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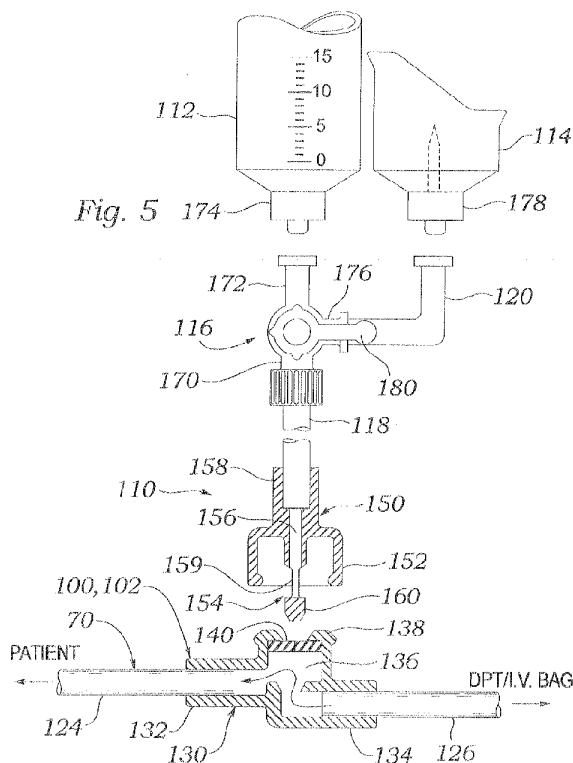
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(54) Title: DISPOSABLE, CLOSED BLOOD SAMPLING SYSTEM FOR USE IN MEDICAL CONDUIT LINE



(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

5 [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

10 [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
15 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.

20 [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
25 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

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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

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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.

5 [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
10 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
15 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
20 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
25 system, especially used in conjunction with a pressure transducer, that is more convenient and safer to use.

Summary of the Invention

30 [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

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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
5 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
10 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
15 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
20 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
25 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
30 sampling site housing leading to the distal port when the bypass cannula engages the sampling site. Furthermore, a sealing member may be positioned in

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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

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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;

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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

5 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.

10 [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:

15 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
20 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.

25 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
30 adjacent the proximal port of the sampling site for occluding the proximal port

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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;

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[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;

5 [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;

10 [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;

15 [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
20 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
25 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
30 pressure monitoring. For instance, intracranial pressures could be monitored and cerebrospinal fluid samples taken by placing the system described herein in

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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 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

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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

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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

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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

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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:

- 5 ☐ 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
- 10 ☐ 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

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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.

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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
5 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
10 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
15 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
20 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
25 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-
30 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

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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.

10 [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.
- 15 ☐ 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.
- 20 ☐ 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.
- 25 ☐ 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
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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.

- 5 □ 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.

10 [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
15 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
20 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.

25 [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
30 212, 214.

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[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
5 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
10 262 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
15 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
20 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
25 282 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
30 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

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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

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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
5 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
10 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.

15 [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
20 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
25 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
30 390 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
5 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
10 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
15 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
20 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
25 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
30 from the site 382. To do so, he/she manipulates the stopcock 370 into a position

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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
5 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
10 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
15 “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
20 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
25 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
30 fluid draw reservoir is removable and disposable. Moreover, the reservoir is closed because it remains in place during the fluid draw and re-infusion.

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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.

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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.

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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;

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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;

5 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
10 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:

15 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
20 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.

25 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.

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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.

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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.

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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:

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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;

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opening fluid communication between the bypass cannula and reservoir while closing fluid communication between the bypass cannula and fluid sampling container;

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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;

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opening fluid communication between the bypass cannula and fluid sampling vessel while closing fluid communication between the bypass cannula and reservoir;

5 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.

10

15 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

20 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:

25 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
30 communication between the bypass cannula and reservoir while closing fluid

- 35 -

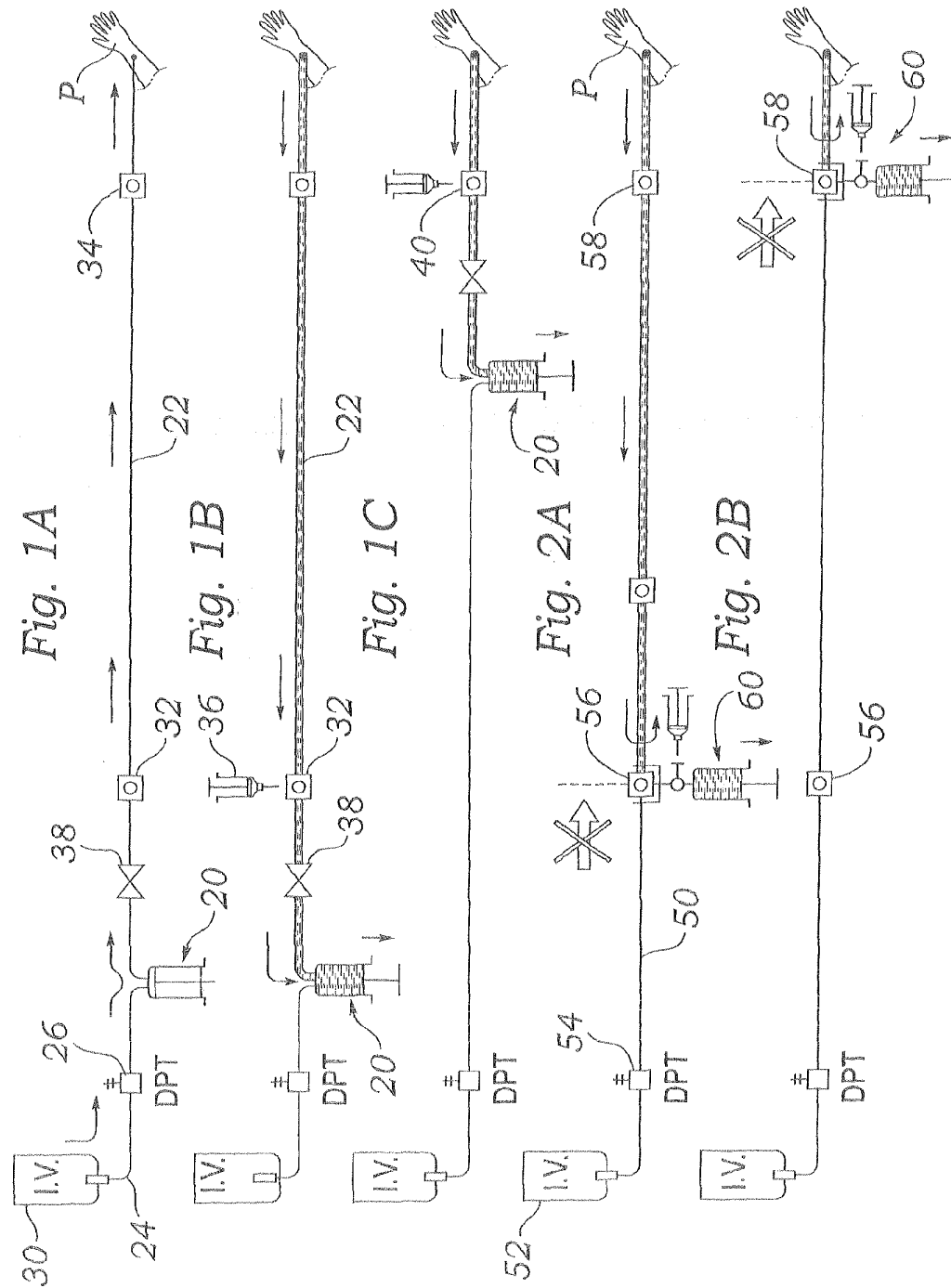
communication between the bypass cannula and fluid sampling vessel is accomplished by the step of engaging the bypass cannula with the sampling site.

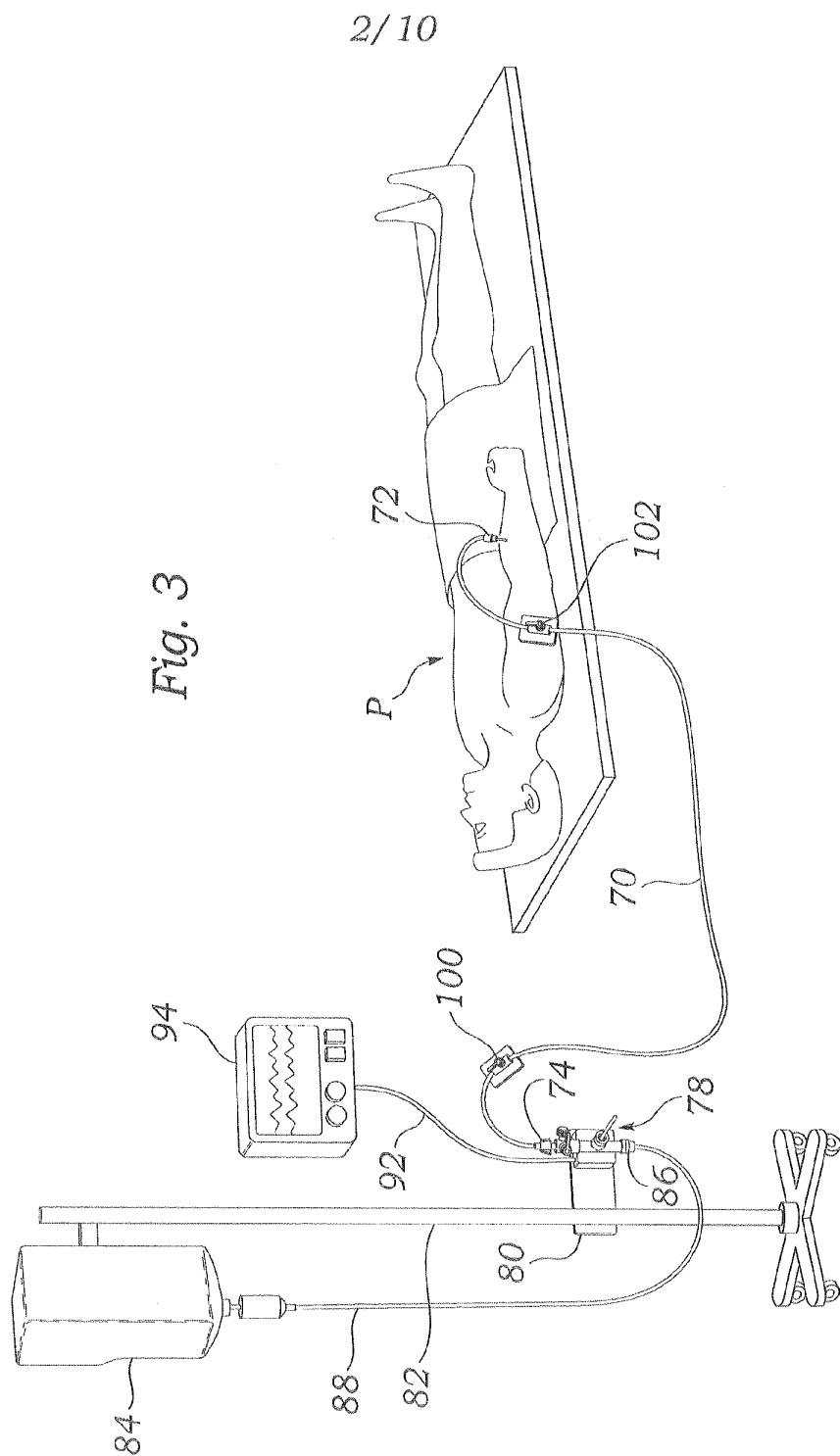
18. The method of claim 17, wherein the probe of the bypass cannula
5 has a size sufficient to contact and occlude a passageway opening leading to the proximal port of the sampling site.

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
10 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
15 occluding the proximal port when fluid is drawn into and expelled from the reservoir and drawn into the fluid sampling container.

1/10





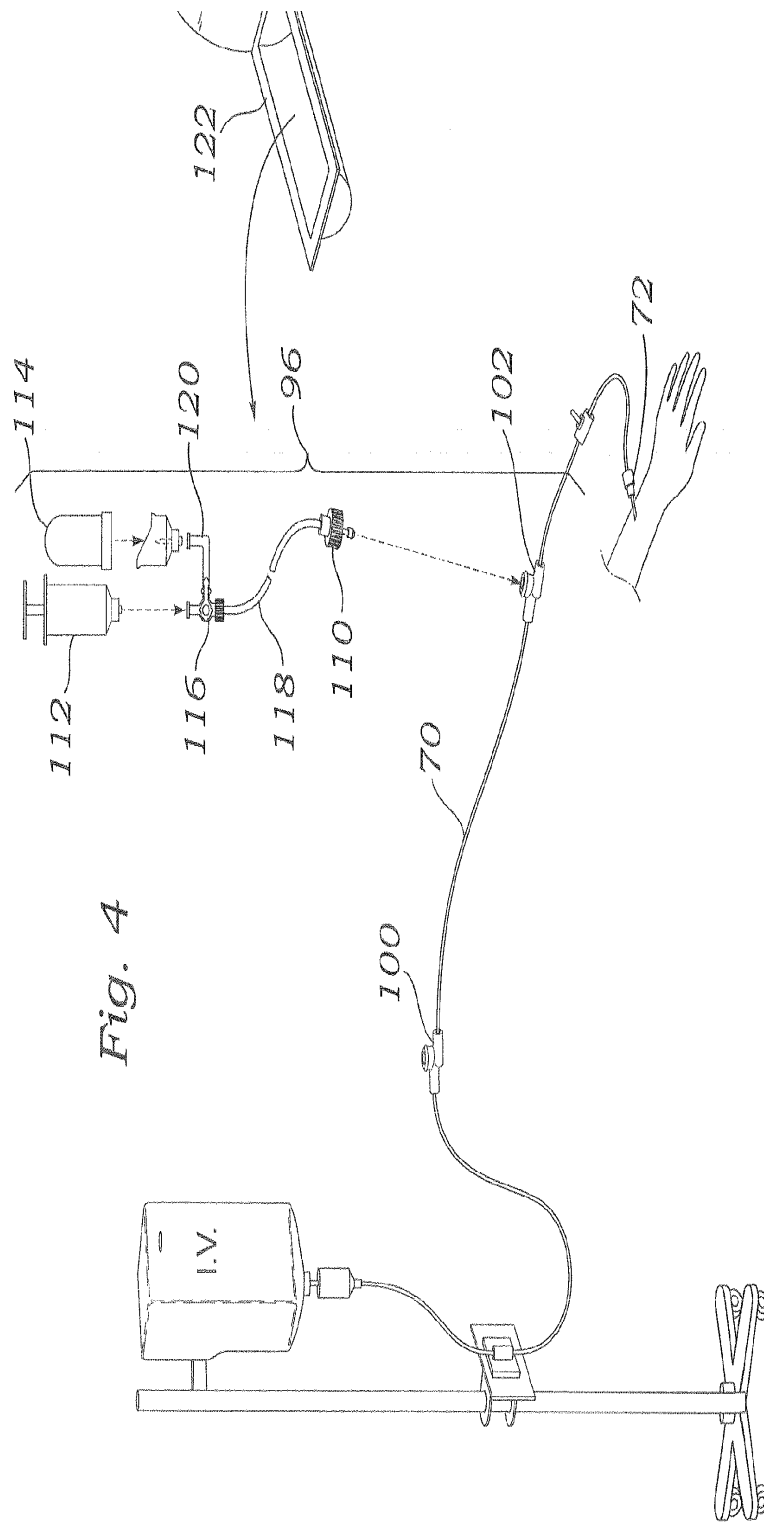
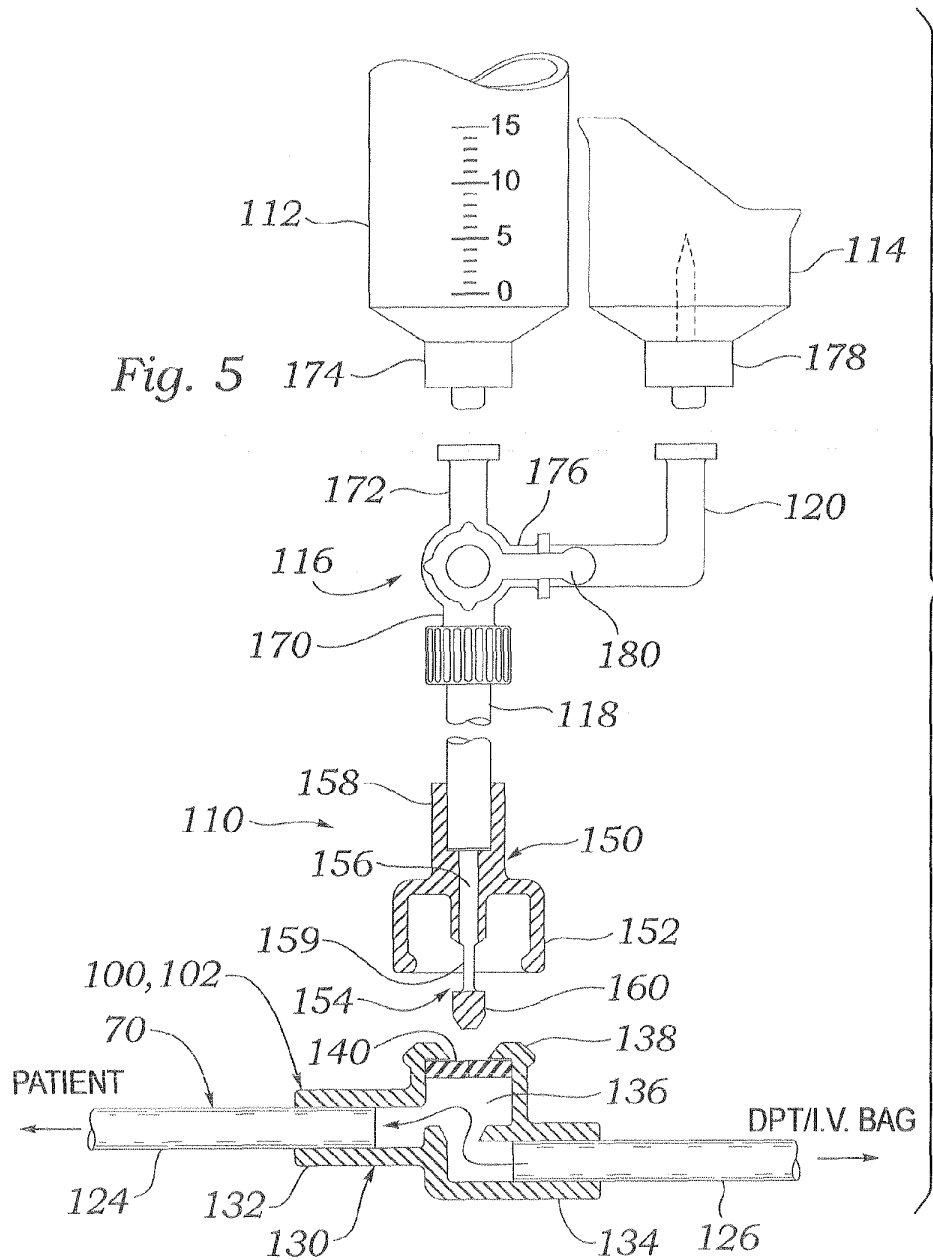


Fig. 4

4/10



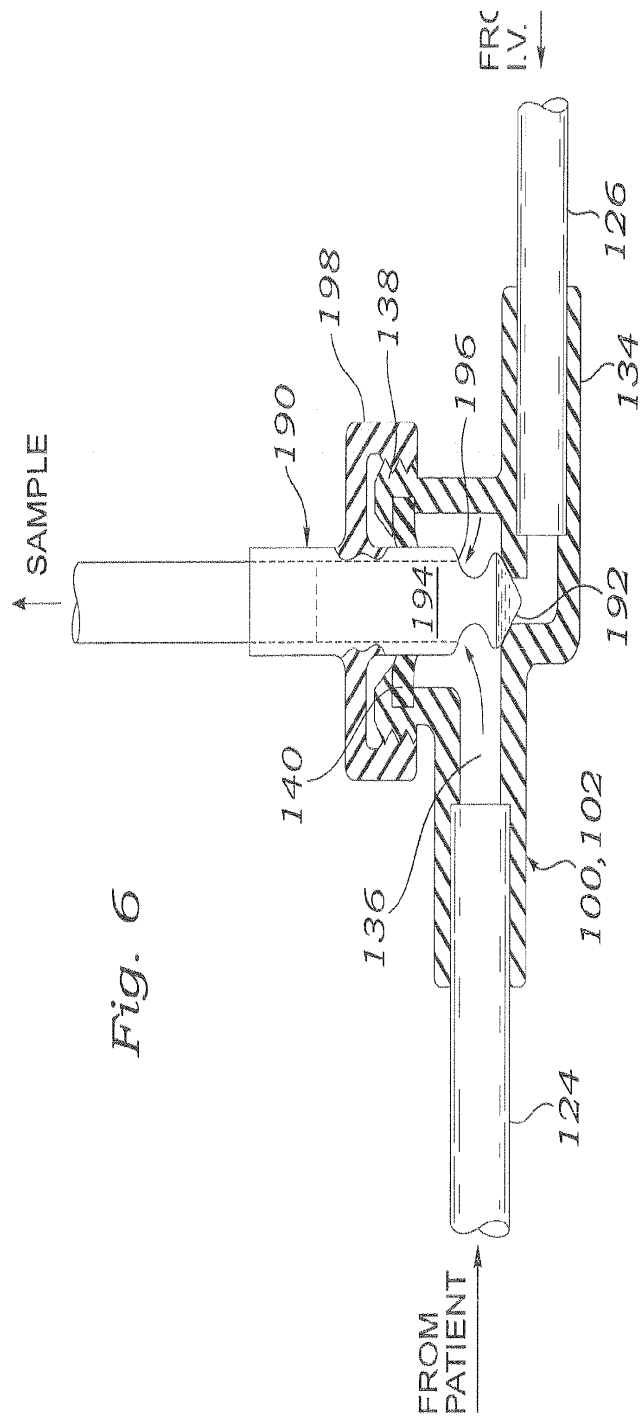
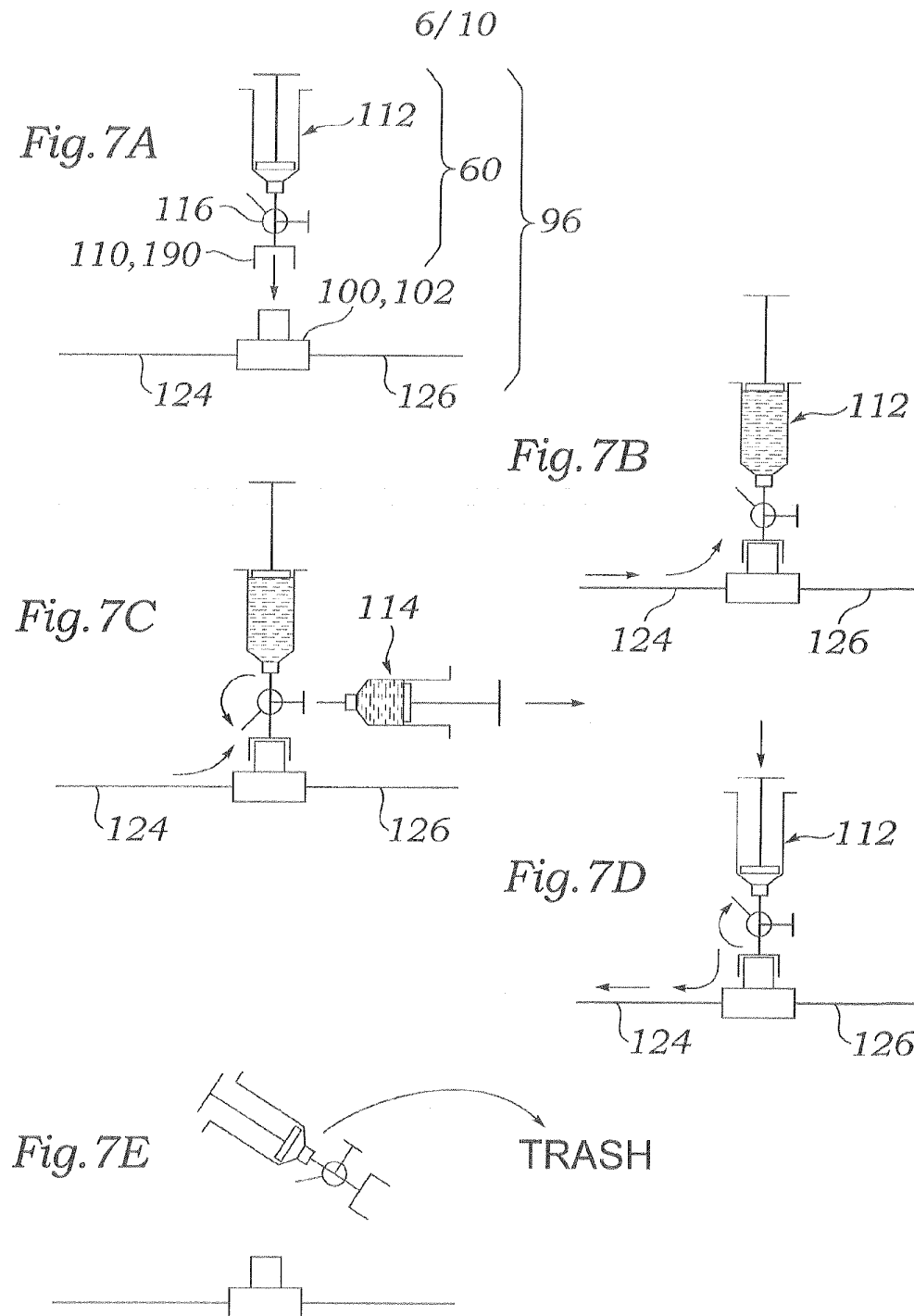
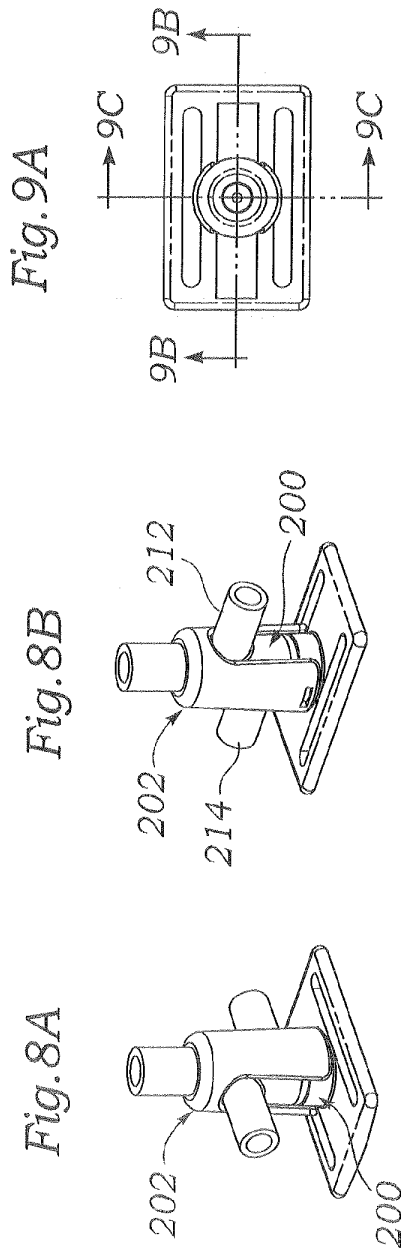
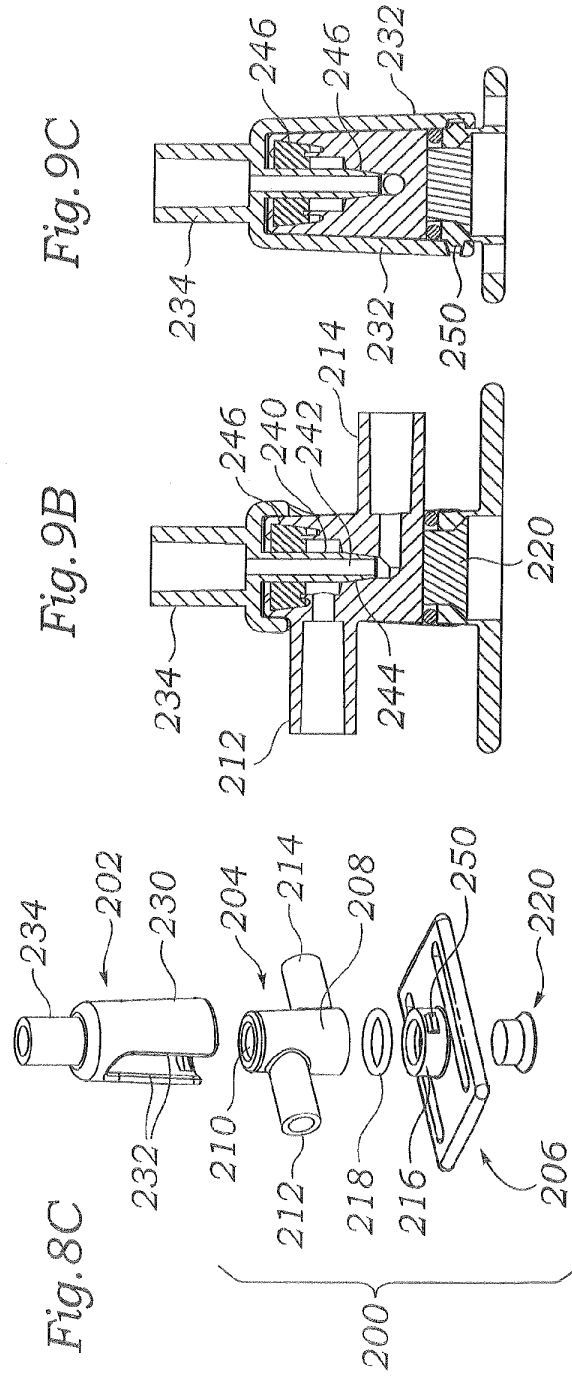


Fig. 6



7/10



8/10

Fig. 10

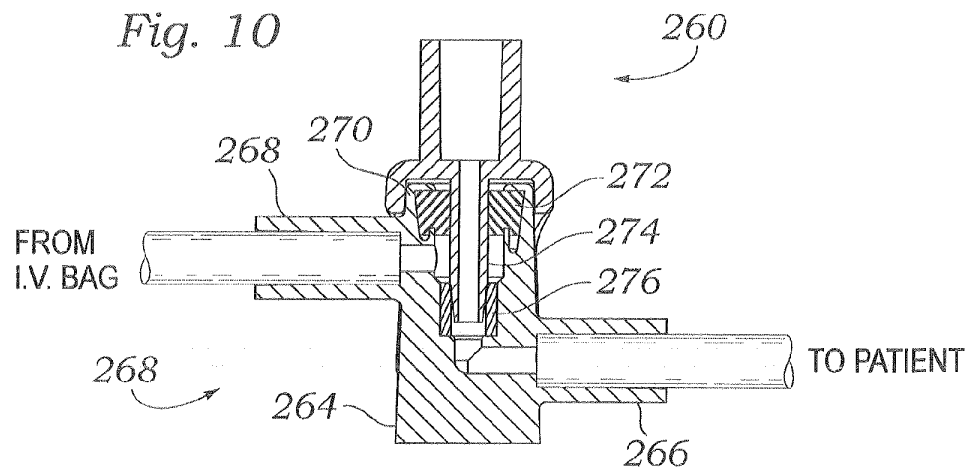
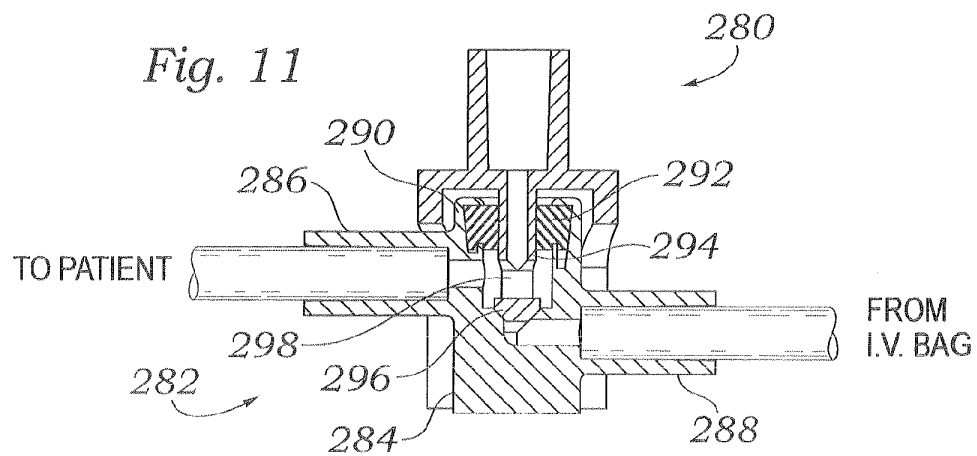
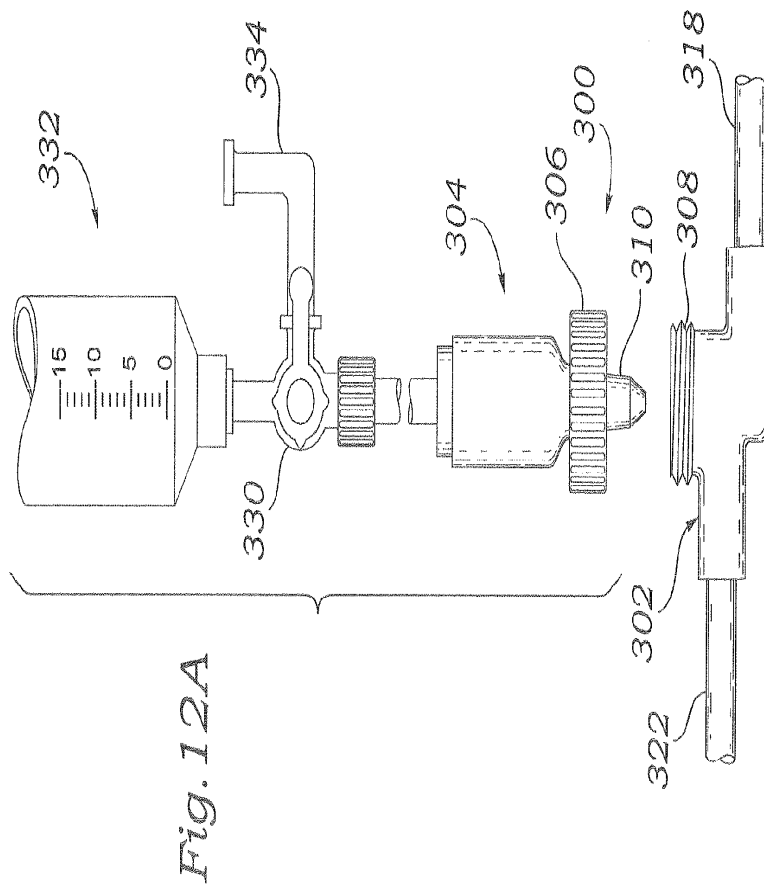
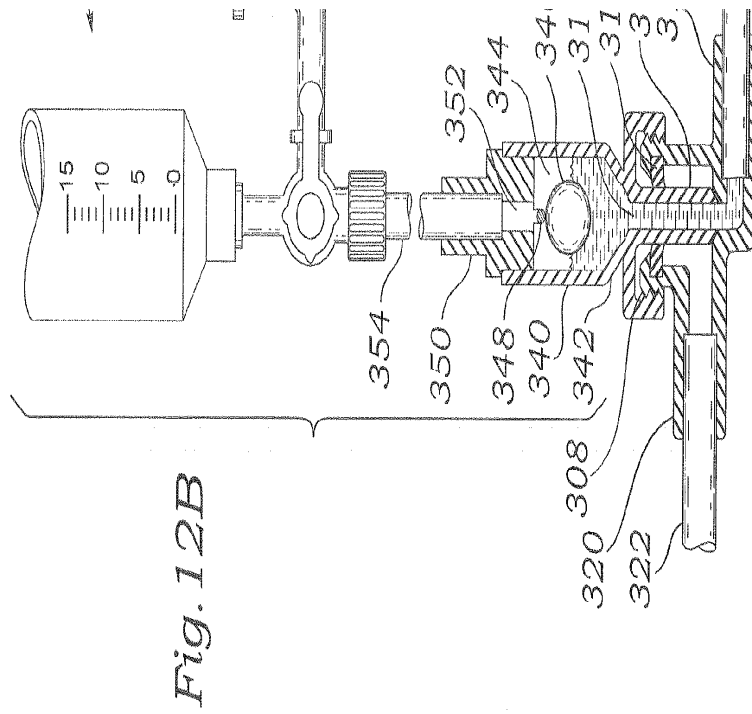
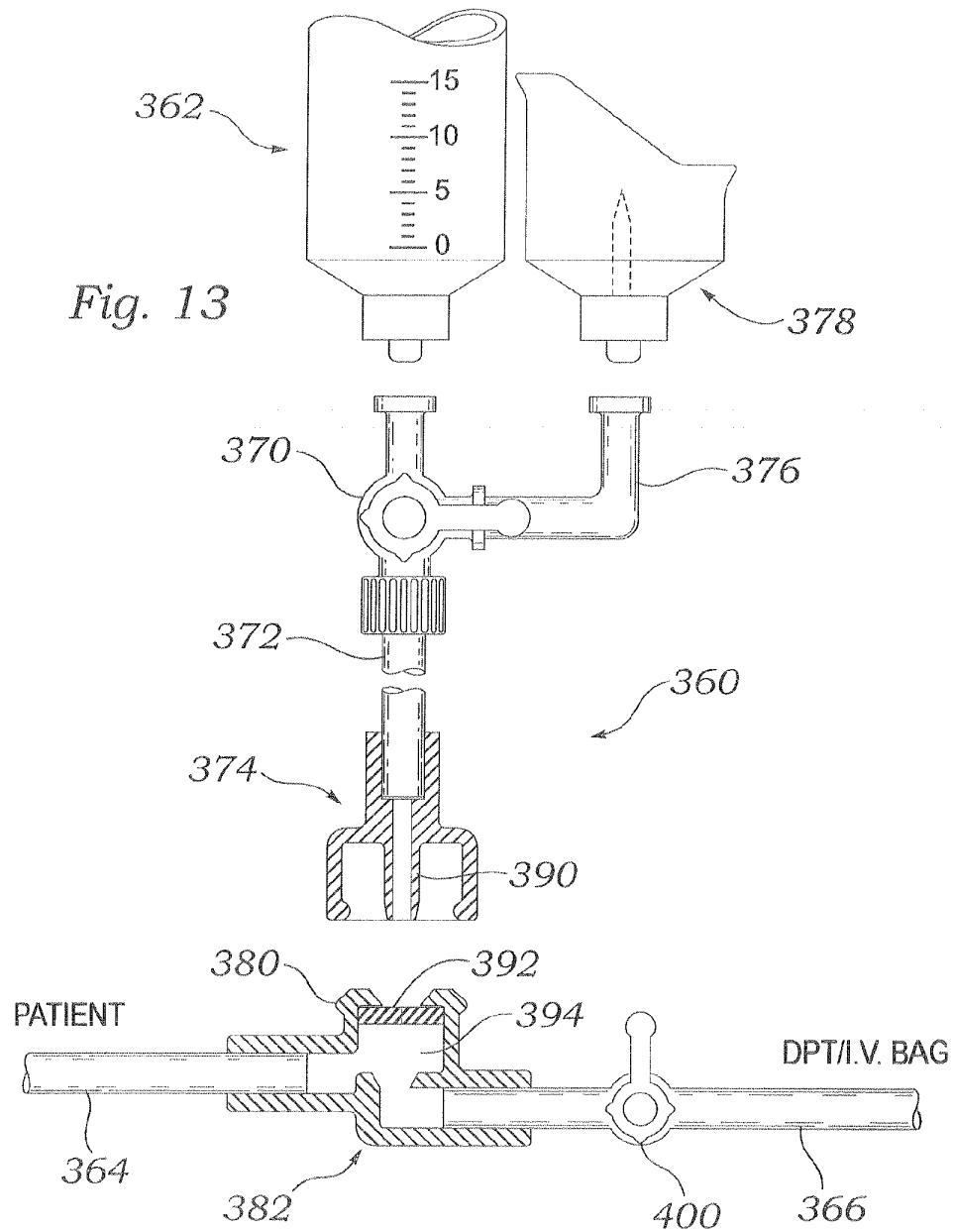


Fig. 11





10/10



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	EP 0 637 455 A (SIEMENS ELEMA AB [SE]) 8 February 1995 (1995-02-08)	1-7
Y	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	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
	----- -/--	
☒ 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 4 July 2008		Date of mailing of the international search report 14/07/2008
Name and mailing address of the ISA/ 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		Authorized officer Böttcher, Stephanie

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. ☒ 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 US 5549582 A	28-02-1995 27-08-1996
EP 0240590	A	14-10-1987	AT 66622 T DE 3681158 D1 JP 1708152 C JP 3062113 B JP 62243563 A US 4819684 A	15-09-1991 02-10-1991 11-11-1992 24-09-1991 24-10-1987 11-04-1989
US 5348542	A	20-09-1994	NONE	
US 6287265	B1	11-09-2001	NONE	

 Literature display

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JP 2009-131273

Registration Gazette

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bibliography

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(43) [Published date]] June 18, 2009 (2009.6.18)
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(51) [International Patent Classification]
C12Q 1/56 (2006.01)
A61K 38/43 (2006.01)
A61P 7/04 (2006.01)
A61P 43/00 (2006.01)
[FI]
C12Q 1/56 ZNA
A61K 37/48
A61P 7/04
A61P 43/00 111
[Request for examination] Yes
[Number of claims] 7

[Application form] OL

[Total number of pages] 25

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(22) [Application date] March 11, 2009 (2009.3.11)

(62) [Indication of division] Division of Japanese Patent Application Hei 11-116411 [Original filing date] April 23, 1999 (1999.4.23)

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(31) [Priority claim number] 19851335:6

(32) [Priority date] November 6, 1998 (1998.11.6)

(33) [Priority claiming country] Germany (DE)

(31) [Priority claim number] 19851336:4

(32) [Priority date]] November 6, 1998 (1998.11.6)

(33) [Country claiming priority] Germany (DE)

(31) [Priority claim number] 19827734:2

(32) [Priority date] June 1998 22 June (1998.6.22)

(33) [Country claiming priority] Germany (DE)

(31) [Priority claim number] 19903693:4

(32) [Priority date] February 1, 1999 (1999.2.1)

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(72) [Inventor]

[Name] Hans-Arnold Steer

(72)) [Inventor]

[Name] Annette Feusner [

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4C084

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4B063QQ36

4B063QQ79 4B063QQ95

4B063QQ97 4B063QR16

4B063QR48

4B063QR6

7 4B063QR82 4B063QX01 4C084AA02 4C084AA07 4C084BA03 4C084BA44 4C084CA62

4C084DC14

4C084NA14

4C084ZA532

4C084ZC022

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close

(57) [Summary]

[Object] To discover a novel FVII-activating protease and its application.

SOLUTION: a) is inhibited by the presence of aprotinin, b) its activity is increased by calcium ions and/or heparin or heparin analogues, and c) in SDS-PAGE, the molecular weight is reduced in subsequent staining under non-reducing conditions. A protease that activates blood coagulation factor VII, which exhibits one or more bands in the range of 50-75 kDa and, under reduced conditions, one or more bands in the molecular weight range of 10-35 kDa, as well as its proenzyme. The proenzyme is obtained from plasma or prothrombin complex (PPSB) concentrates by prior anion exchange chromatography followed by affinity chromatography using heparin or heparin analogues or dextran sulfate.

The present invention provides a test system for the qualitative and quantitative detection of said protease or its proenzyme, as well as a test system for its diagnostic application and said protease activating an amount of blood coagulation factor VII suitable for the lysis of fibrin-containing thrombi. and/or pharmaceutical preparations containing the proenzyme thereof.

[Selection figure] None

The scope of the claims

open

Claims:

1.

a) inhibited by the presence of aprotinin,
 b) its activity is increased by calcium ions and/or heparin or heparin sulfate,
 c) subsequent non-reducing conditions in SDS-PAGE. shows one or more bands in the molecular weight range of 50-75 kDa by staining with , and in reducing conditions one band in the molecular weight range of 40-55 kDa and one or more bands in the molecular weight range of 10-35 kDa. and

d) the band obtained in the reducing state in the molecular weight range 40-55 kDa in SDS-PAGE has the amino acid sequence: LLESLDP and the band obtained in the molecular weight range 10-35 kDa has the amino acid sequence: IYGGFKSTAGK. and/or

for the qualitative and quantitative detection of the proenzyme of said protease, the band obtained in reducing conditions in SDS-PAGE has a molecular weight in the range of 60-65 kDa and contains the amino acid sequences: LLESLDP and IYGGFKSTAGK. In the test system, its protease activity is characterized by:

- a) its activity to inactivate blood coagulation factor VIII/VIIIa or factor V/Va or b
-) its activity to reduce blood clotting time in a comprehensive blood coagulation test or
- c) its activity to activate the plasminogen activator or
- d) its activity to activate FVII

2. The test system of claim 1

, wherein the activity of lowering blood clotting time comprises:

A test system measured by a) non-activated partial thromboplastin time (NAPTT) or
b) prothrombin time (PT) or
c) plasma recalcification time or
d) activated partial thromboplastin time (APTT).

3. In the test system according to claims 1 and 2, the activity of activating and/or enhancing plasminogen activator comprises: a) single-chain urokinase PA (scuPA, single-chain urokinase plasminogen activator); or b) a test system measuring by activation of single-chain tPA (sctPA, single-chain tissue plasminogen activator).
4. A test system according to any one of claims 1 to 3, which contains calcium ions in an amount of 0.001 mM or more.
5. a) inhibited by the presence of aprotinin, b) its activity increased by calcium ions and/or heparin or heparin sulfate, c) in SDS-PAGE with a molecular weight of 50 by subsequent staining under non-reducing conditions, showing one or more bands in the range of ~75 kDa, one band in the molecular weight range of 40-55 kDa and one or more bands in the molecular weight range of 10-35 kDa in the reduced state, and

and/or

Bands obtained in SDS-PAGE under reduced conditions are molecules in the range of 60-65 kDa

A mixture of the proenzyme of said protease containing the amino acid sequences: LLES LDP and IYGGFKSTAGK and a suitable proenzyme activator is used to test for prothrombin time-displaced tissue factor/thromboplastin.

6.

a) inhibited by the presence of aprotinin,
b) its activity is increased by calcium ions and/or heparin or heparin sulfate,
c) molecular weight 50 by subsequent staining in non-reducing conditions in SDS-PAGE. 1 or 2 or more bands in the range of ~75 kDa, in the reduced state 1 band in the molecular weight range of 40-55 kDa and 1 or 2 or more bands in the molecular weight range of 10-35 kDa, an

d d

) The band obtained in the range of molecular weight 40-55 kDa under reducing conditions in SDS-PAGE has the amino acid sequence: LLESLDP, the band obtained in the range of molecular weight 10-35 kDa has the amino acid sequence: IYGGFKSTAGK, and/or

SDS- The bands obtained under reduced conditions in PAGE have molecular weights in the range of 60-65 kDa and contain the amino acid sequences: LLESLDP and IYGGFKSTAGK. Assay system used for sex testing and quantification of single-chain plasminogen activator forms.

7.

In the test system according to claims 1 to 6, the plasminogen activator enhancing activity is

a) measured using a chromogen test or

b) A test system measuring the formation of plasmin itself or the lysis of fibrin clots brought about by plasmin in a coupling reaction in the presence of plasminogen.

detailed description

open

Description: FIELD OF THE INVENTION

The

present

invention relates to a protease for the activation of blood coagulation factor VII, methods for isolating, detecting and inactivating it and pharmaceutical preparations comprising this protease. . BACKGROUND

OF THE INVENTION The blood coagulation system consists of two different cascade-like pathways that activate blood coagulation factors present in plasma. Depending on the induction mechanism, the intrinsic or extrinsic pathway is preferentially used to initiate blood coagulation. [0003] When tissues are injured, thromboplastin (tissue factor, TF and phospholipids) is exposed by the affected cells as starters of the extrinsic coagulation pathway. Membrane-localized thromboplastin can bind both blood coagulation factor VII (FVII) and circulating, activated FVII (FVIIa). In the presence of calcium ions and lipids, this TF-FVIIa complex leads to binding of FX, which is converted to its activated form (FXa) by limited proteolysis. FXa then activates prothrombin to form thrombin, leading to the formation of fibrin, which ultimately causes wound closure. [0004] Further activation of thromboplastin-binding FVII occurs initially by autocatalytic reactions, but especially after initiation of the coagulation cascade it is supported by FXa and thrombin, leading to a marked enhancement of the reaction cascade among others. [0005]

Administration of FVIIa or FVIIa-containing concentrates has been indicated for certain clinical conditions. For example, in patients with hemophilia A who develop antibodies to FVIII as a result of administration of FVIII.

used the so-called FVIII alternative pathway activity (FEIBA) of FVIIa. Based on presently known findings, FVIIa is well tolerated in this relationship, it does not produce thrombotic tendencies, and is sufficient to ensure that a limited but adequate degree of clotting occurs. Are suitable. Recombinant FVIIa is already used therapeutically and prophylactically. FVII isolated from plasma can also be used after activation. Proteases such as thrombin can be used for this activation, however, these proteases themselves are capable of strongly activating blood clots and may pose a thrombotic risk. For this reason, subsequent removal or inactivation of thrombin is necessary, resulting in losses. As a result of the thrombotic risk associated therewith, the use of FXa or FIIa (thrombin) is often contraindicated and indicated only in emergencies, eg in connection with significant loss of blood and uncontrolled bleeding.

SUMMARY OF THE INVENTION

[
0006]

FVIIa is found in very low concentrations in the plasma of healthy individuals. Little is known so far about the formation and origin of FVIIa circulating in the blood. Traces of thromboplastin expressed or released with cell destruction may play a role in this association. Factor XIIa, for example, is known to cause activation of FVII under certain conditions, but the physiological relevance of this response has not yet been clarified.

[0007]

Surprisingly, a FVII-activating protease, distinct from all previously known proteases, has now been discovered associated with the fractionation of human plasma and certain prothrombin complex concentrates. A study of this protease showed that it exhibited a particularly high amidolytic activity towards the peptide substrate S2288 (HD-isoleucyl-L-prolyl-L-arginine-pNA) from Chromogenix AB, Sweden. A special property of this protease is that its amidolytic activity is effectively inhibited by aprotinin. Other inhibitors such as the antithrombin III/heparin complex are also suitable for its inhibition. On the other hand, its activity is increased by heparin and heparin-related substances such as heparin sulfate or dextran sulfate and calcium ions. Finally, it was found that this protease is capable of converting FVII to FVIIa in a time- and concentration-dependent manner. This reaction is also inhibited by aprotinin. SUMMARY

OF THE INVENTION Accordingly, part of the subject matter of the present invention is that

a) aprotinin is inhibited by the presence and b) its activity is elevated by calcium ions and/or heparin or heparin-related substances. and c) in SDS-PAGE, subsequent staining in non-reducing conditions shows one or more bands in the molecular weight range of 50-75 kDa, and in reducing conditions one band in the molecular weight range of 40-55 kDa and molecular weight It is a protease that activates blood coagulation factor VII, exhibiting one or more bands ranging from 10 to 35 kDa . BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows protease concentration and inactivation of FVIII when protease and FVIII are incubated for a certain period of time.

FIG. 2 shows the inactivation of FVIII when the protease concentration is constant and FVIII is incubated for various times.

FIG. 3 shows the inactivation of FVIII when protease and FVIII are incubated with varying calcium concentrations in the mixture.

[Mode for carrying out the invention]

In the following

specification, the activated form of the protease is called "protease" and the non-activated form is called "proenzyme".

[0011]

This protease was further investigated and after concentration or isolation underwent a rapid loss of activity, which was observed in a solution containing 20 mM tris, 0.15 M NaCl, pH 7.5. Addition of albumin at a concentration of 0.1% also failed to prevent the activity of this protease from dropping to 50% after 1 hour at room temperature. On the other hand, very good stabilization of this protease was observed in solutions buffered to pH 6.5 with 50 mM sodium citrate. No or very little loss of activity was observed when the solution was adjusted to pH 4-7.2, preferably pH 5.0-7.0, even without the addition of specific stabilizers to the protease solution. However, it is expedient to add stabilizers to the solution, suitable stabilizers being, in addition to citrate, especially glutamate, amino acids such as arginine, glycine or lysine, calcium ions and sugars such as glucose, arabinose or An amount of 1 to 200 mmol/L, preferably 5 to 100 mmol/L of mannose can be mentioned. Effective stabilization is also achieved by the addition of glycols such as ethylene glycol or glycerol 5-80% by weight, preferably 10-60% by weight is used. In that case, the pH value of the stabilized solution should be between 4 and 9.

[0012]

The novel proteases, and also their proenzymes, are obtained by recombinant DNA methods or, for example, by production in the milk of suitable transgenic animals, in particular by fractionation of plasma or prothrombin complex (PPSB) concentrates. can be done. The starting material is then first subjected to anion exchange chromatography, followed by affinity chromatography of the eluate. Heparin or heparin-related substances immobilized on a matrix, such as heparin sulfate or dextran sulfate, are particularly suitable for affinity chromatography. Using such chromatographic methods, the novel proteases and/or proenzymes are selectively bound and can then be eluted again using known methods. The use of spacers can be recommended for coupling ligands to matrix. A heparin-lysine matrix has been found to be particularly suitable for the isolation of novel proteases.

[0013]

In SDS-PAGE followed by staining, the proteases isolated by this method show one to several closely spaced bands in the molecular weight range of 55-75 kDa under non-reducing conditions. After reduction, one to several bands were observed in the molecular weight range of 15-35 kDa and one band was observed at 40-55 kDa. One additional band at 60-65 kDa was shown to constitute 5-10% of the total protein after scanning and quantitative evaluation, and that non-activated proenzyme was also present. This result was supported by a suitable study using a monoclonal antibody directed against this protease. It was therefore concluded that the proenzyme of this protease could also be prepared, sterilized and used according to the method of the invention. Part of the subject matter of the present invention is therefore the proenzymes of proteases that activate blood coagulation factor VII. The proportion of proenzyme is indicated by the 60-65 kDa band. Examples of suitable physiological activators of proenzymes correspond to amino acid sequences constituting the activation region of proenzymes, thrombin, kallikrein or FVIIa, depending on their substrate specificity. Some of the properties of the novel protease mentioned above, namely the fact that it can be isolated from plasma or plasma-derived prothrombin complex (PPSB) concentrates, inhibition of its amidolytic activity by aprotinin and reduction and non-reduction

The migration behavior described above in SDS-PAGE under both reducing conditions has been demonstrated by Hunfeld et al. 1999, 78: A42)

It recalls a protease isolated from a PPSB concentrate that has not been defined in detail. In that case, preparation was primarily accomplished using an aprotinin matrix. The activity has been described as a thrombin-like activity as a result of the amidolytic cleavage of certain peptide substrates. Hunfeld et al. found no effect on global coagulation parameters such as prothrombin time, quick or platelet aggregation.

[0015]

N-terminal sequencing of the protease described by Hunfeld et al. shows that its cDNA is consistent with that of the protein reported by Choi-Miura et al. (J. Biochem. 119:1157-1165, 1996). In its primary structure, the corresponding protein exhibits homology with an enzyme na

med hepatocyte growth factor activating enzyme (HGFA). Two bands isolated from SDS-PAGE under reducing conditions were subjected to N-terminal sequencing and the following identities were established

Molecular weight range of bands	Amino acid sequence	Reporter
10-35 kDa	IYGGFK	
STAGK Present invention	30 kDa IYGGFKSTAG	Hunfeld et al.
17 kDa IYGGFKSTAGK		
H Choi-Miura et al.	40-55 kDa LLESLDP	Present invention

50 kDa SLDP Hunfeld et al.

57 kDa SLLESLDPWTPD Choi-Miura et

al.

Nevertheless, at present it is still not possible to presume that these proteins are identical. In any event, none of the previously studied proteins described above have been reported to have FVIIa or other factor activating properties (see below).

[0017]

Based on its above-mentioned properties, the novel protease can be used diagnostically and therapeutically.

1

Test Systems Using the Novel Proteases

The novel proteases can be used diagnostically in test reagents. Thus the presence of factor VII can be determined qualitatively and quantitatively in blood coagulation tests by adding novel proteases.

Conversely

, the test system developed for measuring FVII activation can also be used for the detection and quantification of proteases. For this, the protease-containing solution is mixed with the FVII-containing solution and the FVIIa produced is quantified after an appropriate incubation time. This is for example Staclot^(R). It can be performed using the FVIIa-rTF test (Stago/Boehringer Mannheim). Using the preferred procedure, this test is not limited to the concentration of FVII supplied. If the amount of protease in the form of a ratio of total protein is known, the ratio is: -

in a pure protease preparation, by the Kjeldahl method or other protein assays well known to those skilled in the art, or

- can be determined using, for example, specific antibody-based antigen tests and suitable immunochemical assay methods such as ELISA, and then the specific activity of the protease p

reparation can be determined in a corresponding manner.

Surprisingly

, with further characterization of proteases, new properties have been discovered that allow additional measurements. Incubation of the proteases with blood coagulation factors VIII/VIIIa and V/Va followed by quantification reveals that the blood coagulation factors are inactivated in a manner independent of protease concentration and length of incubation. made rice field.

Another part of the subject matter of the present invention is therefore a novel test system

for the qualitative and quantitative detection of proteases that activate blood coagulation factor VII, in which proteases are blood It can be quantified by its activity to inactivate coagulation factor VIII/VIIIa or V/Va. This test system involves incubating a solution containing a protease with Factor VIII/VIIIa or Factor V/Va and determining the amount of residual Factor VIII/VIIIa or the amount of residual Factor V/Va by a conventional activity test. It is based on measuring and then determining from this the amount of protease by comparison with a standard curve. In carrying out this test, the incubation of the protease activity is inhibited by the addition of limited amounts of aprotinin for a predetermined period of time, which has the advantage that these concentrations do not affect the subsequent measurements of the test system. The residual activity of the blood clotting factor is then determined by test methods well known to those skilled in the art. For this, the so-called Coamatic factor VIII test (Chromogenix AB), which mainly contains factors IX and X and quantifies the amount of FXa obtained by conversion of a chromogenic substrate in the presence of a thrombin inhibitor, is used. In terms of enabling (see description in [0007]), especially test systems have proven their worth. On the other hand, this amount is proportional to the amount of FVII or FVIIa. Determining the residual FVIII activity then makes it possible to derive the concentration of protease present.

[0022]

Degradation of FVIII/FVIIIa or FV/FVa factors by proteolytic action can be clearly demonstrated by SDS-PAGE. Depending on how long the protease was incubated with, for example, the FVIII concentrate, the bands typical of FVIII disappear, while other new bands develop or the intensity of weaker bands increases. Thus, protease activity can also be correlated by quantifying the attenuation or enhancement of a band, and thus can be quantitatively measured using, for example, protease preparations. Band intensities in SDS-PAGE electropherograms, or changes in band intensities by other electrophoretic methods, can be quantified using, for example, a scanner and appropriate programs well known to those skilled in the art. Additionally, antibodies to the blood clotting factors described above can be used in Western blots and can be employed for evaluation in the methods described above. Antibodies that specifically detect attenuated bands or specifically developed bands are particularly suitable. In this connection, these antibodies can also be used to establish other immunochemical tests, such as ELISA.

[0023]

The proteolytic inactivation described for FVIII/FVIIIa is also observed when the protease is incubated with Factor V/Va, which exhibits some degree of structural homology with FVIII. Degradation can be monitored in a suitable activity test system and SDS-PAGE/Western blotting. [0024]

Despite the inactivation of FV and FVIII, the addition of proteases to blood, platelet-rich plasma or plasma at this time shortens the blood clotting time, i.e. It was found to exhibit gult activity. These test systems are understood to be, for example, non-activated partial thromboplastin time (NAPTT), prothrombin time (PT) and recalcification time. These shortenings of time, measured for example in so-called coagulometers, by thrombus elastographs or otherwise in chromogenic tests, correlate with the concentration of the procoagulant substance, so that the concentration of that substance in the sample is, can be inferred inversely using the calibration curve for blood clotting time. Concentrations of "FVII activators" can also be determined using selected comprehensive coagulation tests.

"

FVII activator" also includes single-chain urokinase (scuPA, single-chain urokinase plasminogen activator), and single-chain tPA (sctPA, single-chain tissue

It has also been surprisingly found that it can provide an effective activator of plasminogen activator), i.e. act as a plasminogen activator activator (PAA). The activity of activated PA can be measured, for example, using a chromogen. This property can therefore be used for the detection and quantification of "FVII activators". Activation of plasminogen activators can also be determined in coupling reactions in the presence of plasminogen, either by formation of plasmin itself or by lysis of fibrin clots brought about by plasmin.

In summary

, therefore, it can be said that the protease can be incubated with a solution containing FVIII or FVIIIa and then the residual amount of FVIII/FVIIIa can be both detected and quantified by a suitable activity test. Fv or Fva can be incubated with protease in the same manner and the amount of Fv/Fva remaining can then be quantified. An unknown protease concentration can be quantitatively determined by comparing the increase in the amount of protease included in the test to a standard curve. Various comprehensive blood coagulation tests are likewise suitable for quantification, and protease concentrations are read from calibration curves based on reduction of clotting times. The PAA activity of proteases can also be used for quantitation purposes. A feature of these tests is that CaCl_2 is added to high concentrations of calcium, preferably $>0.001 \text{ mM}$, particularly preferably $>0.005 \text{ mM}$, suitable for FV and FVIII inactivation and PAA activity

.

It is particularly well exhibited when present in the form of As noted above, FV/FVIII inactivation is not enhanced by heparin or Only non-significant enhancement is observed. In contrast, PAA activity is stimulated in the presence of any substance, namely calcium and/or heparin or heparin-like substances. The protease-induced reaction can be performed in the presence of

a protease inhibitor, particularly heparin or a heparin-like substance (preferably in the presence of heparin) antithrombin III, C1-esterase inhibitor, α_2 -antiplasmin, inter- α -trypsin inhibitor or known inhibitors

. can be very efficiently attenuated or prevented by incubation with a low molecular weight protease inhibitor such as guanidinocaproic acid-p-ethoxycarbonylphenyl ester available under the tradename FOY®. These substances can thus be used to stop the reaction, for example to accurately determine the incubation time or to further increase the specificity of the test. Reduction of free calcium ions in the mixture, for example with chelating agents, can also be used for this purpose. 2. Stabilized preparations of Factors V and VIII

From the above observations regarding the proteolytic activity of novel proteases against blood coagulation factors V and VIII, the problem of inhibiting the protease activity or attenuating its activity is due to the loss of production and the formation of fragments which are presumably fragments of interfering proteins. occur to avoid All this is all the more important since FV and FVIII are usually prepared from cryoprecipitates obtained from plasma in the presence of calcium ions, the latter being required for maintenance of protein conformation. Another part of the subject-matter of the present invention thus includes proteolytically formed Factor V and VIII fragments as a result of the fact that the proteases that activate blood coagulation Factor VII are inhibited

. is a stabilized preparation of free FV or FVIII. Further investigation revealed that the inactivation of factors V and VIII by the proteases was particularly

It has been shown to occur efficiently in the presence of calcium ions at concentrations of 0.5 mM or higher, suggesting that the coagulation factor V or factor VIII preparations for inhibition of proteases that activate blood coagulation factor VII. Adjusting the concentration of calcium ions to less than 1.0 mM, preferably less than 0.5 mM can effectively stabilize the Factor V and Factor VIII preparations. Although the factor V and factor VIII inactivating action of the protease is significantly reduced at these concentrations, the amount of calcium ions is still sufficient to stabilize the conformation of the FV and FVIII molecules. The amount of calcium ions mentioned above should not be excessive not only in the final product, but also in the cryoprecipitate itself and in subsequent purification steps. Due to the aforementioned affinity of the protease or proenzyme for heparin and heparin-like substances, the protease/proenzyme can be isolated from FVIII- or FV-containing solutions by incubation with immobilized heparin or other immunological or affinity adsorbents

. can be removed. Polyclonal or monoclonal antibodies, respectively antibody fragments, useful for the preparation of immunoadsorbents can be readily obtained by techniques known in the

art using all or part of the protease or proenzyme as the antigen.

However ,

in order to prevent proteolytic degradation of FV or FVIII, natural or synthetic protease inhibitors may optionally be used in addition to lowering the amount of calcium ions. Aprotinin, α_2 -Proteins such as antiplasmin, C1-esterase inhibitor or intertrypsin inhibitor can also be used as inhibitors. Low molecular weight substances known to those skilled in the art as synthetic serine protease inhibitors can also be used in this context. Inhibitors such as antithrombin III, whose inhibitory potency is increased by heparin or heparinoids, can be added as well. Thus, although heparin by itself can increase the amidolytic activity of proteases on small chromogens, it was surprisingly found that it does not support the inactivation of FV/FVIII.

3

. Pharmaceuticals Comprising the Novel Proteases

The novel proteases and/or proenzymes can be used therapeutically.

They can be used alone or with substances that increase the activity of proteases, such as heparin or heparin-related substances, such as heparin sulfate, and/or calcium ions. In addition, factor VII can be added to this drug as well. The use of such agents that utilize their FVIII alternative pathway activity (FEIBA) is, for example, well tolerated due to the presence of, for example, antibodies against FVIII and/or FIX and/or FXI and/or contact phase proteins such as FXII. is present, or other types of missing conditions are present. In this context, FVII can be activated either in vitro, in plasma, in concentrated fractions, or by action on purified FVII. The novel blood clotting agents can also be used ex vivo for prevention of systemic bleeding or to stop bleeding.

[0034]

On the other hand, the observed inhibition of novel proteases by aprotinin or the inhibitors mentioned above can be used to develop drugs comprising protease inhibitors with reduced ability to clot blood. In addition to this, the novel proteases can also be used to identify physiological and non-physiological factors such as synthetic peptides that impair blood coagulation through their protease inhibitory action. Particularly efficiently transformed chromogenic substrates, such as the peptide sequence of S2288 (see above for details), can be used as a structural basis for this. If these preparations do not contain proteolytic activity, the addition of suitable inhibitors to the clot preparations may also be necessary during their preparation.

[0035]

As the protease was further characterized, properties were discovered that open up additional potential uses as so-called "Factor VII activator" proteases. single-stranded plasmid Incubation of a nogen activator, e.g., pro-urokinase (single-chain urokinase, scuPA, single-chain urokinase plasminogen activator) or tctPA (single-chain tissue plasminogen activator) results in the activation of these positive 'factor VII activators'. Resulting in activation of the plasminogen activator (PA). In this connection, the proteolysis of single-chain PA is limited, resulting in the formation of double-chain proteases, which are particularly suitable for plasminogen activation.

tion. The plasmin produced is the effector of fibrinolysis, the physiological system involved in the dissolution of thrombi. PA, such as pro-urokinase or tPA, is an endogenous protein that is released on demand and, as is known, activated by plasmin or kallikrein (scuPA). The mechanism by which scuPA is activated in health has not yet been fully elucidated. The plasminogen activator is for therapeutic use as an isolated or recombinantly prepared protein in pharmaceutical preparations associated with thrombotic diseases or complications such as femoral vein thrombosis, myocardial infarction or stroke

can be done.

[0037]

The nature of the now discovered "Factor VII activator" allows the latter to be used for in vivo or ex vivo activation of plasminogen activators such as urokinase or scuPA. This activity also applies to the use of this protease, particularly in combination with single- or double-chain plasminogen activators or anticoagulants, as well for the prevention or treatment of thromboembolic disease. This potential use is consistent with the fact that proteases can also act in a procoagulant fashion. The question of which of the two responses takes precedence is presumably resolved by the availability of physiological substances. According to current knowledge, factor VII is moderately activated in plasma and is constantly maintained at a certain concentration so that sudden vascular injury can be dealt with immediately. On the other hand, tissue plasminogen activator as well as urokinase plasminogen activator are present in only nanogram quantities in 1 ml of plasma. Its concentration is elevated by secretion or synthesis of plasminogen activators only when fibrin deposition or thrombi occur, which are then activated locally, especially when they bind to thrombi, and then activate plasminogen to exert their thrombolytic action. When single-chain PAs are present, their activation exceeds that of FVII, especially in a locally restricted manner, thereby allowing regulation to physiological conditions. Therefore, this protease also modulates hemostasis, thereby potentially applying to replacement by proteases and/or proenzymes in cases of congenital or acquired defect conditions.

[0038]

Another part of the subject matter of the present invention is therefore a pharmaceutical preparation consisting of an amount of blood coagulation factor VII-activating protease and/or its proenzyme form sufficient to lyse fibrin-containing thrombi. The formulation can also contain a single chain plasminogen activator (PA) and/or an anticoagulant. If a proenzyme is present, it may also be advantageous to use a suitable activating agent within or together with the pharmaceutical formulations described above.

[0039]

Since it has been found that the plasminogen activator potentiating action of the "FVII activator" is enhanced in particular by calcium and/or heparin and heparin-like substances such as dextran sulfate, soluble calcium salts and/or heparin. Alternatively, pharmaceutical preparations containing heparin-like substances can be advantageously used for lysing fibrin-containing thrombi.

ombi according to the present invention. In this context, the protease/proenzyme, alone or in combination with a single- or double-chain plasminogen activator, optionally exerts a specific affinity for the protease, thereby increasing plasma half-life. It can be used as an extended carrier material or as a mediator to the surface together with a material that increases its activity.

[0040]

Pharmaceutical preparations consisting of blood coagulation factor VII-activating protease can be used for the treatment of diseases caused by fibrin-containing thrombi due to their specific fibrinolytic action. The fibrinolytic process is also involved in the wound healing process. In this connection, the proteases and/or proenzymes can be administered intravenously or topically, subcutaneously, intradermally or intramuscularly or topically in the case of injuries or wounds or bound to a suitable carrier matrix. Both proteases/proenzymes isolated from body fluids such as blood or plasma and recombinantly or transgenically prepared proteases/proenzymes can be used in this context. The protease/proenzyme is also suitable as a component of so-called fibrin glues, which must not contain substances that inhibit the protease/proenzyme, such as aprotinin. In this case, the clot-shortening action of proteases is utilized. The above proteases/proenzymes can be used for congenital or acquired hemostatic defects, (generalized) bleeding episodes, various thrombosis-related complications

When used to treat bleeding, it is advantageous to add the protease/proenzyme together with FVIII and, if desired, further clotting factors.

4

. Method for Sterilizing FVII-Activating Protease

Being a protein isolated from human plasma, the novel protease and/or its proenzyme can only be used as a pharmaceutical preparation if it has been previously subjected to virus-inactivating treatment. can do. The sterilization process is recognized as the most important process, especially for virus inactivation. However, the proteins to be processed require adequate stability to heating at about 60° C. for up to 10 hours. Optimal stabilizers must be determined separately for each protein and their concentrations optimized.

In the case of novel proteases and/or their proenzymes, the conditions for stabilizing proteins in non-sterilized solutions have already been described above. A slightly acidic pH has proven to be particularly advantageous in this case. However, novel proteases and/or their proenzymes typically lose 50% or more of their original activity upon sterilization under these conditions. The sterilization of the pharmaceutical formulations comprising the novel proteases and/or their proenzymes is carried out by subjecting the preparation to a

-) pH range 3.5-8.0, preferably pH range 4.0-6.8; and/or
- c) one added sugar or combination of different sugars at a total concentration of 0.01 mol/L or more, preferably 0.05 mol/L or more . 05 g/ml or more, preferably 0.2 g/ml or more; and/or
- d) one or more substances capable of forming a complex with added calcium ions such as citric acid, oxalic acid, ethylenedia

minetetraacetic acid, etc. Preparing in the presence ensures optimum stabilization results. Additives such as albumin, Haemaccel®, heparin and heparinoids, glycerol, glycols and polyethylene glycols can be used separately or mixed together. After sterilization is complete, sugars, amino acids and other additives added as stabilizers can be reduced or completely removed from the preparation using methods well known to those skilled in the art. The results of the sterilization process are shown in Examples 12 and 13. [Example]

Example 1

Activation of FVII by the proteases prepared was demonstrated using the Staclot® FVIIa-rTF test system (Stago/Boehringer Mannheim). This detection system has the specific property that preformed activated FVII (FVIIa) can only be used to inhibit the extrinsic coagulation pathway.

It is based on (recombinant) soluble tissue factor (rTF). This allows the actual content of FVIIa to be accurately determined, as opposed to using intact tissue factor.

Activation experiments were

performed using isolated FVII (Enzyme Research Labs). This FVII itself contains traces of FVIIa since it was isolated from human plasma. The concentration was adjusted to 0.05 IU/ml of FVII by dilution with buffer. FVII was incubated with test substances for 10 minutes at room temperature and then tested for true FVIIa content. FVIIa content was quantified using a standard curve constructed in parallel.

In preliminary

experiments, not described here, aprotinin completely inhibited the activity of the prepared protease at the concentrations used, but had no direct effect on FVIIa and showed no direct effect on the FVIIa-rTF test system. It was confirmed that there was no significant effect on

The results listed below relate in each case to triplicate measurements. That is, the following experiments were set up as follows.

1

. FVII:

Non-activated FVII was used as a control assay. It already contains traces of FVIIa (see above)

e) in the order of 10 mIU/ml of FVIIa.

2

. FVII+Aprotinin:

In this assay, FVII was incubated in the presence of aprotinin and the FVIIa-rTF assay was used to demonstrate that FVIIa itself was not inhibited nor was the test affected by the aprotinin used. This was confirmed (by comparison with Assay 1).

[0050]

3. Protease + FVII (incubation) then addition of aprotinin:

Result: FVIIa 18 mIU/ml

In this case the protease was given time to activate FVIIa. Aprotinin was added only to wash out the protease, after 10 minutes of incubation. The resulting FVIIa was quantified by the FVIIa-rTF assay. Thus, subtracting the basal value of FVIIa (assay 1), 8 mIU/ml of FVIIa was formed by the activity of the protease under the conditions chosen.

4

. Protease + aprotinin then addition of FVII:

Results: FVIIa 11 mIU/ml

In this assay the protease was inhibited with aprotinin prior to contact with FVII. Neither subsequent incubation with FVII nor subsequent quantification of FVIIa resulted in a significant increase in FVIIa content (the range of variation in the assay, ie 11 and 10 mIU/ml in assay 1, is not considered significant).

5

. Protease:

Results: FVIIa 0 mIU/ml

This assay demonstrated that the protease itself had no effect on the FVIIa-rTF test system at the concentrations chosen.

In summary, from the above

- the described proteases activate FVII;
- the activation of FVII by proteases occurs "directly", i.e. independently of the presence of rTF;
- FVII activation is inhibited by aprotinin; aprotinin itself has no significant effect on the test system;

is concluded. Example 2 This example illustrates how FVII is activated in a reaction that is independent of the concentration of protease and the time the protease is incubated with FVII.

. The test system and reagents were selected to correspond to those described in Example 1.

In the first series of experiments, the initially introduced FVII was preincubated (5 min at room temperature) with protease-containing solutions at various dilutions (1:5, 1:10 and 1:20), followed by aprotinin (a protease inhibiting) and subsequently tested for their FVIIa content in the FVIIa-rTF assay. Again, a parallel assay in which the protease was inhibited by aprotinin before contacting with FVII served as a control. Results are given as activation factors. ie x ti

mes the value measured in the control assay described above. Assay: protease + FVII, incubation, + aprotinin Control: protease + aprotinin, incubation + FVII

[Table 1]

<u>プロテアーゼ溶液の希釈度</u>	<u>活性化係数</u>	
	<u>アッセイ</u>	<u>対 照</u>
1 : 5	2.6	1.0
1 : 10	2.0	1.0
1 : 20	1.6	1.0

From this it is concluded that FVII is activated by proteases in a protease concentration-dependent manner. It was also demonstrated that FVII was activated by proteases in a manner that was independent of the length of incubation when the co-reactant concentration was kept constant

When equal volumes of a solution containing 0.2 IU/ml FVII and a 1:10-diluted protease solution were incubated together, aprotinin was added (to stop activation) after a corresponding period of incubation, followed by: of FVIIa content was obtained.

[Table 2]

<u>インキュベーションの長さ</u>	<u>活性化係数</u>
0 分	1.0
2.5 分	1.3
5.0 分	2.0
10.0 分	2.8
40.0 分	> 3.8

From this it is concluded that FVII is activated in a time-dependent manner by proteases. Example 3 This example will be used to demonstrate that protease activation of FVII is enhanced

ed by the presence of calcium ions and heparin

. 25 µl of protease-containing solution was added to 50 µl of

- buffer (control)
- 15 mM CaCl₂
- heparin 50 USP units/ml
- Pathromtin (lipid mixture, aliquot dissolved according to manufacturer's instructions) for 5 minutes at room temperature, then 150 µl of tris/NaCl buffer (pH 8). .2) and 25 µl of chromogenic substrate S2288 (3 mM), followed by measurement of absorbance over time at 405 nm (37° C.). Activation factors (x-fold) relative to buffer controls are shown in the table below.

[Table 3]

<u>アッセイ</u>	<u>活性化係数（緩衝液 対照に対する倍数 x）</u>
緩衝液対照	1.0
+ CaCl ₂	3.6
+ ヘパリン	2.6
+ 脂質	0.9
+ CaCl ₂ + ヘパリン	4.3
+ CaCl ₂ + 脂質	3.3
+ ヘパリン + 脂質	2.7
+ CaCl ₂ + ヘパリン + 脂質	3.7

Under the conditions used in this example, a significant increase in protease activity can be observed in the presence of calcium ions and/or heparin. Example 4 In each case a solution containing 10, 1 or 0.1 µg/ml of protease was mixed with 25 µl of FVII (2 IU/ml) followed by 25 µl of CaCl₂ (25 mM) and 25 µl of Pathromtin® (Dade Behring GmbH) was added. After incubation for 0, 3, 10 and 20 minutes at 37° C., the reaction was stopped by adding 400 µl of aprotinin (500 KIU/mg). A sample to which aprotinin was added first was used as a control. Each sample was diluted in tris buffer/BSA. In each case 50 µl of this solution were mixed with 50 µl of the factor reagent [mainly consisting of FIXa, FX and thrombin inhibitors, modified according to the Cosmatic®^F VIII test, Chromogenix AB] and incubated at 37° C. for 10 minutes. 50 µl of substrate (eg S2765, Na-Cbo-D-Arg-Gly-Arg-pNA) was added, followed by the addition of 50 µl of acetic acid (5

0%) to stop the reaction after a defined time of incubation, OD 405 nm was then measured. A standard curve of FVIII was used to determine the concentrations in the samples. Results :

In the first assay, the protease incubation time with FVIII (2 IU/ml) was kept constant (10 min), but the protease concentration was varied (0.1, 1 and 10 µg/ml). The reaction was stopped and the residual concentration of active FVIII was determined. Increasing protease concentrations resulted in a corresponding inactivation of FVIII (Fig. 1).

The protease content of samples can be quantified using a suitable standard curve.

In the second assay, the concentration of protease was held constant (10 µg/ml), FVIII (2 IU/ml) and incubation time were varied. A significant decrease in the residual concentration of active FVIII was observed with increasing incubation time (Fig. 2).

Example 5 The effect of "FVII activator

" on factor V activity was examined.

25 µl of protease-containing solution (0-100 µg/ml) was incubated with 50 µl of FV (5 IU/ml) and 25 µl of CaCl₂ (0-20 min), then 400 µl of buffer containing 100 KIU/ml aprotinin was added.

In both cases, 100 µl of each incubation assay was then incubated with 100 µl of FV-deficient plasma for 1 minute at 37° C., then 200 µl of Thromborel S® were added, mixed and clotting time was measured using a Schnitger & Gross ^{coagulometer}. was measured. Residual activity of FV was determined.

result:

[Table 4]

プロテアーゼ濃度 (µg/ml)	F Vの残留活性		
	プロテアーゼとF Vのインキュベーション時間(分)		
	0	10	20
10	93	91	100
30	100	93	28
100	100	29	13

This example demonstrates that FV was inactivated by proteases over time. Example 6 The effect of "FVII activators" on blood clotting

times in a so-called global test was investigated using a Schnitger & Gross coagulometer. All the difference values given correspond to a shortened blood clotting time by this amount. NAP TT (non-activated partial thromboplastin time) protease-containing solutions were diluted with buffer to 100, 30, 10 and 3 µg/ml. 100 µl of each of these solutions were incubated with 100 µl of citrated plasma (from standard plasma pools or individual donors) and 100 µl of Pathromtin® for 2 minutes at 37° C., then 100 µl of 25 mM CaCl₂ were added, followed by blood. Clotting time was measured. Differences between these measurements and the corresponding blood clotting times obtained using buffer instead of protease were determined.

[Table 5]

サンプル番号	血液凝固時間の差（緩衝液－サンプル、秒）				
	プロテアーゼ濃度（µg/ml）				
	0	3	10	30	100
標準ヒト血漿(213秒)	0	13	20	42	43
1	0	20	33	42	41
2	0	27	31	45	47
3	0	13	14	23	29
4	0	18	37	51	50
5	0	25	49	54	46

Addition of the FVII activator resulted in a concentration-dependent shortening of NAPTT. Plasma Calcium Reprecipitation Time Protease-containing solutions were diluted with buffer to 100, 30, 10 and 3 µg/ml. 100 µl of each of these solutions were incubated with 100 µl of citrated plasma (either from standard plasma pools or from individual donors) at 37° C. for 1 minute, then 100 µl of 25 mM CaCl₂ were added and clotting times were measured. Differences between these measurements and the corresponding blood clotting times obtained using buffer instead of protease were determined.

[Table 6]

血液凝固時間の差（緩衝液－サンプル、秒）

サンプル番号	プロテアーゼ濃度 ($\mu\text{g}/\text{ml}$)				
	0	3	10	30	100
標準ヒト血漿(283秒)	0	17.2	15.1	30.5	50.4
1	0	29.8	51.7	60.3	90.1
2	0	25.2	51.7	69.5	101.3
3	0	28.0	—	39.0	74.6
4	0	27.3	42.7	55.6	91.8
5	0	44.3	69.1	101.2	134.2

PT (prothrombin time).

protease-containing solutions were diluted with buffer to 100, 30, 10 and 3 $\mu\text{g}/\text{ml}$. 100 μl of each of these solutions are incubated with 100 μl of citrated plasma (either from standard plasma pools or from individual donors) at 37° C. for 1 minute, then 200 μl of Thromborel S® (Dade Behring GmbH) are added, followed by blood clotting. time was measured.

Differences between these measurements and the corresponding clotting times obtained using buffer instead of protease were determined.

[Table 7]

血液凝固時間の差（緩衝液－サンプル、秒）

サンプル番号	プロテアーゼ濃度 ($\mu\text{g}/\text{ml}$)				
	0	3	10	30	100
標準ヒト血漿(13.6秒)	0	1.0	1.7	1.5	2.4
1	0	0.7	1.3	2.4	2.7
2	0	0.3	0.4	1.7	3.1
3	0	0.4	0.7	1.5	1.8
4	0	0.1	0.7	1.8	3.1
5	0	0.3	0.5	1.2	2.8

Example 7 The

plasminogen activator activating action of "FVII activator" was examined using single-chain urokinase (scuPA) and single-chain tPA (sctPA).

Assay:

0.1 ml PA solution (20 µg/ml scuPA or 100 µg/ml sctPA)

+ 0.1 ml test buffer or

100 U/ml heparin in test buffer or

20 mM CaCl₂

in test buffer + 0.5 ml test buffer + 0.1 ml test buffer

1 ml protease/sample (increasing concentrations; 2-10 µg/ml scuPA
or 50-200 µg/ml sctPA)

incubation at 37° C.

+ 0.1 ml aprotinin at 100 KIU/ml in test buffer

2 min incubation at 37° C.

+ 0.1 ml For the substrate S-2444 (3 mM)

control, aprotinin is first introduced instead of plasminogen activator (PA) prior to the first incubation, and so on through each case. On the other hand, PA was not added thereafter until it was added instead of aprotinin.

The difference in measurements (Δ) Δ OD_{405 nm} was measured optically. The control values obtained were subtracted from the sample/protease values and in this way the PA activity produced by the PAA activity was measured (mIU/min).

Results

:

Activation of scuPA (20 µg/ml scuPA, 2-10 µg/ml "FVII activator")

[Table 8]

A. 刺激物質：なし

インキュベーション時間 (分)	得られたPA活性 ($\Delta mIU/\text{分}$) FVIIアクティベーター ($\mu g/ml$)		
	2	5	10
2	25	60	117
5	79	179	165
10	186	449	517

B. 刺激物質：ヘパリン

インキュベーション時間 (分)	得られたPA活性 ($\Delta mIU/\text{分}$) FVIIアクティベーター ($\mu g/ml$)		
	2	5	10
2	190	332	425
5	330	455	458
10	417	462	460

C. 刺激物質：CaCl₂

インキュベーション時間 (分)	得られたPA活性 ($\Delta mIU/\text{分}$) FVIIアクティベーター ($\mu g/ml$)		
	2	5	10
2	255	370	401
5	338	424	438
10	416	445	448

The table illustrates the fact that scuPA is activated in a manner that depends on the concentration of the "FVII activator" and the length of incubation. At the same time, both heparin and calcium showed a stimulatory effect on the activation of PA induced by proteases. Activation of scuPA (100 $\mu g/ml$ sctPA, 50-200 $\mu g/ml$ "FVII activator"). The turnover rate of activated tPA is only increased by a factor of 3-4 compared to the tPA proenzyme. (In the case of uPA it increases by a factor of 1000-1500), so high concentrations of the two co-reactants had to be chosen in order to obtain an analyzable measurement signal.

[Table 9]

A.

<u>インキュベーション時間 (分)</u>	<u>得られたPA活性 (Δ mIU/分) FVIIアクティベーター (200 μg/ml)</u>
1	10.2
2	16.8
5	38.8
10	60.2
20	73.3

B. 「FVIIアクティベーター」の濃度依存性(インキュベーション、時間：20分、37℃)、刺激物質：ヘパリン (100IU/ml)

<u>FVIIアクティベーター (μg/ml)</u>	<u>PA活性 (Δ mIU/分)</u>
50	33.6
100	51.0
200	71.9

C. 刺激物質 (インキュベーション、時間：20分、37℃)

<u>刺激物質</u>	<u>PA活性 (Δ mIU/分)</u>
なし	5.9
CaCl ₂	25.3
ヘパリン	63.8

The table demonstrates that sctPA was also activated in a protease concentration- and incubation time-dependent manner. Both heparin and calcium ions showed a stimulatory effect on the ability of the 'FVII activator' to activate PA. Example 8 Two FVIII-containing solutions, one essentially free of von Willebrand Factor and the other containing vWF, were incubated in the presence of the protease described above and calcium. Residual FVIII activity was measured by a chromogen test after a predetermined time and correlated with a protease-free control assay. For this, 25 μ l of a solution containing 0.1 IU/ml of FVIII were treated with an equ

al volume of protease solution ($\mu\text{g/ml}$) and the whole was mixed with 25 μl of CaCl_2 (25 mM). After incubation at 37° C. for 0, 5, 10 and 20 minutes, it was treated in each case with 400 μl of a solution containing 200 KIU/ml aprotinin in order to terminate the proteolytic activity of the protease. Preliminary experiments have shown that this concentration of aprotinin has no significant interfering effect on the FVIII activity test (assays 1+3) described below. In Assay 2, the protease was incubated with aprotinin prior to contact with FVIII and then manipulated as described above.

In each case 50 μl of the stopped sample (or after further dilution) were then treated with so-called factor reagents, consisting mainly of FIX, FX and thrombin inhibitors, and incubated at 37° C. for 10 minutes. Addition of 50 μl of chromogenic substrate which is cleaved by activated FX was followed by incubation for 5 minutes before adding 50 μl of acetic acid (50%) to stop the reaction and $\Delta\text{OD}_{405\text{ nm}}$ was measured. FVIII activity (mIU) was determined using a standard curve prepared from FVIII concentrates and constructed using the dilution series included in the test.

FVIII activity is

expressed as a percentage of the control to which no protease was added.

result:

[Table 10]

アッセイ	FVIII活性(%)			
	インキュベーション時間(分)			
	0	5	10	20
1. FVIII	97	27	11	<1
2. FVIII/アプロチニン	98	97	97	96
3. FVIII/vWF	98	16	14	1

In the presence of CaCl_2 (6.25 mM in this case), FVIII was inactivated by proteases in a length-of-incubation-dependent manner. vWF did not protect FVIII from inactivation by proteases. Inhibition of the protease with aprotinin prior to contact with FVIII prevented inactivation of the former.

Example

9

In this series of experiments, Example 1/Assay 1 was performed, but in this case the calcium concentration in the mixture of protease and FVIII was varied. For this, CaCl_2 was added from a calcium stock solution to the final concentrations shown in FIG.

Results:

Approximately 50% FVIII remains under these conditions when the calcium concentration in the assay is reduced to less than 1 mM. Below 0.5 mM calcium the residual percentage is greater than 60% (Fig. 1). Example 10 The effect of "FVII activators" on blood clotting times in a so-called global

test was investigated by thrombus elastography. Changes in shear elasticity or strength of associated clots were recorded continuously using a Hilgard TEG meter (from Hellige). The so-called r and k values, the time from the onset of blood arrest and from the onset of clotting reaction respectively, for citrated plasma the time of recalcification to the TEG curve extends up to 1 mm, the r value The time from the end point to the curve extended to 20 mm (clotting time). [0074]

For this, 150 μl aliquots of blood or plasma from 5 donors were in each case incubated at 37° C. for 2 minutes in the measurement cuvette, then 50 μl of sample (protease) were added and mixed. 100 μl of 25 mM CaCl_2 was added to initiate the reaction. The final concentration of "FVII activator" in the assay was 15 $\mu\text{g/ml}$. Reduction in r time was measured for assays containing buffer instead of sample.

result:

[Table 11]

血液番号	サンプル	r 時間(分)	k 時間(分)	r + k 時間(分)
1	プロテアーゼ	5.2	3.4	8.6
1	緩衝液	7.8	5.6	13.4
2	プロテアーゼ	5.2	5.1	10.3
2	緩衝液	6.8	7.1	13.9
3	プロテアーゼ	4.0	5.2	9.2
3	緩衝液	6.5	6.3	12.8
4	プロテアーゼ	4.5	4.8	9.3
4	緩衝液	4.8	6.0	10.8
5	プロテアーゼ	4.2	3.8	8.0
5	緩衝液	7.0	5.8	12.8

血漿番号	サンプル	r 時間(分)
1	プロテアーゼ	9.0
1	緩衝液	11.3
2	プロテアーゼ	9.2
2	緩衝液	12.5
3	プロテアーゼ	9.5
3	緩衝液	9.6
4	プロテアーゼ	8.2
4	緩衝液	12.1
5	プロテアーゼ	9.7
5	緩衝液	14.1

This

example demonstrates that in almost all cases the addition of protease causes a marked reduction in blood clotting time. In the example shown here the fibrinolytic effect of the "FVII activator" was hidden in the background. The reason for this is that in "normal subjects" the concentration of plasminogen activator in plasma is in the nanogram range and has no effect on in vitro coagulation tests. Example 11 Protease FVIII alternative

pathway activity was demonstrated by the following experimental assays. That is, thrombus elastography was used as a measurement technique. The r time was evaluated (see Example 10). Whole blood samples were incubated with monoclonal antibodies known to inhibit FVIII activity (antibodies against FVIII) in order to stimulate the presence of natural FVIII inhibitors. Samples were compared to a whole blood sample control (buffer instead of Mab). FE of protease

IB activity was tested by adding protease (17 µg/ml final concentration) to Mab-inhibited whole blood samples. Additionally, protease was added to the samples to determine the effect of the protease itself on rtime.

Results

:

[Table 12]

	<u>r 時間</u>
全血対照	8.0
全血+mAb	11.0
全血+mAb+プロテアーゼ	8.0
全血+プロテアーゼ	3.5

The rtime prolongation caused by the anti-FVIII mAb was again normalized by the presence of the protease, demonstrating the FEIB activity of the protease. As already demonstrated above, the protease itself shortened the blood clotting time. Example 12 To a solution containing 50 µg/ml FVII-activating protease was added the following substances to the corresponding final concentrations

. 25 mM sodium citrate 25 mM HEPES 100 mM arginine 0.75 g/ml sucrose This solution was divided into portions and in each case aliquots were adjusted to various pH values from 5.0 to 8.6 and then heated to 60° C. for 10 hours. bottom. The activity of the heated protease solution was determined by the chromogenic assay, recording deamidation of the chromogenic substrate S2288 (HD-Ile-Pro-Arg-pHA x 2HCl, Chromogenix AB, Sweden) over time. The activity was expressed as a percentage of aliquots measured in parallel without heating. Results :

[Table 13]

<u>アッセイ</u>	<u>活性(%)</u>
出発原料	100
pH 5.0	76
pH 5.5	65
pH 6.1	81
pH 6.5	50
pH 7.1	43
pH 7.5	46
pH 8.1	46
pH 8.6	32

This series of experiments showed that stabilization, especially in the acidic pH range, markedly inactivated proteases.

decreased sharply. The slight "breakthrough" at pH 5.5 can be explained by the fact that the isoelectric point of the protease lies in this range. Sodium citrate prevents the >50% loss of activity that occurs in the preferred pH range. Example 13 The assay at pH 6.1 (Example 1) showed the best stabilization of the protease

. Therefore, various activities were tested and evaluated at pH 6.0 as described in Example 1.

The following final concentrations were set and the protease concentration was 50 µg/ml. 50 mM sodium citrate/50 mM NaCl, pH 6.0 0.75 g/ml sucrose 100 mM glycine 100 mM arginine Results:

[Table 14]

アッセイ	活性(%)
出発原料	100
クエン酸ナトリウム／NaCl	54
クエン酸ナトリウム／NaCl／スクロース	85
クエン酸ナトリウム／NaCl／スクロース／グリシン	92
クエン酸ナトリウム／NaCl／スクロース／アルギニン	97

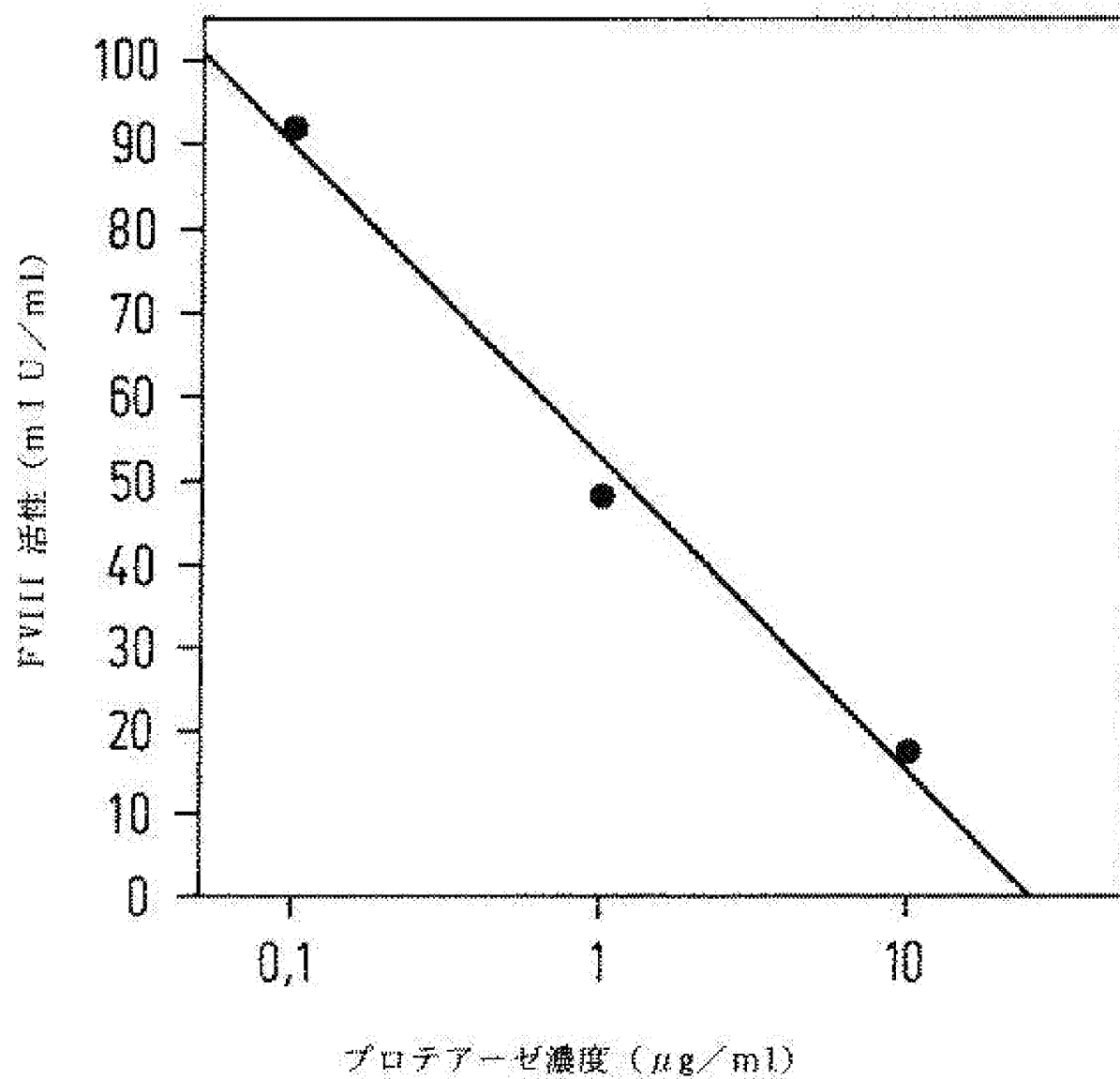
Addition of sucrose and one amino acid in each case demonstrated a significant stabilization of the protease.

drawing

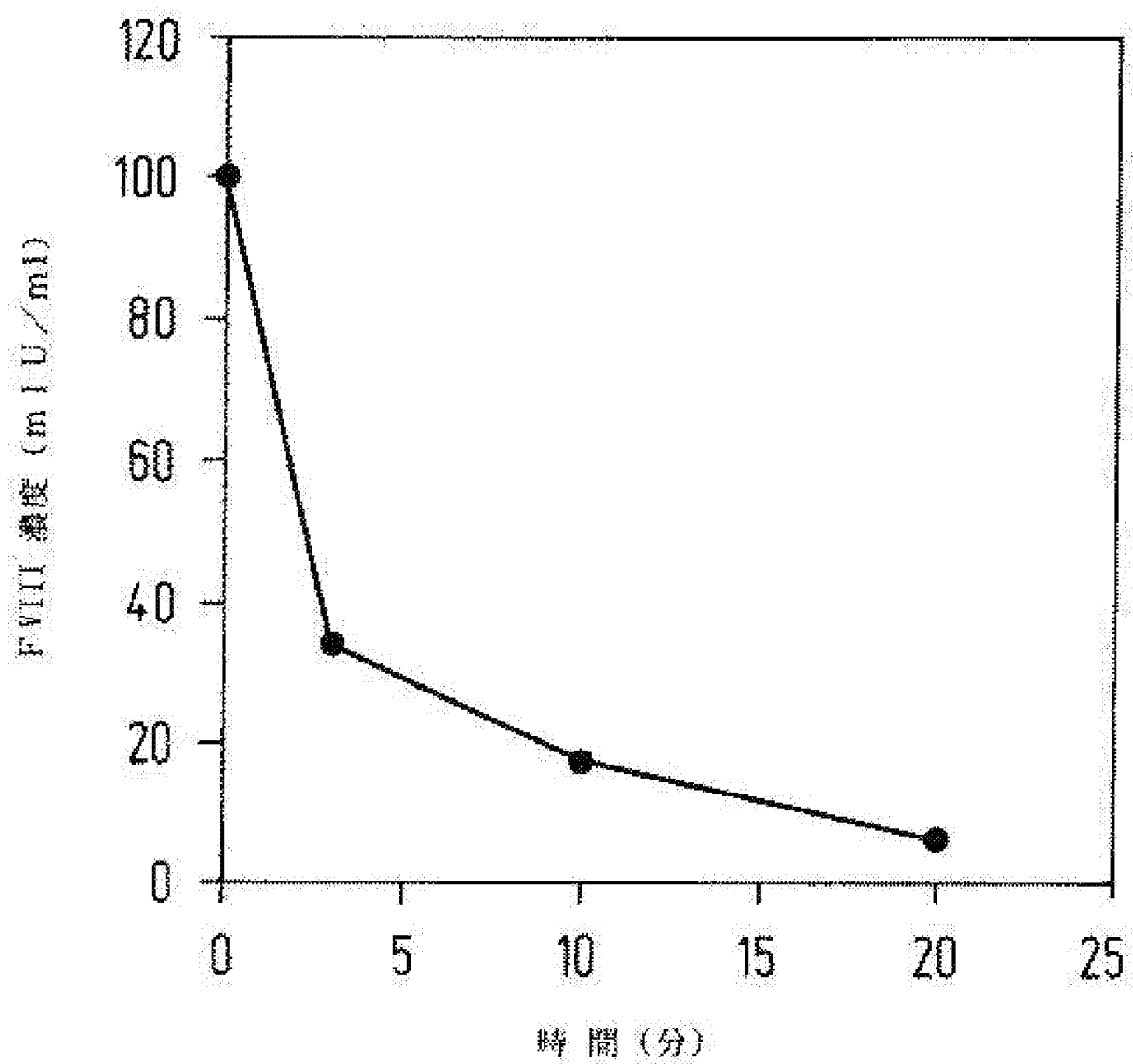
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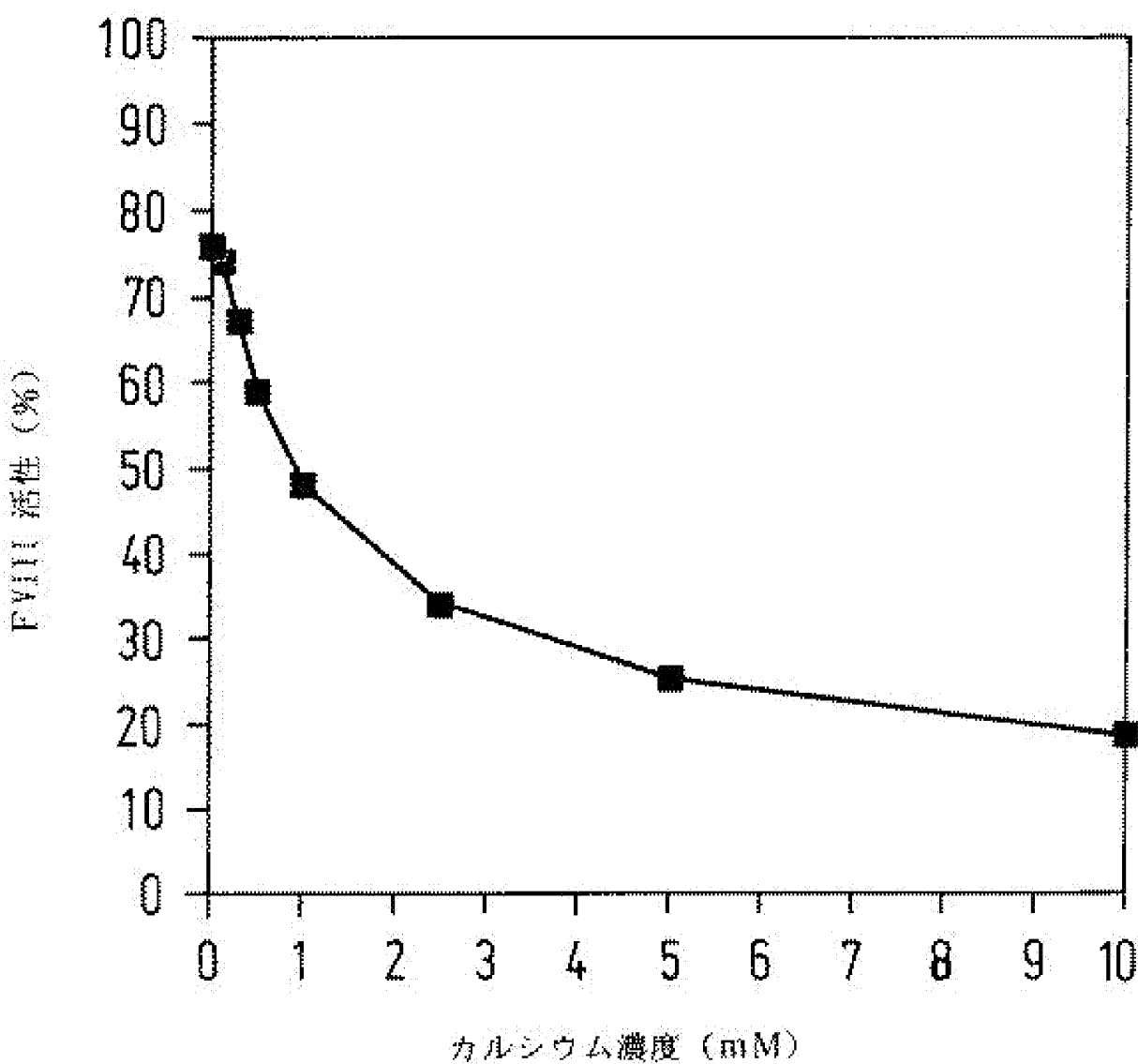
[Fig. 1]



[Figure 2]



[Figure 3]



drawing

open

1 | 2 | 3

Magnify and Rotate

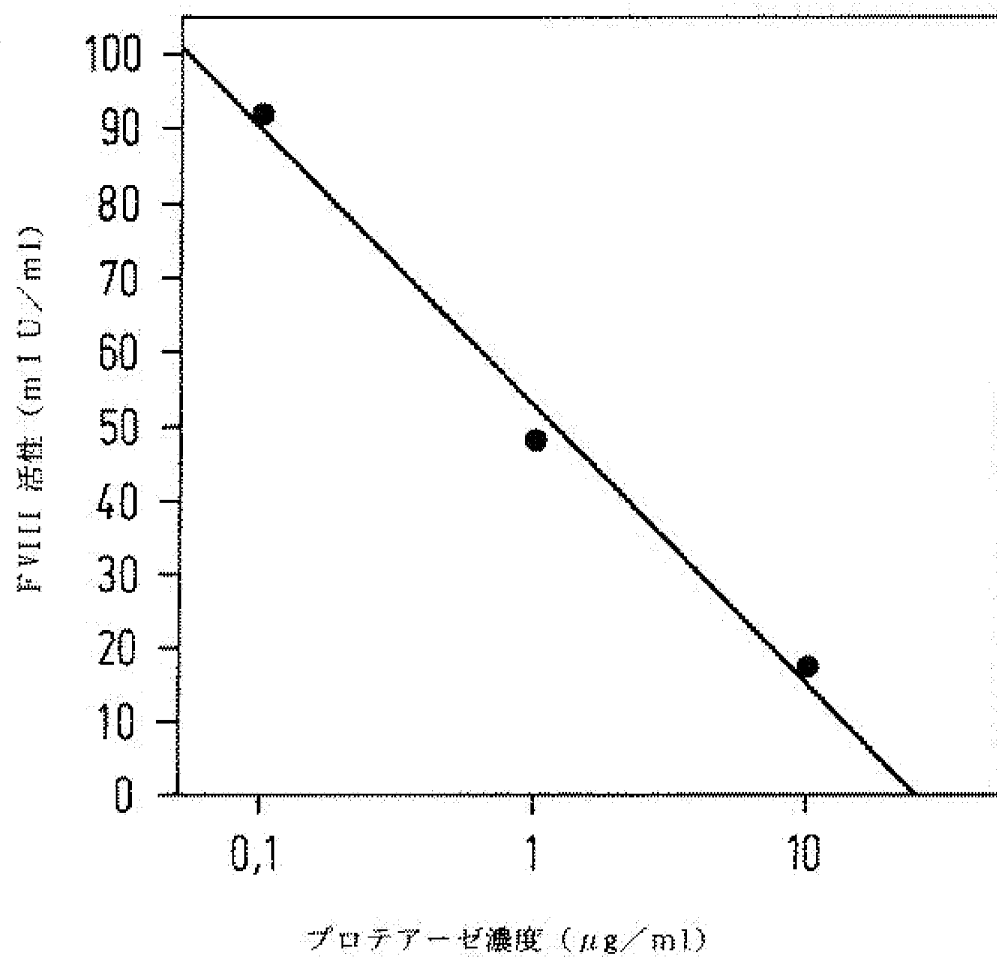


Figure 1

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最終頁に続く

(54) 【発明の名称】 血液凝固第VII因子を活性化するプロテアーゼ

(57) 【要約】

【課題】 新規なFVII活性化プロテアーゼの発見とその応用。

【解決手段】 a) アプロチニンの存在によって阻害され、b) カルシウムイオンおよび／またはヘパリンもしくはヘパリン類縁物質によってその活性が上昇し、またc) SDS-PAGEにおいて、以後の非還元状態での染色では分子量 50～75 kDaの範囲の1個もしくは2個以上のバンドを示し、還元状態では分子量10～35 kDaの範囲の1個もしくは2個以上のバンドを示す、血液凝固第VII因子を活性化するプロテアーゼならびにそのプロ酵素は、血漿またはプロトロンビン複合体 (PPSB) 濃縮物から予め陰イオン交換クロマトグラフィーに付したのち、ヘパリンもしくはヘパリン類縁物質またはデキストラン硫酸を用いる親和性クロマトグラフィーによって得られる。

本発明は、上記プロテアーゼまたはそのプロ酵素の定性的および定量的検出、ならびにその診断的応用のための試験システムおよびフィブリン含有血栓の溶解に適当な量の血液凝固第VII因子を活性化する上記プロテアーゼおよび／またはそのプロ酵素を含有する医薬製剤が含まれる。

【選択図】 なし

【特許請求の範囲】

【請求項1】

- a) アプロチニンの存在によって阻害され、
- b) カルシウムイオンおよび／またはヘパリンもしくはヘパリン硫酸によりその活性は上昇し、
- c) SDS-PAGEにおいて、それに続く非還元状態での染色により分子量50～75 kDaの範囲の1個もしくは2個以上のバンドを示し、還元状態では分子量40～55 kDaに1個のバンドおよび分子量10～35 kDaの範囲に1個または2個以上のバンドを示し、そして
- d) SDS-PAGEにおいて還元状態で分子量40～55 kDaの範囲に得られるバンドはアミノ酸配列：LLES LDPを有し、分子量10～35 kDaの範囲に得られるバンドはアミノ酸配列：IYGGFKSTAGKを有するプロテアーゼ、および／または SDS-PAGEにおいて還元状態で得られるバンドは60～65 kDaの範囲の分子量を有し、アミノ酸配列：LLES LDPおよびIYGGFKSTAGKを含有する前記プロテアーゼのプロ酵素の定性的および定量的検出のための試験システムにおいて、そのプロテアーゼ活性は、

- a) 血液凝固第VIII/VIIIa因子もしくは第V/Va因子を不活性化するその活性または
 - b) 包括的血液凝固試験における血液凝固時間を低下させるその活性または
 - c) プラスミノゲンアクティベーターを活性化するその活性または
 - d) FVIIを活性化するその活性
- によって測定する試験システム。

【請求項2】

請求項1に記載の試験システムにおいて、血液凝固時間を低下させる活性は、

- a) 非活性化部分トロンボプラスチン時間 (NAPTT) または
 - b) プロトロンビン時間 (PT) または
 - c) 血漿カルシウム再沈着時間または
 - d) 活性化部分トロンボプラスチン時間 (APTT)
- によって測定する試験システム。

【請求項3】

請求項1および2に記載の試験システムにおいて、プラスミノゲンアクティベーターを活性化および／または増強する活性は、

- a) 一本鎖ウロキナーゼPA (scuPA、一本鎖ウロキナーゼプラスミノゲンアクティベーター) または
- b) 一本鎖 tPA (scfPA、一本鎖組織プラスミノゲンアクティベーター) の活性化により測定する試験システム。

【請求項4】

請求項1～3に記載の試験システムにおいてカルシウムイオン0.001 mM以上の量を含む試験システム。

【請求項5】

- a) アプロチニンの存在によって阻害され、
- b) カルシウムイオンおよび／またはヘパリンもしくはヘパリン硫酸によりその活性は上昇し、
- c) SDS-PAGEにおいて、それに続く非還元状態での染色により分子量50～75 kDaの範囲の1個もしくは2個以上のバンドを示し、還元状態では分子量40～55 kDaに1個のバンドおよび分子量10～35 kDaの範囲の1個または2個以上のバンドを示し、そして
- d) SDS-PAGEにおいて還元状態で分子量40～55 kDaの範囲に得られるバンドはアミノ酸配列：LLES LDPを有し、分子量10～35 kDaの範囲に得られるバンドはアミノ酸配列：IYGGFKSTAGKを有するプロテアーゼ、および／または

SDS-PAGEにおいて還元状態で得られるバンドは60～65kDaの範囲の分子量を有し、アミノ酸配列：LLES LDPおよびIYGGFKSTAGKを含有する前記プロテアーゼのプロ酵素と適当なプロ酵素アクティベーターの混合物をプロトロンビン時間置換組織因子／トロンボプラスチンの試験に使用するアッセイシステム。

【請求項6】

- a) アプロチニンの存在によって阻害され、
- b) カルシウムイオンおよび／またはヘパリンもしくはヘパリン硫酸によりその活性は上昇し、
- c) SDS-PAGEにおいて、それに続く非還元状態での染色により分子量50～75kDaの範囲の1個もしくは2個以上のバンドを示し、還元状態では分子量40～55kDaに1個のバンドおよび分子量10～35kDaの範囲の1個または2個以上のバンドを示し、そして

d) SDS-PAGEにおいて還元状態で分子量40～55kDaの範囲に得られるバンドはアミノ酸配列：LLES LDPを有し、分子量10～35kDaの範囲に得られるバンドはアミノ酸配列：IYGGFKSTAGKを有するプロテアーゼ、および／または

SDS-PAGEにおいて還元状態で得られるバンドは60～65kDaの範囲の分子量を有し、アミノ酸配列：LLES LDPおよびIYGGFKSTAGKを含有する前記プロテアーゼのプロ酵素と適当なプロ酵素アクティベーターの混合物を、プラスミノゲンアクティベーターの機能性の試験ならびに一本鎖プラスミノゲンアクティベーター型の定量に使用するアッセイシステム。

【請求項7】

請求項1～6に記載の試験システムにおいて、プラスミノゲンアクティベーターを増強する活性は、

- a) 色素原試験を用いて測定するかまたは
- b) プラスミノゲンの存在下におけるカップリング反応でプラスミン自体の形成もしくはプラスミンによってもたらされるフィブリン凝血の溶解で測定する試験システム。

【発明の詳細な説明】

【技術分野】

【0001】

本発明は血液凝固第VII因子の活性化のためのプロテアーゼ、それを単離、検出および不活性化する方法ならびにこのプロテアーゼからなる医薬製剤に関する。

【背景技術】

【0002】

血液凝固系は、血漿中に存在する血液凝固因子を活性化する2つの異なるカスケード経路から構成される。その誘導機構によって、内因系または外因系経路が血液凝固の開始に優先的に使用される。

【0003】

組織が傷害された場合、トロンボプラスチン（組織因子、TFとリン脂質）が外因性凝血経路のスターターとして冒された細胞により暴露される。膜局在性のトロンボプラスチンは、血液凝固第VII因子（FVII）および循環する、活性化FVII（FVIIa）の両者を結合することができる。カルシウムイオンおよび脂質の存在下に、このTF-FVIIa複合体はFXの結合を招き、これは限定された蛋白分解によってその活性化型（FXa）に変換される。続いてFXaはプロトロンビンを活性化してトロンビンを形成させることにより、フィブリンの形成を招来し、それによって最終的に創傷の閉鎖が起こる。

【0004】

トロンボプラスチン結合FVIIの更なる活性化は最初は自触反応によって起こるが、特に、凝血カスケードの開始後には、それはFXaおよびトロンビンによって支持され、特に反応カスケードの著しい強化を招くことになる。

【0005】

FVIIaまたはFVIIa含有濃縮物の投与はある種の臨床状態に適用されている。たとえば、血友病Aに冒されFVIII投与の結果としてFVIIIに対する抗体が発生している患者で

は、FVIIaのいわゆるFVIII副経路活性 (FEIBA) が用いられる。現時点で分かっている所見によれば、FVIIaはこの関係で十分な耐容性を有し、それは血栓傾向を生じることではなく、限られているが適切な程度の凝固が起こることを保証するのに適している。組換えFVIIaは既に治療的におよび予防的に使用されている。血漿から単離されたFVIIIはまた、活性化されてから用いることもできる。トロンビンのようなプロテアーゼをこの活性化に使用できるが、しかしながら、これらのプロテアーゼは、それら自体凝固を強力に活性化することが可能で、血栓の危険を招くことがある。この理由から、以後のトロンビンの除去または不活性化が必要であり、損失を生じることになる。それに伴う血栓の危険の結果として、多くの場合、FXaもしくはFIIa (トロンビン) の使用は禁忌とされ、緊急時、たとえば血液の著しい喪失および止血不能の出血の関連でのみ適用される。

【図面の簡単な説明】

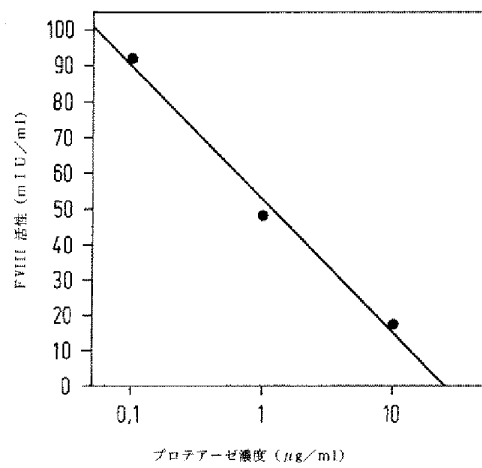
【0009】

【図1】プロテアーゼとFVIIIを一定時間インキュベートした場合のプロテアーゼ濃度とFVIIIの不活性化を示す。

【図2】プロテアーゼ濃度を一定とし、FVIIIを様々な時間インキュベートした場合のFVIIIの不活性化を示す。

【図3】プロテアーゼとFVIIIを混合物中におけるカルシウム濃度を変動させインキュベートした場合のFVIIIの不活性化を示す。

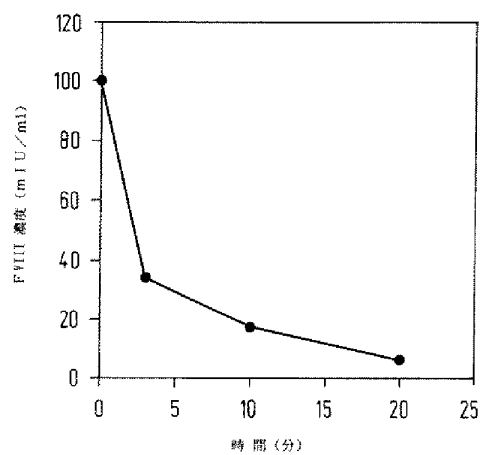
【図1】



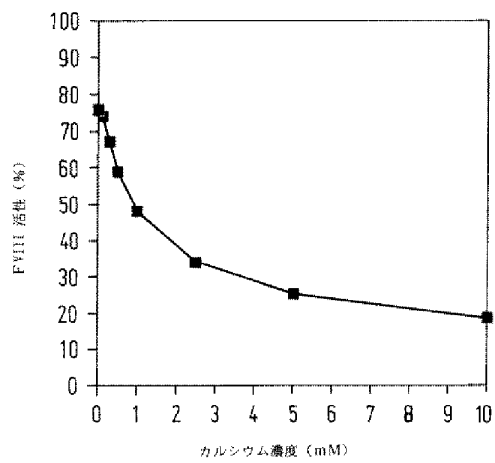
(6)

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【図2】



【図3】



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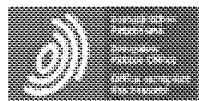
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Fターム(参考) 4B063 QA05 QQ36 QQ79 QQ95 QQ97 QR16 QR48 QR67 QR82 QX01

4C084 AA02 AA07 BA03 BA44 CA62 DC14 NA14 ZA532 ZC022



Espacenet

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

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

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

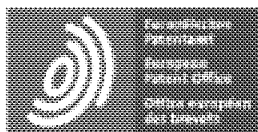
Priority number(s): AT19710009545 19711105

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 plasmapheresis; 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 plasmapheresis.



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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 ulutbehltext-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 leukocytapheresis and thrombocytapheresis, 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 elements 4'" and 4M closed, the system is completely filled with physiological saline before inserting the venipuncture needle into the vein, avoiding air bubbles. Then the shut-off element 4M in the line 7 is closed and the venipuncture needle inserted into the vein is connected to the bag 11 by connecting the coupling piece 10 to the attachment 12, the shut-off element 4M 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 .

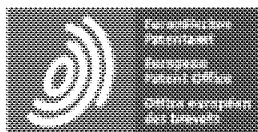
143 In the next phase, the shut-off device 4n in the line 7 is closed, the blood bag 11 is connected to one of the connectors 13 or 14 with the coupling piece 6 of the line 5, 4" is closed. 41 is opened and physiological saline solution is transferred into the bag 11 until a infusible suspension of erythrocytes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

147 Then the obturator 4 is

[0016]

151 closed, reopened 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

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AT 27.01.72

Pr 05.11.71 Österreich A9545-71

Bez: Kombiniertes Blutabnahme- und
Infusionsgerät.

Anm: Immuno Aktiengesellschaft für che-
misch-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;

lbm

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: 4 34

(Bitte freilassen!)

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3891746 DE

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Patentanwälte
Dr. Richard Glawe **Dipl.-Ing. Klaus Delfs** **Dr. Walter Moil**
München Hamburg München

1368

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bezieht, übereinstimmend mit dem Titel der
Beschreibung;
keine Phantasiebezeichnung!)

Kombiniertes Blutabnahme- und Infusionsgerät

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Auslandspriorität der Voranmeldung
(Reihenfolge: Anmeldetag, Land, Aktenzeichen;
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Ausstellungspriorität
(Reihenfolge: 1. Schaustellungstag, amtl.
Bestimmung und Ort der Ausstellung mit
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5. November 1971, Österreich, A 9545/71

05.11.71 DE A 9545-71

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- ☒ Ein Satz Aktenzeichnungen mit Blatt
- ☒ zwei gleiche Modelle
- ☒ Vertretervollmacht
- ☒ Anmeldung
- ☒ ankreuzen!

1. ☒
2. ☒
3. ☒
4. ☒
5. ☒

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Raum für Gebührenmarken —

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(Patentamt)

4

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 Abnahmeapparates 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 verteilhaft aus flexiblem transparentem Kunststoffmaterial, bestehen.

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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

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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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geschlossen, 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 Plasmaphereseprozedur 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.

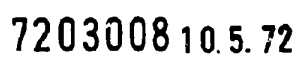
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~~Patent~~ Ansprüche :

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.

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2



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.

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

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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. Szama [1]

estimated that 10% of blood transfusion-associated deaths are caused by bacterial contamination of the transfused product.

In the last decade, increased attention has been given to the prevention of possible systematic contamination during the collection (i.e. by disinfection) and preparation stages (i.e. closed systems, by the use of sterile-docking devices, etc.) of blood components. Reliable data on the frequency of bacterial contamination of donated whole blood, used for component preparation, is needed in order to validate the occurrence of systemic contamination, or to evaluate measures taken to decrease contamination. Recently, we showed that 0.34% of whole blood units were contaminated with bacteria [2]. That

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study compromised a number of units tested, resulting in a narrow 95% confidence interval (CI) of 0.27–0.44%.

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

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

Materials and methods

Blood collection

Whole blood (500 ± 50 ml) was collected under standardized blood bank conditions in four-bag Compoflex CPD/SAGM systems (Fresenius Hemocare, NPBI International, Emmer-Compascuum, the Netherlands), with an additional fifth bag. These blood-collection systems were designed and validated

[2] for use in this particular study (see Fig. 1). They allow both diversion of the whole blood (by Composampler) and sampling in a closed system, with the only aseptic handling being the transfer (in a laminar airflow cabinet) of a sample from the final donation to anaerobic and aerobic culture bottles (BacT/Alert; Organon Teknika, Boxtel, the Netherlands).

At all different collection sites of the De Meierij and CLB Sanquin Blood Banks, standardized methods for disinfection (double-swab method with isopropyl alcohol swabs), blood collection and storage were used. After venepuncture, an EDTA-vacutainer tube (nominal volume 10 ml; Becton-Dickinson, Franklin Lakes, NJ) was filled via the Composampler device (the mean collected volume was 9.8 ml with ≈ 1 ml of anti-coagulant 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

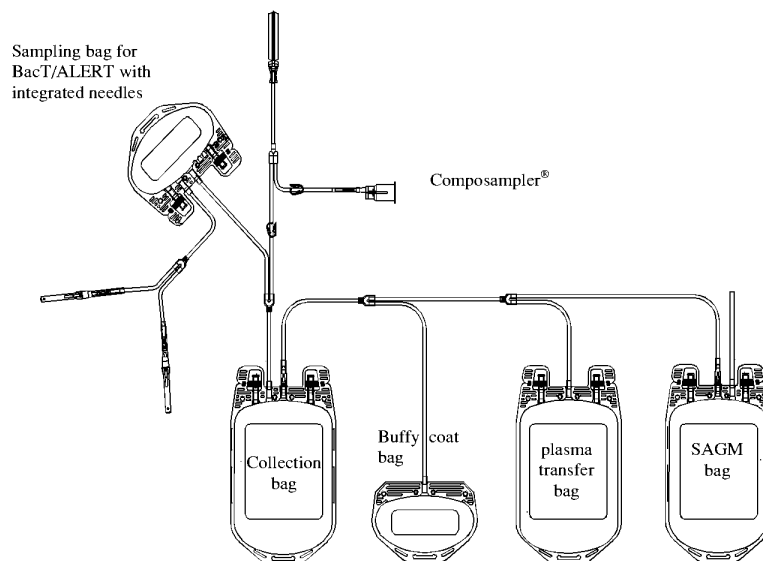


Fig. 1 Special five-bag Compoflex® blood-collection system, consisting of a conventional four-bag system with an additional BacT/ALERT sampling bag (the fifth bag) containing integrated transfer needles and equipped with a Composampler® to allow vacutainer sampling.

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 CO₂ [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	<i>n</i> = 7087	<i>n</i> = 18 257
Positive cultures	<i>n</i> = 15	<i>n</i> = 63
Contamination rate ^a	0.21%	0.35%
95% CI of rate ^b	0.12–0.35%	0.27–0.44%

^aSignificant difference, *P* < 0.05 (χ^2 -test; one-sided).

^bDifference 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		
<i>Staphylococcus</i> ^{a,b}	2 (0.03)	25 (0.14)
<i>Propionibacterium</i> ^c	10 (0.14)	27 (0.15)
<i>Micrococcus</i>	0	1 (0.01)
Diptheroids,	0	5 (0.03)
<i>Corynebacterium</i> spp		
Transient skin flora		
<i>Bacillus</i>	0	3 (0.02)
<i>Gemella morbillorum</i>	1 (0.01)	0
<i>Klebsiella pneumoniae</i>	1 (0.01)	0
(Upper) Gastrointestinal flora		
<i>Streptococcus bovis</i>	1 (0.01)	0
<i>Peptostreptococcus</i>	0	1 (0.01)
Not identified ^d	0	1 (0.01)

Values are expressed as absolute numbers per series (% prevalence).

^aCoagulase-negative isolates, i.e. no occurrence of *Staphylococcus aureus*. Isolates were mainly *Staphylococcus epidermidis*.

^bSignificant difference, *P* = 0.015.

^cMainly *Propionibacterium acnes*.

^dGrowth 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 diptheroids and *Bacillus* spp were lower after diversion of the first 10 ml of the blood donation, but not significantly so.

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 $\approx$ 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 ($\approx$ 1%), despite the reduced contamination rate of whole blood. Therefore, in addition to diversion of the first volume during blood collection, all platelet concentrates should be tested for bacterial contamination in order to increase the safety of the blood supply.

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

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Bacterial Contamination of Blood Components

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INTRODUCTION

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

to achieve this level of safety, despite relatively poor cost-effectiveness, in order to assuage the public’s fears (32).

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

TRANSFUSION-TRANSMITTED BACTERIAL INFECTION OF RED CELLS

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

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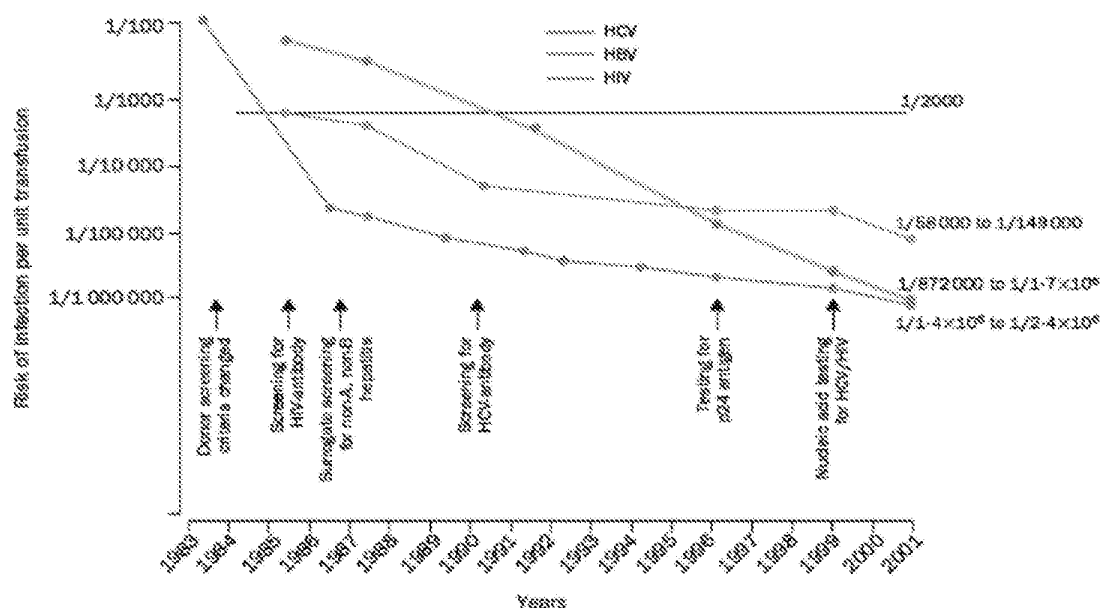


FIG. 1. Risk of infectious disease transmission per unit transfused by year, 1983 to 2001. Reprinted from reference 27 with permission of the publisher.

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

Interestingly, more recent passive reporting studies of bac-

terially 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)
<i>Streptococcus</i> spp.			4 ^d	4
<i>Staphylococcus aureus</i>			2 ^b	2
<i>Enterococcus faecalis</i>			1 ^c	1
<i>Bacillus cereus</i>			2	2
<i>Propionibacterium acnes</i>			1	1
Subtotal	2 (1 or 50%)	2 (0 or 0%)	13 (0 or 0%)	17 (1 or 6%)
Gram negative				
<i>Serratia liquifaciens</i>	2 (2)	1	2 (1)	5 (3)
<i>Serratia marcescens</i>	1			1
<i>Yersinia enterocolitica</i>		1 (1)	1	2 (1)
<i>Enterobacter</i> spp.			1 (1)	1 (1)
<i>Acinetobacter</i> spp.			5 (1) ^b	5 (1)
<i>Pseudomonas</i> spp.			2 (1)	2 (1)
<i>Escherichia coli</i>			3 ^c	3
<i>Klebsiella pneumoniae</i>			1	1
<i>Proteus mirabilis</i>			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				
<i>Bacillus cereus</i>	1	4 (1)	2	7 (1)
Coagulase-negative staphylococci	9	6 (1)	5	20 (1)
<i>Streptococcus</i> spp.	3 (1)	2		5 (1)
<i>Staphylococcus aureus</i>	4	2 (1)		6 (1)
<i>Propionibacterium acnes</i>			3	3
Subtotal	17 (1 or 6%)	14 (3 or 21%)	10 (0 or 0%)	41 (4 or 10%)
Gram negative				
<i>Klebsiella</i> spp.			2 (1)	2 (1)
<i>Serratia</i> spp.	2 (2)		1 (1)	3 (3)
<i>Escherichia coli</i>	5 (1)	2 (1)	1	8 (2)
<i>Acinetobacter</i> spp.			1	1
<i>Enterobacter</i> spp.	2 (1)	1 (1)	1	4 (2)
<i>Providencia rettgeri</i>	1 (1)			1 (1)
<i>Yersinia enterocolitica</i>	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).

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-

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 be 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 Hospi-

tal 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 CO₂ 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

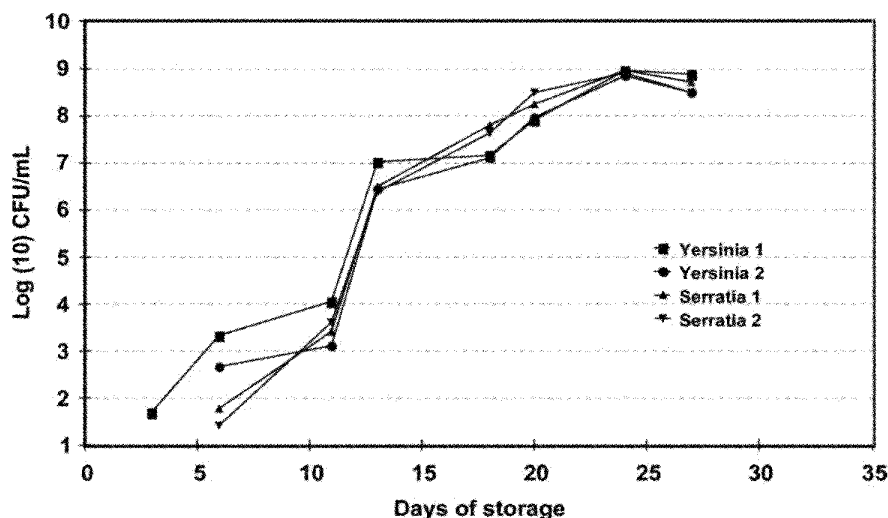


FIG. 2. Growth curves of four units of AS-3 red blood cells inoculated with *S. liquefaciens* (two units inoculated to 4.2 CFU/ml) and *Y. enterocolitica* (two units inoculated to 11.6 CFU/ml) (5a). Bacteria were not detectable by culture until days 3 to 6. Isolates were from strains actually implicated 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

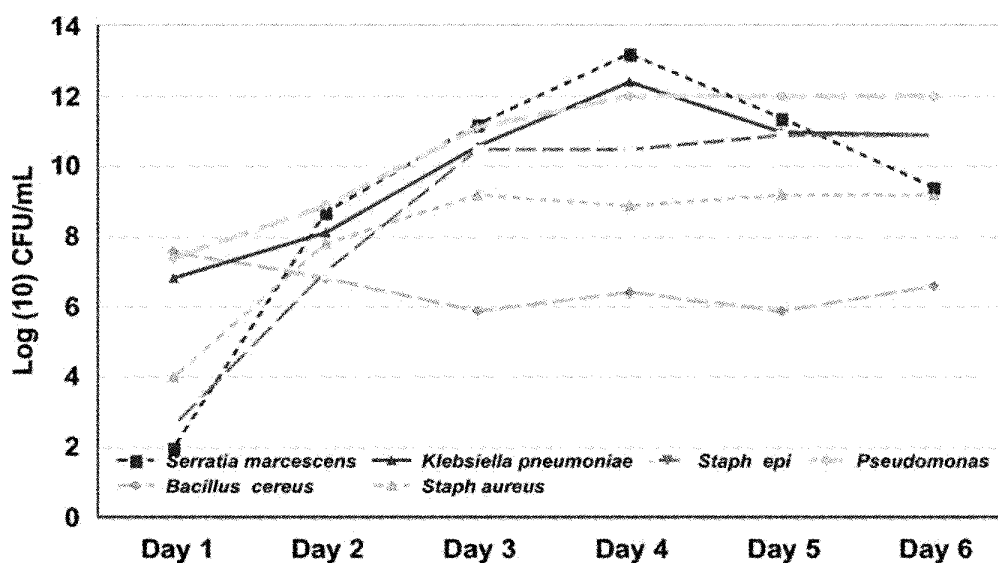


FIG. 3. Growth curves of six bacteria species (*S. marcescens*, $n = 7$; *K. pneumoniae*, $n = 21$; *S. epidermidis*, $n = 21$; *Pseudomonas* sp., $n = 15$; *B. cereus*, $n = 9$; *S. aureus*, $n = 22$) in 95 platelet units. All bacteria were inoculated on day zero at 10–50 CFU/ml (10).

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

Center	No. (rate) of results ^b		No. tested
	True positive	False positive	
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 10⁶ to 10⁷ 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 10⁴ to 10⁵ CFU/ml. In some cases, *S. aureus* was detected at levels as low as 10² to 10³ 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 10³ CFU/ml [P. Morel, M. Deschaseaux, X. Bertrand, C. Naegele, 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 10³ to 10⁵ 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 10³ to 10⁴ 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 pursuing 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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Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	9839	FILED BY	Trent Tercenio
PATENT CENTER #	65207430	FILING DATE	10/25/2023
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 97

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Fibronectin (cold insoluble globulin) in the neonate

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FIBRONECTIN (referred to in older literature as cold insoluble globulin), a ubiquitous glycoprotein, participates in cellular, vascular, and plasma coagulant functions.¹ Acting as a nonspecific opsonin, plasma fibronectin potentiates reticuloendothelial clearance of intravascular debris to protect against organ dysfunction secondary to microvascular occlusion and altered vascular permeability.¹ Found on cell surfaces, fibronectin is important in wound healing and embryogenesis.² Fibronectin is a substrate for thrombin, plasmin, and activated fibrin-stabilizing factor (factor XIII), and can be lysed by granulocyte and other proteases.³

Fibronectin has potentially important roles in hemostasis and control of infection in the neonate. Decreased plasma values of fibronectin, measured by Laurell immunoelectrophoresis, have been reported in apparently healthy full-term infants.⁴ We present the fibronectin values measured by immunoelectrophoresis in reference full-term and preterm infants and in neonates with sepsis of early onset.

MATERIALS AND METHODS

For adult reference values, blood samples were collected from healthy laboratory personnel who were not receiving any medication (including birth control pills or aspirin), had no chronic or recent acute illness, and had not exercised vigorously just prior to blood sampling.

Cord blood samples were collected from 18 healthy full-term infants (gestational age mean 40 weeks, range 37

to 41 weeks) and 15 healthy preterm infants (gestational age mean 35 weeks, range 32 to 36 weeks). Infants met the following criteria: (1) definite maternal dates that agreed within two weeks with the Dubowitz score; (2) Apgar scores at 1 minute of ≥ 7 and at 5 minutes of ≥ 8 in preterm infants (32 to 36 weeks gestational age), and Apgar scores of ≥ 8 at 1 minute and ≥ 9 at 5 minutes in full-term infants; (3) appropriate weight for gestational age; (4) no hypoxia, acidosis, hypotension, or hypothermia by gestational and postnatal age-appropriate definitions; (5) healthy during the first 48 hours of life; (6) inborn; (7) no family history of bleeding disorders; (8) the mothers had not received medications during pregnancy except vitamins, iron, inhibitors of uterine activity, steroids for maturation of fetal lung, and local, general, or epidural anesthesia; (9) the mothers had uncomplicated pregnancies; (10) the mothers of full-term infants delivered by cesarean section did not have labor.

Other preterm infants studied (gestational age mean 35 weeks) did not fit the above criteria because of intrauterine growth retardation (seven infants) or diabetic mothers (two infants). These infants had otherwise uncomplicated, uneventful perinatal courses. The eight ill neonates studied (mean gestational age 33 weeks) had birth asphyxia or hypotension.

Because adults with sepsis have decreased plasma values for fibronectin,⁵ we studied infants with early-onset sepsis. In all infants blood cultures were positive for either β -hemolytic streptococcus (two infants) or *Listeria monocytogenes* (four infants) (mean gestational age 37 weeks, range 30 to 40 weeks).

This study was approved by the Hospital and University Ethical Review Committees. Informed parental consent was obtained prior to collection of blood specimens.

All blood samples tested were collected by the two-syringe technique, in which the first 0.5 ml blood drawn

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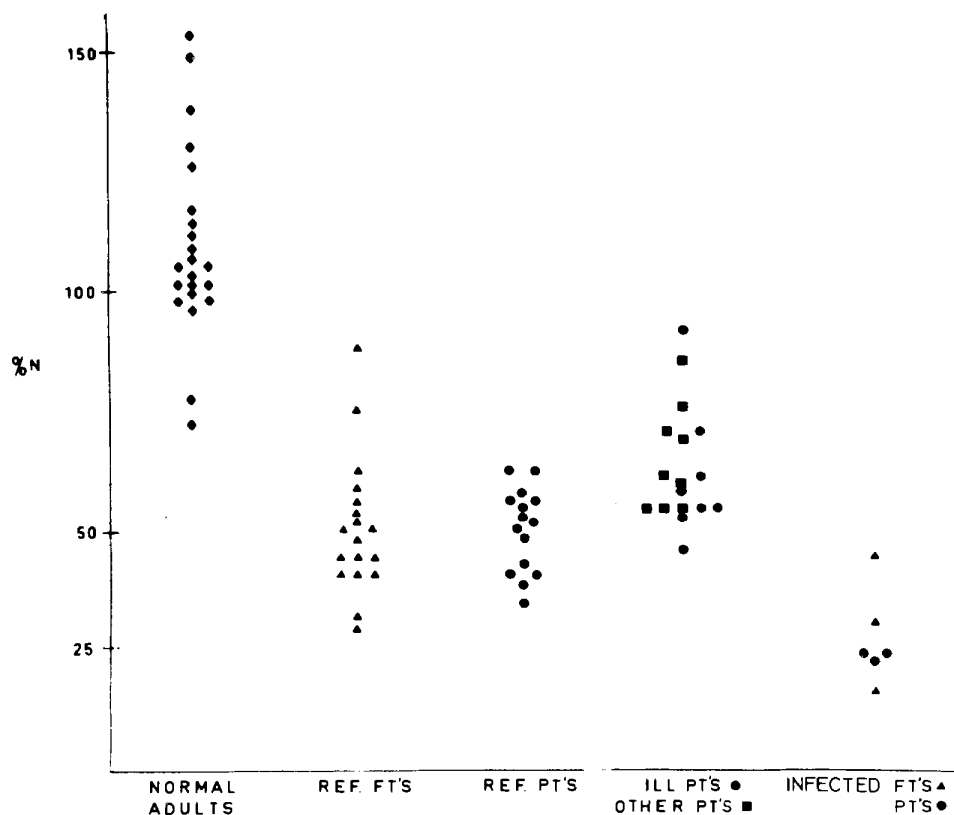


Figure. Fibrinogen values in adults, in infected infants, and in healthy infants. FT, Full-term; PT, preterm.

into a dry syringe was discarded or used for other tests (to prevent contamination of the test sample by tissue thromboplastin). The test sample was then drawn into a syringe containing the anticoagulant to give a ratio of 1 volume anticoagulant to 9 volumes blood. To rule out in vitro artifact from platelet release or thrombin or protease action, the anticoagulant used was buffered citrate (anticoagulant A) or buffered citrate with inhibitors (anticoagulant B). Inhibitors added to the buffered citrate were: theophylline, an inhibitor of platelet release reaction, 1.8 mg/ml (Sigma Chemical, St. Louis); hirudin, an inhibitor of thrombin, 2 antithrombin units/ml (Sigma); and aprotinin, an inhibitor of plasmin and protease, 100 Kunitz IU/ml (Boehringer-Mannheim, Canada).

Cord blood samples were drawn from the umbilical vein of double-clamped cords obtained before placental separation. Samples were collected randomly, first into anticoagulant A or B. Immediately after collection, plasma was separated by refrigerated centrifugation at 5000 *g* for 20 minutes, respun to remove all platelets, and kept frozen at -80°C until assayed. Pooled plasma from normal adults (obtained from George King Ltd., Kansas) was used as

control plasma. Our samples were collected by venipuncture, but conceivably samples could be obtained by heel-stick using anticoagulated Miale pipettes.

Fibrinogen was measured by Laurell immunoelectrophoresis.⁵ Plasma samples were diluted with barbital-EDTA buffer (0.03 M barbiturate, 1.0 gm sodium ethylenediaminetetraacetate, 0.1 gm sodium azide in 1000 ml distilled water). The same buffer was used to make 1% agarose (Seakem Marine Colloids, Lockland, Me.). Rabbit antiserum to human fibrinogen (lot 153955) was obtained from Cappel Laboratories (Cochranville, Pa.). Glass slides (7.5 cm $\times$ 5 cm) were prepared with 4 ml agarose per slide (antiserum concentration approximately 1.675%). Eleven holes (2 mm diameter) were punched per slide. Three lambda samples were applied to each well. The standard curve was made with 100%, 50%, and 25% normal pooled plasma. A normal control plasma was run in duplicate at 50% on each slide. The chamber buffer was a 0.75 M barbital (pH 8.6, 2.07 gm diethylbarbituric acid, 13.14 gm sodium barbitone, 1.0 gm EDTA, 0.1 gm sodium azide in 1000 ml distilled water). Slides were electrophoresed at 15 mamp (constant current) for two hours.

Normally, slides were washed for 24 hours in 0.5 M sodium chloride and subsequently rinsed in tap water. However, slides can be washed and stained immediately. Interassay coefficient of variation was $\pm 8\%$.

The paired and unpaired *t* tests were used for statistical analysis.

RESULTS

Plasma values for fibronectin in 18 reference full-term infants were decreased, compared with values in 22 reference adults (Figure). Measurements of plasma fibronectin in 15 reference preterm infants 32 to 36 weeks gestational age were not statistically different from those in 18 reference full-term infants. Cord blood fibronectin concentrations from nine other preterm infants were not different from values found in the 15 reference preterm infants. The eight ill neonates had cord plasma fibronectin measurements comparable to those of the reference preterm infants. In contrast, six infants, at the time of diagnosis of early-onset sepsis, had decreased plasma values of fibronectin when compared with healthy neonates.

There was no statistical difference by paired *t* test in plasma fibronectin measurements in paired samples randomly collected first into buffered citrate (anticoagulant A) or into buffered citrate plus inhibitors (anticoagulant B) ($53 \pm 2\%$ versus $55 \pm 2\%$, mean $\pm$ SD).

DISCUSSION

Several thorough reviews have been published recently stressing potential physiologic roles for fibronectin.^{1,2,7,8}

Our results confirm the previously reported decreased plasma fibronectin values measured by immunoelectrophoresis in plasma of cord blood from 22 healthy neonates (adult $101 \pm 27\%$, neonates $39 \pm 6\%$).⁴ Fibronectin measurements by immunoelectrophoresis were decreased in plasma obtained from cord blood samples of newborn infants when compared with measurements of plasma fibronectin in normal adults; values for normal full-term and healthy preterm infants were not statistically different. Three healthy, extremely premature infants (gestational age 29 weeks) had cord plasma fibronectin values of 27%, 35%, and 45%, respectively (D. Barnard, unpublished data). Because samples collected randomly first into buffered citrate or buffered citrate plus additional inhibitors were not statistically different, the decreased plasma fibronectin measurements in neonates are not related to *in vitro* proteolysis.

The six full-term and preterm neonates with early-onset sepsis (mean age 14 hours, range 4 to 20 hours at testing) had depressed fibronectin concentrations in plasma from venous blood collected into anticoagulant B. The two infants who died had the lowest plasma fibronectin values

measured. Decreased survival⁹ has been reported in adults with sepsis and persistently low plasma fibronectin values. In an uncontrolled study, adult patients with sepsis and pulmonary dysfunction (ventilation-perfusion imbalance and presumed increase of lung water) improved after infusion of cryoprecipitate containing approximately 1 gm fibronectin.¹⁰ Decreased levels of fibronectin in neonates may increase their susceptibility to and morbidity from septicemia.

Intrauterine growth retardation, maternal diabetes, and birth asphyxia or hypotension apparently do not affect plasma cord values of fibronectin.

Low plasma fibronectin measurements in adults with trauma, disseminated intravascular coagulation, or sepsis are thought to result from utilization of fibronectin in reticuloendothelial system clearance function, consumption by incorporation into intravascular thrombin, proteolytic destruction by granulocyte or tissue protease, binding to areas of tissue damage or denatured collagen, or decreased synthesis.¹ The cause of the decreased plasma values of fibronectin in neonates is speculative.

We acknowledge the excellent cooperation of the nurses and physicians of the Grace Maternity Hospital in obtaining cord blood specimens, and Drs. R. A. Bortolussi, A. Allen, D. Stinson, and E. Rees for blood specimens from septic infants.

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

DISC REMOVAL

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

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

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

With the above technique, the great majority of cases can be operated on within thirty minutes. The short time of operation is important because the patient is under local anaesthesia, and also this short period may be significant in preventing infection of the disc, of which several

cases have been reported in the recent literature. An intravenous drip or blood transfusion is never necessary.

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

SUMMARY

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

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

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THE INVESTIGATION of the clotting time of whole blood has for a long time been a routine procedure in medical practice. Though clotting-time values in health and in various pathological conditions are recorded in many textbooks and publications, these observations are difficult to interpret because different and not properly standardized techniques are used. Even the well known and widely used Lee-White method¹ has been shown to give varying results due to subjective differences in the performance of the test.²

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

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

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

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

MATERIALS

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

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

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

METHOD

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

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

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

(b) If we do not wish to discard the blood drawn into the syringe (which may be important in small animal experiments, where a 5 to 8 ml. blood-loss is considerable), we can use the three-way stop-cock between the needle and the syringe. We draw the blood

into the syringe, and then switch the stop-cock between the needle and the third side opening, and through this we collect the first blood drops in the capillary tube. By switching back we connect the needle with the syringe and reinject the blood into the vein.

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

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

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

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

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

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

DISCUSSION

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

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

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

We had some objections to this proposal and adopted 21° C. temperature. Firstly, 37° C. is not physiological, as the temperature of blood in the body is higher than this. Secondly, for maintaining a 37° C. temperature, one would need an electric water-bath carried to the bedside, while a lower temperature such as 21° C. can be easily maintained in an inexpensive large thermos-flask. Thirdly, at 37° C. the clotting time is too short to detect minor differences. Fowler⁸ has noted that 10 minutes after intravenous injection of 25 mgm. heparin the clotting time at room temperature was prolonged, but it was within normal limits when the test was carried out at 37° C. We have noted also that the higher temperature decreases the sensitivity of the test.

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

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

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

ACCURACY OF THE METHOD

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

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

NORMAL VALUES

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

SUMMARY

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

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

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

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COMPLICATIONS FOLLOWING CEREBRAL ARTERIOGRAPHY

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

PATENT SPECIFICATION (11)

1 378 602

1 378 602

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 (31) Convention Application No. 266 996 (32) Filed 28 June 1972 in
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 A5R 33D
 F2V D4X E1L2 E3B2 J2D M1F
 (72) Inventor WALDEMAR ALEXANDER AYRES



(54) IMPROVEMENTS IN NEEDLE ASSEMBLIES FOR USE WITH APPARATUS FOR COLLECTING SAMPLES OF BLOOD

(71) We, BECTON, DICKINSON & COMPANY, a Corporation organised and existing under a laws of the State of New Jersey, United States of America, and having a principle place of business at East Rutherford, New Jersey, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

In the blood sampling field, there are several well known systems. One of the commonly used systems collects blood from a vein through a needle assembly into an evacuated container. The evacuated container provides the pressure differential necessary to transfer the blood from the vein through the needle assembly into the container. The basic system and apparatus for collecting blood in this manner is disclosed in U.S. Patent Specification No. 2,689,564 to Kleiner.

Improvements have been made in recent years to the basic evacuated container system for blood sampling such as by the provision of a valve on the assembly to automatically open and close the flow path through the assembly as the evacuated containers are coupled in succession with the assembly. In this manner, a multiplicity of samples can be collected in a multiplicity of containers with only one venapuncture being required. Needle assemblies with automatic valves are shown and described in British Patent Specification No. 1,132,197 to Nehring and U.S. Patent No. 3,494,352 to Russo et al.

Frequently the evacuated containers contain chemical materials, useful in the clinical laboratory tests to be conducted after mixing with the patient's blood. However, these chemical materials may be harmful to a patient if any were to flow from the evacuated container into the patient's blood system. This problem has been successfully eliminated by the use of a one-way valve as

shown and described in our co-pending Application No. 20921/73 (Serial No. 1,378,603) filed on 2 May 1973.

In systems such as those referred to above, it has often been found that it is desirable to provide an indication means on the needle assembly to inform an operator that a venapuncture has been successfully accomplished. Consequently, it is desirable to provide a single device which includes a one-way valve for use in collecting multiple samples of blood from a single venapuncture into a multiplicity of collection containers whilst eliminating the danger of back flow of fluid into the patient and which includes a blood flow indication means which indicates that a venapuncture has successfully been accomplished so that the evacuated collection container can be coupled to the needle assembly to withdraw a blood sample from the patient.

According to our invention a needle assembly for use with apparatus for collecting blood samples from a patient has means for indicating when a venapuncture has been accomplished and then for transferring blood from the patient into an evacuated container, whilst preventing any back flow from the container into the patient, and means for automatically blocking the blood flow due to venous pressure while changing from one container to a successive container to be filled from the same venapuncture, the means for indicating when a venapuncture has been accomplished and for preventing backflow comprising an at least partly transparent housing having a chamber therein, a forward penetrating end including a cannula extending from the housing for penetration into the blood vessel of a patient, a rearward end extending from the housing and adapted to be coupled in fluid communication with the interior of the evacuated container, a passage-way for directing blood from the blood vessel through the housing to the container when the forward end is in the blood vessel and the rearward end is in com-

[P]

5 munication with the evacuated container, a
 valve assembly mounted in the chamber and
 normally in an unarmed position in which
 passages therein permit blood to flow from
 10 the vein into the chamber upon venapunc-
 ture and being movable to an armed posi-
 tion in which the valve assembly forms a
 non-return valve and in which the passage-
 way from the vein to the chamber is closed
 15 by means of a resilient elastomeric valve
 member in the chamber, the valve member
 being responsive to a reduction in pressure at
 the rearward end of the assembly upon coup-
 20 ling with the evacuated container to deform
 the valve member and automatically open the
 passageway to permit blood to flow from the
 blood vessel to the rearward end and into
 25 the container, the valve member thereafter
 being responsive to an increase in pressure
 at the rearward end to automatically return
 to the closed position and thereby prevent
 the backflow of fluid from the rear end of
 the assembly to the blood vessel when a pre-
 determined pressure differential exists be-
 tween the forward and rearward end of the
 assembly.

30 Preferably the needle assembly also in-
 cludes a second cannula which is slidably
 mounted in a bore in the rearward end of
 the housing, the second cannula having its
 forward end in the chamber and its rear
 end extending from the rear end of the
 housing for connection to the container.

35 The needle assembly may have the rear
 end of the first cannula extending into the
 chamber and have an elastomeric sleeve,
 having an open end and a closed end, slidably
 40 mounted on the rear end of the first
 cannula in sealing engagement therewith, the
 sleeve being movable between the unarmed
 position and the armed position on the first
 cannula, a transverse hole in the wall of the
 sleeve which permits communication between
 45 the rear end of the first cannula and the ex-
 terior of the sleeve when the sleeve is in the
 unarmed position and the hole being ob-
 scured when the sleeve is moved to the
 armed position, a slit in the wall of the
 sleeve, the slit normally being closed when
 50 the sleeve is in the armed and unarmed
 position but which opens automatically when
 there is a reduction in pressure at the rear-
 ward end as the container is coupled with
 the assembly and the slit thereafter auto-
 55 matically closing when there is an increase
 in pressure at the rearward end and when a
 predetermined pressure differential exists be-
 tween the forward and rearward end of the
 assembly, and an annular flange extending
 60 around the forward open end of the sleeve.

The invention also includes a method of
 transferring blood from a patient into an
 evacuated container whilst indicating that
 a venapuncture has been accomplished and

65 preventing the back flow of fluid from the
 container into the patient during and after
 the collection of a blood sample with the
 use of a needle assembly having a forward
 end for penetration into the blood vessel
 70 of a patient, a rearward end adapted to be
 coupled in fluid communication with the
 evacuated container, a continuous passage-
 way through the assembly, and a valve
 assembly including means for visu-
 75 ally indicating a venapuncture and in-
 cluding a resilient elastomeric valve mem-
 ber on the assembly adapted to deform
 and open when subjected to pressure in one
 direction and adapted to close when the pres-
 80 sure in the one direction is relieved, the
 method comprising, inserting the forward
 penetrating end of the assembly into the
 blood vessel of a patient until the visual indi-
 85 cating means denotes a successful venapunc-
 ture, coupling the evacuated container to the
 rearward end of the needle assembly and
 initially shifting the resilient elastomeric
 valve member to an armed position in which
 the valve member prevents flow between the
 90 ends of the assembly and subsequently coup-
 ling the evacuated interior of the container
 to the passageway through the needle assem-
 bly so that the elastomeric valve is sub-
 95 jected to a pressure differential in one direc-
 tion and automatically responds to the pres-
 sure differential to deform and open and
 permit blood to flow from the patient to
 the container, and removing the container
 from coupling engagement with the needle
 assembly after the pressure differential has
 100 been relieved so that the valve has auto-
 matically returned to the normally closed
 position thereby preventing flow between
 the ends of the needle assembly.

An example of a needle assembly in ac-
 cordance with our invention will now be de-
 scribed with reference to the accompanying
 drawings in which:—

Figure 1 is a side elevation of a needle as-
 105 sembly attached to a holder and with an
 evacuated container in a position ready for
 coupling with the needle assembly;

Figure 2 is an enlarged fragmentary sec-
 110 tion of the apparatus shown in Figure 1 after
 it has been used to achieve a venapuncture
 prior to the initial closure of a valve mem-
 ber;

Figure 3 is an enlarged section of the
 needle assembly shown in Figure 2;

Figure 4 is a similar view to Figure 2 but
 120 showing the valve member in an armed po-
 sition;

Figure 5 is an enlarged section of the
 needle assembly shown in Figure 4;

Figure 6 is a similar view to Figure 2 and
 125 Figure 4 but showing the evacuated con-
 tainer coupled to the needle assembly and
 the valve member in the opened position to

permit blood to flow from a vein to the container;

Figure 7 is an enlarged section of the needle assembly shown in Figure 6;

5 Figure 8 is a similar view to Figure 6 but showing the assembly after the container has been removed and showing a second valve member in a closed position preventing the flow of blood between the ends of the needle assembly;

10 Figure 9 is an enlarged section of the needle assembly shown in Figure 8; and

Figure 10 is an exploded fragmentary perspective view of the needle assembly.

15 The separate components of a needle assembly 20 are shown in Figure 10. The assembly includes a housing 21 which is in two parts, a forward part 22 and a rear part 23. Mounted in the forward part 22 is a cannula 24 and mounted in the rear part 23 is a second cannula 25. When the forward part 22 is engaged with the rear part 23 a chamber 26 is formed as shown in Figures 1 to 9. Housed within chamber 26 is an elastomeric sleeve 27, a rigid cage 28, a retaining disc 29, and an elastomeric sealing disc 30.

25 The forward part 22 has a frusto-conical surface 31 which fits into and engages with an inner cylindrical surface 32 of a tubular portion of the rear part 23. The engagement between parts 22 and 23 is tight enough to keep the parts of housing 21 together during operation of the assembly. If required, to ensure this engagement of the parts of housing 21, an epoxy resin adhesive may be employed between surfaces 31 and 32 to achieve a positive locking engagement.

30 A bore 33 in the forward part 22 provides communication between the space in front of the forward part 22 and the chamber 26. The cannula 24 is mounted in the bore 33 with a rear blunt end 34 extending into the chamber 26 and a forward end terminating in a tip 35 extending forward from the part 22 and fixed in the bore by an epoxy resin adhesive 51. The tip 35 is pointed to enable it to penetrate a patient's vein.

35 The rear part 23 of the housing 21 has a sleeve 36 for engagement with the forward part 22 and to provide the sidewalls of the chamber 26. The remainder of the part 23 is a reduced diameter cylinder having a screw thread 37 formed on its outer surface to connect the needle assembly 20 to a holder 38. The holder 38 forms a guide for an evacuated container 39. The container 39 is formed by a tube 40 which is evacuated and is closed at its open end by a self-sealing puncturable stopper 41.

40 The rear part 23 has an axial bore 42 providing communication between the rear end of the part 23 and chamber 26. The cannula 25 is slidably mounted in the bore 42.

65 The rear end of the cannula 25 extends

rearwardly from the housing 21 and has a pointed tip 43 for penetration through the stopper 41 of the evacuated container 39.

70 The cannula 25 is slidably mounted in the bore 42 and has a forward blunt end 44 extending into the chamber 26. Adjacent the forward end of the cannula 25 is a side opening 45 which is movable into and out of the chamber 26 as the cannula 25 slides through the bore 42. The elastomeric sealing disc 30 rests against a rear wall of the chamber 26 and has a central hole, the diameter of which is smaller than the external diameter of the cannula 25, so that the elastomeric sealing disc 30 maintains a seal with the external surface of the cannula 25 as it slides through the disc 30. Thus the chamber is liquid-tight so that liquid flow into and out of the chamber 26 only occurs through the cannulae 24 and 25. The sealing disc 30 is held in place by the rigid disc 29 which is a 'push fit' in the rear of the housing 21. The sealing disc 30 is sandwiched between the disc 29 and the rear wall of the housing 21. An annular bead 46 projecting from the rear wall of the housing engages with the under surface of the disc 30 to ensure a seal between the disc 30 and the rear wall of the chamber and prevent leakage from the chamber 26 through the bore 42 in the rear part 23.

75 The cage 28 is stuck on the end 44 of the cannula 25 with an epoxy resin adhesive 47. The cage 28 is constructed from a plastics material and it seals the open end of the end 44 of cannula 25. This means that the access from the chamber 26 into the bore of cannula 25 is solely by the side opening 45. The cage 28 is a hollow cylinder and has a closed end mounted on cannula 25 and an opposite open end. Adjacent to the closed end are four transverse side ports 48. The side ports are equi-spaced about the circumference of the cage 28. The external diameter of the cage 28 is less than the internal diameter of the housing 21 so the cage 28 is free to slide axially with the cannula 25. The hollow cage 28 receives the major portion of the sleeve 27 and there is a clearance between the cage 28 and the elastomeric sleeve 27 to enable the cage 28 to slide with respect to sleeve 27. A cylindrical rim at the open end of the cage 28 engages with a flange 50 formed at the open end of sleeve 27. The open end portion of sleeve 27 is slidably mounted on the rear, blunt end 34 of cannula 24. To achieve this the sleeve 27 has its open end expanded so that it surrounds and frictionally engages with the end 34 of the cannula 24 and seals with it. The sleeve 27 is movable to an armed position as shown in Figures 4 to 9 in contrast to its initial unarmed position as shown in Figures 2 and 3. The operational sequence of the needle assembly will be discussed in detail 130

below. The sleeve 27 is formed as a hollow cylinder having a closed end and an open end. As described above a flange 50 is formed about its open end and the bore 52 of the cylindrical sleeve receives the rear end 34 of the cannula 24.

Initially, in the unarmed position only the forward open end of the sleeve 27 is mounted on the cannula 24 and, rearwardly of blunt end 53 of the cannula 24, the sleeve 27 has one or more transverse holes 54 which pass from the interior to the exterior of the sleeve 27. Additionally, adjacent the rear, closed, end of the sleeve 27 is a slit 55 which is normally in the closed position due to the self-sealing elastomeric properties of the sleeve 27. Any well known elastomeric self-sealing material such as natural or synthetic rubber can be utilized for the sleeve 27.

The housing 21 and the cage 28 are made from a transparent plastics material so that the presence of blood within the chamber 26 is readily visible through them for indication purposes. The housing may not be wholly transparent, but may merely include a transparent portion and the presence of blood within the chamber 26 be observed through the transparent portion. Additionally, sleeve 27 may be constructed of a transparent elastomeric material, however, this is not generally utilized, since the blood will flow into the surrounding spaces provided and will be visible through the transparent portions of the housing during the indication procedures and this will be discussed in detail below. All of the components of the assembly with the exception of the cannula and the sleeve may be constructed of a standard low cost, transparent, plastics material or any readily available substitute.

The cannula 25 is slidable into and out of the housing 21 a predetermined distance, its travel being limited in the downward direction by the cage 28 engaging the disc 29 and in the opposite direction by the rim 49 engaging the flange 50 and pressing this against the face 57 of the part 22. The cannula 25 is moved as the evacuated tube 39 is reciprocated within holder 38 during the blood collection procedure since the cannula 25 when inserted through the stopper 41 is gripped tightly by the stopper 41 and thus caused to move by movement of the evacuated tube 39 and stopper 41.

Although slidable, the cannula 25 is continuously hermetically sealed relative to the bore 42 by the elastomeric sealing disc 30 which has been penetrated by the cannula 25.

Figure 1 shows the needle assembly ready for use having been screwed into the holder 38, the holder having the evacuated container 39 in a position ready for engagement with the assembly. The needle assembly 20 is in the initial position as shown in Figures

1 to 3, with the transverse holes 54 behind the end 34 of the cannula 24. In this manner, an open air way exists from the tip 35 of the cannula 24 through the assembly to the side opening 45 in the sliding cannula 25.

When sleeve 27 is pushed forward to encompass all of the rear portion 34 of cannula 24 so that the forward edge of flange 50 of the sleeve rests against inner wall of the housing, the cannula will be positioned so as to occlude transverse openings 54 and cannula 24 will be sealed by the sleeve 27.

Sliding cannula 25 supports valve cage 28. The tip of forward end 44 of cannula 25 is inserted into a recess in the rear end of the valve cage 28 and is sealed therein by epoxy 47 or any other common sealing means. The inner diameter of cylindrical cage 28 is substantially greater than the outer diameter of sleeve 27 so that blood or air can readily flow out of the valve sleeve 27 around the spaces between sleeve 27 and cage 28, and out through one or more of the ports 48 of cage 28.

As shown in Figure 10, portion 22 of housing 21 has a tapered exterior surface 31 which mechanically fits and supports and seals portion 32 of the cylindrical rear portion 23 of housing 21. Rear portion 23 supports sliding needle 25 which is mounted in a close sliding fit within passageway 42 through rear end portion 23. Rear end portion 23 also supports elastomeric sealing disc 30 and the retaining disc 29. Retaining disc 29 is a plastic moulded part. It may be constructed of any other common material for the purpose required. It has an outside diameter which has a push fit in a narrowed region of the inside of rear housing portion 23. In assembly of this seal, rear portion 23 is positioned vertically. Then the elastomeric sealing disc 30 is dropped inside. It is positioned to lie flat across the end of passageway 42. Then the sealing disc 29 is dropped in and stops at the narrowed portion 56 of rear end 23, then a small press or similar device is used to push disc 29 down as far as it will go. The annular bead 46 projecting from the inner surface of portion 23 bites into the elastomeric disc 30 under this pressure thereby assuring a continuous seal.

Then the cage 28 is joined to the tip of needle 25 by epoxy or any other common affixing means. Thereafter, the pointed end 43 of needle 25 is passed through the central hole of retainer disc 29 and pierces the elastomeric disc 30 and is then pushed into the position shown in Figures 1 to 3. The cylindrical member forming end portion 22 including cannula 24 is inserted into rear end portion 23 until the respective walls meet and seal. This action also inserts a partial amount of end portion 34 of cannula 24 into the open end of sleeve 27. The assembly is

then positioned for use as depicted in Figure 3.

In operation, threaded outer surface 37 of rear end 23 is screwed into the threaded receiving surface of holder 38 in a conventional manner. The evacuated container 39 is then positioned in the rear part of holder 38 in position for use. This arrangement is depicted in Figure 1 of the drawings. The operator should not couple any portion of the stopper 41 with the rear end of cannula 25 before inserting cannula 24 into the vein of a patient. In this manner, effectiveness of the blood flow indication portion of the needle assembly will be assured.

Then, as shown in Figures 2 and 3, the tip 35 of the cannula 24 is inserted into a patient's vein. Blood will start to flow from the patient's vein through the airway from the tip 35 to the side opening 45 as follows. The blood will pass through the cannula 24 and out through the transverse holes 54 in the sleeve 27. It will then flow through the space between the outside of the sleeve 27 and the inside of the cage 28 until it passes out through the ports 48 in the wall of the cage 28. The blood will then begin to fill the annular space between the outside of the cage 28 and the inside of the chamber 26. If the blood is allowed to continue to flow from the vein, it will pass through the side opening 45 in the sliding cannula 25 and out through the tip 43 of the cannula 25. The pressure in the patient's blood vessels causes the blood to flow through this series of open passageways. When blood is present in the chamber 26, it will be visible to an operator, who will be watching for this indication. The operator will then push the evacuated container 39 further into the holder 38 so that the cannula 25 penetrates through the stopper 41. The action of pushing the tube 39 into holder 38 forces the cannula 25, firstly to slide forward so that the sleeve 27 is forced further onto the end 34 of the cannula 24 until the flange 50 abuts the interior surface 57 of the housing 21 which acts as a positive stop. In this position the transverse openings 54 will be occluded by the wall of the cannula 24. The only restriction to the sliding of the cannula 25 is the friction acting between the sealing disc 30 and the external surface of the cannula 25. This friction is considerably less than the friction between the cannula 25 and the stopper 41 when the cannula 25 penetrates the stopper 41. Thus the sleeve 27 will be moved forward to its position in which it operates as a valve member before the cannula 25 enters the evacuated space in the container 29. The sleeve 27 stays in its forward position and operates as a valve member thereafter. Figures 4 and 5 show the assembly after the sleeve 27 has been transferred to its forward position just prior to

the penetration of the stopper 41 by the cannula 25.

As the evacuated container 39 is pushed further into the holder 38 the cannula 25 pierces the stopper 41 and the cannula 25 enters the evacuated space within the container 39. Figures 6 and 7 show the evacuated container after the forward movement has been completed and with the cannula 25 in the interior of the tube 40. The slit 55 opens because of the large pressure differential that exists between the vacuum within the container 39 and the blood pressure within the patient's vein, thus blood flows into the tube 40 via the path shown by the arrows in Figure 7. As blood flows into the tube 40 the pressure differential across the slit 55 is reduced and eventually the slit 55 closes when a predetermined pressure differential is reached. After the tube 40 is filled with blood, and it is desired to fill one or more additional tubes, the operator pulls the container 39 out of the holder 38. In doing this, because the friction between the stopper 41 and the cannula 25 is greater than the friction between the cannula 25 and the sealing disc 30, the cannula 25 is moved rearwardly until the rear end of the cage 28 abuts the retaining disc 29 which provides a positive stop. This action is completed before the cannula 25 is pulled out of the stopper 41. In this position, the side opening 45 of the cannula 25 is behind the sealing disc 30 and is no longer in communication with the chamber 26. Therefore, no more blood can flow out of the cannula 25. However when another container is inserted this will once again force the cannula 25 and the cage 28 forward exposing the opening 45 to the chamber 26 and thus permitting blood to flow into the container when the cannula 25 has pierced the stopper on this other container. The closed position at the end of the collection of the first sample of blood and prior to the insertion of a second collection container is shown in Figures 8 and 9 of the drawings. It should be noted that the tip 35 remains in the vein thereby enabling multiple samples to be taken in a succession of collecting containers with only a single venapuncture. After the desired number of samples have been taken, the assembly is discarded.

Thus, the needle assembly 20 performs a combination of functions. It provides a one-way valve which is normally closed and alleviates the danger of the back flow during blood sampling procedures whilst at the same time providing an indication to notify the operator when a proper venapuncture has been accomplished as well as providing a multiple sampling device.

WHAT WE CLAIM IS:—

1. A needle assembly for use with appar- 130

atus for collecting blood samples from a patient, the needle assembly having means for indicating when a venapuncture has been accomplished and then for transferring blood from the patient into an evacuated container, whilst preventing back flow from the container into the patient, and means for automatically blocking the blood flow due to venous pressure while changing from one container to a successive container to be filled from the same venapuncture, the means for indicating when a venapuncture has been accomplished and for preventing backflow comprising an at least partly transparent housing having a chamber therein, a forward penetrating end including a cannula extending from the housing for penetration into the blood vessel of a patient, a rearward end extending from the housing and adapted to be coupled in fluid communication with the interior of the evacuated container, a passageway for directing blood from the blood vessel through the housing to the container when the forward end is in the blood vessel and the rearward end is in communication with the evacuated container, a valve assembly mounted in the chamber and normally in an unarmed position in which passages therein permit blood to flow from the vein into the chamber upon venapuncture and being movable to an armed position in which the valve assembly forms a non-return valve and in which the passageway from the vein to the chamber is closed by means of a resilient elastomeric valve member in the chamber, the valve member being responsive to a reduction in pressure at the rearward end of the assembly upon coupling with the evacuated container to deform the valve member and automatically open the passageway to permit blood to flow from the blood vessel to the rearward end and into the container, the valve member thereafter, being responsive to an increase in pressure at the rearward end to automatically return to the closed position and thereby prevent the back flow of fluid from the rear end of the assembly to the blood vessel when a predetermined pressure differential exists between the forward and rearward end of the assembly.

2. A needle assembly according to claim 1, in which a second cannula is slidably mounted in a bore in the rearward end of the housing, the cannula having its forward end in the chamber and its rear end extending from the rear end of the housing for connection to the container.

3. A needle assembly according to claim 2, in which an elastomeric sealing member is in sealing engagement with the external surface of the second cannula and the wall of the rear end of the housing to thereby eliminate leakage between the wall of the

rear end of the housing and the second, sliding cannula.

4. A needle assembly according to claim 3, in which a retaining disc is frictionally mounted in the chamber so that the elastomeric sealing disc is sandwiched between the retaining disc and the housing, the retaining disc having a bore through which the sliding cannula passes.

5. A needle assembly according to claim 3 or claim 4, in which an annular bead projects from the inner surface of the housing into the chamber and engages with the elastomeric sealing disc to provide the seal at the rear end of the housing.

6. A needle assembly according to any one of the preceding claims, in which the rear end of the first cannula mounted in the forward penetrating end of the housing extends rearwardly into the chamber, an elastomeric sleeve having an open end and a closed end is slidably mounted on the rear end of the first cannula in sealing engagement therewith, the sleeve being movable between the unarmed position and the armed position on the cannula, a transverse hole in the wall of the sleeve which permits the communication between the rear end of the first cannula and the exterior of the sleeve when the sleeve is in the unarmed position and the hole being obscured when the sleeve is moved to the armed position, a slit in the wall of the sleeve, the slit normally being closed when the sleeve is in the armed and unarmed position but which opens automatically when there is a reduction in pressure at the rearward end as the container is coupled with the assembly and the slit thereafter automatically closing when there is an increase in pressure at the rearward end and when there is a predetermined pressure differential between the forward and rearward end of the assembly, and an annular flange extending around the forward open end of the sleeve.

7. A needle assembly according to claim 6 when dependent on any of claims 2 to claim 5, in which a tubular hollow cage is mounted in the chamber, on the forward end of the sliding cannula and surrounding the elastomeric sleeve, the cage being in engagement with the flange on the sleeve so that moving the sliding cannula will move the cage and the engaged sleeve from the unarmed to the armed position when the cannula is moved towards the sleeve and will disengage the cage from the sleeve when the sliding cannula is moved away from the sleeve.

8. A needle assembly according to claim 7, in which there is a transverse opening in the side wall of the cage so that when the sleeve is in the unarmed position and a venapuncture is accomplished, blood will flow through the penetration cannula, through the

transverse opening in the sleeve and through the transverse opening in the cage into the chamber where its presence can be seen and this provides an indication that the venapuncture has been accomplished.

9. A needle assembly according to claim 7 or claim 8, in which the cage is mounted on the forward end of the sliding cannula to seal the end thereof and the sliding cannula has a side opening therein adjacent its forward end, the side opening being positioned within the chamber when the sliding cannula is in its forward position and outside the chamber and being sealed therefrom by the elastomeric sealing disc when the sliding cannula is in its rearmost position in which a surface on the cage engages with a surface on the housing to provide a stop and limit the further withdrawal of the sliding cannula.

10. A needle assembly according to any one of the preceding claims in which the housing is formed in two separate parts a forward end portion and a rearward end portion, the two portions being held together in frictional engagement.

11. A needle assembly according to any one of the preceding claims having a holder coupled to it, the holder being of a hollow cylindrical configuration so that, in use, it receives the evacuated container within and directs the container to couple with the needle assembly.

12. A needle assembly according to any one of claims 2 to claim 10 or claim 11 when dependent on any one of claims 2 to claim 10, having an evacuated container coupled with it, the container including a puncturable self-sealing stopper pierced by and engaged with the sliding cannula.

13. A method of transferring blood from a patient into an evacuated container whilst indicating that a venapuncture has been accomplished and preventing the back flow of fluid from the container into the patient during and after the collection of a blood sample with the use of a needle assembly having a forward end for penetration into the blood vessel of a patient, a rearward end adapted to be coupled in fluid communication with the evacuated container, a continuous passageway through the assembly, and a valve assembly including means for visually indicating a venapuncture and including a resilient elastomeric valve member in the assembly adapted to deform and open when subjected to pressure in one direction and adapted to close when the pressure in the one direction is relieved, the method comprising, inserting the forward penetrating end of the assembly into the blood vessel of a patient until the visual indicating means denotes a successful venapuncture, coupling the evacuated container to the rearward end of the needle assembly and initially shifting

the resilient elastomeric valve member to an armed position in which the valve member prevents flow between the ends of the assembly and subsequently coupling the evacuated interior of the container to the passageway through the needle assembly so that the elastomeric valve is subjected to a pressure differential in the one direction and automatically responds to the pressure differential to deform and open and permit blood to flow from the patient to the container, and removing the container from coupling engagement with the needle assembly after the pressure differential has been delivered so that the valve has automatically returned to the normally closed position thereby preventing flow between the ends of the needle assembly.

14. A method according to claim 13, in which a multiplicity of evacuated containers are coupled successively with the needle assembly to thereby collect a multiplicity of successive blood samples without leakage of blood from the needle assembly and without back flow of fluid from the rear end of the assembly into the patient.

15. A needle assembly for use with apparatus for collecting blood samples from a patient, the needle assembly having means for indicating when a venapuncture has been accomplished and then transferring blood from the patient into an evacuated container, whilst preventing back flow from the container into the patient, and means for automatically blocking the blood flow due to venous pressure while changing from one container to a successive container to be filled from the same venapuncture, the means for indicating when a venapuncture has been accomplished and for preventing back flow comprising an at least partly transparent housing having a chamber therein, a forward penetrating end including a cannula extending from the housing for penetration into the blood vessel of a patient, a rearward end extending from the housing and adapted to be coupled in fluid communication with the interior of the evacuated container, a passageway for directing blood from the blood vessel through the housing to the container when the forward end is in the blood vessel and the rearward end is in communication with the evacuated container, a resilient elastomeric valve member in the chamber forming a non-return valve which closes the passageway, the valve member being responsive to a reduction in pressure at the rearward end of the assembly upon coupling with the evacuated container to deform the valve member and automatically open the passageway to permit blood to flow from a blood vessel to the rearward end and into the container, the valve member thereafter being responsive to an increase in pressure at the rearward end to automatically return to the

- closed position and thereby prevent the back flow of fluid from the rear end of the assembly to the blood vessel when a predetermined pressure differential exists between the forward and rearward end of the assembly, the means for automatically blocking the blood flow due to venous pressure while changing from one container to a successive container including a second valve means adapted to permit or prevent the flow of blood through the rearward end and into the evacuated container as successive containers are filled with successive blood samples.
- 5 16. A needle assembly according to claim 1 constructed substantially as described with reference to the accompanying drawings. 15

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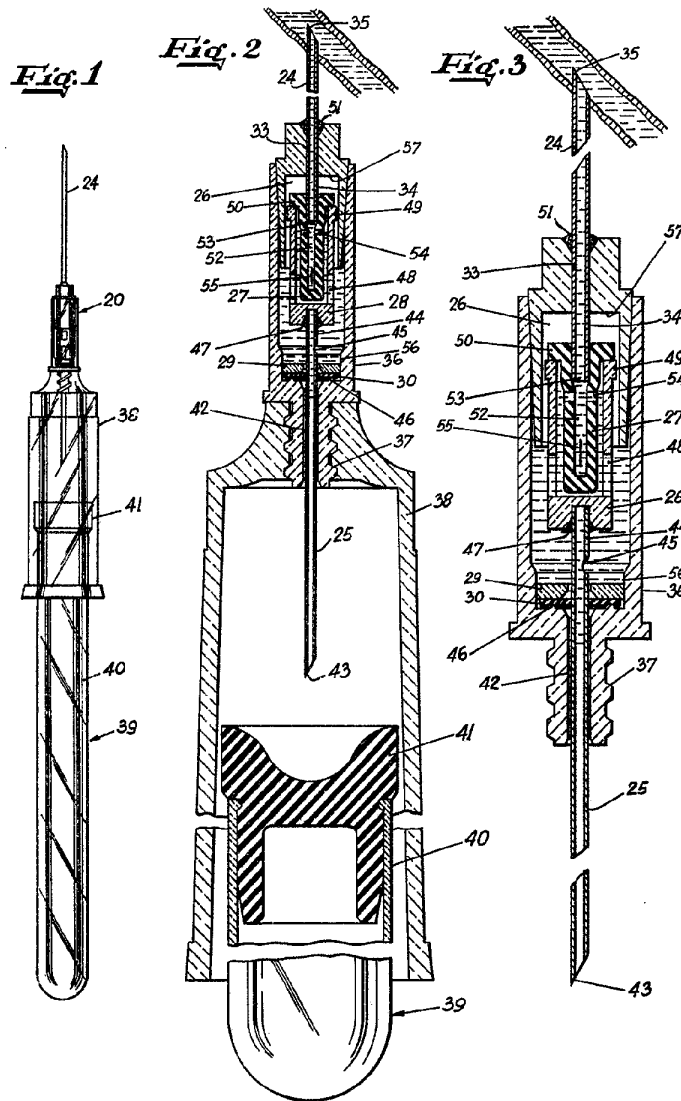


Fig. 4

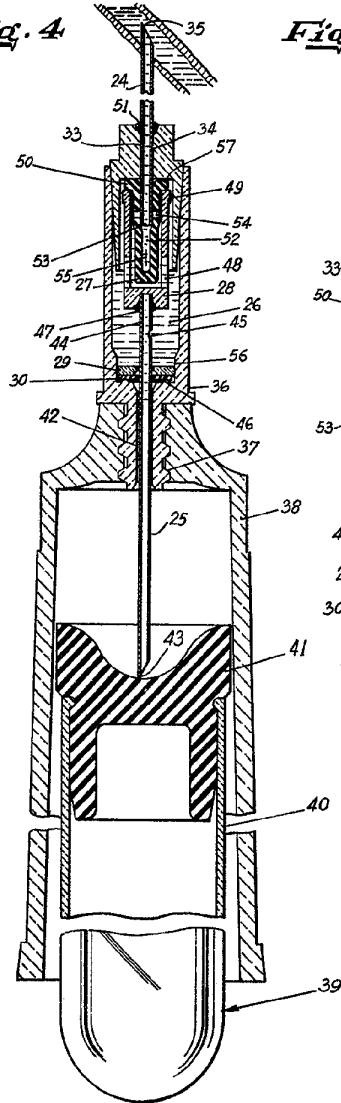


Fig. 5

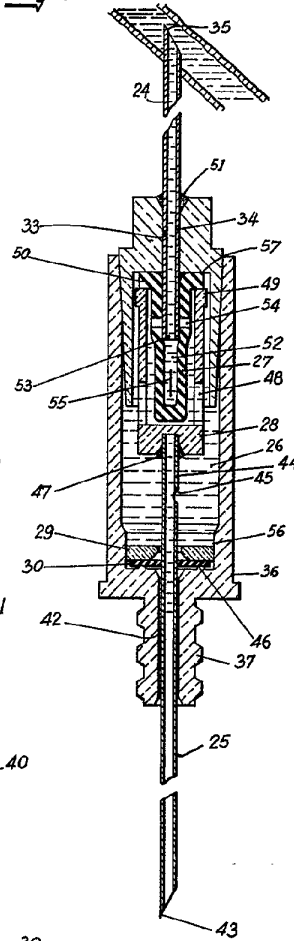


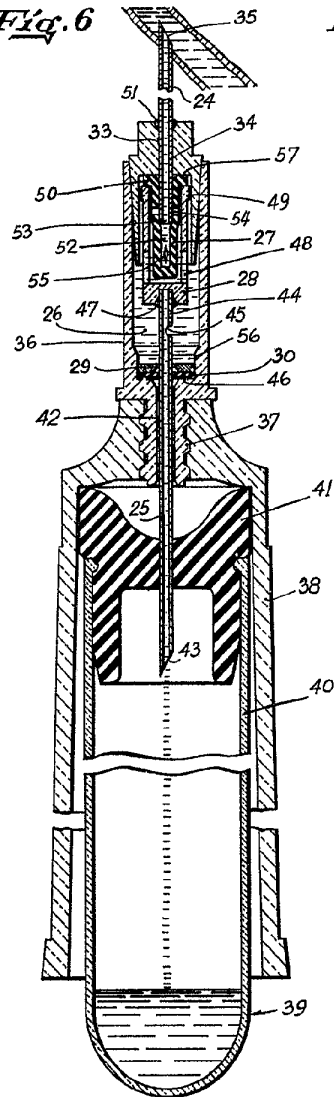
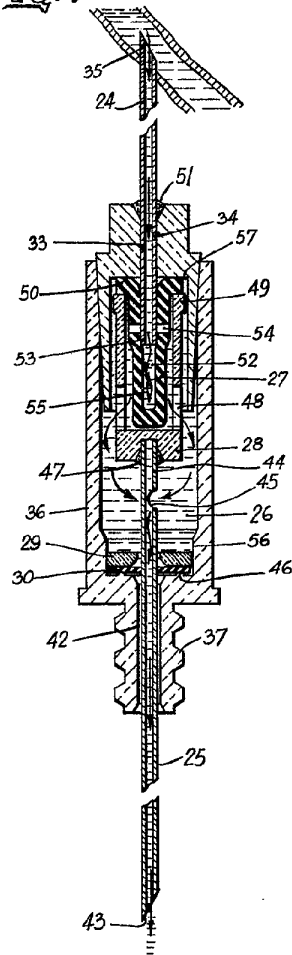
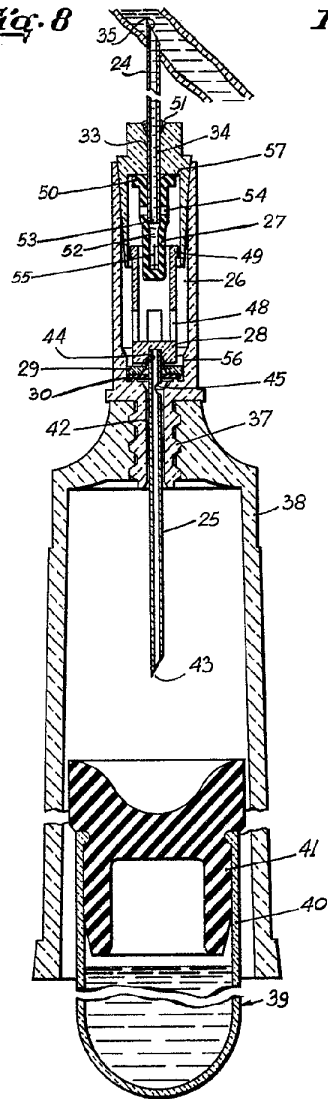
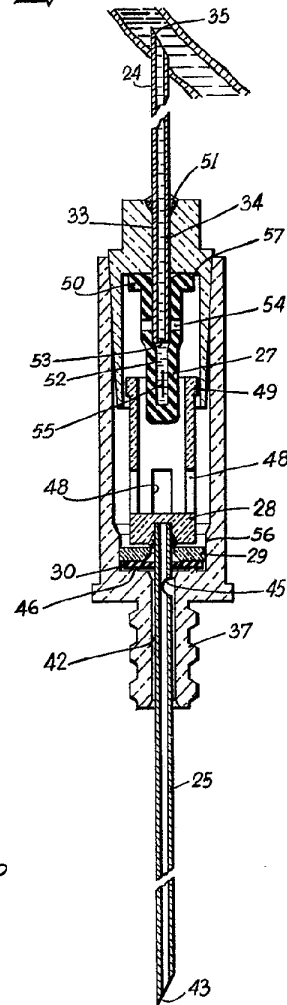
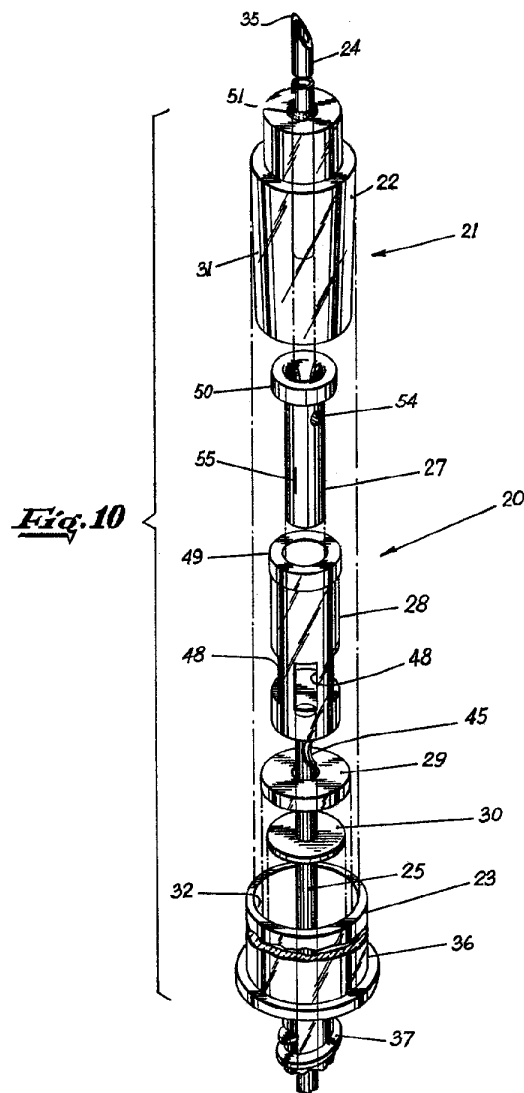
Fig. 6*Fig. 7*

Fig. 8*Fig. 9*



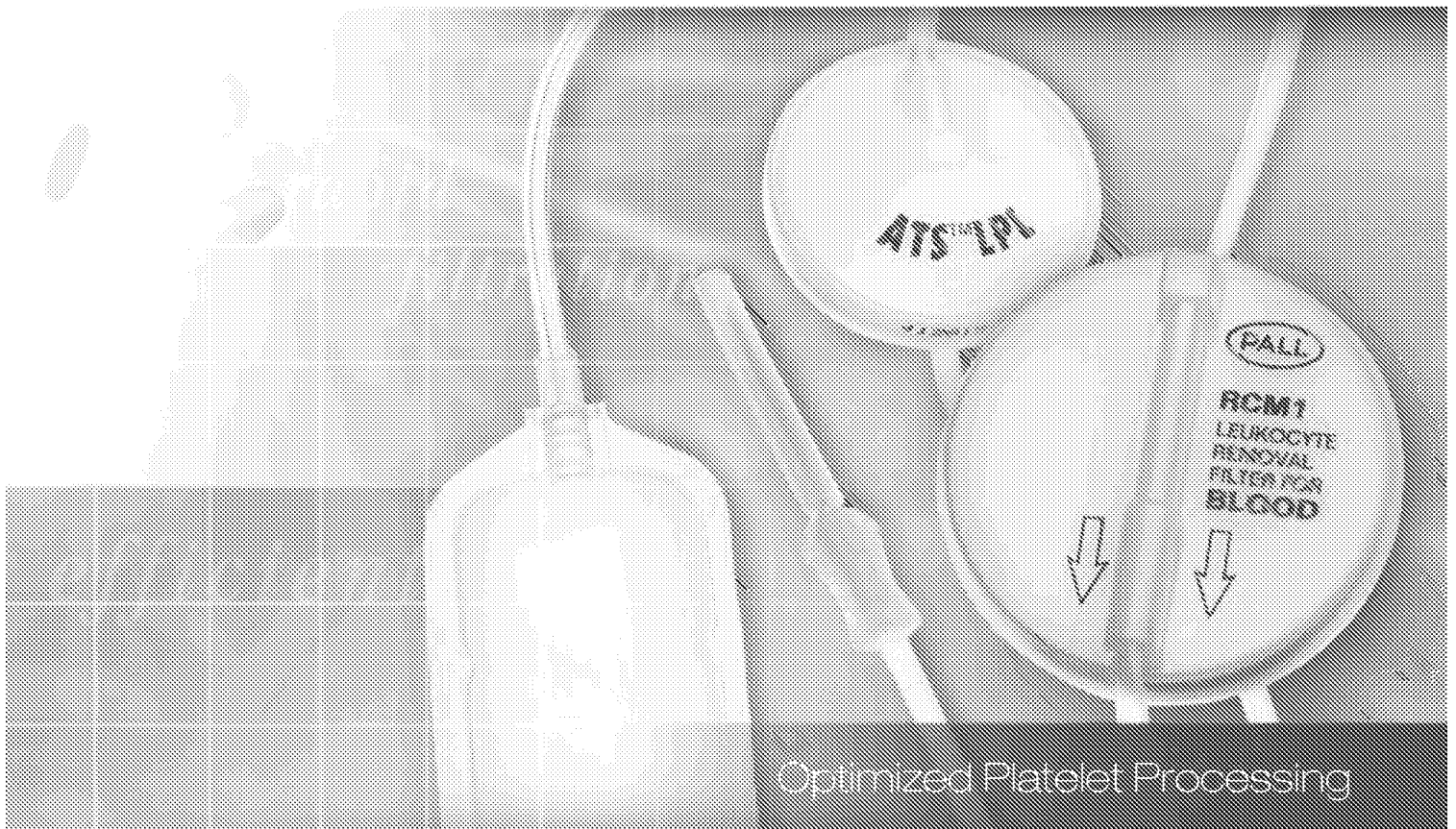


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Leukotrap RC PL and Leukotrap PL Systems



Optimized Platelet Processing

Better Blood, Better Care.™

KUR-MAG-DE005537

Improving the Availability of Safer Whole Blood Derived Platelets

*Pall offers the Only In-line
Collection, Filtration and Storage
Systems Capable of Producing
Leukocyte Reduced Whole Blood
Derived Platelets*



Leukotrap® RC PL System produces leukocyte reduced red blood cells, platelets, and plasma.

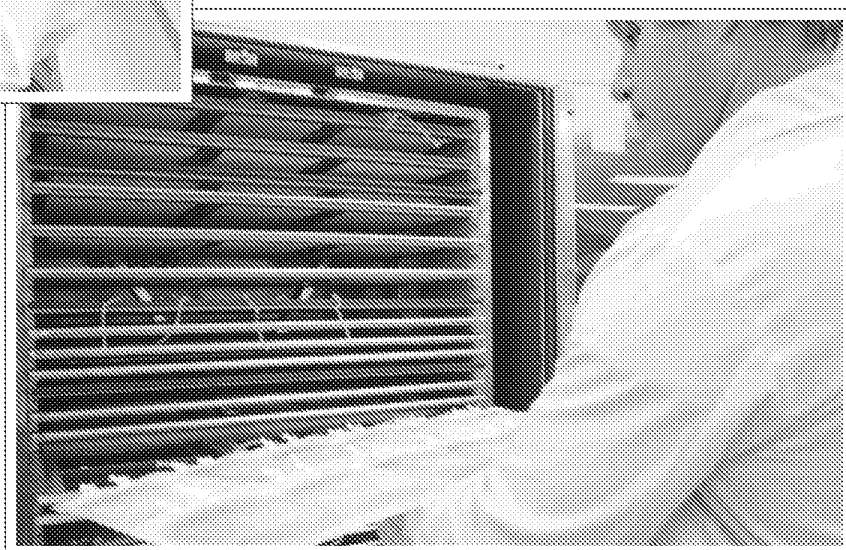
Leukotrap PL System produces leukocyte reduced platelets and plasma.

- ▶ Fits into routine operating procedures without additional labeling and handling
- ▶ Requires no sterile connection which eliminates the rework process of dockable leukoreduction and associated errors and product loss
- ▶ Features easy, snap-open closures for fast opening of fluid paths between bags

Makes cGMP compliance easier than ever.

- ▶ High efficiency filtration providing consistently low residual leukocytes in processed RBC*, platelets and plasma
- ▶ RBC recovery enhanced by auto-drainage*
- ▶ Allows for semi-automatic processing and filtration of the entire platelet rich plasma layer
- ▶ Greater QC assurance of meeting platelet recovery requirements

**Applies to Leukotrap RC PL System only.*



A Unique Combination of Technologies to Enhance Transfusion Safety and Operating Efficiency

Proprietary CLX® Platelet Storage Container

- ▶ Transparent, flexible and gas permeable
- ▶ Designed to maintain acceptable pH over the component's shelf life

Pall ATS LPL Filter

- ▶ High efficiency filtration for platelet-rich plasma
- ▶ Allows for semi-automatic processing and filtration of the entire platelet rich plasma layer.

Ultra Thin Wall 16-Gauge Needle

- ▶ User friendly, finger contoured hub with "bevel-up" indicator
- ▶ Needle sharpness 100% tested for donor safety and comfort
- ▶ Tamper evident needle cover

Sample Diversion Pouch

- ▶ Diverts up to 42 mL of blood collected
- ▶ Provides test sample access while collection bag is filling – reducing donor chair time

Pall RCM1 Filter*

- ▶ High efficiency filtration for RBCs
- ▶ RBC recovery enhanced by auto-drainage.

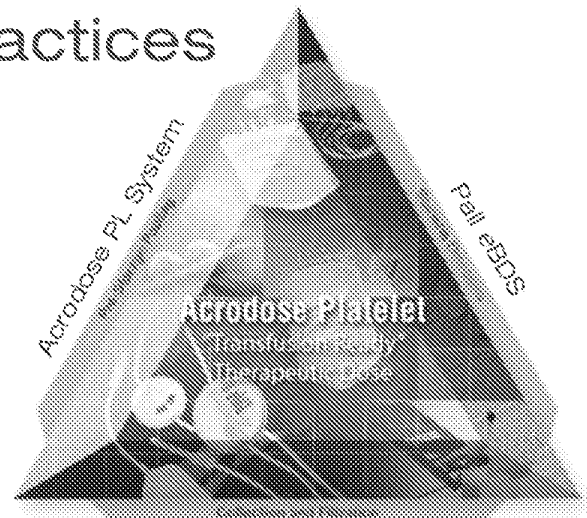
*Applies to Leukotrap® RC PL System only

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A Synergy of Best Practices

Supports your Bacteria Risk Management Program.

- Pre-donation Diversion Pouch Sampling System: Up to 72% predicted reduction in bacteria contamination by diverting initial 13.5 mL¹
- Leukocyte reduction filters have been shown to reduce bacteria from blood components^{2,3,4}
- Produce leukoreduced platelets ready for bacterial testing with the Pall eBDS



Leukotrap RC PL and
Leukotrap PL Systems

Collection and Filtration

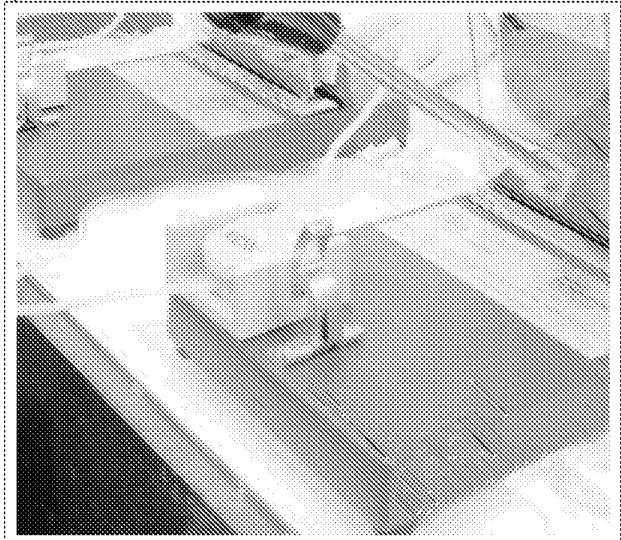
Pall Sample Diversion Pouch



1

Automatically divert initial blood with the Pall Sample Diversion Pouch

Leukotrap RC PL or
Leukotrap PL System



2

Prepare leukoreduced platelets with the Leukotrap RC PL or PL System

Provide Greater Platelet Transfusion Safety

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

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

Pre-storage Pooling and Bacteria Detection

Acrodose™ PL System



3

Pool leukoreduced platelets with the Pall Acrodose PL System.

Pall eBDS and Pall Data



4

Detect bacteria with Pall eBDS, a market cleared quality control culture based system.

Consistent and Reliable Performance

Greater QC Assurance of Meeting White Blood Cell Residual Requirements

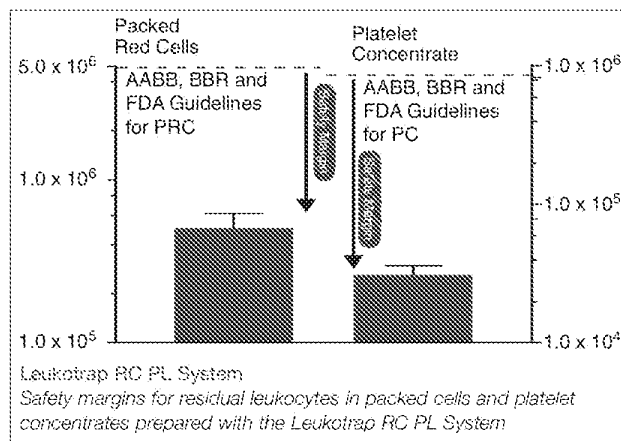


Figure 1

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

Data from actual field use.

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

Greater QC Assurance of Platelet Recovery Requirements

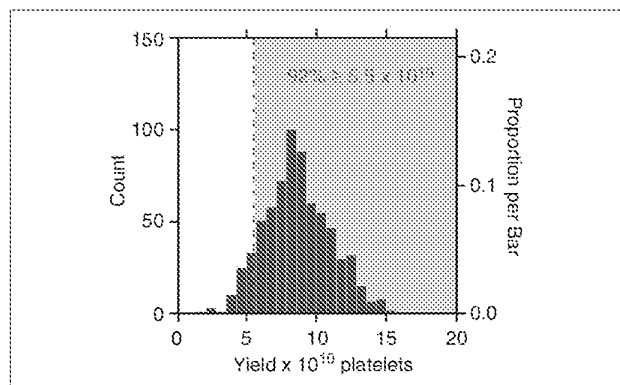


Figure 2

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

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

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

Ninety-two percent (92%) of PCs had a platelet count greater than the AABB Standards⁷ for platelets prepared from whole blood ($\geq 5.5 \times 10^{10}$).

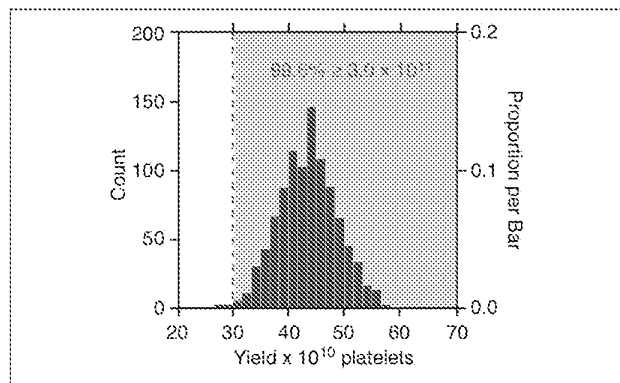


Figure 3

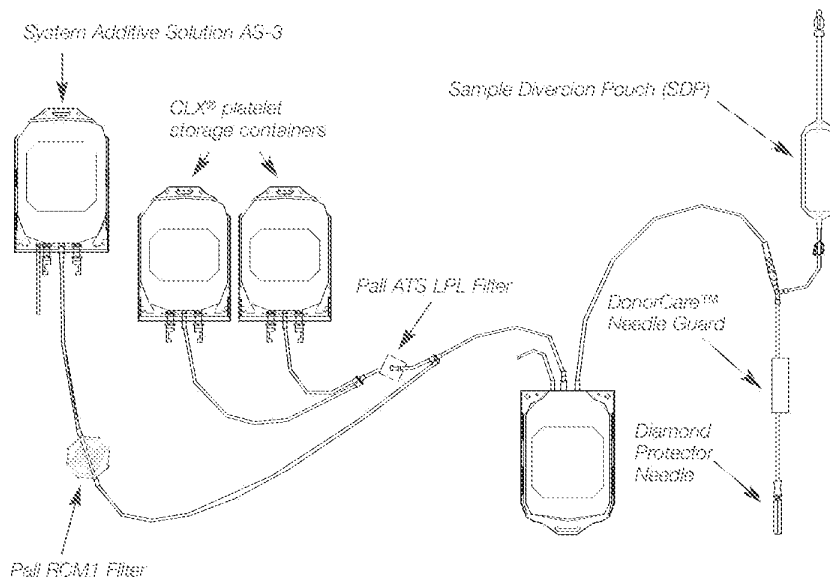
Platelet yield distribution of a pool of five (5) individual platelet concentrates (PC) prepared using the Leukotrap RC PL System.

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

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

Over ninety-nine percent (99.6%) of the PC pools had a platelet yield greater than the AABB Standard for platelets prepared by cytophoresis⁸ ($\geq 3.0 \times 10^{11}$).

Leukotrap® RC PL System

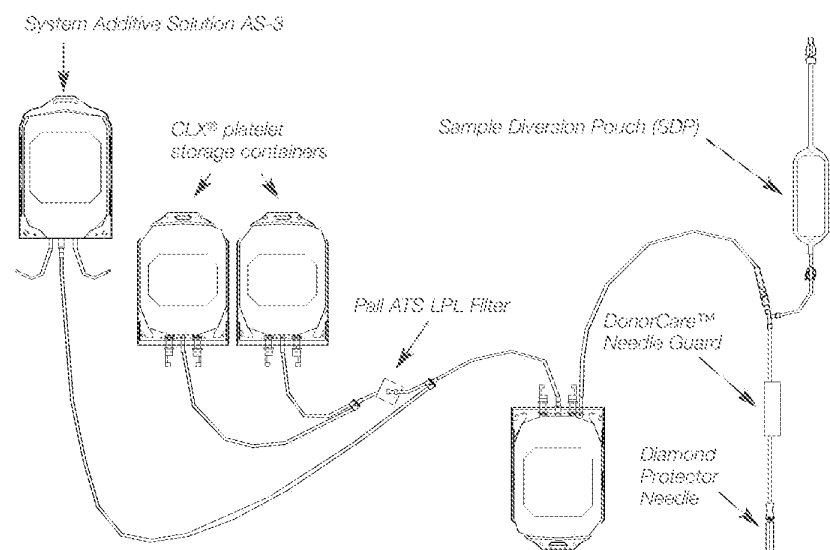


Ordering Information*

Leukotrap RC PL System

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

Leukotrap PL System



Ordering Information*

Leukotrap PL System

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

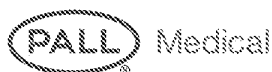
*All sets come with DonorCare™ Needle Guard for reducing needlestick injury, enhanced paper labels for improved adhesion of overlabels and a QC tag on the collection bag for improved QC sampling. The System Additive Solution AS-3 (Nutrical® System) for RBC maintains viability for 42 days without manitol.

Pall filters cover all of your leukoreduction needs.



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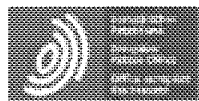
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Better Blood, Better Care.™

9.05.24K, GN/5 1242

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KUR-MAG-DE005544



Espacenet

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BLOOD DRAWING DEVICE WITH FLASH DETECTION

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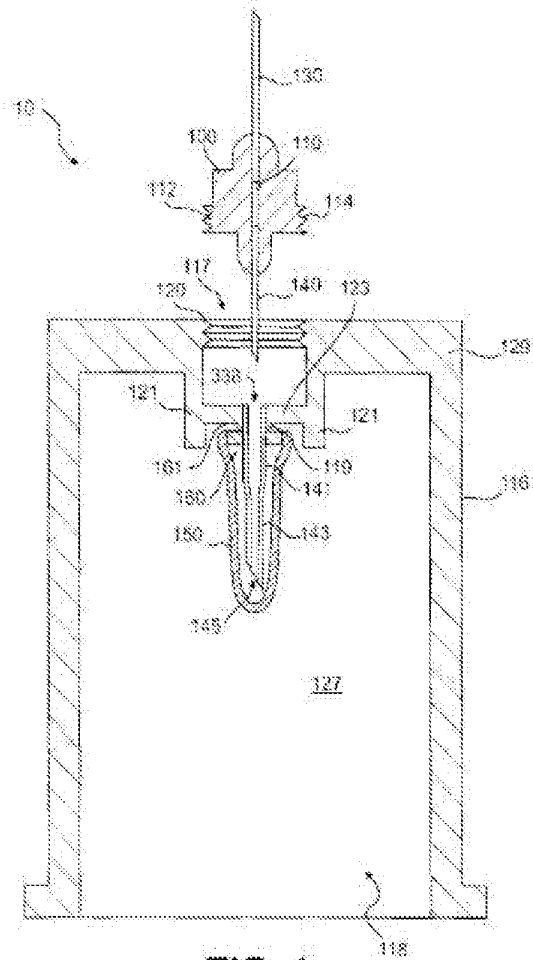
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Application number: WO2010US40030 20100625 [Global Dossier](#)

Priority number(s): [US20100822931](#) 20100624

Abstract of WO2011162772 (A1)

A device for drawing fluid from a lumen, and particularly blood from a blood vessel, is disclosed. The device may provide indication of the entry of an intravenous cannula into the lumen. The device may include a guide tube for receiving a blood sample container and which may be connected to a needle for drawing blood from a lumen. A rear cannula may extend into the guide tube from the well. A flexible sleeve may be mounted on a barb connected to the guide tube. The flexible sleeve may extend into the guide tube from the well and surround at least a tip portion of the rear cannula. A venting member may be provided between the interior of the sleeve and the ambient.





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[Continued on next page]

(54) Title: BLOOD DRAWING DEVICE WITH FLASH DETECTION

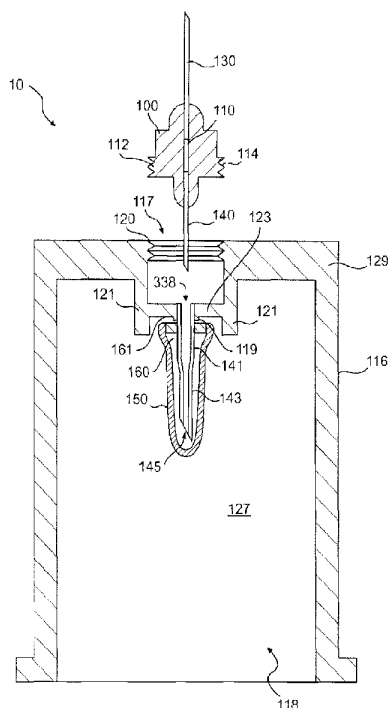


FIG. 1

(57) Abstract: A device for drawing fluid from a lumen, and particularly blood from a blood vessel, is disclosed. The device may provide indication of the entry of an intravenous cannula into the lumen. The device may include a guide tube for receiving a blood sample container and which may be connected to a needle for drawing blood from a lumen. A rear cannula may extend into the guide tube from the well. A flexible sleeve may be mounted on a barb connected to the guide tube. The flexible sleeve may extend into the guide tube from the well and surround at least a tip portion of the rear cannula. A venting member may be provided between the interior of the sleeve and the ambient.

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Published:

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

BLOOD DRAWING DEVICE WITH FLASH DETECTION

FIELD OF THE INVENTION

[0001] The present invention relates to an apparatus for drawing bodily fluids, and particularly blood, from an animal.

BACKGROUND OF THE INVENTION

[0002] Intravenous blood collection assemblies have long been used to draw bodily fluids, such as blood, from patients. With respect to drawing blood in particular, the vessel or lumen from which the blood is drawn is often rather small and or not visible. If the needle tip is not in communication with the interior of the blood vessel during the procedure, the procedure is likely to be unsuccessful, causing error, undermining the integrity of the specimen, and the patient may be harmed additionally by the penetration of delicate underlying structures. Accordingly, confirmation of accurate placement of the needle tip into a blood vessel is desirable for blood drawing procedures.

[0003] Past intravenous blood collection assemblies have included mechanisms for indicating when a needle tip is in communication with the interior of a blood vessel. These needle kits have included a transparent portion in the needle body from which the presence of blood can be observed. The observation of blood in the needle body is known as "flash." Flash detection has been less than satisfactory for many such collection assemblies. In some instances, the flow of blood into the transparent portion of the needle body is impeded by air backpressure in the needle, and thus flash confirmation is not visible or delayed. This delay can impede the determination of the precise moment at which the needle tip enters the blood vessel, which may cause the healthcare worker inserting the needle to miss or perforate the vessel and penetrate into delicate surrounding structures. In other instances, while flash occurs, the visual indication of flash is not easily detected because the amount of flash is small or obscured due to the positioning of the collection assembly. Accordingly, there is a need

for a blood-drawing device that provides flash relatively rapidly and to an extent that a user may readily detect it.

[0004] There are also many needles that are currently used that do not provide for flash detection. It would be advantageous to be able to retrofit such needles so that they may be used to draw blood and provide detection of flash.

SUMMARY OF THE INVENTION

[0005] Responsive to the foregoing challenges, Applicant has developed a guide tube assembly for connection to a device for drawing fluid from a lumen, comprising: a guide tube (116) having an open end (118) and a well (117); a flexible sleeve (150, 151) having an interior space in fluid communication with the well (117) and extending into the guide tube (116); one or more passages (332, 334, 336, 338) extending through the guide tube (116) which are in fluid communication with the flexible sleeve (150) interior space; and a venting member (160) connected to the guide tube (116) or incorporated into the flexible sleeve (150, 151), said venting member in fluid communication with the one or more passages (332, 334, 336, 338) and disposed between the flexible sleeve (150, 151) interior space and an ambient.

[0006] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only, and are not restrictive of the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] In order to assist the understanding of this invention, reference will now be made to the appended drawings, in which like reference characters refer to like elements.

[0008] Figure 1 is a side view in cross-section of a blood drawing needle and guide tube having a venting member in accordance with a first embodiment of the present invention prior to connection with a blood drawing needle.

[0009] Figure 2 is a side view in cross-section of the guide tube shown in Figure 1

after connection to the blood drawing needle.

[0010] Figure 3 is a side view in cross-section of a guide tube having a venting member in accordance with an second embodiment of the present invention prior to connection with a blood drawing needle.

[0011] Figure 4 is an end view of the raised dimple surface of a well bottom wall provided in the guide tube in accordance with an alternative embodiment of the invention shown in Figures 1-3.

[0012] Figure 5 is an end view of the raised radial line surface of a well bottom wall provided in the guide tube in accordance with an alternative embodiment of the invention shown in Figures 1-3.

[0013] Figure 6 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a guide tube opening in accordance with a third embodiment of the present invention.

[0014] Figure 7 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a guide tube opening with well bottom extensions surrounding the venting member in accordance with a fourth embodiment of the present invention.

[0015] Figure 8 is a side view in cross-section of a blood drawing device with a guide tube having a venting member and viewing window located in a guide tube side wall in accordance with a fifth embodiment of the present invention.

[0016] Figure 9 is a side view in cross-section of a blood drawing device with a guide tube having a venting member and viewing window located in a guide tube side wall in accordance with a sixth embodiment of the present invention.

[0017] Figure 10 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a guide tube opening in accordance with a seventh embodiment of the present invention.

[0018] Figure 11 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a guide tube opening and a viewing

window located in a guide tube side wall in accordance with an eighth embodiment of the present invention.

[0019] Figure 12 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a guide tube opening surrounded by well bottom extensions and having a viewing window located in a guide tube side wall in accordance with a ninth embodiment of the present invention.

[0020] Figure 13 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a guide tube opening with well bottom extensions surrounding the venting member in accordance with a tenth embodiment of the present invention.

[0021] Figure 14 is a side view in cross-section of a blood drawing device with a guide tube having a sealing membrane in a guide tube well and a venting member and viewing window located in a guide tube side wall in accordance with an eleventh embodiment of the present invention.

[0022] Figure 15 is a side view in cross-section of a blood drawing device with a guide tube having a venting member and viewing window located in a guide tube side wall in accordance with a twelfth embodiment of the present invention.

[0023] Figure 16 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a guide tube well in accordance with a thirteenth embodiment of the present invention.

[0024] Figure 17 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a sleeve tubulation and a viewing window located in a guide tube side wall in accordance with a fourteenth embodiment of the present invention.

[0025] Figure 18 is a side view in cross-section of a blood drawing device with a guide tube having an air-permeable sleeve and a viewing window located in a guide tube side wall in accordance with a fifteenth embodiment of the present invention.

[0026] Figure 19 is a side view in cross-section of a blood drawing device with a

guide tube having a sleeve with a venting portion and a viewing window located in a guide tube side wall in accordance with a sixteenth embodiment of the present invention.

[0027] Figure 20 is a side view in cross-section of a blood drawing device with a guide tube having a venting member located in a sleeve tubulation and a viewing window located in a guide tube side wall in accordance with a seventeenth embodiment of the present invention.

[0028] Figure 21 is a side view in cross-section of a blood drawing device with a guide tube having an air-permeable sleeve and a viewing window located in a guide tube side wall in accordance with an eighteenth embodiment of the present invention.

[0029] Figure 22 is a side view in cross-section of a blood drawing device with a guide tube having a sleeve with a venting portion and a viewing window located in a guide tube side wall in accordance with a nineteenth embodiment of the present invention.

[0030] Figure 23 is a side view in partial cross-section of a first Luer-adapter type butterfly needle attachment which may be used to connect with the guide tubes shown in Figures 1-22.

[0031] Figure 24 is a side view in cross-section of a second butterfly needle attachment that may be used to directly connect to the guide tubes shown in Figures 1-22.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

[0032] Reference will now be made in detail to a first embodiment of the present invention, an example of which is illustrated in the accompanying drawings. With reference to Figs. 1 and 2, a guide tube **116** is shown. The guide tube **116** is provided for connection to a central body **100** which may include one or more constituent elements, such as a threaded connector **112** with interlocking threads **114** or other connection means, for connecting the central body to the guide tube. The threaded connector **112** may be integrally formed with, or connected to the central body using

adhesive, male-female interfaces, threaded interfaces, or any other connection means. It is appreciated that the guide tube **116** may be connected to the central body **100** by any connection means, including without limitation the threaded interfaces shown, male-female interfaces, pressure-fit connectors, slot and key connectors, snap-on connectors, and the like. The type of connection between the guide tube **116** and the central body **100** is not intended to be limiting to the scope or use of any of the present embodiments of the invention.

[0033] A fluid passage **110** within the central body **100** may communicate with, and in the embodiment shown, be connected to the front cannula **130** and the first rear cannula **140**, respectively, using adhesive, threaded interfaces, pressure fit, or other connection means. Alternatively, the central body **100** may be integrally formed with the front and/or first rear cannulae **130** and **140**. It is further appreciated the front and first rear cannulae **130** and **140** may be formed of a continuous material and eliminate the need to fluid passage **110**. It is also appreciated that the front and/or rear cannulae may be transparent or translucent, in whole or part, to provide flash detection in alternative embodiments of the present invention. If included, the fluid passage **110** may be defined by the opening within the central body between the front and rear cannulae when the cannulae are directly connected to the central body. The fluid passage **110** may be adapted to receive a sufficient amount of fluid to allow observation of the fluid (*i.e.*, "flash") from outside the blood-drawing device **10**. At the same time, the fluid passage **110** may have a sufficiently small volume so as to rapidly fill with fluid during the use of the blood-drawing device.

[0034] Preferably, the central body **100** may be constructed of plastic material suitable for medical use. Further, in any embodiment of the present invention, all, or portions, of the central body **100** may be transparent, translucent, connected to transparent or translucent I.V. tubing, or otherwise adapted to permit detection of fluids passing through the central body and/or I.V. tubing from a vantage point outside of the blood-drawing device **10**. For example, with reference to Fig. 1, the central body **100**

may include a transparent wall that is adapted to permit the observation of "flash" when it occurs. In an alternate embodiment of the present invention, the side wall of the central body **100** also may be adapted to magnify or otherwise enhance the detection of fluid passing through the central body, although it is appreciated that a magnifying or enhancement feature is not necessarily required.

[0035] It is further appreciated that the front cannula **130** may be replaced with or connected to a flexible butterfly connection tube **182** that is part of a butterfly needle **180** as shown in Fig. 23. When connected to a flexible butterfly connection tube **182**, the front cannula **130** extending from the central body **100** may be eliminated and replaced with a Luer-adapter including a female connector **102** and male connector **103** which is connected via the butterfly connection tube **182** to a butterfly cannula **184** which substitutes for the front cannula **130**. The flexible butterfly connection tube **182** may be translucent or transparent when combined with the embodiments shown in Figs. 1-22 so that the "flash" of blood that enters the device **10** may be visible first in the butterfly connection tube. In a further alternative, shown in Fig. 24 and applicable to the embodiments shown in Figs. 1-22, the female connector **102** of the Luer-adapter may connect directly to a specially formed mating male connector **103** integrally formed with the guide tube **116**. It is appreciated that the placement of the male and female connectors could be reversed or replaced with other connector types in alternative embodiments of the invention.

[0036] With renewed reference to Figs. 1-2, the front cannula **130** may extend from the front end of the central body **100** and terminate at a tapered or pointed end **132** which is adapted to be inserted into a lumen. The first rear cannula **140** may extend from the rear of the central body **100** and terminate at a tapered or pointed end.

[0037] A generally cylindrical guide tube **116** is adapted to be connected to the central body **100**. Preferably, the guide tube **116** may be made in whole or part of transparent or translucent material that permits viewing of the interior space of the guide tube. The guide tube **116** may include a substantially closed end **129**, an open

end **118** at one end communicating with an interior opening **127**, and a well **117** at the opposite end defined in part by a well bottom wall **123**. The open end **118** may be adapted to receive a blood or fluid sample container. The upper edge of the well **117** may include threads or other connection means **120** adapted to mate with the threads **114** of the threaded connector **112** provided on the central body **100**.

[0038] The well bottom wall **123** may include a centrally located opening through which a second rear cannula **141** extends towards the guide tube open end **118**. The second rear cannula **141** may be sufficiently fastened to the well bottom wall **123** by any means such that the application of pressure from a fluid sample container pressed against the second rear cannula will not dislodge the second rear cannula. The guide tube **116** may extend coaxially with the second rear cannula **141** sufficiently beyond the tapered end **145** to provide some degree of protection against inadvertent “needle sticks” by a user of the blood-drawing device **10** as well as to guide the reception of a fluid sample container.

[0039] The bottom surface of the well bottom wall **123** located within the interior of the guide tube **116** may include a shoulder **119** against which a venting member **160** may be disposed. The shoulder **119** may create an air space **161** between the bottom surface of the well **117** and the venting member **160**. In one alternative embodiment of the invention, shown in Fig. 4, the shoulder **119** may be replaced by or incorporate a surface having raised dimples **217**, or in another alternative embodiment, as shown in Fig. 5, the shoulder may be replaced by or incorporate a surface having raised radial lines **219**, or some other surface which both supports the venting member **160** and provides for air flow between the venting member and the interior of the guide tube **116**. In still other alternative embodiments of the present invention, an air-permeable spacer may be provided between the venting member **160** and the bottom surface of the well bottom wall **123** to provide the required air flow in place of any raised features on the bottom of the well bottom wall.

[0040] The second rear cannula **141** may include a stepped diameter **143** or other

narrowing feature that results in the second rear cannula having a narrower diameter at the pointed end **145** compared with the end extending from the well **117**. The end of the second rear cannula **141** nearest to the well **117** may have a diameter sufficient to receive the first rear cannula **140** within it. In alternative embodiments of the invention, the second rear cannula **141** may have a uniform diameter over its entire length.

[0041] One or more well bottom extensions **121** may also extend from the well bottom wall **123** into the guide tube opening **118** adjacent to the venting member **160**. The well bottom extensions **121** may surround the venting member **160** in whole or in part and may be formed so as to leave an air space for air to flow from the interior of the sleeve **150** through the venting member **160** to the ambient in the guide tube interior opening **127**. The well bottom extensions **121** may be semi-circular, or prong shaped, and surround the venting member **160**. Further, the well bottom extensions **121** may extend into the guide tube **116** a distance sufficient to protect the venting member **160** from being impacted against, damaged or dislodged by, the stopper of a container inserted into the guide tube. The well bottom extensions **121** may be formed of plastic material which is integral with the rest of the guide tube **116** and well bottom wall **123**. The well bottom extensions **121** may also contact the venting member **160** and/or flexible sleeve **150** so as to assist in retaining the sleeve and venting member in the guide tube **116**.

[0042] The venting member **160** may be constructed out of any material which is capable of substantially preventing blood from passing through it while permitting air to vent through it. Preferably, for purposes of ease of manufacturing, the venting member **160** may be formed as a stamped disk with a central opening from a sheet of venting member material for the embodiment shown in Figs. 1-2.

[0043] The venting member **160** may be constructed of any of a number of materials that provide the desired level of porosity, which may include, but are not limited to sintered, layered, rolled, foamed, perforated, or impregnated, hydrophilic/hydrophobic compositions, porous polyethylene, porous polypropylene,

porous polyfluorocarbon, absorbent paper, materials impregnated with dilute Russell Viper venom molded fiber, fiberglass, felt, granular starch, cellulose, polyacrylamide gel, hydrogel, a molded admixture of porous hydrophobic/hydrophilic granules and sufficiently low density silicone, molded open cell polyurethane, and like polymeric materials. Examples of materials that may be used to construct the venting (i.e., porous) member **160** are discussed in U.S. Patent No. 4,207,870 to Eldridge, and U.S. Patent No. 4,340,068 to Kaufman, each of which are hereby incorporated by reference.

[0044] The venting member **160** (i.e., a means for venting air) may be inserted over the second rear cannula **141** and pressed against or near to the rear portion of the well bottom wall **123**. The venting member **160** may form a seal against the second rear cannula **141** that is sufficient to prevent blood from escaping past the venting member. In the embodiments of the present invention, the venting member **160** may be gas, and particularly air, permeable, but at least partially, and preferably wholly, impermeable to a liquid, such as blood. Preferably, the venting member **160** may be substantially porous for gas constituents less than about 5 microns in size, and substantially non-porous for liquid constituents about 5 microns or greater in size, however, it is appreciated that these approximate sizes should not be limiting for the invention.

[0045] For each of the embodiments discussed in connection with Figs. 3-24, the venting member **160** may be constructed in accordance with the description of the venting members described in connection with the embodiment of the invention described in connection with Figs. 1-2.

[0046] A flexible sleeve **150** may be disposed over and around the second rear cannula **141**. The sleeve **150** may isolate the second rear cannula **141** from the ambient, wherein the ambient includes any space outside of the sleeve **150**, irrespective of whether or not the space is contained within the guide tube **116** or any other structure. The flexible sleeve **150** may be stretched over all or part of the side wall of the venting member **160**, or in alternate embodiments, otherwise contact the venting member **160**. The flexible sleeve **150** may be made of a shape memory

material, such as elastic rubber or elastomeric silicone or latex, or the like, which will return to the shape shown in Fig. 1 as long as no other structure obstructs it. Examples of materials that may be used to construct the flexible sleeve **150** are discussed in U.S. Patent No. 3,877,465 to Miyake, U.S. Patent No. 5,086,780 to Schmitt, U.S. Patent No. 6,110,160 to Farber, U.S. Patent No. 6,533,760 to Leong, U.S. Patent Pub. No. US 2002/0004647 A1 to Leong, and U.S. Patent Pub. No. US 2003/0078544 A1 to Chen, each of which is hereby incorporated by reference. It is appreciated that any suitable material may be used for the flexible sleeve without departing from the intended scope of the present invention.

[0047] The flexible sleeve **150**, also known as a multiple sample sleeve, may preferably be transparent or translucent such that the presence of blood within the flexible sleeve may be visually detected. When the flexible sleeve **150** is transparent or translucent in any of the embodiments shown in Figs. 1-24, the guide tube **116** may also be transparent or translucent so that the "flash" of blood may be visible through both the guide tube and the flexible sleeve to the person drawing blood. The length of the flexible sleeve **150** may be sufficient to accommodate the second rear cannula **141** but not so long as to present serious risk of the second rear cannula piercing the side wall of the flexible sleeve when a fluid sample container is pushed into the guide tube **116**.

[0048] Prior to using the device **10** to draw blood, the central body **100** may be connected to the guide tube **116** at the threaded end **112** as shown in Fig. 2, in which like reference characters refer to like elements. When so connected, the combination of the guide tube **116** with a venting member **160** and the flexible sleeve **150** may be used to effectively "retrofit" a non-venting blood drawing device to become a venting blood drawing device. It is appreciated that each of the embodiments of the present invention shown in Figs. 1-24 may be used to retrofit existing non-venting blood drawing devices to become devices which vent air without substantially venting blood. The well **117** may be designed to provide sufficient space to accommodate the rear portion of

the central body **100** of a conventional or known blood drawing device within it to provide retro-fitting.

[0049] The function of the first embodiment of the blood-drawing device **10** will now be described with reference to Figs. 1-2. With reference to Figs. 1-2, the tapered end **132** of the front cannula **130** (or some extension thereof) may be inserted into a fluid containing body lumen prior to the insertion of a fluid sample container into the guide tube **116**. In a preferred embodiment of the present invention, the front cannula **130** is inserted into a lumen containing a visually detectable fluid, such as blood. At the time that the front cannula **130** is inserted into the body lumen, it is assumed that the internal passages within the blood-drawing device (*i.e.*, the passage through the front cannula **130**, the fluid passage **110**, the passage through the rear cannula **140**, and the space inside the flexible sleeve **150**) may be filled with atmospheric air or some other gas. When the front cannula **130** establishes communication with the fluid in the body lumen, fluid pressure in the lumen may force the fluid through the front cannula **130** towards the fluid passage **110**.

[0050] The flow of fluid through the front cannula may begin to compress the air in the fluid passage **110**, the rear cannula **140**, the second rear cannula **141**, and the space between the rear cannulae and the flexible sleeve **150**, driving the air towards the venting member **160**. Air within the blood drawing device **10** that would otherwise prevent or slow the flow of blood into it, may vent through the flexible sleeve **150** and the venting member **160** to the ambient within the guide tube **116**. The air may vent from the venting member **160** through the air space **161** that may be created by the shoulder **119** or the dimples **217** (Fig. 4) or radial lines **219** (Fig. 5). As a result, there may be insufficient air pressure within the fluid passage **110** to resist the flow of the fluid, where it may be detected or observed as "flash" by a user.

[0051] Blood that flows into the blood drawing device may be viewed either through the central body **100**, the butterfly connection tube **182** (in embodiments that use a butterfly needle) or through a transparent or translucent flexible sleeve **150** and/or a

transparent or translucent guide tube **116**. The visual detection of blood indicates positive vein entry, known as flash. It is appreciated that "flash" may be detected at any point along the device that includes a transparent or translucent member, which may include, but not be limited to, a transparent or translucent cannula, central body, I.V. tubing, flexible sleeve, or other constituent member.

[0052] Once flash is detected, a fluid sample container may be pressed into the open end **118** of the guide tube **116**, the second rear cannula **141** may pierce the flexible sleeve **150**, and the flexible sleeve is pushed back towards the base of the second rear cannula. As shown in Fig. 2, the first rear cannula **140** may slide into the second rear cannula **141** and the second rear cannula may extend into the guide tube **116** a distance which is sufficient to pierce the stopper provided on the top of a fluid sample container. The one or more well bottom extensions **121** may prevent the fluid sample container from crushing, dislodging or otherwise damaging the venting member **160**. A sample of blood may then be received in the fluid sample container.

[0053] An alternative embodiment of the present invention is shown in Fig. 3, in which like reference characters refer to like elements in the other drawing figures. The embodiment shown in Fig. 3 differs from that shown in Figs. 1-2 in that the second rear cannula **141** is truncated. In this embodiment the first rear cannula **140** is of sufficient length to pierce a fluid sample container. It is also appreciated that the second rear cannula **141** could be replaced with an integral portion of the well bottom wall **123** shaped to receive the venting member **160**. In all other respects the embodiment shown in Fig. 3 operates like the embodiment shown in Figs. 1-2.

[0054] With reference to Fig. 6, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The well bottom wall upper surface **125** may prevent blood from flowing into the well **117** when the central body **100** is seated against the well bottom wall **123**.

[0055] With continued reference to Fig. 6, the second rear cannula **141** may have a

venting member **160** disposed about it at a base portion against the inner end wall of the guide tube **116**. The venting member **160** may have a base **300** and a barb portion **302**. The base **300** may be adhered to the end wall of the guide tube **116**, pressure fit onto the second cannula **141**, or otherwise fixed into position within the guide tube **116** without being directly connected to the central body **100** or any element of the central body, such as the first rear cannula **140**. The venting member **160** base **300** may be defined in part by an annular recess which separates the base from the barb portion **302** that is adapted to have the open end of a flexible sleeve **150** mounted thereon. Alternatively, the venting member **160** need not have any annular recess so long as the flexible sleeve **150** has a base portion **300** which provides an air path for air to flow from inside the flexible sleeve **150** to the interior of the guide tube **116**. The air path may be provided in whole or in part by well bottom wall **123** features such as dimples **217** (Fig. 4), radial lines **219** (Fig. 5) or the like. The embodiment shown in Fig. 6, as well as the embodiments of the invention shown in Figs. 1-5 and 7-24, may be used to retrofit an existing and non-air venting needle central body **100** into an air venting blood drawing device after being connected to the guide tube **116**.

[0056] With continued reference to Fig. 6, when the front cannula **130** (or butterfly cannula **184** with respect to Figs. 23-24) is introduced to a lumen, such as a vein, to draw fluid, such as blood, the blood may readily flow through the front cannula, the first rear cannula **140**, the second rear cannula **141** and into the interior of the flexible sleeve **150**. Air within the blood drawing device **10** that would otherwise prevent or slow the flow of blood into it, may vent through the flexible sleeve **150** and the venting member **160** through the venting member base **300** to the ambient within the guide tube **116**. The venting member base **300** may provide a surface for air to escape from the venting member **160**. Blood that flows into the blood drawing device may be viewed either through the central body **100**, the butterfly connection tube **182** (in embodiments that use a butterfly needle) or through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**. The visual detection of blood indicates

positive vein entry, known as flash. Once flash is detected, a fluid sample container may be pressed into the open end **118** of the guide tube **116**, the second rear cannula **141** may pierce the flexible sleeve **150** and the flexible sleeve is pushed back towards the base of the second rear cannula. The shape of the venting member **160** with a wide base **300** and barb portion **302** may be such as to withstand the force of a fluid sample container being inserted into the guide tube and against the venting member without the venting member being crushed or otherwise damaged. This is necessary so that multiple sample containers can be filled with blood without the risk of leakage past a damaged venting member.

[0057] With reference to Fig. 7, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 7 is identical in all respects to that shown in Fig. 6 with the following exception. With respect to Fig. 7, one or more well bottom extensions **121** may extend from the well bottom wall **123**. The well bottom extensions **121** may surround the venting member **160** in whole or in part and may be formed so as to leave an air space for air to flow from the interior of the sleeve **150** through the venting member **160** to the ambient in the guide tube opening **118**. The well bottom extensions **121** may be semi-circular or prong shaped and surround the venting member **160**. Further, the well bottom extensions **121** may extend into the guide tube **116** a distance sufficient to protect the venting member **160** from being impacted against, damaged or dislodged by, the stopper of a container inserted into the guide tube. The well bottom extensions **121** may be formed of plastic material which is integral with the rest of the guide tube **116** and well bottom wall **123**. The well bottom extensions **121** may also be used to secure the venting member **160** and more particularly, the base portion **300** of the venting member so that the venting member is retained in place without the need to use an adhesive or other connection means to the guide tube **116**.

[0058] With reference to Fig. 8, another embodiment of the present invention is

shown in which all reference characters refer to like elements shown in the previous drawing figures. As noted above with respect to Figs. 6-7, the well bottom wall upper surface **125** may prevent blood from flowing into the well **117** when the central body **100** is seated against the well bottom wall **123**.

[0059] With continued reference to Fig. 8, the flexible sleeve **150** may be mounted or fitted onto a sleeve connector **330** which is integrally formed with the guide tube **116** within the guide tube opening **118**. A sleeve connector passage **332** may extend through the sleeve connector **330** and connect with a lateral passage **334** that extends from the sleeve connector passage **332** to a guide tube aperture **342** located along the guide tube outer wall. The guide tube aperture **342** may have a venting member **160** disposed in it, and an optional viewing window **340** disposed in it. The viewing window **340** may be transparent or translucent and may permit blood to be viewed by a user through the viewing window so as to detect flash. The viewing window **340** may be disposed next to, circumferentially about, or within the venting member **160** without departing from the intended scope of the invention. In fact, the viewing window **340** and the venting member **160** may be disposed in separate apertures in alternative embodiments. The viewing window **340** also may be unnecessary if flash is detected elsewhere, such as through a translucent or transparent butterfly connection tube, central body, flexible sleeve and/or guide tube.

[0060] The blood drawing device shown in Fig. 8 may be used as follows. The central body **100** may be connected to the guide tube **116** such that the rear portion of the central body seals against the well bottom wall upper surface **125**. Such sealing is not required in this or any other embodiments discussed, but is preferred to limit the amount of blood that may flow into the well space **117** if the central body **100** is disconnected from the guide tube **116**.

[0061] Once the central body **100** is connected to the guide tube **116**, the front cannula **130** or butterfly cannula **184** may be introduced into a lumen, such as a vein, to draw fluid, such as blood. The blood may readily flow through the front cannula **130**,

the first rear cannula **140**, the second rear cannula **141** and into the interior of the flexible sleeve **150**. Air within the blood drawing device **10** that would otherwise prevent or slow the flow of blood into it, may vent through the flexible sleeve **150**, the sleeve connector passage **332**, the lateral passage **334**, and the venting member **160** to the ambient outside the guide tube **116**. Blood that flows into the blood drawing device may be viewed either through the central body **100**, the butterfly connection tube **182** (in embodiments that use a butterfly needle), through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**, or through the optional viewing window **340**. The visual detection of blood indicates positive vein entry, known as flash. Once flash is detected, a fluid sample container may be pressed into the open end **118** of the guide tube **116**, the second rear cannula **141** may pierce the flexible sleeve **150** and the flexible sleeve is pushed back towards the base of the second rear cannula.

[0062] With reference to Fig. 9, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 9 is identical in all respects to that shown in Fig. 8 with the following exception. With respect to Fig. 9, a well passage **336** extends from the well **117** to the aperture **342**. Air may vent from the rear cannula **140** up through the second rear cannula **141** and into the well **117**. The air may then flow through the well passage **336** and the venting member **160**. Blood may fill the well passage **336** and the aperture **340**. Blood may be viewed either through the central body **100**, the butterfly connection tube **182** (in embodiments that use a butterfly needle), through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**, or through the optional viewing window **340**.

[0063] With reference to Fig. 10, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. A venting member **160** may be disposed against the well bottom wall **123** of the guide tube **116**. The venting member **160** base portion **300** may be adhered

to the well bottom wall of the guide tube **116**, pressure fit onto the cannula **140**, or otherwise fixed into position. A central well opening **338** may extend through the venting member **160** and the well bottom wall **123** to permit air and blood to flow into the well **117**. Alternatively, the central well opening **338** may be reduced in diameter so that the cannula **140** seals against the well bottom wall **123** and/or the venting member **160**. The venting member **160** may have a base **300** separated from a barb portion **302** by an annular recess. The barb portion **302** may be adapted to have an open end of a flexible sleeve **150** mounted thereon. Alternatively, the venting member **160** need not have any annular recess so long as the flexible sleeve **150** has a base portion **300** which provides an air path for air to flow from inside the flexible sleeve **150** to the interior of the guide tube **116**. The air path may be provided in whole or in part by well bottom wall **123** features such as dimples **217** (Fig. 4), radial lines **219** (Fig. 5) or the like.

[0064] With continued reference to Fig. 10, when the front cannula **130** or butterfly cannula **184** is introduced to a lumen, such as a vein, to draw fluid, such as blood, the blood may readily flow through the front cannula, the first rear cannula **140** and into the interior of the flexible sleeve **150**. Air within the blood drawing device **10** that would otherwise prevent or slow the flow of blood into it, may vent through the flexible sleeve **150** and the venting member **160** through the venting member base **300** to the ambient within the guide tube **116**. The venting member base **300** may provide a surface for air to escape from the venting member **160**. Blood that flows into the blood drawing device may be viewed either through the central body **100**, the butterfly connection tube **182** (in embodiments that use a butterfly needle) or through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**. The visual detection of blood indicates positive vein entry, known as flash. Once flash is detected, a fluid sample container may be pressed into the open end **118** of the guide tube **116**, the rear cannula **140** may pierce the flexible sleeve **150** and the flexible sleeve is pushed back towards the base of the second rear cannula.

[0065] With reference to Fig. 11, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 11 is identical in all respects to that shown in Fig. 10 with the following exception. With respect to Fig. 11, a well passage **336** extends from the well **117** to the aperture **342**. After air vents through the venting member **160**, blood may flow from the rear cannula **140** up through the central well opening **338** and into the well **117**. The blood may then flow through the well passage **336** and to the viewing window **340**. Blood may be viewed either through the central body **100**, the butterfly connection tube **182** (in embodiments that use a butterfly needle), through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**, or through the optional viewing window **340**. The well **117** may be formed with sufficient space to permit blood to flow to the viewing window without creating significant air back-pressure in the well passage **336** and aperture **342**.

[0066] With reference to Fig. 12, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 12 is identical in all respects to that shown in Fig. 11 with the following exception. With respect to Fig. 12, one or more well bottom extensions **121** may extend from the well bottom wall **123**. The well bottom extensions **121** may surround the venting member **160** in whole or in part and may be formed so as to leave an air space for air to flow from the interior of the sleeve **150** through the venting member **160** to the ambient in the guide tube opening **118**. The well bottom extensions **121** may be semi-circular or prong shaped and surround the venting member **160**. Further, the well bottom extensions **121** may extend into the guide tube **116** a distance sufficient to protect the venting member **160** from being impacted against, damaged or dislodged by, the stopper of a container inserted into the guide tube. The well bottom extensions **121** may be formed of plastic material which is integral with the rest of the guide tube **116** and well bottom wall **123**. The well bottom extensions **121** may also be used to secure the venting member **160** and more

particularly, the base portion **300** of the venting member so that the venting member is retained in place without the need to use an adhesive or other connection means to the guide tube **116**.

[0067] With reference to Fig. 13, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 13 is identical in all respects to that shown in Fig. 10 with the following two exceptions. With respect to Fig. 13, one or more well bottom extensions **121** may extend from the well bottom wall **123**. The well bottom extensions **121** may surround the venting member **160** in whole or in part and may be formed so as to leave an air space for air to flow from the interior of the sleeve **150** through the venting member **160** to the ambient in the guide tube opening **118**. The well bottom extensions **121** may be semi-circular or prong shaped and surround the venting member **160**. Further, the well bottom extensions **121** may extend into the guide tube **116** a distance sufficient to protect the venting member **160** from being impacted against, damaged or dislodged by, the stopper of a container inserted into the guide tube. The well bottom extensions **121** may be formed of plastic material which is integral with the rest of the guide tube **116** and well bottom wall **123**. The well bottom extensions **121** may also be used to secure the venting member **160** and more particularly, the base portion **300** of the venting member so that the venting member is retained in place without the need to use an adhesive or other connection means to the guide tube **116**. Further, in Fig. 13 the central body **100** may be connected to the guide tube **116** such that the rear portion of the central body seals against the well bottom wall upper surface **125**. Such sealing is not required in this or any other embodiments discussed, but is preferred to limit the amount of blood that may flow into the well space **117** if the central body **100** is disconnected from the guide tube **116**.

[0068] With reference to Fig. 14, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The well bottom wall **123** may have a sealing membrane **310** made of

material similar to or the same as the flexible sleeve **150** which may prevent blood from flowing into the well **117** when the cannula **140** is inserted through and/or withdrawn from it.

[0069] With continued reference to Fig. 14, the flexible sleeve **150** may be mounted or fitted onto a sleeve connector **330** which is integrally formed with the guide tube **116** within the guide tube interior opening **127**. A central well opening **338** may extend through the sleeve connector **330** and connect with a lateral passage **334** that extends from the central well opening **338** to a guide tube aperture **342** located along the guide tube outer wall. The guide tube aperture **342** may have a venting member **160** disposed in it, and an optional viewing window **340** disposed in it. The viewing window **340** may be transparent or translucent and may permit blood to be viewed by a user through the viewing window so as to detect flash. The viewing window **340** may be disposed next to, circumferentially about, or within the venting member **160** without departing from the intended scope of the invention. In fact, the viewing window **340** and the venting member **160** may be disposed in separate apertures in alternative embodiments. The viewing window **340** also may be unnecessary if flash is detected elsewhere, such as through a translucent or transparent butterfly connection tube, central body, flexible sleeve and/or guide tube. The blood drawing device shown in Fig. 14 may be used in the same manner as that described above in connection with Fig. 8.

[0070] With reference to Fig. 15, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 15 is identical in all respects to that shown in Fig. 9 with the following exception. With respect to Fig. 15, the central well opening **338** is defined by the well bottom wall **123** and the sleeve connector **330**. The second rear cannula (shown in Fig. 9) is not provided. When the front cannula **130** is introduced to the vein of a patient air may vent from the rear cannula **140** up through the central well opening **338** and into the well **117**. The air may then flow through the well passage **336** and the venting member **160**. After the air is vented, blood may fill

the well passage 336 and the aperture 340. Blood may be viewed either through the central body 100, the butterfly connection tube 182 (in embodiments that use a butterfly needle), through a transparent or translucent flexible sleeve 150 and transparent or translucent guide tube 116, or through the optional viewing window 340.

[0071] With reference to Fig. 16, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The flexible sleeve 150 may be mounted or fitted onto a sleeve connector 330 which is integrally formed with the guide tube 116 within the guide tube opening 118. A central well opening 338 may extend through the sleeve connector 330 and connect with a well 117. A venting member 160 which may be a flexible membrane or other porous material may be disposed along the interior of the well bottom wall 123 so as to provide a blood barrier between the central well opening 338 and the well 117. A well passage 336 may extend from the well 117 to the outside of the guide tube 116 outer wall. One or more raised features 344 may be provided adjacent to the end of the well passage 336 to assist a user in tactically sensing the location of the well passage so as not to block it with the user's fingers or hand.

[0072] The blood drawing device shown in Fig. 16 may be used as follows. The central body 100 may be connected to the guide tube 116 such that the rear cannula 140 extends through the venting member 160. Once the central body 100 is connected to the guide tube 116, the front cannula 130 or butterfly cannula 184 (in alternative embodiments that utilize a butterfly needle) may be introduced into a lumen, such as a vein, to draw fluid, such as blood. The blood may readily flow through the front cannula 130, the rear cannula 140 and into the interior of the flexible sleeve 150. Air within the blood drawing device 10 that would otherwise prevent or slow the flow of blood into it, may vent through the flexible sleeve 150, the central well opening 338, the venting member 160 and the well passage 336 to the ambient outside the guide tube 116. Blood that flows into the blood drawing device may be viewed either through the central body 100, the butterfly connection tube 182 (in embodiments that use a butterfly

needle), or through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**. The visual detection of blood indicates positive vein entry, known as flash. Once flash is detected, a fluid sample container may be pressed into the open end **118** of the guide tube **116**, the second rear cannula **141** may pierce the flexible sleeve **150** and the flexible sleeve is pushed back towards the base of the second rear cannula.

[0073] With reference to Fig. 17, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The flexible sleeve **150** may be mounted or fitted onto a sleeve connector **330** which is integrally formed with the guide tube **116** within the guide tube opening **118**. A central well opening **338** may be defined by a second rear cannula **141** and provide fluid communication between the interior of a flexible sleeve **150** and a well **117** provided in the guide tube **116**. A well passage **336** may extend from the well **117** to a guide tube aperture **342** located along the guide tube **116** outer wall. The guide tube aperture **342** may have a viewing window **340** disposed in it. The viewing window **340** may be transparent or translucent and may permit blood to be viewed by a user through the viewing window so as to detect flash. The flexible sleeve **150** may include a side tubulation **154** in which a venting member **160** is inserted.

[0074] The blood drawing device shown in Fig. 17 may be used as follows. The central body **100** may be connected to the guide tube **116**. Once the central body **100** is connected to the guide tube **116**, the front cannula **130** or butterfly cannula **184** may be introduced into a lumen, such as a vein, to draw fluid, such as blood. The blood may readily flow through the front cannula **130**, the first rear cannula **140**, the second rear cannula **141** and into the interior of the flexible sleeve **150**. Air within the blood drawing device **10** that would otherwise prevent or slow the flow of blood into it, may vent through the venting member **160** provided in the side tubulation **154** in the flexible sleeve **150** to the ambient inside the guide tube **116**. Blood that flows into the blood drawing device may be viewed either through the central body **100**, the butterfly

connection tube **182** (in embodiments that use a butterfly needle), through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**, or through the optional viewing window **340**. The viewing window **340** may be unnecessary if flash is detected elsewhere, such as through a translucent or transparent butterfly connection tube, central body, flexible sleeve and/or guide tube.

[0075] With reference to Fig. 18, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 18 is identical in all respects to that shown in Fig. 17 with the following exception. In Fig. 18, an air-permeable, blood impermeable flexible sleeve **151** replaces the flexible sleeve **150** shown in Fig. 17. The air-permeable, blood-impermeable sleeve **151** serves as a venting member.

[0076] The air-permeable, completely or partially blood-impermeable flexible sleeve **151** may be constructed of a material that is largely air-permeable, but partially, largely or entirely impermeable to blood. The air-permeable sleeve **151** may be used to isolate the rear cannula **140** of a blood drawing device from the ambient in the same manner as conventional sleeve may isolate rear cannulae. During a blood drawing procedure using a device not equipped with a means for venting air from the sleeve, blood from a lumen may be slowed or prevented from entering the device due to air back pressure in the device. In these devices the air in the device may be trapped because there is no vent provided. In the present embodiment, an air-permeable sleeve **151** replaces a conventional sleeve in the guide tube **116**. The air-permeable sleeve **151** may provide a pathway to vent air from the device interior, through the sleeve wall, to the ambient. As the air is vented, the blood filling the device may contact the air-permeable sleeve **151**. However, the air-permeable sleeve **151** may prevent or retard the flow of blood through its wall because the pore size of the air-permeable sleeve may be large enough to allow the passage of air, but too small to allow much or any blood to pass. This air passage-blood blockage may permit blood to fill the needle and/or the sleeve **151** more readily because there is reduced or no air back pressure inhibiting the flow of blood into

the blood drawing device. As a result, a blood drawing device equipped with the air-permeable sleeve **151** may indicate flash (the visual indication of blood flow into the needle) more readily. The air-permeable sleeve **151** may be used with conventional needle drawing or infusion sets (such as butterfly needles), hypodermic needles, or the like, to enhance flash indication.

[0077] The air-permeable sleeve **151** may be made of any suitable material that is completely or at least partially air-permeable and substantially blood impermeable, such as for example, low density polyethylene or low density rubber. One example of a method of making such material is described in U.S. Patent No. 5,641,442. A second example may be made of crumbed material of sufficiently low density/high flexibility to allow the required flexibility in spite of the use of thermal binders like polyethylene. Low density material such as low density silicone may be sifted using a #80 mesh and mixed with #100 mesh low density polyethylene. This mixture may be heated at approximately 280° F and injected into a cavity mold to form the selectively porous sleeve **151**.

[0078] An air-permeable sleeve may be constructed of porous material formed from the combination of a hydrophobic porous material with a hydrophilic porous agent. The hydrophobic porous material, for example, may be a polymeric matrix of either thermoplastic resins such as polyvinyl chloride or copolymers thereof, or synthetic or natural thermosetting rubber-like polymers. In a second example, the polymeric matrix may be rubber-like polymers combined with additives such as anti-degradants, cross-linking agents, cure inhibitors, platinum and other type catalysts, inert fillers, or like materials used to compound thermosetting compounds, and intimately mixed with a hydrophilic porous agent such as silica hydrogel, precipitated hydrated silica, for example such as that sold under the trademark Hi-Sil from PPG Industries, or polyacrylamide gel, cross-linked homopolymer of acrylamide, for example such as that sold under the trademark Agrosoake from Agrosoake International, inert fillers and/or water or solvent soluble porosics. In a third example, the polymeric matrix may be

made of a synthetic or natural thermosetting polymer or copolymer, such as those that may be made in accordance with the methods disclosed in U.S. Patent No. 4,548,835 to Takahashi, et al. and U.S. Patent No. 4,153,760 to Sundberg et al, for example, each of which is hereby incorporated by reference.

[0079] The porous agent may be prepared by polymerizing acrylamide in the presence of an aqueous sodium carbonate to produce a partially hydrolyzed, lightly cross-linked, polyacrylamide gel in accordance with the method disclosed in U.S. Patent No. 3,022,279 to Proffitt, for example, which is hereby incorporated by reference. The polyacrylamide gel may be produced in bead or granular form using an inverse suspension polymerization method for water-soluble monomer, which is disclosed in U.S. Patent No. 2,982,749 to Friedrich et al., for example, and which is hereby incorporated by reference.

[0080] In one embodiment, for example, the hydrophilic granules may be added to the hydrophobic material in sufficient quantities to create a hydrophilic/hydrophobic porous material. The porosity of the hydrophobic material may be manifested by a network of voids/pores extending throughout the matrix or binder, between neighboring particles of the dispersed filler and portions of the polymeric matrix, which may be achieved by the shrinking of the swollen hydrophilic granules during the dehydration/curing phase. The resultant degree of porosity may be controlled by the amount of water or water substitute added to the polymeric matrix binder material during the mixing phase, the vulcanization of the polymeric matrix (such as for example, under hydrostatic conditions in a steam autoclave to a state of cure using the pressurized steam as a source of heat), the proportion and size of the hydrophilic granules added, the duration of the mixing phase, and the wall thickness of the elastomeric sleeve. The hydrophilic granules may be mixed with a normally hydrophobic binder (and water or a water substitute may be added to control porosity) in a mixing type extruder.

[0081] When this material is formed into an air-permeable flexible sleeve **151**, water-

based liquids such as blood may rapidly soak into the pores/voids containing the granular material, causing the granules to swell and seal the pores/voids contained within the polymeric matrix. Thus, the air-permeable flexible sleeve, which is initially permeable to air, may become relatively impermeable to liquids, such as blood, due to the swelling of the moisture reactive granules entrapped within the pores/voids within the polymeric matrix.

[0082] With reference to Fig. 19, another embodiment of the present invention is shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiment shown in Fig. 19 is identical in all respects to that shown in Fig. 17 with the following exception.

[0083] In the embodiment shown in Fig. 19, a portion of the flexible sleeve **150** may be made to be porous to air. A challenge associated with making the flexible porous sleeve **150** shown in Fig. 19 is that many methods of making a material porous may render the material less flexible. For example, porous "soaker" hoses are made by mixing ground rubber with a thermoplastic such as polyethylene which allows the ground rubber to be "sintered" or stuck together by melting the polyethylene. The addition of the polyethylene makes the hose much stiffer than a plain rubber hose. The same may be true when making a fully porous multiple sample sleeve as shown in Fig. 18 – the resulting sleeve may be less flexible than required. As a result, one solution is to restrict the porous portion of the flexible sleeve **150** to the area near but not all the way at the open end of the sleeve as shown in Fig. 19, so that air can vent from the sleeve while still permitting the open end of the sleeve and the closed end of the sleeve to be made of relatively more flexible material which does not vent. This way the open end of the sleeve may be flexible enough to be stretched over the sleeve connector **330** and the closed end of the sleeve may be flexible enough to be pierced by the second rear cannula **141** without breaking apart while reverting to its original shape after being compressed by the vacuum tube after its removal. This ability to maintain the sleeve's compressibility and "memory" function may be important to the proper functioning of the

sleeve.

[0084] With reference to Fig. 19, the flexible sleeve **150** may be made of a first type of flexible sleeve material which does not substantially vent air (i.e., is the air-impermeable portion of the sleeve) such as the material described in U.S. Patent No. 3,877,465 to Miyake, for example, and of a second type of flexible sleeve material that makes up the venting member **160** which is air-permeable and completely or partially blood-impermeable (i.e., the air-permeable blood-impermeable portion of the sleeve) and formed as a venting port or wall portion added to or incorporated or integrated into the sleeve **150**. The venting member **160** may be of any shape or size suitable for permitting air to vent from the interior of the sleeve **150** while completely or substantially preventing the passage of blood. The venting member **160** may be made of some flexible material other than just air, meaning that the venting member **160** is not merely an opening, but rather a second type of material having numerous small air passages as distinguished from the first type of material that makes up the flexible sleeve **150** or a single larger opening or hole in the first type of material.

[0085] In the embodiment of the invention shown in Fig. 19, the venting member **160** may be constructed of a material that is largely air-permeable, but partially, largely, or entirely impermeable to blood, and preferably made of similar or the same material as used to construct the sleeve **151** shown in Figure 18. Preferably, the venting member **160** may be provided as near to the open end of the flexible sleeve **150** as is practically possible, however, in alternative embodiments, the venting member may be placed in alternate locations closer to or near the closed end of the flexible sleeve **150**.

[0086] The porous venting member **160** shown in Fig. 19 could be achieved by forming a part of the sleeve wall by partially hydrating an absorbent such as polyacrylamide gel with water and mixing it with a heat cured injection molding silicone. When subjected to the typical curing temperatures of 120-200° degrees Celsius the water may convert to steam once the sleeve is ejected from the mold. This may create an open cell structure which contains granules of polyacrylamide. These granules may

be processed further during a post cure phase where the granules are further dehydrated with heated dry air. This drying process may create open spaces around each granule which allows air to escape. These same granules absorb water and swell when exposed to blood, thereby sealing the venting portion to prevent leakage. With particular reference to Fig. 19, the resulting porous blood-impermeable air-permeable ring shaped venting member **160** can be inserted into sleeve molds where transparent silicone can be injected adjacent to both edges of the venting port, thus bonding the venting portion with the transparent, more flexible body portion material of the sleeve.

[0087] With reference to Figs. 20-22, three other embodiments of the present invention are shown in which all reference characters refer to like elements shown in the previous drawing figures. The embodiments shown in Figs. 20-22 are identical in all respects to those shown in Figs. 17-19, respectively, with the following exception. With respect to Figs. 20-22, the central well opening **338** is defined by the well bottom wall **123** and the sleeve connector **330**. The second rear cannula (shown in Figs. 17-19) is not provided. When the front cannula **130** is introduced to the vein of a patient air may vent from the rear cannula **140** through the venting members **160** or air-permeable, blood-impermeable flexible sleeve **151** shown in Figs. 20-22. After the air is vented, blood may fill the well passage **336** and the aperture **340**. Blood may be viewed either through the central body **100**, the butterfly connection tube **182** (in embodiments that use a butterfly needle), through a transparent or translucent flexible sleeve **150** and transparent or translucent guide tube **116**, or through the optional viewing window **340**. As noted above, the size of the well **117** may be sufficient to permit blood to fill the aperture **342** without developing sufficient air back-pressure to prevent such filling.

[0088] It is appreciated that the embodiments of the invention shown in Figs. 1-24 may be altered as follows without departing from the intended scope of the invention. The shoulder **119**, the dimples **217** and the radial lines **219** on the bottom of the well **117** could be replaced by a shoulder, raised dimples or raised radial lines on the surface of the venting member **160** closest to the well bottom wall **123**. Accordingly, the

illustrations provided in Figs. 1, 4 and 5 of the shoulder **119**, the dimples **217** and the radial lines **219** are intended to also illustrate such features as they may be provided on a venting member.

[0089] With regard to Figs. 23-24, the butterfly needle **180** may be connected to the Luer-type hub **102** via a butterfly connection tube **182**. The butterfly needle **180** may include a butterfly (*i.e.*, front) cannula **184** and one or more wings **186**. The butterfly cannula **184** may be inserted directly into the body lumen for blood collection. Flash may be observed in the transparent or translucent butterfly connection tube **182**, in which case the central body **100** need not be transparent or translucent (although it could be).

[0090] With continued reference to Figs. 23-24, known butterfly needles may use a butterfly connection tube **182** approximately 12 or more inches in length. This length of tubing is used so as to provide a sufficiently long column of air to permit flash observation when the blood-drawing device **10** is not provided with an air vent. Specifically, when a butterfly connection tube is used without an air vent, the flow of fluid through the butterfly needle may compress the volume of air in the butterfly connection tube **182**, the fluid passage **110**, the rear cannula **140**, and the space between the rear cannula and the flexible sleeve **150**. Because there is no vent provided, as blood flows into the device, the air in the device exerts an increasing level of backpressure on the blood, which may prevent blood flow and flash detection. The inclusion of a butterfly connection tube approximately 12 inches in length or greater increases the relative volume of air in the blood collection device. The increased volume of air in the device may permit flash detection before the air backpressure in the device rises to a level that prevents further blood flow into the device and could frustrate flash detection. Butterfly connection tubes of this length may be coiled in packaging, and retain some coil memory after they are removed from their packaging. Previously coiled butterfly connection tubes may resist being straightened for use and have an inherent bias towards returning to their coiled shape. Accordingly, manipulation of a

butterfly needle attached to a previously coiled butterfly connection tube may be difficult due to the connection tube's tendency to recoil. This action can be the cause of accidental needle sticks for the healthcare worker and the patient. Furthermore, the coil memory of the tubing may make handling generally difficult for lumen insertion, and/or maintenance of the needle in the lumen.

[0091] The butterfly connection tube **182** used in the devices shown in Figs. 23-24 may be less than approximately 12 inches in length, and more preferably, may be only a few inches in length as a result of the inclusion of a venting member **160** in the blood-drawing device **10**. The inclusion of the venting member **160** may obviate the need for a relatively long column of air in the butterfly connection tube that otherwise may be needed to indicate flash. The use of a shortened butterfly connection tube **182** may also obviate the need to coil the tube prior to use, thereby eliminating the issues associated with coil memory in the tube, as well as make it possible to use rigid or semi-rigid connection tubes that may better enable placement of the front cannula into the body lumen.

[0092] Each of the embodiments of the present invention shown in all of the afore-noted figures may also utilize a transparent or translucent flexible sleeve **150** to provide flash detection. An example of a transparent sleeve is disclosed in U.S. Patent No. 3,886,930 to Ryan, which is hereby incorporated by reference. Use of a transparent or translucent sleeve **150** may make it unnecessary for the central body **100** or other elements of the device to be constructed of transparent or translucent material because the flash may be detected through the wall of the sleeve itself and thereby allow for the retrofitting of known blood-drawing devices to provide air venting and flash detection without other modification of the device. Use of a transparent or translucent sleeve **150** may also obviate the need to have discreet front and rear cannulae **130** and **140**. The front and rear cannulae may be constructed from a single integral piece of material because in this embodiment of the invention there may be no need to view flash in the central body **100**.

[0093] Each of the embodiments of the invention described above may also be modified such that the porous member **160** includes or is constructed of any one or more of a number of substances that may permit air venting, and limit and reduce blood seepage, but not completely prevent blood seepage through the particular porous structure. For example, hydrophilic and/or hydrophobic substances such as polyethylene and granular starch, cellulose, polyacrylamide gel, or the like may be used. Such substances are known in the art, and may be used to permit gas (e.g., air) to flow through them, but absorb or block liquid substances. Accordingly, a porous member comprised of these materials may be used to permit the air in a blood drawing device to vent past it until it is contacted by a liquid, such as blood, at which time the blood may be absorbed.

[0094] Similarly, glass powder or fiber may be used to simulate clotting, or a clotting agent, such as dilute Russell Viper Venom, may be used to permit air venting with little or reduced blood seepage. Russell Viper Venom is known in the art as a clotting agent. A porous member **160** impregnated with a clotting agent or simulating clotting agent may be used to permit the air in a blood drawing device to vent until it is contacted by blood, at which time the blood may clot or act as clotted and reduce further blood seepage through the porous member. As a result, use of hydrophilic and/or clotting agents in the previously described porous member may permit improved blood flow into a blood drawing device and flash detection.

[0095] It will be apparent to those skilled in the art that variations and modifications of the present invention can be made without departing from the scope or spirit of the invention. For example, the shape, size, and material selection for the various components of the blood-drawing device may be changed without departing from the intended scope of the invention and appended claims. It is further appreciated that forming one or more elements of the apparatus embodiments of the present invention integrally as opposed to separately is intended to fall within the scope of the invention and appended claims.

WHAT IS CLAIMED IS:

1. A guide tube assembly for connection to a device for drawing fluid from a lumen, comprising:

a guide tube (116) having an open end (118) and a well (117);

a flexible sleeve (150, 151) having an interior space in fluid communication with the well (117) and extending into the guide tube (116);

one or more passages (332, 334, 336, 338) extending through the guide tube (116) which are in fluid communication with the flexible sleeve (150) interior space; and

a venting member (160) connected to the guide tube (116) or incorporated into the flexible sleeve (150, 151), said venting member in fluid communication with the one or more passages (332, 334, 336, 338) and disposed between the flexible sleeve (150, 151) interior space and an ambient.

2. The guide tube assembly of Claim 1, wherein:

the guide tube (116) has an interior opening (127) and a substantially closed end (129);

the well (117) is defined by a well bottom wall (123) and is formed in the substantially closed end (129) of the guide tube (116);

one of the one or more passages is a central well opening (338) extending from the well (117) to the guide tube interior opening (127);

the venting member (160) is connected to the guide tube (116) within the guide tube interior opening (127);

the flexible sleeve (150) is mounted on the venting member (160) and extends into the guide tube interior opening (127), said sleeve defining an interior space; and

one or more well bottom extensions (121) extend into the guide tube interior opening (127) adjacent to the venting member (160).

3. The guide tube of Claim 2 wherein the venting member (160) has a base (300) exposed to the ambient and a barb portion (302) adapted to receive the flexible sleeve (150).

4. The guide tube of Claim 3 wherein the venting member (160) is adhered to the well bottom wall (123).
5. The guide tube of Claim 3 wherein the venting member (160) contacts raised dimples (217) provided on the well bottom wall (123).
6. The guide tube of Claim 3 wherein the venting member (160) contacts a raised shoulder (119) provided on the well bottom wall (123).
7. The guide tube of Claim 3 wherein the venting member (160) contacts raised radial lines (219) provided on the well bottom wall (123).
8. The guide tube of Claim 2 wherein the central well opening (338) is defined by a rear cannula (141) connected to the guide tube (116) and extending into the guide tube interior opening (127).
9. The guide tube of Claim 8 wherein the rear cannula (141) has a stepped diameter (143).
10. The guide tube of Claim 2 further comprising a well bottom wall (123) upper surface (125) adapted to seal against a central body (100) of a blood drawing device (10).
11. The guide tube of Claim 2 wherein the one or more well bottom extensions (121) are adapted to retain the venting member (160) by a frictional fit.
12. The guide tube of Claim 2 wherein the one or more well bottom extensions (121) extend an equal to greater distance into the guide tube interior opening (127) than the venting member (160).
13. The guide tube of Claim 2 further comprising:
 - a well passage (336) extending from the well (117) to an aperture (342) provided in a side wall of the guide tube (116); and
 - a viewing window (344) disposed in the aperture (342).
14. The guide tube of Claim 2 wherein the guide tube (116) and the flexible sleeve (150) are transparent or translucent.
15. The guide tube assembly of Claim 1, wherein:

the guide tube (116) has an interior opening (127) and a substantially closed end (129);

the well (117) is defined by a well bottom wall (123) and is formed in the substantially closed end (129) of the guide tube (116);

one of the one or more passages is a central well opening (338) extending from the well (117) to the guide tube interior opening (127);

the venting member (160) is connected to the guide tube (116) within the guide tube interior opening (127), said venting member having a base (300) and a barb portion (302); and

the flexible sleeve (150) is mounted on the venting member (160) and extends into the guide tube interior opening (127), said sleeve defining an interior space and being mounted on said venting member so that the base (300) of the venting member is exposed to an ambient.

16. The guide tube of Claim 15 wherein the venting member (160) is adhered to the well bottom wall (123).

17. The guide tube of Claim 15 wherein the central well opening (338) is defined by a rear cannula (141) connected to the guide tube (116) and extending into the guide tube interior opening (127).

18. The guide tube of Claim 17 wherein the rear cannula (141) has a stepped diameter (143).

19. The guide tube of Claim 15 further comprising a well bottom wall (123) upper surface (125) adapted to seal against a central body (100) of a blood drawing device (10).

20. The guide tube of Claim 15 further comprising:

a well passage (336) extending from the well (117) to an aperture (342) provided in a side wall of the guide tube (116); and

a viewing window (344) disposed in the aperture (342).

21. The guide tube of Claim 15 wherein the guide tube (116) and the flexible sleeve

(150) are transparent or translucent.

22. The guide tube assembly of Claim 1 further comprising:

a sleeve connector (330) extending from a well bottom wall (123) into a guide tube interior opening (127), and wherein

the guide tube (116) has a substantially closed end (129);

the well (117) is defined by the well bottom wall (123) and is formed in the substantially closed end (129) of the guide tube (116);

one of the one or more passages is a central well opening (338) extending from the well (117) to the guide tube interior opening (127) through the sleeve connector (330);

the flexible sleeve (150) is mounted on the sleeve connector (330) and extends into the guide tube interior opening (127), said sleeve defining an interior space; and

the one or more passages (332, 334, 336, 338) connect the sleeve interior space with an aperture (342) provided in a wall of the guide tube (116).

23. The guide tube of Claim 22 wherein the venting member (160) is disposed in the aperture (342).

24. The guide tube of Claim 23 further comprising a viewing window (340) disposed in the aperture (342).

25. The guide tube of Claim 24 wherein the viewing window (340) is disposed within the venting member (160).

26. The guide tube of Claim 24 wherein the viewing window (340) is disposed about the venting member (160).

27. The guide tube of Claim 24 wherein the viewing window (340) is disposed adjacent to the venting member (160).

28. The guide tube of Claim 22 further comprising a viewing window (340) disposed in the aperture (342).

29. The guide tube of Claim 22 further comprising:

a second aperture in the guide tube (116) wall communicating with the one or

more passages (332, 334, 336, 338); and

a viewing window (340) disposed in the second aperture.

30. The guide tube of Claim 22 wherein the central well opening (338) is defined by a rear cannula (141) connected to the guide tube (116) and extending into the guide tube interior opening (127).

31. The guide tube of Claim 30 wherein the rear cannula (141) has a stepped diameter (143).

32. The guide tube of Claim 22 further comprising a well bottom wall (123) upper surface (125) adapted to seal against a central body (100) of a blood drawing device (10).

33. The guide tube of Claim 22 further comprising a sealing membrane (310) disposed in the well (117) along the well bottom wall (123).

34. The guide tube of Claim 22 wherein the one or more passages (332, 334, 336, 338) communicate with the well (117).

35. The guide tube of Claim 22 wherein the venting member (160) is disposed in the well (117) along the well bottom wall (123).

36. The guide tube of Claim 22 wherein the aperture (340) is surrounded by one or more raised features (344) on the wall of the guide tube (116).

37. The guide tube of Claim 22 wherein the venting member (160) is disposed in a tubulation (154) provided in the side wall of the flexible sleeve (150).

38. The guide tube of Claim 37 further comprising a viewing window (340) disposed in the aperture (342).

39. The guide tube of Claim 37 wherein the central well opening (338) is defined by a rear cannula (141) connected to the guide tube (116) and extending into the guide tube interior opening (127).

40. The guide tube of Claim 39 wherein the rear cannula (141) has a stepped diameter (143).

41. The guide tube of Claim 22 wherein the venting member (160) comprises an air-

permeable sleeve (151) or is integrated into a portion of the flexible sleeve (150).

42. The guide tube of Claim 41 further comprising a viewing window (340) disposed in the aperture (342).

43. The guide tube of Claim 41 wherein the central well opening (338) is defined by a rear cannula (141) connected to the guide tube (116) and extending into the guide tube interior opening (127).

44. The guide tube of Claim 43 wherein the rear cannula (141) has a stepped diameter (143).

45. The guide tube of Claim 22 wherein the guide tube (116) and the flexible sleeve (150) are transparent or translucent.

46. The device of Claims 2, 15 and 22 wherein the venting member (160) is permeable to air and impermeable to blood.

47. The device of Claim 1, further comprising:

a first connector (103) of a Luer-adapter connected to the guide tube (116); and

a butterfly needle (180) connected to the first connector of the Luer-adapter by a second connector (102).

48. The device of Claim 1, further comprising:

a first connector (103) of a Luer-adapter integrally formed in an end of the guide tube (116) opposite the guide tube open end (118); and

a butterfly needle (180) connected to the first connector of the Luer-adapter by a second connector (102).

