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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

[1130] Furthermore, a user (e.g., a physician, a nurse, a technician, or the like) can engage the transfer device 800 to physically and fluidically couple the first lock mechanism 813 to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC. In this manner, the external fluid reservoir can define a negative pressure within an inner volume of the reservoir. Therefore, when the flow control mechanism 840 is in the first configuration, a negative pressure differential introduces a suction force within the first proximal cannula 812, the first lumen 846 defined by the flow control mechanism 840, the distal cannula 817, and the cannula assembly 820. In this manner, the first proximal cannula 812, the first lumen 846 defined by the flow control mechanism 840, the distal cannula 817, and the cannula assembly 820 collectively define a fluid flow path configured to transfer a flow of a bodily fluid to the external fluid reservoir, as indicated by the arrow WW in FIG. 37. In addition, the flow of bodily fluid can be such that dermally residing microbes dislodged during a venipuncture event (e.g., the insertion of the cannula 824) are entrained in the flow of bodily fluid and are transferred to the external fluid reservoir.

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

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

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

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

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

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

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

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

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

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

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

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

[1139] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Where methods and steps described above indicate certain events occurring in certain order, those of ordinary skill in the art having the benefit of this disclosure would recognize that the ordering of certain steps may be modified and that such modifications are in accordance with the variations of the invention. Additionally, certain of the steps may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above. Additionally, certain steps may be partially completed before proceeding to subsequent steps.

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

[1141] Although various embodiments have been described as having particular features and/or combinations of components, other embodiments are possible having any combination or sub-combination of any features and/or components from any of the embodiments described herein.

[1142] The specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different from the embodiments shown, while still providing the functions as described herein. More specifically, the size and shape of the various components can be specifically selected for a desired rate of bodily fluid flow into a fluid reservoir or for a desired rate of parenteral fluid flow into the patient.

Claims

1. An apparatus, comprising:

a cannula assembly;

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

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

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

an actuator operably coupled to the flow control mechanism and configured to move the flow control mechanism from the first configuration in which the inlet port is placed in fluid communication with the fluid reservoir such that bodily fluid can flow from the cannula assembly, through inlet port via the fluid flow path and to the fluid reservoir, to the second configuration, in which the fluid reservoir is fluidically isolated from the cannula assembly.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

38. The method of clam 37, further comprising:

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

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

40. The method of claim 35, further comprising:

delivering fluid from the fluid source to the patient.

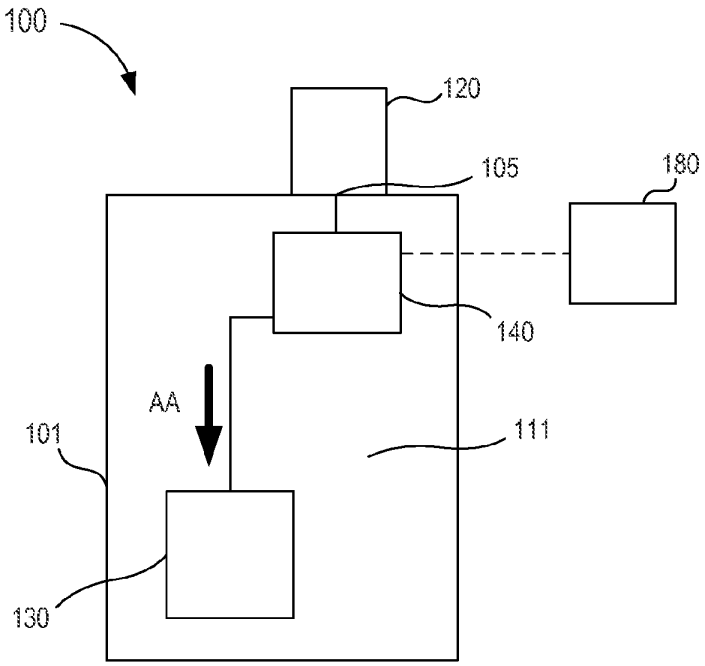

100
120
105
180
140
AA
101
111
130

FIG. 1

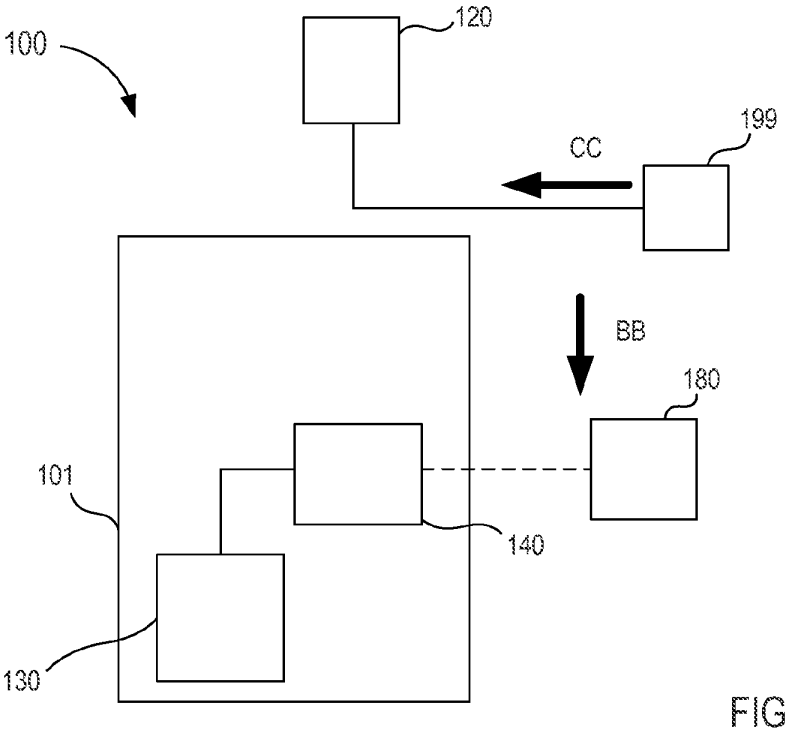

100
120
199
CC
BB
180
101
140
130

FIG. 2

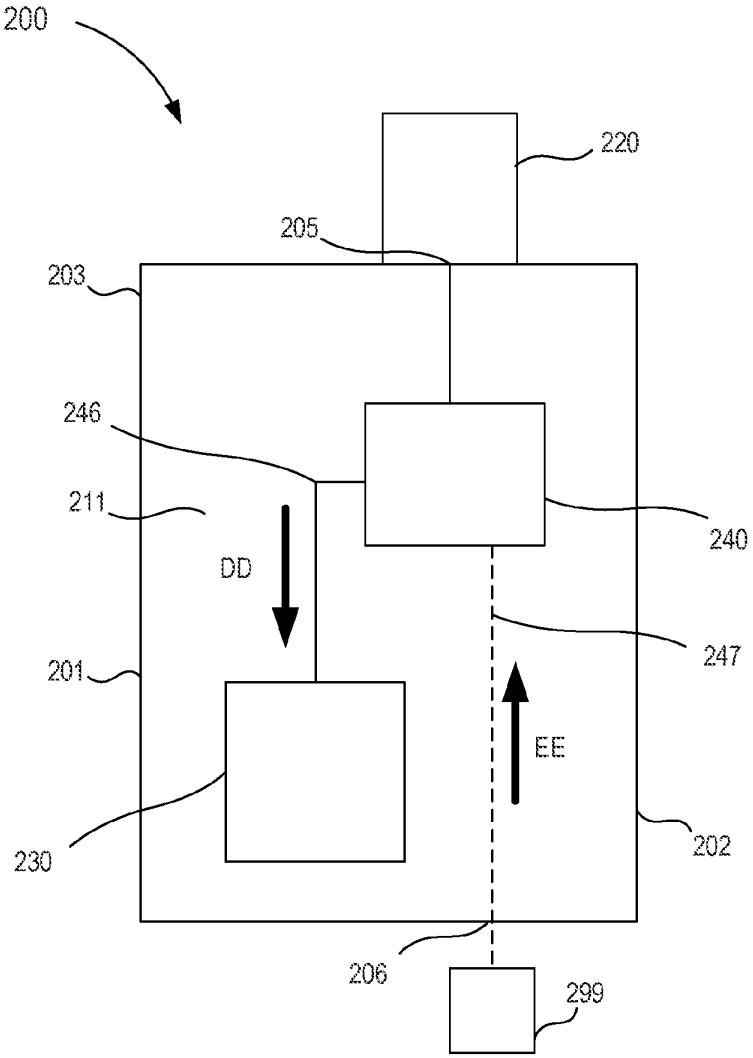


FIG. 3

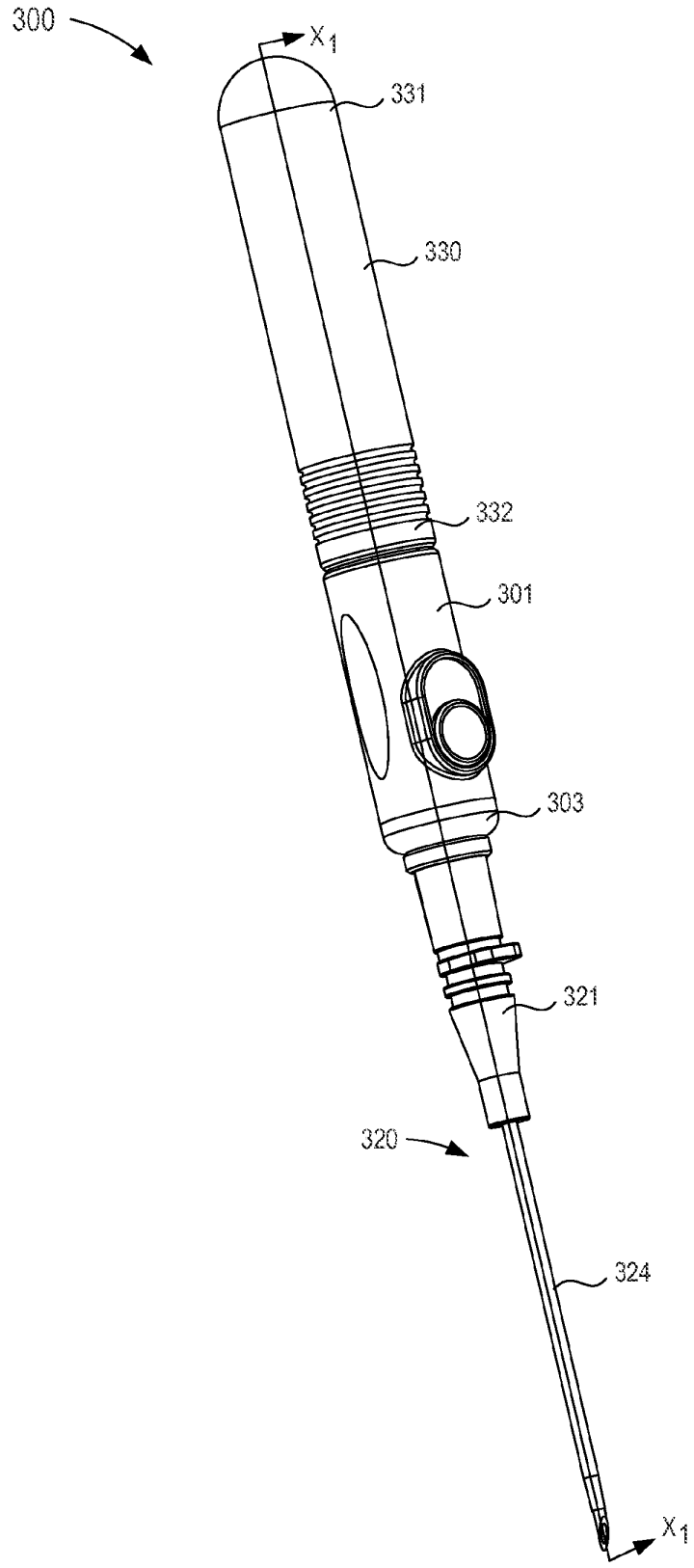


FIG. 4

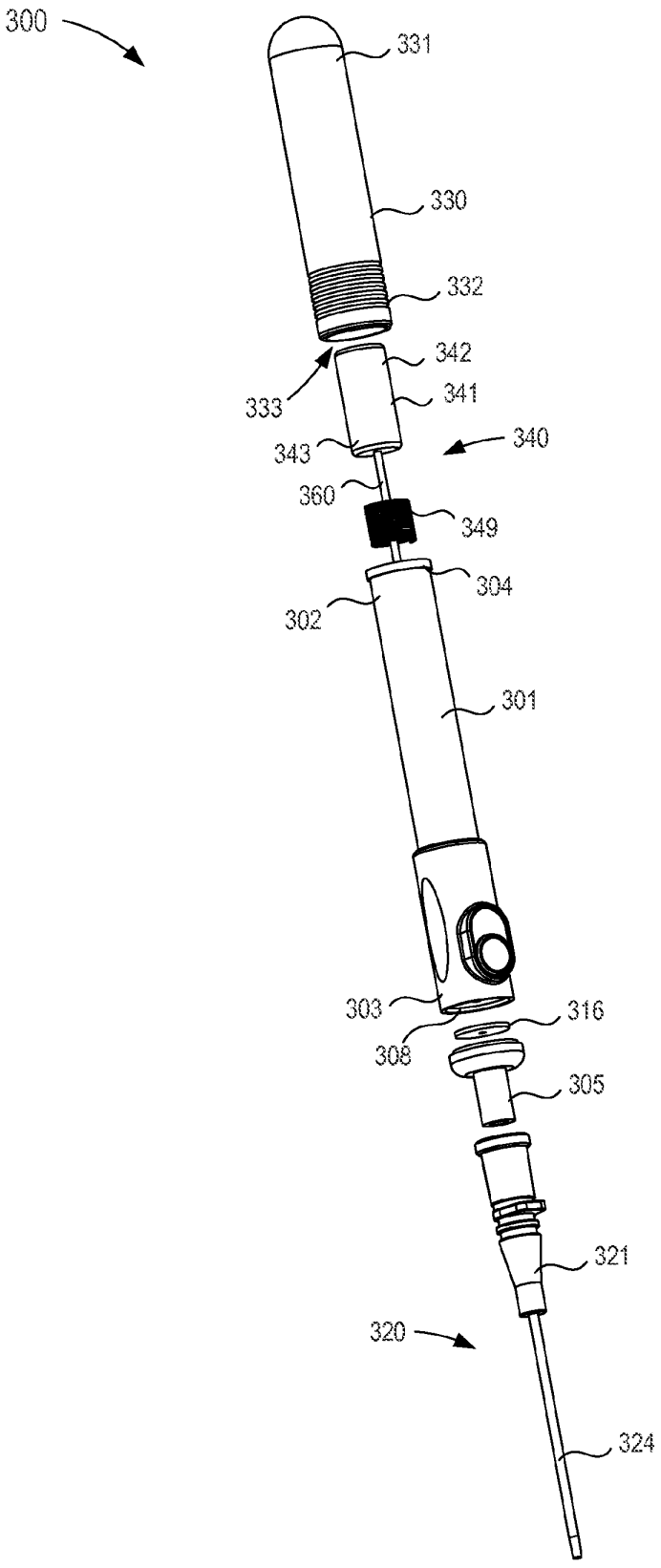

300
331
330
332
342
341
333
340
343
360
349
304
302
301
303
316
308
305
321
320
324

FIG. 5

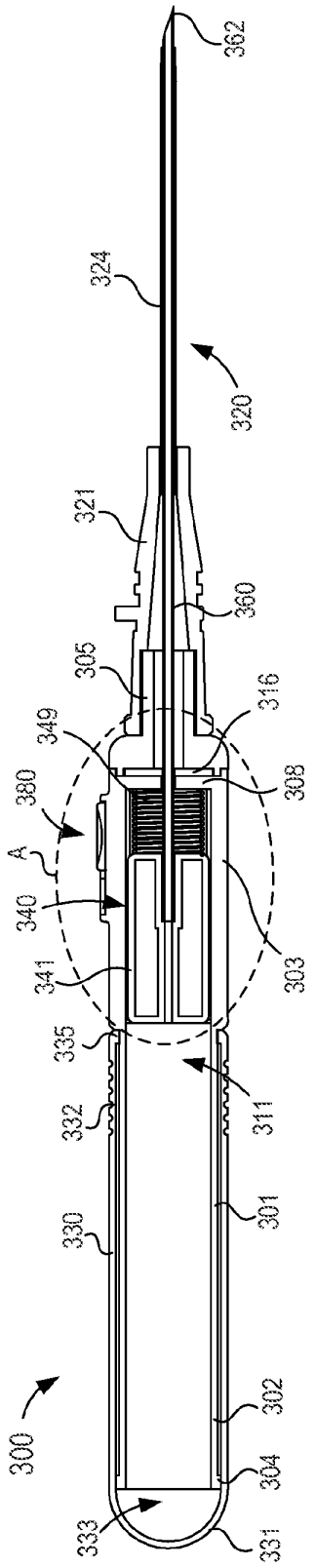

362
324
320
321
360
305
316
349
308
380
A
340
341
303
335
311
332
301
330
300
302
304
333
331

FIG. 6

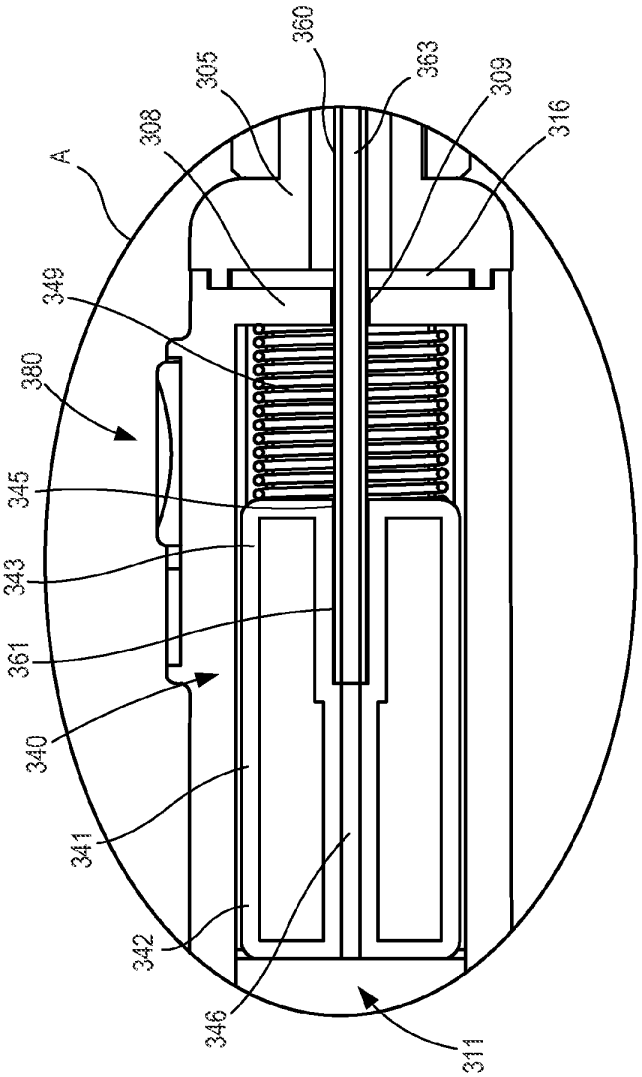

360
305
363
309
316
308
A
349
380
345
343
361
340
341
342
346
311

FIG. 7

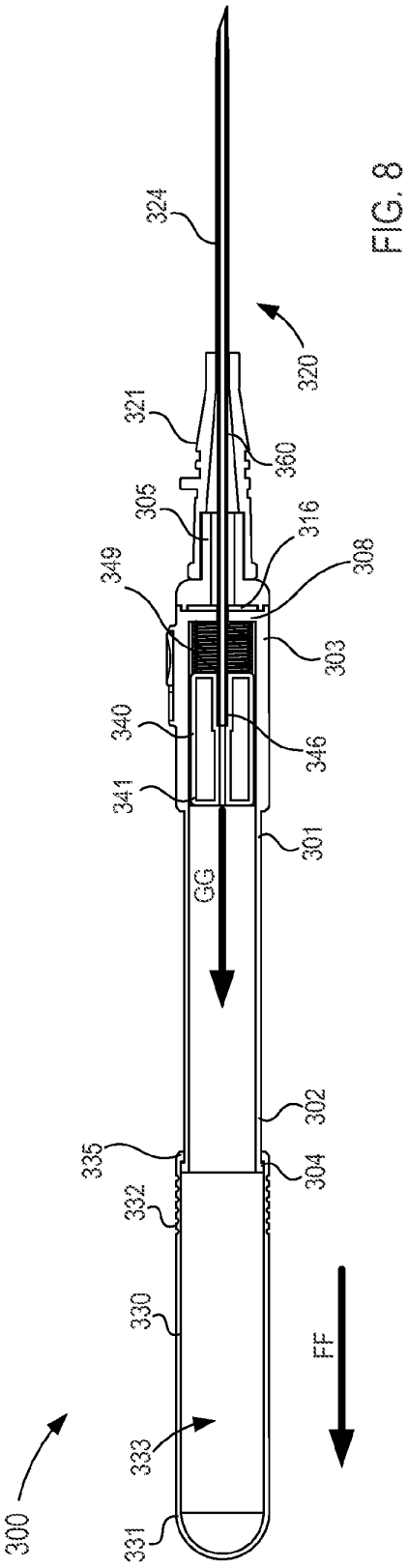

324
320
321
360
305
316
308
349
303
340
346
341
301
GG
302
335
304
332
330
FF
333
300
331

FIG. 8

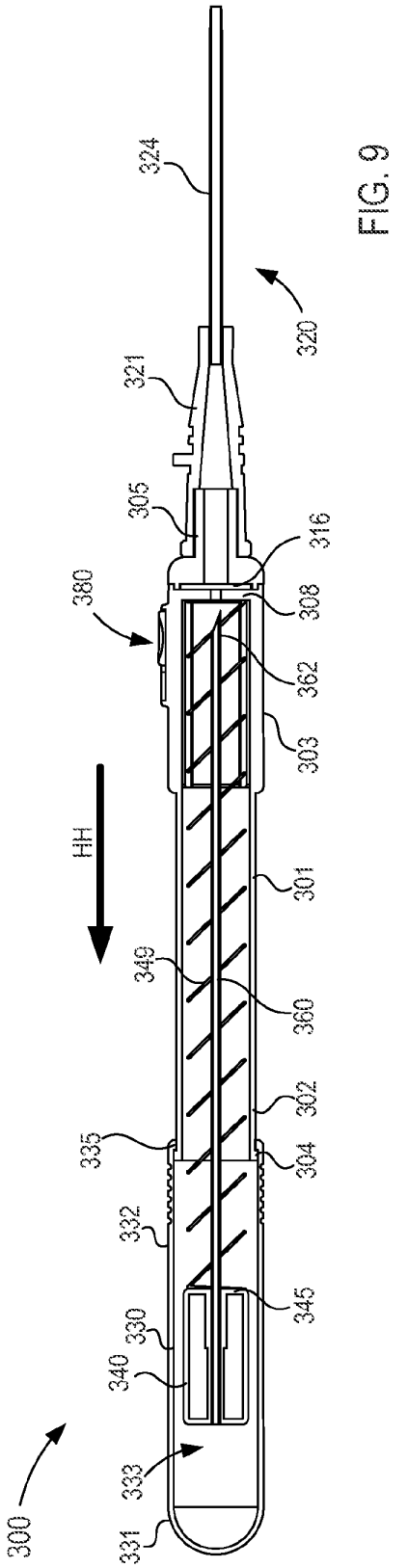

324
320
321
305
316
308
380
362
303
HH
301
349
360
302
335
304
332
345
330
340
333
300
331

FIG. 9

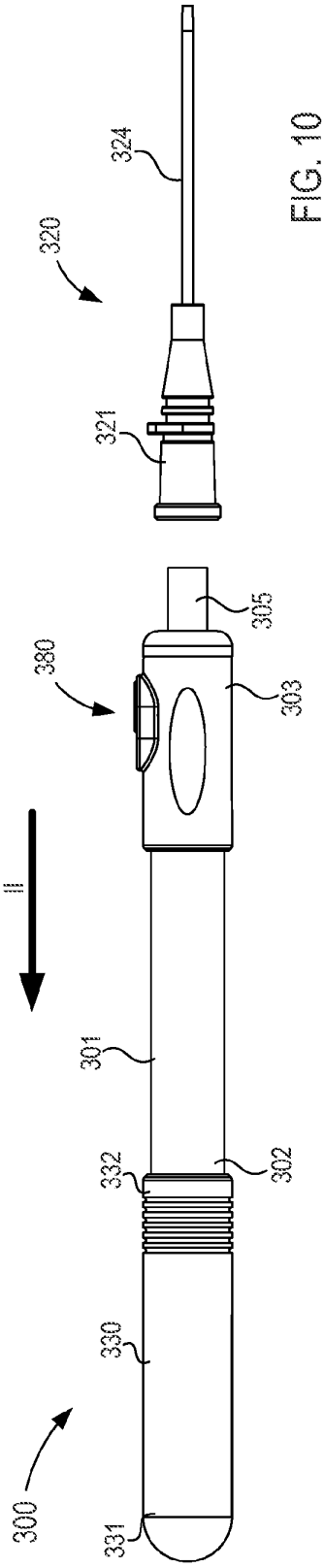


FIG. 10

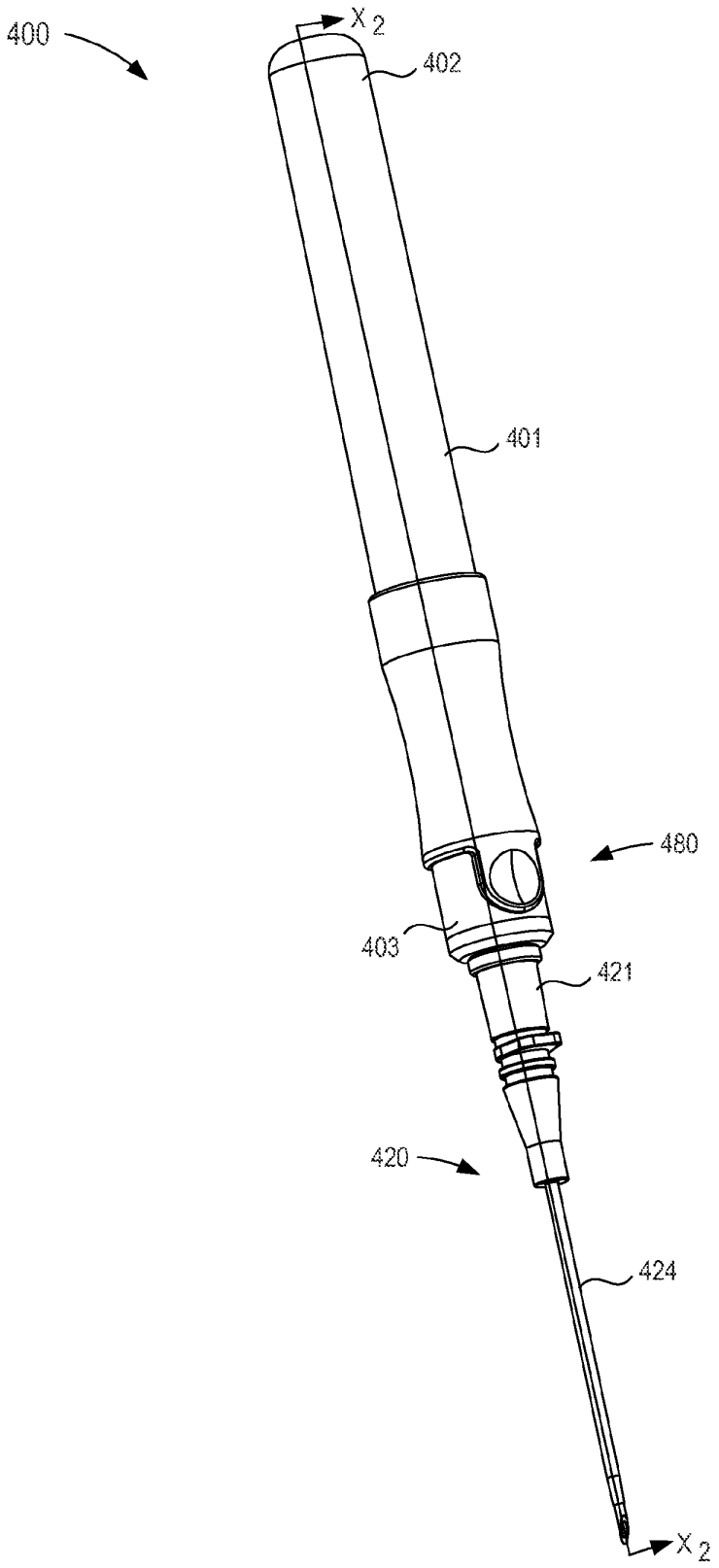


FIG. 11

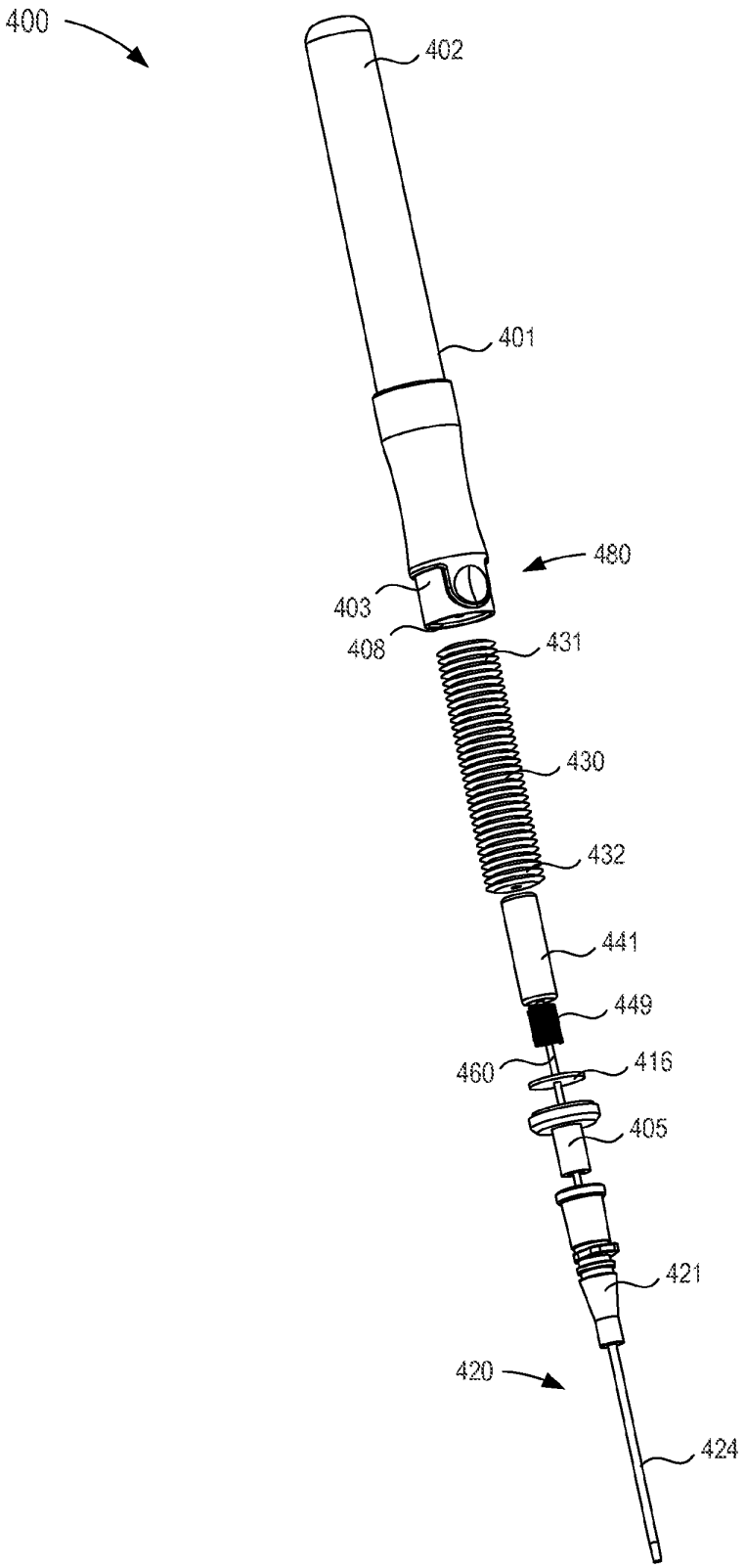

400
402
401
480
403
408
431
430
432
441
449
460
416
405
421
420
424

FIG. 12

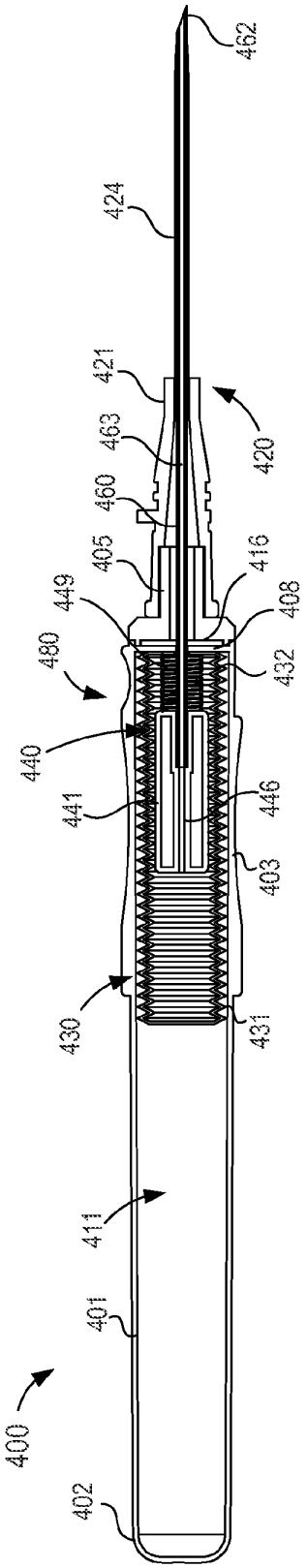

462
424
421
463
460
405
449
480
440
441
430
411
401
400
402
420
416
408
432
446
403
431

FIG. 13

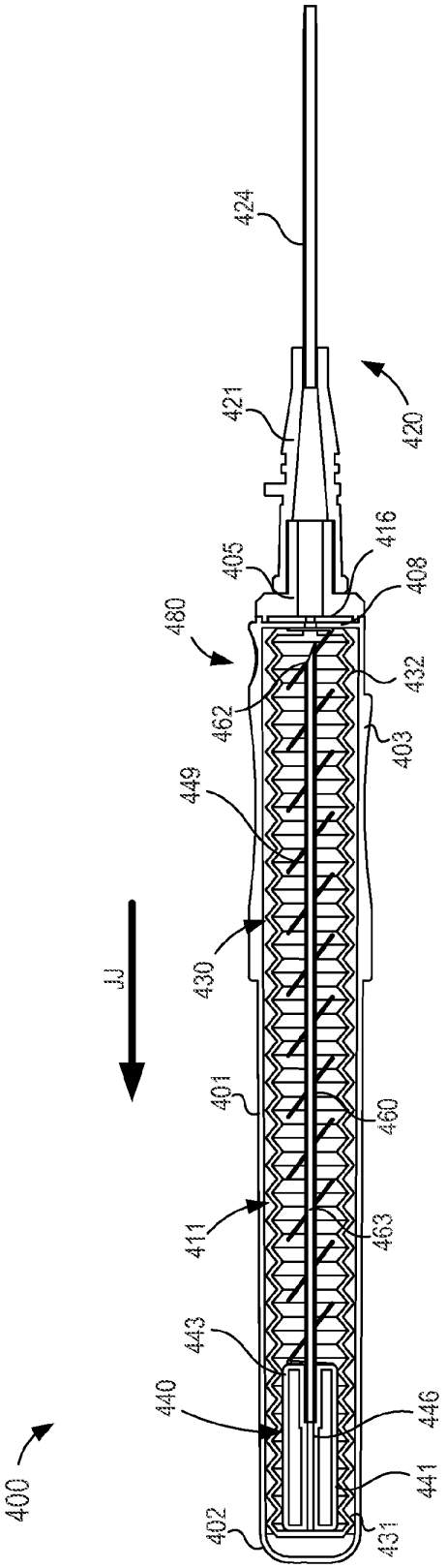

424
421
420
405
416
408
480
462
432
403
449
430
JJ
401
460
411
463
443
440
446
441
400
402
431

FIG. 14

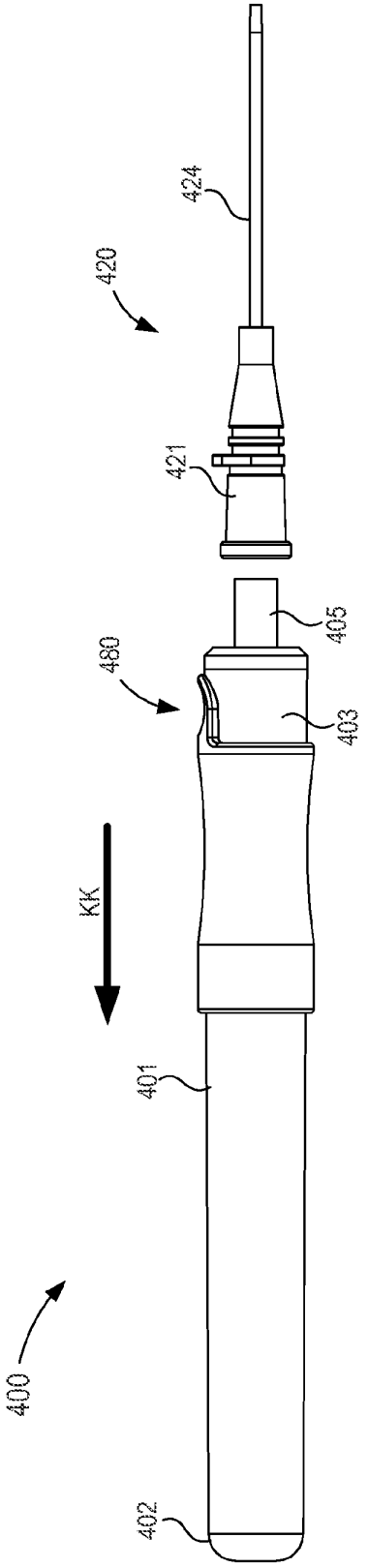


FIG. 15

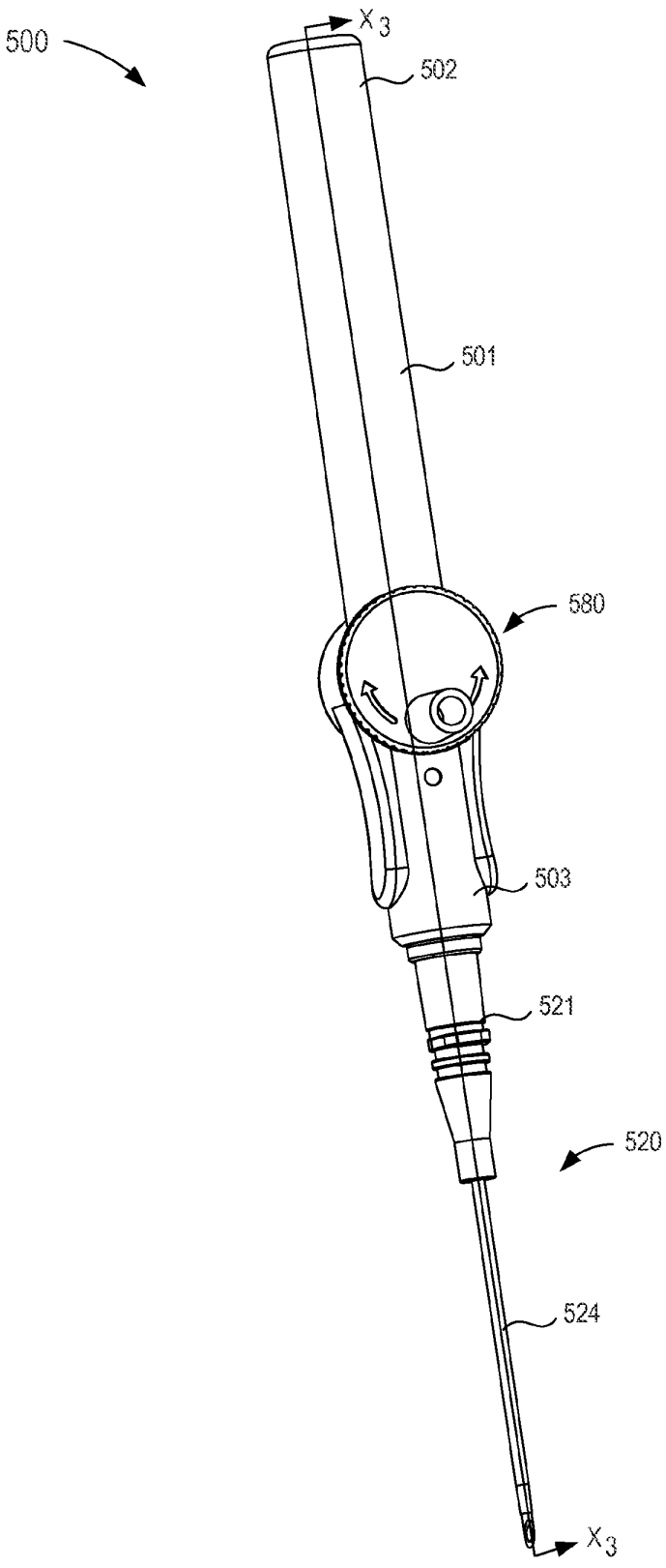


FIG. 16

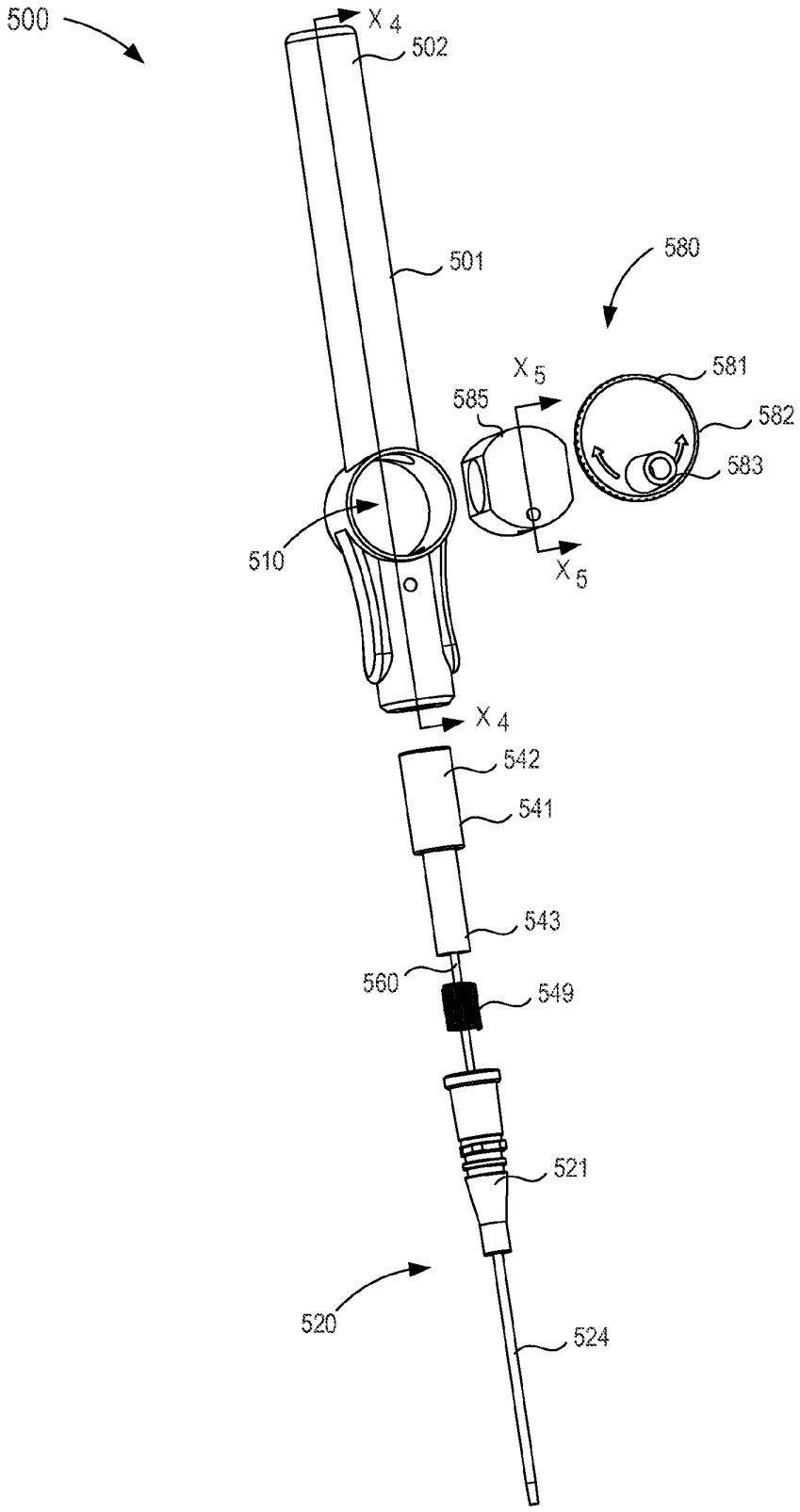

500
X 4
502
501
580
581
X 5
585
582
583
510
X 5
X 4
542
541
543
560
549
521
520
524

FIG. 17

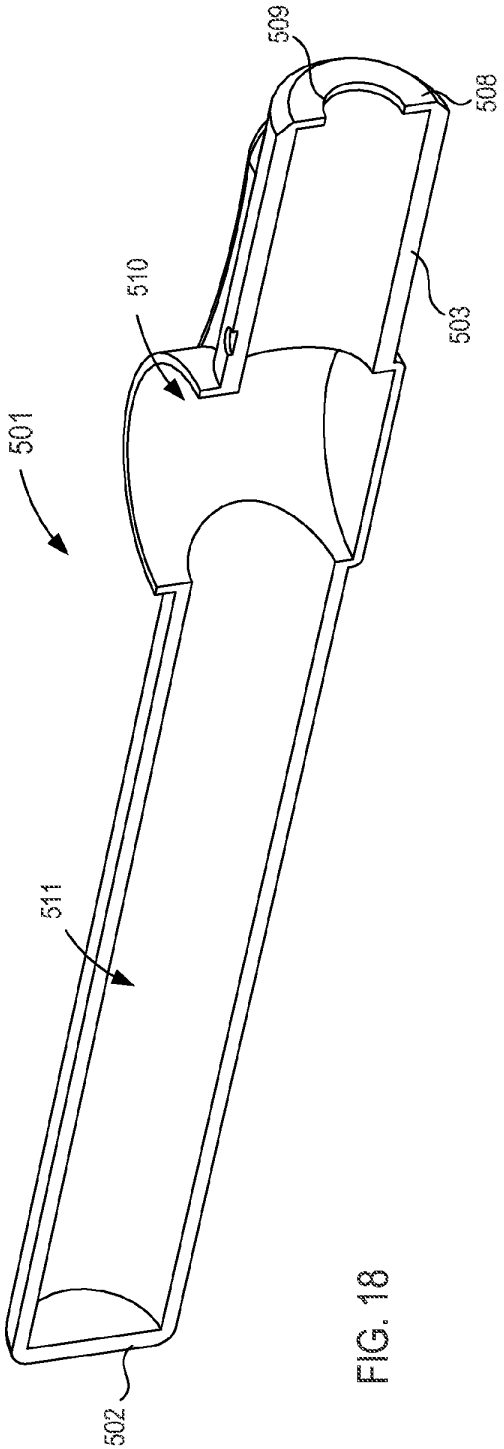


FIG. 18

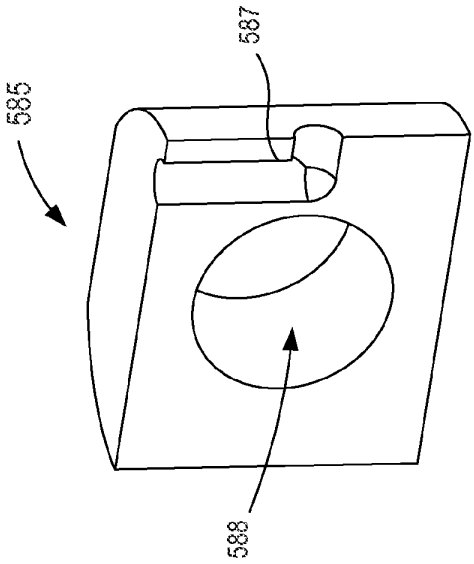


FIG. 19

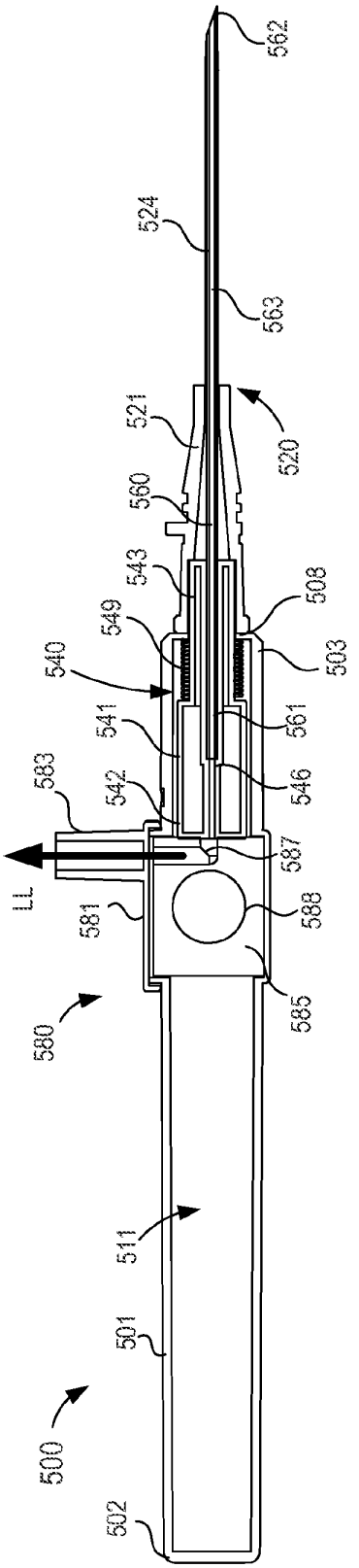

562
524
563
521
520
560
543
549
508
503
540
541
561
583
542
546
587
LL
581
588
580
585
511
501
500
502

FIG. 20

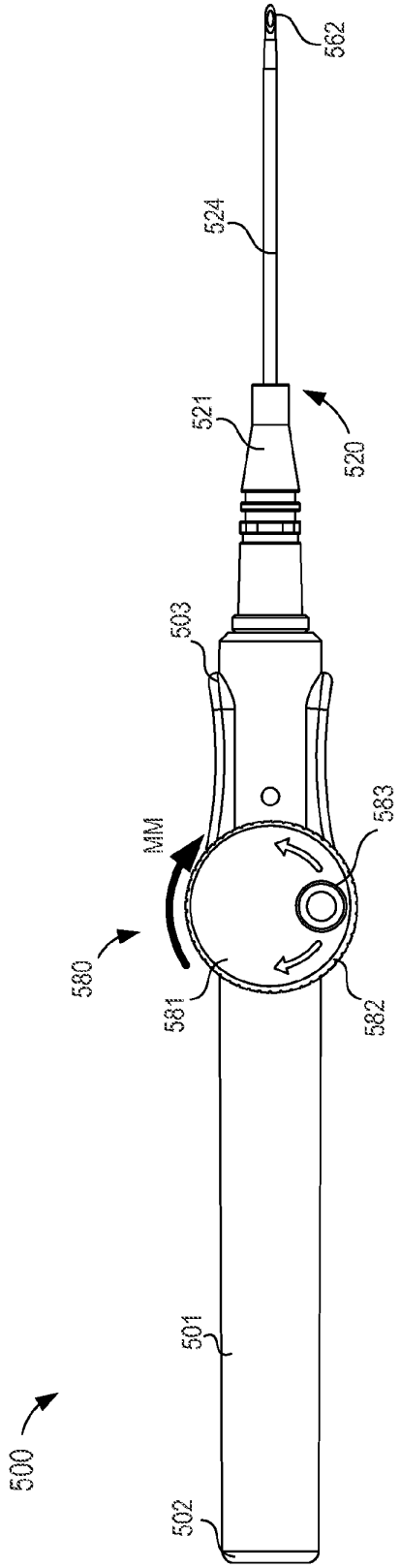

562
524
521
520
503
583
MM
580
581
582
501
500
502

FIG. 21

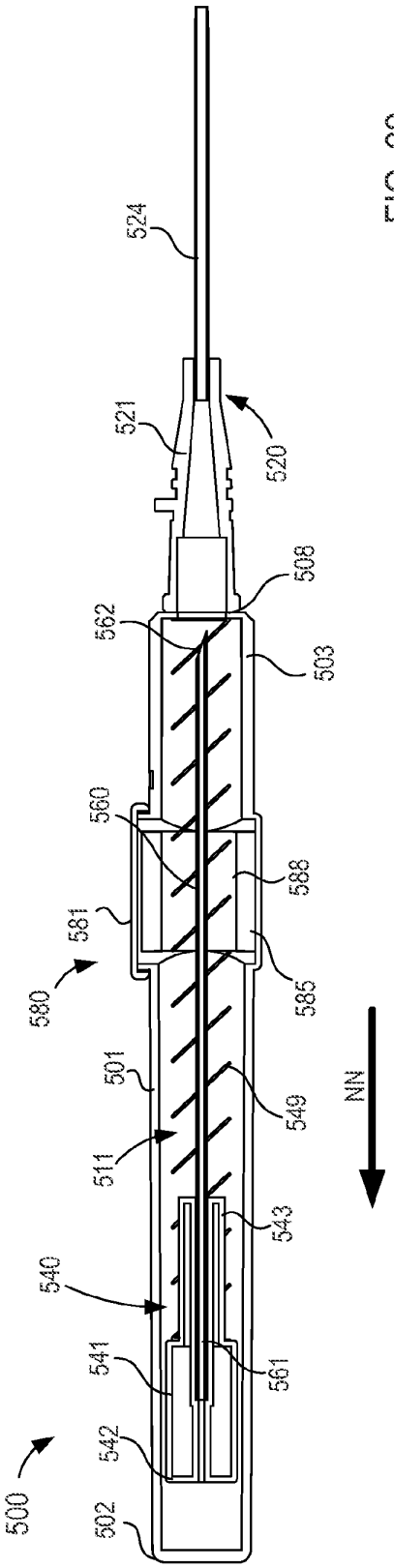

524
521
520
508
562
503
560
588
581
580
585
501
549
511
543
540
541
561
542
500
502
NN

FIG. 22

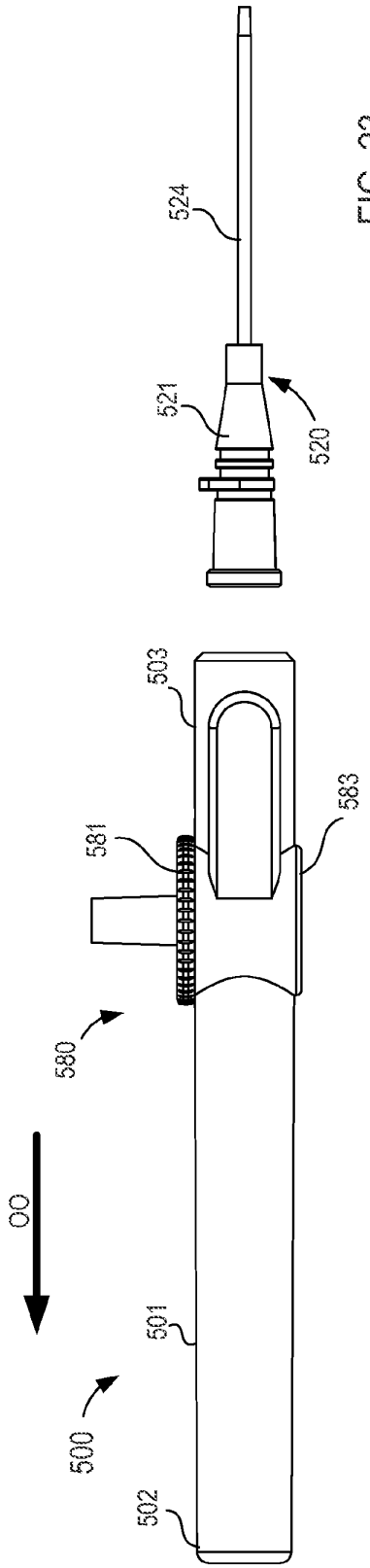

524
521
520
503
583
581
580
OO
501
500
502

FIG. 23

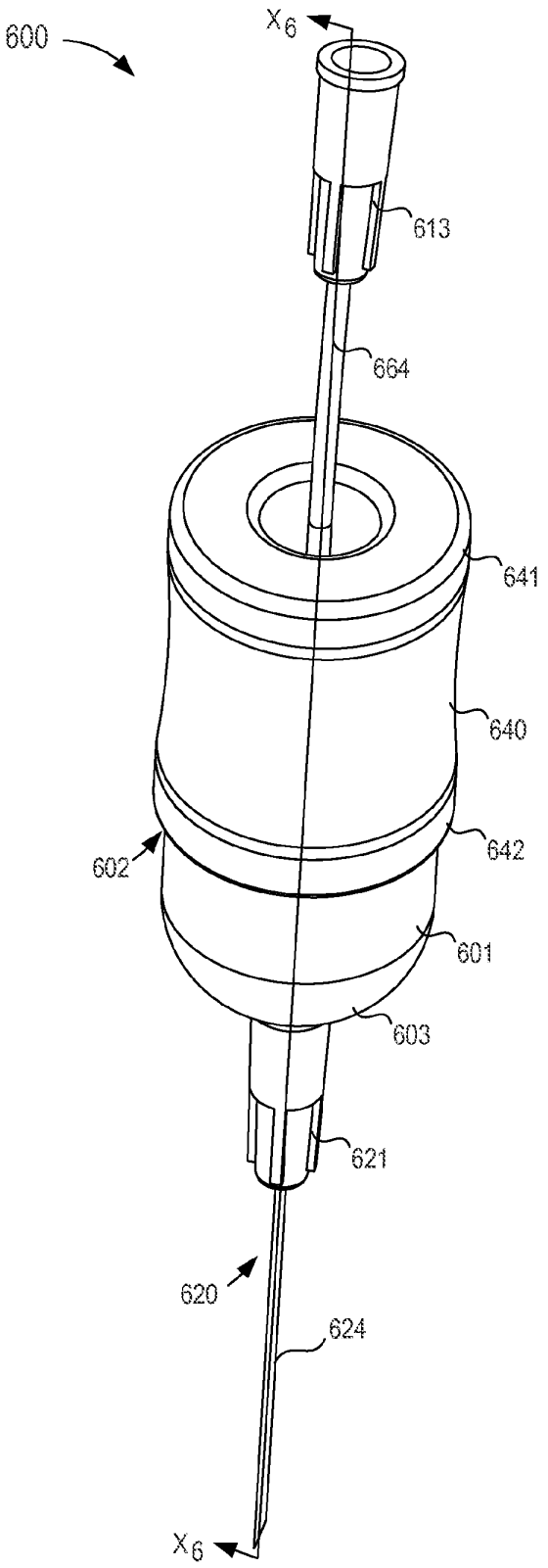


FIG. 24

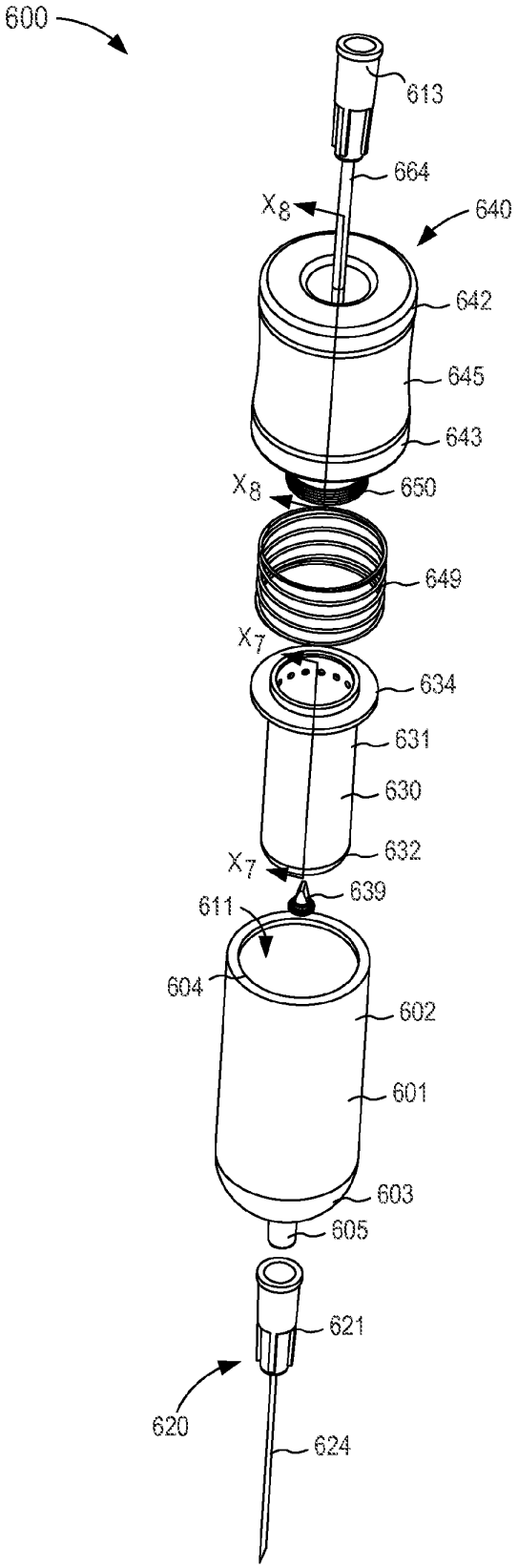

600
613
664
X8
640
642
645
643
X8
650
649
X7
634
631
630
632
X7
639
611
604
602
601
603
605
621
620
624

FIG. 25

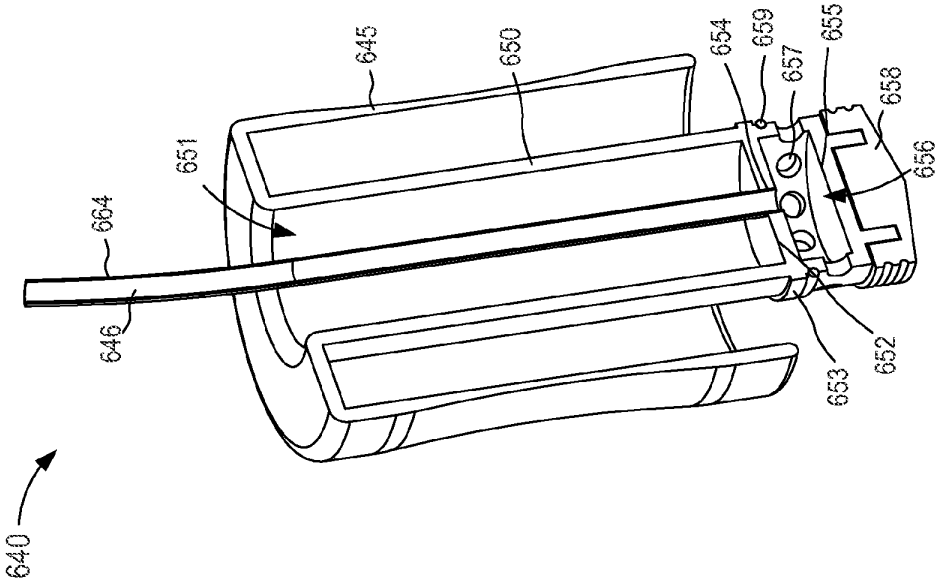

640
646
664
651
645
650
654
659
657
655
658
656
653
652

FIG. 27

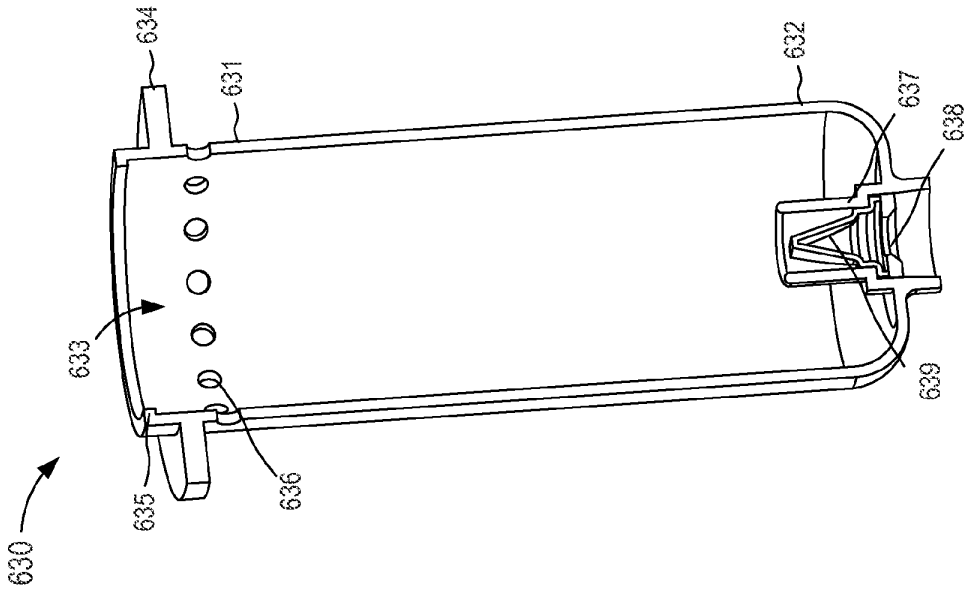

630
635
636
633
634
631
632
637
638
639

FIG. 26

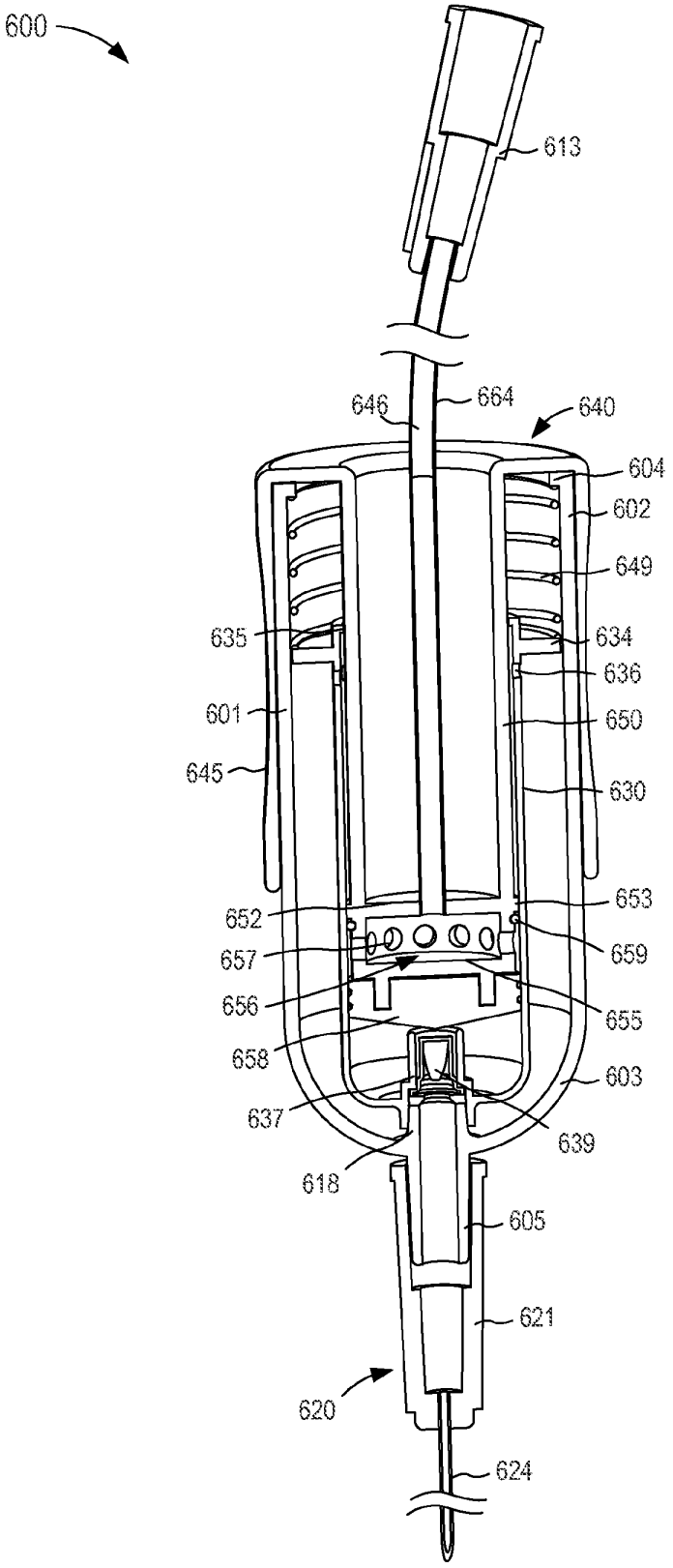

600
613
646
664
640
604
602
649
635
634
636
601
650
645
630
653
652
659
657
656
655
658
603
637
639
618
605
621
620
624

FIG. 28

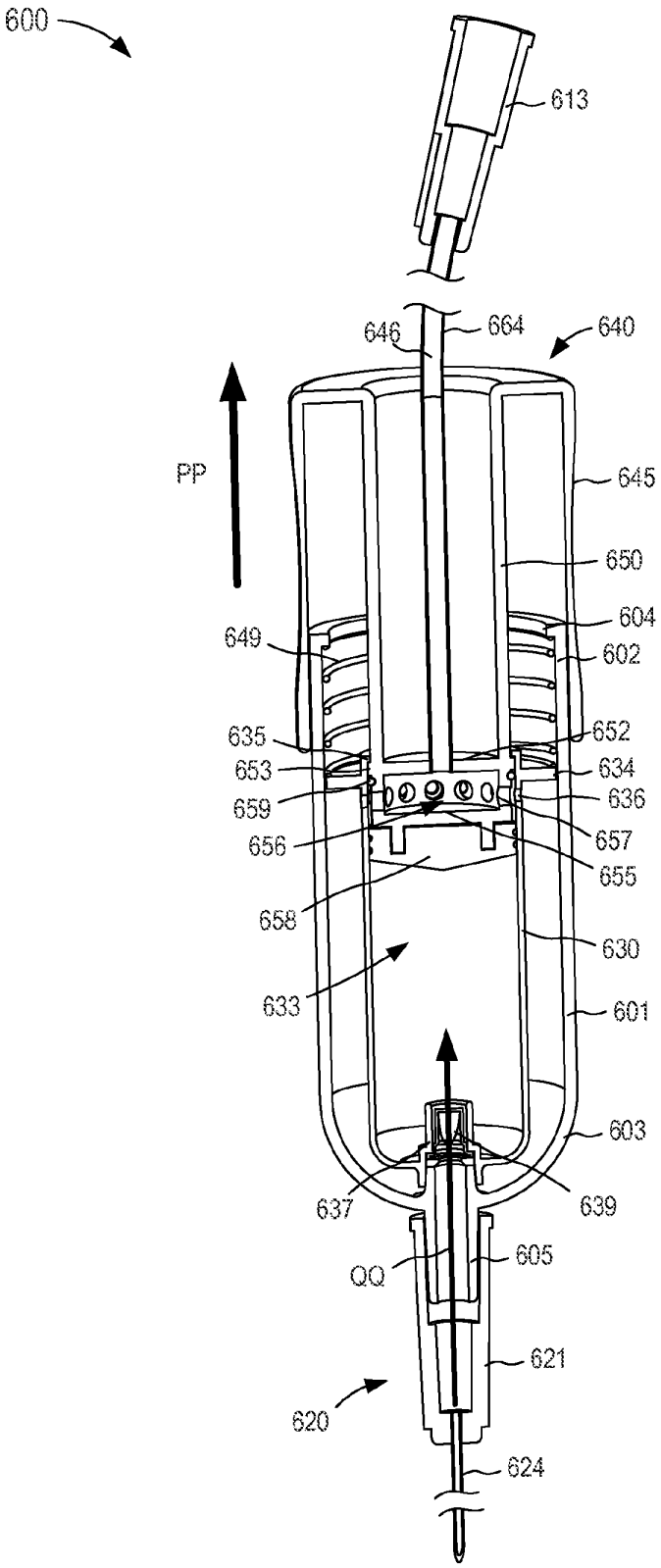

600
613
646
664
640
PP
645
650
604
649
602
635
652
653
634
659
636
656
657
655
658
630
633
601
603
637
639
QQ
605
621
620
624

FIG. 29

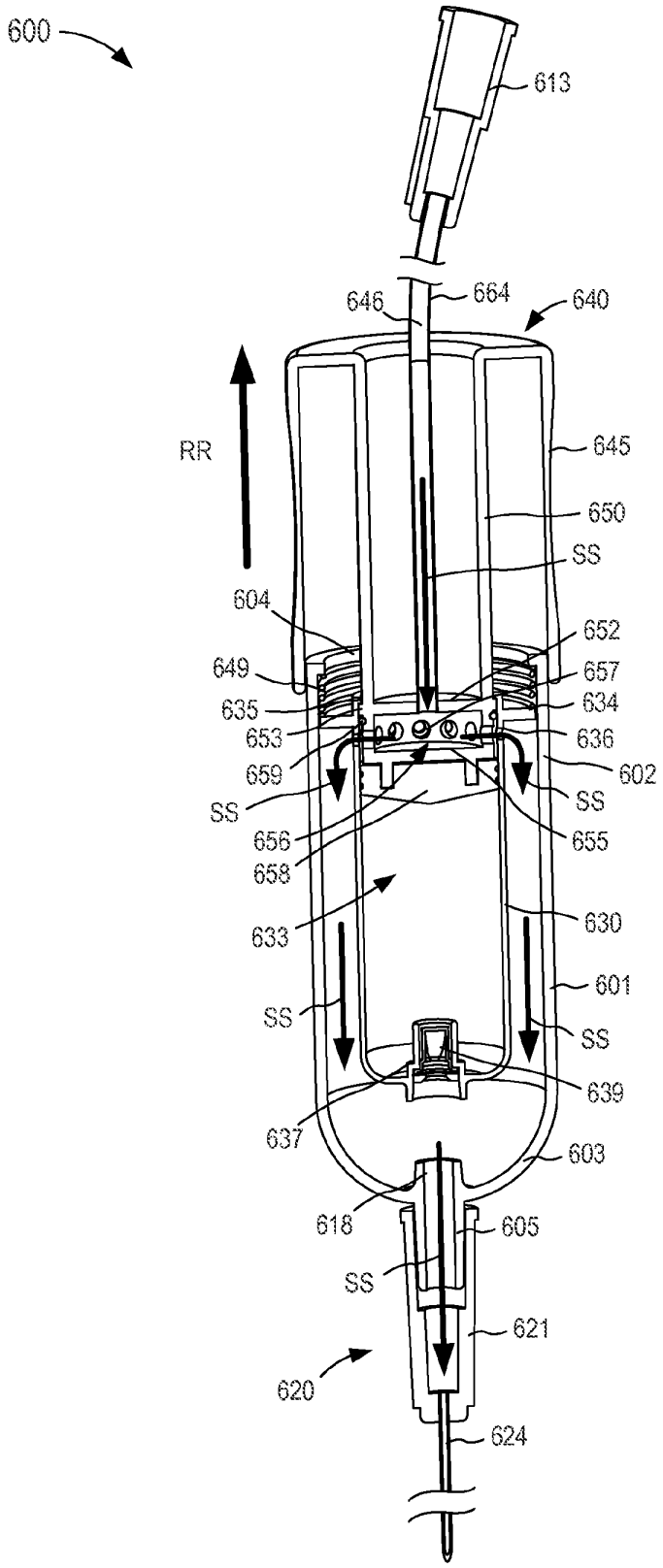

600
613
646
664
640
RR
645
650
SS
604
652
649
657
635
634
653
636
659
602
SS
SS
656
655
658
633
630
601
SS
SS
639
637
603
618
605
SS
621
620
624

FIG. 30

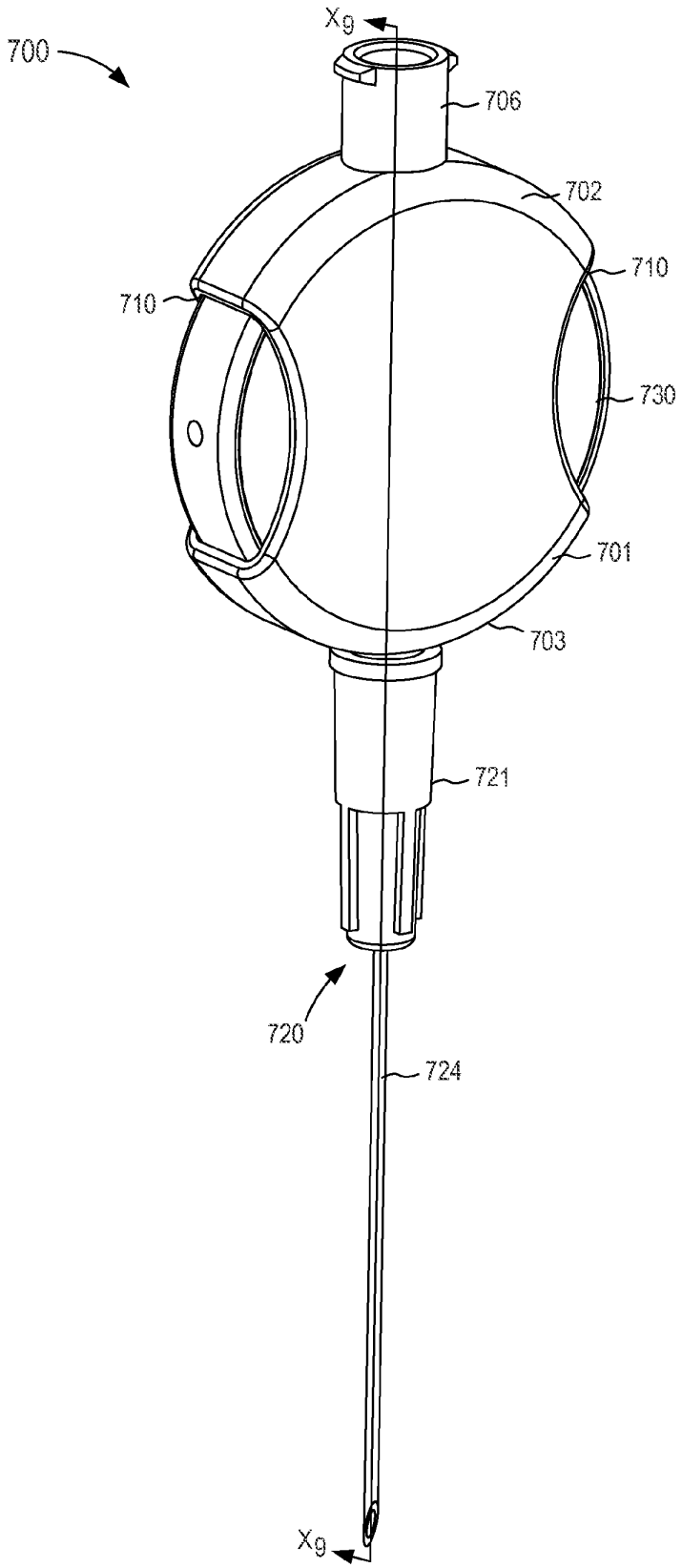


FIG. 31

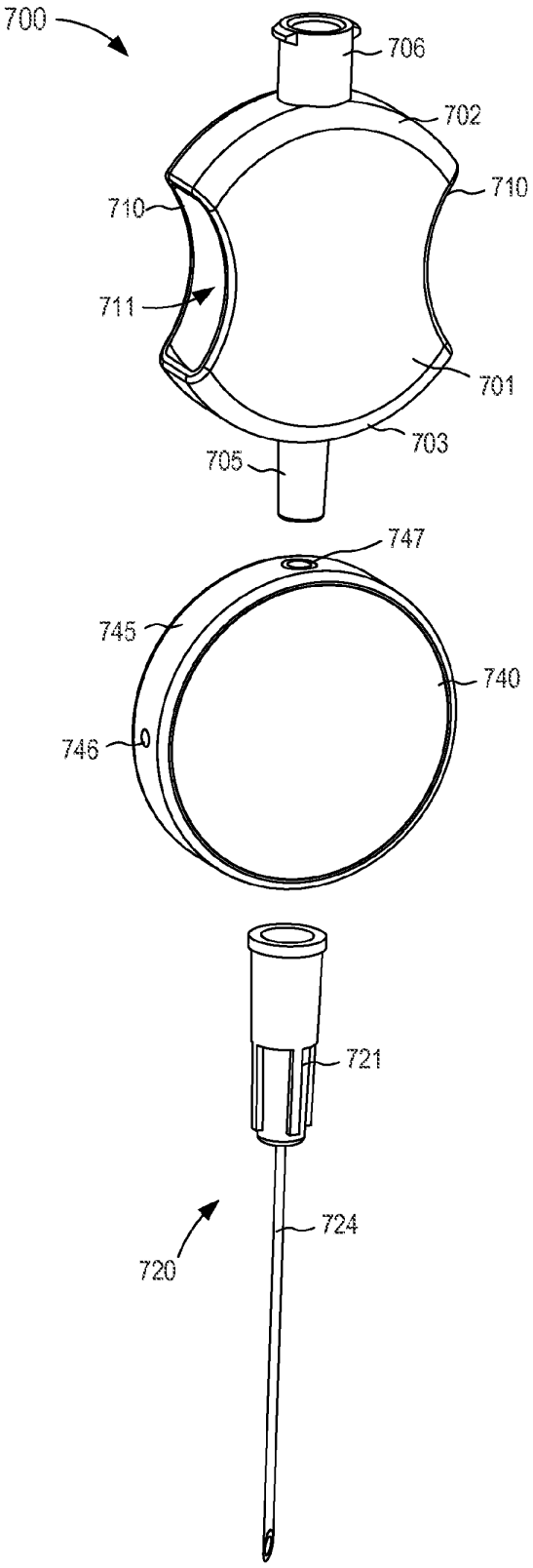


FIG. 32

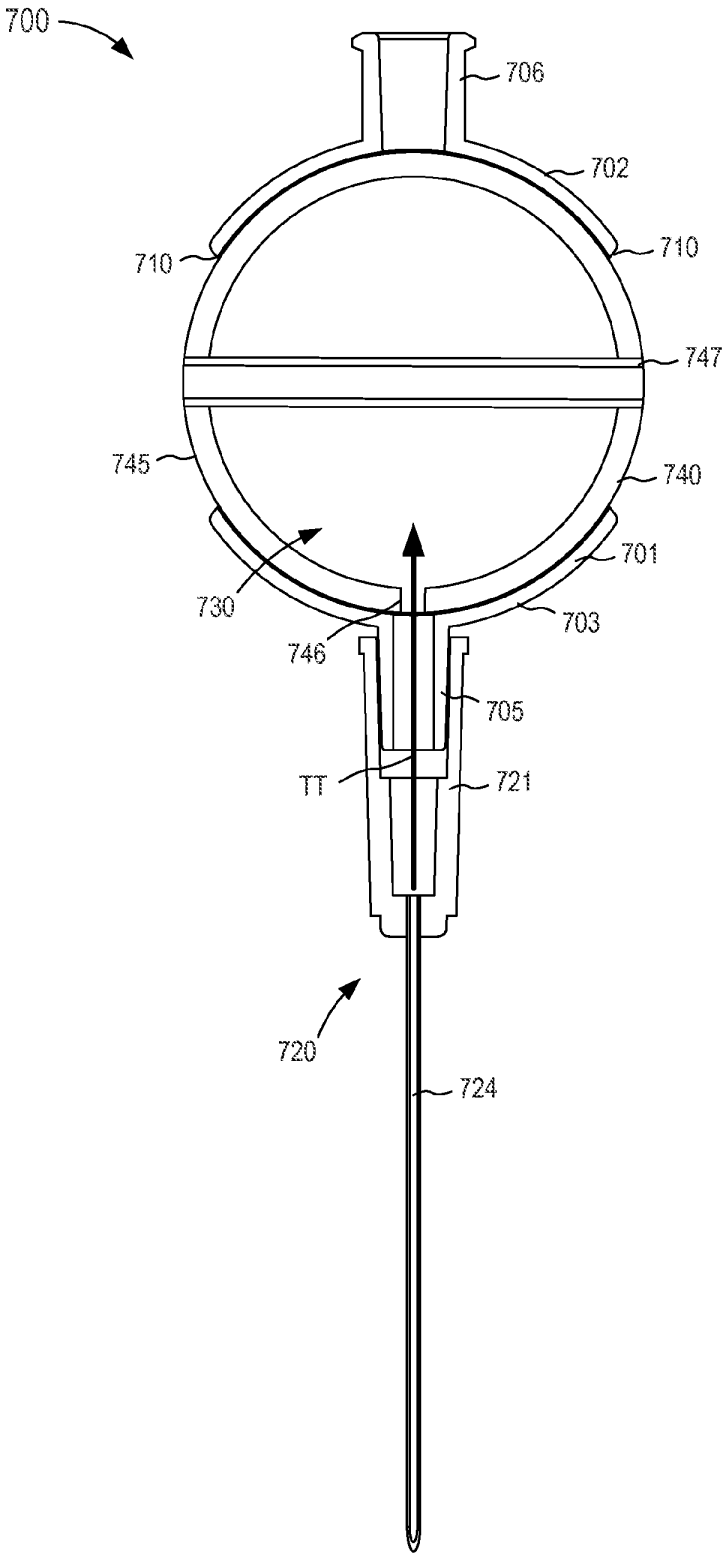

700
706
702
710
710
747
745
740
701
730
703
746
705
TT
721
720
724

FIG. 33

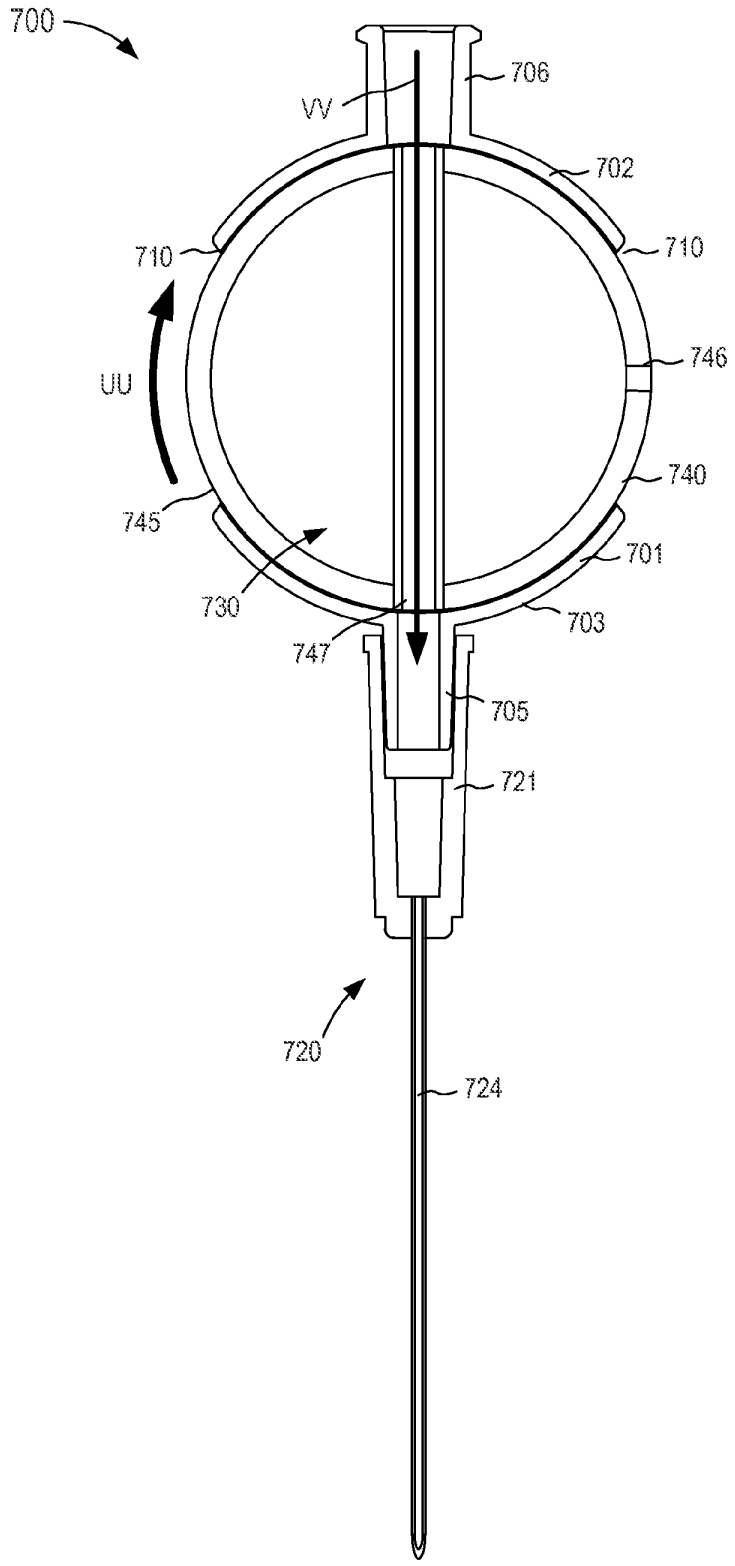

700
706
VV
702
710
710
746
UU
740
745
701
730
703
747
705
721
720
724

FIG. 34

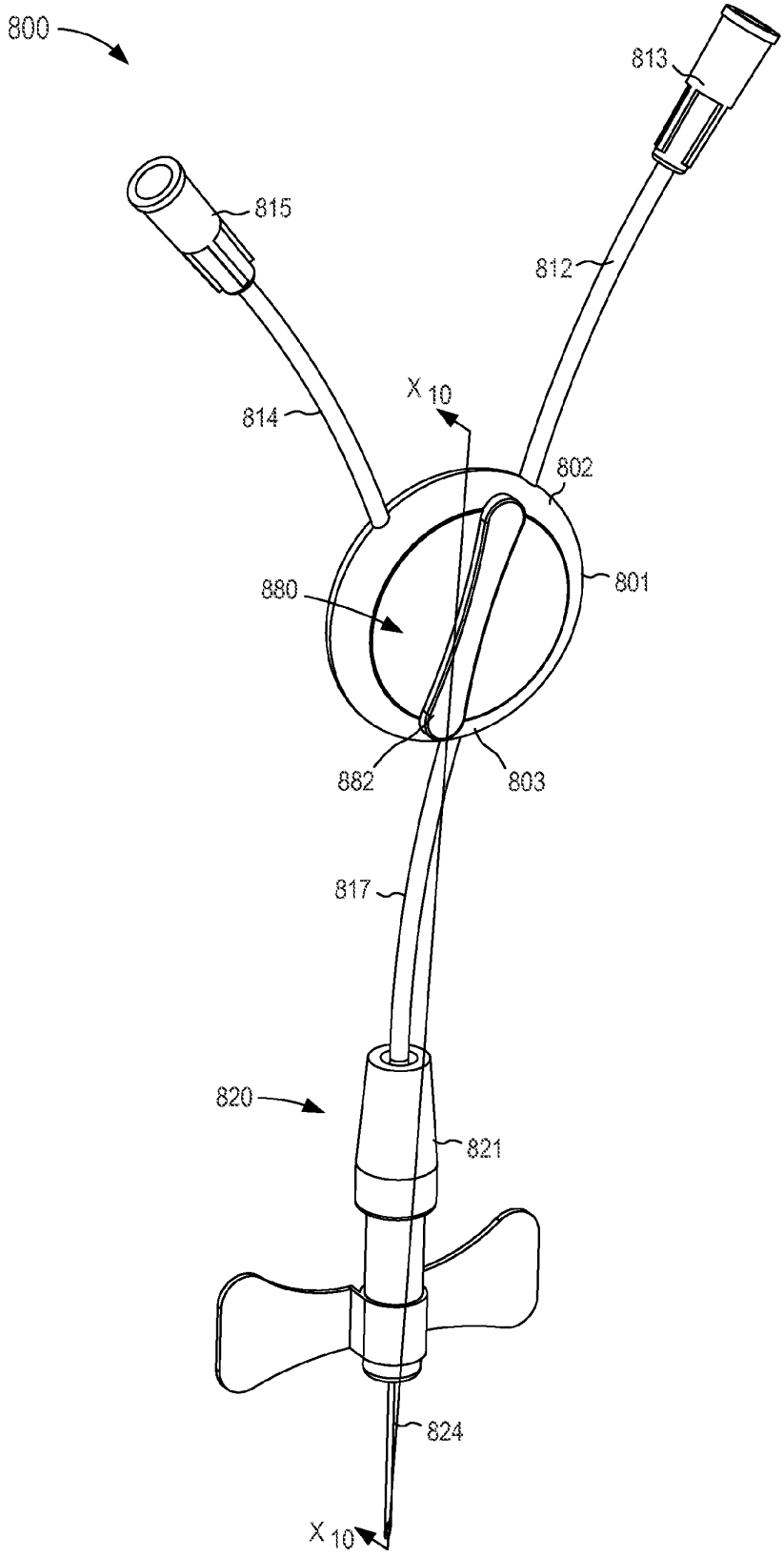


FIG. 35

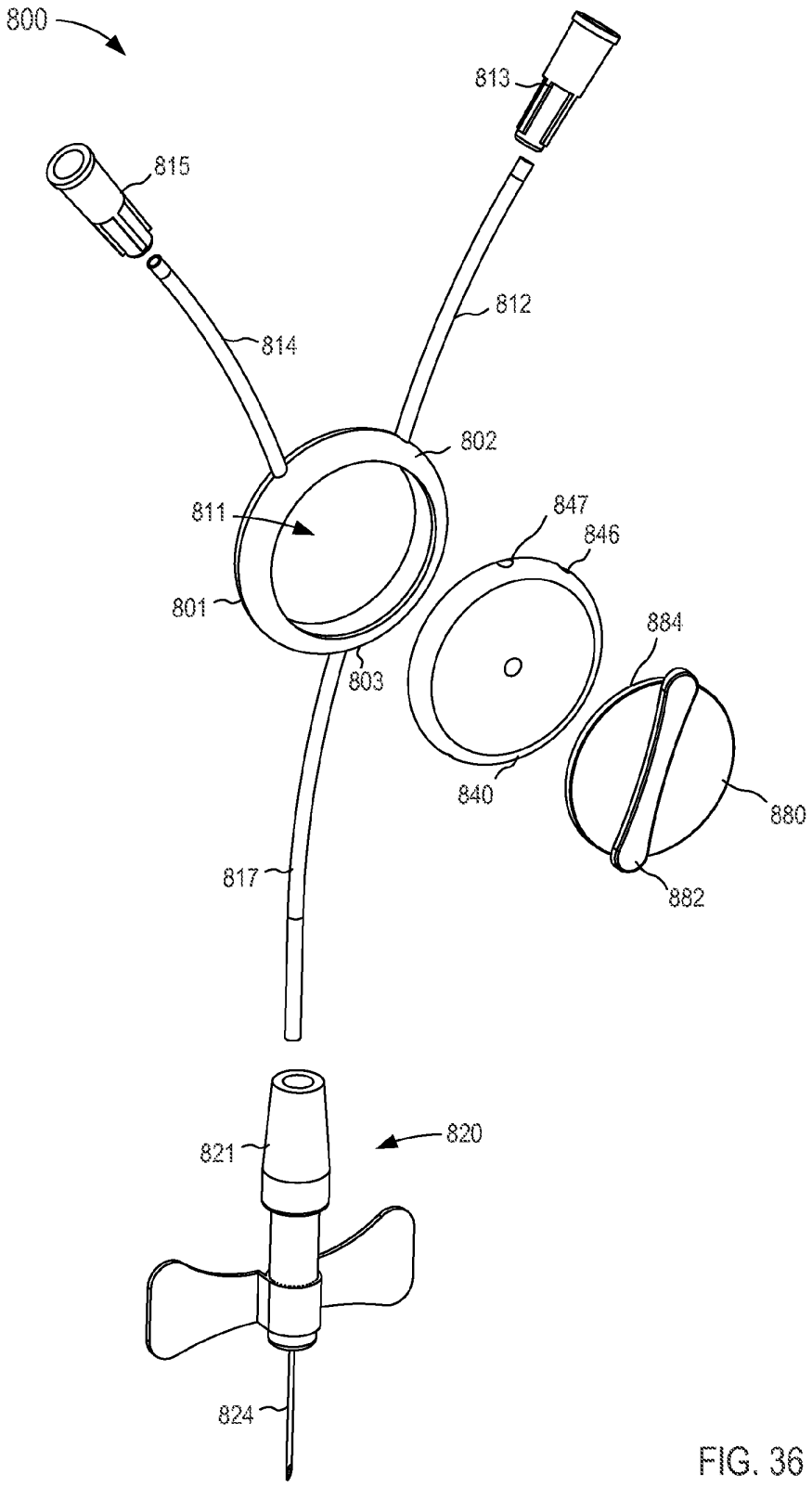

800
813
815
812
814
802
811
847
846
801
884
803
840
880
817
882
820
821
824

FIG. 36

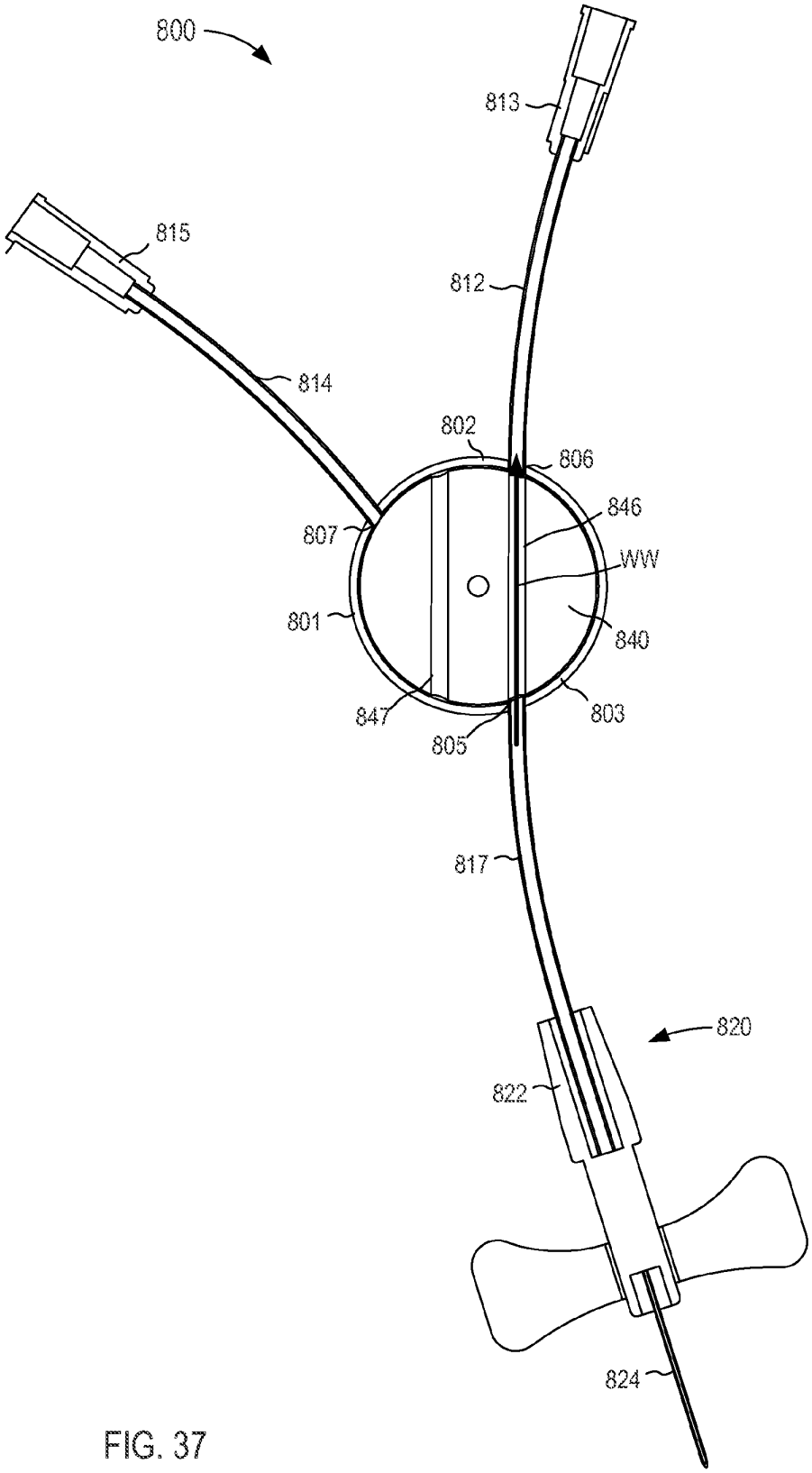

800
813
815
812
814
802
806
846
807
WW
801
840
847
803
805
817
820
822
824

FIG. 37

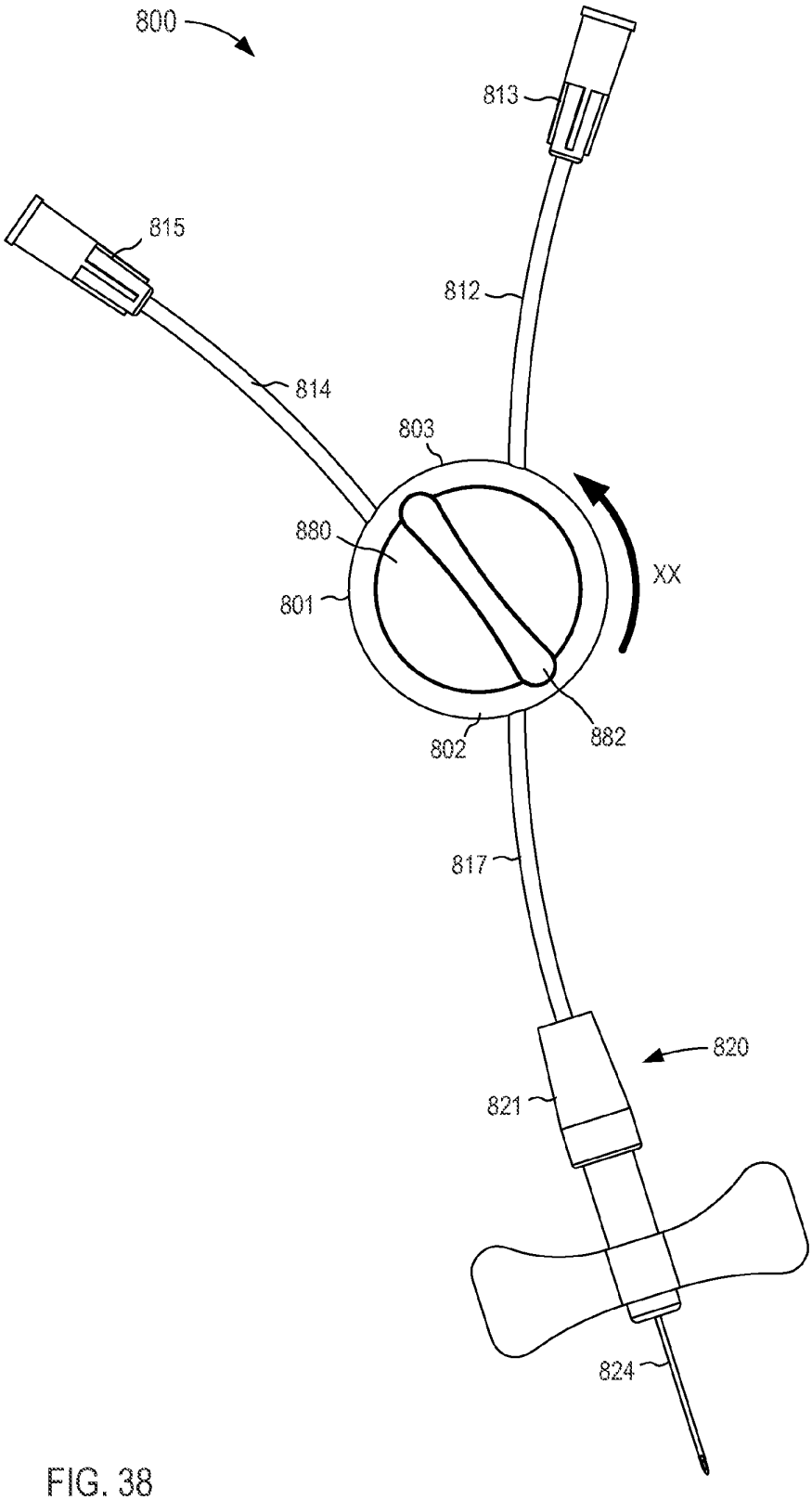


FIG. 38

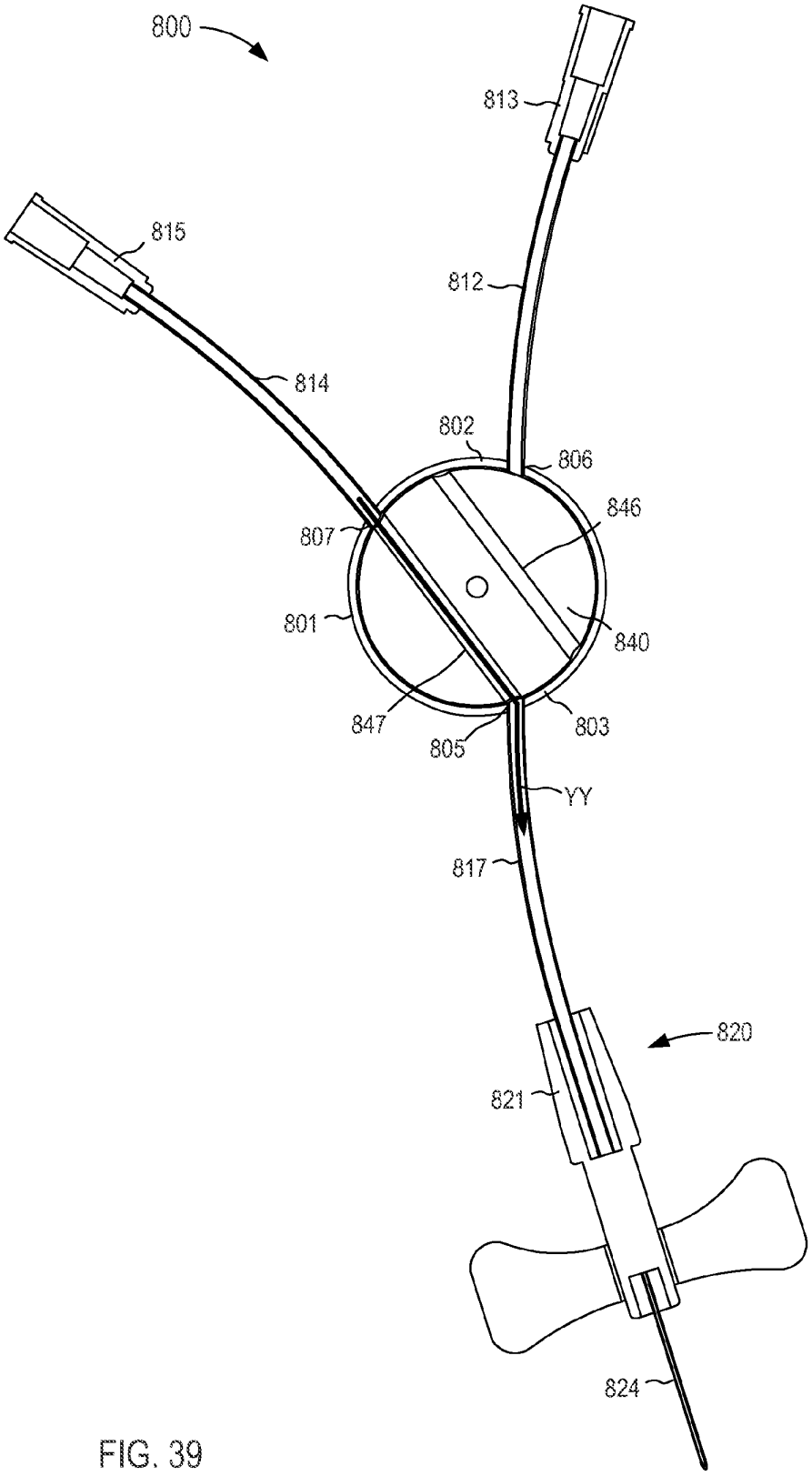

800
813
815
812
814
802
806
846
807
801
840
847
805
803
YY
817
820
821
824

FIG. 39

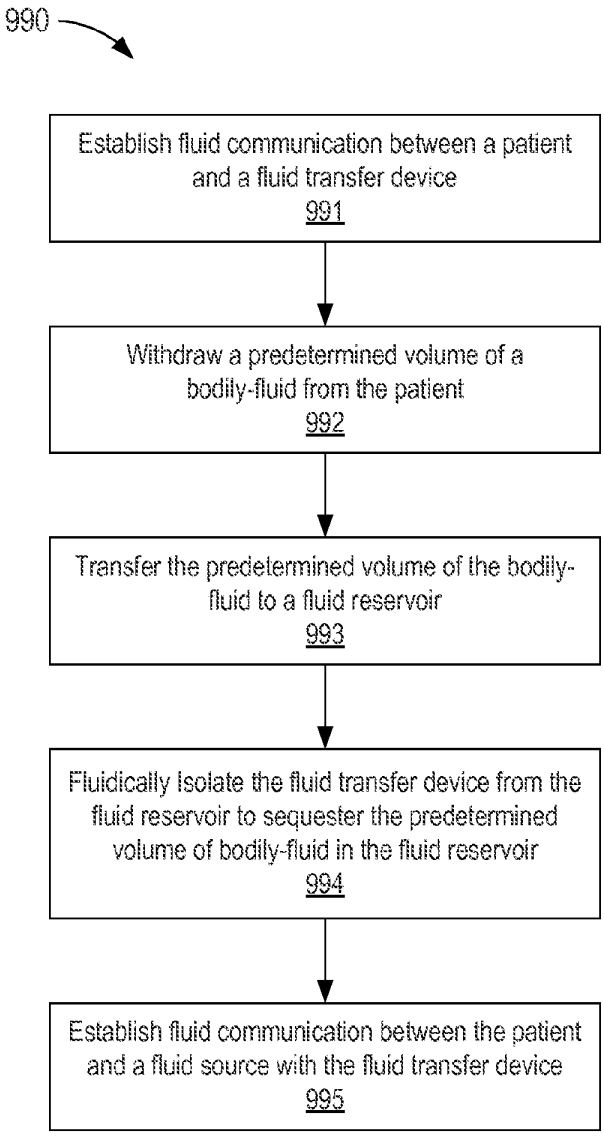

990
Establish fluid communication between a patient and a fluid transfer device
991
Withdraw a predetermined volume of a bodily-fluid from the patient
992
Transfer the predetermined volume of the bodily-fluid to a fluid reservoir
993
Fluidically isolate the fluid transfer device from the fluid reservoir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

FIG. 40

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/063975

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/155 (2014.01)
USPC - 600/575
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61B 5/15, 5/155; A61M 1/00, 5/00, 5/31, 5/32, 5/178, 5/315, 25/06; B01L 3/14 (2014.01)
USPC - 600/573, 575, 576, 577, 578, 579; 604/110, 164.01, 164.08, 191, 228, 246, 403, 411

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

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

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

Date of the actual completion of the international search	Date of mailing of the international search report
06 March 2014	20 MAR 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/063975

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

SEE CONTINUATION SHEET ATTACHED

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-34

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2013/063975

CONTINUATION OF BOX III

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-34 are drawn to an apparatus.