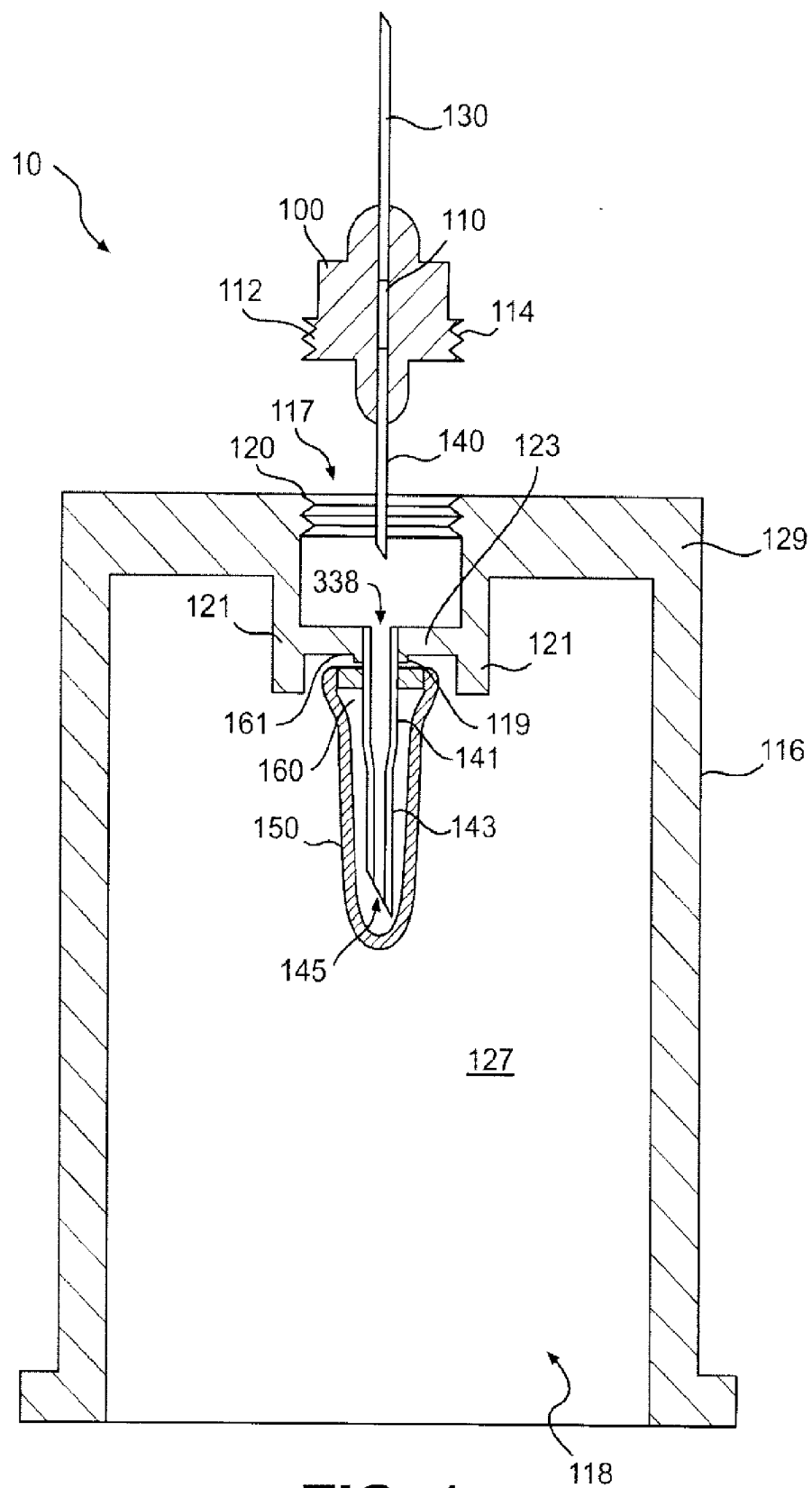


FIG. 1

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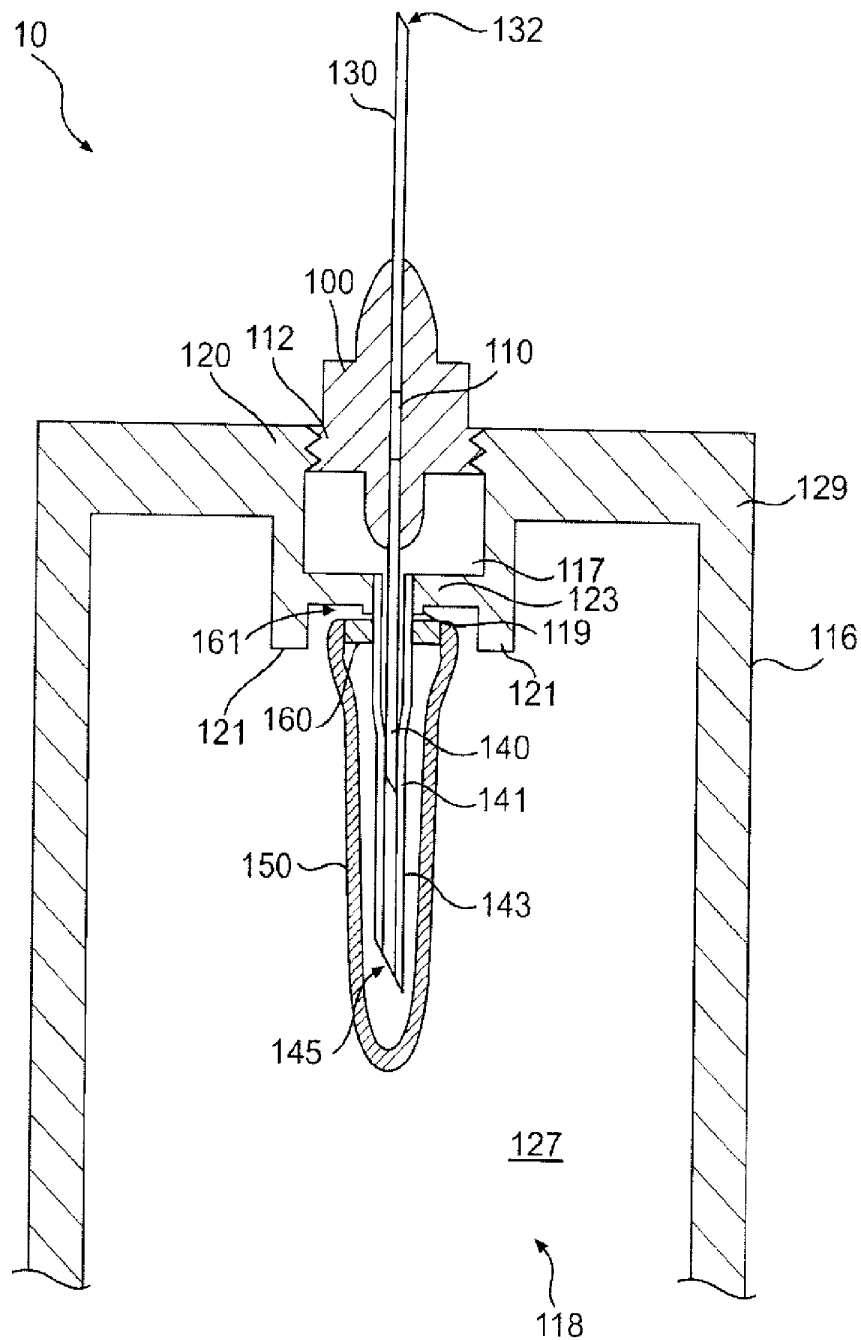


FIG. 2

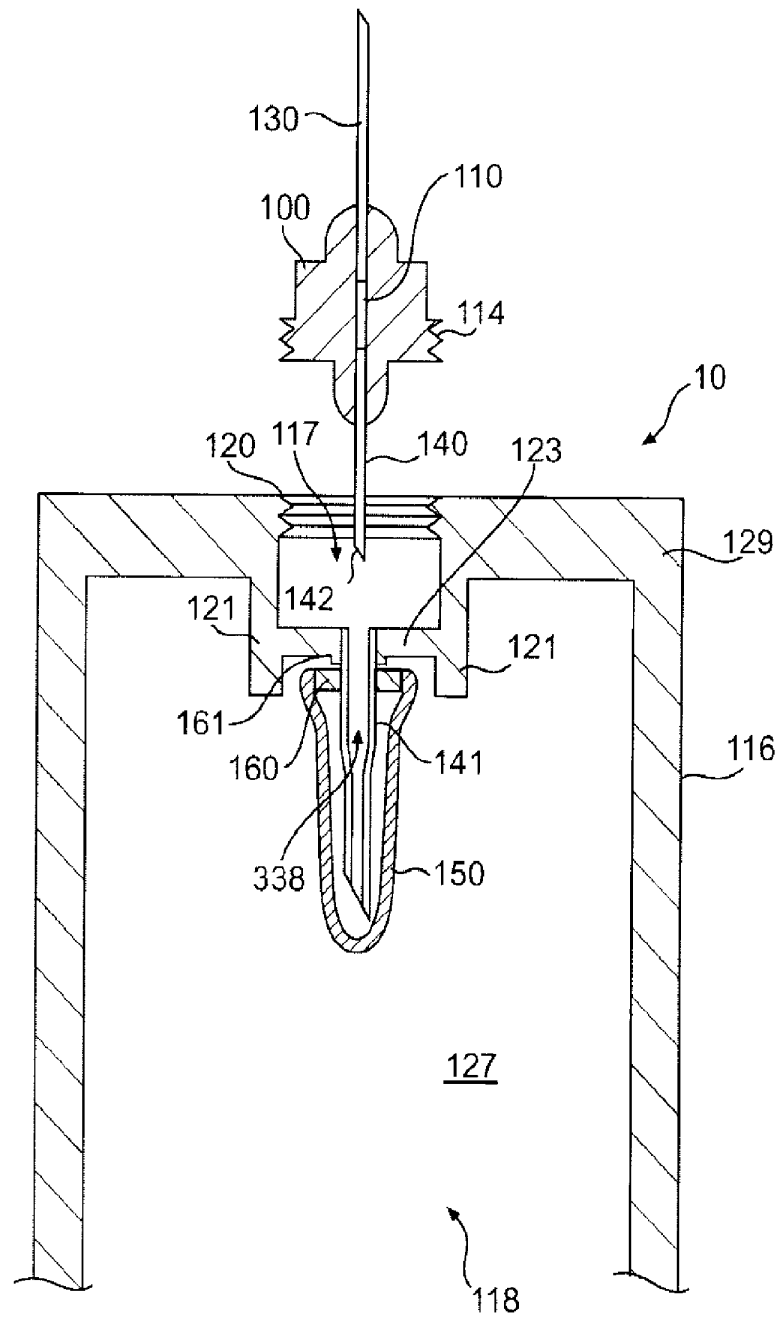


FIG. 3

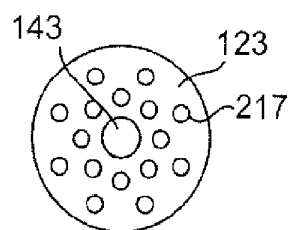


FIG. 4

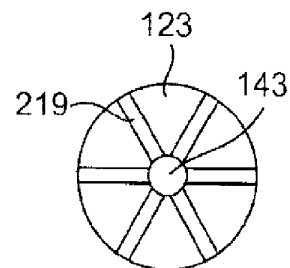
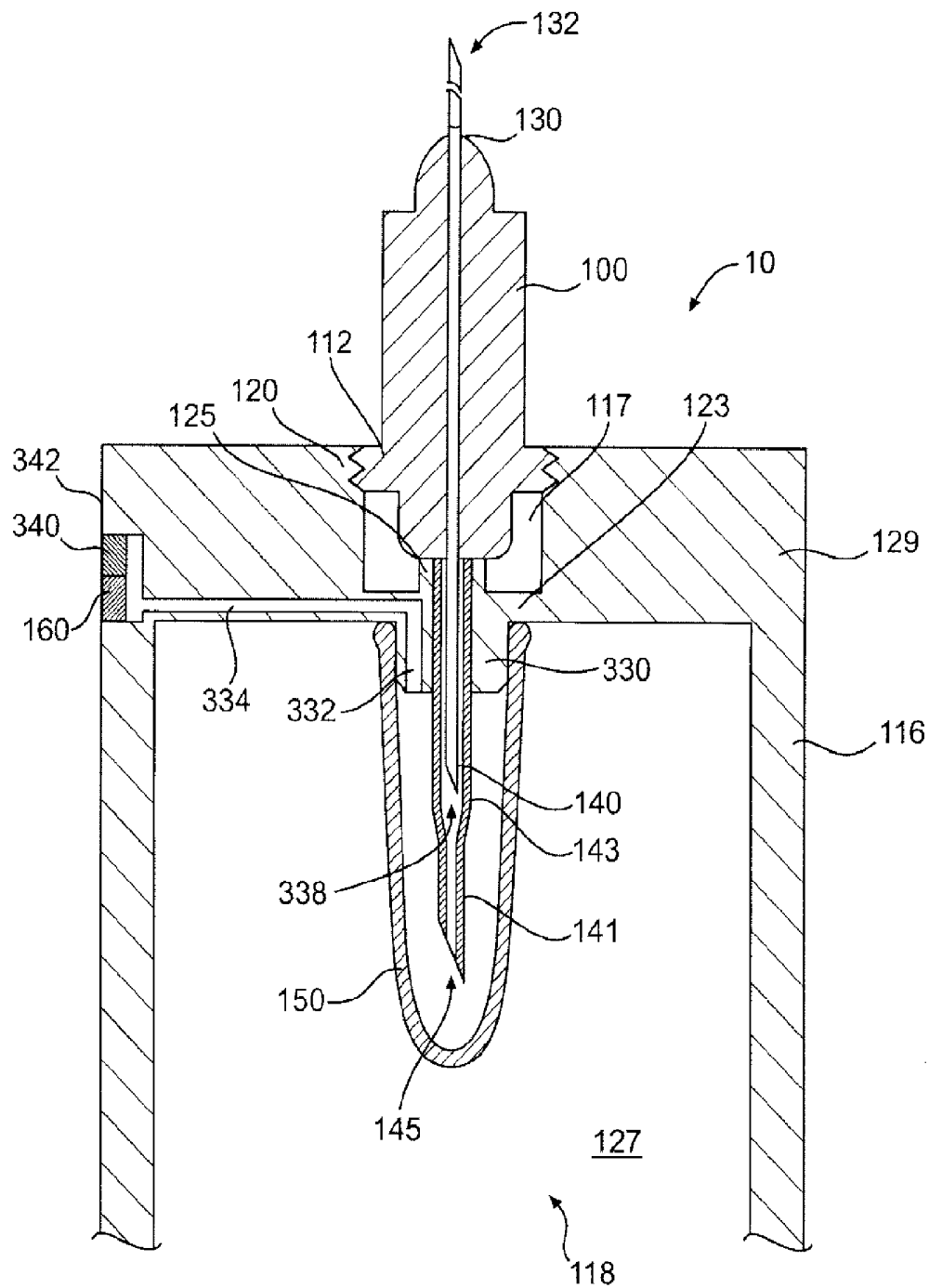


FIG. 5

**FIG. 8**

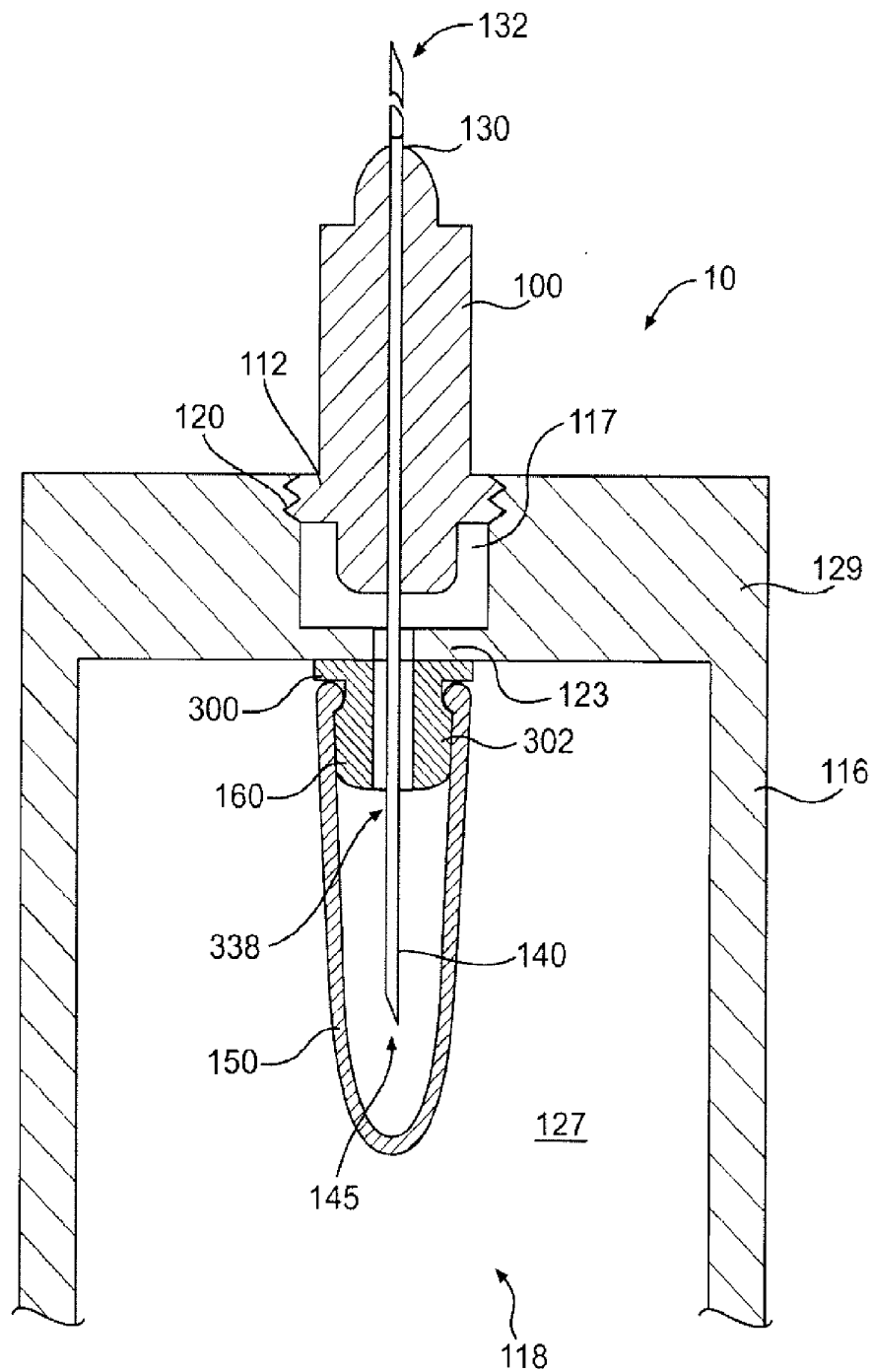


FIG. 10

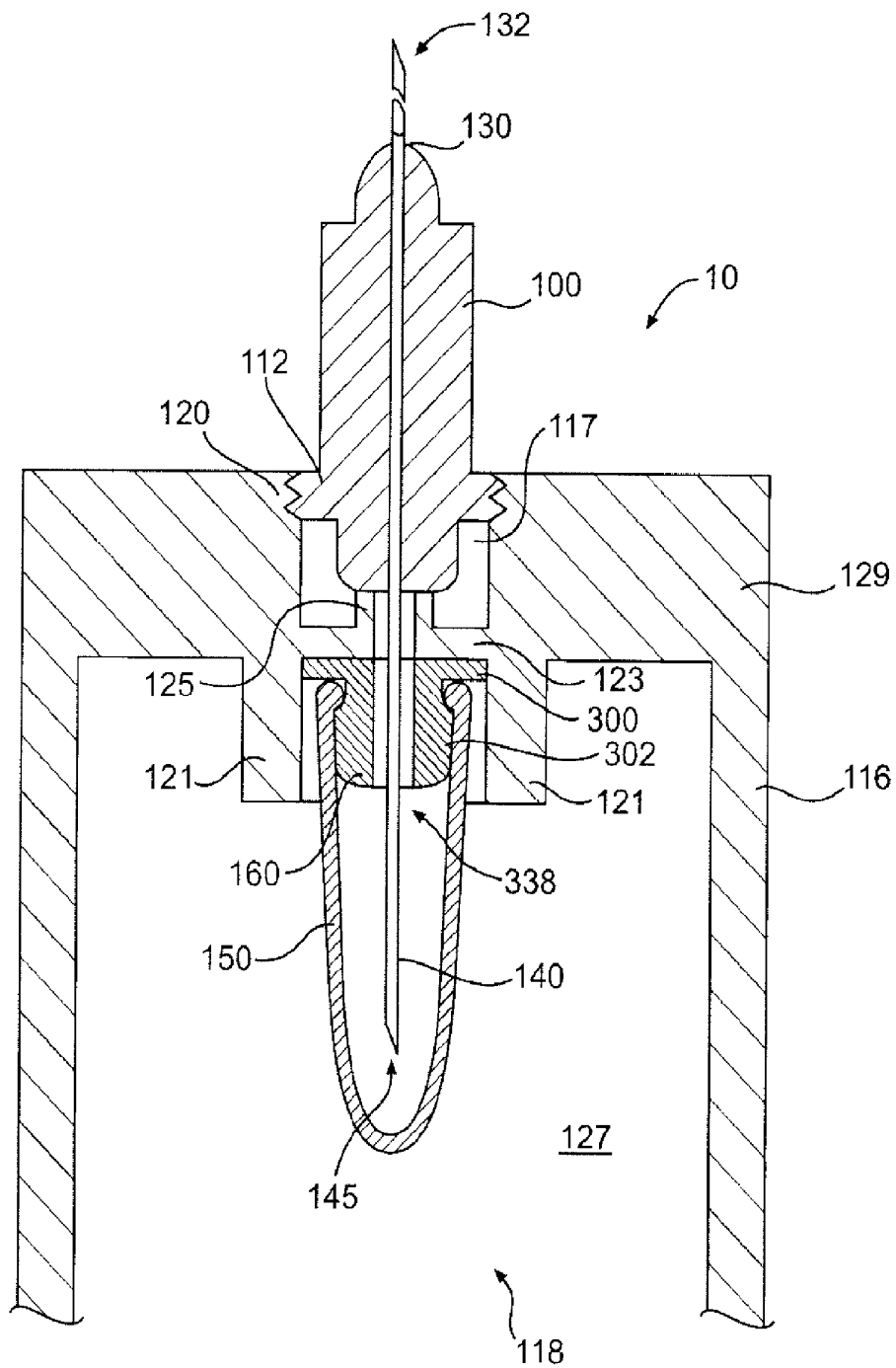


FIG. 13

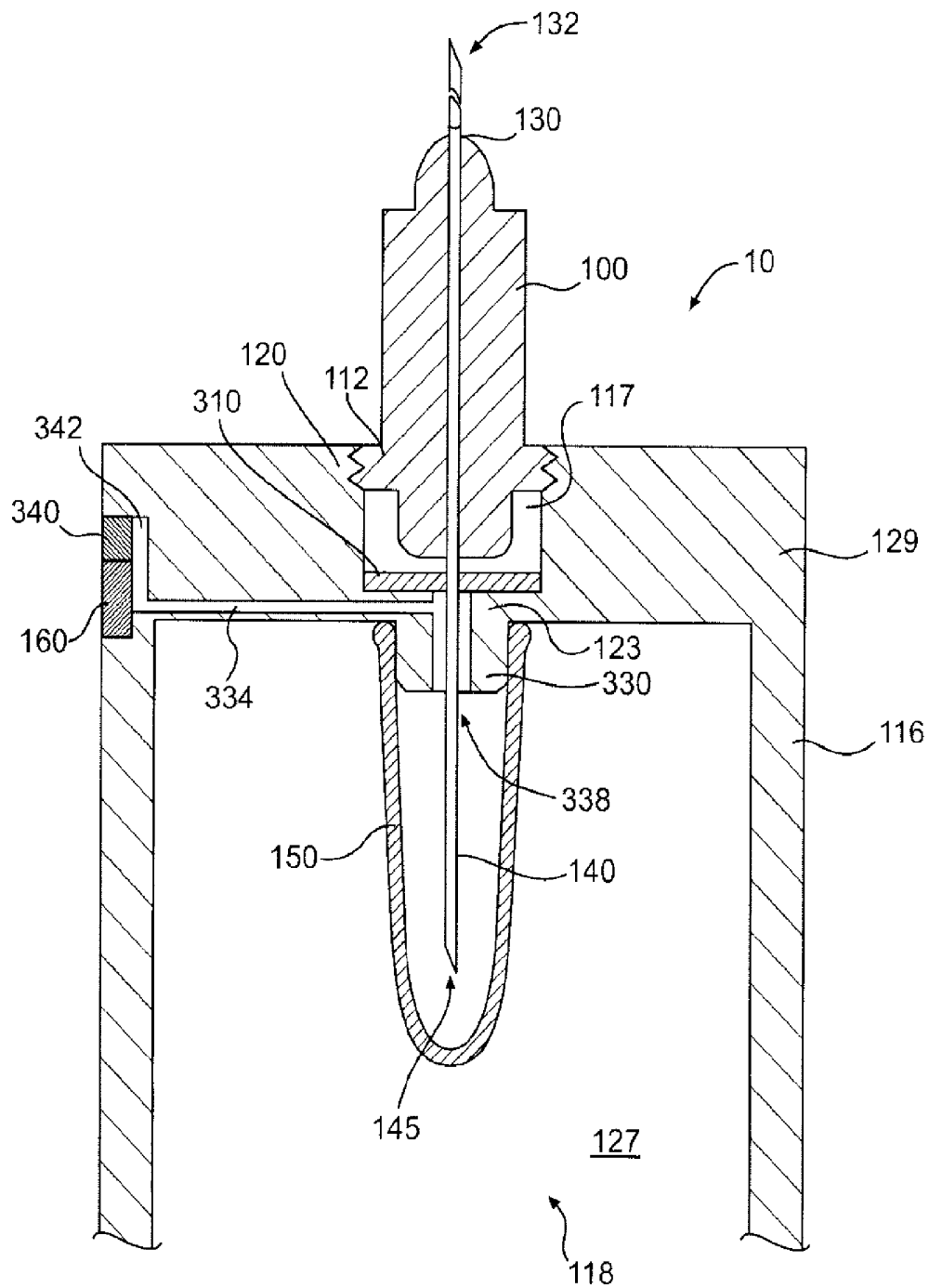
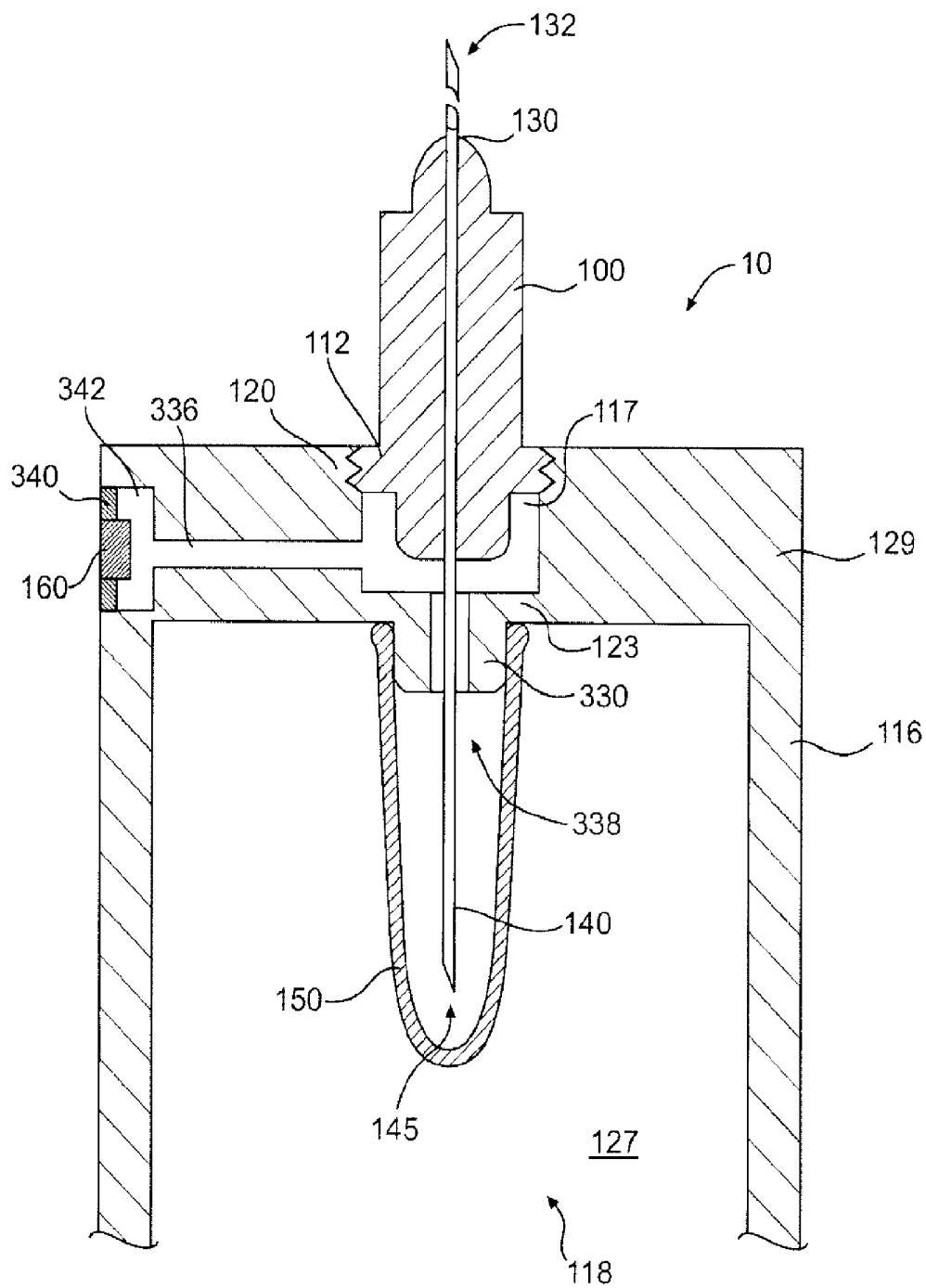


FIG. 14

**FIG. 15**

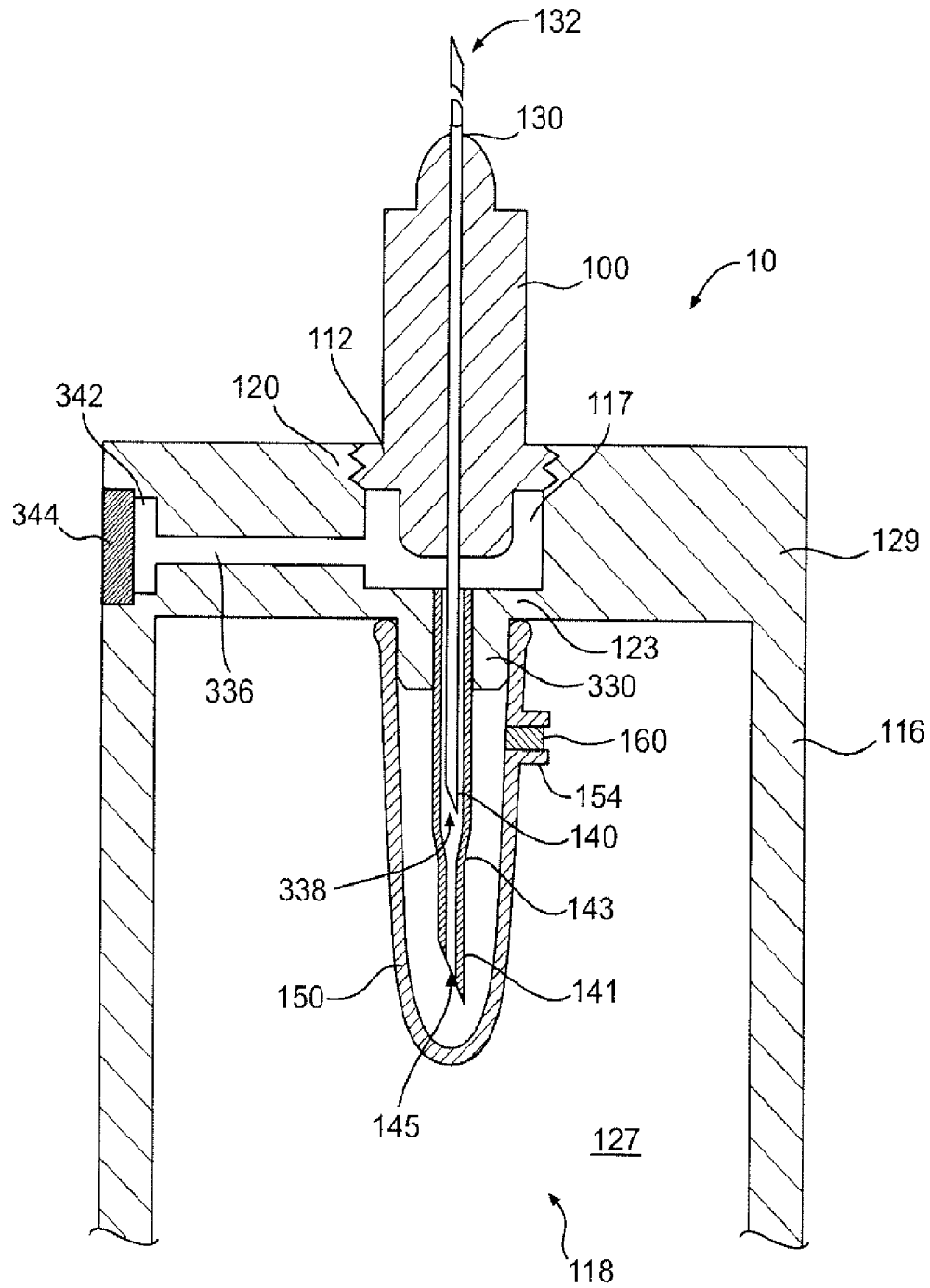


FIG. 17

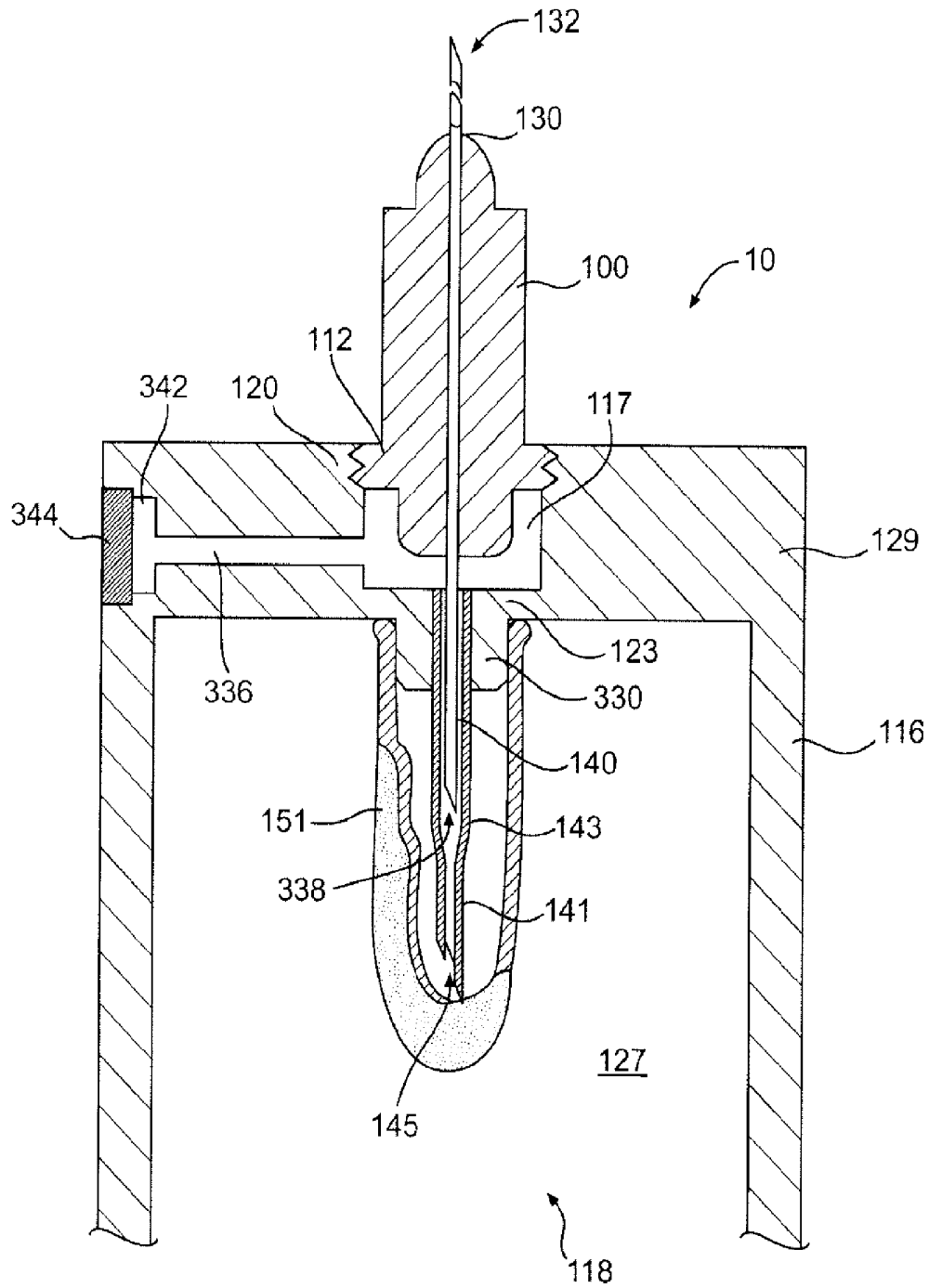


FIG. 18

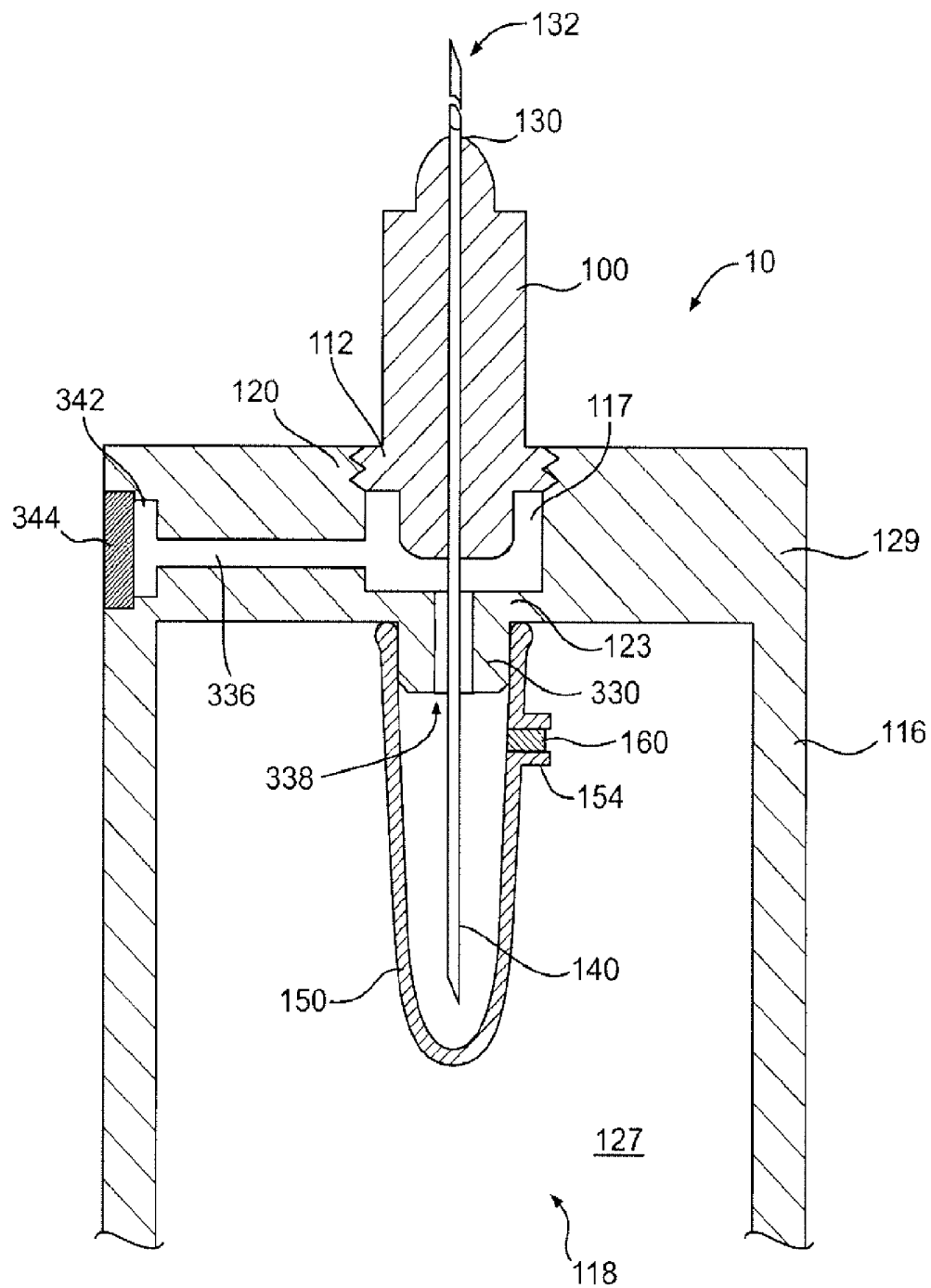


FIG. 20

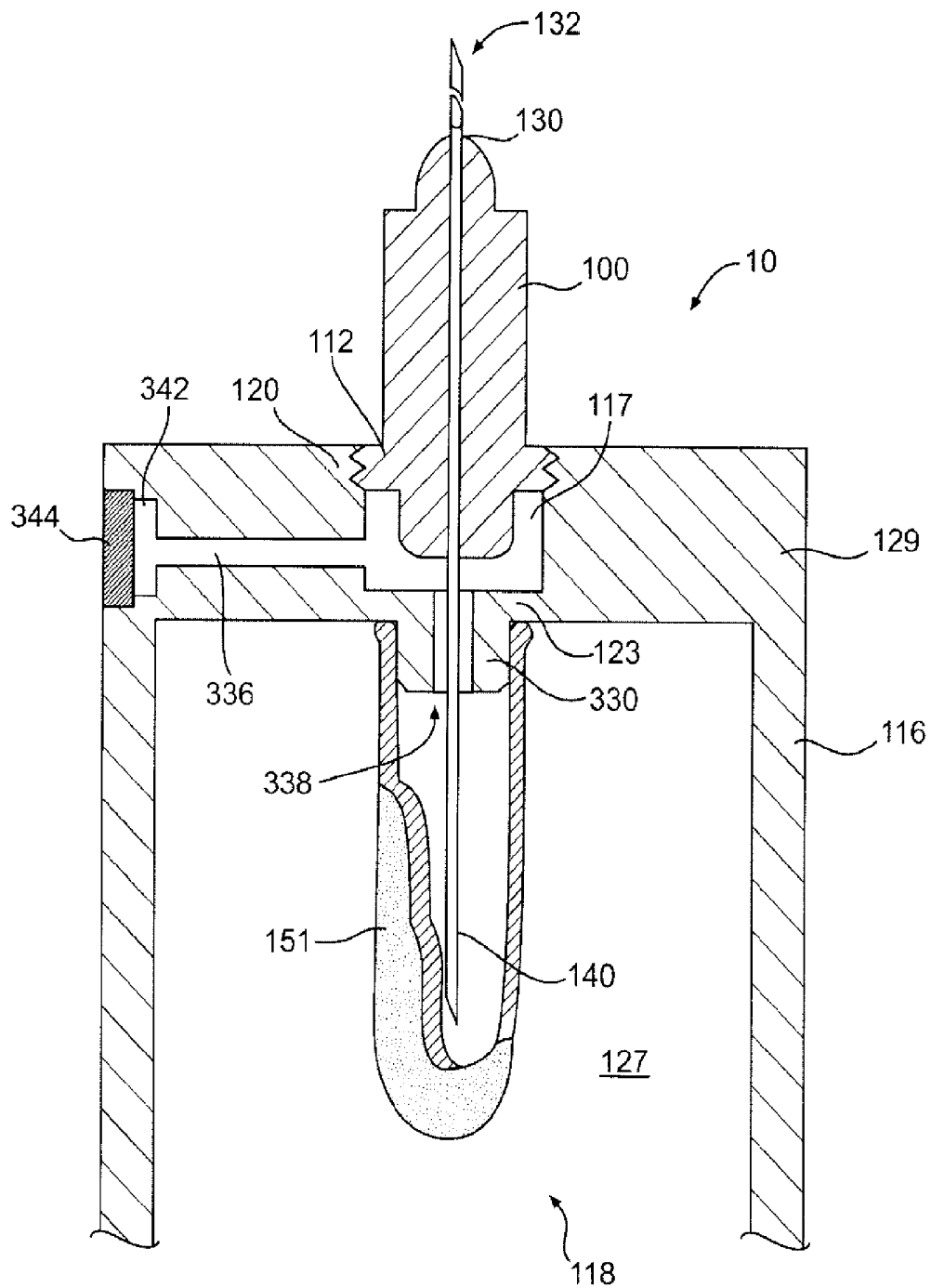


FIG. 21

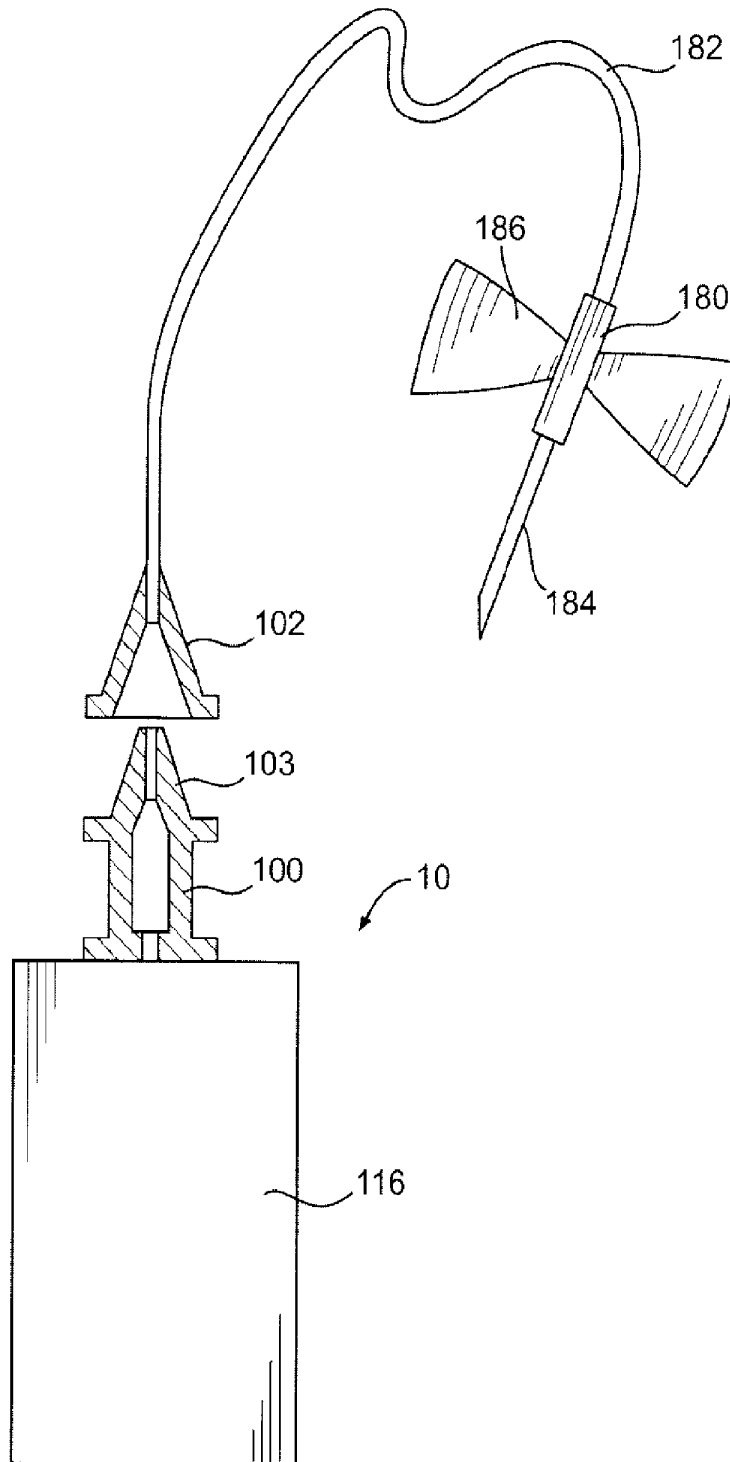


FIG. 23

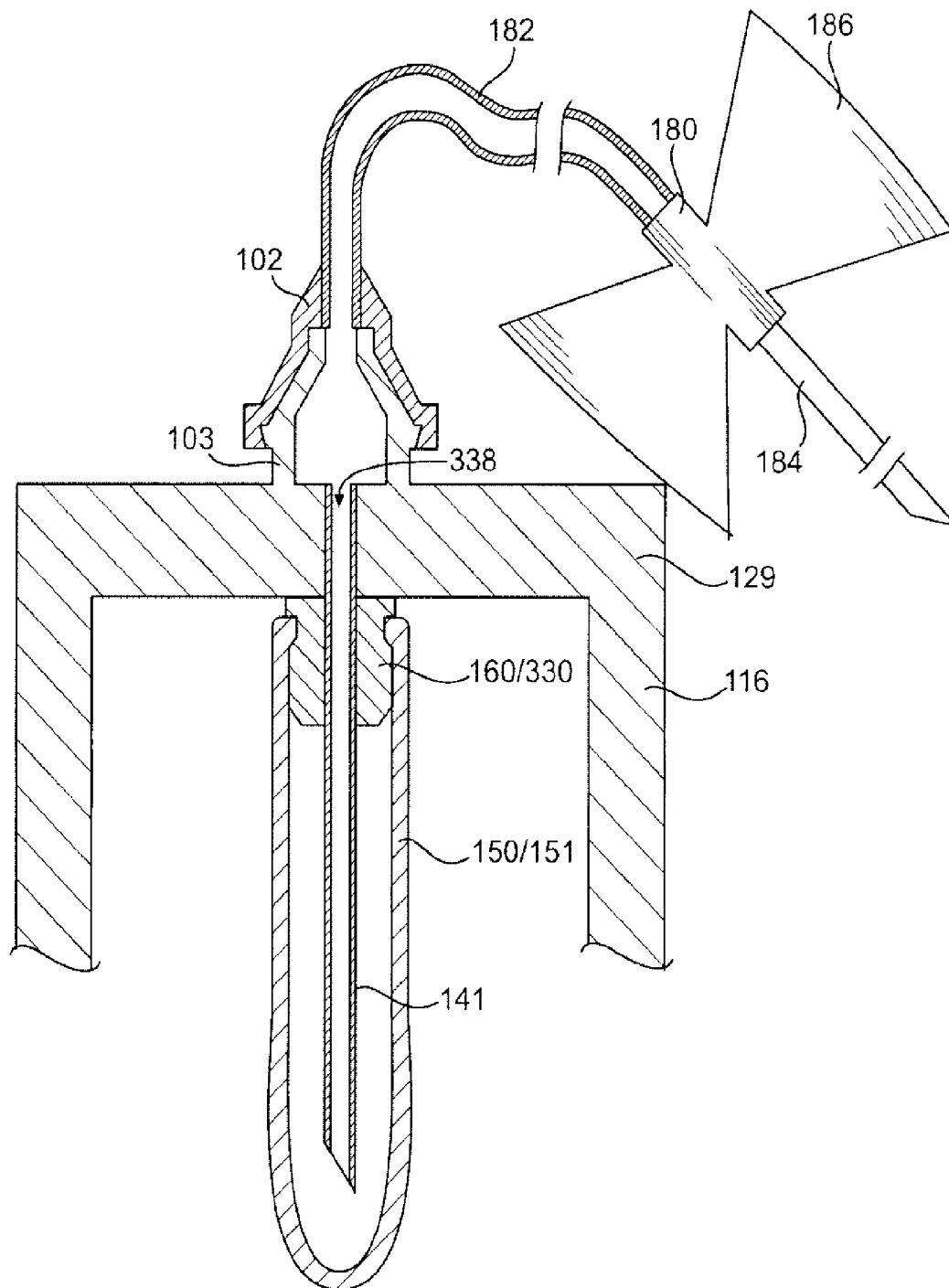


FIG. 24

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2010/040030

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61M 5/36 (2010.01)

USPC - 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)

IPC(8) - A61M 5/36, 5/178 (2010.01)

USPC - 604/122, 164

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

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

MicroPatent, Freepatentsonline, Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2008/0086085 A1 (BROWN) 10 April 2008 (10.04.2008) entire document	1-48
Y	US 2003/0153874 A1 (TAL) 14 August 2003 (14.08.2003) entire document	1-48
Y	EP0 440 479 B1 (VAN HEUGTEN) 07 August 1991 (07.08.1991) entire document	2-14

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

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"E" earlier application or patent but published on or after the international filing date

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

"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

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Date of the actual completion of the international search

12 August 2010

Date of mailing of the international search report

30 AUG 2010

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[Request for examination: Unclaimed
[Number of claims] 4
[Application form] OL
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(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.

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(72) [Inventor]

[Name] Suzuki Issei

[Theme code (reference)]

4C038

[F term (reference)]

4C038 TA06 UJ02 UJ06

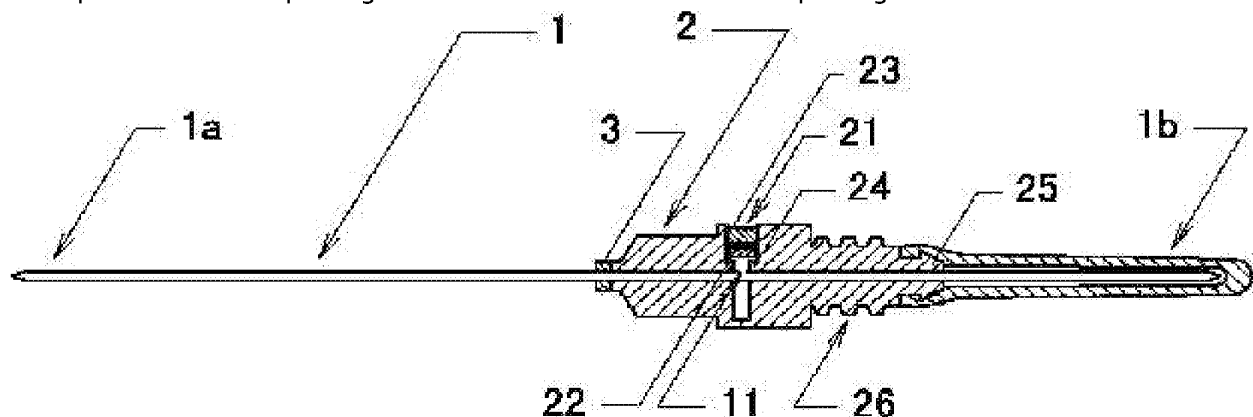
wrap up

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(57) [Summary]

[Problem] To provide a blood collection needle that enables confirmation immediately after puncturing that the needle has definitely punctured a vein of a subject at the time of blood collection.

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 outside and the inside of the needle tube through the hole. an air-permeable, blood-impermeable member (C) engaged with the open end of the passageway; and a needle tube support member (C) engaged with the needle tube support so as to seal one end of the needle tube. A blood collection needle having a rubber-like cap (D) that is closed and a sealing member (E) that 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 blood 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 enters 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 INVENTION 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 immediate confirmation of flashback after one end of the needle is punctured into a vein. Means for Solving 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 through 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 for blocking the inside of the needle tube from the outside when the blood collection tube is attached 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 part of its side wall and blade surfaces at both ends, a needle tube (A) provided so as to cover the hole, and communicating the outside and the inside of the needle tube through the hole. an 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 needle having a rubber-like cap (D) engaged with a support and a sealing member (E) provided in 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 reference to the drawings. FIG. 1 is a sectional view showing one embodiment of the blood collection needle of the present invention. The needle tube 1 is preferably made of stainless steel. 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 provided in any part of the needle tube 1 as long as it is inside the needle tube support 2. The needle tube 1 is provided with a transparent or translucent needle tube support 2 so as to cover the hole 11. The needle tube support 2 is hermetically fixed to the needle tube 1 on the one end 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 the 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 surface of one end 1a of the needle tube 1 is punctured into a vein of a subject through the passage 21, the blood that has entered the inside of the needle tube 1 enters the passage 21 through 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 materials such as polypropylene, Teflon (registered trademark) and silicon rubber can be used. It may 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 passage 21 air-permeable and prevents the blood that has flowed in during blood collection from leaking 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 blood that has flowed from the inside of the needle tube 1 through the hole 11 into the passage 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. After that, when the vacuum blood collection tube is attached to the other end 1b of the needle tube 1, the negative pressure of the vacuum blood collection tube pulls the sealing member 22 toward the needle tube 1 and closes the passage 21, as shown in FIG. As a result, negative pressure is not directly applied to the air-permeable blood-impermeable member 23, so that a predetermined amount of blood can be collected. Further, considering the sealing performance inside the needle tube 1, it is more preferable that the passage 21 is provided with a protrusion 24 for locking the sealing member 22 therein. As for the shape of the projection 24, in addition 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. When one end 1a of the needle tube 1 is punctured into the subject, the air-permeable blood-impermeable 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 passage 21. As a result, immediately after confirming the flash bag, the inside of the needle tube 1 part is sealed. Further, when the vacuum blood collection tube is attached, the negative pressure of the vacuum blood collection tube further brings the sealing member 22 into close contact 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 blade 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

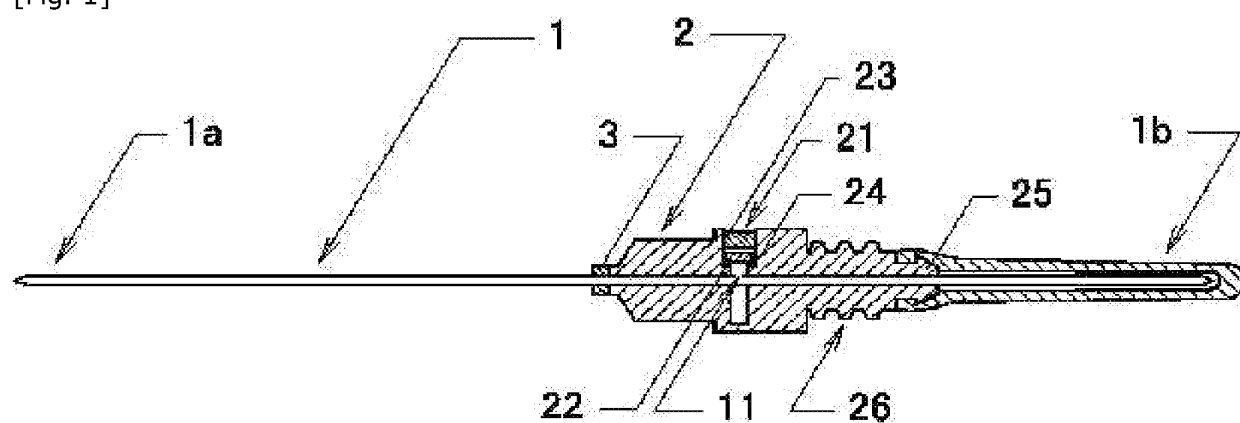
24 Convex portion

4 Rubber cap

drawing

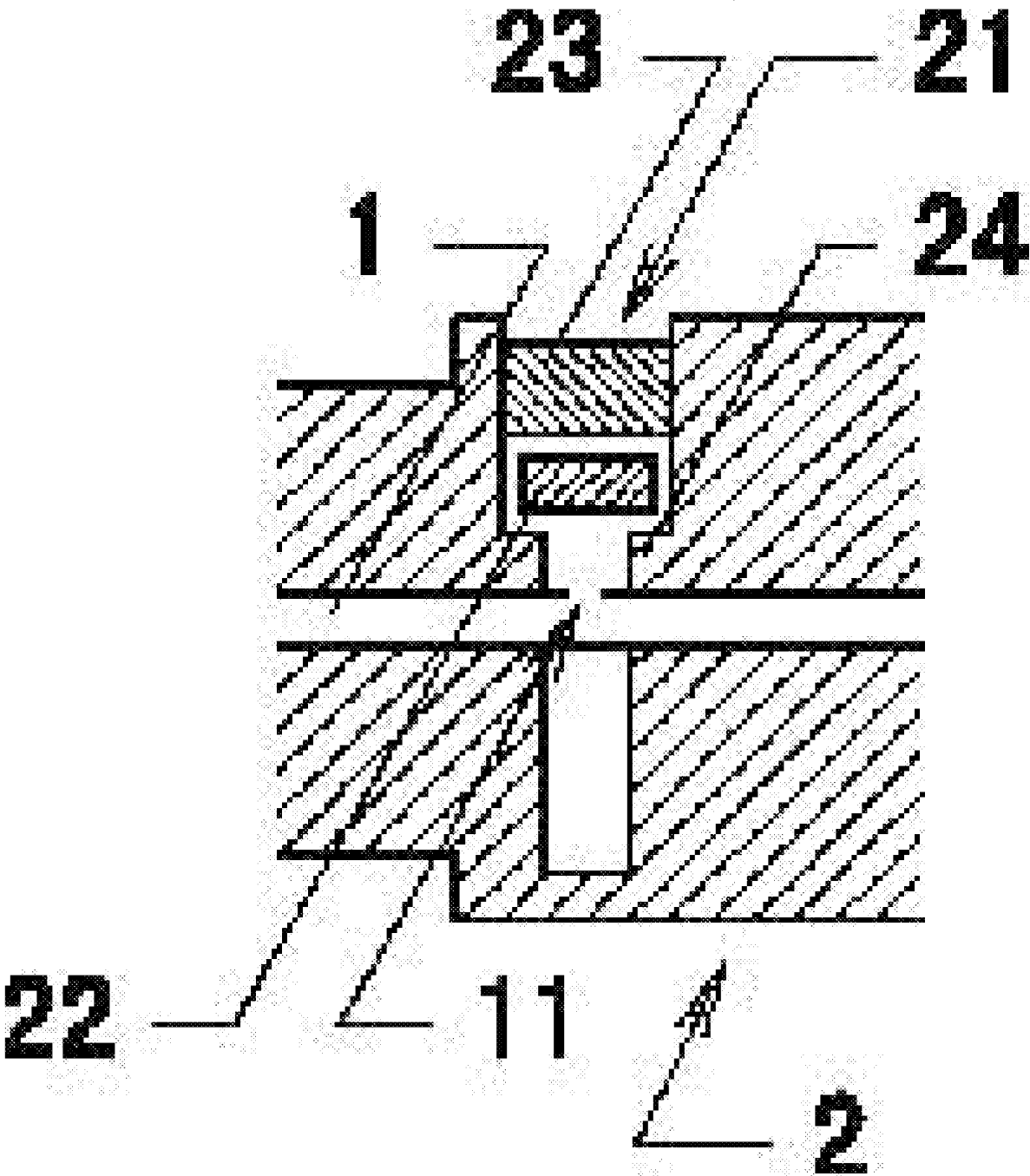
open

[Fig. 1]

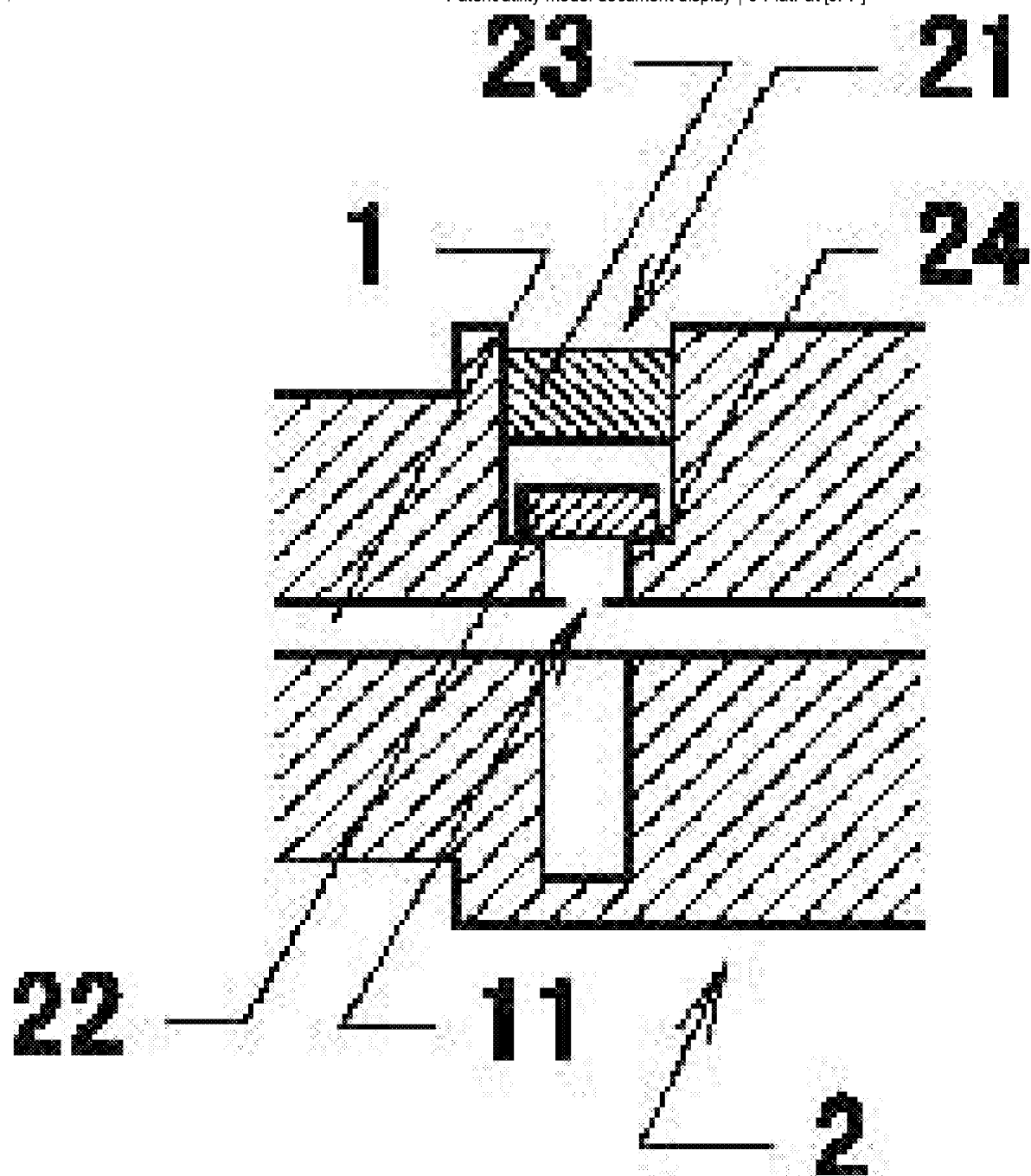


[Figure 2]

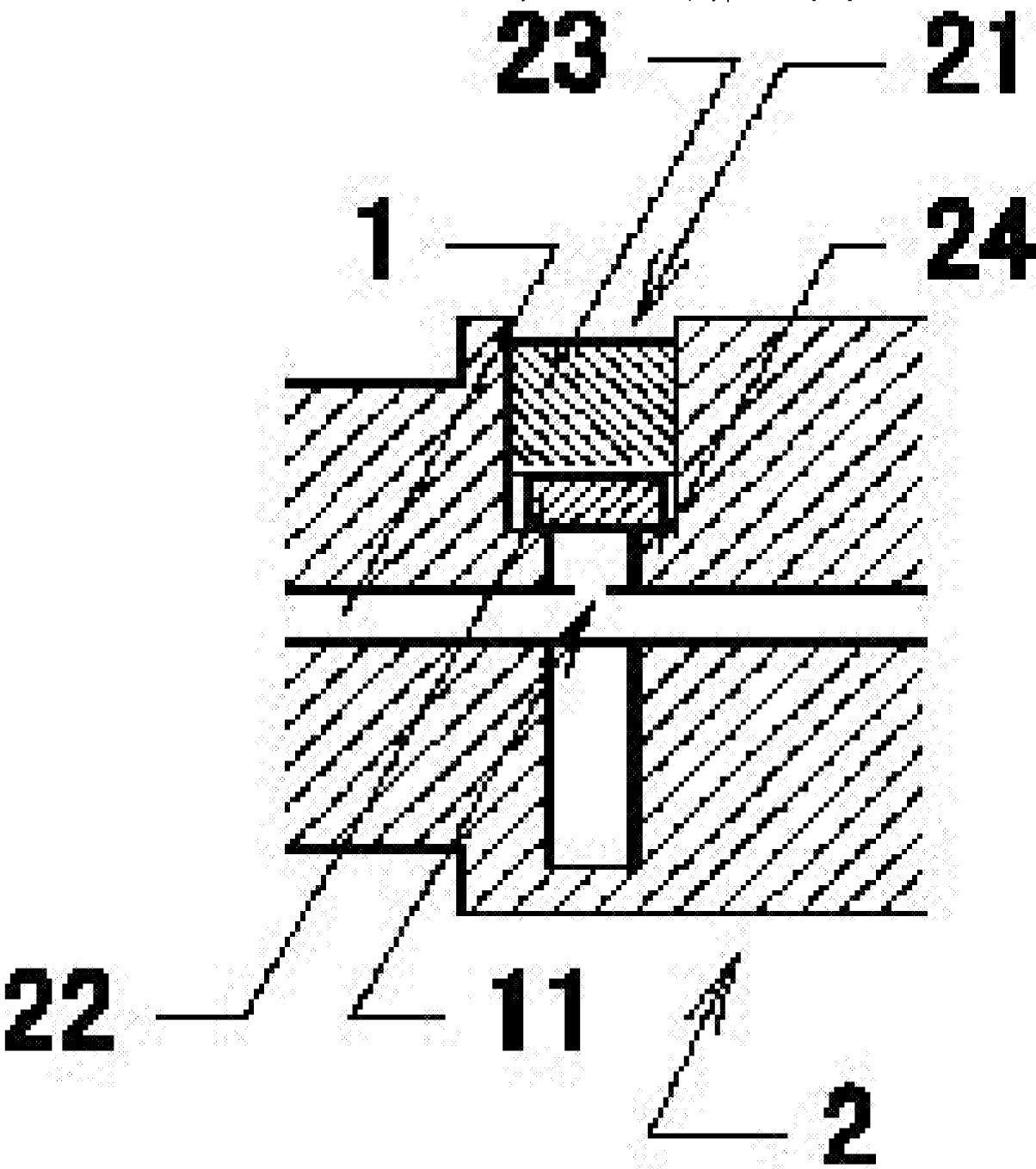




[Figure 3]



[Figure 4]

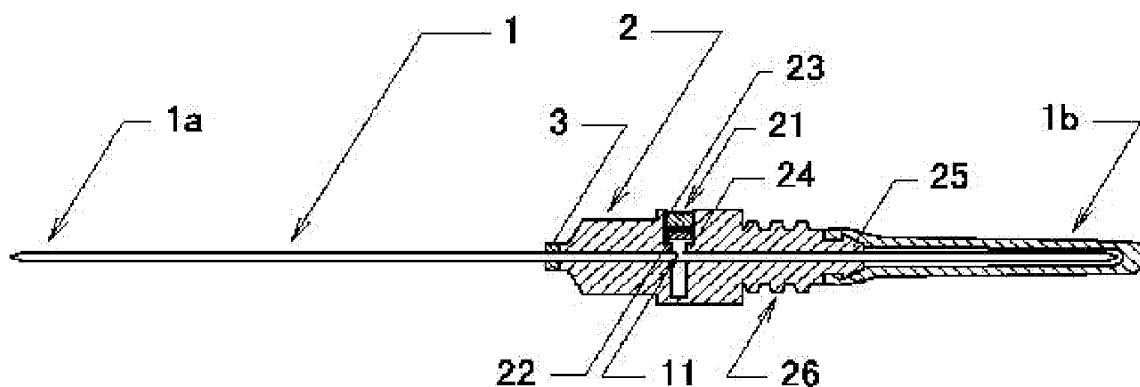


drawing

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Representative drawing | 1 | 2 | 3 | Four

Magnify and Rotate



Representative drawing

< 1 / 1 display >



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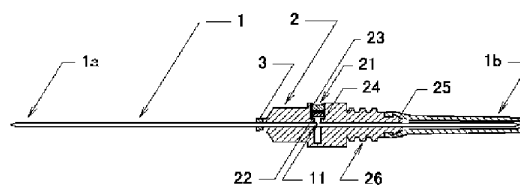
Fターム(参考) 4C038 TA06 UJ02 UJ06

(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】 通路が封止部材に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が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、一端が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の刃面が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を通して前記通路21に侵入し、侵入した血液は針管支持体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を通して通路21内に流入してきた血液は、封止部材22と針管支持体2との間隙を通して、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に示される断面がし字状であるものの他に、開放端に向かってテーパ状に広がるものや、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。

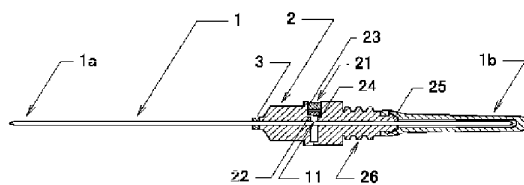
【図3】真空採血管取り付け時の、図1の採血針における、針管支持体部分の拡大断面図である。

【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。

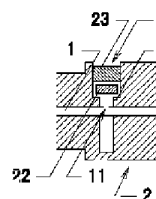
【符号の説明】

- 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

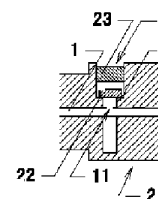
【図1】



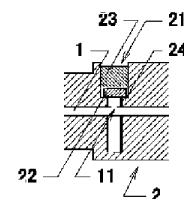
【図2】



【図3】



【図4】



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[F term (reference)]

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4C038TA10

4C038UA10

4C038UB07

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4C038UF14 4C066 AA07

4C066BB10 4C066FF05 4C066JJ08

wrap up

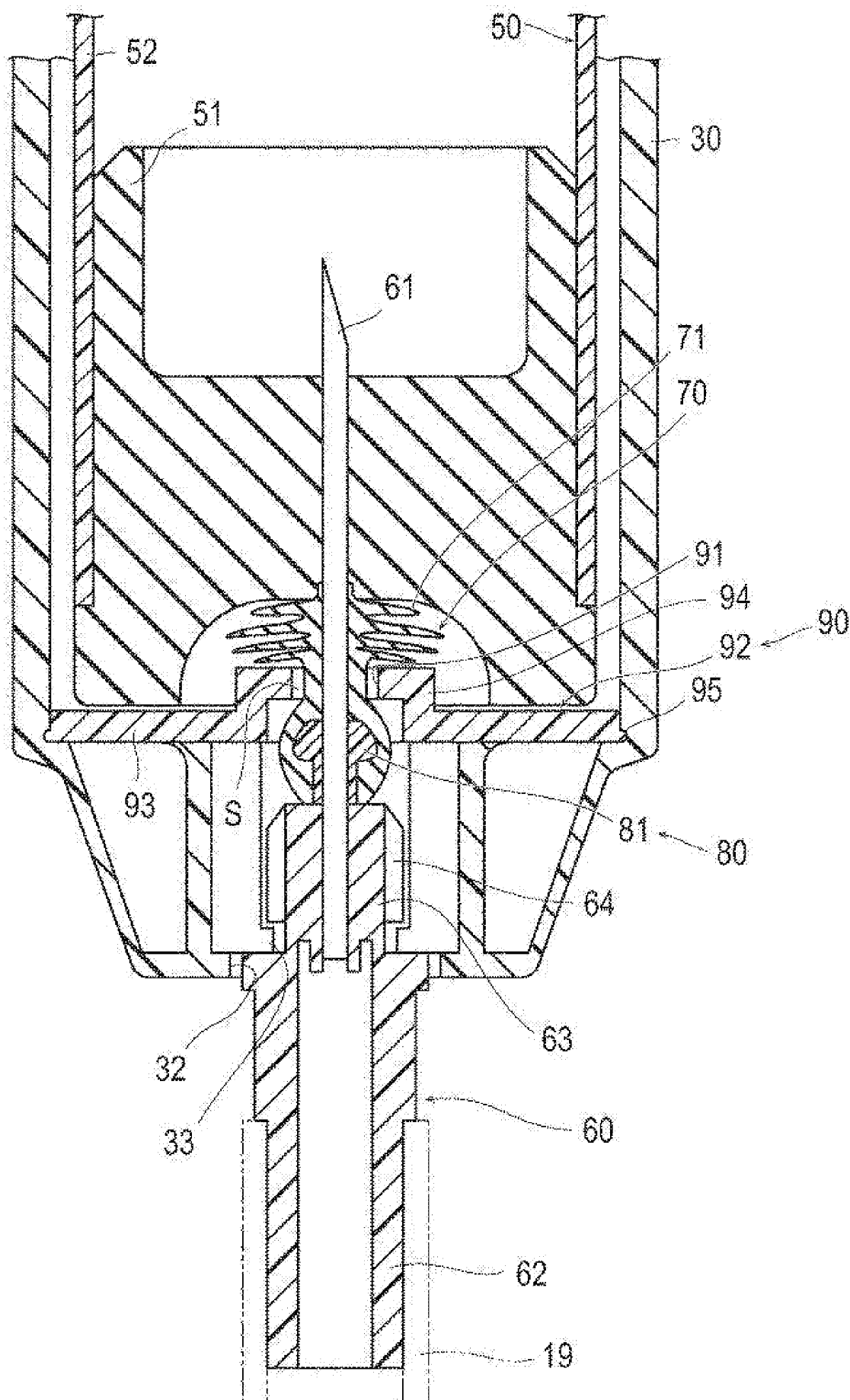
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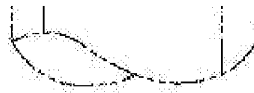
(57) [Summary]

[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 collection tube. To provide a sampling port capable of maintaining force and sufficiently preventing leakage of blood.

A sampling port (20) includes a main body (30) formed with an opening (31) for inserting a blood collection tube (50) having a rubber plug (51), a hollow needle (61) that can be freely inserted into the rubber plug of the blood collection tube, and a hollow needle. a needle assembly 60 attached to the main body, comprising a hub 64 supporting the proximal end of the needle, an elastic rubber cap 70 covering the hollow needle, and a holding portion 80 holding the rubber cap; A through hole 91 through which a hollow needle covered with a rubber cap penetrates is provided, and wrinkles 71 generated by elastic contraction of the rubber cap accompanying 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





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 cap 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 penetrates, and wrinkles generated by elastic contraction of the rubber cap as the hollow needle is inserted into the rubber plug reach the holding portion. and a suppression member that suppresses 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 rubber cap, 2. The sampling port of claim 1, having clearance to allow rotation of said body portion.

3.

The main body has a cylindrical shape, and the suppressing member has a disk shape and includes a projection projecting toward the opening 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 protruding radially outward is provided on the outer peripheral edge of said suppressing member.

[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 shrunk 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 collection 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 hollow needle is covered with an elastic rubber cap to prevent leakage of blood. [0003] As the blood collection tube is inserted into the body of the sampling port and the hollow needle is passed through the rubber plug, the rubber cap is elastically contracted and wrinkled to expose the hollow needle. The exposed hollow needle is used to collect blood into a collection tube. When the blood collection tube is pulled out after blood collection, the rubber cap elastically stretches from the contracted state as if smoothing the wrinkles, and restores to the state where it covers the hollow needle again. This prevents leakage of blood from the hollow needle. The rubber cap is held on the needle assembly by, for example, fitting the root portion to the needle assembly. [Prior Art Document] [Patent Document] [Patent Document 1] Japanese Patent Application 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 contraction of the rubber cap may reach the base of the rubber cap. There is In such a case, the root 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 insertion hole of the rubber stopper of the blood collection tube, the rubber cap will be pulled together when the blood collection tube is pulled out, and the position of the rubber cap will be affected. 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 invention 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 preventing leakage of blood. [0007] A sampling port of the present invention for achieving the above objects comprises a main body having an opening for inserting 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 base end of the hollow needle, an elastic rubber cap that covers the hollow needle, and a holding portion that holds the rubber cap a needle assembly attached to the main body, and a through hole through which the hollow needle covered with the rubber cap passes, wherein the rubber cap is elastic as the hollow needle is inserted into the rubber plug and a suppressing member that suppresses wrinkles generated by the contraction from reaching the holding portion.

[0008] The suppressing

member suppresses wrinkles generated by elastic contraction of the rubber cap as the hollow 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 position of the rubber cap will not be displaced, and blood leakage can be sufficiently prevented. Thus, even if the rubber cap is elastically contracted and wrinkled as the hollow needle is passed through the rubber plug of the blood collection tube, the holding force for holding the rubber cap to the needle assembly can be maintained, Thus, a sampling port that can sufficiently 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; FIG. 2 is a perspective view showing the initial blood bag shown in FIG. 1 and a sampling port; FIG. 3 is a cross-sectional view showing essential parts of a sampling port before a blood collection tube is inserted;

FIG. 4 is a cross-sectional view showing the essential parts of the sampling port after the blood collection tube has been inserted;

5(A) is a perspective view showing a plate as a suppressing member, FIG. 5(B) is a cross-sectional view along line 5B-5B in FIG. 5(A), and FIG. It is sectional drawing which expands and shows 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 FIG. 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 drawings, the same elements are denoted by the same reference numerals, and overlapping descriptions 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 collected blood when collecting blood, and uses the initial blood flow as test blood. It is a blood collection device. Bacteria present on and under the skin enter along with the skin fragments at the time of puncture, so the initial blood flow is removed. A blood bag system 10 includes a blood collecting needle 11, a blood bag 12 containing blood collected through the blood collecting needle 11, a blood collecting tube 13 connecting the blood collecting needle 11 and the blood bag 12, and a blood collecting tube

13, an initial blood flow bag 16 communicating with the blood collection tube 13 via a branch tube 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 member 17 that seals communication with the blood bag 12 . The sealing member 17 seals the communication with the blood bag 12 until the collection of the initial blood flow into the initial blood 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 member 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 collected as test blood. A sampling port 20 is connected to a blood extraction tube 19 connected to an 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 the initial blood bag 16 as test blood, a reduced-pressure blood collection tube 50 (corresponding to a blood collection tube) having a rubber plug 51 is inserted into the sampling port 20 through the opening 31 .

A reduced

-pressure blood collection tube 50 is an instrument for collecting the initial blood that is stored in the initial blood bag 16 . The vacuum blood collection tube 50 has a blood collection tube body 52 and a rubber plug 51 fitted into the opening of the blood collection tube body 52 . The vacuum blood collection tube 50 is in a vacuum or a reduced pressure state. When the vacuum blood collection tube 50 is connected to the sampling port 20 , the rubber stopper 51 is pierced 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 generally 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 freely 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 80 . The sampling port 20 further suppresses wrinkles 71 (see FIG. 4) caused by elastic contraction of the rubber cap 70 as the hollow needle 61 is inserted into the rubber plug 51 from reaching the holding portion 80. It has a member 90 . The suppressing member 90 has a through 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 lower 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 preventing the inserted needle assembly 60 from coming off.

Body

portion 30 is rotatably attached to needle assembly 60 . By making it rotatable, the body portion 30 can be rotated with respect to the needle assembly 60 to easily finely adjust the position 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 . The needle assembly 60 is attached to the body portion 30 with the hub 64 overcoming the locking 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 to the needle assembly 60, the clearance between the connecting portion 62 of the needle assembly 60 and the receptacle 32 of the body portion 30 and the outer circumference of the hub 64

are

and the body portion 30 are adjusted. 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 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 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

.

[0021]

The holding portion 80 includes a lock member 81 through which the hollow needle 61 is inserted and which is attached to the boss portion 63 of the needle assembly 60 . The locking member 81 has an undercut shape in which the base end side of the hollow needle 61 has a smaller diameter than the tip end side. The undercut shape of the locking member 81 holds the rubber 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 91 through which the hollow needle 61 with the rubber cap 70 is attached is formed in the convex portion 94 . As shown in FIG. 5C , a ring-shaped projection 95 projecting radially outward is provided integrally with the flat plate portion 93 on the outer peripheral edge of the flat plate portion 93 . 3 and 4, the plate 92 is mounted inside the main body 30 at a position above the 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 wrinkles 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 holding 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 dimension 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 possible.

By providing the plate 92 with the protrusions 94, it is possible to increase the area of the rubber cap 70 in the longitudinal direction that is not affected by the wrinkles 71. As shown in FIG. 4, as a result, a decrease in holding force for holding the rubber cap 70 to the needle assembly 60 can be further suppressed. Even if the arrangement position of the plate 92 is shifted upward from the position shown in FIG. 4, the area in the longitudinal direction of the rubber cap 70 that is not affected by the wrinkles 71 can be increased. However, in this case, since the position of the blood collection tube 50 is also shifted upward, it may be necessary to slightly 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 by 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 the hollow needle 61, the holding part 80, and the plate 92 is not particularly limited, but examples thereof include polycarbonate, polyethylene, polypropylene, ethylene- Examples include polyolefins such as vinyl acetate copolymers and modified polyolefins. The material of the hollow needle 61 is not particularly limited, but examples include various metal materials such as 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, chloroprene rubber, butyl rubber, acrylic rubber, ethylene-propylene rubber, hydride rubber, Various 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, the body portion 30 is made of a resin material that shrinks more than the resin material forming the plate 92 when heat is applied. This is because the plate 92 can be fixed to the body po

portion 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 projection 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 assembly 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 does. 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 combination of resin materials as described above, for example, polypropylene can be used as the molding material for the main body 30 and polycarbonate can be used as the molding material for the plate 92

. [0033]

The operation of this embodiment will be described. When collecting blood, the blood collection 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 through the rubber stopper 51, the rubber cap 70 is elastically contracted to form wrinkles 71, thereby exposing the hollow needle 61. As shown in FIG. Referring to FIG. 7B, in the case of contrast without plate 92, rubber cap 170 is elastically closed as hollow needle 161 is inserted into 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 displaced, 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 member 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 contraction 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 body 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 from 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 overall 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) in 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 rubber cap 70 from coming off and holding it in the needle assembly 60. For example, the holding 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 needle 61 by ultrasonic fusion, or a clip. For example, a configuration in which the rubber cap 70 is held on the hollow needle 61 by fitting is exemplified. These holding portions 80 may be used 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);

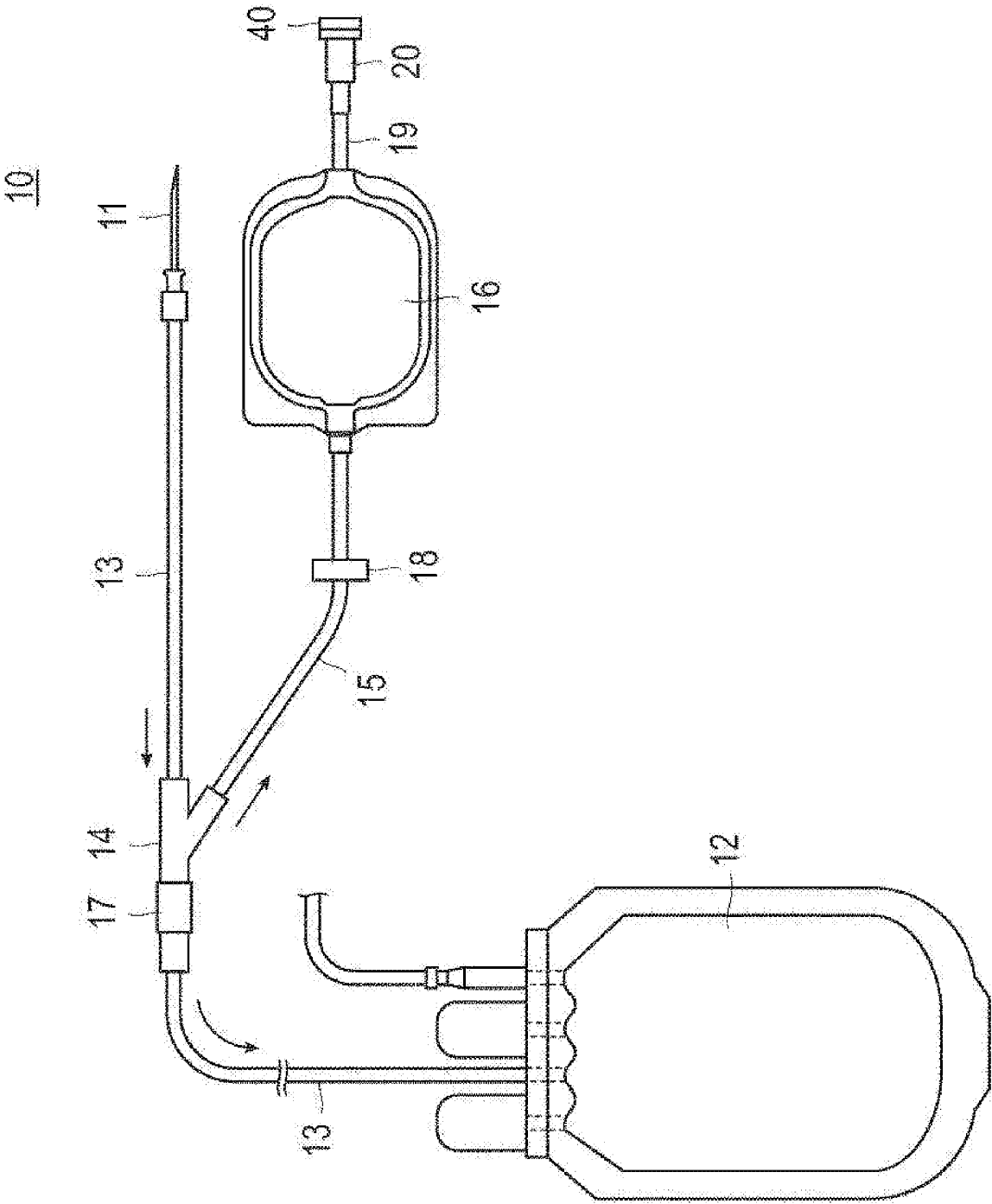
93 flat plate portion,
94 convex portion,
95 ring-shaped projection,
S clearance.

drawing

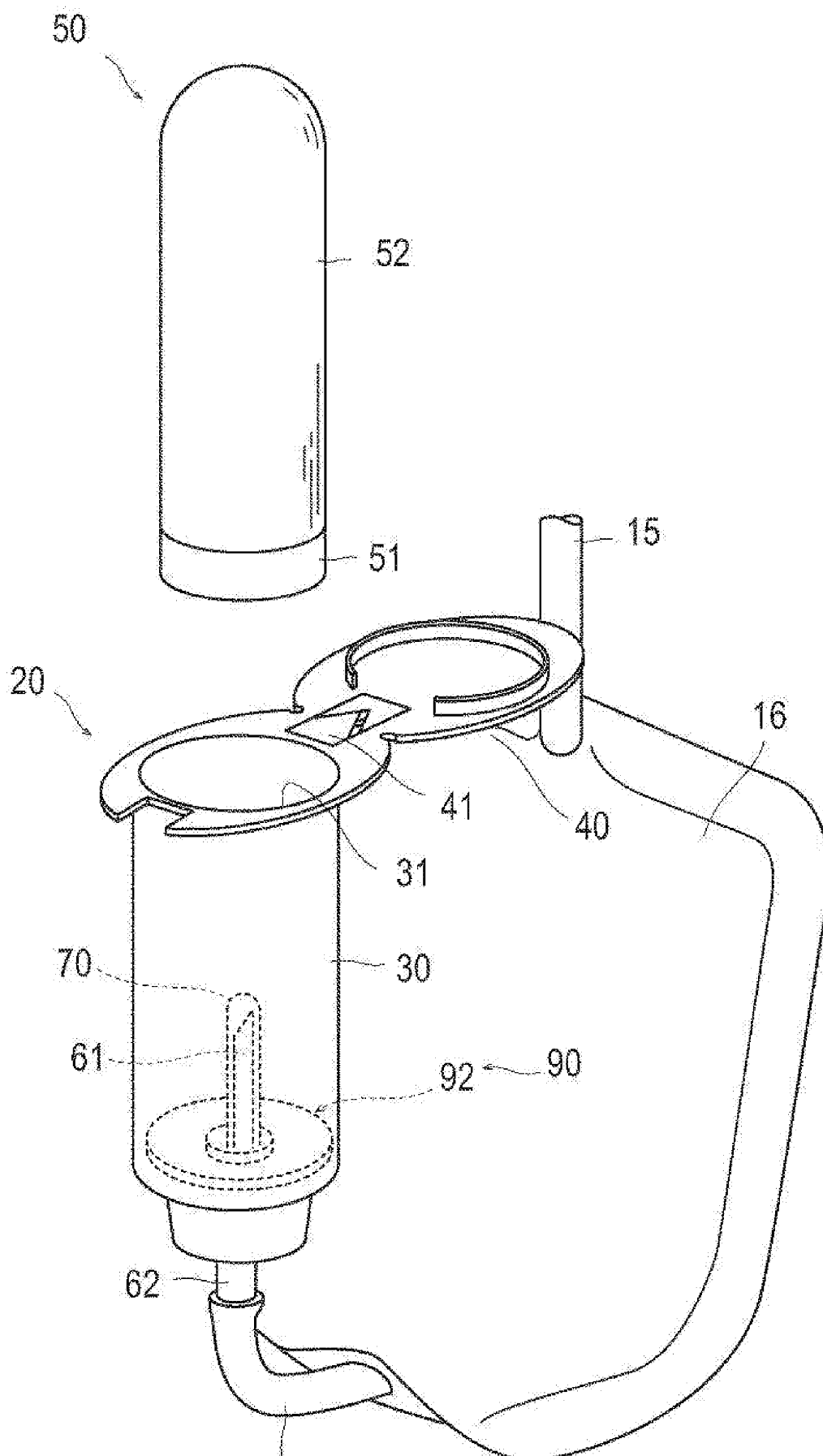
open



[Fig. 1]

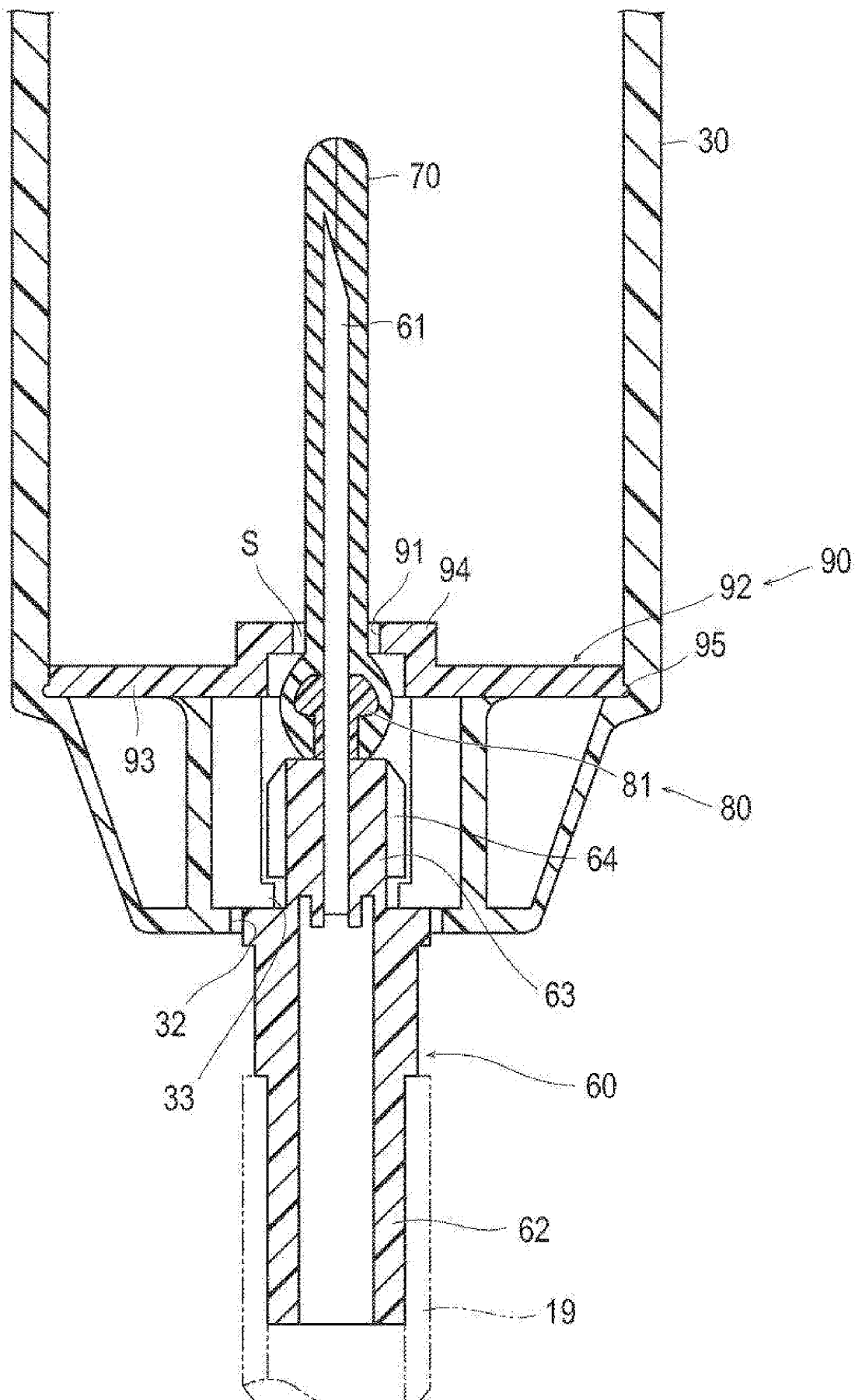


[Figure 2]

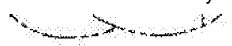


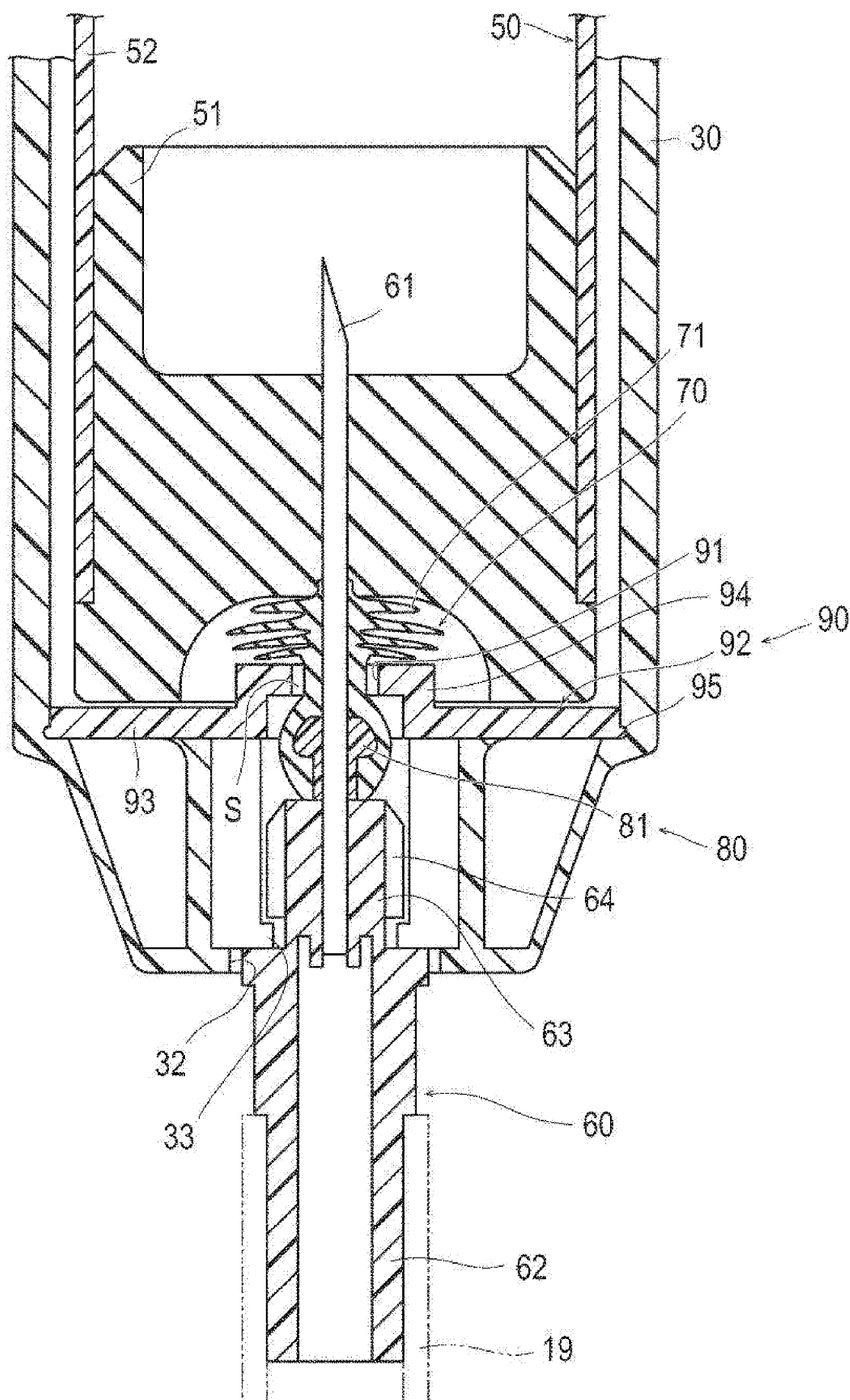
[Figure 3]

19



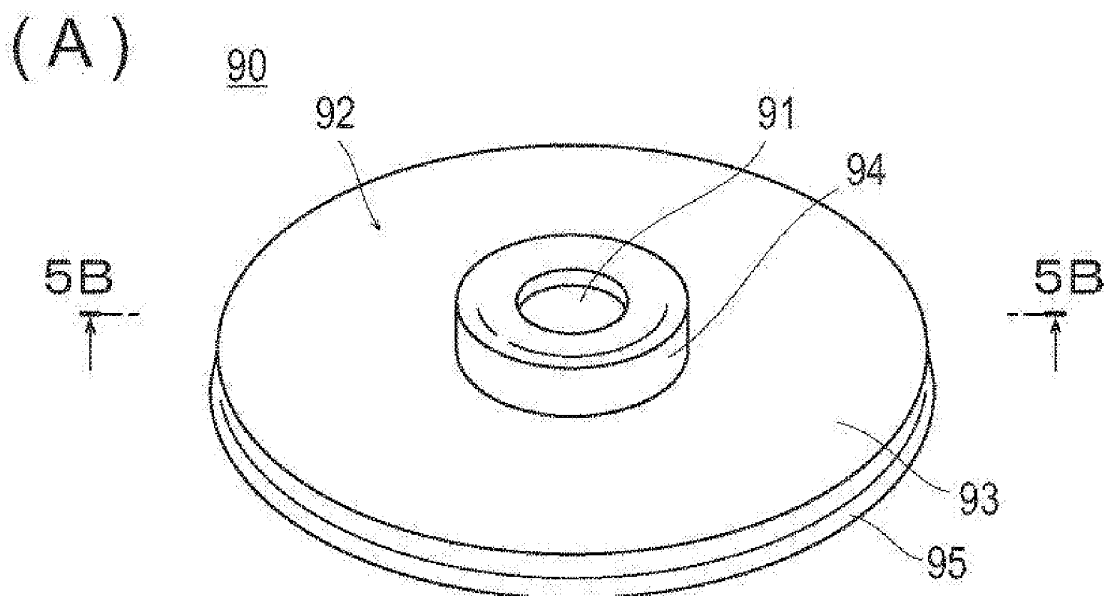
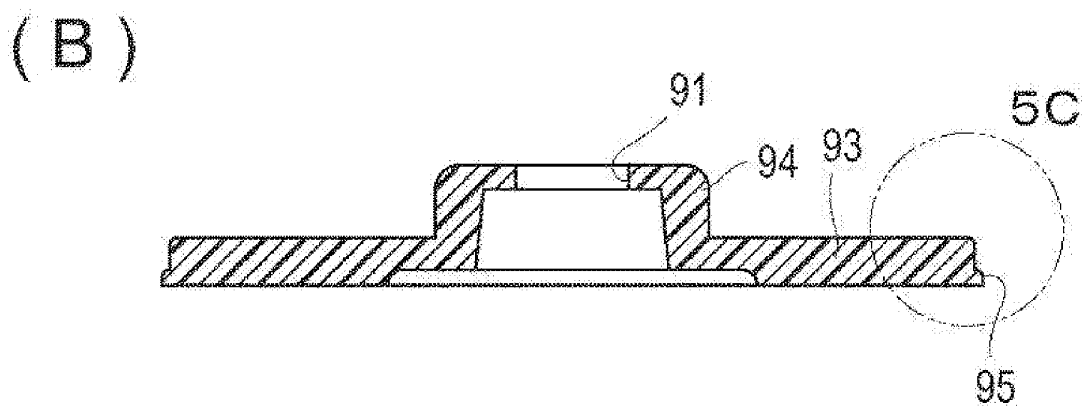
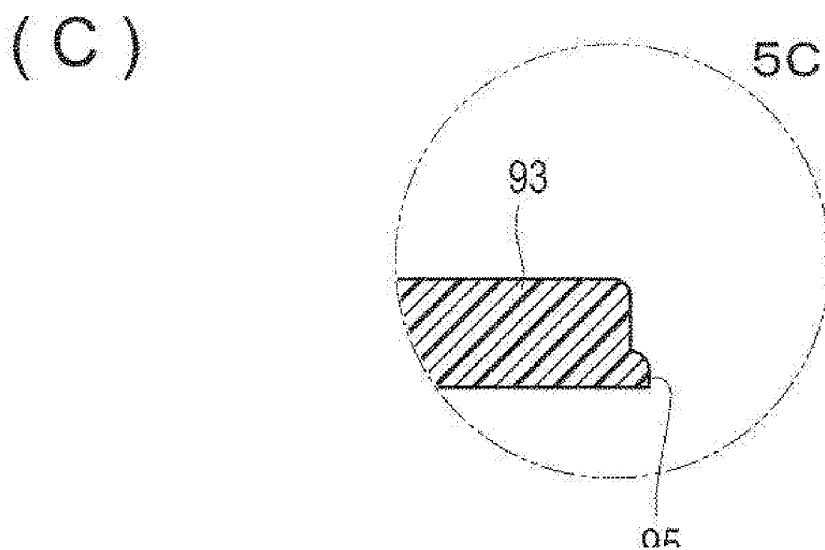
[Figure 4]





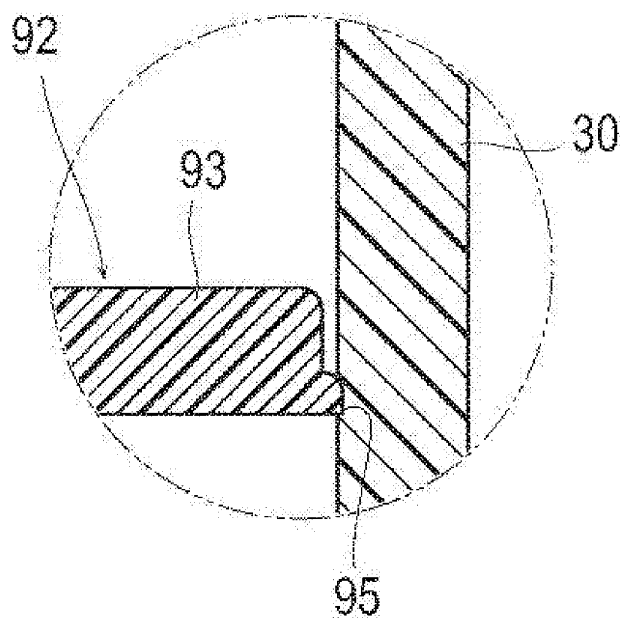
[Figure 5]



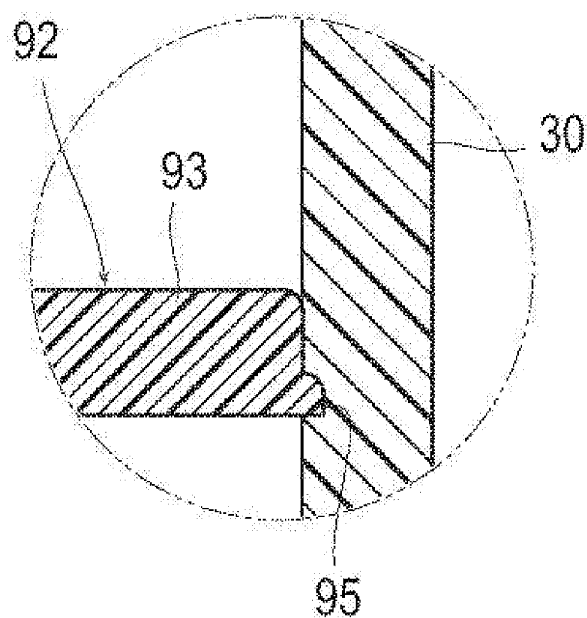


[Fig. 6]

(A)

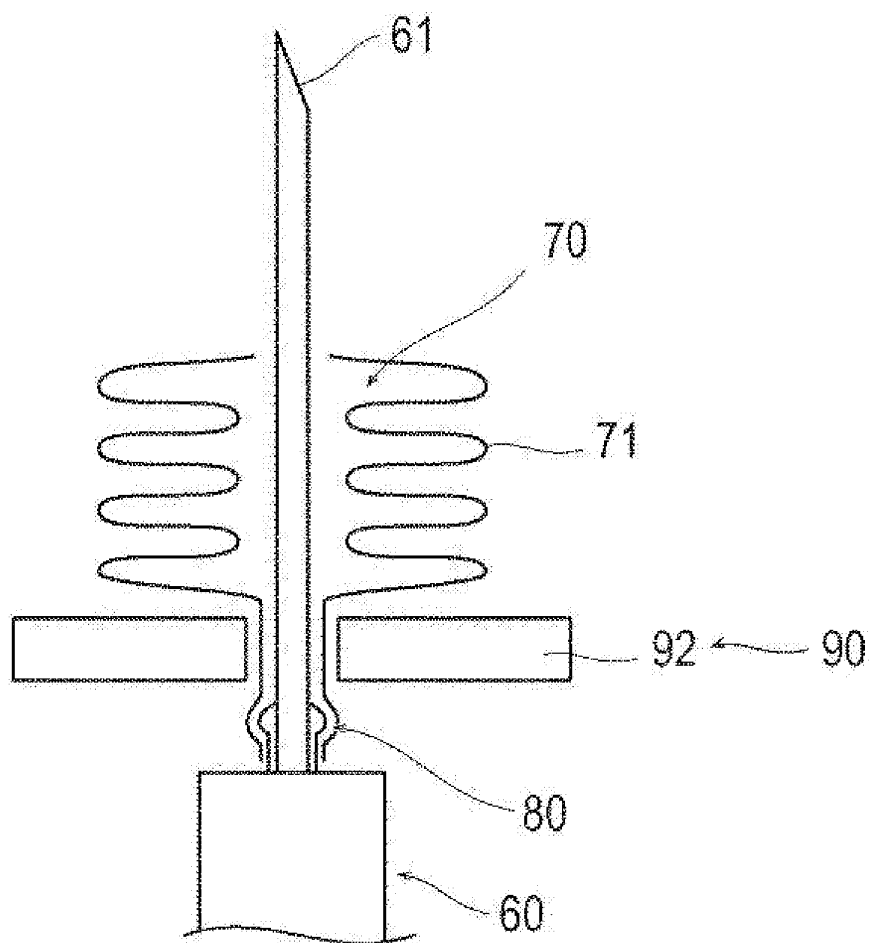


(B)

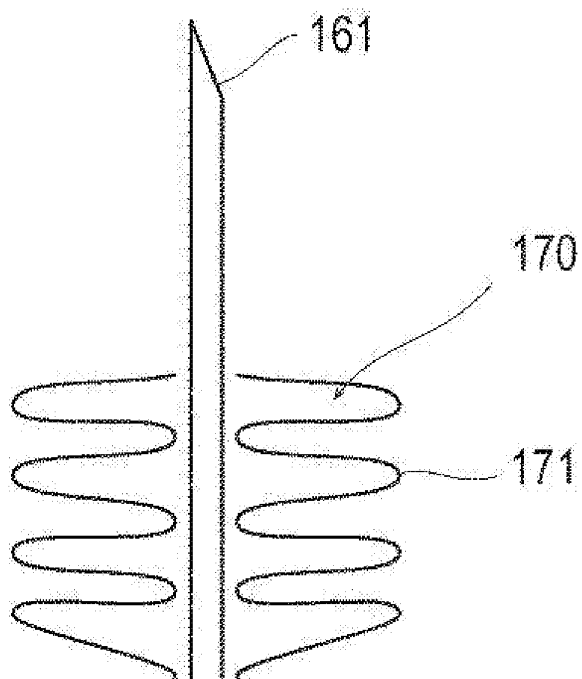


[Fig. 7]

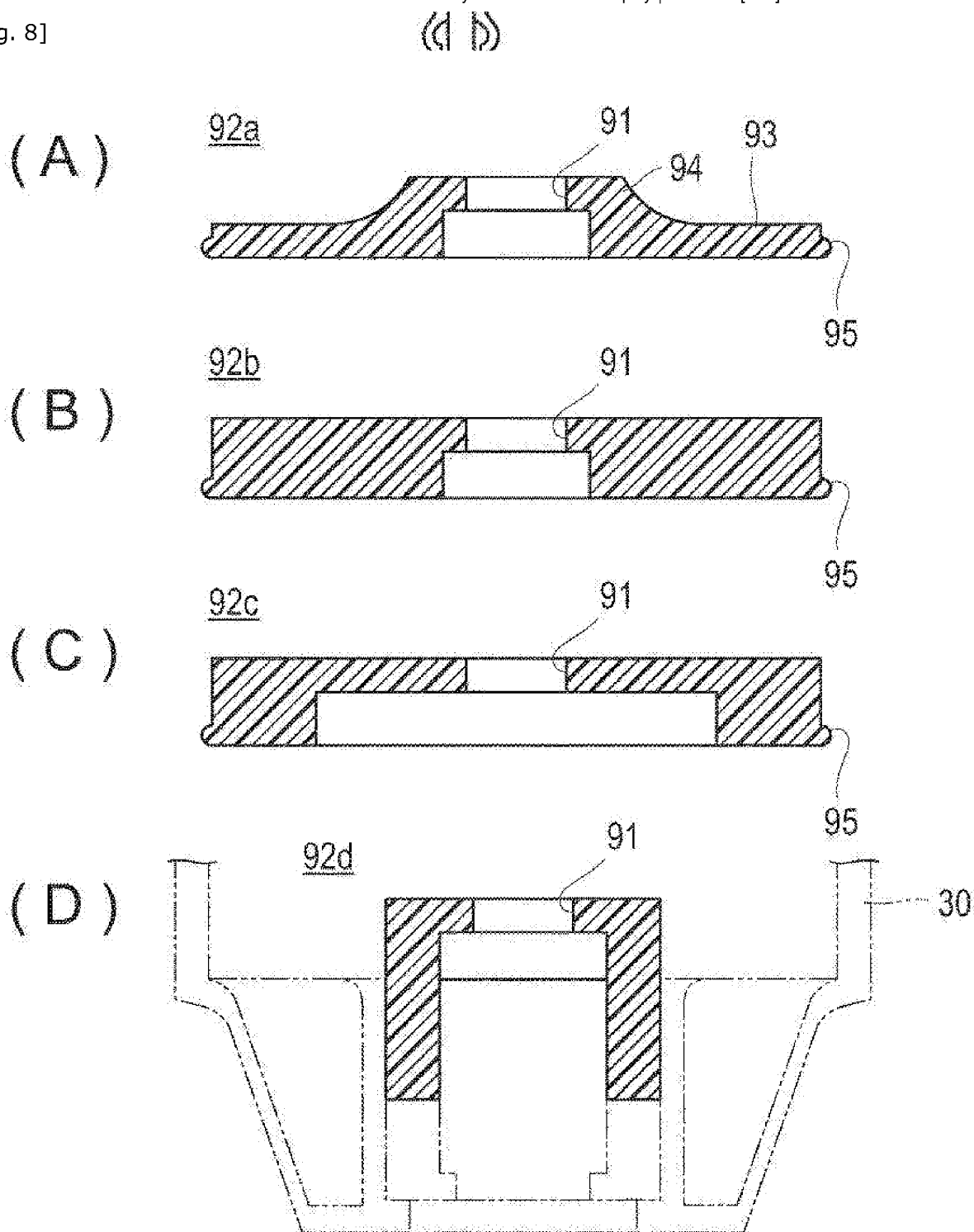
(A)



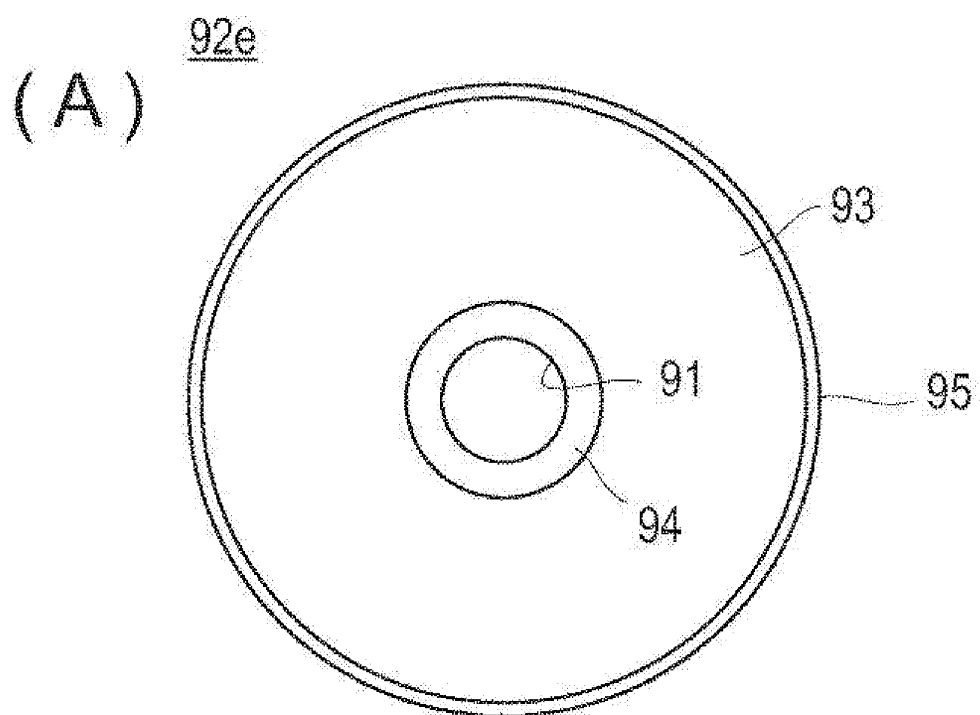
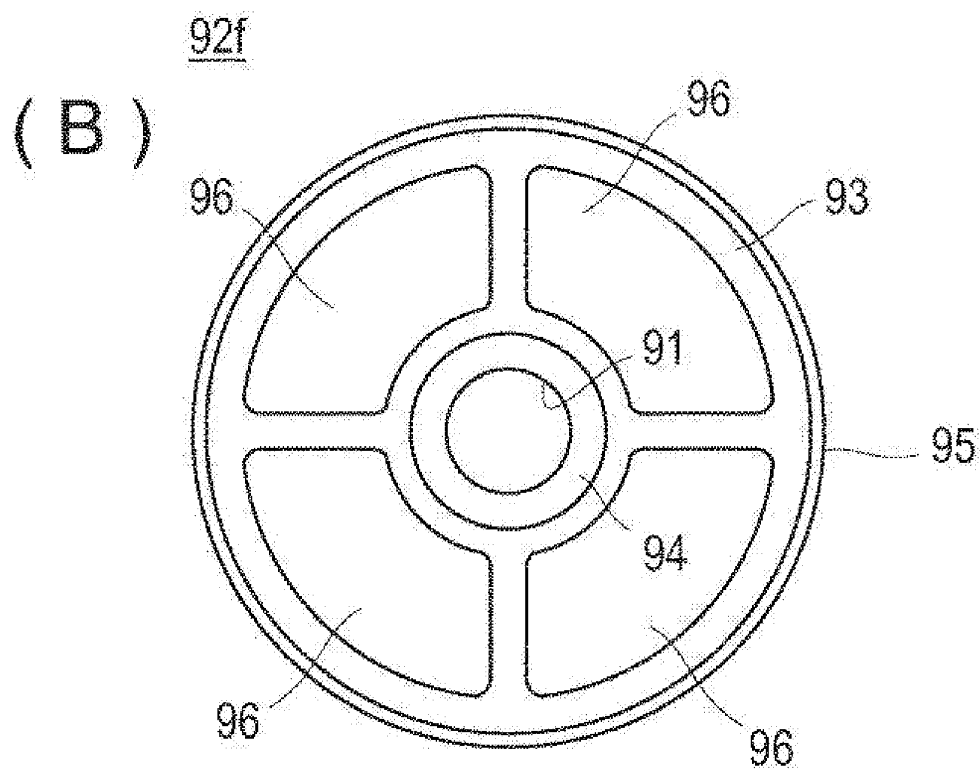
(B)



[Fig. 8]



[Fig. 9]



drawing

open

Representative drawing

1

2

3

Four

Five

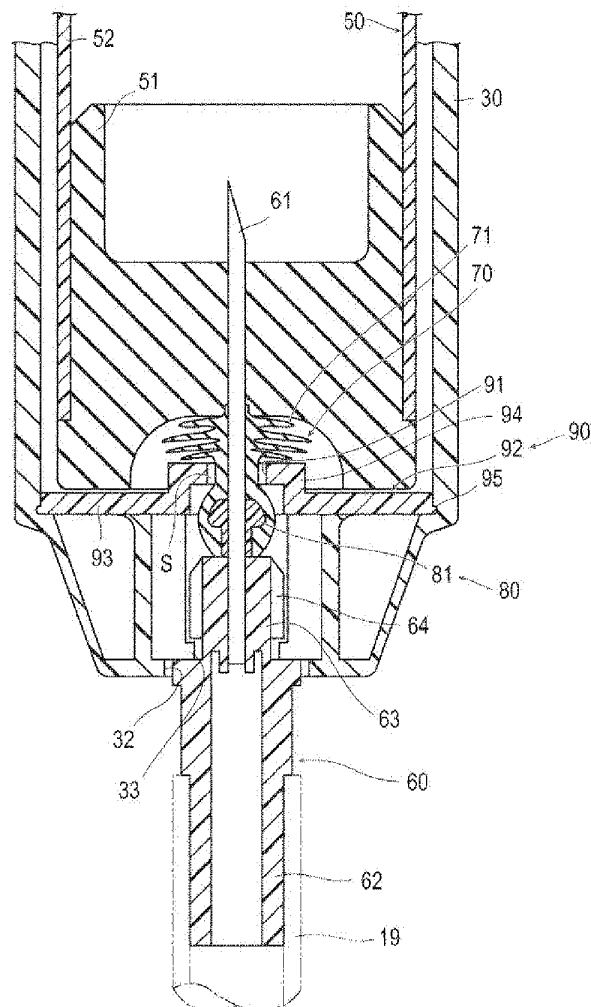
6

7

8

9

Magnify and Rotate



Representative drawing

<

1

/ 1

display

>



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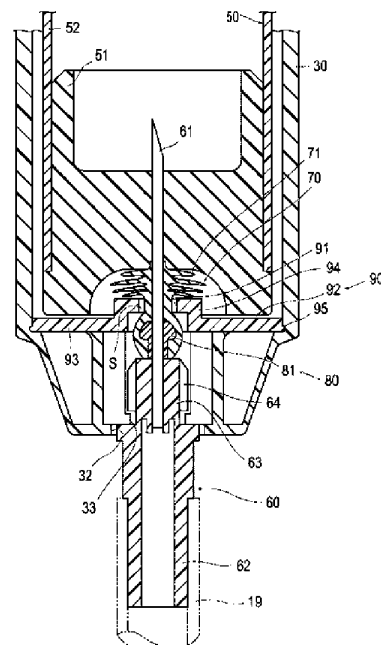
(54) 【発明の名称】 サンプリングポート

(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。

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【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。

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【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。

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【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。

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【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】

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【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と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】

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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、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、

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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と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、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。

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【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。

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【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。

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【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げらとともに侵入するため、初流血を除去している。

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【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。

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【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。

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【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。

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【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

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、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。

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【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。

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【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。

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【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)。

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【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。

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【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。

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【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。

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【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。

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【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。

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【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

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針 6 1 をゴム栓 5 1 に挿通させる。ゴム栓 5 1 に中空針 6 1 が挿通するのに伴って、ゴムキャップ 7 0 は、弾性的に縮められて皺 7 1 を生じながら中空針 6 1 を露出させる。

【0035】

図 7 (B) を参照して、プレート 9 2 を設けていない対比例の場合には、採血管 5 0 のゴム栓 5 1 への中空針 1 6 1 の挿通に伴ってゴムキャップ 1 7 0 が弾性的に縮められることによって生じる皺 1 7 1 が、ゴムキャップ 1 7 0 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 1 7 0 の根元部が膨らんでしまい、ゴムキャップ 1 7 0 を針組立体 1 6 0 に保持するための保持力が弱くなる。このため、採血管 5 0 を引き抜くときにゴムキャップ 1 7 0 が一緒に引っ張られてしまい、ゴムキャップ 1 7 0 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。

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【0036】

これに対して、図 4 および図 7 (A) を参照して、本実施形態にあつては、プレート 9 2 を、保持部 8 0 をなすロック部材 8 1 よりも上部側の位置において、本体部 3 0 内に取り付けている。このプレート 9 2 によって、採血管 5 0 のゴム栓 5 1 への中空針 6 1 の挿通に伴ってゴムキャップ 7 0 が弾性的に縮められることによって生じる皺 7 1 がロック部材 8 1 に達することが抑制される。ロック部材 8 1 の部分でゴムキャップ 7 0 が膨らむことがないので、ゴムキャップ 7 0 を針組立体 6 0 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 6 1 は、ゴム栓 5 1 に挿通されて、採血管 5 0 に採血する。採血後に採血管 5 0 を引き抜くと、ゴムキャップ 7 0 は、縮んだ状態から、皺 7 1 を伸ばすように弾性的に伸び、中空針 6 1 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 6 1 からの血液の漏洩を防止する。ゴムキャップ 7 0 は、ロック部材 8 1 の部分で針組立体 6 0 に保持されている。

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【0038】

採血管 5 0 のゴム栓 5 1 の微小な挿通孔にゴムキャップ 7 0 の先端部が食い込んだ状態で採血管 5 0 を引き抜くと、ゴムキャップ 7 0 が一緒に引っ張られる。しかし、ロック部材 8 1 の部分は皺 7 1 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 7 0 は、中空針 6 1 から抜けずに、採血管 5 0 のゴム栓 5 1 への食い込みが解除される。これによって、ゴムキャップ 7 0 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。

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【0039】

このように、採血管 5 0 のゴム栓 5 1 への中空針 6 1 の挿通に伴ってゴムキャップ 7 0 が弾性的に縮められて皺 7 1 が生じても、ゴムキャップ 7 0 を針組立体 6 0 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 2 0 を提供できる。

【0040】

また、本体部 3 0 は針組立体 6 0 に対して回動自在に取り付けられ、プレート 9 2 は本体部 3 0 に固定されており、貫通孔 9 1 とゴムキャップ 7 0 との間に本体部 3 0 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 6 0 に対する本体部 3 0 の回動位置などを簡単に微調整することが可能となる。

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【0041】

また、プレート 9 2 は、本体部 3 0 の開口部 3 1 の側に向けて突出する凸部 9 4 を備えているため、本体部 3 0 の長手方向の長さを維持したまま、ゴムキャップ 7 0 の長手方向のうち皺 7 1 の影響を受けない範囲を大きくして、ゴムキャップ 7 0 を針組立体 6 0 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 9 2 の外周縁に径方向外方に突出するリング状突起 9 5 を設けているため、リング状突起 9 5 を若干寸法だけ本体部 3 0 に食い込ませるようにしてプレート 9 2 を本体部 3 0 内に挿入させることができ、簡単にプレート 9 2 の組み込み作業を行うこと

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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。

【符号の説明】

【0048】

20 サンプリングポート、
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)、

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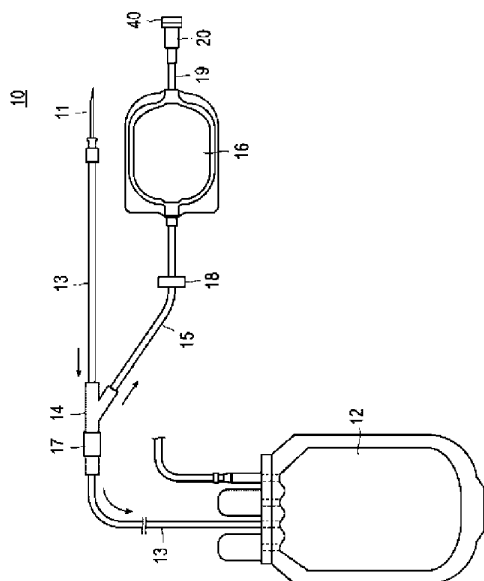
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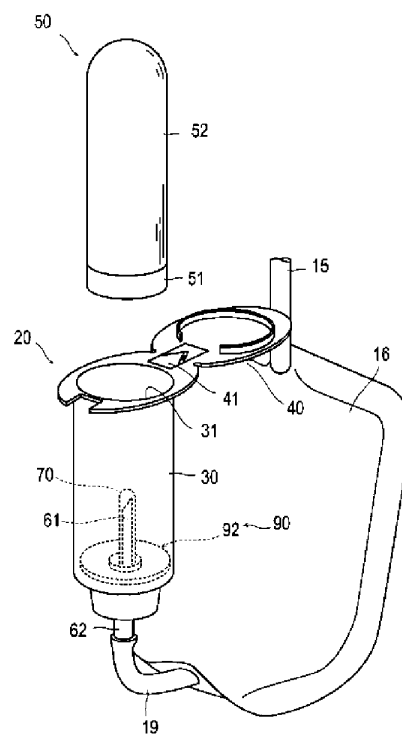
50

- 9 3 平板部、
 9 4 凸部、
 9 5 リング状突起、
 S クリアランス。

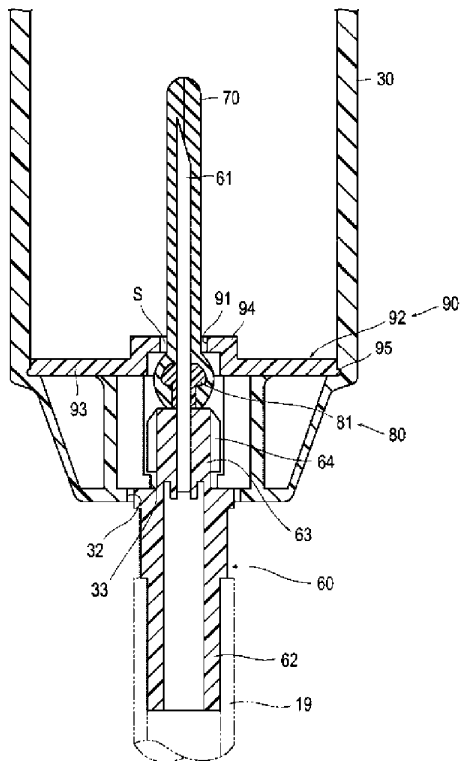
【図 1】



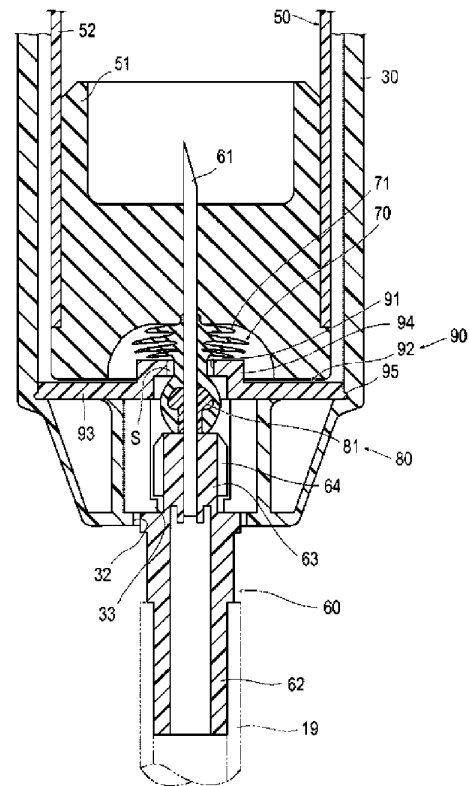
【図 2】



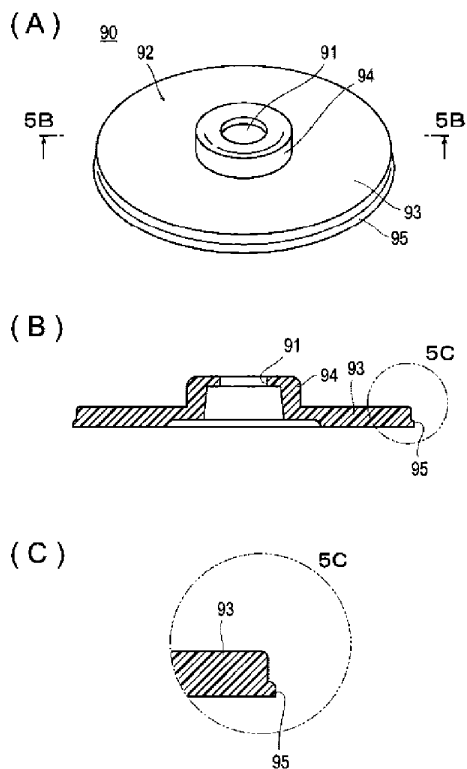
【図 3】



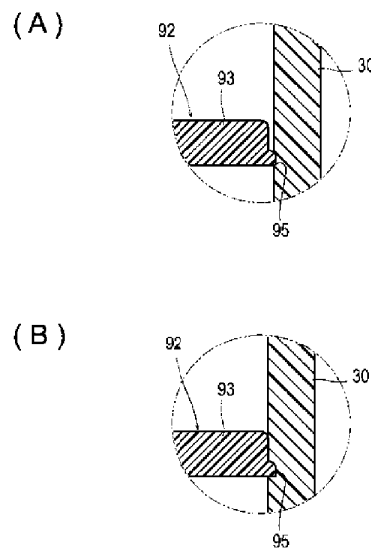
【図 4】



【図 5】

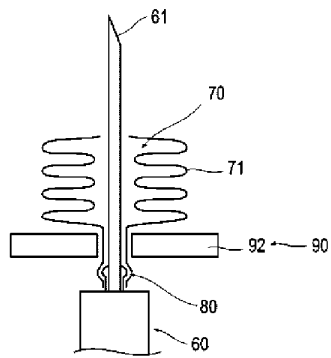


【図 6】

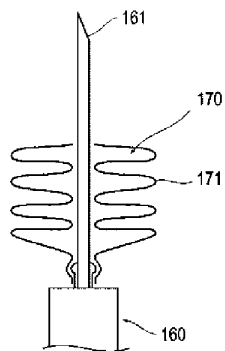


【図 7】

(A)

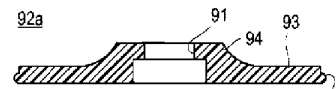


(B)

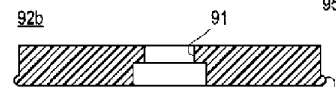


【図 8】

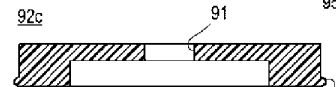
(A)



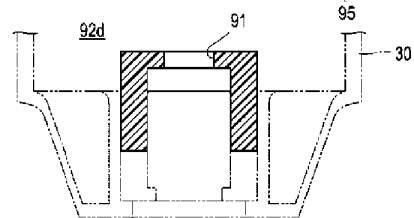
(B)



(C)

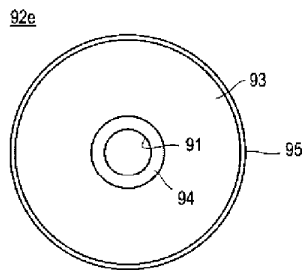


(D)

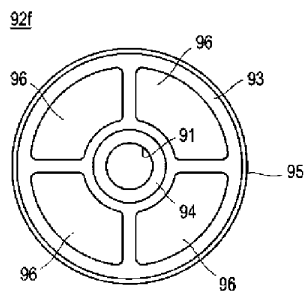


【図 9】

(A)



(B)



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[FI]
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[Application form] OL
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[Theme code (reference)]

4C038

[F term (reference)]

4C038TA01

4C038TA03

4C038UJ02

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(57) [Summary] (Modified)

[Problem] To provide a cheaper and simpler phlebotomy needle that facilitates visualization of flashbacks.

A central portion (106) of the needle (100) includes a hole or opening (110) that communicates with the flow path defined by the needle (100), and a transparent housing (112) covers the opening (110). Positioned around to facilitate visualization of blood flow through needle 100 .

A material that allows passage of air and provides an indication of blood flow through needle

100 is positioned over opening 110 . The material is in the form of plugs or alternatively in the form of patches or collars. The phlebotomy needle includes a needle 100, a housing 112 having a passive vent, and an observation area for visualizing blood flow in the housing 112. FIG. [Selection drawing] Fig. 2-1

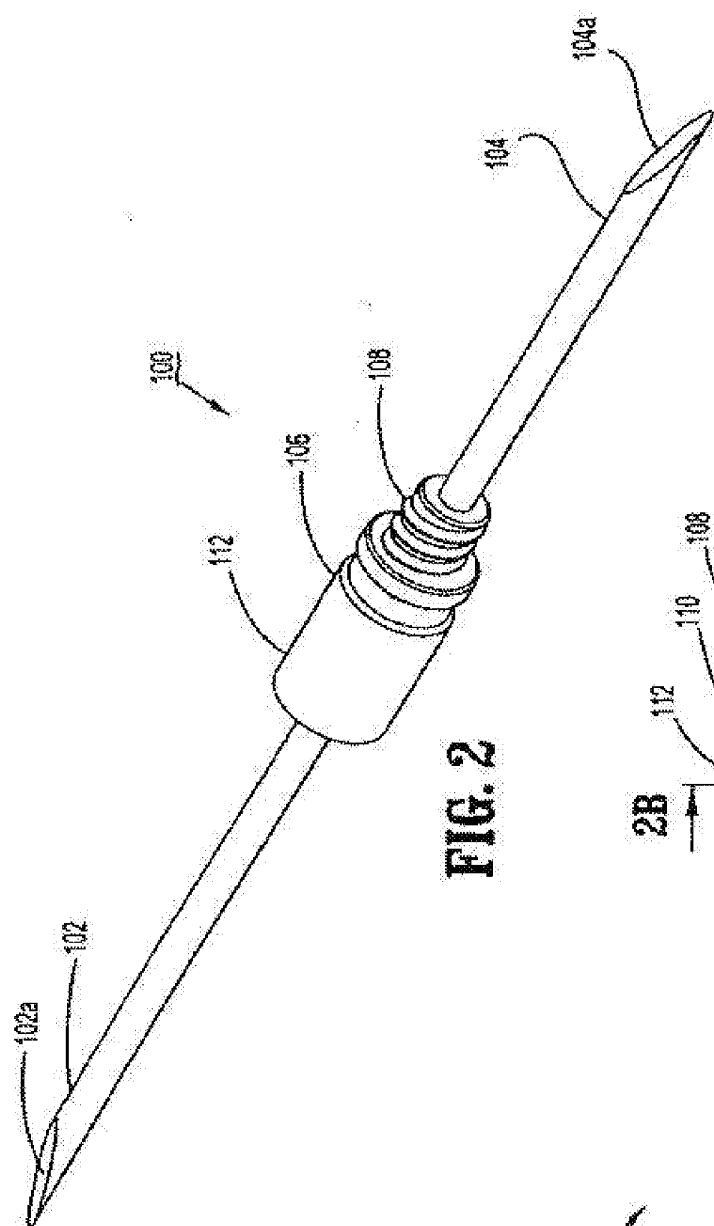


FIG. 2

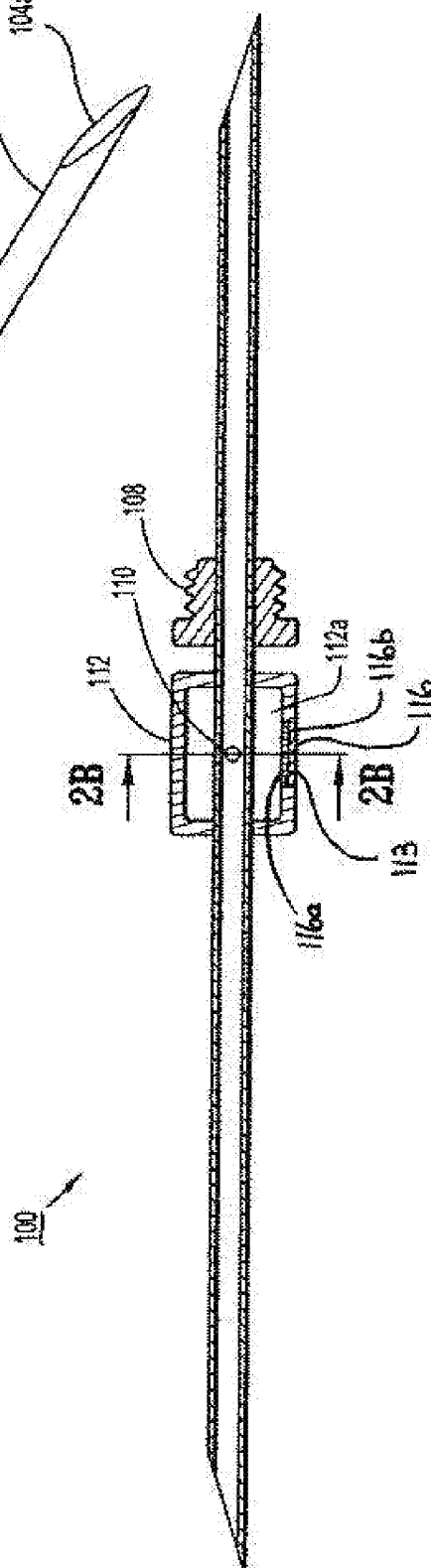


FIG. 2A

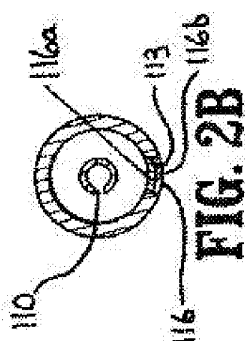


FIG. 2B

The scope of the claims

open

Claims:

1. A

phlebotomy needle: a distal needle portionhaving a sharpened distal end configured to pierce tissue; and a distal needle portion configured to pierce a stopper of a blood collection tube. a proximal needle portion having a sharpened proximal end, the distal needle portion and the proximal needle portion defining a fluid channel; a housing supported over the needle; a housing, comprising a passive vent, the housing defining a viewing area for viewing blood in the housing; and an elastomeric shield positioned about the proximal needle portion, A phlebotomy needle comprising an elastomeric shield and an elastomeric shield wherein the proximal needle portion defines a fluid flow path into the housing.

2. The phlebotomy needle of claim 1

, further comprising a fluted member positioned within said housing, said fluted member defining a plurality of fluid channels.

3.

The phlebotomy needle of claim 2, wherein said fluted member extends distally beyond said elastomeric shield.

4.

The phlebotomy needle of claim 2, wherein the fluid channel of the fluted member is configured to allow the passage of blood.

5.

The phlebotomy needle of claim 2, further comprising a hydrophilic material supported within said housing. 6. The phlebotomy of claim 5, wherein said flow path directs blood from the proximal end of said needle into the fluid channel of said fluted member and into contact with said hydrophilic material.needle.

[Claim 7]

6. The phlebotomy needle of claim 5, wherein a portion of said fluted member is surrounded by said hydrophilic material.

8. The method of claim

5, wherein a proximal end of said fluted member is surrounded by said elastomeric shield and a distal end of said fluted member is surrounded by said hydrophilic material. Phlebotomy needle.

9.

The phlebotomy needle of claim 5, wherein the proximal portion of the housing includes an inwardly extending annular rib.

10.

The elastomeric shield has an open distal end including an annular flange, and an annular rib of the housing engages the flange to extend the distal end of the elastomeric shield into the housing.

11.

The phlebotomy needle of claim 10, wherein the elastomeric shield flange is positioned adjacent to the hydrophilic material.

12.

The phlebotomy needle of claim 1, wherein the distal end of said elastomeric shield is received in said housing and the proximal end of said elastomeric shield extends proximally from said housing.

detailed description

open

Description: BACKGROUND 1.

Technical Field The present disclosure relates to medical needles having structures that facilitate visualization of flashback. More particularly, the present disclosure provides vented phlebotomy needles that include structures that facilitate visualization of flashback.

Regarding. 2. Background of Related Art

Medical devices for drawing blood from a patient are well known. These devices include standard needle-syringes, butterfly needle sets, and phlebotomy needles. A butterfly needle set typically includes a hollow needle having a sharpened distal end and a proximal end secured to a needle hub. A proximal portion of the needle hub is connected to flexible tubing. The needle hub defines a fluid conduit in communication with the tubing and includes a pair of flexible, radially extending wings that facilitate grasping of the butterfly needle set by a medical practitioner. Generally, the flexible tubing is formed of a transparent material that allows medical personnel to visualize blood flow, or flashback, through the tubing proximate to the needle hub. Flashback visualization allows medical personnel to confirm that the needle has been correctly inserted into the patient. [0003] Some clinicians utilize a hypodermic needle-syringe with a clear needle hub to take blood samples. During insertion, these clinicians usually observe flashb

acks in the needle hub. Phlebotomy needles generally do not include structures for visualizing flashback. The lack of a flashback visualization feature on the phlebotomy needle is not a major drawback for more experienced HCWs, but for HCWs with little experience of drawing blood with a phlebotomy needle, the needle may be a problem. Not having any means of confirming proper positioning in the patient can increase the time required to draw blood and can increase patient discomfort. [0005]

In an attempt to overcome the above disadvantages, US Pat. No. 6,200,300 to Norris et al. discloses a phlebotomy needle, which is attachable to a blood collection tube, comprises an outer needle, an inner needle, and a valve (bulb). The valve is transparent, allowing medical personnel to visualize the blood when the outer needle is correctly positioned within the patient's vein. The valve also includes a button that can be depressed by a medical practitioner to vent air from within the needle. Air in the needle prevents blood from flowing through the needle and must be vented.

[0006]

[

0006] US Pat.

No. 5,450,856 . SUMMARY OF THE INVENTION [0007] The Norris phlebotomy needle is a H owever, a cheaper and simpler phlebotomy needle that facilitates flashback visualization is desired. SUMMARY OF THE INVENTION The present disclosure relates to a phlebotomy needle having a sharpened distal end configured to penetrate tissue.

a proximal needle portion having a sharpened proximal end configured to penetrate a blood collection tube stopper; and a central needle portion defining an opening. The distal needle portion, the proximal needle portion and the central needle portion define a fluid channel in communication with the opening. A material is positioned adjacent to the opening. The material is

of a type that allows air to exit the fluid channel through the openings while preventing the passage of blood. In one embodiment, the material provides a visual indication of blood flow, or flashback, adjacent the opening.

[0009]

In one embodiment, the material comprises a hydrophobic material. In alternative embodiments, the material comprises a hydrophilic capillary action material. In yet another embodiment, the material includes hydrophobic plugs. Alternatively, the material may define a collar positioned around the opening.

[0010]

In one embodiment, the opening is circular. Alternatively, the openings are envisioned to be of various configurations, such as rectangular or slot-shaped.

[0011]

In one embodiment, a transparent housing is positioned around the opening to facilitate visualization of the flashback. A housing may also be positioned to contain the material and may include a vent for venting air from the needle.

[0012]

In one embodiment, the phlebotomy needle includes engagement structure configured to engage the needle holder.

In one

embodiment, a check valve is provided to prevent air from entering the fluid channel through the opening. In yet another embodiment, the phlebotomy needle includes a needle holder. For example, the present invention provides the following items.

(Item 1)

A phlebotomy needle,
a distal needle portion having a sharpened distal end configured to penetrate tissue and a sharpened
proximal end configured to pierce a stopper of a blood collection tube. and a central needle portion
defining an opening, wherein the distal needle portion, the proximal needle portion and the central needle portion are in fluid communication with the opening a central needle portion defining a channel;

A material positioned adjacent to the opening of a type that allows air to exit the fluid channel through the opening while preventing the passage of blood to reduce blood flow.

A phlebotomy needle comprising a material that further enables visual indication .

(Item 2)

The phlebotomy needle of item 1, wherein the material comprises a hydrophobic material.
3.

The phlebotomy needle of claim 1, wherein said material comprises a hydrophilic capillary action material.

4.

The phlebotomy needle of claim 1, wherein said material comprises an inner layer of hydrophilic material facing towards said opening and an outer layer of hydrophobic material.

(Item 5)

The phlebotomy needle according to item 1, wherein the opening is circular.

6.

The phlebotomy needle of claim 1, wherein the opening defines an elongated slot.

7.

The phlebotomy needle of claim 1, further comprising a transparent housing positioned around the opening. Clause 8.

The phlebotomy needle of claim 1, further comprising an engagement structure supported by the phlebotomy needle, the engagement structure configured to engage a needle holder.

9.

The phlebotomy needle of claim 1, wherein the material defines a collar covering the opening and positioned about the needle.

10.

The phlebotomy needle of claim 9, further comprising a transparent housing positioned around the collar material.

11.

The phlebotomy needle of claim 1, further comprising a check valve for preventing air from entering the fluid channel through the opening.

12.

The phlebotomy needle of claim 1, further comprising a needle holder.

13.

The phlebotomy needle of claim 1, wherein the material provides a visual indication of blood flow through the opening.

(Item 14)

A phlebotomy needle, a distal needle portion having a sharpened distal end configured to penetrate tissue and a sharpened proximal end configured to pierce a stopper of a blood collection tube. and a central needle portion

defining an opening, wherein the distal needle portion, the proximal needle portion and the central needle portion are in fluid communication with the opening A central needle portion defining a channel and

a hydrophobic material positioned adjacent the opening to permit air to exit the fluid channel through the opening while allowing blood to exit the fluid channel. A hydrophobic material of a type that prevents passage and further permits visual indication of blood flow, a

transparent housing positioned around the opening, and

an engagement supported by the phlebotomy needle. A phlebotomy needle comprising: a structure, and an engagement structure configured to engage the needle holder .

(Item 15)

The phlebotomy needle of item 14, further comprising the needle holder.

(Item 16)

A phlebotomy needle,
a distal needle portion having a sharp distal tip configured to penetrate tissue;
a proximal needle portion having a sharpened proximal end configured to penetrate a blood collection tube stopper; and a central needle portion
defining an opening, the distal needle portion, the proximal The needle portion and the central needle portion define a fluid channel in communication with the opening, a hydrophilic capillary action material positioned adjacent the central needle portion and the opening, wherein air flows into the a hydrophilic capillary active material of a type that allows exiting the fluid channel through the opening while preventing the passage of blood, further permitting a visual indication of blood flow; and the opening
. and an engagement structure supported by the phlebotomy needle
, the engagement structure configured to engage a needle holder
.

(Item 17)

The phlebotomy needle of item 16, further comprising the needle holder.

(Item 18)

A phlebotomy needle, the phlebotomy needle
penetrating a distal needle portion having a sharpened distal end configured to penetrate tissue and a stopper of a blood collection tube. a proximal needle portion having a pointed proximal end configured to define a fluid channel
; a housing that includes a passive vent and
defines an observation area for visualizing blood in the housing
.

(Item 19)

19, further comprising an elastomeric shield positioned about the proximal needle portion, the elastomeric shield and the proximal needle portion defining a fluid flow path into the housing; Phlebotomy needle as described.

(Item 20)

20. The phlebotomy needle of any one of items 18 and 19, further comprising a fluted member positioned within the housing, the fluted member defining a plurality of fluid channels.

(Item 21)

The phlebotomy needle according to any one of items 18 to 20, further including a hydrophilic material supported within the housing.

22.

The phlebotomy needle of any one of items 18-21, wherein the needle has a central portion defining an opening into the housing.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014]

An embodiment of the presently disclosed vented phlebotomy needle with a flashback chamber is disclosed herein with reference to the drawings.

1 is a perspective view, with parts separated, of a "prior art" phlebotomy needle with a needle holder, a protective needle cover and a blood collection tube shown in phantom; FIG.

1A is a side cross-sectional view of an assembled "prior art" phlebotomy needle, needle holder, and blood collection tube shown in phantom, with the distal portion of the phlebotomy needle positioned within a vein; It is

2-1 is a side perspective view of one embodiment of the presently disclosed phlebotomy needle; FIG. 2A is a cross-sectional view of the phlebotomy needle shown in FIG. 2; FIG. 2B is a cross-sectional view along section line 2B-2B of FIG. 2A.

2-2C is a side cross-sectional view of another embodiment of a phlebotomy needle of the present disclosure; FIG.

3 is a side cross-sectional view of an alternate embodiment of the phlebotomy needle of the present disclosure; FIG. FIG. 3A is a cross-sectional view taken along section line 3A--3A of FIG.

FIG. 4 is a side perspective cutaway view of another embodiment of the phlebotomy needle of the present disclosure; FIG. FIG. 4A is a cross-sectional view along section line 4A--4A of FIG.

FIG. 5 is a side perspective cutaway view of another embodiment of the phlebotomy needle of the present disclosure; FIG.

6 is a side cross-sectional view of another embodiment of the phlebotomy needle of the present disclosure; FIG.

7 is a cross-sectional view along section line 7-7 of FIG. 6; FIG. DETAILED DESCRIPTION OF EMBODIMENTS

Embodiments of vented phlebotomy needles of the present disclosure with flashback chambers will now be described in detail with reference to the drawings

, In the drawings, like reference numbers indicate identical or corresponding elements in each of the several drawings. FIG. 1 shows a known phlebotomy needle 10, needle holder 12, and needle covers 14 and 16. As shown in FIG. A blood collection tube 17 is shown in phantom. Phlebotomy needle 10 includes a distal needle portion 20, a proximal needle portion 22 and an intermediate needle hub 23 with an engaging portion 24. Engaging portion 24 is provided to facilitate connecting phlebotomy needle 10 to needle holder 12. In one embodiment, the engaging portion includes a male fitting 24a configured to engage a female fitting or engaging member 26, which engages the distal end of needle holder 12. Alternatively, oth

er engagement structures may be used, including screws, snap-type connectors, and the like. An elastomeric shield 28 is positioned over the proximal needle portion 22 to seal the proximal needle portion 22, as described in further detail below . [0017]

Needle holder 12 includes a substantially cylindrical body 30 having a distal end including engagement member 26 and a proximal end including a pair of flange members 32 . Flange member 32 facilitates grasping and insertion of blood collection tube 17 by medical personnel. Cylindrical body 30 defines cavity 34 (FIG. 1A) for receiving blood collection tube 17 . Blood collection tube, usually

17 is sealed by a penetrable stopper 17a to define a low pressure cavity 17b (FIG. 1A). The distal end of holder 12 defines an opening 36 through engagement member 26 , opening 36 sized to receive proximal needle portion 22 . In use, needle 10 is secured to the distal end of needle holder 12 via engagement portion 24 and engagement member 26, as shown in FIG. 1A .

When needle 10 is secured to needle holder 12 , proximal needle portion 22 is positioned within cavity 34 of body 30 of needle holder 12 and elastomeric shield 28 is positioned over proximal needle portion 22 . A blood collection tube 17 (shown in phantom) containing a penetrable stopper 17a is then positioned within cavity 34 . When blood collection tube 17 is inserted into cavity 34 , proximal needle portion 22 engages stopper 17 a and penetrates shield 28 . Shield 28 is compressed downward (FIG. 1A) so that proximal needle portion 22 penetrates stopper 40 and enters cavity 17b of blood collection tube 17 . Once the distal needle portion 20 is properly positioned in the patient's vein 38 and the blood collection tube 17 is positioned within the cavity 34, blood is typically flowed through the needle 10 and into the blood collection tube 17. The blood collection tube 17 is maintained under vacuum. When the blood collection tube 17 is removed from the needle holder 12 , the resilient elastomeric shield 28 returns to its original configuration, covering and sealing the proximal needle portion 22 .

[0019]

FIGS. 2 and 2A illustrate one embodiment of the phlebotomy needle of the present disclosure with a flashback chamber, generally indicated as 100. FIG. Needle 100 includes distal end 102 , proximal end 104 and central portion 106 . Distal end 102 has a pointed end 102a configured to penetrate patient tissue, and proximal end 104 is configured to pierce stopper 17a of blood collection tube 17 (see FIG. 1A). It has a sharp edge 104a. Central portion 106 includes an engagement member 108, as discussed above, which is configured to engage a needle holder (FIG. 1). Central portion 106 also includes an opening or hole 110 and a translucent or tra

transparent housing 112 positioned around central portion 106 of the portion defining opening 110. Although opening 110 is shown as circular, other configurations are envisioned, such as rectangular, square, oval, elongated slot 39 (FIG. 5), and the like. A transparent housing 112 defines a blood reservoir 112a. Vent openings 113 are preferably formed in transparent housing 112. Vent opening 113 facilitates venting needle 100 and allows blood flow through needle 100. As discussed below, the vent opening 113 of the housing 112 may be covered with a material that allows passage of air but not liquid, such as blood, for example. Referring to FIGS. 2A and 2B, vent opening 113 may be covered with filter 116.

Filter 116 preferably includes an inner layer 116a of hydrophilic material and an outer layer 116b of hydrophobic material. Preferably, at least one of layers 116a and 116b has a pore size of less than 0.45 microns. Such a pore size allows air to pass through but prevents bacteria from entering the housing 112.

[0021]

Referring to FIG. 2C, in an alternative embodiment, filter 116 may be replaced by a hydrophobic check valve, such as flap valve 150, for example. As shown, flap valve 150 is configured to flex outward from housing 112 to expose vent opening 113 and vent housing 112 when blood begins to flow into housing 112.

A hydrophobic sheet 152 is positioned over opening 113 to prevent blood from exiting vent opening 113 when the check valve is open. Prior to blood beginning to flow into housing 112, flap valve 150 seals opening 113 to prevent material from entering housing 112. Alternatively, flap valve 150 may be formed from a hydrophilic material if the pore size of the hydrophilic material is sized to block the passage of blood components. When the distal end 102 of needle 100 is properly positioned within the patient's vein, ie, blood

The transparent housing 112 allows the medical practitioner to visualize blood flow through the needle 100 as air flows through the needle 100 and air is vented and blood enters the reservoir 112a through the opening 110. make it possible. This allows the medical practitioner to confirm that the distal end 102 of the needle 100 has been properly positioned within the patient's vein for drawing blood. This provides a significant benefit to medical practitioners attempting to draw blood from patients, especially those who have limited experience with drawing blood from patients with phlebotomy needles.

[0023]

FIG. 3 illustrates an alternative embodiment of the vented phlebotomy needle of the present disclosure with a flashback chamber generally indicated as 200. As shown in FIG. Needle 200 is substantially similar to needle 100, except as described below. Needle 200 includes distal end 202, proximal end 204 and central portion 206. Distal end 202 has a sharpened end 202a configured to pierce patient tissue, and proximal end 204 has a sharpened end 202a configured

d to pierce a stopper of a blood collection tube (see FIG. 1A). It has a tapered end 204a. Central portion 206 includes an opening or hole 210 and an engagement member 212a. Material 214 is positioned over hole 210. Material 214 may be a hydrophilic material that wicks blood in to the material so that blood flow through needle 200 can be readily discerned by medical personnel. To facilitate venting of needle 200, material 214 may be a hydrophilic material that is permeable to air but impermeable to liquids, such as blood. In one embodiment, the hydrophilic material can be of the type that changes color when in contact with blood. The material may be in the form of collar 250 (Fig. 3) or plug 252 (Fig. 4). Additionally, the material may be positioned within a transparent housing or hub 212, or alternatively positioned adjacent opening 210 without any housing. In an alternative embodiment, the material is a hydrophobic material that is air permeable but blood impermeable. It is noted that ventilation openings 226 may be provided in housing 212 to facilitate ventilation of the housing. A vent can be in the form of an opening in housing 212 that allows air to flow out of housing 212 as blood enters.

[0024]

In an alternative embodiment, further illustrated in FIGS. 3 and 3A, material 214 may be formed of an expandable material that allows air to pass through vent openings 226 before contacting the expandable material with blood. Material 214 may expand upon contact with blood, closing vent opening 226. Although only hydrophilic and hydrophobic materials have been disclosed herein, other materials that facilitate the passage of air while preventing the passage of blood and provide an indication of blood flow are disclosed in the present disclosure.

phlebotomy needles. The material may have other configurations not disclosed herein. For example, the material may define a pad that covers the opening.

FIGS.

6 and 7 illustrate another embodiment of the phlebotomy needle of the present disclosure with a flashback chamber, generally indicated as device 398. FIG. Phlebotomy needle 398 includes needle 400 and stepped housing 408. Needle 400 includes distal end 402, proximal end 404 and central portion 406. Distal end 402 has a pointed end 402a configured to penetrate tissue of a patient, and proximal end 404 is adapted to pierce a stopper (not shown) of a blood collection tube (not shown). It has a configured pointed end 404a.

The

stepped housing 408 has a distal portion 408a and a larger diameter proximal portion 408b. A stepped housing 408 is supported at the central portion 406. Distal portion 408a defines a throughbore 412 sized to receive central portion 406 of the needle. Distal portion 408a is sealed and secured to needle 400 using adhesive 410, for example. Alternatively, other known techniques such as crimping, clamping, screws, welding, etc. may be used to secure needle 400 to housing 408. Proximal portion 408b is a transparent or translucent material.

formed to facilitate visualization within proximal portion 408b of housing 408. Proximal portion 408b also defines a through hole 414 that communicates with through hole 412 but has a

larger diameter than through hole 412 . Proximal portion 408 b defines an annular recess 416 between portion 408 b and proximal end 404 of needle 400 . Recess 416 is sized to receive hydrophilic material 418 and inner fluted member 420 . An inner fluted member 420 is positioned around proximal end 404 of needle 400 and defines a plurality of channels 422 in communication with hydrophilic material 418 . A ventilation opening 409 is provided through housing 408 .

[0028]

An elastomeric shield 428 is positioned over the proximal end 404 of the needle 400 . As discussed above, elastomeric shield 428 may be resilient, sealing proximal end 404 of needle 400 when proximal end 404 of needle 400 is not connected to a blood collection tube (not shown). function to Elastomeric shield 428 includes a closed proximal end 428a and an open distal end 428b. Open distal end 428 b includes an annular flange 430 positioned adjacent material 418 within recess 416 of housing 408 . A proximal portion 408b of the housing 408 includes an inwardly extending annular rib 432 that engages a flange 430 of an elastomeric shield 428 and a distal end 428b of the shield 428. within recess 416 of housing 408 . A channel 436 is defined between elastomeric shield 428 and proximal end 404 of needle 400 , as indicated by arrow 434 . Channel 436 directs blood from proximal end 404 of needle 400 into fluted channel 422 of fluted member 420 and into contact with hydrophilic material 418 . In use, when blood contacts material 418 , material 418 provides a visual indication of blood flow that is visible through proximal portion 408 b of housing 408 .

[0029]

defined with filter 116 (FIGS. 2A-2B), defined with filter 252 (FIGS. 4-4A), or defined with filter 39 (FIG. 5), or defined with check valve 150 (FIG. 5). FIG. 2C) Vent opening 113, as well as openings 226 (FIGS. 3-3A) and opening 409 (FIG. 6) can all be described as passive vent openings, which are positioned within the needle cannula. Allows gases with pressures greater than atmospheric pressure to automatically leak into the atmosphere. These passive ventilation openings do not require any action by the user of the device according to the invention.

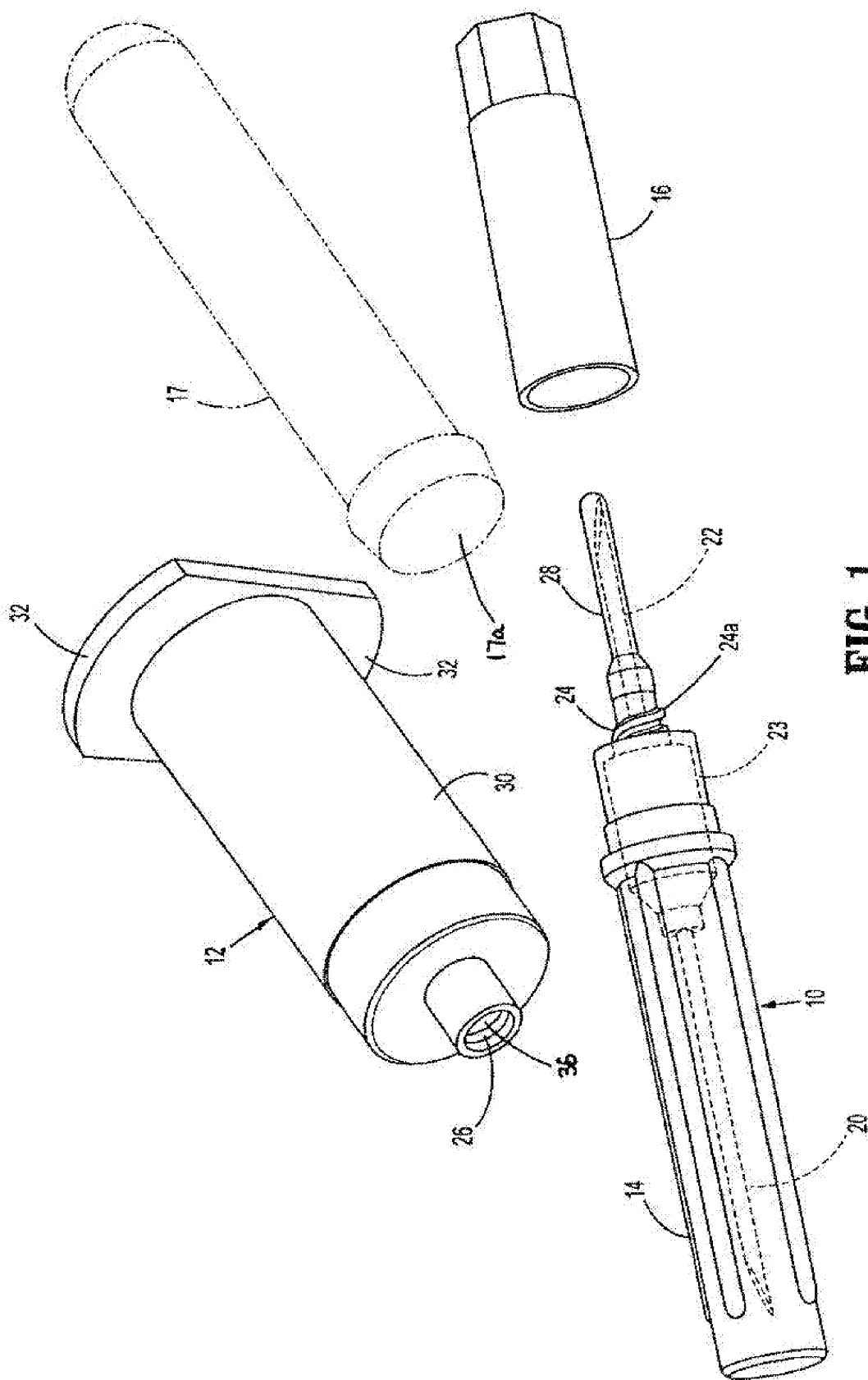
[0030]

It is understood that various modifications may be made to the embodiments disclosed herein. Therefore, the above should not be construed as limiting, but merely as exemplifications of preferred embodiments. Those skilled in the art will envision other modifications within the scope and spirit of the claims appended hereto.

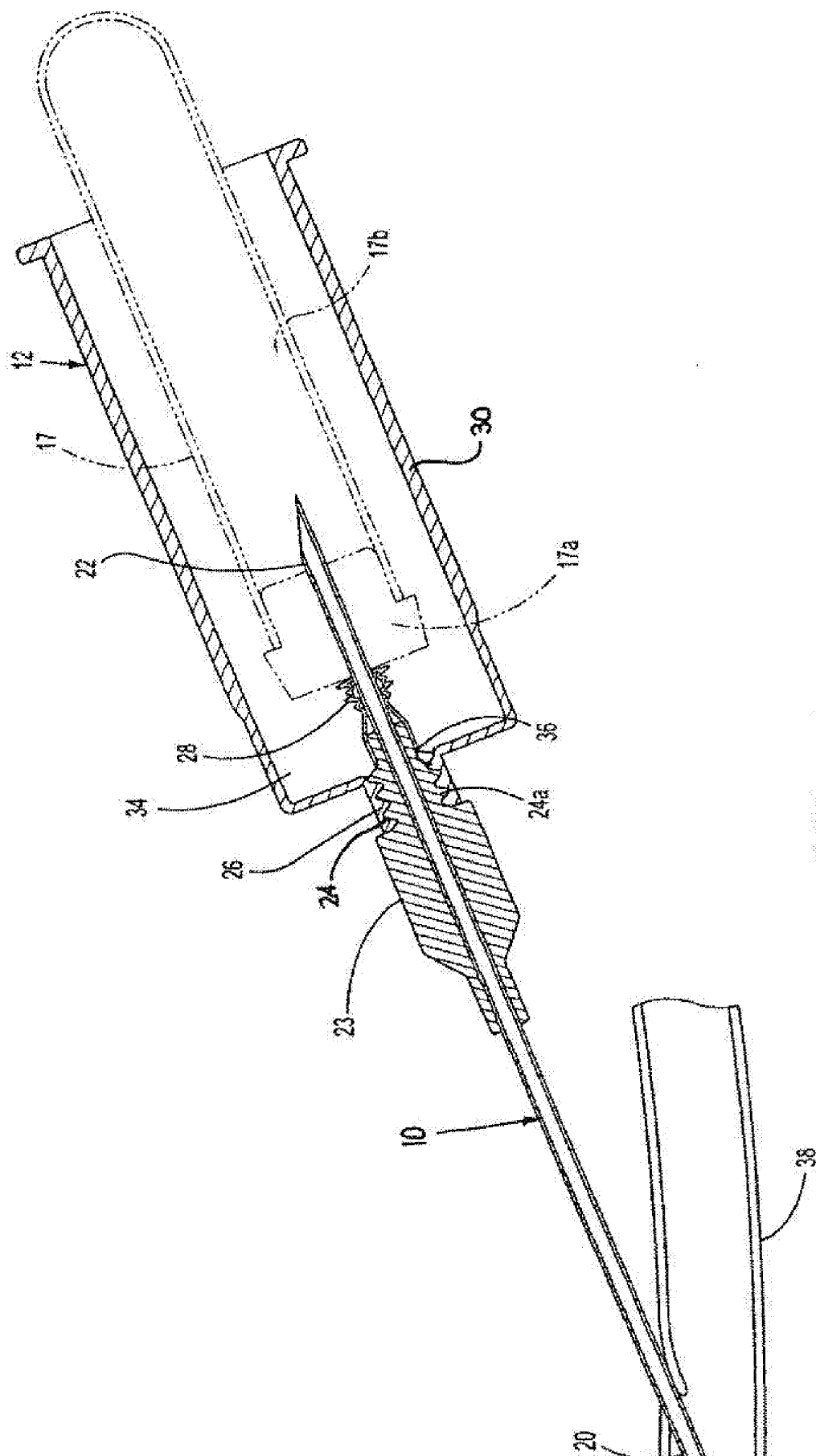
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[Fig. 1-1]



[Figure 1-2]



[Figure 2-1]



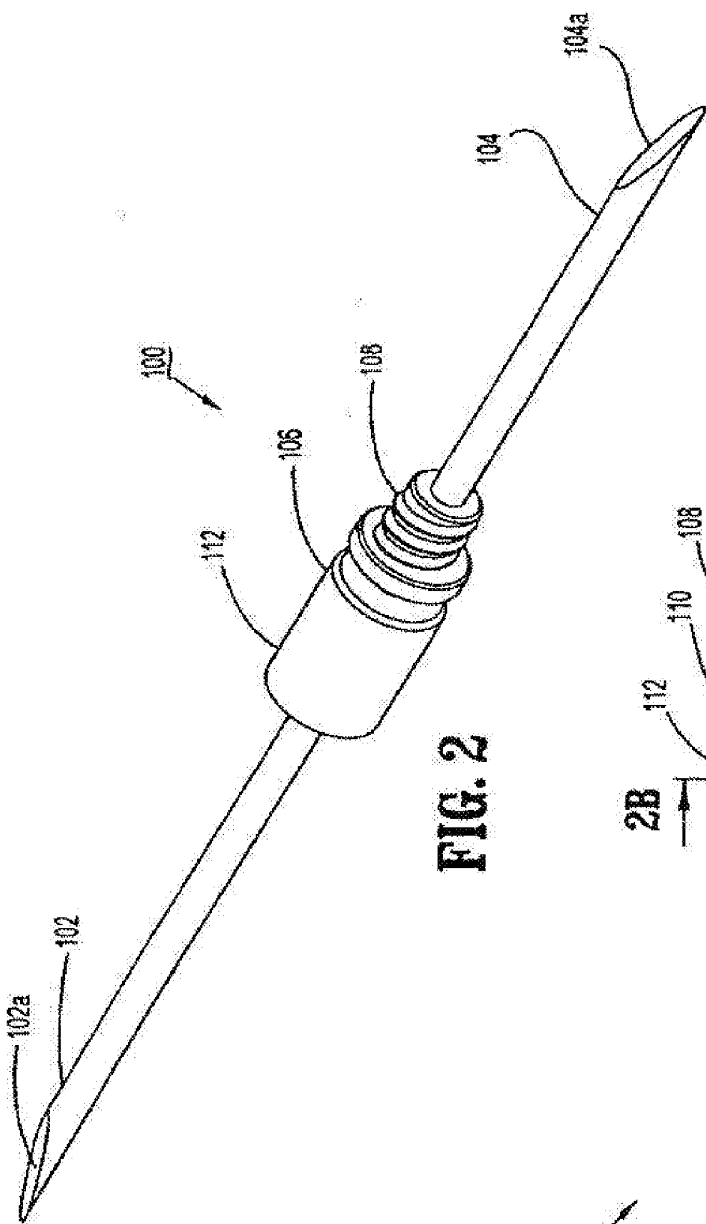


FIG. 2

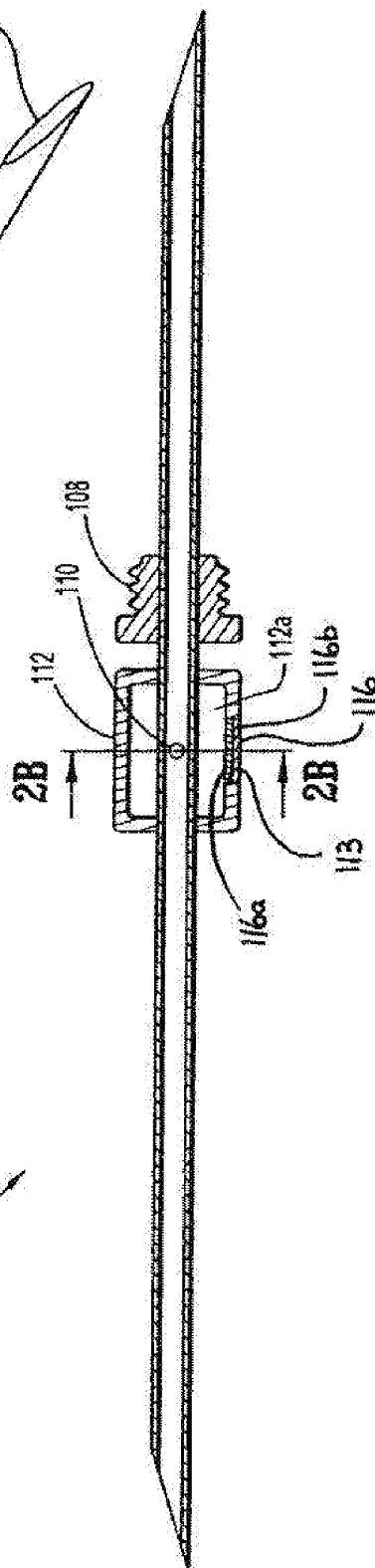


FIG. 2A

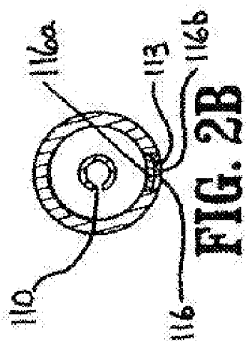


FIG. 2B

[Figure 2-2]

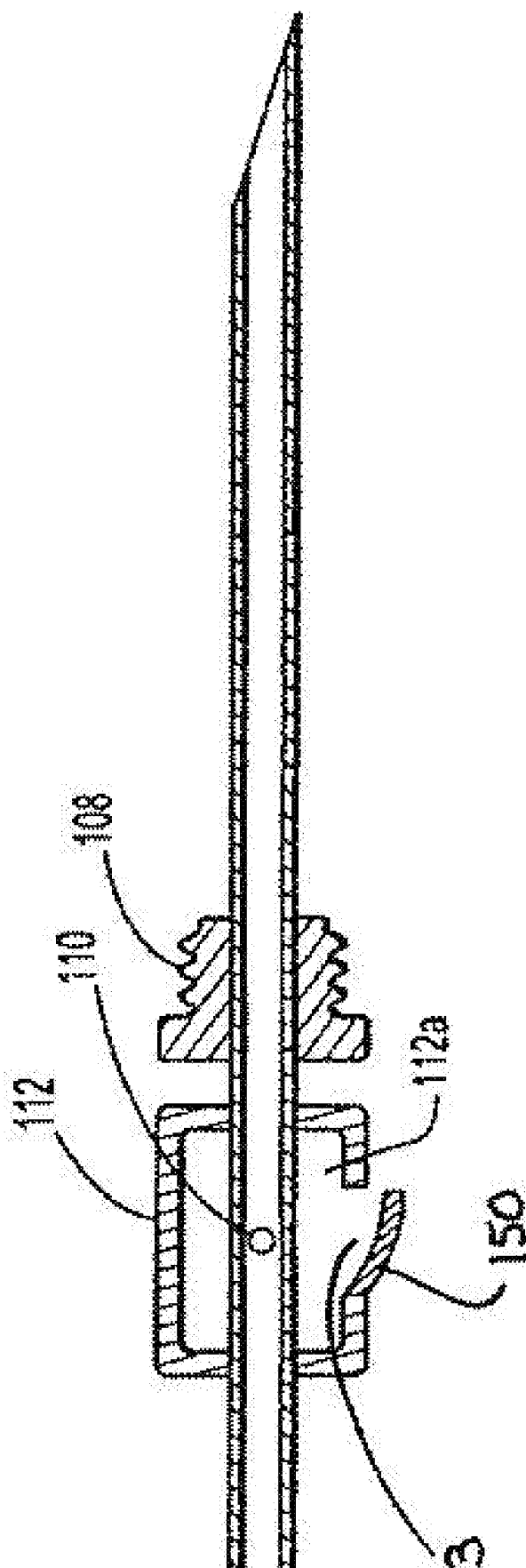


FIG. 20

[Figure 3]

100



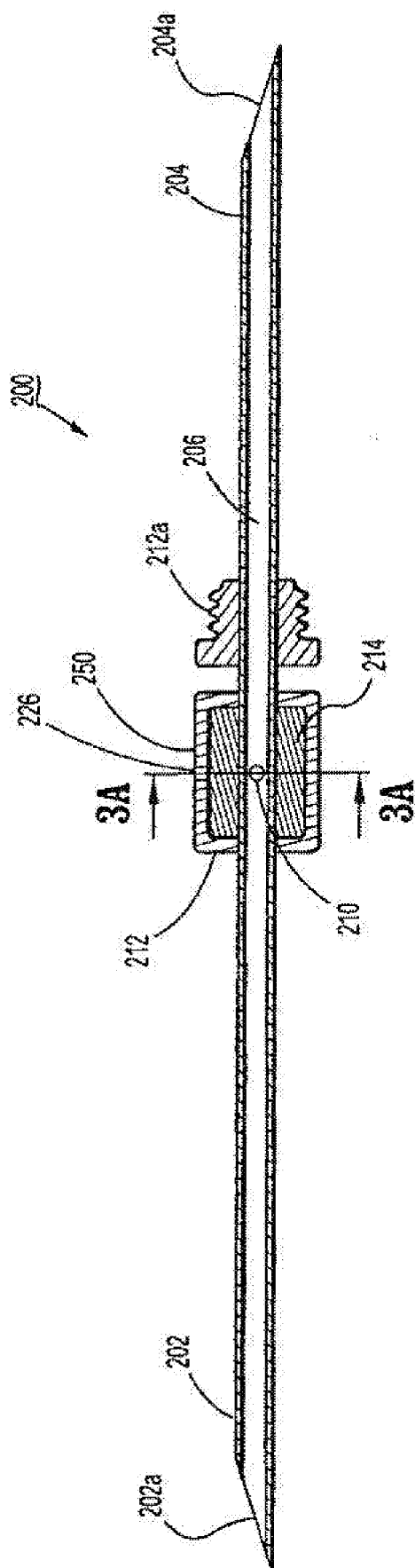


Fig. 3

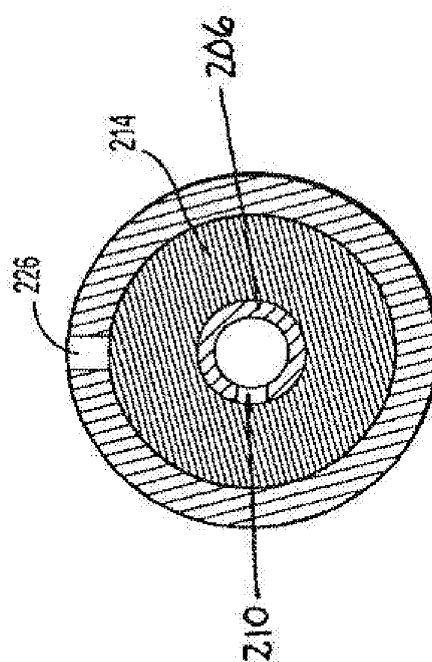
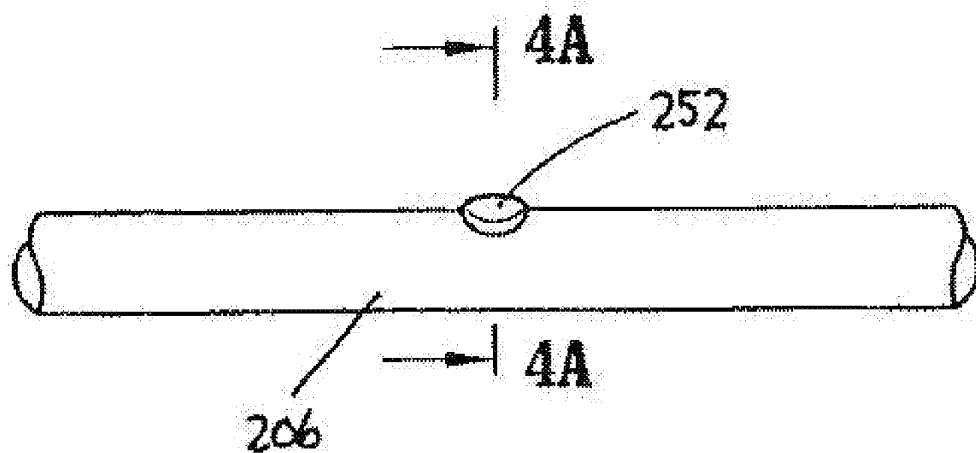
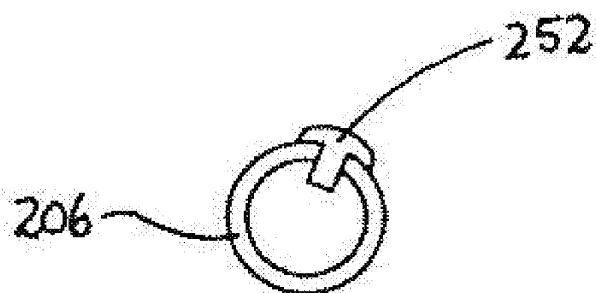


FIG. 3A

[Figure 4]

**FIG. 4****FIG. 4A**

[Figure 5]

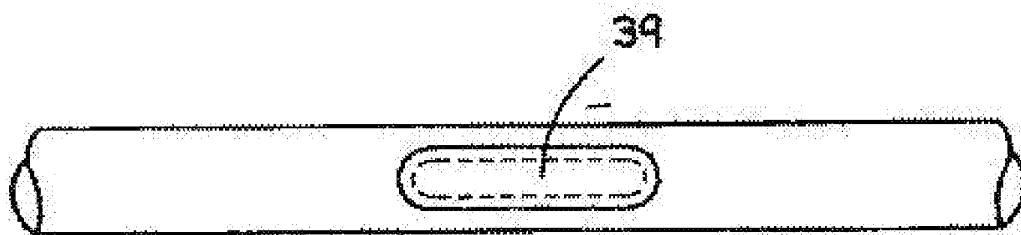
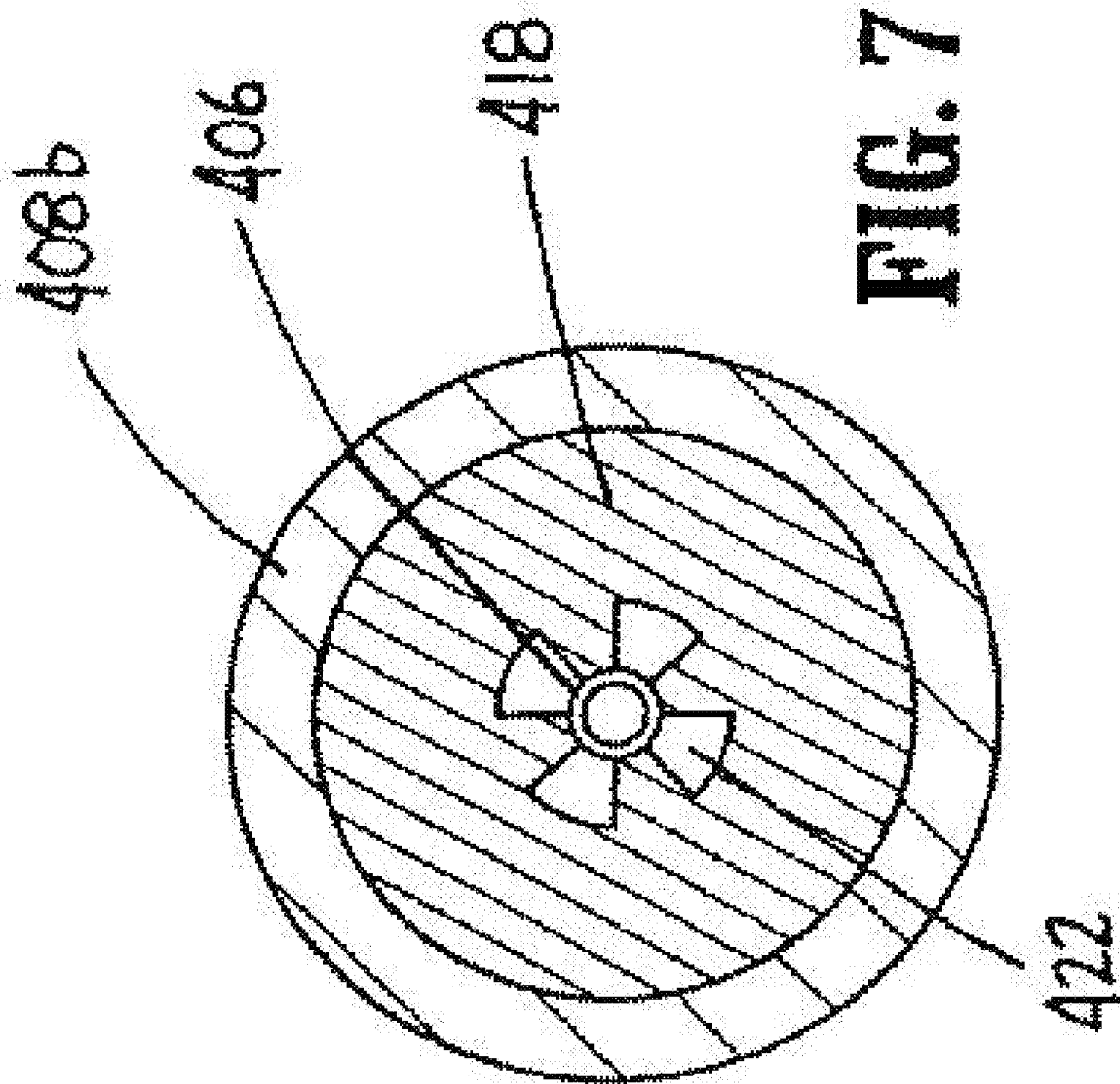


FIG. 5

[Fig. 6]

[Fig. 7]



Foreign language statement, etc.

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[Foreign language specification] [2013240628000001.pdf](#)

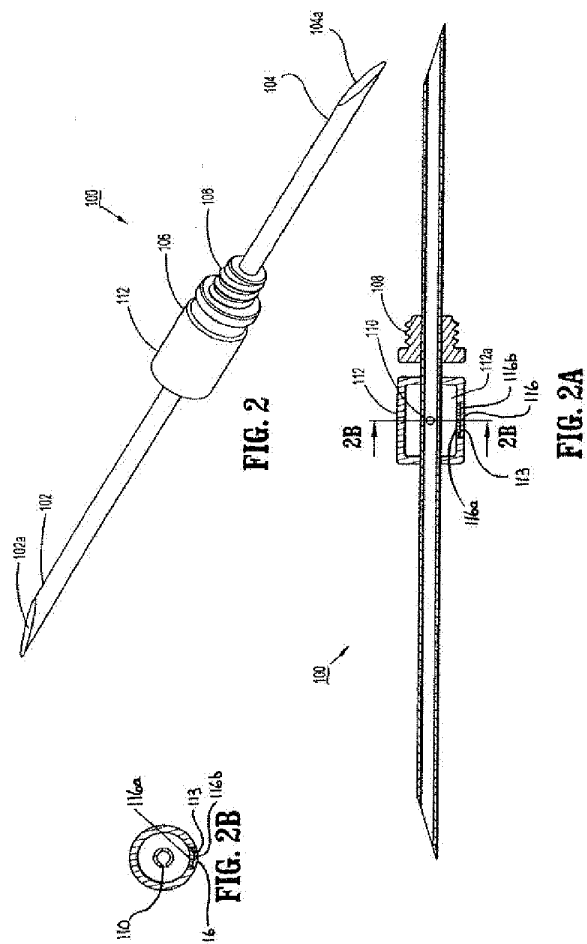
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Representative drawing

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VENTED PHLEBOTOMY NEEDLE WITH FLASHBACK CHAMBER

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Applicant(s): COVIDIEN LP ± (COVIDIEN LP)

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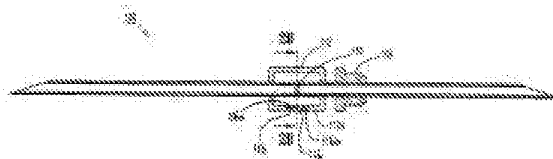
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Abstract of JP2013240628 (A)

PROBLEM TO BE SOLVED: To provide a less expensive, less complex phlebotomy needle which facilitates visualization of flashback. SOLUTION: A central portion 106 of a needle 100 includes a hole or opening 110 which communicates with a flow channel defined by the needle 100 and a transparent housing 112 is positioned about the opening 110 to facilitate visualization of blood flow through the needle 100. A material which allows passage of air and provides an indication of blood flow through the needle 100 is positioned over the opening 110. The material is in the form of a plug or, alternately, in the form of a patch or collar. The phlebotomy needle includes the needle 100 and the housing 112 having a passive vent and a viewing region for visualizing blood flow in the housing 112.



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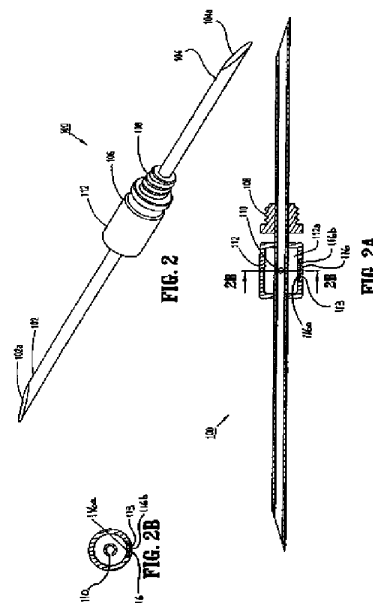
(54) 【発明の名称】 フラッシュバックチャンバを備えた通気型瀉血針

(57) 【要約】 (修正有)

【課題】フラッシュバックの可視化を容易にするより安価な、より簡単な瀉血針の提供。

【解決手段】針100の中央部分106は穴または開口部110を含み、該穴または開口部110は、針100によって画定された流路と連通し、透明の筐体112が、開口部110の周りに位置決めされ、針100を通る血流の可視化を容易にする。空気の通過を可能にし、針100を通る血流の表示を提供する材料が、開口部110を覆い位置決めされる。材料は、プラグの形であるか、または代替として、パッチまたはカラーの形である。瀉血針は、針100と、受動通気孔を有する筐体112と、筐体112の血流を可視化するための観察領域とを含む。

【選択図】 図2-1



【特許請求の範囲】

【請求項 1】

瀉血針であって：

組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分とを有し、該遠位の針部分と該近位の針部分が流体チャンネルを画定する、針；

該針上に支持される筐体であって、受動通気孔を含み、該筐体が該筐体中に血液を観察するための観察領域を画定する、筐体；および

該近位の針部分の周りに位置決めされるエラストマーのシールドであって、該エラストマーのシールドおよび該近位の針部分が該筐体中への流体の流路を画定する、エラストマーのシールド、を備える、瀉血針。

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【請求項 2】

前記筐体内に位置決めされる縦溝のある部材をさらに含み、該縦溝のある部材が複数の流体チャンネルを画定する、請求項 1 に記載の瀉血針。

【請求項 3】

前記縦溝のある部材が、前記エラストマーのシールドを超えて遠位方向に延びる、請求項 2 に記載の瀉血針。

【請求項 4】

前記縦溝のある部材の流体チャンネルが血液の通過を可能にするように構成されている、請求項 2 に記載の瀉血針。

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【請求項 5】

前記筐体内に支持される親水性材料をさらに含む、請求項 2 に記載の瀉血針。

【請求項 6】

前記流路が、血液を、前記針の近位端から前記縦溝のある部材の流体チャンネル中に、および前記親水性材料との接触に向ける、請求項 5 に記載の瀉血針。

【請求項 7】

前記縦溝のある部材の一部分が、前記親水性材料によって取り囲まれる、請求項 5 に記載の瀉血針。

【請求項 8】

前記縦溝のある部材の近位端が前記エラストマーのシールドによって取り囲まれ、そして該縦溝のある部材の遠位端が前記親水性材料によって取り囲まれる、請求項 5 に記載の瀉血針。

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【請求項 9】

前記筐体の近位部分が、内方に延びる環状のリブを含む、請求項 5 に記載の瀉血針。

【請求項 10】

前記エラストマーのシールドが環状のフランジを含む開いた遠位端を有し、前記筐体の環状のリブが該フランジに係合し、該エラストマーのシールドの遠位端を該筐体内に保持する、請求項 9 に記載の瀉血針。

【請求項 11】

前記エラストマーのシールドのフランジが、前記親水性材料に隣接して位置決めされる、請求項 10 に記載の瀉血針。

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【請求項 12】

前記エラストマーシールドの遠位端が前記筐体中に受容され、そして該エラストマーシールドの近位端が該筐体から近位方向に延びる、請求項 1 に記載の瀉血針。

【発明の詳細な説明】

【技術分野】

【0001】

(1. 技術分野)

本開示は、フラッシュバックの可視化を容易にする構造を有する医療用針に関する。より詳細には、本開示は、フラッシュバックの可視化を容易にする構造を含む通気型瀉血針

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に関する。

【背景技術】

【0002】

(2. 関連技術の背景)

患者から血液を抜き取る医療用デバイスは周知である。これらのデバイスは、標準的な針-注射器、蝶型針セット、および瀉血針を含む。通常、蝶型針セットは、尖った遠位端および針ハブに固定された近位端を有する中空の針を含む。針ハブの近位部分は、可撓性の配管に接続されている。針ハブは、配管と連通する流体導管を画定し、一对の可撓性の、半径方向に延びるウィングを含み、該ウィングは、医療従事者による蝶型針セットの把持を容易にする。一般に、可撓性の配管は、医療従事者が、針ハブに直近の配管を通る血流、すなわちフラッシュバックを可視化することを可能にする透明の材料で形成される。フラッシュバックの可視化は、針が患者の中に正しく挿入されたことを、医療従事者が確認することを可能にする。

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【0003】

一部の臨床医は、血液サンプルを採取するために、透明の針ハブを備えた皮下針-注射器を利用する。挿入の間、これらの臨床医たちは通常、針ハブの中のフラッシュバックを観察する。

【0004】

一般に、瀉血針は、フラッシュバックを可視化するための構造を含んでいない。瀉血針にフラッシュバックを可視化するための構造がないことは、より経験のある医療従事者にとっては大きな欠点ではないが、瀉血針によって血液を抜き取る経験をほとんど有しない医療従事者にとっては、針が正しく患者の中に位置決めされたことを確認するいかなる手段もないことは、血液を抜き取るために必要な時間を増加させ得、患者の不快感を増加させ得る。

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【0005】

上記の不利を克服する試みとして、Norrisらへの特許文献1は、瀉血針を開示し、該瀉血針は、採血管に取り付け可能であり、外側針、内側針、およびそれらの間にバルブ(bulb)を含む。バルブは、透明であり、外側針が正しく患者の静脈内に位置決めされたとき、医療従事者が血液を可視化することを可能にする。バルブは、針内から空気を通気するために医療従事者によって押し下げられ得るボタンも含む。針内の空気は、血液が針を通して流れることを妨げ、通気されなければならない。

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【先行技術文献】

【特許文献】

【0006】

【特許文献1】米国特許第5,450,856号明細書

【発明の概要】

【発明が解決しようとする課題】

【0007】

Norrisの瀉血針は、フラッシュバックの可視化を容易にするが、フラッシュバックの可視化を容易にするより安価な、より簡単な瀉血針が望まれる。

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【課題を解決するための手段】

【0008】

本開示は瀉血針に関し、該瀉血針は、組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、および開口部を画定する中央の針部分とを含む。遠位の針部分、近位の針部分および中央の針部分は、開口部と連通する流体チャンネルを画定する。材料が、開口部に隣接して位置決めされる。材料は、空気が開口部を通して流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものである。一実施形態において、材料は、開口部に隣接する血流、すなわちフラッシュバックの可視表示を提供する。

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【0009】

一実施形態において、材料は疎水性材料を含む。代替の実施形態において、材料は親水性毛管作用材料を含む。さらに別の実施形態において、材料は疎水性のプラグを含む。あるいは、材料は開口部の周りに位置決めされたカラー部を画定し得る。

【0010】

一実施形態において、開口部は円形である。あるいは、開口部は様々な構成、例えば長方形またはスロット形状であることが想定されている。

【0011】

一実施形態において、透明の筐体が開口部の周りに位置決めされ、フラッシュバックの可視化を容易にする。筐体はまた、材料を包含するように位置決めされ得、針から空気を通気するための通気孔を含み得る。

【0012】

一実施形態において、瀉血針は、針ホルダーと係合するように構成された係合構造を含む。

【0013】

一実施形態において、空気が開口部を通して流体チャンネルの中に入ることを阻止するために、逆止弁が提供される。さらに別の実施形態において、瀉血針は、針ホルダーを含む。

例えば、本発明は以下の項目を提供する。

(項目1)

瀉血針であって、
組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、
採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、
開口部を画定する中央の針部分であって、該遠位の針部分、該近位の針部分および該中央の針部分は、該開口部と連通する流体チャンネルを画定する、中央の針部分と、
該開口部に隣接して位置決めされた材料であって、空気が該開口部を通して該流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものであり、血流の可視表示をさらに可能にする、材料と
を備えている、瀉血針。

(項目2)

上記材料は疎水性材料を含む、項目1に記載の瀉血針。

(項目3)

上記材料は親水性毛管作用材料を含む、項目1に記載の瀉血針。

(項目4)

上記材料は、上記開口部の方に向かう親水性材料の内側層と、疎水性材料の外側層とを含む、項目1に記載の瀉血針。

(項目5)

上記開口部は円形である、項目1に記載の瀉血針。

(項目6)

上記開口部は細長いスロットを画定する、項目1に記載の瀉血針。

(項目7)

上記開口部の周りに位置決めされた透明の筐体をさらに含む、項目1に記載の瀉血針。

(項目8)

上記瀉血針で支持された係合構造であって、針ホルダーと係合するように構成された、係合構造をさらに含む、項目1に記載の瀉血針。

(項目9)

上記材料は、上記開口部を覆い上記針の周りに位置決めされたカラー部を画定する、項目1に記載の瀉血針。

(項目10)

上記カラー部の材料の周りに位置決めされた透明の筐体をさらに含む、項目9に記載の瀉血針。

(項目 1 1)

空気が、上記開口部を通して上記流体チャンネルの中に入ることを阻止するための逆弁をさらに含む、項目 1 に記載の瀉血針。

(項目 1 2)

針ホルダーをさらに含む、項目 1 に記載の瀉血針。

(項目 1 3)

上記材料は、上記開口部を通る血流の可視表示を提供する、項目 1 に記載の瀉血針。

(項目 1 4)

瀉血針であって、

組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、

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採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、

開口部を画定する中央の針部分であって、該遠位の針部分、該近位の針部分および該中央の針部分は、該開口部と連通する流体チャンネルを画定する、中央の針部分と、

該開口部に隣接して位置決めされた疎水性材料であって、空気が該開口部を通して該流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものであり、血流の可視表示をさらに可能にする、疎水性材料と、

該開口部の周りに位置決めされた透明の筐体と、

該瀉血針で支持された係合構造であって、針ホルダーと係合するように構成された、係合構造と

を備えている、瀉血針。

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(項目 1 5)

上記針ホルダーをさらに含む、項目 1 4 に記載の瀉血針。

(項目 1 6)

瀉血針であって、

組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、

採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分と、

開口部を画定する中央の針部分であって、該遠位の針部分、該近位の針部分および該中央の針部分は、該開口部と連通する流体チャンネルを画定する、中央の針部分と、

該開口部に隣接して位置決めされた親水性毛管作用材料であって、空気が該開口部を通して該流体チャンネルを出ることを可能にし、一方、血液の通過を防止するタイプのものであり、血流の可視表示をさらに可能にする、親水性毛管作用材料と、

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該開口部の周りに位置決めされた透明の筐体と、

該瀉血針で支持された係合構造であって、針ホルダーと係合するように構成された、係合構造と

を備えている、瀉血針。

(項目 1 7)

上記針ホルダーをさらに含む、項目 1 6 に記載の瀉血針。

(項目 1 8)

瀉血針であって、該瀉血針は、

針であって、組織を貫通するように構成された尖った遠位端を有する遠位の針部分と、採血管のストッパを貫通するように構成された尖った近位端を有する近位の針部分とを含み、該遠位の針部分および該近位の針部分は、流体チャンネルを画定する、針と、

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該針で支持された筐体であって、受動通気孔を含み、該筐体の血液を可視化するための観察領域を画定する、筐体と

を備えている、瀉血針。

(項目 1 9)

上記近位の針部分の周りに位置決めされたエラストマーのシールドをさらに含み、該エラストマーのシールドおよび該近位の針部分が、上記筐体の中への流体の流路を画定する、項目 1 8 に記載の瀉血針。

(項目 2 0)

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上記筐体内に位置決めされた縦溝のある部材をさらに含み、該縦溝のある部材は、複数の流体チャンネルを画定する、項目 18 および項目 19 のうちのいずれか一項に記載の瀉血針。

(項目 21)

上記筐体内に支持された親水性材料をさらに含む、項目 18 ～項目 20 のうちのいずれか一項に記載の瀉血針。

(項目 22)

上記針は、上記筐体の中への開口部を画定する中央部分を有する、項目 18 ～項目 21 のうちのいずれか一項に記載の瀉血針。

【図面の簡単な説明】

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【0014】

フラッシュバックチャンバを備えた本開示の通気型瀉血針の実施形態が、図面を参照して本明細書に開示される。

【図 1-1】図 1 は、針ホルダー、保護針カバーおよび幻影で示された採血管を備えた「従来技術」の瀉血針の斜視図であり、部品は分離されている。

【図 1-2】図 1 A は、組み立てられた「従来技術」の瀉血針、針ホルダー、および幻影で示された採血管の側面断面図であり、瀉血針の遠位部分は静脈内に位置決めされている。

【図 2-1】図 2 は、本開示の瀉血針の一実施形態の側面斜視図である。図 2 A は、図 2 で示された瀉血針の断面図である。図 2 B は、図 2 A の切断線 2 B-2 B に沿った断面図である。

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【図 2-2】図 2 C は、本開示の瀉血針の別の実施形態の側面断面図である。

【図 3】図 3 は、本開示の瀉血針の代替の実施形態の側面断面図である。図 3 A は、図 3 の切断線 3 A-3 A に沿った断面図である。

【図 4】図 4 は、本開示の瀉血針の別の実施形態の側面斜視切取り図である。図 4 A は、図 4 の切断線 4 A-4 A に沿った断面図である。

【図 5】図 5 は、本開示の瀉血針の別の実施形態の側面斜視切取り図である。

【図 6】図 6 は、本開示の瀉血針の別の実施形態の側面断面図である。

【図 7】図 7 は、図 6 の切断線 7-7 に沿った断面図である。

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【発明を実施するための形態】

【0015】

(実施形態の詳細な記述)

フラッシュバックチャンバを備えた本開示の通気型瀉血針の実施形態がここで、図面を参照して詳細に記述され、該図面においては、同様の参照番号は、幾つかの図面の各々において同一のまたは対応する要素を示す。

【0016】

図 1 は、公知の瀉血針 10、針ホルダー 12、ならびに針カバー 14 および 16 を示す。採血管 17 が幻影で示されている。瀉血針 10 は、遠位の針部分 20 と、近位の針部分 22 と、係合部分 24 を備えた中間の針ハブ 23 とを含む。係合部分 24 は、瀉血針 10 を針ホルダー 12 に接続することを容易にするように提供される。一実施形態において、係合部分は、雄継手 24 a を含み、雄継手 24 a は、雌継手または係合部材 26 と係合するように構成され、係合部材 26 は、針ホルダー 12 の遠位端に提供される。あるいは、ねじ、スナップ型コネクタ、その他を含む他の係合構造が使用され得る。下にさらに詳細に記述されるように、エラストマーのシールド 28 が近位の針部分 22 を覆い位置決めされ、近位の針部分 22 をシールする。

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【0017】

針ホルダー 12 は、実質的に円筒状の本体 30 を含み、実質的に円筒状の本体 30 は、係合部材 26 を含む遠位端および一對のフランジ部材 32 を含む近位端を有する。フランジ部材 32 は、医療従事者による採血管 17 の把持および挿入を容易にする。円筒状の本体 30 は、採血管 17 を受け入れるための空洞 34 (図 1 A) を画定する。通常、採血管

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17は、貫通可能ストッパ17aによってシールされ、低圧の空洞17b（図1A）を画定する。ホルダー12の遠位端は、係合部材26を通る開口部36を画定し、開口部36は、近位の針部分22を受け入れる大きさとされる。

【0018】

図1Aに示されるように、使用に際して、針10は、係合部分24および係合部材26を介して針ホルダー12の遠位端に固定される。針10が針ホルダー12に固定されると、近位の針部分22は、針ホルダー12の本体30の空洞34内に位置決めされ、エラストマーのシールド28は、近位の針部分22を覆い位置決めされる。次に、貫通可能ストッパ17aを含む採血管17（幻影で示される）が、空洞34内に位置決めされる。採血管17が空洞34の中に挿入されると、近位の針部分22が、ストッパ17aと係合し、シールド28を貫通する。近位の針部分22が、ストッパ40を貫通し、採血管17の空洞17bに入るように、シールド28は下向きに圧縮（図1A）される。遠位の針部分20が患者の静脈38に正しく位置決めされ、採血管17が空洞34内に位置決めされると、血液が、針10を通して採血管17の中に流入するように、通常、採血管17は、真空に維持される。採血管17が針ホルダー12から取り外されると、弾力的なエラストマーのシールド28は、その元の構成に戻り、近位の針部分22を被覆し、近位の針部分22をシールする。

【0019】

図2および図2Aは、概して100として示されるフラッシュバックチャンバを備えた本開示の瀉血針の一実施形態を示す。針100は、遠位端102と、近位端104と、中央部分106とを含む。遠位端102は、患者の組織を貫通するように構成された尖った端102aを有し、近位端104は、採血管17（図1Aを参照）のストッパ17aを貫通するように構成された尖った端104aを有する。中央部分106は、上に論議されたように、係合部材108を含み、係合部材108は針ホルダー（図1）と係合するように構成される。中央部分106はまた、開口部または穴110と、開口部110を画定する部分の中央部分106の周りに位置決めされた半透明または透明の筐体112とを含む。開口部110は円形として示されているが、他の構成、例えば長方形、正方形、楕円形、細長いスロット39（図5）、その他が想定されている。透明の筐体112は、血液レザバ112aを画定する。通気開口部113は好ましくは、透明の筐体112に形成される。通気開口部113が針100の通気を容易にし、針100を通る血流を可能にする。下に論議されるように、筐体112の通気開口部113は、空気の通過は許すが、例えば血液のような液体の通過は許さない材料によって被覆され得る。

【0020】

図2Aおよび図2Bを参照して、通気開口部113は、フィルタ116で被覆され得る。フィルタ116は好ましくは、親水性材料の内側層116aと、疎水性材料の外側層116bとを含む。好ましくは、層116aおよび層116bのうちの少なくとも1つは、0.45ミクロンを下回る孔サイズを有する。かかる孔サイズは、空気の通過は可能にするが、バクテリアが筐体112の中に入ることを防止する。

【0021】

図2Cを参照して、代替の実施形態において、フィルタ116は、例えばフラップ弁150のような疎水性逆止弁によって置き換えられ得る。図示のように、フラップ弁150は、筐体112の中に血液が流入し始めると、筐体112から外向きに曲がり、通気開口部113を露出させ、筐体112を通気するように構成される。逆止弁が開いたとき、血液が通気開口部113から出ることを防止するために、疎水性シート152が開口部113を覆い位置決めされる。血液が筐体112の中に流入し始めるのに先立って、フラップ弁150は開口部113をシールし、物質が筐体112の中に入ることを防止する。あるいは、フラップ弁150は、親水性材料の孔サイズが血液成分の通過を遮るサイズである場合は、該親水性材料から形成され得る。

【0022】

針100の遠位端102が患者の静脈内に正しく位置決めされたとき、すなわち、血液

が針１００を通して流れ、空気が通気されて、血液が開口部１１０を通してレザバ１１２ａの中に入るとき、透明の筐体１１２は、医療実施者が針１００を通る血流を可視化することを可能にする。これによって、医療実施者は、針１００の遠位端１０２が、血液を抜き取るために患者の静脈内に正しく位置決めされたことを確認することができる。これは、患者から血液を抜き取ろうと試みる医療実施者に対して、特に瀉血針によって患者から血液を抜き取ることに限られた経験しか有しないような実施者に対して大きな利益を提供する。

【００２３】

図３は、概して２００として示されるフラッシュバックチャンバを備えた本開示の通気型瀉血針の代替の実施形態を示す。針２００は、下に記述されたとおりを除いて、針１００と実質的に同様である。針２００は、遠位端２０２と、近位端２０４と、中央部分２０６とを含む。遠位端２０２は、患者の組織を貫通するように構成された尖った端２０２ａを有し、近位端２０４は、採血管（図１Ａを参照）のストッパを貫通するように構成された尖った端２０４ａを有する。中央部分２０６は、開口部または穴２１０と係合部材２１２ａとを含む。材料２１４は、穴２１０を覆い位置決めされている。医療従事者が針２００を通る血流を容易に識別し得るように、材料２１４は、材料の中に血液を毛管作用で吸い込む親水性の材料であり得る。針２００の通気を容易にするために、材料２１４は、空気に対しては透過性があるが、例えば血液のように液体に対しては透過性がない親水性材料であり得る。一実施形態において、親水性材料は、血液と接触したとき、色が変わるタイプのものであり得る。材料は、カラー２５０（図３）またはプラグ２５２（図４）の形であり得る。さらに、材料は、透明の筐体もしくはハブ２１２内に位置決めされ得るか、または代替的に、いかなる筐体もなく開口部２１０に隣接して位置決めされ得る。代替の実施形態において、材料は、空気は通すが血液は通さない疎水性の材料である。通気開口部２２６は筐体２１２に提供され得、筐体の通気を容易にし得ることに留意される。通気孔は、筐体２１２における開口部の形であり得、該開口部は、血液が入ると筐体２１２から空気が流れ出ることを可能にする。

【００２４】

図３および図３Ａでさらに示される代替の実施形態において、材料２１４は、膨張可能な材料で形成され得、該膨張可能な材料が血液と接触する前に、空気が通気開口部２２６を通ることを可能にする。材料２１４は、血液と接触すると膨張し得、通気開口部２２６を閉じ得る。

【００２５】

本明細書において、親水性材料および疎水性材料のみが開示されたが、血液の通過を防止しながら空気の通過を容易にし、血流の表示を提供する他の材料が、本開示の瀉血針に対して使用され得る。材料は、本明細書に開示されていない他の構成を有し得る。例えば、材料は、開口部を被覆するパッドを画定し得る。

【００２６】

図６および図７は、概してデバイス３９８として示されるフラッシュバックチャンバを備えた本開示の瀉血針の別の実施形態を示す。瀉血針３９８は、針４００と段付き筐体４０８とを含む。針４００は、遠位端４０２と、近位端４０４と、中央部分４０６とを含む。遠位端４０２は、患者の組織を貫通するように構成された尖った端４０２ａを有し、近位端４０４は、採血管（図示されず）のストッパ（図示されず）を貫通するように構成された尖った端４０４ａを有する。

【００２７】

段付き筐体４０８は、遠位部分４０８ａおよびより大きな直径の近位部分４０８ｂを有する。段付き筐体４０８は、中央部分４０６で支持されている。遠位部分４０８ａは、針の中央部分４０６を受け入れる大きさとされた通し穴４１２を画定する。遠位部分４０８ａは、例えば接着剤４１０を使用して、針４００にシールされ、固定される。あるいは、他の公知の技術、例えばクリンプ加工、クランプ、ねじ、溶接その他が使用され得、針４００を筐体４０８に固定し得る。近位部分４０８ｂは、透明の材料または半透明の材料で

形成され、筐体 408 の近位部分 408 b 内の可視化を容易にする。近位部分 408 b はまた、通し穴 414 を画定し、通し穴 414 は通し穴 412 と連通するが、通し穴 412 よりも直径が大きい。近位部分 408 b は、部分 408 b と針 400 の近位端 404 との間に環状のリセス 416 を画定する。リセス 416 は、親水性材料 418 および内側の縦溝のある部材 420 を受け入れるような大きさとされる。内側の縦溝のある部材 420 が、針 400 の近位端 404 の周りに位置決めされ、親水性材料 418 と連通する複数のチャンネル 422 を画定する。通気開口部 409 は、筐体 408 を通して提供される。

【0028】

エラストマーのシールド 428 は、針 400 の近位端 404 を覆い位置決めされる。上に論議されたように、エラストマーのシールド 428 は弾力的であり得、針 400 の近位端 404 が採血管（図示されず）に接続されていないとき、針 400 の近位端 404 をシールドするように機能する。エラストマーのシールド 428 は、閉じた近位端 428 a と開いた遠位端 428 b とを含む。開いた遠位端 428 b は環状のフランジ 430 を含み、環状のフランジ 430 は、筐体 408 のリセス 416 内で材料 418 に隣接して位置決めされる。筐体 408 の近位部分 408 b は、内向きに延びる環状のリブ 432 を含み、内向きに延びる環状のリブ 432 は、エラストマーのシールド 428 のフランジ 430 と係合し、シールド 428 の遠位端 428 b を筐体 408 のリセス 416 内に保持するように位置決めされる。矢印 434 によって示されるように、流路 436 は、エラストマーのシールド 428 と針 400 の近位端 404 との間に画定される。流路 436 は、針 400 の近位端 404 から縦溝のある部材 420 の縦溝のあるチャンネル 422 の中に血液を導き、親水性材料 418 と接触させる。使用に際して、血液が材料 418 と接触すると、材料 418 は、筐体 408 の近位部分 408 b を通して目視可能となる血流の可視表示を提供する。

【0029】

フィルタ 116 と共に画定された（図 2 A ～図 2 B）、フィルタ 252 と共に画定された（図 4 ～図 4 A）、もしくはフィルタ 39 と共に画定された（図 5）、または逆止弁 150 と共に画定された（図 2 C）通気開口部 113、ならびに開口部 226（図 3 ～図 3 A）および開口部 409（図 6）はすべて、受動通気開口部として記述され得、該受動通気開口部は、針カニューレ内において大気圧よりも大きな圧力の気体が大気中に自動的に漏れることを可能にする。これらの受動通気開口部は、本発明によるデバイスのユーザによるいかなる行動も必要としない。

【0030】

本明細書に開示された実施形態には、様々な変更がなされ得ることは理解される。したがって、上述は、限定するものとして解釈されるべきではなく、好ましい実施形態の単なる例示として解釈されるべきである。当業者は、本明細書に添付された請求項の範囲および精神内で他の変更にも想到する。

【图 1-1】

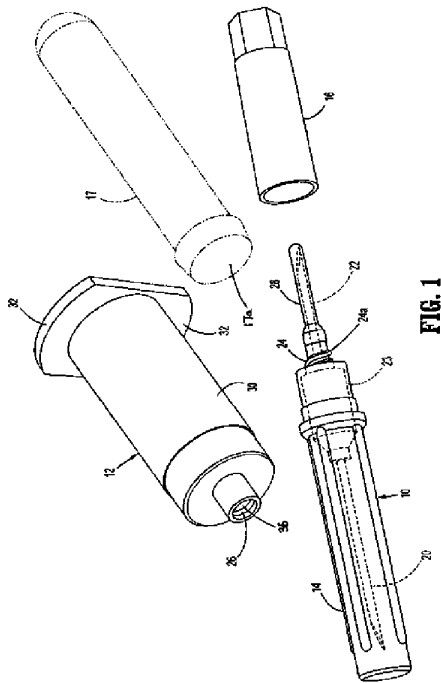


FIG. 1

【圖 1-2】

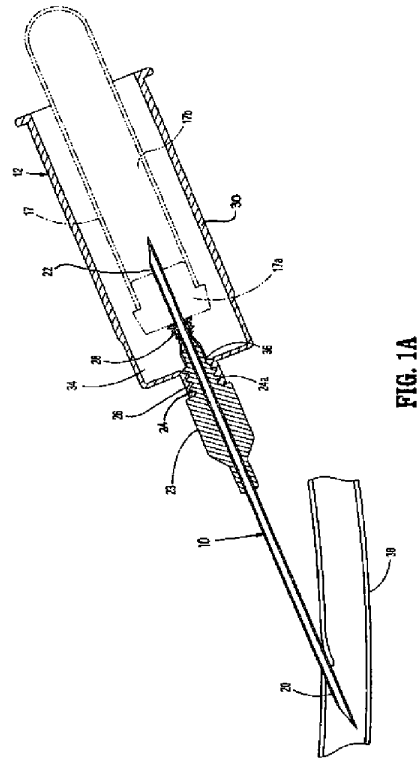


FIG. 1A

【圖 2-1】

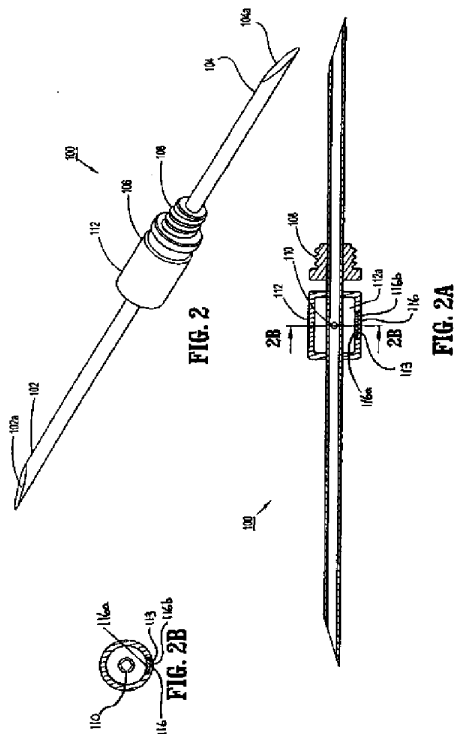


FIG. 2A

【图 2-2】

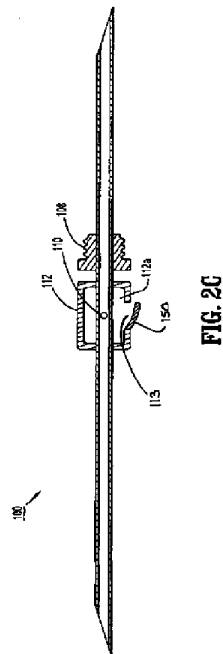
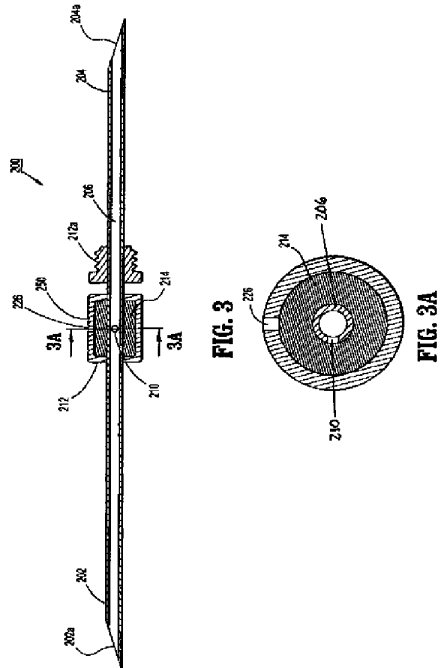


FIG. 2C

【 図 3 】



【 図 4 】

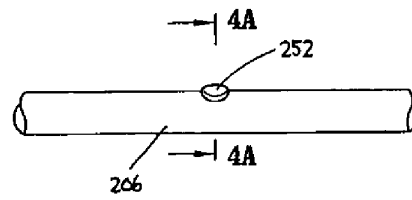


FIG. 4



FIG. 4A

【 図 5 】

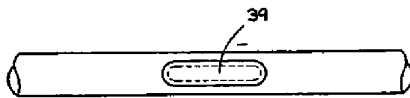
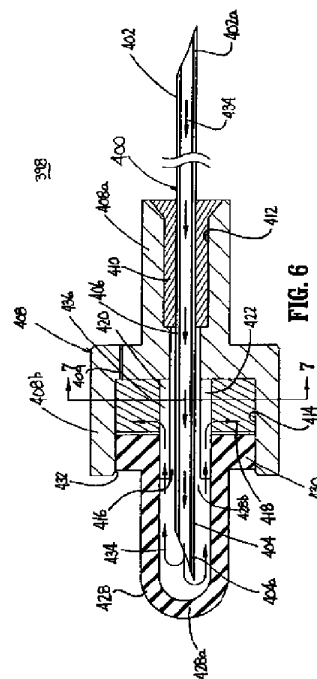
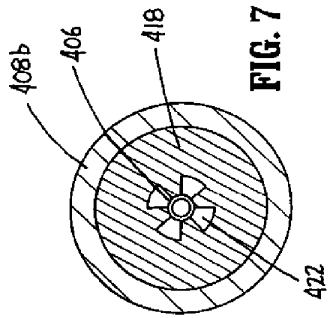


FIG. 5

【图 6】



【図 7】



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[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 or 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 detection 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 that generates sensor data including position data indicating whether a detection area is being touched; and based on the sensor data, whether or not the driver is gripping the grip and the touch

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 operation 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 the specific input operation, wherein the touch sensor includes a part of the plurality of detection areas

, a grip detection area for detecting the contact of the driver's palm, and an operation detection 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 based 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 for an operation target device in a vehicle, wherein the specific input operation is detected by data, and the

control unit disables control of the operation target device when the vehicle is in a specific state.

5.

The controller controls, as the specific input operation, two points spaced apart in the circumferential direction in a cross section of the steering wheel when the grip is cut in the radial direction 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 according to claim 3 or 4, characterized in that :

6.

The controller determines that the vehicle is in a specific state when the rotation angle of the steering wheel exceeds a predetermined angle, and invalidates the control of the device to be 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 grip portion gripped with the left hand of the driver and a second touch sensor mounted in a predetermined 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 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. The control

device for an operation target device in a vehicle according to any one of claims 1 to 6, characterized 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. detecting 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 specific state, it is detected that the driver is gripping the touch sensor, and it is detected that the specific 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 detected that the vehicle is in a specific state in which a direction indicator is operated. A control method 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 operation target.

14. The method for controlling an operation target device in a vehicle according to any one of 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 system installed in a vehicle, or a transmission, a direction indicator, or the like. The present invention 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 operation switches for operating vehicle-mounted equipment such as a navigation system are arranged 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 equipment 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 not the annular portion of the steering wheel, which is the grip portion that the driver grips, but 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 annular 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 Documents] [Patent Documents] [Patent Document 1] Japanese Patent Laid-Open Publication No. 2007-106353 [Patent Document 2] Japanese Patent Laid-Open Publication No. 2005-348123 [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 operation

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 t he operation target device to be operated by the touch sensorand, when it is detected that th e 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 device to be operated in the vehicle of the present invention, the device to be operated can be operated without releasing the hand from the grip portion or moving the hand largely

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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 for an operation-targeted device according to one embodiment;

FIG. 3 is a diagram showing an example of positions and ranges where touch sensors are mounted 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 wheel;

FIG. 6 is a partial perspective view showing an example of a portion of the steering wheel from 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 cross-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 sensor 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 touch sensor;

13A and 13B are schematic diagrams showing still another example of a specific input operation 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 control method

for

an operation target device in a vehicle according to the present invention will be described below with reference to the accompanying drawings. 1 and 2, the in-vehicle device 100 is mounted inside the dashboard of the vehicle. In the example shown in FIG. 1, the in-vehicle device 100 includes a control unit 10, a navigation processing unit 11, an audio reproduction unit 12, a television (TV) tuner 13, a video signal processing unit 14, a video display unit 15, an audio signal processing unit 16, a display element 17 and a storage unit 18. The control unit 10 includes a detection unit 10a. The navigation processing unit 11 has a storage unit for holding 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 tuner 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 11 or the TV tuner 13 is input to the video signal processing unit 14 via the control unit 10, processed, 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 the 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 from the in-vehicle device 100 and arranged near the steering wheel 200 of the vehicle. The storage 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 example 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 sensor 21 is a so-called multi-point detection (multi-touch) touch sensor capable of detecting co

contact at multiple points. The touch sensor 21 is preferably mounted on the circumference of the cross section in the radial direction of the annular portion 200r within a range of 360°. Even if the range is less than 360°, it is sufficient that it covers substantially the entire circumference 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 the sensor data generator 22. Based on the input contact detection signal, the sensor data generation unit 22 generates sensor data including position data indicating from which position on 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 integrated, 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 used. As the touch sensor 21 attached to the annular portion 200r, for example, a flexible touch panel 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 touch sensor 21 does not have unevenness that can be sensed by the hand or fingers, so that it hardly 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 the 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 steering wheel 200. As shown in FIG.

The direction indicator sensor 32 detects operation of the direction indicator 320. The shift lever 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 supplied to the control section 10 via the in-vehicle communication section 34. An example of the position and range of mounting the touch sensor 21 on the annular portion 200r of the steering 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 200 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 sensor 21 is attached to the entire circumference of the annular portion 200r. FIG. 3B is the same as FIG. 2, and shows an example in which the touch sensors 21 are mounted separately from e

each 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.

FIG. 3(D) shows an example in which the touch sensors 21 are spaced apart from each other within predetermined angular ranges on the left and right sides below the annular portion 200r. FIG. 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.

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 sensor 21 is attached to the left and right straight portions 201s of the modified steering wheel 201. The driver grips the linear portion 201s, which is the grip portion, while driving, and the touch 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 which the palm and fingers are in contact when the driver grips the touch sensor 21 on the right side of FIG. The manner in which the driver grips the annular portion 200r and the size of the hand are not uniform, and FIG. 6 is merely an example. In the example shown in FIG. 6, a plurality of detection areas R indicated by hatched Tp are portions where the contact of the palm is detected, and a plurality of detection areas R indicated by hatched Tt are those of the thumb

.

This is the part that detects contact. Hereinafter, they are referred to as a palm contact detection section Tp and a thumb contact detection section Tt. The back side of the touch sensor 21, which is not visible in FIG. 6, is in contact with the forefinger.

As shown in FIG.

FIG. 6, the touch sensor 21 has a plurality of detection regions R as detection portions for detecting contact of palms and fingers. Coordinates are set in each detection area R of the touch sensor 21. As shown in FIG. 6, in the circumferential direction of the annular portion 200r, the detection 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 circumferential direction are set. Let the circumferential coordinate of the annular portion 200r in t

the 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 annular 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 shown in FIG. 7 from the inner diameter side to the front side, from the front side to the outer diameter side, from the outer diameter side to the back side, and from the back side to the inner diameter side in the counterclockwise direction of FIG. are set to 1, 2, . . . , 21, 22. Let the coordinate 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 touch 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.

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. FIG. 8 and 9, in addition to the palm contact detection portion Tp and the thumb contact detection portion Tt, the index finger contact detection portion Ti, which is a plurality of detection regions R in contact with the index finger, is also shown. If the touch sensor 21 is touched by the 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 performing 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. Based on the sensor data output from the sensor data generator 22, the detector 10a of the controller 10 detects that an input operation has been performed on the touch sensor 21 with the thumb or forefinger. Based on the sensor data output from the sensor data generation unit 22, the 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, the 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 specific input operation.

Another

example of the device to be operated is a vehicle motion control device for controlling the motion of a vehicle. Specifically, the control unit 10 may control the transmission, the direction indicator, the on/off of the air conditioner, the set temperature of the air conditioner, and the like, through the in-vehicle communication unit 34. When the operation target device is a vehicle 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. The control unit that controls the operation target device may be the control unit 10 in the vehicle-mounted device 100 or may be a control unit outside the vehicle-mounted device 100 provided in the vehicle. According to this embodiment, the extremely thin touch sensor 21 is attached to the annular portion 200r gripped by the driver, and the device to be operated is operated by operating the touch sensor 21.

.

The device to be operated can be operated without releasing the hand or moving the hand largely. 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 steering 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 embodiment, the following measures are taken to avoid erroneous operations not intended by the driver. As shown in FIGS. 8 and 9, a plurality of detection areas R on the touch sensor 21 are provided with a grip detection area Arg for detecting contact of the palm and an operation input by the thumb or forefinger

.

An operation detection area Arv for detecting an input and an operation invalid area Ariv which is an intermediate area between the grip detection area Arg and the operation detection area Arv and invalidates an operation input are set. The palm contact detection portion Tp is located within the grip detection area Arg, and the thumb contact detection portion Tt and the forefinger 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 Ariv has a detection area R for detecting the contact of the palm or fingers

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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 detection 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 detection portion Tp, the thumb contact detection portion Tt, and the index finger contact detection portion Ti are relatively close to each other. Therefore, in order to accurately distinguish between the case where the driver simply grips the annular portion 200r and the case where the driver touches the touch sensor 21 to operate the operation target device, the operation invalid area Ariv is provided. When the driver intends to operate the device to be operated, the driver intentionally 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 operation 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 driver carelessly touches the operation detection area Arv without gripping the annular portion 200r 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 predetermined area or more is obtained in the grip detection area Arg. The control unit 10 is configured to control the operation target device when the annular portion 200r is gripped and a specific operation is performed within the operation detection area Arv. The area of the palm contact 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 steering 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 section of the annular portion 200r cut at the portion of the grip detection area Arg of the touch sensor 21. As shown in FIG. The detection unit 10a can determine that the annular portion 200r 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 predetermined 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 possible to avoid an erroneous operation when the operation detection area Arv is carelessly touched. In this embodiment, as a preferred configuration, the operation detection area Arv is provided 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 reduced. In this embodiment, the area of the palm contact detection portion Tp in the grip detection

n area Arg and the angle θ in the circumferential direction of the cross section are used as requirements 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 portion 200r. Therefore, it is possible to avoid an erroneous operation when the driver carelessly touches 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 21) based on the sensor data based on the contact detection signal from the grip detection area Arg, the control unit

10

The display element 17 is turned on in order to inform the driver that the operation input by the operation detection area Arv is possible. The driver can determine whether or not the operation target device can be operated by the touch sensor 21 by turning on/off the display element 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 touch sensor 21. Must be set.

Therefore ,

when the touch sensor 21 is gripped while the grip detection area Arg and the like are not set, the control section 10 sets the area including the palm contact detection portion Tp as the grip detection area Arg. A predetermined range of Y coordinates including the palm contact detection 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 detected 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 sensor 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 operation detection area Arv

.

In this case, if necessary, a predetermined range of Y coordinates adjacent to the grip detection area Arg is set as the operation invalid area Ariv, and the grip detection area Arg is positioned away from the grip detection area Arg. 11 to 13, examples of specific input operations p

performed by the driver on the touch sensor 21 using his thumb or forefinger will now be described.

.

FIGS. 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 performed 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 D_L 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; D_D is a downward drag that slides in the 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 touch sensor 21 is flicked with the thumb or forefinger in the respective directions. It may be a flick.

FIG.

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. FIG. 11(D) shows a zigzag drag DZ in which the thumb or forefinger is dragged on the touch sensor 21 in a zigzag pattern. 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 of the touch sensor 21, and a rear portion 21r, which is the rear half of the touch sensor 21, when the touch sensor 21 is opened. The front portion 21f is the portion of X coordinates 0 to 11 shown in FIGS. 8 and 9, and the rear portion 21r is the portion of X coordinates 12 to 22. As shown in FIG. Strictly speaking, in the examples shown in FIGS. 8 and 9, the front portion 21f and the back portion 21r do not have the same area, but in FIGS. Shown in area. 12A to 12D, for ease of understanding, the rear surface portion 21r is not viewed from the rear surface side of the annular portion 200r, but is seen through the rear surface portion 21r from the front surface portion 21f. state. As shown in FIGS. 12A to 12D, a combination of an input operation with the thumb on the front portion 21f and an input operation with the index finger on the back portion 21r can be used as a specific input operation on the touch sensor 21.

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FIG. 12A shows an example of performing both a rightward drag D_{TR} in which the thumb slides rightward on the front portion 21f and a rightward drag D_{IR} in which the index finger slides rightward 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 pattern 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 DTR in which the index finger slides rightward on the back portion 21r. is. FIG. 12B is realized by dragging the thumb from the outer peripheral side to the inner peripheral side of the annular portion 200r 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 index finger slides leftward on the back portion 21r. FIG. 12C is realized by dragging the thumb from the inner circumference side to the outer circumference side of the annular portion 200r and dragging the index finger from the outer circumference side to the inner circumference side of the annular portion 200r. FIG. 12(D) shows an example of performing both an upward drag DTU

in which the thumb slides upward on the front portion 21f and a downward drag DD in which the index finger slides downward on the back portion 21r. is. A pattern in which the thumb is 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 adopted. 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 combined. [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. Furthermore, 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 right hands when the left touch sensor 21 in FIG. 3B is the left touch sensor 21L and the right touch 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 sliding the thumb rightward on the right touch sensor 21R. This pattern is a combination of FIG. 13B shows a combination of a rightward drag DTR in which the thumb slides rightward on the left 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 upward on both the left touch sensor 21L and the right touch sensor 21R.

This pattern is a combination of TUs . FIG. 13(D) shows a pattern in which a downward drag DTD of sliding the thumb downward is combined for both the left touch sensor 21L and the right touch sensor 21R. If a combination of input operations with left and right 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 contributes to safe driving because the touch sensor 21 is mounted at the most appropriate position for gripping the annular portion 200r with both hands. An input operation may be accepted when the left and right touch sensors 21 are gripped with both hands. A state may be adopted in which input operations are not accepted when one hand is removed from the touch sensor 21 . When one hand leaves the touch sensor 21, the state of accepting the input operation may be continued. Even when a specific input operation with only one hand is used, if the input operation is accepted when the left and right touch sensors 21 are gripped with both hands, it contributes to safe driving.

When the driver grips the annular portion 200r for normal driving and does not intend to operate the device to be operated, he accidentally combines the input operation with the thumb 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 which an input operation with the thumb and an input operation with the index finger are combined, 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-described erroneous operation. The storage unit 18 stores a table that associates the above-described specific input operations or patterns of combinations of specific input operations with types of control for the device to be operated

The control unit 10 controls the operation target device according to the operation input to the touch sensor 21 according to the table stored in the storage unit 18 . The storage unit 18 may be provided within the control unit 10 .

[0064]

The processing executed by the control unit 10 in this embodiment will be described again using the flowchart of FIG. 14 . In FIG. 13, the control unit 10 acquires sensor data output from

in the sensor data generation unit 22 in step S1. In step S2, the control unit 10 determines whether or not the annular portion 200r is being gripped based on the detection output from the detection unit 10a. If it is determined that the annular portion 200r is gripped (YES), the control 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 control unit 10 determines whether or not there is an input operation based on the detection output from the detection section 10a.

If it is determined that an input operation has been performed (YES), the control unit 10 moves the process to step S4, and if it is not determined that an operation input has been performed (NO), the control unit 10 returns the process to step S1. In step S4, the control unit 10 determines whether or not to permit the operation of the operation target device by the input operation in step S3. If it is determined that the operation is permitted (YES), the control unit 10 moves the process to step S5, and if it is not determined that the operation is permitted (NO), the control unit 10 returns the process to step S1. As described above, the control 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 operation 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 operation is performed within the operation detection area Arv, the control unit 10 does not permit the operation to the operation target device unless the above-described specific input operation is performed, and only when the specific input operation is performed. Permission to operate 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 returns 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 be operated. As shown in FIG. 15, a state in which the steering wheel 200 is not rotated is assumed 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 exceeds $\pm 30^\circ$, the input operation to the touch sensor 21 is disabled and not permitted.

When the turning angle exceeds $\pm 30^\circ$, 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 occur. In other words, there is a high possibility that an operation input in such a specific state is an operation input unintended by the user. Moreover, it is not preferable in terms of safety. Therefore, in this embodiment, when the vehicle is in a specific state, control of the operation target device is disabled. As described above, the rotation angle of the steering wheel 200 detected by the steering angle sensor 31 is input to the controller 10.

The control unit 10 switches between enabling and disabling the input operation to the touch sensor 21 according to the rotation angle of the steering wheel 200 detected by the steering angle sensor 31. A detection signal from the direction indicator sensor 32 is also input to the control unit 10. Therefore, the control unit 10 may invalidate the input operation to the touch sensor 21 when the direction indicator 320 is operated by the detection signal from the direction indicator sensor 32. When the direction indicator 320 is operated, it can be considered to be in a specific state in which the steering wheel 200 is rotated over a predetermined rotation angle. In some cases, the direction indicator 320 is also used for operations other than signaling a right turn or left turn, but the operation of the direction indicator 320 here is an operation for signaling a right turn or a left turn.

[0071]

Furthermore, it is not preferable to perform a specific input operation on the touch sensor 21 to control the operation target device while the vehicle is being reversed. There is a high possibility that an erroneous operation will occur, and this is not preferable in terms of safety. Therefore, it is preferable that the control unit 10 invalidates the input operation to the touch sensor 21 even when the shift position of the shift lever 330 is reversed by the detection signal from the shift lever sensor 33. When the rotation angle of the steering wheel 200 exceeds a predetermined angle of $\pm 30^\circ$, for example, or when the direction indicator 320 is operated, and when the shift position of the shift lever 330 is reversed, the operation target device. Although it is preferable to disable the control for , only one of them may be disabled. It should be noted that disabling the control of the operation target device means disabling the control of the operation target device by disabling the specific input operation even if the above-described specific input operation is performed.

Even if some sensor data is input from the sensor data generation unit 22 to the control unit 10, the control unit 10 may invalidate the sensor data. As a result, it is sufficient to invalidate the control on the operation target device.

[0073]

A specific example of the processing of step S4 in FIG. 14 will be described with reference to the flowchart in FIG. In FIG. 16, in step S41, the control unit 10 determines whether or not the shift position of the shift lever 330 is reverse. If the shift position is reverse (YES), in step S45, the control unit 10 disallows the input operation in step S3, and proceeds to step S1 in FIG.

G. If the shift position is not reverse (NO), control unit 10 determines in step S42 whether direction indicator 320 has been operated. If the direction indicator 320 is operated (YES), the controller 10 disallows the input operation in step S3 in step S45, and proceeds to step S1 in FIG. If the direction indicator 320 has not been operated (NO), the controller 10 determines in step S43 whether or not the rotation angle of the steering wheel 200 has exceeded a predetermined angle

.

If the rotation angle of the steering wheel 200 exceeds the predetermined angle (YES), in step 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 (NO), 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 performed (NO), in step S45, the control unit 10 disallows the input operation in step S3, and proceeds to step S1 in FIG. If the input operation is disallowed in step S45, control of the operation 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. Although all steps S41, S42 and S43 are provided in the example shown in FIG. 16, only one or two of these steps may be provided

.

Moreover, when providing all of steps S41, S42, and S43 or two of these steps, the order is arbitrary. Although referred to as a shift lever 330 here, the shape of the operating portion for switching between straight forward and backward movement of the vehicle and for changing the gear ratio of the transmission is arbitrary, and may be any of floor shift, column shift, paddle 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 reverse, 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 10a (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 the driver. Detects that the An example of the first area is the grip detection area Arg. The detection 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 the first area may be the second area. When the first area is touched and a specific input operation

ion is performed, the touch sensor 21 controls the operation target device to be operated according 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 first area is being touched over a predetermined area.

[0079]

Moreover, from another viewpoint, it is as follows. The detection unit 10a (first detection unit) is mounted in a predetermined range of the grip portion (annular portion 200r or linear portion 201s) of the steering wheels 200 and 201 that the driver grips so as to cover the grip portion. The touch sensor 21 touches the first area on the touch sensor 21 at a predetermined angle 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 (second 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 predetermined angle or more. Detect what has been done. When the first area is touched at the predetermined angle or more and a specific input operation is performed, the operation target device to be operated by the touch sensor 21 is controlled according to the specific input operation.

The second

area is preferably an area located above the first area. The area located above is an area located above the first area when the driver grips the grip portion while the steering wheel 200 is not rotated.

FIGS.

17 and 18 show examples of construction for effectively informing the driver that the touch sensor 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 example 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 sensor 21, the driver can see the color of the color change sheet 41 arranged on the lower surface of the touch sensor 21 through the touch sensor 21. The driver can recognize that the touch sensor 21 has been operated by changing the color of the color change sheet 41 at the portion 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 (hand feeling) is provided on the upper surface side of the touch sensor 21. As the tactile feedback sheet 42, for example, a sheet called "E-Sense" developed by Senseg of Finland can be adopted. This sheet provides tactile feedback by charging the film. Even if the tactile feedback sheet 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 changing 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 operation 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 omitted as appropriate. As shown in FIG. 19, the steering wheel 210 includes, for example, a sensor data generation unit 23 similar to the sensor data generation unit 22 in FIG. 1. The controller 24 has a detector 24a similar to the detector 10a and a control signal generator 24b. When the steering wheel 210 is mounted on the vehicle, the control signal generator 24b generates a control signal for controlling the device to be operated in accordance with a specific input operation to the touch sensor 21. FIG.

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The control signal output from the control signal generator 24b is output to the output terminal 26 via the cable 25. FIG. By connecting the output terminal 26 to the device to be operated, 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 to generate the control signal are the same as those described above. The present invention is not limited to the embodiments described above, and various modifications can be made without departing from the gist of the present invention.

.

The touch sensor 21 may be detachably attached to the annular portion 200r using a hook-and-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 plurality of touch sensor pieces. If the touch sensor 21 is composed of a plurality of touch sensor pieces, the shape of each touch sensor piece can be simplified, which is advantageous in manufacturing 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. The touch panel 21 of the present embodiment is mounted so as to cover the grip portion. It also 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 portion (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 connection 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 connecting portion, and the operation detection area Arv may be set at a position near the grip portion of the connecting portion. If the position is close to the grip portion, the driver can operate the operation target device without releasing the hand from the grip portion or moving the hand largely during driving. Therefore, even if the touch sensor 21 is extended to the surface of the 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 television tuner 14 video signal processing unit 15 video display unit 16 audio signal processing unit 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

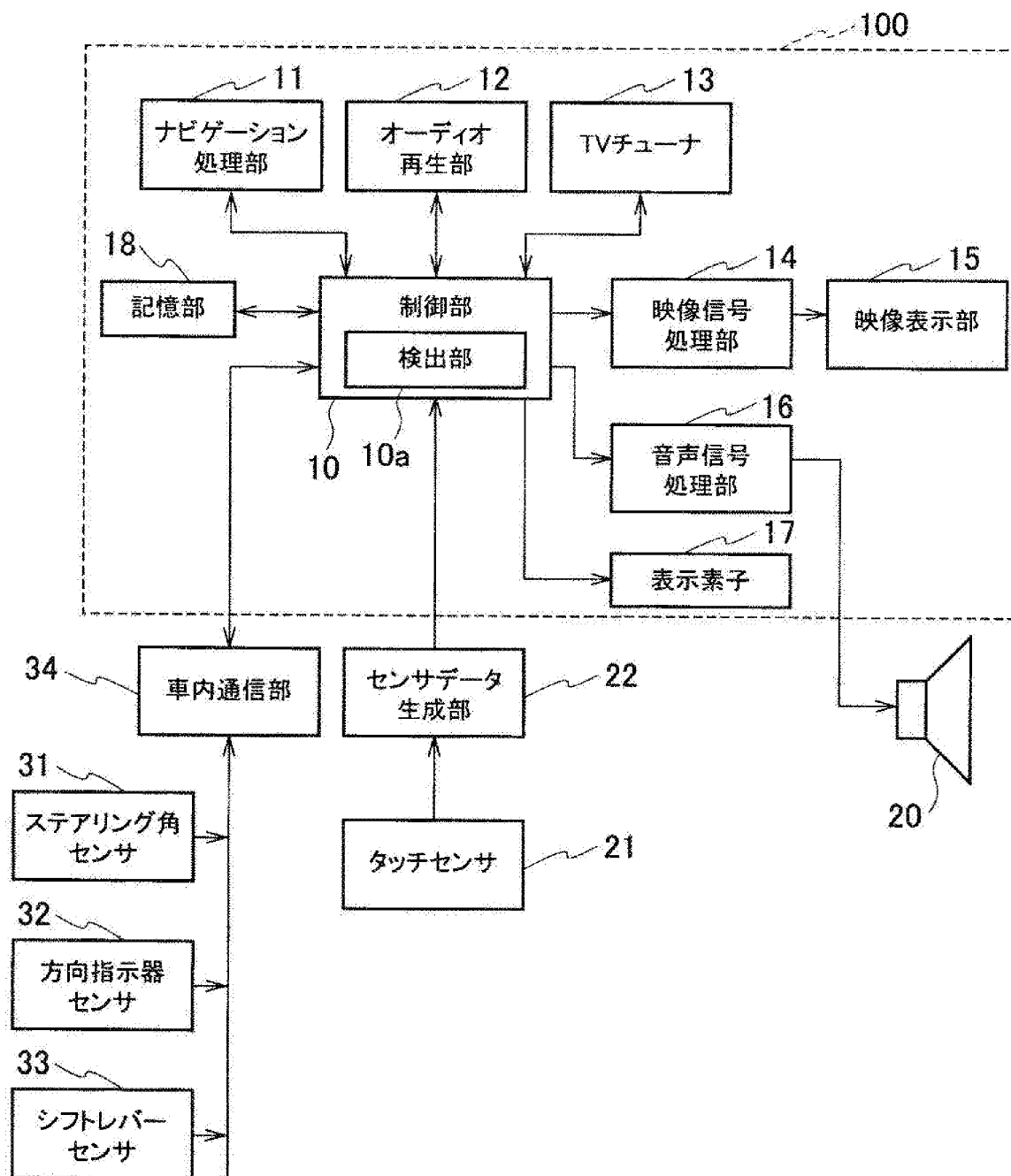
200, 201, 210 steering wheel

200r annular section (grip section)

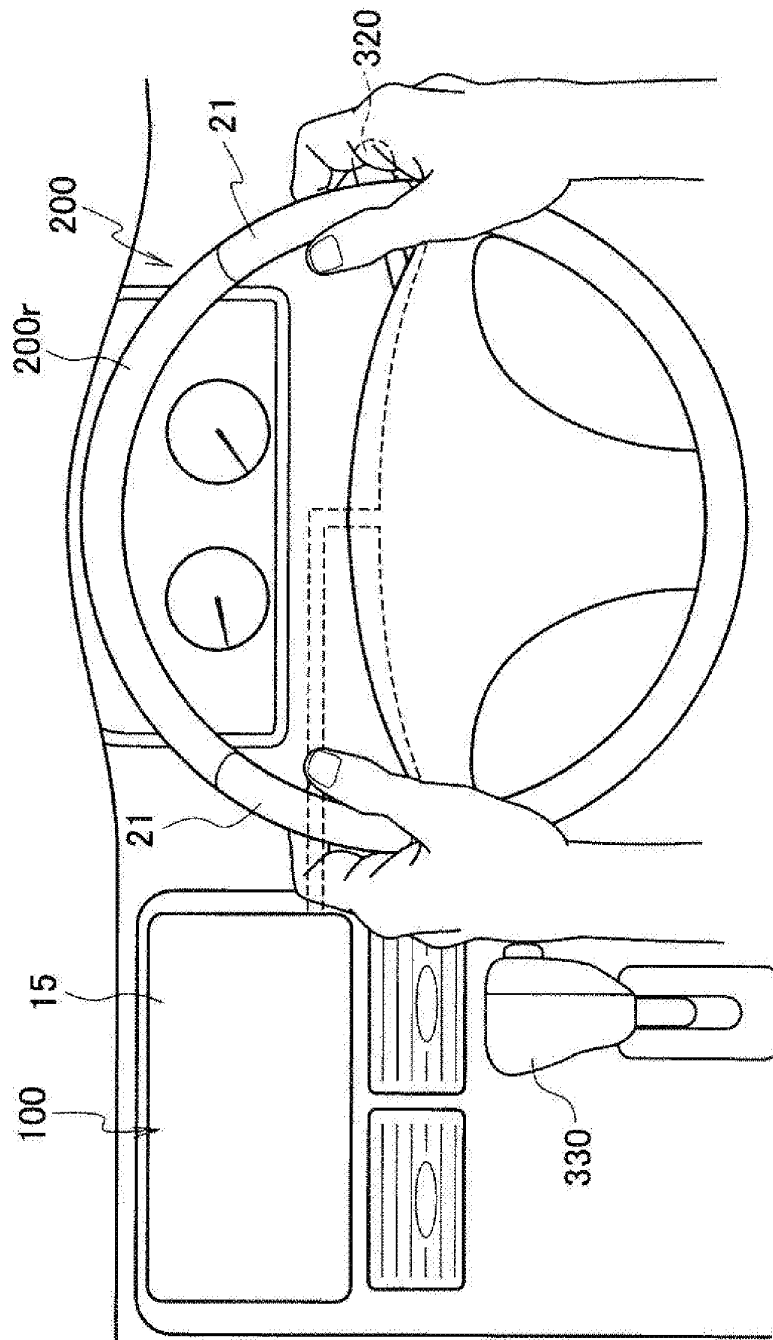
201s linear section (grip section)

drawing	open
---------	------

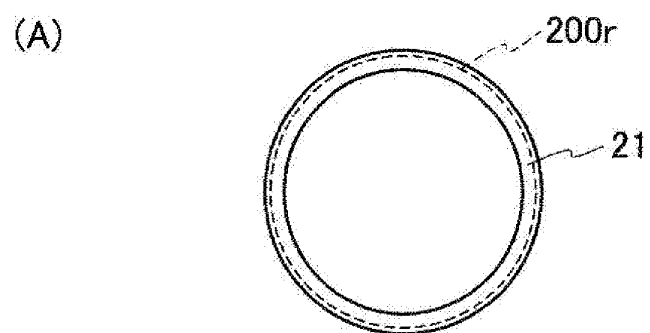
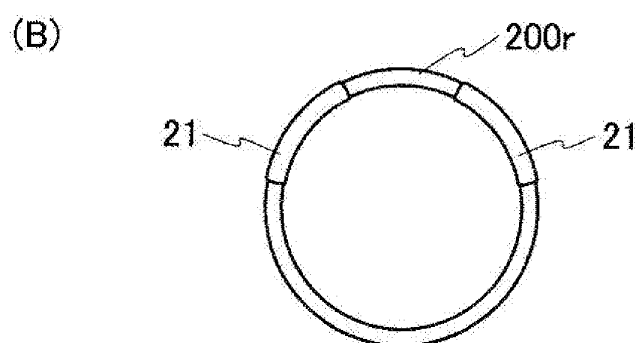
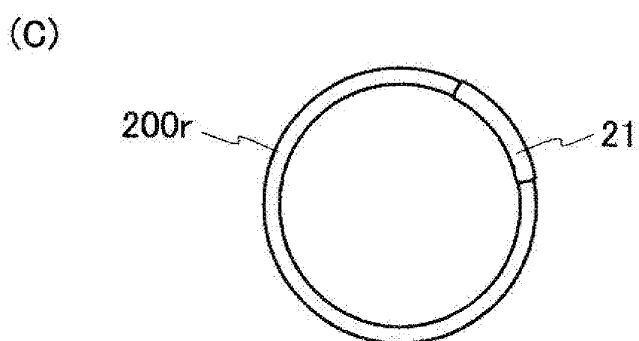
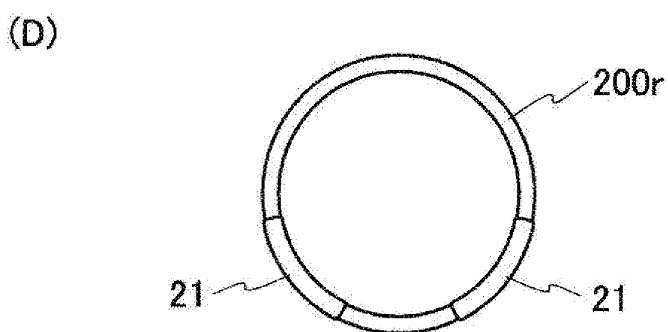
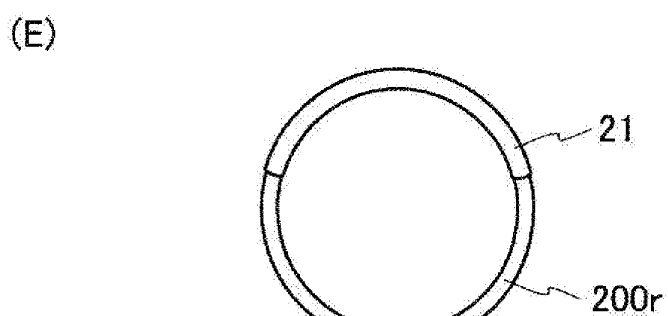
[Fig. 1]



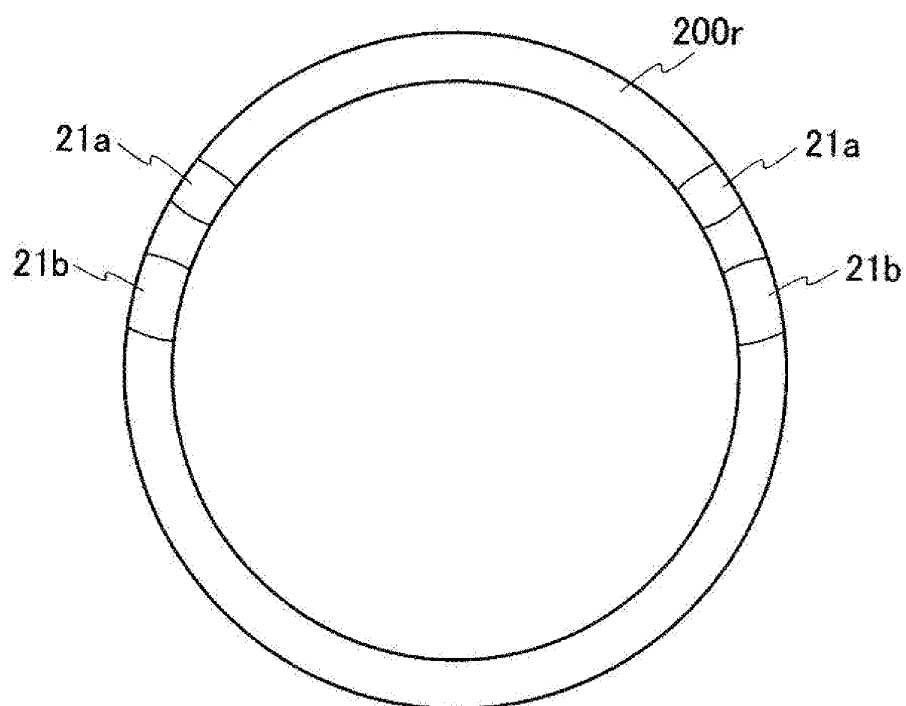
[Figure 2]



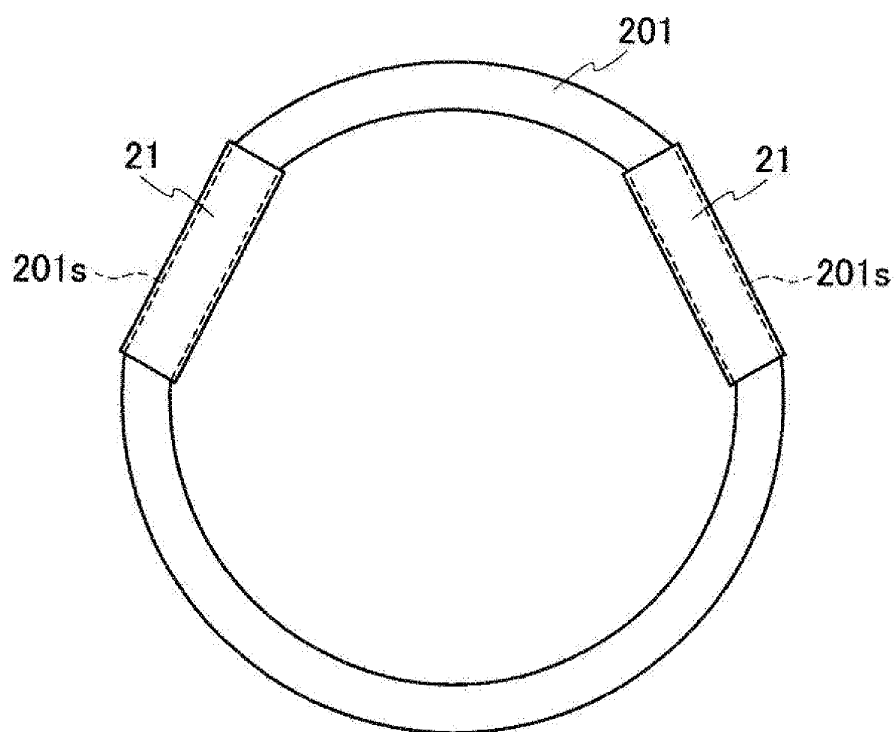
[Figure 3]



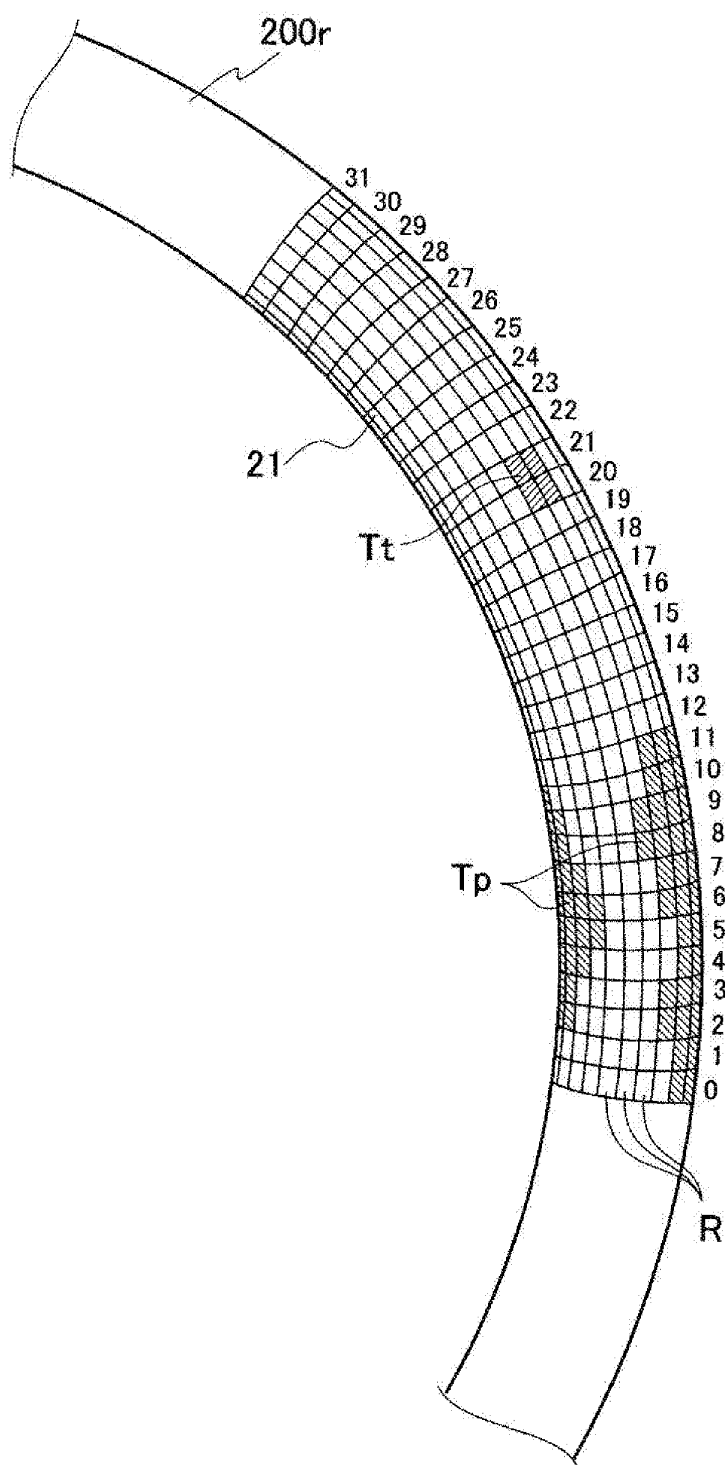
[Figure 4]



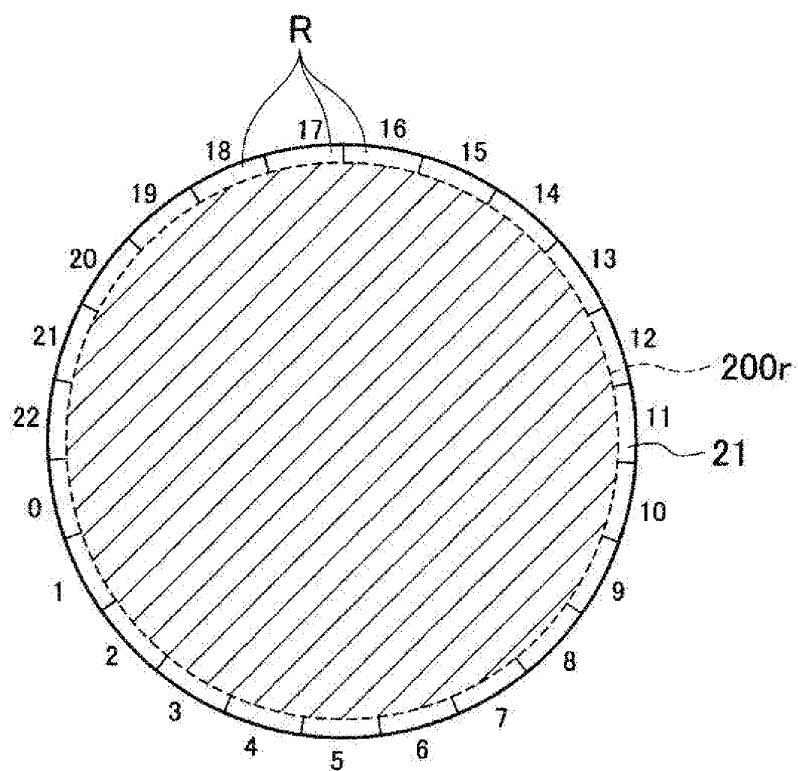
[Figure 5]



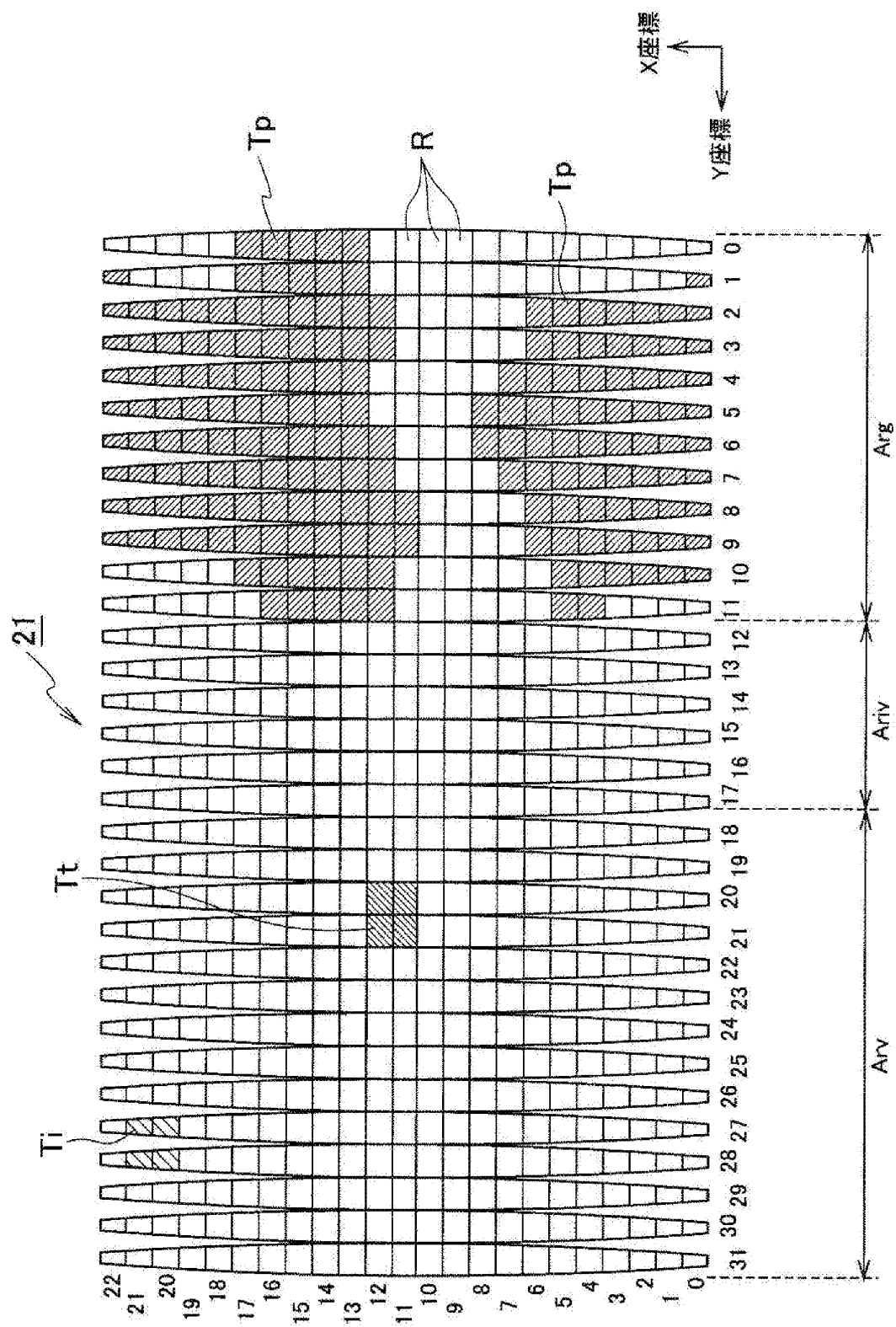
[Fig. 6]



[Fig. 7]

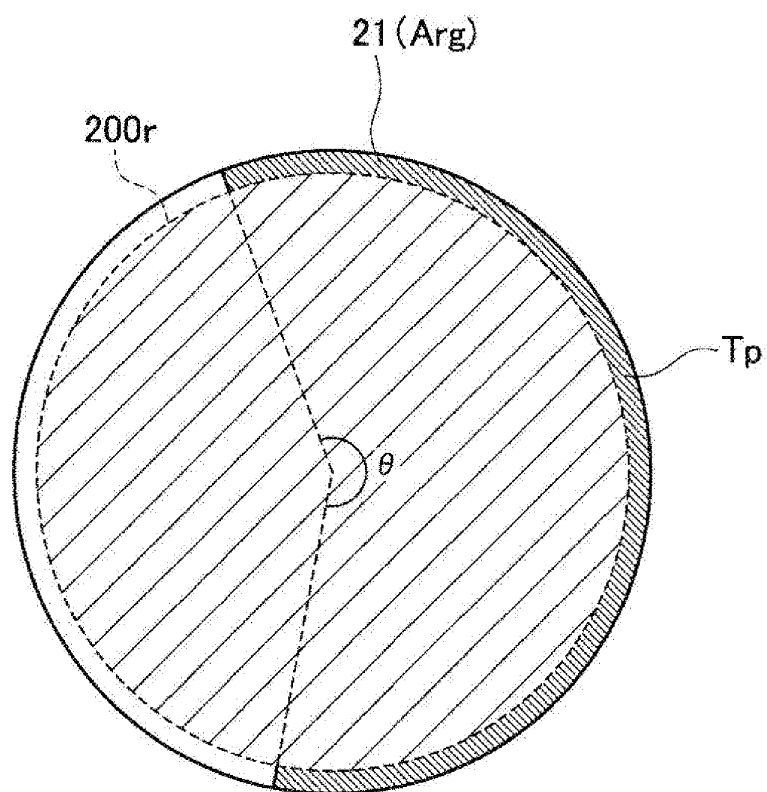


[Fig. 8]

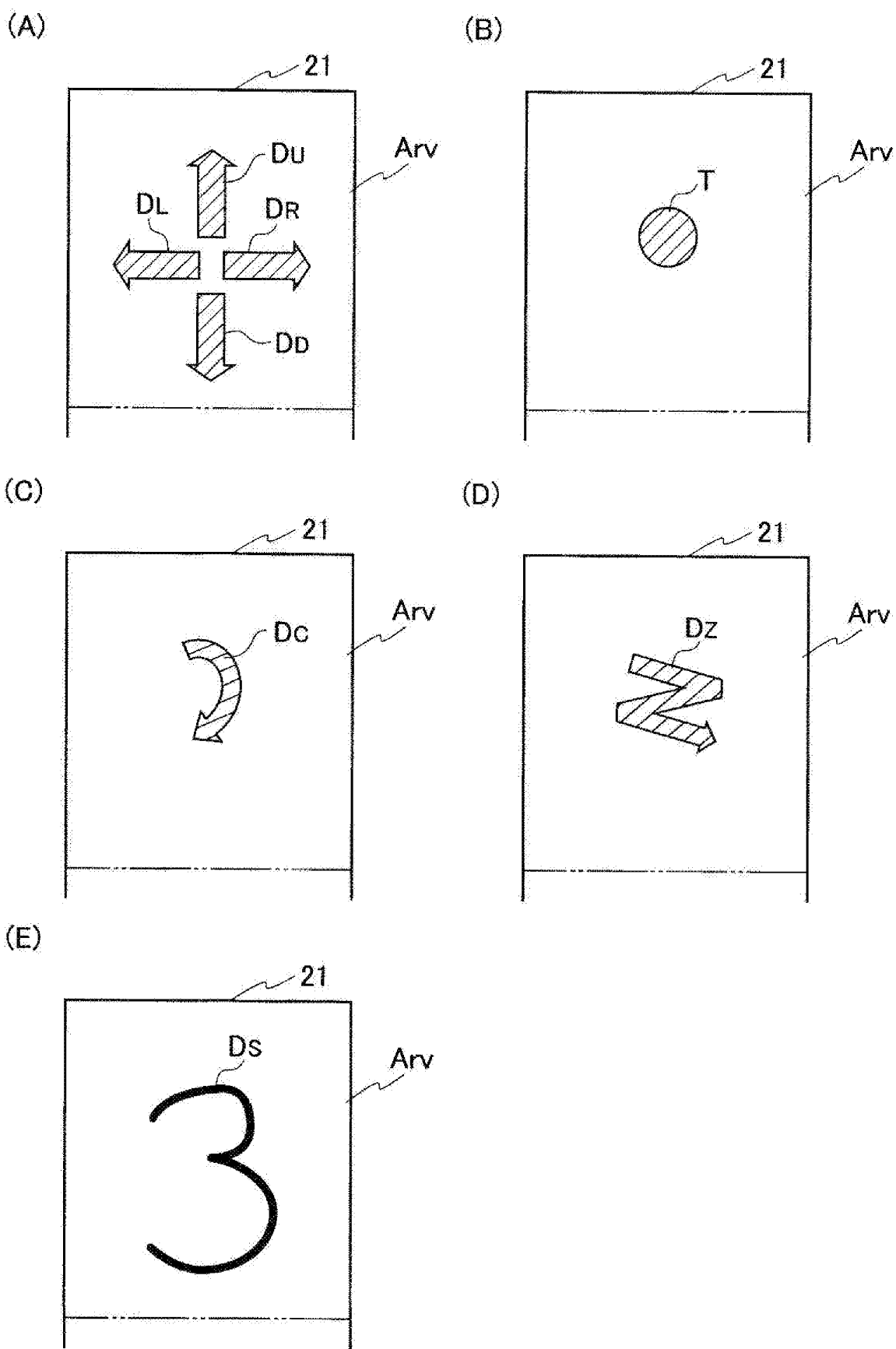


[Fig. 9]

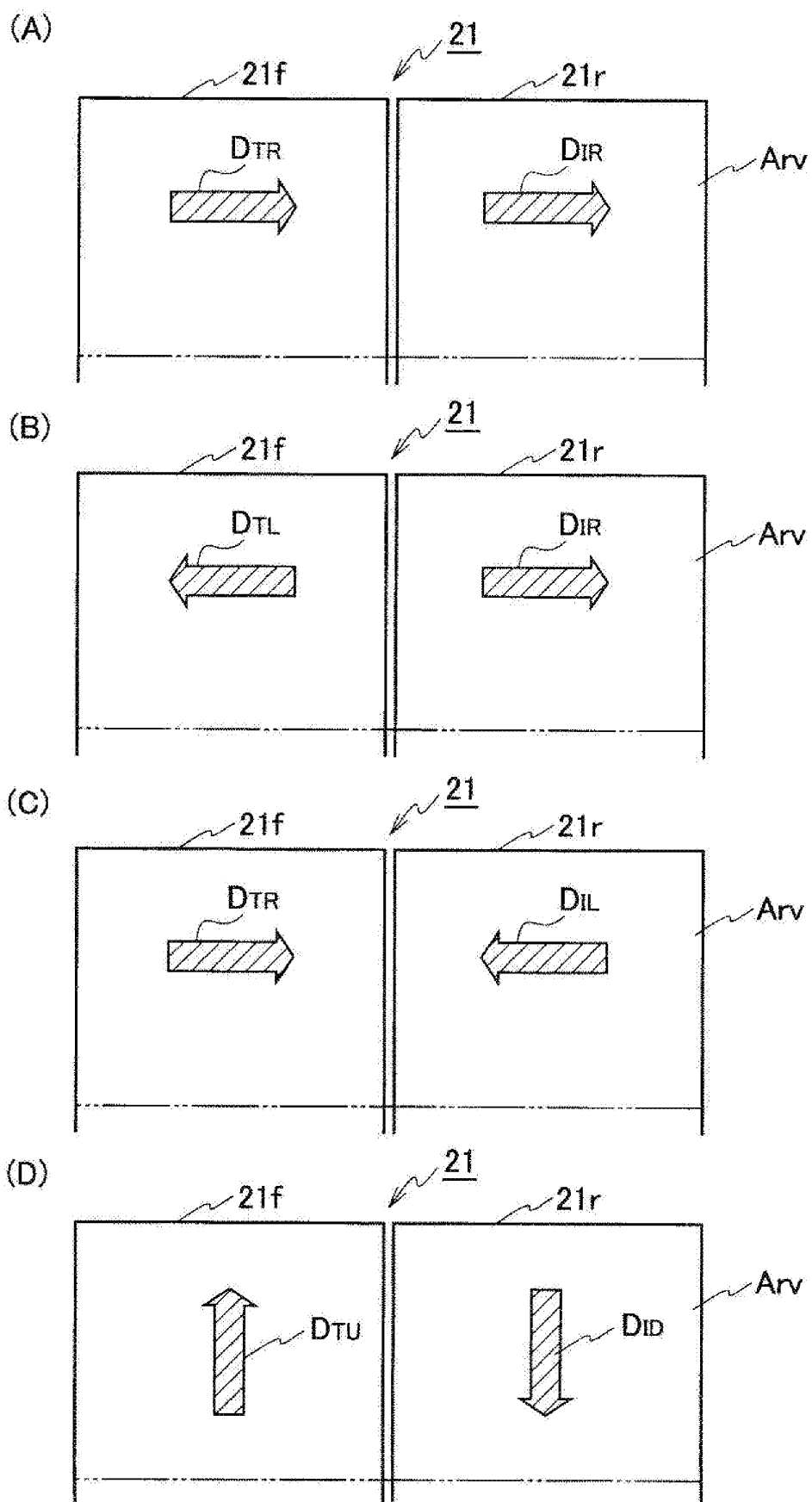
[Fig. 10]



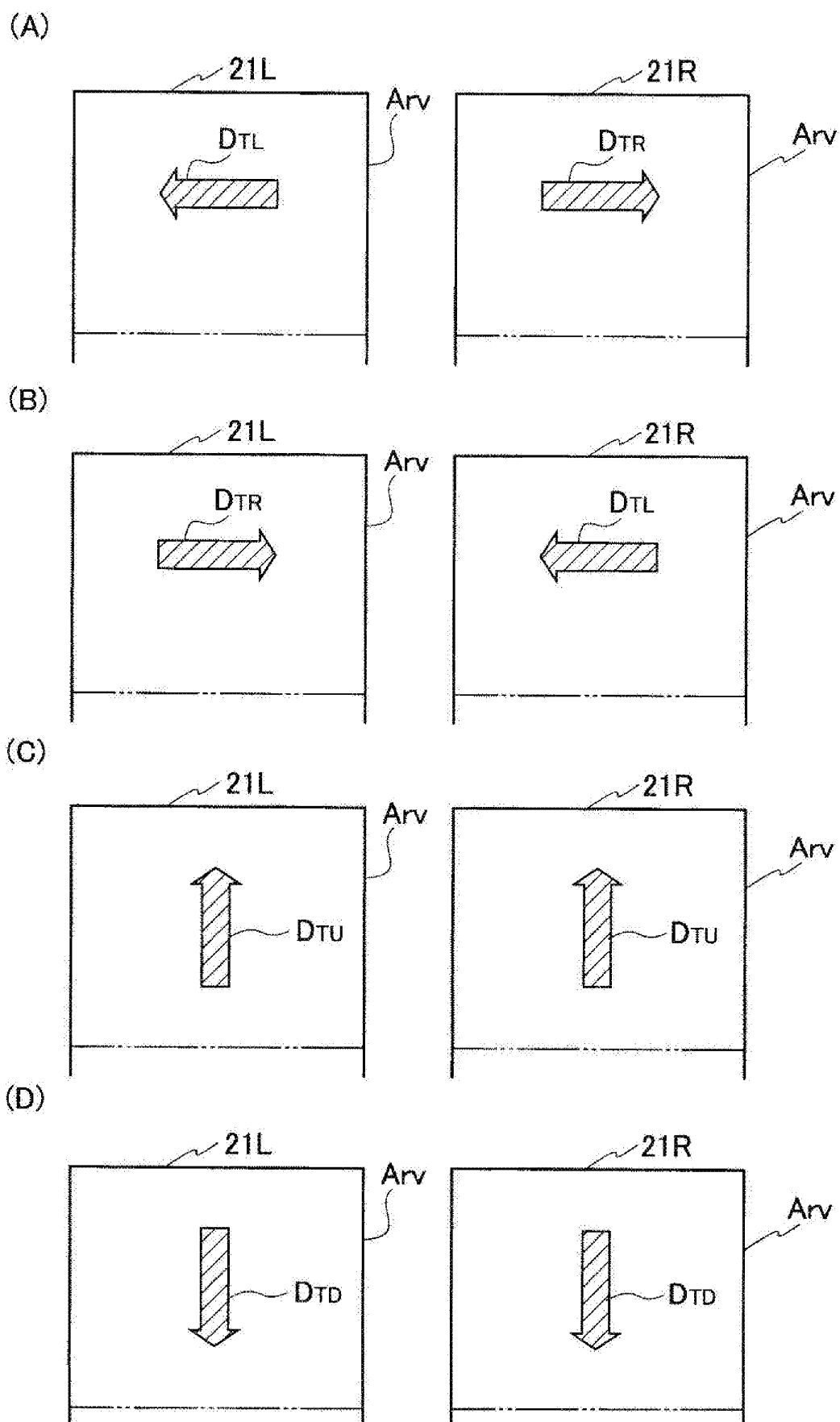
[Fig. 11]



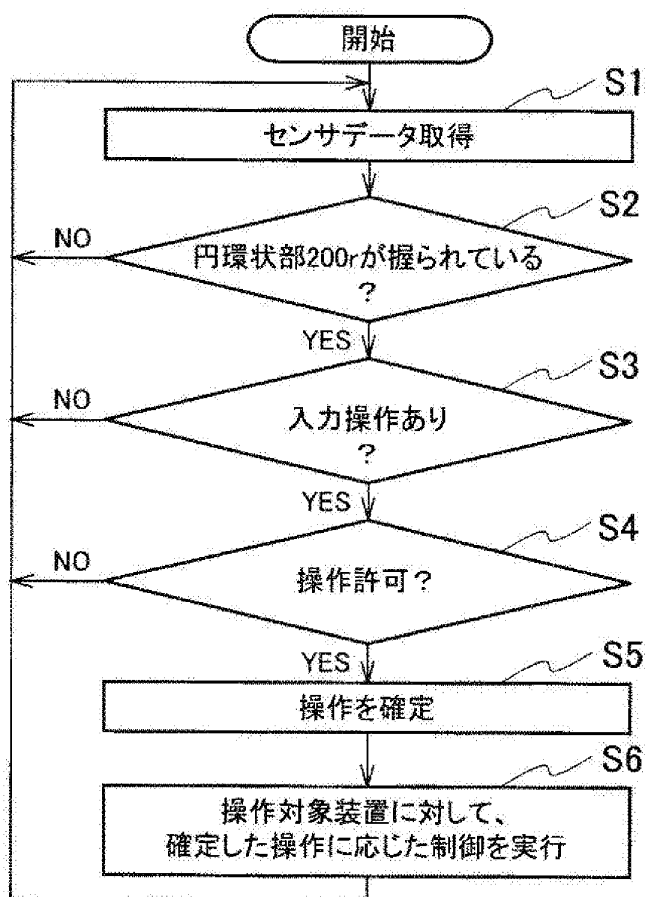
[Fig. 12]



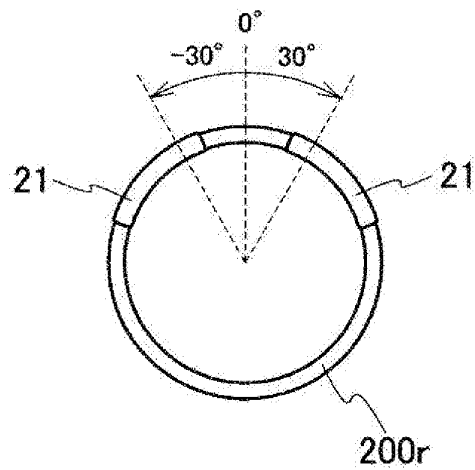
[Fig. 13]



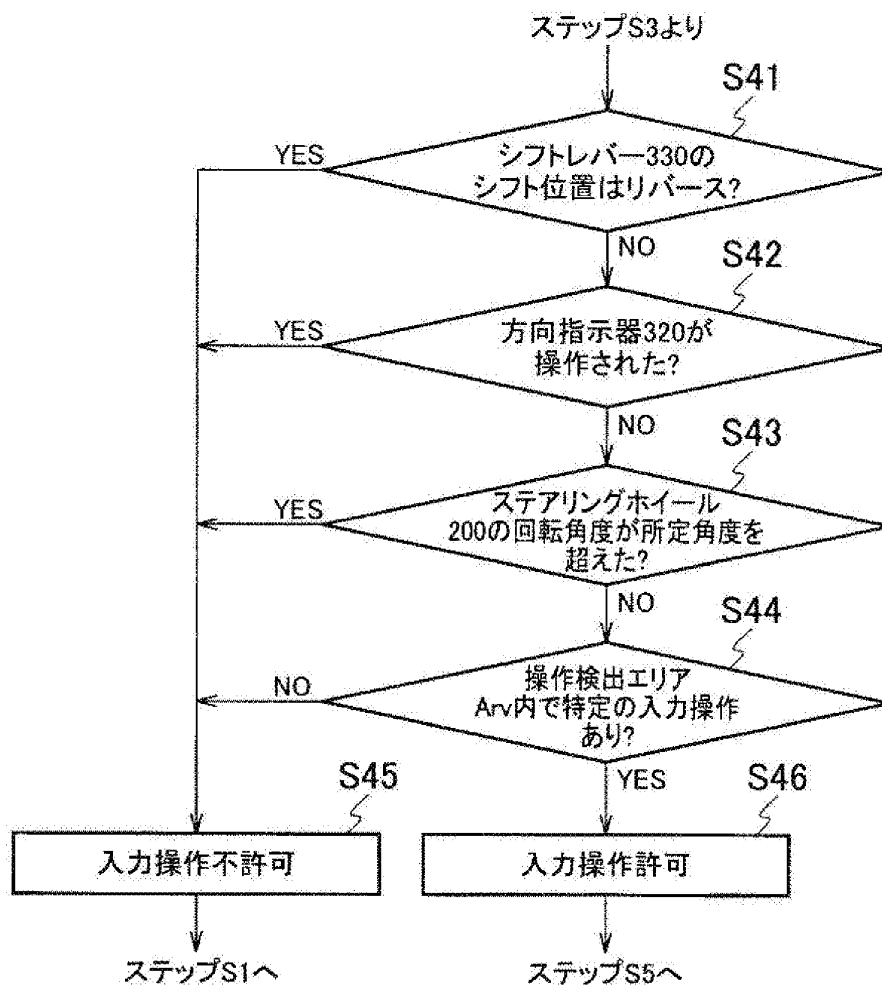
[Fig. 14]



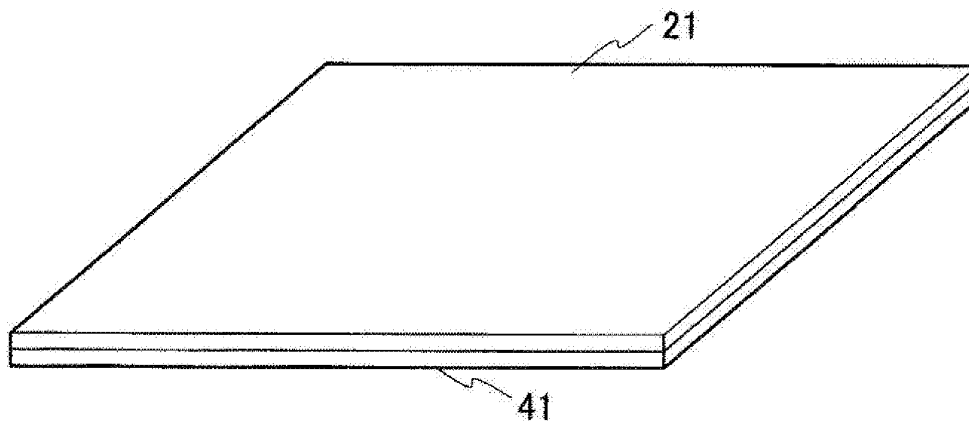
[Fig. 15]



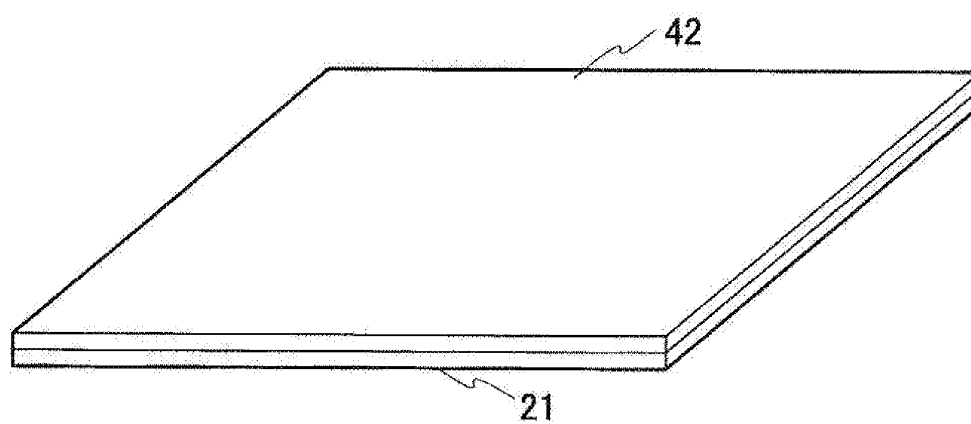
[Fig. 16]



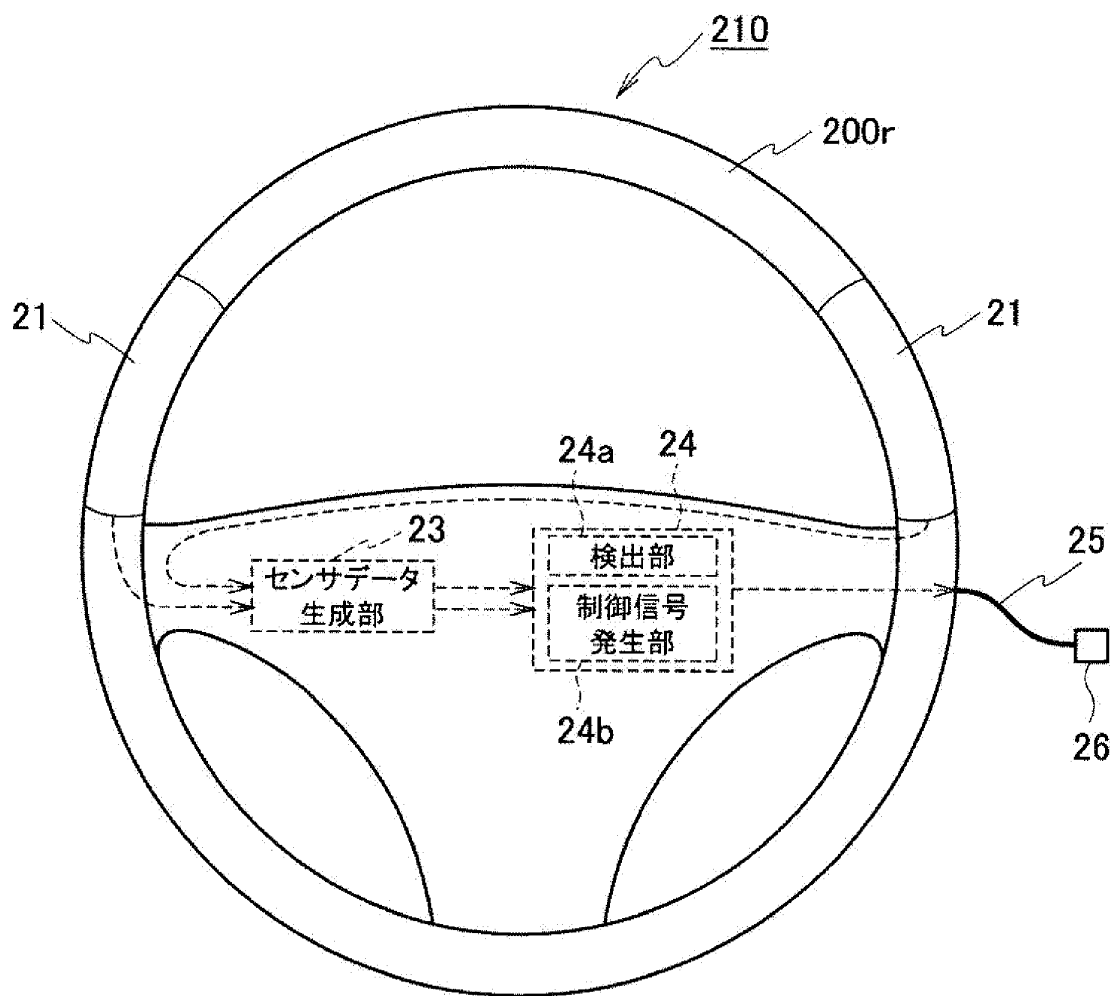
[Fig. 17]



[Fig. 18]



[Fig. 19]



drawing

open

1 2 3 Four Five 6 7 8 9 Ten ...

Magnify and Rotate

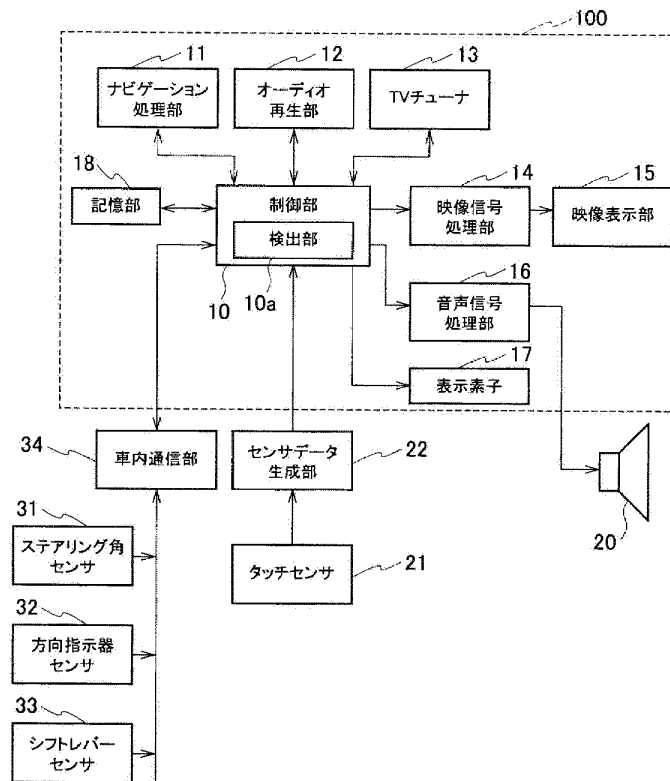


Figure 1





Espacenet

Bibliographic data: JP5825146 (B2) — 2015-12-02

DEVICE AND METHOD FOR CONTROLLING OPERATION TARGET DEVICE IN
VEHICLE

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Applicant(s): JVC KENWOOD CORP, ; 株式会社 J V C ケンウッド

Classification: - international: B60R16/02; B60R16/027
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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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(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、

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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。

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【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、

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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、

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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。

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【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、

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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 1 2】

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 1 0 または 1 1 に記載の車両における操作対象装置の制御方法。

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【請求項 1 3】

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 ～ 1 1 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 1 4】

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

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ことを特徴とする請求項 8 ～ 1 3 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】

【0 0 0 1】

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】

【0 0 0 2】

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。

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【先行技術文献】

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【特許文献】

【0 0 0 3】

【特許文献 1】特開 2 0 0 7 - 1 0 6 3 5 3 号公報

【特許文献 2】特開 2 0 0 5 - 3 4 8 1 2 3 号公報

【特許文献 3】特開 2 0 0 8 - 1 9 5 2 2 0 号公報

【発明の概要】

【発明が解決しようとする課題】

【0 0 0 4】

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

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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りとして、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

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 200 r 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 200 r 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 200 r 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。

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【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 200 r 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 0.02～0.05 mm 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 200 r 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。

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【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。

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【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 200 r 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 200 r 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 200 r 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 200 r 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。

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【0027】

図 3（D）は、円環状部 200 r 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 200 r 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 21 a と下側のタッチセンサ 21 b 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 21 a 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 21 b 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

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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。

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【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。

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【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。

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【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。

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【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

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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、エアコンディショナのオン・オフ、エア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 200 r 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 200 r 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 200 r 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 200 r 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 A r g 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 A r v と、グリップ検出エリア A r g と操作検出エリア A r v 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 A r iv とを設定している。手のひら接触検出部 T p はグリップ検出エリア A r g 内に位置し、親指接触検出部 T t 及び人差し指接触検出部 T i は操作検出エリア A r v 内に位置する。

【0040】

操作無効エリア A r iv は、グリップ検出エリア A r g と操作検出エリア A r v 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 10 a）またはセンサデータ生成部 22 が操作無効エリア A r iv 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 A r iv 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 200 r を握っている場合には、手のひら接触検出部 T p と親指接触検出部 T t 及び人差し指接触検出部 T i 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 200 r 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 A r iv 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 A r v 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。

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【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、正面側であれば親指で、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、DR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、DL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。DU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、DD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。

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【0051】

図11(A)において、右方向ドラッグDR、左方向ドラッグDL、上方向ドラッグDU、下方向ドラッグDD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DC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DZ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DS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。

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【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。

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【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DTR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D1R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。

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【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_{TR} 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_{TL} 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_{TD} 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

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【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。

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【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。

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【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。

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【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

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に対する入力操作を有効として許可し、回転角度が $\pm 30^\circ$ 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 $\pm 30^\circ$ 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る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、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 $\pm 30^\circ$ 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 (N0)、制御部 10 は、ステップ S 44 にて、操作検出エリア A r v 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 (N0)、制御部 10 は、ステップ S 45 にて、ステップ S 3 での入力操作を不許可として、図 14 のステップ S 1 に移行させる。ステップ S 45 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 S 46 にて、ステップ S 3 での入力操作を許可して、図 14 のステップ S 5 に移行させる。

【0075】

図 16 に示す例では、ステップ S 41、S 42、S 43 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 S 41、S 42、S 43 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が無効とすれば、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 10 a (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 200 r または直線部 201 s) 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 A r g である。検出部 10 a (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 A r v 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のが好ましい。

【0079】

また、別の観点では、次の通りである。検出部 10 a (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 200 r または直線部 201 s) 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 10 a (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と同様のセンサデータ生成部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 2 1 を設ける範囲を、運転者が運転時に握る握持部（円環状部 2 0 0 r または直線部 2 0 1 s）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 2 0 0 r との間を連結する連結部の表面まで広げてよい。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 1 9 においては、センサデータ生成部 2 3 及び制御部 2 4 が設けられている部分である。このようにタッチセンサ 2 1 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 A r v 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 2 1 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 2 0 0, 2 0 1, 2 1 0 を操作する際に支障となる可能性はほとんどない。

10

【符号の説明】

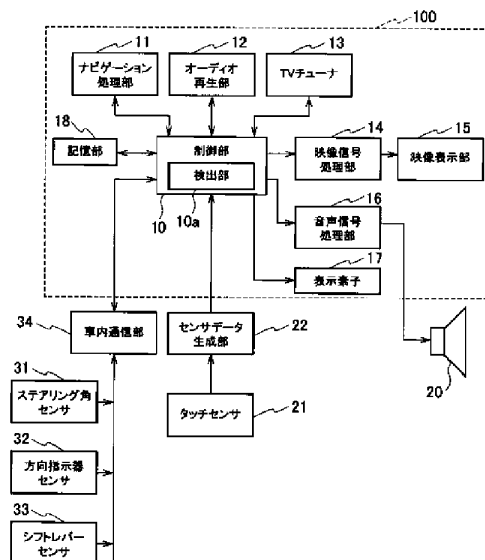
【0 0 8 8】

- 1 0, 2 4 制御部
- 1 0 a, 2 4 a 検出部
- 1 1 ナビゲーション処理部
- 1 2 オーディオ再生部
- 1 3 テレビジョンチューナ
- 1 4 映像信号処理部
- 1 5 映像表示部
- 1 6 音声信号処理部
- 1 7 表示素子
- 1 8 記憶部
- 2 0 スピーカ
- 2 1 タッチセンサ
- 2 2, 2 3 センサデータ生成部
- 2 4 b 制御信号発生部
- 2 5 ケーブル
- 2 6 出力端子
- 3 1 ステアリング角センサ
- 3 2 方向指示器センサ
- 3 3 シフトレバーセンサ
- 3 4 車内通信部
- 2 0 0, 2 0 1, 2 1 0 ステアリングホイール
- 2 0 0 r 円環状部（握持部）
- 2 0 1 s 直線部（握持部）

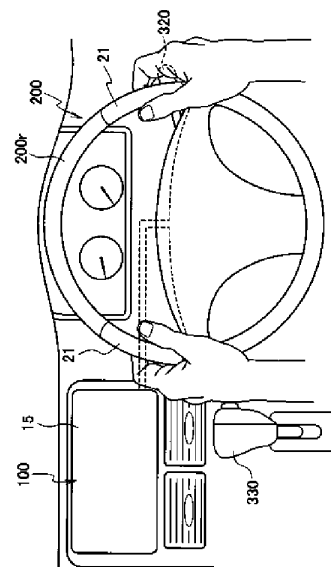
20

30

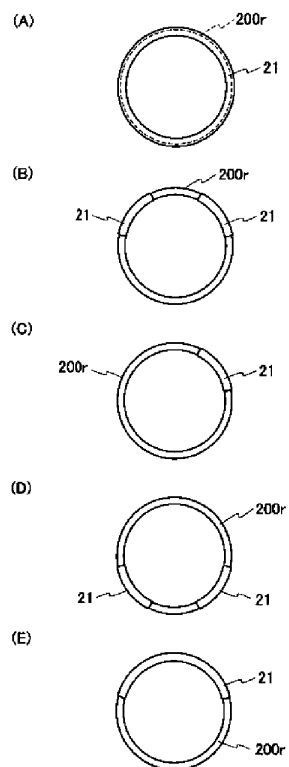
【図 1】



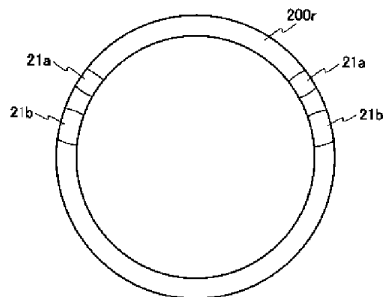
【図 2】



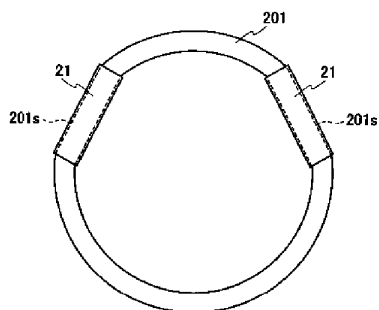
【図 3】



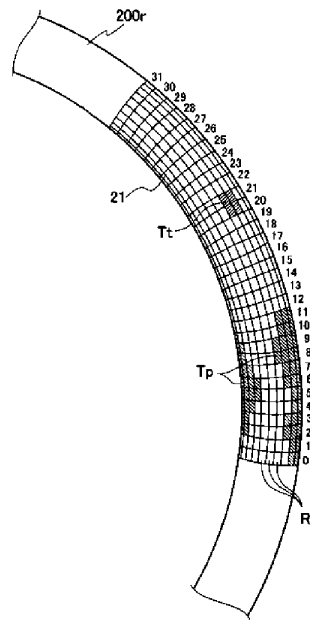
【図 4】



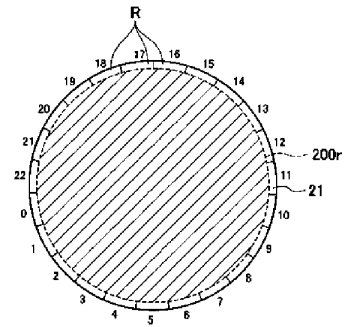
【図 5】



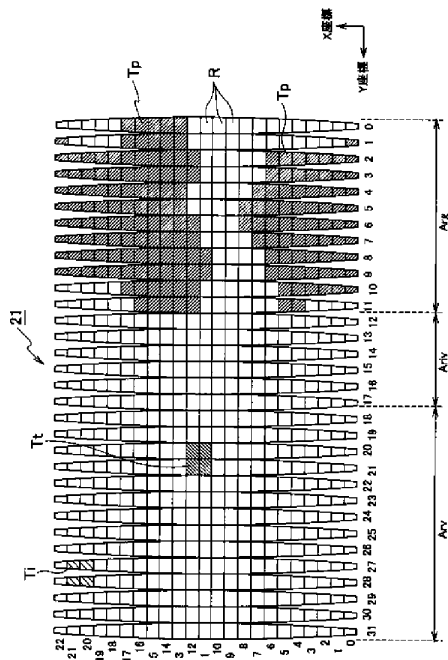
【図 6】



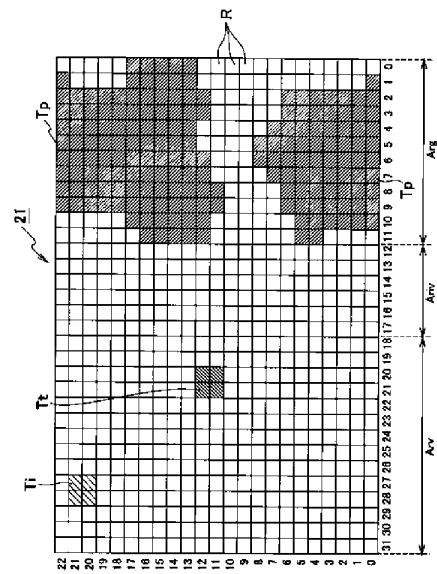
【図 7】



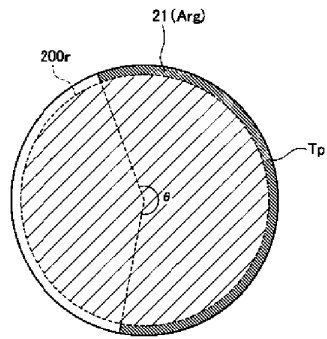
【図 8】



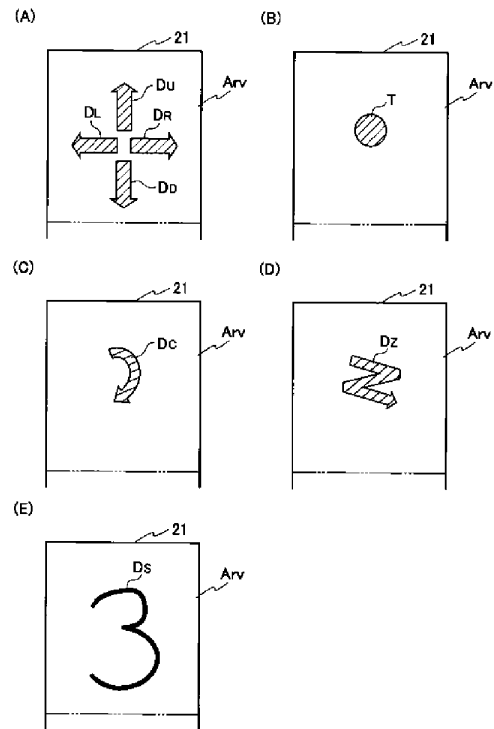
【図 9】



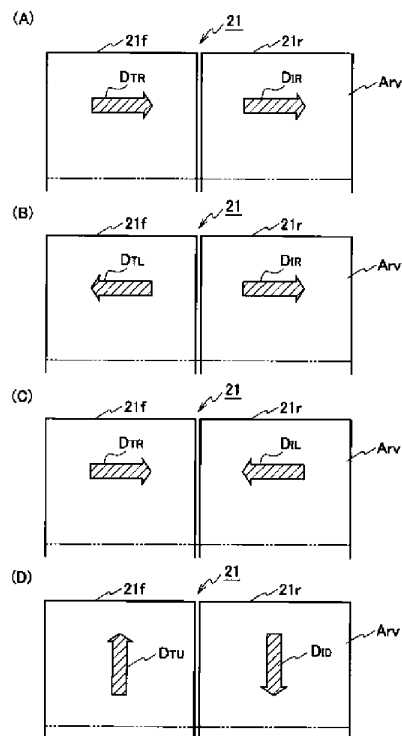
【図 10】



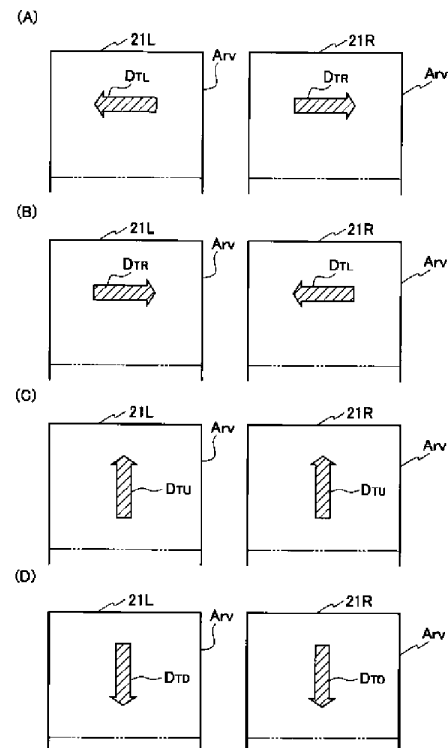
【図 11】



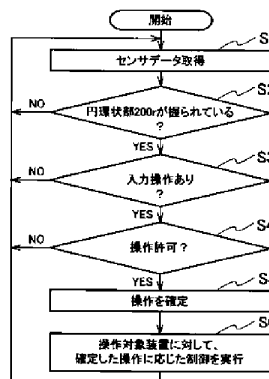
【図 12】



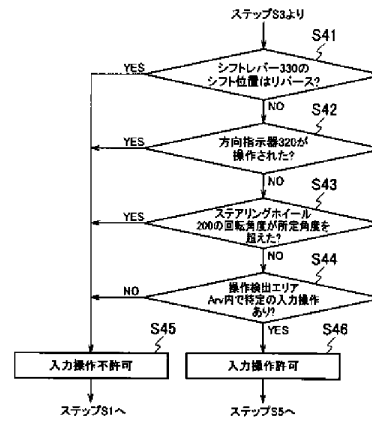
【図 13】



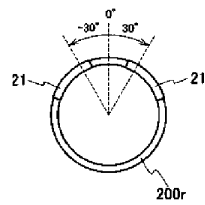
【図14】



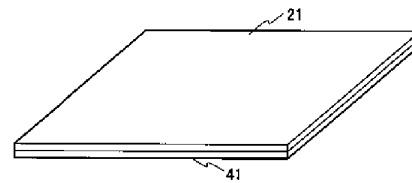
【図16】



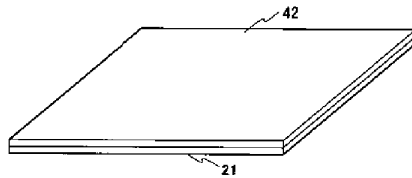
【図15】



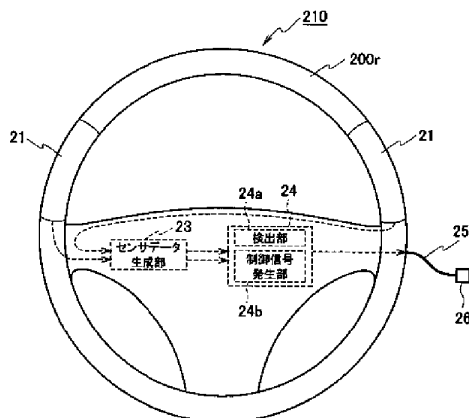
【図17】



【図18】



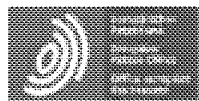
【図19】



フロントページの続き

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(58)調査した分野(Int. Cl., DB名)
B60R 16/02
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Hypodermic needle blood taking device - has valves at needle end and at attachable evacuated chamber connection

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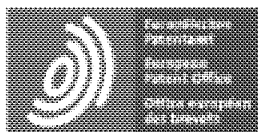
Application number: DE19752541494 19750917

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Also published as: FR2321262 (A1) GB1506449 (A)

Abstract of DE2541494 (A1)

The blood-taking device is of the type where a hypodermic needle is inserted into a blood vessel and one or more evacuated containers in successions are connected to the needle for collecting blood samples. The device has two valves. The first valve closes the proximal end of the needle section when a container is not connected to it and the second valve makes it possible to control the difference of pressure utilized for drawing blood from a subject. The second valve can be closed rapidly in the event it is discovered that the needle lies in tissue exterior to a blood vessel rather than in a blood vessel itself, thereby preventing extravasation and haematoma.



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DESCRIPTION DE2541494A1

[0001]

¹³ blood collection device

[0002]

¹⁷ The invention relates to a blood sampling device for draining blood from a blood vessel.

[0003]

²¹ It is routine in modern hospitals to draw blood samples from patients by sequentially inserting one or more evacuated test tubes into a holder having a double-tipped cannula; one pointed end of the cannula pierces the patient's vein and the other pointed end pierces the stopper of the evacuated test tube, thereby allowing blood to flow from the vein into the evacuated tube.

[0004]

²⁸ However, vacuum tube holders are relatively expensive and therefore not disposable; they are also bulky devices subject to contamination (see U.S. Patent 3,520,292).

³⁰ Unless dual-tipped cannulas are already installed in the holders, they must be attached to the holders by a user.

³² However, handling these double-tipped cannulas is dangerous because the user could prick their fingers or infect the cannula.

³⁴ In addition, double-ended needles do not readily permit the injection of soluble drugs into the vein. In medical practice, however, it is sometimes desirable to inject drugs after the blood has been drawn through the cannula in order to save the patient the pain of re-inserting a vein. Another disadvantage of using double-pointed cannulas is that when the tube is withdrawn,

some blood from the vein will flow back through the cannula to its inner end and soil the surrounding area. Of particular note when vacuum tubes are used with double-pointed cannulas is the risk that if the outer tip is not in a vein but in tissue, puncture of the inner tip of the cannula through the tube will result in blood leaking from the vein and a hematoma is coming. Then the user must pull out the cannula as quickly as possible. Even then, the user cannot grasp the situation quickly enough to avoid damage because the full pressure differential is applied to the outer tip of the cannula when the stopper of the evacuated tube is punctured.

[0005]

- 48 The conventional device has a holder surrounding the proximal end of the double-pointed cannula to receive the plugged end of the evacuated tube.
- 50 The diameter of the holder part is so large that the cannula penetrates the skin at a relatively acute angle, which increases the risk that the cannula will also puncture the other wall of the blood vessel, so that the tip of the cannula will then be in the tissue rather than in the blood vessel comes to rest. Even without an evacuated reservoir attached to the proximal end of the cannula, blood can clot at the tip, making the device inoperable if another sample is to be taken.

[0006]

- 58 The invention seeks to provide an improved blood sampling device that avoids the above deficiencies.
- 60 With the device according to the invention, it should be possible to take a plurality of blood samples with a single puncture of a cannula in a blood vessel without the risk of blood clotting in the space between the successive blood withdrawals. Furthermore, the angle at which the cannula penetrates the patient's skin should be determined by the device itself.

[0007]

- 67 In order to achieve this, the invention provides a blood sampling device as described in the characterizing part of the first claim.

[0008]

- 72 The device according to the invention has two valves.
- 73 The first valve closes the proximal end of the needle part when no container is connected; the second valve makes it possible to control the pressure difference used to aspirate blood from the patient.
- 76 The second valve can be quickly closed if it is discovered that the needle is not in a blood vessel but outside of it in the tissue. In this way, leakage of blood into the environment and a flamatoma are avoided.

[0009]

82 The device according to the invention consists of two composable parts; the first part comprises a cannula and a holder, the second part comprises an evacuated container closed with a stopper through which an axially slidable and rotatable tube passes.

85 The first and second parts, hereinafter referred to as the holder part and the container part, can be firmly joined together to form a continuous channel for blood to flow through the cannula, holder part and tube into the container. In the holder part is arranged the first valve, which is usually closed, so that when the tube and the container part are not connected to the holder part, the blood trapped in the holder part does not come into contact with air and thus possible infection is avoided. A second valve is mounted in the reservoir portion to allow control of the pressure differential acting across the distal tip of the cannula and to shut off negative pressure from the tip if the cannula is improperly seated in a blood vessel from which blood is being drawn to avoid the risk of a hematoma. The second valve is operated by rotating the container around the tube.

[0010]

98 The distal end of the tube can be inserted into the proximal end of the holder member so that a continuous channel is formed.

100 In one embodiment the distal end of the tube is provided with a protruding flange which opens the first valve when the container part and the holder part are connected to each other. In a second embodiment, the distal end of the tube itself opens the first valve and the container part can be detached from the holder part only when the second valve is closed.

[0011]

107 The invention thus has the advantage, among other things, that the negative pressure at the tip of a cannula is shut off by a valve if the cannula is not correctly positioned in a blood vessel.

109 The invention also eliminates the need for a holder and double-pointed needles by providing a novel vacuum container stopper and hypodermic applicator.

[0012]

114 The hypodermic applicator allows both the injection of soluble drugs into a blood vessel and the collection of blood samples without splashing back blood.

[0013]

119 Assembling the cannula containing part with the container part automatically opens the valve in the holder part so that a continuous and unobstructed channel is formed from the tip of the cannula to the proximal end of the tube which opens into the container.

122 Controlling the negative pressure applied to a vein can prevent the vein from collapsing.

[0014]

126 Further details and advantages of the invention result from the following description of exemplary embodiments with reference to the accompanying drawings.

128 1 shows a side view of a device according to the invention, in which the part containing the cannula is separated from the container part; Figure 2 shows a side elevation of the device according to the invention, in which the two parts are ready for assembly; Figure 3 is a side elevation showing the two parts of the device connected together and showing the valve in the container part closed; Figure 4 is a side elevation similar to Figure 3 but with the valve in the container part open; Figure 5 is a sectional view taken along line 5-5 of Figure 4; Figure 6 is a sectional view taken along line 6-6 of Figure 4; Figure 7 is a side perspective view of a second embodiment of the invention; Figure 8 is a partially sectioned view of the two parts of the second embodiment of the invention separated; Figure 9 is a view similar to Figure 8 but showing the two parts combined; Figure 10 shows the same two parts of the second embodiment but with the container advanced so that the second valve is open; Figure 11 is a view taken along line 11-11 of Figure 10; Figure 12 is a view taken along line 12-12 of Figure 10; and FIG. 13 is a sectional view taken along line 13-13 of FIG.

[0015]

144 The blood sampling device according to the invention consists of two parts that can be joined together, a holder part and a container part, which are shown separately from one another in FIG.

147 A cannula 23 has a tip 24 for piercing a blood vessel through a patient's skin.

148 The proximal end 25 (FIG. 2) of the cannula 23 is fastened in a holder part 22 through which a channel 26 runs. A flexible walled plug 27 sits in the end 28 of the channel. A flexible wall of the ben lies across an opening 29 so that the plug 27 simultaneously seals the opening 29 and the end 28 of the channel.

[0016]

155 The holder part 22 has a projection 30 which serves to hold the holder part at a certain distance from the patient's skin, thereby adjusting the angle at which the cannula 23 penetrates the skin and the manipulation of the holder part and the cannula is facilitated.

[0017]

161 A container 12 is closed with a stopper 10 having a flange 11 seated on the open end of the container 12 .

163 The plug 10 is penetrated by an axial passage in which is inserted a tube 14 which fits tightly

enough in the plug 10 to prevent air from entering between the tube 14 and the axial passage in the plug 10, yet is loose enough That they can move or rotate in the plug 10 in the axial direction.

[0018]

- 170 The tube 14 is closed at its proximal end, preferably with a disc cemented or otherwise secured onto the end of the tube 14 after the tube 14 is inserted into the stopper 10.
- 172 The washer 15 performs the dual function of sealing the end of the tube 14 and at the same time limiting the axial movement of the tube 14 away from the container 12.
- 174 The tube 14 also has a rigidly attached or molded stop 18 at a location such that the movement of the tube 14 axially toward the container 12 is limited.

[0019]

- 179 The tube 14 is provided with a side opening 16 located a small distance from the sealed tube end.
- 181 As shown in Figure 2, the opening 16 lies within the passage through the stopper 10 so that the container 12 is protected against ingress of air during evacuation. In a convenient embodiment, the axial passage through the plug 10 is threaded from its outer part to just short of where the orifice 16 comes to rest when the disc 15 is brought into contact with the plug 10. In this case, of course, the tube 14 must also be equipped with a suitable thread.

[0020]

- 189 Figure 2 shows the container part of the device being assembled with the holder part.
- 190 The connection is made by inserting the distal end 19 of the tube 14 into a socket 29. The tube end and socket are shaped to fit flush and prevent air from entering between them. A flange 20 is attached to the tube end 19 which bears against the flexible wall 29' of the plug 27 when the two parts are joined together. When the tube end 19 is pushed into the receptacle 29, the flange 20 pushes aside the top of the stopper 27 so that a continuous channel is established between the tip of the cannula 23 and the interior of the tube 14. This can be seen in Figure 3 where the top wall of the flexible plug 27 is depressed by the flange 20. The appearance of the holder portion of the device after insertion of the tube end 19 into the socket 29 is shown in the sectional views of Figs.

[0021]

- 202 When a blood sample is to be taken, the container 12 is gently rotated in the direction indicated by the arrow in FIG.
- 204 The axial movement of the container 12 towards the stop 18 results from the fact that the tube 14 is provided with a thread 13 which engages with a threaded part 13' of the stopper 10.

[0022]

209 It should be noted that the plug 10 has an unthreaded portion at its proximal end which ensures a tight seal when the opening 16 is within the plug 10.

[0023]

214 If blood does not flow through opening 16 into container 12 substantially immediately, the container 12 is rotated in the opposite direction to bring opening 16 back into stopper 10, thereby avoiding the full pressure differential being applied to the tissue in where the cannula must lie.

218 This avoids extravasation of blood and the resulting hematoma.

219 The cannula can then be pulled out and properly inserted again so that its tip comes to rest in a blood vessel.

[0024]

224 Then the container 12 is turned again according to FIG. 4 in order to start again with the blood collection.

226 If blood flows through the opening 16, the container 12 is rotated further until the stopper 10 hits the stop 18 on the holder part 22. The container then remains in this position until the desired amount of blood has been aspirated or until the container is filled.

[0025]

232 A second embodiment of the invention is shown in FIGS.

233 Again the device consists of two parts, a holder part, generally designated 221, containing the cannula, and a container part, generally designated 351. The container part 351 has a container 121 which is closed with a stopper 101 in which a through hole is made. A tube 141 having a threaded portion 131 is mounted in the bore of plug 101. The tube 141 has two parts 141a and 141b which form an angle with each other. A passage 161a through tube 141 is closed at its end by a conical portion 151 which fits into a corresponding portion 151a of the bore in plug 101. A lateral opening 161 is provided in the channel 161a near the conical part 151. The threaded portion 131 of the tube 141 terminates short of the side opening 161 so that when the container 121 is in a position such that the conical portion 151 is snugly received in section 151a, the opening 161 passes through the cylindrical portion of the stopper 101 is tightly closed.

[0026]

247 To assemble the holder portion and container portion of the device, end 191 of tube 141 is

inserted into a receptacle 291 in holder portion 221, lugs 301a slide into grooves 301b in holder portion 221, and rotation of container portion 351 establishes a bayonet fitting between lugs 301a and 301a grooves 301b.

251 In addition, the receptacle 29a has a spherical portion 311b which mates with a corresponding spherical portion 311a on the tube 141 to provide a tight seal between the holder portion and the container portion.

[0027]

257 When the tube end 191 is inserted into the socket 291 and the bayonet fitting is made, the pointed tube end 191 pushes down the top of a flexible plug 271 which is preferably hollow.

259 In doing so, the pointed end of the tube itself serves as a means to push the upper part 271' of the plug 271 aside. This displacement creates an uninterrupted line between the channel 161a in the container part and the cannula 23. The hollow plug 271 closes the end of the socket 291 and acts as a valve upon insertion of the tube end 191 due to the depressed top plug wall 271'. A portion 401 of the tube end is preferably received in a snug fit in receptacle 29a so that a seal is formed between these portions.

[0028]

268 When the container 121 is rotated in the direction indicated by an arrow in Fig. 10, it moves distally as shown in Fig. 10 and communicates the side opening 161 with the container interior; so that a connection is made from the cannula 23 to the container.

271 If the container is evacuated before the two parts are joined, then blood will flow through the cannula and through the associated channels into the container 121 after the side opening 161 enters the conical portion of the bore in the stopper 101. The range of movement of the container in a distal direction - the threads on the tube 141 are right-hand in this case - is restricted by the contact between the plug 101 and the rear part 321 of the border of the holder part 221.

[0029]

280 Conveniently, the plug 271 carries a ridge 271a which nests in a groove 271b in the retainer portion 221 to help hold the plug 271 in place.

[0030]

285 The manner in which the lugs 301a are fixed in the grooves 301b can be clearly seen from FIGS.

287 The path by which liquid enters the container 121 from the cannula is clear from FIGS. 10 and 12.

[0031]

292 Once the container is filled, the tip 191 of the tube 141 is removed from the channel, i. pulled out of the socket 29a and the flexible wall of the plug 27a springs back so that it blocks a channel 261 in the holder part 221.

295 This process can be repeated any number of times, each time using a new container to collect a sample.

[0032]

300 The distance between the border 321 of the holder part 221 and the outer surface 38a of the plug 101 is chosen so that the container part cannot lift off the corner 361 until the conical part 151 seals tightly in the bore portion 151a, and this sealing engagement is achieved by Turning the container 351 produced with simultaneous displacement of the same in the proximal direction.

305 The dashed curve shows how the distance at which the tip 371 of the plug 101 clears the corner 361 is determined.

307 The purpose of this arrangement is to ensure that the container is properly sealed before container portion 351 is removed from holder portion 221.

[0033]

312 The container portion can then be handled separately without risk of contamination of its contents.

[0034]

317 It should be noted that the seal between the tube end portion 401 and the receptacle 291 prevents air ingress when unlocking the bayonet fitting if unlocking is attempted when the container portion 351 at the side opening 161 is only partially closed.

[0035]

323 If desired, a soluble drug can be injected without causing pain to the patient by drawing the drug into an ordinary syringe fitted with a thin gauge needle and piercing the stopper 271 through an opening 28a with the needle tip of the syringe.

326 The drug is then injected into the channel 26a and from there goes to the cannula 23, to its tip 24 and finally into the patient's blood vessel, provided that the passageway serving as receptacle 291 remains sealed.

329 A new reservoir portion can be attached to the holder portion 221 that remains in place to aspirate more blood, or the cannula 23 can be withdrawn from the blood vessel and then discarded.

³³² The filled part of the container is sent to an appropriate biochemical laboratory, where the valve of the side opening 161 is first opened, after which the plug 101 can be easily removed, the tests can be carried out and the whole unit can then be destroyed.

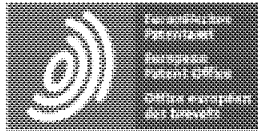
[0036]

³³⁸ Since receptacle 291 is blocked each time a container is removed, blood cannot continue to ooze out of channel 261, nor is it drawn back into the blood vessel.

[0037]

³⁴³ The object of the invention is thus fulfilled.

³⁴⁴ Modifications are possible with respect to the exemplary embodiments described.



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CLAIMS DE2541494A1

1.

¹³ L n 8 p r u c h e 9 Blood extraction device for draining blood from a blood vessel, characterized in that it consists of a holder part (22, 221) and a container part (351), that the holder part has a cannula (23) with a pointed distal end (24) and a proximal end (25) and is traversed by a channel (26, 261), in whose distal end the proximal end (25) of the cannula is received in a sealed manner and which communicates with an opening (29, 291) of the holder part and that a first valve (27, 271) is seated in the proximal end of the duct (26, 261) to close the duct, normally blocking communication between the opening (29, 291) and the duct, that further the container part has an evacuable container (12, 121), the opening of which is closed by a stopper (10, 101), and that a tube (14, 141) is provided, the proximal end of which passes through the stopper (10, 101). and is connected at its distal end to the opening (29, 291) in the holder part in such a way that a sealing connection can be established between the tube and the holder part at this opening, and that at the distal end of the tube an actuating element (20, 191) is provided which opens the first valve (27, 271) thereby connecting the orifice (29, 291) to the channel (26, 261) when the tube (14, 141) is attached to the holder part (22, 221) with the plug (10,101) being attached to the container (12,121) so that it is movable with the container relative to the tube but is sufficiently tight in the container opening to prevent air ingress between the two prevent sharing.

2.

³³ Device according to Claim 1, characterized in that the first valve consists of a flexible plug (27, 271) which fits into the proximal end (28, 281) of the channel (26, 261) and closes this end (28, 281). and which extends across the opening (29, 291) and completely seals this opening when the tube (14, 141) is not connected to the holder part (22, 221).

3.

⁴⁰ Apparatus according to claim 2 characterized in that the actuator on the tube (14) is a flange (20) projecting from the distal end of the tube and positioned to engage that portion (29) of the hollow flexible plug (27) blocking the opening (29), pushing aside and thereby establishing communication with the channel (26) so that blood can flow through the holder part (22) into the tube (14).

4.

⁴⁸ Apparatus according to any one of the preceding paragraphs characterized in that the opening (29, 291) is shaped as a socket and the distal end of the tube (14, 141) is receivable in the socket-shaped opening with a snug fit.

5.

⁵⁴ Device according to one of the preceding claims, characterized in that the holder part is provided with a projection (30) which can be placed on the surface into which the cannula (2#) is to be inserted and thus defines the angle under which the cannula is inserted into the surface, and also maintains the holder portion at a distance from the surface and provides a means for more conveniently retaining the holder portion.

6.

⁶² Device according to any one of the preceding claims, characterized in that the plug (10, 101) is traversed by an axial channel in which the tube (14, 141) fits tightly enough to permit a flow of fluid between the tube and the channel wall preventing, and that the tube (14, 141) is closed at its proximal end and has an opening (16, 161) in its side wall near the proximal end, and that the container (12, 121) relative to this proximal end of the tube is axially movable sufficiently so that in a first position the opening (16, 161) is within the container and communicates between the tube and the container and in a second position within the channel in the stopper (10, 101) and thus the container is sealed against the ingress of air or liquid from the tube into the container, the opening (16, 161) in the side wall of the tube constituting a second valve.

7.

⁷⁴ Device according to claim 6, characterized in that the distal end of the channel in the stopper (10, 101) and the proximal end of the tube are externally provided with mating threads (13, 13'; 131, 131') so that through Rotating the container around the tube gradually establishes a connection between the tube and the container or the connection can be broken.

8.

⁸¹ Device according to claim 6 or 7, characterized in that the tube (14) is provided on both sides of the stopper (10) with protruding parts (18, 15) serving as stops to limit the relative axial freedom of movement of the container and the stopper to limit the tube.

9.

⁸⁷ A device according to any one of claims 6 to 8, characterized in that the proximal end of the tube and the proximal end of the channel in the stopper are shaped to match each other so that a seal is formed between the two parts when the tube is inserted into the channel.

10.

⁹³ Apparatus according to claim 9, characterized in that the mating parts (151, 151a) of the tube and duct are conically shaped.

11.

⁹⁸ Apparatus according to any one of the preceding claims characterized in that the first valve is a hollow plug (27, 271) through which a hypodermic needle can be inserted to inject fluid into a patient once the patient's skin has been punctured for blood collection .

12.

¹⁰⁴ Device according to one of claims 6 to 11, characterized in that the axial range of movement of the container (121) relative to the tube (141) in the proximal direction is determined by the contact of the proximal end (151) of the tube with the stopper (101) and in the distal Direction is limited by the contact of the plug (101) with the holder part (221).

13.

¹¹¹ Device according to Claim 12, characterized in that the distance between the holder part (221) and the stopper (101) is selected in such a way that the container part (351) can only be removed from the holder part (221) if the container has reached the am position furthest from the holder part, which position corresponds to the limit of movement of the container in the proximal direction, thereby ensuring that the second valve (161) is closed.

51

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A n s p r ü c h e

1. Blutentnahmevorrichtung zum Abzapfen von Blut aus einem Blutgefäß, dadurch gekennzeichnet, daß sie aus einem Halterteil (22, 221) und einem Behälterteil (351) besteht, daß der Halterteil eine Kanüle (23) mit einem zugespitzten distalen Ende (24) und einem proximalen Ende (25) aufweist und von einem Kanal (26, 261) durchzogen ist, in dessen distalem Ende das proximale Ende (25) der Kanüle dichtend aufgenommen ist und der mit einer Öffnung (29, 291) des Halterteils in Verbindung steht, und daß ein erstes Ventil (27, 271) in dem proximalen Ende des Kanals (26, 261) sitzt, um den Kanal zu schließen, das normalerweise die Verbindung zwischen der Öffnung (29, 291) und dem Kanal sperrt, daß ferner der Behälterteil einen evakuierbaren Behälter (12, 121) aufweist, dessen Öffnung durch einen Stöpsel (10, 101) verschlossen ist, und daß eine Röhre (14, 141) vorgesehen ist, die mit ihrem proximalen Ende durch den Stöpsel (10, 101) tritt und an ihrem distalen Ende derart mit der Öffnung (29, 291) in dem Halterteil verbunden ist, daß an dieser Öffnung eine abdichtende Verbindung zwischen der Röhre und dem Halterteil herstellbar ist, und daß an dem distalen Ende der Röhre ein Betätigungselement (20, 191) vorgesehen ist, das das erste Ventil (27, 271) öffnet und dabei die Öffnung (29, 291) mit dem Kanal (26, 261) verbindet, wenn die Röhre (14, 141) an den Halterteil (22, 221) angeschlossen wird, wobei der Stöpsel (10, 101) derart an dem Behälter (12, 121) angebracht ist, daß er mit dem Behälter relativ zur Röhre bewegbar ist, aber fest genug in der Behälteröffnung sitzt, um ein Eindringen von Luft zwischen den beiden Teilen zu verhindern.
2. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß das erste Ventil aus einem flexiblen Stopfen (27, 271) besteht, der in dem proximalen Ende (28, 281) des Kanals (26, 261) sitzt und dieses Ende (28, 281) verschließt und der sich quer über die Öffnung (29, 291) erstreckt und die-

- se Öffnung vollständig abdichtet, wenn die Röhre (14, 141) nicht mit dem Halterteil (22, 221) verbunden ist.
3. Vorrichtung nach Anspruch 2, dadurch gekennzeichnet, daß das Betätigungselement an der Röhre (14) ein Flansch (20) ist, der vom distalen Ende der Röhre absteht und eine solche Lage hat, daß er denjenigen Teil (29) des hohlen flexiblen Stopfens (27), der die Öffnung (29) versperrt, beiseite-drückt und dadurch eine Verbindung mit dem Kanal (26) herstellt, so daß Blut durch den Halterteil (22) in die Röhre (14) fließen kann.
 4. Vorrichtung nach einem der vorangehenden Ansprüche, dadurch gekennzeichnet, daß die Öffnung (29, 291) als Muffe geformt ist und das distale Ende der Röhre (14, 141) im Paßsitz in der muffenförmigen Öffnung aufnehmbar ist.
 5. Vorrichtung nach einem der vorangehenden Ansprüche, da-durch gekennzeichnet, daß der Halterteil mit einem Vorsprung (30) versehen ist, der an der Oberfläche, in die die Kanüle (23) eingeführt werden soll, aufsetzbar ist und damit den Winkel festlegt, unter dem die Kanüle in die Oberfläche eingeführt wird, und zudem den Halterteil in einem Abstand von der Oberfläche hält und ein Mittel zum bequemeren Festhalten des Halterteils darstellt.
 6. Vorrichtung nach einem der vorangehenden Ansprüche, da-durch gekennzeichnet, daß der Stöpsel (10, 101) von einem axialen Kanal durchzogen ist, in dem die Röhre (14, 141) fest genug sitzt, um einen Fluß von Fluid zwischen der Röhre und der Kanalwand zu verhindern, und daß die Röhre (14, 141) an ihrem proximalen Ende verschlossen ist und in ihrer Seitenwand nahe dem proximalen Ende eine Öffnung (16, 161) hat, und daß der Behälter (12, 121) relativ zu diesem proximalen Ende der Röhre in Achsrichtung weit genug bewegbar ist, so daß die Öffnung (16, 161) in einer

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ersten Stellung sich in dem Behälter befindet und eine Verbindung zwischen der Röhre und dem Behälter herstellt und in einer zweiten Stellung innerhalb des Kanals in dem Stöpsel (10, 101) liegt und damit der Behälter gegen das Eindringen von Luft oder Flüssigkeit aus der Röhre in den Behälter abgedichtet ist, wobei die Öffnung (16, 161) in der Seitenwand der Röhre ein zweites Ventil darstellt.

7. Vorrichtung nach Anspruch 6, dadurch gekennzeichnet, daß das distale Ende des Kanals im Stöpsel (10, 101) und das proximale Ende der Röhre auf der Außenseite mit zusammenpassenden Gewinden (13, 13'; 131, 131') versehen sind, so daß durch Drehen des Behälters um die Röhre allmählich eine Verbindung zwischen der Röhre und dem Behälter herstellbar ist bzw. die Verbindung unterbrechbar ist.
8. Vorrichtung nach Anspruch 6 oder 7, dadurch gekennzeichnet, daß die Röhre (14) zu beiden Seiten des Stöpsels (10) mit vorstehenden Teilen (18, 15) versehen ist, die als Anschläge dienen, um den axialen Bewegungsspielraum des Behälters und des Stöpsels relativ zur Röhre zu begrenzen.
9. Vorrichtung nach einem der Ansprüche 6 bis 8, dadurch gekennzeichnet, daß das proximale Ende der Röhre und das proximale Ende des Kanals im Stöpsel zueinander passend geformt sind, so daß beim Einsetzen der Röhre in den Kanal eine Abdichtung zwischen beiden Teilen zustandekommt.
10. Vorrichtung nach Anspruch 9, dadurch gekennzeichnet, daß die zusammenpassenden Teile (151, 151a) von Röhre und Kanal konisch geformt sind.
11. Vorrichtung nach einem der vorangehenden Ansprüche, dadurch gekennzeichnet, daß das erste Ventil ein hohler Stopfen (27, 271) ist, durch den eine Injektionsnadel eingeführt werden kann, um Fluid einem Patienten zu injizieren,

wenn die Haut des Patienten zur Blutentnahme bereits einmal durchstoßen ist.

12. Vorrichtung nach einem der Ansprüche 6 bis 11, dadurch gekennzeichnet, daß der axiale Bewegungsspielraum des Behälters (121) relativ zur Röhre (141) in proximaler Richtung durch den Kontakt des proximalen Endes (151) der Röhre mit dem Stöpsel (101) und in distaler Richtung durch den Kontakt des Stöpsels (101) mit dem Halterteil (221) begrenzt ist.
13. Vorrichtung nach Anspruch 12, dadurch gekennzeichnet, daß der Abstand zwischen dem Halterteil (221) und dem Stöpsel (101) so gewählt ist, daß ein Wegnehmen des Behälterteils (351) vom Halterteil (221) nur dann möglich ist, wenn der Behälter die am weitesten von dem Halterteil entfernte Lage einnimmt, wobei diese Lage der Bewegungsgrenze des Behälters in proximaler Richtung entspricht, wodurch sichergestellt ist, daß das zweite Ventil (161) geschlossen ist.

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Blutentnahmevorrichtung

Die Erfindung betrifft eine Blutentnahmevorrichtung zum Abzapfen von Blut aus einem Blutgefäß.

In modernen Krankenhäusern gehört es zur Routine, von Patienten Blutproben zu entnehmen, indem man eine oder mehrere evakuierte Teströhren nacheinander in einen Halter einsetzt, der eine Kanüle mit zwei Spitzen hat; das eine zugespitzte Ende der Kanüle sticht in die Vene des Patienten ein und das andere spitze Ende durchsticht den Stöpsel der evakuierten Teströhre, um auf diese Weise Blut aus der Vene in die evakuierte Röhre fließen zu lassen.

Halter für Vakuumröhren sind jedoch verhältnismäßig teuer und daher keine Wegwerfartikel; außerdem sind sie unhandliche Geräte, die einer Verunreinigung ausgesetzt sind (siehe US-PS 3 520 292). Wenn in den Haltern nicht bereits Kanülen mit zwei Spitzen eingebaut sind, müssen sie von einem Benutzer an den Haltern angebracht werden. Die Handhabung dieser Kanülen mit zwei Spitzen ist jedoch gefährlich, weil der Benutzer sich in die Finger stechen oder die Kanüle infizieren kann. Außerdem erlauben doppelseitig zugespitzte Kanülen nicht ohne weiteres die Injektion von löslichen Arzneimitteln in die Vene. In der medizinischen Praxis ist es jedoch manchmal erwünscht, nach der Blutentnahme durch die Kanüle Arzneimittel zu injizieren,

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weil man so dem Patienten den Schmerz beim nochmaligen Einstechen in eine Vene erspart. Ein weiterer Nachteil in der Verwendung doppelt zugespitzter Kanülen ist, daß beim Herausziehen der Röhre etwas Blut aus der Vene durch die Kanüle zu deren innerem Ende zurückfließt und die Umgebung verschmutzt. Besonders beachtlich ist bei der Verwendung von Vakuumröhren zusammen mit doppelt zugespitzten Kanülen die Gefahr, daß, wenn die äußere Spitze nicht in einer Vene sondern im Gewebe liegt, es beim Durchstechen der inneren Spitze der Kanüle durch die Röhre zu einem Blutaustritt aus der Vene und einem Hämatom kommt. Dann muß der Benützer die Kanüle so rasch wie möglich herausziehen. Selbst dann kann der Benützer die Situation nicht schnell genug erfassen, um Schaden zu vermeiden, weil der volle Druckunterschied an die äußere Spitze der Kanüle angelegt wird, wenn der Stöpsel der evakuierten Röhre durchstoßen wird.

Das herkömmliche Gerät hat einen Halter, der das proximale Ende der doppelt zugespitzten Kanüle umgibt, um das zugestöpselte Ende der evakuierten Röhre aufzunehmen. Der Durchmesser des Halterteils ist so groß, daß die Kanüle in die Haut unter einem verhältnismäßig spitzen Winkel eindringt, was die Gefahr erhöht, daß die Kanüle auch noch die andere Wand des Blutgefäßes durchsticht, so daß die Spitze der Kanüle dann im Gewebe statt im Blutgefäß zu liegen kommt. Auch wenn auf dem proximalen Ende der Kanüle kein evakuierter Behälter angebracht ist, kann es an der Spitze zu einer Blutgerinnung kommen, wodurch die Funktion des Gerätes gestört ist, wenn eine weitere Probe entnommen werden soll.

Die Erfindung will eine verbesserte Blutentnahmevorrichtung schaffen, die die obigen Mängel vermeidet. Mit der erfindungsgemäßen Vorrichtung sollen mit einem einzigen Einstich einer Kanüle in ein Blutgefäß mehrere Blutproben entnommen werden können, ohne daß die Gefahr einer Blutgerinnung in dem Zwischenraum zwischen den aufeinanderfolgenden Blutentnahmen besteht. Ferner soll der Winkel, unter dem die Kanüle in die

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Haut des Patienten eindringt, durch das Gerät selbst festgelegt sein.

Um dies zu erreichen, sieht die Erfindung eine Blutentnahmevorrichtung vor, wie sie im kennzeichnenden Teil des ersten Anspruchs beschrieben ist.

Die erfindungsgemäße Vorrichtung hat zwei Ventile. Das erste Ventil schließt das proximale Ende des Nadelteils, wenn kein Behälter angeschlossen ist; das zweite Ventil macht es möglich, den Druckunterschied, der zum Absaugen von Blut aus dem Patienten genützt wird, zu steuern. Das zweite Ventil kann rasch geschlossen werden, falls man entdeckt, daß die Nadel nicht in einem Blutgefäß sondern außerhalb desselben im Gewebe liegt. Auf diese Weise wird ein Blutaustritt in die Umgebung und ein Hämatom vermieden.

Die erfindungsgemäße Vorrichtung besteht aus zwei zusammensetzbaren Teilen; der erste Teil umfaßt eine Kanüle und einen Halter, der zweite Teil umfaßt einen evakuierten Behälter, der mit einem Stöpsel geschlossen ist, durch den eine axial verschiebbare und drehbare Röhre tritt. Der erste und zweite Teil, die nachstehend als der Halterteil und der Behälterteil bezeichnet werden, können fest miteinander vereinigt werden, so daß ein durchgehender Kanal für das fließende Blut durch die Kanüle, den Halterteil und die Röhre in den Behälter gebildet ist. In dem Halterteil ist das erste Ventil angeordnet, das gewöhnlich geschlossen ist, so daß, wenn die Röhre und der Behälterteil nicht mit dem Halterteil verbunden sind, das in dem Halterteil eingeschlossene Blut nicht mit Luft in Berührung kommt und somit eine mögliche Infizierung vermieden ist. In dem Behälterteil ist ein zweites Ventil angebracht, das die Steuerung der Druckdifferenz, die an der distalen Spitze der Kanüle wirksam wird, ermöglicht und den Unterdruck von der Spitze absperren kann, falls die Kanüle nicht ordnungsgemäß in einem Blutgefäß liegt, aus dem Blut entnommen werden soll, um so die Gefahr eines Hämatoms auszuschließen. Das zweite Ven-

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til wird durch Drehung des Behälters um die Röhre betätigt. Das distale Ende der Röhre kann in das proximale Ende des Halterteils eingesetzt werden, so daß ein durchgehender Kanal gebildet wird. In einer Ausführungsform ist das distale Ende der Röhre mit einem vorstehenden Flansch versehen, der das erste Ventil öffnet, wenn der Behälterteil und der Halterteil miteinander verbunden werden. In einer zweiten Ausführungsform öffnet das distale Ende der Röhre selbst das erste Ventil und der Behälterteil kann von dem Halterteil nur dann abgenommen werden, wenn das zweite Ventil geschlossen ist.

Die Erfindung hat also u.a. den Vorteil, daß der Unterdruck an der Spitze einer Kanüle von einem Ventil abgesperrt wird, falls die Kanüle nicht richtig in einem Blutgefäß liegt. Die Erfindung macht außerdem durch einen neuartigen Stöpsel für einen Vakuumbehälter und einen neuartigen hypodermischen Applikator einen Halter und doppelt zugespitzte Kanülen überflüssig. Der hypodermische Applikator erlaubt sowohl die Injizierung löslicher Arzneimittel in ein Blutgefäß als auch das Entnehmen von Blutproben, ohne ein Verspritzen von rückschießendem Blut. Durch das Zusammensetzen des die Kanüle enthaltenden Teils mit dem Behälterteil wird automatisch das Ventil in dem Halterteil geöffnet, so daß ein durchgehender und unbehinderter Kanal von der Kanülenspitze bis zum proximalen Ende der Röhre, das in den Behälter mündet, gebildet ist. Durch die Steuerung des an eine Vene angelegten Unterdruckes kann ein Kollaps der Vene vermieden werden.

Weitere Einzelheiten und Vorzüge der Erfindung ergeben sich aus der nachfolgenden Beschreibung von Ausführungsbeispielen anhand der beigefügten Zeichnungen. Darin zeigen:

Fig.1 eine Seitenansicht einer erfindungsgemäßen Vorrichtung, in der der die Kanüle enthaltende Teil von dem Behälterteil getrennt ist;

Fig.2 einen Seitenriß der erfindungsgemäßen Vorrichtung, in dem die beiden Teile in der Lage zum Zusammensetzen sind;

Fig.3 einen Seitenriß, der die zwei Teile der Vorrichtung miteinander verbunden zeigt und in dem das Ventil im Behälterteil geschlossen dargestellt ist;

Fig.4 einen der Fig.3 ähnlichen Seitenriß, bei dem jedoch das Ventil im Behälterteil offen ist;

Fig.5 eine Schnittansicht nach der Linie 5-5 der Fig.4;

Fig.6 eine Schnittansicht nach der Linie 6-6 der Fig.4;

Fig.7 eine perspektivische Seitenansicht einer zweiten Ausführungsform der Erfindung;

Fig.8 eine teilweise geschnittene Ansicht der beiden Teile der zweiten Ausführungsform der Erfindung im getrennten Zustand;

Fig.9 eine der Fig.8 ähnliche Ansicht, in der jedoch die beiden Teile vereinigt sind;

Fig.10 die gleichen beiden Teile der zweiten Ausführungsform, wobei jedoch der Behälter vorgeschoben ist, so daß das zweite Ventil offen ist;

Fig.11 eine Ansicht nach der Linie 11-11 der Fig.10;

Fig.12 eine Ansicht nach der Linie 12-12 der Fig.10; und

Fig.13 eine Schnittansicht nach der Linie 13-13 der Fig.9.

Die erfindungsgemäße Blutentnahmevorrichtung besteht aus zwei zusammenfügbaren Teilen, einem Halterteil und einem Behälterteil, die in Fig.1 getrennt voneinander dargestellt sind. Eine Kanüle 23 hat eine Spitze 24 zum Einstechen in ein Blutgefäß durch die Haut eines Patienten. Das proximale Ende 25 (Fig.2) der Kanüle 23 ist in einem Halterteil 22 befestigt, der von einem Kanal 26 durchzogen ist. Ein Stopfen 27 mit flexiblen Wänden sitzt im Ende 28 des Kanals. Eine flexible Wand desselben liegt quer über einer Öffnung 29, so daß der Stopfen 27 zugleich die Öffnung 29 und das Ende 28 des Kanals abdichtet. Der Halterteil 22 hat einen Vorsprung 30, der dazu dient, den Halterteil in einem bestimmten Abstand von der Haut des Patienten zu halten.

ten zu halten, wodurch der Winkel eingestellt wird, unter dem die Kanüle 23 in die Haut eindringt, und die Handhabung des Halterteils und der Kanüle erleichtert wird.

Ein Behälter 12 ist mit einem Stöpsel 10 verschlossen, der einen auf dem offenen Ende des Behälters 12 aufsitzenden Flansch 11 hat. Der Stöpsel 10 ist von einem axialen Kanal durchzogen, in dem eine Röhre 14 steckt, die fest genug in dem Stöpsel 10 sitzt, um ein Eindringen von Luft zwischen die Röhre 14 und den axialen Kanal im Stöpsel 10 zu verhindern, aber andererseits doch so locker, daß sie sich im Stöpsel 10 in Achsrichtung verschieben oder drehen kann.

Die Röhre 14 ist an ihrem proximalen Ende verschlossen, vorzugsweise mit einer Scheibe, die auf dem Ende der Röhre 14 festgekittet oder sonstwie befestigt wird, nachdem die Röhre 14 in den Stöpsel 10 eingeführt ist. Die Scheibe 15 erfüllt eine doppelte Aufgabe, nämlich das Ende der Röhre 14 abzudichten und zugleich den axialen Bewegungsspielraum der Röhre 14 von dem Behälter 12 weg zu begrenzen. Die Röhre 14 hat auch noch einen starr angebrachten oder angeformten Anschlag 18 an einer solchen Stelle, daß der Bewegungsspielraum der Röhre 14 in axialer Richtung zum Behälter 12 hin begrenzt wird.

Die Röhre 14 ist mit einer seitlichen Öffnung 16 versehen, die in einem kleinen Abstand von dem abgedichteten Röhrenende angeordnet ist. Wie in Fig.2 gezeigt, liegt die Öffnung 16 innerhalb des den Stöpsel 10 durchziehenden Kanals, so daß der Behälter 12 gegen ein Eindringen von Luft beim Evakuieren geschützt ist. In einer zweckmäßigen Ausführungsform ist der axiale Kanal durch den Stöpsel 10 von seinem äußeren Teil bis kurz vor die Stelle, wo die Öffnung 16 zu liegen kommt, wenn die Scheibe 15 mit dem Stöpsel 10 in Kontakt gebracht ist, mit einem Gewinde versehen. Selbstverständlich ist in diesem Fall auch die Röhre 14 mit einem passenden Gewinde auszustatten.

Fig.2 zeigt den Behälterteil der Vorrichtung gerade beim Zu-

sammenfügen mit dem Halterteil. Die Verbindung wird in der Weise hergestellt, daß das distale Ende 19 der Röhre 14 in eine Aufnahme 29 eingesetzt wird. Das Röhrenende und die Aufnahme sind so geformt, daß sie bündig zusammenpassen und keine Luft zwischen ihnen eindringen kann. An dem Röhrenende 19 ist ein Flansch 20 angebracht, der sich gegen die flexible Wand 29' des Stopfens 27 anlegt, wenn die beiden Teile miteinander vereinigt sind. Wenn das Röhrenende 19 in die Aufnahme 29 eingeschoben wird, drückt der Flansch 20 den oberen Teil des Stopfens 27 beiseite, so daß ein durchgehender Kanal zwischen der Spitze der Kanüle 23 und dem Inneren der Röhre 14 hergestellt wird. Dies ist in Fig.3 zu sehen, in der die obere Wand des flexiblen Stopfens 27 von dem Flansch 20 niedergedrückt ist. Das Aussehen des Halterteils der Vorrichtung nach dem Einführen des Röhrenendes 19 in die Aufnahme 29 ist in den Schnittansichten der Fig.5 und 6 gezeigt.

Wenn eine Blutprobe entnommen werden soll, wird der Behälter 12 vorsichtig in der durch den Pfeil in Fig.4 angegebenen Richtung gedreht, bis die Öffnung 16 eben von dem proximalen Ende des Stöpsels 10 freikommt. Die axiale Bewegung des Behälters 12 in Richtung zum Anschlag 18 ergibt sich aus der Tatsache, daß die Röhre 14 mit einem Gewinde 13 versehen ist, das mit einem Gewindeteil 13' des Stöpsels 10 im Eingriff ist. Zu beachten ist, daß der Stöpsel 10 an seinem proximalen Ende einen gewindefreien Teil hat, wodurch eine feste Abdichtung sichergestellt ist, wenn sich die Öffnung 16 innerhalb des Stöpsels 10 befindet.

Wenn nicht praktisch sofort Blut durch die Öffnung 16 in den Behälter 12 fließt, wird der Behälter 12 in der entgegengesetzten Richtung gedreht, um die Öffnung 16 wieder in den Stöpsel 10 zurückzubringen, wodurch man vermeidet, daß die volle Druckdifferenz auf das Gewebe einwirkt, in dem die Kanüle liegen muß. Auf diese Weise werden eine Extravasation von Blut und das dabei entstehende Hämatom vermieden. Die Kanüle kann dann herausgezogen und noch einmal richtig eingestochen wer-

den, so daß ihre Spitze in einem Blutgefäß zu liegen kommt. Dann wird der Behälter 12 wieder gemäß Fig.4 gedreht, um noch einmal mit der Blutentnahme zu beginnen. Falls Blut durch die Öffnung 16 fließt, wird der Behälter 12 weitergedreht, bis der Stöpsel 10 auf den Anschlag 18 am Halterteil 22 trifft. In dieser Lage bleibt dann der Behälter, bis die gewünschte Blutmenge abgesaugt ist oder bis der Behälter gefüllt ist.

In den Fig.7-12 ist eine zweite Ausführungsform der Erfindung dargestellt. Wieder besteht die Vorrichtung aus zwei Teilen, einem die Kanüle enthaltenden Halterteil, der insgesamt mit 221 bezeichnet ist, und einem insgesamt mit 351 bezeichneten Behälterteil. Der Behälterteil 351 weist einen Behälter 121 auf, der mit einem Stöpsel 101 verschlossen ist, in dem eine durchgehende Bohrung angebracht ist. Eine Röhre 141, die einen Gewindeteil 131 hat, ist in der Bohrung des Stöpsels 101 angebracht. Die Röhre 141 hat zwei Teile 141a und 141b, die miteinander einen Winkel bilden. Ein die Röhre 141 durchziehender Kanal 161a ist an seinem Ende mit einem konischen Teil 151 verschlossen, das in einen entsprechenden Abschnitt 151a der Bohrung im Stöpsel 101 paßt. In dem Kanal 161a ist nahe dem konischen Teil 151 eine seitliche Öffnung 161 vorgesehen. Der Gewindeteil 131 der Röhre 141 hört kurz vor der seitlichen Öffnung 161 auf, so daß, wenn der Behälter 121 eine solche Lage hat, daß das konische Teil 151 im Paßsitz im Abschnitt 151a aufgenommen ist, die Öffnung 161 durch den zylindrischen Teil des Stöpsels 101 dichtend verschlossen ist.

Um den Halterteil und den Behälterteil der Vorrichtung zusammenzufügen, wird das Ende 191 der Röhre 141 in eine Aufnahme 291 im Halterteil 221 eingeführt. Nasen 301a schieben sich in Nuten 301b im Halterteil 221 und eine Drehung des Behälterteils 351 stellt einen Bajonettverschluß zwischen den Nasen 301a und Nuten 301b her. Außerdem hat die Aufnahme 29a einen kugelförmigen Teil 311b, der mit einem entsprechenden kugelförmigen Teil 311a an der Röhre 141 zusammenpaßt, so daß eine feste Abdich-

tung zwischen dem Halterteil und dem Behälterteil zustande kommt.

Wenn das Röhrenende 191 in die Aufnahme 291 eingeschoben und der Bajonettverschluß hergestellt ist, drückt das zugespitzte Röhrenende 191 den oberen Teil eines flexiblen Stopfens 271 nach unten, der vorzugsweise hohl ist. Dabei dient das zugespitzte Röhrenende selbst als ein Mittel, um den oberen Teil 271' des Stopfens 271 beiseite zu schieben. Durch diese Verlagerung entsteht eine ununterbrochene Leitung zwischen dem Kanal 161a im Behälterteil und der Kanüle 23. Der hohle Stopfen 271 schließt das Ende der Aufnahme 291 und wirkt beim Einführen des Röhrenendes 191 als Ventil infolge der herabgedrückten oberen Stopfenwand 271'. Ein Teil 401 des Röhrenendes ist vorzugsweise im Paßsitz in der Aufnahme 29a aufgenommen, so daß zwischen diesen Teilen eine Abdichtung hergestellt ist.

Wenn der Behälter 121 in der durch einen Pfeil in Fig.10 angedeuteten Richtung gedreht wird, bewegt er sich gemäß Fig.10 in distaler Richtung und verbindet die seitliche Öffnung 161 mit dem Behälterinnenraum; damit ist eine Verbindung von der Kanüle 23 zum Behälter hergestellt. Falls der Behälter vor dem Vereinigen der beiden Teile evakuiert ist, fließt dann Blut durch die Kanüle und durch die verbundenen Kanäle in den Behälter 121, nachdem die seitliche Öffnung 161 in den konischen Abschnitt der Bohrung im Stöpsel 101 gelangt ist. Der Bewegungsspielraum des Behälters in distaler Richtung - das Gewinde an der Röhre 141 ist in diesem Fall rechtsgängig - wird durch den Kontakt zwischen dem Stöpsel 101 und dem hinteren Teil 321 der Begrenzung des Halterteils 221 eingeschränkt.

Zweckmäßigerweise trägt der Stopfen 271 einen Wulst 271a, der sich in eine Nut 271b im Halterteil 221 einbettet, um dazu beizutragen, daß der Stopfen 271 in seiner Lage gehalten wird.

Auf welche Weise die Nasen 301a sich in den Nuten 301b festsetzen, ist deutlich aus den Fig.11 und 12 ersichtlich. Der

Weg, auf dem Flüssigkeit von der Kanüle in den Behälter 121 gelangt, wird aus den Fig. 10 und 12 deutlich.

Sobald der Behälter gefüllt ist, wird die Spitze 191 der Röhre 141 von dem Kanal, d.i. aus der Aufnahme 29a herausgezogen und die flexible Wand des Stopfens 27a schnellt zurück, so daß sie einen Kanal 261 im Halterteil 221 versperrt. Dieser Vorgang kann beliebig oft wiederholt werden, wobei man jedesmal einen neuen Behälter zum Entnehmen einer Probe verwendet.

Der Abstand zwischen der Begrenzung 321 des Halterteils 221 und der Außenfläche 38a des Stöpsels 101 ist so gewählt, daß der Behälterteil von der Ecke 361 nicht abheben kann, bevor nicht das konische Teil 151 fest in dem Bohrungsabschnitt 151a abdichtet, und diese dichtende Anlage wird durch Drehen des Behälters 351 mit gleichzeitiger Verschiebung desselben in proximaler Richtung hergestellt. Die gestrichelte Kurve zeigt, wie der Abstand, bei dem die Spitze 371 des Stöpsels 101 von der Ecke 361 freikommt, bestimmt wird. Zweck dieser Anordnung ist es, sicherzustellen, daß der Behälter gut abgedichtet ist, bevor der Behälterteil 351 vom Halterteil 221 weggenommen wird. Der Behälterteil kann dann getrennt gehandhabt werden, ohne daß die Gefahr einer Verunreinigung seines Inhalts besteht.

Zu beachten ist, daß die Abdichtung zwischen dem Röhrenenden- teil 401 und der Aufnahme 291 ein Eindringen von Luft beim Entriegeln des Bajonettverschlusses verhindert, falls ein Entriegeln versucht wird, wenn der Behälterteil 351 an der seitlichen Öffnung 161 nur teilweise verschlossen ist.

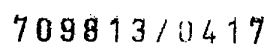
Nach Wunsch kann ein lösliches Arzneimittel ohne Schmerzen für den Patienten injiziert werden, indem man das Arzneimittel in eine übliche Spritze aufzieht, an der eine dünnkalibrige Nadel angesetzt ist, und den Stopfen 271 durch eine Öffnung 28a hindurch mit der Nadelspitze der Spritze durchsticht. Das Arzneimittel wird dann in den Kanal 26a eingespritzt und geht

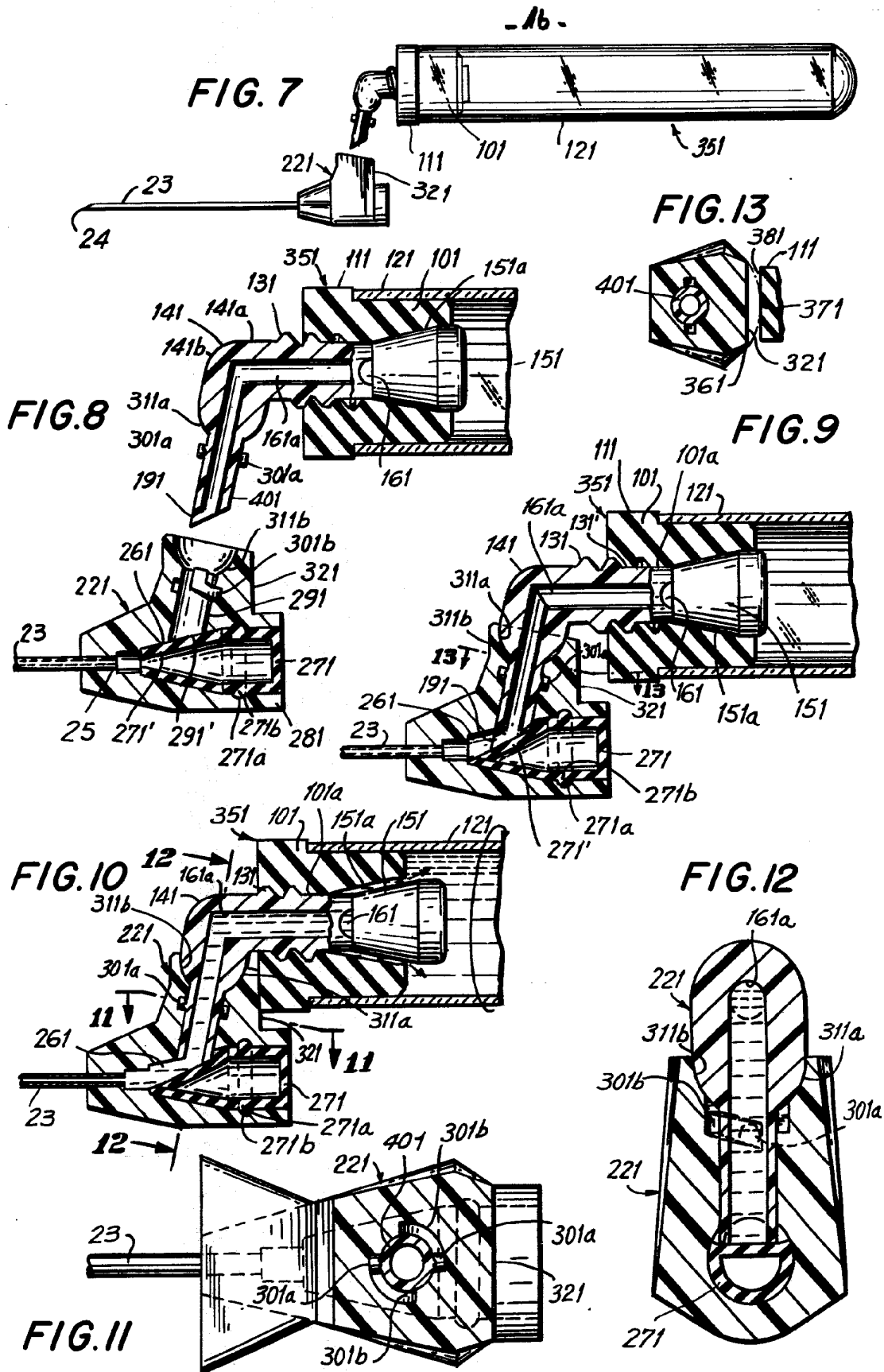
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von dort zur Kanüle 23, zu deren Spitze 24 und schließlich in das Blutgefäß des Patienten, vorausgesetzt, daß der als Aufnahme 291 dienende Durchgang abgedichtet bleibt. An den am Ort bleibenden Halterteil 221 kann ein neuer Behälterteil angesetzt werden, um mehr Blut abzusaugen, oder es kann auch die Kanüle 23 aus dem Blutgefäß herausgezogen und dann weggeworfen werden. Der gefüllte Behälterteil wird an ein entsprechendes biochemisches Labor geschickt, wo das Ventil der seitlichen Öffnung 161 zuerst geöffnet wird, worauf der Stöpsel 101 ohne weiteres entfernt, die Untersuchungen vorgenommen und die ganze Einheit dann vernichtet werden kann.

Da die Aufnahme 291 jedesmal versperrt wird, wenn ein Behälter weggenommen wird, kann Blut weder weiter aus dem Kanal 261 aussickern, noch wird es in das Blutgefäß zurückgesaugt.

Die der Erfindung gestellte Aufgabe ist somit erfüllt. Gegenüber den beschriebenen Ausführungsbeispielen sind Abänderungen möglich.







Espacenet

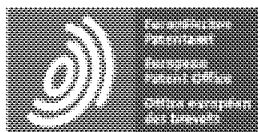
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DEVICE AND METHOD FOR PREPARING BLOOD

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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 as 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]

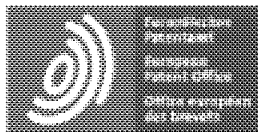
624 In a method according to the invention for blood preparation, the following single-chamber centrifugation can be provided in deviation from the centrifugation of the entire preparation

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.



①⑨ **BUNDESREPUBLIK
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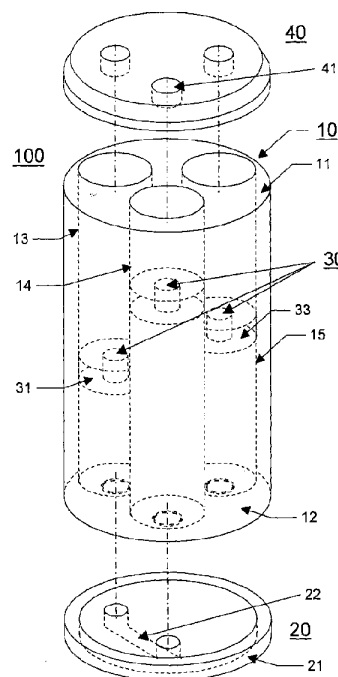
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WO 00 38 762

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

[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 Kryoadditivs 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 Zentrifu-

gationstechniken 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 Präparationschritte 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 Präparationschritte nicht die Präparationsvorrichtung. Eine Verwechslung z. B. von Blut verschiedener Spender oder eine Kontamination durch Fremdblut oder Mikroorganismen sind ausgeschlossen. Die Identität des Spenderblutes ist garantiert. Der Präparationsvorgang wird stark beschleunigt, da Arbeitsschritte, die bei herkömmlichen Systemen ggf. mehrfach notwendig sind, erfindungsgemäß vollständig entfallen können. Ein teilweiser oder vollständiger Probenverlust oder eine Kontamination der Arbeitsumgebung einschließlich des Laborpersonals durch undichte Schlauchverbindungen werden bei der erfindungsgemäßen Präparationsvorrichtung ausgeschlossen.

[0019] Die erfindungsgemäße Präparationsvorrichtung bildet ein festes Behältnis, das im Vergleich mit herkömmlich verwendeten Blutbeuteln ein definiertes und reproduzierbares Greifen und Handhaben der Vorrichtung und der an dieser angebrachten Ventile und/oder Stutzen ermöglicht. Das Greifen oder Positionieren und Klemmen von Verbindungsschläuchen entfällt, wenn die mindestens eine Verbindungsleitung in die Präparationsvorrichtung integriert ist und somit ein reproduzierbares und mehrfaches Verbinden der einzelnen Kammern auf kürzestem Weg ermöglicht. Durch die kurzen Wege und die Wahl eines geeigneten Querschnittes der jeweiligen Verbindungsleitung lässt sich die Transferzeit zur Übertragung von Proben zwischen den Kammern optimieren. Der Aufbau der Vorrichtung ermöglicht ein definiertes Positionieren der mindestens einen Verbindungsleitung. Ein versehentliches Verbinden von aktuell nicht kooperierenden Kammern wird ausgeschlossen. Ein Deformieren oder Quetschen der Kammern wird erfindungsgemäß vermieden. Eine z. B. durch Zentrifugation eingestellte Phasentrennung von Probenbestandteilen kann durch einen Greifvorgang nicht verwischt werden.

[0020] Die feste und vorzugsweise symmetrische Anordnung der Kammern in einer erfindungsgemäßen Präparationsvorrichtung ermöglicht ein schnelles und definiertes Positionieren der jeweils interessierenden Kammer in einem Präparationssystem unabhängig vom Verfahrensschritt. Alle Sensoren und Aktoren sind automatisch korrekt positioniert. Es wird ein erhöhter, fehlerfreier Durchsatz erzielt. Beispielsweise lassen sich mit einer erfindungsgemäß Präparationsvorrichtung rund dreifach mehr Kryokonserven pro Zeiteinheit präparieren. Die Präparationsvorrichtung ermöglicht eine freie Materialwahl und Dimensionierung der Außenform der Kammeranordnung. Vorteilhafterweise kann die Vorrichtung ohne Weiteres mit herkömmlichen Zentrifugiereinrichtungen verwendet werden.

[0021] Durch die Herstellung der Präparationsvorrichtung aus kostengünstigen Kunststoffmaterialien können große Stückzahlen der Vorrichtung in Spritzgieß- oder Extrusionstechniken hergestellt werden. Dies ist für die erfindungsgemäße Verwendung der fest bewandeten Kammern als Einwegprodukte von Vorteil.

[0022] Insbesondere bei der Präparation von Blutproben ergeben sich zusätzlich die folgenden Vorteile. Für Blutspendedienste entsteht bei Einsatz der erfindungsgemäßen Präparationsvorrichtung kein wesentlicher Zusatzaufwand. Es werden keine Mehrfachbeutelsysteme erforderlich. Die Präparationsvorrichtung kann direkt mit einem einfachen

Spendebeutel (Einfachblutbeutel) gekoppelt werden. Der bei herkömmlichen Verfahren ggf. in den Abfall gelangende oder nur mit großem Aufwand gewinnbare Überstand (Plasma und "Buffy Coat") steht erfindungsgemäß bei Bedarf als zusätzliches Endprodukt zur Verfügung. Die Präparationsvorrichtung liefert auch Vorteile bei der nach der Präparation vorgesehenen Befüllung von Einfrierbeuteln. Ein befüllter Einfrierbeutel kann im angedockten Zustand an der Präparationsvorrichtung mit dieser einfach und steril entlüftet werden, in dem die jeweilige Kammer mit einem Unterdruck beaufschlagt wird.

[0023] Weitere Vorteile und Einzelheiten der Erfindung ergeben sich aus der folgenden Beschreibung der beigefügten Zeichnungen. Es zeigen:

[0024] Fig. 1 eine schematische Phantomansicht einer Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung in teilweise auseinander gezogenem Zustand,

[0025] Fig. 2 eine Illustration der Einbindung der Präparationsvorrichtung gemäß Fig. 1 in eine Vorrichtung zur Herstellung von Blutkonserven,

[0026] Fig. 3 eine vergrößerte Teilansicht eines Kammerendes der Präparationsvorrichtung gemäß Fig. 1,

[0027] Fig. 4 Illustration einer abgewandelten Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung,

[0028] Fig. 5 eine schematische Schnittansicht einer erfindungsgemäß verwendeten Einzelkammer, und

[0029] Fig. 6 eine Illustration einer herkömmlichen Präparationstechnik (Stand der Technik).

[0030] In Fig. 1 ist eine Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung 100 in schematischer Phantomansicht dargestellt. Die Präparationsvorrichtung 100 umfasst einen Kammerkörper 10, in dem drei Kammern zur Aufnahme von Suspensionsproben gebildet sind, eine Übertragungseinrichtung 20, bestehend aus einer Ventilplatte 21 und mindestens einer Verbindungsleitung 22, eine Stempelinrichtung 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 Kammerkörpers 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 Ventilplatte 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 Ventalfunktion, 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 erzwingenden Vorgabe einer bestimmten Drehrichtung und/oder einer Wiederhol Sperre 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 Beschickung 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 Stempelinrichtung 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 Durchlaufen 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 zentrale 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 Durchtrittsöffnungen 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-Kryokonserven 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, Widerstandsmessgerät 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 Kryokonserven einfriefertig. Es folgt die Übertragung in den anwendungsabhängig gewählten Behälter, z. B. einen Kryobbeutel, 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 vorher-

gehenden 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 Zentrifugation 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-Kryokonserven hergestellt wird.

Hierzu 5 Seite(n) Zeichnungen

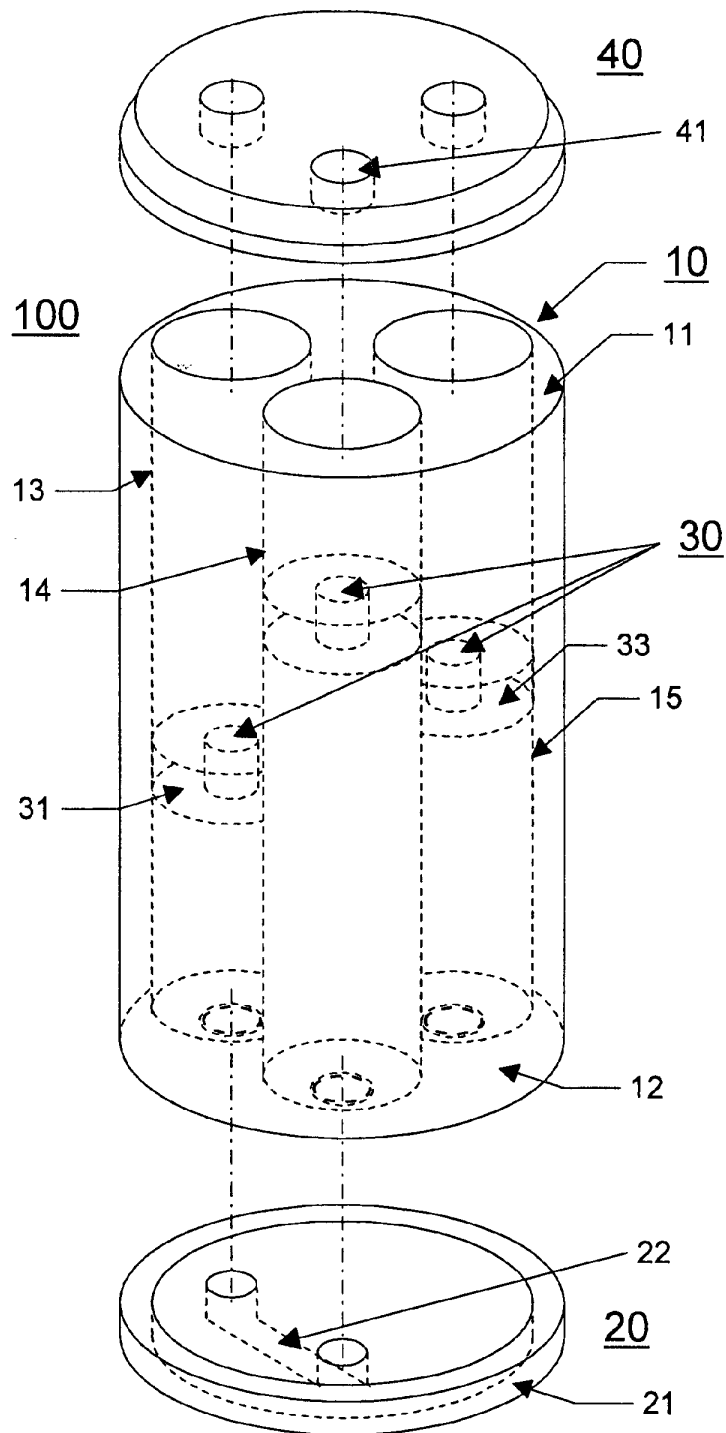


Fig. 1

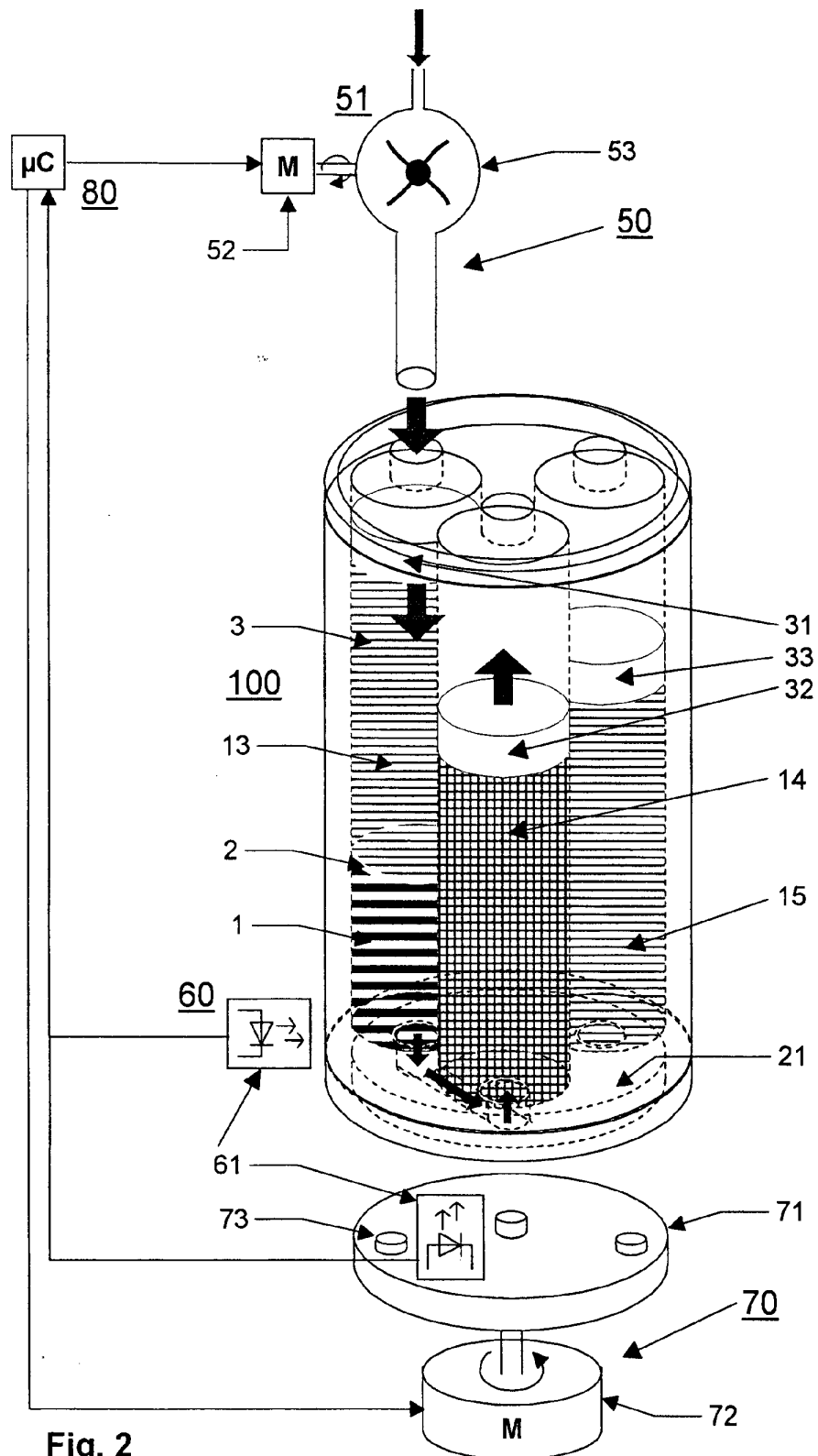


Fig. 2

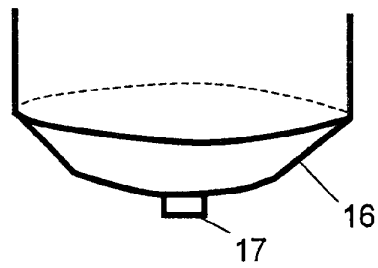


Fig. 3

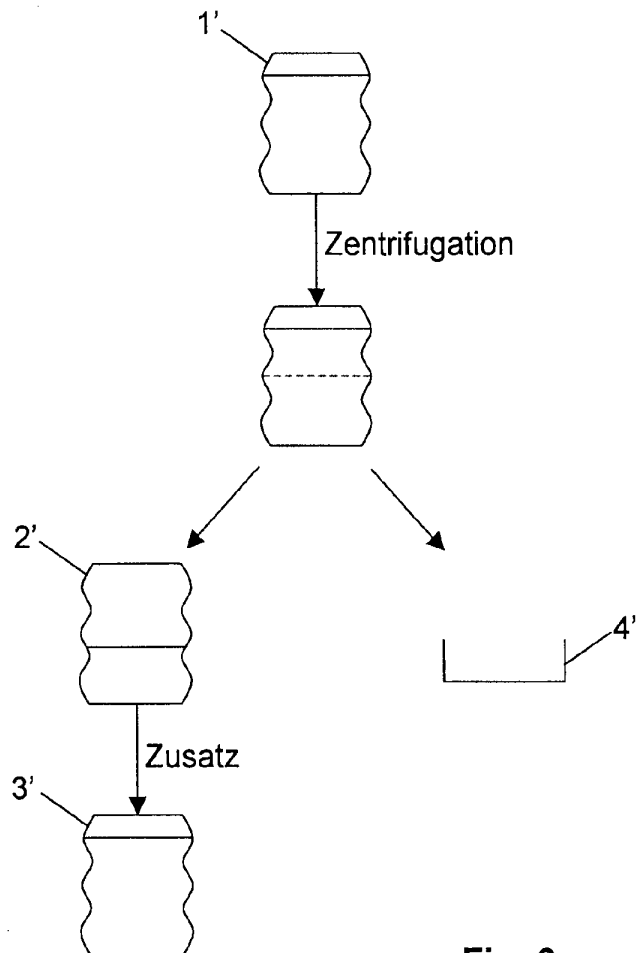


Fig. 6
(Stand der Technik)

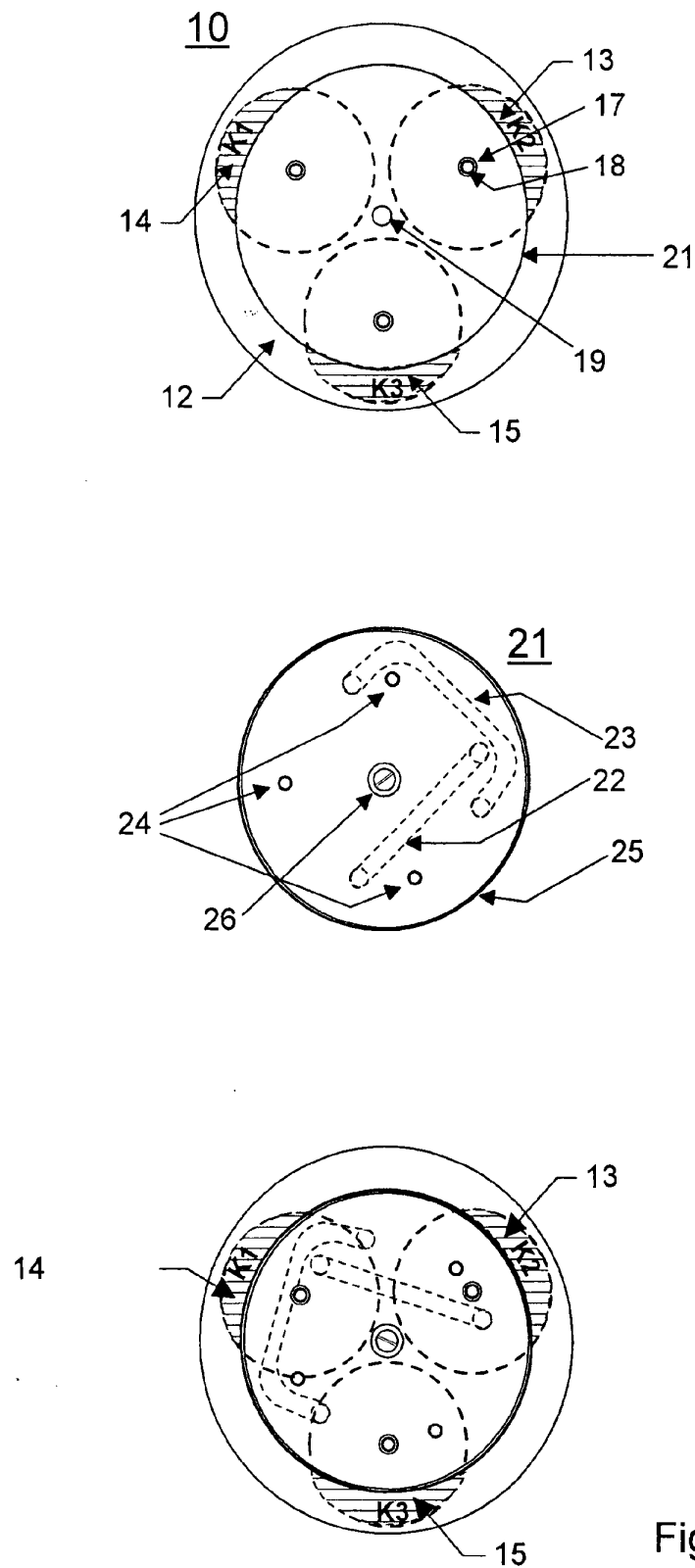


Fig. 4

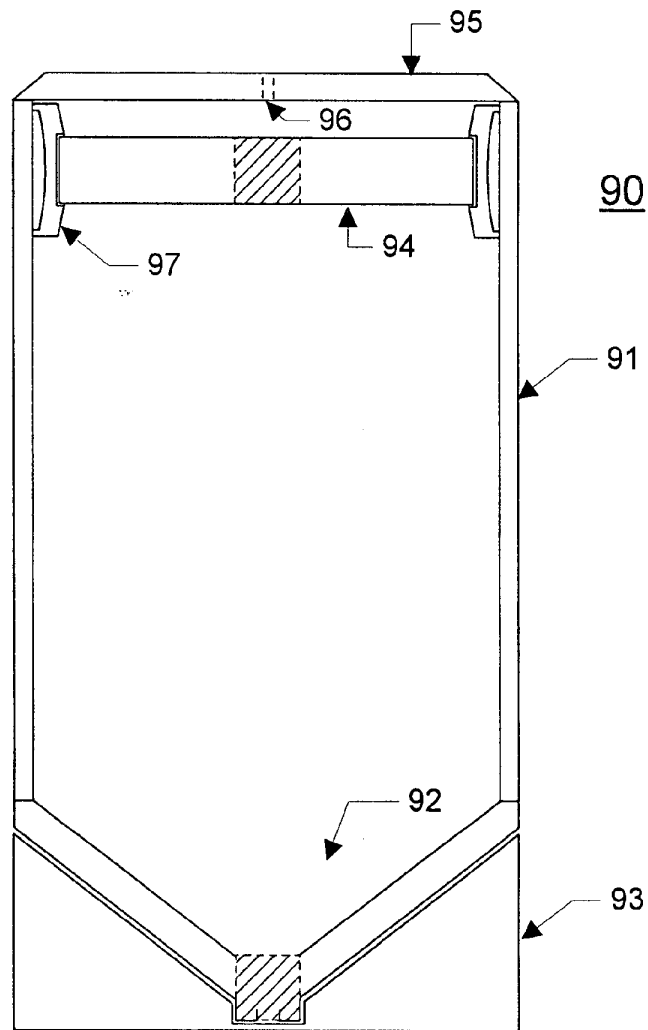


Fig. 5

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 (<i>day/month/year</i>) 15 June 2015 (15.06.2015)	(Earliest) Priority Date (<i>day/month/year</i>) 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 43.6bis(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	WO 2013/082301 A1 (TELEFLEX MEDICAL, INC.) 06.06.2013 claims, [0006]-[0008], [0037], [0041], [0044]-[0054], fig. 1-5	1-9
Y		10-13, 15-16, 18-19
Y	JP 2009131273 A (CSL BEHRING GMBH) 18.06.2009 abstract	10-13
X	EP 2593169 A1 (BECTON DICKINSON CO) 22.05.2013 abstract, [0006]-[0013]	14, 17
Y		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

19 October 2015 (19.10.2015)

Date of mailing of the international search report

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

PATENT COOPERATION TREATY

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

From the INTERNATIONAL SEARCHING AUTHORITY

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.
PCT/US 2015/035870

International filing date (*day/month/year*)
15 June 2015 (15.06.2015)

Priority date (*day/month/year*)
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:

- ☒ 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 43bis.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 66.1bis(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:
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

Date of completion of this opinion
19 October 2015 (19.10.2015)

Authorized officer
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:
☒ 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 43bis.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 13ter.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 13ter.1(a)).
☐ on paper or in the form of an image file (Rule 13ter.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 43bis.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 in D1 ([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.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference KURIN4PCT		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US 20/23617	International filing date (day/month/year) 19 March 2020 (19.03.2020)	(Earliest) Priority Date (day/month/year) 13 March 2020 (13.03.2020)	
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 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 43.6bis(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. 35
☐ 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 20/23617

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61B 5/15, A61B 5/153, A61B 5/154, A61B 5/157 (2020.01)

CPC - A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946

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	US 2018/0177445 A1 (Kurin, Inc.) 28 June 2018 (28.06.2018), entire document	1-4, 10-12, 18
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Y		5-9, 13-17, 19-20
Y	US 4,349,035 A (Thomas et al.) 14 September 1982 (14.09.1982), entire document	5-6, 8-9, 13-14, 16-17, 19-20
Y	US 5,401,262 A (Karwoski et al.) 28 March 1995 (28.03.1995), entire document	5, 7, 13, 15
A	US 2018/0271425 A1 (Kurin, Inc.) 27 September 2018 (27.09.2018), entire document	1-20
A	US 2018/0353117 A1 (Magnolia Medical Technologies, Inc.) 13 December 2018 (13.12.2018), entire document	1-20

☐ 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

"D" document cited by the applicant in the international application

"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

07 JUNE 2020

Date of mailing of the international search report

19 JUN 2020

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 Young

Telephone No. PCT Helpdesk: 571-272-4300

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: JAMES SCOTT NOLAN
P.O. BOX 371710
SAN DIEGO, CA 92110

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

19 JUN 2020

Applicant's or agent's file reference

KURIN4PCT

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US 20/23617

International filing date (day/month/year)

19 March 2020 (19.03.2020)

Priority date (day/month/year)

13 March 2020 (13.03.2020)

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

IPC - A61B 5/15, A61B 5/153, A61B 5/154, A61B 5/157 (2020.01)

CPC - A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946

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 43bis.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 66.1bis(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/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Date of completion of this opinion

07 JUNE 2020

Authorized officer

Lee Young

PCT Help Desk

Telephone No. 571-272-4300

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/23617

Box No. 1 Basis of this 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 43bis.1(b)).

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 13ter.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 13ter.1(a)).
☐ on paper or in the form of an image file (Rule 13ter.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:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/23617

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement			
1. Statement				
Novelty (N)	Claims	5-9, 13-20		YES
	Claims	1-4, 10-12		NO
Inventive step (IS)	Claims	none		YES
	Claims	1-20		NO
Industrial applicability (IA)	Claims	1-20		YES
	Claims	none		NO
2. Citations and explanations:				
Claims 1-4 and 10-12 lack novelty under PCT Article 33(2) as being anticipated by US 2018/0177445 A1 to Kurin, Inc. (hereinafter Kurin).				
<p>Regarding claim 1, Kurin teaches a blood sequestration device (see fig. 30A-G; para [0156]) comprising; an inlet path (fig. 30A see inlet path 3002; para [0156]); an outlet path (fig. 30A see outlet path 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first portion of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A-D see vent 3010; para [0161]; para [0163]-[0165]), the junction being configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, it is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see para[0156], [0160]-[0161], [0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first amount of blood is received by the sequestration chamber (para [0160]-[0170]).</p> <p>Regarding claim 2, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction is angled from the inlet path toward the sequestration chamber (fig. 30A; fig. 17A see junction 3007 is angled from the inlet path to the sequestration chamber; para [0160]) .</p> <p>Regarding claim 3, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction has a cross-sectional area that is smaller than a cross-sectional area of the inlet path (fig. 30A; fig. 17A see junction 3007 has a cross-sectional area closest to the inlet path that is smaller than a cross-sectional area of the inlet path below where it meets the junction; para [0160]).</p> <p>Regarding claim 4, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction has a cross-sectional area that is larger than a cross-sectional area of the inlet path (fig. 30A; fig. 17A see junction 3007 has a cross-sectional area near the sequestration chamber 3008 that is larger than a cross-sectional area of the inlet path where the inlet path opens to the junction; para [0160]; para [0163] junction cross-sectional area widens towards the sequestration chamber to direct blood).</p> <p>Regarding claim 10, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the vent includes two or more vent apertures (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060] air permeable blood barrier may comprise a mesh, a mesh inherently comprises two or more vent apertures).</p> <p>Regarding claim 11, Kurin teaches a blood sequestration device (see fig. 30A-G; para [0156]) comprising; a housing (fig. 30A see housing 3001; para [0161]) having an inlet port (fig. 30A see inlet path 3002 has port opening in housing 3001; para [0156]; para [0161]) and an outlet port (fig. 30A see outlet path 3004 has outlet opening in housing 3001; para [0159]; para [0161]), the housing containing; an inlet path connected to the inlet port (fig. 30A see inlet path 3002; para [0156]); an outlet path connected with the outlet port (fig. 30A see outlet path 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first amount of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A see vent 3010; para [0161]; para [0163]-[0165]), the vent further being further configured to close upon the sequestration chamber being filled with the first portion of blood (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060]; para [0160]-[0170]), the junction being configured to inhibit a return of the first portion of blood out of the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, it is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see also para[0156],[0160]-[0161],[0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first portion of blood is received by the sequestration chamber (para [0160]-[0170]).</p>				
-Continued in Supplemental Box--				

Form PCT/ISA/237 (Box No. V) (revised January 2019)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 20/23617

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:

Regarding claim 18, the claim language is confusing and lacks clarity. Specifically, the recitation "the patient needle and the sample needle", lack proper antecedent basis. In order to give meaning to this claim and to give proper antecedent basis, based on the specification (para [0063]), this recitation has been interpreted as the following: "and a blood sequestration device connected along the blood sampling pathway between a patient needle and a sample needle, wherein the venipuncture apparatus includes the patient needle and the reservoir includes the sample needle".

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

-Box V.2 - Citations and Explanations-

Regarding claim 12, Kurin teaches the blood sequestration device in accordance with claim 11, wherein the vent further comprises a closure mechanism that inhibits air from reentering the sequestration chamber after it has been displaced (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060]).

Claim 18 lacks an inventive step under PCT Article 33(3) as being obvious over Kurin.

Regarding claim 18, Kurin teaches a blood sample optimization system (fig. 30A-G; para [0156]) comprising: a blood sampling system (para [0156]) comprising: a venipuncture apparatus configured for venipuncture of a patient to access a sample of blood of a patient (para [0156] inlet port 3002 with opening connects to patient needle, needle is a suitable venipuncture apparatus); a blood sampling pathway connected with the venipuncture apparatus for conveying the sample of blood (fig. 30A see system 3000 comprises blood sampling pathway from inlet 3002 to outlet 3004 through sampling channel 3006; para [0156]); and a reservoir (fig. 30A see reservoir 3004; para [0158]); and a blood sequestration device connected along the blood sampling pathway between a patient needle and the reservoir (see fig. 30A-G; para [0156]), wherein the venipuncture apparatus includes the patient needle (para [0156] inlet port 3002 with opening connects to patient needle), the blood sequestration device comprising: an inlet path connected with the patient needle (fig. 30A see inlet path 3002; para [0156]); an outlet path connected with the reservoir (fig. 30A see outlet path through outlet reservoir 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first portion of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A see vent 3010; para [0161]; para [0163]-[0165]), the junction being configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, is is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see para[0156], [0160]-[0161], [0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first amount of blood is received by the sequestration chamber (para [0160]-[0170]); but Kurin does not explicitly teach wherein the reservoir is configured for receiving an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood, nor wherein reservoir and connected outlet path comprise a sample needle. However, in another embodiment, Kurin teaches a sample needle at an outlet path of a blood sample collection device facilitates connection to an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood (fig. 1 see sample needle 5; para [0065]; see fig. 7). Combining embodiments is within the ordinary skill of a person within the art. Accordingly, it would have been obvious to a person having ordinary skill in the art to have provided a sample needle such that the reservoir is configured for receiving an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood in order to provide blood collection means with the blood sampling device.

Claims 5-6, 8-9, 13-14, 16-17 and 19-20 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 4,349,035 A to Thomas et al. (hereinafter Thomas).

Regarding claim 5, Kurin teaches the blood sequestration device in accordance with claim 1, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, in 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, in 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, in 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, in 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 6, Kurin in view of Thomas teaches the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a conical baffle having a tapered end directed toward the sequestration chamber (see Thomas fig. 4-5 passive structure tapers to a point towards chamber, thus restricting flow; see column 5, in 13-17).

Regarding claim 8, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a divider wall extending across a cross-section of the junction (see Thomas fig. 4-5 divider wall 25; column 6, in 7-13).

-Continued in next Supplemental Box-

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

-*-Supplemental Box - Box V.2 - Citations and Explanations.-*-

Regarding claim 9, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a flow director extending from an inner surface of the junction (see Thomas fig. 4-5 valve 22 is a flow director; column 4, In 23-38; column 5, In 13-17), the flow director being configured to control a flow of blood (see Thomas column 4, In 23-28 flow director valve 22 controls flow by directing into chamber 21 and preventing backflow).

Regarding claim 13, Kurin teaches the blood sequestration device in accordance with claim 11, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, In 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, In 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, In 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, In 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 14, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a conical baffle having a tapered end directed toward the sequestration chamber (see Thomas fig. 4-5 passive structure tapers to a point towards chamber, thus restricting flow; see column 5, In 13-17).

Regarding claim 16 Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a divider wall extending across a cross-section of the junction. (see Thomas fig. 4-5 divider wall 25; column 6, In 7-13).

Regarding claim 17 Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a flow director extending from an inner surface of the junction (see Thomas fig. 4-5 valve 22 is a flow director; column 4, In 23-38; column 5, In 13-17), the flow director being configured to control a flow of blood (see Thomas column 4, In 23-28 flow director valve 22 controls flow by directing into chamber 21 and preventing backflow).

Regarding claim 19, Kurin teaches the blood sample optimization system in accordance with claim 18, but does not explicitly teach wherein the junction of the blood sequestration device includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, In 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, In 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, In 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, In 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 20, Kurin in view of Thomas teach the blood sample optimization system in accordance with claim 19, and Kurin modified by Thomas further teaches wherein the one or more passive structures includes a wall extending from an inner surface of the junction to control a flow of the first portion of blood (see Thomas fig. 4-5 divider wall 25; column 6, In 7-13).

-*-Continued in next Supplemental Box.-*-

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

-*-Supplemental Box - Box V.2 - Citations and Explanations-*

Claim 5, 7 and 13, 15 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 5,401,262 A to Karwoski et al. (hereinafter Karwoski).

Regarding claim 5, Kurin teaches the blood sequestration device in accordance with claim 1, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Karwoski teaches a blood collection device (see fig. 1; column 4, In 20-40). Karwoski further teaches wherein a pathway of the blood collection devices includes one or more passive structures configured to inhibit a return to an inlet path of any of a sample of blood (fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structures as taught by Karwoski in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 7, Kurin in view of Karwoski teach the blood sequestration device in accordance with claim 5, and Kurin modified by Karwoski further teaches wherein the one or more passive structures include two or more staggered baffles extending from an inner surface of the junction (Karwoski fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65).

Regarding claim 13, Kurin teaches the blood sequestration device in accordance with claim 11, wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Karwoski teaches a blood collection device (see fig. 1; column 4, In 20-40). Karwoski further teaches wherein a pathway of the blood collection devices includes one or more passive structures configured to inhibit a return to an inlet path of any of a sample of blood (fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structures as taught by Karwoski in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 15, Kurin in view of Karwoski teach the blood sequestration device in accordance with claim 13, and Kurin modified by Karwoski further teaches wherein the one or more passive structures include two or more staggered baffles extending from an inner surface of the junction (Karwoski fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65).

Claims 1-20 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used by industry.

SEARCH HISTORY

Application Number	PCT/US 20/23617
Search Conducted By	EAW
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CPC/IPC Classifications Searched	IPC(8): A61B 5/15, A61B 5/153, A61B 5/154, A61B5/157 (2020.01) CPC: A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946
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Documentation Searched	IPC(8): A61B 5/15, A61B 5/153, A61B 5/154, A61B5/157 (2020.01) CPC: (keyword limited; see below)
Search Terms Used	baffle*, prevent*, inhibit*, back*, return*, sequestration*, flow*, blood*, sample*, restrict*
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Electronic Database Searched	PatBase
Files Searched	Full-text: AU BE BR CA CH CN DE DK EP ES FI FR GB IN JP KR SE TH TW US WO Bibliographic: (European) AT BA BE BG CH CS CY CZ DD DK EE ES FI GE GR HR HU IE IS IT LT LU LV MC MD MT NL NO PL PT RO RS SE SI SK SM TR UA YU (Asia) EA GC HK ID IL IN KZ MN MY PH RU SG SU TH TJ TW UZ VN (North America) CA CR CU DO GT HN MX NI PA SV TT (South America) AR BR CL CO EC PE UY (Australasia) AU NZ (Africa) AP DZ EG KE MA MW OA ZA ZM ZW
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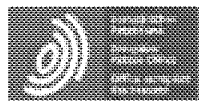
Search Logic:

Search 1: PA=(Kurin inc) (Results 5)
 Search 2: PN=(US2018/0177445) (Results 1)
 Search 3: ctb 2 or ctf 2 (Results 5)
 Search 4: CPC=(A61B5/15003) (Results 2650)
 Search 5: 4 and ft=(baffle%) (Results 36)
 Search 6: 4 and ft=((prevent* or inhibit*) near (back* or return*)) (Results 226)
 Search 7: 6 and ft=(sequestration) (Results 3)
 Search 8: 6 and ft=(flow*) (Results 182)
 Search 9: IPC=(A61B5/15 or A61B5/153 or A61B5/154 or A61B5/157) (Results 13750)
 Search 10: CPC=(A61B5/15003 or A61B5/150213 or A61B5/150251 or A61B5/150992 or A61B5/150206 or A61B5/150221 or A61B5/150946) (Results 3410)
 Search 11: 9 or 10 (Results 14204)
 Search 12: 11 and ft=(sequestration) (Results 32)
 Search 13: 11 and ft=((prevent* or inhibit*) near (back* or return*)) (Results 535)
 Search 14: 13 and ft=(blood* near sample*) (Results 335)
 Search 15: 14 not 8 (Results 198)
 Search 16: ft=(sequestration* and baffle* and blood*) (Results 170)
 Search 17: 16 not (14 or 8) (Results 170)
 Search 18: ft=(blood* and sequestration* and (restrict* near flow*)) (Results 176)

Electronic Database Searched	Google
Files Searched	Patents
Date Conducted	7 June 2020 (07.06.2020)
<p style="text-align: center;">Search Logic:</p> <p>blood sampling sequestration device prevent backflow</p> <p>blood sampling sequestration device baffle directs flow</p> <p>blood sampling collection device prevent backflow</p> <p>blood sampling device valve restricts backflow controls flow</p>	

blood sequestration junction prevents backflow
blood sequestration junction flow restriction

Electronic Database Searched	Google
Files Searched	Web
Date Conducted	7 June 2020 (07.06.2020)
<p>Search Logic:</p> <p>blood sampling sequestration device prevent backflow</p> <p>blood sampling sequestration device baffle directs flow</p> <p>blood sampling collection device prevent backflow</p> <p>blood sampling device valve restricts backflow controls flow</p> <p>blood sequestration junction prevents backflow</p> <p>blood sequestration junction flow restriction</p>	



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CLOSED BLOOD SAMPLING SYSTEM WITH ISOLATED PRESSURE MONITORING

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A closed blood sampling system within a pressure monitoring line having a control valve that enables a clearance reservoir to be isolated from the pressure column when no samples are being taken. The valve is a stopcock-like device that includes a rotating valve member and attached control handle with clear visible and tactile indicators for the mode of operation. The rotating valve member has a number of internal and circumferential channels for connecting or disconnecting select ports in the core of the valve. By isolating the clearance reservoir, the quality of the pressure signal is improved such that the sampling line can be lengthened for greater convenience in the intensive care or operating room. The valve may also incorporate a blunt cannula sampling site therewithin.

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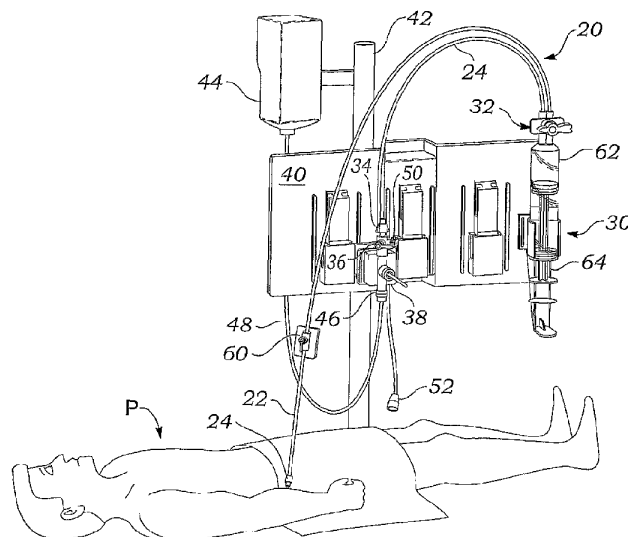
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(54) Title: CLOSED BLOOD SAMPLING SYSTEM WITH ISOLATED PRESSURE MONITORING



(57) Abstract: A closed blood sampling system within a pressure monitoring line having a control valve that enables a clearance reservoir to be isolated from the pressure column when no samples are being taken. The valve is a stopcock-like device that includes a rotating valve member and attached control handle with clear visible and tactile indicators for the mode of operation. The rotating valve member has a number of internal and circumferential channels for connecting or disconnecting select ports in the core of the valve. By isolating the clearance reservoir, the quality of the pressure signal is improved such that the sampling line can be lengthened for greater convenience in the intensive care or operating room. The valve may also incorporate a blunt cannula sampling site therewithin.

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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

CLOSED BLOOD SAMPLING SYSTEM WITH ISOLATED PRESSURE MONITORING

Field of the Invention

5 **[0001]** The present invention relates to blood sampling systems and, in particular, to closed blood sampling systems with a clearing reservoir and pressure monitoring.

Background of the Invention

10 **[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. Patients that are in the critical care units or the operating room sometimes require as many as twelve samples a day. Such frequent
15 sampling injections potentially expose 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,
20 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 preclude flow from
25 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 proximal 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.

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[0004] Most early systems required a two-step operation where a first sample of fluid, generally about 5ml 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] In response to the drawbacks associated with earlier two-step sampling systems, closed systems were developed as described in U.S. Patent No. 4,673,386 to Gordon, and more recently in U.S. Patent No. 5,961,472 to Swendson, which are expressly incorporated by reference herein. 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 reservoir in the tubing line from the patient that can draw fluid past a sampling port. The clearing volume is held in the in-line reservoir, and not set-aside in a syringe for re-infusion later. The sampling systems are often used in conjunction with a pressure monitor having a transducer continually or periodically sensing pressure within the sampling line except during the draw of a blood sample.

[0006] The VAMP Plus® system conveniently utilizes a reservoir with one-handed operability, and includes a line from the patient into and out of the reservoir and 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). A stopcock valve at the reservoir controls the mode of operation. Prior to drawing a blood sample, the reservoir plunger is latched closed, though a reservoir gap allows a continuous drip of IV flushing fluid through an inlet port to an outlet port. A pressure transducer in the line proximal to the reservoir senses fluid pressure within the line and conveys the signal to a monitor. One exemplary pressure transducer used with both the VAMP® and

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VAMP Plus® systems is the Edwards TruWave® Disposable Pressure Transducer.

[0007] When a blood sample is to be taken, the flow of flushing or infusion fluid is halted by turning the handle of the reservoir stopcock valve.

5 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 fluid sampling sites. After full retraction of the plunger, the stopcock valve closes off the reservoir from the patient and a sample of blood is taken at one or the other sampling sites. Subsequently, the clinician manipulates the stopcock
10 valve so that the volume within the reservoir can be reinfused back into the patient by depressing the plunger, and the flushing drip and pressure monitoring resumes.

[0008] In the closed blood sampling/pressure monitoring systems described above, the pressure transducer typically includes a diaphragm
15 exposed to the in-line fluid on one side and has a device for measuring deflection of the diaphragm on the other. Such pressure lines typically make use of relatively stiff tubing primed with a suitable physiological fluid such as saline or 5% dextrose solution as a pressure column. For adults, a bag pressurized with air surrounds the fluid supply bag to maintain a constant
20 pressure differential in the line urging fluid toward the patient through a restrictor orifice. The slow drip of physiological fluid flushes the line to prevent clotting. Some transducers such as the TruWave® Disposable Pressure Transducer include a flush device that also can be used for sending transient pressure waves through the line. A Snap-Tab™ device of the
25 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, such as the sampling ports and reservoir. Proper system frequency response is necessary for reliable blood pressure measurements. In general, a
30 more accurate signal may be obtained with a shorter sampling line and fewer

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components so that the transducer is closer to the patient and there is less delay between the generation and receipt of the blood pressure signal, and less interference. However the limited amount of space available or the location of the anesthesiologist during a surgical procedure often necessitates a relatively long tubing line which degrades the signal. Furthermore, minimum functionality of the system requires various components such as sampling sites be included.

[0009] In view of the foregoing, there is a need for a blood sampling system used in conjunction with a pressure transducer that produces more accurate pressure readings.

Summary of the Invention

[0010] The present invention provides a fluid sampling system within a pressure monitoring line having a control valve that enables a clearance reservoir to be isolated from the pressure column when no samples are being taken. The control valve further permits complete flushing of the system with no dead spaces. Additionally, control valve desirably incorporates a sampling port therein capable of isolating the sampling port from the clearance reservoir. By isolating the clearance reservoir, the quality of the pressure signal is improved such that the sampling line can be lengthened for greater convenience in the intensive care or operating room.

[0011] In accordance with a first embodiment of the invention, a medical system for fluid sampling and pressure monitoring of a fluid system of a patient is provided. The system includes a conduit line with a proximal segment adapted to be supplied with a physiological fluid (e.g., saline) and a distal segment adapted to be in communication with a fluid system of a patient. A control valve has a manifold defining an interior chamber. The manifold has a proximal port fluidly connected to the proximal segment, a distal port fluidly connected to the distal segment, and a reservoir port,

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wherein each of the manifold ports opens to the interior chamber. A system further includes a fluid sampling port and pressure transducer connected to the conduit line for sensing the pressure of the fluid therein. A reservoir fluidly communicates with the reservoir port of the control valve manifold. The control valve further includes a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports. The valve member is movable into at least two positions:

a first position that provides open fluid communication from the proximal segment to the patient through the control valve so as to eliminate any dead spaces therein, wherein reduced pressure within the reservoir pulls fluid from the distal segment through the control valve and into the reservoir sufficient to draw fluid from the fluid system of the patient past the sampling port, and

a second position that provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member to the distal segment while bypassing the reservoir, such that the pressure of fluid within the conduit line exclusive of the reservoir can be sensed by the pressure transducer.

[0012] Desirably, the valve member also has a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

[0013] In a preferred embodiment the valve member comprises a core rotatable within the interior chamber of the manifold and a control handle external to the manifold, wherein mating features on the valve member core and manifold provide tactile feedback and positive positioning of the core in both first and second positions. Alternatively, or in addition, coordinated visible features on the control handle and manifold provide symbolic indicators of both first and second positions of the valve member.

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[0014] The sampling port may be formed within the control valve or along the distal segment of the conduit line. If within the control valve, the sampling port may be formed within the valve member and communicates with a sampling cavity formed internally within the valve member open to at least one of the channels. Alternatively, the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the interior chamber of the manifold. Furthermore, the system may include a second sampling port having a sampling cavity positioned along the distal segment of the conduit line.

10 [0015] In accordance with one embodiment, the valve member comprises a core movable within the interior chamber of the manifold and a control handle external to the manifold, the core having an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core. The internal channel desirably opens to the exterior surface of the core at two separated locations spaced from the external channel.

[0016] System further may include means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position. Desirably, the reservoir has an inlet open to an outlet port of the control valve manifold and an outlet open to an inlet port of the control valve manifold. In this embodiment, the first position of the valve member provides open fluid communication between the control valve flow passages through the inlet and outlet of the reservoir to flush a chamber of the reservoir.

25 [0017] A second embodiment of the present invention comprises a medical system for fluid sampling of a fluid system of a patient. The system encompasses 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 control valve connects between the proximal segment and the distal segment of the conduit line. A

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fluid sampling port defines a flow path therethrough whose opposite ends open to internal channels in the control valve. A reservoir fluidly communicates with a reservoir port of the control valve manifold. The control valve further includes a valve member movable into at least three positions:

- 5 a first position that provides open fluid communication from the proximal segment through the control valve to the distal segment,
- a second position that provides open fluid communication from the proximal segment to the distal segment while bypassing the reservoir and sampling port, and
- 10 a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

[0018] Desirably, the control valve further includes a manifold
15 defining an interior chamber. The manifold has a proximal port fluidly connected to the proximal segment of the conduit line, a distal port fluidly connected to the distal segment, an outlet port, and an inlet port, wherein each of the manifold ports opens to the interior chamber. The valve member also comprises a core movable within the interior chamber of the manifold and
20 having channels therein that selectively communicate with the manifold ports. The reservoir has an inlet open to the manifold outlet port and an outlet open to the manifold inlet port. In this embodiment:

 the first position provides open fluid communication from the proximal segment to the proximal port and the outlet port of the control valve,
25 through the inlet and outlet of the reservoir, to the inlet port and the distal port of the control valve to the distal segment,

 the second position provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member core to the distal segment while bypassing the reservoir and
30 sampling port, and

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the third position provides open fluid communication from the distal segment to distal port and one of the channels of the valve member core, and to the sampling port.

- 5 **[0019]** The valve member core may have an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core. Desirably, the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.
- 10 **[0020]** Another aspect of the invention is a method of taking samples and measuring the pressure of a fluid system of a patient. The method provides a fluid sampling system with a conduit line and a reservoir connected thereto between a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with
15 a fluid system of a patient. A control valve interposed between the reservoir and the conduit line has a movable valve member with a control handle, the valve member movable into at least a first position and a second position. A pressure transducer connects to the conduit line for sensing the pressure of the fluid therein, and a fluid sampling port is provided in the sampling system.
- 20 **[0021]** The method includes selecting the first position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve and the reservoir, and creating a reduced pressure within the reservoir such that fluid flows from the distal segment through the control valve into the reservoir sufficient to draw fluid
25 from the fluid system of the patient past the sampling port. The method further includes selecting the second position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve while bypassing the reservoir, and monitoring the pressure sensed by the pressure transducer. Desirably, the valve member has a
30 third position, and the method includes selecting the third position of the valve

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member to provide open fluid communication from the distal segment to the sampling port but prevent communication between the sampling port and both the reservoir and the proximal segment, and sampling fluid from the conduit line through the sampling port.

- 5 **[0022]** In a preferred embodiment, the fluid system of the patient is the blood system, and the method further including means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position. In this instance, the method including the steps of:
- 10 selecting the first position of the valve member such that the physiological fluid flows through the conduit line to the patient; then
 creating a reduced pressure within reservoir and collecting sufficient fluid therein such that blood flows past the sampling port; then
 selecting the third position of the valve member; then
- 15 sampling blood from the conduit line through the sampling port; then
 creating an elevated pressure within the reservoir to expel blood therefrom into the distal segment of the conduit line; then
 selecting the first position of the valve member such that the
- 20 physiological fluid flows through the conduit line to the patient and flushes the reservoir of blood; and then
 selecting the second position of the valve member and monitoring the pressure sensed by the pressure transducer.
- 25 **[0023]** Preferably, the control valve has a manifold defining an interior chamber within which the valve member rotates, and further including mating features on the valve member and manifold that provide tactile feedback and positive positioning of the core in both first and second positions, the method of selecting the first and second positions further including rotating the valve
- 30 member until the tactile feedback is sensed. Or, the control valve includes

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visible features that provide symbolic indicators of the first and second positions of the control handle, the method of selecting the first and second positions further includes interpreting the symbolic indicators to determine the placement of the control handle corresponding to the first and second positions.

5 [0024] Another useful aspect of the present invention is a medical system for fluid sampling of a fluid system of a patient. The sampling system includes a conduit line with a proximal end adapted to be supplied with a physiological fluid and a distal end adapted to be in communication with a fluid system of a patient. A pressure transducer connects to the conduit line for sensing the pressure of the fluid therein, and a fluid sampling port is provided having a sampling cavity. A control valve interposes between the conduit line and the sampling port and has a manifold defining an interior chamber. The manifold further includes a proximal port fluidly connected to the conduit line, a distal port fluidly connected to the conduit line, an outlet port, and an inlet port, wherein each of the manifold ports opens to the interior chamber. The control valve also has a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports, the valve member being movable into at least three positions:

20 a first position that provides open fluid communication from the conduit line to the proximal port and the outlet port of the control valve to the sampling cavity, and to the inlet port and the distal port of the control valve to the conduit line,

25 a second position that provides open fluid communication from the conduit line to the proximal port and through at least one channel in the valve member and back to the conduit line while bypassing the sampling port, such that the pressure of fluid within the conduit line exclusive of the sampling port can be sensed by the pressure transducer, and

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a third position that provides open fluid communication from the distal end of the conduit line through the control valve to the sampling port but prevents communication between the sampling port and the proximal end of the conduit line.

5

[0025] 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.

10

Brief Description of the Drawings

[0026] 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:

15

[0027] Fig. 1 illustrates a typical hospital room setup of a fluid sampling system of the present invention incorporating a reservoir, the sampling port, and a pressure transducer within a conduit line to a patient;

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[0028] Figure 2 is a perspective view of a reservoir of the fluid sampling system in Figure 1 having an attached control valve of the present invention;

[0029] Figures 3A-3C are several orthogonal views of one end of the reservoir showing the control valve;

25

[0030] Figure 4 is a close-up perspective view of the control valve on the end of the reservoir having a central sampling port in a rotatable valve member;

[0031] Figure 5 is an exploded perspective view of the control valve;

[0032] Figures 6-11 are various external and sectional views of the rotatable valve member used in the control valve shown in Figures 4 and 5;

30

[0033] Figures 12-15 are various external and sectional views of a manifold of the control valve of Figures 4 and 5;

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[0034] Figures 16 and 17 are axial sectional views of the control valve of the present invention taken along lines 16-16 and 17-17, respectively, of Figure 4;

5 [0035] Figures 18A-18C are axial sectional views of the control valve taken along line 18-18 of Figure 4 showing the positions of interior fluid flow channels for different positions of the valve member;

[0036] Figures 19A-19C are views similar to Figures 18A-18C of the interior fluid flow channels for the three different positions of the control valve showing selective interconnections between the various manifold ports;

10 [0037] Figures 20A-20E are various external and sectional views of an alternative control valve of the present invention with a different arrangement of internal flow paths and a central sampling port;

[0038] Figures 21A-21E are various external and sectional views of an alternative control valve with a different arrangement of internal flow paths and a luer-style central sampling port;

15 [0039] Figures 22A-22E are various external and sectional views of an alternative control valve with a sampling port extending from the side of a manifold;

[0040] Figures 23A-23E are various external views of a luer-style valved sampling port;

20 [0041] Figure 24 is an axial sectional view of the valved sampling port of Figures 23A-23E; and

[0042] Figures 25A-25E are various external and sectional views of a further alternative valved sampling port with the sampling port extending from the side of a manifold.

Detailed Description of the Preferred Embodiments

[0043] The present invention provides an improved closed blood sampling system in conjunction with pressure monitor. As mentioned above, continuous or periodic blood pressure monitoring is a common and extremely

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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.

[0044] The present invention comprises an improved, closed, one-handed fluid sampling system especially useful for sampling blood in the operating room or critical care unit (CCU). The overall functioning of the system is similar to those in the prior art, in particular the VAMP Plus® Venous Arterial blood Management Protection system available from Edwards Lifesciences of Irvine, CA. Furthermore, the blood sampling function is desirably combined with a pressure transducer and monitoring hardware. The term “closed fluid sampling system” should be understood to include both systems that have a dedicated reservoir (i.e., one that remains connected) and that utilize a removable reservoir (or syringe) that gains access to the fluid column through a port. As explained above, dedicated reservoirs are preferred because of their enhanced sterility, but the feature of the present invention that isolates the reservoir from the fluid pressure column may also be useful with removable reservoirs.

[0045] Figure 1 illustrates an exemplary blood sampling system 20 of the present invention in the environment of a typical set up in a hospital room and connected to a patient P. The blood sampling system 20 comprises a conduit line having a distal segment 22 toward the patient and a proximal segment 24. The conduit line is primarily medical grade pressure tubing. The distal segment 22 may terminate in a male luer connector 26 for attaching to a female luer connector (not shown) of an injection site, or other conduit leading to the patient. A reservoir 30 connects to the conduit line via a control valve

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32 interposed between the distal segment 22 proximal segment 24. The control valve 32 externally resembles a stopcock and controls fluid flow between the conduit line and the reservoir 30.

[0046] The proximal segment 24 extends from the control valve 32 and terminates in a female luer connector 34 attached to a stopcock 36 of a pressure transducer 38. The reservoir 30 and pressure transducer 38 removably mount to a bracket 40 which, in turn, may be secured to a conventional pole support 42 with the reservoir in a vertical orientation.

[0047] As mentioned above, the blood sampling system 20 forms a portion of a pressure monitoring system, and the fluid pressure transducer 36 may be a TruWave™ Disposable Pressure Transducer available from Edwards Lifesciences of Irvine, CA. A supply of flush solution 44 connects to a flush port 46 of the transducer 38 via tubing 48. Typically for adults, the flush solution 44 comprises a bag of physiological fluid such as saline surrounded by a pressurized sleeve that squeezes the fluid and forces it through the tubing 48. In addition, an infusion fluid supply (not shown) may be provided in communication with an infusion port 50 of the stopcock 36. The pressure transducer 38 is thus placed in fluid communication with the arterial or venous system of the patient through the conduit line, and preferably includes a cable and plug 52 to connect to a suitable display monitor (not shown). Though the pressure transducer 38 is shown positioned within the proximal segment 24, it could also be located in the distal segment 22.

[0048] The sampling system 20 further comprises a fluid sampling site 60 that desirably defines a Z-shaped flow passage adjacent a pre-slit septum (not numbered). With this configuration, a minimal amount of flush volume is needed to clear the line after sampling. The septum preferably comprises an 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. Such sampling site is described in U.S. Patent No. 5,135,489 to Jepson, et al., which is hereby expressly incorporated by reference.

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[0049] Figure 2 better illustrates one embodiment of a blood sampling reservoir 30 of the present invention removed from the bracket 40. The reservoir 30 desirably includes a syringe-type variable volume chamber 62, though other reservoirs that have constant volume chambers or other
5 receptacles for receiving fluid may be used. Preferably, the reservoir 30 is of a type that includes a constantly open flow channel through the variable volume chamber 62 for passage of flushing fluid therethrough. A particularly useful such reservoir 30 is the Edwards VAMP Plus® system mentioned above.

[0050] In one mode of operation of the system 20, a reduced pressure
10 is created within the variable volume chamber 62 by withdrawing the plunger 64 such that a fluid sample from the distal segment 22 is drawn into the chamber. The chamber 62 has a sufficient volume, typically 12 ml, to draw blood from the patient P passed the sampling site 60. The clinician can then take a sample of undiluted blood from the site 60. Subsequently, the blood
15 and other fluids drawn into the reservoir 30 during the sampling operation are re-infused by depressing the plunger 64. It should be noted that the pressure transducer 38 may include a flow restrictor or flow control means to prevent flushed solution from going proximally through the sensor rather than back to the patient. For instance, the stopcock 36 may be used to close off the fluid
20 path through the pressure transducer 38 prior to re-infusing the reservoir clearance volume.

[0051] The entire sampling system 20 is thus closed as the “priming” volume that ensures a pure sample of blood reaches the sampling site 60 remains within the system 20 and is reinfused into the patient. It will be
25 understood by those skilled in the art that the syringe-type reservoir 30 shown in Figures 1-2 is only exemplary and other configurations may be designed to adequately provide the variable volume chamber.

[0052] With reference now to Figures 3A-3C and 4-5, the proximate relationship between the reservoir 30 and the control valve 32 will be
30 described. Desirably, the reservoir 30 and control valve 32 are molded plastic

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pieces that are rigidly mounted together such as with adhesive or ultrasonic welding. However, the reservoir 30 simply needs to be in proximity with the control valve 32 such that they are connected by two fluid flow paths. For convention, the ordinary flow path of the whole system as seen in Figure 1 is from proximal to distal, or from the fluid bag 44 to the patient P. With reference back to Figure 2, the saline or other physiological fluid flows into the reservoir 30 and control valve 32 combination through the proximal segment 24 of the conduit line and flows out of the distal segment 22. In this regard, therefore, the reservoir 30 has an inlet that receives saline from an outlet port of the control valve 32, and also an outlet through which saline flows to an inlet port of the control valve. These internal flow paths and channels will become clearer below, and as mentioned are desirably molded into the mating sections of the reservoir 30 and control valve 32. It is entirely feasible, however, to separate these two components with short lengths of tubing.

[0053] The control valve 32 as best seen in Figures 4-5 comprises a manifold 70 that receives a movable valve member 72. In the exemplary embodiment, the manifold 70 defines a cylindrical interior chamber 74 sized to rotatably receive a generally cylindrical core 76 of the valve member 72. A control handle 78 extends externally from the chamber 74 and provides leverage for rotating the core 76 within the chamber. The interior chamber 74 is shown oriented 90° from the axis of the reservoir 30, although other arrangements are possible.

[0054] Figures 4 and 5 further illustrate an exemplary fluid sampling port 84 provided in an outer portion of the control handle 78. The fluid sampling 44 may take a variety of forms, but as illustrated includes an elastomeric slit septum 86 captured by a cap 88 over a sampling cavity 90 within the valve member 72. The assembly seen in Figure 4 provides access for a blunt cannula through the slit septum 86 to withdraw fluid from within the sampling cavity 90. The sampling site 84 is located along the center line

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of the rotating valve member 72, although as will be explained below, other locations for a sampling site within the control valve are contemplated.

[0055] Figures 4 and 5 also illustrate exemplary indicators for the various rotational positions of the valve member 72 within the manifold 70. More specifically, the preferred form of the invention includes both tactile and visual indicators to help reduce clinician errors, speed up and clarify the process. The visual indicators include an arrow-shaped control handle 78 with a pointed end 92 that registers with one of three symbols 94a, 94b, 94c raised and/or printed on a faceplate 96 of the control valve 32. The valve member 72 may be rotated to one of the three positions with the pointed end 92 registering with one of the three symbols 94a, 94b, 94c. The indicator plate 96 shows the three position indicators 94 at the 0°, 90°, and 180° locations relative to a 0° horizontal reference line to the right (3:00). The 90° angular separation between the positions of the valve member 72 facilitates selection of one of three modes. An arc-shaped lip 98 projecting from an outer end of the interior chamber body desirably interferes with a small tooth 99 (see Fig. 6A) on the valve member 72 to prevent its rotation into the fourth, unmarked quadrant. The meaning of the symbols 94a, 94b, 94c will become apparent below. 91 psuedo inlet/outlet port, good flushing

[0056] In addition to visual indicators, the control valve 32 also desirably provides tactile feedback to the operator when the valve member 72 is in one of the three discrete positions. There are a number of ways to indicate tactilely the proper positioning of a rotating body within another, but the means used in the present context also preferably provide positive positioning of the valve member 72 within the interior chamber 74. For example, a small rib or bump 100 extending inward from the chamber 74 or lip 78 may be sized in position to register with small grooves or depressions 102 formed in the valve member core 76. These mating features are preferably sized large enough for the male portion to fit within the female portion and nominally restrain motion of the valve member 72, but small

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enough to allow the user to relatively easily overcome their engagement and further rotate the valve member. As the engaging pieces are molded plastic, and the assembly is designed to be used once and disposed of, small rounded bumps engaging equal sized depressions are an effective short-term tactile
5 indicator. It should be understood that the bumps and depressions could be provided on the parts as shown, or on the opposite elements in a reverse configuration. Moreover, these physical mating features desirably emit a small click when engaging, which provides a third, aural indicator.

[0057] Figures 6A-6E and 7-11 provide details of the exemplary valve
10 member 72 having the central sampling port 84 therein. With reference to Figure 6A, the core 76 has a generally cylindrical exterior that slightly narrows away from the control handle 78 and is interrupted at a lower end by a trough 110 bordered by two shoulders 112. A pair of channels 114, 116 through the interior of the core 76 open to the core exterior at two locations
15 separated circumferentially by almost 90° but in a common radial plane (as used herein, “radial” is relative to the rotational axis of the valve member 72). Looking at the reverse orientation of Figure 6E, the core 76 further features an arc-shaped groove or channel 120 that extends around the circumference of the core in a radial plane, preferably the same plane as that of the openings of
20 the channels 114, 116. Figure 9 is a radial sectional view through that common plane and illustrates the relative positions and orientations of the channels 114, 116, 120.

[0058] The generally cylindrical portion of the core 76 is sized to closely fit within the interior chamber 74 of the manifold 70 (see Figure 5)
25 such that the valve member 72 can rotate within the manifold but there is no unintended fluid leakage between the various ports and channels. The openings of the channels 14, 16 and the circumferential channel 120 lying in a common radial plane provide the only avenue for fluid passage around or through the valve member 72 when it is closely fit within the interior chamber
30 74. It should be understood that alternative configurations are possible with,

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for example, the openings to the channels 114, 116 and circumferential channel 120 being spaced apart axially with respect to one or the others.

[0059] Figure 7 is an axial cross-sectional view through the valve member 72 that illustrates the inner components of the sampling port 84. Namely, the cap 88 restrains the elastomeric slit septum 86 over the sampling cavity 90. Figure 8 illustrates the sampling cavity 90 along a different axial plane that passes directly between a pair of axially-oriented channels 130, 132 seen in Figure 7 that communicate, respectively, with the radial channels 114, 116. Figure 8 further illustrates the generally semi-circular cross-section of the circumferential channel 120. With reference again to Figure 9, it should therefore be apparent that the radial channels 114, 116 are in constant fluid communication with each other via the respective connecting channels 130, 132 opening into the common sampling cavity 90. As will be explained below, these bifurcated channels through the valve member 72 function to permit blood or other body fluid into the sampling cavity 90, and also effectively flush the sampling cavity 90 in between samples. An axial extension 134 of the wall separating the connecting channels 130, 132 continues into close proximity with the slit septum 86. The extension 134 creates a pseudo inlet/outlet to the sampling cavity 90 such that a flow of flushing fluid therethrough is directed all the way to the slit septum 86 before turning the corner and continuing through the valve member 72. The extension 134 therefore enhances the efficacy of the flushing step and helps eliminate dead zones within the sampling cavity 90 that might otherwise be a source of blood coagulation and contamination.

[0060] Structural details of the manifold 70 are seen in Figures 12-15. Specifically, the manifold 70 features a plurality of ports that opened into the interior chamber 74. A distal port 140 and a proximal port 142 extend upward from the chamber 74 in the orientation where the reservoir 30 plunger points downward. These ports 140, 142 are shown respectively connected to the distal segment 22 and proximal segment 24 of the conduit line in Figures 1

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and 2. Therefore these ports 140, 142 represent the two diverging segments of the conduit line, the former extending toward the patient and the latter to the pressure transducer 38 and saline drip.

[0061] On the opposite side of the chamber 74, a manifold outlet port 144 leads to an inlet 146 to the reservoir variable volume chamber 62. An outlet 148 of the reservoir 30 leads directly into a manifold inlet port 150. The distal and proximal ports 140, 142 and outlet and inlet ports 144, 150 all open directly to the interior chamber 74 of the manifold 70. Note that one possible configuration is a reservoir connected through the control valve 32 using only a single reservoir port as opposed to inlet and outlet ports. For example, a syringe-type removable reservoir may be connected to a single port of the control valve 32. In such a system, the benefit of isolating the reservoir remains although the flush mode of operation will not pass through the reservoir. The term "reservoir port" therefore includes one or both of the outlet and inlet ports 144, 150.

[0062] Figures 13-14 show the manifold 70 having relatively long outlet and inlet ports 144, 150 leading to and from the reservoir 30 to provide some clearance for rotation of the valve member 72. Desirably, the manifold 70 is a single molded piece that is rigidly secured to the end of the reservoir 30. However, the manifold 70 could be a combination of more than one piece, and could be connected to the reservoir 30 through short tubes.

[0063] Figures 15A and 15B show the gradual taper of the interior chamber 74 at the narrow end of the chamber 74, a circular rib 160 projects inward for engaging and retaining the valve member 72, as will be explained next.

[0064] Figures 16 and 17 illustrate in cross-section the coupling of the valve member 72 within the manifold 70. Specifically, the gradual tapers of both closely match and provide an effective fluid seal at the point that the inward rib 160 of the manifold passes over the first shoulder 112 of the valve member 72 and resides within the trough 110. A cavity 162 in the narrow end

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of the valve member 72 permits inward flexing of the shoulder 112 such that it can be forced passed the rib 160. Interference between the outwardly-sprung shoulder 112 and rib 160 effectively locks the valve member 72 within the manifold 70 and ensures good fluid sealing around the various ports and openings. Figure 16 shows the alignment of the proximal port 142 with the circumferential groove 120 two valve member 72. Likewise, the radial channel 114 also lies in the same plane. It is worth mentioning again at this stage that the coplanar nature of all of the ports and openings is an efficient and relatively straightforward design, but more complex fluid pathways between the rotating valve member 72 and manifold 70 could be designed to perform the same function. For example, one or more of the internal channels could be curvilinear, or there could be more than one circumferential surface channel.

[0065] Now with reference to Figures 18A-18C and 19A-1C, the fluid flow paths for the three positions of the valve member 72 will be explained.

[0066] The reader will recall from the description of the system of Figure 1 that there is a physiological fluid flush drip, preferably pressurized. When such flush is needed, the clinician rotates the valve member 72 to the downward position, as indicated by the arrow F/C in Figure 18A. This corresponds to a "Flush/Clear" mode of operation, and is symbolically indicated by the symbol 94a of three divergent flow paths in Figure 5, meaning all fluid communications are open. When pressure monitoring is desirable, the clinician rotates the valve member 72 to the left position, as indicated by the arrow M in Figure 18B. This corresponds to a "Monitoring" mode of operation, and is symbolically indicated by the symbol 94b of a pressure wave in Figure 5. Finally, when the clinician requires a fluid sample, he/she rotates the valve member 72 to the right position, as indicated by the arrow S in Figure 18C. This corresponds to a "Sampling" mode of operation, and is symbolically indicated by the symbol 94c of a drop of fluid in Figure 5. As mentioned above, the symbolic indicators 94a, 94b, and 94c are desirably

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supplemented by the clear directional nature of the arrow-shaped control handle 78, and by tactile and audible feedback measures, to help avoid error.

[0067] Figures 18A-18C further illustrate the change in rotational orientation of the valve member 72 within the internal chamber of the manifold 70, in particular through the radial plane passing through the flow channels that open to the exterior of the valve member core 76. The same illustrations of the flow channels in the three positions are shown more clearly in Figures 19A-19C with relevant labels and fluid flows indicated. The two sets of diagrams further indicate the four manifold ports 140, 142, 144, and 150.

[0068] In the F/C position of the valve member 72 of Figures 18A and 19A, a slow drip of flushing fluid travels from the supply of flush solution 44 (Figure 1) through the proximal segment 24 (Figure 2) to the manifold proximal port 142, through the circumferential channel 120 and the outlet port 144. As indicated by the flow arrows in Figure 19A, the drip continues through the inlet 146 and outlet 148 of the reservoir 30 passing through the variable volume chamber 62. The fluid then passes through the inlet port 150 into the radial channel 114, and along the axial channel 130 into the sampling reservoir 90 (see Figure 7), and back through the parallel axial channel 132 into the other radial channel 132. Finally, the fluid exits the valve member 72 into the manifold distal port 140 and from there continues through the distal segment 22 of the conduit line to the patient.

[0069] In the F/C position of the valve member 72, all of the internal flow paths within the reservoir 30 and control valve 32 are open to form a single continuous flushing pathway. This desirably permits any blood or other bodily fluid to be completely flushed from within the system 20, leaving no dead spots for bubbles to form or blood to coagulate. This "pocket-less" fluid pathway through the system in conjunction with the ability to isolate components that degrade the pressure signal is extremely useful. Furthermore, the control valve 32 is desirably made of transparent or frosted plastic that

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permits the user to visualize blood flow therethrough, thus insuring blood as been completely flushed out of the system after a sample is taken.

[0070] The F/C position also enables a clearing volume to be pulled into the reservoir 30. Specifically, a reduced pressure within the variable
5 volume chamber 62 pulls fluid from the distal segment 22 into the reservoir 30 in a reverse flow from that shown in Fig. 19A. The volume of the chamber 62 is sufficient to draw blood from the patient past the sampling port 84 (sampling cavity 90), that is, through the internal channels of the valve member 72. A flow restrictor or control valve at the pressure transducer 38
10 toward the proximal segment 24 ensures that the reservoir 30 fills with fluid from the distal segment 22. That is, there is greater resistance to flow into the reservoir from the proximal segment 24 as compared to the distal segment 22.

[0071] Before a sample is taken, however, the control handle 78 must be rotated into the third S position shown in Figures 18C and 19C. In this
15 position, the channels of the valve member 72 provide open fluid communication only from the distal port 140 to the radial channel 114 as shown, and from there to the sampling cavity 90 (Figure 7). A fluid sample is taken from the port 84 using a blunt cannula or other sampling device.

[0072] Pressure monitoring occurs with the valve member 72 in the
20 second M position shown in Figures 18B and 19B. In that position, the pressure transducer 38 (or DPT, Disposable Pressure Transducer), is in fluid communication with the patient directly through the circumferential channel 120, bypassing the reservoir 30 and sampling port 84. This feature of the control valve 32 isolates the elastomeric elements of the reservoir 30 and
25 sampling port 84, as well as the associated channels leading thereto, from the fluid pressure column. The fluid pressure column therefore extends directly from the patient through the distal segment 22, making a U-turn in the circumferential channel 120 to the proximal segment 24. Bypassing the reservoir 30, and in particular the elastomeric seal of the plunger 64, and the
30 sampling port 84 (elastomeric septum 86), greatly improves the signals

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received by the pressure transducer 38. A distal sampling port 60 in the distal segment 22 may be of a conventional type which includes an elastomeric septum that would affect the pressure signal, or that sampling port may also be isolated from the pressure column as will be described below. One benefit of improving the pressure response of the system by isolating the various functional elements is that the entire conduit line can be lengthened to move the reservoir 30 farther away from the patient. In conventional blood sampling systems, where the elastomeric components remain in contact with the pressure column, the maximum length of the conduit line from the reservoir to the patient is about __ cm. By isolating just the reservoir 30 as indicated above, the conduit line can be lengthened to about __ cm. [Mark, please fill in these distances]

[0073] It is important to understand that the principles of the control valve 32 described above are applicable to other configurations of fluid sampling systems. In the exemplary system described above, a sampling port 84 is incorporated centrally in the rotating valve member 72 of the control valve 32, which is connected or adjacent to the reservoir 30. The control valve 32 isolates both the reservoir and the sampling port in the sampling mode. However, the sampling port in the control valve may connect through the manifold 70 instead of the valve member 72. Also, the exemplary valve member has three positions 90° apart from each other, but the arrangement of the channels within the valve member and manifold may be altered to change the amount of the valve member rotates in each position. Furthermore, the principles of isolating the elastomeric elements of the reservoir and sampling port can be transferred to a stand-alone sampling port in the conduit line. Examples of each of these alternatives will be described below, and it should be clear that these are representative of numerous other alternatives.

[0074] Figures 20A-20E illustrate an alternative control valve 170 of the present invention adjacent a reservoir 30 with a modified arrangement of internal flow paths than the exemplary embodiment described above. The

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control valve 170 is similar to the first embodiment in that a housing or manifold 172 connects to the reservoir 30 and rotatably receives therein a valve member 174. Furthermore, the valve member 174 carries a central sampling port 176, which is illustrated as a slit septum-type but could be any number of kinds of sampling ports. Figure 20B shows a control handle 178 of the valve member 174 oriented with its pointed end 180 down into the right at about a 45° angle. The indicator plate 182 shows the three position indicators at the 45°, 90°, and 180° locations relative to a horizontal reference line to the right at 0°. This is a departure from the 90° separation between the valve member positions in the first embodiment.

[0075] The control handle 178 in Figure 20B is in the “S” or sampling position. The internal flow channels defined within the valve member 174 in the radial plane of the ports of the manifold 172 are illustrated in Figure 20E. Comparing this view with a similar view shown in Figure 18C, the reader will discern the slightly different orientations of the internal channels within the valve member 174. By rotating the valve member 174 clockwise another 45°, the control valve 170 will be placed in the F/C mode wherein all of the internal flow paths are in series so that the system can be flushed. Rotating the valve member 174 a further 90° into the M position isolates both the reservoir 30 and the sampling port 176 from the attached conduit line for undegraded pressure monitoring. Although the relative spacing between the S position and the F/C position is only 45°, in contrast with 90° in the first embodiment, the flow channels are modified to prevent cross-talk or pressure perturbations transmitted to the proximal segment and pressure transducer when switching positions. Furthermore, the channels are arranged so that there is greater separation between the internal channels in the sampling mode.

[0076] Figures 21A-21E show another alternative control valve 190 similar to the valve 170 of Figure 20A-20E, but with a luer-style central sampling port. Specifically, the control valve 190 includes the modified internal flow paths such that the three operating positions of a control handle

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192 seen in Figure 21B are other than 90° apart. More particularly, the cross-section of Figure 21E is the same as that of Figure 20E. Also, the control valve 190 includes a sampling port 194 provided in the center of a rotatable valve member 196. In contrast to the embodiments of Figures 20A-20E, however, the sampling port 194 includes a luer-style connector 198, best seen in Figure 21C. The male luer-style connector 198 mates with a female luer connector on a sampling syringe (not shown). Because of the typically larger sizes of the blunt cannulas in such sampling syringes, the septum 200 of the sampling port 194 is highly compliant, or at least more compliant than the slit septum 86 used in the sampling port 84 described above. The ability to isolate the luer-style sampling port 194 using the control valve 190 is therefore highly desirable as it greatly improves the quality of the pressure signal received by the pressure transducer by removing the compliance of the septum 200 from the pressure column.

15 [0077] Figures 22A-22E illustrates a control valve 210 that, as before, may be associated with or connected to a reservoir 30, but includes an alternative fluid sampling port 212. Specifically, the fluid sampling port 212 comprises a side port from a control valve manifold 214 rather than being formed centrally in a rotatable valve member 216. The sampling port 212 is shown in cross-section in Figure 22E which reveals an elastomeric septum 220 captured by a cap 222 over a sampling cavity 224. A pair of flow channels 226, 228 open into the sampling cavity 224. The opposite ends of the flow channels 226, 228 opened to an interior chamber of the control valve manifold 214. In this sense, the sampling port 212 communicates with internal channels in the control valve 210 via a through flow path defined by the channels 226, 228.

20 [0078] Figure 22E also shows six openings to the internal channel of the manifold 214, two of which lead to the sampling port channels 226, 228. Another two openings lead to proximal and distal ports 230, 232 that connect to the proximal and distal conduit line segments. Finally, two more openings

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- 27 -

lead respectively to the inlet and outlet of the reservoir 30. The valve member 216 includes circumferential channels that selectively communicate with these 6 ports depending on the rotational position of a handle 234. As with the earlier embodiments, there are 3 positions of flush, monitor, and sample. In the monitor position, the control valve 210 isolates both the reservoir 30 and sampling port 212 from the conduit line for a more accurate pressure signal. Also, the valve 210 prevents flow from the proximal conduit line segment in the sampling mode. This embodiment illustrates the alternative of having the sampling port connected with the control valve manifold as opposed to the rotating valve member. ;

Figures 23A-23E are various views of a luer-style valved sampling station 250 which can be incorporated into a pressure monitoring line in conjunction with a reservoir or independently. The valved sampling station 250 includes a housing or manifold 252 that defines therewithin an internal chamber 254 as seen in Figure 24 with which a pair of ports 256, 258 communicate. The downstream port 256 may be connected to the patient, while an upstream port 258 is connected to a pressure transducer (not shown), in like manner as the manifold ports 140, 142 seen in Figure 12. Additionally, a loop-shaped channel 260 formed in the manifold 252 has opposite ends that open to the internal chamber 254. A valve member 262 rotates within the internal chamber 254. The valve member 262 has the same configuration as the valve member 196 shown in Figures 21A-21E. That is, the internal flow channels are the same and the valve member 262 carries a central luer-type sampling port 264.

[0079] With reference to Figure 23B, the manifold 252 includes an indicator plate 266 on which are provided the familiar three operational mode symbols of sampling, flush, and pressure monitoring. A control handle 268 is used to rotate the valve member 262 into the three operational positions. The reader will recognize that the three positions have the same spacing as the positions for the control valve 190 in Figures 21A-21E. Indeed, the valved

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sampling station 250 functions analogously to the control valve 190 in that in the pressure monitoring position of the control handle 268, the central sampling port 264 is isolated from the ports 256, 258, and thus the attached conduit line and pressure column. The sole difference between the valved sampling station 250 and the control valve 190 is the substitution of the loop-shaped channel 260 for the clearance reservoir. The channel 260 is important in that a flow of fluid passes through it and through all of the internal channels of the valved sampling station 250 when the control handle 268 is in the flush position, seen in Figure 23B. Again, the valved sampling station 250 can be used in a conduit line of a pressure monitoring system where a clearance volume of fluid is pulled past the sampling port using a reservoir as described above, or other such clearing device.

[0080] Finally, Figures 25A-25E illustrate a further alternative valved sampling station 280 with a sampling port 282 extending from one side of a manifold 284. The manifold 284 is configured in a T-shape with a pair of ports 286, 288 that open to an internal chamber projecting outward at 90° with respect to one another, and with respect to the sampling port 282. The valve member 290 rotates within the internal chamber. As seen in Figure 25E, the valve member 290 includes two circumferential channels 292, 294 that selectively communicate with the ports 286, 288, and with two ports 296, 298 leading to and from the sampling port 282. As in the valved sampling station 250 of Figures 23-24, the valve member 290 rotates into three positions corresponding to flush, sampling, and pressure monitoring. The ports 286, 288 attach to proximal and distal segments of a conduit line in a manner described above. In the pressure monitoring mode, the sampling station 280 excludes the sampling port 282 from the conduit line. This embodiment is similar to the immediately preceding sampling station 250, but illustrates a sampling port 282 that connects directly to the manifold 284 rather than to the rotating valve member 290. Furthermore, the sampling port 282 has a slit

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septum 299 for receiving a blunt cannula (not shown), but a luer-type sampling port could also be used.

[0081] While the invention has been described in its preferred embodiments, it is to be understood that the words which have been used are
5 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 fluid sampling and pressure monitoring of a fluid system of a patient, 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 control valve with a manifold defining an interior chamber, the manifold having a proximal port fluidly connected to the proximal segment, a distal port fluidly connected to the distal segment, and a reservoir port, wherein each of the manifold ports opens to the interior chamber,

a pressure transducer connected to the conduit line for sensing the pressure of the fluid therein;

a fluid sampling port in the medical system;

a reservoir in fluid communication with the reservoir port of the control valve manifold;

the control valve further including a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports, the valve member being movable into at least two positions:

a first position that provides open fluid communication from the proximal segment to the patient through the control valve so as to eliminate any dead spaces therein, wherein reduced pressure within the reservoir pulls fluid from the distal segment through the control valve and into the reservoir sufficient to draw fluid from the fluid system of the patient past the sampling port, and

a second position that provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member to the

distal segment while bypassing the reservoir, such that the pressure of fluid within the conduit line exclusive of the reservoir can be sensed by the pressure transducer.

2. The system of claim 1, wherein the valve member has a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

3. The system of claim 1, wherein the valve member comprises a core rotatable within the interior chamber of the manifold and a control handle external to the manifold, and further including mating features on the valve member core and manifold that provide tactile feedback and positive positioning of the core in both first and second positions.

4. The system of claim 1, wherein the valve member comprises a core rotatable within the interior chamber of the manifold and a control handle external to the manifold, further including coordinated visible features on the control handle and manifold that provide symbolic indicators of both first and second positions of the valve member.

5. The system of claim 1, wherein the sampling port is formed within the control valve.

6. The system of claim 5, wherein the sampling port is formed within the valve member and communicates with a sampling cavity formed internally within the valve member open to at least one of the channels.

7. The system of claim 5, wherein the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the interior chamber of the manifold.

8. The system of claim 5, further including a second sampling port having a sampling cavity positioned along the distal segment of the conduit line.

9. The system of claim 8, further including a second control valve interposed between the second sampling port and the distal segment and having a valve member movable into at least three positions:

a first position that provides open fluid communication from the conduit line through the control valve to the sampling cavity and back to the conduit line,

a second position that provides open fluid communication from the conduit line through the valve member and back to the conduit line while bypassing the second sampling port, such that the pressure of fluid within the conduit line exclusive of the second sampling port can be sensed by the pressure transducer, and

a third position that provides open fluid communication from the distal segment through the control valve to the second sampling port but prevents communication between the second sampling port and the conduit line proximal from the second sampling port.

10. The system of claim 1, wherein the sampling port is positioned along the distal segment of the conduit line.

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11. The system of claim 10, further including a second control valve interposed between the sampling port and the distal segment and having a valve member movable into at least three positions:

a first position that provides open fluid communication from the conduit line through the control valve to the sampling cavity and back to the conduit line,

a second position that provides open fluid communication from the conduit line through the valve member and back to the conduit line while bypassing the sampling port, such that the pressure of fluid within the conduit line exclusive of the sampling port can be sensed by the pressure transducer, and

a third position that provides open fluid communication from the distal segment through the control valve to the sampling port but prevents communication between the sampling port and the conduit line proximal from the sampling port.

12. The system of claim 1, wherein the valve member comprises a core movable within the interior chamber of the manifold and a control handle external to the manifold, the core having an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core.

13. The system of claim 12, wherein the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.

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14. The system of claim 1, further including means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position.

15. The system of claim 1, wherein the reservoir has an inlet open to an outlet port of the control valve manifold and an outlet open to an inlet port of the control valve manifold, and wherein the first position of the valve member provides open fluid communication between the control valve flow passages through the inlet and outlet of the reservoir to flush a chamber of the reservoir.

16. A medical system for fluid sampling of a fluid system of a patient, 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 control valve connected between the proximal segment and the distal segment of the conduit line;

- a fluid sampling port having a flow path therethrough whose opposite ends open to internal channels in the control valve;

- a reservoir in fluid communication with a reservoir port of the control valve manifold;

- the control valve further including a valve member movable into at least three positions:

- a first position that provides open fluid communication from the proximal segment through the control valve to the distal segment,

- a second position that provides open fluid communication from the proximal segment to the distal segment while bypassing the reservoir and sampling port, and

a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

17. The system of claim 16, wherein:

the control valve further includes a manifold defining an interior chamber, the manifold having a proximal port fluidly connected to the proximal segment of the conduit line, a distal port fluidly connected to the distal segment, an outlet port, and an inlet port, wherein each of the manifold ports opens to the interior chamber, and wherein the valve member comprises a core movable within the interior chamber of the manifold and having channels therein that selectively communicate with the manifold ports, and the reservoir has an inlet open to the manifold outlet port and an outlet open to the manifold inlet port, and wherein:

the first position provides open fluid communication from the proximal segment to the proximal port and the outlet port of the control valve, through the inlet and outlet of the reservoir, to the inlet port and the distal port of the control valve to the distal segment,

the second position provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member core to the distal segment while bypassing the reservoir and sampling port, and

the third position provides open fluid communication from the distal segment to distal port and one of the channels of the valve member core, and to the sampling port.

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18. The system of claim 17, wherein the valve member core has an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core.

19. The system of claim 18, wherein the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.

20. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber in which the valve member moves, and wherein the sampling port is formed within the valve member and includes a sampling cavity open to channels within the valve member that communicate with the manifold interior chamber.

21. The system of claim 20, wherein the valve member comprises a cylindrical core rotatable within the manifold interior chamber, and wherein the fluid sampling port opens in a control handle of the valve member and is centered along the axis of rotation of the valve member core.

22. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber in which the valve member moves, and wherein the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the manifold interior chamber.

23. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber and the valve member comprises a core movable within the interior chamber of the manifold, and further including mating features on the valve member core and manifold that

provide tactile feedback and positive positioning of the core in all three positions of the valve member.

24. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber and the valve member comprises a movable within the interior chamber of the manifold and a control handle external to the manifold, and further including coordinated visible features on the control handle and manifold that provide symbolic indicators of all three positions of the valve member.

25. A method of taking samples and measuring the pressure of a fluid system of a patient, comprising:

- providing a fluid sampling system with a conduit line and a reservoir connected thereto between 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;

- interposing a control valve between the reservoir and the conduit line having a movable valve member with a control handle, the valve member movable into at least a first position and a second position;

- providing a pressure transducer connected to the conduit line for sensing the pressure of the fluid therein;

- providing a fluid sampling port in the sampling system;

- selecting the first position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve and the reservoir, and creating a reduced pressure within the reservoir such that fluid flows from the distal segment through the control valve into the reservoir sufficient to draw fluid from the fluid system of the patient past the sampling port; and

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selecting the second position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve while bypassing the reservoir, and monitoring the pressure sensed by the pressure transducer.

26. The method of claim 25, wherein the valve member has a third position, and the method includes selecting the third position of the valve member to provide open fluid communication from the distal segment to the sampling port but prevent communication between the sampling port and both the reservoir and the proximal segment, and sampling fluid from the conduit line through the sampling port.

27. The method of claim 26, wherein the fluid system of the patient is the blood system, and further including means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position, the method including the steps of:

selecting the first position of the valve member such that the physiological fluid flows through the conduit line to the patient; then
creating a reduced pressure within reservoir and collecting sufficient fluid therein such that blood flows past the sampling port;
then

selecting the third position of the valve member; then
sampling blood from the conduit line through the sampling port; then

creating an elevated pressure within the reservoir to expel blood therefrom into the distal segment of the conduit line; then

selecting the first position of the valve member such that the physiological fluid flows through the conduit line to the patient and flushes the reservoir of blood; and then

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selecting the second position of the valve member and monitoring the pressure sensed by the pressure transducer.

28. The method of claim 25, wherein the control valve has a manifold defining an interior chamber within which the valve member rotates, and further including mating features on the valve member and manifold that provide tactile feedback and positive positioning of the core in both first and second positions, the method of selecting the first and second positions further including rotating the valve member until the tactile feedback is sensed.

29. The method of claim 25, wherein the control valve includes visible features that provide symbolic indicators of the first and second positions of the control handle, the method of selecting the first and second positions further includes interpreting the symbolic indicators to determine the placement of the control handle corresponding to the first and second positions.

30. A medical system for fluid sampling of a fluid system of a patient, comprising:

- a conduit line with a proximal end adapted to be supplied with a physiological fluid and a distal end adapted to be in communication with a fluid system of a patient;

- a pressure transducer connected to the conduit line for sensing the pressure of the fluid therein;

- a fluid sampling port having a sampling cavity;

- a control valve interposed between the conduit line and the sampling port and having a manifold defining an interior chamber, the manifold having a proximal port fluidly connected to the conduit line, a distal port fluidly connected to the conduit line, an outlet port, and an

inlet port, wherein each of the manifold ports opens to the interior chamber,

the control valve further including a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports, the valve member being movable into at least three positions:

a first position that provides open fluid communication from the conduit line to the proximal port and the outlet port of the control valve to the sampling cavity, and to the inlet port and the distal port of the control valve to the conduit line,

a second position that provides open fluid communication from the conduit line to the proximal port and through at least one channel in the valve member and back to the conduit line while bypassing the sampling port, such that the pressure of fluid within the conduit line exclusive of the sampling port can be sensed by the pressure transducer, and

a third position that provides open fluid communication from the distal end of the conduit line through the control valve to the sampling port but prevents communication between the sampling port and the proximal end of the conduit line.

31. The system of claim 30, wherein the valve member comprises a core movable within the interior chamber of the manifold and having an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core.

32. The system of claim 31, wherein the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.

33. The system of claim 30, wherein the sampling port is formed within the valve member and includes a sampling cavity open to the valve member channels.

34. The system of claim 33, wherein the valve member comprises a cylindrical core rotatable within the manifold interior chamber, and wherein the fluid sampling port opens in a control handle of the valve member and is centered along the axis of rotation of the valve member core.

35. The system of claim 30, wherein the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the manifold interior chamber.

36. The system of claim 30, wherein the valve member comprises a core movable within the interior chamber of the manifold and a control handle external to the manifold.

37. The system of claim 36, further including mating features on the valve member core and manifold that provide tactile feedback and positive positioning of the core in all three positions of the valve member.

38. The system of claim 36, further including coordinated visible features on the control handle and manifold that provide symbolic indicators of all three positions of the valve member.

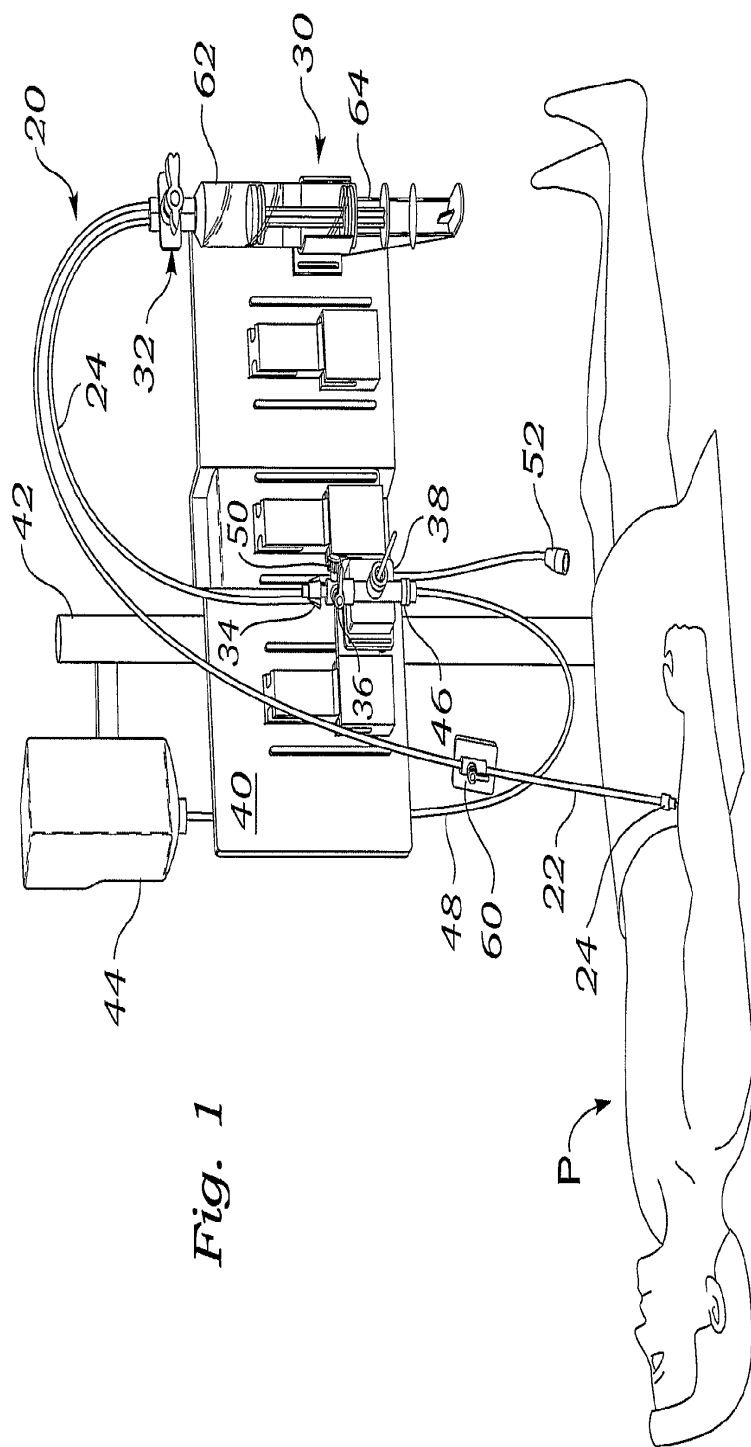


Fig. 1

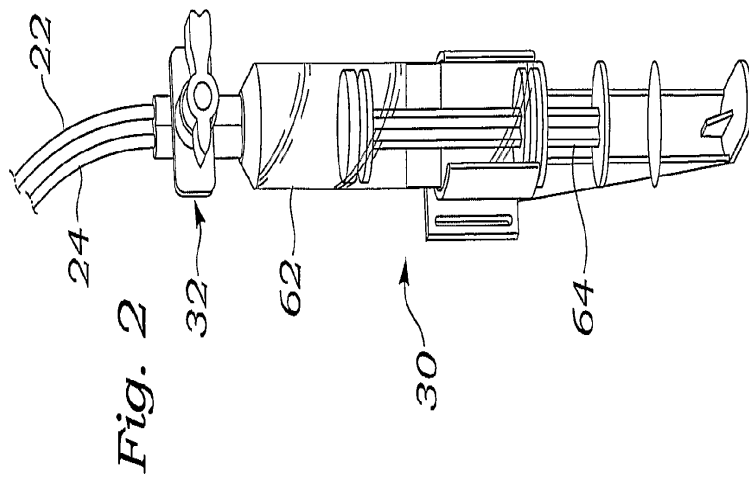


Fig. 2

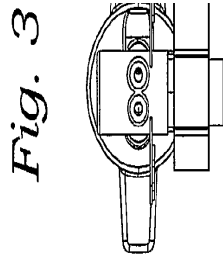


Fig. 3

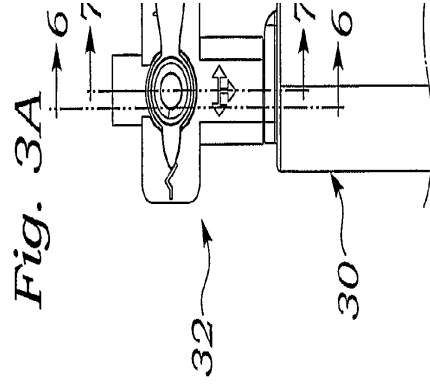


Fig. 3A

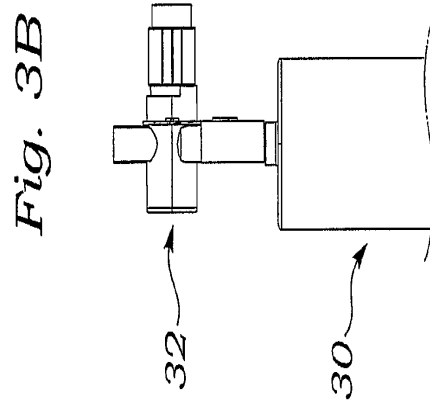


Fig. 3B



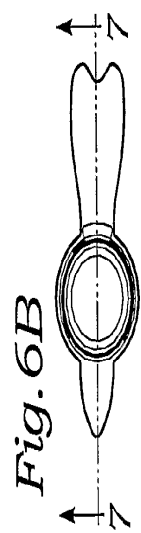
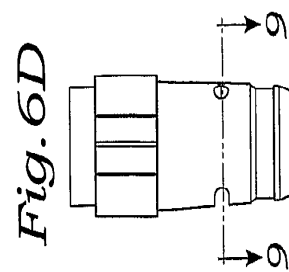
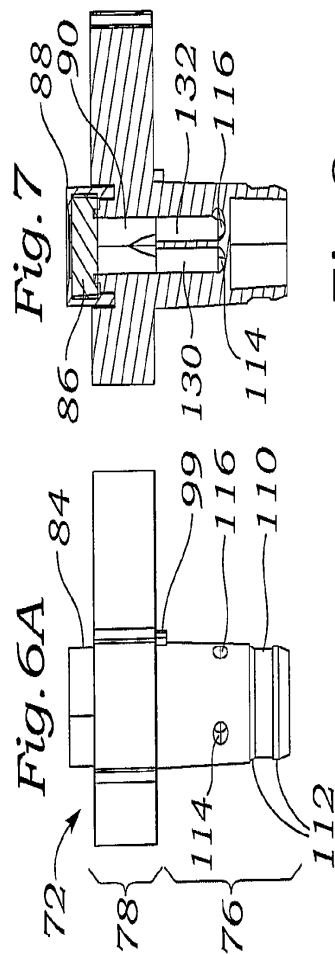
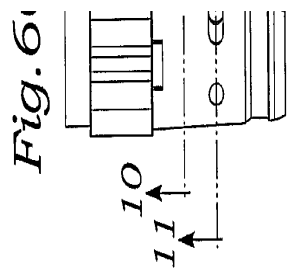
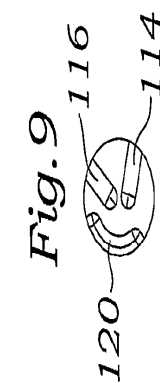
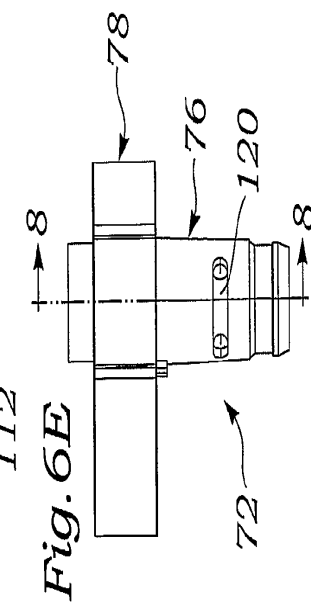
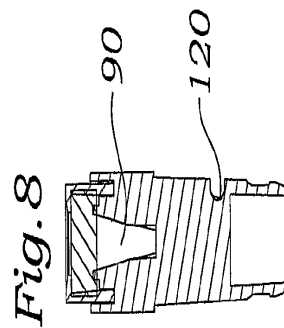
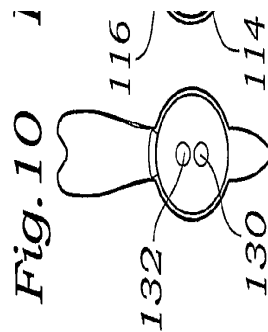


Fig. 12

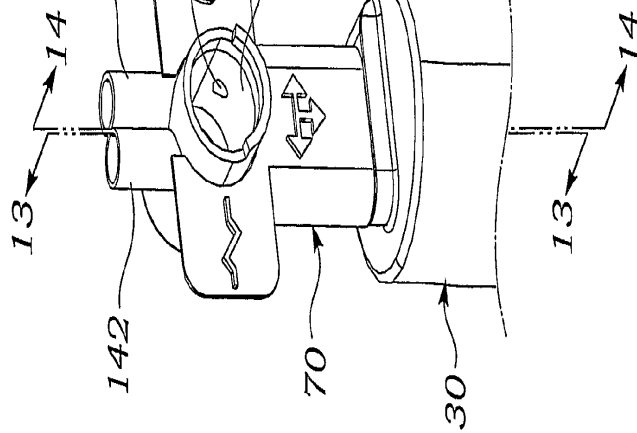


Fig. 13

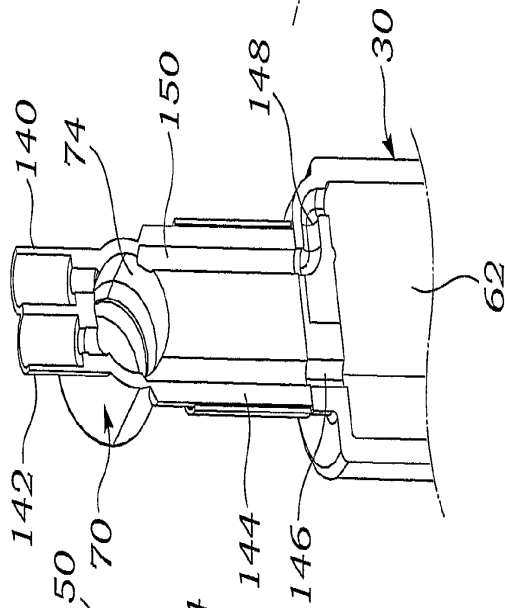
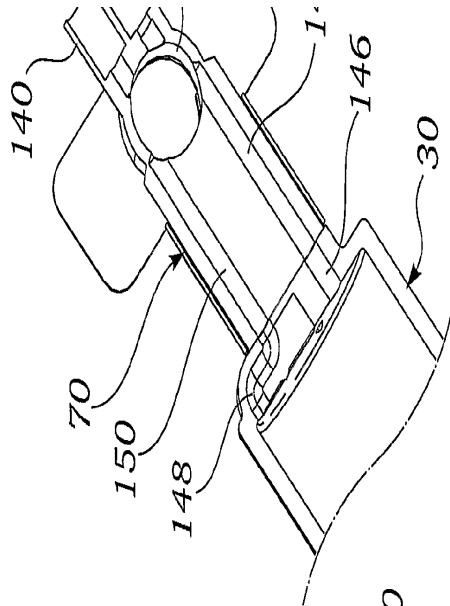


Fig. 14



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Fig. 15B

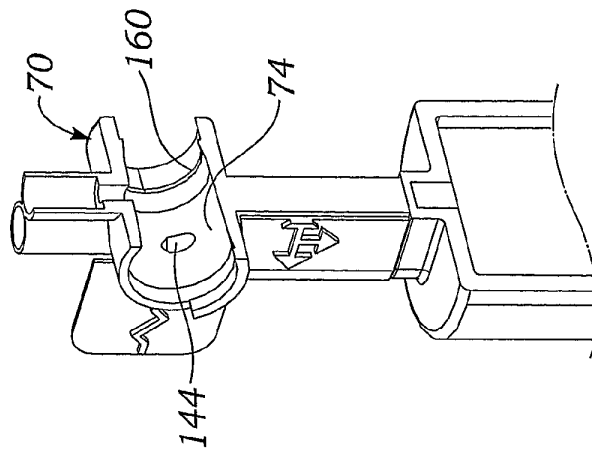


Fig. 15A

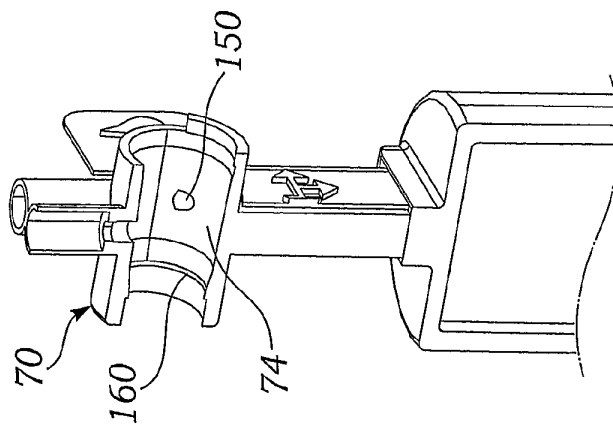


Fig. 16

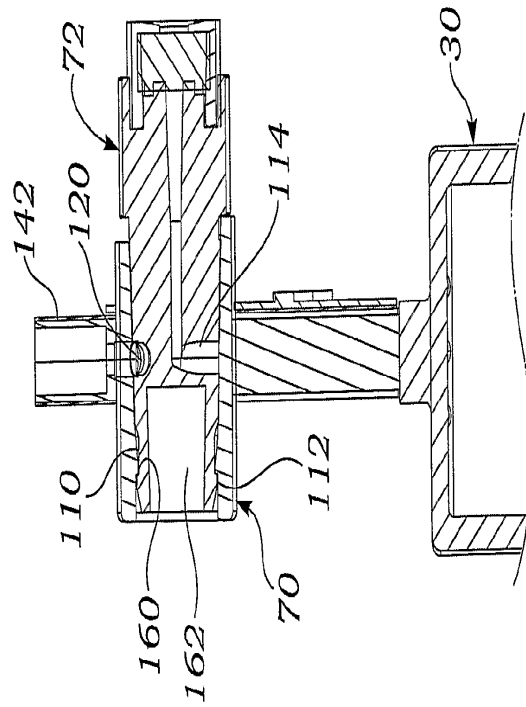
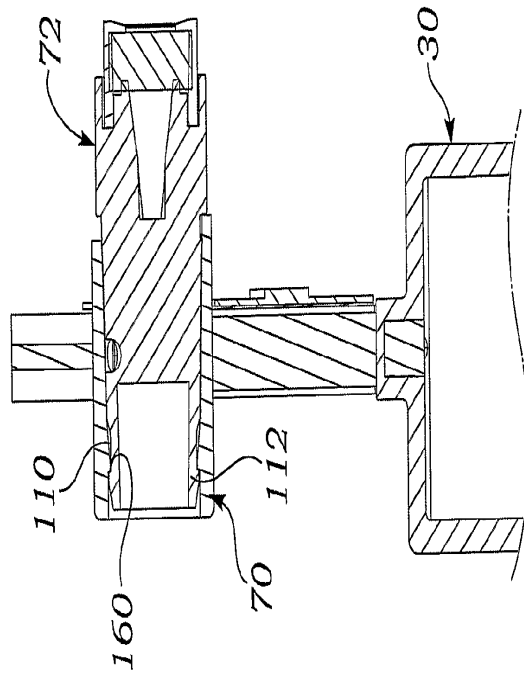
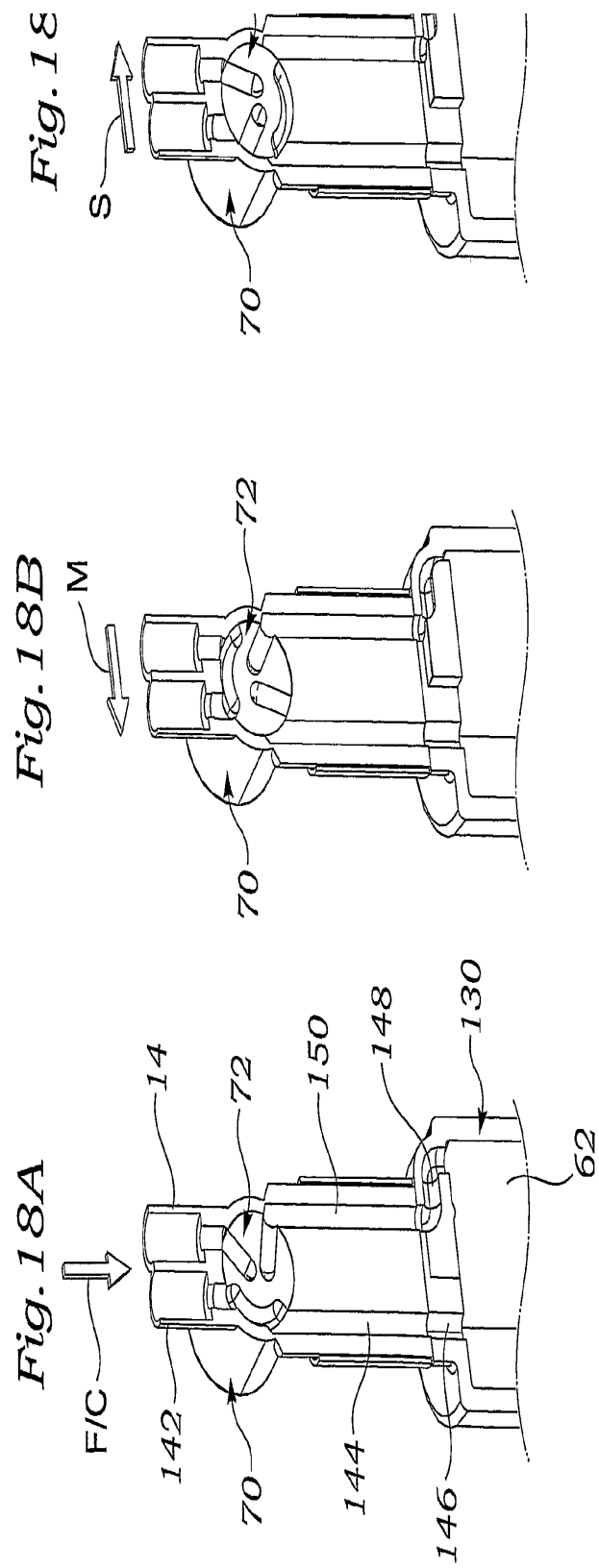


Fig. 17





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Fig. 19A
F/C POSITION

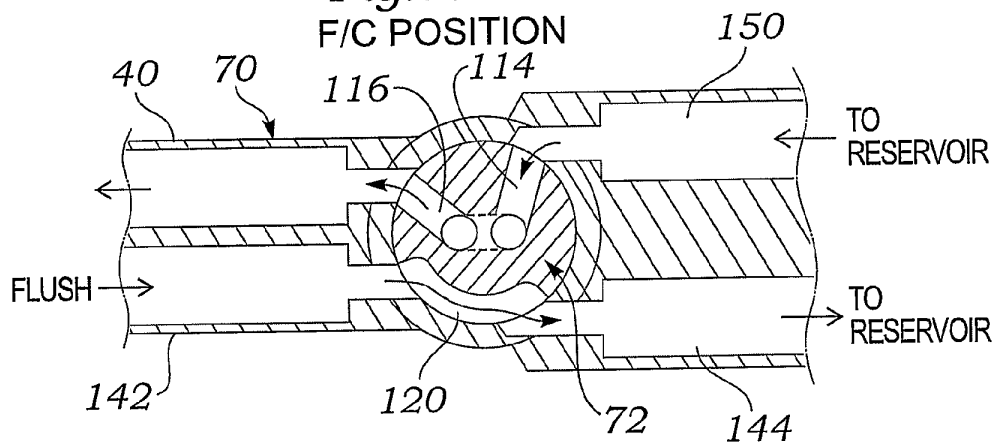


Fig. 19B
M POSITION

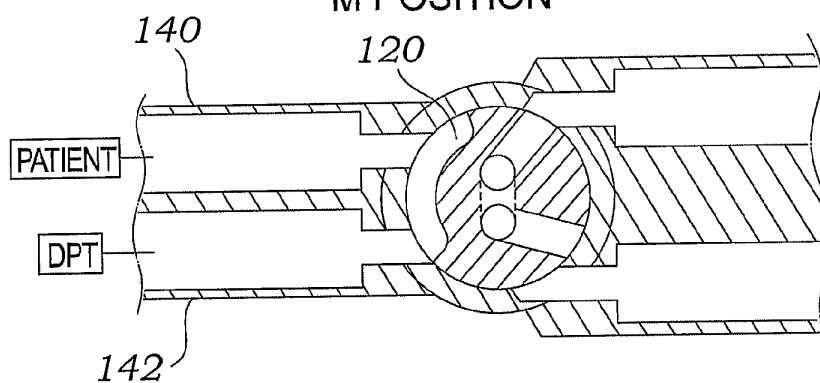
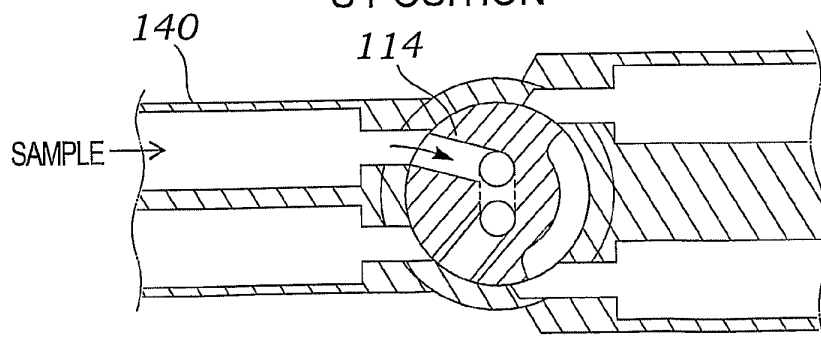


Fig. 19C
S POSITION



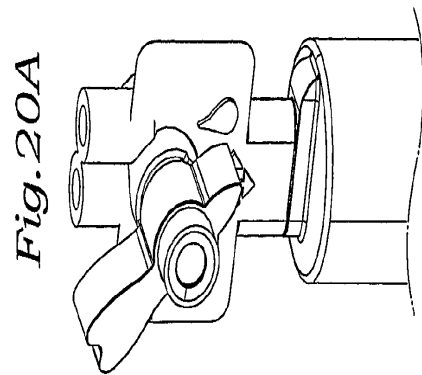


Fig. 20D

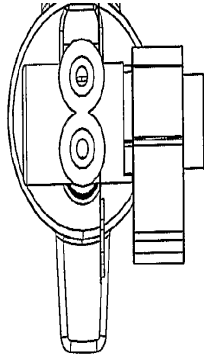


Fig. 20B

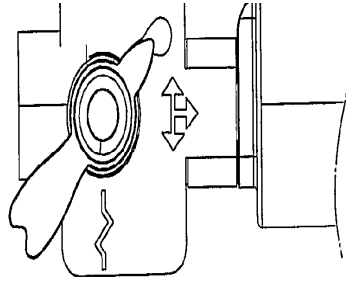


Fig. 20C

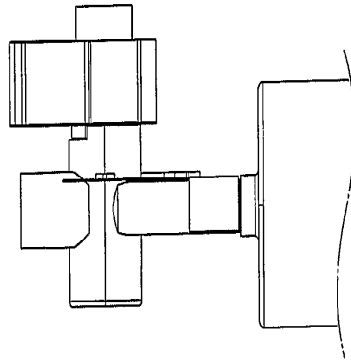


Fig. 21A

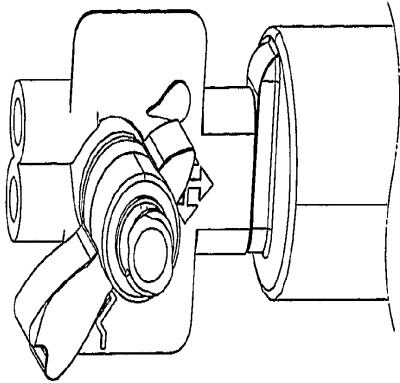


Fig. 21L

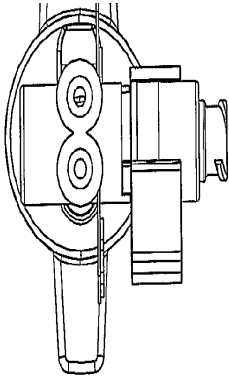


Fig. 21B

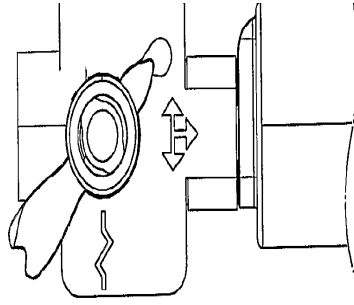


Fig. 21C

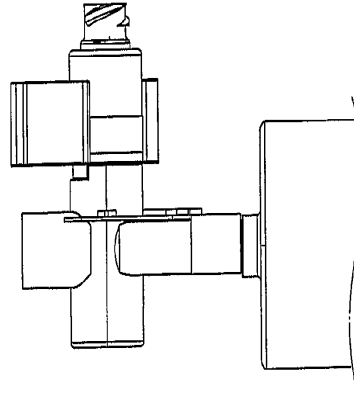


Fig. 22A

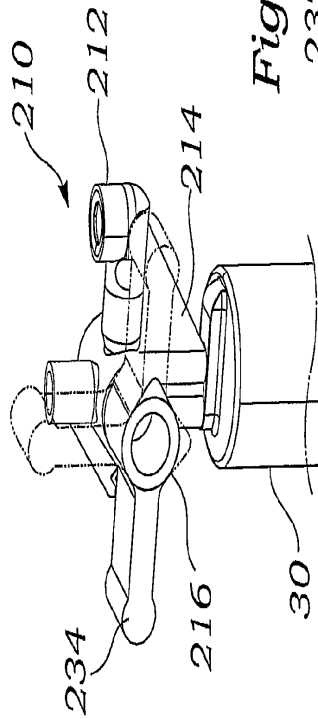


Fig. 22

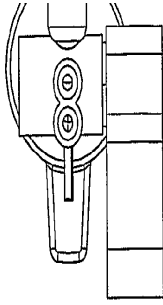


Fig. 22E

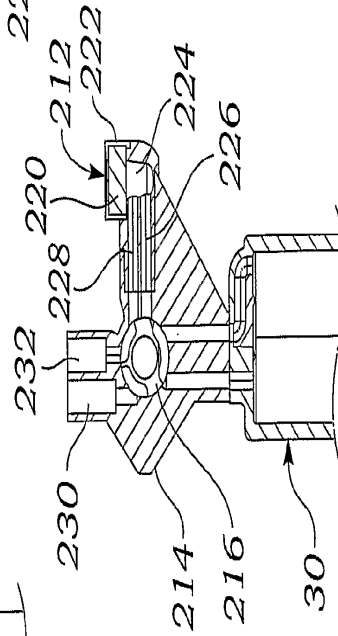


Fig. 22C

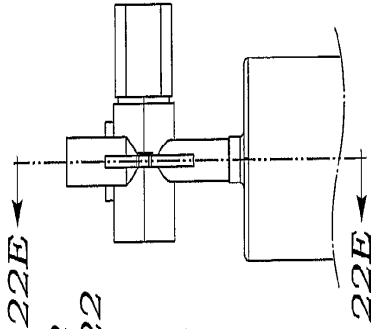
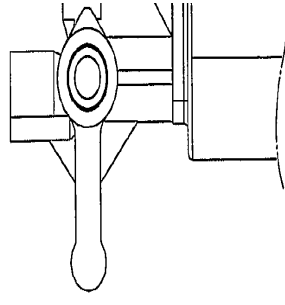


Fig. 22'



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Fig. 24D

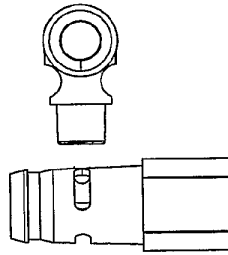


Fig. 24B

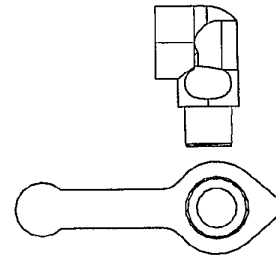


Fig. 24A

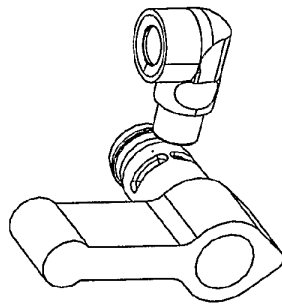
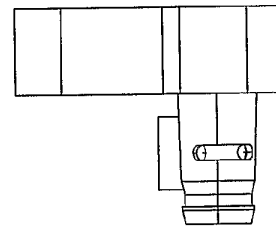


Fig. 24C



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Fig. 25D

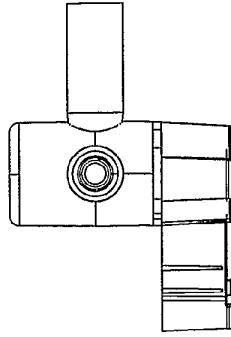


Fig. 25B

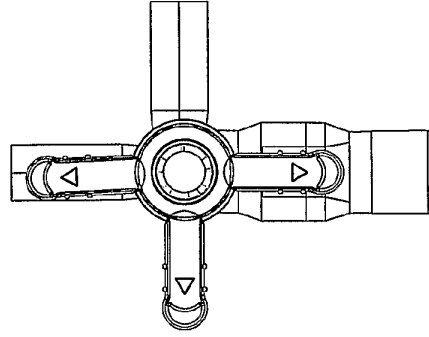


Fig. 25A

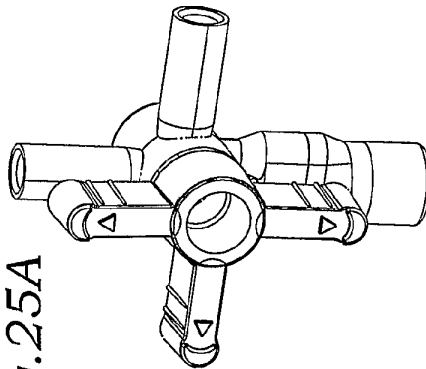
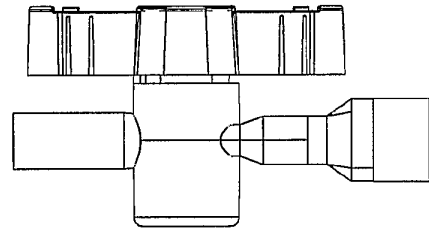


Fig. 25C



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/035832

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61B5/15

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 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.
A	US 5 643 218 A (LYNN LAWRENCE A [US] ET AL) 1 July 1997 (1997-07-01) column 13, line 42 - column 14, line 57	1-24, 30-38
A	US 5 961 472 A (SWENDSON DAVID L [US] ET AL) 5 October 1999 (1999-10-05) cited in the application column 12, line 31 - column 14, line 64	1-24, 30-38
A	EP 0 376 603 A (MEDEX INC [US]) 4 July 1990 (1990-07-04) column 3, line 53 - column 4, line 58	1-24, 30-38

☐ 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

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

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the International search

5 December 2006

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Authorized officer

Manschot, Jan

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/035832

Box 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.: 25-29
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 surgery
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 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 all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/035832

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5643218	A	01-07-1997	US 5743886 A	28-04-1998
US 5961472	A	05-10-1999	AT 309743 T	15-12-2005
			AU 732501 B2	26-04-2001
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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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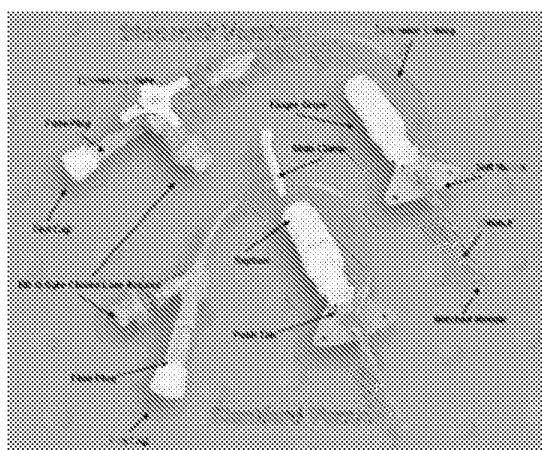


Fig. 1. — The new integrated completely closed IV catheter system (BD Nexiva™). Shown are two versions: the top one has a three-way valve to which the Q-Syte™ is attached; the bottom one, with the Q-Syte™ closed Luer Lok access. Both devices have a flow plug for venting out the air during insertion.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

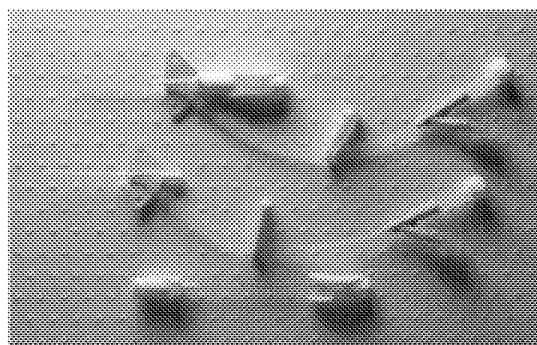


Fig. 2. — Non-activated (top) and activated (bottom) versions of the BD Nexiva™.

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 Ventlon™	Yes	No	No	No
BD Ventlon 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

<ul style="list-style-type: none"> • 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 with-

drawal, 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

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,

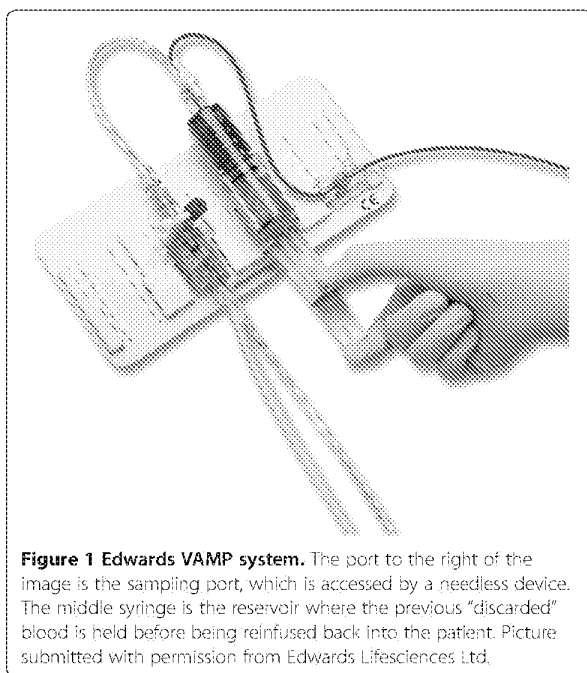
Table 1 Current studies relating to the use of blood conservation devices in critical care

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 ($p = \text{nonsignificant}$). 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



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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NCCLS simplifies the order of draw: a brief history.

Print

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The order in which tubes should be filled seems to mutate daily into increasingly creative incarnations. In fact, it mutated right out of existence last year when one workshop presenter astonished her attendees by stating, "There is no order of draw." Adding to the confusion are Internet phlebotomy sites, training manuals, certification study guides, and textbooks that perpetuate many variations.

The proper order in which blood-collection tubes should be filled is designed to prevent the carryover of additives from one tube to the next. Such carryover alters the composition of the next tube and can lead to erroneous results--with the potential to mislead physicians and invite catastrophic errors in patient management. For the record, the order of draw has been established by NCCLS--the National Committee for Clinical Laboratory Standards, which develops voluntary standards--through its consensus process with industry, government, and laboratory professionals and is published by NCCLS in document H3, Procedure for the Collection of Blood Specimens for Diagnostic Testing by Venipuncture.

The order was revised and simplified this past December to one that works for both glass and plastic tubes, regardless of whether the specimen is drawn by using a tube holder and needle assembly or syringe. To understand the necessity for the order of draw and to clarify the widespread confusion on the matter, let us examine the history on how the order came about and how it has evolved through the years.

Historical perspective

The order has its origins in the literature as early as 1977, when evidence that additive carryover occurs was first published in the American Society of Clinical Pathologists' (ASCPs') Summary Report. (1) Authors Nilda Sun and Rita Knauf at the St. Barnabas Medical Center in Livingston, NJ, reported their observation of an asymptomatic patient who had a potassium level of 25.4 mEq/L (normal 3.5-5.3 mEq/L) obtained from a nonhemolyzed specimen. Upon investigation, the authors discovered that the phlebotomist filled the lavender-stopper tube containing potassium EDTA immediately prior to filling the tube from which the elevated potassium was obtained.

The first recommendation on establishing a formal order of draw for blood collection was published in a letter to the editor of Clinical Chemistry by Roger Calam, PhD, and Marsha Cooper of St. John Hospital in Detroit, MI, in 1982. (2) Although tube manufacturer Becton Dickinson (BD) had been recommending as early as 1976 that all additive tubes be drawn after nonadditive tubes, with citrate tubes being

the first additive tube filled, Calam and Cooper postulated that a more detailed order was necessary for additive tubes. They reported five cases in which they observed spuriously abnormal potassium and calcium levels, all of which resulted when a lavender-stopper tube containing potassium EDTA was filled immediately prior to the gel tube intended for chemistry tests. When specimens were re-collected, potassium and calcium fell within normal limits. Based on these observations and those of Sun and Knoff, Calam and Cooper concluded that not only should additive tubes be drawn after nonadditive tubes, as BD had been suggesting, but that heparin, EDTA, and potassium-oxalate/sodium-fluoride tubes (gray stoppers) should have a specific "order of draw."

The reasoning for their proposed order was based on the fact that if EDTA could carryover into nonadditive tubes, it could also carryover into tubes containing other additives. Such proof suggested that the additive of any tube could also carryover into a subsequent tube, threatening the accuracy of results.

The authors proposed that heparin tubes be drawn before the EDTA tube, and EDTA tube should precede oxalate/fluoride tubes. Since oxalate/fluoride is disruptive to cell membranes, placing it subsequent to the EDTA tube prevents problems with cell morphology that might otherwise occur. Also, with the gray top drawn after the green top, neither potassium oxalate nor sodium fluoride in the gray-top tubes would contaminate sodium or potassium testing.

The order proposed by Calam and Cooper for filling additive tubes (following nonadditive tubes) was adopted by the NCCLS in 1984 in document H3-A2 as: (1) sodium-citrate tube; (2) heparin tube; (3) EDTA tube; and (4) oxalate/fluoride tube. (3)

Gel separator tubes and clot activators

The introduction of serum gel tubes (1976) and plasma gel tubes (1987) provided a convenience to specimen-processing personnel who had been required to remove the stoppers of nongel tubes after centrifugation and physically remove the serum or plasma for testing or storage. The gel tubes provided a physical barrier between the serum or plasma following centrifugation, preventing the changes that occur when serum or plasma is allowed to remain in contact with the cells for prolonged periods of time prior to testing. Serum separator tubes contain a clot activator (glass or silica particles) to facilitate clotting. Although clot activators may shorten the time it takes for the specimen to clot, manufacturers stress that such tubes facilitate complete clotting, not rapid clotting, yielding serum that is less likely to contain fibrin strands that can interfere in testing.

Historically, tubes with anticoagulants (e.g., EDTA) or preservatives (e.g., sodium fluoride) were referred to as "additive tubes." In 1998, it was proposed that separator tubes containing gels and either a clotting activator or an anticoagulant also be considered as additive tubes. (4) The NCCLS incorporated these tubes into the order of draw in its 1998 revision (H3-A4). (5) The order evolved with the gel tubes (serum and plasma separators) following the citrate tube (blue stopper):

1. blood-culture tubes,
2. nonadditive tube,
3. additive tubes (in the following order):
 - a. sodium-citrate tube,
 - b. gel separator tube,
 - c. heparin tube,
 - d. EDTA tube, and
 - e. oxalate/fluoride tube.

Since possible carryover of the clot activator could conceivably alter results, a gel tube with a clot activator had to be drawn after the blue top. Although not spelled out, the serum gel tube should be drawn before the plasma gel tube, as the latter often contains lithium heparin, which could affect the accuracy of a patient's lithium test in the serum tube.

If required, a plastic red-stopper tube (plastic tubes contain a clot activator) can precede a heparin (green top) or EDTA (lavender top) tube without concern for carryover. The logic is that any carryover of the clot activator into tubes other than blue tops is irrelevant, since carryover should be neutralized by the excess anticoagulant. In contrast, carryover of a clot activator into a sodium citrate tube (blue top) could interfere with clotting factors, leading to inaccurate results.

Some facilities maintain the necessity for a different order for syringe transfer because not all syringe draws go quickly and, therefore, the potential exists for clotting to occur in the syringe prior to blood transfer to successive tubes. (6,7) To prevent clotting within the syringe, an order is implemented that fills all additive tubes first and then the nonadditive tubes. NCCLS consensus concluded, however, that the potential for carryover from the needle of the syringe had the potential to be a more significant problem than any clotting that might take place in the syringe during a properly performed venipuncture. Therefore, the 1998 NCCLS revision also recommended that the same order of draw be followed when transferring blood specimens from a syringe to multiple blood-collection tubes.

Plastic tubes

Motivated by increasing concern over broken-glass exposures, high biohazardous waste-disposal costs, and Occupational Safety and Health Agency (OSHA) guidelines mandating substitution, many laboratories began switching from glass collection tubes to plastic (see "Richard Fairfax of OSHA Talks About the Bloodborne Pathogens Standard" February 2003 MLO, p. 32.) This industry-wide transition from glass to plastic necessitated a modification to the order of draw. Plastic serum tubes are now positioned the same as gel separator tubes, which contain a clot activator. The revised order,* published in December 2003, is now as follows:

1. blood-culture tubes,
2. sodium-citrate tube (e.g., blue-stopper),
3. serum tubes with or without clot activator, with or without gel separator (e.g., red-, gold-, speckled-stopper),
4. heparin tubes with or without gel (e.g., green-stopper),
5. EDTA tubes (e.g., lavender-stopper), and
6. glycolytic inhibitor (e.g., gray-stopper). (8)

In the revised standard, NCCLS recognizes that some facilities may still be using glass serum tubes without a clot activator to serve as a waste tube before collecting special coagulation assays. Although the revised order functions well regardless of the presence of a clot activator in the facility's serum tube, a provision within H3-A5 affords the option of keeping the nonadditive serum tube before the citrate tube in the following passage: "The order of draw has been revised to reflect the increased use of plastic blood-collection tubes. Plastic serum tubes containing a clot activator may cause interference in coagulation testing. Glass nonadditive serum tubes may be drawn before the coagulation tube."

The NCCLS order of draw has gone through several revisions dictated by technology, publication, and common sense. The latest revision should make it easier for educators and trainers to teach the order of draw and prevent additive carryover, which can affect patient results.

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RELATED ARTICLE: Alternatives to current order of draw

Some facilities have conducted internal studies that support a variation to NCCLS' order of draw. When reliable documentation supports an alternative order, the facility's protocol should take precedence. The Mayo Clinic in Rochester, MN, developed its own when it found that calcium levels drawn early in the order of draw can be significantly different than those drawn later in the order. Since immediate tourniquet removal is not always feasible (nor appropriate for ionized calcium collection), phlebotomists there follow an order of draw designed to protect against potentially erroneous calcium results, which includes a separate order of draw for syringes. In addition, tubes for trace-metal analysis are always first in order of draw at Mayo, since such specimens have been found to be contaminated by penetration of the sheathed back-end of the needle into any nontrace metal tube stoppers. Mayo's current order of draw is:

1. trace-metal collection tube (nonadditive)
2. gel separator tube (glass and plastic)
3. nongel serum tube (glass and plastic)
4. citrate tube
5. heparin tube
6. EDTA tube

7. oxalate/fluoride tube
8. ACD tube

Mayo also advocates a previous NCCLS order of dispensing from a syringe, i.e., tubes containing anticoagulants are dispensed first in order to minimize microclot formation in the syringe.

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Better Blood Transfusion

There has been renewed interest in the safety and effectiveness of transfusion practice in recent years because of:-

- data from the Serious Hazards of Transfusion (SHOT) scheme showing that the safety of transfusion practice in hospitals should be improved,
- increases in the cost of blood associated with the introduction by Blood Services of safety measures such as universal leucocyte-depletion of blood components and nucleic acid testing,
- concerns about the transmission of variant Creutzfeldt-Jakob disease (vCJD) by blood transfusion and the potential

effect that measures to minimise this risk might have on the blood supply.

Research is being carried out both on new approaches for the safety of the transfusion process, and to determine the appropriate indications for transfusion. The use of blood components only when there is a real clinical need is arguably the best way of avoiding the risks of transfusion. These issues apply to critical care as much if not more than to other clinical areas where transfusions are regularly used.

Risks of transfusion and new approaches to reducing the risks

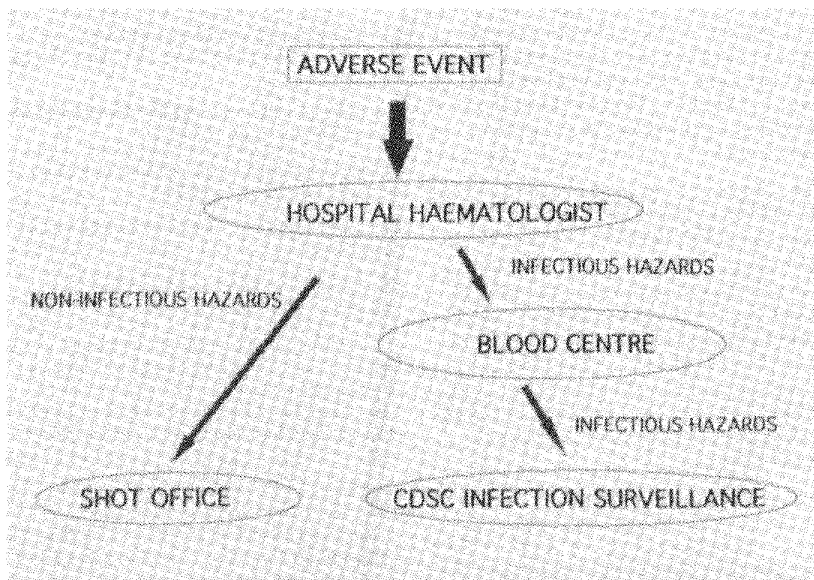
The Serious Hazards of Transfusion (SHOT) scheme was established in 1996 to collect reports of major adverse events associated

with the transfusion of blood components in the UK (1). Figure 1 shows the mechanism for reporting. 92% of eligible hospitals participated in 2001/02.

It is striking that the most frequent event is incorrect blood transfused (IBCT). Immune complications of transfusion are all represented to varying degree, but episodes of transfusion-transmitted infection are infrequent. Recent figures from the National Blood Service indicate that the risk of HIV transmission has been reduced to less than 1 in 8 million (less than the risk of being struck by lightning), the risk of hepatitis B transmission is 1 in 900,000, and the risk of HCV has decreased to less than 1 in 30 million since the introduction of nucleic acid testing.

The increase in reports over the 5 years of the SHOT scheme is due to an increase in incidents of IBCT. This may be due to better reporting or a real increase in the number of incidents; the latter is thought to be less likely, but cannot be excluded. IBCT is defined as an episode where a patient was transfused with blood which did not meet the appropriate requirements or was intended for another patient. Out of the 699 incidents reported between 1996/97 and 2000/01, there were 161 ABO incompatible transfusions (resulting in 9 deaths and 37 cases of major morbidity), 73 RhD incompatible transfusions, and 37 cases involving other red cell incompatibilities. 195 wrong transfusions were by chance ABO and RhD compatible. Analysis of the distribution of errors causing IBCT shows that they occur throughout the transfusion process. The most frequent site of error is at the time of collection and/or

Figure 1. Mechanism of SHOT reporting.
(CDSC- Communicable Disease Surveillance Centre)





administration of blood (55%), followed by errors in the laboratory (28%), and errors at the time of request, sampling or prescription of blood (13%). The SHOT data have clearly demonstrated that multiple errors often contribute to IBCT; in 2001/02, 54% of IBCT cases involved multiple errors. IBCT was found to occur in all sites where blood is used, with both elective and emergency transfusion, and to involve many types and grades of staff.

In over 70% of cases, there was minor or no morbidity. However, 14% of incidents were associated with major morbidity e.g. admission to an intensive care unit, renal dysfunction, or confirmed infection. The death of the patient was definitely attributed to transfusion in 37 cases (3%), and was possibly associated with transfusion in a further 32 cases (2%). The most frequent cause of death was transfusion-associated graft-versus-host disease (TA-GvHD) (13 cases). The most frequent cause of death or major morbidity was IBCT (71 cases) followed by transfusion-related acute lung injury (TRALI) (67 cases).

TRALI is a complication of transfusion particularly relevant to critical care. It is severe acute reaction characterized by respiratory distress, hypoxia and pulmonary infiltrates soon after transfusion with no other apparent cause. In many cases, preformed leucocyte antibodies have been found in the plasma of the donors, and these are thought to cause pulmonary leucostasis and leucocyte activation resulting in capillary leak and pulmonary damage. TRALI has been reported to occur after the transfusion of all types of blood components, but is particularly likely to occur with those with a large volume of plasma such as fresh frozen plasma (FFP). TRALI is clinically indistinguishable from acute respiratory distress syndrome (ARDS), and the occurrence of ARDS with a possible association with transfusion provides grounds to consider TRALI as the cause. Unlike ARDS, TRALI is self-

limiting, and there is usually clinical improvement within 48–96 hours provided prompt respiratory support is provided. The production of FFP from only male donors, and reducing the volume of plasma in platelet concentrates are under consideration as measures to reduce the risk of TRALI.

The SHOT scheme has no mechanism for implementing its recommendations, and is reliant on other organisations to do so. Some parallel initiatives have supported the work of the SHOT scheme, including the development of national guidelines for transfusion practice by the British Committee for Standards in Haematology (BCSH), for example on the administration of blood (2). The SHOT scheme has recommended that further research should be carried out into information technology solutions for safer transfusion. An example is the use of barcode technology for patient identification and for the confirmation that the right blood will be transfused. A barcode patient identification system was recently found to simplify the clinical transfusion process and improve practice (3). Further work is required on the development of such systems for transfusion, and also for other hospital procedures requiring patient identification such as drug administration. These systems are particularly relevant for clinical areas such as critical care where the patient cannot verbally confirm their identification.

SHOT has also recommended the introduction of new strategies for reducing the risk of bacterial contamination. New methods are being introduced for cleaning the arms of blood donors and for diverting the initial 20ml of donor blood into a pouch for laboratory testing, and bacterial testing of platelet concentrates is being considered.

Measures to encourage the appropriate use of blood components and blood products

Concerns about blood safety have probably been the main driver for changes in transfusion practice in recent years. The threat of transfusion-transmitted infection has outweighed other risks of transfusion, and maybe it is time to 'realign transfusion safety with risks' using data from schemes such as SHOT about the observed risks of transfusion (4). At a clinical level, evidence does influence practice, but the level of evidence is critical. Guidelines and recommendations from experts appear to have limited impact, but level 1 evidence from systematic reviews or randomised controlled trials can have a major impact. For example, in the field of critical care, the publication of a systematic review on the absence of benefit of the use of albumin and possible increased mortality rapidly reduced its use (5), and a randomised controlled trial on transfusion triggers for red cell transfusion resulted in a change in practice in many centres (6). Greater efforts are needed to develop a sound evidence-base for the use of blood components and blood products in critical care as well as other clinical areas.

Better Blood Transfusion is an initiative led by the UK Chief Medical Officers to improve the safety and effectiveness of transfusion practice. Its output has been two Health Service Circulars (HSCs) setting out a number of recommended actions to hospital Chief Executives (7, 8). An audit of the implementation of the HSC 1998/224 Better Blood Transfusion showed that most hospitals had established Hospital Transfusion Committees (HTCs), were participating in the SHOT scheme, and had protocols for the administration of blood (9). However, there was evidence of poor provision of training for clinical staff and patient information, few protocols for the appropriate use of blood, few

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audits of transfusion practice, and limited use of outologous transfusion. The HSC 2002/009 Better Blood Transfusion – Appropriate Use of Blood was published in July 2002, and it included an action plan and an ongoing programme for Better Blood Transfusion to be taken forward in each Trust. It recommended the establishment of a Hospital Transfusion Team (HTT) in each Trust. The HTT is tasked with implementing the agreed actions recommended by the HTC; it should be led by a senior doctor interested in transfusion medicine (not necessarily a haematologist) and include one or more Transfusion Nurses (depending on the size of the Trust), senior blood bank laboratory staff and specialists who work in clinical areas with large or high risk blood usage. It should be provided with managerial, information technology, and administrative support. The main work of the HTT and HTC is directed to:-

- the development and implementation of local policies for safe and appropriate transfusion based on national guidelines, and the use of alternatives to blood where appropriate,
- the provision of training for the many staff involved in transfusion,
- the provision of better information for patients.

The Chief Medical Officer's National Blood Transfusion Committee (NBTC) was established in England in 2001 (for details, see www.doh.gov.uk/blood/nbtrcommittee.htm). It provides a potentially powerful framework through its Regional Transfusion Committees for improving transfusion practice and supporting the work of the HTCs. It oversees the national Better Blood Transfusion initiative, and acts as the Steering Group for an initiative for national comparative audit of clinical transfusion practice based on an earlier pilot scheme (10). The NBTC reviews the

findings of the SHOT scheme, and supports its recommendations. One of its main roles is to provide educational material for hospitals and patients, for example it has recently developed a national patient information leaflet, recommendations on the resources to implement Better Blood Transfusion, and an audit tool for the use of blood (available on www.doh.gov.uk/bbr2). Recommendations on strategies for the avoidance of transfusion are in preparation. Specific measures which could be considered in critical care practice include better compliance with evidence-based triggers for transfusion, greater use of near patient testing to determine the need for transfusion, and minimising blood loss due to sampling. ■

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- (1) Notify the designated first-aid trained personnel.
- (2) Where practical, lay the patient flat or lower his/her head and arms, if the patient is sitting.
- (3) Loosen tight clothing.
- (4) The use of ammonia inhalants may be associated with untoward effects and is not recommended.

11.8.2 Nausea

The procedure for dealing with a patient who is experiencing nausea is to:

- (1) Make the patient as comfortable as possible.
- (2) Instruct the patient to breathe deeply and slowly.
- (3) Apply cold compresses to the patient's forehead.
- (4) Notify the designated first-aid trained personnel.

11.8.3 Vomiting

The procedure for dealing with a patient who vomits is to:

- (1) Give the patient an emesis basin or carton, and have tissues ready.
- (2) Give the patient water to rinse out his/her mouth.
- (3) Notify the designated first-aid trained personnel.

11.8.4 Convulsions

The procedure for dealing with a patient who is having convulsions is to:

- (1) Prevent the patient from injuring himself/herself. Do not restrain the movements of the patient's extremities completely, but try to prevent him/her from being injured.
- (2) Notify the designated first-aid trained personnel.

11.8.5 Incident Reports

Incident reports should be filed according to institutional policy.

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NCCLS consensus procedures include an appeals process that is described in detail in Section 8 of the Administrative Procedures. For further information, contact the Executive Offices or visit our website at www.nccls.org.

Summary of Comments and Subcommittee Responses

H3-A4: Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fourth Edition

General

1. NCCLS has inconsistencies in their own publications (H3 and H21) when it comes to the order of draw for coagulation testing relative to tissue thromboplastin contamination and procurement of a “discard tube.” In performing intra-laboratory studies at our institution and sister institutions, results showed no significant clinical or statistical significance on any of the assays between each of the specimen tubes performed at each individual laboratory. Also, our results indicated that NCCLS guidelines for obtaining a second tube when performing coagulation testing should be eliminated when the revised document is published.
- **The text has been revised (see Section 8.10.2), including the order of draw, and several notes have been added to address the use of discard tubes for coagulation test collection. The next version of H21—*Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays* is due to be released by the end of 2003. The documents are now consistent.**

Section 7.9.3.4, Intravenous Therapy (Now Section 8.6.7.4)

2. The text of this section states, “Optimally, specimens should not be collected from an arm with an intravenous site. If this is impossible the attending physician should be consulted (see Section 10.3). Blood should never be collected from above any active intravenous site (see Section 10.6). We would like a clearer definition of what is considered to be “active.” What defining factors are present that would classify an “active” intravenous site?
- **The term “active” has been removed from the text. The text in Sections 8.6.7.4 and 11.6 has been revised to describe the procedure for specimen collection in relation to intravenous fluids.**

Section 7.13.3.3, Coagulation Testing (Now Section 8.10.3)

3. The text of this section states, “if only a coagulation tube is drawn for routine coagulation testing (APTT and PT tests) the first tube drawn may be used for testing.” This statement has raised some discussion regarding the definition of the phrase “routine coagulation testing.” Does this include coumadin patient samples?
- **Specimens collected from patients on warfarin sodium (Coumadin™) are considered for routine coagulation testing.**

Section 10, Special Situations (Now Section 11)

4. H3-A4 does not list recommendations for obtaining venipuncture specimens during blood transfusions. Information on this topic would be greatly appreciated.
- **The directions outlined in Section 11.6 should be followed during transfusions as it is described for intravenous fluids.**

Summary of Delegate Comments and Working Group Responses

H3-A5: *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition*

General

1. Nothing was included about pain management (EMLA, coldspray, etc.) or age-specific consideration on developmental stages of children. I can send you what we have if you like.
- **The working group recognizes the availability of pain reducing techniques. Topical sprays and treatments are available and are used at the discretion of each institution.**

Age-specific considerations are outside the scope of this document. Please refer to the current edition of NCCLS document H4—*Procedures and Devices for the Collection of Diagnostic Blood Specimens by Skin Puncture*.

2. Add a Section 11.2.6, RNA Specimen. Since RNA is unstable, the whole blood should be transported to the laboratory at 2 to 25 °C within six hours of collection.

References: de Gerbehay A-I, et al. Stable hepatitis C virus RNA detection by RT-PCR during four days storage. *BMC Infectious Diseases*. 2002;2:22, and Halfon P, et al. Impact of various handling and storage conditions on quantitative defection of hepatitis C virus RNA. *J Hepatol*. 1996;25:307-311.

- **This comment is more related to specimen handling than collection and is beyond the scope of this document. This comment will be considered during the revision of NCCLS document H18-A2—*Procedures for the Handling and Processing of Blood Specimens; Approved Guideline*.**

Foreword

3. Page vii should include hemolysis and clotting of samples, as these are common problems with hematology or coagulation samples. “The errors that can occur during the collection and handling of blood specimens are potentially numerous (e.g., inaccurate identification of specimens, the use of incorrect anticoagulant, the formation of hematomas, hemoconcentration).”
- **The text has been revised to include specimen hemolysis and improper handling of anticoagulants.**

Section 8. Venipuncture Procedure

4. Consider switching steps 14 and 15 so that bandaging occurs after specimens are labeled, not before. This helps assure that specimen labeling will occur before leaving the patient’s side. It also accommodates situations in which the patient assists in applying pressure while the phlebotomist labels tubes.
- **The working group appreciates the comment; we believe, however, that the order is correct as written. The text in Section 8.15 emphasizes the need to label the tube before leaving the side of the patient.**
5. Between steps 5 and 6, add the following: “Inquire as to patient’s sensitivity to latex products.” Step 7, change as follows: “Put on appropriate gloves based on patient’s response to Step 6.”
- **The working group agrees with the comment. The text of step 3 has been revised as follows: “Verify patient’s diet restrictions, as appropriate, and inquire if the patient has a latex sensitivity. Select appropriate gloves and tourniquet.”**
6. Modify step 6 to new “step 6: Inquire on patient’s allergy to latex products.” Also add: “Due to the prevalence of latex sensitivity, the phlebotomist should inquire as the patient’s sensitivity to latex products (tourniquet and gloves.)”
- **The text of Step 3 and Section 8.3 has been revised to include asking the patient if he/she has a latex sensitivity. The text in Section 8.6 has been revised to refer the reader to Section 7.7.**
7. The patient should be asked to open his/her hand just when entering the vein, therefore eliminating some of the pain a tense closed fist may cause. Also, recommend performing venipuncture using the correct order of draw.
- **In response to this comment, the text of step 9 has been revised as follows: “Perform venipuncture; once blood flow begins, request patient to open hand.” Step 10 has been revised to recommend the use of the correct order of draw.**

8. Following the removal of the needle, pressure should be applied to the venipuncture site (either by the patient or phlebotomist).

- **In response to this comment, the text of step 14 has been revised as follows: “Apply pressure to the site, making sure bleeding has stopped, and then bandage the arm.”**

Section 8.1.1, Information for Test Request Form

9. “May include” should be utilized.

- **The working group believes that the test request form information listed should be included.**

Section 8.1.2, Accessioning Blood Bank Specimens

10. Neither AABB nor CAP requires “time of collection” on the specimen tube label.

- **Time of collection is important for some specimens (e.g., therapeutic drug monitoring). The subcommittee confirmed that AABB does not require “time of collection” on the specimen tube label. The text, “Blood bank specimens must be labeled according to the standards set by the American Association of Blood Banks (AABB),” has been incorporated into Section 8.15, Label Blood Collection Tubes and Record Time of Collection. The remainder of Section 8.1.2 has been deleted.**
11. This passage is more about patient identification and labeling specimens than accessioning. Passages are important, but seem out of place. Consider moving the passage on identifying blood bank patients to Section 8.2 (“Step 2: Approach and Identify the Patient.”) and the passage about labeling to Section 8.15 (“Step 15: Label Blood Collection Tubes and Record Time of Collection”).
- **See response to comment 10.**

Section 8.2.3, Patient Who Is Semiconscious, Comatose, or Sleeping

12. This passage does not address identification and is out of place. Consider moving to Section 8.5.4.

- **The location of this text is appropriate. Section 8.2 addresses both approaching and identifying the patient. The following has been added to the end of the paragraph: “If unable to identify the patient, then contact the nurse or physician.”**

Section 8.2.4, Patient Who Is Unconscious, Too Young, Mentally Incompetent, or Does Not Speak the Language of the Phlebotomist

13. The first bullet states, “Ask the nurse, a relative, or a friend to identify the patient by name, address, and identification number and/or birth date.” This is inconsistent with Section 8.2.2, re: asking for patient’s address and identification number. Suggest changing “and” to “or” for consistency with step 1 of 8.2.2.

- **The text in Section 8.2.4 has been revised for consistency with Section 8.2.2.**

Section 8.4.1, Supplies

14. “Inspect all supplies for possible defects” should include inspection of expiration dates on blood collection tubes.

- **The text has been revised to include applicable expiration dates during inspection of supplies.**

15. Supplies, sharps, or other disposal container is missing from the list (as discussed in Section 8.13). This should be available at the bedside for safe disposal.

- **The following bullet point has been added to the list: “Sharps container, consistent with OSHA regulations.”**

16. Supplies such as tubes and needles should be checked before use to ensure they are not outdated. Sterile conditions or tube vacuum could be lost in old supplies. NCCLS document H4-A discusses tube stability and dating; H1-A4 discusses expiration date. Therefore, this step should be added to the collection procedure.

- **See response to comment 13.**

Section 8.6.3, Blood Pressure Cuff

17. In Section 7.7 the blood pressure cuff is said to be inflated to 40 mmHg. However, in Section 8.6.3 it is said that a blood pressure is taken first (an activity performed by NO phlebotomists I know) and maintained below the diastolic pressure of the patient. I would recommend using the specific 40 mm Hg found in Section 7.7 and replace the language in Section 8.6.3 with the same.

- **The text has been revised as recommended. The following text has been added to replace the previous text: “If a blood pressure cuff is used as a tourniquet, inflate it to 40 mm Hg.”**

Section 8.6.5, Select Vein

18. “Brachial” is misspelled in Figure 1.

- **The spelling error in Figure 1 has been corrected.**

Section 8.7, Step 7: Put on Gloves

19. Step 7: Add the following after the existing sentence: “...is performed. The type of gloves (latex, vinyl or nitrile) used for venipuncture will depend on the patient’s and/or phlebotomist’s sensitivity to latex products.” General note—As both a patient and laboratorian, I know the importance of covering the issue of latex sensitivity with both patients and the phlebotomists. I highly recommend that you incorporate the information presented here into the document.

- **The text has been revised as follows: “The phlebotomist must put gloves on before the venipuncture is performed, for each patient, with consideration for latex sensitivity as discussed in Section 7.3.”**

Section 8.9.1, Venipuncture Procedure When Venous Blood Collection Tubes Are Used

20. The illustration on page 14 is very primitive and would be improved if the proper angle included a view of the needle bevel up just as the needle enters the skin.

- **The illustrations (Figures 2 and 3) have been replaced with comparable photographs.**

Section 8.9.3, Fill the Tubes If Syringe and Needle Are Used

21. The third bullet suggests a straight needle be applied to the syringe after removing the winged collection set. Consider substituting “attach a 19- to 21-gauge sterile needle” with “attach a safety transfer device.”

- **The text of the third bullet has been revised as follows: “To transfer the blood from the syringe to a venous blood collection tube, activate the safety feature of the needle or winged blood collection set used to withdraw the specimen, remove and discard the needle or winged collection set, and apply a safety transfer device.”**

22. The fourth bullet seems to define the third bullet. Consider combining the two.

- **The working group agrees with the comment and has deleted the fourth bullet.**

23. The fifth bullet is not necessary in light of the third bullet. If standards are being followed, a transfer device protects the user, and holding the tubes should be safe.

- **The fifth bullet has been deleted as suggested.**

Section 8.9.4, Blood Specimen That Cannot Be Obtained

24. Consider making the passage about trying another tube into a bullet. Consider differentiating between probing and a calculated needle relocation in an additional bullet so that the section is rewritten as follows:

- ▶ Try another tube to ensure the tube selected is not defective.
- ▶ Change the position of the needle. If the needle has penetrated too far into the vein, pull it back a bit. If it has not penetrated far enough, advance it farther into the vein. Rotate the needle half a turn.
- ▶ Lateral needle relocation should be attempted only if the phlebotomist has a high degree of confidence that so doing will access the vein successfully without risking injury to the patient. Lateral needle relocation should never be attempted in an effort to access the basilic vein, since nerves and the brachial artery are in close proximity.

- ▶ Manipulation other than that recommended above is considered probing. Probing is not recommended. Probing is painful to the patient. In most cases, another puncture in a site below the first site (or use of another vein on the other arm) is advisable.
 - ▶ It is not advisable to attempt a venipuncture more than twice. If possible, have another person attempt to draw the specimen or notify the physician.
- **The following text has been added to the first bullet point: “Lateral needle relocation should never be attempted in an effort to access the basilic vein, since nerves and the brachial artery are in close proximity.”**

Section 8.10.2, Glass and Plastic Venous Blood Collection Tubes

25. Consider deleting tube 4: gel serum separator tube. Since gel does not carryover, its presence or absence should not affect the order of draw. It seems more fitting for the second italicized paragraph to immediately follow the order of draw than the first paragraph.
- **Gel serum separator tube has been deleted from the fourth position on the order of draw. The third position has been revised as follows: “Serum tube with or without clot activator, with or without gel (e.g., red closure).”**
- The italicized paragraphs have been reorganized as suggested; the note regarding the revised order of draw appears immediately following the order of draw.**

Section 8.13, Step 13: Remove and Dispose of the Needle

26. Removal of a needle (after the safety feature is activated) is necessary and acceptable to OSHA if applying a safety transfer device. Consider modifying to read: “Needles should not be resheathed, bent, broken, or cut, nor should they be removed from disposable syringes unless attaching a safety transfer device...”
- **The text of the third sentence has been revised as follows: “Needles should not be resheathed, bent, broken, or cut, nor should they be removed from disposable syringes unless attaching a safety transfer device prior to disposal.”**

Section 8.14.2, Continued Bleeding

27. “When a patient continues to bleed,” indicates that it is inevitable. Consider revising to “If a patient continues to bleed or a hematoma develops, ...”
- **The text has been revised as recommended. The first paragraph now reads as follows: “If a hematoma develops or bleeding persists longer than five minutes, a nurse should be alerted so that the attending physician can be notified.”**

Section 8.15, Step 15: Label Blood Collection Tubes and Record Time of Collection

28. Step 15: Consider revising the paragraph after the bullet list to accommodate handwritten identification of tubes. Suggested revision: “The label must be attached to the tube or the tube inscribed with complete information before leaving the side of the patient”
- **The text has been revised as recommended. The following text has been added to the second paragraph: “Alternatively, the manufacturer’s tube label can be inscribed with the patient’s complete information.”**
29. Tubes should be labeled in accordance with the laboratory requirements. These may not meet all requirements for all laboratories.
- **The text in this section has been revised in response to comment 9.**

Section 9, Venipuncture in Children and Difficult Collections

30. Passage states, “If a venipuncture is done on a child younger than one year of age, the site should be limited to superficial veins.” As opposed to what? This statement is unclear.
- **The first sentence has been revised for clarity. The revision is as follows: “If a venipuncture is requested on a child younger than one year of age, the phlebotomist should consult with the physician or follow institutional policy.”**

Section 9.2, Equipment

31. Consider modifying the range of needles to be used on pediatrics from 20-23 to 22-23 for patient comfort unless platelet aggregation studies are required.

- The needle gauge range has been revised as suggested. The following text has also been added: “For pediatric patients, through the age of 16, larger gauge needles may be appropriate.”

Section 11.6, Intravenous Fluids

32. Add the following reference: Savage R, ed. Q&A column. *CAP Today*. 2002;16(4):102-103.

- The recommended reference, regarding performance of venipunctures above intravenous sites, has been added as suggested.

NOTES

The Quality System Approach

NCCLS subscribes to a quality system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents through a gap analysis. The approach is based on the model presented in the most current edition of NCCLS HS1—*A Quality System Model for Health Care*. The quality system approach applies a core set of “quality system essentials (QSEs),” basic to any organization, to all operations in any healthcare service’s path of workflow. The QSEs provide the framework for delivery of any type of product or service, serving as a manager’s guide. The quality system essentials (QSEs) are:

Documents & Records	Equipment	Information Management	Process Improvement
Organization	Purchasing & Inventory	Occurrence Management	Service & Satisfaction
Personnel	Process Control	Assessment	Facilities & Safety

H3-A5 addresses the quality system essentials (QSEs) indicated by an “X.” For a description of the other NCCLS documents listed in the grid, please refer to the Related NCCLS Publications section on the next page.

Documents & Records	Organization	Personnel	Equipment	Purchasing & Inventory	Process Control	Information Management	Occurrence Management	Assessment	Process Improvement	Service & Satisfaction	Facilities & Safety
				X H1	X T/DM6						X M29

Adapted from NCCLS document HS1—*A Quality System Model for Health Care*.

Path of Workflow

A path of workflow is the description of the necessary steps to deliver the particular product or service that the organization or entity provides. For example, GP26-A2 defines a clinical laboratory path of workflow which consists of three sequential processes: preanalytical, analytical, and postanalytical. All clinical laboratories follow these processes to deliver the laboratory’s services, namely quality laboratory information.

H3-A5 addresses the clinical laboratory path of workflow steps indicated by an “X.” For a description of the other NCCLS documents listed in the grid, please refer to the Related NCCLS Publications section on the next page.

Preanalytic					Analytic		Postanalytic	
Patient Assessment	Test Request	Specimen Collection	Specimen Transport	Specimen Receipt	Testing Review	Laboratory Interpretation	Results Report	Post-test Specimen Management
X	X	X C38 H4 HJ1 H21	X C38 H4 HJ1 H21	X H18	X T/DM6			

Adapted from NCCLS document HS1—*A Quality System Model for Health Care*.

Related NCCLS Publications*

- C38-A** **Control of Analytic Variation in Trace Element Analysis; Approved Guideline (1997).** This document provides guidelines for patient preparation, specimen collection, transport, and processing for the analysis of trace metals in a variety of biological matrices.
- H1-A4** **Evacuated Tubes and Additives for Blood Specimen Collection—Fourth Edition; Approved Standard (1996).** This document provides requirements for blood collection tubes and additives.
- H4-A4** **Procedures and Devices for the Collection of Diagnostic Blood Specimens by Skin Puncture; Approved Standard—Fourth Edition (1999).** A consolidation of H4-A3 and H14-A2, this standard provides detailed descriptions and explanations of proper collection techniques, as well as hazards to patients from inappropriate specimen collection by skin puncture procedures.
- H11-A3** **Procedure for the Collection of Arterial Blood Specimens; Approved Standard—Third Edition (1999).** *American National Standard.* This standard describes principles of collecting, handling, and transporting arterial blood specimens. The document is aimed at reducing collection hazards and ensuring integrity of the arterial specimen.
- H18-A2** **Procedures for the Handling and Processing of Blood Specimens; Second Edition—Approved Guideline (1999).** This guideline addresses multiple factors associated with handling and processing specimens, as well as factors that can introduce imprecision of systematic bias into results.
- H21-A3** **Collection, Transport, and Processing of Blood Specimen for Coagulation Testing and General Performance of Coagulation Assays; Approved Guideline—Third Edition (1998).** This guideline contains procedures for collecting, transporting, and storing blood; processing blood specimens; storing plasma for coagulation testing; and provides general recommendations for performing the tests.
- M29-A2** **Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline—Second Edition (2001).** This document provides guidance on the risk of transmission of hepatitis viruses and human immunodeficiency viruses in any laboratory setting; specific precautions for preventing the laboratory transmission of blood-borne infection from laboratory instruments and materials; and recommendations for the management of blood-borne exposure.
- T/DM6-A** **Blood Alcohol Testing in the Clinical Laboratory; Approved Guideline (1997).** This document gives technical and administrative guidance on laboratory procedures related to blood alcohol testing.

* Proposed- and tentative-level documents are being advanced through the NCCLS consensus process; therefore, readers should refer to the most recent edition.

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Canadian Standards Association
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Innovation for Reducing Blood Culture Contamination: Initial Specimen Diversion Technique

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ABSTRACT

We hypothesized that diversion of the first milliliter of venipuncture blood—the initial specimen diversion technique (ISDT)—would eliminate incompletely sterilized fragments of skin from the culture specimen and significantly reduce our blood culture contamination rate (R). We studied our hypothesis prospectively beginning with our control culture (C) definition: one venipuncture with two sequentially obtained specimens, 10 ml each, the first specimen (M_1) for aerobic and the second (M_2) for anaerobic media. The test ISDT culture (D) was identical, with the exception that each was preceded by diverting a 1-ml sample (D_S) from the same venipuncture. During the first of two sequential 9-month periods, we captured D versus C data ($n = 3,733$), where D_{MXR} and C_{MXR} are R for D and C specimens. Our hypothesis predicted D_S would divert soiled skin fragments from D_{M_1} , and therefore, C_{M_1R} would be significantly greater than D_{M_1R} . This was confirmed by C_{M_1R} (30/1,061 [2.8%]) less D_{M_1R} (37/2,672 [1.4%]; $P = 0.005$), which equals 1.4%. For the second 9-month follow-up period, data were compiled for all cultures ($n = 4,143$), where AD_{MXR} is R for all (A) diversion specimens, enabling comparison to test ISDT. Our hypothesis predicted no significant differences for test ISDT versus all ISDT. This was confirmed by D_{M_1R} (37/2,672 [1.4%]) versus AD_{M_1R} (42/4,143 [1.0%]; $P = 0.17$) and D_{M_2R} (21/2,672 [0.80%]) versus AD_{M_2R} (39/4,143 [0.94%]; $P = 0.50$). We conclude that our hypothesis is valid: venipuncture needles soil blood culture specimens with unsterilized skin fragments and increase R , and ISDT significantly reduces R from venipuncture-obtained blood culture specimens.

As a clinical laboratory test, blood culture has played a major diagnostic role in medicine for decades. One limitation of this diagnostic role is false-positive results, which increase expenses and have an adverse patient safety impact (1, 2). Consequently, numerous interventions with blood culture processes have been employed by laboratories to reduce contamination (3, 4). The purpose of this report is to introduce a new blood culture technique that significantly reduced the blood culture contamination rate (*R*) in this study. This innovation, the initial specimen diversion technique (ISDT), omits the first approximately 1-ml portion of venipuncture blood from the culture specimen without compromising or diminishing the volume of blood optimum for culture. The basis for ISDT is the hypothesis that skin fragments incompletely sterilized by skin surface antisepsis and dislodged by venipuncture increase *R*. We evaluated our hypothesis prospectively first with test ISDT versus control cultures for a 9-month period (group 1; *n* = 3,733 cultures). Next, we collected data for a second 9-month period with an all-cultures ISDT (group 2; *n* = 4,143) for comparison to test ISDT.

MATERIALS AND METHODS

Patients and phlebotomists. The blood cultures in this study were from adults suspected of having sepsis who were hospitalized, evaluated in the emergency room, or seen as outpatients in a not-for-profit urban community hospital setting. Venipunctures (peripheral vein sites only) were performed by laboratory-trained and supervised phlebotomists who wore safety gloves during the procedure. No indwelling-catheter-obtained specimens were included in this study. Our standard procedure of monitoring needle puncture and other laboratory staff issues was continued during and after the study.

Skin preparation. Prior to venipuncture, the skin antiseptic agent 2% chlorhexidine-70% alcohol (Medi-Flex Hospital Products, Inc., Overland Park, KS) was applied with a sponge using vertical and horizontal strokes in a washboard manner for 30 s over a 5- by 5-cm area. The scrubbed area was allowed to dry and was not repalpated prior to venipuncture.

Blood culture definition and initial specimen diversion technique. A blood culture was defined as two separate 10-ml specimens obtained serially from one venipuncture for sequential inoculation of bottled media, M1 (aerobic) and M2 (anaerobic). Medium bottle stoppers were cleaned with a 70% isopropyl alcohol wipe, which was left in place prior to inoculation. The culture medium bottles were incubated in an automated computer-monitored system (BacT/Alert SN Microbial Detection System; bioMérieux S.A, Durham, NC) and in the event of growth were Gram stained and subcultured for identification. We used a pushbutton blood collection apparatus (Becton Dickinson and Company, Franklin Lakes, NJ) with a 21-gauge venipuncture needle for blood culture specimen collection and inoculation (Fig. 1). The apparatus included a venipuncture needle (1), wings (2) to aid insertion of the venipuncture needle, tubing (3) for blood transfer, and a protective adapter (4) that facilitated medium bottle inoculation. Inoculation was enabled within the adapter by a second needle (Fig. 1, inset). The venipuncture and inoculation needles had safety covers. The inoculation needle cover was rubberized and re-covered the needle between medium inoculations. Blood culture specimens (10 ml each) were collected sequentially directly to M1 and then to M2 (Fig. 2). The medium bottle volume in 5-ml increments was shown on the medium bottles, providing precision in measuring the culture specimen volume. The medium bottles were held vertically, and the desired 10-ml increment was marked with a pen or the phlebotomist's thumb nail. The procedure was the same for ISDT blood culture (D), with the exception that each was preceded by diverting the first milliliter (Ds) of the same venipuncture blood into a 3-ml sterile Vacutainer collection tube (Becton Dickinson and Company, Franklin Lakes, NJ) (Fig. 1). For patients with small veins, syringes and 23-gauge needles were used for blood collection as

follows. The collection needle/adapter attachment apparatus (Fig. 1, inset, 5) was removed, enabling a syringe connector (6) to be attached. Syringes (3 ml and 10 ml) collected the 1-ml D_S and culture samples, respectively. A separate safety needle was attached to the 10-ml syringes for transferring culture specimens to medium containers. The medium bottles were placed in racks for the syringe/safety needle inoculation; hand-held medium inoculation was not permitted.

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FIG. 1.

ISDT diversion step prior to culture. 1, venipuncture needle; 2, wings to aid insertion of the venipuncture needle; 3, tubing for blood transfer; 4, protective adapter to facilitate medium bottle inoculation; 5, collection needle/adapter attachment apparatus; 6, syringe connector; 7, diversion tube. (Inset) Diversion inoculation needle detail.

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FIG. 2.

ISDT direct-to-medium inoculation step.

Blood cultures were classified as false positive if one or more of the following organisms were isolated from only one of a series of blood culture specimens: coagulase-negative *Staphylococcus* spp., *Propionibacterium acnes*, *Micrococcus* spp., “viridans” group streptococci, *Corynebacterium* spp., or *Bacillus* spp. (2).

Data groups. For the first of two 9-month periods, June 2007 through February 2008, culture specimen collection was tracked for test ISDT versus C (group 1). Training for ISDT commenced prior to and continued at the beginning of the period, followed by randomization of test-ISDT versus C. Before randomization was fully implemented, significant reduction of *R* by ISDT became obvious; therefore, in the best interest of our patients and our institution, randomization was discontinued and all cultures were obtained with ISDT. For a second 9-month period, April through December 2008, blood culture specimens were obtained with all ISDT (group 2). Confirmation of receipt in the laboratory and the blood volume of D_S were also tracked. D_S was not cultured.

Statistical method. Pearson's chi-square test was used to evaluate the significance of the blood culture groups compared; significance was defined as a *P* value of ≤ 0.05 .

RESULTS

During the first of two sequential 9-month periods, we captured test ISDT data, D versus C data ($n = 3,733$), which can be expressed as

$$D_T R = D_S R + D_{M1} R + D_{M2} R \quad (1)$$

and

$$C_T R = C_{M1} R + C_{M2} R \quad (2)$$

where $D_{MX}R$, $C_{MX}R$, and $D_S R$ are R for D , C , and D_S specimens and $D_T R$ and $C_T R$ are total R for D and C . Our ISDT hypothesis predicted that D_S would divert soiled skin fragments from D_{M1} , and therefore, $C_{M1} R$ would be significantly greater than $D_{M1} R$. This was confirmed by $C_{M1} R$ (30/1,061 [2.8%]) less $D_{M1} R$ (37/2,672 [1.4%]; $P = 0.005$) equaling 1.4%. Also predicted was that ISDT would show no significant difference between $C_{M2} R$ and $D_{M2} R$. Confirmation came as $C_{M2} R$ (11/1,061 [1.0%]) less $D_{M2} R$ (21/2,672 [0.8%]; $P = 0.31$) equaling 0.2%. Additionally, we assumed $D_T R$ was equal to $C_T R$, and therefore,

$$D_S R = C_{M1} R + C_{M2} R - D_{M1} R - D_{M2} R \quad (3)$$

Thus, $D_S R$ was discrete, could be calculated, and was 1.6%. Regarding the second 9-month follow-up period for comparison to test ISDT, ISDT data were compiled for all (A), $AD_T R$, and $AD_{MX} R$, cultures ($n = 4,143$),

$$AD_T R = AD_{M1} R + AD_{M2} R \quad (4)$$

Our hypothesis predicted no significant differences for test ISDT versus all ISDT. This was confirmed by $D_{M1} R$ (37/2,672 [1.4%]) versus $AD_{M1} R$ (42/4,143 [1.0%]; $P = 0.17$) and $D_{M2} R$ (21/2,672 [0.80%]) versus $AD_{M2} R$ (39/4,143 [0.94%]; $P = 0.50$). The data are shown in Table 1 for all cultured specimens, as are comparison contamination rates for control versus test ISDT and all ISDT versus test ISDT. The only significant comparison difference was test ISDT M_1 versus control M_1 (1.4%). This difference can be attributed to the diversion of unsterilized skin fragments from control M_1 by ISDT (formulas 1 and 2), and this difference in the study can be quantified (formula 3) as 1.6%. The lack of significant differences between test ISDT M_1 and M_2 and AD_{M1} and M_2 rates are consistent with our hypothesis: ISDT significantly reduces contamination in venipuncture-obtained blood culture specimens.

TABLE 1.

Comparison of R for control versus test ISDT and all ISDT versus test ISDT culture groups

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^aTest ISDT rate from first 9 months less all ISDT rate from second 9 months used for comparison.

For one randomly chosen month (February 2008), the diversion volume distribution was 152 (40%) >0.5 ml and ≤ 1.0 ml, 256 (68%) ≤ 1.5 ml, 351 (93%) ≤ 2.0 ml, and ≤ 3.0 ml (100%) ($n = 376$). We conclude that ≥ 0.5 ml and ≤ 2.0 ml is adequate diversion volume to significantly reduce contamination.

The clinical service distribution of blood cultures during the study was inpatients 77.2%, emergency department 15.9%, and outpatients 6.9% ($n = 11,330$). None of these were ≤ 16 years of age.

Phlebotomists did not suffer needle sticks or other injuries as a result of this study.

DISCUSSION

Every pathologist who has examined numerous needle aspirations of bone marrow and other viscera has observed skin fragments (mini-biopsy specimens) contaminating these aspiration specimens. Based on this experience, we sought improvement in our blood culture contamination rate. We hypothesized that small fragments of skin dislodged by a venipuncture needle harbor bacteria not killed by skin surface antisepsis and that they are a discrete cause of contamination. Additionally, we hypothesized that diverting the first milliliter of venipuncture blood and subsequently obtaining a culture specimen from the same venipuncture would eliminate some of these fragments from the culture specimen and significantly reduce contamination and that it would do so without compromising blood culture sensitivity. We refer to this diversion method as ISDT.

Our results show that ISDT significantly reduces contamination of blood cultures by excluding contaminants from the first portion of venipuncture-obtained culture specimens. Given this, several questions arise. What other studies have been done that may corroborate our findings? What is the optimum volume of blood for diversion? What is the cost of ISDT, and are there laboratory worker safety issues? Finally, do we recommend ISDT to other laboratories?

Regarding other studies, to our knowledge, reduction of contamination by diversion has not been previously studied in detail or quantified for venipuncture-obtained blood culture specimens. In contrast, diversion has been extensively studied and quantified for donor blood components. Diversion of the first part of donor blood to reduce the risk of bacterial contamination in recipients is a worldwide standard. Diversion volumes ranging from 10 to 50 ml are credited with having reduced contamination of blood components by 40 to 90% between 1995 and 2007 (7). Similar reductions in contamination of blood cultures may be realized with less diversion volume, as a blood culture needle is commonly a smaller gauge than a donor needle. The usual 16-gauge donor needle (bore, 1.19 mm) captures numerous plugs of skin contaminants (3). One would expect less contamination from our 21-gauge culture needle (bore, 0.514 mm), which has a cross-sectional area less than 1/5 that of the donor needle.

As for the optimum diversion volume for blood cultures, this study showed significant improvement in contamination with a volume of ≥ 0.5 ml and ≤ 2 ml. More diversion volume is likely better. Our data show that all specimens subsequent to ≥ 2.0 ml of diversion (C_{M2} , D_{M1} , D_{M2} , AD_{M1} , and AD_{M2}) had an average R of 1%. Hence, 20 ml of diversion would very likely decrease contamination further. However, with meticulous oversight, increased experience with diversion, and both initial and remedial training using a video of our diversion technique, our phlebotomists have achieved an R of $<1\%$ in the first 6 months of 2010, an R which a short time ago we would have thought impossible. We are satisfied with our current diversion volume but are considering increasing the volume to 3 or possibly 5 ml. Another improvement tactic is drawing blood for other tests (blood counts, chemistry, etc.) prior to blood culture.

ISDT can be cost-effective by lowering patient care charges. Recently, in a large emergency department (ED), patient charges were increased by \$8,720 for each contaminated blood culture (4). If our IDST procedure were implemented in this ED, with 5,432 blood cultures in 13 months, annual charges would decrease by \$699,575 for an increase in supply costs of \$3,510. Our costs for ISDT supplies are minimal (blood collection apparatus, \$1.28, and diversion tube, \$0.07), replacing a theoretical 20-ml syringe and two safety needles (\$0.65). Reduced contamination is based on our calculated $D_{50}R$ of 1.6%, and these cost savings can accrue without employee safety issues. We had no needle sticks or other injuries to our phlebotomists or other laboratory workers during this study.

For venipuncture-obtained specimens, we believe ISDT significantly reduces blood culture contamination, has a high benefit/cost ratio, is practical and safe for laboratory personnel and patients, and does not compromise blood culture sensitivity. We recommend ISDT to other laboratories.

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FOOTNOTES

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REVIEW

Detecting Bacterial Contamination in Platelet Products

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SUMMARY

Bacterial contamination of platelets is an important cause of transfusion-associated morbidity and mortality. It is currently the most frequent infectious complication of transfusion therapy, with between 1 in 1,000 and 1 in 3,000 platelet units being bacterially contaminated at time of transfusion. Several factors have contributed to the persistence of this problem including lack of sensitive detection methods, lack of recognition of the frequency of the problem, inadequate recognition of septic reactions by clinicians treating patients receiving platelet transfusions, differences in transfusion reactions between bacterial species and bacterial inocula transfused, and differing methodologies and time of testing for detection of bacteria in platelet units. There are also important correlations between the receipt of bacterially contaminated platelet units and the development of transfusion reactions and bacteremia. In the last few years the recognition of the importance of platelet bacterial contamination prompted the College of American Pathologists (CAP) and the American Association of Blood Banks (AABB) to set new standards requiring the screening of platelets for bacterial contamination. In the wake of these standards, an increasing number of approaches have been and are being developed to deal with this problem. The clinical sensitivity, specificity and predictive value of these detection methods vary considerably and need to be defined for routine laboratory practice. In this review, we focus on the practical aspects and feasibility of implementing FDA-cleared detection methods for identifying bacterially contaminated platelet units. We also present details of a number of methods under development for at-issue use. (Clin. Lab. 2006;52:443-456)

BACKGROUND

Platelets are currently administered as single donor plasmapheresis (SDP) and whole-blood derived, random donor platelet (RDP) units, with the latter typically being administered in pools of 4-6 units. Bacterial contamination of these platelet products is an ongoing problem associated with significant transfusion-associated morbidity and mortality.¹⁻¹⁰ Currently, platelet-transfusion-associated sepsis is the most frequent infectious complication of transfusion therapy, with between 1 in 1,000 and 1 in 3,000 platelet units being bacterially contaminated at time of transfusion.^{1, 8, 11} Transfusion of contaminated units is estimated to cause life-threatening sepsis in between 10% and 40% of recipients receiving a bacterially contaminated platelet unit. Based on passive-reporting studies from the United States, the United

Kingdom and France, the risk of death from a platelet transfusion due to bacterial contamination is between 1 in 7,500 and 1 in 100,000 transfusions.⁸ These risks are up to two orders of magnitude higher than the incidence of transfusion-associated viral transmission.^{1, 6, 7} Platelet units are more susceptible to contamination than other blood products because of the requirement to store platelets at room temperature to preserve platelet function.¹² At 22-24 °C, a small bacterial inoculum can grow into very high numbers within a short time period and therefore, older ("at-risk") units are most likely to be contaminated with a large number of organisms and to cause a septic reaction in the recipient.^{11, 13, 14} In recognition that older platelets are at risk for significant bacterial contamination, the storage period of platelets was shortened by the United States Food and Drug Administration (US-FDA) from seven to five days in 1986 in response to an increased number of reports of transfusion-related sepsis in older platelet units.^{9, 15} Only in

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Table 1: Bacteria associated with 60 cases of fatalities resulting from transfusion of platelet products as reported to the US-FDA, 1995-2004.¹⁷

Bacterial species	No. of cases
Gram-positive organisms (n = 22)	
<i>Staphylococcus epidermidis</i>	11
<i>Staphylococcus aureus</i>	4
<i>Streptococcus group G</i>	2
<i>Clostridium perfringens</i> (anaerobe)	1
<i>Enterococcus spp</i>	1
<i>Streptococcus group B</i>	1
<i>Streptococcus group F/Eikenella</i>	1
Gram + rods (unidentified)	1
Gram-negative organisms (n = 38)	
<i>Klebsiella pneumoniae</i>	10
<i>Escherichia coli</i>	9
<i>Serratia marcescens</i>	5
<i>Enterobacter aerogenes</i>	2
<i>Enterobacter cloacae</i>	2
<i>Pseudomonas aeruginosa</i>	2
<i>Salmonella spp</i>	2
<i>Bacillus spp</i>	1
<i>Enterobacter agglomerans</i>	1
<i>Klebsiella oxytoca</i>	1
<i>Morganella/Providencia</i>	1
<i>Pasteurella multocida</i>	1
Gram-negative rods (unidentified)	1

2005, with the advent of licensed storage containers for single donor apheresis platelets combined with aerobic and anaerobic culture testing under an US-FDA-approved post-market surveillance protocol, did it become permissible once again to store platelets (SDP only) for up to seven days following collection.¹⁶

The predominant organisms implicated in platelet bacterial contamination are the skin flora, including staphylococci (*Staphylococcus aureus* and coagulase-negative staphylococci), *Corynebacterium* species, and *Propionibacterium* species. Other contaminants include streptococci, Gram-negative bacilli and *Bacillus* species. Although Gram-positive organisms cause the majority of septic reactions, Gram-negative organisms are implicated in the majority of fatalities.^{1, 3, 6} Among the Gram-negative organisms reported to contaminate platelet units are *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella* species, *Enterobacter* species, *Morganella morganii*, and *Serratia* species.^{9, 17} Indeed, *Klebsiella pneumoniae* was responsible for the majority of platelet transfusion-associated deaths related to Gram-negative organisms reported to the US-FDA from 1995 to 2004 (Table 1).¹⁷ Although some of these organisms have a preference for anaerobic conditions, all are able to grow in aerobic conditions, with the ex-

ception of *Propionibacterium* spp., which grows only under anaerobic conditions. A single case of contamination of a platelet unit with *Clostridium perfringens*, also a strict anaerobe, has been reported.¹⁷

PREVALENCE OF BACTERIAL CONTAMINATION OF PLATELETS

The reported prevalence of bacterial contamination of platelets is highly variable and, in many cases, is difficult to assess due to differences in surveillance and testing methodologies and in case definitions. However, it is generally accepted that approximately 1 in 1,000 to 1 in 3,000 platelet units are contaminated with bacteria.^{1, 8} Based on 1999 data, over 4 million platelet units are transfused per year in the USA, in the form of 1 million SDP units and 3 million RDP units, the latter administered in 0.5 to 0.75 million pools of 4-6 units.^{10, 18} On this basis, it is likely that 1,300 to 4,000 platelet units and 500 to 1,500 platelet transfusions per year are bacterially contaminated. Projected fatalities from these transfusions, based on extrapolation from surveillance and other studies, vary from 15 to over 200 per year. Our nearly 15-year experience with bacterial contami-

nation surveillance in a university hospital using passive (transfusion-reaction triggered) and active (culture at issue) surveillance demonstrated that, while active surveillance detected 38 instances of bacterial contamination (1:2,090 RDP units and 1:2,213 SDP units), only one instance of contamination was detected by passive surveillance (0:48,067 SDP units and 1:168,216 RDP units).¹¹ The failure of passive surveillance to detect instances of bacterial contamination is attributed to the widespread lack of recognition of septic versus nonseptic reactions, and failure to associate signs of bacterial sepsis with the transfusion of a platelet unit. Additionally, transfusion of platelet units contaminated with bacterial species of low virulence such as coagulase-negative staphylococci frequently does not elicit signs and symptoms of a transfusion reaction.

Thus, there remain important outstanding questions relating to the clinical significance of detecting, defining and quantitating bacterial contamination in platelet units. Although the search for the perfect method is elusive, in the last few years a variety of different methodologies have been developed and evaluated for detection of bacteria in platelet units. Currently, three commercial methods have been cleared by the US-FDA for screening of platelets for bacterial contamination, BacT/ALERT (bioMérieux, Inc, Durham, NC), Pall eBDS (Medsep Corporation, Covina, CA), and Scansystem (Hemosystem, Marseilles, France). Based on the published information from centers that have used one or more of these systems for screening single donor platelet products,¹⁹⁻²³ these methods are sensitive and specific, but the culture-based systems have not detected all contaminated units in the clinical setting.^{10, 24} Therefore, patients are still at risk for being transfused with bacterially contaminated platelet units due to false negative results. In addition to these US-FDA-cleared methods, there are several additional methods in various stages of development. It is our goal to present the feasibility and logistics of the application of various methods – both cleared and under development – for bacterial detection testing in platelet units and to describe their advantages and disadvantages.

CORRELATION OF TRANSFUSION OF BACTERIALLY CONTAMINATED PLATELET UNITS, BACTERIAL LOAD AND TRANSFUSION REACTIONS

The critical factor for the clinical use of any detection method is defining the number of bacteria, expressed as colony-forming units per mL (CFU/mL) that will result in a clinically significant transfusion reaction. Transfusion reactions may occur with as few as 10^2 to 10^3 CFU/mL, even with organisms of low virulence such as *S. epidermidis*.^{1, 11, 25}

Transfusion of a contaminated platelet unit is often not recognized or directly associated with subsequent sepsis. Over a 3-year period, 1998 through 2000, from sus-

pected cases reported to the CDC during the BaCon study, a voluntary reporting study with very restricted criteria for case definition, the rate of transfusion-transmitted bacteremia (in events/million) was estimated to be 9.98 for SDP and 10.64 for pooled RDP units. The rates of fatal reactions were 1.94 and 2.22 respectively.⁶ Overall, the BaCon study estimated a fatality rate of 1 in 500,000 units for both SDP and RDP units.⁶

In France, over a 2-year period, of 16 cases of bacterial contamination associated with platelet transfusion 9 (56%) resulted in severe sepsis or shock. Estimates of the incidence of life-threatening reactions were 9.4 per million (1:106,000) units for RDP units and 17.7 per million (1:56,500) for SDP units.²⁶ A more recent report from the French Haemovigilance System identified seven confirmed cases of transfusion-transmitted bacterial contamination. Of these two were related to SDP and two to RDP pools, while the other cases were related to transfusion of red blood cells.²⁷ In the United Kingdom during six years of voluntary participation of blood services, the SHOT (Serious Hazards of Transfusion) study identified 26 episodes of bacterial contamination out of 40 transfusion-transmitted infection incidents reported. Twenty-two of these episodes were related to the transfusion of platelets, accounting for 5 of 6 deaths.²⁸

A major problem in determining the magnitude of the problem of platelet bacterial contamination is the lack of recognition and reporting of cases, due in large measure to the failure to associate chills, rigors and fever – signs and symptoms common in patients receiving platelet transfusion therapy – with the possibility of transfusion of a bacterially contaminated platelet unit.^{11, 25} Based on the reported prevalence of transfusion reactions and the detection rate of contaminated platelet units, however, it is estimated that a severe episode of transfusion-associated bacterial sepsis occurs in connection with about 17% of contaminated units transfused.¹ More serious clinical events, such as shock and death occurring in immunocompromised platelet transfusion recipients, are likewise often not linked to transfusion of a bacterially contaminated platelet unit.¹¹

The data obtained by our group during more than 14 years of surveillance for bacterial contamination of platelets showed, for the first time, the correlation between the organism load in bacterially contaminated units, transfusion reactions and positive blood cultures.¹¹ From this study, it was clear that bacteremia did not correlate with transfusion reactions, with bacteremia not being documented in the three patients with fatal outcomes, while two patients showing no signs of a transfusion reaction were bacteremic. Absence of bacteremia was likely related to patients receiving antimicrobial agents and delays in obtaining blood cultures following transfusion. Correlation of organism load with occurrence of transfusion reactions showed that a system with a sensitivity of 10^3 CFU/ml would detect 10/11 (91%) serious reactions and 15/19 (79%) of all reactions, while one with a sensitivity of 10^4 CFU/ml would detect all 11

serious reactions and 16/19 (84%) of all reactions.^{11, 29} Additionally, our study showed that rates of bacterial contamination, transfusion of contaminated units, transfusion reactions and bacteremia for RDP pool transfusions were significantly higher than those for SDP unit transfusions. These differences, however, were associated with the use of pools of 5 RDP units per transfusion as these rates were not statistically different based on the number of individual platelet units transfused. Our study also demonstrated the superiority of active surveillance over passive surveillance in detecting platelet bacterial contamination, with 38 of the 39 instances of platelet bacterial contamination being detected only by active surveillance. While our experience also highlights the finding that the vast majority of transfusion reactions with signs and symptoms consistent with sepsis are not due to transfusion of bacterially contaminated platelet units, paradoxically it demonstrates that the majority of patients who received bacterially contaminated platelet units and developed signs and symptoms of sepsis were not recognized or reported to the Blood Bank or Transfusion Service for further evaluation. In 2004, the Infectious Diseases Society of America conducted a survey to assess clinician experience with transfusion-associated bacterial infections among infectious diseases specialists who are members of the Emerging Infections Network in the United States.¹⁰ Among the 399 members that responded, 48 (12%) recalled consulting on 85 reactions to blood transfusions potentially caused by bacterial contamination, with 10 of these cases being fatal. A total of 143 (36%) respondents were aware that bacterial contamination of platelets is now the most common infectious risk of transfusion therapy while only 78 (20%) were aware of the new AABB standard for testing platelets for bacterial contamination. It is clear from this survey that efforts should be made to communicate with clinicians not only the new requirements from AABB and CAP, but also to recognize and request the appropriate testing to confirm the diagnosis of sepsis related to transfusion of potentially bacterially contaminated platelet units.¹⁰

STRATEGIES TO REDUCE OR PREVENT CONTAMINATION OF BLOOD PRODUCTS

In March of 2004, the AABB, an accrediting organization for Advancing Transfusion and Cellular Therapies Worldwide, added a new standard that requires members of this organization to implement measures to detect and limit bacterial contamination in all platelet components.³⁰ In an effort to assist blood banks and transfusion services, the AABB, in a supplemental guideline, suggested various strategies for reducing transfusion of bacterially contaminated platelet units and described several methods for detecting bacterial contamination,³¹ which will be described in more detail below. In addition to the AABB, in 2002 the CAP added a re-

quirement for laboratories to have a system in place to detect the presence of bacteria in platelet components.^{32, 33} Thus, in order to be in compliance with the CAP Laboratory Accreditation Program, blood banks and transfusion medicine services need to have a system to detect the presence of bacteria in platelet components. While bacterial detection methods garner most of the attention, additional strategies have been developed to reduce the risk of transfusion of bacterially contaminated platelets. These strategies include bacterial contamination avoidance methods, and bacterial growth inhibition or inactivation methods.¹⁵ In order to accomplish the goal of eliminating bacterial contamination of platelets, these strategies likely will need to be used in combination with a detection method. Ideally, the responsibility for limiting bacterial contamination is shared between the collection center, which needs to insure suitable donor selection, proper aseptic collection technique and absence of measurable bacteria by using a sensitive detection method shortly after product collection, and by the transfusion service, which should ideally use a rapid test for detecting bacterial contamination at the time the platelet unit is issued for transfusion.