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

The inventions listed as Groups I - II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I, housing including a proximal end portion and a distal end portion; a fluid reservoir fluidically coupled to the housing; and a flow control mechanism, are not present in Group II; and the special technical features of Group II, establishing fluid communication between the patient and the fluid transfer device; fluidically isolating the fluid transfer device from the fluid reservoir to sequester the predetermined volume of bodily fluid in the fluid reservoir, are not present in Group I.

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

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

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

JP 2009-131273

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

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

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] JP 2009-131273 (P2009-131273A)
(43) [Published date]] June 18, 2009 (2009.6.18)
(54) [Title of Invention] Protease that activates blood coagulation factor VII
(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

(21) [Application number] Patent application 2009-57232 (P2009-57232)

(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)

(31) [Priority claim number] 19818495:6

(32) [Priority date] April 24, 1998 (1998.4.24)

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

(31) [Priority Claim number] 19851332:1

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

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

(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)

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

(71) [Applicant]

[Identification number] 597070264

[Name] T.S.L. Bering GMBH

(74) [Attorney]

[Identification number] 100127926

[Patent attorney]

[Name] Junji Yuida

(74) [Agent]

[Identification number] 100105290

[Patent attorney]

[Name] Shoji Miwa

(74) [Agent]

[Identification number] 100140132

[Patent attorney]

[Name] Noriyuki Takebayashi
(74) [Attorney]
[Identification number] 100091731
[Patent attorney]
[Name] Chika Takagi
(72) [Inventor]
[Name] Jürgen Remisch
(72) [Inventor]
[Name] Hans-Arnold Steer
(72)) [Inventor]
[Name] Annette Feusner [
Theme code (reference)] 4B063
4C084
[
F term (reference)]
4B063QA05
4B063QQ36
4B063QQ79 4B063QQ95
4B063QQ97 4B063QR16
4B063QR48
4B063QR6
7 4B063QR82 4B063QX01 4C084AA02 4C084AA07 4C084BA03 4C084BA44 4C084CA62

4C084DC14
4C084NA14
4C084ZA532
4C084ZC022

wrap up 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 i ons and/or heparin or heparin analogues, and c) in SDS-PAGE, the molecular weight is reduce d in subsequent staining under non-reducing conditions. A protease that activates blood coag ulation factor VII, which exhibits one or more bands in the range of 50-75 kDa and, under red uced conditions, one or more bands in the molecular weight range of 10-35 kDa, as well as its 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-co ntaining 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 molec ular 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 r ange 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 ob tained 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 p rotease 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) singl e- 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 ac tivator). 4. A test system according to any one of claims 1 to 3, which contains calcium ions i n an amount of 0.001 mM or more. 5. a) inhibited by the presence of aprotinin, b) its activi ty increased by calcium ions and/or heparin or heparin sulfate, c) in SDS-PAGE with a molec ular 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: LLESLDP a nd IYGGFKSTAGK and a suitable proenzyme activator is used to test for prothrombin time-dis placed 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 i n SDS-PAGE has the amino acid sequence: LLESLDP, the band obtained in the range of molec ular 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 ra nge 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 i s

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 protea se. . BACKGROUND

OF THE INVENTION The blood coagulation system consists of two different cascade-like path ways that activate blood coagulation factors present in plasma. Depending on the induction m echanism, the intrinsic or extrinsic pathway is preferentially used to initiate blood coagulation. [0003] When tissues are injured, thromboplastin (tissue factor, TF and phospholipids) is exp osed by the affected cells as starters of the extrinsic coagulation pathway. Membrane-localize d thromboplastin can bind both blood coagulation factor VII (FVII) and circulating, activated F VII (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 wou nd closure. [0004] Further activation of thromboplastin-binding FVII occurs initially by autoc atalytic reactions, but especially after initiation of the coagulation cascade it is supported by F Xa and thrombin, leading to a marked enhancement of the reaction cascade among others. [0 005]

Administration of FVIIa or FVIIa-containing concentrates has been indicated for certain clinic al 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 kno wn findings, FVIIa is well tolerated in this relationship, it does not produce thrombotic tendenc ies, and is sufficient to ensure that a limited but adequate degree of clotting occurs. Are suita ble. 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 acti vation, however, these proteases themselves are capable of strongly activating blood clots an d 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 us e of FXa or FIIa (thrombin) is often contraindicated and indicated only in emergencies, eg in c onnection 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 thromboplasti n expressed or released with cell destruction may play a role in this association. Factor XIIa, f or example, is known to cause activation of FVII under certain conditions, but the physiologica l relevance of this response has not yet been clarified.
[0007]
Surprisingly, a FVII-activating protease, distinct from all previously known proteases, has no w 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 am idolytic activity towards the peptide substrate S2288 (HD-isoleucyl-L-prolyl-L-arginine-pNA) fr om 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 com plex 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. Fi nally, it was found that this protease is capable of converting FVII to FVIIa in a time- and conc entration-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 fracti onation of plasma or prothrombin complex (PPSB) concentrates. can be done. The starting ma terial is then first subjected to anion exchange chromatography, followed by affinity chromato graphy 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 mattrex. A heparin-lysine matrix has been found to be particularly suit able for the isolation of novel proteases.

[0013]

In SDS-PAGE followed by staining, the proteases isolated by this method show one to severa l closely spaced bands in the molecular weight range of 55-75 kDa under non-reducing conditi ons. 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 sho wn to constitute 5-10% of the total protein after scanning and quantitative evaluation, and th at non-activated proenzyme was also present. This result was supported by a suitable study u sing 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 meth od of the invention. Part of the subject matter of the present invention is therefore the proenz ymes of proteases that activate blood coagulation factor VII. The proportion of proenzyme is i ndicated by the 60-65 kDa band. Examples of suitable physiological activators of proenzymes correspond to amino acid sequences constituting the activation region of proenzymes, thrombi n, 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 plasm a-derived prothrombin complex (PPSB) concentrates, inhibition of its amidolytic activity by ap rotinin and reduction and non-

reduction

The migration behavior described above in SDS-PAGE under both reducing conditions has bee n 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 t hat case, preparation was primarily accomplished using an aprotinin matrix. The activity has b een described as a thrombin-like activity as a result of the amidolytic cleavage of certain pepti de substrates. Hunfeld et al. found no effect on global coagulation parameters such as prothro mbin time, quick or platelet aggregation.

[0015]

N-terminal sequencing of the protease described by Hunfeld et al. shows that its cDNA is con sistent with that of the protein reported by Choi-Miura et al. (J. Biochem. 119:1157-1165, 19 96). 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-PAG E under reducing conditions were subjected to N-terminal sequencing and the following identit ies 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 hav e 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 no vel 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 FV II-containing solution and the FVIIa produced is quantified after an appropriate incubation tim e. This is for example Staclot(R) It can be performed using the FVIIa-rTF test (Stago/Boehring er Mannheim). Using the preferred procedure, this test is not limited to the concentration of F VII supplied. If the amount of protease in the form of a ratio of total protein is known, the rati o is: -

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

- can be determined using, for example, specific antibody-based antigen tests and suitable i mmunochemical 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/VIII a and V/Va followed by quantification reveals that the blood coagulation factors are inactivate d 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 fac tor VII, in which proteases are blood It can be quantified by its activity to inactivate coagulati on factor VIII/VIIIa or V/Va. This test system involves incubating a solution containing a prote ase with Factor VIII/VIIIa or Factor V/Va and determining the amount of residual Factor VIII/V IIIa or the amount of residual Factor V/Va by a conventional activity test. It is based on meas uring and then determining from this the amount of protease by comparison with a standard c urve. In carrying out this test, the incubation of the protease activity is inhibited by the additi on of limited amounts of aprotinin for a predetermined period of time, which has the advantag e that these concentrations do not affect the subsequent measurements of the test system. T he 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 conversi on of a chromogenic substrate in the presence of a thrombin inhibitor, is used In terms of en abling (see description in [0007]), especially test systems have proven their worth. On the ot her hand, this amount is proportional to the amount of FVII or FVIIa. Determining the residua l 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 demonstrat ed by SDS-PAGE. Depending on how long the protease was incubated with, for example, the F VIII concentrate, the bands typical of FVIII disappear, while other new bands develop or the i ntensity of weaker bands increases. Thus, protease activity can also be correlated by quantifyi ng 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 chan ges in band intensities by other electrophoretic methods, can be quantified using, for exampl e, a scanner and appropriate programs well known to those skilled in the art. Additionally, anti bodies 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 at tenuated bands or specifically developed bands are particularly suitable. In this connection, th ese 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 i ncubated with Factor V/Va, which exhibits some degree of structural homology with FVIII. De gradation 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 plas ma or plasma at this time shortens the blood clotting time, i. It was found to exhibit gulent ac tivity. These test systems are understood to be, for example, non-activated partial thrombopla stin 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 c hromogenic 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 calibratio n curve for blood clotting time. Concentrations of "FVII activators" can also be determined usi ng selected comprehensive coagulation tests.

"

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

It has also been surprisingly found that it can provide an effective activator of plasminogen ac tivator), ie 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 detec tion and quantification of "FVII activators". Activation of plasminogen activators can also be d etermined in coupling reactions in the presence of plasminogen, either by formation of plasmi n 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 th e amount of Fv/Fva remaining can then be quantified. An unknown protease concentration ca n 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 sui table for quantification, and protease concentrations are read from calibration curves based o n reduction of clotting times. The PAA activity of proteases can also be used for quantitation p urposes. A feature of these tests is that $CaCl_2$ is added to high concentrations of calcium, preferably >0.001 mM, particularly preferably >0.005 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 inactivat ion 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 presenc e 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 pr otease inhibitor such as guanidinocaproic acid-p-ethoxycarbonylphenyl ester available under t he 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. Red uction 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 blo od coagulation factors V and VIII, the problem of inhibiting the protease activity or attenuatin g its activity is due to the loss of production and the formation of fragments which are presum ably fragments of interfering proteins. occur to avoid All this is all the more important since F V 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 p art 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 Fa ctor VII are inhibited

.

is a stabilized preparation of free FV or FVIII. Further investigation revealed that the inactivati on 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 inhibitio n of proteases that activate blood coagulation factor VII. Adjusting the concentration of calciu m 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 pr otease is significantly reduced at these concentrations, the amount of calcium ions is still suffi cient 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 cryopre cipitate 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 o ther 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, α2-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, sucPA, single-chain urokinase plasminogen activator) or sctPA (single-chain tissue plasminogen activator) results in the activation of these positive 'factor VII activators'. Resulting in activation of the minogen 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 activa

tion. The plasmin produced is the effector of fibrinolysis, the physiological system involved in t he dissolution of thrombi. PA, such as pro-urokinase or tPA, is an endogenous protein that is r eleased on demand and, as is known, activated by plasmin or kallikrein (scuPA). The mechani sm 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 pharmaceu tical preparations associated with thrombotic diseases or complications such as femoral vein t hrombosis, 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 viv o or ex vivo activation of plasminogen activators such as urokinase or sctPA. This activity also applies to the use of this protease, particularly in combination with single- or double-chain pla sminogen activators or anticoagulants, as well for the prevention or treatment of thromboemb olic disease. This potential use is consistent with the fact that proteases can also act in a proc oagulant fashion. The question of which of the two responses takes precedence is presumably resolved by the availability of physiological substances. According to current knowledge, facto r 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 plasm inogen activator as well as urokinase plasminogen activator are present in only nanogram qua ntities in 1 ml of plasma. Its concentration is elevated by secretion or synthesis of plasminoge n activators only when fibrin deposition or thrombi occur, which are then activated locally, esp ecially when they bind to thrombi, and then Activating plasminogen to exert their thrombolyti c action. When single-chain PAs are present, their activation exceeds that of FVII, especially i n a locally restricted manner, thereby allowing regulation to physiological conditions. Therefor e, this protease also modulates hemostasis, thereby potentially applying to replacement by pr oteases 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 pre paration 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 pha rmaceutical formulations described above.

[0039]

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

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 ca rrier material or as a mediator to the surface together with a material that increases its activit y.

[0040]

Pharmaceutical preparations consisting of blood coagulation factor VII-activating protease ca n be used for the treatment of diseases caused by fibrin-containing thrombi due to their specif ic fibrinolytic action. The fibrinolytic process is also involved in the wound healing process. In t his connection, the proteases and/or proenzymes can be administered intravenously or topical ly, subcutaneously, intradermally or intramuscularly or topically in the case of injuries or woun ds or bound to a suitable carrier matrix. . Both proteases/proenzymes isolated from body fluid s such as blood or plasma and recombinantly or transgenically prepared proteases/proenzyme s can be used in this context. The protease/proenzyme is also suitable as a component of so-c alled fibrin glues, which must not contain substances that inhibit the protease/proenzyme, suc h as aprotinin. In this case, the clot-shortening action of proteases is utilized. The above pro teases/proenzymes can be used for congenital or acquired hemostatic defects, (generalized) b leeding 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 o nly be used as a pharmaceutical preparation if it has been previously subjected to virus-inacti vating treatment. can do. The sterilization process is recognized as the most important proces s, especially for virus inactivation. However, the proteins to be processed require adequate sta bility to heating at about 60° C. for up to 10 hours. Optimal stabilizers must be determined se parately for each protein and their concentrations optimized.

In the case of novel proteases and/or their proenzymes, the conditions for stabilizing protein s in non-sterilized solutions have already been described above. A slightly acidic pH has prove n to be particularly advantageous in this case. However, novel proteases and/or their proenzy mes typically lose 50% or more of their original activity upon sterilization under these conditio ns. 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 combinatio n 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 cap able 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. A dditives such as albumin, Haemaccel® ′ heparin and heparinoids, glycerol , glycols and polyet hylene glycols can be used separately or mixed together. After sterilization is complete, sugar s, 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 s terilization 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 th at preformed activated FVII (FVIIa) can only be used to inhibit the extrinsic coagulation pathw ay.

It is based on (recombinant) soluble tissue factor (rTF). This allows the actual content of FVII a 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 FVI Ia 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 t emperature and then tested for true FVIIa content. FVIIa content was quantified using a stan dard 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 ef fect 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 abov

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 u sed to demonstrate that FVIIa itself was not inhibited nor was the test affected by the aprotini n 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 FV IIa-rTF assay. Thus, subtracting the basal value of FVIIa (assay 1), 8 mIU/ml of FVIIa was for med 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 sub sequent incubation with FVII nor subsequent quantification of FVIIa resulted in a significant in crease in FVIIa content (the range of variation in the assay, ie 11 and 10 mIU/ml in assay 1, i s 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 r TF;

- 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 in dependent 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 roo m temperature) with protease-containing solutions at various dilutions (1:5, 1:10 and 1:20), f ollowed 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 b efore 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, incub ation, + aprotinin Control: protease + aprotinin, incubation + FVII

[Table 1]

プロテアーゼ溶液の希釈度	活性化係数	
	アッセイ	対 照
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-depe ndent manner. It was also demonstrated that FVII was activated by proteases in a manner t hat 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 solut ion were incubated together, aprotinin was added (to stop activation) after a corresponding pe riod of incubation, followed by: of FVIIa content was obtained.

[Table 2]

インキュベーションの長さ	活性化係数
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. Ex ample 3 This example will be used to demonstrate that protease activation of FVII is enhanc

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 $CaCl_2$
- 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]

アッセイ	活性化係数（緩衝液対照に対する倍数x）
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 CaCl 2 (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 s tandard 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 m in), but the protease concentration was varied (0.1, 1 and 10 µg/ml). The reaction was stoppe d and the residual concentration of active FVIII was determined. Increasing protease concentr ations 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 I U/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 $CaCl_2$ (0-20 min), then 400 µl of buffer containing 100 KIU/ml aprotinin was add ed. .

In both cases, 100 µl of each incubation assay was then incubated with 100 µl of FV-deficien t plasma for 1 minute at 37° C., then 200 µl of Thromborel S® were added, mixed and clottin g 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)	FVの残留活性 プロテアーゼとFVのインキュベート時間(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. NAPTT (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 $CaCl_2$ 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]

	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）				
サンプル番号	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 CaCl 2 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）				
	プロテアーゼ濃度（μg／ml）				
サンプル番号	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 μg/ml . 100 μl of each of these solutions are incubated with 100 μl of citrated plasma (either from standard pla sma pools or from individual donors) at 37° C. for 1 minute, then 200 μl of Thromborel S® (D ade Behring GmbH) are added, followed by blood clotting . time was measured.

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

[Table 7]

	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）				
サンプル番号	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 $CaCl_2$

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 in cubation, and so on through each case. On the other hand, PA was not added thereafter until i t was added instead of aprotinin.

The difference in measurements (Δ) $\Delta OD_{405\ nm}$ was measured optically. The control values obtained were subtracted from the sample/protease values and in this way the PA activity pro duced 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（ΔｍＩＵ／分） FVIIアクティベーター（μg／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（ΔｍＩＵ／分） FVIIアクティベーター（μg／ml）		
	2	5	10
2	190	332	425
5	330	455	458
10	417	462	460

C．刺激物質：$CaCl_2$

インキュベーション時間（分）	得られたＰＡ活性（ΔｍＩＵ／分） FVIIアクティベーター（μg／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 µg/ml sctPA, 50-200 µg/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.

インキュベーション時間（分）	得られたＰＡ活性（ΔｍＩＵ／分） ＦＶＩＩアクティベーター(200μg／ml)
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）

ＦＶＩＩアクティベーター（μg／ml）	ＰＡ活性(ΔmIU／分)
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℃）

刺激物質	ＰＡ活性(ΔmIU／分)
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 µl of a solution containing 0.1 IU/ml of FVIII were treated with an equ

al volume of protease solution (μg/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 o f the protease. Preliminary experiments have shown that this concentration of aprotinin has n o significant interfering effect on the FVIII activity test (assays 1+3) described below. In Assa y 2, the protease was incubated with aprotinin prior to contact with FVIII and then manipulate d as described above.

In each case 50 μl of the stopped sample (or after further dilution) were then treated with s o-called factor reagents, consisting mainly of FIX, FX and thrombin inhibitors, and incubated a t 37° C. for 10 minutes . Addition of 50 μl of chromogenic substrate which is cleaved by activa ted FX was followed by incubation for 5 minutes before adding 50 μl of acetic acid (50%) to st op the reaction and ΔOD 405 nm was measured . FVIII activity (mIU) was determined using a s tandard curve prepared from FVIII concentrates and constructed using the dilution series inclu ded in the test.

FVIII activity is

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

result:

[Table 10]

	FVIII活性(%)			
	インキュベーション時間(分)			
アッセイ	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 len gth-of-incubation-dependent manner. vWF did not protect FVIII from inactivation by protease s. 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 µg/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 a ctivity (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 protea se

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

Results

:

[Table 12]

	r時間
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 ab ove, the protease itself shortened the blood clotting time. Example 12 To a solution containin g 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 protea se solution was determined by the chromogenic assay, recording deamidation of the chromog enic 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. Resul ts :

[Table 13]

アッセイ	活性(%)
出発原料	100
pH5.0	76
pH5.5	65
pH6.1	81
pH6.5	50
pH7.1	43
pH7.5	46
pH8.1	46
pH8.6	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:

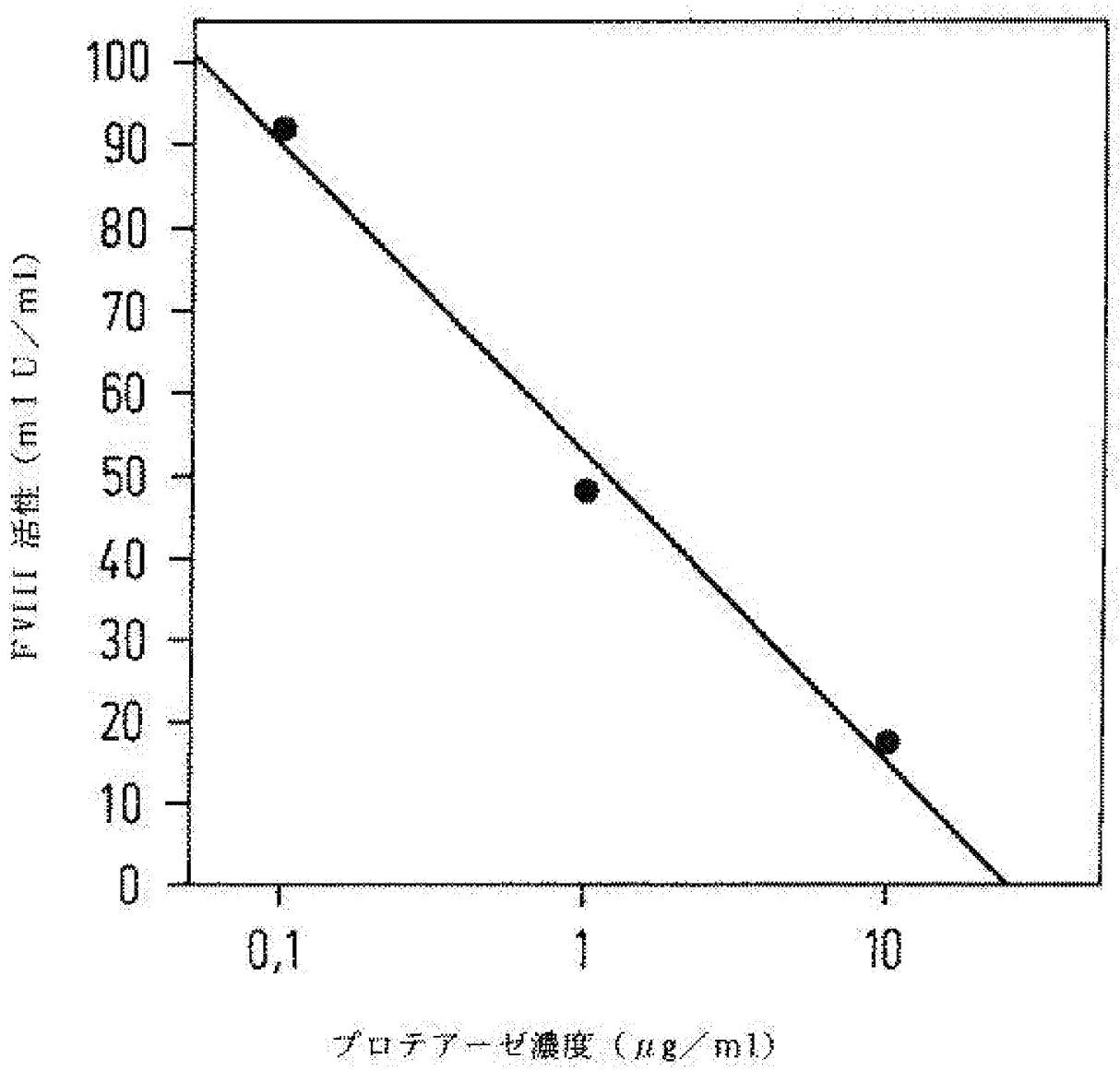
[Table 14]

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

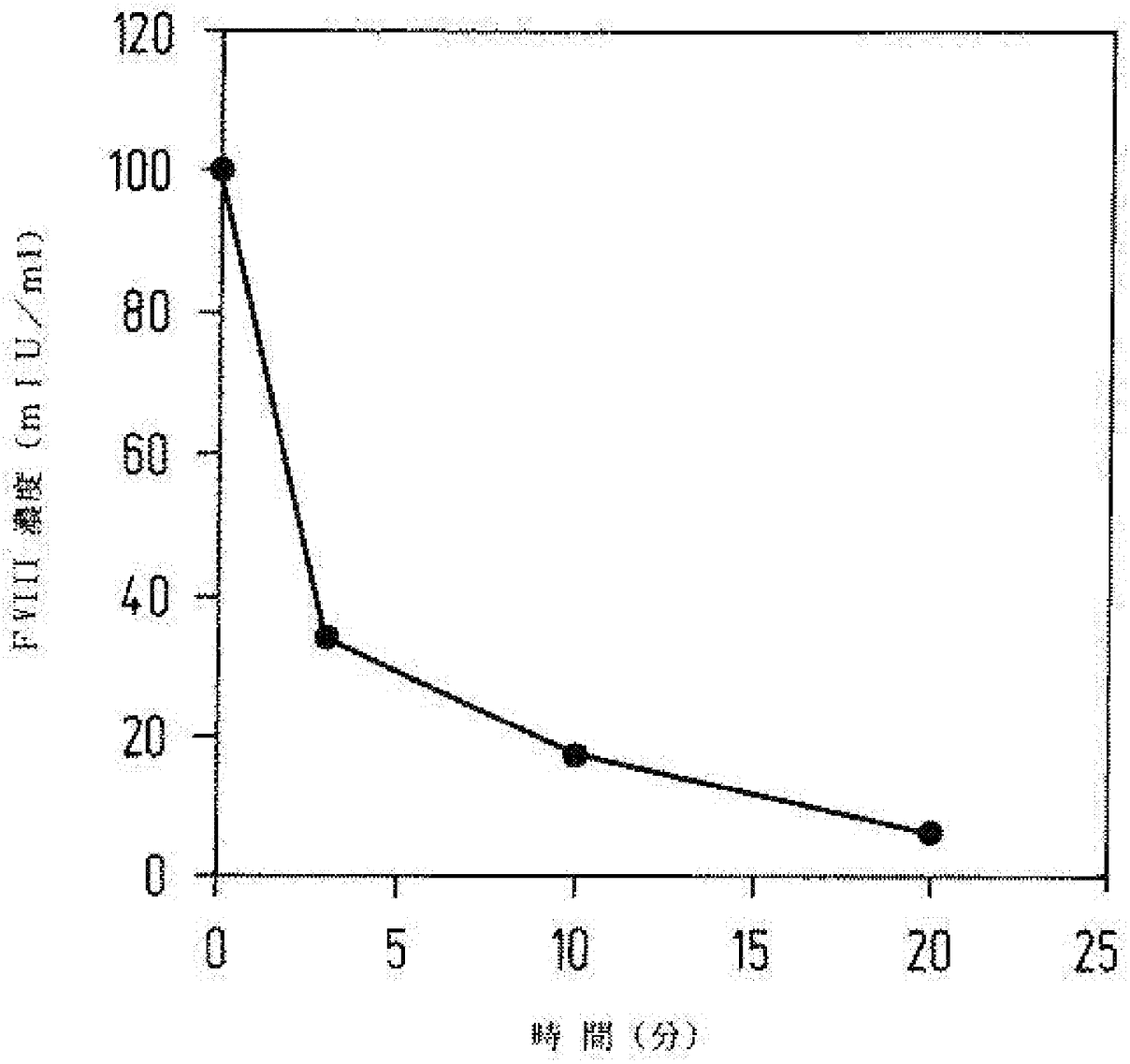
Addition of sucrose and one amino acid in each case demonstrated a significant stabilization of the protease.

drawing open —

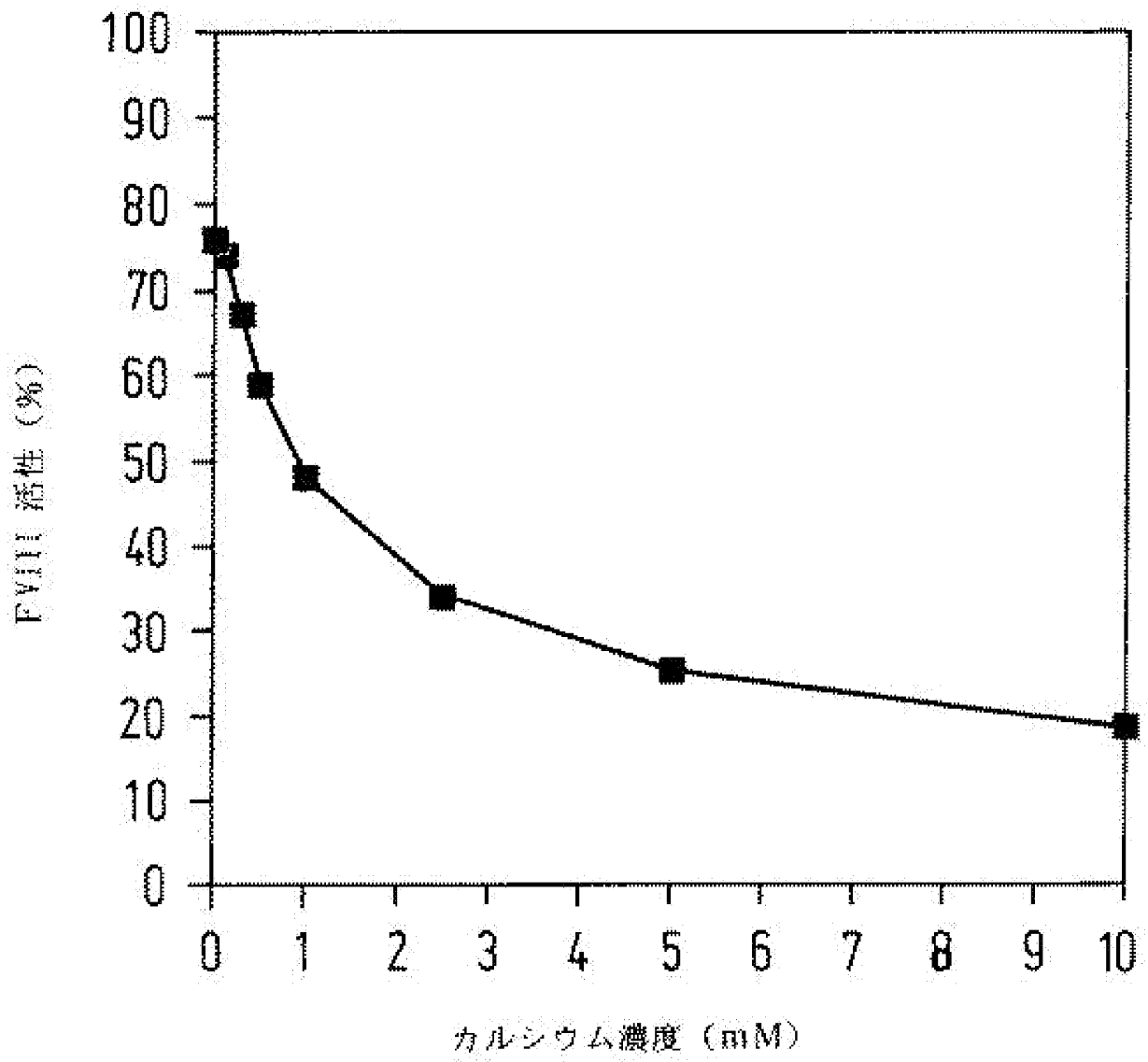
[Fig. 1]



[Figure 2]



[Figure 3]



drawing open —

1 2 3

Magnify and Rotate

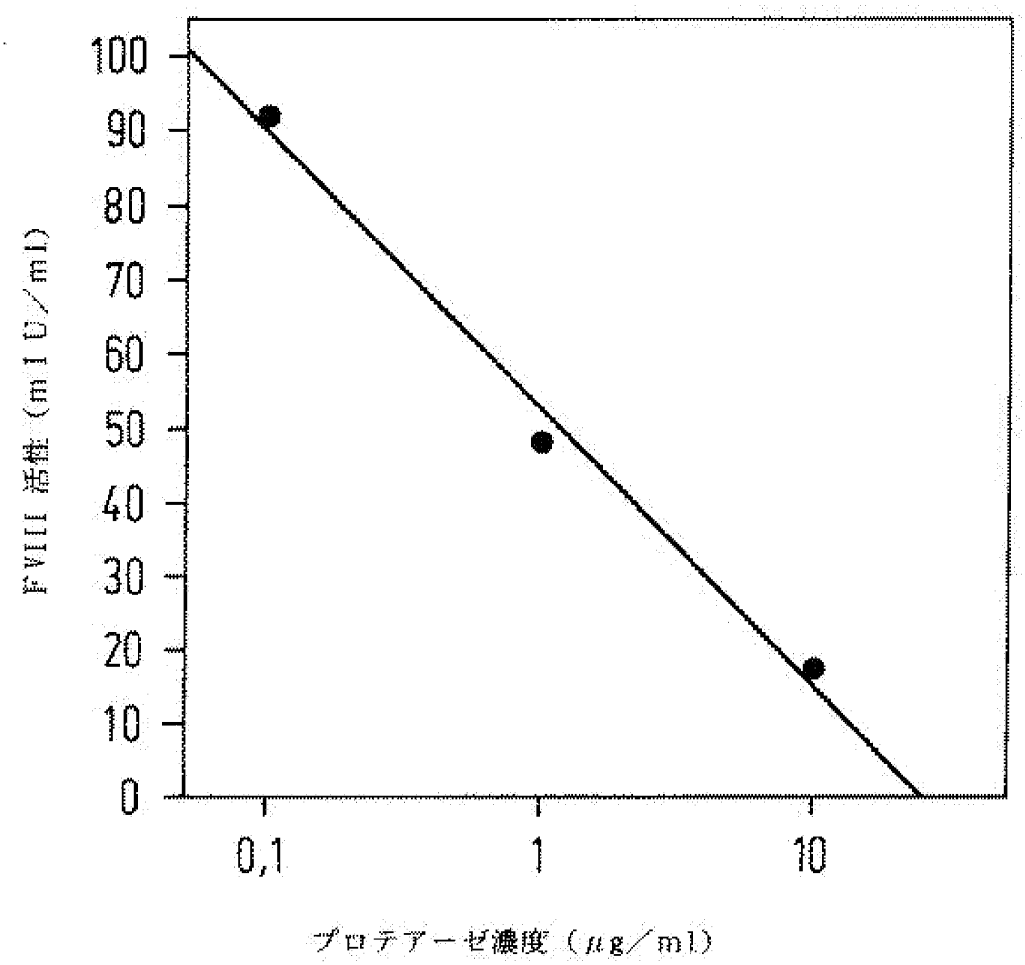


Figure 1

1 / 1 display

Copyright JPO and INPIT (P0200)

(19)日本国特許庁(JP)　(12)公開特許公報(A)　(11)特許出願公開番号
特開2009-131273
(P2009-131273A)
(43)公開日　平成21年6月18日(2009.6.18)

(51)Int.Cl.			F I			テーマコード（参考）
C12Q	1/56	(2006.01)	C12Q	1/56	ZNA	4B063
A61K	38/43	(2006.01)	A61K	37/48		4C084
A61P	7/04	(2006.01)	A61P	7/04		
A61P	43/00	(2006.01)	A61P	43/00	111	

審査請求 有　請求項の数 7　OL　（全 25 頁）

(21)出願番号　特願2009-57232 (P2009-57232)
(22)出願日　平成21年3月11日 (2009.3.11)
(62)分割の表示　特願平11-116411の分割
原出願日　平成11年4月23日 (1999.4.23)
(31)優先権主張番号　19818495:6
(32)優先日　平成10年4月24日 (1998.4.24)
(33)優先権主張国　ドイツ(DE)
(31)優先権主張番号　19851332:1
(32)優先日　平成10年11月6日 (1998.11.6)
(33)優先権主張国　ドイツ(DE)
(31)優先権主張番号　19851335:6
(32)優先日　平成10年11月6日 (1998.11.6)
(33)優先権主張国　ドイツ(DE)
(31)優先権主張番号　19851336:4
(32)優先日　平成10年11月6日 (1998.11.6)
(33)優先権主張国　ドイツ(DE)

(71)出願人　597070264
ツェー・エス・エル・ベーリング・ゲー・エム・ベー・ハー
ドイツ連邦共和国Ｄ－３５０４１　マルブルク．エミル　フォン　ベーリング　シュトラーセ　７６
(74)代理人　100127926
弁理士　結田　純次
(74)代理人　100105290
弁理士　三輪　昭次
(74)代理人　100140132
弁理士　竹林　則幸
(74)代理人　100091731
弁理士　高木　千嘉

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　５０～７５ｋＤａ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１０～３５ｋＤａ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５０～７５ｋＤａ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４０～５５ｋＤａの範囲に得られるバンドはアミノ酸配列：ＬＬＥＳＬＤＰ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：ＬＬＥＳＬＤＰ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）プラスミノー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、プラスミノー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ーゲンアクティベーター）または
ｂ）一本鎖 ｔＰＡ（sctＰＡ、一本鎖組織プラスミノー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０．００１ｍM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５０～７５ｋＤａ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：ＬＬＥＳＬＤＰ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：ＬＬＥＳＬＤＰ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：ＬＬＥＳＬＤＰ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：ＬＬＥＳＬＤＰ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、プラスミノー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ー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、プラスミノー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）プラスミノー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様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はなく、限られているが適切な程度の凝血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ＦＶＩＩ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、それら自体凝血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】

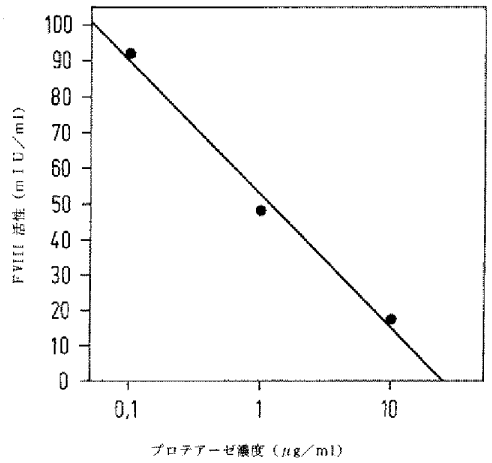
【0009】

【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。

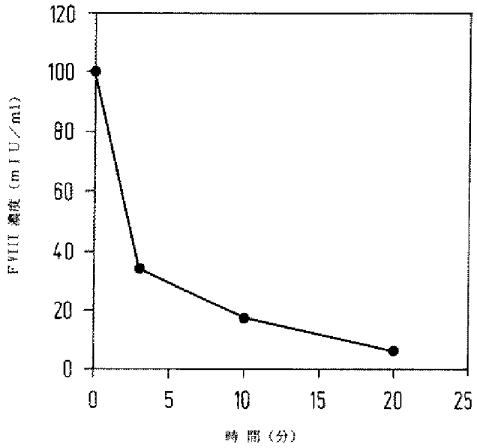
【図2】プロテアーゼ濃度を一定とし、ＦＶＩＩＩを様々な時間インキュベートした場合のＦＶＩＩＩの不活性化を示す。

【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。

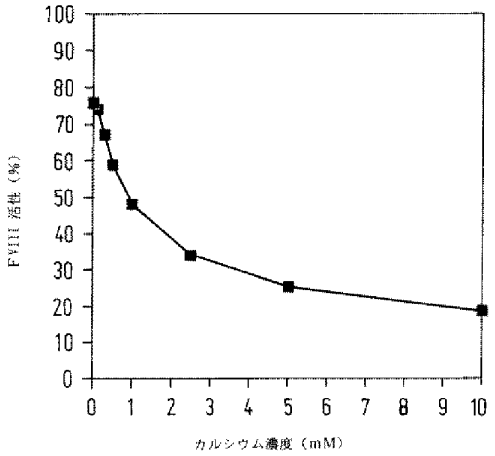
【図1】


100
90
80
70
60
50
40
30
20
10
0
FVIII 活性（mIU/ml）
0,1
1
10
プロテアーゼ濃度（μg/ml）

【図2】



【図3】


100
90
80
70
60
50
40
30
20
10
0
FVIII 活性（%）
0 1 2 3 4 5 6 7 8 9 10
カルシウム濃度（mM）

(31)優先権主張番号　19827734:2
(32)優先日　　平成10年6月22日(1998.6.22)
(33)優先権主張国　　ドイツ(DE)
(31)優先権主張番号　19903693:4
(32)優先日　　平成11年2月1日(1999.2.1)
(33)優先権主張国　　ドイツ(DE)

(72)発明者　イェルゲン・レーミシュ
ドイツ連邦共和国デー－３５０４１マルブルク．ツム・アイゼンベルク８
(72)発明者　ハンス－アルノルト・シュテーア
ドイツ連邦共和国デー－３５０８３ヴェター．シュールシュトラーセ６６
(72)発明者　アネッテ・フォイスナー
ドイツ連邦共和国デー－３５０４３マルブルク．ランゲヴィーゼンヴェーク１０

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

Australian Government
IP Australia

Delivering a world leading IP system

www.ipaustralia.gov.au

ABN: 38 113 072 755

29 April 2020

Examination report No. 1 for standard patent application

Griffith Hack
GPO Box 4164
Sydney NSW 2001
Australia

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

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

Dear Griffith Hack,

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

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

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

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

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

Yours sincerely,

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

Report details

Basis of the report

In examining this application I have considered:

- the PCT pamphlet as originally filed

Summary of novelty, inventive step and patentable subject matter

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

Detailed objections on issues that have been identified

Documents cited or considered relevant

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

[1] Cited in WO 2017019552

Special categories of cited documents:

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

Novelty and inventive step

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

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

> an inlet port (100); an outlet port (330); a sequestration chamber connected with the inlet port (117), the sequestration chamber having a vent (160) comprising an air permeable blood barrier (Para [0042]); a sampling channel (130) having a proximal end connected with the inlet port and a distal end connected with the outlet port; and a housing (116) that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

Claims **8 and 17** define a blood sequestration device with a similar scope to claim 1, only differing by the additional features of a blood sampling pathway or blood sampling system

connected to said device. **D1** also discloses a blood sampling pathway or system connected to the blood sequestration device (Fig. 23; patient needle 184, connected to inlet 100).

Furthermore, appended **claims 2-7, 9-16, 18-20** are not considered to make any patentable contribution over the teachings of the cited document **D1** or are common general knowledge in the art or workshop improvements and which therefore cannot contribute to providing novelty or an inventive step. For example, **D1** discloses features of **claims 2, 11, 20** of the air permeable blood barrier sealing upon contact with blood (Para [0081], [0085]). Features of dependent **claim 3** are considered matters of workshop improvement over **D1**. It would be obvious to the person skilled in the art that a sequestration channel be implemented to improve transport of blood to the sequestration chamber.

END OF REPORT

Contamination Rates of Blood Cultures Obtained by Dedicated Phlebotomy vs Intravenous Catheter

Alonna Norberg, MD
Norman C. Christopher, MD
Maria L. Ramundo, MD
John R. Bower, MD
Shirley A. Berman, RN

Context Blood culture is the criterion standard for identifying children with bacteremia. However, elevated false-positive rates are common and are associated with substantial health care costs.

Objective To compare contamination rates in blood culture specimens obtained from separate sites vs through newly inserted intravenous catheters.

Design, Setting, and Participants Observational study conducted January 1998 through December 1999 among patients aged 18 years or younger who were seen at a US children's hospital emergency department and had a blood culture obtained as part of their care. Medical records were reviewed in all cases with a positive blood culture. Patients with indwelling vascular catheters were excluded.

Intervention All phlebotomy was performed by emergency department registered nurses. During the baseline phase, blood specimens for culture were obtained simultaneously with intravenous catheter insertion. During the postintervention phase, specimens were obtained by a separate, dedicated procedure.

Main Outcome Measure Contamination rate in the postintervention period compared with the baseline period.

Results A total of 4108 blood cultures were evaluated, including 2108 during the baseline phase and 2000 in the postintervention phase. The false-positive blood culture rate decreased from 9.1% to 2.8% ($P<.001$). A statistical process control chart demonstrated a steady-state process in the baseline phase and the establishment of a significantly improved steady state in the postintervention phase. Young age was associated with increased contamination rate in both the baseline and postintervention periods.

Conclusion Blood culture contamination rates were lower when specimens were drawn from a separate site compared with when they were drawn through a newly inserted intravenous catheter.

JAMA. 2003;289:726-729 www.jama.com

FEVER IS THE PRIMARY COMPLAINT in up to 20% of children presenting to emergency departments,[1] and bacteremia is the source of fever in 1.5% to 2.3% of these patients.[2,3] Blood culture is the criterion standard for identifying children with bacteremia[4-7]; however, false-positive blood cultures are common and may add significantly to health care costs.[8-11] High rates of contamination are common among pediatric patients, likely related to difficulties inherent to phlebotomy in young patients.[12] To minimize the number of venipunctures in children, blood culture specimens are obtained simultaneously with intravenous catheter placement in many emergency departments. The impact of using intravenous catheters to obtain blood cultures is unclear.[13-16] We hypothesized that the blood culture contamination rate would be less when blood culture specimens were obtained from a remote site rather than through a newly inserted intravenous catheter.

METHODS

A preintervention and postintervention observational study of patients who had a blood culture obtained as part of their routine emergency department course was conducted. Patients 18 years old or younger who presented to the emergency department at a free-standing tertiary care children's hospital that evaluates more than 65 000 children annually and required a blood culture as part of their routine care were eligible. Patients were identified by computerized search of the hospital database.

Laboratory specimens were obtained based on clinical and laboratory indications and were drawn by an emergency department registered nurse. The protocols for skin antisepsis and

Author Affiliations: Divisions of Emergency Medicine (Drs Norberg, Christopher, Ramundo, and Ms Berman) and Infectious Diseases (Dr Bower), Department of Pediatrics, Children's Hospital Medical Center of Akron, Akron, Ohio; and Departments of Emergency Medicine and Pediatrics, Northeastern Ohio Universities College of Medicine, Rootstown (Drs Norberg, Christopher, Ramundo, and Bower).
Corresponding Author and Reprints: Norman C. Christopher, MD, Division of Emergency Medicine, Children's Hospital Medical Center, One Perkins Square, Akron, OH 44308 (e-mail: Nchristopher@CHMCA.org).

©2003 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 04/10/2019

for specimen collection and inoculation were standardized and remained unchanged during the study. Nursing staff members were unaware of ongoing data collection and analysis. In cases where a positive blood culture was reported, the patient's medical record was reviewed. Patients with indwelling devices (central venous lines, ventricular catheters) were excluded.

Baseline Phase

During the baseline phase (January 1, 1998-November 19, 1998), culture specimens were obtained through a newly inserted peripheral intravenous catheter using the standard over-the-needle approach. A sterile 5-mL syringe was attached to the catheter hub, and blood for both culture and for laboratory studies was withdrawn; the first portion of the sample was used for culture.

During the first 4 months of the baseline phase, focused efforts to decrease the contamination rate were implemented. Because these interventions failed to reduce the contamination rate, the standard technique was abandoned in favor of obtaining specimens from a separate phlebotomy site. Data from a 6-week implementation phase (November 20, 1998-December 31, 1998) were not included in the analysis.

Postintervention Phase

During the postintervention phase (January 1, 1999-December 31, 1999), culture specimens were obtained by venipuncture at a dedicated site. If a patient required an intravenous catheter, it was placed using the standard approach at a site distant from the blood culture venipuncture site. While laboratory specimens were sometimes obtained through the newly inserted intravenous catheter, all specimens for culture were obtained by phlebotomy dedicated to that procedure.

Classification of Blood Culture Isolates

Blood culture isolates were categorized as contaminants or pathogens. In all cases, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Salmonella* species, *Haemophilus influenzae*, and group A or group B β-hemolytic streptococci were considered pathogens. A contaminant was defined as a nonpathogenic microorganism.[15] If pathogenicity was uncertain or variable, assignment was made in consultation with an infectious disease expert (J.R.B.), with consideration of patient demographics and the clinical setting. Assignment was made without knowledge of the intervention phase. Because the presence of even a single nonpathogenic species in the blood culture specimen represented improper phlebotomy technique, a specimen with multiple bacteria was considered contaminated.

Decisions regarding treatment and follow-up of patients were made by clinicians in the emergency department based on current practice. The institutional review board of the Children's Hospital Medical Center of Akron approved the study protocol. Consent was not obtained from families. The intervention was adopted as our standard of care, and data was collected in a blinded database for analysis.

Data Analysis

Data were analyzed using STATA Version 7.0 (Dallas, Tex, 2001). Univariate analysis was performed unless stated otherwise. Pearson χ^2 was used to analyze categorical data. Descriptive analysis of continuous data was performed. $P<.05$ was the level of significance.

Statistical process control methodology was also used to examine the impact of the intervention over time. A run chart was constructed showing the blood culture contamination rate for each month of the study ([number of contaminated specimens × 100]/[number of blood cultures obtained]). The mean blood culture contamination rate and the upper and lower control limits were established based on the preintervention data, with control limits representing ±3 SD from the mean.[16-18]

Table 1. Patient Demographics

	Baseline (n = 2106)	Postintervention (n = 2000)
Age, median (IQR), y	1.4 (0.47-3.8)	1.4 (0.42-3.4)
Emergency department disposition, No. (%)		
Admit	1099 (52.0)	1042 (52.0)
Discharge	1009 (48.0)	958 (48.0)
Age category, No. (%)		
<12 wk	385 (18.3)	353 (17.7)
3 mo-≤2 y	887 (42.1)	891 (44.6)
>2 - ≤5 y	391 (18.5)	381 (19.1)
>5 y	445 (21.1)	375 (18.8)

Abbreviation: IQR, interquartile range.

RESULTS

During the study, 4448 blood culture specimens were obtained. We excluded 289 specimens obtained during the 6-week implementation phase, 14 with incomplete data in the medical record and 37 because of the presence of central venous catheters, leaving 4108 emergency department visits for analysis (2108 in the baseline phase and 2000 in the postintervention phase). Overall, there were 324 positive blood culture specimens.

Patient demographics are presented in TABLE 1. There were no statistically or clinically important differences between patients in the baseline and in the postintervention phases.

During the baseline phase, 223 positive blood culture specimens were reported; of these, 32 specimens grew a pathogen. In the 191 blood culture specimens categorized as contaminated, 243 organisms were cultured (TABLE 2). The overall false-positive rate was 9.1% and the true-positive rate was 1.5%. In the postintervention period, there were 101 positive blood cultures; of these, 45 grew a pathogen. In the 56 contaminated specimens, 65 organisms were cultured (Table 2). The overall false-positive rate during the

©2003 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 04/10/2019

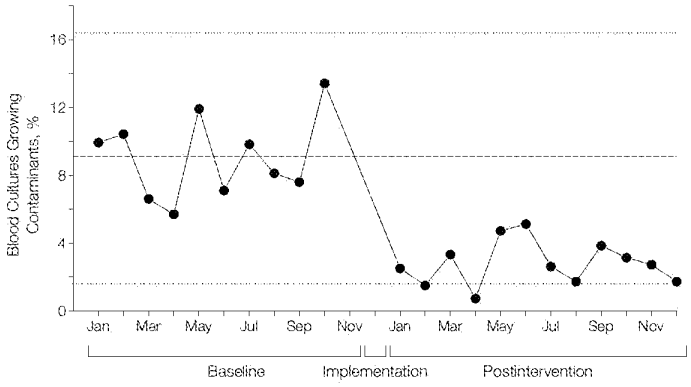
KUR-MAG-DE004379

Table 2. Blood Culture Contaminants in the Baseline and Postintervention Periods of Study

Contaminants	No. of Organisms (% of Total Contaminated Specimens)	
	Baseline*	Postintervention
Coagulase-negative staphylococci	140 (73)	37 (67)
Streptococcus viridans	57 (30)	8 (14)
Corynebacterium species	13 (7)	7 (12)
Micrococcus species	13 (7)	5 (8)
Bacillus species	3 (1.6)	3 (5)
Propionibacterium acnes	4 (2)	0
Neisseria species	3 (1.6)	0
Others	10 (5)	5 (8)
Total No. of Organisms	**243**	**65**

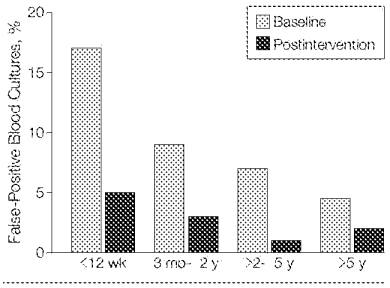
*There were 191 contaminated specimens growing 243 organisms in the baseline phase and 56 contaminated specimens growing 65 organisms in the postintervention phase of the study.

Figure 1. Statistical Process Control Chart Showing the Percentage of All Blood Cultures Growing Contaminants by Month, for the 2-Year Study Period



The upper and lower control limits (dotted lines) represent ±3 SD from the mean (dashed line). The mean, upper control limit, and lower control limit are calculated based on data in the baseline phase of the study.

Figure 2. Blood Culture Contamination Rate, by Age Category, During the Baseline and Postintervention Phases of Study



postintervention period was 2.8%, with a true-positive rate of 2.3%. Using a 2-sample test of proportions, the contaminated blood culture rate in the postintervention phase is significantly decreased when compared with the baseline phase ($P<.001$). The increase in true-positive rates did not reach statistical significance ($P=.20$).

The statistical process control chart (FIGURE 1) shows 12 consecutive data points below the mean established in the baseline phase in the postintervention phase, indicating a special cause effect (the intervention) and a significant change in the measured outcome (the contamination rate).[19]

The contamination rates in the baseline and postintervention phases are higher the younger the child (FIGURE 2). For example, in the baseline phase, the contamination rate in patients younger than 12 weeks was 17%, compared with 4.5% in those older than 5 years.

COMMENT

The contamination rates were significantly lower when blood culture specimens were drawn from a separate and dedicated venipuncture site compared with through a newly inserted intravenous catheter in children seen in a busy emergency department. The low rates have been sustained since the end of the study.

The statistical quality control methodology we applied provides a simple graphical display of process data that enhances our ability to understand outcomes that occur over time.[17] This methodology has been used increasingly in the evaluation of processes occurring in the health care setting.[16,20,21] The premise is that when a process achieves steady state, it is likely to remain there until events cause it to shift to a new steady state.[18,19]

This study addresses a common problem that has been linked to substantial and unnecessary resource utilization.[9,10,22-24] The contamination rate in our emergency department was resistant to change in spite of several specific interventions intended to address the problem. The sole procedural change was in the method by which blood culture specimens were obtained. During the baseline phase, the overall false-positive blood culture rate was 9.1% compared with a rate of 2.8% after the intervention, representing a decrease of 70%. While not statistically significant, the true-positive rate increased from 1.5% at baseline to 2.3% after the intervention. We believe that at least some of this increase is due to more selective ordering of blood cultures during the postintervention phase, when all cultures were obtained in response to other diagnostic tests obtained during the patient's emergency department evaluation. Since it is easier to obtain blood for culture from an intravenous catheter, cultures may have been obtained more indiscriminately in the baseline phase.

Previous studies comparing contamination rates in specimens obtained through newly inserted intravenous catheters or by phlebotomy at a remote

©2003 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 04/10/2019

KUR-MAG-DE004380

site suggest that the 2 techniques are essentially equivalent. Smart and Baggoley[22] failed to show a difference in the contamination rate in 940 adult patients randomized to phlebotomy by either venipuncture or by placement of an intravenous catheter. Isaacman and Karasic[14] prospectively evaluated a convenience sample of 99 pediatric patients, each of whom had 2 blood cultures obtained, one by venipuncture and one through a newly inserted intravenous catheter. The authors demonstrated a low contamination rate with both techniques, concluding that newly inserted intravenous catheters offer an alternative to a separate venipuncture procedure in patients requiring blood culture. The small number of patients enrolled and the impact of the nursing staff's awareness of the study protocol may have biased the results.

On the other hand, a study by Ramsook et al[15] suggested that blood culture contamination rates were decreased when using dedicated phlebotomy compared with those obtained through a newly inserted intravenous catheter. Importantly, this study demonstrated the highest contamination rates in patients younger than 3 months of age, regardless of the collection method used, a finding confirmed in our study. Because staff members were aware of ongoing data collection, the potential effect on their phlebotomy technique is unknown.

However, our study also has limitations; because medical records were reviewed only for those patients with positive blood cultures, detailed information about patients with negative blood cultures is not known. In particular, information about antibiotic pretreatment is unknown. While it is likely that some patients were prescribed systemic antibiotic therapy prior to or during their emergency department evaluation, the rates of antibiotic pretreatment in the baseline and postintervention phases of the study are likely to be similar and unlikely to affect the study's conclusions. In addition, this protocol was implemented in a single unit and may not be generalizable to other settings. Finally, no concurrent control group was included to account for secular temporal changes.

Obtaining blood cultures from a separate site requires the patient to undergo an additional procedure for phlebotomy, but the overall benefit in terms of costs associated with a high contamination rate is likely to be substantial. During the baseline period, there were 6 contaminated specimens for every true-positive blood culture, compared with a ratio of 1.2:1 after implementation of the intervention. If subsequent patient management is based on preliminary blood culture results, false-positive test results will result in repeat emergency department visits, unnecessary medical interventions, unnecessary antibiotic therapy, and even hospital admission. One study[5] found that 26% of children followed as outpatients who had false-positive blood cultures were hospitalized unnecessarily, and that unnecessary use of antibiotics was significantly increased in the presence of false-positive blood culture results. Additional costs that are more difficult to quantify include staff effort and time required to arrange follow-up for patients, exposure of patients to unnecessary procedures, and cost and inconvenience related to repeat emergency department and/or hospital visits.[10,24]

Author Contributions: *Study concept and design:* Norberg, Christopher, Ramundo, Berman.
Acquisition of data: Norberg, Christopher, Ramundo, Berman.
Analysis and interpretation of data: Norberg, Christopher, Bower.
Drafting of the manuscript: Norberg, Christopher, Bower.
Critical revision of the manuscript for important intellectual content: Norberg, Christopher, Ramundo, Bower, Berman.
Statistical expertise: Christopher.
Administrative, technical, or material support: Norberg, Berman.
Study supervision: Christopher, Ramundo, Bower.

REFERENCES

1. Nelson DS, Walsh K, Fleisher GR. Spectrum and frequency of pediatric illness presenting to a general community hospital emergency department. *Pediatrics*. 1992;90:5-10.
2. Alpern ER, Alessandrini EA, Bell LM, et al. Occult bacteremia from a pediatric emergency department: current prevalence, time to detection, and outcome. *Pediatrics*. 2000;106:505-511.
3. Lee GM, Harper MB. Risk of bacteremia for febrile young children in the post-*Haemophilus influenza* type b era. *Arch Pediatr Adolesc Med*. 1998; 152:624-628.
4. Baraff LJ, Bass JW, Fleisher GR, et al. Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. *Ann Emerg Med*. 1993;22:1198-1210.
5. Kupperman N. Occult bacteremia in young febrile children. *Pediatr Clin North Am*. 1999;46:1073-1109.
6. Downs SM, McNutt RA, Margolis PA. Management of infants at risk for occult bacteremia: a decision analysis. *J Pediatr*. 1991;118:11-20.
7. Yamamoto LG, Worthley RG, Melish ME, et al. A revised decision analysis of strategies in the management of febrile children at risk for occult bacteremia. *Am J Emerg Med*. 1998;16:193-207.
8. Weinbaum FI, Lavie S, Danek M, et al. Doing it right the first time: quality improvement and the contaminant blood culture. *J Clin Microbiol*. 1997;35:563-565.
9. Thuler LCS, Jenicek M. Impact of a false positive blood culture result on the management of febrile children. *Pediatr Infect Dis J*. 1997;16:846-851.
10. Bates DW, Goldman L. Contaminant blood culture and resource utilization: the true consequences of false-positive results. *JAMA*. 1991;265:365-369.
11. Lieu TA, Schwartz JS. Strategies for diagnosis and treatment of children at risk for occult bacteremia: clinical effectiveness and cost effectiveness. *J Pediatr*. 1991; 118:21-29.
12. Campos JM. Detection of blood stream infections in children. *Eur J Clin Microbiol Infect Dis*. 1989; 8:815-824.
13. Tonnesen A, Peuler M, Lockwood WR. Cultures of blood drawn by catheter vs venipuncture. *JAMA*. 1976;235:1877-1879.
14. Isaacman DJ, Karasic RB. Utility of collecting blood cultures through newly inserted intravenous catheters. *Pediatr Infect Dis J*. 1990;9:815-818.
15. Ramsook C, Childers K, Cron SG, Nirken M. Comparison of blood culture contamination rates in a pediatric emergency room: newly inserted intravenous catheters versus venipuncture. *Infect Control Hosp Epidemiol*. 2000;21:649-651.
16. Schwab RA, DelSorbo SM, Cunningham MR, Craven K, Watson WA. Using statistical process control to demonstrate the effect of operational interventions on quality indicators in the emergency department. *J Healthc Qual*. 1999;21:38-41.
17. Benneyan JC. Statistical quality control methods in infection control and hospital epidemiology, part I: introduction and basic theory. *Infect Control Hosp Epidemiol*. 1998;19:194-214.
18. Benneyan JC. Statistical quality control methods in infection control and hospital epidemiology, part II: chart use, statistical properties, and research issues. *Infect Control Hosp Epidemiol*. 1998;19:265-283.
19. Humble C. Caveats regarding the use of control charts. *Infect Control Hosp Epidemiol*. 1998;19:865-868.
20. Mylotte JM, White D, McDermott C, Hodan C. Nosocomial bloodstream infection at a veterans hospital: 1979-1987. *Infect Control Hosp Epidemiol*. 1989; 10:455-464.
21. Koska MT. Using CQI methods to lower postsurgical wound infection rates. *Hospitals*. 1992;66:62-64.
22. Smart D, Baggoley C. Effect of needle changing and intravenous cannula collection on blood culture contamination rates. *Ann Emerg Med*. 1993;22:1164-1168.
23. Komberg A. Evaluation of false positive blood cultures: guidelines for early detection of contaminated cultures in febrile children. *Pediatr Emerg Care*. 1994; 10:20-23.
24. Segal GS, Chamberlain JM. Resource utilization and contaminated blood cultures in children at risk for occult bacteremia. *Arch Pediatr Adolesc Med*. 2000; 154:469-473.

©2003 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ on 04/10/2019

however, it is hypertonia rather than muscle twitching that occurs. Glavinia and Robertshaw described a case of myoclonic spasm in a 59-year-old woman who received a bolus of 3 mg of intrathecal morphine for intractable pain [2] while Jayawardena and Hill described a case of myoclonus in a 65-year-old woman 24 h after discontinuing a diamorphine infusion into the epidural space [3].

In both the previously reported cases of myoclonic spasms following the administration of morphine and diamorphine, the drugs had been infused spinally in much smaller doses. The 100-fold difference in dose before the development of myoclonus is probably related to the concentration gradient between the intravenous and cerebrospinal compartments, this being a function of a lipid solubility of diamorphine. Terminally ill patients at the Hospice commonly receive comparable doses of diamorphine and morphine to that initially given to this patient without developing myoclonic spasms, but ureteric obstruction leading to chronic renal insufficiency may have accelerated central neuronal toxicity in this patient as it would impair excretion of unconjugated active morphine.

Ashgate Hospice D. TURNER
Chesterfield

References

[1] Martindale. *The Extra Pharmacopoeia*, 29th edn. p 1311.
[2] GLAVINIA ML, ROBERTSHAW R. Myoclonic spasms following intrathecal morphine. *Anaesthesia* 1988; **43:** 389–90.
[3] JAYAWARDENA B, HILL DJ. Myoclonic spasms after epidural diamorphine infusion. *Anaesthesia* 1991; **46:** 473–4.

Venous/arterial blood management protection system

We have recently assessed the function of the venous/arterial blood management protection system (VAMP) manufactured by Baxter and have been impressed with its simplicity and ease of operation. This disposable system, consisting of a length of pressure monitoring tubing, reservoir, shut-off valve and blood sampling site (Fig. 1) is attached distally to a pressure transducer and allows a convenient method for the periodic withdrawal of blood samples. It may be used with arterial, pulmonary artery or central venous catheters.

Five millilitres of heparinised blood/saline mixture are drawn from the patient into the VAMP reservoir over 3–5 s using the reservoir plunger. After turning the shut-off valve, undiluted blood samples are drawn from the sampling site using a guarded needleless cannula attached to either a syringe or a direct draw blood transfer unit (BTU). If the latter is used, individual vacuumed blood sample tubes may be attached directly to the BTU for filling. Following completion of blood sampling, the shut-off valve is re-opened and the reservoir volume slowly returned to the patient using firm, even pressure on the reservoir plunger. The sampling site is cleansed using an alcohol swab before and after sampling.

The VAMP system may be useful in an Intensive Care Unit for several reasons. Firstly, it is likely to reduce the risk of sampling-related anaemia which has been reported, particularly in children [1, 2]. Although some of the reduction in haemoglobin may be related to the removal of the blood samples themselves, it is often the case that the initial volume of blood/heparinised saline mixture removed from the patient is discarded. The use of a closed sampling system will reduce this effect. Secondly, the absence of potentially messy and infected three-way taps as sampling points for blood, and the use of the VAMP sampling

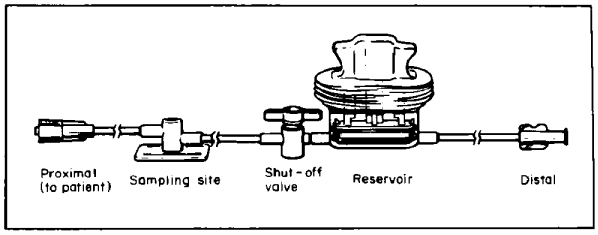


Fig. 1. Baxter venous/arterial blood management protection system (VAMPTM).

system, may reduce the risk of catheter-related sepsis. Finally, the use of needles during blood sampling is potentially hazardous to health workers [3]; the fact that the VAMP system employs a needleless sampling method will reduce the incidence of needlestick injuries.

Queen Alexandra Hospital, A. CHALLINER
Portsmouth PO6 3LY G.B. SMITH
B.L. TAYLOR

References

[1] BALAKRISHNAN G, GIBSON B, MORTON NS, HALLWORTH D. Anaemia due to blood sampling. *British Journal of Intensive Care* 1991; **1:** 104–105.
[2] TARPEY J, LAWLER PG. Iatrogenic anaemia? A survey of venesection of patients in the Intensive Therapy Unit. *Anaesthesia* 1990; **45:** 396–8.
[3] ANDERSON DC, BLOWER AL, PACKER JMV, GANGULI LA. Preventing needlestick injuries. *British Medical Journal* 1991; **302:** 769–70

Dural puncture and depth of the extradural space

We read with interest the article by Sutton and Linter (*Anaesthesia* 1991; **46:** 97–8) concerning the relative risk of dural puncture as a function of the depth of the extradural space. This study prompted us to examine our own data about the same subject. Since 1989, we have recorded prospectively, and collected on standardised forms, the technical characteristics of all the epidurals performed in obstetric patients, either for labour or for elective Caesarean section. The depth of extradural space was one of the collected items, as well as the occurrence of dural

INFORMATION DISCLOSURE STATEMENT BY APPLICANT		
	Application Number	17538990
	Filing Date	11/30/2021
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Client Number	069366
Page 1 of 1	**Matter Number**	0572201_KUR2C03US

GENERAL

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

Although the information submitted herewith may be "material" to the Examiner's consideration of the subject application, this submission is not intended to constitute an admission that such information is "prior art" as to the claimed invention.

In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

TIMING

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

CERTIFICATION STATEMENT

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

FEE

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

ADDITIONAL COMMENTS

SIGNATURE

Signature	/ Benjamin F. Hudson /	**Date**	2023-05-16
Name	Benjamin F. Hudson	**Registration Number**	71,474

SyncIDS.com

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Patent 6734490

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

Display format of the document display screen:

text display / PDF display

primary literature

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Patent publication (B2)
(11) [Patent number] Patent No. 6734490 (P6734490)
(24) [Registration date] Reiwa 2 July 13, 2020 (2020.7.13)
(45) [Date of issue] August 5, 2020 (2020.8.5)
(54) [Title of invention] Blood isolation device, body fluid isolation device, and blood isolation system
(51) [International Patent Classification]
A61B 5/15 (2006.01)
A61B 5/154 (2006.01)
[FI]
A61B 5/15 200
A61B 5/154 200
[Number of Claims] 26
[Foreign language application]
[All pages Number] 39
(21) [Application number] Patent application 2020-340 (P2020-340)

(22) [Application date] January 6, 2020 (2020.1.6)
(62) [Indication of division] Patent application Division of 2018-523384 (P2018-523384) [Original filing date] July 22, 2016 (2016.7.22) (65) [Publication number] JP 2020-96843 (P2020-96843A) (43) [Publication date]] June 25, 2020 (2020.6.25)

[Date of request for examination] January 31, 2020 (January 31, 2020)
(31) [Priority claim number] 62/238,636
(32) [Priority date] October 7, 2015 (October 7, 2015)
(33) [Country/region or organization claiming priority] United States (US)
(31) [Priority claim number] 62/318,194
(32) [Priority date] April 4, 2016 (2016.4.4)
(33) [Priority claiming country/region or organization] United States (US)
(31) [Priority claim number] 62/196,797
(32) [Priority date] July 24, 2015 (2015.7.24)
(33) [Priority Country/Territory or Organization] United States (US)
(31) [Priority claim number] 15/140,448
(32) [Priority date] April 27, 2016 (2016.4.27)
(33) [Priority claim Country/region or organization] United States (US)
(31) [Priority claim number] 15/140,443
(32) [Priority date] April 27, 2016 (2016.4.27)
(33) [Priority claim country/ Region or institution] United States (US)
[Application subject to accelerated examination]
(73) [Patent holder]
[Identification number] 518026730
[Name] Klin Inc.
(74) [Agent]
[Identification number] 100083806
[Patent attorney]]
[Name] Hidekazu Miyoshi
(74) [Agent]
[Identification number] 100095500
[Patent attorney]
[Name] Masakazu Ito
(74) [Agent]
[Identification number] 100111235 [
Patent attorney]
[Name or name] Yuko Hara

(74) [Agent]
[Identification number] 100195257
[Patent Attorney]
[Name] Kazushi Obuchi
(72) [Inventor]
[Name] Rogers, Bobby
(72) [Inventor]
[Name] Kan, Gino
(72) [Inventor]
[Name] Detrov, John
[Examiner] Hirokatsu Shimizu
(56) [Reference]
[Reference] Japanese Patent Application Laid-Open No. 58-025146 (JP, A) [Reference] Japanese Patent Application Laid-Open No. 58-067238 (JP, A) [Reference] Japanese Patent Application Laid- Open No. 2012-016496 (JP, A) [Document] JP-A-57-089869 (JP, A) [Document] JP-A-09-504726 (JP, A) [Document] JP-A-02-224742 (JP, A) 2005-349196 (JP, A) [Reference]

US Patent No. 04207870 (US, A)
[Reference] US Patent Application Publication No. 2013/0116599 (US, A1) [Reference] US Patent Application Publication No. 2011/0306899 (US, A1) (58) [Fields searched] (Int.Cl., DB name)A61B 5/153-5/154

The scope of the claims open —

(57) [Claims]
[Claim 1]
A blood isolation device comprising
an inlet port, an

outlet port, an

isolation chamber and a sampling channel, wherein each of the isolation chamber and the sa mpling channel has an isolation chamber connected to the inlet port via a bifurcation, the isol ation chamber having a vent containing an air permeable blood barrier, and the sampling chan nel having a distal end connected to the outlet port; a sampling channel, and a housing contai ning

and defining the inlet port, the outlet port, the isolation chamber, and the sampling channel, wherein the isolation chamber, the sampling channel, and the bifurcation point are connecte d to the flow of blood. A first portion of blood flows into the isolation chamber toward the air p ermeable blood barrier for sequestration within the isolation chamber and a second portion of the blood flows into the isolation chamber and the blood isolated within the isolation chamber. A blood isolation device sized and configured to bypass the first portion and direct the samplin g channel toward the outlet port. 2. A blood isolation device, comprising: an inlet port;

an isolation chamber having an exit port,

a vent containing an air permeable blood barrier, a sampling channel

having a distal end connected to said exit port, said

entrance port, said exit port, said isolation chamber, and said a housing containing and defini ng a sampling flow path

,

each of said isolation chamber and said sampling flow path being connected to said inlet port via a bifurcation point, said bifurcation point connecting said first portion of blood to said isola tion fluid; a second portion of blood flowing into the chamber to expel air in the isolation cha mber through the air permeable blood barrier and to be isolated in the isolation chamber; a bl ood isolation device sized and configured to bypass the first portion of the blood that has been drawn and directed into the sampling flow path toward the outlet port.

3.

The blood isolation device of claim 1, wherein the air permeable blood barrier comprises an air permeable material that at least partially seals upon contact with blood.

4.

The blood isolation device of claims 1 or 2, wherein the isolation chamber includes an isolati on channel defined within the housing.

5. The housing

includes a lower member mating with an upper member, each of said lower member and sai d upper member being associated with each of said inlet port, said outlet port, said isolation c

hamber and said sampling channel. 4. A blood isolation device according to any one of claims 1 to 3, which defines part of a

6.

A blood isolation device connected to a blood collection path having a patient needle and a sample collection device, comprising:

an inlet port connected to the patient needle,

an isolation chamber and a sampling channel, wherein each of the isolation chamber and the sampling channel is connected to the inlet port through a branch point, and the isolation chamber is air permeable a vent including an air permeable blood barrier, the isolation chamber and the bifurcation configured to direct a first portion of blood into the isolation chamber toward the air permeable blood barrier; Having a distal end connected with an outlet port, the sampling channel and the branch point bypass the isolation chamber and the first portion of the blood with the second portion of blood isolated within the isolation chamber. , an isolation chamber and a sampling channel configured to allow the sampling channel to be directed toward the outlet port, the outlet port being connected with the sample-collecting device

;

A blood isolation device comprising a housing containing and defining an outlet port, said isolation chamber, and said sampling flow path .

7.

A blood isolation device connected to a blood collection path having a patient needle and a sample collection device, wherein an

inlet port connected to the patient needle and

an outlet port connected to the sample collection device;

an isolation chamber having a vent containing an air permeable blood barrier; a sampling channel

having a distal end connected to said outlet port;

said inlet port, said outlet port, said isolation chamber and said sampling channel; a housing containing and defining

;

Each of the isolation chamber and the sampling channel are connected to the inlet port via a branch point, the junction allowing a first portion of blood to flow into the isolation chamber and through the air permeable blood barrier to the isolation chamber. to expel the air inside and into the isolation chamber

allowing a second portion of blood to be sequestered, bypassing said isolation chamber and a first portion of said blood isolated within said isolation chamber, towards said outlet port and said sampling device; A blood isolation device sized and configured to allow it to be directed into a tract.

8.

A blood isolation device according to claim 6 or 7, wherein said entry port is connected to sai

d patient needle through said first portion of said blood collection path.

9.

A blood isolation device according to any one of claims 6 to 8, wherein said outlet port is con nected to said sample collection device via a second portion of said blood collection pathway.

10.

The blood isolation device of claim 6 or 7, wherein said air permeable blood barrier comprise s an air permeable material that at least partially seals upon contact with blood.

11.

The blood isolation device of claim 6 or 7, wherein said isolation chamber includes an isolatio n channel defined within said housing.

12. The blood isolation of claim 11,

wherein said isolation channel has a proximal end connected with said inlet port and a distal end with said vent containing an air permeable blood barrier. Device.

13. A

body fluid isolation device, comprising

an inlet port,

an outlet port connected to said inlet port, and an

isolation chamber connected to said inlet port via a branch point, wherein said air permeable body fluid barrier comprises: an isolation chamber having a vent containing

a housing containing and defining the inlet port, the outlet port, and the isolation chamber,

wherein the isolation chamber and the junction direct a first portion of bodily fluid from the i nlet port to the air permeable bodily fluid barrier; The air permeable bodily fluid barrier compr ises an air permeable material that forms a barrier to bodily fluids upon contact with bodily flu ids, such that contact with bodily fluids results in an increase in air flow within the isolating ch ambers. and a second portion of bodily fluid from the inlet port to the outlet port through the bifurcation bypasses the isolation chamber and the first portion of the bodily fluid. Become a b ody fluid isolation device.

14. A

body fluid isolation device, comprising

an inlet port,

an outlet port connected to said inlet port, and an

isolation chamber connected to said inlet port via a branch point, wherein said air permeable body fluid barrier comprises: and a housing containing and defining said inlet port, said outlet port, and said isolation chamber , said isolation chamber and said branch point

being adapted for a first flow of bodily fluid from said inlet port. configured to direct one po rtion toward said isolation chamber toward said air permeable body fluid barrier, said air perm eable body fluid barrier comprising an air permeable material that forms a barrier to body flui ds upon contact therewith, such that: Formation of the barrier permits isolation of a first porti

on of bodily fluid within the isolation chamber and allows a second portion of bodily fluid from the inlet port to pass through the junction toward the outlet port and into the isolation chamb er and into the isolation chamber. A bodily fluid isolation device configured to allow a first port ion of the bodily fluid to be bypassed.

15.

The body fluid isolation device of claim 13 or 14, wherein the air permeable body fluid barrie r comprises an air permeable material that seals upon contact with body fluids.

16.

A body fluid isolation device according to claim 13 or 14, wherein said isolation chamber incl udes an isolation channel defined within said housing.

17. The method according to claim

13 or 14, further comprising a blood collection path connected to said inlet port, said blood c ollection path conveying a second portion of said body fluid from said inlet port to said outlet port through said branch point. A bodily fluid isolation device as described.

18. The housing

includes a lower member mating with an upper member, the lower member and the upper m ember each defining a portion of each of the inlet port, the outlet port and the isolation cham ber. 15. A body fluid isolation device according to claim 13 or 14, wherein

19. A body fluid isolation device according to claim 13 or 14,

further comprising .

20. The housing

includes a lower member mating with an upper member, each of said lower member and sai d upper member being associated with each of said inlet port, said outlet port, said isolation c hamber and said sampling channel. 20. A bodily fluid isolation device according to claim 19, w hich defines a portion of a.

21.

A blood isolation system comprising:

a blood collection path having a patient needle and a sample collection device; and a

blood isolation device

, said blood isolation device comprising:

an isolation chamber having an inlet port connected to the patient needle; an

outlet port connected to the sample collection device; an

isolation chamber having a vent containing an air permeable blood barrier; and a

distal end connected to the outlet port. a sampling channel, and a housing containing

and defining said inlet port, said outlet port, said isolation chamber, and said sampling chann el, said isolation chamber and said sampling channel each diverging through said branch poi nt. Connected with an inlet port, the junction allows a first portion of blood to flow into the iso

lation chamber, expel air within the isolation chamber through the air permeable blood barrier, and be sequestered within the isolation chamber. and a second portion of blood bypasses the i solation chamber and the first portion of the blood isolated within the isolation chamber and is directed into the sampling channel toward the exit port and the sample collection device. A bl ood isolation system sized and configured to enable. 22. The blood isolation system of claim 2 1 , wherein said entry port is connected to said patient needle through said first portion of s aid blood collection path. 23. The blood isolation system of claim 21 , wherein said exit port i s connected to said sample collection device via a second portion of said blood collection path way. 24. The blood isolation system of claim 21, wherein said air permeable blood barrier co mprises an air permeable material that at least partially seals upon contact with blood. [Claim 25]

25. The blood isolation system of Claim 24, wherein the isolation chamber includes an isolati on channel defined within the housing. 26. The blood isolation of claim 25, wherein said isola tion channel has a proximal end connected with said inlet port and a distal end with said vent containing an air permeable blood barrier

.

system.

detailed description open —

Description:

CROSS -REFERENCE TO RELATED APPLICATIONS This application is entitled "Blood Sample Op timization System and Blood Contaminant Isolation Apparatus and Method," filed on Apr. 27, 2016

. U.S. Nonprovisional Application No. 15/140,443, entitled "Blood Sample Optimization Syste m and Blood Contaminant Isolation Apparatus and , 448, and both of these U.S. nonprovision al applications are U.S. Provisional 62/196,797, U.S. Provisional Application No. 62/ 238,636 e

ntitled "Blood Isolation System for Clean Blood Collection," filed Oct. 7, 2015; No. 62/318,19 4, entitled "Blood Sample Optimization System and Blood Contaminant Isolation Apparatus an d Method," filed herein, the disclosure of which is incorporated herein by reference in its entir ety. shall be included in the Bacteremia is the presence of microorganisms in the blood. Seps is, on the other hand, is bacteremia with clinical symptoms and signs such as fever, tachycardi a, tachypnea and hypotension. Bacteremia and sepsis are associated with high mortality, hosp italization incidence and length of stay and associated costs. many bacteremia

, sepsis, fungemia, and other pathogens do occur in hospitals or other health care facilities, a nd
catheters and venipunctures are sources of contamination as potential carriers of these patho gens.

[0003] Blood cultures are the standard test used
to detect microbial pathogens associated with bacteremia and sepsis in the blood of patients .
The term blood culture refers to a single venipuncture from a peripheral site or central or arte rial line in which blood is inoculated into one or more blood culture bottles
or vessels
. One bottle is considered one blood culture and two or more are considered a set. Multiple sets are obtained from multiple venipunctures and are associated with different sites in the pa tient.

[0004]
Although these methods enable microbial identification and susceptibility testing, which are i mportant factors in the management of sepsis, their

lack of rapid results and low sensitivity to nasty pathogens pose challenges for improvement . This has .

[0005]

The collection of blood samples for blood culture is an important component of modern patient care, both positively impacting patient outcome by providing an accurate diagnosis and eliminating unnecessary antibacterial treatments. It can also adversely therapy affect .

One consequence of blood culture collection is contamination. Contamination of blood cultures can lead to false positive culture results and and/or significantly increase healthcare-related costs. Sources of blood culture contamination include inadequate skin disinfection, inadequate collection tube disinfection, and contamination of the initial blood draw, which can skew results. Blood culture collection kits generally include a "butterfly" set, infusion set, or other type of venipuncture device provided and an aerobic

It consists of a blood culture bottle and an anaerobic blood culture bottle. A variety of different bottles are also available depending on inspection requirements . These bottles are specially designed to optimize the collection of both aerobic and anaerobic organisms. In conventional kits, the bottle used is commonly known as a "vacutainer", which is used to create a vacuum inside the tube to facilitate the collection of a predetermined amount of liquid, such as blood. A blood collection tube formed from a sterile glass .

False positive blood cultures are generally the result of poor sampling techniques. They cause antibiotics to be used when they are not needed, increasing hospital costs and patient anxiety. Blood cultures are taken from a needle prick into the skin, after which a Vacutainer® . Contamination can result from improper or . It can also result from the piercing of the skin by the needle during insertion, which draws pierced skin cells and associated contaminants into the sample . [0009] Blood flow through a hypodermic needle is laminar, which causes a flow velocity gradient across the flow tube when . Strong aspiration of the blood or use of a very small hypodermic needle causes lysis and

release of potassium from the red blood cells, thereby obtaining a blood sample.

The pull may become abnormal.

[0010]

In another example, some patients have delicate veins which are subject to pressure drop or for the patient's condition. Can collapse under vacuum. Such venous collapse is dangerous and very difficult to control because such a condition cannot be known in advance . Various strategies have been implemented to reduce the contamination rate of blood cultures, such as staff training in sterile collection techniques , feedback on contamination rates, and the introduction of blood culture collection kits . Skin antisepsis can reduce contamination concerns, but more than 20% of skin microbes are located deep in the dermis and are not affected by antisepsis. Changing needles prior to bottle inoculation is not recommended as it increases the risk of needlestick injuries without reducing contamination rates. [0012] Some conventional systems and techniques for reducing contamination of blood cultures involve discarding the initial aliquot of blood taken from central venous catheters, venous punctures and other vascular access systems. . However, these systems either require the user to mechanically manipulate the intravascular device or require a complicated series of steps that are difficult to ensure. SUMMARY OF THE INVENTION [Problem to be Solved by the Invention]

The present specification presents systems

and . In some implementations, the systems and methods can eliminate variability in user disi nfection
and also eliminate the risk of skin cells entering blood culture samples. Other than potentially indicating when to attach a Vacutainer® or other blood collection device (i.e., a syringe) to ob tain a contaminant-free blood sample, the systems and methods disclosed
herein are does not require changes to existing clinical processes. [0014] In some implemen tations of the systems and methods disclosed herein, blood sampling is accomplished passivel y through the use of the patient's own blood pressure, thereby reducing the risk of venous ru pture and reducing current practice. Eliminates additional user steps beyond duties. The syste m and method can be adapted to suit short-path direct puncture or butterfly venipuncture sys tems. catheter

It can also be used with samples taken through the tube.
SUMMARY OF THE INVENTION In
one
aspect, a blood isolation device is presented. A blood isolation device includes an inlet port a nd an outlet
port . The blood isolation device further includes an isolation chamber connected to the inlet p ort, the
isolation chamber having a vent including an air permeable blood barrier. The blood isolation 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 isolation device is described that is connected to a blood collectio n path. The blood collection path has a
patient needle and a sample collection device. The blood isolation device includes an entry por t connected to the patient needle and an
isolation chamber connected to the entry port, the isolation chamber having a vent including a n air permeable blood barrier
. The blood isolation device further includes a sampling channel having a proximal end connec ted to the inlet port
, and an outlet port connected to the distal end of the sampling channel and the sample collec

tion device . [0017] In yet another aspect, a blood isolation device is described that interfac es with a blood collection system. The blood collection system includes a patient needle for all owing a blood sample to be drawn from a patient and a sample needle that is sealed and adap ted to receive an evacuated blood collection tube. A blood isolation device includes an inlet po rt connected to a patient needle for receiving a blood sample from . blood isolation device

The device is an isolation
chamber isolating an initial
portion of the blood sample before the sample needle is unsealed by the evacuated blood coll ection tube. further includes an isolation chamber for The blood isolation
device
further includes a sampling channel having a proximal end connected to the inlet port, the sa mpling channel carrying a subsequent portion of the blood sample when the sample needle is opened by the evacuated blood collection tube. . The blood isolation device further includes an exit port connected
with the distal end of the sampling channel for carrying subsequent portions of the blood sam ple 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 collection s ystem for enabling and obtaining one or more samples of a patient's blood, a blood collection system for potentially contaminated by the venipuncture process and a false pathogen in the patient's blood. a blood isolation device for receiving and isolating an initial portion of one or more samples of patient blood that may result in a positive identification . A blood collection s ystem includes a patient needle configured for venipuncture of a patient to enable withdrawa l of a sample of the patient's blood , a blood collection channel connected to the patient needl e for carrying the blood sample, and a blood sample. a sample needle configured to receive th e evacuated blood collection container for withdrawing and containing a subsequent portion of the sample . [0020]

In yet another aspect, a blood isolation device is disclosed and described. In some implementations, a blood isolation device can include an
inlet port, an outlet port connected to the inlet port, and an isolation chamber connected to the inlet port . The isolation chamber can have a vent
containing an air permeable blood barrier . A blood isolation device is connected along the blood collection path between the patient needle and the sample needle and includes an entry port for receiving a blood sample . A blood isolation device is an isolation chamber connected with an inlet port for receiving and an air permeable blood barrier to isolate at least a first portion of the initial volume of blood sample. further comprising an isolation chamber having a vent containing a . The blood sequestration device is a sampling , the sequestration chamber receiving at least a first portion of an initial volume of blood sample.

Further includes a sampling channel that, when isolated, conveys subsequent amounts of the blood sample to the evacuated blood collection container.
The blood isolation device further includes an outlet port connected to the distal end of the sampling channel for outputting a subsequent volume of blood
sample . The details of one or more embodiments are set forth in the accompanying drawings and the description below
.
Other features
and advantages will be apparent from the specification and drawings, and from the claims.
BRIEF DESCRIPTION OF THE DRAWINGS
[0023]
These and other aspects will now be described in detail with reference to the following drawings.
1 shows a blood sample optimization system; FIG.

FIG. 2 shows a blood sample optimization system according to an alternative implementation;
FIG. 3 shows a blood sample optimization system according to another alternative implement ation;
FIG. 4 shows a blood sample optimization system according to another alternative implement ation;
FIG. 5 shows a blood sample optimization system according to another alternative implement ation;
FIG. 6 shows a blood sample optimization system according to an alternative implementation;
FIG. 7 is a flowchart of a method for optimizing blood culture quality;
FIG. 8A illustrates a blood isolation system for non-contaminated blood collection, according t o some implementations;
FIG. 8B illustrates a blood isolation system for clean blood collection, according to some imple mentations.
FIG. 8C illustrates a blood isolation system for clean blood collection, according to some imple mentations;
FIG. 8D illustrates a blood isolation system for clean blood collection, according to some imple mentations.
FIG. 8E illustrates a blood isolation system for clean blood collection, according to some imple mentations.
FIG. 9 shows a path splitter for use in a blood sequestration system;
FIG. 10A shows a blood isolation system for non-contaminated blood collection according to a n alternative implementation;
FIG. 10B shows a blood isolation system for non-contaminated blood collection according to a n alternative implementation;
FIG. 10C shows a blood isolation system for non-contaminated blood collection according to a n alternative implementation;
FIG. 10D shows a blood isolation system for non-contaminated blood collection according to a n alternative implementation;
FIG. 11A shows a blood isolation system for non-contaminated blood collection according to a nother alternative implementation;
FIG. 11B shows a blood isolation system for non-contaminated blood collection according to a nother alternative implementation;
FIG. 11C shows a blood isolation system for non-contaminated blood collection according to a nother alternative implementation;
FIG. 11D shows a blood isolation system for non-contaminated blood collection according to a nother alternative implementation;
FIG. 11E shows a blood isolation system for non-contaminated blood collection according to a nother alternative implementation;
FIG. 12A shows a blood sample optimization system including a blood isolation device accordi

ng to yet another alternative implementation;

12B shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation; FIG.

FIG. 12C shows a blood sample optimization system including a blood isolation device accordi ng to yet another alternative implementation;

FIG. 12D shows a blood sample optimization system including a blood isolation device accordi ng to yet another alternative implementation;

FIG. 13A shows blood sample optimization system 1300 according to yet another alternative i mplementation.

FIG. 13B shows blood sample optimization system 1300 according to yet another alternative i mplementation.

FIG. 13C shows blood sample optimization system 1300 according to yet another alternative i mplementation.

FIG. 13D shows blood sample optimization system 1300 according to yet another alternative i mplementation.

FIG. 14A illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14B illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14C. False positives in blood cultures or tests performed on patient blood samples.

FIG. 10 illustrates yet another implementation of a blood collection system that isolates initial aliquots or samples of contaminants to reduce them.

FIG. 14D illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14E shows yet another implementation of a blood collection system that isolates contami nants in the initial aliquot or sample to reduce false positives in blood cultures or tests perfor med on patient blood samples.

15A-B illustrate a blood isolation device and method of using the same according to yet anoth er implementation.

15B illustrates a blood isolation device and method of using the same according to yet anothe r implementation; FIG.

FIG. 15C illustrates a blood isolation device and method of using the same according to yet an other implementation;

FIG. 15D illustrates a blood isolation device and method of using the same according to yet an other implementation;

FIG. 15E illustrates a blood isolation device and method of using the same according to yet an

other implementation;

Figure 15F illustrates a blood isolation device and method of using the same according to yet another implementation;

FIG. 15G shows a blood isolation device and method of using the same according to yet another implementation;

FIG. 16A shows a blood isolation device according to yet another implementation;

16B shows a blood isolation device according to yet another implementation; FIG.

16C shows a blood isolation device according to yet another implementation; FIG.

16D shows a blood isolation device according to yet another implementation; FIG.

Figure 17A shows a lower member of a housing for a blood isolation device;

Figure 17B shows a lower member of a housing for a blood isolation device;

Figure 17C shows a lower member of a housing for a blood isolation device;

Figure 17D shows a lower member of a housing for a blood isolation device;

Figure 17E shows a lower member of a housing for a blood isolation device;

Figure 18A shows a top member of a housing for a blood isolation device;

Figure 18B shows a top member of a housing for a blood isolation device;

Figure 18C shows a top member of a housing for a blood isolation device;

Figure 18D shows a top member of a housing for a blood isolation device;

Figure 18E shows a top member of a housing for a blood isolation device;

Figure 18F shows a top member of a housing for a blood isolation device;

Figure 19A shows a blood isolation device having an upper member that mates with a lower member.

Figure 19B shows a blood isolation device having an upper member that mates with a lower member.

FIG. 20 shows a blood sample optimization system including a blood sequestration device;

Figure 21 shows a non-vented blood isolation device using a wicking material chamber.

Figure 22A shows the material composition of a filter for isolating blood in an isolation chamber of a blood isolation device;

Figure 22B shows the material composition of a filter for isolating blood in an isolation chamber of a blood isolation device;

FIG. 23A shows another implementation of a blood isolation device using vacuum force from a blood collection device;

Figure 23B shows another implementation of a blood isolation device using vacuum force from a blood collection device. Like numbers in the various drawings indicate like elements.

DETAILED DESCRIPTION OF THE INVENTION

[0024]

The present invention provides blood sample optimization that reduces or eliminates contaminants in a drawn blood sample and, as a result, reduces or eliminates false positive readings in blood cultures or other tests of the dr

awn blood sample.

A system and method are described. In some implementations, the blood sample optimization system includes a patient needle for vascular access to the patient's bloodstream and a blood collection container such as a vacutainer or evacuated blood collection tube or other and a blood

isolation device positioned between the patient needle and the sample needle. The blood isola tor will remove the first aliquot of potentially contaminated blood.

and bypasses

the isolation chamber to carry potentially uncontaminated blood between the patient needle a nd the sample needle after the first aliquot of blood has been isolated in the isolation chambe r.

A sampling channel can be further included.

FIG .

1 shows a blood sample optimization system according to some implementations. The syste m includes a patient needle 1 for puncturing the patient's

skin to access the patient's vein and intravenous blood therein

.

The system is housed within

a resealable boot 10, luer-activated valve, or other collection interface or device and initially s ealed by the resealable boot 10, luer-activated valve, or other collection interface or device. It further includes a sample needle (ie

, a resealably sealed needle for use with a Vacutainer® or the like) 5, which may be included. The resealable boot 10 can be pushed

by or around the sample needle 5 by using a Vacutainer® bottle (not shown) for collecting th e patient's blood.

The system

can further include a low volume chamber 30 leading to the sample needle 5, but

also includes a hole or one or more channels 45 leading to the isolation chamber 55 formed b y the housing 50. FIG. Isolation chamber 55 is a chamber for receiving and holding an initial aliquot of the patient's blood, which can be

.

, channels, passages, locks, or other structures. Initial blood draws

generally contain or are more

susceptible to contain microorganisms or other pathogens that cause bacteremia and sepsis t han subsequent blood draws. The isolation chamber 55 can be contained within a rigid housin g, can be a container formed in or defined by the

housing itself, or

can be realized as a tube or lumen.

Isolation chamber 55 can have a predetermined volume, regardless of how it is formed and i mplemented. In some implementations

, the predetermined volume is based on the volume of the patient needle, i.e.,

ranges from a volume less than the volume of the patient needle to any volume to a volume g reater than 20 times the volume of the patient needle. can be done

.

The predetermined volume of isolation chamber 55 can also be set to conserve or minimize th e amount of blood that is isolated and disposed of . Isolation chamber 55 may be formed, co ntained, or housed within chamber housing 50 and may be made of plastic, rubber, steel, alu minum, or other suitable material

. For example, isolation chamber 55 can be formed from flexible tubing or other elastomeric material . The isolation chamber 55 further includes an air permeable blood barrier 20 that all ows air to exit the isolation chamber 55 . As used herein, the term "air permeable blood barri er " refers to an air permeable but substantially blood impermeable substance, material or str ucture.

means. Representative examples are hydrophobic membranes and coatings, hydrophilic mem branes or hydrophilic

coatings combination with hydrophobic membranes or coatings, meshes, filters, mechanical v alves

, antimicrobial materials, or the isolation chamber 55 is Any other means capable of expelling air from isolation chamber 55 when filled with blood may be included. In various exemplary e mbodiments

, the air permeable blood barrier can be formed by one or more materials

that allow , such materials comprising: Completely or partially sealed to prevent or block the passage of air and/or

liquids . In other words,

the material forms an air permeable barrier prior to contact with the liquid. After contact with liquid, the material

substantially or completely prevents further passage of air and/or liquid. Holes or channels 4 5 may be of any desired length, cross-sectional shape or size and/or be formed away from lo w volume chamber 30 at any desired angle or orientation

. can be done. The hole or channel 45 may also include a one-way flap or valve 60 that retain

s the first aliquot of blood sample within the isolation chamber 55 . In some particular implem entations , the holes or channels 45 allow unidirectional blood flow from the low volume cham ber 30 to the isolation chamber 55 .

can include a "duckbill" valve or flapper valve 60 or the like for Air permeable blood barrier 20 may also be constructed of a material that allows air to escape but seals upon cont act with blood , thereby not allowing outside air to enter isolation chamber 55 . This seal eliminates the need for valves.