Bacterial Contamination Avoidance Methods

Platelet units are most commonly contaminated at the time of collection when bacteria from the skin or from bacteremia in the donor gain entry into the collection set during the phlebotomy process. Exhaustive donor screening and deferral if a history or symptoms of possible bacteremia is elicited has reduced contamination of blood products. Additional measures to minimize the entrance of bacteria into the blood collection system include improved disinfection of the skin, and diversion or removal of the first 20-30 mL of blood collected.^{34, 35} Overall, rates of bacterial contamination of SDP and RDP units have been similar, but the rate of transfusion of contaminated products is proportionately higher in RDP pools than in SDP units.^{11, 25, 36}

Bacterial Growth Inhibition and Inactivation Methods

While bacteria may gain entry into a platelet unit during collection, the number of bacteria entering the collection system is usually very small and it is only during room temperature platelet storage that the organisms may grow into large numbers. This problem can potentially be prevented by using a substance that inactivates bacteria or that inhibits bacterial growth during storage. The use of substances that inhibit or inactivate organisms present within a platelet bag should be implemented by the collection center. In order for this strategy to be feasible and practical, these substances should not cause substantial damage to platelet function, and the process should be automated and linked to the collection instrument. These

inhibitory substances need to be added in a particular concentration, and the instrument should be able to calculate and dispense the pathogen inhibitory reagent in a closed system and according to the volume collected. Although the cost is substantial, and safety concerns about the additive solutions remain, the potential application of inactivation methods seems to be a promising approach to avoiding bacterial contamination of blood products.³⁷ Two inhibitory substances are being evaluated for use in platelets: amotosalen S59, which is being developed as the Intercept PLT System (Cerus, Concord, CA), and riboflavin, which is being developed by Navigant (Lakewood, CO). When activated by light, amotosalen S59 binds to the nucleic acid of pathogens and prevents replication.^{38,39} A pilot study assessing the use of 7-day-old buffy-coat platelets treated photochemically with amotosalen S59 to transfuse patients with thrombocytopenia showed that treated platelets produced acceptable efficacy and safety compared to 7-day-old untreated platelets.⁴⁰ The Intercept PLT System obtained regulatory approval in 2002 in Europe to treat platelets for transfusion, and regulatory approval is being pursued in the United States. The other pathogen inhibitory system under development for platelets is a photochemical decontamination process utilizing riboflavin, and preliminary reports are encouraging.^{41,42}

Bacterial Detection Methods

At present, the focus in identifying and preventing bacterial contamination of platelet components by the collection centers as well as the transfusion services is on detection methods. The ideal detection method should be sensitive and specific, have a rapid turn-around time, require a small sample volume for testing and be inexpensive.

For SDP platelets, the CAP and AABB recommend the use of one of the commercial systems that have been cleared by the US-FDA for in-process quality control testing of platelet units. For RDP units, where application of testing with an US-FDA-cleared method may be impractical unless applied to pooled units, a variety of less sensitive testing methods are permissible. These include detection of decreased pH, detection of decreased glucose concentration, microscopic examination of dried smears stained with acridine orange or Gram stain, plate culture, and broth culture. These methods should be validated by the user.

As discussed above, the methods that have been cleared for bacterial contamination testing of platelet products by the US-FDA are two culture-based instruments, the BacT/ALERT and PALL eBDS. More recently, the US-FDA has also cleared the Scansystem, a scanning cytometry method that uses an automated microscopic analysis of particles stained with a fluorescent stain. Both culture-based methods (BacT/ALERT and eBDS) may potentially delay the use of platelets and shift the inventory to the use of older platelets because they require a

24-h holding period prior to sampling and a generally 24-h incubation period after sampling.

Description of US-FDA Cleared Bacterial Detection Methods for Quality Control Testing of SDP units

BacT/ALERT

A sample of platelet rich plasma from a leukocyte-reduced SDP unit is inoculated into aerobic (BPA) and anaerobic (BPN) culture bottles containing broth media and then placed into an instrument that automatically monitors the production of CO₂ as a result of growth of bacteria. This and similar systems have been used for many years for the routine culture of blood for clinical purposes. The manufacturer strongly recommends using one aerobic and one anaerobic bottle, each inoculated with 4 ml of the platelet product. For optimal bacterial detection, the manufacturer recommends that the platelet specimen should be taken at least 24 hours after collection to allow for natural proliferation in the platelet product. During this time bacteria, if present at the time of collection, would have an opportunity, in most instances, to reach a level adequate for sampling and subsequent growth in the culture system. Although procurement of the aliquot from the platelet unit is achieved with the use of a sterile docking device, the subsequent inoculation of the sample into the culture bottle involves an open system using a needle and syringe. Therefore, strict adherence to the manufacturer's instructions for antisepsis of the septum of the blood culture bottle and inoculation instructions are critical factors to prevent the occurrence of false positive results due to contamination during inoculation of the platelet unit itself. Distinguishing false positive culture results from true contamination is often confounded by the fact that the same bacterial species are commonly detected in both circumstances. According to the manufacturer's directions, the inoculated culture bottles are held for the shelf-life of the platelet unit unless a signal indicating bacterial growth is generated before this time period has elapsed.

Once the system identifies a bottle as being "positive", indicating that the CO₂ content is above the baseline, an aliquot is removed for Gram stain and subculture to agar media. Most collection centers send positive bottles and a sample from the original unit to a microbiology laboratory for further testing. Absolute proof that a true positive result is correct requires that the same organism be isolated from original platelet unit and positive culture bottle. If the culture from the original platelet unit is negative, it is likely that the positive culture bottle is a false positive.

In the USA, the BacT/ALERT culture bottles are accompanied by product inserts indicating that BacT/ALERT System (3D and 240) and culture bottles may be used for quality control testing of platelets and that the laboratory should follow its own quality control pro-

cedures for this use.⁴³ The product inserts also state that the BacT/ALERT System, including the culture bottles, should not be used in determining suitability for release of platelets for transfusion and that users considering such release testing should first consult the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) for the appropriate clinical studies. A report of "negative" should not be interpreted as meaning that the original product is sterile. The negative status could be due to underinoculation of the bottle, no organisms present in the inoculum, the number of organisms were too small for detection, or a culture bottle/medium that does not support the growth of the organism.⁴³

eBDS

This method is a novel culture-based system, which assesses the reduction of the O₂ content in the head space of a sample pouch containing an enriched medium, compared to ambient O₂, as a marker for bacterial growth.²³ This method involves docking an eBDS sample pouch onto the tubing of a platelet bag, transfer of an aliquot of 2-3 mL of the platelet product into the sample pouch, which is then separated from the platelet unit using a heat sealer. The eBDS pouch is then incubated at 35 °C for 24 hrs. Pouches are then removed from the incubator, kept at room temperature for at least 2 minutes and the probe of the oxygen analyzer inserted into the sample port of the pouch. The oxygen analyzer automatically reads the oxygen concentration in the sample pouch. The instrument then gives a reading with a positive or negative interpretation for bacterial contamination.

Scansystem

This method detects bacteria using a laser-based, solid-phase scanning cytometry detection method. This method is a highly sensitive bacterial screening system, and can detect very low levels of bacteria after concentration from a larger volume by filtration.⁶⁰ The Scansystem solid-phase cytometry analyzer includes four modules: (i) a scan module, in which the black membrane is placed; (ii) an argon laser module (488 nm excitation light), which is connected directly to the scan module to scan the black membrane; (iii) an epifluorescence microscope with a suitable light source and filters, which has an automated motor-driven stage, for visual discrimination by the operator of fluorescent particles detected by the laser scan as bacteria or nonbacterial particles; and (iv) a computer with proprietary software to monitor the other modules.

The Scansystem is used by drawing a 3 ml sample of platelets into the syringe of a Scansystem Platelet kit through the sample injection port. The kit is then agitated in a platelet incubator at 22 °C for forty minutes in order to achieve platelet aggregation. The contents of the syringe are then expressed through a filter, which retains the aggregated platelets and allows passage of bacteria into the second portion of the kit. The kit is then

incubated at room temperature for twenty minutes to allow labeling of any bacteria present with the fluorescent stain. A black membrane in a holder attached to a vacuum pump is then attached to the bottom port, and the contents of the pouch are then filtered through the black membrane. Any bacteria present will be deposited on the surface of this membrane. The membrane is then removed from the holder and placed into the Scansystem scan module for detection of fluorescent particles by laser scanning. The final step is visual determination, using the epifluorescence microscope, of the identity of fluorescent particles as bacteria or as other particles.

Other Detection methods

Although traditional culture and culture-based methods are far more sensitive than staining and measurement of pH or glucose, the latter methods have the advantage of having a rapid turn-around time and therefore the testing can be done at or near the time of releasing the platelet unit, while final culture results may not be available until after transfusion. For this reason, and because these non-culture based methods are among the suggested methods in the current AABB and CAP guidelines for testing of RDP units, many transfusions services and blood banks have adopted them for routine testing; and, as is discussed below, despite poor sensitivity for detection of bacterially contaminated platelet units, their use may reduce the fatalities associated with transfusion of bacterially contaminated platelet units.

Staining Methods

Among the staining methods recommended by AABB and CAP are the Gram stain and the acridine orange stain.

Gram stain procedure: A smear is prepared using a sterile pipette or syringe to transfer 1 or 2 drops from a platelet unit to a clean glass slide. The drop is spread into an even film and allowed to either air dry or heat dry on a slide warmer. Smears can also be prepared using a cytospin slide centrifuge to concentrate the sample. Cytospin preparations deposit the concentrated sample within a limited area for viewing.⁴⁴ The Gram stain procedure includes sequential staining steps with crystal violet, alcohol decolorization, and counterstaining with safranin or neutral red. Bacteria stain either Gram-positive (deep violet) or Gram-negative (red) on the basis of differences in their cell wall composition. Gram-positive bacteria have a thick peptidoglycan layer and they are unaffected by the decolorization step and retain the initial stain, appearing deep violet. Gram-negative bacteria have a thin peptidoglycan layer attached to an outer membrane containing lipids. This membrane is damaged by the decolorizer, allowing the initial stain to leak out and be replaced by the red counterstain. The smear is examined microscopically using a light microscope with a 100X oil objective. The sensitivity of the

Gram stain is 10^5 CFU/mL, or 10^4 CFU/mL if the specimen has been prepared with a cytocentrifuge.⁴⁴ Use of the Gram stain has been successful in interdicting platelet units heavily contaminated with bacteria prior to transfusion.⁵

Acridine orange stain procedure: Acridine orange is a fluorochromatic dye that binds to nucleic acids of bacteria and other cells. Under UV light, bacteria stain bright orange, whereas human cells and background debris stain pale green to yellow, although nuclei of activated leukocytes may also stain orange or red. The smear is prepared as for a Gram stain and stained with acridine orange (0.1 g/L in 0.5M acetate buffer) for 2 min. The smear is read on a suitable fluorescent microscope with a 40X dry or 100X oil objective. The sensitivity of the acridine orange stain is approximately 10^4 CFU/mL.⁴⁵

Interpretation of Gram and acridine orange stains involve consideration of staining characteristics and cell size, shape, and arrangement. Sample preparation, reagents, and staining procedures may influence these characteristics. Therefore, use of quality control slides and competency training of the personnel reading the stains is essential. It is advisable that these staining methods be done in a clinical microbiology laboratory. In institutions where a microbiology laboratory is not available, the Gram stain can be performed by blood bank or transfusion service personnel that have been adequately trained to perform and interpret Gram stains. In addition, these laboratories should be participating in a Gram stain proficiency testing program.

pH and glucose analysis: Testing can be done separately using a handheld device or pH paper, or in combination on a multi-reagent dipstick. Although, handheld pH meters provide a more accurate result than do dipsticks, both methods are easy and rapid to perform and, for that reason, they have been adopted for many blood banks and transfusion services for testing RDP units.⁴⁶⁻⁴⁹

The sensitivity of pH and glucose testing, using one or both methods, is approximately 10^6 to 10^7 CFU/mL. Because of this limited sensitivity, the AABB recommends that facilities use these methods on individual units rather than pooled units. A recent study showed that as platelets age, the rate of pH failures increases, and only 4 of 405 random platelet units that failed pH were culture positive.⁴⁹ A lower rate of pH failure has been demonstrated in random units that have undergone pre-storage leukoreduction compared to non-leukoreduced, random platelets.⁵⁰

IMPLEMENTATION OF DETECTION METHODOLOGY

A summary of the AABB fall 2004 survey of members on practices related to the new guidelines on detection and prevention of bacterial contamination in platelet units was presented at the US-FDA Blood Products Advisory Committee Meeting in January of 2005.⁵¹ The survey results showed that the majority (88%) of blood centers were using a culture method – usually BacT/ALERT – to screen for bacterial contamination of SDP units. Most centers (85%) using BacT/ALERT did only aerobic cultures and held the cultures for 5 to 7 days. Four out of the 34 blood centers surveyed used glucose or pH by dipstick or meters. A few transfusion services cultured platelets by plate culture or performed Gram stains. Among hospital blood banks, most cultured platelets if their supplier did not, or if the platelets were collected in-house. Half of the blood banks performing cultures used anaerobic and aerobic cultures, while the remainder used only aerobic culture.⁵¹

It is clear from the results of the survey that many transfusion services are using less sensitive techniques – glucose, pH or Gram stain as compared to methods cleared by the US-FDA – for quality control of platelets, particularly RDP units. The advantage of using these methods is that they are easy to implement in any hospital blood bank or transfusion service and they can be performed at or near the time of issue. However, there have been reports of false negatives with fatal consequences with these methods,¹⁰ and investigators have strongly advised against the use of surrogate markers of bacterial metabolism, such as pH and glucose concentration, for detecting bacterial contamination of platelets due to the analytic insensitivity of these methods.⁵²

Some of the practical aspects relating to implementation of the US-FDA-cleared detection methods are discussed below. In addition, the BacT/ALERT and the eBDS systems have also been evaluated for screening of individual and of pooled RDP units, and have been found to be reliable for monitoring bacterial contamination in these products.^{53, 54} Table 2 summarizes the published contamination rates found by routine testing in a clinical setting using different detection methods. The rates of bacterial contamination varied considerably between and within methods, with methods such as plate culture, eBDS and BacT/ALERT generally reflecting realistic true positivity rates (0.02-0.05% for SDP and RDP units, and 0.1-0.25% for RDP pools), while Gram stain, pH determination and glucose determination resulted in low true positive rates while in the case of pH and glucose determination, very high false positive rates were also found. In many instances especially when the BacT/ALERT method was positive, the platelet product had already been transfused and was no longer available for retesting, and these cases are regarded as unconfirmed positives.

Table 2: Results of various methods used for routine testing of platelet products to detect bacterial contamination. Realistic true positive rates based on 1:1,000 to 1:3,000 units being contaminated are 0.03-0.1% for SDP and RDP units, and 0.17-0.5 for RDP pools of 5 units. Data was obtained or derived from the references indicated.

Method	Platelet product (total tested)	Overall positive rate (%)	True positive rate (%)	False positive rate (%)	Unconfirmed positive rate* (%)	False negative rate (%)	Reference #
Gram stain at issue	RDP pools of 5 units (N=7716)	0.12	0.078	0.039	0	0.16	11
	SDP (N=8761)	0	0	0	0	0.046	
pH at issue	Individual RDP (N=37067)	1.09	0.01	1.08	0	NR	49
	Individual RDP (N=6590)	1.97	0	1.97	0	0.03	11
	SDP (N=671)	1.93	0	1.93	0	0.30	
pH + glucose at issue	Individual RDP (N=3093)	0.96	0.06	0.9	0	0 (N=203)	47
	SDP (N=350658)	0.06	0.02	0.03	0.01	0.0008	55
BacT/ALERT at 12-24 h	RDP pools and SDP (N=4000)	1.2	0.13	0.9	0.02	NR	57
	Individual RDP units (N=10141)	1.4	0.02	0.75	0.64	NR	54
	RDP pools of 5 units (N=2063)	3.4	1.9	1.5	0	NR	
	RDP pools (N=28104)	0.72	0.65	0.06	0	NR	24
	RDP pools of 4 units and SDP (N=36896)	0.24	0.03	0.04	0.12	0.18 (N=1061)	20
	Individual RDP units (N=12062)	0.04	0.02	0.008	0.008	NR	53
eBDS at 24 h	RDP pools of 5-6 units (N=2201)	3.6	0.04	3.5	0	NR	
Plate culture at issue	RDP pools of 5 units (N=12,961)	0.26	0.24	0.023	0	0.0077	11
	SDP (N=15,493)	0.077	0.045	0.032	0	0	

SDP: Single donor platelets; RDP: Random donor platelets; NR: Not reported

* Unconfirmed positives are those where the platelet product had been used at the time the bacterial detection system became positive

Implementation of BacT/ALERT: Laboratory and clinical studies have demonstrated the efficacy of this system in identifying many instances of bacterial contamination of platelets.¹⁹⁻²² The American Red Cross implemented routine quality control testing for bacterial contamination in SDP products with BacT/Alert in all 36 regional blood centers in March 2004.⁵⁵ Platelet samples (4 ml) were obtained at least 24 h after collection and cultured in BacT/ALERT aerobic bottle only until the end of the product shelf life or until a positive reaction occurred.⁵⁵ Products were released for use if negative after incubation for at least 12 h, and, if not used, removed from supply when culture became positive. Reports and investigations of potential septic reactions to SDP platelets were also reviewed. In the first 10 months of bacterial testing, 226 of 350,658 collections tested initially positive. Sixty-eight (30%) were confirmed as true positives. Of the 354 apheresis platelet products derived from all 226 initial test-positive cases, 38 (10.7%) had been transfused by the time of the initial

positive result, although none of these were confirmed positive. During this period, three septic episodes probably related to transfusion of bacterially contaminated platelets, which had negative screening, were documented, with *S. lugdunensis* implicated in one and other coagulase-negative staphylococci in the other two instances. In Norway, from May 1999 to May 2004, RDP pools were monitored for bacterial growth using BacT/ALERT during an average period of 6.5 days. The investigators found that from 88 platelet pools that were initially positive, only 12 (13.6%) were confirmed as true positives.²⁰ The main limitations related to culturing, either using traditional culture or using an automated system, is the time required to obtain results. In order to increase the sensitivity of culture, sample for testing should be taken 24 hours after collection, inoculated into culture media and incubated for at least five days before reporting it as negative. Although most of the bacterial organisms implicated in bacterial contamination of platelets are detected after 24 hours of incuba-

tion (48 hours after collection), slow growing organisms cannot be detected for several days. As documented in the survey described above, in most instances, because of the logistics of sample handling, BacT/ALERT testing is performed at the collection center rather than the transfusion service. Documentation of training of the personnel performing the testing is required by accrediting organizations. While inter-laboratory proficiency testing is currently not required due to lack of available defined methodologies, it is anticipated that this will soon be required.⁵⁶

The survey did not evaluate whether the blood centers were performing Gram stains or confirmation cultures from positive BacT/ALERT bottles on site or whether the bottles were sent to an external microbiology laboratory. Because it is known that false positive bacterial contamination results may occur with this system,⁵⁷ if the bottles are sent out for confirmation results could be delayed, which may lead to an increase in wastage of products and unnecessary treatment of patients who received these units.

Another limitation of culturing using an automated system is the specimen volume required for testing, usually 4 ml per bottle, which for a SDP unit represents only 1.5% of the unit volume if using aerobic bottles only, or 3% if using both aerobic and anaerobic bottles, but if testing is done on a single RDP unit, the volume required for testing could represent 10% to 40% of the unit volume. This limitation makes routine culturing of individual random units impractical.

Implementation of Pall eBDS: The features of this culture-based US-FDA cleared test are similar to those of the BacT/ALERT. This system also requires that a large sample (3 ml) be obtained at least 24 hours after collection and requires an incubation period of 24 hours. Published laboratory studies have shown that the Pall eBDS system is able to detect 1 to 15 CFU/ml of aerobic bacteria in a contaminated unit.⁵⁸ The initial version of this system (BDS) gave some invalid or negative readings with organisms that rapidly consume O₂ during their metabolism, particularly *Klebsiella pneumoniae*, but the newer enhanced version (eBDS) has overcome this problem.^{15, 58, 59}

There are several potential advantages of the eBDS system compared to automated blood culture systems: (1) it is easier to utilize in a laboratory environment not generally familiar with bacterial testing instrumentation; (2) the sampling and inoculation occurs in a closed system, reducing the opportunity for false positive culture results; and, (3) unlike the BacT/ALERT system in which continuous monitoring of the culture bottles is performed throughout the shelf-life of the platelet unit, the eBDS system is read at a single, discreet time point, eliminating the possibility that a positive result will be generated after the platelet unit has been transfused. It is believed that many of the positive results generated after the platelet unit has been transfused are either false

positives or are not clinically significant, while adding a significant burden of work. A potential disadvantage of the eBDS compared to the BacT/ALERT is that only aerobic organisms are detected. And with a smaller sample volume than the BacT/ALERT, it is possibly slightly less sensitive. With both systems, since sampling is done relatively early in the storage period when the bacteria have had limited time for growth, it is possible that bacterial contamination will be missed entirely. While the number of such "breakthrough" cases is uncertain they have occurred, and some have been clinically significant.²⁹

Implementation of the Scansystem: Our group and other investigators have evaluated this system and found that this method is able to detect most typical bacterial platelet contaminants in leukocyte-reduced SDP units 30 h after contamination, with a sensitivity equal to that of BacT/ALERT.^{60, 61} The Scansystem can detect both live and dead bacteria, so that the presence of bacterial species such as *Pseudomonas aeruginosa* and *Staphylococcus epidermidis*, which are frequently inhibited or killed in the presence of human plasma,^{62, 63} may still be detected, provided some bacterial growth occurred.

Advantages of the Scansystem method are that platelets, from 30 to 72 h after collection, can rapidly be tested for the presence of bacteria, with a total test time of approximately ninety minutes.^{60, 64} Thus the Scansystem allows testing of platelets closer to time of use, and allows platelet units to be used as early as 32 h after collection, compared to typically 48 h for the BacT/ALERT and eBDS methods. Moreover, the Scansystem method is able to detect both live and dead bacteria, which may prevent transfusion of endotoxin-containing products. Disadvantages of the Scansystem are the labor-intensive nature of the system, the need to verify visually the presence or absence of bacteria for each positive test, and the need to test platelet units within 72 hours of collection as platelet aggregation – a requisite of the testing methodology as noted above – is less efficient after 3 days of storage.

Implementation of non US-FDA cleared culture methods: Traditional culture using plated or broth media as well as commercially available automated blood culture systems other than BacT/ALERT can be used for platelet bacterial contamination testing but requires strict validation to ensure that the performance of the technique is as expected.^{11, 65, 66} The validation plan should be developed by each institution or laboratory before routine testing can be in place. AABB Association Bulletins, published to supplement the required AABB Standard, provide guidance on acceptable validation methods.^{31, 67} Published studies have documented these systems to reliably detect bacterial contamination of platelets.^{65, 66} In many cases, the burden of the internal validation pro-

cess is placed on the microbiology laboratory⁶⁸ and the cost of testing is passed on to the hospital. The legal risks of using a non-US-FDA-cleared detection system for quality control of platelets for which US-FDA cleared tests are available also need to be considered.

It is important to note that in emergency situations, as promulgated by the FDA any standard procedure may be bypassed if the clinical need is paramount. (see 21 Code of Federal Regulations 606.121(h) and www.fda.gov/ora/inspect_ref/igs/blood.html)

CHANGES IN REGULATIONS FOR PLATELET STORAGE

As discussed above, in 1984 the US-FDA extended the platelet storage from five to seven days based on the functional quality of the platelets. However, in response to an increasing number of reports of bacterial contamination episodes, the US-FDA reduced the storage time back to five days in 1986. Nevertheless, to comply with the new AABB and CAP recommendation for screening platelet products for bacterial contamination, the average time between collection and issuing the product has been increased and most SDP products are released three days after collection, making a difficult task for blood centers to satisfy the need for platelet products. In 2005, the US-FDA approved platelet bags made by Gambro BCT and Baxter for 7-day storage of SDP platelets provided that a US-FDA-cleared detection method is used,¹⁵ and the US-FDA-approved protocol, the PASSPORT Study (www.passportstudy.com) is followed. The extended storage time would improve detection and confirmation of positive results before units have been used, and could limit the wastage of units.

SDP VERSUS RDP UNITS

Although several reports have demonstrated a reduced incidence of transfusion-associated platelet bacterial contamination with the use of SDP platelets compared with pooled RDP units,^{11, 25, 36} the difficulty of maintaining a SDP platelet inventory has forced transfusion services to continue using pooled RDP units. However, if RDP units are screened for bacterial contamination with a sensitive method at the time of issue, the risk of transfusing a bacterially contaminated unit should be similar to that of SDP units. The obstacle in reaching that goal is that the US-FDA-approved methods for detection of bacterial contamination have been approved for quality control of SDP and, in some cases, RDP units, but not until recently (see below) for RDP pools, making approved systems prohibitively expensive to use on each RDP unit used to prepare a pool. Most hospital blood banks are therefore using methods such as pH or glu-

cose determination, which have low sensitivity, but are rapid and easy to perform at the time of issue. The main reason that transfusion services and blood banks need to do the testing of RDP units is because the pooling of the units is done just before releasing the product for transfusion. This problem could be overcome by the allowance of early pooling along with screening for bacterial contamination with one of the methods already cleared by the US-FDA for SDP units.

Investigators have assessed the effectiveness of storing RDP platelets as a pool compared to SDP platelets and found that there is no detrimental effect of pooling RDP platelets as relates to platelet quality for products stored for up to 7 days.^{69, 70} In February 2006, the US-FDA approved a platelet storage bag, the Pall Acrodose PL system, for the pooling of 4 to 6 ABO identical, leukocyte-reduced, RDP units shortly after collection and subsequent storage for up to 5 days after blood collection when coupled with a device cleared by US-FDA for detection of bacterial contamination in pooled, leukoreduced RDP units.⁷¹

Although some investigators have stated that the sensitivity of culture testing of pools may be insufficient to detect all contaminated products, and that manipulation of pools can also increase false positive results,⁵⁴ others have found pool testing to be reliable.⁷²⁻⁷⁴ In addition, the use of both aerobic and anaerobic BacT/ALERT bottles may enhance the detection of contaminated units. This finding seems to be related to the volume of sample cultured rather than the isolation of strict anaerobic organisms.⁷⁴

DETECTION METHODS UNDER DEVELOPMENT

Several detection methods suitable for use at the time of issue of platelet products are currently being developed, and include the following:

Detection of bacterial 16S ribosomal RNA with oligonucleotide probes. A chemiluminescence-linked universal bacterial rRNA probe for the detection of bacterial contamination in 0.4 mL aliquots of platelet concentrates detected the majority of samples containing 10^4 CFU/mL of *Bacillus cereus*, *P. aeruginosa*, *S. aureus* and *S. epidermidis*, and all samples with 2.1×10^5 CFU/mL or greater of these species.⁷⁵ Further development of this method is currently not being pursued.

Detection of conserved regions of bacterial 23S rRNA and a heat shock protein by real-time, reverse transcriptase PCR assay. Two real-time reverse transcriptase PCR (RT-PCR) assays performed in a LightCycler instrument were developed and compared regarding specificity and sensitivity by the use of different templates to detect the majority of the clinically important bacterial species in platelets.⁷⁶ Primers and probes specific for the conserved regions of the eubacterial 23S rRNA

gene or the *groEL* gene (encoding the 60-kDa heat shock protein Hsp60) were designed. With *rTth* DNA polymerase in a one-enzyme system, 500 CFU/mL of *Escherichia coli* or *Staphylococcus epidermidis* were detected. With a two-enzyme system consisting of Moloney murine leukemia virus RT and *Taq* DNA polymerase, 16 CFU/mL were detected. With *groEL* mRNA as the target of RT-PCR under optimized conditions, 125 CFU/mL of *E. coli* were detected. False-positive results caused by reagent contamination or a cross-reaction with human nucleic acids were found with the 23S rRNA, but not with the *groEL* gene detection systems.

BacSTAT Antibody-based lateral flow device for detection of bacteria. This system, being developed by GenPrime Inc., Spokane, WA, (www.genprime.com) is a broad-spectrum, antibody-based lateral flow device for detection of bacteria in SDP or RDP units, and uses a unique lateral-flow scanning system and a reader with pass/fail software.⁷⁷ The antibody targets used in this system are unique surface antigens. Specimen processing is simple, and total test time is less than 20 minutes. The expected sensitivity of this method is 10^3 to 10^4 CFU/mL.

Rapid Bioluminescent Bacterial Detection System using Luciferase. This method, which detects bacterial ATP by generation of light in the presence of bioluminescent luciferase firefly extract, is being developed by SUBC Inc., Rochester, Minnesota.⁷⁸ The method consists of removing platelets and cellular debris from 2-3 mL platelet concentrate samples, isolation and immobilization of any bacteria present in an isolation chamber, rinsing the isolation chamber with buffer, adding a lysing solution in combination with localized heat to rapidly lyse bacterial membranes and release bacterial ATP, adding bioluminescent firefly extract, and detecting generated light with a photon counter. The burst of light is then converted into a bacterial inoculum in CFU/mL. The sensitivity of this method is claimed to be 10^2 to 10^3 CFU/mL. A fully automated, microprocessor-driven instrument with an internal reagent cartridge, GloBac, has been developed for this application, and processing time is 4 min per specimen.

Bacterial lipotechoic acid and lipopolysaccharide detection by lateral flow immunoprecipitation. This test is being developed as the Verax Biomedical Platelet PGD Test by Verax Biomedical Inc., Worcester, MA (www.veraxbiomedical.com).⁷⁹ This system consists of test kits with a double-sided, lateral flow test cartridge and a central specimen well. Testing is performed by adding 8 drops of a platelet lysis reagent to 0.5 mL of a platelet sample, and centrifuging for 5 min to sediment any bacteria present. The supernatant is decanted off and 8 drops of a resuspension agent and 4 drops of a bacterial lysis reagent are then added, and the fluid is then added to the central well of the lateral flow test cartridge. The test cartridge contains antibodies to bac-

terial lipotechoic acid on one side and lipopolysaccharide on the other side to detect Gram-positive and -negative bacteria, respectively. A positive test is shown by the development of a pink precipitation line on one side. The system is designed for use with leukoreduced or non-leukoreduced RDPs, pooled RDPs and SDPs, with testing taking 30 min, with 2 to 3 minutes attended labor per test. The sensitivity of this method is claimed to be 10^3 to 10^4 CFU/mL.

Bacteriological Biosensor using engineered spores as fluorogenic nanodetectors. This system, being developed by BCR Diagnostics, Jamestown, Rhode Island (www.bcrbiotech.com), is able to detect and count low bacterial levels quantitatively in less than 20 minutes with a linear detection response over a range of one to 10,000 bacteria per sample.⁸⁰ The instrumentation cost is low and the system is suitable for automated high-throughput operations. A 0.5 mL platelet sample is processed to separate bacteria, and the resulting suspension is mixed with engineered bacterial spores. The mixture is then combined with a germinogenic substrate and then filtered through a filter mounted on a biochip – the filter contains 80,000 micro-colanders, which are 20 μ m in diameter and contain engineered biosensor bacterial spores. The presence of a bacterial aminopeptidase, present in all bacteria, in the platelet specimen triggers the biosensors on the spores, resulting in production of fluorescent light, which is detected by a camera. The expected sensitivity of this method is 10^3 CFU/mL.

Bacterial peptidoglycan chromogenic immunoassay. This method is being developed as BacTx by Immunetics, Inc., Boston, MA (www.immunetics.com) and consists of a test kit containing all needed reagents and a chromogenic reader.⁸¹ The system has a turnaround time of less than one hour, a 1 mL sample volume, and premeasured vial reagent dispensers. The system detects bacterial peptidoglycan in Gram-positive and Gram-negative bacteria when a peptidoglycan binding protein triggers enzymatic conversion of a chromogenic substrate to a visible product with measurable absorbance. A 1 mL platelet sample is centrifuged for 10 min, the sediment incubated for 30 min with reagents, and absorbance is read on a reader. Assay sensitivity is claimed to be 10^3 to 10^4 CFU/mL.

CONCLUSIONS

Bacterial contamination of platelet units is the most prevalent infectious risk of blood products in the United States. In the last 3 years, a unified effort from professional and regulatory agencies has been committed to limiting bacterial contamination of platelet products. Strategies beginning with donor selection, collection guidelines, use of detection methods after collection and at time of issue have been developed in order to deal with this problem. Because of the multi-factorial etio-

logy of bacterial contamination and the heterogeneous growth and metabolic characteristics of the organisms involved, different strategies should be used in combination. Now that FDA-cleared methods and guidelines are available to meet the requirement that all platelet units be tested for bacterial contamination, it is hoped that data will continue to be collected and new strategies will be developed to reduce the occurrence and the fatalities associated with bacterial contamination of platelets. Several promising methods for at-issue testing are being developed and will hopefully obtain regulatory approval soon.

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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 units³⁻⁸ 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 contaminants identified in retrospective analysis of platelet units.¹² Three reporting systems have suggested that 70% of contaminants 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 enterocolitica* septicemia in which many of the donors retrospectively reported diarrhea in the days preceding donation.²⁰

An Open Letter to the Blood Community and AABB Standard 5.1.5.1

Physicians concerned that the risk from infected units was too high and that there were technologies that could address the issue at least in part wrote an "open letter" to the transfusion medicine community urging implementation of a method to stem this complication.²¹ In 2003, AABB Standard 5.1.5.1 was released after considerable discussion, debate, and a public comment period. To be implemented within 1 year, the Standard

read, "The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components."

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

Clinical Relevance

Typically at the time of collection, the level of contamination is relatively low (between 1 to 10 colony forming units (CFU)/mL.²³ However, once the product is inoculated, the bacteria can proliferate to levels of 10⁶/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.

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 CO₂ generation or O₂ 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

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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Quality control of bacterial contamination of blood components: the feasibility of diversion system testing

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Quality controls and retrospective investigations indicate that the majority of bacterial strains isolated from platelet concentrates (PC) derives from bacterial flora contaminating the skin^{1,2}, while about 50% of cases of bacterial contamination of red cell concentrates (RCC) are caused by transitory episodes of asymptomatic bacteraemia in the donor³. For the recipient, the risk of receiving PC contaminated by bacteria is 10-1,000 higher than the combined risk of receiving product contaminated by viruses such as HBV, HCV and HIV. The available epidemiological data show that 1: 2-3,000 PC can be contaminated by bacteria and that the risk of severe sepsis is about 1 case for every 1:50,000 platelet transfusions¹. The risk of severe sepsis from transfusion of RCC is estimated to be about 1:500,000⁴. In the United States bacterial contamination of blood components is the second cause, after human error, of transfusion-related deaths².

The recognized preventive measures include: careful selection of the donor in order to avoid periods of possible bacteraemia (recent dental procedures or diarrhoea), scrupulous disinfection of the venipuncture site with appropriate disinfectants not contaminated by bacteria, diversion – for diagnostic purposes – of the first millilitres of donated blood. Widespread use of pathogen inactivation is currently only available for plasma. Assessment of microbiological contamination of blood components by automated culture systems is increasing and is the subject of considerable debate.

Microbiological cultures of blood components have two aims: to avoid assigning contaminated blood components and to control the quality of the process of producing the blood components themselves. Given the low prevalence of potentially contaminated blood components, preventive bacteriological screening should include all blood components produced: this is an onerous and demanding strategy. Again, in consideration of the low prevalence of contamination, the efficacy of the bacteriological controls on samples can be challenged. Nevertheless, statistically and epidemiologically interesting results can be obtained from co-operation among centres which share the same investigation methods and aims.

We analyzed the technical feasibility of a study on microbiological contamination, using a simple system of diversion into a satellite bag, which allows the blood component to be sampled without compromising its clinical usefulness.

The system allows samples of the contents of the primary bag to be analysed, so the results are applicable to all the blood components produced by fractionating that unit of whole blood, or to conserve the satellite bag in the same conditions as those of the blood component to test, thus exactly reproducing the times and methods of storing the component.

Triple or quadruple bags with SAG-M are used. After having carried out the fractionation and having detached the plasma bag, the SAG-M is allowed to flow into the bag with the red blood cells. After mixing, about 20 mL of the product are allowed to flow into the bag containing SAG-M. This bag is then destined for sampling for microbiological tests.

We used this system to investigate microbial contamination of RCC. The satellite bags were stored in the blood bank in the same conditions as those used for

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the RCC to be transfused. The samples were taken in a sterile environment, under a laminar flow hood, on day + 16 of storage (this being the mean time of use of RCC in our centre) and on day + 42 (expiry date). The cultures were carried out with the MiniVITAL system (BioMerieux SA, Marcy-l'Etoile, France).

The presence of aerobic and anaerobic bacteria and mycetes was investigated. The sampling was carried out using two blood culture bottles with 5 mL of sample in each bottle. Overall, 340 cultures were set up for 170 units of RCC. One blood culture was positive for *Micrococcus spp.*, a saprophytic skin contaminant, weakly pathogenic

for humans. This positive culture was found in the group of samples taken on day + 42. Our results, indicating a higher than expected percentage of contamination, support the fact that the most prevalent type of contamination is that from the skin; the data are also of interest with the aim of controlling the production process of blood components⁵. It goes without saying that the number of investigations carried out is too low to attribute any statistical significance to the results.

We believe that it would be worthwhile building a multicentre collaboration on the basis of our methodological approach and in the light of our results.

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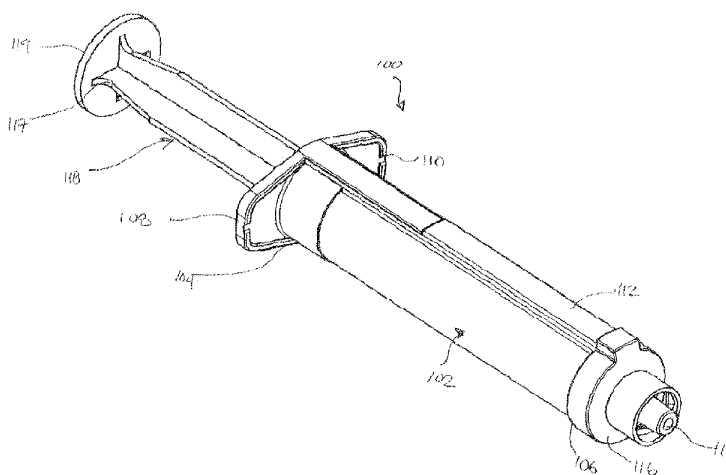
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(54) Title: DEVICE WITH INTEGRATED ALLERGY TESTING



(57) Abstract: The disclosure provides an allergy detection system for use during catheterization. The allergy detection system is incorporated into specialized syringes, connectors for use with standard syringes, or can be an independent test module designed for the sole purpose of allergy detection. The detection system features a test strip, such as an immunochromatographic test strip, and a structure to couple the system to a connector, syringe, or a housing, to form an independent test module. The detection system, by way of test strips, is used to detect potential allergic reactions.

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INTERNATIONAL APPLICATION FOR DEVICE WITH INTEGRATED ALLERGY TESTING

Related applications

[0001] This application claims the full Paris Convention priority to and benefit of U.S. Provisional Application Serial No. 61/564,593, filed on November 29, 2011, the contents of which are hereby incorporated by this reference, as if fully set forth herein in their entirety.

Field of the disclosure

[0002] The present disclosure generally relates to a medical testing device. More particularly, the present disclosure pertains to a device having an integrated allergy testing system.

Background of the disclosure

[0003] During surgical procedures and other medical procedures, it is often necessary to determine if a patient has any allergies that may be aggravated during the procedure. Testing for allergies can be a long process. Often, an immediate answer is needed during the procedure.

[0004] Extensive use of certain compounds in home and health care products (oral care products, contact lens care products, dressings, ointments, soaps, cosmetics) is causing a larger population to become pre-sensitized to such particular agents. When a pre-sensitized person comes in contact with such an agent, there is a high probability that person could develop much stronger symptoms as severe as anaphylactic shock with cardiac arrest. Currently known tests for such allergies cannot be performed at the patient bedside as they are time consuming, and involve numerous steps and equipment.

[0005] It is therefore desirable to provide a device for integrating allergy testing into a medical device.

Summary of the disclosure

[0006] The disclosure provides an allergy detection system for use during catheterization. The allergy detection system is incorporated into specialized syringes, connectors for use with standard syringes, or can be an independent test module designed for the sole purpose of allergy detection. The detection system features a test strip, such as an immunochromatographic test strip, and a structure to couple the system to a connector, syringe, or a housing, to form an independent test module. The detection system, by way of test strips, is used to detect potential allergic reactions.

[0007] In embodiments, the present disclosure provides a device for testing the presence or absence of a substance in blood, comprising: a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; a first chamber for receiving the withdrawn blood; a second chamber configured for holding a test strip; a test strip that is held within the second chamber; a wall or panel that separates the first chamber from the second chamber; at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber; wherein the second chamber comprises a window for viewing the test strip, wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and, wherein the window is configured to allow visual detection of the visible signal.

[0008] Also provided is the above device, that comprises a syringe and wherein the first chamber is defined by the housing of the syringe. Also provided is the above device, that does not comprises a syringe. Also provided is the above device, that is capable of being coupled to a syringe and to a needle, wherein the device has a hub that is capable of coupling to the hub of the syringe, and wherein the device has a coupler that is capable of coupling to a needle. Moreover, what is provided is the above device, wherein the substance is an antibody. Furthermore, what is contemplated is the above device, wherein the substance is an antibody of the class IgG, IgA, or IgE. Additionally,

what is embraced is the above device, wherein the substance is an antibody that specifically binds to an antimicrobial agent, e.g., antiseptic or antibiotic.

[0009] In embodiments, what is provided is the above device that is capable of: testing for the presence or absence of a first substance in the blood; and, testing for the presence or absence of a second substance in the blood; wherein the test strip is capable of separately providing a first visual signal for the first substance and a second visual signal for the second substance. Also, what is provided is the above device, wherein the first substance is an IgE antibody that specifically binds latex and the second substance is an IgE antibody that specifically binds an antiseptic. What is further embraced is the above device, wherein the second chamber comprises a flexible dome, and wherein the flexible dome is capable of flexing radially outward; wherein in use the flexible dome flexes radially outwards and creates a partial vacuum that is capable of drawing blood out of the first chamber and into the second chamber; wherein a sliding latch is operably linked with the flexible dome; wherein in use the sliding latch is capable of being slid over the dome to compress the flexible dome radially downwards and increase the pressure within the second chamber; and wherein in use the sliding latch is capable of being slid away from the dome to release the dome and allow the dome to flex radially outwards thereby creating a partial vacuum in the second chamber. Alternatively, the first substance can be an antibody of the IgG, IgA, IgM, or IgD class. Alternatively, the second substance can be an antibody of the IgG, IgA, IgM, or IgD class.

[0010] In yet another aspect, what is provided is the above device, further comprising an end-cap, wherein the end-cap is configured for contacting and stabilizing the test strip, and configured for contacting and stabilizing the proximal portion of a needle that is coupled to said device. Also provided is the above device, wherein the second chamber comprises a proximal end and a distal end, and wherein one or both of the proximal end and distal ends comprises an opening for installing the test strip from the second chamber. In yet another aspect, what is provided is the above device, wherein the second chamber comprises a proximal end and a distal end, and wherein one or both of the proximal end and distal ends comprises an opening for installing the test

strip from the second chamber, further comprising one or more end caps that capable of capping one or both of the proximal end and the distal end.

[0011]What is further embraced, is the above device further comprising a needle, wherein the needle is reversibly coupled to the coupler. Also contemplated is the above device that does not comprise a needle.

[0012]In yet another embodiment, what is contemplated is a device for testing the presence or absence of IgE in blood, comprising: a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; a first chamber for receiving the withdrawn blood; a second chamber configured for holding a test strip; a test strip that is held within the second chamber; a wall or panel that separates the first chamber from the second chamber; at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber; wherein the second chamber comprises a window for viewing the test strip; wherein the test strip is capable of producing a visible signal that indicates the presence or absence, in the withdrawn blood, of an antibody of the IgE class that specifically binds to an antiseptic or an antibiotic; and, wherein the window is configured to allow visual detection of the visible signal. Also provided is the above device, wherein the test strip is an immunochromatographic test strip.

[0013]In a process embodiment, what is provided is a process for allergy detection during catheterization, comprising: the step of drawing blood from a subject into the first chamber of a device that comprises: (a) a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; (b) a first chamber for receiving the withdrawn blood; (c) a second chamber configured for holding a test strip; (d) a test strip that is held within the second chamber; (e) a wall or panel that separates the first chamber from the second chamber; (f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber; (g) wherein the second chamber comprises a window for viewing the test strip, (h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and, (i) wherein the window is configured to allow

visual detection of the visible signal; the step of allowing at least some of the drawn blood to enter the second chamber of the device; wherein a needle is coupled to the device; and, wherein in use, at least some of the withdrawn blood enters the needle and then enters the first chamber, then enters the second chamber, and then contacts the test strip.

[0014] In yet another process embodiment, what is provided is the above process, further comprising a reaction that is mediated by the test strip, wherein the reaction produces a visual signal that indicates presence or absence of a substance that mediates an allergy. Also provided is the above process, wherein the drawing blood into the first chamber is urged by one or more of: (a) Blood pressure of the subject; (b) Vacuum produced by a syringe plunger of the device; (c) Vacuum produced by a flexible dome of the device; and (d) Capillary action of the test strip of the device. In yet another process embodiment, the disclosure provides the above process wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent, e.g., antiseptic or antibiotic; wherein in use the test strip provides a visual signal that the blood does not contain detectable antibodies that specifically bind to the specific antimicrobial agent, e.g., antiseptic or antibiotic; followed by the step of inserting a catheter into the subject, wherein the catheter is impregnated or coated with the antimicrobial agent, e.g., antiseptic or antibiotic.

[0015] Also provided is the above process, wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent, e.g., antiseptic or antibiotic; wherein in use the test strip provides a visual signal that the blood does contain detectable antibodies that specifically bind to the specific antiseptic or antibiotic; followed by the step of making a decision on whether or not to insert a catheter that is impregnated or coated with the antiseptic or antibiotic; and, wherein the decision is to refrain from inserting the catheter in the subject, followed by the step of inserting a catheter into the subject, wherein the catheter is not impregnated or coated with the antiseptic or antibiotic.

[0016] In a system embodiment, the disclosure provides a system comprising, in combination, a medical instrument that is capable of holding blood, and a medical device that comprises: (a) a coupler or hub that is capable of coupling with a needle,

wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device; (b) a first chamber for receiving the withdrawn blood; (c) a second chamber configured for holding a test strip; (d) a test strip that is held within the second chamber; (e) a wall or panel that separates the first chamber from the second chamber;

[0017] (f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber; (g) wherein the second chamber comprises a window for viewing the test strip, (h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and, (i) wherein the window is configured to allow visual detection of the visible signal. What is also embraced, is the above system, wherein the combination is a reversible combination or a permanent combination. Furthermore, what is provided is the above system, wherein the combination is a reversible combination, wherein the device and the medical instrument are held in combination by one or more of a clip, snap, lock, or tab. Also disclosed, is the above system, wherein the combination is a permanent combination, wherein the device and the medical instrument are held in combination by one or more of an adhesive or integral molding. In yet another system embodiment, what is provided is the above system, wherein the medical instrument comprises one or more of a syringe, trocar, catheter, introducer, sheath, hub, pump, or valve.

[0018] The foregoing needs are met, to a great extent, by the present disclosure, wherein in some embodiments a device with an integrated allergy testing system that is capable of overcoming the disadvantages described herein at least to some extent is provided.

[0019] In accordance with an embodiment of the present disclosure an allergy testing device for testing a sample includes a housing having a proximal end and a distal end. The housing can also include an outer wall defining an inner chamber extending through at least a portion of the housing. The device can also include a needle extending from a distal end of the housing. Additionally, the device can include an immunochromatographic test strip configured to indicate whether a predetermined antibody is present in the sample. The test strip can be positioned in the housing.

[0020] In accordance with another embodiment of the present disclosure, a syringe with an integrated allergy testing system includes a syringe housing having an outer wall defining an inner chamber extending through at least a portion of the syringe housing and the syringe housing having a proximal end and a distal end. The syringe can also include a needle extending from a distal end of the housing. Additionally a syringe plunger can be movably disposed within the inner chamber of the syringe housing. The syringe can also include an immunochromatographic test component configured to indicate whether a predetermined antibody is present in a sample, where the sample can be aspirated into the syringe, and wherein the test component is positioned in the syringe housing.

[0021] In accordance with another embodiment of the present disclosure, an attachment for a medical device having an integrated allergy testing system can include a housing having a proximal end and a distal end, wherein the proximal end is configured to couple to a medical device and the distal end is configured to receive a needle. The attachment can also include an immunochromatographic test component configured to indicate whether a predetermined antibody is present in a sample, wherein the test component is positioned in the housing. The sample can be aspirated into the housing. Additionally, the attachment can include a window disposed in the housing such that the test component is viewable.

[0022] There has thus been outlined, rather broadly, certain embodiments of the invention in order that the detailed description thereof, herein may be better understood, and in order that the present contribution to the art may be better appreciated. There are, of course, additional embodiments of the invention that will be described below and which will form the subject matter of the claims appended hereto.

[0023] In this respect, before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and to the arrangements of the components set forth in the following description or illustrated in the drawings. The invention is capable of embodiments in addition to those described and of being practiced and carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein, as well as the abstract, are for the purpose of description and should not be regarded as limiting.

[0024] As such, those skilled in the art will appreciate that the conception upon which this disclosure is based may readily be utilized as a basis for the designing of other structures, methods and systems for carrying out the several purposes of the present disclosure. It is important, therefore, that the claims be regarded as including such equivalent constructions insofar as they do not depart from the spirit and scope of the present disclosure.

[0025] Components for the methods and devices of the disclosure are available, for example, from any major medical device company, for example, Medtronic of Minneapolis, MN; Advanced Cardiovascular Systems in Santa Clara, CA; Baxter International of Deerfield, IL; Abbott Laboratories at Abbott Park, IL, Edwards Lifesciences, Irvine, CA, and Boston Scientific of Natick, MA. Components of the present disclosure can be made, without limitation, by molding, blow molding, slush molding, injection molding, rotational molding, compression molding, extrusion, thermoforming, stamping, calendaring, and so on (Brazel, CS; Rosen, SL (2012) Fundamental Principles of Polymeric Materials. Wiley, Hoboken, NJ).

Brief descriptions of the drawings

[0026] FIG. 1 illustrates a test strip in accordance with an embodiment of the invention.

[0027] FIGS. 2 and 3 illustrate a perspective view of an independent allergy testing module in accordance with an embodiment of the invention.

[0028] FIGS. 4 and 5 illustrate a sectional view of the independent allergy testing module illustrated in FIGS. 2 and 3 in accordance with an embodiment of the invention.

[0029] FIG. 6 illustrates an exploded view of the independent allergy testing module illustrated in FIGS. 2-5 in accordance with an embodiment of the invention.

[0030] FIG. 7 illustrates a syringe with integrated allergy testing in accordance with an embodiment of the invention.

[0031] FIG. 8 illustrates a sectional view of the syringe with integrated allergy testing illustrated in FIG. 7 in accordance with an embodiment of the invention.

[0032] FIG. 9 illustrates an exploded view of the syringe with integrated allergy testing illustrated in FIGS. 7 and 8 in accordance with an embodiment of the invention.

[0033] FIG. 10 illustrates a connector with integrated allergy testing in accordance with an embodiment of the invention.

[0034] FIG. 11 illustrates a sectional view of the connector with integrated allergy testing illustrated in FIG. 10 in accordance with an embodiment of the invention.

[0035] FIG. 12 illustrates an exploded view of the connector with integrated allergy testing illustrated in FIGS. 10 and 11 in accordance with an embodiment of the invention.

[0036] FIG. 13 (A, B) illustrates the cap that is a part of the module embodiment, and structures in the vicinity of the cap.

Detailed description

[0037] The present disclosure provides in some embodiments, an allergy detection system for integration into medical devices. For instance, in accordance with embodiments of this invention, the allergy detection system can be incorporated into a specialized syringe, a connector for use with a standard syringe, or an independent test module, designed for the sole purpose of allergy detection. The detection system can include, without limitation, an immunochromatographic membrane and structure to couple it to a connector or syringe or a housing to form an independent test module. The detection system can be used to detect any potential allergies that can be identified using immunochromatography.

[0038] In embodiments, what is provided is a device and related methods for point of care testing. For example, where a needle is introduced for use in the Seldinger technique, the needle can be used in conjunction with device and method of the present disclosure for detecting antibodies and predicting adverse allergic reactions. The *Seldinger* technique, includes the initial step of inserting a needle into a patient's blood vessel, where the Seldinger technique concludes with replacing the needle with a catheter or other medical device. The end-result is that the catheter or other medical device is situated in a subject's blood vessel or other body cavity. The *Seldinger* technique, and variations thereof, and devices used to perform this technique, are described in Seldinger (1953) *Acta Radiologica* 39:368-376; U.S. Pat. No. 7,722,567 issued to Tal, 7,972,307 issued to Kraus, et al, and 7,938,806 issued to Fisher, et al, which are incorporated by reference. Following testing by device and method of the present disclosure, and where the test gives a negative result (indicating that the subject is not allergic), the clinician can proceed with the *Seldinger* technique, and replace the needle with a catheter that contains the antigenic drug, antigenic antiseptic,

antigenic adhesive, or antigenic latex. Alternatively, if the test gives a positive result and indicates that the subject is likely to be allergic to the antigenic drug, antigenic antimicrobial agent, antigenic antiseptic, antigenic adhesive, or antigenic latex, then the clinician refrains from using the medical device. Where the test gives a positive result, the clinician can use an alternative medical device that does not contain the offending drug, antiseptic, adhesive, or latex, and the like.

[0039] In this way, the device and procedure of the present disclosure is used at the point of care, and is integrated into the procedure for using any medical device of interest, and where the device and procedure of the present disclosure can give the clinician a yes/no answer. The device of the present disclosure can be a physical part of a device used for the medical procedure of interest, for example, the device can be connected to a syringe that is used in the *Seldinger* technique or other procedure. This connection can be by way of a luer lock, Storz lock, or other coupler. Alternatively, the device of the present procedure can be integrated into a syringe, that is, permanently molded into the syringe, that is used in the *Seldinger* technique or other procedure.

[0040] In exclusionary embodiments, the present disclosure includes only test-strip devices that are integrated into a syringe. In another exclusionary embodiment, the present disclosure excludes test-strip devices that are not integrated into a syringe. In exclusionary embodiments, the present disclosure includes only test-strip devices that are integrated into a needle hub, trocar, dilator, syringe, syringe barrel, introducer, and the like. In another exclusionary embodiment, the present disclosure excludes test-strip devices that are not integrated into a needle hub, that are not integrated into a trocar, that are not integrated into a dilator, that are not integrated into a syringe or syringe barrel, that are not integrated into an introducer, and the like.

Immune disorders arising from exposure to medical devices and pharmaceuticals

[0041] In embodiments, the present disclosure provides a device and related methods, for detecting antibodies against components of medical devices or components of pharmaceuticals, and for quantitating or for predicting allergic reactions in a subject to be exposed to the medical device or the pharmaceutical. What can be quantitated is, for example, antibodies of one or more of the classes IgG, IgA, IgM, IgD, or IgE, that are present in a subject's bloodstream or in any biological fluid. The device and related methods are configured for quantifying or for predicting anaphylactic-type reactions or

bronchospasm (Layton et al (1989) Clin. Exp. Allergy. 19:307-314; Terazawa et al(1998) Anesthesiology. 89:1298-1300), allergic contact dermatitis, irritant contact dermatitis, photoallergic contact dermatitis, or immediate type contact reactions (Kutzscher (2012) Clin. J. Oncol. Nurs. 16:E48-55; Krasteva (1999) Eur. J. Dermatol. 9:144-159), arising from exposure to an antimicrobial agent or an antiseptic, e.g., a biguanide antiseptic.

Allergic reactions against and antibodies to antimicrobial agents, and to other components of medical devices

[0042] Device and methods of the present disclosure can detect antibodies, present in a subject's blood, serum, or other biological fluid, where the antibodies specifically bind to an antimicrobial agent, such as an antiseptic or antibiotic (Torres et al (2009) 19:67-68), antibiotics such as rifampicin (Feng et al (2011) Eur. J. Dermatol. 21:696-699), adhesives on catheters (Meikle et al (2012) Can. J. Anaesth. 59:815-816), thimerosol or other preservatives in medical devices (Ancona et al (1990) Dermatol. Clin. 8:95-105). Allergic reactions to latex, and antibodies against latex, have been described (Patriarca et al (2002) J. Investig. Allergol. Clin. Immunol. 12:169-176; Unsel et al (2012) Int. Arch. Allergy Immunol. 158:281-287). Allergic reactions (anaphylaxis) can occur in response to medical devices impregnated with one or more antiseptics (Darouiche and Raad (1999) New Engl. J. Med. 1762 (1 page)). Antibodies of the classes IgG and IgA are associated with drug-induced eruptions (pemphigus foliaceus) (Feng et al (2011) Eur. J. Dermatol. 21:696-699). Antibodies of the classes IgG and IgE are associated with allergic reactions to antiseptics (Layton et al (1987) Mol. Immunol. 24:133-141). Antibodies of the IgE class have been identified that are responsible for hypersensitivity to various beta-lactam antibiotics (Gunez et al (2012) J. Investig. Allergol. Clin. Immunol. 22:41-47). IgE antibodies have also been identified that specifically react against latex (Galindo et al (2011) J. Investig. Allergol. Clin. Immunol. 21:459-465).

[0043] The term "antimicrobial" encompasses, but is not limited to, antiseptics and antibiotics.

Detecting antibodies and other molecules that can provoke adverse events

[0044] Antibodies in blood or in other biological fluids can be detected, for example, by way of reagents in a test strip. The reagents can be covalently or non-covalently attached to the surface of a test strip, the reagents can be adsorbed to a test strip, the

reagents can be absorbed to a test strip, the reagents can be covalently or non-covalently bound to interior of test strip, such as porous interior or fibrous interior, or any combination of the above. Reagents, test strips, substrates, for immune assays, including color reactions, and the like, are provided, for example, from US 7,544,324 issued to Tung et al, US 7,438,852 issued to Tung et al, US 7,989,217 issued to Yee et al, 7,910,381 of Ford et al, each of which is individually incorporated herein by reference, each in its entirety. The present disclosure encompasses detection of antibodies, such as IgG, IgA, IgM, IgD, or IgE, detecting B cells that express IgE or other classes of antibodies, by way of test strip technology. Several antibody classes can be simultaneously expressed in the body, and that recognize the same antigen. Accordingly, the present disclosure provides a test strip that can detect antibodies two or more of the classes IgG, IgA, IgM, IgA, IgD, or IgE. In one embodiment, the test strip detects two different classes, and provides two different colors. In another embodiment, the test strip detects two different classes, and provides the same color for both of the respective color reactions, but at different locations in the test strip. In yet another embodiment, the test strip detects a plurality of different antibody classes (or detects a plurality of different specific antibodies that bind to respective different antigens, where all of these specific antibodies are in one particular class). Combinations of the previous embodiments are also provided, e.g., detecting IgG that binds to an antibiotic, and detecting IgE that binds to latex, or detecting an antibody that binds to an antimicrobial and an antibody that binds to a pathogen. Color reaction can be provided by a label that comprises a metal, a colloidal particle such as colloidal gold, a dye particle, or results from a reaction catalyzed by peroxidase or alkaline phosphatase (see US 7,262,019 issued to Kovalenko, US 5,200,312 issued to Oprandy, US 5,637,468 issued to Mason, and US 6,503,726 issued to Anne, which are each incorporated herein in their entirety). Where a gold labeled anti-IgE antibody is used, for example, a test sample (e.g., blood) reacts with the gold labeled anti-IgE antibody, forming a complex. The complex travels across a membrane where immobilized allergens capture the complex, resulting in a colored line (see US 7,629,127 issued to Hubscher, which is incorporated herein by reference).

[0045] The following provides a non-limiting example. For detection of anti-antiseptic antibodies, blood can be deposited at a sample receiving area located at a first end of

the test strip. Flow of solvent from the first end of the test strip towards the opposite end of the test strip draws any antibodies towards the test strip, and draws the antibodies over a region of the test strip that contains conjugates of gold-antiseptic. When the antibodies migrate over the area that contains gold-antiseptic, the result is an insoluble complex that forms a visually detectable line. Conjugates of gold-antiseptic that are not trapped as part of this insoluble complex continue to migrate on the test strip, and do not contribute to the visual signal of the line. As an alternative to using a conjugate of gold-antiseptic, what can be used is a conjugate of gold with an antibody that specifically binds to anti-antiseptic antibodies (anti-idiotypic antibodies). The above narrative applies to anti-antiseptic antibodies, but also to embodiments where the antigen is an antibiotic, a pharmaceutical, a drug, latex, an adhesive, and the like.

[0046] In a non-limiting embodiment, what is provided is a device that encompasses an immunoassay with all reagents embedded on a test strip that performs without the use of instruments. Total IgE in a biological fluid is bound by anti-human IgE immobilized on test strips in the IgE reactive field of the test strip. Visualization of captured IgE is indicated by colloidal gold labeled anti-human IgE. Excess labeled antibodies are captured by antibodies in the control field. A control line appears in the control field and determines when enough of the biological fluid has been collected. The presence of IgE in the sample is visualized by the appearance of a dark-colored line, e.g., a red line, in the reactive field and the control field. Absence of a line in the control field, regardless of the presence of line in the reactive field, indicates an invalid assay result. The area on the support identifying the reactive field and control field are on the back surface of the support in two colors. A sample with IgE in the normal reference range lacks a line in the reactive field but has a line in the control field. The presence of lines in the reactive and control fields indicates a sample with elevated total IgE levels. The device provides a qualitative/semi-quantitative measure of total IgE in the biological fluid when the intensity of color on the test strip is visually observed. The skilled artisan can divide or classify the different intensities of signal as negative or as positive, and the skilled artisan can prepare a standard operating procedure (SOP) that sets forth these different intensities. What is also provided is the above embodiment, but where it applies to other antibody classes, e.g., IgG, IgA, IgM, or IgD.

[0047] In a non-limiting embodiment, what is provided is a device that comprises a series of capillary beds (elements), for example, made of cellulose. The first element (a sample pad) acts as a sponge and can hold an excessive amount of biological fluid. Then, the fluid migrates to the second element (conjugate pad). The second element is manufactured with a conjugate, a dried format of particles in a soluble matrix that contains reagents that promote the desired chemical reaction between the target molecule (antigen) and its binding partner (antibody) that has been immobilized on the surface of the particle. At the time that the sample fluid dissolves the soluble matrix, it also dissolves the particles and the sample and conjugate mix while flowing through the porous structure. In this way, the analyte binds to the particles while migrating further through the third capillary bed. This material has one or more regions or stripes where a third molecule has been immobilized. By the time the sample-conjugate mix has migrated to these stripes, analyte has been bound on the particle and the third capture molecule binds the complex. When additional fluid passes the stripes, particles accumulate and the stripe-area changes color. In embodiments, there can be two stripes: one (the control) that captures any particle and demonstrates that reaction is in working order, the second contains a specific capture molecule and only captures those particles on which an analyte molecule has been immobilized.

Duration of detection

[0048] In embodiments, what is provided is a device that is capable of detecting an antibody responsible for an allergic reaction, for example, to an antibiotic or antiseptic, (1) During a blood draw that is dedicated to this detection;

(2) Only during a blood draw that is dedicated to this detection, with no capability during subsequent procedures, e.g., during insertion of a catheter or other medical instrument. This is an exclusionary embodiment;

(3) During a period of time when a catheter or other medical instrument is indwelling in a subject, that is, when a catheter or other medical instrument is operably linked to a subject. This period of time can be, e.g., at least ten minutes, at least one hour, at least one day, at least one week, at least one month, and the like;

(4) Only during a period of time when a catheter or other medical instrument is indwelling in a subject, but not capable of detecting the antibody during a blood draw

that is solely dedicated to the detection of the antibody. This is an exclusionary embodiment.

Antibodies and other reagents

[0049] "Specifically" or "selectively" binds, when referring to a ligand/receptor, nucleic acid/complementary nucleic acid, antibody/antigen, or other binding pair (e.g., a cytokine to a cytokine receptor) indicates a binding reaction which is determinative of the presence of the protein in a heterogeneous population of proteins and other biologics. Thus, under designated conditions, a specified ligand binds to a particular receptor and does not bind in a significant amount to other proteins present in the sample. Specific binding can also mean, e.g., that the binding compound, nucleic acid ligand, antibody, or binding composition derived from the antigen-binding site of an antibody, of the contemplated method binds to its target with an affinity that is often at least 25% greater, more often at least 50% greater, most often at least 100% (2-fold) greater, conventionally at least ten times greater, more normally at least 20-times greater, more typically at least 100-times greater, and most typically at least 1000-fold than the affinity with any other binding compound (see, e.g., US 2012/0121643 of Dubensky, which is incorporated by reference).

[0050] In a typical embodiment an antibody will have an affinity that is greater than about 10^9 liters/mol, as determined, e.g., by Scatchard analysis (Munsen, et al. (1980) *Analyt. Biochem.* 107:220-239). It is recognized by the skilled artisan that some binding compounds can specifically bind to more than one target, e.g., an antibody specifically binds to its antigen, binds to lectins by way of the antibody's oligosaccharide, and also binds to an Fc receptor by way of the antibody's Fc region.

[0051] In embodiments, the disclosure provides test strip that is capable of detecting antibodies in blood, where the antibodies specifically bind to a pathogen. Anti-pathogen antibodies have been characterized. Reagents and kits are available for detecting antibodies that specifically bind to viruses (e.g., HIV, HCV, HBV), fungi, and bacteria (see, e.g., Novack et al (2006) *J. Clin. Microbiol.* 44:2909-2913; Hennessey et al (2009) *J. Urban Health.* 86:93-105; Thurman et al (2009) *Clin. Infect. Dis.* 48:1244-1249; Alexander et al (1996) *J. Clin. Microbiol.* 34:1180-1183).

[0052] "Sample" refers to a sample from a human, animal, placebo, or research sample, e.g., a cell, tissue, organ, fluid, gas, aerosol, slurry, colloid, or coagulated material. The "sample" may be tested in vivo, e.g., without removal from the human or animal, or it may be tested in vitro. The sample may be tested after processing, e.g., by histological methods. "Sample" also refers, e.g., to a cell comprising a fluid or tissue sample or a cell separated from a fluid or tissue sample. "Sample" may also refer to a cell, tissue, organ, or fluid that is freshly taken from a human or animal, or to a cell, tissue, organ, or fluid that is processed or stored.

[0053] A composition that is "labeled" is detectable, either directly or indirectly, by spectroscopic, photochemical, biochemical, immunochemical, isotopic, or chemical methods. For example, useful labels include ^{32}P , ^{33}P , ^{35}S , ^{14}C , ^3H , ^{125}I , stable isotopes, epitope tags fluorescent dyes, electron-dense reagents, substrates, or enzymes, e.g., as used in enzyme-linked immunoassays, or fluorettes (see, e.g., Rozinov and Nolan (1998) Chem. Biol. 5:713-728).

Detailed descriptions of the figures

[0054] The invention will now be described with reference to the drawing figures, in which like reference numerals refer to like parts throughout. As illustrated in FIG. 1, the allergy detection system can include an immunochromatographic membrane 2 (PVDF or nitrocellulose material) in strip or cassette format that can detect elevated levels of an allergen by employing a highly sensitive detecting antibody and a carrier-protein conjugated hapten. The antibody is labeled with a signal generator (e.g., colloidal gold), which is placed in the dry state at a predetermined site on the membrane. Using this novel approach the clinician (catheter inserters) would be able to determine if a patient is at risk of developing an allergic reaction before potentially introducing an allergen into a patient's system. The system also provides ease of use to the hospital staff as it does not require any additional step, equipment or time other than what is needed for standard procedures.

[0055] FIGS. 2 and 3 illustrate an independent testing module in accordance with an embodiment of this invention. FIG. 2 illustrates the independent testing module 10 in its inactive state and FIG. 3 illustrates the independent testing module 10 in its active state. The independent testing module 10 includes a housing 12 having a proximal end 14 and a distal end 16. A needle 18 can extend from the distal end 16 of the housing 12.

The needle 18 can include a sharpened distal end 20 and a proximal end 22 that extends into the housing 12. The needle 18 can be generally configured as a hypodermic-type needle with a bore 24 extending through its length. The testing module 10 can also include a viewing window 26, through which test strip 28 can be observed. The test strip 28 is disposed within the housing 12 behind the window 26, such that the operator can view any changes in the strip 28 during use. The testing module 10 can also include a slide 30 and a vacuum button 32 (as illustrated in FIGS. 4-6). In the inactive state illustrated in FIG. 2, the slide 30 is positioned toward the distal end of the testing module 10. When the needle 18 is inserted into the patient and testing is required the slide 30 can be moved from its distal, forward position to a proximal position. Slot 34, positioned on a side 36 of housing 12 in FIGS. 2 and 3, is configured to lock the slide 30 into place after it has been activated into the proximal position.

[0056] The button can comprise an elastic material, for example, silicone, latex, or polyurethane. In one non-limiting embodiment, button is thinner at the peak of the button's dome, and is thicker at the base of the dome.

[0057] FIGS. 4 and 5 illustrate a sectional view of the independent testing module 10 illustrated in FIGS. 2 and 3. FIG. 4 is a sectional view of the independent testing module 10 in the inactive position, as illustrated in FIG. 2, and FIG. 5 is a sectional view of the independent testing module 10 in the active position, as illustrated in FIG. 3. The housing 12 can define an inner space 38 near the proximal end 14 of the testing module 10. The test strip 28 can be disposed in this inner space 38. In addition, an absorbent pad 40 can be integrated into the bottom of the test strip 28 in this inner space 38. The test strip 28 can include a proximal end 42 and a distal end 44. Cap 46 is positioned on top of the junction between the proximal end of the needle 22 and the distal end 44 of the test strip 28.

[0058] The following concerns non-limiting embodiments of cap (46). The cap holds or positions the test strip. The cap holds or positions the proximal end of the needle. Also, the cap creates or defines small vacuum pathways from the vacuum button to the proximal end of the needle. In a preferred embodiment, the cap (46), is not removable.

[0059] In a non-limiting embodiment of the present disclosure, the absorbent pad is an integrated part of the test strip. In another non-limiting embodiment, the absorbent pad

is separate from, and does not occupy the same space as, the test strip. The absorbent pad increases the total volume of sample that enters the test strip. The absorbent pad can block the migration of blood cells, and thereby provide a clean field for development and detection (by clinician's eyes) of the color reaction. In addition, or alternatively, the absorbent pad can draw the biological fluid by way of capillary attraction, resulting in wetting of a broad area of the test strip. In another embodiment, the device comprises only a test strip and does not contain any absorbent pad. In one embodiment that does not contain an absorbent pad, the test strip does not disperse fluid by way of capillary attraction, and the biological fluid is sufficiently dispersed without capillary attraction. In another embodiment, the test strip is sufficiently thick (or thin but sufficiently opaque) that it blocks passage of red blood cells to the viewable area where the color reaction takes place. In yet another embodiment, the test strip has capillary attraction and is also sufficiently thick (or thin but sufficiently opaque) to block passage of red blood cells, and to prevent the red blood cells from residing in the viewable area where the color reaction takes place). Absorbent pad can comprise cellulose, polyvinylidene fluoride (PVDF), nitrocellulose, and the like. Filter material suitable as a matrix for test strips, and for serving as a reaction area for color reagents, and optionally for blocking red blood cells, and optionally for serving as a capillary attractant for attracting and dispersing a biological fluid, are available (EMD Millipore, Darmstadt, Germany; Millipore, Billerica, MA; Membrane Solutions, Plano, TX). US 4,855,240 of Rosenstein, US 4,703,017 of Campbell, and US 4,376,110 of David et al, disclose absorbent materials, capillary materials, test strips, labels, and immunoassays, are incorporated herein by reference in their entirety.

[0060] FIGS. 4 and 5 also illustrate a vacuum button 32 of the independent testing module 10. In the inactivated position illustrated in FIG. 4, the vacuum button 32 is depressed by slide 30. This keeps the vacuum button 32 depressed until the needle 18 is inserted and ready to extract blood. As illustrated in FIG. 5, once the device is in position, the slide 30 is retracted to the active position, releasing vacuum button 32, thus creating a vacuum and allowing blood to flow into the bore 24 of the needle 18. Locking the slide 30 in the active position prevents depression of the vacuum button 32, when the needle 18 is inserted into a vein of the patient, in turn preventing air from potentially being pushed into the access point or blood being squirted from the device

after it has been used. The blood aspirated into the testing module 10 is absorbed from the bottom end of the testing strip 28. The absorbent pad 40 can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad 40 can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within approximately 10 minutes within the viewing window 26, but could take less time or more time depending on the detecting antibodies contained in the test strip.

[0061] FIG. 6 illustrates an exploded view of the independent testing module 10 as shown in FIGS. 2-5. As shown in FIG. 6, the testing module includes the housing 12 and a needle 18 coupled to a distal end 16 of the housing 12. The housing 12 also defines the inner space 38 near the proximal end 14 of the testing module 10. The test strip 28 can be disposed in this inner space 38. In addition, an absorbent pad 40 can be integrated into the test strip 28 in this inner space 38. The test strip 28 can include a proximal end 42 and a distal end 44. Cap 46 is positioned on top of the junction between the proximal end of the needle 22 and the distal end 44 of the absorbent pad 40. FIG. 6 also illustrates the slide 30 and the vacuum button 32 which work together to release the vacuum for the independent testing module such that it can aspirate the blood sample. The slide 30 and vacuum button 32 also prevent the vacuum button from being re-depressed to prevent pushing any air into the entry site or allowing any blood to spurt out after use. The vacuum button 32 sits within an opening 48 defined by the housing 12. The slide 30 can lock into position via the slot 34, also illustrated in FIGS. 2 and 3. As illustrated, tab 31 interacts with a notch 31' in the architecture of slot 34 in order to lock the slide 30 into place. However, any suitable means of locking the slide into place can be used. Locking the slide 30 in the active position prevents depression of the vacuum button 32, when the needle 18 is inserted into a vein of the patient, in turn preventing air from potentially being pushed into the access point or blood being squirted from the device after it has been used. Cap 46 is also shown and is placed over the junction between the testing strip 28 and the proximal end 22 of the needle 18.

[0062] FIG. 7 illustrates a syringe with integrated allergy testing, in accordance with another embodiment of the integrated allergy testing system. As shown in FIG. 7, the syringe 100 includes a housing 102 having a proximal end 104 and a distal end 106. The proximal end 104 of the housing 102 can include flanges 108, 110 which can serve

as finger rests during use of the syringe 100. The housing 102 can include a window 112 positioned such that test strip positioned below the window is visible to a user of the syringe 100. The test strip resides within its own lumen or channel, such that only the distal end of the test strip is exposed to the blood that is aspirated within the syringe housing 102. A needle hub 114 can be positioned at the distal end 106 of the housing 102 and can be configured to couple to a hypodermic-type needle for aspirating blood into a lumen of the syringe 100. A syringe housing cap 116 can be coupled to the distal end 106 to hold the test strip in the housing 102. The syringe 100 can also include a plunger 118 extending into the lumen of the housing 102 for creating negative pressure to aspirate blood into the lumen of the syringe. The plunger 118 can include a thumb rest 119 positioned at a proximal end 117 of the plunger 118.

[0063] In embodiments, where test strip resides in its own lumen or channel, blood or other biological sample enters channel through a hole, slit, passage, or crevice, that is about 5% the distal-to-proximal length of the channel, about 10% the distal-to-proximal length of the channel, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or longer, than the distal-to-proximal length of the channel. Where the slit or crevice is about 100% the distal-to-proximal length of the channel, the result is that blood entering the syringe, or entering a corresponding structure in the module (10), contacts that entire test strip essentially simultaneously.

[0064] Regarding the orientation of the channel with respect to the hole, slit, passage, or crevice, the hole, slit, or crevice, can start at a point corresponding to the distal-most portion of the channel, and then migrate proximally. Alternatively, the hole, slit, or crevice, can start at a point corresponding to the proximal-most portion of the channel, and then migrate distally. In yet another alternative, the hole, slit, passage, or crevice, can be situated entirely between the distal-most and proximal-most portions of the channel. For example, the hole or passage can be situated near the half-way point of the channel, where blood entering the hole migrates both in the proximal and in the distal directions.

[0065] In embodiments where the hole, slit, passage, or crevice, is about 5% the distal-to-proximal length of the channel, it may be the case that only about 5% of the

test strip is wetted by the blood or other biological sample. Alternatively, in embodiments where the hole, slit, passage, or crevice, is about 5% the distal-to-proximal length of the channel, it may be the case that greater than about 5% of the test strip is wetted by the blood or other biological sample, where this greater than amount results from migration of the biological sample through the test strip. Migration can be via diffusion, capillary force, or by a combination of diffusion and capillary force. The above narrative also applies to configurations where the hole, slit, passage, or crevice, is less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, less than 5%, of the length of the distal-to-proximal length of the channel.

[0066] FIG. 8 illustrates a sectional view of the syringe illustrated in FIG. 7. As shown in FIG. 8, the syringe 100 includes the housing 102 defining a lumen 120, extending therethrough. The plunger 118 is shown extending into the lumen 120 of the housing 102. Additionally, FIG. 8 illustrates test strip 122 positioned within the housing 102 beneath window 112. The syringe housing cap 116 holds the test strip 122 in place beneath the window 112 for observation by the practitioner. Alternately, the test strip 122 can take the form of a cassette or any other appropriate form for positioning within the syringe 100. In addition, an absorbent pad 124 can be integrated into the test strip 122. The absorbent pad 124 can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad 124 can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within approximately 10 minutes within the viewing window 112, but could take less time or more time depending on the antibodies contained in the test strip.

[0067] FIG. 9 illustrates an exploded view of the syringe illustrated in FIGS. 7 and 8. FIG. 9 shows the housing 102 having a window 112 for the test strip 122. The syringe housing cap 116 can be used to hold the test strip in place, such that it does not move during testing. The plunger 118 can be configured to slide within the lumen 120 of the housing 102.

[0068] FIG. 10 illustrates a connector design for the integrated testing system in accordance with an embodiment of the invention. The connector 200, includes a housing 201, having a proximal end 202 and a distal end 204, and can be configured for

placement between a syringe body and a needle for the syringe. The connector 200 can be connected to the syringe body in a variety of different ways such as frictional hold, tabs, or any other suitable coupling. As illustrated in FIG. 10, the connector 200 can be coupled to the syringe via luer threads 206 positioned at the proximal end 202 of the connector 200. The connector 200 can also include a coupling 208 for coupling the connector 200 to a needle. The needle can take the form of a hypodermic-type needle or any other needle suitable for aspirating blood through the connector 200. The connector also includes a window 210 through which test strip (not shown) can be visualized.

[0069] FIG. 11 illustrates a sectional view of the embodiment shown in FIG. 10 and FIG. 12 illustrates an exploded view of the embodiment illustrated in FIGS. 10 and 11. FIGS. 11 and 12 illustrate the test strip 214 disposed within the connector housing 201. As illustrated, the test strip 214 is spirally wound within the connector housing 201. The test strip 214 can be viewed through window 210 in the housing 201. Blood can be aspirated into a lumen 212 defined by housing 201, when testing is required. In addition, an absorbent pad 216 can be positioned beneath the test strip 214. The absorbent pad 216 integrated into the test strip 228 can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad 216 can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within approximately 10 minutes within the viewing window 210, but could take less time or more time depending on the antibodies contained in the blood sample.

[0070] Alternately test strip, for example, an immunochromatographic test strip, can be incorporated into a number of different medical devices. One such example is a test strip incorporated into a "hemo-hopper," such as a blood reservoir in a medical tray or kit. The blood aspirated during access to the vessel would be disposed into the hemo-hopper. The sample could then be absorbed into the test strip. In addition, an absorbent pad can be positioned beneath the test strip. The absorbent pad can absorb the plasma sample after the completion of the signal detection reaction. The absorbent pad can also include a porous backing and an absorbent dispersed, adsorbed, or coated into the pores of the porous backing. A color signal can appear within

approximately 10 minutes, but could take less time or more time depending on the antibodies contained in the blood sample.

[0071] FIG. 13 (A, B) illustrates the end-cap that is a part of the module embodiment, and structures in the vicinity of the cap. The end-cap (346) is in contact with needle (318). The end-cap (346) defines part of cavity (348) where the vacuum button (32) can fit. A non-limiting embodiment of vacuum button (32) is shown in FIGS. 4-6. FIG. 13(A) shows cap without test strip, and FIG. 13 (B) shows cap with test strip.

[0072] While the method and apparatus have been described in terms of what are presently considered to be the most practical and preferred embodiments, it is to be understood that the disclosure need not be limited to the disclosed embodiments. It is intended to cover various modifications and similar arrangements included within the spirit and scope of the claims, the scope of which should be accorded the broadest interpretation so as to encompass all such modifications and similar structures. The present disclosure includes any and all embodiments of the following claims.

[0073] It should also be understood that a variety of changes may be made without departing from the essence of the invention. Such changes are also implicitly included in the description. They still fall within the scope of this invention. It should be understood that this disclosure is intended to yield a patent covering numerous aspects of the invention both independently and as an overall system and in both method and apparatus modes.

[0074] Further, each of the various elements of the invention and claims may also be achieved in a variety of manners. This disclosure should be understood to encompass each such variation, be it a variation of an embodiment of any apparatus embodiment, a method or process embodiment, or even merely a variation of any element of these.

[0075] Particularly, it should be understood that as the disclosure relates to elements of the invention, the words for each element may be expressed by equivalent apparatus terms or method terms -- even if only the function or result is the same.

[0076] Such equivalent, broader, or even more generic terms should be considered to be encompassed in the description of each element or action. Such terms can be

substituted where desired to make explicit the implicitly broad coverage to which this invention is entitled.

[0077] It should be understood that all actions may be expressed as a means for taking that action or as an element which causes that action.

[0078] Similarly, each physical element disclosed should be understood to encompass a disclosure of the action which that physical element facilitates.

[0079] Any patents, publications, or other references mentioned in this application for patent are hereby incorporated by reference.

[0080] Finally, all references listed in the Information Disclosure Statement or other information statement filed with the application are hereby appended and hereby incorporated by reference; however, as to each of the above, to the extent that such information or statements incorporated by reference might be considered inconsistent with the patenting of this/these invention(s), such statements are expressly not to be considered as made by the applicant.

[0081] In this regard it should be understood that for practical reasons and so as to avoid adding potentially hundreds of claims, the applicant has presented claims with initial dependencies only.

[0082] Support should be understood to exist to the degree required under new matter laws -- including but not limited to United States Patent Law 35 USC §132 or other such laws -- to permit the addition of any of the various dependencies or other elements presented under one independent claim or concept as dependencies or elements under any other independent claim or concept.

[0083] To the extent that insubstantial substitutes are made, to the extent that the applicant did not in fact draft any claim so as to literally encompass any particular embodiment, and to the extent otherwise applicable, the applicant should not be understood to have in any way intended to or actually relinquished such coverage as the applicant simply may not have been able to anticipate all eventualities; one skilled in the art, should not be reasonably expected to have drafted a claim that would have literally encompassed such alternative embodiments.

[0084] Further, the use of the transitional phrase “comprising” is used to maintain the “open-end” claims herein, according to traditional claim interpretation. Thus, unless the context requires otherwise, it should be understood that the term “comprise” or variations such as “comprises” or “comprising”, are intended to imply the inclusion of a stated element or step or group of elements or steps but not the exclusion of any other element or step or group of elements or steps.

[0085] Such terms should be interpreted in their most expansive forms so as to afford the applicant the broadest coverage legally permissible.

[0086] The many features and advantages of the invention are apparent from the detailed specification, and thus, it is intended by the appended claims to cover all such features and advantages of the invention which fall within the true spirit and scope of the invention. Further, because numerous modifications and variations will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and operation illustrated and described, and accordingly, all suitable modifications and equivalents may be resorted to falling within the scope of the invention.

What is claimed is:

Claim 1. A device for testing the presence or absence of a substance in blood, comprising:

- a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;

- a first chamber for receiving the withdrawn blood;

- a second chamber configured for holding a test strip;

- a test strip that is held within the second chamber;

- a wall or panel that separates the first chamber from the second chamber;

- at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;

- wherein the second chamber comprises a window for viewing the test strip,

- wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and,

- wherein the window is configured to allow visual detection of the visible signal.

Claim 2. The device of claim 1, that comprises a syringe and wherein the first chamber is defined by the housing or barrel of the syringe.

Claim 3. The device of claim 1 that is capable of being coupled to a syringe and to a needle, wherein the device has a hub that is capable of coupling to the hub of the syringe, and wherein the device has a coupler that is capable of coupling to a hub of a needle.

Claim 4. The device of claim 1, wherein the substance is an antibody that specifically binds to an antimicrobial agent.

Claim 5. The device of claim 1, wherein the substance is an antibody of the class IgG, IgA, IgM, or IgE.

Claim 6. The device of claim 1, wherein the second chamber comprises a flexible dome, and

wherein the flexible dome is capable of flexing radially outward;

wherein in use the flexible dome flexes radially outwards and creates a partial vacuum that is capable of drawing blood out of the first chamber and into the second chamber;

wherein a sliding latch is operably linked with the flexible dome;

wherein in use the sliding latch is capable of being slid over the dome to compress the flexible dome radially downwards and increase the pressure within the second chamber; and

wherein in use the sliding latch is capable of being slid away from the dome to release the dome and allow the dome to flex radially outwards thereby creating a partial vacuum in the second chamber.

Claim 7. The device of claim 1, further comprising an end-cap, wherein the end-cap is configured for contacting and stabilizing the test strip, and configured for contacting and stabilizing the proximal portion of a needle that is coupled to said device.

Claim 8. The device of claim 1, further comprising a needle, wherein the needle is reversibly coupled to the coupler.

Claim 9. The device of claim 1 that does not comprise a needle.

Claim 10. The device of claim 1, wherein the test strip is an immunochromatographic test strip.

Claim 11. A device for testing the presence or absence of an antibody in blood, wherein the antibody specifically binds to an antimicrobial agent, comprising:

a coupler that is capable of coupling with a hub of a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;

a first chamber for receiving the withdrawn blood;

a second chamber configured for holding a test strip;
a test strip that is held within the second chamber;
a wall or panel that separates the first chamber from the second chamber;
at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;
wherein the second chamber comprises a window for viewing the test strip;
wherein the test strip is capable of producing a visible signal that indicates the presence or absence, in the withdrawn blood, of the antibody that specifically binds to the antimicrobial agent; and,
wherein the window is configured to allow visual detection of the visible signal.

Claim 12. A process for allergy detection during catheterization, comprising:
the step of drawing blood from a subject into the first chamber of a device that comprises:

- (a) a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;
 - (b) a first chamber for receiving the withdrawn blood;
 - (c) a second chamber configured for holding a test strip;
 - (d) a test strip that is held within the second chamber;
 - (e) a wall or panel that separates the first chamber from the second chamber;
 - (f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;
 - (g) wherein the second chamber comprises a window for viewing the test strip,
 - (h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and,
 - (i) wherein the window is configured to allow visual detection of the visible signal;
- the step of allowing at least some of the drawn blood to enter the second chamber of the device;

wherein a needle is coupled to the device; and,
wherein in use, at least some of the withdrawn blood enters the needle and then enters the first chamber, then enters the second chamber, and then contacts the test strip.

Claim 13. The process of claim 12, further comprising a reaction that is mediated by the test strip, wherein the reaction produces a visual signal that indicates presence or absence of a substance that mediates an allergy.

Claim 14. The process of claim 12, wherein the drawing blood into the first chamber is urged by one or more of: (a) Blood pressure of the subject; (b) Vacuum produced by a syringe plunger of the device; (c) Vacuum produced by a flexible dome of the device; and (d) Capillary action of the test strip of the device.

Claim 15. The process of claim 12, wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent;
wherein in use the test strip provides a visual signal that the blood does not contain detectable antibodies that specifically bind to the specific antimicrobial agent;
followed by the step of inserting a catheter into the subject, wherein the catheter is impregnated or coated with the antimicrobial agent.

Claim 16. The process of claim 12, wherein the test strip is configured for detecting an antibody that specifically binds an antimicrobial agent;
wherein in use the test strip provides a visual signal that the blood does contain detectable antibodies that specifically bind to the specific antimicrobial agent;
followed by the step of making a decision on whether or not to insert a catheter that is impregnated or coated with the antimicrobial agent; and,
wherein the decision is to refrain from inserting the catheter in the subject,
followed by the step of inserting a catheter into the subject, wherein the catheter is not impregnated or coated with the antimicrobial agent.

Claim 17. A system comprising, in combination, a medical instrument that is capable of holding blood, and a medical device that comprises:

- (a) a coupler or hub that is capable of coupling with a needle, wherein the needle is for withdrawing blood from a subject and for introducing the withdrawn blood into the device;
- (b) a first chamber for receiving the withdrawn blood;
- (c) a second chamber configured for holding a test strip;
- (d) a test strip that is held within the second chamber;
- (e) a wall or panel that separates the first chamber from the second chamber;
- (f) at least one aperture in the wall or panel configuring for allowing blood to pass from the first chamber to the second chamber;
- (g) wherein the second chamber comprises a window for viewing the test strip,
- (h) wherein the test strip is capable of producing a visible signal that indicates the presence or absence of the substance in the withdrawn blood; and,
- (i) wherein the window is configured to allow visual detection of the visible signal.

Claim 18. The system of claim 17, wherein the combination is a reversible combination or a permanent combination.

Claim 19. The system of claim 17, wherein the combination is a reversible combination, wherein the device and the medical instrument are held in combination by one or more of a clip, snap, lock, or tab.

Claim 20. The system of claim 17, wherein the medical instrument comprises one or more of a syringe, trocar, catheter, introducer, sheath, hub, pump, or valve.

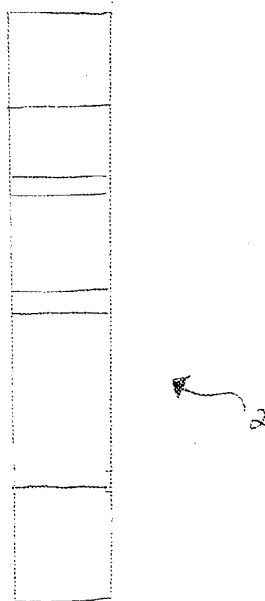


FIG. 1

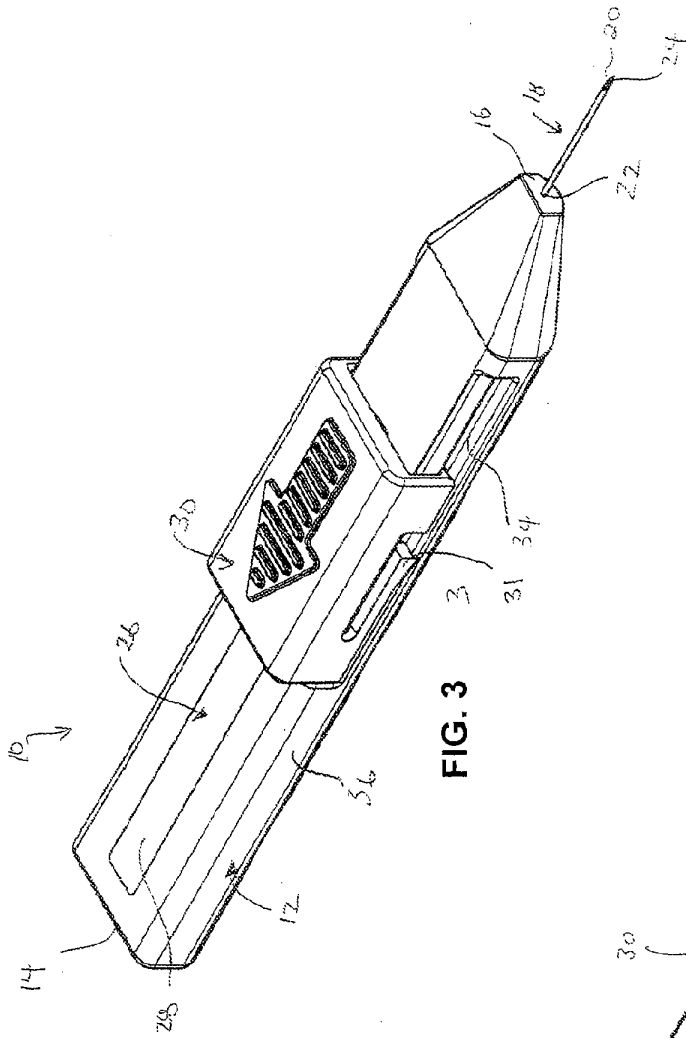


FIG. 3

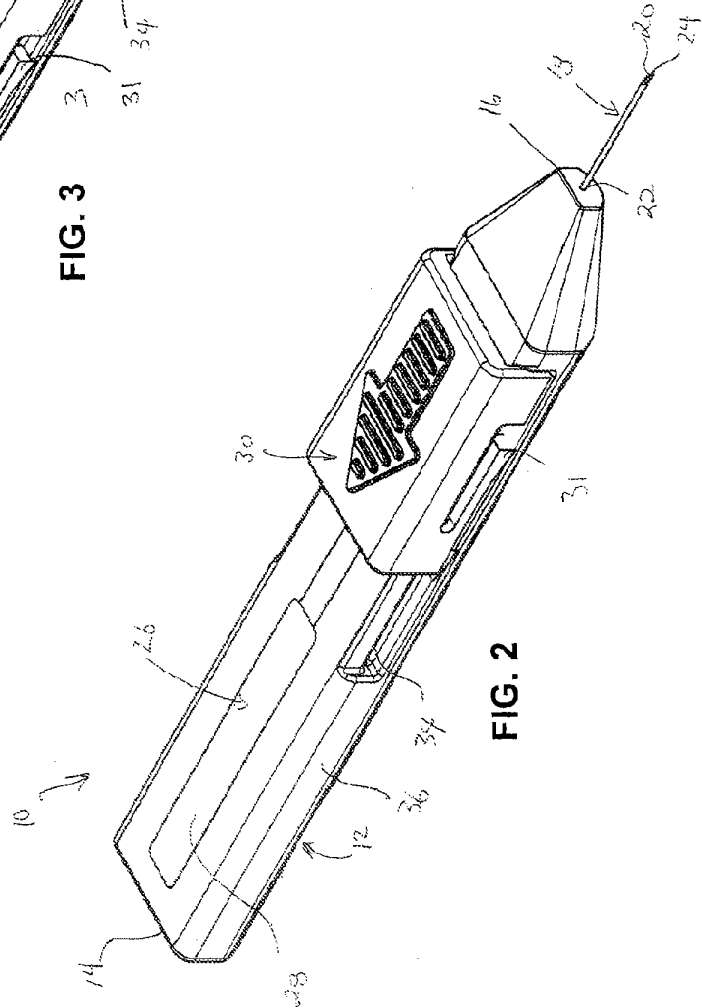
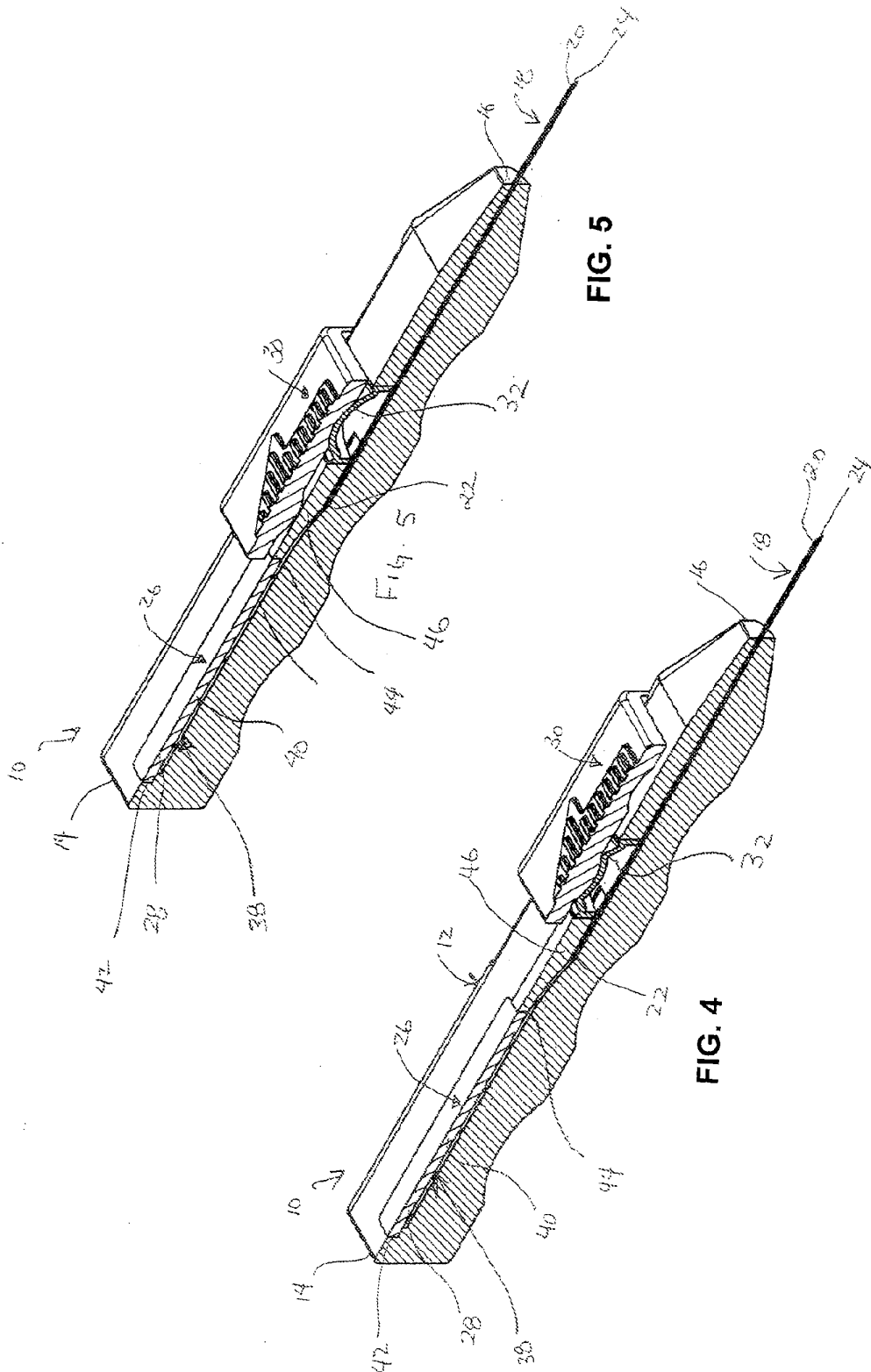
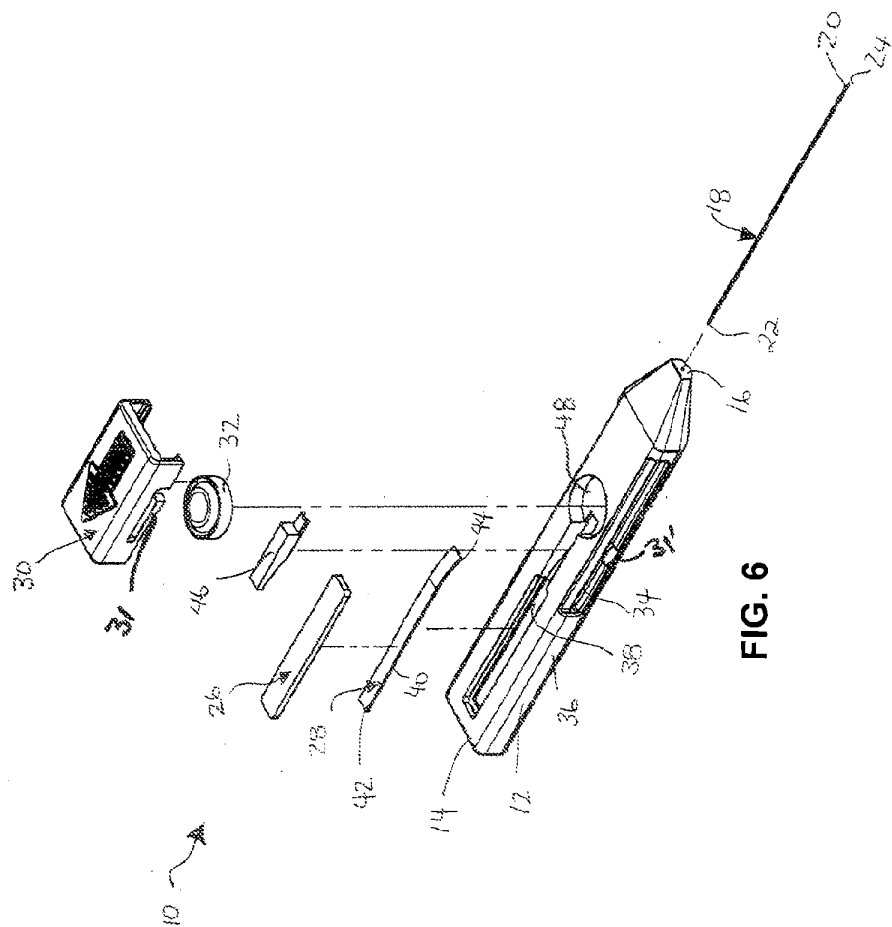
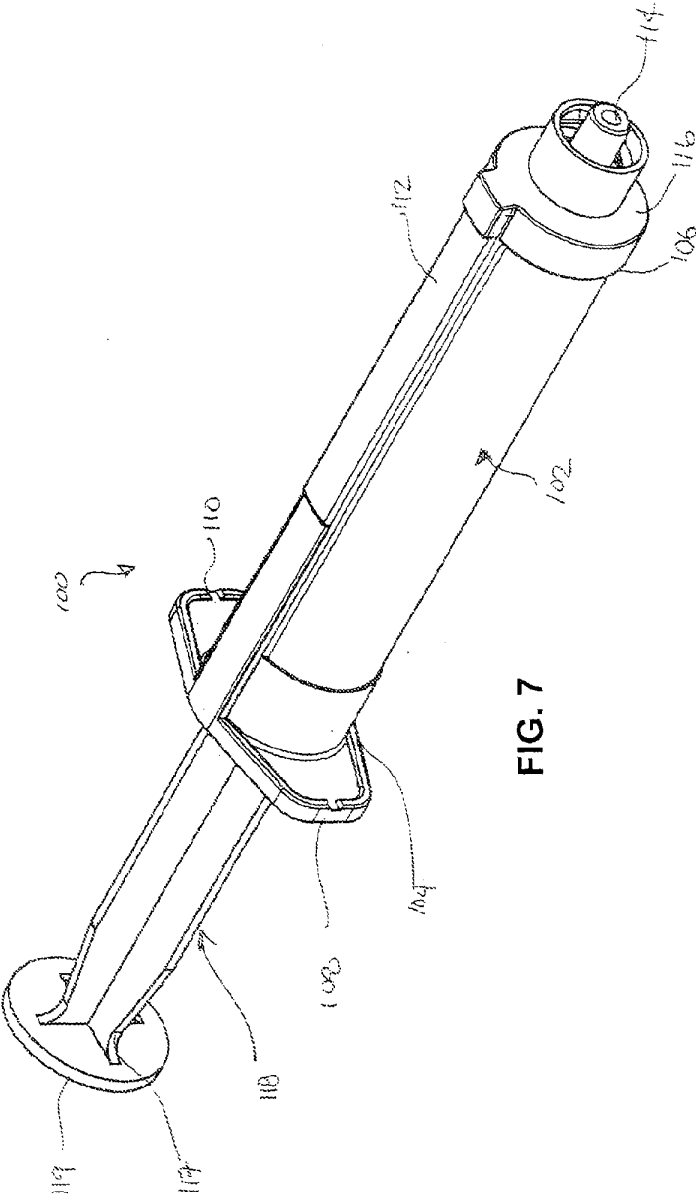


FIG. 2







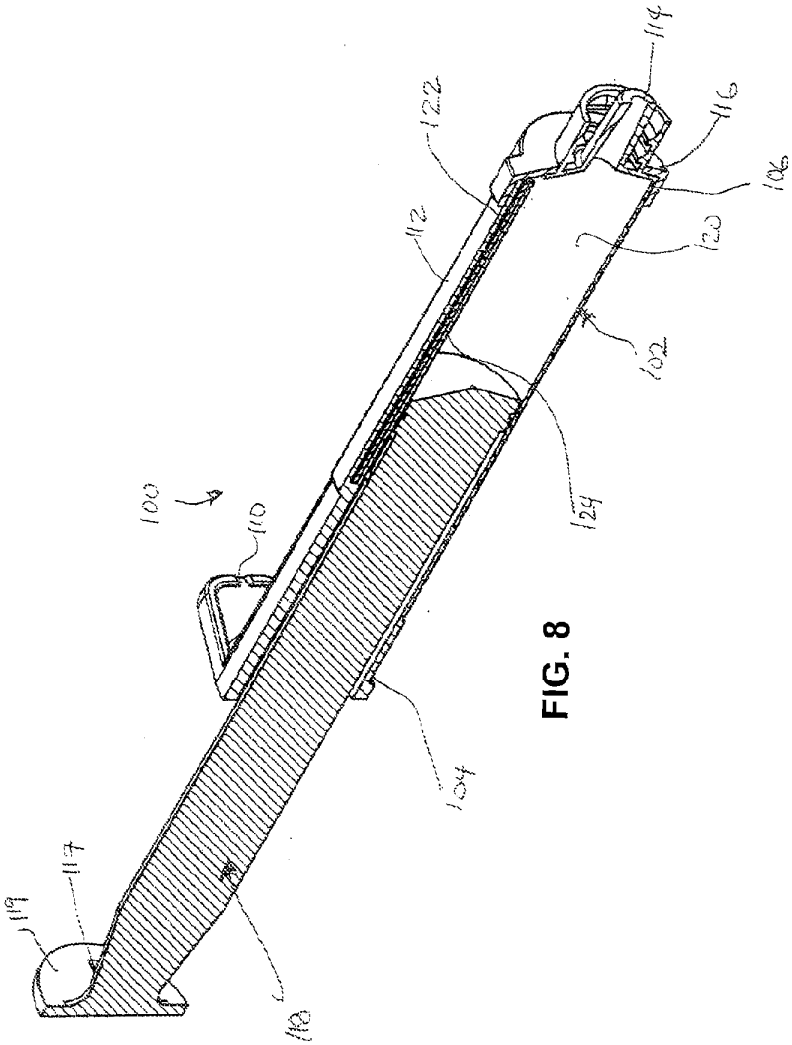


FIG. 8

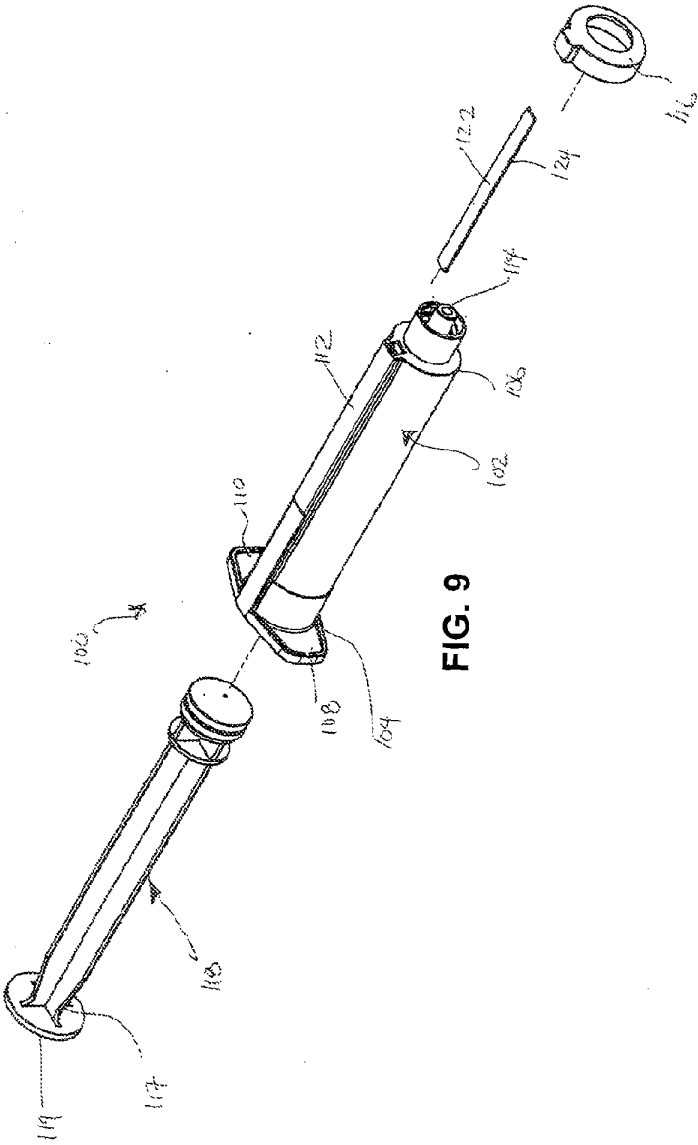
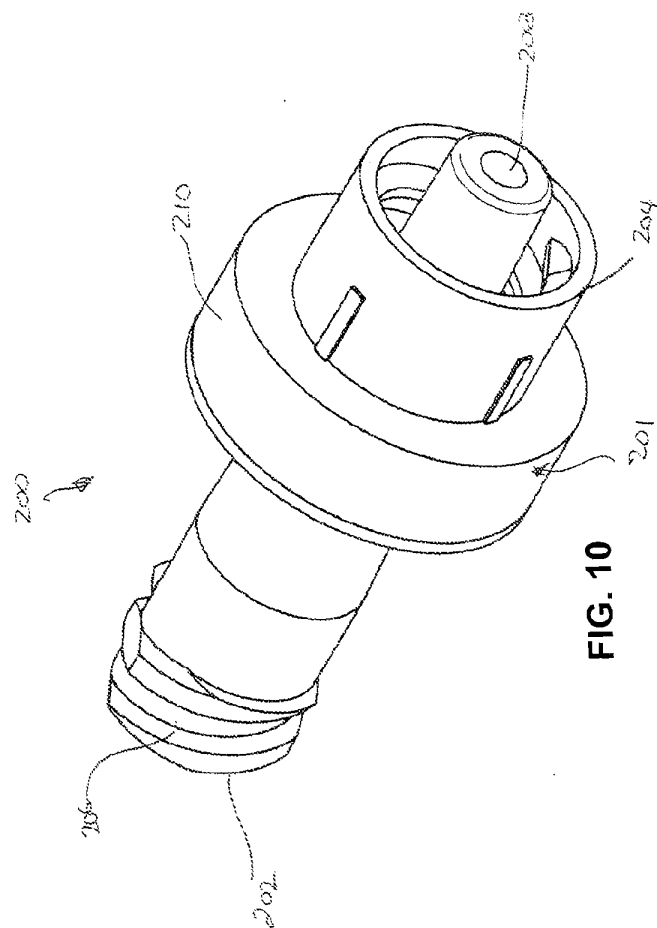
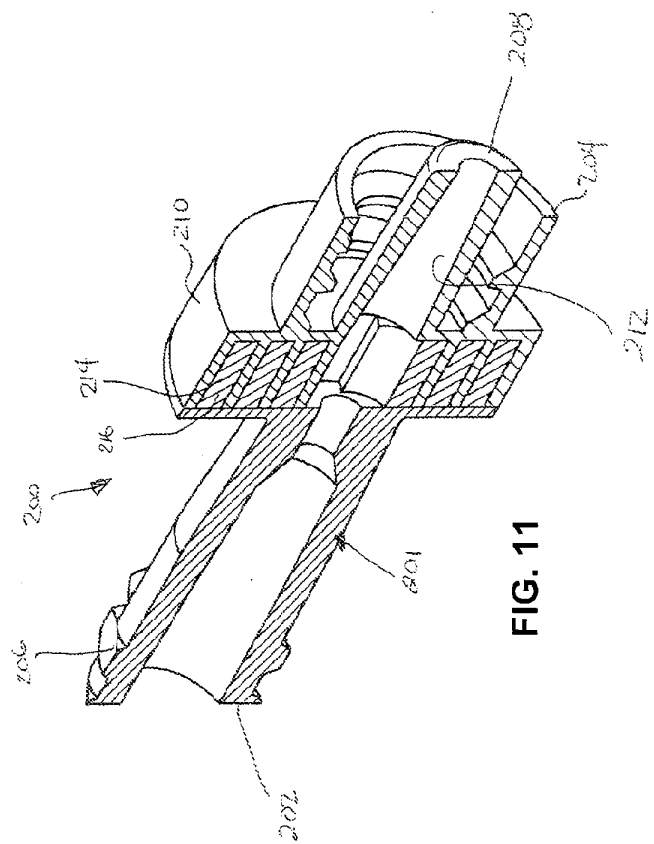


FIG. 9





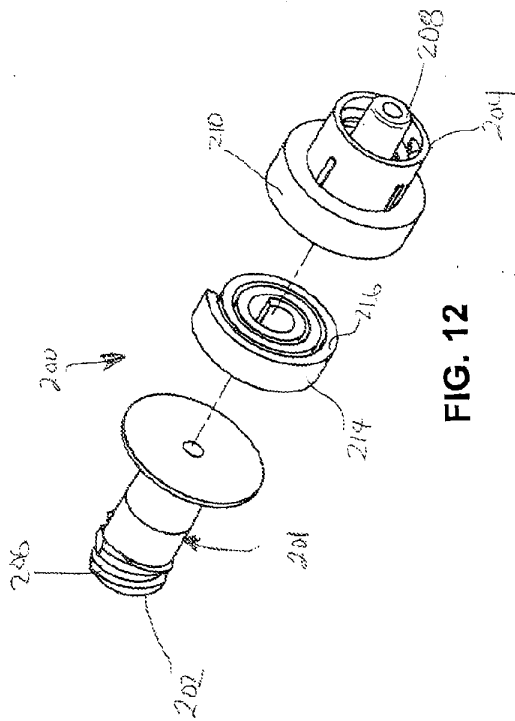
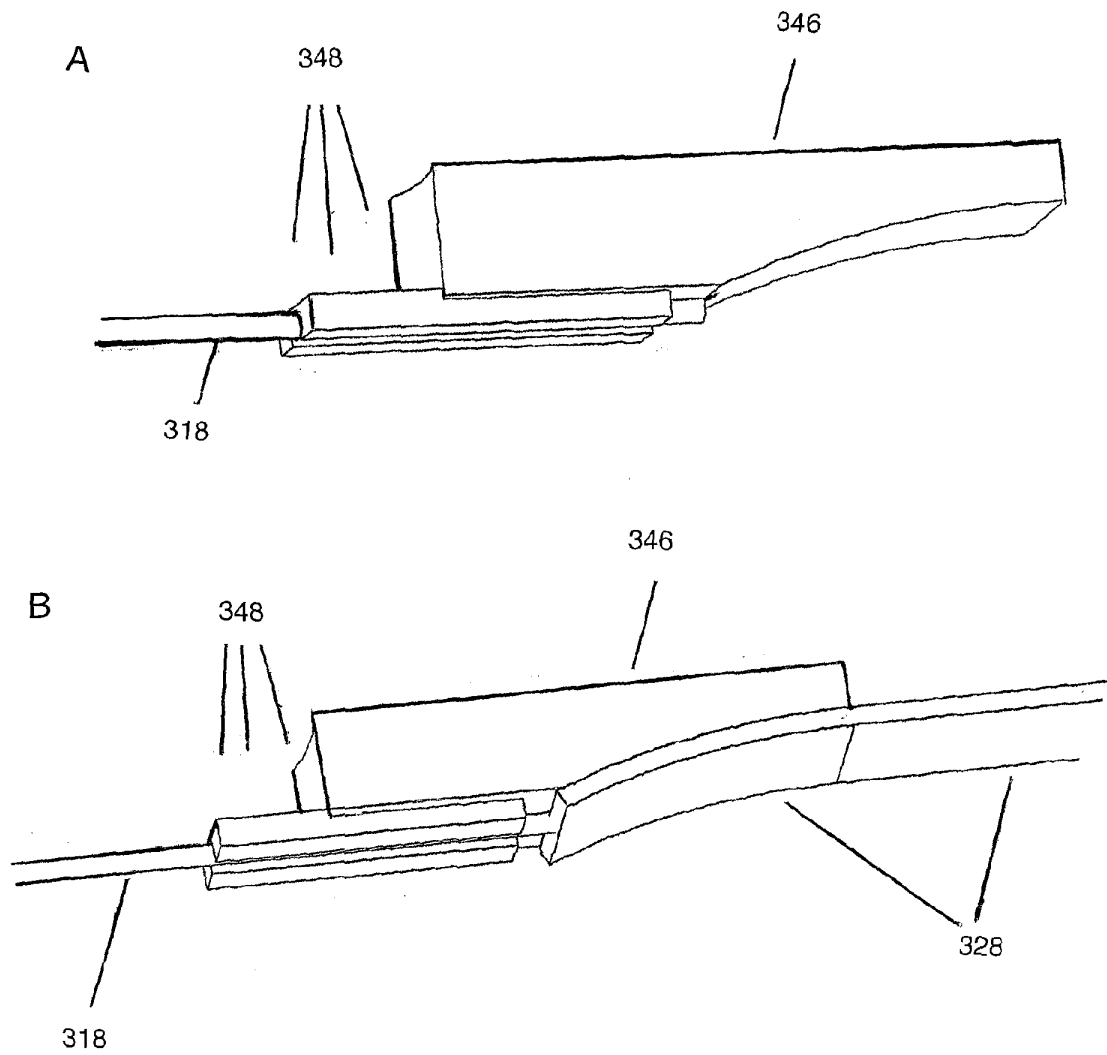


FIG. 12

Fig. 13



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/067095**A. CLASSIFICATION OF SUBJECT MATTER***G01N 33/50(2006.01)i, G01N 33/52(2006.01)i, G01N 33/53(2006.01)i*

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01N 33/50; C25C 3/02; A61B 5/151; G01N 17/00; B32B 38/04; A61B 5/00

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & keywords: test strip, coupling, needle, chamber, window

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2009-0112125 A1 (TAMIR, NILI) 30 April 2009 See paragraph [0100]; claims 1 and 5-6; figure 5.	1-20
A	US 2003-0109777 A1 (KLOEPFER, HANS G. et al.) 12 June 2003 See paragraph [0107]; claim 1; figures 1 and 5.	1-20
A	US 2003-0150745 A1 (TEODORCZYK, MARIA et al.) 14 August 2003 See claims 1, 8 and 13; figure 3.	1-20
A	US 2007-0161926 A1 (IMAMURA, TAKESHI et al.) 12 July 2007 See paragraph [0032]; claim 1; figure 2A.	1-20
A	US 2011-0046453 (KEIL, MICHAEL) 24 February 2011 See paragraphs [0017] and [0019]; claims 14-16; figures 1 and 7.	1-20



Further documents are listed in the continuation of Box C.



See patent family annex.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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PCT/US2012/067095

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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Bibliographic data: EP3324845 (A1) — 2018-05-30

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE

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

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

Application number: EP20160747682 20160722 Global Dossier

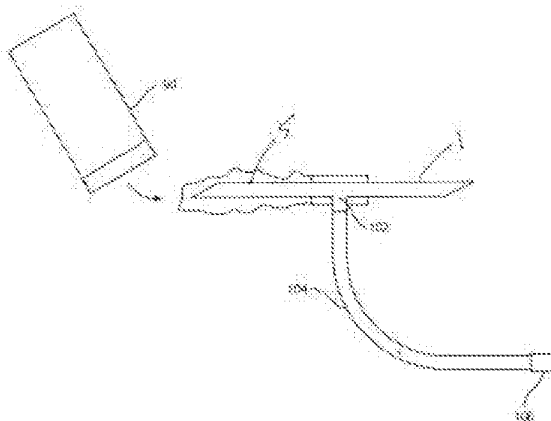
Priority number(s): US201562196797P 20150724 ; US201562238636P 20151007 ; US201662318194P 20160404 ; US201615140448 20160427 ; US201615140443 20160427 ; WO2016US43709 20160722

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Abstract not available for EP3324845 (A1)

Abstract of corresponding document: US2017020427 (A1)

Blood sample optimization systems and methods are described that reduce or eliminate contaminants 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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15/140,448 27 April 2016 (27.04.2016) US
15/140,443 27 April 2016 (27.04.2016) US

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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,
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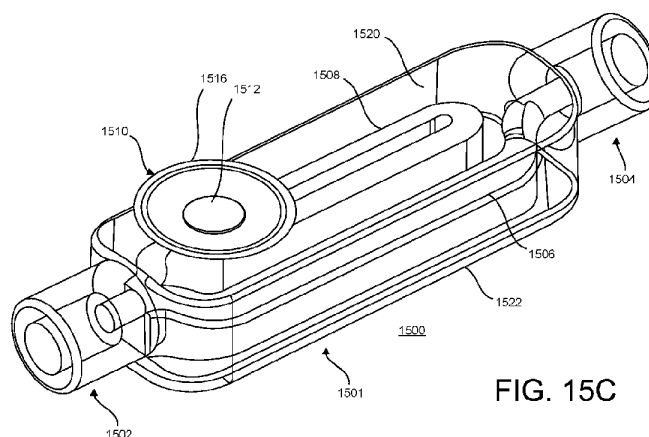


FIG. 15C

(57) Abstract: Blood sample optimization systems and methods are described that reduce or eliminate contaminants 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.

WO 2017/019552 A1

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 contaminants 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 contaminants 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 indicator 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 contaminants 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 decontaminant, 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.

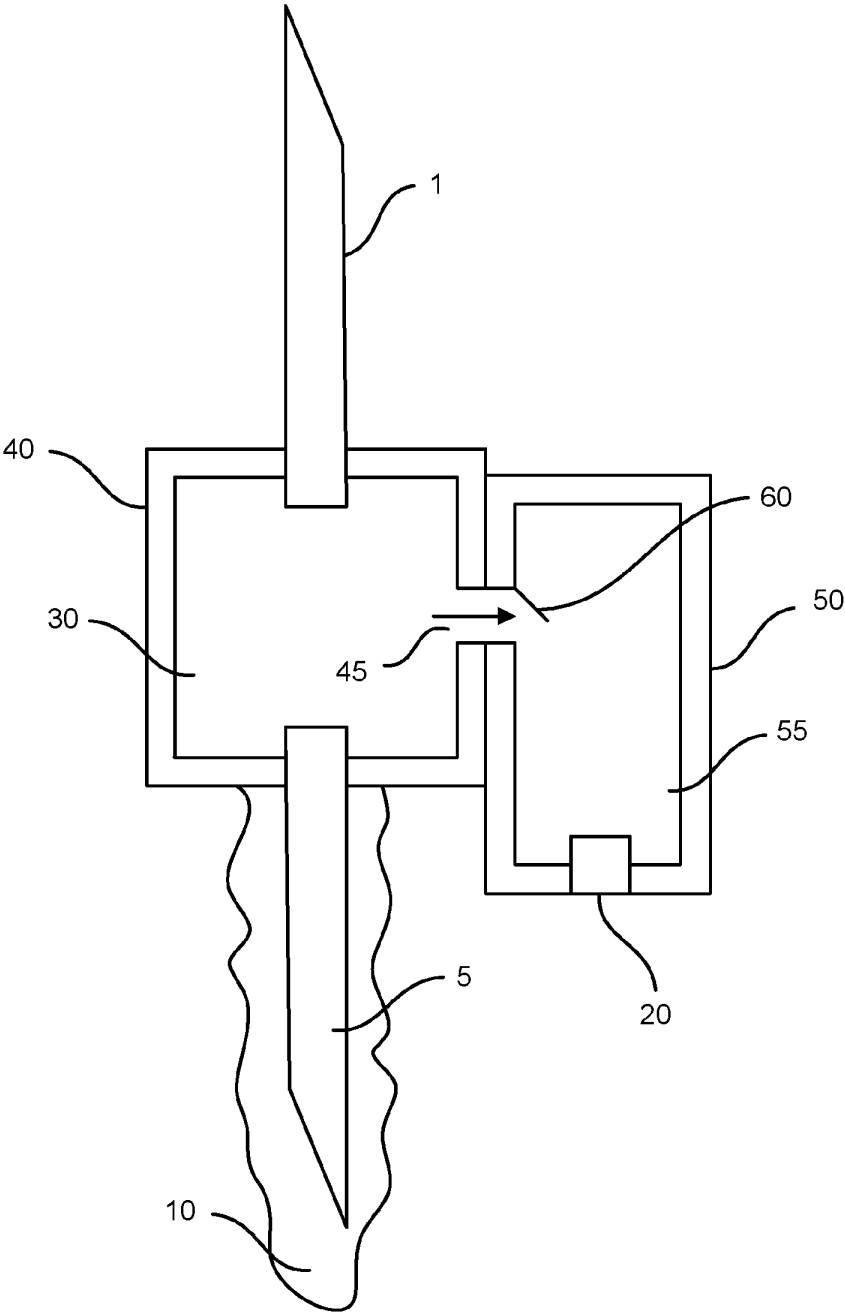


FIG. 1

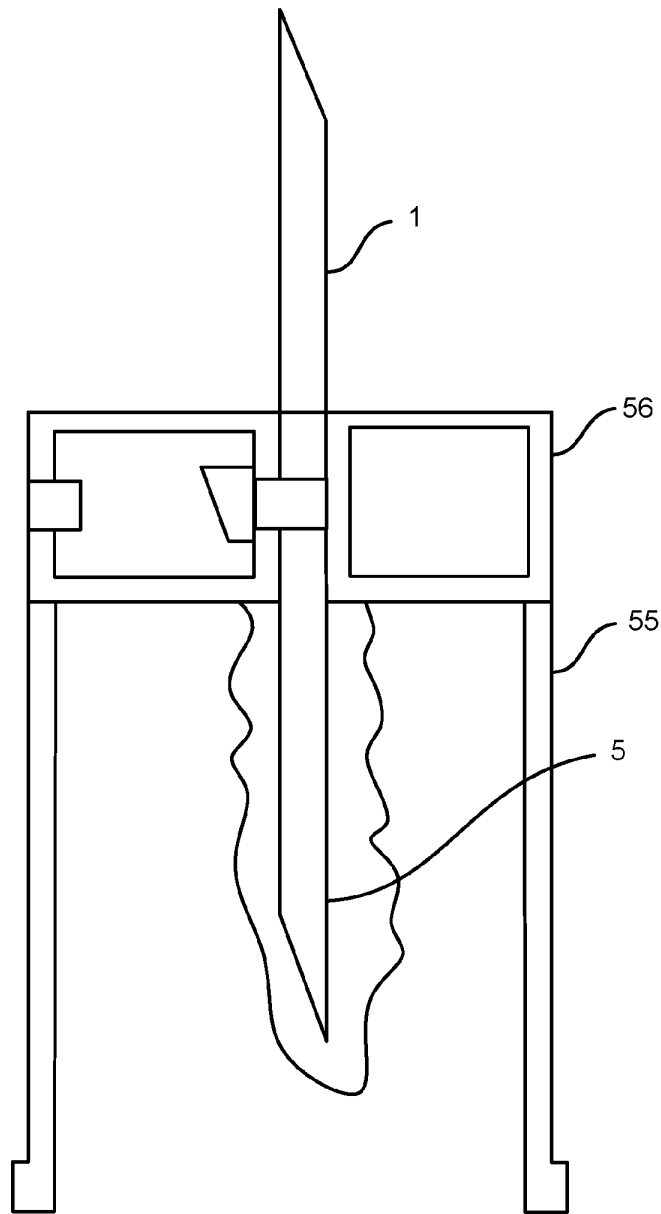


FIG. 2

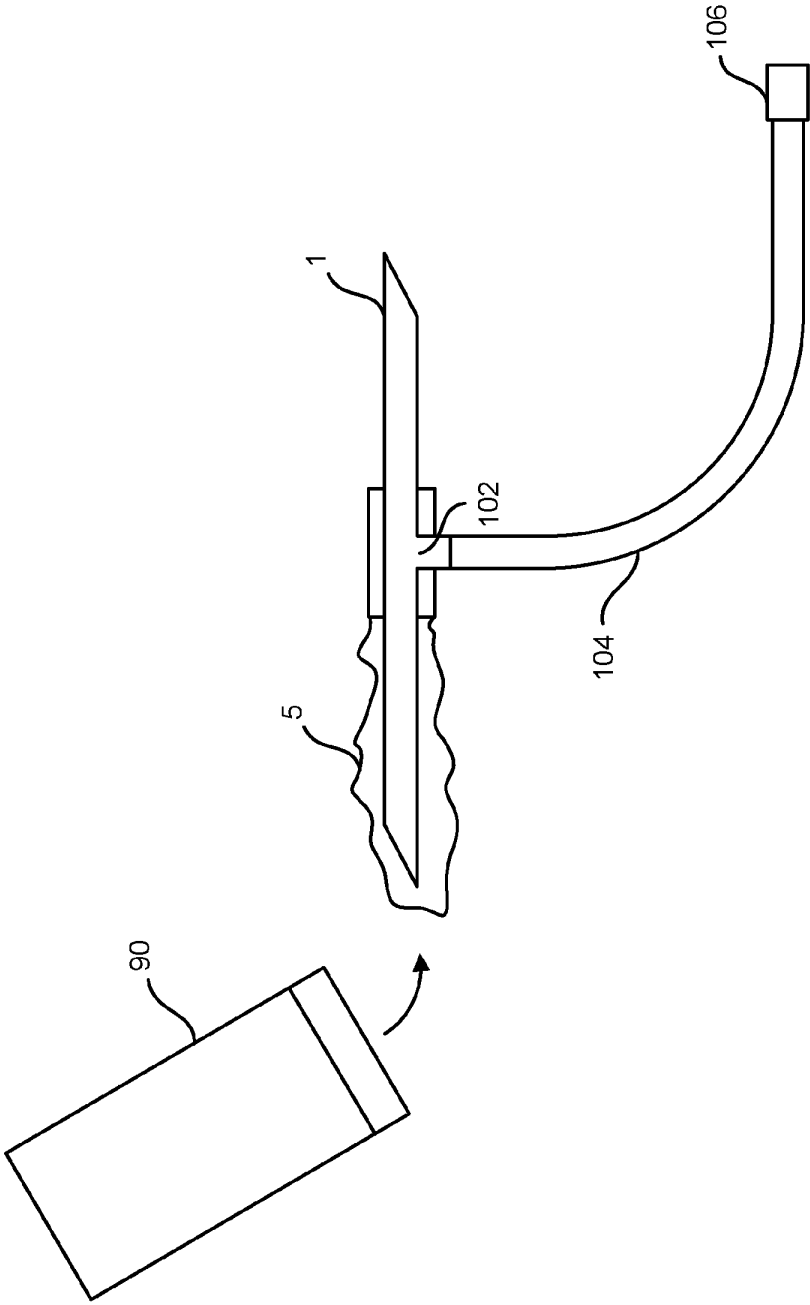


FIG. 3

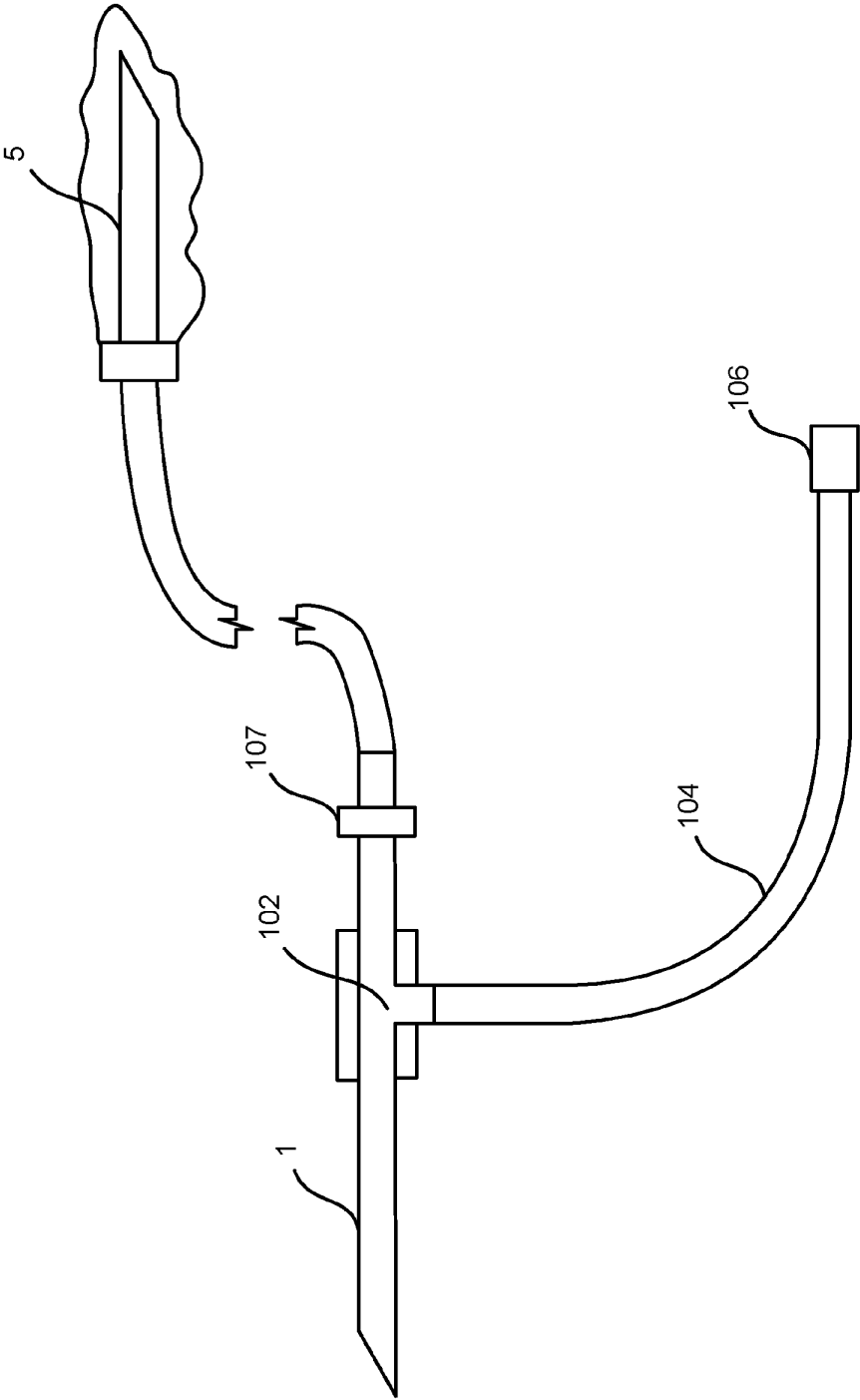


FIG. 4

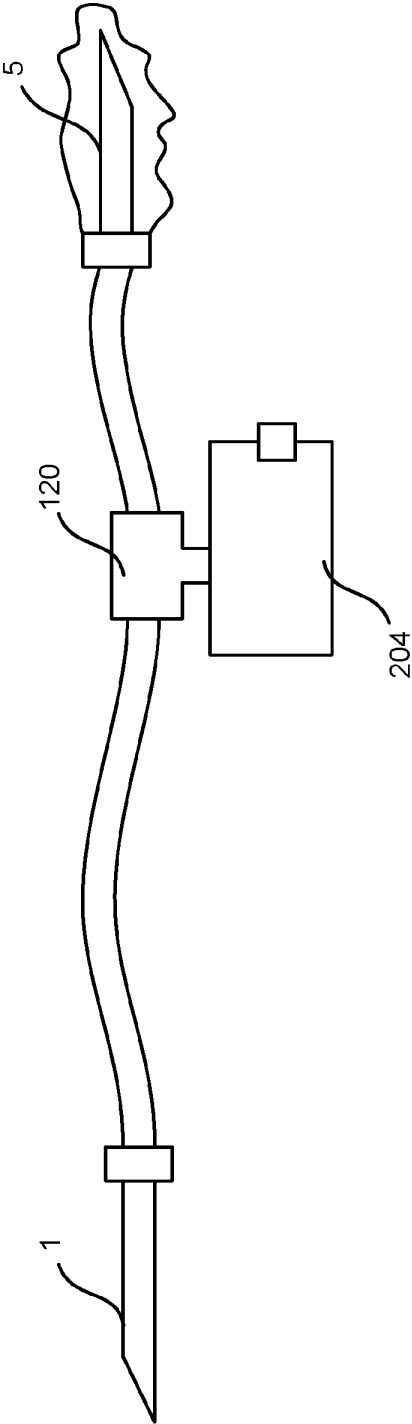


FIG. 5

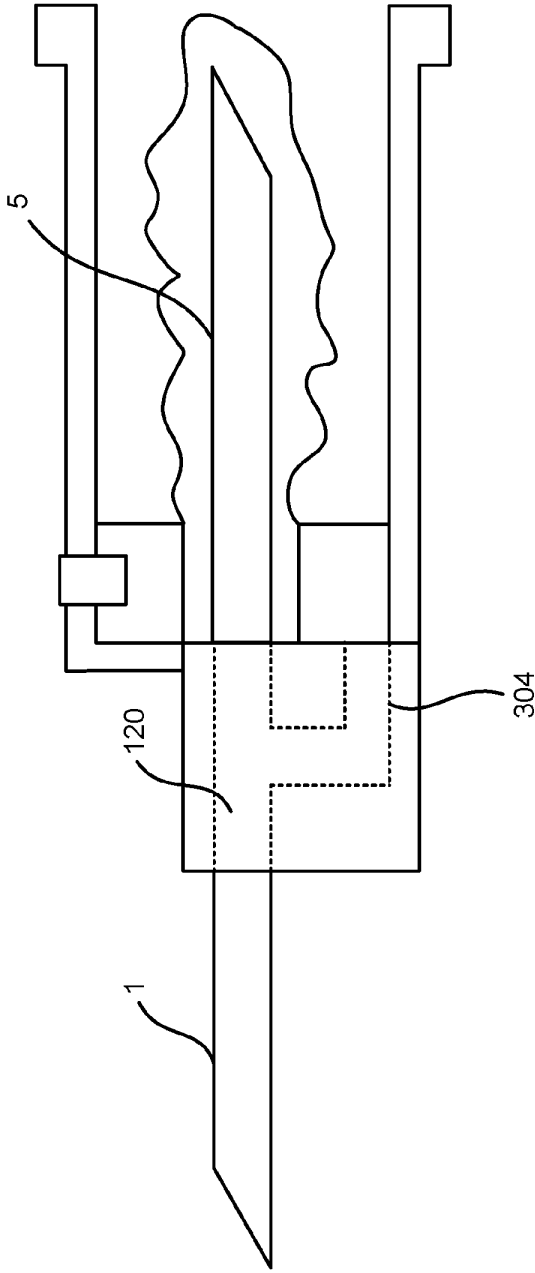
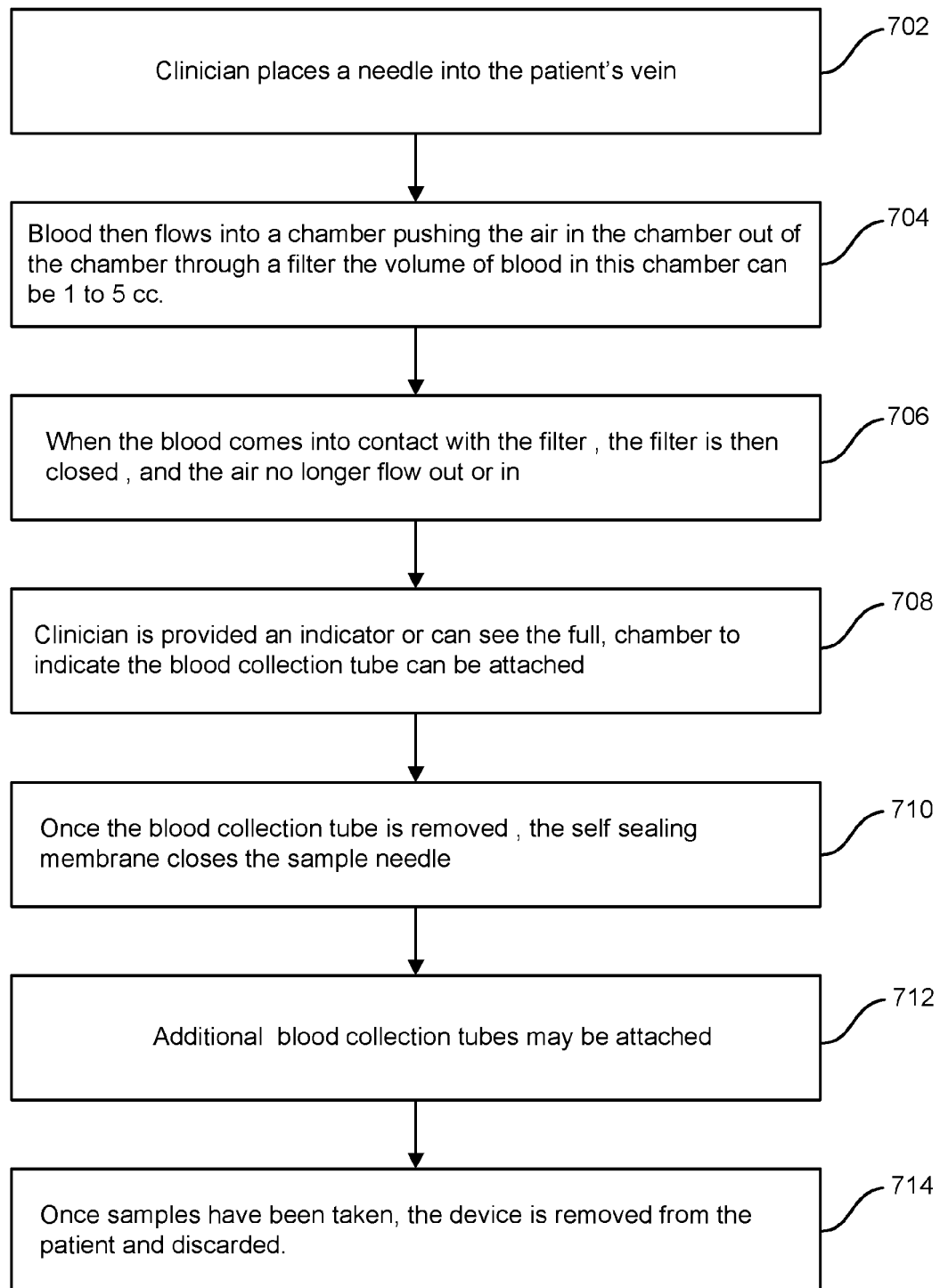
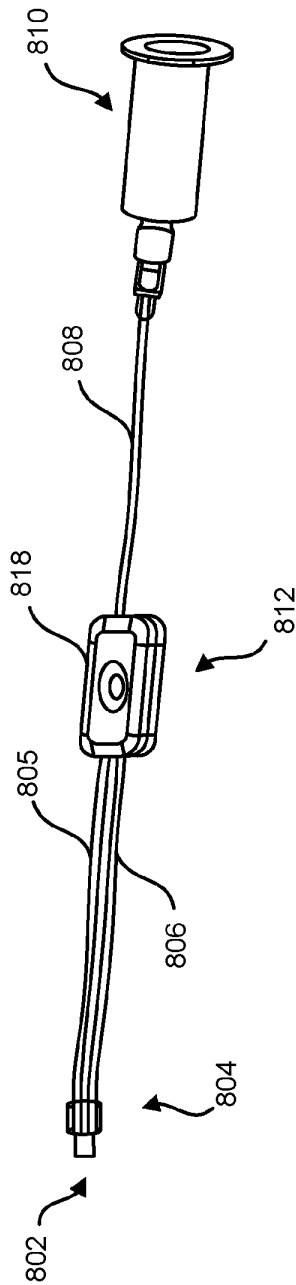


FIG. 6

**FIG. 7**



800

FIG. 8A

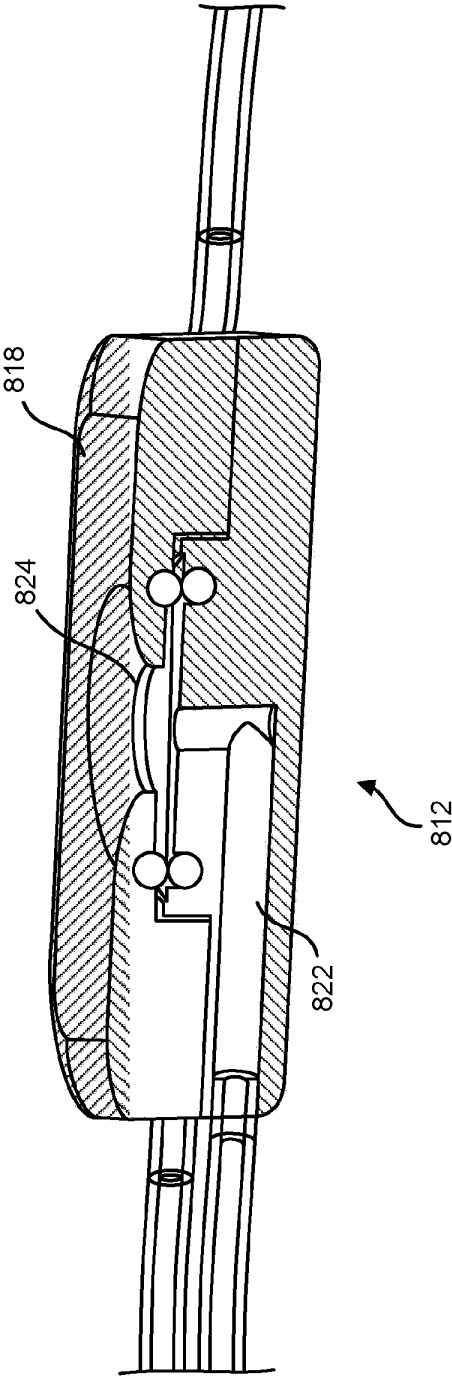


FIG. 8B

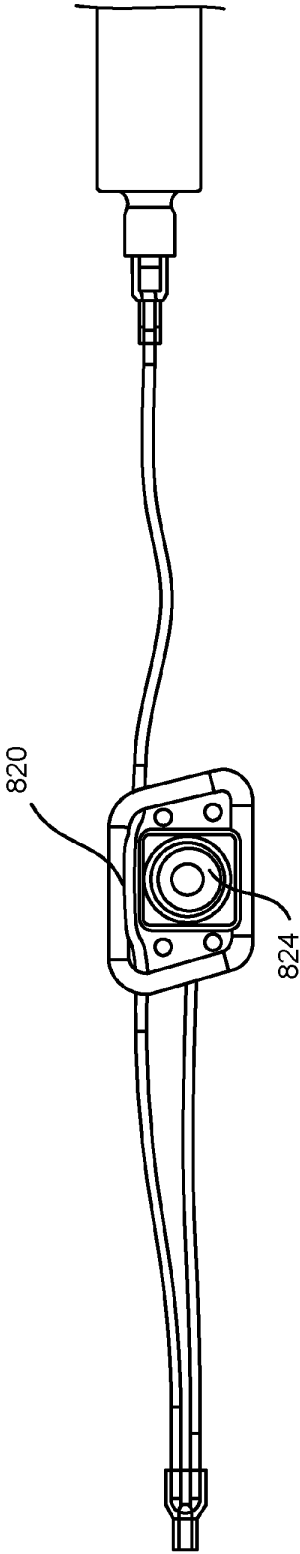


FIG. 8C

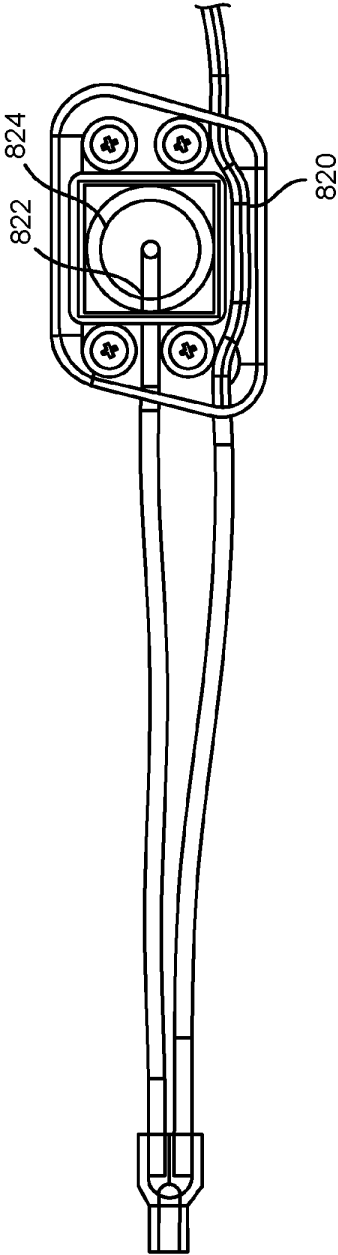


FIG. 8D

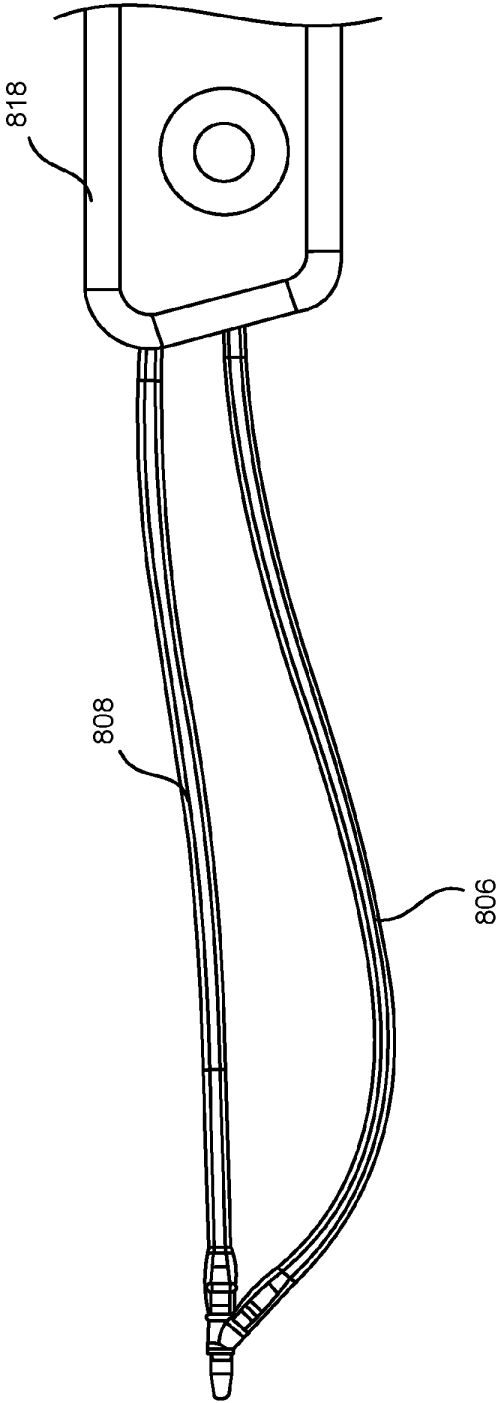


FIG. 8E

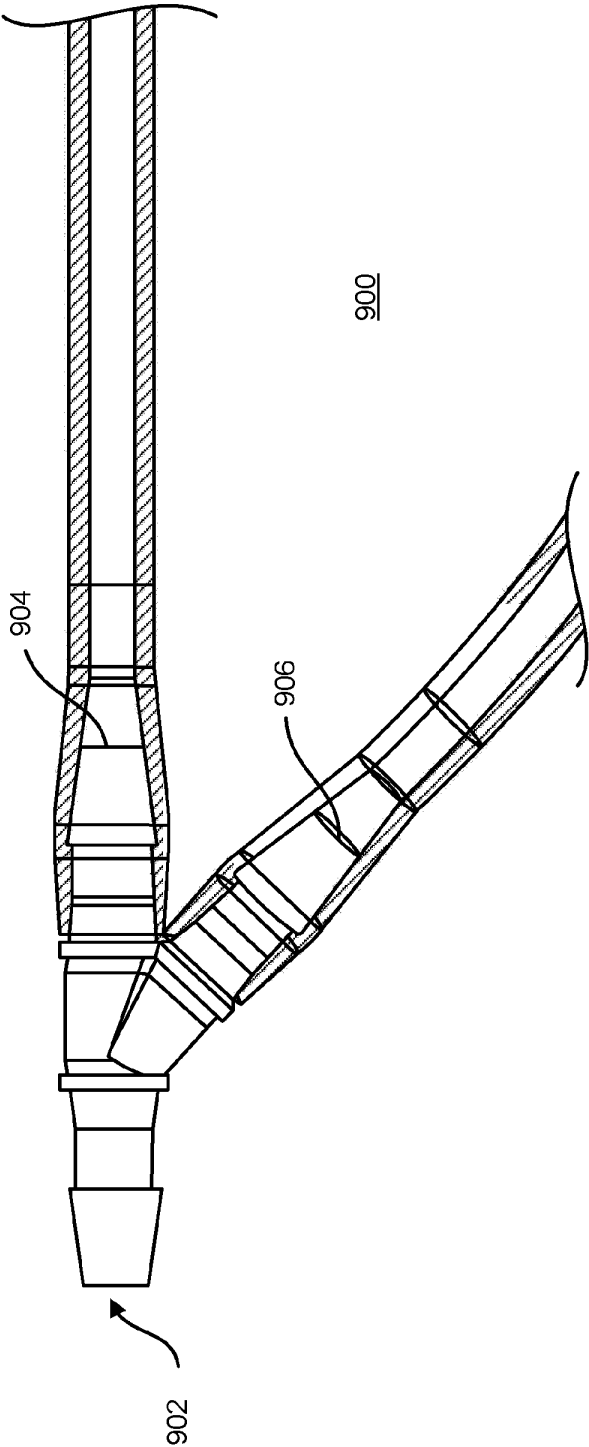


FIG. 9

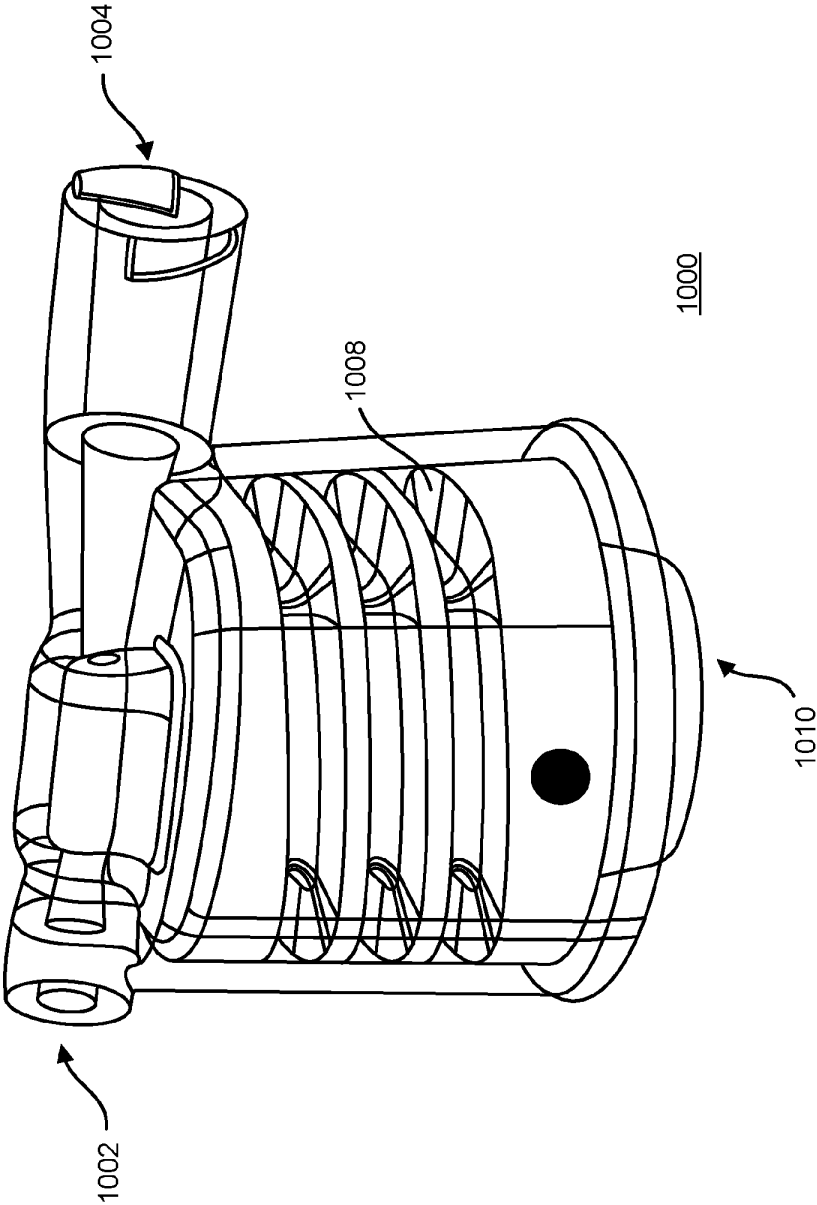


FIG. 10A

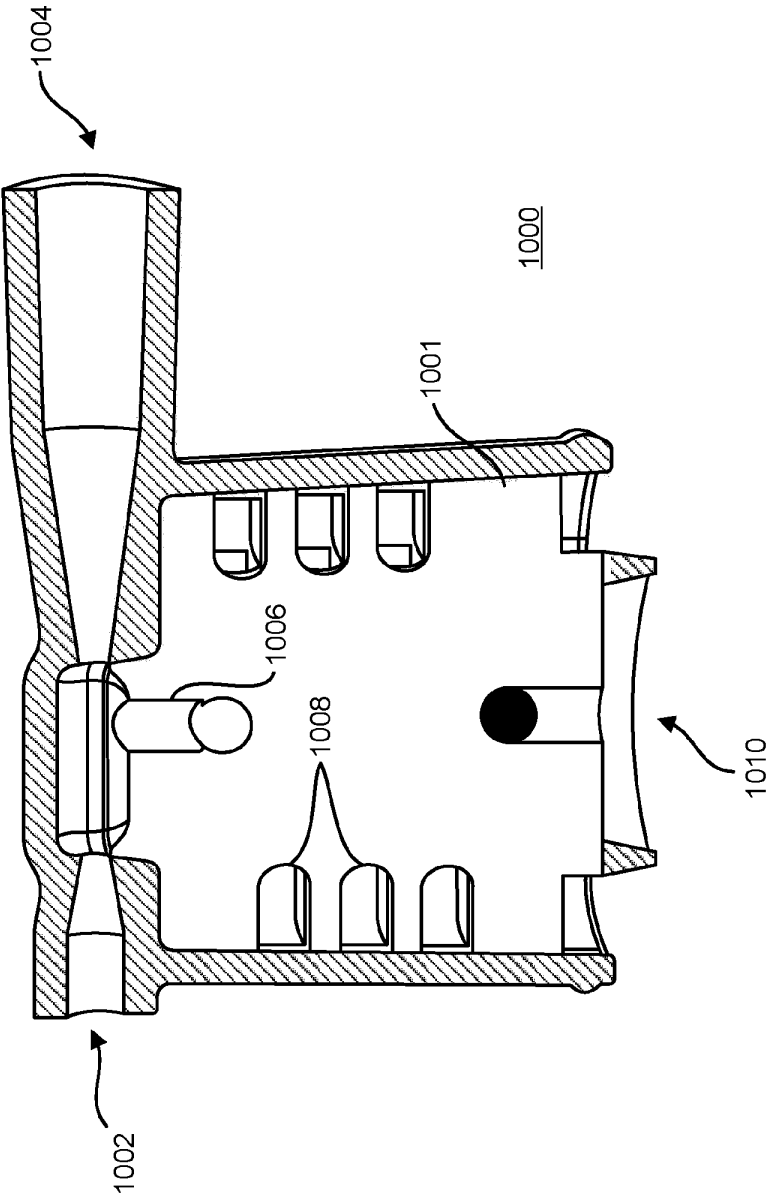


FIG. 10B

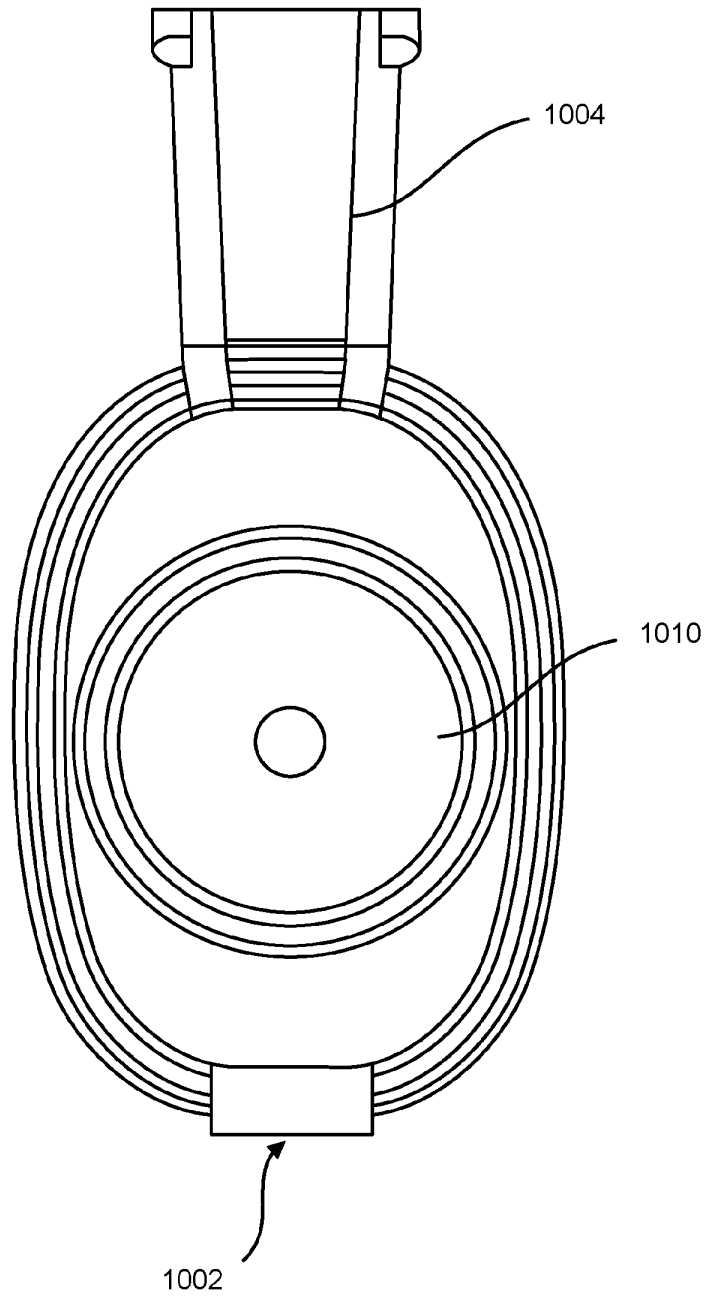


FIG. 10C

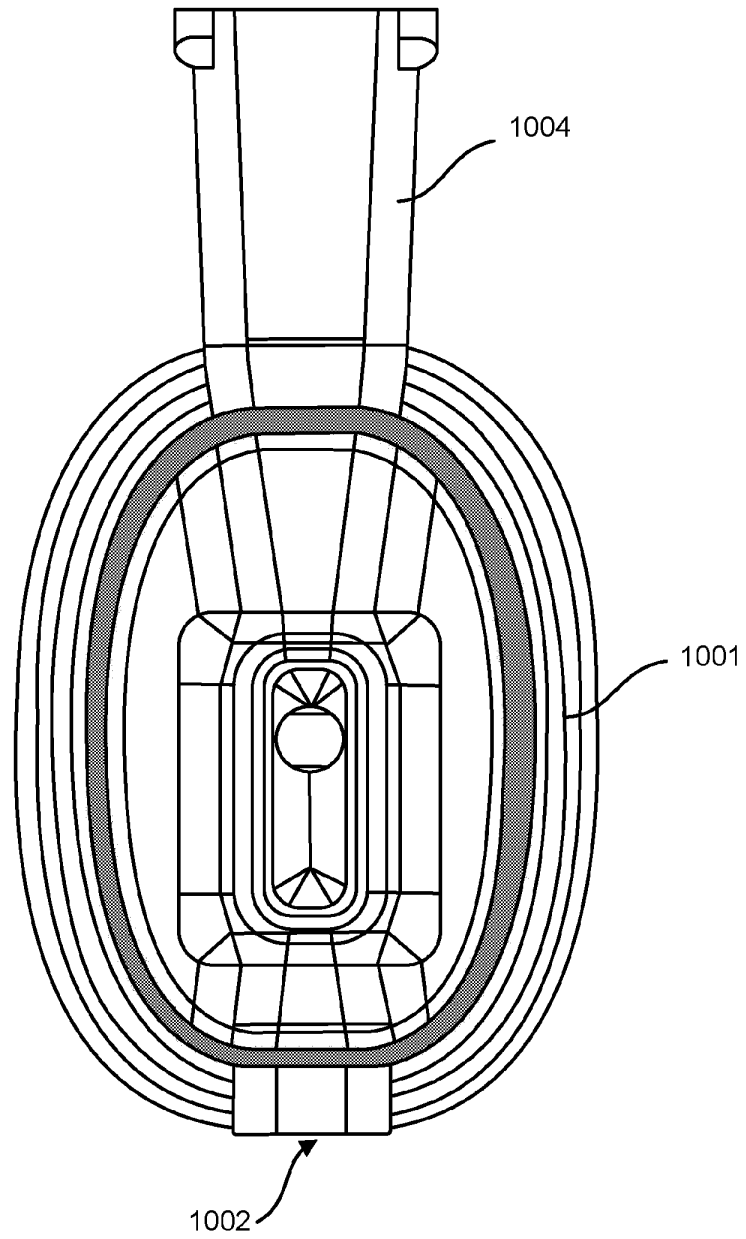


FIG. 10D

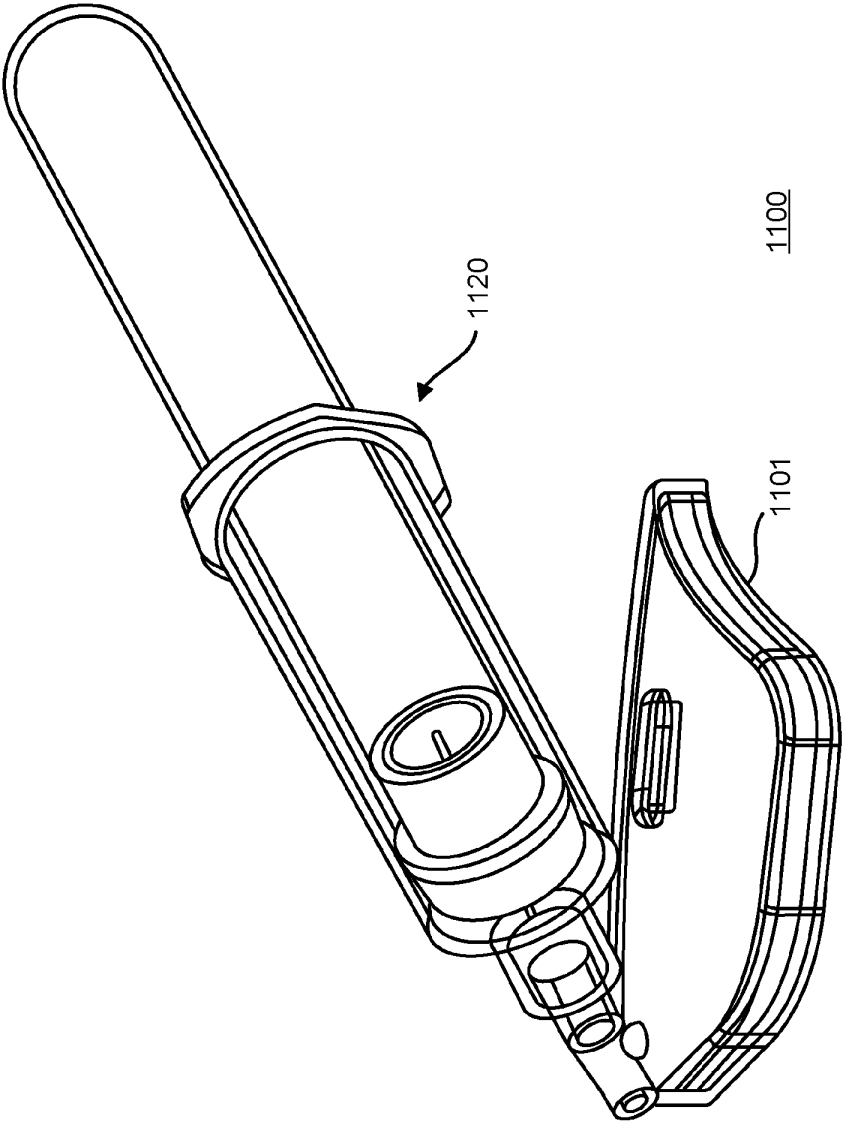


FIG. 11A

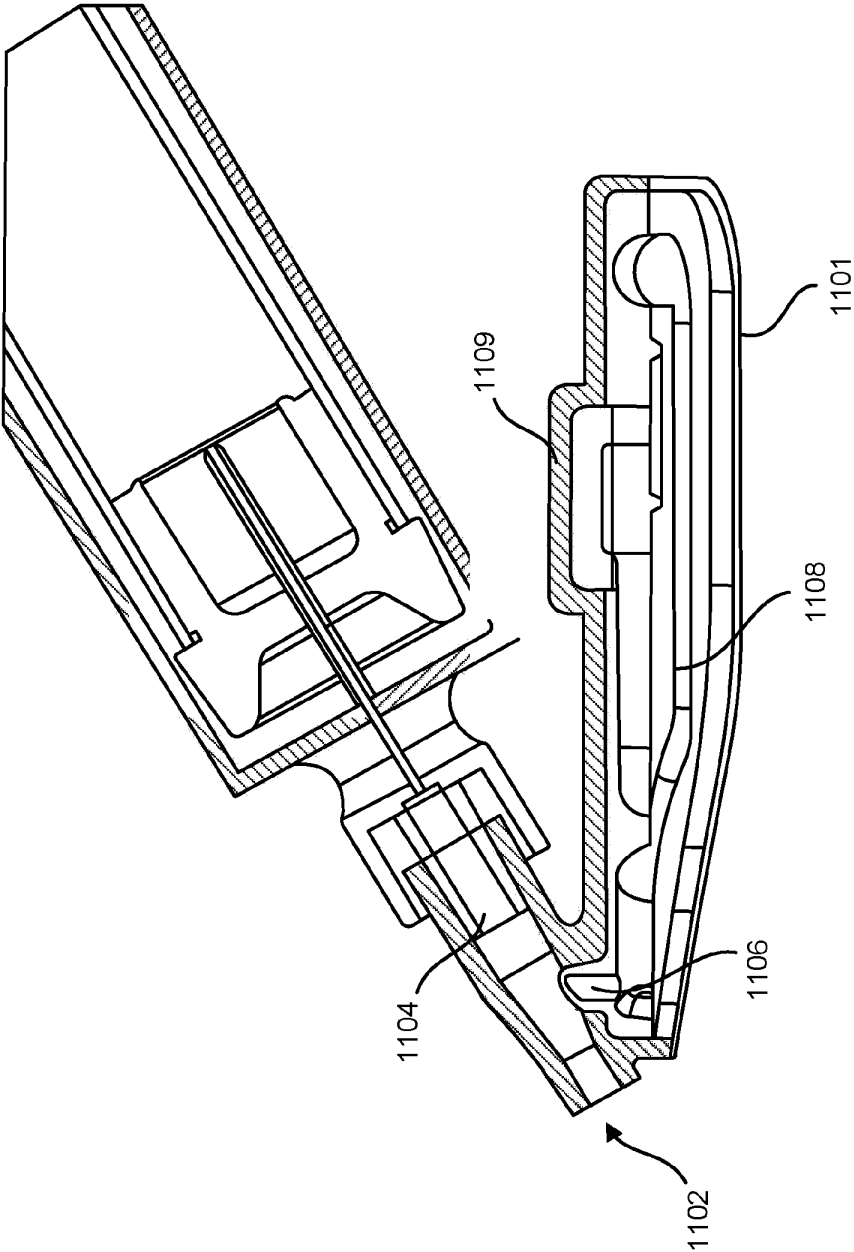


FIG. 11B

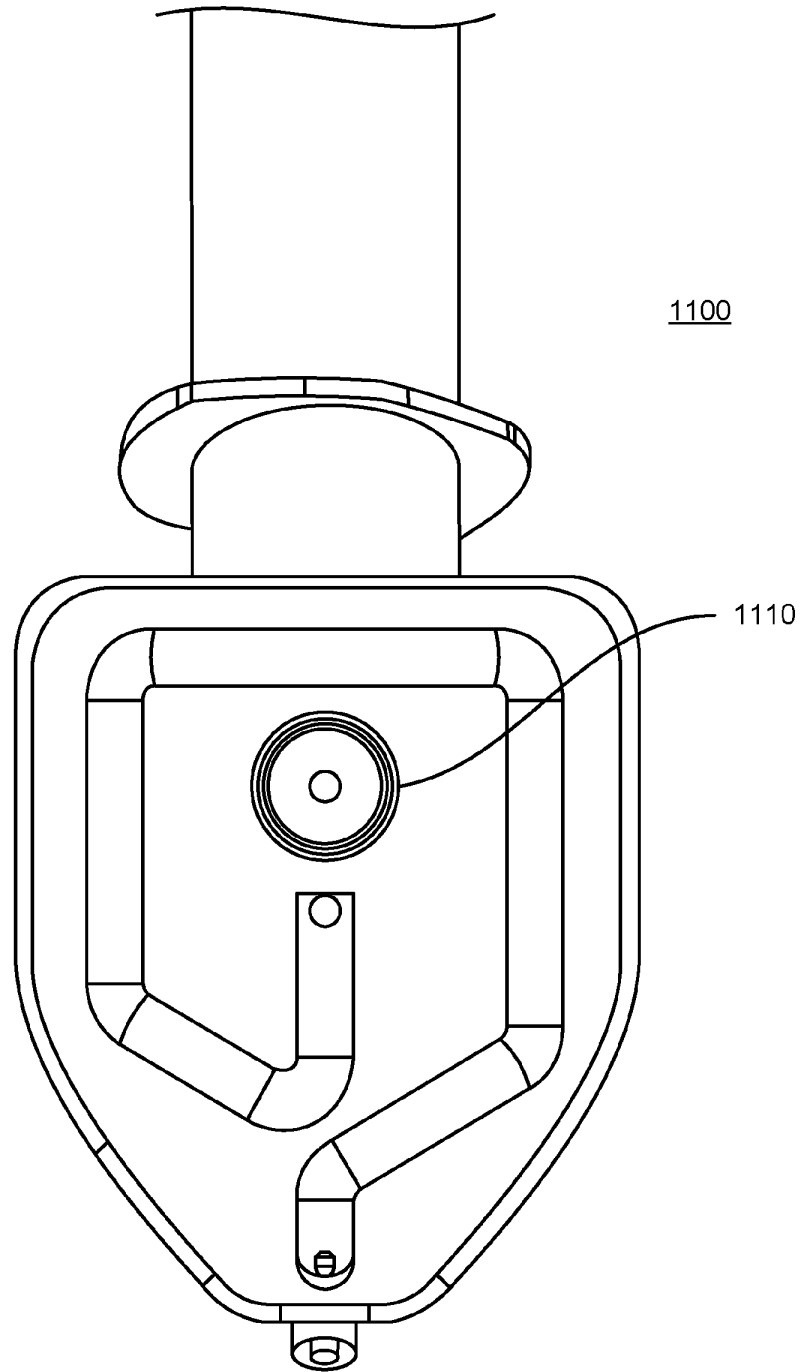


FIG. 11C

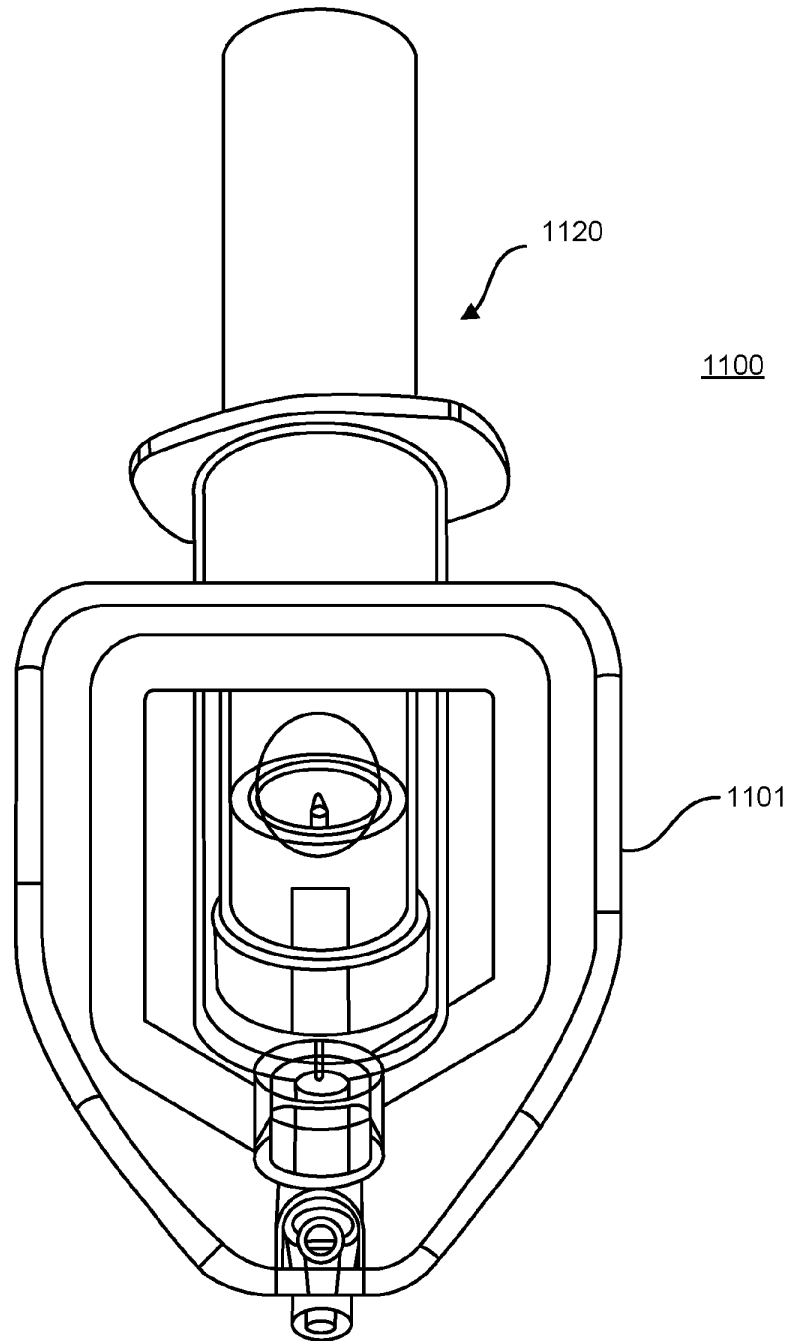


FIG. 11D

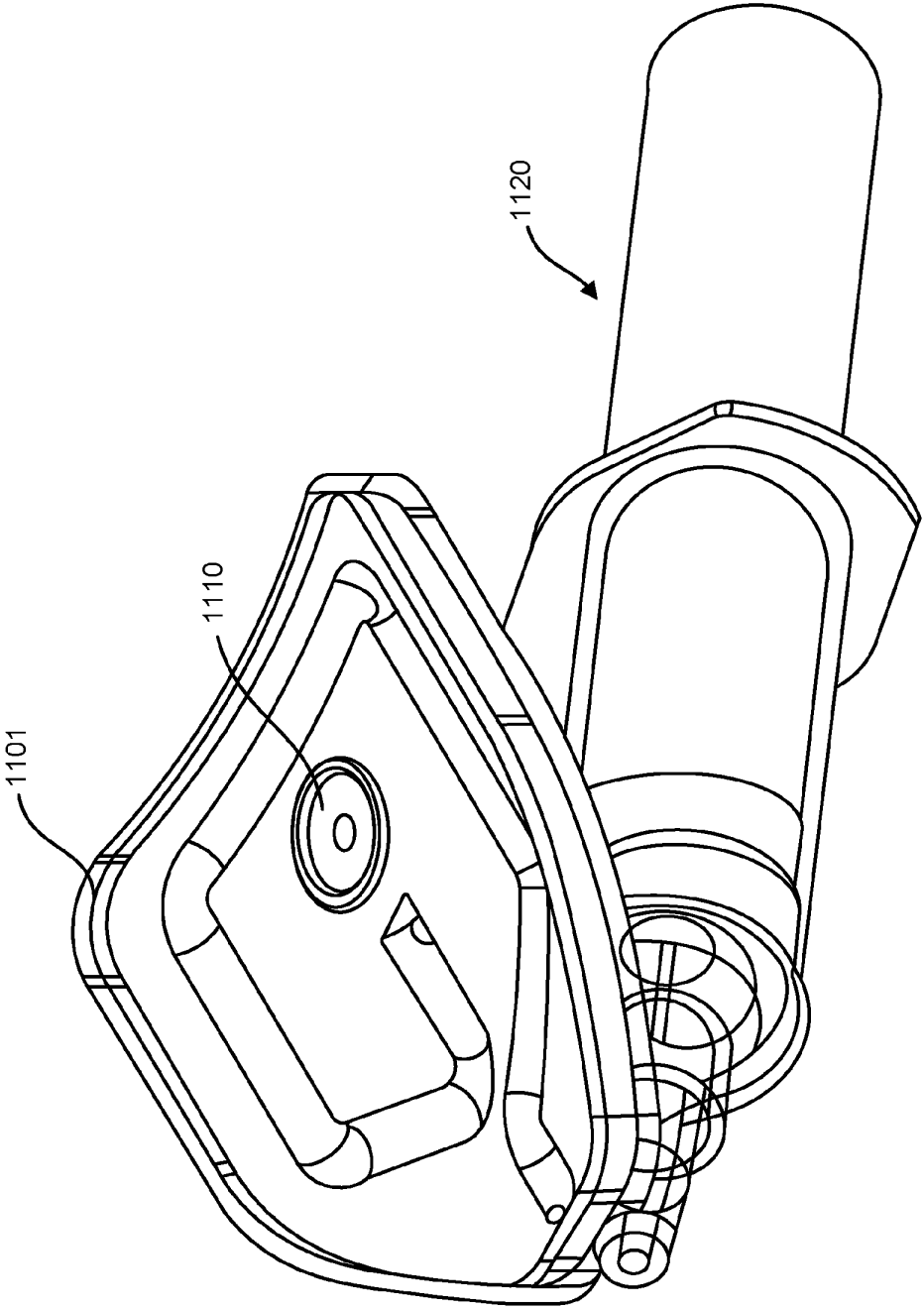


FIG. 11E

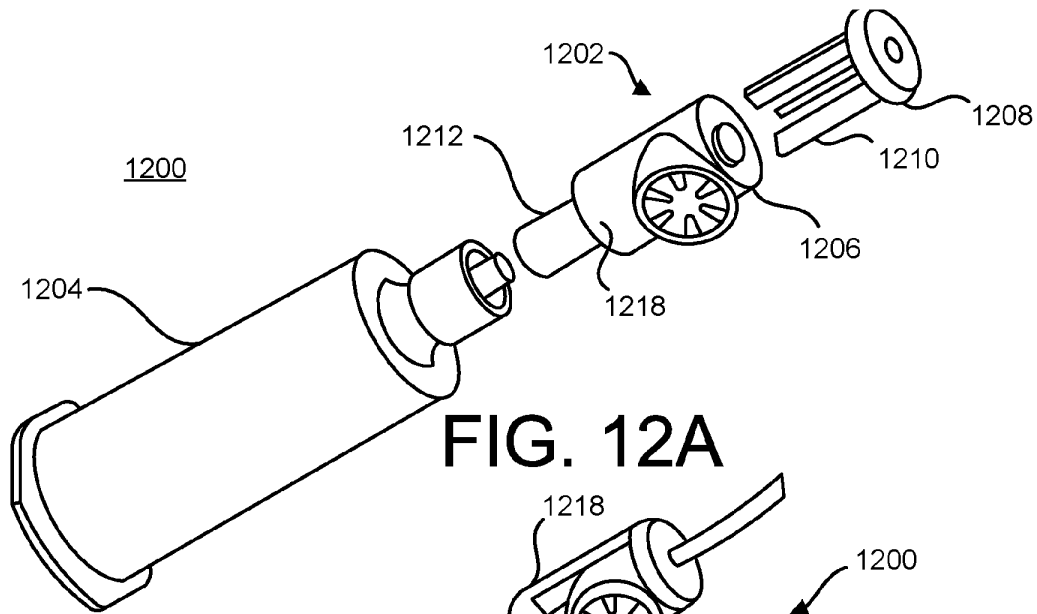


FIG. 12A

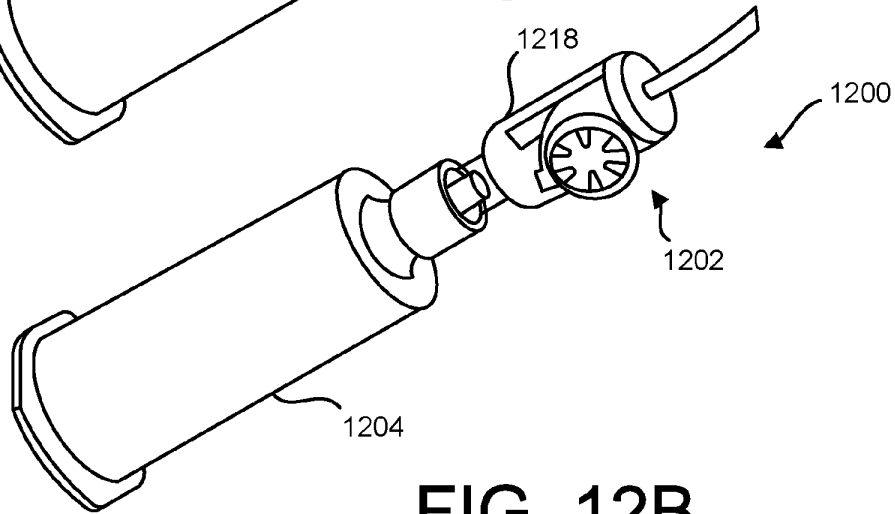


FIG. 12B

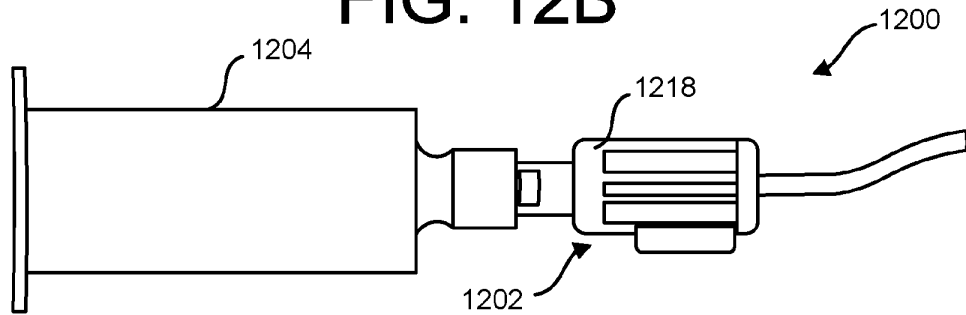


FIG. 12C

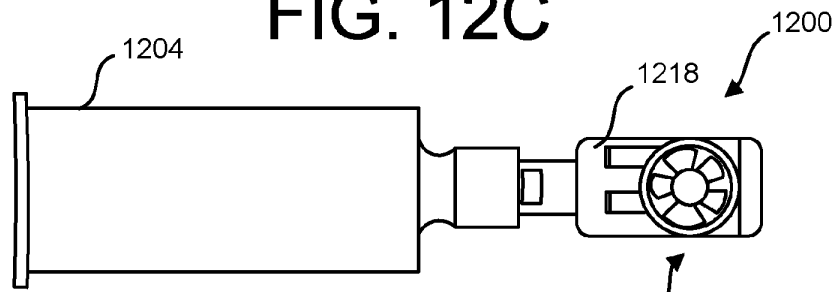


FIG. 12D

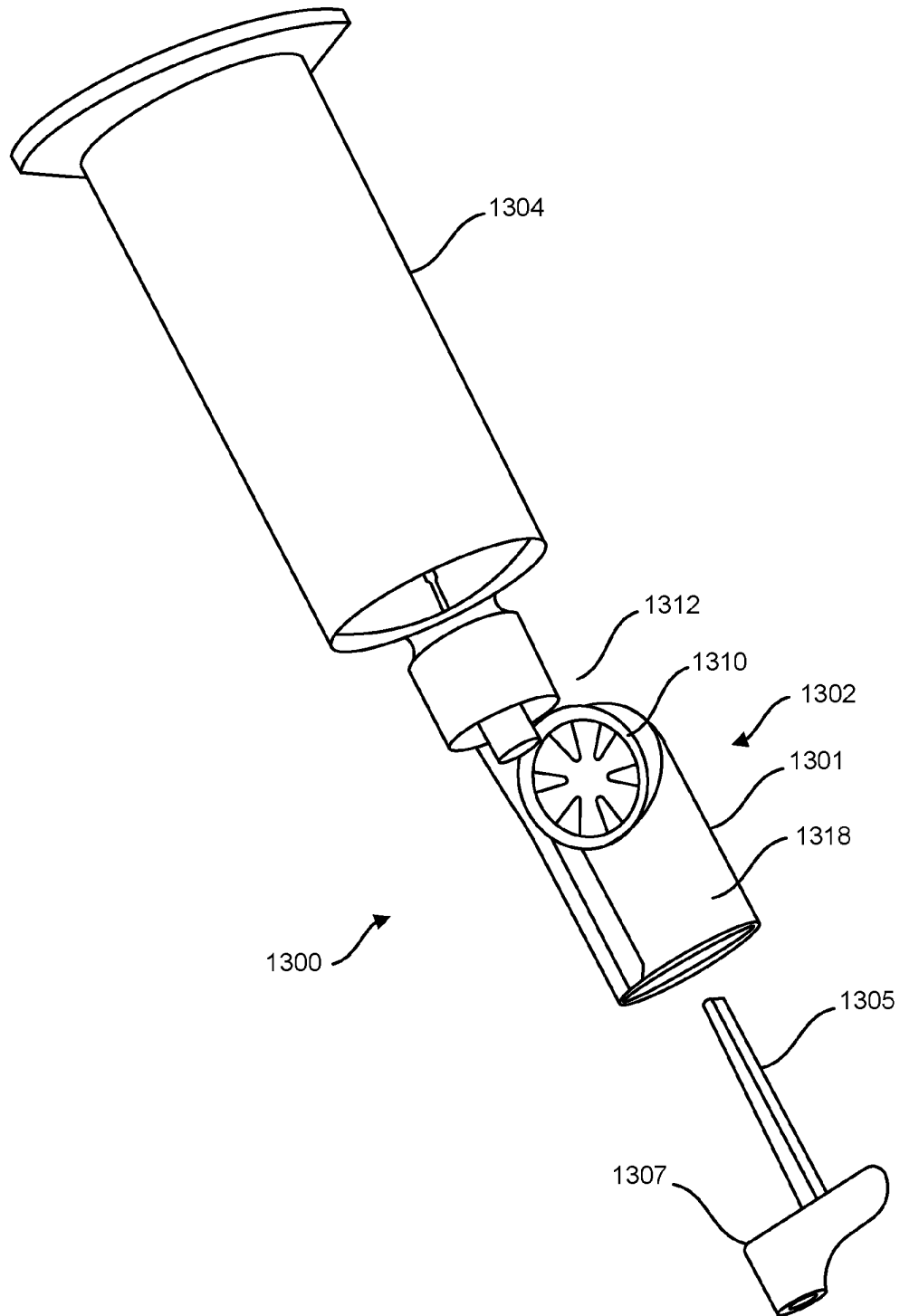


FIG. 13A

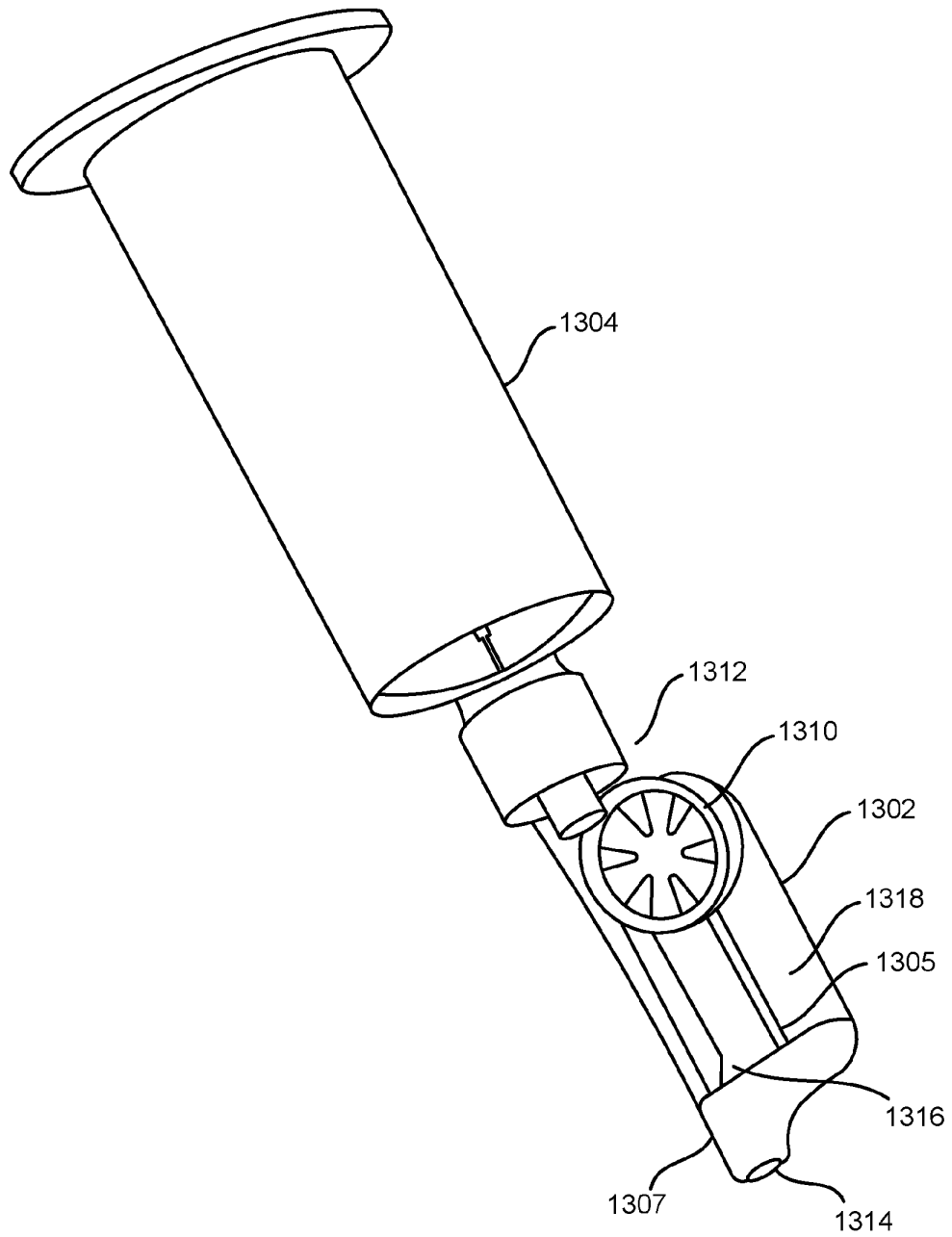


FIG. 13B

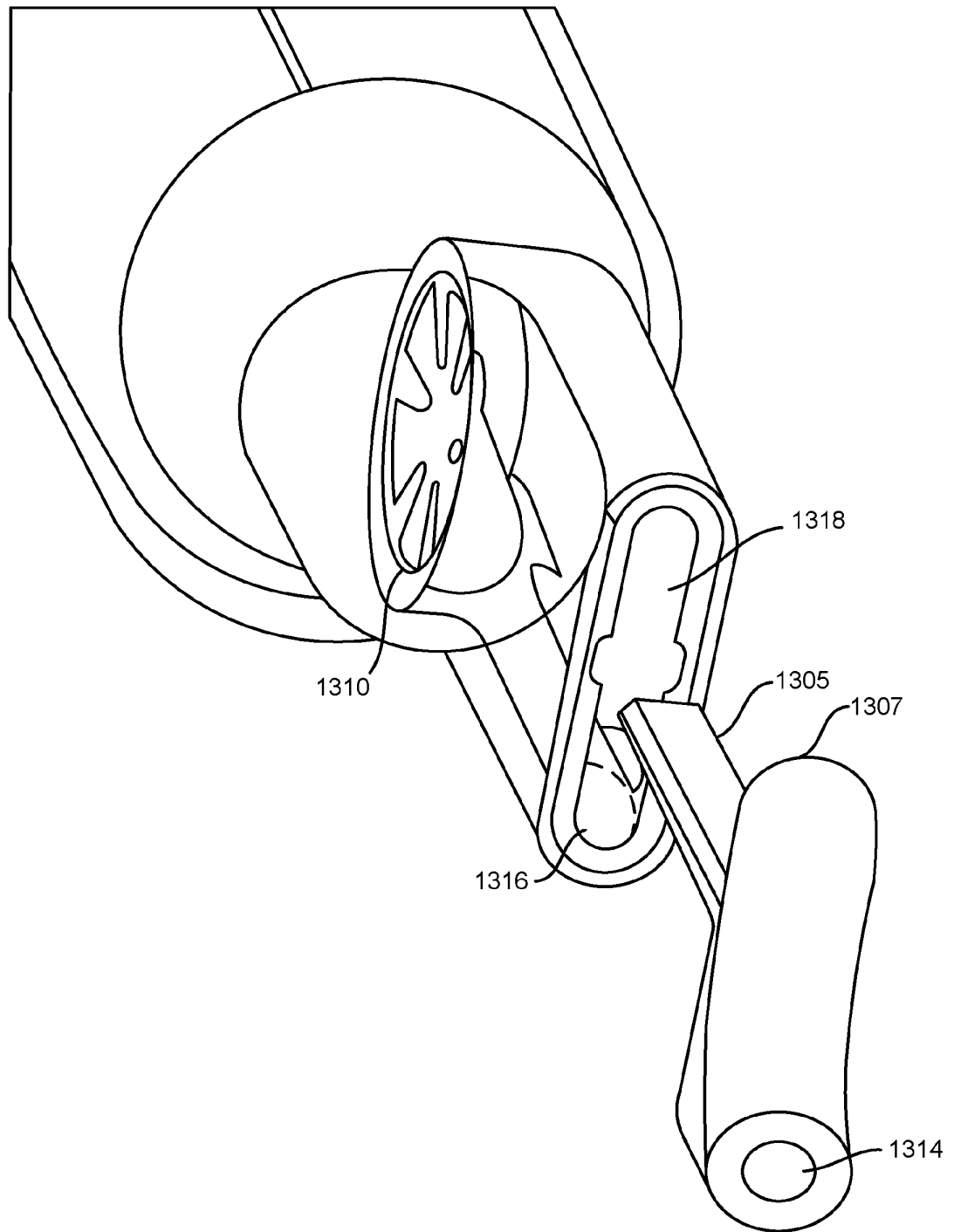


FIG. 13C

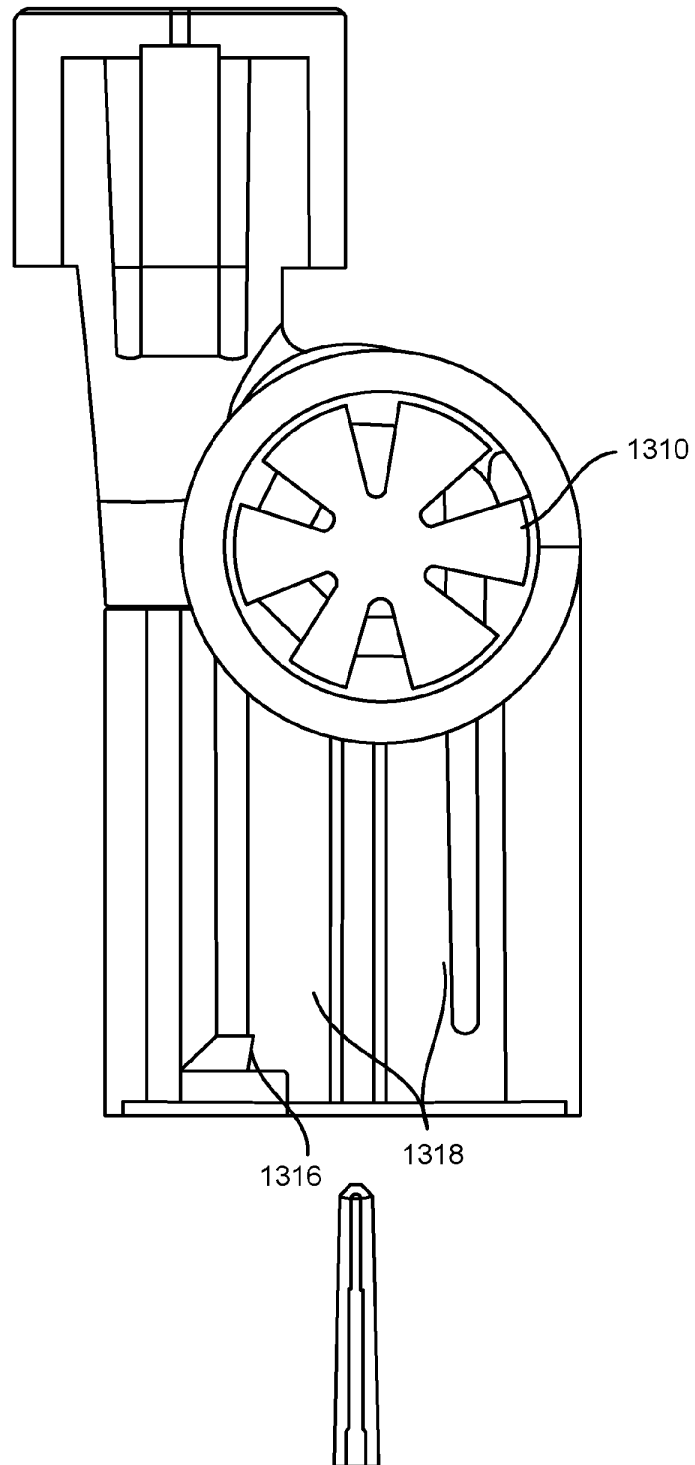


FIG. 13D

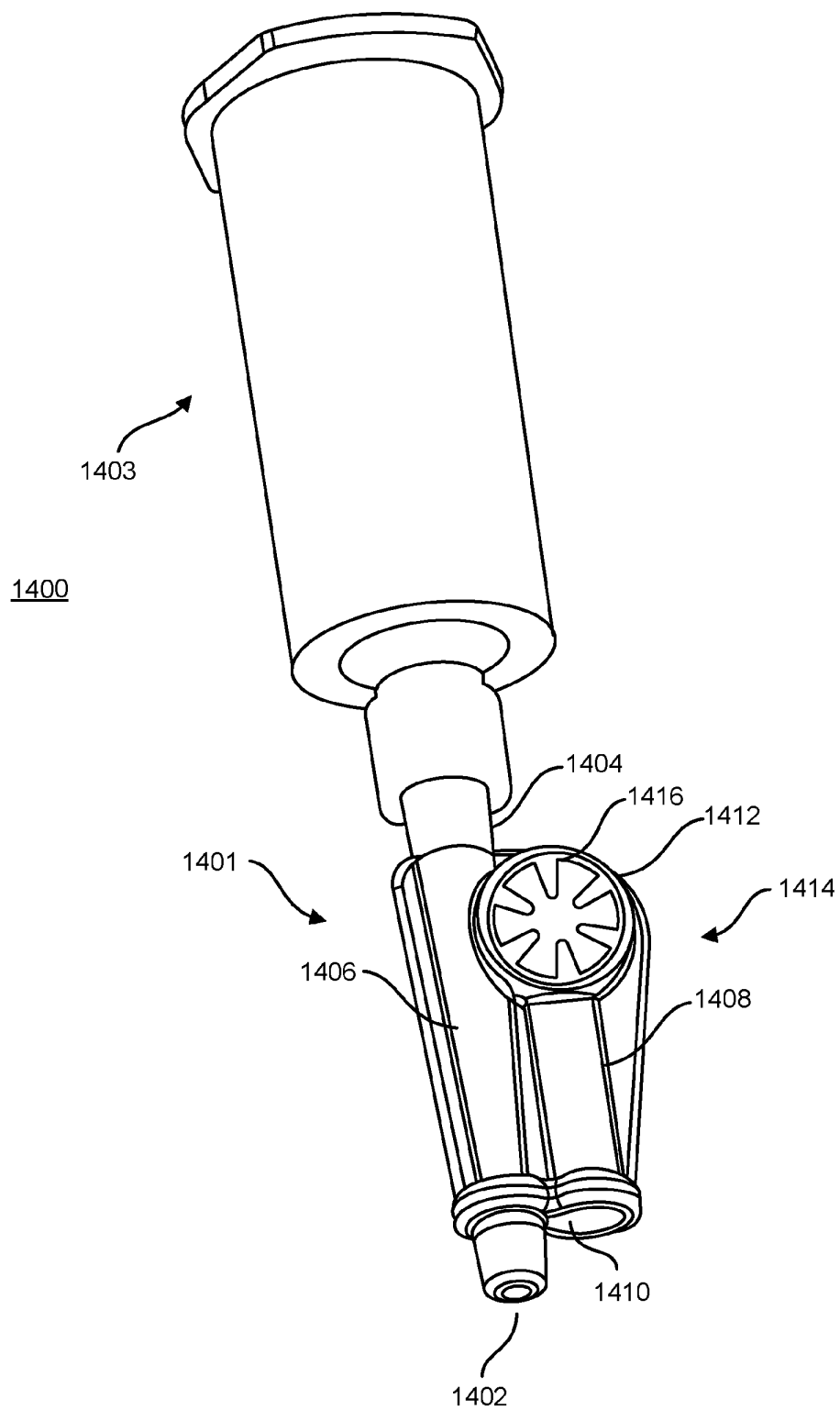


FIG. 14A

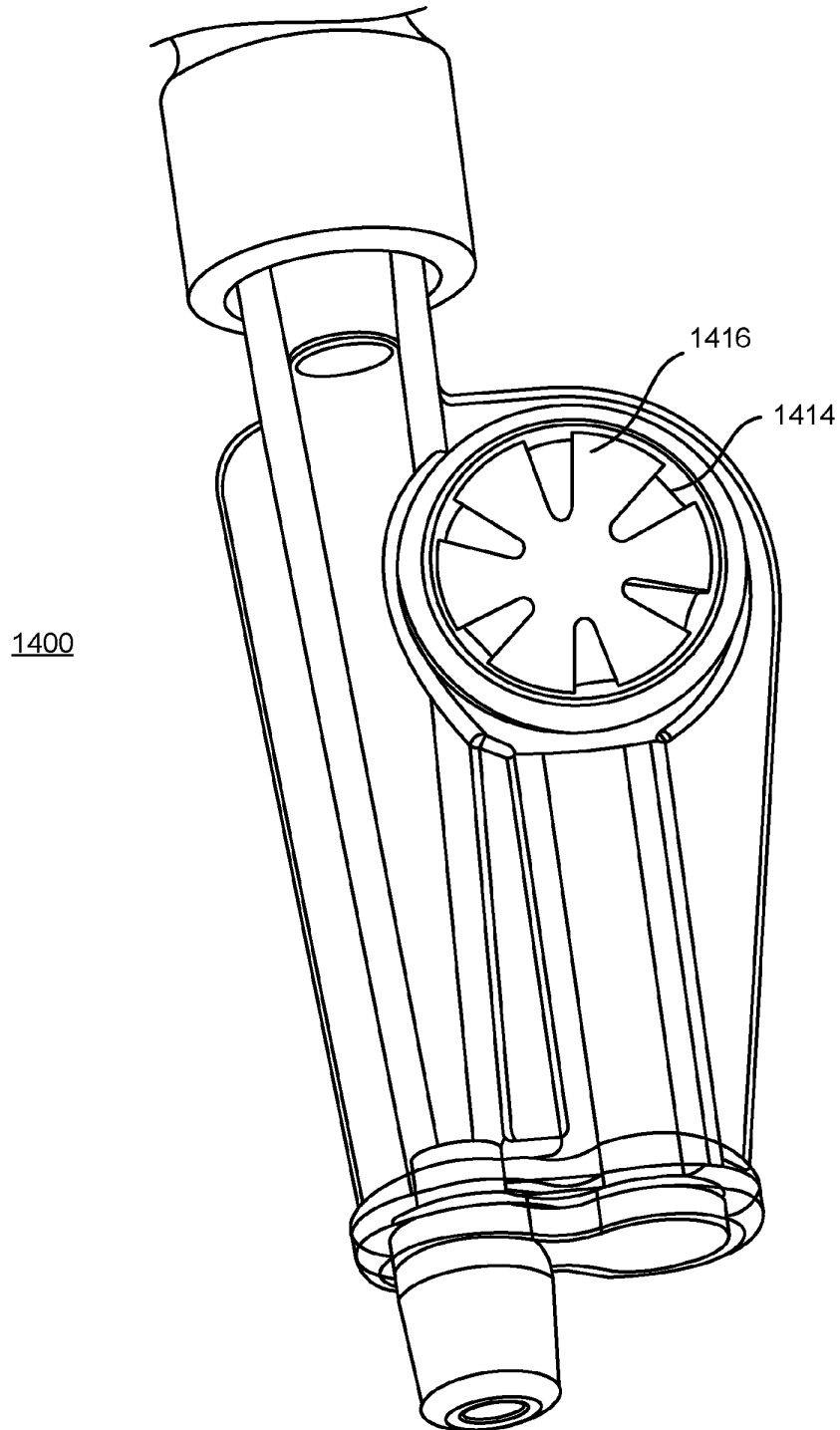


FIG. 14B

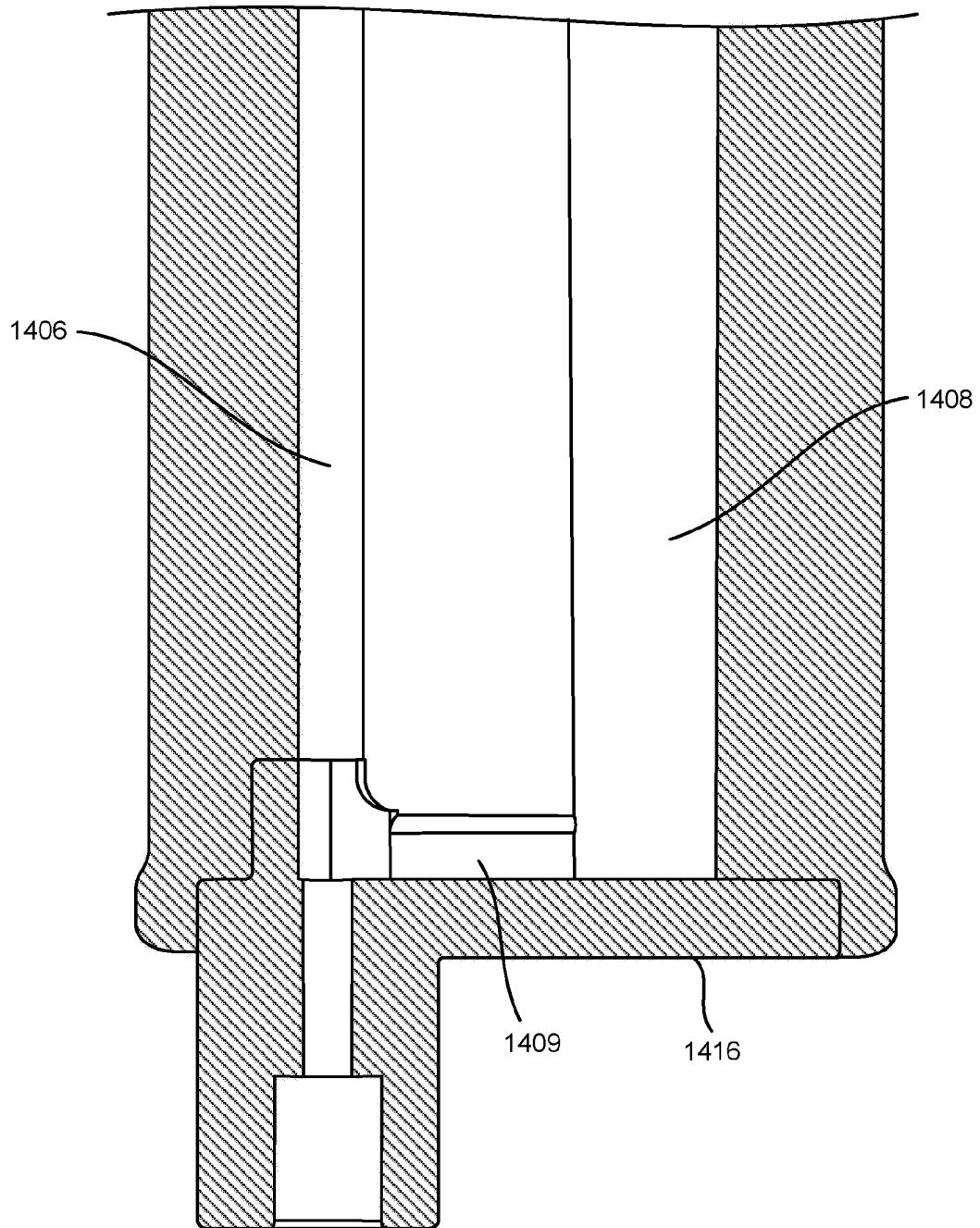


FIG. 14C

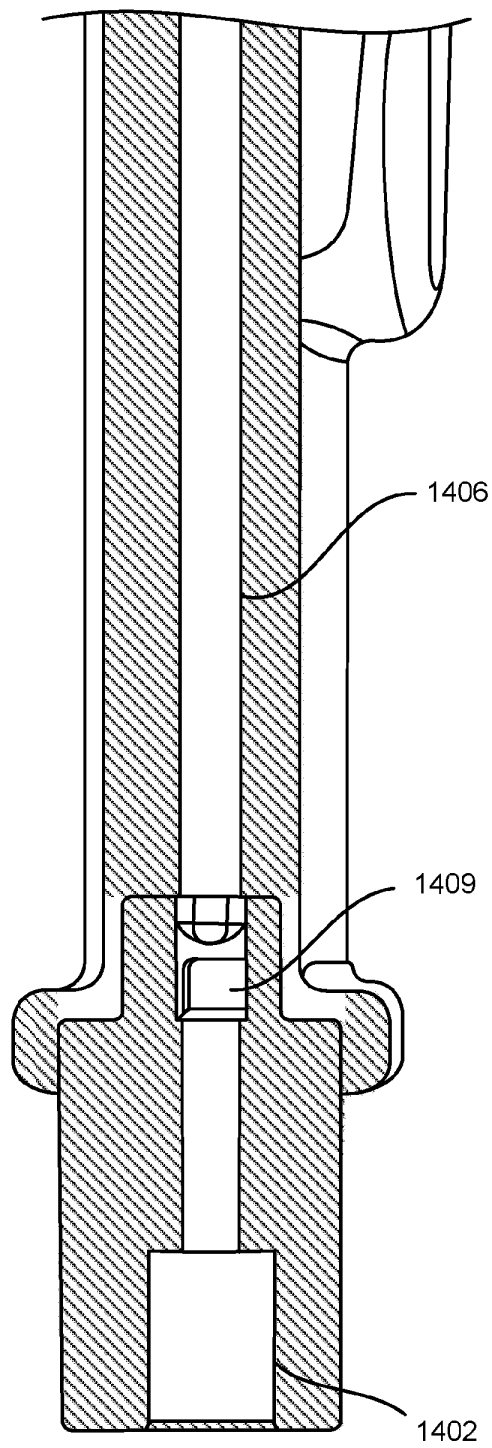


FIG. 14D

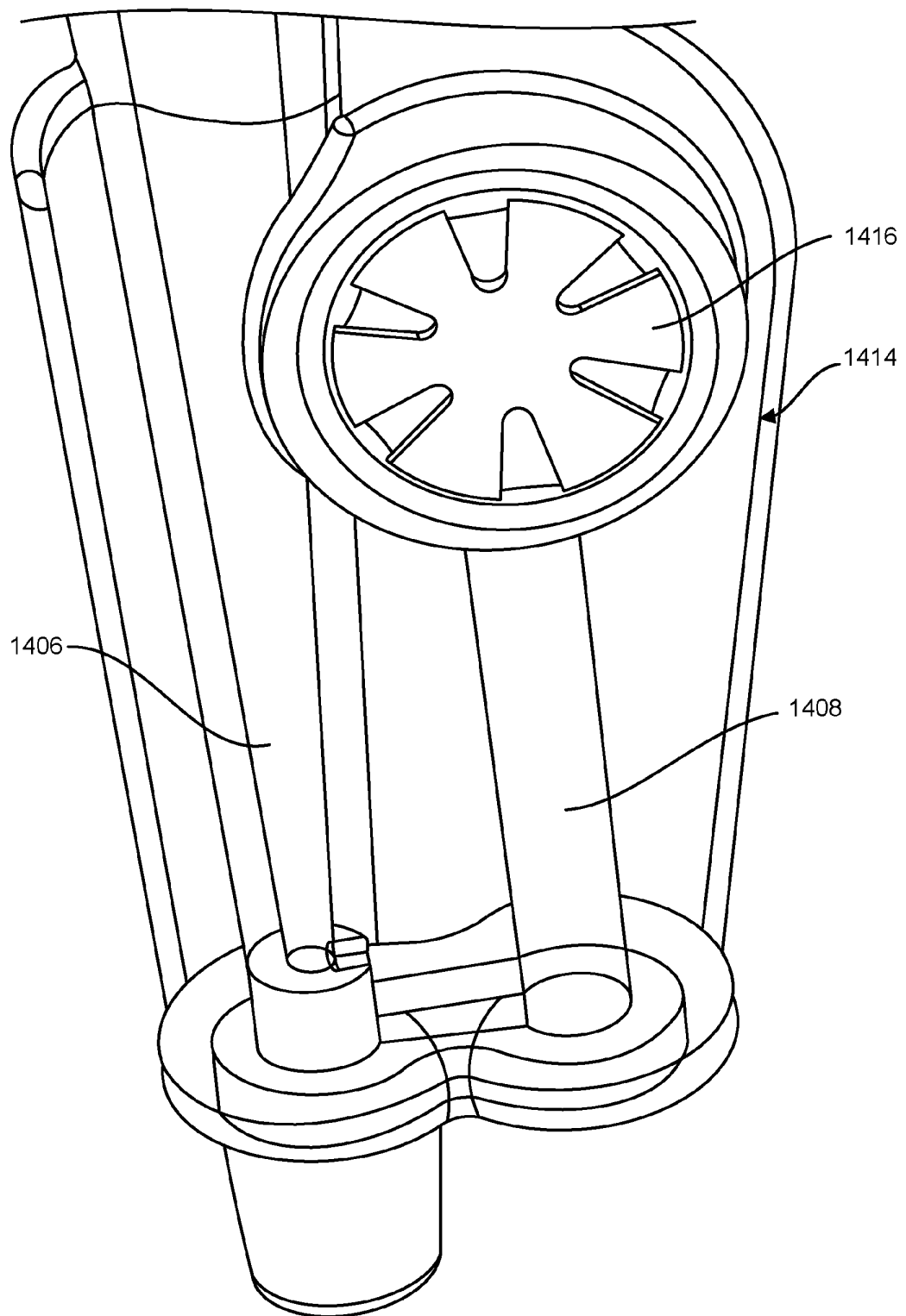


FIG. 14E

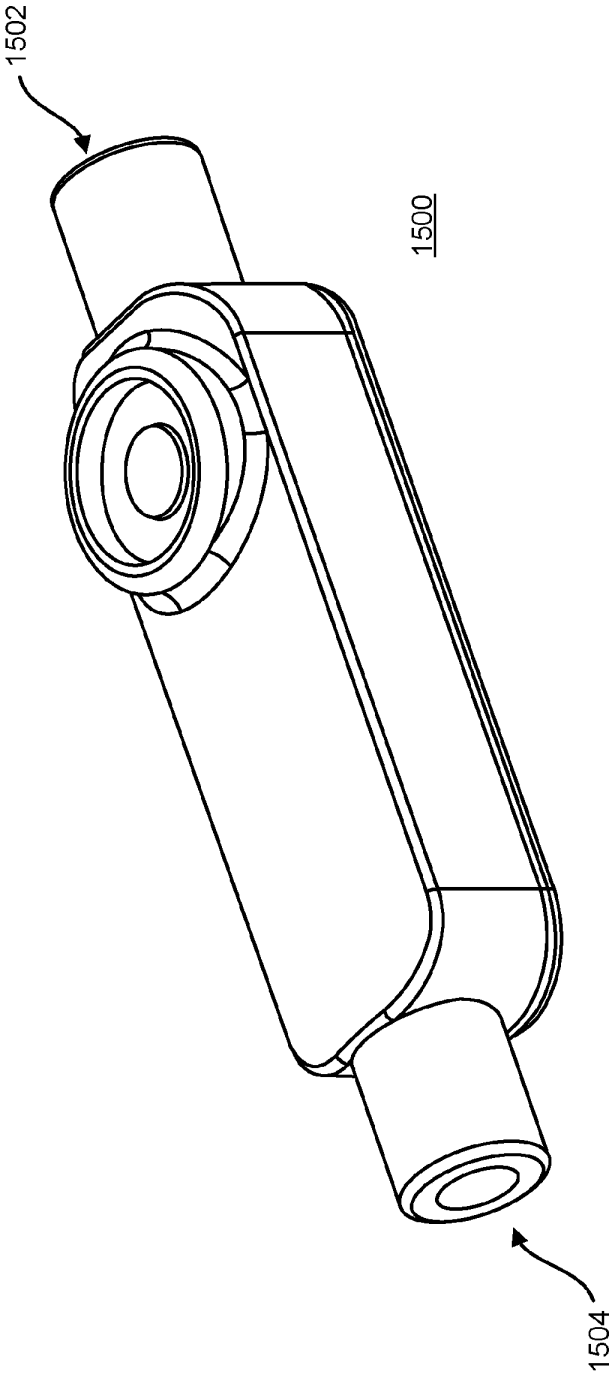


FIG. 15A

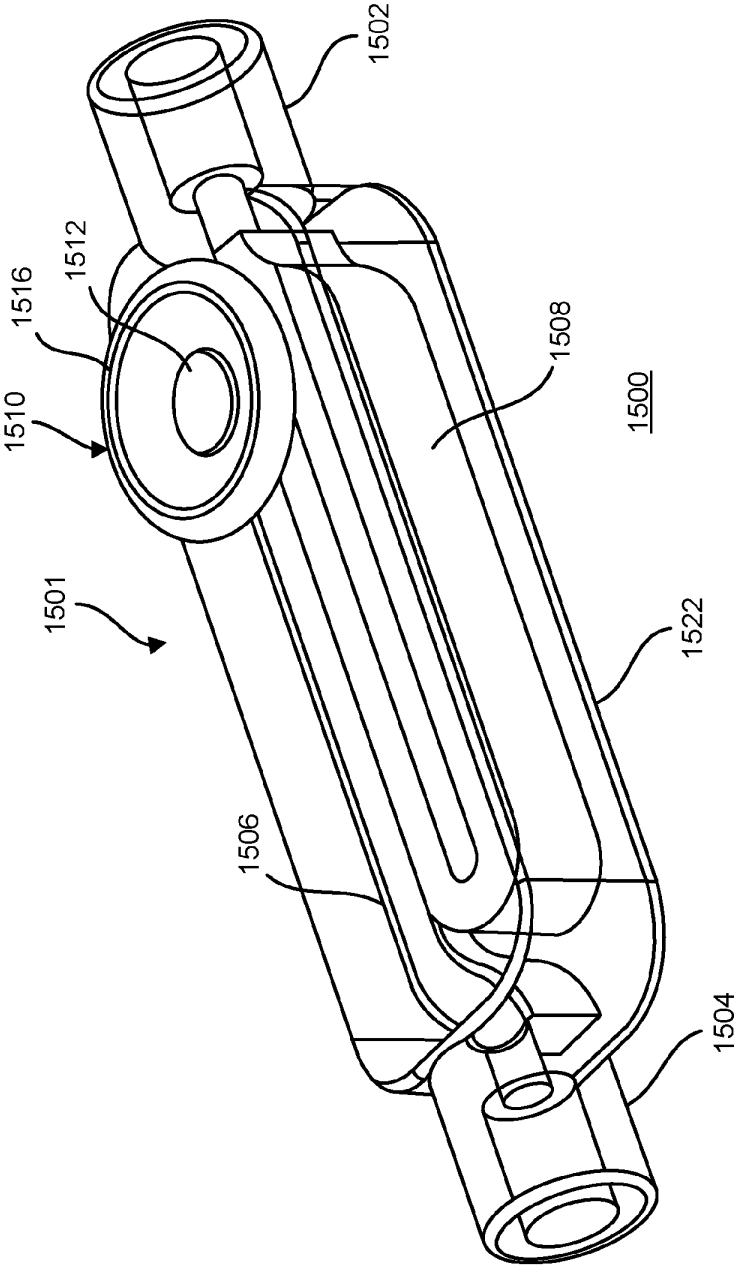


FIG. 15B

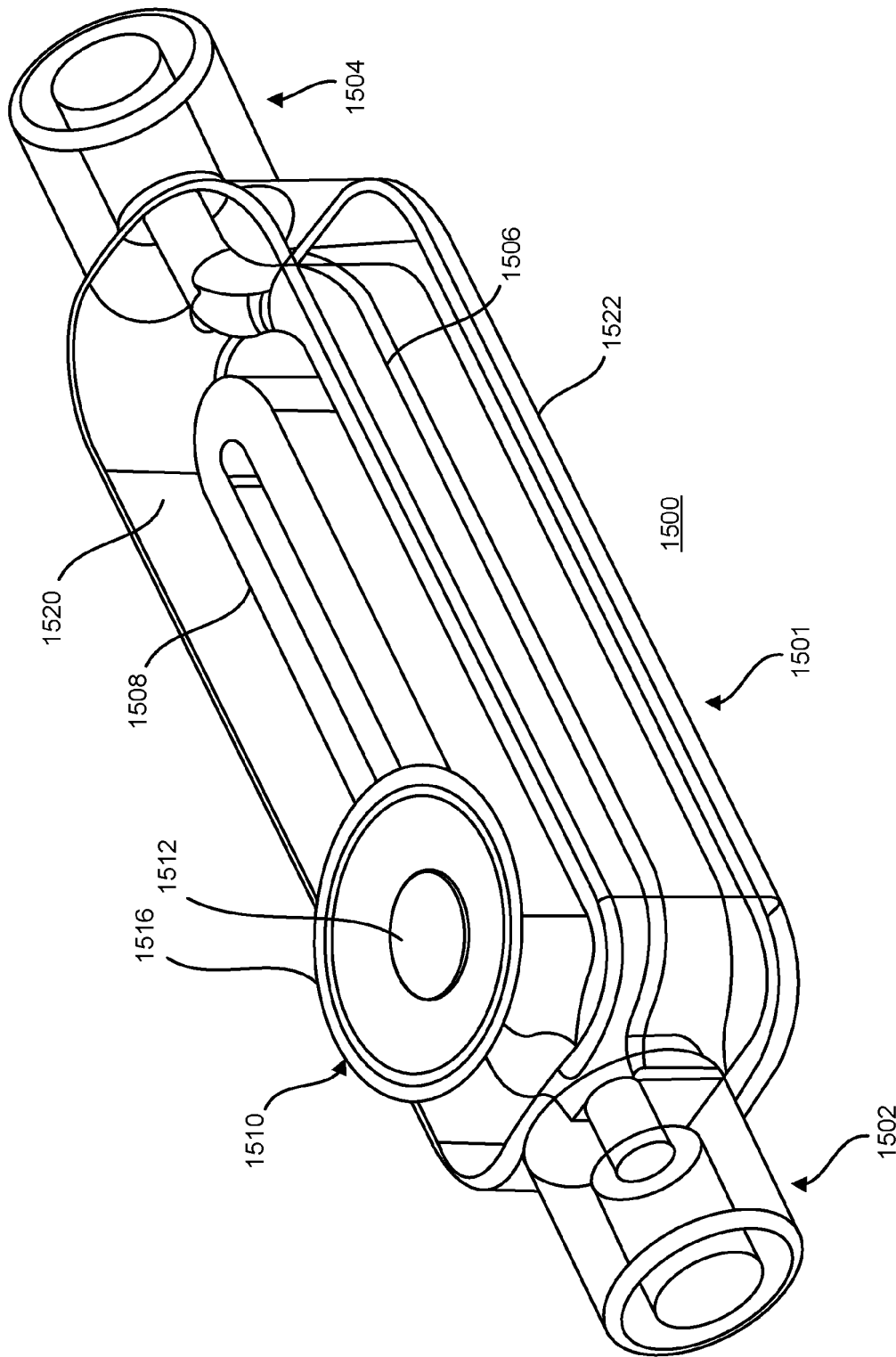


FIG. 15C

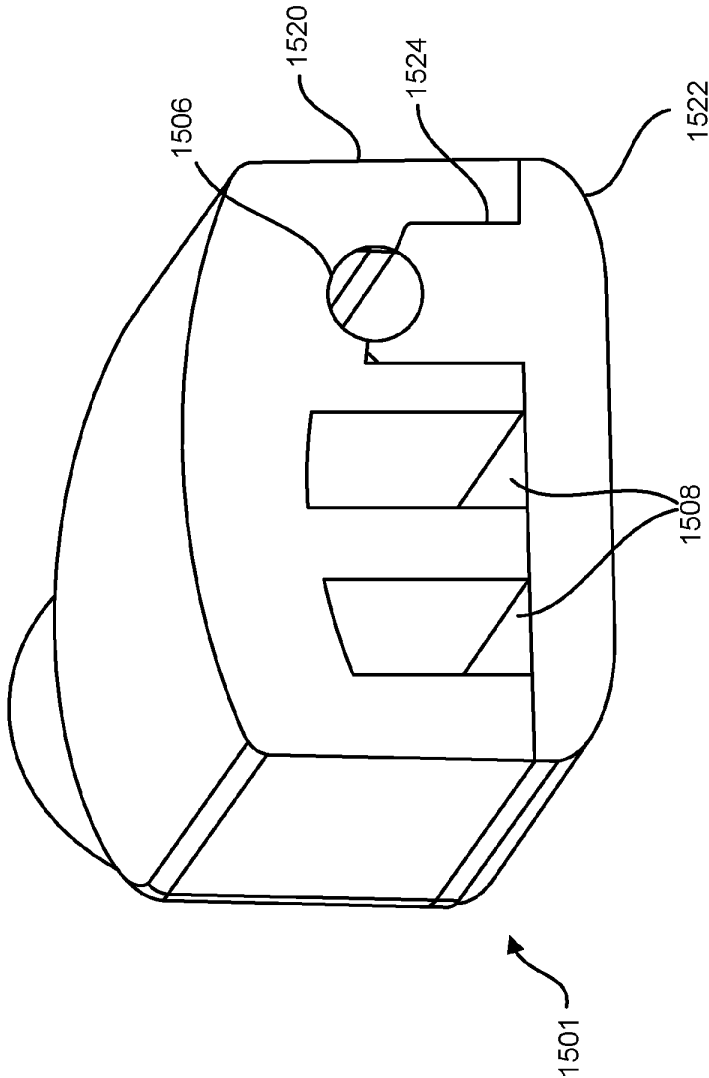


FIG. 15D

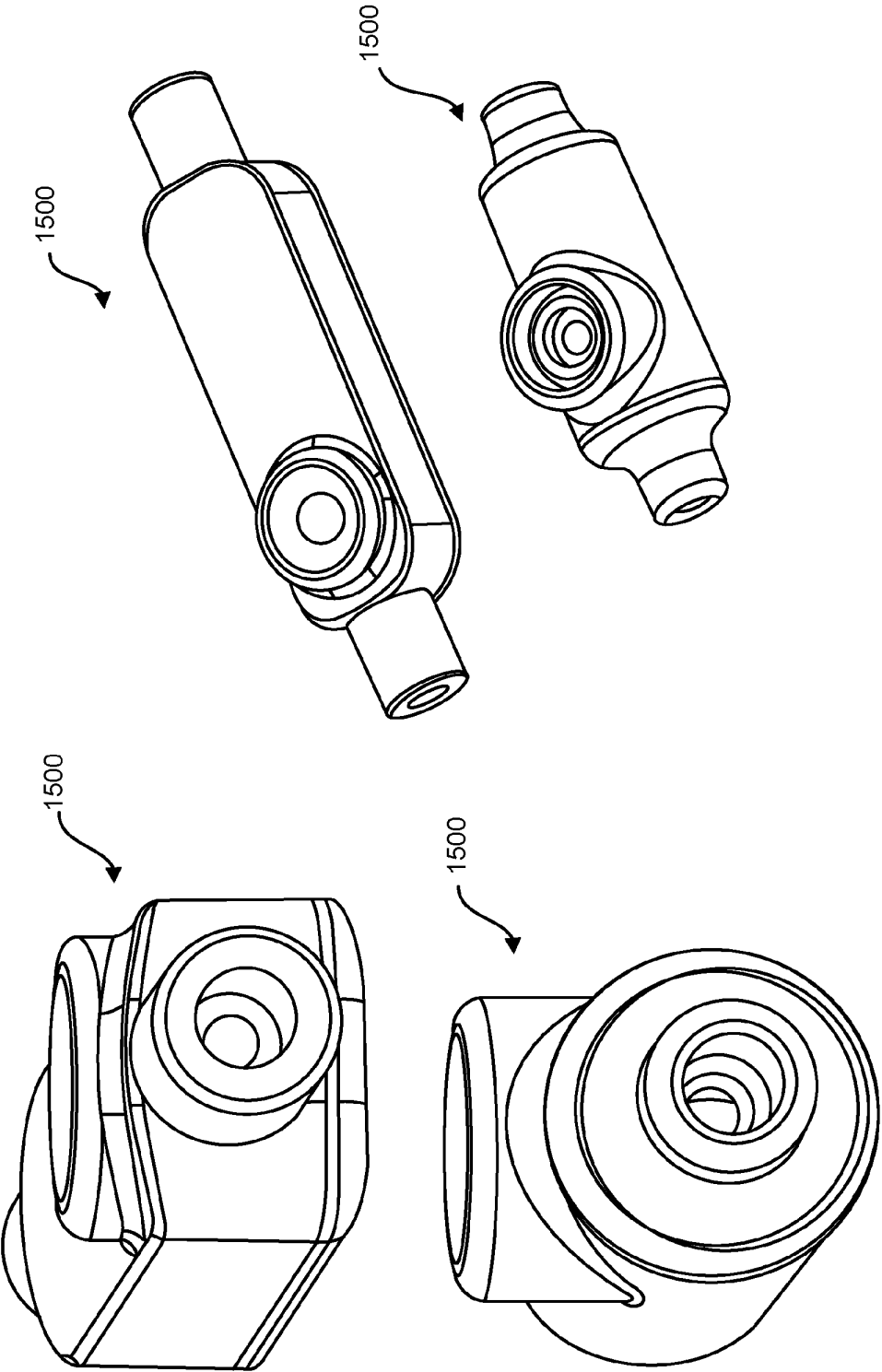


FIG. 15F

FIG. 15E

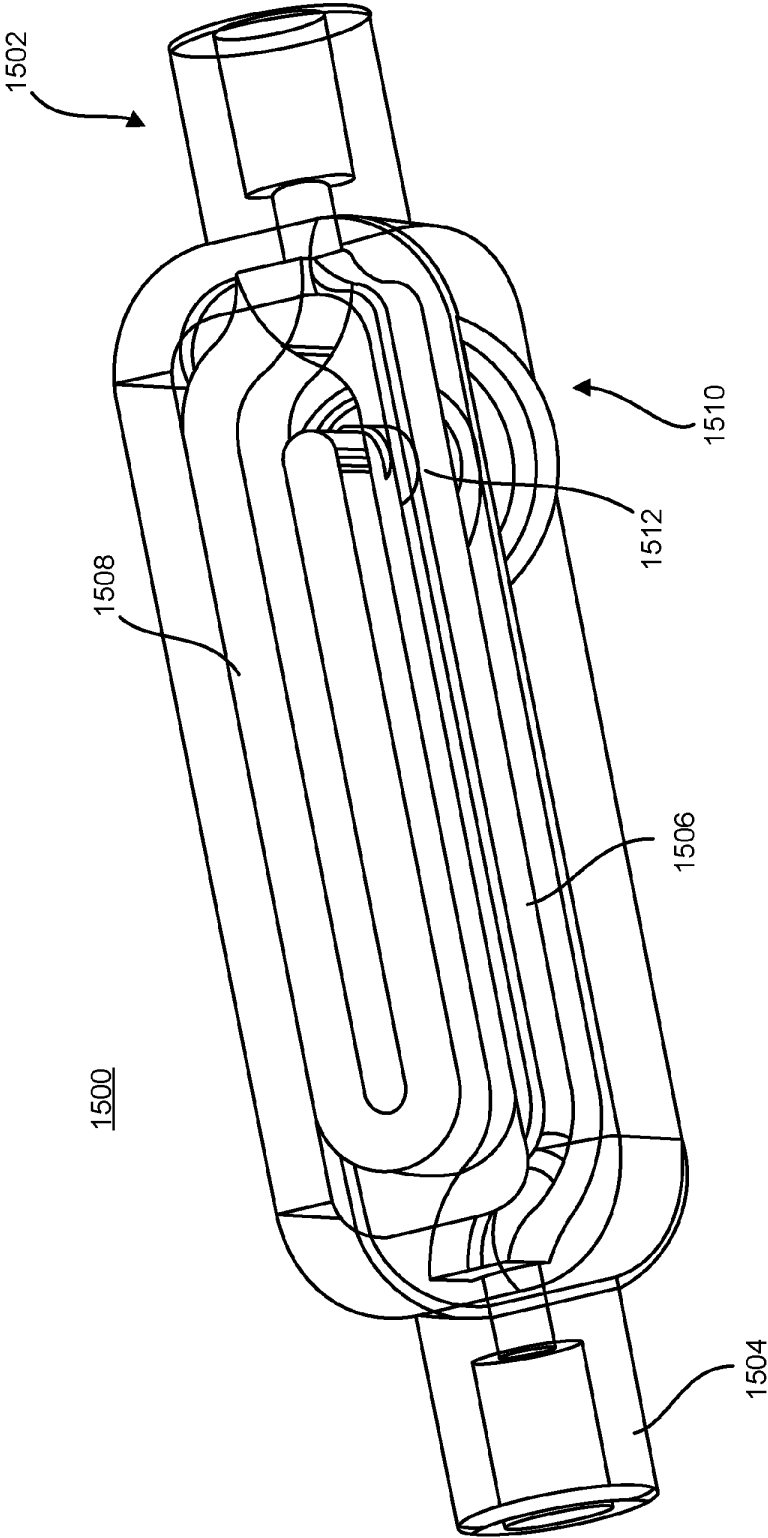


FIG. 15G

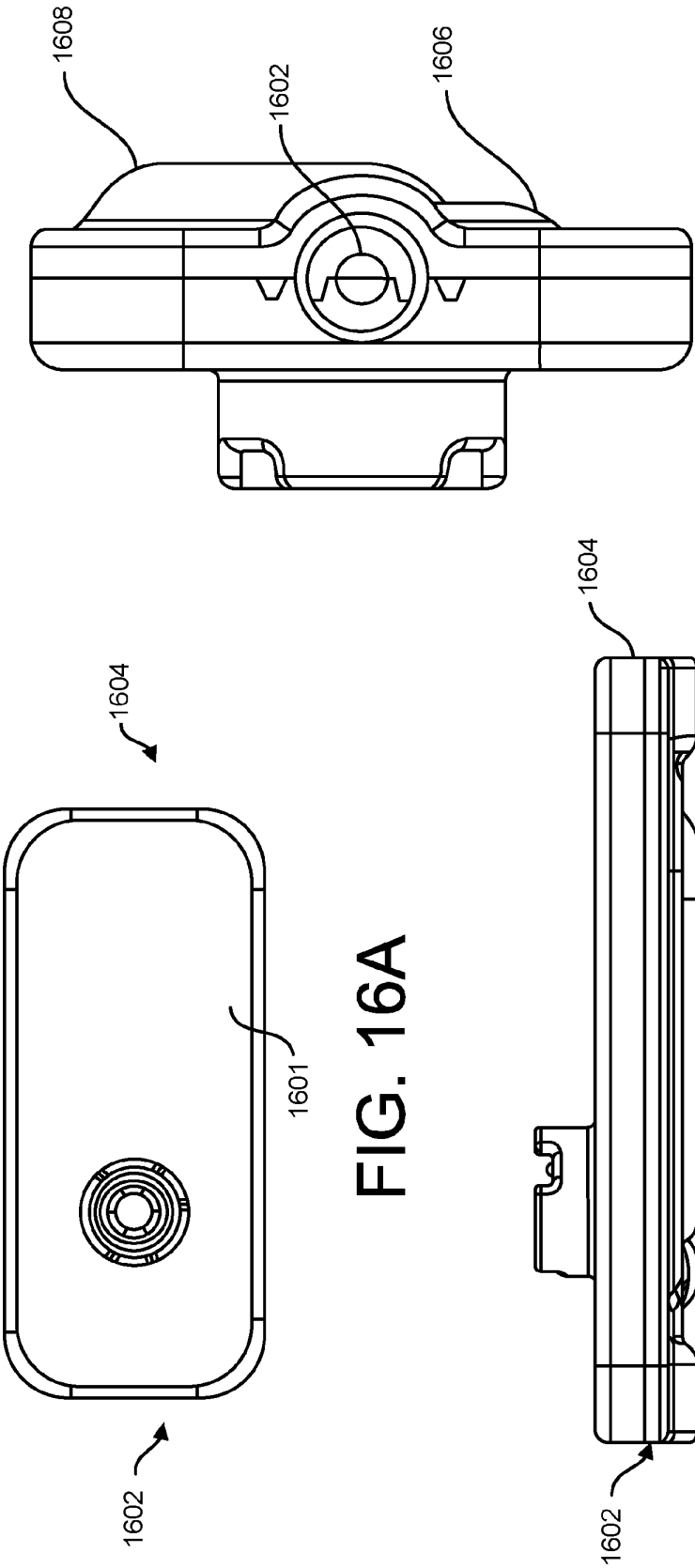


FIG. 16A

FIG. 16B

FIG. 16C

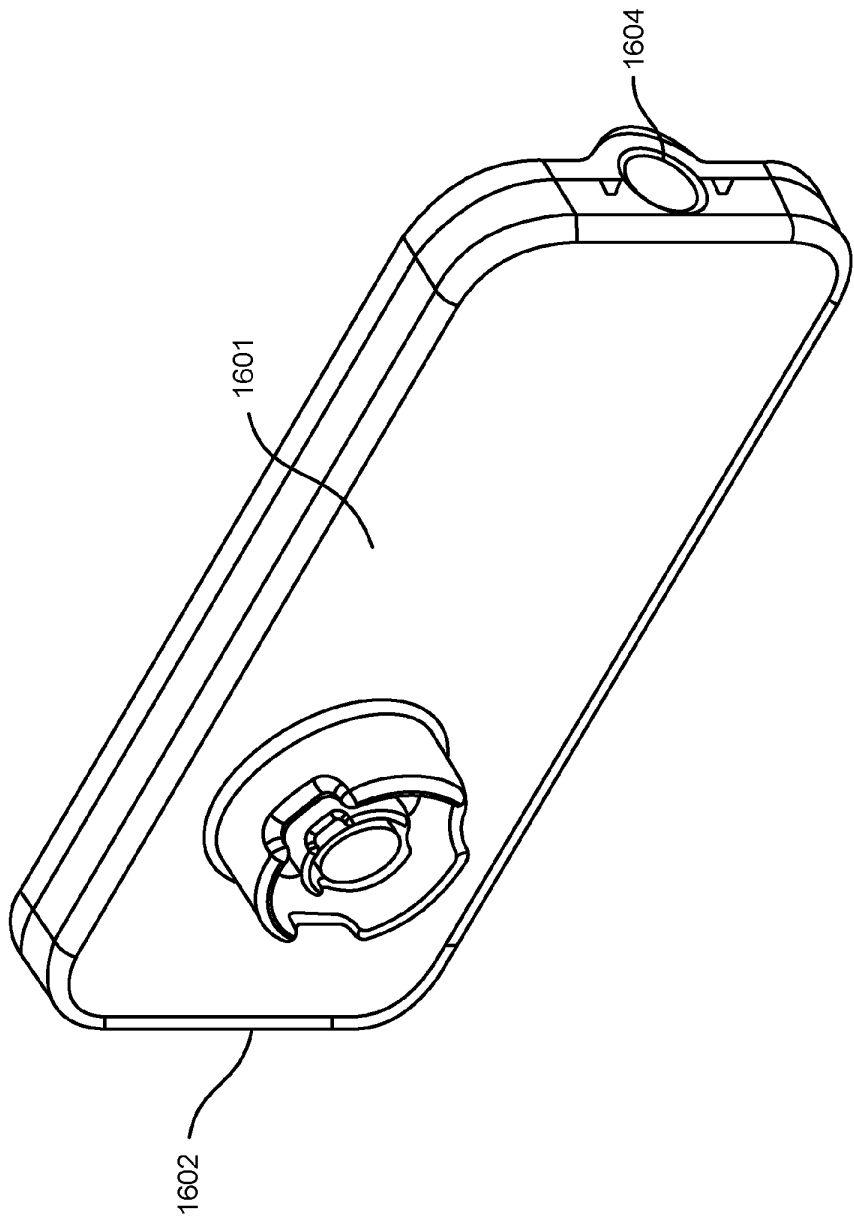


FIG. 16D

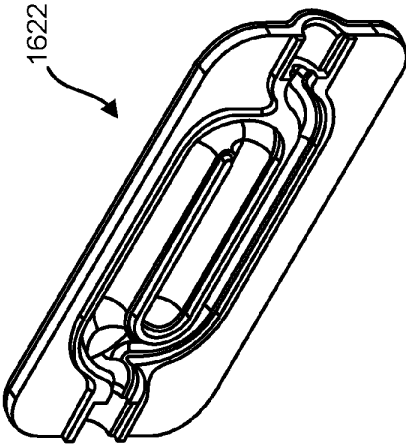


FIG. 17B

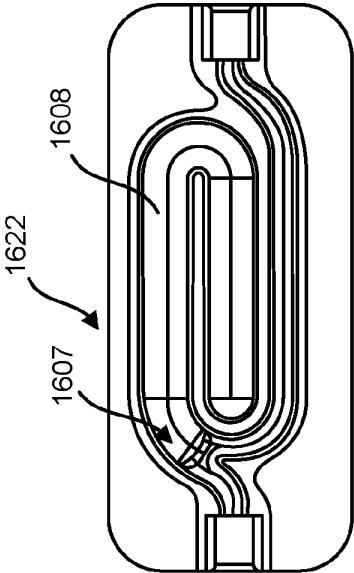


FIG. 17A

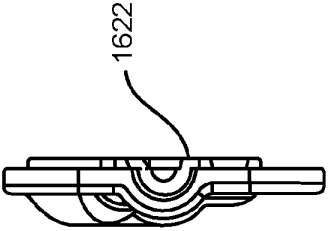


FIG. 17C

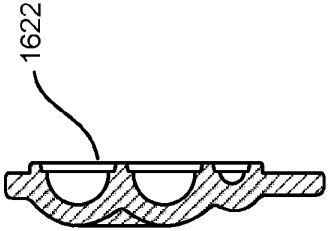


FIG. 17D



FIG. 17E

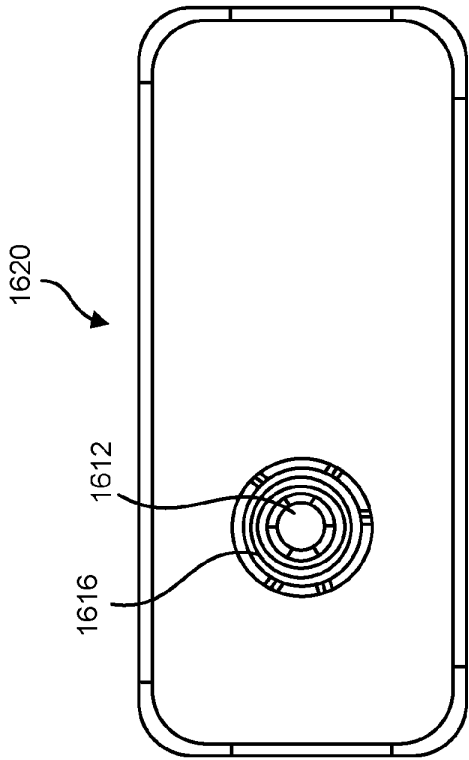


FIG. 18A

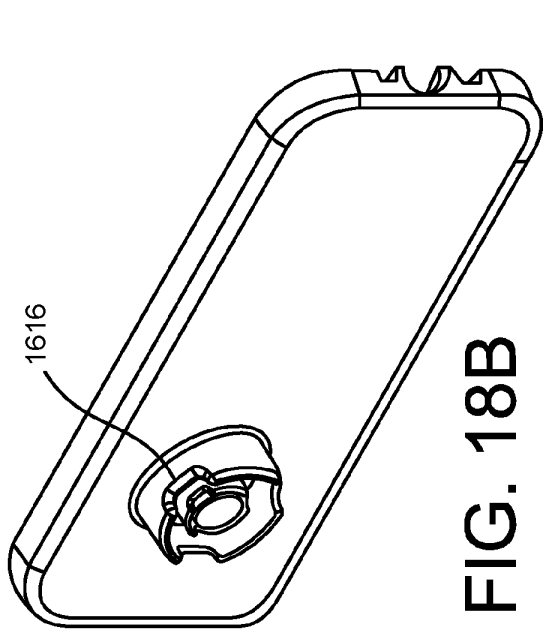


FIG. 18B

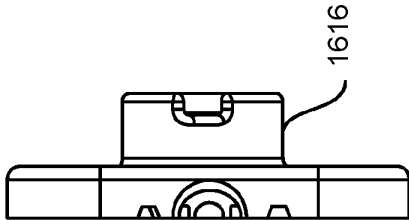


FIG. 18C

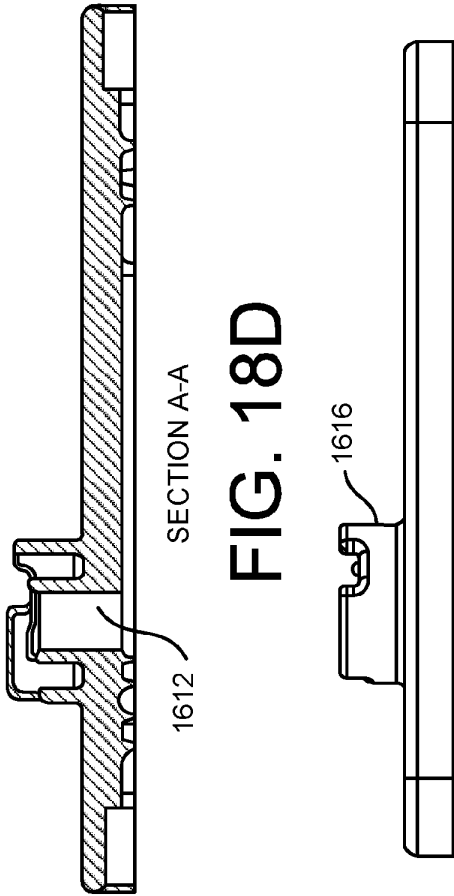


FIG. 18D

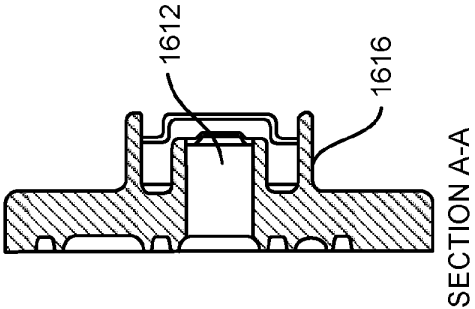


FIG. 18E

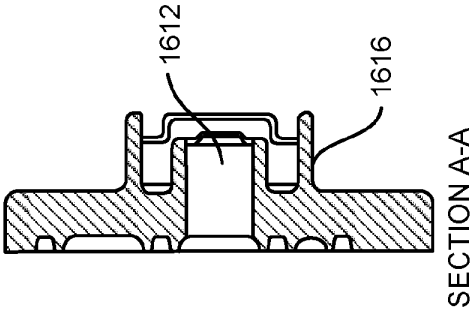


FIG. 18F

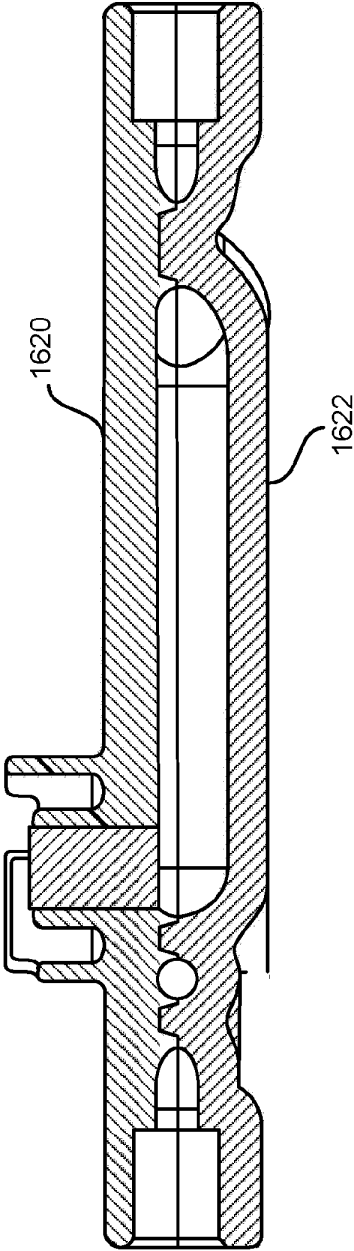


FIG. 19A

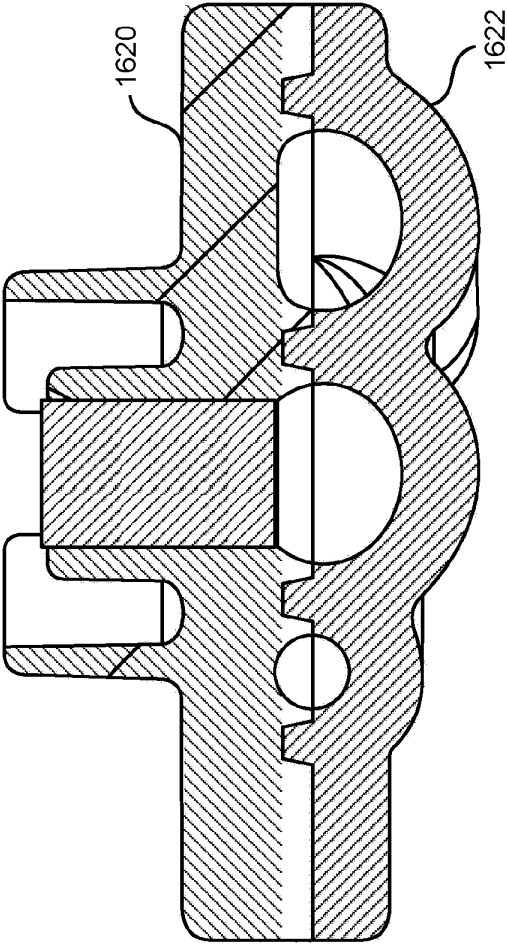


FIG. 19B

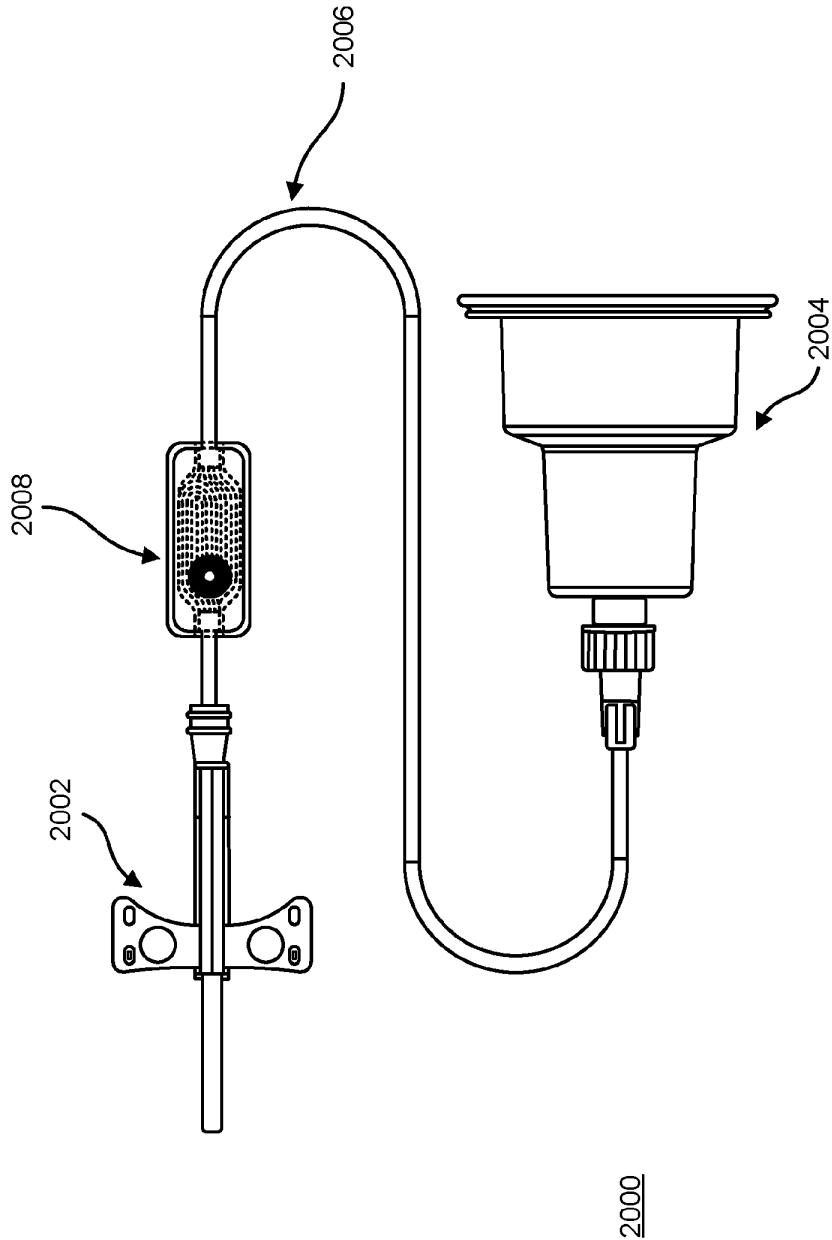


FIG. 20

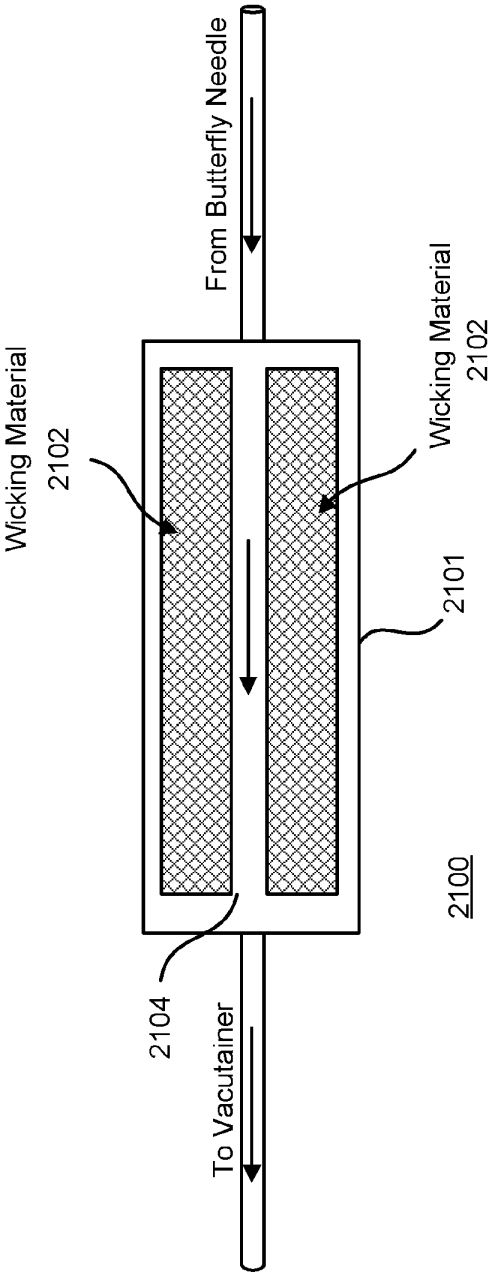


FIG. 21

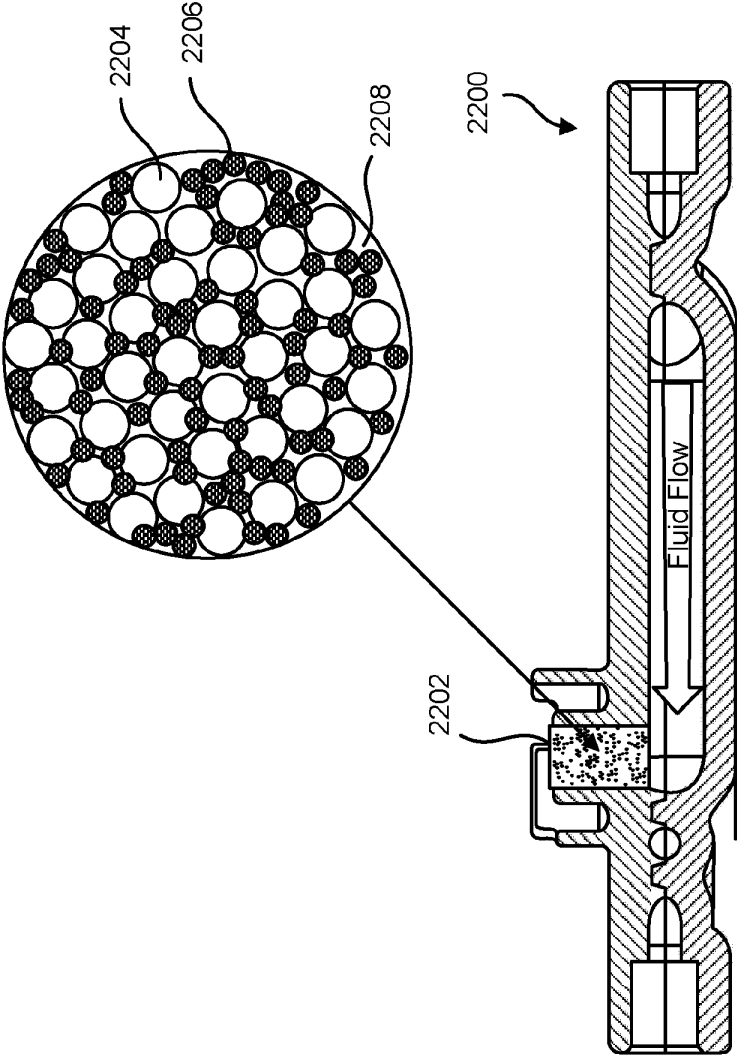


FIG. 22A

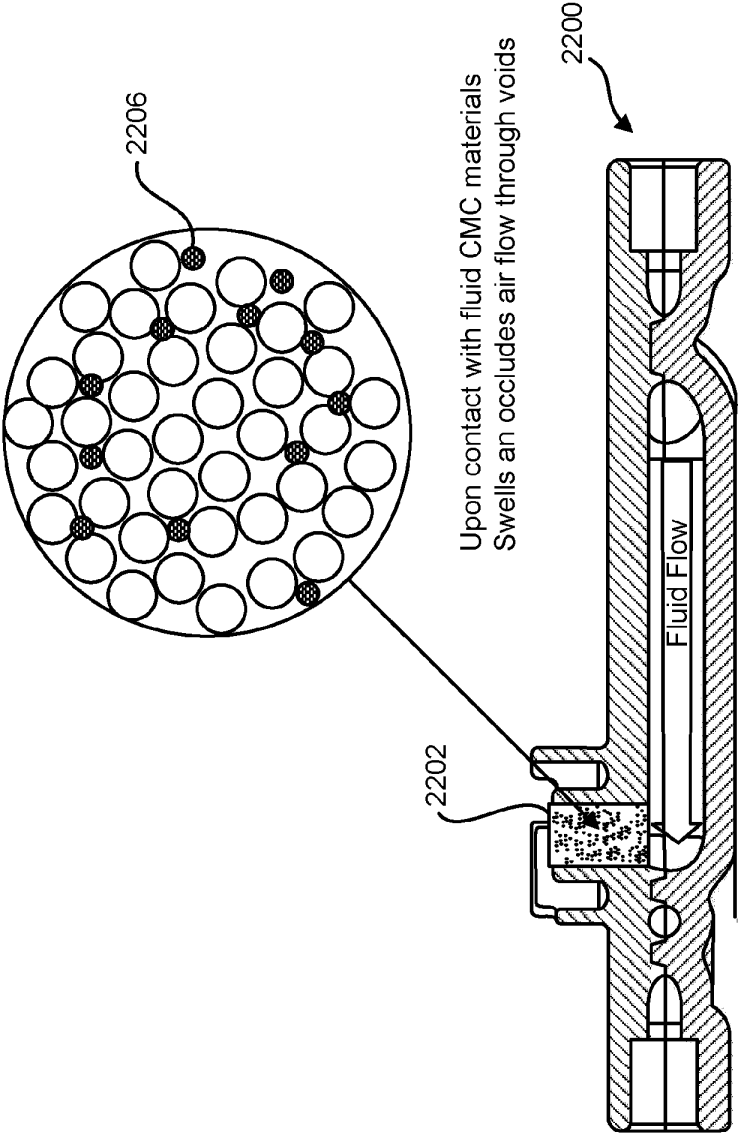


FIG. 22B

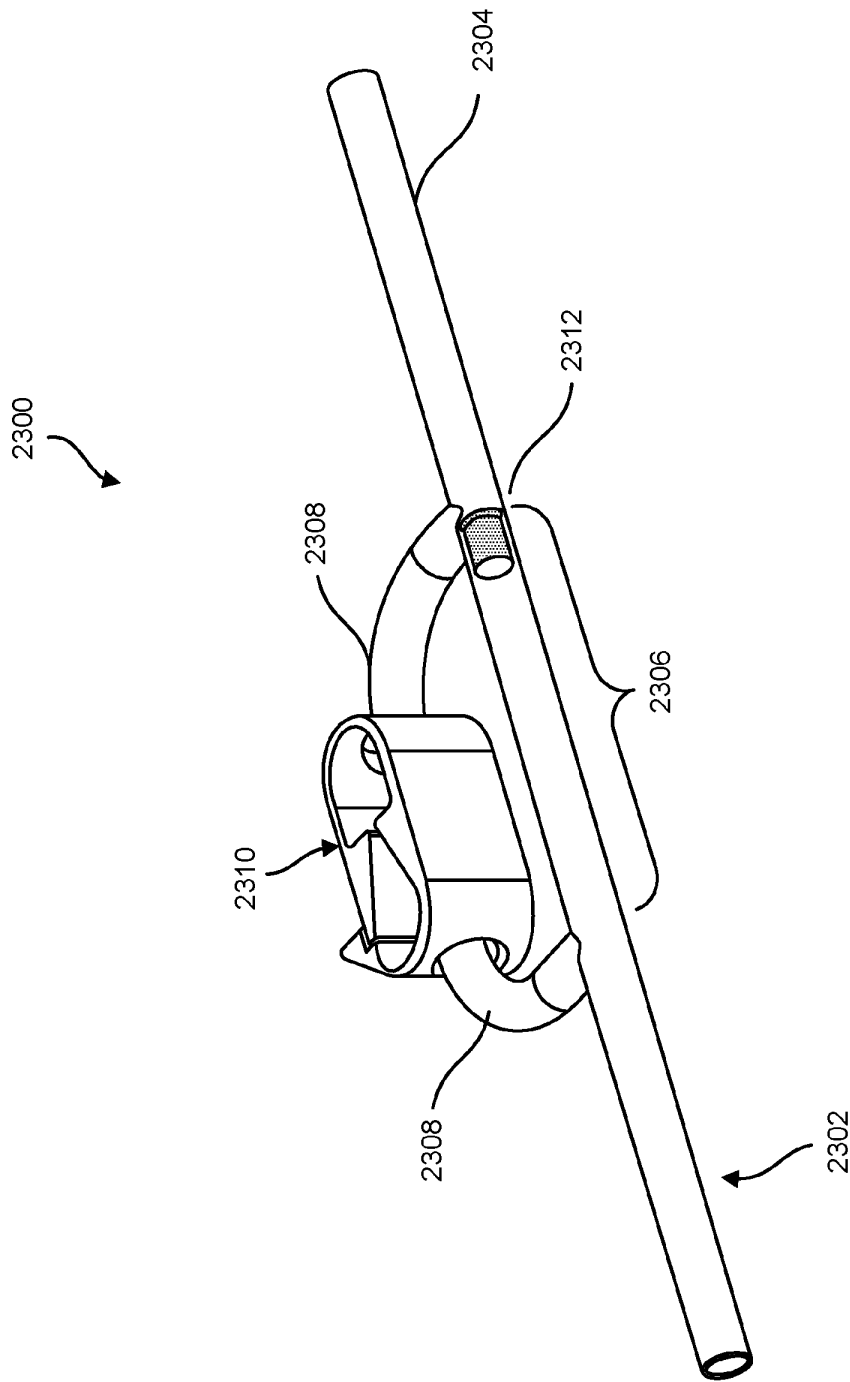


FIG. 23A

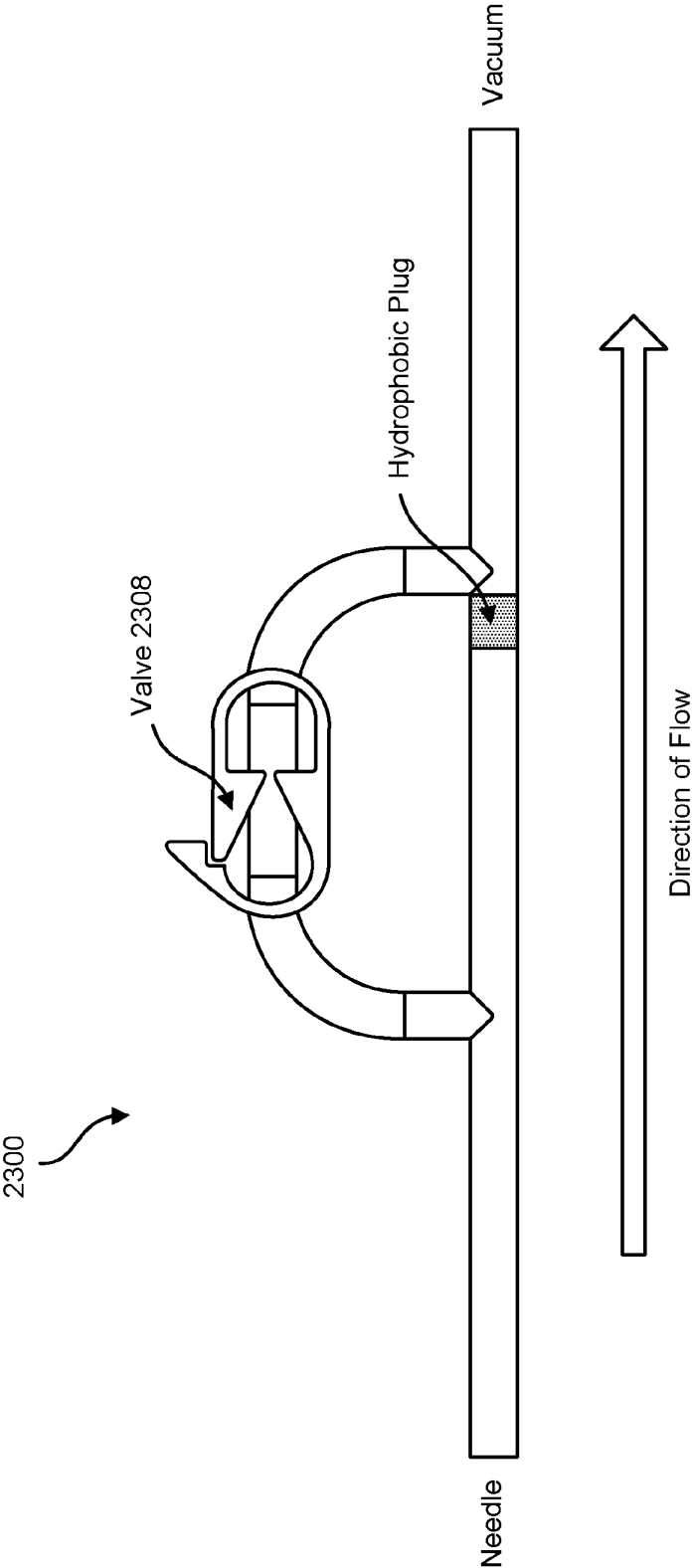


FIG. 23B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

A. CLASSIFICATION OF SUBJECT MATTER INV. A61B5/15 A61B5/153 A61B5/154 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHER LLOYD [US]; BR) 29 December 2011 (2011-12-29) paragraph [0070] figure 15 abstract	1-5, 7-13, 15-20
A	-----	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	-----	1-20
A	JP H08 257018 A (NISSHO KK) 8 October 1996 (1996-10-08) abstract; figures	1-20

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☒ 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 "Z" 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/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel: (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Schultz, Ottmar

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

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures -----	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures -----	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14 -----	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures -----	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18 -----	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2016/043709

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			US 2010262038 A1	14-10-2010
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			US 2015099996 A1	09-04-2015
			US 2015351678 A1	10-12-2015

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

(19) World Intellectual Property
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International Bureau

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



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

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PCT/US2016/043709

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

(25) Filing Language: English

(26) Publication Language: English

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

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

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

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
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(84) Designated States (unless otherwise indicated, for every
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TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
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SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Published:

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

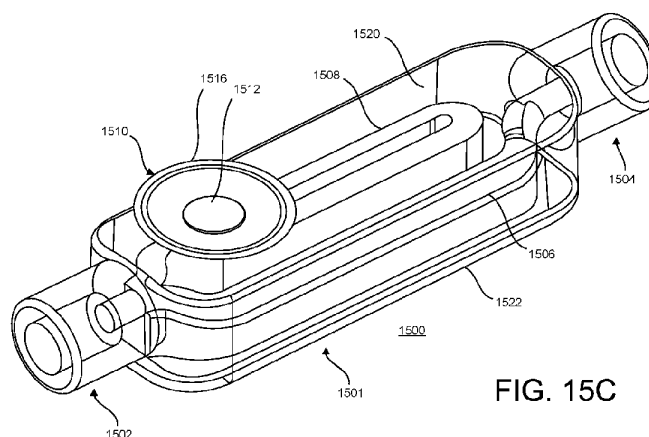


FIG. 15C

(57) Abstract: Blood sample optimization systems and methods are described that reduce or eliminate contaminants 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 contaminants 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 contaminants 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 indicator 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 contaminants 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 decontaminant, 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.

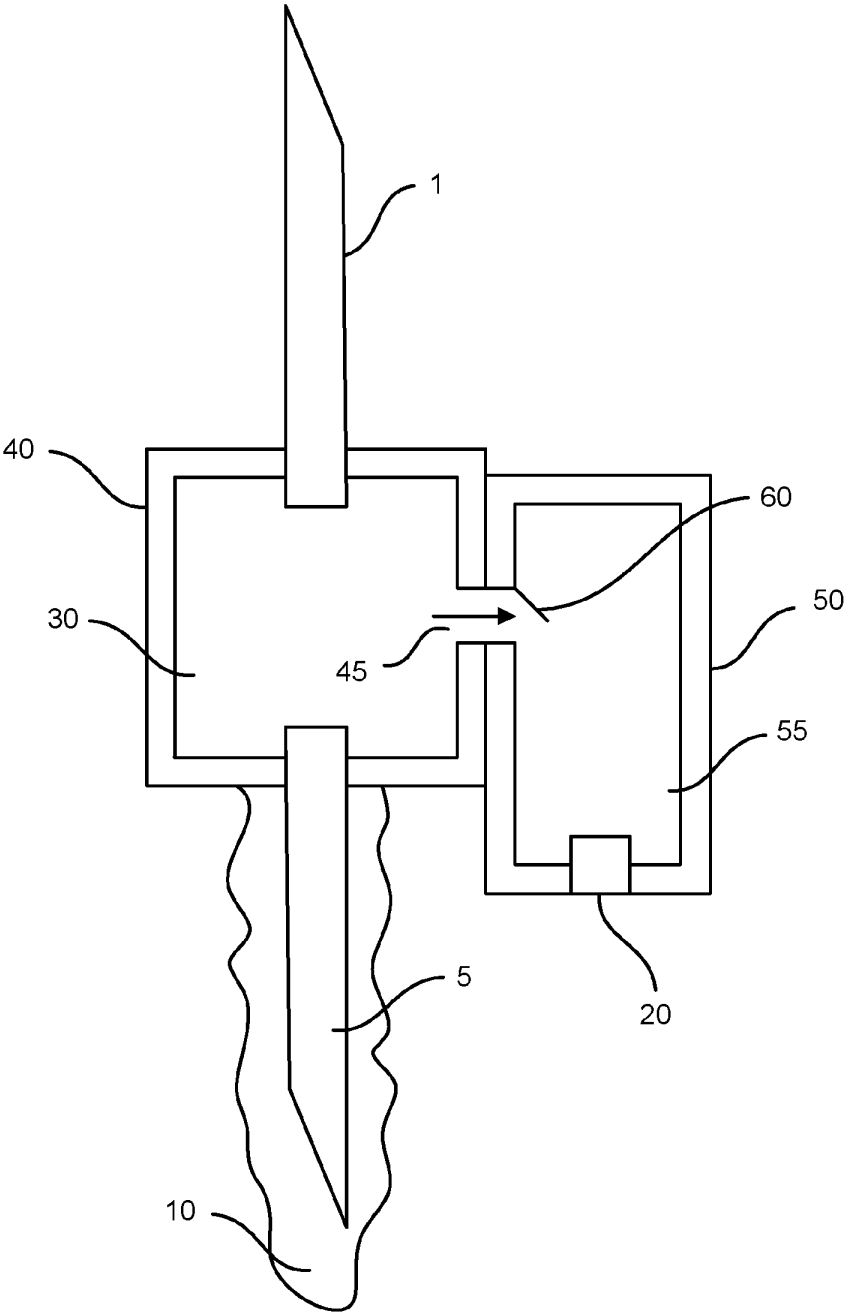


FIG. 1

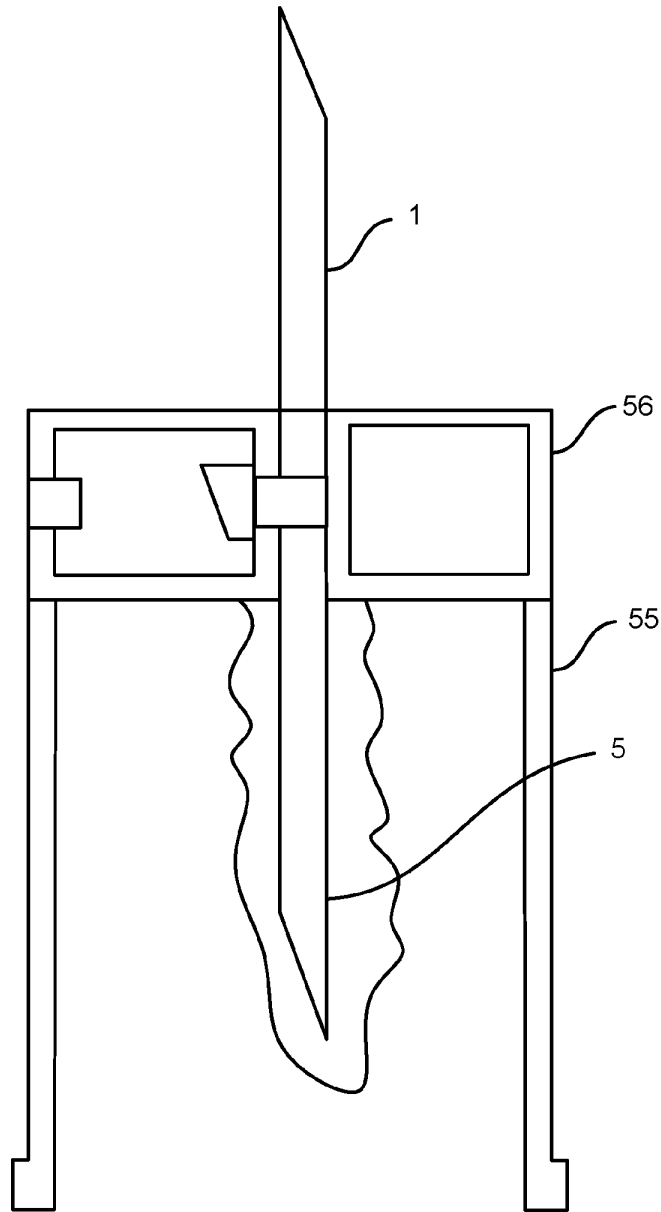


FIG. 2

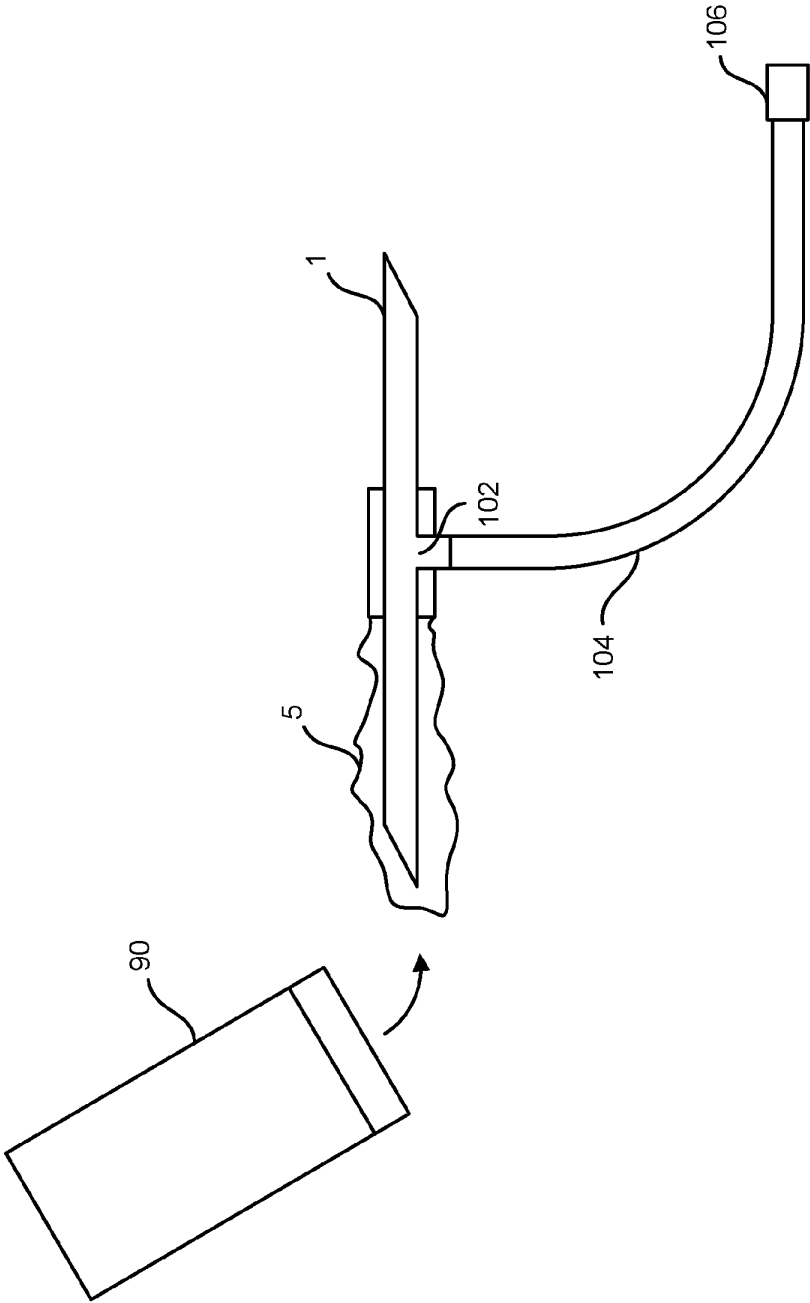


FIG. 3

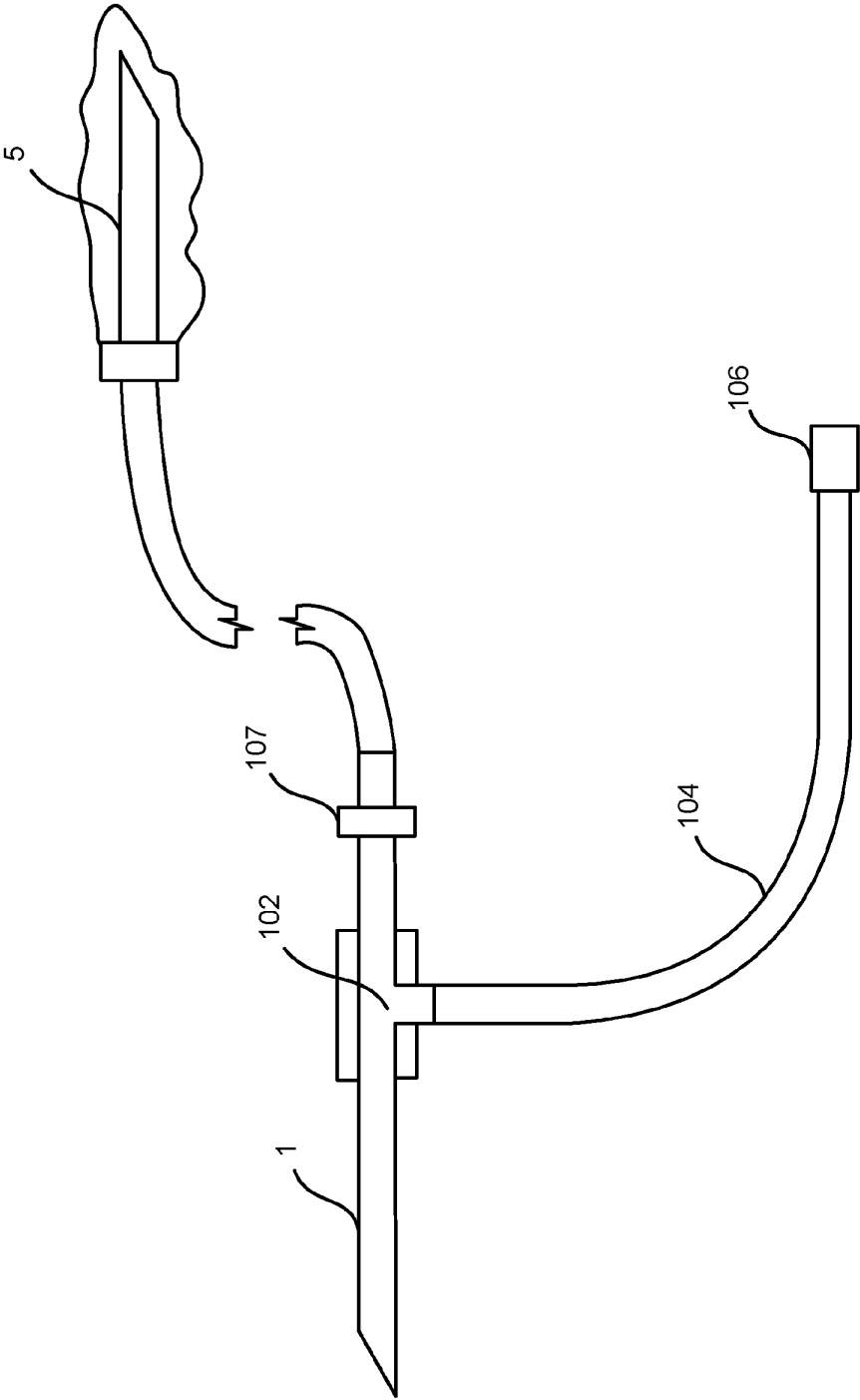


FIG. 4

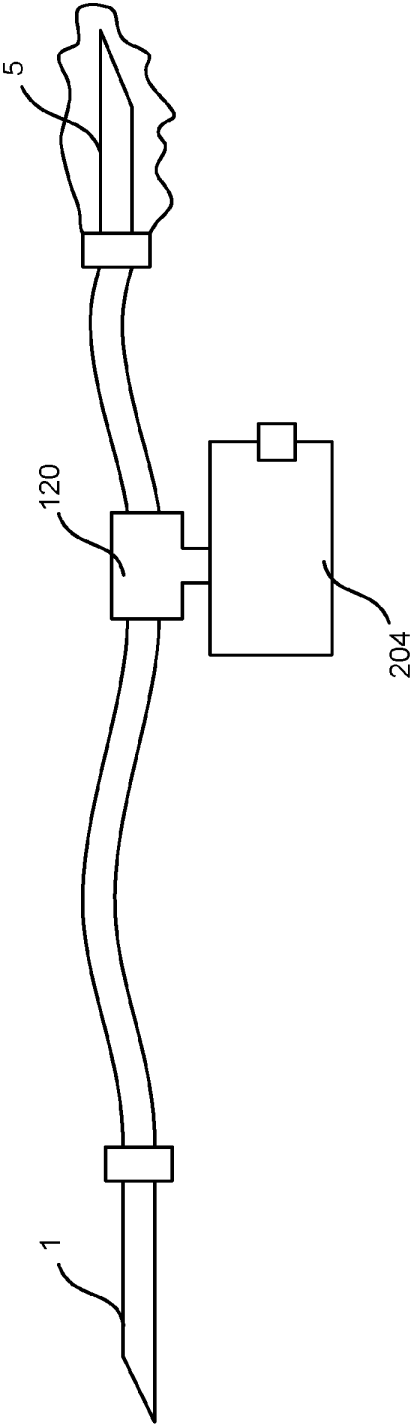


FIG. 5

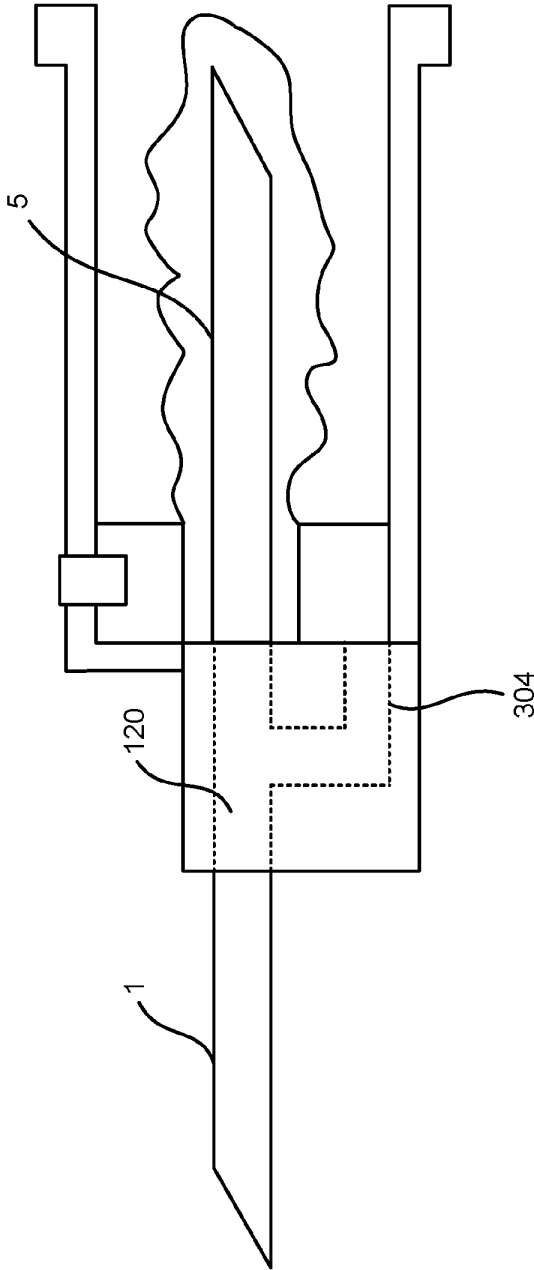
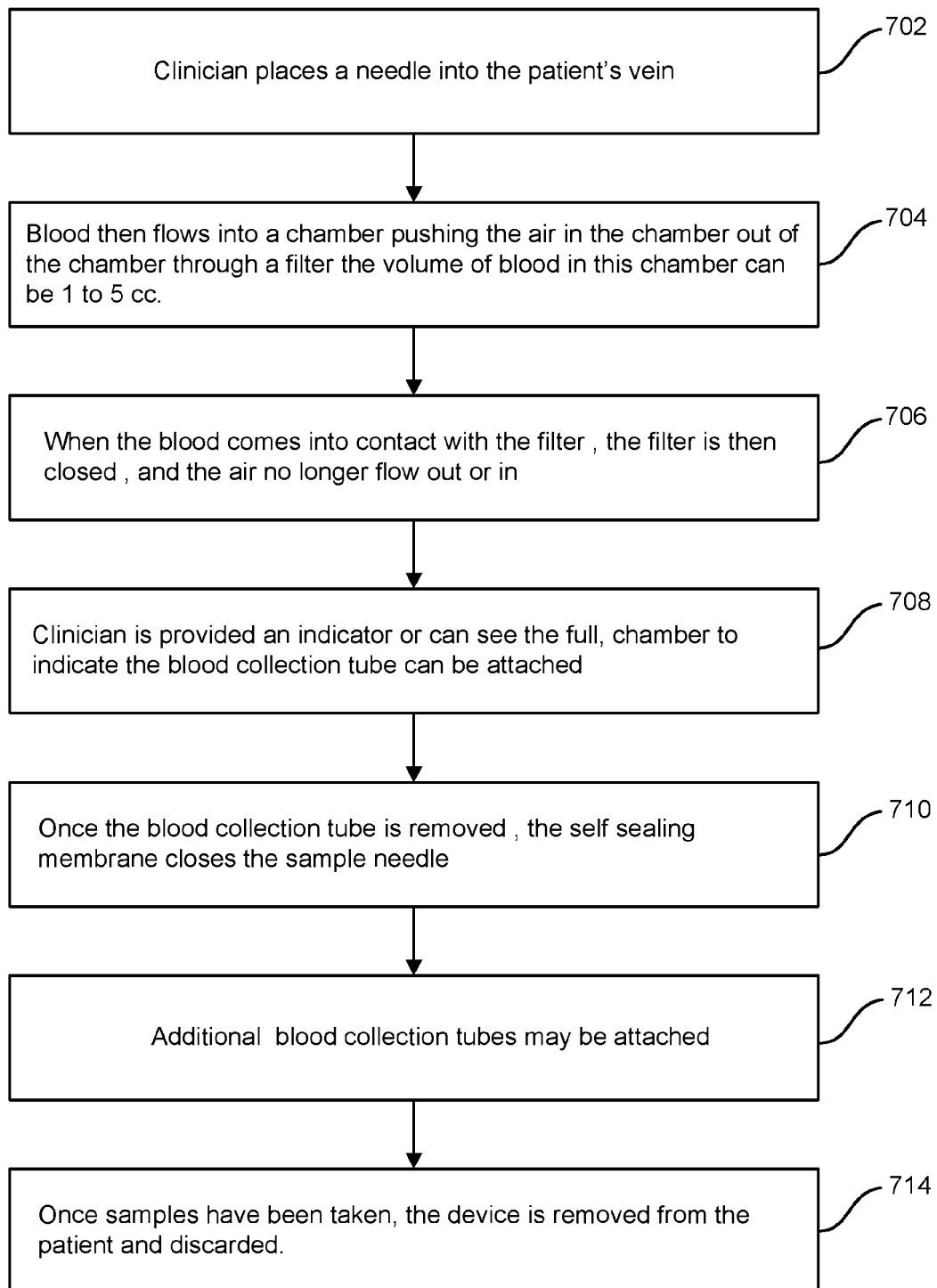
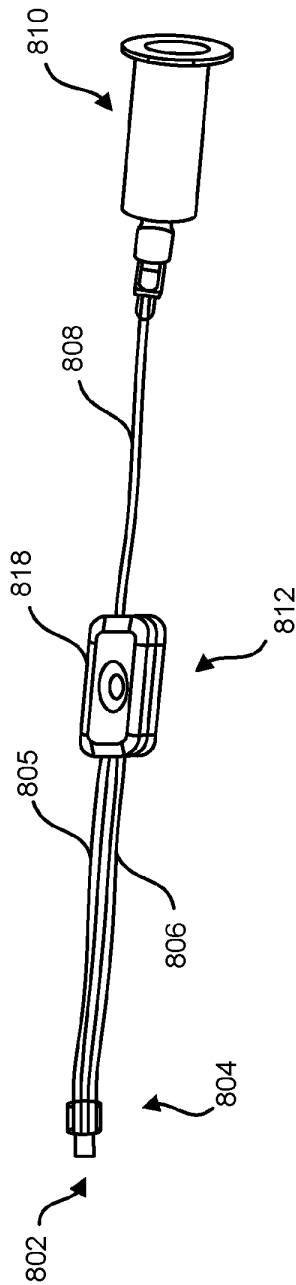


FIG. 6

**FIG. 7**



800

FIG. 8A

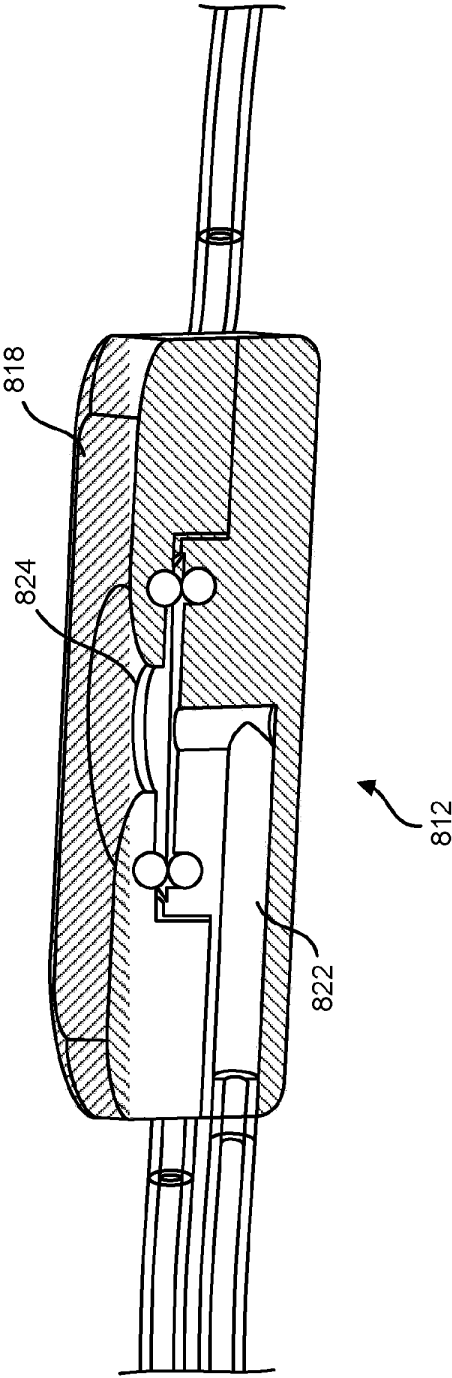


FIG. 8B

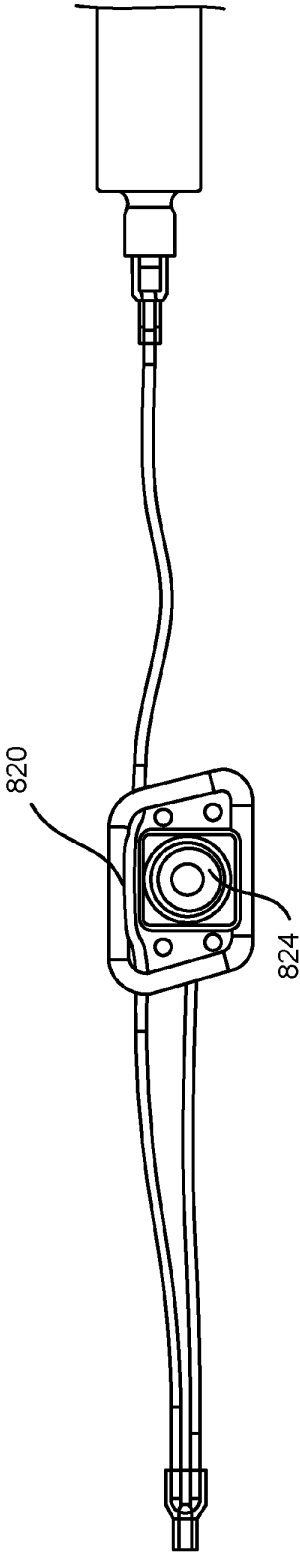


FIG. 8C

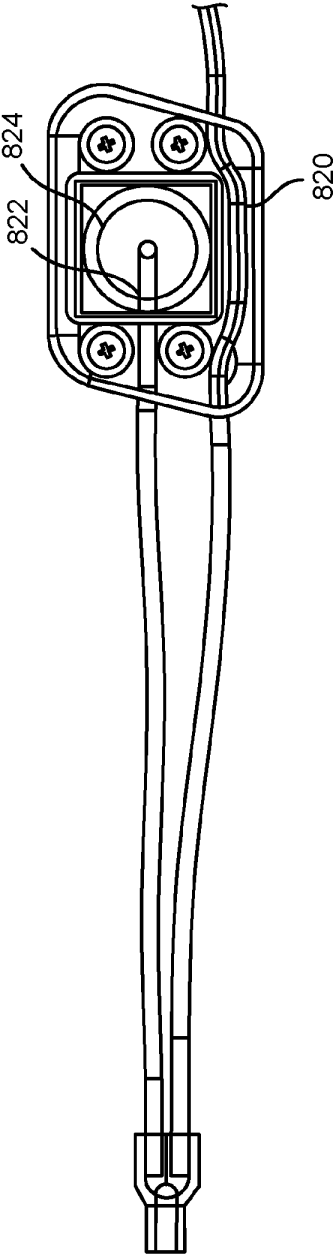


FIG. 8D

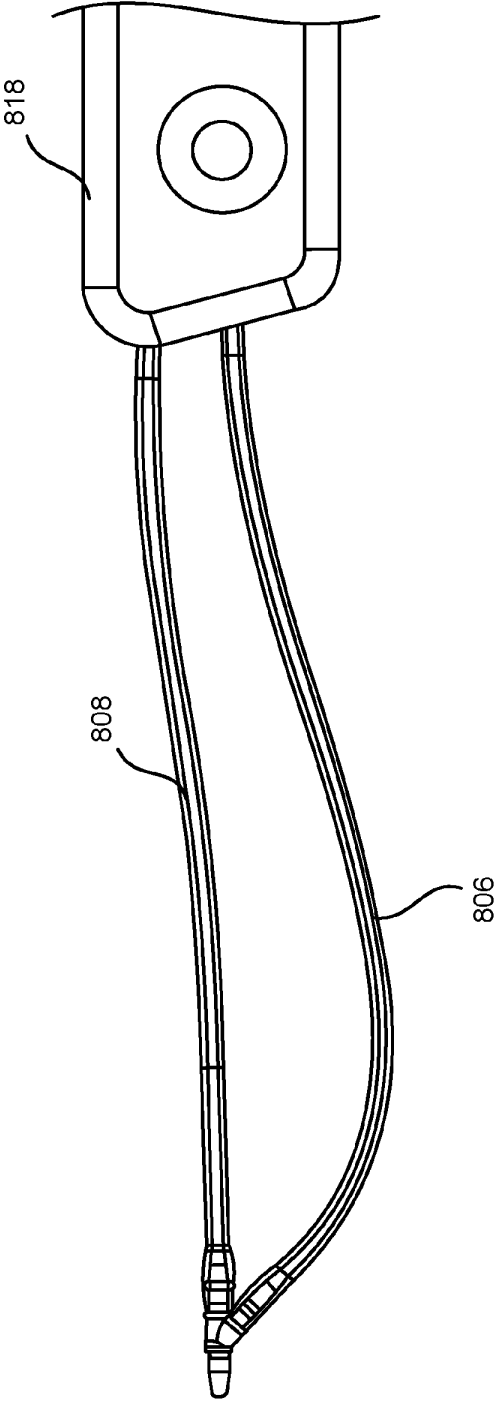


FIG. 8E

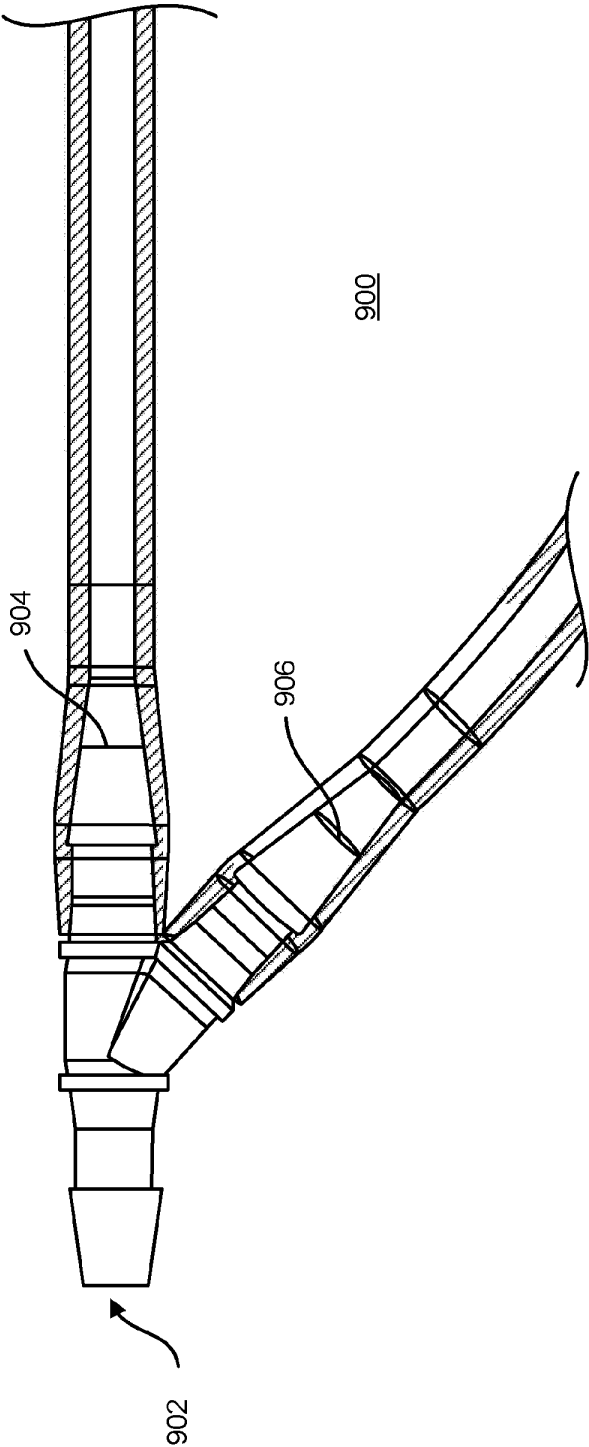


FIG. 9

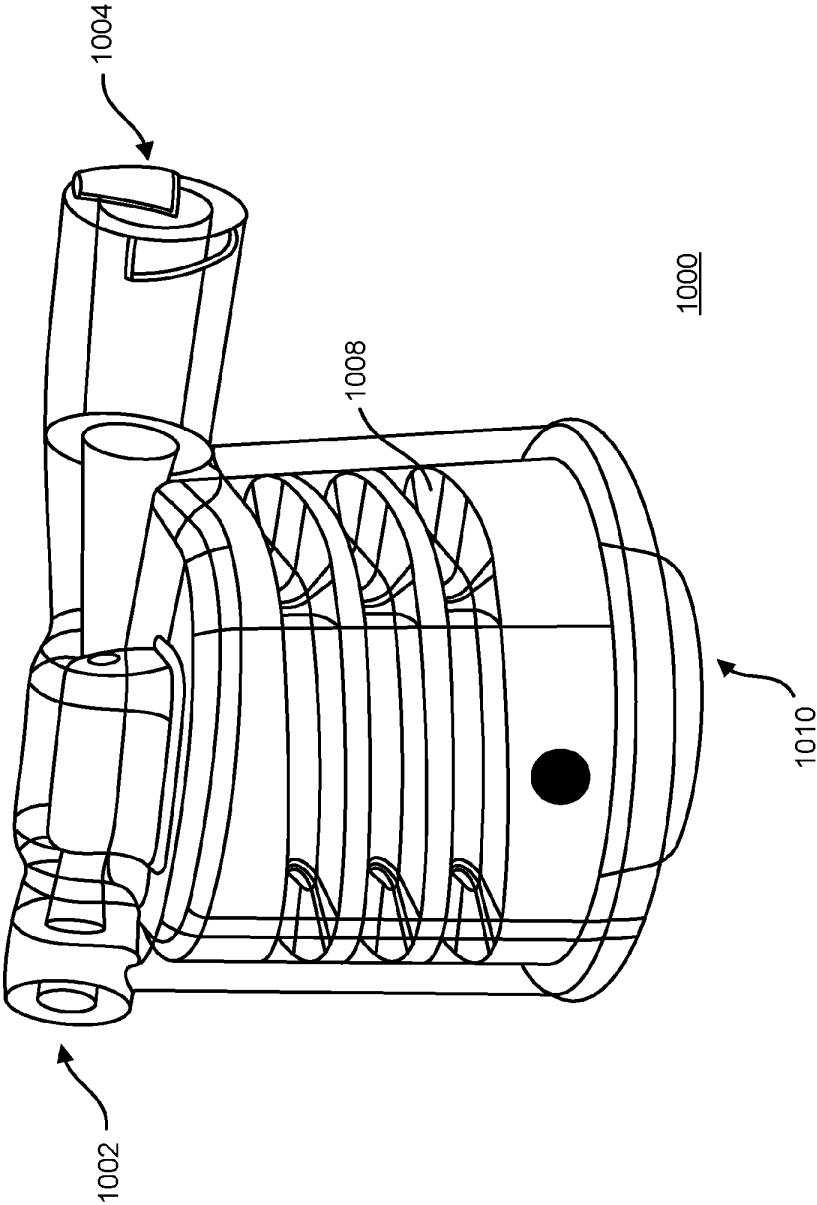


FIG. 10A

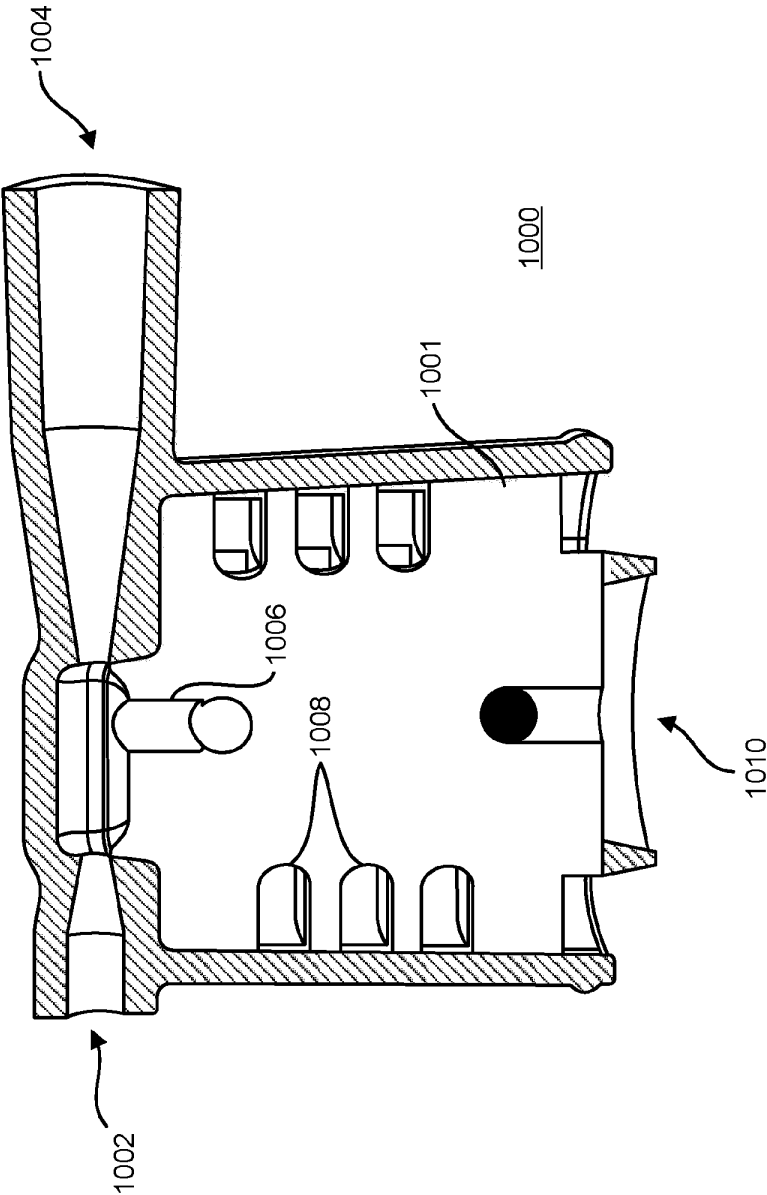


FIG. 10B

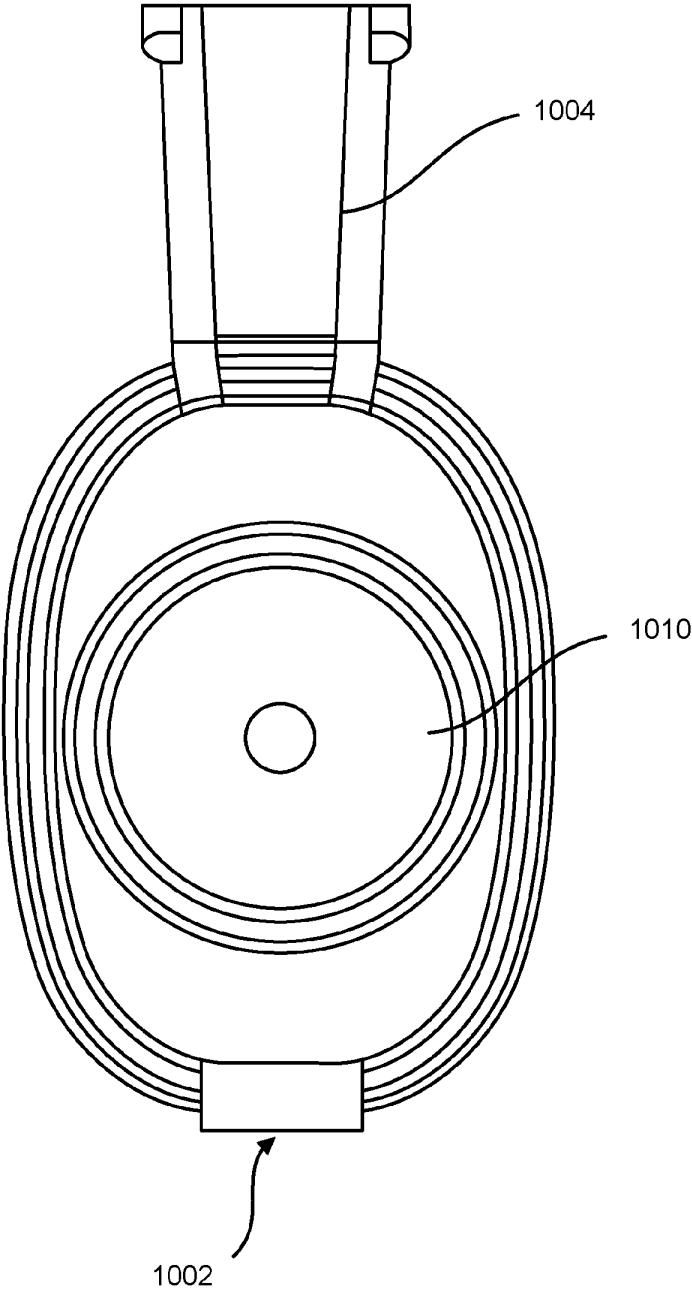


FIG. 10C

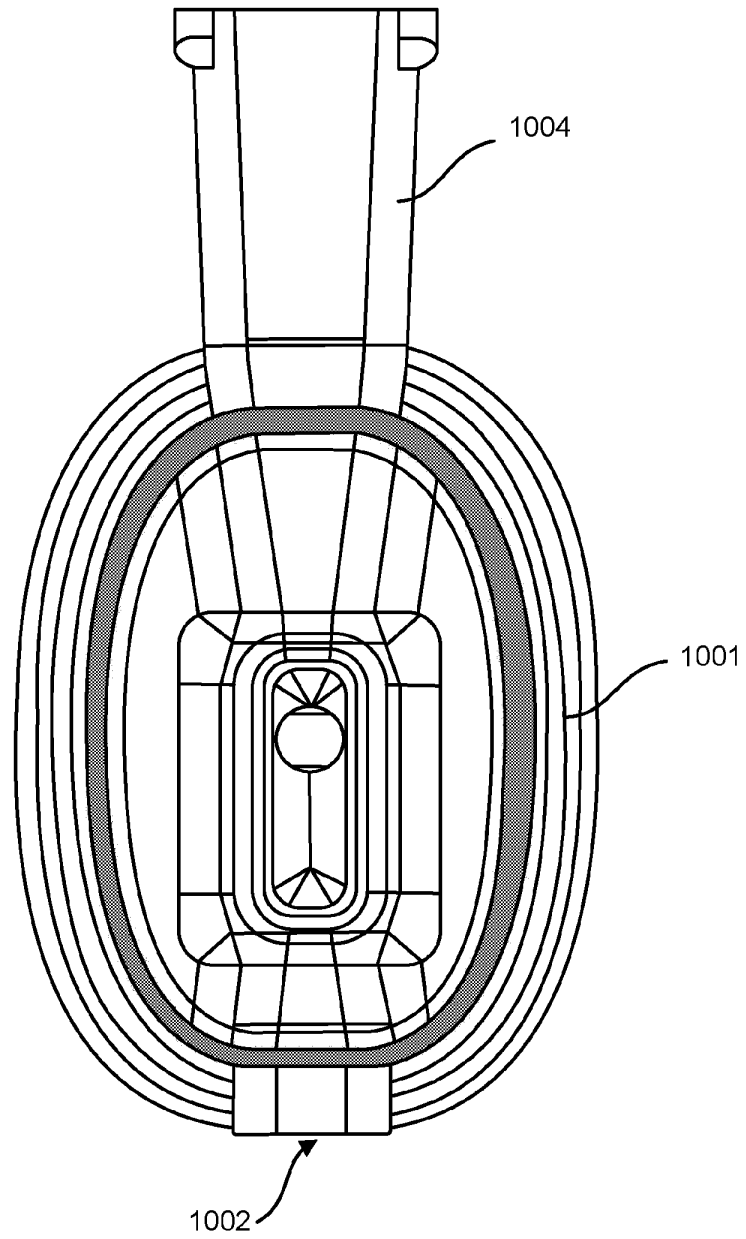


FIG. 10D

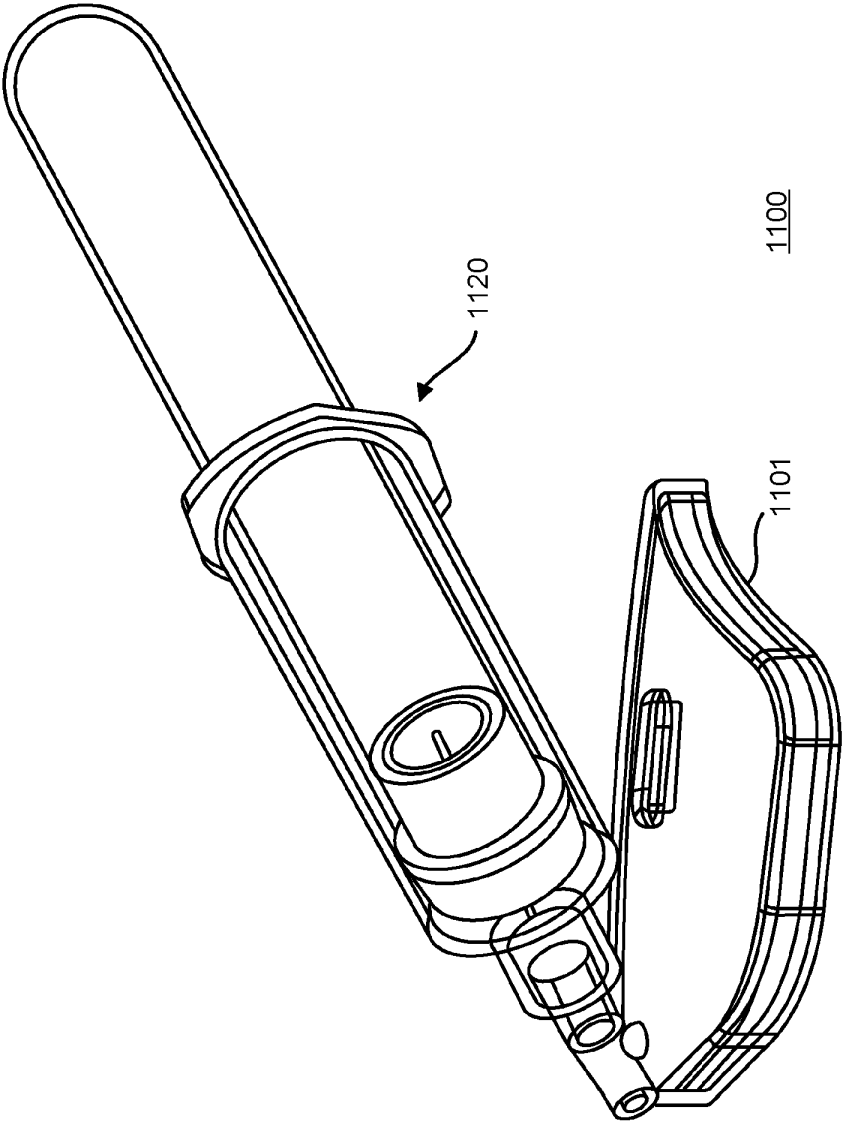


FIG. 11A

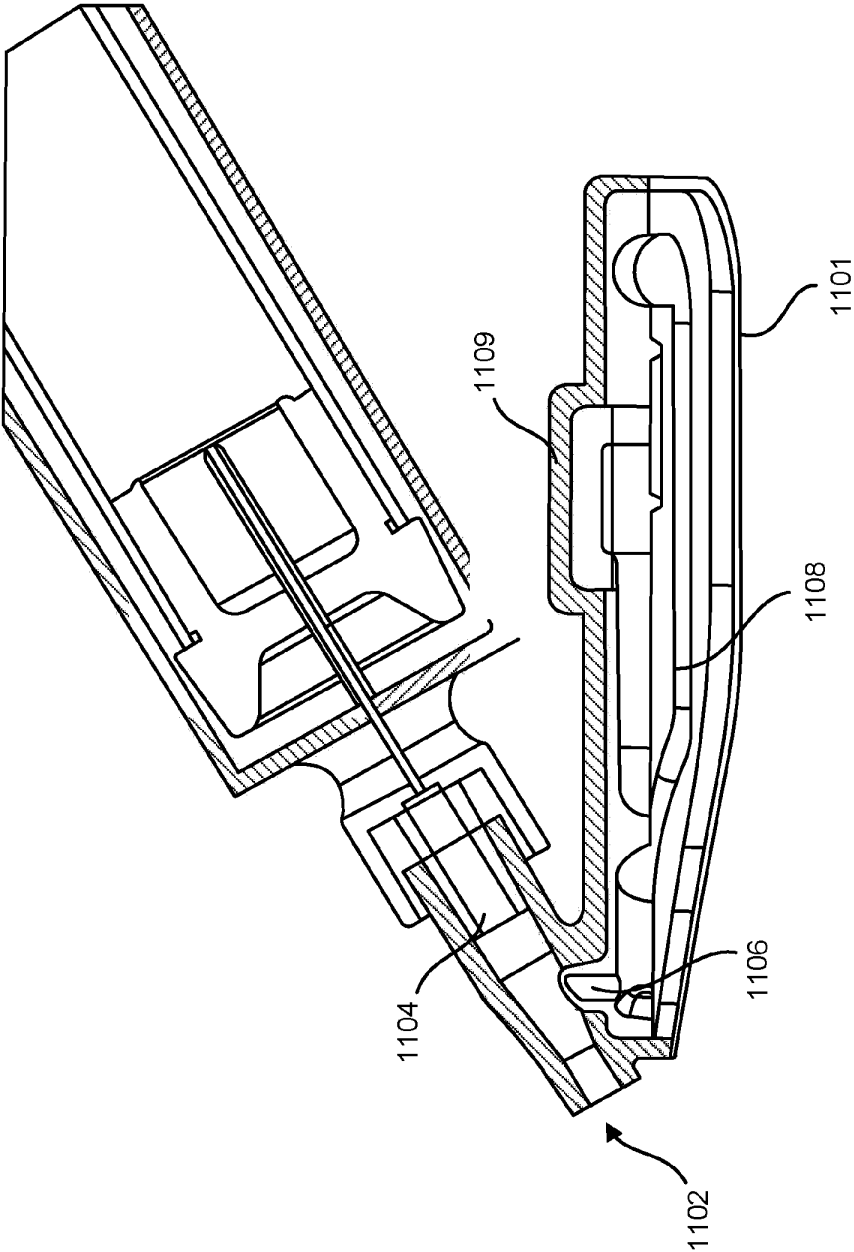


FIG. 11B

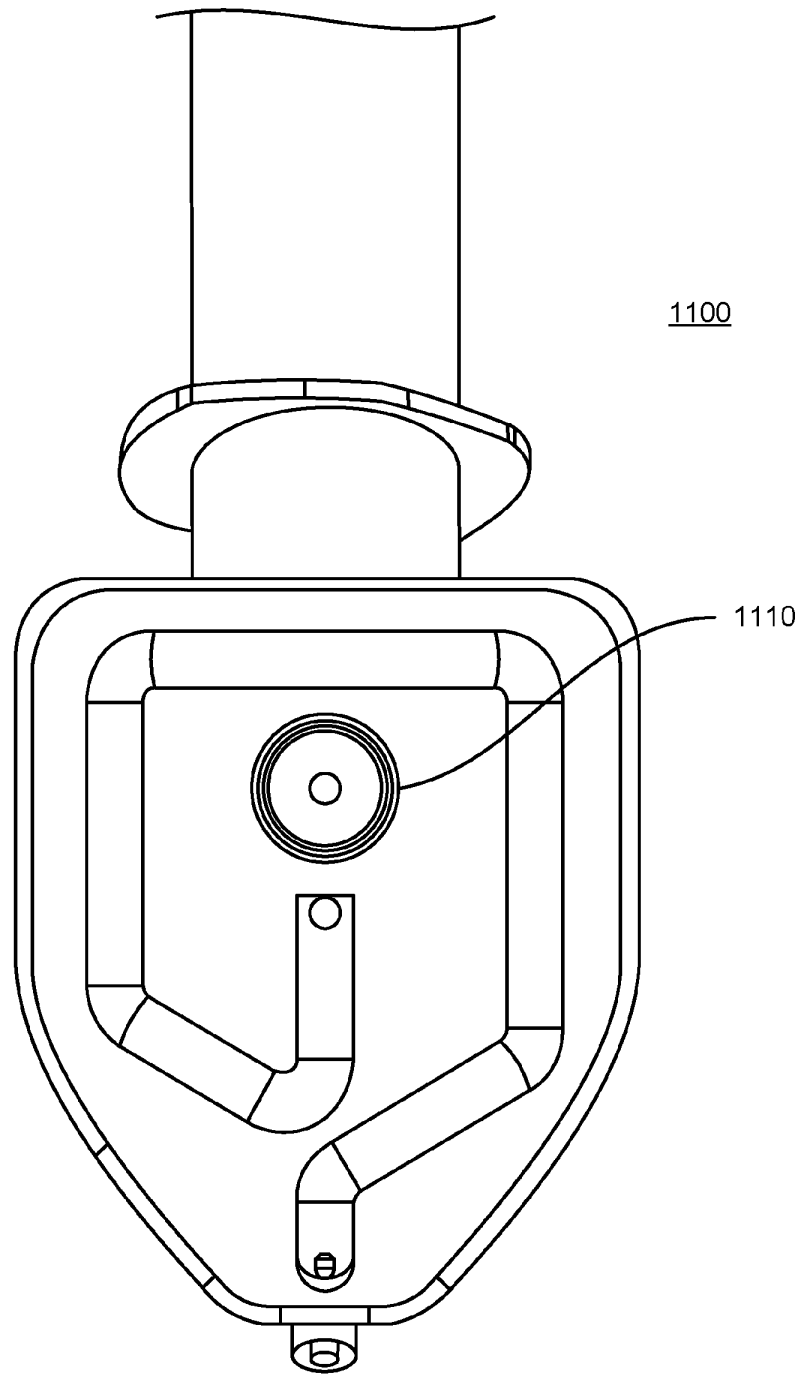


FIG. 11C

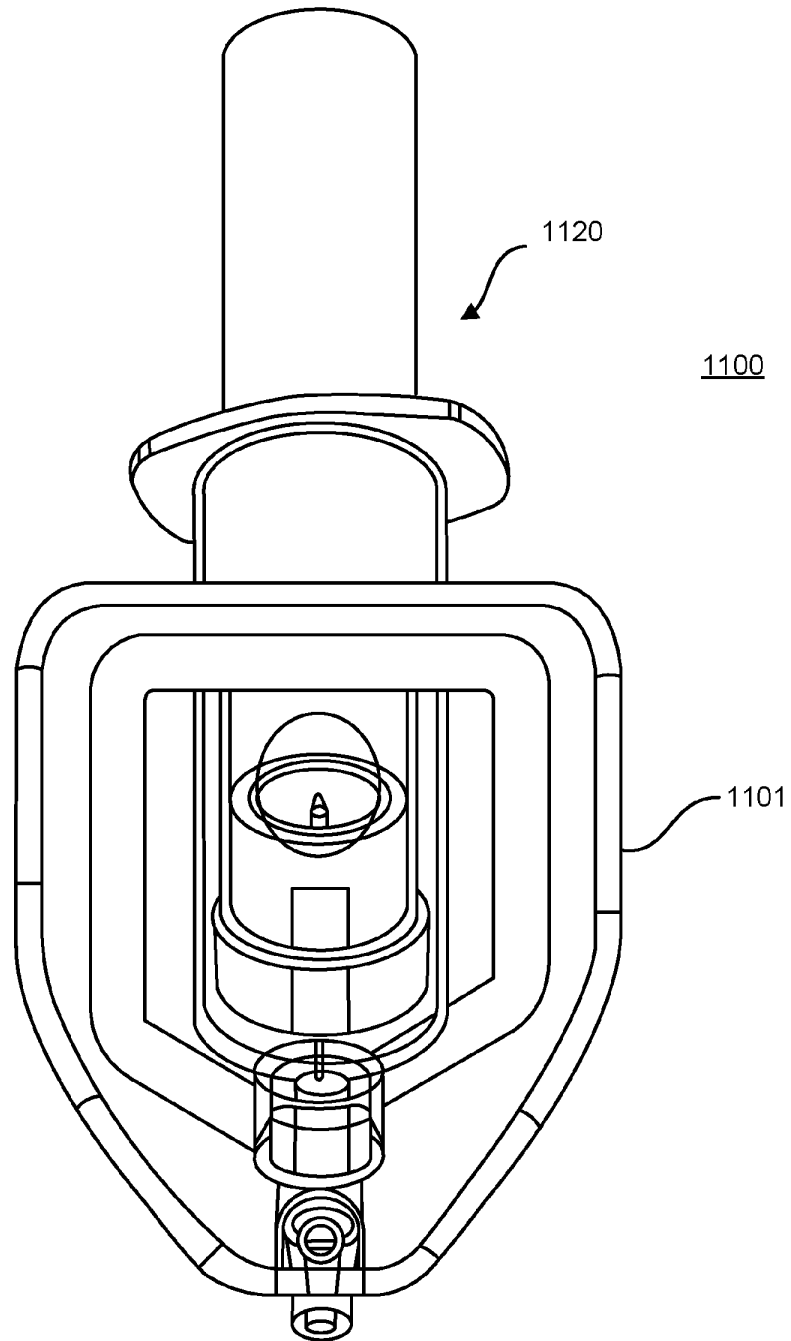


FIG. 11D

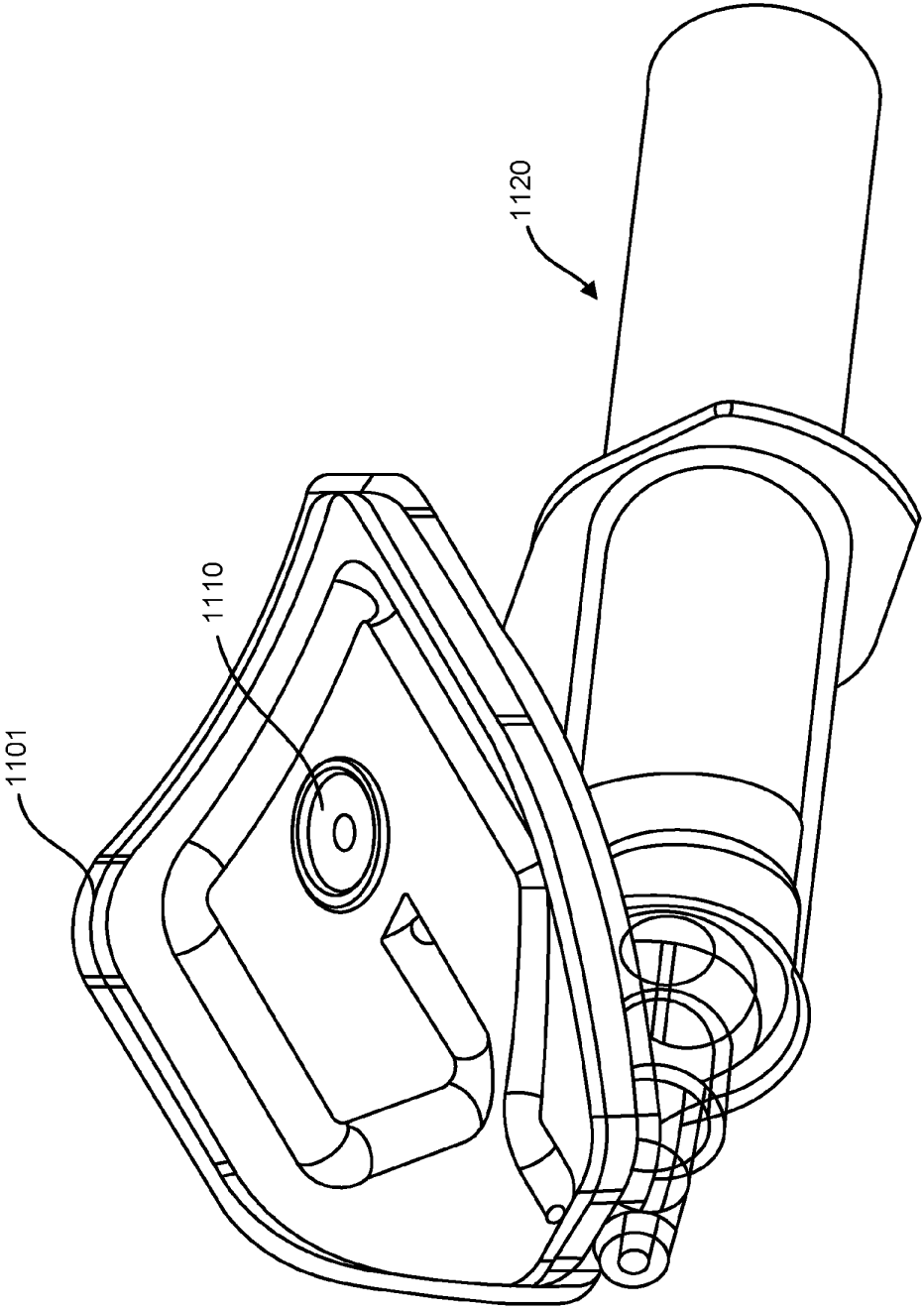


FIG. 11E

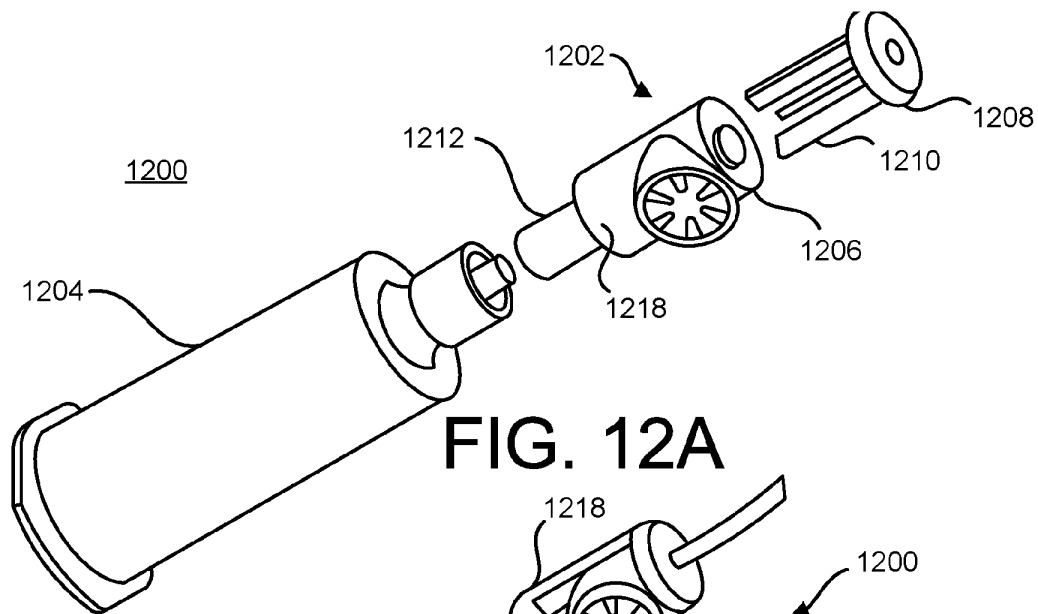


FIG. 12A

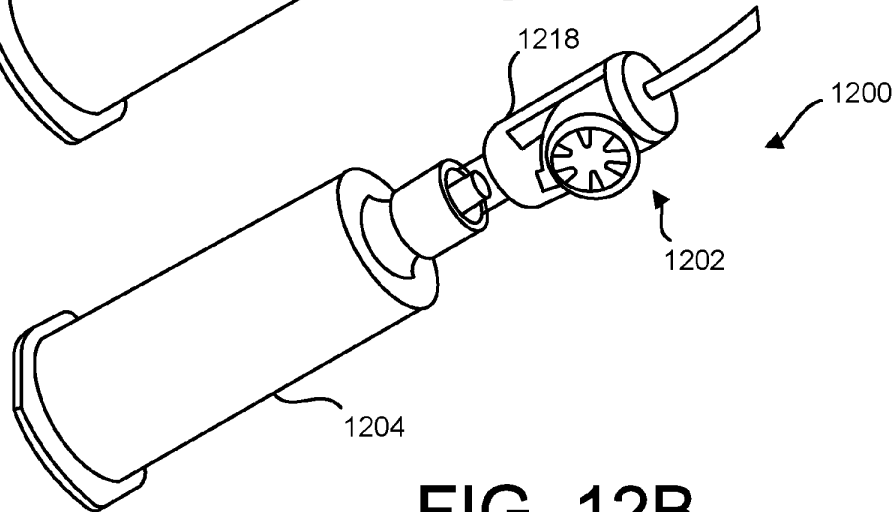


FIG. 12B

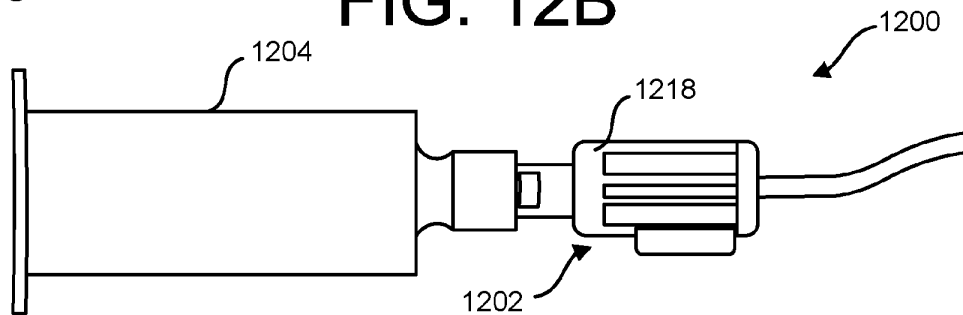


FIG. 12C

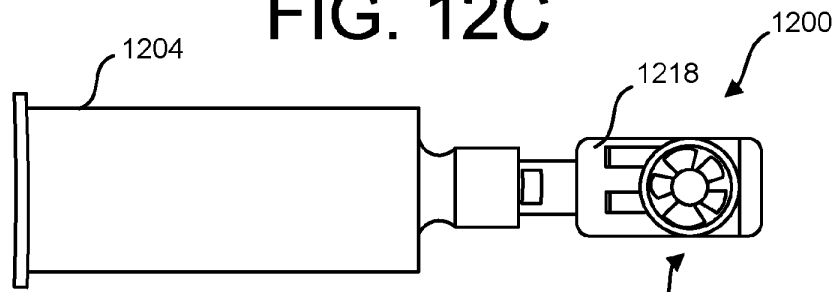


FIG. 12D

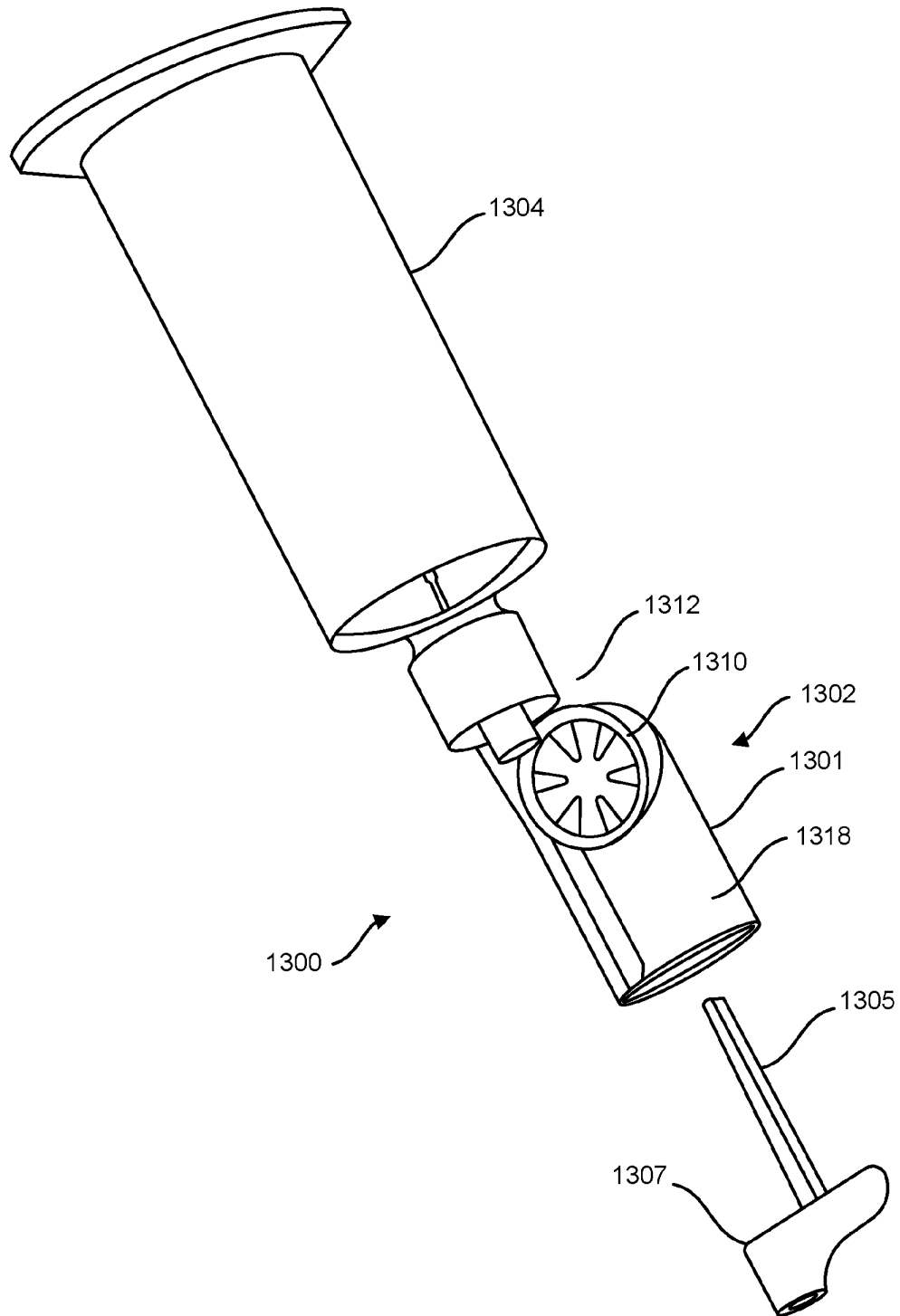


FIG. 13A

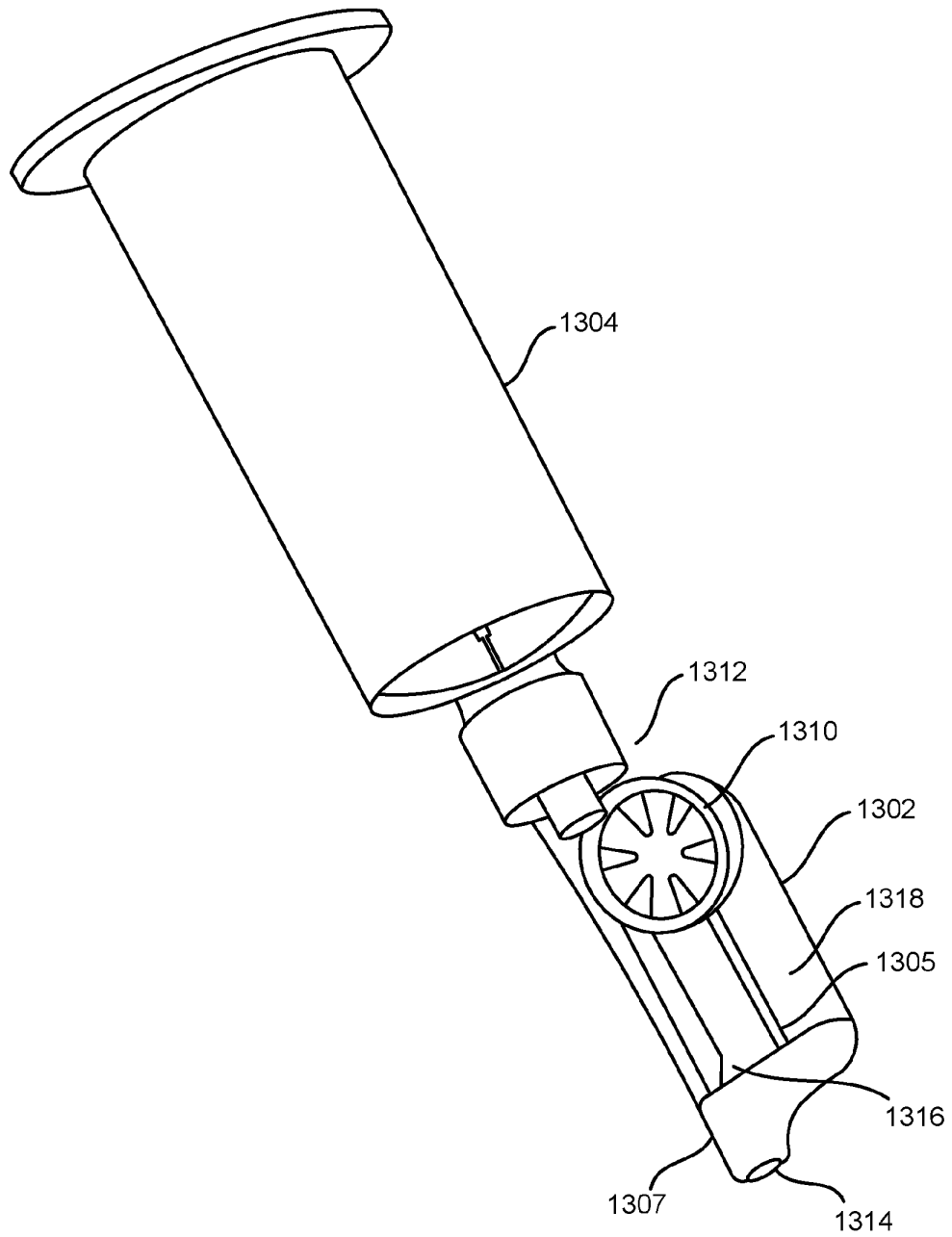


FIG. 13B

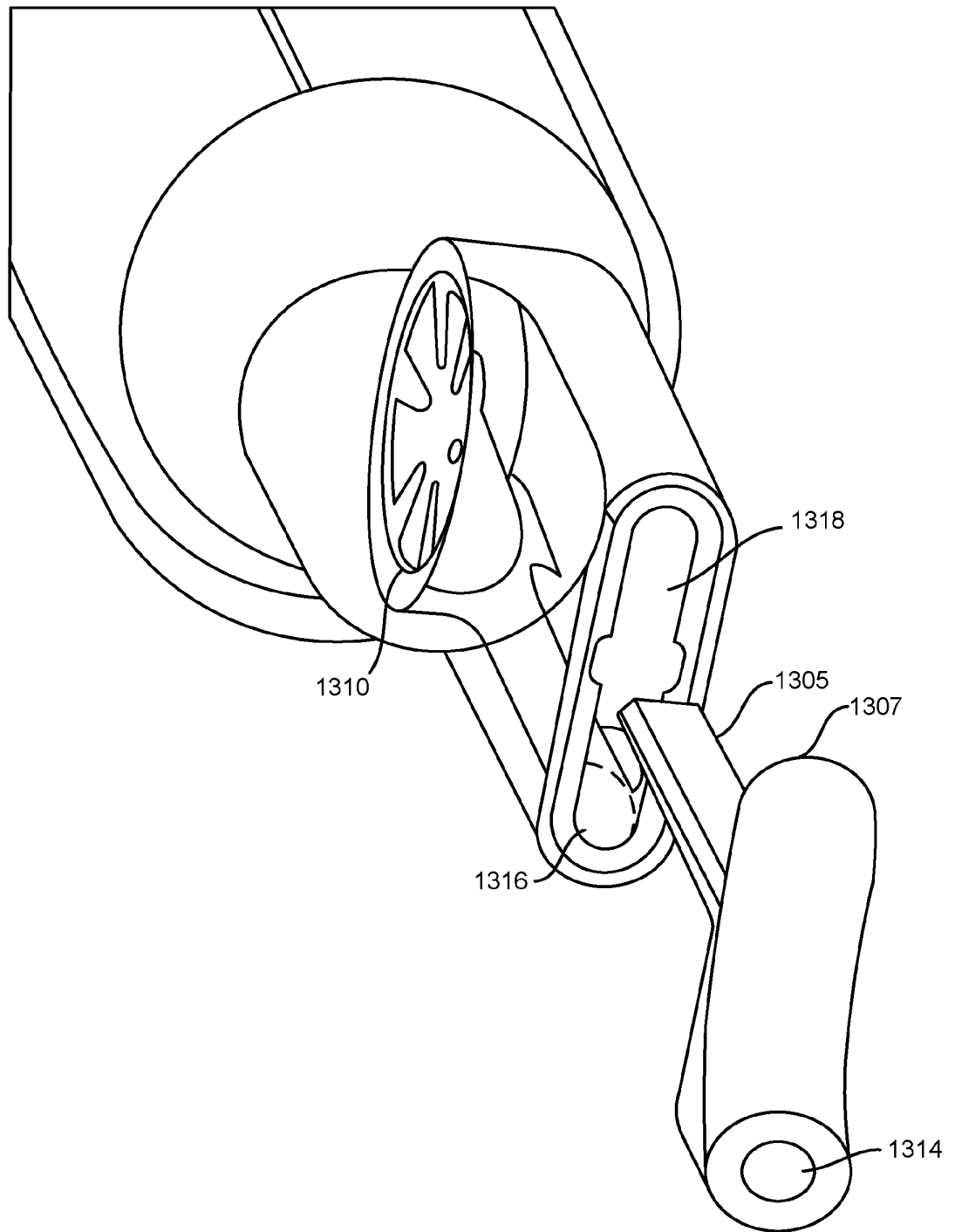


FIG. 13C

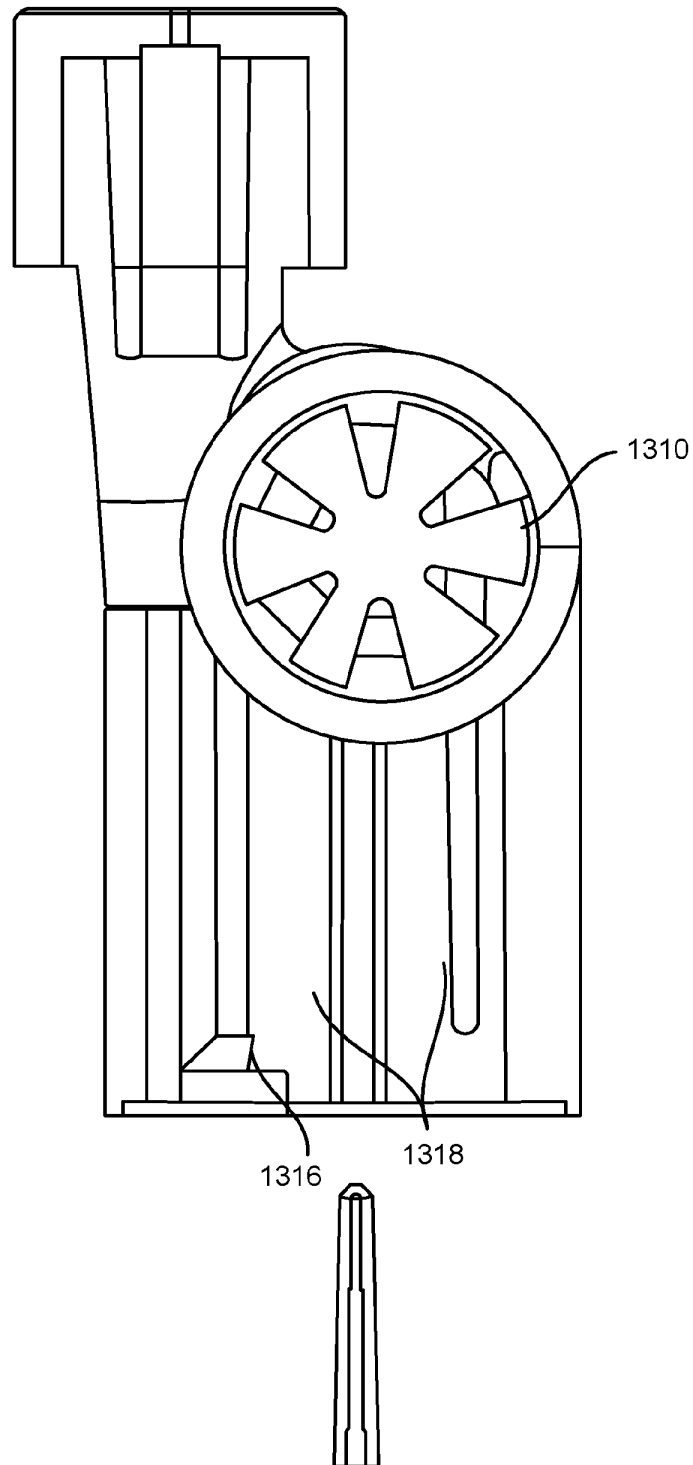


FIG. 13D

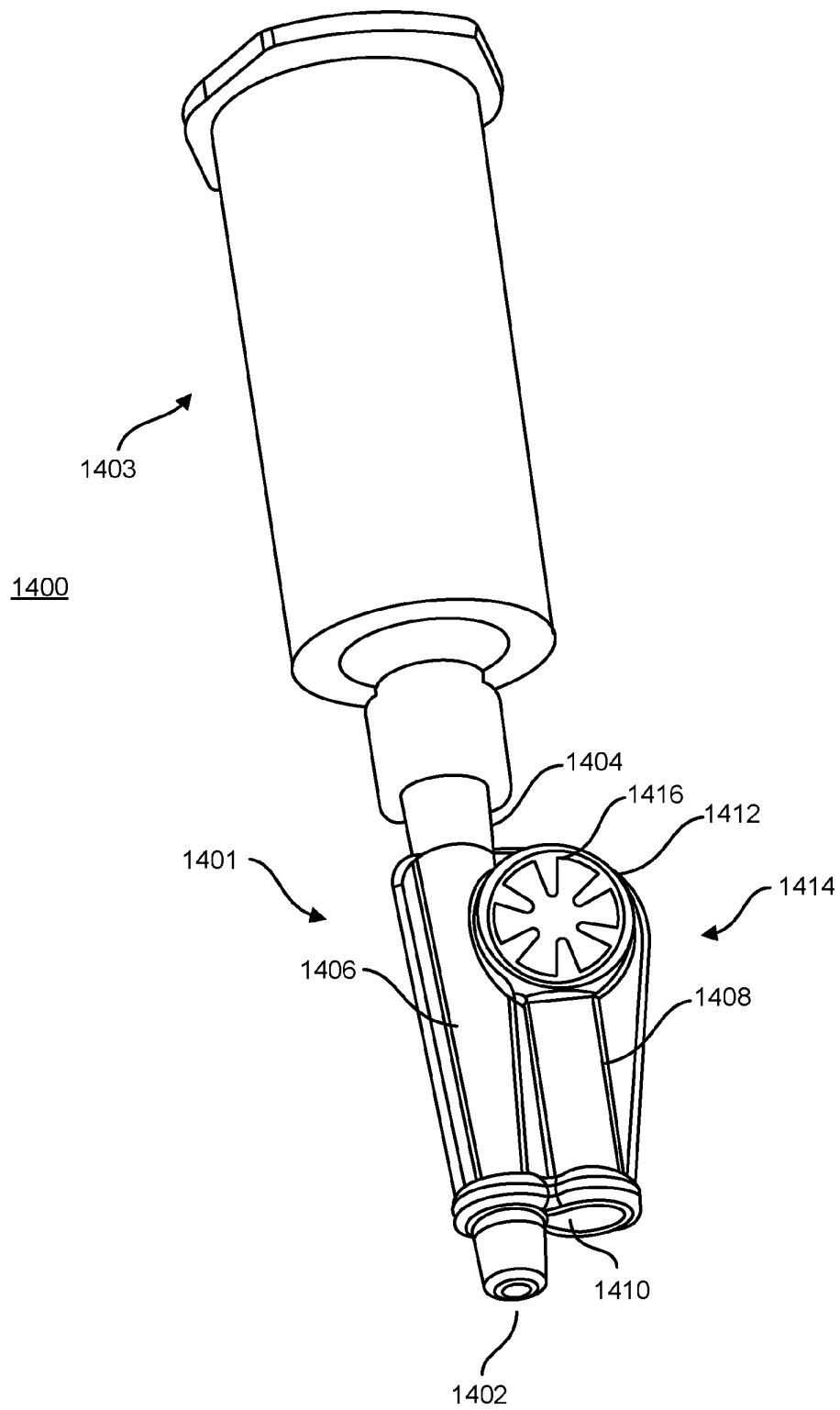


FIG. 14A

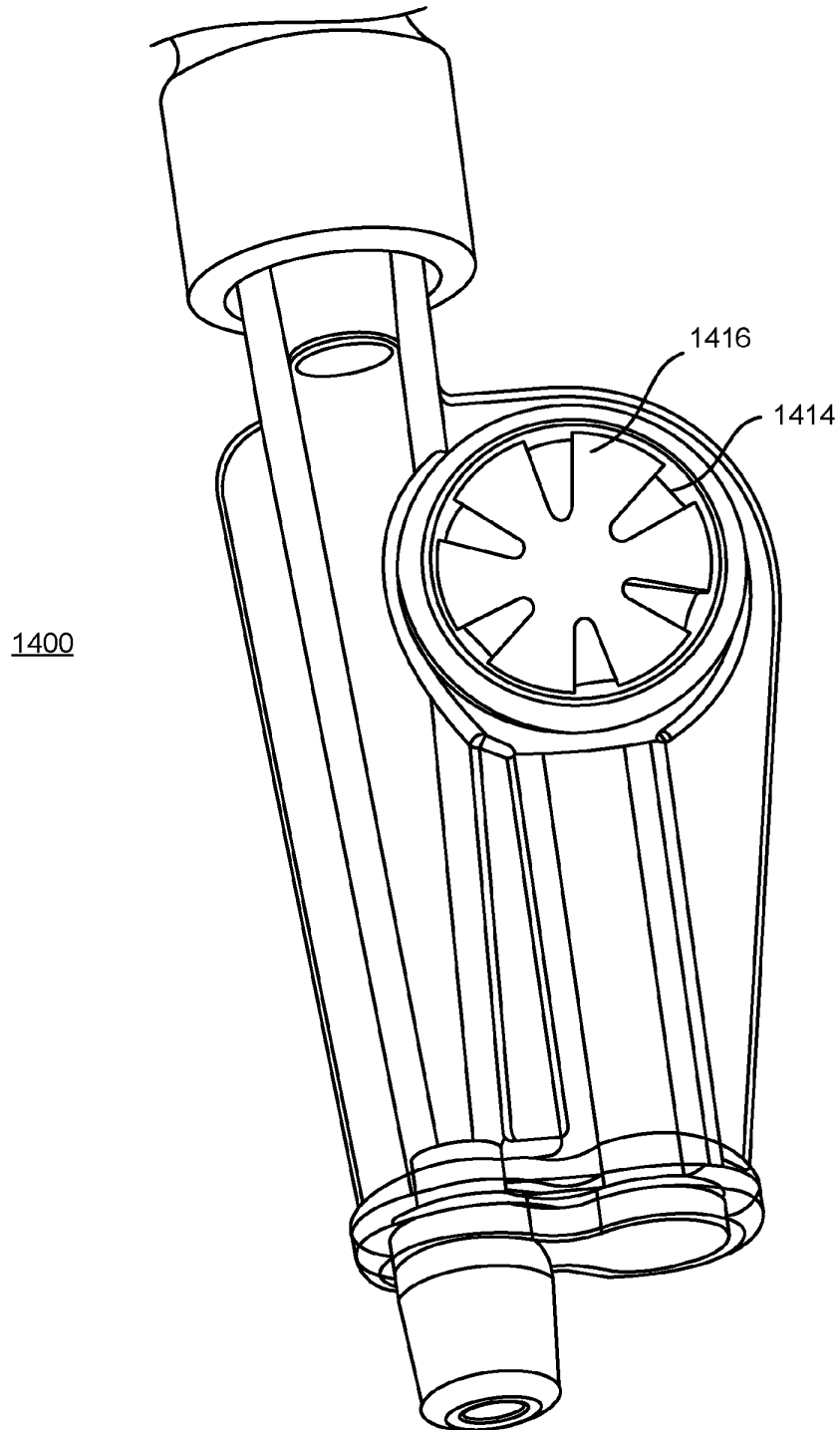


FIG. 14B

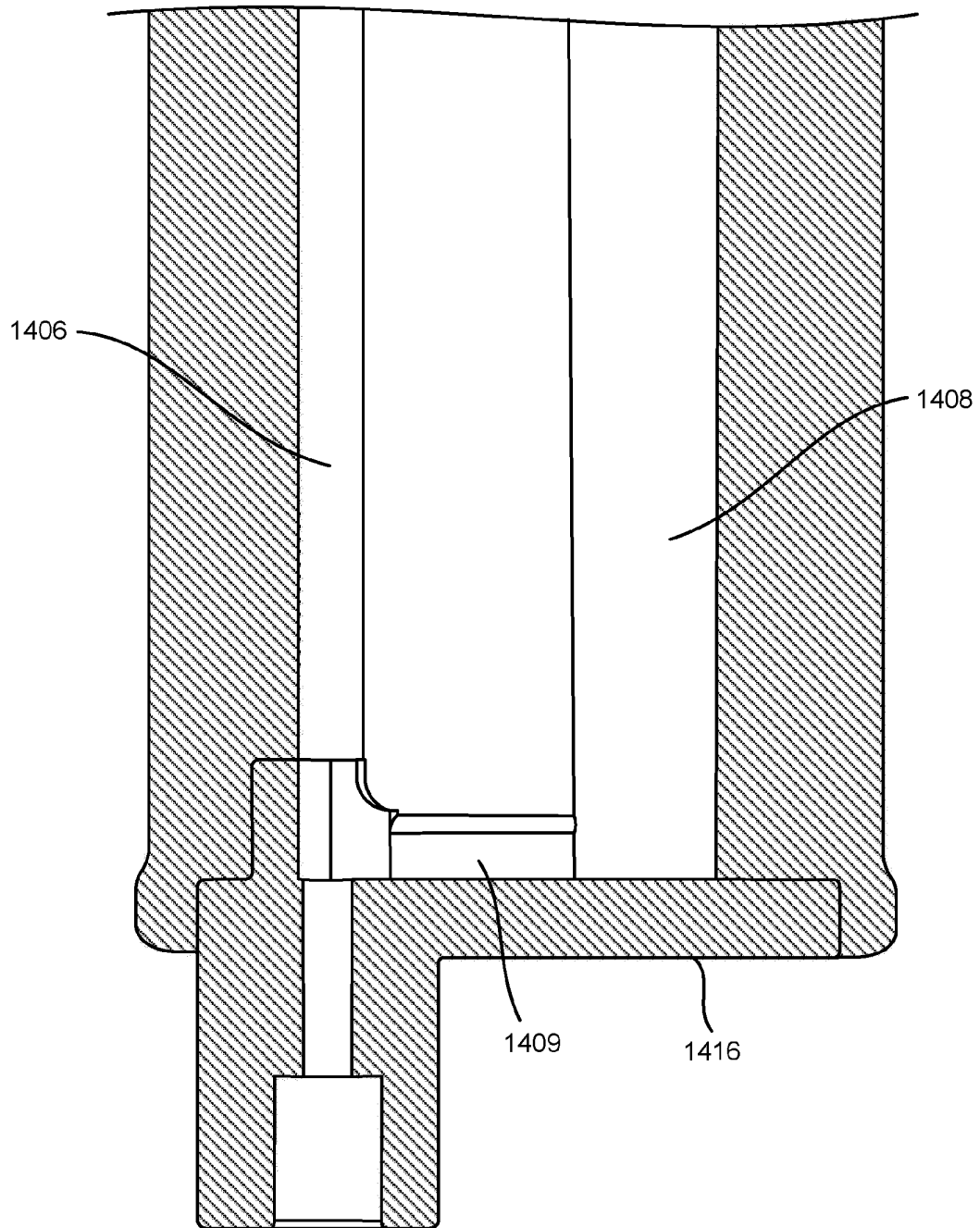


FIG. 14C

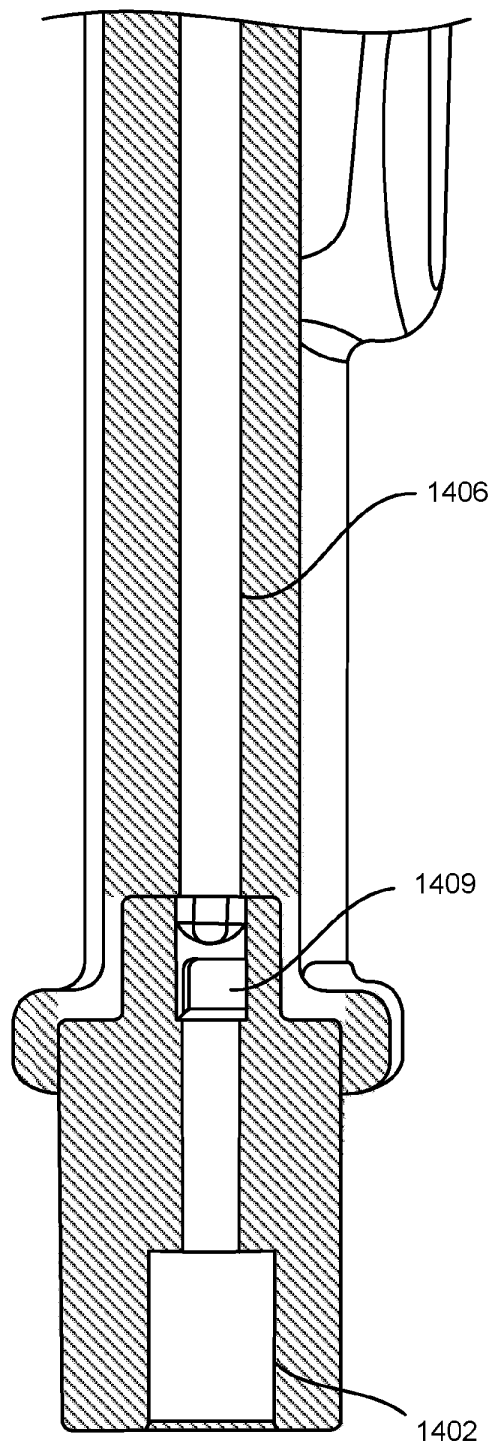


FIG. 14D

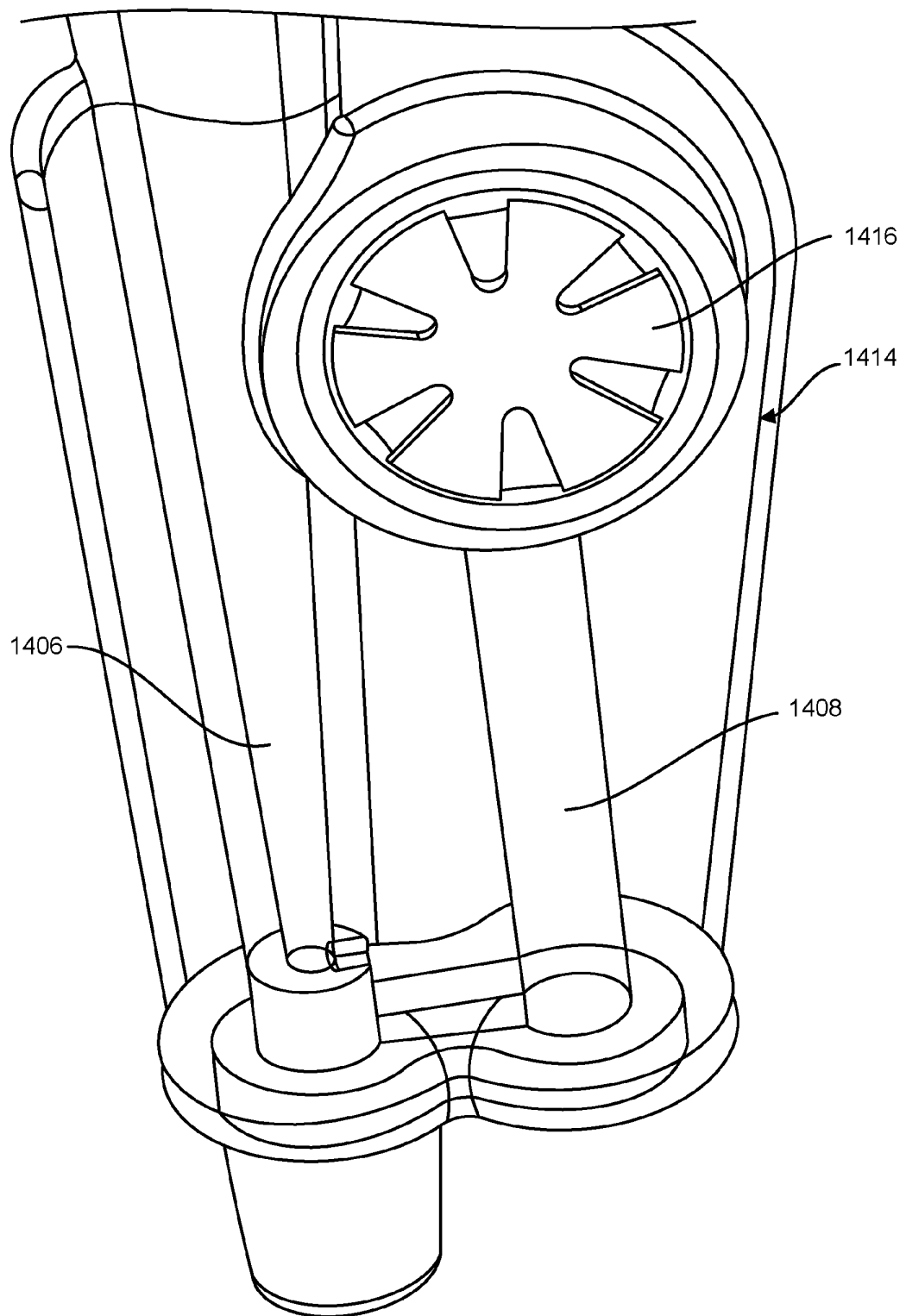


FIG. 14E

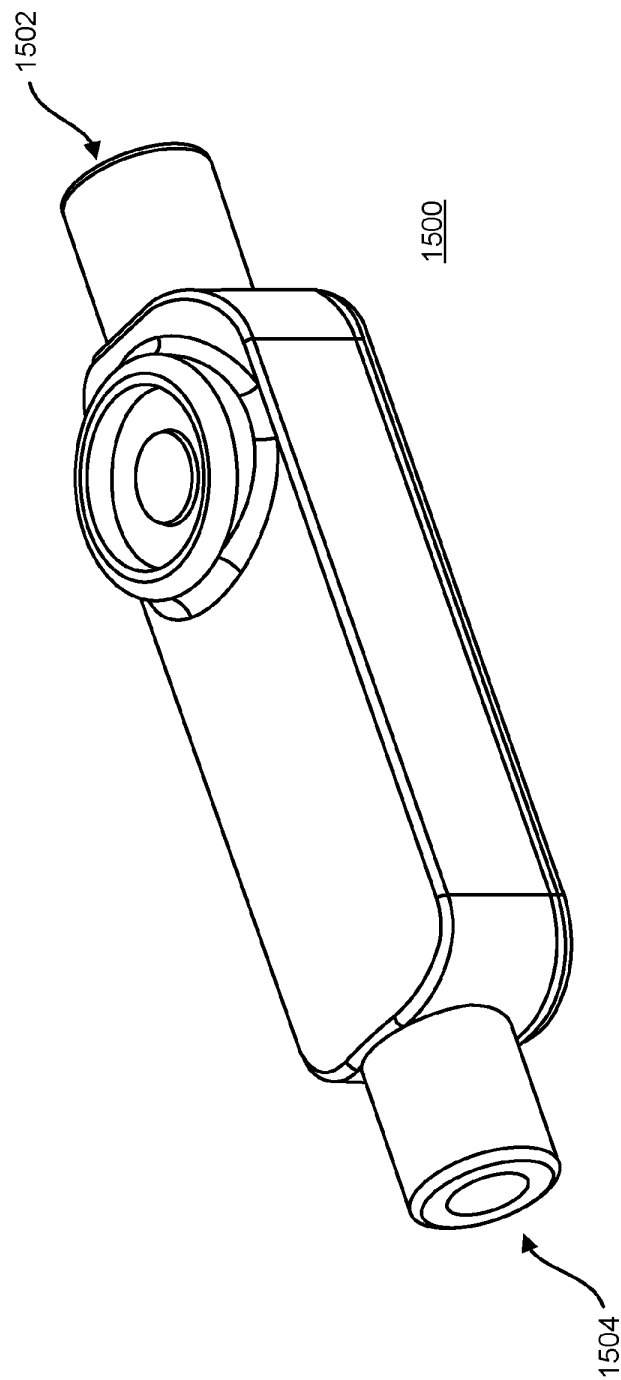


FIG. 15A

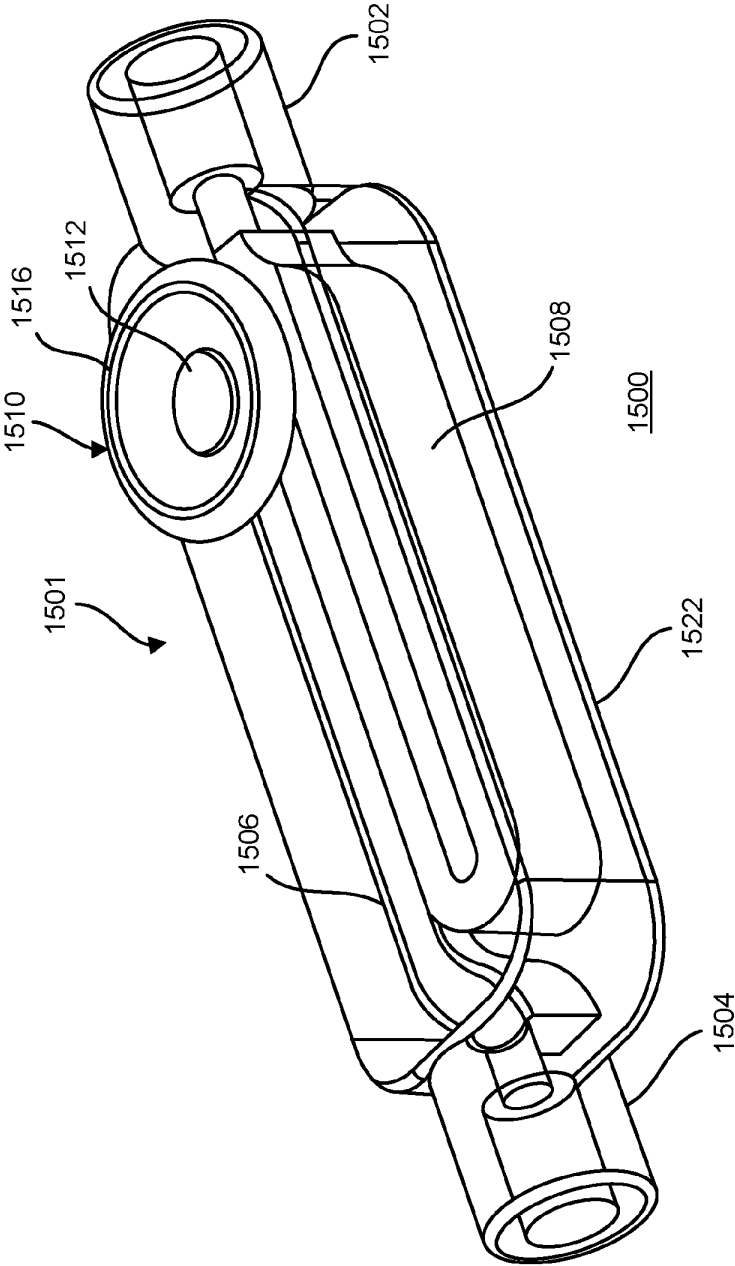


FIG. 15B

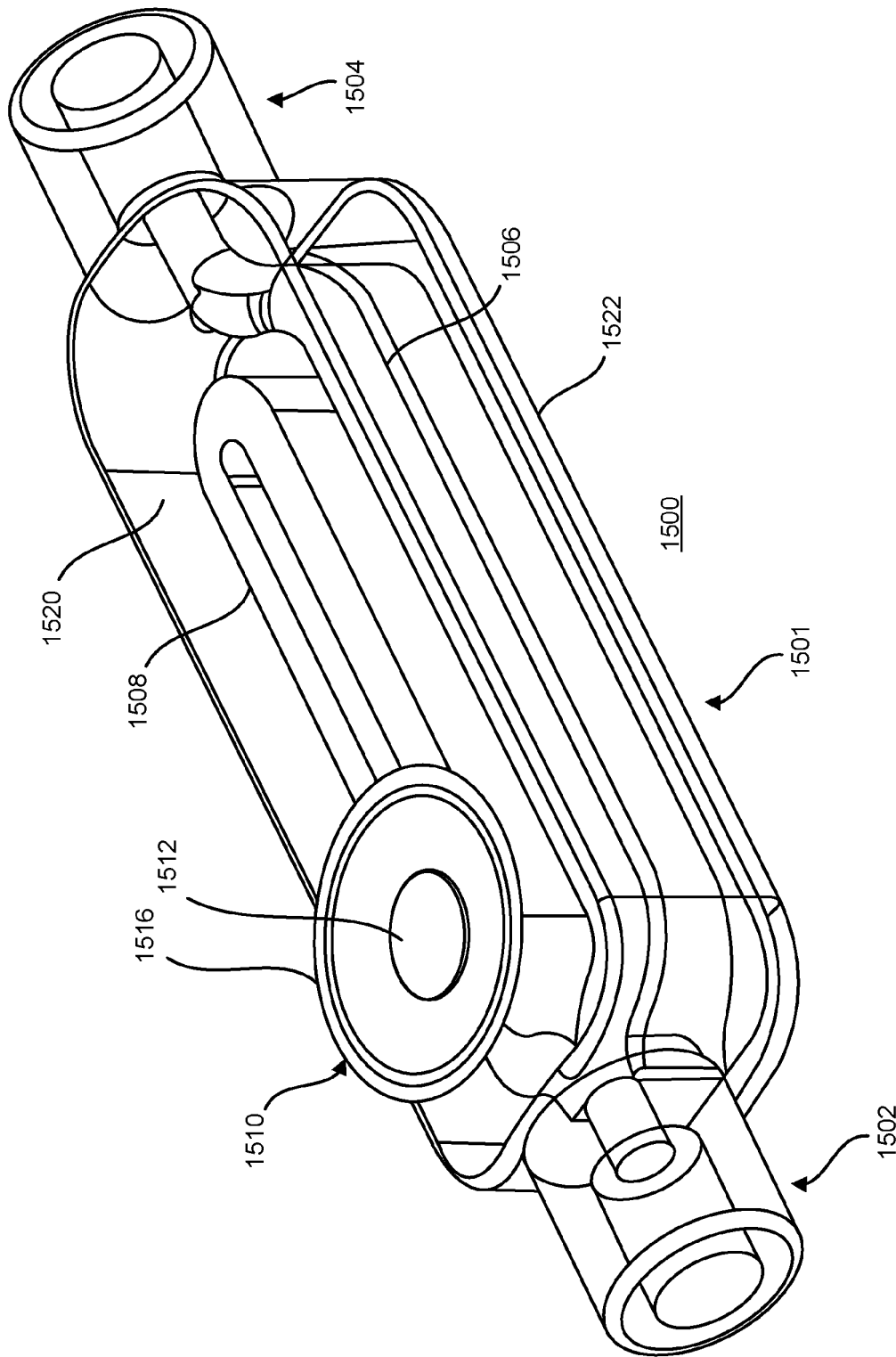


FIG. 15C

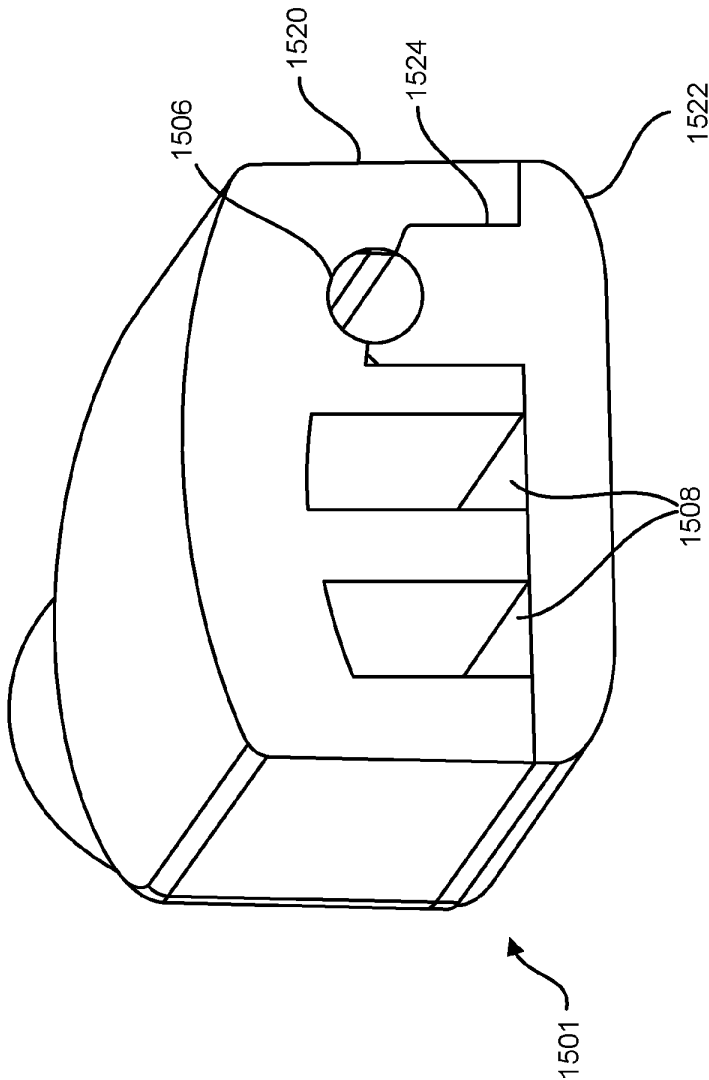


FIG. 15D

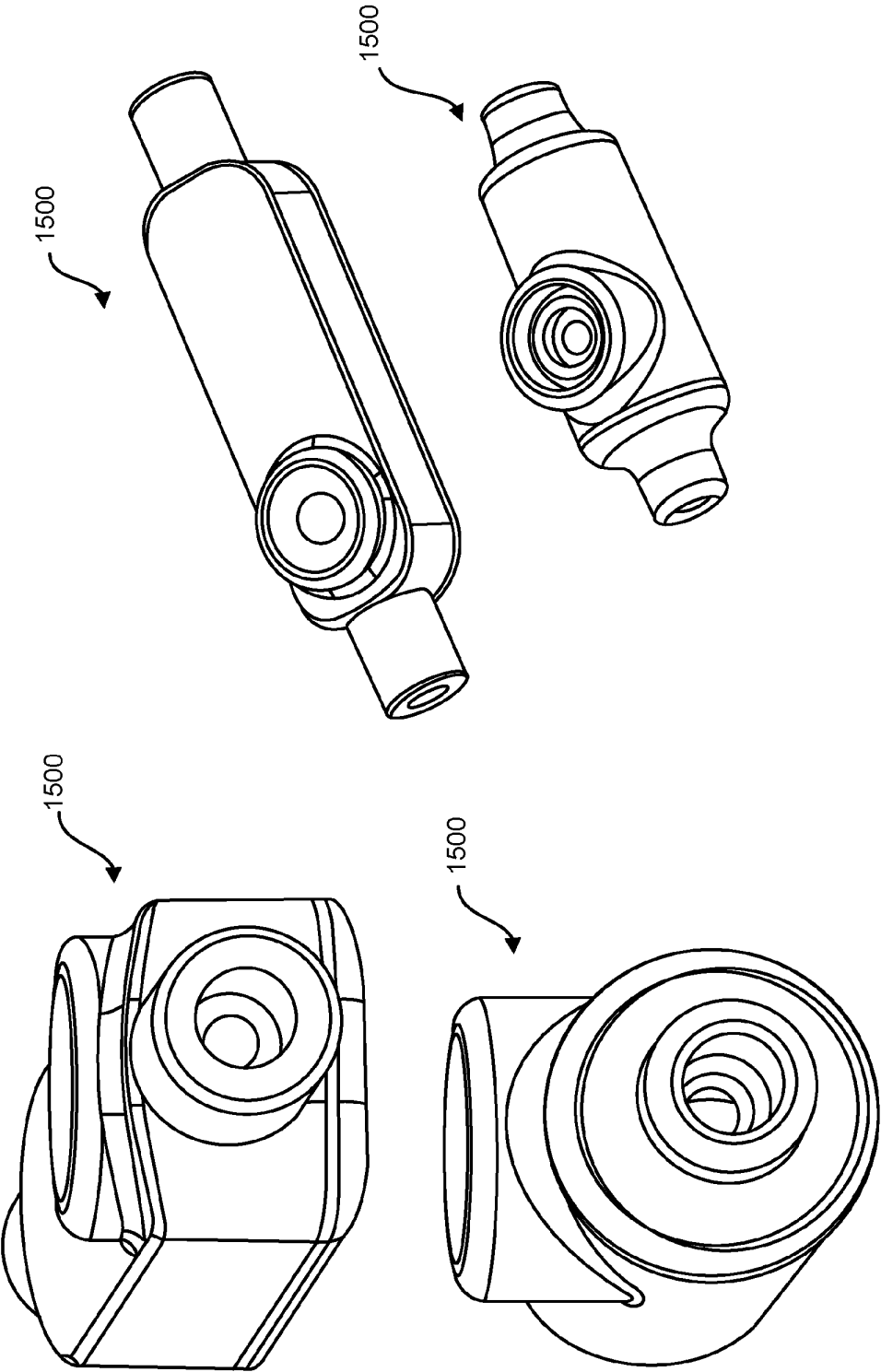


FIG. 15F

FIG. 15E

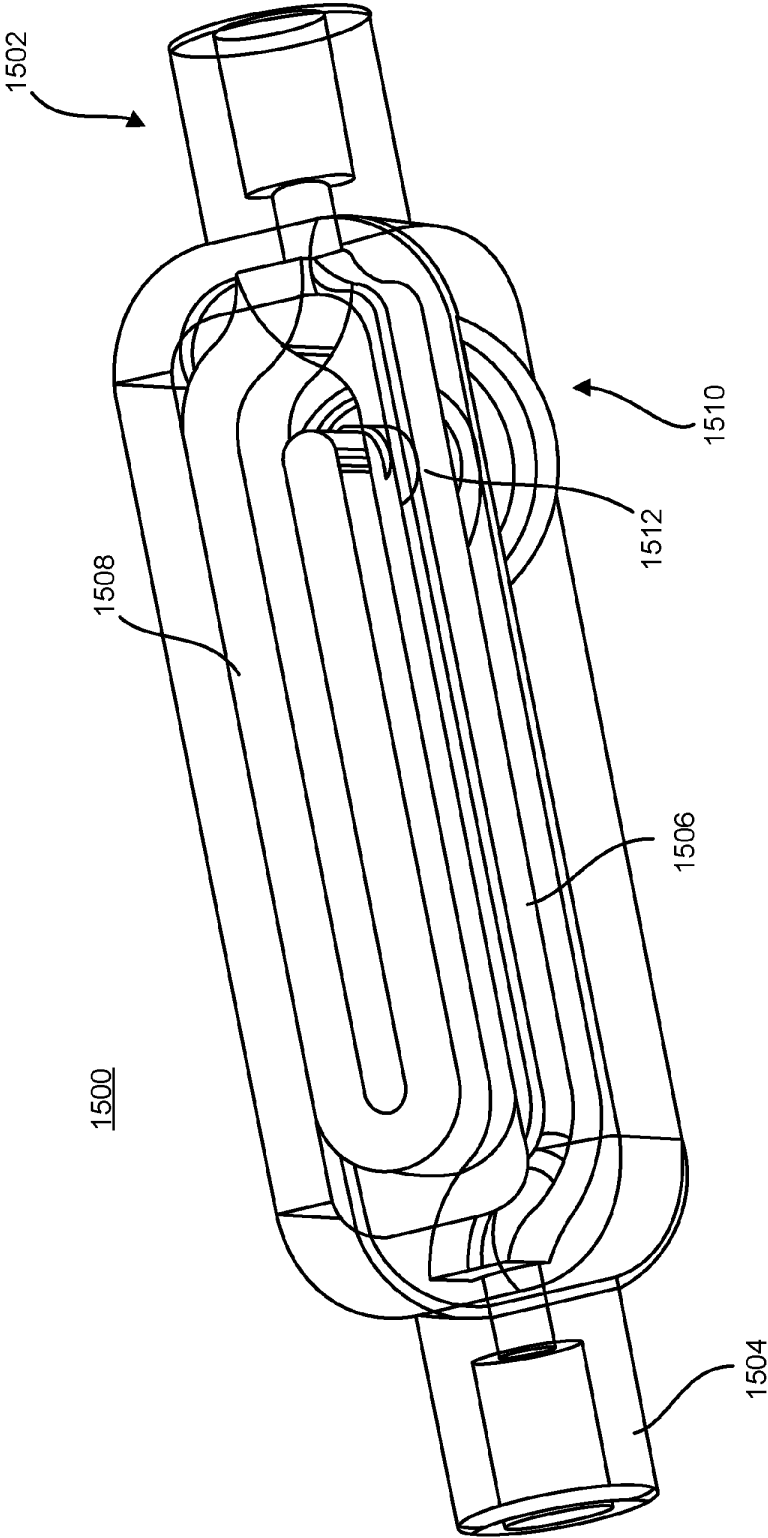


FIG. 15G

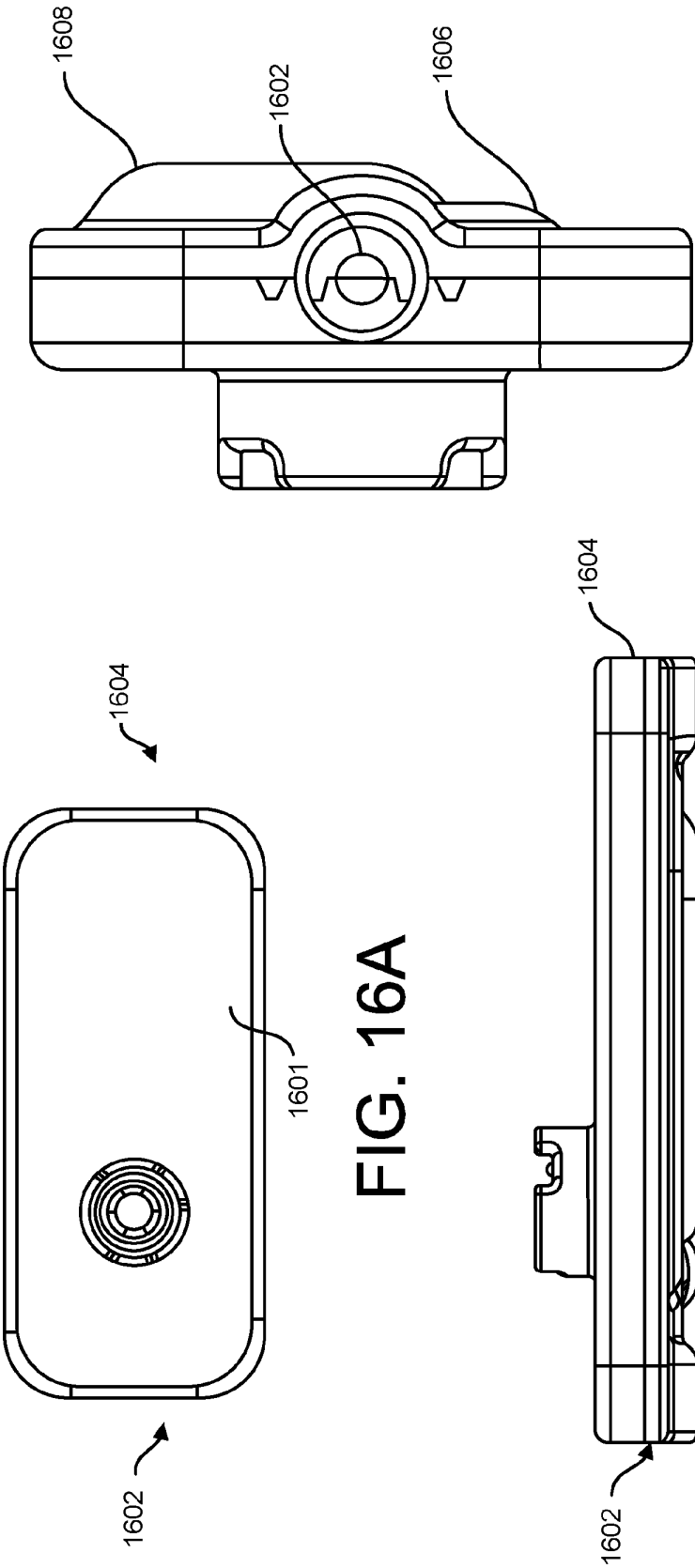


FIG. 16A

FIG. 16B

FIG. 16C

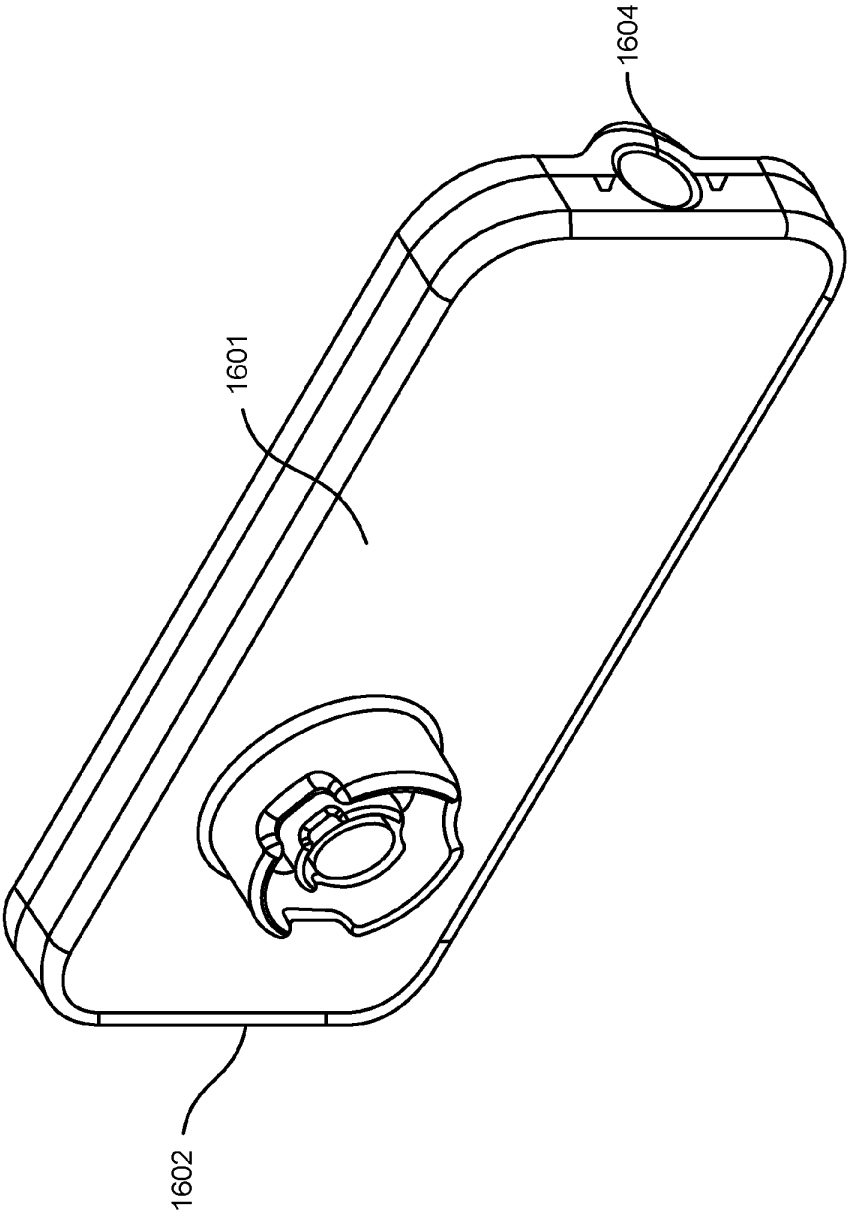


FIG. 16D

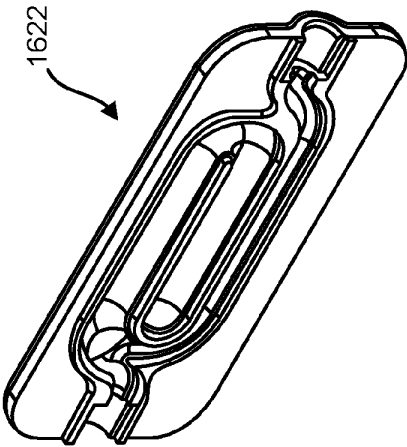


FIG. 17B

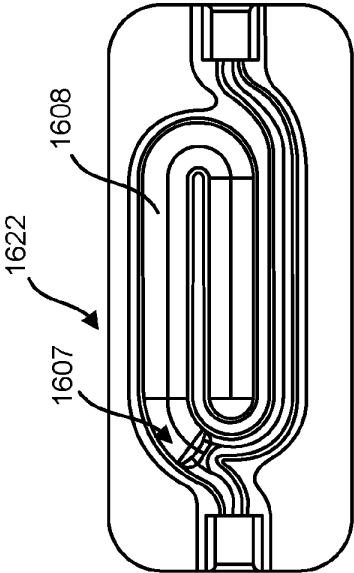


FIG. 17A

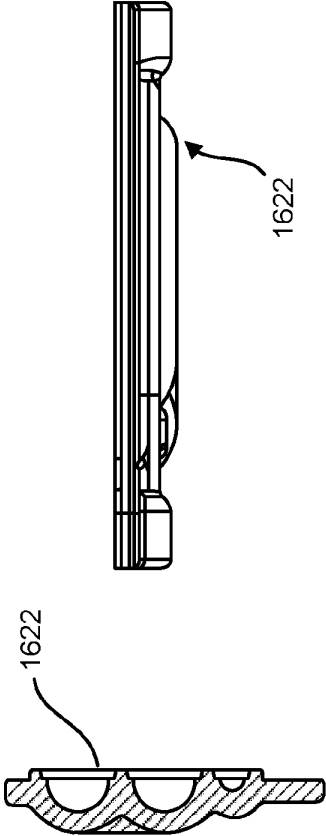


FIG. 17D

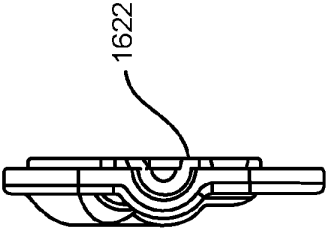


FIG. 17C



FIG. 17E

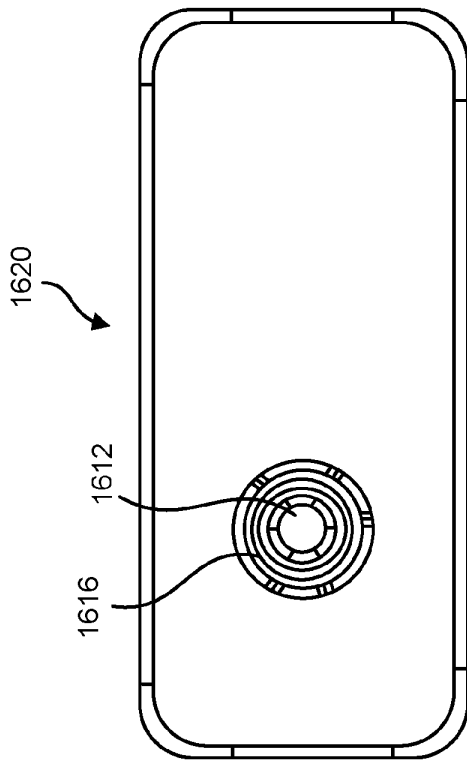


FIG. 18A

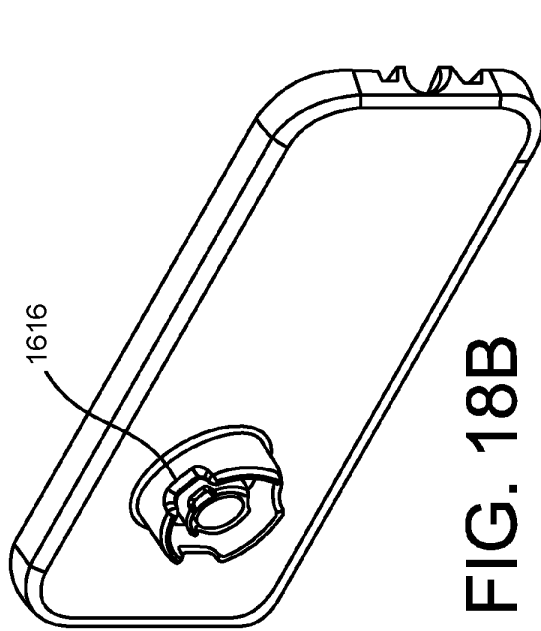


FIG. 18B

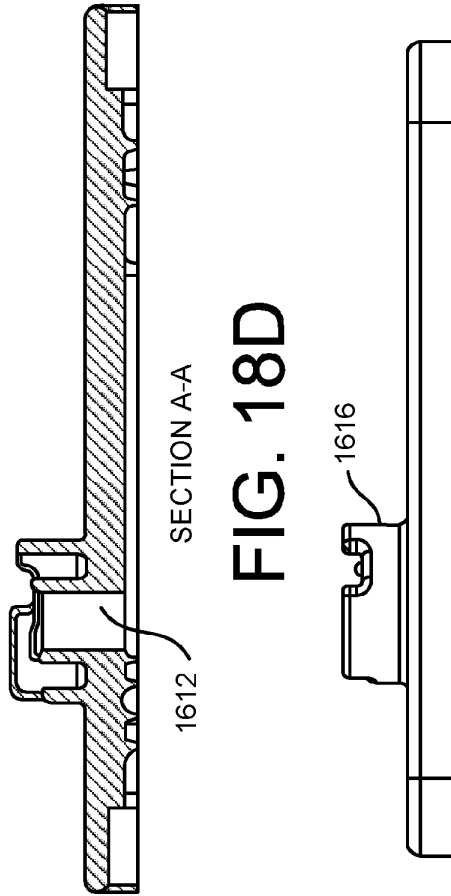


FIG. 18D

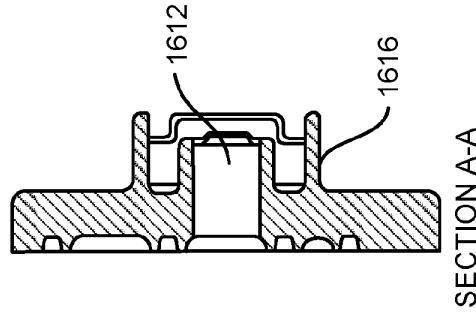


FIG. 18F

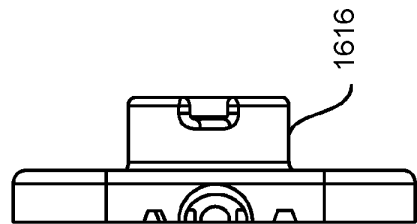


FIG. 18C

FIG. 18E

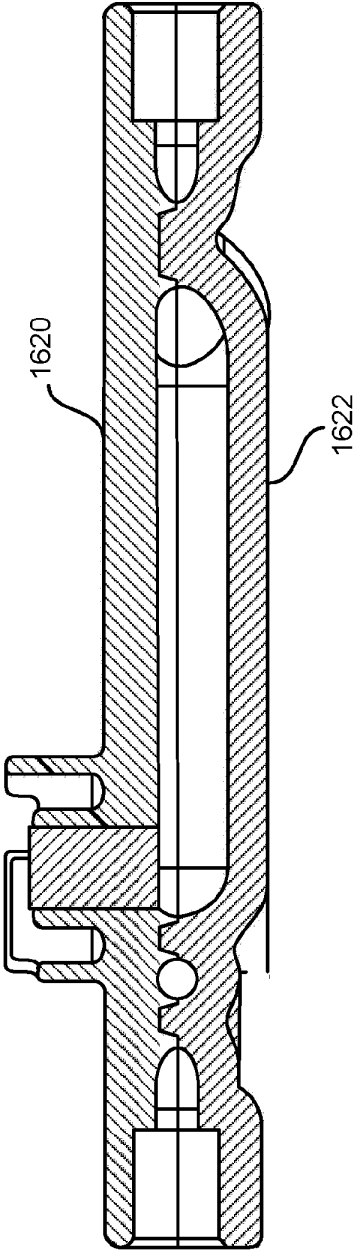


FIG. 19A

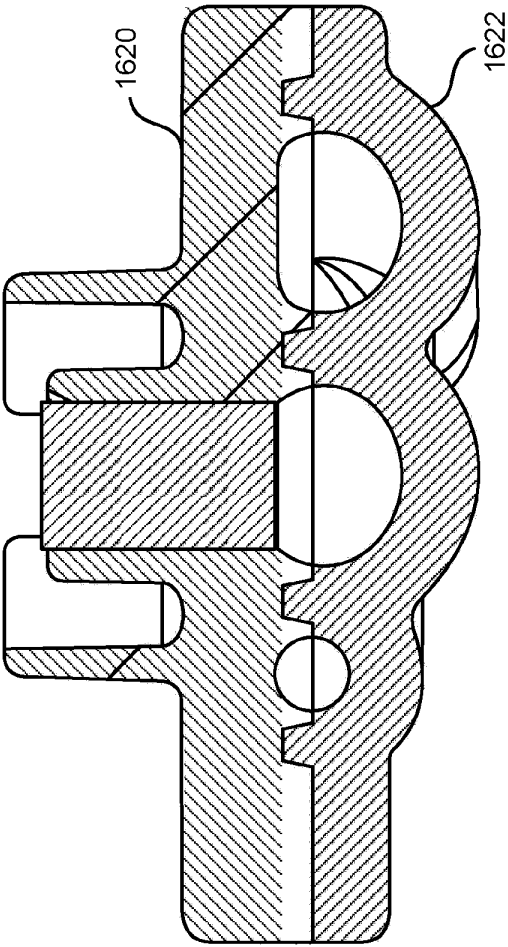


FIG. 19B

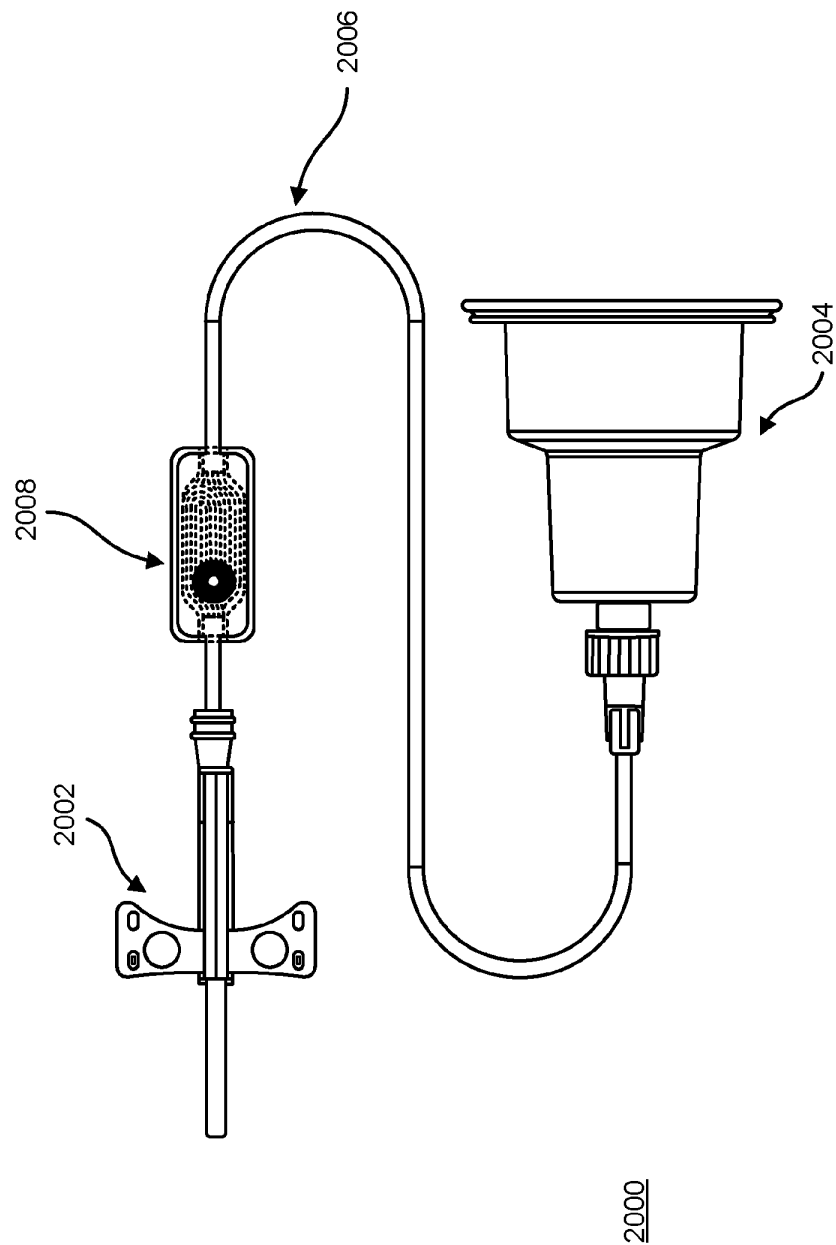


FIG. 20

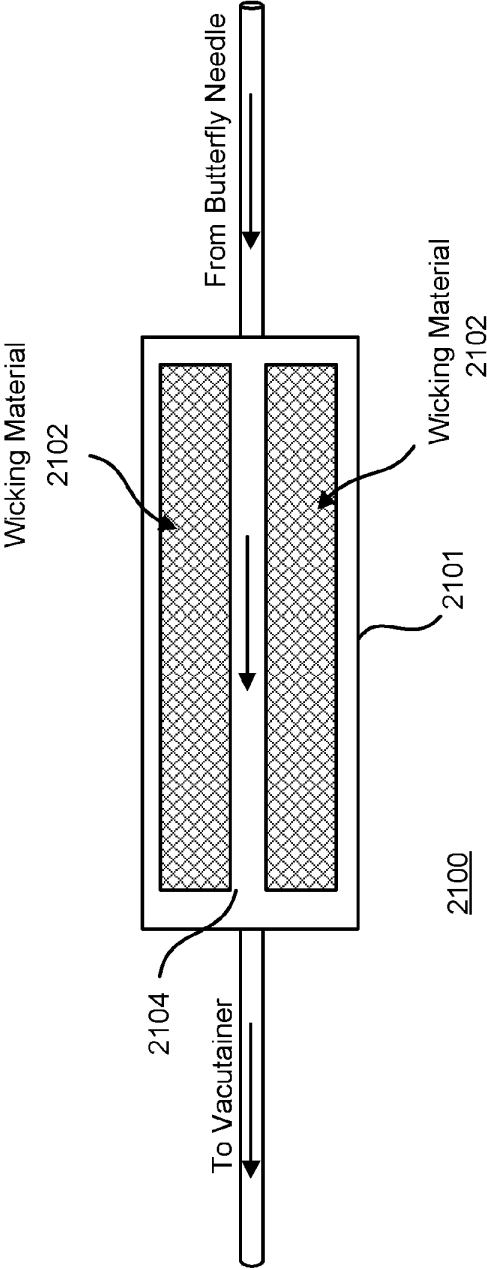


FIG. 21

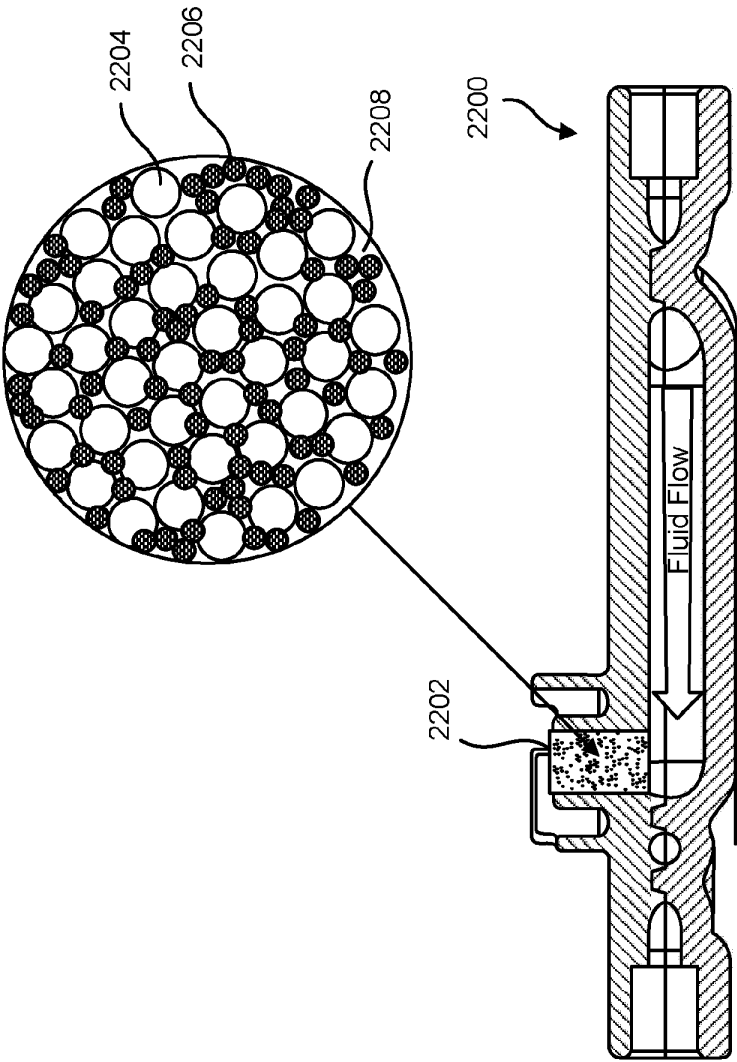


FIG. 22A

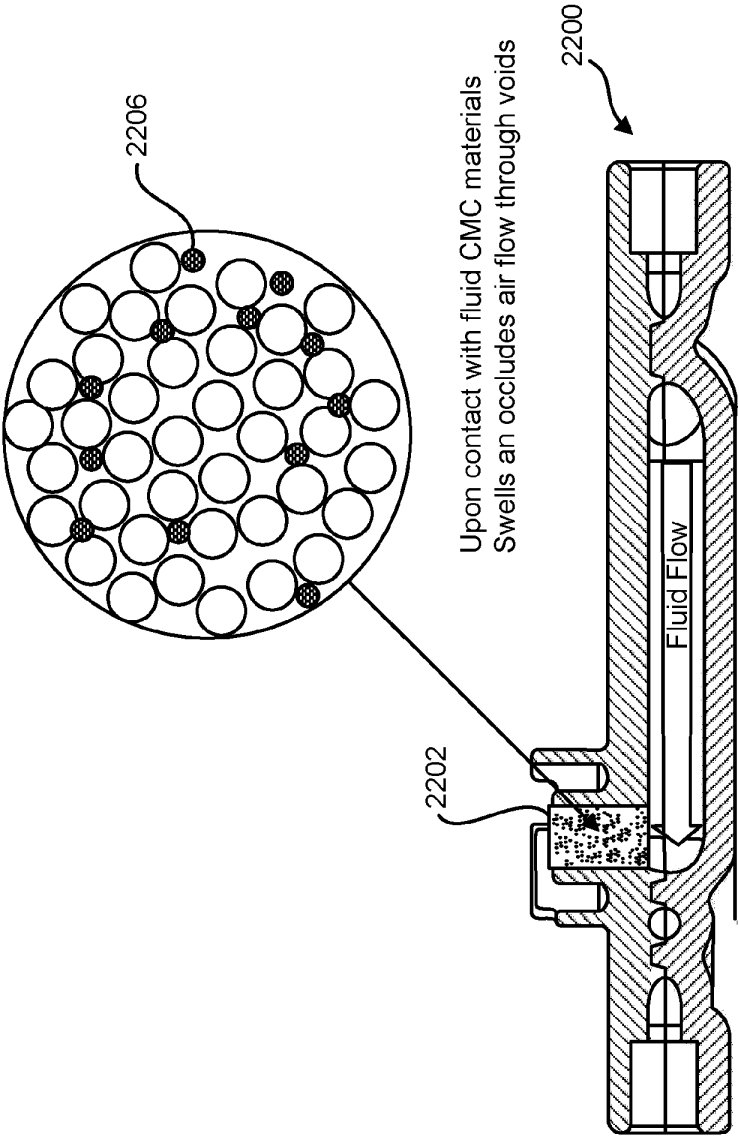


FIG. 22B

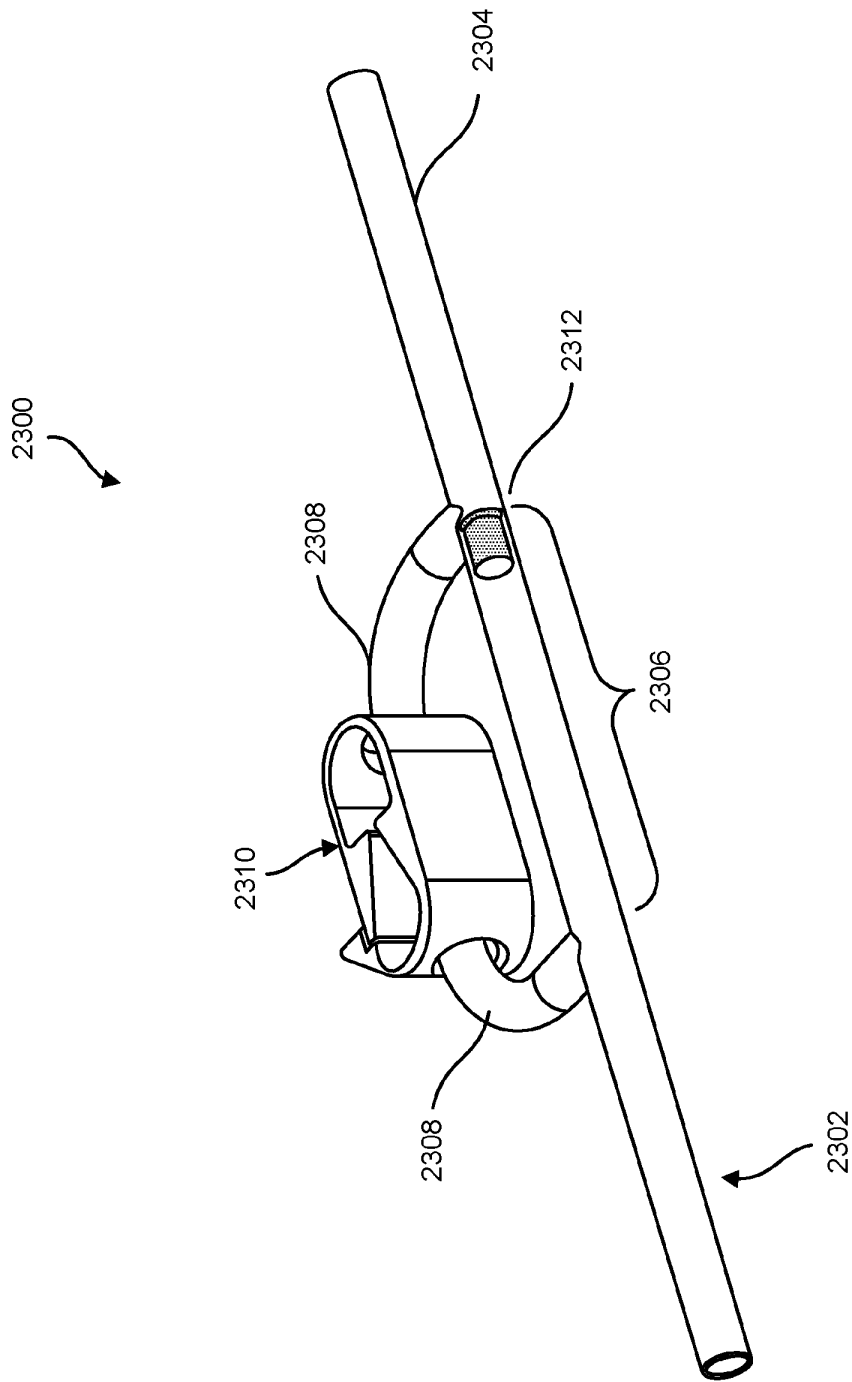


FIG. 23A

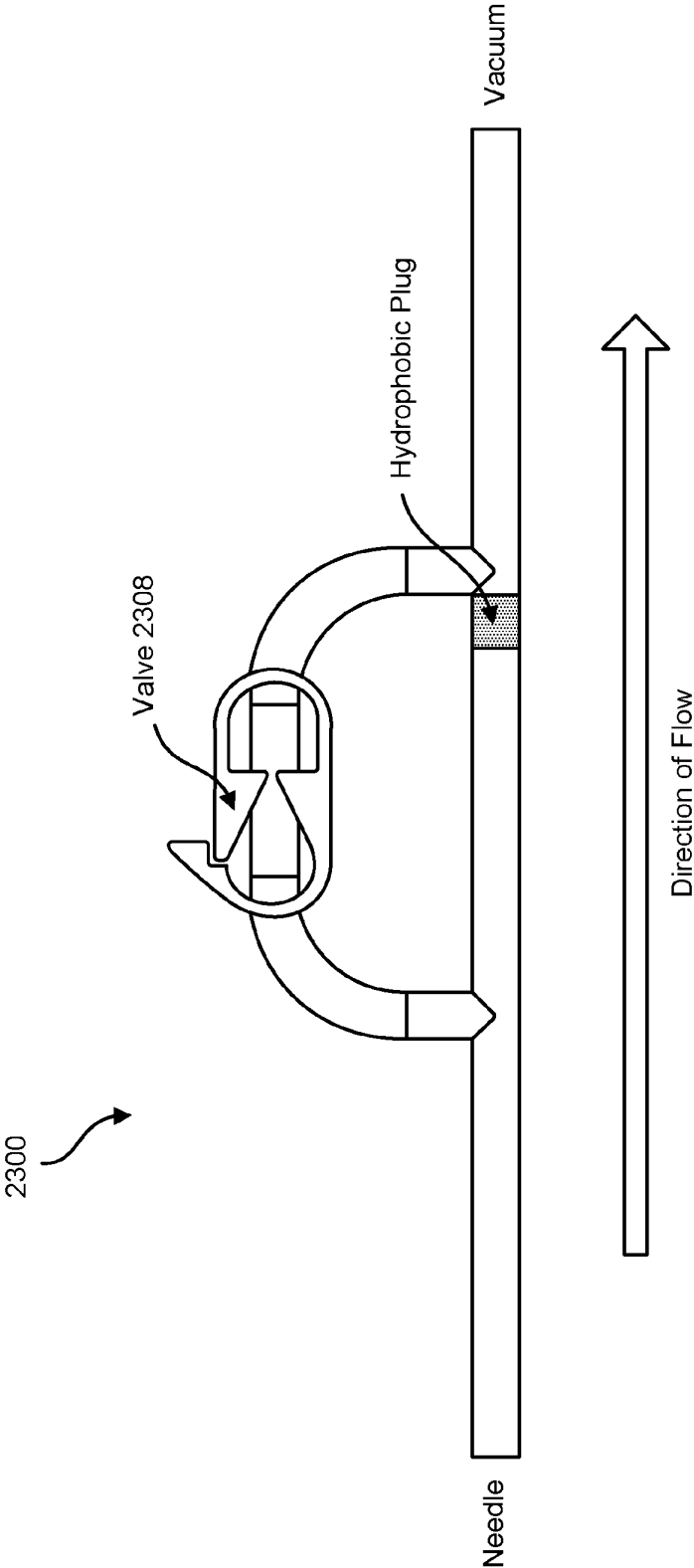


FIG. 23B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures -----	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures -----	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14 -----	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures -----	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18 -----	1-20

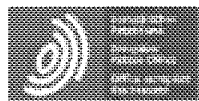
INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2016/043709

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WO 2011162772	A1	29-12-2011	NONE	
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			US 2015099996 A1	09-04-2015
			US 2015351678 A1	10-12-2015



Espacenet

Bibliographic data: EP3324845 (A1) — 2018-05-30

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE

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

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

Classification: - international: A61B5/15; A61B5/153; A61B5/154; A61M39/02; A61M39/04; A61M39/06
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Application number: EP20160747682 20160722 Global Dossier

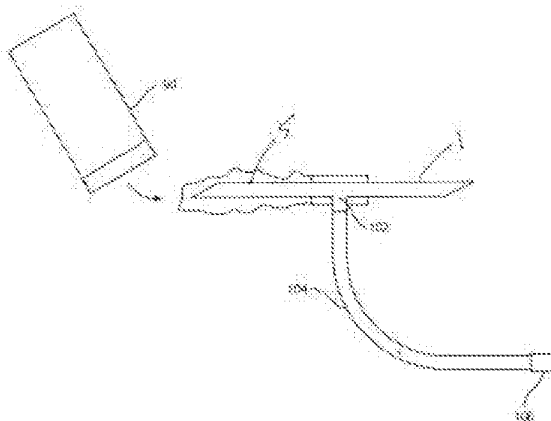
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Blood sample optimization systems and methods are described that reduce or eliminate contaminants in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples.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



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(54) [Title of Invention] Auxiliary Plate for Polishing Pad and Equipped with Auxiliary Plate for Polishing Pad Polishing Apparatus

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2014) [Matters to be stated regarding results of research commissioned by the government] (report by applicant) commissioned by the government Patent application related to research results (FY2010 Ministry of Economy, Trade and Industry "Strategic Fundamental Technology Advancement Support Project" commissioned research, patent application subject to Article 19 of the Industrial Technology Enhancement Act) (73) [Patentee] [Identification number] 599 096053

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(56) [References] [Reference] Japanese Patent Application

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The scope of the claims

open

(57) [Scope of Claims]

[Claim 1] A

polishing pad auxiliary plate mounted on a rotating surface plate of a polishing apparatus for detachably attaching a polishing pad to the rotating surface plate, wherein

:

a first fixing means for fixing the lower auxiliary plate to the rotating surface plate; and
a pad supporting surface on which the polishing pad is superposed and fixed. an upper auxiliary plate superimposed on the upper surface of the lower auxiliary plate;

second fixing means for fixing the upper auxiliary plate to the lower auxiliary plate;

the lower auxiliary plate and the upper side; positioning means for aligning the center axis of the auxiliary plate with respect to each other

, and the lower auxiliary plate is fixed to the rotating surface plate of the polishing apparatus by the first fixing means. By removing the upper auxiliary plate from the lower auxiliary plate held and fixed to the rotating surface plate, the polishing pad can be rotated while being fixed to the pad supporting surface of the upper auxiliary plate. The upper auxiliary plate can be removed from the surface plate, and the removed upper auxiliary plate can be fixed and attached again to the lower auxiliary plate while being aligned by the positioning means, and,

the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is smaller than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means;

Auxiliary plate for a polishing pad, characterized in that :

[Claim 2]

2. The auxiliary plate for a polishing pad according to claim 1 , wherein said positioning means is located inside the outer peripheral surfaces of said lower auxiliary plate and said upper auxiliary plate.

3. The positioning means

includes an engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate and protruding toward the other, and the lower auxiliary plate and the upper auxiliary plate. 3. An auxiliary plate for a polishing pad according to claim 2 , wherein said auxiliary plate for a polishing pad comprises an engaging concave portion provided on the other side thereof and with which said engaging convex portion is engaged .

4. The polishing pad according to claim 3

, wherein said engaging projections and said engaging recesses are formed with engaging portions located on the outer peripheral portions of said lower auxiliary plate and said upper auxiliary plate. Auxiliary plate. 5. An annular engagement in which the engaging portions of the engaging protrusion and the engaging recess extend continuously in the circumferential direction of the lower auxiliary plate and the upper auxiliary plate and are fitted to each other. 5. The auxiliary plate for a polishing pad according to claim 4 , comprising an outer peripheral surface and an engaging inner peripheral surface . 6. At a plurality of locations on the circumference of the outer peripheral portions of the lower auxiliary plate and the upper auxiliary plate

e, the lower auxiliary plate and the upper auxiliary plate are overlapped on one side toward the other. The engaging concave portion that opens and the engaging convex portion that protrudes toward one side of the other of the mutual overlapping surfaces of the lower auxiliary plate and the upper auxiliary plate are formed at positions corresponding to each other, wherein said engaging portion is formed by fitting said engaging convex portion into said engaging concave portion.

5. The polishing pad auxiliary plate according to 4.

7.

The engaging protrusions projecting from a plurality of locations on the circumference of one of the lower auxiliary plate and the upper auxiliary plate toward the other are formed of an elastic material, and the engagement portion is formed by engaging the tip of the engagement projection with the engagement recess provided in the outer peripheral surface of the other of the side auxiliary plate and the upper auxiliary plate. 5. The polishing pad auxiliary plate according to claim 4.

8. A polishing pad auxiliary plate according to claim 3

, wherein said engaging projections and said engaging recesses are provided on the central axes of said lower auxiliary plate and said upper auxiliary plate. 9. An outer peripheral surface of said engaging projection and an inner peripheral surface of said engaging recess are formed with screw grooves for engaging with each other, and said engaging projection and said engaging portion constituting said positioning means are formed with thread grooves for engaging with each other. 9. The auxiliary plate for a polishing pad according to claim 8, wherein said second fixing means is formed by screwing with said mating recess. 10. The engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate is formed of the same material as one of the lower auxiliary plate and the upper auxiliary plate. The auxiliary plate for a polishing pad according to any one of claims 3, 4, 5, 6, 8 and 9.

11. The auxiliary plate for a polishing pad according to any one of claims 1 to 10 is mounted on the upper surface of a rotating surface plate, and a protective member is provided on the outer peripheral side of the rotating surface plate with a gap

therebetween. 11. The positioning means according to any one of claims 1 to 10, wherein the positioning means is disposed on the inner peripheral side of the outer peripheral end faces of the rotating platen and the polishing pad auxiliary plate. 2. A polishing apparatus comprising the polishing pad auxiliary plate according to 1 or 2 above.

detailed description

open

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to the polishing of substrates such as silicon wafers, semiconductor substrates, glass substrates, etc., which are workpieces requiring high flatness accuracy. It relates to a related technique, and more particularly to a technique that makes it possible to reuse a polishing pad used in polishing the surface of such a substrate.

is. 2.

Description of the Related Art As is well known, in manufacturing a semiconductor, a polishing process is performed to flatten the surface of a substrate such as a silicon wafer, a semiconductor substrate, a glass substrate, or the like. Such a polishing process generally involves fixing a disc-shaped polishing pad made of a resin material or the like directly on a rotating surface plate of a polishing apparatus with a double-sided tape, and supplying a polishing liquid containing abrasive grains to the polishing pad. Polishing is performed by rotating the substrates relative to each other. [0003] Polishing pads for carrying out such a polishing process are made of foamed or non-foamed urethane or the like, as described in Japanese Patent Application Laid-Open No. 2002-11630 (Patent Document 1). A resin pad is used. Further, in many cases, the polishing surface of such a polishing pad is provided with grooves such as concentric circles, grids, or radial grooves, or the bubbles of foamed resin are opened. [0004] By the way, when performing a polishing process using a polishing pad, when changing the type of substrate to be polished, the polishing pad used for the polishing process is peeled off from the rotating platen and replaced with another polishing pad. sometimes you have to. Also, for example, when a polishing pad that has deteriorated due to polishing is to be re-processed, such as by grooving the surface, with another processing device for the purpose of reusing the polishing pad, the polishing pad is removed from the rotating platen. Needs to be pulled off. [0005]

However, since the thin disk-shaped polishing pad is firmly fixed to the rotating surface plate

of the polishing apparatus with an adhesive tape, when the polishing pad is peeled off from the rotating surface plate, Damage such as bending, breaking, wrinkling, and tearing is likely to occur. Therefore, due to such damage, there is often a problem that such polishing pads cannot be reused and must be discarded even though their service life has not expired.

[0006]

Moreover, the work of peeling off the polishing pad from the rotating surface plate while paying close attention not to damage it requires skill and caution, and there is also the problem of placing a heavy burden on the operator. In addition, since it takes a considerable amount of time to peel off the polishing pad from the rotating surface plate, the polishing apparatus, which is expensive and valuable equipment, must be stopped for a long time, which shortens the operation time of the equipment. There was also the problem that the

[0007]

Therefore, the present inventor previously described in Japanese Patent Application Laid-Open No. 2010-214579 (Patent Document 2) that an auxiliary plate is attached to the back surface of the polishing pad, and the polishing pad is rotated by the polishing apparatus through this auxiliary plate. We proposed a polishing pad with an auxiliary plate that is fixed to the surface plate with double-sided tape. With such a polishing pad with auxiliary plate, since the polishing pad is attached to and detached from the rotating surface plate while being supported by the auxiliary plate, damage to the polishing pad during attachment and detachment is reinforced by the auxiliary plate. Therefore, it is possible to attach and detach the polishing pad to and from the rotating platen with good workability while preventing the polishing pad from being damaged.

[0008]

However, as a result of further studies and studies by the present inventors, it has been found that it is difficult to say that the polishing pad with an auxiliary plate proposed in Patent Document 2 is easily compatible with all polishing apparatuses.

[0009]

That is, when the polishing pad is overlaid and fixed to the rotating surface plate, it is necessary to align the center of the polishing pad with the rotation center of the rotating surface plate. Accuracy is required for center alignment. If the number of attachment/detachment of the polishing pad to/from the rotating platen increases by adopting the auxiliary plate as described above, it becomes more difficult and labor-intensive to align the center position when attaching the polishing pad to the rotating platen.

It becomes a problem. Further, in the polishing pad with auxiliary plate proposed in Patent Document 2, in order to detachably attach the auxiliary plate while aligning the center of the auxiliary plate with respect to the rotary surface plate, the following are provided between the auxiliary plate and the rotary surface plate

:

For example, fixing means such as an outer peripheral ring may be provided on the outer periphery

peripheral surface of the rotating surface plate. On the other hand, in some polishing apparatuses, a protective cover or the like is attached to the outer peripheral side of the rotary platen, so that the space on the outer peripheral side of the rotary platen is extremely narrow. Therefore, if such an outer peripheral ring were to be adopted, and a polishing device with a narrow space on the outer peripheral side of the rotating surface plate was used, there was a possibility that the polishing device would need to be modified. of.

[Prior Art Documents]

[Patent Documents]

[0011]

[Patent Document 1] [Japanese Unexamined Patent Application Publication No. 2002-11630](#) [Patent Document 2] [Japanese Unexamined Patent Application Publication No. 2010-214579](#) [Summary of the Invention] [Problems to be Solved by the Invention] SUMMARY OF THE INVENTION It is an object of the present invention to provide a polishing pad which can be easily attached to and detached from a rotating surface plate while sufficiently securing the fixing force of the polishing pad to the rotating surface plate. For a polishing pad with a novel structure, which can prevent damage to the polishing pad when the polishing pad is removed from the rotating platen, and which can be advantageous for reuse of the polishing pad, for example. To provide an auxiliary plate. [0013]

In addition, according to the present invention, the work of aligning the center when mounting the polishing pad on the rotating surface plate can be performed easily and accurately, and the labor burden can be reduced. Another object of the present invention is to provide an auxiliary plate for a polishing pad with an improved structure, which can be easily and advantageously applied to a rotating surface plate in a polishing machine without requiring any special modification. A further object of the present invention is to provide a polishing apparatus having such a novel polishing pad auxiliary plate

. Means for Solving the Problems In order to solve the above problems, a first aspect of the present invention relating to an auxiliary plate for a polishing pad is: (A) mounted on a rotating surface plate of a polishing apparatus; A polishing pad auxiliary plate for detachably attaching a pad to the rotary platen, comprising: (B) a lower auxiliary plate disposed on the upper surface of the rotary platen; and (C) the lower auxiliary plate. and (D) a pad supporting surface on which the polishing pad is superimposed and fixed, which is superimposed on the upper surface of the lower auxiliary plate. (E) a second fixing means for fixing the upper auxiliary plate to the lower auxiliary plate; The lower auxiliary plate is held in a fixed state by the first fixing

g means to the rotating surface plate of the polishing apparatus, and is fixed to the rotating surface plate. Further, by removing the upper auxiliary plate from the lower auxiliary plate, the polishing pad can be removed from the rotating surface plate while being fixed to the pad supporting surface of the upper auxiliary plate. At the same time, it is possible to attach the removed upper auxiliary plate to the lower auxiliary plate by fixing it again in a state of being aligned by the positioning means.

and the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is stronger than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means. It features a smaller auxiliary plate for the polishing pad. In the polishing pad auxiliary plate constructed according to the present invention, the polishing pad is composed of the upper auxiliary plate and the upper auxiliary plate

.

It is fixedly attached to the rotating surface plate via the lower auxiliary plate. Thereby, the upper auxiliary plate can be removed from the lower auxiliary plate while the lower auxiliary plate is fixed to the rotating surface plate, and the polishing pad can be removed from the rotating surface plate while being fixed to the upper auxiliary plate. becomes possible. Therefore, in a state in which the polishing pad is reinforced and protected by the upper auxiliary plate, the polishing pad can be removed from the rotating surface plate while preventing damage to the polishing pad, and the thin polishing pad can be easily handled

.

becomes. For example, when the polishing pad is repeatedly attached and detached when the object to be polished or the polishing conditions are changed, or when the worn polishing pad is detached and reattached after reprocessing, the attachment and detachment of the polishing pad to and from the rotating platen and the polishing are difficult. It is also possible to easily perform operations such as reproduction processing for pads. Moreover, since the lower auxiliary plate still fixed to the rotating surface plate and the upper auxiliary plate removed together with the polishing pad are aligned with each other by the positioning means, the position on the rotating surface plate can be easily adjusted

.

The attachment and detachment work of the polishing pad, which requires alignment, can be performed more easily. In particular, since the positioning means is provided between the lower auxiliary plate and the upper auxiliary plate, there is no need to apply special processing or the like to the rotating surface plate. In addition, it is possible to prevent such positioning means from protruding to the outer peripheral side of the rotating surface plate. applicable without In the polishing pad auxiliary plate according to the first aspect of the present invention

, the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is smaller than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means; A certain aspect is employed. According to the first aspect, the fixing forces of the first and second fixing means are mutually adjusted, so that the upper auxiliary plate to which the polishing pad is fixed can be rotated. This makes it easier to remove the lower auxiliary plate that is still fixed to the surface plate. In short, there is no need for a special operation or the like to keep the lower auxiliary plate fixed to the rotating platen, and the polishing pad can be attached to the upper supporting plate while the lower auxiliary plate remains fixed to the rotating platen. It becomes possible to easily remove the plate from the rotating surface plate while it is fixed to the plate. According to a second aspect of the present invention, in the polishing pad auxiliary plate according to the first aspect, the positioning means is arranged on the inner peripheral side of the outer peripheral surfaces of the lower auxiliary plate and the upper auxiliary plate. It is located and provided. [0022] In the polishing pad auxiliary plate of this aspect, the projection of the upper and lower auxiliary plates to the outer peripheral side of the positioning means is completely avoided. Therefore, for example, even when the outer diameter of the upper and lower auxiliary plates is set to be the same as or slightly smaller than the outer diameter of the rotating surface plate, the supporting surface of the polishing pad can be secured sufficiently large and the It is possible to prevent the positioning means from protruding to the outer peripheral side, and even if a protective cover or the like is installed on the outer peripheral side of the rotating surface plate, it will not become an obstacle when applying the polishing pad auxiliary plate according to the present invention. Avoided.

A third

aspect of the present invention is the polishing pad auxiliary plate according to the second aspect, wherein the positioning means is provided on one of the lower auxiliary plate and the upper auxiliary plate and on the other. It is composed of an engaging projection projecting to the forward and an engaging recess provided in the other of the lower auxiliary plate and the upper auxiliary plate with which the engaging projection is engaged. In the polishing pad auxiliary plate of this aspect, it is possible to easily obtain a mechanically large positioning force based on the mutual engagement between the engaging projections and the engaging recesses. Further, by adjusting the shape, size, number, etc. of the engaging projections and engaging recesses, it is possible to easily set the direction and acting force of the positioning action with a large degree of freedom.

A fourth aspect

of the present invention is the auxiliary plate for a polishing pad according to the third aspect, wherein the engaging projections and the engaging recesses are located on the outer periphery of the lower auxiliary plate and the upper auxiliary plate. It is formed with an engaging portion located in the portion. In the polishing pad auxiliary plate of this aspect, the engagement outer peripheral surface of the engagement projection and the engagement recess are positioned in the outer peripheral portion away from the center of the polishing pad auxiliary plate and are engaged with each other in a concave-convex manner. By forming the engagement inner peripheral surface of the upper and lower auxiliary plates, the relative positioning accuracy, particularly the radial positioning accuracy, can be improved. As shown in the sixth and seventh aspects below, the engaging outer peripheral surface of the engaging convex portion and the engaging inner peripheral surface of the engaging concave portion are arranged around the center of the polishing pad auxiliary plate. It may extend in the circumferential direction along the outer peripheral edge of the polishing pad auxiliary plate, or it may extend on the circumference like the engaging protrusions and engaging recesses formed on the outer peripheral portion of the polishing pad auxiliary plate. It may be in a partially positioned form.

A fifth aspect of the present invention is the auxiliary plate for a polishing pad according to the fourth aspect, wherein the engaging portions of the engaging projections and the engaging recesses correspond to the lower auxiliary plate and the It is composed of an annular engaging outer peripheral surface and an engaging inner peripheral surface that extend continuously in the circumferential direction of the upper auxiliary plate and are fitted to each other. [0028]

In the polishing pad auxiliary plate of this aspect, more preferably, the engaging concave portion and the engaging convex portion are formed with an annular inner and outer peripheral engaging surface that spreads around the central axis of the polishing pad auxiliary plate. Therefore, when the upper auxiliary plate is attached to the lower auxiliary plate, it is not necessary to align the upper auxiliary plate with each other in the circumferential direction, and the work can be performed easily and quickly. A sixth aspect of the present invention is a polishing pad auxiliary plate according to the fourth aspect, wherein the lower auxiliary plate and the upper auxiliary plate are provided at a plurality of locations on the periphery of the outer peripheral portions of the lower auxiliary plate and the upper auxiliary plate. The engaging recess opening toward the other on one of the overlapping surfaces of the lower auxiliary plate and the upper auxiliary plate, and the other of the mutually overlapping surf

aces of the lower auxiliary plate and the upper auxiliary plate and the engaging projection projecting toward one side are formed at positions corresponding to each other, and the engaging portion is formed by fitting the engaging projection into the engaging recess. is. In the polishing pad auxiliary plate of this mode, the mutual positioning of the upper and lower auxiliary plates can be easily realized not only in the direction perpendicular to the axis but also in the circumferential direction around the central axis. In a seventh aspect of the present invention, in the polishing pad auxiliary plate according to the fourth aspect, the outer peripheral portion of one of the lower auxiliary plate and the upper auxiliary plate has a plurality of points on the circumference of the other. The engaging convex portion protruding toward the upper auxiliary plate is formed of an elastic material, and engages with the engaging concave portion provided in an opening on the outer peripheral surface of the other of the lower auxiliary plate and the upper auxiliary plate. The engaging portion is configured by engaging the tip of the engaging projection.

In the polishing pad auxiliary plate of this aspect, it is possible to form the engaging portions so as to be exposed on the outer peripheral surfaces of the upper and lower auxiliary plates. can be confirmed. In addition, in this aspect, the engagement state of the engagement portion can be stably maintained by utilizing the elasticity of the engagement convex portion. An eighth aspect of

the present invention is the polishing pad auxiliary plate according to the third aspect, where in the engaging projections and the engaging recesses are located at the centers of the lower auxiliary plate and the upper auxiliary plate. It is provided on the shaft. In the polishing pad auxiliary plate of this aspect, the engaging projections and the engaging recesses are formed on the central axis of the upper and lower auxiliary plates.

By providing this, it becomes possible to align the central axes of the upper and lower auxiliary plates with one engaging portion. Further, when the engaging projections and the engaging recesses provided on the central axis are aligned with each other, it is not necessary to align the upper and lower auxiliary plates with each other in the circumferential direction. can be easily brought into engagement. According to a ninth aspect of the present invention, in the polishing pad auxiliary plate according to the eighth aspect, the outer peripheral surface of the engaging projection and the inner peripheral surface of the engaging recess are screwed together.

her

. A groove is formed, and the second fixing means is formed by screwing the engaging projection and the engaging recess that constitute the positioning means. [0036] In the polishing pad auxiliary plate of this mode, the fixing force between the upper auxiliary plate and the lower auxiliary plate can be obtained by the positioning means. Therefore, it is possible to configure the second fixing means only by such positioning means, or to configure the fixing force between the upper and lower auxiliary plates by the second fixing means as an auxiliary means by the positioning means. A tenth aspect of the present invention is the third , fourth , fifth , sixth , eighth and ninth

2. In the polishing pad auxiliary plate according to any one of the above aspects, the engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate is arranged between the lower auxiliary plate and the upper auxiliary plate. It is made of the same material as the one. In the polishing pad auxiliary plate of this aspect, it is possible to prevent the support characteristics of the polishing pad of the auxiliary plates superimposed one on top of the other from greatly differing locally at the portions where the engaging projections are formed

.

. Therefore, when a pressing force acts on the surface of the polishing pad during pad polishing, the pressure reaction force and the elasticity of the polishing pad are reduced at the formation portions of the engaging convex portions and the engaging concave portions of the upper and lower auxiliary plates that support the polishing pad. It is possible to reduce or avoid defects such as polishing accuracy caused by local differences in such characteristics. Further, according to the present invention, the auxiliary plate for a polishing pad according to any one of the first to tenth aspects of the present invention is mounted on the upper surface of a rotating platen, and is attached to the outer peripheral side of the rotating platen

. A polishing apparatus in which a protective member is arranged with a gap in between, and the positioning means is provided on the inner peripheral side of the outer peripheral end surfaces of the rotating platen and the polishing pad auxiliary plate, Characterized by EFFECTS OF THE INVENTION By adopting the polishing pad auxiliary plate structured according to the present invention or using the polishing apparatus structured according to the present invention, the polishing pad can be prevented from being damaged and polished. can be easily removed from and attached to the rotating surface plate, and positioning of the polishing pad on the rotating surface plate can be performed easily and accurately. [Brief Description of the Drawings]

FIG. 1 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a first embodiment of the present invention;

2 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 1; FIG.

FIG. 3 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a second embodiment of the present invention;

4 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 3; FIG.

FIG. 5 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a third embodiment of the present invention;

6 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 5; FIG.

FIG. 7 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a fourth embodiment of the present invention;

8 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 7; FIG.

FIG. 9 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a fifth embodiment of the present invention;

10 is a side view of a lower auxiliary plate that constitutes the polishing pad auxiliary plate shown in FIG. 9; FIG.

11 is a plan view of the lower auxiliary plate shown in FIG. 10; FIG.

FIG. 12 is a longitudinal sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a sixth embodiment of the present invention;

FIG. 13 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a seventh embodiment of the present invention;

FIG. 14 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to an eighth embodiment of the present invention;

FIG. 15 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a ninth embodiment of the present invention is removed;

FIG. 16 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate is removed according to a tenth embodiment of the present invention;

FIG. 17 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to an eleventh embodiment of the present invention is removed;

FIG. 18 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a twelfth embodiment of the present invention is removed;

FIG. 19 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a thirteenth embodiment of the present invention is removed;

FIG. 20 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a fourteenth embodiment of the present invention is positioned;

FIG. 21 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a fifteenth embodiment of the present invention is positioned;

FIG. 22 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a sixteenth embodiment of the present invention is removed;

DETAILED DESCRIPTION OF THE INVENTION Embodiments of the present invention will be described below

below

with reference to the drawings. First, FIGS. 1 and 2 show a polishing pad auxiliary plate 10 as a first embodiment of the present invention. This polishing pad auxiliary plate 10 is used by being attached to a rotary surface plate 14 of a polishing apparatus 12, and a polishing pad 16 is detachably attached to the rotary surface plate 14. As shown in FIG.

The polishing apparatus is used ,

for example, as a CMP apparatus as described in Japanese Patent Application Laid-Open No. 2010-141155, for example. A rotating shaft extending vertically is rotatably supported by the main body of the apparatus fixedly installed above, and a disk-shaped rotating platen 14 is fixed to the upper end of the rotating shaft. The rotating surface plate 14 has a flat upper surface 18 extending horizontally, and the upper surface 18 serves as a support surface for the polishing pad 16. The rotating shaft is connected to the rotating output shaft of an electric motor, and the driving force of the electric motor is transmitted so that the rotating shaft and thus the rotating surface plate 14 are rotated about the central axis. there is A nozzle for supplying polishing slurry is arranged above the upper surface 18 supporting the polishing pad 16, and a wafer or the like to be polished (an object to be polished) is held and rotated while being moved to the polishing pad 16. A polishing head is provided for polishing by pressing. In such a polishing apparatus, the polishing pad auxiliary plate 10 mounted on the rotating platen 14 is

includes a lower auxiliary plate 20 and an upper auxiliary plate 22 . A lower auxiliary plate 20 is fixed to the upper surface 18 of the rotating platen 14 by first fixing means 24 , and an upper auxiliary plate 22 is attached to the upper surface of the lower auxiliary plate 20 . It is fixed by two fixing means 26 . That is, the lower auxiliary plate 20 and the upper auxiliary plate 22 are overlapped and fixed to each other via the second fixing means 26, thereby forming the polishing pad auxiliary plate 10 having a two-layer structure as a whole. , and is attached to the upper surface 18 of the rotating surface plate 14 by the first fixing means 24 .

Each of the lower auxiliary plate 20 and the upper

auxiliary plate 22 has a thin, substantially circular flat plate shape, and has a flat front surface (upper surface) and a rear surface (lower surface). These upper and lower auxiliary plates 22 and 20 are desirably made of a harder material than the polishing pad 16 to which it is attached, or having a higher member rigidity than the polishing pad 16 . Although it depends on the method of use, as will be described later, the lower auxiliary plate 20 can be used without being repeatedly attached and detached after being attached to the rotary surface plate 14, while the upper auxiliary plate 22 can be attached and detached after being attached to the rotary surface plate 14. is expected to be repeated, it is desirable that at least the upper auxiliary plate 22 should have higher member rigidity than the polishing pad 16 .

[0046]

Of course, the upper auxiliary plate 22 supports the polishing pad 16 and provides the strength, rigidity, and rigidity required for various treatments such as polishing, cleaning, and re-grinding of the polishing pad surface, in addition to polishing by the polishing device 12 . Any material that satisfies shape stability and accuracy may be used, and its material and thickness are not limited. In particular, not only the lower auxiliary plate 20 but also the upper auxiliary plate 22 alone bears the supporting strength and rigidity of the polishing pad 16. Since the lower surface is supported by the rotating surface plate 14 by being superimposed on each other and used, the strength and rigidity of the single unit are not required so much. Therefore, in addition to metals such as stainless steel, synthetic resins, fiber-reinforced resins, and the like can be employed as materials for forming the lower auxiliary plate 20 and the upper auxiliary plate 22 . In particular, synthetic resin materials are lighter than metal materials and easier to process and handle. . In order to obtain a stable supporting force over the entire polishing pad 16, it is desirable to set the outer diameter dimension of the upper auxiliary plate 22 to be equal to or larger than the outer diameter dimension of the polishing pad 16, and

It is desirable to set the outer diameter of the lower auxiliary plate 20 to be equal to or larger than the outer diameter of the upper auxiliary plate 22, and set the outer diameter of the lower auxiliary plate 20 to be equal to or smaller than the outer diameter of the rotating surface plate 12. should be set to In particular, as shown in FIGS. 1 and 2, the outer diameters of the lower auxiliary plate 20 and the upper auxiliary plate 22 are made substantially the same, and the outer diameter of the rotating surface plate 14 to be mounted is also substantially the sa

me. By doing so, it becomes possible to ensure a sufficiently large support area for the polishing pad 16. As a result, the polishing pad 16 having approximately the same size as the rotating surface plate 14 can be attached to the rotating surface plate 14 with approximately the same supporting force over the entirety thereof.

[0048]

Furthermore, as the first fixing means 24 and the second fixing means 26, the lower auxiliary plate 20 and the upper auxiliary plate 22 are fixed to the upper surface 18 of the rotating plate 14 against the external force exerted during polishing. It is not particularly limited as long as it can be held at. Specifically, an adhesive, a pressure-sensitive adhesive, or a double-sided tape having an adhesive or a pressure-sensitive adhesive attached to both sides of a base sheet may be employed as the first and second fixing means 24, 26. In addition, negative pressure suction using negative pressure air or the like, or magnetic suction using a permanent magnet or an electromagnet can be employed. In addition, it is desirable that the fixing means made of adhesive or the like apply substantially uniform fixing force over substantially the entire surface of the flat overlapping surfaces of the lower auxiliary plate 20 and the upper auxiliary plate 22. Adhesive strength can be obtained, and problems such as locally different support characteristics of the polishing pad 16 on the surface of the polishing pad auxiliary plate 20 can be avoided.

For example,

the fixing force can be turned ON/OFF by negative pressure suction or an electromagnet. auxiliary

It is desirable to set the fixing force of the upper auxiliary plate 22 to the lower auxiliary plate 20 by the second fixing means 26 to be smaller than the fixing force of the plate 20. As a result, when the upper auxiliary plate 22 is peeled off from the lower auxiliary plate 20 and removed, the lower auxiliary plate 20 can be easily left fixed on the rotating surface plate 14.例文帳に追加 The specific realization of such a difference in adhesion force is achieved by differentiating the adhesion means itself such as the material of the adhesive and pressure-sensitive adhesive, as well as the adhesion area and the condition of the adhesion surface (surface roughness, presence or absence of plasma treatment, etc.) can also be realized by making the.

Further, the surface (upper surface) of the upper auxiliary plate 22 serves as a

polishing pad supporting surface, and the polishing pad 16 is superimposed and mounted thereon. As such a polishing pad 16, conventionally known various types of polishing pads can be employed. The back surface of the polishing pad 16 is fixed to the surface of the upper auxiliary plate 22 using a conventionally known adhesive tape or suitable adhesive for attaching the polishing pad.

It is desirable that the fixing means for fixing

the polishing pad 16 to the upper auxiliary plate 22 has a larger fixing force than the second fixing means 26 described above. As a result, when the upper auxiliary plate 22 is removed from the lower auxiliary plate 20 with the polishing pad 16 still fixed, the polishing pad 16 does

not move from the upper auxiliary plate 22 even if the upper auxiliary plate 22 is bent or the like. It is possible to effectively prevent the peeling off. The outer diameter of the polishing pad 16 is generally a standard value, but in many cases it is set equal to or smaller than the outer diameter of the upper surface 18 of the rotating surface plate 14 to which it is attached . [0053]

Further, for example, at least one of between the upper surface 18 of the rotating surface plate 14 and the lower auxiliary plate 20, between the lower auxiliary plate 20 and the upper auxiliary plate 22, and between the upper auxiliary plate 22 and the polishing pad 16 A suitable cushioning layer may be provided. By providing such a cushion layer, it becomes possible to achieve uniform polishing efficiency over the entire surface of the workpiece when polishing with the polishing pad 16 .

[0054]

As such a cushion layer, for example, a resin sheet, an elastomer sheet, a rubber sheet, or the like to which a certain degree of compressibility is imparted by foaming can be suitably employed. A cushion layer can also be configured by the first fixing means 24 , the second fixing means 26 , and the means for fixing the polishing pad 16 to the upper auxiliary plate 22 . In order to prevent local distortion on the support surface of the polishing pad 16, the cushion layer is formed so as to have a size and a constant thickness over substantially the entire support area of the polishing pad 16. is desirable. Positioning means 28 are provided between the lower auxiliary plate 20 and the upper auxiliary plate 22 that constitute the polishing pad auxiliary plate 10 to align the centers of the plates with each other .

In the present embodiment, a circular stepped surface 30 is formed on the outer peripheral portion of the lower auxiliary plate 20 and extends around the central axis of the lower auxiliary plate 20 over the entire circumference. By reducing the thickness of the lower auxiliary plate 20 on the outer peripheral side of the stepped surface 30, the notch cross-sectional shape that opens to the outer peripheral surface of the lower auxiliary plate 20 continues to the entire circumference in the circumferential direction. An annular engaging recess 32 that extends inward is formed integrally with the lower auxiliary plate 20 so as to protrude therefrom.

[0056]

On the other hand, in the present embodiment, a circular stepped surface 34 is formed on the outer peripheral portion of the upper auxiliary plate 22 so as to extend around the central axis of the upper auxiliary plate 22 over the entire circumference. Since the thickness of the upper auxiliary plate 22 is increased on the outer peripheral side of the stepped surface 34, an annular engagement continuously extends along the outer peripheral edge of the upper auxiliary plate 22 along the entire circumference in the circumferential direction. A mating projection 36 is integrally formed so as to protrude from the upper auxiliary plate 22 . Incidentally, the e

engaging convex portion 36 and the engaging concave portion 32 may be formed on either of the upper and lower auxiliary plates 22 and 20 .

The stepped surface 30 and the engaging recess 32 of the lower auxiliary plate 20 are aligned with the stepped surface 34 and the engaging projection 36 of the upper auxiliary plate 22 . It constitutes an engagement outer peripheral surface and an engagement inner peripheral surface. When the upper auxiliary plate 22 is superimposed on the lower auxiliary plate 20, the engaging convex portion 36 is fitted into the engaging concave portion 32, and the stepped surface 34 is superimposed on the stepped surface 30 in the radial direction. is formed. As a result, the engaging concave portion 32 and the engaging convex portion 36 constitute the positioning means 28, and the lower auxiliary plate 20 and the upper side support plate 20 are aligned in the radial direction with their central axes aligned with each other. Auxiliary plates 22 are superimposed. In addition, the positioning means 28 is positioned on the inner peripheral side of the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20, thereby preventing the upper and lower auxiliary plates 22 and 20 and the polishing apparatus 12 from becoming large. . In the polishing apparatus 12 provided with the polishing pad auxiliary plate 10 having such a structure, the upper and lower auxiliary plates 22 are mounted on the upper surface 18 of the rotating platen 14 as shown in FIG

, 20 is fixedly attached, and the polishing pad 16 is fixedly supported on the upper surface of the upper auxiliary plate 22. Then, the rotating platen 14 is driven to rotate, and the substrate or the like is processed. CMP (Chemical Mechanical Polishing) is applied to objects. The polishing apparatus 12 can exhibit the following special technical effects by being provided with the polishing pad auxiliary plate 10 having a specific structure.

[0059]

First, as shown in FIG. 2, while the polishing pad 16 is fixed to the upper surface of the upper auxiliary plate 22, the upper auxiliary plate 22 is fixed to the rotating surface plate 14 by the first fixing means 24. By removing the side auxiliary plate 20, the polishing pad 16 can be removed from the rotating surface plate 14. - 特許庁 Even when the surface (polishing surface) of the polishing pad 16 is removed from the rotating platen 14 and cleaned or reprocessed, the polishing pad 16 can be kept fixed to the upper surface of the upper auxiliary plate 22 . As a result, the upper auxiliary plate 22 provides reinforcement not only when the polishing pad 16 is attached to and detached from the rotating surface plate 14, when the polishing pad 16 is cleaned and reprocessed, but also when the polishing pad 16 is transported or stored. By this action, the polishing pad 16 can be prevented from being bent or damaged, and the polishing pad 16 can be kept in good condition.

Further

, even when the polishing pad 16 is removed from the rotating surface plate 14 together with the upper auxiliary plate 22 , the lower auxiliary plate 20 remains on the upper surface 18 o

f the rotating surface plate 14 . When the polishing pad 16 is again mounted on the rotating platen 14, the positioning means 28 provided between the upper auxiliary plate 22 and the lower auxiliary plate 20 moves the upper auxiliary plate 22 and thus the polishing pad 16 to the lower auxiliary plate. The center axis of the plate 20 and thus the rotating platen 14 can be aligned with high accuracy and easily.

[0061]

Here, since the engaging concave portion 32 and the engaging convex portion 36 constituting the positioning means 28 are overlapped with almost no gap in a mutually fitted state, the supporting characteristics of the polishing pad 16 are improved. can be prevented from adversely affecting Of the outer peripheral portions of the upper and lower auxiliary plates 22 and 20, particularly in the present embodiment, an engaging portion, in other words, a positioning means 28, is formed on the outer peripheral edge portion, and the diameter of the polishing pad 16 that serves as the main region for polishing is formed. Since it is out of the middle part in the direction, even if there is a slight gap between the engaging concave portion 32 and the engaging convex portion 36, the supporting characteristics of the polishing pad 16 are such that a serious problem occurs in the polishing characteristics. can be avoided. Moreover, the engaging concave portion 32 and the engaging convex portion 36 constituting the positioning means 28 are formed on the superimposed surfaces of the upper and lower auxiliary plates 22 and 20, in other words, on the outer circumferences of the rotating surface plate 14 and the polishing pad auxiliary plate 10

Since it is formed on the inner peripheral side of the end face, the upper and lower auxiliary plates 22 and 20 can be prevented from projecting onto the outer peripheral surface. Therefore, as shown in FIGS. 1 and 2, for example, even when the protective member 38 is installed close to the outer peripheral side of the rotating surface plate 14 in the polishing apparatus 12, the protective member 38 cannot be protected. Polishing provided with upper and lower auxiliary plates 22, 20 provided with positioning means 28 while avoiding interference

A device 12 is made possible. Furthermore, as described above, while preventing damage to the polishing pad 16, the polishing pad 16 can be quickly attached to and detached from the rotating platen 14 with accurate positioning accuracy

The operating time of the expensive polishing equipment is not unnecessarily limited for such work, and the operating efficiency of the polishing equipment can be improved, and thus the production efficiency of substrates and the like (polishing work efficiency) can be improved. In addition, since the polishing pad 16 can be easily attached to and detached from the rotating surface

plate 14, the reuse of the polishing pad 16 can be realized on a practical level without special skill or knowledge. That is, for example, the polishing pad 16 once removed from the rotating platen 14 can be reused when changing the type of the object to be polished such as a subs

trate, or the polishing pad 16 can be re-processed by another processing device such as surface grooving as a countermeasure against deterioration. It is also possible to consider reusing the polishing pad 16 once removed from the rotating surface plate 14 after reprocessing at a practical level. Although the first embodiment of the present invention has been described above, the specific structure of the present invention should not be construed as limited by the first embodiment

.

A plurality of other embodiments of the present invention having different positioning means between the upper and lower auxiliary plates 22 and 20 are illustrated below, but these embodiments are not intended to limit the configuration of the present invention. In the following embodiments, members and parts having the same structure as in the first embodiment are denoted by the same reference numerals as those in the first embodiment in the corresponding parts in each figure. , their detailed description is omitted. 3 and 4 show a polishing apparatus 42 provided with a polishing pad auxiliary plate 40 as a second embodiment of the present invention

.

In this polishing pad auxiliary plate 40, an engaging recess 44 is formed by an annular groove continuously extending in the circumferential direction on the outer peripheral portion of the upper surface of the lower auxiliary plate 20. As shown in FIG . On the other hand, on the outer peripheral portion of the lower surface of the upper auxiliary plate 22, an engagement convex portion 46 is formed by an annular protrusion extending continuously in the circumferential direction. The engaging projection 46 may be formed integrally with the upper auxiliary plate 22, or may be formed separately as illustrated. That is, in this embodiment, an annular circumferential groove 48 that opens in the lower surface of the upper auxiliary plate 22 and extends in the circumferential direction is formed. block is fitted and fixed at one end in the axial direction to form an engagement convex portion 46 . The engaging concave portion 44 of the lower auxiliary plate 20 and the engaging convex portion 46 of the upper auxiliary plate 22 are both formed at corresponding radial positions around the central axis

.

are overlapped, the engagement projections 46 are fitted into the engagement recesses 44, thereby aligning the upper and lower auxiliary plates 22 and 20 with each other in the radial direction. In the present embodiment, two side walls of the engaging recess 44 of the lower auxiliary plate 20 and the inner and outer peripheral surfaces of the engaging protrusion 46 of the upper auxiliary plate 20 are superimposed on each other in the corresponding radial direction. A pair of inner and outer engagement surfaces are provided. 5 and 6 show a polishing apparatus 52 provided with a polishing pad auxiliary plate 50 as a third embodiment of the present invention

. [0070]

In this polishing pad auxiliary plate 50, the lower auxiliary plate 20 has a stepped surface 54 as a circular engagement inner peripheral surface extending all around the central axis on the outer peripheral portion thereof. By increasing the thickness of the lower auxiliary plate 20 on the outer peripheral side of the stepped surface 54, an annular shape continuously extends along the outer peripheral edge of the lower auxiliary plate 20 along the entire circumference in the circumferential direction. The engaging convex portion 56 of

It is formed integrally with the side auxiliary plate 20 . On the other hand, on the outer peripheral portion of the upper auxiliary plate 22, there is formed a stepped surface 58 as a circular engagement outer peripheral surface extending all around the central axis

Since the thickness of the upper auxiliary plate 22 is reduced on the outer peripheral side of the step surface 58, the upper auxiliary plate 22 has a notched cross-sectional shape that opens to the outer peripheral surface and extends continuously along the entire circumference in the circumferential direction. An annular engaging recess 60 is formed integrally with the upper auxiliary plate 22 .

Further, the step surface 54 of the lower auxiliary plate 20 is formed with

female threads, while the step surface 58 of the upper auxiliary plate 22 is formed with male threads. Then, the female thread of the stepped surface 54 of the lower auxiliary plate 20 is screwed with the male thread of the stepped surface 58 of the upper auxiliary plate 22 so that the stepped surface 54 of the lower auxiliary plate 20 and the stepped surface 58 of the upper auxiliary plate 22 are screwed together. are superimposed on each other in the radial direction, the upper auxiliary plate 22 is superimposed on the upper surface of the lower auxiliary plate 20 . Further, in such a superimposed state, the screwing structure of the stepped surfaces 58, 54 of the upper and lower auxiliary plates 22, 20 constitutes a second fixing means 62 for detachably fixing the upper and lower auxiliary plates 22, 20. . The direction of the male and female threads in such a threaded structure is set in consideration of the rotational reaction force exerted on the rotating surface plate 14 of the polishing device 12 during polishing so that the screws do not loosen

It is desirable that

FIGS.

7 and 8 show a polishing apparatus 66 having a polishing pad auxiliary plate 64 as a fourth embodiment of the present invention.

[0075]

In this polishing pad auxiliary plate 64 , a cylindrical engaging convex portion 68 projecting upward is formed at the central portion of the upper surface of the lower auxiliary plate 20 . T

he engaging projection 68 may be formed integrally with the lower auxiliary plate 20, or may be formed separately as shown in the drawing. That is, in this embodiment, a circular fitting recess 70 is formed on the central axis of the lower auxiliary plate 20, and a cylindrical block formed separately from the fitting recess 70 is provided. An engaging convex portion 68 is formed by being fitted and fixed at one end in the axial direction. On the other hand, in the central portion of the lower surface of the upper auxiliary plate 22, there is formed a bottomed circular engaging recess 72 that opens to the lower surface on the central axis. Incidentally, the engaging convex portion 68 and the engaging concave portion 72 may be formed on either of the upper and lower auxiliary plates 22 and 20. As shown in FIG. When the upper and lower auxiliary plates 22 and 20 are superimposed, the engaging convex portion 68 is fitted into the engaging concave portion 72, thereby aligning the upper and lower auxiliary plates 22 and 20 with each other in the radial direction

It is designed to be In this embodiment, the engagement outer peripheral surface and the engagement inner peripheral surface are formed by the outer peripheral surface of the engaging protrusion 68 of the lower auxiliary plate 20 and the inner peripheral surface of the engaging recess 72 of the upper auxiliary plate 22. It is configured.

FIG.

9 shows a polishing apparatus 76 provided with a polishing pad auxiliary plate 74 as a fifth embodiment of the present invention.

[0078]

In this polishing pad auxiliary plate 74, a cylindrical engaging convex portion 78 projecting upward is formed on the outer peripheral portion of the upper surface of the lower auxiliary plate 20. This engaging projection 78 may be formed integrally with the lower auxiliary plate 20, or may form a fitting recess in the lower auxiliary plate 20 like the engaging projection in the fourth embodiment. Alternatively, a separate pin or the like may be fixed by press-fitting or the like. Also, as shown in FIGS. 10 and 11, a plurality of such engaging projections 78 are formed independently of each other at the outer peripheral portion of the lower auxiliary plate 20 at predetermined intervals in the circumferential direction. Particularly preferably, the plurality of engaging protrusions 78 are formed at regular intervals in the circumferential direction and positioned on the same circle on the central axis.

On the other hand, on the outer peripheral portion of the lower surface of the upper auxiliary plate 22, bottomed circular engagement grooves are provided at positions corresponding to the formation positions of the plurality of engaging projections 78 on the lower auxiliary plate 20, respectively. A concave portion 80 is formed to open downward. Incidentally, the engaging convex portion 78 and the engaging concave portion 80 may be formed on either of the upper and lower auxiliary plates 22 and 20. As shown in FIG. When the upper and lower auxiliary plates 22 and 20 are superimposed, the engaging convex portions 78 are fitted into the eng

aging concave portions 80, respectively, so that the upper and lower auxiliary plates 22 and 20 are positioned radially relative to each other

.

are designed to be matched. In the present embodiment, the outer circumferences of the lower auxiliary plate 20 and the upper auxiliary plate 22 are formed by the outer circumference of the engagement projection 78 of the lower auxiliary plate 20 and the inner circumference of the engagement recess 80 of the upper auxiliary plate 22. An engaging outer peripheral surface and an engaging inner peripheral surface located in a portion are configured. In particular, as in this embodiment, by adopting positioning means consisting of a plurality of engaging projections 78 and engaging recesses 80 independent in the circumferential direction, the superimposed upper and lower auxiliary plates 22, 20 can be diametrically aligned

.

Mutual positioning is possible not only in the direction but also in the circumferential direction. Instead of the plurality of independent engaging recesses 80 formed in the upper auxiliary plate 22,

a circumferential groove continuously extending circularly in the circumferential direction around the central axis of the upper auxiliary plate 22 may be employed. Alternatively, as shown in the sixth embodiment of the present invention in FIG. 12, a circular stepped surface 82 is formed around the central axis of the outer peripheral portion of the upper auxiliary plate 22 and extends over the entire circumference. By making the thickness dimension of the outer peripheral side smaller than 82, it is also possible to form an annular engagement concave portion 83 that has a notched cross-sectional shape that opens to the outer peripheral surface of the upper auxiliary plate 22 and that extends continuously all around in the circumferential direction. It is possible.

[0083]

In this way, in the upper auxiliary plate 22, the engaging surfaces of the engaging projections 78 of the lower auxiliary plate 20 are formed continuously over the entire circumference, so that when the upper and lower auxiliary plates 20 and 22 are superimposed, the upper and lower auxiliary plates 20 and 22 can be overlapped. Since it is no longer necessary to align the auxiliary plates 20 and 22 with each other in the circumferential direction, the mounting work can be easily performed.

FIG.

13 shows a polishing pad auxiliary plate 84 as a seventh embodiment of the present invention.

In this polishing pad auxiliary plate 84, the upper portion of the outer peripheral surface of the lower auxiliary plate 20 and the lower portion of the outer peripheral surface of the upper auxiliary plate 22 are each provided with a small diameter portion. By superimposing the upper and lower auxiliary plates 22 and 20, the small diameter portions of the upper and lower auxiliary plates 22 and 20 form an annular ring that extends across the entire circumference i

n the circumferential direction by widening a predetermined width across the upper and lower auxiliary plates 22 and 20. A shaped receiving recess 86 is formed. A groove-shaped engaging recess 88 is formed at the lower end of the small diameter portion of the lower auxiliary plate 20.

The engagement recess 88 opens to the outer peripheral surface of the lower auxiliary plate 20 at the bottom surface of the accommodation recess 86. Here, the bottom surface of the accommodation recess 86 refers to an annular surface extending over the upper and lower auxiliary plates 22 and 20 and extending in the vertical direction in FIG. On the other hand, a plate-shaped engaging projection 90 made of an elastic material is attached to the small-diameter portion of the upper auxiliary plate 22 that constitutes the accommodation recess 86 so that its proximal end is fixed by a fixing pin 92. The engaging protrusions 90 are accommodated in accommodation recesses 86 formed on the outer peripheral surfaces of the upper and lower auxiliary plates 22, 20 and extend from the upper auxiliary plate 22 onto the outer peripheral surface of the lower auxiliary plate 20. There is an engaging claw portion 94 formed at the tip portion of the engaging projection portion 90 is engaged with an engaging recess portion 88 formed in the small diameter portion of the lower auxiliary plate 20, and the engaging projection portion 90 is locked. It is held in a locked state based on elasticity.

Furthermore, a plurality of such engaging projections 90 are provided on the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20 at predetermined intervals in the circumferential direction. And attached to the outer peripheral surface of the upper auxiliary plate 22

Each of the engaging projections 90 is elastically pressed against the outer peripheral surface of the lower auxiliary plate 20, thereby forming positioning means for positioning the upper and lower auxiliary plates 22, 20 relative to each other on the central axis. Further, by engaging the engaging claw portion 94 of the engaging convex portion 90 with the engaging concave portion 88, a fixing means is also configured to hold the upper and lower auxiliary plates 22 and 20 in a superimposed state and apply a fixing force. There is. Instead of the engaging protrusions 90 having the engaging claws 94 that engage with the engaging recesses 88 as described above, for example, an eighth embodiment of the present invention shown in FIG

In addition, a connecting plate 100 extending across the upper and lower auxiliary plates 22 and 20 and superimposed on the bottom surface of the housing recess 86 is adopted, and both ends of the connecting plate 100 are connected to one of the upper and lower auxiliary plates 22 and 20. It is also possible to fix to the outer peripheral surface of the by connecting pins 102, 102. At least one of the connecting pins 102, 102 is detachable from the lower auxiliary plate 20 or the upper auxiliary plate 22, so that the connection of the upper and lower auxiliary plates 22, 20 by the connecting plate 100 can be released. , the attachment and detachment

t of the upper auxiliary plate 22 to which the polishing pad 16 is fixed with respect to the lower auxiliary plate 20 is permitted. The first fixing means 24 and the second fixing means 26 made of double-faced tape or the like shown in the first to eighth embodiments are used when removing the upper and lower auxiliary plates 22 and 20 and the rotating surface plate 14.

In addition, it is desirable to be held on the fixing surface on the side of a specific member. This facilitates handling of the upper and lower auxiliary plates 22, 20 and the first and second fixing means 24, 26 in a detached state. In addition, the fixing surfaces on which the first and second fixing means 24 and 26 remain are determined by making the fixing force of both surfaces of the first fixing means and the second fixing means 24 and 26 themselves different from each other. It is possible to set by differentiating the surface roughness, material, etc. of the fixed upper and lower auxiliary plates 22 and 20 and the rotating platen 14 from each other. In particular, it

is desirable that the first fixing means 24 is held on the fixing surface on the side of the lower auxiliary plate 20 when the lower auxiliary plate 20 is removed, becomes easier. On the other hand, as shown in FIG. 2 in the first embodiment, the second fixing means 26 is held on the fixing surface on the side of the upper auxiliary plate 22 when the upper auxiliary plate 22 is removed. Alternatively, it may remain on the upper surface of the lower auxiliary plate 20 as in the ninth embodiment of the present invention shown in FIG. By holding the second fixing means 26 on the fixing surface on the side of the upper auxiliary plate 22, the removed upper auxiliary plate 22 can be attached to the rotating surface plate of the device for reprocessing such as grooving of the polishing pad 16. At the time of mounting, it is also possible to use the second fixing means 26 held by the upper auxiliary plate 22 for mounting. On the other hand, by holding the second fixing means 26 on the fixing surface of the lower auxiliary plate 20, when mounting another upper auxiliary plate 22 with another polishing pad 16 mounted thereon to the lower auxiliary plate 20, it is also possible to attach using the second fixing means 26 held by the lower auxiliary plate 20.

Further, the engaging recesses 32, 44, 60, 72, 80, (83), 88 and the engaging projections 36, 46, 56,

70, 78, 90 shown in the first to seventh embodiments may be provided on opposite sides of the lower auxiliary plate 20 side and the upper auxiliary plate 22 side. For example, as the tenth embodiment of the present invention is shown in FIG. The stepped surface 30 and the engaging recess 32 may be formed on the upper auxiliary plate 22, while the stepped surface 34 and the engaging convex portion 36 forming the inner peripheral surface of the engagement may be formed on the lower auxiliary plate 20. It is possible.

[0092]

Furthermore, the engaging recesses 32, 44, 60, 72, 80, (83) and the engaging protrusions 36, 46, 56, 70, 78 shown in the first to sixth embodiments are overlapped with each other. It is also possible to form an inclination angle with respect to the outer peripheral surface of the en

gaging projection and the inner peripheral surface of the engaging recess for positioning the upper and lower auxiliary plates 22 and 20 by using the upper and lower auxiliary plates 22 and 20 as shown in FIG. For example, as an eleventh embodiment of the present invention is shown in FIG. On the other hand, while the engaging convex portion 36 is tapered in the inclined direction in which it gradually tapers in the projecting direction,

A stepped surface 30 serving as an engaging outer peripheral surface of an engaging recess 32 formed in the outer peripheral portion of the upper auxiliary plate 22 can be tapered at an inclination direction and an inclination angle corresponding to the stepped surface 34. As a result, the operation of fitting the engaging convex portion 36 into the engaging concave portion 32 and overlapping the upper and lower auxiliary plates 22, 20 can be further facilitated by using the tapers provided on both the stepped surfaces 34, 30 as guide surfaces. It becomes possible to do it easily. Incidentally, as shown in the twelfth embodiment of the invention shown in FIG. 18 and the thirteenth embodiment of the invention shown in FIG.

.

Even when adopting a plurality of projection-shaped engaging projections 78 formed independently in the direction and a plurality of hole-shaped engaging recesses 80 formed at respective corresponding positions of the upper auxiliary plate 22, the engagement A tapered portion 104 having a tapered shape can be formed by giving an inclination angle to the outer peripheral surface of the projecting tip portion of the convex portion 78. In FIG. 19, an engagement pin 106 formed separately is press-fitted into a fitting hole 105 formed in the lower auxiliary plate 20 to form the engagement convex portion 78. The lower end of the locking pin 106 also has a tapered portion 104 similar to the upper end. As a result, the locking pin 106 has no directivity and is easy to handle, and the operation of press-fitting it into the fitting hole 105 is also facilitated.

[0094]

Further, in the fourteenth embodiment of the present invention shown in FIG. 20, a straddle between the upper and lower auxiliary plates 22, 20 is used as a kind of positioning means for aligning the central axis of the upper and lower auxiliary plates 22, 20 in a superimposed state. A locating sleeve 108 is thus shown fitted over. The positioning sleeve 108 has an inner diameter that is the same as or slightly larger than the outer diameter of the upper and lower auxiliary plates 22 and 20, which are disk-shaped and have substantially the same outer diameter. Such a positioning sleeve 108 is used when superimposing the upper and lower auxiliary plates 22 and 20, and by superimposing the upper and lower auxiliary plates 22 and 20 within the positioning sleeve 108, the central axes of the upper and lower auxiliary plates 22 and 20 are aligned. They can be axially superimposed and secured to each other with a second securing means 26. Therefore, the positioning sleeve 108 can be removed after the upper and lower auxiliary plates 22 and 20 are superimposed and fixed to each other, thereby positioning the upper and lower auxiliary plates 22 and 20 so as to protrude on the outer peripheral surface. It is possible to attach them to each other without means and in precise alignment.

[0095]

Furthermore, in the fifteenth embodiment of the present invention shown in FIG. 21, a slit-shaped engagement groove 110 is formed extending across the overlapping direction when the upper and lower auxiliary plates 22 and 20 are overlapped. The engaging grooves 110 are open to the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20 and have a predetermined depth radially inward. It is a plate-shaped engaging plate 112 is fitted into the engaging groove 110 from the opening of the outer peripheral surface, so that the upper and lower auxiliary plates 22 and 20 are positioned by the engaging plate 112 and is in a connected state. Although the engaging plate 112 is formed separately from the upper and lower auxiliary plates 22 and 20, it may be formed integrally with one of the upper and lower auxiliary plates 22 and 20 so as to protrude toward the other. In that case, the engagement groove 110 is formed only in the other auxiliary plate.

Furthermore, in the sixteenth embodiment of the present invention shown in FIG. 22 ,

a fitting recess 114 is formed as an engaging recess opening in the lower surface of the upper auxiliary plate 22 . In particular, in this embodiment, the fitting recess 114 is formed as an annular groove extending continuously in the circumferential direction around the central axis of the upper auxiliary plate 22 . On the other hand, the lower auxiliary plate 20 has a fitting convex portion 116 as an engaging convex portion that protrudes upward on the upper surface that overlaps with the upper auxiliary plate 22 . In addition, in this embodiment, the fitting protrusion 116 is formed as an annular protrusion corresponding to the fitting recess 114 . When the upper and lower auxiliary plates 22 and 20 are superimposed, the fitting convex portion 116 is positioned so as to enter the fitting concave portion 114 .

[0097]

The fitting projection 116 has a hollow structure, and the inside of the fitting projection 116 is provided with an external space.

A fluid reservoir 118 is formed which is sealed between them. Further, at least the inner peripheral wall and the outer peripheral wall of the wall portion of the fitting convex portion 116 that defines the fluid reservoir 118 are bulged and deformable in the radial direction. Specifically, for example, by forming the fitting convex portion 116 with a rubber elastic material or the like, it is possible to realize an inner peripheral wall that can bulge radially inward and an outer peripheral wall that can bulge radially outward. Further, the lower auxiliary plate 22 is formed with a fluid passage 120 that communicates with the fluid reservoir 118 and extends radially outward and opens to the outer peripheral surface.

A pressure screw 122 is screwed into the end opening. In addition, a sealed area composed of the fluid passage 120 and the fluid reservoir 118 sealed by the pressurizing screw 122 is filled with an incompressible fluid such as oil.

Thus

, by screwing the pressure screw 122, the internal pressure of the fluid reservoir 118 can be

increased through the fluid passage 120, and the inner and outer peripheral walls of the fluid reservoir 118 can be expanded outward. As a result, the fitting convex portion 116 is expanded and pressed against the inner surface of the fitting concave portion 114, so that the upper and lower auxiliary plates 22 and 20 can be positioned by mutual frictional force and the like, and can also exert a fixing force. there is

When removing the upper auxiliary plate 22 from the lower auxiliary plate 20 ,

the pressure screw 122 is rotated in the direction of loosening and moved to the outer peripheral side of the lower auxiliary plate 20, whereby the fluid reservoir 118 is removed. , the pressing force of the fitting protrusion 116 against the fitting recess 114 can be released.

[0101]

In addition, although not listed individually, the present invention can be implemented with various changes, modifications, improvements, etc. based on the knowledge of those skilled in the art. It is also possible to attach an O-ring or a sealing material to the portion to prevent foreign matter from entering the overlapping surfaces of the upper and lower auxiliary plates.

In addition to the auxiliary plates 20 and 22 having the two-layer structure described above, it

is also possible to add additional auxiliary plates in a laminated state and fixed by fixing means. By adopting the auxiliary plate of the third layer in this way, it becomes possible to realize an elastic support state or to dispose of the intermediate layer.

[Description of Reference Symbols]

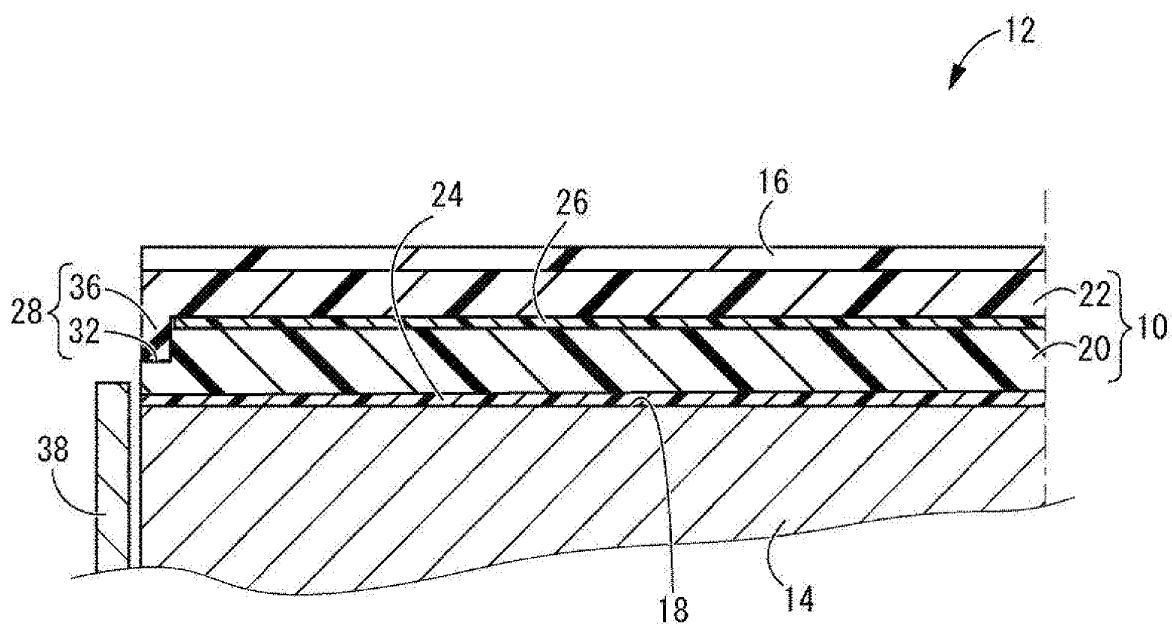
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, 40, 50, 64, 74, 84: polishing pad auxiliary plate, 12, 42, 52, 66, 76: polishing device, 14: rotating platen, 16: polishing pad, 18: upper surface, 20: lower auxiliary plate, 22: upper auxiliary plate, 24: first fixing means, 26, 62: second fixing means, 28: positioning means, 30, 58: step surface (engagement outer circumference surface), 32, 44, 60, 72, 80, 88: engagement concave portion, 34, 54: step surface (engagement inner peripheral surface), 36, 46, 56, 68, 78, 90: engagement convex portion, 38: Protective member

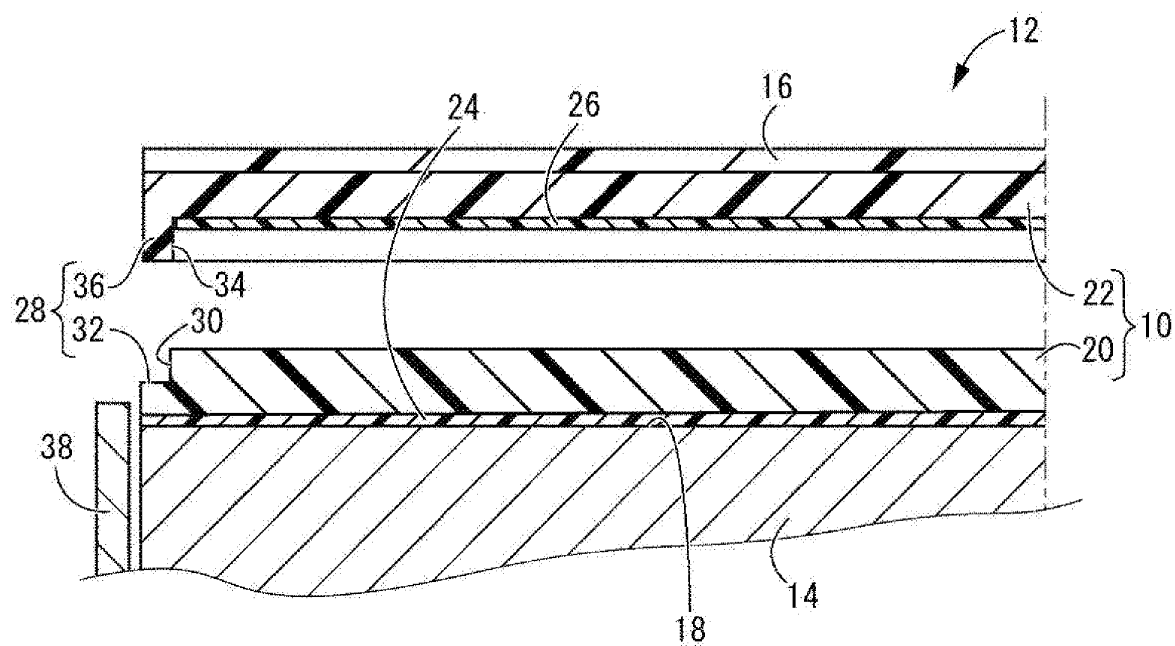
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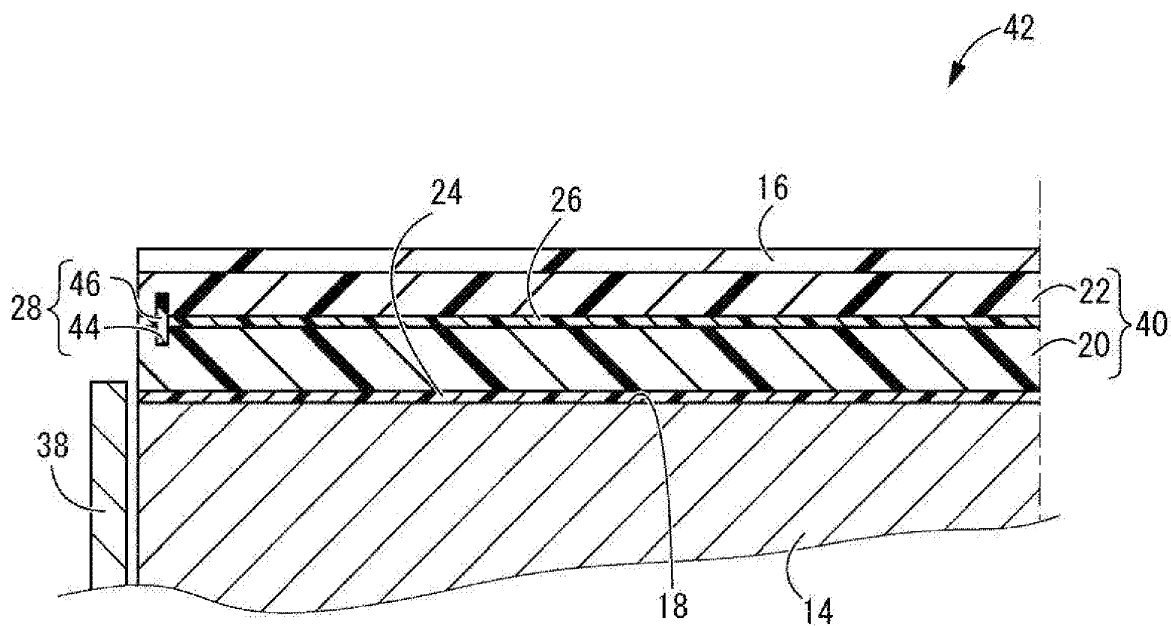
[Fig. 1]



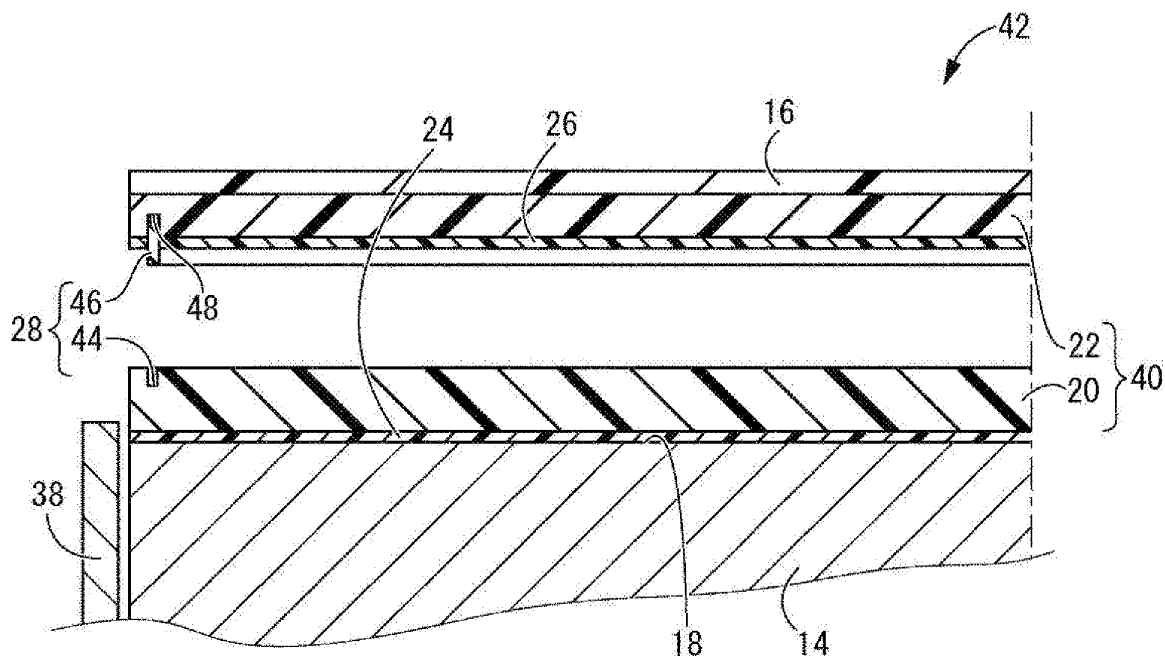
[Figure 2]



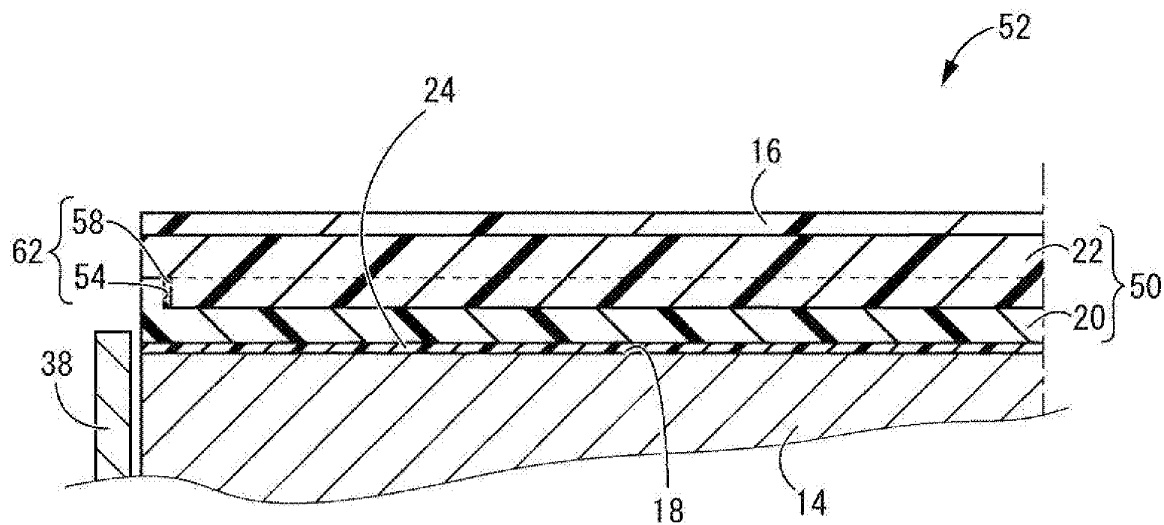
[Figure 3]



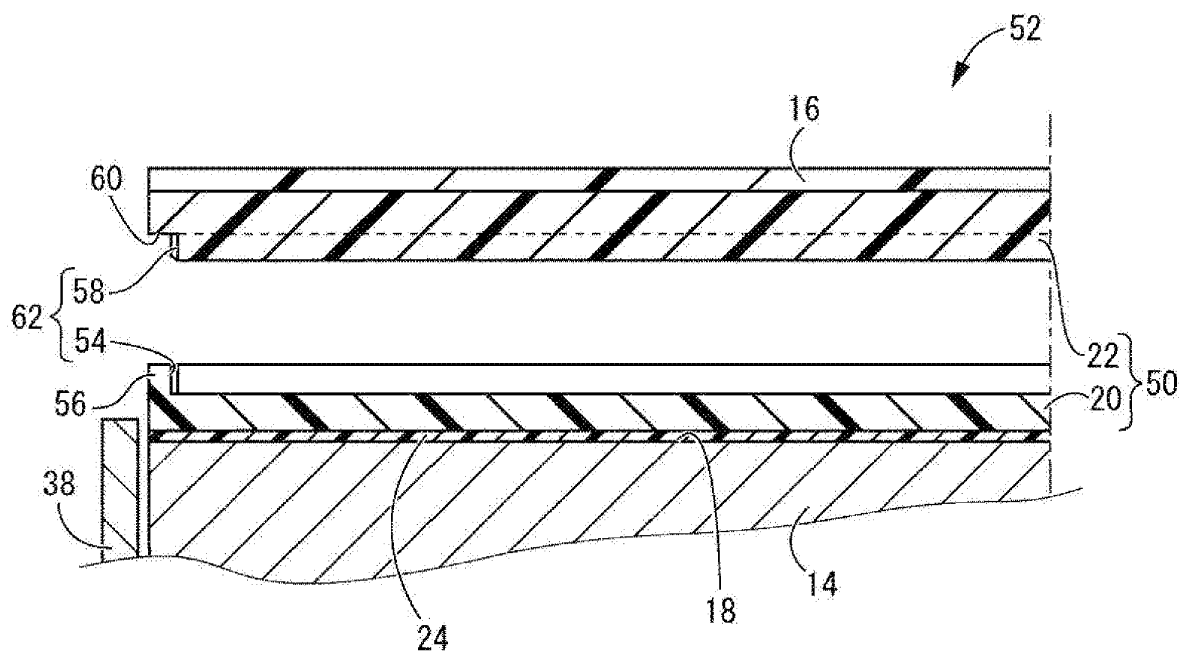
[Figure 4]



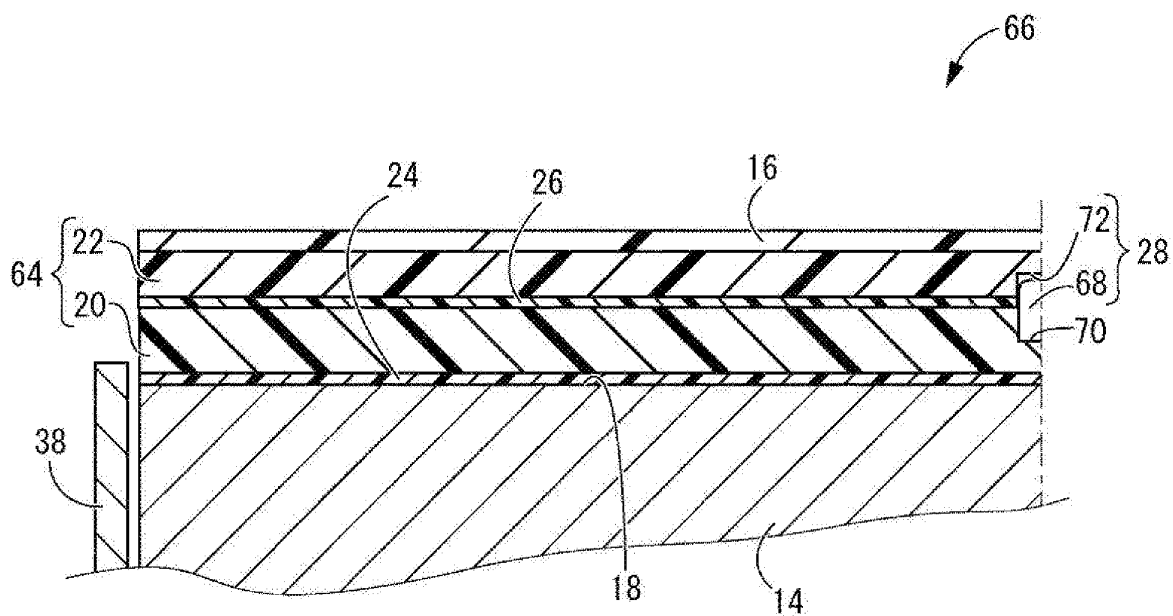
[Figure 5]



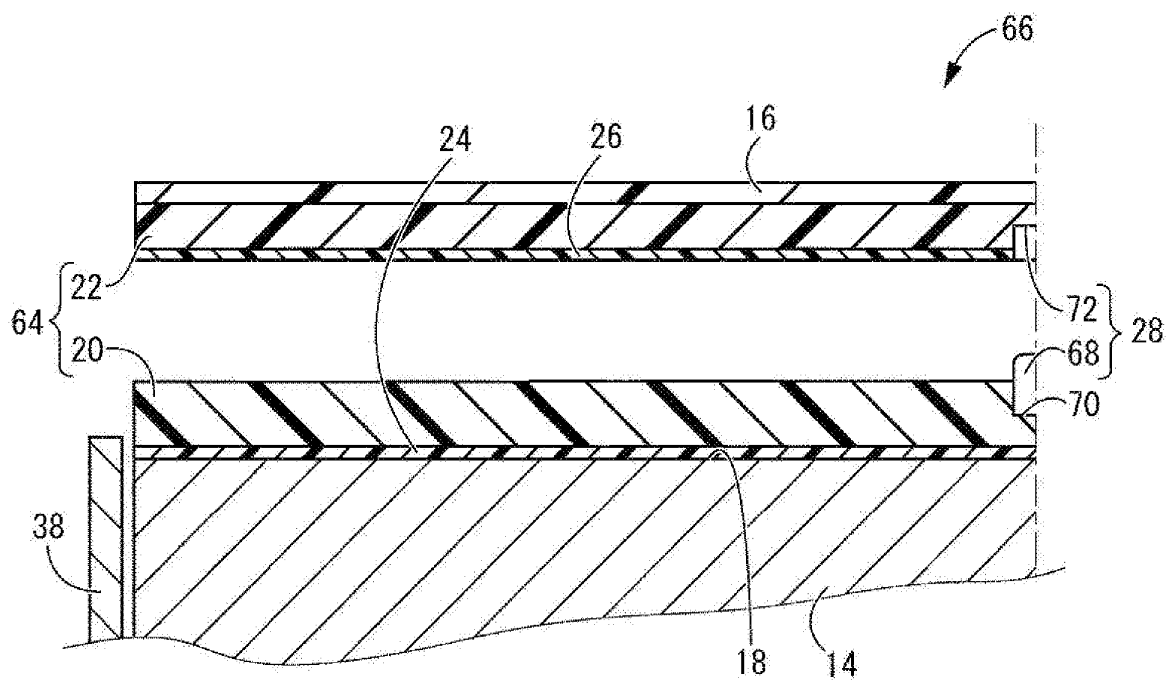
[Fig. 6]



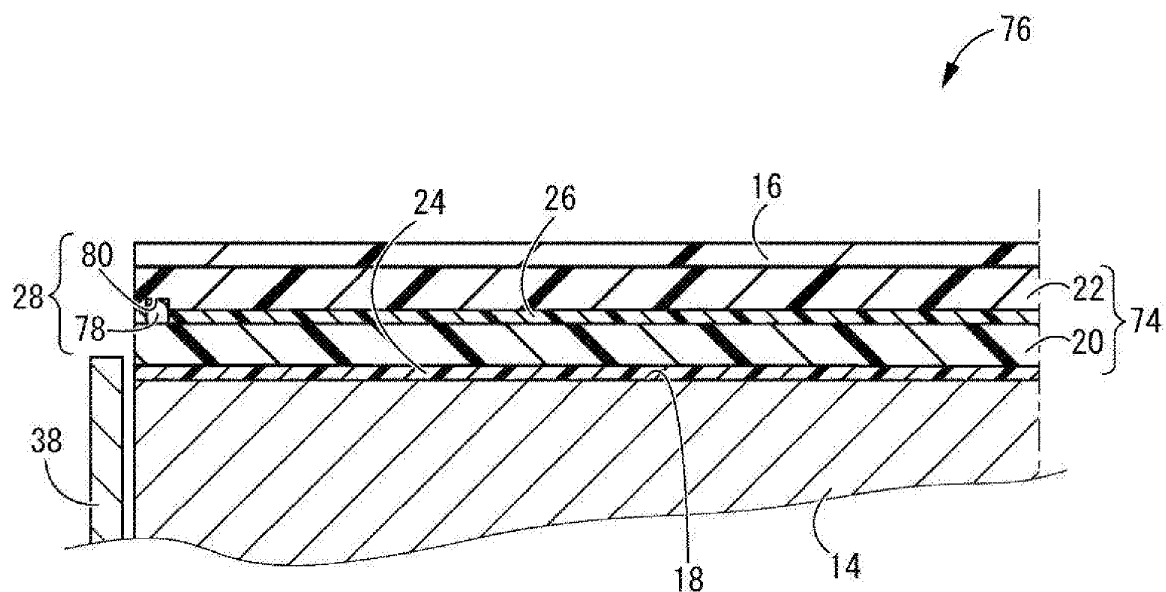
[Fig. 7]



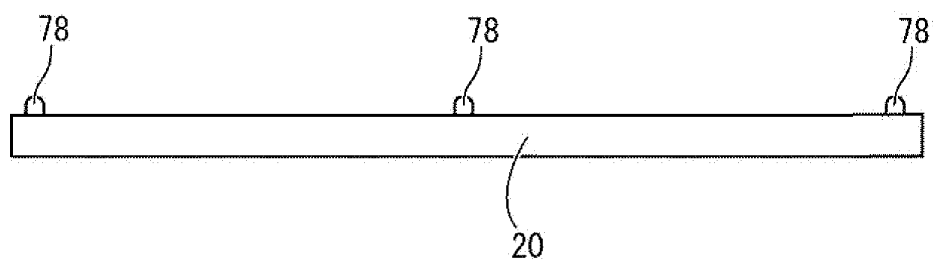
[Fig. 8]



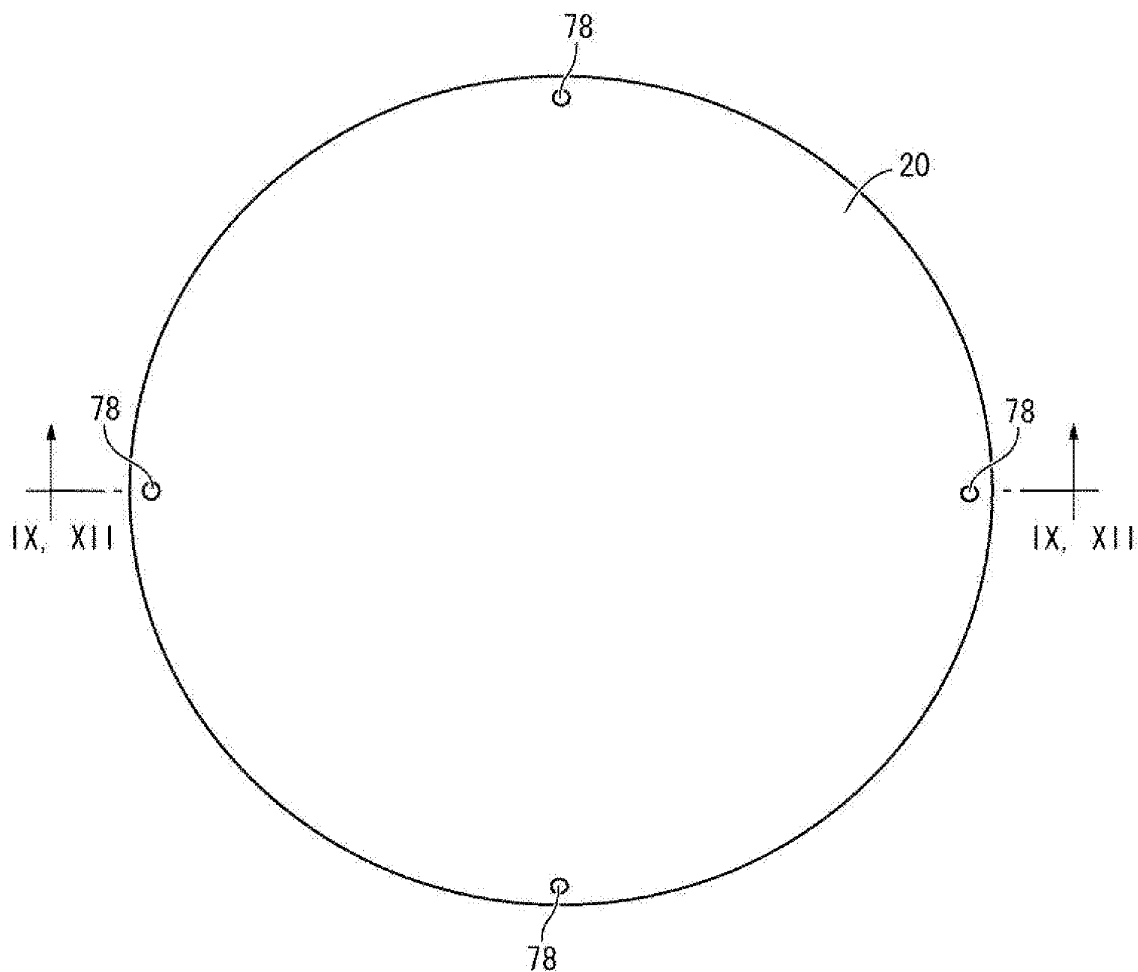
[Fig. 9]



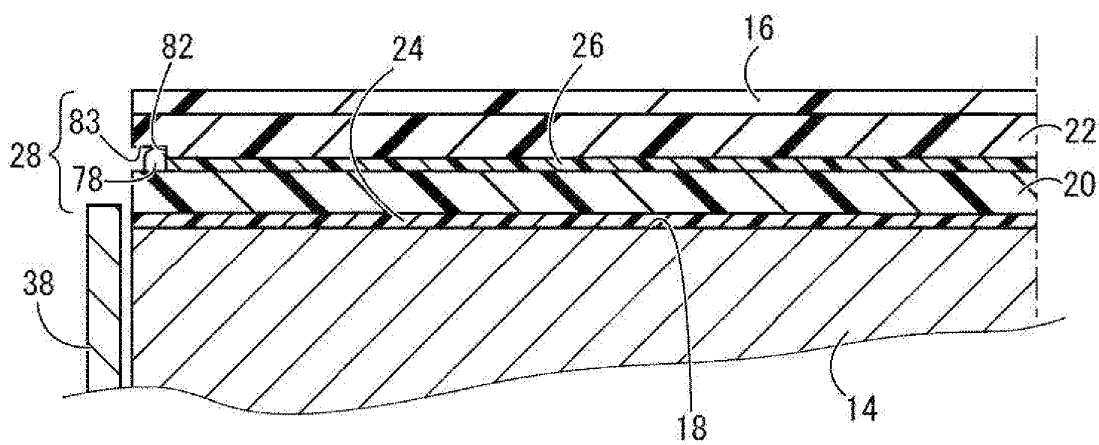
[Fig. 10]



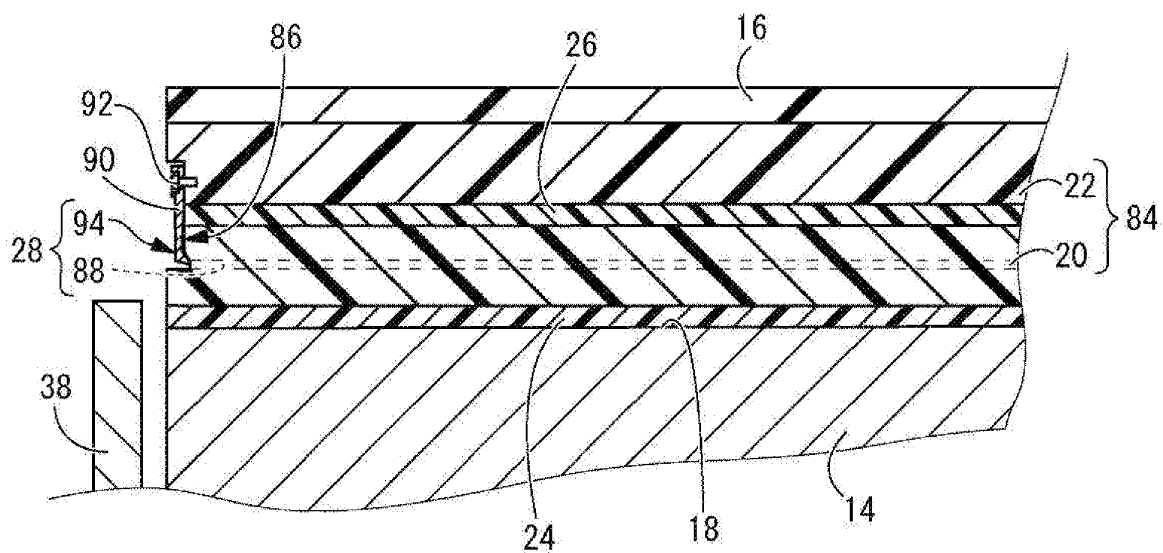
[Fig. 11]



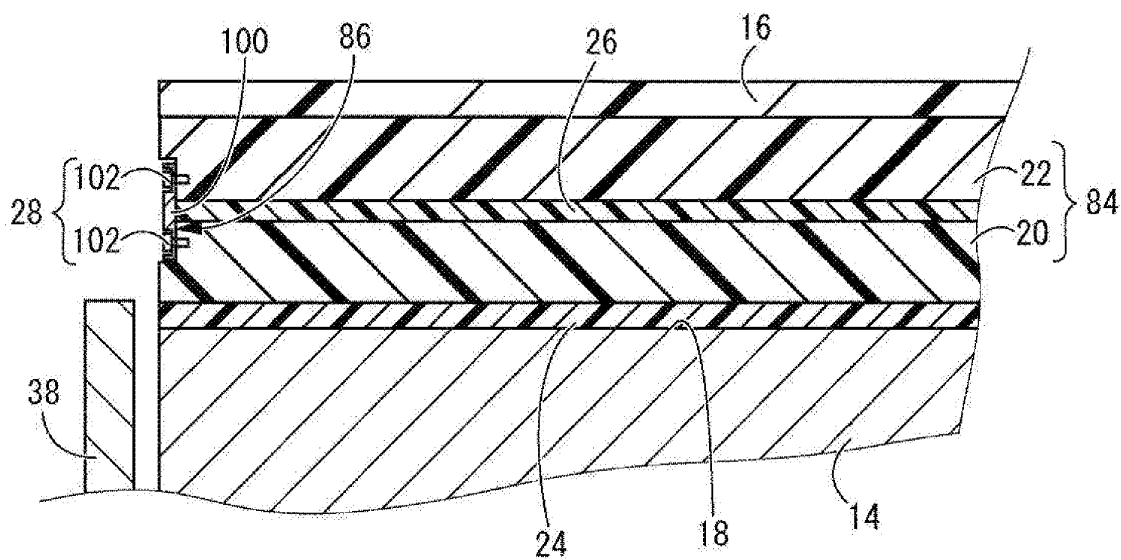
[Fig. 12]



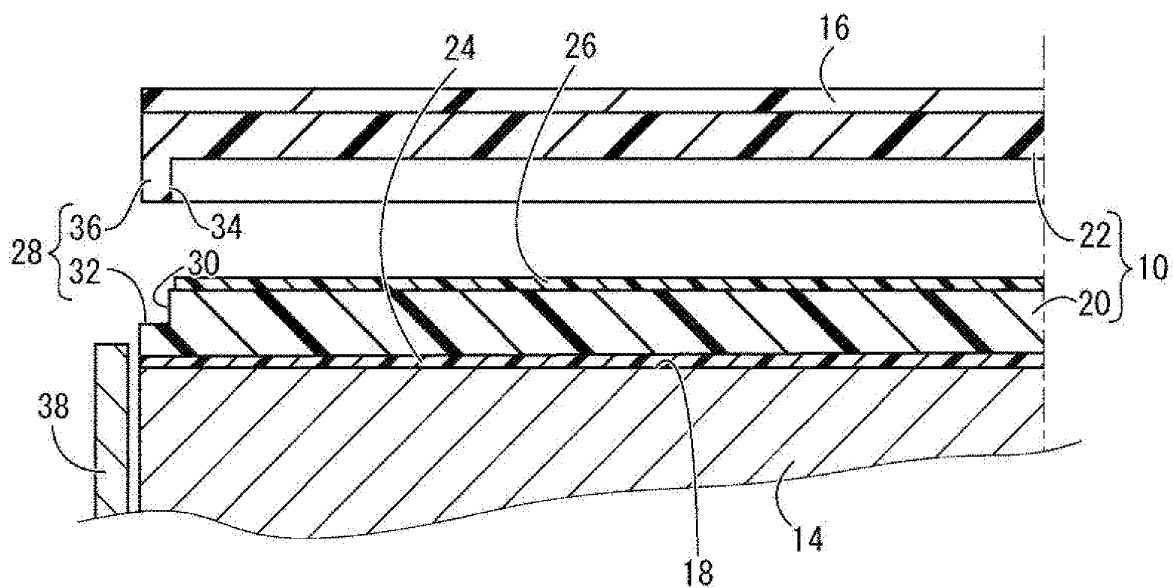
[Fig. 13]



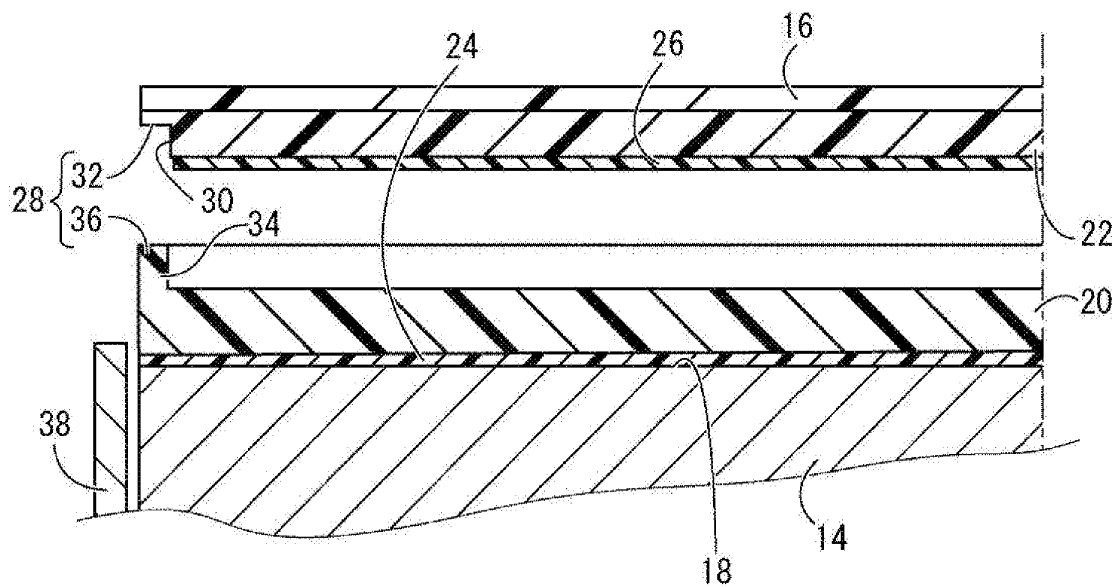
[Fig. 14]



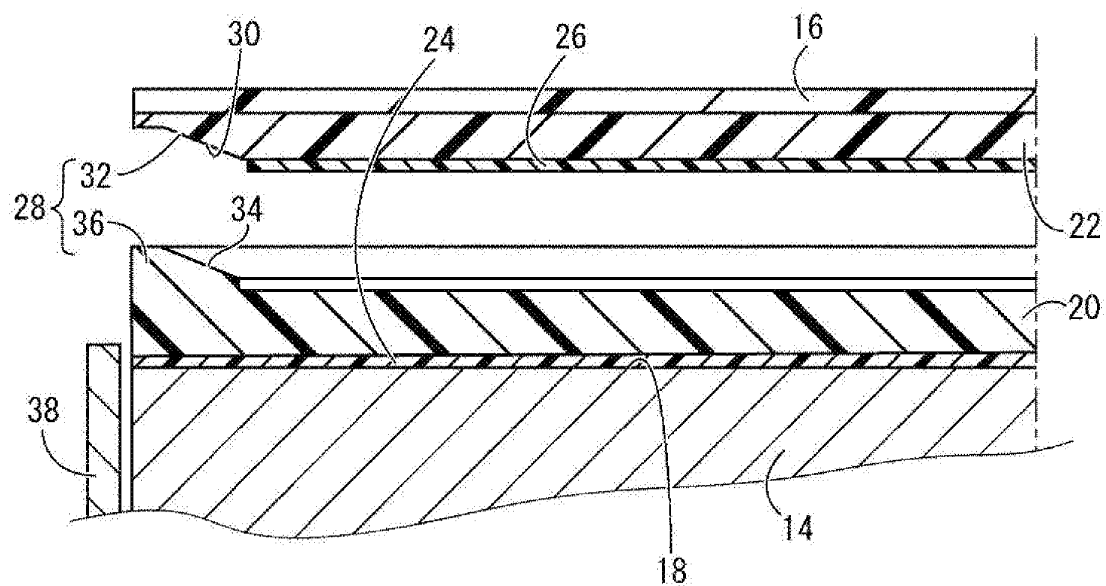
[Fig. 15]



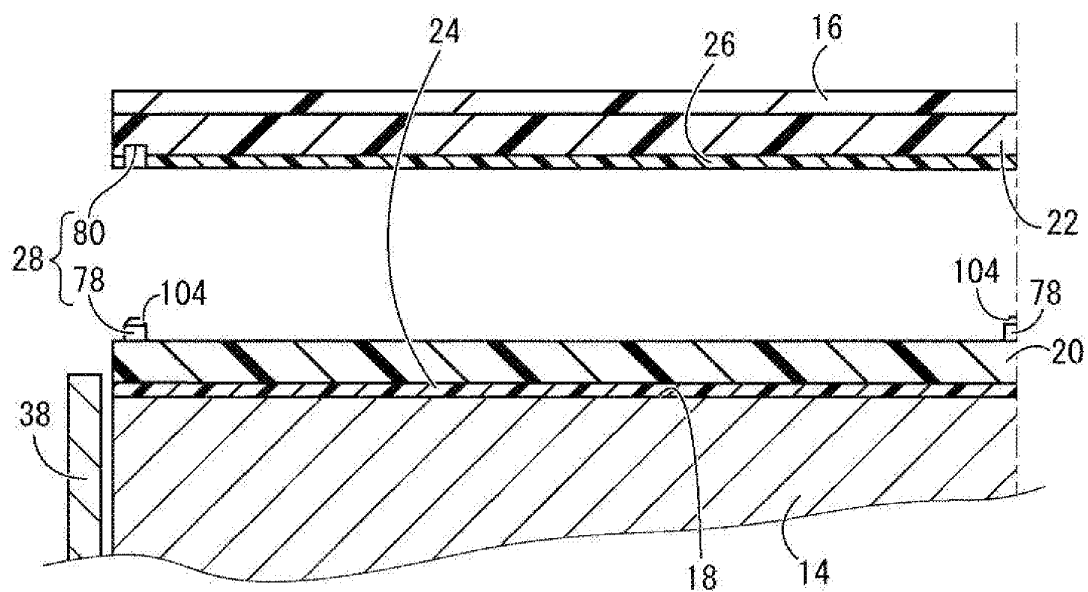
[Fig. 16]



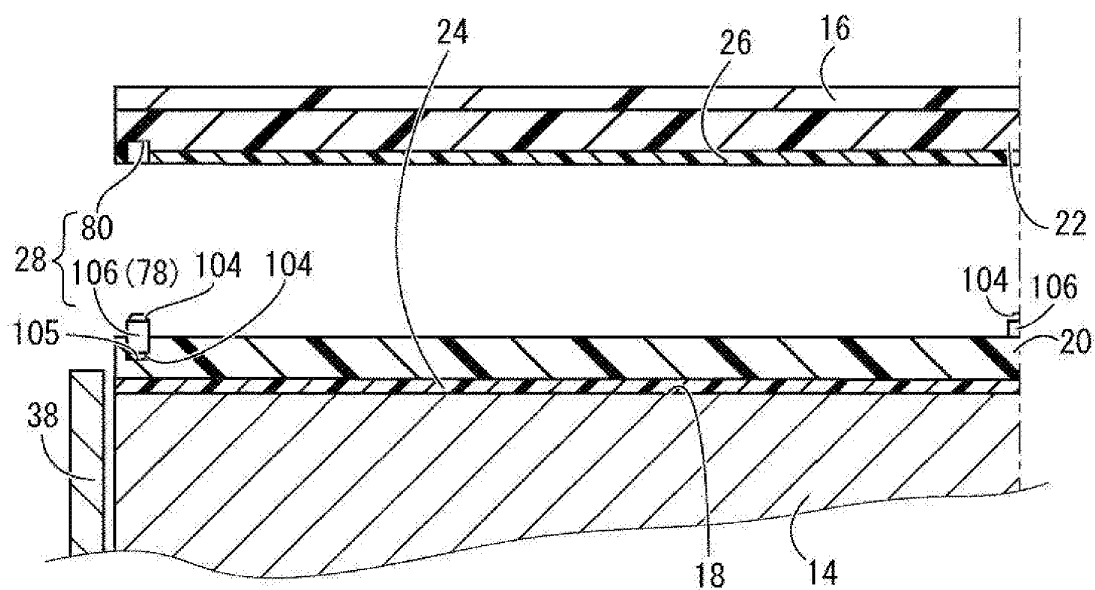
[Fig. 17]



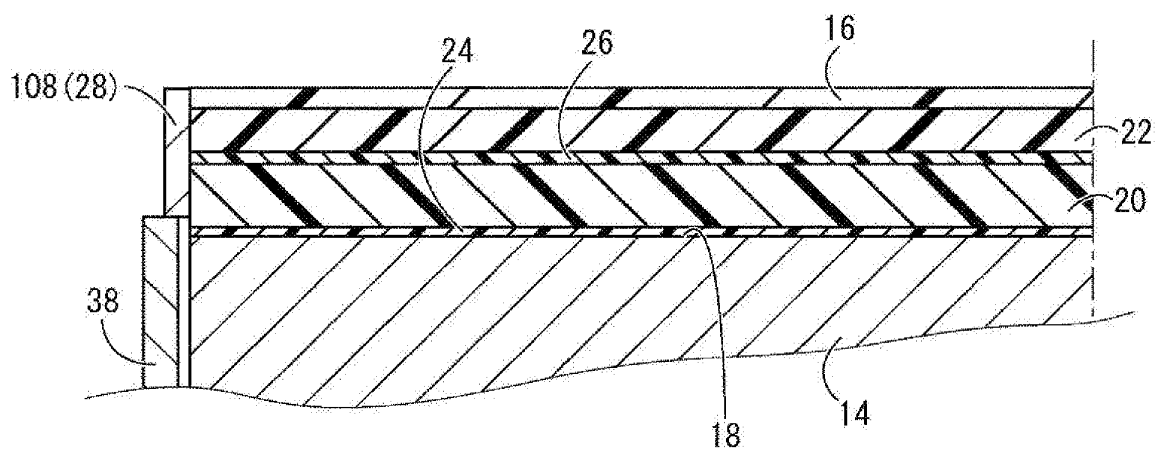
[Fig. 18]



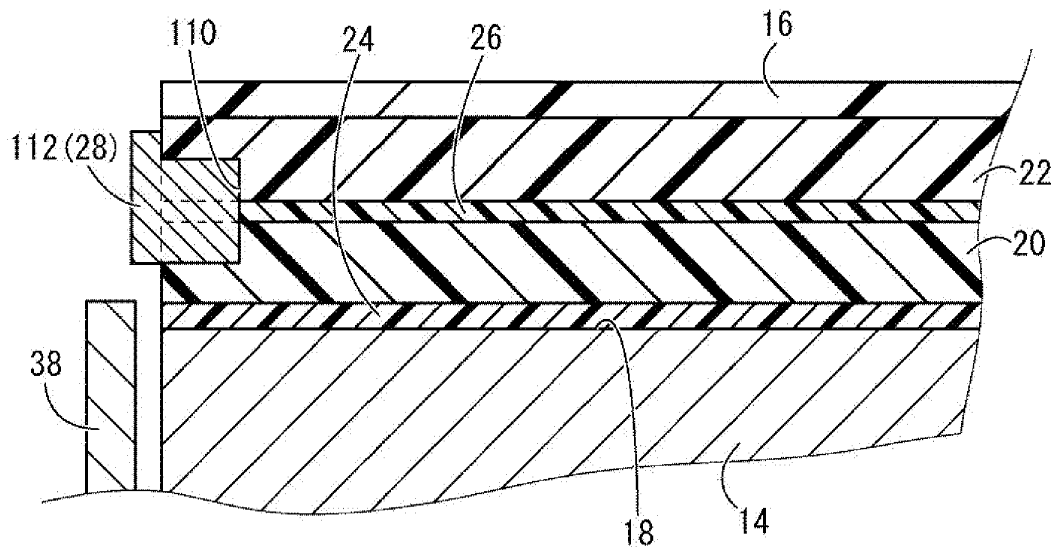
[Fig. 19]



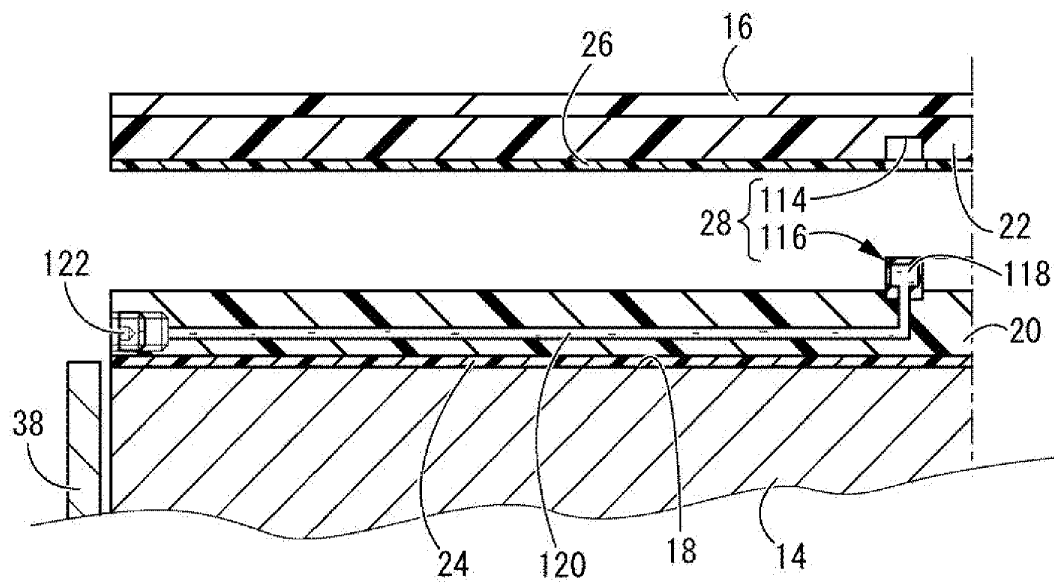
[Fig. 20]



[Fig. 21]



[Fig. 22]



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1 | 2 | 3 | Four | Five | 6 | 7 | 8 | 9 | Ten | ...

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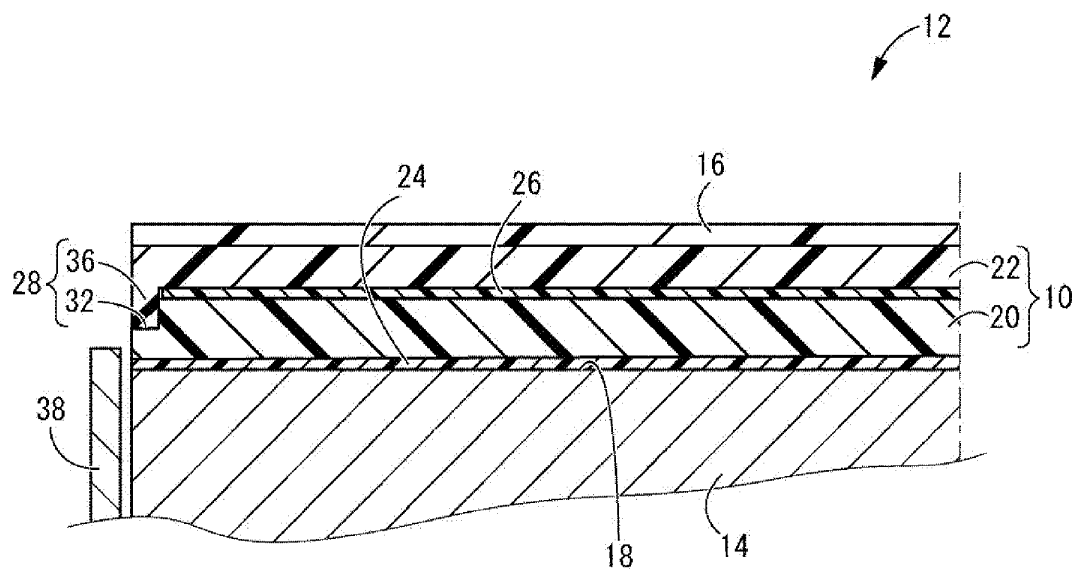


Figure 1

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(54) [Title of Invention] Auxiliary Plate for Polishing Pad and Equipped with Auxiliary Plate for Polishing Pad Polishing Apparatus

(51) [International Patent Classification]

B24B 37/12 (2012.01)

[FI]

B24B 37/04 A

[Number of Claims] 11

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2014) [Matters to be stated regarding results of research commissioned by the government] (report by applicant) commissioned by the government Patent application related to research results (FY2010 Ministry of Economy, Trade and Industry "Strategic Fundamental Technology Advancement Support Project" commissioned research, patent application subject to Article 19 of the Industrial Technology Enhancement Act) (73) [Patentee] [Identification number] 599 096053

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(72) [Inventor]

[Name] Eiji Suzuki

[Examiner] Takashi Kameda

(56) [References] [Reference] Japanese Patent Application

Laid- Open No. 08- 118231 (JP.A) [Reference] JP-A-07-328915 (JP.A) (58) [Field investigate d] (Int.Cl., DB name) B24B 37/12 H01L 21/304...

The scope of the claims

open

(57) [Scope of Claims]

[Claim 1] A

polishing pad auxiliary plate mounted on a rotating surface plate of a polishing apparatus for detachably attaching a polishing pad to the rotating surface plate, wherein

:

a first fixing means for fixing the lower auxiliary plate to the rotating surface plate; and
a pad supporting surface on which the polishing pad is superposed and fixed. an upper auxiliary plate superimposed on the upper surface of the lower auxiliary plate;

second fixing means for fixing the upper auxiliary plate to the lower auxiliary plate;

the lower auxiliary plate and the upper side; positioning means for aligning the center axis of the auxiliary plate with respect to each other

, and the lower auxiliary plate is fixed to the rotating surface plate of the polishing apparatus by the first fixing means. By removing the upper auxiliary plate from the lower auxiliary plate held and fixed to the rotating surface plate, the polishing pad can be rotated while being fixed to the pad supporting surface of the upper auxiliary plate. The upper auxiliary plate can be removed from the surface plate, and the removed upper auxiliary plate can be fixed and attached again to the lower auxiliary plate while being aligned by the positioning means, and,

the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is smaller than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means;

Auxiliary plate for a polishing pad, characterized in that :

[Claim 2]

2. The auxiliary plate for a polishing pad according to claim 1 , wherein said positioning means is located inside the outer peripheral surfaces of said lower auxiliary plate and said upper auxiliary plate.

3. The positioning means

includes an engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate and protruding toward the other, and the lower auxiliary plate and the upper auxiliary plate. 3. An auxiliary plate for a polishing pad according to claim 2 , wherein said auxiliary plate for a polishing pad comprises an engaging concave portion provided on the other side thereof and with which said engaging convex portion is engaged .

4. The polishing pad according to claim 3

, wherein said engaging projections and said engaging recesses are formed with engaging portions located on the outer peripheral portions of said lower auxiliary plate and said upper auxiliary plate. Auxiliary plate. 5. An annular engagement in which the engaging portions of the engaging protrusion and the engaging recess extend continuously in the circumferential direction of the lower auxiliary plate and the upper auxiliary plate and are fitted to each other. 5. The auxiliary plate for a polishing pad according to claim 4 , comprising an outer peripheral surface and an engaging inner peripheral surface . 6. At a plurality of locations on the circumference of the outer peripheral portions of the lower auxiliary plate and the upper auxiliary plate

e, the lower auxiliary plate and the upper auxiliary plate are overlapped on one side toward the other. The engaging concave portion that opens and the engaging convex portion that protrudes toward one side of the other of the mutual overlapping surfaces of the lower auxiliary plate and the upper auxiliary plate are formed at positions corresponding to each other, wherein said engaging portion is formed by fitting said engaging convex portion into said engaging concave portion.

5. The polishing pad auxiliary plate according to 4.
7.

The engaging protrusions projecting from a plurality of locations on the circumference of one of the lower auxiliary plate and the upper auxiliary plate toward the other are formed of an elastic material, and the engagement portion is formed by engaging the tip of the engagement projection with the engagement recess provided in the outer peripheral surface of the other of the side auxiliary plate and the upper auxiliary plate. 5. The polishing pad auxiliary plate according to claim 4.

8. A polishing pad auxiliary plate according to claim 3

, wherein said engaging projections and said engaging recesses are provided on the central axes of said lower auxiliary plate and said upper auxiliary plate. 9. An outer peripheral surface of said engaging projection and an inner peripheral surface of said engaging recess are formed with screw grooves for engaging with each other, and said engaging projection and said engaging portion constituting said positioning means are formed with thread grooves for engaging with each other. 9. The auxiliary plate for a polishing pad according to claim 8, wherein said second fixing means is formed by screwing with said mating recess. 10. The engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate is formed of the same material as one of the lower auxiliary plate and the upper auxiliary plate. The auxiliary plate for a polishing pad according to any one of claims 3, 4, 5, 6, 8 and 9.

11. The auxiliary plate for a polishing pad according to any one of claims 1 to 10 is mounted on the upper surface of a rotating surface plate, and a protective member is provided on the outer peripheral side of the rotating surface plate with a gap

therebetween. 11. The positioning means according to any one of claims 1 to 10, wherein the positioning means is disposed on the inner peripheral side of the outer peripheral end faces of the rotating platen and the polishing pad auxiliary plate. 2. A polishing apparatus comprising the polishing pad auxiliary plate according to 1 or 2 above.

detailed description

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Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to the polishing of substrates such as silicon wafers, semiconductor substrates, glass substrates, etc., which are workpieces requiring high flatness accuracy. It relates to a related technique, and more particularly to a technique that makes it possible to reuse a polishing pad used in polishing the surface of such a substrate.

is. 2.

Description of the Related Art As is well known, in manufacturing a semiconductor, a polishing process is performed to flatten the surface of a substrate such as a silicon wafer, a semiconductor substrate, a glass substrate, or the like. Such a polishing process generally involves fixing a disc-shaped polishing pad made of a resin material or the like directly on a rotating surface plate of a polishing apparatus with a double-sided tape, and supplying a polishing liquid containing abrasive grains to the polishing pad. Polishing is performed by rotating the substrates relative to each other. [0003] Polishing pads for carrying out such a polishing process are made of foamed or non-foamed urethane or the like, as described in Japanese Patent Application Laid-Open No. 2002-11630 (Patent Document 1). A resin pad is used. Further, in many cases, the polishing surface of such a polishing pad is provided with grooves such as concentric circles, grids, or radial grooves, or the bubbles of foamed resin are opened. [0004] By the way, when performing a polishing process using a polishing pad, when changing the type of substrate to be polished, the polishing pad used for the polishing process is peeled off from the rotating platen and replaced with another polishing pad. sometimes you have to. Also, for example, when a polishing pad that has deteriorated due to polishing is to be re-processed, such as by grooving the surface, with another processing device for the purpose of reusing the polishing pad, the polishing pad is removed from the rotating platen. Needs to be pulled off. [0005]

However, since the thin disk-shaped polishing pad is firmly fixed to the rotating surface plate

of the polishing apparatus with an adhesive tape, when the polishing pad is peeled off from the rotating surface plate, Damage such as bending, breaking, wrinkling, and tearing is likely to occur. Therefore, due to such damage, there is often a problem that such polishing pads cannot be reused and must be discarded even though their service life has not expired.

[0006]

Moreover, the work of peeling off the polishing pad from the rotating surface plate while paying close attention not to damage it requires skill and caution, and there is also the problem of placing a heavy burden on the operator. In addition, since it takes a considerable amount of time to peel off the polishing pad from the rotating surface plate, the polishing apparatus, which is expensive and valuable equipment, must be stopped for a long time, which shortens the operation time of the equipment. There was also the problem that the

[0007]

Therefore, the present inventor previously described in Japanese Patent Application Laid-Open No. 2010-214579 (Patent Document 2) that an auxiliary plate is attached to the back surface of the polishing pad, and the polishing pad is rotated by the polishing apparatus through this auxiliary plate. We proposed a polishing pad with an auxiliary plate that is fixed to the surface plate with double-sided tape. With such a polishing pad with auxiliary plate, since the polishing pad is attached to and detached from the rotating surface plate while being supported by the auxiliary plate, damage to the polishing pad during attachment and detachment is reinforced by the auxiliary plate. Therefore, it is possible to attach and detach the polishing pad to and from the rotating platen with good workability while preventing the polishing pad from being damaged.

[0008]

However, as a result of further studies and studies by the present inventors, it has been found that it is difficult to say that the polishing pad with an auxiliary plate proposed in Patent Document 2 is easily compatible with all polishing apparatuses.

[0009]

That is, when the polishing pad is overlaid and fixed to the rotating surface plate, it is necessary to align the center of the polishing pad with the rotation center of the rotating surface plate. Accuracy is required for center alignment. If the number of attachment/detachment of the polishing pad to/from the rotating platen increases by adopting the auxiliary plate as described above, it becomes more difficult and labor-intensive to align the center position when attaching the polishing pad to the rotating platen.

It becomes a problem. Further, in the polishing pad with auxiliary plate proposed in Patent Document 2, in order to detachably attach the auxiliary plate while aligning the center of the auxiliary plate with respect to the rotary surface plate, the following are provided between the auxiliary plate and the rotary surface plate

:

For example, fixing means such as an outer peripheral ring may be provided on the outer periphery

peripheral surface of the rotating surface plate. On the other hand, in some polishing apparatuses, a protective cover or the like is attached to the outer peripheral side of the rotary platen, so that the space on the outer peripheral side of the rotary platen is extremely narrow. Therefore, if such an outer peripheral ring were to be adopted, and a polishing device with a narrow space on the outer peripheral side of the rotating surface plate was used, there was a possibility that the polishing device would need to be modified. of.

[Prior Art Documents]

[Patent Documents]

[0011]

[Patent Document 1] [Japanese Unexamined Patent Application Publication No. 2002-11630](#) [Patent Document 2] [Japanese Unexamined Patent Application Publication No. 2010-214579](#) [Summary of the Invention] [Problems to be Solved by the Invention] SUMMARY OF THE INVENTION It is an object of the present invention to provide a polishing pad which can be easily attached to and detached from a rotating surface plate while sufficiently securing the fixing force of the polishing pad to the rotating surface plate. For a polishing pad with a novel structure, which can prevent damage to the polishing pad when the polishing pad is removed from the rotating platen, and which can be advantageous for reuse of the polishing pad, for example. To provide an auxiliary plate. [0013]

In addition, according to the present invention, the work of aligning the center when mounting the polishing pad on the rotating surface plate can be performed easily and accurately, and the labor burden can be reduced. Another object of the present invention is to provide an auxiliary plate for a polishing pad with an improved structure, which can be easily and advantageously applied to a rotating surface plate in a polishing machine without requiring any special modification. A further object of the present invention is to provide a polishing apparatus having such a novel polishing pad auxiliary plate

. Means for Solving the Problems In order to solve the above problems, a first aspect of the present invention relating to an auxiliary plate for a polishing pad is: (A) mounted on a rotating surface plate of a polishing apparatus; A polishing pad auxiliary plate for detachably attaching a pad to the rotary platen, comprising: (B) a lower auxiliary plate disposed on the upper surface of the rotary platen; and (C) the lower auxiliary plate. and (D) a pad supporting surface on which the polishing pad is superimposed and fixed, which is superimposed on the upper surface of the lower auxiliary plate. (E) a second fixing means for fixing the upper auxiliary plate to the lower auxiliary plate; The lower auxiliary plate is held in a fixed state by the first fixing

g means to the rotating surface plate of the polishing apparatus, and is fixed to the rotating surface plate. Further, by removing the upper auxiliary plate from the lower auxiliary plate, the polishing pad can be removed from the rotating surface plate while being fixed to the pad supporting surface of the upper auxiliary plate. At the same time, it is possible to attach the removed upper auxiliary plate to the lower auxiliary plate by fixing it again in a state of being aligned by the positioning means.

and the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is stronger than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means. It features a smaller auxiliary plate for the polishing pad. In the polishing pad auxiliary plate constructed according to the present invention, the polishing pad is composed of the upper auxiliary plate and the upper auxiliary plate

.

It is fixedly attached to the rotating surface plate via the lower auxiliary plate. Thereby, the upper auxiliary plate can be removed from the lower auxiliary plate while the lower auxiliary plate is fixed to the rotating surface plate, and the polishing pad can be removed from the rotating surface plate while being fixed to the upper auxiliary plate. becomes possible. Therefore, in a state in which the polishing pad is reinforced and protected by the upper auxiliary plate, the polishing pad can be removed from the rotating surface plate while preventing damage to the polishing pad, and the thin polishing pad can be easily handled

.

becomes. For example, when the polishing pad is repeatedly attached and detached when the object to be polished or the polishing conditions are changed, or when the worn polishing pad is detached and reattached after reprocessing, the attachment and detachment of the polishing pad to and from the rotating platen and the polishing are difficult. It is also possible to easily perform operations such as reproduction processing for pads. Moreover, since the lower auxiliary plate still fixed to the rotating surface plate and the upper auxiliary plate removed together with the polishing pad are aligned with each other by the positioning means, the position on the rotating surface plate can be easily adjusted

.

The attachment and detachment work of the polishing pad, which requires alignment, can be performed more easily. In particular, since the positioning means is provided between the lower auxiliary plate and the upper auxiliary plate, there is no need to apply special processing or the like to the rotating surface plate. In addition, it is possible to prevent such positioning means from protruding to the outer peripheral side of the rotating surface plate. applicable without In the polishing pad auxiliary plate according to the first aspect of the present invention

, the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is smaller than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means; A certain aspect is employed. According to the first aspect, the fixing forces of the first and second fixing means are mutually adjusted, so that the upper auxiliary plate to which the polishing pad is fixed can be rotated. This makes it easier to remove the lower auxiliary plate that is still fixed to the surface plate. In short, there is no need for a special operation or the like to keep the lower auxiliary plate fixed to the rotating platen, and the polishing pad can be attached to the upper supporting plate while the lower auxiliary plate remains fixed to the rotating platen. It becomes possible to easily remove the plate from the rotating surface plate while it is fixed to the plate. According to a second aspect of the present invention, in the polishing pad auxiliary plate according to the first aspect, the positioning means is arranged on the inner peripheral side of the outer peripheral surfaces of the lower auxiliary plate and the upper auxiliary plate. It is located and provided. [0022] In the polishing pad auxiliary plate of this aspect, the projection of the upper and lower auxiliary plates to the outer peripheral side of the positioning means is completely avoided. Therefore, for example, even when the outer diameter of the upper and lower auxiliary plates is set to be the same as or slightly smaller than the outer diameter of the rotating surface plate, the supporting surface of the polishing pad can be secured sufficiently large and the It is possible to prevent the positioning means from protruding to the outer peripheral side, and even if a protective cover or the like is installed on the outer peripheral side of the rotating surface plate, it will not become an obstacle when applying the polishing pad auxiliary plate according to the present invention. Avoided.

A third

aspect of the present invention is the polishing pad auxiliary plate according to the second aspect, wherein the positioning means is provided on one of the lower auxiliary plate and the upper auxiliary plate and on the other. It is composed of an engaging projection projecting to the forward and an engaging recess provided in the other of the lower auxiliary plate and the upper auxiliary plate with which the engaging projection is engaged. In the polishing pad auxiliary plate of this aspect, it is possible to easily obtain a mechanically large positioning force based on the mutual engagement between the engaging projections and the engaging recesses. Further, by adjusting the shape, size, number, etc. of the engaging projections and engaging recesses, it is possible to easily set the direction and acting force of the positioning action with a large degree of freedom.

A fourth aspect

of the present invention is the auxiliary plate for a polishing pad according to the third aspect, wherein the engaging projections and the engaging recesses are located on the outer periphery of the lower auxiliary plate and the upper auxiliary plate. It is formed with an engaging portion located in the portion. In the polishing pad auxiliary plate of this aspect, the engagement outer peripheral surface of the engagement projection and the engagement recess are positioned in the outer peripheral portion away from the center of the polishing pad auxiliary plate and are engaged with each other in a concave-convex manner. By forming the engagement inner peripheral surface of the upper and lower auxiliary plates, the relative positioning accuracy, particularly the radial positioning accuracy, can be improved. As shown in the sixth and seventh aspects below, the engaging outer peripheral surface of the engaging convex portion and the engaging inner peripheral surface of the engaging concave portion are arranged around the center of the polishing pad auxiliary plate. It may extend in the circumferential direction along the outer peripheral edge of the polishing pad auxiliary plate, or it may extend on the circumference like the engaging protrusions and engaging recesses formed on the outer peripheral portion of the polishing pad auxiliary plate. It may be in a partially positioned form.

A fifth aspect of the present invention is the auxiliary plate for a polishing pad according to the fourth aspect, wherein the engaging portions of the engaging projections and the engaging recesses correspond to the lower auxiliary plate and the It is composed of an annular engaging outer peripheral surface and an engaging inner peripheral surface that extend continuously in the circumferential direction of the upper auxiliary plate and are fitted to each other. [0028]

In the polishing pad auxiliary plate of this aspect, more preferably, the engaging concave portion and the engaging convex portion are formed with an annular inner and outer peripheral engaging surface that spreads around the central axis of the polishing pad auxiliary plate. Therefore, when the upper auxiliary plate is attached to the lower auxiliary plate, it is not necessary to align the upper auxiliary plate with each other in the circumferential direction, and the work can be performed easily and quickly. A sixth aspect of the present invention is a polishing pad auxiliary plate according to the fourth aspect, wherein the lower auxiliary plate and the upper auxiliary plate are provided at a plurality of locations on the periphery of the outer peripheral portions of the lower auxiliary plate and the upper auxiliary plate. The engaging recess opening toward the other on one of the overlapping surfaces of the lower auxiliary plate and the upper auxiliary plate, and the other of the mutually overlapping surf

aces of the lower auxiliary plate and the upper auxiliary plate and the engaging projection projecting toward one side are formed at positions corresponding to each other, and the engaging portion is formed by fitting the engaging projection into the engaging recess. is. In the polishing pad auxiliary plate of this mode, the mutual positioning of the upper and lower auxiliary plates can be easily realized not only in the direction perpendicular to the axis but also in the circumferential direction around the central axis. In a seventh aspect of the present invention, in the polishing pad auxiliary plate according to the fourth aspect, the outer peripheral portion of one of the lower auxiliary plate and the upper auxiliary plate has a plurality of points on the circumference of the other. The engaging convex portion protruding toward the upper auxiliary plate is formed of an elastic material, and engages with the engaging concave portion provided in an opening on the outer peripheral surface of the other of the lower auxiliary plate and the upper auxiliary plate. The engaging portion is configured by engaging the tip of the engaging projection.

In the polishing pad auxiliary plate of this aspect, it is possible to form the engaging portions so as to be exposed on the outer peripheral surfaces of the upper and lower auxiliary plates. can be confirmed. In addition, in this aspect, the engagement state of the engagement portion can be stably maintained by utilizing the elasticity of the engagement convex portion. An eighth aspect of

the present invention is the polishing pad auxiliary plate according to the third aspect, where in the engaging projections and the engaging recesses are located at the centers of the lower auxiliary plate and the upper auxiliary plate. It is provided on the shaft. In the polishing pad auxiliary plate of this aspect, the engaging projections and the engaging recesses are formed on the central axis of the upper and lower auxiliary plates.

By providing this, it becomes possible to align the central axes of the upper and lower auxiliary plates with one engaging portion. Further, when the engaging projections and the engaging recesses provided on the central axis are aligned with each other, it is not necessary to align the upper and lower auxiliary plates with each other in the circumferential direction. can be easily brought into engagement. According to a ninth aspect of the present invention, in the polishing pad auxiliary plate according to the eighth aspect, the outer peripheral surface of the engaging projection and the inner peripheral surface of the engaging recess are screwed together.

her

. A groove is formed, and the second fixing means is formed by screwing the engaging projection and the engaging recess that constitute the positioning means. [0036] In the polishing pad auxiliary plate of this mode, the fixing force between the upper auxiliary plate and the lower auxiliary plate can be obtained by the positioning means. Therefore, it is possible to configure the second fixing means only by such positioning means, or to configure the fixing force between the upper and lower auxiliary plates by the second fixing means as an auxiliary means by the positioning means. A tenth aspect of the present invention is the third , fourth , fifth , sixth , eighth and ninth

2. In the polishing pad auxiliary plate according to any one of the above aspects, the engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate is arranged between the lower auxiliary plate and the upper auxiliary plate. It is made of the same material as the one. In the polishing pad auxiliary plate of this aspect, it is possible to prevent the support characteristics of the polishing pad of the auxiliary plates superimposed one on top of the other from greatly differing locally at the portions where the engaging projections are formed

. Therefore, when a pressing force acts on the surface of the polishing pad during pad polishing, the pressure reaction force and the elasticity of the polishing pad are reduced at the formation portions of the engaging convex portions and the engaging concave portions of the upper and lower auxiliary plates that support the polishing pad. It is possible to reduce or avoid defects such as polishing accuracy caused by local differences in such characteristics. Further, according to the present invention, the auxiliary plate for a polishing pad according to any one of the first to tenth aspects of the present invention is mounted on the upper surface of a rotating platen, and is attached to the outer peripheral side of the rotating platen

. A polishing apparatus in which a protective member is arranged with a gap in between, and the positioning means is provided on the inner peripheral side of the outer peripheral end surfaces of the rotating platen and the polishing pad auxiliary plate, Characterized by EFFECTS OF THE INVENTION By adopting the polishing pad auxiliary plate structured according to the present invention or using the polishing apparatus structured according to the present invention, the polishing pad can be prevented from being damaged and polished. can be easily removed from and attached to the rotating surface plate, and positioning of the polishing pad on the rotating surface plate can be performed easily and accurately. [Brief Description of the Drawings]

FIG. 1 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a first embodiment of the present invention;

2 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 1; FIG.

FIG. 3 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a second embodiment of the present invention;

4 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 3; FIG.

FIG. 5 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a third embodiment of the present invention;

6 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 5; FIG.

FIG. 7 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a fourth embodiment of the present invention;

8 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 7; FIG.

FIG. 9 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a fifth embodiment of the present invention;

10 is a side view of a lower auxiliary plate that constitutes the polishing pad auxiliary plate shown in FIG. 9; FIG.

11 is a plan view of the lower auxiliary plate shown in FIG. 10; FIG.