Valve 60 can be any type of valve or opening/closing mechanism. Chamber 30 is designed to retain substantially no residual blood and can be configured to retain or pass a ce rtain volume or percentage of blood to isolation chamber 55 . Similarly, the isolation chamber 55 may also include any type of coating, such as an antimicrobial coating, or a coating that assists in identifying a nd/or diagnosing components of the isolated primary blood draw . Housings 50 and 40 may be formed from any suitable material, including plastics such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric materials, rubber, steel, or aluminum . The air permeable blood barrier 20 is activated upon contact with blood from the first draw o r when the expulsion of air is stopped, or any combination of events and blood in the isolation chamber 55. , color-providing substances or other signaling mechanisms. Air permeable barri ers may also include hydrophobic membranes or covers that block or prevent inadvertent or p remature sealing of the filter by external fluid sources, splashes, etc.

An outer layer can be included. The isolation chamber 55 can also be translucent or transpare nt to allow the user .

FIG.

2 shows a blood sample optimization system according to some alternative implementations. In the implementation shown in FIG. 2 , an isolation chamber 55 or waste chamber surrounds the patient needle 1 and an open-ended
cuff or housing is connected to the waste chamber and surrounds the sample needle housing base and
housing . The patient needle 1 and the sample needle 5 are connected to each other by a boo t 56
which forms a continuous blood collection flow path therethrough. Boot 56
includes a single hole or channel leading from the blood collection channel to isolation chambe r 55 .
The device can include multiple holes or channels in other implementations . Each hole or cha nnel can include a one-way valve
and can be sized and adapted for a predetermined amount of blood flow.
Isolation
chamber 55 contains an air permeable blood barrier. The
filter
may further include sensors or indicators, respectively, for sensing and/or indicating when a p redetermined volume of blood has been collected in the isolation chamber 55 .
The instructions alert the user to attach an evacuated blood collection tube or bottle, such as a Vacutainer®, to the sample needle 5 . The housing for the isolation chamber 55
can be of any size or shape, and the internal space within the housing or
can include any type of material to define the volume. The interior space is initially filled with air only, but
can also be coated with agents or substances such as decontamination agents, coagulants, an d the like. When the evacuated blood collection tube is attached to the sample needle 5, blood automatically
flows into the patient needle 1, through the blood collection channel and the sample needle 5 into the bottle. The sample needle 5
is
covered by a resealable boot, coating or membrane that seals the sample needle when no blo od collection bottle is attached to the sample needle.
FIG.
3 shows a blood sample optimization system according to some alternative implementations. In the illustrated implementation
, sample needle 5 is surrounded by a resealable boot or membrane and is also
connected . A blood flow path is formed through the sample needle and the patient needle.
The connection between
the sample needle and the patient needle includes a 'T' or 'Y' connector 102 that includes a flo w path, port or opening leading from the main blood flow path to the isolation chamber 104 .

The T or Y connector 102 includes a flap or one-way valve and has holes sized and adapted for a predetermined flow rate of blood .

Isolation chamber 104 is formed from a tube

or can be formed by a rigid housing, initially filled with air. The isolation

chamber 104 receives blood

flowing . The isolation chamber 104 preferably includes an air permeable blood barrier 106 at the distal end of the tube forming the isolation chamber 104

and connected at the proximal end to the T or Y connector 102 . The T or Y connector 102 can branch at any desired angle

for most efficient blood flow , minimizing or eliminating mixing of the initial aliquot of blood wi th the main blood sample. To this end, the openings and junctions between the channels and t he main blood flow channel can be shaped to minimize. In some alternative implementation s, the sample needle is attached to any length of tubing whose opposite end is connected to a T or . I can . The isolation chamber 104 can be of any shape or volume so long as the initial al iquot contains a predetermined amount of blood sample . The T or Y connector 102 can also i nclude openings or channels 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 predeter mined amount of blood has been collected in the isolation chamber or when the released air h as reached a certain threshold, i.e. zero. can. The tube also includes a clip 109 that can be us ed to pinch and prevent fluid flow through the tube

can be done. Once the air permeable blood barrier and primary chamber are sealed, the first aliquot of blood is confined to the isolation chamber 104 and an evacuated blood collection tu be, such as a Vacutainer® bottle, is

used to obtain the sample. It is attached to the sample needle 5 . The blood collection tube ca n be removed and the sample needle 5 resealed. Any number of subsequent blood collection t ubes can be attached for additional blood draws or samples. When all blood draws are comple ted, the system is discarded, leaving the first aliquot of blood trapped in isolation chamber 10

4 . FIG. 5 shows a blood sample optimization system according to some alternative impleme ntations. In the illustrated implementation , the sample needle 5 is connected by tubing to the patient needle. A "T" or "Y" connector 120 is added at any desired location along the tube to i nclude an opening, port or flow path leading to isolation chamber 204, substantially as describ ed above. FIG. 6 illustrates a blood sample according to some alternative implementations in which an isolation chamber 304 configured as the primary collection channel receives the first aliquot of blood and is provided adjacent to the blood collection channel. An optimization syst em is shown. The isolation chamber 304 can surround the blood collection channel, patient ne edle 1 and/or sample needle 5 . The primary collection channel may include T or Y connectors 120, or other types of openings or channels. The isolation chamber 304 is an air permeable bl ood barrier

and may also include an indication that a fluid, such as blood, has been contacted, as describe d above. In some implementations, either or both of the patient needle 1 or the sample nee dle 5 can be replaced with luer lock
or luer lock female connectors. However, in various implementations , the connector at the sa mple needle end of the blood sample optimization system is first sealed and the first aliquot al low to divert the blood of the In this way, the system passively and automatically uses the pat ient's own blood pressure to overcome the ambient air pressure in the isolation chamber, forc e air through the air permeable blood barrier, and replace the air in the isolation chamber with blood. FIG . 7 is a flowchart of an exemplary method for optimizing blood culture quality. At 702 , a clinician inserts a needle into a patient's vein. At 704, blood flows into the isolation ch amber, forcing . In some implementations, the volume of the isolation chamber is less than 0.

1 cubic centimeters (cc).

From full to 5 cubic centimeters (cc) or more. The isolation chamber is sized and adapted to c
ollect
a second portion of the blood sample and other subsequent portions or a first portion of the bl
ood sample that is more susceptible to contamination than subsequent collections .
The isolation chamber has an air permeable blood barrier
through which air can be expelled by the blood expelled from the patient's veins
so that such blood is
a vacutainer Before being drawn into or otherwise entering a ® or other bottle, it inevitably a
nd
automatically flows into the isolation chamber. As the isolation chamber fills, blood collects o
r otherwise contacts an air permeable blood barrier that
blocks or prevents blood from passing through. At 706, once the blood contacts the entire inte
rnal surface area of the air permeable blood barrier, the air permeable blood barrier is closed
and air no longer flows out or in. At 708, the clinician is provided an indication or can view the
full chamber indicating that an evacuated blood collection tube , such as a Vacutainer®, can b
e attached. The indicator may include visibility of the primary chamber to see if the primary c
hamber is full , eg, a blood barrier that changes color, or other indicator . Since the fill time of
the isolation chamber may be substantially instantaneous, such an indication, if present, may
simply be that the isolation chamber is filled. [0042]

Before the evacuated blood collection tube is attached, communication between the needle, the sampling channel, and the isolation chamber
is restricted by the sealing of the isolation chamber's blood barrier, thus isolation does not allo w air to re-enter
the system . Sealing of the communication path is accomplished by mechanical twisting or oth er
action , small hole or tortuous path,
obviating the need for a separate valve or mechanical action or manipulation by the clinician. At 710, the evacuated blood collection tube is removed, a self-
sealing membrane seals the sample needle, and at 712, a further subsequent evacuated bloo d collection tube
can be attached. At 714, once the sample has been taken, the device is removed from the pat ient and discarded
.

[0043]

Figures 8A-8E illustrate an exemplary blood sample optimization
system . Blood sample optimization system 800 includes an
entry port 802 that can be connected to tubing, a patient needle (or both), or other vascular o r venous access device, and a
first exit to isolation chamber tubing 806 and sample collection tubing.
a path splitter 804 with a second exit to 808 ; One or both of isolation chamber tube 806 and sample collection
tube 808 can be formed from tubing. In some implementations , isolation chamber tube 806 i s sized
to accommodate a specific amount of initial blood sample .
The sample collection tube 808 is used once the isolation chamber tube 806 is full.
When prompted, accept a blood sample. The sample collection tube 808 can be
connected to a Vacutainer® base or housing 810, or other blood sample collection device . B lood isolation system 800 further includes blood isolation device 812, which includes housing 818, shown in more detail in FIGS . It includes a sampling channel 820 that defines a pathwa y or is connected at either end with a clean sample collection tube 808 . The sampling flow pa th 820 can be curved through the housing 818 to better secure and stabilize the housing 818 i n position along the clean sample collection tube 808 . Blood isolation device 812 further inclu des an isolation chamber 822 or other chamber connected with isolation chamber tube 806 . Isolation chamber 822 terminates . The air-permeable blood barrier 824 also reacts upon full contact with blood as an indicator that proper collection of a blood sample (i.e., an uncontami

nated blood sample) can begin.

It may contain a colorant that changes to a different color. Other indicators such as small light s, sound generating mechanisms, etc.
can be used. In some implementations, the air permeable blood barrier is positioned perpendi cular to
the orientation , but
may be positioned at any distance or orientation to conserve space and materials used for ho using 818. can Housing 818 and its contents
can be formed from any rigid or semi-rigid material or range of materials.
FIG.
9
shows a path splitter 900 for use in, for example, blood isolation systems such as those show n in FIGS. 8A-8E. Path splitter 900 includes inlet port 902 , main conduit outlet port 904
and isolation channel outlet port 906 .
The entry port 902 can be connected to a main tube that is also connected to the patient nee dle system or directly to the patient needle. The main line outlet port 904 can be connected to a
main line tube to a blood collection system, such as a Vacutainer® base or housing, or directl y to such a blood collection system.
The isolation channel
outlet port 906
can be connected to an isolation tube for receiving and isolating the first sample of blood up t o a measured volume or predetermined threshold. Alternatively, the isolation flow path outlet port
906 can connect to the isolation chamber. The isolation channel outlet port 906
is preferably angled from 20 to 70 degrees from the main conduit outlet port 904, while the m

ain conduit outlet port
Port 904 is preferably in line with inlet port 902 . Once an initial blood
sample
has been isolated in an isolation tube or isolation chamber according to the mechanisms and t echniques described herein, subsequent blood samples flow into inlet port 902 unobstructed. directly out of the main conduit outlet port 904 at . 10A-10D show blood isolation device 100 0 according to another implementation
.
Blood isolation device 1000 includes
inlet port 1002 , main outlet port 1004 , and isolation flow port 1006
. Entry port 1002 can be connected with a patient needle or associated tubing.
The main exit port 1004 can be connected to a blood sampling device such as a Vacutainer®, associated tubing, or a luer-
actuated valve. An isolation flow port 1006
separates from the main exit port 1004 into an isolation chamber 1008 . In some implementa tions, isolation
chamber 1008 is formed as a spiral channel within housing or other container 1001 .
Isolation chamber 1008 is connected
at its distal end to air permeable blood barrier 1010, substantially as described above . Air w ithin the isolation chamber 1008 is expelled by the first aliquot of blood directed into the isolat ion flow path
port 1006
through .
Once the isolation chamber 1008 is filled, further
blood draws through the main exit port 1004 are accomplished and these samples are clean.
11A -
11E show blood isolation device 1100 according to another alternative implementation. Bloo d isolation device 1100 includes an
inlet port 1102 similar to the inlet ports described above, a main outlet port 1104
and an isolation flow port 1106 separate from main outlet port 1104 and inlet port 1102 .
The isolation flow port is connected to isolation chamber 1108 .
In the implementation shown in FIGS. 11A-11E , the blood isolation device
includes a base member 1101 having a flow path therein that functions as an isolation chamb er 1108 .
The flow path can be formed as a tortuous path through the base member 1101 while the bas e member 1101
is shaped and shaped to rest on the patient's limb. A portion of isolation chamber 1108 may p rotrude from or near the top surface of the base member just prior to exiting air permeable . Indicator 1109 can be made of a transparent material or a material that changes color when

in contact with blood . In some implementations, the blood isolation device 1100 includes a n ormally closed needle, vacutainer.RTM.

A blood collection device 1120, such as a shield or other collection device, may be included. Bl ood collection device 1 120 is manufactured and sold with blood isolation device 1100 for effic iency and convenience so that the
first aliquot of blood that may be contaminated by the patient needle insertion process can be isolated. be able to. Accordingly, the blood collection device 1120 can collect and ensure a cle an blood sample so as to reduce the risk of false positive tests . [0052] Figures 12A-12D illust rate a blood sample optimization system 1200 according to yet another alternative impleme ntation . System 1200 includes a blood isolation device 1202 for attachment to a blood collect ion device 1204, such as a Vacutainer® or other collection and sampling device. Blood isolatio n device 1202 receives an initial aliquot or volume of blood before a Vacutainer® container or vial is attached to the collection needle of blood collection device 1204 and transfers that initi al aliquot or volume to blood isolation device 1202 . Constructed and . [0053] In some imple mentations, the blood isolation device 1202 can include an inlet port 1212, a main outlet port, and an isolation flow path port. Entry port 1212 can be connected to a patient needle or assoc iated tubing . The main exit port 1214 is an evacuated blood collection container or vacutaine r.

can be connected to a normally closed needle or device to allow connection with other collecti on devices such as ®, associated tubing, luer connectors, syringes,
luer actuated valves
. The isolation flow port separates the isolation chamber 1218 from the main exit port. In so me implementations, isolation chamber 1218 is formed
. The isolation chamber 1218 can be a tortuous channel, such as a U-shaped channel, an S-sh aped channel, a spiral channel, or any other tortuous channel. Isolation device 1202 can inclu de a housing or other enclosure and one or more channels formed therein . As shown in FIGS. 12A and 12B, isolation device 1202 includes body 1206 and cap 1208 . One or more cavities o r channels are formed in the body 1206, and the cavities or channels are further formed with one or more arms 1210 extending from the cap 1208, the one or more arms 1210 extending f rom the cavities or channels of the body 1206. A primary collection port and a main outlet por t . [0055] Figures 13A-13D illustrate a blood sample optimization system 1300 according to yet another alternative implementation . System 1300 includes a blood isolation device 1302 f or attachment to a blood collection device 1304, such as a Vacutainer® or other body fluid col lection and sampling device. Blood isolation device 1302 is a Vacutainer® container or vial blo od collection device 1304 .

to receive an initial aliquot or volume of blood and sequester that
initial
constructed and arranged. Blood isolation device 1302 includes housing 1301 having inlet po rt 1314 , main outlet port 1312 and isolation flow path port 1316
. Entry port 1314 can be connected to a patient needle or associated tubing. The main exit po rt 1312 is a normally closed needle or needle to allow connection with other collection devices such as evacuated blood collection containers or vacutainers, associated tubing, luer connecto

rs , syringes, luer actuated valves. It can be connected to a device . An isolation flow port 131 6 separates from the main inlet port 1314 into an isolation chamber 1318 . In the embodime nt shown in FIGS. 13A-13D, isolation chamber 1318 is formed as a cavity or chamber within h ousing 1301 or by walls defining housing 1301 .

be done. The isolation chamber 1318 can be a
tortuous
defined by the cooperation and connection of the housing 1301 and the cap 1307. The cap 13 07
can
include protrusions 1305 that provide one or more walls or directors for the tortuous flow path within the isolation chamber 1318 . Projections 1305 from cap 1307
can be straight or curved,
can extend from cap 1307 at any angle or orientation. be able to.
When the cap 1307 is connected with the housing 1301 to complete the formation of
the isolation chamber 1318 , the projection 1305 forms at least a portion of the tortuous flow path
formed by the tortuous flow path within the isolation chamber 1318 . An initial aliquot or volu me of blood or
other bodily fluid is sequestered in the sequestration channel .
Isolation chamber 1318
includes air permeable blood barrier 1310 substantially as described above
.
Air within the isolation chamber 1318 is expelled through the air permeable blood barrier 131 0 by the first aliquot of blood supplied into the isolation chamber 1318 by the patient's blood pressure
. Once the isolation chamber 1318 is filled and the air within the isolation chamber 1318 is ex pelled,
a
The patient's blood pressure forces more blood into the blood isolation device 1302, and in pa

rticular the exit port 1312 , until a force such as a vacuum or other pressure is provided
Inadequate to drive or provide.
Additional blood draws can be taken through the main exit port 1312 and
these samples are not contaminated because any contaminants are sequestered in the isolatio n chamber 1318 along with the blood of the first aliquot.
FIGS. 14A-14E further illustrate a blood collection system 1400 for isolating contaminants of i nitial aliquots or samples to reduce false positives in
blood cultures or tests performed on patient blood samples. Show another implementation.
Blood collection system 1400 includes a blood isolation device 1401 that can be connected bet ween blood sample collection device 1 403 and a patient needle (not shown) . The blood sam ple collection device 1403 can . Blood isolation device 1401 includes an entry port 1402 that c an be connected to a patient needle that is inserted into the patient's vasculature for access t o and collection of a blood sample . Inlet port 1402 can also be connected to a tube or other c onduit that is also connected to a patient needle . Inlet port 1402 defines an opening to bloo d isolation device 1401, which opening can be of the same cross-sectional dimensions as a tu be or other conduit connected to the patient needle or the patient needle itself.

be. For example, the opening can
be , but may be 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm
) or less. can have diameters equal to or greater than Blood isolation device 1401 further incl udes
an exit port 1404 that defines an opening from blood isolation device 1 401 and to blood sam pling device 1403 . Exit port 1404 can also be connected to
a tube or other conduit that is also connected to blood isolation device 1403 . The exit port 14 04 may be a connector such as an unthreaded interference or glue joint for attachment to a v ariety of devices including, but not limited to,
threaded caps,
luer connectors (male or female), tubing, and the like.

A device
can also be included. Blood isolation device 1401 further includes a sampling
serves as a blood sample pathway once the first aliquot of blood has been isolated. do. Sampli ng channel 1406 can be a channel or conduit of any size , shape or configuration. In some im plementations, sampling channel 1406 has a cross-sectional area substantially similar to the o pening of inlet port 1402 . other fruits

In practice, sampling channel 1406
can gradually diverge from inlet port 1402 to outlet port 1404 . Blood isolation device 1401 f urther includes isolation chamber 1408 , which is connected to and separated from sampling c hannel 1406 anywhere between inlet port 1402 and outlet port 1404
. or diverted, but preferably connected to the proximal end of the sampling channel 1406 near the inlet port 1402 and separated or diverted from . The isolation chamber 1408 is initially ma intained at atmospheric pressure and includes an air outlet 1412 at or near the distal end of t he isolation chamber 1408 opposite the turning point from the sampling channel 1406 . Air ou tlet 1412 includes air permeable blood barrier 1412 . The air permeable blood barrier 1412 ca n be covered with a protective cover 1416, as shown in FIG. 14B . The protective cover 1416 can be sized and configured to prevent a user from touching the air permeable blood barrier 1 412 with their fingers or other external instruments , while still allowing the patient's own blo od pressure to force the isolation chamber. A forced blood supply into 1408 allows air to exit t he air permeable . The protective cover 1416 also prevents or prevents accidental exposure of the air permeable blood barrier to surrounding fluids or droplets.

can be configured.
This can be done in a variety of mechanical ways including, but not limited to, adding a hydro phobic membrane to the protective cover . As shown in FIGS. 14C and 14D, the sampling cha nnel 1406 is cylindrical or frusto-conical in shape from smaller diameters to larger diameters t o minimize the possibility of
. can be done. Similarly, the sampling channel 1406 is formed with a minimal amount or no s harp bends or sharp angles that could lyse red blood cells. Sampling channel 1406 splits near inlet port 1402 through diverting path 1409 into isolation chamber 1408 . Diversion pathway 1409 can , but is preferably similar to the cross-sectional shape of at least a portion of inlet p ort 1402 . In some implementations, sampling channel 1406 and isolation chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414 . Housing 1 41 4 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can ha ve a lower member that sealably mates with the upper member. One or both of the lower and upper members includes a sampling channel 1406 and an isolation chamber 1408 as well as a diversion channel 1409, an inlet port 1402 and an outlet port 1404.

can be read. In some other embodiments,
one or more of diverting path 1409, inlet port 1402, and/or outlet port 1404 are
at least partially closed by a cap member connected to either end of housing 1414. can be for med in
In
membersome
can be connected together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations,
some

can be coated or filled with agents or substances such as decontamination agents, coagulants, and the like. For example, when the sequestration chamber 1408 fills and the first aliquot of b lood
returns to the diversion path 1409 , the final volume of sequestered blood clots, creating a barrier between the sequestration chamber 1408 and the sampling channel 1406 .
A coagulant can be provided in the turning path 1409 to create . 15A-15G show a blood isola tion device 1500. FIG
.
The blood isolation device 1500
is
a needle that is normally closed to allow connection with other collection devices such as evac uated blood collection containers or vacutainers, associated tubing, luer connectors, syringes, luer actuated valves, and the like. or connected to
the device .
Blood isolation device 1500 includes an entry port 1502 that can be connected to a patient ne edle that is inserted into the patient's vasculature
for access to and withdrawal of a blood sample . Entry port 1502 can also be . Entry port 15 02 defines an opening to blood isolation device 1500, which opening can be of the same cross -sectional dimensions as a tube or other conduit connected to the patient needle or the patien t needle itself. For example, the opening can be circular with , but may be 0.01 inch (0.254 m m) to 0.2 inch (5.08 mm) or It can have a larger diameter. Inlet port 1502 may also include a sealed or fluid tight connector or connection such as a threaded or luer fitting or the like . In some implementations, a tube or other conduit that is coupled to the patient needle can be int egrated with the entry port 1502, such as by co-molding, gluing, laser welding, or heat bondi ng the parts together. This allows the blood isolation device 1500 to be manufactured and sol d as a single unit with the patient needle, eliminating the need to connect the patient needle t o the blood isolation device 1500 during blood draw or sampling. The blood isolation device 1 500 has open connections from the blood isolation device 1500 and to the blood sampling de vice.

Further includes an exit port 1504 defining a mouth. Exit port 1504
may also be connected to a tube or other conduit that is also connected to a blood isolation d evice and may include a sealed or fluid tight connector or connection such as a threaded or lu er
fitting . Thus
, as noted above, the blood isolation device 1500 is manufactured and sold as a single unit wit h the patient needle and/or tubing and blood
sample device, and
is attached to the patient needle and blood sample collection device during blood collection or sampling. to the blood isolation device 1500
. Blood isolation device 1500 further includes a sampling
functions as a blood sample channel once the first aliquot of blood has been isolated. do. Sam pling channel 1506 can be a channel or conduit of any size , shape, or configuration. In some implementations, sampling channel 1506 has a cross-sectional area substantially similar to th e opening of inlet port 1502 . In other implementations, sampling channel 1506 can gradually diverge from inlet port 1502 to . Blood isolation device 1500 further includes isolation chamb er 1508 , which is connected to sampling channel 150 at any location between inlet port 1502 and outlet port 1504 .

6 and separated or diverted from the sampling channel 1506 , preferably connected
to and separated or diverted
from . In some implementations, the diversion channel includes a Y-junction. The isolation cha mber 1508
is preferably maintained at atmospheric pressure and includes a

vent . Vent 1510 includes air permeable blood barrier 1512 . FIG. 15C shows blood isolation d evice 1500

with isolation chamber 1508 filled with an initial aliquot or sample of blood from a patient . A ir permeable blood barrier 1512 may be covered with protective cover 1516 . The protective c over 1516 can be sized and configured to prevent a user from touching the air permeable bloo d barrier 1 512 with their fingers or other external instruments , while still allowing the patien t's own blood pressure to force the isolation chamber. A forced blood supply allows air to exit t he air permeable blood barrier 1512 as the air is expelled from the isolation chamber. Protecti ve cover 1516 protects the filter from accidental contact with surrounding fluids or splashes.

can be configured to inhibit or prevent exposure to This can be

done in a variety of mechanical ways including, but not limited to, adding a hydrophobic mem brane to the protective cover. FIG. 15B is a perspective view of blood isolation device 1500 fr om the top of housing blood isolation device 1500 , showing the sampling flow path before th e sample collection device is activated. A first aliquot of blood fills isolation . Figure 15G is a p erspective view of the blood isolation device 1500 from the bottom of the housing 1501 and t he exit port 1504 of the blood isolation device 1500, initially while the sampling channel 1506 is empty before the sample collection device is activated. aliquot of blood fills isolation chamb er 1508 . FIG. 15C is another perspective view of blood isolation device 1500 from the top of housing 1501 including inlet port 1502 and vent 1510 of blood isolation device 1500 , with the isolated blood substantially within isolation chamber 1508 . Blood is drawn through sampling c hannel 1506 while remaining at . FIG . 15D is a cross-sectional view of blood isolation device 1500 according to some implementations, showing housing 1501 defining sampling channel 1 506 and isolation chamber 1508 . Figure 15E and

and 15F illustrate various form factors of housings for blood isolation devices according to one or more implementations described herein . Isolation chamber 1508 can have a larger cross-sectional area than sampling channel 1506 , and the cross-sectional area or length can be con figured such that a predetermined or specific blood volume is isolated or locked
. can. The sampling channel 1506 can be sized to fit tubing for either or both the patient need le tubing or the blood collection device tubing. Housing 1501 can be formed from multiple pi eces or from a single unitary piece. In some implementations, as shown in FIG. 15D, housing 1501 includes an upper member 1520 and a lower member 1522 that mate with each other, o ne or both of which are formed, for example, by an injection molding process or by etching, H aving grooves, channels, locks, conduits drilling or the like. The upper member 1520 may be attached by laser welding, thermal bonding, ultrasonic welding , adhesives, screws, rivets, bol ts, etc., or by latches, grooves, tongues, or the like. Other mating mechanisms, such as pins, flanges, etc., can connect with lower member 1522 . In some implementations, upper memb er 1520 includes grooves, channels, locks, guides, etc., as shown in FIG. 15D .

A tube or other passageway can be included, while the lower member 1522 is sized and adapted to
fit into at least one of a groove, channel, lock or other passageway in the upper member 1520.
can include raised protrusions 1524 . Protrusions 1524 can provide surface features
such as
partial . In some implementations,
the protrusions 1524
can be formed with one or more slanted sides or faces to more closely fit within corresponding grooves, channels, locks or other pathways. can. In still other implementations, both the upper member 1520 and the lower member
can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524 . In some implementations, sampling channel 1506 and isolation chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501
. Housing 1 501 may be made of any suitable material including rubber, plastic, metal or other material.

can be Housing 1501 can be formed from a transparent or translucent material, or from an opaque or non-
translucent material.
In other implementations, the housing 1501 can
be largely opaque or non-transparent, but the housing surfaces directly adjacent the sampling channel 1506 and/or the isolation chamber 1508 are transparent or translucent and initially A visual cue or sign that the isolation
chamber 1508 is filled to the required or desired degree
and/or is isolated while a subsequent uncontaminated blood sample is
taken Gives the
practitioner . Other visual cues or signs of isolation include, but are not limited to,
contact, penetration, or partial penetration of blood, causing the air permeable blood barrier 1512 to
turn
color-coded tabs or indicators, audible, vibratory, or other signals at any location along or adjacent to the isolation chamber . After venipuncture by a patient needle (not shown), which can collect many pathogens from the patient's skin, the patient's own blood pressure overcomes the atmospheric pressure in isolation chamber 1508 to form an air permeable blood
barrier
. As the air in the isolation chamber 1508 is expelled through 1512, the initial volume of pati

ent blood with these pathogens enters the blood isolation device 1500 inlet port 1502 and the most

It flows into isolation chamber 1508 by following the path of least resistance. The patient's blo od pressure
is not sufficient to overcome the rising air pressure within the sealed sampling channel 1506 . Ultimately, an isolation chamber 1508 of predetermined volume
is filled with blood that drives air out through the air permeable blood barrier 1 512 . When bl ood
impinges , the blood interacts with the material of air permeable blood barrier 1512
to completely or partially seal vent 1510 . A signal or indication can be provided that the pract itioner can now
utilize the VACUTAINER® capsule or other blood sampling device to obtain the next volume of the patient's blood for sampling.
The blood in the isolation chamber 1508
is now effectively isolated within the isolation chamber.
Upon filling blood isolation channel 1508 and prior to use of a Vacutainer
™ or other blood
sampling device, the patient's blood pressure
causes compression of air within sampling channel 1506, possibly A small amount of blood tra vels past the turning point to the isolation chamber 1508 and into
the sampling channel 1506 ,
queuing clean blood to be drawn through the sampling channel 1506 .
Figures 16-19
show yet another implementation of a blood isolation device. Figures 16A-16D illustrate a bl ood sample collection device, such as an evacuated blood collection container such as
a Vacutainer® (not shown), and a patient.
A blood isolation device 1600 that can be connected between a needle (not shown) and/or ass ociated tubing is
shown. FIG. 17 shows the lower member of the blood isolation device and FIG. 18 shows the upper member of the blood isolation
device , the upper and lower members
being interfitted and configured as described in more detail below. Inlet ports, outlet ports, iso lation chambers and sampling channels
can . Figures 19A and 19B show the upper and lower members mating together. 16-19 show one exemplary method of constructing the blood isolation devices described herein, and it sho uld be understood that other forms of construction are possible. 16A-16D, blood isolation de

vice 1600 has an entry port that can . 1602 included. Inlet port 1602 can also be connected t o a tube . The inlet port 1602 defines an opening to the blood isolation device 1600, which op ening can be of the same cross-sectional dimensions as the tubing or other conduit connected to the patient needle or the patient needle itself. For example, the opening can be circular wit h a diameter of about 0.045 inch (1.143 mm), but may be 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm) or less. can have a diameter of

.

Inlet port 1602 may

also include a sealed or fluid tight connector or connection such as a threaded or luer fitting or the like . In some implementations, a tube or other conduit coupled

to the patient needle can be integrated with the entry port 1602, such as by co-molding, gluin g, laser welding, or heat bonding the parts together. This allows the blood isolation device 160 0 to be manufactured and sold as a single unit along with the patient needle and/or tubing, eli minating the need to connect the patient needle to the blood isolation device 1600 during blo od draw or sampling. . Blood isolation device 1600 further includes an exit port 1604 that de fines an opening . Exit port 1604 may also be connected to a tube or other conduit that is also connected to a blood isolation device and may include a sealed or fluid tight connector or con nection such as a threaded or luer fitting . Thus , as noted above, the blood isolation device 1 600 is manufactured and sold as a single unit with the patient needle and/or tubing and blood sample device, and is attached to the patient needle and blood sample collection device durin g blood collection or sampling. to the blood isolation device 1600 . Blood isolation device 160 0 has a sampling port between inlet port 1602 and outlet port 1604 .

and an isolation chamber 1608 connected to and separated or diverted from the sampling
. Sampling channel 1606 functions as a blood collection path once the first aliquot of blood is sequestered in sequestration chamber 1608 . Sampling channel 1606 can be a channel or conduit of any size, shape or configuration . In some implementations, sampling channel 1606
has a cross-sectional area substantially similar to the opening of inlet port 1602 . In other implementations, sampling channel 1606
can gradually widen from inlet port 1602 to outlet port 1604 . The isolation chamber 1608 widens toward the path of the isolation channel so that blood first attempts to enter the reservoir as opposed to entering the
smaller diameter of the sampling channel 1606, as shown in more detail in FIGS . It can have a larger cross-section to form a reservoir. In some exemplary implementations, the diversion between sampling channel 1606 and isolation chamber 1608 is accomplished by diversion junction 1607 . Turning junction 1607 can be substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations , redirection junction 1607 is configured such that flow from . isolation chamber

1608 can also include or form a curve or ramp to move the initial blood flow toward and into the isolation chamber 1608 . The isolation chamber 1608 is preferably maintained at atmospheric pressure and includes a vent 1610 at or near the distal end of the isolation chamber 1608 . Vent 1610 can include an air permeable blood . Blood isolation device 1600 can include

a housing 1601 that can be formed from multiple pieces or a single unitary piece . In some implementations, as shown in FIGS. 17A-17D and 18A-18F, housing 1601 includes an upper member 1620 and a lower . Blood isolation device 1600 includes a gasket or other sealing member such that when upper member 1620 is mechanically attached to lower member 1622, the interface therebetween is sealed by A member (not shown) may also be included.

17A-17D show the lower member 1622 of the housing for the blood isolation device 1600. FIG.

The lower member 1622 includes pre-formed grooves, channels, locks, or the like by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channels 1606, the isolation chambers 1608, and the turning junctions
1607.

Conduits or other pathways may be included
.

Isolation chamber 1608
has a larger cross-section than sampling channel 1606
so that blood preferentially moves into the isolation chamber first as opposed
to can be done.

FIGS.
18A-18F may be connected by any mating or connecting mechanism such as using laser welding, thermal bonding, gluing, screws, rivets, bolts, etc.,
or by latches, grooves, tongues, pins, flanges, etc.

Upper member 1620 is
shown . Top member 1620 can include
some or all of grooves, channels, locks, conduits or other pathways to form sampling channels 1606 , isolation chambers 1608 and turning junctions 1607 .

In still other implementations,
both upper member 1620 and lower member 1622 can include grooves, channels, locks or other pathways. In some implementations, sampling channel 1606 and isolation chamber 1608 are located in a housing

.

formed by grooves, channels, locks or other pathways formed in 1601; Housing 1
601 can be made of rubber, plastic, metal or any other suitable material
. Housing 1601 can be formed from a transparent or translucent material, or
from .
In other implementations, housing 1601 can be largely opaque or non-translucent, but housing surfaces directly adjacent sampling channel 1606 and/or isolation chamber 1608 can be transparent or translucent. , first a visual cue or sign that the isolation
chamber 1608 has been filled to the required or desired degree
, and/or subsequently while a clean blood sample is
taken through the sampling channel 1606. ,
giving the practitioner a visual cue or sign that the sequestered blood remains sequestered .
Other visual cues or signs of isolation include, but are not limited to,
contact, penetration, or partial penetration of blood, causing the air permeable blood barrier 1
612 to turn a different color
; Color-coded tabs or indicators at any location along or adjacent to the isolation chamber
, audible, vibratory, or other signals may be included. As shown in FIGS. 18A-18F, air perme
able blood barrier 1612
can be covered or surrounded by protective member 1616 . Protective material

1616 can be sized and configured to prevent a user from
touching , while still
expelling air from the isolation chamber 1608.
allows air to exit the air permeable blood barrier 1612 . In some implementations, protective member 1616
includes protrusions that extend from the top surface of top member 1620 up and around air permeable blood barrier 1612 . The protective cover 1616 can be configured
to block or prevent accidental exposure of the filter to ambient fluids or splashes . This can be done in a variety of mechanical ways
including, but not limited to, adding a hydrophobic membrane to the protective cover . In use, blood isolation device 1600 includes sampling channel 1606 and isolation chamber 1608 . Bo
th paths are initially filled with air at atmospheric pressure, but sampling channel 1 606 is initi
ally sealed by The isolation chamber 1608 terminates in a vent 1610 to the atmosphere that i
ncludes an air permeable blood barrier 1612 . [0093]

After
venipuncture with a patient needle (not shown), which can collect many pathogens from the patient's skin, an initial volume of the patient's blood with these pathogens is delivered to inle t port 1602 of blood isolation device 1600 .
pass through. This initial volume of potentially contaminated blood
preferentially enters isolation chamber 1608 by finding the path of least resistance. The patie nt's
own blood pressure overcomes the atmospheric pressure in the vented isolation chamber 160 8
and expels air within the isolation chamber 1608 through the air permeable blood barrier 161 2, but builds up in the sealed
sampling channel 1606. insufficient to overcome the air pressure that is present. In
various exemplary embodiments, the isolation chamber 1608 and sampling channel 1606 are configured such that the force generated by the patient's blood pressure is sufficient to overco me the effects of gravity regardless of the orientation of the blood isolation device. can be con figured to Ultimately , the isolation chamber 1608 fills with blood that drives . When blood c ontacts the air permeable blood barrier, the blood interacts with the material of air permeable blood barrier 1612 to completely or partially seal vent 1610 . A signal or indication can be pro vided that the practitioner can now utilize the Vacutainer® or other blood collection device .
Once the blood isolation path 1608 is satisfied, a Vacutainer™ or other blood sample collecti on is performed .

Prior to use of the aspiration device, the patient's blood pressure
causes , possibly
moving a small amount of blood past the turning point into the sampling channel 1606 and int

o the sampling channel.

Queue .

FIG .

19A is a side view of blood isolation device 1600 and FIG. 19B is a cross-sectional view of bl ood isolation device 1600

showing upper member 1620 mating with lower member 1622 .

FIG.

20 illustrates a patient needle 2002 for vascular access to a patient's bloodstream, a blood s ample collection device 2004 facilitating the collection of one or more blood

samples patient needle 2002 and the blood

sample . Blood sample

optimization . In some implementations, the blood sample collection device 2004

includes a protective shield that includes a sealed collection needle such that once a sealed va cuum container is placed on the collection needle and the container is pierced once by the coll ection

needle, the patient needle is exposed to the patient needle. A blood sample is drawn from 200 2 through conduit 2006 with vacuum pressure

or force.

Blood sample optimization system 2000 further includes a blood isolation device 2008 located at any point on conduit 2006 between

patient needle 2002 and blood sampling device 2004, as described herein. . [0099]

FIG. 21 shows a non-vented blood isolation device 2100 that uses wicking material chamber s . Blood isolation device 2100 includes a housing 2101

having a sampling channel 2104 at least partially surrounded or abutted by an isolation cham ber 2102 filled with wicking material .

A first aliquot of blood is

drawn from the patient needle into the sampling channel 2104 where it immediately escapes i nto the

wicking . The wicking material and/or isolation chamber 2102 is filled with a predetermined vo lume such

that subsequent or subsequent blood draws flow past the wicking material and

through the sampling channel 2104 directly to a sampling device such as a vacutainer.

Dimensioned and adapted to receive and retain blood. The wicking

material can include substances such as solidifying agents, decontaminating agents, or other additives. As described herein, air permeable blood barriers can be of a wide variety of differ

ent constructions and materials

.

can be made using a fee. As shown in Figures 22A and 22B, the
air permeable blood barrier 2202 of the blood isolation device 2200
can include a polymeric bead matrix 2204 that has been treated to render at least some of th e beads hydrophilic. Air permeable blood
barrier 2202
further comprises a self-sealing material 2206 such as carboxymethylcellulose (CMC) or cellul ose gum, or other sealing material. Air permeable blood barrier
2202
may further include voids 2208 that allow air flow prior to or during partial contact with a fluid such as blood. Upon contact with fluid, self-sealing material 2206
expands close void 2208 and occlude air flow through void 2208, completely or
partially sealing, as shown in FIG. 22B. Figures 23A and 23B show an entry port 2302 for co nnection with a patient needle, an exit port 2304 for connection with a blood sampling device, an isolation chamber 2306, an isolation chamber 2306 and a contamination to be isolated
. 23 shows yet another implementation of a blood isolation device 2300 having a sampling ch annel 2308 that bypasses the isolation . The isolation chamber 2306 includes a hydrophobic pl ug 2312 at the distal end of the isolation chamber 2306 furthest from the inlet port 2302 . Ap plied from exit port 2304, such as from a Vacutainer® or the like.

The applied vacuum or other suction force
draws blood into inlet port 2302 and directly into isolation chamber 2306 where a first aliquot of blood contacts hydrophobic plug 2312
, isolating the first aliquot of blood. Return to chamber 2306 and isolate there. A small amoun t of
blood
can enter sampling channel 2308 which is initially closed by valve 2308 . When valve 2308 is released, a subsequent volume of blood, under additional vacuum or other force, flows into inl et port 2302, bypasses isolation chamber 2306, and through
sampling channel 2308 to the outlet port.
It flows towards 2304 and is sent to the collection device. Sampling channel 2308 can have

any suitable geometry and can be formed from plastic
tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pin ch, deflect, bend, or otherwise close the sampling channel before the first aliquot of blood is s equestered in sequestration chamber 2306 . can. [0103] While various embodiments have b een described in detail above, other modifications are possible. Other embodiments may be wi thin the scope of the following claims.

drawing open ----

[Fig. 1]

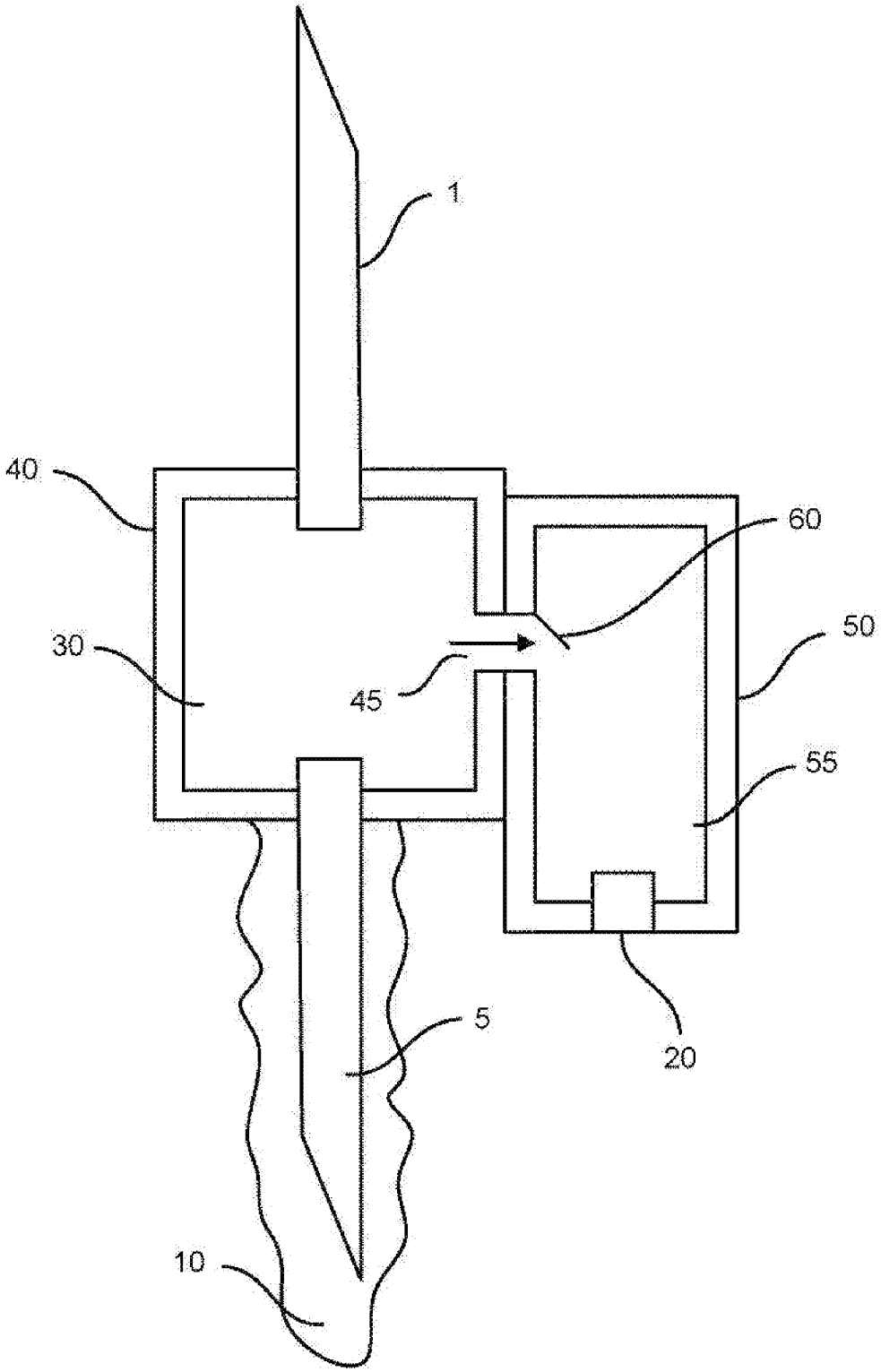


FIG. 1

[Figure 2]



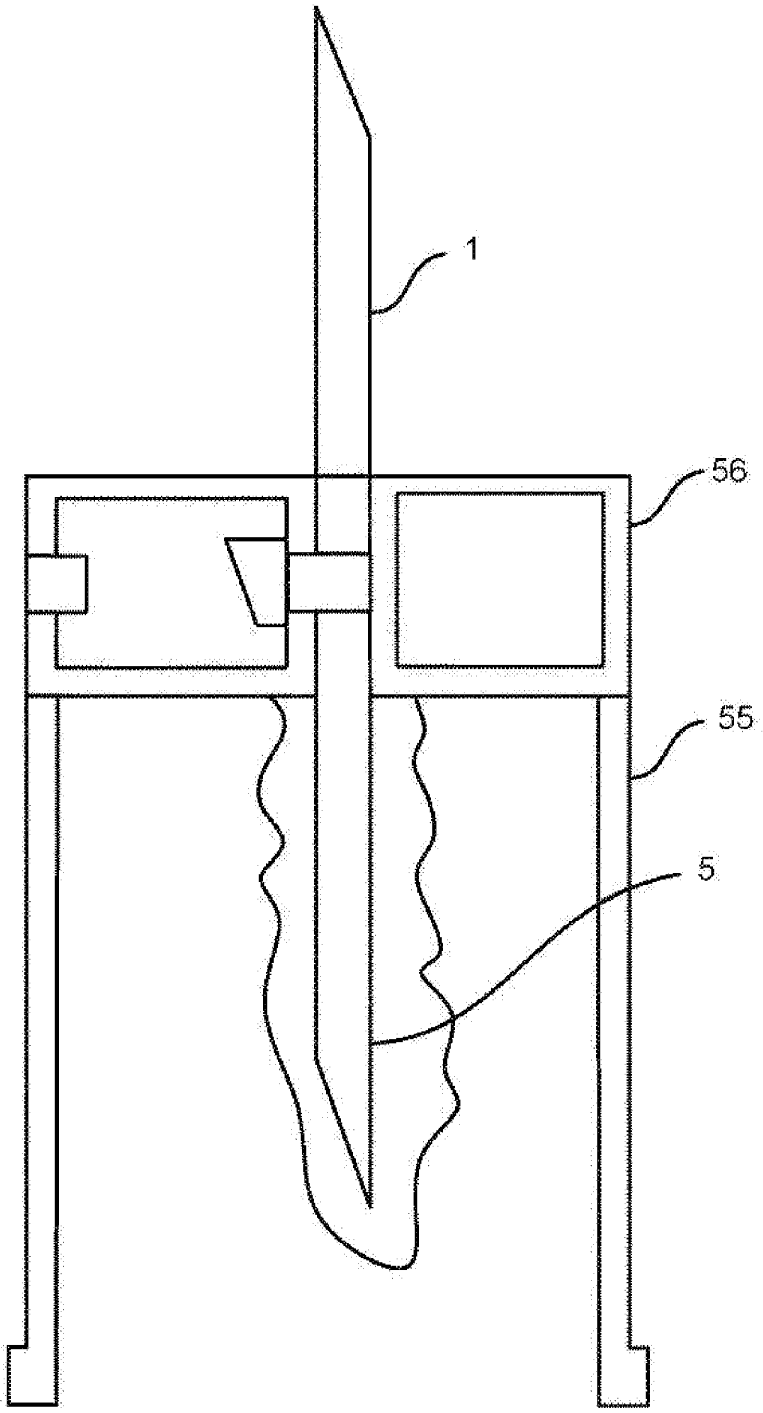


FIG. 2

[Figure 3]

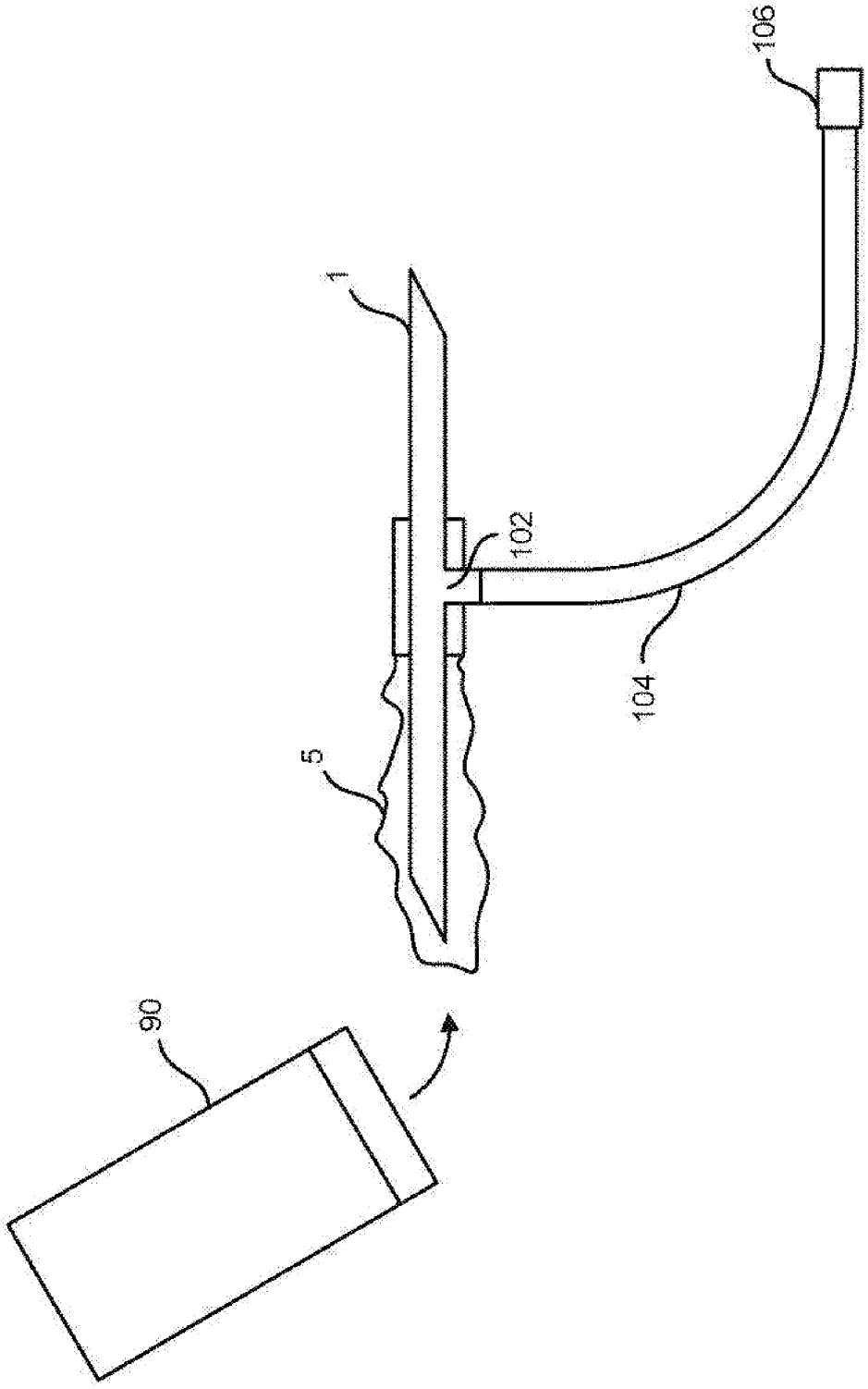


FIG. 3

[Figure 4]

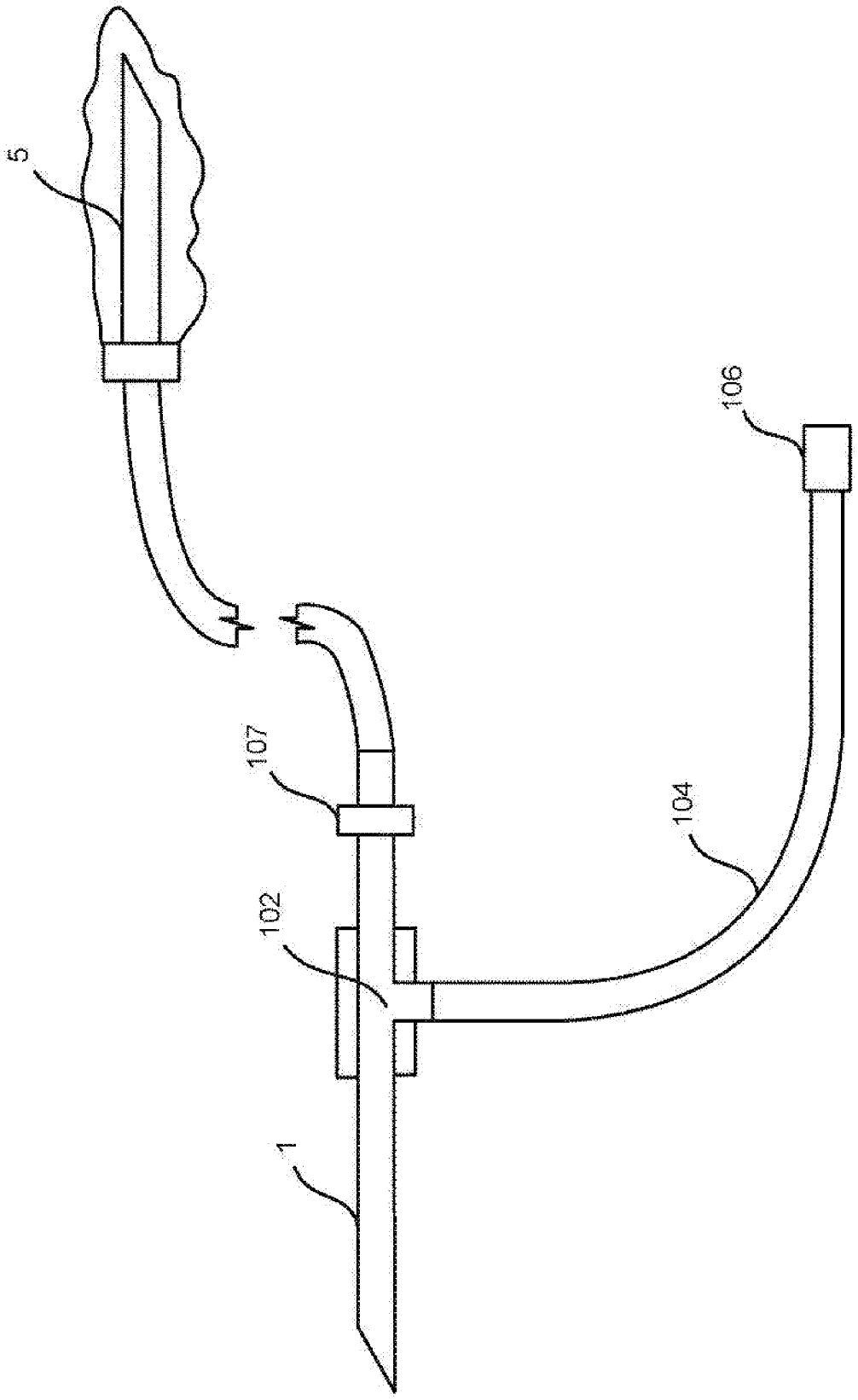


FIG. 4

[Figure 5]

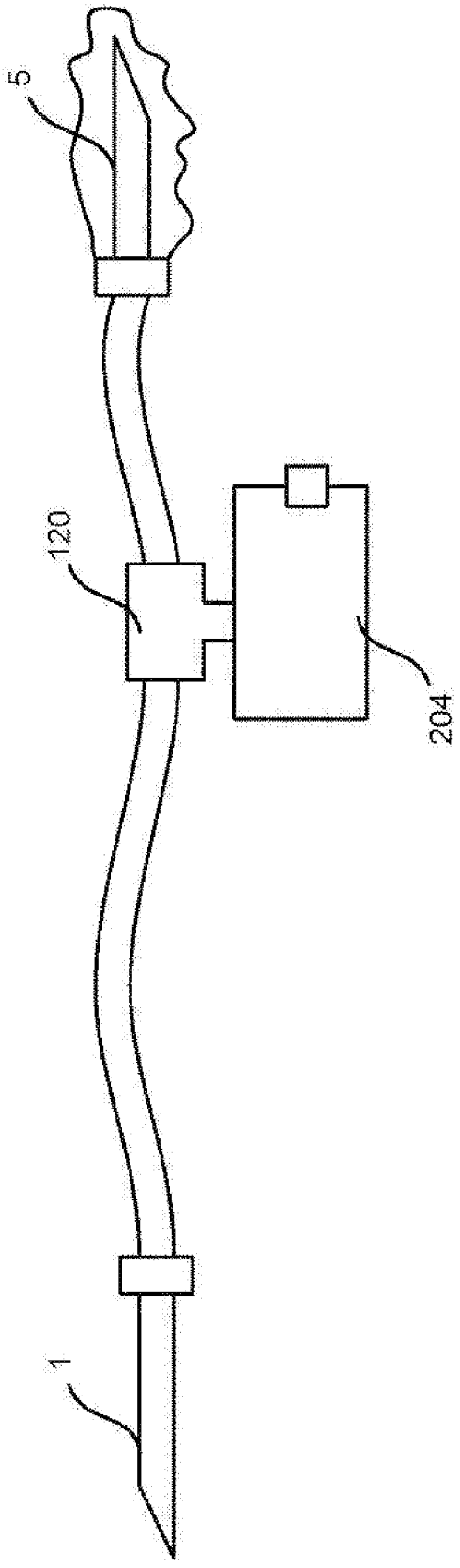


FIG. 5

[Fig. 6]

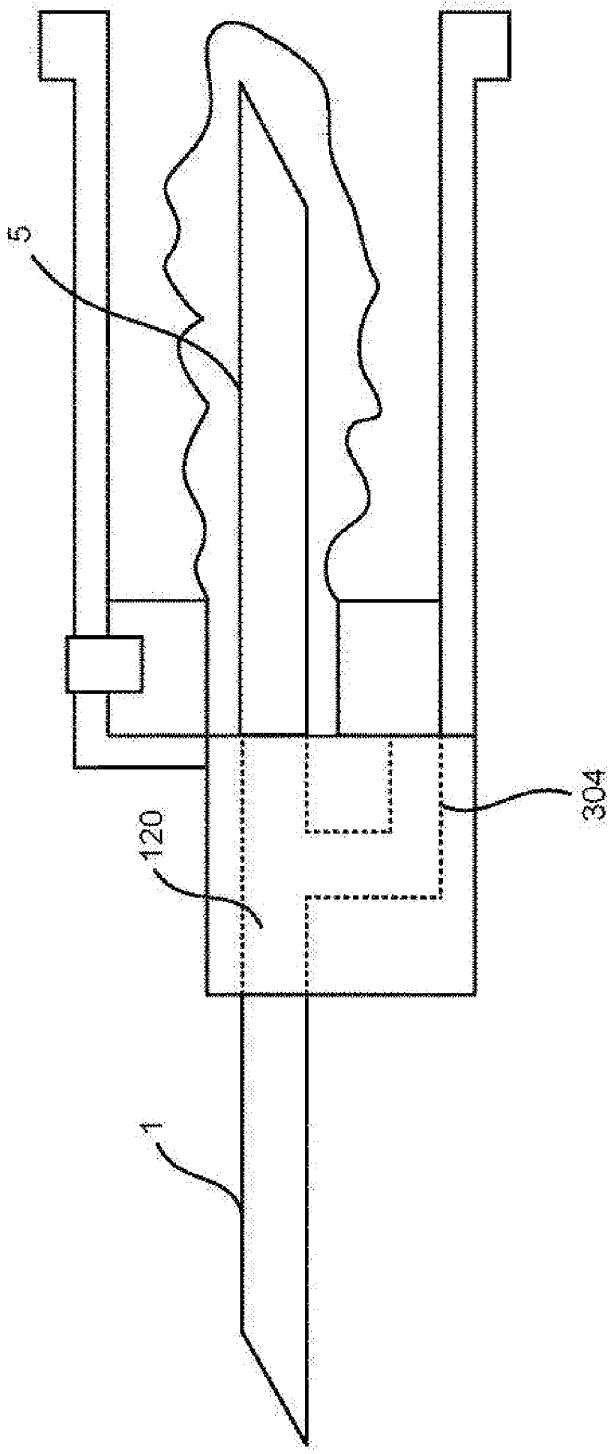


FIG. 6

[Fig. 7]

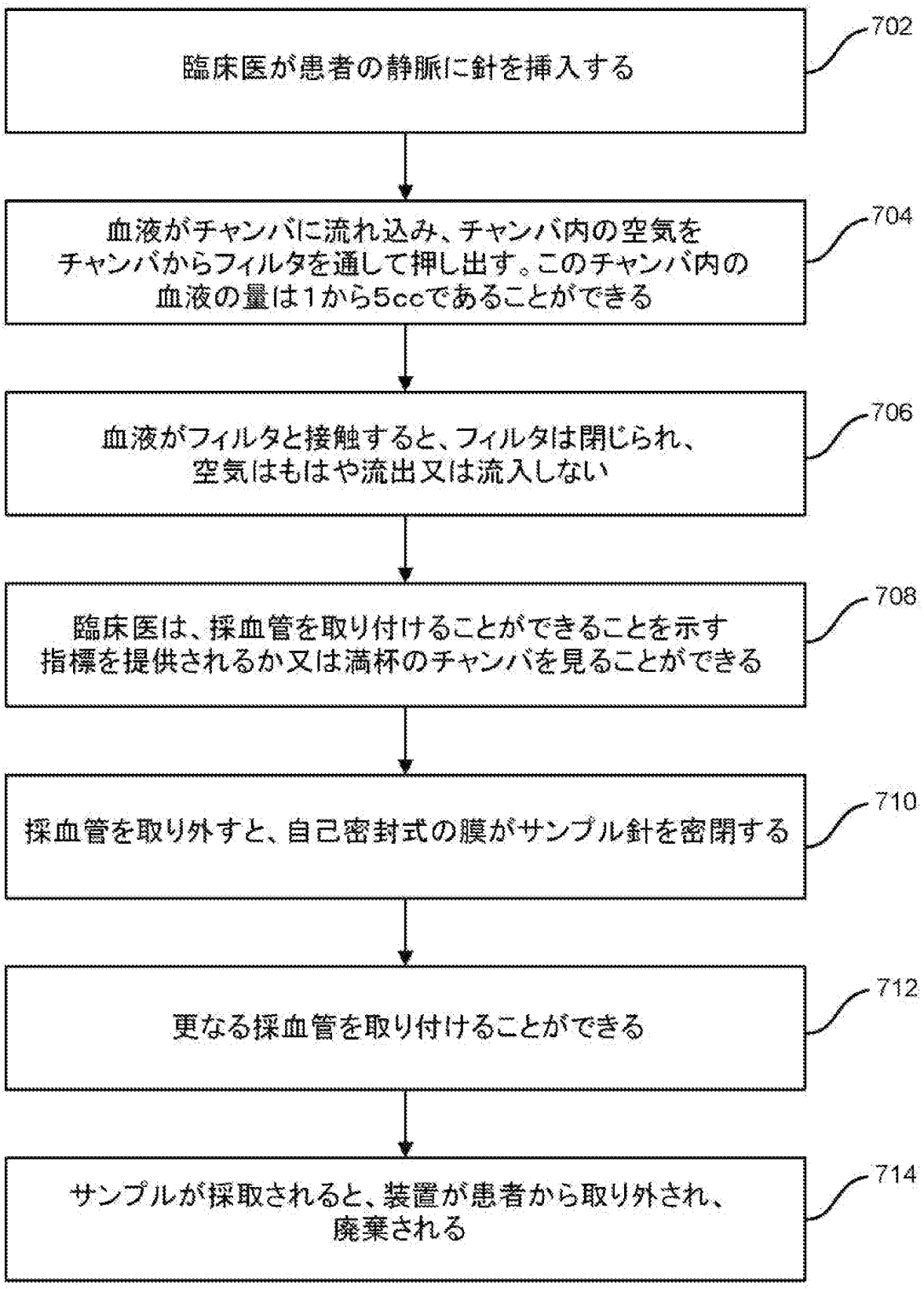

臨床医が患者の静脈に針を挿入する
702
血液がチャンバに流れ込み、チャンバ内の空気を
チャンバからフィルタを通して押し出す。このチャンバ内の
血液の量は1から5ccであることができる
704
血液がフィルタと接触すると、フィルタは閉じられ、
空気はもはや流出又は流入しない
706
臨床医は、採血管を取り付けることができることを示す
指標を提供されるか又は満杯のチャンバを見ることができる
708
採血管を取り外すと、自己密封式の膜がサンプル針を密閉する
710
更なる採血管を取り付けることができる
712
サンプルが採取されると、装置が患者から取り外され、
廃棄される
714

FIG. 7

[Fig. 8A]

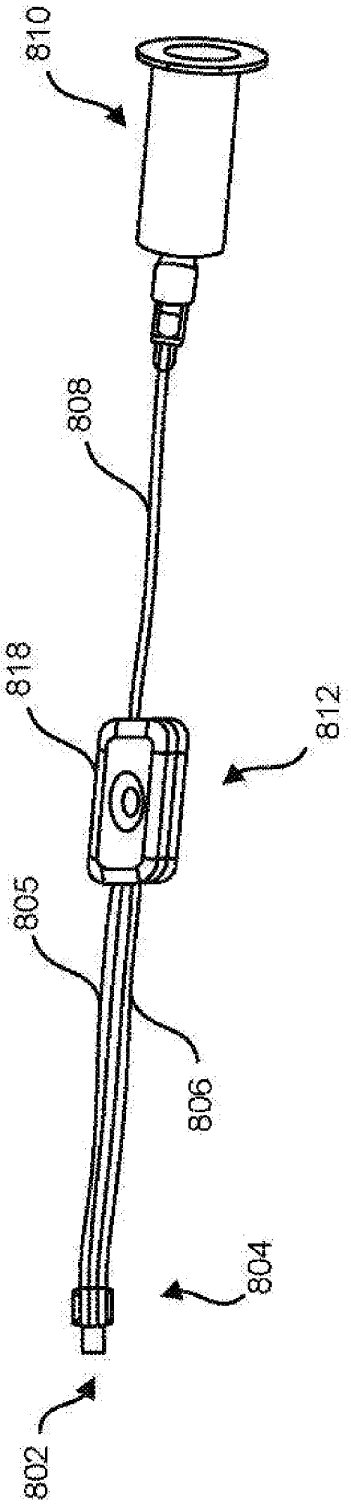


FIG. 8A

[Fig. 8B]

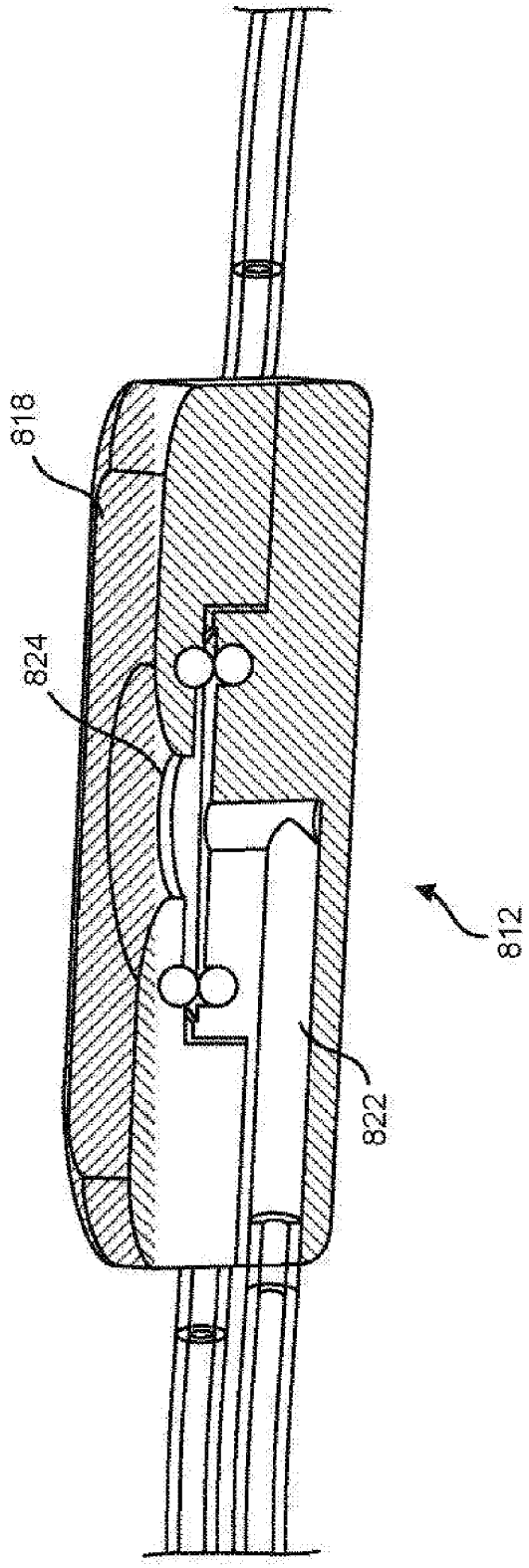


FIG. 8B

[Fig. 8C]

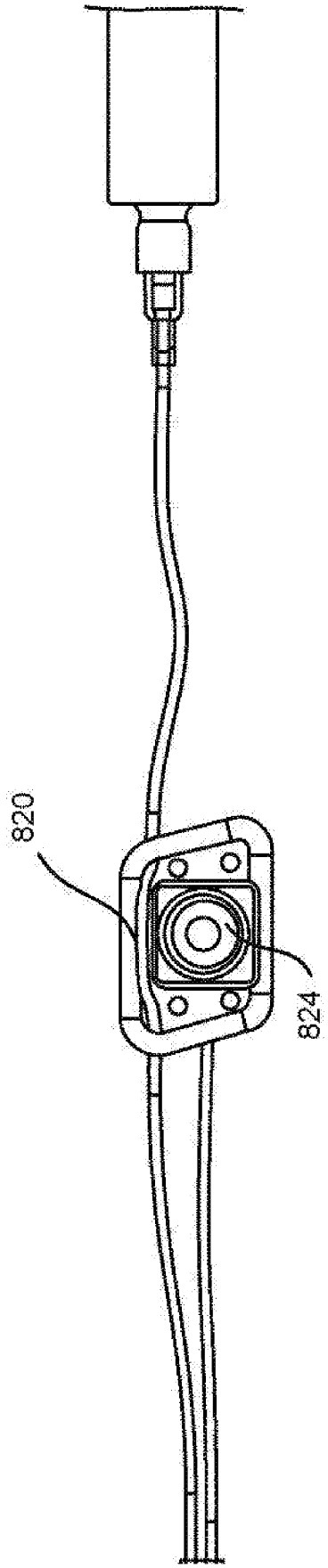


FIG. 8C

[Fig. 8D]



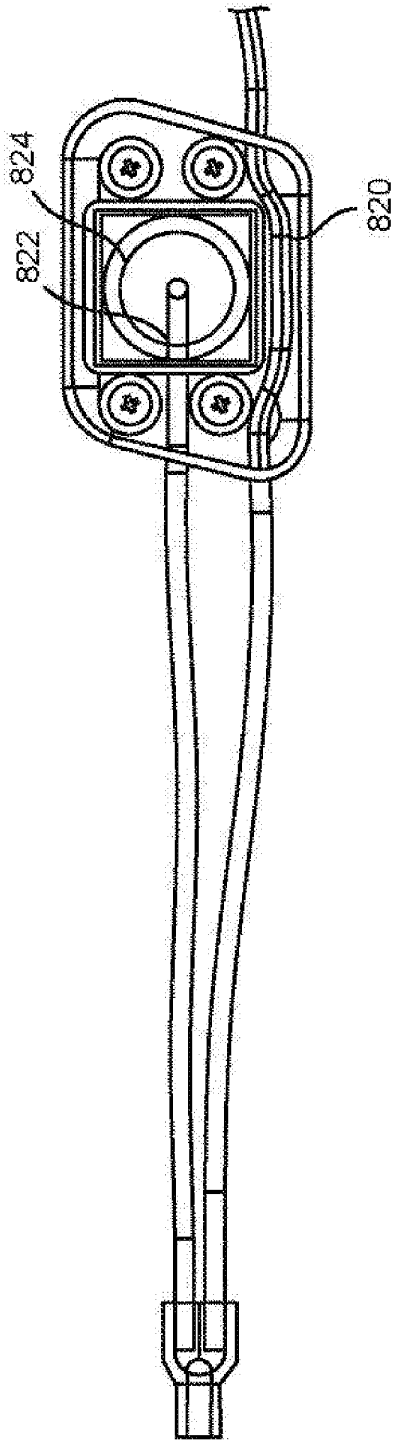


FIG. 8D

[Fig. 8E]

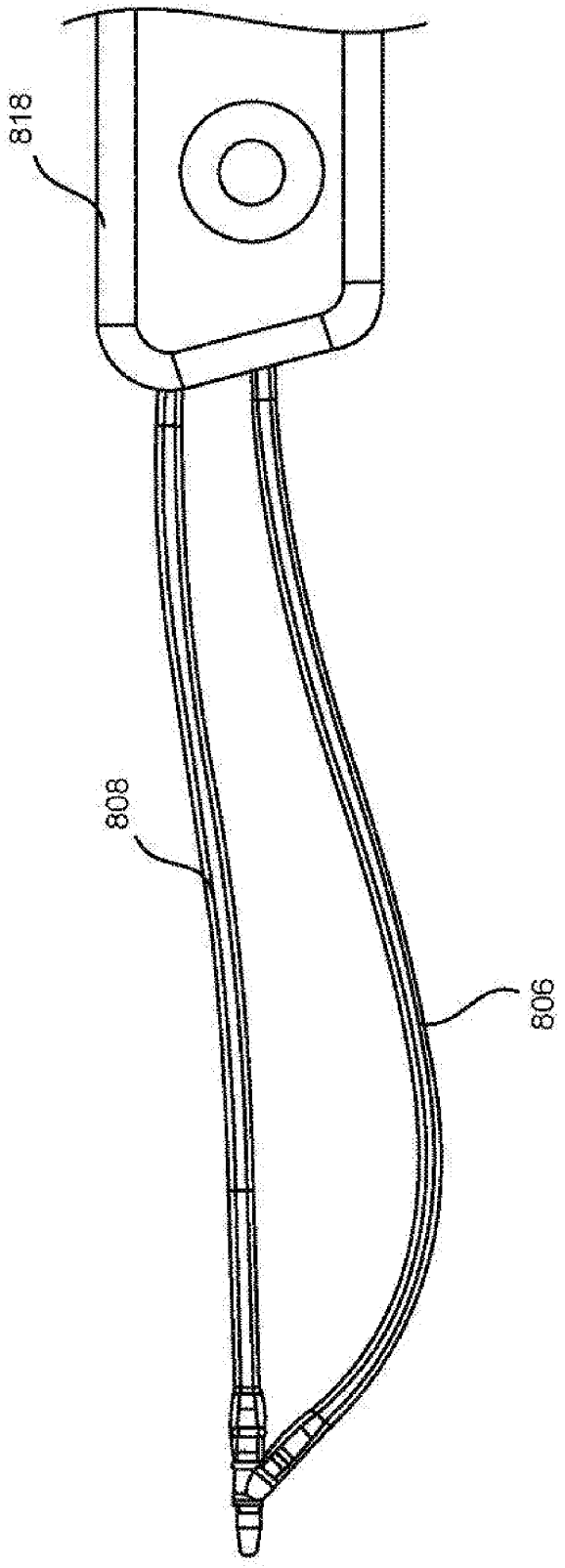


FIG. 8E

[Fig. 9]

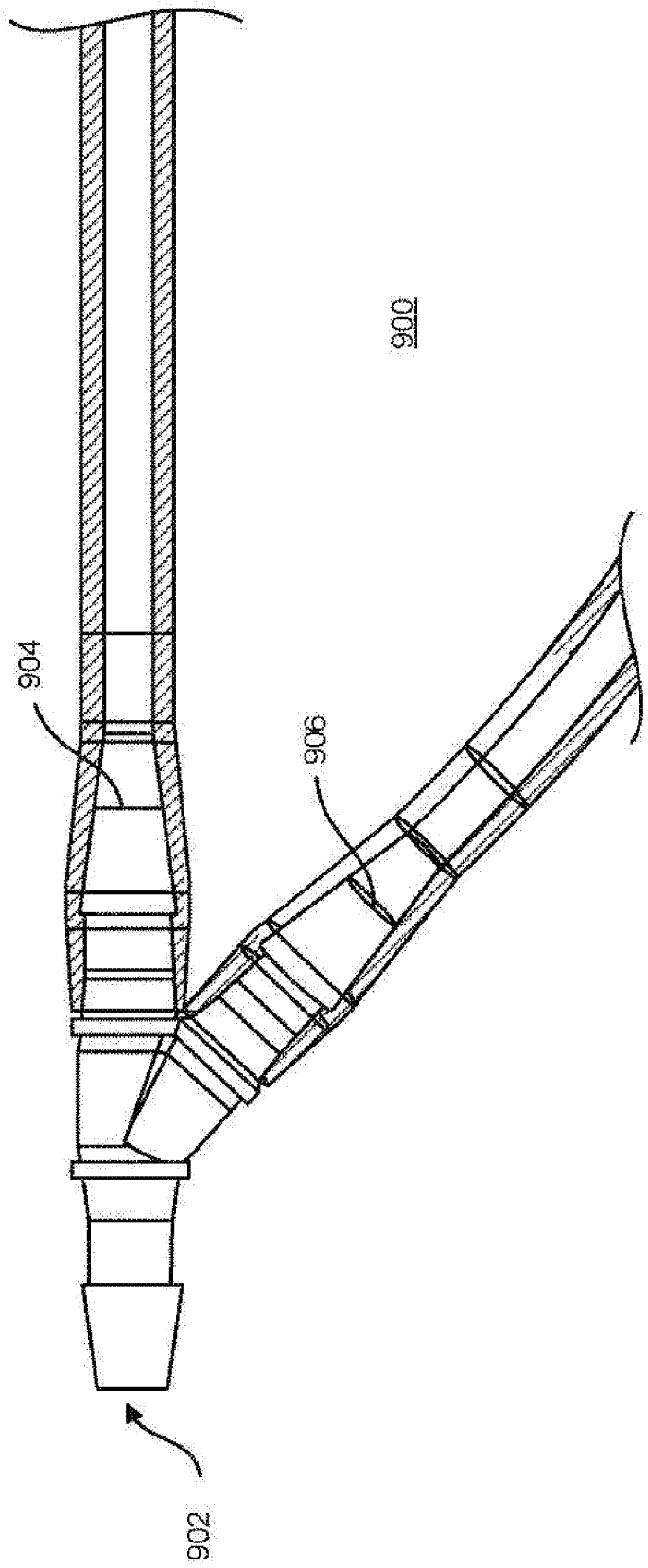


FIG. 9

[Fig. 10A]

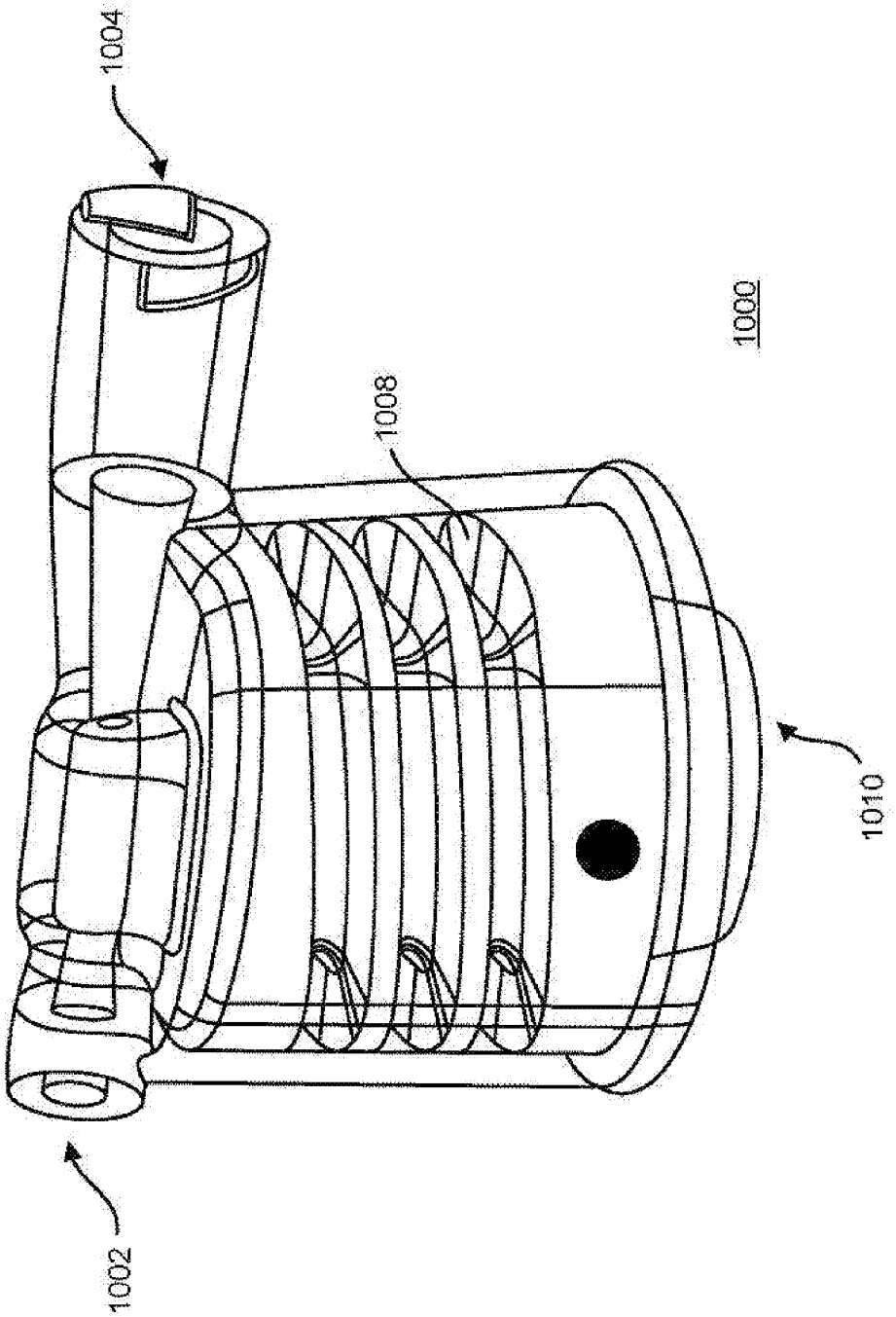


FIG. 10A

[Fig. 10B]

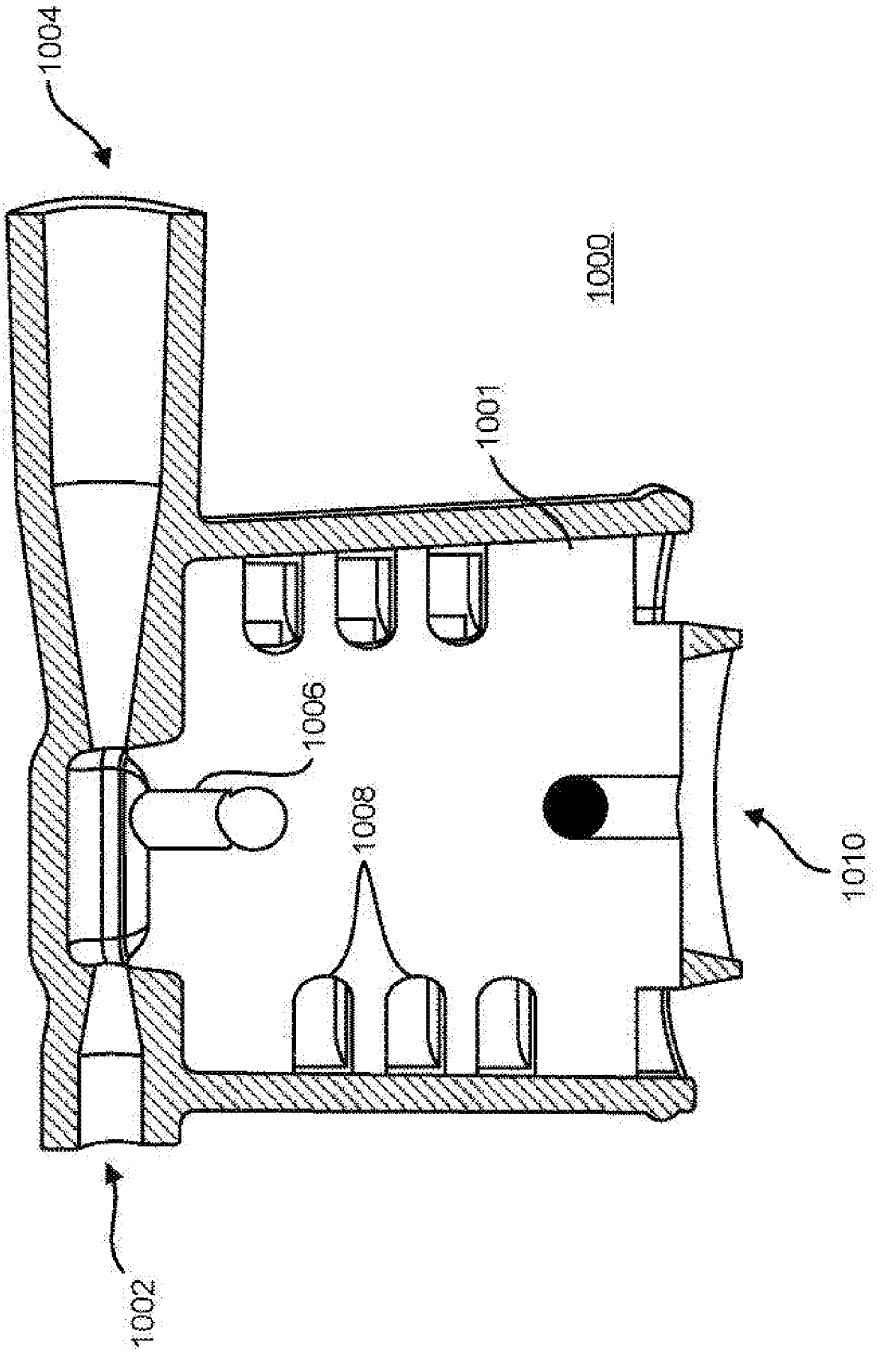


FIG. 10B

[Fig. 10C]

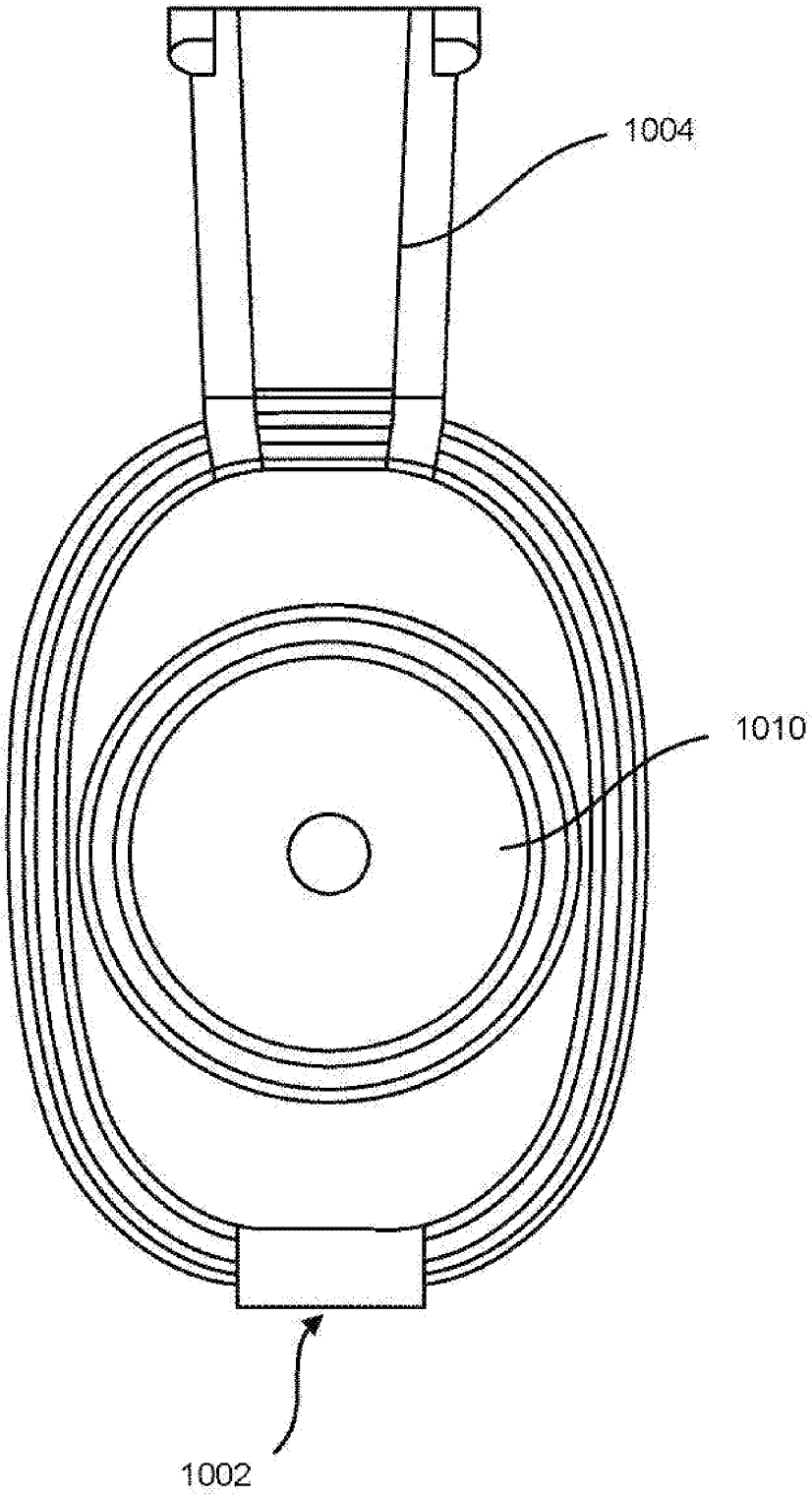
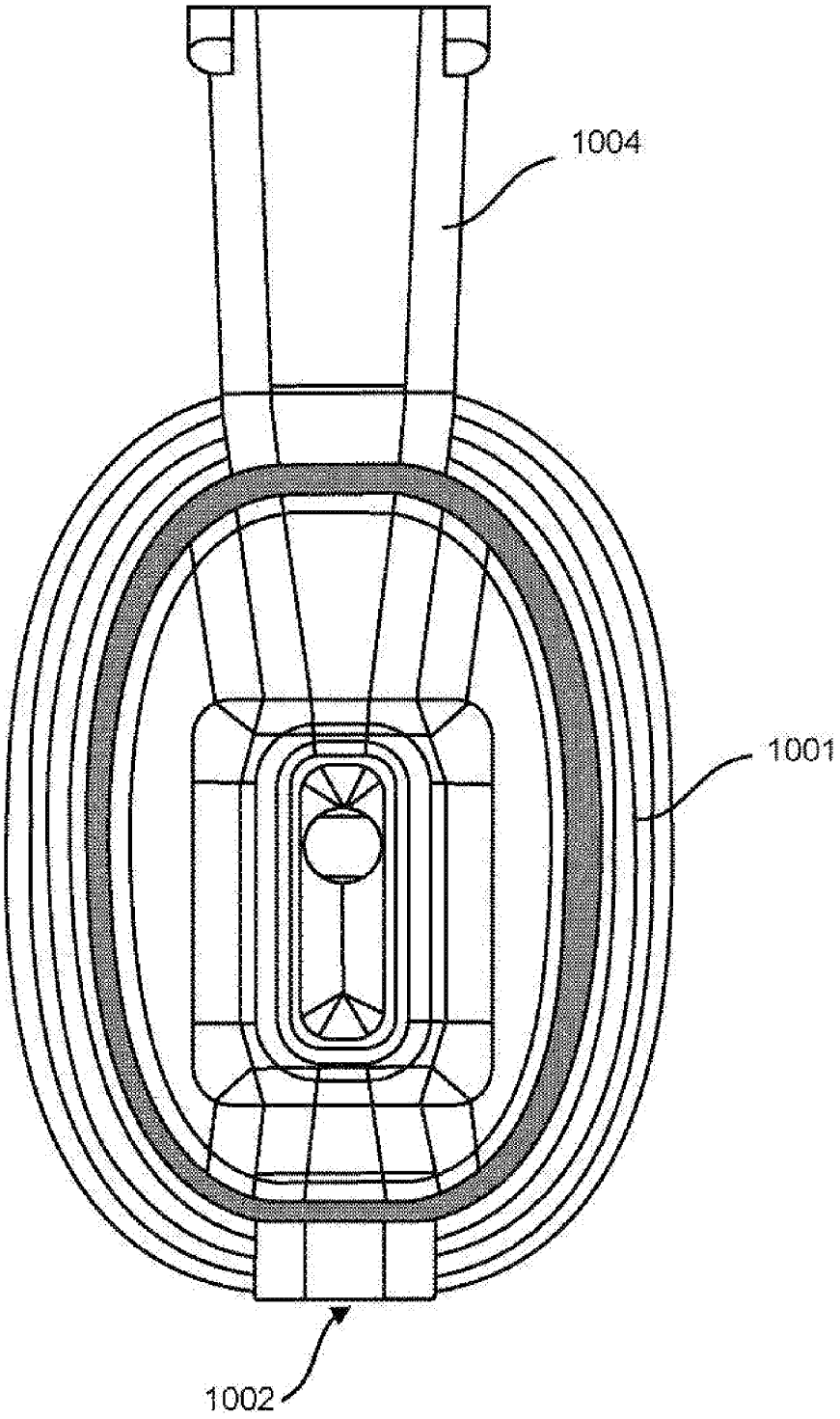


FIG. 10C

[Fig. 10D]




1004
1001
1002

[Fig. 11A]

FIG. 10D

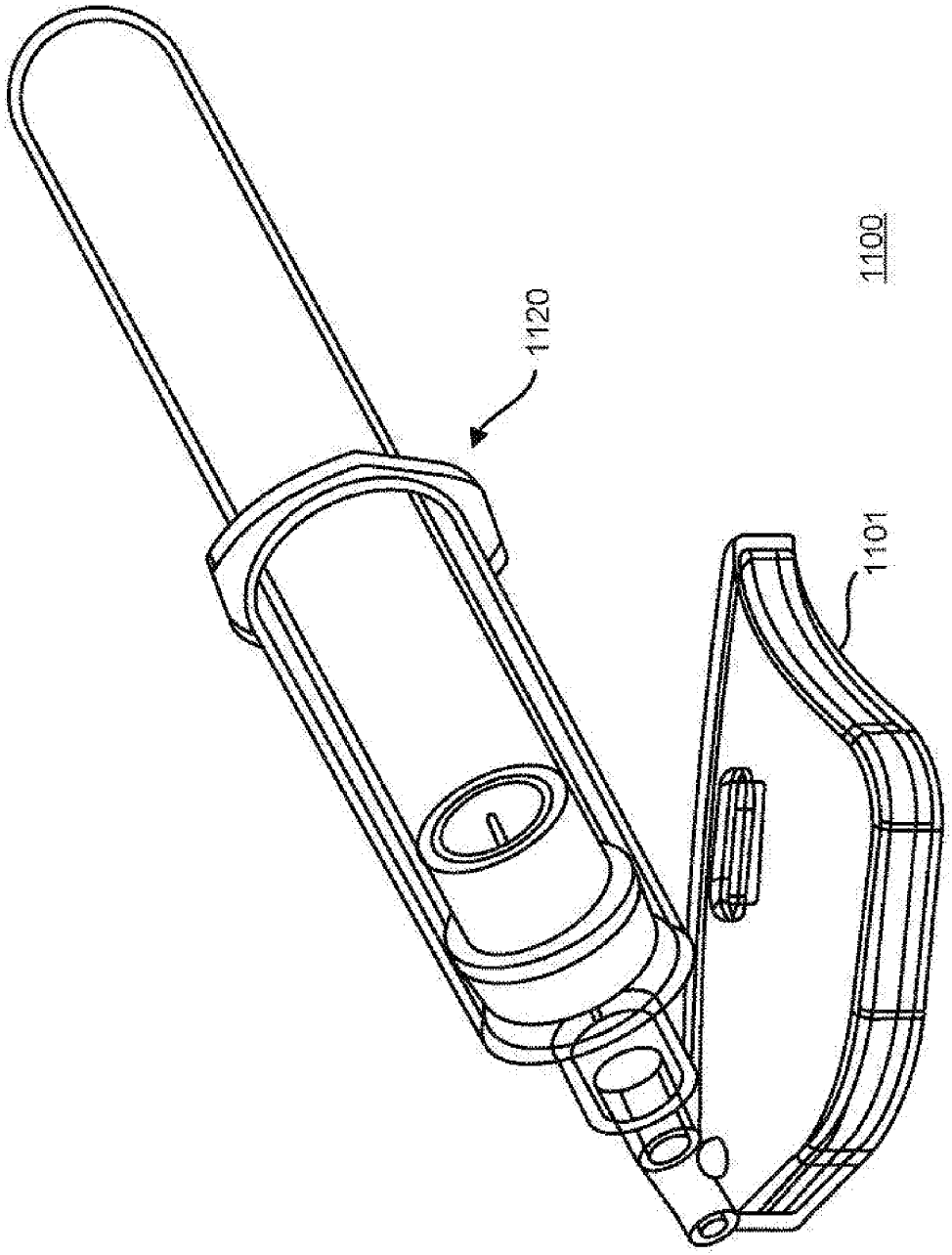


FIG. 11A

[Fig. 11B]

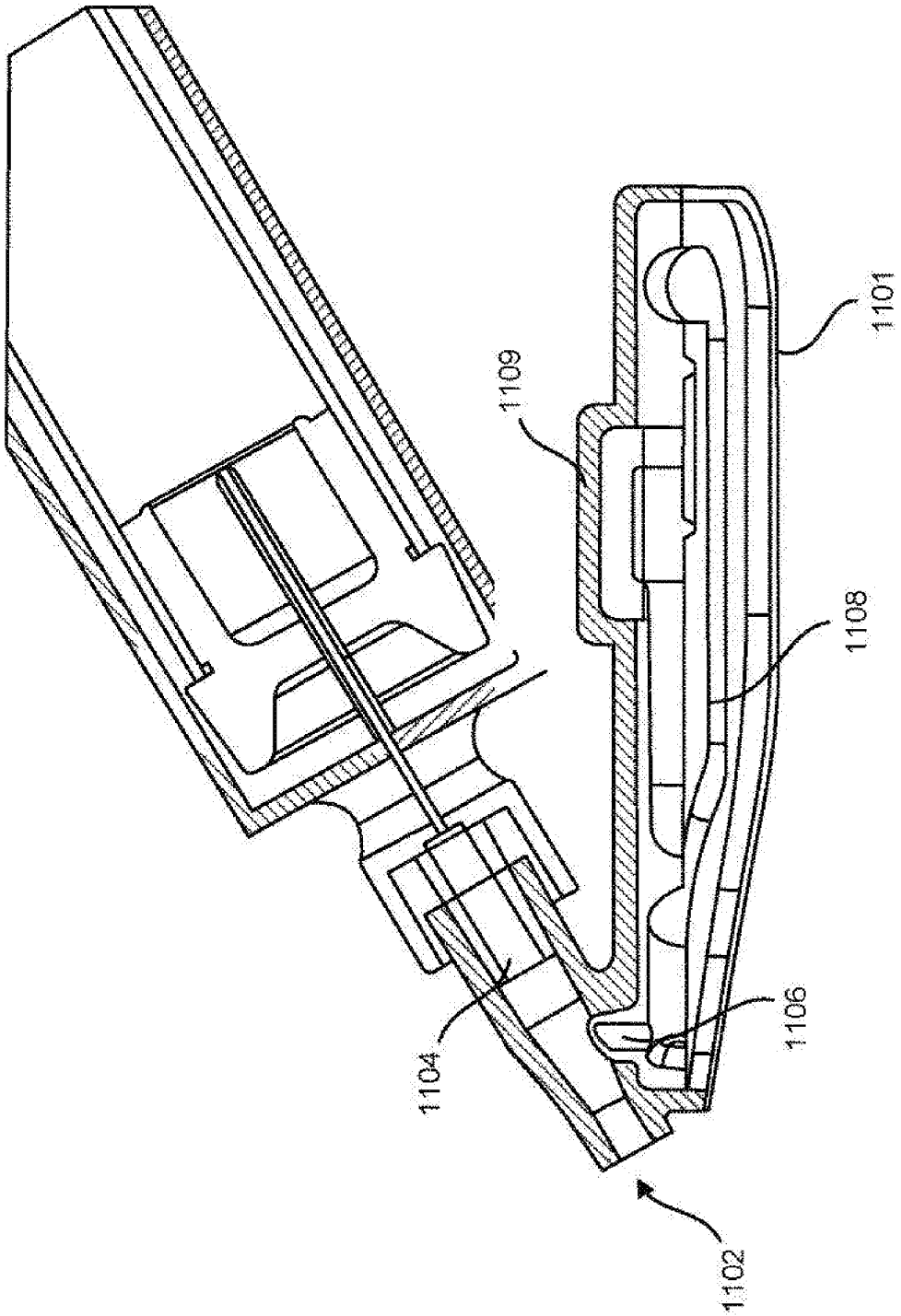
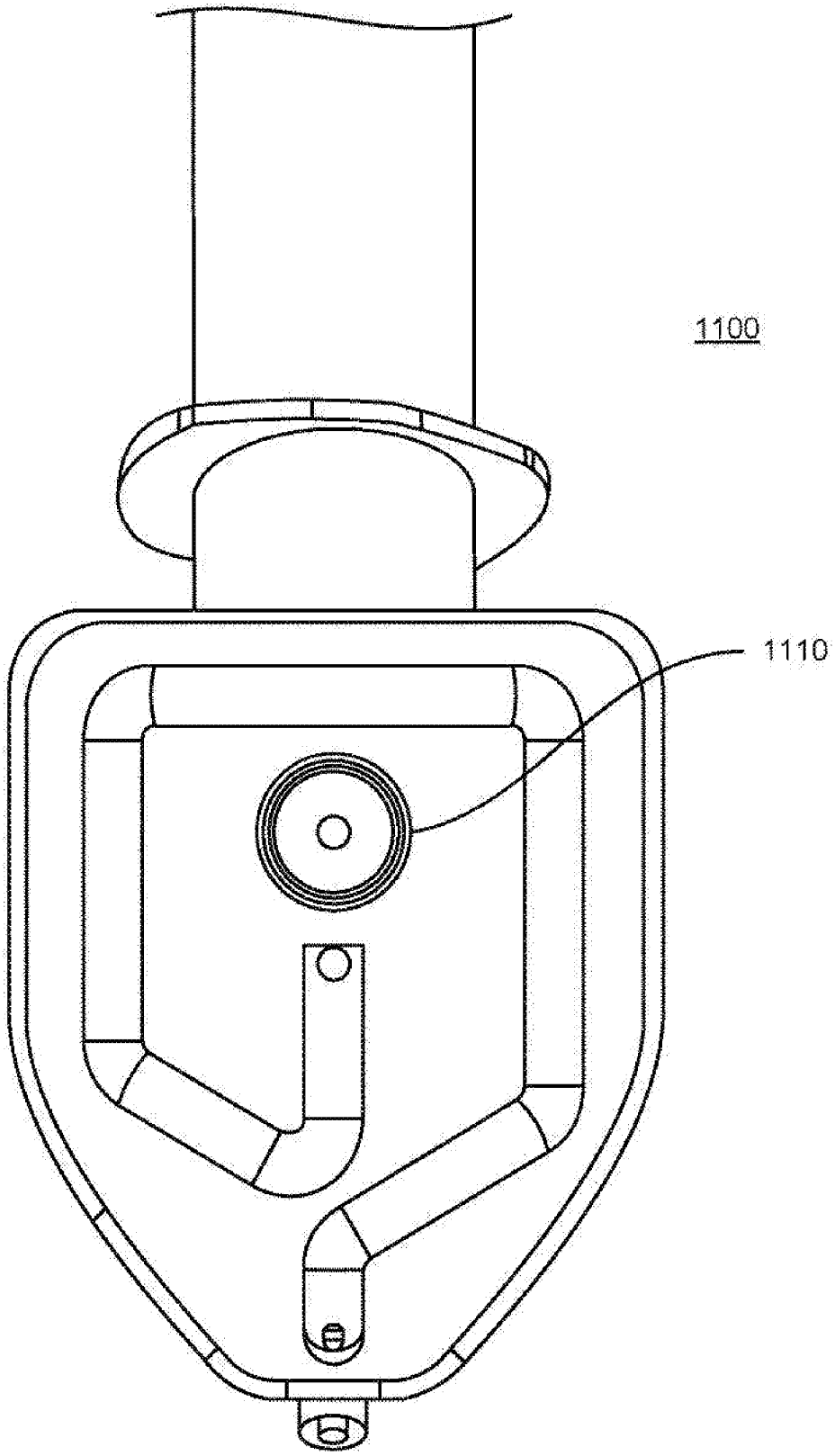