FIG. 12 is a longitudinal sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a sixth embodiment of the present invention;

FIG. 13 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a seventh embodiment of the present invention;

FIG. 14 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to an eighth embodiment of the present invention;

FIG. 15 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a ninth embodiment of the present invention is removed;

FIG. 16 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate is removed according to a tenth embodiment of the present invention;

FIG. 17 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to an eleventh embodiment of the present invention is removed;

FIG. 18 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a twelfth embodiment of the present invention is removed;

FIG. 19 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a thirteenth embodiment of the present invention is removed;

FIG. 20 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a fourteenth embodiment of the present invention is positioned;

FIG. 21 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a fifteenth embodiment of the present invention is positioned;

FIG. 22 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a sixteenth embodiment of the present invention is removed;

DETAILED DESCRIPTION OF THE INVENTION Embodiments of the present invention will be described below

below

with reference to the drawings. First, FIGS. 1 and 2 show a polishing pad auxiliary plate 10 as a first embodiment of the present invention. This polishing pad auxiliary plate 10 is used by being attached to a rotary surface plate 14 of a polishing apparatus 12, and a polishing pad 16 is detachably attached to the rotary surface plate 14. As shown in FIG.

The polishing apparatus is used ,

for example, as a CMP apparatus as described in Japanese Patent Application Laid-Open No. 2010-141155, for example. A rotating shaft extending vertically is rotatably supported by the main body of the apparatus fixedly installed above, and a disk-shaped rotating platen 14 is fixed to the upper end of the rotating shaft. The rotating surface plate 14 has a flat upper surface 18 extending horizontally, and the upper surface 18 serves as a support surface for the polishing pad 16. The rotating shaft is connected to the rotating output shaft of an electric motor, and the driving force of the electric motor is transmitted so that the rotating shaft and thus the rotating surface plate 14 are rotated about the central axis. there is A nozzle for supplying polishing slurry is arranged above the upper surface 18 supporting the polishing pad 16, and a wafer or the like to be polished (an object to be polished) is held and rotated while being moved to the polishing pad 16. A polishing head is provided for polishing by pressing. In such a polishing apparatus, the polishing pad auxiliary plate 10 mounted on the rotating platen 14 is

includes a lower auxiliary plate 20 and an upper auxiliary plate 22 . A lower auxiliary plate 20 is fixed to the upper surface 18 of the rotating platen 14 by first fixing means 24 , and an upper auxiliary plate 22 is attached to the upper surface of the lower auxiliary plate 20 . It is fixed by two fixing means 26 . That is, the lower auxiliary plate 20 and the upper auxiliary plate 22 are overlapped and fixed to each other via the second fixing means 26, thereby forming the polishing pad auxiliary plate 10 having a two-layer structure as a whole. , and is attached to the upper surface 18 of the rotating surface plate 14 by the first fixing means 24 .

Each of the lower auxiliary plate 20 and the upper

auxiliary plate 22 has a thin, substantially circular flat plate shape, and has a flat front surface (upper surface) and a rear surface (lower surface). These upper and lower auxiliary plates 22 and 20 are desirably made of a harder material than the polishing pad 16 to which it is attached, or having a higher member rigidity than the polishing pad 16 . Although it depends on the method of use, as will be described later, the lower auxiliary plate 20 can be used without being repeatedly attached and detached after being attached to the rotary surface plate 14, while the upper auxiliary plate 22 can be attached and detached after being attached to the rotary surface plate 14. is expected to be repeated, it is desirable that at least the upper auxiliary plate 22 should have higher member rigidity than the polishing pad 16 .

[0046]

Of course, the upper auxiliary plate 22 supports the polishing pad 16 and provides the strength, rigidity, and rigidity required for various treatments such as polishing, cleaning, and re-grinding of the polishing pad surface, in addition to polishing by the polishing device 12 . Any material that satisfies shape stability and accuracy may be used, and its material and thickness are not limited. In particular, not only the lower auxiliary plate 20 but also the upper auxiliary plate 22 alone bears the supporting strength and rigidity of the polishing pad 16. Since the lower surface is supported by the rotating surface plate 14 by being superimposed on each other and used, the strength and rigidity of the single unit are not required so much. Therefore, in addition to metals such as stainless steel, synthetic resins, fiber-reinforced resins, and the like can be employed as materials for forming the lower auxiliary plate 20 and the upper auxiliary plate 22 . In particular, synthetic resin materials are lighter than metal materials and easier to process and handle. . In order to obtain a stable supporting force over the entire polishing pad 16, it is desirable to set the outer diameter dimension of the upper auxiliary plate 22 to be equal to or larger than the outer diameter dimension of the polishing pad 16, and

It is desirable to set the outer diameter of the lower auxiliary plate 20 to be equal to or larger than the outer diameter of the upper auxiliary plate 22, and set the outer diameter of the lower auxiliary plate 20 to be equal to or smaller than the outer diameter of the rotating surface plate 12. should be set to In particular, as shown in FIGS. 1 and 2, the outer diameters of the lower auxiliary plate 20 and the upper auxiliary plate 22 are made substantially the same, and the outer diameter of the rotating surface plate 14 to be mounted is also substantially the sa

me. By doing so, it becomes possible to ensure a sufficiently large support area for the polishing pad 16. As a result, the polishing pad 16 having approximately the same size as the rotating surface plate 14 can be attached to the rotating surface plate 14 with approximately the same supporting force over the entirety thereof.

[0048]

Furthermore, as the first fixing means 24 and the second fixing means 26, the lower auxiliary plate 20 and the upper auxiliary plate 22 are fixed to the upper surface 18 of the rotating plate 14 against the external force exerted during polishing. It is not particularly limited as long as it can be held at. Specifically, an adhesive, a pressure-sensitive adhesive, or a double-sided tape having an adhesive or a pressure-sensitive adhesive attached to both sides of a base sheet may be employed as the first and second fixing means 24, 26. In addition, negative pressure suction using negative pressure air or the like, or magnetic suction using a permanent magnet or an electromagnet can be employed. In addition, it is desirable that the fixing means made of adhesive or the like apply substantially uniform fixing force over substantially the entire surface of the flat overlapping surfaces of the lower auxiliary plate 20 and the upper auxiliary plate 22. Adhesive strength can be obtained, and problems such as locally different support characteristics of the polishing pad 16 on the surface of the polishing pad auxiliary plate 20 can be avoided.

For example,

the fixing force can be turned ON/OFF by negative pressure suction or an electromagnet. auxiliary

It is desirable to set the fixing force of the upper auxiliary plate 22 to the lower auxiliary plate 20 by the second fixing means 26 to be smaller than the fixing force of the plate 20. As a result, when the upper auxiliary plate 22 is peeled off from the lower auxiliary plate 20 and removed, the lower auxiliary plate 20 can be easily left fixed on the rotating surface plate 14.例文帳に追加 The specific realization of such a difference in adhesion force is achieved by differentiating the adhesion means itself such as the material of the adhesive and pressure-sensitive adhesive, as well as the adhesion area and the condition of the adhesion surface (surface roughness, presence or absence of plasma treatment, etc.) can also be realized by making the.

Further, the surface (upper surface) of the upper auxiliary plate 22 serves as a

polishing pad supporting surface, and the polishing pad 16 is superimposed and mounted thereon. As such a polishing pad 16, conventionally known various types of polishing pads can be employed. The back surface of the polishing pad 16 is fixed to the surface of the upper auxiliary plate 22 using a conventionally known adhesive tape or suitable adhesive for attaching the polishing pad.

It is desirable that the fixing means for fixing

the polishing pad 16 to the upper auxiliary plate 22 has a larger fixing force than the second fixing means 26 described above. As a result, when the upper auxiliary plate 22 is removed from the lower auxiliary plate 20 with the polishing pad 16 still fixed, the polishing pad 16 does

not move from the upper auxiliary plate 22 even if the upper auxiliary plate 22 is bent or the like. It is possible to effectively prevent the peeling off. The outer diameter of the polishing pad 16 is generally a standard value, but in many cases it is set equal to or smaller than the outer diameter of the upper surface 18 of the rotating surface plate 14 to which it is attached . [0053]

Further, for example, at least one of between the upper surface 18 of the rotating surface plate 14 and the lower auxiliary plate 20, between the lower auxiliary plate 20 and the upper auxiliary plate 22, and between the upper auxiliary plate 22 and the polishing pad 16 A suitable cushioning layer may be provided. By providing such a cushion layer, it becomes possible to achieve uniform polishing efficiency over the entire surface of the workpiece when polishing with the polishing pad 16 .

[0054]

As such a cushion layer, for example, a resin sheet, an elastomer sheet, a rubber sheet, or the like to which a certain degree of compressibility is imparted by foaming can be suitably employed. A cushion layer can also be configured by the first fixing means 24 , the second fixing means 26 , and the means for fixing the polishing pad 16 to the upper auxiliary plate 22 . In order to prevent local distortion on the support surface of the polishing pad 16, the cushion layer is formed so as to have a size and a constant thickness over substantially the entire support area of the polishing pad 16. is desirable. Positioning means 28 are provided between the lower auxiliary plate 20 and the upper auxiliary plate 22 that constitute the polishing pad auxiliary plate 10 to align the centers of the plates with each other .

In the present embodiment, a circular stepped surface 30 is formed on the outer peripheral portion of the lower auxiliary plate 20 and extends around the central axis of the lower auxiliary plate 20 over the entire circumference. By reducing the thickness of the lower auxiliary plate 20 on the outer peripheral side of the stepped surface 30, the notch cross-sectional shape that opens to the outer peripheral surface of the lower auxiliary plate 20 continues to the entire circumference in the circumferential direction. An annular engaging recess 32 that extends inward is formed integrally with the lower auxiliary plate 20 so as to protrude therefrom.

[0056]

On the other hand, in the present embodiment, a circular stepped surface 34 is formed on the outer peripheral portion of the upper auxiliary plate 22 so as to extend around the central axis of the upper auxiliary plate 22 over the entire circumference. Since the thickness of the upper auxiliary plate 22 is increased on the outer peripheral side of the stepped surface 34, an annular engagement continuously extends along the outer peripheral edge of the upper auxiliary plate 22 along the entire circumference in the circumferential direction. A mating projection 36 is integrally formed so as to protrude from the upper auxiliary plate 22 . Incidentally, the e

engaging convex portion 36 and the engaging concave portion 32 may be formed on either of the upper and lower auxiliary plates 22 and 20 .

The stepped surface 30 and the engaging recess 32 of the lower auxiliary plate 20 are aligned with the stepped surface 34 and the engaging projection 36 of the upper auxiliary plate 22 . It constitutes an engagement outer peripheral surface and an engagement inner peripheral surface. When the upper auxiliary plate 22 is superimposed on the lower auxiliary plate 20, the engaging convex portion 36 is fitted into the engaging concave portion 32, and the stepped surface 34 is superimposed on the stepped surface 30 in the radial direction. is formed. As a result, the engaging concave portion 32 and the engaging convex portion 36 constitute the positioning means 28, and the lower auxiliary plate 20 and the upper side support plate 20 are aligned in the radial direction with their central axes aligned with each other. Auxiliary plates 22 are superimposed. In addition, the positioning means 28 is positioned on the inner peripheral side of the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20, thereby preventing the upper and lower auxiliary plates 22 and 20 and the polishing apparatus 12 from becoming large. . In the polishing apparatus 12 provided with the polishing pad auxiliary plate 10 having such a structure, the upper and lower auxiliary plates 22 are mounted on the upper surface 18 of the rotating platen 14 as shown in FIG

, 20 is fixedly attached, and the polishing pad 16 is fixedly supported on the upper surface of the upper auxiliary plate 22. Then, the rotating platen 14 is driven to rotate, and the substrate or the like is processed. CMP (Chemical Mechanical Polishing) is applied to objects. The polishing apparatus 12 can exhibit the following special technical effects by being provided with the polishing pad auxiliary plate 10 having a specific structure.

[0059]

First, as shown in FIG. 2, while the polishing pad 16 is fixed to the upper surface of the upper auxiliary plate 22, the upper auxiliary plate 22 is fixed to the rotating surface plate 14 by the first fixing means 24. By removing the side auxiliary plate 20, the polishing pad 16 can be removed from the rotating surface plate 14. - 特許庁 Even when the surface (polishing surface) of the polishing pad 16 is removed from the rotating platen 14 and cleaned or reprocessed, the polishing pad 16 can be kept fixed to the upper surface of the upper auxiliary plate 22 . As a result, the upper auxiliary plate 22 provides reinforcement not only when the polishing pad 16 is attached to and detached from the rotating surface plate 14, when the polishing pad 16 is cleaned and reprocessed, but also when the polishing pad 16 is transported or stored. By this action, the polishing pad 16 can be prevented from being bent or damaged, and the polishing pad 16 can be kept in good condition.

Further

, even when the polishing pad 16 is removed from the rotating surface plate 14 together with the upper auxiliary plate 22 , the lower auxiliary plate 20 remains on the upper surface 18 o

f the rotating surface plate 14 . When the polishing pad 16 is again mounted on the rotating platen 14, the positioning means 28 provided between the upper auxiliary plate 22 and the lower auxiliary plate 20 moves the upper auxiliary plate 22 and thus the polishing pad 16 to the lower auxiliary plate. The center axis of the plate 20 and thus the rotating platen 14 can be aligned with high accuracy and easily.

[0061]

Here, since the engaging concave portion 32 and the engaging convex portion 36 constituting the positioning means 28 are overlapped with almost no gap in a mutually fitted state, the supporting characteristics of the polishing pad 16 are improved. can be prevented from adversely affecting Of the outer peripheral portions of the upper and lower auxiliary plates 22 and 20, particularly in the present embodiment, an engaging portion, in other words, a positioning means 28, is formed on the outer peripheral edge portion, and the diameter of the polishing pad 16 that serves as the main region for polishing is formed. Since it is out of the middle part in the direction, even if there is a slight gap between the engaging concave portion 32 and the engaging convex portion 36, the supporting characteristics of the polishing pad 16 are such that a serious problem occurs in the polishing characteristics. can be avoided. Moreover, the engaging concave portion 32 and the engaging convex portion 36 constituting the positioning means 28 are formed on the superimposed surfaces of the upper and lower auxiliary plates 22 and 20, in other words, on the outer circumferences of the rotating surface plate 14 and the polishing pad auxiliary plate 10

Since it is formed on the inner peripheral side of the end face, the upper and lower auxiliary plates 22 and 20 can be prevented from projecting onto the outer peripheral surface. Therefore, as shown in FIGS. 1 and 2, for example, even when the protective member 38 is installed close to the outer peripheral side of the rotating surface plate 14 in the polishing apparatus 12, the protective member 38 cannot be protected. Polishing provided with upper and lower auxiliary plates 22, 20 provided with positioning means 28 while avoiding interference

A device 12 is made possible. Furthermore, as described above, while preventing damage to the polishing pad 16, the polishing pad 16 can be quickly attached to and detached from the rotating platen 14 with accurate positioning accuracy

The operating time of the expensive polishing equipment is not unnecessarily limited for such work, and the operating efficiency of the polishing equipment can be improved, and thus the production efficiency of substrates and the like (polishing work efficiency) can be improved. In addition, since the polishing pad 16 can be easily attached to and detached from the rotating surface

plate 14, the reuse of the polishing pad 16 can be realized on a practical level without special skill or knowledge. That is, for example, the polishing pad 16 once removed from the rotating platen 14 can be reused when changing the type of the object to be polished such as a sub

trate, or the polishing pad 16 can be re-processed by another processing device such as surface grooving as a countermeasure against deterioration. It is also possible to consider reusing the polishing pad 16 once removed from the rotating surface plate 14 after reprocessing at a practical level. Although the first embodiment of the present invention has been described above, the specific structure of the present invention should not be construed as limited by the first embodiment

.

A plurality of other embodiments of the present invention having different positioning means between the upper and lower auxiliary plates 22 and 20 are illustrated below, but these embodiments are not intended to limit the configuration of the present invention. In the following embodiments, members and parts having the same structure as in the first embodiment are denoted by the same reference numerals as those in the first embodiment in the corresponding parts in each figure. , their detailed description is omitted. 3 and 4 show a polishing apparatus 42 provided with a polishing pad auxiliary plate 40 as a second embodiment of the present invention

.

In this polishing pad auxiliary plate 40, an engaging recess 44 is formed by an annular groove continuously extending in the circumferential direction on the outer peripheral portion of the upper surface of the lower auxiliary plate 20. As shown in FIG . On the other hand, on the outer peripheral portion of the lower surface of the upper auxiliary plate 22, an engagement convex portion 46 is formed by an annular protrusion extending continuously in the circumferential direction. The engaging projection 46 may be formed integrally with the upper auxiliary plate 22, or may be formed separately as illustrated. That is, in this embodiment, an annular circumferential groove 48 that opens in the lower surface of the upper auxiliary plate 22 and extends in the circumferential direction is formed. block is fitted and fixed at one end in the axial direction to form an engagement convex portion 46 . The engaging concave portion 44 of the lower auxiliary plate 20 and the engaging convex portion 46 of the upper auxiliary plate 22 are both formed at corresponding radial positions around the central axis

.

are overlapped, the engagement projections 46 are fitted into the engagement recesses 44, thereby aligning the upper and lower auxiliary plates 22 and 20 with each other in the radial direction. In the present embodiment, two side walls of the engaging recess 44 of the lower auxiliary plate 20 and the inner and outer peripheral surfaces of the engaging protrusion 46 of the upper auxiliary plate 20 are superimposed on each other in the corresponding radial direction. A pair of inner and outer engagement surfaces are provided. 5 and 6 show a polishing apparatus 52 provided with a polishing pad auxiliary plate 50 as a third embodiment of the present invention

. [0070]

In this polishing pad auxiliary plate 50, the lower auxiliary plate 20 has a stepped surface 54 as a circular engagement inner peripheral surface extending all around the central axis on the outer peripheral portion thereof. By increasing the thickness of the lower auxiliary plate 20 on the outer peripheral side of the stepped surface 54, an annular shape continuously extends along the outer peripheral edge of the lower auxiliary plate 20 along the entire circumference in the circumferential direction. The engaging convex portion 56 of

It is formed integrally with the side auxiliary plate 20. On the other hand, on the outer peripheral portion of the upper auxiliary plate 22, there is formed a stepped surface 58 as a circular engagement outer peripheral surface extending all around the central axis

Since the thickness of the upper auxiliary plate 22 is reduced on the outer peripheral side of the step surface 58, the upper auxiliary plate 22 has a notched cross-sectional shape that opens to the outer peripheral surface and extends continuously along the entire circumference in the circumferential direction. An annular engaging recess 60 is formed integrally with the upper auxiliary plate 22.

Further, the step surface 54 of the lower auxiliary plate 20 is formed with

female threads, while the step surface 58 of the upper auxiliary plate 22 is formed with male threads. Then, the female thread of the stepped surface 54 of the lower auxiliary plate 20 is screwed with the male thread of the stepped surface 58 of the upper auxiliary plate 22 so that the stepped surface 54 of the lower auxiliary plate 20 and the stepped surface 58 of the upper auxiliary plate 22 are screwed together. are superimposed on each other in the radial direction, the upper auxiliary plate 22 is superimposed on the upper surface of the lower auxiliary plate 20. Further, in such a superimposed state, the screwing structure of the stepped surfaces 58, 54 of the upper and lower auxiliary plates 22, 20 constitutes a second fixing means 62 for detachably fixing the upper and lower auxiliary plates 22, 20. The direction of the male and female threads in such a threaded structure is set in consideration of the rotational reaction force exerted on the rotating surface plate 14 of the polishing device 12 during polishing so that the screws do not loosen

It is desirable that

FIGS.

7 and 8 show a polishing apparatus 66 having a polishing pad auxiliary plate 64 as a fourth embodiment of the present invention.

[0075]

In this polishing pad auxiliary plate 64, a cylindrical engaging convex portion 68 projecting upward is formed at the central portion of the upper surface of the lower auxiliary plate 20. T

he engaging projection 68 may be formed integrally with the lower auxiliary plate 20, or may be formed separately as shown in the drawing. That is, in this embodiment, a circular fitting recess 70 is formed on the central axis of the lower auxiliary plate 20, and a cylindrical block formed separately from the fitting recess 70 is provided. An engaging convex portion 68 is formed by being fitted and fixed at one end in the axial direction. On the other hand, in the central portion of the lower surface of the upper auxiliary plate 22, there is formed a bottomed circular engaging recess 72 that opens to the lower surface on the central axis. Incidentally, the engaging convex portion 68 and the engaging concave portion 72 may be formed on either of the upper and lower auxiliary plates 22 and 20. As shown in FIG. When the upper and lower auxiliary plates 22 and 20 are superimposed, the engaging convex portion 68 is fitted into the engaging concave portion 72, thereby aligning the upper and lower auxiliary plates 22 and 20 with each other in the radial direction

It is designed to be In this embodiment, the engagement outer peripheral surface and the engagement inner peripheral surface are formed by the outer peripheral surface of the engaging protrusion 68 of the lower auxiliary plate 20 and the inner peripheral surface of the engaging recess 72 of the upper auxiliary plate 22. It is configured.

FIG.

9 shows a polishing apparatus 76 provided with a polishing pad auxiliary plate 74 as a fifth embodiment of the present invention.

[0078]

In this polishing pad auxiliary plate 74, a cylindrical engaging convex portion 78 projecting upward is formed on the outer peripheral portion of the upper surface of the lower auxiliary plate 20. This engaging projection 78 may be formed integrally with the lower auxiliary plate 20, or may form a fitting recess in the lower auxiliary plate 20 like the engaging projection in the fourth embodiment. Alternatively, a separate pin or the like may be fixed by press-fitting or the like. Also, as shown in FIGS. 10 and 11, a plurality of such engaging projections 78 are formed independently of each other at the outer peripheral portion of the lower auxiliary plate 20 at predetermined intervals in the circumferential direction. Particularly preferably, the plurality of engaging protrusions 78 are formed at regular intervals in the circumferential direction and positioned on the same circle on the central axis.

On the other hand, on the outer peripheral portion of the lower surface of the upper auxiliary plate 22, bottomed circular engagement grooves are provided at positions corresponding to the formation positions of the plurality of engaging projections 78 on the lower auxiliary plate 20, respectively. A concave portion 80 is formed to open downward. Incidentally, the engaging convex portion 78 and the engaging concave portion 80 may be formed on either of the upper and lower auxiliary plates 22 and 20. As shown in FIG. When the upper and lower auxiliary plates 22 and 20 are superimposed, the engaging convex portions 78 are fitted into the eng

aging concave portions 80, respectively, so that the upper and lower auxiliary plates 22 and 20 are positioned radially relative to each other

.

are designed to be matched. In the present embodiment, the outer circumferences of the lower auxiliary plate 20 and the upper auxiliary plate 22 are formed by the outer circumference of the engagement projection 78 of the lower auxiliary plate 20 and the inner circumference of the engagement recess 80 of the upper auxiliary plate 22. An engaging outer peripheral surface and an engaging inner peripheral surface located in a portion are configured. In particular, as in this embodiment, by adopting positioning means consisting of a plurality of engaging projections 78 and engaging recesses 80 independent in the circumferential direction, the superimposed upper and lower auxiliary plates 22, 20 can be diametrically aligned

.

Mutual positioning is possible not only in the direction but also in the circumferential direction. Instead of the plurality of independent engaging recesses 80 formed in the upper auxiliary plate 22,

a circumferential groove continuously extending circularly in the circumferential direction around the central axis of the upper auxiliary plate 22 may be employed. Alternatively, as shown in the sixth embodiment of the present invention in FIG. 12, a circular stepped surface 82 is formed around the central axis of the outer peripheral portion of the upper auxiliary plate 22 and extends over the entire circumference. By making the thickness dimension of the outer peripheral side smaller than 82, it is also possible to form an annular engagement concave portion 83 that has a notched cross-sectional shape that opens to the outer peripheral surface of the upper auxiliary plate 22 and that extends continuously all around in the circumferential direction. It is possible.

[0083]

In this way, in the upper auxiliary plate 22, the engaging surfaces of the engaging projections 78 of the lower auxiliary plate 20 are formed continuously over the entire circumference, so that when the upper and lower auxiliary plates 20 and 22 are superimposed, the upper and lower auxiliary plates 20 and 22 can be overlapped. Since it is no longer necessary to align the auxiliary plates 20 and 22 with each other in the circumferential direction, the mounting work can be easily performed.

FIG.

13 shows a polishing pad auxiliary plate 84 as a seventh embodiment of the present invention.

In this polishing pad auxiliary plate 84, the upper portion of the outer peripheral surface of the lower auxiliary plate 20 and the lower portion of the outer peripheral surface of the upper auxiliary plate 22 are each provided with a small diameter portion. By superimposing the upper and lower auxiliary plates 22 and 20, the small diameter portions of the upper and lower auxiliary plates 22 and 20 form an annular ring that extends across the entire circumference i

n the circumferential direction by widening a predetermined width across the upper and lower auxiliary plates 22 and 20. A shaped receiving recess 86 is formed. A groove-shaped engaging recess 88 is formed at the lower end of the small diameter portion of the lower auxiliary plate 20.

The engagement recess 88 opens to the outer peripheral surface of the lower auxiliary plate 20 at the bottom surface of the accommodation recess 86. Here, the bottom surface of the accommodation recess 86 refers to an annular surface extending over the upper and lower auxiliary plates 22 and 20 and extending in the vertical direction in FIG. On the other hand, a plate-shaped engaging projection 90 made of an elastic material is attached to the small-diameter portion of the upper auxiliary plate 22 that constitutes the accommodation recess 86 so that its proximal end is fixed by a fixing pin 92. The engaging protrusions 90 are accommodated in accommodation recesses 86 formed on the outer peripheral surfaces of the upper and lower auxiliary plates 22, 20 and extend from the upper auxiliary plate 22 onto the outer peripheral surface of the lower auxiliary plate 20. There is an engaging claw portion 94 formed at the tip portion of the engaging projection portion 90 is engaged with an engaging recess portion 88 formed in the small diameter portion of the lower auxiliary plate 20, and the engaging projection portion 90 is locked. It is held in a locked state based on elasticity.

Furthermore, a plurality of such engaging projections 90 are provided on the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20 at predetermined intervals in the circumferential direction. And attached to the outer peripheral surface of the upper auxiliary plate 22

Each of the engaging projections 90 is elastically pressed against the outer peripheral surface of the lower auxiliary plate 20, thereby forming positioning means for positioning the upper and lower auxiliary plates 22, 20 relative to each other on the central axis. Further, by engaging the engaging claw portion 94 of the engaging convex portion 90 with the engaging concave portion 88, a fixing means is also configured to hold the upper and lower auxiliary plates 22 and 20 in a superimposed state and apply a fixing force. There is. Instead of the engaging protrusions 90 having the engaging claws 94 that engage with the engaging recesses 88 as described above, for example, an eighth embodiment of the present invention shown in FIG

In addition, a connecting plate 100 extending across the upper and lower auxiliary plates 22 and 20 and superimposed on the bottom surface of the housing recess 86 is adopted, and both ends of the connecting plate 100 are connected to one of the upper and lower auxiliary plates 22 and 20. It is also possible to fix to the outer peripheral surface of the by connecting pins 102, 102. At least one of the connecting pins 102, 102 is detachable from the lower auxiliary plate 20 or the upper auxiliary plate 22, so that the connection of the upper and lower auxiliary plates 22, 20 by the connecting plate 100 can be released. , the attachment and detachment

t of the upper auxiliary plate 22 to which the polishing pad 16 is fixed with respect to the lower auxiliary plate 20 is permitted. The first fixing means 24 and the second fixing means 26 made of double-faced tape or the like shown in the first to eighth embodiments are used when removing the upper and lower auxiliary plates 22 and 20 and the rotating surface plate 14.

In addition, it is desirable to be held on the fixing surface on the side of a specific member. This facilitates handling of the upper and lower auxiliary plates 22, 20 and the first and second fixing means 24, 26 in a detached state. In addition, the fixing surfaces on which the first and second fixing means 24 and 26 remain are determined by making the fixing force of both surfaces of the first fixing means and the second fixing means 24 and 26 themselves different from each other. It is possible to set by differentiating the surface roughness, material, etc. of the fixed upper and lower auxiliary plates 22 and 20 and the rotating platen 14 from each other. In particular, it

is desirable that the first fixing means 24 is held on the fixing surface on the side of the lower auxiliary plate 20 when the lower auxiliary plate 20 is removed, becomes easier. On the other hand, as shown in FIG. 2 in the first embodiment, the second fixing means 26 is held on the fixing surface on the side of the upper auxiliary plate 22 when the upper auxiliary plate 22 is removed. Alternatively, it may remain on the upper surface of the lower auxiliary plate 20 as in the ninth embodiment of the present invention shown in FIG. By holding the second fixing means 26 on the fixing surface on the side of the upper auxiliary plate 22, the removed upper auxiliary plate 22 can be attached to the rotating surface plate of the device for reprocessing such as grooving of the polishing pad 16. At the time of mounting, it is also possible to use the second fixing means 26 held by the upper auxiliary plate 22 for mounting. On the other hand, by holding the second fixing means 26 on the fixing surface of the lower auxiliary plate 20, when mounting another upper auxiliary plate 22 with another polishing pad 16 mounted thereon to the lower auxiliary plate 20, it is also possible to attach using the second fixing means 26 held by the lower auxiliary plate 20.

Further, the engaging recesses 32, 44, 60, 72, 80, (83), 88 and the engaging projections 36, 46, 56,

70, 78, 90 shown in the first to seventh embodiments may be provided on opposite sides of the lower auxiliary plate 20 side and the upper auxiliary plate 22 side. For example, as the tenth embodiment of the present invention is shown in FIG. The stepped surface 30 and the engaging recess 32 may be formed on the upper auxiliary plate 22, while the stepped surface 34 and the engaging convex portion 36 forming the inner peripheral surface of the engagement may be formed on the lower auxiliary plate 20. It is possible.

[0092]

Furthermore, the engaging recesses 32, 44, 60, 72, 80, (83) and the engaging protrusions 36, 46, 56, 70, 78 shown in the first to sixth embodiments are overlapped with each other. It is also possible to form an inclination angle with respect to the outer peripheral surface of the en

gaging projection and the inner peripheral surface of the engaging recess for positioning the upper and lower auxiliary plates 22 and 20 by using the upper and lower auxiliary plates 22 and 20 as shown in FIG. For example, as an eleventh embodiment of the present invention is shown in FIG. On the other hand, while the engaging convex portion 36 is tapered in the inclined direction in which it gradually tapers in the projecting direction,

A stepped surface 30 serving as an engaging outer peripheral surface of an engaging recess 32 formed in the outer peripheral portion of the upper auxiliary plate 22 can be tapered at an inclination direction and an inclination angle corresponding to the stepped surface 34. As a result, the operation of fitting the engaging convex portion 36 into the engaging concave portion 32 and overlapping the upper and lower auxiliary plates 22, 20 can be further facilitated by using the tapers provided on both the stepped surfaces 34, 30 as guide surfaces. It becomes possible to do it easily. Incidentally, as shown in the twelfth embodiment of the invention shown in FIG. 18 and the thirteenth embodiment of the invention shown in FIG.

.

Even when adopting a plurality of projection-shaped engaging projections 78 formed independently in the direction and a plurality of hole-shaped engaging recesses 80 formed at respective corresponding positions of the upper auxiliary plate 22, the engagement A tapered portion 104 having a tapered shape can be formed by giving an inclination angle to the outer peripheral surface of the projecting tip portion of the convex portion 78. In FIG. 19, an engagement pin 106 formed separately is press-fitted into a fitting hole 105 formed in the lower auxiliary plate 20 to form the engagement convex portion 78. The lower end of the locking pin 106 also has a tapered portion 104 similar to the upper end. As a result, the locking pin 106 has no directivity and is easy to handle, and the operation of press-fitting it into the fitting hole 105 is also facilitated.

[0094]

Further, in the fourteenth embodiment of the present invention shown in FIG. 20, a straddle between the upper and lower auxiliary plates 22, 20 is used as a kind of positioning means for aligning the central axis of the upper and lower auxiliary plates 22, 20 in a superimposed state. A locating sleeve 108 is thus shown fitted over. The positioning sleeve 108 has an inner diameter that is the same as or slightly larger than the outer diameter of the upper and lower auxiliary plates 22 and 20, which are disk-shaped and have substantially the same outer diameter. Such a positioning sleeve 108 is used when superimposing the upper and lower auxiliary plates 22 and 20, and by superimposing the upper and lower auxiliary plates 22 and 20 within the positioning sleeve 108, the central axes of the upper and lower auxiliary plates 22 and 20 are aligned. They can be axially superimposed and secured to each other with a second securing means 26. Therefore, the positioning sleeve 108 can be removed after the upper and lower auxiliary plates 22 and 20 are superimposed and fixed to each other, thereby positioning the upper and lower auxiliary plates 22 and 20 so as to protrude on the outer peripheral surface. It is possible to attach them to each other without means and in precise alignment.

[0095]

Furthermore, in the fifteenth embodiment of the present invention shown in FIG. 21, a slit-shaped engagement groove 110 is formed extending across the overlapping direction when the upper and lower auxiliary plates 22 and 20 are overlapped. The engaging grooves 110 are open to the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20 and have a predetermined depth radially inward. It is a plate-shaped engaging plate 112 is fitted into the engaging groove 110 from the opening of the outer peripheral surface, so that the upper and lower auxiliary plates 22 and 20 are positioned by the engaging plate 112 and is in a connected state. Although the engaging plate 112 is formed separately from the upper and lower auxiliary plates 22 and 20, it may be formed integrally with one of the upper and lower auxiliary plates 22 and 20 so as to protrude toward the other. In that case, the engagement groove 110 is formed only in the other auxiliary plate.

Furthermore, in the sixteenth embodiment of the present invention shown in FIG. 22 ,

a fitting recess 114 is formed as an engaging recess opening in the lower surface of the upper auxiliary plate 22 . In particular, in this embodiment, the fitting recess 114 is formed as an annular groove extending continuously in the circumferential direction around the central axis of the upper auxiliary plate 22 . On the other hand, the lower auxiliary plate 20 has a fitting convex portion 116 as an engaging convex portion that protrudes upward on the upper surface that overlaps with the upper auxiliary plate 22 . In addition, in this embodiment, the fitting protrusion 116 is formed as an annular protrusion corresponding to the fitting recess 114 . When the upper and lower auxiliary plates 22 and 20 are superimposed, the fitting convex portion 116 is positioned so as to enter the fitting concave portion 114 .

[0097]

The fitting projection 116 has a hollow structure, and the inside of the fitting projection 116 is provided with an external space.

A fluid reservoir 118 is formed which is sealed between them. Further, at least the inner peripheral wall and the outer peripheral wall of the wall portion of the fitting convex portion 116 that defines the fluid reservoir 118 are bulged and deformable in the radial direction. Specifically, for example, by forming the fitting convex portion 116 with a rubber elastic material or the like, it is possible to realize an inner peripheral wall that can bulge radially inward and an outer peripheral wall that can bulge radially outward. Further, the lower auxiliary plate 22 is formed with a fluid passage 120 that communicates with the fluid reservoir 118 and extends radially outward and opens to the outer peripheral surface.

A pressure screw 122 is screwed into the end opening. In addition, a sealed area composed of the fluid passage 120 and the fluid reservoir 118 sealed by the pressurizing screw 122 is filled with an incompressible fluid such as oil.

Thus

, by screwing the pressure screw 122, the internal pressure of the fluid reservoir 118 can be

increased through the fluid passage 120, and the inner and outer peripheral walls of the fluid reservoir 118 can be expanded outward. As a result, the fitting convex portion 116 is expanded and pressed against the inner surface of the fitting concave portion 114, so that the upper and lower auxiliary plates 22 and 20 can be positioned by mutual frictional force and the like, and can also exert a fixing force. there is

When removing the upper auxiliary plate 22 from the lower auxiliary plate 20 ,

the pressure screw 122 is rotated in the direction of loosening and moved to the outer peripheral side of the lower auxiliary plate 20, whereby the fluid reservoir 118 is removed. , the pressing force of the fitting protrusion 116 against the fitting recess 114 can be released.

[0101]

In addition, although not listed individually, the present invention can be implemented with various changes, modifications, improvements, etc. based on the knowledge of those skilled in the art. It is also possible to attach an O-ring or a sealing material to the portion to prevent foreign matter from entering the overlapping surfaces of the upper and lower auxiliary plates.

In addition to the auxiliary plates 20 and 22 having the two-layer structure described above, it

is also possible to add additional auxiliary plates in a laminated state and fixed by fixing means. By adopting the auxiliary plate of the third layer in this way, it becomes possible to realize an elastic support state or to dispose of the intermediate layer.

[Description of Reference Symbols]

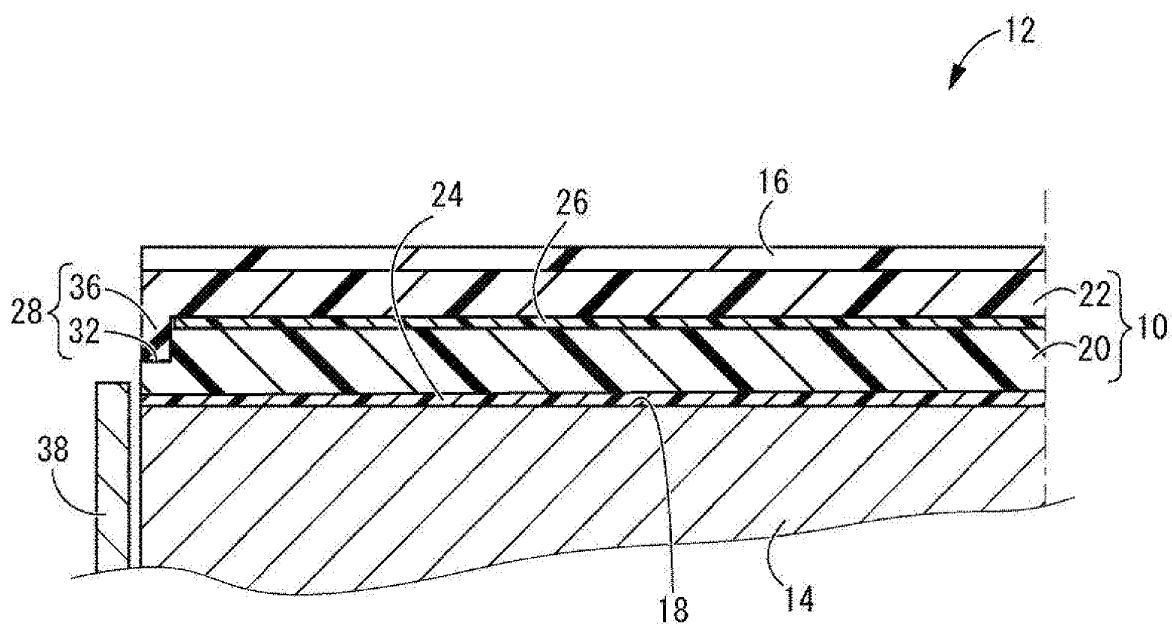
10

, 40, 50, 64, 74, 84: polishing pad auxiliary plate, 12, 42, 52, 66, 76: polishing device, 14: rotating platen, 16: polishing pad, 18: upper surface, 20: lower auxiliary plate, 22: upper auxiliary plate, 24: first fixing means, 26, 62: second fixing means, 28: positioning means, 30, 58: step surface (engagement outer circumference surface), 32, 44, 60, 72, 80, 88: engagement concave portion, 34, 54: step surface (engagement inner peripheral surface), 36, 46, 56, 68, 78, 90: engagement convex portion, 38: Protective member

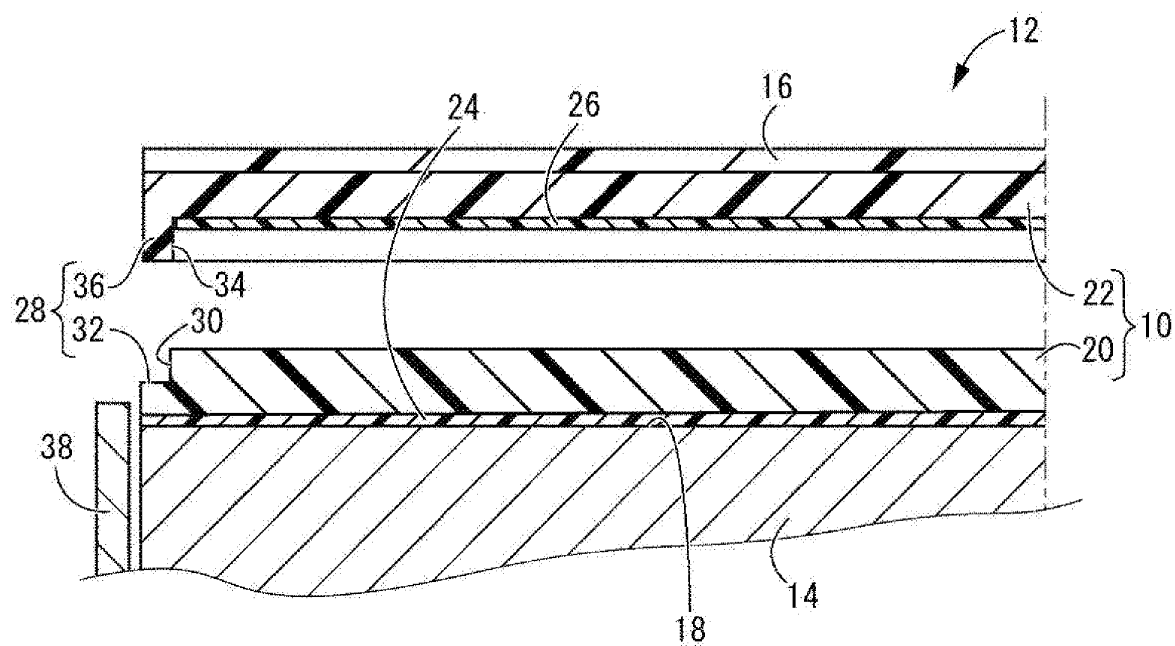
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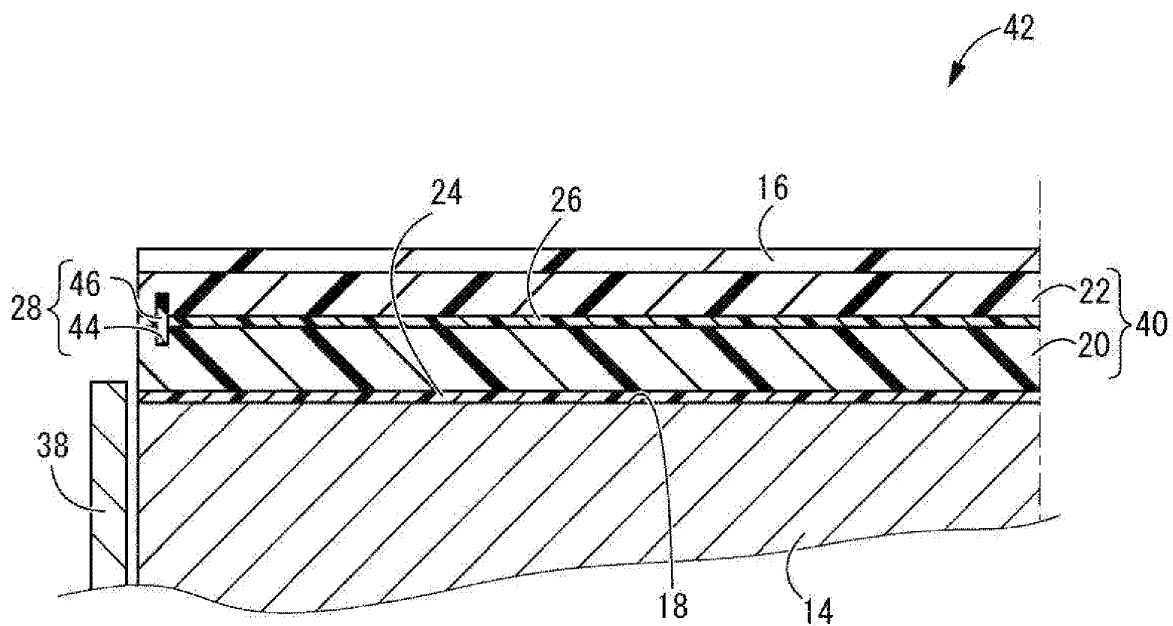
[Fig. 1]



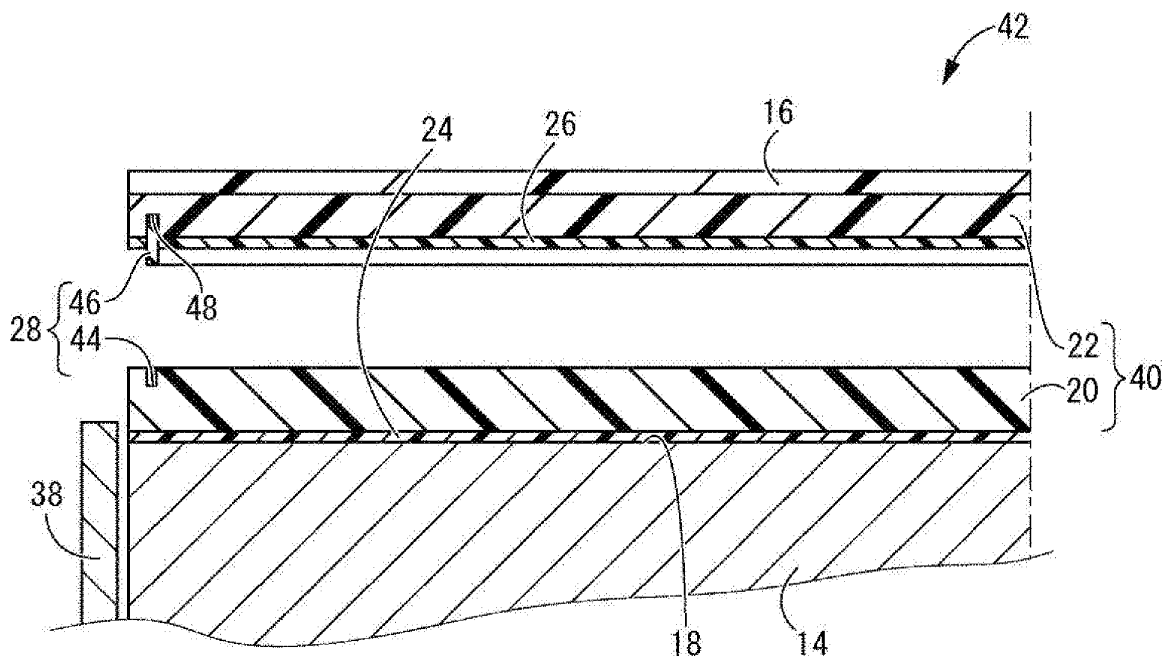
[Figure 2]



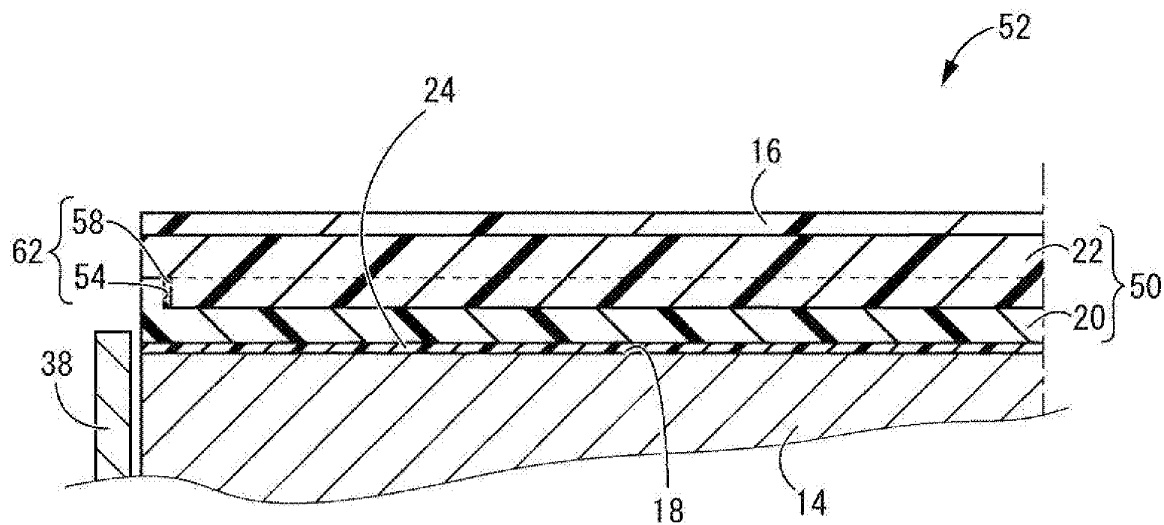
[Figure 3]



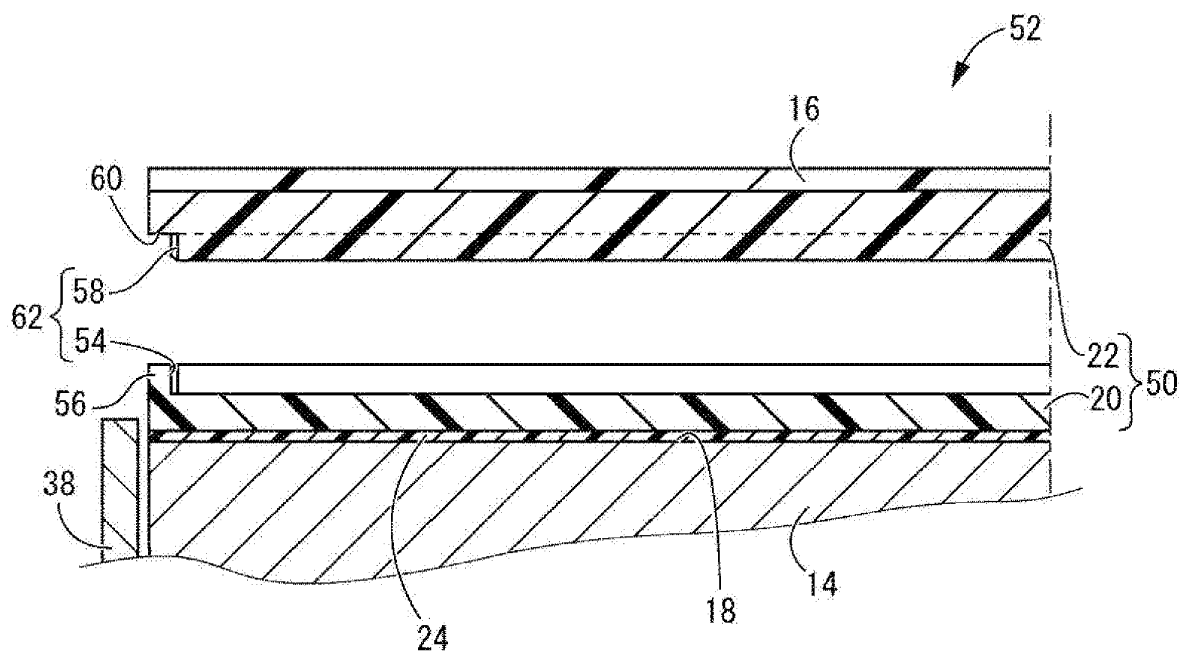
[Figure 4]



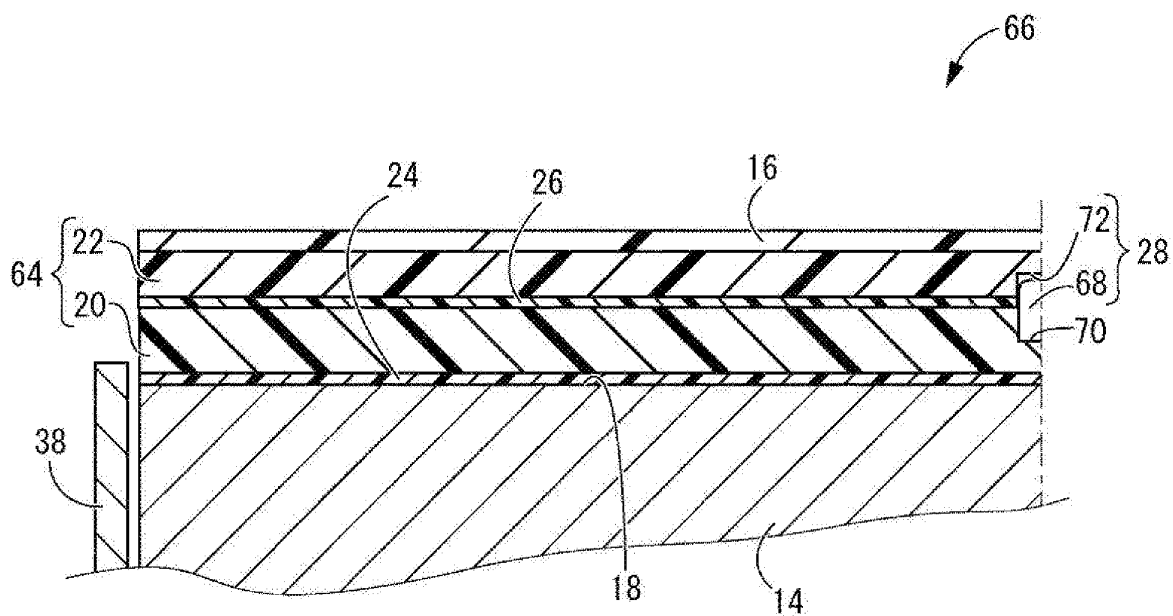
[Figure 5]



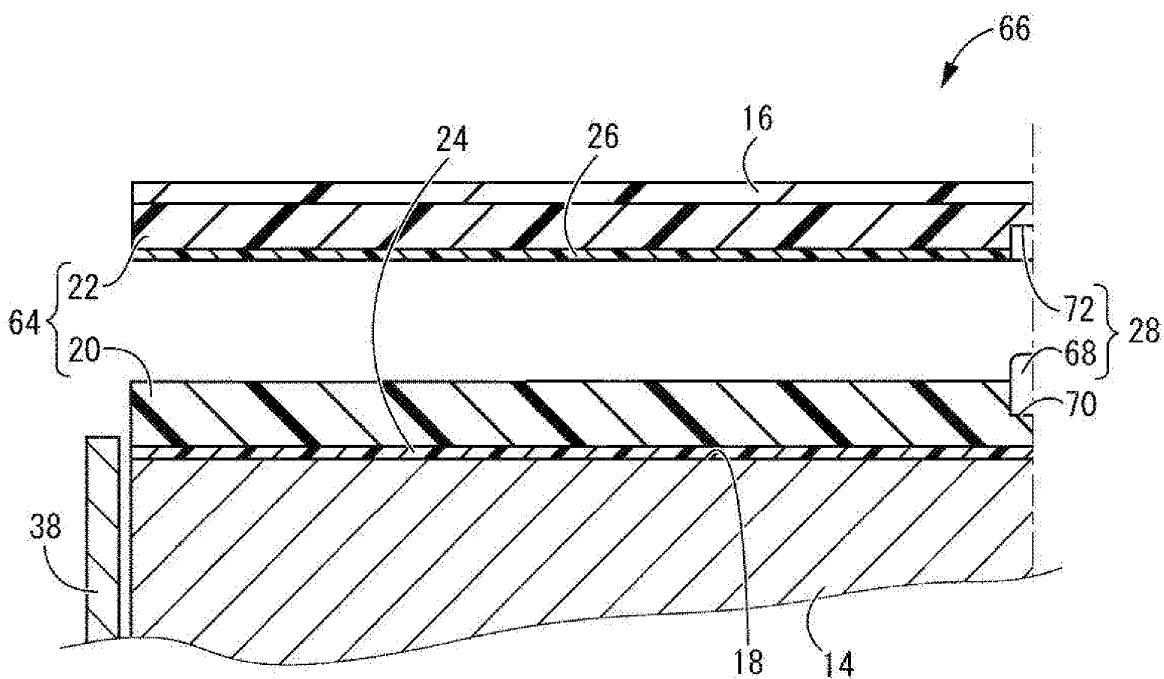
[Fig. 6]



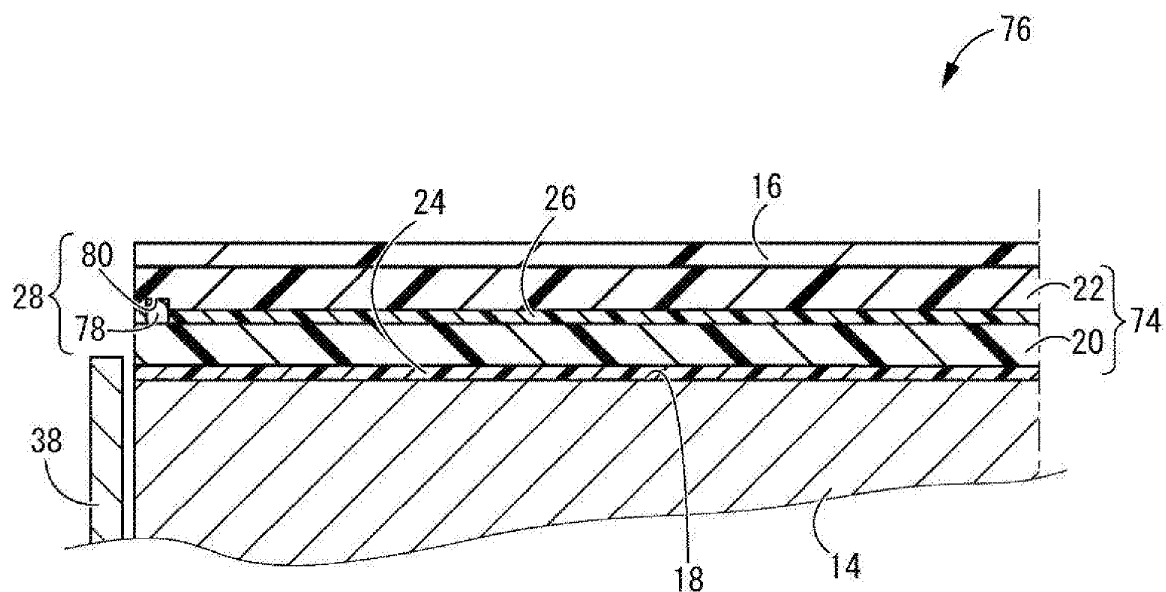
[Fig. 7]



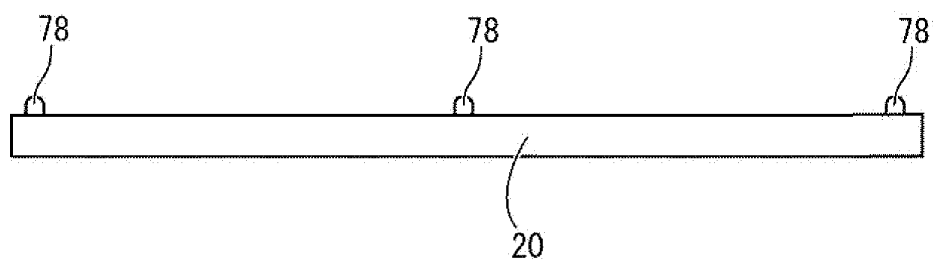
[Fig. 8]



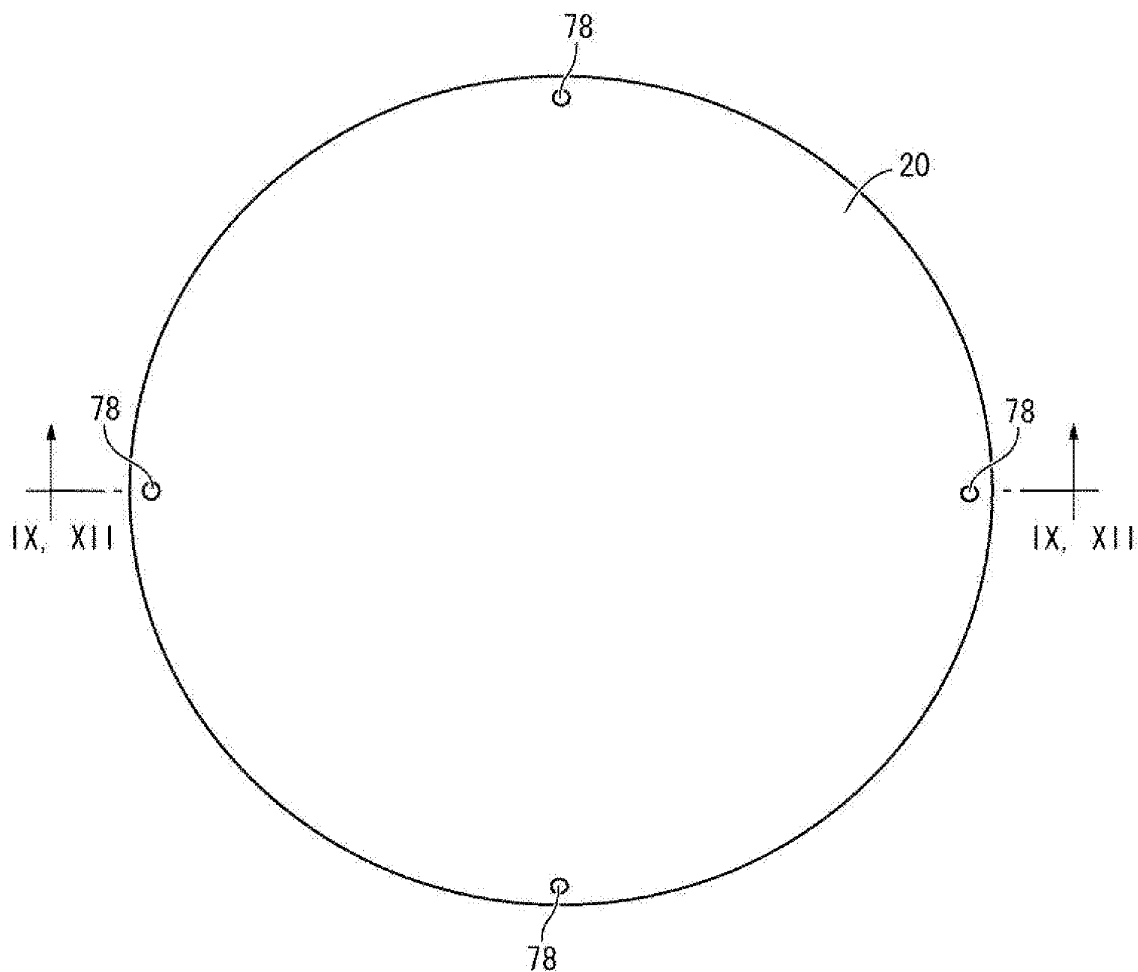
[Fig. 9]



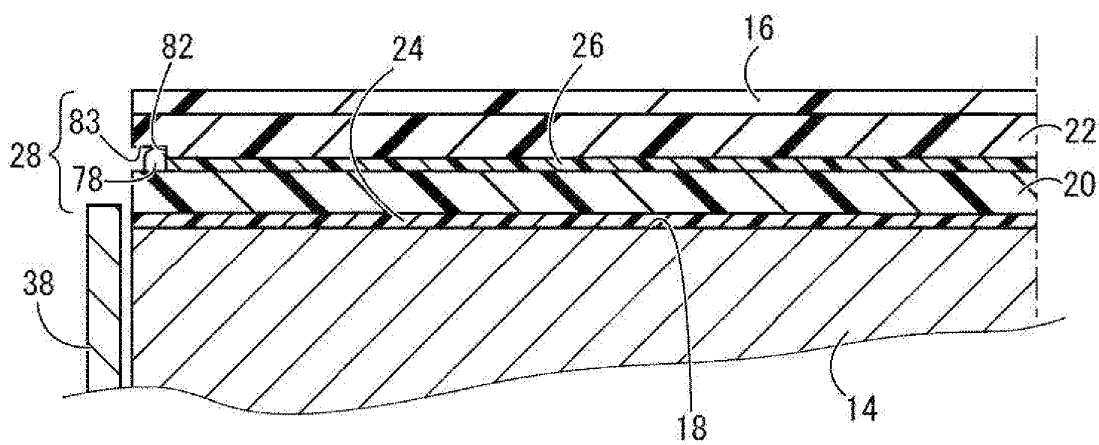
[Fig. 10]



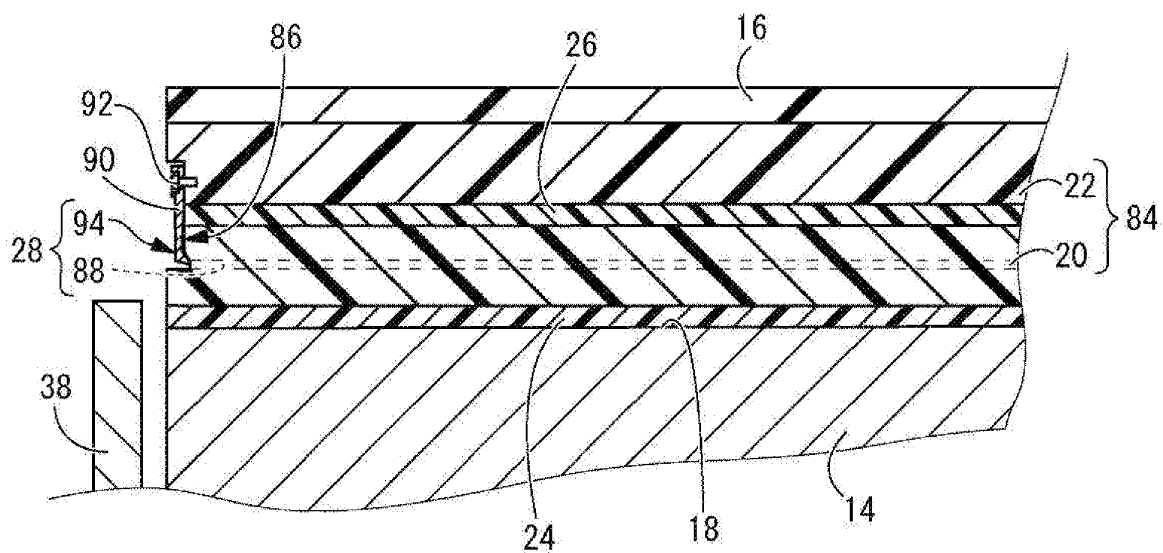
[Fig. 11]



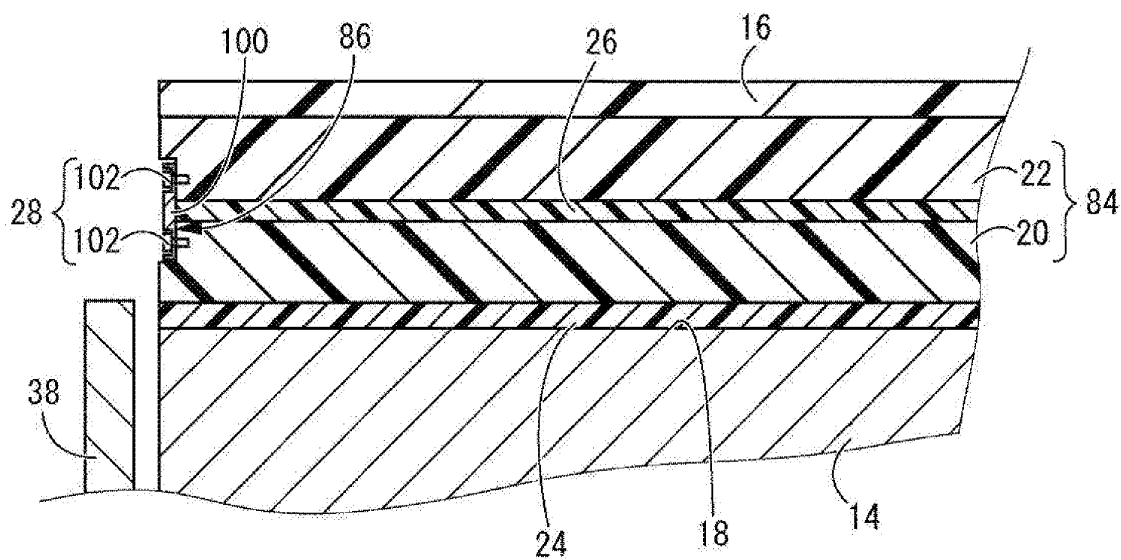
[Fig. 12]



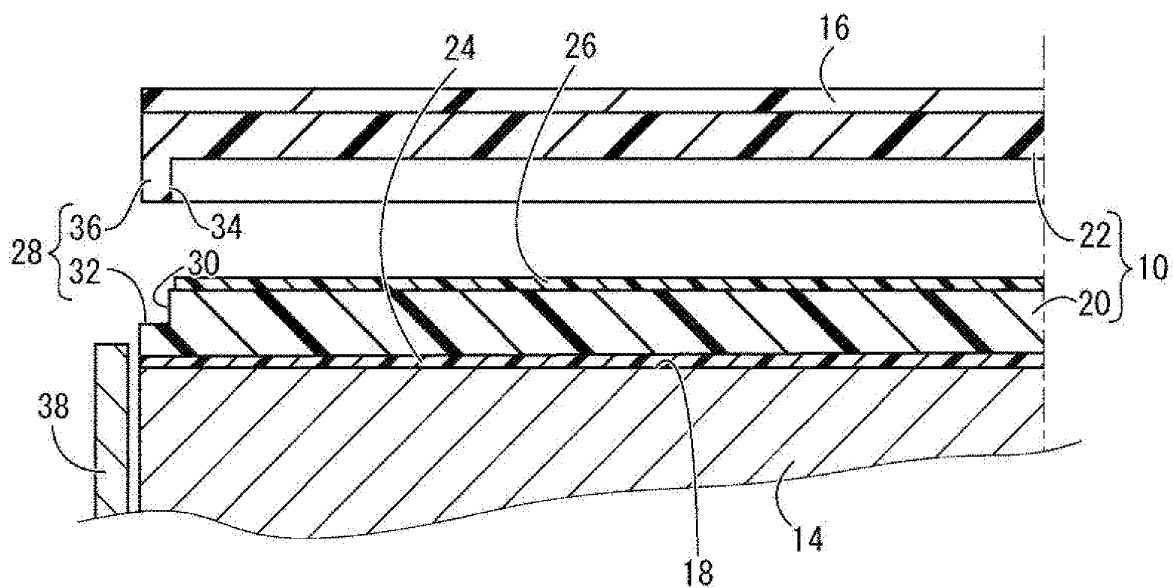
[Fig. 13]



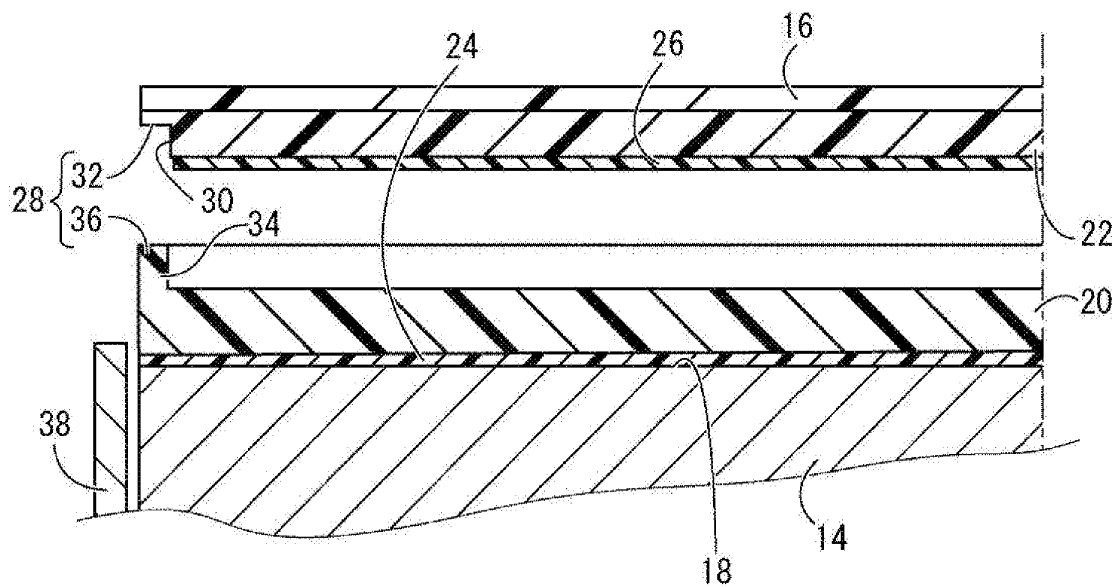
[Fig. 14]



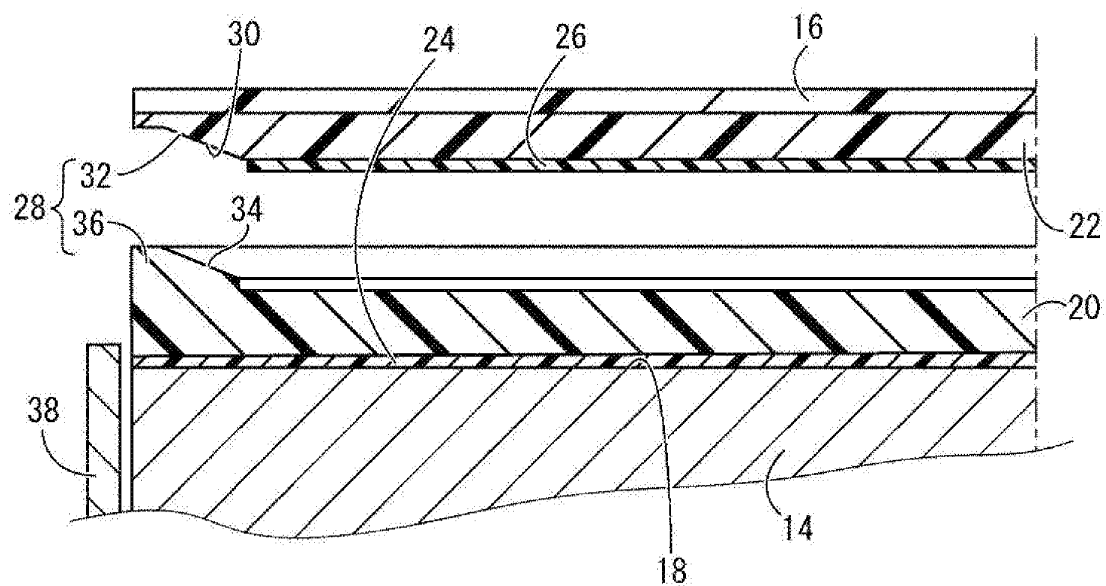
[Fig. 15]



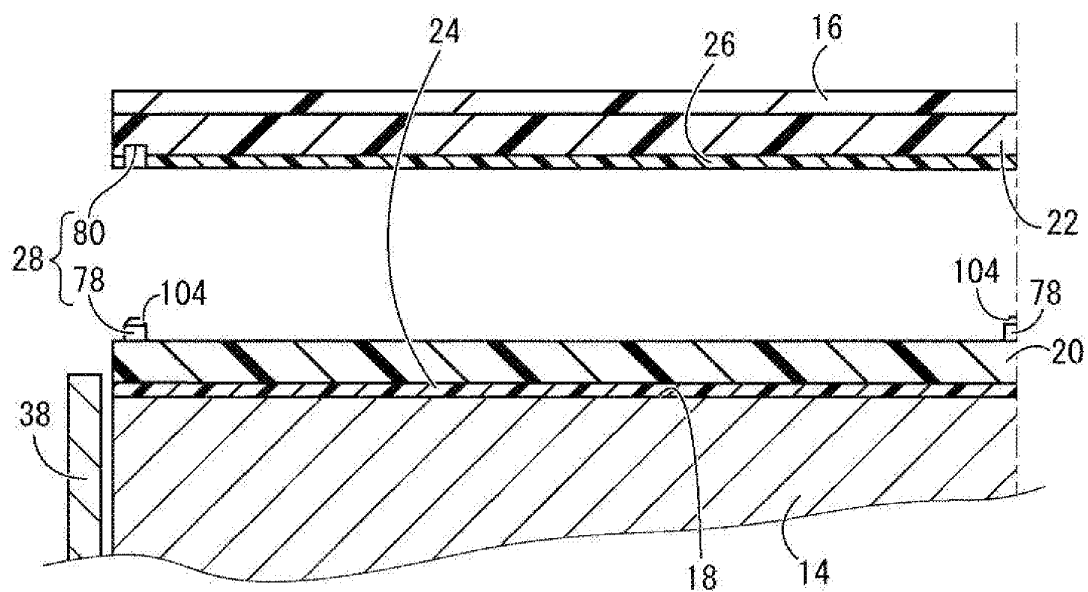
[Fig. 16]



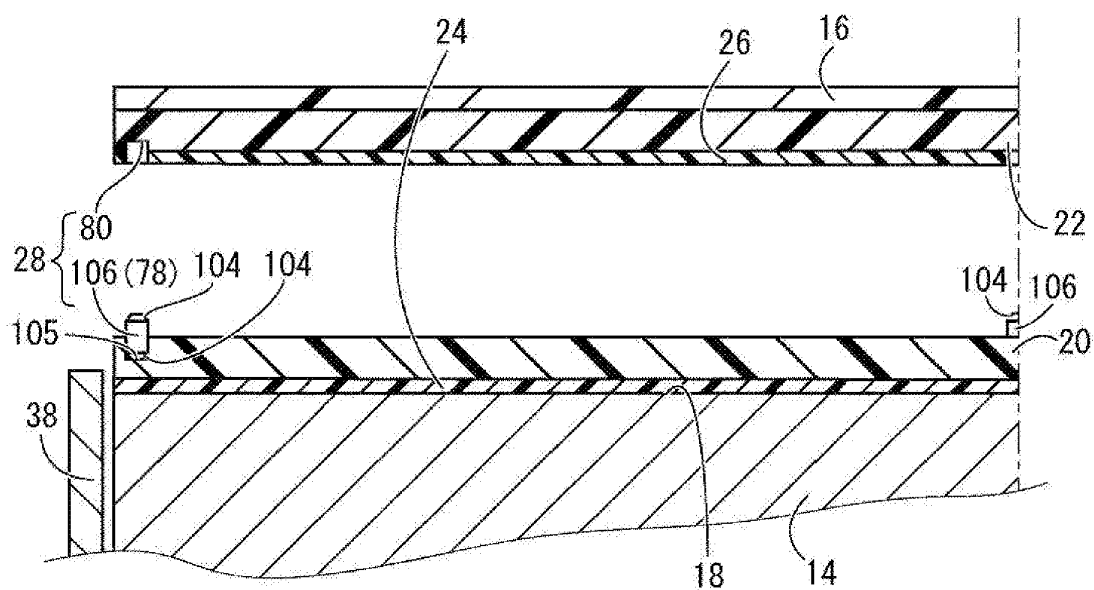
[Fig. 17]



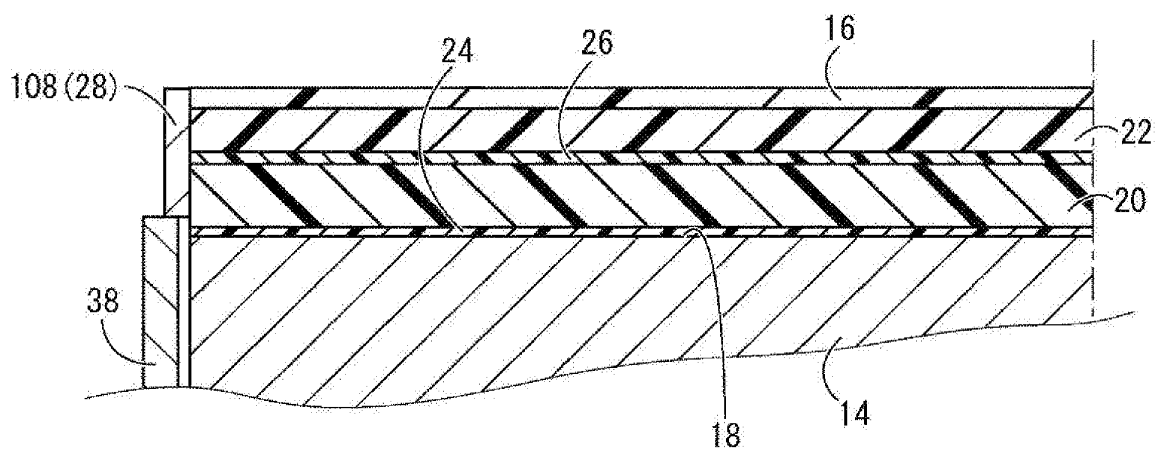
[Fig. 18]



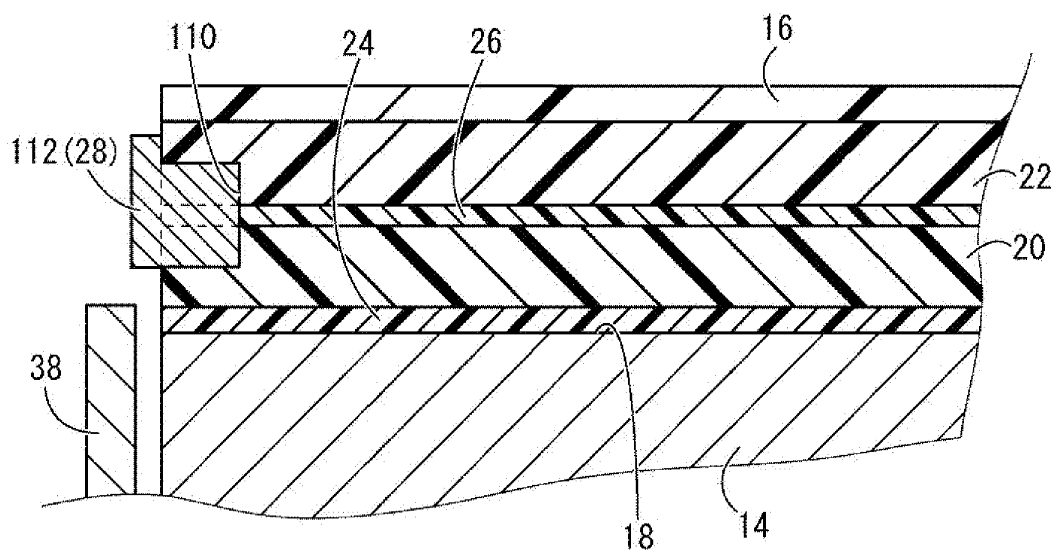
[Fig. 19]



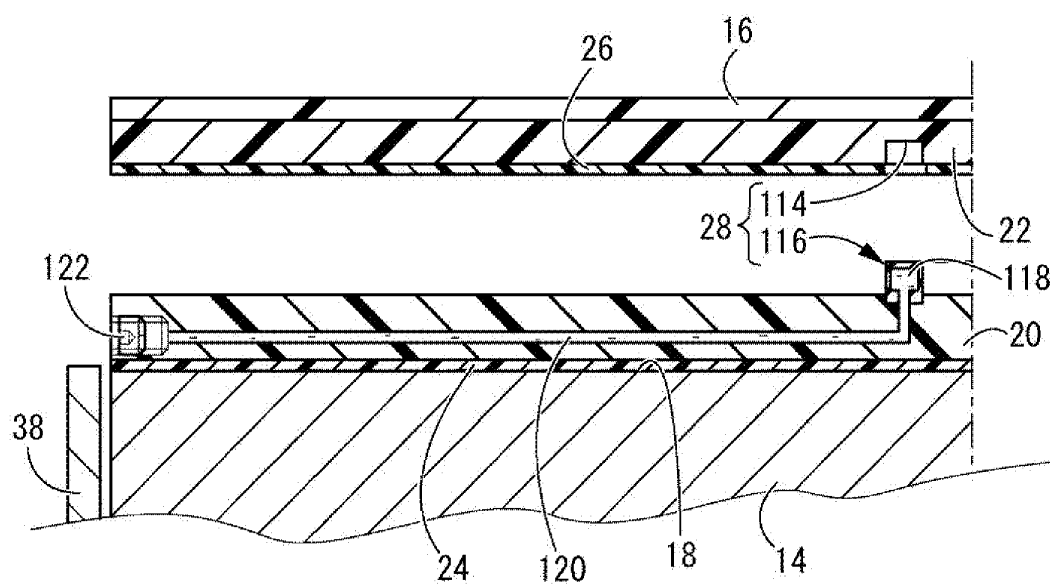
[Fig. 20]



[Fig. 21]



[Fig. 22]



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1 | 2 | 3 | Four | Five | 6 | 7 | 8 | 9 | Ten | ...

Magnify and Rotate

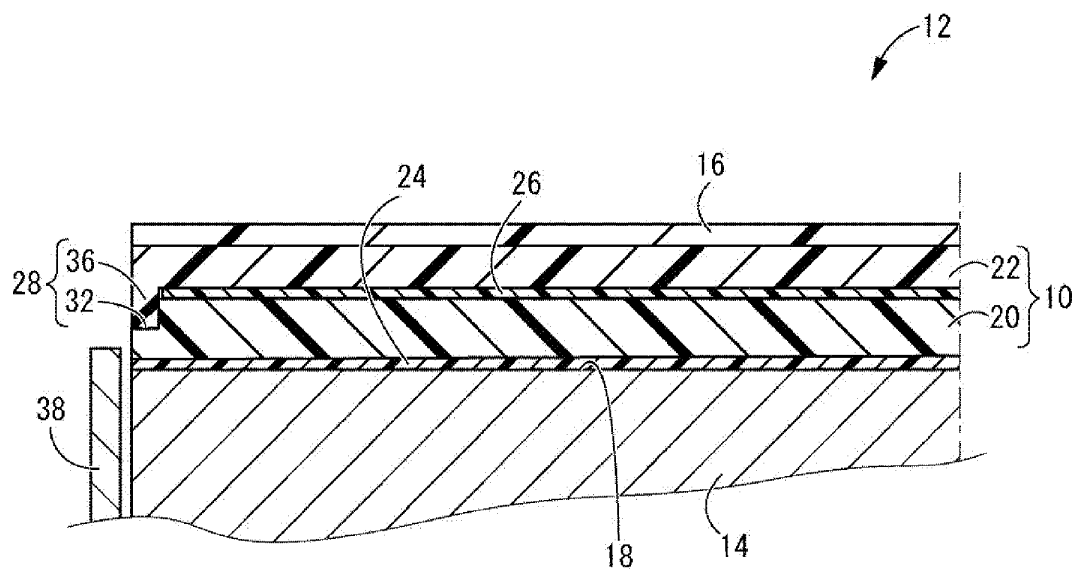


Figure 1

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(出願人による申告) 国等の委託研究の成果に係る特許出願(平成22年度経済産業省「戦略的基盤技術高度化支援事業」委託研究、産業技術力強化法第19条の適用を受ける特許出願)		(72) 発明者	鈴木 辰俊
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			最終頁に続く

(54) 【発明の名称】 研磨パッド用補助板および研磨パッド用補助板を備えた研磨装置

(57) 【特許請求の範囲】

【請求項1】

研磨装置の回転定盤に装着されて、研磨パッドを該回転定盤に対して着脱可能に取り付ける研磨パッド用補助板において、

前記回転定盤の上面に重ね合わされて配される下側補助板と、

該下側補助板を該回転定盤に固着する第一の固着手段と、

前記研磨パッドが重ね合わされて固着されるパッド支持面を備えており、該下側補助板の上面に重ね合わされて配される上側補助板と、

該上側補助板を該下側補助板に固着する第二の固着手段と、

該下側補助板と該上側補助板とを相互に位置決めして中心軸を合わせる位置決め手段とを、有しており、前記研磨装置の前記回転定盤に対して前記下側補助板が前記第一の固着手段による固着状態に保持されて、該回転定盤に固着された該下側補助板から前記上側補助板を取り外すことにより、該上側補助板の前記パッド支持面に固着されたままの状態の前記研磨パッドを該回転定盤から取り外すことが可能とされていると共に、取り外した該上側補助板を該下側補助板に対して前記位置決め手段による位置合わせ状態で再び固着せしめて取り付けることが可能とされており、且つ、

前記第二の固着手段による前記下側補助板と前記上側補助板との固着力が、前記第一の固着手段による前記回転定盤と該下側補助板との固着力よりも小さくされていることを特徴とする研磨パッド用補助板。

【請求項2】

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前記位置決め手段が、前記下側補助板および前記上側補助板の外周面よりも内周側に位置して設けられている請求項 1 に記載の研磨パッド用補助板。

【請求項 3】

前記位置決め手段が、

前記下側補助板と前記上側補助板との一方に設けられて他方に向かって突出する係合凸部と、該下側補助板と前記上側補助板との他方に設けられて該係合凸部が係合せしめられる係合凹部とによって構成されている請求項 2 に記載の研磨パッド用補助板。

【請求項 4】

前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の外周部分に位置する係合部をもって形成されている請求項 3 に記載の研磨パッド用補助板。

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【請求項 5】

前記係合凸部および前記係合凹部における前記係合部が、前記下側補助板および前記上側補助板の周方向に連続して延びて相互に嵌め合わされる環状の係合外周面および係合内周面によって構成されている請求項 4 に記載の研磨パッド用補助板。

【請求項 6】

前記下側補助板および前記上側補助板の外周部分における周上の複数箇所において、前記下側補助板と前記上側補助板との相互の重ね合わせ面の一方において他方に向かって開口する前記係合凹部と、該下側補助板と前記上側補助板との相互の重ね合わせ面の他方において一方に向かって突出する前記係合凸部とが、互いに対応する位置に形成されており、該係合凹部に対する該係合凸部の嵌まり込みによって前記係合部が構成されている請求項 4 に記載の研磨パッド用補助板。

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【請求項 7】

前記下側補助板と前記上側補助板との一方の外周部分における周上の複数箇所から他方に向かって突出する前記係合凸部が弾性材によって形成されており、該下側補助板と前記上側補助板との他方における外周面に開口して設けられた前記係合凹部に対して該係合凸部の先端が係合されることにより前記係合部が構成されている請求項 4 に記載の研磨パッド用補助板。

【請求項 8】

前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の中心軸上に設けられている請求項 3 に記載の研磨パッド用補助板。

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【請求項 9】

前記係合凸部の外周面と前記係合凹部の内周面とにおいて互いに螺合するねじ溝が形成されており、前記位置決め手段を構成する該係合凸部と該係合凹部との螺合により前記第二の固着手段が構成されている請求項 8 に記載の研磨パッド用補助板。

【請求項 10】

前記下側補助板と前記上側補助板との一方に設けられた前記係合凸部が、該下側補助板と該上側補助板との一方と同じ材質で形成されている請求項 3、4、5、6、8、9 の何れか 1 項に記載の研磨パッド用補助板。

【請求項 11】

請求項 1 ～ 10 の何れか 1 項に記載の研磨パッド用補助板が回転定盤の上面に装着されると共に、該回転定盤の外周側に隙間を隔てて保護部材が配設されており、該回転定盤および該研磨パッド用補助板の外周端面よりも内周側に位置して、前記位置決め手段が設けられていることを特徴とする請求項 1 ～ 10 の何れか 1 項に記載の研磨パッド用補助板を備えた研磨装置。

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【発明の詳細な説明】

【技術分野】

【0001】

本発明は、シリコンウエハや半導体基板、ガラス基板等のような高い平坦加工精度が要求される被加工物である基板を対象とする研磨に関連する技術に係り、特に、かかる基板の表面を研磨する際に用いられる研磨パッドの再使用を実現可能とする技術に関するもの

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である。

【背景技術】

【0002】

良く知られているように、半導体の製造に際しては、構成材となるシリコンウエハや半導体基板、ガラス基板等の基板の表面を平坦化する研磨処理が行われている。かかる研磨処理は、一般に、樹脂材等からなる円板形状の研磨パッドを研磨装置の回転定盤の上に両面テープで直接固定し、砥粒を含んだ研磨液を供給しつつ、研磨パッドと基板を相対的に回転運動させて研磨を行うことによって実施されている。

【0003】

そして、このような研磨処理を実施するための研磨パッドとしては、特開2002-11630号公報（特許文献1）等に記載されているように、発泡又は無発泡のウレタン等からなる樹脂パッドが採用されている。また、かかる研磨パッドの研磨表面には、多くの場合、同心円状や格子状、放射状等の溝加工が施されたり、発泡樹脂の気泡が開口される等している。

【0004】

ところで、研磨パッドを用いた研磨加工を行う場合には、研磨対象である基板の品種切り替え等に際して、研磨加工に使用する研磨パッドを回転定盤から引き剥がして別の研磨パッドに交換しなければならない場合がある。また、例えば、研磨加工に伴って劣化した研磨パッドを、その再使用等を目的として、別の加工装置で表面溝入れ等の再加工するような場合等においても、研磨パッドを回転定盤から引き剥がすことが必要となる。

【0005】

ところが、薄肉円板形状の研磨パッドは、研磨装置の回転定盤に対して粘着テープで強固に固着されていることから、この研磨パッドを回転定盤から引き剥がす際に、研磨パッドに対して曲がりや折れ、シワ、破れ等の損傷が発生し易い。それ故このような損傷が原因で、かかる研磨パッドを、寿命がきていないにもかかわらず、再使用できずに廃棄せざるを得なくなることが多いという問題があった。

【0006】

しかも、損傷しないように細心の注意を払いつつ研磨パッドを回転定盤から引き剥がす作業は、熟練と注意を要することから作業者に大きな負担をかけるという問題もあった。加えて、研磨パッドを回転定盤から引き剥がす作業に相当の時間が必要となることから、高価で貴重な設備である研磨装置を長時間に亘って停止させなければならず、設備の稼働時間が制限されてしまうという問題もあった。

【0007】

そこで、本発明者は、先に特開2010-214579号公報（特許文献2）において、研磨パッドの裏面に補助板を取り付け、この補助板を介して、研磨パッドを研磨装置の回転定盤に対して両面テープ等で固着するようにした補助板付き研磨パッドを提案した。かかる補助板付き研磨パッドでは、研磨パッドが補助板で支持されたままの状態を保ちつつ回転定盤に対して着脱されることから、着脱に際しての研磨パッドの損傷が補助板で補強される。それ故、研磨パッドの損傷を防止しつつ、回転定盤に対して研磨パッドを良好な作業性をもって着脱することが可能となる。

【0008】

ところが、本発明者が更なる研究と検討を重ねたところ、特許文献2で提案した補助板付き研磨パッドでは、必ずしも全ての研磨装置への対応が容易であると言えないことがわかった。

【0009】

すなわち、研磨パッドを回転定盤に重ね合わせて固着する際には、研磨パッドの中心を回転定盤の回転中心に位置合わせする必要がある、特に研磨表面に溝等が施された研磨パッドでは中心位置合わせに精度が要求される。そして、上述の如き補助板を採用することで回転定盤に対する研磨パッドの着脱回数が増加すると、より一層、研磨パッドを回転定盤に装着する際の中心位置合わせの作業が難しくて労力負担が大きいということが大きな

問題となるのである。

【0010】

また、特許文献2で提案した補助板付き研磨パッドでは、補助板を回転定盤に対して中心位置合わせしつつ着脱可能に取り付けるために、補助板と回転定盤との間において、例えば回転定盤の外周面上に外周リングなどの固着手段が設けられる場合がある。一方、研磨装置のなかには、回転定盤の外周側に保護カバー等が装着されて、回転定盤の外周側のスペースが非常に狭くなっているものもある。それ故、仮に、そのような外周リングを採用しようとした場合に、たまたま回転定盤の外周側のスペースが狭い研磨装置を用いる際には、研磨装置の改造が必要となるおそれもあったのである。

【先行技術文献】

【特許文献】

【0011】

【特許文献1】特開2002-11630号公報

【特許文献2】特開2010-214579号公報

【発明の概要】

【発明が解決しようとする課題】

【0012】

本発明は上述の如き事情を背景として為されたものであり、回転定盤に対する研磨パッドの固着力を十分に確保しつつ、回転定盤に対する研磨パッドの着脱を容易に行うことを可能と為し、特に回転定盤から研磨パッドを取り外すに際しての研磨パッドの損傷を防止することが出来て、例えば研磨パッドの再利用の実現にも有利とされ得る、新規な構造の研磨パッド用補助板を提供することにある。

【0013】

それに加えて、本発明は、研磨パッドを回転定盤に装着する際の中心合わせの作業を容易に且つ精度良く行うことが出来て、労力負担も軽減され得ると共に、従来の各種仕様の研磨装置における回転定盤にも特別な改造を必要とすることなく容易に且つ有利に適用され得る、改良された構造の研磨パッド用補助板を提供することも、目的とする。

【0014】

さらに、本発明は、かかる新規な構造とされた研磨パッド用補助板を備えた研磨装置を提供することも、目的とする。

【課題を解決するための手段】

【0015】

かかる課題を解決するために、研磨パッド用補助板に関する本発明の第一の態様は、(A) 研磨装置の回転定盤に装着されて、研磨パッドを該回転定盤に対して着脱可能に取り付ける研磨パッド用補助板において、(B) 前記回転定盤の上面に重ね合わされて配される下側補助板と、(C) 該下側補助板を該回転定盤に固着する第一の固着手段と、(D) 前記研磨パッドが重ね合わされて固着されるパッド支持面を備えており、該下側補助板の上面に重ね合わされて配される上側補助板と、(E) 該上側補助板を該下側補助板に固着する第二の固着手段と、(F) 該下側補助板と該上側補助板とを相互に位置決めして中心軸を合わせる位置決め手段とを、有しており、前記研磨装置の前記回転定盤に対して前記下側補助板が前記第一の固着手段による固着状態に保持されて、該回転定盤に固着された該下側補助板から前記上側補助板を取り外すことにより、該上側補助板の前記パッド支持面に固着されたままの状態の前記研磨パッドを該回転定盤から取り外すことが可能とされていると共に、取り外した該上側補助板を該下側補助板に対して前記位置決め手段による位置合わせ状態で再び固着せしめて取り付けることが可能とされており、且つ、前記第二の固着手段による前記下側補助板と前記上側補助板との固着力が、前記第一の固着手段による前記回転定盤と該下側補助板との固着力よりも小さくされている研磨パッド用補助板を特徴とする。

【0016】

本発明に従う構造とされた研磨パッド用補助板では、研磨パッドを、上側補助板および

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下側補助板を介して、回転定盤に固着して装着することとなる。これにより、下側補助板を回転定盤に固着したまま、下側補助板から上側補助板を取り外すことが出来、研磨パッドを上側補助板に固着されたままの状態での回転定盤から取り外すことが可能となる。

【0017】

それ故、研磨パッドが上側補助板で補強および保護された状態で、研磨パッドの損傷を防止しつつ、研磨パッドを回転定盤から取り外すことが出来、薄肉の研磨パッドの取り扱いも容易となる。そして、例えば研磨対象物や研磨条件の変更等に際して研磨パッドの着脱を繰り返す際や、磨耗した研磨パッドを取り外して再生処理後に再装着する際などにおいて、回転定盤への研磨パッドの着脱や研磨パッドに対する再生処理等の作業を容易に行うことも可能となる。

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【0018】

しかも、回転定盤に固着されたままの下側補助板と、研磨パッドと共に取り外される上側補助板とが、位置決め手段により相互に中心軸合わせされることから、回転定盤への位置合わせが必要となる研磨パッドの着脱作業を一層容易に行うことができる。特に、かかる位置決め手段が、下側補助板と上側補助板との間に設けられていることから、回転定盤に対して特別な加工等を施す必要がない。また、かかる位置決め手段が、回転定盤よりも外周側に大きく突出することが回避され得、例えば回転定盤の外周側に保護カバー等が設けられている研磨装置などにも、特別な改造を施すことなく適用可能とされる。

【0019】

上記本発明の第一の態様に係る研磨パッド用補助板においては、前記第二の固着手段による前記下側補助板と前記上側補助板との固着力が、前記第一の固着手段による前記回転定盤と該下側補助板との固着力よりも小さくされている態様が、採用されている。

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【0020】

このような第一の態様に従えば、第一及び第二の固着手段における固着力を相互に調整して設定したことにより、研磨パッドが固着されたままの上側補助板を、回転定盤に固着されたままの下側補助板から取り外す作業が一層容易となる。要するに、下側補助板を回転定盤に対して固着状態に保つための特別な操作等を必要とすることなく、下側補助板を回転定盤への固着状態に残しつつ研磨パッドを上側補助板に固着されたままの状態での回転定盤から容易に取り外すことが可能になる。

【0021】

本発明の第二の態様は、前記第一の態様に係る研磨パッド用補助板において、前記位置決め手段が、前記下側補助板および前記上側補助板の外周面よりも内周側に位置して設けられているものである。

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【0022】

本態様の研磨パッド用補助板では、位置決め手段における上下補助板の外周側への突出が完全に回避される。それ故、例えば上下補助板の外径寸法を回転定盤の外径寸法と同じか僅かに小さく設定して装着する場合でも、研磨パッドの支持面を十分に大きく確保しつつ、回転定盤から外周側に位置決め手段が突出することを回避することが出来、回転定盤の外周側に保護カバー等が設置されていても、本発明に係る研磨パッド用補助板の適用に際して障害となることが回避される。

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【0023】

本発明の第三の態様は、前記第二の態様に係る研磨パッド用補助板において、前記位置決め手段が、前記下側補助板と前記上側補助板との一方に設けられて他方に向かって突出する係合凸部と、該下側補助板と前記上側補助板との他方に設けられて該係合凸部が係合せしめられる係合凹部とによって構成されているものである。

【0024】

本態様の研磨パッド用補助板では、係合凸部と係合凹部との相互係合作用に基づいて、機械的に大きな位置決め力を容易に得ることが可能となる。また、係合凸部や係合凹部の形状や大きさ、数などを調節することにより、位置決め作用の方向や作用力を大きな自由度で容易に設定することも可能となる。

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【0025】

本発明の第四の態様は、前記第三の態様に係る研磨パッド用補助板において、前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の外周部分に位置する係合部をもって形成されているものである。

【0026】

本態様の研磨パッド用補助板では、研磨パッド用補助板の中央から離れた外周部分に位置して、相互に凹凸嵌合せしめられる係合凸部の係合外周面と係合凹部の係合内周面とを形成することにより、上下補助板の相対的な位置決め精度、特に径方向の位置決め精度の向上が図られ得る。なお、後述の第六及び第七の態様にも示されているように、係合凸部の係合外周面および係合凹部の係合内周面は、研磨パッド用補助板の中心周りで研磨パッド用補助板の外周縁部に沿って周方向に延びる形態であっても良いし、研磨パッド用補助板の外周部分に形成された係合凸部と係合凹部のように周上で部分的に位置する形態であっても良い。

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【0027】

本発明の第五の態様は、前記第四の態様に係る研磨パッド用補助板において、前記係合凸部および前記係合凹部における前記係合部が、前記下側補助板および前記上側補助板の周方向に連続して延びて相互に嵌め合わされる環状の係合外周面および係合内周面によって構成されているものである。

【0028】

本態様の研磨パッド用補助板において、より好適には、研磨パッド用補助板の中心軸回りに広がる環状の係合内外周面をもって係合凹部と係合凸部が形成されることとなり、それによって、上側補助板の下側補助板への装着時に周方向での相互の位置合わせが必要なくなり、容易且つ速やかに作業することが可能となる。

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【0029】

本発明の第六の態様は、前記第四の態様に係る研磨パッド用補助板であって、前記下側補助板および前記上側補助板の外周部分における周上の複数箇所において、前記下側補助板と前記上側補助板との相互の重ね合わせ面の一方において他方に向かって開口する前記係合凹部と、該下側補助板と前記上側補助板との相互の重ね合わせ面の他方において一方に向かって突出する前記係合凸部とが、互いに対応する位置に形成されており、該係合凹部に対する該係合凸部の嵌まり込みによって前記係合部が構成されているものである。

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【0030】

本態様の研磨パッド用補助板では、上下補助板の相互の位置合わせを軸直角方向だけでなく中心軸回りの周方向でも容易に実現することが可能となる。

【0031】

本発明の第七の態様は、前記第四の態様に係る研磨パッド用補助板において、前記下側補助板と前記上側補助板との一方の外周部分における周上の複数箇所から他方に向かって突出する前記係合凸部が弾性材によって形成されており、該下側補助板と前記上側補助板との他方における外周面に開口して設けられた前記係合凹部に対して該係合凸部の先端が係合されることにより前記係合部が構成されているものである。

【0032】

本態様の研磨パッド用補助板では、上下補助板の外周面上に係合部を露出させて形成することが可能であり、それによって係合部の係合状態を目視等で容易に確認することが可能となる。また、本態様では、係合凸部の弾性を利用して係合部における係合状態が安定して保たれ得る。

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【0033】

本発明の第八の態様は、前記第三の態様に係る研磨パッド用補助板において、前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の中心軸上に設けられているものである。

【0034】

本態様の研磨パッド用補助板では、上下補助板の中心軸上に係合凸部および係合凹部を

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設けたことにより、一つの係合部によって上下補助板の中心軸合わせを行うことが可能になる。また、中心軸上に設けられた係合凸部と係合凹部の相互の位置合わせに際しては、上下補助板の周方向での相互の位置合わせが必要なく、それら係合凸部と係合凹部を容易に係合状態とすることも可能になる。

【0035】

本発明の第九の態様は、前記第八の態様に係る研磨パッド用補助板において、前記係合凸部の外周面と前記係合凹部の内周面とにおいて互いに螺合するねじ溝が形成されており、前記位置決め手段を構成する該係合凸部と該係合凹部との螺合により前記第二の固着手段が構成されているものである。

【0036】

本態様の研磨パッド用補助板では、位置決め手段により、上側補助板と下側補助板との固着力を得ることができる。それ故、かかる位置決め手段のみによって第二の固着手段を構成したり、第二の固着手段による上下補助板間の固着力を位置決め手段で補助的に構成することも可能となる。

【0037】

本発明の第十の態様は、前記第三、四、五、六、八、九の何れかの態様に係る研磨パッド用補助板において、前記下側補助板と前記上側補助板との一方に設けられた前記係合凸部が、該下側補助板と該上側補助板との一方と同じ材質で形成されているものである。

【0038】

本態様の研磨パッド用補助板では、上下で重ね合わされた補助板における研磨パッドの支持特性が、係合凸部の形成部分で局所的に大きく異なることを防止することが可能となる。それ故、パッド研磨加工に際して押圧力が研磨パッド表面に作用した際、かかる研磨パッドを支持している上下補助板における係合凸部や係合凹部の形成部位において、押圧反力や研磨パッド弾性などの特性が局所的に異なることに起因する研磨精度などの不具合を軽減乃至は回避することが可能になる。

【0039】

さらに、本発明は、前記第一～十の何れかの態様に記載の本発明に係る研磨パッド用補助板が回転定盤の上面に装着されると共に、該回転定盤の外周側に隙間を隔てて保護部材が配設されており、該回転定盤および該研磨パッド用補助板の外周端面よりも内周側に位置して、前記位置決め手段が設けられている研磨装置も、特徴とする。

【発明の効果】

【0040】

本発明に従う構造とされた研磨パッド用補助板を採用し、または本発明に従う構造とされた研磨装置を用いることによって、研磨パッドの損傷を防止しつつ、研磨パッドを回転定盤から容易に取り外したり装着したりすることが可能となるのであり、研磨パッドの装着に際しての回転定盤への位置合わせも容易に且つ精度良く行うことが可能となる。

【図面の簡単な説明】

【0041】

【図1】本発明の第一の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図2】図1に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図3】本発明の第二の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図4】図3に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図5】本発明の第三の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図6】図5に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図 7】本発明の第四の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 8】図 7 に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図 9】本発明の第五の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 10】図 9 に示された研磨パッド用補助板を構成する下側補助板の側面図。

【図 11】図 10 に示された下側補助板の平面図。

【図 12】本発明の第六の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 13】本発明の第七の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 14】本発明の第八の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 15】本発明の第九の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 16】本発明の第十の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 17】本発明の第十一の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 18】本発明の第十二の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 19】本発明の第十三の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 20】本発明の第十四の実施形態としての研磨パッド用補助板を位置決めした状態を示す縦断面の説明図。

【図 21】本発明の第十五の実施形態としての研磨パッド用補助板を位置決めした状態を示す縦断面の説明図。

【図 22】本発明の第十六の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【発明を実施するための形態】

【0042】

以下、本発明の実施形態について、図面を参照しつつ説明する。先ず、図 1～2 には、本発明の第一の実施形態としての研磨パッド用補助板 10 が示されている。この研磨パッド用補助板 10 は、研磨装置 12 の回転定盤 14 に装着されて用いられ、回転定盤 14 に対して研磨パッド 16 を着脱可能に取り付けるようになっている。

【0043】

研磨装置は、例えば特開 2010-141155 号公報等に記載されているように例えば CMP 装置として用いられるものであって、基本構造は周知であるが要部を説明すると、先ず基礎ベース上に固定設置された装置本体によって鉛直方向に延びる回転軸が回転可能に支持されており、この回転軸の上端部に円盤形状の回転定盤 14 が固設されている。かかる回転定盤 14 は、水平方向に広がる平坦な上面 18 を有しており、この上面 18 が研磨パッド 16 の支持面とされている。また、回転軸には、電気モータの回転出力軸が連結されており、電気モータの駆動力が伝達されることで回転軸ひいては回転定盤 14 が中心軸回りに回転駆動されるようになっている。なお、研磨パッド 16 を支持する上面 18 の上方には、研磨用スラリを供給するノズルが配置されると共に、研磨対象（被研磨物）であるウェハ等を保持して回転させつつ研磨パッド 16 に押し付けることで研磨加工を施す研磨ヘッドが配設されている。

【0044】

このような研磨装置において、その回転定盤 14 に装着された研磨パッド用補助板 10

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は、下側補助板 20 および上側補助板 22 を含んでいる。そして、回転定盤 14 の上面 18 に対して、下側補助板 20 が第一の固着手段 24 で固着されており、更に、下側補助板 20 の上面に対して、上側補助板 22 が第二の固着手段 26 で固着されている。即ち、下側補助板 20 と上側補助板 22 は、第二の固着手段 26 を介して相互に重ね合わされて固着されることにより、全体として二層構造とされた研磨パッド用補助板 10 を構成しており、第一の固着手段 24 により回転定盤 14 の上面 18 に取り付けられている。

【0045】

下側補助板 20 および上側補助板 22 は、何れも、薄肉の略円形平板形状とされており、平坦な表面（上面）と裏面（下面）を有している。これらの上下補助板 22, 20 は、装着される研磨パッド 16 よりも硬質材料であるものや、研磨パッド 16 よりも部材剛性が大きいものが望ましい。使用方法にもよるが、後述するように下側補助板 20 は回転定盤 14 への取り付け後に着脱を繰り返さない使用も可能である一方、上側補助板 22 は回転定盤 14 への取り付け後に着脱を繰り返すことが予定されることから、少なくとも上側補助板 22 は、研磨パッド 16 よりも部材剛性が大きいものを採用することが望ましい。

【0046】

尤も、上側補助板 22 は、研磨パッド 16 を支持せしめて、研磨装置 12 による研磨加工の他、研磨パッド表面へのドレッシング、清掃、再溝入などの各種の処理に際して要求される強度や剛性、形状安定性及び精度を満足するものであれば良く、その材質や厚さ寸法は限定されるものでない。特に、下側補助板 20 だけでなく上側補助板 22 も、それ単体で、研磨パッド 16 の支持強度や剛性等を負うものでなく、例えば研磨加工に際しては研磨装置 12 の回転定盤 14 の上に重ね合わされて使用されることで、回転定盤 14 で下面を支持されるものであることから、単体での強度や剛性がそれ程迄に要求されるものでない。それ故、ステンレス鋼等の金属の他、合成樹脂や繊維強化樹脂等も、下側補助板 20 や上側補助板 22 の形成材料として採用され得る。特に、合成樹脂材は金属材に比して軽量で加工や取扱いが容易であり、例えばポリカーボネート等は、厚さ寸法精度の安定性や温度変化に対する低歪み特性にも優れているといった利点がある。

【0047】

また、研磨パッド 16 の全体に亘って安定した支持力を得るためには、上側補助板 22 の外径寸法を研磨パッド 16 の外径寸法の値以上に設定することが望ましく、且つ下側補助板 20 の外径寸法を上側補助板 22 の外径寸法の値以上に設定することが望ましく、更に下側補助板 20 の外径寸法を回転定盤 12 の外径寸法の値以下に設定することが望ましい。特に、図 1, 2 に示されているように、下側補助板 20 および上側補助板 22 の外径寸法を略同じにすると共に、装着される回転定盤 14 の外径寸法とも略同じとすることにより、研磨パッド 16 の支持面積を十分に大きく確保することが可能になる。これにより、回転定盤 14 と略同じ大きさの研磨パッド 16 を、その全体に亘って略同じ支持力をもって回転定盤 14 に装着することが可能となる。

【0048】

更にまた、第一の固着手段 24 および第二の固着手段 26 としては、研磨に際して及ぼされる外力に対抗して、回転定盤 14 の上面 18 へ下側補助板 20 および上側補助板 22 を固着状態に保持し得るものであればよく、特に限定されるものでない。具体的には、接着剤や粘着剤、または基材シートの両面に接着剤や粘着剤が付着等された両面テープなどが、第一及び第二の固着手段 24, 26 として採用され得るが、その他、負圧エア等を利用した負圧吸引や、永久磁石又は電磁石を利用した磁力吸引なども採用可能である。また、これらの接着剤等からなる固着手段は、下側補助板 20 や上側補助板 22 において平坦な重ね合わせ面の略全面に亘って略均一に固着力を及ぼすことが望ましく、それによって、大きな固着力を得ることが出来ると共に、研磨パッド用補助板 10 の表面において研磨パッド 16 の支持特性が局所的に異なる不具合等を回避できる。

【0049】

例えば負圧吸引や電磁石では固着力を ON/OFF できるが、接着剤等のように一定の固着力が及ぼされる場合には、第一の固着手段 24 による回転定盤 14 に対する下側補助

板 2 0 の固着力に比して、第二の固着手段 2 6 により下側補助板 2 0 に対する上側補助板 2 2 の固着力が小さくなるように設定されることが望ましい。これにより、上側補助板 2 2 を下側補助板 2 0 から引き剥がして取り外す際、下側補助板 2 0 を回転定盤 1 4 上に固着せしめたまま残置させておくことが容易に実現可能となる。このような固着力の相違の具体的な実現は、接着剤や粘着剤の材質など固着手段そのものを相互に異ならせる他、固着面積や固着面の状態（面粗さやプラズマ等の処理有無など）を相互に異ならせること等によっても実現可能である。

【0050】

さらに、上側補助板 2 2 の表面（上面）は研磨パッド支持面となっており、研磨パッド 1 6 が重ね合わされて取り付けられている。かかる研磨パッド 1 6 は、従来から公知の各種の研磨パッドを採用することが出来る。そして、この研磨パッド 1 6 の裏面が、上側補助板 2 2 の表面に対して、研磨パッド貼付用として従来公知の粘着テープや適当な接着剤等を利用して固着されている。

【0051】

なお、研磨パッド 1 6 の上側補助板 2 2 への固着手段は前述の第二の固着手段 2 6 よりも、大きな固着力を設定することが望ましい。これにより、研磨パッド 1 6 が固着されたままの状態の上側補助板 2 2 を下側補助板 2 0 から取り外す際に、上側補助板 2 2 が湾曲等しても研磨パッド 1 6 が上側補助板 2 2 から予期せずに剥がれることが効果的に防止され得る。

【0052】

また、研磨パッド 1 6 の外径寸法は、一般に規格値とされるが、多くの場合、装着される回転定盤 1 4 の上面 1 8 の外径寸法と同じか小さく設定される。

【0053】

さらに、例えば回転定盤 1 4 の上面 1 8 と下側補助板 2 0 との間、下側補助板 2 0 と上側補助板 2 2 との間、上側補助板 2 2 と研磨パッド 1 6 との間の少なくとも一つにおいて、適当なクッション層を設けても良い。このようなクッション層を設けることにより、研磨パッド 1 6 による研磨加工に際して、被加工物に対する研磨効率の全面に亘る均一化を図ることが可能となる。

【0054】

かかるクッション層としては、例えば発泡によってある程度の圧縮性が付与された樹脂シートや、エラストマーシート、ゴムシート等が好適に採用され得る。また、第一の固着手段 2 4 や第二の固着手段 2 6、研磨パッド 1 6 の上側補助板 2 2 への固着手段によって、クッション層を構成することも可能である。なお、クッション層は、研磨パッド 1 6 の支持面における局所的な歪を防止するために、研磨パッド 1 6 の支持領域の略全体に亘る大きさをもって一定厚さで存在するように、形成されることが望ましい。

【0055】

また、研磨パッド用補助板 1 0 を構成する下側補助板 2 0 と上側補助板 2 2 との間には、相互に位置決めして中心軸を合わせる位置決め手段 2 8 が設けられている。本実施形態では、下側補助板 2 0 の外周部分に、下側補助板 2 0 の中心軸回りで全周に亘って延びる円形の段差面 3 0 が形成されている。そして、この段差面 3 0 よりも外周側では下側補助板 2 0 の厚さ寸法が小さくされることで、下側補助板 2 0 の外周面に開放する切欠断面形状をもって周方向の全周に連続して延びる環状の係合凹部 3 2 が、下側補助板 2 0 に突出して一体形成されている。

【0056】

一方、本実施形態では、上側補助板 2 2 の外周部分には、上側補助板 2 2 の中心軸回りで全周に亘って延びる円形の段差面 3 4 が形成されている。そして、この段差面 3 4 よりも外周側では上側補助板 2 2 の厚さ寸法が大きくなることで、上側補助板 2 2 の外周端縁に沿って周方向の全周に連続して延びる環状の係合凸部 3 6 が、上側補助板 2 2 に突出して一体形成されている。なお、係合凸部 3 6 および係合凹部 3 2 は、上下補助板 2 2、2 0 のどちらに形成されていても良い。

【0057】

上述の下側補助板20の段差面30および係合凹部32は、上側補助板22の段差面34および係合凸部36に対して相互に位置合わせされており、本実施形態において係合外周面および係合内周面を構成している。そして、下側補助板20に上側補助板22が重ね合わされる際、係合凹部32に係合凸部36が嵌まり込み、段差面30に段差面34が径方向で重ね合わされ、係合部が形成される。これにより、係合凹部32と係合凸部36とによって位置決め手段28が構成されており、中心軸が相互に一致させられて径方向で位置合わせされた状態で、下側補助板20と上側補助板22が重ね合わされるようになっている。なお、位置決め手段28は、上下補助板22、20の外周面よりも内周側に位置して設けられ、それにより、上下補助板22、20、ひいては研磨装置12が大型化しないようにしている。

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【0058】

このような構造とされた研磨パッド用補助板10を備えた研磨装置12にあっては、図1に示されているように、回転定盤14の上面18に上下の補助板22、20からなる研磨パッド用補助板10を固着せしめて装着すると共に、上側補助板22の上面に研磨パッド16を固着支持せしめた状態で、回転定盤14を回転駆動させて基板等の被加工物に対してCMP（化学機械研磨）を施すようにされる。そして、かかる研磨装置12は、特定構造の研磨パッド用補助板10を備えていることにより、以下の如き特別な技術的效果を発揮し得る。

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【0059】

先ず、図2に示されているように、研磨パッド16を上側補助板22の上面に固着させたまま、上側補助板22を、第一の固着手段24により回転定盤14に固着された下側補助板20から取り外すことにより、研磨パッド16を回転定盤14から取り外すことが出来る。そして、回転定盤14から取り外して研磨パッド16の表面（研磨面）をクリーニングや再加工等する場合でも、研磨パッド16を上側補助板22の上面に固着させたままで行うことが出来る。これにより、回転定盤14に対する研磨パッド16の着脱の際や、研磨パッド16のクリーニングや再加工の際などは勿論、研磨パッド16の移送時や保存時等においても、上側補助板22による補強作用により研磨パッド16の曲がりや損傷を防止できて、研磨パッド16を良好な状態に保つことが出来る。

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【0060】

また、研磨パッド16を上側補助板22と共に回転定盤14から取り外した際にも、回転定盤14の上面18には下側補助板20が残置される。そして、研磨パッド16を再び回転定盤14に装着する際、上側補助板22と下側補助板20との間に設けられた位置決め手段28により、上側補助板22ひいては研磨パッド16が下側補助板20ひいては回転定盤14に対して高精度に且つ容易に中心軸合わせされ得る。

【0061】

ここにおいて、かかる位置決め手段28を構成する係合凹部32と係合凸部36は、相互に嵌合された状態で殆ど隙間なく重ね合わされるようになっていることから、研磨パッド16の支持特性への悪影響が防止され得る。また、上下補助板22、20の外周部分のうち特に本実施形態では外周端縁部に係合部、言い換えると位置決め手段28が形成されており、研磨パッド16において研磨用の主たる領域となる径方向中間部分を外れていることから、係合凹部32と係合凸部36の嵌合部分に多少の隙間があっても、研磨特性に大きな問題が発生する程の研磨パッド16の支持特性への悪影響が回避され得る。

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【0062】

しかも、位置決め手段28を構成する係合凹部32と係合凸部36は、上下補助板22、20の重ね合わせ面、換言すると、回転定盤14および研磨パッド用補助板10の外周端面よりも内周側に形成されており、上下補助板22、20の外周面上への突出が回避され得る。それ故、例えば図1、2に示されているように、研磨装置12において回転定盤14の外周側に近接して保護部材38が設置されている場合でも、そのような保護部材38への干渉を回避しつつ、位置決め手段28を備えた上下補助板22、20を備えた研磨

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装置 1 2 が実現可能とされる。

【0063】

さらに、上述のように研磨パッド 1 6 の損傷を防止しつつ、正確な位置合わせ精度で速やかに研磨パッド 1 6 を回転定盤 1 4 に対して着脱することが出来る結果、研磨パッド 1 6 の着脱等の作業のために高価な研磨設備の稼働時間が不必要に制限されることがなくなり、研磨設備の稼働効率の向上ひいては基板等の生産効率（研磨作業効率）の向上が達成され得る。

【0064】

また、研磨パッド 1 6 の回転定盤 1 4 に対する着脱が容易に実現されることから、特別な熟練や知識がなくとも研磨パッド 1 6 の再利用が実用レベルで実現可能となる。即ち、例えば、基板等の被研磨物の品種切り替え等に際して一旦回転定盤 1 4 から外した研磨パッド 1 6 を再利用したり、劣化対策として別の加工装置で表面溝入れ等の再加工するのに一旦回転定盤 1 4 から取り外した研磨パッド 1 6 を再加工後に再利用したりすることなども、実用化レベルで検討することが可能となるのである。

【0065】

以上、本発明の第一の実施形態について説明してきたが、本発明の具体的構造はかかる第一の実施形態によって限定的に解釈されるものでない。上下補助板 2 2, 2 0 間において別構造の位置決め手段を備えた、本発明の別の実施形態の複数を以下に例示するが、これらの実施形態も本発明の構成を限定的に示すものでない。なお、以下の実施形態において、第一の実施形態と同様な構造とされた部材および部位については、それぞれ、第一の実施形態と同一の符号を各図中の対応する部位に記載することにより、それらの詳細な説明を省略する。

【0066】

図 3～4 には、本発明の第二の実施形態としての研磨パッド用補助板 4 0 を備えた研磨装置 4 2 が示されている。

【0067】

この研磨パッド用補助板 4 0 においては、下側補助板 2 0 の上面の外周部分を周方向に連続して延びる円環形状の溝によって係合凹部 4 4 が形成されている。一方、上側補助板 2 2 の下面の外周部分には、周方向に連続して延びる円環形状の突起によって係合凸部 4 6 が形成されている。この係合凸部 4 6 は、上側補助板 2 2 に一体形成されていても良いが、図示されているように、別体形成されていても良い。即ち、本実施形態では、上側補助板 2 2 の下面に開口して周方向に延びる円環形状の周溝 4 8 が形成されており、この周溝 4 8 に対して、別体形成された円環形状のブロックが軸方向一端側で嵌め込まれて固着されることにより係合凸部 4 6 が形成されている。

【0068】

下側補助板 2 0 の係合凹部 4 4 と、上側補助板 2 2 の係合凸部 4 6 は、何れも中心軸回りで対応する径方向位置に形成されており、上下補助板 2 2, 2 0 が重ね合わされた際、係合凹部 4 4 に対して係合凸部 4 6 が嵌め入れられることにより、上下補助板 2 2, 2 0 が相互に径方向で位置合わせされるようになっている。なお、本実施形態では、下側補助板 2 0 の係合凹部 4 4 における両側壁面と、上側補助板の係合凸部 4 6 における内外周面との、各対応する径方向の重ね合わせ面によって、二組の係合内周面および係合外周面が構成されている。

【0069】

図 5～6 には、本発明の第三の実施形態としての研磨パッド用補助板 5 0 を備えた研磨装置 5 2 が示されている。

【0070】

この研磨パッド用補助板 5 0 においては、下側補助板 2 0 の外周部分には、中心軸回りで全周に亘って延びる円形の係合内周面としての段差面 5 4 が形成されている。そして、この段差面 5 4 よりも外周側では下側補助板 2 0 の厚さ寸法が大きくされることで、下側補助板 2 0 の外周端縁に沿って周方向の全周に連続して延びる環状の係合凸部 5 6 が、下

側補助板 20 に一体形成されている。

【0071】

一方、上側補助板 22 の外周部分には、中心軸回りで全周に亘って延びる円形の係合外周面としての段差面 58 が形成されている。そして、この段差面 58 よりも外周側では上側補助板 22 の厚さ寸法が小さくされることで、上側補助板 22 の外周面に開放する切欠断面形状をもって周方向の全周に連続して延びる環状の係合凹部 60 が、上側補助板 22 に一体形成されている。

【0072】

さらに、下側補助板 20 の段差面 54 には雌ねじが形成されている一方、上側補助板 22 の段差面 58 には雄ねじが形成されている。そして、下側補助板 20 の段差面 54 の雌ねじに対して上側補助板 22 の段差面 58 の雄ねじを螺合させて、下側補助板 20 の段差面 54 と上側補助板 22 の段差面 58 とを径方向に重ね合わせることで、下側補助板 20 の上面に上側補助板 22 が重ね合わされるようになっている。また、かかる重ね合わせ状態では、上下補助板 22, 20 の段差面 58, 54 の螺着構造により、上下補助板 22, 20 を取り外し可能に固着する第二の固着手段 62 が構成されている。

【0073】

なお、このような螺着構造における雌雄ねじは、研磨装置 12 の回転定盤 14 に対して及ぼされる研磨時の回転反力を考慮して、ねじが緩まないようにねじ方向が設定されることが望ましい。

【0074】

図 7～8 には、本発明の第四の実施形態としての研磨パッド用補助板 64 を備えた研磨装置 66 が示されている。

【0075】

この研磨パッド用補助板 64 においては、下側補助板 20 の上面の中央部分で上方に向かって突出する円柱形状の係合凸部 68 が形成されている。この係合凸部 68 は、下側補助板 20 に一体形成されていても良いが、図示されているように、別体形成されていても良い。即ち、本実施形態では、下側補助板 20 の中心軸上に円形の嵌着凹所 70 が形成されており、この嵌着凹所 70 に対して、別体形成された円柱形状のブロックが軸方向一端側で嵌め込まれて固着されることにより係合凸部 68 が形成されている。一方、上側補助板 22 の下面の中央部分には、中心軸上で下面に開口する有底円形の係合凹部 72 が形成されている。なお、係合凸部 68 および係合凹部 72 は上下補助板 22, 20 のどちらに形成されていても良い。

【0076】

そして、上下補助板 22, 20 が重ね合わされた際、係合凹部 72 に対して係合凸部 68 が嵌め入れられることにより、上下補助板 22, 20 が相互に径方向で位置合わせされるようになっている。なお、本実施形態では、下側補助板 20 の係合凸部 68 の外周面と上側補助板 22 の係合凹部 72 の内周面とによって、係合外周面と係合内周面とが構成されている。

【0077】

図 9 には、本発明の第五の実施形態としての研磨パッド用補助板 74 を備えた研磨装置 76 が示されている。

【0078】

この研磨パッド用補助板 74 においては、下側補助板 20 の上面の外周部分で上方に向かって突出する円柱形状の係合凸部 78 が形成されている。この係合凸部 78 は、下側補助板 20 に一体形成されていても良いし、前記第四の実施形態における係合凸部のように下側補助板 20 に嵌着凹所を形成して別体のピンなどを圧入等で固着しても良い。また、図 10～11 に示されているように、かかる係合凸部 78 は、下側補助板 20 の外周部分で周方向で所定距離を隔てて互いに独立して複数形成されている。特に好適には、周方向で等間隔に且つ中心軸上の同一円上に位置して、それら複数の係合凸部 78 が形成される。

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【0079】

一方、上側補助板22の下面の外周部分には、下側補助板20における複数の係合凸部78の形成位置に対して各対応する位置に、それぞれ、有底円形の係合凹部80が下方に向かって開口して形成されている。なお、係合凸部78および係合凹部80は上下補助板22、20のどちらに形成されていても良い。

【0080】

そして、上下補助板22、20が重ね合わされた際、係合凹部80に対してそれぞれ係合凸部78が嵌め入れられることにより、上下補助板22、20が相互に径方向で位置合わせされるようになっている。なお、本実施形態では、下側補助板20の係合凸部78の外周面と上側補助板22の係合凹部80の内周面とによって、下側補助板20および上側補助板22の外周部分に位置する係合外周面と係合内周面とが構成されている。

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【0081】

特に本実施形態のように、周方向で独立した複数の係合凸部78と係合凹部80とからなる位置決め手段を採用することにより、重ね合わされた上下補助板22、20を径方向だけでなく周方向においても相互に位置決めすることが可能となる。

【0082】

なお、上側補助板22に形成される独立した複数の係合凹部80に代えて、上側補助板22の中心軸回りで周方向に連続して円形に延びる周溝を採用したり、或いは図12における本発明の第六の実施形態に示されているように、上側補助板22の外周部分を中心軸回りで全周に亘って延びる円形の段差面82を形成し、この段差面82よりも外周側の厚さ寸法を小さくすることで、上側補助板22の外周面に開放する切欠断面形状をもって周方向の全周に連続して延びる環状の係合凹部83を形成することも可能である。

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【0083】

このように上側補助板22において、下側補助板20の係合凸部78の係合面を全周に亘って連続して形成することにより、上下補助板20、22の重ね合わせに際して、上下補助板20、22を相互に周方向で位置合わせする必要がなくなって装着作業を容易に行うことが可能となる。

【0084】

図13には、本発明の第七の実施形態としての研磨パッド用補助板84が示されている。

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【0085】

この研磨パッド用補助板84においては、下側補助板20の外周面の側面部分と、上側補助板22の外周面の側面部分とに、それぞれ小径部が設けられている。そして、これら上下補助板22、20が重ね合わされることにより、それぞれの小径部によって、上下補助板22、20間に跨がって所定幅で広がって周方向の全周に亘って延びる円環形状の収容凹所86が形成されている。

【0086】

また、下側補助板20の小径部下端には、溝状の係合凹部88が形成されている。この係合凹部88は、収容凹所86の底面において、下側補助板20の外周面に開口せしめられている。ここで、収容凹所86の底面とは、収容凹所86を構成する面のうち、上下補助板22、20に跨り、図13の上下方向に広がる環状の面を指す。一方、収容凹所86を構成する上側補助板22の小径部には、弾性材からなる板状の係合凸部90が、その基端部において固定ピン92で固定されて取り付けられている。この係合凸部90は、上下補助板22、20の外周面に形成された収容凹所86に収容配置されており、上側補助板22から下側補助板20の外周面上に延び出している。そして、係合凸部90の先端部分に形成された係合爪部94が、下側補助板20の小径部に形成された係合凹部88に対して係止され、係合凸部90の弾性に基づいて係止状態に保持されるようになっている。

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【0087】

更にまた、このような係合凸部90が、上下補助板22、20の外周面上で周方向に所定距離を隔てて複数設けられている。そして、上側補助板22の外周面に取り付けられた

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各係合凸部90が、下側補助板20の外周面に対して弾性的に押し付けられることで、上下補助板22、20が中心軸上で相互に位置決めする位置決め手段が構成されている。また、係合凸部90の係合爪部94が係合凹部88に係止されることにより、上下補助板22、20を重ね合わせ状態に保持せしめて固着力を及ぼす固着手段も構成されている。

【0088】

なお、上述の如き係合凹部88に係合する係合爪部94を備えた係合凸部90に代えて、例えば図14に示された本発明の第八の実施形態のように、上下補助板22、20間に跨がって延びて收容凹所86の底面に重ね合わされる連結板100を採用し、かかる連結板100の両端部分を上下補助板22、20の各一方の外周面に対して連結ピン102、102で固着することも可能である。なお、連結ピン102、102の少なくとも一方は下側補助板20又は上側補助板22に対して着脱可能とされることにより、上下補助板22、20の連結板100による連結が解除可能とされて、研磨パッド16が固着された上側補助板22の下側補助板20に対する着脱が許容されることとなる。

【0089】

また、第一～八の実施形態に示された両面テープ等からなる第一の固着手段24や第二の固着手段26は、上下補助板22、20や回転定盤14を取り外す際に、特定の部材側の固着面に保持されることが望ましい。これにより、取り外した状態での上下補助板22、20や第一及び第二の固着手段24、26の取り扱いが容易となるからである。なお、第一及び第二の固着手段24、26が何れの固着面に残るかは、第一の固着手段や第二の固着手段24、26自体における両面の固着力を相互に異ならせる他、固着される上下補助板22、20や回転定盤14の面粗度や材質等を相互に異ならせることなどによって設定することが可能である。

【0090】

特に、第一の固着手段24は、下側補助板20を取り外す際に下側補助板20側の固着面に保持されることが望ましく、それによって回転定盤14の上面18のメンテナンスが容易となる。一方、第二の固着手段26は、第一の実施形態における図2に示されているように、上側補助板22を取り外す際に上側補助板22側の固着面に保持されるようになっていても良いし、例えば図15に示す本発明の第九の実施形態のように、下側補助板20の上面に残るようにしても良い。なお、第二の固着手段26を上側補助板22側の固着面に保持させることにより、研磨パッド16の溝入れなどの再加工用装置の回転定盤に対して、取り外した上側補助板22を装着する際に、上側補助板22に保持された第二の固着手段26を利用して取り付けることも可能となる。一方、第二の固着手段26を下側補助板20側の固着面に保持させることにより、別の研磨パッド16を装着した別の上側補助板22を下側補助板20に装着する際に、下側補助板20に保持された第二の固着手段26を利用して取り付けることも可能となる。

【0091】

また、第一～七の実施形態に示された係合凹部32、44、60、72、80、(83)、88と係合凸部36、46、56、70、78、90は、下側補助板20側と上側補助板22側とにおいて相互に反対側に設けられていても良い。例えば本発明の第十の実施形態が図16に示されているように、第一の実施形態として図1～2に示された研磨パッド用補助板10に対して、その係合外周面を構成する段差面30と係合凹部32とを上側補助板22に形成する一方、係合内周面を構成する段差面34と係合凸部36とを下側補助板20に形成することも可能である。

【0092】

更にまた、第一～六の実施形態に示された係合凹部32、44、60、72、80、(83)と係合凸部36、46、56、70、78において、相互に重ね合わされて上下補助板22、20を位置決めする係合凸部の外周面と係合凹部の内周面とに対して傾斜角を付すことも可能である。例えば本発明の第十一の実施形態が図17に示されているように、下側補助板20の外周部分に突出形成した係合凸部36の係合内周面としての段差面34に対して、係合凸部36が突出方向で次第に先細となる傾斜方向のテーパを付す一方、

上側補助板２２の外周部分に形成した係合凹部３２の係合外周面としての段差面３０に対して、段差面３４に対応する傾斜方向および傾斜角度のテーパを付すことができる。これにより、係合凸部３６を係合凹部３２に嵌め入れて上下補助板２２、２０を重ね合わせる作業を、両段差面３４、３０に付されたテーパを案内面として利用することで、一層容易に行うことが可能となる。

【００９３】

因みに、図１８に記載の本発明の第十二の実施形態や、図１９に記載の本発明の第十三の実施形態に示されているように、下側補助板２０の周方向で独立して複数形成される突起形状の係合凸部７８と、上側補助板２２の各対応する位置に形成される複数の穴形状の係合凹部８０とを採用する場合でも、係合凸部７８の突出先端部分の外周面に対して傾斜角を付して、先細形状のテーパ部１０４を形成することができる。なお、図１９では、下側補助板２０に形成された嵌着穴１０５に対して、別体形成された係止ピン１０６が圧入等で固着されて係合凸部７８が構成されており、かかる係止ピン１０６の下端にも、上端と同様なテーパ部１０４が付されている。これにより、係止ピン１０６に方向性が無くなって取り扱いが容易となると共に、嵌着穴１０５への圧入作業も容易となる。

【００９４】

また、図２０に示された本発明の第十四の実施形態では、上下補助板２２、２０の重ね合わせ状態で中心軸を合わせる位置決め手段の一種として、それら上下補助板２２、２０間に跨がって外挿される位置決めスリーブ１０８が示されている。この位置決めスリーブ１０８は、互いに略同じ外径寸法の円板形状とされた上下補助板２２、２０の外径寸法と同じか僅かに大きな内径寸法を有しており、金属材や合成樹脂材によって形成されている。このような位置決めスリーブ１０８を、上下補助板２２、２０の重ね合わせに際して用いて、位置決めスリーブ１０８内で上下補助板２２、２０を重ね合わせるとにより、上下補助板２２、２０を中心軸合わせしつつ軸方向に重ね合わせて、第二の固着手段２６で相互に固着することができる。それ故、上下補助板２２、２０を重ね合わせて相互に固着せしめた後で、位置決めスリーブ１０８を取り外すことが出来るのであり、それによって、上下補助板２２、２０を、外周面上に突出する位置決め手段を有しない状態で且つ正確な位置合わせ状態で相互に固着することが可能となる。

【００９５】

更にまた、図２１に示された本発明の第十五の実施形態では、上下補助板２２、２０の重ね合わせ状態で重ね合わせ方向に跨がって延びるスリット状の係合溝１１０が形成されている。この係合溝１１０は、上下補助板２２、２０の外周面に開口して径方向内方に所定深さを有しており、上下補助板２２、２０の周方向で互いに独立して複数設けられている。そして、かかる係合溝１１０に対して、外周面の開口部からプレート形状の係合板１１２が嵌め入れられることにより、かかる係合板１１２で上下補助板２２、２０が相互に位置決めされると共に、相互に連結状態とされている。なお、かかる係合板１１２は、上下補助板２２、２０と別体形成されているが、例えば上下補助板２２、２０の何れか一方において他方に向かって突出する形状をもって一体形成されていても良い。その場合には、係合溝１１０は、当該他方の補助板にだけ形成されることとなる。

【００９６】

さらに、図２２に示された本発明の第十六の実施形態では、上側補助板２２の下面に開口する係合凹部としての嵌合凹部１１４が形成されている。特に本実施形態では、かかる嵌合凹部１１４が、上側補助板２２の中心軸回りで周方向に連続して延びる環状溝として形成されている。一方、下側補助板２０には、上側補助板２２に重ね合わされる上面において上方に突出する係合凸部としての嵌合凸部１１６が形成されている。なお、本実施形態では、かかる嵌合凸部１１６が、嵌合凹部１１４に対応する環状凸部として形成されている。そして、上下補助板２２、２０の重ね合わせ状態で、嵌合凸部１１６が嵌合凹部１１４に入り込んで位置せしめられるようになっている。

【００９７】

また、嵌合凸部１１６は中空構造とされており、嵌合凸部１１６の内部において外部空

間に対して密閉された流体溜 1 1 8 が形成されている。更に、この流体溜 1 1 8 を画成する嵌合凸部 1 1 6 の壁部は、少なくとも内周壁と外周壁が径方向に向かって膨出変形可能にされている。具体的には、例えば嵌合凸部 1 1 6 をゴム弾性体などで形成することによって、径方向内方に膨出可能な内周壁と径方向外方に膨出可能な外周壁とが実現可能である。

【0098】

更にまた、下側補助板 2 2 には、流体溜 1 1 8 に連通して、径方向外方に延び出し外周面に開口する流体通路 1 2 0 が形成されていると共に、この流体通路 1 2 0 の外周端開口部に加圧ねじ 1 2 2 がねじ込まれている。また、加圧ねじ 1 2 2 で封止された流体通路 1 2 0 と流体溜 1 1 8 からなる密閉領域には、オイルなどの非圧縮性流体が充填されている。

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【0099】

これにより、加圧ねじ 1 2 2 をねじ込むことにより、流体通路 1 2 0 を通じて流体溜 1 1 8 の内圧を上昇させて、流体溜 1 1 8 の内周壁および外周壁を外方に膨出させることが出来る。その結果、嵌合凸部 1 1 6 が拡張されて、嵌合凹部 1 1 4 の内面に押し付けられ、相互の摩擦等によって上下補助板 2 2, 2 0 を相互に位置決めすると共に固着力も及ぼし得るようになっている。

【0100】

なお、上側補助板 2 2 を下側補助板 2 0 から取り外すに際しては、加圧ねじ 1 2 2 を緩ませる方向に回転操作して下側補助板 2 0 の外周側に移動させることにより、流体溜 1 1 8 の圧力を低下させて嵌合凸部 1 1 6 の嵌合凹部 1 1 4 への押し付け力を解除することができる。

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【0101】

その他、一々列挙はしないが、本発明は当業者の知識に基づいて種々なる変更、修正、改良などを加えて実施することが可能であり、例えば、係合凸部と係合凹部の係合部分に Oリングやシール材を装着して上下補助板の重ね合わせ面等への異物の侵入を防止することも可能である。

【0102】

また、上述の二層構造の補助板 2 0, 2 2 に加えて、更に補助板を積層状態で且つ固着手段で固着せしめて追加することも可能である。このように第三層の補助板を採用することで、弾性支持状態を実現したり、或いは中間層を使い捨てる等の態様も可能となる。

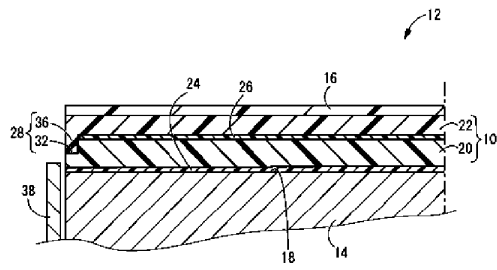
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【符号の説明】

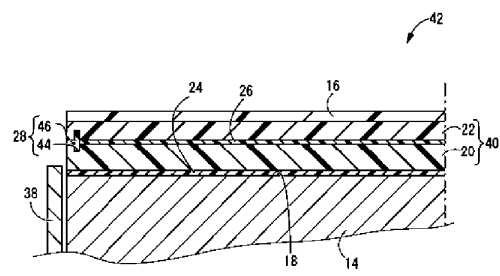
【0103】

1 0, 4 0, 5 0, 6 4, 7 4, 8 4 : 研磨パッド用補助板、1 2, 4 2, 5 2, 6 6, 7 6 : 研磨装置、1 4 : 回転定盤、1 6 : 研磨パッド、1 8 : 上面、2 0 : 下側補助板、2 2 : 上側補助板、2 4 : 第一の固着手段、2 6, 6 2 : 第二の固着手段、2 8 : 位置決め手段、3 0, 5 8 : 段差面 (係合外周面)、3 2, 4 4, 6 0, 7 2, 8 0, 8 8 : 係合凹部、3 4, 5 4 : 段差面 (係合内周面)、3 6, 4 6, 5 6, 6 8, 7 8, 9 0 : 係合凸部、3 8 : 保護部材

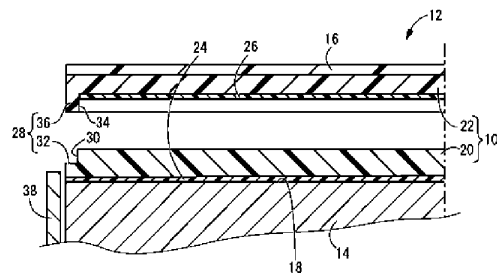
【図 1】



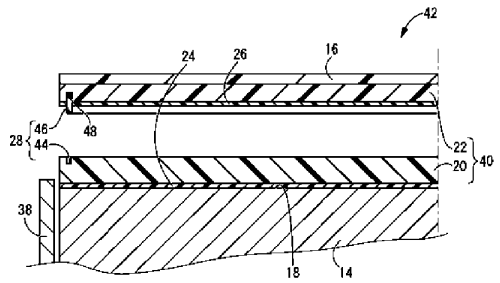
【図 3】



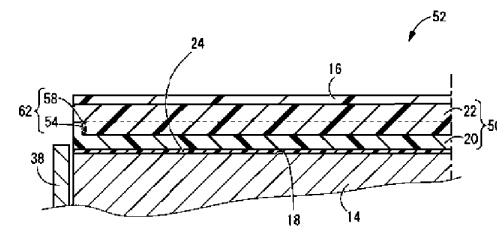
【図 2】



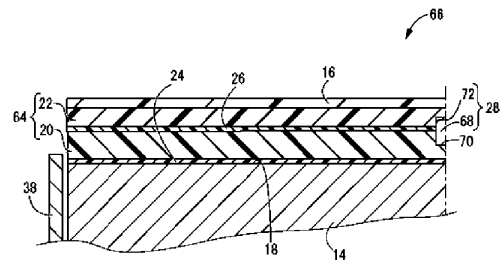
【図 4】



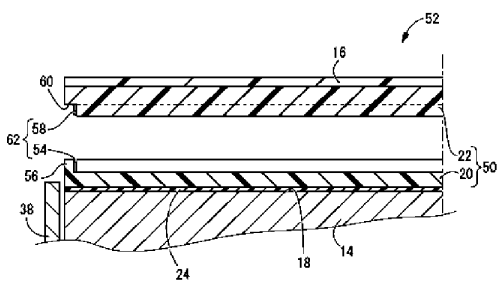
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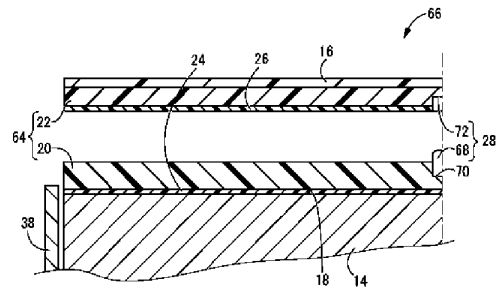
【図 7】



【図 6】



【図 8】



フロントページの続き

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wrap up

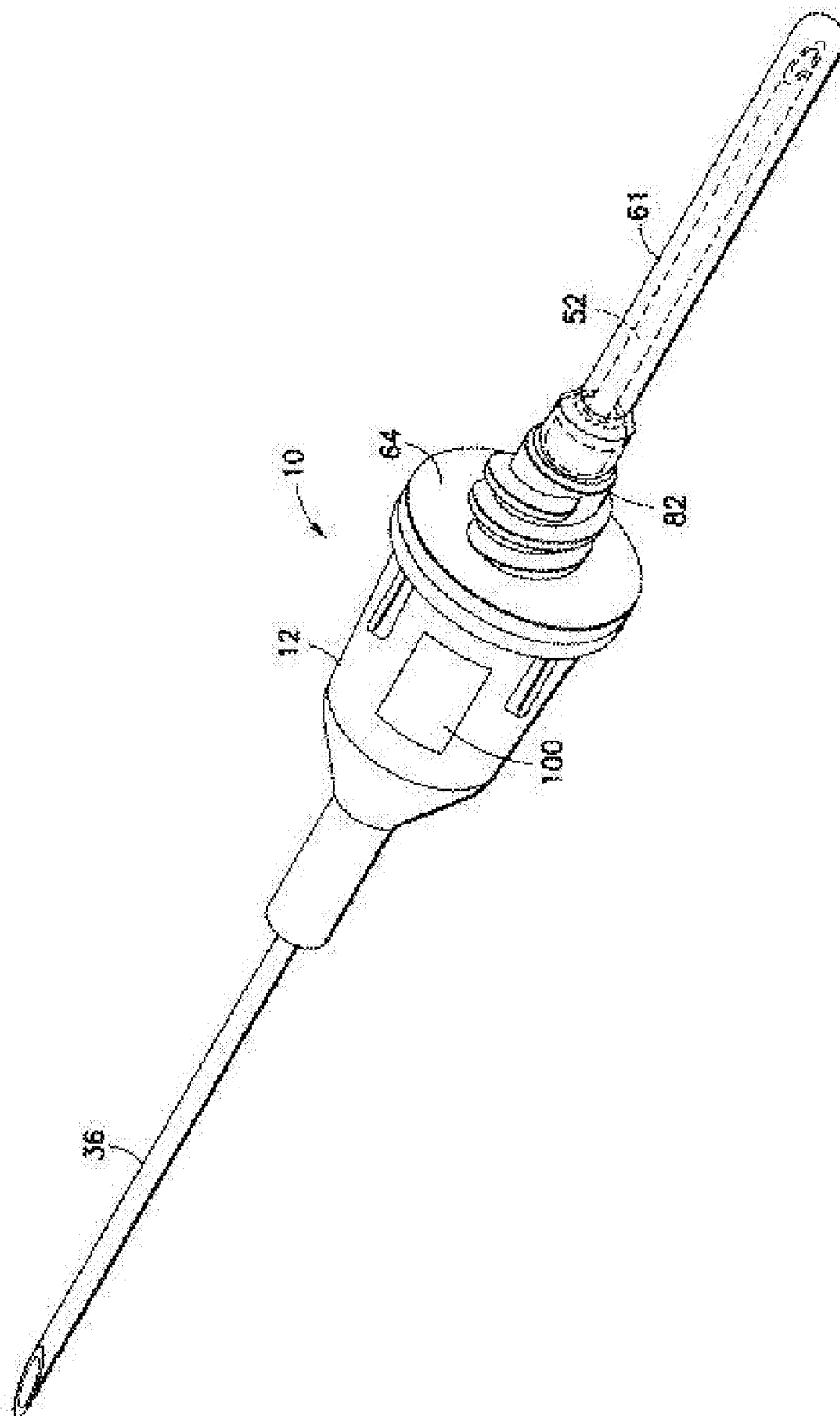
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(57) [Summary] (Modified)

[Problem] To easily confirm that puncturing has been performed reliably when collecting blood, 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 blood 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 blood, during use. Thus, air under venous pressure can be expelled from the blood collection needle assembly by the time the blood reaches the venting mechanism.

[Selection drawing] Fig. 1



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 cannula and having a lumen attached to the hub in communication with the chamber; an outlet cannula 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 multiple 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 outflow 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 communicating 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 venting medium.

[Claim 4]

3. The needle assembly of claim 2, wherein said venting mechanism includes at least one opening 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 surrounding the inlet cannula, the vent ring being positioned through the hub in the chamber proximate 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 passage

e beyond the proximal end of said exit cannula.

8.

The needle assembly as recited in claim 7, wherein said venting mechanism comprises a venting medium.

9.

The needle assembly of claim 1, wherein said hub further comprises a non-patient locking projection, 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 venting medium.

11.

The needle assembly of claim 9, wherein said venting mechanism comprises a passageway through 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 extending 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 non-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 projection, at least a portion of said non-patient locking projection comprising said venting mechanism. .

15. The

needle assembly as recited in claim 14, wherein said venting mechanism comprises a venting medium.

16.

At least part of said non-patient side locking projection is made of a porous hydrophobic material, or at least part of said non-patient side locking projection is made of a porous material having a hydrophobic surface. 15. The needle assembly of claim 14, wherein the needle assembly is made of material.

17.

A needle assembly as in claim 14, wherein said venting mechanism comprises a porous material 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 non-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 venting sleeve.

[Claim 20]

20. The needle assembly of claim 19, wherein said vent sleeve comprises a porous hydrophobic 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 vent cord.

22.

The needle assembly of claim 18, wherein said venting mechanism comprises a textile surface.

23.

The needle assembly of claim 1, wherein said multiple sample sleeve includes said venting mechanism.

24. The

needle assembly as recited in claim 23, wherein said venting mechanism comprises a venting medium.

25. Said

multiple sample sleeve is formed of a porous hydrophobic material or said multiple sample sleeve comprises a porous material having a hydrophobic surface. A needle assembly as described in .

26.

The needle assembly of claim 1, wherein at least a portion of said hub is formed by a venting 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 said 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 assembly 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 located 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 thread 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 thread assembly formed of a porous material such that the non-patient thread assembly constitutes 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 medium.

33.

The needle assembly of claim 1, further comprising a shield selectively covering said first cannula.

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 proximal 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 the 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 venting mechanism to the external atmosphere and substantially prevents fluid from exiting the needle assembly through the venting mechanism to the external atmosphere. A needle assembly,

comprising: a venting mechanism.

35.

The needle assembly as recited in claim 34, wherein said venting mechanism is disposed in said passageway beyond said proximal end of said exit cannula.

36.

The needle assembly of claim 35, wherein said venting mechanism comprises a venting medium.

37.

The needle assembly of claim 34, wherein the hub further comprises a non-patient locking projection, and wherein the vent mechanism extends through the non-patient locking projection. .

38. The

needle assembly as recited in claim 37, wherein said venting mechanism comprises a venting medium.

39. The needle assembly of claim 37,

wherein said venting mechanism comprises a passageway through said non-patient stop projection and a vent plug disposed in said passageway.

[Claim 40]

The vent mechanism includes a notch extending through the non-patient side locking projection 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 least 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 venting medium.

44.

At least part of said non-patient side locking projection is formed of a porous hydrophobic material, 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 material 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 puncture on a patient to obtain a blood sample. More particularly, the present invention is useful for collecting multiple blood samples when collecting blood samples from a patient into a vacuum blood collection tube, where the self-venting feature allows the phlebotomist to know if the vessel has been punctured. of the needle assembly. **BACKGROUND OF THE INVENTION** Vascular puncture is the primary method used to obtain blood samples for clinical examination. Performing a vascular puncture requires the phlebotomist to perform multiple steps simultaneously. 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 collect and identify fluid samples for clinical examination. All of these concurrent factors must be identified 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 developed to address the aforementioned problems. These devices include a needle assembly having a hub defining a chamber therein with a single pointed cannula secured to the hub. The vascular 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 within 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 cannula into the sealable sleeve and into the hub's chamber, which is transparent or translucent for 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 phlebotomist 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 chamber and/or

Unnecessarily repeated vascular punctures requiring replacement of the needle assembly itself. Repetition of such procedures prolongs the physical and emotional discomfort experienced by 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. push out to

[0007]

Accordingly, to provide a rapid, accurate and cost-effective solution to conventional blood sampling 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 assembly and no leakage of blood from the assembly. As used herein, ventilation media refers to elements that actually allow air to pass, such as plugs, coatings, surface treatments, and the like. 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-venting 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 allow air to escape but prevent the passage of liquids. Thus, air under venous pressure can be expelled from the blood collection needle assembly by the time it reaches the venting mechanism. The venting mechanism then blocks or prevents the flow of blood around or through it, allowing blood to be collected into a vacuum collection tube or other suitable blood collection container. The present invention provides good instant visualization within the flashback chamber 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 sample from a patient and subsequently expelling it into at least one vacuum vessel. The self vented blood collection needle assembly of the present invention includes a hub having a fluid inlet defined by a cylindrical outer wall. The wall defines a flashback chamber for retaining the blood 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 extends outwardly therefrom. The first cannula has an inner proximal end located at the proximal 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 exit 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 opposite 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 instead of two cannulas. Another alternative cannula configuration is to use a single cannula without a notch to pass through the proximal end of the non-patient cannula, around multiple sample sleeves and through a vent before flashback occurs. The outer portion of the hub near the proximal end is formed with a single external thread, or other mounting structure, for receiving blood.

A collection needle assembly can be attached to a collection tube holder or other medical device. 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 this configuration. The vent mechanism thereby communicates the fluid passageway with the outside atmosphere via the hub.

In another embodiment, a venting mechanism is placed over the proximal end of the non-patient cannula which

allows air to pass through the proximal end of the non-patient cannula from which blood is aspirated and then through the vent. A single cannula without a notch is suitable in this case, but any cannula construction can be used. Specifically, air flows through the space between the outside of the needle and the multiple sample sleeve and exits the fluid passageway out the proximal end of the non-patient cannula. The air is then directed to the non-patient 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-patient 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 prevents contact of the blood sample with the vent, which could potentially lead to platelet activation or contamination or other undesirable consequences. This also prevents air from being drawn back into the fluid passageway when a vacuum tube is installed. It should also be noted that this embodiment requires a smaller ejection chamber than the previous embodiment in which the vent is located in the hub.

[0012]

Another embodiment of the invention has a venting mechanism comprising an integral hub at least partially formed of a porous material such as sintered plastic, ceramic or metal. This porous material either before air enters the non-patient cannula or after air exits the proximal end and flows through the non-patient cannula into the space between the cannula and the multiple sample sleeve. can be arranged so that the evacuation takes place at the same time. The porous material allows air to pass through but prevents blood from leaking. In typical embodiments, 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 be permanently joined to the tube holder to eliminate the need and inconvenience of a threaded 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 manufactured efficiently, and the holder can be discarded together with the needle, thereby increasing the safety of medical procedures.

[0013]

In yet another embodiment, the vent mechanism vents air out through a side opening located 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 the surface tension is also such that it prevents leakage. The vent media material of this embodiment 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 twisting of the shape requires the vent medium to extend over the receiving structure on the hub. When the vent media is placed on the support structure, it releases and uses its own elasticity 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 the 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 more vacuum tubes. An assembly is provided that provides a visual indication of vascular insertion ("flashback") as it is drawn into a blood collection tube. The aeration medium may be a separate physical element, such as a plug or insert, or an integral part of the device, treated, such as by laser drilling, or made wholly or partially of a porous material, or impregnated, for example

Note that it may be a film, layer, etc., formed by depositing the material on the device by coating, 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 through the hub 12 and is immediately visible in the flashback chamber through the translucent window.

ndow 100, and with the aid of the venting mechanism, at the appropriate time that a proper vessel puncture has occurred. give proper instructions.

[0017]

Figures 2-28 illustrate various embodiments of the present invention including various configurations 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 portion. Figures 5-12 show embodiments in which the venting mechanism is located beyond the proximal end 60 of the non-patient cannula. Figures 13 and 14 show an embodiment in which a portion of the hub of the needle acts as the vent medium. FIG. 15 shows an embodiment in which the venting mechanism is a unified hub 132. Figures 16-26 show embodiments in which the ventilation mechanism is a breathable cord. Figures 27A and 27B show an embodiment 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 cannula can be used as well.

FIGS.

2, 3, 4A, 4B and 4C illustrate a venting mechanism in which a venting ring 300 is placed around 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 openings 303 to the outside atmosphere through this ventilation ring. These openings can be located 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 longitudinal 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 reduces the amount of air exhausted from the hub assembly 12 compared to the previous embodiments such as FIGS. 2, 3, 4A, 4B, 4C. It is advantageous for The next embodiment uses a larger 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 the surface of the hub and/or part of the flashback chamber for better visibility of the flash. Note that a flashback chamber or window can be placed in the air/blood passageway, especially for embodiments using a single cannula without a notch. In the embodiment of FIG. 5, air flows from the fluid passageway 306 to the proximal end 60 of the non-patient cannula and through the space 307 between the outside 308 of the needle and the inside of the multiple sample 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 escaping 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 of 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 the vent is close to the exterior through which air is exhausted. 8A and 8B show an embodiment in which the notch 313 in the non-patient locking projection 314 is configured to allow air to escape to the vent disc 315. FIG. 9A and 9B show another embodiment in which the notch 316 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 modified 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 cannula 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 described.

[0023]

12 shows that air passes through narrow passage 353 between the outside of non-patient needle 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 reservoir 355 of the hub 356 and is discharged to the outside atmosphere via a passageway 358 at the 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 assembly 322 is made of a porous material and thus acts as a venting medium. FIG. 13 shows hub 321 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 chamber 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 of 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 to be an integral one-piece hub 325 with the air further passing through the space 307 between the outside of the needle 308 and the inside of the multiple specimen sleeve 61 and then through 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 the 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 projection 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, placement, 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 shapes and combinations of these shapes are also available. The cord is made by extruding, spinning 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 the fluid passageway. This valve allows air to pass through but closes when a vacuum is applied, so when a vacuum collection tube is attached to the tip of the needle, this tube will draw blood 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 306 , but is preferably located at hub 328 . The valve 349 itself may be a thin flap such as a plastic 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 valve 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 and is pulled out of fluid passageway 306 by venous pressure during an initial venipuncture. Air is pushed through the porous vent plug 352 and out under the free edge of the plastic film 349 . However, when a vacuum is applied to the fluid passageway 306 (via the blood collection tube attachment), the thin plastic film 349 sucks tightly against the porous vent plug 352, sealing the vent to keep air out. Prevents re-entry into the fluid passageway. Thus, this embodiment serves the primary or backup function of preventing air from re-entering the system after evacuation 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 remains in fluid communication therewith. When cannula 360 is properly positioned, it frictionally engages hole 34 or is secured thereto, such as by adhesive. During venipuncture, air flows from fluid passageway 306, exits proximal end 362 of cannula, and flows into space 307 between 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 mechanisms described herein are applicable to various devices other than blood collection needle assemblies. Venting media, as used herein, include, for example : a generally hydrophobic substrate or carrier coated, impregnated, or containing a hydrophilic material that swells on contact 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, tortuous passages ; vent holes provided by a porous material or holes, gaps or passages large enough 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 coagulation and/or cell agglutination to block the vent, or a super plug that seals the vent by swelling 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 containing a hydrophilic material such as carboxymethylcellulose (CMC) or polyacrylate, or a hydrophobic material such as high density polyethylene (HDPE)

.
formed by Alternative hydrophobic materials include, but are not limited to, polytetrafluoroethylene (PTFE), ultra high molecular weight polyethylene (UHMPE), nylon 6, polypropylene (PP), polyvinylidene fluoride, or polyethersulfone. (PES). As will be described in further detail below, the venting media of the present invention are suitable for venting mechanisms and devices, including one or more micro-dimensioned matte-finished passages, laser-drilled holes, ventable 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 plug, is referred to herein, it is intended to be non-limiting and to include other suitable members of venting media.

[0032]

One embodiment of the venting media consists of micro-sized holes formed in the outer wall. These holes are large enough to allow air to pass, but small enough to prevent blood leakage. The vent can be any number, including one, but multiple holes are preferred for reliable function. These holes are laser drilled, i.e. they are burned through the wall using one or more laser 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 mechanism may be located at any convenient space along the fluid passageway within the syringe or patient cannula, hub, or additional component, but to produce a flush along the entire length of the tube, a vent 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 small pores between parts. or by placing a biological agent in the space. The vent may be of any conventional shape. Venting may occur at any location(s) in the fluid passageway, but preferably at the proximal end, such as the hub, close to the collection device. The vent is made of and includes a stimulant that interacts with blood to promote clotting and/or cell clumping such that clotted and/or congealed cells inhibit flow through the vent. , preferably adjacent to or cooperating with. Examples of clotting stimulants are silica, crushed glass, or glass fibers. One example of a glue is a lectin. Examples of platelet activators are collagen or thrombin. Neutralizing agents for anticoagulants such as protomin sulfate may be included. The biological stimulant can be applied as a powder, solution, suspension, slurry, or other form using any convenient 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 invention, all of which are intended to be within the scope of the invention

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 the 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 present 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 invention;

FIG. 7 is a cross-sectional view similar to FIG. 5, but showing another embodiment of the invention;

8A is a cross-sectional view similar to FIG. 5, but showing another embodiment of the invention; 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 invention; 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 invention; 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 invention;

Figure 19 is a cross-sectional view similar to Figure 17 but showing another embodiment of the invention;

Figure 20 is a cross-sectional view similar to Figure 17 but showing another embodiment of the invention;

Figure 21 is a cross-sectional view similar to Figure 17 but showing another embodiment of the invention;

Figure 22 is a cross-sectional view similar to Figure 17 but showing another embodiment of the invention;

Figure 23 is a cross-sectional view similar to Figure 17 but showing another embodiment of the invention;

FIG. 24 is a cross-sectional view similar to FIG. 17 but showing another embodiment of the invention;

Figure 25 is a cross-sectional view similar to Figure 17 but showing another embodiment of the invention;

Figure 26 is a cross-sectional view similar to Figure 17 but showing another embodiment of the invention;

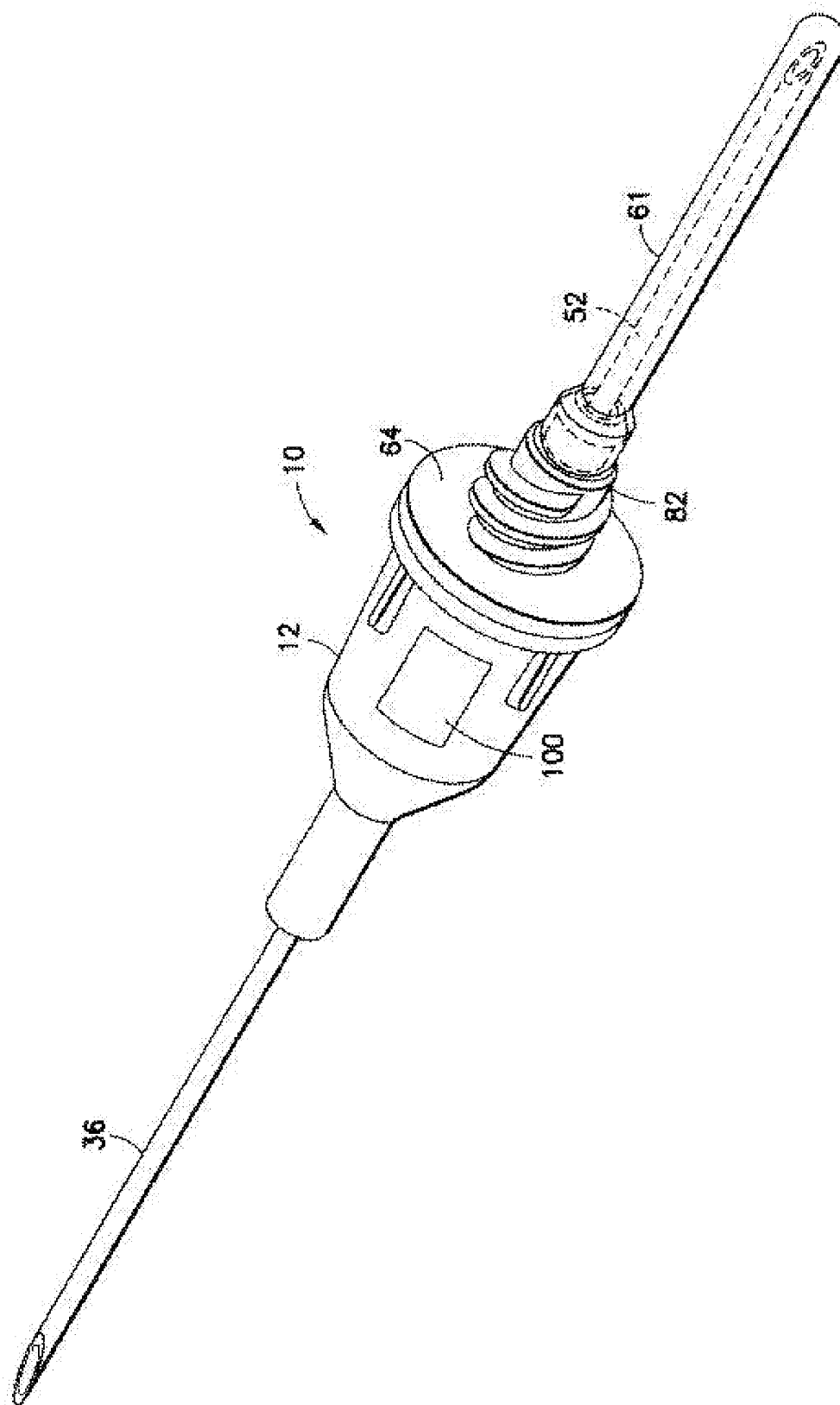
Figure 27A is a cross-sectional view of one embodiment of a blood collection needle assembly; 27B is an enlarged view of FIG. 27A viewed from region R; FIG.

Figure 28 is a cross-sectional view of one embodiment of a blood collection needle assembly;

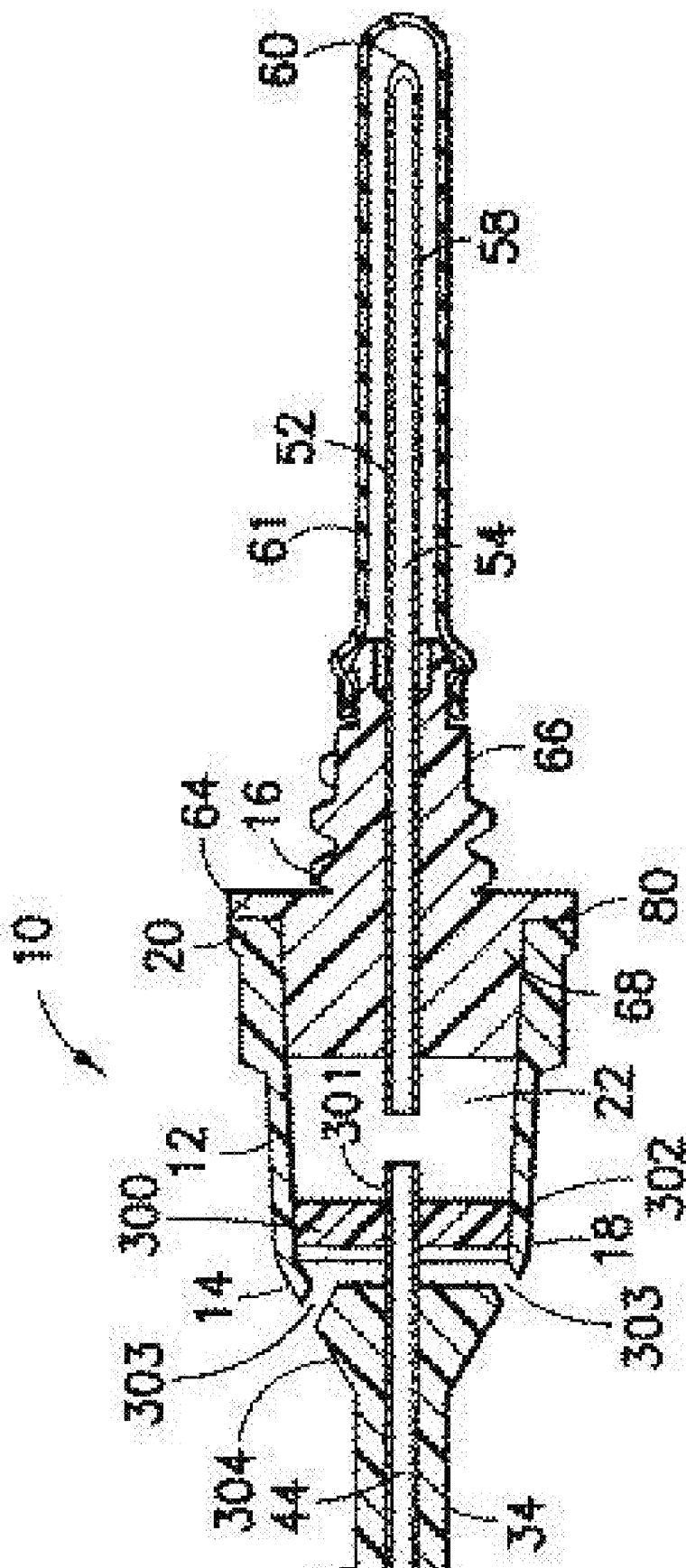
drawing

open

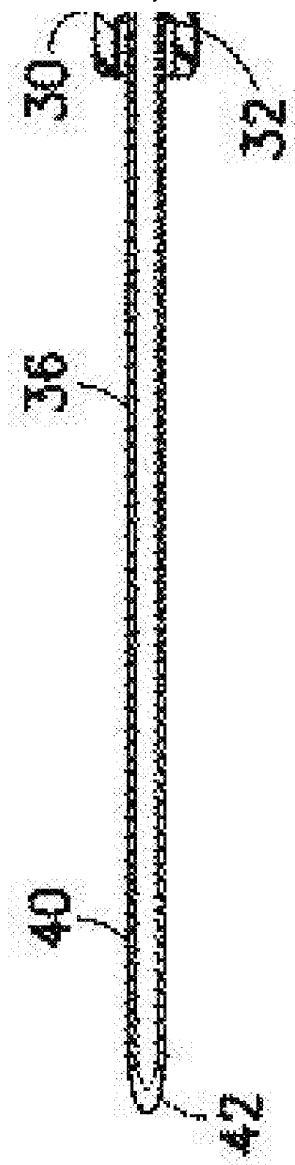
[Fig. 1]

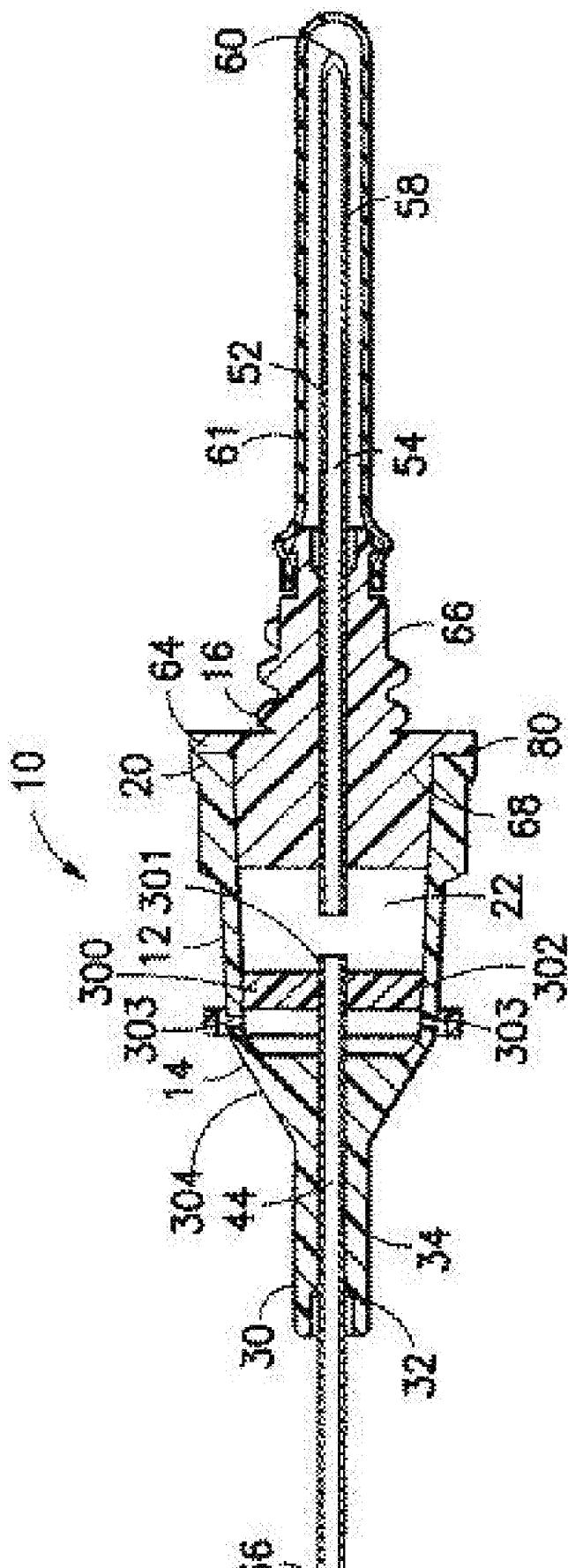


[Figure 2]

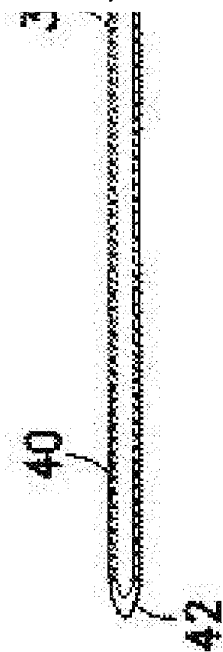


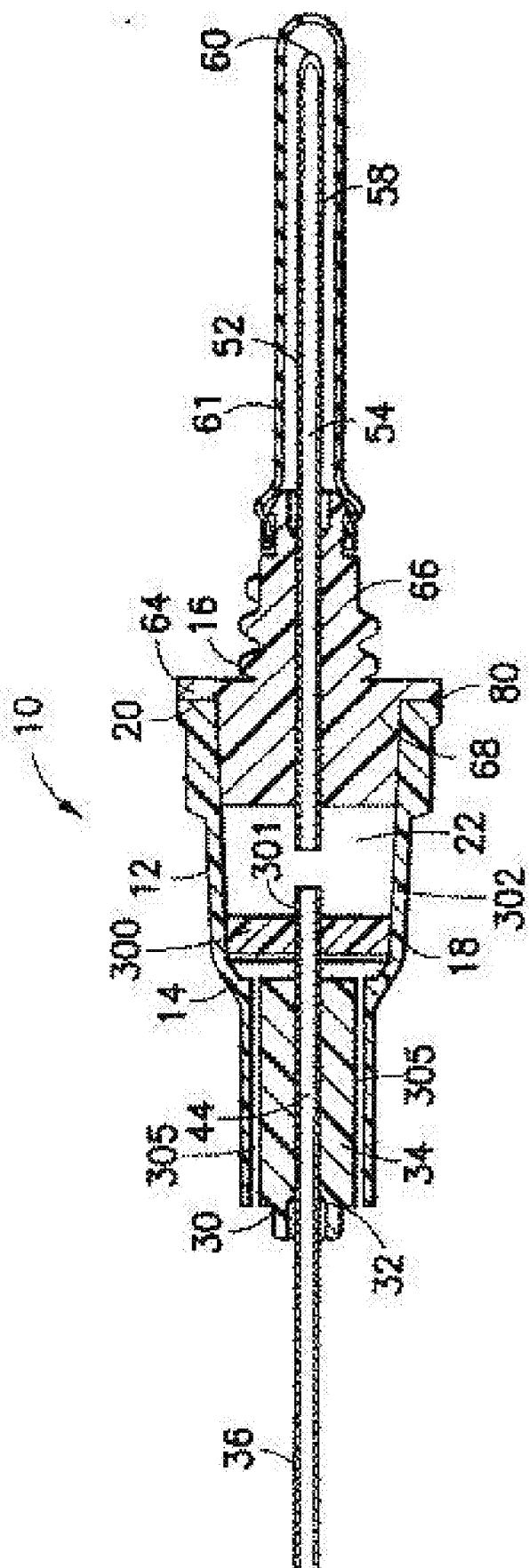
[Figure 3]



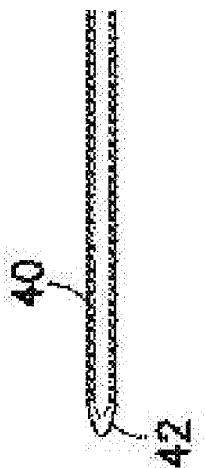


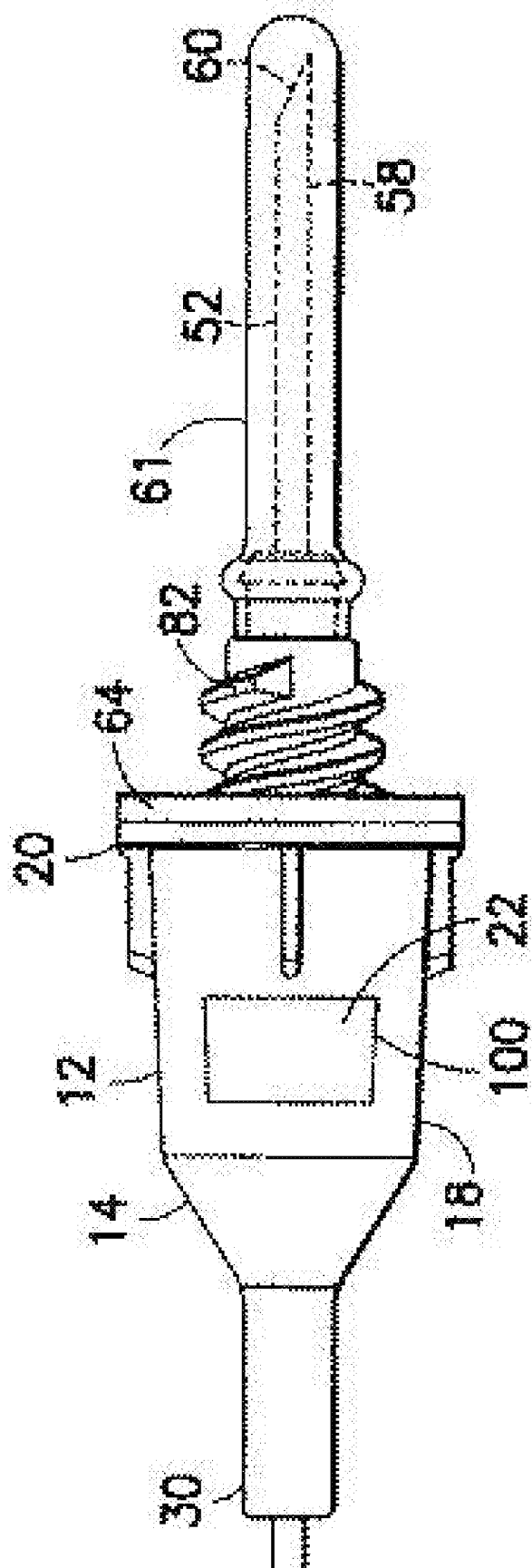
[Fig. 4A]



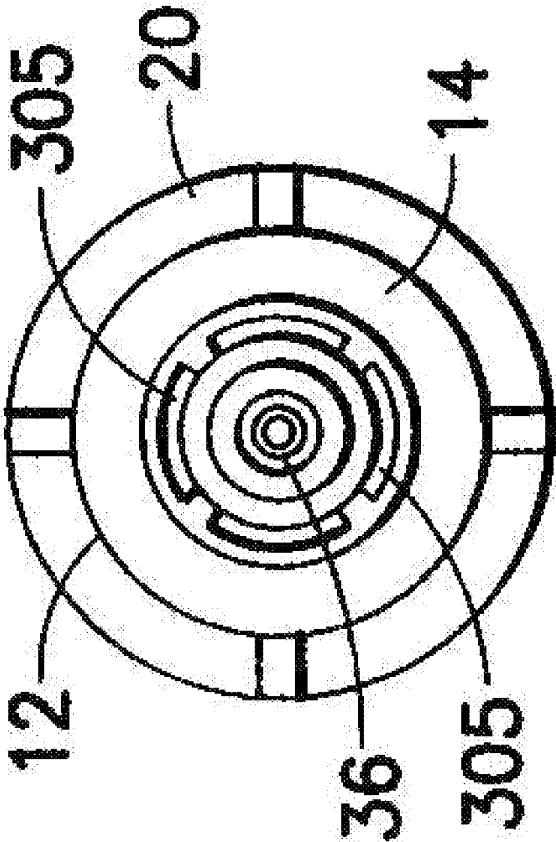


[Fig. 4B]

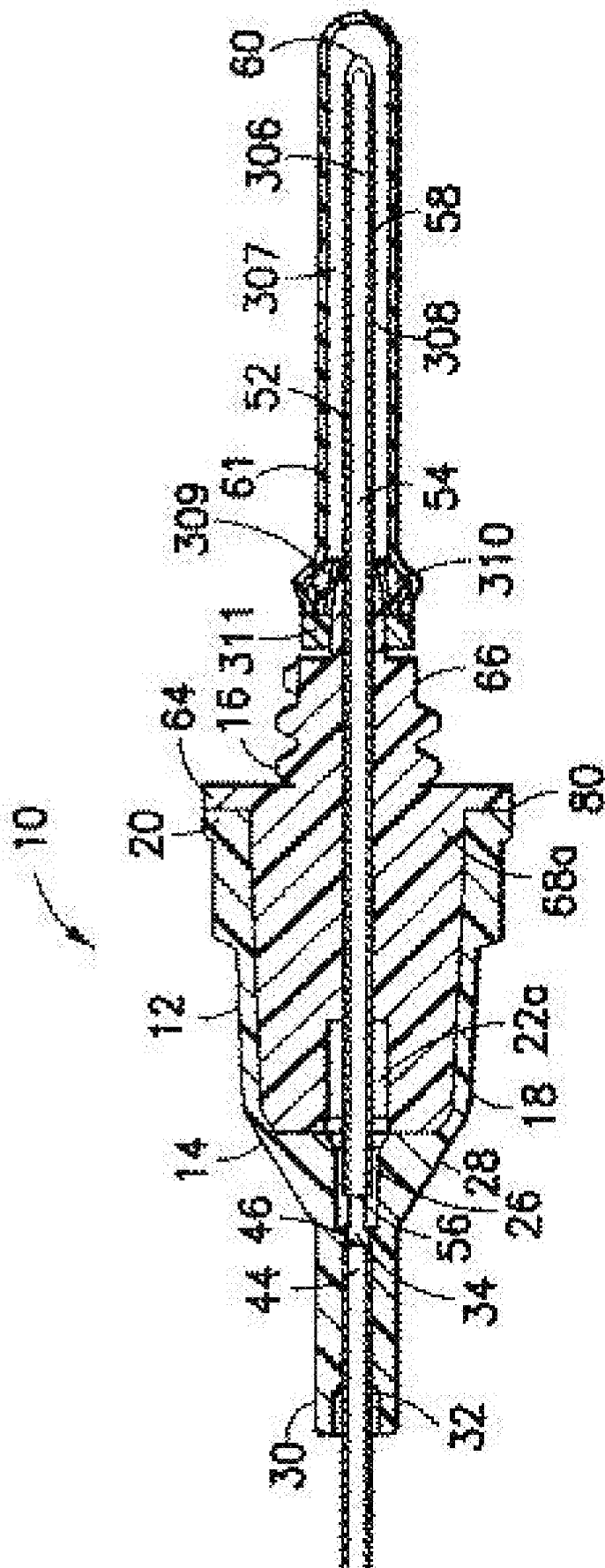




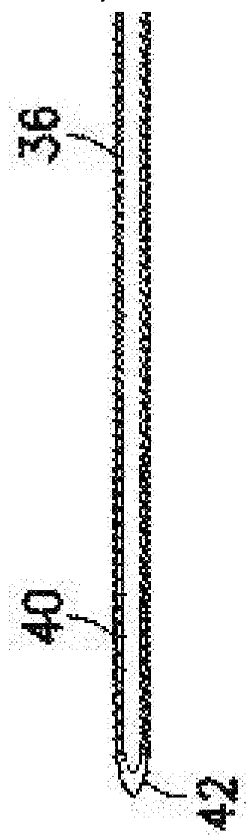
[Fig. 4C]

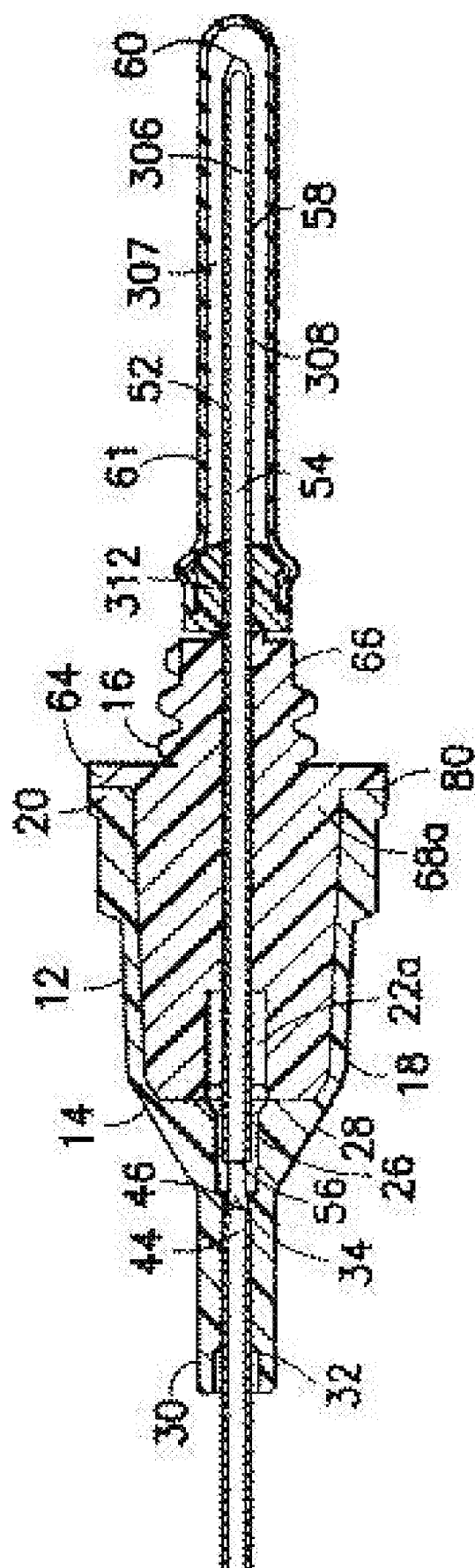


[Figure 5]

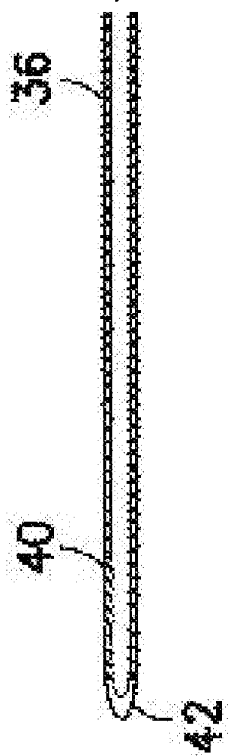


[Fig. 6]

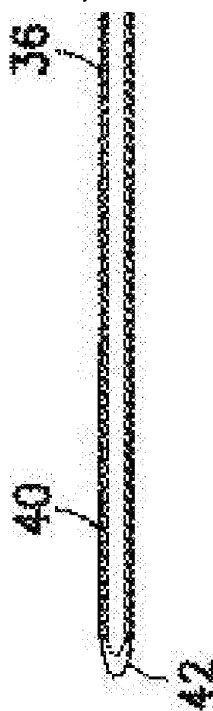


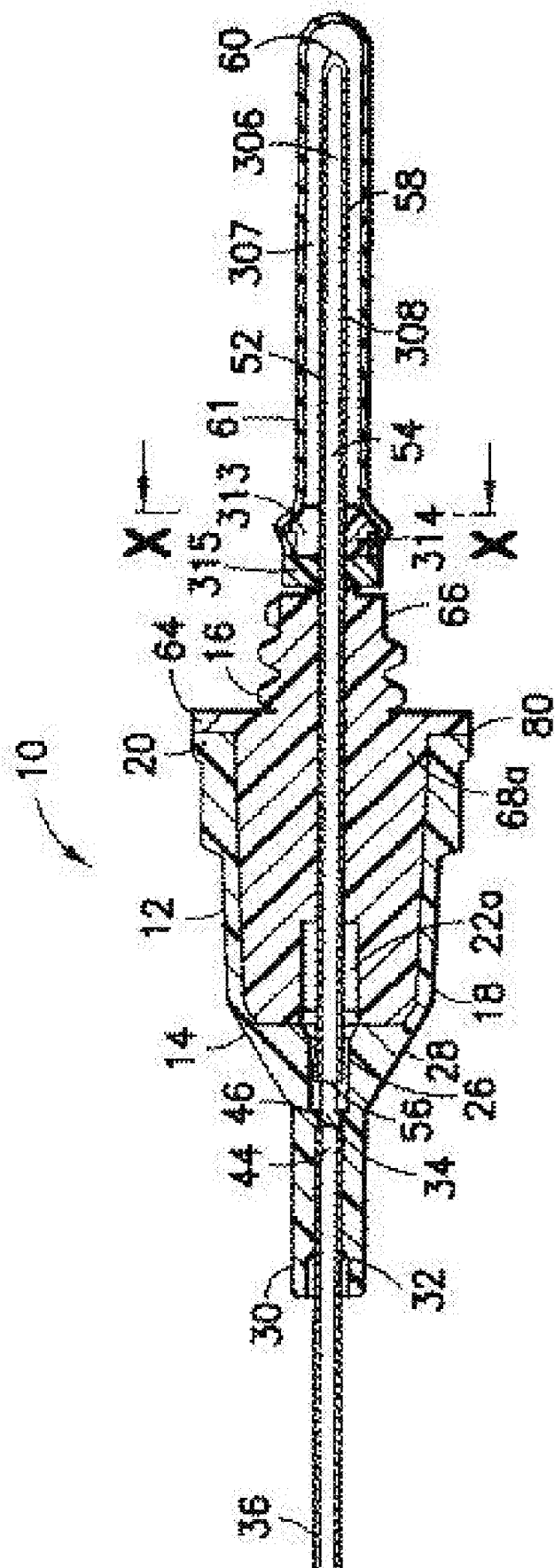


[Fig. 7]

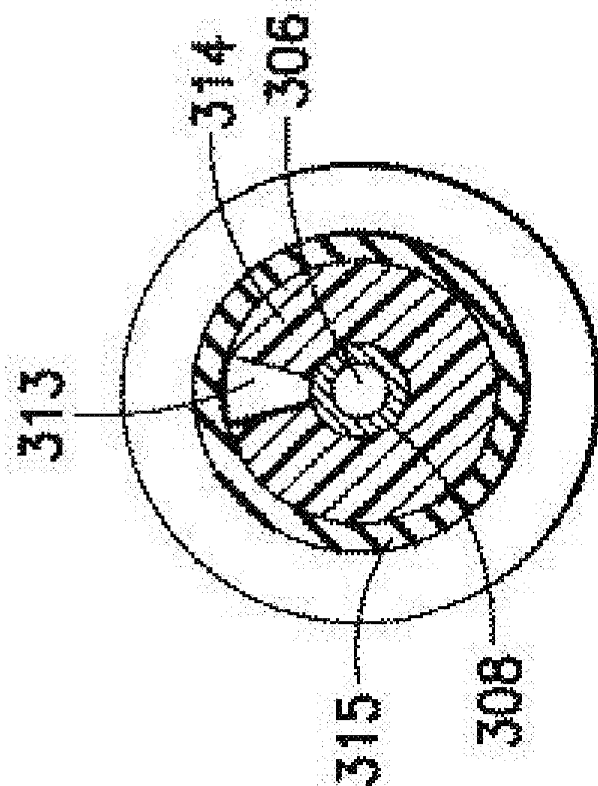


[Fig. 8A]

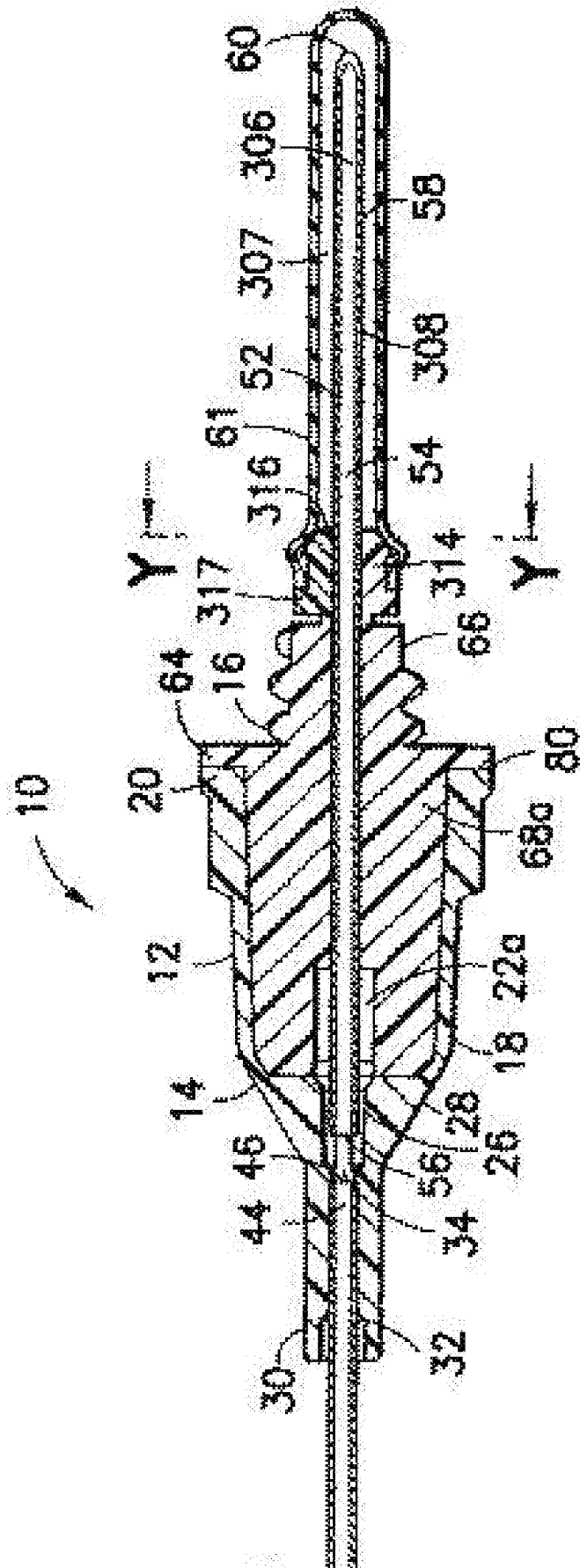




[Fig. 8B]

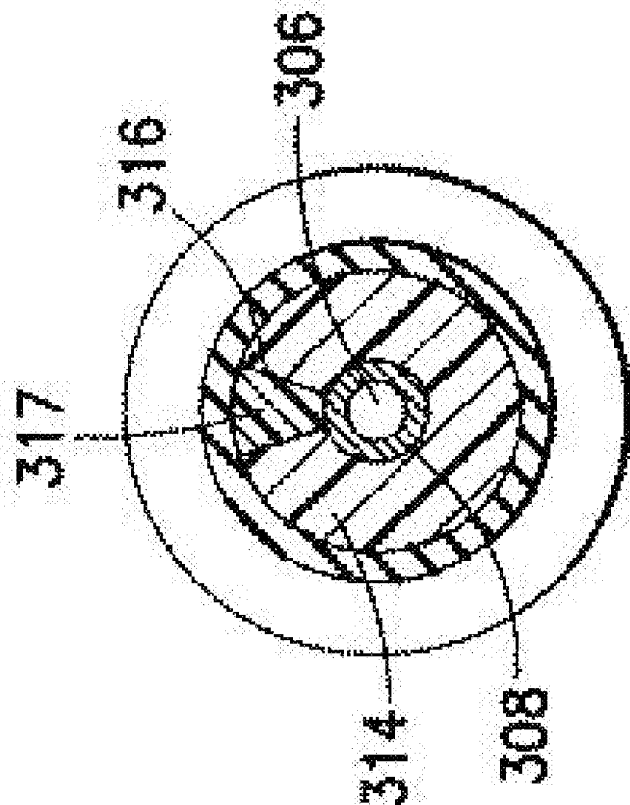


[Fig. 9A]

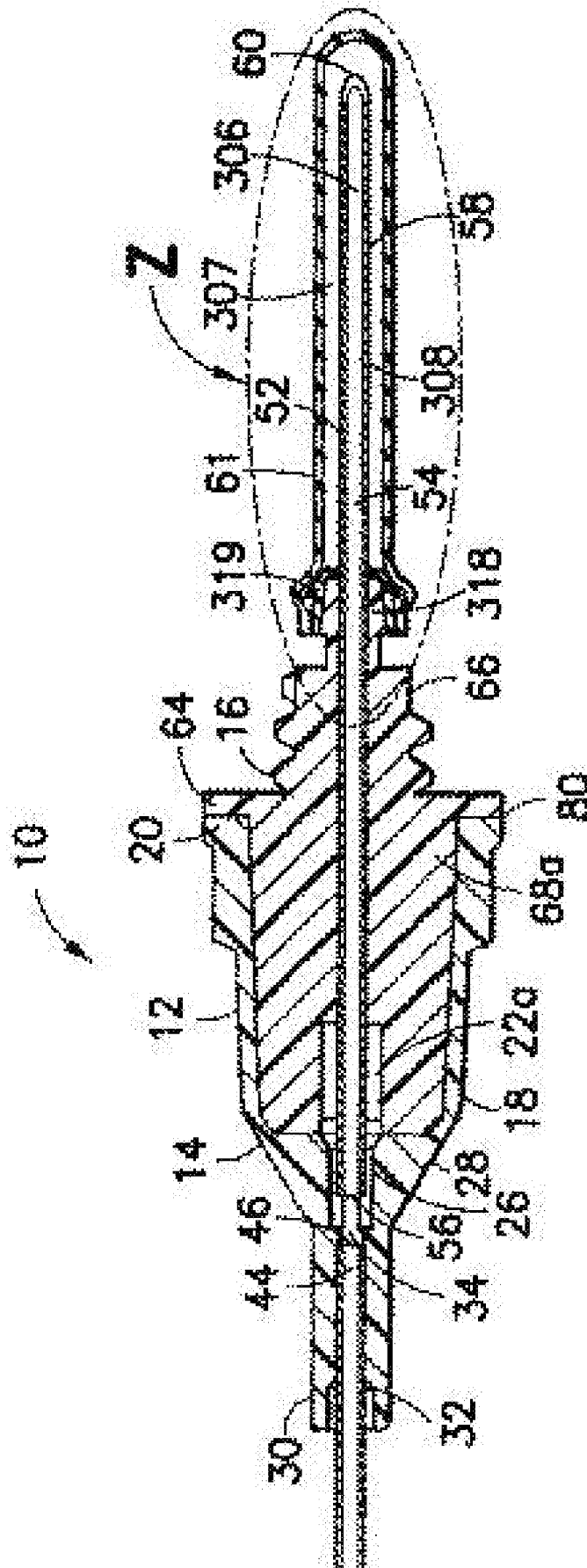


[Fig. 9B]

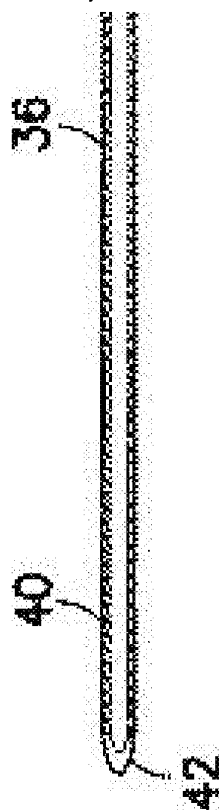
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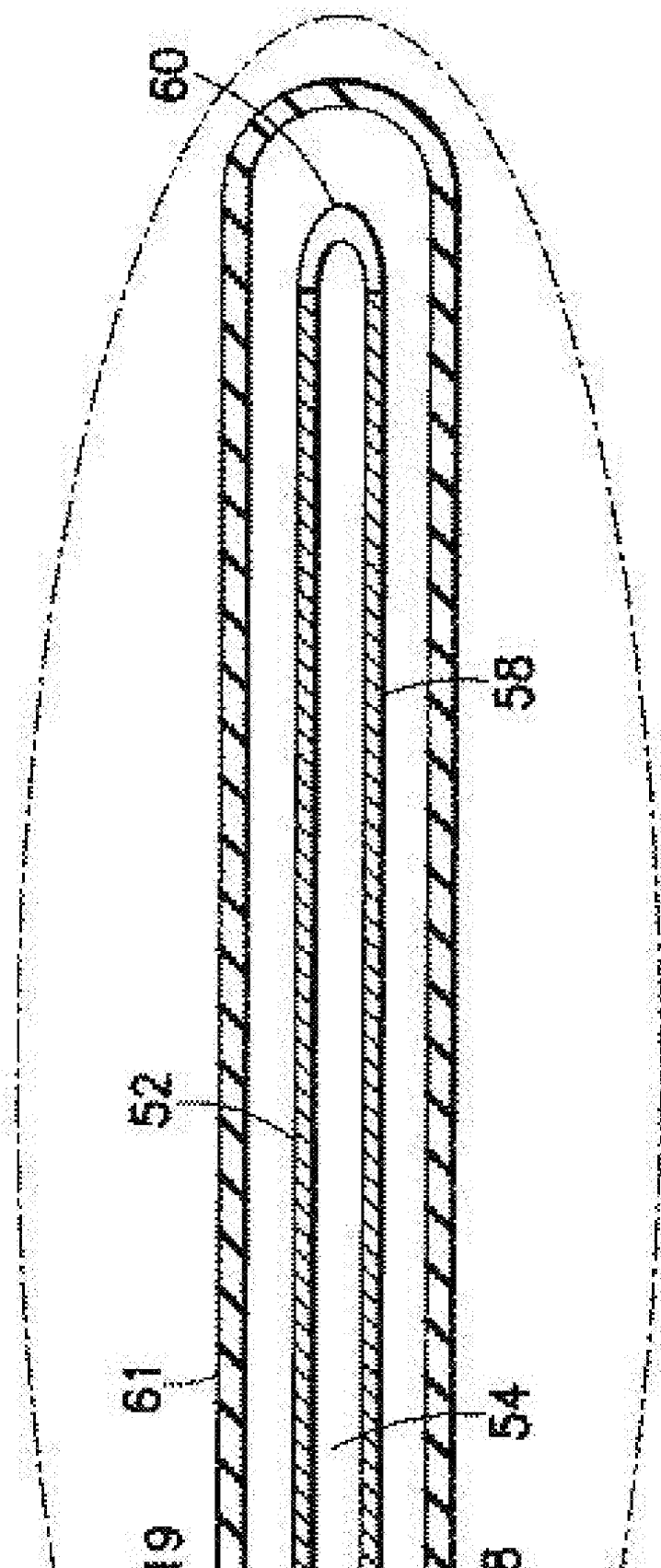


[Fig. 10A]

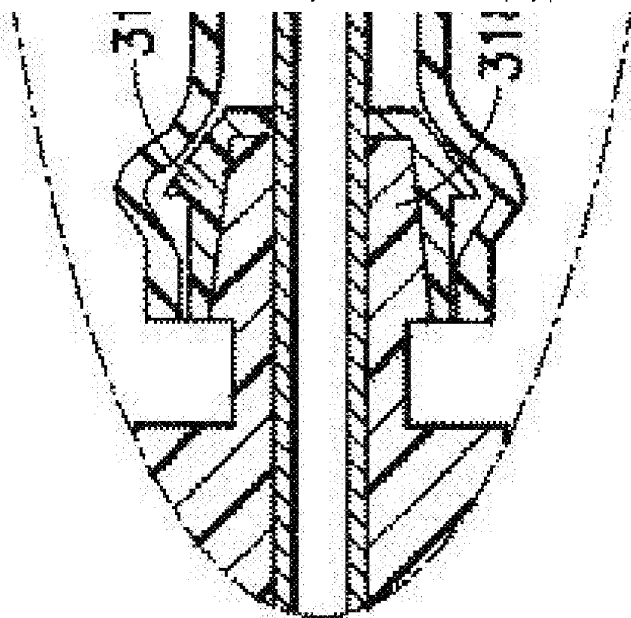


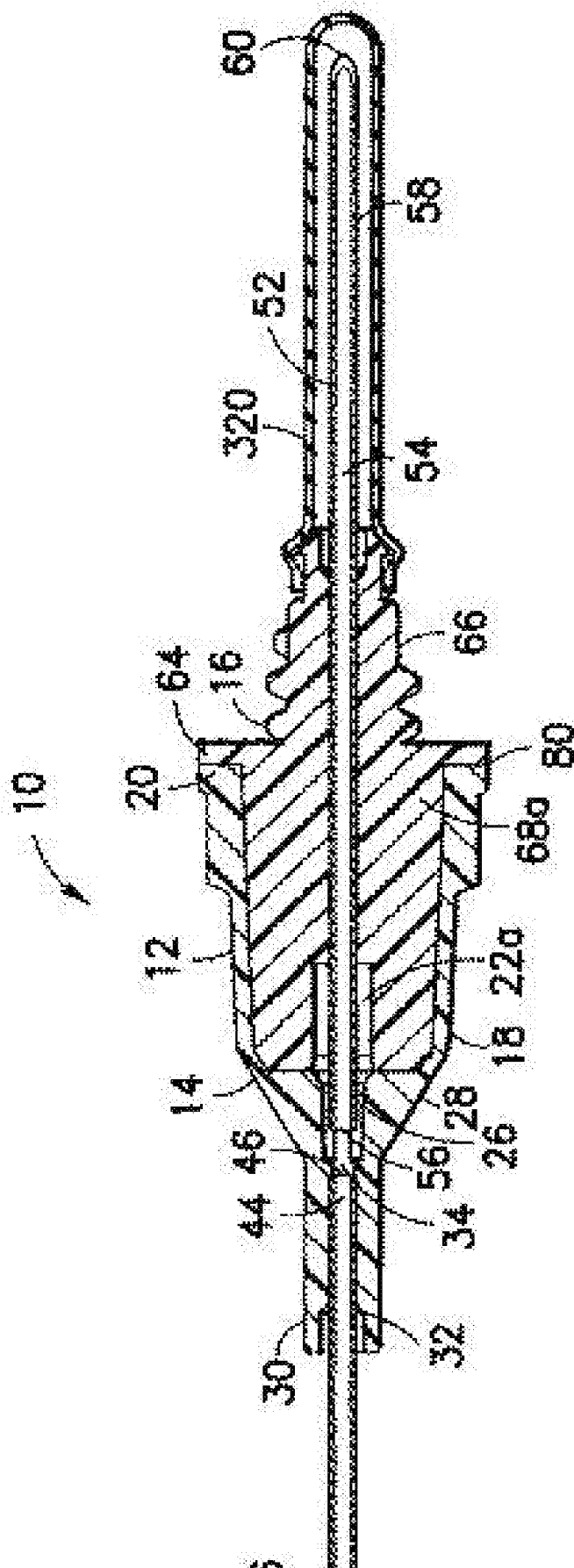
[Fig. 10B]



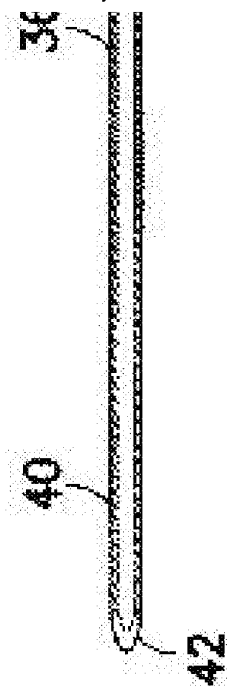


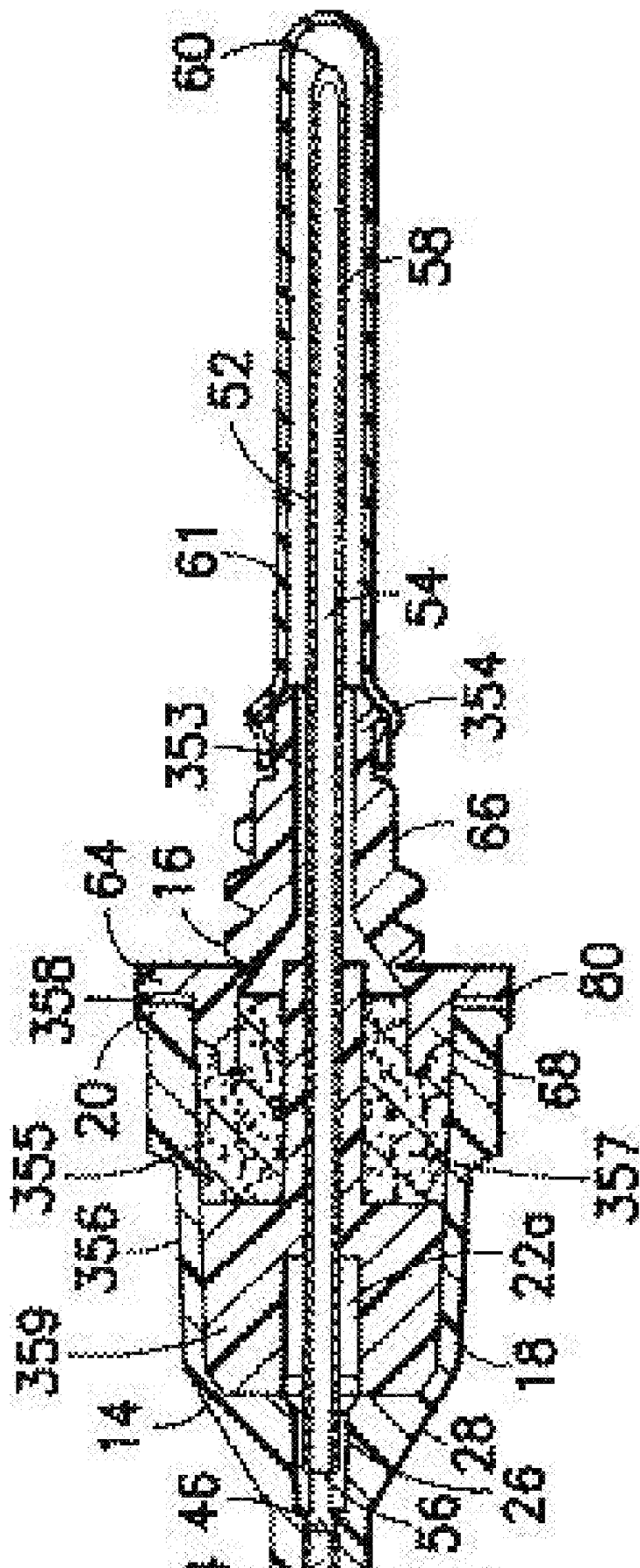
[Fig. 11]



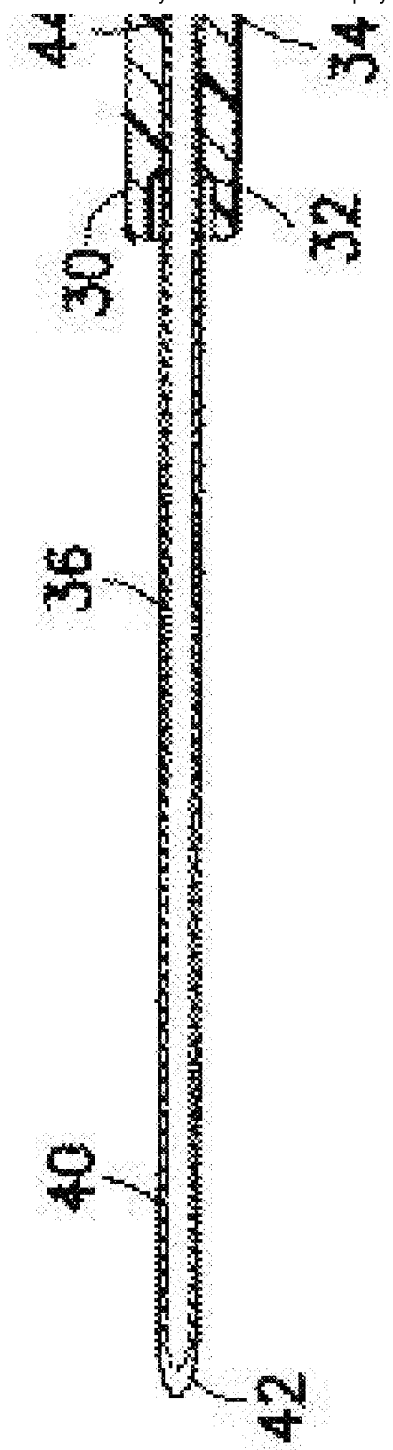


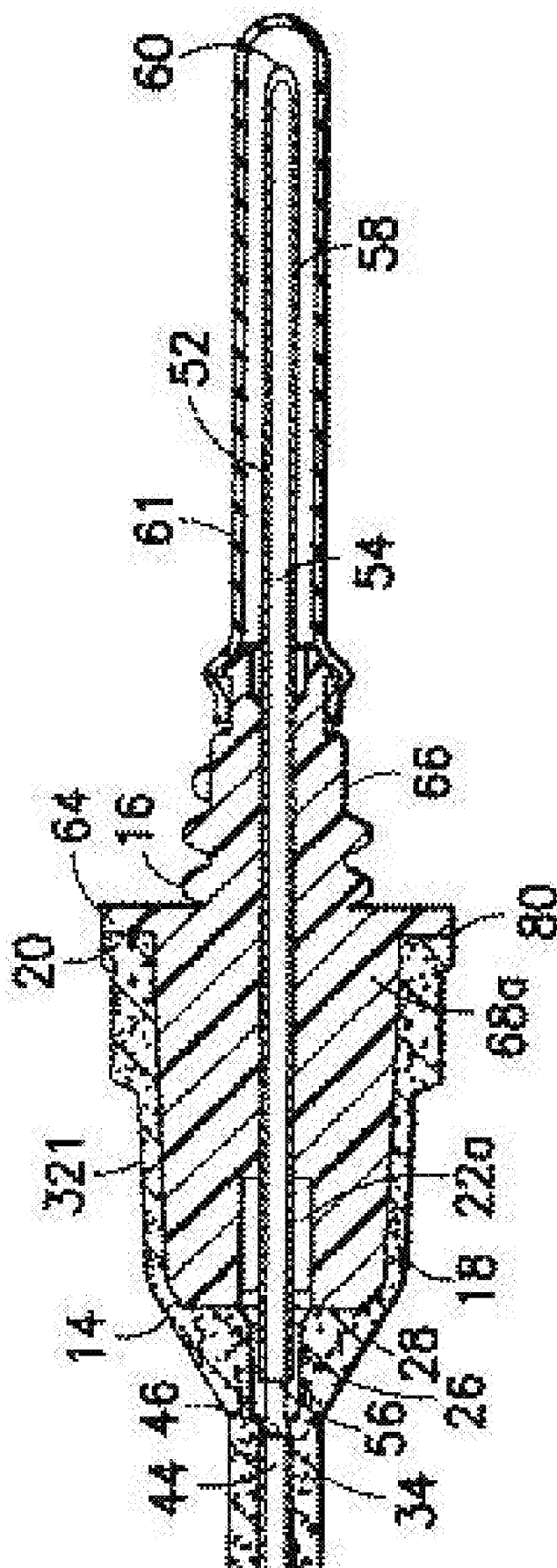
[Fig. 12]



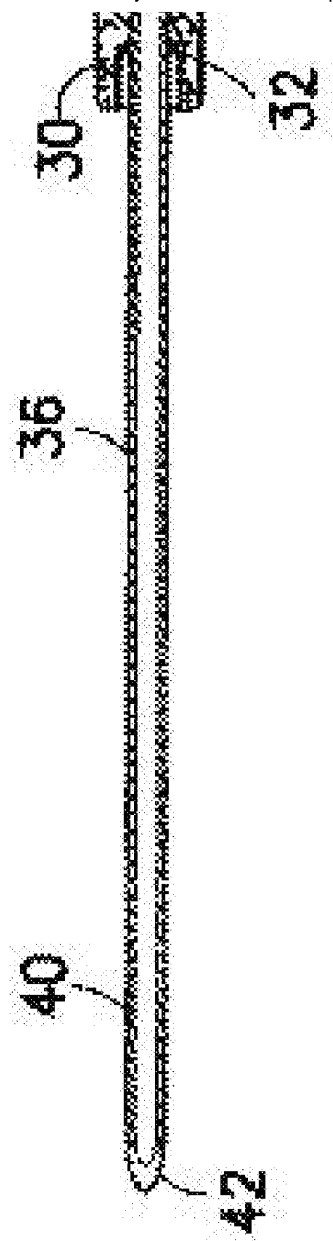


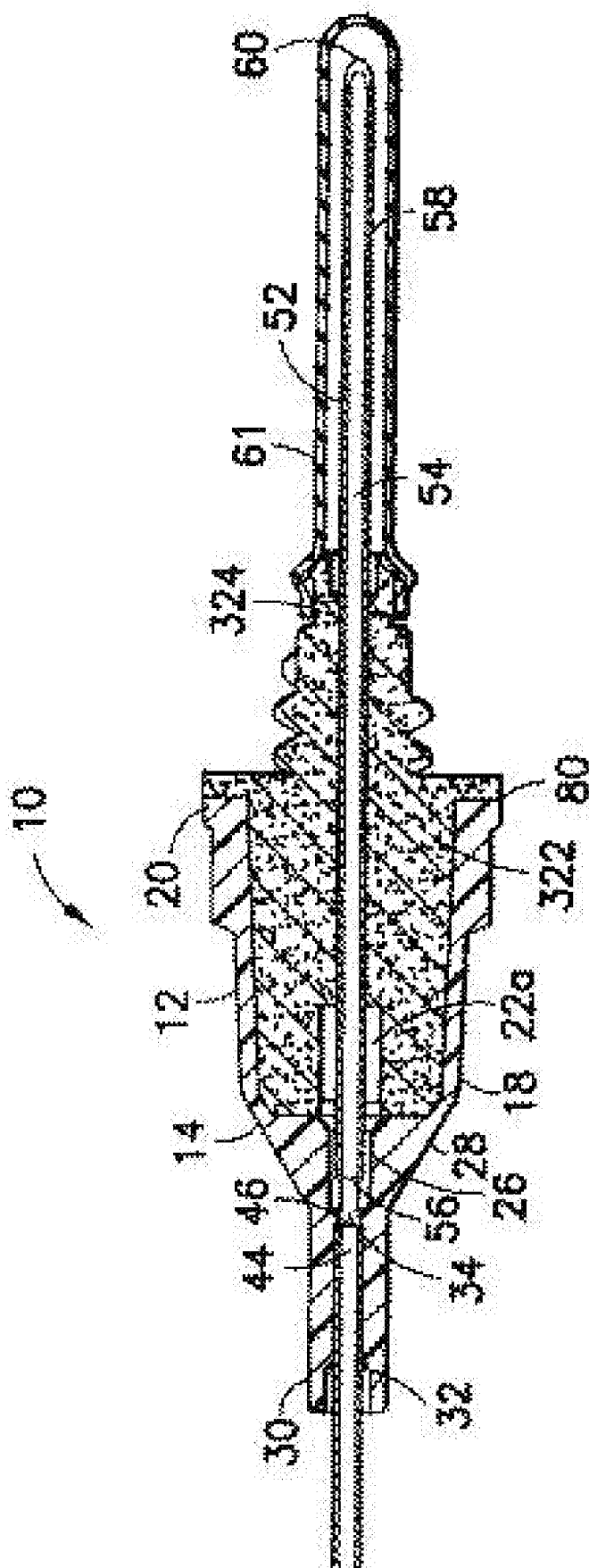
[Fig. 13]



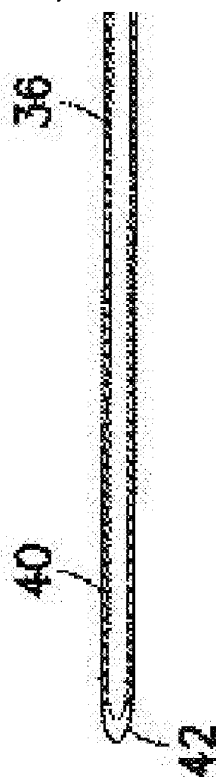


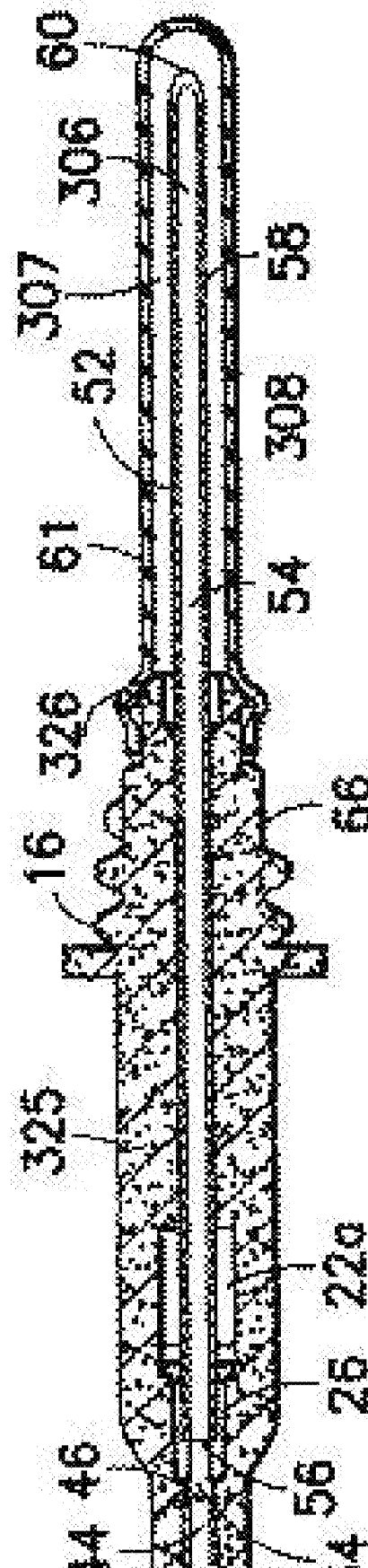
[Fig. 14]



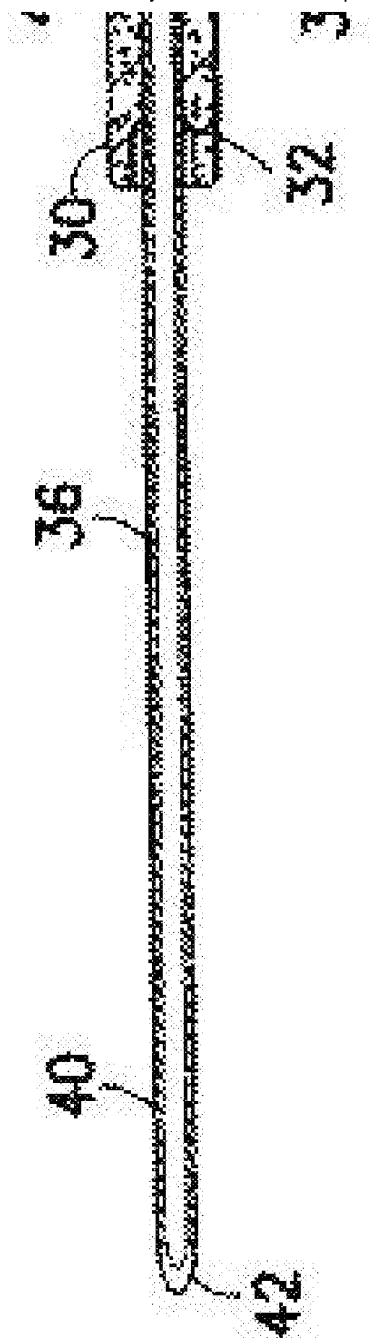


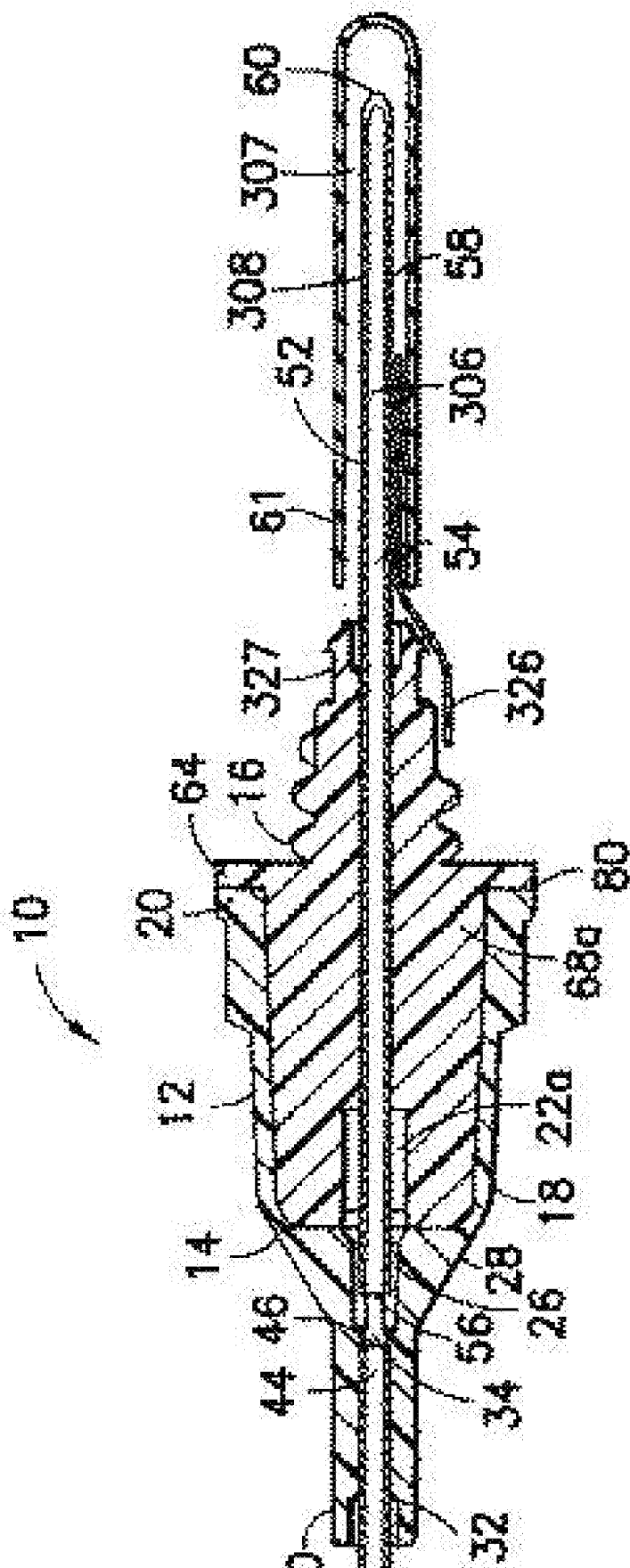
[Fig. 15]



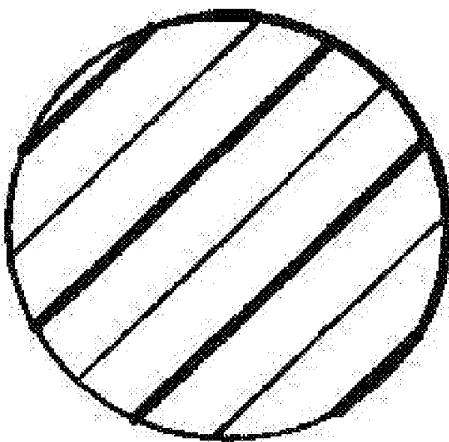


[Fig. 16]



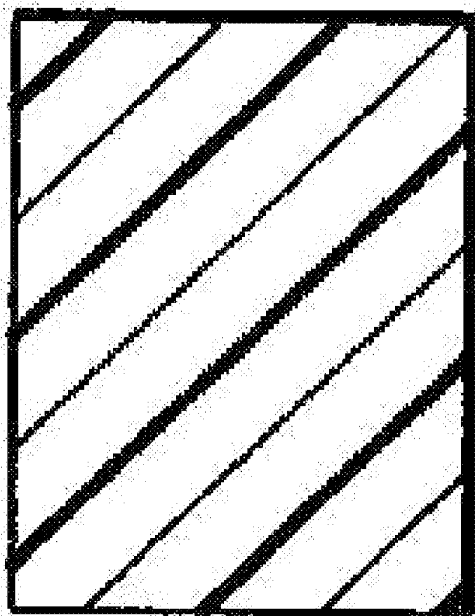


[Fig. 17]

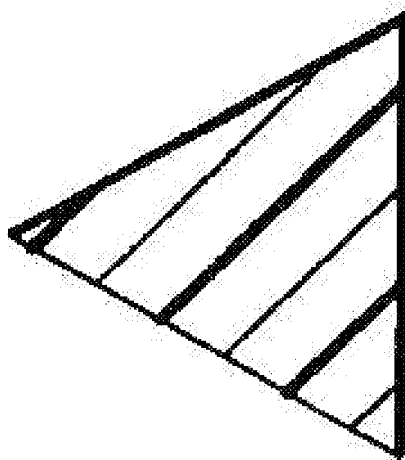


[Fig. 18]

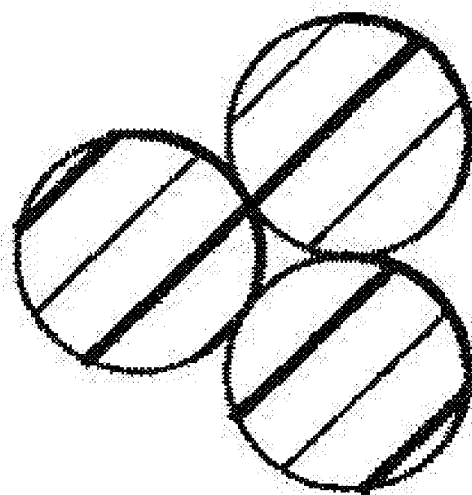




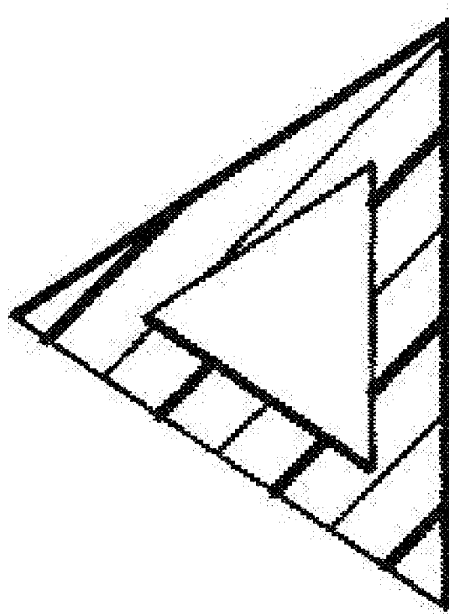
[Fig. 19]



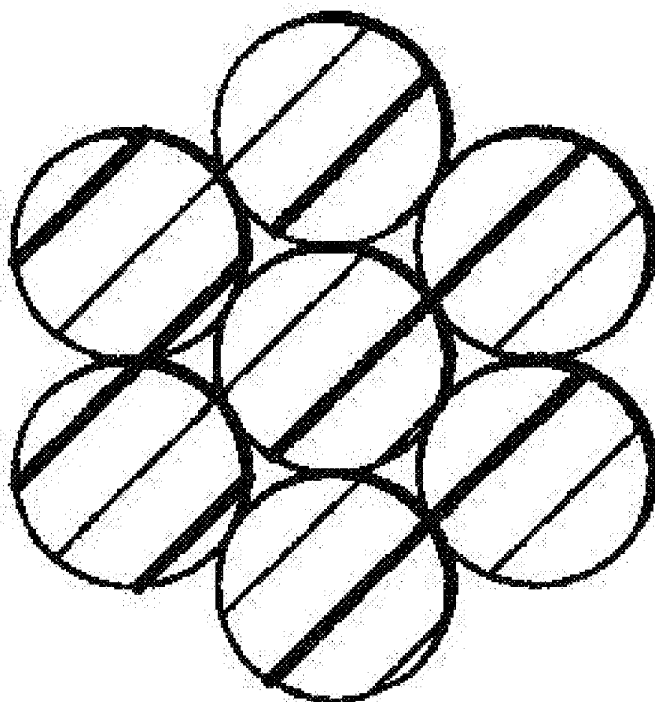
[Fig. 20]



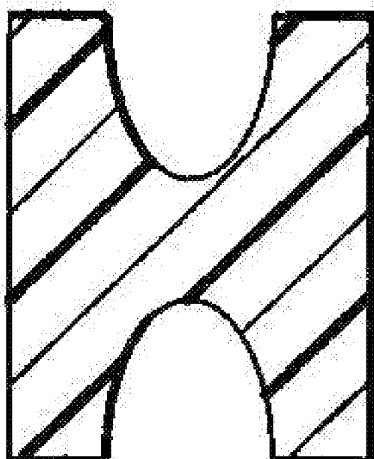
[Fig. 21]



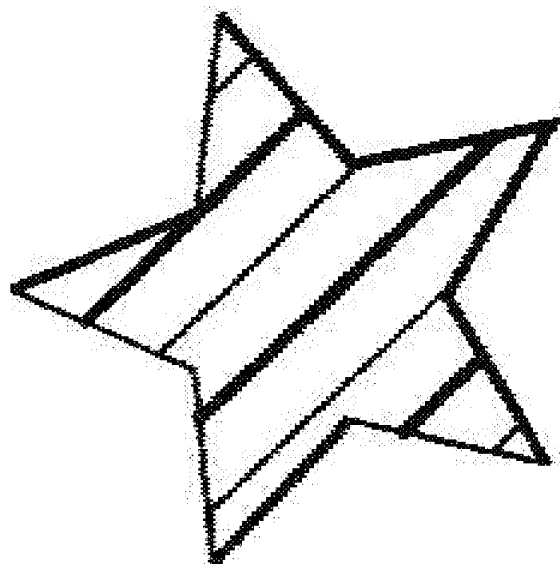
[Fig. 22]



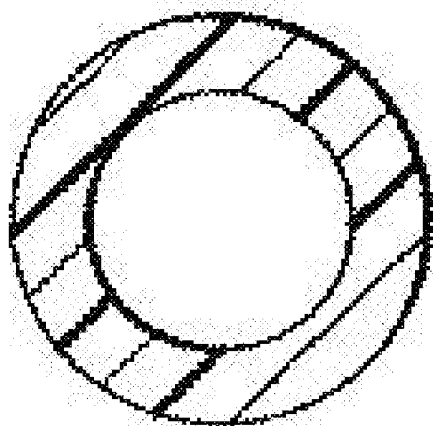
[Fig.23]



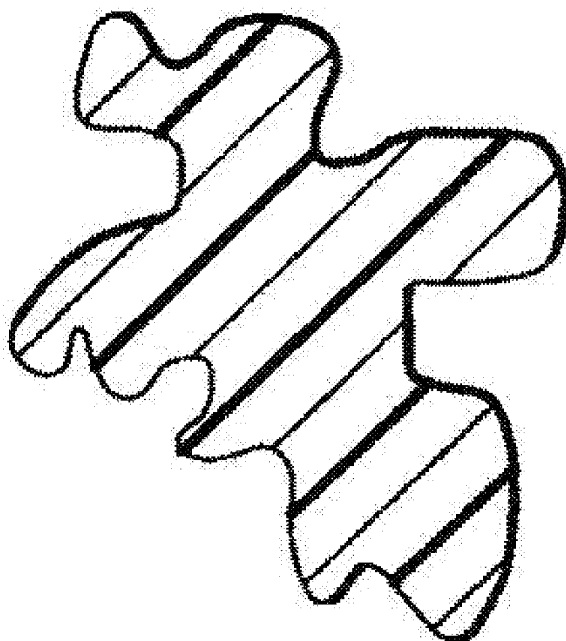
[Fig.24]



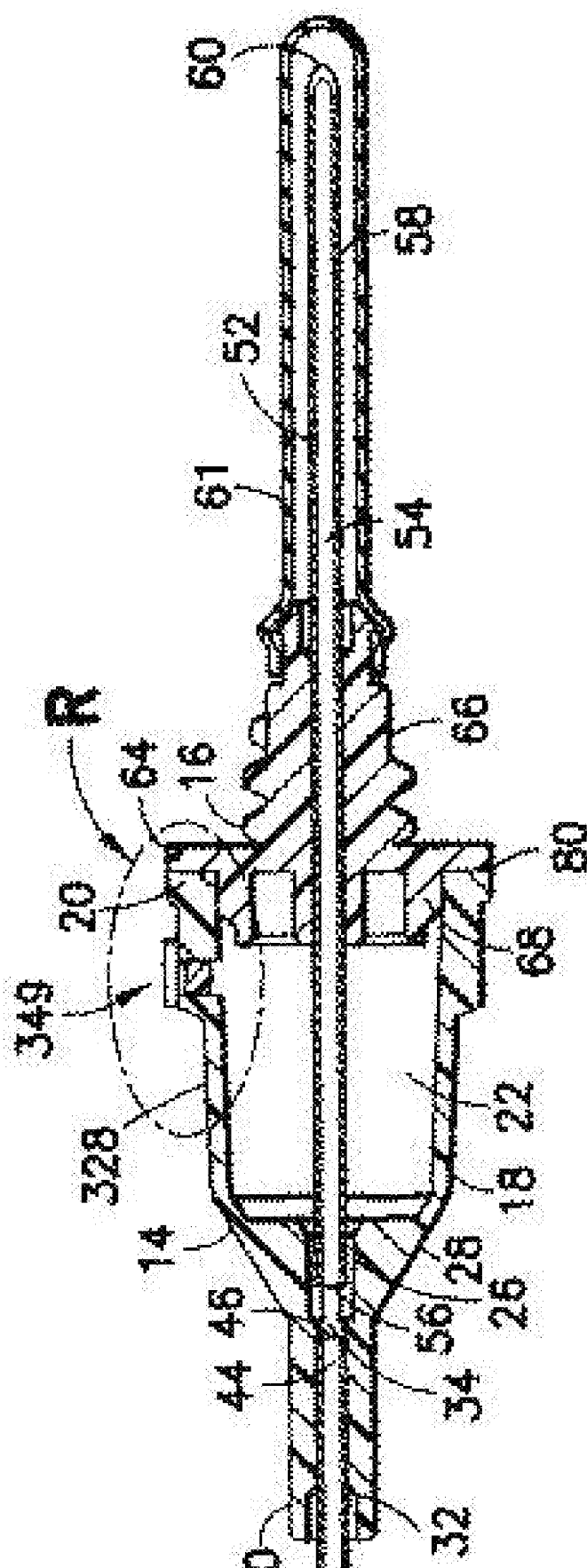
[Fig.25]



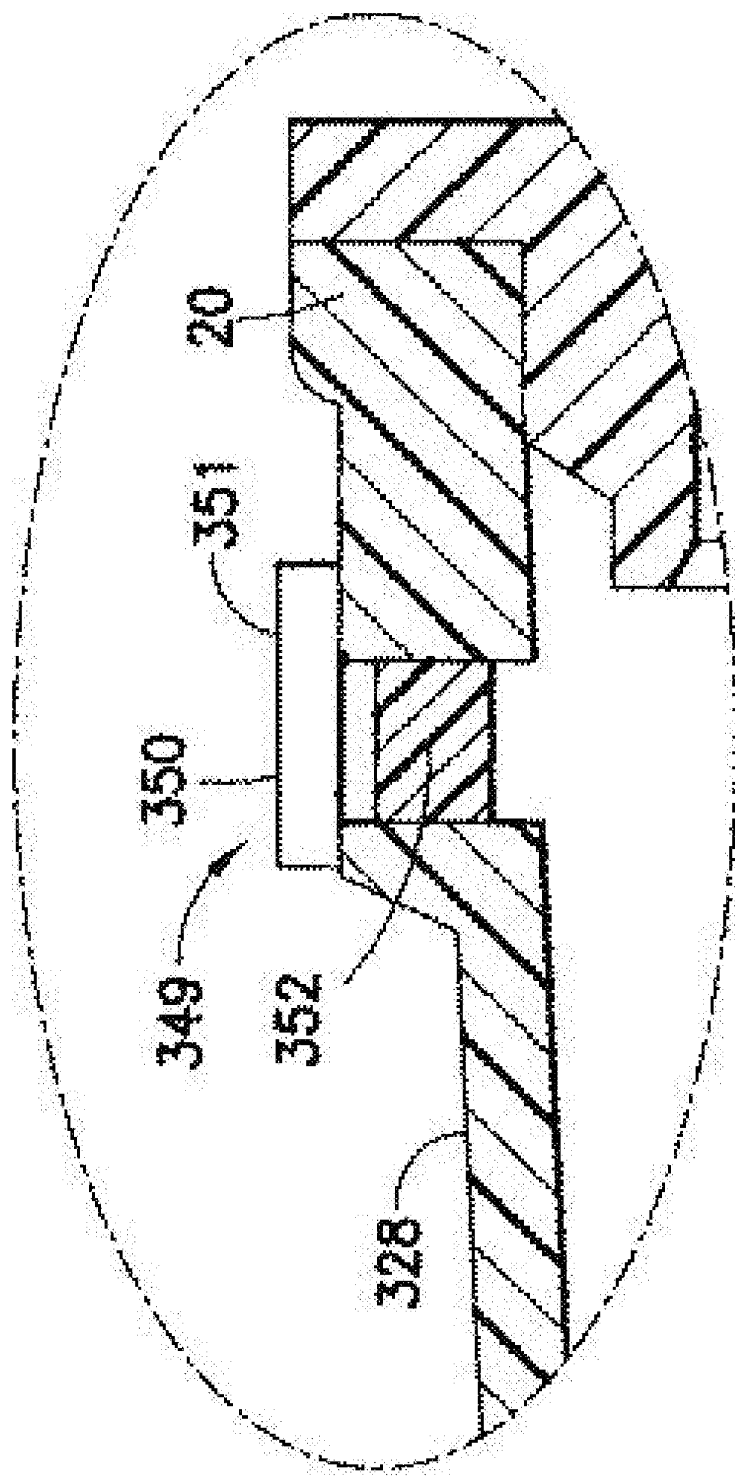
[Fig.26]



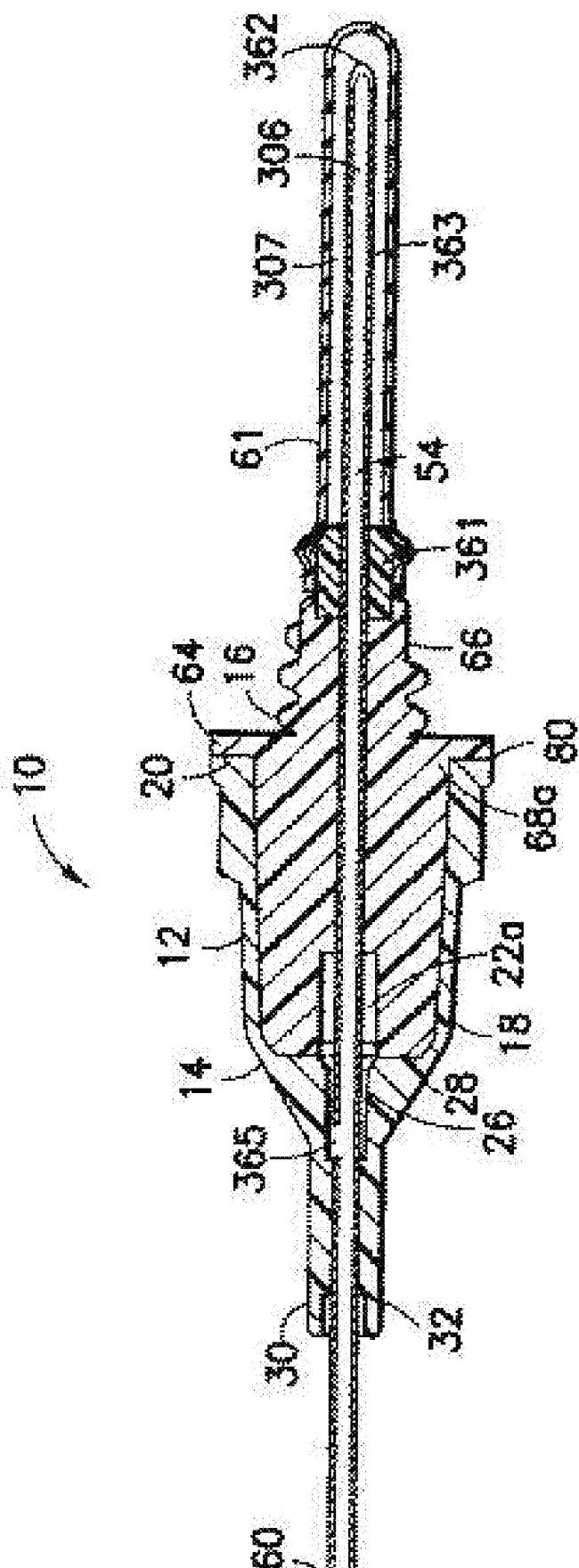
[Fig. 27A]



[Fig. 27B]



[Fig.28]





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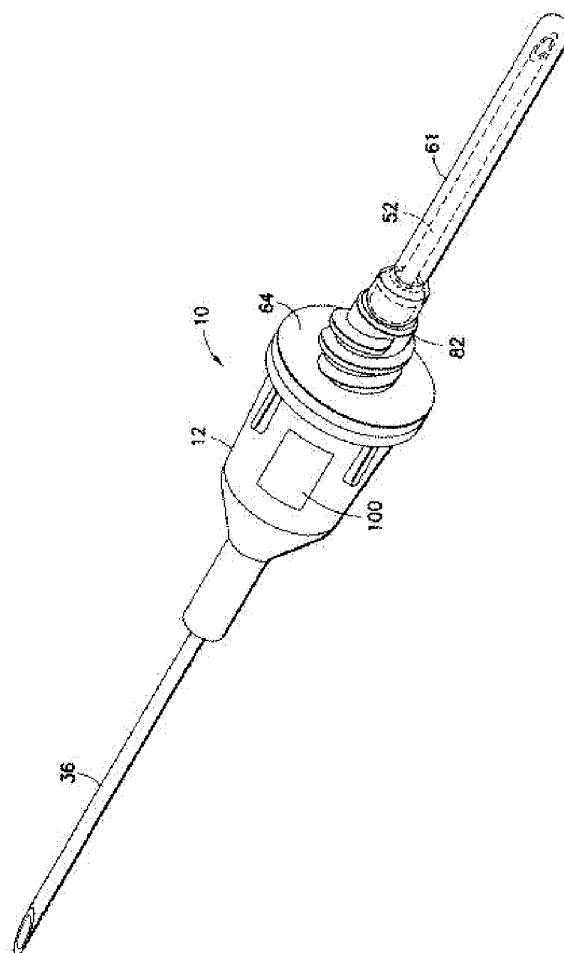
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Espacenet

Bibliographic data: JP2005349196 (A) — 2005-12-22

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)

Classification: - international: A61B5/00; A61B5/15; A61M5/158; A61M5/32; (IPC1-7): A61B5/15; A61M5/158; A61M5/32
- 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)

Application number: JP20050163169 20050602 Global Dossier

Priority number(s): US20040576217P 20040602

Also published as: BRPI0502219 (A) CN1736332 (A) EP1602328 (A1) US2005283093 (A1) US2008275364 (A1) more

Abstract of JP2005349196 (A)

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&NCIP



FIG.2

(19) 日本国特許庁 (JP)

(12) 公開特許公報(A)

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特開2005-349196

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(51) Int. Cl.⁷

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4 C 0 6 6

A 6 1 M 5/32

A 6 1 M 5/14 3 6 9 F

A 6 1 M 5/14 3 6 9 H

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(32) 優先日 平成16年6月2日 (2004.6.2)

(33) 優先権主張国 米国 (US)

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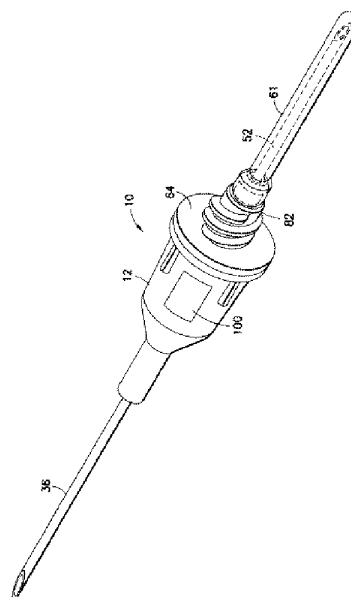
(54) 【発明の名称】 フラッシュバック式血液採取針

(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れ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れ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し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し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し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42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狀態を評価して、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し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へと流入する。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すことになる。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1の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し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し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いが、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、全採取経路に亘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わ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亘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カニユーレ）36を、反対側に非患者側の流体出口針（第2カニユーレ）52を支えるハブ12を具えている。第1カニユ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ユーレの基端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ユーレを具えた実施形態を示している。2本のカニユ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ユ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カニユーレ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の内壁と締め嵌めを形成する。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、非患者側カニユーレの基端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本のカニユ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から非患者側カニユーレの基端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を通して、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要素）が空気を流出させるが、血液その他の流体が外部雰囲気へ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自体の材料を通して排気される。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との間を通して通気媒体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へ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を通して環状溝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を通し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わ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わせであってよい。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十分に大きい、血液の漏洩を防ぐためには十分に小さい、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わ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、レーザー穿孔孔、通気可能なコード、超吸水性逆止め弁、または他の手段、あるいはこれらの任意の組み合わ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十分に大きい、血液の漏洩を阻止するには十分に小さい。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、管の全長に亘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、破碎ガラス、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。

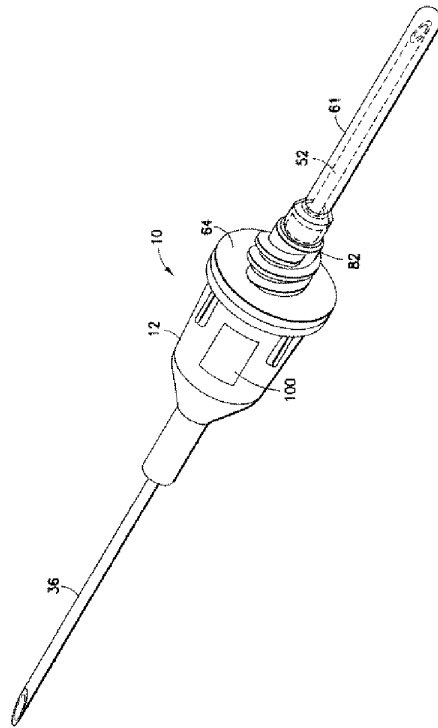
【図4A】図2と同様な側断面図であるが、本発明の別の実施形態を示している。

【図4B】図4Bの側面図である。

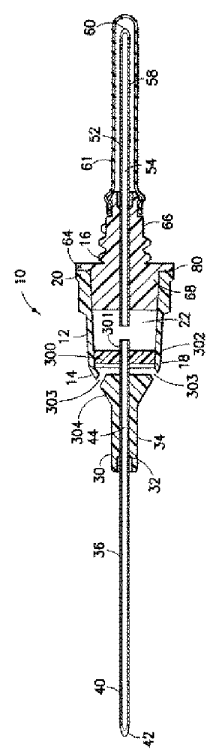
【図4C】R-Rの方向から見た図4BAの正面図である。

- 【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。

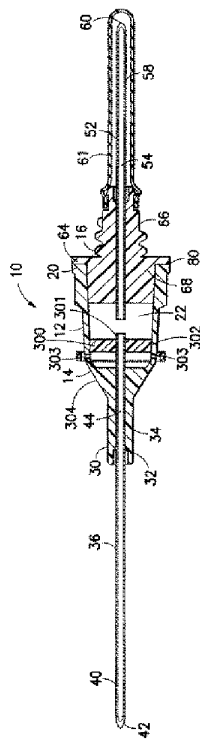
【図1】



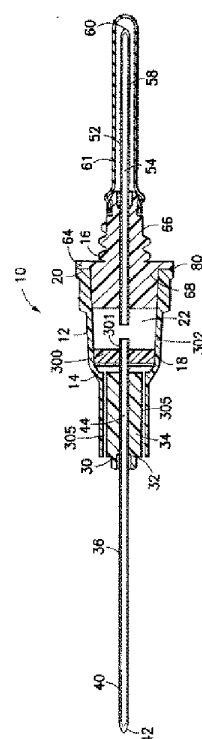
【図2】



【図3】



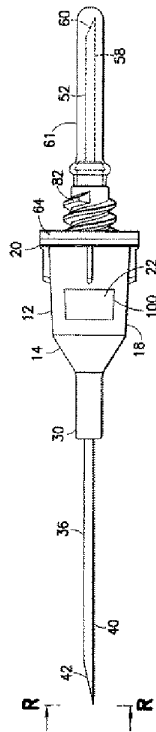
【図4A】



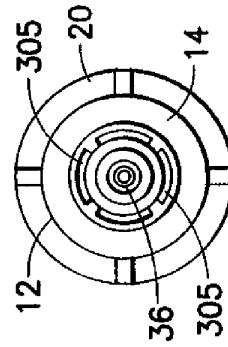
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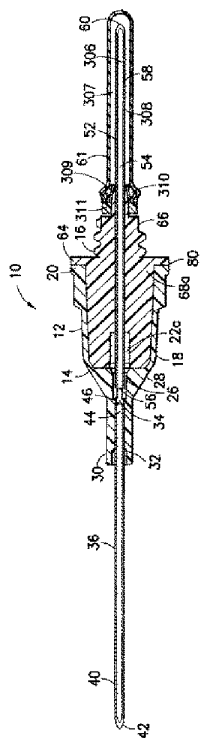
【図4B】



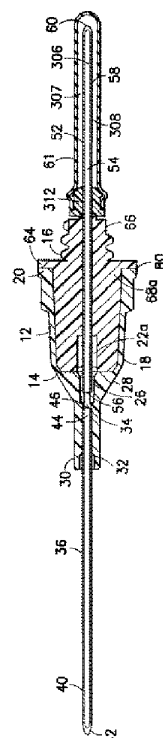
【 図4C 】



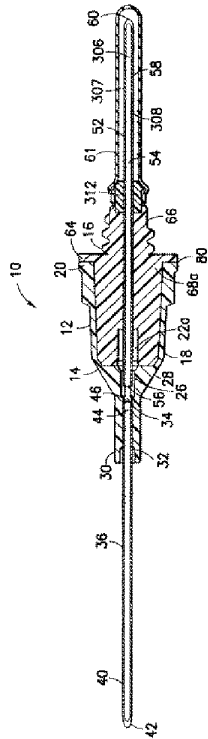
【図5】



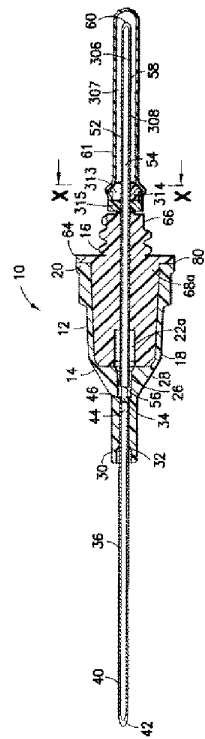
【图6】



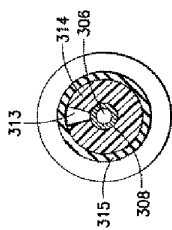
【图7】



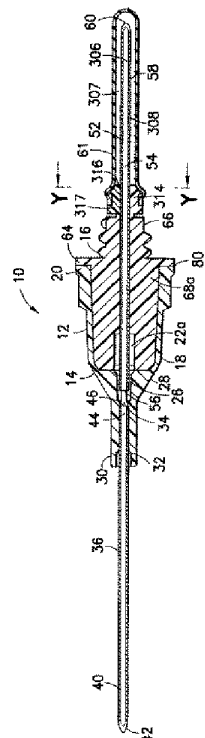
【 ㊦8A 】



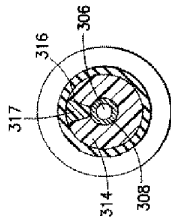
【図8B】



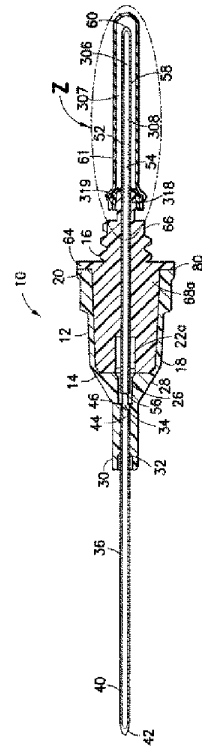
【 図9A 】



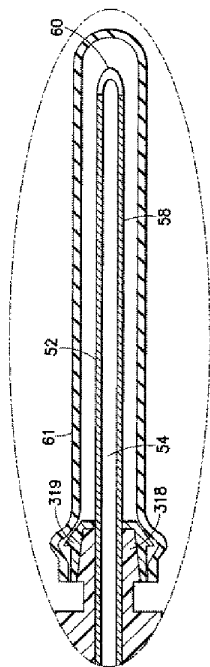
【図9B】



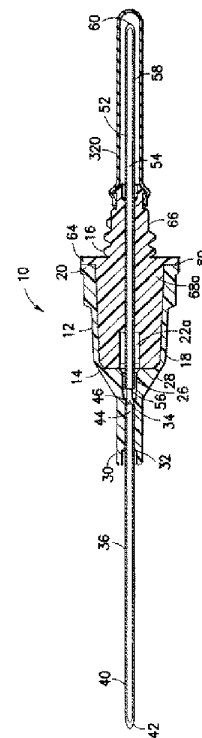
【図10A】



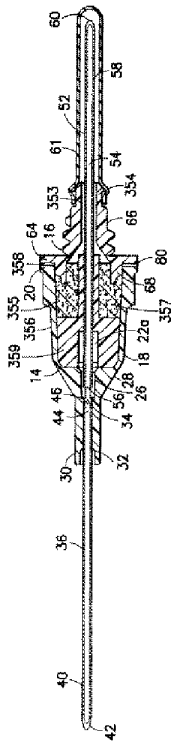
【図10B】



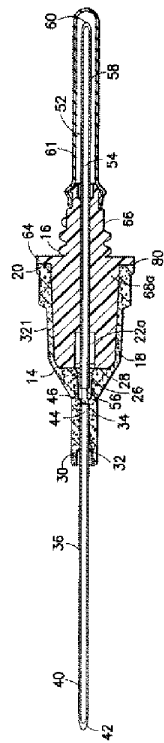
【図11】



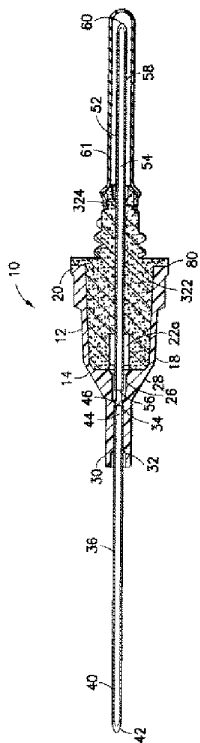
【図12】



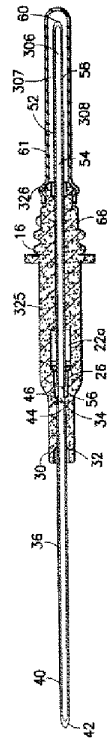
【图13】



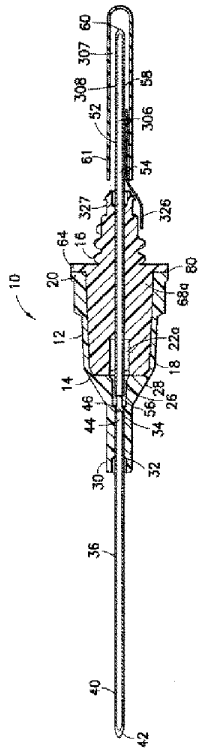
【図14】



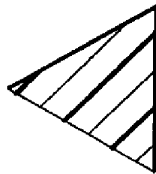
【図15】



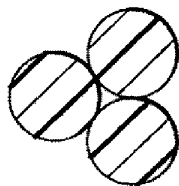
【図16】



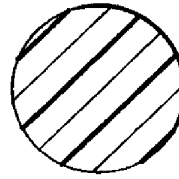
【図19】



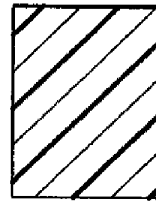
【図20】



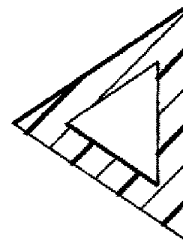
【図17】



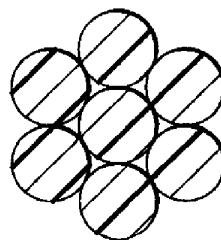
【図18】



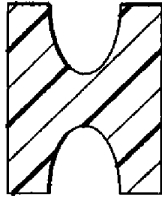
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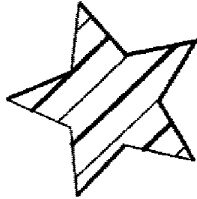
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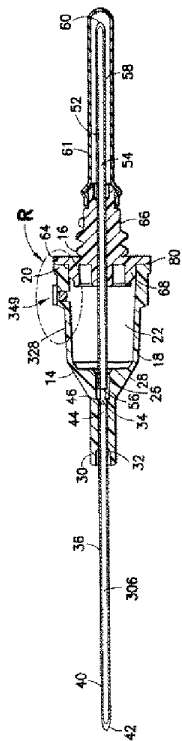
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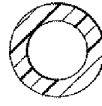
【図24】



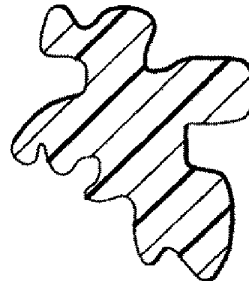
【図27A】



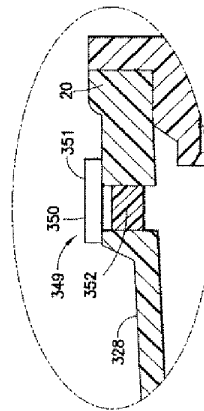
【図25】



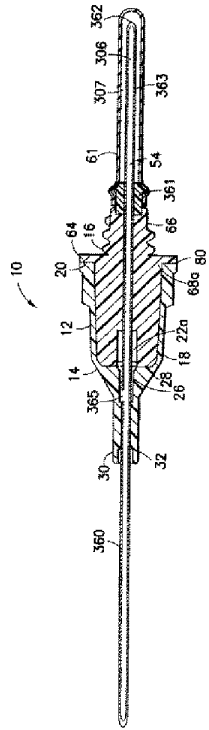
【図26】



【図27B】



【図28】



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- Fターム(参考) 4C038 TA06 UJ02
4C066 AA09 BB01 CC01 DD06 FF05 GG12 GG15 KK05 KK06

【外国語明細書】
2005349196000001.pdf

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference KURIN7PCT		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US20/26276	International filing date (day/month/year) 01 April 2020 (01.04.2020)	(Earliest) Priority Date (day/month/year) 01 April 2019 (01.04.2019)	
Applicant Bobby E. Rogers			

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 43.6bis(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. 1A
☒ 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/US20/26276

A. CLASSIFICATION OF SUBJECT MATTER

IPC - G01N 1/10, 1/02; A61B 5/15 (2020.01)

CPC - G01N 1/10, 1/02; B01L 3/0203

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	US 2018/0271425 A1 (KURIN, INC.) 27 September 2018; abstract; figures 24A-24D;	1-10, 14-18
--	paragraphs [0066], [0096], [0144]-[0148]	--
Y		11-13, 19-20
Y	GB 1 3786 02 A (AYERS, WA) 02 May 1974; page 5, lines 34-95; figures 4, 6	11-12, 19-20
Y	US 2014/0112841 A1 (SCHOEN, C) 24 April 2014; abstract; paragraph [0035]	13
A	WO 2019/055487 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 21 March 2019;	13
	paragraphs [1071], [1080]; figures 2-5	
P, X	WO 2019/232196 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 05 December 2019;	1, 6, 14
	entire document	

☐ 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

"D" document cited by the applicant in the international application

"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

25 June 2020 (25.06.2020)

Date of mailing of the international search report

16 JUL 2020

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

Shane Thomas

Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/210 (second sheet) (July 2019)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: James Scott Nolan
P.O. Box 371710
San Diego, California 92110
United States of America

Date of mailing
(day/month/year)

16 JUL 2020

Applicant's or agent's file reference
KURIN7PCT

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US20/26276

International filing date (day/month/year)

01 April 2020 (01.04.2020)

Priority date (day/month/year)

01 April 2019 (01.04.2019)

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

IPC - G01N 1/10, 1/02; A61B 5/15 (2020.01)**CPC - G01N 1/10, 1/02; B01L 3/0203**

Applicant

Bobby E. Rogers

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 43bis.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 66.1bis(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/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Date of completion of this opinion

25 June 2020 (25.06.2020)

Authorized officer

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US20/26276

Box No. I	Basis of this opinion
<p>1. With regard to the language, this opinion has been established on the basis of:</p> <p>☒ the international application in the language in which it was filed.</p> <p>☐ 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)).</p> <p>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<i>bis</i>.1(b)).</p> <p>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:</p> <p style="margin-left: 20px;">a. ☐ forming part of the international application as filed:</p> <p style="margin-left: 40px;">☐ in the form of an Annex C/ST.25 text file.</p> <p style="margin-left: 40px;">☐ on paper or in the form of an image file.</p> <p style="margin-left: 20px;">b. ☐ furnished together with the international application under PCT Rule 13<i>ter</i>.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.</p> <p style="margin-left: 20px;">c. ☐ furnished subsequent to the international filing date for the purposes of international search only:</p> <p style="margin-left: 40px;">☐ in the form of an Annex C/ST.25 text file (Rule 13<i>ter</i>.1(a)).</p> <p style="margin-left: 40px;">☐ on paper or in the form of an image file (Rule 13<i>ter</i>.1(b) and Administrative Instructions, Section 713).</p> <p>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.</p> <p>5. Additional comments:</p>	

Form PCT/ISA/237 (Box No. I) (revised January 2019)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US20/26276

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement			
1. Statement				
Novelty (N)	Claims	4, 9, 11-13, 18-20	YES	
	Claims	1-3, 5-8, 10, 14-17	NO	
Inventive step (IS)	Claims	NONE	YES	
	Claims	1-20	NO	
Industrial applicability (IA)	Claims	1-20	YES	
	Claims	NONE	NO	
2. Citations and explanations:				
<p>Claims 1-3, 5-8, 10, and 14-17 lack novelty under PCT Article 33(2) as being anticipated by US 2018/0271425 A1 to Kurin, Inc. (hereafter 'Kurin')</p> <p>As per claim 1, Kurin discloses a fluid sample optimization device for optimizing a fluid sample collected by a fluid collection device from a fluid source, a first portion of the fluid sample potentially having contaminants (sample optimization systems that reduce or eliminate contaminants in collected blood samples by including a blood sequestration device; abstract), the fluid sample optimization device comprising: an inlet configured to connect with the fluid source (blood sequestration device 2408 includes an inlet port 2412; figure 24B; paragraph [0146]); an outlet configured to connect with the fluid collection device (blood sequestration device 2408 includes an outlet port 2414; figure 24B; paragraph [0146]); a sample path connected between the inlet and the outlet (a blood sample channel 2422; figure 24C; paragraph [0147]); and a contaminant containment reservoir connected between the inlet and the outlet (blood sequestration chamber 2418; figure 24B; paragraph [0147]), the contaminant containment reservoir having an air permeable fluid resistor proximate the outlet (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]), the contaminant containment reservoir being arranged to receive, when a pressure differential is applied between the inlet and the outlet, a first portion of the fluid sample from the fluid source to displace air therein through the air permeable fluid resistor and the outlet (upon drawing of blood by way of a syringe or Vacutainer (pressure differential is applied) initial aliquot of blood flows into the blood sequestration chamber 2418 displacing air through blood barrier 2420 (air permeable fluid) and the outlet; figures 24B-24C; paragraph [0148]), such that upon receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir, subsequent portions of the fluid sample can be conveyed by the sample path from the inlet to the outlet when subsequent pressure differentials are applied between the inlet and the outlet (the blood in the sequestration chamber 2418 forces the inner chamber housing to the second position allowing one or more apertures 2424 to open 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 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraph [0148]).</p> <p>As per claim 2, Kurin discloses the fluid sample optimization device in accordance with claim 1, and Kurin further discloses comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the contaminant containment reservoir (blood sequestration device 2408 houses the inlet, the outlet, the sample path, and the contaminant containment reservoir; figures 24B-24D; paragraph [0147]).</p> <p>As per claim 3, Kurin discloses the fluid sample optimization device in accordance with claim 1, and Kurin further discloses wherein the air permeable fluid resistor (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]) includes a material that seals upon contact with the first portion of the fluid sample (the term "air permeable blood barrier" is 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; paragraph [0066]).</p> <p>As per claim 5, Kurin discloses the fluid sample optimization device in accordance with claim 1, and Kurin further discloses wherein each pressure differential is provided by a vacuum pressure provided by the fluid collection device (in a blood sample under vacuum pressure or force through the conduit 2006 [2406] from the patient needle 2402 using a syringe or Vacutainer; figure 24B; paragraphs [0144], [0148]).</p> <p>----Continued Within the Next Supplemental Box----</p>				

Form PCT/ISA/237 (Box No. V) (revised January 2019)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US20/26276

Box No. VI Certain documents cited1. Certain published documents (Rules 43*bis*.1 and 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 2019/232196 A1	05/12/2019	30/05/2019	31/05/2018

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)
_____	_____	_____

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US20/26276

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

---Continued from Box V: Citations and Explanations---

As per claim 6, Kurin discloses a fluid sample optimization device for optimizing a fluid sample collected by a fluid collection device from a fluid source, a first portion of the fluid sample potentially having contaminants (sample optimization systems that reduce or eliminate contaminants in collected blood samples by including a blood sequestration device; abstract), the fluid sample optimization device comprising: an inlet configured to connect with the fluid source (blood sequestration device 2408 includes an inlet port 2412, for blood sample; figure 24B; paragraph [0146]); an outlet configured to connect with the fluid collection device (blood sequestration device 2408 includes an outlet port 2414 for blood sample; figure 24B; paragraph [0146]); a sample path connected between the inlet and the outlet (a blood sample channel 2422; figure 24C; paragraph [0147]), the sample path further having a resistive plug that is configured to inhibit at least a part of the first portion of the fluid sample and the contaminants from entering the sample path (in the first position one or more apertures 2424 are closed to flow blood into sequestration chamber 2418 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraphs [0147]-[0148]); and a contaminant containment reservoir connected between the inlet and the outlet (blood sequestration chamber 2418; figure 24B; paragraph [0147]), the contaminant containment reservoir further having an air permeable fluid resistor proximate the outlet (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]), the contaminant containment reservoir being arranged to receive, when a pressure differential is applied between the inlet and the outlet, the first portion of the fluid sample from the fluid source to displace air therein through the air permeable fluid resistor and the outlet (upon drawing of blood by way of a syringe or Vacutainer (pressure differential is applied) initial aliquot of blood flows into the blood sequestration chamber 2418 displacing air through blood barrier 2420 (air permeable fluid) and the outlet; figures 24B-24C; paragraph [0148]), such that upon receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir, subsequent portions of the fluid sample can be forced through the resistive plug and conveyed by the sample path from the inlet to the outlet when subsequent pressure differentials are applied between the inlet and the outlet (the blood in the sequestration chamber 2418 forces the inner chamber housing to the second position allowing one or more apertures 2424 to open 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 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraph [0148]).

As per claim 7, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin further discloses further comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the contaminant containment reservoir (blood sequestration device 2408 houses the inlet, the outlet, the sample path, and the contaminant containment reservoir; figures 24B-24D; paragraph [0147]).

As per claim 8, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin further discloses wherein the air permeable fluid resistor (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]) includes a material that seals upon contact with the first portion of the fluid sample (the term "air permeable blood barrier" is 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; paragraph [0066]).

As per claim 10, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin further discloses wherein each pressure differential is provided by a vacuum pressure provided by the fluid collection device (in a blood sample under vacuum pressure or force through the conduit 2006 [2406] from the patient needle 2402 using a syringe or Vacutainer; figure 24B; paragraphs [0144], [0148]).

As per claim 14. A fluid sample optimization device for optimizing a fluid sample, a first portion of the fluid sample potentially having contaminants (sample optimization systems that reduce or eliminate contaminants in collected blood samples by including a blood sequestration device; abstract), the fluid sample optimization device comprising: an inlet (blood sequestration device 2408 includes an inlet port 2412; figure 24B; paragraph [0146]); an outlet (blood sequestration device 2408 includes an outlet port 2414; figure 24B; paragraph [0146]); a sample path connected between the inlet and the outlet (a blood sample channel 2422; figure 24C; paragraph [0147]); and a contaminant containment reservoir connected between the inlet and the outlet (blood sequestration chamber 2418; figure 24B; paragraph [0147]), the contaminant containment reservoir having an air permeable fluid resistor proximate the outlet (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]), the contaminant containment reservoir being arranged to receive, when a pressure differential is applied between the inlet and the outlet, a first portion of the fluid sample to displace air therein through the air permeable fluid resistor and the outlet (upon drawing of blood by way of a syringe or Vacutainer (pressure differential is applied) initial aliquot of blood flows into the blood sequestration chamber 2418 displacing air through blood barrier 2420 (air permeable fluid) and the outlet; figures 24B-24C; paragraph [0148]), such that upon receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir, subsequent portions of the fluid sample can be conveyed by the sample path from the inlet to the outlet when subsequent pressure differentials are applied between the inlet and the outlet (the blood in the sequestration chamber 2418 forces the inner chamber housing to the second position allowing one or more apertures 2424 to open 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 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraph [0148]).

---Continued Within the Next Supplemental Box---

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US20/26276

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

---Continued from Previous Supplemental Box---

As per claim 15, Kurin discloses the fluid sample optimization device in accordance with claim 14, and Kurin further discloses wherein the sample path further includes a resistive plug that is configured to inhibit at least a part of the first portion of the fluid sample and the contaminants from entering the sample path during receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir (in the first position one or more apertures 2424 are closed to flow blood into sequestration chamber 2418 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraphs [0147]-[0148]).

As per claim 16, Kurin discloses the fluid sample optimization device in accordance with claim 14, and Kurin further discloses further comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the contaminant containment reservoir (blood sequestration device 2408 houses the inlet, the outlet, the sample path, and the contaminant containment reservoir; figures 24B-24D; paragraph [0147]).

As per claim 17, Kurin discloses the fluid sample optimization device in accordance with claim 14, and Kurin further discloses wherein the air permeable fluid resistor (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]) includes a material that seals upon contact with the first portion of the fluid sample (the term "air permeable blood barrier" is 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; paragraph [0066]).

Claims 4, 9, 18 lack an inventive step under PCT Article 33(3) as being obvious over Kurin,

As per claim 4, Kurin discloses the fluid sample optimization device in accordance with claim 1, but Kurin does not disclose, in the first embodiment, wherein the contaminant containment reservoir includes a tortuous path. In a different embodiment, Kurin further discloses wherein the contaminant containment reservoir includes a tortuous path (a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of inner conduit 2620; figures 26C-26D; paragraph [0154]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of the first embodiment of Kurin to provide wherein the contaminant containment reservoir includes a tortuous path, as taught by the second embodiment of Kurin, in order to provide an associated amount of the sequestered fluid (paragraph [0096]).

As per claim 9, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin does not disclose, in the first embodiment, wherein the contaminant containment reservoir includes a tortuous path. In a different embodiment, Kurin further discloses wherein the contaminant containment reservoir includes a tortuous path (a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of inner conduit 2620; figures 26C-26D; paragraph [0154]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of the first embodiment of Kurin to provide wherein the contaminant containment reservoir includes a tortuous path, as taught by the second embodiment of Kurin, in order to provide an associated amount of the sequestered fluid (paragraph [0096]).

As per claim 18, Kurin discloses the fluid sample optimization device in accordance with claim 14, but Kurin does not disclose, in the first embodiment, wherein the contaminant containment reservoir includes a tortuous path. In a different embodiment, Kurin further discloses wherein the contaminant containment reservoir includes a tortuous path (a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of inner conduit 2620; figures 26C-26D; paragraph [0154]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of the first embodiment of Kurin to provide wherein the contaminant containment reservoir includes a tortuous path, as taught by the second embodiment of Kurin, in order to provide an associated amount of the sequestered fluid (paragraph [0096]).

Claims 11-12, 19-20 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of GB 1378602 A (AYERS).

As per claim 11, Kurin discloses the fluid sample optimization device in accordance with claim 6, but Kurin does not disclose wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials. Ayers discloses a resistive plug includes a film that is pierceable by a first of a subsequent pressure differentials (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US20/26276

Supplemental Box

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As per claim 12, Kurin and Ayers, in combination, disclose the fluid sample optimization device in accordance with claim 11, but Kurin does not disclose wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film. Ayers discloses a resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

As per claim 19, Kurin discloses the fluid sample optimization device in accordance with claim 15, but Kurin does not disclose wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

As per claim 20, Kurin and Ayers, in combination, disclose the fluid sample optimization device in accordance with claim 19, but Kurin does not disclose wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film. Ayers discloses a resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

Claim 13 lacks an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 2014/0112841 A1 to Schoen, et al. (hereafter 'Schoen') as evidenced by WO 2019/055487 A1 to Magnolia Medical Technologies (hereafter 'Magnolia').