FIG. 11B

[Fig. 11C]


1100
1110

[Fig. 11D]

FIG. 11C

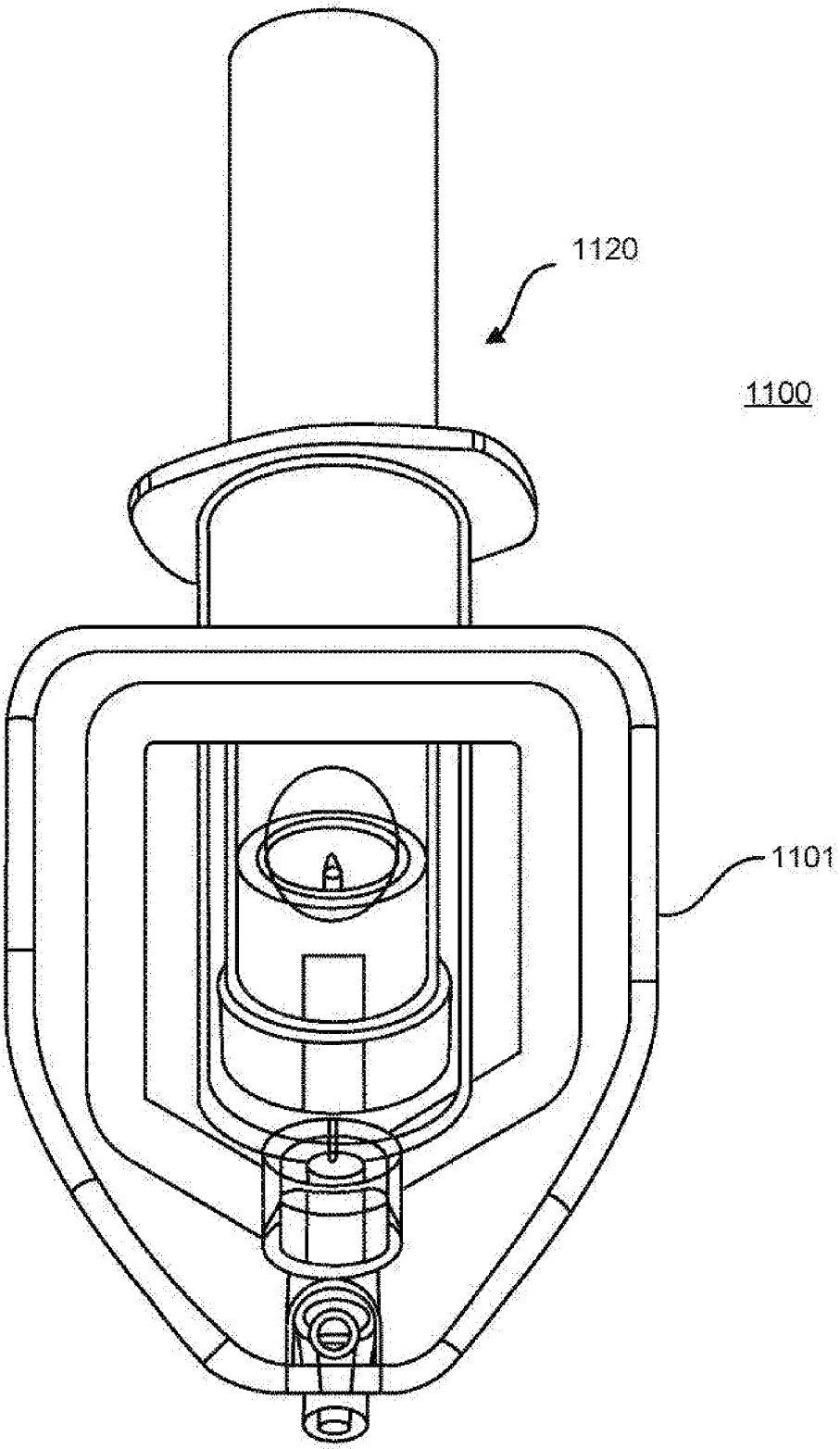


FIG. 11D

[Fig. 11E]

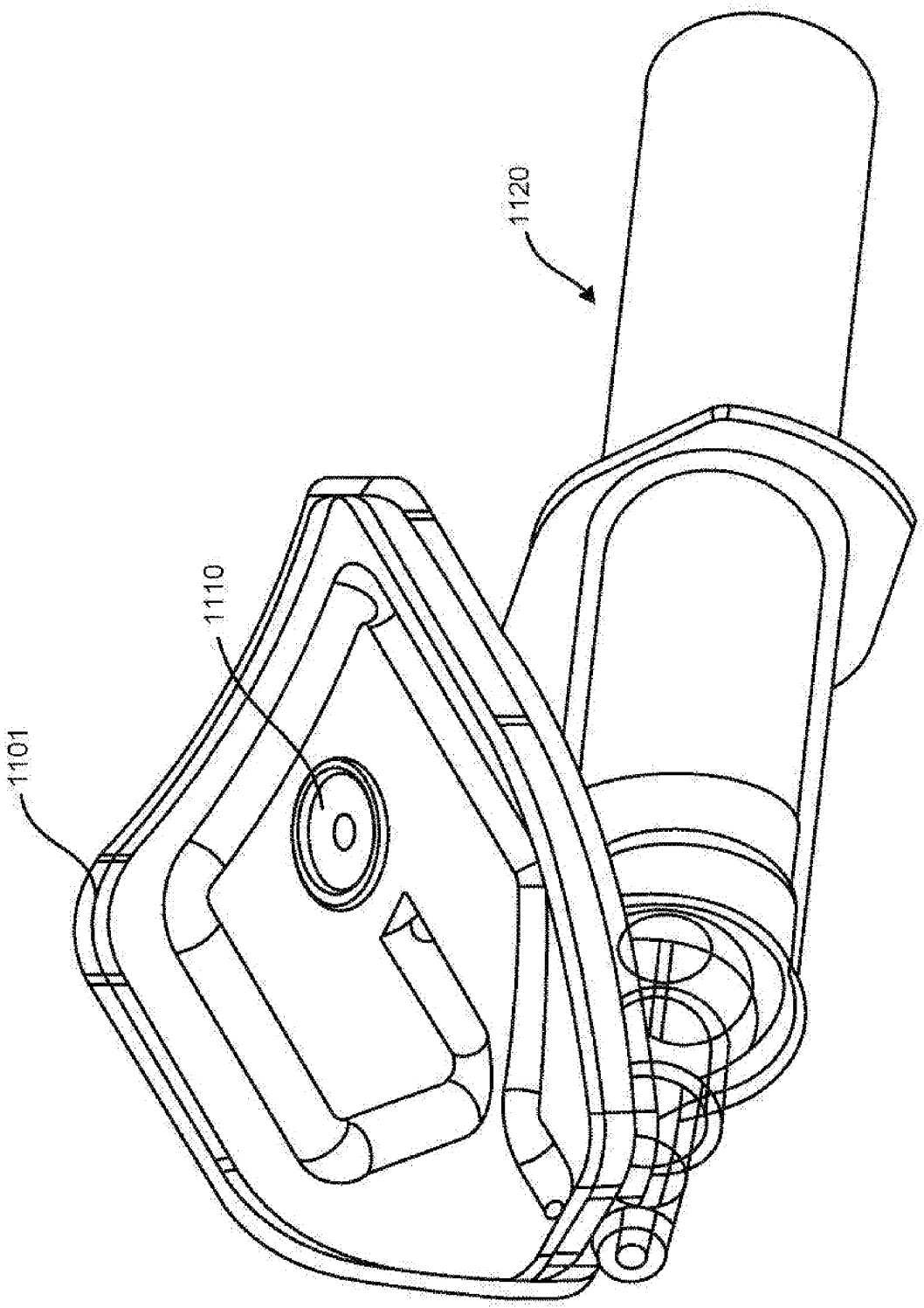


FIG. 11E

[Fig. 12A]

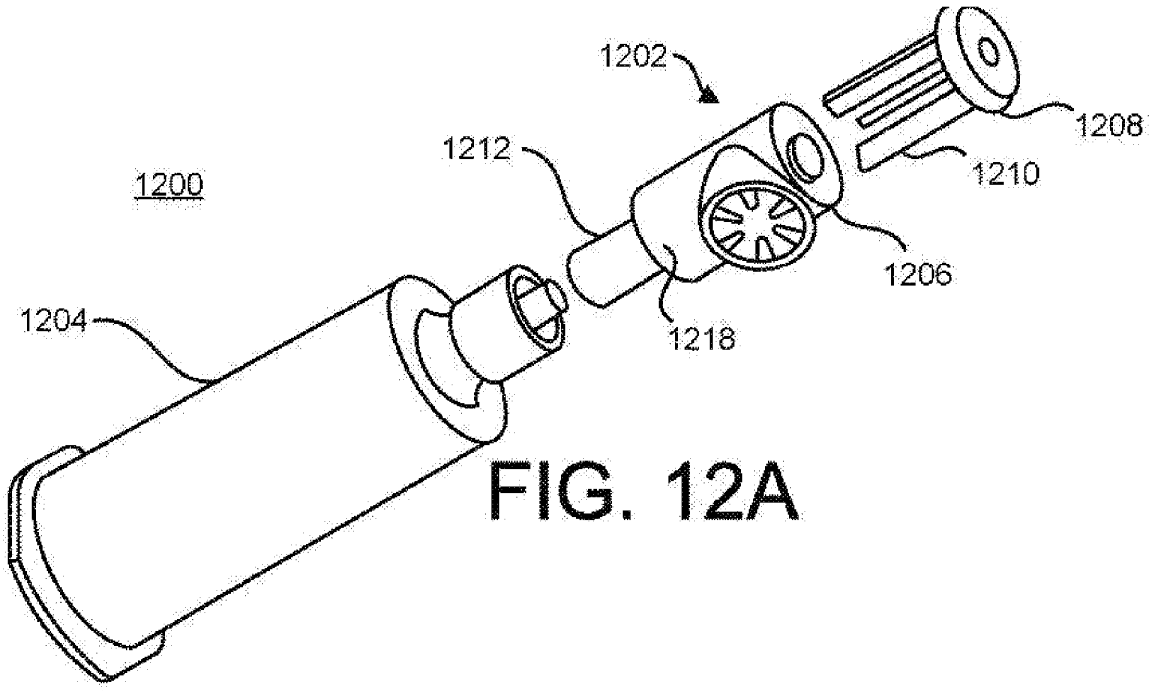


FIG. 12A

[Fig. 12B]

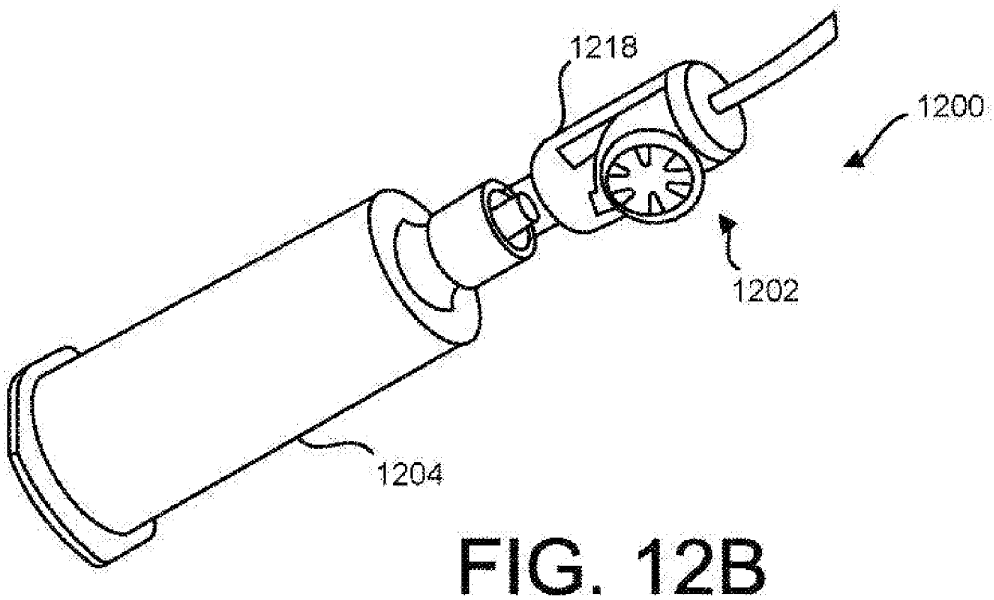


FIG. 12B

[Fig. 12C]

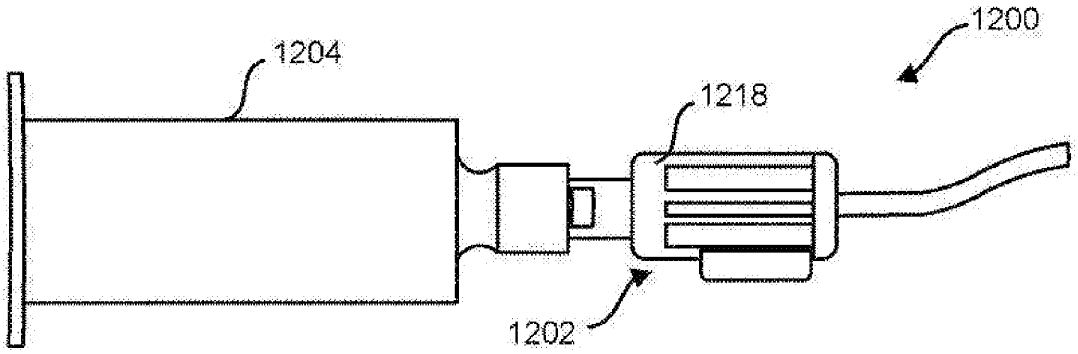


FIG. 12C

[Fig. 12D]

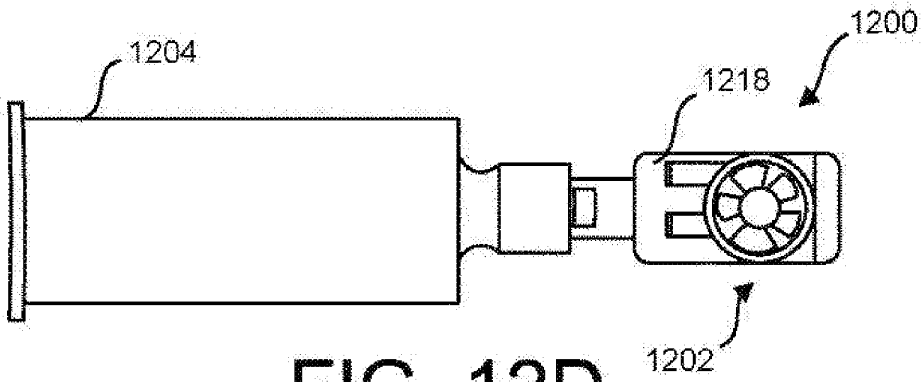


FIG. 12D

[Fig. 13A]

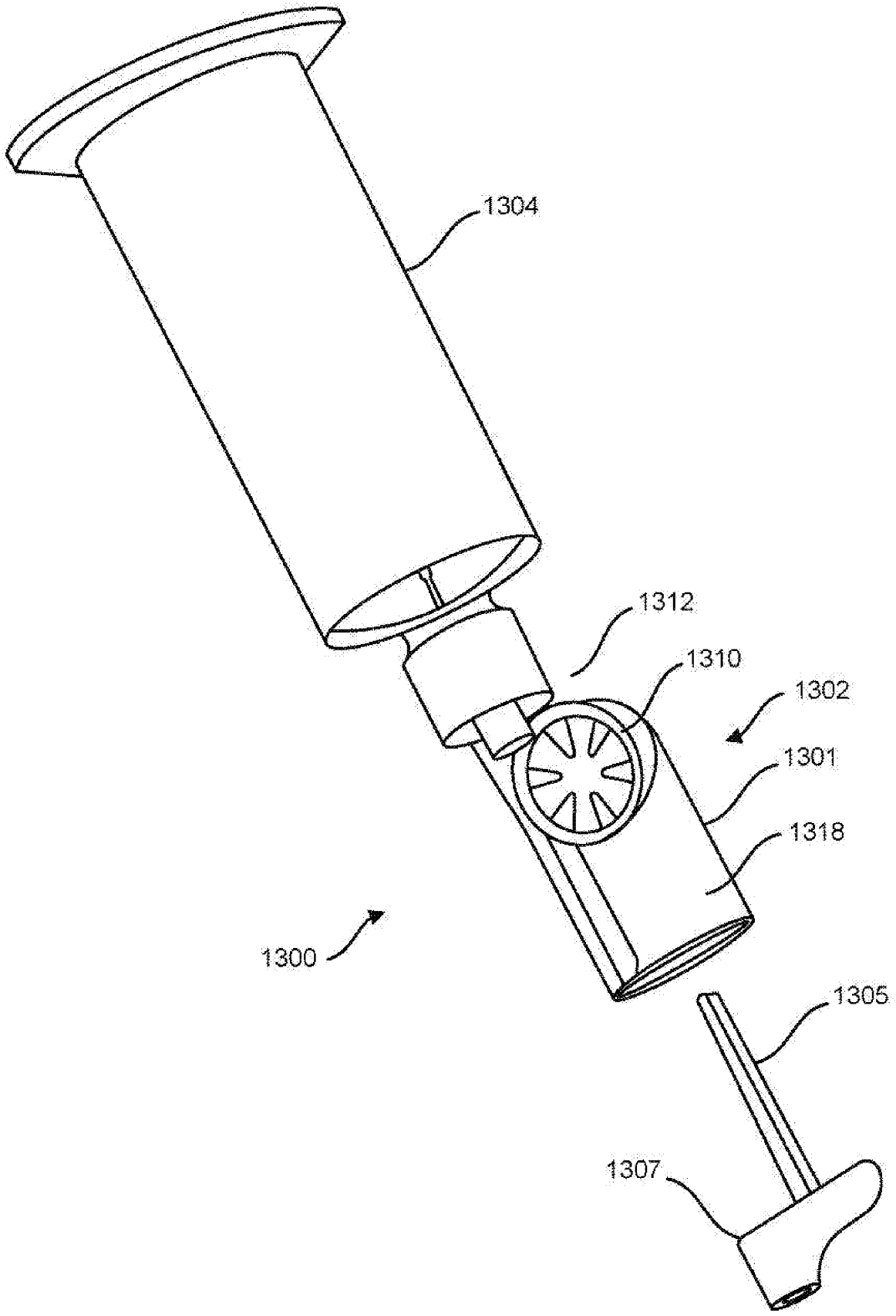


FIG. 13A

[Fig. 13B]

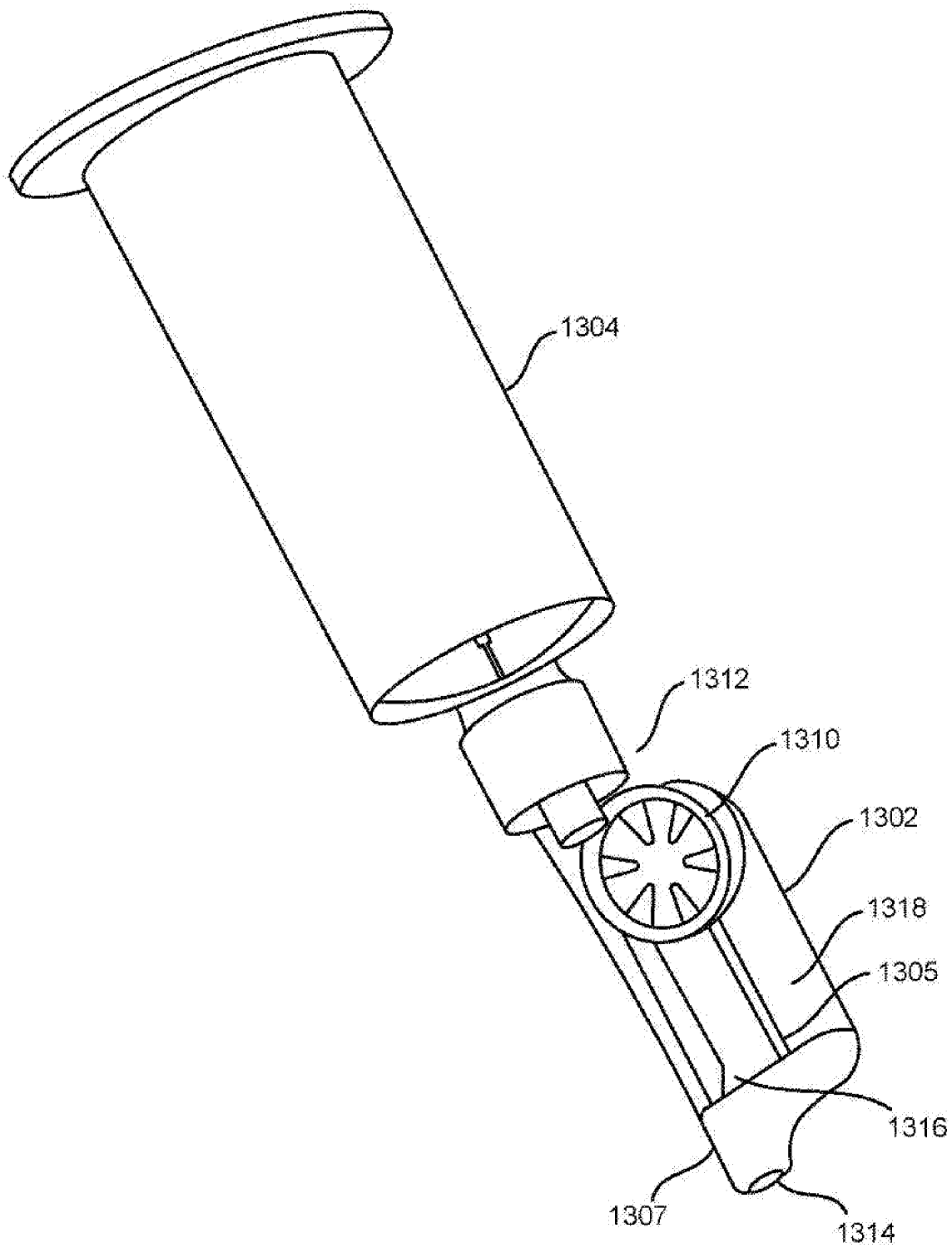


FIG. 13B

[Fig. 13C]

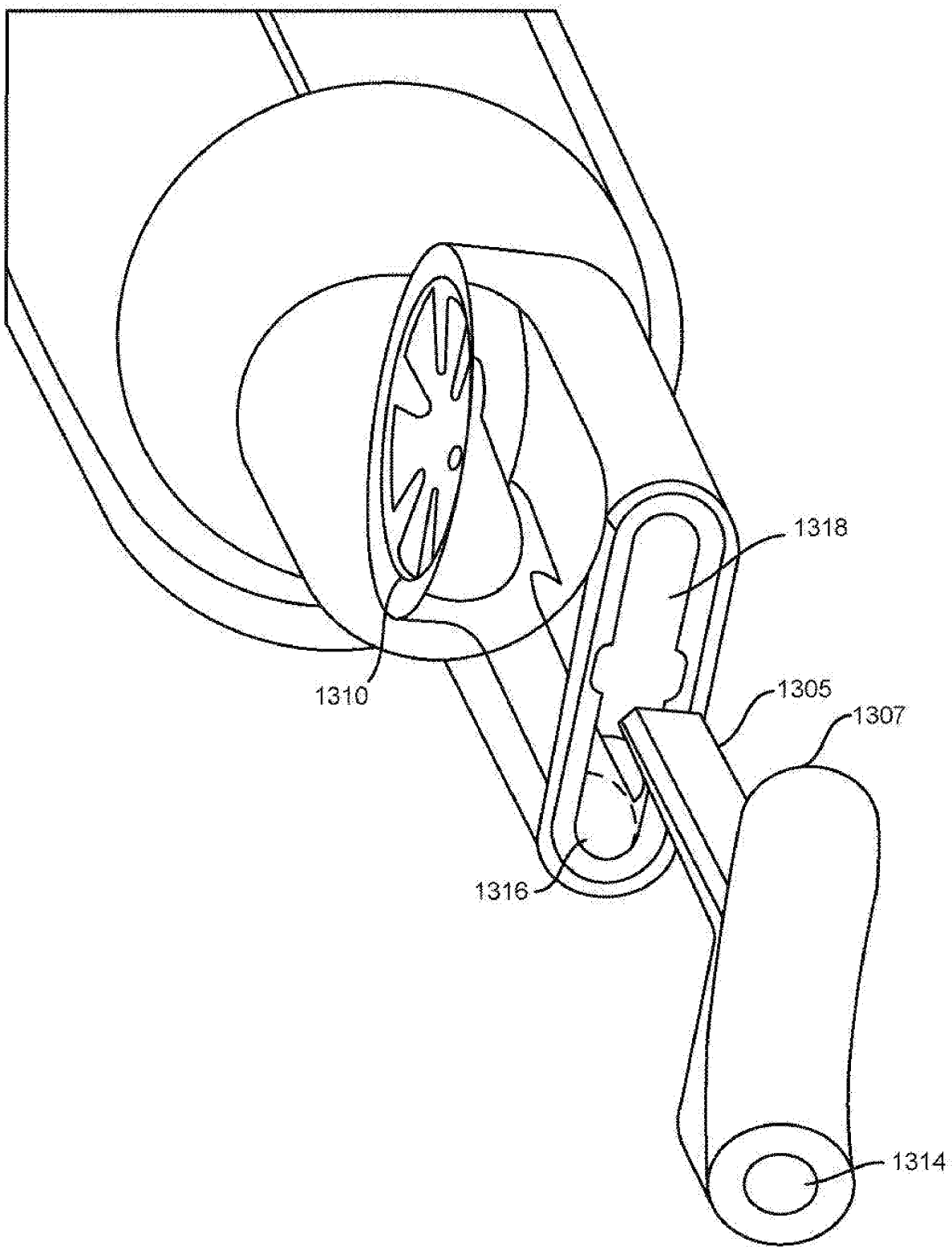
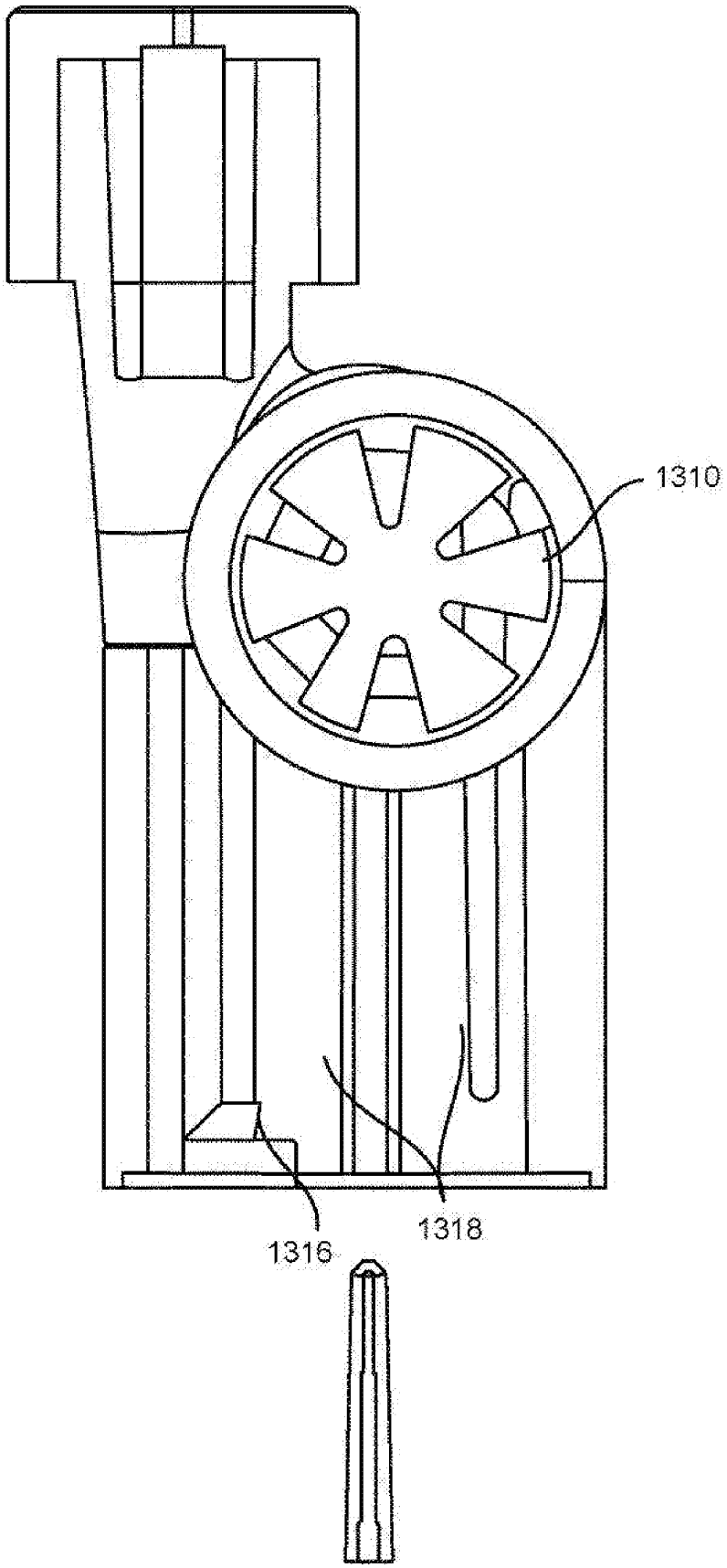


FIG. 13C

[Fig. 13D]


1310
1316
1318

[Fig. 14A]

FIG. 13D

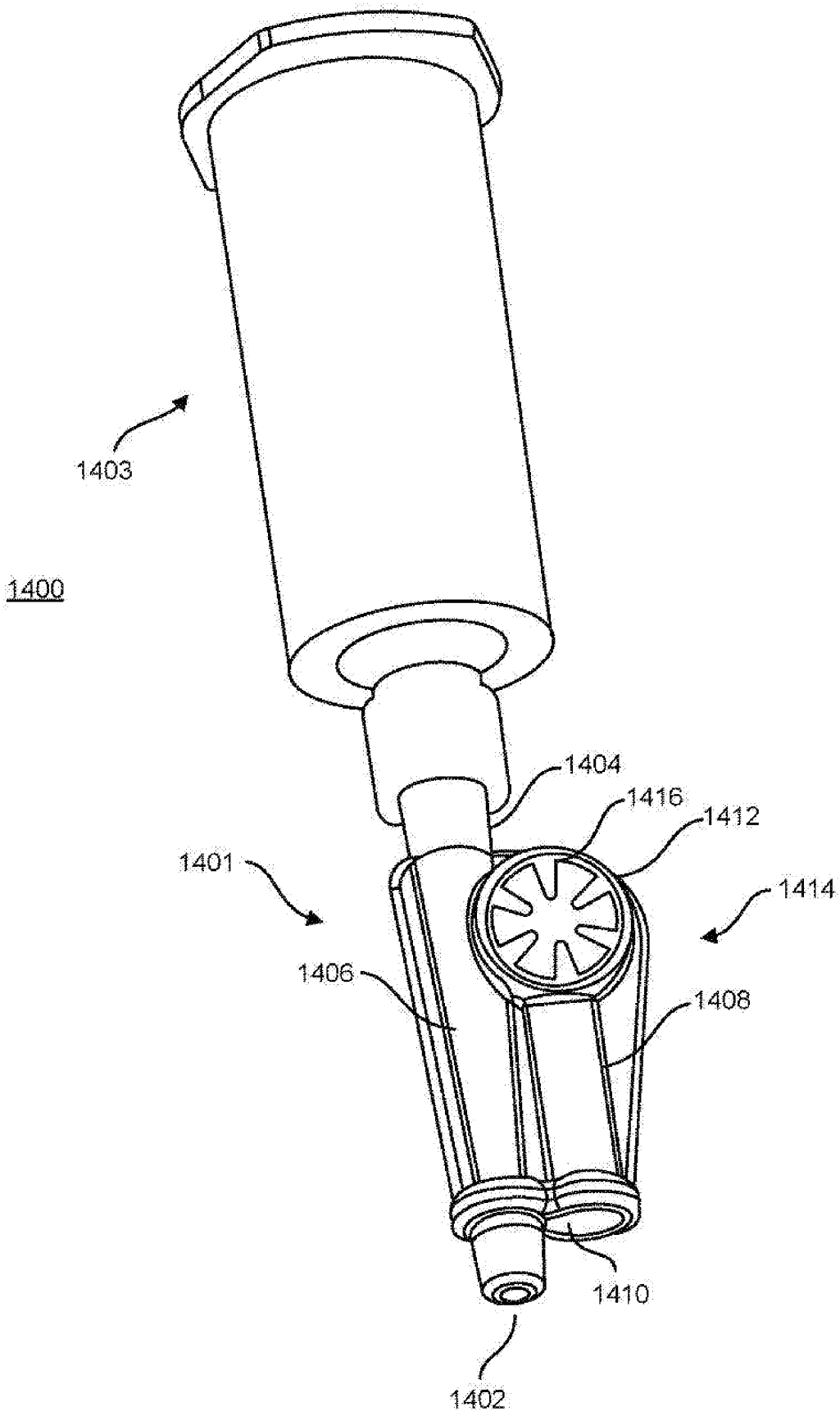
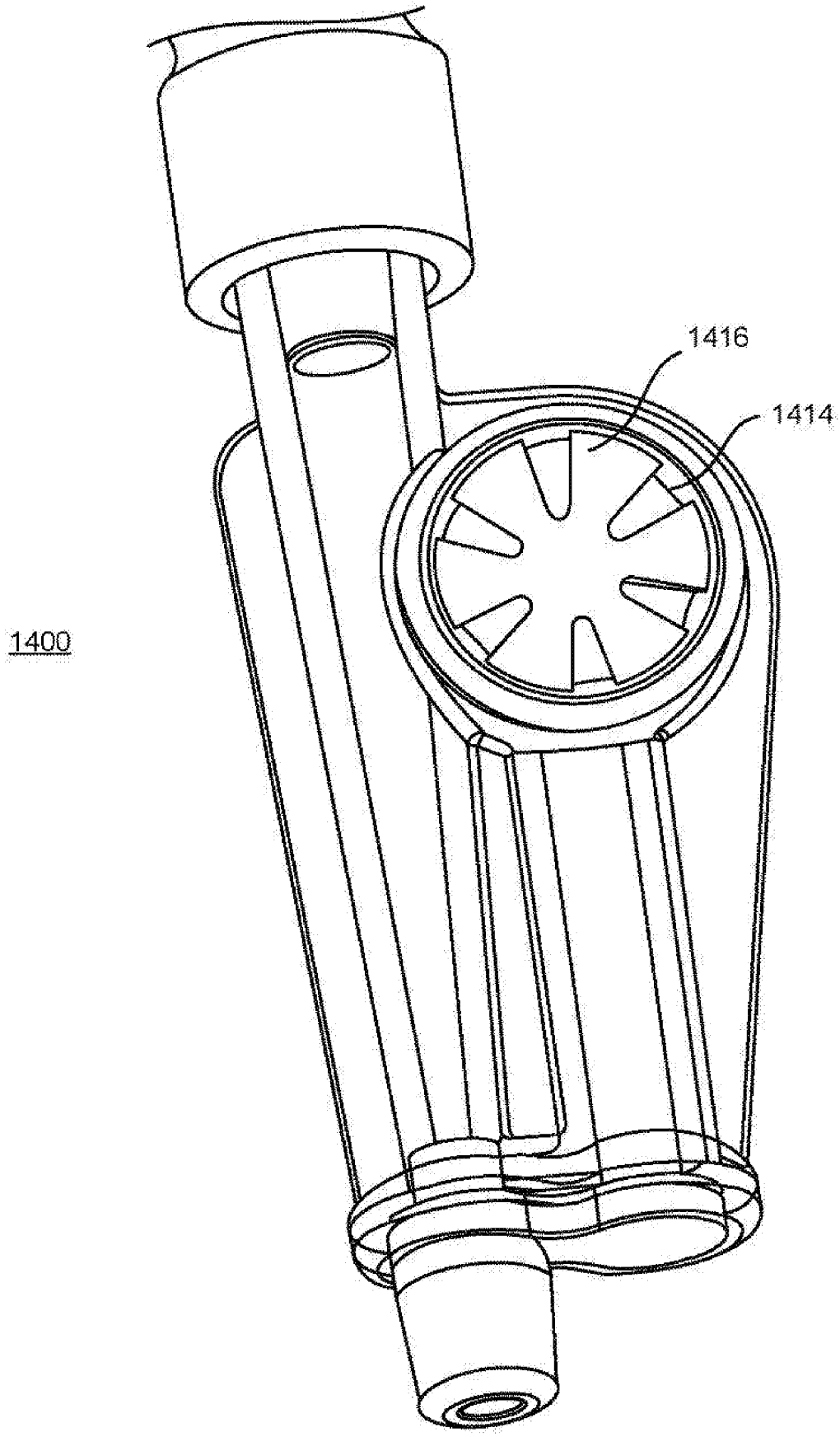


FIG. 14A

[Fig. 14B]


1416
1414
1400

[Fig. 14C]

FIG. 14B

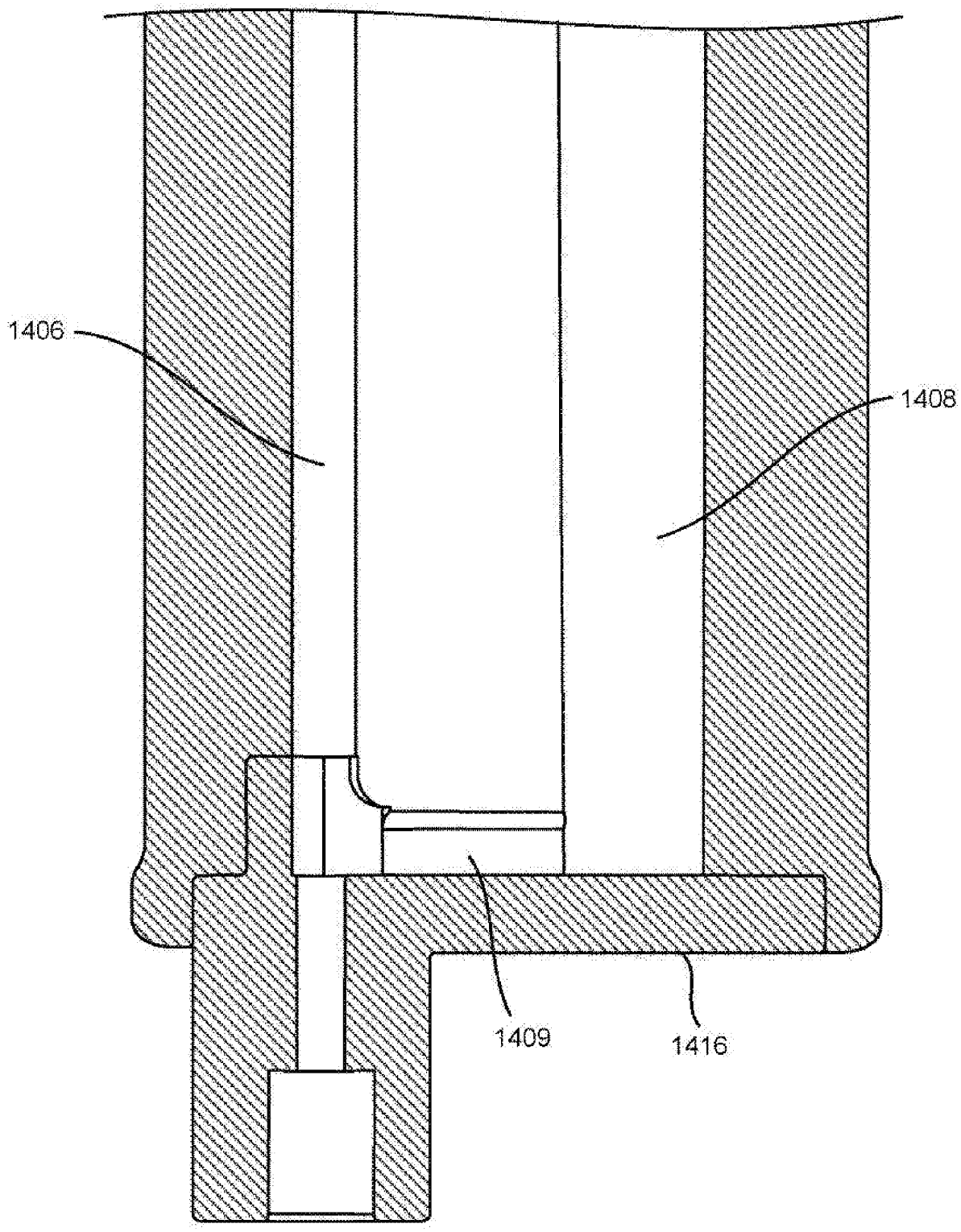
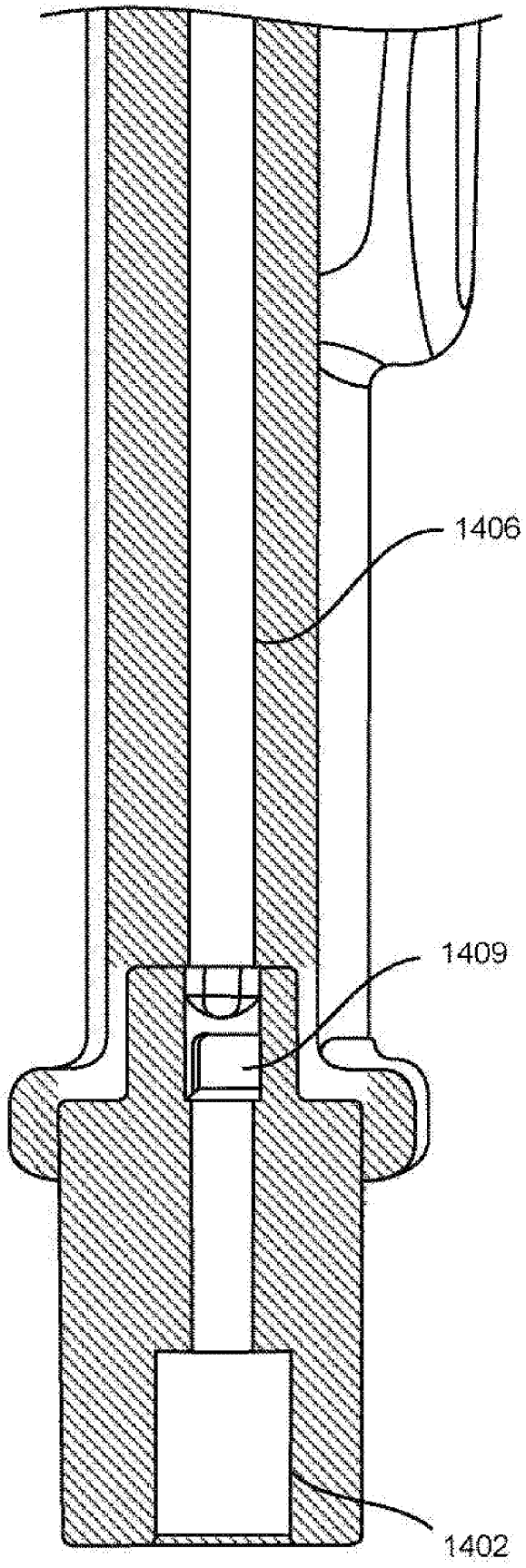


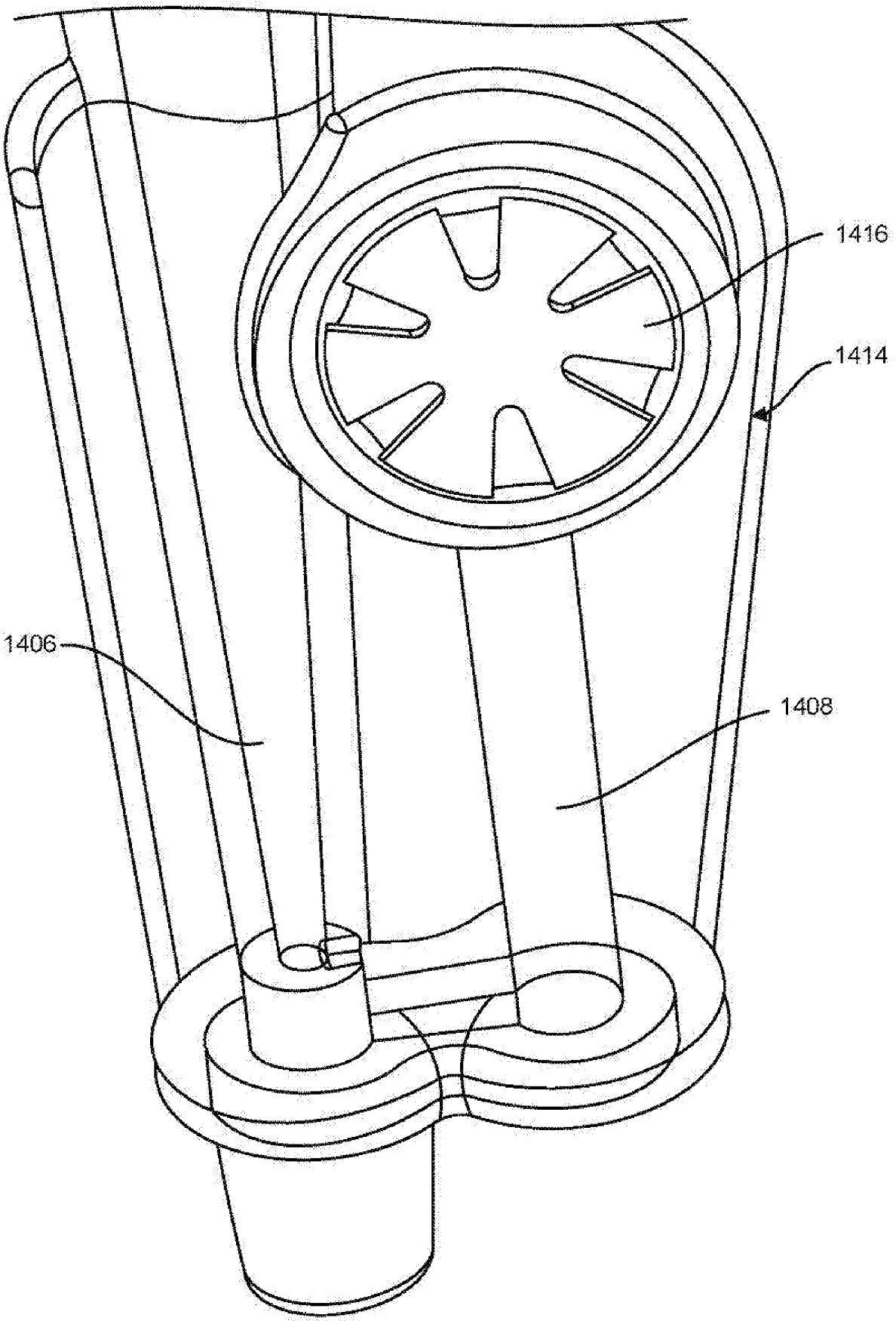
FIG. 14C

[Fig. 14D]


1406
1409
1402

[Fig. 14E]

FIG. 14D


1416
1414
1406
1408

[Fig. 15A]

FIG. 14E

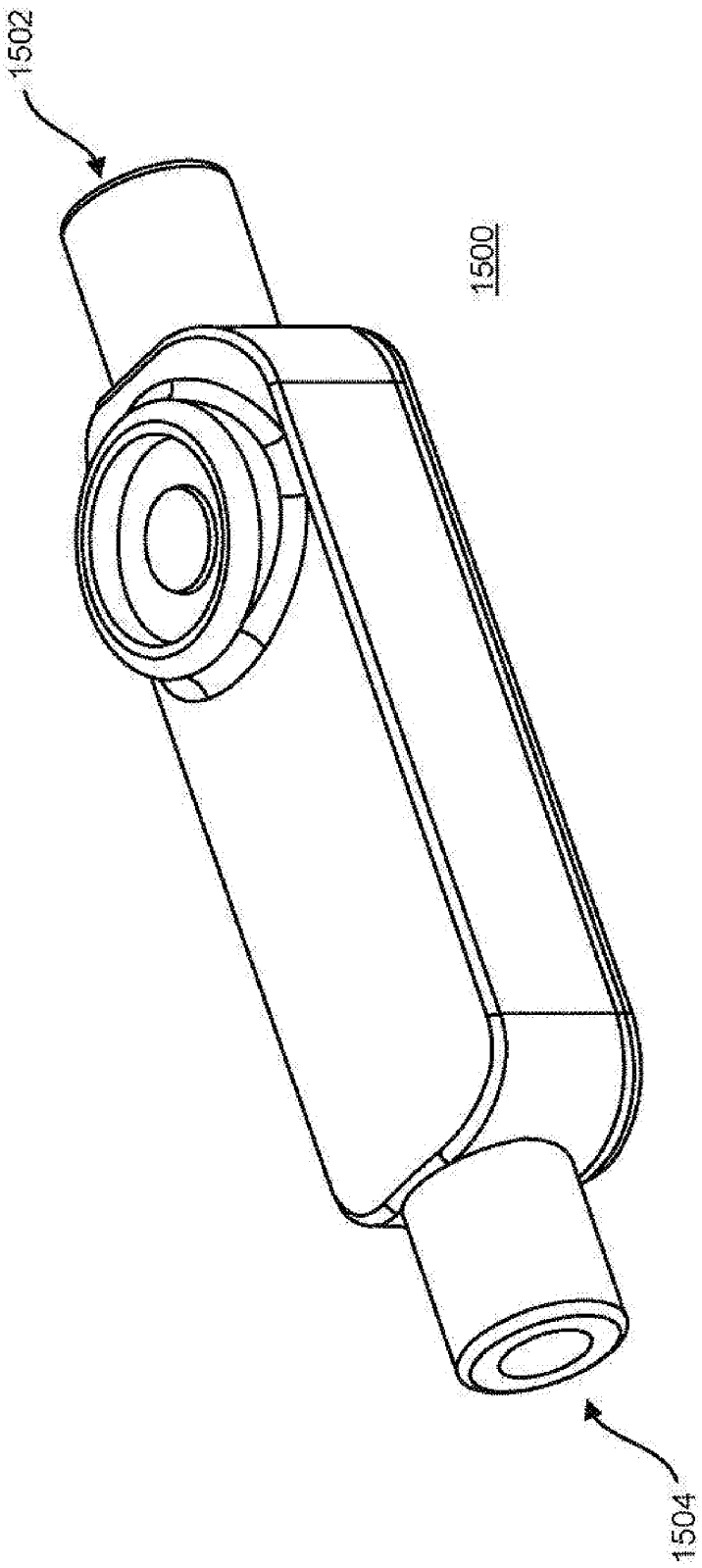


FIG. 15A

[Fig. 15B]

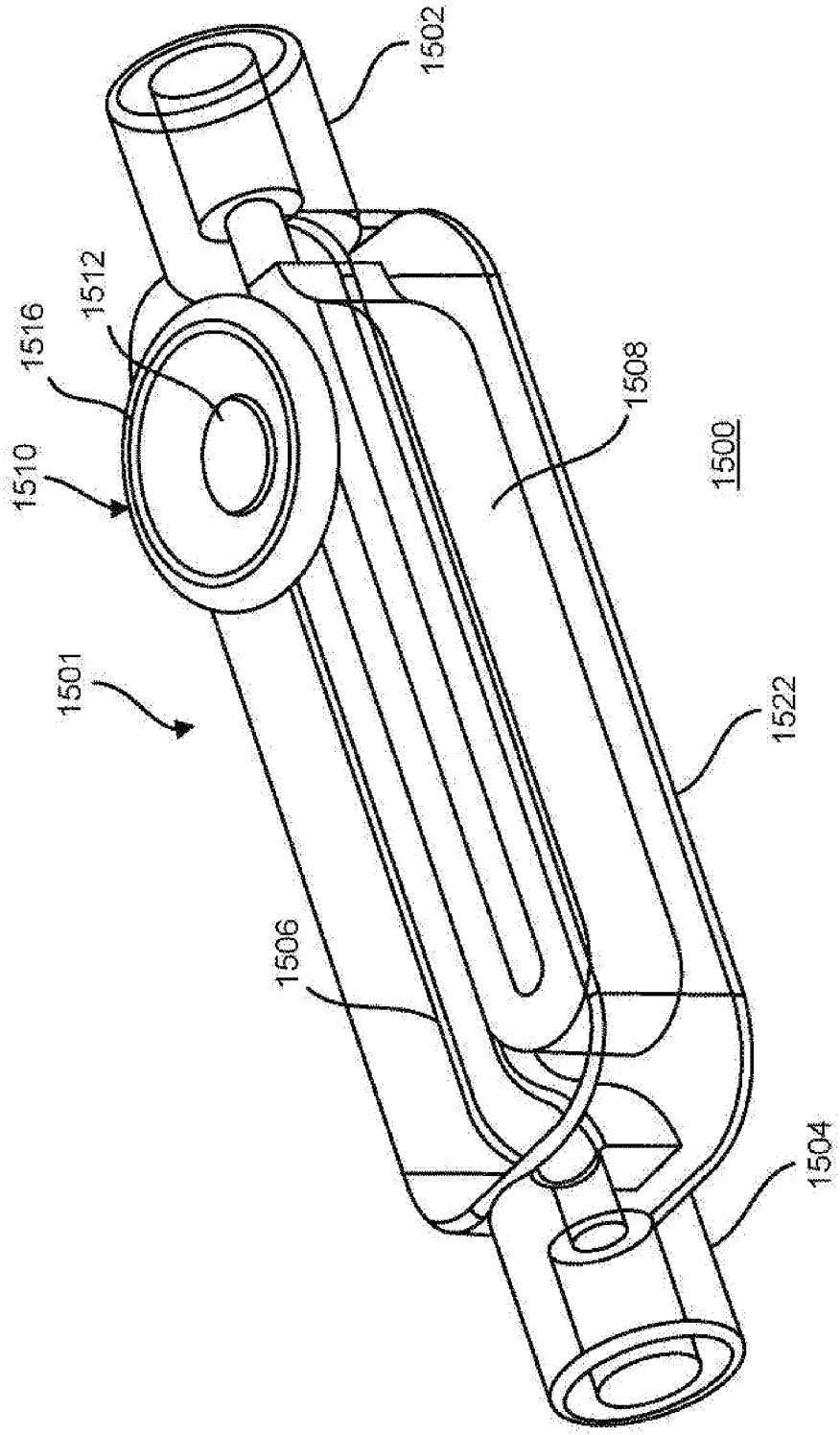


FIG. 15B

[Fig. 15C]

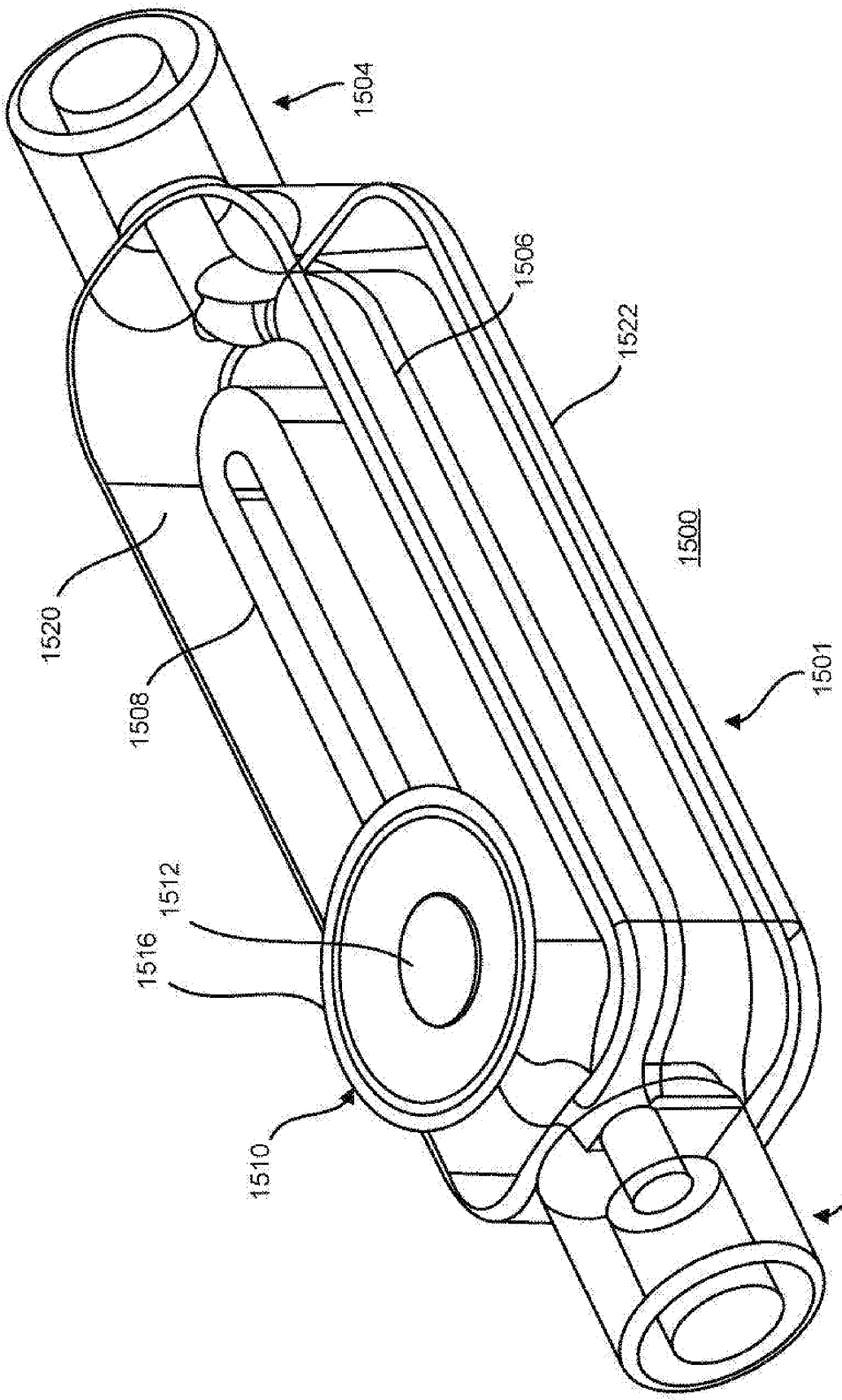


FIG. 15C

[Fig. 15D]

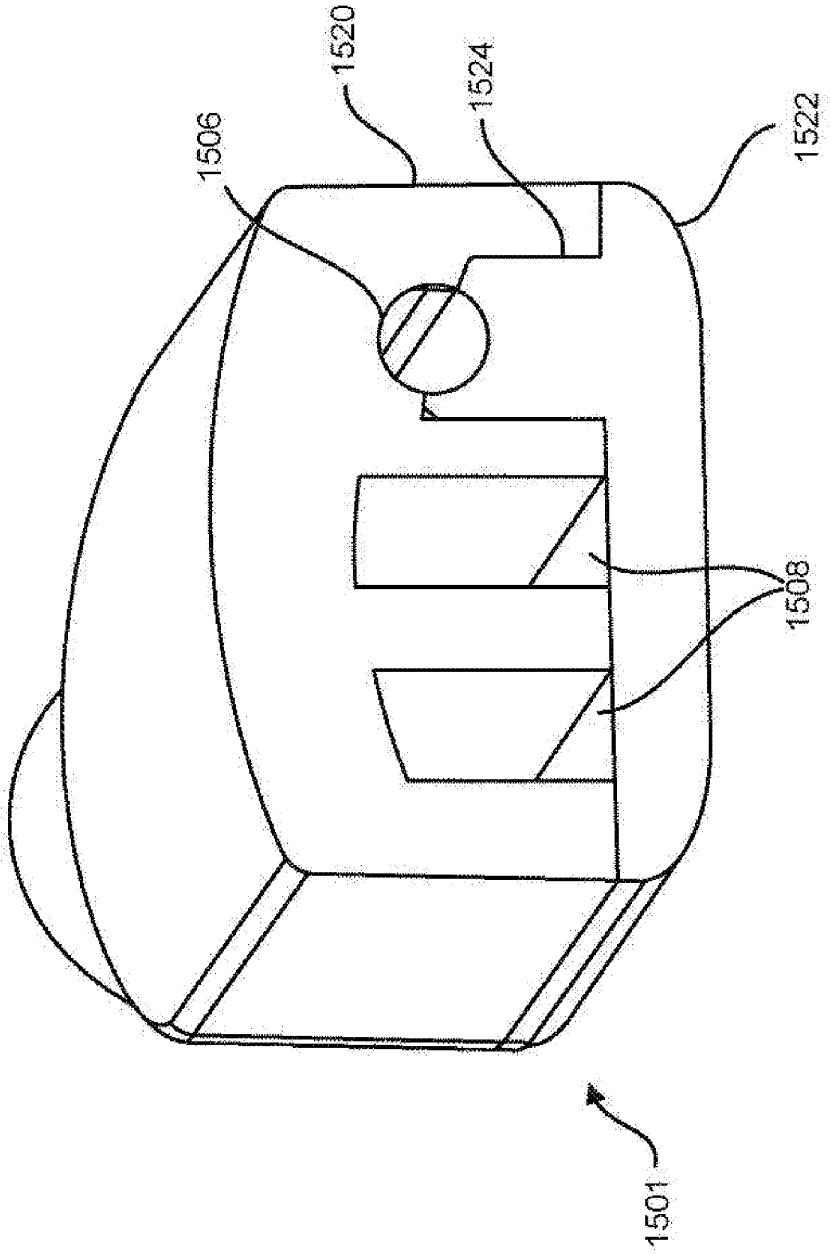


FIG. 15D

[Fig. 15E]

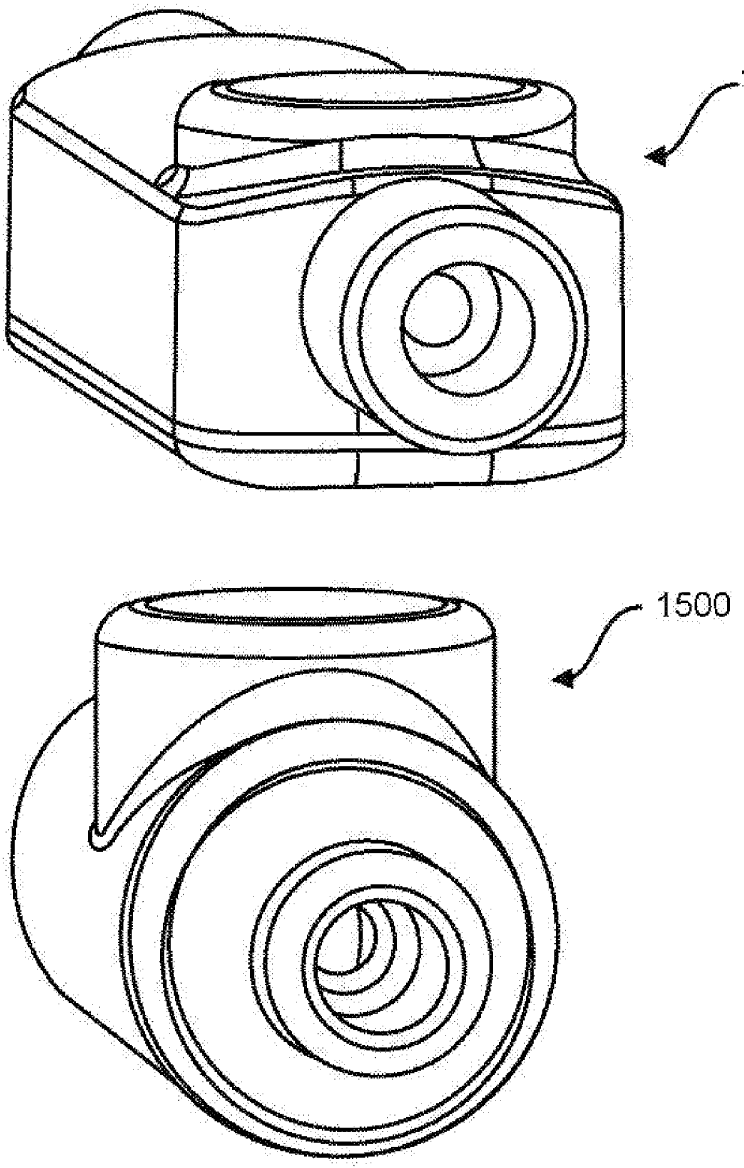


FIG. 15E

[Fig. 15F]

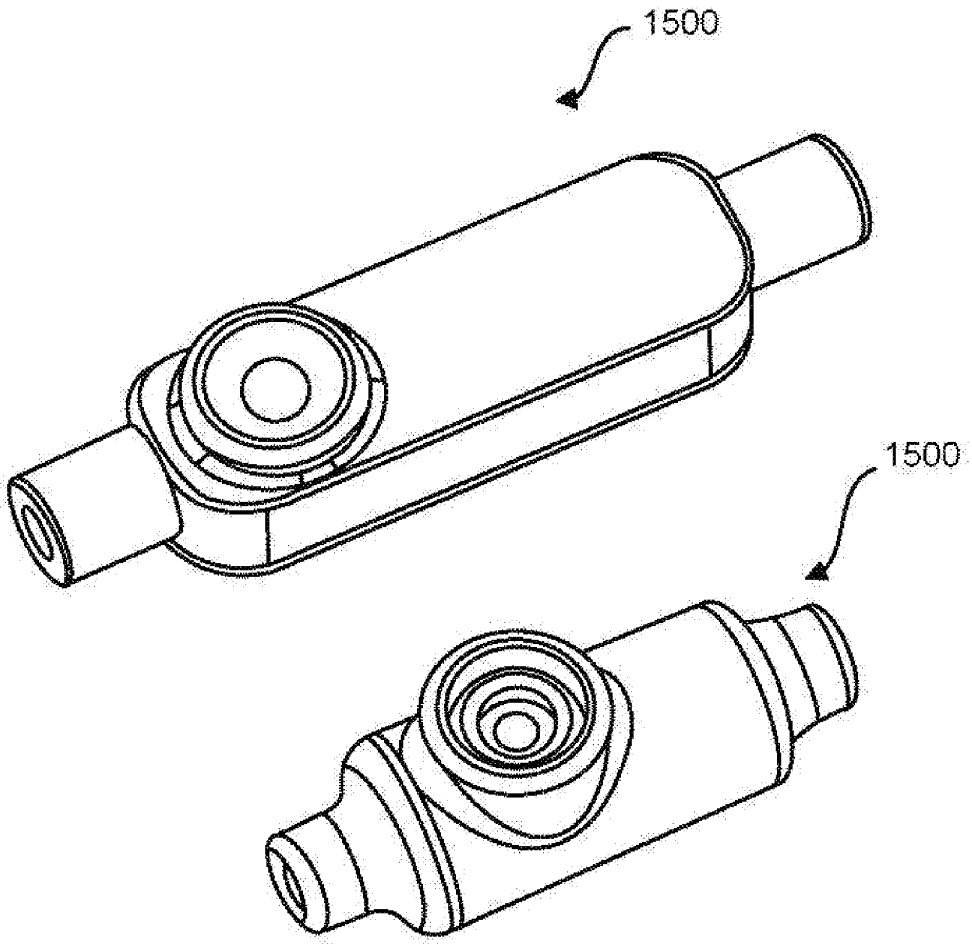


FIG. 15F

[Fig. 15G]

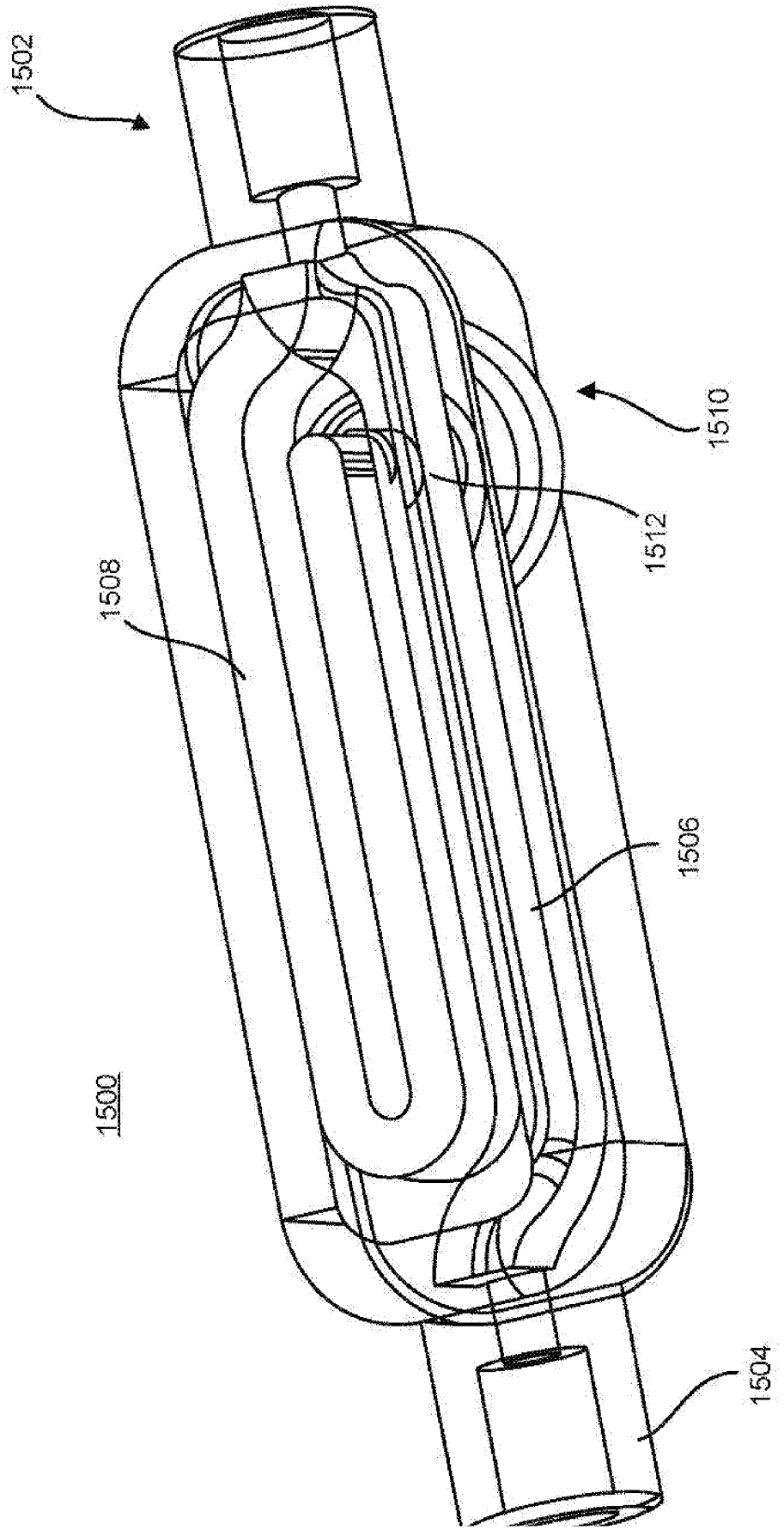


FIG. 15G

[Fig. 16A]

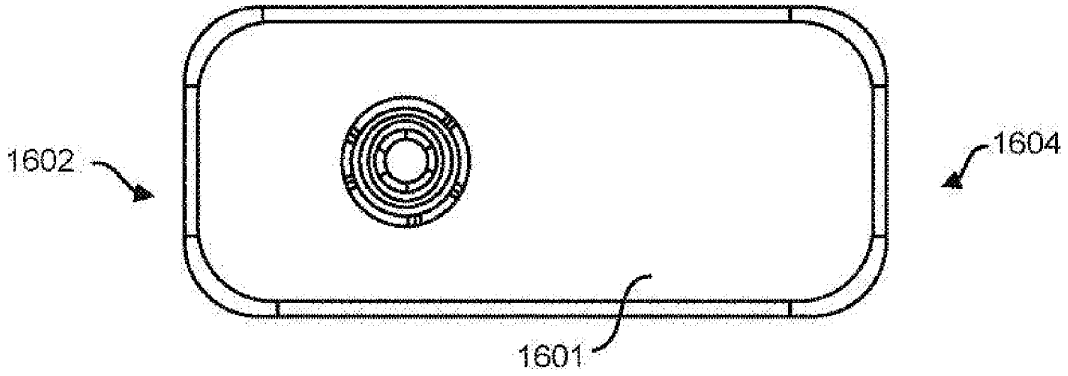


FIG. 16A

[Fig. 16B]

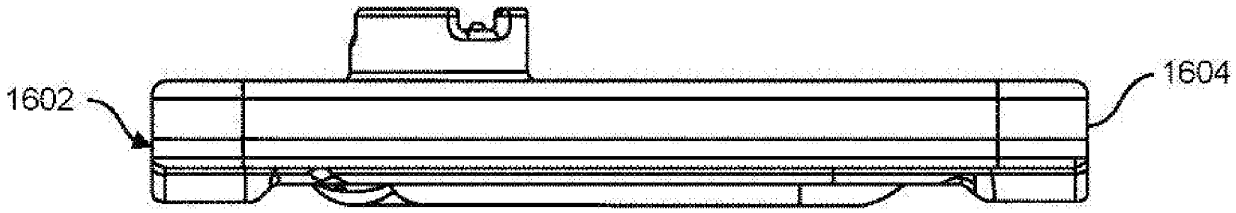


FIG. 16B

[Fig. 16C]

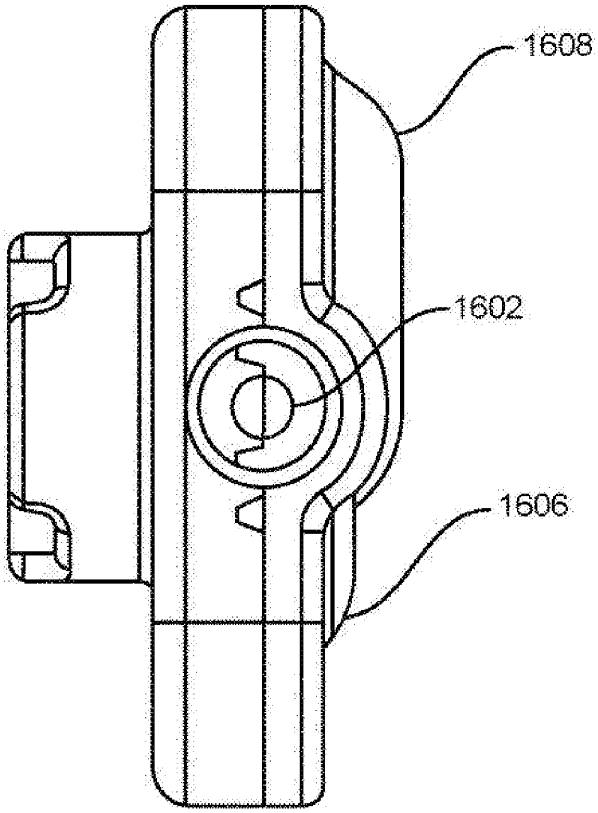


FIG. 16C

[Fig. 16D]

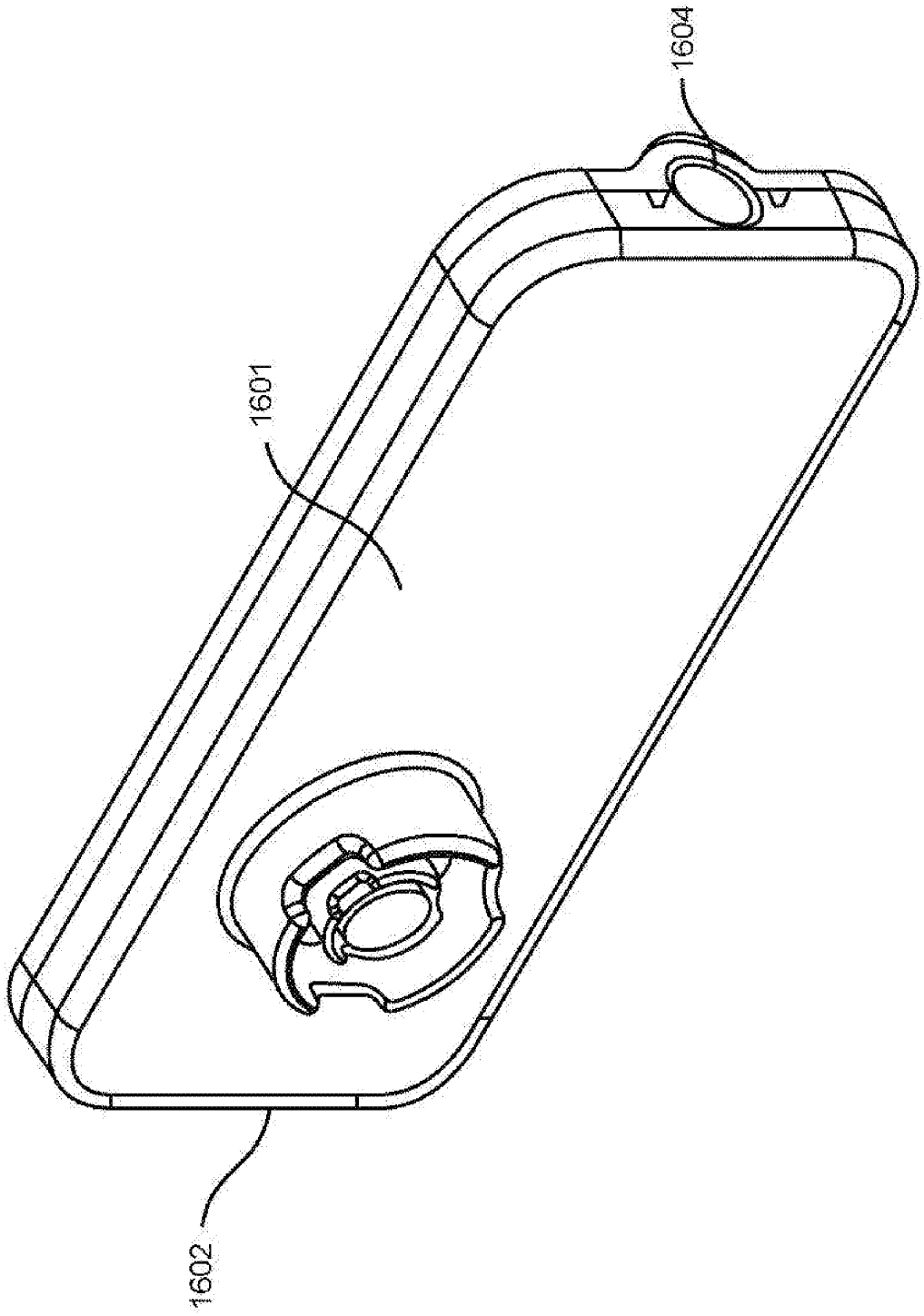


FIG. 16D

[Fig. 17A]

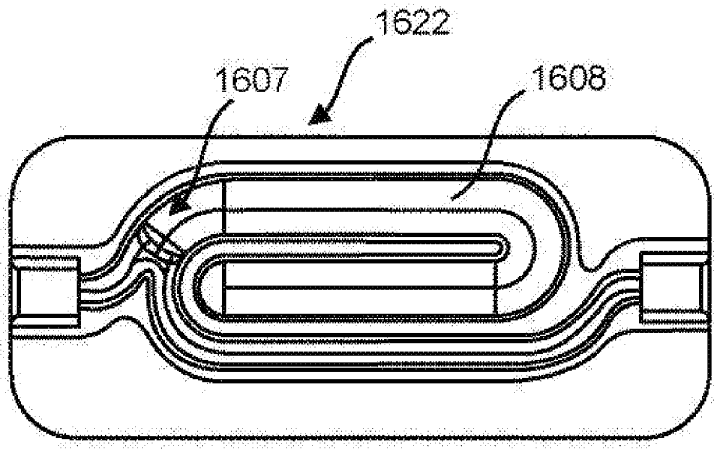


FIG. 17A

[Fig. 17B]

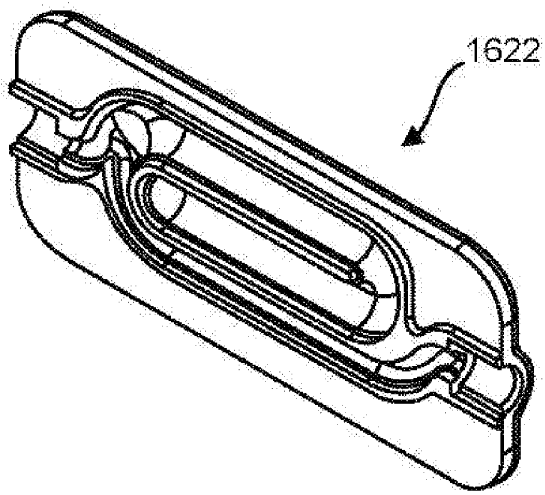


FIG. 17B

[Fig. 17C]

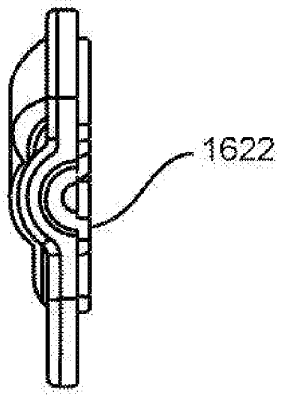


FIG. 17C

[Fig. 17D]

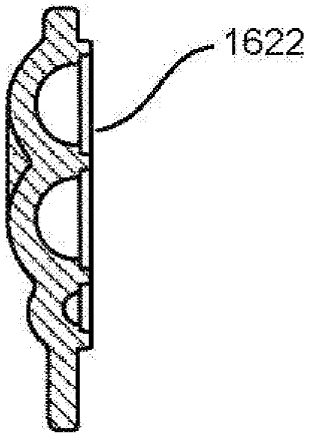


FIG. 17D

[Fig. 17E]

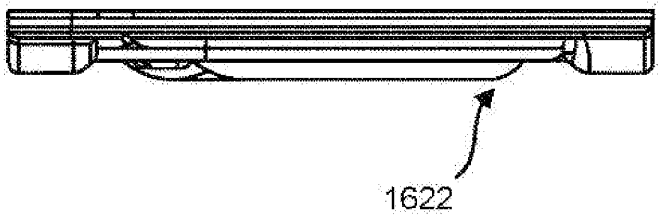


FIG. 17E

[Fig. 18A]

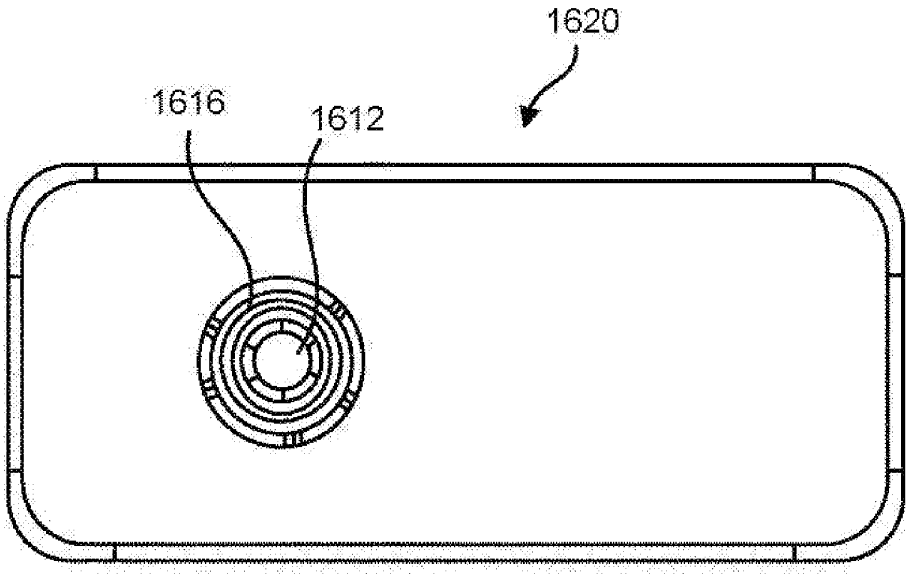


FIG. 18A

[Fig. 18B]

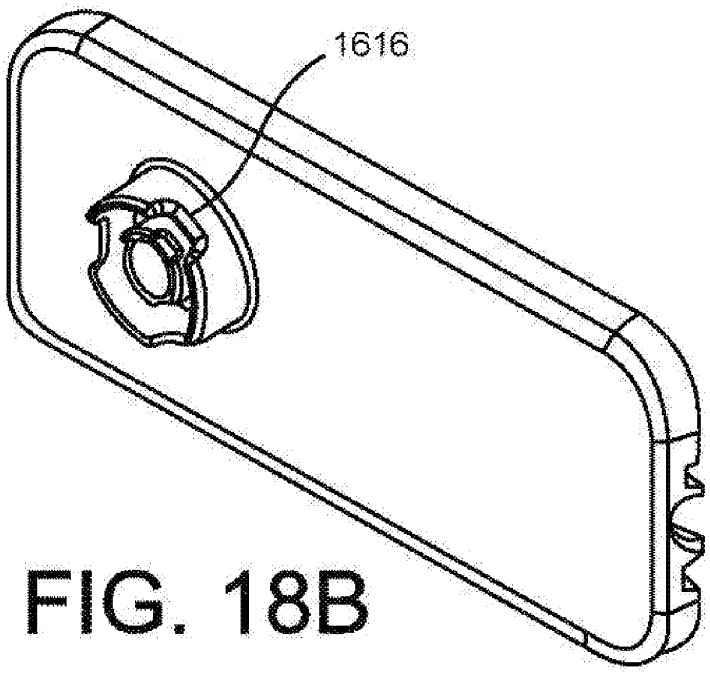


FIG. 18B

[Fig. 18C]

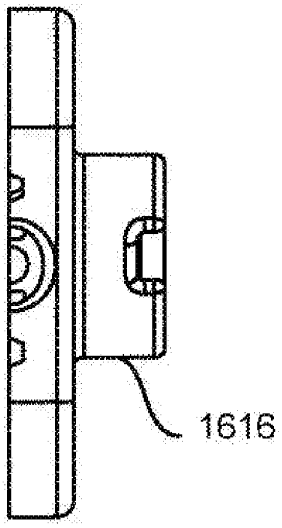


FIG. 18C

[Fig. 18D]

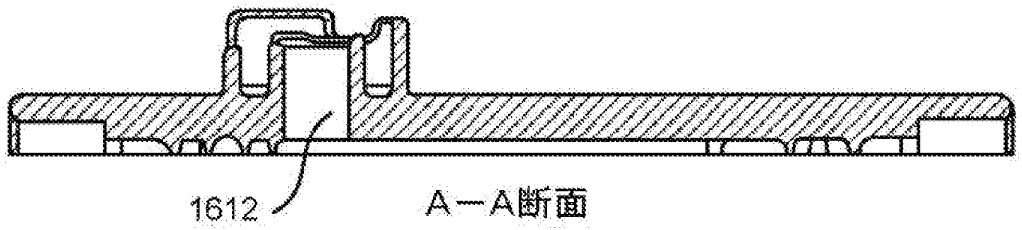


FIG. 18D

[Fig. 18E]

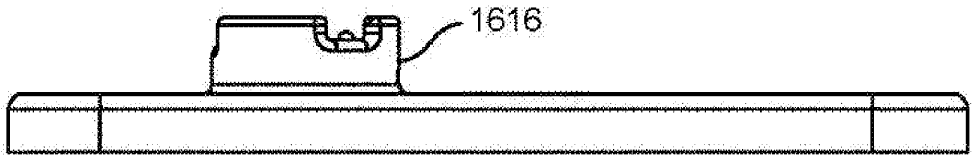


FIG. 18E

[Fig. 18F]

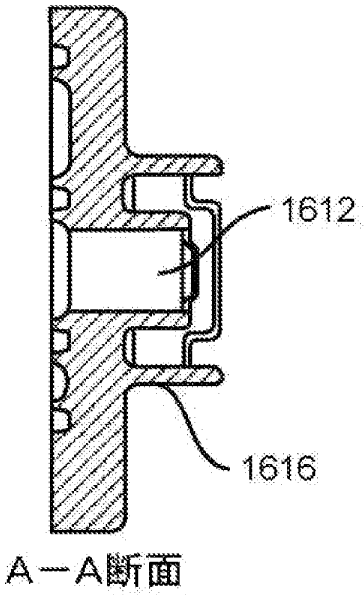


FIG. 18F

[Fig. 19A]

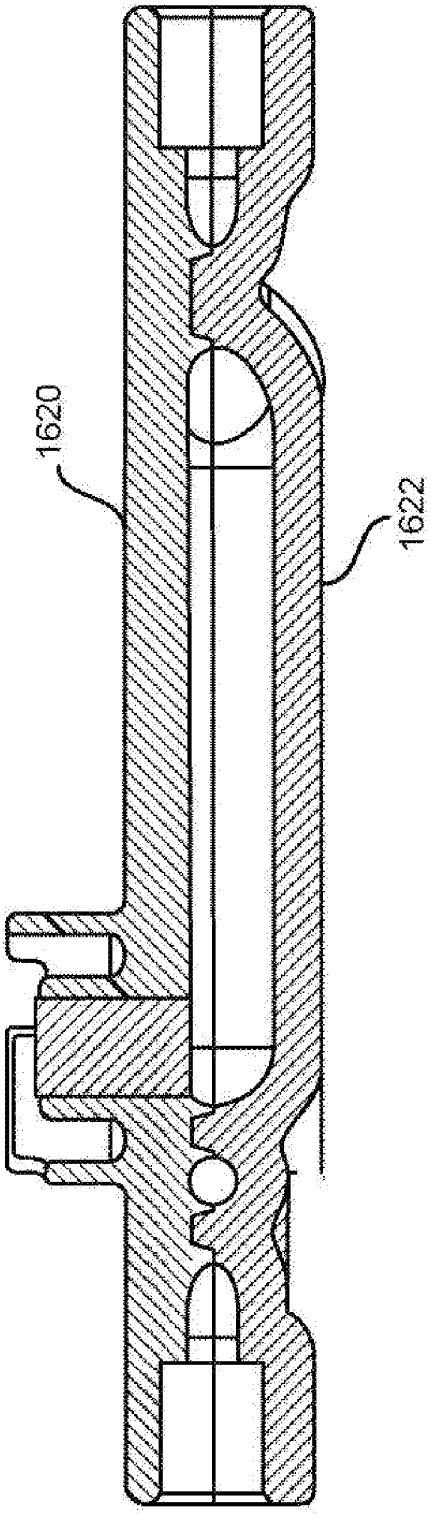


FIG. 19A

[Fig. 19B]

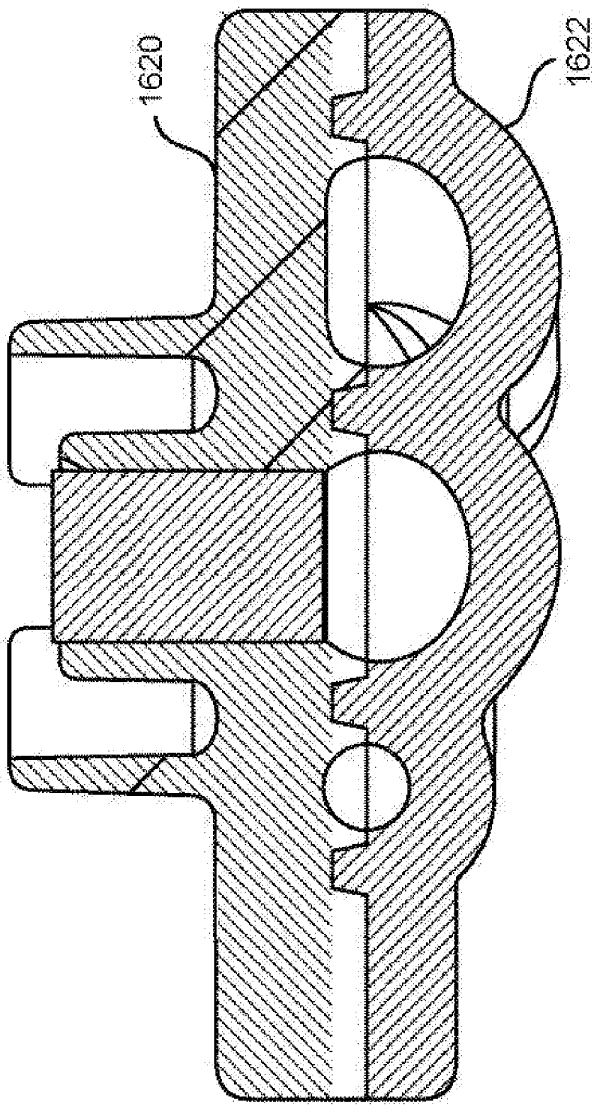


FIG. 19B

[Fig. 20]

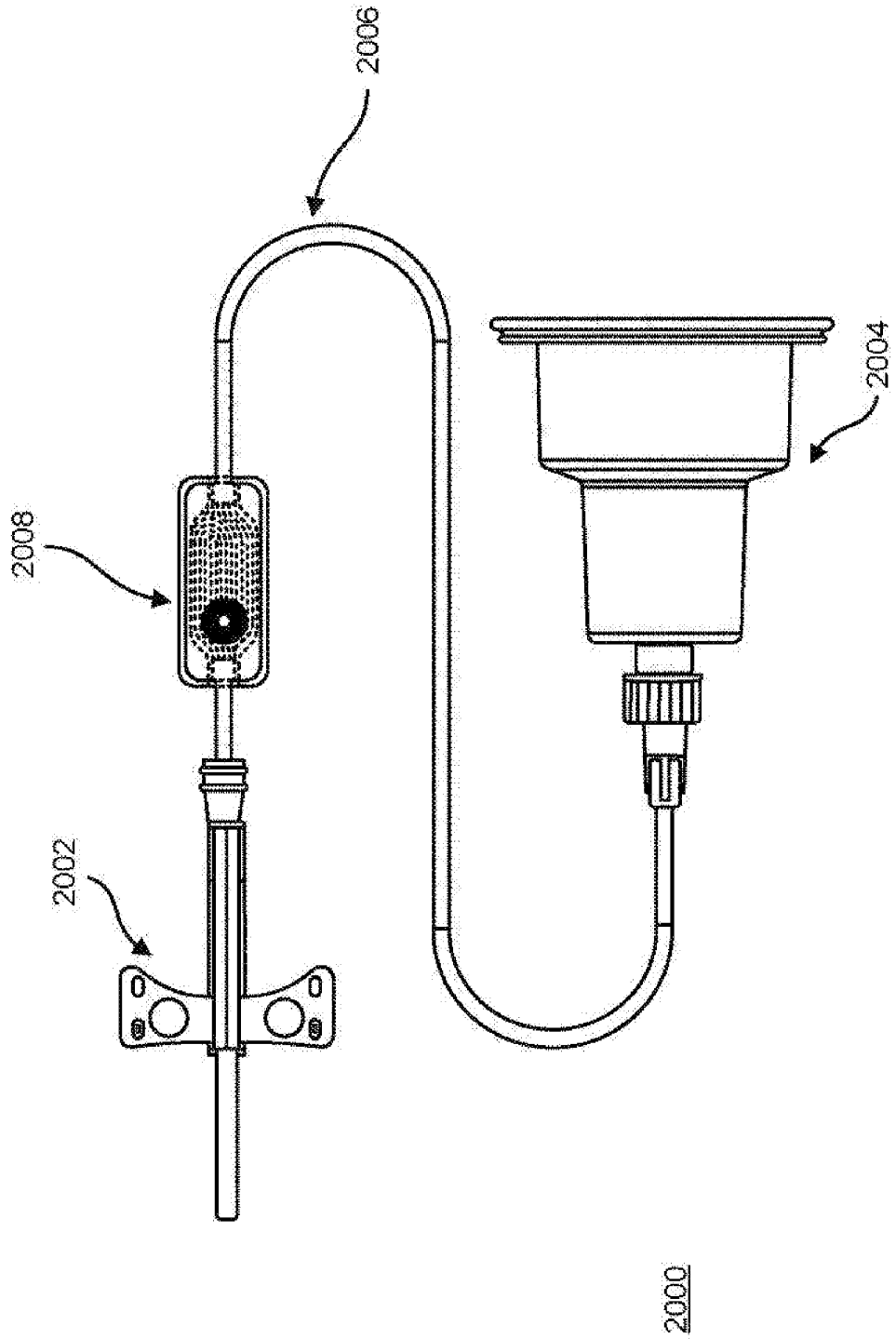


FIG. 20

[Fig. 21]

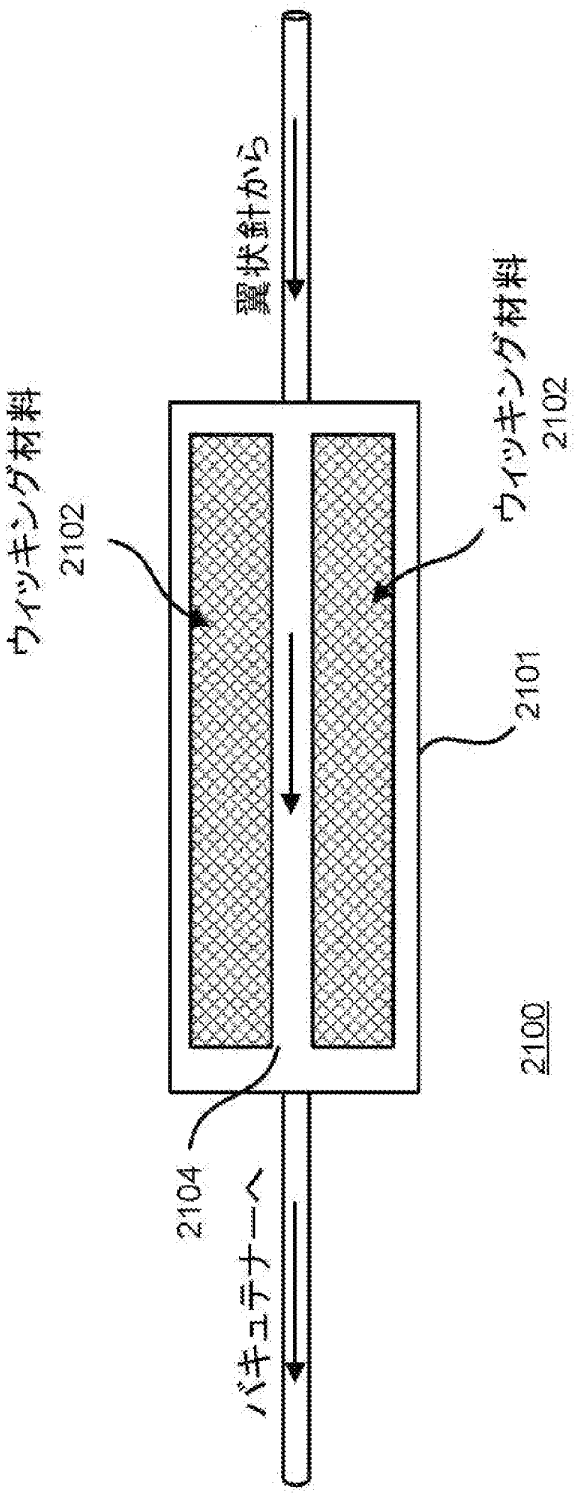


FIG. 21

[Fig. 22A]

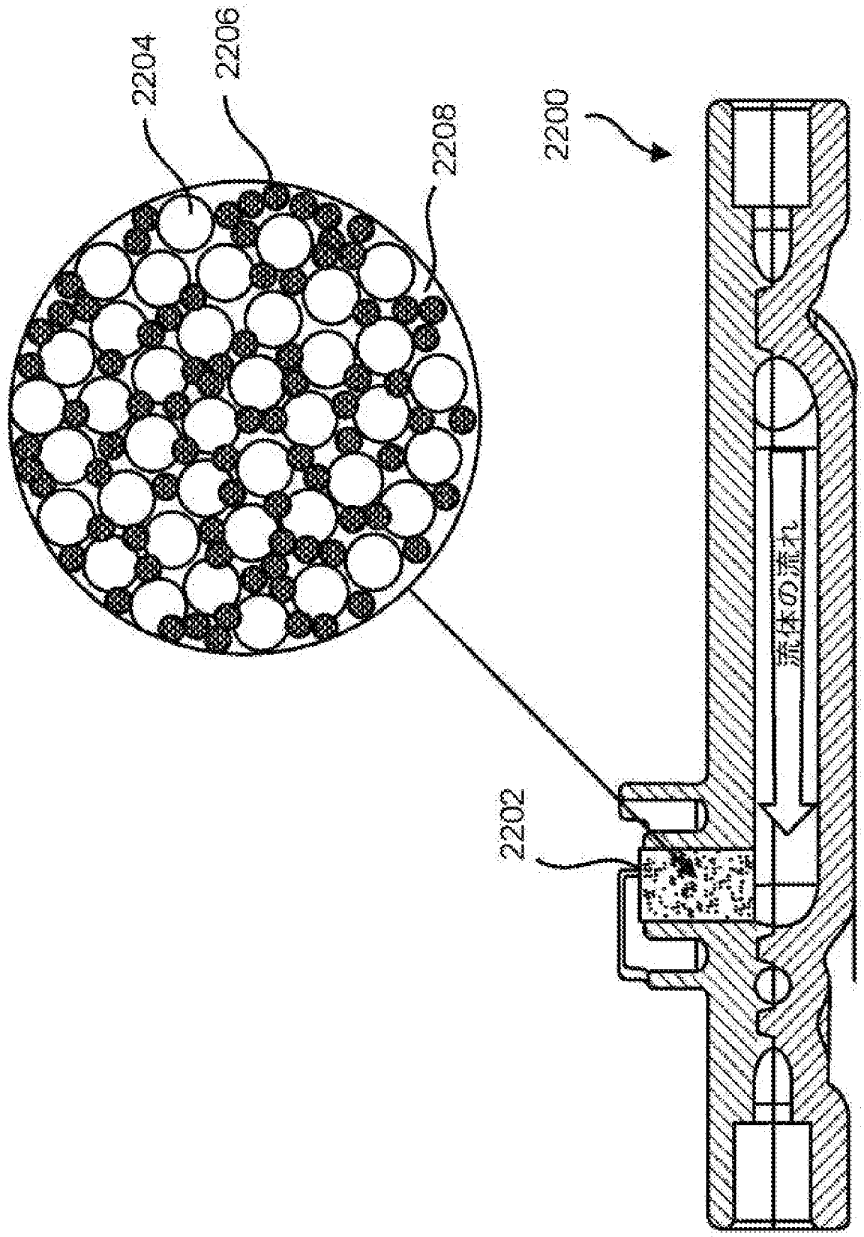


FIG. 22A

[Fig. 22B]

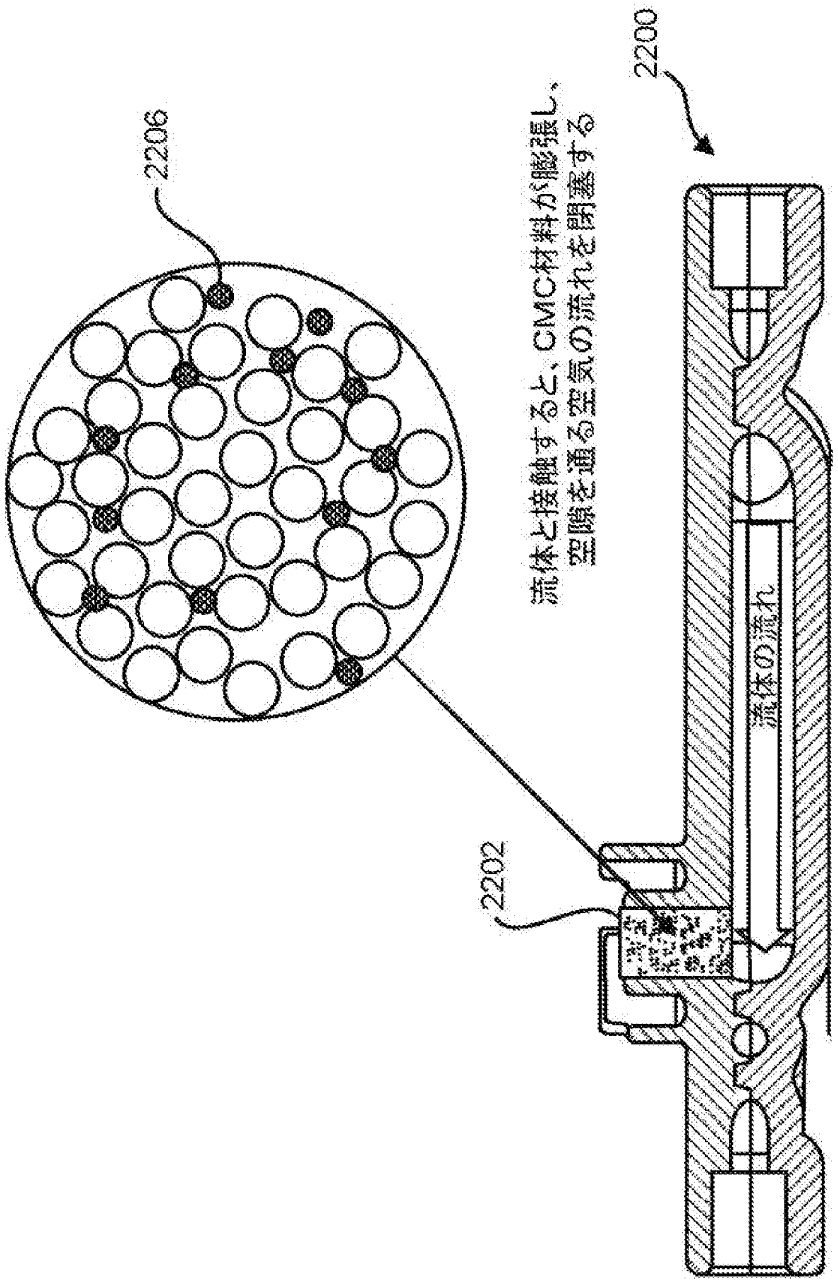


FIG. 22B

[Fig. 23A]

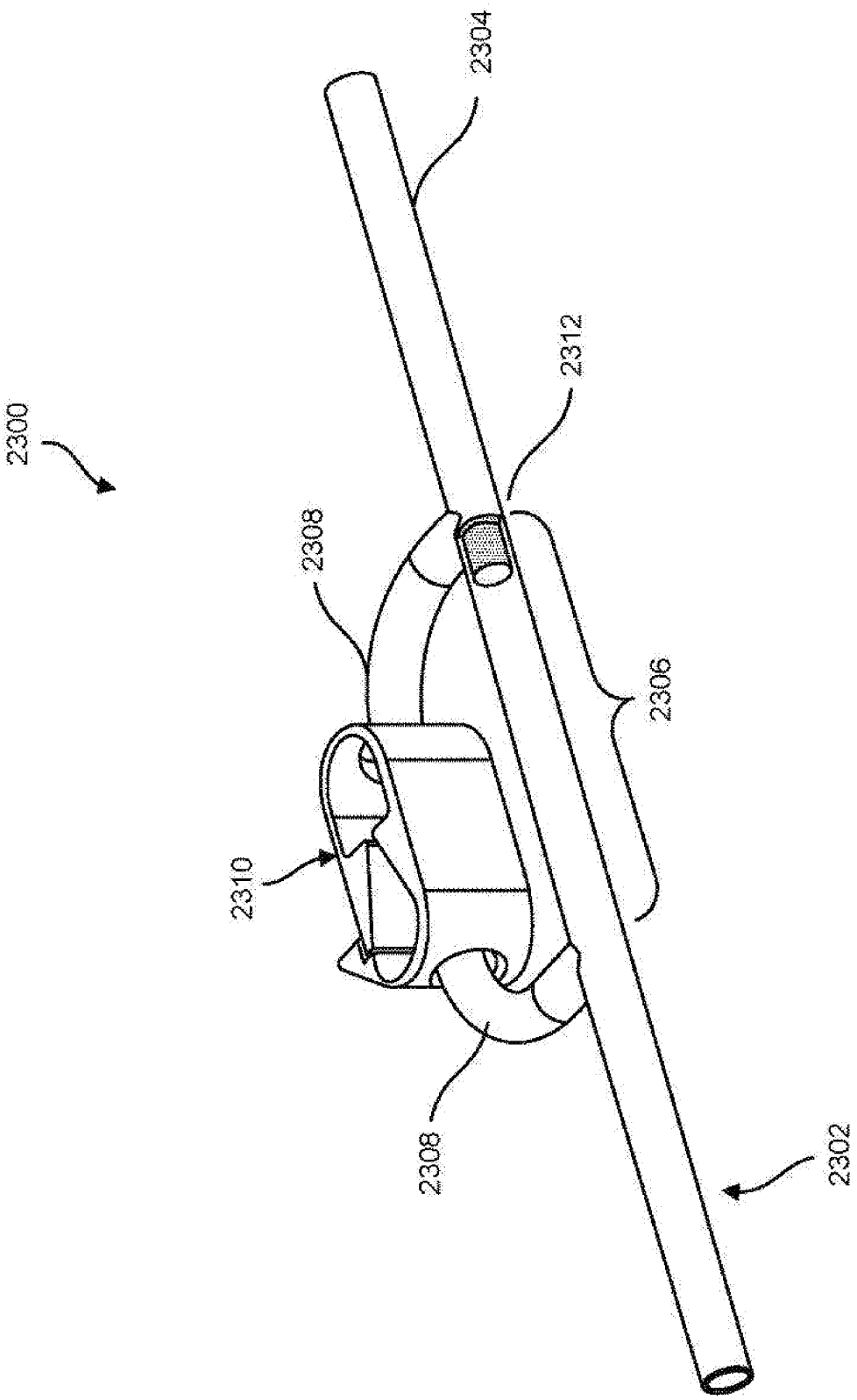


FIG. 23A

[Fig. 23B]

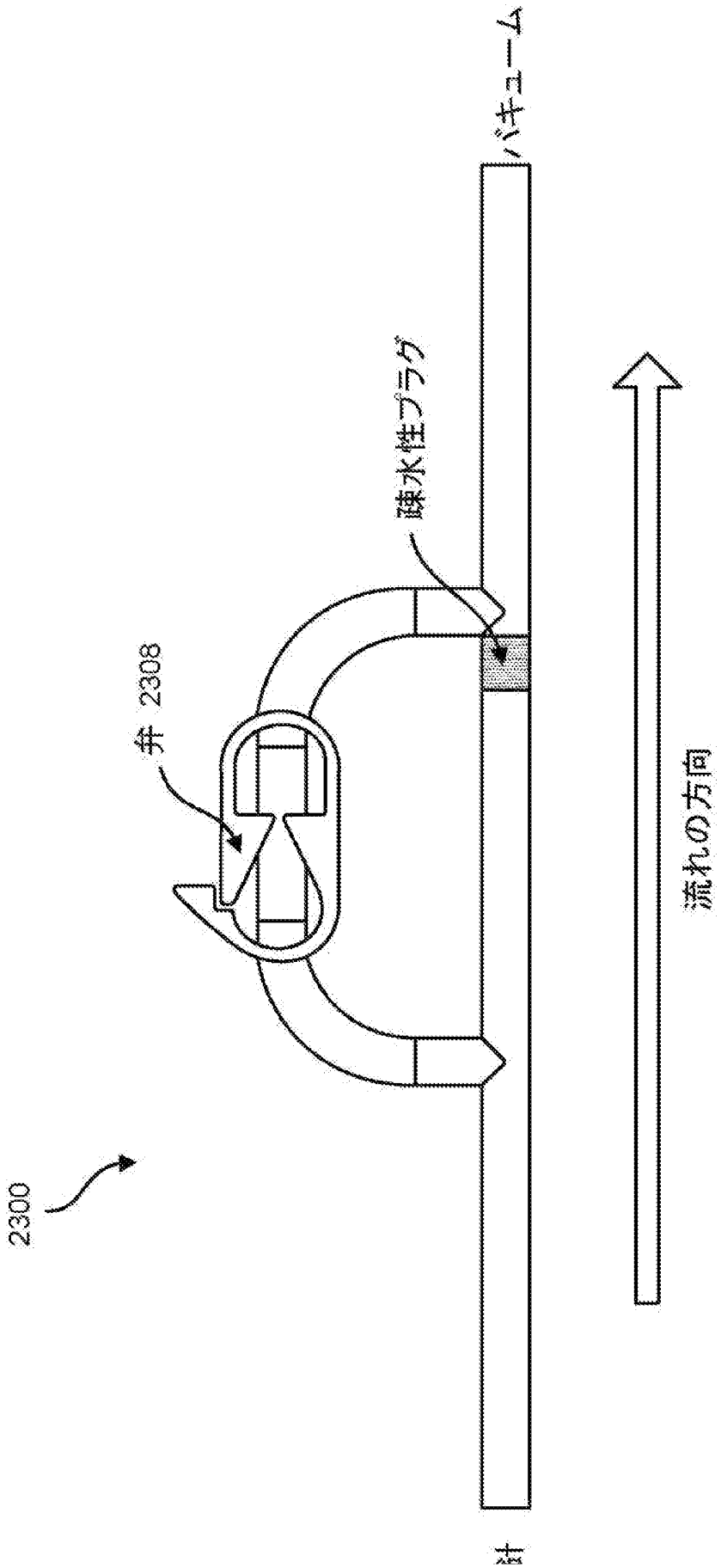


FIG. 23B

drawing open

1 2 3 Four Five 6 7 8A 8B 8C ...

Magnify and Rotate

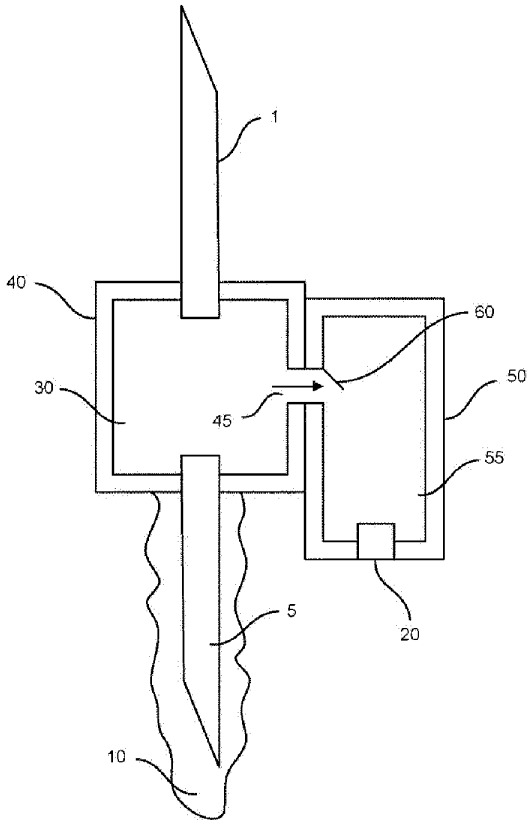


FIG. 1

Figure 1

1 / 1 display

Copyright JPO and INPIT (P0200)

(19)日本国特許庁(JP)　(12)特　許　公　報(B2)　(11)特許番号
特許第6734490号
(P6734490)
(45)発行日　令和2年8月5日(2020.8.5)　(24)登録日　令和2年7月13日(2020.7.13)

(51)Int.Cl.　　F I
A61B 5/15 (2006.01)　　A61B 5/15 200
A61B 5/154 (2006.01)　　A61B 5/154 200

請求項の数 26　外国語出願　(全 39 頁)

(21)出願番号　特願2020-340(P2020-340)
(22)出願日　令和2年1月6日(2020.1.6)
(62)分割の表示　特願2018-523384(P2018-523384)の分割
原出願日　平成28年7月22日(2016.7.22)
(65)公開番号　特開2020-96843(P2020-96843A)
(43)公開日　令和2年6月25日(2020.6.25)
審査請求日　令和2年1月31日(2020.1.31)
(31)優先権主張番号　62/238,636
(32)優先日　平成27年10月7日(2015.10.7)
(33)優先権主張国・地域又は機関　米国(US)
(31)優先権主張番号　62/318,194
(32)優先日　平成28年4月4日(2016.4.4)
(33)優先権主張国・地域又は機関　米国(US)

(73)特許権者　518026730
クリン　インコーポレイテッド
アメリカ合衆国　９２１３１　カリフォルニア州　サンディエゴ　スクリップス　ポーウェイ　パークウェイ　１０７５５　ナンバー　２５７
(74)代理人　100083806
弁理士　三好　秀和
(74)代理人　100095500
弁理士　伊藤　正和
(74)代理人　100111235
弁理士　原　裕子
(74)代理人　100195257
弁理士　大渕　一志

最終頁に続く

(54)【発明の名称】血液隔離装置、体液隔離装置、及び血液隔離システム

【特許請求の範囲】
【請求項１】
血液隔離装置であって、
入口ポートと、
出口ポートと、
隔離チャンバ及びサンプリング流路であって、前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記隔離チャンバは空気透過性血液バリアを含む通気口を有し、前記サンプリング流路は前記出口ポートと接続される遠位端を有する、隔離チャンバ及びサンプリング流路と、
前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含み、
前記隔離チャンバ、前記サンプリング流路、及び前記分岐点は、血液の第１部分が前記隔離チャンバ内での隔離のために前記空気透過性血液バリアに向かって前記隔離チャンバに流れ込み、血液の第２部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第１部分を迂回し、前記出口ポートに向かって前記サンプリング流路に向けられるように寸法設定され且つ構成される、血液隔離装置。
【請求項２】
血液隔離装置であって、
入口ポートと、

出口ポートと、
空気透過性血液バリアを含む通気口を有する隔離チャンバと、
前記出口ポートと接続される遠位端を有するサンプリング流路と、
前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含み、
前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記分岐点は、血液の第１部分が前記隔離チャンバに流れ込み、前記空気透過性血液バリアを通して前記隔離チャンバ内の空気を追い出し、前記隔離チャンバ内に隔離されることを可能にし、血液の第２部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第１部分を迂回し、前記出口ポートに向かって前記サンプリング流路に向けられることを可能にするように寸法設定され且つ構成される、血液隔離装置。
【請求項３】
前記空気透過性血液バリアは、血液と接触すると少なくとも部分的に密封する空気透過性材料を含む、請求項１又は２に記載の血液隔離装置。
【請求項４】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項１又は２に記載の血液隔離装置。
【請求項５】
前記ハウジングは、上部部材と嵌合する下部部材を含み、前記下部部材及び前記上部部材のそれぞれは、前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路のそれぞれの一部を画定する、請求項１から３のいずれか一項に記載の血液隔離装置。
【請求項６】
患者針とサンプル採取装置とを有する採血経路と接続される血液隔離装置であって、
前記患者針と接続される入口ポートと、
隔離チャンバ及びサンプリング流路であって、前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記隔離チャンバは空気透過性血液バリアを含む通気口を有し、前記隔離チャンバ及び前記分岐点は、血液の第１部分を前記空気透過性血液バリアに向かって前記隔離チャンバに向けるように構成され、前記サンプリング流路は出口ポートと接続される遠位端を有し、前記サンプリング流路及び前記分岐点は、血液の第２部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第１部分を迂回し、前記出口ポートに向かって前記サンプリング流路に向けられることを可能にするように構成され、前記出口ポートは前記サンプル採取装置と接続される、隔離チャンバ及びサンプリング流路と、
前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含む、血液隔離装置。
【請求項７】
患者針とサンプル採取装置とを有する採血経路と接続される血液隔離装置であって、
前記患者針と接続される入口ポートと、
前記サンプル採取装置と接続される出口ポートと、
空気透過性血液バリアを含む通気口を有する隔離チャンバと、
前記出口ポートと接続される遠位端を有するサンプリング流路と、
前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含み、
前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記分岐点は、血液の第１部分が前記隔離チャンバに流れ込み、前記空気透過性血液バリアを通して前記隔離チャンバ内の空気を追い出し、前記隔離チャンバ内に

隔離されることを可能にし、血液の第２部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第１部分を迂回し、前記出口ポート及び前記サンプル採取装置に向かって前記サンプリング流路に向けられることを可能にするように寸法設定され且つ構成される、血液隔離装置。

【請求項８】

前記入口ポートは、前記採血経路の第１の部分を介して前記患者針と接続される、請求項６又は７に記載の血液隔離装置。

【請求項９】

前記出口ポートは、前記採血経路の第２の部分を介して前記サンプル採取装置と接続される、請求項６から８のいずれか一項に記載の血液隔離装置。

【請求項１０】

前記空気透過性血液バリアは、血液と接触すると少なくとも部分的に密封する空気透過性材料を含む、請求項６又は７に記載の血液隔離装置。

【請求項１１】

前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項６又は７に記載の血液隔離装置。

【請求項１２】

前記隔離流路は、前記入口ポートと接続される近位端と、空気透過性血液バリアを含む前記通気口を有する遠位端とを有する、請求項１１に記載の血液隔離装置。

【請求項１３】

体液隔離装置であって、

入口ポートと、

前記入口ポートと接続される出口ポートと、

分岐点を介して前記入口ポートと接続される隔離チャンバであって、空気透過性体液バリアを含む通気口を有する隔離チャンバと、

前記入口ポート、前記出口ポート、及び前記隔離チャンバを収容し且つ画定するハウジングと

を含み、

前記隔離チャンバ及び前記分岐点は、前記入口ポートからの体液の第１部分を前記空気透過性体液バリアに向かって前記隔離チャンバに向けるように構成され、前記空気透過性体液バリアは、体液と接触すると体液に対するバリアを形成する空気透過性材料を含み、その結果、体液との接触により、前記隔離チャンバ内の前記体液の第１部分の隔離が可能になり、前記分岐点を通る前記入口ポートから前記出口ポートへの体液の第２部分が前記隔離チャンバ及び前記体液の第１部分を迂回することが可能になる、体液隔離装置。

【請求項１４】

体液隔離装置であって、

入口ポートと、

前記入口ポートと接続される出口ポートと、

分岐点を介して前記入口ポートと接続される隔離チャンバであって、空気透過性体液バリアを含む通気口を有する隔離チャンバと、

前記入口ポート、前記出口ポート、及び前記隔離チャンバを収容し且つ画定するハウジングと

を含み、

前記隔離チャンバ及び前記分岐点は、前記入口ポートからの体液の第１部分を前記空気透過性体液バリアに向かって前記隔離チャンバに向けるように構成され、前記空気透過性体液バリアは、体液と接触すると体液に対するバリアを形成する空気透過性材料を含み、その結果、前記バリアの形成は、前記隔離チャンバ内の体液の第１部分の隔離を可能にし、前記入口ポートからの体液の第２の部分が前記出口ポートに向かって前記分岐点を通って前記隔離チャンバ及び前記体液の第１部分を迂回することを可能にするように構成される、体液隔離装置。

【請求項１５】
前記空気透過性体液バリアは、体液と接触すると密封する空気透過性材料を含む、請求項１３又は１４に記載の体液隔離装置。
【請求項１６】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項１３又は１４に記載の体液隔離装置。
【請求項１７】
前記入口ポートと接続される採血経路を更に含み、前記採血経路は、前記分岐点を通して前記体液の第２部分を前記入口ポートから前記出口ポートに運ぶ、請求項１３又は１４に記載の体液隔離装置。
【請求項１８】
前記ハウジングは、上部部材と嵌合する下部部材を含み、前記下部部材及び前記上部部材のそれぞれは、前記入口ポート、前記出口ポート、及び前記隔離チャンバのそれぞれの一部を画定する、請求項１３又は１４に記載の体液隔離装置。
【請求項１９】
前記分岐点を介して前記入口ポートと接続される近位端を有するサンプリング流路をさらに含む、請求項１３又は１４に記載の体液隔離装置。
【請求項２０】
前記ハウジングは、上部部材と嵌合する下部部材を含み、前記下部部材及び前記上部部材のそれぞれは、前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路のそれぞれの一部を画定する、請求項１９に記載の体液隔離装置。
【請求項２１】
血液隔離システムであって、
患者針とサンプル採取装置とを有する採血経路と、
血液隔離装置と
を含み、前記血液隔離装置は、
前記患者針と接続される入口ポートと、
前記サンプル採取装置と接続される出口ポートと、
空気透過性血液バリアを含む通気口を有する隔離チャンバと、
前記出口ポートと接続される遠位端を有するサンプリング流路と、
前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含み、
前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記分岐点は、血液の第１部分が前記隔離チャンバに流れ込み、前記空気透過性血液バリアを通して前記隔離チャンバ内の空気を追い出し、前記隔離チャンバ内に隔離されることを可能にし、血液の第２部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第１部分を迂回し、前記出口ポート及び前記サンプル採取装置に向かって前記サンプリング流路に向けられることを可能にするように寸法設定され且つ構成される、血液隔離システム。
【請求項２２】
前記入口ポートは、前記採血経路の第１の部分を介して前記患者針と接続される、請求項２１に記載の血液隔離システム。
【請求項２３】
前記出口ポートは、前記採血経路の第２の部分を介して前記サンプル採取装置と接続される、請求項２１に記載の血液隔離システム。
【請求項２４】
前記空気透過性血液バリアは、血液と接触すると少なくとも部分的に密封する空気透過性材料を含む、請求項２１に記載の血液隔離システム。
【請求項２５】

前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項２４に記載の血液隔離システム。
【請求項２６】
前記隔離流路は、前記入口ポートと接続される近位端と、空気透過性血液バリアを含む前記通気口を有する遠位端とを有する、請求項２５に記載の血液隔離システム。
【発明の詳細な説明】
【背景技術】
【０００１】
関連出願との相互参照
本出願は、２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４３号及び２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４８号の優先権の利益を主張するものであり、これらの米国非仮出願の両方が２０１５年７月２４日に出願された「血液培養改良システム及び方法」と題する米国仮特許出願第６２／１９６，７９７号、２０１５年１０月７日に出願された「非汚染採血用の血液隔離システム」と題する米国仮出願第６２／２３８，６３６号、及び２０１６年４月４日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国仮特許出願第６２／３１８，１９４号の優先権を主張しており、これらの開示はその全体が参照により本明細書に含まれるものとする。
【０００２】
菌血症は、血液中に微生物が存在することである。一方、敗血症は、発熱、頻脈、頻呼吸及び低血圧などの臨床症状及び臨床兆候がある場合の菌血症である。菌血症及び敗血症は、高い死亡率、入院発生率及び入院期間と関連する費用の増加とを伴う。多くの菌血症、敗血症、真菌血症及び他の病原体が実際に病院又は他の医療施設内で発生し、カテーテル及び静脈穿刺がこれらの病原体の潜在的なキャリアとしての汚染源である。
【０００３】
血液培養は、患者の血液中の菌血症及び敗血症に関連する微生物病原体を検出するのに使用される標準検査である。血液培養という用語は、血液が１つ以上の血液培養ボトル又は容器に接種される、末梢部位又は中心ライン又は動脈ラインからの１回の静脈穿刺を指す。１つのボトルが１つの血液培養と見なされ、２つ以上がセットと見なされる。複数のセットは複数の静脈穿刺から得られ、患者の異なる部位に関連する。
【０００４】
これらの方法は、敗血症を管理する上で重要な要素である微生物同定及び感受性検査を可能にするが、迅速な結果が得られないことと危険な病原体に対する感度が低いことが、改良されたシステムの開発及び補助的な分子検査又はプロテオミクス検査につながっている。
【０００５】
血液培養を行うための血液サンプルの採取は、現代の患者ケアの重要な要素であり、正確な診断を提供することによって患者の結果に良い影響を与えることも、不必要な抗菌療法を長引かせ、入院期間を長くし、コストを増加させることによって結果に悪影響を与えることもある。
【０００６】
血液培養の採取の１つの結果は、汚染である。血液培養の汚染は、偽陽性の培養結果及び／又は医療関連コストの著しい増加につながる可能性がある。血液培養の汚染の原因は、不適切な皮膚消毒、不適切な採取管の消毒、最初の採血の汚染を含み、これらは結果を歪める可能性がある。
【０００７】
血液培養採取キットは、一般に、ＢＤ、スミス、ビー・ブラウンなどの会社によって提供される「バタフライ」セット、輸液セット、又は他のタイプの静脈穿刺装置と、好気性

血液培養ボトル及び嫌気性血液培養ボトルとで構成される。様々な異なるボトルも検査要件に応じて利用可能である。これらのボトルは、好気性生物と嫌気性生物の両方の回収を最適化するように特別に設計されている。従来のキットでは、使用されるボトルは一般に「バキュテナー（登録商標）」として知られており、これは、所定の量の血液などの液体の採取を容易にするべく管の内部に真空を作り出すために排気される蓋を備える滅菌ガラス管又は滅菌プラスチック管から形成される採血管である。

【０００８】

偽陽性の血液培養は、一般的に、不十分なサンプリング技術の結果である。それらは、必要でないときに抗生物質を使用させ、病院費及び患者の不安を増大させる。血液培養は、皮膚内への針刺しから採取され、その後で血液のサンプルを取り込むためにバキュテナー（登録商標）が取り付けられる。汚染は、穿刺部位及びその周辺の皮膚領域の不適切又は不完全な消毒によって生じ得る。それはまた、挿入中の針による皮膚のくりぬきから、くりぬかれた皮膚細胞と関連する汚染物質とがサンプル中に引き込まれることで生じることもある。

【０００９】

皮下注射針を通る血流は層流であり、このため、皮下注射針に圧力降下が加えられるときに流管にわたって流速勾配が発生する。血液を強く吸引するか又は非常に小さな皮下注射針を使用すると、溶解及び赤血球からのカリウムの放出が起こり、それにより血液サンプルが異常になる可能性がある。

【００１０】

他の例では、一部の患者は繊細な静脈を有し、繊細な静脈は、特に患者の状態に対してあまりにも急速に引き出される注射器のプランジャによって加えられるような圧力低下又は真空の下で崩壊し得る。このような状態は事前に知ることが不可能であるため、このような静脈崩壊は危険であり、制御することは非常に困難である。

【００１１】

血液培養の汚染率を低下させるために、例えば、無菌採取技術に関するスタッフの訓練、汚染率に関するフィードバック、及び血液培養採取キットの導入など、様々な戦略が実施されている。皮膚消毒は汚染の心配を減らすことができるが、２０％以上の皮膚の微生物は真皮の深部に位置し、消毒の影響を受けない。ボトル接種の前に針を交換することは、汚染率を低下させることなく針刺し損傷を受ける危険性を高めるので推奨されない。

【００１２】

血液培養の汚染を低減するための一部の従来のシステム及び技術は、中心静脈カテーテル、静脈穿刺及び他の血管アクセスシステムから採取された最初のアリコートの血液を捨てることを含む。しかしながら、これらのシステムは、ユーザーが血管内装置を機械的に操作することを必要とするか又は確実にすることが困難な複雑な一連のステップを踏むこと必要とする。

【発明の概要】

【発明が解決しようとする課題】

【００１３】

本明細書は、血液培養の汚染、細胞の溶解、及び静脈崩壊を低減するためのシステム及び方法を提示する。一部の実施では、システム及び方法は、ユーザーの消毒のばらつきをなくし、また皮膚細胞が血液培養サンプルに入り込む危険性をなくすこともできる。本明細書に開示されたシステム及び方法は、汚染物質のない血液サンプルを採取するためにバキュテナー（登録商標）又は他の採血装置（すなわち、注射器）をいつ取り付けるべきかを潜在的に示す以外は、既存の臨床プロセスの変更を必要としない。

【００１４】

本明細書に開示されたシステム及び方法の一部の実施では、採血は、患者自身の血圧の使用によって受動的に成し遂げられ、それによって静脈崩壊の危険性を低減し、現行の実務を超える更なるユーザーのステップを排除する。システム及び方法は、短経路の直接刺し又はバタフライ静脈穿刺システムに適合するように適用されることができる。カテーテ

ルを通して採取されたサンプルと共に使用されることもできる。
【課題を解決するための手段】
【００１５】
一態様では、血液隔離装置が提示されている。血液隔離装置は、入口ポートと出口ポートとを含む。血液隔離装置は、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端と、出口ポートと接続される遠位端とを有する、サンプリング流路を更に含む。
【００１６】
別の態様では、採血経路と接続される血液隔離装置が記載されている。採血経路は、患者針とサンプル採取装置とを有する。血液隔離装置は、患者針と接続される入口ポートと、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバとを含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路と、サンプリング流路の遠位端及びサンプル採取装置と接続される出口ポートとを更に含む。
【００１７】
更に別の態様では、採血システムと接続される血液隔離装置が記載されている。採血システムは、患者から血液サンプルを取り出せるようにするための患者針と、密封され且つ真空採血管を受け入れるように適合されたナンプル針とを含む。血液隔離装置は、患者からの血液サンプルを受け入れるために患者針と接続される入口ポートを含む。血液隔離装置は、入口ポートと接続され且つ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、サンプル針が真空採血管によって開封されるより前に血液サンプルの最初の部分を受け入れ且つ隔離する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、真空採血管によってナンプル針が開封されると血液サンプルの後続の部分を運ぶサンプリング流路を更に含む。血液隔離装置は、血液サンプルの後続の部分をサンプル針に運ぶためにサンプリング流路の遠位端と接続される出口ポートを更に含む。
【００１８】
更に別の態様では、血液サンプル最適化システムが開示され、記載されている。血液サンプル最適化システムは、患者の血液の１つ以上のサンプルを取り出せるようにし且つ得るための採血システムと、静脈穿刺プロセスによって汚染されている恐れがあり且つ患者の血液中の病原体の偽陽性同定をもたらす可能性がある患者の血液の１つ以上のサンプルの最初の部分を受け入れ且つ隔離するための血液隔離装置とを含む。
【００１９】
採血システムは、患者の血液のサンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、血液ナンプルを運ぶために患者針と接続される採血経路と、血液サンプルの後続の部分を採取し且つ収容するために真空採血容器を受け入れるように構成されたサンプル針とを含む。
【００２０】
更に別の態様では、血液隔離装置が開示され、記載されている。一部の実施では、血液隔離装置は、入口ポートと、入口ポートと接続される出口ポートと、入口ポートと接続される隔離チャンバとを含むことができる。隔離チャンバは、空気透過性血液バリアを含む通気口を有することができる。
【００２１】
血液隔離装置は、患者針とサンプル針との間で採血経路に沿って接続され、血液サンプルを受け入れるための入口ポートを含む。血液隔離装置は、血液サンプルの最初の量を受け入れるために入コポートと接続される隔離チャンバであって、血液サンプルの最初の量の少なくとも最初の部分を隔離するために空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、隔離チャンバが血液ナンプルの最初の量の少なくとも最初の部分を

隔離すると血液サンプルの後続の量を真空採血容器に運ぶサンプリング流路を更に含む。血液隔離装置は、サンプリング流路の遠位端と接続される出口ポートであって、血液サンプルの後続の量を出力する出口ポートを更に含む。

【００２２】

１つ以上の実施形態の詳細が、添付の図面及び以下の説明に記載されている。他の特徴及び利点は、明細書及び図面並びに特許請求の範囲から明らかになるであろう。

【図面の簡単な説明】

【００２３】

以下、これら及び他の態様について、以下の図面を参照して詳細に説明する。

【図１】血液サンプル最適化システムを示す。

【図２】代替的な実施に従う血液サンプル最適化システムを示す。

【図３】別の代替的な実施に従う血液サンプル最適化システムを示す。

【図４】別の代替的な実施に従う血液サンプル最適化システムを示す。

【図５】別の代替的な実施に従う血液サンプル最適化システムを示す。

【図６】代替的な実施に従う血液サンプル最適化システムを示す。

【図７】血液培養の質を最適化するための方法のフローチャートである。

【図８Ａ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｂ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｃ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｄ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｅ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図９】血液隔離システムに用いる経路スプリッタを示す。

【図１０Ａ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１０Ｂ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１０Ｃ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１０Ｄ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ａ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｂ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｃ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｄ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｅ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１２Ａ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。

【図１２Ｂ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。

【図１２Ｃ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。

【図１２Ｄ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。

【図１３Ａ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。

【図１３Ｂ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。

【図１３Ｃ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。

【図１３Ｄ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。

【図１４Ａ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。

【図１４Ｂ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。

【図１４Ｃ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を

低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｄ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｅ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１５Ａ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｂ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｃ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｄ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｅ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｆ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｇ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１６Ａ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｂ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｃ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｄ】更に別の実施に従う血液隔離装置を示す。
【図１７Ａ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｂ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｃ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｄ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｅ】血液隔離装置用のハウジングの下部部材を示す。
【図１８Ａ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｂ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｃ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｄ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｅ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｆ】血液隔離装置用のハウジングの上部部材を示す。
【図１９Ａ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図１９Ｂ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図２０】血液隔離装置を含む血液サンプル最適化システムを示す。
【図２１】ウィッキング材料チャンバを使用する通気口付きでない血液隔離装置を示す。
【図２２Ａ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２２Ｂ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２３Ａ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。
【図２３Ｂ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。　様々な図面における同様の符号は同様の要素を示す。
【発明を実施するための形態】
【００２４】
本明細書は、採取される血液サンプル中の汚染物質を低減又は排除し、その結果、採取される血液サンプルの血液培養又は他の検査における偽陽性の判断を減少又は排除する血液サンプル最適化システム及び方法を記載している。一部の実施では、血液サンプル最適化システムは、患者の血流への血管アクセスのための患者針と、バキュテナー（登録商標）のような真空採血容器又は真空採血管などの採血容器か又は他のサンプリング装置に血液サンプルを供給するためのサンプル針と、患者針とサンプル針との間に位置する血液隔離装置とを含む。血液隔離装置は、汚染されている可能性のある最初のアリコートの血液

を隔離するための隔離チャンバを含み、最初のアリコートの血液が隔離チャンバ内に隔離された後に患者針とサンプル針との間の汚染されていない可能性のある血液を運ぶために隔離チャンバを迂回するサンプリング流路を更に含むことができる。

【００２５】

図１は、一部の実施に従う血液サンプル最適化システムを示す。システムは、患者の皮膚を穿刺してその中の患者の静脈及び静脈内の血液にアクセスするための患者針１を含む。システムは、再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース又は装置内に収容され且つ再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース又は装置によって当初は密封されていることができる、サンプル針（すなわち、バキュテナー（登録商標）などと共に使用するための再密封可能に密封された針）５を更に含む。再密封可能なブーツ１０は、患者の血液を採取するためのバキュテナー（登録商標）ボトル（図示せず）を用いることによって、サンプル針５のそばに又はサンプル針５の周りに押し付けることができる。システムは、サンプル針５に通じる低容量チャンバ３０を更に含むことができるが、ハウジング５０によって形成される隔離チャンバ５５に通じる穴又は１つ以上の流路４５も含む。

【００２６】

隔離チャンバ５５は、隔離チャンバ５５の容積に応じて、所定の又は測定された量であることができる、患者の血液の最初のアリコートを受け入れ且つ保持するためのチャンバ、流路、通路、ロック、又は他の構造である。最初の採血は、一般的に、後続の採血に比べて菌血症及び敗血症を引き起こす微生物又は他の病原体を含有しているか又はより含有の影響を受けやすい。隔離チャンバ５５は、硬いハウジング内に収容されるか、ハウジング自体に形成され又はハウジング自体によって画定された容器であることができ、或いはチューブ又は内腔として実現されることができる。隔離チャンバ５５は、どのように形成され且つ実施されるかにかかわらず、所定の容積を有することができる。一部の実施では、所定の容積は、患者針の容積に基づくこと、すなわち、患者針の容積よりも少ない容積から任意の容積から患者針の容積の２０倍以上大きい容積までの範囲であることができる。隔離チャンバ５５の所定の容積は、隔離され且つ処分される血液の量を節約又は最小化するように設定されることもできる。

【００２７】

隔離チャンバ５５は、チャンバハウジング５０内に形成、包含、又は収容されることができ、プラスチック、ゴム、鋼、アルミニウム又は他の適切な材料で作られることができる。例えば、隔離チャンバ５５は、可撓性チューブ又は他のエラストマー材料から形成されることができる。隔離チャンバ５５は、空気が隔離チャンバ５５から出ることを可能にする空気透過性血液バリア２０を更に含む。本明細書で使用される「空気透過性血液バリア」という用語は、空気透過性であるが実質的に血液不透過性の物質、材料又は構造体を意味する。代表的な例は、疎水性膜及び疎水性コーティング、疎水性膜又は疎水性コーティングと組み合わせた親水性膜又は親水性コーティング、メッシュ、フィルタ、機械的弁、抗菌性材料、又は隔離チャンバ５５が血液で満たされるときに隔離チャンバ５５から空気を追い出すことができる他の任意の手段を含むことができる。様々な例示的な実施形態において、空気透過性血液バリアは、空気が液体と接触するまで通過することを可能にする１つ以上の材料によって形成されることができ、このような材料は、空気及び／又は液体の通過を防止又は阻止するために完全に又は部分的に密封される。言い換えれば、液体との接触より前に、材料は空気透過性のバリアを形成している。液体との接触後、材料は、空気及び／又は液体の更なる通過を実質的に又は完全に防止する。

【００２８】

穴又は流路４５は、任意の所望の長さ、断面形状又はサイズであることができ、且つ／又は任意の所望の角度又は向きで低容量チャンバ３０から離れるように形成されることができる。穴又は流路４５はまた、最初のアリコートの血液サンプルを隔離チャンバ５５内に保持する一方向フラップ又は一方向弁６０を含むことができる。一部の特定の実施では、穴又は流路４５は、低容量チャンバ３０から隔離チャンバ５５への一方向の血液の流れ

のための「ダックビル」弁又はフラッパ弁６０などを含むことができる。空気透過性血液バリア２０は、空気が出ることを可能にするが血液と接触すると密封する材料で構成することもでき、それによって外気が隔離チャンバ５５に入ることを許容しない。この密封は弁を不要にする。

【００２９】

弁６０は、任意のタイプの弁又は開閉機構であることができる。チャンバ３０は、実質的に残留血液を保持しないように設計されており、特定の容積又は割合の血液を隔離チャンバ５５に保持し又は通過させるように構成することができる。同様に、隔離チャンバ５５は、抗菌コーティングのような任意のタイプのコーティング、又は隔離された最初の採血の成分の同定及び／又は診断を支援するコーティングも含むことができる。

【００３０】

ハウジング５０及び４０は、アクリロニトリルブタジエンスチレン（ＡＢＳ）又は他の熱可塑性材料又はポリマー材料などのプラスチック、ゴム、鋼、又はアルミニウムを含む任意の適切な材料から形成されることができる。空気透過性血液バリア２０は、最初の採血による血液と接触すると又は空気の追い出しが停止されたときに、又は事象と隔離チャンバ５５内の血液との任意の組み合わせの場合に活性化される、色提供物質又は他の信号伝達機構を含むことができる。空気透過性のバリアはまた、外部流体源、しぶき等によるフィルタの不注意による又は早過ぎる密封を阻止又は防止する疎水性膜又はカバーなどの外層を含むことができる。隔離チャンバ５５はまた、チャンバが充填されたことをユーザーが視覚的に確認することを可能にするために半透明又は透明であることができる。

【００３１】

図２は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図２に示す実施では、隔離チャンバ５５又は廃棄チャンバが患者針１を取り囲み、端部が開放されたカフ又はハウジングが廃棄チャンバと接続され、サンプル針ハウジングベース及びハウジングを取り囲んでいる。患者針１とサンプル針５とは、ブーツ５６によって互いと接続されており、ブーツ５６は、それを貫通する連続的な採血流路を形成している。ブーツ５６は、採血流路から隔離チャンバ５５に通じる単一の穴又は流路を含む。装置は、他の実施では、複数の穴又は流路を含むことができる。各穴又は流路は、一方向弁を含むことができ、所定の量の血流のために寸法設定され且つ適合されることができる。

【００３２】

隔離チャンバ５５は、空気透過性血液バリアを含む。フィルタは、所定容積の血液が隔離チャンバ５５に集められたときに、それぞれ、感知及び／又は指示するためのセンサ又は指標を更に含むことができる。その指示は、バキュテナー（登録商標）などの真空採血管又はボトルをサンプル針５に取り付けるようにユーザーに警告する。隔離チャンバ５５用のハウジングは、任意のサイズ又は形状であることができ、ハウジング内の内部空間又は容積を画定するために任意のタイプの材料を含むことができる。内部空間は、最初は空気のみで満たされているが、汚染除去剤、凝固剤などの薬剤又は物質でコーティングされることもできる。真空採血管がサンプル針５に取り付けられると、血液は自動的に患者針１に、採血流路及びサンプル針５を通ってボトルに流入する。サンプル針５は、採血ボトルがサンプル針に取り付けられていないときにサンプル針を密封する再密封可能なブーツ、コーティング又は膜によって覆われている。

【００３３】

図３は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図示の実施では、サンプル針５は、再密封可能なブーツ又は膜によって取り囲まれ、更に患者針１と接続される。サンプル針及び患者針を通って血液流路が形成される。サンプル針と患者針との間の接続は、主血液流路から隔離チャンバ１０４へと導く流路、ポート又は開口部を含む「Ｔ」又は「Ｙ」コネクタ１０２を含む。

【００３４】

Ｔ又はＹコネクタ１０２は、フラップ又は一方向弁を含み、所定の流量の血液のために寸法設定され且つ適合された穴を有する。隔離チャンバ１０４は、チューブから形成され

又は硬いハウジングによって形成されることができ、最初は空気で満たされている。隔離チャンバ１０４は、自動的に、すなわち、患者自身の血圧による圧力下で患者から流出する血液を受け入れる。隔離チャンバ１０４は、好ましくは隔離チャンバ１０４を形成し且つ近位端がＴ又はＹコネクタ１０２に接続されたチューブの遠位端に、空気透過性血液バリア１０６を含む。Ｔ又はＹコネクタ１０２は、最も効率的な血流のために任意の所望の角度で分岐することができ、最初のアリコートの血液と主要な採血サンプルとの混合を最小限に抑え又は排除するために、開口部及び流路と主血液流路との間の接合部分を最小化するように形成されることができる。

【００３５】

一部の代替的な実施では、サンプル針は、図４に示すように、その反対側の端部がＴ又はＹコネクタ１０２と接続している任意の長さのチューブに取り付けられることができる。隔離チャンバ１０４は、最初のアリコートに所定量の血液サンプルを含む限り、任意の形状又は容積であることができる。Ｔ又はＹコネクタ１０２はまた、主血液流路に対して平行な開口部又は流路を含むことができる。空気透過性血液バリアは、所定量の血液が隔離チャンバに集められたとき、又は放出される空気が特定の閾値、すなわちゼロに達したときを示す指標１０７又は他の機構を更に含むことができる。チューブはまた、挟んでチューブを通る流体の流れを防止するのに使用することができるクリップ１０９を含むことができる。

【００３６】

空気透過性血液バリア及び一次チャンバが密封されると、最初のアリコートの血液が隔離チャンバ１０４に閉じ込められ、サンプルを得るためにバキュテナー（登録商標）ボトルのような真空採血管がサンプル針５に取り付けられる。採血管は取り外すことができ、サンプル針５は再密封される。更なる採血又はサンプルのために、任意の数の後続の採血管を取り付けることができる。全ての採血が完了すると、最初のアリコートの血液が隔離チャンバ１０４に閉じ込められたまま、システムは廃棄される。

【００３７】

図５は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図示の実施では、サンプル針５が患者針とチューブによって接続されている。「Ｔ」又は「Ｙ」コネクタ１２０が、チューブに沿って任意の所望の位置に追加され、実質的に上記のように、隔離チャンバ２０４に通じる開口部、ポート又は流路を含む。

【００３８】

図６は、一次採取流路として形成された隔離チャンバ３０４が最初のアリコートの血液を受け入れ、採血流路に隣接して設けられている、一部の代替的な実施に従う血液サンプル最適化システムを示す。隔離チャンバ３０４は、採血流路、患者針１及び／又はサンプル針５を取り囲むことができる。一次採取流路は、Ｔ又はＹコネクタ１２０、又は他のタイプの開口部又は流路を含むことができる。隔離チャンバ３０４は空気透過性血液バリアを含み、上記のように、血液などの流体が接触したことの指標を含むこともできる。

【００３９】

一部の実施では、患者針１又はサンプル針５のいずれか又は両方をルアーロック雄コネクタ又はルアーロック雌コネクタで置き換えることができる。しかしながら、様々な実施で、血液サンプル最適化システムのサンプル針端部にあるコネクタを最初に密封し、周囲空気圧で加圧され且つ空気透過性血液バリアの空気出口を含む隔離チャンバへ最初のアリコートの血液をそらすことを可能にする。このようにして、システムは受動的且つ自動的に患者自身の血圧を用いて隔離チャンバの周囲空気圧に打ち勝ち、空気透過性血液バリアを通して空気を押し出し、隔離チャンバ内の空気を血液に置き換える。

【００４０】

図７は、血液培養の質を最適化するための例示的な方法のフローチャートである。７０２において、臨床医が患者の静脈に針を挿入する。７０４において、血液が隔離チャンバに流れ込み、隔離チャンバ内の空気を隔離チャンバから空気透過性血液バリアを通して押し出す。一部の実施では、隔離チャンバの容積は、０．１立方センチメートル（ｃｃ）未

満から５立方センチメートル（ｃｃ）以上である。隔離チャンバは、血液ナンブルの第２部分及び他の後続の部分又は後続の採取よりも汚染しやすい血液サンプルの第１部分を採取するように寸法設定され且つ適合されている。隔離チャンバは空気透過性血液バリアを有し、この血液バリアを通して空気を患者の静脈から押し出された血液で追い出すことができるので、このような血液は、血液サンプルを受け入れ且つ保管するためのバキュテナー（登録商標）又は他のボトルに引き込まれるか又は他の方法で入る前に、必然的に且つ自動的に隔離チャンバに流入する。

【００４１】

隔離チャンバがいっぱいになると、血液は、血液が通過するのを阻止又は防止する空気透過性血液バリアに集まるか、さもなければ接触する。７０６において、血液が空気透過性血液バリアの全内部表面積と接触すると、空気透過性血液バリアは閉じられ、空気はもはや流出又は流入しない。７０８において、臨床医は、バキュテナー（登録商標）などの真空採血管を取り付けることができることを示す指標を提供されるか又は満杯のチャンバを見ることができる。指標は、一次チャンバがいっぱいであるか否かを確認するための一次チャンバの可視性、例えば、色を変える血液バリア、又は他の指標を含むことができる。隔離チャンバの充填時間は、実質的に瞬間的であり得るので、このような指標は、存在する場合、隔離チャンバが満たされているというだけである可能性がある。

【００４２】

真空採血管が取り付けられる前、針、サンプリング流路、及び隔離チャンバの間の連通は、隔離チャンバの血液バリアの密封によって制限され、従って隔離によって空気がシステムに再び入ることを可能にしない。連通経路の密封は、機械的にねじること又は他の動作、小さな穴又は曲がりくねった経路によって達成され、臨床医による別個の弁又は機械的な動作又は操作の必要性をなくす。７１０において、真空採血管を取り外すと、自己密封式の膜がサンプル針を密封し、７１２で、更なる後続の真空採血管を取り付けることができる。７１４において、サンプルが採取されると、装置が患者から取り外され、廃棄される。

【００４３】

図８Ａ～８Ｅは、一部の実施に従う、非汚染採血用の例示的な血液サンプル最適化システム８００を示す。血液サンプル最適化システム８００は、チューブ、患者針（又は両方）、又は他の血管又は静脈アクセス装置に接続されることができる入口ポート８０２と、隔離チャンバチューブ８０６への第１出口とサンプル採取チューブ８０８への第２出口とを有する経路スプリッタ８０４とを含む。隔離チャンバチューブ８０６及びサンプル採取チューブ８０８の一方又は両方は、チューブから形成されることができる。一部の実施では、隔離チャンバチューブ８０６は、特定の量の当初血液サンプルを収容するように寸法設定される。サンプル採取チューブ８０８は、ひとたび隔離チャンバチューブ８０６が満たされると、血液サンプルを受け入れる。サンプル採取チューブ８０８は、バキュテナー（登録商標）ベース又はハウジング８１０、又は他の血液サンプル採取装置に接続されることができる。

【００４４】

血液隔離システム８００は血液隔離装置８１２を更に含み、血液隔離装置８１２は、図８Ｂ～８Ｄにより詳細に示すようにハウジング８１８を含み、ハウジング８１８は、非汚染サンプル採取チューブ８０８用の経路を固定するか又はいずれかの端部が非汚染サンプル採取チューブ８０８と接続されるサンプリング流路８２０を含む。サンプリング流路８２０は、非汚染サンプル採取チューブ８０８に沿った位置でハウジング８１８をより良好に固定し且つ安定させるように、ハウジング８１８を通って曲線状であることができる。

【００４５】

血液隔離装置８１２は、隔離チャンバチューブ８０６と接続される隔離チャンバ８２２又は他のチャンバを更に含む。隔離チャンバ８２２は、空気透過性血液バリア８２４で終端している。空気透過性血液バリア８２４はまた、血液サンプル（すなわち、非汚染血液サンプル）の正式な採取を開始することができる指標として、血液との完全な接触時に異

なる色に変わる着色剤を含むことができる。小さい光、音発生機構などの他の指標を使用することができる。一部の実施では、空気透過性血液バリアは、隔離チャンバ８２２の方向から直角に配置されているが、ハウジング８１８に使用される空間及び材料を節約するために任意の距離又は向きに配置されることができる。ハウジング８１８及びその内容物は、任意の剛性材料又は半剛性材料又は一連の材料から形成されることができる。

【００４６】

図９は、例えば、図８Ａ～８Ｅに示すような血液隔離システムに用いる経路スプリッタ９００を示す。経路スプリッタ９００は、入口ポート９０２と、主管路出口ポート９０４と、隔離流路出口ポート９０６とを含む。入口ポート９０２は、同様に患者針システムに接続される主チューブに、又は直接患者針に接続されることができる。主管路出口ポート９０４は、バキュテナー（登録商標）ベース又はハウジングなどの採血システムへの主管路チューブに、又は直接そのような採血システムに接続されることができる。隔離流路出口ポート９０６は、測定された量又は所定の閾値まで血液の第１サンプルを受け入れ且つ隔離するための隔離チューブに接続されることができる。代わりに、隔離流路出口ポート９０６は、隔離チャンバに接続することができる。隔離流路出口ポート９０６は、好ましくは、主管路出口ポート９０４から２０～７０度の角度に曲げられ、一方、主管路出口ポート９０４は、好ましくは、入口ポート９０２と一直線である。所定の量の最初の血液サンプルが、本明細書に記載された機構及び技術に従って隔離チューブ又は隔離チャンバ内に隔離されると、後続の血液サンプルは、入口ポート９０２に流入し、障害物なしで主管路出口ポート９０４から直接流出する。

【００４７】

図１０Ａ～１０Ｄは、別の実施に従う血液隔離装置１０００を示す。血液隔離装置１０００は、入口ポート１００２と、主出口ポート１００４と、隔離流路ポート１００６とを含む。入口ポート１００２は、患者針又は関連するチューブと接続されることができる。主出口ポート１００４は、バキュテナー（登録商標）、関連するチューブ、又はルアー作動弁などの血液サンプル採取装置に接続されることができる。隔離流路ポート１００６は、主出口ポート１００４から隔離チャンバ１００８に分離する。一部の実施では、隔離チャンバ１００８は、ハウジング又は他の容器１００１内に螺旋流路として形成される。

【００４８】

隔離チャンバ１００８は、実質的に上記のように、遠位端が空気透過性血液バリア１０１０に接続される。隔離チャンバ１００８内の空気は、空気透過性血液バリア１０１０を通して、隔離流路ポート１００６内に案内される最初のアリコートの血液によって追い出される。ひとたび隔離チャンバ１００８が満たされると、主出口ポート１００４を通る更なる採血が成し遂げられ、これらのサンプルは汚染されていない。

【００４９】

図１１Ａ～１１Ｅは、他の代替的な実施に従う血液隔離装置１１００を示す。血液隔離装置１１００は、上述の入口ポートと同様の入口ポート１１０２と、主出口ポート１１０４と、主出口ポート１１０４及び入口ポート１１０２から分離する隔離流路ポート１１０６とを含む。隔離流路ポートは、隔離チャンバ１１０８に接続されている。図１１Ａ～１１Ｅに示す実施では、血液隔離装置は、隔離チャンバ１１０８として機能する流路を内部に有するベース部材１１０１を含む。流路は、ベース部材１１０１を通る曲がりくねった経路として形成されることができ、一方、ベース部材１１０１は、患者の四肢に載るように成形され且つ形成される。

【００５０】

隔離チャンバ１１０８の一部は、血液隔離指標１１０９として機能するように、空気透過性血液バリア１１１０に出る直前に、ベース部材から又はベース部材の上面付近に突出することができる。指標１１０９は、透明な材料、又は血液と接触すると変色する材料で形成されることができる。

【００５１】

一部の実施では、血液隔離装置１１００は、常時閉じている針、バキュテナー（登録商

標）シールド又は他の採取装置などの採血装置１１２０を含むことができる。採血装置１１２０は、患者針の挿入プロセスによって汚染される恐れがある最初のアリコートの血液を隔離することができるように、効率及び利便性のために血液隔離装置１１００と共に製造及び販売されることができる。従って、採血装置１１２０は、偽陽性の検査のリスクを低減するように非汚染血液サンプルを採取し且つ非汚染サンプルを確実にすることができる。

【００５２】

図１２Ａ～１２Ｄは、更に他の代替的な実施に従う血液サンプル最適化システム１２００を示す。システム１２００は、バキュテナー（登録商標）又は他の採取及びサンプリング装置のような採血装置１２０４に取り付けるための血液隔離装置１２０２を含む。血液隔離装置１２０２は、バキュテナー（登録商標）容器又はバイアルが採血装置１２０４の採取針に取り付けられる前に、最初のアリコート又は量の血液を受け入れ、且つその最初のアリコート又は量を血液隔離装置１２０２の隔離流路内に隔離するように、構成され且つ配置されている。

【００５３】

一部の実施では、血液隔離装置１２０２は、入口ポート１２１２と、主出口ポートと、隔離流路ポートとを含むことができる。入口ポート１２１２は、患者針又は関連するチューブに接続されることができる。主出口ポート１２１４は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁との接続を可能にするために、常時閉じている針又は装置に接続されることができる。隔離流路ポートは、主出口ポートから隔離チャンバ１２１８に分離する。

【００５４】

一部の実施では、隔離チャンバ１２１８は、隔離装置１２０２の本体内の流路として形成される。隔離チャンバ１２１８は、Ｕ字形流路、Ｓ字形流路、螺旋流路、又は任意の他の曲がりくねった流路などの曲がりくねった流路であることができる。隔離装置１２０２は、ハウジング又は他の収容体、及びその中に形成された１つ以上の流路を含むことができる。図１２Ａ及び１２Ｂに示すように、隔離装置１２０２は、本体１２０６とキャップ１２０８とを含む。本体１２０６には１つ以上の空洞又は流路が形成され、空洞又は流路にはキャップ１２０８から延びる１つ以上のアーム１２１０が更に形成され、１つ以上のアーム１２１０は、本体１２０６の空洞又は流路に当接して一次採取ポート及び主出口ポートを形成している。

【００５５】

図１３Ａ～１３Ｄは、更に他の代替的な実施に従う血液サンプル最適化システム１３００を示す。システム１３００は、バキュテナー（登録商標）又は他の体液採取及びサンプリング装置などの採血装置１３０４に取り付けるための血液隔離装置１３０２を含む。血液隔離装置１３０２は、バキュテナー（登録商標）容器又はバイアルが採血装置１３０４の採取針に取り付けられる前に、最初のアリコート又は量の血液を受け入れ、且つその最初のアリコート又は量の血液又は他の体液を血液隔離装置１３０２の隔離流路内に隔離するように、構成され且つ配置されている。

【００５６】

血液隔離装置１３０２は、入口ポート１３１４と、主出口ポート１３１２と、隔離流路ポート１３１６とを有するハウジング１３０１を含む。入口ポート１３１４は、患者針又は関連するチューブに接続されることができる。主出口ポート１３１２は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁との接続を可能にするために、常時閉じている針又は装置に接続されることができる。隔離流路ポート１３１６は、主入口ポート１３１４から隔離チャンバ１３１８に分離する。

【００５７】

図１３Ａ～１３Ｄに示す実施例では、隔離チャンバ１３１８は、ハウジング１３０１内の空洞又はチャンバとして形成され、又はハウジング１３０１を画定する壁によって形成

される。隔離チャンバ１３１８は、Ｕ字形流路、Ｓ字形流路、螺旋流路などの曲がりくねった流路、又はハウジング１３０１とキャップ１３０７との協働及び接続によって画定される任意の他の曲がりくねった流路であることができ、キャップ１３０７は、隔離チャンバ１３１８内の曲がりくねった流路のための１つ以上の壁又はディレクタを提供する突出部１３０５を含むことができる。キャップ１３０７からの突出部１３０５は、真っ直ぐであるか湾曲していることができ、様々な流路、開口部又は溝が埋め込まれていることができ、キャップ１３０７から任意の角度又は向きで延びることができる。隔離チャンバ１３１８の形成を完了するためにキャップ１３０７がハウジング１３０１と接続されると、突出部１３０５は曲がりくねった流路の少なくとも一部を形成し、隔離チャンバ１３１８内に曲がりくねった流路によって形成される隔離流路に最初のアリコート又は量の血液又は他の体液を隔離する。

【００５８】

隔離チャンバ１３１８は、実質的に上記のように空気透過性血液バリア１３１０を含む。隔離チャンバ１３１８内の空気は、患者の血圧によって隔離チャンバ１３１８内に供給される最初のアリコートの血液によって空気透過性血液バリア１３１０を通して追い出される。隔離チャンバ１３１８が満たされ、隔離チャンバ１３１８内の空気が追い出されると、バキュテナー（登録商標）のような血液サンプル採取装置によって提供されるような真空又は他の圧力のような力が次のアリコート又は量の血液又は体液を引き抜くために提供されるまで、患者の血圧は、血液隔離装置１３０２、特に、出口ポート１３１２に更なる血液を追い込み又は提供するのには不十分である。主出口ポート１３１２を通して更なる採血を行うことができ、あらゆる汚染物質が最初のアリコートの血液と共に隔離チャンバ１３１８内に隔離されているので、これらのサンプルは汚染されない。

【００５９】

図１４Ａ～１４Ｅは、患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システム１４００の更に別の実施を示す。採血システム１４００は、血液サンプル採取装置１４０３と患者針（図示せず）との間に接続されることができる血液隔離装置１４０１を含む。血液サンプル採取装置１４０３は、バキュテナー（登録商標）などであることができる。血液隔離装置１４０１は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１４０２を含む。入口ポート１４０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。

【００６０】

入口ポート１４０２は、血液隔離装置１４０１への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有する円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。血液隔離装置１４０１は、血液隔離装置１４０１から及び血液サンプル採取装置１４０３への開口部を画定する出口ポート１４０４を更に含む。出口ポート１４０４は、同様に血液隔離装置１４０３と接続されるチューブ又は他の導管と接続されることもできる。出口ポート１４０４は、ねじ付きキャップ、ルアーコネクタ（雄型又は雌型）、チューブなどを含むがそれらに限定されない様々な装置の取り付け用のねじが切られていない締め代又は接着継手などのコネクタ装置を更に含むことができる。

【００６１】

血液隔離装置１４０１は、入口ポート１４０２と出口ポート１４０４との間にサンプリング流路１４０６を更に含み、サンプリング流路１４０６は、最初のアリコートの血液が隔離されると血液サンプル経路として機能する。サンプリング流路１４０６は、任意のサイズ、形状又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１４０６は、入口ポート１４０２の開口部と実質的に同様の断面積を有する。他の実

施では、サンプリング流路１４０６は、入口ポート１４０２から出口ポート１４０４まで徐々に広がることができる。

【００６２】

血液隔離装置１４０１は隔離チャンバ１４０８を更に含み、隔離チャンバ１４０８は、入口ポート１４０２と出口ポート１４０４との間の任意の位置でサンプリング流路１４０６に接続され且つサンプリング流路１４０６から分離又は方向転換されるが、好ましくは入口ポート１４０２の近くのサンプリング流路１４０６の近位端に接続され且つ近位端から分離又は方向転換される。隔離チャンバ１４０８は、最初は大気圧に維持され、サンプリング流路１４０６からの方向転換点と反対側の隔離チャンバ１４０８の遠位端又はその近傍に空気出口１４１２を含む。空気出口１４１２は、空気透過性血液バリア１４１２を含む。図１４Ｂに示すように、空気透過性血液バリア１４１２は、保護カバー１４１６で覆われていることができる。保護カバー１４１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１４１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも患者自身の血圧によって隔離チャンバ１４０８内に強制的に血液が供給されることによって空気が隔離チャンバから追い出されるときに空気が空気透過性血液バリア１４１２から出ることを可能にする。また、保護カバー１４１６は、空気透過性血液バリアが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００６３】

図１４Ｃ及び１４Ｄに示すように、サンプリング流路１４０６は、赤血球を溶解する可能性を最小限に抑えるために、より小さい直径からより大きい直径になる円筒形又は円錐台形であることができる。同様に、サンプリング流路１４０６は、赤血球を溶解する可能性がある急カーブ又は鋭角が最小限の量で又はなしで形成される。サンプリング流路１４０６は、方向転換経路１４０９を通して入口ポート１４０２の近くで隔離チャンバ１４０８へと分離する。方向転換経路１４０９は、任意の断面形状又はサイズを有することができるが、好ましくは、入口ポート１４０２の少なくとも一部の断面形状と同様である。

【００６４】

一部の実施では、サンプリング流路１４０６及び隔離チャンバ１４０８は、ハウジング１４１４に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１４１４は、プラスチック、金属又は他の剛性又は半剛性材料で作られることができる。ハウジング１４１４は、上部部材と密封可能に嵌合する下部部材を有することができる。下部部材及び上部部材の一方又は両方は、サンプリング流路１４０６及び隔離チャンバ１４０８、並びに方向転換経路１４０９、入口ポート１４０２、及び出口ポート１４０４を含むことができる。一部の他の実施態様では、方向転換経路１４０９、入口ポート１４０２、及び／又は出口ポート１４０４のうちの１つ以上が、ハウジング１４１４のいずれかの端部に接続されるキャップ部材によって少なくとも部分的に形成されることができる。一部の実施では、上部部材及び下部部材、並びにキャップ部材は、レーザ溶接、ヒートシール、接着、スナップ止め、ねじ止め、ボルト止めなどによって互いに連結されることができる。他の実施では、方向転換経路１４０９及び／又は隔離チャンバ１４０８の内面の一部又は全部が、汚染除去剤、凝固剤などの薬剤又は物質でコーティング又は充填されることができる。例えば、隔離チャンバ１４０８が満たされて最初のアリコートの血液が方向転換経路１４０９に戻るとき、隔離された血液の最後の量が凝固し、隔離チャンバ１４０８とサンプリング流路１４０６との間に障壁を作り出すように、方向転換経路１４０９に凝固剤を設けることができる。

【００６５】

図１５Ａ～１５Ｇは、血液隔離装置１５００を示す。血液隔離装置１５００は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁などとの接続を可能にするために常時閉じている針又は装置に接続されることができる。

【００６６】
血液隔離装置１５００は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１５０２を含む。入口ポート１５０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。入口ポート１５０２は、血液隔離装置１５００への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有する円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。
【００６７】
入口ポート１５０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封のコネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザ溶接、又は熱接合などによって、入口ポート１５０２と一体化されることができる。これによって、血液隔離装置１５００は、患者針と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針を血液隔離装置１５００に接続する必要性をなくすことができる。
【００６８】
血液隔離装置１５００は、血液隔離装置１５００から及び血液サンプル採取装置への開口部を画定する出口ポート１５０４を更に含む。出口ポート１５０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１５００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１５００に接続する必要性をなくすことができる。
【００６９】
血液隔離装置１５００は、入口ポート１５０２と出口ポート１５０４との間にサンプリング流路１５０６を更に含み、サンプリング流路１５０６は、最初のアリコートの血液が隔離されると血液サンプル経路として機能する。サンプリング流路１５０６は、任意のサイズ、形状、又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１５０６は、入口ポート１５０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１５０６は、入口ポート１５０２から出口ポート１５０４まで徐々に広がることができる。
【００７０】
血液隔離装置１５００は隔離チャンバ１５０８を更に含み、隔離チャンバ１５０８は、入口ポート１５０２と出口ポート１５０４との間の任意の位置でサンプリング流路１５０６に接続され且つサンプリング流路１５０６から分離又は方向転換されるが、好ましくは入口ポート１５０２の近くのサンプリング流路１５０６の近位端に接続され且つ近位端から分離又は方向転換される。一部の実施では、分水路はＹ字路を含む。隔離チャンバ１５０８は、好ましくは大気圧に維持され、隔離チャンバ１５０８の遠位端又はその近傍に通気口１５１０を含む。通気口１５１０は、空気透過性血液バリア１５１２を含む。図１５Ｃは、隔離チャンバ１５０８が患者からの血液の最初のアリコート又はサンプルで満たされた血液隔離装置１５００を示す。
【００７１】
空気透過性血液バリア１５１２は、保護カバー１５１６で覆されていることができる。保護カバー１５１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１５１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも患者自身の血圧によって隔離チャンバ１５０８内に強制的に血液が供給されることによって空気が隔離チャンバから追い出されるときに空気が空気透過性血液バリア１５１２から出ることを可能にする。保護カバー１５１６は、フィルタが周囲の流体又は飛沫に偶発的

に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００７２】

図１５Ｂは、血液隔離装置１５００の出口ポート１５０４及び通気口１５１０を含むハウジング１５０１の上面からの血液隔離装置１５００の斜視図であり、サンプル採取装置が起動される前、サンプリング流路１５０６が空である間に最初のアリコートの血液が隔離チャンバ１５０８を満たすことを示す。図１５Ｇは、血液隔離装置１５００の出口ポート１５０４及びハウジング１５０１の底面からの血液隔離装置１５００の斜視図であり、サンプル採取装置が起動される前、サンプリング流路１５０６が空である間に最初のアリコートの血液が隔離チャンバ１５０８を満たすことを示す。図１５Ｃは、血液隔離装置１５００の入口ポート１５０２及び通気口１５１０を含むハウジング１５０１の上面からの血液隔離装置１５００の別の斜視図であり、隔離された血液は実質的に隔離チャンバ１５０８内にとどまっている間に血液がサンプリング流路１５０６を通って採取されることを示す。

【００７３】

図１５Ｄは、一部の実施に従う血液隔離装置１５００の断面図であり、サンプリング流路１５０６及び隔離チャンバ１５０８を画定するハウジング１５０１を示す。図１５Ｅ及び１５Ｆは、本明細書に記載される１つ以上の実施に従う血液隔離装置用のハウジングの様々なフォームファクタを示す。

【００７４】

隔離チャンバ１５０８は、サンプリング流路１５０６よりも大きい断面積を有することができ、断面積又は長さは、所定の又は特定の血液量が隔離又はロックされるように構成されることができる。サンプリング流路１５０６は、患者針のチューブ又は採血装置のチューブのいずれか又は両方のためのチューブに適合するように寸法設定されることができる。

【００７５】

ハウジング１５０１は、複数の部品又は単一の一体部品から形成されることができる。一部の実施では、図１５Ｄに示すように、ハウジング１５０１は、互いに嵌合する上部部材１５２０と下部部材１５２２とを含み、それらの一方又は両方は、例えば、射出成形プロセスによって又はエッチング、切削、穿孔などによって予め形成された溝、流路、ロック、導管又は他の経路を有する。上部部材１５２０は、レーザ溶接、熱接合、超音波溶接、接着、ねじ、リベット、ボルトなどを使用することなどの任意の嵌合又は接続機構によって、又はラッチ、溝、舌状部、ピン、フランジなどの他の嵌合機構によって、下部部材１５２２と接続されることができる。

【００７６】

一部の実施では、図１５Ｄに示すように、上部部材１５２０は、溝、流路、ロック、導管又は他の経路を含むことができ、一方、下部部材１５２２は、上部部材１５２０の溝、流路、ロック又は他の経路のうちの少なくとも１つに嵌合するように寸法設定され且つ適合された突出部１５２４を含むことができる。突出部１５２４は、例えば、サンプリング流路１５０６及び／又は隔離チャンバ１５０８のいずれかの形成を完了させるために、部分的な溝又は部分的な流路などの表面特徴を提供することができる。一部の実施では、突出部１５２４は、対応する溝、流路、ロック又は他の経路内によりぴったりと嵌合するために、１つ以上の傾斜した側面又は面を形成されることができる。更に他の実施では、上部部材１５２０と下部部材の両方が、溝、流路、ロック又は他の経路、並びに１つ以上の突出部１５２４を含むことができる。

【００７７】

一部の実施では、サンプリング流路１５０６及び隔離チャンバ１５０８は、ハウジング１５０１に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１５０１は、ゴム、プラスチック、金属又は他の材料を含む任意の適切な材料で作られるこ

とができる。ハウジング１５０１は、透明又は半透明の材料から、又は不透明又は非半透明の材料から形成されることができる。他の実施では、ハウジング１５０１は、大部分が不透明又は非透明であることができるが、サンプリング流路１５０６及び／又は隔離チャンバ１５０８に直接隣接するハウジング表面は、透明又は半透明であり、最初に隔離チャンバ１５０８が必要又は所望の程度まで満たされているという視覚的な合図又はサイン、及び／又は、次に汚染されていない血液サンプルがサンプリング流路１５０６を通して採取される間、隔離された血液が隔離されたままであるという視覚的な合図又はサインを施術者に与える。隔離の他の視覚的な合図又はサインは、以下に限定されるものではないが、血液の接触、浸透、又は部分的な浸透で空気透過性血液バリア１５１２が異なる色に変わること、隔離チャンバに沿った又は隔離チャンバに隣接する任意の位置にある色分けされたタブ又は指標、可聴信号、振動信号、又は他の信号を含むことができる。

【００７８】

患者の皮膚から多数の病原体を集める可能性がある患者針（図示せず）による静脈穿刺の後、患者自身の血圧が隔離チャンバ１５０８内の大気圧に打ち勝って空気透過性血液バリア１５１２を通して隔離チャンバ１５０８内の空気を追い出すので、これらの病原体を有する患者の血液の最初の量が、血液隔離装置１５００入口ポート１５０２に入り、最も抵抗の少ない経路をたどることによって隔離チャンバ１５０８に流入する。患者の血圧は、密封されたサンプリング流路１５０６内で高まっている空気圧に打ち勝つのに十分ではない。最終的に、所定の容積を有する隔離チャンバ１５０８は、空気透過性血液バリア１５１２を通して空気を追い出す血液で満たされる。血液が空気透過性血液バリアに衝突すると、血液は空気透過性血液バリア１５１２の材料と相互作用して、通気口１５１０を完全に又は部分的に密封する。施術者がいまやバキュテナー（登録商標）カプセル又は他の血液サンプル採取装置を利用してサンプリングのために患者の血液の次の量を得ることができるという信号又は表示を提供することができる。隔離チャンバ１５０８内の血液は、このとき隔離チャンバ内で事実上隔離されている。

【００７９】

血液隔離経路１５０８を満たすと、バキュテナー（登録商標）又は他の血液サンプル採取装置の使用より前に、患者の血圧は、サンプリング流路１５０６内の空気の圧縮を引き起こし、場合によっては少量の血液が隔離チャンバ１５０８への方向転換点を過ぎてサンプリング流路１５０６に移動し、サンプリング流路１５０６を通して採取される汚染されていない血液を待ち行列に入れる。

【００８０】

図１６～１９は、血液隔離装置の更に別の実施を示す。図１６Ａ～１６Ｄは、バキュテナー（登録商標）（図示せず）のような真空採血容器のような血液サンプル採取装置と患者針（図示せず）及び／又は関連するチューブとの間に接続されることができる血液隔離装置１６００を示す。図１７は、血液隔離装置の下部部材を示し、図１８は、血液隔離装置の上部部材を示し、上部部材及び下部部材は、以下でより詳しく説明するように、相互に嵌合して、入口ポート、出口ポート、隔離チャンバ及びサンプリング流路を形成することができる。図１９Ａ及び１９Ｂは、互いに嵌合する上部部材及び下部部材を示す。図１６～１９は本明細書に記載される血液隔離装置を構成する１つの例示的な方法を示しており、他の形態の構成も可能であることを理解されたい。

【００８１】

図１６Ａ～１６Ｄを参照すると、血液隔離装置１６００は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１６０２を含む。入口ポート１６０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。入口ポート１６０２は、血液隔離装置１６００への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有する円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる

。
【００８２】
入口ポート１６０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封コネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザー溶接、又は熱接合などによって、入口ポート１６０２と一体化されることができる。これによって、血液隔離装置１６００は、患者針及び／又はチューブと共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針を血液隔離装置１６００に接続する必要性をなくすことができる。
【００８３】
血液隔離装置１６００は、血液隔離装置１６００から及び血液サンプル採取装置への開口部を画定する出口ポート１６０４を更に含む。出口ポート１６０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１６００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１６００に接続する必要性をなくすことができる。
【００８４】
血液隔離装置１６００は、入口ポート１６０２と出口ポート１６０４との間のサンプリング流路１６０６と、入口ポート１６０２と出口ポート１６０４との間の任意の位置でサンプリング流路１６０６に接続され且つサンプリング流路１６０６から分離又は方向転換される隔離チャンバ１６０８とを更に含む。サンプリング流路１６０６は、最初のアリコートの血液が隔離チャンバ１６０８内に隔離されると、採血経路として機能する。サンプリング流路１６０６は、任意のサイズ、形状又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１６０６は、入口ポート１６０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１６０６は、入口ポート１６０２から出口ポート１６０４まで徐々に広がることができる。隔離チャンバ１６０８は、図１７及び１９により詳しく示すように、血液がサンプリング流路１６０６のより小さい直径に入るのに対して、まずリザーバに入ろうとするように、隔離流路の経路に向かって大きいリザーバを形成するべくより大きい断面を有することができる。
【００８５】
一部の例示的な実施では、サンプリング流路１６０６と隔離チャンバ１６０８との間の方向転換は、方向転換分岐点１６０７によって行われる。方向転換分岐点１６０７は、実質的にＹ字形、Ｔ字形、又はＵ字形であることができる。一部の好ましい例示的な実施では、図１７Ａ～１７Ｂに示すように、方向転換分岐点１６０７は、入口ポート１６０２からの流れが優先的に隔離チャンバ１６０８に向けられるように構成される。隔離チャンバ１６０８はまた、最初の血液流を隔離チャンバ１６０８に向かって且つ隔離チャンバ１６０８内に移動させるための湾曲部又は傾斜路を含むか又は形成することができる。
【００８６】
隔離チャンバ１６０８は、好ましくは大気圧に維持され、隔離チャンバ１６０８の遠位端又はその近傍に通気口１６１０を含む。通気口１６１０は、上記のように空気透過性血液バリア１６１２を含むことができる。
【００８７】
血液隔離装置１６００は、複数の部品又は単一の一体部品から形成されることができるハウジング１６０１を含むことができる。一部の実施では、図１７Ａ～１７Ｄ及び図１８Ａ～１８Ｆに示すように、ハウジング１６０１は、互いに嵌合する上部部材１６２０と下部部材１６２２とを含む。血液隔離装置１６００は、上部部材１６２０が下部部材１６２２に機械的に取り付けられたときに、両者の間の接合部分がガスケット又は密封部材によって密封されるように、ガスケット又は他の密封部材（図示せず）を含むこともできる。

図１７Ａ～１７Ｄは、血液隔離装置１６００用のハウジングの下部部材１６２２を示す。下部部材１６２２は、サンプリング流路１６０６、隔離チャンバ１６０８、及び方向転換分岐点１６０７を形成するために、射出成形プロセスによって又はエッチング、切削、穿孔などによって予め形成された溝、流路、ロック、導管又は他の経路を含むことができる。

【００８８】

隔離チャンバ１６０８は、血液がサンプリング流路１６０６のより小さい直径に入るのに対して、まず隔離チャンバ内に優先的に移動するように、サンプリング流路１６０６よりも大きい断面を有することができる。

【００８９】

図１８Ａ～１８Ｆは、レーザ溶接、熱接合、接着、ねじ、リベット、ボルトなどを使用することなどの任意の嵌合又は接続機構によって、又はラッチ、溝、舌状部、ゴン、フランジなどの他の嵌合機構によって、下部部材１６２２と接続可能な上部部材１６２０を示す。上部部材１６２０は、サンプリング流路１６０６、隔離チャンバ１６０８、及び方向転換分岐点１６０７を形成するために、溝、流路、ロック、導管又は他の経路の一部又はすべてを含むことができる。更に他の実施では、上部部材１６２０と下部部材１６２２の両方が、溝、流路、ロック又は他の経路を含むことができる。

【００９０】

一部の実施では、サンプリング流路１６０６及び隔離チャンバ１６０８は、ハウジング１６０１に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１６０１は、ゴム、プラスチック、金属又は任意の他の適切な材料で作られることができる。ハウジング１６０１は、透明又は半透明の材料から、又は不透明又は非半透明の材料から形成されることができる。他の実施では、ハウジング１６０１は、大部分が不透明又は非半透明であることができるが、サンプリング流路１６０６及び／又は隔離チャンバ１６０８に直接隣接するハウジング表面は、透明又は半透明であることができ、最初に隔離チャンバ１６０８が必要又は所望の程度まで満たされているという視覚的な合図又はサイン、及び／又は、次に汚染されていない血液サンプルがサンプリング流路１６０６を通して採取される間、隔離された血液が隔離されたままであるという視覚的な合図又はサインを施術者にうえる。隔離の他の視覚的な合図又はサインは、以下に限定されるものではないが、血液の接触、浸透、又は部分的な浸透で空気透過性血液バリア１６１２が異なる色に変わること、隔離チャンバに沿った又は隔離チャンバに隣接する任意の位置にある色分けされたタブ又は指標、可聴信号、振動信号、又は他の信号を含むことができる。

【００９１】

図１８Ａ～１８Ｆに示すように、空気透過性血液バリア１６１２は、保護部材１６１６で覆われているか又は保護部材１６１６によって包囲されていることができる。保護部材１６１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１６１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも空気が隔離チャンバ１６０８から追い出されるときに空気が空気透過性血液バリア１６１２から出ることを可能にする。一部の実施では、保護部材１６１６は、上部部材１６２０の上面から上に空気透過性血液バリア１６１２の周りに延びる突出部を含む。保護カバー１６１６は、フィルタが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００９２】

使用時、血液隔離装置１６００は、サンプリング流路１６０６と隔離チャンバ１６０８とを含む。両方の経路が、最初は大気圧で空気を充填されているが、サンプリング流路１６０６は、最初はバキュテナー（登録商標）又は他のこのような密封された採血装置によって密封されている出口ポート１６０４に向けられ、隔離チャンバ１６０８は、空気透過性血液バリア１６１２を含む大気への通気口１６１０で終端している。

【００９３】

患者の皮膚から多数の病原体を集める可能性がある患者針（図示せず）による静脈穿刺の後、これらの病原体を有する患者の血液の最初の量が、血液隔離装置１６００の入口ポート１６０２を通過する。この汚染されている可能性のある血液の最初の量は、最も抵抗の少ない経路を見出すことによって、隔離チャンバ１６０８に優先的に流入する。患者自身の血圧は、通気口付きの隔離チャンバ１６０８内の大気圧に打ち勝ち、空気透過性血液バリア１６１２を通して隔離チャンバ１６０８内の空気を追い出すが、密封されたサンプリング流路１６０６内で高まっている空気圧に打ち勝つには不十分である。様々な例示的な実施形態では、隔離チャンバ１６０８及びサンプリング流路１６０６は、患者の血圧によって生じた力が、血液隔離装置の向きに関わらず、重力の影響に打ち勝つのに十分であるように構成されることができる。

【００９４】

最終的に、隔離チャンバ１６０８は、空気透過性血液バリア１６１２を通して空気を追い出す血液で満たされる。血液が空気透過性血液バリアと接触すると、血液は空気透過性血液バリア１６１２の材料と相互作用して通気口１６１０を完全に又は部分的に密封する。施術者がいまやバキュテナー（登録商標）又は他の採血装置を利用することができるという信号又は表示を提供することができる。

【００９５】

血液隔離経路１６０８を満たすと、バキュテナー（登録商標）又は他の血液サンプル採取装置の使用より前に、患者の血圧は、サンプリング流路１６０６内の空気の圧縮を引き起こし、場合によっては少量の血液が方向転換点を過ぎてサンプリング流路１６０６に移動しサンプリング流路１５０６を通して採取される汚染されていない血液を待ち行列に入れる。

【００９６】

図１９Ａは、血液隔離装置１６００の側面図であり、図１９Ｂは、血液隔離装置１６００の断面図であり、下部部材１６２２と嵌合する上部部材１６２０を示す。

【００９７】

図２０は、患者の血流への血管アクセスのための患者針２００２と、１つ以上の血液サンプルの採取を容易にする血液サンプル採取装置２００４と、患者針２００２と血液サンプル採取装置２００４との間の流体接続を提供する導管２００６とを含む血液サンプル最適化システム２０００を示す。一部の実施では、血液サンプル採取装置２００４は、密封された採取針を含む保護シールドを含み、採取針に密封された真空容器が置かれ、容器は採取針によって一度穿孔されると、患者針２００２から導管２００６を通して真空圧力又は真空力で血液サンプルを吸い込む。

【００９８】

血液サンプル最適化システム２０００は、本明細書で説明するように、患者針２００２と血液サンプル採取装置２００４との間の導管２００６上の任意の点に位置する血液隔離装置２００８を更に含む。

【００９９】

図２１は、ウィッキング材料チャンバを使用する通気口付きでない血液隔離装置２１００を示す。血液隔離装置２１００は、ウィッキング材料で満たされた隔離チャンバ２１０２によって少なくとも部分的に囲まれ又は当接されるサンプリング流路２１０４を有するハウジング２１０１を含む。最初のアリコートの血液が患者針からサンプリング流路２１０４に引き込まれ、サンプリング流路２１０４において隔離チャンバ２１０２のウィッキング材料の中に直ちに逃がされる。ウィッキング材料及び／又は隔離チャンバ２１０２は、後続の又はそれ以降の採血がウィッキング材料を通り過ぎ、サンプリング流路２１０４を通って直接バキュテナー（登録商標）などのサンプリング装置に流れるように、所定量の血液を受け入れ且つ保持するように寸法設定され且つ適合されている。ウィッキング材料は、固化剤、汚染除去剤、又は他の添加剤などの物質を含むことができる。

【０１００】

本明細書に記載されるように、空気透過性血液バリアは、多種多様な異なる構造及び材

料を用いて作られることができる。図２２Ａ及び２２Ｂに示すように、血液隔離装置２２００の空気透過性血液バリア２２０２は、少なくとも一部のビーズが親水性になるように処理されたポリマービーズマトリックス２２０４を含むことができる。空気透過性血液バリア２２０２は、カルボキシメチルセルロース（ＣＭＣ）又はセルロースガムなどの自己密封材料２２０６、又は他の密封材料を更に含む。空気透過性血液バリア２２０２は、血液などの流体との接触前又は部分接触中の空気の流れを可能にする空隙２２０８を更に含むことができる。図２２Ｂに示すように、流体と接触すると、自己密封材料２２０６が膨張して空隙２２０８を閉鎖し、空隙２２０８を通る空気の流れを閉塞し、完全に又は部分的に密封する。

【０１０１】

図２３Ａ及び２３Ｂは、患者針と接続するための入口ポート２３０２と、血液サンプル採取装置と接続するための出口ポート２３０４と、隔離チャンバ２３０６と、隔離チャンバ２３０６と、隔離するべき汚染されている可能性のある血液の最初のアリコートまで隔離チャンバが満たされると隔離チャンバ２３０６を迂回するサンプリング流路２３０８とを有する、血液隔離装置２３００の更に別の実施を示している。隔離チャンバ２３０６は、入口ポート２３０２から最も遠い隔離チャンバ２３０６の遠位端に疎水性プラグ２３１２を含む。バキュテナー（登録商標）などからのような、出口ポート２３０４から加えられる真空力又は他の吸引力は、血液を入口ポート２３０２内に、そして隔離チャンバ２３０６内に直接吸い込み、そこで最初のアリコートの血液が疎水性プラグ２３１２に接触し、最初のアリコートの血液を隔離チャンバ２３０６に戻してそこで隔離させる。少量の血液が、最初は弁２３０８によって閉鎖されているサンプリング流路２３０８に入ることができる。弁２３０８が解放されると、真空の更なる力又は他の力の下で、後続の量の血液が入口ポート２３０２に流れ、隔離チャンバ２３０６を迂回し、サンプリング流路２３０８を通り抜けて出口ポート２３０４に向かって流れ、採取装置に送られる。

【０１０２】

サンプリング流路２３０８は、任意の適切な幾何学的形状を有することができ、プラスチックチューブ又は任意の他の適切な材料から形成されることができる。弁２３０８は、最初のアリコートの血液が隔離チャンバ２３０６内に隔離される前にサンプリング流路を挟み、脇へそらし、曲げ、又は他の方法で閉じるためにクリップ又は他の包囲装置であることができる。