As per claim 13, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin discloses the use of mesh for resistive plugs (barriers are made from mesh or filter material; paragraph [0066]), but Kurin does not disclose wherein the resistive plug includes a mesh with a dissolvable material that dissolves upon contact with a first of the subsequent portions of the fluid sample. Schoen discloses a resistive plug includes a mesh with a dissolvable material that dissolves upon contact with a first of the subsequent portions of the fluid sample (water-soluble membrane (mesh) used for temporarily retaining a liquid in a holding chamber, where the membrane dissolves after a certain amount of time; abstract; paragraph [0035]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug includes a mesh with a dissolvable material that dissolves upon contact with a first of the subsequent portions of the fluid sample, as taught by Schoen, as evidenced by Magnolia that discloses an actuator that changes a sample device from sequestration to flow through upon dissolving (Magnolia: actuator 250, used to change sample flow from sequestration to flow through, is transitioned by a change of configuration such as dissolving; paragraphs [1071], [1080]; figures 2-5).

Claims 1-20 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.

Effect of Portal Venous Blood Flow Diversion on Portal Pressure

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Research Article

To anticipate the hepatic vascular response to portacaval anastomosis, we studied portal pressure during diversion of portal blood through a temporary extracorporeal umbilical vein to saphenous vein shunt. The relationship of portal pressure to shunted flow was approximately linear. In five schistosomiasis patients (controls) portal diversion to 1,250 ml/min gave portal pressure-shunted flow curve slopes ranging from 0.13 to 0.57 cm water/100 ml per min (0.31 ± 0.18 , mean $\pm$ SD). In 17 cirrhotic patients with portal hypertension a continuum of slopes was observed from within mean ± 2 SD of control (type A) to larger slopes (type B) indicating failure of portal pressure regulation. When portal flow was augmented by shunting from saphenous vein to portal vein, cirrhotic patients who had slopes less than mean ± 2 SD of controls during diversion (type A) exhibited a compliant system with small increases in portal pressure, whereas type B patients had significantly greater pressure increases. Selective investigations suggested that changes in portal pressure provoked compensatory changes in hepatic arterial blood flow that tended to maintain portal pressure at a set point. Type B patients demonstrated failure of this mechanism to varying degrees.

After end-to-side portacaval shunt, seven type A cirrhotic patients maintained residual intrahepatic venous pressure unchanged from prior portal pressure, whereas six type B patients had a significant decrease. Residual intrahepatic venous pressure was measured after portacaval shunt [...]

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Effect of Portal Venous Blood Flow Diversion on Portal Pressure

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ABSTRACT To anticipate the hepatic vascular response to portacaval anastomosis, we studied portal pressure during diversion of portal blood through a temporary extracorporeal umbilical vein to saphenous vein shunt. The relationship of portal pressure to shunted flow was approximately linear. In five schistosomiasis patients (controls) portal diversion to 1,250 ml/min gave portal pressure-shunted flow curve slopes ranging from 0.13 to 0.57 cm water/100 ml per min (0.31 ± 0.18 , mean $\pm$ SD). In 17 cirrhotic patients with portal hypertension a continuum of slopes was observed from within mean ± 2 SD of control (type A) to larger slopes (type B) indicating failure of portal pressure regulation. When portal flow was augmented by shunting from saphenous vein to portal vein, cirrhotic patients who had slopes less than mean ± 2 SD of controls during diversion (type A) exhibited a compliant system with small increases in portal pressure, whereas type B patients had significantly greater pressure increases. Selective investigations suggested that changes in portal pressure provoked compensatory changes in hepatic arterial blood flow that tended to maintain portal pressure at a set point. Type B patients demonstrated failure of this mechanism to varying degrees.

After end-to-side portacaval shunt, seven type A cirrhotic patients maintained residual intrahepatic venous pressure unchanged from prior portal pressure, whereas six type B patients had a significant decrease. Residual intrahepatic venous pressure was measured after portacaval shunt in 40 cirrhotic patients who were followed

for as long as 9 yr (median survival 4.0 yr). The 13 patients who developed chronic encephalopathy had significantly lower pressure (21.1 ± 4.4 cm, mean $\pm$ SD) and shorter survival (median 0.6 yr) than the other 27 patients (32.6 ± 5.3 cm, 5.0 yr). The preoperative estimation of portal pressure-diverted portal flow curve slope anticipates the hepatic vascular response to portacaval anastomosis and identifies a group of patients in whom loss of portal blood flow results in a low residual intrahepatic venous pressure that is associated with early death and chronic encephalopathy.

INTRODUCTION

The increase in hepatic vascular resistance accompanying liver disease raises portal pressure and diminishes portal venous flow to the liver. Prograde portal flow may cease or even become retrograde as portal-systemic collaterals divert portal flow (1, 2). Increased hepatic arterial flow is presumed to compensate for reduced portal flow and account for normal values of total hepatic flow observed occasionally in cirrhotic patients with portal hypertension and portal systemic collateral circulation (3-6). An abrupt compensatory increase in hepatic arterial flow has been documented during acute portal flow diversion at the creation of a portacaval anastomosis (7-9). These facts imply homeostatic activity of the splanchnic vascular system to maintain portal pressure and/or hepatic blood flow when portal blood flow decreases (10-12). To evaluate the splanchnic hemodynamic response to portal blood flow diversion, we studied the response of portal pressure to acute incremental diversion of portal venous blood through a temporary extracorporeal umbilical vein to saphenous vein portal-systemic shunt (13).

METHODS

Subjects. In the schistosomiasis patients (Table I) described here, portal pressure and liver function tests including Bromsulfalein retention were normal. These patients were assumed to have normal splanchnic hemodynamics. They

This work was presented in part at the annual meetings of the American Association for the Study of Liver Disease, 4 November 1970, 1 November 1972, and 8 November 1978, Chicago Illinois; of the American Federation of Clinical Research, 12 May 1971 and 29 April 1973; and of the American College of Surgery, 14 November 1969. Abstracts were published in *Gastroenterology*, **60**: 169 (1970), **64**: 166 (1973), **75**: 996 (1978); *Clin. Res.* **19**: 406 (1971), **21**: 529 (1973); and *Surg. Forum*, **22**: 351-352 (1971), **23**: 334-336 (1972). Address reprint requests to Dr. Zimmon.

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were studied after heparinization, but before the administration of tartar emetic (13). The initial 17 cirrhotic patients (Table I) with documented esophageal varices were studied after umbilical vein catheterization for measurement of portal pressure (14), for umbilical vein angiography before portal-systemic shunt surgery (15), or for the establishment of an extracorporeal portal-systemic shunt to reduce portal pressure and control life threatening variceal hemorrhage (16). Subsequent patients evaluated before and after or during portacaval shunt received internal therapeutic end-to-side portacaval anastomosis after endoscopically documented variceal hemorrhage (17). In our institution umbilical vein catheterization is the preferred method for evaluating the portal circulation because of its safety and reliability (18). Informed consent was obtained from all subjects. These studies were performed under a research protocol approved by the Research Committee of the Veterans Administration Medical Center, New York, and the New York University School of Medicine.

Except where specifically indicated all procedures were performed under local anesthesia. The umbilical vein was catheterized extraperitoneally (19) and connected to a saphenous catheter by a silicon rubber tube with an occluding roller pump (solid state varistaltic pump; Manostat Corp., New York) and cannulating square wave electromagnetic flow meter (model E-3000; Statham Instruments Inc., Oxnard, Calif.). The umbilical vein catheter has an integral molded wire to prevent collapse and a second 1-mm lumen within its wall to allow continuous recording of portal pressure (model 1956 SP-BJBI, U. S. Catheter and Instrument Co., Glen Falls, N. Y.). Pres-

ures were recorded using Statham P37 perfused strain gauges that permitted a continuous infusion of heparin (0.1 mg/min). Electrical mean pressures were used to obviate respiratory fluctuation. Zero pressure level was taken as 12 cm above the couch.

The hepatic vein was catheterized from an antecubital vein (20, 21). The achievement of a wedged position was confirmed by the demonstration of an arterial pulse in the pressure recording, by the identity of wedged hepatic venous pressure and portal pressure, and by injection of radiopaque contrast at the completion of a study.

Flow through the extracorporeal shunt was monitored by the cannulating square wave flow meter calibrated for zero flow with the shunt occluded. In vitro calibration for flow rates to 3,000 ml/min with pumped whole blood and occluding roller pump yields an accuracy of $\pm 5\%$. The pumping circuit was primed with 200 ml of normal saline.

Procedure. After catheter placement and shunt construction, portal pressure was recorded and portal to systemic shunting initiated at 100 ml/min. Stabilization of pump rate required 5–10 s. By that time, pressures were stable and were recorded. Shunting was increased in 100 ml/min increments. When maximum hepatofugal flow was achieved as evidenced by portal vein flutter, shunting was stopped and pressure recorded. Systemic to portal shunting was then begun in 100 ml/min increments until limited by saphenous vein flutter. The shunting portion of the procedure required 15–20 min.

The response of portal pressure to shunting at different

TABLE I
Effect of Portal Venous Flow Diversion or Augmentation on Portal Pressure

Case	Diagnosis etiology	Documentation	Ascites (-4+)	Direction portal flow	Basal PP	Hepatofugal pumping			Hepatopetal pumping		
						Max flow	Pressure change	Pressure-flow slope	Max flow	Pressure change	Pressure-flow slope
					cm	ml/min	cm	cm/100 ml	ml/min	cm	cm/100 ml
1	C,A	Biopsy	0	Prograde	37	1,100	0	0.00	500	+2	+0.40
2	S	—	—	Prograde	15	750	-1	-0.13			
3	S	—	—	Prograde	11	1,200	-2	-0.17			
4	C,A	Biopsy	+1	Prograde	35	1,450	-3	-0.20			
5	S	—	—	Prograde	15	1,250	-3.5	-0.28			
6	C	Biopsy	3+	Prograde	27	1,600	-6	-0.38	1,000	+3	+0.30
7	S	—	—	Prograde	14	1,100	-5	-0.43			
8	C,A	Biopsy	0	Retrograde	37	900	-4	-0.44			
9	C,A	Biopsy	0	Prograde	36	1,000	-5	-0.50	700	+1	+0.14
10	S	—	—	Prograde	8	700	-4	-0.57	1,100	0	0.0
11	C,A	Biopsy	2+	Retrograde	39	1,700	-10	-0.59	1,200	+1	+0.08
12	C,A	W,biopsy	0	Prograde	35	2,500	-15	-0.60	900	+2.5	+0.27
13	C,HEM	Biopsy	+1	Prograde	29	1,500	-9	-0.60	600	+3	+0.50
14	C,A	Biopsy	0	Prograde	39	1,500	-13	-0.87	1,000	+16	+1.6
15	C,A	W,biopsy	2+	Prograde	42	600	-6	-1.00	1,400	+6	+0.43
16	C,A	Biopsy	1+	Prograde	26	1,000	-10	-1.00	750	+9	+1.20
17	C,CR	Biopsy	1+	Prograde	29	850	-18	-2.11			
18	C,A	Autopsy	0	Prograde	37	900	-28	-3.10	700	+11	+1.57
19	C,A	Biopsy	2+	Prograde	39	900	-31	-3.44	700	+9	+1.28
20	C,A	Biopsy	4+	Prograde	35	800	-31	-3.87			
21	C,A,HEP	Biopsy	0	Prograde	55	1,100	-48	-4.36			
22	C,A	Biopsy	0	Prograde	35	500	-30	-6.00	500	+18	+3.6

Abbreviations used in this table: C, cirrhosis; S, schistosomiasis; A, alcoholism; HEM, hemachromatosis; HEP, hepatoma; CR, cryptogenic; W, wedged hepatic venous pressure; PP, portal pressure; max, maximum.

vascular volumes was studied after phlebotomy accomplished by draining the extracorporeal circuit into a sterile infusion bottle containing 20 mg of heparin. 1 liter of blood was withdrawn in 3 min. After studying the response of portal pressure to shunting the blood was reinfused. Then, for volume expansion 5% dextran or blood was infused. Final volume was dictated by the patient's clinical status (22). Since the elapsed time for phlebotomy and volume expansion was <15 min, vascular volume shifts were considered to be negligible. Therefore, changes in blood volume were calculated from the measured quantity withdrawn or infused.

At the completion of a study the direction of portal venous flow (prograde or retrograde) was determined by observing the course of a gentle hand injection of 50% sodium diazotrate (Hypaque, Winthrop Laboratories, Sterling Drug Co., New York) through the primary lumen of the umbilical vein catheter (3). Radiopaque contrast media were not administered before pressure or flow measurements because of their effect on systemic and splanchnic hemodynamics (23). Finally, a pressure injection with serial x rays was used to visualize the portal vasculature (15).

Definition of residual intrahepatic venous pressure. Wedged hepatic venous pressure and portal pressure measured by umbilical vein catheterization are identical in patients with cirrhosis when the portal circulation is intact (24). Simultaneous measurement of wedged hepatic venous pressure and umbilical portal pressure in two cirrhotic patients during shunting of portal flow agreed within ± 1 cm water (Fig. 1). After disconnection of the extrahepatic portal venous system from the liver by end-to-side portacaval shunt, residual intrahepatic venous pressure was measured by wedged hepatic venous catheterization or by umbilical vein catheterization of the intrahepatic portal vein. The extrahepatic portal venous system drains into the vena cava.

Construction of portal pressure-shunted portal flow curves. Curves constructed for controls with *Schistosoma mansoni* infections and cirrhotic patients with portal pressure-shunted portal flow curve slopes < -0.67 cm water/100 ml per min diverted flow were linear (Figs. 1 and 2) and allow a simple arithmetic expression of slope as change in pressure/100 ml per min shunted flow. Cirrhotic patients with steep slopes have a smaller range of flow and curves that are increasingly convex (Figs. 2 and 3). For the purpose of this paper, the arithmetic portal pressure-shunted portal flow curve slope is derived from the sum change in pressure divided by maximum flow before vein flutter was detected by palpation of the shunt or pumping was stopped because of increased portal pressure. As indicated, certain patients were studied at laparotomy under anesthesia or during resuscitation from hemorrhage. These circumstances provide unique opportunities to gain physiologic insights in man but undoubtedly influence to a greater or lesser extent the data obtained. Therefore, we confined data in Table I describing the control (schistosomiasis) patients and values in cirrhotic patients with portal hypertension for portal pressure-shunted portal flow curve slope to subjects studied without anesthesia or laparotomy when hemodynamically stable.

Statistical significance was determined with the Wilcoxon two sample ranked test, unpaired *t* test, and log rank test (25, 26).

RESULTS

Schistosomiasis (control) subjects

During portal to systemic shunting averaging 1,000 ml/min (range, 700–1,350) in five schistosomiasis pa-

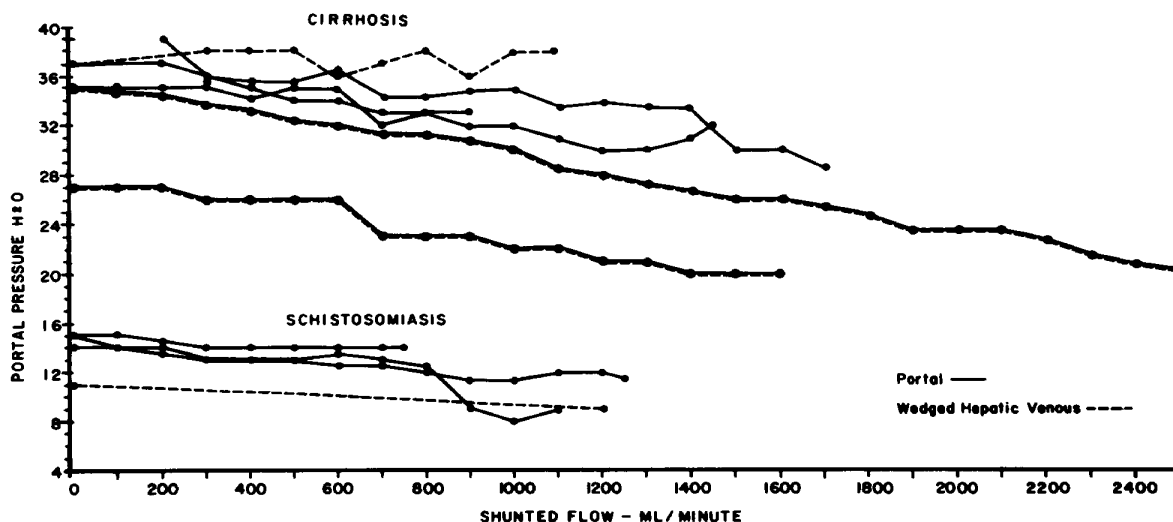


FIGURE 1 Response of portal pressure to portal venous blood flow diversion in type A cirrhotic patients and control subjects. Portal pressure (centimeters water) is plotted against volume of shunted portal venous flow (milliliters per minute) diverted through an umbilicosaphenous shunt. Six representative cirrhotic patients are shown in order of decreasing basal portal pressure (case Nos. 11, 1, 8, 4, 12, and 6, Table I). Four representative controls (2, 5, 7, and 3, Table I) are shown in order of decreasing basal portal pressure. The solid line indicates portal pressure measured through an umbilical vein catheter in the left portal vein. The interrupted line indicates portal pressure measured by wedged hepatic venous catheterization. The combined solid and interrupted lines in two cirrhotic patients (11, 1, Table I) indicate simultaneous measurement of portal and wedged hepatic venous pressures.

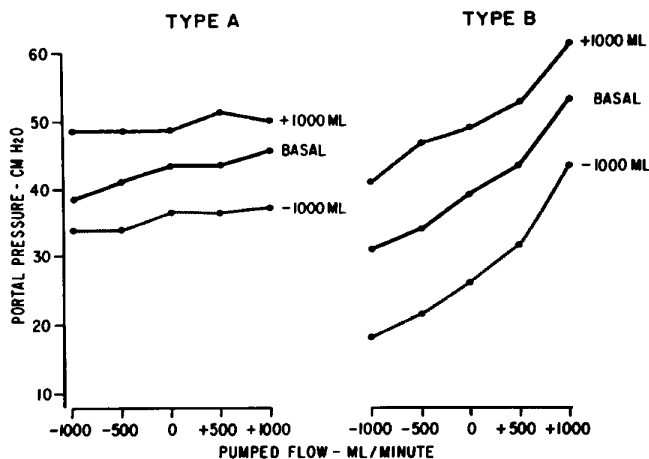


FIGURE 2 Effect of changes in blood volume on portal pressure and portal pressure-shunted flow curve slope. In a single type A patient (left) basal portal pressure of 43 cm was reduced to 36 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000 ml-volume load in addition to replacement of the 1,000-ml phlebotomy, whereas portal pressure-shunted flow slope varied from 0.35 to 0.15 to 0.10 cm/100 ml per min shunted flow, respectively. In a single type B patient, a basal portal pressure of 39 cm was reduced to 26 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000-ml volume load after replacement of the phlebotomy, whereas portal pressure-shunted flow curve slope varied from 1.15 to 1.25 to 1.05, respectively.

tients portal pressure decreased an average of 3.1 cm water (range, 1–4). Portal pressure-shunted portal flow slope averaged -0.31 ± 0.18 (mean $\pm$ SD) cm water/100 ml per min diverted flow (range -0.13 to -0.57) (Table I).

Cirrhotic patients

In cirrhotic patients ($n = 17$) with portal hypertension, the response to portal diversion was varied and the portal pressure-shunted portal flow slope ranged from -0.0 to -6.0 . In patient 1 (Table I) portal pressure was unchanged by portal diversion of 1,000 ml/min, whereas in patient 22 (Table I) portal pressure fell to central venous levels with diversion of only 500 ml/min (Table I). A histogram (Fig. 4, upper) of portal pressure-shunted portal flow slope during diversion in cirrhotic patients with portal hypertension shows a continuum from slopes similar to *S. mansoni* patients with normal portal pressure (Fig. 4, hatched bars) to extremely high values. A relationship between basal portal pressure and portal pressure-shunted portal flow slope is not apparent (Table I). The lack of correlation between portal pressure and portal pressure-shunted portal flow slope arises, in part, from the influence of blood volume on portal pressure (Fig. 2). Increasing or decreasing blood volume produces a corresponding shift in portal pressure (22) with little change in portal pressure-shunted portal flow slope.

Definition of type A and B cirrhotic patients

Type A cirrhotic patients (Figs. 1 and 2) are defined as those with portal pressure-shunted portal flow slopes < -0.67 cm/100 ml per min (control mean ± 2 SD). Type B cirrhotic patients have portal pressure-shunted portal flow slopes in excess of -0.67 cm/100 ml per min diverted flow (Table I, Figs. 2 and 3). In the initial 17 patients studied (Table I) the mean basal portal pressure (34.4 ± 4.2 cm of water, mean $\pm$ SD) of eight cirrhotic patients with portal pressure-shunted flow slopes for portal flow diversion within the mean ± 2 SD of the five control (schistosomiasis) patients was not significantly different from the mean basal portal pressure (37.4 ± 8.3 cm) of the nine cirrhotic patients with greater slopes. Similarly, in a group of 13 patients clinically considered candidates for portacaval anastomosis (Fig. 5), the basal portal pressures of seven type A patients were not significantly different from the six type B patients. The 23 cirrhotic patients with endoscopically documented bleeding esophageal varices classified as type A or type B when hemodynamically stable under local anesthesia had basal portal pressure ranging from 55 to 26 cm. The 55-cm value (Table I, No. 21) occurred in a patient with hepatoma. Although the three highest values (55, 45, and 42 cm) and the two lowest values (26 and 28 cm) were found in type B patients, the pressures of type A patients were not significantly different (Wilcoxon rank test) from type B.

Mechanism for maintenance of portal pressure during portal venous flow diversion

Hepatic arterial response to extracorporeal portal diversion. Hepatic arterial flow was measured at laparotomy for portacaval anastomosis by noncannulating square wave electromagnetic flow meter in two type A cirrhotic patients before and during diversion of 1 liter/min. Hepatic arterial flow increased 40 and 46%.

Spontaneous total retrograde portal flow in type A portal hypertension. Two (Nos. 8 and 11) of 17 cirrhotic patients described had total retrograde portal venous flow (Table I) (3). Both had type A portal hypertension with portal pressure-shunted portal flow slopes of 0.44 and 0.59 cm/100 ml per min. The presence of total retrograde portal flow implies sufficient portal-systemic collateral vessels for egress from the splanchnic chamber of all splenic and mesenteric inflow and a portion of hepatic arterial flow. The most likely source for additional splanchnic inflow to maintain portal pressure during portal diversion in this situation is the hepatic artery.

Portal pressure response to portal flow augmentation by systemic to portal shunting. In portal hypertension an added load should increase portal pressure, since mechanisms for reducing splanchnic inflow or in-

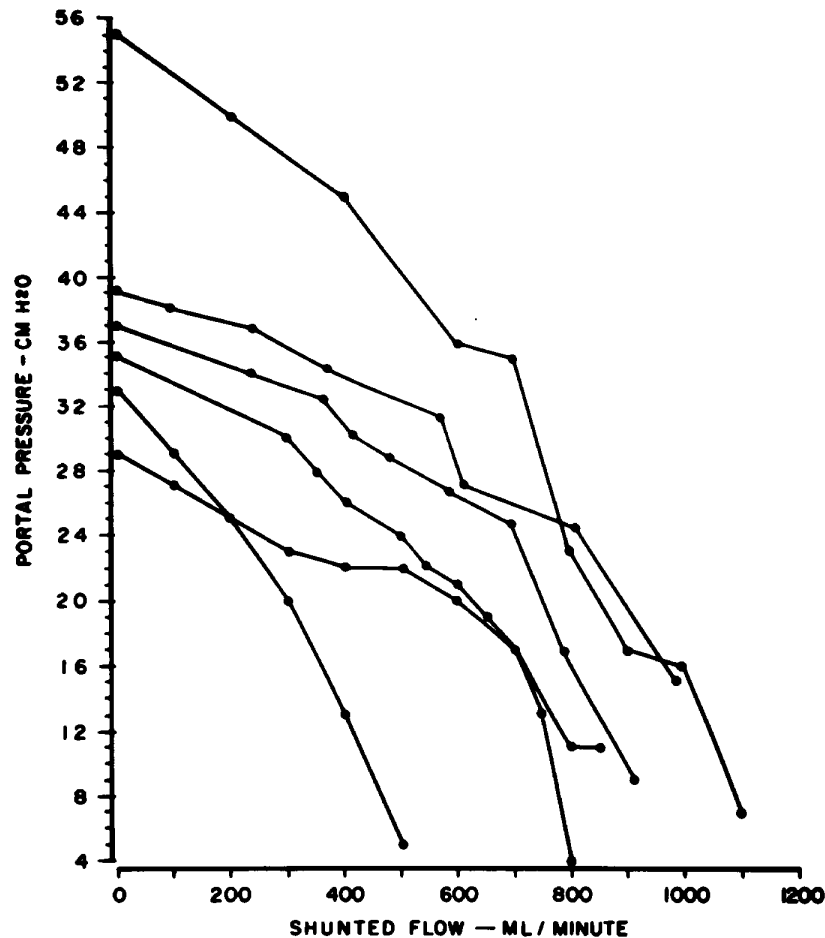


FIGURE 3 Response of portal pressure to portal diversion in type B cirrhotic patients. Portal pressure (centimeters water) is plotted against volume of portal venous flow diverted through the umbilicosaphenous shunt. Six representative type B cases in order of decreasing basal portal pressure (case Nos. 21, 19, 18, 20, 22, and 17, Table I) are shown.

creasing outflow already would be activated by existing portal hypertension. Type A patients accommodate their portal pressure as well to portal flow augmentation as diversion (Table I, Figs. 2 and 4). Portal pressure-shunted portal flow curve slopes are more varied for augmentation but are similar to slopes (Table I) for diversion in the 12 patients where both maneuvers were performed (Fig. 4).

Type A cirrhotic subjects who during portal diversion had portal pressure-shunted portal flow slopes less than the mean ± 2 SD of control exhibit a compliant system in that relatively small increases in portal pressure were observed (range, $+0.08$ to $+0.50$, mean $\pm$ SD, 0.3 ± 1.6 cm/100 ml per min, $n = 6$). Cirrhotic patients with steep type B slopes during portal diversion demonstrated steep slopes during augmentation (range, $+0.43$ to $+3.60$, mean $\pm$ SD, 1.6 ± 1.1 cm/100 ml per min, $n = 6$) that were increased ($P < 0.01$) when compared to the

compliant group. The basal portal pressures of the eight cirrhotic patients with type A slopes (34.4 ± 4.2 cm water, mean $\pm$ SD) were not significantly different from the nine cirrhotic patients with type B slopes (37.4 ± 8.3 cm water).

Induced retrograde portal flow during portal venous flow diversion. If increasing hepatic arterial flow, rather than changing portal-systemic collateral, splenic, or mesenteric inflow, accounts for the maintenance of portal pressure during portal diversion, sampling of indocyanine green from the umbilicosaphenous shunt during diversion should demonstrate extraction of indocyanine green from portal blood when increased hepatic arterial flow reverses through hepatic sinusoids to enter the extracorporeal circuit. At laparotomy for portacaval shunt with 750 ml/min portal diversion, prograde portal flow was evidenced by absence of extraction. Retrograde flow of hepatic arterial blood into the

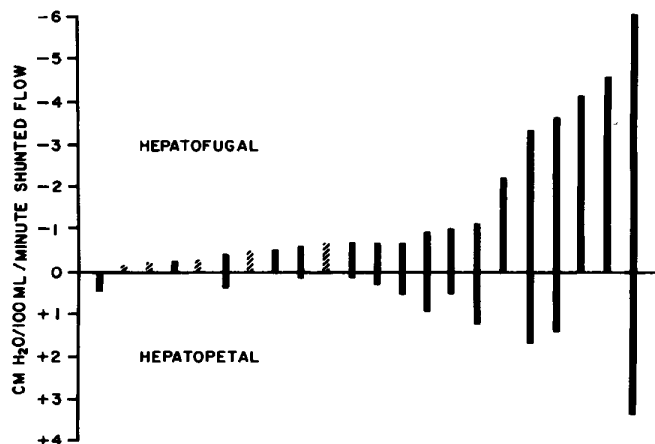


FIGURE 4 Histogram of portal pressure-shunted portal venous flow slope. Patients 1 (left) through 22 (right) are presented in order of increasing slope (Table I). The upper bars refer to the slope for portal diversion (hepatofugal shunting). The lower bars refer to the slope for portal blood flow augmentation (hepatopetal shunting) performed in 12 patients. Hatched bars indicate schistosomiasis patients (controls).

portal vein with extraction occurred at diversion rates in excess of 1,000 ml/min. This type A patient (Table IIA) accommodated to 1,000 ml/min portal diversion or augmentation (portal pressure-shunted portal flow slope -0.3 , $+0.0$) with little change in portal pressure.

Portal pressure and intrahepatic venous pressure response to occlusion of hepatic artery or portal vein. Intraoperative occlusion of hepatic artery or portal vein before and during diversion of blood from the hepatic side of the occluded portal vein was studied in two patients to compare hepatic artery and portal venous (splenic and mesenteric) capacity to sustain intrahepatic venous pressure (Table II). Intrahepatic venous pressure was measured and blood was shunted through the umbilical catheter on the hepatic side of the occluded portal vein.

The type A patient maintained intrahepatic venous pressure with flow from either hepatic artery or portal vein (Table II experiments 5A and 6A). Portal venous flow alone maintained portal venous pressure when the hepatic artery was occluded (experiment 5A) suggesting adequate portal flow to support pressure. When portal flow is stopped, hepatic artery flow is adequate to prevent a reduction in intrahepatic venous pressure (experiment 6A). The response to 1,000 ml/min portal to systemic shunting between the site of portal vein occlusion and the liver (experiment 7A) shows the hepatic artery to have a greater capacity to support intrahepatic venous pressure than mesenteric and splenic vessels, since pressure falls less when the portal vein is occluded and the hepatic artery supplies the liver (experiment 8A) than when the hepatic artery is

occluded and the portal vein supplies liver (experiment 7A). This suggests that increased hepatic artery flow is the most important mechanism in maintaining portal pressure during portal diversion in this type A patient.

In a type B patient (Table II) occlusion of the portal vein precipitated an 11-cm decrease in intrahepatic venous pressure (experiment 6B) indicating the failure of hepatic artery flow to maintain pressure. This inadequacy was exaggerated by simultaneous portal vein occlusion and portal diversion (Experiment 8B). This type B patient relies on portal flow to sustain intrahepatic venous pressure. The failure of hepatic artery occlusion to reduce portal pressure (experiment 5B) indicates a small hepatic artery contribution to maintenance of portal pressure in this patient. The steep portal pressure-shunted portal flow slope when the portal vein is patent (experiment 2B) demonstrates the failure of portal-systemic collateral flow to compensate for increasing or decreasing portal flow.

Maintenance of residual intrahepatic venous pressure after end-to-side portacaval anastomosis. If the portal pressure-shunted portal flow slope estimates he-

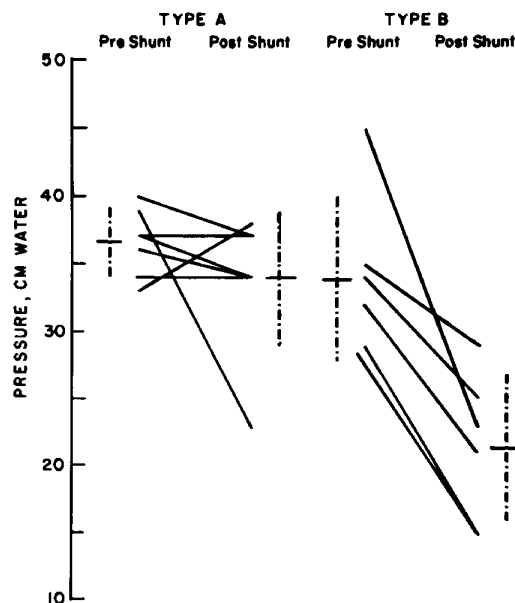


FIGURE 5 Effect of total portal venous flow diversion by end-to-side portacaval anastomosis on intrahepatic venous pressure in type A and type B patients. The horizontal solid bar indicates the mean. The vertical interrupted line indicates SD. Preoperative portal pressures for type A and type B patients were not significantly different. After portacaval shunt mean intrahepatic venous pressure in type B patients (21.3 ± 5.6 , $n = 6$) is significantly decreased ($P < 0.01$) when compared to preshunt portal pressure or postshunt intrahepatic venous pressure in type A patients (33.9 ± 5.0 , $n = 7$). Four type A and four type B patients shown here had portal pressure-shunted portal flow slope determined under anesthesia at laparotomy for portacaval anastomosis and are excluded from Table I.

TABLE II
*Response of Intrahepatic Venous Pressure to Occlusion
of Hepatic Artery and Portal Vein*

Experiment	Hemodynamic type	A	B
1	Basal portal pressure	46	29
2	Portal pressure during diversion, 1,000 ml/min	43	16
3	Portal pressure during augmen- tation, 1,000 ml/min	46	37
4	Pressure-flow slope (cm water/100 ml per min) diversion	-0.3	-1.3
	augmentation	+0.0	+0.8
5	Portal pressure with hepatic artery occluded	44	31
6	Intrahepatic pressure with portal vein occluded	44	18
7	Portal pressure with hepatic artery occluded plus diversion, 1,000 ml/min	35	22
8	Intrahepatic pressure portal vein occluded plus diversion, 1,000 ml/min	39	3

patic vascular capacity to sustain portal pressure during portal venous diversion, the residual intrahepatic venous pressure after end-to-side portacaval anastomosis when the hepatic artery alone supplies the liver should correlate with the preoperative portal pressure and postoperative intrahepatic venous pressure. In 13 patients undergoing end-to-side portacaval anastomosis (Fig. 5) after determination of portal pressure-shunted portal flow slope preoperative portal pressure in seven type A patients (36.6 ± 2.5 cm, mean $\pm$ SD) was not significantly different from six type B patients (33.8 ± 6.1 cm). After end-to-side portacaval anastomosis in type A patients intrahepatic venous pressure was not significantly changed (33.9 ± 5.0) indicating hepatic vascular compensation for loss of portal venous flow. Type B patients suffered a decrease in intrahepatic venous pressure (21.3 ± 5.6) that was significant when compared to their preoperative portal pressure ($t = 3.38$, $P < 0.01$) or to the postoperative intrahepatic venous pressure of the type A patients ($t = 3.90$, $P < 0.01$).

Residual intrahepatic venous pressure after end-to-side portacaval shunt and prognosis. Our initial clinical observations suggested that type B patients in whom residual intrahepatic venous pressure fell after portacaval anastomosis (Fig. 5) frequently died shortly after surgery or suffered from chronic encephalopathy. Therefore, residual intrahepatic venous pressure was measured in 40 patients with cirrhosis associated with

ethanol abuse shortly after interval end-to-side portacaval anastomosis when they were hemodynamically stable. The patients were followed clinically for as long as 9 yr (median, 4.0 yr). 13 patients developed chronic hepatic encephalopathy defined as diminished mental function that was improved by and required continued dietary protein restriction and antibiotic or lactulose therapy. Six of these died within 1 mo of surgery and were classified as early deaths (Fig. 6). The mean residual intrahepatic venous pressure of these 13 patients (21.1 ± 4.4 cm) was significantly less ($P < 0.001$) than the 27 patients that did not have chronic encephalopathy (32.6 ± 5.3 cm).

Life table analysis (25, 26) demonstrated a significantly ($P < 0.01$) shorter survival (median, 0.6 yr) for the 13 patients with lower pressures when compared to the other patients (median, 5.0 yr) (Fig. 7). None of the 27 patients with relatively favorable postoperative courses had a residual intrahepatic venous pressure < 25 cm. 6 of 8 patients who died within 1 mo, 8 of 10 patients who died within 1 yr, and 6 of 7 patients who survived the postoperative period, but suffered from chronic encephalopathy, were unable to maintain residual intrahepatic venous pressure above 25 cm. These findings suggest that 25 cm is a critical lower limit of pressure, below which hepatic function is not maintained and chronic encephalopathy with early death supervenes.

DISCUSSION

A lesser fall in portal pressure than would be expected for a given quantity of portal blood flow diversion indicates a compensatory vascular mechanism. Therefore, the steepest portal pressure-shunted portal flow slope observed (Table I, patient 22) most clearly approaches the absence of this postulated mechanism. Lesser slopes result from its activity. The failure of the portal pressure-shunted portal flow slope to be altered by changing blood volume, portal pressure, and presumably cardiac output (27) points to a splanchnic rather than systemic origin of the proposed mechanism. The small portal pressure-shunted portal flow slopes recorded in control subjects may reflect both low and variable hepatic resistance to flow (28, 29). Similarly, a lesser increase in portal pressure than expected during portal blood flow augmentation by systemic to portal shunting in the presence of portal hypertension suggests a compensatory decrease in arterial inflow to the splanchnic chamber since hepatic and portal-systemic collateral outflow resistance should be limiting when cirrhosis and portal hypertension are present (30-32). Failure or absence of this mechanism in some patients with cirrhosis is indicated by the continuum of portal pressure-shunted portal flow slopes observed.

An increase of mesenteric and splenic venous flow

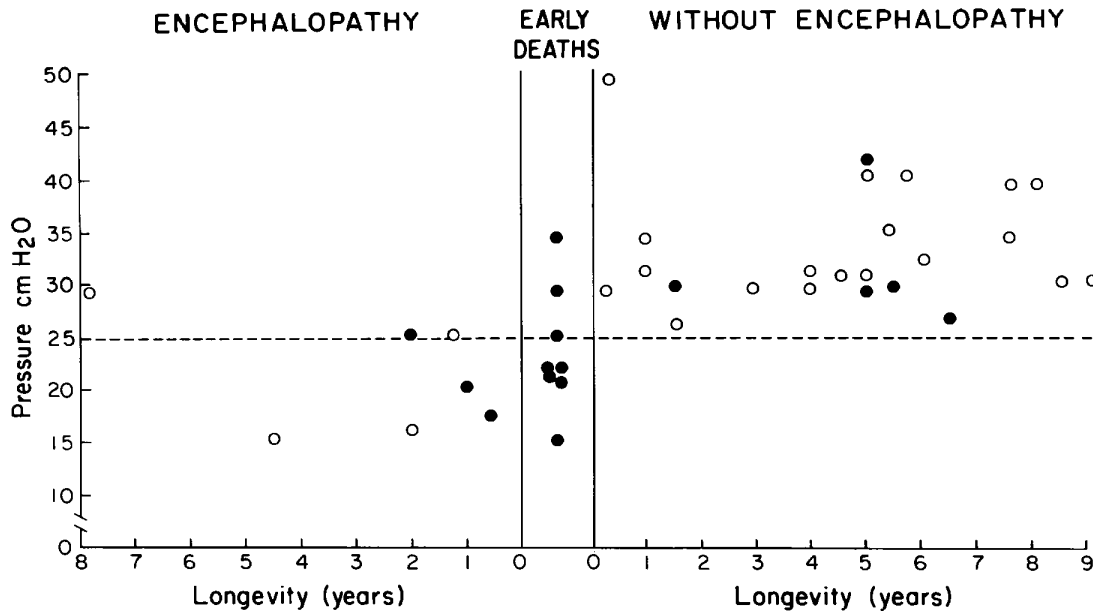


FIGURE 6 Relationship of survival and clinical status (encephalopathy) to residual intrahepatic venous pressure after end-to-side portacaval anastomosis (open circle, alive; closed circle, dead). The 13 patients with encephalopathy (left) had significantly lower pressures than those without encephalopathy (right, $n = 27$) and a significantly shorter survival (median, 0.6 vs. 5.0 yr). Early mortality is defined as death within 1 mo of surgery.

in response to reduced portal pressure is suggested by the maintenance of portal pressure despite hepatic artery occlusion (Table II) and published studies demonstrating an increase in portal and splenic flow after

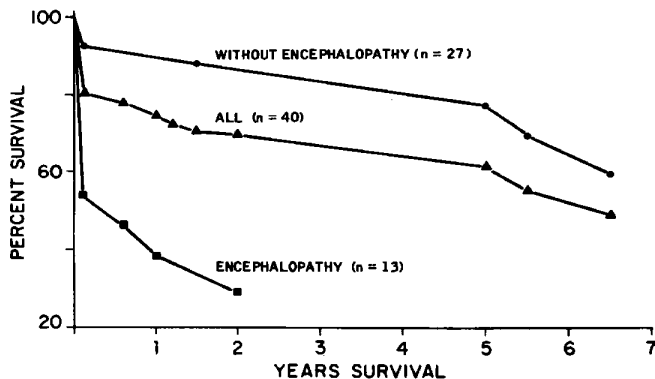


FIGURE 7 Life table analysis of 40 patients followed for up to 9 yr after end-to-side portacaval anastomosis (center curve, all patients). The 13 patients with chronic encephalopathy had a lower residual intrahepatic venous pressure and reduce median survival (0.6 yr, lower curve) when compared to the 27 patients with residual intrahepatic venous pressure > 25 cm and median survival 5.0 yr who did not have chronic encephalopathy (highest curve). The highest and lowest curves are significantly different (log rank test, $P = 0.01$). Cumulative survival for the 13 patients in the lower curve was not carried beyond 2 yr because experience was limited to only two patients surviving beyond this point.

portacaval anastomosis (10, 33). Hepatic (9, 34–36), mesenteric, and splenic (33) arteries may all contribute to maintenance of portal pressure in type A patients when the portal circulation is intact. Conversely, the steep portal pressure-shunted portal flow slopes in type B patients indicate a limited response of all these vessels to changing portal flow and suggests a widespread defect in vascular function.

Abnormal vascular responses in the cardiac (37, 38), pulmonary (39), renal (40), integumentary (41), and splanchnic (36) systems have been demonstrated in patients with liver disease. The increased cardiac output (37) functional renal failure (42) and portal hypertension (43) of liver disease may be reversible. The portal hypertension of cirrhotic patients in this study consisting of an elevated portal pressure setpoint and a variable limitation of the response to changing portal flow also, at least in part, may be a reversible alteration in vascular responsiveness (44) rather than a consequence of the presumed fixed anatomic hepatic outflow block previously conceived as the cause of portal hypertension (45).

Alternatively, the continuum of response to changing portal flow could result from anatomic alterations in the hepatic artery associated with cirrhosis (46, 47). Herrick (48), and later Dock (49), perfused the livers of alcoholic hypertrophic cirrhotic patients in vitro and demonstrated a reciprocal relationship between hepatic arterial pressure and portal pressure. They speculated on the role

of relatively increased hepatic arterial flow as a factor in the portal hypertension of cirrhosis associated with alcoholism. The investigations reported here were based upon their early studies and imply similar conclusions.

Moreno et al. (1) and Burchell et al. (9) have studied portal and hepatic arterial blood flow at laparotomy for portacaval anastomosis. They demonstrated an elevated setpoint for portal pressure of 40 cm of water since this pressure was found despite wide variation in portal blood flow (10). Attempts to correlate portal or hepatic arterial flow measured before or immediately after portacaval anastomosis with prognosis failed (9).

After our initial publications, Reynolds (50) attempted and failed to correlate wedge hepatic venous pressure measured after portacaval shunt with prognosis. His data were drawn retrospectively from studies of hepatic blood flow after portacaval shunt (51, 52) and, therefore, excluded patients who died early or had poor liver function that precluded blood flow measurement. Furthermore, the additional variable of inferior vena caval pressure was introduced by subtracting inferior vena caval pressure from the wedged hepatic venous pressure. Subsequently, Burchell et al. (53) retrospectively correlated a limited increment in hepatic arterial flow occurring after portacaval shunt with early death and encephalopathy. Patients with less than a 200 ml/min increase in hepatic arterial flow after diversion of portal flow by portacaval shunt accounted for 90% of the patients with encephalopathy or early mortality. Unfortunately, their hemodynamic data did not include residual intrahepatic venous pressure. Nevertheless, their retrospective analysis of intraoperative data and correlation of hemodynamic response to long-term prognosis confirms the data presented here.

The prolonged survival and absence of hepatic encephalopathy in patients with residual intrahepatic pressures >25 cm suggests that this is the minimum pressure required to sustain hepatic function. The elevated portal pressure set point of 40 cm, maintained in these patients before portacaval shunt when they were at risk for variceal hemorrhage, is on the average 15 cm greater. This 15-cm excess of portal pressure appears to increase the risk of variceal hemorrhage without serving an essential role in maintaining hepatic perfusion.

There is general agreement that prior hemodynamic measurements have been of "inconsistent value in selecting the proper shunt to be done or in predicting its physiologic outcome" (54). The preoperative hemodynamic classification presented here allows a prospective quantitative stratification of cirrhotic patients that identifies the type B patients who require portal blood flow to maintain hepatic perfusion and the type A patients who tolerate the loss of portal flow produced by portacaval anastomosis relatively well.

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wrap up

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(57) [Summary]

An apparatus includes a pre-sample reservoir, a flow dividing mechanism and a flow metering mechanism. The flow diverting mechanism includes an inlet port couplable to the lumen-defining device to receive bodily fluid from the patient, a first outlet port fluidly couplable to the pre-sample reservoir, and a second outlet port fluidly couplable to the sample reservoir. and an exit port. The flow diverter mechanism defines a first fluid flow path and a second fluid flow path configured to place the first outlet port and the second outlet port in fluid communication with the inlet port, respectively. The flow metering mechanism meters flow of a predetermined volume of bodily fluid through the first fluid flow path to the pre-sample reservoir, meters flow of a second volume of bodily fluid through the second fluid flow path to the sample reservoir, It is configured to display a volume indicator associated with the volume and the second volume.

[Selection drawing] Fig. 2

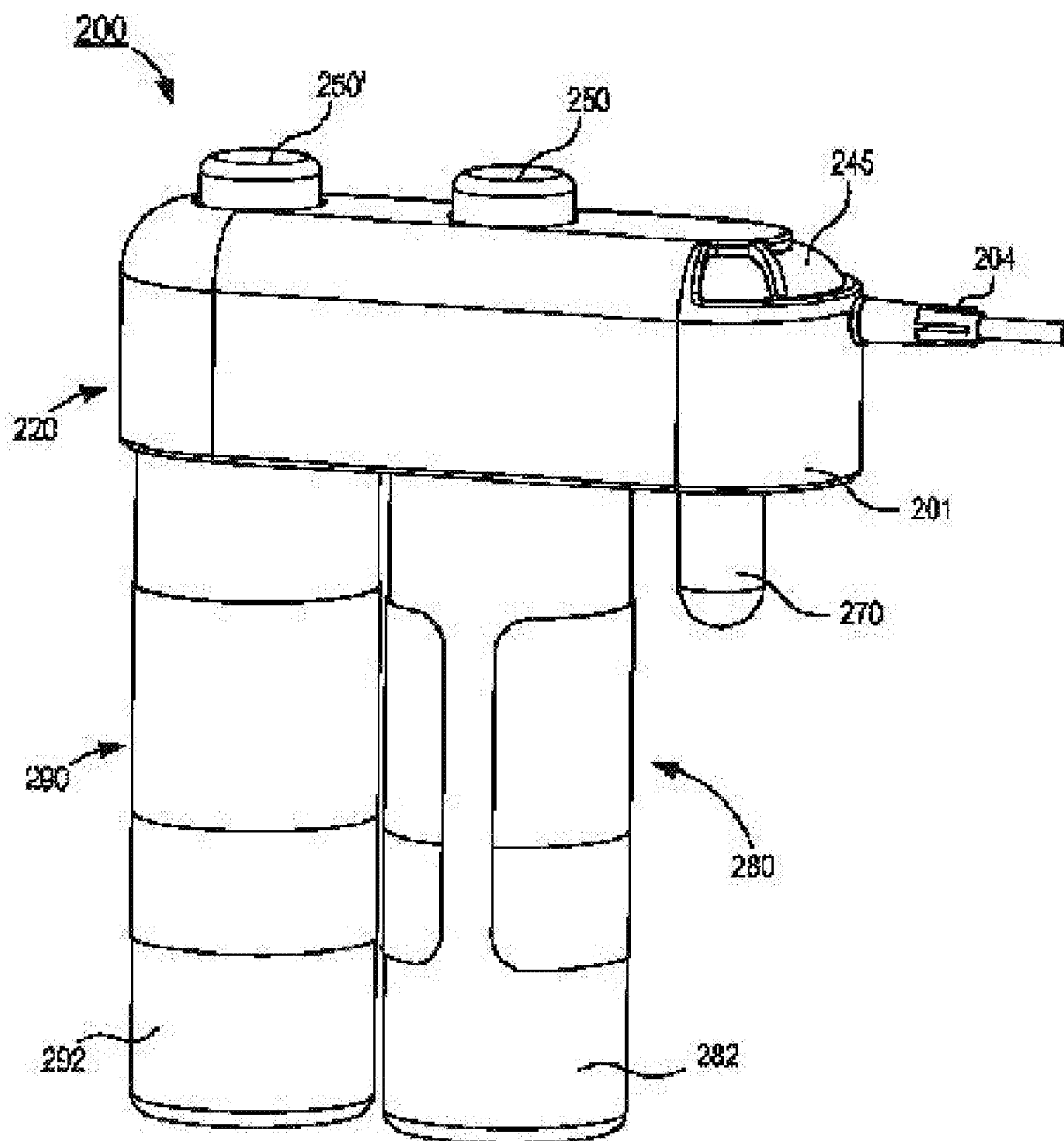


FIG. 2

The scope of the claims

open

1. An apparatus for obtaining a bodily fluid sample from a patient, comprising a pre-sample reservoir configured to receive a first volume of bodily fluid withdrawn from the

patient; an

inlet port; A flow diverting mechanism including an outlet port and a second outlet port, wherein the inlet port is configured to be coupled to a lumen defining device to receive bodily fluid from a patient, and the first outlet port is connected to the flow diverting mechanism. and the second outlet port is configured to fluidly couple the sample reservoir to the flow diverting mechanism, the flow diverting mechanism configured to fluidly couple the pre-sample reservoir to the first outlet port. a first fluid flow path configured to place a in fluid communication with the inlet port; and a second fluid flow path configured to place the second outlet port in fluid communication with the inlet port. and a flow metering mechanism in fluid communication with said first fluid flow path and said second fluid flow path, wherein a first volume of bodily fluid passes through said first fluid flow path. configured to meter flow into a pre-sample reservoir and meter flow of a second volume of bodily fluid through said second fluid flow path into said sample reservoir; and a flow metering mechanism configured to display an associated volume indicator.

2. A

first volume of said bodily fluid flows in said first fluid flow path during a first period of time, and a second volume of said bodily fluid flows in said second volume of fluid during a second period of time after said first period of time. 2. The device of claim 1, which flows in a two-fluid flow path.

3. The apparatus of claim

1, wherein the first volume of bodily fluid comprises contaminants present on the skin and the second volume of bodily fluid is substantially free of contaminants present on the skin. .

4.

The apparatus of claim 1, wherein said pre-sample reservoir is at least partially defined by a portion of said flow divider mechanism.

5.

The apparatus of claim 1, wherein said volume indicator is a visual indicator.

6.

The flow diverting mechanism includes a moveable member configured to move through the second outlet port to place the sample reservoir in fluid communication with the second fluid flow path. Item 1. The device according to item 1.

7.

The apparatus of claim 6, wherein said flow metering mechanism is at least partially disposed within a portion of said movable member.

8. The

flow diverting mechanism fluidly isolates the pre-sample reservoir and at least a portion of the first fluid flow path when the first volume of blood is disposed within the pre-sample reservoir. 2. The device of claim 1, wherein the device comprises:

9.

The flow diverter mechanism includes a third outlet port configured to fluidly couple a second sample reservoir to the flow diverter mechanism, the third outlet port being in fluid communication with the inlet port. 2. The device of claim 1, defining a third fluid flow path configured to be positioned in the .

10.

A flow controller defining a first lumen and a second lumen, the first configuration placing the first fluid flow path in fluid communication with the inlet port. and a second configuration in which the second lumen places the second fluid flow path in fluid communication with the inlet port, further comprising a flow controller configured to move between Apparatus as described.

11. The method of claim 10,

wherein the flow controller is configured to move from the first configuration to the second configuration after the first volume of bodily fluid is placed in the pre-sample reservoir. Apparatus as described.

12.

An apparatus for obtaining a bodily fluid sample from a patient, comprising a pre-sample reservoir configured to receive a first volume of bodily fluid withdrawn from the patient, an

inlet port, a first outlet port and a second outlet. A flow diverting mechanism comprising a port, wherein the inlet port is configured to be coupled to a lumen defining device to receive bodily fluid from a patient, and the first outlet port directs the pre-sample reservoir to the flow diverting mechanism. a flow diverting mechanism configured for fluid coupling, wherein the second outlet port is configured to fluidly couple a sample reservoir to the flow diverting mechanism; and a flow diverting mechanism disposed at least partially within the flow diverting mechanism

. a flow controller, wherein the flow controller defines at least a portion of a fluid flow path between the inlet port and the first outlet port in a first configuration; a flow controller configured to move between a second configuration defining at least a portion of a fluid flow path between the port;

a first configuration of a movable member movably coupled to the flow diverting mechanism, wherein the sample reservoir is fluidly isolated from a fluid flow path between the inlet port and the second outlet port; a reservoir configured to move through the second outlet port between a second configuration in fluid communication with the fluid flow path between the inlet port and the second outlet port, the sample reservoir a movable member configured to receive a second volume of bodily fluid withdrawn from the patient when the flow controller is in its second configuration and the movable member is in its second configuration.

13. The apparatus of claim 12,

wherein the first volume of bodily fluid comprises contaminants present on the skin and the second volume of bodily fluid is substantially free of contaminants present on the skin. .

14.

The apparatus of claim 12, wherein the flow controller rotates between its first configuration and its second configuration relative to the flow diverter mechanism.

15.

The apparatus of claim 12, wherein said flow controller moves in linear motion relative to said flow diverter mechanism.

16. The apparatus of claim 12,

wherein the flow controller is configured to fluidly isolate the pre-sample reservoir when in its second configuration.

17.

The apparatus of claim 12, wherein said movable member includes a piercing member configured to pierce a portion of said sample reservoir when in its second configuration.

18. The apparatus of claim 12

, wherein said movable member is coupled to a biasing member configured to at least temporarily maintain said movable member in its first configuration.

19.

The apparatus of claim 12, wherein said flow diverter mechanism includes a third outlet port configured to fluidly couple a second sample reservoir to said flow diverter mechanism.

20. The

movable member is a first movable member, the device

is a second movable member, and the second sample reservoir is defined between the inlet port and the third outlet port. a first configuration fluidly isolated from the fluid flow path; and the second sample.

a reservoir configured to move through the third outlet port between a second configuration in fluid communication with the fluid flow path defined between the inlet port and the third outlet port; A second movable member configured to receive a third volume of bodily fluid withdrawn from the patient when the flow controller is in its second configuration and the second movable member is in its second configuration. 20. The device of Claim 19, further comprising a member.

21.

An apparatus for obtaining a bodily fluid sample from a patient, the

flow diverting mechanism comprising a pre-sample reservoir configured to receive a first volume of bodily fluid withdrawn from the patient, a

housing and a distribution member. said housing defining a first opening and a second opening, said first opening being in fluid communication with said pre-sample reservoir, said distribution member being disposed at least partially within said housing; and defining a fluid flow path in fluid communication with the second opening, wherein the distribution member is configured to be in fluid communication with the flow path and physically and fluidly coupled to a sample reservoir. and an

inlet port configured to be coupled to a lumen-defining device to receive bodily fluid from the patient, the flow controller being rotatably coupled to the flow diversion mechanism, and a flow controller configured to move between a first configuration in which the inlet port is in fluid communication with the first opening and a second configuration in which the inlet port is in fluid communication with the second opening; Equipment to equip.

22. The apparatus of claim 21,

wherein the first volume of bodily fluid comprises contaminants present on the skin and the second volume of bodily fluid is substantially free of contaminants present on the skin. .

[Claim 23]

22. The apparatus of claim 21, wherein said pre-sample reservoir is at least partially defined by a portion of said distribution member.

24. The method of claim 21,

wherein the coupling portion includes a piercing member configured to pierce a portion of the sample reservoir to place the sample reservoir in fluid communication with the fluid flow path. Apparatus as described.

25. Said

piercing of said portion of said sample reservoir by said piercing member causes bodily fluids from said patient to enter said sample reservoir through said inlet port and said flow path when said flow controller is in its second configuration. 25. The device of claim 24, which initiates inward flow.

26.

The first volume of bodily fluid is a first predetermined volume of bodily fluid, the fluid flow path is configured to receive a second predetermined volume of bodily fluid, and the second predetermined volume of bodily fluid is a sample volume. 22. Apparatus according to claim 21, related to volume.

27.

The apparatus of claim 26, wherein said sample volume is between about 10 milliliters and about 50 milliliters.

28.

The apparatus of claim 26, wherein said sample volume is approximately 30 milliliters.

[Claim 29]

said flow diverter mechanism including a seal member, said seal member forming a substantially fluid tight seal with a surface of said flow controller and a surface of said housing when said flow controller is coupled to said flow diverter mechanism; Disposed between the housing and the flow controller, the seal member defines a first opening and a second opening, the first opening of the seal member substantially flush with the first opening of the housing. and wherein said second opening of said seal member is substantially coaxial with said second opening of said housing.

The apparatus described in .

30.

A method of obtaining a predetermined sample volume of bodily fluid from a patient using a flow metering transfer device, wherein the flow metering transfer device is selectively placed in fluid communication with a pre-sample reservoir and a sample reservoir. and a flow metering mechanism configured to meter the flow of bodily fluid from the patient to the pre-sample reservoir and to the sample reservoir; A method comprising: establishing fluid communication between the patient

and the port of the flow metering transfer device; establishing fluid communication between the

port and the pre-sample reservoir;

metering a flow of bodily fluid transferred to a pre-sample reservoir; and

via said flow metering mechanism of said flow metering transfer device, a pre-sample volume of bodily fluid disposed within said pre-sample reservoir to a predetermined pre-sample of bodily fluid.

fluidly isolating the pre-sample reservoir from the port to confine a pre-sample volume of the bodily fluid within the pre-sample reservoir

; metering

a flow of bodily fluid transferred from the patient to the sample reservoir; and

via the flow metering mechanism of the flow metering transfer device disposed within the sample reservoir. and C. verifying that the obtained sample volume of bodily fluid is a predetermined sample volume of bodily fluid.

[Claim 31]

The flow metering transfer device has a first configuration in which fluid communication is established between the patient and the pre-sample reservoir, and a second configuration in which fluid communication is established between the patient and the sample reservoir. 31. The method of claim 30, including a flow controller configured to move between.

32.

The method of claim 30, wherein said bodily fluid is blood.

33. The method of claim 32

, wherein the sample reservoir comprises at least one of an aerobe medium or an anaerobe medium.

34.

The method of claim 30, wherein said predetermined pre-sample volume is between about 1 milliliter and about 10 milliliters.

35.

The method of claim 30, wherein said predetermined sample volume is between about 20 milliliters and about 60 milliliters.

36.

The method of claim 30, wherein said predetermined sample volume is approximately 60 mil

liliters.

37. verified that

said sample reservoir is a first sample reservoir, said sample volume is a first sample volume, and said first sample volume within said first sample reservoir is said predetermined sample volume;

subsequently establishing fluid communication between the port and a second sample reservoir;

metering the flow of bodily fluid transferred from the patient to the second sample reservoir ; verifying, via a metering mechanism, that a second sample volume of bodily fluid disposed within the second sample reservoir is the predetermined sample volume of bodily fluid;

31. The method of claim 30, further comprising:

38. The method of claim 37, wherein

said first sample volume and said second sample volume collectively equal between about 20 milliliters and about 60 milliliters.

39.

After verifying that said second sample volume in said second sample reservoir is said predetermined sample volume, establishing fluid communication between said port and a third sample reservoir

; metering a flow of bodily fluid transferred from a patient to said third sample reservoir; and a third sample volume of bodily fluid

disposed within said third sample reservoir via said flow metering mechanism of said flow metering transfer device. 38. The method of claim 37, further comprising verifying that is the predetermined sample volume of bodily fluid.

40.

The method of claim 39, wherein said first sample volume, said second sample volume and said third sample volume collectively equal between about 30 milliliters and about 60 milliliters.

41.

The method of claim 39, wherein said first sample volume, said second sample volume and said third sample volume collectively equal approximately 60 milliliters.

detailed description

open

Description: CROSS-REFERENCE TO RELATED APPLICATIONS

[

1001] This application is entitled "Sterile Bodily-Fluid Collection Device and Method", filed De

c. 4, 2012. and Methods),” the disclosure of which is hereby incorporated by reference in its entirety. [1002] Embodiments described herein relate generally to the parenteral procurement of bodily fluid samples, and more particularly to microbial or other external sources of bodily fluids, such as those present on the skin. Devices and methods for obtaining bodily fluid samples parenterally with reduced contamination from contaminants. BACKGROUND ART [0003]

[1003] Health care practitioners routinely perform various types of microbiological tests on patients using parenterally obtained bodily fluids. In some cases, a patient sample (eg, bodily fluid) is tested for the presence of one or more potentially unwanted microorganisms, such as bacteria, fungi or yeast (eg, Candida). Microbial testing may involve culturing patient samples in one or more sterile containers containing media that promote microbial growth, real-time diagnostics and/or molecular PCR-based techniques. Generally, when such microorganisms are present in a patient sample, they will multiply in the culture medium over time. After a variable amount of time (eg, hours to days), automated continuous monitoring can detect organism growth. Such automated monitoring can detect carbon dioxide produced by the growth of organisms. The medium can then be tested for the presence of microorganisms. The presence of microorganisms in the medium indicates the presence of the same microorganisms in the patient sample, which in turn indicates the presence of the same microorganisms in the patient's bodily fluid from which the sample was obtained. Therefore, if it is determined that microorganisms are present in the culture medium, the patient is administered one or more antibiotics or other treatments specifically designed to treat or otherwise eliminate the undesirable microorganisms from the patient. may be prescribed.

[0004]

[1004] However, patient samples can be contaminated during acquisition and/or otherwise prone to false positive results. One process by which contamination of patient samples can occur is microbes from the body surface (e.g., microbes present on the skin) that are removed during needle insertion into the patient's body and subsequently transferred to the culture medium with the patient sample.) by transfer. Surface microbes and/or other unwanted external microbes may be removed either directly or through removed tissue debris, hair follicles, sweat glands and other skin appendage structures. Another possible source of contamination comes from the person who draws the patient sample. For example, doctors, phlebotomists, nurses, etc. may transfer contaminants from their bodies (eg, fingers, arms, etc.) to patient samples and/or to equipment containing patient samples. To further elaborate, the instruments and/or devices used during the patient sample acquisition process (e.g., patient to needle, needle/tu

be to sample container, etc.) can each introduce potential points of contamination. It often contains multiple fluid interfaces. Use of such instruments and/or devices typically involves manual intervention to connect and/or fluidly couple various interfaces. Because these interfaces are pre-assembled and non-sterilized as a single, fluidly coupled system, the user (e.g., physician, phlebotomist, etc.) and/or other sources of contamination (e.g., ambient air, hospital room contaminants on table and counter surfaces, microorganisms transferred from linens or clothing, etc.) may be introduced into the patient sample. In some cases, these contaminants can grow in the culture medium and ultimately result in a positive microbial test result, thereby falsely indicating the presence of such organisms in the body.

[0005]

[1005] In some cases, false positive and/or false negative results may result from a given volume of patient sample. For example, by overfilling volume-sensitive blood culture bottles, as noted in the instructions for use and/or warning labels from the manufacturers of such culture bottles and associated automated continuous monitoring microbial detection systems, can lead to false positive results. On the other hand, as another example, insufficient patient sample volume in culture medium can lead to false negative results. As an example, in a study conducted by the Mayo Clinic entitled "Optimized Pathogen Detection with 30- Compared to 20-Milliliter Blood Culture Draws", published in the December 2011 issue of the Journal of Clinical Microbiology, 20 milliliters (mL) of A patient sample volume allows detection of the presence of approximately 80% of bacteremia present in a patient sample, a patient sample volume of 40 mL allows detection of approximately 88% of bacteremia, and a patient sample volume of 60 mL allows detection of approximately 88% of bacteremia. Approximately 99% of bacteremia can be detected by sample volume.

[0006]

[1006] Such inaccurate results as a result of contamination, insufficient patient sample volume, etc. are a problem when trying to diagnose or treat a suspected disease or condition. For example, a false negative result from a microbiological test can lead to misdiagnosis and/or delay in treatment of a patient's illness, which in some cases can lead to death of the patient. Conversely, a false-positive result from a microbiological test can lead to the patient receiving one or more antimicrobial therapies unnecessarily, thereby causing serious side effects in the patient, including death, for example. Together, this can result in unnecessary burden and expense to the health care system due to prolonged hospitalization of the patient and/or other complications associated with the wrong treatment. In addition, the use of diagnostic imaging equipment due to these false positive results also increases the cost and unnecessary exposure of high doses of radiation associated with various imaging procedures (e.g., CT scans) to long-term patient health. It is also problematic from a patient safety perspective, as it has many known adverse effects.

[1007]

] Thus, for example, reducing microbial contamination in bodily fluid test samples by minimizi

ng exposure to non-sterile conditions and/or other external sources of contamination around patient samples and/or fluid interfaces. There is a need for a sterile "one-piece" bodily fluid collection device and method. Further, such fluid collection devices provide visual, calculated, or must include means for accurately weighing, measuring, and/or otherwise assessing body fluids transferred from the patient to the sample reservoir or culture medium, which can be otherwise communicated. It is

SUMMARY OF THE INVENTION [

1008

] The present invention provides a non-toxic method for treating a body fluid sample by reducing contamination from microorganisms external to the body fluid source, such as microorganisms present on the skin and/or other undesirable external contaminants. An orally acquired device is described. In some embodiments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reservoir, a flow diversion mechanism and a flow metering mechanism. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverting mechanism includes an inlet port, a first outlet port and a second outlet port and defines a first fluid flow path and a second fluid flow path. An inlet port can be coupled to the lumen-defining device to receive bodily fluid from the patient. A first outlet port and a second outlet port are configured to fluidly couple the pre-sample reservoir and the sample reservoir, respectively, to the flow diverting mechanism. The first fluid flow path is configured to place the first outlet port in fluid communication with the inlet port and the second fluid flow path is configured to place the second outlet port in fluid communication with the inlet port. A flow metering mechanism is in fluid communication with the first fluid flow path and the second fluid flow path. A flow metering mechanism meters a flow of a first volume of bodily fluid through the first fluid flow path into the pre-sample reservoir and a second volume of bodily fluid through the second fluid flow path into the sample reservoir. The flow metering mechanism is configured to display volume indicators associated with the first volume and the second volume.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009]

FIG. 1 is a schematic diagram of a bodily fluid collection device according to an embodiment;

2 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

3 is an exploded perspective view of the bodily fluid collection device of FIG. 2; FIG.

4 is a side cross-sectional view taken along line X₁-X₁ of FIG. 3 of a housing included in the bodily fluid collection device of FIG. 2;

5 is a cross-sectional view taken along line X₂-X₂ of FIG. 3 of a movable member included in the bodily fluid collection device of FIG. 2;

6 is a cross-sectional view taken along line X₃-X₃ of FIG. 3 of the flow controller included in the bodily fluid collection device of FIG. 2;

7 is a cross-sectional view taken along line X₄-X₄ of FIG. 3 of the flow controller included in the bodily fluid

d collection device of FIG. 2;

8 is a top view of the bodily fluid collection device of FIG. 2 in a first configuration; FIG.

9 is a cross-sectional view taken along line X 5 -X 5 of FIG. 8 of the body fluid collection device of FIG. 2 in the first configuration;

10 is a top view of the bodily fluid collection device of FIG. 2 in a second configuration; FIG.

11 is line X 6 -X 6 of FIG. 10 of the body fluid collection device of FIG. 2 in a second configuration; 1 is a cross-sectional view taken along .

12 is a cross-sectional view taken along line X 6 -X 6 of FIG. 10 of the bodily fluid collection device of FIG. 2 in a third configuration;

13 is a cross-sectional view taken along line X 6 -X 6 of FIG. 10 of the bodily fluid collection device of FIG. 2 in a fourth configuration;

14 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

15 is a side cross-sectional view taken along line X 7 -X 7 of the bodily fluid collection device of FIG. 14; FIG.

16 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

17 is an exploded perspective view of a flow diverting mechanism included in the body fluid collection device of FIG. 16; FIG.

18 along line X 8 -X 8 of FIG. 16 of a distribution member included in the bodily fluid collection device of FIG. 16; is a side cross-sectional view taken out.

19 is a top view of the bodily fluid collection device of FIG. 16 in a first configuration; FIG.

20 is a cross-sectional view taken along line X 9 -X 9 of FIG. 19 of the partial bodily fluid collection device of FIG. 16 in the first configuration;

21 is a top view of the bodily fluid collection device of FIG. 16 in a second configuration; FIG.

22 is a cross-sectional view taken along line X 10 -X 10 of FIG. 21 of the bodily fluid collection device of FIG. 16 in a second configuration;

FIG. 23 is a perspective view of a bodily fluid collection device according to an embodiment; Figure 24 is a cross-sectional view taken along line X 11 - X 11

of a portion of the bodily fluid collection device of Figure 23 in a first configuration ; 25 is a cross-sectional view taken along line X 11 -X 11 of the bodily fluid collection device of FIG. 23, in a second configuration; FIG.

FIG. 26 is a perspective view of a bodily fluid collection device according to an embodiment; 27 is an exploded perspective view of a flow diverting mechanism included in the bodily fluid collection device of FIG. 26; FIG.

28 is a cross-sectional view taken along line X 13 - X 13 of FIG. 27 of a distribution member included in the bodily fluid collection device of FIG. 27;

29 is a cross-sectional view taken along line X 14 -X 14 of FIG. 27 of a coupling member included in the bodily fluid collection device of FIG. 26;

30 is a cross-sectional view taken along line X 15 -X 15 of FIG. 27 of the dial included in the bodily fluid collection device of FIG. 26;

31 is a cross-sectional view taken along line X 16 -X 16 of FIG. 27 of the valve included in the bodily fluid collection device of FIG. 26;

32 is a cross-sectional view taken along line X 12 -X 12 of the bodily fluid collection device of FIG. 26 in the first configuration; FIG.

33 is a cross-sectional view taken along line X 12 -X 12 of the bodily fluid collection device of FIG. 26 in a second configuration; FIG.

34 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

35 is an exploded perspective view of a flow diverting mechanism included in the bodily fluid collection device of FIG. 34; FIG.

36 is a cross-sectional view taken along line X 17 -X 17 of a distribution member included in the flow diverting mechanism of FIG. 35; FIG.

37 is a top view of a portion of the bodily fluid collection device of FIG. 34 in a first configuration; FIG.

38 is a cross-sectional view taken along line X 18 -X 18 of the partial bodily fluid collection device of FIG. 37 in the first configuration; FIG.

39 is a top view of the bodily fluid collection device of FIG. 33 in a second configuration; FIG.

Figure 40 is a cross-sectional view taken along line X 19 - X 19

of Figure 39 of the body fluid collection device of Figure 33 in a second configuration ; 41 is a perspective view of a bodily fluid collection device in a first configuration according to embodiments; FIG. 42 is an exploded perspective view of a portion of the bodily fluid collection device of FIG. 41; FIG. 43 is a cross-sectional view taken along line X 20 -X 20 of the bodily fluid collection device of FIG. 41 in the first configuration; FIG. Figure 44 is a cross-sectional view taken along line X 20 -

X 20 of the bodily fluid collection device of Figure 41 in a second configuration ; Figure 45 is a cross-sectional view taken along line X 20 - X 20 of the body fluid collection device of Figure 41 in a third configuration ; Figure 46 is a perspective view of a bodily fluid collection device in a first configuration according to an embodiment; 47 is an exploded perspective view of a portion of the bodily fluid collection device of FIG. 45; FIG. 48 shows the distribution member included in the bodily fluid collection device of FIG. 46, line X of FIG. 47. FIG.

Figure 21 is a side sectional view taken along line X 21 - X 21 ;

49 is a side sectional view taken along line X 22 -X 22 of FIG. 47 of a movable member included in the bodily fluid collection device of FIG. 46, line X of FIG. 47. FIG.

y fluid collection device of FIG. 46;

50 is a top view of the bodily fluid collection device of FIG. 46 in a first configuration; FIG. Figure 51 is a cross-sectional view taken along line x23 - x23

of Figure 50 of the partial bodily fluid collection device of Figure 46 in the first configuration ;

52 is a top view of the bodily fluid collection device of FIG. 46 in a second configuration; FIG. Figure 53 is a cross-sectional view taken along line x24 - x24 of Figure 52 of the body fluid collection device of Figure 46 in a second configuration ; FIG. 54 is a perspective view of a bodily fluid collection device according to an embodiment; 55 is a top view of the bodily fluid collection device of FIG. 54; FIG. FIG. 56 is a flowchart illustrating a method of obtaining bodily fluid samples with reduced contamination using a collection device according to embodiments; DETAILED DESCRIPTION OF THE INVENTION [0010]

[1063] Described herein are devices for obtaining bodily fluid samples parenterally with reduced contamination from microorganisms external to the bodily fluid source, such as microorganisms present on the skin and/or other undesirable external contaminants. It is In some embodiments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reservoir, a flow diversion mechanism and a flow metering mechanism. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverting mechanism includes an inlet port, a first outlet port and a second outlet port and defines a first fluid flow path and a second fluid flow path. An inlet port can be coupled to the lumen-defining device to receive bodily fluid from the patient. A first outlet port and a second outlet port are configured to fluidly couple the pre-sample reservoir and the sample reservoir, respectively, to the flow diverting mechanism. The first fluid flow path is configured to place the first outlet port in fluid communication with the inlet port and the second fluid flow path is configured to place the second outlet port in fluid communication with the inlet port. is configured to A flow metering mechanism is in fluid communication with the first fluid flow path and the second fluid flow path. A flow metering mechanism meters a flow of a first volume of bodily fluid through the first fluid flow path into the pre-sample reservoir and a second volume of bodily fluid through the second fluid flow path into the sample reservoir. is configured to The flow metering mechanism is configured to display volume indicators associated with the first volume and the second volume.

[0011]

[1064] In some embodiments, an apparatus for obtaining a bodily fluid sample from a patient

includes a pre-sample reservoir, a flow diversion mechanism, a flow controller, and a movable member. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverting mechanism includes an inlet port, a first outlet port and a second outlet port. The inlet port is couplable to the lumen-defining device to receive bodily fluid from the patient. A first outlet port fluidly couples the pre-sample reservoir to the flow diverter mechanism and a second outlet port fluidly couples the sample reservoir to the flow diverter mechanism. A flow controller is disposed at least partially within the flow diverting mechanism and comprises a first configuration in which the flow controller defines at least a portion of a fluid flow path between the inlet port and the first outlet port; is movable between a second configuration that defines at least a portion of the fluid flow path between the inlet port and the second outlet port. The movable member is movably coupled to the flow diverting mechanism in a first configuration in which the sample reservoir is fluidly isolated from the fluid flow path between the inlet port and the second outlet port; It is movable through the second outlet port to and from a second configuration in fluid communication with the fluid flow path between the outlet port. The sample reservoir is configured to receive a second volume of bodily fluid withdrawn from the patient when the flow controller is in its second configuration and the movable member is in its second configuration.

[1065

] In some embodiments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reservoir, a flow diversion mechanism and a flow controller. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverting mechanism includes a housing and a distribution member. The housing has a first opening in fluid communication with the pre-sample reservoir.

defines a portion and a second opening. A distribution member defines a fluid passageway disposed at least partially within the housing and in fluid communication with the second opening. The distribution member includes a coupling portion configured to be in fluid communication with the flow path and physically and fluidly coupled to the sample reservoir. The flow controller includes an inlet port configured to be coupled to the lumen defining device to receive bodily fluid from the patient. A flow controller is rotatably coupled to the flow diverter mechanism and is movable between a first configuration in which the inlet port is in fluid communication with the first opening and a second configuration in which the inlet port is in fluid communication with the second opening. is.

[0013]

[1066] In some embodiments, a flow diverting mechanism including an inlet port configured to be selectively placed in fluid communication with the pre-sample reservoir and the sample reservoir, and bodily fluid from the patient to the pre-sample reservoir. and a flow metering mechanism configured to meter flow into a sample reservoir comprising the steps of: establishing fluid communication between a patient and an inlet port of the flow metering transfer device; including. Fluid communication is then established between the port and the pre-sample re

servoir. A flow of bodily fluid transferred from the patient to the pre-sample reservoir is metered. The method includes verifying, via a flow metering mechanism of the flow metering transfer device, that a pre-sample volume of bodily fluid disposed within a pre-sample reservoir is a first pre-sample volume of bodily fluid. With the pre-sample volume disposed within the pre-sample reservoir, the pre-sample reservoir is fluidly isolated from the port to seal the pre-sample volume of bodily fluid within the pre-sample reservoir. With the pre-sample reservoir fluidly isolated, the method includes establishing fluid communication between the port and the sample reservoir. A flow of bodily fluid transferred from the patient to the sample reservoir is metered. The method includes verifying, via the flow metering mechanism of the flow metering transfer device, that the sample volume of bodily fluid disposed within the sample reservoir is a first sample volume of bodily fluid.

[0014]

[1067] In some embodiments, an apparatus includes a flow diversion mechanism and a flow controller. The flow diverting mechanism can define an inlet port, a first outlet port, a second outlet port and a third outlet port. a first outlet port fluidly coupled to the pre-sample reservoir, a second outlet port fluidly coupled to the first sample reservoir, a third outlet port fluidly coupled to the second sample reservoir; etc. All of the fluid reservoirs can be fluidly isolated from each other. The flow controller includes various fluid channels, which can allow fluid movement in specified directions and can be configured to be operatively coupled to the flow diverting mechanism. In use, the flow controller can allow bodily fluid flow into the pre-sample reservoir when the flow diverter mechanism is in the first configuration. The flow diverter mechanism can be moved to a second configuration, in which the flow controller can allow bodily fluid flow to enter the first sample reservoir. In addition, the flow diverter mechanism can then be moved to the third configuration so that the flow controller can allow bodily fluid flow to enter the second sample reservoir.

[0015]

[1068] In some embodiments, the bodily fluid collection device allows a second volume of bodily fluid to flow into the first sample reservoir and/or a third volume of bodily fluid to flow into the second sample reservoir. previously, it can be configured to selectively divert a first predetermined volume of bodily fluid to a pre-sample reservoir. In this way, the second and/or third volume of bodily fluid can be used for diagnosis or other testing, while the presence of microorganisms from the body surface or other microbial sources external to the patient from whom the sample is obtained. A first volume of bodily fluid that may contain is isolated. In some embodiments, the bodily fluid collection device can include additional sample reservoirs (eg, 3, 4, 5, 6 or more) depending on the analysis and/or testing protocols to be performed.

[1069]

] In some embodiments, the bodily fluid collection device is configured such that an appropriate volume of bodily fluid is collected from the patient and/or transferred to a predetermined pre-sample reservoir and/or sample reservoir.

Flow metering can be included to ensure that the A bodily fluid collection device can be configured to automatically divert and/or control fluid flow after a metered volume of bodily fluid has been collected. For example, once a first metric pre-sample volume has been collected, the flow diverter mechanism can be configured to divert body fluid flow to a first sample reservoir, and then divert the flow after the first metric sample volume has been collected. The mechanism can be configured to divert body fluid flow to a second sample reservoir, and so on. In some embodiments, the bodily fluid collection device includes a metered volume display, such as a liquid crystal display (LCD), to provide a visual indication of how much bodily fluid has been collected in each predetermined individual sample reservoir. can be provided to the user. In some embodiments, multiple displays can be provided to allow for customized pre-sample and/or sample volume collection.

[1070]

] As used in this specification and the appended claims, the singular forms "a, an" and "the" refer to the plural unless the context clearly dictates otherwise. including referents of Thus, for example, the term "(a) member" is intended to mean a single member or combination of members, and "(a) material" is intended to mean one or more materials or combinations thereof. intended to mean

[1071]

] As used herein, "bodily fluid" includes, but is not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, etc., or any combination thereof. , can include any fluid obtained from the patient's body.

[0019]

[1072] As used herein, the terms "first predetermined amount," "first amount," and "first volume" are configured to be received or contained by a first reservoir or a pre-sample reservoir. s tate the amount of body fluid The terms "first amount" and "first volume" do not explicitly state a predetermined amount, but unless explicitly stated otherwise, the first amount may be a first predetermined amount. should be understood.

[1073]

] As used herein, the terms "second volume" and "second volume" describe the amount of bodily fluid configured to be received or contained by a second reservoir or sample reservoir. . T he second amount can be any suitable amount of bodily fluid and it need not be a predetermined amount. Conversely, when so explicitly stated, the second volume received and contained by the second reservoir or sample reservoir may be the second predetermined volume.

[1074]

] As used herein, the term "set" can refer to a single feature comprising multiple features or multiple parts. For example, when referring to a set of walls, the set of walls can be considered a single wall with separate portions, or the set of walls can be considered multiple walls. Similarly, an integrally constructed article can include a set of walls. Such a set of walls can include, for example, multiple portions that are discontinuous from each other. A set of walls can

also be made from multiple articles that are manufactured separately and later joined together (eg, via welding, adhesives, or any suitable method).

[0022]

[1075] As used herein, the terms "proximal" and "distal" refer to directions toward and away from, respectively, a user placing the device in contact with a patient. Thus, for example, the end of the device that first contacts the patient's body would be the distal end, and the opposite end of the device (eg, the end of the device being operated by the user) would be the proximal end of the device. becomes.

[1076]

] As used herein, the terms "about," "approximately," and "substantially," when used in connection with numerical values, are nominally indicative of the value so defined. is intended to mean that the value In other words, the terms about, approximately and substantially when used in connection with numerical values generally include the indicated value plus or minus a given tolerance.

nothing. For example, in some cases a suitable tolerance may be $\pm 10\%$ of the indicated value, thus about 0.5 includes 0.45 and 0.55; 11, and about 1000 includes 900-1100. In other cases, a suitable tolerance may be plus or minus an acceptable percentage of the last significant digits of the indicated value. For example, a suitable tolerance might be $\pm 10\%$ of the last significant digit, so approximately 10.1 includes 10.09 and 10.11, and approximately 25 includes 24.5 and 25.5. including. Such variations may result from manufacturing tolerances or other practical considerations (eg, tolerances associated with measurement equipment, acceptable human error, etc.).

[0024]

[1077] When describing the relationship between a given volume of bodily fluid and a collected volume of bodily fluid, it should be understood that these values include suitable tolerances such as those set forth above. For example, when stating that a collected volume of bodily fluid is substantially equal to a predetermined volume of bodily fluid, the collected volume and the predetermined volume are nominally equal within suitable tolerances. In some cases, tolerance can be determined by the intended use of the collected volume of bodily fluid. For example, in some cases, blood culture assays are performed when the collected volume of blood is within 1.0% to 5.0% of the manufacturer's (or evidence-based best practice) recommended volume. It can be about 99% accurate. As an example, the manufacturer's recommended volume for the body fluid assay is 10 milliliters (mL) (ie total volume is 40 ml to 60 ml) $\pm 5\%$. Thus, a collection volume of 10.5 mL provides results with greater than about 99% confidence, and a collection volume of 11 mL provides results with less than about 99% confidence. In other cases suitable tolerances are 0.1%, 0.5%, 1.0%, 2.0%, 3.0%, 4.0%, 5.0%, 6.0% , 7.0%, 8.0%, 9.0%, 10.0% or any fractional value therebetween. In still other cases, the tolerance can exceed 10.0%. Accordingly, any of the embodiments described herein may be any suitable flow rate configured to meter the flow rate of body fluid and/or otherwise measure the volume o

f body fluid within suitable tolerances. It can include and/or be used with measurement mechanisms and/or devices. Additionally, flow metering mechanisms and/or devices can be arranged to minimize or eliminate tolerance build-up that can result from a combination of inaccurate measurements, human error, and the like.

[0025]

[1078] FIG. 1 is a schematic illustration of a portion of a bodily fluid collection device 100, according to an embodiment. In general, the bodily fluid collection device 100 (also referred to herein as a "fluid collection device" or "collection device") allows for the withdrawal of bodily fluid from a patient, wherein a first portion or a first portion of the withdrawn bodily fluid is so that a quantity separates from a second portion or volume and/or a third portion or volume of the withdrawn bodily fluid used as a biological sample, such as to be tested for medical diagnostic and/or therapeutic purposes configured to be shunted. In other words, as described in more detail herein, the collection device 100 can transfer a first predetermined volume of bodily fluid to a pre-sample collection reservoir, second and third volumes of bodily fluid (or, in some implementations, 4th, 5th, etc.) to one or more sample collection reservoirs (eg, sample reservoirs) fluidly isolated from the pre-sample reservoir.

[1079

] The collection device 100 includes a flow diverter mechanism 120 , a flow controller 140 , a pre-sample reservoir 170 , a first sample reservoir 180 , and a second sample reservoir 190 that is different from the first sample reservoir 180 . The flow diverting mechanism 120 includes an inlet port 121 and at least two outlet ports, such as a first outlet port 125 and a second outlet port 126, as shown in FIG. In some embodiments, flow diverter 120 can include a set of exit ports equal to the total number of pre-sample and sample reservoirs. For example, if collection device 100 has one pre-sample and four sample reservoirs, flow diverter 120 may include five outlet ports. In some embodiments, a flow divider

Mechanism 120 can be operably coupled to an actuator (not shown in FIG. 1) that can facilitate movement of flow diverter mechanism 120 between configurations. Inlet port 121 is configured to be fluidly coupled to a medical device that defines a pathway X for withdrawing and/or transporting bodily fluid from a patient to collection device 100 . For example, entry port 121 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). As such, the flow diverting mechanism 120 can receive bodily fluid from the patient via a needle or any other lumen defining device.

[1080

] The first outlet port 125 of the flow diverter mechanism 120 may be fluidly coupled to the pre-sample reservoir 170 . In some embodiments, pre-sample reservoir 170 is integrally formed with first outlet port 125 and/or part of flow diverter mechanism 120 . In other embodiments, the pre-sample reservoir 170 is attached via adhesives, resistance fits, mechanical fasteners, any number of mating recesses, threaded connections and/or any other suitable connection or combination thereof. , can be mechanically and/or fluidly coupled to the flow diverting mechanism

hanism 120 . Similarly, pre-sample reservoir 170 can be physically (e.g., mechanically) coupled to flow diverting mechanism 120 such that the volume defined by pre-sample reservoir 170 is the flow diverting mechanism. 120 in fluid communication with a first outlet port 125 . In still other embodiments, the pre-sample reservoir 170 is operably coupled to the first outlet port 125 of the flow diverting mechanism 120 via an intervening structure (not shown in FIG. 1) such as flexible sterile tubing. can be done. More particularly, the intervening structure can define a lumen configured to place the pre-sample reservoir 170 in fluid communication with the first outlet port 125 .

[1081

] The pre-sample reservoir 170 is configured to receive and contain a first predetermined volume of bodily fluid. In some embodiments, the pre-sample reservoir 170 stores a first volume of bodily fluid (which may be the same as or different from the first volume of bodily fluid), a second volume of bodily fluid that is subsequently withdrawn from the patient, and a second volume of bodily fluid. /or configured to receive in a fluidly isolated manner from the third volume. Pre-sample reservoir 170 is described in "Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination", which is incorporated herein by reference in its entirety. It can be any suitable reservoir for containing bodily fluids, such as the pre-sample reservoir described in detail in US Pat. No. 8,197,420.

[0029]

[1082] In some embodiments, the second outlet port 126 of the flow diverting mechanism 120 is fluidly coupled to a lumen defining device that can be coupled to the first sample reservoir 180 and the second sample reservoir 190. is configured to Optionally, in other embodiments, the second outlet port 126 of the flow diverter 120 can be coupled to the first sample reservoir 180, and the flow diverter 120 was coupled to the second sample reservoir 190 (Fig. (not shown) can have a third exit port. In some embodiments, the first sample reservoir 180 can be integrally formed with the second outlet port 126 and/or part of the flow diverting mechanism 120 . In other embodiments, the first sample reservoir 180 is mechanically coupled or operably coupled to the second outlet port 126 via intervening structures such as those described above with respect to the pre-sample reservoir 170. can be combined. First sample reservoir 180 is configured to receive and contain a second volume of bodily fluid. For example, the second volume of bodily fluid can be the amount withdrawn from the patient following the withdrawal of the first pre-sample volume. In some embodiments, first sample reservoir 180 is configured to contain a second volume of bodily fluid such that the second volume is fluidly isolated from the first volume of pre-sample bodily fluid.

[1083

] First sample reservoir 180 and second sample reservoir 190 may be, for example, It can be any suitable sterile reservoir for containing bodily fluids, including a sample reservoir as described in the incorporated '420 patent. In some embodiments, the second volume can be any suitable volume of bodily fluid and it need not be a predetermined volume. In other e

embodiments, the transfer of bodily fluid to the first sample reservoir 180 and/or the second sample reservoir 190 can be metered or the like such that the second volume is a second predetermined volume.

[1084]

] The second sample reservoir 190 can be any suitable sample reservoir. In some embodiments, the second sample reservoir 190 can be substantially similar to the first sample reservoir 180 described above. A second sample reservoir 190 can be fluidly coupled to the second outlet port 126 as described above. The fluidic coupling of the second outlet port 126 to the second sample reservoir 190 can be substantially similar to the fluidic coupling of the second outlet port 126 to the first sample reservoir 180, as detailed above. Accordingly, such portions are not described in further detail herein and should be considered substantially similar unless explicitly described to the contrary. Additionally, additional outlet ports and sample reservoirs of flow diverter 120 (not shown in FIG. 1) may be substantially similar to second outlet port 126 and first sample reservoir 180 .

[0032]

[1085] In some embodiments, the pre-sample reservoir 170, the first sample reservoir 180 and the second sample reservoir 190 can be similarly coupled to (or formed with) the flow diverting mechanism 120. FIG. In other embodiments, pre-sample reservoir 170 , first sample reservoir 180 and second sample reservoir 190 need not be similarly coupled to flow diverting mechanism 120 . For example, in some embodiments, the pre-sample reservoir 170 can be integrally formed with the flow diverting mechanism 120 (eg, the first outlet port 124) and the first sample reservoir 180 and/or the second sample reservoir 190. can be operably coupled to flow diverting mechanism 120 (eg, second outlet port 126) via an intervening structure such as flexible sterile tubing or any combination thereof.

[0033]

[1086] In some embodiments, the collection device 100 includes an actuator (not shown in FIG. 1) and a first fluid flow path 142, a second fluid flow path 144 and optionally (not shown in FIG. 1). and a flow controller 140 that defines additional fluid flow paths. In some embodiments, an actuator may be included in or otherwise operably coupled to the flow diverting mechanism 120 . As such, actuators can be configured to control fluid movement (eg, between different configurations) within flow controller 140 . For example, the actuator may be movable between a first position corresponding to a first configuration of flow controller 140, a second position different from the first position corresponding to a second configuration of flow controller 140, and so on. In some embodiments, the actuator can be configured to move in one direction. For example, an actuator can be moved from its first position to its second position, but cannot be moved from its second position to its first position. Similarly, the actuator can be moved from its second position to its third position, but cannot be moved from its third position back to its second position. In this manner, flow controller 140 is prevented from moving to its second or third configuration before its first configuration, thus directing a first volume of bodily

y fluid to pre-sample reservoir 170 for medical diagnosis. and/or sample reservoirs 180 and/or 190 designed to contain a second and/or third volume of withdrawn fluid used as a biological sample, such as for testing for therapeutic purposes. It is necessary not to be directed to [0034]

[1087] The flow controller 140 has a first fluid flow path 142 fluidly coupling the inlet port 121 to the first outlet port 125 when in the first configuration and a second fluid flow path 142 when in the second configuration. 144 is configured to fluidly couple inlet port 121 to second outlet port 126. In some embodiments, actuators such as those described above are incorporated into the flow controller 140.

140 can be configured to move in translation between the first and second configurations, and optionally between the third or fourth configuration. For example, in some embodiments, flow controller 140 may be in a first configuration when in a distal position relative to collection device 100. In such embodiments, the actuator can be actuated to move flow controller 140 proximally to a proximal position relative to collection device 100, thereby placing flow controller 140 in the second configuration. In other embodiments, the actuator can be actuated to move the flow controller 140 between the first and second configurations, or optionally between the third or fourth configurations, in a rotary motion.

[1088]

] Thus, when the flow controller 140 is in the first configuration, the second outlet port 126 (and optionally an additional outlet port coupled to the sample reservoir) is fluidly routed from the inlet port 121. Similarly, first outlet port 125 is fluidly isolated from inlet port 121 when flow controller 140 is in the second configuration. Optionally, first outlet port 125 and second outlet port 126 are fluidly isolated from inlet port 121 when flow controller 140 is in a third configuration (not shown in FIG. 1). Thus, the flow controller 140 can direct or divert a first volume of bodily fluid through the first outlet port 125 to the pre-sample fluid reservoir 170 when in the first configuration and in the second configuration. A second volume of bodily fluid can then be directed or diverted to the first sample fluid reservoir 180 via the second outlet port 126.

[0036]

[1089] In some embodiments, at least a portion of the actuator can be operably coupled to the pre-sample fluid reservoir 170. As shown in FIG. In this manner, the actuator (or at least a portion of the actuator) causes or otherwise facilitates the creation of a vacuum within the "pre-sample" fluid reservoir 170, thereby causing the flow diverter mechanism 120 to assume its first configuration. At some point, it can be configured to initiate flow through the bodily fluid collection device 100 and into the pre-sample fluid reservoir 170. Actuators may be any suitable mechanism for driving bodily fluid flow into collection device 100, such as, for example, rotating discs, plungers, slides, dials, buttons, handles, levers, and/or any other suitable mechanism or combination thereof. Examples of suitable actuators are described in more detail herein with reference to specific embodiments.

[0037]

[1090] In some embodiments, the flow diverter mechanism 120 is configured such that the flow of the second volume of bodily fluid is transported through the flow diverter mechanism 120 to the first sample fluid reservoir 180 and/or to the second sample fluid reservoir 190. can be configured such that a first volume of bodily fluid needs to be transported to the pre-sample fluid reservoir 170 before allowing for . In this manner, the flow diverting mechanism 120 can be used by a healthcare professional to collect a first predetermined amount of bodily fluid (e. g., a pre-sample) before collecting a second amount and/or a third amount of bodily fluid (e. g., a sample). can be characterized as requiring compliance with respect to Similarly, the flow diverter mechanism 120 can be used by a medical practitioner to transfer a second volume of bodily fluid, i.e., a sample, into a first sample fluid reservoir without first diverting the first volume of bodily fluid, i.e., a pre-sample, into a pre-sample reservoir 170. It can be configured to prevent collection within 180 . In this manner, a healthcare professional may (intentionally or not) add a first volume of bodily fluid that is more likely to contain surface microbes and/or other undesirable external contaminants into the bodily fluid sample used for analysis. (either unintentionally or unintentionally). In other embodiments, the fluid collection device 100 need not include mandatory compliance features or components.

[1091

] In some embodiments, the flow diverter mechanism 120 can have a fourth configuration (not shown in FIG. 1) that is different from the first, second, and third configurations. When in the fourth configuration, the flow diverter mechanism 120 can simultaneously fluidly isolate the inlet port 121 from the first outlet port 125, the second outlet port 126 and, optionally, the third outlet port. Therefore, the shunting

When mechanism 120 is in its fourth configuration, body fluid is prevented from flowing from inlet port 121 to pre-sample fluid reservoir 170, first sample fluid reservoir 180 and second sample fluid reservoir 190. FIG. In use, for example, the flow diverter mechanism 120 is placed (eg, manually or automatically) in a first configuration such that bodily fluid can flow from the inlet port 121 to the pre-sample fluid reservoir 170 . actuated and then moved to a second configuration such that bodily fluids can flow from inlet port 121 to first sample fluid reservoir 180 and, optionally, bodily fluids can flow from inlet port 121 to second sample fluid reservoir 190 It can be moved to a third configuration so that it can be used, and then moved to a fourth configuration so as to stop the flow of bodily fluids into and/or through the flow diverting mechanism 120 . In this manner, the device is effectively "cleaned" such that any residual bodily fluids within the device 100 are prevented from becoming contaminated and/or otherwise exposing medical personnel and/or patients to potentially hazardous fluids. Locked" and self-contained in the fourth form. This optional safety feature can prevent possible exposure to bodily fluid samples that may be infected with pathogens such as HIV, Hepatitis C, and the like.

[0039]

[1092] In some embodiments, one or more portions of the collection device 100 are disposed

within a housing (not shown in FIG. 1). For example, in some embodiments, at least a portion of one or more of flow diverting mechanism 120, first pre-sample reservoir 170 and sample reservoirs 180 and 190 can be disposed within the housing. In such embodiments, at least a portion of the flow diverter mechanism 120 is configured so that the user can activate the flow controller 140 to control the flow of bodily fluid from the patient (e.g., vein) to the collection device 100. Accessible through the housing. Examples of suitable housings are described in more detail herein with reference to specific embodiments.

[0040]

[1093] In some embodiments, the collection device 100 can optionally include one or more flow metering devices that can meter the flow of bodily fluid through the collection device. For example, a flow metering device can be in fluid communication with the first fluid flow path 142 and/or the second fluid flow path 144 to meter the flow of bodily fluid therethrough. In other embodiments, a flow metering device can be in fluid communication with and/or otherwise disposed in first port 125 and/or second port 126. The flow metering device can be configured to provide the user with an indication related to the predetermined volume being transferred to the pre-sample reservoir 170, the first sample reservoir 180 and/or the second sample reservoir 190, such as an indicator (For example, electrical signal output devices such as dials, displays, colors, tactile output devices, wireless radio signals, Bluetooth radio signals, etc.). In some embodiments, a flow metering device can be operably coupled to an actuator, such as, for example, those described above. In such embodiments, the flow metering device operates an actuator to move flow controller 140 between its first configuration and its second configuration based on the desired volume of bodily fluid that has flowed through the flow metering device. may be operable as such. Thus, using the flow metering device, a desired volume of bodily fluid is transferred to the pre-sample reservoir 170, the first sample reservoir 180 and/or the second sample reservoir 190, thereby providing an insufficient volume, such as in microbiological testing, for example on patient samples. can ensure that incorrect and/or erroneous results can be prevented.

[0041]

[1094] Referring now to FIGS. Includes reservoir 290. As further described herein, the collection device 200 is used to deliver a bodily fluid stream that is substantially free of extracorporeal microbes, such as microbes present on the skin and/or other undesirable external contaminants. It can be moved between a first configuration, a second configuration and a third configuration. collection de

Vise 200 may be of any suitable shape, size or configuration. For example, while sample reservoirs 280 and/or 290 are shown oriented perpendicular to housing 201 in FIGS. 2-13, collection device 200 is oriented planar to housing 201. It can have sample reservoirs 280 and/or 290, such as or arranged conically with respect to housing 201.

[0042]

[1095] The flow diverter mechanism 220 includes a housing 201 and movable members 250 a

nd 250'. As shown in FIGS. 2-4, housing 201 is coupled to pre-sample reservoir 270 , first sample reservoir 280 and second sample reservoir 290 . Housing 201 includes an inlet port 221, a first outlet port 230, a second outlet port 231, a third outlet port 232, and an internal flow path 235 that can define a fluid flow path for collecting bodily fluids from a patient. stipulated. Inlet port 221 can be selectively placed in fluid communication with internal flow path 235 . More specifically, inlet port 221 defines an inlet lumen 202 that can be placed in fluid communication with internal flow path 235 . Inlet port 221 is thus part of housing 201 such that internal flow path 235 can be placed in fluid communication with a space substantially outside housing 201 via inlet lumen 202 . extends from Inlet port 221 can be fluidly coupled to a medical device (not shown) that defines a fluid flow path for drawing bodily fluid from a patient and/or transporting it to collection device 200 . For example, entry port 221 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing) directly or indirectly via adapter 204 . Similarly, inlet lumen 202 defined by inlet port 221 is arranged to be in fluid communication with the lumen defined by the lumen-defining device when the lumen-defining device is coupled to inlet port 221 . . More specifically, when the lumen defining device is positioned within a portion of a patient's body (e.g., within a patient's vein or spinal space), the interior passageway 235 of the housing 201 is aligned with that portion of the patient's body. It can be arranged in fluid communication with the portion.

[0043]

[1096] The internal passageway 235 defined by the housing 201 is a central lumen that extends along the length of the housing 201 and is used for venipuncture (fluid access) as described herein. (other methods employed to enable the patient to be placed in fluid communication with the patient's bodily fluids). Internal channels 235 form fluid flow paths that transport bodily fluids between inlet port 221 and first, second, and third outlet ports 230 , 231 , and 232 . More specifically, when the internal flow path 235 is placed in fluid communication with a patient (eg, via a medical device coupled to the inlet port 221), the first outlet port 230, the second outlet port 231 are and third outlet port 232 are selectively placed in fluid communication with internal flow path 235 to allow bodily fluids to flow into at least one of pre-sample reservoir 270 , first sample reservoir 280 or second sample reservoir 290 . can be allowed to flow. In some embodiments, bodily fluid is prevented from flowing to second outlet port 231 and third outlet port 232 before a predetermined volume of bodily fluid has been collected in pre-sample reservoir 270 . In some embodiments, the second outlet port 231 and the third outlet port 232 can be placed in fluid communication with the internal flow path 235 at the same time. In some embodiments, the second outlet port 231 and the third outlet port 232 can be arranged in fluid communication with the internal flow path 235 sequentially.

[0044]

[1097] Movable members 250, 250' are actuated (eg, moved) by a user from first and second positions relative to housing 201 to direct fluid flow to first sample reservoir 280 and second sample reservoir. 290. Movable members 250 and 250 ' are substantially identical and therefor

e will be described with respect to a single movable member 250 . As shown in FIG. 5, moveable member 250 includes a boss 251 defining an interior cavity 252 , an inlet port 253 , a first outlet port 254 , and lumen 256 fluidly coupled to interior cavity 252 .

and a piercing member 255 defining 6. Inlet port 253 and outlet port 254 extend through the wall of boss 251 that defines interior chamber 252 of movable member 250 . Movable member 250 is positioned within support 257 (see FIG. 4) of housing 201 such that boss 251 is disposed within bore 258 (see FIG. 4) and at least a portion of movable member 250 is disposed within annular chamber 260 (see FIG. 4). configured to be attached to the housing. Optionally, a biasing member 259 (eg, a spring) can be disposed within the annular chamber 260 to return the movable member 250 to its first position after actuation by the user. In some embodiments, movable member 250, annular chamber 260, bore 258 or boss 251 are configured to retain movable member 250 in a second position (e.g., depressed position) after being actuated by a user. A mechanical locking mechanism can be included.

[0045]

[1098] As described herein, in the first configuration, the movable member 250 is arranged to be spaced apart from the internal channel 235. As shown in FIG. In such configurations, a fluid flow path cannot be established between a portion of the patient's body (eg, a vein, spinal cavity, etc.) and sample reservoirs 280 and/or 290 . In other words, when movable member 250 is in its first configuration, first sample reservoir 280 and second sample reservoir 290 are fluidly isolated from internal flow path 235 defined by housing 201 . Movable member 250 can be actuated by a user to move movable member 250 from the first configuration to the second configuration and into alignment with internal channel 235 . The force applied by the user may be sufficient to deform (eg, compress) biasing member 259, thereby inserting piercing member 255 into sample reservoirs 280 and/or 290. can be done. In the second configuration, inlet port 253 and outlet port 254 are substantially aligned with internal flow path 235 to place internal cavity 252 in fluid communication with internal flow path 235 . Thus, when movable member 250 is in the second configuration, a fluid flow path is established between internal channel 235 , internal cavity 252 , lumen 256 of piercing member 255 and sample reservoir 280 . In other words, in such a configuration, bodily fluids flow from the patient (eg, veins, spinal spaces, etc.) through the flow diverting mechanism 220 into the first sample reservoir 280 and/or the second sample reservoir 280, as described in further detail herein. It can flow into the sample reservoir 290 .

[0046]

[1099] The pre-sample reservoir 270 can be any suitable reservoir for containing bodily fluids, such as, for example, a single-use disposable collection tube, a vacuum-assisted collection tube, and the like. Pre-sample reservoir 270 is configured to be fluidly coupled in any suitable manner (either directly or via an intervening structure such as sterile flexible tubing) to first outlet port 230 of collection device 200. . For example, in some embodiments, a portion of pre-sample reservoir 270 can form a friction fit within a portion of first outlet port 230 . In other em

bodiments, pre-sample reservoir 270 can be coupled to first outlet port 230 via threaded coupling, adhesives, snap fits, mechanical fasteners and/or any other suitable coupling method. . In some embodiments, pre-sample reservoir 270 can be integrally formed with housing 201 . Pre-sample reservoir 270 is subjected to a negative pressure condition (vacuum condition) that can enable bodily fluid to be drawn into pre-sample reservoir 270 via vacuum suction from inlet port 221 through outlet port 230 (pre-sample reservoir 270) can be configured to be maintained internally. Pre-sample reservoir 270 is configured to contain a first volume of bodily fluid, where the first volume of bodily fluid can be a predetermined volume or an unquantified volume, thereby is fluidly isolated from a second and/or a third volume of bodily fluid subsequently withdrawn from the patient.

[

1100] Sample reservoirs 280 and/or 290 may be single-use disposable collection tubes, vacuum driven collection tubes, sample reservoirs such as those described in the '420 patent incorporated herein by reference above, or the like. It can be any suitable reservoir for containing bodily fluids, including: In some embodiments, sample reservoirs 280 and/or 290 include, for example

It can be substantially similar or identical to known sample containers, such as the Vacutainer®. Sample reservoirs 280 and 290 include sample vessels 282 and 292, respectively, and vacuum seals 284 and 294, respectively. A vacuum seal 284 or 294 can allow bodily fluid to be drawn into the sample container 282 or 292, respectively, from the internal channel 235 via vacuum suction into the sample container 282 or 292, respectively. state). Sample containers 280 and/or 290 are fluidically connected in any suitable manner (directly or via an intervening structure such as sterile flexible tubing) to second and third outlet ports 231 and 232, respectively, of collection device 200. It can be configured to be coupled. Sample reservoirs 280 and/or 290 can be moved relative to exit ports 231 and/or 232 so as to be placed in fluid communication with exit ports 231 and/or 232 . Sample reservoirs 280 and 290 can be configured to contain a second volume or a third volume of bodily fluid. The second or third amount of bodily fluid can be a predetermined amount or an unquantified amount, whereby the second or third amount of bodily fluid is the first amount of bodily fluid withdrawn from the patient. fluidly isolated from In some configurations, sample reservoirs 280 and/or 290 may be coupled to collection device 200 by being integrally formed with housing 201, similar to pre-sample reservoir 270, and are therefore not discussed in detail herein. not described in In some cases, the sample reservoirs 280 and/or 290 can be transparent so that the user has visual feedback to confirm the flow of bodily fluid into the sample reservoirs 280 and/or 290. can be done.

[0048]

[1101] In some embodiments, sample reservoirs 280 and 290 and flow diverter mechanism 220 (and/or portions of collection device 200 other than sample reservoirs 280 and 290) are independently formed (e.g., integrally formed) and bonded together during the manufacturing process, for example. In some cases, sample reservoirs 280 and 290 can be coupled to flow div

erter mechanism 220 in a substantially sterile or sealed environment (eg, filled with ethylene oxide or the like). Accordingly, the interface between sample reservoirs 280 and 290 and flow diverter 220 is substantially sterile prior to use. Further, collection device 200 can be transported and/or stored pre-assembled, such as to maintain a substantially sterile interface between sample reservoirs 280 and 290 and flow diverting mechanism 220 .

[0049]

[1102] As shown in FIGS. First member 241 is configured to be disposed within recess 266 (see, eg, FIG. 4) of housing 201 and is made of, for example, titanium, graphite, pyrolytic carbon, polyester, polycarbonate, polyurethane, or the like. , elastomeric materials, etc., that are biocompatible. In some embodiments, second member 245 acts as an actuator to move first member 241 from the first configuration to the second configuration. More specifically, once the first member 241 is positioned within the recess 266, the second member 245 is moved between the first and second positions to move the flow controller 240 from the first configuration to the second configuration. It can be moved between two forms. In some embodiments, housing 201 can selectively restrict movement of second member 245 from its first position to its second position. In some embodiments, the housing 201 can be configured to prevent movement of the second member 245 moved to the second position. In other words, housing 201 can include a locking mechanism that prevents second member 245 from moving back from the second position to the first position. Second member 245 and/or housing 201 may also include mechanical detents and/or other indicators that provide visual or tactile feedback to ensure correct positioning of second member 245. is.

[1103]

] The first member 241 is used for venipuncture (and/or other methods of accessing a patient's bodily fluids).

A plurality of channels can be included to direct fluid flow subsequent to the . For example, as shown in FIGS. 6 and 7, first member 241 includes first channel 242 and second channel 244 . When the second member 245 is in the first position (see, for example, FIGS. 8 and 9), the flow controller 240 is arranged in the first configuration and the first channel 242 connects the inlet port 221 from the internal channel 235. Fluid communication is established between inlet port 221 and first outlet port 230 while being fluidly isolated. When the second member 245 is in the second position (see, eg, FIGS. 10-13), the flow controller 240 is disposed in the second configuration and the second flow path 244 connects the inlet port 221 to the first outlet port 230. Fluid communication is established between the inlet port 221 and the internal channel 235 while being fluidly isolated from the . The position of the additional second member 245 corresponding to the flow path of the additional first member 241 and/or the configuration of the flow controller 240 to further direct/isolate the fluid flow between the patient and the collection device 200. can be included. For example, the second member 245 can have a third position corresponding to a third configuration of the flow controller 240 that substantially prevents fluid flow between the patient and the collection device 200 as a whole. In other words, in

some embodiments, after all bodily fluid samples have been removed from the patient, moving the dial to the third position substantially seals the sample within the collection device 200 from the external environment. can be done.

[0051]

[1104] In operation, the collection device 200 can be used to collect bodily fluids (eg, blood) from a patient with reduced contamination from microorganisms present on the skin and/or other undesirable external contaminants. can. For example, inlet port 221 of collection device 200 is fluidly coupled via adapter 204 to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other fluid access method), second member 245 is rotated until it reaches the first position, as shown in FIGS. Alternatively, the second member 245 can be preset to the first position and the collection device 200 is otherwise sealed to maintain the vacuum within the pre-sample reservoir 270 and the sterility of the collection device 200. can do. For example, inlet port 221 and/or adapter 204 can include a valve that opens when collection device 200 is coupled to a needle or other lumen defining device.

[0052]

[1105] As described above, when the second member 245 is in the first position, the flow controller 240 is disposed in the first configuration and the first passageway 242 of the first member 241 connects the inlet port 221 to the internal passageway. Fluid communication is established between inlet port 221 and first outlet port 230 while being fluidly isolated from 235. Further, the first sample reservoir 280 and the second sample reservoir 290 are fluidly isolated from the inlet port 221 in the first configuration and are located in a portion of the patient's body (eg, a vein), as indicated by arrows AA in FIG. and a pre-sample reservoir 270 are defined. As described above, the fluid reservoirs used in collection device 200, such as pre-sample reservoir 270 and sample reservoirs 280 and 290, are exposed to a negative pressure (i.e., the pressure of the body part from which collection device 200 is used to draw bodily fluids). pressure less than the fluid pressure), thereby establishing fluid communication between a portion of the patient's body (e.g., a vein) and pre-sample reservoir 270, the negative pressure within pre-sample reservoir 270 causes, the pressure differential between the pre-sample reservoir 270 and that portion of the patient's body causes fluid to be drawn into the pre-sample reservoir 270. In this first configuration, flow controller 240 also fluidly isolates pre-sample reservoir 270 from internal flow path 235. Thus, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 270 (for example) immediately after venipuncture and isolated from subsequent samples. Thus, with the collection device 200, a first volume of bodily fluid most likely to contain surface microorganisms and/or other undesirable external contaminants may be diagnosed or affected by the contaminants. Subsequent volumes of bodily fluid samples collected and used for other tests can be uncontaminated.

[0053]

[1106] Following collection of the body fluid pre-sample volume in the pre-sample reservoir 270,

, the second member 245 can be rotated until it reaches a second position as shown in FIGS. When the second member 245 is in the second position, the flow controller 240 is placed in the second configuration and the second flow path 244 of the first member 241 enters the first outlet port 230 (i.e., the pre-sample reservoir 270). Fluid communication is established between inlet port 221 and internal channel 235 while being fluidly isolated from port 221. In other words, in the second configuration, the flow controller 240 provides flow between a portion of the patient's body (eg, a vein) and the internal flow path 235 via the second flow path 244, as indicated by arrow BB in FIG. establish a fluid flow path in the

[0054]

[1107] With flow controller 240 in the second configuration, movable member 250 and/or 250' is actuated (i.e., depressed) by a user from a first position to a second position to move the patient's body. Fluid communication can be established between a portion (eg, a vein) and the first sample reservoir 280 and/or the second sample reservoir 290. More specifically, movable member 250 moves from its first position to its second configuration such that piercing member 255 pierces vacuum seal 284 of first sample reservoir 280, as indicated by arrow CC in FIG. The piercing member 255 passes through the exit port 231 so that it can be opened and placed inside the sample container 282. When in the second position, inlet port 253 and outlet port 254 of movable member 250 are substantially aligned with and in fluid communication with internal channel 235 such that bodily fluids flow from internal channel 235 to the movable member. It can flow into the internal cavity 252 of 250 and out of the lumen 256 of the piercing member 255 into the first sample reservoir 280. A pressure differential between sample reservoir 280 (eg, vacuum or negative pressure) and internal channel 235 draws bodily fluid in to sample reservoir 280. In other words, in the second configuration, movable member 250 establishes a fluid flow path between internal flow path 235 and first sample reservoir 280, as indicated by arrow DD in FIG. Once a desired amount of bodily fluid (eg, a second amount) has been collected in first sample reservoir 280, the user releases movable member 250 such that biasing member 259 returns the button to its first position. can be enabled to move to When movable member 250 returns to its first position, piercing member 255 is removed from first sample reservoir 280 and seal 284 (e.g., a self sealing septum) opens first sample reservoir 280 to internal flow. It is fluidly isolated from channel 235.

[0055]

[1108] Similarly, while the flow controller 240 is in the second configuration, the movable member 250' is actuated (depressed) by a user from its first position to its second position, as indicated by arrow EE in FIG.)be able to. Thus, in a manner similar to the movable member 250 and the first sample reservoir 280 described above, a portion of the patient's body (eg, a vein) and the second sample reservoir 290 (via the exit port 232). Fluid communication is established. In other words, in the second configuration, movable member 250' establishes a fluid flow path between internal flow path 235 and second sample reservoir 290, as indicated by arrow FF in FIG. Once a desired amount of bodily fluid (eg, a third amount) has been collected in

second sample reservoir 290, the user releases movable member 250' such that biasing member 259' causes button 250' to move to its third position. It can be allowed to move back to one position. Although shown and described as being a sequential process, the order and/or sequencing of filling is not necessary (i.e., sample reservoir 280 may not necessarily fill before sample reservoir 290, etc.). In other words, when the flow controller 240 is moved to the second configuration, the first sample reservoir 280 and the second sample reservoir 290 (and any additional sample reservoirs) are activated in any order at the same time (eg, simultaneously) and/or Or they can be filled in overlapping time intervals. For example, a user can initiate filling of the first sample reservoir 280, and then after the first sample reservoir 280 is partially filled, the user presses the movable member 250' to Filling of the second sample reservoir 290 can begin while the first sample reservoir 280 finishes filling. Additionally, adjustment of the volume of bodily fluid collected in sample reservoirs 280 and/or 290 can be achieved by moving member 2

It can be enabled by repeatedly actuating (inserting) 50 and/or 250'. As noted above, the second member 245 can have a third position corresponding to the third configuration of the flow controller 240, thereby substantially reducing fluid flow between the patient and the collection device 200 as a whole. to substantially seal the sample within the collection device 200 from the external environment.

[1109]

] Although not shown in FIGS. 2-13, the collection device 200 meters the volume of bodily fluid transferred to the pre-sample reservoir 270, the first sample reservoir 280 and/or the second sample reservoir 290. A flow metering device or the like can be included that can be configured to. For example, in some embodiments, first member 241 of flow controller 240 can include a flow metering device in fluid communication with first flow path 242 and second flow path 244. In other embodiments, a flow metering device can be positioned within the internal cavity 252 of the moveable member 250 and/or 250'. Accordingly, the volume of the bodily fluid sample transferred to and placed in the first sample reservoir 280 and the second sample reservoir 290 may be such that the volume of the bodily fluid sample placed in each sample reservoir 280 and 290 is e.g. It can be metered and/or controlled to have a predetermined volume, such as 30 mL.

[0057]

[1110] Although the collection device 200 is shown and described as including a first sample reservoir 280 and a second sample reservoir 290, other embodiments may include any number of pre-sample reservoirs and/or sample reservoirs. can contain. For example, Figures 14 and 15 show a collection device 300 according to embodiments. As shown, some aspects of the collection device 300 may be substantially similar to corresponding aspects of the collection device 200 described above with reference to FIGS. 2-13. Accordingly, similar aspects are not described in further detail herein.

[0058]

[1111] As shown in Figs. A fourth sample reservoir 390' is included. Pre-sample reservoir 370 may be substantially similar to pre-sample reservoir 270 described in detail above. In some embodiments, sample reservoirs 380, 380', 390 and 390' can be substantially similar to sample reservoirs 280 and 290 described in detail above. In some embodiments, sample reservoirs 380, 380', 390 and 390' can have substantially the same shape and size, eg, contain substantially the same medium. In other embodiments, sample reservoirs 380, 380', 390 and 390' can have substantially the same shape and size and contain one of aerobic or anaerobe media. can be done. For example, in some embodiments, the first sample reservoir 380 and the third sample reservoir 390 can contain an aerobic culture medium, and the second sample reservoir 380' and the fourth sample reservoir 390' can contain an anaerobe culture medium. A culture medium can be included. In other embodiments, sample reservoirs 380, 380', 390 and 390' may each contain aerobic or anaerobe media in any arrangement or combination.

[0059]

[1112] The flow diverter mechanism 320 includes a housing 301 and a set of moveable members 350, 350', 350'' and 350'''. Movable members 350, 350', 350'' and 350''' are substantially similar to movable member 250 described above with reference to FIG. 5, for example. Accordingly, movable members 350, 350', 350'' and 350''' are positioned in a first position relative to housing 301 such that they are placed in fluid communication with sample reservoirs 380, 380', 390 and 390', respectively. and a second position. The housing 301 is in fluid communication with an inlet port 321, a first outlet port 330 configured to be arranged in fluid communication with a pre-sample reservoir 370, and a first sample reservoir 380.

a second outlet port 331 configured to be arranged to be in fluid communication with a second sample reservoir 380' and a third outlet port 332 configured to be arranged in fluid communication with a third sample reservoir 390'; and a fifth outlet port 334 configured to be placed in fluid communication with a fourth sample reservoir 390'. Further, housing 301 can be selectively placed in fluid communication with inlet port 321 and outlet ports 331, 332, 333 and 334 in a manner similar to that described above with respect to interior passageway 235 of housing 201. An internal channel 335 is defined.

[1113]

] The flow controller 340 is substantially similar to the flow controller 240 described above, eg, with reference to FIGS. 6-13. Accordingly, the flow controller 340 is rotated between the first and second configurations to provide a portion of the fluid flow path between the patient and the pre-sample reservoir 370 or the sample reservoirs 380, 380', 390 and 390'. can be selectively defined. In this manner, a user can operate collection device 300 in a manner similar to that described above with respect to collection device 200 in FIGS. 8-13. Thus, a first volume of bodily fluid can be transferred to and placed in pre-sample reservoir 370, and subsequent volumes of bodily fluid can be transferred to and placed in sample reservoirs 380, 380', 390 and 390'. can be placed.

[0061]

[1114] FIGS. 16-22 illustrate a collection device 400 according to an embodiment. Collection device 400 includes flow diverter mechanism 420, flow controller 440 and sample reservoirs 480, 480', 490 and 490'. As further described herein, the collection device 400 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorganisms and/or microorganisms present on the skin. or a body fluid stream that is substantially free of extracorporeal microorganisms, such as other undesirable external contaminants. Collection device 400 may be of any suitable shape, size or configuration. For example, although sample reservoirs 480, 480', 490 and 490' are shown oriented perpendicular to housing 401 in FIGS. It is possible to have the sample reservoirs 480, 480', 490 and 490' oriented in a plane, arranged conically with respect to the housing 401, or the like.

[0062]

[1115] The sample reservoirs 480, 480', 490 and 490' are substantially similar or identical in form and function to the sample reservoirs 280 and/or 290 of the collection device 200; No details are given. As described above, the sample reservoirs 480, 480', 490 and 490' are negative pressure conditions that can allow fluid to be drawn from the patient into the sample reservoirs 480, 480', 490 and 490' via suction. (vacuum state) is maintained. In some embodiments, sample reservoirs 480 and 480' can be aerobic culture bottles, sample reservoirs 490 and 490' can be anaerobic culture bottles, and collection device 400 can be used to Thus, multiple aerobic and multiple anaerobic blood culture samples can be collected from a single venipuncture. As described in further detail herein, sample reservoirs 480, 480', 490 and 490' are each arranged in fluid communication with at least a portion of flow diverting mechanism 420 to receive a volume of bodily fluid sample. can do. The volume of the bodily fluid sample can be either predetermined or unquantified. Further, once a desired volume of bodily fluid has been placed within sample reservoirs 480, 480', 490, 490', each sample reservoir 480, 480', 490 and 490' will be displaced as described in further detail herein. can be fluidly isolated from at least a portion of flow diverting mechanism 420 .

[1116

] Flow diverting mechanism 420 includes housing 401 and distribution member 429 . Housing 401 of flow diverter mechanism 420 is physically and fluidly coupled to distribution member 429 to provide patient-to-body flow.

It provides and/or defines a set of fluid flow paths for collecting liquid. Housing 401 defines a recess 466 and a set of exit openings 403 . Recess 466 is configured to receive seal member 441 included in flow controller 440, as described in further detail herein. The set of outlet openings 403 is configured to define a different fluid flow path, each of which is in fluid communication with a different portion of the distribution member 429, a first outlet opening 403a, a second outlet opening 403b. , a third exit opening 403c, a fourth exit opening 403d and a fifth exit opening 403e. More specifically, distribution member 429 includes at least a portion of pre-sample reservoir 470 in fluid communication with first outlet opening 403a and a first channel 435a in fluid communication with second outlet opening 403b. , a second channel 435b in fluid

d communication with the third outlet opening 403, a third channel 435c in fluid communication with the fourth outlet opening 403d, and a third channel 435c in fluid communication with the fifth outlet opening 403e. defines and/or forms four channels 435;

[0064]

[1117] As shown in FIGS. Pre-sample reservoir 470 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. A first outlet opening 403a of housing 401 can be substantially aligned with an open portion of pre-sample reservoir 470 to allow pre-sample reservoir 470 to receive the flow of bodily fluid from the patient. For example, pre-sample reservoir 470 can receive and contain a first amount or first volume of bodily fluid, where the first amount of bodily fluid can be a predetermined amount or an unquantified amount. Additionally, the arrangement of the flow diverter mechanism 420 may be such that the pre-sample reservoir 470 may be configured to allow fluid from the flow paths 435a, 435b, 435c and 435d and/or subsequent volumes of bodily fluid withdrawn from the patient, as described in further detail herein. can be maintained in a systematically isolated manner. Although pre-sample reservoirs 270 and 370 are described above as maintaining a negative pressure, pre-sample reservoir 470 does not maintain a negative pressure (vacuum) and therefore uses other mechanisms such as gravity for example. can be used to draw bodily fluid into the pre-sample reservoir 470 .

[0065]

[1118] Channels 435a-435d extend radially from the center of distribution member 429 such that each channel 435a, 435b, 435c and 435d is fluidly isolated from pre-sample reservoir 470 and the other channels. are placed in In this manner, channels 435a, 435b, 435c and 435d are fluid flow channels between first and second ends substantially aligned with outlet openings 403b, 403c, 403d and 403e, respectively. can be oriented and/or otherwise defined. As shown in FIGS. 17 and 18, the distribution member 429 includes a first outlet port 431 positioned at the second end of the first flow path 435a and a second outlet port 431 positioned at the second end of the second flow path 435b. defining a second outlet port 432, a third outlet port 433 positioned at the second end of the third flow path 435c, and a fourth outlet port 434 positioned at the second end of the fourth flow path 435d; are doing. Further, the distribution member 429 includes a first piercing member 455a, a second piercing member 455b, a third piercing member 455c and a fourth piercing member 455d, which are the first outlet port 431, the second outlet port 432, the third It is physically and fluidly coupled to outlet port 433 and fourth outlet port 434, respectively. Thus, as described in further detail herein, piercing members 455a-455d can be used to pierce the vacuum seals of sample reservoirs 480, 480', 490 and 490', thereby allowing bodily fluids to flow. Flow can be started. Although not shown in Figures 17 and 18, sample reservoirs 480, 480', 490 and 490' are in fluid communication with outlet ports 431, 432, 433 and 434, respectively. can be physically coupled (either directly or via an intervening structure, such as a sterile flexible tube) to a portion of distribution member 429 in any suitable manner that can allow the can.

[0066]

[1119] The flow controller 440 includes a dial 445 and a seal member 441 . C

Lel member 441 is positioned within recess 466 of housing 401 (see, eg, FIG. 20). More particularly, coupling flow controller 440 to housing 401 such that seal member 441 is positioned between and in contact with the surface of housing 401 defining recess 466 and the surface of dial 445 . can be done. In addition, seal member 441 may be positioned against the surface of housing 401 defining dial 445 and recess 466 when flow controller 440 is coupled to housing 401, as described in further detail herein. can be sized and shaped to form a substantially fluid-tight seal with. The sealing member 441 is made of, for example, silicone, polylactic acid, polyglycolic acid, polylactic-co-glycolic acid (PLGA), polyanhydride, polyorthoester, polyetherester, polycaprolactone, polyesteramide, poly(butyric acid).), poly(valeric acid), polyurethanes, nylons, polyesters, polycarbonates, polyacrylates, polymers of ethylene-vinyl acetate and other acyl-substituted cellulose acetates, polystyrene, polyvinyl chloride, polyvinyl fluoride, poly(vinylimidazole), chloro It can be made from any material that is biocompatible, such as sulfonate polyolefins, polyethylene oxides and/or mixtures and copolymers thereof.

[0067]

[1120] As shown in FIG. 17, the sealing member 441 defines a set of openings 444 through which the flow of bodily fluids can be directed following venipuncture (or other method of accessing bodily fluids). . For example, the set of openings 444 defined by the seal member 441 includes a first opening 444a, a second opening 444b, a third opening 444c, a fourth opening 444d and a fifth opening 444e. The arrangement of the sealing member 441 is such that when the sealing member 441 is arranged in the recess 446, the first opening 444a, the second opening 444b, the third opening 444c, the fourth opening 444d, and the fifth opening 444e are , the first outlet opening 403a, the second outlet opening 403b, the third outlet opening 403c, the fourth outlet opening 403d and the fifth outlet opening 403e of the housing 401, respectively. is.

[0068]

[1121] The dial 445 of the flow controller 440 is rotatably coupled to the housing 401 and is movable between a first position, a second position, a third position, a fourth position and a fifth position relative to the housing 401. . Dial 445 includes an entry port 421 that defines lumen 402 . Inlet port 421 can be fluidly coupled to a medical device (not shown) that defines a fluid flow path for withdrawing and/or transporting bodily fluid from the patient's body to collection device 400 . For example, entry port 421 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing) either directly or indirectly via adapter 404 . Similarly, inlet lumen 402 defined by inlet port 421 is arranged to be in fluid communication with the lumen defined by the lumen-defining device when the lumen-defining device is coupled to inlet port 421 . be. Inlet port 421 thus connects to pre-sample reservoir 470, first sample reservoir 480, second sample reservoir 480', third sample reservoir 490 and fourth sample reservoir 490, as described in further detail herein. ' can be configured to be selectively placed in fluid

communication with a patient.

[0069]

[1122] As described above, the dial 445 is movable between a first position, a second position, a third position, a fourth position, and a fifth position. When the dial 445 is in the first position, the flow controller 440 is arranged in a first configuration, aligning the inlet port 421 substantially with the first opening 444a of the seal member 441 and the first outlet opening 403a of the housing 401. can be combined. Thus, the first opening 444a of the seal member 441 fluidly isolates the inlet port 421 from the outlet openings 403b, 403c, 403d and 403e, thereby fluidly isolating the inlet port 421 from the flow paths 435a-435d. Fluid communication is established between the inlet port 421 and the first outlet opening 403a while isolating to the first outlet port 403a. When the first outlet port 403a is aligned with the open portion of the pre-sample reservoir 470, the first opening 444a and the first outlet port 403a are aligned.

Mouth opening 403a establishes fluid communication between inlet port 421 and pre-sample reservoir 470. When the dial 445 is rotated (or driven) to the second position, the flow controller 440 is placed in the second configuration and the second outlet opening 444b connects the inlet port 421 to the outlet openings 403a, 403c, 403d and 403e. Fluid communication is established between inlet port 421 and second outlet opening 403b while being fluidly isolated from. When the second outlet opening 403b is aligned with the first end of the first flow path 435a, the second opening 444b and the second outlet opening 403b are between the inlet port 421 and the first flow path 435a. establish fluid communication with the

[0070]

[1123] The collection device 400 operates similarly when the dial 445 is rotated to the third, fourth and fifth positions. Thus, when inlet lumen 402 is placed in fluid communication with a patient (eg, via a medical device coupled to inlet port 421), first outlet port 430, second outlet port 431, third outlet Port 432, fourth outlet port 433, and fifth outlet port 434 are selectively placed in fluid communication with inlet lumen 402 so that all body fluids are present in at least one of pre-sample reservoirs 470 or sample. It can be enabled to flow into one or more of reservoirs 480, 480'490 and 490'. In some embodiments, additional seal outlet openings and/or additional dials 445 corresponding to the configuration of the flow controller 440 are provided to further direct/isolate fluid flow between the patient and the collection device 400. Can include location. For example, dial 445 can have a sixth position corresponding to a sixth configuration of flow controller 440 that substantially prevents fluid flow between the patient and collection device 400 as a whole. In other words, in some embodiments, after all bodily fluid samples have been removed from the patient, dial 445 may be moved to the sixth position to substantially seal the sample within collection device 400 from the external environment. can.

[0071]

[1124] In some embodiments, until after a predetermined volume of bodily fluid has been collected in the pre-sample reservoir 470, the bodily fluid does not flow to the outlet ports associated with the sample reservoir (eg, outlet ports 431-434). prevented. In some embodiments,

the exit ports associated with the sample reservoirs (eg, exit ports 431-434) can be placed in fluid communication with the entrance lumen 402 only sequentially (eg, exit ports 431-434). 431 must be in fluid communication with the inlet lumen 402 before the outlet port 432, etc.). In some embodiments, outlet ports associated with subsequent sample reservoirs (eg, outlet ports 432-434) are placed in fluid communication with inlet lumen 402 only after a defined volume of bodily fluid has been collected. can be placed. In some embodiments, the outlet ports associated with the sample reservoirs (eg, outlet ports 431-434) can be arranged in fluid communication with the inlet lumen 402 in any random manner without any order preference. (eg, outlet port 434 can be in fluid communication with inlet lumen 402 before outlet port 431, outlet port 432 can be in fluid communication with inlet lumen 402 before outlet port 433, etc.).

[0072]

[1125] In some embodiments, the housing 401 can selectively restrict movement of the dial 445 from its first position to its second, third, fourth and fifth positions. . In some embodiments, housing 401 can be configured to prevent movement of dial 445 moved to the fifth position. In other words, housing 401 may include a locking mechanism that prevents dial 445 from moving back from the fifth position to the first position. Dial 445 and/or housing 401 may also include mechanical detents and/or other detents that provide visual or tactile feedback to ensure correct positioning of dial 445 relative to exit openings 403a-403e of housing 401. It is also possible to include an indicator.

[0073]

[1126] In operation, the collection device 400 can be used to collect bodily fluids (eg, blood, plasma, urine, etc.) from a patient with reduced contamination. For example, entry port 421 of collection device 400 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), dial 445 is actuated (or turned) until it reaches the first position, as shown in FIGS. Alternatively, dial 445 can be preset to the first position and collection device 400 can be otherwise sealed to maintain sterility of collection device 400 . For example, inlet port 421 can include a valve that opens when collection device 400 is coupled to a needle or other lumen defining device.

[0074]

[1127] As described above, when the dial 445 is in the first position, the flow controller 440 is disposed in the first configuration, and the first opening 444a of the seal member 441 connects the inlet port 421 to the four flow paths 435a through 435d. Fluid communication is established between inlet port 421 (contained within housing 401) and first outlet port 430 while being fluidly isolated from 435d. Further, sample reservoirs 480, 480', 490 and 490' are fluidly isolated from inlet port 421 in the first configuration and are part of the patient's body (e.g., A fluid flow path is defined between the vein) and the pre-sample reservoir 470 . In this first configuration, bodily fluid passes from that portion of the patient's body through the inlet lumen 402 of the inlet port 421, the first opening 444a of the seal member 441, the first outlet port 4

30, and into the pre-sample reservoir 470 (for example, by gravity, vacuum, etc.). In the first form, flow controller 440 also fluidly isolates pre-sample reservoir 470 from channels 435a-335d. Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 470 immediately after venipuncture and isolated from subsequent samples. Thus, with the collection device 400, a first volume of bodily fluid most likely to contain surface microorganisms and/or other undesirable external contaminants may be diagnosed or affected by the contaminants. Subsequent volumes of bodily fluid samples collected and used for other tests can be uncontaminated.

[0075]

[1128] Following the collection of the bodily fluid pre-sample into the pre-sample reservoir 470, the dial 445 can be actuated (rotated) until it reaches the second position, as shown in FIG. S. When dial 445 is in the second position, flow controller 440 is disposed in the second configuration, and second opening 444b of seal member 441 fluidly isolates pre-sample reservoir 470 from inlet port 421 while allowing inlet port 421 to flow. Establish fluid communication between 421 and channel 435a. In other words, in the second configuration, flow controller 440 establishes a fluid flow path between a portion of the patient's body (eg, a vein) and flow path 435a, as indicated by arrow HH in FIG. With the flow controller 440 in the second configuration, the sample reservoir 480 is actuated by the user from the first configuration to the second configuration (e.g., by pushing the piercing member 455a) into a portion of the patient's body (e.g., A vein) and the first sample reservoir 480 can be in fluid communication.

[0076]

[1129] As described above, the piercing member 455a is positioned inside the sample reservoir 480 by piercing the vacuum seal of the sample reservoir 480 by moving the sample reservoir 480 to the second configuration. In this second configuration, a portion of the patient's body (eg, a vein) is exposed to a vacuum suction force from the sample reservoir 480 due to the negative pressure (vacuum) within the sample reservoir 480. A pressure differential between the sample reservoir 480 (eg, vacuum or negative pressure) and that portion of the patient's body draws fluid into the sample reservoir 480. Bodily fluid passes from that portion of the patient's body through the inlet lumen 402 of the inlet port 421, the second opening 444b of the seal member 441, the second outlet opening 403b of the housing 401, and into the first flow path 435a. flow in. Vacuum suction draws the flow of bodily fluid through first channel 435a and into sample reservoir 480 via second outlet port 431 and piercing member 455a.

. In other words, in the second configuration, flow controller 440 establishes a fluid flow path between inlet port 421 and sample reservoir 480. Once a desired amount of bodily fluid (eg, a second amount) has been collected in sample reservoir 480, the user actuates (rotates) flow controller 440 to a third position and/or rotates sample reservoir 480 to its The first sample reservoir 480 can be isolated from the channel 435a by moving it back to the first configuration. When sample reservoir 480 returns to the first configuration, piercing member 455a is removed from sample reservoir 480 and a seal (eg, self-sealing membrane) in sample reservoir 480

isolates first sample reservoir 480 from flow path 435a. Filling of the other sample reservoirs is done similarly with the flow controller 440 positioned in the third, fourth and fifth configurations, respectively.

[0077]

[1130] It should be noted that the order and/or sequencing of filling is not necessary (ie, sample reservoir 480 does not necessarily need to be filled before sample reservoir 490, etc.). In other words, first sample reservoir 480 and second sample reservoir 490 (and any additional sample reservoirs) can be filled in any order. For example, the user can start filling the first sample reservoir 480, and then after the first sample reservoir 480 is partially filled, the user can fill the second sample reservoir 490. Further, adjustment of the volume of bodily fluid collected in sample reservoirs 480 and/or 490 can be enabled by repeated filling of sample reservoirs 480 and/or 490. However, in other embodiments, the order of filling is such that the second sample reservoir cannot be accessed until it is verified that a specified amount of bodily fluid has been placed in the first reservoir. It can be operated mechanically. As described above, the dial 445 can substantially prevent fluid flow between the patient and the collection device 400 as a whole, substantially sealing the sample within the collection device 400 from the external environment. A sixth position for a sixth configuration of the flow controller 440 can be provided.

[0078]

[1131] The collection device 400 includes a set of four sample reservoirs (eg, a first sample reservoir 480, a second sample reservoir 480', a third reservoir 490 and a fourth reservoir 490') and/or to which other. Although shown and described above as being coupled in a manner, in other embodiments the collection device may include and/or be coupled to any suitable number of sample reservoirs. For example, Figures 23-25 show a collection device 500 according to an embodiment. As shown, some aspects of the collection device 500 can be substantially similar to corresponding aspects of the collection device 500 described above with reference to FIGS. 16-22. Accordingly, similar aspects are not described in further detail herein.

[1132

] The collection device 500 includes a flow diverter mechanism 520, a flow controller 540, a first sample reservoir 580 and a second sample reservoir 590. Sample reservoirs 580 and 590 can be substantially similar to the sample reservoirs described in detail above. In some embodiments, sample reservoirs 580 and 590 can have substantially the same shape and size and contain substantially the same medium. In other embodiments, sample reservoirs 580 and 590 can have substantially the same shape and size and can contain one of an aerobic medium or an anaerobic medium. In still other embodiments, first sample reservoir 580 can have a first size that is substantially larger than the size of second sample reservoir 590.

[0080]

[1133] As shown in FIGS. Housing 501 of flow diverter mechanism 520 is physically and fluidly coupled to distribution member 529 to provide a set of fluid flow paths for collecting bodily f

fluids from a patient and/or

stipulates. As described above with respect to housing 401, housing 501 can define a recess and first, second, and third outlet openings 503a, 503b, and 503c. The recess is configured to receive a seal member 541 included in flow controller 540, as described in detail above. First outlet opening 503a, second outlet opening 503b and third outlet opening 503c correspond to first outlet opening 403a, second outlet opening 403b and third outlet opening 403c defined by housing 401, respectively. They can be substantially similar in form and function. Similarly, distribution member 529 includes pre-sample reservoir 470, first flow channel 435a and second flow channel 435b that are substantially similar to pre-sample reservoir 470, first flow channel 435a and second flow channel 435b included in flow diverter member 429. Two flow paths 435b are defined. Thus, pre-sample reservoir 570 is in fluid communication with first outlet opening 503a, first channel 535a is in fluid communication with second outlet opening 503b, and as described above with respect to flow diverter mechanism 420; The second flow path 535b is in fluid communication with the third outlet opening 503c. As shown in FIG. 25, distribution member 529 is in fluid communication with first outlet port 531, which is in fluid communication with first channel 535a and first piercing member 555a, and second channel 535b, with second piercing member 555b. A second outlet port 532 is defined. As described above, piercing members 555a and 555b can be used to pierce the vacuum seals of sample reservoirs 580 and 590, thereby initiating bodily fluid flow, as described in further detail herein. can do.

[0081]

[1134] The flow controller 540 includes a dial 545 and a seal member 541. The seal member 541 is positioned within the recess of the housing 501 as described above. Thus, when flow controller 540 is coupled to housing 501, seal member 541 forms a substantially fluid-tight seal with the surface of dial 545 and the surface of housing 501 that defines the recess. As shown in FIGS. 24 and 25, seal member 541 is substantially configured with first outlet opening 503a, second outlet opening 503b and third outlet opening 503c, respectively, as described in detail above with respect to seal member 441. defines a first opening 544a, a second opening 544b and a third opening 544c, which are aligned with each other.

[0082]

[1135] The dial 545 of the flow controller 540 may be substantially similar in form and function to the dial 445 while having a suitable size to be coupled to the housing 501. Accordingly, dial 545 may be rotatably coupled to housing 501 and movable relative to housing 501 between first, second and third positions. Dial 545 includes an entry port 521 defining lumen 502 that defines a fluid flow path for withdrawing and/or transporting bodily fluid from a patient to collection device 500. Medical device (not shown) can be fluidly coupled to In this way, inlet port 521 can be configured to selectively locate pre-sample reservoir 570, first sample reservoir 580 and second sample reservoir 590. More specifically, when the dial 545 is in the first position, the flow controller 540 is arranged in the first configuration and the inlet port 521 communicates with the first opening 544a of the seal member 541 and the first outlet opening 503a of

the housing 501. is substantially aligned with Thus, as described in detail above with respect to collection device 400, first opening 544a of seal member 541 establishes fluid communication between inlet port 521 and first outlet opening 503a, and thus the inlet port. 521 is placed in fluid communication with pre-sample reservoir 570 . Similarly, when the dial 545 is turned (or driven) to the second position, the flow controller 540 is placed in the second configuration and the second outlet opening 544b is connected to the inlet port 521 and the second outlet opening 503b. , thus establishing fluid communication with the first flow path 535a, and when the dial 545 is turned to the third position, the flow controller 540 is disposed in the third configuration, and the third outlet opening 544c communicates with the inlet port. Fluid communication is established between 521 and the third outlet opening 503c and thus the second flow path 535a. Thus, the collection device 500 is applied to the pre-sample 570 as described in detail above with respect to the collection device 400 .

It can be used to transfer second and third volumes of bodily fluid to reservoir 580 and second sample reservoir 590, respectively.

[1136

] Figures 26-33 show a collection device 600 according to an embodiment. Collection device 600 includes flow diverter mechanism 620, flow controller 640 and sample reservoirs 680, 680', 690 and 690'. As further described herein, the collection device 600 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorganisms and/or microorganisms present on the skin. A fluid stream can be delivered that is substantially free of extracorporeal microorganisms, such as or other undesirable external contaminants. Collection device 600 may be of any suitable shape, size or configuration. For example, aspects and/or portions of collection device 600 may be similar in form and/or function to corresponding aspects and/or portions of any of collection devices 100, 200, 300, 400 and/or 500 described above. . Accordingly, such similar aspects and/or parts will not be described in further detail herein. By way of example, in some embodiments sample reservoirs 680, 680', 690 and 690' of collection device 600 are similar to sample reservoirs 480, 480', 490 and 490' included in collection device 400 of FIGS. may be substantially similar and/or the same in form and/or function as each.

[0084]

[1137] The flow diverting mechanism 620 includes a distribution member 629 and a set of coupling members 637a, 637b, 637c and 637d (see, eg, FIG. 27). Distribution member 629 is in fluid communication with coupling members 637a, 637b, 637c and 637d and is configured to provide and/or define a set of fluid flow paths for collecting bodily fluid from a patient. As shown in FIGS. 27 and 28, distribution member 629 includes a first outlet port 630 in fluid communication with pre-sample reservoir 670, a second outlet port 631 in fluid communication with first coupling member 637a; A third outlet port 632 in fluid communication with the second coupling portion 637b, a fourth outlet port 633 in fluid communication with the third coupling portion 637c, and a fifth outlet in fluid communication with the fourth coupling portion 637d. def

ines and/or forms a port 634;

[0085]

[1138] As shown in FIG. Pre-sample reservoir 670 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. For example, the pre-sample reservoir 670 can receive and contain a first amount or volume of bodily fluid from a patient, where the first amount of bodily fluid can be a predetermined amount or an unquantified amount. Additionally, the arrangement of flow diverter mechanism 620 and flow controller 640 allows pre-sample reservoir 670 to follow coupling portions 637a, 637b, 637c and 637d and/or bodily fluids with drawn from the patient, as described in further detail herein. It may be maintained fluidly isolated from the volume. Thus, outlet ports 631, 632, 633 and 634 direct fluid flow paths between flow controller 640 and coupling members 637a, 637b, 637c and 637d, respectively, as described in further detail herein. may be attached and/or otherwise defined. In some embodiments, the arrangement of first exit port 630 and pre-sample reservoir 670 can be substantially similar in form and function to pre-sample reservoirs 470 and/or 570. Accordingly, pre-sample reservoir 670 will not be described in further detail herein.

[0086]

[1139] As shown in FIG. 29, the first coupling member 637a defines a channel 638a that is fluidly coupled to the piercing member 655a. Coupling member 637a can be physically and fluidly coupled to distribution member 629, as described above. For example, channel 638a can receive a portion of distribution member second outlet port 631 and coupling member 637a can be physically and fluidly coupled thereto. In some embodiments, the surface of the second outlet port 631 forms a substantially fluid-tight seal (e.g., fluid-tight seal) with the inner surface of the coupling portion 637a that defines the flow path 638a.

(e.g., a friction fit) that can form a substantially hermetic seal. The piercing member 655a of the coupling portion 637a can be substantially similar in form and function to the piercing member 455a included in the collection device 400 of FIGS. 16-22. Accordingly, piercing member 655a will not be further described herein. The second coupling member 637b, the third coupling member 637c and the fourth coupling member 637d are similarly arranged. Accordingly, the second coupling member 637b, the third coupling member 637c and the fourth coupling member 637d each include piercing members 655b, 655c and 655d respectively and define channels 638b, 638c and 638d respectively. As described in further detail herein, first coupling member 637a, second coupling member 637b, third coupling member 637c and fourth coupling member 637d are used to connect flow diverting mechanism 620 to first sample reservoir 680, It can be selectively placed in fluid communication with each of the second sample reservoir 680', the third sample reservoir 690 and the fourth sample reservoir 690'.

[0087]

[1140] The flow controller 640 includes a dial 645 and a seal member 641, as shown in FIGS. A dial 645 of flow controller 640 is rotatably disposed within distribution member 629 (see FIGS. 32 and 33) and is movable between first, second, third and fourth positions. . Dial 645 inc

ludes an inlet port 621, a first outlet port 647 and a second outlet port 648, each in fluid communication with interior space 646 (see, eg, FIG. 30). Interior space 646 is configured to receive a portion of seal member 641, as described in further detail herein. Inlet port 621 can be fluidly coupled to a medical device (not shown) that defines a fluid flow path for drawing bodily fluid from a patient and/or transporting it to collection device 600. For example, inlet port 621 may be fluidly coupled to a needle or other lumen-defining device (e.g., flexible sterile tubing) directly or indirectly via an adapter 604 (see, e.g., FIGS. 26 and 27). First outlet port 647 is in fluid communication with pre-sample reservoir 670. For example, first outlet port 647 can be rotatably disposed within first outlet port 630 of distribution member 629. When dial 645 is in its first, second, third and fourth positions respectively, second outlet port 648 is connected to second outlet port 631, third outlet port 632, fourth outlet port 633 and It can be selectively placed in fluid communication with the fifth outlet port 634. Thus, the interior space 646 of the dial 645 is divided into a pre-sample reservoir 670, a first sample reservoir 680, a second sample reservoir 680', a third sample reservoir 690 and a fourth sample reservoir, as described in further detail herein. It can be selectively placed in fluid communication with the sample reservoir 690'.

[0088]

[1141] At least a portion of the sealing member 641 of the flow controller 640 is rotatably disposed within an interior space 646 of the dial 645 and is movable between a first position and a second position. Further, seal member 641 can be sized and shaped such that an outer surface of seal member 641 forms a substantially fluid-tight seal with an inner surface of dial 645 that defines at least a portion of interior space 646. As shown in FIG. 31, the sealing member 641 defines a first flow path 642 and a second flow path 644. As shown in FIG. When seal member 641 is in its first position within interior space 646, passage 642 fluidly isolates inlet port 621 from second outlet port 648 while allowing inlet port 621 and first outlet port 647 to communicate with each other. establish fluid communication therebetween. Similarly, when seal member 641 is in its second position within interior space 646, second flow path 644 fluidly isolates inlet port 621 from first outlet port 647 while allowing inlet port 621 and second outlet port 647 to flow through inlet port 621 and second outlet port 647. Establish fluid communication with outlet port 648. Collection device 600 operates similarly when dial 645 is rotated within dispensing member 629 to second, third and fourth positions. Accordingly, when inlet port 621 is placed in fluid communication with a patient (e.g., via a medical device coupled to inlet port 621 and/or adapter 604), first outlet port 630 of distribution member 629; 2 outlet port 631, third outlet port 632, fourth outlet port 633 and fifth outlet port 634 are in fluid communication with inlet port 621.

to allow bodily fluids to flow into pre-sample reservoir 670, first sample reservoir 680, second sample reservoir 680', third sample reservoir 690 and fourth sample reservoir 690', respectively. can be

[1142]

] In operation, the collection device 600 can be used to collect bodily fluids (eg, blood, plasma, urine, etc.) from a patient with reduced contamination. For example, entry port 621 of collection device 600 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), the seal member can be actuated (or rotated) to its first position, as shown in FIG. Alternatively, the seal member 641 can be preset in the first position and the collection device 600 can be otherwise sealed to maintain the sterility of the collection device 600. When seal member 641 is in its first position, flow controller 640 causes inlet port 621 and a first outlet port of distribution member 629 to flow through inlet port 621 from coupling members 637a, 637b, 637c and 637d while fluidly isolating inlet port 621 from coupling members 637a, 637b, 637c and 637d. 630 to establish fluid communication. Thus, in a manner similar to that described above with respect to collection device 400, as indicated by arrow II in FIG. It can be transferred into pre-sample reservoir 670 via first exit port 630 of member 629.

[0090]

[1143] Following collection of the bodily fluid pre-sample within pre-sample reservoir 670, seal member 641 may be actuated (rotated) relative to dial 645 from its first position to its second position. Similarly, dial 645 can be actuated (or rotated) until it reaches the second position relative to distribution member 629, as shown in FIG. When seal member 641 and dial 645 are in their second positions, flow controller 640 is disposed in a second configuration and second flow path 644 of seal member 641 fluidly isolates pre-sample reservoir 670 from inlet port 621. While establishing fluid communication between inlet port 621 and channel 638a of first coupling member 637a. With flow controller 640 in its second configuration, sample reservoir 680 is actuated by a user from its first configuration to its second configuration (e.g., by pushing piercing member 655a) to force a portion of the patient's body (e.g., vein) and the first sample reservoir 680. By moving the sample reservoir 680 to the second configuration, as described in detail above, the piercing member 655a is positioned inside the sample reservoir 680 piercing the vacuum seal of the sample reservoir 680. In this second configuration, that portion of the patient's body (eg, a vein) is exposed to a vacuum suction force from the sample reservoir 680 due to the negative pressure (vacuum) within the sample reservoir 680. Thus, as shown by arrows JJ in FIG. 33, body fluid is directed from that portion of the patient's body through inlet port 621, second channel 644, second outlet port 631 and channel 638a and through the piercing member of first coupling member 637a. It can be forced through 655a into the first sample reservoir 680.

[0091]

[1144] Once a desired volume of bodily fluid (eg, a second amount) has been collected in sample reservoir 680, the user may actuate (rotate) flow controller 640 to a third position and/or can be moved back to its first configuration to isolate the first sample reservoir 680 from the second flow path 644. When the sample reservoir 680 returns to the first configuration, the piercing member 655a is removed from the sample reservoir 680 and the seal (eg, self-sealing

membrane) of the sample reservoir 680 fluidly removes the first sample reservoir 680 from the flow path 635a. isolate to Filling of the other sample reservoirs is similarly performed with the flow controller 640 positioned in the third, fourth and fifth configurations, respectively.

[1145]

] Figures 34-40 show a collection device 700 according to an embodiment. The collection device 700 includes a flow diverter 720, a flow controller 740 and sample reservoirs 780 and 780. 90 (although there are holders for four sample reservoirs, only two sample reservoirs are included in the figure for clarity, and as part of the collection device 700 additional sample reservoirs (e.g. 5th, 6th, etc.). As further described herein, the collection device 700 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorganisms and/or microorganisms present on the skin. A bodily fluid stream can be delivered that is substantially free of extracorporeal microorganisms, such as other undesirable external contaminants. Collection device 700 may be of any suitable shape, size or configuration. For example, aspects and/or portions of collection device 700 may be substantially similar in form and/or function to corresponding aspects and/or portions of any of collection devices 100, 200, 300, 400, 500 and/or 600 described above. can be similar to Accordingly, such similar aspects and/or parts will not be described in further detail herein. By way of example, in some embodiments, sample reservoirs 780 and 790 of collection device 700 are substantially similar and/or similar in form and function to sample reservoirs 480 and 490, respectively, included in collection device 400 of FIGS. or may be the same.

[0093]

[1146] The flow diverter mechanism 720 includes a housing 701, a distribution member 729 and a base plate 771. As shown in FIG. As described above with respect to collection device 400, housing 701 has a first outlet opening 703a, a second outlet opening 703b, a second outlet opening 703a, a second outlet opening 703b, and a second outlet opening 703a, each configured to be in fluid communication with a different portion of distribution member 729. It defines three exit openings 703c, a fourth exit opening 703d and a fifth exit opening 703e. More specifically, distribution member 729 includes at least a portion of pre-sample reservoir 770 in fluid communication with first outlet opening 703a and a first fluid chamber 735a in fluid communication with second outlet opening 703b. , a second fluid chamber 735b in fluid communication with the third outlet opening 703b, a third fluid chamber 735c in fluid communication with the fourth outlet opening 703d, and a second fluid chamber 735c in fluid communication with the fifth outlet opening 703e. defines and/or forms four fluid chambers 735d. Additionally, housing 701 defines a recess 766 configured to movably receive at least a portion of flow controller 740, as described further herein.

[0094]

[1147] As shown in FIG. Pre-sample reservoir 770 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. The first outlet opening 703a of the housing 701 is substantially aligned with the open portion of the pre-sample reservoir 770 so that the

e pre-sample reservoir 770 can receive the flow of bodily fluid from the patient, as described in detail above. be able to. More specifically, distribution member 729 includes a set of walls 736 that can, for example, divide the interior space of distribution member 729 into portions and/or spaces that are fluidly isolated from one another. For example, as shown in FIG. 36, a set of walls 736 divides the interior space of distribution member 729 into pre-sample reservoir 770, first fluid chamber 735a, second fluid chamber 735b, third fluid chamber 735c and fourth fluid chamber 735c. It can be divided into chambers 735d. In some embodiments, wall 736 can equally define and/or form pre-sample reservoir 770 and fluid chambers 735a-735d. In other embodiments, pre-sample reservoir 770 can define a space that is different than the space defined by fluid chambers 735a-735d.

[0095]

[1148] The distribution member 729 is in fluid communication with the first piercing member 755a, the second piercing member 755b, respectively, with the first fluid chamber 735a, the second fluid chamber 735b, the third fluid chamber 735c and the fourth fluid chamber 735d. , a third piercing member 755c and a fourth piercing member 755d. Thus, piercing members 755a-755d can be used to pierce sample reservoirs 780 and 790 (and corresponding sample reservoirs not shown in FIGS. 34-40), as described in further detail herein. , thereby initiating bodily fluid flow.

[1149]

] The flow controller 740 of the collection device 700 includes a dial 745 and a seal member 741 . Seal member 741 is positioned within recess 766 of housing 701 (see, eg, FIGS. 38 and 40). More particularly, coupling flow controller 740 to housing 701 such that seal member 741 is positioned between and in contact with the surface of housing 701 defining recess 766 and the surface of dial 745 . can be done. Seal member 741 may be configured to form a substantially fluid-tight seal with the surface of dial 745 and the surface of housing 701 defining recess 766, as described in detail above. As shown in FIG. 35, the sealing member 741 defines a first opening 744a, a second opening 744b, a third opening 744c, a fourth opening 744d and a fifth opening 744e. The arrangement of the sealing member 741 is such that when the sealing member 741 is arranged in the recess 766, the first opening 744a, the second opening 744b, the third opening 744c, the fourth opening 744d, and the fifth opening 744e are formed. , the first outlet opening 703a, the second outlet opening 703b, the third outlet opening 703c, the fourth outlet opening 703d and the fifth outlet opening 703e of the housing 701, respectively. is.

[0097]

[1150] The dial 745 of the flow controller 740 is rotatably coupled to the housing 701 and is movable relative to the housing 701 between a first position, a second position, a third position, a fourth position, and a fifth position. be. Dial 745 includes an entry port 721 that connects entry port 721 to a medical device (either directly or indirectly via adapter 704) that defines a fluid flow path for withdrawing bodily fluid from a patient and/or transporting it to collection d

evice 700.) can be fluidly coupled. Inlet port 721 thus connects to pre-sample reservoir 770, first sample reservoir 780, second sample reservoir 780', third sample reservoir 790 and fourth sample reservoir 790, as described in further detail herein. ' can be configured to be selectively placed in fluid communication with a patient. When dial 745 is in the first position, flow controller 740 is disposed in a first configuration, aligning inlet port 721 substantially with first opening 744a of seal member 741 and first outlet opening 703a of housing 701. can be combined. Thus, the first opening 744a of the seal member 741 fluidly isolates the inlet port 721 from the outlet openings 703b, 703c, 703d and 703e, thereby fluidly isolating the inlet port 721 from the fluid chambers 735a-735d. Fluid communication is established between the inlet port 721 and the first outlet opening 703a while isolating to the first outlet port 703a. When the dial 745 is turned (or driven) to the second position, the flow controller 740 is placed in the second configuration and the second outlet opening 744b connects the inlet port 721 to the pre-sample reservoir 770 and the fluid chambers 735b-735b. Fluid communication is established between inlet port 721 and second outlet opening 703b while being fluidly isolated from 735d. Collection device 700 operates similarly when dial 745 is turned to the third, fourth and fifth positions. Accordingly, inlet port 721 is in fluid communication with the patient (eg, via a medical device coupled to inlet port 721).

[1151

] In some embodiments, housing 701 selectively limits movement of dial 745 from its first position to its second, third, fourth and fifth positions. be able to. In some other embodiments, the housing 701 can be configured to prevent movement of the dial moved to the fifth position. In other words, housing 701 can include a locking mechanism that prevents dial 745 from moving back from the fifth position to the first position. This feature allows flow chambers 735a-735d and/or

This reduces the risk that bodily fluids collected in pull reservoirs 780 and 790 are contaminated from bodily fluids contained in pre-sample reservoir 770 (which has a high risk of containing surface-bound microorganisms and/or other undesirable external contaminants). can be reduced. This locking mechanism can also protect medical personnel from exposure to blood-borne pathogens in patient samples, which may include HIV, hepatitis C, and the like. Dial 745 and/or housing 701 may also have mechanical detents that provide visual or tactile feedback to ensure correct alignment of dial 745 with respect to exit port 703a and exit openings 703a-703d in housing 701. and/or other indicators may also be included.

[0099]

[1152] Similar to the embodiment of the collection device 400 shown in FIGS. The pre-sample reservoir 770 can contain bodily fluids such as, for example, blood, plasma, urine, and the like. Pre-sample reservoir 770 is configured to be fluidly coupled to first outlet port 703a of collection device 700 (located within housing 701). During operation of the collection device 700, when the flow controller 740 is in the first position, body fluid flows from a portion of the patient's body (eg, a vein) through the inlet port 721, into the pre-sample reservoir 770, into the s

seal member 741. is drawn into the opening for the pre-sample reservoir 744a and the first exit port 703a located at . Pre-sample reservoir 770 is configured to contain a first volume of fluid to be drawn from a patient, where the first volume of bodily fluid can be a predetermined volume or an unquantified volume. Thereby the first volume of bodily fluid is fluidly isolated from a second and/or third and/or fourth and/or fifth volume of bodily fluid subsequently withdrawn from the patient.

[0100]

[1153] In operation, the collection device 700 can be used to collect bodily fluids (eg, blood, plasma, urine, etc.) from a patient with reduced contamination. For example, entry port 721 of collection device 700 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture, dial 745 is turned until it reaches the first position, as shown in FIGS. Alternatively, the dial 745 can be preset in the first position and the collection device 700 can be otherwise sealed to maintain the sterility of the collection device 700, as described above. With the dial 745 in the first position, the flow controller 740 is placed in a first configuration and the first outlet opening 744a of the seal member 741 fluidly connects the inlet port 721 from the four sample flow paths 735a-735d. While in isolation, fluid communication is established between inlet port 721 (contained within housing 701) and first outlet port 741 . In this first configuration, bodily fluids are directed from that portion of the patient's body, as indicated by arrows KK in FIG. through and into the pre-sample reservoir 770 defined by the distribution member 770 . Accordingly, as described in detail above, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 770 immediately after venipuncture and segregated from subsequent samples.

[0101]

[1154] Following the collection of the bodily fluid pre-sample within the pre-sample reservoir 770, the dial 745 can be actuated (or rotated) until it reaches the second position, as shown in FIGS. When dial 745 is in the second position, flow controller 740 is placed in a second configuration, and second outlet opening 744 a of seal member 741 fluidly isolates pre-sample reservoir 770 from inlet port 721 while allowing inlet port 721 to flow. Fluid communication is established between port 721 and first fluid chamber 735a. Once the first fluid chamber 735a is filled with bodily fluid, the flow controller 740 can be moved to the third position to isolate and seal the first flow path 735a from the external environment. Additionally, the sample reservoir 780 is actuated from the first configuration to the second configuration to transfer bodily fluid from the first fluid chamber 735a to the sample reservoir 780.

can be sent. For example, sample reservoir 780 may be user or automatically actuated from a first configuration to a second configuration (pressing piercing member 755a) to allow a portion of the patient's body (e.g., a vein) to move between sample reservoir 780 and sample reservoir 780. can establish fluid communication with the As described above, moving the sample reservoir 780 to the second configuration causes the piercing member 755a to pierce the vacuum seal of the sample reservoir 780 and be positioned inside the sample reservoir 780 . In a

second configuration, that portion of the patient's body (eg, a vein) is subjected to vacuum suction from the sample reservoir 780 due to the negative pressure (vacuum) existing within the sample reservoir 780 in some embodiments. Thus, as indicated by arrow LL in FIG. 40, bodily fluids flow from that portion of the patient's body through inlet port 721, second outlet opening 744b in seal member 741, second outlet opening 703b in housing 701, second It flows into the first sample reservoir 780 through the fluid chamber 735b.

[1155]

] Once a desired amount of bodily fluid (eg, a second amount) has been collected in sample reservoir 780, the user may actuate (rotate) flow controller 740 to a third position and/or The sample reservoir 780 can be moved back to its first configuration to isolate the first sample reservoir 780 from the inlet port 721 . When the sample reservoir 780 returns to the first configuration, the piercing member 755a is removed from the sample reservoir 780 and the seal (eg, self-sealing membrane) of the sample reservoir 780 allows the first sample reservoir 780 to enter the second fluid chamber 735b and the exterior. Fluid isolation from the environment. Filling of the other sample reservoirs is done in the same manner with the flow controller 740 in the third, fourth and fifth configurations respectively.

[0103]

[1156] In some embodiments, the collection device 700 can be configured such that there is no set of walls 736 separating the different fluid chambers 735a-735d within the distribution member 729 (detailed in FIG. 16). (see cross section). In such embodiments, the distribution member 729 is divided between the pre-sample reservoir 770 and the associated fluid chamber 735 (ie, the fluid chamber is not separated into four separate portions by wall 736). In such embodiments, the user can fill all four sample reservoirs at once by actuating (rotating) dial 745 to either the second, third, fourth or fifth position. can be done.

[0104]

[1157] Any of the embodiments described herein can be used, for example, to meter (e.g., quantify) the flow of bodily fluid into a pre-sample reservoir and/or a sample reservoir. Can be used with metering devices. In some cases, laboratory standard practice limits the exact inoculation volume of bodily fluids (e.g., blood samples) due to the fact that fill volumes are judged visually by clinicians and/or phlebotomists and are therefore subject to human error. Consistent compliance is not ensured. The volume indicator on the blood collection bottle is difficult to read when held, and the fact that the collection bottle is not held upright during the withdrawal procedure contributes to the inaccurate volume of the bodily fluid sample received from the patient. could be a factor. Insufficient sample volume (eg, less than the manufacturer's recommendation) can reduce the sensitivity of the culture test and lead to false-negative results. In addition, briefing materials and instructions for certain types of test supplies and equipment (e.g., blood culture bottles designed for use with automated microbial detection systems produced by manufacturers such as Becton Dickinson of Franklin Lakes, NJ). Filling volumes in excess of the manufacturer's recommendations, as indicated in the literature, may result in false

positives. Thus, flow metering and volume display capabilities allow laboratory technicians and/or medical personnel (e.g., phlebotomists) to transfer sample reservoirs to incubators or other laboratories, depending on how the sample needs to be processed. The volume of bodily fluid collected in each individual sample reservoir can be verified prior to placement within the testing device. The laboratory technician and/or phlebotomist may also provide accurate volume information (e.g., in medical records, databases, spreadsheets, etc.) for clinician evaluation when results are received.

), which helps reduce the likelihood of misinterpretation of false negative and/or false positive results.

[1158]

] By way of example, FIGS. 41-45 illustrate a collection device 800 that can include one or more metering devices. Collection device 800 includes flow diverter mechanism 820, flow controller 840, display 875 and sample reservoir 880. As further described herein, the collection device 800 can be moved between first, second and third configurations to remove, for example, microorganisms present on the skin and/or other undesirable external contaminants, and the like. , can deliver a body fluid stream that is substantially free of extracorporeal microorganisms. Collection device 800 may be of any suitable shape, size or configuration. For example, aspects and/or portions of collection device 600 may be similar in form and/or function to corresponding aspects and/or portions of any of collection devices 100, 200, 300, 400, 500, 600 and/or 700 described above. can be substantially similar. Accordingly, such similar aspects and/or parts will not be described in further detail herein. By way of example, in some embodiments, sample reservoir 880 of collection device 800 is substantially similar and/or identical in form and function to sample reservoir 480 included in collection device 400 of FIGS. could be.

[0106]

[1159] As shown in FIGS. 41-43, the flow diverter mechanism 820 includes an actuator portion 822 (eg, a first portion), an intermediate portion 823 (eg, a second portion) and a coupling portion 824 (eg, a third portion). including. Actuator portion 822 of flow diverter mechanism 820 is substantially cylindrical including a set of actuator walls that define interior space 806. More specifically, actuator portion 822 has a first end that is substantially closed and an opposite end that is substantially open to allow access to interior space 806. a side second end. As such, actuator portion 822 can movably receive at least a portion of flow controller 840, as described in further detail herein. Actuator portion 822 further includes inlet port 821 and outlet port 831. Inlet port 821 is fluidly connected (either directly or indirectly via adapter 804) to a medical device that defines a fluid flow path for withdrawing bodily fluid from a patient and/or transporting it to collection device 800, as described in detail above. can be linked together.

[0107]

[1160] The outlet port 831 of the actuator portion 822 may be selectively positioned to place a portion of the interior space 806 of the actuator portion 822 in fluid communication with the interior space 807 defined by the intermediate portion 823. As shown in FIG. 43, intermediate

portion 823 is positioned between actuator portion 822 and coupling portion 824 . Although not shown in FIGS. 41-45, intermediate portion 823 can include a metering device that can be configured to meter a volume of bodily fluid transferred to sample reservoir 880, for example. For example, in some embodiments, a flow metering device can be fluidly coupled to outlet port 831 to meter the flow of bodily fluid therethrough. As shown in FIGS. 41 and 42, the intermediate portion 823 includes a display 875 that provides a user with visual indicators and/or information related to the volume of bodily fluid that has flowed through the outlet port 831, for example. can provide. In other embodiments, the flow metering device may be placed at any other suitable location within or along the flow diverter 820 .

[1161

] The coupling portion 824 can be physically and fluidly coupled to the intermediate portion 823 . For example, in some embodiments, coupling portion 824 is partially disposed within interior space 807 of intermediate portion 823 and attached thereto at least temporarily via a friction fit, press fit, snap fit, threaded connection, adhesive, or the like. can be linked together. Coupling portion 824 is configured to receive a portion of sample reservoir 880, as described in detail above, so that it can puncture the vacuum seal of sample reservoir 880, thereby initiating bodily fluid flow. includes a piercing member 855 that can be used to

[1162

] The flow controller 840 of the collection device 800 is disposed at least partially within the interior space 806 defined by the actuator portion 822 and is movable between first, second and third configurations. is. As shown in FIGS. 42 and 43, the flow controller 840 includes a movable member 850 having a first sealing member 861, a second sealing member 862 and a third sealing member 863, and a biasing member 859 (eg, a spring or the like). including. Seal members 861 , 862 and 863 are in contact with the inner surface of actuator portion 822 that defines interior space 806 . Accordingly, as described in further detail herein, each of the seal members 861, 862 and 863 has an inner surface that can, for example, divide the interior space 806 of the actuator portion 822 into fluidly isolated portions; A fluid-tight seal can be formed.

[0110]

[1163] The movable member 850 is movable within the interior space 806 between a first position, a second position and a third position. The arrangement of movable member 850 is such that seal members 861, 862 and 863 selectively move within interior space 806 as movable member 850 moves between its first, second and third positions. It can be. More specifically, the first sealing member 861 can move simultaneously with the movable member 850 as the movable member 850 moves between its first, second and third positions. A second seal member 862 and a third seal member 863 can be fixedly coupled to each other (eg, positioned at a fixed distance from each other) and slidably disposed about a portion of the movable member 850, which This causes movable member 850 to move from its first position (see, eg, FIG. 43) to its first position while second sealing member 862 and third sealing member 863 remain

in a substantially fixed position relative to actuator portion 822 . It may be possible to move to two positions (see, eg, FIG. 44). For example, as movable member 850 moves between its first and second positions, second sealing member 862 and third sealing member 863 can remain in a substantially fixed position, thereby providing an inlet port. Port 821 is located on a first side of second sealing member 862 and exit port 831 is located on a second side of second sealing member 862 opposite the first side. Thus, when movable member 850 is in its first position (FIG. 43) and its second position (FIG. 44), inlet port 821 is in contact with first sealing member 861, as described in further detail herein. is in fluid communication with a portion of the interior space 806 defined between the second seal member 862 and the exit port is in the interior space 806 defined between the second seal member 862 and the third seal member 863. in fluid communication with the part.

[0111]

[1164] The arrangement of the flow controller 840 is such that the first sealing member 861 moves relative to the second sealing member 862 and the third sealing member 863 when the movable member 850 moves from its first position to its second position. , can be Movement of first seal member 861 relative to second seal member 862 can enlarge the space defined therebetween, thereby forming and/or otherwise defining pre-sample reservoir 870 . can do. In addition, seal members 861 and 862 form a substantially fluid-tight seal with the inner surface of actuator portion 822 such that pre-sample reservoir 870 defined between first seal member 861 and second seal member 862 is , are fluidly isolated from the rest of the interior space 806 . Thus, inlet port 821 can be in fluid communication with pre-sample reservoir 870 when moveable member 850 moves from its first position to its second position. As movable member 850 moves from its second position (see, eg, FIG. 44) to its third position (see, eg, FIG. 45), a portion of movable member 850 contacts third sealing member 863. , the first sealing member 861 , the second sealing member 862 and the third sealing member 863 can be moved substantially simultaneously within the interior space 806 . Accordingly, both the inlet port 821 and the outlet port 831 provide fluid communication to the portion of the interior space 806 defined between the second sealing member 862 and the third sealing member 863, as described in further detail herein. A second sealing member 862 can be moved relative to the inlet port 821 in communication.

[0112]

[1165] In operation, the collection device 800 can be used to collect bodily fluids (eg, blood, plasma, urine, etc.) from a patient with reduced contamination. For example, entry port 821 of collection device 800 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). With inlet port 821 coupled to the lumen defining device, flow controller 840 can be moved from its first configuration to its second configuration. Thus, a user can apply a force to move movable member 850 from its first position to its second position, as indicated by arrow MM in FIG. As described above, the first sealing member 861 moves simultaneously with the movable member 850, thereby enlarging the space defined between the first seal

ng member 861 and the second sealing member 862, thereby A sample reservoir 870 is formed and/or defined. First sealing member 861 and second sealing member 862 form a substantially fluid-tight seal with the inner surface of actuator portion 822 that defines interior space 806 such that first sealing member 861 and second sealing member 862 are in contact with each other. A negative pressure is created in the pre-sampling reservoir 870 by the increase in volume between . Accordingly, once fluid communication is established between a portion of the patient's body (eg, a vein) and the pre-sample reservoir 870 (eg, via inlet port 821 in FIG. 44), indicated by arrows NN in FIG. As such, the negative pressure differential between pre-sample reservoir 870 and that portion of the patient's body draws fluid into pre-sample reservoir 870 through inlet port 821 . In this first configuration, flow controller 840 also fluidly isolates pre-sample reservoir 870 from outlet port 831 . Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 870 (for example) immediately after venipuncture and isolated from subsequent samples. In this manner, the collection device 800 can be used to collect surface microorganisms and/or other undesirable A first volume of bodily fluid most likely to contain an external contaminant contaminates a subsequent volume of bodily fluid sample collected and used for diagnosis or other testing that may be affected by the contaminant can be prevented. In some embodiments, the metering device can meter a volume of bodily fluid placed in pre-sample reservoir 870 and present a value associated with that volume on display 875 .

[0113]

[1166] Following collection of the body fluid pre-sample volume in pre-sample reservoir 870, moveable member 850 is moved from its second position to its third position, as indicated by arrow OO in FIG. It can be arranged in a third configuration. As described above, when movable member 850 moves from its second position to its third position, a portion of movable member 850 is placed in contact with third sealing member 863 . Accordingly, the movable member 850 moves the first sealing member 861 , the second sealing member 862 and the third sealing member 863 substantially simultaneously within the interior space 806 . Accordingly, the second sealing member 862 is positioned such that both the inlet port 821 and the outlet port 831 are in fluid communication with the portion of the interior space 806 defined between the second sealing member 862 and the third sealing member 863 . It can be moved relative to port 821 . Furthermore, because the volume of body fluid is fluidly isolated within the pre-sample reservoir 870, movement of the second seal member 862 and the third seal member 863 in the direction of the first seal member 861 is restricted (i.e., body fluid is a substantially incompressible fluid). Thus, the pre-sample volume of bodily fluid is sequestered within pre-sample reservoir 870 and the space defined between second sealing member 862 and third sealing member 863 is separated by inlet port 821 and outlet port 821 . 831 defines a fluid flow path. Further, flow controller 840 is positioned such that when in its third configuration, first sealing member 861 is in contact with biasing member 859 such that at least a portion of the force exerted by the user on movable member 850 is The biasing member 859 is operable to deform,

compress, bend and/or otherwise reconfigure. Accordingly, the biasing member 859 acts against the first sealing member 861 to resist movement of the flow controller 840 from its second configuration to its third configuration, as described in further detail herein. can affect

[1167]

] As described in detail above, piercing member 855 provides a vacuum seal for sample reservoir 880.

The sample reservoir 880 can be positioned relative to the collection device 800 such that the hole is pierced and placed inside the sample reservoir. A pressure differential between the sample reservoir 880 (eg, vacuum or negative pressure) and that part of the body draws body fluid into the sample reservoir 880. In other words, in the second configuration, flow controller 840 and flow diverter mechanism 820 direct body fluid from the patient through inlet port 821, second sealing member 862, and third sealing member 863, as indicated by arrow PP in FIG. through the portion of the interior space 806 defined therebetween, and the exit port 831 of the actuator portion 822, through the piercing member 855 of the intermediate portion 823 and the coupling portion 824, and into the sample reservoir 880; Establish a fluid flow path. As discussed above, a metering device (not shown) can meter the volume of bodily fluid transferred, for example, through outlet port 831 and can present a value associated with the volume of bodily fluid on display 875.

[0115]

[1168] Once a desired volume of bodily fluid (eg, a second amount) has been collected in the sample reservoir 880, the user can remove and/or reduce the force applied to the movable member 850, thereby, a biasing member 859 can move the first sealing member 861 and the movable member 850 from their third position toward their second position. Further, due to the substantially incompressible nature of the bodily fluid disposed within pre-sample reservoir 870, movement of first sealing member 861 transfers force through the volume of bodily fluid, thereby increasing second sealing member 862 and third sealing member 862. Seal members 863 are moved from their third position toward their second position. In some embodiments, the biasing member 859 is operable to move the second seal member 862 relative to the actuator portion 822, for example, to a fourth position where the inlet port 821 can be substantially blocked. The resulting force can be applied to the first sealing member 861. Accordingly, inlet port 821 can be fluidly isolated from interior space 806 of actuator portion 822. Additionally, the piercing member 855 can be removed from the sample reservoir 880 and a seal (eg, a self-sealing membrane) can fluidly isolate the bodily fluid sample from the space outside the sample reservoir 880. Subsequent filling of the sample reservoir is similarly accomplished by placing piercing member 855 into the sample reservoir and moving flow controller 840 to the third configuration to allow bodily fluid to flow from the patient into the sample reservoir. can be done.

[0116]

[1169] FIGS. 46-53 illustrate a collection device 900 according to an embodiment. Collection

device 900 includes flow diverter mechanism 920, flow controller 940 and sample reservoirs 980, 980', 990 and 990'. As further described herein, the collection device 900 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorganisms and/or microorganisms present on the skin. or a body fluid stream that is substantially free of extracorporeal microorganisms, such as other undesirable external contaminants. Collection device 900 may be of any suitable shape, size or configuration. For example, aspects and/or portions of collection device 900 may be corresponding aspects and/or portions and configurations and/or of any of collection devices 100, 200, 300, 400, 500, 600, 700 and/or 800 described above. They may be substantially similar in function. Accordingly, such similar aspects and/or parts will not be described in further detail herein. By way of example, in some embodiments, sample reservoirs 980, 980', 990 and 990' of collection device 900 are similar to sample reservoirs 680, 680', 690 and 690 included in collection device 600 of FIGS. ' can be substantially similar and/or the same in form and function.

[1170]

] The flow diverter mechanism 920 includes a housing 901, a distribution member 929 and movable members 950a, 950b, 950c and 950d. Housing 901 is physically and fluidly coupled to distribution member 929 to provide and/or define a set of fluid flow paths for collecting bodily fluids from a patient. Housing 901 may be included in a flow metering device and/or otherwise (e.g., electrically and/or mechanically) as described in further detail herein. and a set of displays 975' (eg, liquid crystal displays (LCDs), etc.) that can be coupled together. Housing 901 defines recess 966, exit openings 903a, 903b, 903c, 903d, 903e and movable member openings 950a, 950b, 950c, 950d (also referred to herein as "openings"). Recess 966 is configured to receive seal member 941 included in flow controller 940, as described in further detail herein. First outlet opening 903a, second outlet opening 903b, third outlet opening 903c, fourth outlet opening 903d and fifth outlet opening 903e are each in fluid communication with different portions of distribution member 929. It is configured to define different fluid flow paths. More specifically, distribution member 929 includes at least a portion of pre-sample reservoir 970 in fluid communication with first outlet opening 903a and a first channel 935a in fluid communication with second outlet opening 903b. , a second passageway 935b in fluid communication with the third outlet opening 903b, a third passageway 935c in fluid communication with the fourth outlet opening 903d, and a second passageway 935c in fluid communication with the fifth outlet opening 903e. defines and/or forms four channels 935;

[0118]

[1171] As shown in FIGS. Pre-sample reservoir 970 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. As described in detail above with respect to pre-sample reservoir 470 in FIGS. 16-22, first outlet opening 903a of housing 901 is pre-mounted to allow pre-sample reservoir 970 to receive a flow of bodily fluid from the patient. It can be substantially aligned with the open portion of sample reservoir 970. Channels 935a-935d extend radially from the center of distribution member 929 and are arranged such that each

channel 935a, 935b, 935c and 935d is fluidly isolated from pre-sample reservoir 970 and the other channels. ing. Thus, channels 935a, 935b, 935c and 935d have first ends defining openings substantially aligned with outlet openings 903b, 903c, 930d and 903e, respectively, and movable members 950a, 950b, A fluid flow path may be directed and/or otherwise defined between the second ends defining openings or ports configured to receive 950c and 950d, respectively. Although distribution member 929 is shown in FIGS. 47 and 48 as including channels 935a-935d that are substantially closed, in other embodiments, with respect to distribution member 429 of FIGS. Channels 935a-935d can be substantially open as shown and described above. Accordingly, distribution member 929 of collection device 900 can function substantially similar to distribution member 429 of collection device 400 .

[0119]

[1172] Movable members 950a, 950b, 950c and 950d are movably disposed in respective openings 905a, 905b, 905c and 905d of housing 901 and corresponding openings defined by the second end of distribution member 929. be. Although not shown in FIGS. 46-53, in some embodiments moveable members 950a, 950b, 950c and 950d are biased members, as described in detail above with respect to moveable members 250 and 250' of collection device 200. etc. can be operatively coupled. Thus, movable members 950a, 950b, 950c and 950d are actuated (moved) by a user from first and second positions relative to housing 901 and distribution member 929 to direct fluid flow to a first sample. It can be directed into each of reservoir 980, second fluid reservoir 980', third fluid reservoir 990 and fourth sample reservoir 990'. Movable members 950a, 950b, 950c and 950d are substantially identical and therefore will be described with respect to a single movable member 950 in FIG. Additionally, some portions of movable member 950 may be substantially similar to movable members 250 and 350 described above. Accordingly, some portions of movable member 950 are not described in further detail herein. Movable member 950 defines an internal cavity 952 in fluid communication with inlet port 953 and piercing member 955 . The piercing member is substantially similar to that detailed above. The inlet port 953 extends through a set of walls that define the interior space 952 of the movable member 950 with corresponding passages 935a, 935b, 935c.

Alternatively, an internal chamber 952 is defined for selective placement in fluid communication with 935d.

[1173

] As shown in FIG. The flow metering mechanism 967 can be, for example, a wheel or the like that can include a set of spokes or fins. In this manner, bodily fluid can enter inlet port 953 of movable member 950 and flow past flow metering device 967 , thereby allowing flow metering device 967 to rotate relative to movable member 950 . Accordingly, the rotational features of the flow metering device 967 may be usable in determining the volume of bodily fluid transferred to the interior space 952 of the movable member 950, the volumetric flow rate, and the like. Although not shown in FIGS. 46-53, flow control mechanism 967 of movable member 950 is operably coupled to display 975 ' of housing 901 . Accordingly, as bodily fluids are transferred

rrred to sample reservoirs 980, 980', 990 and/or 990', for example, volumetric information related to the flow of bodily fluids can be presented on display 975'. In this way, a user can operate the collection device 900 to collect a bodily fluid sample from a patient, e.g. One can be visualized.

[0121]

[1174] The flow controller 940 of the collection device 900 includes a dial 945 and a seal member 941. Seal member 941 is disposed within recess 966 of housing 901. More particularly, flow controller 940 is coupled to housing 901 such that seal member 941 is positioned between and in contact with the surface of housing 901 defining recess 966 and the surface of dial 945. be able to. As described in detail herein, sealing member 941 can be configured to form a substantially fluid-tight seal with the surface of dial 945 and the surface of housing 901 defining recess 966. As shown in FIG. 47, the sealing member 941 defines a first opening 944a, a second opening 944b, a third opening 944c, a fourth opening 944d and a fifth opening 944e. As for the arrangement of the sealing member 941, when the sealing member 941 is arranged in the recess 966, the first opening 944a, the second opening 944b, the third opening 944c, the fourth opening 944d, and the fifth opening 944e are opened. , the first outlet opening 903a, the second outlet opening 903b, the third outlet opening 903c, the fourth outlet opening 903d and the fifth outlet opening 903e of the housing 901, respectively. is.

[0122]

[1175] The dial 945 of the flow controller 940 is rotatably coupled to the housing 901 and is movable relative to the housing 901 between a first position, a second position, a third position, a fourth position, and a fifth position. be. Dial 945 includes an entry port 921 that connects entry port 921 to a medical device (either directly or indirectly via adapter 904) that defines a fluid flow path for drawing bodily fluid from a patient and/or transporting it to collection device 900.) can be fluidly coupled. Inlet port 921 thus connects to pre-sample reservoir 970, first sample reservoir 980, second sample reservoir 980', third sample reservoir 990 and fourth sample reservoir 990, as described in further detail herein. ' can be configured to be selectively placed in fluid communication with a patient. configuring dial 945 to rotate through first, second, third, fourth and fifth positions in a manner substantially similar to that described above with respect to dial 445 of collection device 400; , and therefore will not be described in further detail here.

[1176]

] As shown, the dial 945 can further include a display 975 that can be configured to present volumetric information related to the flow of bodily fluids. For example, although not shown in FIGS. 46-53, a dial may be a flow metering device included in movable member 950 967, can include flow metering devices and the like. Thus, the flow metering device can, for example, meter the flow of bodily fluid through inlet port 921 such that volumetric information associated with the flow of bodily fluid through inlet port 921 is presented on display 975 of dial 945. , may be operatively coupled to the display 975.

[1177

] In operation, the collection device 900 can be used to collect bodily fluids (eg, blood, plasma, urine, etc.) from a patient with reduced contamination. For example, entry port 921 of collection device 900 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), dial 945 is actuated (or turned) until it reaches the first position, as shown in FIGS. Alternatively, dial 945 can be preset to the first position and collection device 900 can be otherwise sealed to maintain sterility of collection device 900 .

[0125]

[1178] As described above, when the dial 945 is in the first position, the flow controller 940 is disposed in the first configuration, and the first opening 944a of the seal member 941 connects the inlet port 921 to the four flow paths 935a to 935d. Fluid communication is established between inlet port 921 (contained within housing 901) and first outlet port 930 while being fluidly isolated from 935d. Further, sample reservoirs 980, 980', 990 and 990' are fluidly isolated from inlet port 921 in the first configuration and are part of the patient's body (e.g., A fluid flow path is defined between the vein) and the pre-sample reservoir 970 . In this first configuration, bodily fluids are forced (e.g., by gravity, vacuum, etc.) from that portion of the patient's body through inlet port 921, first opening 944a in seal member 941, and first outlet port 903a in housing 901. through and into the pre-sample reservoir 970 . In the first form, flow controller 940 also fluidly isolates pre-sample reservoir 970 from flow paths 935a-935d. Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 970 immediately after venipuncture and isolated from subsequent samples. In this way, using the collection device 900, a first volume of bodily fluid most likely to contain surface microorganisms and/or other undesirable contaminants may be diagnosed or otherwise affected by the contaminant. Subsequent amounts of bodily fluid samples collected and used for testing can be avoided from contaminating. Additionally, the display 975 can present information received from a flow control mechanism (not shown) related to, for example, the volume of bodily fluid transferred to the pre-sample reservoir 970 . Thus, a precise volume of bodily fluid can be transferred to and fluidly isolated within the pre-sample reservoir.

[0126]

[1179] Following the collection of the bodily fluid pre-sample within the pre-sample reservoir 970, the dial 945 can be actuated (or rotated) until it reaches the second position, as shown in FIGS. When the dial 945 is in the second position, the flow controller 940 is disposed in the second configuration, and the second opening 944b of the seal member 941 fluidly isolates the pre-sample reservoir 970 from the inlet port 921 while allowing the inlet port 921 to flow. Fluid communication is established between 921 and channel 935a. With flow controller 940 in the second configuration, movable member 950a is actuated (i.e., depressed) by a user from a first position to a second position to allow patient (eg, vein) and first sample reservoir 880 to move. can establish fluid communication between the More specifically, as indicated by arrow

RR in FIG. to be placed in the first sample reservoir 980 .

[1180

] While in the second position, the inlet port 953 of the movable member 950 is substantially aligned with and in fluid communication with the first flow path 935a, thereby allowing body fluid to flow through the first flow path 935a. can flow from into the internal cavity 952 of the working member 950 and out of the piercing member 955 into the first sample reservoir 980 . Sample reservoir 980 (e.g. vacuum or negative pressure)

) and the first channel 935 a draws bodily fluid into the sample reservoir 980 . In other words, in the second configuration, flow controller 940 and movable member 950a establish a fluid flow path between inlet port 921 of dial 945 and first sample reservoir 980, as indicated by arrow SS in FIG. In addition, flow of bodily fluids through movable member 950 a causes flow metering mechanism 967 to rotate relative to movable member 950 . Thus, rotation of flow metering mechanism 967 may be usable in determining the volume of bodily fluid sample transferred to sample reservoir 980 . Additionally, display 975 ' can present information received from flow control mechanism 967 related to, for example, the volume of bodily fluid transferred to sample reservoir 980 . Therefore, a precise volume of bodily fluid can be transferred to the sample reservoir 980 . For example, in some cases, collection device 900 is used to collect three sample volumes of 20 mL each in first sample reservoir 980, second sample reservoir 980', and third sample reservoir 990 (i.e., a total of 60 mL of sample volume is collected).

[0128]

[1181] Once a desired volume of bodily fluid (eg, a second amount) has been collected in the first sample reservoir 980, the user releases the movable member 950 to cause the biasing member (not shown) to It can be allowed to move back to the first position. When movable member 950 returns to its first position, piercing member 955 is removed from first sample reservoir 980 and a seal (eg, a self-sealing membrane) fluidly disconnects first sample reservoir 980 from internal flow path 935 . isolate to Using the collection device 900, transfer the second sample volume to the second sample reservoir 980' and the third sample volume to the third sample by rotating the dial 945 to its third, fourth and fifth positions, respectively. A fourth sample volume can be similarly transferred to reservoir 990 to fourth sample reservoir 990'.

[0129]

[1182] In some cases, the fluid collection device 900 allows the clinician and/or phlebotomist to open the package containing the fluid collection device 900, remove only the housing 901 (including the dispensing member 929), and remove the housing 901. It can be carried by the patient's bedside. The clinician and/or phlebotomist performs a venipuncture (or employs any other method of accessing the patient's bodily fluids) into a portion of the patient's body (e.g., a vein) using any standardized technique be able to. Following venipuncture, the clinician and/or phlebotomist can collect the total blood volume required for all samples. For example, a clinician and/or phlebotomist can collect a 2.5 mL pre-sample diversion volume and a 10 mL sample volume for each of the four sample reservoirs, whereby the collected bodily fluid (e.g., b

lood) totals 42.5 mL. Following collection of a desired amount of bodily fluid, the hypodermic needle can be removed from that portion of the patient's body (e.g., a vein) and the clinician and/or phlebotomist can access the housing 901 (which contains the bodily fluid). can be placed on top of 4-pack (or 2-pack) pre-sterilized sample reservoirs with the membrane tops pre-placed in custom trays that match the shape of housing 901. By using such pre-sterilized packs of sample reservoirs, the clinician does not have to perform the process step of "wiping" the sample reservoir tops with a sterilant, thereby, for example, sterilizing the reservoir tops. Reduced potential for contamination if inappropriate and/or insufficient. A clinician and/or phlebotomist can then trigger automatic inoculation of a sample reservoir containing bodily fluid with precise volume control. In some embodiments, after inoculation of the sample reservoirs is complete, the entire device 900 with volume information displayed for each individual sample reservoir can be sent to a laboratory for analysis. In other embodiments, sample reservoirs 980 and/or 990 are individually

[1183

] The collection device 900, with reference to FIGS.

Although shown and described as including 975 and 975', in other embodiments the collection device can include any suitable flow metering mechanism with any suitable output indicator. For example, Figures 54 and 55 show a flow diverter 1020 and a flow controller 1040 according to embodiments. Flow diverter 1020 and flow controller 1040 may be substantially similar in form and function to flow diverter 920 and flow controller 940, respectively. Accordingly, similar parts will not be described further herein. However, flow diverter 1020 and flow controller 1040 may differ in the placement of set of displays 1075. For example, flow diverting mechanism 1020 includes housing 1001 configured to movably receive a set of movable members 1050a, 1050b, 1050c and 1050d, each of which can include a flow metering mechanism, as described above with respect to movable member 950. include. Accordingly, movable members 1050a, 1050b, 1050c and 1050d can be used to determine the precise volume of bodily fluid that is transported through them. As shown in FIG. 55, the display 1075 of the housing 1001 provides a first illumination for a small volume (eg, 5 mL), a second illumination associated with an intermediate volume (eg, 20 mL), and an acceptable and/or large volume. A set of three lights can be included, including a third light associated with (eg, 40 mL). In this manner, when the flow of bodily fluid is transferred through the flow controller 1040 and the flow diverter mechanism 1020, for example into the first movable member 1050a, the flow metering mechanism contained therein can send a signal or the like to the display. , the display is operable to illuminate the first light, the second light and/or the third light according to the volume of bodily fluid transferred through the movable member 1050.

[0131]

[1184] In other embodiments, movable members 1050a, 1050b, 1050c, and 1050d can be moved from a first position to a second position, a third position, or a fourth position relative to housing 1001. In such embodiments, their positions can be associated with, for example, the

intended volume of bodily fluid to be transferred to the sample reservoir. For example, in some embodiments, a user can actuate (eg, move) movable member 1050a from its first position to its second position. In such embodiments, the second position can be associated with, for example, a small volume (eg, 10 mL) of bodily fluid to be transferred to the sample reservoir. In some embodiments, housing 1001 and/or moveable member 1050a can temporarily hold moveable member 1050a in a second position until a low volume of sample has been transferred to the sample reservoir. , locks, fasteners, protrusions, recesses, and the like. Further, when positioned in the second position, display 1075 is configured to illuminate a first illumination associated with the smaller volume to indicate to the user the preset volume of bodily fluid to be transferred to the sample reservoir. can do. Once a desired volume of bodily fluid has been transferred to and fluidly isolated within the sample reservoir, the flow diverter mechanism 1020 can be configured to automatically return the movable member 1050a to its first position. In this manner, flow diverter mechanism 1020 and flow controller 1040 can be physically and fluidly coupled to any number of sample reservoirs and used to transfer precise volumes of bodily fluid to each sample reservoir.

[0132]

[1185] FIG. 56 is a flowchart illustrating a method 1190 of obtaining a predetermined sample volume of bodily fluid from a patient using a flow metering transfer device. A flow metering transfer device can be any of the transfer devices described herein (also referred to herein as a "collection device"). By way of example, in some embodiments the transfer device can be the collection device 900 described above with reference to FIGS. 46-53. Thus, the transfer device includes an inlet port configured to be selectively placed in fluid communication with a patient, a pre-sample reservoir and a sample reservoir, and fluid flow from the patient to the pre-sample reservoir and to the sample reservoir. and a flow metering mechanism configured to meter the flow of bodily fluid. The method 1190 includes, at 1191, establishing fluid communication between a patient and a port of a flow metering transfer device. For example, the port may be connected to a needle or other lumen-defining device (e.g., a flexible A needle or other lumen-defining device can be inserted into the patient's body (eg, a venipuncture event or other method of accessing bodily fluids).

[1186]

] With the port in fluid communication with the patient, at 1192, fluid communication is established between the port and the pre-sample reservoir. In some embodiments, the flow metering transfer device can include a flow controller or the like (eg, flow controller 940 included in collection device 900) that provides fluid communication between the port and the pre-sample reservoir. It can be actuated and/or manipulated (eg rotated) to an established position (eg first position). In some embodiments, actuation of the flow controller may cause the flow controller and flow diversion mechanism to collectively define at least a portion of a fluid flow path between the port and the pre-sample reservoir. In some embodiments, the pre-sample reservoir can include negative pressure or the like that can initiate the flow of bodily fluid from the patient.

ient to the pre-sample reservoir. In other embodiments, bodily fluid flow can be initiated in any other suitable manner (eg, gravity, etc.).

[0134]

[1187] At 1193, the flow of bodily fluid transferred from the patient to the pre-sample reservoir is metered. For example, in some embodiments, the port has a flow control mechanism that can meter the flow of bodily fluid through the port (eg, in a manner similar to that described above with respect to flow control mechanism 967 of collection device 900). can contain. Thus, a pre-sample volume of bodily fluid is transferred to the pre-sample reservoir. The method 1190 includes, at 1194, verifying, via the flow metering mechanism of the flow metering transfer device, that the pre-sample volume of bodily fluid disposed within the pre-sample reservoir is a predetermined pre-sample volume of bodily fluid. For example, the flow metering mechanism can include and/or be operably coupled to a display or the like (eg, display 975 and/or 975' of collection device 900). The flow metering mechanism can be configured to present volumetric information on a display, as described above.

[0135]

[1188] Once the pre-sample volume of bodily fluid is disposed within the pre-sample reservoir, at 1195, the pre-sample reservoir is fluidly isolated from the port to seal the pre-sample volume of bodily fluid within the pre-sample reservoir. For example, in some cases, the flow controller and/or flow diverter mechanism can be actuated (or rotated) from a first position and/or configuration to a second position and/or configuration. When the flow controller and/or flow diverter mechanism are in the second configuration, the pre-sample reservoir is fluidly isolated from the space outside the pre-sample reservoir. In some embodiments, when the flow controller and/or flow diversion mechanism is driven to its second position and/or configuration, at 1196 fluid communication is established between the port and the sample reservoir. For example, in some embodiments, the flow metering transfer device can include a piercing member (e.g., movable member 950) configured to pierce a portion of the sample reservoir (e.g., membrane, etc.) etc. Thus, when the flow controller and/or flow diverter mechanism is in its second position and/or second configuration, the perforation of that portion of the sample reservoir places the sample reservoir in fluid communication with the port. As noted above, the sample reservoir can contain, for example, a negative pressure or the like that can initiate the flow of bodily fluid from the patient to the sample reservoir.

[0136]

[1189] At 1197, the flow of bodily fluid transferred from the patient to the pre-sample reservoir is metered. For example, as described above, the port may include a flow control mechanism capable of metering the flow of bodily fluid through the port (eg, in a manner similar to that described above with respect to flow control mechanism 967 of collection device 900). can be done. In some embodiments, the flow control mechanism can be included in a movable member, such as, for example, movable member 950 in FIG. A sample volume of bodily fluid is thus transferred to the sample reservoir. The method 1190 includes, at 1198, removing the bo

dy disposed within the sample reservoir via the flow metering mechanism of the flow metering transfer device.

This includes verifying that the sample volume of liquid is a predetermined sample volume of volume. For example, as described above, a display or the like can be configured to present volumetric information.

[0137]

[1190] In this manner, a predetermined pre-sample volume of bodily fluid is collected, which may include, for example, externally present microorganisms. For example, in some embodiments, the predetermined pre-sample volume is about 0.1 mL, about 0.3 mL, about 0.5 mL, about 1.0 mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, It can be about 5.0 mL, about 10 mL, about 20 mL, about 50 mL, and/or any volume or volume fraction value therebetween. In other embodiments, the pre-sample volume can be greater than 50 mL or 0.1 mL. In other embodiments, the predetermined pre-sample volume can be between about 2 mL and about 5 mL. In one embodiment, the predetermined pre-sample volume can be approximately 3 mL. Additionally, by collecting the predetermined pre-sample volume, the predetermined sample volume disposed within the one or more sample reservoirs can be substantially free of externally present microorganisms. In some embodiments, the predetermined sample volume can be between 10 mL and 60 mL. In other embodiments, the predetermined sample volume can be between 30 mL and 60 mL. In still other embodiments, the predetermined sample volume can be 60 mL. Although described above as transferring a sample volume of bodily fluid to a single sample reservoir, in other embodiments, a flow metering transfer device can be used to transfer a given sample volume to two or more sample reservoirs. For example, in some embodiments, a predetermined pre-sample volume of bodily fluid can be collected in and fluidly isolated within a pre-sample reservoir, as described above. A predetermined sample volume into a first sample reservoir, a predetermined sample volume into a second sample reservoir, and a predetermined sample volume into a third sample reservoir using a flow metering transfer device while the pre-sample volume is fluidly isolated. can be transferred to In such a case, the predetermined sample volume can be, for example, 20 mL, so that the total sample volume placed in the first, second and third reservoirs is 60 mL.

[0138]

[1191] Various embodiments of the bodily fluid collection devices described herein enable collection of two (or more) sets of bodily fluid (e.g., blood) samples from a single venipuncture. can do. The current standard of care is to perform some tests (e.g., blood cultures) on separate, independent samples (e.g., via two separate venipunctures, via catheter + venipuncture, and/or combinations thereof). They are asked to do so by obtaining it from a fluid access point. Embodiments described herein can facilitate obtaining multiple samples for a given diagnostic test (e.g., blood culture test) from a single bodily fluid access point (e.g., venipuncture); thereby, the annual number of venipunctures required to obtain these samples can be reduced by a factor of two. This is advantageous for both patients and medical personnel alike. Reducing

the number of venipunctures (and/or other blood access procedures) significantly reduces the risk of needlestick injuries to health care workers and reduces patient-related complications resulting from these procedures (e.g., hematoma, thrombosis, phlebitis, infection, etc.) can be reduced. Further, reducing the number of fluid access procedures (eg, venipuncture) reduces the supply utilization, labor and waste associated with these procedures. The cost reductions realized by the healthcare system are significant, as are patient concerns for improved sample integrity resulting in more accurate patient diagnoses that inform treatment plan development and implementation, as well as more efficient resource consumption. presents an opportunity to promote improved outcomes in The bodily fluid collection device also greatly reduces the incidence of false positives from post-collection analysis. The fluid collection devices described herein can also streamline the fluid collection process, reducing the number of manual steps and "touch points", thereby reducing the chances of external contamination. The devices described herein can also minimize the risk of needle stick injury and infection to the laboratory technician and/or phlebotomist.

[1192

] In some embodiments, the bodily fluid collection devices described herein (eg, 100, 200, 300, 400, 500, 600, 700, 800 and 900) are sterile saturated.

It may include and/or be formed in part from a composite material (eg, housing 401). Current standards rely on medical personnel to place individual antiseptic materials (eg, isopropyl alcohol swabs) on top of individual sample reservoirs (eg, 480, 480', 490 and 490'). To ensure compliance with this protocol, (for example) the device 400 may include antiseptic material disposed within the device 400 so that the housing 401, as shown in FIG. 2 pack), the first point of contact from the top of housing 401 and sample reservoirs 480, 480', 490, 490' is the disinfectant material. In this way, the tops of the sample reservoirs 480, 480', 490, 490' are ensured that proper disinfection is applied before bodily fluids are inoculated into the sample reservoirs.

[0140]

[1193] While various embodiments have been particularly shown and described, various changes in form and detail can be made. For example, although dial 445 (actuator) is shown and described with reference to FIGS. 19-22 as rotating in a single direction, in other embodiments, dial 445 (actuator) rotates in a first direction. and a second direction opposite the first direction. In such embodiments, rotation in the second direction can be configured to move the collection device through any number of configurations. In other embodiments, rotation of the actuator in the second direction can be restricted. In some embodiments, the dial can include a mechanical stop or lock to fluidly isolate the first volume of bodily fluid received from the patient (ie, the contaminated sample). In other words, when the first reservoir (pre-sample reservoir) is filled with a predetermined volume of bodily fluid and the user rotates the dial (actuator) to start drawing in additional sample, the dial (actuator) is turned to (It cannot be moved back to establish fluid communication with the first sample volume (contained within the pre-s

ample reservoir).

[0141]

[1194] While several embodiments have been described above, it should be understood that they have been presented by way of example only and not limitation. Although various embodiments have been described as including combinations of particular features and/or components, any combination or sub-combination of any feature and/or component from any of the embodiments described herein may be described. Other embodiments with combinations are possible. For example, with reference to FIGS. 34-40, although collection device 700 is shown and described as having a first, second, third, fourth or fifth configuration, other implementations are possible. In form, the collection devices described herein can have more or fewer forms. Further, while the collection device 200 is shown and described with reference to FIGS. 2-13 as having a vacuum-assisted collection tube as the pre-sample reservoir 270, in other embodiments, the collection device 200 includes a dispensing member. The collection device 400 of the embodiment presented in FIGS. 16-22 can have chambers housed in a housing 201 similar to the collection device 400 of the embodiment presented in FIGS. It is possible.

[0142]

[1195] It is also possible to vary the specific arrangement of the various components. For example, the sizes and specific shapes of various components may differ from the illustrated embodiments while still providing functionality as described herein. More specifically, the sizes and shapes of the various components can be specifically selected for the desired flow rate of bodily fluid flow into the fluid reservoir. For example, although flow metering mechanism 967 is specifically shown in FIG. 49, any of the collection devices described herein can be used with any suitable flow metering mechanism. For example, in some embodiments, the collection device includes a flow metering mechanism and/or, for example, pressure sensors, voltage sensors, optical sensors, velocity sensors, flow meters, strain gauges, valves, turbines, floats, displacement analysis, Density Analysis, Gravimetric Analysis, Optical Analysis, Ultrasound Analysis, Thermal Analysis, Doppler Analysis, Electromagnetic Field (emf) Analysis, Reflection Analysis, Obstacle Analysis, Area Analysis, Venturi Analysis, Coriolis Analysis, Visual Analysis and/or any other suitable sensor, analysis and/or (e.g., applying and/or using Boyle's law, the ideal gas law, force calculations (force = mass x acceleration), etc., as examples), other Any mechanism, device or method can be included.

drawing

open

[Fig. 1]

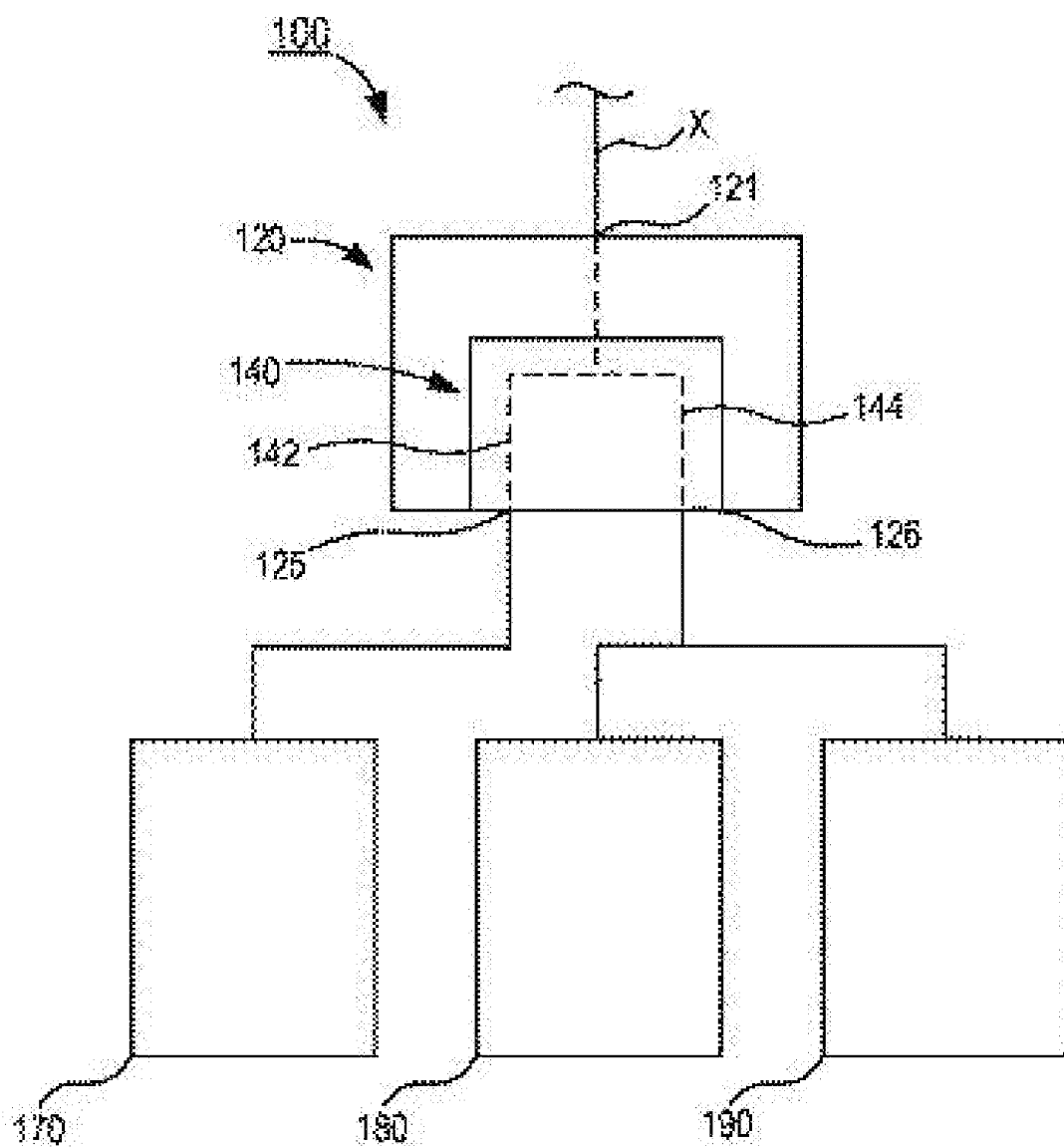


FIG. 1

[Figure 2]

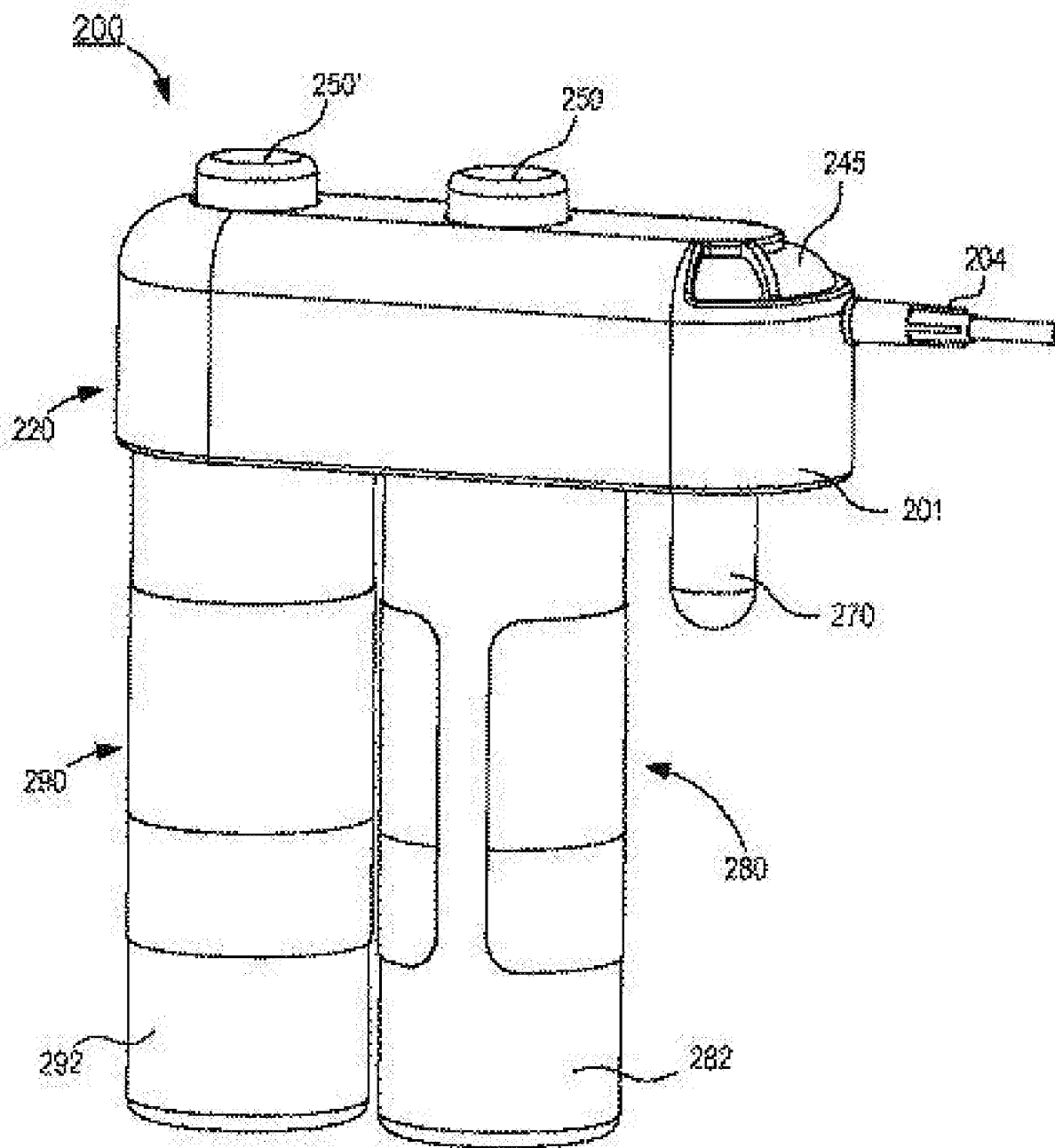
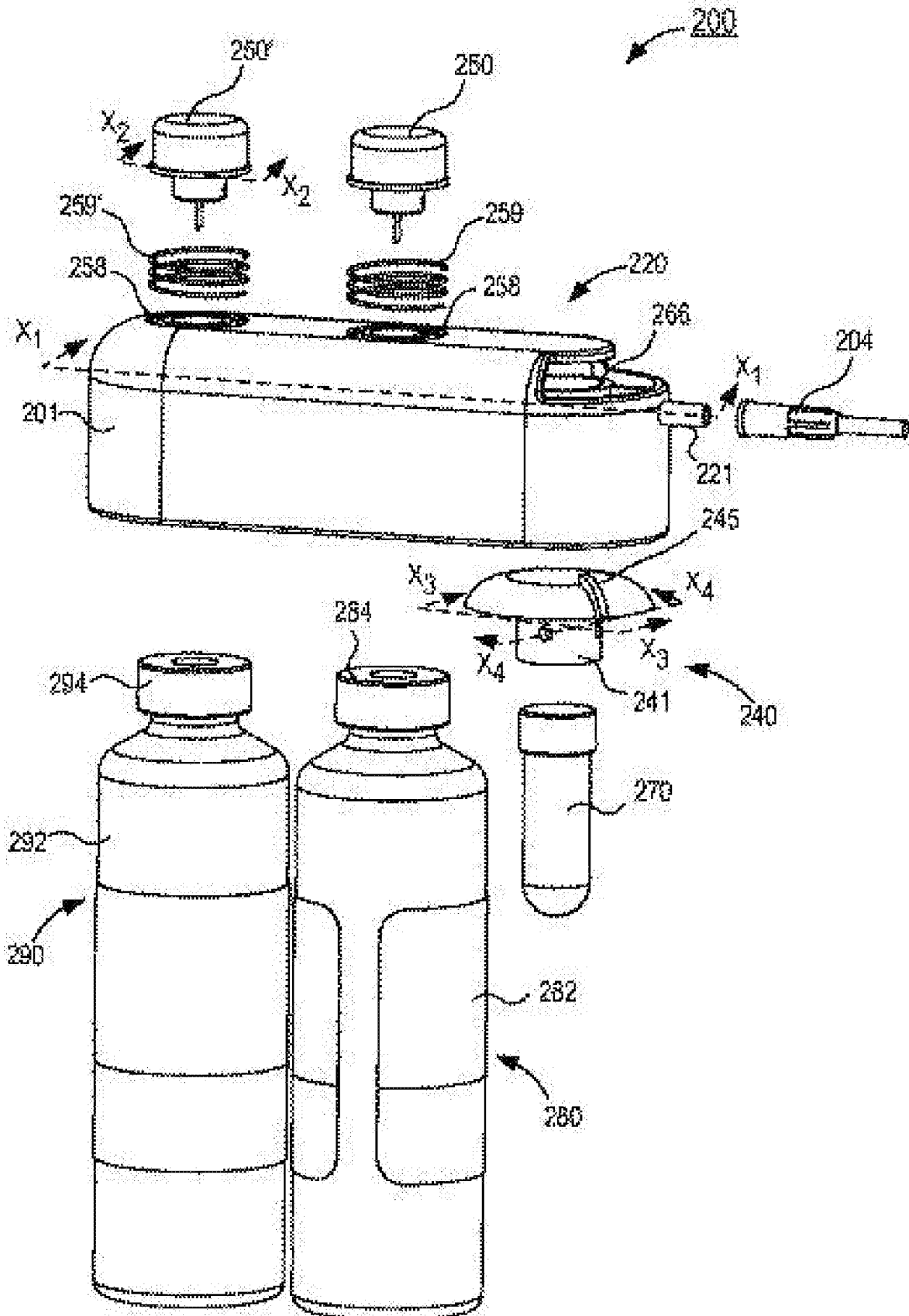


FIG. 2

[Figure 3]



[Figure 4]

FIG. 3

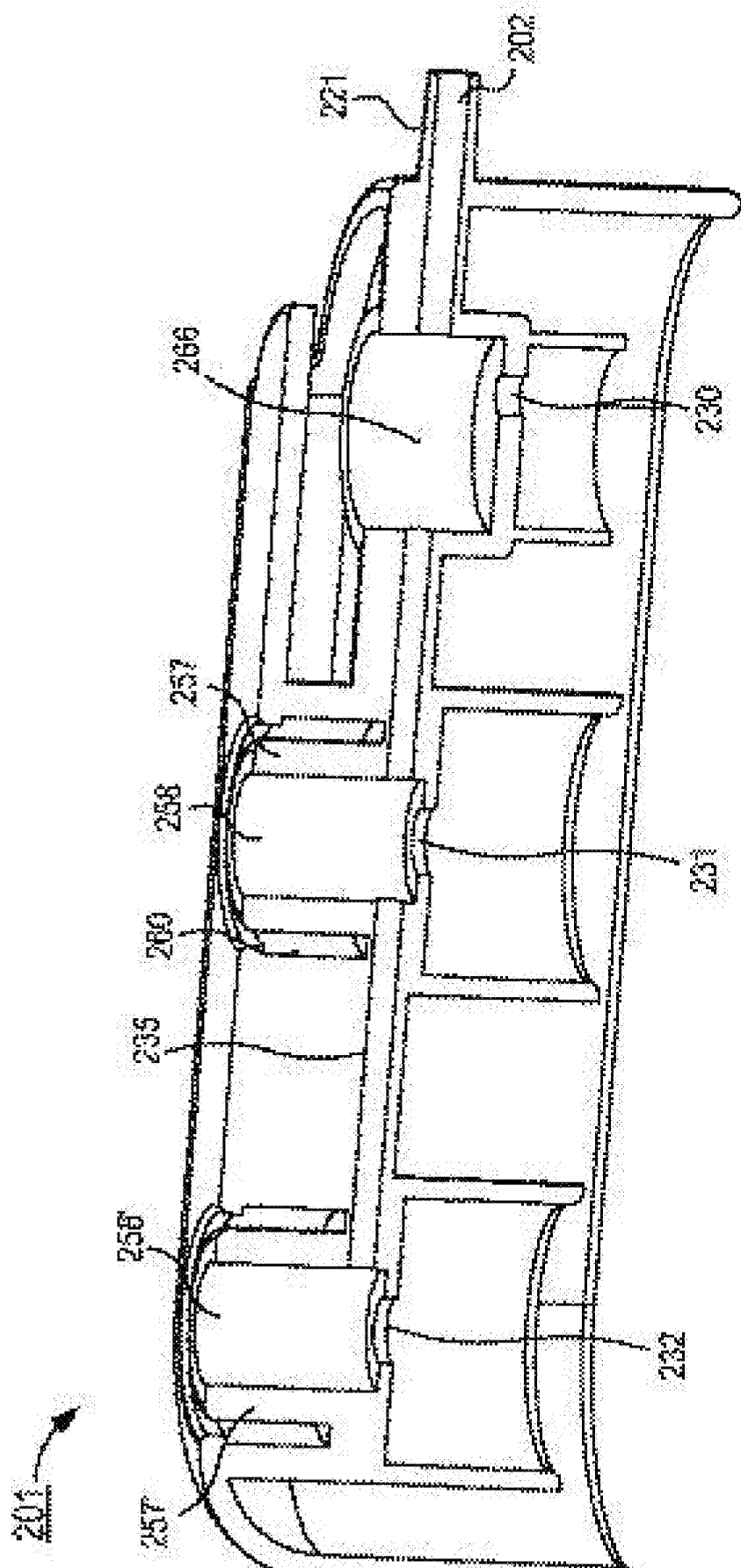


FIG. 4

[Figure 5]

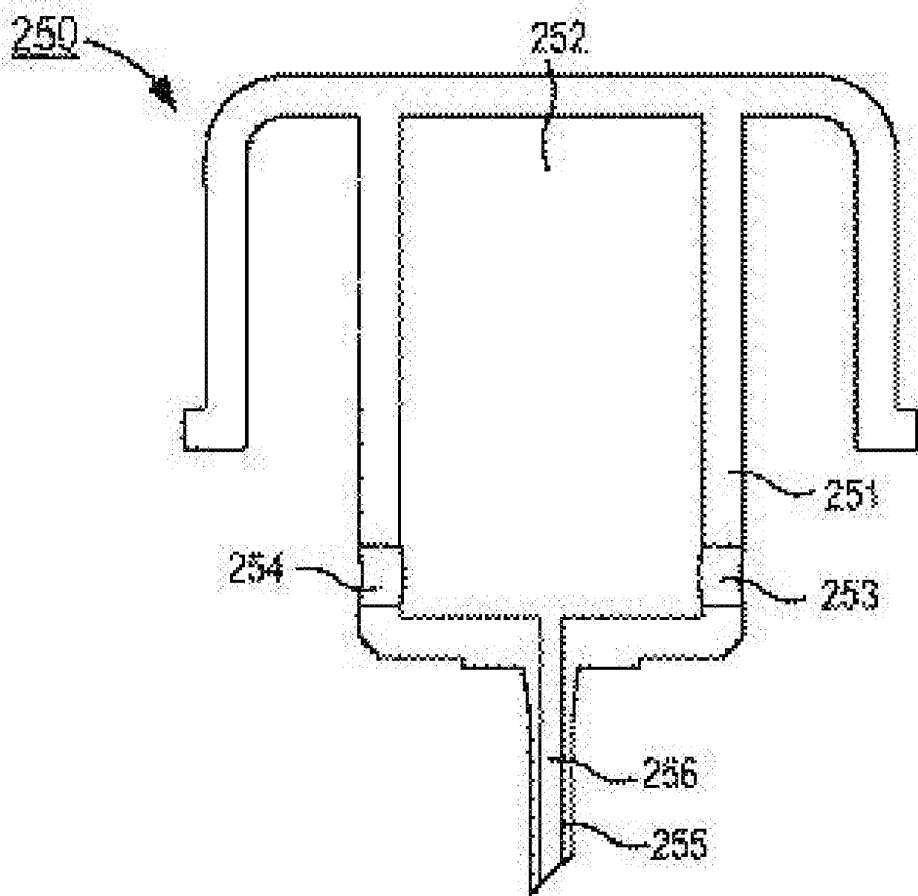


FIG. 5

[Fig. 6]

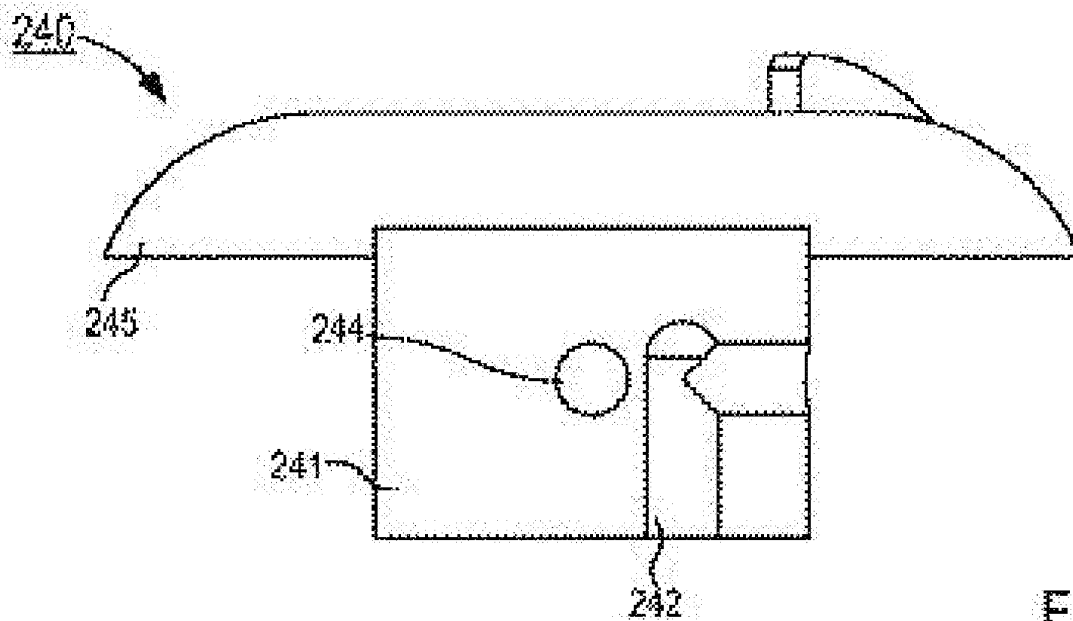


FIG. 6

[Fig. 7]

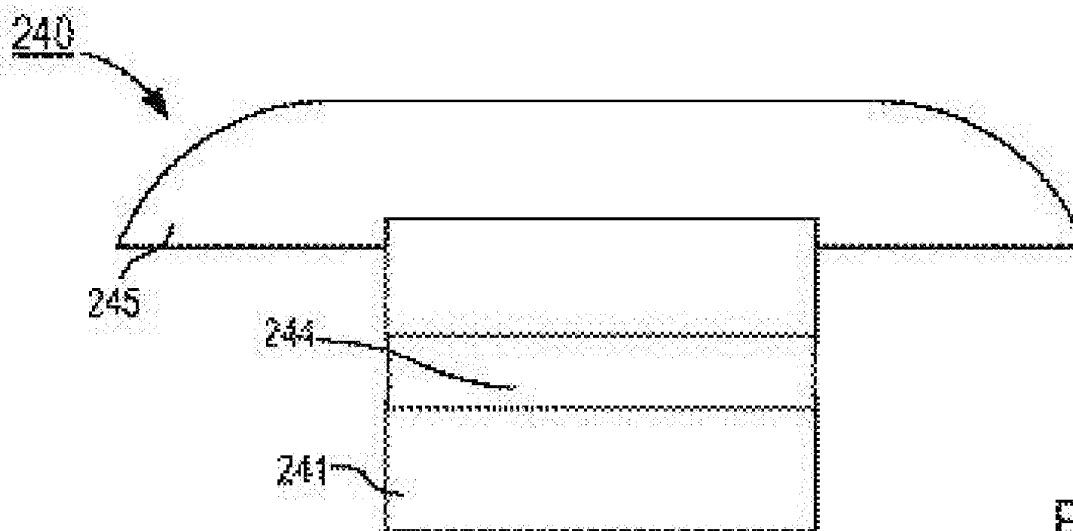


FIG. 7

[Fig. 8]

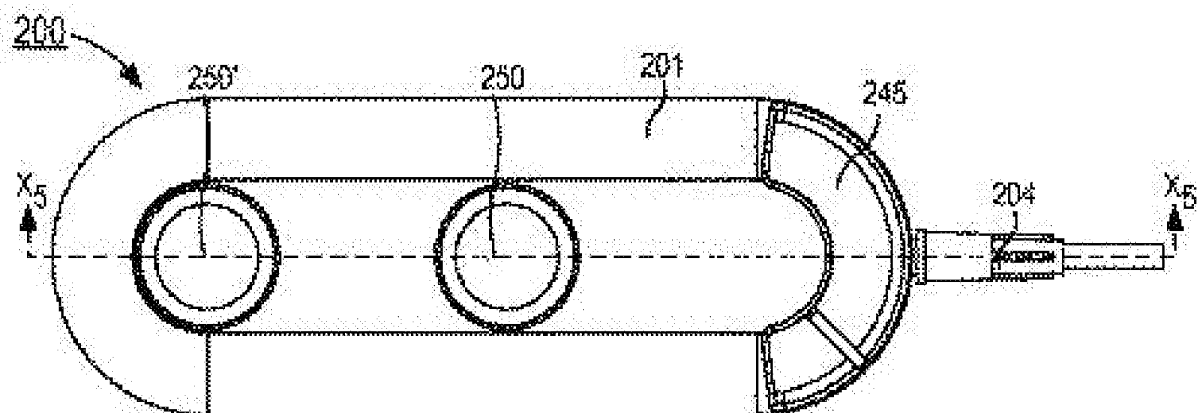


FIG. 8

[Fig. 9]

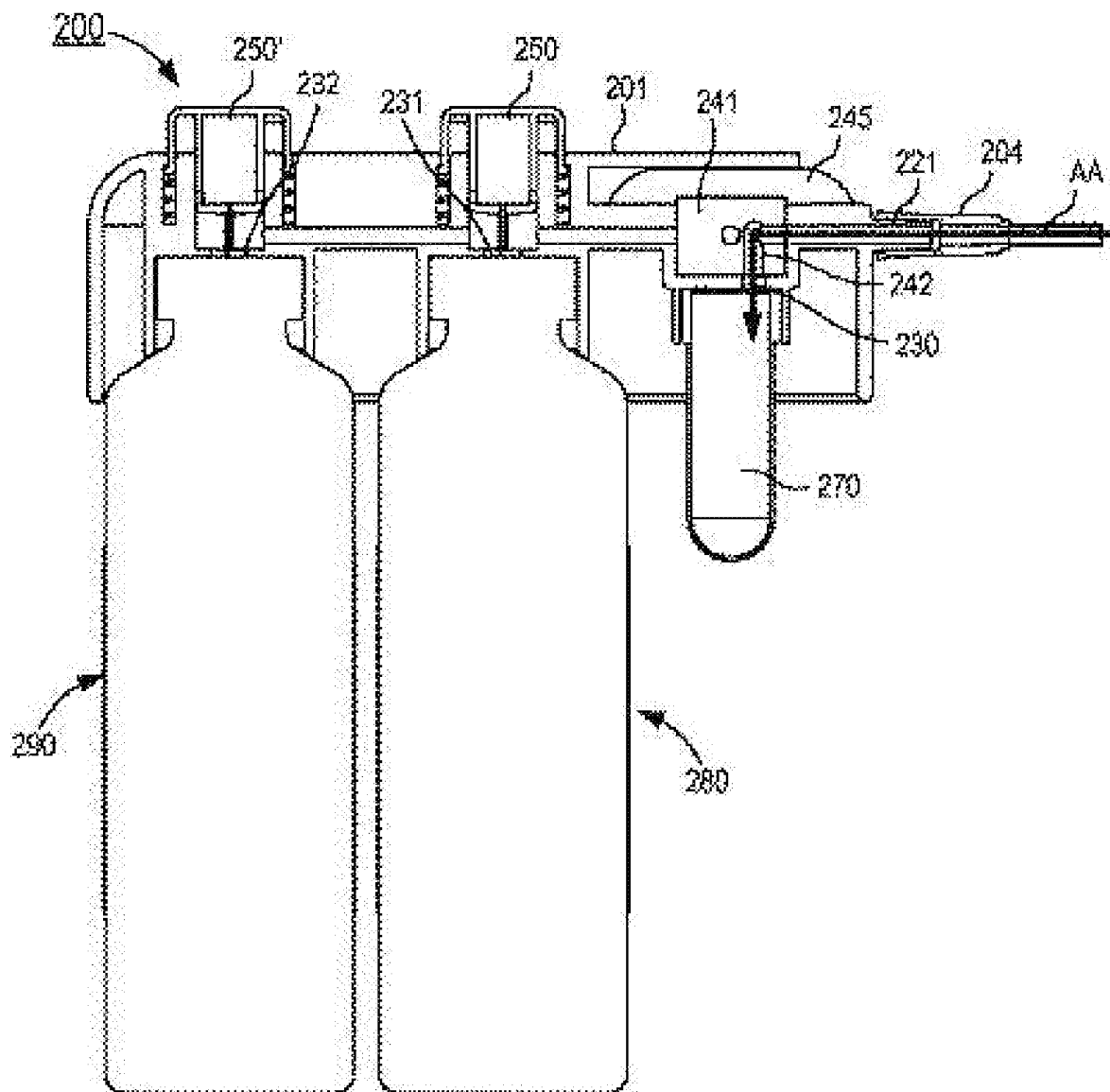


FIG. 9

[Fig. 10]

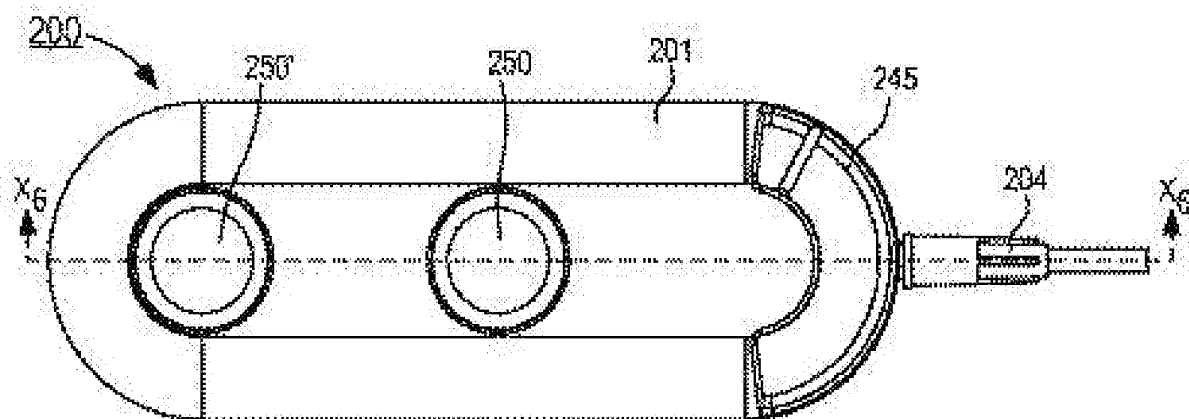


FIG. 10

[Fig. 11]

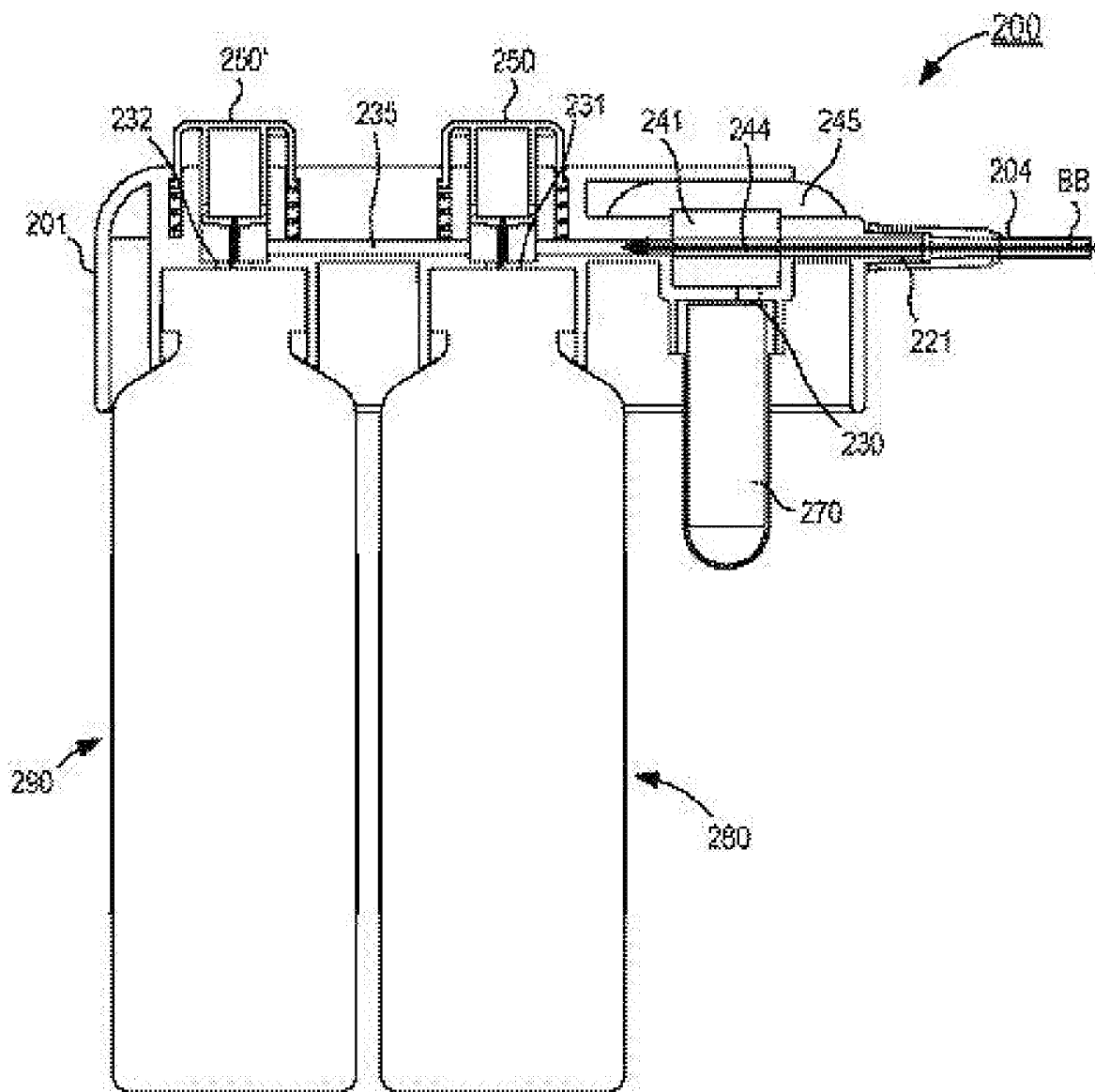


FIG. 11

[Fig. 12]

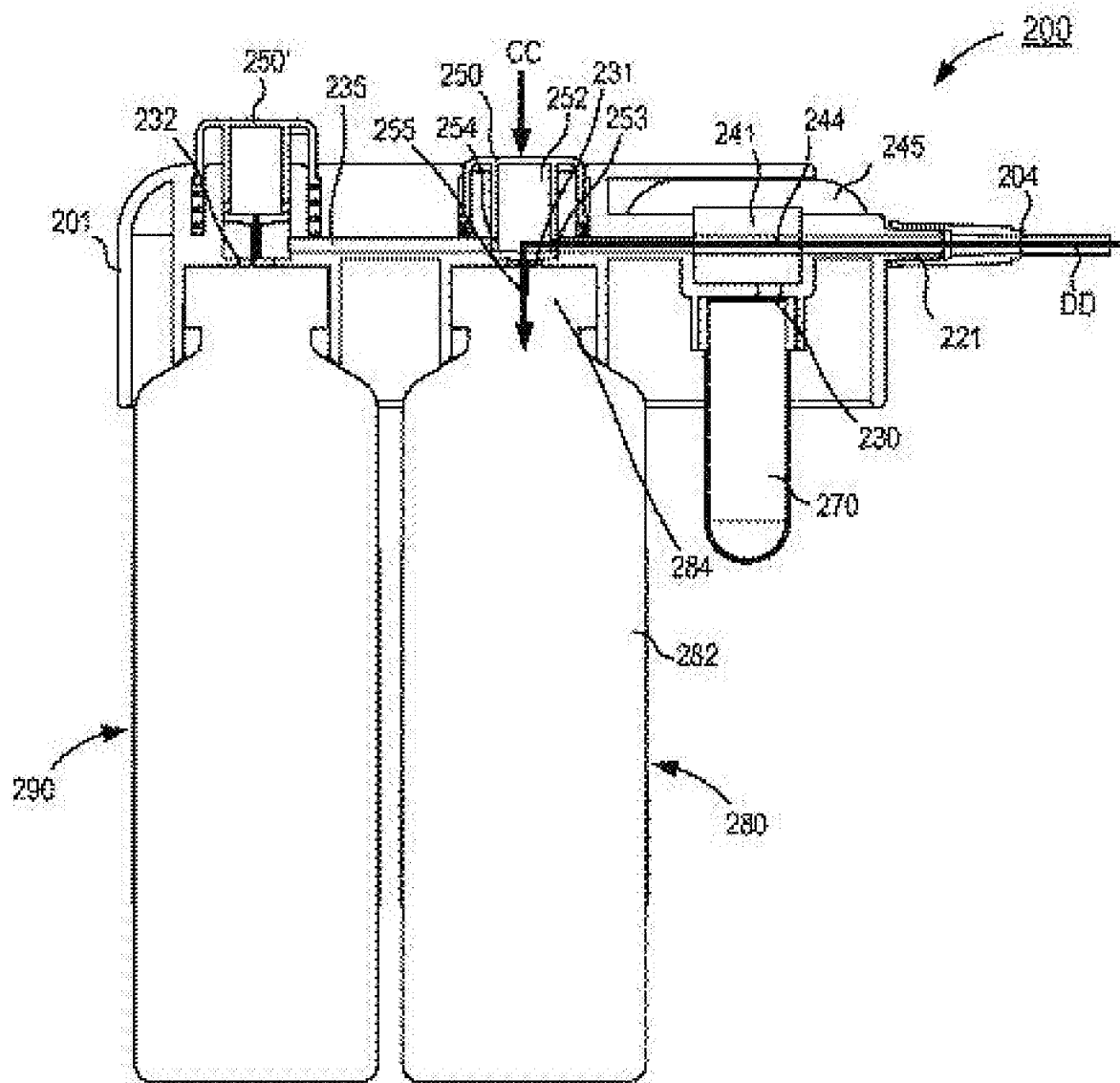


FIG. 12

[Fig. 13]

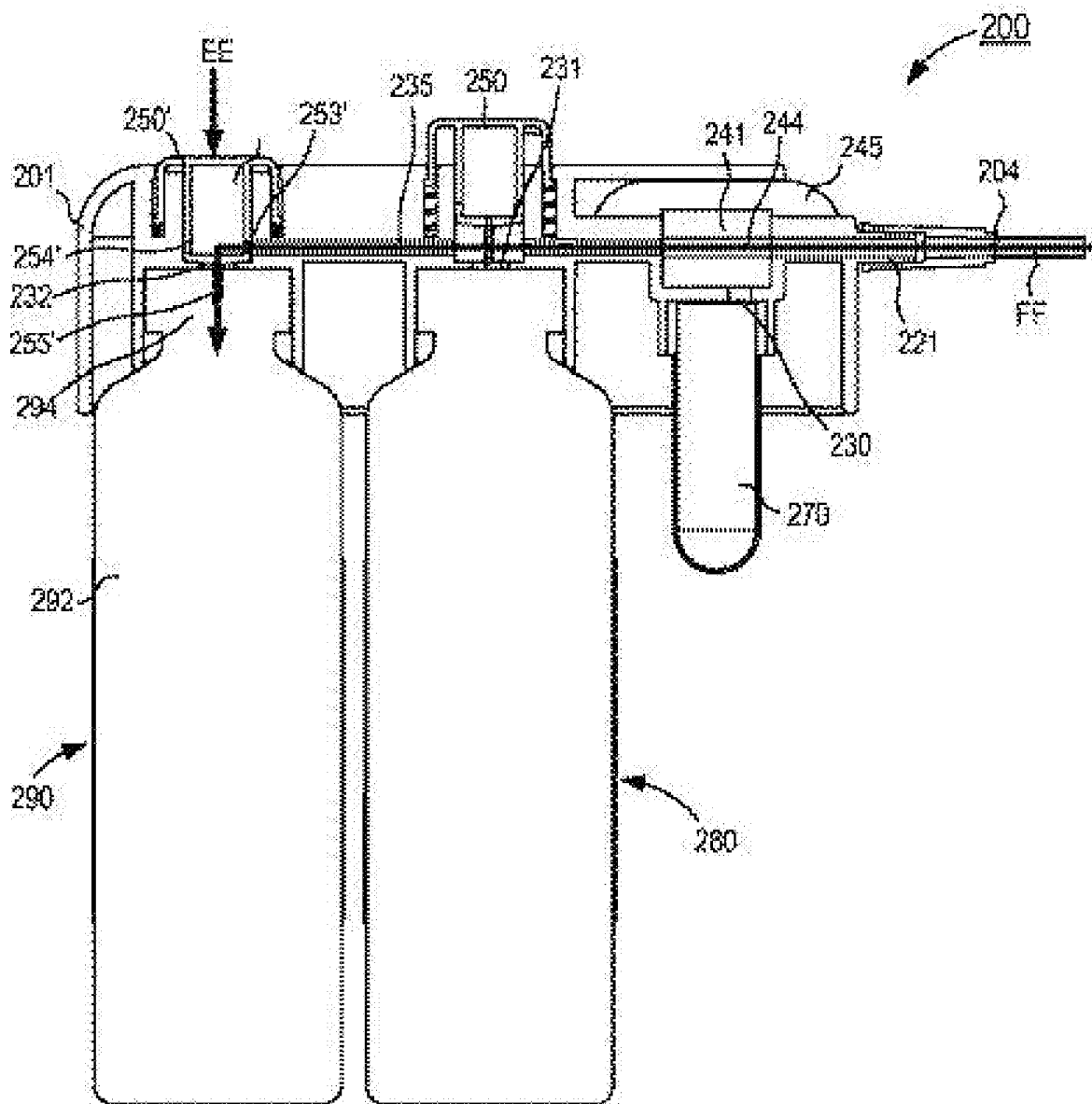
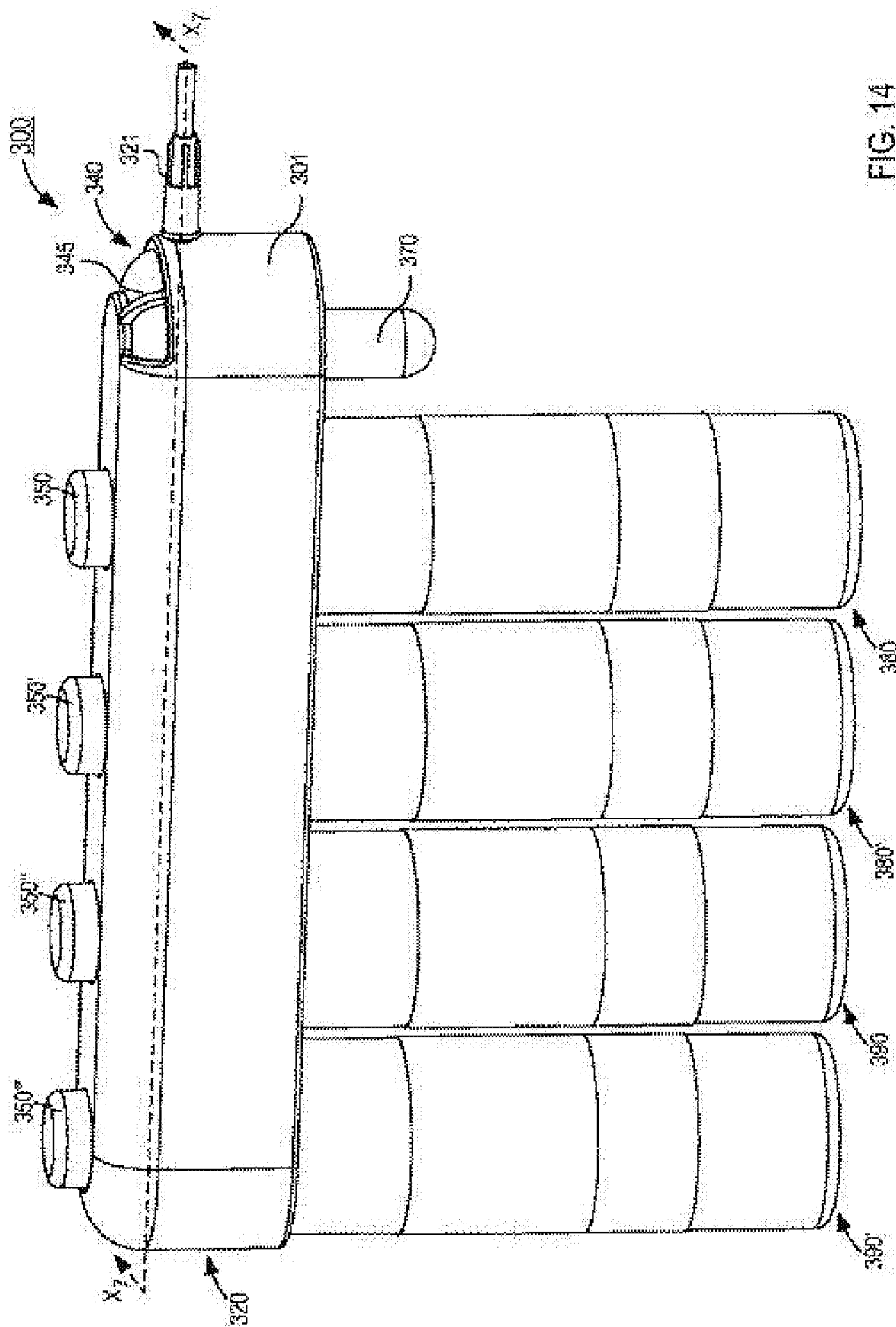


FIG. 13

[Fig. 14]



[Fig. 15]

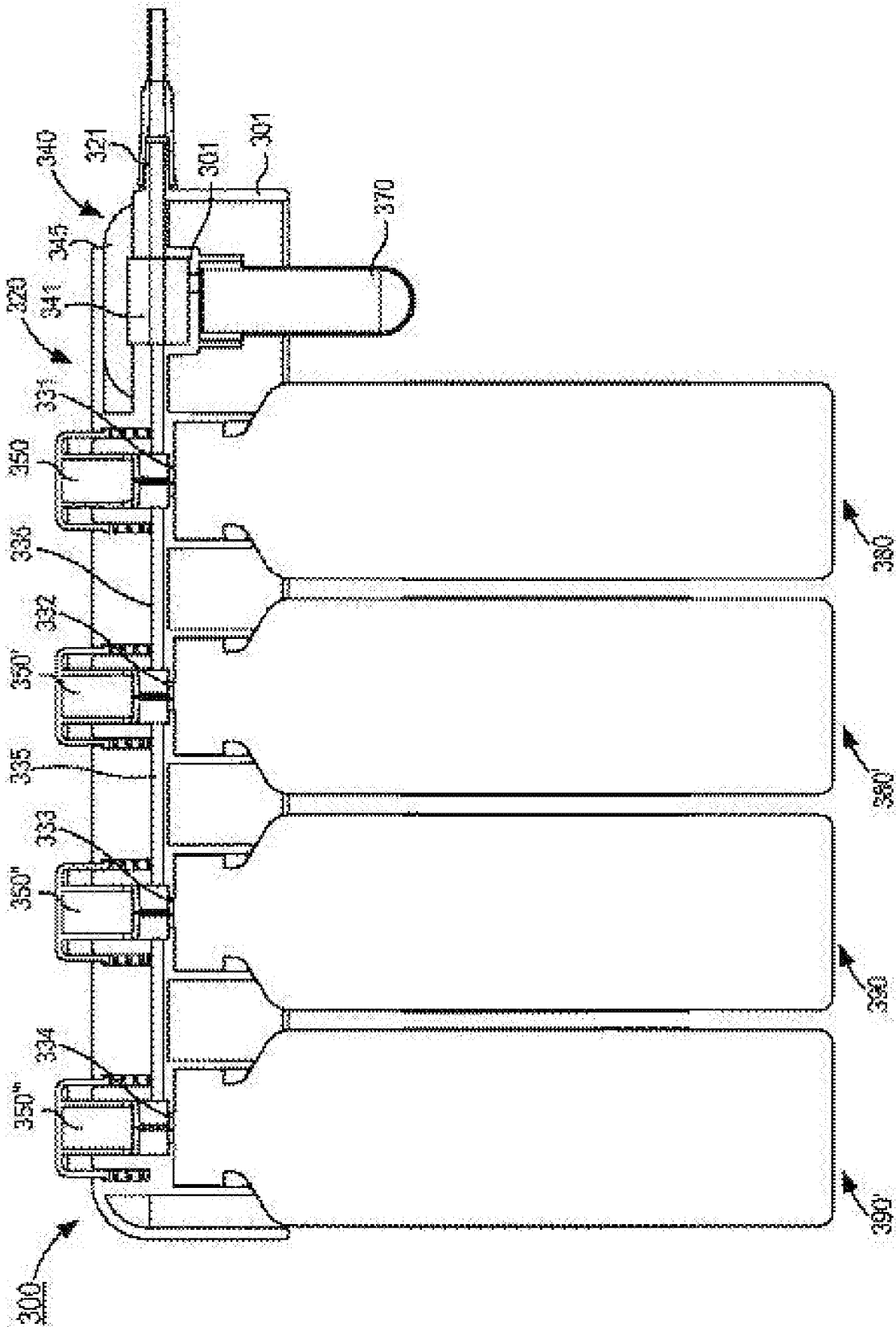
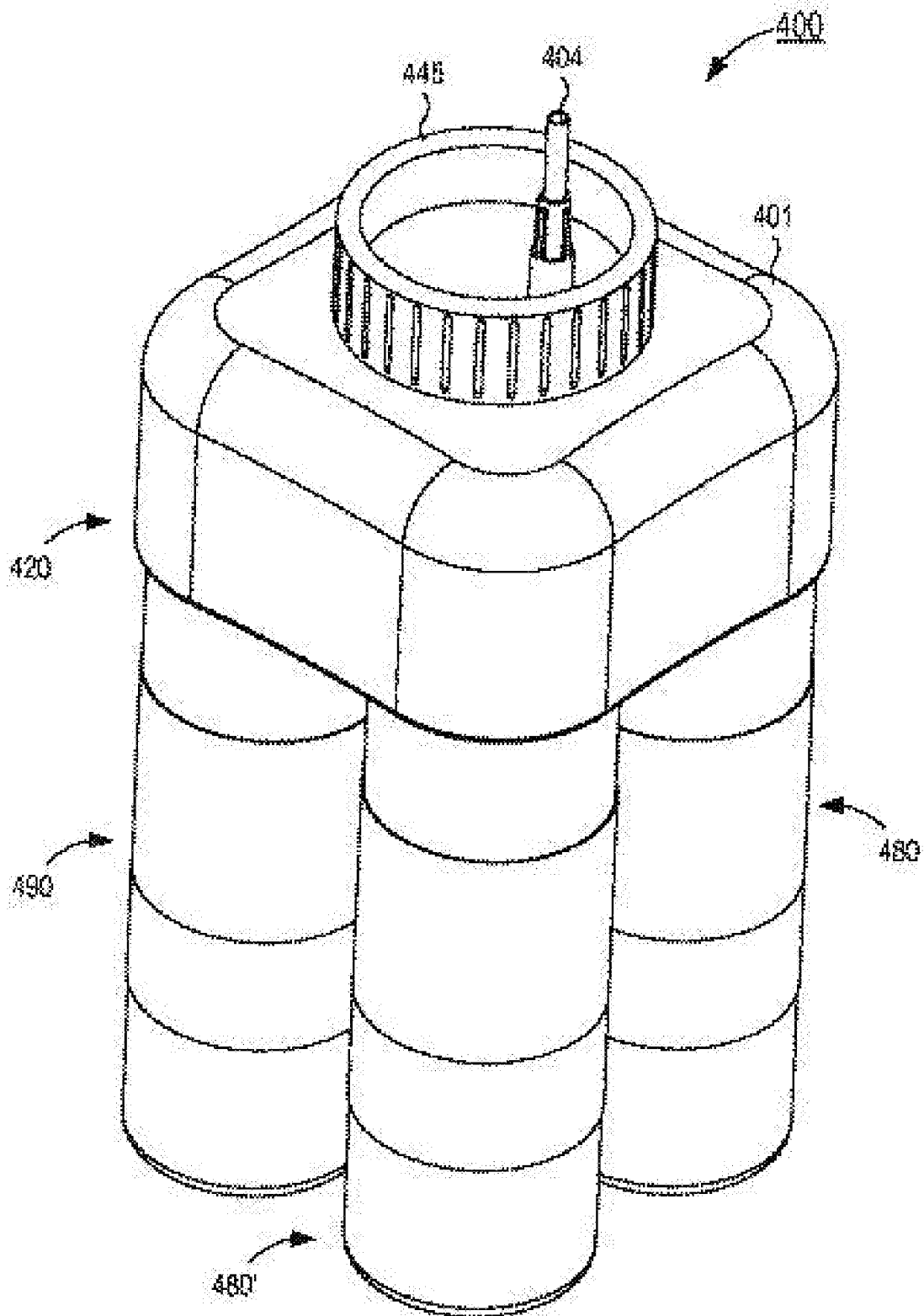


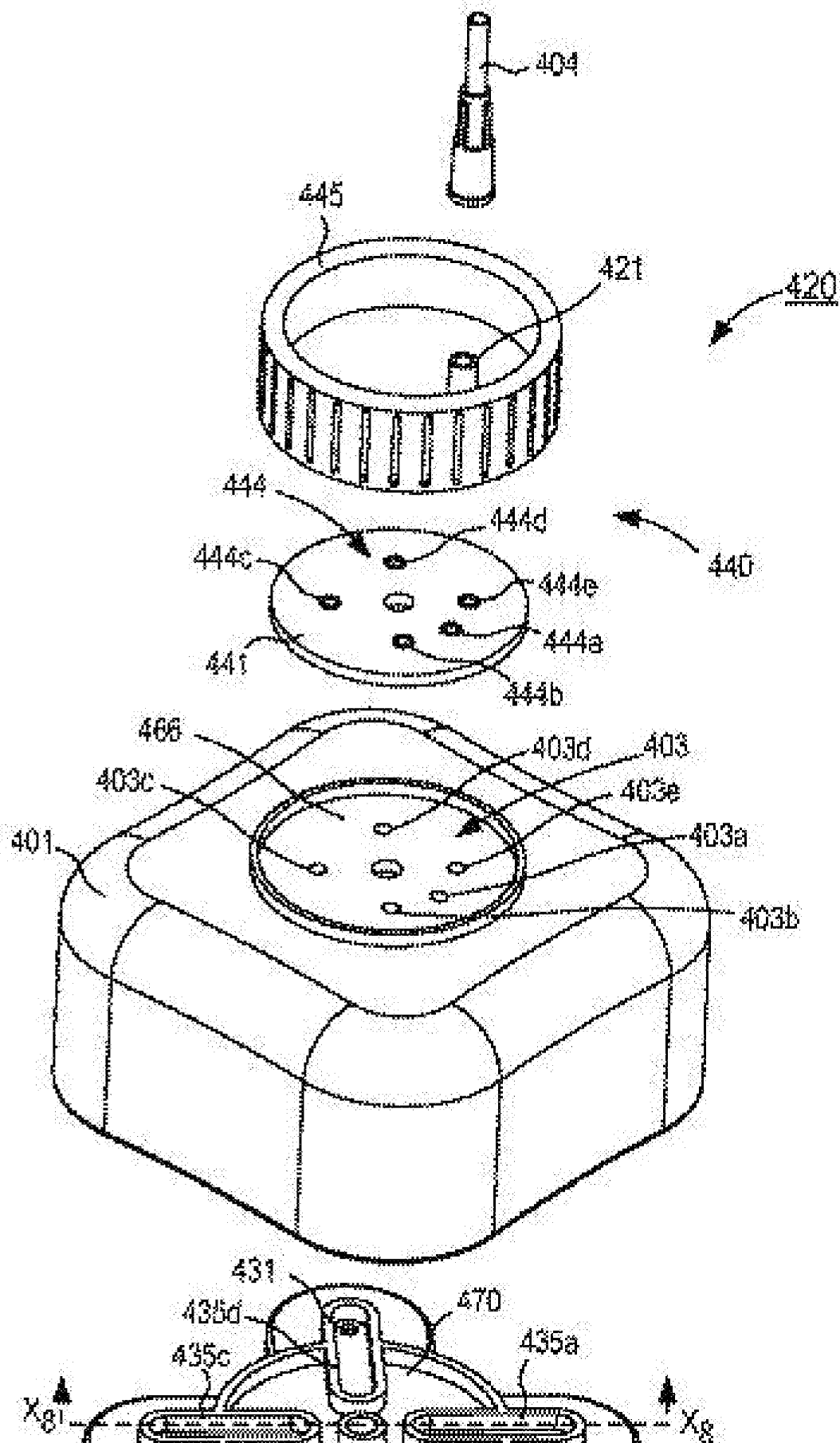
FIG. 15

[Fig. 16]



[Fig. 17]

FIG. 16



[Fig. 18]

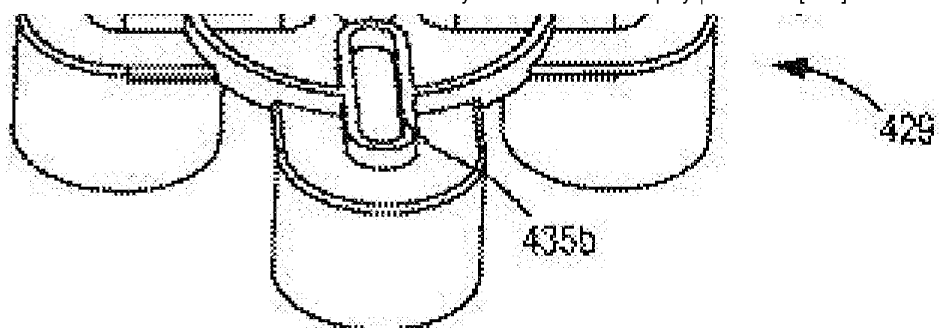


FIG. 17

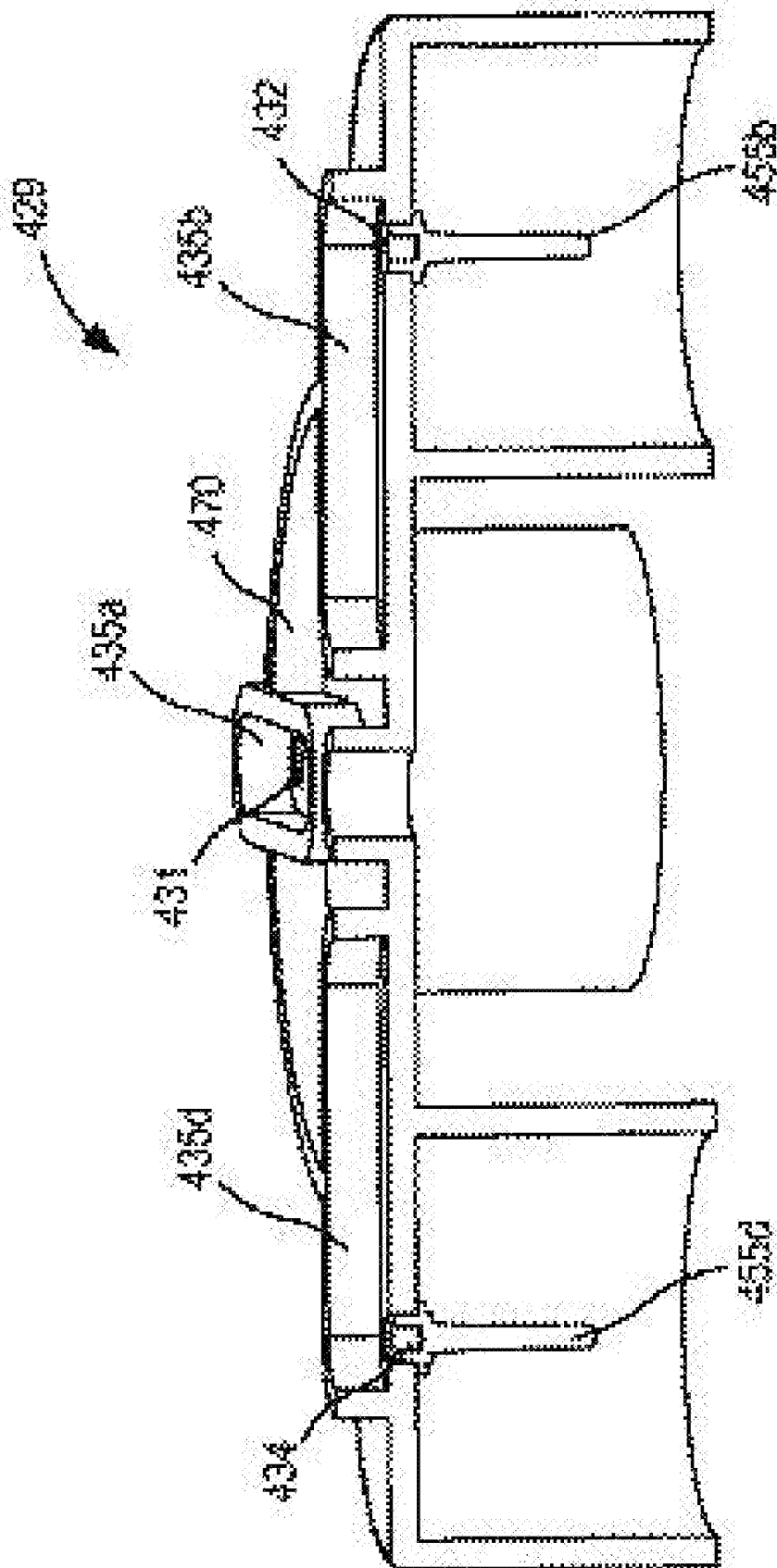


FIG. 18

[Fig. 19]

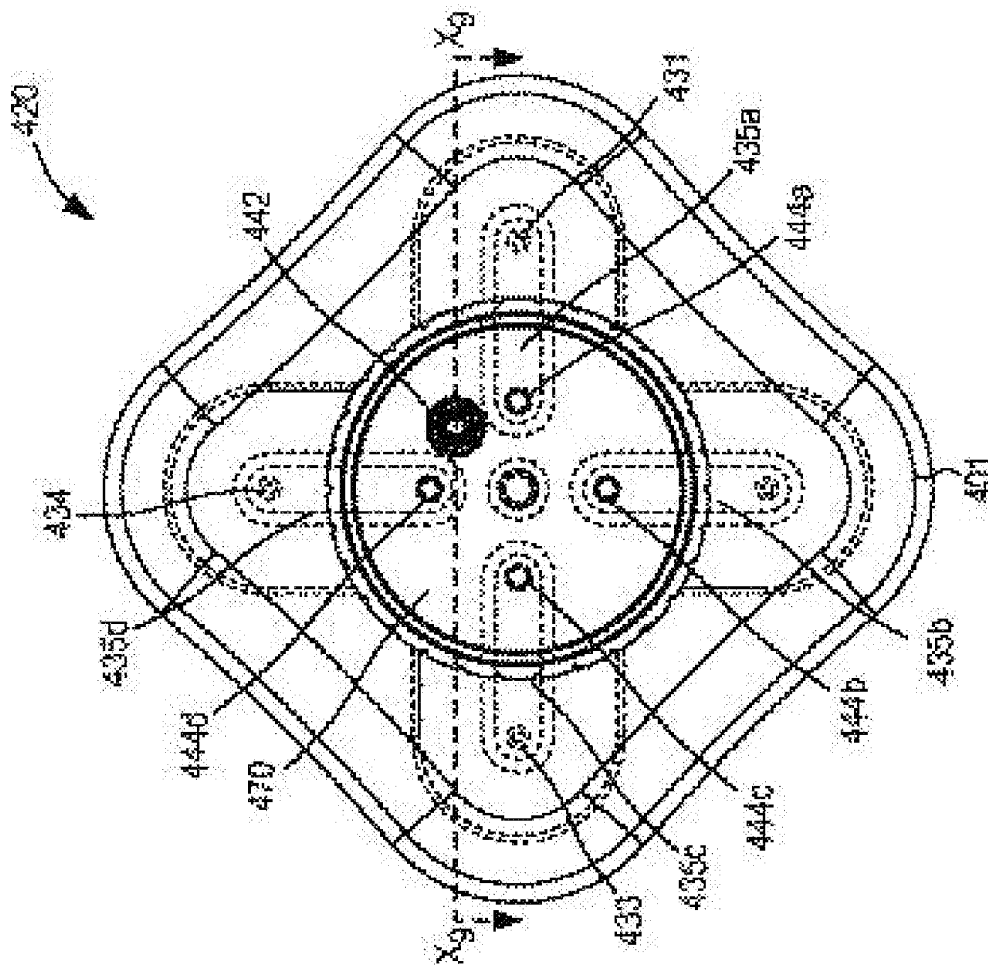
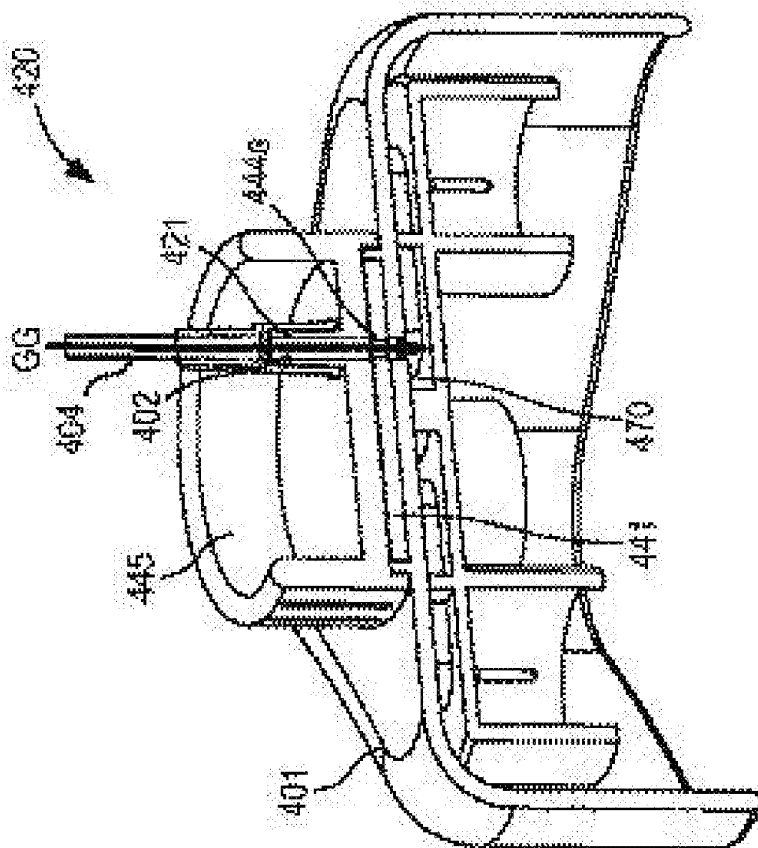


FIG. 19

[Fig. 20]



6-29

[Fig. 21]

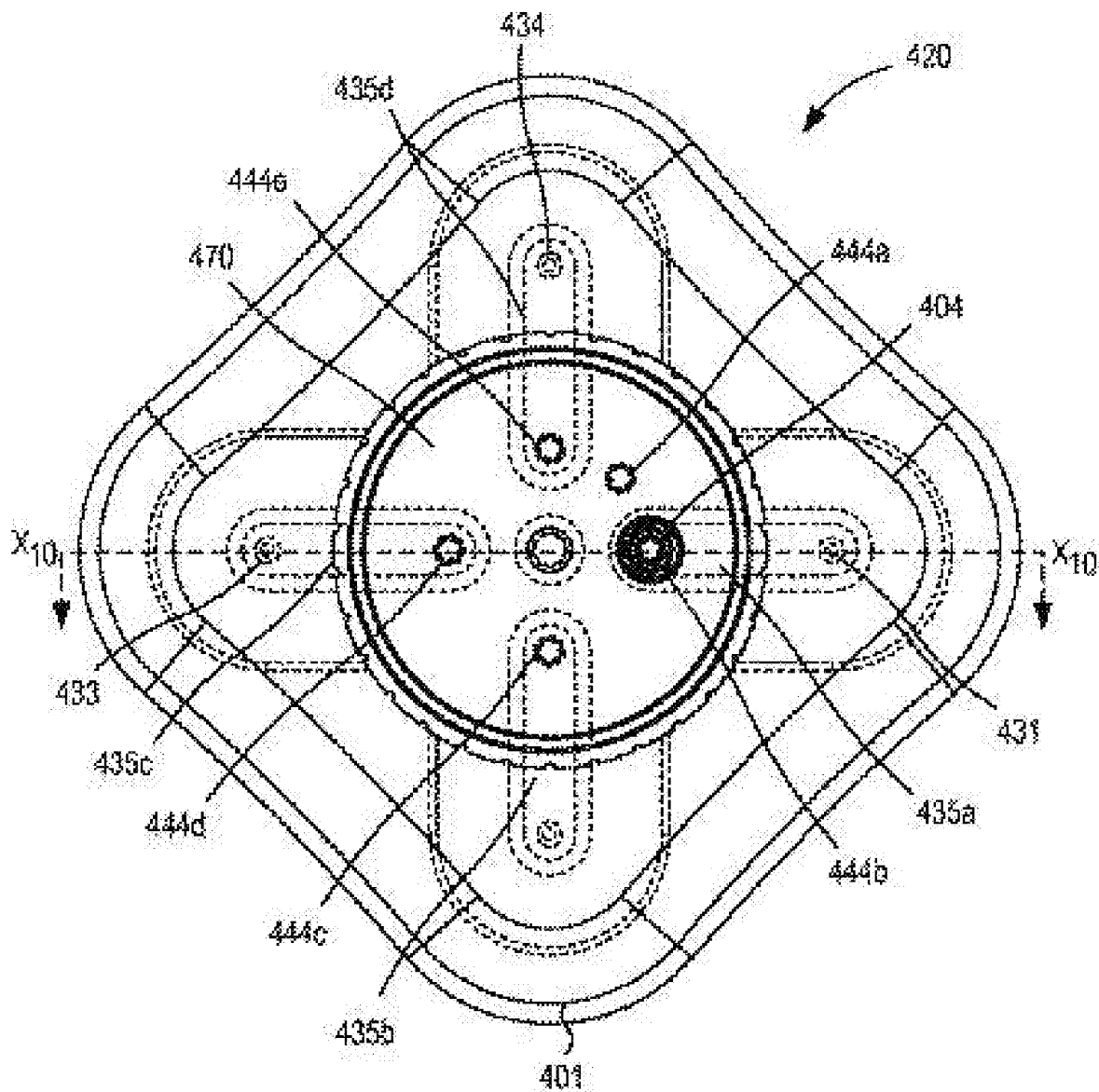
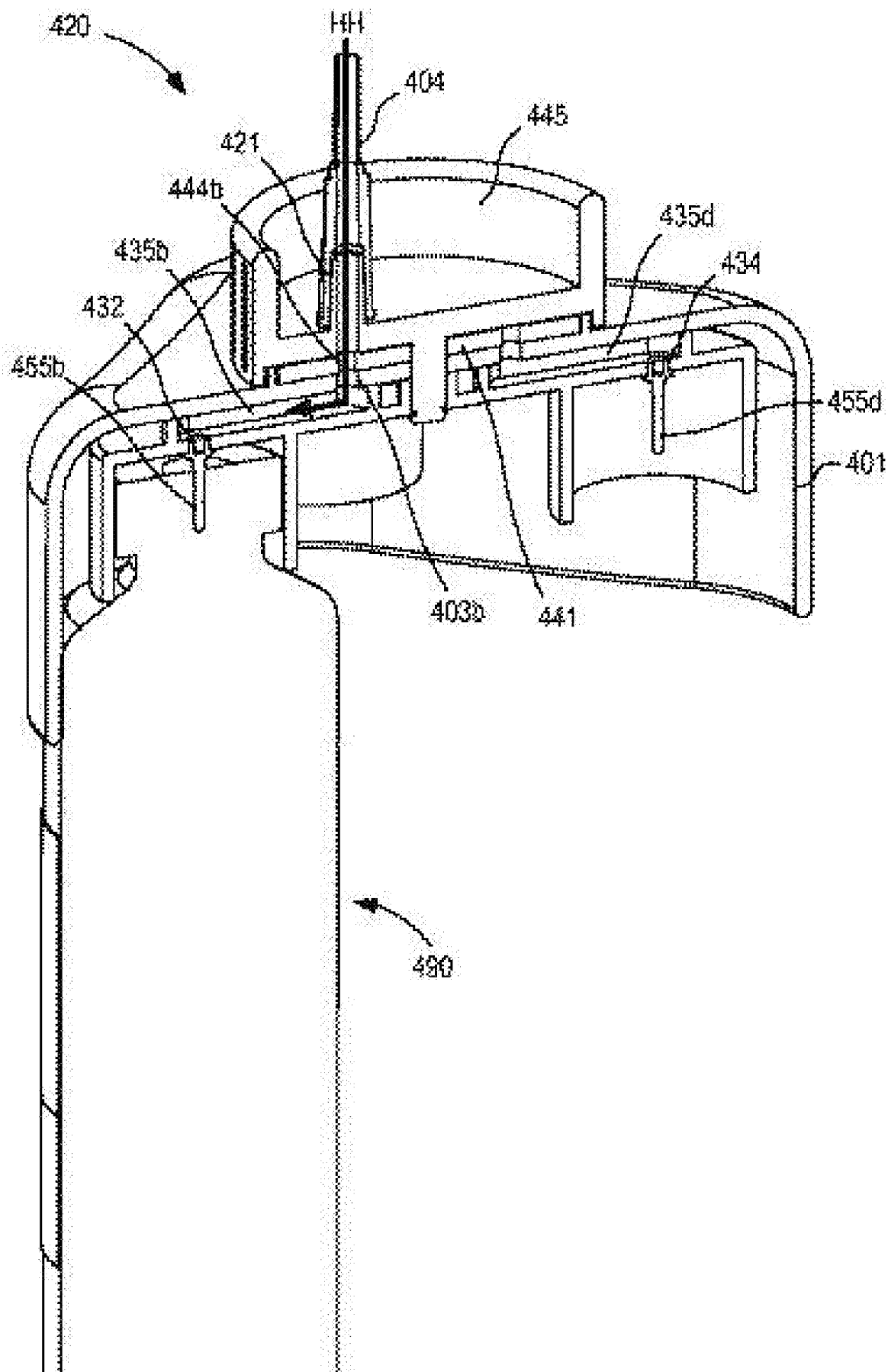


FIG. 21

[Fig. 22]



[Fig.23]