【０１０３】

様々な実施形態を上記で詳細に説明してきたが、他の変更も可能である。他の実施形態は、添付の特許請求の範囲内に含まれ得る。

【図１】

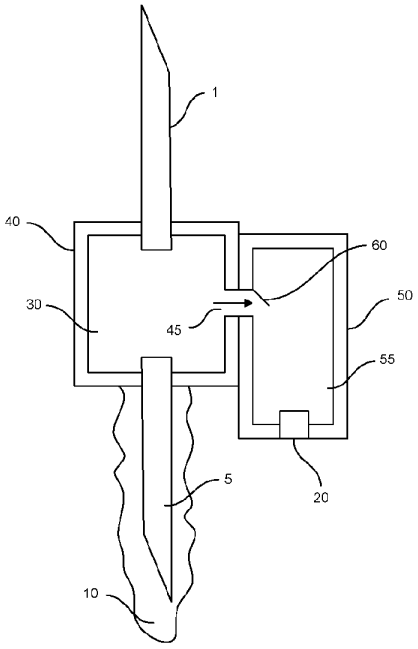


FIG. 1

【図２】

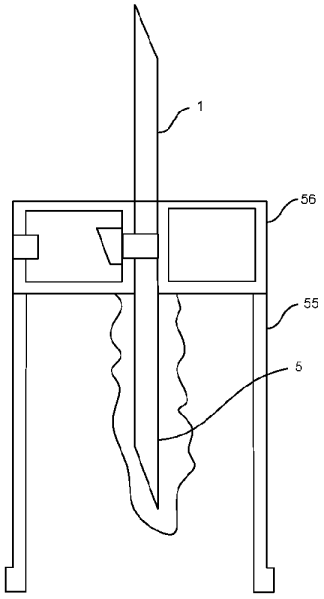


FIG. 2

【図３】

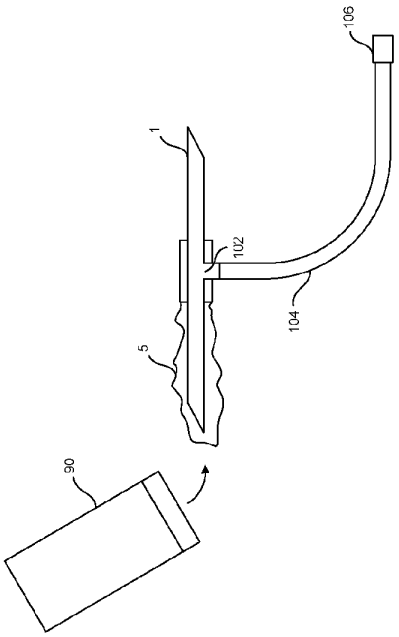


FIG. 3

【図４】

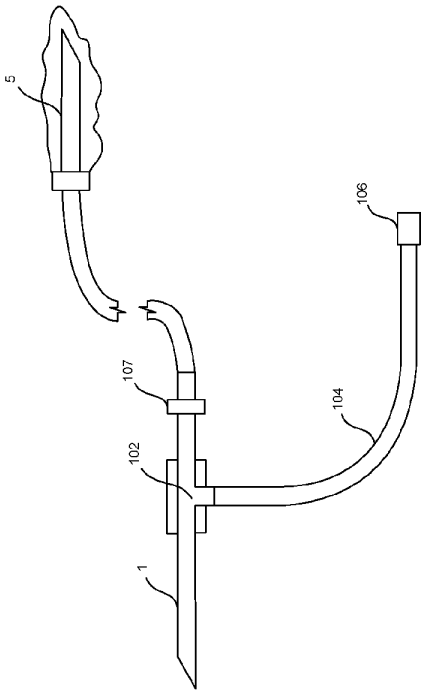


FIG. 4

【図５】

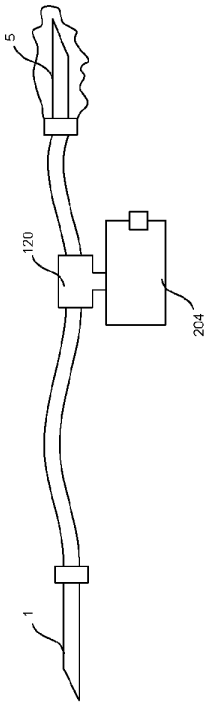


FIG. 5

【図６】

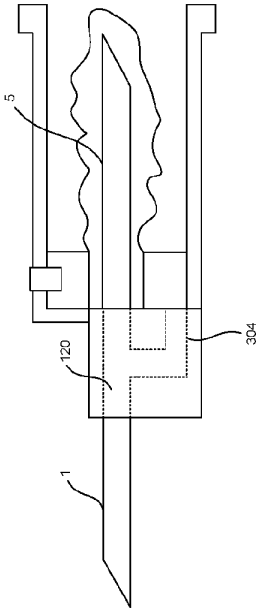


FIG. 6

【図７】

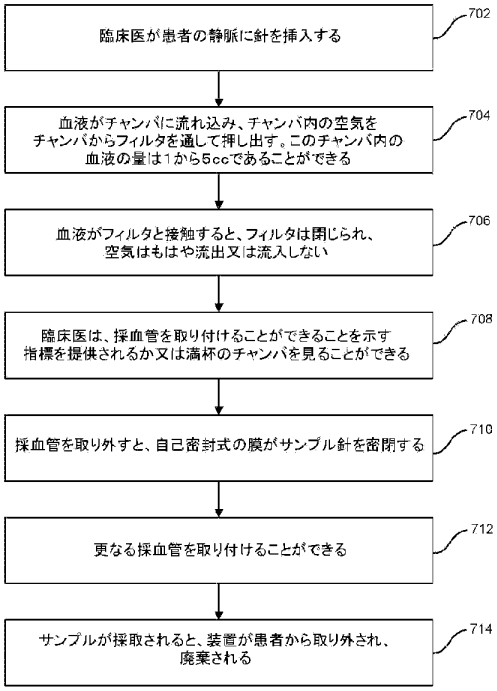


FIG. 7

【図８Ａ】

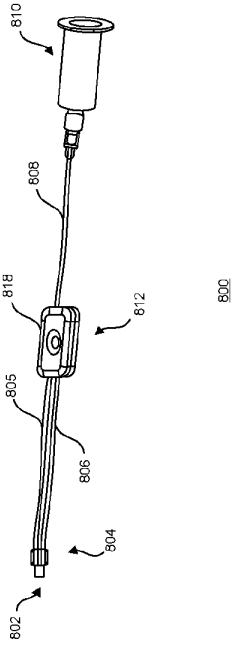


FIG. 8A

【図８Ｂ】

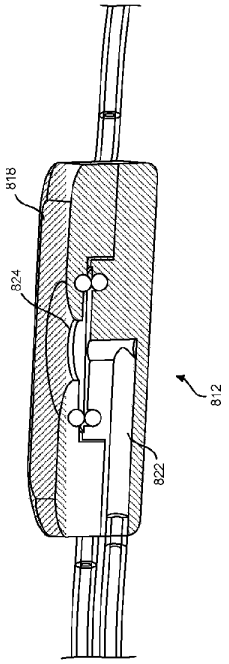


FIG. 8B

【図８Ｃ】

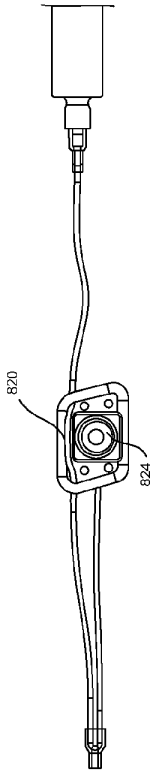


FIG. 8C

【図８Ｄ】

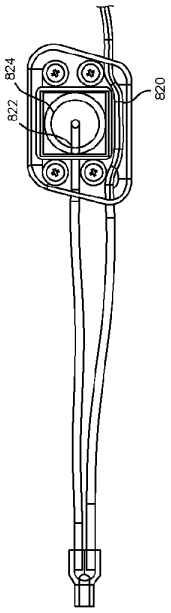


FIG. 8D

【図８Ｅ】

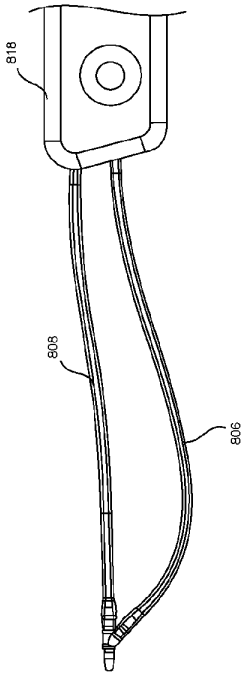


FIG. 8E

【図９】

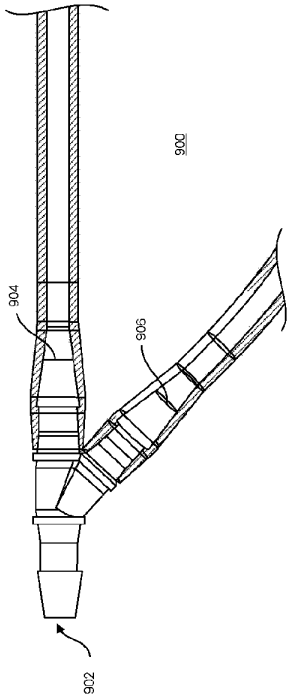


FIG. 9

【図１０Ａ】

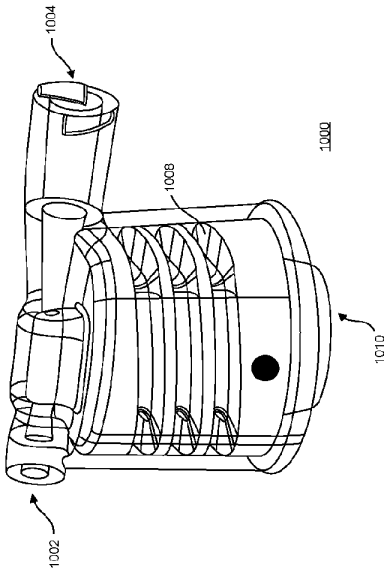


FIG. 10A

【図１０Ｂ】

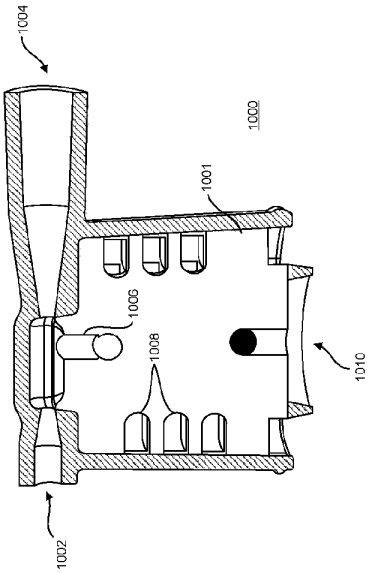


FIG. 10B

【図１０Ｃ】

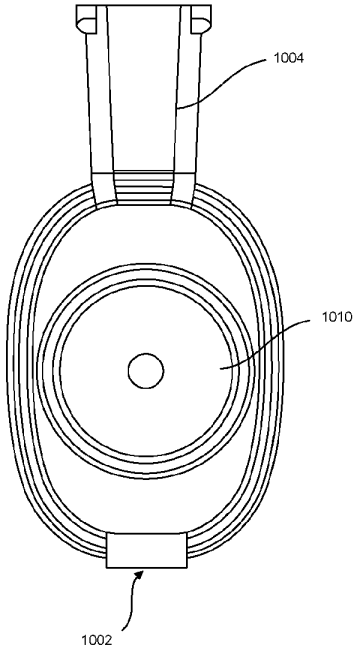


FIG. 10C

【図１０Ｄ】

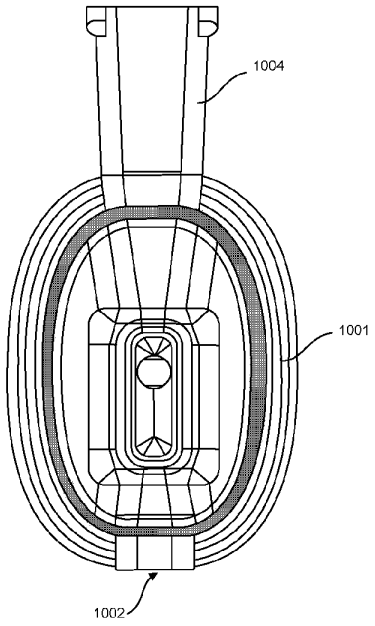


FIG. 10D

【図１１Ａ】

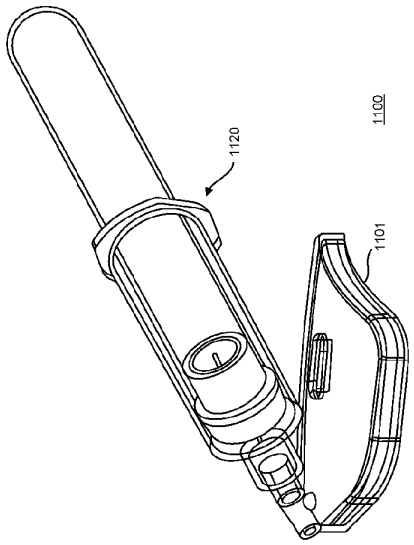


FIG. 11A

【図１１Ｂ】

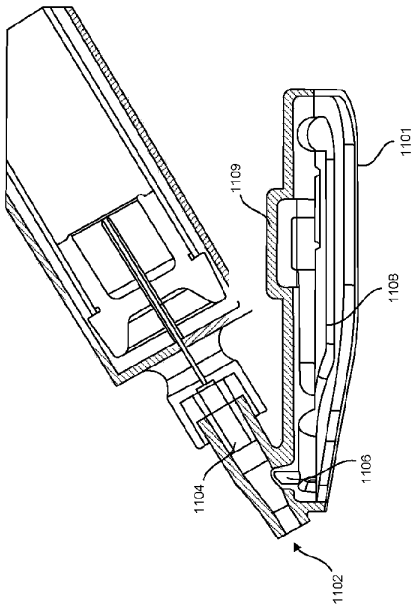


FIG. 11B

【図１１Ｃ】

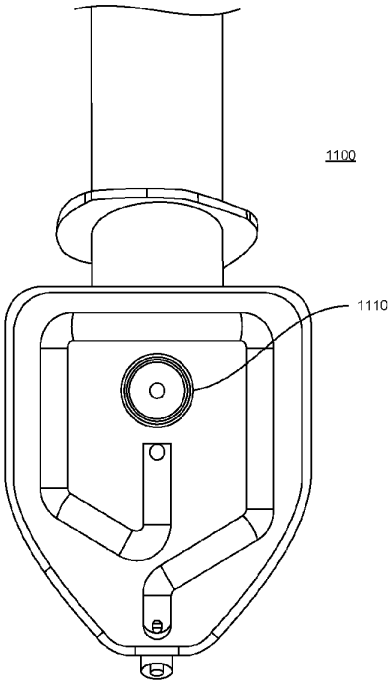


FIG. 11C

【図１１Ｄ】

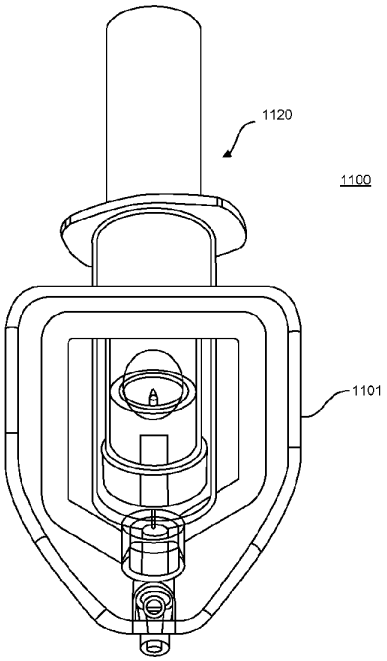


FIG. 11D

【図１１Ｅ】

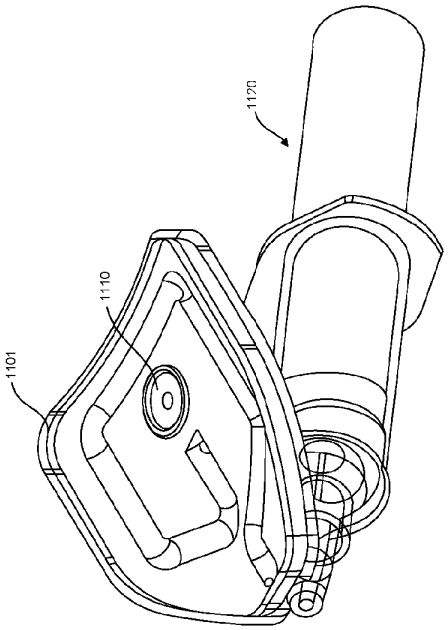


FIG. 11E

【図１２Ａ】

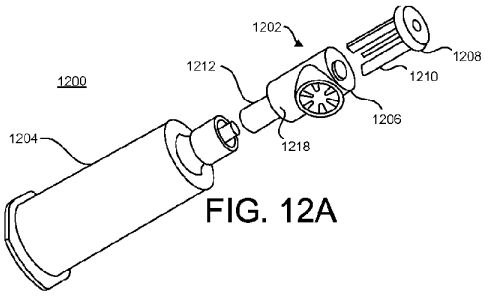


FIG. 12A

【図１２Ｂ】

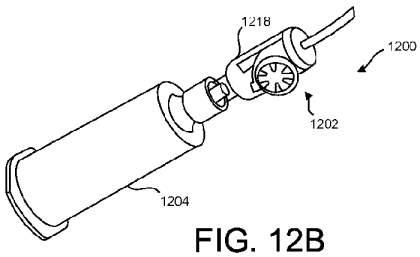


FIG. 12B

【図１２Ｃ】

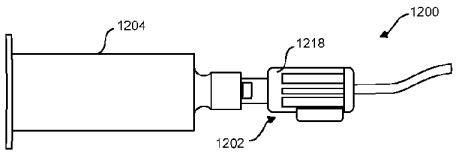


FIG. 12C

【図１２Ｄ】

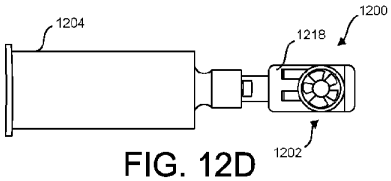


FIG. 12D

【図１３Ａ】

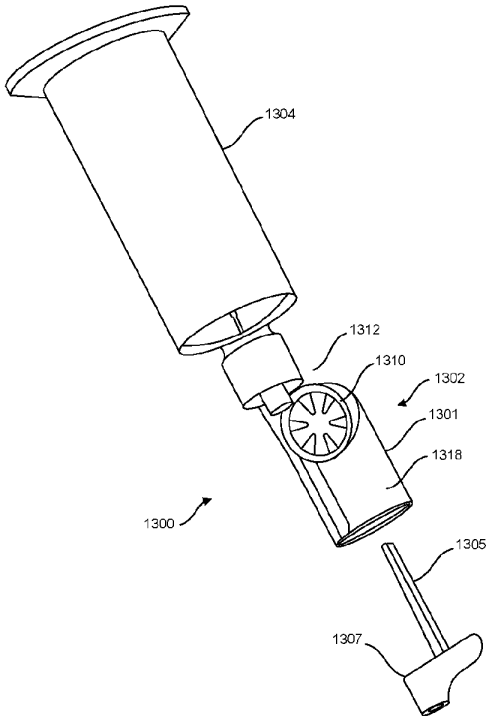


FIG. 13A

【図１３Ｂ】

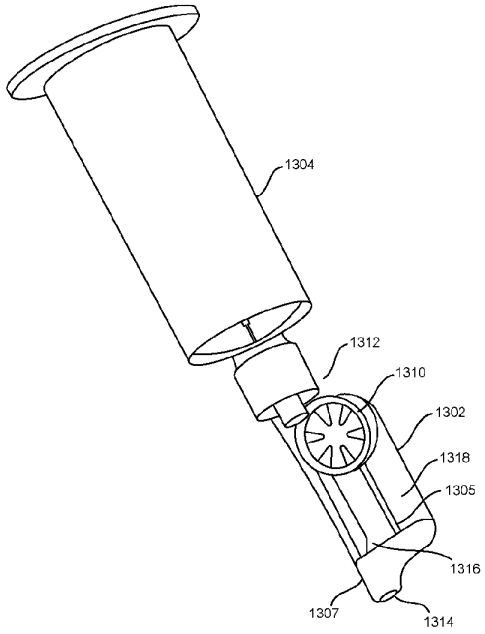


FIG. 13B

【図１３Ｃ】

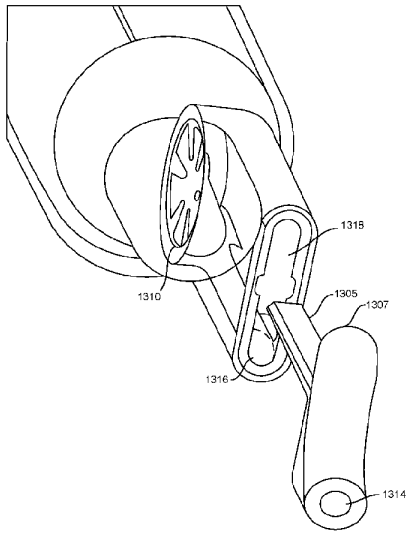


FIG. 13C

【図１３Ｄ】

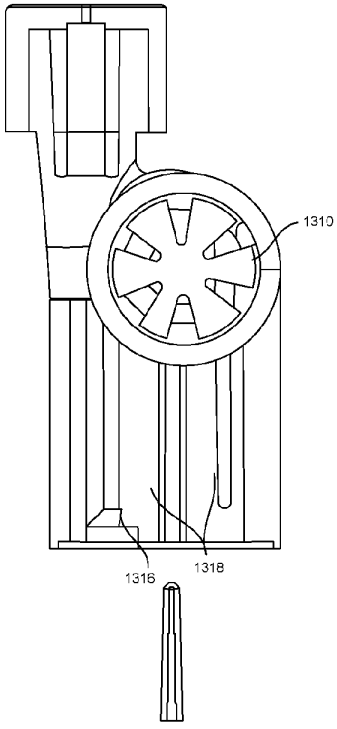


FIG. 13D

【図１４Ａ】

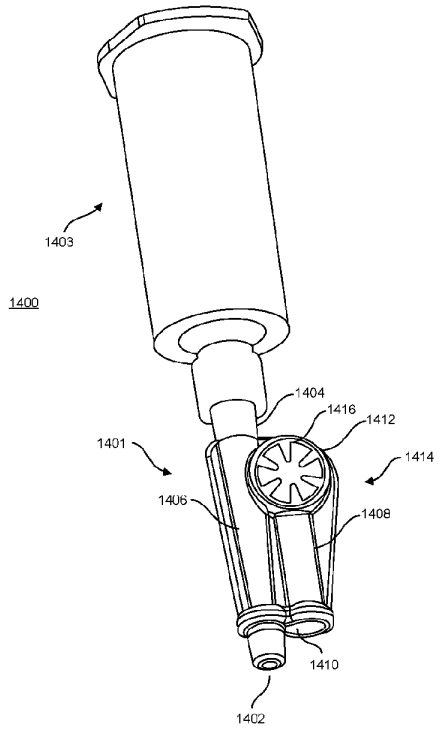


FIG. 14A

【図１４Ｂ】

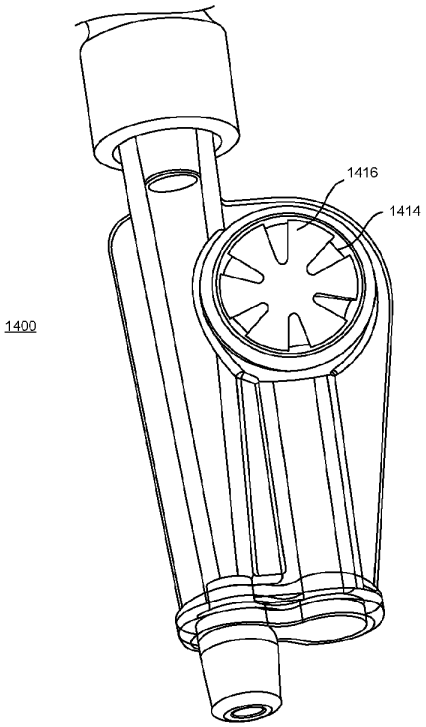


FIG. 14B

【図１４Ｃ】

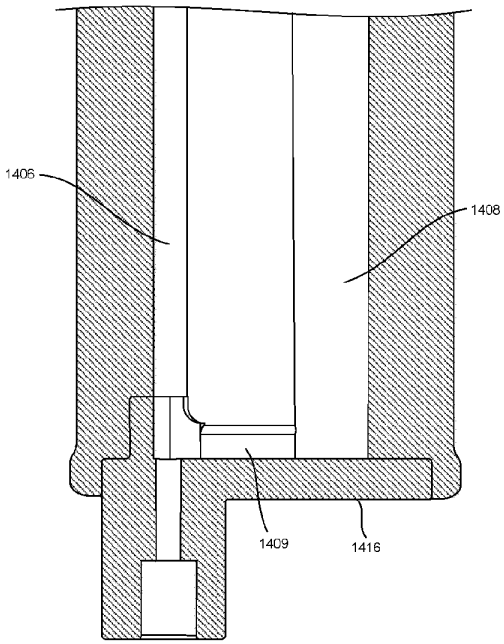


FIG. 14C

【図１４Ｄ】

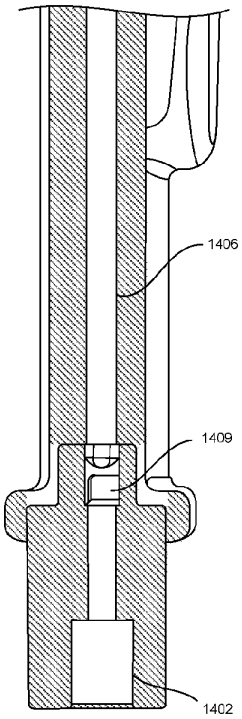


FIG. 14D

【図１４Ｅ】

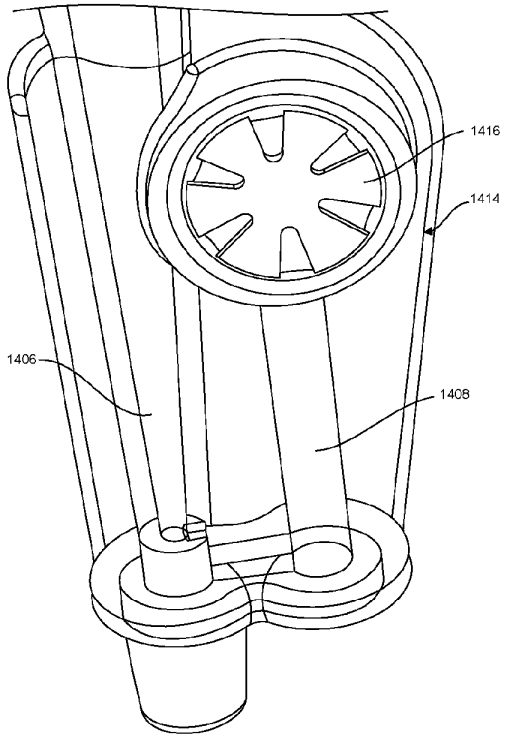


FIG. 14E

【図１５Ａ】

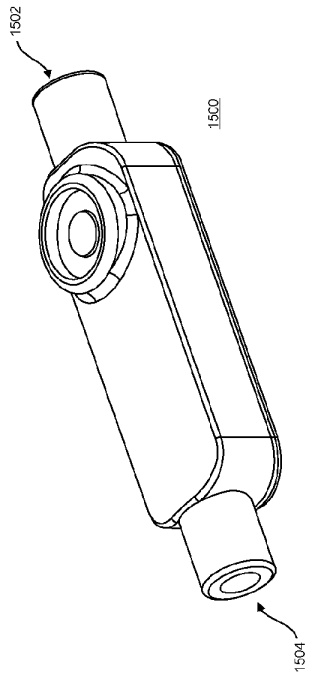


FIG. 15A

【図１５Ｂ】

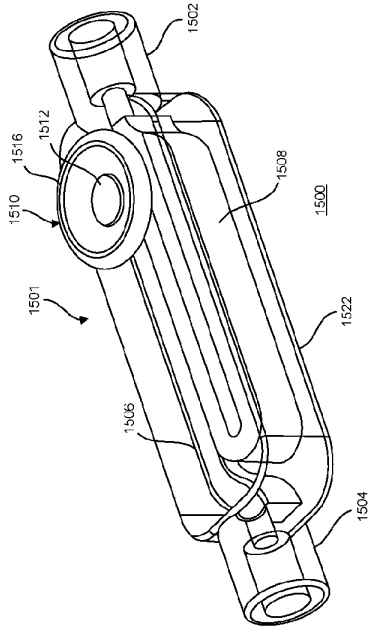


FIG. 15B

【図１５Ｃ】

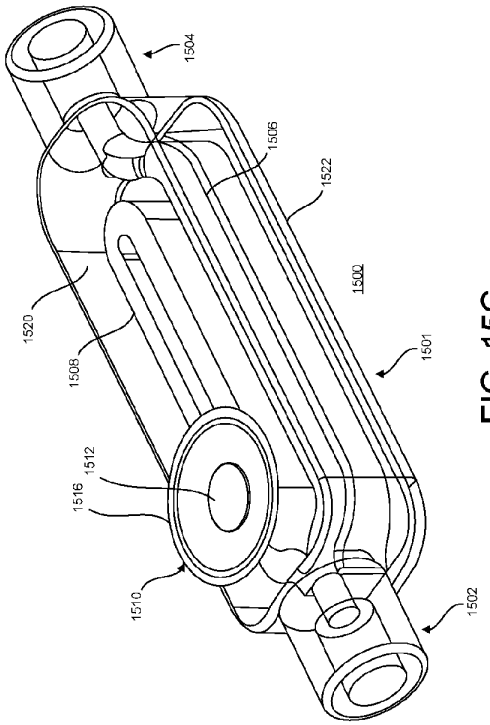


FIG. 15C

【図１５Ｄ】

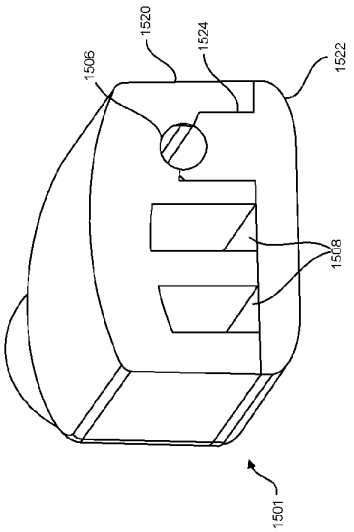


FIG. 15D

【図１５Ｅ】

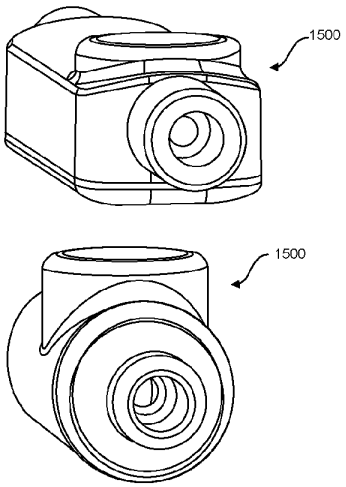


FIG. 15E

【図１５Ｆ】

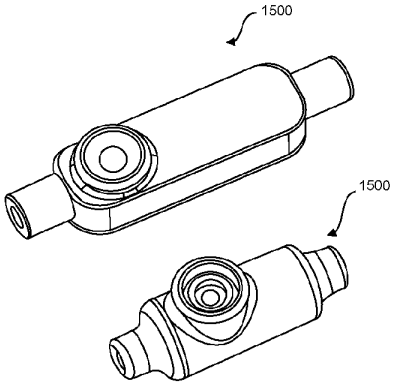


FIG. 15F

【図１５Ｇ】

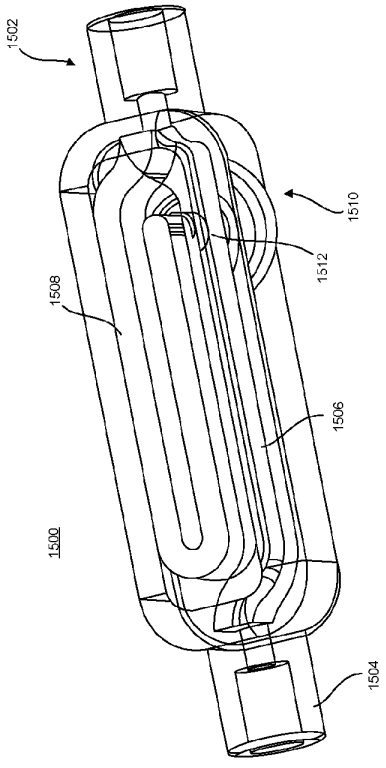


FIG. 15G

【図１６Ａ】

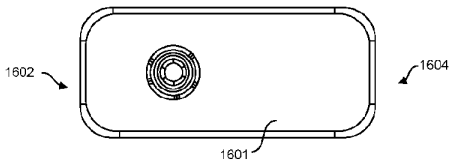


FIG. 16A

【図１６Ｂ】

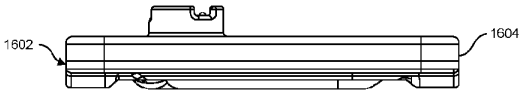


FIG. 16B

【図１６Ｃ】

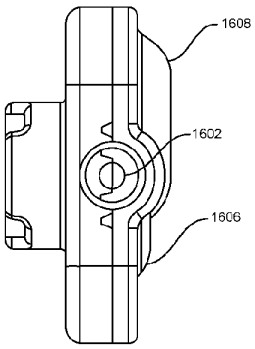


FIG. 16C

【図１６Ｄ】

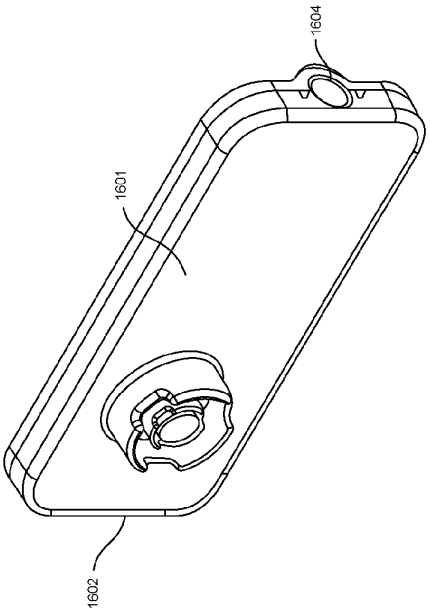


FIG. 16D

【図１７Ａ】

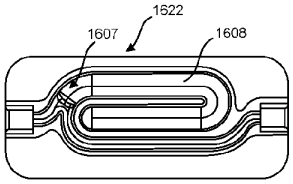


FIG. 17A

【図１７Ｂ】

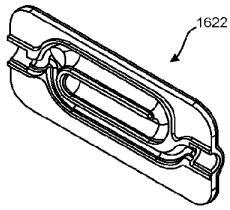


FIG. 17B

【図１７Ｃ】

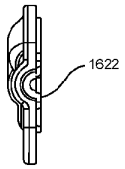


FIG. 17C

【図１７Ｄ】

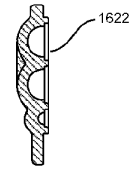


FIG. 17D

【図１７Ｅ】



FIG. 17E

【図１８Ａ】

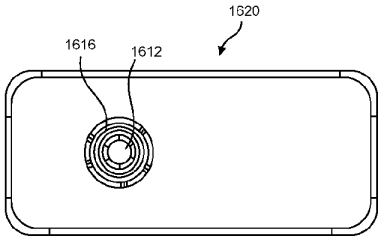


FIG. 18A

【図１８Ｂ】

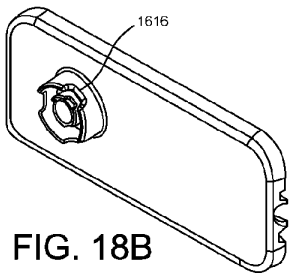


FIG. 18B

【図１８Ｃ】

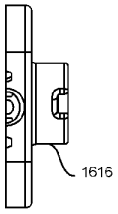


FIG. 18C

【図１８Ｄ】

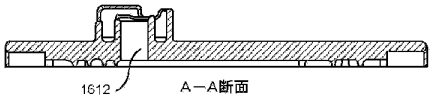


FIG. 18D

【図１８Ｅ】

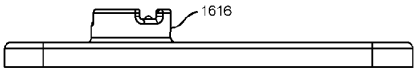


FIG. 18E

【図１８Ｆ】

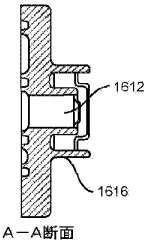


FIG. 18F

【図１９Ａ】

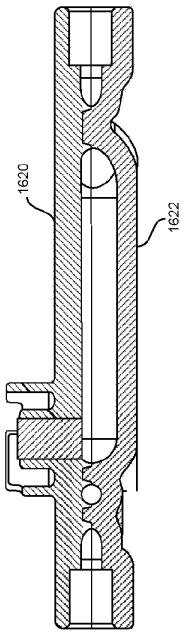


FIG. 19A

【図１９Ｂ】

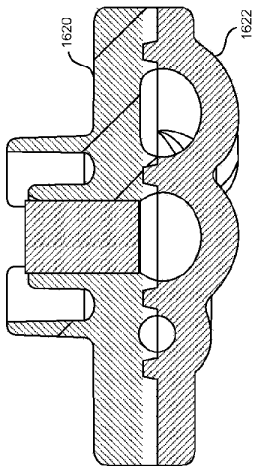


FIG. 19B

【図２０】

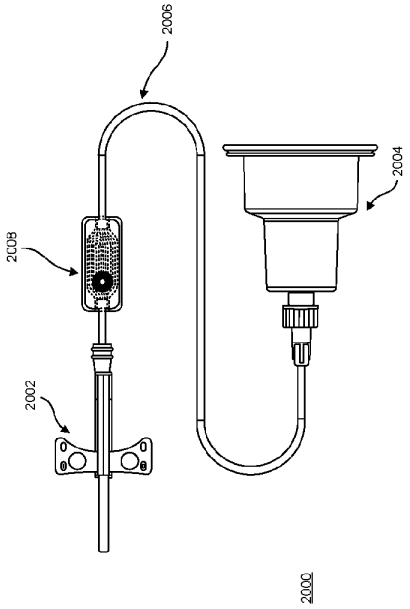


FIG. 20

【図２１】

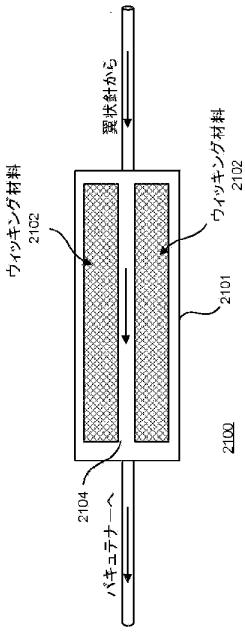


FIG. 21

【図２２Ａ】

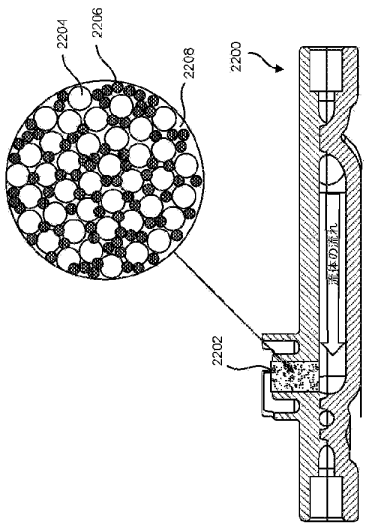


FIG. 22A

【図２２Ｂ】

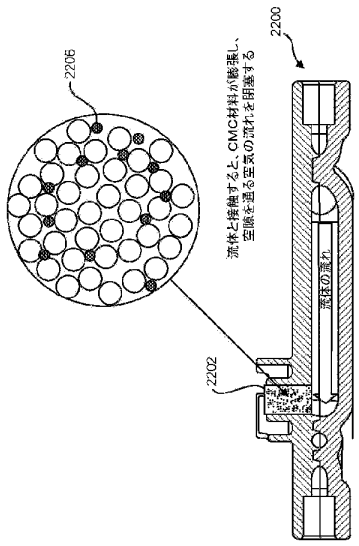


FIG. 22B

【図２３Ａ】

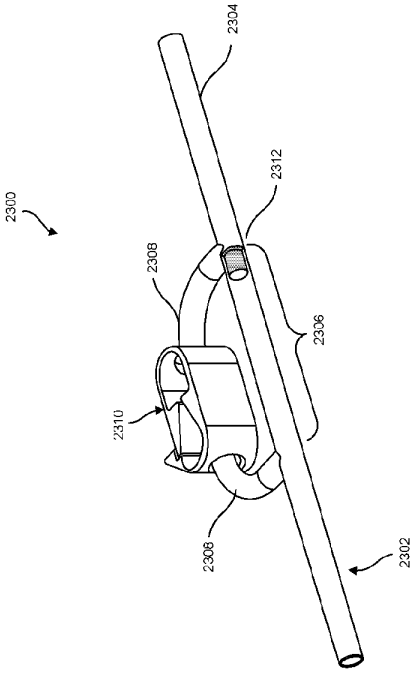


FIG. 23A

【図２３Ｂ】

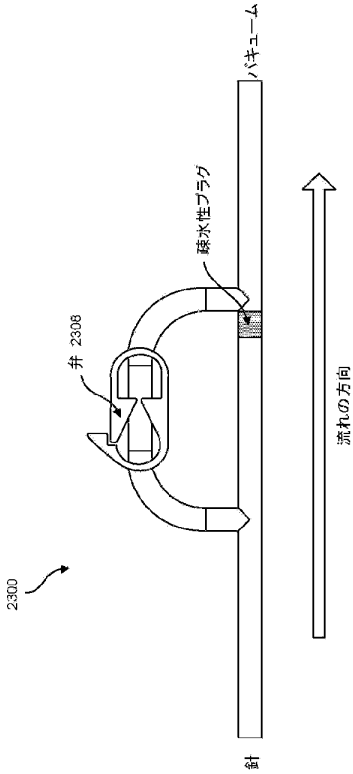


FIG. 23B

フロントページの続き

優先権主張番号
優先日　　平成　年 月　日
優先権主張国・地域又は機関
　　米国
優先権主張番号
優先日　　平成　年 月　日
優先権主張国・地域又は機関
　　米国
優先権主張番号
優先日　　平成　年 月　日
優先権主張国・地域又は機関
　　米国

早期審査対象出願

発明者　ロジャーズ、　ボビー
　　アメリカ合衆国　９２１３１　カリフォルニア州　サンディエゴ　スクリップス　ポーウェイ　パークウェイ　１０７５５　ナンバー　２５７
発明者　カン、　ジーノ
　　アメリカ合衆国　９２１３１　カリフォルニア州　サンディエゴ　スクリップス　ポーウェイ　パークウェイ　１０７５５　ナンバー　２５７
発明者　デトロフ、　ジョン
　　アメリカ合衆国　９２１３１　カリフォルニア州　サンディエゴ　スクリップス　ポーウェイ　パークウェイ　１０７５５　ナンバー　２５７

審査官　清水　裕勝

参考文献　特開昭５８－０２５１４６（ＪＰ，Ａ）
　　特開昭５８－０６７２３８（ＪＰ，Ａ）
　　特開２０１２－０１６４９６（ＪＰ，Ａ）
　　特開昭５７－０８９８６９（ＪＰ，Ａ）
　　特表平０９－５０４７２６（ＪＰ，Ａ）
　　特開平０２－２２４７４２（ＪＰ，Ａ）
　　特開２００５－３４９１９６（ＪＰ，Ａ）
　　米国特許第０４２０７８７０（ＵＳ，Ａ）
　　米国特許出願公開第２０１３／０１１６５９９（ＵＳ，Ａ１）
　　米国特許出願公開第２０１１／０３０６８９９（ＵＳ，Ａ１）

調査した分野　　，ＤＢ名
　　Ａ６１Ｂ　　５／１５３－５／１５４

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Special table 2016-504075

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

Display format of the document display screen:
text display PDF display
primary literature

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] Special table 2016-504075 (P2016-504075A)
(43) [Publication date] February 12, 2016 (2016.2.12)
(54) [Title of Invention] Sterilized Body Fluid Collection Device and Method
(51) [International Patent Classification]
A61B 5/154 (2006.01)
A61B 5/15 (2006.01)
[FI]
A61B 5/14 300E
A61B 5/14 300H
[Request for examination] Unclaimed
[Request for preliminary examination] Unclaimed
[Total number of pages] 64
(21) [Application number] Patent application 2015-545813 (P2015-545813)
(86)(22) [Filing date] December 4, 2013 (2013.12.4)
(85) [Translation submission date] July 24, 2015 (2015.7.24)

(86) [International application number] PCT /US2013/073080
(87) [International publication number] WO2014/089186 (87) [International publication date] June 12, 2014 (2014.6.12) (31) [Priority claim number] 61/733,199 (32) [Priority date] December 4, 2012 (2012.12.4) (33) [Country claiming priority] United States (US)

(81) [Designated country] AP (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), EA (AM, AZ, BY,KG,KZ,RU,TJ,TM),EP(AL,AT,BE,BG,CH,CY,CZ,DE,DK,EE,ES,FI,FR,GB, GR,HR,HU,IE ,IS,IT,LT,LU,LV,MC,MK,MT,NL,NO,PL,PT,RO,RS,SE,SI,SK,SM,TR),OA(BF,BJ,CF,CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG), AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH ,BN,BR,BW,BY,BZ,CA,CH,CL,CN,CO,CR,CU,CZ,DE,DK,DM,DO,DZ,EC,EE,EG,ES,FI,GB,GD ,GE,GH,GM,GT,HN,HR,HU,ID,IL,IN,IR,IS,JP,KE,KG,KN,KP,KR,KZ,LA,LC,LK,LR,LS,LT ,LU,LY,MA,MD,ME,MG,MK,MN,MW,MX,MY,MZ,NA,NG,NI,NO,NZ,OM,PA,PE,PG,PH,PL,PT,QA ,RO,RS,RU,RW,SA,SC,SD,SE,SG,SK,SL,SM,ST,SV,SY,TH,TJ,TM,TN,TR,TT,TZ,UA,UG,US
(71) [Applicant]
[Identification number] 514113555
[Name] Magnolia Medical Technologies, Inc.
(74) [Agent]
[Identification number] 100079108
[Patent attorney]
[Name] Yoshiyuki Inaba
(74) [Agent]
[Identification number] 100109346
[Patent Attorney]
[Name] Toshifumi Onuki
(74) [Agent]
[Identification Number] 100117189 [
Patent Attorney]
[Name] Akihiko Eguchi
(74) [Agent]
[Identification Number] 100134120
[Patent Attorney]
[Name] Kazuhiko Naito
(72) [Inventor]
[Name] Barrington, Gregory, Jay.
(72) [Inventor]
[Name] Patton, Richard Gee. , M. , D.

(72) [Inventor]
[Name] Gau, Shan, Yi.
[Theme code (reference)]
4C038
[F term (reference)]
4C038TA01
4C038UA10
4C038UB07

wrap up close

(57) [Summary]
An apparatus includes a pre-sample reservoir, a flow dividing mechanism and a flow meterin g mechanism. The flow diverting mechanism includes an inlet port couplable to the lumen-defi ning device to receive bodily fluid from the patient, a first outlet port fluidly couplable to the p re-sample reservoir, and a second outlet port fluidly couplable to the sample reservoir. and an exit port. The flow diverter mechanism defines a first fluid flow path and a second fluid flow p ath configured to place the first outlet port and the second outlet port in fluid communication with the inlet port, respectively. The flow metering mechanism meters flow of a predetermine d volume of bodily fluid through the first fluid flow path to the pre-sample reservoir, meters fl ow of a second volume of bodily fluid through the second fluid flow path to the sample reserv oir, It is configured to display a volume indicator associated with the volume and the second v olume.
[Selection drawing] Fig. 2

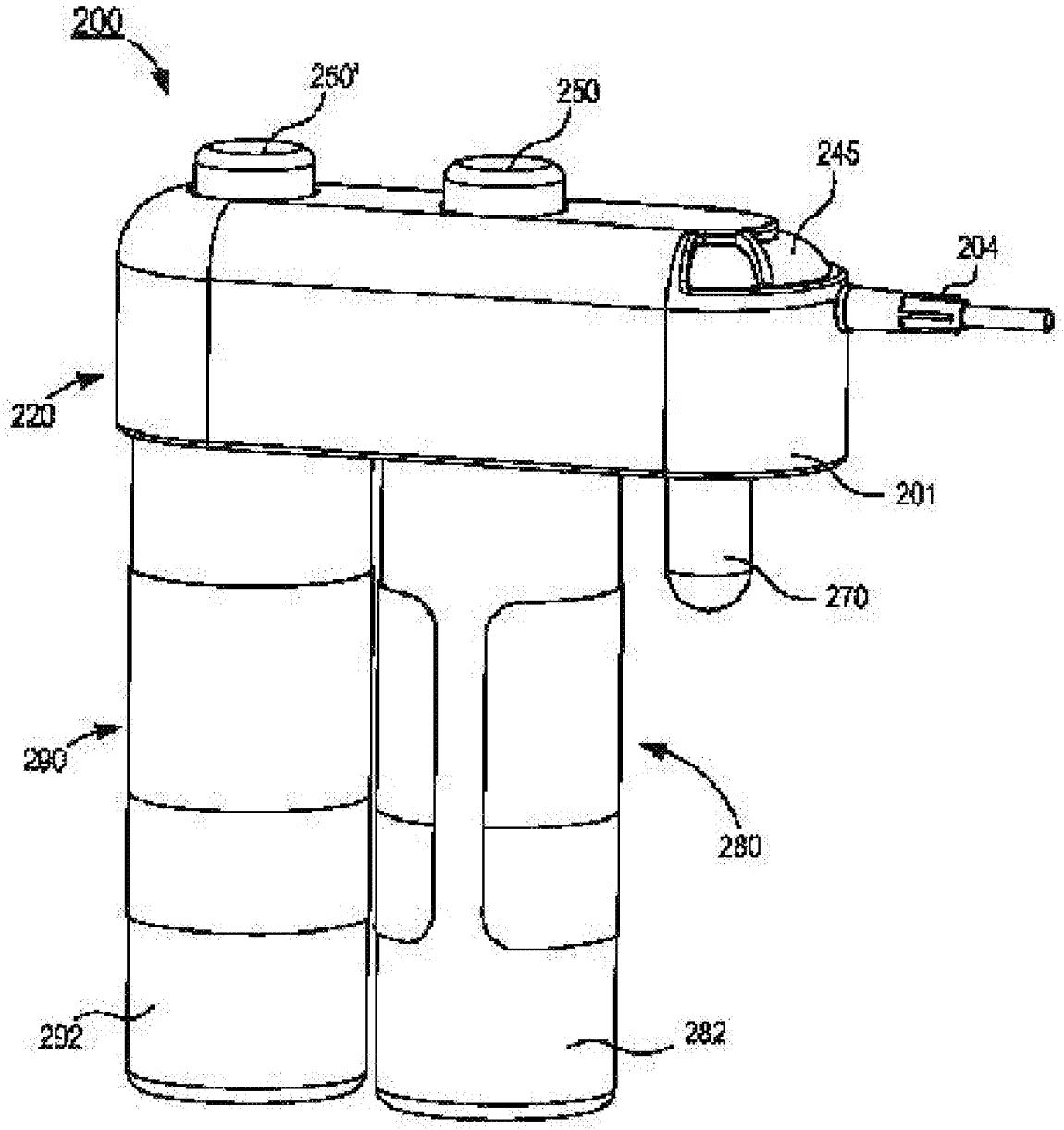


FIG. 2

The scope of the claims open

1. An apparatus for
obtaining a bodily fluid sample from a patient, comprising a
pre-sample reservoir configured to receive a first volume of bodily fluid withdrawn from the

patient; an

inlet port; A flow diverting mechanism including an outlet port and a second outlet port, whe rein the inlet port is configured to be coupled to a lumen defining device to receive bodily fluid from a patient, and the first outlet port is connected to the flow diverting mechanism. and the second outlet port is configured to fluidly couple the sample reservoir to the flow diverting me chanism, the flow diverting mechanism configured to fluidly couple the pre-sample reservoir t o the first outlet port. a first fluid flow path configured to place a in fluid communication with t he inlet port; and a second fluid flow path configured to place the second outlet port in fluid c ommunication with the inlet port. and a flow metering mechanism in fluid communication with

said first fluid flow path and said second fluid flow path, wherein a first volume of bodily fluid passes through said first fluid flow path. configured to meter flow into a pre-sample reservoir and meter flow of a second volume of bodily fluid through said second fluid flow path into said sample reservoir; and a flow metering mechanism configured to display an associated volume indicator.

2. A

first volume of said bodily fluid flows in said first fluid flow path during a first period of time, and a second volume of said bodily fluid flows in said second volume of fluid during a second period of time after said first period of time. 2. The device of claim 1, which flows in a two-flui d flow path.

3. The apparatus of claim

1, wherein the first volume of bodily fluid comprises contaminants present on the skin and t he second volume of bodily fluid is substantially free of contaminants present on the skin. .

4.

The apparatus of claim 1, wherein said pre-sample reservoir is at least partially defined by a portion of said flow divider mechanism.

5.

The apparatus of claim 1, wherein said volume indicator is a visual indicator.

6.

The flow diverting mechanism includes a moveable member configured to move through the second outlet port to place the sample reservoir in fluid communication with the second fluid f low path. Item 1. The device according to item 1.

7.

The apparatus of claim 6, wherein said flow metering mechanism is at least partially dispose d within a portion of said movable member.

8. The

flow diverting mechanism fluidly isolates the pre-sample reservoir and at least a portion of t he first fluid flow path when the first volume of blood is disposed within the pre-sample reserv oir. 2. The device of claim 1, wherein the device comprises:

9.

The flow diverter mechanism includes a third outlet port configured to fluidly couple a secon d sample reservoir to the flow diverter mechanism, the third outlet port being in fluid commun ication with the inlet port. 2. The device of claim 1, defining a third fluid flow path configured t o be positioned in the .

10.

A flow controller defining a first lumen and a second lumen, the first configuration placing th e 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 inle t port, further comprising a flow controller configured to move between Apparatus as describe d.

11. The method of claim 10,

wherein the flow controller is configured to move from the first configuration to the second c onfiguration after the first volume of bodily fluid is placed in the pre-sample reservoir. Apparat us as described.

12.

An apparatus for obtaining a bodily fluid sample from a patient, comprising a

pre-sample reservoir configured to receive a first volume of bodily fluid withdrawn from the patient, an

inlet port, a first outlet port and a second outlet. A flow diverting mechanism comprising a p ort, wherein the inlet port is configured to be coupled to a lumen defining device to receive bo dily fluid from a patient, and the first outlet port directs the pre-sample reservoir to the flow d iverting mechanism. a flow diverting mechanism configured for fluid coupling, wherein the sec ond outlet port is configured to fluidly couple a sample reservoir to the flow diverting mechani sm; and a flow diverting mechanism disposed at least partially within the flow diverting mech anism

. a flow controller, wherein the flow controller defines at least a portion of a fluid flow path b etween the inlet port and the first outlet port in a first configuration; a flow controller configur ed to move between a second configuration defining at least a portion of a fluid flow path bet ween the port;

a first configuration of a movable member movably coupled to the flow diverting mechanism, wherein the sample reservoir is fluidly isolated from a fluid flow path between the inlet port a nd the second outlet port; a reservoir configured to move through the second outlet port betw een a second configuration in fluid communication with the fluid flow path between the inlet p ort and the second outlet port, the sample reservoir a movable member configured to receive a second volume of bodily fluid withdrawn from the patient when the flow controller is in its se cond configuration and the movable member is in its second configuration.

13. The apparatus of claim 12,

wherein the first volume of bodily fluid comprises contaminants present on the skin and the second volume of bodily fluid is substantially free of contaminants present on the skin. .

14.

The apparatus of claim 12, wherein the flow controller rotates between its first configuration and its second configuration relative to the flow diverter mechanism.

15.

The apparatus of claim 12, wherein said flow controller moves in linear motion relative to sai d flow diverter mechanism.

16. The apparatus of claim 12,

wherein the flow controller is configured to fluidly isolate the pre-sample reservoir when in it s second configuration.

17.

The apparatus of claim 12, wherein said movable member includes a piercing member config ured to pierce a portion of said sample reservoir when in its second configuration.

18. The apparatus of claim 12

, wherein said movable member is coupled to a biasing member configured to at least tempo rarily 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 p ort 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 outle t port; A second movable member configured to receive a third volume of bodily fluid withdra wn from the patient when the flow controller is in its second configuration and the second mo vable member is in its second configuration. 20. The device of Claim 19, further comprising a member.

21.

An apparatus for obtaining a bodily fluid sample from a patient, the

flow diverting mechanism comprising a pre-sample reservoir configured to receive a first vol ume of bodily fluid withdrawn from the patient, a

housing and a distribution member. said housing defining a first opening and a second openi ng, said first opening being in fluid communication with said pre-sample reservoir, said distrib ution member being disposed at least partially within said housing; and defining a fluid flow p ath in fluid communication with the second opening, wherein the distribution member is confi gured to be in fluid communication with the flow path and physically and fluidly coupled to a s ample reservoir. and an

inlet port configured to be coupled to a lumen-defining device to receive bodily fluid from the patient, the flow controller being rotatably coupled to the flow diversion mechanism, and a flo w controller configured to move between a first configuration in which the inlet port is in fluid communication with the first opening and a second configuration in which the inlet port is in fl uid communication with the second opening; Equipment to equip.

22. The apparatus of claim 21,

wherein the first volume of bodily fluid comprises contaminants present on the skin and the second volume of bodily fluid is substantially free of contaminants present on the skin. .

[Claim 23]

22. The apparatus of claim 21, wherein said pre-sample reservoir is at least partially defined by a portion of said distribution member.

24. The method of claim 21,

wherein the coupling portion includes a piercing member configured to pierce a portion of th e sample reservoir to place the sample reservoir in fluid communication with the fluid flow pat h. Apparatus as described.

25. Said

piercing of said portion of said sample reservoir by said piercing member causes bodily fluids from said patient to enter said sample reservoir through said inlet port and said flow path whe n said flow controller is in its second configuration. 25. The device of claim 24, which initiates inward flow.

26.

The first volume of bodily fluid is a first predetermined volume of bodily fluid, the fluid flow p ath is configured to receive a second predetermined volume of bodily fluid, and the second pr edetermined volume of bodily fluid is a sample volume. 22. Apparatus according to claim 21, r elated to volume.

27.

The apparatus of claim 26, wherein said sample volume is between about 10 milliliters and a bout 50 milliliters.

28.

The apparatus of claim 26, wherein said sample volume is approximately 30 milliliters.

[Claim 29]

said flow diverter mechanism including a seal member, said seal member forming a substant ially fluid tight seal with a surface of said flow controller and a surface of said housing when s aid flow controller is coupled to said flow diverter mechanism; Disposed between the housing and the flow controller, the seal member defines a first opening and a second opening, the firs t opening of the seal member substantially flush with the first opening of the housing. and wh erein said second opening of said seal member is substantially coaxial with said second openi ng of said housing.

The apparatus described in .

30.

A method of obtaining a predetermined sample volume of bodily fluid from a patient using a flow metering transfer device, wherein the flow metering transfer device is selectively placed i n fluid communication with a pre-sample reservoir and a sample reservoir. and a flow meterin g mechanism configured to meter the flow of bodily fluid from the patient to the pre-sample r eservoir and to the sample reservoir; A method comprising: establishing fluid communication between the patient

and the port of the flow metering transfer device; establishing fluid communication between the

port and the pre-sample reservoir;

metering a flow of bodily fluid transferred to a pre-sample reservoir; and

via said flow metering mechanism of said flow metering transfer device, a pre-sample volum e of bodily fluid disposed within said pre-sample reservoir to a predetermined pre-sample of b odily fluid.

fluidly isolating the pre-sample reservoir from the port to confine a pre-sample volume of th e bodily fluid within the pre-sample reservoir

; metering

a flow of bodily fluid transferred from the patient to the sample reservoir; and

via the flow metering mechanism of the flow metering transfer device disposed within the sa mple reservoir. and C. verifying that the obtained sample volume of bodily fluid is a predeterm ined sample volume of bodily fluid.

[Claim 31]

The flow metering transfer device has a first configuration in which fluid communication is es tablished between the patient and the pre-sample reservoir, and a second configuration in whi ch fluid communication is established between the patient and the sample reservoir. 31. The method of claim 30, including a flow controller configured to move between.

32.

The method of claim 30, wherein said bodily fluid is blood.

33. The method of claim 32

, wherein the sample reservoir comprises at least one of an aerobe medium or an anaerobe medium.

34.

The method of claim 30, wherein said predetermined pre-sample volume is between about 1 milliliter and about 10 milliliters.

35.

The method of claim 30, wherein said predetermined sample volume is between about 20 mi lliliters and about 60 milliliters.

36.

The method of claim 30, wherein said predetermined sample volume is approximately 60 mil

liliters.

37. verified that

said sample reservoir is a first sample reservoir, said sample volume is a first sample volum e, and said first sample volume within said first sample reservoir is said predetermined sampl e volume;

subsequently establishing fluid communication between the port and a second sample reservo ir;

metering the flow of bodily fluid transferred from the patient to the second sample reservoir ; verifying, via a metering mechanism, that a second sample volume of bodily fluid disposed within the second sample reservoir is the predetermined sample volume of bodily fluid;

31. The method of claim 30, further comprising:

38. The method of claim 37, wherein

said first sample volume and said second sample volume collectively equal between about 2 0 milliliters and about 60 milliliters.

39.

After verifying that said second sample volume in said second sample reservoir is said prede termined sample volume, establishing fluid communication between said port and a third sam ple reservoir

; metering a flow of bodily fluid transferred from a patient to said third sample reservoir; an d a third sample volume of bodily fluid

disposed within said third sample reservoir via said flow metering mechanism of said flow m etering transfer device. 38. The method of claim 37, further comprising verifying that is the pr edetermined sample volume of bodily fluid.

40.

The method of claim 39, wherein said first sample volume, said second sample volume and s aid third sample volume collectively equal between about 30 milliliters and about 60 milliliter s.

41.

The method of claim 39, wherein said first sample volume, said second sample volume and s aid third sample volume collectively equal approximately 60 milliliters.

detailed description open —

Description: CROSS-REFERENCE TO RELATED APPLICATIONS

[

1001] This application is entitled "Sterile Bodily-Fluid Collection Device and Method", filed De

c. 4, 2012. and Methods)," the disclosure of which is hereby incorporated by reference in its e ntirety. [1002] Embodiments described herein relate generally to the parenteral procurement of bodily fluid samples, and more particularly to microbial or other external sources of bodily f luids, such as those present on the skin. Devices and methods for obtaining bodily fluid sampl es parenterally with reduced contamination from contaminants. BACKGROUND ART [0003]

[1003] Health care practitioners routinely perform various types of microbiological tests on pa tients using parenterally obtained bodily fluids. In some cases, a patient sample (eg, bodily flu id) is tested for the presence of one or more potentially unwanted microorganisms, such as ba cteria, fungi or yeast (eg, Candida). Microbial testing may involve culturing patient samples in one or more sterile containers containing media that promote microbial growth, real-time diag nostics and/or molecular PCR-based techniques. Generally, when such microorganisms are pre sent in a patient sample, they will multiply in the culture medium over time. After a variable a mount of time (eg, hours to days), automated continuous monitoring can detect organism gro wth. Such automated monitoring can detect carbon dioxide produced by the growth of organis ms. The medium can then be tested for the presence of microorganisms. The presence of mic roorganisms in the medium indicates the presence of the same microorganisms in the patient sample, which in turn indicates the presence of the same microorganisms in the patient's bodi ly fluid from which the sample was obtained. Therefore, if it is determined that microorganism s are present in the culture medium, the patient is administered one or more antibiotics or ot her treatments specifically designed to treat or otherwise eliminate the undesirable microorga nisms from the patient. may be prescribed.

[0004]

[1004] However, patient samples can be contaminated during acquisition and/or otherwise pr one to false positive results. One process by which contamination of patient samples can occu r is microbes from the body surface (e.g., microbes present on the skin) that are removed dur ing needle insertion into the patient's body and subsequently transferred to the culture mediu m with the patient sample.) by transfer. Surface microbes and/or other unwanted external mi crobes may be removed either directly or through removed tissue debris, hair follicles, sweat glands and other skin appendage structures. Another possible source of contamination comes from the person who draws the patient sample. For example, doctors, phlebotomists, nurses, etc. may transfer contaminants from their bodies (eg, fingers, arms, etc.) to patient samples and/or to equipment containing patient samples. To further elaborate, the instruments and/or devices used during the patient sample acquisition process (e.g., patient to needle, needle/tu

be to sample container, etc.) can each introduce potential points of contamination. It often co ntains multiple fluid interfaces. Use of such instruments and/or devices typically involves man ual intervention to connect and/or fluidly couple various interfaces. Because these interfaces a re pre-assembled and non-sterilized as a single, fluidly coupled system, the user (e.g., physici an, phlebotomist, etc.) and/or other sources of contamination (e.g., ambient air, hospital roo m contaminants on table and counter surfaces, microorganisms transferred from linens or clot hing, etc.) may be introduced into the patient sample. In some cases, these contaminants can grow in the culture medium and ultimately result in a positive microbial test result, thereby fal sely indicating the presence of such organisms in the body.

[0005]

[1005] In some cases, false positive and/or false negative results may result from a given vol ume of patient sample. For example, by overfilling volume-sensitive blood culture bottles, as noted in the instructions for use and/or warning labels from the manufacturers of such culture bottles and associated automated continuous monitoring microbial detection systems, can lea d to false positive results. On the other hand, as another example, insufficient patient sample volume in culture medium can lead to false negative results. As an example, in a study condu cted by the Mayo Clinic entitled "Optimized Pathogen Detection with 30- Compared to 20-Millil iter Blood Culture Draws", published in the December 2011 issue of the Journal of Clinical Micr obiology, 20 milliliters (mL) of A patient sample volume allows detection of the presence of ap proximately 80% of bacteremia present in a patient sample, a patient sample volume of 40 m L allows detection of approximately 88% of bacteremia, and a patient sample volume of 60 m L allows detection of approximately 88% of bacteremia. Approximately 99% of bacteremia ca n be detected by sample volume.

[0006]

[1006] Such inaccurate results as a result of contamination, insufficient patient sample volum e, etc. are a problem when trying to diagnose or treat a suspected disease or condition. For e xample, a false negative result from a microbiological test can lead to misdiagnosis and/or del ay in treatment of a patient's illness, which in some cases can lead to death of the patient. Co nversely, a false-positive result from a microbiological test can lead to the patient receiving on e or more antimicrobial therapies unnecessarily, thereby causing serious side effects in the pa tient, including death, for example. Together, this can result in unnecessary burden and expen se to the health care system due to prolonged hospitalization of the patient and/or other com plications associated with the wrong treatment. In addition, the use of diagnostic imaging equ ipment due to these false positive results also increases the cost and unnecessary exposure of high doses of radiation associated with various imaging procedures (e.g., CT scans) to long-te rm patient health. It is also problematic from a patient safety perspective, as it has many kno wn adverse effects.

[1007

] Thus, for example, reducing microbial contamination in bodily fluid test samples by 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 co llection device and method. Further, such fluid collection devices provide visual, calculated, or must include means for accurately weighing, measuring, and/or otherwise assessing body flui ds transferred from the patient to the sample reservoir or culture medium, which can be other wise communicated. It is

SUMMARY OF THE INVENTION [

1008

] The present invention provides a non-toxic method for treating a body fluid sample by reduc ing contamination from microorganisms external to the body fluid source, such as microorgani sms present on the skin and/or other undesirable external contaminants. An orally acquired d evice is described. In some embodiments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reservoir, a flow diversion mechanism and a flow metering mec hanism. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdra wn from the patient. The flow diverting mechanism includes an inlet port, a first outlet port an d a second outlet port and defines a first fluid flow path and a second fluid flow path. An inlet port can be coupled to the lumen-defining device to receive bodily fluid from the patient. A fir st outlet port and a second outlet port are configured to fluidly couple the pre-sample reservoi r and the sample reservoir, respectively, to the flow diverting mechanism. The first fluid flow p ath is configured to place the first outlet port in fluid communication with the inlet port and th e second fluid flow path is configured to place the second outlet port in fluid communication w ith the inlet port. is configured to A flow metering mechanism is in fluid communication with t he first fluid flow path and the second fluid flow path. A flow metering mechanism meters a fl ow of a first volume of bodily fluid through the first fluid flow path into the pre-sample reservo ir and a second volume of bodily fluid through the second fluid flow path into the sample reser voir. is configured to The flow metering mechanism is configured to display volume indicators associated with the first volume and the second volume.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009]

FIG. 1 is a schematic diagram of a bodily fluid collection device according to an embodiment; 2 is a perspective view of a bodily fluid collection device according to an embodiment; FIG. 3 is an exploded perspective view of the bodily fluid collection device of FIG. 2; FIG. 4 is a side cross-sectional view taken along line X 1 -X 1 of FIG. 3 of a housing included in the bodily fluid c ollection device of FIG. 2;

5 is a cross-sectional view taken along line X 2 -X 2 of FIG. 3 of a movable member included i n the bodily fluid collection device of FIG. 2 ;

6 is a cross-sectional view taken along line X 3 -X 3 of FIG. 3 of the flow controller included in the bodily flui d collection device of FIG. 2;

7 is a cross-sectional view taken along line X 4 -X 4 of FIG. 3 of the flow controller included in the bodily flui

d collection device of FIG. 2;

8 is a top view of the bodily fluid collection device of FIG. 2 in a first configuration; FIG.

9 is a cross-sectional view taken along line X 5 -X 5 of FIG. 8 of the body fluid collection device of FIG. 2 in t he first configuration;

10 is a top view of the bodily fluid collection device of FIG. 2 in a second configuration; FIG.

11 is line X 6 -X 6 of FIG. 10 of the body fluid collection device of FIG. 2 in a second configuration; 1 is a cross-sec tional view taken along .

12 is a cross-sectional view taken along line X 6 -X 6 of FIG. 10 of the bodily fluid collection device of FIG. 2 in a third configuration;

13 is a cross-sectional view taken along line X 6 -X 6 of FIG. 10 of the bodily fluid collection device of FIG. 2 in a fourth configuration;

14 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

15 is a side cross-sectional view taken along line X 7 -X 7 of the bodily fluid collection device of FIG. 14; FI G.

16 is a perspective view of a bodily fluid collection device according to an embodiment; FIG.

17 is an exploded perspective view of a flow diverting mechanism included in the body fluid co llection device of FIG. 16; FIG.

18 along line X 8 -X 8 of FIG. 16 of a distribution member included in the bodily fluid collection device of FIG. 16;

is a side cross-sectional view taken out.

19 is a top view of the bodily fluid collection device of FIG. 16 in a first configuration; FIG.

20 is a cross-sectional view taken along line X 9 -X 9 of FIG. 19 of the partial bodily fluid collection device of FIG. 16 in the first configuration;

21 is a top view of the bodily fluid collection device of FIG. 16 in a second configuration; FIG.

22 is a cross-sectional view taken along line X 10 -X 10 of FIG. 21 of the bodily fluid collection device of FI G. 16 in a second configuration;

FIG. 23 is a perspective view of a bodily fluid collection device according to an embodiment; F igure 24 is a cross-sectional view taken along line X11 - X11

of a portion of the bodily fluid collection device of Figure 23 in a first configuration ; 25 is a cr oss-sectional view taken along line X 11 -X 11 of the bodily fluid collection device of FIG. 23, in a second config uration; FIG. FIG. 26 is a perspective view of a bodily fluid collection device according to an emb odiment; 27 is an exploded perspective view of a flow diverting mechanism included in the bo dily fluid collection device of FIG. 26; FIG. 28 is a cross-sectional view taken along line X 13 - X 13 of FIG. 27 of a distribution member included in the bodily fluid collection device of FIG. 27;

29 is a cross-sectional view taken along line X 14 -X 14 of FIG. 27 of a coupling member included in the bod ily fluid collection device of FIG. 26;

30 is a cross-sectional view taken along line X 15 -X 15 of FIG. 27 of the dial included in the bodily fluid coll ection 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 co llection 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 se cond 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 c ollection 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 diverti ng 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 configurati on; FIG.

38 is a cross-sectional view taken along line X 18 -X 18 of the partial bodily fluid collection device of FIG. 37 in the first configuration; FIG.

39 is a top view of the bodily fluid collection device of FIG. 33 in a second configuration; FIG.

Figure 40 is a cross-sectional view taken along line X19 - X19

of Figure 39 of the body fluid collection device of Figure 33 in a second configuration ; 41 is a perspective view of a bodily fluid collection device in a first configuration according to embodi ments; FIG. 42 is an exploded perspective view of a portion of the bodily fluid collection devic e of FIG. 41; FIG. 43 is a cross-sectional view taken along line X 20 -X 20 of the bodily fluid collection device of FIG. 41 in the first configuration; FIG. Figure 44 is a cross-sectional view taken along line X20 - X20 of the bodily fluid collection device of Figure 41 in a second configuration ; Figure 45 is a c ross-sectional view taken along line X20 - X20 of the body fluid collection device of Figure 41 in a third configuration ; Figure 46 is a perspective view of a bodily fluid collection device in a fir st 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 include d in the bodily fluid collection device of FIG. 46, line X of FIG. 47. FIG.

Figure 21 is a side sectional view taken along 21 - X21 ;

49 is a side sectional view taken along line X 22 -X 22 of FIG. 47 of a movable member included in the bodil

y fluid collection device of FIG. 46;

50 is a top view of the bodily fluid collection device of FIG. 46 in a first configuration; FIG. Fig ure 51 is a cross-sectional view taken along line X23 - X23

of Figure 50 of the partial bodily fluid collection device of Figure 46 in the first configuration ; 52 is a top view of the bodily fluid collection device of FIG. 46 in a second configuration; FIG. Figure 53 is a cross-sectional view taken along line X24 - X24 of Figure 52 of the body fluid coll ection device of Figure 46 in a second configuration ; FIG. 54 is a perspective view of a bodily fluid collection device according to an embodiment; 55 is a top view of the bodily fluid collecti on device of FIG. 54; FIG. FIG. 56 is a flowchart illustrating a method of obtaining bodily fluid samples with reduced contamination using a collection device according to embodiments; DET AILED DESCRIPTION OF THE INVENTION [0010]

[1063] Described herein are devices for obtaining bodily fluid samples parenterally with reduc ed contamination from microorganisms external to the bodily fluid source, such as microorgan isms present on the skin and/or other undesirable external contaminants. It is In some embod iments, a device for obtaining a bodily fluid sample from a patient includes a pre-sample reser voir, a flow diversion mechanism and a flow metering mechanism. The pre-sample reservoir is configured to receive a first volume of bodily fluid withdrawn from the patient. The flow diverti ng mechanism includes an inlet port, a first outlet port and a second outlet port and defines a first fluid flow path and a second fluid flow path. An inlet port can be coupled to the lumen-def ining device to receive bodily fluid from the patient. A first outlet port and a second outlet por t are configured to fluidly couple the pre-sample reservoir and the sample reservoir, respectiv ely, to the flow diverting mechanism. The first fluid flow path is configured to place the first ou tlet port in fluid communication with the inlet port and the second fluid flow path is configured to place the second outlet port in fluid communication with the inlet port. is configured to A flo w metering mechanism is in fluid communication with the first fluid flow path and the second f luid flow path. A flow metering mechanism meters a flow of a first volume of bodily fluid throu gh the first fluid flow path into the pre-sample reservoir and a second volume of bodily fluid th rough the second fluid flow path into the sample reservoir. is configured to The flow metering mechanism is configured to display volume indicators associated with the first volume and the second volume.

[0011]

[1064] In some embodiments, an apparatus for obtaining a bodily fluid sample from a 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 meter ed. The method includes verifying, via a flow metering mechanism of the flow metering transf er device, that a pre-sample volume of bodily fluid disposed within a pre-sample reservoir is a first pre-sample volume of bodily fluid. With the pre-sample volume disposed within the pre-s ample reservoir, the pre-sample reservoir is fluidly isolated from the port to seal the pre-samp le volume of bodily fluid within the pre-sample reservoir. With the pre-sample reservoir fluidly isolated, the method includes establishing fluid communication between the port and the sam ple reservoir. A flow of bodily fluid transferred from the patient to the sample reservoir is met ered. The method includes verifying, via the flow metering mechanism of the flow metering tr ansfer device, that the sample volume of bodily fluid disposed within the sample reservoir is a first sample volume of bodily fluid.

[0014]

[1067] In some embodiments, an apparatus includes a flow diversion mechanism and a flow c ontroller. The flow diverting mechanism can define an inlet port, a first outlet port, a second o utlet port and a third outlet port. a first outlet port fluidly coupled to the pre-sample reservoir, a second outlet port fluidly coupled to the first sample reservoir, a third outlet port fluidly cou pled to the second sample reservoir; etc. All of the fluid reservoirs can be fluidly isolated from each other. The flow controller includes various fluid channels, which can allow fluid movemen t in specified directions and can be configured to be operatively coupled to the flow diverting mechanism. In use, the flow controller can allow bodily fluid flow into the pre-sample reservoi r when the flow diverter mechanism is in the first configuration. The flow diverter mechanism can be moved to a second configuration, in which the flow controller can allow bodily fluid flo w to enter the first sample reservoir. In addition, the flow diverter mechanism can then be mo ved to the third configuration so that the flow controller can allow bodily fluid flow to enter the second sample reservoir.

[0015]

[1068] In some embodiments, the bodily fluid collection device allows a second volume of bod ily fluid to flow into the first sample reservoir and/or a third volume of bodily fluid to flow into the second sample reservoir. previously, it can be configured to selectively divert a first predet ermined volume of bodily fluid to a pre-sample reservoir. In this way, the second and/or third volume of bodily fluid can be used for diagnosis or other testing, while the presence of microo rganisms from the body surface or other microbial sources external to the patient from whom the sample is obtained. A first volume of bodily fluid that may contain is isolated. In some em bodiments, the bodily fluid collection device can include additional sample reservoirs (eg, 3, 4, 5, 6 or more) depending on the analysis and/or testing protocols to be performed.

[1069

] In some embodiments, the bodily fluid collection device is configured such that an appropria te volume of bodily fluid is collected from the patient and/or transferred to a predetermined pr e-sample reservoir and/or sample reservoir.

Flow metering can be included to ensure that the A bodily fluid collection device can be config ured to automatically divert and/or control fluid flow after a metered volume of bodily fluid ha s been collected. For example, once a first metric pre-sample volume has been collected, the f low diverter mechanism can be configured to divert body fluid flow to a first sample reservoir, and then divert the flow after the first metric sample volume has been collected. The mechani sm can be configured to divert body fluid flow to a second sample reservoir, and so on. In so me embodiments, the bodily fluid collection device includes a metered volume display, such a s a liquid crystal display (LCD), to provide a visual indication of how much bodily fluid has bee n collected in each predetermined individual sample reservoir. can be provided to the user. In some embodiments, multiple displays can be provided to allow for customized pre-sample an d/or sample volume collection.

[1070

] As used in this specification and the appended claims, the singular forms "a, an" and "the" r efer to the plural unless the context clearly dictates otherwise. including referents of Thus, for example, the term "(a) member" is intended to mean a single member or combination of me mbers, and "(a) material" is intended to mean one or more materials or combinations thereof. intended to mean

[1071

] As used herein, "bodily fluid" includes, but is not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, etc., or any combin ation thereof. , can include any fluid obtained from the patient's body.

[0019]

[1072] As used herein, the terms "first predetermined amount," "first amount," and "first volu me" are configured to be received or contained by a first reservoir or a pre-sample reservoir. s tate the amount of body fluid The terms "first amount" and "first volume" do not explicitly stat e a predetermined amount, but unless explicitly stated otherwise, the first amount may be a fi rst predetermined amount. should be understood.

[1073

] As used herein, the terms "second volume" and "second volume" describe the amount of bo dily fluid configured to be received or contained by a second reservoir or sample reservoir. . T he second amount can be any suitable amount of bodily fluid and it need not be a predetermi ned amount. Conversely, when so explicitly stated, the second volume received and contained by the second reservoir or sample reservoir may be the second predetermined volume.

[1074

] As used herein, the term "set" can refer to a single feature comprising multiple features or multiple parts. For example, when referring to a set of walls, the set of walls can be considere d a single wall with separate portions, or the set of walls can be considered multiple walls. Si milarly, an integrally constructed article can include a set of walls. Such a set of walls can incl ude, for example, multiple portions that are discontinuous from each other. A set of walls can

also be made from multiple articles that are manufactured separately and later joined togethe r (eg, via welding, adhesives, or any suitable method).

[0022]

[1075] As used herein, the terms "proximal" and "distal" refer to directions toward and away f rom, respectively, a user placing the device in contact with a patient. Thus, for example, the e nd of the device that first contacts the patient's body would be the distal end, and the opposit e end of the device (eg, the end of the device being operated by the user) would be the proxi mal end of the device. becomes.

[1076

] As used herein, the terms "about," "approximately," and "substantially," when used in conne ction with numerical values, are nominally indicative of the value so defined. is intended to m ean that the value In other words, the terms about, approximately and substantially when use d in connection with numerical values generally include the indicated value plus or minus a giv en tolerance.

nothing. For example, in some cases a suitable tolerance may be ±10% of the indicated valu e, thus about 0.5 includes 0.45 and 0.55; 11, and about 1000 includes 900-1100. In other ca ses, a suitable tolerance may be plus or minus an acceptable percentage of the last significant digits of the indicated value. For example, a suitable tolerance might be ±10% of the last sign ificant digit, so approximately 10.1 includes 10.09 and 10.11, and approximately 25 includes 24.5 and 25.5. including. Such variations may result from manufacturing tolerances or other p ractical considerations (eg, tolerances associated with measurement equipment, acceptable h uman error, etc.).

[0024]

[1077] When describing the relationship between a given volume of bodily fluid and a collecte d volume of bodily fluid, it should be understood that these values include suitable tolerances such as those set forth above. For example, when stating that a collected volume of bodily flui d is substantially equal to a predetermined volume of bodily fluid, the collected volume and th e predetermined volume are nominally equal within suitable tolerances. In some cases, tolera nce can be determined by the intended use of the collected volume of bodily fluid. For exampl e, in some cases, blood culture assays are performed when the collected volume of blood is wi thin 1.0% to 5.0% of the manufacturer's (or evidence-based best practice) recommended vol ume. It can be about 99% accurate. As an example, the manufacturer's recommended volum e for the body fluid assay is 10 milliliters (mL) (ie total volume is 40 ml to 60 ml) ± 5%. Thu s, a collection volume of 10.5 mL provides results with greater than about 99% confidence, an d a collection volume of 11 mL provides results with less than about 99% confidence. In other cases suitable tolerances are 0.1%, 0.5%, 1.0%, 2.0%, 3.0%, 4.0%, 5.0%, 6.0% , 7.0%, 8. 0%, 9.0%, 10.0% or any fractional value therebetween. In still other cases, the tolerance can exceed 10.0%. Accordingly, any of the embodiments described herein may be any suitable flo w rate configured to meter the flow rate of body fluid and/or otherwise measure the volume o

f body fluid within suitable tolerances. It can include and/or be used with measurement mech anisms and/or devices. Additionally, flow metering mechanisms and/or devices can be arrange d to minimize or eliminate tolerance build-up that can result from a combination of inaccurate measurements, human error, and the like.

[0025]

[1078] FIG. 1 is a schematic illustration of a portion of a bodily fluid collection device 100, acc ording to an embodiment. In general, the bodily fluid collection device 100 (also referred to h erein as a "fluid collection device" or "collection device") allows for the withdrawal of bodily flu id from a patient, wherein a first portion or a first portion of the withdrawn bodily fluid is so th at a quantity separates from a second portion or volume and/or a third portion or volume of t he withdrawn bodily fluid used as a biological sample, such as to be tested for medical diagno stic and/or therapeutic purposes configured to be shunted. In other words, as described in mo re detail herein, the collection device 100 can transfer a first predetermined volume of bodily f luid to a pre-sample collection reservoir, second and third volumes of bodily fluid (or, in some i mplementations, 4th, 5th, etc.) to one or more sample collection reservoirs (eg, sample reser voirs) fluidly isolated from the pre-sample reservoir.

[1079

] The collection device 100 includes a flow diverter mechanism 120 , a flow controller 140 , a pre-sample reservoir 170 , a first sample reservoir 180 , and a second sample reservoir 190 t hat is different from the first sample reservoir 180 . The flow diverting mechanism 120 include s an inlet port 121 and at least two outlet ports, such as a first outlet port 125 and a second o utlet port 126, as shown in FIG. In some embodiments, flow diverter 120 can include a set of exit ports equal to the total number of pre-sample and sample reservoirs. For example, if coll ection device 100 has one pre-sample and four sample reservoirs, flow diverter 120 may inclu de five outlet ports. In some embodiments, a flow divider

Mechanism 120 can be operably coupled to an actuator (not shown in FIG. 1) that can facilitat e movement of flow diverter mechanism 120 between configurations. Inlet port 121 is configu red to be fluidly coupled to a medical device that defines a pathway X for withdrawing and/or transporting bodily fluid from a patient to collection device 100 . For example, entry port 121 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). As such, the flow diverting mechanism 120 can receive bodily fluid from the patient via a nee dle or any other lumen defining device.

[1080

] The first outlet port 125 of the flow diverter mechanism 120 may be fluidly coupled to the pr e - sample reservoir 170 . In some embodiments, pre-sample reservoir 170 is integrally forme d with first outlet port 125 and/or part of flow diverter mechanism 120 . In other embodiment s, the pre-sample reservoir 170 is attached via adhesives, resistance fits, mechanical fastener s, any number of mating recesses, threaded connections and/or any other suitable connection or combination thereof. , can be mechanically and/or fluidly coupled to the flow diverting mec

hanism 120 . Similarly, pre-sample reservoir 170 can be physically (e.g., mechanically) couple d to flow diverting mechanism 120 such that the volume defined by pre-sample reservoir 170 is the flow diverting mechanism. 120 in fluid communication with a first outlet port 125 . In st ill other embodiments, the pre-sample reservoir 170 is operably coupled to the first outlet por t 125 of the flow diverting mechanism 120 via an intervening structure (not shown in FIG. 1) such as flexible sterile tubing. can be done. More particularly, the intervening structure can de fine a lumen configured to place the pre-sample reservoir 170 in fluid communication with the first outlet port 125 .

[1081

] The pre-sample reservoir 170 is configured to receive and contain a first predetermined volu me of bodily fluid. In some embodiments, the pre-sample reservoir 170 stores a first volume of bodily fluid (which may be the same as or different from the first volume of bodily fluid), a second volume of bodily fluid that is subsequently withdrawn from the patient, and a second v olume of bodily fluid. /or configured to receive in a fluidly isolated manner from the third volu me. Pre-sample reservoir 170 is described in "Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination", which is incorporated herein by reference in its entirety. It can be any suitable reservoir for containing bodily fluids, such as the pre-sa mple reservoir described in detail in US Pat. No. 8,197,420.

[0029]

[1082] In some embodiments, the second outlet port 126 of the flow diverting mechanism 12 0 is fluidly coupled to a lumen defining device that can be coupled to the first sample reservoi r 180 and the second sample reservoir 190. is configured to Optionally, in other embodiments, the second outlet port 126 of the flow diverter 120 can be coupled to the first sample reservoi r 180, and the flow diverter 120 was coupled to the second sample reservoir 190 (Fig. (not sh own) can have a third exit port. In some embodiments, the first sample reservoir 180 can be i ntegrally formed with the second outlet port 126 and/or part of the flow diverting mechanism 120 . In other embodiments, the first sample reservoir 180 is mechanically coupled or operabl y coupled to the second outlet port 126 via intervening structures such as those described ab ove with respect to the pre-sample reservoir 170. can be combined. First sample reservoir 18 0 is configured to receive and contain a second volume of bodily fluid. For example, the secon d volume of bodily fluid can be the amount withdrawn from the patient following the withdraw al of the first pre-sample volume. In some embodiments, first sample reservoir 180 is configu red to contain a second volume of bodily fluid such that the second volume is fluidly isolated f rom the first volume of pre-sample bodily fluid.

[1083

] First sample reservoir 180 and second sample reservoir 190 may be, for example,

It can be any suitable sterile reservoir for containing bodily fluids, including a sample reservoi r as described in the incorporated '420 patent. In some embodiments, the second volume can be any suitable volume of bodily fluid and it need not be a predetermined volume. In other e

mbodiments, the transfer of bodily fluid to the first sample reservoir 180 and/or the second sa mple reservoir 190 can be metered or the like such that the second volume is a second predet ermined volume.

[1084

] The second sample reservoir 190 can be any suitable sample reservoir. In some embodiment s, the second sample reservoir 190 can be substantially similar to the first sample reservoir 1 80 described above. A second sample reservoir 190 can be fluidly coupled to the second outle t port 126 as described above. The fluidic coupling of the second outlet port 126 to the second sample reservoir 190 can be substantially similar to the fluidic coupling of the second outlet p ort 126 to the first sample reservoir 180, as detailed above. Accordingly, such portions are not described in further detail herein and should be considered substantially similar unless explicit ly described to the contrary. Additionally, additional outlet ports and sample reservoirs of flow diverter 120 (not shown in FIG. 1) may be substantially similar to second outlet port 126 and first sample reservoir 180 .

[0032]

[1085] In some embodiments, the pre-sample reservoir 170, the first sample reservoir 180 a nd the second sample reservoir 190 can be similarly coupled to (or formed with) the flow dive rting mechanism 120. FIG. In other embodiments, pre-sample reservoir 170 , first sample res ervoir 180 and second sample reservoir 190 need not be similarly coupled to flow diverting m echanism 120 . For example, in some embodiments, the pre-sample reservoir 170 can be inte grally formed with the flow diverting mechanism 120 (eg, the first outlet port 124) and the fir st sample reservoir 180 and/or the second sample reservoir 190. can be operably coupled to f low diverting mechanism 120 (eg, second outlet port 126) via an intervening structure such a s flexible sterile tubing or any combination thereof.

[0033]

[1086] In some embodiments, the collection device 100 includes an actuator (not shown in FI G. 1) and a first fluid flow path 142, a second fluid flow path 144 and optionally (not shown in FIG. 1). and a flow controller 140 that defines additional fluid flow paths. In some embodimen ts, an actuator may be included in or otherwise operably coupled to the flow diverting mechan ism 120 . As such, actuators can be configured to control fluid movement (eg, between differe nt configurations) within flow controller 140 . For example, the actuator may be movable betw een a first position corresponding to a first configuration of flow controller 140, a second positi on different from the first position corresponding to a second configuration of flow controller 1 40, and so on. In some embodiments, the actuator can be configured to move in one directio n. For example, an actuator can be moved from its first position to its second position, but ca nnot be moved from its second position to its first position. Similarly, the actuator can be mov ed from its second position to its third position, but cannot be moved from its third position ba ck to its second position. In this manner, flow controller 140 is prevented from moving to its s econd or third configuration before its first configuration, thus directing a first volume of bodil

y fluid to pre-sample reservoir 170 for medical diagnosis. and/or sample reservoirs 180 and/o r 190 designed to contain a second and/or third volume of withdrawn fluid used as a biological sample, such as for testing for therapeutic purposes. It is necessary not to be directed to

[0034]

[1087] The flow controller 140 has a first fluid flow path 142 fluidly coupling the inlet port 121 to the first outlet port 125 when in the first configuration and a second fluid flow path 142 wh en in the second configuration. 144 is configured to fluidly couple inlet port 121 to second outl et port 126 . In some embodiments, actuators such as those described above are incorporate d into the flow controller 14

0 can be configured to move in translation between the first and second configurations, and o ptionally between the third or fourth configuration. For example, in some embodiments, flow c ontroller 140 may be in a first configuration when in a distal position relative to collection devi ce 100 . In such embodiments, the actuator can be actuated to move flow controller 140 proxi mally to a proximal position relative to collection device 100, thereby placing flow controller 1 30 in the second configuration. In other embodiments, the actuator can be actuated to move t he flow controller 140 between the first and second configurations, or optionally between the t hird or fourth configurations, in a rotary motion. .

[1088

] Thus, when the flow controller 140 is in the first configuration, the second outlet port 126 (a nd optionally an additional outlet port coupled to the sample reservoir) is fluidly routed from t he inlet port 121. isolated to Similarly, first outlet port 125 is fluidly isolated from inlet port 12 1 when flow controller 140 is in the second configuration. Optionally, first outlet port 125 and second outlet port 126 are fluidly isolated from inlet port 121 when flow controller 140 is in a third configuration (not shown in FIG. 1). Thus, the flow controller 140 can direct or divert a fi rst volume of bodily fluid through the first outlet port 125 to the pre-sample fluid reservoir 17 0 when in the first configuration and in the second configuration. A second volume of bodily fl uid can then be directed or diverted to the first sample fluid reservoir 180 via the second outl et port 126 .

[0036]

[1089] In some embodiments, at least a portion of the actuator can be operably coupled to th e pre-sample fluid reservoir 170. As shown in FIG. In this manner, the actuator (or at least a portion of the actuator) causes or otherwise facilitates the creation of a vacuum within the "pr e-sample" fluid reservoir 170, thereby causing the flow diverter mechanism 120 to assume its first configuration. At some point, it can be configured to initiate flow through the bodily fluid collection device 100 and into the pre-sample fluid reservoir 170 . Actuators may be any suita ble mechanism for driving bodily fluid flow into collection device 100, such as, for example, ro tating discs, plungers, slides, dials, buttons, handles, levers, and/or any other suitable mecha nism or combination thereof. can include Examples of suitable actuators are described in more detail herein with reference to specific embodiments.

[0037]

[1090] In some embodiments, the flow diverter mechanism 120 is configured such that the fl ow of the second volume of bodily fluid is transported through the flow diverter mechanism 12 0 to the first sample fluid reservoir 180 and/or to the second sample fluid reservoir 190. can b e configured such that a first volume of bodily fluid needs to be transported to the pre-sample fluid reservoir 170 before allowing for . In this manner, the flow diverting mechanism 120 can be used by a healthcare professional to collect a first predetermined amount of bodily fluid (e. g., a pre-sample) before collecting a second amount and/or a third amount of bodily fluid (e. g., a sample). can be characterized as requiring compliance with respect to Similarly, the flow diverter mechanism 120 can be used by a medical practitioner to transfer a second volume of bodily fluid, i.e., a sample, into a first sample fluid reservoir without first diverting the first vol ume of bodily fluid, i.e., a pre-sample, into a pre-sample reservoir 170. It can be configured t o prevent collection within 180 . In this manner, a healthcare professional may (intentionally o r not) add a first volume of bodily fluid that is more likely to contain surface microbes and/or other undesirable external contaminants into the bodily fluid sample used for analysis. (either unintentionally or unintentionally). In other embodiments, the fluid collection device 100 need not include mandatory compliance features or components.

[1091

] In some embodiments, the flow diverter mechanism 120 can have a fourth configuration (no t shown in FIG. 1) that is different from the first, second, and third configurations. When in th e fourth configuration, the flow diverter mechanism 120 can simultaneously fluidly isolate the inlet port 121 from the first outlet port 125, the second outlet port 126 and, optionally, the thi rd outlet port. Therefore, the shunting

When mechanism 120 is in its fourth configuration, body fluid is prevented from flowing from i nlet port 121 to pre-sample fluid reservoir 170, first sample fluid reservoir 180 and second sa mple fluid reservoir 190. FIG. In use, for example, the flow diverter mechanism 120 is placed (eg, manually or automatically) in a first configuration such that bodily fluid can flow from the inlet port 121 to the pre-sample fluid reservoir 170 . actuated and then moved to a second co nfiguration such that bodily fluids can flow from inlet port 121 to first sample fluid reservoir 1 80 and, optionally, bodily fluids can flow from inlet port 121 to second sample fluid reservoir 1 90 It can be moved to a third configuration so that it can be used, and then moved to a fourth configuration so as to stop the flow of bodily fluids into and/or through the flow diverting mec hanism 120 . In this manner, the device is effectively "cleaned" such that any residual bodily fl uids within the device 100 are prevented from becoming contaminated and/or otherwise expo sing medical personnel and/or patients to potentially hazardous fluids. Locked" and self-contai ned in the fourth form. This optional safety feature can prevent possible exposure to bodily flu id samples that may be infected with pathogens such as HIV, Hepatitis C, and the like.

[0039]

[1092] In some embodiments, one or more portions of the collection device 100 are 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 sa mple reservoir 280 and second sample reservoir 290 . Housing 201 includes an inlet port 221, a first outlet port 230, a second outlet port 231, a third outlet port 232, and an internal flow p ath 235 that can define a fluid flow path for collecting bodily fluids from a patient. stipulated. Inlet port 221 can be selectively placed in fluid communication with internal flow path 235 . M ore specifically, inlet port 221 defines an inlet lumen 202 that can be placed in fluid communic ation with internal flow path 235 . Inlet port 221 is thus part of housing 201 such that internal flow path 235 can be placed in fluid communication with a space substantially outside housing 201 via inlet lumen 202 . extends from Inlet port 221 can be fluidly coupled to a medical devi ce (not shown) that defines a fluid flow path for drawing bodily fluid from a patient and/or tra nsporting it to collection device 200 . For example, entry port 221 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing) directly or indirectly via ada pter 204 . Similarly, inlet lumen 202 defined by inlet port 221 is arranged to be in fluid comm unication with the lumen defined by the lumen-defining device when the lumen-defining devic e is coupled to inlet port 221 . . More specifically, when the lumen defining device is positione d within a portion of a patient's body (e.g., within a patient's vein or spinal space), the interior passageway 235 of the housing 201 is aligned with that portion of the patient's body. It can b e arranged in fluid communication with the portion.

[0043]

[1096] The internal passageway 235 defined by the housing 201 is a central lumen that exten ds along the length of the housing 201 and is used for venipuncture (fluid access) as describe d herein. (other methods employed to enable the patient to be placed in fluid communication with the patient's bodily fluids). Internal channels 235 form fluid flow paths that transport bod ily fluids between inlet port 221 and first, second, and third outlet ports 230 , 231 , and 232 . More specifically, when the internal flow path 235 is placed in fluid communication with a pati ent (eg, via a medical device coupled to the inlet port 221), the first outlet port 230, the seco nd outlet port 231 are and third outlet port 232 are selectively placed in fluid communication with internal flow path 235 to allow bodily fluids to flow into at least one of pre-sample reserv oir 270 , first sample reservoir 280 or second sample reservoir 290 . can be allowed to flow. I n some embodiments, bodily fluid is prevented from flowing to second outlet port 231 and thir d outlet port 232 before a predetermined volume of bodily fluid has been collected in pre-sam ple reservoir 270 . In some embodiments, the second outlet port 231 and the third outlet port 232 can be placed in fluid communication with the internal flow path 235 at the same time. In some embodiments, the second outlet port 231 and the third outlet port 232 can be arranged in fluid communication with the internal flow path 235 sequentially.

[0044]

[1097] Movable members 250, 250' are actuated (eg, moved) by a user from first and second positions relative to housing 201 to direct fluid flow to first sample reservoir 280 and second s ample reservoir. 290. Movable members 250 and 250 ′ are substantially identical and therefor

e will be described with respect to a single movable member 250 . As shown in FIG. 5, movea ble member 250 includes a boss 251 defining an interior cavity 252 , an inlet port 253 , a first outlet port 254 , and lumen 25 fluidly coupled to interior cavity 252 .

and a piercing member 255 defining 6. Inlet port 253 and outlet port 254 extend through the wall of boss 251 that defines interior chamber 252 of movable member 250 . Movable membe r 250 is positioned within support 257 (see FIG. 4) of housing 201 such that boss 251 is dispo sed within bore 258 (see FIG. 4) and at least a portion of movable member 250 is disposed wi thin annular chamber 260 (see FIG. 4). configured to be attached to the Optionally, a biasing member 259 (eg, a spring) can be disposed within the annular chamber 260 to return the mo vable member 250 to its first position after actuation by the user. In some embodiments, mov able member 250, annular chamber 260, bore 258 or boss 251 are configured to retain mova ble member 250 in a second position (e.g., depressed position) after being actuated by a user. A mechanical locking mechanism can be included.

[0045]

[1098] As described herein, in the first configuration, the movable member 250 is arranged to be spaced apart from the internal channel 235. As shown in FIG. In such configurations, a flui d flow path cannot be established between a portion of the patient's body (eg, a vein, spinal c avity, etc.) and sample reservoirs 280 and/or 290 . In other words, when movable member 25 0 is in its first configuration, first sample reservoir 280 and second sample reservoir 290 are fl uidly isolated from internal flow path 235 defined by housing 201 . Movable member 250 can be actuated by a user to move movable member 250 from the first configuration to the secon d configuration and into alignment with internal channel 235 . The force applied by the user m ay be sufficient to deform (eg, compress) biasing member 259, thereby inserting piercing me mber 255 into sample reservoirs 280 and/or 290. can be done. In the second configuration, in let port 253 and outlet port 254 are substantially aligned with internal flow path 235 to place i nternal cavity 252 in fluid communication with internal flow path 235 . Thus, when movable m ember 250 is in the second configuration, a fluid flow path is established between internal cha nnel 235 , internal cavity 252 , lumen 256 of piercing member 255 and sample reservoir 280 . In other words, in such a configuration, bodily fluids flow from the patient (eg, veins, spinal s paces, etc.) through the flow diverting mechanism 220 into the first sample reservoir 280 an d/or the second sample reservoir 280, as described in further detail herein. It can flow into th e sample reservoir 290 .

[0046]

[1099] The pre-sample reservoir 270 can be any suitable reservoir for containing bodily fluids, such as, for example, a single-use disposable collection tube, a vacuum-assisted collection tub e, and the like. Pre-sample reservoir 270 is configured to be fluidly coupled in any suitable ma nner (either directly or via an intervening structure such as sterile flexible tubing) to first outl et port 230 of collection device 200. . For example, in some embodiments, a portion of pre-sa mple reservoir 270 can form a friction fit within a portion of first outlet port 230 . In other em

bodiments, pre-sample reservoir 270 can be coupled to first outlet port 230 via threaded coup ling, adhesives, snap fits, mechanical fasteners and/or any other suitable coupling method. . I n some embodiments, pre-sample reservoir 270 can be integrally formed with housing 201 . P re-sample reservoir 270 is subjected to a negative pressure condition (vacuum condition) that can enable bodily fluid to be drawn into pre-sample reservoir 270 via vacuum suction from inl et port 221 through outlet port 230 (pre-sample reservoir 270) can be configured to be maint ained internally. Pre-sample reservoir 270 is configured to contain a first volume of bodily flui d, where the first volume of bodily fluid can be a predetermined volume or an unquantified vol ume, thereby is fluidly isolated from a second and/or a third volume of bodily fluid subsequent ly withdrawn from the patient.

[

1100] Sample reservoirs 280 and/or 290 may be single-use disposable collection tubes, vacuu m driven collection tubes, sample reservoirs such as those described in the '420 patent incorp orated herein by reference above, or the like. It can be any suitable reservoir for containing b odily fluids, including: In some embodiments, sample reservoirs 280 and/or 290 include, for e xample

It can be substantially similar or identical to known sample containers, such as the Vacutainer ®. Sample reservoirs 280 and 290 include sample vessels 282 and 292, respectively, and vac uum seals 284 and 294, respectively. A vacuum seal 284 or 294 can allow bodily fluid to be dr awn into the sample container 282 or 292, respectively, from the internal channel 235 via vac uum suction into the sample container 282 or 292, respectively. state). Sample containers 28 0 and/or 290 are fluidically connected in any suitable manner (directly or via an intervening st ructure such as sterile flexible tubing) to second and third outlet ports 231 and 232, respectiv ely, of collection device 200. It can be configured to be coupled. Sample reservoirs 280 and/or 290 can be moved relative to exit ports 231 and/or 232 so as to be placed in fluid communica tion with exit ports 231 and/or 232 . Sample reservoirs 280 and 290 can be configured to con tain a second volume or a third volume of bodily fluid. The second or third amount of bodily fl uid can be a predetermined amount or an unquantified amount, whereby the second or third amount of bodily fluid is the first amount of bodily fluid withdrawn from the patient. fluidly isol ated from In some configurations, sample reservoirs 280 and/or 290 may be coupled to collec tion device 200 by being integrally formed with housing 201, similar to pre-sample reservoir 2 70, and are therefore not discussed in detail herein. not described in In some cases, the samp le reservoirs 280 and/or 290 can be transparent so that the user has visual feedback to confir m the flow of bodily fluid into the sample reservoirs 280 and/or 290. can be done.

[0048]

[1101] In some embodiments, sample reservoirs 280 and 290 and flow diverter mechanism 2 20 (and/or portions of collection device 200 other than sample reservoirs 280 and 290) are in dependently formed (e.g., integrally formed) and bonded together during the manufacturing p rocess, for example. In some cases, sample reservoirs 280 and 290 can be coupled to flow 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, movin g the dial to the third position substantially seals the sample within the collection device 200 f rom the external environment. can be done.

[0051]

[1104] In operation, the collection device 200 can be used to collect bodily fluids (eg, blood) f rom a patient with reduced contamination from microorganisms present on the skin and/or ot her undesirable external contaminants. can. For example, inlet port 221 of collection device 2 00 is fluidly coupled via adapter 204 to a needle or other lumen defining device (eg, flexible st erile tubing). Following venipuncture (or other fluid access method), second member 245 is ro tated until it reaches the first position, as shown in FIGS. Alternatively, the second member 2 45 can be preset to the first position and the collection device 200 is otherwise sealed to main tain the vacuum within the pre-sample reservoir 270 and the sterility of the collection device 200. can do. For example, inlet port 221 and/or adapter 204 can include a valve that opens w hen collection device 200 is coupled to a needle or other lumen defining device.

[0052]

[1105] As described above, when the second member 245 is in the first position, the flow con troller 240 is disposed in the first configuration and the first passageway 242 of the first mem ber 241 connects the inlet port 221 to the internal passageway. Fluid communication is establi shed between inlet port 221 and first outlet port 230 while being fluidly isolated from 235 . Fu rther, the first sample reservoir 280 and the second sample reservoir 290 are fluidly isolated f rom the inlet port 221 in the first configuration and are located in a portion of the patient's bo dy (eg, a vein), as indicated by arrows AA in FIG. and a pre-sample reservoir 270 are defined. As described above, the fluid reservoirs used in collection device 200, such as pre-sample res ervoir 270 and sample reservoirs 280 and 290, are exposed to a negative pressure (i.e., the p ressure of the body part from which collection device 200 is used to draw bodily fluids). press ure less than the fluid pressure), thereby establishing fluid communication between a portion of the patient's body (e.g., a vein) and pre-sample reservoir 270, the negative pressure within pre-sample reservoir 270 causes , the pressure differential between the pre-sample reservoir 270 and that portion of the patient's body causes fluid to be drawn into the pre-sample reserv oir 270 . In this first configuration, flow controller 240 also fluidly isolates pre-sample reservoi r 270 from internal flow path 235 . Thus, a first volume (predetermined or unquantified) of bo dily fluid can be received in pre-sample reservoir 270 (for example) immediately after venipun cture and isolated from subsequent samples. Thus, with the collection device 200, a first volu me of bodily fluid most likely to contain surface microorganisms and/or other undesirable exte rnal contaminants may be diagnosed or affected by the contaminants. Subsequent volumes of bodily fluid samples collected and used for other tests can be uncontaminated.

[0053]

[1106] Following collection of the body fluid pre-sample volume in the pre-sample reservoir 2 70,

, the second member 245 can be rotated until it reaches a second position as shown in FIGS. When the second member 245 is in the second position, the flow controller 240 is placed in th e second configuration and the second flow path 244 of the first member 241 enters the first outlet port 230 (i.e., the pre-sample reservoir 270). Fluid communication is established betwe en inlet port 221 and internal channel 235 while being fluidly isolated from port 221 . In other words, in the second configuration, the flow controller 240 provides flow between a portion of the patient's body (eg, a vein) and the internal flow path 235 via the second flow path 244, as indicated by arrow BB in FIG. establish a fluid flow path in the

[0054]

[1107] With flow controller 240 in the second configuration, movable member 250 and/or 25 0' is actuated (i.e., depressed) by a user from a first position to a second position to move the patient's body. Fluid communication can be established between a portion (eg, a vein) and the first sample reservoir 280 and/or the second sample reservoir 290 . More specifically, movable member 250 moves from its first position to its second configuration such that piercing memb er 255 pierces vacuum seal 284 of first sample reservoir 280, as indicated by arrow CC in FI G. The piercing member 255 passes through the exit port 231 so that it can be opened and pl aced inside the sample container 282 . When in the second position, inlet port 253 and outlet port 254 of movable member 250 are substantially aligned with and in fluid communication wi th internal channel 235 such that bodily fluids flow from internal channel 235 to the movable member. It can flow into the internal cavity 252 of 250 and out of the lumen 256 of the pierci ng member 255 into the first sample reservoir 280 . A pressure differential between sample r eservoir 280 (eg, vacuum or negative pressure) and internal channel 235 draws bodily fluid in to sample reservoir 280 . In other words, in the second configuration, movable member 250 e stablishes a fluid flow path between internal flow path 235 and first sample reservoir 280, as i ndicated by arrow DD in FIG. Once a desired amount of bodily fluid (eg, a second amount) ha s been collected in first sample reservoir 280, the user releases movable member 250 such th at biasing member 259 returns the button to its first position. can be enabled to move to Whe n movable member 250 returns to its first position, piercing member 255 is removed from firs t sample reservoir 280 and seal 284 (e.g., a self sealing septum) opens first sample reservoir 280 to internal flow. It is fluidly isolated from channel 235 .

[0055]

[1108] Similarly, while the flow controller 240 is in the second configuration, the movable me mber 250' is actuated (depressed) by a user from its first position to its second position, as in dicated by arrow EE in FIG.)be able to. Thus, in a manner similar to the movable member 25 0 and the first sample reservoir 280 described above, a portion of the patient's body (eg, a ve in) and the second sample reservoir 290 (via the exit port 232). Fluid communication is establ ished. In other words, in the second configuration, movable member 250' establishes a fluid fl ow path between internal flow path 235 and second sample reservoir 290, as indicated by arr ow FF in FIG. Once a desired amount of bodily fluid (eg, a third amount) has been collected in

second sample reservoir 290, the user releases movable member 250' such that biasing mem ber 259' causes button 250' to move to its third position. It can be allowed to move back to o ne position. Although shown and described as being a sequential process, the order and/or se quencing of filling is not necessary (i.e., sample reservoir 280 may not necessarily fill before s ample reservoir 290, etc.). . In other words, when the flow controller 240 is moved to the sec ond configuration, the first sample reservoir 280 and the second sample reservoir 290 (and a ny additional sample reservoirs) are activated in any order at the same time (eg, simultaneou sly) and/or Or they can be filled in overlapping time intervals. For example, a user can initiate filling of the first sample reservoir 280, and then after the first sample reservoir 280 is partiall y filled, the user presses the movable member 250' to Filling of the second sample reservoir 2 90 can begin while the first sample reservoir 280 finishes filling. Additionally, adjustment of th e volume of bodily fluid collected in sample reservoirs 280 and/or 290 can be achieved by mo ving member 2

It can be enabled by repeatedly actuating (inserting) 50 and/or 250'. As noted above, the sec ond member 245 can have a third position corresponding to the third configuration of the flow controller 240, thereby substantially reducing fluid flow between the patient and the collection device 200 as a whole. to substantially seal the sample within the collection device 200 from t he external environment.

[1109

] Although not shown in FIGS. 2-13, the collection device 200 meters the volume of bodily flui d transferred to the pre-sample reservoir 270, the first sample reservoir 280 and/or the secon d sample reservoir 290. A flow metering device or the like can be included that can be configu red to. For example, in some embodiments, first member 241 of flow controller 240 can includ e a flow metering device in fluid communication with first flow path 242 and second flow path 244 . In other embodiments, a flow metering device can be positioned within the internal cavi ty 252 of the moveable member 250 and/or 250'. Accordingly, the volume of the bodily fluid s ample transferred to and placed in the first sample reservoir 280 and the second sample reser voir 290 may be such that the volume of the bodily fluid sample placed in each sample reserv oir 280 and 290 is e.g. It can be metered and/or controlled to have a predetermined volume, such as 30 mL.

[0057]

[1110] Although the collection device 200 is shown and described as including a first sample r eservoir 280 and a second sample reservoir 290, other embodiments may include any number of pre-sample reservoirs and/or sample reservoirs. can contain. For example, Figures 14 and 15 show a collection device 300 according to embodiments. As shown, some aspects of the co llection device 300 may be substantially similar to corresponding aspects of the collection devi ce 200 described above with reference to FIGS. 2-13. Accordingly, similar aspects are not des cribed in further detail herein.

[0058]

[1111] As shown in Figs. A fourth sample reservoir 390' is included. Pre-sample reservoir 370 may be substantially similar to pre-sample reservoir 270 described in detail above. In some e mbodiments, sample reservoirs 380, 380', 390 and 390' can be substantially similar to sample reservoirs 280 and 290 described in detail above. In some embodiments, sample reservoirs 3 80, 380', 390 and 390' can have substantially the same shape and size, eg, contain substanti ally the same medium. In other embodiments, sample reservoirs 380, 380', 390 and 390' can have substantially the same shape and size and contain one of aerobic or anaerobe media. ca n be done. For example, in some embodiments, the first sample reservoir 380 and the third s ample reservoir 390 can contain an aerobic culture medium, and the second sample reservoir 380' and the fourth sample reservoir 390' can contain an anaerobe culture medium. A culture medium can be included. In other embodiments, sample reservoirs 380, 380', 390 and 390' m ay each contain aerobic or anaerobe media in any arrangement or combination.

[0059]

[1112] The flow diverter mechanism 320 includes a housing 301 and a set of moveable memb ers 350, 350', 350'' and 350'''. Movable members 350, 350', 350'' and 350''' are substantially similar to movable member 250 described above with reference to FIG. 5, for example. Accor dingly, movable members 350, 350', 350'' and 350''' are positioned in a first position relative t o housing 301 such that they are placed in fluid communication with sample reservoirs 380, 3 80', 390 and 390', respectively. and a second position. The housing 301 is in fluid communicat ion with an inlet port 321 , a first outlet port 330 configured to be arranged in fluid communic ation with a pre-sample reservoir 370 , and a first sample reservoir 380 .

a second outlet port 331 configured to be arranged to be in fluid communication with a secon d sample reservoir 380' and a third outlet port 332 configured to be arranged in fluid commun ication with a third sample reservoir 390'; and a fifth outlet port 334 configured to be placed i n fluid communication with a fourth sample reservoir 390'. Further, housing 301 can be selecti vely placed in fluid communication with inlet port 321 and outlet ports 331 , 332 , 333 and 33 4 in a manner similar to that described above with respect to interior passageway 235 of hous ing 201 . An internal channel 335 is defined.

[1113

] The flow controller 340 is substantially similar to the flow controller 240 described above, e g, with reference to FIGS. 6-13. Accordingly, the flow controller 340 is rotated between the fir st and second configurations to provide a portion of the fluid flow path between the patient an d the pre-sample reservoir 370 or the sample reservoirs 380, 380', 390 and 390'. can be sele ctively defined. In this manner, a user can operate collection device 300 in a manner similar t o that described above with respect to collection device 200 in FIGS. 8-13. Thus, a first volum e of bodily fluid can be transferred to and placed in pre-sample reservoir 370, and subsequent volumes of bodily fluid can be transferred to and placed in sample reservoirs 380, 380', 390 a nd 390'. can be placed.

[0061]

[1114] FIGS. 16-22 illustrate a collection device 400 according to an embodiment. Collection device 400 includes flow diverter mechanism 420, flow controller 440 and sample reservoirs 480, 480', 490 and 490'. As further described herein, the collection device 400 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorganisms and/or microorganisms present on the skin. or a body fluid stream that is substantially free of extracorporeal microorganisms, such as other undesirable external contaminants. Collection device 400 may be of any suitable shape, size or configuration. For example, although sample reservoirs 480, 480', 490 and 490' are shown oriented perpendicular to housing 401 in FIGS. It is possible to have the sample reservoirs 480, 480', 490 and 490' oriented in a plane, arranged conically with respect to the housing 401, or the like.

[0062]

[1115] The sample reservoirs 480, 480', 490 and 490' are substantially similar or identical in form and function to the sample reservoirs 280 and/or 290 of the collection device 200; No details are given. As described above, the sample reservoirs 480, 480', 490 and 490' are negative pressure conditions that can allow fluid to be drawn from the patient into the sample reservoirs 480, 480', 490 and 490' via suction. (vacuum state) is maintained. In some embodiments, sample reservoirs 480 and 480′ can be aerobe culture bottles, sample reservoirs 490 and 490′ can be anaerobe culture bottles, and collection device 400 can be used to Thus, multiple aerobic and multiple anaerobic blood culture samples can be collected from a single venipuncture. As described in further detail herein, sample reservoirs 480, 480', 490 and 490' are each arranged in fluid communication with at least a portion of flow diverting mechanism 420 to receive a volume of bodily fluid sample. can do. The volume of the bodily fluid sample can be either predetermined or unquantified. Further, once a desired volume of bodily fluid has been placed within sample reservoirs 480, 480', 490, 490', each sample reservoir 480, 480', 490 and 490' will be displaced as described in further detail herein. can be fluidly isolated from at least a portion of flow diverting mechanism 420 .

[1116

] Flow diverting mechanism 420 includes housing 401 and distribution member 429 . Housing 401 of flow diverter mechanism 420 is physically and fluidly coupled to distribution member 429 to provide patient-to-body flow.

It provides and/or defines a set of fluid flow paths for collecting liquid. Housing 401 defines a recess 466 and a set of exit openings 403 . Recess 466 is configured to receive seal member 441 included in flow controller 440, as described in further detail herein. The set of outlet openings 403 is configured to define a different fluid flow path, each of which is in fluid communication with a different portion of the distribution member 429, a first outlet opening 403a, a second outlet opening 403b. , a third exit opening 403c, a fourth exit opening 403d and a fifth exit opening 403e. More specifically, distribution member 429 includes at least a portion of pre-sample reservoir 470 in fluid communication with first outlet opening 403a and a first channel 435a in fluid communication with second outlet opening 403b. , a second channel 435b in flui

d communication with the third outlet opening 403, a third channel 435c in fluid communicati on with the fourth outlet opening 403d, and a third channel 435c in fluid communication with the fifth outlet opening 403e. defines and/or forms four channels 435;

[0064]

[1117] As shown in FIGS. Pre-sample reservoir 470 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. A first outlet opening 403a of housing 401 can be substantially aligned with an open portion of pre-sample reservoir 470 to allow pre-sa mple reservoir 470 to receive the flow of bodily fluid from the patient. For example, pre-sampl e reservoir 470 can receive and contain a first amount or first volume of bodily fluid, where th e first amount of bodily fluid can be a predetermined amount or an unquantified amount. Addi tionally, the arrangement of the flow diverter mechanism 420 may be such that the pre-sampl e reservoir 470 may be configured to allow fluid from the flow paths 435a, 435b, 435c and 43 5d and/or subsequent volumes of bodily fluid withdrawn from the patient, as described in furt her detail herein. can be maintained in a systematically isolated manner. Although pre-sample reservoirs 270 and 370 are described above as maintaining a negative pressure, pre-sample r eservoir 470 does not maintain a negative pressure (vacuum) and therefore uses other mecha nisms such as gravity for example. can be used to draw bodily fluid into the pre-sample reser voir 470 .

[0065]

[1118] Channels 435a-435d extend radially from the center of distribution member 429 such that each channel 435a, 435b, 435c and 435d is fluidly isolated from pre-sample reservoir 47 0 and the other channels. are placed in In this manner, channels 435a, 435b, 435c and 435d are fluid flow channels between first and second ends substantially aligned with outlet openin gs 403b, 403c, 403d and 403e, respectively. can be oriented and/or otherwise defined. As sho wn in FIGS. 17 and 18, the distribution member 429 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 se cond end of the second flow path 435b. defining a second outlet port 432, a third outlet port 4 33 positioned at the second end of the third flow path 435c, and a fourth outlet port 434 posit ioned at the second end of the fourth flow path 435d; are doing. Further, the distribution me mber 429 includes a first piercing member 455a, a second piercing member 455b, a third pier cing member 455c and a fourth piercing member 455d, which are the first outlet port 431, th e second outlet port 432, the third It is physically and fluidly coupled to outlet port 433 and fo urth outlet port 434, respectively. Thus, as described in further detail herein, piercing member s 455a-355d 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 Figure s 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 i n 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 positio n, a third position, a fourth position, and a fifth position. When the dial 445 is in the first posit ion, the flow controller 440 is arranged in a first configuration, aligning the inlet port 421 subs tantially with the first opening 444 a of the seal member 441 and the first outlet opening 403 a of the housing 401 . can be combined. Thus, the first opening 444a of the seal member 441 fluidly isolates the inlet port 421 from the outlet openings 403b, 403c, 403d and 403e, thereb y fluidly isolating the inlet port 421 from the flow paths 435a-335d. Fluid communication is es tablished between the inlet port 421 and the first outlet opening 403a while isolating to the fir st outlet port 403a. When the first outlet port 403a is aligned with the open portion of the pre -sample reservoir 470, the first opening 444a and the first outlet port 403a are aligned. Mouth opening 403 a establishes fluid communication between inlet port 421 and pre-sample reservoir 470 . When the dial 445 is rotated (or driven) to the second position, the flow contro ller 440 is placed in the second configuration and the second outlet opening 444b connects th e inlet port 421 to the outlet openings 403a, 403c, 403d and 403e. Fluid communication is est ablished between inlet port 421 and second outlet opening 403b while being fluidly isolated fr om. When the second outlet opening 403b is aligned with the first end of the first flow path 4 35a, the second opening 444b and the second outlet opening 403b are between the inlet port 421 and the first flow path 435a. establish fluid communication with the

[0070]

[1123] The collection device 400 operates similarly when the dial 445 is rotated to the third, f ourth and fifth positions. Thus, when inlet lumen 402 is placed in fluid communication with a p atient (eg, via a medical device coupled to inlet port 421), first outlet port 430, second outlet port 431, third outlet Port 432, fourth outlet port 433, and fifth outlet port 434 are selectively placed in fluid communication with inlet lumen 402 so that all body fluids are present in at lea st one of pre-sample reservoirs 470 or sample. It can be enabled to flow into one or more of r eservoirs 480, 480'490 and 490'. In some embodiments, additional seal outlet openings and/o r additional dials 445 corresponding to the configuration of the flow controller 440 are provide d to further direct/isolate fluid flow between the patient and the collection device 400. Can inc lude location. For example, dial 445 can have a sixth position corresponding to a sixth configu ration of flow controller 440 that substantially prevents fluid flow between the patient and coll ection device 400 as a whole. In other words, in some embodiments, after all bodily fluid sam ples have been removed from the patient, dial 445 may be moved to the sixth position to sub stantially seal the sample within collection device 400 from the external environment. can.

[0071]

[1124] In some embodiments, until after a predetermined volume of bodily fluid has been coll ected in the pre-sample reservoir 470, the bodily fluid does not flow to the outlet ports associ ated with the sample reservoir (eg, outlet ports 431-434). prevented. In some embodiments,

the exit ports associated with the sample reservoirs (eg, exit ports 431-434) can be placed in fluid communication with the entrance lumen 402 only sequentially (eg, exit ports 431-434). 431 must be in fluid communication with the inlet lumen 402 before the outlet port 432, etc.). In some embodiments, outlet ports associated with subsequent sample reservoirs (eg, outlet ports 432-434) are placed in fluid communication with inlet lumen 402 only after a defined vol ume of bodily fluid has been collected. can be placed. In some embodiments, the outlet ports associated with the sample reservoirs (eg, outlet ports 431-434) can be arranged in fluid com munication with the inlet lumen 402 in any random manner without any order preference. (e g, outlet port 434 can be in fluid communication with inlet lumen 402 before outlet port 431, outlet port 432 can be in fluid communication with inlet lumen 402 before outlet port 433, et c.)).

[0072]

[1125] In some embodiments, the housing 401 can selectively restrict movement of the dial 4 45 from its first position to its second, third, fourth and fifth positions. . In some embodiment s, housing 401 can be configured to prevent movement of dial 445 moved to the fifth positio n. In other words, housing 401 may include a locking mechanism that prevents dial 445 from moving back from the fifth position to the first position. Dial 445 and/or housing 401 may also include mechanical detents and/or other detents that provide visual or tactile feedback to ens ure correct positioning of dial 445 relative to exit openings 403a-403e of housing 401. It is als o possible to include an indicator.

[0073]

[1126] In operation, the collection device 400 can be used to collect bodily fluids (eg, blood, p lasma, urine, etc.) from a patient with reduced contamination. For example, entry port 421 of collection device 400 can be fluidly coupled to a needle or other lumen defining device (eg, fle xible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), dial 445 is actuated (or turned) until it reaches the first position, as shown in FIGS. Alternatively, dial 445 can be preset to the first position and collection device 400 can be otherwise sealed t o maintain sterility of collection device 400 . For example, inlet port 421 can include a valve t hat opens when collection device 400 is coupled to a needle or other lumen defining device.

[0074]

[1127] As described above, when the dial 445 is in the first position, the flow controller 440 is disposed in the first configuration, and the first opening 444a of the seal member 441 connect s the inlet port 421 to the four flow paths 435a through 435a. Fluid communication is establis hed between inlet port 421 (contained within housing 401) and first outlet port 430 while bein g fluidly isolated from 335d. Further, sample reservoirs 480, 480', 490 and 490' are fluidly isol ated from inlet port 421 in the first configuration and are part of the patient's body (e.g., A flu id flow path is defined between the vein) and the pre-sample reservoir 470 . In this first confi guration, bodily fluid passes from that portion of the patient's body through the inlet lumen 4 02 of the inlet port 421, the first opening 444a of the seal member 441, the first outlet port 4

30, and into the pre-sample reservoir 470 (for example, by gravity, vacuum, etc.). In the firs t form, flow controller 440 also fluidly isolates pre-sample reservoir 470 from channels 435a-3 35d. Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be receive d in pre-sample reservoir 470 immediately after venipuncture and isolated from subsequent s amples. Thus, with the collection device 400, a first volume of bodily fluid most likely to conta in surface microorganisms and/or other undesirable external contaminants may be diagnosed or affected by the contaminants. Subsequent volumes of bodily fluid samples collected and us ed for other tests can be uncontaminated.

[0075]

[1128] Following the collection of the bodily fluid pre-sample into the pre-sample reservoir 47 0, the dial 445 can be actuated (rotated) until it reaches the second position, as shown in FIG S. When dial 445 is in the second position, flow controller 440 is disposed in the second config uration, and second opening 444b of seal member 441 fluidly isolates pre-sample reservoir 47 0 from inlet port 421 while allowing inlet port 421 to flow. Establish fluid communication betw een 421 and channel 435a. In other words, in the second configuration, flow controller 440 es tablishes a fluid flow path between a portion of the patient's body (eg, a vein) and flow path 4 35a, as indicated by arrow HH in FIG. With the flow controller 440 in the second configuratio n, 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 reservo ir 480 by piercing the vacuum seal of the sample reservoir 480 by moving the sample reservoi r 480 to the second configuration. In this second configuration, a portion of the patient's body (eg, a vein) is exposed to a vacuum suction force from the sample reservoir 480 due to the ne gative pressure (vacuum) within the sample reservoir 480 . A pressure differential between th e sample reservoir 480 (eg, vacuum or negative pressure) and that portion of the patient's bo dy draws fluid into the sample reservoir 480 . Bodily fluid passes from that portion of the pati ent's body through the inlet lumen 402 of the inlet port 421, the second opening 444b of the seal member 441, the second outlet opening 403b of the housing 401, and into the first flow path 435a. flow in. Vacuum suction draws the flow of bodily fluid through first channel 435a a nd into sample reservoir 480 via second outlet port 431 and piercing member 455a.

. In other words, in the second configuration, flow controller 440 establishes a fluid flow path between inlet port 421 and sample reservoir 480 . Once a desired amount of bodily fluid (eg, a second amount) has been collected in sample reservoir 480, the user actuates (rotates) flow controller 440 to a third position and/or rotates sample reservoir 480 to its The first sample re servoir 480 can be isolated from the channel 435a by moving it back to the first configuration. When sample reservoir 480 returns to the first configuration, piercing member 455a is remov ed from sample reservoir 480 and a seal (eg, self-sealing membrane) in sample reservoir 480

isolates first sample reservoir 480 from flow path 435a. Filling of the other sample reservoirs i s done similarly with the flow controller 440 positioned in the third, fourth and fifth configurati ons, respectively.

[0077]

[1130] It should be noted that the order and/or sequencing of filling is not necessary (ie, sam ple reservoir 480 does not necessarily need to be filled before sample reservoir 490, etc.). In other words, first sample reservoir 480 and second sample reservoir 490 (and any additional sample reservoirs) can be filled in any order. For example, the user can start filling the first sa mple reservoir 480, and then after the first sample reservoir 480 is partially filled, the user ca n fill the second sample reservoir 490. . Further, adjustment of the volume of bodily fluid colle cted in sample reservoirs 480 and/or 490 can be enabled by repeated filling of sample reservo irs 480 and/or 490 . However, in other embodiments, the order of filling is such that the secon d sample reservoir cannot be accessed until it is verified that a specified amount of bodily flui d has been placed in the first reservoir. It can be operated mechanically. As described above, t he dial 445 can substantially prevent fluid flow between the patient and the collection device 400 as a whole, substantially sealing the sample within the collection device 400 from the ext ernal environment. A sixth position for a sixth configuration of the flow controller 440 can be provided.

[0078]

[1131] The collection device 400 includes a set of four sample reservoirs (eg, a first sample re servoir 480, a second sample reservoir 480', a third reservoir 490 and a fourth reservoir 490') and/or to which other Although shown and described above as being coupled in a manner, in o ther embodiments the collection device may include and/or be coupled to any suitable numbe r of sample reservoirs. For example, Figures 23-25 show a collection device 500 according to an embodiment. As shown, some aspects of the collection device 500 can be substantially sim ilar to corresponding aspects of the collection device 500 described above with reference to FI GS. 16-22. Accordingly, similar aspects are not described in further detail herein.

[1132

] The collection device 500 includes a flow diverter mechanism 520 , a flow controller 540 , a f irst sample reservoir 580 and a second sample reservoir 590 . Sample reservoirs 580 and 590 can be substantially similar to the sample reservoirs described in detail above. In some embo diments, sample reservoirs 580 and 590 can have substantially the same shape and size and contain substantially the same medium. In other embodiments, sample reservoirs 580 and 59 0 can have substantially the same shape and size and can contain one of an aerobe medium o r an anaerobe medium. In still other embodiments, first sample reservoir 580 can have a first size that is substantially larger than the size of second sample reservoir 590 .

[0080]

[1133] As shown in FIGS. Housing 501 of flow diverter mechanism 520 is physically and fluidl y coupled to distribution member 529 to provide a set of fluid flow paths for collecting bodily f

luids from a patient and/or

stipulates. As described above with respect to housing 401, housing 501 can define a recess a nd first, second, and third outlet openings 503a, 503b, and 503c. The recess is configured to r eceive a seal member 541 included in flow controller 540, as described in detail above. First o utlet opening 503a, second outlet opening 503b and third outlet opening 503c correspond to f irst outlet opening 403a, second outlet opening 403b and third outlet opening 403c defined by housing 401, respectively. They can be substantially similar in form and function. Similarly, di stribution member 529 includes pre-sample reservoir 470 , first flow channel 435 a and secon d flow channel 435 a that are substantially similar to pre-sample reservoir 470 , first flow cha nnel 435 a and second flow channel 435 b included in flow diverter member 429 . Two flow pa ths 435b are defined. Thus, pre-sample reservoir 570 is in fluid communication with first outle t opening 503a, first channel 535a is in fluid communication with second outlet opening 503b, and as described above with respect to flow diverter mechanism 420; The second flow path 5 35b is in fluid communication with the third outlet opening 503c. As shown in FIG. 25, distribu tion member 529 is in fluid communication with first outlet port 531, which is in fluid commun ication with first channel 535a and first piercing member 555a, and second channel 535b, wit h second piercing member 555b. A second outlet port 532 is defined. As described above, pier cing members 555a and 555b can be used to pierce the vacuum seals of sample reservoirs 58 0 and 590, thereby initiating bodily fluid flow, as described in further detail herein. can do.

[0081]

[1134] The flow controller 540 includes a dial 545 and a seal member 541 . The seal member 541 is positioned within the recess of the housing 501 as described above. Thus, when flow co ntroller 540 is coupled to housing 501, seal member 541 forms a substantially fluid-tight seal with the surface of dial 545 and the surface of housing 501 that defines the recess. As shown in FIGS. 24 and 25, seal member 541 is substantially configured with first outlet opening 503 a, second outlet opening 503b and third outlet opening 503c, respectively, as described in det ail above with respect to seal member 441. defines a first opening 544a, a second opening 54 4b and a third opening 544c, which are aligned with each other.

[0082]

[1135] The dial 545 of the flow controller 540 may be substantially similar in form and functio n to the dial 445 while having a suitable size to be coupled to the housing 501 . Accordingly, d ial 545 may be rotatably coupled to housing 501 and movable relative to housing 501 betwee n first, second and third positions. Dial 545 includes an entry port 521 defining lumen 502 tha t defines a fluid flow path for withdrawing and/or transporting bodily fluid from a patient to col lection device 500. Medical device (not shown) can be fluidly coupled to In this way, inlet port 521 can be configured to selectively locate pre-sample reservoir 570 , first sample reservoir 5 80 and second sample reservoir 590 . More specifically, when the dial 545 is in the first positio n, the flow controller 540 is arranged in the first configuration and the inlet port 521 communi cates with the first opening 544a of the seal member 541 and the first outlet opening 503a of

the housing 501. is substantially aligned with Thus, as described in detail above with respect t o collection device 400, first opening 544a of seal member 541 establishes fluid communicatio n between inlet port 521 and first outlet opening 503a, and thus the inlet port. 521 is placed i n fluid communication with pre-sample reservoir 570 . Similarly, when the dial 545 is turned (or driven) to the second position, the flow controller 540 is placed in the second configuratio n and the second outlet opening 544b is connected to the inlet port 521 and the second outlet opening 503b. , thus establishing fluid communication with the first flow path 535a, and when the dial 545 is turned to the third position, the flow controller 540 is disposed in the third conf iguration, and the third outlet opening 544c communicates with the inlet port. Fluid communic ation is established between 521 and the third outlet opening 503c and thus the second flow path 535a. Thus, the collection device 500 is applied to the pre-sample 570 as described in de tail above with respect to the collection device 400 .

It can be used to transfer second and third volumes of bodily fluid to reservoir 580 and secon d sample reservoir 590, respectively.

[1136

] Figures 26-33 show a collection device 600 according to an embodiment. Collection device 6 00 includes flow diverter mechanism 620, flow controller 640 and sample reservoirs 680, 68 0', 690 and 690'. As further described herein, the collection device 600 can be moved betwee n first, second, third, fourth and fifth configurations to, for example, collect microorganisms a nd/or microorganisms present on the skin. A fluid stream can be delivered that is substantiall y free of extracorporeal microorganisms, such as or other undesirable external contaminants. Collection device 600 may be of any suitable shape, size or configuration. For example, aspect s and/or portions of collection device 600 may be similar in form and/or function to correspon ding aspects and/or portions of any of collection devices 100, 200, 300, 400 and/or 500 descr ibed above. . Accordingly, such similar aspects and/or parts will not be described in further de tail herein. By way of example, in some embodiments sample reservoirs 680, 680′, 690 and 6 90′ of collection device 600 are similar to sample reservoirs 480, 480′, 490 and 490′ included in collection device 400 of FIGS. may be substantially similar and/or the same in form and/or function as each.

[0084]

[1137] The flow diverting mechanism 620 includes a distribution member 629 and a set of co upling members 637a, 637b, 637c and 637d (see, eg, FIG. 27). Distribution member 629 is in fluid communication with coupling members 637a, 637b, 637c and 637d and is configured to provide and/or define a set of fluid flow paths for collecting bodily fluid from a patient. As sho wn in FIGS. 27 and 28, distribution member 629 includes a first outlet port 630 in fluid comm unication with pre-sample reservoir 670, a second outlet port 631 in fluid communication with first coupling member 637a; A third outlet port 632 in fluid communication with the second co upling portion 637b, a fourth outlet port 633 in fluid communication with the third coupling po rtion 637c, and a fifth outlet in fluid communication with the fourth coupling portion 637d. 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 a s, for example, blood, plasma, urine, and the like. For example, the pre-sample reservoir 670 can receive and contain a first amount or volume of bodily fluid from a patient, where the first amount of bodily fluid can be a predetermined amount or an unquantified amount. Additionall y, the arrangement of flow diverter mechanism 620 and flow controller 640 allows pre-sample reservoir 670 to follow coupling portions 637a, 637b, 637c and 637d and/or bodily fluids with drawn from the patient, as described in further detail herein. It may be maintained fluidly isol ated from the volume. Thus, outlet ports 631, 632, 633 and 634 direct fluid flow paths betwe en flow controller 640 and coupling members 637a, 637b, 637c and 637d, respectively, as des cribed in further detail herein. may be attached and/or otherwise defined. In some embodime nts, the arrangement of first exit port 630 and pre-sample reservoir 670 can be substantially similar in form and function to pre-sample reservoirs 470 and/or 570 . Accordingly, pre-sampl e reservoir 670 will not be described in further detail herein.

[0086]

[1139] As shown in FIG. 29, the first coupling member 637a defines a channel 638a that is flu idly coupled to the piercing member 655a. Coupling member 637a can be physically and fluidl y coupled to distribution member 629, as described above. For example, channel 638a can re ceive a portion of distribution member second outlet port 631 and coupling member 637a can be physically and fluidly coupled thereto. In some embodiments, the surface of the second out let 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 t he coupling portion 637a can be substantially similar in form and function to the piercing me mber 455a included in the collection device 400 of FIGS. 16-22. Accordingly, piercing member 655a will not be further described herein. The second coupling member 637b, the third coupli ng member 637c and the fourth coupling member 637d are similarly arranged. Accordingly, th e second coupling member 637b, the third coupling member 637c and the fourth coupling me mber 637d each include piercing members 655b, 655c and 655d respectively and define chan nels 638b, 638c and 638d respectively. As described in further detail herein, first coupling me mber 637a, second coupling member 637b, third coupling member 637c and fourth coupling member 637d are used to connect flow diverting mechanism 620 to first sample reservoir 68 0, It can be selectively placed in fluid communication with each of the second sample reservoi r 680', the third sample reservoir 690 and the fourth sample reservoir 690'.

[0087]

[1140] The flow controller 640 includes a dial 645 and a seal member 641, as shown in FIGS. A dial 645 of flow controller 640 is rotatably disposed within distribution member 629 (see FI GS. 32 and 33) and is movable between first, second, third and fourth positions. . Dial 645 inc

ludes an inlet port 621, a first outlet port 647 and a second outlet port 648, each in fluid com munication with interior space 646 (see, eg, FIG. 30). Interior space 646 is configured to rece ive a portion of seal member 641, as described in further detail herein. Inlet port 621 can be f luidly coupled to a medical device (not shown) that defines a fluid flow path for drawing bodily fluid from a patient and/or transporting it to collection device 600 . For example, inlet port 62 1 may be fluidly coupled to a needle or other lumen-defining device (e.g., flexible sterile tubin g) directly or indirectly via an adapter 604 (see, e.g., FIGS. 26 and 27). can do. First outlet po rt 647 is in fluid communication with pre-sample reservoir 670 . For example, first outlet port 647 can be rotatably disposed within first outlet port 630 of distribution member 629 . When dial 645 is in its first, second, third and fourth positions respectively, second outlet port 648 is connected to second outlet port 631, third outlet port 632, fourth outlet port 633 and It can b e selectively placed in fluid communication with the fifth outlet port 634 . Thus, the interior sp ace 646 of the dial 645 is divided into a pre-sample reservoir 670, a first sample reservoir 68 0, a second sample reservoir 680', a third sample reservoir 690 and a fourth sample reservoir, as described in further detail herein. It can be selectively placed in fluid communication with t he sample reservoir 690'.

[0088]

[1141] At least a portion of the sealing member 641 of the flow controller 640 is rotatably dis posed within an interior space 646 of the dial 645 and is movable between a first position and a second position. Further, seal member 641 can be sized and shaped such that an outer surf ace of seal member 641 forms a substantially fluid-tight seal with an inner surface of dial 645 that defines at least a portion of interior space 646 . As shown in FIG. 31, the sealing member 641 defines a first flow path 642 and a second flow path 644. As shown in FIG. When seal me mber 641 is in its first position within interior space 646 , passage 642 fluidly isolates inlet po rt 621 from second outlet port 648 while allowing inlet port 621 and first outlet port 647 to co mmunicate with each other. establish fluid communication therebetween. Similarly, when seal member 641 is in its second position within interior space 646 , second flow path 644 fluidly is olates inlet port 621 from first outlet port 647 while allowing inlet port 621 and second outlet port 647 to flow through inlet port 621 and second outlet port 647 . Establish fluid communica tion with outlet port 648 . Collection device 600 operates similarly when dial 645 is rotated wit hin dispensing member 629 to second, third and fourth positions. Accordingly, when inlet port 621 is placed in fluid communication with a patient (e.g., via a medical device coupled to inlet port 621 and/or adapter 604), first outlet port 630 of distribution member 629; 2 outlet port 631 , third outlet port 632 , fourth outlet port 633 and fifth outlet port 634 are in fluid commu nication with inlet port 621 .

to allow bodily fluids to flow into pre-sample reservoir 670, first sample reservoir 680, second sample reservoir 680', third sample reservoir 690 and fourth sample reservoir 690', respectiv ely. can be

[1142

] In operation, the collection device 600 can be used to collect bodily fluids (eg, blood, plasm a, urine, etc.) from a patient with reduced contamination. For example, entry port 621 of colle ction device 600 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), the seal m ember can be actuated (or rotated) to its first position, as shown in FIG. Alternatively, the sea l member 641 can be preset in the first position and the collection device 600 can be otherwis e sealed to maintain the sterility of the collection device 600 . When seal member 641 is in its first position, flow controller 640 causes inlet port 621 and a first outlet port of distribution me mber 629 to flow through inlet port 621 from coupling members 637a, 637b, 637c and 637d while fluidly isolating inlet port 621 from coupling members 637a, 637b, 637c and 637d. 630 t o establish fluid communication. Thus, in a manner similar to that described above with respe ct to collection device 400, as indicated by arrow II in FIG. It can be transferred into pre-sam ple reservoir 670 via first exit port 630 of member 629 .

[0090]

[1143] Following collection of the bodily fluid pre-sample within pre-sample reservoir 670, sea l member 641 may be actuated (rotated) relative to dial 645 from its first position to its secon d position. Similarly, dial 645 can be actuated (or rotated) until it reaches the second position relative to distribution member 629, as shown in FIG. When seal member 641 and dial 645 ar e in their second positions, flow controller 640 is disposed in a second configuration and secon d flow path 644 of seal member 641 fluidly isolates pre-sample reservoir 670 from inlet port 6 21 . while establishing fluid communication between inlet port 621 and channel 638a of first c oupling member 637a. With flow controller 640 in its second configuration, sample reservoir 6 80 is actuated by a user from its first configuration to its second configuration (e.g., by pushin g piercing member 655a) to force a portion of the patient's body (e.g., , vein) and the first sa mple reservoir 680 . By moving the sample reservoir 680 to the second configuration, as desc ribed in detail above, the piercing member 655 a is positioned inside the sample reservoir 680 piercing the vacuum seal of the sample reservoir 680 . In this second configuration, that porti on of the patient's body (eg, a vein) is exposed to a vacuum suction force from the sample re servoir 680 due to the negative pressure (vacuum) within the sample reservoir 680 . Thus, as shown by arrows JJ in FIG. 33, body fluid is directed from that portion of the patient's body th rough inlet port 621, second channel 644, second outlet port 631 and channel 638a and throu gh the piercing member of first coupling member 637a. It can be forced through 655a into th e first sample reservoir 680.

[0091]

[1144] Once a desired volume of bodily fluid (eg, a second amount) has been collected in sam ple reservoir 680, the user may actuate (rotate) flow controller 640 to a third position and/or can be moved back to its first configuration to isolate the first sample reservoir 680 from the s econd flow path 644 . When the sample reservoir 680 returns to the first configuration, the pi ercing member 655a is removed from the sample reservoir 680 and the seal (eg, self-sealing

membrane) of the sample reservoir 680 fluidly removes the first sample reservoir 680 from th e flow path 635a. isolate to Filling of the other sample reservoirs is similarly performed with t he flow controller 640 positioned in the third, fourth and fifth configurations, respectively.

[1145

] Figures 34-40 show a collection device 700 according to an embodiment. The collection devi ce 700 includes a flow diverter 720, a flow controller 740 and sample reservoirs 780 and 780. 90 (although there are holders for four sample reservoirs, only two sample reservoirs are incl uded in the figure for clarity, and as part of the collection device 700 additional sample reserv oirs (e.g. 5th, 6th, etc.). As further described herein, the collection device 700 can be moved between first, second, third, fourth and fifth configurations to, for example, collect microorgan isms and/or microorganisms present on the skin. A bodily fluid stream can be delivered that is substantially free of extracorporeal microorganisms, such as other undesirable external conta minants. Collection device 700 may be of any suitable shape, size or configuration. For examp le, aspects and/or portions of collection device 700 may be substantially similar in form and/o r function to corresponding aspects and/or portions of any of collection devices 100, 200, 300, 400, 500 and/or 600 described above. can be similar to Accordingly, such similar aspects and/ or parts will not be described in further detail herein. By way of example, in some embodimen ts, sample reservoirs 780 and 790 of collection device 700 are substantially similar and/or sim ilar in form and function to sample reservoirs 480 and 490, respectively, included in collection device 400 of FIGS. or may be the same.

[0093]

[1146] The flow diverter mechanism 720 includes a housing 701, a distribution member 729 a nd a base plate 771. As shown in FIG. As described above with respect to collection device 40 0, housing 701 has a first outlet opening 703a, a second outlet opening 703b, a second outlet opening 703a, a second outlet opening 703b, and a second outlet opening 703a, each configu red to be in fluid communication with a different portion of distribution member 729. It define s three exit openings 703c, a fourth exit opening 703d and a fifth exit opening 703e. More spe cifically, distribution member 729 includes at least a portion of pre-sample reservoir 770 in flu id communication with first outlet opening 703a and a first fluid chamber 735a in fluid commu nication with second outlet opening 703b. , a second fluid chamber 735b in fluid communicati on with the third outlet opening 703b, a third fluid chamber 735c in fluid communication with the fourth outlet opening 703d, and a second fluid chamber 735c in fluid communication with the fifth outlet opening 703e. defines and/or forms four fluid chambers 735d. Additionally, ho using 701 defines a recess 766 configured to movably receive at least a portion of flow control ler 740, as described further herein.

[0094]

[1147] As shown in FIG. Pre-sample reservoir 770 is configured to contain bodily fluids such a s, for example, blood, plasma, urine, and the like. The first outlet opening 703a of the housin g 701 is substantially aligned with the open portion of the pre-sample reservoir 770 so that th

e pre-sample reservoir 770 can receive the flow of bodily fluid from the patient, as described i n detail above. be able to. More specifically, distribution member 729 includes a set of walls 7 36 that can, for example, divide the interior space of distribution member 729 into portions a nd/or spaces that are fluidly isolated from one another. For example, as shown in FIG. 36, a s et of walls 736 divides the interior space of distribution member 729 into pre-sample reservoir 770, first fluid chamber 735a, second fluid chamber 735b, third fluid chamber 735c and fourth fluid chamber 735c. It can be divided into chambers 735d. In some embodiments, wall 736 ca n equally define and/or form pre-sample reservoir 770 and fluid chambers 735a-735d. In othe r embodiments, pre-sample reservoir 770 can define a space that is different than the space d efined by fluid chambers 735a-735d.

[0095]

[1148] The distribution member 729 is in fluid communication with the first piercing member 755a, the second piercing member 755b, respectively, with the first fluid chamber 735a, the s econd fluid chamber 735b, the third fluid chamber 735c and the fourth fluid chamber 735d. , a third piercing member 755c and a fourth piercing member 755d. Thus, piercing members 7 55a-355d can be used to pierce sample reservoirs 780 and 790 (and corresponding sample re servoirs not shown in FIGS. 34-40), as described in further detail herein. , thereby initiating b odily fluid flow.

[1149

] The flow controller 740 of the collection device 700 includes a dial 745 and a seal member 7 41 . Seal member 741 is positioned within recess 766 of housing 701 (see, eg, FIGS. 38 and 40). More particularly, coupling flow controller 740 to housing 701 such that seal member 741 is positioned between and in contact with the surface of housing 701 defining recess 766 and the surface of dial 745 . can be done. Seal member 741 may be configured to form a substant ially fluid-tight seal with the surface of dial 745 and the surface of housing 701 defining recess 766, as described in detail above. As shown in FIG. 35, the sealing member 741 defines a first opening 744a, a second opening 744b, a third opening 744c, a fourth opening 744d and a fift h opening 744e. The arrangement of the sealing member 741 is such that when the sealing m ember 741 is arranged in the recess 766, the first opening 744a, the second opening 744b, th e third opening 744c, the fourth opening 744d, and the fifth opening 744e are formed. , the fi rst outlet opening 703a, the second outlet opening 703b, the third outlet opening 703c, the fo urth outlet opening 703d and the fifth outlet opening 703e of the housing 701, respectively. i s.

[0097]

[1150] The dial 745 of the flow controller 740 is rotatably coupled to the housing 701 and is movable relative to the housing 701 between a first position, a second position, a third positio n, a fourth position, and a fifth position. be. Dial 745 includes an entry port 721 that connects entry port 721 to a medical device (either directly or indirectly via adapter 704) that defines a fluid flow path for withdrawing bodily fluid from a patient and/or transporting it to collection 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 fourt h sample reservoir 790, as described in further detail herein. ' can be configured to be selectiv ely placed in fluid communication with a patient. When dial 745 is in the first position, flow co ntroller 740 is disposed in a first configuration, aligning inlet port 721 substantially with first o pening 744 a of seal member 741 and first outlet opening 703 a of housing 701 . can be comb ined. Thus, the first opening 744a of the seal member 741 fluidly isolates the inlet port 721 fr om the outlet openings 703b, 703c, 703d and 703e, thereby fluidly isolating the inlet port 721 from the fluid chambers 735a-335d. Fluid communication is established between the inlet port 721 and the first outlet opening 703a while isolating to the first outlet port 703a. When the di al 745 is turned (or driven) to the second position, the flow controller 740 is placed in the sec ond configuration and the second outlet opening 744b connects the inlet port 721 to the pre-s ample reservoir 770 and the fluid chambers 735b-735b. Fluid communication is established b etween inlet port 721 and second outlet opening 703b while being fluidly isolated from 735d. Collection device 700 operates similarly when dial 745 is turned to the third, fourth and fifth p ositions. Accordingly, inlet port 721 is in fluid communication with the patient (eg, via a medic al device coupled to inlet port 721).

[1151

] In some embodiments, housing 701 selectively limits movement of dial 745 from its first pos ition to its second, third, fourth and fifth positions. be able to. In some other embodiments, th e housing 701 can be configured to prevent movement of the dial moved to the fifth position. In other words, housing 701 can include a locking mechanism that prevents dial 745 from mo ving back from the fifth position to the first position. This feature allows flow chambers 735a-735d and/or

This reduces the risk that bodily fluids collected in pull reservoirs 780 and 790 are contaminat ed from bodily fluids contained in pre-sample reservoir 770 (which has a high risk of containin g surface-bound microorganisms and/or other undesirable external contaminants). can be red uced. This locking mechanism can also protect medical personnel from exposure to blood-bor ne pathogens in patient samples, which may include HIV, hepatitis C, and the like. Dial 745 an d/or housing 701 may also have mechanical detents that provide visual or tactile feedback to ensure correct alignment of dial 745 with respect to exit port 703a and exit openings 703a-70 3d in housing 701. and/or other indicators may also be included.

[0099]

[1152] Similar to the embodiment of the collection device 400 shown in FIGS. The pre-sample reservoir 770 can contain bodily fluids such as, for example, blood, plasma, urine, and the lik e. Pre-sample reservoir 770 is configured to be fluidly coupled to first outlet port 703a of colle ction device 700 (located within housing 701). During operation of the collection device 700, when the flow controller 740 is in the first position, body fluid flows from a portion of the patie nt's body (eg, a vein) through the inlet port 721, into the pre-sample reservoir 770, into the s

eal member 741. is drawn into the opening for the pre-sample reservoir 744a and the first exi t port 703a located at . Pre-sample reservoir 770 is configured to contain a first volume of flui d to be drawn from a patient, where the first volume of bodily fluid can be a predetermined vo lume or an unquantified volume. Thereby the first volume of bodily fluid is fluidly isolated fro m a second and/or third and/or fourth and/or fifth volume of bodily fluid subsequently withdra wn from the patient.

[0100]

[1153] In operation, the collection device 700 can be used to collect bodily fluids (eg, blood, p lasma, urine, etc.) from a patient with reduced contamination. For example, entry port 721 of collection device 700 can be fluidly coupled to a needle or other lumen defining device (eg, fle xible sterile tubing). Following venipuncture, dial 745 is turned until it reaches the first positio n, as shown in FIGS. Alternatively, the dial 745 can be preset in the first position and the colle ction device 700 can be otherwise sealed to maintain the sterility of the collection device 700, as described above. With the dial 745 in the first position, the flow controller 740 is placed in a first configuration and the first outlet opening 744a of the seal member 741 fluidly connects the inlet port 721 from the four sample flow paths 735a-735d. While in isolation, fluid commu nication is established between inlet port 721 (contained within housing 701) and first outlet port 741 . In this first configuration, bodily fluids are directed from that portion of the patien t's body, as indicated by arrows KK in FIG. through and into the pre-sample reservoir 770 defi ned by the distribution member 770 . Accordingly, as described in detail above, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 770 im mediately after venipuncture and segregated from subsequent samples.

[0101]

[1154] Following the collection of the bodily fluid pre-sample within the pre-sample reservoir 770, the dial 745 can be actuated (or rotated) until it reaches the second position, as shown i n FIGS. When dial 745 is in the second position, flow controller 740 is placed in a second confi guration, and second outlet opening 744 a of seal member 741 fluidly isolates pre-sample res ervoir 770 from inlet port 721 while allowing inlet port 721 to flow. Fluid communication is est ablished between port 721 and first fluid chamber 735a. Once the first fluid chamber 735a is f illed with bodily fluid, the flow controller 740 can be moved to the third position to isolate and seal the first flow path 735a from the external environment. Additionally, the sample reservoir 780 is actuated from the first configuration to the second configuration to transfer bodily fluid from the first fluid chamber 735a to the sample reservoir 780.

can be sent. For example, sample reservoir 780 may be user or automatically actuated from a first configuration to a second configuration (pressing piercing member 755a) to allow a portio n of the patient's body (e.g., a vein) to move between sample reservoir 780 and sample reser voir 780. can establish fluid communication with the As described above, moving the sample r eservoir 780 to the second configuration causes the piercing member 755a to pierce the vacu um seal of the sample reservoir 780 and be positioned inside the sample reservoir 780 . In a

second configuration, that portion of the patient's body (eg, a vein) is subjected to vacuum su ction from the sample reservoir 780 due to the negative pressure (vacuum) existing within th e sample reservoir 780 in some embodiments. Thus, as indicated by arrow LL in FIG. 40, bodil y fluids flow from that portion of the patient's body through inlet port 721, second outlet open ing 744b in seal member 741, second outlet opening 703b in housing 701, second It flows int o the first sample reservoir 780 through the fluid chamber 735b.

[1155

] Once a desired amount of bodily fluid (eg, a second amount) has been collected in sample r eservoir 780, the user may actuate (rotate) flow controller 740 to a third position and/or The sample reservoir 780 can be moved back to its first configuration to isolate the first sample re servoir 780 from the inlet port 721 . When the sample reservoir 780 returns to the first config uration, the piercing member 755a is removed from the sample reservoir 780 and the seal (e g, self-sealing membrane) of the sample reservoir 780 allows the first sample reservoir 780 to enter the second fluid chamber 735b and the exterior. Fluid isolation from the environment. Fi lling of the other sample reservoirs is done in the same manner with the flow controller 740 in the third, fourth and fifth configurations respectively.

[0103]

[1156] In some embodiments, the collection device 700 can be configured such that there is no set of walls 736 separating the different fluid chambers 735a-735d within the distribution member 729 (detailed in FIG. 16). (see cross section). In such embodiments, the distribution member 729 is divided between the pre-sample reservoir 770 and the associated fluid chamb er 735 (ie, the fluid chamber is not separated into four separate portions by wall 736). In suc h embodiments, the user can fill all four sample reservoirs at once by actuating (rotating) dial 745 to either the second, third, fourth or fifth position. can be done.

[0104]

[1157] Any of the embodiments described herein can be used, for example, to meter (e.g., qu antify) the flow of bodily fluid into a pre-sample reservoir and/or a sample reservoir. Can be u sed with metering devices. In some cases, laboratory standard practice limits the exact inocul ation volume of bodily fluids (e.g., blood samples) due to the fact that fill volumes are judged visually by clinicians and/or phlebotomists and are therefore subject to human error. Consiste nt compliance is not ensured. The volume indicator on the blood collection bottle is difficult to read when held, and the fact that the collection bottle is not held upright during the withdraw al procedure contributes to the inaccurate volume of the bodily fluid sample received from the patient. could be a factor. Insufficient sample volume (eg, less than the manufacturer's recom mendation) can reduce the sensitivity of the culture test and lead to false-negative results. In addition, briefing materials and instructions for certain types of test supplies and equipment (e.g., blood culture bottles designed for use with automated microbial detection systems prod uced by manufacturers such as Becton Dickinson of Franklin Lakes, NJ). Filling volumes in exc ess of the manufacturer's recommendations, as indicated in the literature, may result in false

positives. Thus, flow metering and volume display capabilities allow laboratory technicians an d/or medical personnel (e.g., phlebotomists) to transfer sample reservoirs to incubators or oth er laboratories, depending on how the sample needs to be processed. The volume of bodily flu id collected in each individual sample reservoir can be verified prior to placement within the te sting device. The laboratory technician and/or phlebotomist may also provide accurate volume tric information (e.g., in medical records, databases, spreadsheets, etc.) for clinician evaluatio n when results are received.

), which helps reduce the likelihood of misinterpretation of false negative and/or false positive results.

[1158

] By way of example, FIGS. 41-45 illustrate a collection device 800 that can include one or mo re metering devices. Collection device 800 includes flow diverter mechanism 820 , flow contro ller 840 , display 875 and sample reservoir 880 . As further described herein, the collection de vice 800 can be moved between first, second and third configurations to remove, for example, microorganisms present on the skin and/or other undesirable external contaminants, and the l ike. , can deliver a body fluid stream that is substantially free of extracorporeal microorganis ms. Collection device 800 may be of any suitable shape, size or configuration. For example, as pects and/or portions of collection device 600 may be similar in form and/or function to corres ponding aspects and/or portions of any of collection devices 100, 200, 300, 400, 500, 600 an d/or 700 described above. can be substantially similar. Accordingly, such similar aspects and/o r parts will not be described in further detail herein. By way of example, in some embodiment s, sample reservoir 880 of collection device 800 is substantially similar and/or identical in for m and function to sample reservoir 480 included in collection device 400 of FIGS. could be.

[0106]

[1159] As shown in FIGS. 41-43, the flow diverter mechanism 820 includes an actuator portio n 822 (eg, a first portion), an intermediate portion 823 (eg, a second portion) and a coupling portion 824 (eg, a third portion). including. Actuator portion 822 of flow diverter mechanism 8 20 is substantially cylindrical including a set of actuator walls that define interior space 806 . More specifically, actuator portion 822 has a first end that is substantially closed and an oppos ite end that is substantially open to allow access to interior space 806 . a side second end. As such, actuator portion 822 can movably receive at least a portion of flow controller 840, as de scribed in further detail herein. Actuator portion 822 further includes inlet port 821 and outlet port 831 . Inlet port 821 is fluidly connected (either directly or indirectly via adapter 804) to a medical device that defines a fluid flow path for withdrawing bodily fluid from a patient and/or transporting it to collection device 800, as described in detail above. can be linked together.

[0107]

[1160] The outlet port 831 of the actuator portion 822 may be selectively positioned to place a portion of the interior space 806 of the actuator portion 822 in fluid communication with the interior space 807 defined by the intermediate portion 823. As shown in FIG. 43, intermediate

portion 823 is positioned between actuator portion 822 and coupling portion 824 . Although n ot shown in FIGS. 41-45, intermediate portion 823 can include a metering device that can be configured to meter a volume of bodily fluid transferred to sample reservoir 880, for example. For example, in some embodiments, a flow metering device can be fluidly coupled to outlet po rt 831 to meter the flow of bodily fluid therethrough. As shown in FIGS. 41 and 42, the interm ediate portion 823 includes a display 875 that provides a user with visual indicators and/or inf ormation related to the volume of bodily fluid that has flowed through the outlet port 831, for example. can provide. In other embodiments, the flow metering device may be placed at any other suitable location within or along the flow diverter 820 .

[1161

] The coupling portion 824 can be physically and fluidly coupled to the intermediate portion 82 3 . For example, in some embodiments, coupling portion 824 is partially disposed within interi or space 807 of intermediate portion 823 and attached thereto at least temporarily via a fricti on fit, press fit, snap fit, threaded connection, adhesive, or the like. can be linked together. Co upling portion 824 is configured to receive a portion of sample reservoir 880, as described in detail above, so that it can puncture the vacuum seal of sample reservoir 880, thereby initiati ng bodily fluid flow. includes a piercing member 855 that can be used to

[1162

] The flow controller 840 of the collection device 800 is disposed at least partially within the in terior space 806 defined by the actuator portion 822 and is movable between first, second an d third configurations. is. As shown in FIGS. 42 and 43, the flow controller 840 includes a mov able member 850 having a first sealing member 861, a second sealing member 862 and a thir d sealing member 863, and a biasing member 859 (eg, a spring or the like). including. Seal m embers 861 , 862 and 863 are in contact with the inner surface of actuator portion 822 that d efines interior space 806 . Accordingly, as described in further detail herein, each of the seal members 861, 862 and 863 has an inner surface that can, for example, divide the interior spa ce 806 of the actuator portion 822 into fluidly isolated portions; A fluid-tight seal can be form ed.

[0110]

[1163] The movable member 850 is movable within the interior space 806 between a first pos ition, a second position and a third position. The arrangement of movable member 850 is such that seal members 861, 862 and 863 selectively move within interior space 806 as movable m ember 850 moves between its first, second and third positions. It can be. More specifically, th e first sealing member 861 can move simultaneously with the movable member 850 as the m ovable member 850 moves between its first, second and third positions. A second seal memb er 862 and a third seal member 863 can be fixedly coupled to each other (eg, positioned at a fixed distance from each other) and slidably disposed about a portion of the movable member 850, which This causes movable member 850 to move from its first position (see, eg, FIG. 4 3) to its first position while second sealing member 862 and third sealing member 863 remain

in a substantially fixed position relative to actuator portion 822 . It may be possible to move t o two positions (see, eg, FIG. 44). For example, as movable member 850 moves between its f irst and second positions, second sealing member 862 and third sealing member 863 can rem ain in a substantially fixed position, thereby providing an inlet port. Port 821 is located on a fir st side of second sealing member 862 and exit port 831 is located on a second side of second sealing member 862 opposite the first side. Thus, when movable member 850 is in its first po sition (FIG. 43) and its second position (FIG. 44), inlet port 821 is in contact with first sealing member 861, as described in further detail herein. is in fluid communication with a portion of the interior space 806 defined between the second seal member 862 and the exit port is in th e interior space 806 defined between the second seal member 862 and the third seal member 863. in fluid communication with the part.

[0111]

[1164] The arrangement of the flow controller 840 is such that the first sealing member 861 moves relative to the second sealing member 862 and the third sealing member 863 when th e movable member 850 moves from its first position to its second position. , can be Movemen t of first seal member 861 relative to second seal member 862 can enlarge the space defined therebetween, thereby forming and/or otherwise defining pre-sample reservoir 870 . can do. I n addition, seal members 861 and 862 form a substantially fluid-tight seal with the inner surf ace of actuator portion 822 such that pre-sample reservoir 870 defined between first seal me mber 861 and second seal member 862 is , are fluidly isolated from the rest of the interior sp ace 806 . Thus, inlet port 821 can be in fluid communication with pre-sample reservoir 870 w hen moveable member 850 moves from its first position to its second position. As movable m ember 850 moves from its second position (see, eg, FIG. 44) to its third position (see, eg, FI G. 45), a portion of movable member 850 contacts third sealing member 863. , the first sealin g member 861 , the second sealing member 862 and the third sealing member 863 can be m oved substantially simultaneously within the interior space 806 . Accordingly, both the inlet po rt 821 and the outlet port 831 provide fluid communication to the portion of the interior space 806 defined between the second sealing member 862 and the third sealing member 863, as d escribed in further detail herein. A second sealing member 862 can be moved relative to the i nlet port 821 in communication.

[0112]

[1165] In operation, the collection device 800 can be used to collect bodily fluids (eg, blood, p lasma, urine, etc.) from a patient with reduced contamination. For example, entry port 821 of collection device 800 can be fluidly coupled to a needle or other lumen defining device (eg, fle xible sterile tubing). With inlet port 821 coupled to the lumen defining device, flow controller 840 can be moved from its first configuration to its second configuration. Thus, a user can app ly a force to move movable member 850 from its first position to its second position, as indica ted by arrow MM in FIG. As described above, the first sealing member 861 moves simultaneou sly with the movable member 850, thereby enlarging the space defined between the first seali

ng member 861 and the second sealing member 862, thereby A sample reservoir 870 is form ed and/or defined. First sealing member 861 and second sealing member 862 form a substant ially fluid-tight seal with the inner surface of actuator portion 822 that defines interior space 8 06 such that first sealing member 861 and second sealing member 862 are in contact with ea ch other. A negative pressure is created in the pre-sampling reservoir 870 by the increase in v olume between . Accordingly, once fluid communication is established between a portion of th e patient's body (eg, a vein) and the pre-sample reservoir 870 (eg, via inlet port 821 in FIG. 4 4), indicated by arrows NN in FIG. As such, the negative pressure differential between pre-sa mple reservoir 870 and that portion of the patient's body draws fluid into pre-sample reservoir 870 through inlet port 821 . In this first configuration, flow controller 840 also fluidly isolates pre-sample reservoir 870 from outlet port 831 . Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample reservoir 870 (for example) immed iately after venipuncture and isolated from subsequent samples. In this manner, the collection device 800 can be used to collect surface microorganisms and/or other undesirable A first vol ume of bodily fluid most likely to contain an external contaminant contaminates a subsequent volume of bodily fluid sample collected and used for diagnosis or other testing that may be aff ected by the contaminant can be prevented. In some embodiments, the metering device can meter a volume of bodily fluid placed in pre-sample reservoir 870 and present a value associa ted with that volume on display 875 .

[0113]

[1166] Following collection of the body fluid pre-sample volume in pre-sample reservoir 870, moveable member 850 is moved from its second position to its third position, as indicated by arrow OO in FIG. It can be arranged in a third configuration. As described above, when movab le member 850 moves from its second position to its third position, a portion of movable mem ber 850 is placed in contact with third sealing member 863 . Accordingly, the movable membe r 850 moves the first sealing member 861 , the second sealing member 862 and the third seal ing member 863 substantially simultaneously within the interior space 806 . Accordingly, the s econd sealing member 862 is positioned such that both the inlet port 821 and the outlet port 831 are in fluid communication with the portion of the interior space 806 defined between the second sealing member 862 and the third sealing member 863 . It can be moved relative to p ort 821 . Furthermore, because the volume of body fluid is fluidly isolated within the pre-sam ple reservoir 870, movement of the second seal member 862 and the third seal member 863 i n the direction of the first seal member 861 is restricted (i.e., body fluid is a substantially inco mpressible fluid). Thus, the pre-sample volume of bodily fluid is sequestered within pre-sampl e reservoir 870 and the space defined between second sealing member 862 and third sealing member 863 is separated by inlet port 821 and outlet port 821 . 831 defines a fluid flow path. Further, flow controller 840 is positioned such that when in its third configuration, first sealing member 861 is in contact with biasing member 859 such that at least a portion of the force ex erted by the user on movable member 850 is The biasing member 859 is operable to deform,

compress, bend and/or otherwise reconfigure. Accordingly, the biasing member 859 acts agai nst the first sealing member 861 to resist movement of the flow controller 840 from its secon d configuration to its third configuration, as described in further detail herein. can affect

[1167

] As described in detail above, piercing member 855 provides a vacuum seal for sample reser voir 880.

The sample reservoir 880 can be positioned relative to the collection device 800 such that the hole is pierced and placed inside the sample reservoir. A pressure differential between the sa mple reservoir 880 (eg, vacuum or negative pressure) and that part of the body draws body fl uid into the sample reservoir 880 . In other words, in the second configuration, flow controller 840 and flow diverter mechanism 820 direct body fluid from the patient through inlet port 82 1, second sealing member 862, and third sealing member 863, as indicated by arrow PP in FI G. through the portion of the interior space 806 defined therebetween, and the exit port 831 of the actuator portion 822, through the piercing member 855 of the intermediate portion 823 and the coupling portion 824, and into the sample reservoir 880; Establish a fluid flow path. A s discussed above, a metering device (not shown) can meter the volume of bodily fluid transfe rred, for example, through outlet port 831 and can present a value associated with the volum e of bodily fluid on display 875 .

[0115]

[1168] Once a desired volume of bodily fluid (eg, a second amount) has been collected in the sample reservoir 880, the user can remove and/or reduce the force applied to the movable m ember 850, thereby , a biasing member 859 can move the first sealing member 861 and the movable member 850 from their third position toward their second position. Further, due to th e substantially incompressible nature of the bodily fluid disposed within pre-sample reservoir 870, movement of first sealing member 861 transfers force through the volume of bodily flui d, thereby increasing second sealing member 862 and third sealing member 862. Seal memb ers 863 are moved from their third position toward their second position. In some embodimen ts, the biasing member 859 is operable to move the second seal member 862 relative to the a ctuator portion 822, for example, to a fourth position where the inlet port 821 can be substan tially blocked. The resulting force can be applied to the first sealing member 861 . Accordingl y, inlet port 821 can be fluidly isolated from interior space 806 of actuator portion 822 . Additi onally, the piercing member 855 can be removed from the sample reservoir 880 and a seal (e g, a self-sealing membrane) can fluidly isolate the bodily fluid sample from the space outside t he sample reservoir 880 . Subsequent filling of the sample reservoir is similarly accomplished by placing piercing member 855 into the sample reservoir and moving flow controller 840 to t he third configuration to allow bodily fluid to flow from the patient into the sample reservoir. c an be done.

[0116]

[1169] FIGS. 46-53 illustrate a collection device 900 according to an embodiment. Collection

device 900 includes flow diverter mechanism 920, flow controller 940 and sample reservoirs 9 80, 980', 990 and 990'. As further described herein, the collection device 900 can be moved b etween first, second, third, fourth and fifth configurations to, for example, collect microorgani sms and/or microorganisms present on the skin. or a body fluid stream that is substantially fr ee of extracorporeal microorganisms, such as other undesirable external contaminants. Collec tion device 900 may be of any suitable shape, size or configuration. For example, aspects an d/or portions of collection device 900 may be corresponding aspects and/or portions and confi gurations and/or of any of collection devices 100, 200, 300, 400, 500, 600, 700 and/or 800 d escribed above. They may be substantially similar in function. Accordingly, such similar aspect s and/or parts will not be described in further detail herein. By way of example, in some embo diments, sample reservoirs 980, 980′, 990 and 990′ of collection device 900 are similar to sa mple reservoirs 680, 680′, 690 and 690 included in collection device 600 of FIGS. ' can be sub stantially similar and/or the same in form and function.

[1170

] The flow diverter mechanism 920 includes a housing 901, a distribution member 929 and m ovable members 950a, 950b, 950c and 950d. Housing 901 is physically and fluidly coupled to distribution member 929 to provide and/or define a set of fluid flow paths for collecting bodily fluids from a patient. Housing 901 may be included in a flow metering device and/or otherwis e (e.g., electrically and/or mechanically) as described in further detail herein.

and a set of displays 975' (eg, liquid crystal displays (LCDs), etc.) that can be coupled togethe r. Housing 901 defines recess 966, exit openings 903a, 903b, 903c, 903d, 903e and movable member openings 950a, 950b, 950c, 950d (also referred to herein as "openings"). Recess 966 is configured to receive seal member 941 included in flow controller 940, as described in furth er detail herein. First outlet opening 903a, second outlet opening 903b, third outlet opening 9 03c, fourth outlet opening 903d and fifth outlet opening 903e are each in fluid communication with different portions of distribution member 929. It is configured to define different fluid flo w paths. More specifically, distribution member 929 includes at least a portion of pre-sample r eservoir 970 in fluid communication with first outlet opening 903a and a first channel 935a in fluid communication with second outlet opening 903b. , a second passageway 935b in fluid co mmunication with the third outlet opening 903b, a third passageway 935c in fluid communicat ion with the fourth outlet opening 903d, and a second passageway 935c in fluid communicatio n with the fifth outlet opening 903e. defines and/or forms four channels 935;

[0118]

[1171] As shown in FIGS. Pre-sample reservoir 970 is configured to contain bodily fluids such as, for example, blood, plasma, urine, and the like. As described in detail above with respect t o pre-sample reservoir 470 in FIGS. 16-22, first outlet opening 903a of housing 901 is pre-mo unted to allow pre-sample reservoir 970 to receive a flow of bodily fluid from the patient. It ca n be substantially aligned with the open portion of sample reservoir 970 . Channels 935a-935 d extend radially from the center of distribution member 929 and are arranged such that 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 openi ngs substantially aligned with outlet openings 903b, 903c, 930d and 903e, respectively, and movable members 950a, 950b, A fluid flow path may be directed and/or otherwise defined bet ween the second ends defining openings or ports configured to receive 950c and 950d, respec tively. Although distribution member 929 is shown in FIGS. 47 and 48 as including channels 9 35a-935d that are substantially closed, in other embodiments, with respect to distribution me mber 429 of FIGS. Channels 935a-935d can be substantially open as shown and described ab ove. Accordingly, distribution member 929 of collection device 900 can function substantially s imilar to distribution member 429 of collection device 400 .

[0119]

[1172] Movable members 950a, 950b, 950c and 950d are movably disposed in respective ope nings 905a, 905b, 905c and 905d of housing 901 and corresponding openings defined by the second end of distribution member 929. be. Although not shown in FIGS. 46-53, in some emb odiments moveable members 950a, 950b, 950c and 950d are biased members, as described i n detail above with respect to moveable members 250 and 250′ of collection device 200. etc. can be operatively coupled. Thus, movable members 950a, 950b, 950c and 950d are actuated (moved) by a user from first and second positions relative to housing 901 and distribution me mber 929 to direct fluid flow to a first sample. It can be directed into each of reservoir 980, se cond fluid reservoir 980', third fluid reservoir 990 and fourth sample reservoir 990'. Movable members 950a, 950b, 950c and 950d are substantially identical and therefore will be describe d with respect to a single movable member 950 in FIG. Additionally, some portions of movable member 950 may be substantially similar to movable members 250 and 350 described above. Accordingly, some portions of movable member 950 are not described in further detail herein. Movable member 950 defines an internal cavity 952 in fluid communication with inlet port 953 and piercing member 955 . The piercing member is substantially similar to that detailed abov e. The inlet port 953 extends through a set of walls that define the interior space 952 of the movable member 950 with corresponding passages 935a, 935b, 935c.

Alternatively, an internal chamber 952 is defined for selective placement in fluid communicatio n with 935d.

[1173

] As shown in FIG. The flow metering mechanism 967 can be, for example, a wheel or the like that can include a set of spokes or fins. In this manner, bodily fluid can enter inlet port 953 of movable member 950 and flow past flow metering device 967 , thereby allowing flow meterin g device 967 to rotate relative to movable member 950 . Accordingly, the rotational features o f the flow metering device 967 may be usable in determining the volume of bodily fluid transf erred to the interior space 952 of the movable member 950, the volumetric flow rate, and the like. Although not shown in FIGS. 46-53, flow control mechanism 967 of movable member 95 0 is operably coupled to display 975 ′ of housing 901 . Accordingly, as bodily fluids are transfe

rred to sample reservoirs 980, 980', 990 and/or 990', for example, volumetric information rel ated to the flow of bodily fluids can be presented on display 975'. In this way, a user can oper ate the collection device 900 to collect a bodily fluid sample from a patient, e.g. One can be vi sualized.

[0121]

[1174] The flow controller 940 of the collection device 900 includes a dial 945 and a seal me mber 941 . Seal member 941 is disposed within recess 966 of housing 901 . More particularly, flow controller 940 is coupled to housing 901 such that seal member 941 is positioned betwee n and in contact with the surface of housing 901 defining recess 966 and the surface of dial 9 45 . be able to. As described in detail herein, sealing member 941 can be configured to form a substantially fluid-tight seal with the surface of dial 945 and the surface of housing 901 defini ng recess 966 . As shown in FIG. 47, the sealing member 941 defines a first opening 944a, a second opening 944b, a third opening 944c, a fourth opening 944d and a fifth opening 944e. As for the arrangement of the sealing member 941, when the sealing member 941 is arrange d in the recess 966, the first opening 944a, the second opening 944b, the third opening 944c, the fourth opening 944d, and the fifth opening 944e are opened. , the first outlet opening 903 a, the second outlet opening 903b, the third outlet opening 903c, the fourth outlet opening 90 3d and the fifth outlet opening 903e of the housing 901, respectively. is.

[0122]

[1175] The dial 945 of the flow controller 940 is rotatably coupled to the housing 901 and is movable relative to the housing 901 between a first position, a second position, a third positio n, a fourth position, and a fifth position. be. Dial 945 includes an entry port 921 that connects entry port 921 to a medical device (either directly or indirectly via adapter 904) that defines a fluid flow path for drawing bodily fluid from a patient and/or transporting it to collection devic e 900.) can be fluidly coupled. Inlet port 921 thus connects to pre-sample reservoir 970, first sample reservoir 980, second sample reservoir 980', third sample reservoir 990 and fourth sa mple reservoir 990, as described in further detail herein. ' can be configured to be selectively placed in fluid communication with a patient. configuring dial 945 to rotate through first, seco nd, third, fourth and fifth positions in a manner substantially similar to that described above w ith respect to dial 445 of collection device 400; , and therefore will not be described in further detail here.

[1176

] As shown, the dial 945 can further include a display 975 that can be configured to present v olumetric information related to the flow of bodily fluids. For example, although not shown in FIGS. 46-53, a dial may be a flow metering device included in movable member 950
967, can include flow metering devices and the like. Thus, the flow metering device can, for e xample, meter the flow of bodily fluid through inlet port 921 such that volumetric information associated with the flow of bodily fluid through inlet port 921 is presented on display 975 of di al 945. , may be operatively coupled to the display 975 .

[1177

] In operation, the collection device 900 can be used to collect bodily fluids (eg, blood, plasm a, urine, etc.) from a patient with reduced contamination. For example, entry port 921 of colle ction device 900 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing). Following venipuncture (or other method of accessing bodily fluids), dial 945 is actuated (or turned) until it reaches the first position, as shown in FIGS. Alternatively, dial 94 5 can be preset to the first position and collection device 900 can be otherwise sealed to main tain sterility of collection device 900 .

[0125]

[1178] As described above, when the dial 945 is in the first position, the flow controller 940 is disposed in the first configuration, and the first opening 944a of the seal member 941 connect s the inlet port 921 to the four flow paths 935a to 935a. Fluid communication is established b etween inlet port 921 (contained within housing 901) and first outlet port 930 while being flui dly isolated from 335d. Further, sample reservoirs 980, 980', 990 and 990' are fluidly isolated from inlet port 921 in the first configuration and are part of the patient's body (e.g., A fluid flo w path is defined between the vein) and the pre-sample reservoir 970 . In this first configurati on, bodily fluids are forced (e.g., by gravity, vacuum, etc.) from that portion of the patient's b ody through inlet port 921, first opening 944a in seal member 941, and first outlet port 903a i n housing 901. through and into the pre-sample reservoir 970 . In the first form, flow controll er 940 also fluidly isolates pre-sample reservoir 970 from flow paths 935a-935d. Accordingly, a first volume (predetermined or unquantified) of bodily fluid can be received in pre-sample re servoir 970 immediately after venipuncture and isolated from subsequent samples. In this wa y, using the collection device 900, a first volume of bodily fluid most likely to contain surface microorganisms and/or other undesirable contaminants may be diagnosed or otherwise affect ed by the contaminant. Subsequent amounts of bodily fluid samples collected and used for tes ting can be avoided from contaminating. Additionally, the display 975 can present information received from a flow control mechanism (not shown) related to, for example, the volume of b odily fluid transferred to the pre-sample reservoir 970 . Thus, a precise volume of bodily fluid can be transferred to and fluidly isolated within the pre-sample reservoir.

[0126]

[1179] Following the collection of the bodily fluid pre-sample within the pre-sample reservoir 970, the dial 945 can be actuated (or rotated) until it reaches the second position, as shown i n FIGS. When the dial 945 is in the second position, the flow controller 940 is disposed in the second configuration, and the second opening 944b of the seal member 941 fluidly isolates th e pre-sample reservoir 970 from the inlet port 921 while allowing the inlet port 921 to flow. Fl uid communication is established between 921 and channel 935a. With flow controller 940 in t he second configuration, movable member 950a is actuated (i.e., depressed) by a user from a first position to a second position to allow patient (eg, vein) and first sample reservoir 880 to move. can establish fluid communication between the More specifically, as indicated by arrow

RR in FIG. to be placed in the first sample reservoir 980 .

[1180

] While in the second position, the inlet port 953 of the movable member 950 is substantially aligned with and in fluid communication with the first flow path 935a, thereby allowing body fl uid to flow through the first flow path 935a. can flow from into the internal cavity 952 of the working member 950 and out of the piercing member 955 into the first sample reservoir 980 . Sample reservoir 980 (e.g. vacuum or negative pressure)

) and the first channel 935 a draws bodily fluid into the sample reservoir 980 . In other words, in the second configuration, flow controller 940 and movable member 950a establish a fluid fl ow path between inlet port 921 of dial 945 and first sample reservoir 980, as indicated by arr ow SS in FIG. In addition, flow of bodily fluids through movable member 950 a causes flow m etering mechanism 967 to rotate relative to movable member 950 . Thus, rotation of flow met ering mechanism 967 may be usable in determining the volume of bodily fluid sample transfer red to sample reservoir 980 . Additionally, display 975 ′ can present information received from flow control mechanism 967 related to, for example, the volume of bodily fluid transferred to sample reservoir 980 . Therefore, a precise volume of bodily fluid can be transferred to the sa mple reservoir 980 . For example, in some cases, collection device 900 is used to collect three sample volumes of 20 mL each in first sample reservoir 980, second sample reservoir 980', an d third sample reservoir 990 (i.e., a total of 60 mL of sample volume is collected).

[0128]

[1181] Once a desired volume of bodily fluid (eg, a second amount) has been collected in the first sample reservoir 980, the user releases the movable member 950 to cause the biasing m ember (not shown) to It can be allowed to move back to the first position. When movable me mber 950 returns to its first position, piercing member 955 is removed from first sample reser voir 980 and a seal (eg, a self-sealing membrane) fluidly disconnects first sample reservoir 98 0 from internal flow path 935 . isolate to Using the collection device 900, transfer the second sample volume to the second sample reservoir 980' and the third sample volume to the third sample by rotating the dial 945 to its third, fourth and fifth positions, respectively. A fourth sa mple volume can be similarly transferred to reservoir 990 to fourth sample reservoir 990'.

[0129]

[1182] In some cases, the fluid collection device 900 allows the clinician and/or phlebotomist to open the package containing the fluid collection device 900, remove only the housing 901 (including the dispensing member 929), and remove the housing 901. It can be carried by the patient's bedside. The clinician and/or phlebotomist performs a venipuncture (or employs any other method of accessing the patient's bodily fluids) into a portion of the patient's body (e.g., a vein) using any standardized technique be able to. Following venipuncture, the clinician an d/or phlebotomist can collect the total blood volume required for all samples. For example, a c linician and/or phlebotomist can collect a 2.5 mL pre-sample diversion volume and a 10 mL sa mple volume for each of the four sample reservoirs, whereby the collected bodily fluid (e.g., 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 plac ed on top of 4-pack (or 2-pack) pre-sterilized sample reservoirs with the membrane tops pre-placed in custom trays that match the shape of housing 901. By using such pre-sterilized pack s of sample reservoirs, the clinician does not have to perform the process step of "wiping" the sample reservoir tops with a sterilant, thereby, for example, sterilizing the reservoir tops. Red uced potential for contamination if inappropriate and/or insufficient. A clinician and/or phlebot omist can then trigger automatic inoculation of a sample reservoir containing bodily fluid with precise volume control. In some embodiments, after inoculation of the sample reservoirs is co mplete, the entire device 900 with volume information displayed for each individual sample re servoir can be sent to a laboratory for analysis. In other embodiments, sample reservoirs 980 and/or 990 are individually

[1183

] The collection device 900, with reference to FIGS.

Although shown and described as including 975 and 975', in other embodiments the collection device can include any suitable flow metering mechanism with any suitable output indicator. F or example, Figures 54 and 55 show a flow diverter 1020 and a flow controller 1040 according to embodiments. Flow diverter 1020 and flow controller 1040 may be substantially similar in f orm and function to flow diverter 920 and flow controller 940, respectively. Accordingly, simila r parts will not be described further herein. However, flow diverter 1020 and flow controller 10 40 may differ in the placement of set of displays 1075 . For example, flow diverting mechanis m 1020 includes housing 1001 configured to movably receive a set of movable members 1050 a, 1050b, 1050c and 1050d, each of which can include a flow metering mechanism, as describ ed above with respect to movable member 950. include. Accordingly, movable members 1050 a, 1050b, 1050c and 1050d can be used to determine the precise volume of bodily fluid that i s transported through them. As shown in FIG. 55, the display 1075 of the housing 1001 provi des a first illumination for a small volume (eg, 5 mL), a second illumination associated with an intermediate volume (eg, 20 mL), and an acceptable and/or large volume. A set of three light s can be included, including a third light associated with (eg, 40 mL). In this manner, when th e flow of bodily fluid is transferred through the flow controller 1040 and the flow diverter mec hanism 1020, for example into the first movable member 1050a, the flow metering mechanis m contained therein can send a signal or the like to the display. , the display is operable to illu minate the first light, the second light and/or the third light according to the volume of bodily fluid transferred through the movable member 1050 .

[0131]

[1184] In other embodiments, movable members 1050a, 1050b, 1050c, and 1050d can be m oved from a first position to a second position, a third position, or a fourth position relative to housing 1001 . In such embodiments, their positions can be associated with, for example, the

intended volume of bodily fluid to be transferred to the sample reservoir. For example, in som e embodiments, a user can actuate (eg, move) movable member 1050a from its first position to its second position. In such embodiments, the second position can be associated with, for e xample, a small volume (eg, 10 mL) of bodily fluid to be transferred to the sample reservoir. I n some embodiments, housing 1001 and/or moveable member 1050a can temporarily hold m oveable member 1050a in a second position until a low volume of sample has been transferre d to the sample reservoir. , locks, fasteners, protrusions, recesses, and the like. Further, when positioned in the second position, display 1075 is configured to illuminate a first illumination a ssociated with the smaller volume to indicate to the user the preset volume of bodily fluid to b e transferred to the sample reservoir. can do. Once a desired volume of bodily fluid has been t ransferred to and fluidly isolated within the sample reservoir, the flow diverter mechanism 102 0 can be configured to automatically return the movable member 1050a to its first position. I n this manner, flow diverter mechanism 1020 and flow controller 1040 can be physically and fl uidly coupled to any number of sample reservoirs and used to transfer precise volumes of bod ily fluid to each sample reservoir.

[0132]

[1185] FIG. 56 is a flowchart illustrating a method 1190 of obtaining a predetermined sample volume of bodily fluid from a patient using a flow metering transfer device. A flow metering tr ansfer device can be any of the transfer devices described herein (also referred to herein as a "collection device"). By way of example, in some embodiments the transfer device can be the collection device 900 described above with reference to FIGS. 46-53. Thus, the transfer devic e includes an inlet port configured to be selectively placed in fluid communication with a patie nt, a pre-sample reservoir and a sample reservoir, and fluid flow from the patient to the pre-s ample reservoir and to the sample reservoir. and a flow metering mechanism configured to m eter the flow of bodily fluid. The method 1190 includes, at 1191, establishing fluid communica tion between a patient and a port of a flow metering transfer device. For example, the port m ay be connected to a needle or other lumen-defining device (e.g., a flexible

A needle or other lumen-defining device can be inserted into the patient's body (eg, a venipun cture event or other method of accessing bodily fluids).

[1186

] With the port in fluid communication with the patient, at 1192, fluid communication is establ ished between the port and the pre-sample reservoir. In some embodiments, the flow meterin g transfer device can include a flow controller or the like (eg, flow controller 940 included in c ollection device 900) that provides fluid communication between the port and the pre-sample reservoir. It can be actuated and/or manipulated (eg rotated) to an established position (eg fir st position). In some embodiments, actuation of the flow controller may cause the flow contro ller and flow diversion mechanism to collectively define at least a portion of a fluid flow path b etween the port and the pre-sample reservoir. In some embodiments, the pre-sample reservoi r can include negative pressure or the like that can initiate the flow of bodily fluid from the pat

ient to the pre-sample reservoir. In other embodiments, bodily fluid flow can be initiated in an y other suitable manner (eg, gravity, etc.).

[0134]

[1187] At 1193, the flow of bodily fluid transferred from the patient to the pre-sample reservo ir is metered. For example, in some embodiments, the port has a flow control mechanism that can meter the flow of bodily fluid through the port (eg, in a manner similar to that described a bove with respect to flow control mechanism 967 of collection device 900). can contain. Thus, a pre-sample volume of bodily fluid is transferred to the pre-sample reservoir. The method 11 90 includes, at 1194, verifying, via the flow metering mechanism of the flow metering transfer device, that the pre-sample volume of bodily fluid disposed within the pre-sample reservoir is a predetermined pre-sample volume of bodily fluid. For example, the flow metering mechanis m can include and/or be operably coupled to a display or the like (eg, display 975 and/or 975′ of collection device 900). The flow metering mechanism can be configured to present volumet ric information on a display, as described above.

[0135]

[1188] Once the pre-sample volume of bodily fluid is disposed within the pre-sample reservoi r, at 1195, the pre-sample reservoir is fluidly isolated from the port to seal the pre-sample vol ume of bodily fluid within the pre-sample reservoir. For example, in some cases, the flow cont roller and/or flow diverter mechanism can be actuated (or rotated) from a first position and/or configuration to a second position and/or configuration. When the flow controller and/or flow diverter mechanism are in the second configuration, the pre-sample reservoir is fluidly isolate d from the space outside the pre-sample reservoir. In some embodiments, when the flow cont roller and/or flow diversion mechanism is driven to its second position and/or configuration, at 1196 fluid communication is established between the port and the sample reservoir. For exam ple, in some embodiments, the flow metering transfer device can include a piercing member (e.g., movable member 950) configured to pierce a portion of the sample reservoir (e.g., me mbrane, etc.) etc. Thus, when the flow controller and/or flow diverter mechanism is in its sec ond position and/or second configuration, the perforation of that portion of the sample reserv oir places the sample reservoir in fluid communication with the port. As noted above, the sam ple reservoir can contain, for example, a negative pressure or the like that can initiate the flo w of bodily fluid from the patient to the sample reservoir.

[0136]

[1189] At 1197, the flow of bodily fluid transferred from the patient to the pre-sample reservo ir is metered. For example, as described above, the port may include a flow control mechanis m capable of metering the flow of bodily fluid through the port (eg, in a manner similar to tha t described above with respect to flow control mechanism 967 of collection device 900). can b e done. In some embodiments, the flow control mechanism can be included in a movable me mber, such as, for example, movable member 950 in FIG. A sample volume of bodily fluid is t hus transferred to the sample reservoir. The method 1190 includes, at 1198, removing the bo

dy disposed within the sample reservoir via the flow metering mechanism of the flow meterin g transfer device.

This includes verifying that the sample volume of liquid is a predetermined sample volume of volume. For example, as described above, a display or the like can be configured to present v olumetric information.

[0137]

[1190] In this manner, a predetermined pre-sample volume of bodily fluid is collected, which may include, for example, externally present microorganisms. For example, in some embodim ents, the predetermined pre-sample volume is about 0.1 mL, about 0.3 mL, about 0.5 mL, ab out 1.0 mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, It can be about 5.0 mL, about 10 mL, about 20 mL, about 50 mL, and/or any volume or volume fraction value therebetween. In oth er embodiments, the pre-sample volume can be greater than 50 mL or 0.1 mL. In other embo diments, the predetermined pre-sample volume can be between about 2 mL and about 5 mL. In one embodiment, the predetermined pre-sample volume can be approximately 3 mL. Additi onally, by collecting the predetermined pre-sample volume, the predetermined sample volume disposed within the one or more sample reservoirs can be substantially free of externally pres ent microorganisms. In some embodiments, the predetermined sample volume can be betwee n 10 mL and 60 mL. In other embodiments, the predetermined sample volume can be betwee n 30 mL and 60 mL. In still other embodiments, the predetermined sample volume can be 60 mL. Although described above as transferring a sample volume of bodily fluid to a single samp le reservoir, in other embodiments, a flow metering transfer device can be used to transfer a given sample volume to two or more sample reservoirs. For example, in some embodiments, a predetermined pre-sample volume of bodily fluid can be collected in and fluidly isolated with in a pre-sample reservoir, as described above. A predetermined sample volume into a first sa mple reservoir, a predetermined sample volume into a second sample reservoir, and a predete rmined sample volume into a third sample reservoir using a flow metering transfer device whil e the pre-sample volume is fluidly isolated. can be transferred to In such a case, the predeter mined sample volume can be, for example, 20 mL, so that the total sample volume placed in t he first, second and third reservoirs is 60 mL.

[0138]

[1191] Various embodiments of the bodily fluid collection devices described herein enable coll ection of two (or more) sets of bodily fluid (e.g., blood) samples from a single venipuncture. c an do. The current standard of care is to perform some tests (e.g., blood cultures) on separat e, independent samples (e.g., via two separate venipunctures, via catheter + venipuncture, a nd/or combinations thereof). They are asked to do so by obtaining it from a fluid access point. Embodiments described herein can facilitate obtaining multiple samples for a given diagnostic test (e.g., blood culture test) from a single bodily fluid access point (e.g., venipuncture); Ther eby, the annual number of venipunctures required to obtain these samples can be reduced by a factor of two. This is advantageous for both patients and medical personnel alike. Reducing

the number of venipunctures (and/or other blood access procedures) significantly reduces the risk of needlestick injuries to health care workers and reduces patient-related complications resulting from these procedures (e.g., hematoma, thrombosis, phlebitis, infection, etc.) can be reduced. Further, reducing the number of fluid access procedures (eg, venipuncture) reduces the supply utilization, labor and waste associated with these procedures. The cost reductions realized by the healthcare system are significant, 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 t hey have been presented by way of example only and not limitation. Although various embodi ments have been described as including combinations of particular features and/or component s, any combination or sub-combination of any feature and/or component from any of the emb odiments described herein may be described. Other embodiments with combinations are possi ble. For example, with reference to FIGS. 34-40, although collection device 700 is shown and described as having a first, second, third, fourth or fifth configuration, other implementations are possible. In form, the collection devices described herein can have more or fewer forms. F urther, while the collection device 200 is shown and described with reference to FIGS. 2-13 as having a vacuum-assisted collection tube as the pre-sample reservoir 270, in other embodime nts, the collection device 200 includes a dispensing member. The collection device 400 of the embodiment presented in FIGS. 16-22 can have chambers housed in a housing 201 similar to the collection device 400 of the embodiment presented in FIGS. It is possible.

[0142]

[1195] It is also possible to vary the specific arrangement of the various components. For exa mple, the sizes and specific shapes of various components may differ from the illustrated emb odiments while still providing functionality as described herein. More specifically, the sizes and shapes of the various components can be specifically selected for the desired flow rate of bodil y fluid flow into the fluid reservoir. For example, although flow metering mechanism 967 is sp ecifically shown in FIG. 49, any of the collection devices described herein can be used with an y suitable flow metering mechanism. For example, in some embodiments, the collection devic e includes a flow metering mechanism and/or, for example, pressure sensors, voltage sensor s, optical sensors, velocity sensors, flow meters, strain gauges, valves, turbines, floats, displa cement analysis, Density Analysis, Gravimetric Analysis, Optical Analysis, Ultrasound Analysis, Thermal Analysis, Doppler Analysis, Electromagnetic Field (emf) Analysis, Reflection Analysis, Obstacle Analysis, Area Analysis, Venturi Analysis, Coriolis Analysis, Visual Analysis and/or an y other suitable sensor, analysis and/or

(e.g., applying and/or using Boyle's law, the ideal gas law, force calculations (force = mass x acceleration), etc., as examples), other Any mechanism, device or method can be included.

drawing open —

[Fig. 1]

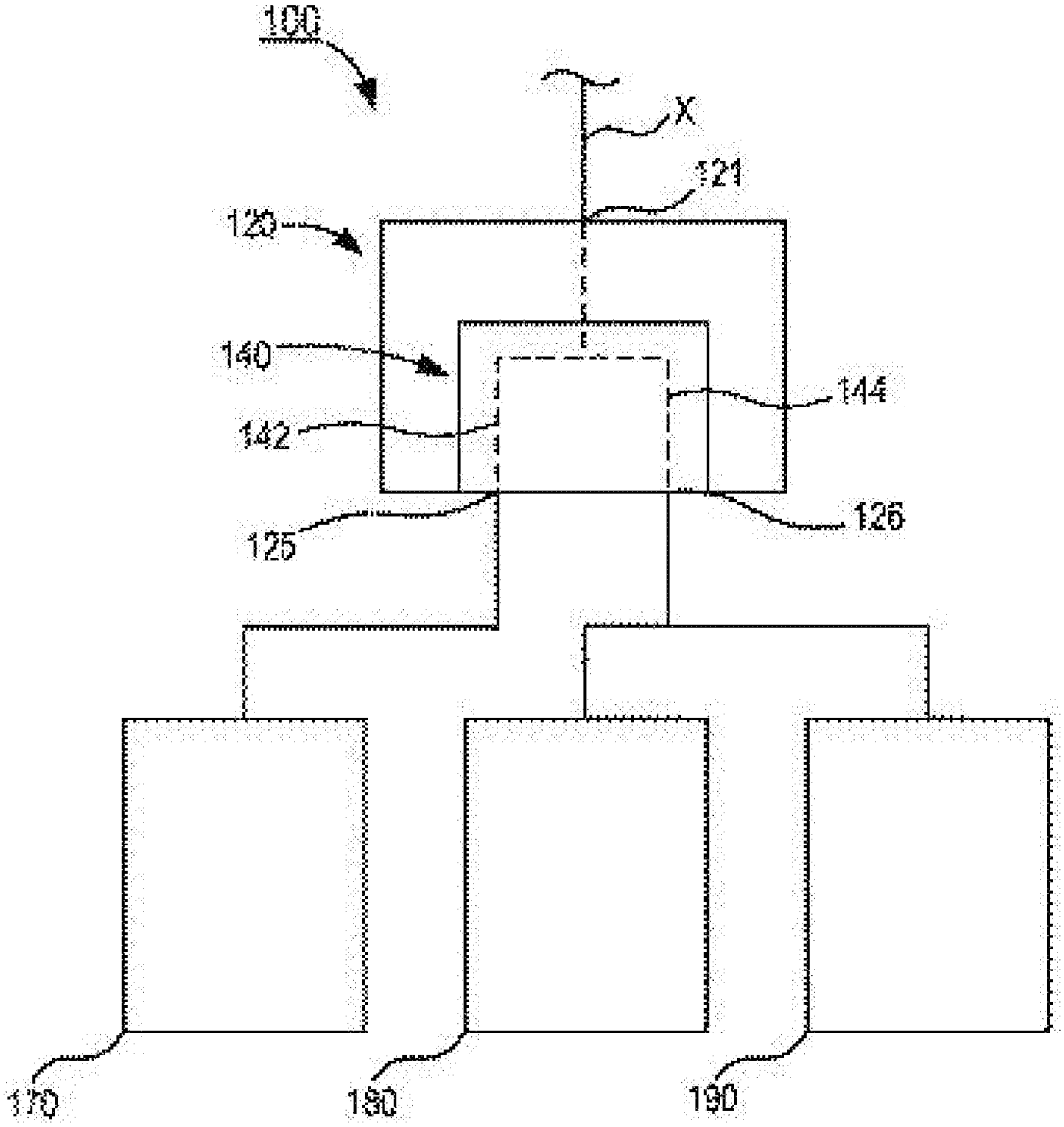


FIG. 1

[Figure 2]

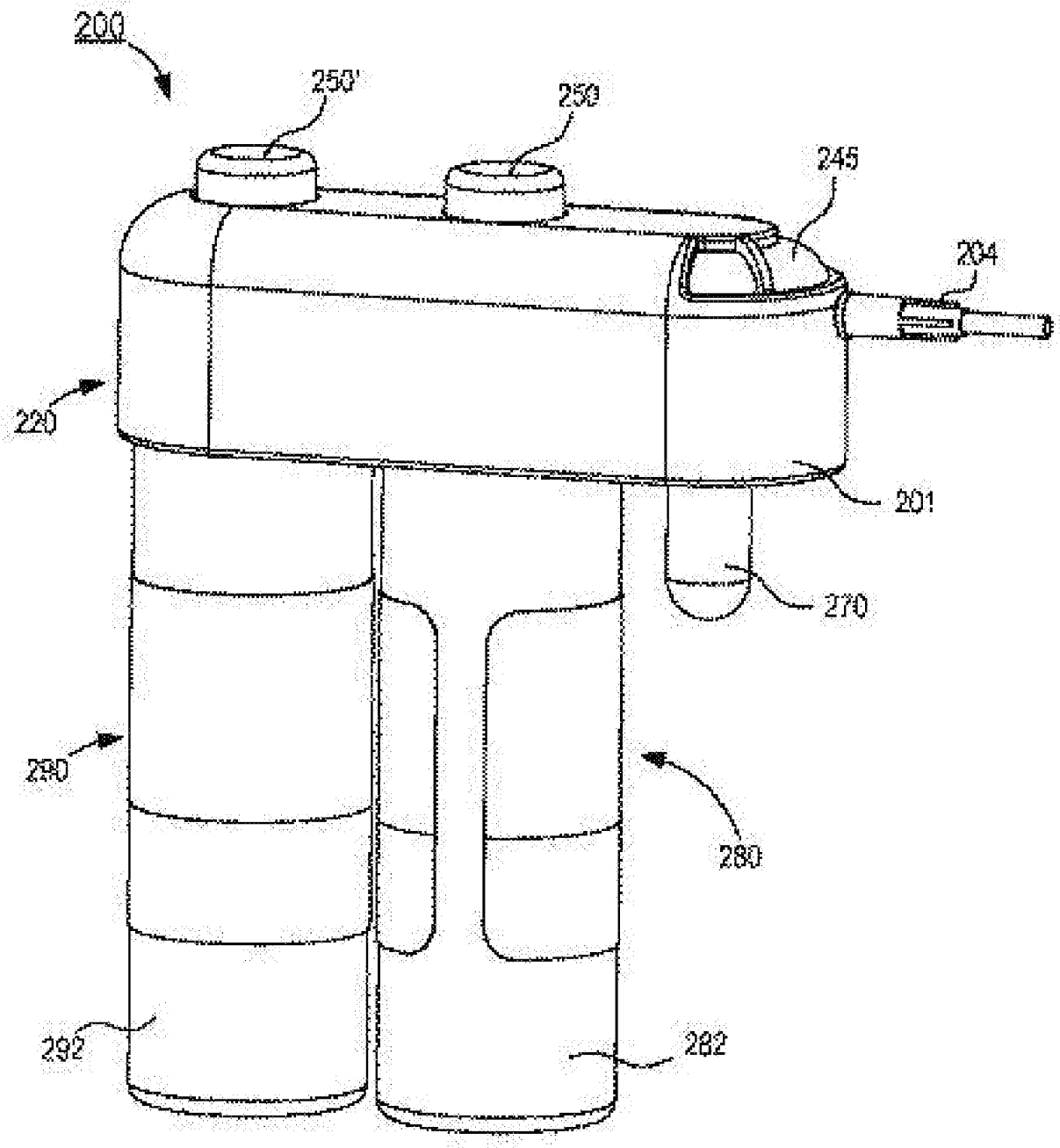
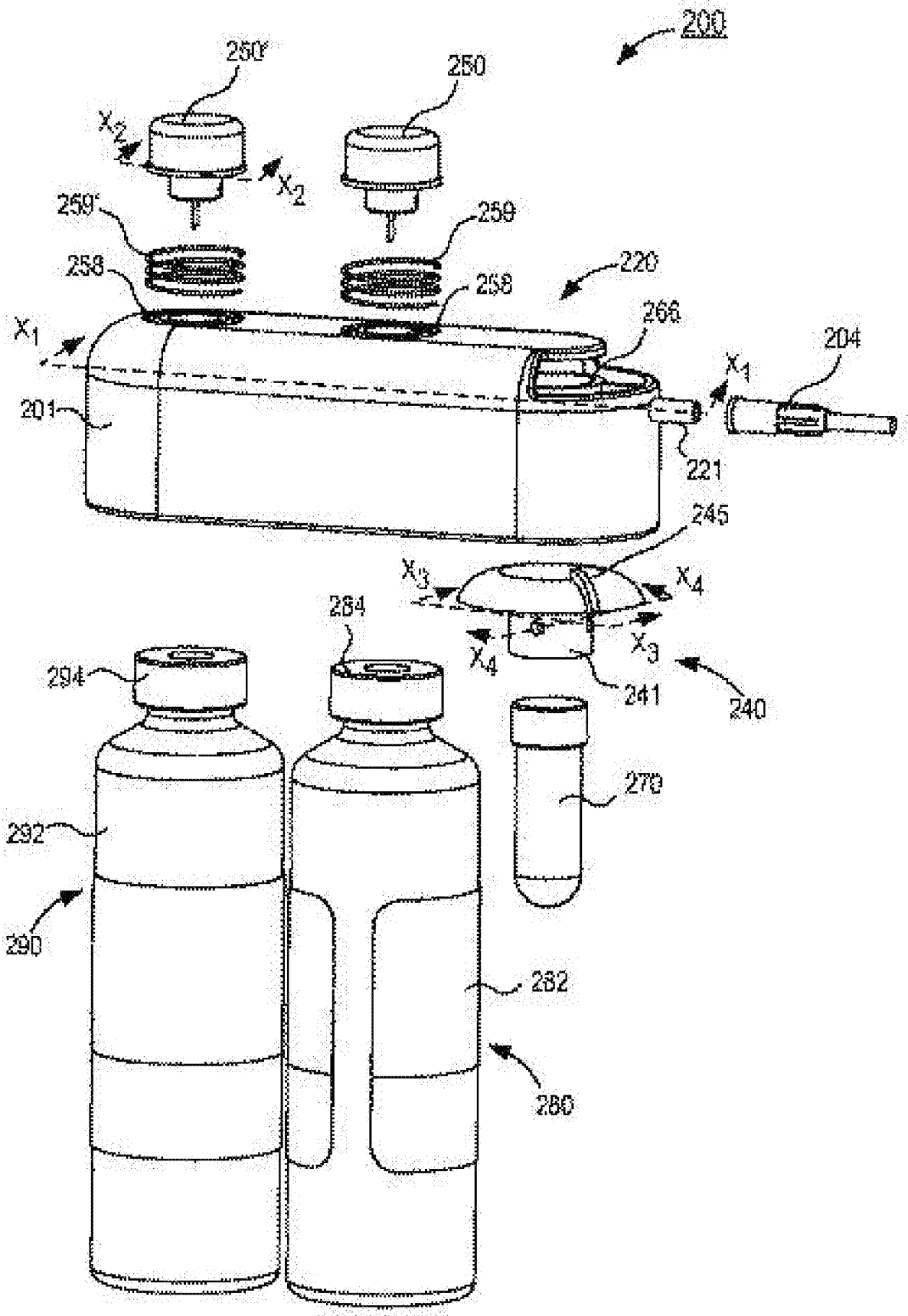


FIG. 2

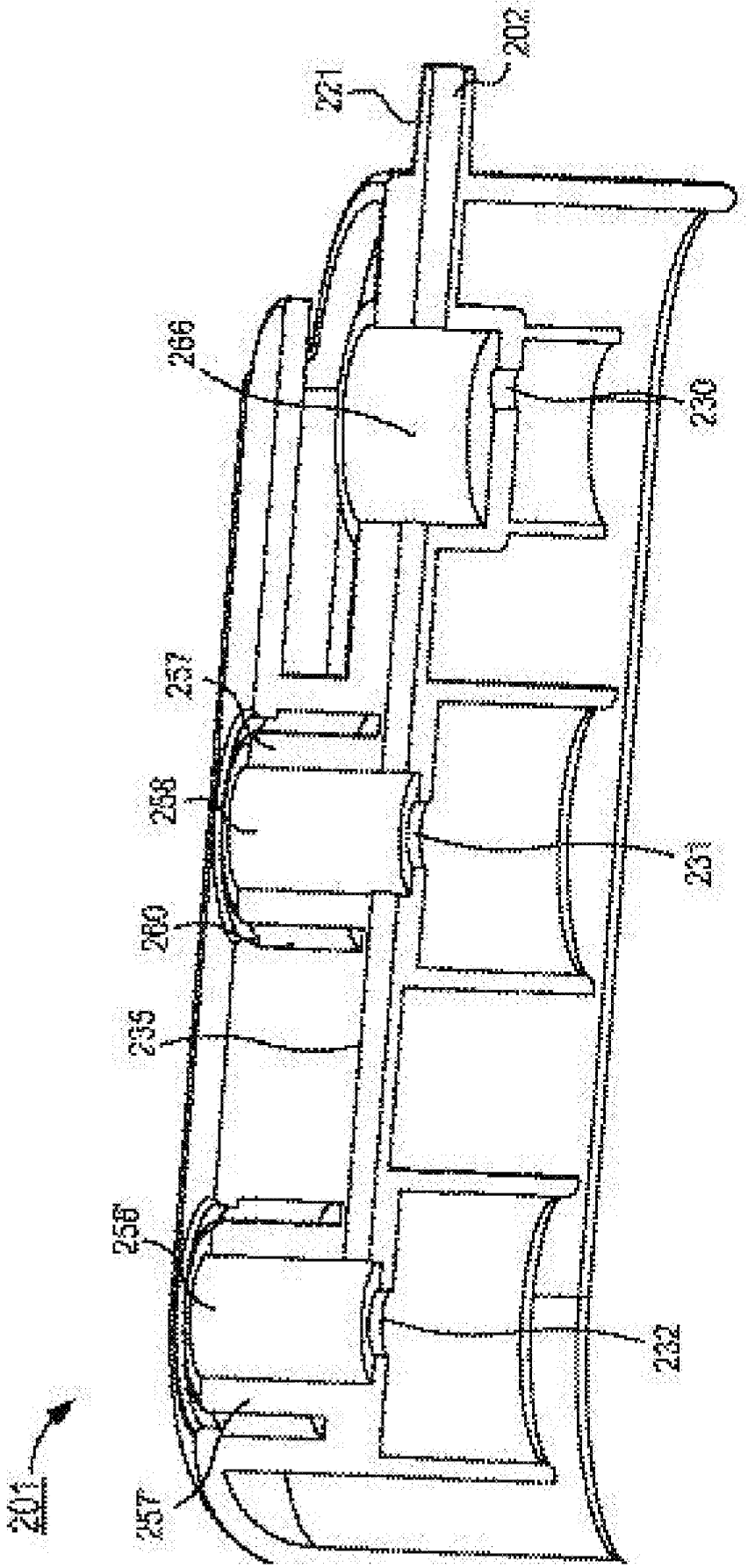
[Figure 3]


200
250'
250
X_2
X_2
259'
259
258
258
220
X_1
266
204
X_1
201
221
245
X_3
X_4
264
X_4
X_3
294
241
240
270
292
290
282
280

[Figure 4]

FIG. 3

FIG. 4



[Figure 5]

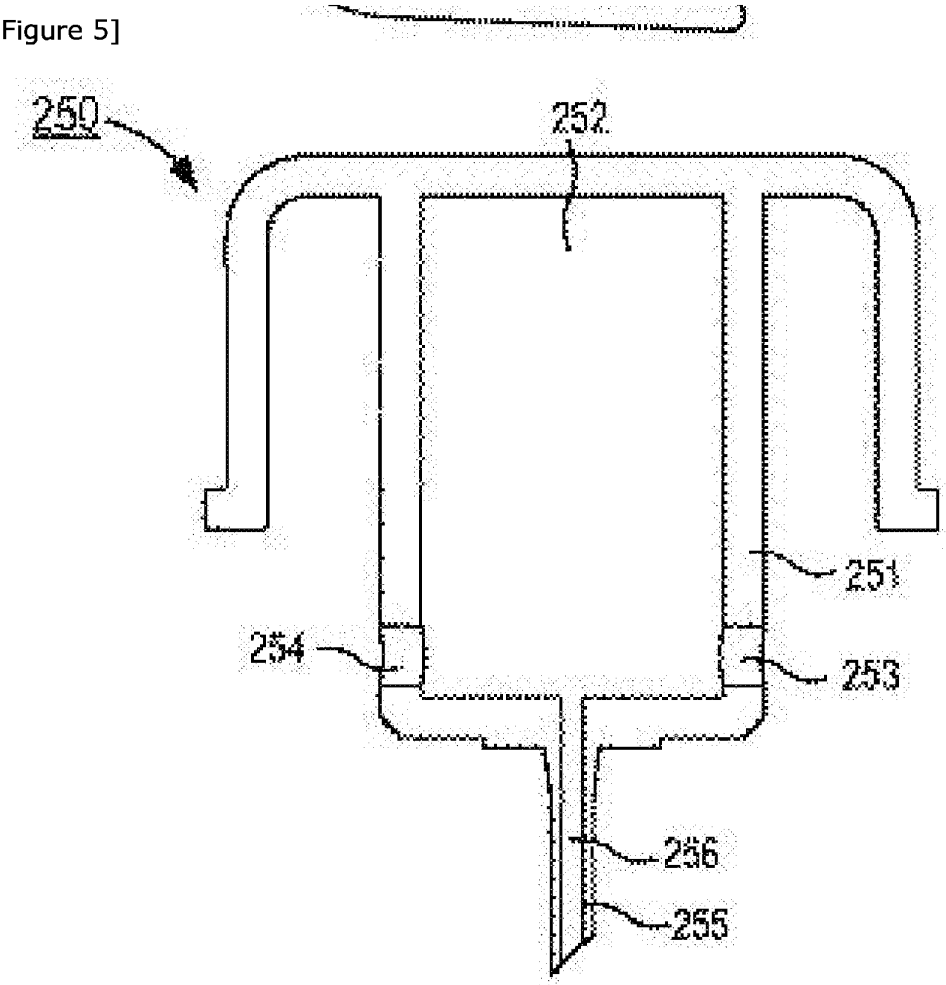


FIG. 5

[Fig. 6]

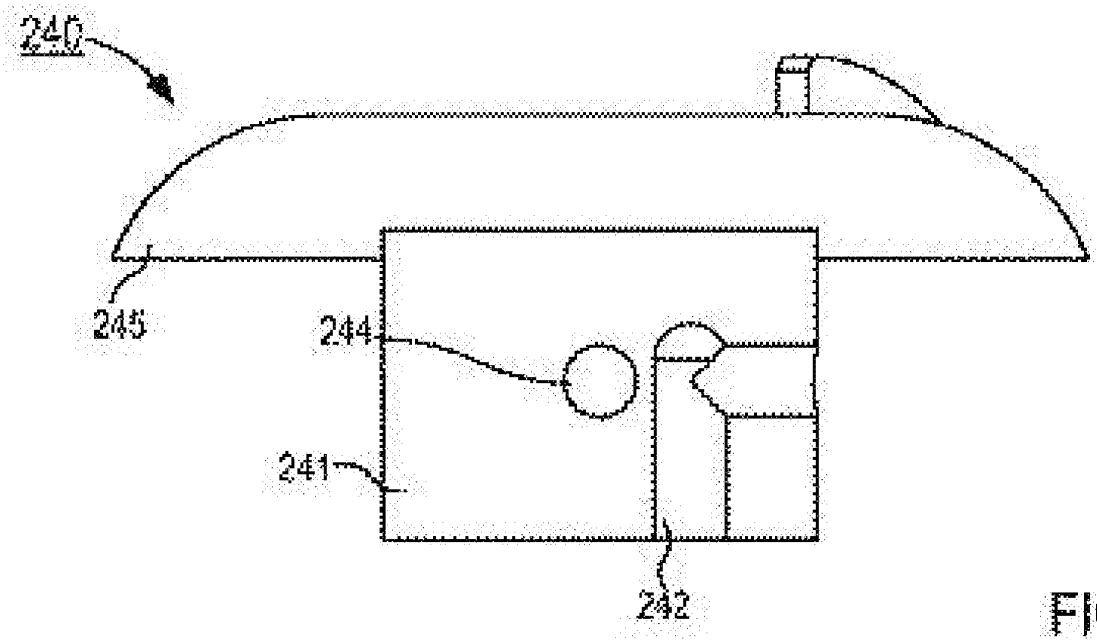


FIG. 6

[Fig. 7]

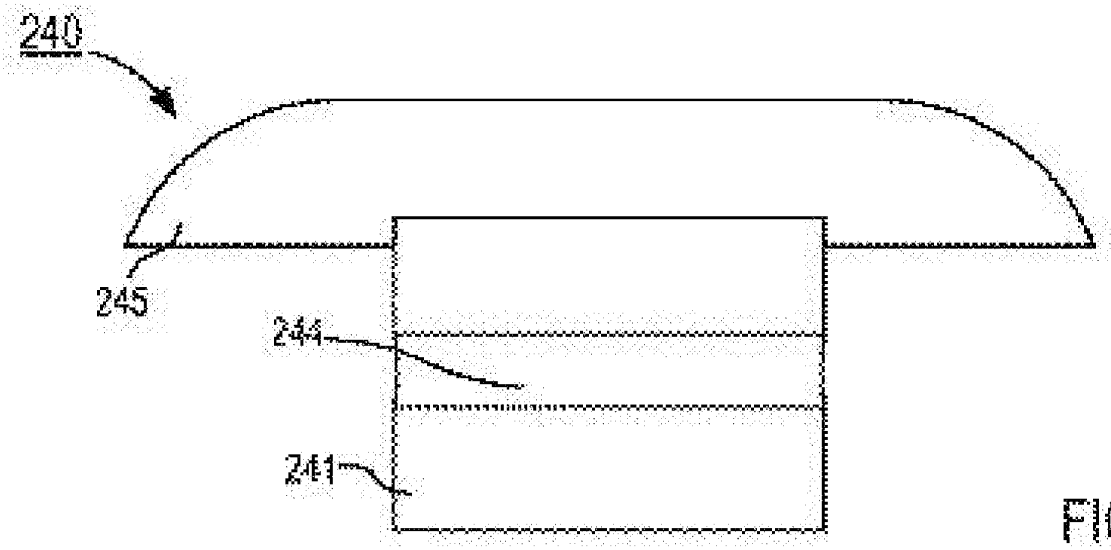


FIG. 7

[Fig. 8]

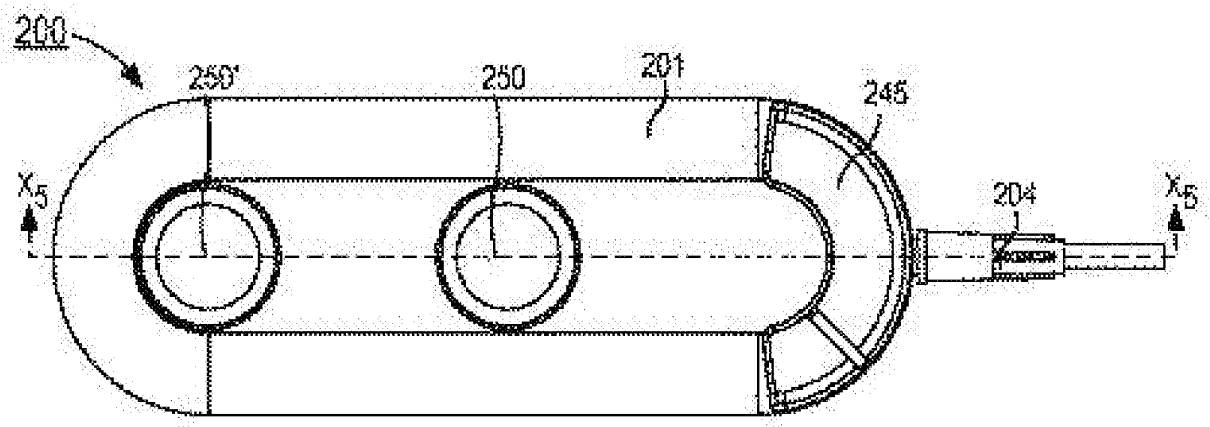


FIG. 8

[Fig. 9]

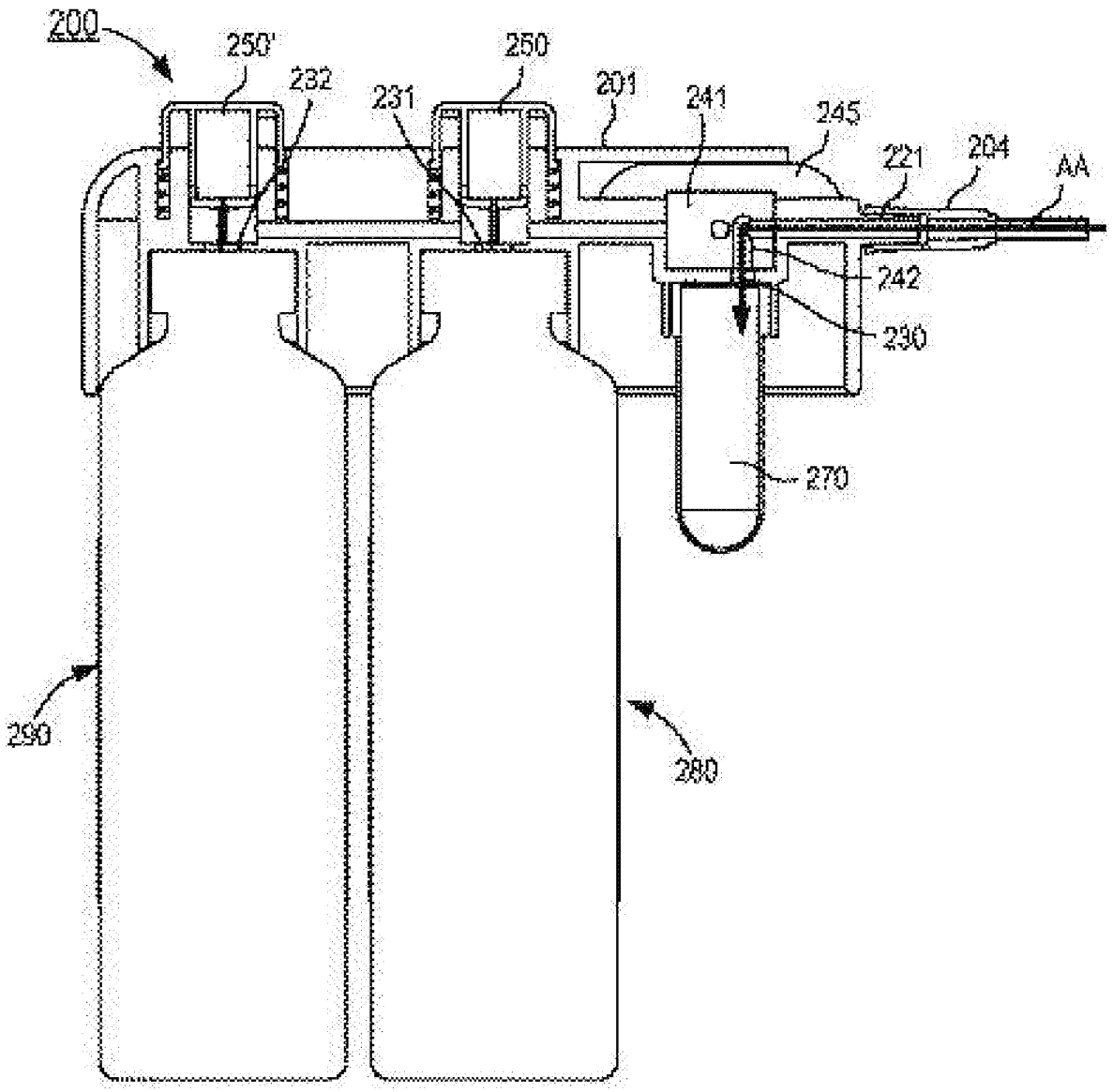


FIG. 9

[Fig. 10]