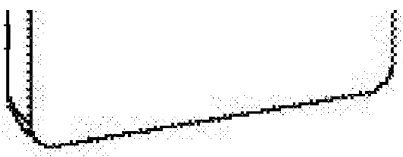
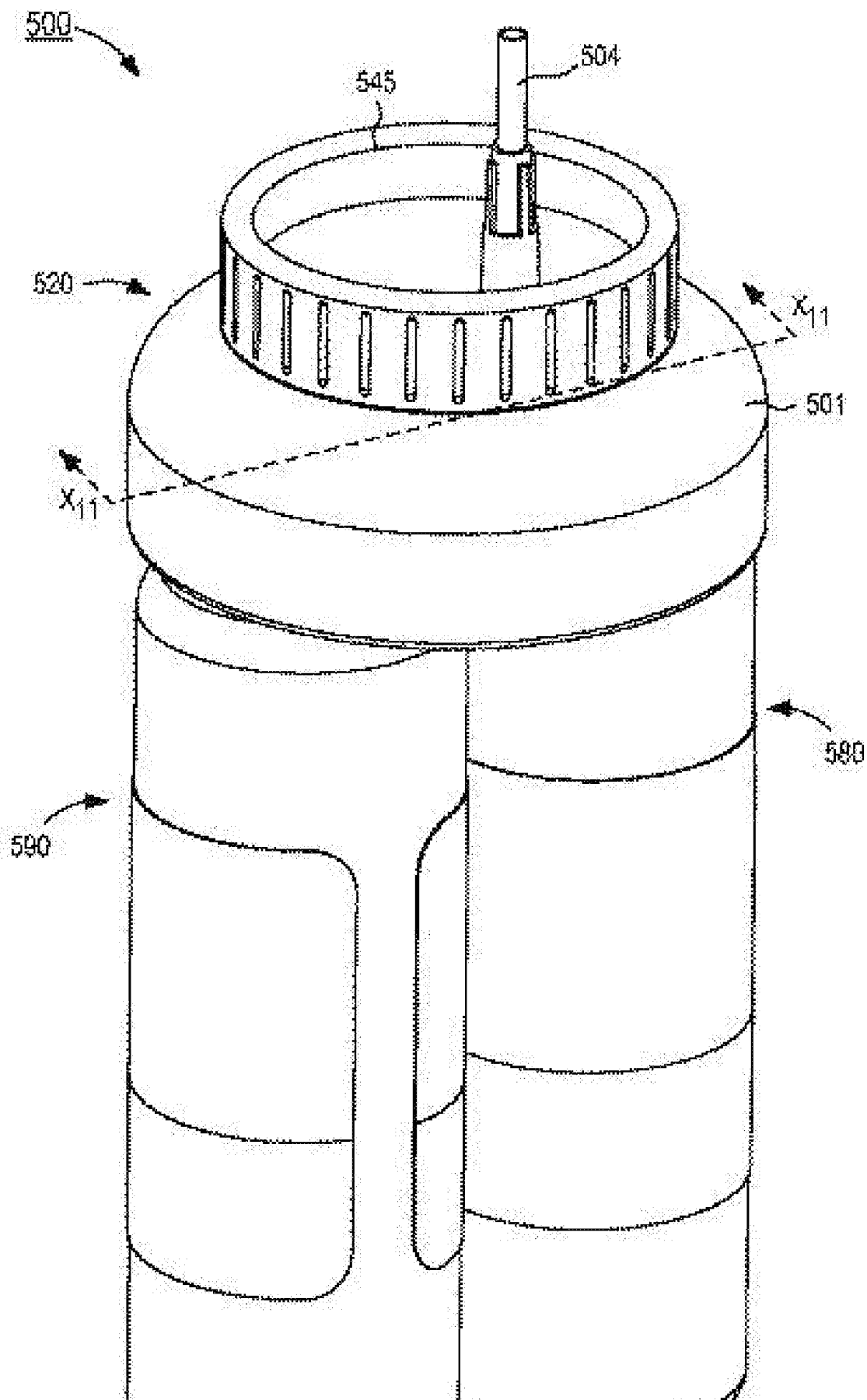


FIG. 22



[Fig.24]

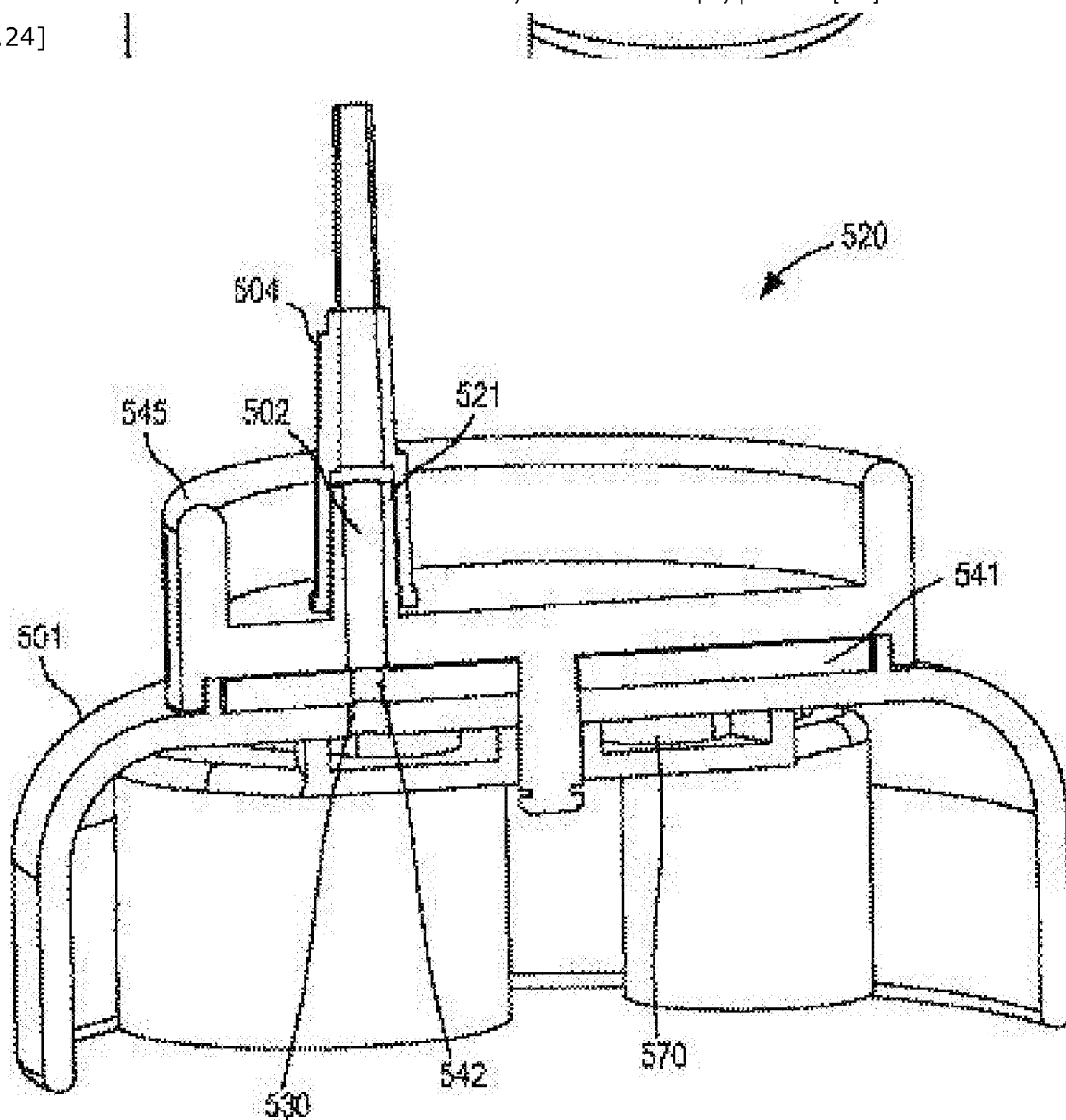
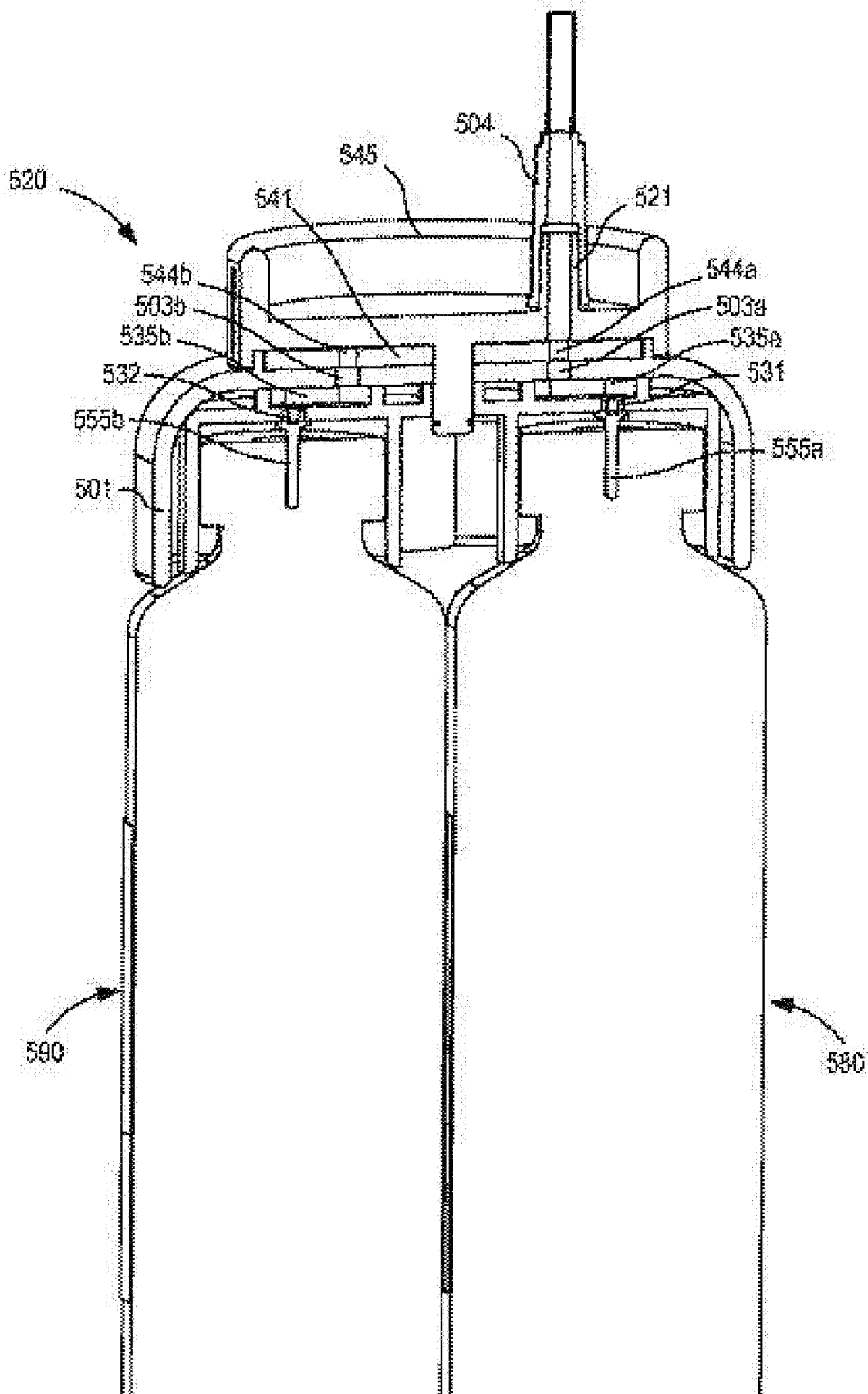


FIG. 24

[Fig.25]



[Fig.26]

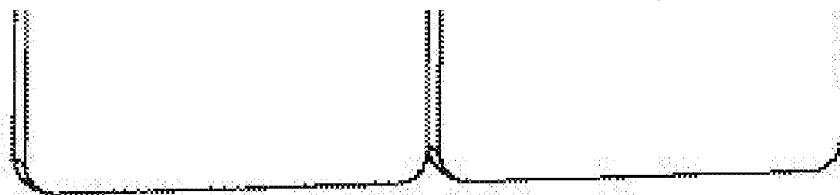
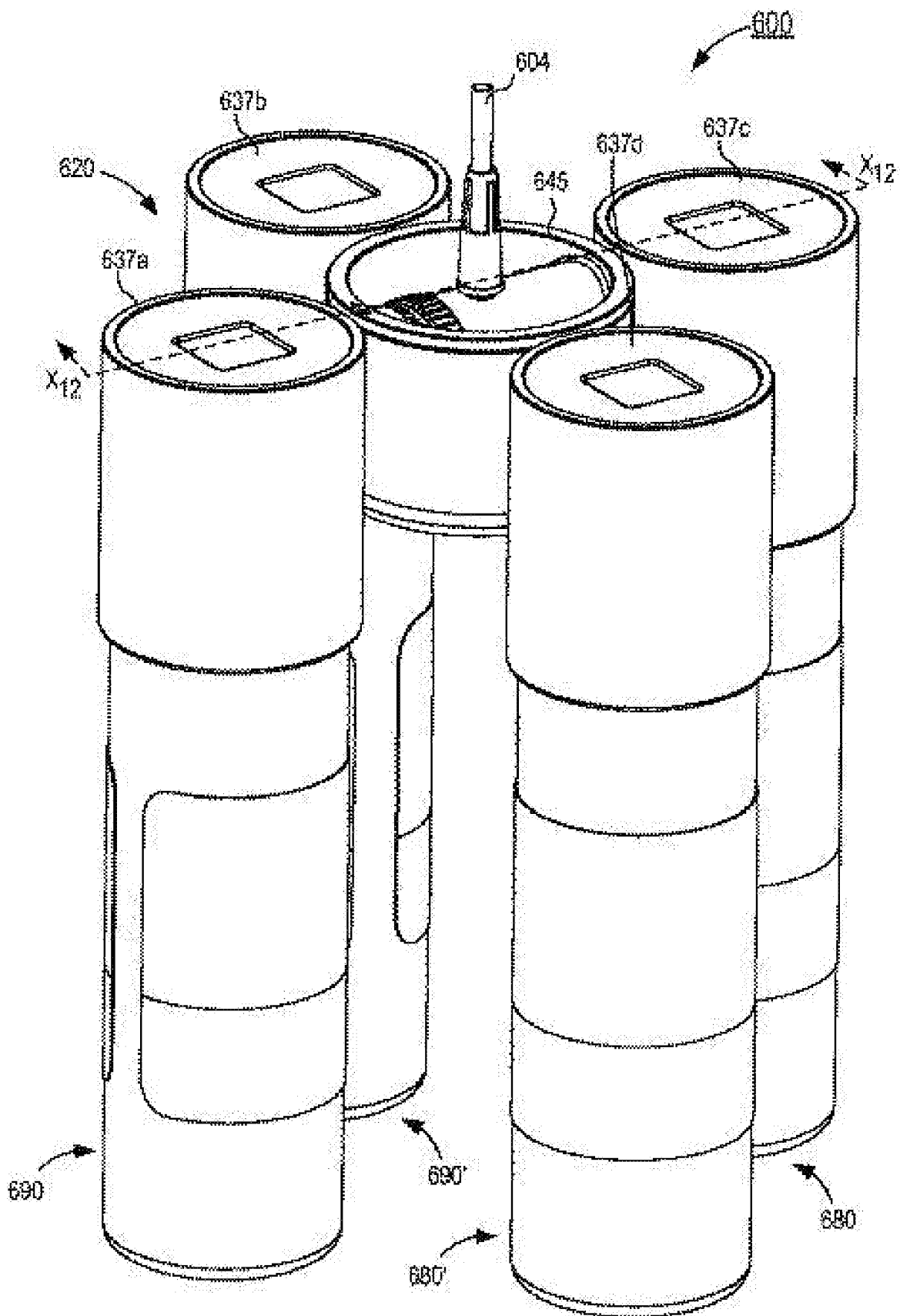


FIG. 25



[Fig.27]

FIG. 26

[Fig.28]

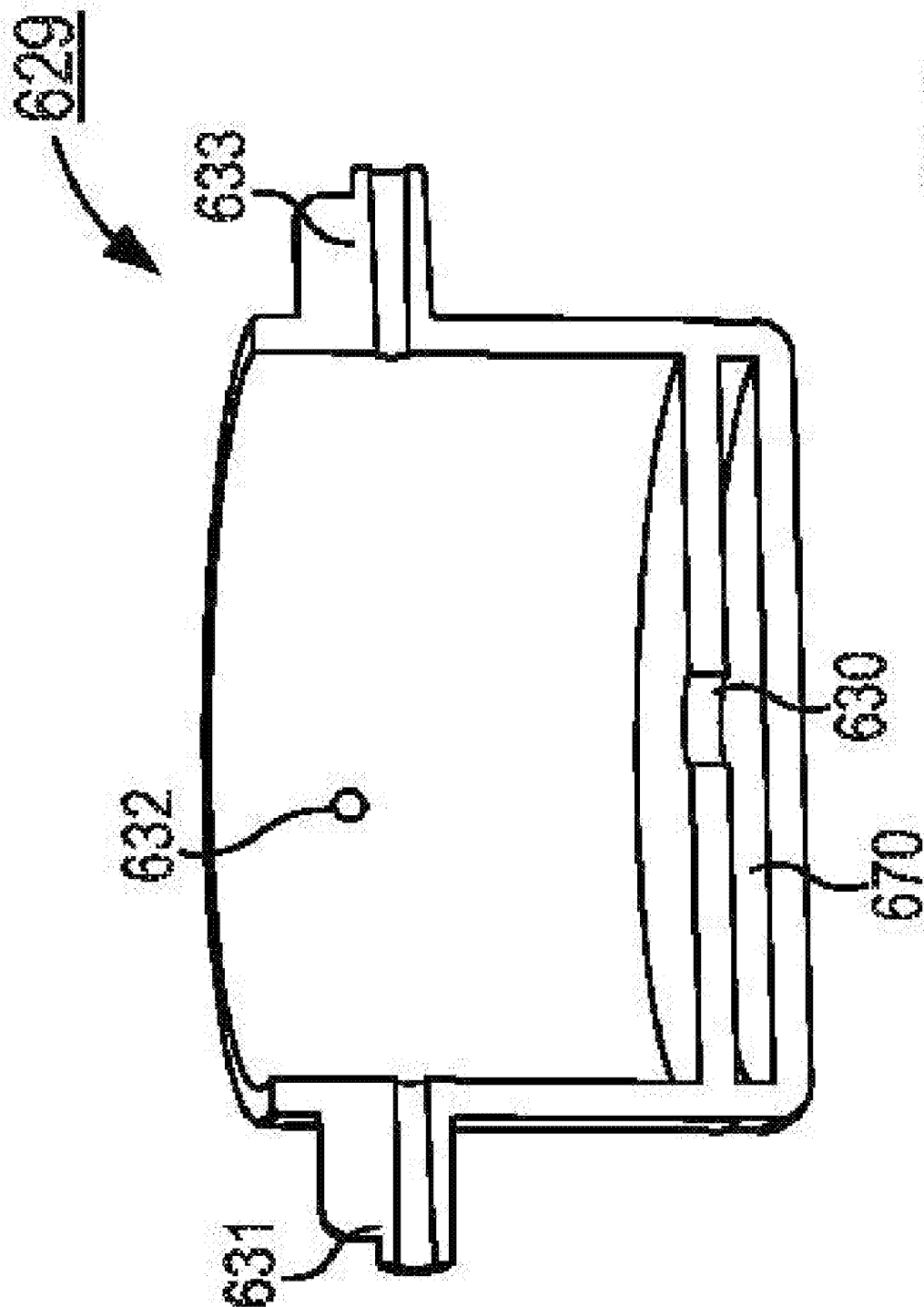


FIG. 28

[Fig.29]

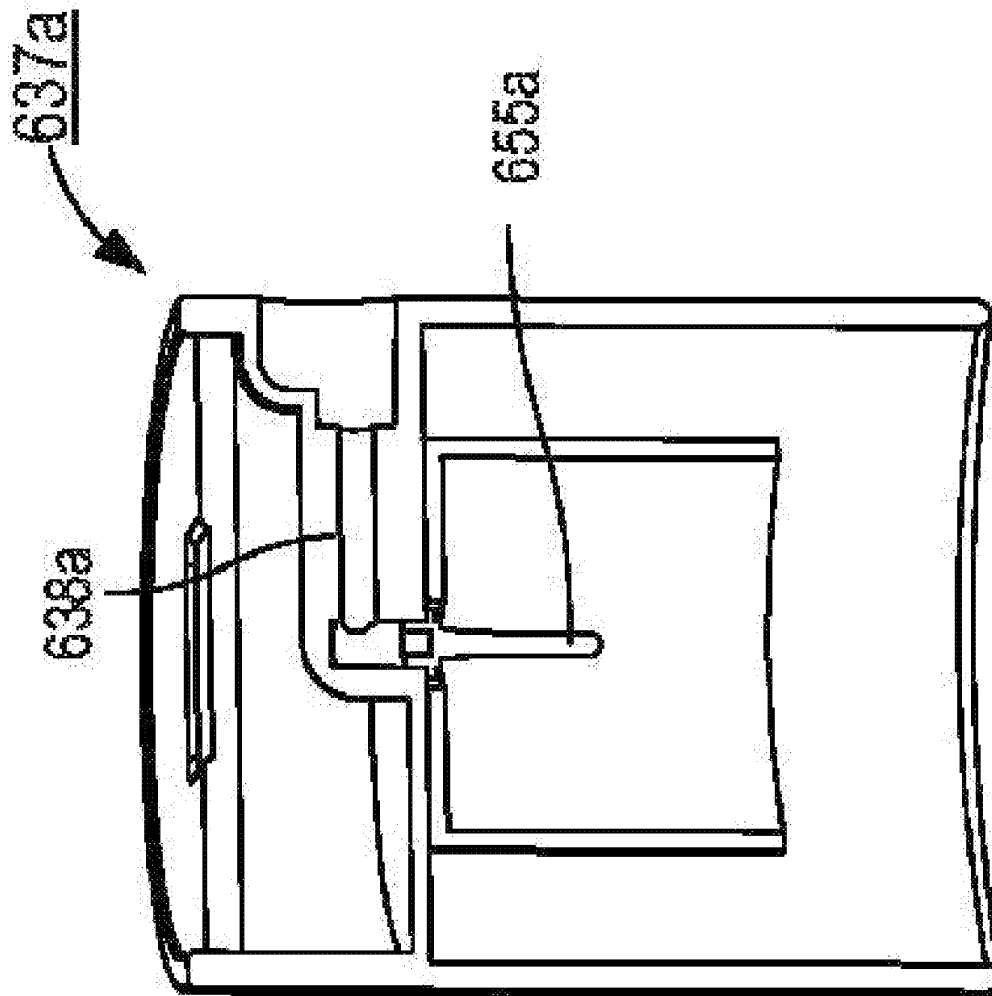
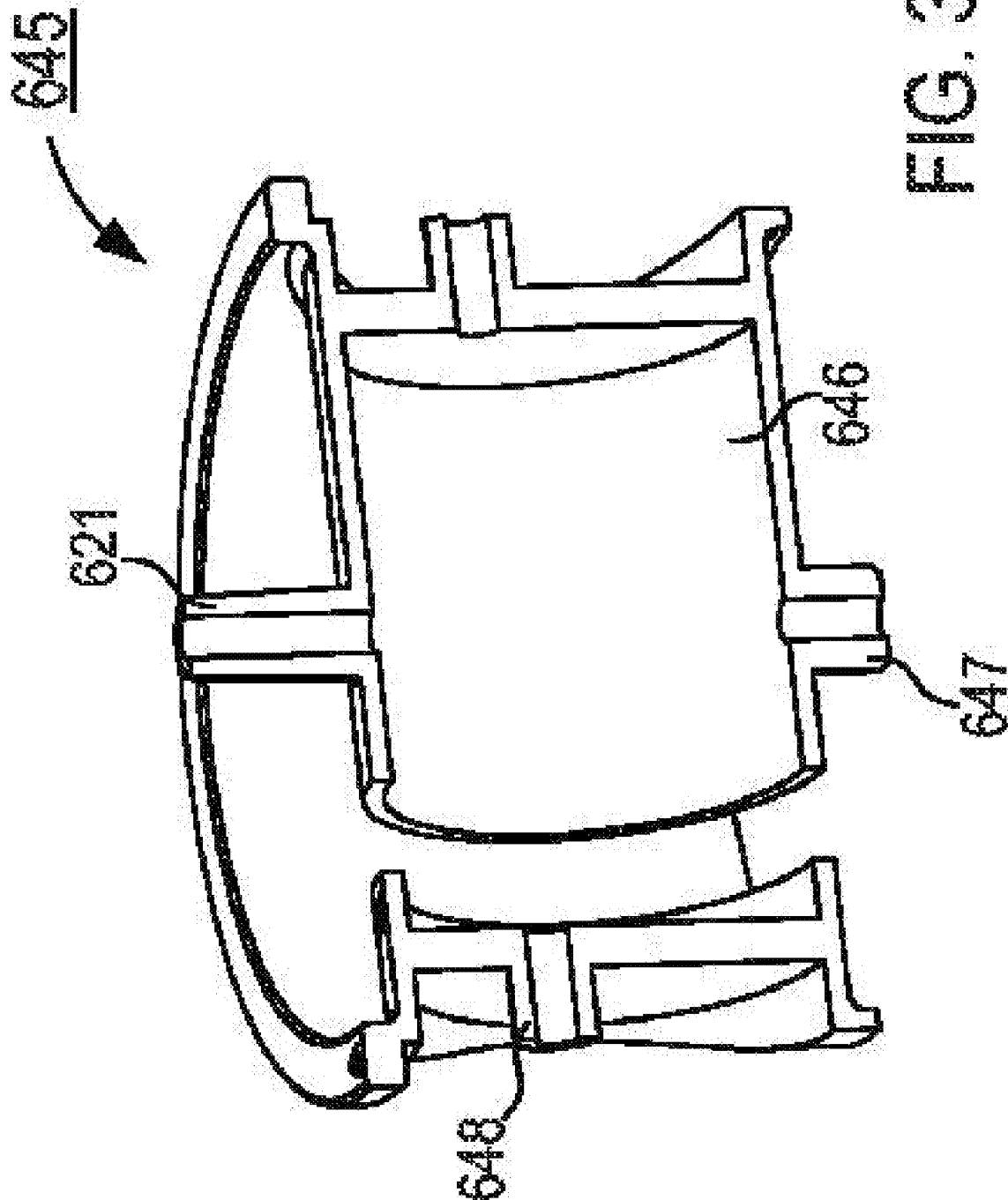


FIG. 29

[Fig. 30]



[Fig. 31]

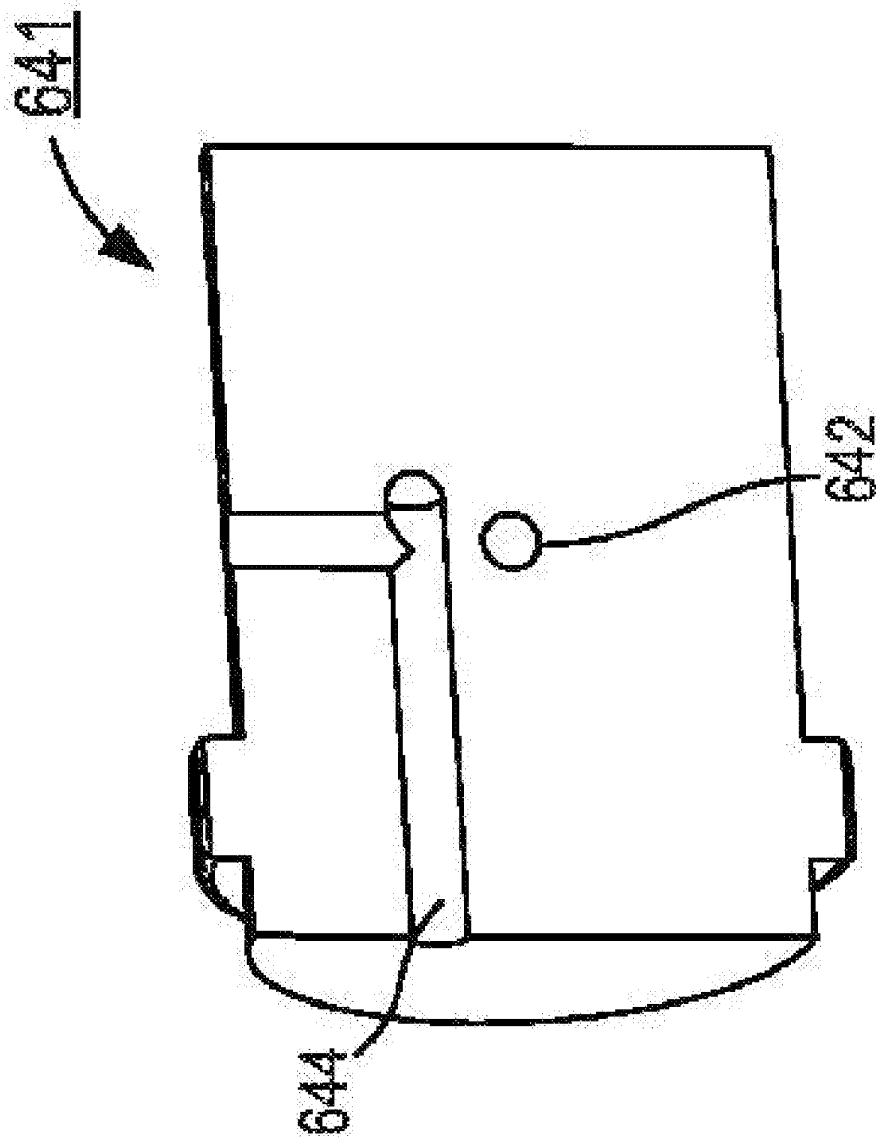


FIG. 31

[Fig. 32]

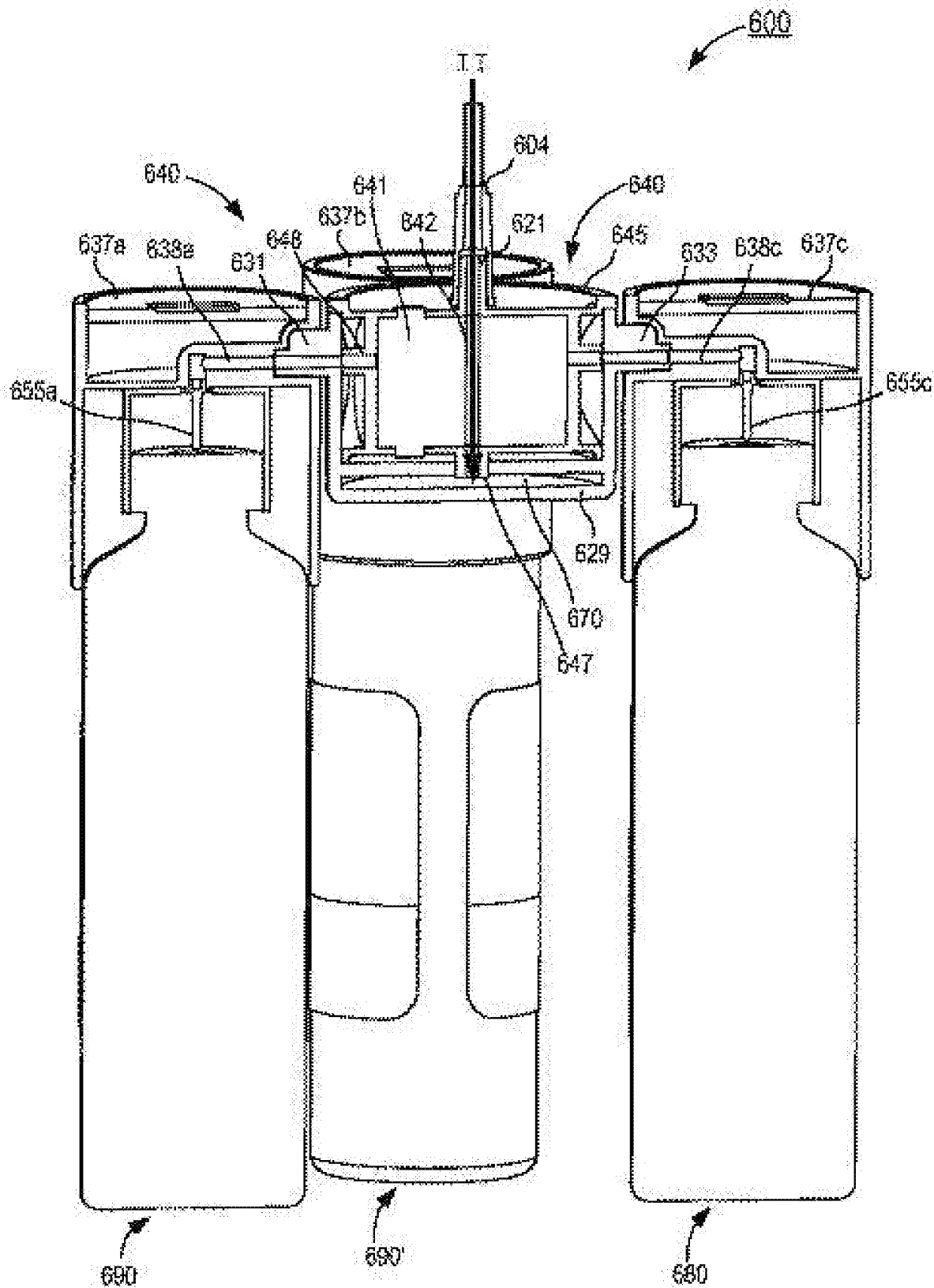


FIG. 32

[Fig. 33]

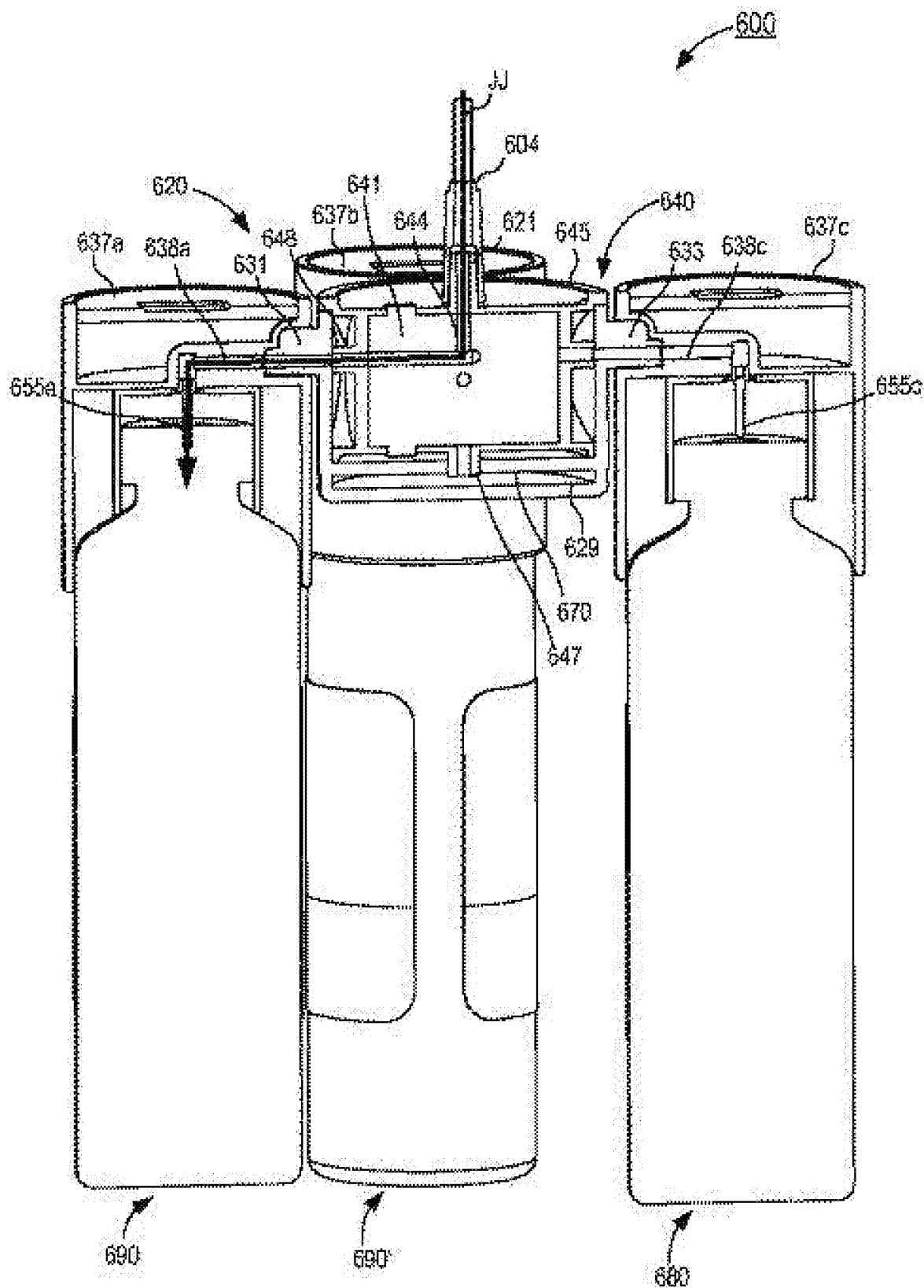
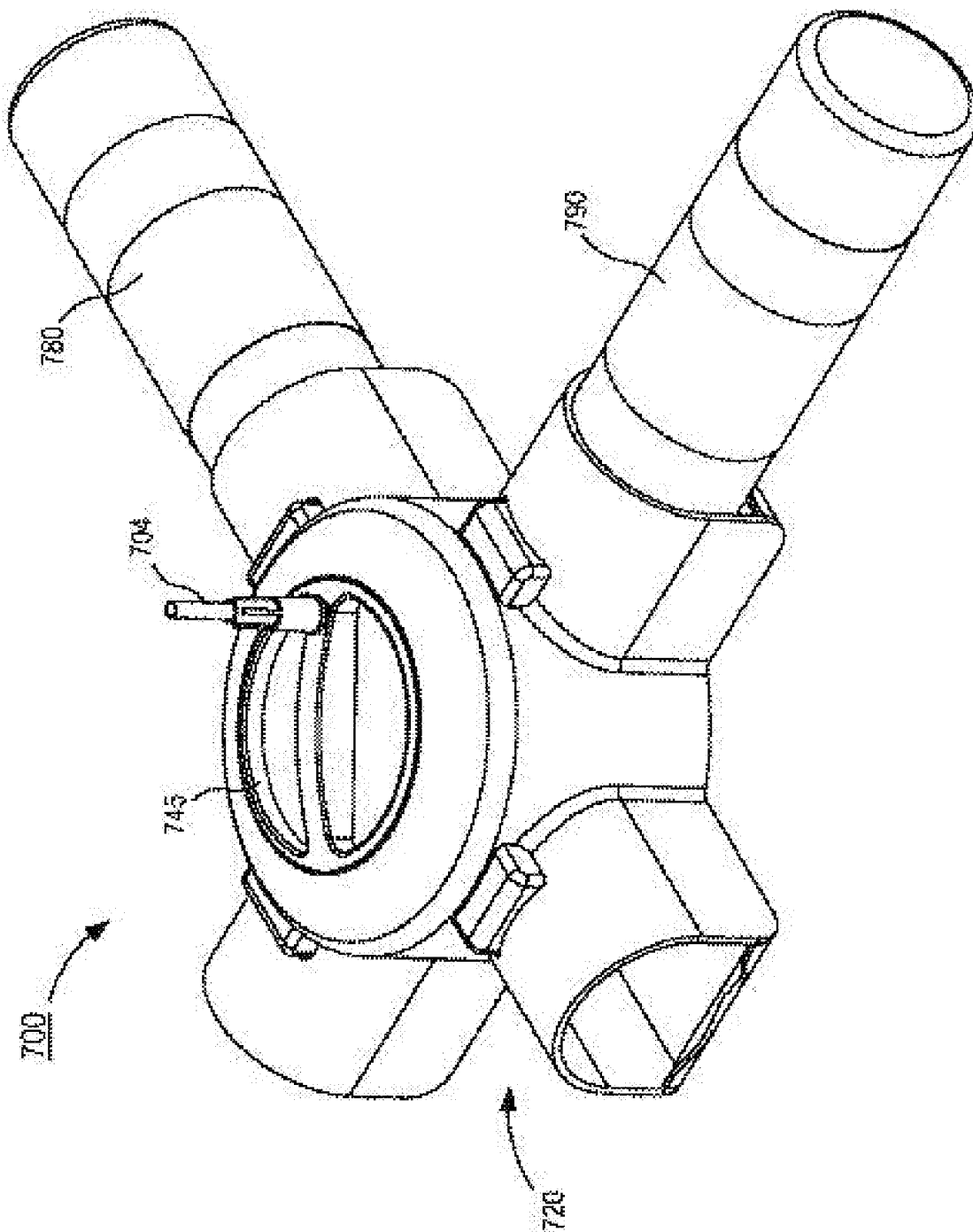


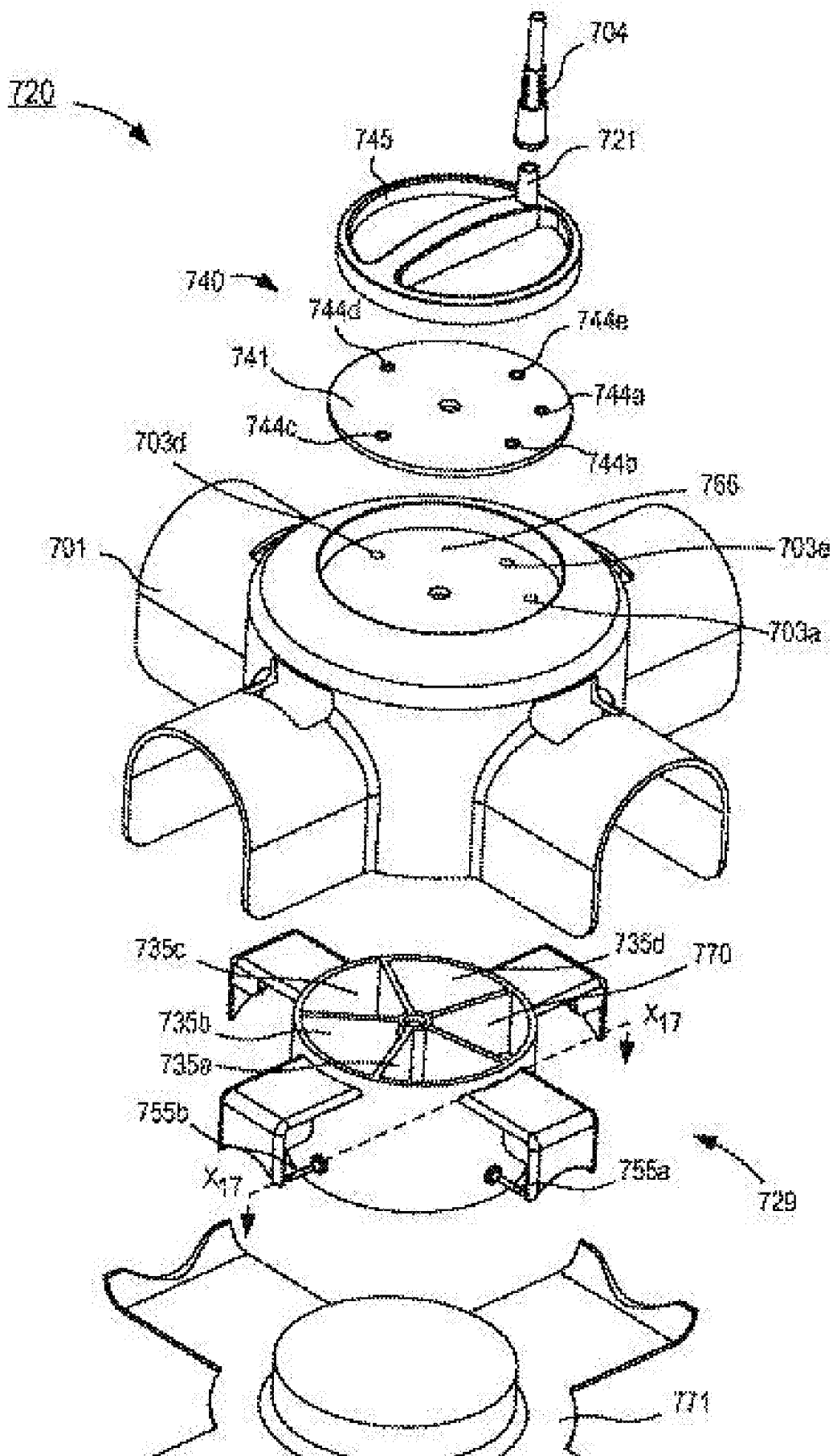
FIG. 33

[Fig. 34]

FIG. 34



[Fig.35]



[Fig. 36]

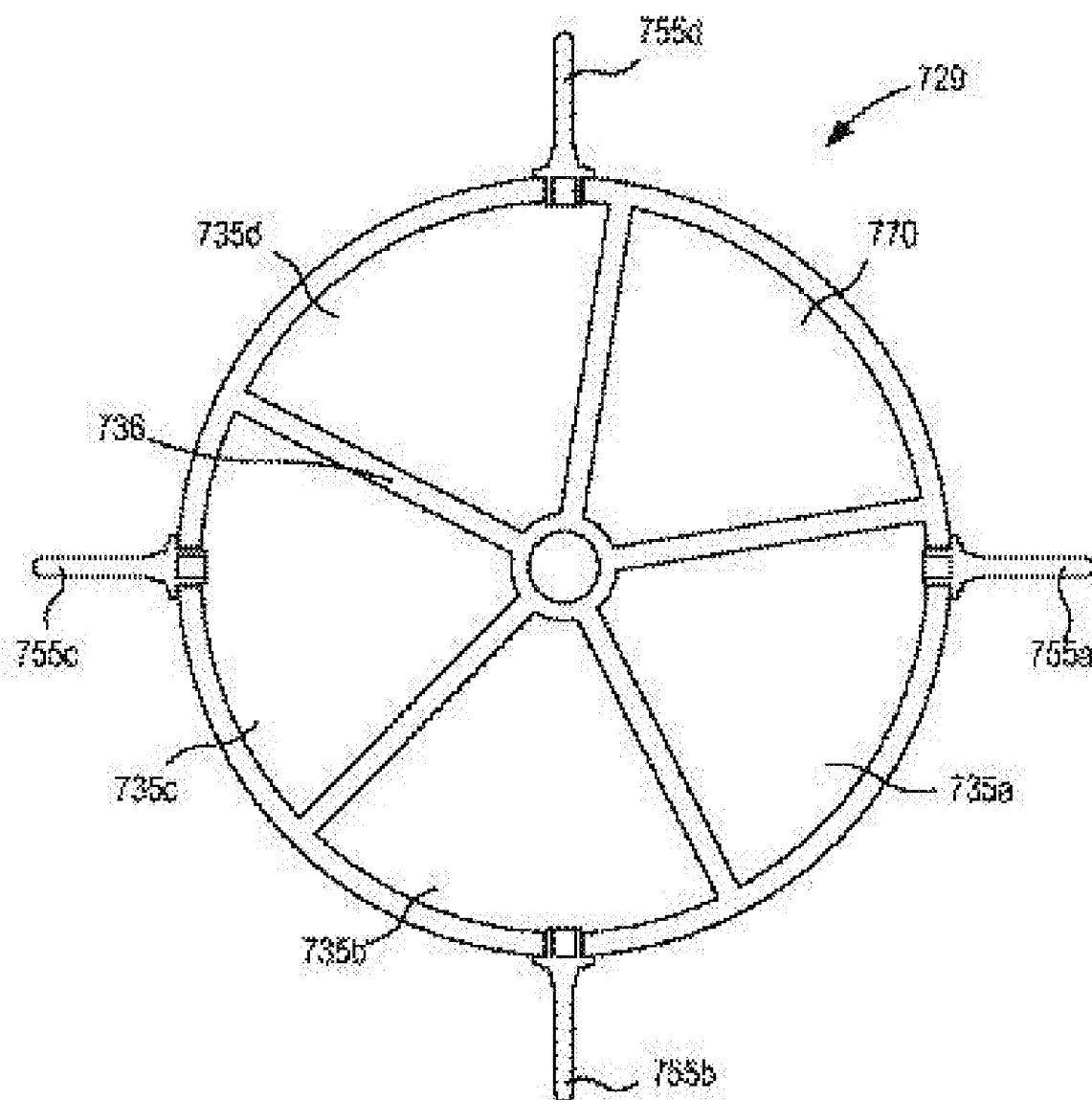


FIG. 36

[Fig. 37]

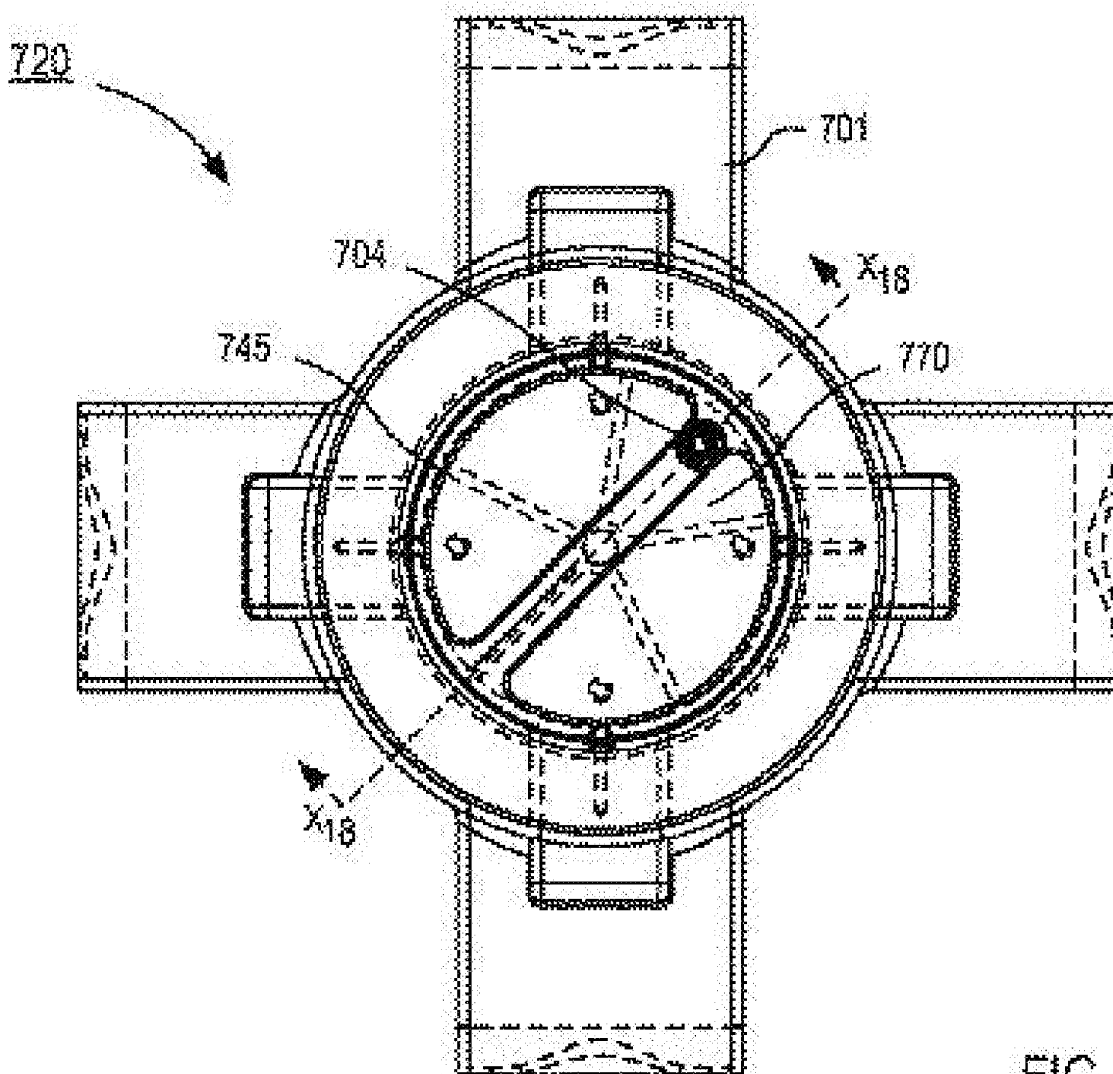
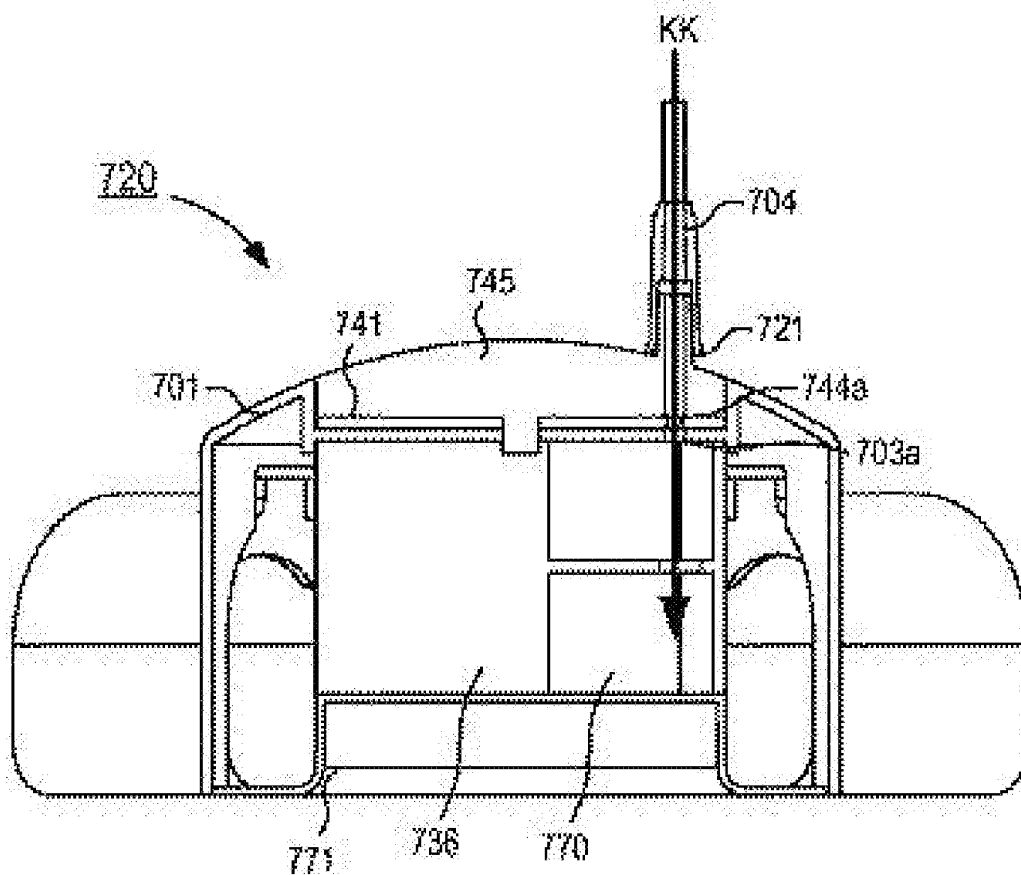


FIG. 37

[Fig. 38]



[Fig.39]

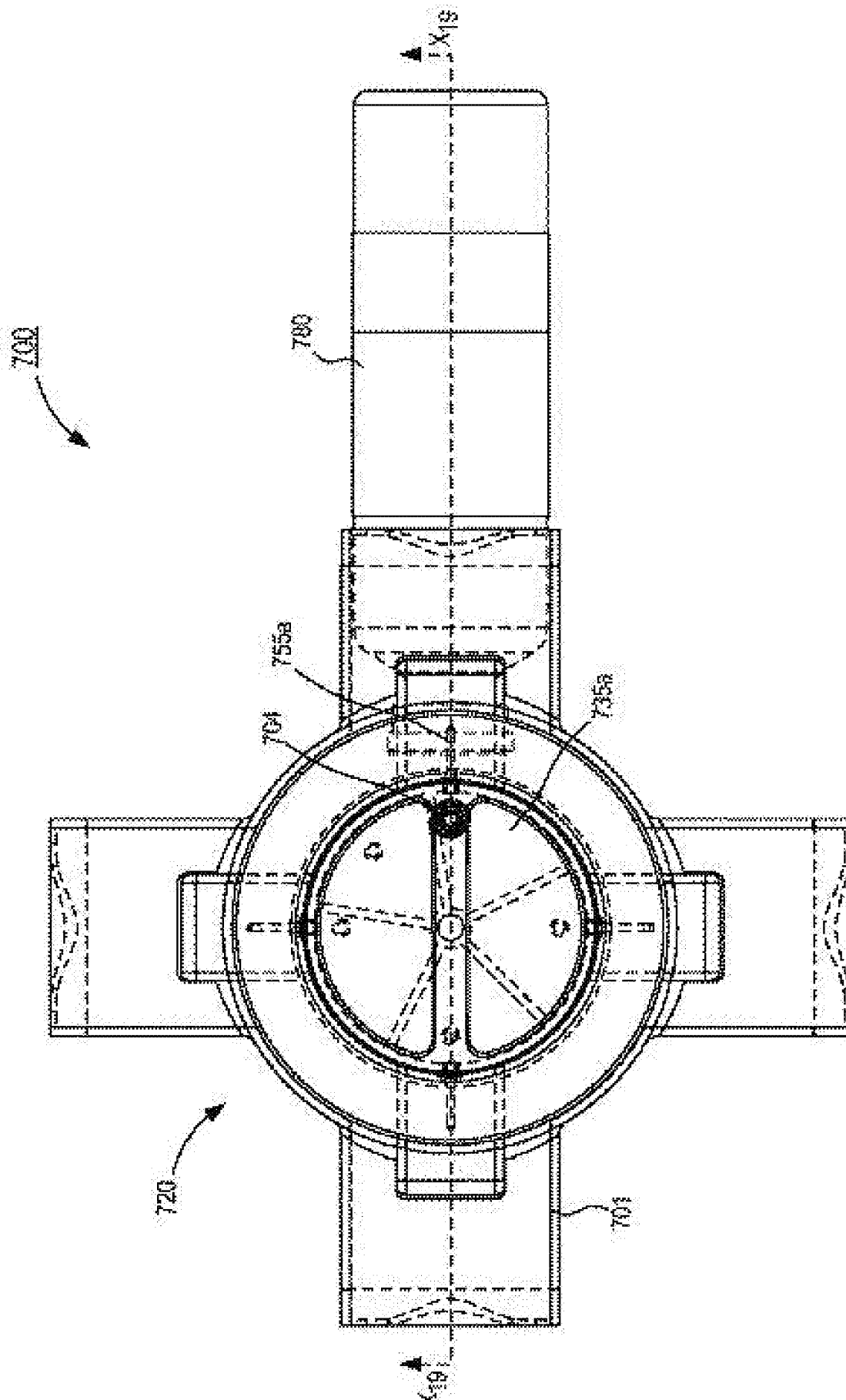


FIG. 39

[Fig. 40]

Fig. 40

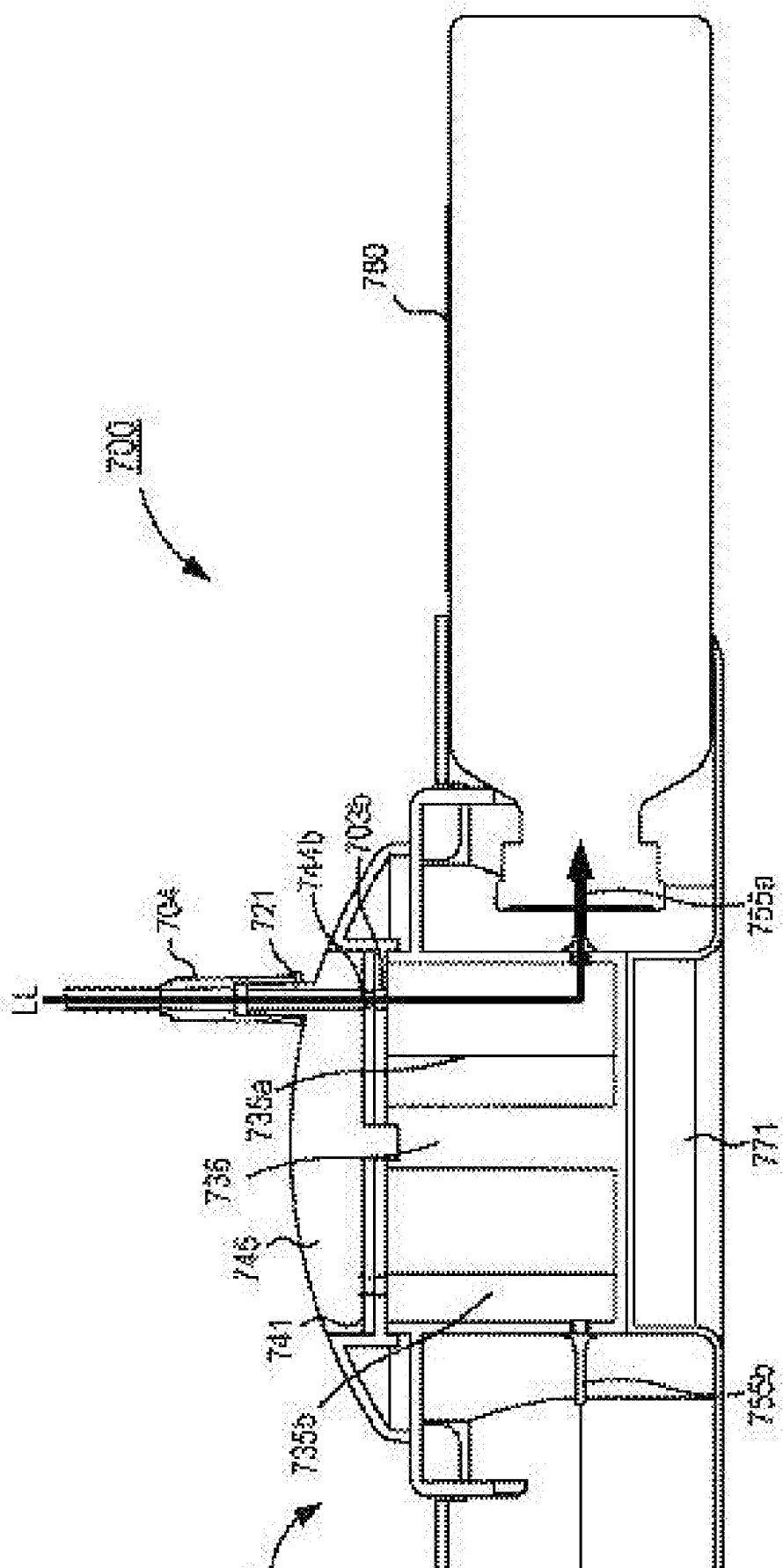
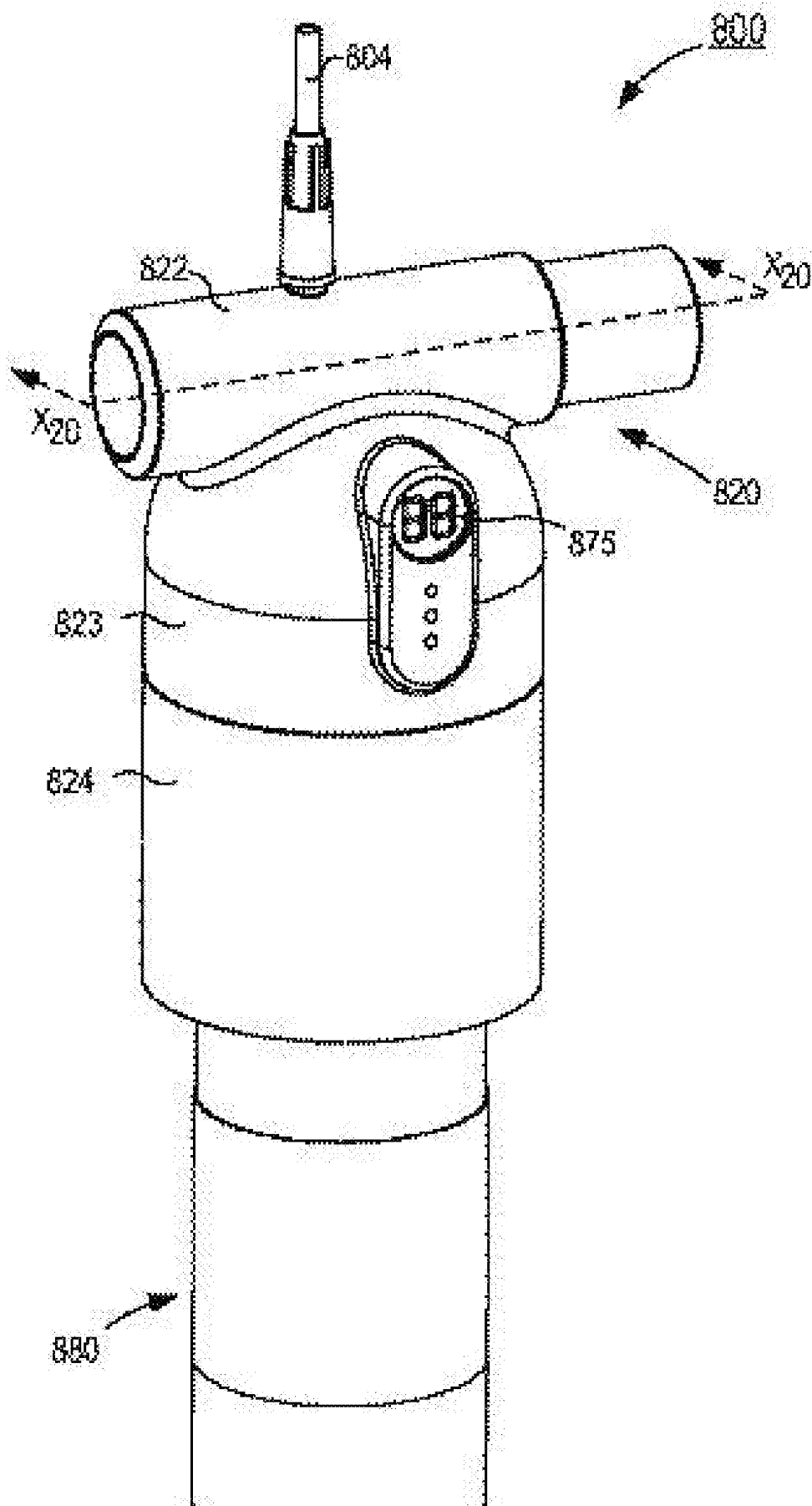


FIG. 40

[Fig. 41]

720





[Fig. 42]

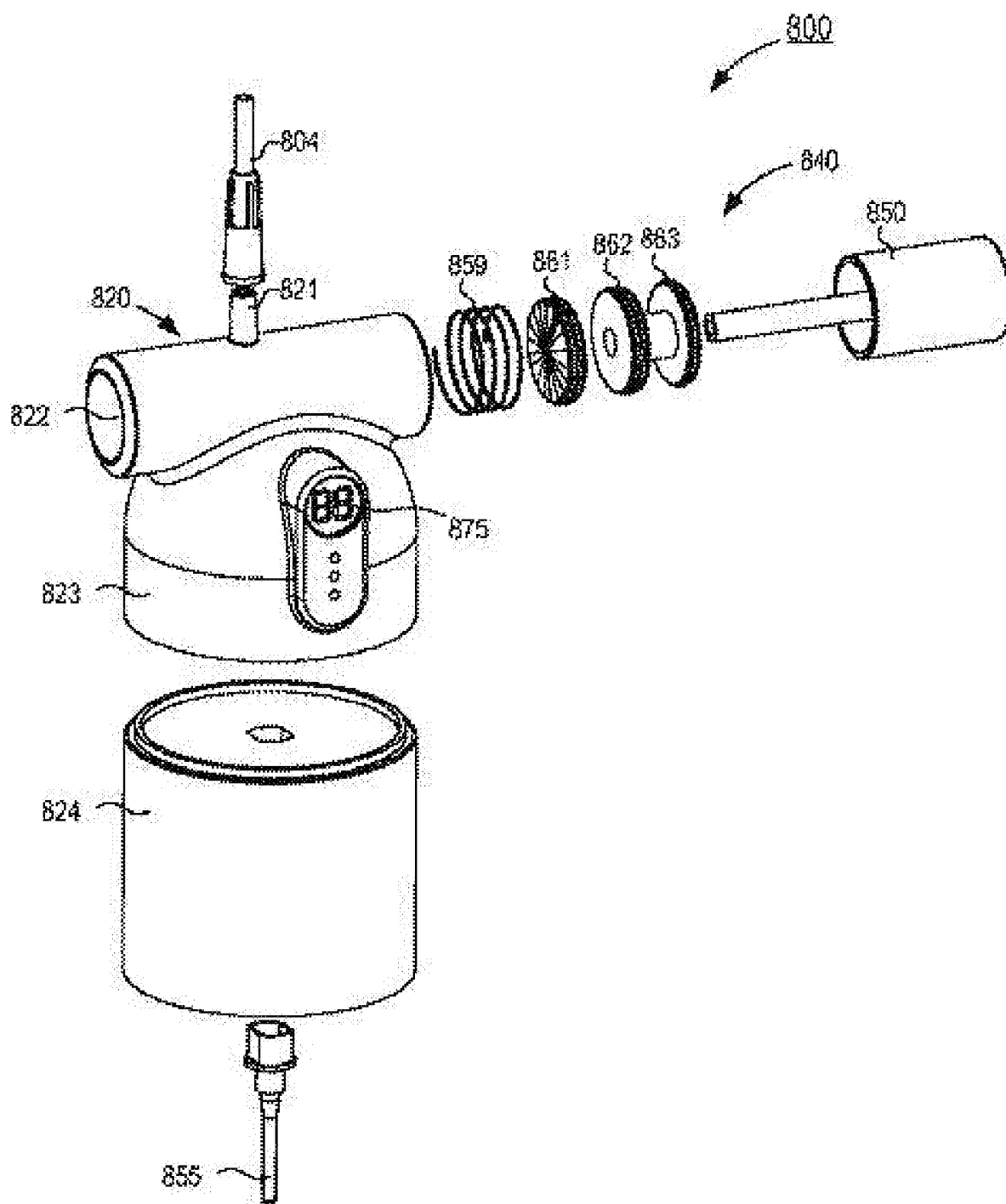
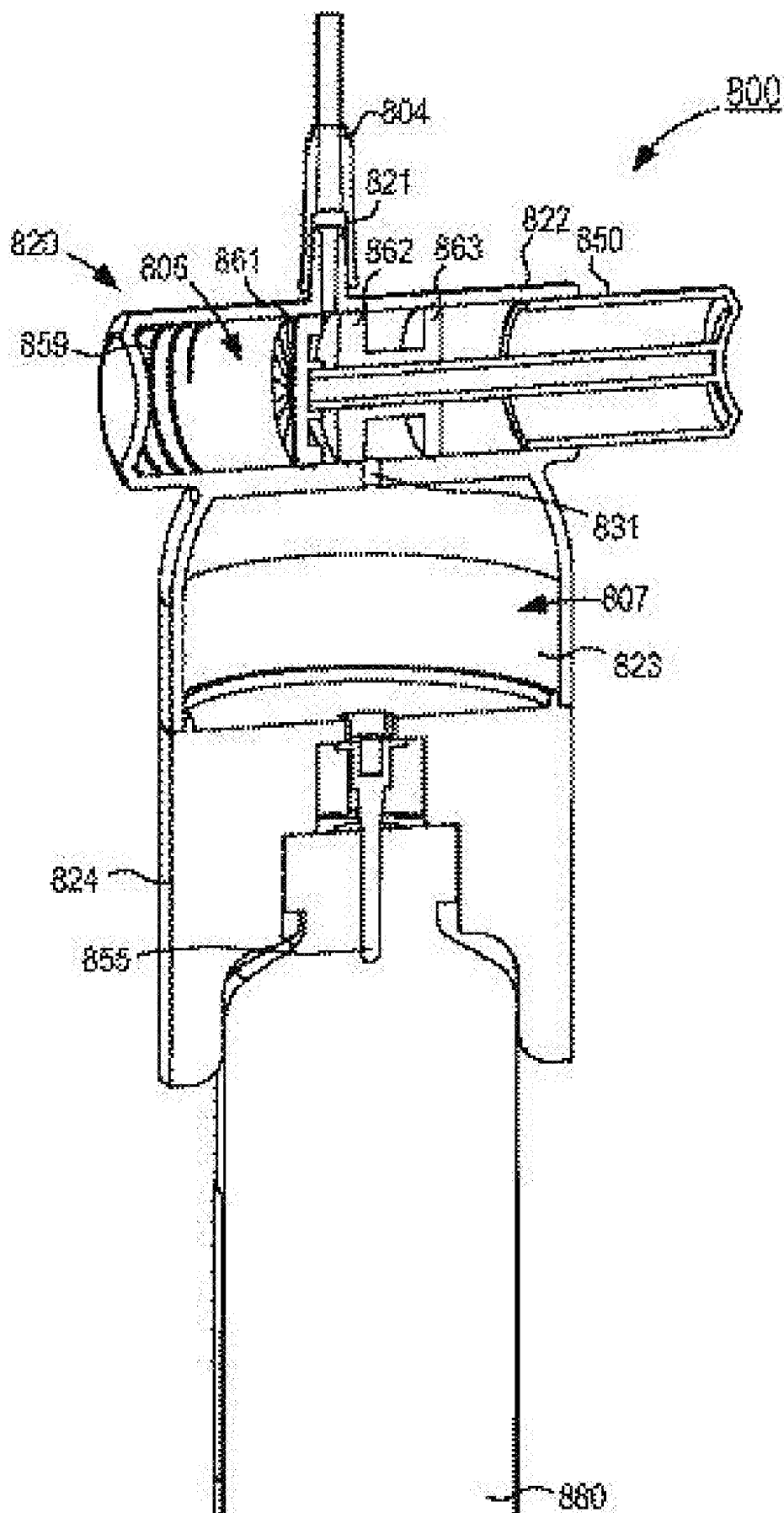


FIG. 42

[Fig. 43]



[Fig. 44]

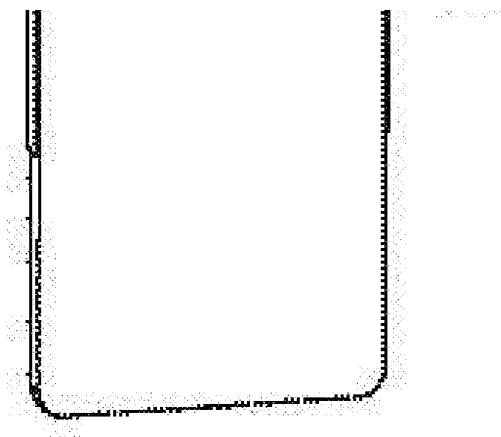
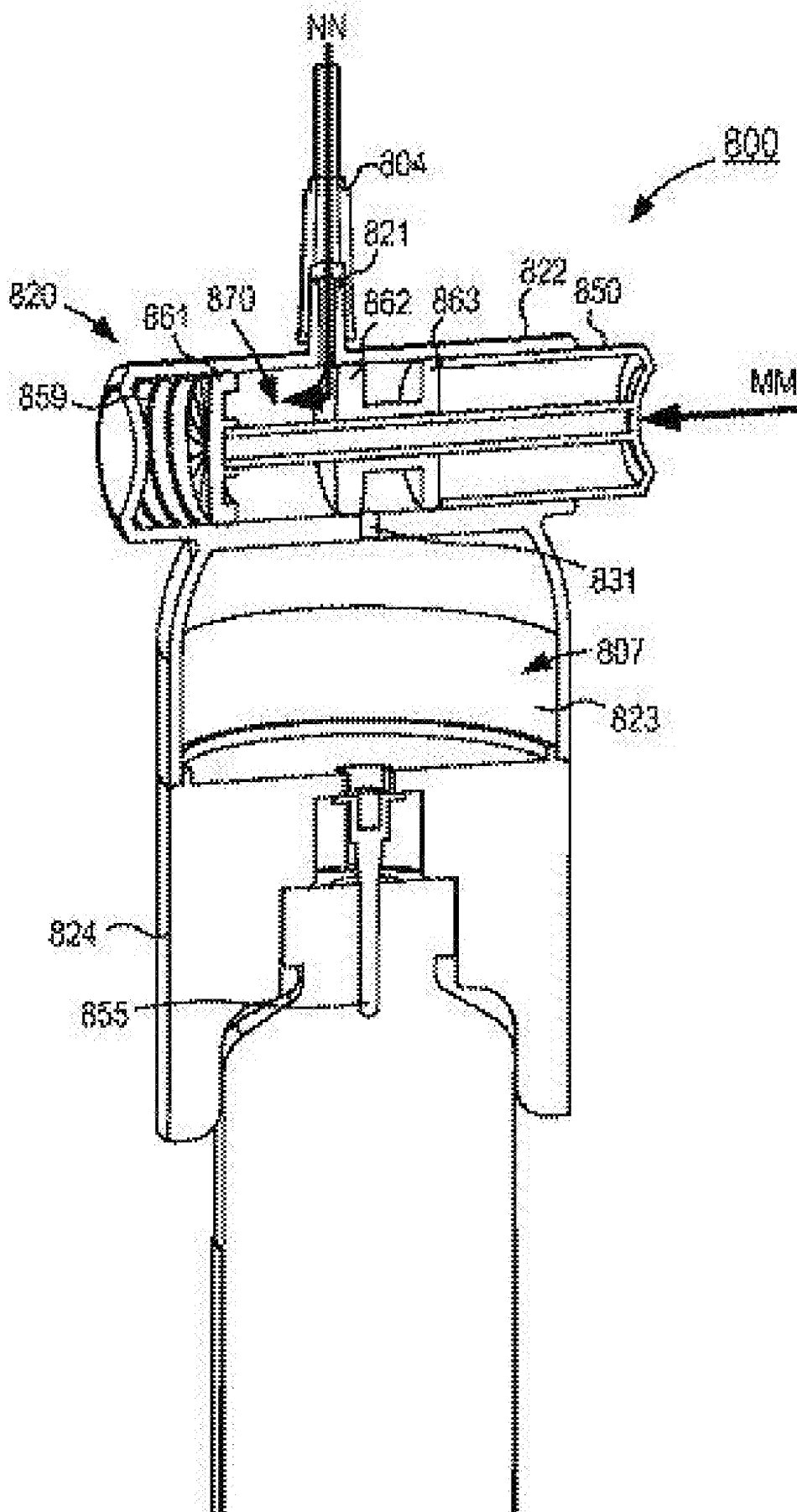


FIG. 43



[Fig. 45]

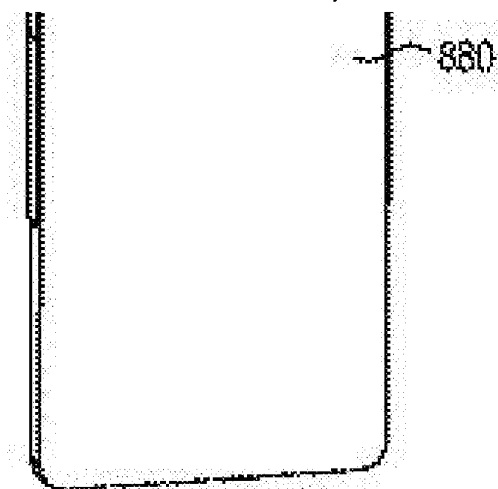


FIG. 44

[Fig. 46]

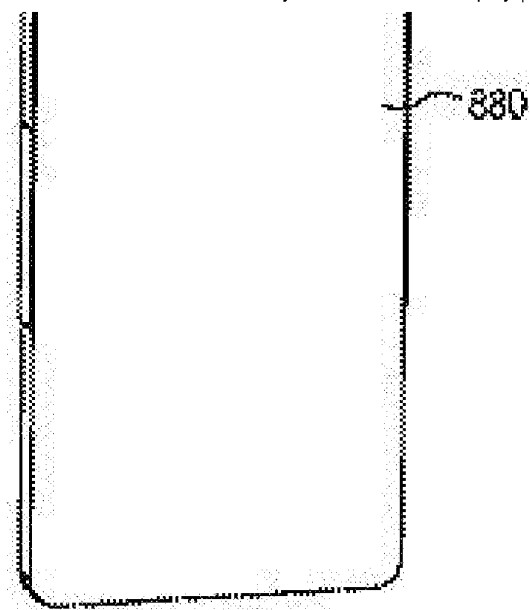


FIG. 45

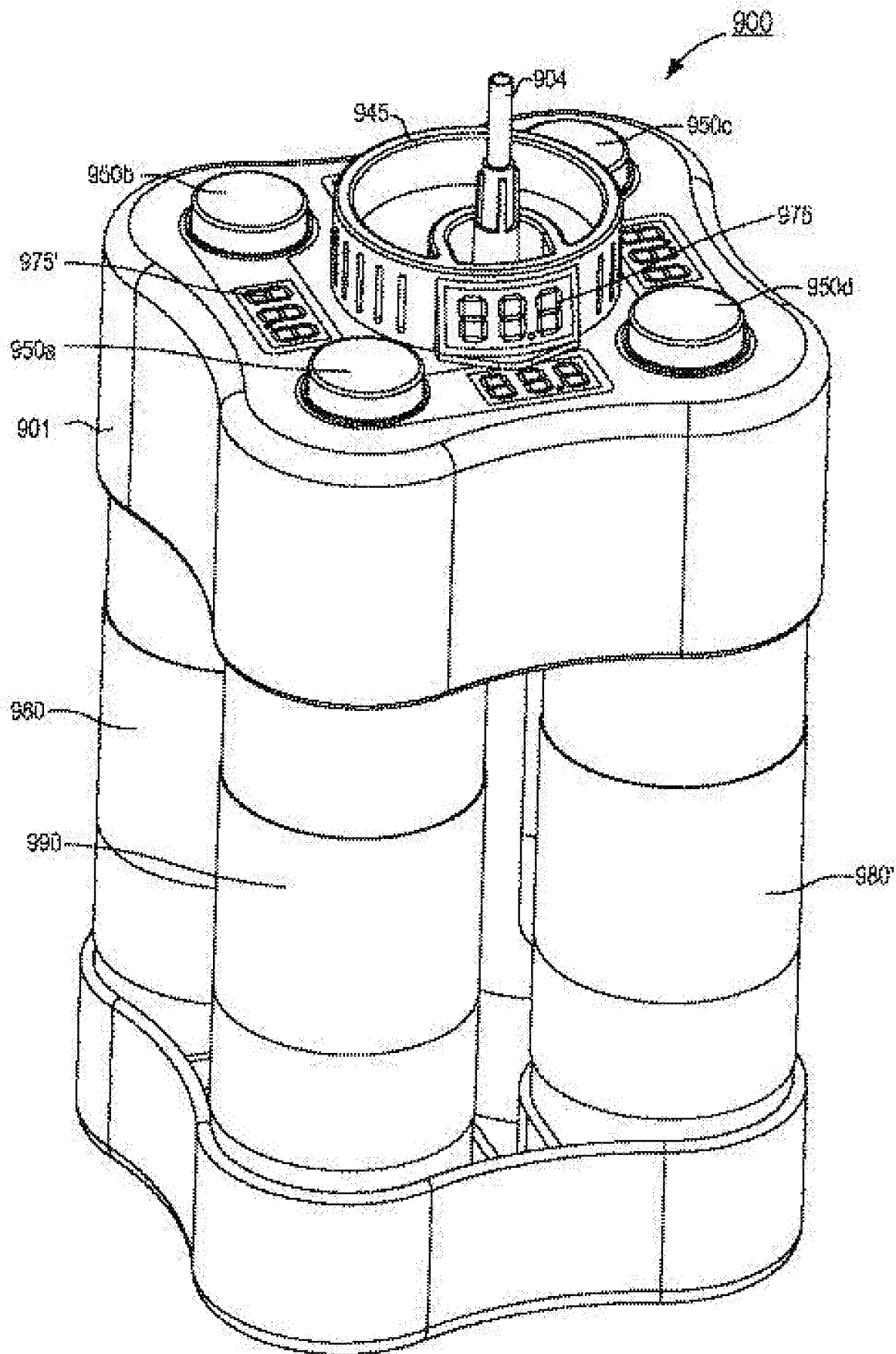


FIG. 46
[Fig. 46]

[Fig. 48]

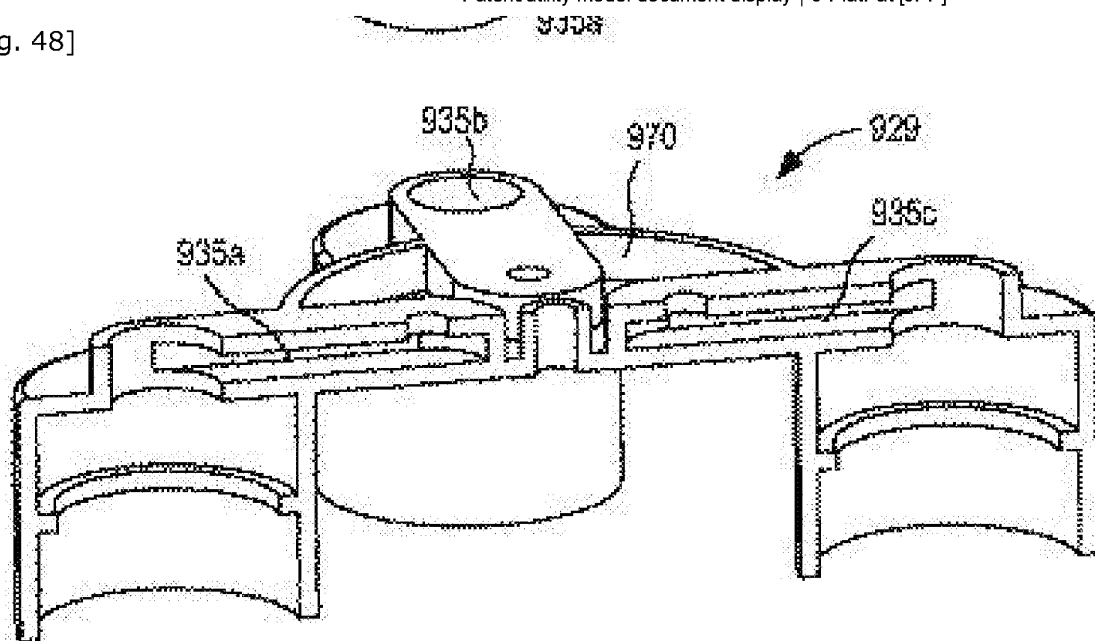


FIG. 48

[Fig. 49]

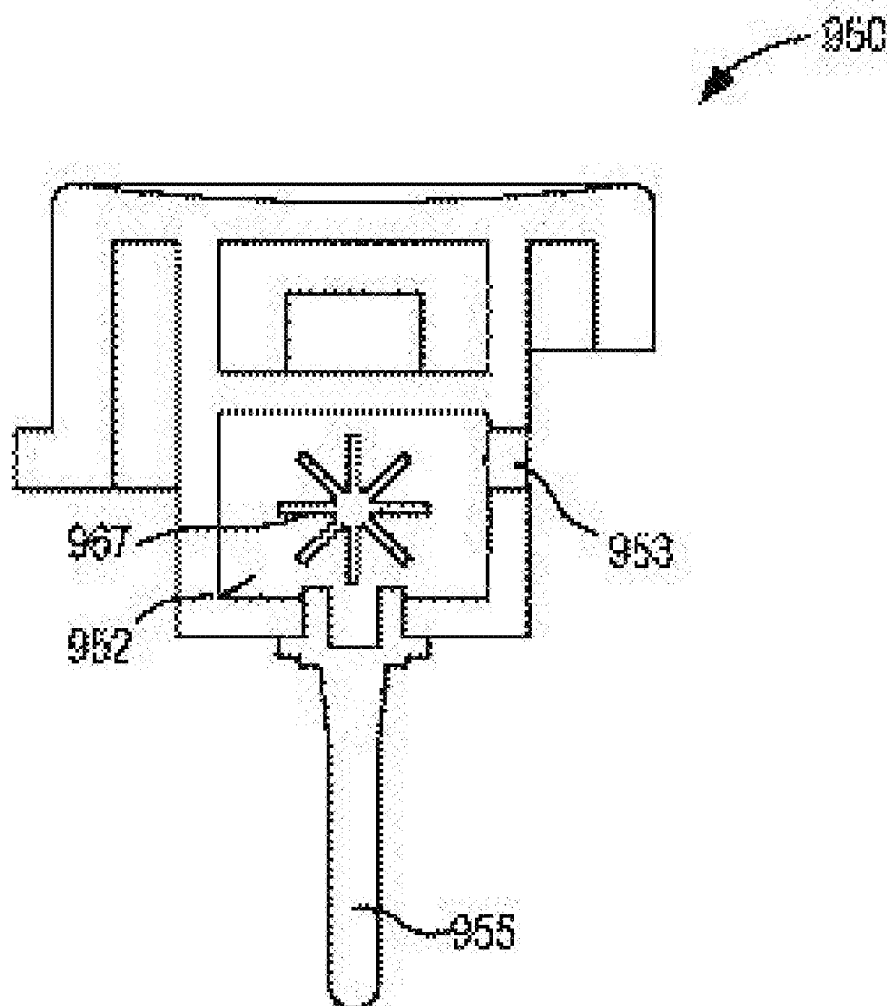


FIG. 49

[Fig. 50]

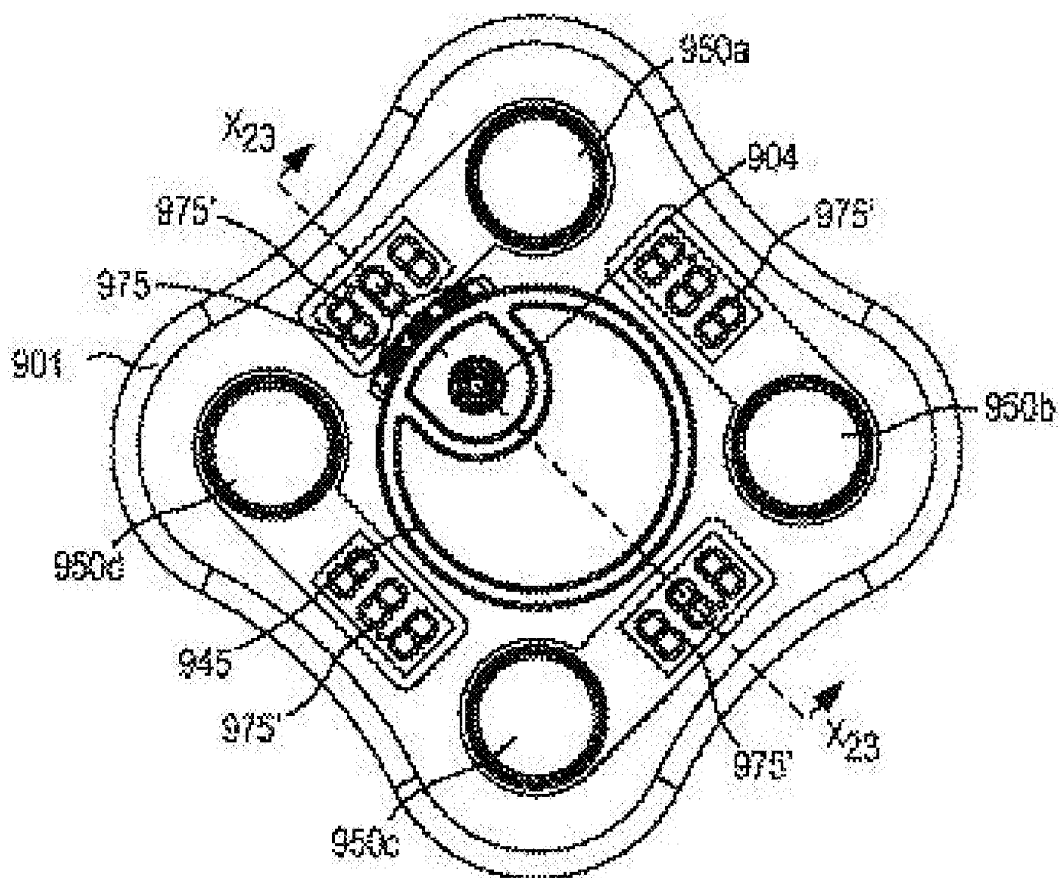


FIG. 50

[Fig. 51]

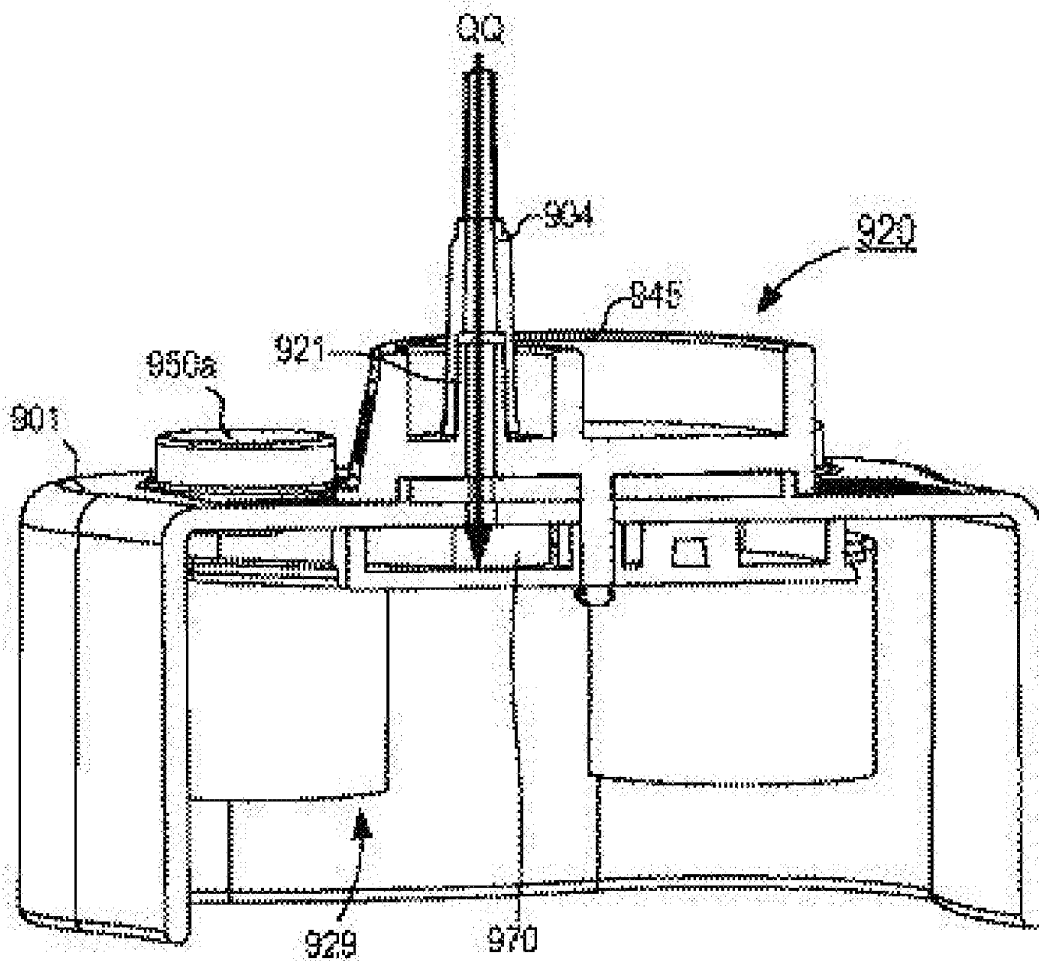


FIG. 51

[Fig. 52]

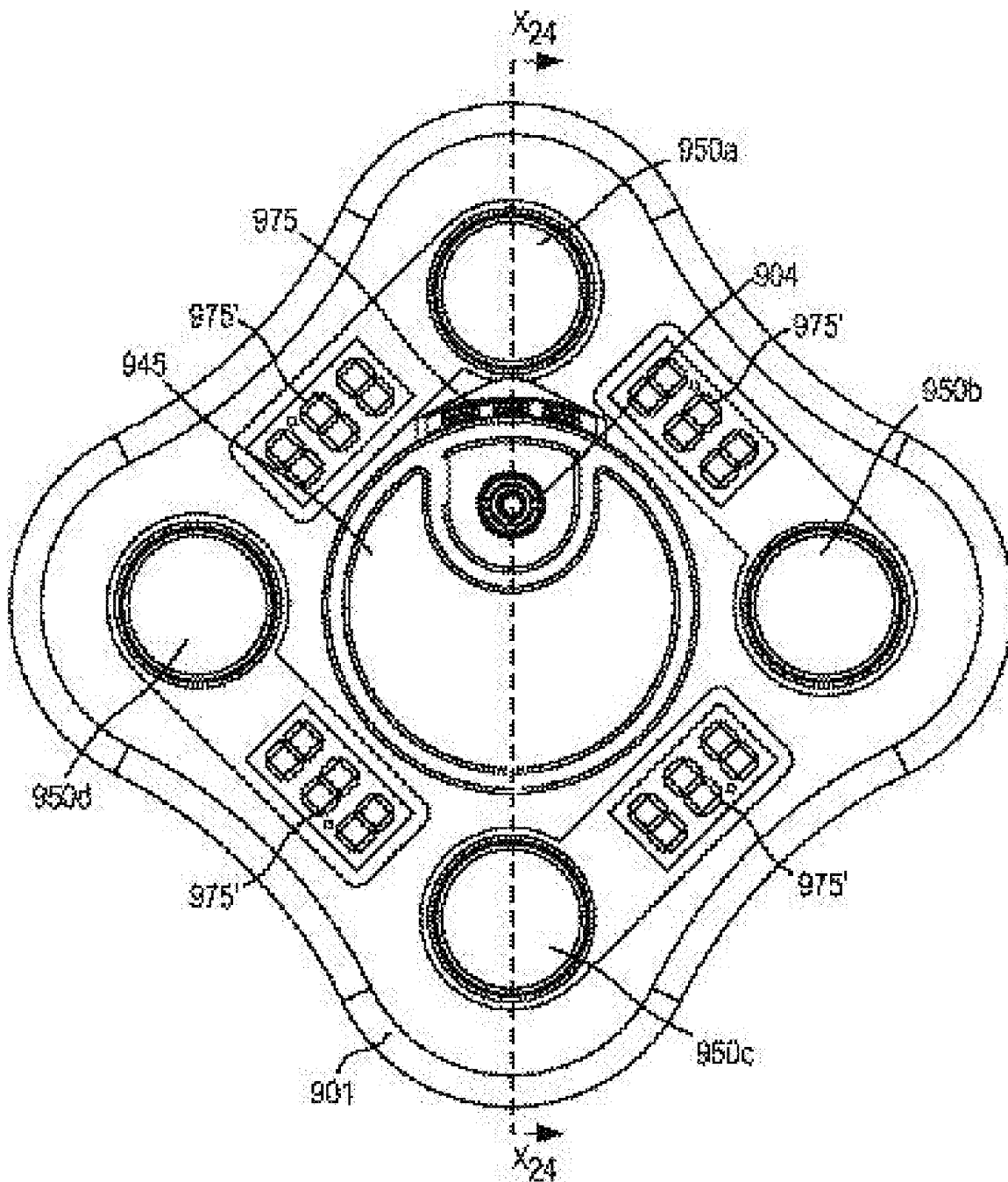
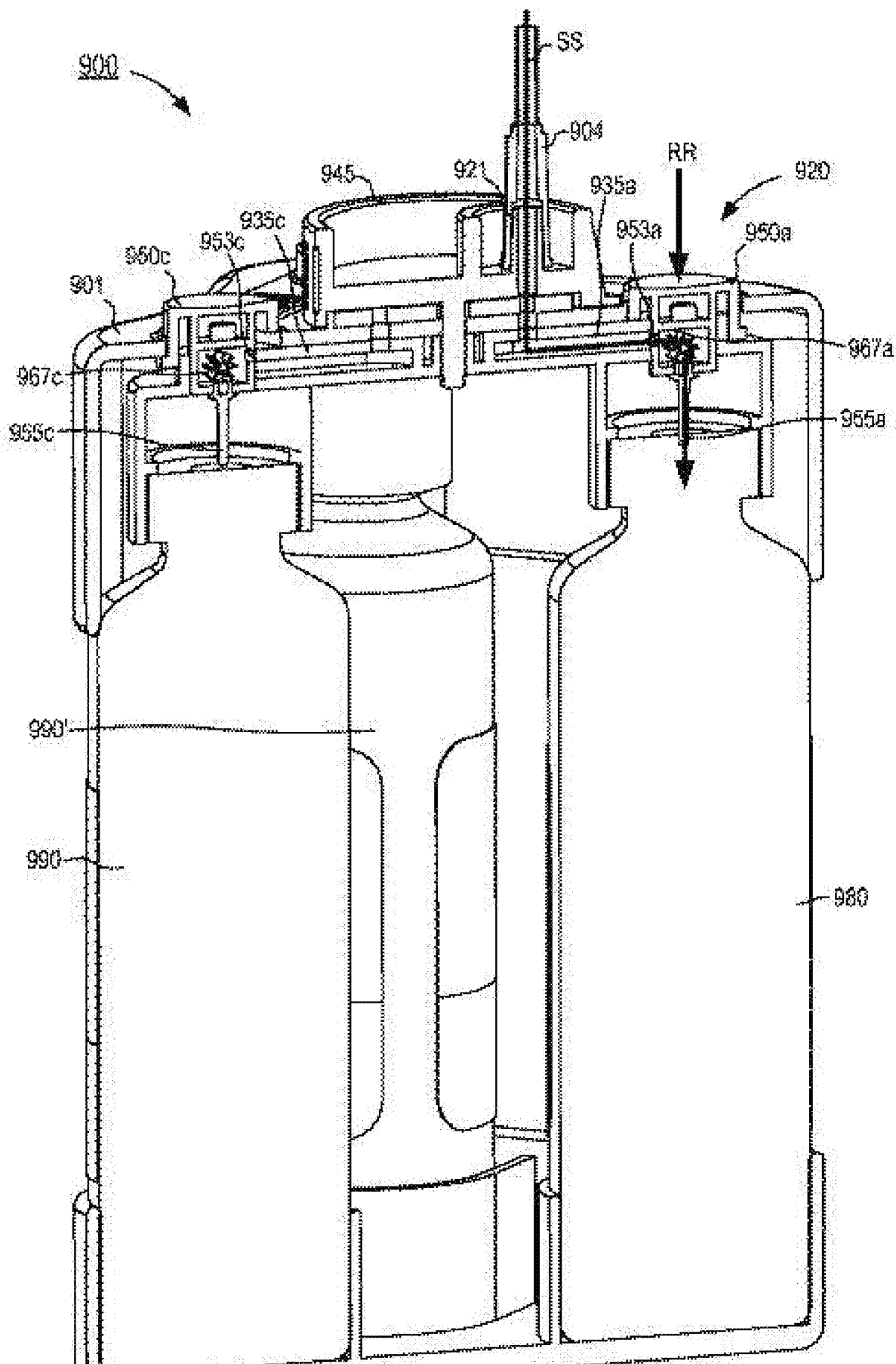
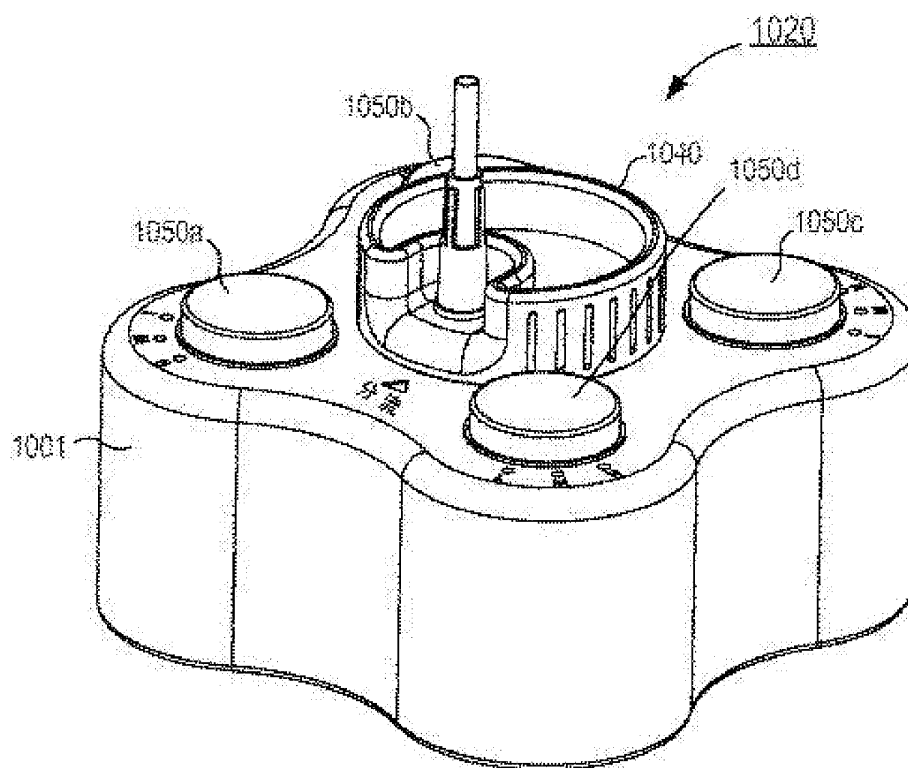


FIG. 52

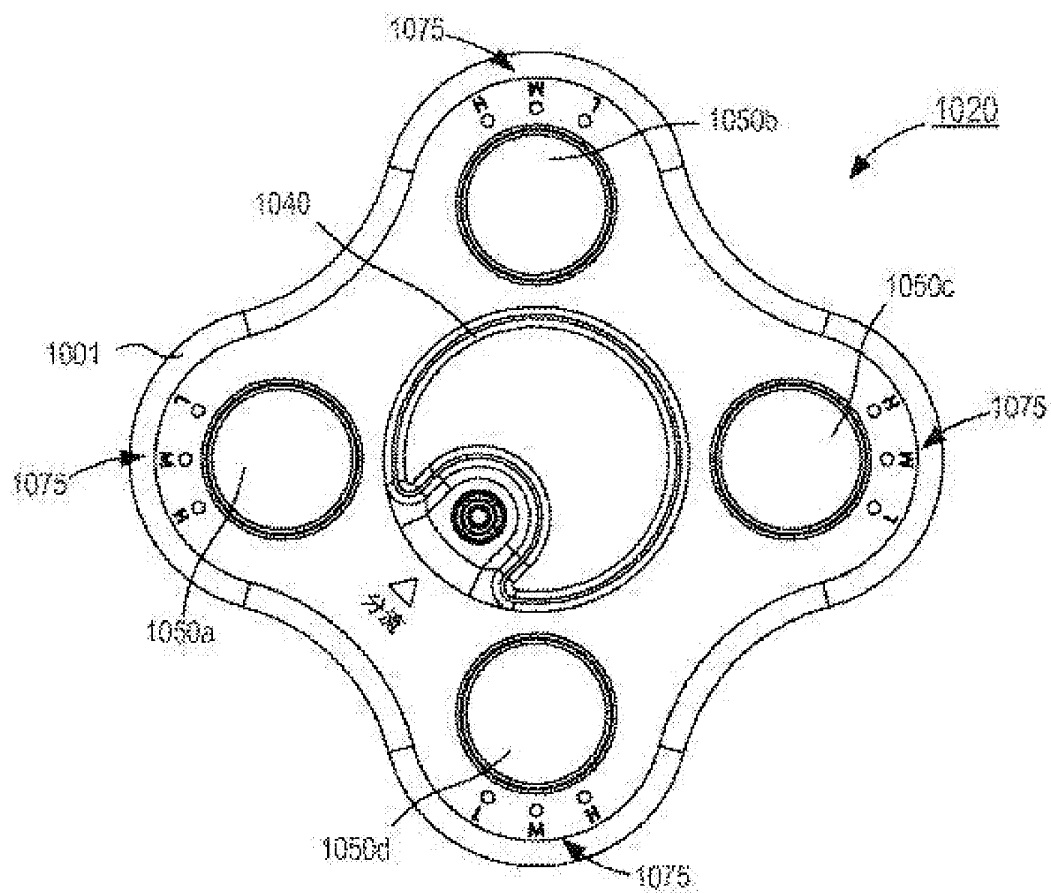
[Fig. 53]



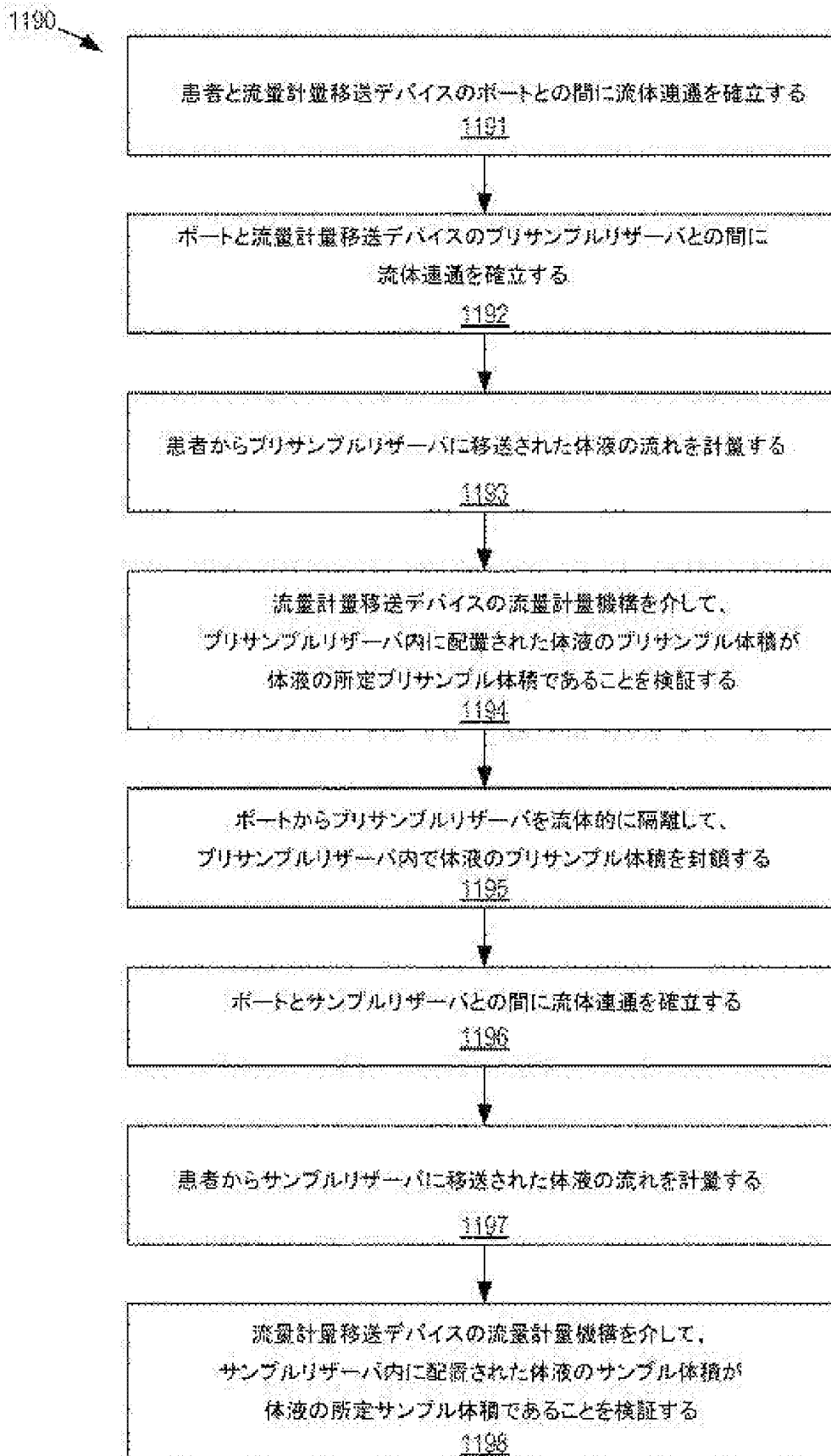
[Fig. 54]



[Fig. 55]



[Fig. 56]



search report	open
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[International search report]

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/073060

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/155 (2014.01)

USPC - 600/575

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - A61B 5/00, 5/15, 5/153, 5/155; A61M 39/22; A61J 1/05; G01N 1/10, 1/14, 1/18 (2014.01)

USPC - 422/559; 435/294.1; 600/573, 575, 576, 577, 578; 604/248, 409

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

CPC - A61B 5/1405, 5/1427, 5/1438, 5/150251; A61M 39/223 (2013.01)

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

PatBase, Google Patents, Google Scholar.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,097,842 A (BONN) 24 March 1992 (24.03.1992) entire document	12, 15, 16, 18
Y		1-11, 13, 14, 17, 19-29
X	US 2008/0145933 A1 (PATTON) 19 June 2008 (19.06.2008) entire document	30-41
Y		3, 13, 17, 22, 24, 25,
Y	US 2005/0148993 A1 (MATHIAS et al) 07 July 2005 (07.07.2005) entire document	1-11
Y	WO 2005/068011 A1 (MEHLHORN) 28 July 2005 (28.06.2005) entire document	14, 21-29
Y	US 3,848,581 A (CINQUALBRE et al) 19 November 1974 (19.11.1974) entire document	9, 19, 20

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

06 February 2014

Date of mailing of the international search report

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Name and mailing address of the ISA/US

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PCT Helpdesk: 571-272-4300
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Form PCT/ISA/210 (second sheet) (July 2009)

drawing

open

Representative drawing

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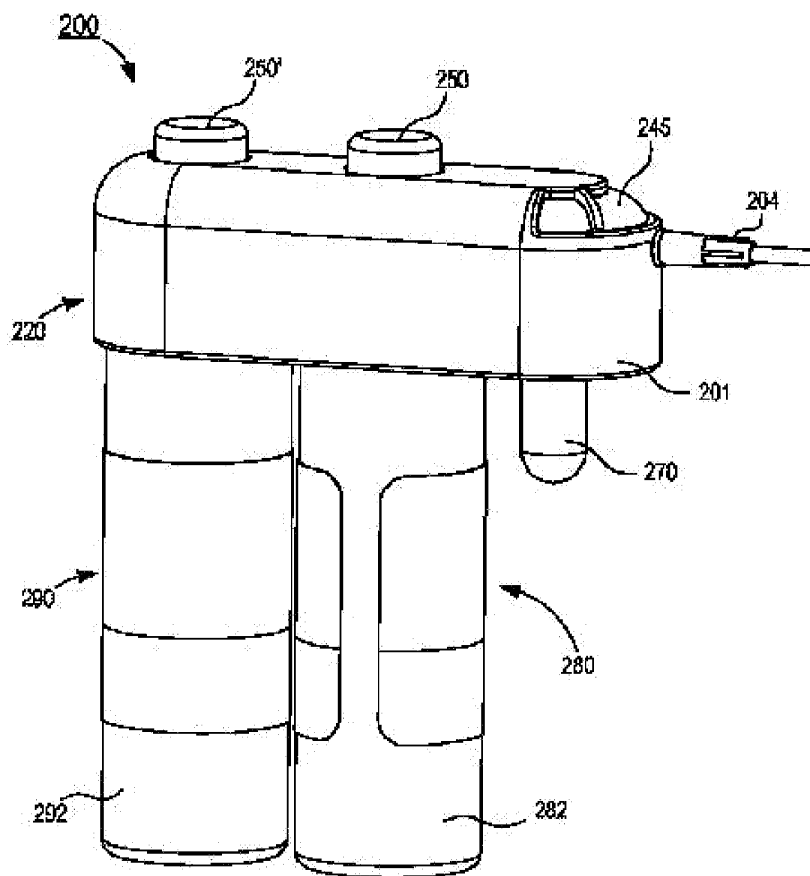


FIG. 2

Representative drawing

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/ 1

display

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(19) 日本国特許庁(JP)

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A 6 1 B 5/15 (2006.01)	A 6 1 B 5/14 3 0 0 H	

審査請求 未請求 予備審査請求 未請求 (全 64 頁)

(21) 出願番号	特願2015-545813 (P2015-545813)	(71) 出願人	514113555 マグノリア メディカル テクノロジーズ 、インコーポレイテッド アメリカ合衆国、ワシントン州 9812 1、シアトル、6番 アベニュー 200 1、スイート 1630
(86) (22) 出願日	平成25年12月4日 (2013.12.4)	(74) 代理人	100079108 弁理士 稲葉 良幸
(85) 翻訳文提出日	平成27年7月24日 (2015.7.24)	(74) 代理人	100109346 弁理士 大貫 敏史
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(87) 国際公開日	平成26年6月12日 (2014.6.12)		
(31) 優先権主張番号	61/733,199		
(32) 優先日	平成24年12月4日 (2012.12.4)		
(33) 優先権主張国	米国 (US)		

最終頁に続く

(54) 【発明の名称】 滅菌体液収集デバイス及び方法

(57) 【要約】

装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。分流機構は、患者から体液を受け取るように内腔規定デバイスに結合可能な入口ポートと、プリサンプルリザーバに流体的に結合可能な第1出口ポートと、サンプルリザーバに流体的に結合可能な第2出口ポートと、を有する。分流機構は、第1出口ポート及び第2出口ポートをそれぞれ入口ポートに流体連通するように配置するように構成された第1流体流路及び第2流路を規定する。流量計量機構は、体液の所定体積の第1流体流路を通るプリサンプルリザーバへの流れを計量し、体液の第2体積の第2流体流路を通るサンプルリザーバへの流れを計量し、所定体積及び第2体積に関連する体積インジケータを表示するように構成される。

【選択図】 図2

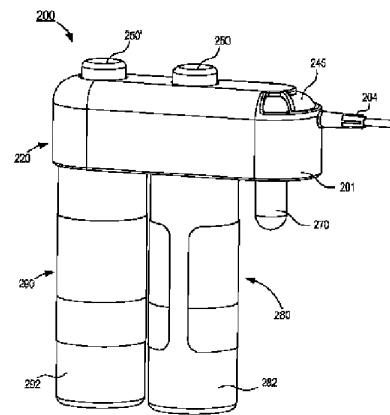


FIG. 2

【特許請求の範囲】

【請求項 1】

患者から体液サンプルを取得する装置であって、

前記患者から抜き取られる体液の第 1 体積を受け取るように構成されたプリサンプルリザーバと、

入口ポート、第 1 出口ポート及び第 2 出口ポートを含む分流機構であって、前記入口ポートが、患者から体液を受け取るように内腔規定デバイスに結合されるように構成され、前記第 1 出口ポートが、前記分流機構に前記プリサンプルリザーバを流体的に結合するように構成され、前記第 2 出口ポートが、前記分流機構にサンプルリザーバを流体的に結合するように構成され、前記分流機構が、前記第 1 出口ポートを前記入口ポートに流体連通するように配置するように構成された第 1 流体流路と、前記第 2 出口ポートを前記入口ポートに流体連通するように配置するように構成された第 2 流体流路と、を規定する、分流機構と、

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前記第 1 流体流路及び前記第 2 流体流路に流体連通する流量計量機構であって、体液の第 1 体積の前記第 1 流体流路を通る前記プリサンプルリザーバ内への流れを計量し、体液の第 2 体積の前記第 2 流体流路を通る前記サンプルリザーバ内への流れを計量するように構成され、前記第 1 体積及び前記第 2 体積に関連する体積インジケータを表示するように構成された流量計量機構と、を備える装置。

【請求項 2】

前記体液の第 1 体積が、第 1 期間中に前記第 1 流体流路内で流れ、前記体液の第 2 体積が、前記第 1 期間の後、第 2 期間中に前記第 2 流体流路内で流れる、請求項 1 に記載の装置。

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【請求項 3】

前記体液の第 1 体積が、皮膚に存在する汚染物質を含み、前記体液の第 2 体積には、皮膚に存在する汚染物質が実質的にない、請求項 1 に記載の装置。

【請求項 4】

前記プリサンプルリザーバが、前記分流機構の一部によって少なくとも部分的に規定される、請求項 1 に記載の装置。

【請求項 5】

前記体積インジケータが視覚的インジケータである、請求項 1 に記載の装置。

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【請求項 6】

前記分流機構が、前記第 2 出口ポートを通して移動して前記サンプルリザーバを前記第 2 流体流路に流体連通するように配置するように構成された可動部材を含む、請求項 1 に記載の装置。

【請求項 7】

前記流量計量機構が、前記可動部材の一部の中に少なくとも部分的に配置される、請求項 6 に記載の装置。

【請求項 8】

前記分流機構が、前記血液の第 1 体積が前記プリサンプルリザーバ内に配置されると、前記プリサンプルリザーバ及び前記第 1 流体流路の少なくとも一部を流体的に隔離するように構成される、請求項 1 に記載の装置。

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【請求項 9】

前記分流機構が、第 2 サンプルリザーバを前記分流機構に流体的に結合するように構成された第 3 出口ポートを含み、前記第 3 出口ポートを前記入口ポートに流体連通するように配置するように構成された第 3 流体流路を規定する、請求項 1 に記載の装置。

【請求項 10】

第 1 内腔及び第 2 内腔を規定する流量コントローラであって、前記第 1 内腔が前記第 1 流体流路を前記入口ポートに流体連通するように配置する第 1 形態と、前記第 2 内腔が前記第 2 流体流路を前記入口ポートに流体連通するように配置する第 2 形態との間で移動するように構成された流量コントローラをさらに備える、請求項 1 に記載の装置。

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【請求項 1 1】

前記流量コントローラが、前記体液の第 1 体積が前記プリサンプルリザーバ内に配置された後、前記第 1 形態から前記第 2 形態に移動するように構成される、請求項 1 0 に記載の装置。

【請求項 1 2】

患者から体液サンプルを取得する装置であって、

前記患者から抜き取られる体液の第 1 体積を受け取るように構成されたプリサンプルリザーバと、

入口ポート、第 1 出口ポート及び第 2 出口ポートを含む分流機構であって、前記入口ポートが、患者から体液を受け取るように内腔規定デバイスに結合されるように構成され、前記第 1 出口ポートが前記プリサンプルリザーバを前記分流機構に流体的に結合するように構成され、前記第 2 出口ポートが、サンプルリザーバを前記分流機構に流体的に結合するように構成される、分流機構と、

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前記分流機構内に少なくとも部分的に配置された流量コントローラであって、前記流量コントローラが前記入口ポートと前記第 1 出口ポートとの間に流体流路の少なくとも一部を規定する第 1 形態と、前記流量コントローラが前記入口ポートと前記第 2 出口ポートとの間に流体流路の少なくとも一部を規定する第 2 形態との間で移動するように構成された流量コントローラと、

前記分流機構に移動可能に結合された可動部材であって、前記サンプルリザーバが前記入口ポートと前記第 2 出口ポートとの間の流体流路から流体的に隔離される第 1 形態と、前記サンプルリザーバが前記入口ポートと前記第 2 出口ポートとの間の前記流体流路に流体連通する第 2 形態との間で、前記第 2 出口ポートを通して移動するように構成され、前記サンプルリザーバが、前記流量コントローラがその第 2 形態にあり、前記可動部材がその第 2 形態にある時、前記患者から抜き取られる体液の第 2 体積を受け取るように構成される、可動部材と、を含む装置。

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【請求項 1 3】

前記体液の第 1 体積が、皮膚に存在する汚染物質を含み、前記体液の第 2 体積には、皮膚に存在する汚染物質が実質的にない、請求項 1 2 に記載の装置。

【請求項 1 4】

前記流量コントローラが、前記分流機構に対してその第 1 形態とその第 2 形態との間で回転する、請求項 1 2 に記載の装置。

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【請求項 1 5】

前記流量コントローラが、前記分流機構に対して線形運動で移動する、請求項 1 2 に記載の装置。

【請求項 1 6】

前記流量コントローラが、その第 2 形態にある時に、前記プリサンプルリザーバを流体的に隔離するように構成される、請求項 1 2 に記載の装置。

【請求項 1 7】

前記可動部材が、その第 2 形態にある時、前記サンプルリザーバの一部を穿孔するように構成された穿孔部材を含む、請求項 1 2 に記載の装置。

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【請求項 1 8】

前記可動部材が、前記可動部材をその第 1 形態で少なくとも一時的に維持するように構成された付勢部材に結合されている、請求項 1 2 に記載の装置。

【請求項 1 9】

前記分流機構が、第 2 サンプルリザーバを前記分流機構に流体的に結合するように構成された第 3 出口ポートを含む、請求項 1 2 に記載の装置。

【請求項 2 0】

前記可動部材が第 1 可動部材であり、前記装置が、

第 2 可動部材であって、前記第 2 サンプルリザーバが前記入口ポートと前記第 3 出口ポートとの間に規定された流体流路から流体的に隔離される第 1 形態と、前記第 2 サンプル

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リザーバが前記入口ポートと前記第 3 出口ポートとの間に規定された前記流体流路に流体連通する第 2 形態との間で、前記第 3 出口ポートを通して移動するように構成され、前記第 2 サンプルリザーバが、前記流量コントローラがその第 2 形態にあり、前記第 2 可動部材がその第 2 形態にある時、前記患者から抜き取られる体液の第 3 体積を受け取るように構成される、第 2 可動部材をさらに含む、請求項 19 に記載の装置。

【請求項 21】

患者から体液サンプルを取得する装置であって、

前記患者から抜き取られる体液の第 1 体積を受け取るように構成されたプリサンプルリザーバと、

ハウジング及び分配部材を含む分流機構であって、前記ハウジングが第 1 開口部及び第 2 開口部を規定し、前記第 1 開口部が前記プリサンプルリザーバに流体連通しており、前記分配部材が、前記ハウジング内に少なくとも部分的に配置され、かつ前記第 2 開口に流体連通している流体流路を規定し、前記分配部材が、前記流路に流体連通しかつサンプルリザーバに物理的にかつ流体的に結合されるように構成された結合部分を含む、分流機構と、

前記患者から体液を受け取るように内腔規定デバイスに結合されるように構成された入口ポートを含む流量コントローラであって、前記分流機構に回転可能に結合され、かつ前記入口ポートが前記第 1 開口部に流体連通する第 1 形態と、前記入口ポートが前記第 2 開口部に流体連通する第 2 形態との間で移動するように構成された流量コントローラと、を備える装置。

【請求項 22】

前記体液の第 1 体積が、皮膚に存在する汚染物質を含み、前記体液の第 2 体積には、皮膚に存在する汚染物質が実質的にない、請求項 21 に記載の装置。

【請求項 23】

前記プリサンプルリザーバが、前記分配部材の一部によって少なくとも部分的に規定される、請求項 21 に記載の装置。

【請求項 24】

前記結合部分が、前記サンプルリザーバの一部を穿孔して前記サンプルリザーバを前記流体流路に流体連通するように配置するように構成された穿孔部材を含む、請求項 21 に記載の装置。

【請求項 25】

前記穿孔部材による前記サンプルリザーバの前記一部の前記穿孔が、前記流量コントローラがその第 2 形態にある時、体液の前記患者から前記入口ポート及び前記流路を通る前記サンプルリザーバ内への流れを開始する、請求項 24 に記載の装置。

【請求項 26】

前記体液の第 1 体積が、体液の第 1 所定体積であり、前記流体流路が、体液の第 2 所定体積を受け取るように構成され、前記体液の第 2 所定体積がサンプル体積に関連する、請求項 21 に記載の装置。

【請求項 27】

前記サンプル体積が、約 10 ミリリットルと約 50 ミリリットルとの間である、請求項 26 に記載の装置。

【請求項 28】

前記サンプル体積が約 30 ミリリットルである、請求項 26 に記載の装置。

【請求項 29】

前記分流機構がシール部材を含み、前記流量コントローラが前記分流機構に結合された時に、前記シール部材が、前記流量コントローラの表面及び前記ハウジングの表面と実質的流体密封シールを形成するように、前記ハウジングと前記流量コントローラとの間に配置され、前記シール部材が第 1 開口部及び第 2 開口部を規定し、前記シール部材の前記第 1 開口部が、前記ハウジングの前記第 1 開口部と実質的に同軸であり、前記シール部材の前記第 2 開口部が、前記ハウジングの前記第 2 開口部と実質的に同軸である、請求項 21

に記載の装置。

【請求項 30】

流量計量移送デバイスを用いて患者から体液の所定サンプル体積を取得する方法であって、前記流量計量移送デバイスが、プリサンプルリザーバ及びサンプルリザーバに流体連通するように選択的に配置されるように構成された入口ポートを含む分流機構と、前記患者からの体液の前記プリサンプルリザーバへの流れ及び前記サンプルリザーバへの流れを計量するように構成された流量計量機構とを含む、方法であり、

前記患者と前記流量計量移送デバイスの前記ポートとの間に流体連通を確立するステップと、

前記ポートと前記プリサンプルリザーバとの間に流体連通を確立するステップと、 10

前記患者から前記プリサンプルリザーバに移送された体液の流れを計量するステップと、

、

前記流量計量移送デバイスの前記流量計量機構を介して、前記プリサンプルリザーバ内に配置された体液のプリサンプル体積が体液の所定プリサンプル体積であることを検証するステップと、

前記プリサンプルリザーバを前記ポートから流体的に隔離して、前記プリサンプルリザーバ内で前記体液のプリサンプル体積を封鎖するステップと、

前記ポートと前記サンプルリザーバとの間に流体連通を確立するステップと、

前記患者から前記サンプルリザーバに移送された体液の流れを計量するステップと、 20

前記流量計量移送デバイスの前記流量計量機構を介して、前記サンプルリザーバ内に配置された体液のサンプル体積が体液の所定サンプル体積であることを検証するステップと、を含む方法。

【請求項 31】

前記流量計量移送デバイスが、前記患者と前記プリサンプルリザーバとの間に流体連通が確立される第1形態と、前記患者と前記サンプルリザーバとの間に流体連通が確立される第2形態との間で移動するように構成された流量コントローラを含む、請求項30に記載の方法。

【請求項 32】

前記体液が血液である、請求項30に記載の方法。

【請求項 33】

前記サンプルリザーバが、好気性菌用培地又は嫌気性菌用培地のうちの少なくとも一方を含む、請求項32に記載の方法。

【請求項 34】

前記所定プリサンプル体積が、約1ミリリットルと約10ミリリットルとの間である、請求項30に記載の方法。

【請求項 35】

前記所定サンプル体積が、約20ミリリットルと約60ミリリットルとの間である、請求項30に記載の方法。

【請求項 36】

前記所定サンプル体積が約60ミリリットルである、請求項30に記載の方法。

【請求項 37】

前記サンプルリザーバが第1サンプルリザーバであり、前記サンプル体積が第1サンプル体積であり、

前記第1サンプルリザーバ内の前記第1サンプル体積が前記所定サンプル体積であることを検証した後、前記ポートと第2サンプルリザーバとの間に流体連通を確立するステップと、

前記患者から前記第2サンプルリザーバに移送された体液の流れを計量するステップと、

、

前記流量計量移送デバイスの前記流量計量機構を介して、前記第2サンプルリザーバ内に配置された体液の第2サンプル体積が体液の前記所定サンプル体積であることを検証す 50

るステップと、をさらに含む、請求項 30 に記載の方法。

【請求項 38】

前記第 1 サンプル体積及び前記第 2 サンプル体積が、まとめて、約 20 ミリリットルと約 60 ミリリットルとの間に等しい、請求項 37 に記載の方法。

【請求項 39】

前記第 2 サンプルリザーバ内の前記第 2 サンプル体積が前記所定サンプル体積であることを検証した後、前記ポートと第 3 サンプルリザーバとの間に流体連通を確立するステップと、

前記患者から前記第 3 サンプルリザーバに移送された体液の流れを計量するステップと、

前記流量計量移送デバイスの前記流量計量機構を介して、前記第 3 サンプルリザーバ内に配置された体液の第 3 サンプル体積が体液の前記所定サンプル体積であることを検証するステップと、をさらに含む、請求項 37 に記載の方法。

【請求項 40】

前記第 1 サンプル体積、前記第 2 サンプル体積及び前記第 3 サンプル体積が、まとめて、約 30 ミリリットルと約 60 ミリリットルとの間に等しい、請求項 39 に記載の方法。

【請求項 41】

前記第 1 サンプル体積、前記第 2 サンプル体積及び前記第 3 サンプル体積が、まとめて、約 60 ミリリットルに等しい、請求項 39 に記載の方法。

【発明の詳細な説明】

【技術分野】

【0001】

関連出願の相互参照

[1001] 本出願は、2012 年 12 月 4 日に出願された「滅菌体液収集デバイス及び方法 (Sterile Bodily-Fluid Collection Device and Methods)」と題する米国仮特許出願第 61, 733, 199 号に対する優先権及びその利益を主張し、その出願の開示内容は、全体として参照により本明細書に組み込まれる。

【0002】

[1002] 本明細書に記載する実施形態は、概して体液サンプルの非経口的獲得 (parenteral procurement) に関し、より詳細には、皮膚に存在する微生物等、体液源の外部の微生物又は他の汚染物質からの汚染を低減して、体液サンプルを非経口的に獲得するデバイス及び方法に関する。

【背景技術】

【0003】

[1003] 医療従事者は、日常的に、非経口的に取得された体液を用いて患者に対してさまざまなタイプの微生物検査を行う。場合によっては、患者サンプル (例えば、体液) は、細菌、真菌又は酵母菌 (例えば、カンジダ) 等、1 種又は複数種の望ましくない可能性がある微生物が存在するか検査される。微生物検査は、微生物増殖を促進する培地を収容する 1 つ又は複数の滅菌容器において患者サンプルを培養すること、リアルタイム診断及び／又は分子 PCR に基づく手法を含む場合がある。一般に、こうした微生物が患者サンプルに存在する場合、それら微生物は、培地において経時的に繁殖する。可変時間 (例えば数時間から数日間) の後、自動化された連続モニタリングにより、生物体の成長を検出することができる。こうした自動化モニタリングは、生物体の増殖によって生成される二酸化炭素を検出することができる。そして、培地に対して、微生物が存在するか検査することができる。培地に微生物が存在する場合、それは、患者サンプルに同じ微生物が存在することを示唆し、それはさらに、サンプルを取得した患者の体液に同じ微生物が存在することを示唆する。従って、培地に微生物が存在すると判断された場合、患者は、患者から望ましくない微生物を処置するか又は他の方法で除去するように特に設計された 1 種あるいは複数種の抗生物質又は他の処置が処方される可能性がある。

【0004】

[1004] しかしながら、患者サンプルは、獲得中に汚染される可能性があり、及び／又は、他の方法で偽陽性結果が出やすい可能性がある。患者サンプルの汚染が発生する可能性がある1つの過程は、患者の体内への針の挿入中に取り除かれ後に患者サンプルとともに培地に移送された体表からの微生物（例えば、皮膚に存在する微生物）の移送による。体表微生物及び／又は他の望ましくない外部微生物は、直接、又は取り除かれた組織片、毛包、汗腺及び他の皮膚付属器構造を介して取り除かれる可能性がある。別のあり得る汚染源は、患者サンプルを抜き取る人から来る。例えば、医師、瀉血専門医、看護師等が、自身の身体（例えば、指、腕等）から患者サンプルに及び／又は患者サンプルを収容している機器に汚染物質を移送する可能性がある。さらに詳述すると、患者サンプル獲得プロセス（例えば、患者から針、針／管からサンプル容器等）の間に使用される機器及び／又はデバイスは、各々が有り得る汚染の箇所を生じさせる可能性がある複数の流体インタフェースを含むことが多い。こうした機器及び／又はデバイスの使用は、通常、さまざまなインタフェースを接続し及び／又は流体的に結合するための手作業による介入を含む。これらのインタフェースは、単一の流体的に結合されたシステムとして事前に組み立てられかつ滅菌されないため、使用者（例えば、医師、瀉血専門医等）及び／又は他の汚染源（例えば、周囲空気、病室のテーブル及びカウンタの表面の汚染物質、リネン又は衣類から移送された微生物等）を介して患者サンプルに導入される可能性がある。場合によっては、こうした汚染物質は、培地で生育し、最終的に陽性の微生物検査結果をもたらす可能性があり、それにより、体内におけるこうした微生物の存在を誤って示す。

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【0005】

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[1005] 場合によっては、偽陽性結果及び／又は偽陰性結果は、患者サンプルの所定体積に起因する可能性がある。例えば、体積に影響されやすい血液培養ボトルを過充填することにより、こうした培養ボトル及び関連する自動連続モニタリング微生物検出システムの製造業者からの使用説明書及び／又は警告ラベルにおいて注記されているように、偽陽性結果に至る可能性がある。一方、別の例として、培地内における患者サンプルの体積が不十分であることにより、偽陰性結果がもたらされる可能性がある。例として、Journal of Clinical Microbiologyの2011年12月号に記載された「Optimized Pathogen Detection with 30- Compared to 20-Milliliter Blood Culture Draws」と題するMayo Clinicによって行われた研究において、20ミリリットル（mL）の患者サンプル体積により、患者サンプルに存在する菌血症の約80%の存在を検出することができ、40mLの患者サンプル体積により、菌血症の約88%を検出することができ、60mLの患者サンプル体積により、菌血症の約99%を検出することができる。

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【0006】

[1006] 汚染、不十分な患者サンプル体積等の結果としてのこうした不正確な結果は、疑いのある病気又は健康状態を診断するか又は治療しようとする時に問題である。例えば、微生物検査からの偽陰性結果により、患者の病気が誤診され及び／又は治療が遅れることになる可能性があり、それによって場合によっては、患者の死に至る可能性がある。逆に、微生物検査からの偽陽性結果により、患者が1つ又は複数の抗微生物療法を不必要に受けることになる可能性があり、それにより、例えば死を含む患者の深刻な副作用が引き起こされるとともに、患者の入院の期間の延長及び／又は間違った治療に関連する他の合併症のために医療制度に対する不必要な負担及び出費がもたらされる可能性がある。さらに、これらの偽陽性結果に起因する診断撮像機器の使用はまた、コストとともに、種々の撮像処置（例えば、CTスキャン）に関連する高濃度放射線の不必要な照射が長期の患者の健康に対して多くの既知の悪影響を及ぼすため、患者の安全性の観点からも問題である。

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【0007】

[1007] 従って、例えば、患者サンプル及び／又は流体インタフェースの周囲の非滅菌状態及び／又は他の外部汚染源への暴露を最小限にすることにより、体液検査サンプルにおける微生物汚染を低減する、滅菌「一体型」体液収集デバイス及び方法が必要とされている。さらに、こうした体液収集デバイスが、患者サンプルを実質的にリアルタイムに（例えば、患者のベッドわきで）獲得している医療従事者に視覚的に、計算された方法で、又

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は他の方法で通信することができる、患者からサンプルリザーバ又は培地に移送された体液の体液を正確に計量し、測定し、及び／又は、他の方法で評価する手段を含むことが必要とされている。

【発明の概要】

【0008】

[1008] 本明細書では、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体液源の外部の微生物からの汚染を低減して体液サンプルを非経口的に獲得するデバイスについて記載されている。いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。プリサンプルリザーバは、患者から抜き取られる体液の第1体積を受け取るように構成されている。分流機構は、入口ポート、第1出口ポート及び第2出口ポートを含み、第1流体流路及び第2流体流路を規定している。入口ポートを、患者から体液を受け取るように内腔規定デバイスに結合することができる。第1出口ポート及び第2出口ポートは、プリサンプルリザーバ及びサンプルリザーバそれぞれを分流機構に流体的に結合するように構成されている。第1流体流路は、第1出口ポートを入口ポートに流体連通するように配置するように構成され、第2流体流路は、第2出口ポートを入口ポートに流体連通するように配置するように構成されている。流量計量機構は、第1流体流路及び第2流体流路に流体連通している。流量計量機構は、体液の第1体積の第1流体流路を通るプリサンプルリザーバ内への流れを計量し、体液の第2体積の第2流体流路を通るサンプルリザーバ内への流れを計量するように構成されている。流量計量機構は、第1体積及び第2体積に関連する体積インジケータを表示するように構成されている。

【図面の簡単な説明】

【0009】

【図1】実施形態による体液収集デバイスの概略図である。

【図2】実施形態による体液収集デバイスの斜視図である。

【図3】図2の体液収集デバイスの組立分解斜視図である。

【図4】図2の体液収集デバイスに含まれるハウジングの図3の線X₁ - X₁に沿って取り出された側断面図である。

【図5】図2の体液収集デバイスに含まれる可動部材の図3の線X₂ - X₂に沿って取り出された断面図である。

【図6】図2の体液収集デバイスに含まれる流量コントローラの図3の線X₃ - X₃に沿って取り出された断面図である。

【図7】図2の体液収集デバイスに含まれる流量コントローラの図3の線X₄ - X₄に沿って取り出された断面図である。

【図8】第1形態にある図2の体液収集デバイスの上面図である。

【図9】第1形態にある図2の体液収集デバイスの図8の線X₅ - X₅に沿って取り出された断面図である。

【図10】第2形態にある図2の体液収集デバイスの上面図である。

【図11】第2形態にある図2の体液収集デバイスの図10の線X₆ - X₆に沿って取り出された断面図である。

【図12】第3形態にある図2の体液収集デバイスの図10の線X₆ - X₆に沿って取り出された断面図である。

【図13】第4形態にある図2の体液収集デバイスの図10の線X₆ - X₆に沿って取り出された断面図である。

【図14】実施形態による体液収集デバイスの斜視図である。

【図15】図14の体液収集デバイスの線X₇ - X₇に沿って取り出された側断面図である。

【図16】実施形態による体液収集デバイスの斜視図である。

【図17】図16の体液収集デバイスに含まれる分流機構の組立分解斜視図である。

【図18】図16の体液収集デバイスに含まれる分配部材の図16の線X₈ - X₈に沿って

て取り出された側断面図である。

【図 1 9】第 1 形態にある図 1 6 の体液収集デバイスの上面図である。

【図 2 0】第 1 形態にある図 1 6 の一部体液収集デバイスの図 1 9 の線 $X_9 - X_9$ に沿って取り出された断面図である。

【図 2 1】第 2 形態にある図 1 6 の体液収集デバイスの上面図である。

【図 2 2】第 2 形態にある図 1 6 の体液収集デバイスの図 2 1 の線 $X_{10} - X_{10}$ に沿って取り出された断面図である。

【図 2 3】実施形態による体液収集デバイスの斜視図である。

【図 2 4】第 1 形態にある、図 2 3 の体液収集デバイスの一部の線 $X_{11} - X_{11}$ に沿って取り出された断面図である。

【図 2 5】第 2 形態にある、図 2 3 の体液収集デバイスの線 $X_{11} - X_{11}$ に沿って取り出された断面図である。

【図 2 6】実施形態による体液収集デバイスの斜視図である。

【図 2 7】図 2 6 の体液収集デバイスに含まれる分流機構の組立分解斜視図である。

【図 2 8】図 2 7 の体液収集デバイスに含まれる分配部材の図 2 7 の線 $X_{13} - X_{13}$ に沿って取り出された断面図である。

【図 2 9】図 2 6 の体液収集デバイスに含まれる結合部材の図 2 7 の線 $X_{14} - X_{14}$ に沿って取り出された断面図である。

【図 3 0】図 2 6 の体液収集デバイスに含まれるダイヤルの図 2 7 の線 $X_{15} - X_{15}$ に沿って取り出された断面図である。

【図 3 1】図 2 6 の体液収集デバイスに含まれる弁の図 2 7 の線 $X_{16} - X_{16}$ に沿って取り出された断面図である。

【図 3 2】第 1 形態にある図 2 6 の体液収集デバイスの線 $X_{12} - X_{12}$ に沿って取り出された断面図である。

【図 3 3】第 2 形態にある図 2 6 の体液収集デバイスの線 $X_{12} - X_{12}$ に沿って取り出された断面図である。

【図 3 4】実施形態による体液収集デバイスの斜視図である。

【図 3 5】図 3 4 の体液収集デバイスに含まれる分流機構の組立分解斜視図である。

【図 3 6】図 3 5 の分流機構に含まれる分配部材の線 $X_{17} - X_{17}$ に沿って取り出された断面図である。

【図 3 7】第 1 形態にある図 3 4 の体液収集デバイスの一部の上面図である。

【図 3 8】第 1 形態にある図 3 7 の一部体液収集デバイスの線 $X_{18} - X_{18}$ に沿って取り出された断面図である。

【図 3 9】第 2 形態にある図 3 3 の体液収集デバイスの上面図である。

【図 4 0】第 2 形態にある図 3 3 の体液収集デバイスの図 3 9 の線 $X_{19} - X_{19}$ に沿って取り出された断面図である。

【図 4 1】実施形態による第 1 形態にある体液収集デバイスの斜視図である。

【図 4 2】図 4 1 の体液収集デバイスの一部の組立分解斜視図である。

【図 4 3】第 1 形態にある図 4 1 の体液収集デバイスの線 $X_{20} - X_{20}$ に沿って取り出された断面図である。

【図 4 4】第 2 形態にある図 4 1 の体液収集デバイスの線 $X_{20} - X_{20}$ に沿って取り出された断面図である。

【図 4 5】第 3 形態にある図 4 1 の体液収集デバイスの線 $X_{20} - X_{20}$ に沿って取り出された断面図である。

【図 4 6】実施形態による第 1 形態にある体液収集デバイスの斜視図である。

【図 4 7】図 4 5 の体液収集デバイスの一部の組立分解斜視図である。

【図 4 8】図 4 6 の体液収集デバイスに含まれる分配部材の図 4 7 の線 $X_{21} - X_{21}$ に沿って取り出された側断面図である。

【図 4 9】図 4 6 の体液収集デバイスに含まれる可動部材の図 4 7 の線 $X_{22} - X_{22}$ に沿って取り出された側断面図である。

【図 5 0】第 1 形態にある図 4 6 の体液収集デバイスの上面図である。

【図 5 1】第 1 形態にある図 4 6 の一部体液収集デバイスの図 5 0 の線 $X_{23} - X_{23}$ に沿って取り出された断面図である。

【図 5 2】第 2 形態にある図 4 6 の体液収集デバイスの上面図である。

【図 5 3】第 2 形態にある図 4 6 の体液収集デバイスの図 5 2 の線 $X_{24} - X_{24}$ に沿って取り出された断面図である。

【図 5 4】実施形態による体液収集デバイスの斜視図である。

【図 5 5】図 5 4 の体液収集デバイスの上面図である。

【図 5 6】実施形態による収集デバイスを用いて、汚染を低減して体液サンプルを取得する方法を示すフローチャートである。

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【発明を実施するための形態】

【0010】

[1063] 本明細書では、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体液源の外部の微生物からの汚染を低減して体液サンプルを非経口的に獲得するデバイスについて記載されている。いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。プリサンプルリザーバは、患者から抜き取られる体液の第 1 体積を受け取るように構成されている。分流機構は、入口ポート、第 1 出口ポート及び第 2 出口ポートを含み、第 1 流体流路及び第 2 流体流路を規定している。入口ポートを、患者から体液を受け取るように内腔規定デバイスに結合することができる。第 1 出口ポート及び第 2 出口ポートは、プリサンプルリザーバ及びサンプルリザーバそれぞれを分流機構に流体的に結合するように構成されている。第 1 流体流路は、第 1 出口ポートを入口ポートに流体連通するように配置するように構成され、第 2 流体流路は、第 2 出口ポートを入口ポートに流体連通するように配置するように構成されている。流量計量機構は、第 1 流体流路及び第 2 流体流路に流体連通している。流量計量機構は、体液の第 1 体積の第 1 流体流路を通るプリサンプルリザーバ内への流れを計量し、体液の第 2 体積の第 2 流体流路を通るサンプルリザーバ内への流れを計量するように構成されている。流量計量機構は、第 1 体積及び第 2 体積に関連する体積インジケータを表示するように構成されている。

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【0011】

[1064] いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構、流量コントローラ及び可動部材を含む。プリサンプルリザーバは、患者から抜き取られる体液の第 1 体積を受け取るように構成されている。分流機構は、入口ポート、第 1 出口ポート及び第 2 出口ポートを含む。入口ポートは、患者から体液を受け取るように内腔規定デバイスに結合可能である。第 1 出口ポートは、プリサンプルリザーバを分流機構に流体的に結合し、第 2 出口ポートは、サンプルリザーバを分流機構に流体的に結合する。流量コントローラは、分流機構内に少なくとも部分的に配置され、流量コントローラを、流量コントローラが入口ポートと第 1 出口ポートとの間に流体流路の少なくとも一部を規定する第 1 形態と、流量コントローラが入口ポートと第 2 出口ポートとの間に流体流路の少なくとも一部を規定する第 2 形態との間で移動させることができる。可動部材は、分流機構に移動可能に結合され、サンプルリザーバが入口ポートと第 2 出口ポートとの間の流体流路から流体的に隔離される第 1 形態と、サンプルリザーバが入口ポートと第 2 出口ポートとの間の流体流路に流体連通する第 2 形態との間で、第 2 出口ポートを通して移動可能である。サンプルリザーバは、流量コントローラがその第 2 形態にあり、可動部材がその第 2 形態にある時、患者から抜き取られる体液の第 2 体積を受け取るように構成されている。

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【0012】

[1065] いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量コントローラを含む。プリサンプルリザーバは、患者から抜き取られる体液の第 1 体積を受け取るように構成されている。分流機構は、ハウジング及び分配部材を含む。ハウジングは、プリサンプルリザーバに流体連通している第 1 開口

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部と第2開口部とを規定している。分配部材は、ハウジング内に少なくとも部分的に配置され、かつ第2開口に流体連通している流体流路を規定している。分配部材は、流路に流体連通しかつサンプリリザーバに物理的にかつ流体的に結合されるように構成された結合部分を含む。流量コントローラは、患者から体液を受け取るように内腔規定デバイスに結合されるように構成された入口ポートを含む。流量コントローラは、分流機構に回転可能に結合され、かつ入口ポートが第1開口部に流体連通する第1形態と、入口ポートが第2開口部に流体連通する第2形態との間で移動可能である。

【0013】

[1066] いくつかの実施形態では、プリサンプリリザーバ及びサンプリリザーバに流体連通するように選択的に配置されるように構成された入口ポートを含む分流機構と、患者からの体液のプリサンプリリザーバへの流れ及びサンプリリザーバへの流れを計量するように構成された流量計量機構とを有する流量計量移送デバイスを用いる方法は、患者と流量計量移送デバイスの入口ポートとの間に流体連通を確立するステップを含む。そして、ポートとプリサンプリリザーバとの間に流体連通が確立される。患者からプリサンプリリザーバに移送された体液の流れが計量される。本方法は、流量計量移送デバイスの流量計量機構を介して、プリサンプリリザーバ内に配置された体液のプリサンプル体積が体液の第1プリサンプル体積であることを検証するステップを含む。プリサンプリリザーバ内にプリサンプル体積が配置された状態で、プリサンプリリザーバがポートから流体的に隔離されて、プリサンプリリザーバ内で体液のプリサンプル体積が封鎖される。プリサンプリリザーバが流体的に隔離された状態で、本方法は、ポートとサンプリリザーバとの間に流体連通を確立するステップを含む。患者からサンプリリザーバに移送された体液の流れが計量される。本方法は、流量計量移送デバイスの流量計量機構を介して、サンプリリザーバ内に配置された体液のサンプル体積が体液の第1サンプル体積であることを検証するステップを含む。

【0014】

[1067] いくつかの実施形態では、装置は、分流機構及び流量コントローラを含む。分流機構は、入口ポート、第1出口ポート、第2出口ポート及び第3出口ポートを規定することができる。第1出口ポートは、プリサンプリリザーバに流体的に結合され、第2出口ポートは、第1サンプリリザーバに流体的に結合され、第3出口ポートは、第2サンプリリザーバに流体的に結合され、等である。流体リザーバのすべてを、互いから流体的に隔離することができる。流量コントローラはさまざまな流体チャネルを含み、流体チャネルは、指定された方向における流体移動を可能にすることができ、分流機構に動作可能に結合されるように構成され得る。使用時、分流機構が第1形態にある時、流量コントローラは、体液の流れがプリサンプリリザーバに入るのを可能にすることができる。分流機構を第2形態に移動させることができ、そこでは、流量コントローラは、体液の流れが第1サンプリリザーバに入るのを可能にすることができる。さらに、分流機構を、その後、第3形態に移動させることができ、それにより、流量コントローラは、体液の流れが第2サンプリリザーバに入るのを可能にすることができる。

【0015】

[1068] いくつかの実施形態では、体液収集デバイスを、体液の第2体積の第1サンプリリザーバ内への流れ及び／又は体液の第3体積の第2サンプリリザーバ内への流れを可能にする前に、体液の第1の所定体積をプリサンプリリザーバに選択的に分流させるように構成することができる。このように、体液の第2体積及び／又は第3体積を、診断又は他の検査に使用することができ、一方で、体表又はサンプルを獲得する患者の外部の他の微生物源からの微生物を含む可能性がある体液の第1体積が隔離される。いくつかの実施形態では、体液収集デバイスは、行われる分析プロトコル及び／又は検査プロトコルに応じて追加のサンプリリザーバ（例えば、3、4、5、6以上）を含むことができる。

【0016】

[1069] いくつかの実施形態では、体液収集デバイスは、体液の適切な体積が患者から収集され及び／又は所定のプリサンプリリザーバ及び／又はサンプリリザーバに移送される

のを確実にするために、流量計量を含むことができる。体液収集デバイスを、体液の計量された体積が収集された後に、流体流を自動的に分流させ及び／又は制御するように構成することができる。例えば、第1計量プリサンプル体積が収集されると、分流機構を、体液流を第1サンプルリザーバに分流させるように構成することができ、その後、第1計量サンプル体積が収集された後、分流機構を、体液流を第2サンプルリザーバに分流させるように構成することができ、等である。いくつかの実施形態では、体液収集デバイスは、例えば液晶ディスプレイ（LCD）等の計量された体積のディスプレイを含み、どれだけの体液が各所定の個々のサンプルリザーバ内に収集されたかの視覚的指示を使用者に提供することができる。いくつかの実施形態では、カスタマイズされたプリサンプル及び／又はサンプル体積収集を可能にするように、複数のディスプレイを設けることができる。

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【0017】

[1070] 本明細書及び添付の特許請求の範囲で用いる単数形「1つの（a、an）」及び「その（the）」は、文脈に明示的に述べられていない限り、複数の指示対象を含む。従って、例えば、「（1つの）部材」という用語は、単一部材又は部材の組合せを意味するように意図され、「（1つの）材料」は、1つあるいは複数の材料又はそれらの組合せを意味するように意図されている。

【0018】

[1071] 本明細書で用いる「体液」は、限定されないが、血液、髄液、尿、胆汁、リンパ液、唾液、滑液、漿液、胸膜液、羊水等又はそれらのあらゆる組合せを含む、患者の体内から得られるあらゆる流体を含むことができる。

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【0019】

[1072] 本明細書で用いる「第1の所定量」、「第1量」及び「第1体積」という用語は、第1リザーバ又はプリサンプルリザーバによって受け取られるか又は収容されるように構成された体液の量を述べる。「第1量」及び「第1体積」という用語は、所定量を明示的に述べないが、明示的に異なるように述べられていない限り、第1量は第1の所定量であることが理解されるべきである。

【0020】

[1073] 本明細書で用いる「第2量」及び「第2体積」という用語は、第2リザーバ又はサンプルリザーバによって受け取られるか又は収容されるように構成された体液の量を述べる。第2量を、体液のあらゆる好適な量とすることができ、それは所定量である必要はない。逆に、そのように明示的に述べられる場合、第2リザーバ又はサンプルリザーバによって受け取られかつ収容される第2量は、第2の所定量であり得る。

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【0021】

[1074] 本明細書で用いる「組」という用語は、複数の機構又は複数の部品を含む単一の機構を指すことができる。例えば、壁の組と言う場合、壁の組を、別個の部分を含む1つの壁とみなすことができ、又は壁の組を、複数の壁とみなすことができる。同様に言えば、一体的に構成された物品は一組の壁を含むことができる。こうした一組の壁は、例えば、互いに不連続である複数の部分を含むことができる。一組の壁を、別個に製造され、後に（例えば、溶接、接着剤又はあらゆる好適な方法を介して）互いに接合される複数の物品から製造することも可能である。

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【0022】

[1075] 本明細書で用いる「近位」及び「遠位」という用語は、デバイスを患者に接触するように配置する使用者に対してそれぞれ近い方の方向及び離れる方向を指す。従って、例えば、患者の身体に最初に接触するデバイスの端部は遠位端となり、デバイスの反対側の端部（例えば、使用者が操作しているデバイスの端部）はデバイスの近位端となる。

【0023】

[1076] 本明細書で用いる「約」、「およそ」及び「実質的に」という用語は、数値と関連して用いられる場合、そのように定義される値が名目上示されている値であることを意味するように意図されている。言い換えれば、約、およそ及び実質的にという用語は、数値に関連して用いられる場合、概して、示されている値プラスマイナス所与の許容差を含

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む。例えば、場合によっては、好適な許容差は、示されている値の±10%である可能性があり、従って、約0.5は0.45及び0.55を含み、約10は9~11を含み、約1000は900~1100を含む。他の場合では、好適な許容差は、プラスマイナス示されている値の最後の有効数字の許容可能な割合であり得る。例えば、好適な許容差は、最後の有効数字の±10%である可能性があり、従って、約10.1は10.09及び10.11を含み、およそ25は24.5及び25.5を含む。こうした変動は、製造公差又は他の実際的な考慮事項（例えば、測定器具に関連する公差、許容可能な人的ミス等）からもたらされ得る。

【0024】

[1077] 体液の所定体積と体液の収集された体積との関係について述べる場合、それらの値は、上述したものの等の好適な許容差を含むことが理解されるべきである。例えば、体液の収集された体積が体液の所定体積と実質的に等しいと述べる場合、収集された体積及び所定体積は、名目上、好適な許容差の範囲内で等しい。場合によっては、許容差を、体液の収集された体積の意図された使用によって求めることができる。例えば、場合によっては、血液培養のアッセイは、血液の収集された体積が製造業者の（又はエビエンスに基づく最適な実践）推奨体積の1.0%から5.0%の範囲内である時、約99%正確であり得る。例として、体液のアッセイに対する製造業者の推奨体積は、約99%の信頼度のために、合計4本又は6本の収集ボトルが使用される場合、1本のサンプル収集ボトル当たり10ミリリットル（mL）（すなわち、総体積は40mL~60mL）±5%であり得る。従って、10.5mLの収集体積により、約99%を超える信頼度での結果が提供され、11mLの収集体積により、約99%未満の信頼度の結果が提供される。他の場合では、好適な許容差は、0.1%、0.5%、1.0%、2.0%、3.0%、4.0%、5.0%、6.0%、7.0%、8.0%、9.0%、10.0%又はそれらの間のあらゆる分数値であり得る。さらに他の場合では、許容差は10.0%を上回る可能性がある。従って、本明細書に記載する実施形態のいずれも、好適な許容差の範囲内で体液の流量を計量し及び／又は体液の体積を他の方法で測定するように構成されたあらゆる好適な流量測定機構及び／又はデバイスを含み及び／又はそれとともに使用することができる。さらに、流量計量機構及び／又はデバイスを、不正確な測定、人的ミス等の組合せからもたらされる可能性がある公差の蓄積を最小限にするか又はなくすように配置することができる。

【0025】

[1078] 図1は、実施形態による体液収集デバイス100の一部の概略図である。概して、体液収集デバイス100（本明細書では、「流体収集デバイス」又は「収集デバイス」とも呼ぶ）は、患者から体液を抜き取ることを可能にし、その際、抜き取られた体液の第1部分又は第1量が、医療診断及び／又は治療の目的で検査されるため等、生物学的サンプルとして使用される、抜き取られた体液の第2部分あるいは体積及び／又は第3部分あるいは体積から離れるように分流されるように構成されている。言い換えれば、本明細書においてより詳細に記載するように、収集デバイス100は、体液の第1の所定体積をプリサンプル収集リザーバに、体液の第2体積及び第3体積（又は、いくつかの実施形態では、第4、第5等）を、プリサンプルリザーバから流体的に隔離された1つ又は複数のサンプル収集リザーバ（例えば、サンプルリザーバ）に移送するように構成されている。

【0026】

[1079] 収集デバイス100は、分流機構120、流量コントローラ140、プリサンプルリザーバ170、第1サンプルリザーバ180、及び第1サンプルリザーバ180とは異なる第2サンプルリザーバ190を含む。分流機構120は、図1に示すように、入口ポート121と、第1出口ポート125及び第2出口ポート126等、少なくとも2つの出口ポートとを含む。いくつかの実施形態では、分流機構120は、プリサンプルリザーバ及びサンプルリザーバの総数に等しい一組の出口ポートを含むことができる。例えば、収集デバイス100が1つのプリサンプル及び4つのサンプルリザーバを有する場合、分流機構120は5つの出口ポートを含むことができる。いくつかの実施形態では、分流機

構 1 2 0 を、複数の形態の間の分流機構 1 2 0 の移動を容易にすることができる（図 1 には示さない）アクチュエータに動作可能に結合することができる。入口ポート 1 2 1 は、患者から体液を抜き取り及び／又は収集デバイス 1 0 0 に輸送するための経路 X を規定している医療デバイスに流体的に結合されるように構成されている。例えば、入口ポート 1 2 1 を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。このように、分流機構 1 2 0 は、針又は他のあらゆる内腔規定デバイスを介して患者から体液を受け取ることができる。

【0027】

[1080] 分流機構 1 2 0 の第 1 出口ポート 1 2 5 を、プリサンプルリザーバ 1 7 0 に流体的に結合することができる。いくつかの実施形態では、プリサンプルリザーバ 1 7 0 は、第 1 出口ポート 1 2 5 及び／又は分流機構 1 2 0 の一部と一体的に形成されている。他の実施形態では、プリサンプルリザーバ 1 7 0 を、接着剤、抵抗嵌め（resistance fit）、機械的締結具、あらゆる数の嵌合凹部、ねじ結合及び／又は他のあらゆる好適な結合あるいはその組合せを介して、分流機構 1 2 0 に機械的に及び／又は流体的に結合することができる。同様に言えば、プリサンプルリザーバ 1 7 0 を、分流機構 1 2 0 に物理的に（例えば、機械的に）結合することができ、それにより、プリサンプルリザーバ 1 7 0 によって規定される内部空間（volume）が分流機構 1 2 0 の第 1 出口ポート 1 2 5 に流体連通する。さらに他の実施形態では、プリサンプルリザーバ 1 7 0 を、可撓性滅菌管等の（図 1 には示さない）介在構造を介して、分流機構 1 2 0 の第 1 出口ポート 1 2 5 に動作可能に結合することができる。より詳細には、介在構造は、プリサンプルリザーバ 1 7 0 を、第 1 出口ポート 1 2 5 に流体連通するように配置するように構成された内腔を規定することができる。

【0028】

[1081] プリサンプルリザーバ 1 7 0 は、体液の第 1 の所定体積を受け取りかつ収容するように構成されている。いくつかの実施形態では、プリサンプルリザーバ 1 7 0 は、体液の第 1 体積を、患者から後に抜き取られる（体液の第 1 体積と同じである場合もあれば異なる場合もある）体液の第 2 体積及び／又は第 3 体積から流体的に隔離するように収容するように構成されている。プリサンプルリザーバ 1 7 0 は、全体として参照により本明細書に組み込まれる、「汚染を低減して体液サンプルを非経口的に獲得するシステム及び方法（Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination）」と題する米国特許第 8, 197, 420 号に詳細に記載されているプリサンプルリザーバ等、体液を収容するあらゆる好適なリザーバであり得る。

【0029】

[1082] いくつかの実施形態では、分流機構 1 2 0 の第 2 出口ポート 1 2 6 は、第 1 サンプルリザーバ 1 8 0 及び第 2 サンプルリザーバ 1 9 0 に結合することができる内腔規定デバイスに流体的に結合されるように構成されている。任意選択的に、他の実施形態では、分流機構 1 2 0 の第 2 出口ポート 1 2 6 を、第 1 サンプルリザーバ 1 8 0 に結合することができ、分流機構 1 2 0 は、第 2 サンプルリザーバ 1 9 0 に結合された（図示せず）第 3 出口ポートを有することができる。いくつかの実施形態では、第 1 サンプルリザーバ 1 8 0 を、第 2 出口ポート 1 2 6 及び／又は分流機構 1 2 0 の一部と一体的に形成することができる。他の実施形態では、第 1 サンプルリザーバ 1 8 0 を、プリサンプルリザーバ 1 7 0 に関して上述したような介在構造を介して、第 2 出口ポート 1 2 6 に機械的に結合し、又は第 2 出口ポート 1 2 6 に動作可能に結合することができる。第 1 サンプルリザーバ 1 8 0 は、体液の第 2 体積を受け取りかつ収容するように構成されている。例えば、体液の第 2 体積は、第 1 プリサンプル体積の抜取りに続いて患者から抜き取られた量であり得る。いくつかの実施形態では、第 1 サンプルリザーバ 1 8 0 は、第 2 体積がプリサンプル体液の第 1 体積から流体的に隔離されるように、体液の第 2 体積を収容するように構成されている。

【0030】

[1083] 第 1 サンプルリザーバ 1 8 0 及び第 2 サンプルリザーバ 1 9 0 は、例えば、上で

参照により組み込んだ‘420特許に記載されているようなサンプルリザーバを含む、体液を収容するあらゆる好適な滅菌リザーバであり得る。いくつかの実施形態では、第2体積を、体液のあらゆる好適な体積とすることができ、それは所定体積である必要はない。他の実施形態では、第1サンプルリザーバ180及び／又は第2サンプルリザーバ190への体液の移送を、第2体積が第2の所定体積であるように、計量等することができる。

【0031】

[1084] 第2サンプルリザーバ190は、あらゆる好適なサンプルリザーバであり得る。いくつかの実施形態では、第2サンプルリザーバ190は、上述した第1サンプルリザーバ180と実質的に同様であり得る。第2サンプルリザーバ190を、上述したように、第2出口ポート126に流体的に結合することができる。第2出口ポート126の第2サンプルリザーバ190への流体的結合は、詳細に上述したように、第2出口ポート126の第1サンプルリザーバ180への流体的結合と実質的に同様であり得る。従って、こうした部分については、本明細書ではそれ以上詳細には記載せず、明示的に異なるように記載されていない限り、実質的に同様であるとみなすべきである。さらに、(図1には示さない)分流機構120の追加の出口ポート及びサンプルリザーバは、第2出口ポート126及び第1サンプルリザーバ180と実質的に同様であり得る。

【0032】

[1085] いくつかの実施形態では、プリサンプルリザーバ170、第1サンプルリザーバ180及び第2サンプルリザーバ190を、分流機構120に同様に結合する(又はともに形成する)ことができる。他の実施形態では、プリサンプルリザーバ170、第1サンプルリザーバ180及び第2サンプルリザーバ190は、分流機構120に同様に結合される必要はない。例えば、いくつかの実施形態では、プリサンプルリザーバ170を、分流機構120(例えば、第1出口ポート124)と一体的に形成することができ、第1サンプルリザーバ180及び／又は第2サンプルリザーバ190を、可撓性滅菌管又はそのあらゆる組合せ等の介在構造を介して、分流機構120(例えば、第2出口ポート126)に動作可能に結合することができる。

【0033】

[1086] いくつかの実施形態では、収集デバイス100は、(図1には示さない)アクチュエータと、第1流体流路142、第2流体流路144及び任意選択的に(図1には示さない)追加の流体流路を規定する流量コントローラ140と、をさらに含むことができる。いくつかの実施形態では、アクチュエータを、分流機構120に含めるか又は他の方法で動作可能に結合することができる。このように、アクチュエータを、流量コントローラ140内の(例えば、異なる形態の間の)流体移動を制御するように構成することができる。例えば、アクチュエータは、流量コントローラ140の第1形態に対応する第1位置、流量コントローラ140の第2形態に対応する、第1位置とは異なる第2位置等の間で移動可能であり得る。いくつかの実施形態では、アクチュエータを、単方向に移動するように構成することができる。例えば、アクチュエータを、その第1位置からその第2位置に移動させることができるが、その第2位置からその第1位置に移動させることはできない。同様に、アクチュエータを、その第2位置から第3位置に移動させることができるが、その第3位置からその第2位置に戻るよう移動させることはできない。このように、流量コントローラ140は、その第1形態の前にその第2形態又は第3形態に移動することが防止され、従って、体液の第1量がプリサンプルリザーバ170に向けられ、医療診断及び／又は治療の目的での検査のため等、生物学的サンプルとして使用される抜き取られた流体の第2体積及び／又は第3体積を収容するように設計されたサンプルリザーバ180及び／又は190に向けられないことが必要である。

【0034】

[1087] 流量コントローラ140は、第1形態にある時、第1流体流路142が入口ポート121を第1出口ポート125に流体的に結合し、第2形態にある時、第2流体流路144が入口ポート121を第2出口ポート126に流体的に結合するように構成されている。いくつかの実施形態では、上述したようなアクチュエータを、流量コントローラ14

0を第1形態及び第2形態、任意選択的に第3形態又は第4形態の間で、並進運動で移動させるように構成することができる。例えば、いくつかの実施形態では、流量コントローラ140は、収集デバイス100に対して遠位位置にある時に第1形態であり得る。こうした実施形態では、アクチュエータを、流量コントローラ140を収集デバイス100に対して近位位置まで近位方向に移動させ、それにより流量コントローラ130を第2形態に配置するように作動させることができる。他の実施形態では、アクチュエータを、流量コントローラ140を第1形態及び第2形態又は任意選択的に第3形態あるいは第4形態の間で、回転運動で移動するように作動させることも可能である。

【0035】

[1088] 従って、流量コントローラ140が第1形態にある時、第2出口ポート126（及び任意選択的に、サンプルリザーバに結合された追加の出口ポート）は、入口ポート121から流体的に隔離される。同様に、流量コントローラ140が第2形態にある時、第1出口ポート125は入口ポート121から流体的に隔離される。任意選択的に、流量コントローラ140が（図1には示さない）第3形態にある場合、第1出口ポート125及び第2出口ポート126は、入口ポート121から流体的に隔離される。このように、流量コントローラ140は、第1形態にある時、体液の第1量を、第1出口ポート125を介してプリサンプル流体リザーバ170に仕向け又は分流させることができ、第2形態にある時、体液の第2量を、第2出口ポート126を介して第1サンプル流体リザーバ180に仕向け又は分流させることができる。

【0036】

[1089] いくつかの実施形態では、アクチュエータの少なくとも一部を、プリサンプル流体リザーバ170に動作可能に結合することができる。このように、アクチュエータ（又はアクチュエータの少なくとも一部）を、「プリサンプル」流体リザーバ170内における真空の発生を引き起こすか又は他の方法で促進し、それにより、分流機構120がその第1形態にある時、体液の収集デバイス100を通りプリサンプル流体リザーバ170に入る流れを開始するように構成することができる。アクチュエータは、例えば、回転ディスク、プランジャ、スライド、ダイヤル、ボタン、ハンドル、レバー及び／あるいは他のあらゆる好適な機構又はそれらの組合せ等、収集デバイス100内への体液の流れを駆動するあらゆる好適な機構を含むことができる。好適なアクチュエータの例については、本明細書において具体的な実施形態を参照してより詳細に記載する。

【0037】

[1090] いくつかの実施形態では、分流機構120を、体液の第2量の流れが分流機構120を通して第1サンプル流体リザーバ180に及び／又は第2サンプル流体リザーバ190に輸送されるのを可能にする前に、体液の第1量をプリサンプル流体リザーバ170に輸送する必要があるように構成することができる。このように、分流機構120を、医療従事者による、体液の第2量及び／又は第3量（例えば、サンプル）を収集する前に体液の第1の所定量（例えば、プリサンプル）を収集することに関するコンプライアンスを必要とするものとして特徴付けることができる。同様に言えば、分流機構120を、医療従事者が、体液の第1量、すなわちプリサンプルをプリサンプルリザーバ170に最初に分流させることなく、体液の第2量すなわちサンプルを第1サンプル流体リザーバ180内に収集するのを防止するように構成することができる。このように、医療従事者は、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性がより高い体液の第1量を、分析に使用される体液サンプル内に（意図的であっても無意図的であっても）含めることが防止される。他の実施形態では、流体収集デバイス100は、強制的コンプライアンスの特徴又は構成要素を含む必要はない。

【0038】

[1091] いくつかの実施形態では、分流機構120は、第1形態、第2形態及び第3形態とは異なる（図1には示さない）第4形態を有することができる。第4形態にある時、分流機構120は、入口ポート121を、第1出口ポート125、第2出口ポート126及び任意選択的に第3出口ポートから同時に流体的に隔離することができる。従って、分流

機構 120 がその第 4 形態にある時、入口ポート 121 からプリサンプル流体リザーバ 170、第 1 サンプル流体リザーバ 180 及び第 2 サンプル流体リザーバ 190 に体液が流れることが防止される。使用時、例えば、分流機構 120 を、体液が入口ポート 121 からプリサンプル流体リザーバ 170 に流れることができるように分流機構 120 を第 1 形態に配置するように（例えば、手で又は自動的に）作動させ、その後、体液が入口ポート 121 から第 1 サンプル流体リザーバ 180 に流れることができるように第 2 形態まで移動させ、任意選択的に、体液が入口ポート 121 から第 2 サンプル流体リザーバ 190 に流れることができるように第 3 形態に移動させることができ、その後、体液の分流機構 120 内への及び／又はそこを通る流れを停止させるように第 4 形態に移動させることができる。このように、デバイスは、デバイス 100 内のいかなる残留体液も汚染され及び／又は他の方法で医療従事者及び／又は患者をあり得る危険な流体にさらすことが防止されるように、有効に「ロックされ」かつ第 4 形態で自己完結する。この任意選択的な安全機能により、HIV、C 型肝炎等の病原体が感染している可能性がある体液サンプルへのあり得る暴露を防止することができる。

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【0039】

[1092] いくつかの実施形態では、収集デバイス 100 の 1 つ又は複数の部分は、（図 1 には示さない）ハウジング内に配置されている。例えば、いくつかの実施形態では、分流機構 120、第 1 プリサンプルリザーバ 170 並びにサンプルリザーバ 180 及び 190 のうちの 1 つ又は複数の少なくとも一部を、ハウジング内に配置することができる。こうした実施形態では、分流機構 120 の少なくとも一部は、使用者が、患者（例えば、静脈）から収集デバイス 100 への体液の流れを制御するように流量コントローラ 140 を作動させることができるように、ハウジングを通してアクセス可能である。好適なハウジングの例については、本明細書において具体的な実施形態を参照してより詳細に記載する。

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【0040】

[1093] いくつかの実施形態では、収集デバイス 100 は、任意選択的に、収集デバイスを通して体液の流れを計量することができる 1 つ又は複数の流量計量デバイスを含むことができる。例えば、流量計量デバイスは、第 1 流体流路 142 及び／又は第 2 流体流路 144 に流体連通してそこを通る体液の流れを計量することができる。他の実施形態では、流量計量デバイスは、第 1 ポート 125 及び／又は第 2 ポート 126 に流体連通し及び／又は他の方法でそこに配置されることが可能である。流量計量デバイスは、プリサンプルリザーバ 170、第 1 サンプルリザーバ 180 及び／又は第 2 サンプルリザーバ 190 に移送されている所定体積に関連する指示を使用者に提供するように構成することができるインジケータ等（例えば、ダイヤル、ディスプレイ、色、触覚出力デバイス、ワイヤレス無線信号、Bluetooth（登録商標）無線信号等の電気信号出力デバイス）を含むことができる。いくつかの実施形態では、流量計量デバイスを、例えば、上述したもののようなアクチュエータ等に動作可能に結合することができる。こうした実施形態では、流量計量デバイスは、流量計量デバイスを通して流れた体液の所望の体積に基づいて、流量コントローラ 140 をその第 1 形態とその第 2 形態との間で移動させるようにアクチュエータを作動させるように、動作可能であり得る。従って、流量計量デバイスを用いて、体液の所望の体積がプリサンプルリザーバ 170、第 1 サンプルリザーバ 180 及び／又は第 2 サンプルリザーバ 190 に移送され、それにより、例えば患者サンプルに対する微生物検査等において不十分な、不正確な及び／又は誤った結果を防止することができることを確実にすることができる。

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【0041】

[1094] ここで図 2 ～ 図 13 を参照すると、収集デバイス 200 は、分流機構 220、流量コントローラ 240、プリサンプルリザーバ 270、第 1 サンプルリザーバ 280、及び第 1 サンプルリザーバ 280 とは異なる第 2 サンプルリザーバ 290 を含む。本明細書においてさらに記載するように、収集デバイス 200 を、例えば皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出するために、第 1 形態、第 2 形態及び第 3 形態の間で移動させることができる。収集デ

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バイス 200 は、いかなる好適な形状、サイズ又は構成でもあり得る。例えば、図 2～図 13 ではサンプルリザーバ 280 及び／又は 290 がハウジング 201 に対して垂直に向けられているように示されているが、収集デバイス 200 は、ハウジング 201 に対して平面に向けられているか又はハウジング 201 に対して円錐状に配置されている等のサンプルリザーバ 280 及び／又は 290 を有することができる。

【0042】

[1095] 分流機構 220 は、ハウジング 201 及び可動部材 250 及び 250' を含む。図 2～図 4 に示すように、ハウジング 201 は、プリサンプルリザーバ 270、第 1 サンプルリザーバ 280 及び第 2 サンプルリザーバ 290 に結合されている。ハウジング 201 は、入口ポート 221、第 1 出口ポート 230、第 2 出口ポート 231、第 3 出口ポート 232 を含み、患者から体液を収集するための流体流路を規定することができる内部流路 235 を規定している。入口ポート 221 を、内部流路 235 に流体連通するように選択的に配置することができる。より具体的には、入口ポート 221 は、内部流路 235 に流体連通するように配置することができる入口内腔 202 を規定している。このように、入口ポート 221 は、内部流路 235 を、入口内腔 202 を介してハウジング 201 の実質的に外側の空間に流体連通するように配置することができるように、ハウジング 201 の一部から延在している。入口ポート 221 を、患者から体液を抜き取り及び／又は収集デバイス 200 に輸送するための流体流路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート 221 を、アダプタ 204 を介して直接又は間接的に針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。同様に言えば、入口ポート 221 によって規定された入口内腔 202 は、内腔規定デバイスが入口ポート 221 に結合された時に内腔規定デバイスによって規定される内腔に流体連通するように配置される。さらに詳述すると、内腔規定デバイスが患者の身体の一部の中に（例えば、患者の静脈又は脊椎腔内に）配置されると、ハウジング 201 の内部流路 235 を、患者の身体その部分に流体連通するように配置することができる。

【0043】

[1096] ハウジング 201 によって規定される内部流路 235 は、ハウジング 201 の長さに沿って延在する中心内腔であり、それを、本明細書に記載するように静脈穿刺（体液へのアクセスを可能にするために採用される他の方法）に続いて患者の体液に流体連通するように配置することができる。内部流路 235 は、入口ポート 221 と第 1 出口ポート 230、第 2 出口ポート 231 及び第 3 出口ポート 232 との間で体液を移送する流体流経路を形成する。より具体的には、内部流路 235 が（例えば、入口ポート 221 に結合された医療デバイスを介して）患者に流体連通するように配置されると、第 1 出口ポート 230、第 2 出口ポート 231 及び第 3 出口ポート 232 を、内部流路 235 に流体連通するように選択的に配置して、体液がプリサンプルリザーバ 270、第 1 サンプルリザーバ 280 又は第 2 サンプルリザーバ 290 のうちの少なくとも 1 つに流れ込むのを可能にすることができる。いくつかの実施形態では、体液は、体液の所定体積がプリサンプルリザーバ 270 内に収集される前に、第 2 出口ポート 231 及び第 3 出口ポート 232 に流れるのが防止される。いくつかの実施形態では、第 2 出口ポート 231 及び第 3 出口ポート 232 を、同時に内部流路 235 に流体連通するように配置することができる。いくつかの実施形態では、第 2 出口ポート 231 及び第 3 出口ポート 232 を、逐次内部流路 235 に流体連通するように配置することができる。

【0044】

[1097] 可動部材 250、250' は、使用者によって、ハウジング 201 に対して第 1 位置及び第 2 位置から作動（例えば、移動）させて、流体流を第 1 サンプルリザーバ 280 及び第 2 サンプルリザーバ 290 内に向けるように構成されている。可動部材 250 及び 250' は、実質的に同じであり、従って、単一の可動部材 250 に関して記載する。図 5 に示すように、可動部材 250 は、内部空洞 252 を規定するボス 251 と、入口ポート 253 と、第 1 出口ポート 254 と、内部空洞 252 に流体的に結合された内腔 25

6を規定する穿孔部材255とを含む。入口ポート253及び出口ポート254は、可動部材250の内部チャンバ252を規定するボス251の壁を通して延在している。可動部材250は、ボス251がボア258（図4参照）内に配置され、可動部材250の少なくとも一部が環状チャンバ260内に配置されるように、ハウジング201の支持体257（図4参照）に取り付けられるように構成されている。任意選択的に、可動部材250を使用者が作動させた後にその第1位置に戻すように、付勢部材259（例えば、ばね）を環状チャンバ260内に配置することができる。いくつかの実施形態では、可動部材250、環状チャンバ260、ボア258又はボス251は、使用者によって作動された後に可動部材250を第2位置（例えば、押下位置）で保持するように構成された機械的係止機構を含むことができる。

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【0045】

[1098] 本明細書に記載するように、第1形態では、可動部材250は、内部流路235から間隔を空けて配置されるように配置されている。こうした形態では、患者の身体の一部（例えば、静脈、脊椎腔等）とサンプルリザーバ280及び／又は290との間に、流体流路を確立することができない。言い換えれば、可動部材250がその第1形態にある時、第1サンプルリザーバ280及び第2サンプルリザーバ290は、ハウジング201によって規定される内部流路235から流体的に隔離される。可動部材250を、使用者により、可動部材250を第1形態から第2形態にかつ内部流路235と整列するように移動させるように作動させることができる。使用者によってかけられる力は、付勢部材259を変形させる（例えば、圧縮する）のに十分である可能性があり、それにより、穿孔部材255をサンプルリザーバ280及び／又は290内に挿入することができる。第2形態では、入口ポート253及び出口ポート254は、内部流路235と実質的に位置合せされて、内部空洞252を内部流路235に流体連通するように配置する。従って、可動部材250が第2形態にある場合、内部流路235と、内部空洞252と、穿孔部材255の内腔256と、サンプルリザーバ280との間に流体流経路が確立される。言い換えれば、こうした形態では、本明細書においてさらに詳細に記載するように、体液は、患者（例えば、静脈、脊椎腔等）から分流機構220を通して、第1サンプルリザーバ280及び／又は第2サンプルリザーバ290内に流れ込むことができる。

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【0046】

[1099] プリサンプルリザーバ270は、例えば、単回使用使い捨て収集チューブ、真空による収集チューブ等、体液を収容するあらゆる好適なリザーバであり得る。プリサンプルリザーバ270は、収集デバイス200の第1出口ポート230に（直接、又は滅菌可撓性管等の介在構造を介して）あらゆる好適な方法で流体的に結合されるように構成されている。例えば、いくつかの実施形態では、プリサンプルリザーバ270の一部は、第1出口ポート230の一部の中に摩擦嵌めを形成することができる。他の実施形態では、プリサンプルリザーバ270を、ねじ結合、接着剤、スナップフィット、機械的締結具及び／又は他のあらゆる好適な結合方法を介して、第1出口ポート230に結合することができる。いくつかの実施形態では、プリサンプルリザーバ270を、ハウジング201と一体的に形成することができる。プリサンプルリザーバ270を、体液を、真空吸引を介して入口ポート221から出口ポート230を通りプリサンプルリザーバ270に引き込むのを可能にすることができる負圧状態（真空状態）を（プリサンプルリザーバ270の）内部で維持するように構成することができる。プリサンプルリザーバ270は、体液の第1量を収容するように構成されており、そこでは、体液の第1量は所定量であることも未定量であることも可能であり、それにより、体液の第1量は、患者から後に抜き取られる体液の第2量及び／又は第3量から流体的に隔離される。

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【0047】

[1100] サンプルリザーバ280及び／又は290は、単回使用使い捨て収集チューブ、真空による収集チューブ、上記参照により本明細書に組み込まれる‘420特許に記載されているようなサンプルリザーバ等を含む、体液を収容するあらゆる好適なリザーバであり得る。いくつかの実施形態では、サンプルリザーバ280及び／又は290は、例えば

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Vacutainer（登録商標）等、既知のサンプル容器と実質的に同様であるか又は同じであり得る。サンプルリザーバ２８０及び２９０は、それぞれサンプル容器２８２及び２９２を含み、それぞれ真空シール２８４及び２９４を含む。真空シール２８４又は２９４は、サンプル容器２８２又は２９２それぞれ内部に、真空吸引を介して内部流路２３５からサンプル容器２８２又は２９２それぞれに体液が引き込まれるのを可能にすることができる負圧状態（真空状態）を維持する。サンプル容器２８０及び／又は２９０を、収集デバイス２００の第２出口ポート２３１及び第３出口ポート２３２それぞれに（直接、又は滅菌可撓管等の介在構造を介して）あらゆる好適な方法で流体的に結合されるように構成することができる。サンプルリザーバ２８０及び／又は２９０を、出口ポート２３１及び／又は２３２に流体連通するように配置するように、出口ポート２３１及び／又は２３２に対して移動させることができる。サンプルリザーバ２８０及び２９０を、体液の第２量又は第３量を収容するように構成することができる。体液の第２量又は第３量は、所定量であることも未定量であることも可能であり、それにより、体液の第２量又は第３量は、患者から抜き取られる体液の第１量から流体的に隔離される。いくつかの構成では、サンプルリザーバ２８０及び／又は２９０を、プリサンプルリザーバ２７０と同様にハウジング２０１と一体的に形成することによって収集デバイス２００に結合することができ、従って、それらについてはここでは詳細に記載しない。場合によっては、サンプルリザーバ２８０及び／又は２９０を透明とすることができ、それにより、使用者は、サンプルリザーバ２８０及び／又は２９０内への体液の流れを確認するように視覚的フィードバックを得ることができる。

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【００４８】

[1101] いくつかの実施形態では、サンプルリザーバ２８０及び２９０と分流機構２２０（及び／又はサンプルリザーバ２８０及び２９０以外の収集デバイス２００の部分）とは、独立して形成され（例えば、一体的に形成されず）例えば製造プロセス中に合わせて結合される。場合によっては、サンプルリザーバ２８０及び２９０を、実質的に滅菌又は密封環境（例えば、エチレンオキシド等で充填された環境）で分流機構２２０に結合することができる。従って、サンプルリザーバ２８０及び２９０と分流機構２２０との間のインタフェースは、使用前に実質的に滅菌される。さらに、収集デバイス２００を、サンプルリザーバ２８０及び２９０と分流機構２２０との間に実質的滅菌インタフェースを維持するため等、事前組立式に輸送及び／又は保管することができる。

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【００４９】

[1102] 図６及び図７に示すように、流量コントローラ２４０は、第１部材２４１及び第２部材２４５を含む。第１部材２４１は、ハウジング２０１の凹部２６６（例えば、図４を参照）内に配置されるように構成され、第１部材２４１を、例えば、チタン、グラファイト、熱分解炭素、ポリエステル、ポリカーボネート、ポリウレタン、エラストマー材料等、生体適合性であるあらゆる材料から作製することができる。いくつかの実施形態では、第２部材２４５は、第１部材２４１を第１形態から第２形態に移動させるアクチュエータとしての役割を果たす。より具体的には、第１部材２４１が凹部２６６内に配置されると、第２部材２４５を、第１位置と第２位置との間で移動させて、流量コントローラ２４０を第１形態と第２形態との間で移動させることができる。いくつかの実施形態では、ハウジング２０１は、第２部材２４５のその第１位置からその第２位置への移動を選択的に制限することができる。いくつかの実施形態では、ハウジング２０１を、第２位置に移動した第２部材２４５の移動を防止するように構成することができる。言い換えれば、ハウジング２０１は、第２部材２４５が第２位置から第１位置に戻るよう移動するのを防止する係止機構を含むことができる。第２部材２４５及び／又はハウジング２０１はまた、第２部材２４５の正確な位置決めを確実にするように視覚的フィードバック又は触覚フィードバックを提供する機械的戻り止め及び／又は他のインジケータを含むことも可能である。

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【００５０】

[1103] 第１部材２４１は、静脈穿刺（及び／又は患者の体液にアクセスする他の方法）

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に続いて流体流を方向付ける複数のチャネルを含むことができる。例えば、図 6 及び図 7 に示すように、第 1 部材 2 4 1 は第 1 流路 2 4 2 及び第 2 流路 2 4 4 を含む。第 2 部材 2 4 5 が第 1 位置にある時（例えば、図 8 及び図 9 を参照）、流量コントローラ 2 4 0 は第 1 形態に配置され、第 1 流路 2 4 2 は、入口ポート 2 2 1 を内部流路 2 3 5 から流体的に隔離しながら、入口ポート 2 2 1 と第 1 出口ポート 2 3 0 との間に流体連通を確立する。第 2 部材 2 4 5 が第 2 位置にある時（例えば、図 10 ～図 13 を参照）、流量コントローラ 2 4 0 は第 2 形態に配置され、第 2 流路 2 4 4 は、入口ポート 2 2 1 を第 1 出口ポート 2 3 0 から流体的に隔離しながら、入口ポート 2 2 1 と内部流路 2 3 5 との間に流体連通を確立する。患者と収集デバイス 2 0 0 との間で流体流をさらに方向付ける／隔離するように、追加の第 1 部材 2 4 1 の流路及び／又は流量コントローラ 2 4 0 の形態に対応する追加の第 2 部材 2 4 5 の位置を含めることができる。例えば、第 2 部材 2 4 5 は、患者と収集デバイス 2 0 0 との間の流体流を全体的に実質的に防止する、流量コントローラ 2 4 0 の第 3 形態に対応する第 3 位置を有することができる。言い換えれば、いくつかの実施形態では、すべての体液サンプルが患者から取り出された後に、収集デバイス 2 0 0 内のサンプルを外部環境から実質的に封止するように、ダイヤルを第 3 位置に移動させることができる。

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【0051】

[1104] 動作時、収集デバイス 2 0 0 を使用して、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質からの汚染を低減して、患者から体液（例えば、血液）を収集することができる。例えば、収集デバイス 2 0 0 の入口ポート 2 2 1 は、アダプタ 2 0 4 を介して針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合される。静脈穿刺（又は他の体液アクセス方法）に続いて、第 2 部材 2 4 5 を、図 8 及び図 9 に示すように第 1 位置に達するまで回転させる。別法として、第 2 部材 2 4 5 を第 1 位置に事前設定することができ、収集デバイス 2 0 0 を、プリサンプルリザーバ 2 7 0 内の真空及び収集デバイス 2 0 0 の無菌状態を保持するように他の方法で封止することができる。例えば、入口ポート 2 2 1 及び／又はアダプタ 2 0 4 は、収集デバイス 2 0 0 が針又は他の内腔規定デバイスに結合された時に開放される弁を含むことができる。

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【0052】

[1105] 上述したように、第 2 部材 2 4 5 が第 1 位置にある時、流量コントローラ 2 4 0 は第 1 形態に配置され、第 1 部材 2 4 1 の第 1 流路 2 4 2 は、入口ポート 2 2 1 を内部流路 2 3 5 から流体的に隔離しながら、入口ポート 2 2 1 と第 1 出口ポート 2 3 0 との間に流体連通を確立する。さらに、第 1 サンプルリザーバ 2 8 0 及び第 2 サンプルリザーバ 2 9 0 は、第 1 形態では入口ポート 2 2 1 から流体的に隔離され、図 9 において矢印 A A によって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ 2 7 0 との間に流体流路が規定される。上述したように、プリサンプルリザーバ 2 7 0 並びにサンプルリザーバ 2 8 0 及び 2 9 0 等、収集デバイス 2 0 0 で使用される流体リザーバを、負圧（すなわち、収集デバイス 2 0 0 が体液を抜き取るために使用されている身体の部分の流体圧力未満の圧力）を規定し、それにより、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ 2 7 0 との間に流体連通が確立されると、プリサンプルリザーバ 2 7 0 内の負圧により、プリサンプルリザーバ 2 7 0 と患者の身体の部分との間の圧力差によってプリサンプルリザーバ 2 7 0 内に体液が引き込まれるようになる。この第 1 形態では、流量コントローラ 2 4 0 はまた、プリサンプルリザーバ 2 7 0 を内部流路 2 3 5 から流体的に隔離する。従って、体液の第 1 量（所定量又は未定量）を、（例えば）静脈穿刺の直後にプリサンプルリザーバ 2 7 0 内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス 2 0 0 を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第 1 量が、診断又は汚染物質によって影響を受ける可能性がある他の検査のために収集され使用される体液サンプルの後続する量を汚染しないようにすることができる。

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【0053】

[1106] プリサンプルリザーバ 2 7 0 内における体液プリサンプルの体積の収集に続いて

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、第2部材245を、図10及び図11に示すような第2位置に達するまで、回転させることができる。第2部材245が第2位置にある時、流量コントローラ240は第2形態に配置され、第1部材241の第2流路244は、第1出口ポート230（すなわち、プリサンプルリザーバ270）を入口ポート221から流体的に隔離しながら、入口ポート221と内部流路235との間に流体連通を確立する。言い換えれば、第2形態では、流量コントローラ240は、図11において矢印BBによって示すように第2流路244を介して、患者の身体の一部（例えば、静脈）と内部流路235との間に流体流路を確立する。

【0054】

[1107] 流量コントローラ240が第2形態にある状態で、可動部材250及び／又は250'を使用者が第1位置から第2位置に作動させて（すなわち、押下して）、患者の身体の一部（例えば静脈）と第1サンプルリザーバ280及び／又は第2サンプルリザーバ290との間に流体連通を確立することができる。より具体的には、可動部材250は、その第1位置からその第2形態に移動して、図12において矢印CCによって示すように、穿孔部材255が第1サンプルリザーバ280の真空シール284に穴をあけサンプル容器282内部に配置されることが可能であるように、穿孔部材255が出口ポート231を通過するようにする。第2位置にある時、可動部材250の入口ポート253及び出口ポート254は、内部流路235と実質的に位置合せされかつそれに流体連通し、それにより、体液が、内部流路235から可動部材250の内部空洞252内に、かつ穿孔部材255の内腔256から出て第1サンプルリザーバ280内に流れることができる。サンプルリザーバ280（例えば、真空又は負圧）と内部流路235との圧力差により、体液がサンプルリザーバ280内に引き込まれる。言い換えれば、第2形態では、図12において矢印DDによって示すように、可動部材250は、内部流路235と第1サンプルリザーバ280との間に流体流路を確立する。第1サンプルリザーバ280に体液の所望の量（例えば、第2量）が収集されると、使用者は、可動部材250を解放して、付勢部材259がボタンをその第1位置に戻るように移動させるのを可能にすることができる。可動部材250がその第1位置に戻ると、穿孔部材255は第1サンプルリザーバ280から取り除かれ、シール284（例えば、自己封止膜（self sealing septum））が、第1サンプルリザーバ280を内部流路235から流体的に隔離する。

【0055】

[1108] 同様に、流量コントローラ240が第2形態にある間、図13において矢印EEによって示すように、可動部材250'を、使用者がその第1位置から第2位置に作動させる（押下する）ことができる。このように、上述した可動部材250及び第1サンプルリザーバ280と同様の方法で、患者の身体の一部（例えば、静脈）と第2サンプルリザーバ290との間に（出口ポート232を介して）流体連通が確立される。言い換えれば、第2形態では、可動部材250'は、図13において矢印FFによって示すように、内部流路235と第2サンプルリザーバ290との間に流体流路を確立する。第2サンプルリザーバ290内に体液の所望の量（例えば、第3量）が収集されると、使用者は、可動部材250'を解放して、付勢部材259'がボタン250'をその第1位置に戻るように移動させるのを可能にすることができる。逐次プロセスであるものとして示しかつ記載しているが、充填の順序及び／又は順序付けは必ずしも必要ではない（すなわち、サンプルリザーバ280は、必ずしもサンプルリザーバ290より前に充填されなくてもよい、等）。言い換えれば、流量コントローラ240が第2形態に移動すると、第1サンプルリザーバ280及び第2サンプルリザーバ290（及び任意の追加のサンプルリザーバ）を、あらゆる順序で、同じ時点で（例えば、同時に）及び／又は一部が重なる時間間隔で充填することができる。例えば、使用者は、第1サンプルリザーバ280への充填を開始することができる。その後、第1サンプルリザーバ280が部分的に充填された後、使用者は、可動部材250'を押下して、第1サンプルリザーバ280が充填を終了している間に、第2サンプルリザーバ290への充填を開始するようにすることができる。さらに、サンプルリザーバ280及び／又は290内に収集された体液の体積の調整を、可動部材2

50及び／又は250'を繰り返し作動させる（挿入する）ことによって可能にすることができる。上述したように、第2部材245は、流量コントローラ240の第3形態に対応する第3位置を有することができ、それにより、患者と収集デバイス200との間の流体流を全体的に実質的に防止して、収集デバイス200内のサンプルを外部環境から実質的に封止することができる。

【0056】

[1109] 図2～図13には示さないが、収集デバイス200は、プリサンプルリザーバ270、第1サンプルリザーバ280及び／又は第2サンプルリザーバ290に移送される体液の体積を計量するように構成することができる流量計量デバイス等を含むことができる。例えば、いくつかの実施形態では、流量コントローラ240の第1部材241は、第1流路242及び第2流路244に流体連通している流量計量デバイスを含むことができる。他の実施形態では、流量計量デバイスを、可動部材250及び／又は250'の内部空洞252内に配置することができる。従って、第1サンプルリザーバ280及び第2サンプルリザーバ290に移送されかつその中に配置される体液サンプルの体積を、各サンプルリザーバ280及び290内に配置される体液サンプルの体積が例えば10mL、20mL、30mL等の所定体積であるように、計量し及び／又は制御することができる。

【0057】

[1110] 収集デバイス200は、第1サンプルリザーバ280及び第2サンプルリザーバ290を含むものとして示されかつ記載されているが、他の実施形態では、あらゆる数のプリサンプルリザーバ及び／又はサンプルリザーバを含むことができる。例えば、図14及び図15は、実施形態による収集デバイス300を示す。図示するように、収集デバイス300のいくつかの態様は、図2～図13を参照して上述した収集デバイス200の対応する態様に実質的に同様であり得る。従って、同様の態様については本明細書ではそれ以上詳細には記載しない。

【0058】

[1111] 図14及び図15に示すように、収集デバイス300は、分流機構320、流量コントローラ340、プリサンプルリザーバ370、第1サンプルリザーバ380、第2サンプルリザーバ380'、第3サンプルリザーバ390及び第4サンプルリザーバ390'を含む。プリサンプルリザーバ370は、詳細に上述したプリサンプルリザーバ270と実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ380、380'、390及び390'は、詳細に上述したサンプルリザーバ280及び290と実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ380、380'、390及び390'は、実質的に同じ形状及びサイズを有することができ、例えば、実質的に同じ培地を含むことができる。他の実施形態では、サンプルリザーバ380、380'、390及び390'は、実質的に同じ形状及びサイズを有することができ、好気性菌用培地又は嫌気性菌用培地のうちの一方を含むことができる。例えば、いくつかの実施形態では、第1サンプルリザーバ380及び第3サンプルリザーバ390は好気性菌用培地を含むことができ、第2サンプルリザーバ380'及び第4サンプルリザーバ390'は嫌気性菌用培地を含むことができる。他の実施形態では、サンプルリザーバ380、380'、390及び390'は、各々、好気性菌用培地又は嫌気性菌用培地をあらゆる配置又は組合せで含むことができる。

【0059】

[1112] 分流機構320は、ハウジング301と一組の可動部材350、350'、350''及び350'''とを含む。可動部材350、350'、350''及び350'''は、例えば、図5を参照して上述した可動部材250と実質的に同様である。従って、可動部材350、350'、350''及び350'''を、サンプルリザーバ380、380'、390及び390'それぞれに流体連通して配置されるように、ハウジング301に対して第1位置と第2位置との間で移動させることができる。ハウジング301は、入口ポート321と、プリサンプルリザーバ370に流体連通するように配置されるように構成された第1出口ポート330と、第1サンプルリザーバ380に流体連通する

ように配置されるように構成された第2出口ポート331と、第2サンプルリザーバ380'に流体連通するように配置されるように構成された第3出口ポート332と、第3サンプルリザーバ390'に流体連通するように配置されるように構成された第4出口ポート333と、第4サンプルリザーバ390'に流体連通するように配置されるように構成された第5出口ポート334とを含む。さらに、ハウジング301は、ハウジング201の内部流路235に関して上述したものと同様の方法で、入口ポート321並びに出口ポート331、332、333及び334に流体連通するように選択的に配置することができる内部流路335を規定している。

【0060】

[1113] 流量コントローラ340は、例えば、図6～図13を参照して上述した流量コントローラ240と実質的に同様である。従って、流量コントローラ340を、第1形態と第2形態との間で回転させて、患者とプリサンプルリザーバ370又はサンプルリザーバ380、380'、390及び390'との間に流体流路の一部を選択的に規定することができる。このように、使用者は、図8～図13において収集デバイス200に関して上述したものと同様の方法で、収集デバイス300を操作することができる。従って、体液の第1体積をプリサンプルリザーバ370に移送しかつその中に配置することができ、体液の後続する体積を、サンプルリザーバ380、380'、390及び390'に移送しかつその中に配置することができる。

【0061】

[1114] 図16～図22は、実施形態による収集デバイス400を示す。収集デバイス400は、分流機構420、流量コントローラ440並びにサンプルリザーバ480、480'、490及び490'を含む。本明細書においてさらに記載するように、収集デバイス400を、第1形態、第2形態、第3形態、第4形態及び第5形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス400は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、図16～図22において、サンプルリザーバ480、480'、490及び490'がハウジング401に対して垂直に向けられて示されているが、収集デバイス400は、ハウジング401に対してあらゆる好適な平面において向けられ、又はハウジング401に対して円錐状に配置される等のサンプルリザーバ480、480'、490及び490'を有することができる。

【0062】

[1115] サンプルリザーバ480、480'、490及び490'は、収集デバイス200のサンプルリザーバ280及び／又は290と形態及び機能が実質的に同様であるか又は同じであり、従って、本明細書では詳細には記載しない。上述したように、サンプルリザーバ480、480'、490及び490'は、吸引を介して患者からサンプルリザーバ480、480'、490及び490'に体液を引き込むのを可能にすることができる負圧状態（真空状態）を維持する。いくつかの実施形態では、サンプルリザーバ480及び480'を好気性菌用培養ボトルとすることができ、サンプルリザーバ490及び490'を嫌気性菌用培養ボトルとすることができ、収集デバイス400を用いて、1回の静脈穿刺から複数の好気性菌用血液培養サンプル及び複数の嫌気性菌用血液培養サンプルを収集することができる。本明細書においてさらに詳細に記載するように、サンプルリザーバ480、480'、490及び490'を、各々、体液サンプルのある体積を受け取るように分流機構420の少なくとも一部に流体連通するように配置することができる。体液サンプルの体積は、所定量でも未定量であり得る。さらに、サンプルリザーバ480、480'、490、490'内に体液の所望の体積が配置されると、本明細書においてさらに詳細に記載するように、各サンプルリザーバ480、480'、490及び490'を、分流機構420の少なくとも一部から流体的に隔離することができる。

【0063】

[1116] 分流機構420は、ハウジング401及び分配部材429を含む。分流機構420のハウジング401は、分配部材429に物理的にかつ流体的に結合され、患者から体

液を収集する一組の流体流経路を提供し及び／又は規定している。ハウジング 401 は、凹部 466 及び一組の出口開口部 403 を規定している。凹部 466 は、本明細書においてさらに詳細に記載するように、流量コントローラ 440 に含まれるシール部材 441 を受け入れるように構成されている。出口開口部 403 の組は、各々が、分配部材 429 の異なる部分に流体連通している異なる流体流路を規定するように構成されている、第 1 出口開口部 403 a、第 2 出口開口部 403 b、第 3 出口開口部 403 c、第 4 出口開口部 403 d 及び第 5 出口開口部 403 e を含む。より具体的には、分配部材 429 は、第 1 出口開口部 403 a に流体連通しているプリサンプルリザーバ 470 の少なくとも一部と、第 2 出口開口部 403 b に流体連通している第 1 流路 435 a、第 3 出口開口部 403 c に流体連通している第 2 流路 435 b、第 4 出口開口部 403 d に流体連通している第 3 流路 435 c 及び第 5 出口開口部 403 e に流体連通している第 4 流路 435 d とを規定し及び／又は形成している。

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【0064】

[1117] 図 17 及び図 18 に示すように、分配部材 429 は、プリサンプルリザーバ 470 の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ 470 は、例えば、血液、血漿、尿等の体液を収容するように構成されている。ハウジング 401 の第 1 出口開口部 403 a を、プリサンプルリザーバ 470 が患者から体液の流れを受け取るのを可能にするように、プリサンプルリザーバ 470 の開放部分と実質的に位置合せすることができ、例えば、プリサンプルリザーバ 470 は、体液の第 1 量又は第 1 体積を受け取りかつ収容することができ、ここで、体液の第 1 量は、所定量でも未定量でもあり得る。さらに、分流機構 420 の配置を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ 470 が流路 435 a、435 b、435 c 及び 435 d 並びに／又は患者から抜き取られた体液の後続する体積から流体的に隔離して維持されるというものとすることができる。プリサンプルリザーバ 270 及び 370 を、負圧を維持するものとして上述しているが、プリサンプルリザーバ 470 は、負圧状態（真空状態）を維持せず、従って、例えば重力等の他の機構を用いて、体液をプリサンプルリザーバ 470 内に引き込むことができる。

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【0065】

[1118] 流路 435 a ~ 435 d は、分配部材 429 の中心から放射状に延在し、各流路 435 a、435 b、435 c 及び 435 d がプリサンプルリザーバ 470 及び他の流路から流体的に隔離されるように配置されている。このように、流路 435 a、435 b、435 c 及び 435 d は、出口開口部 403 b、403 c、403 d 及び 403 e それぞれと実質的に位置合せされる第 1 端部と第 2 端部との間で流体流路を方向付け及び／又は他の方法で規定することができる。図 17 及び図 18 に示すように、分配部材 429 は、第 1 流路 435 a の第 2 端部に配置された第 1 出口ポート 431 と、第 2 流路 435 b の第 2 端部に配置された第 2 出口ポート 432 と、第 3 流路 435 c の第 2 端部に配置された第 3 出口ポート 433 と、第 4 流路 435 d の第 2 端部に配置された第 4 出口ポート 434 とを規定している。さらに、分配部材 429 は、第 1 穿孔部材 455 a、第 2 穿孔部材 455 b、第 3 穿孔部材 455 c 及び第 4 穿孔部材 455 d を含み、それらは、第 1 出口ポート 431、第 2 出口ポート 432、第 3 出口ポート 433 及び第 4 出口ポート 434 それぞれに、物理的にかつ流体的に結合されている。従って、本明細書においてさらに詳細に記載するように、穿孔部材 455 a ~ 455 d を用いて、サンプルリザーバ 480、480'、490 及び 490' の真空シールに穴をあけることができ、それにより、体液の流れを開始することができる。図 17 及び図 18 には示さないが、サンプルリザーバ 480、480'、490 及び 490' を、サンプルリザーバ 480、480'、490 及び 490' が出口ポート 431、432、433 及び 434 それぞれに流体連通するように配置されるのを可能にするようにできるあらゆる好適な方法で、分配部材 429 の一部に（直接、又は滅菌可撓性管等の介在構造を介して）物理的に結合することができる。

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【0066】

[1119] 流量コントローラ 440 は、ダイヤル 445 及びシール部材 441 を含む。シー

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ル部材 4 4 1 は、ハウジング 4 0 1 の凹部 4 6 6 内に配置される（例えば、図 2 0 を参照）。より詳細には、流量コントローラ 4 4 0 を、シール部材 4 4 1 が凹部 4 6 6 を規定するハウジング 4 0 1 の表面とダイヤル 4 4 5 の表面との間にかつそれらと接触して配置されるように、ハウジング 4 0 1 に結合することができる。さらに、シール部材 4 4 1 は、本明細書においてさらに詳細に記載するように、流量コントローラ 4 4 0 がハウジング 4 0 1 に結合された時、シール部材 4 4 1 が、ダイヤル 4 4 5 の表面及び凹部 4 6 6 を規定するハウジング 4 0 1 の表面と実質的流体密封シールを形成するような、サイズ及び形状を有することができる。シール部材 4 4 1 を、例えば、シリコン、ポリ乳酸、ポリグリコール酸、ポリ乳酸-グリコール酸共重合体（PLGA）、ポリ酸無水物、ポリオルトエステル、ポリエーテルエステル、ポリカプロラクトン、ポリエステルアミド、ポリ（酪酸）、ポリ（吉草酸）、ポリウレタン、ナイロン、ポリエステル、ポリカーボネート、ポリアクリレート、エチレン-ビニルアセテート及び他のアシル置換セルロースアセテートのポリマー、ポリスチレン、ポリ塩化ビニル、ポリフッ化ビニル、ポリ（ビニルイミダゾール）、クロロスルホネートポリオレフィン、ポリエチレンオキシド並びに／又はそれらの混合物及びコポリマー等、生体適合性であるあらゆる材料から作製することができる。

【0067】

[1120] 図 1 7 に示すように、シール部材 4 4 1 は、静脈穿刺（又は体液にアクセスする他の方法）に続いて体液の流れを方向付けることができる一組の開口部 4 4 4 を規定している。例えば、シール部材 4 4 1 によって規定される一組の開口部 4 4 4 は、第 1 開口部 4 4 4 a、第 2 開口部 4 4 4 b、第 3 開口部 4 4 4 c、第 4 開口部 4 4 4 d 及び第 5 開口部 4 4 4 e を含む。シール部材 4 4 1 の配置は、シール部材 4 4 1 が凹部 4 4 6 内に配置された時、第 1 開口部 4 4 4 a、第 2 開口部 4 4 4 b、第 3 開口部 4 4 4 c、第 4 開口部 4 4 4 d 及び第 5 開口部 4 4 4 e が、ハウジング 4 0 1 の第 1 出口開口部 4 0 3 a、第 2 出口開口部 4 0 3 b、第 3 出口開口部 4 0 3 c、第 4 出口開口部 4 0 3 d 及び第 5 出口開口部 4 0 3 e それぞれと実質的に位置合せされる、というものである。

【0068】

[1121] 流量コントローラ 4 4 0 のダイヤル 4 4 5 は、ハウジング 4 0 1 に回転可能に結合され、かつハウジング 4 0 1 に対する第 1 位置、第 2 位置、第 3 位置、第 4 位置及び第 5 位置の間で移動可能である。ダイヤル 4 4 5 は、内腔 4 0 2 を規定する入口ポート 4 2 1 を含む。入口ポート 4 2 1 を、患者の体内から体液を抜き取り及び／又は収集デバイス 4 0 0 に輸送するための流体流経路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート 4 2 1 を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に直接又はアダプタ 4 0 4 を介して間接的に流体的に結合することができる。同様に言えば、入口ポート 4 2 1 によって規定される入口内腔 4 0 2 は、内腔規定デバイスが入口ポート 4 2 1 に結合された時、内腔規定デバイスによって規定される内腔に流体連通するように配置される。このように、入口ポート 4 2 1 を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ 4 7 0、第 1 サンプルリザーバ 4 8 0、第 2 サンプルリザーバ 4 8 0'、第 3 サンプルリザーバ 4 9 0 及び第 4 サンプルリザーバ 4 9 0' を、患者に流体連通するように選択的に配置するように構成することができる。

【0069】

[1122] 上述したように、ダイヤル 4 4 5 は、第 1 位置、第 2 位置、第 3 位置、第 4 位置及び第 5 位置の間で移動可能である。ダイヤル 4 4 5 が第 1 位置にある時、流量コントローラ 4 4 0 は第 1 形態で配置され、入口ポート 4 2 1 を、シール部材 4 4 1 の第 1 開口部 4 4 4 a 及びハウジング 4 0 1 の第 1 出口開口部 4 0 3 a と実質的に位置合せすることができる。このように、シール部材 4 4 1 の第 1 開口部 4 4 4 a は、入口ポート 4 2 1 を出口開口部 4 0 3 b、4 0 3 c、4 0 3 d 及び 4 0 3 e から流体的に隔離し、それにより入口ポート 4 2 1 を流路 4 3 5 a ~ 3 3 5 d から流体的に隔離しながら、入口ポート 4 2 1 と第 1 出口開口部 4 0 3 a との間に流体連通を確立する。第 1 出口ポート 4 0 3 a がプリサンプルリザーバ 4 7 0 の開放部分と位置合せされると、第 1 開口部 4 4 4 a 及び第 1 出

口開口部 4 0 3 a は、入口ポート 4 2 1 とプリサンプルリザーバ 4 7 0 との間に流体連通を確立する。ダイヤル 4 4 5 が第 2 位置まで回転した（又は駆動された）時、流量コントローラ 4 4 0 は第 2 形態に配置され、第 2 出口開口部 4 4 4 b は、入口ポート 4 2 1 を出口開口部 4 0 3 a、4 0 3 c、4 0 3 d 及び 4 0 3 e から流体的に隔離しながら、入口ポート 4 2 1 と第 2 出口開口部 4 0 3 b との間に流体連通を確立する。第 2 出口開口部 4 0 3 b が第 1 流路 4 3 5 a の第 1 端部と位置合せされると、第 2 開口部 4 4 4 b 及び第 2 出口開口部 4 0 3 b は、入口ポート 4 2 1 と第 1 流路 4 3 5 a との間に流体連通を確立する。

【0070】

[1123] 収集デバイス 4 0 0 は、ダイヤル 4 4 5 が第 3 位置、第 4 位置及び第 5 位置まで回転した時、同様に作用する。従って、入口内腔 4 0 2 が（例えば、入口ポート 4 2 1 に結合された医療デバイスを介して）患者に流体連通するように配置されると、第 1 出口ポート 4 3 0、第 2 出口ポート 4 3 1、第 3 出口ポート 4 3 2、第 4 出口ポート 4 3 3 及び第 5 出口ポート 4 3 4 を、入口内腔 4 0 2 に流体連通するように選択的に配置して、体液のすべてがプリサンプルリザーバ 4 7 0 のうちの少なくとも 1 つ、又はサンプルリザーバ 4 8 0、4 8 0' 4 9 0 及び 4 9 0' のうちの 1 つあるいは複数に流れ込むのを可能にすることができる。いくつかの実施形態では、患者と収集デバイス 4 0 0 との間で流体流をさらに方向付け／隔離するために、追加のシール出口開口部及び／又は流量コントローラ 4 4 0 の形態に対応する追加のダイヤル 4 4 5 の位置を含めることができる。例えば、ダイヤル 4 4 5 は、患者と収集デバイス 4 0 0 との間の流体流を全体として実質的に防止する、流量コントローラ 4 4 0 の第 6 形態に対応する第 6 位置を有することができる。言い換えれば、いくつかの実施形態では、すべての体液サンプルが患者から取り出された後、収集デバイス 4 0 0 内のサンプルを外部環境から実質的にシールするようにダイヤル 4 4 5 を第 6 位置に移動させることができる。

【0071】

[1124] いくつかの実施形態では、プリサンプルリザーバ 4 7 0 内に体液の所定体積が収集される後まで、体液は、サンプルリザーバに関連する出口ポート（例えば、出口ポート 4 3 1～4 3 4）に流れるのが防止される。いくつかの実施形態では、サンプルリザーバに関連する出口ポート（例えば、出口ポート 4 3 1～4 3 4）を、逐次的にのみ、入口内腔 4 0 2 に流体連通するように配置することができる（例えば、出口ポート 4 3 1 は、出口ポート 4 3 2 の前に入口内腔 4 0 2 に流体連通しなければならない、等）。いくつかの実施形態では、後続するサンプルリザーバに関連する出口ポート（例えば、出口ポート 4 3 2～4 3 4）を、体液の確定された体積が収集された後にのみ、入口内腔 4 0 2 に流体連通するように配置することができる。いくつかの実施形態では、サンプルリザーバに関連する出口ポート（例えば、出口ポート 4 3 1～4 3 4）を、いかなる順序の優先もなくあらゆるランダムな方法で入口内腔 4 0 2 に流体連通するように配置することができる（例えば、出口ポート 4 3 4 は、出口ポート 4 3 1 の前に入口内腔 4 0 2 に流体連通することができ、出口ポート 4 3 2 は、出口ポート 4 3 3 の前に入口内腔 4 0 2 に流体連通することができる等）。

【0072】

[1125] いくつかの実施形態では、ハウジング 4 0 1 は、ダイヤル 4 4 5 のその第 1 位置からその第 2 位置、第 3 位置、第 4 位置及び第 5 位置への移動を選択的に制限することができる。いくつかの実施形態では、ハウジング 4 0 1 を、第 5 位置まで移動したダイヤル 4 4 5 の移動を防止するように構成することができる。言い換えれば、ハウジング 4 0 1 は、ダイヤル 4 4 5 が第 5 位置から第 1 位置に戻るよう移動するのを防止する係止機構を含むことができる。ダイヤル 4 4 5 及び／又はハウジング 4 0 1 は又はウジング 4 0 1 の出口開口部 4 0 3 a～4 0 3 e に対するダイヤル 4 4 5 の正確な位置決めを確実にするように視覚的フィードバック又は触覚フィードバックを提供する、機械的戻り止め及び／又は他のインジケータを含むことも可能である。

【0073】

[1126] 動作時、収集デバイス400を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス400の入口ポート421を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は体液にアクセスする他の方法）に続いて、図19及び図20に示すように、ダイヤル445が第1位置に達するまで駆動される（又は回される）。別法として、ダイヤル445を第1位置に事前設定することができ、収集デバイス400を、収集デバイス400の無菌状態を維持するように他の方法で封止することができる。例えば、入口ポート421は、収集デバイス400が針又は他の内腔規定デバイスに結合されると開放する弁を含むことができる。

【0074】

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[1127] 上述したように、ダイヤル445が第1位置にある時、流量コントローラ440は第1形態に配置され、シール部材441の第1開口部444aは、入口ポート421を4つの流路435a～335dから流体的に隔離しながら、（ハウジング401内に含まれる）入口ポート421と第1出口ポート430との間で流体連通を確立する。さらに、サンプリリザーバ480、480'、490及び490'は、第1形態では入口ポート421から流体的に隔離されており、図20において矢印GGによって示すように、患者の身体の一部（例えば、静脈）とプリサンプリリザーバ470との間に、流体流路が規定される。この第1形態では、体液は、患者の身体の部分から入口ポート421の入口内腔402、シール部材441の第1開口部444a、第1出口ポート430を通り、プリサンプリリザーバ470内に（例えば、重力、真空等により）流れ込む。第1形態では、流量コントローラ440はまた、プリサンプリリザーバ470を流路435a～335dから流体的に隔離する。従って、体液の第1量（所定量又は未定量）を、静脈穿刺の直後にプリサンプリリザーバ470内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス400を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第1量が、診断又は汚染物質によって影響を受ける可能性がある他の試験に対して収集され使用される体液サンプルの後続する量を汚染しないようにすることができる。

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【0075】

[1128] プリサンプリリザーバ470内への体液プリサンプルの収集に続き、図21及び図22に示すように、ダイヤル445を、第2位置に達するまで作動させる（回転させる）ことができる。ダイヤル445が第2位置にある時、流量コントローラ440は第2形態に配置され、シール部材441の第2開口部444bは、プリサンプリリザーバ470を入口ポート421から流体的に隔離しながら、入口ポート421と流路435aとの間に流体連通を確立する。言い換えれば、第2形態では、図22において矢印HHによって示すように、流量コントローラ440は、患者の身体の一部（例えば、静脈）と流路435aとの間に流体流路を確立する。流量コントローラ440が第2形態にある状態で、サンプリリザーバ480を、使用者が、第1形態から第2形態に作動させて（例えば、穿孔部材455aを押して）患者の身体の一部（例えば、静脈）と第1サンプリリザーバ480との間に流体連通を確立することができる。

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【0076】

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[1129] 上述したように、サンプリリザーバ480を第2形態に移動させることにより、穿孔部材455aが、サンプリリザーバ480の真空シールに穴をあけてサンプリリザーバ480の内側に配置される。この第2形態では、患者の身体の一部（例えば、静脈）が、サンプリリザーバ480内の負圧状態（真空）によるサンプリリザーバ480からの真空吸引力にさらされる。サンプリリザーバ480（例えば、真空又は負圧）と患者の身体の部分との圧力差により、サンプリリザーバ480内に体液が引き込まれる。体液は、患者の身体の部分から、入口ポート421の入口内腔402、シール部材441の第2開口部444b、ハウジング401の第2出口開口部403bを通して、第1流路435a内に流れ込む。真空吸引により、体液の流れが第1流路435aを通して、第2出口ポート431及び穿孔部材455aを介してサンプリリザーバ480内に引き込まれる

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。言い換えれば、第2形態では、流量コントローラ440は、入口ポート421とサンプルリザーバ480との間に流体流路を確立する。サンプルリザーバ480内に体液の所望の量（例えば、第2量）が収集されると、使用者は、流量コントローラ440を第3位置まで作動させ（回転させ）、及び／又はサンプルリザーバ480をその第1形態に戻るよう移動させて、第1サンプルリザーバ480を流路435aから隔離することができる。サンプルリザーバ480が第1形態に戻ると、穿孔部材455aはサンプルリザーバ480から取り除かれ、サンプルリザーバ480のシール（例えば、自己封止膜）が、第1サンプルリザーバ480を流路435aから隔離する。他のサンプルリザーバの充填は、流量コントローラ440が第3形態、第4形態及び第5形態それぞれに配置されて同様に行われる。

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【0077】

[1130] 充填の順序及び／又は順序付けは必ずしも必要ではない（すなわち、サンプルリザーバ480は必ずしもサンプルリザーバ490の前に充填されなくてもよい等）ことに留意されたい。言い換えれば、第1サンプルリザーバ480及び第2サンプルリザーバ490（及び任意の追加のサンプルリザーバ）をあらゆる順序で充填することができる。例えば、使用者は、第1サンプルリザーバ480の充填を開始することができ、その後、第1サンプルリザーバ480が部分的に充填された後、使用者は第2サンプルリザーバ490を充填することができる。さらに、サンプルリザーバ480及び／又は490内に収集された体液の体積の調整を、サンプルリザーバ480及び／又は490の繰り返される充填によって可能とすることができる。しかしながら、他の実施形態では、充填の順序を、

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【0078】

[1131] 収集デバイス400を、4つのサンプルリザーバの組（例えば、第1サンプルリザーバ480、第2サンプルリザーバ480'、第3リザーバ490及び第4リザーバ490'）を含み及び／又はそれらに他の方法で結合しているものとして上に示し記載しているが、他の実施形態では、収集デバイスは、あらゆる好適な数のサンプルリザーバを含むことができ及び／又はそれらに結合され得る。例えば、図23～図25は、実施形態による収集デバイス500を示す。図示するように、収集デバイス500のいくつかの態様は、図16～図22を参照して上述した収集デバイス500の対応する態様と実質的に同様であり得る。従って、同様の態様については本明細書ではそれ以上詳細には記載しない。

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【0079】

[1132] 収集デバイス500は、分流機構520、流量コントローラ540、第1サンプルリザーバ580及び第2サンプルリザーバ590を含む。サンプルリザーバ580及び590は、詳細に上述したサンプルリザーバと実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ580及び590は、実質的に同じ形状及びサイズを有することができる、実質的に同じ培地を含むことができる。他の実施形態では、サンプルリザーバ580及び590は、実質的に同じ形状及びサイズを有することができ、好気性菌用培地又は嫌気性菌用培地のうちの一方を含むことができる。さらに他の実施形態では、第1サンプルリザーバ580は、第2サンプルリザーバ590のサイズより実質的に大きい第1サイズを有することができる。

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【0080】

[1133] 図24及び図25に示すように、分流機構520は、ハウジング501及び分配部材529を含む。分流機構520のハウジング501は、分配部材529に物理的にかつ流体的に結合されており、患者から体液を収集する一組の流体流経路を提供し及び／又

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は規定している。ハウジング401に関して上述したように、ハウジング501は、凹部と、第1出口開口部503a、第2出口開口部503b及び第3出口開口部503cとを規定することができる。凹部は、詳細に上述したように、流量コントローラ540に含まれるシール部材541を受け入れるように構成されている。第1出口開口部503a、第2出口開口部503b及び第3出口開口部503cは、ハウジング401によって規定された第1出口開口部403a、第2出口開口部403b及び第3出口開口部403cそれぞれと形態及び機能が実質的に同様であり得る。同様に、分配部材529は、分流部材429に含まれるプリサンプルリザーバ470、第1流路435a及び第2流路435bと実質的に同様である、プリサンプルリザーバ470、第1流路435a及び第2流路435bを規定している。従って、分流機構420に関して上述したように、プリサンプルリ
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ザーバ570は、第1出口開口部503aに流体連通しており、第1流路535aは、第2出口開口部503bに流体連通しており、第2流路535bは、第3出口開口部503cに流体連通している。図25に示すように、分配部材529は、第1流路535a及び第1穿孔部材555aに流体連通している第1出口ポート531と、第2流路535b及び第2穿孔部材555bに流体連通している第2出口ポート532とを規定している。上述したように、穿孔部材555a及び555bを用いて、本明細書においてさらに詳細に記載するように、サンプルリザーバ580及び590の真空シールに穴をあけることができ、それにより、体液の流れを開始することができる。

【0081】

[1134] 流量コントローラ540は、ダイヤル545及びシール部材541を含む。シール部材541は、上述したように、ハウジング501の凹部内に配置される。このように、流量コントローラ540がハウジング501に結合されると、シール部材541は、ダイヤル545の表面及び凹部を規定するハウジング501の表面と実質的な流体密封シールを形成する。図24及び図25に示すように、シール部材541は、シール部材441に関して詳細に上述したように、第1出口開口部503a、第2出口開口部503b及び第3出口開口部503cそれぞれと実質的に位置合せされる、第1開口部544a、第2開口部544b及び第3開口部544cを規定している。
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【0082】

[1135] 流量コントローラ540のダイヤル545は、ハウジング501に結合されるのに好適なサイズを有していながら、ダイヤル445と形態及び機能が実質的に同様であり得る。従って、ダイヤル545を、ハウジング501に回転可能に結合し、ハウジング501に対して第1位置、第2位置及び第3位置の間で移動可能とすることができる。ダイヤル545は、内腔502を規定する入口ポート521を含み、入口ポート521を、患者から体液を抜き取り及び／又は収集デバイス500に輸送するための流体流経路を規定する医療デバイス（図示せず）に流体的に結合することができる。このように、入口ポート521を、プリサンプルリザーバ570、第1サンプルリザーバ580及び第2サンプルリザーバ590を選択的に配置するように構成することができる。より詳細には、ダイヤル545が第1位置にある時、流量コントローラ540は第1形態に配置され、入口ポート521は、シール部材541の第1開口部544a及びハウジング501の第1出口開口部503aと実質的に位置合せされる。このように、収集デバイス400に関して詳細に上述したように、シール部材541の第1開口部544aは、入口ポート521と第1出口開口部503aとの間に流体連通を確立し、従って、入口ポート521を、プリサンプルリザーバ570に流体連通するように配置する。同様に、ダイヤル545が第2位置まで回される（又は駆動される）と、流量コントローラ540は第2形態に配置され、第2出口開口部544bは、入口ポート521と第2出口開口部503b、従って第1流路535aとの間に流体連通を確立し、ダイヤル545が第3位置まで回されると、流量コントローラ540は第3形態に配置され、第3出口開口部544cは、入口ポート521と第3出口開口部503c、従って第2流路535aとの間に流体連通を確立する。このように、収集デバイス400に関して詳細に上述したように、収集デバイス500を、プリサンプル570に体液の第1体積を移送するために使用し、その後、第1サンプルリ
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ザーバ５８０及び第２サンプルリザーバ５９０それぞれに体液の第２体積及び第３体積を移送するために使用することができる。

【００８３】

[1136] 図２６～図３３は、実施形態による収集デバイス６００を示す。収集デバイス６００は、分流機構６２０、流量コントローラ６４０並びにサンプルリザーバ６８０、６８０'、６９０及び６９０'を含む。本明細書においてさらに記載するように、収集デバイス６００を、第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的な体液の流れを送出することができる。収集デバイス６００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス６００の態様及び／又は部分

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【００８４】

[1137] 分流機構６２０は、分配部材６２９並びに一組の結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄを含む（例えば、図２７を参照）。分配部材６２９は、結合部材６３７

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【００８５】

[1138] 図２８に示すように、分配部材６２９は、プリサンプルリザーバ６７０の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ６７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。例えば、プリサンプルリザーバ６７０は、患者から体液の第１量又は第１体積を受け取りかつ収容することができ、そこでは、体液の第１量は所定量でも未定量でもあり得る。さらに、分流機構６２０及び流量コントローラ６４０の配置は、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ６７０が結合部分６３７

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【００８６】

[1139] 図２９に示すように、第１結合部材６３７ａは、穿孔部材６５５ａに流体的に結合されている流路６３８

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ば、実質的気密シールを形成することができる摩擦嵌め)を形成することができる。結合部分637aの穿孔部材655aは、図16～図22の収集デバイス400に含まれる穿孔部材455aと形態及び機能が実質的に同様であり得る。従って、穿孔部材655aについては本明細書ではそれ以上記載しない。第2結合部材637b、第3結合部材637c及び第4結合部材637dは同様に配置される。従って、第2結合部材637b、第3結合部材637c及び第4結合部材637dは各々、穿孔部材655b、655c及び655dそれぞれを含み、各々、流路638b、638c及び638dそれぞれを規定している。本明細書においてさらに詳細に記載するように、第1結合部材637a、第2結合部材637b、第3結合部材637c及び第4結合部材637dを用いて、分流機構620を、第1サンプルリザーバ680、第2サンプルリザーバ680'、第3サンプルリザーバ690及び第4サンプルリザーバ690'それぞれに流体連通するように選択的に配置することができる。

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【0087】

[1140] 図30及び図31に示すように、流量コントローラ640は、ダイヤル645及びシール部材641を含む。流量コントローラ640のダイヤル645は、分配部材629内に回転可能に配置され(図32及び図33を参照)、第1位置、第2位置、第3位置及び第4位置の間で移動可能である。ダイヤル645は、各々が内部空間646に流体連通している入口ポート621、第1出口ポート647及び第2出口ポート648を含む(例えば、図30を参照)。内部空間646は、本明細書においてさらに詳細に記載するように、シール部材641の一部を受け入れるように構成されている。入口ポート621を、患者から体液を抜き取り及び/又は収集デバイス600に輸送するための流体流経路を規定する(図示せず)医療デバイスに流体的に結合することができる。例えば、入口ポート621を、針又は他の内腔規定デバイス(例えば、可撓性滅菌管)に直接又はアダプタ604(例えば、図26及び図27を参照)を介して間接的に流体的に結合することができる。第1出口ポート647は、プリサンプルリザーバ670に流体連通している。例えば、第1出口ポート647を、分配部材629の第1出口ポート630内に回転可能に配置することができる。ダイヤル645が、その第1位置、第2位置、第3位置及び第4位置にそれぞれある時、第2出口ポート648を、第2出口ポート631、第3出口ポート632、第4出口ポート633及び第5出口ポート634に流体連通するように選択的に配置することができる。このように、本明細書においてさらに詳細に記載するように、ダイヤル645の内部空間646を、プリサンプルリザーバ670、第1サンプルリザーバ680、第2サンプルリザーバ680'、第3サンプルリザーバ690及び第4サンプルリザーバ690'に流体連通するように選択的に配置することができる。

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【0088】

[1141] 流量コントローラ640のシール部材641の少なくとも一部が、ダイヤル645の内部空間646内に回転可能に配置され、第1位置と第2位置との間で移動可能である。さらに、シール部材641は、シール部材641の外面が、内部空間646の少なくとも一部を規定するダイヤル645の内面と実質的流体密封シールを形成するようなサイズ及び形状を有することができる。図31に示すように、シール部材641は、第1流路642及び第2流路644を規定している。シール部材641が内部空間646内でその第1位置にある時、流路642は、入口ポート621を第2出口ポート648から流体的に隔離しながら、入口ポート621と第1出口ポート647との間に流体連通を確立する。同様に、シール部材641が内部空間646内でその第2位置にある時、第2流路644は、入口ポート621を第1出口ポート647から流体的に隔離しながら、入口ポート621と第2出口ポート648との間に流体連通を確立する。収集デバイス600は、ダイヤル645が分配部材629内で第2位置、第3位置及び第4位置まで回転する時に同様に作用する。従って、入口ポート621が(例えば、入口ポート621及び/又はアダプタ604に結合された医療デバイスを介して)患者に流体連通するように配置されると、分配部材629の第1出口ポート630、第2出口ポート631、第3出口ポート632、第4出口ポート633及び第5出口ポート634を、入口ポート621に流体連通す

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るように選択的に配置して、体液がプリサンプルリザーバ 670、第 1 サンプルリザーバ 680、第 2 サンプルリザーバ 680'、第 3 サンプルリザーバ 690 及び第 4 サンプルリザーバ 690' それぞれの中に流れ込むのを可能にすることができる。

【0089】

[1142] 動作時、収集デバイス 600 を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス 600 の入口ポート 621 を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は体液にアクセスする他の方法）に続き、図 32 に示すように、シール部材をその第 1 位置になるまで作動（又は回転）させることができる。別法として、シール部材 641 を第 1 位置に事前設定することができ、収集デバイス 600 を、収集デバイス 600 の無菌状態を維持するように他の方法で封止することができる。シール部材 641 がその第 1 位置にある時、流量コントローラ 640 は、入口ポート 621 を結合部材 637 a、637 b、637 c 及び 637 d から流体的に隔離しながら、入口ポート 621 と分配部材 629 の第 1 出口ポート 630 との間に流体連通を確立する。従って、図 32 において矢印 I I によって示すように、収集デバイス 400 に関して上述したものと同様の方法で、体液を、患者から入口ポート 621、第 1 流路 642、ダイヤル 645 の第 1 出口ポート 647、分配部材 629 の第 1 出口ポート 630 を介してプリサンプルリザーバ 670 内に移送することができる。

【0090】

[1143] プリサンプルリザーバ 670 内における体液プリサンプルの収集に続いて、シール部材 641 をダイヤル 645 に対してその第 1 位置からその第 2 位置に作動させる（回転させる）ことができる。同様に、図 33 に示すように、ダイヤル 645 を、それが分配部材 629 に対して第 2 位置に達するまで作動させる（又は回転させる）ことができる。シール部材 641 及びダイヤル 645 がその第 2 位置にある時、流量コントローラ 640 は第 2 形態に配置され、シール部材 641 の第 2 流路 644 は、プリサンプルリザーバ 670 を入口ポート 621 から流体的に隔離しながら、入口ポート 621 と第 1 結合部材 637 a の流路 638 a との間に流体連通を確立する。流量コントローラ 640 が第 2 形態にある状態で、サンプルリザーバ 680 を、使用者によりその第 1 形態から第 2 形態に作動させて（例えば、穿孔部材 655 a を押して）、患者の身体の一部（例えば、静脈）と第 1 サンプルリザーバ 680 との間に流体連通を確立することができる。詳細に上述したように、サンプルリザーバ 680 を第 2 形態に移動させることにより、穿孔部材 655 a が、サンプルリザーバ 680 の真空シールに穴をあけてサンプルリザーバ 680 の内側に配置される。この第 2 形態では、患者の身体の部分（例えば、静脈）が、サンプルリザーバ 680 内の負圧状態（真空）のためにサンプルリザーバ 680 からの真空吸引力にさらされる。従って、図 33 において矢印 J J によって示すように、体液を、患者の身体の部分から入口ポート 621、第 2 流路 644、第 2 出口ポート 631 及び流路 638 a 並びに第 1 結合部材 637 a の穿孔部材 655 a を通って第 1 サンプルリザーバ 680 内に強制的に流すことができる。

【0091】

[1144] サンプルリザーバ 680 内に体液の所望の体積（例えば、第 2 量）が収集されると、使用者は、流量コントローラ 640 を第 3 位置まで作動させ（回転させ）及び／又はサンプルリザーバ 680 をその第 1 形態に戻るよう移動させて、第 1 サンプルリザーバ 680 を第 2 流路 644 から隔離することができる。サンプルリザーバ 680 が第 1 形態に戻ると、穿孔部材 655 a は、サンプルリザーバ 680 から取り除かれ、サンプルリザーバ 680 のシール（例えば、自己封止膜）が、第 1 サンプルリザーバ 680 を流路 635 a から流体的に隔離する。他のサンプルリザーバの充填は、流量コントローラ 640 が第 3 形態、第 4 形態及び第 5 形態それぞれに配置されている状態で同様に行われる。

【0092】

[1145] 図 34～図 40 は、実施形態による収集デバイス 700 を示す。収集デバイス 700 は、分流機構 720、流量コントローラ 740 並びにサンプルリザーバ 780 及び 7

90を含む(4つのサンプルリザーバに対してホルダが存在するが、明確にするために図では2つのサンプルリザーバのみが含まれており、収集デバイス700の一部として、追加のサンプルリザーバ(例えば、第5、第6等)を含めることができる)。本明細書においてさらに記載するように、収集デバイス700を第1形態、第2形態、第3形態、第4形態及び第5形態の間で移動させて、例えば、皮膚に存在する微生物及び/又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス700は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス700の態様及び/又は部分は、上述した収集デバイス100、200、300、400、500及び/又は600のいずれかの対応する態様及び/又は部分と形態及び/又は機能が実質的に同様であり得る。従って、こうした同様の態様及び/又は部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス700のサンプルリザーバ780及び790は、図16～図22の収集デバイス400に含まれるサンプルリザーバ480及び490それぞれと形態及び機能が実質的に同様及び/又は同じであり得る。

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【0093】

[1146] 分流機構720は、ハウジング701、分配部材729及びベースプレート771を含む。収集デバイス400に関して上述したように、ハウジング701は、各々、分配部材729の異なる部分に流体連通しているように構成されている、第1出口開口部703a、第2で出口開口部703b、第3出口開口部703c、第4出口開口部703d及び第5出口開口部703eを規定している。より具体的には、分配部材729は、第1出口開口部703aに流体連通しているプリサンプルリザーバ770の少なくとも一部と、第2出口開口部703bに流体連通している第1流体チャンバ735a、第3出口開口部703bに流体連通している第2流体チャンバ735b、第4出口開口部703dに流体連通している第3流体チャンバ735c、第5出口開口部703eに流体連通している第4流体チャンバ735dとを規定し及び/又は形成している。さらに、本明細書においてさらに記載するように、ハウジング701は、流量コントローラ740の少なくとも一部を移動可能に受け入れるように構成された凹部766を規定している。

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【0094】

[1147] 図36に示すように、分配部材729は、プリサンプルリザーバ770の少なくとも一部を形成するチャンバ又は空間を規定している。プリサンプルリザーバ770は、例えば、血液、血漿、尿等の体液を収容するように構成されている。ハウジング701の第1出口開口部703aを、詳細に上述したように、プリサンプルリザーバ770が患者から体液の流れを受け取ることができるように、プリサンプルリザーバ770の開放部分と実質的に位置合せすることができる。さらに詳述すると、分配部材729は一組の壁736を含み、それらは、例えば、分配部材729の内部空間を互いに流体的に隔離されている部分及び/又は空間に分割することができる。例えば、図36に示すように、一組の壁736は、分配部材729の内部空間を、プリサンプルリザーバ770、第1流体チャンバ735a、第2流体チャンバ735b、第3流体チャンバ735c及び第4流体チャンバ735dに分割することができる。いくつかの実施形態では、壁736は、プリサンプルリザーバ770及び流体チャンバ735a～735dを等しく規定し及び/又は形成することができる。他の実施形態では、プリサンプルリザーバ770は、流体チャンバ735a～735dによって規定される空間とは異なる空間を規定することができる。

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【0095】

[1148] 分配部材729は、第1流体チャンバ735a、第2流体チャンバ735b、第3流体チャンバ735c及び第4流体チャンバ735dそれぞれに流体連通している、第1穿孔部材755a、第2穿孔部材755b、第3穿孔部材755c及び第4穿孔部材755dをさらに含む。従って、穿孔部材755a～755dを用いて、本明細書においてさらに詳細に記載するように、サンプルリザーバ780及び790(並びに図34～図40には示さない対応するサンプルリザーバ)に穴をあけることができ、それにより、体液の流れを開始することができる。

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【0096】

[1149] 収集デバイス700の流量コントローラ740は、ダイヤル745及びシール部材741を含む。シール部材741は、ハウジング701の凹部766内に配置される（例えば、図38及び図40を参照）。より詳細には、シール部材741が、凹部766を規定するハウジング701の表面とダイヤル745の表面との間にかつそれらと接触して配置されるように、流量コントローラ740をハウジング701に結合することができる。シール部材741を、詳細に上述したように、ダイヤル745の表面及び凹部766を規定するハウジング701の表面と実質的流体密封シールを形成するように構成することができる。図35に示すように、シール部材741は、第1開口部744a、第2開口部744b、第3開口部744c、第4開口部744d及び第5開口部744eを規定している。シール部材741の配置は、シール部材741が凹部766内に配置された時、第1開口部744a、第2開口部744b、第3開口部744c、第4開口部744d及び第5開口部744eが、ハウジング701の第1出口開口部703a、第2出口開口部703b、第3出口開口部703c、第4出口開口部703d及び第5出口開口部703eそれぞれと実質的に位置合せされる、というものである。

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【0097】

[1150] 流量コントローラ740のダイヤル745は、ハウジング701に回転可能に結合され、ハウジング701に対して第1位置、第2位置、第3位置、第4位置及び第5位置の間で移動可能である。ダイヤル745は入口ポート721を含み、入口ポート721を、患者から体液を抜き取り及び／又は収集デバイス700に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ704を介して間接的に）流体的に結合することができる。このように、入口ポート721を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ770、第1サンプルリザーバ780、第2サンプルリザーバ780'、第3サンプルリザーバ790及び第4サンプルリザーバ790'を患者に流体連通するように選択的に配置するように構成することができる。ダイヤル745が第1位置にある時、流量コントローラ740は第1形態に配置され、入口ポート721を、シール部材741の第1開口部744a及びハウジング701の第1出口開口部703aと実質的に位置合せすることができる。このように、シール部材741の第1開口部744aは、入口ポート721を出口開口部703b、703c、703d及び703eから流体的に隔離し、それにより入口ポート721を流体チャンバ735a～735dから流体的に隔離しながら、入口ポート721と第1出口開口部703aとの間に流体連通を確立する。ダイヤル745が第2位置まで回される（又は駆動される）と、流量コントローラ740は第2形態に配置され、第2出口開口部744bは、入口ポート721をプリサンプルリザーバ770及び流体チャンバ735b～735dから流体的に隔離しながら、入口ポート721と第2出口開口部703bとの間に流体連通を確立する。収集デバイス700は、ダイヤル745が第3位置、第4位置及び第5位置まで回される時、同様に作用する。従って、入口ポート721が（例えば、入口ポート721に結合された医療デバイスを介して）患者に流体連通するように配置されると、体液のすべてがプリサンプルリザーバ770、第1サンプルリザーバ780又は第2サンプルリザーバ790（又はそれらに結合された他の任意の流体リザーバ）内に流れ込むことができるように、第1出口開口部703a、第2出口開口部703b、第3出口開口部703c、第4出口開口部703d及び第5出口開口部703eを入口ポート721に流体連通するように選択的に配置することができる。

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【0098】

[1151] いくつかの実施形態では、ハウジング701は、ダイヤル745のその第1位置からその第2位置、第3位置、第4位置及び第5位置への移動を選択的に制限することができる。いくつかの他の実施形態では、ハウジング701を、第5位置まで移動したダイヤルの移動を防止するように構成することができる。言い換えれば、ハウジング701は、ダイヤル745が第5位置から第1位置に戻るよう移動するのを防止する係止機構を含むことができる。この特徴により、流量チャンバ735a～735d並びに／又はサン

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ブリザーバ780及び790内に収集された体液が（表面に結合された微生物及び／又は他の望ましくない外部汚染物質を含むリスクが高い）プリサンプルリザーバ770内に収容された体液から汚染されるリスクを低減することができる。この係止機構により、医療従事者を、HIV、C型肝炎等を含む可能性がある患者サンプル内の血液媒介病原体にさらされることから保護することも可能である。ダイヤル745及び／又はハウジング701は又はウジング701における出口ポート703a及び出口開口部703a～703dに対するダイヤル745の正確な位置合せを確実にするように視覚的フィードバック又は触覚フィードバックを提供する、機械的戻り止め及び／又は他のインジケータも含むことができる。

【0099】

[1152] 図16～図22に示す収集デバイス400の実施形態と同様に、収集デバイス700は、分配部材729内に収容されるチャンバであるプリサンプルリザーバ770を含む。プリサンプルリザーバ770は、例えば、血液、血漿、尿等の体液を収容することができる。プリサンプルリザーバ770は、（ハウジング701内に位置する）収集デバイス700の第1出口ポート703aに流体的に結合されるように構成されている。収集デバイス700の動作中、流量コントローラ740が第1位置にある時、体液は、患者の身体の一部（例えば、静脈）から、入口ポート721を介して、プリサンプルリザーバ770、シール部材741内に位置するプリサンプルリザーバ744a用の開口部及び第1出口ポート703a内に引き込まれる。プリサンプルリザーバ770は、患者から抜き取られる流体の第1量を収容するように構成され、そこでは、体液の第1量は、所定量であることも未定量であることも可能であり、それにより、体液の第1量は、患者から後に抜き取られる体液の第2量及び／又は第3量及び／又は第4量及び／又は第5量から流体的に隔離される。

【0100】

[1153] 動作時、収集デバイス700を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス700の入口ポート721を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺に続き、図37及び図38に示すように、ダイヤル745が第1位置に達するまで回される。別法として、上述したように、ダイヤル745を第1位置で事前設定することができ、収集デバイス700の無菌状態を維持するように、収集デバイス700を他の方法で封止することができる。ダイヤル745が第1位置にある状態で、流量コントローラ740は第1形態に配置され、シール部材741の第1出口開口部744aは、入口ポート721を4つのサンプル流路735a～735dから流体的に隔離しながら、（ハウジング701内に含まれる）入口ポート721と第1出口ポート741との間に流体連通を確立する。この第1形態では、体液は、図38において矢印KKによって示すように、患者の身体のその部分から、入口ポート721、シール部材741の第1出口開口部744a、ハウジング701の第1出口ポート703aを通して、分配部材770によって規定されたプリサンプルリザーバ770内に流れ込む。従って、詳細に上述したように、体液の第1量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ770内に受け取り、後続するサンプルから隔離することができる。

【0101】

[1154] プリサンプルリザーバ770内における体液プリサンプルの収集に続き、ダイヤル745を、図39及び図40に示すように第2位置に達するまで作動させる（又は回転させる）ことができる。ダイヤル745が第2位置にある時、流量コントローラ740は第2形態に配置され、シール部材741の第2出口開口部744aは、プリサンプルリザーバ770を入口ポート721から流体的に隔離しながら、入口ポート721と第1流体チャンバ735aとの間に流体連通を確立する。第1流体チャンバ735aに体液が充填されると、流量コントローラ740を第3位置に移動させて、第1流路735aを外環境から隔離し封止することができる。さらに、サンプルリザーバ780を第1形態から第2形態に作動させて、体液を第1流体チャンバ735aからサンプルリザーバ780に移

送することができる。例えば、サンプルリザーバ780を使用者が又は自動的に第1形態から第2形態に作動させて（穿孔部材755aを押して）、患者の身体の一部（例えば、静脈）とサンプルリザーバ780との間に流体連通を確立することができる。上述したように、サンプルリザーバ780を第2形態まで移動させることにより、穿孔部材755aがサンプルリザーバ780の真空シールに穴をあけ、サンプルリザーバ780の内側に配置される。第2形態では、患者の身体の一部（例えば、静脈）は、幾つかの実施形態ではサンプルリザーバ780内部に存在する負圧状態（真空）によりサンプルリザーバ780からの真空吸引にさらされる。従って、図40において矢印LLによって示すように、体液は、患者の身体の一部から、入口ポート721、シール部材741の第2出口開口部744b、ハウジング701の第2出口開口部703b、第2流体チャンバ735bを通して第1サンプルリザーバ780内に流れ込む。

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【0102】

[1155] サンプルリザーバ780内に体液の所望の量（例えば、第2量）が収集されると、使用者は、流量コントローラ740を第3位置まで作動させ（回転させ）及び／又はサンプルリザーバ780をその第1形態に戻るように移動させて、第1サンプルリザーバ780を入口ポート721から隔離することができる。サンプルリザーバ780が第1形態に戻ると、穿孔部材755aはサンプルリザーバ780から取り除かれ、サンプルリザーバ780のシール（例えば、自己封止膜）が、第1サンプルリザーバ780を第2流体チャンバ735b及び外部環境から流体的に隔離する。他のサンプルリザーバの充填は、流量コントローラ740が第3形態、第4形態及び第5形態それぞれにある状態で同じ方法で行われる。

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【0103】

[1156] いくつかの実施形態では、収集デバイス700を、分配部材729内で異なる流体チャンバ735a～735dを分離する一組の壁736が存在しないように構成することができる（図16における詳細な断面図を参照）。こうした実施形態では、分配部材729は、プリサンプルリザーバ770と結合された流体チャンバ735との間で分割される（すなわち、流体チャンバは、壁736によって4つの別個の部分に分離されない）。こうした実施形態では、使用者は、ダイヤル745を第2位置、第3位置、第4位置又は第5位置のいずれかに作動（回転）させることによって、一度に4つのサンプルリザーバすべてを充填することができる。

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【0104】

[1157] 本明細書に記載する実施形態のうちのいずれも、例えば、プリサンプルリザーバ及び／又はサンプルリザーバ内への体液の流れを計量する（例えば、定量化する）ために使用することができる計量デバイスと使用することができる。場合によっては、検査標準実施により、充填体積が臨床医及び／又は瀉血専門医によって視覚的に判断され従って人的ミスを受けやすいという事実により、体液（例えば、血液試料）の正確な接種体積との一貫したコンプライアンスが確保されない。血液収集ボトルの体積インジケータは、保持されている時に読み取ることが困難であり、収集ボトルは引込み処置の間、直立して保持されないという事実が、患者から受け取られた体液サンプルの不正確な体積の要因となる可能性がある。サンプル体積が不十分である（例えば、製造業者の推奨未満である）ことにより、培養検査の感度が低下し、偽陰性結果に至る可能性がある。さらに、所定タイプの検査供給品及び装置（例えば、Franklin Lakes, NJのBecton Dickinson等の製造業者によって生成される自動微生物検出システムと使用するように設計された血液培養ボトル）に対する概要資料及び使用説明書において指示されているように、製造業者の推奨を上回る充填体積は、偽陽性をもたらす可能性がある。従って、流量計量及び体積表示機能により、検査技師及び／又は医療従事者（例えば、瀉血専門医）は、サンプルがいかに処理される必要があるかに応じて、サンプルリザーバをインキュベータに又は他の研究室検査機器内に配置する前に各個々のサンプルリザーバ内に収集される体液の体積を確認することができる。検査技師及び／又は瀉血専門医はまた、結果が受け取られる時に臨床医が評価するための正確な体積情報を（例えば、診療記録、データベース、スプレッドシート等に

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）記録することも可能であり、それにより、偽陰性結果及び／又は偽陽性結果の誤った解釈の可能性を低減するのに役立つ。

【0105】

[1158] 例として、図41～図45は、1つ又は複数の計量デバイスを含むことができる収集デバイス800を示す。収集デバイス800は、分流機構820、流量コントローラ840、ディスプレイ875及びサンプルリザーバ880を含む。本明細書においてさらに記載するように、収集デバイス800を第1形態、第2形態及び第3形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス800は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス600の態様及び／又は部分は、上述した収集デバイス100、200、300、400、500、600及び／又は700のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／又は部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス800のサンプルリザーバ880は、図16～図22の収集デバイス400に含まれるサンプルリザーバ480と形態及び機能が実質的に同様であり及び／又は同じであり得る。

【0106】

[1159] 図41～図43に示すように、分流機構820は、アクチュエータ部分822（例えば、第1部分）、中間部分823（例えば、第2部分）及び結合部分824（例えば、第3部分）を含む。分流機構820のアクチュエータ部分822は、内部空間806を規定する一組のアクチュエータ壁を含む実質的に円筒状である。より具体的には、アクチュエータ部分822は、実質的に閉鎖されている第1端部と、内部空間806へのアクセスを可能にするように実質的に開放されている、第1端部と反対側の第2端部とを含む。このように、アクチュエータ部分822は、本明細書においてさらに詳細に記載するように、流量コントローラ840の少なくとも一部を移動可能に受け入れることができる。アクチュエータ部分822は、入口ポート821及び出口ポート831をさらに含む。入口ポート821を、詳細に上述したように、患者から体液を抜き取り及び／又は収集デバイス800に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ804を介して間接的に）流体的に結合することができる。

【0107】

[1160] アクチュエータ部分822の出口ポート831は、アクチュエータ部分822の内部空間806の一部を、中間部分823によって規定される内部空間807に流体連通するように選択的に配置することができる。図43に示すように、中間部分823は、アクチュエータ部分822と結合部分824との間に配置されている。図41～図45には示さないが、中間部分823は、例えばサンプルリザーバ880に移送される体液の体積を計量するように構成することができる計量デバイスを含むことができる。例えば、いくつかの実施形態では、流量計量デバイスを出口ポート831に流体的に結合して、そこを通る体液の流れを計量することができる。図41及び図42に示すように、中間部分823はディスプレイ875を含み、ディスプレイ875は、例えば、出口ポート831を通して流れた体液の体積に関連する視覚的インジケータ及び／又は情報を使用者に提供することができる。他の実施形態では、流量計量デバイスを、分流機構820内の又はそれに沿った他のあらゆる好適な位置に配置することができる。

【0108】

[1161] 結合部分824を、中間部分823に物理的にかつ流体的に結合することができる。例えば、いくつかの実施形態では、結合部分824を、中間部分823の内部空間807内に部分的に配置し、それに、摩擦嵌め、圧入、スナップフィット、ねじ結合、接着剤等を介して少なくとも一時的に結合することができる。結合部分824は、詳細に上述したように、サンプルリザーバ880の一部を受け入れるように構成されており、サンプルリザーバ880の真空シールに穴をあけ、それにより体液の流れを開始することができるように使用することができる穿孔部材855を含む。

【0109】

[1162] 収集デバイス800の流量コントローラ840は、アクチュエータ部分822によって規定された内部空間806内に少なくとも部分的に配置され、第1形態、第2形態及び第3形態の間で移動可能である。図42及び図43に示すように、流量コントローラ840は、第1シール部材861、第2シール部材862及び第3シール部材863を有する可動部材850と、付勢部材859（例えば、ばね等）を含む。シール部材861、862及び863は、内部空間806を規定するアクチュエータ部分822の内面と接触している。従って、本明細書においてさらに詳細に記載するように、シール部材861、862及び863は各々、例えばアクチュエータ部分822の内部空間806を流体的に隔離された部分に分割することができる内面と、実質的流体密封シールを形成することができる。

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【0110】

[1163] 可動部材850は、内部空間806内で第1位置、第2位置及び第3位置の間で移動可能である。可動部材850の配置は、可動部材850がその第1位置、第2位置及び第3位置の間で移動する際に、シール部材861、862及び863が内部空間806内で選択的に移動する、というものであり得る。より具体的には、可動部材850がその第1位置、第2位置及び第3位置の間で移動する際、第1シール部材861を可動部材850と同時に移動させることができる。第2シール部材862及び第3シール部材863を、互いに固定して結合し（例えば、互いに固定距離で配置し）、可動部材850の一部の周囲に摺動可能に配置することができ、それにより、可動部材850は、第2シール部材862及び第3シール部材863がアクチュエータ部分822に対して実質的固定位置にあり続ける間に、その第1位置（例えば、図43を参照）からその第2位置（例えば、図44を参照）に移動することを可能にすることができる。例えば、可動部材850がその第1位置と第2位置との間で移動する際、第2シール部材862及び第3シール部材863は、実質的固定位置にあり続けることができ、それにより、入口ポート821は第2シール部材862の第1側に配置され、出口ポート831は、第2シール部材862の第1側とは反対側の第2側に配置される。従って、本明細書においてさらに詳細に記載するように、可動部材850がその第1位置（図43）及びその第2位置（図44）にある時、入口ポート821は、第1シール部材861と第2シール部材862との間に規定された内部空間806の部分に流体連通しており、出口ポートは、第2シール部材862と第3シール部材863との間に規定された内部空間806の部分に流体連通している。

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【0111】

[1164] 流量コントローラ840の配置は、可動部材850がその第1位置からその第2位置に移動した時に、第1シール部材861が第2シール部材862及び第3シール部材863に対して移動する、というものであり得る。第2シール部材862に対する第1シール部材861の移動により、それらの間に規定された空間が拡大することが可能であり、それにより、プリサンプルリザーバ870を形成し及び／又は他の方法で規定することができる。さらに、シール部材861及び862がアクチュエータ部分822の内面と実質的流体密封シールを形成していることにより、第1シール部材861と第2シール部材862との間に規定されたプリサンプルリザーバ870は、内部空間806の他の部分から流体的に隔離される。従って、可動部材850がその第1位置からその第2位置に移動する時、入口ポート821はプリサンプルリザーバ870に流体連通することができる。可動部材850がその第2位置（例えば、図44を参照）からその第3位置（例えば、図45を参照）まで移動する時、可動部材850の一部は第3シール部材863と接触して、内部空間806内で第1シール部材861、第2シール部材862及び第3シール部材863を実質的に同時に移動させることができる。従って、本明細書においてさらに詳細に記載するように、入口ポート821及び出口ポート831の両方が、第2シール部材862と第3シール部材863との間に規定された内部空間806の部分に流体連通するように、第2シール部材862を入口ポート821に対して移動させることができる。

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【0112】

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[1165] 動作時、収集デバイス 800 を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス 800 の入口ポート 821 を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。入口ポート 821 が内腔規定デバイスに結合された状態で、流量コントローラ 840 をその第 1 形態からその第 2 形態に移動させることができる。このように、使用者は、図 44 において矢印 MM によって示すように、可動部材 850 をその第 1 位置からその第 2 位置に移動させるように力をかけることができる。上述したように、第 1 シール部材 861 は、可動部材 850 と同時に移動し、それによって、第 1 シール部材 861 と第 2 シール部材 862 との間に規定された空間が拡大し、それにより、プリサンプルリザーバ 870 が形成され及び／又は規定される。第 1 シール部材 861 及び第 2 シール部材 862 が、内部空間 806 を規定するアクチュエータ部分 822 の内面と実質的流体密封シールを形成していることにより、第 1 シール部材 861 と第 2 シール部材 862 との間の容積の増大によって、プリサンプルリザーバ 870 内に負圧がもたらされる。従って、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ 870 との間に（例えば、図 44 における入口ポート 821 を介して）流体連通が確立されると、図 44 において矢印 NN によって示すように、プリサンプルリザーバ 870 と患者の身体の部分との間の負圧の差により、入口ポート 821 を通してプリサンプルリザーバ 870 内に体液が引き込まれる。この第 1 形態では、流量コントローラ 840 はまた、プリサンプルリザーバ 870 を出口ポート 831 から流体的に隔離する。従って、体液の第 1 量（所定量又は未定量）を、（例えば）静脈穿刺の直後にプリサンプルリザーバ 870 内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス 800 を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第 1 量が、診断又は汚染物質によって影響を受ける可能性がある他の検査のために収集されかつ使用される体液サンプルの後続する量を汚染するのを防止することができる。いくつかの実施形態では、計量デバイスは、プリサンプルリザーバ 870 内に配置された体液の体積を計量し、その体積に関連する値をディスプレイ 875 に提示することができる。

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【0113】

[1166] プリサンプルリザーバ 870 内における体液プリサンプルの体積の収集に続き、図 45 において矢印 OO によって示すように、可動部材 850 をその第 2 位置からその第 3 位置に移動させて、流量コントローラを第 3 形態に配置することができる。上述したように、可動部材 850 がその第 2 位置からその第 3 位置に移動すると、可動部材 850 の部分は、第 3 シール部材 863 と接触するように配置される。従って、可動部材 850 は、内部空間 806 内で、第 1 シール部材 861、第 2 シール部材 862 及び第 3 シール部材 863 を実質的に同時に移動させる。従って、入口ポート 821 及び出口ポート 831 両方が、第 2 シール部材 862 と第 3 シール部材 863 との間に規定された内部空間 806 の部分に流体連通するように、第 2 シール部材 862 を、入口ポート 821 に対して移動させることができる。さらに、体液の体積がプリサンプルリザーバ 870 内で流体的に隔離されているため、第 2 シール部材 862 及び第 3 シール部材 863 の第 1 シール部材 861 の方向における移動が制限される（すなわち、体液は実質的に非圧縮性流体である）。このように、体液のプリサンプル体積は、プリサンプルリザーバ 870 内で封鎖（sequester）され、第 2 シール部材 862 と第 3 シール部材 863 との間に規定された空間は、入口ポート 821 と出口ポート 831 との間に流体流路を規定する。さらに、流量コントローラ 840 の配置は、その第 3 形態にある時、第 1 シール部材 861 が付勢部材 859 と接触するように配置され、使用者により可動部材 850 にかかる力の少なくとも一部が、付勢部材 859 を変形させ、圧縮し、屈曲させ及び／又は他の方法で再構成するように動作可能である、というものである。従って、付勢部材 859 は、本明細書においてさらに詳細に記載するように、第 1 シール部材 861 に対して、流量コントローラ 840 のその第 2 形態からその第 3 形態への移動に抵抗する反力を及ぼすことができる。

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【0114】

[1167] 詳細に上述したように、穿孔部材 855 が、サンプルリザーバ 880 の真空シー

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ルに穴をあけてサンプルリザーバ内部に配置されるように、サンプルリザーバ 880 を収集デバイス 800 に対して配置することができる。サンプルリザーバ 880（例えば、真空又は負圧）と身体との部分との間の圧力差により、体液がサンプルリザーバ 880 内に引き込まれる。言い換えれば、第 2 形態では、流量コントローラ 840 及び分流機構 820 は、図 45 において矢印 PP によって示すように、体液を、患者から、入口ポート 821、第 2 シール部材 862 と第 3 シール部材 863 との間に規定された内部空間 806 の部分、及びアクチュエータ部分 822 の出口ポート 831 を通って、中間部分 823 及び結合部分 824 の穿孔部材 855 を通って、サンプルリザーバ 880 内に引き込むことができるように、流体流路を確立する。上述したように、（図示せず）計量デバイスが、例えば出口ポート 831 を通して移送される体液の体積を計量することができ、体液の体積に関連する値をディスプレイ 875 に提示することができる。

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【0115】

[1168] サンプルリザーバ 880 内に体液の所望の体積（例えば、第 2 量）が収集されると、使用者は、可動部材 850 にかげられた力を取り除き及び／又は低減することができる、それにより、付勢部材 859 が、第 1 シール部材 861 及び可動部材 850 をそれらの第 3 位置からそれらの第 2 位置に向かって移動させることができる。さらに、プリサンプルリザーバ 870 内に配置された体液が実質的に非圧縮性であることにより、第 1 シール部材 861 の移動が、体液の体積を通して力を移送し、第 2 シール部材 862 及び第 3 シール部材 863 をそれらの第 3 位置からそれらの第 2 位置に向かって移動させる。いくつかの実施形態では、付勢部材 859 は、第 2 シール部材 862 をアクチュエータ部分 822 に対して例えば入口ポート 821 を実質的に遮断することができる第 4 位置に移動させるように作用可能であり得る力を、第 1 シール部材 861 にかけることができる。従って、入口ポート 821 を、アクチュエータ部分 822 の内部空間 806 から流体的に隔離することができる。さらに、穿孔部材 855 をサンプルリザーバ 880 から取り除くことができ、シール（例えば、自己封止膜）が、体液サンプルをサンプルリザーバ 880 の外側の空間から流体的に隔離することができる。後続するサンプルリザーバの充填を、穿孔部材 855 をサンプルリザーバ内に配置し、流量コントローラ 840 を第 3 形態まで移動させて体液が患者からサンプルリザーバに流れるのを可能にすることによって、同様に行うことができる。

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【0116】

[1169] 図 46～図 53 は、実施形態による収集デバイス 900 を示す。収集デバイス 900 は、分流機構 920、流量コントローラ 940 及びサンプルリザーバ 980、980'、990 及び 990' を含む。本明細書においてさらに記載するように、収集デバイス 900 を、第 1 形態、第 2 形態、第 3 形態、第 4 形態及び第 5 形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス 900 は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス 900 の態様及び／又は部分は、上述した収集デバイス 100、200、300、400、500、600、700 及び／又は 800 のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス 900 のサンプルリザーバ 980、980'、990 及び 990' は、図 26～図 33 の収集デバイス 600 に含まれる、サンプルリザーバ 680、680'、690 及び 690' と形態及び機能が実質的に同様であり及び／又は同じであり得る。

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【0117】

[1170] 分流機構 920 は、ハウジング 901、分配部材 929 並びに可動部材 950 a、950 b、950 c 及び 950 d を含む。ハウジング 901 は、分配部材 929 に物理的にかつ流体的に結合されており、患者から体液を収集する一組の流体流経路を提供し及び／又は規定している。ハウジング 901 は、本明細書においてさらに詳細に記載するように、流量計量デバイスに含め及び／又は他の方法で（例えば、電氣的に及び／又は機械

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的に)結合することができる一組のディスプレイ975' (例えば、液晶ディスプレイ(LCD)等)を含む。ハウジング901は、凹部966、出口開口部903a、903b、903c、903d、903e及び(本明細書において「開口」とも呼ぶ)可動部材開口950a、950b、950c、950dを規定している。凹部966は、本明細書においてさらに詳細に記載するように、流量コントローラ940に含まれるシール部材941を受け入れるように構成されている。第1出口開口部903a、第2出口開口部903b、第3出口開口部903c、第4出口開口部903d及び第5出口開口部903eは、各々、分配部材929の異なる部分に流体連通している異なる流体流路を規定するように構成されている。より具体的には、分配部材929は、第1出口開口部903aに流体連通しているプリサンプルリザーバ970の少なくとも一部と、第2出口開口部903bに流体連通している第1流路935a、第3出口開口部903bに流体連通している第2流路935b、第4出口開口部903dに流体連通している第3流路935c、第5出口開口部903eに流体連通している第4流路935とを規定し及び/又は形成している。

【0118】

[1171] 図47及び図48に示すように、分配部材929は、プリサンプルリザーバ970の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ970は、例えば、血液、血漿、尿等の体液を収容するように構成されている。図16～図22においてプリサンプルリザーバ470に関して詳細に上述したように、プリサンプルリザーバ970が患者から体液の流れを受け取るのを可能にするように、ハウジング901の第1出口開口部903aを、プリサンプルリザーバ970の開放部分と実質的に位置合せすることができる。流路935a～935dは、分配部材929の中心から放射状に延在し、各流路935a、935b、935c及び935dがプリサンプルリザーバ970及び他の流路から流体的に隔離されるように配置されている。このように、流路935a、935b、935c及び935dは、出口開口部903b、903c、930d及び903eそれぞれと実質的に位置合せされた開口を規定する第1端部と、可動部材950a、950b、950c及び950dそれぞれを受け入れるように構成された開口又はポートを規定する第2端部との間で、流体流路を方向付け及び/又は他の方法で規定することができる。図47及び図48において、分配部材929は、実質的に閉鎖されている流路935a～935dを含むものとして示されているが、他の実施形態では、図17及び図18の分配部材429に関して上に示しかつ記載したように、流路935a～935dを実質的に開放することができる。従って、収集デバイス900の分配部材929は、収集デバイス400の分配部材429と実質的に同様に機能することができる。

【0119】

[1172] 可動部材950a、950b、950c及び950dは、ハウジング901の開口905a、905b、905c及び905dそれぞれと、分配部材929の第2端部によって規定される対応する開口とに移動可能に配置される。図46～図53には示さないが、いくつかの実施形態では、可動部材950a、950b、950c及び950dを、収集デバイス200の可動部材250及び250'に関して詳細に上述したように、付勢部材等に動作可能に結合することができる。このように、可動部材950a、950b、950c及び950dを、使用者が、ハウジング901及び分配部材929に対して第1位置及び第2位置から作動させ(移動させ)て、流体流を第1サンプルリザーバ980、第2流体リザーバ980'、第3流体リザーバ990及び第4サンプルリザーバ990'それぞれの中に仕向けることができる。可動部材950a、950b、950c及び950dは、実質的に同じであり、従って、図49において単一の可動部材950に関して記載する。さらに、可動部材950のいくつかの部分は、上述した可動部材250及び350と実質的に同様であり得る。従って、可動部材950のいくつかの部分については、本明細書においてそれ以上詳細に説明しない。可動部材950は、入口ポート953及び穿孔部材955に流体連通している内部空洞952を規定している。穿孔部材は、詳細に上述したものと実質的に同様である。入口ポート953は、一組の壁を通して延在し、一組の壁は、可動部材950の内部空間952を対応する流路935a、935b、935c

又は 935d に流体連通するように選択的に配置するように内部チャンバ 952 を規定している。

【0120】

[1173] 図 49 に示すように、可動部材 950 は、内部空間 952 内に回転可能に配置されかつ入口ポート 953 と実質的に直接流体連通している流量制御機構 967 を含む。流量計量機構 967 は、例えば、一組のスプーク又はフィンを含むことができるホイール等であり得る。このように、体液は、可動部材 950 の入口ポート 953 に入り、流量計量デバイス 967 を通過して流れることができ、それにより、流量計量デバイス 967 が可動部材 950 に対して回転することができる。従って、流量計量デバイス 967 の回転の特徴は、可動部材 950 の内部空間 952 に移送される体液の体積、体積流量等を求める際に使用可能であり得る。図 46～図 53 には示さないが、可動部材 950 の流量制御機構 967 は、ハウジング 901 のディスプレイ 975' に動作可能に結合される。従って、体液が、例えばサンプリライザバ 980、980'、990 及び／又は 990' に移送される際、体液の流れに関連する体積情報をディスプレイ 975' に提示することができる。このように、使用者は、患者から体液サンプルを収集するように収集デバイス 900 を操作することができ、例えばサンプリライザバ 980 に移送される体液サンプルの正確な体積を求めるためにディスプレイ 975' の少なくとも 1 つを視覚化することができる。

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【0121】

[1174] 収集デバイス 900 の流量コントローラ 940 は、ダイヤル 945 及びシール部材 941 を含む。シール部材 941 は、ハウジング 901 の凹部 966 内に配置される。より詳細には、シール部材 941 が、凹部 966 を規定するハウジング 901 の表面とダイヤル 945 の表面との間にかつそれらと接触するように配置されるように、流量コントローラ 940 をハウジング 901 に結合することができる。本明細書において詳細に記載するように、シール部材 941 を、ダイヤル 945 の表面及び凹部 966 を規定するハウジング 901 の表面と実質的流体密封シールを形成するように構成することができる。図 47 に示すように、シール部材 941 は、第 1 開口部 944a、第 2 開口部 944b、第 3 開口部 944c、第 4 開口部 944d 及び第 5 開口部 944e を規定している。シール部材 941 の配置は、シール部材 941 が凹部 966 内に配置されると、第 1 開口部 944a、第 2 開口部 944b、第 3 開口部 944c、第 4 開口部 944d 及び第 5 開口部 944e が、ハウジング 901 の第 1 出口開口部 903a、第 2 出口開口部 903b、第 3 出口開口部 903c、第 4 出口開口部 903d 及び第 5 出口開口部 903e それぞれと実質的に位置合せされる、というものである。

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【0122】

[1175] 流量コントローラ 940 のダイヤル 945 は、ハウジング 901 に回転可能に結合され、ハウジング 901 に対して第 1 位置、第 2 位置、第 3 位置、第 4 位置及び第 5 位置の間で移動可能である。ダイヤル 945 は入口ポート 921 を含み、入口ポート 921 を、患者から体液を抜き取り及び／又は収集デバイス 900 に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ 904 を介して間接的に）流体的に結合することができる。このように、入口ポート 921 を、本明細書においてさらに詳細に記載するように、プリサンプリライザバ 970、第 1 サンプリライザバ 980、第 2 サンプリライザバ 980'、第 3 サンプリライザバ 990 及び第 4 サンプリライザバ 990' を患者に流体連通するように選択的に配置するように構成することができる。ダイヤル 945 を、収集デバイス 900 のダイヤル 945 に関して上述したものと実質的に同様な方法で、第 1 位置、第 2 位置、第 3 位置、第 4 位置及び第 5 位置を通して回転するように構成することができ、従って、それについては本明細書においてそれ以上詳細に記載しない。

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【0123】

[1176] 図示するように、ダイヤル 945 は、体液の流れに関連する体積情報を提示するように構成することができるディスプレイ 975 をさらに含むことができる。例えば、図 46～図 53 には示さないが、ダイヤルは、可動部材 950 に含まれる流量計量デバイス

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967等、流量計量デバイス等を含むことができる。このように、流量計量デバイスは、例えば入口ポート921を通る体液の流れを計量することができ、入口ポート921を通る体液の流れに関連する体積情報がダイヤル945のディスプレイ975に提示されるように、ディスプレイ975に動作可能に結合され得る。

【0124】

[1177] 動作時、収集デバイス900を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス900の入口ポート921を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は、体液にアクセスする他の方法）に続き、図50及び図51に示すように、ダイヤル945は、第1位置に達するまで駆動される（又は回される）。別法として、ダイヤル945を第1位置に事前設定することができ、収集デバイス900の無菌状態を維持するように、収集デバイス900を他の方法で封止することができる。

【0125】

[1178] 上述したように、ダイヤル945が第1位置にある時、流量コントローラ940は第1形態に配置され、シール部材941の第1開口部944aは、入口ポート921を4つの流路935a～935dから流体的に隔離しながら、（ハウジング901内に含まれる）入口ポート921と第1出口ポート930との間に流体連通を確立する。さらに、サンプルリザーバ980、980'、990及び990'は、第1形態では入口ポート921から流体的に隔離されており、図51において矢印QQによって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ970との間に、流体流路が規定される。この第1形態では、体液は、（例えば、重力、真空等により）、患者の身体の部分から、入口ポート921、シール部材941の第1開口部944a、ハウジング901の第1出口ポート903aを通して、プリサンプルリザーバ970内に流れ込む。第1形態では、流量コントローラ940はまた、流路935a～935dからプリサンプルリザーバ970を流体的に隔離する。従って、体液の第1量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ970内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス900を用いて、体表微生物及び／又は他の望ましくない汚染物質を含む可能性が最も高い体液の第1量が、診断又は汚染物質によって影響を受ける可能性がある他の検査に対して収集されかつ使用される体液サンプルの後続する量を汚染しないようにすることができる。さらに、ディスプレイ975は、例えば、プリサンプルリザーバ970に移送される体液の体積に関連する、（図示せず）流量制御機構から受け取られる情報を提示することができる。従って、体液の正確な体積を、プリサンプルリザーバに移送し、かつその中で流体的に隔離することができる。

【0126】

[1179] プリサンプルリザーバ970内における体液プリサンプルの収集に続き、図52及び図53に示すように、ダイヤル945を、第2位置に達するまで作動させる（又は回転させる）ことができる。ダイヤル945が第2位置にある時、流量コントローラ940は第2形態に配置され、シール部材941の第2開口部944bは、プリサンプルリザーバ970を入口ポート921から流体的に隔離しながら、入口ポート921と流路935aとの間に流体連通を確立する。流量コントローラ940が第2形態にある状態で、可動部材950aを、使用者が第1位置から第2位置に作動させて（すなわち押下して）、患者（例えば、静脈）と第1サンプルリザーバ880との間に流体連通を確立することができる。より具体的には、図53において矢印RRによって示すように、可動部材950は、その第1位置からその第2位置に移動して、穿孔部材955が、第1サンプルリザーバ980の真空シールを通過して第1サンプルリザーバ980内に配置されるようにする。

【0127】

[1180] 第2位置にある間、可動部材950の入口ポート953は、第1流路935aと実質的に位置合せされかつ流体連通し、それにより、体液が、第1流路935aから稼働部材950の内部空洞952内に入り、穿孔部材955から出て第1サンプルリザーバ980に入るように流れることができる。サンプルリザーバ980（例えば、真空又は負圧

）と第1流路935aとの圧力差により、サンプルリザーバ980内に体液が引き込まれる。言い換えれば、第2形態では、図53において矢印SSによって示すように、流量コントローラ940及び可動部材950aは、ダイヤル945の入口ポート921と第1サンプルリザーバ980との間に流体流路を確立する。さらに、体液の可動部材950aを通る流れにより、可動部材950に対して流量計量機構967が回転する。従って、流量計量機構967の回転は、サンプルリザーバ980に移送される体液サンプルの体積を求める際に使用可能であり得る。さらに、ディスプレイ975'は、例えば、サンプルリザーバ980に移送される体液の体積に関連する、流量制御機構967から受け取られる情報を提示することができる。従って、体液の正確な体積をサンプルリザーバ980に移送することができる。例えば、場合によっては、収集デバイス900を用いて、第1サンプルリザーバ980、第2サンプルリザーバ980'及び第3サンプルリザーバ990の各々に20mLの3つのサンプル体積を収集する（すなわち、合計60mLのサンプル体積が収集される）ことができる。

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【0128】

[1181] 第1サンプルリザーバ980内に体液の所望の体積（例えば、第2量）が収集されると、使用者は、可動部材950を解放して、（図示せず）付勢部材がその第1位置に戻るよう移動するのを可能にすることができる。可動部材950がその第1位置に戻ると、穿孔部材955は、第1サンプルリザーバ980から取り除かれ、シール（例えば、自己封止膜）が、第1サンプルリザーバ980を内部流路935から流体的に隔離する。収集デバイス900を用いて、ダイヤル945をその第3位置、第4位置及び第5位置までそれぞれ回転させることにより、第2サンプル体積を第2サンプルリザーバ980'に、第3サンプル体積を第3サンプルリザーバ990に、第4サンプル体積を第4サンプルリザーバ990'に、同様に移送することができる。

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【0129】

[1182] 場合によっては、体液収集デバイス900により、臨床医及び／又は瀉血専門医は、体液収集デバイス900を収容するパッケージを開封し、（分配部材929を含む）ハウジング901のみを取り出し、ハウジング901を患者のベッドわきに持って行くことができる。臨床医及び／又は瀉血専門医は、あらゆる標準化技法を用いて患者の身体の一部（例えば、静脈）に対して静脈穿刺を行う（又は、患者の体液にアクセスする他のあらゆる方法を採用する）ことができる。静脈穿刺に続き、臨床医及び／又は瀉血専門医は、すべてのサンプルに対して必要な総血液体積を収集することができる。例えば、臨床医及び／又は瀉血専門医は、2.5mLプリサンプル分流体積及び4つのサンプルリザーバの各々に対して10mLサンプル体積を収集することができ、それにより、収集された体液（例えば、血液）は合計42.5mLになる。体液の所望の量の収集に続き、皮下注射針を患者の身体の一部（例えば、静脈）から取り除くことができ、臨床医及び／又は瀉血専門医は、（体液を収容している）ハウジング901を、膜頂部がハウジング901の形状に一致するカスタムトレイ内に事前に配置された状態で、4パック（又は2パック）の事前滅菌されたサンプルリザーバの上に配置することができる。サンプルリザーバのこうした事前滅菌されたパックを使用することにより、臨床医は、滅菌剤を用いてサンプルリザーバの頂部を「拭く」プロセスステップを行う必要がなく、それにより、例えば、リザーバ頂部の滅菌が不適切及び／又は不十分である場合に、汚染の可能性が低減する。そして、臨床医及び／又は瀉血専門医は、体液を含むサンプルリザーバの自動接種を正確な体積制御で起動させることができる。いくつかの実施形態では、サンプルリザーバの接種が完了した後、各個々のサンプルリザーバに対して体積情報が表示されているデバイス900全体を、分析のために研究室に送ることができる。他の実施形態では、サンプルリザーバ980及び／又は990を個々に取り除き、分析のために研究室に送ることができる。

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【0130】

[1183] 収集デバイス900を、図46～図53を参照して、収集デバイスの一部を通して移送される体液の体積に関する体積データを提示することができる一組のディスプレイ

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