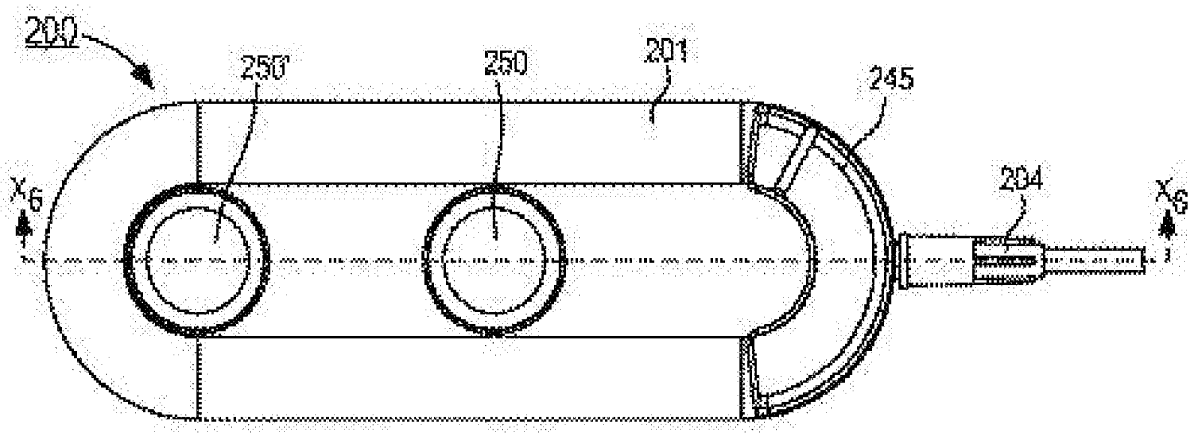


FIG. 10

[Fig. 11]

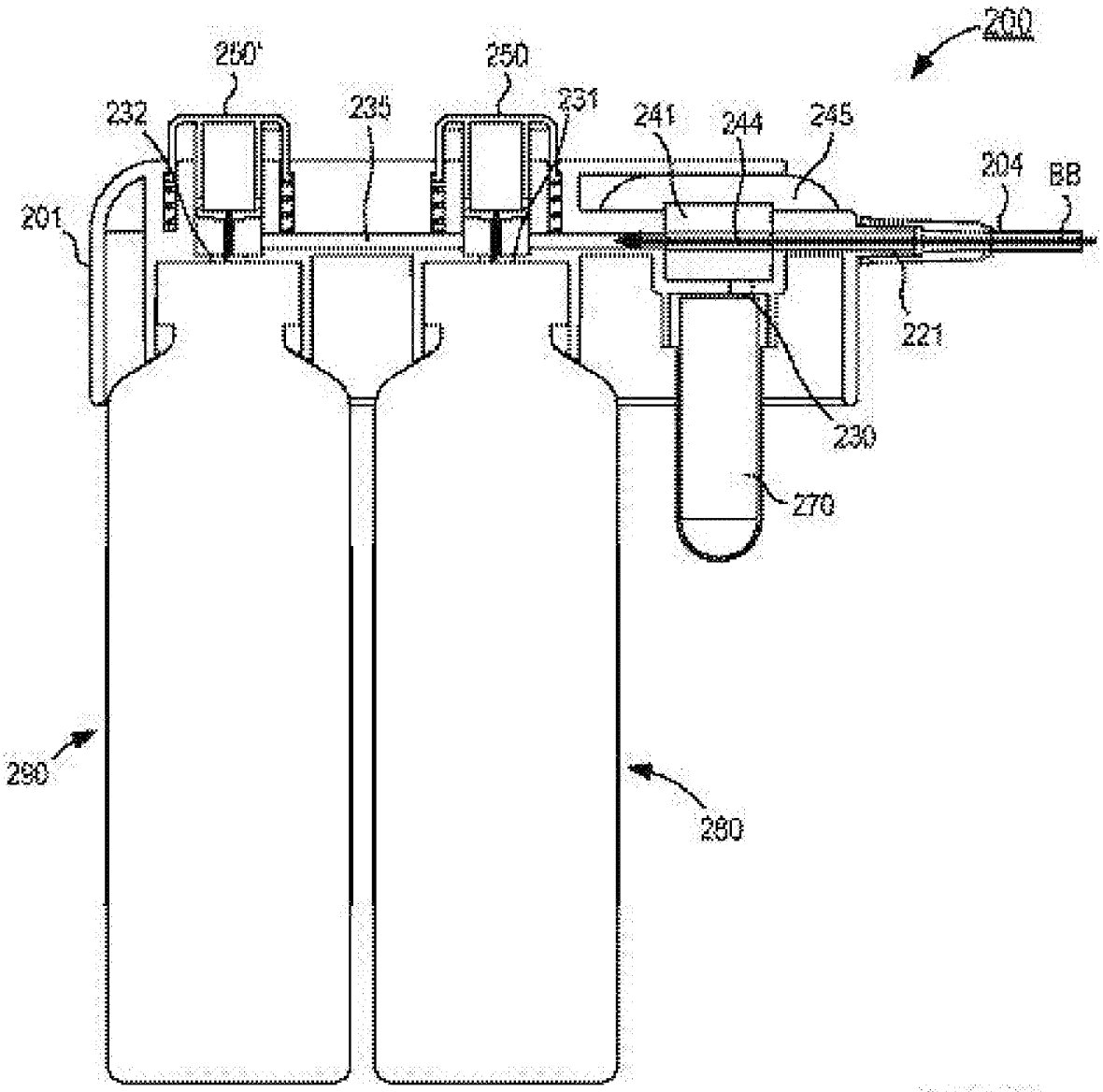

200
250'
250
232
235
231
241
244
245
204
BB
201
221
239
270
280
280

FIG. 11

[Fig. 12]

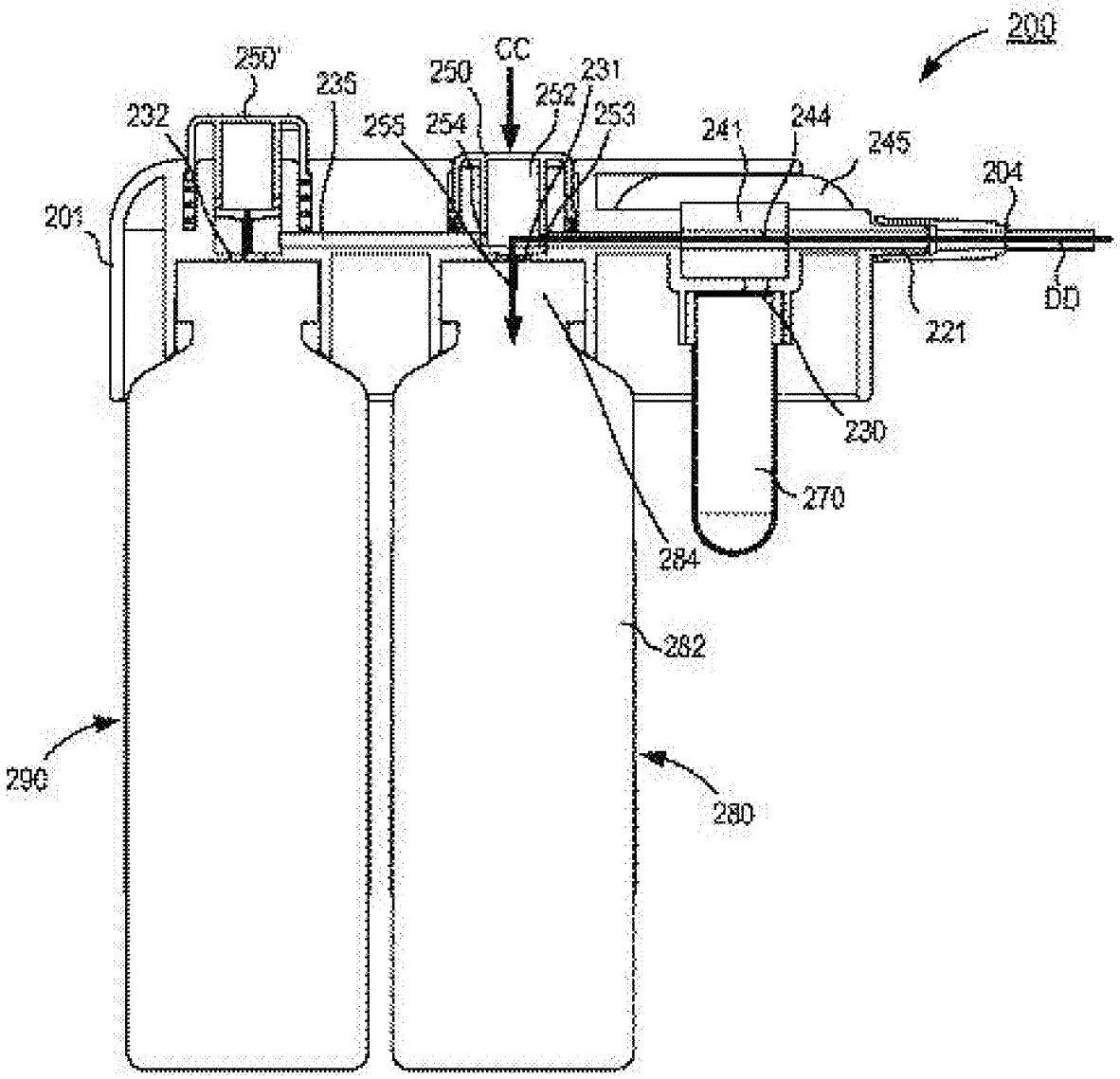

200
250'
236
CC
250
231
232
252
255
254
253
241
244
245
204
201
DD
221
230
270
284
282
290
280

FIG. 12

[Fig. 13]

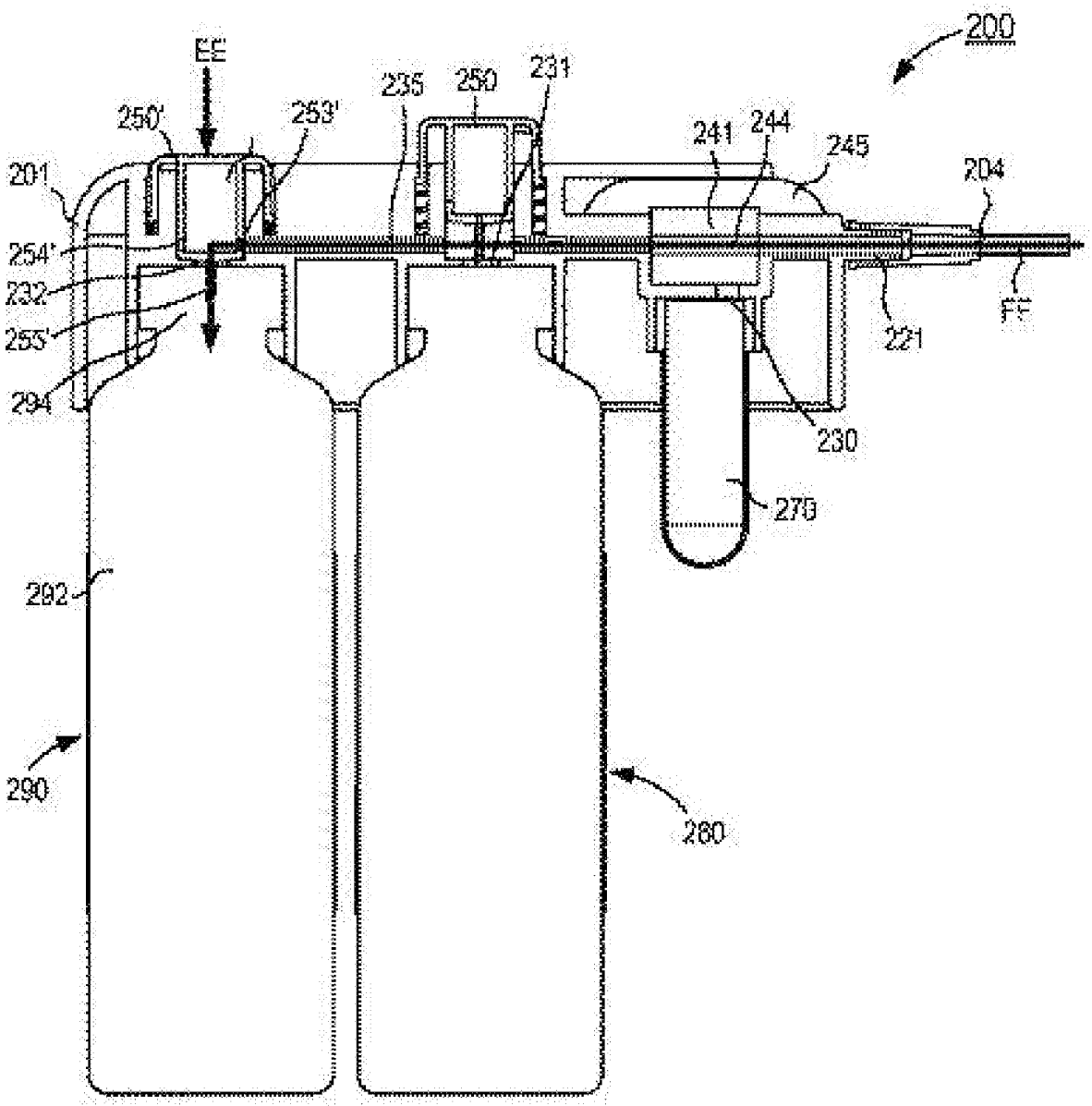

200
EE
250'
253'
235
250
231
241
244
245
204
201
254'
232
255'
294
221
FF
230
270
292
290
280

FIG. 13

[Fig. 14]

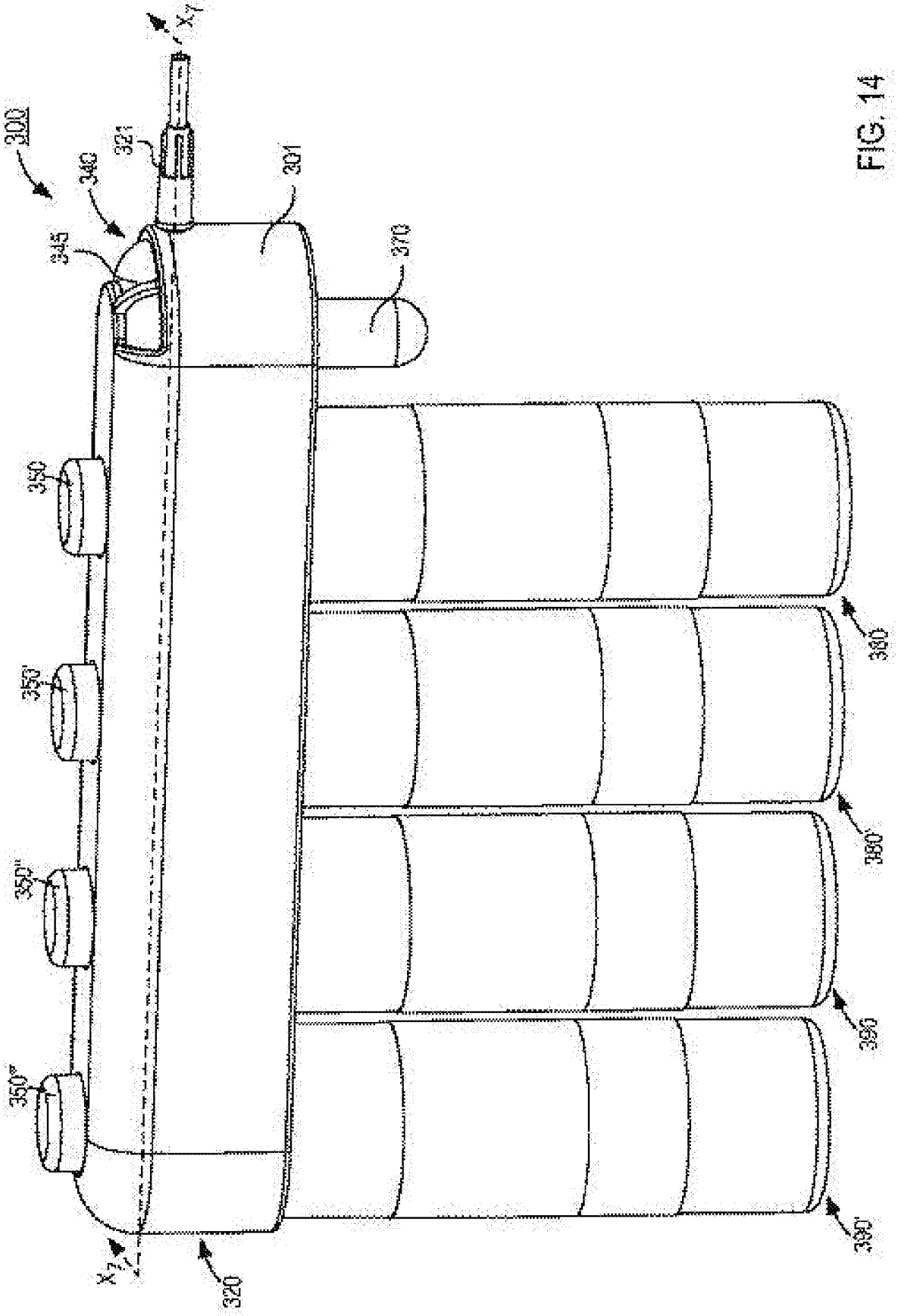
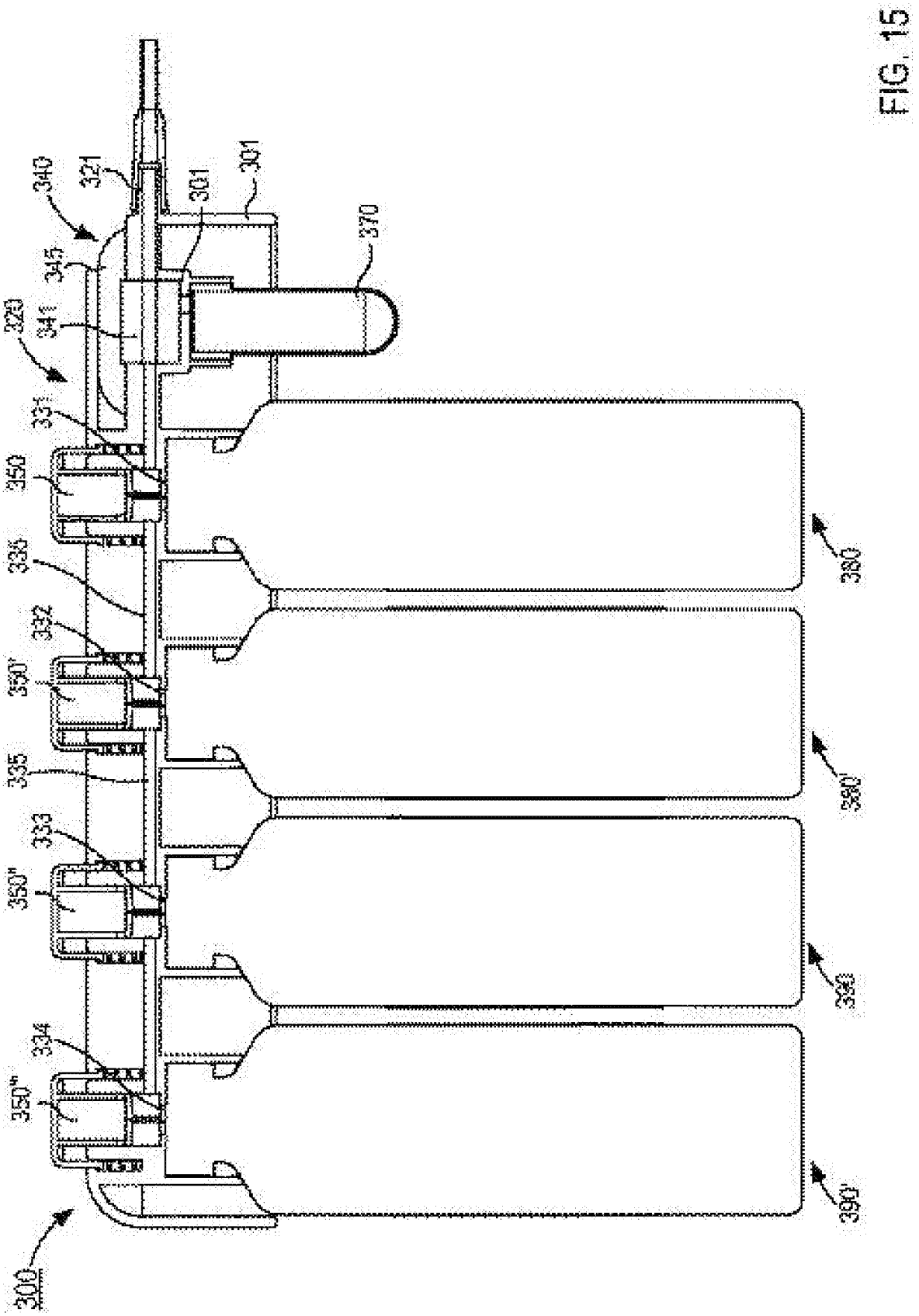
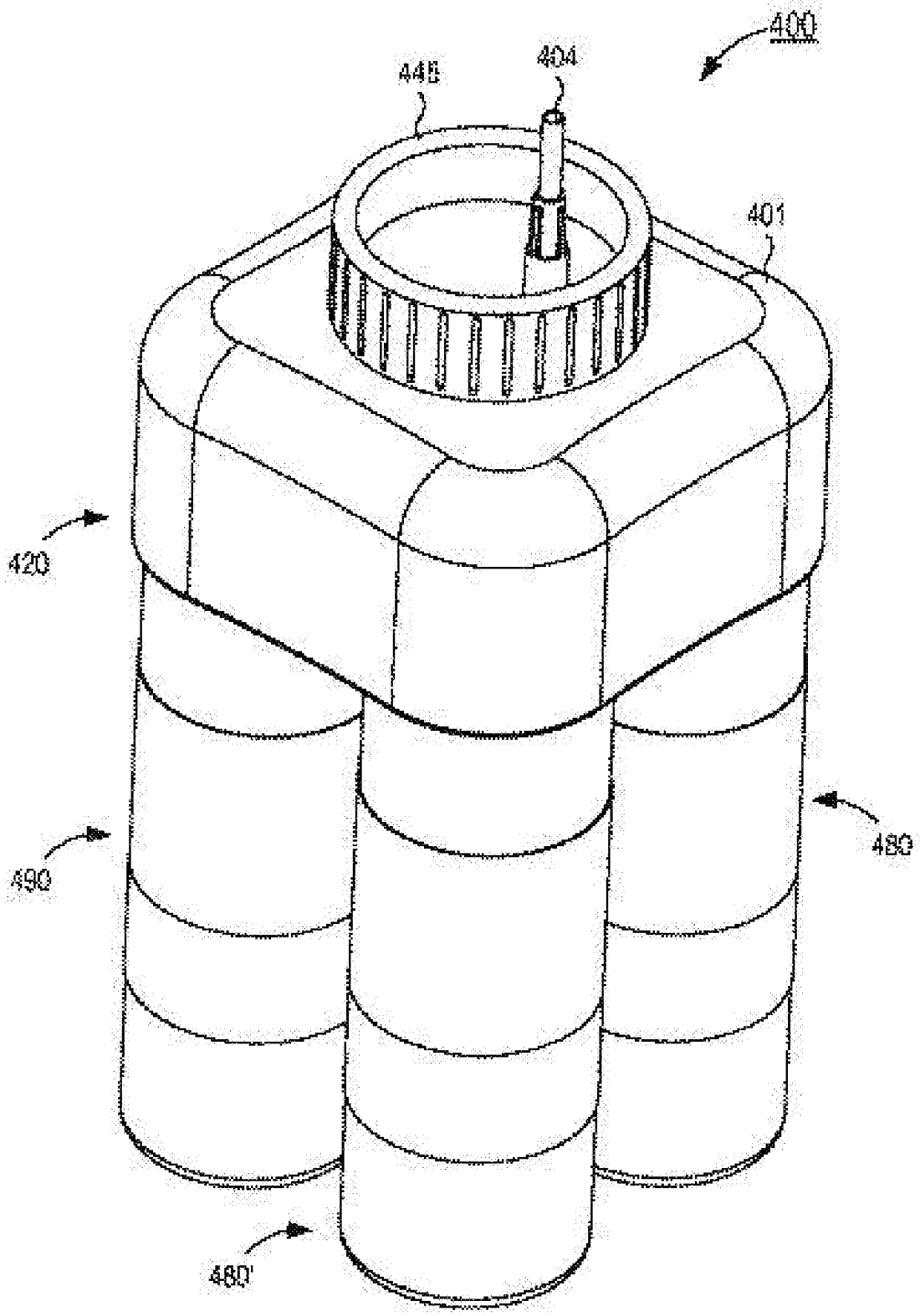


FIG. 14

[Fig. 15]

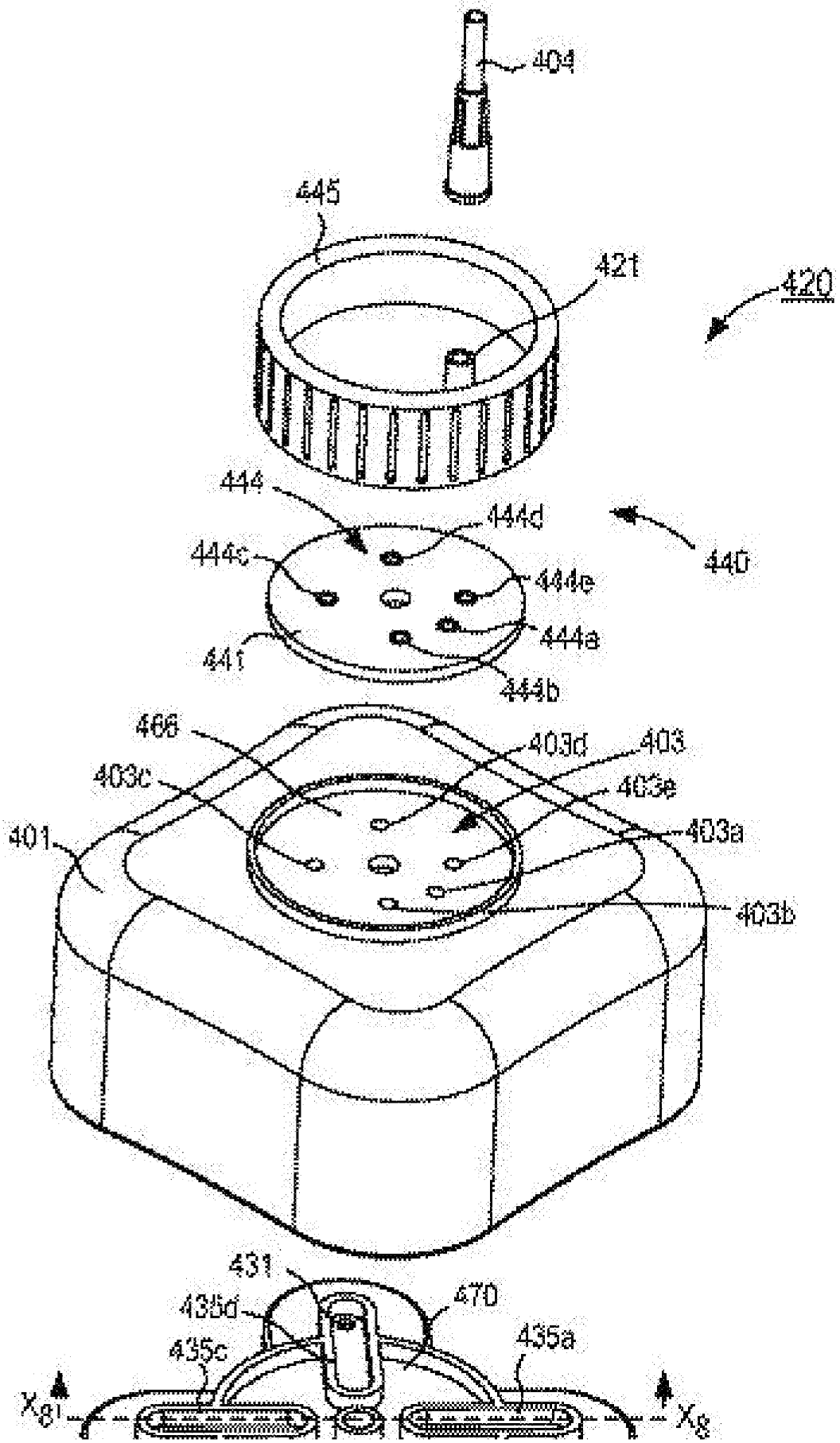

FIG. 15
340
321
301
301
370
345
343
223
333
350
335
332
350'
335
333
350"
334
350"
300
380
380'
380"
390'

[Fig. 16]


400
404
445
401
420
490
480
480'

[Fig. 17]

FIG. 16


404
445
421
420
444
444d
444c
444e
440
444a
441
444b
466
403d
403
403c
403e
401
403a
403b
431
470
435d
435a
435c
X81
X8

[Fig. 18]

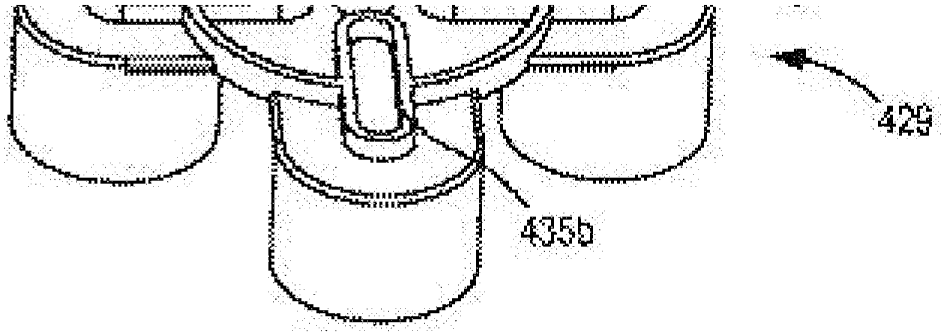


FIG. 17

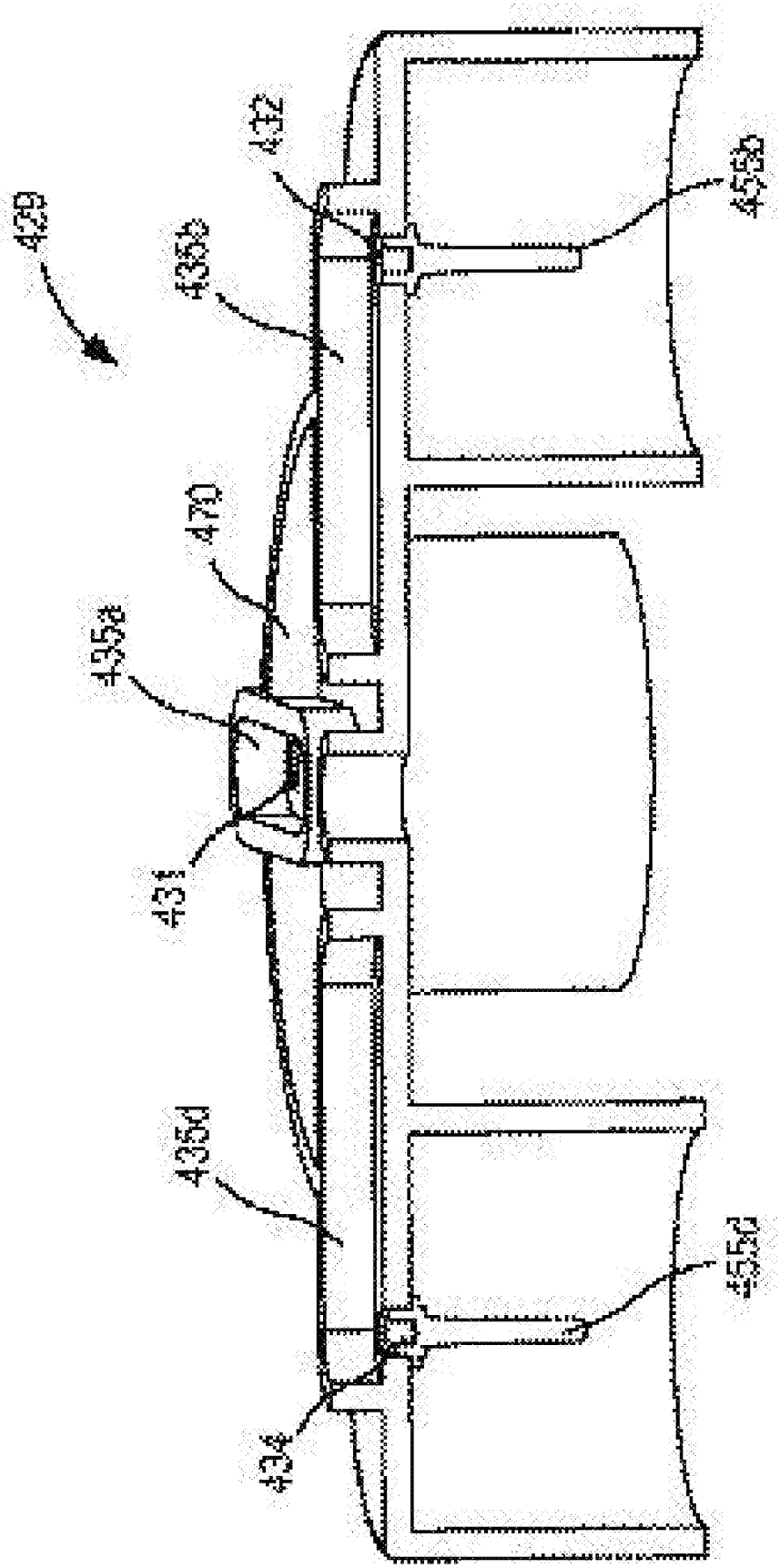


FIG. 18

[Fig. 19]

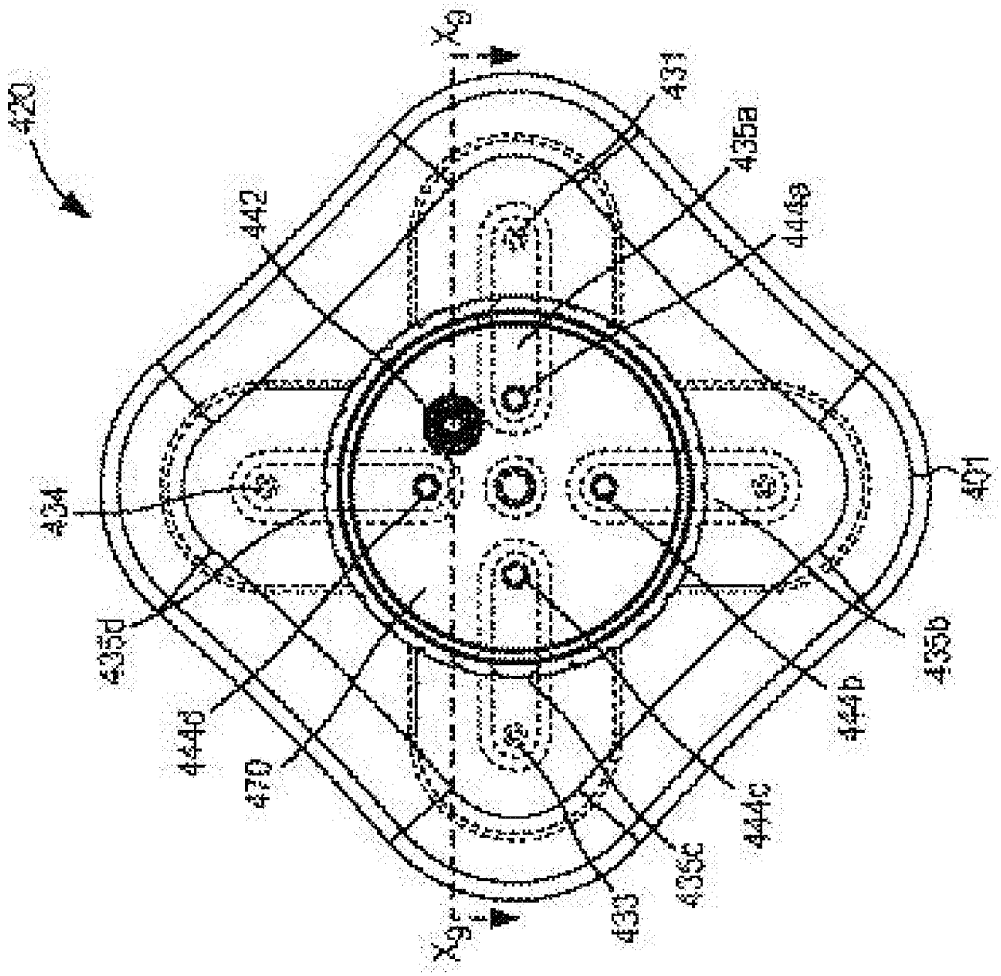


FIG. 19

[Fig. 20]

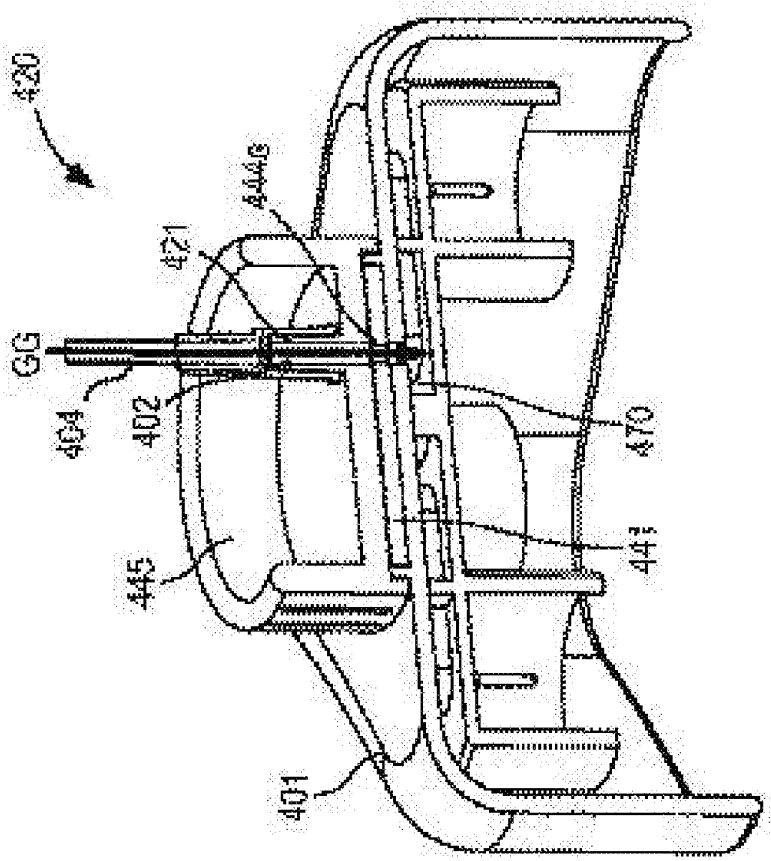


FIG. 20

[Fig. 21]

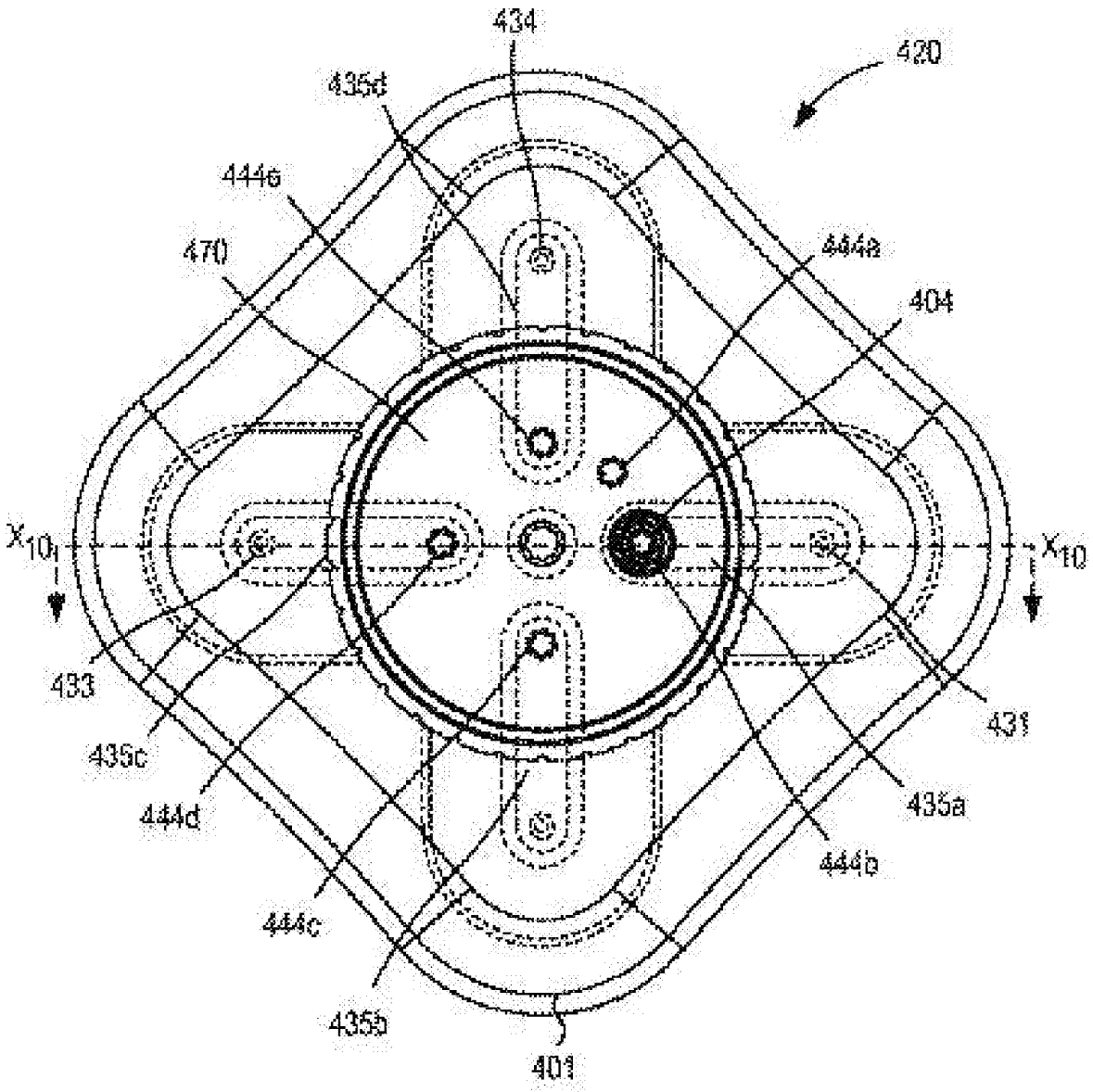
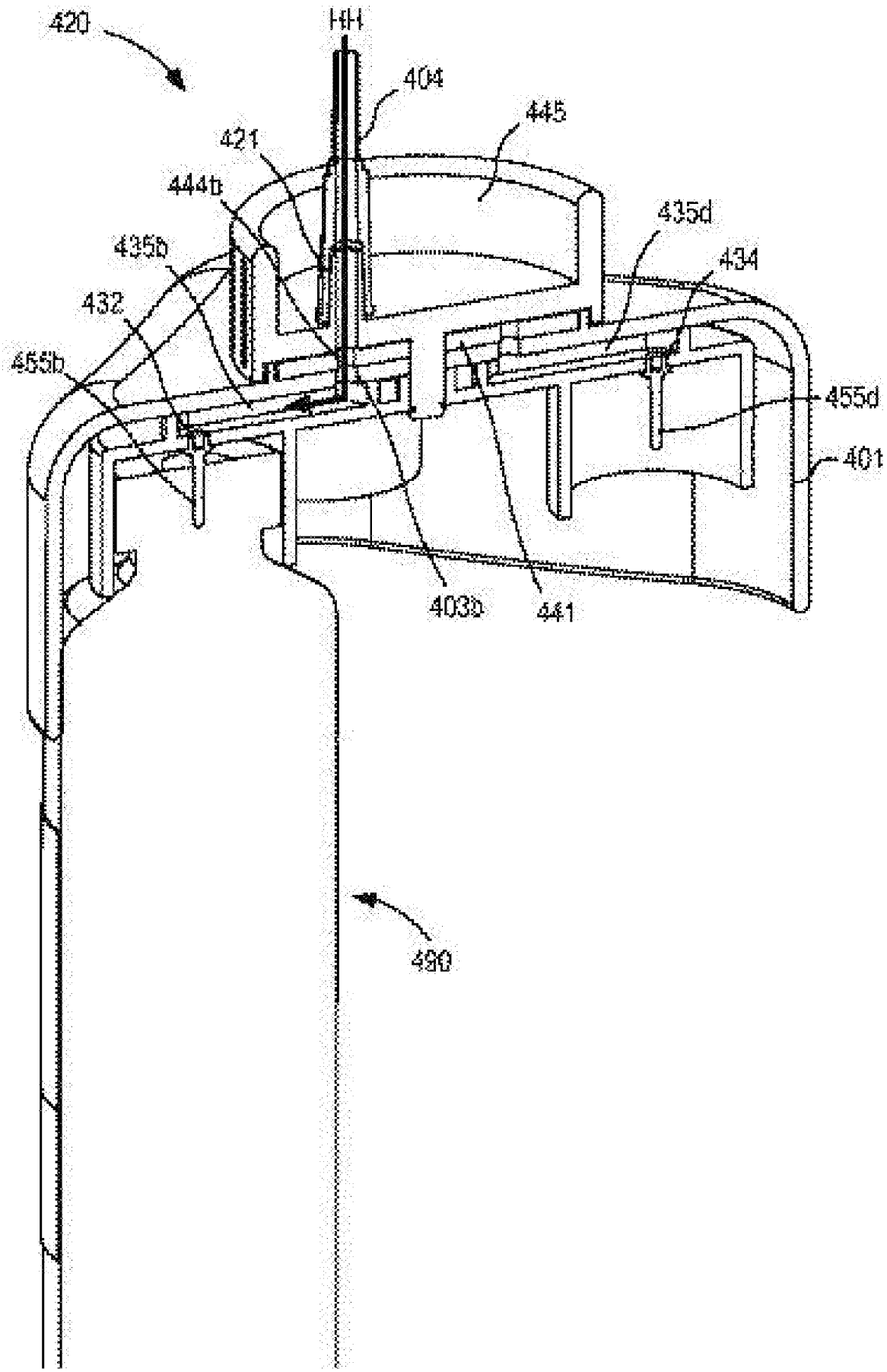

434
420
435d
444e
470
444a
404
X_{10}
X_{10}
433
439c
444d
444c
435b
401
444b
435a
431

FIG. 21

[Fig. 22]


420
HH
404
445
421
444b
435d
435b
434
432
455b
455d
401
403b
441
490

[Fig.23]

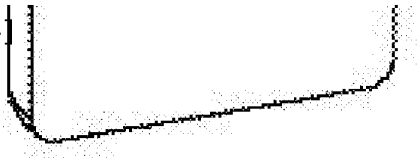
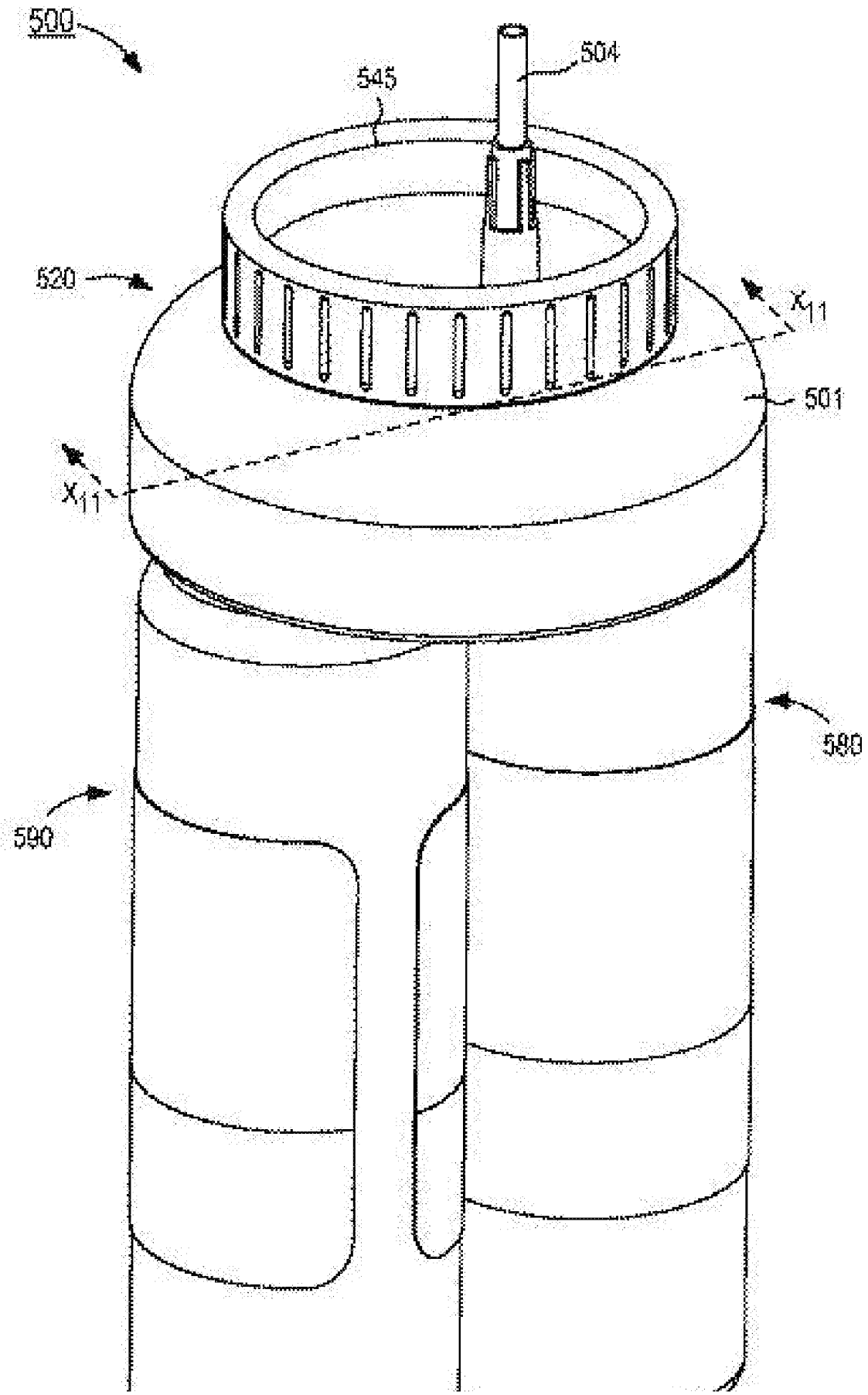


FIG. 22


500
504
545
520
X_{11}
501
X_{11}
590
590

[Fig.24]

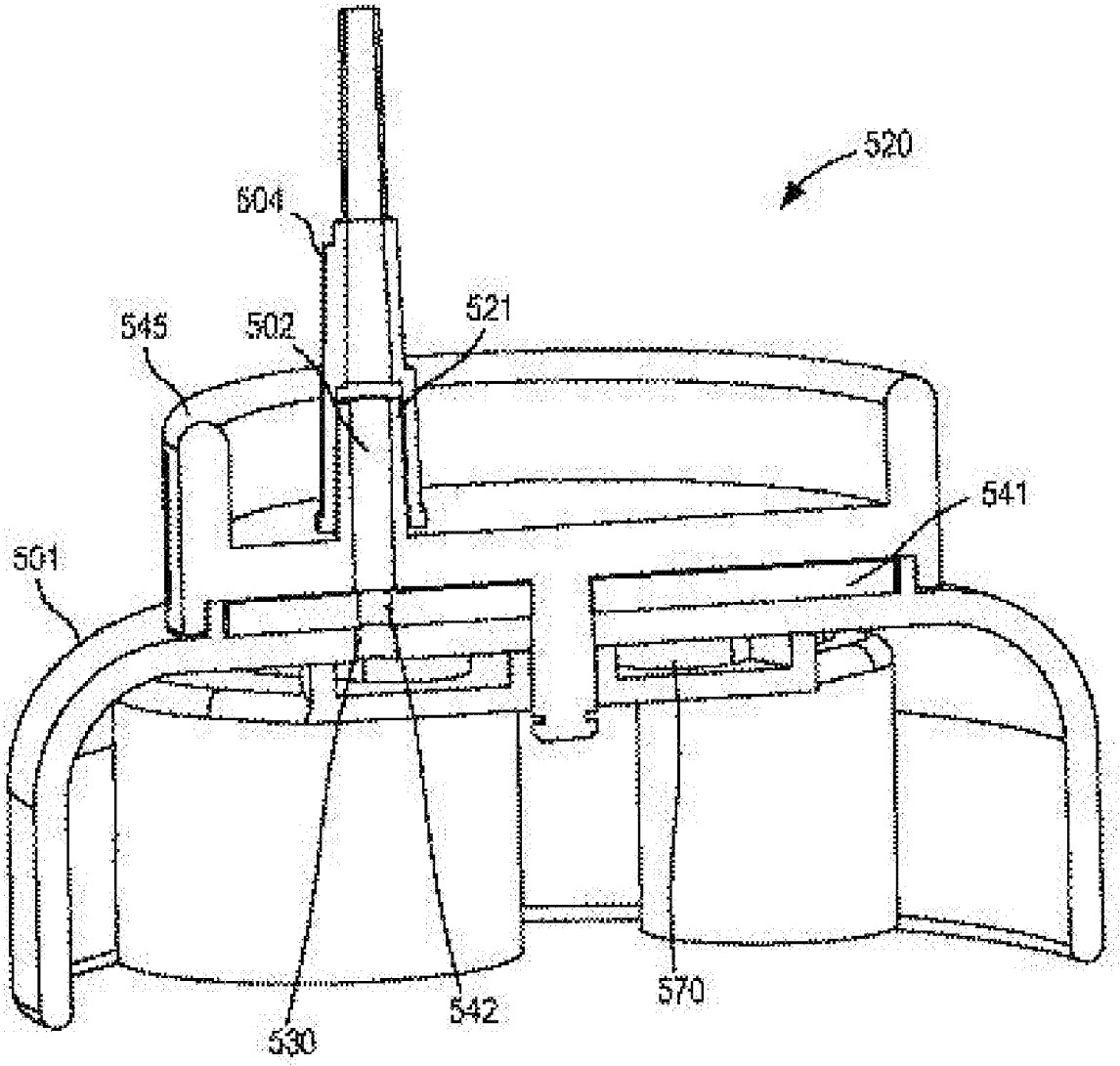
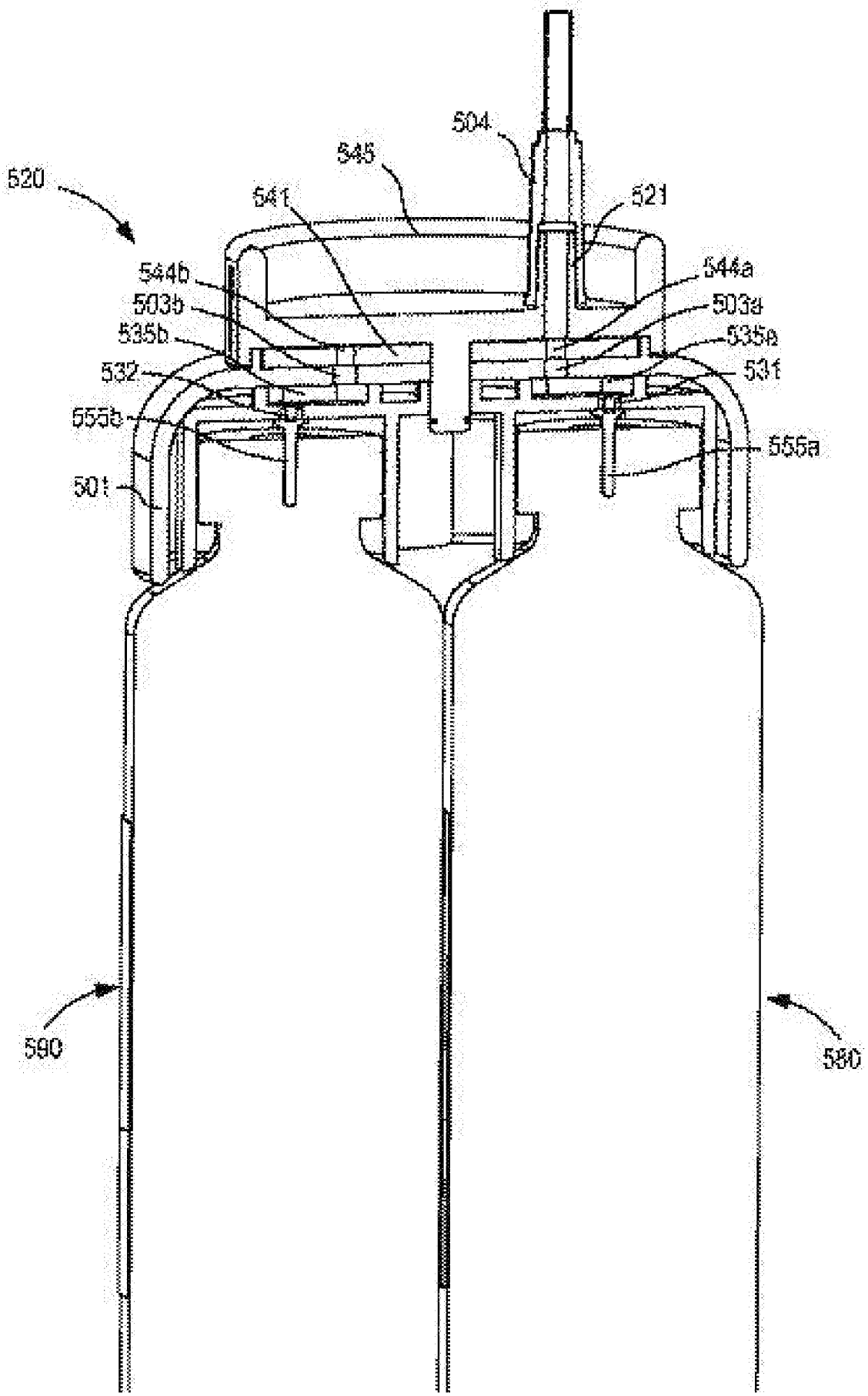


FIG. 24

[Fig.25]


504
545
520
541
521
544b
544a
503b
503a
535b
535a
532
531
555b
555a
501
590
580

[Fig.26]

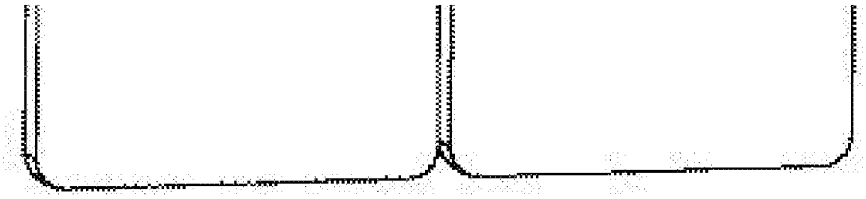
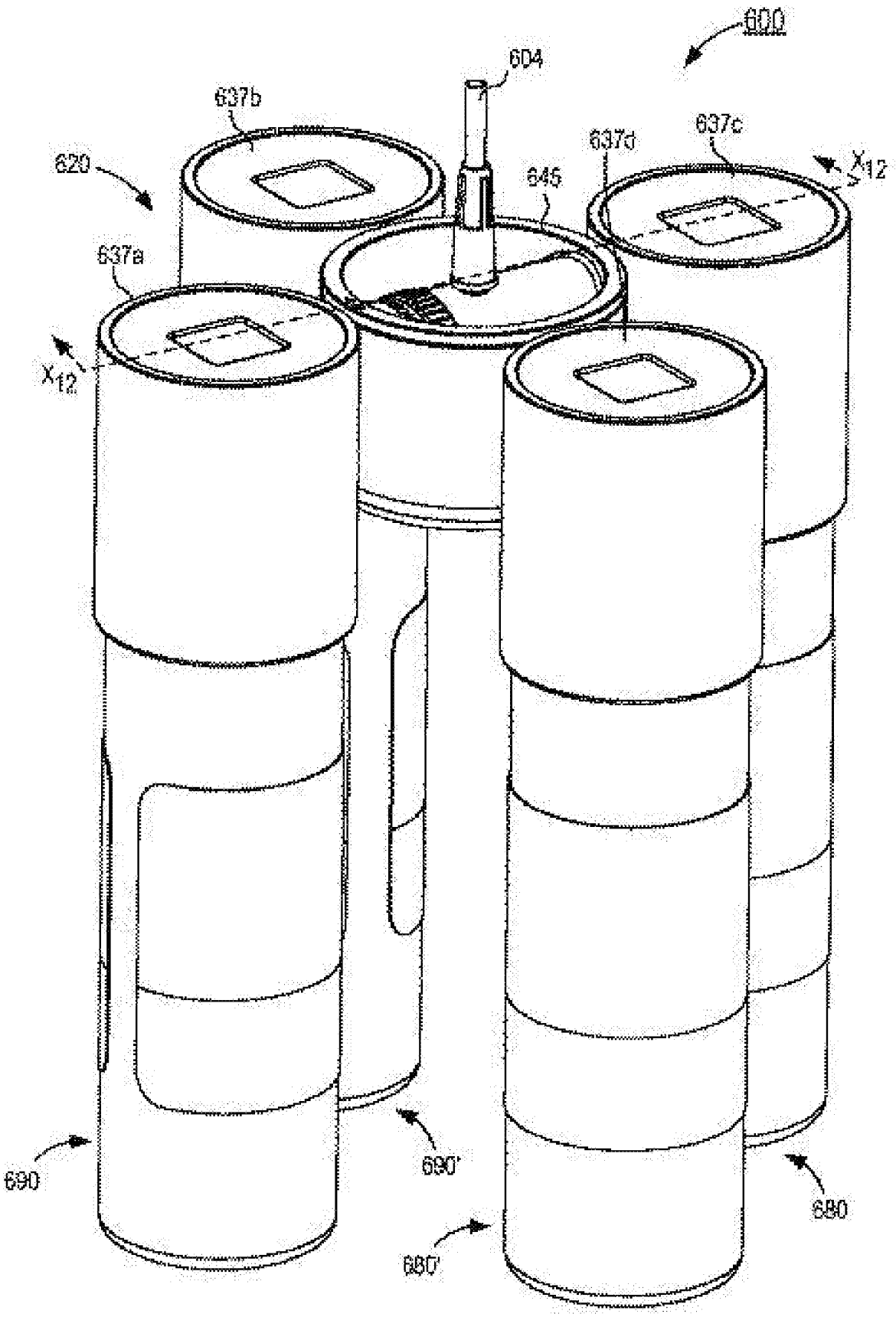


FIG. 25


600
604
637b
637d
637c
620
645
637a
X12
X12
690
690'
680
680'

[Fig.27]

FIG. 26

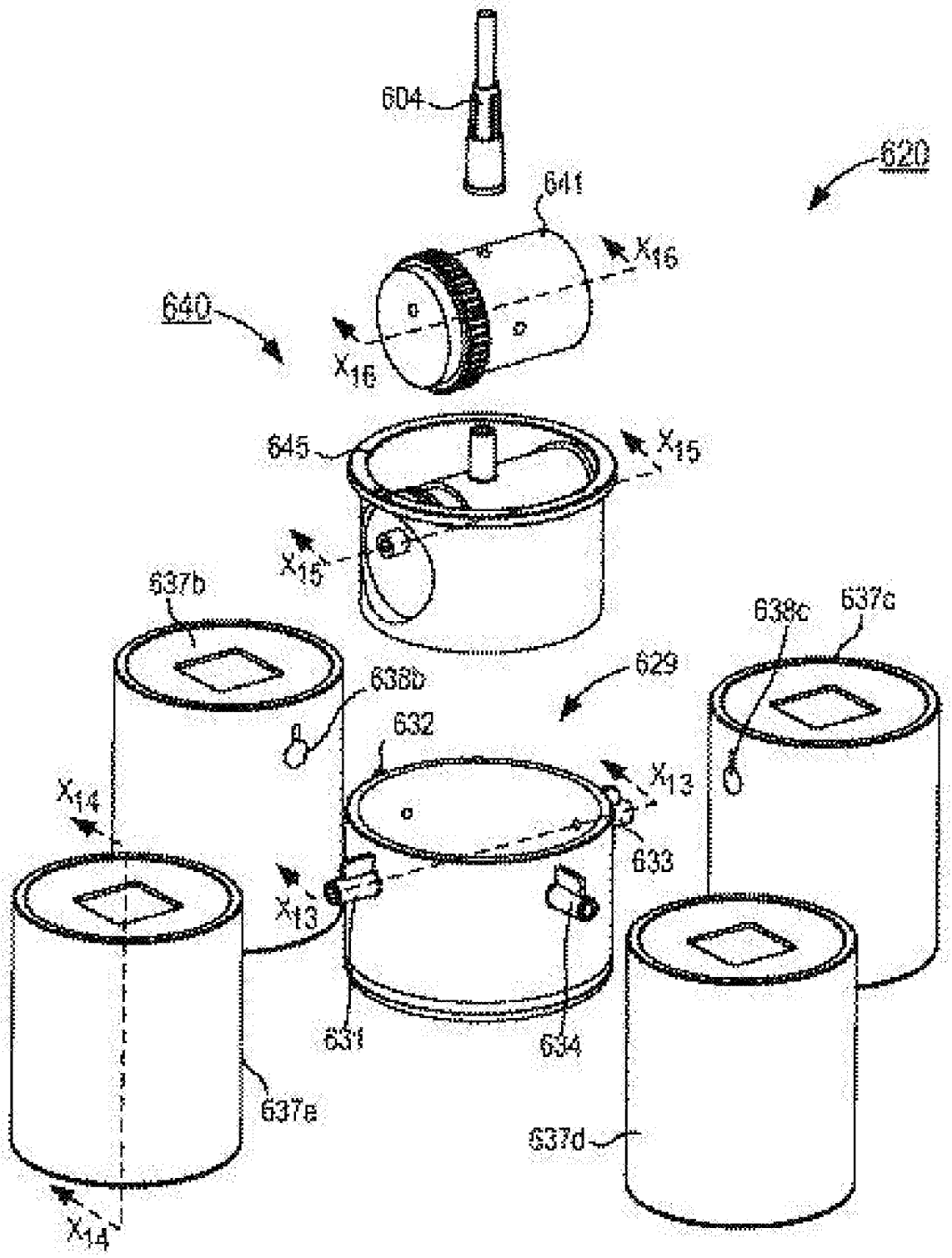

604
620
641
X_{16}
640
X_{16}
645
X_{15}
X_{15}
637b
638c
637c
638b
629
632
X_{14}
X_{13}
633
X_{13}
631
634
637e
637d
X_{14}

FIG. 27

[Fig.28]

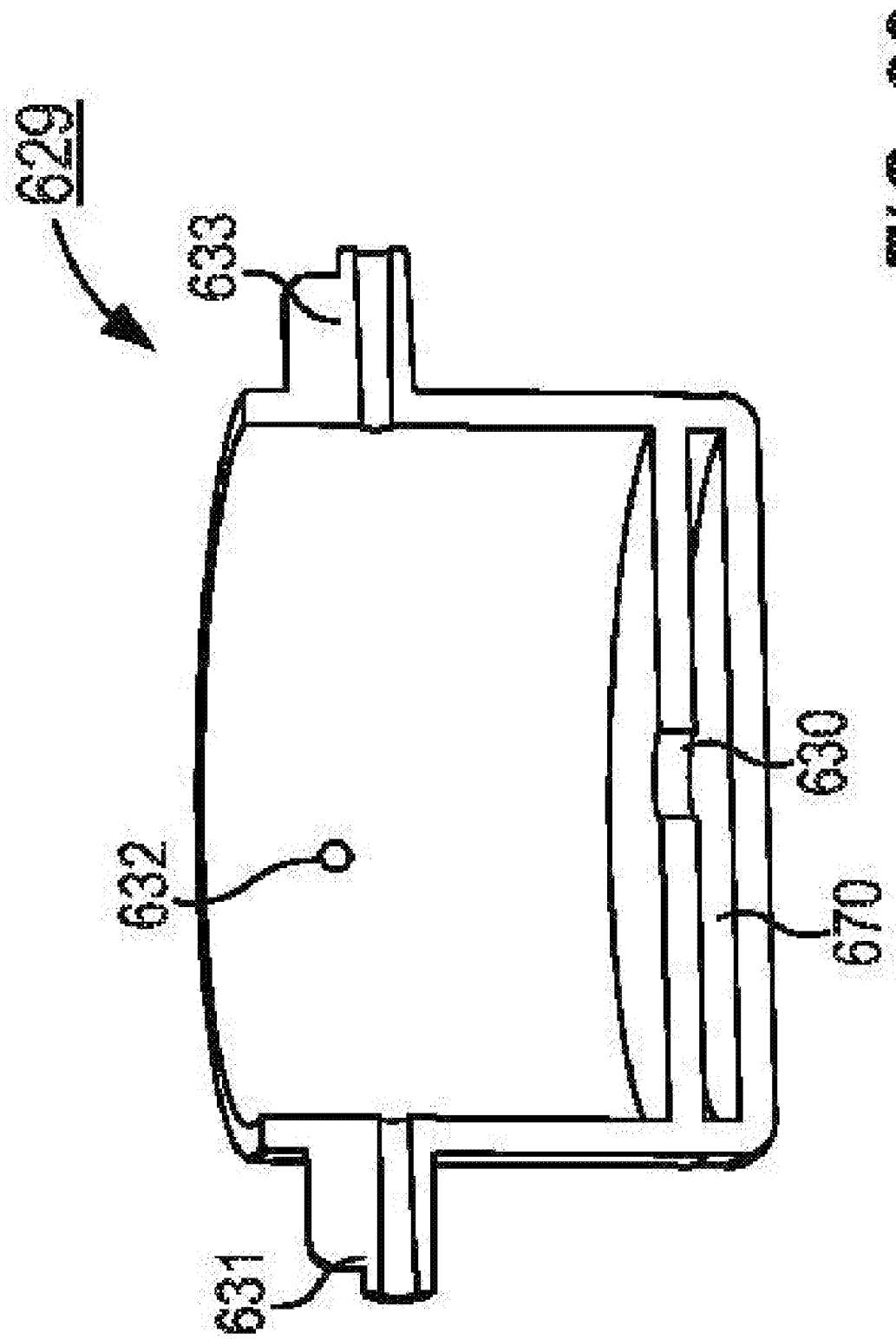


FIG. 28

[Fig.29]

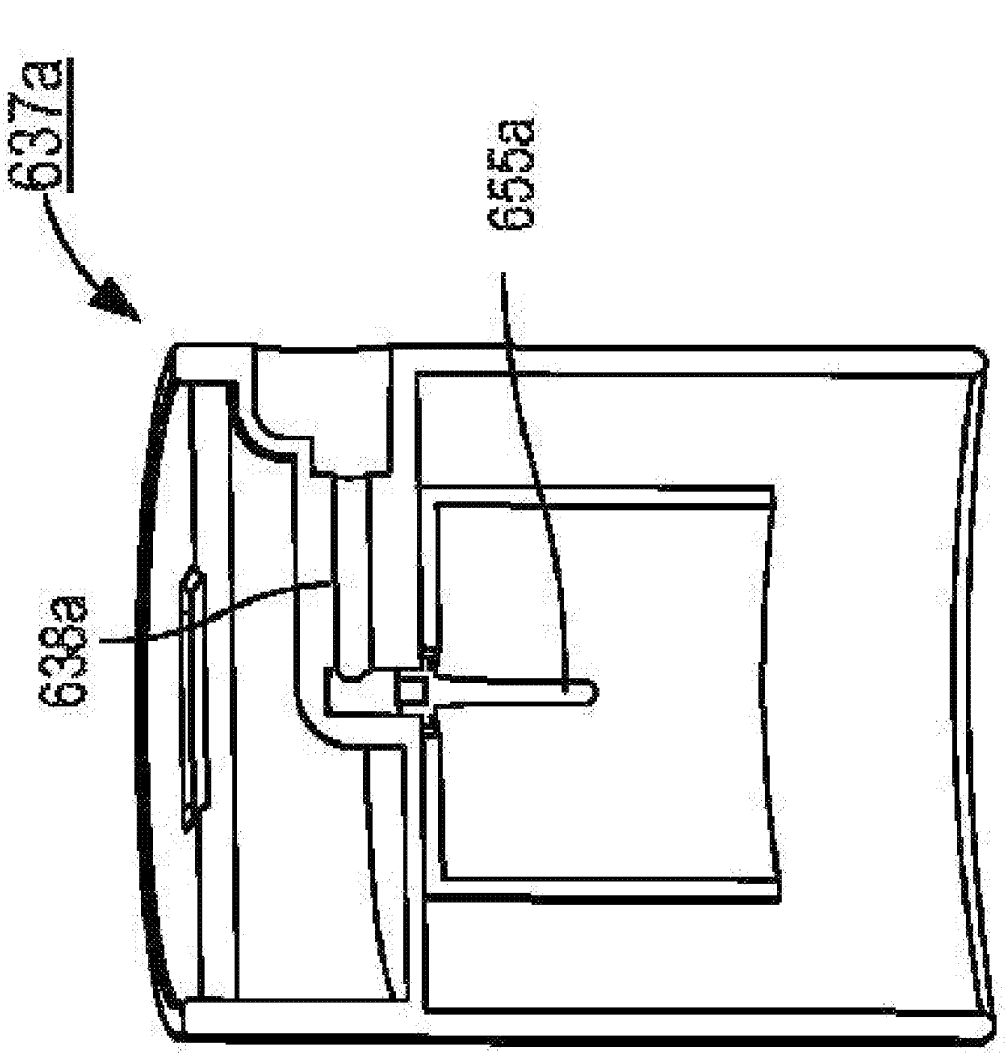
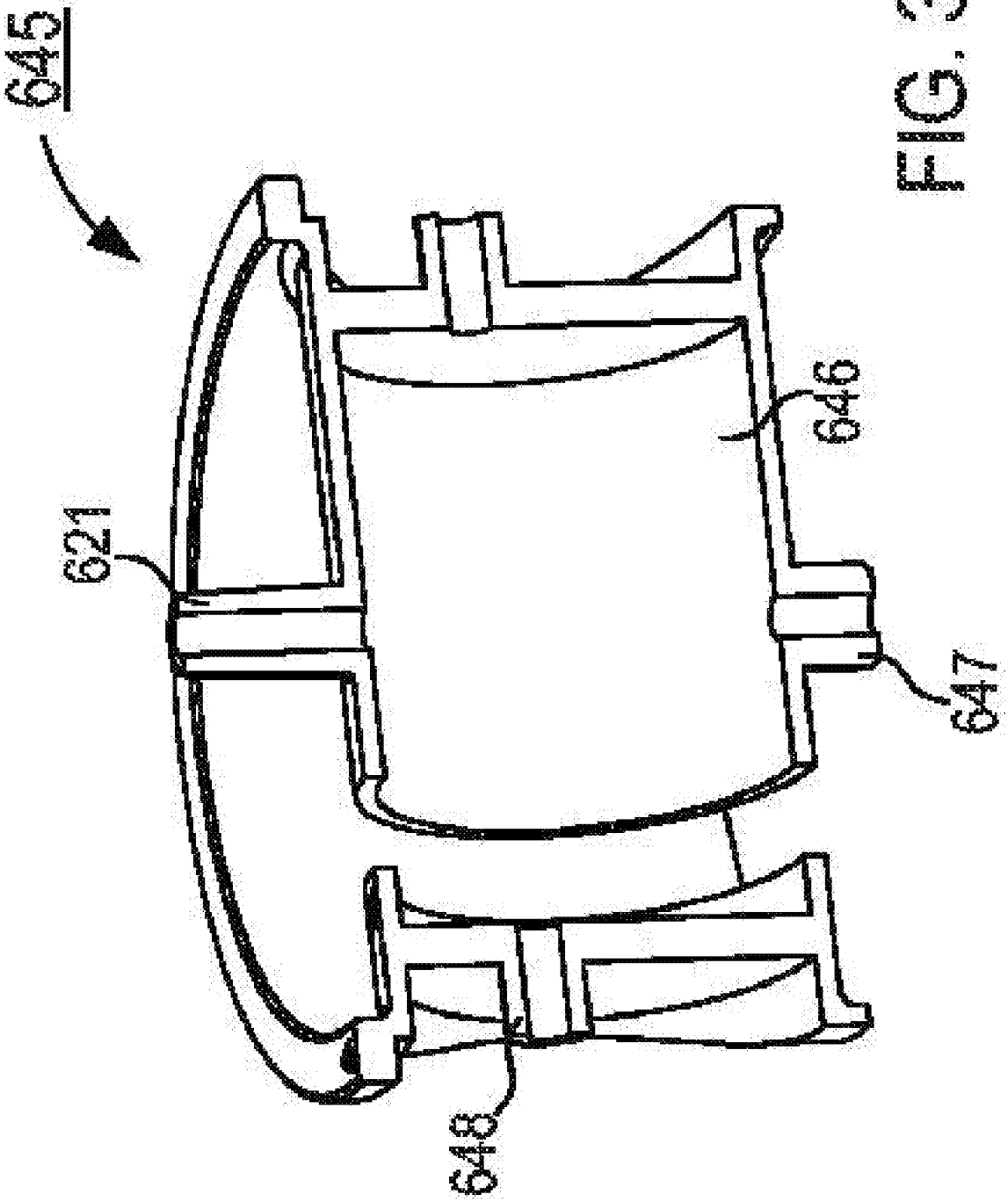


FIG. 29

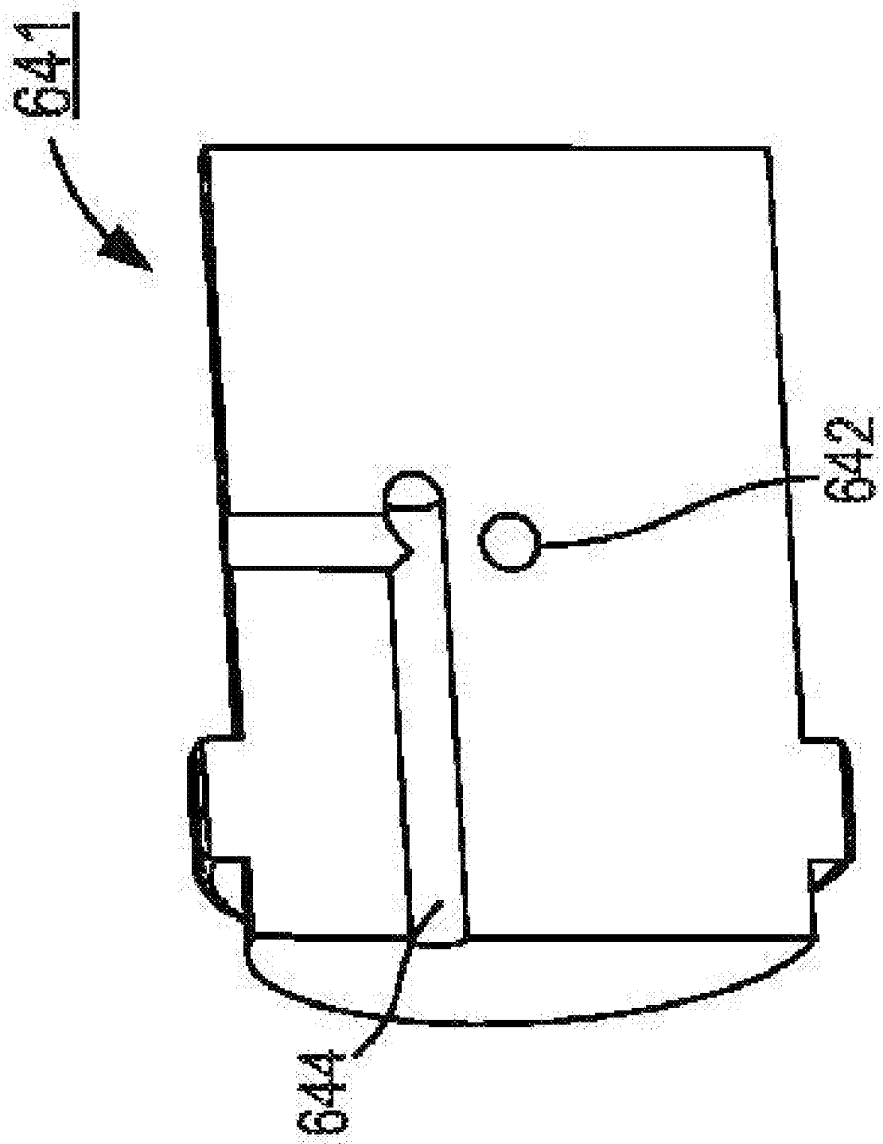
[Fig. 30]

FIG. 30



[Fig. 31]

FIG. 31



[Fig. 32]

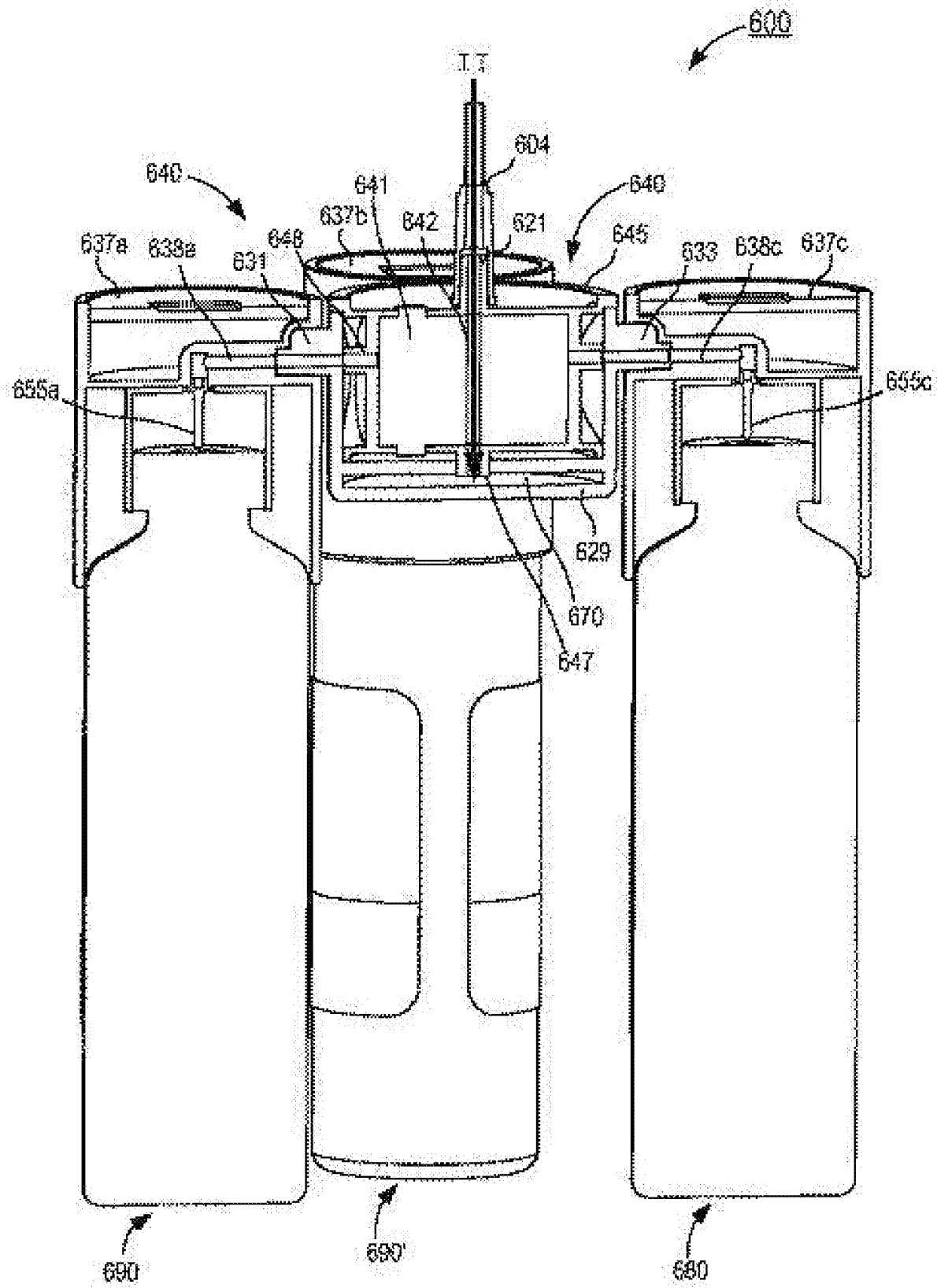

600
I
I
604
640
641
637b
642
621
640
645
637a
638a
631
648
633
638c
637c
655a
655c
629
670
647
690
690'
680

FIG. 32

[Fig. 33]

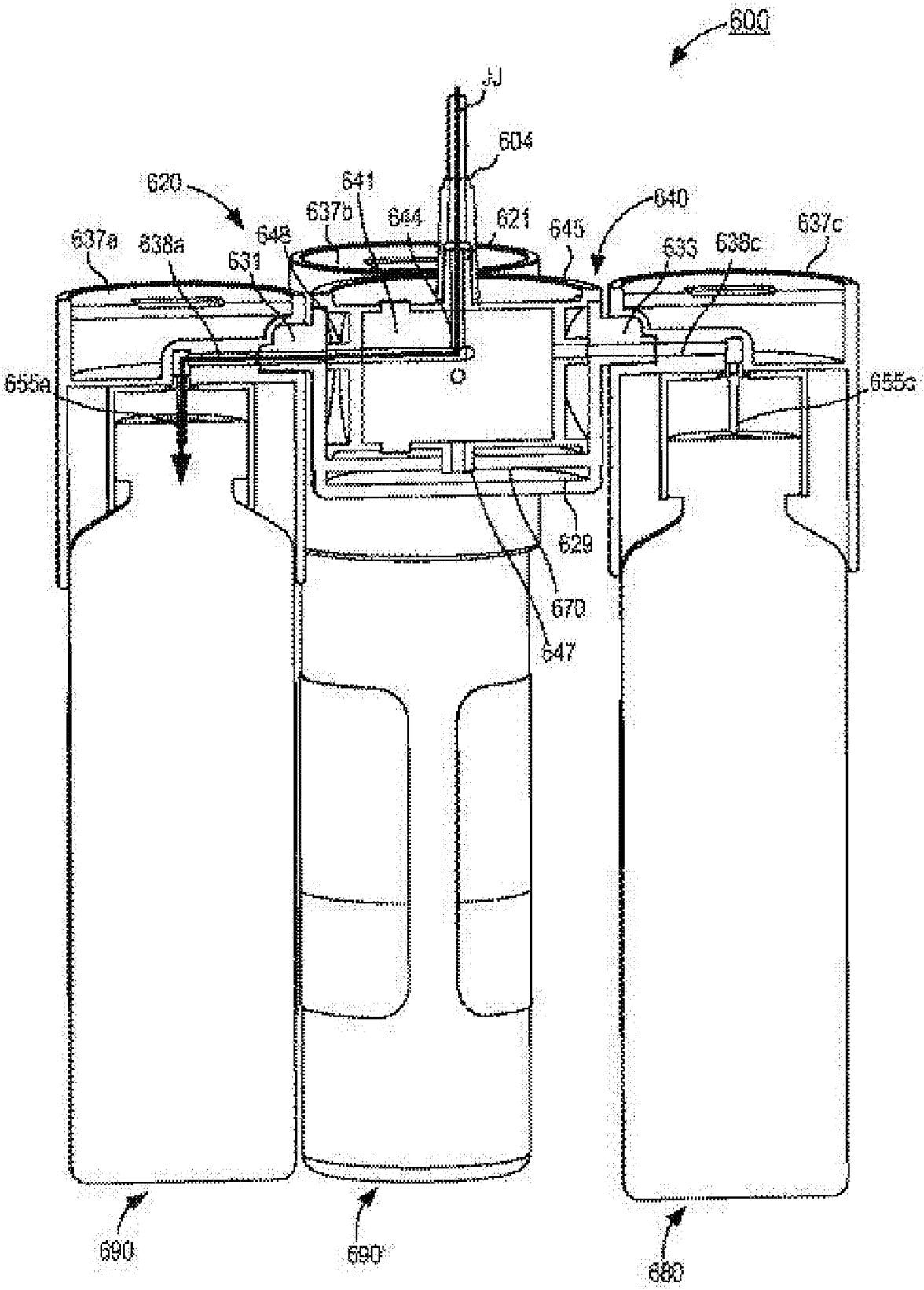

600
JJ
604
620
641
637b
644
621
645
640
637c
637a
638a
648
631
633
638c
655a
655c
629
670
647
690
690
680

FIG. 33

[Fig. 34]

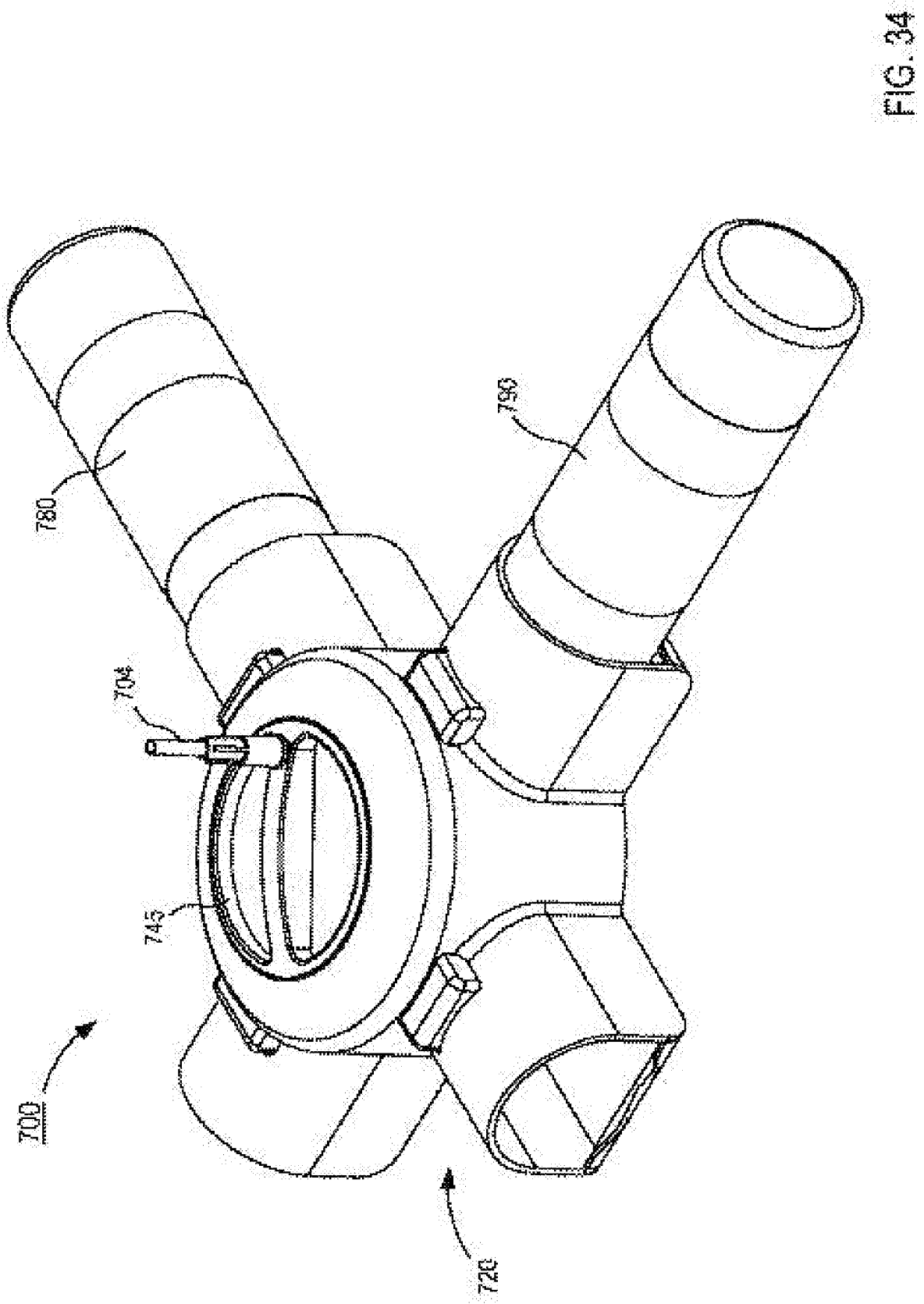
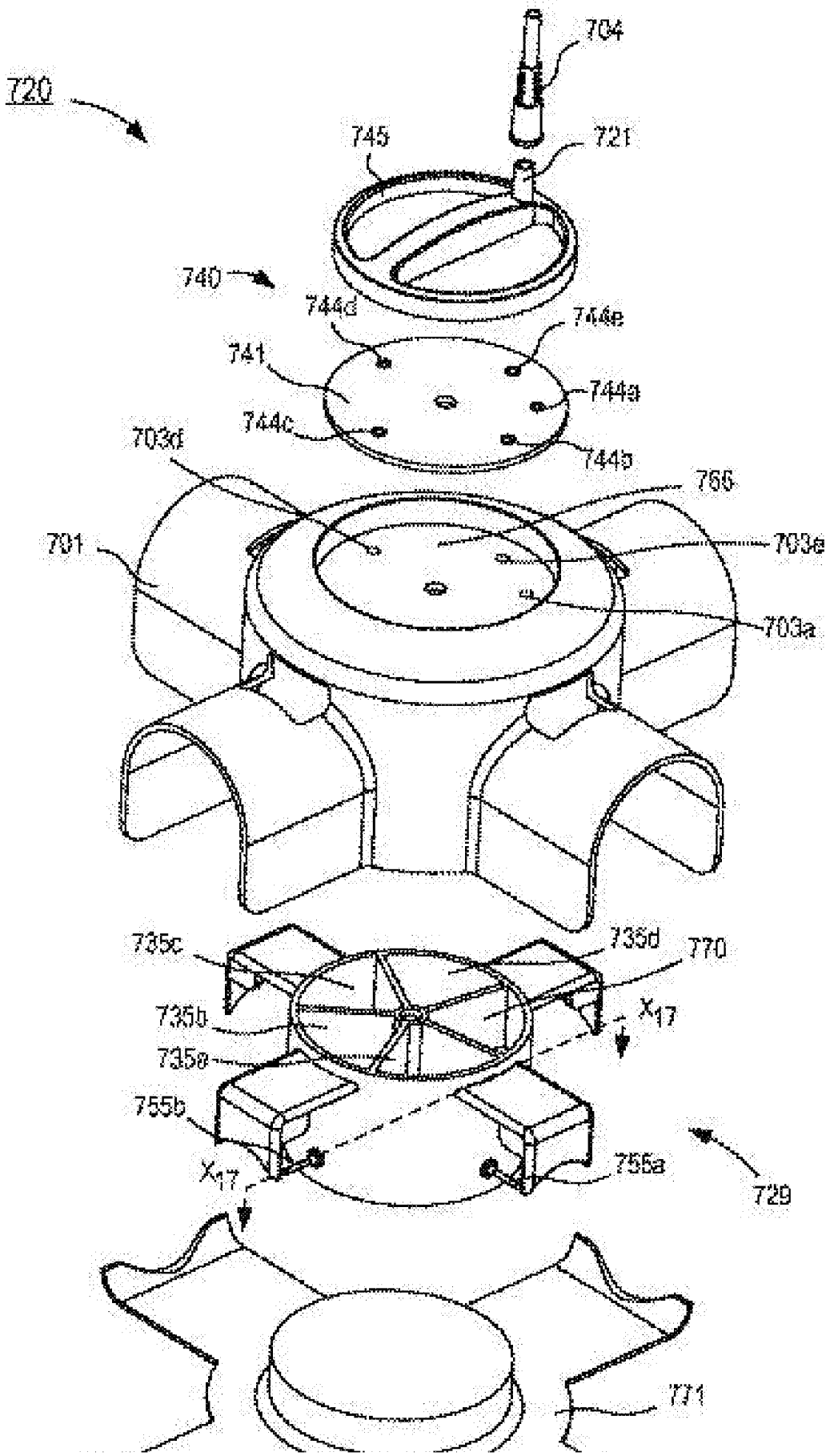


FIG. 34

[Fig.35]


720
704
745
721
740
744d
744e
741
744a
744c
744b
703f
766
701
703e
703a
735c
735d
770
735b
X_{17}
735a
755b
X_{17}
755a
729
771

[Fig. 36]

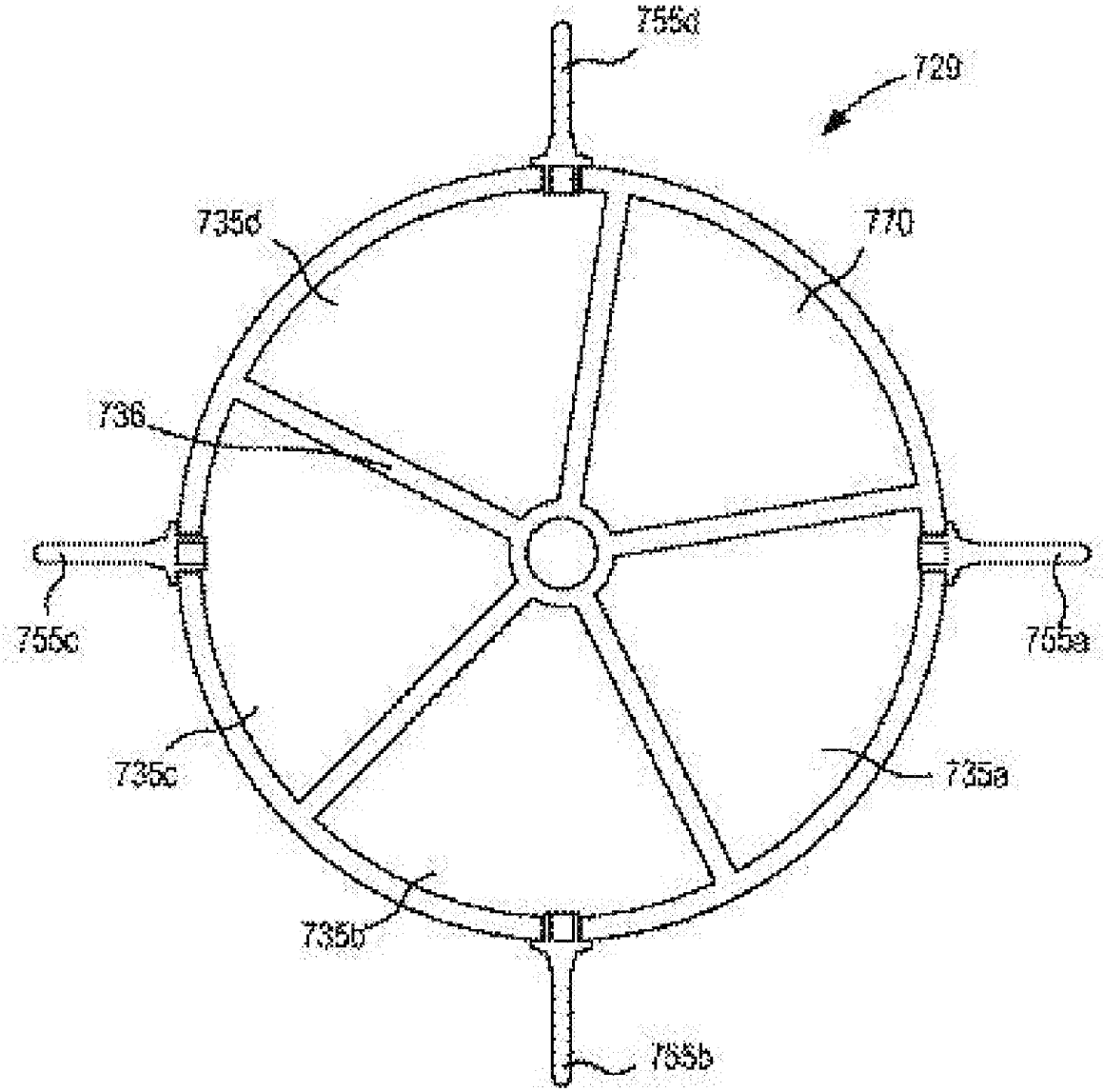


FIG. 36

[Fig. 37]

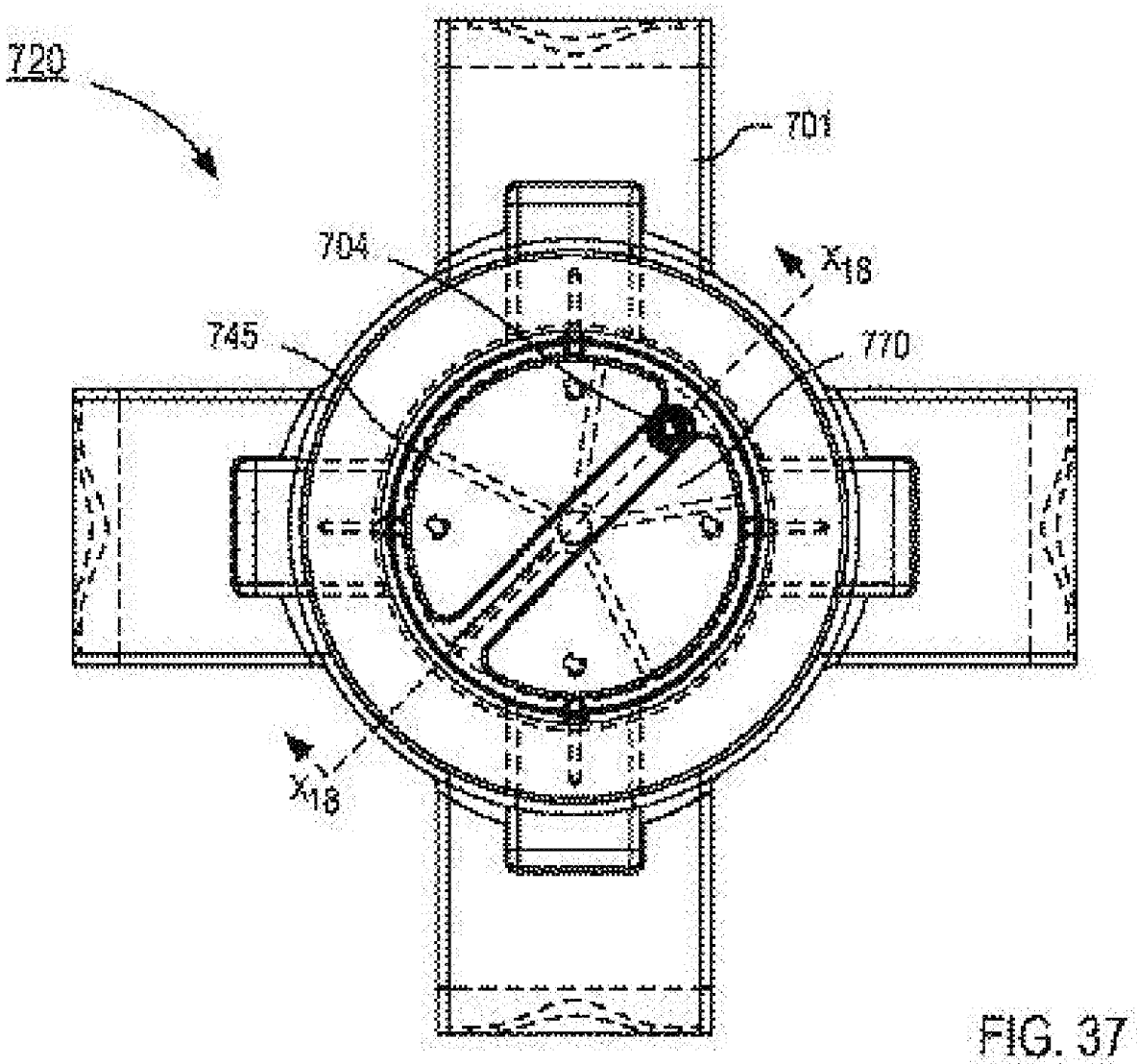


FIG. 37

[Fig. 38]

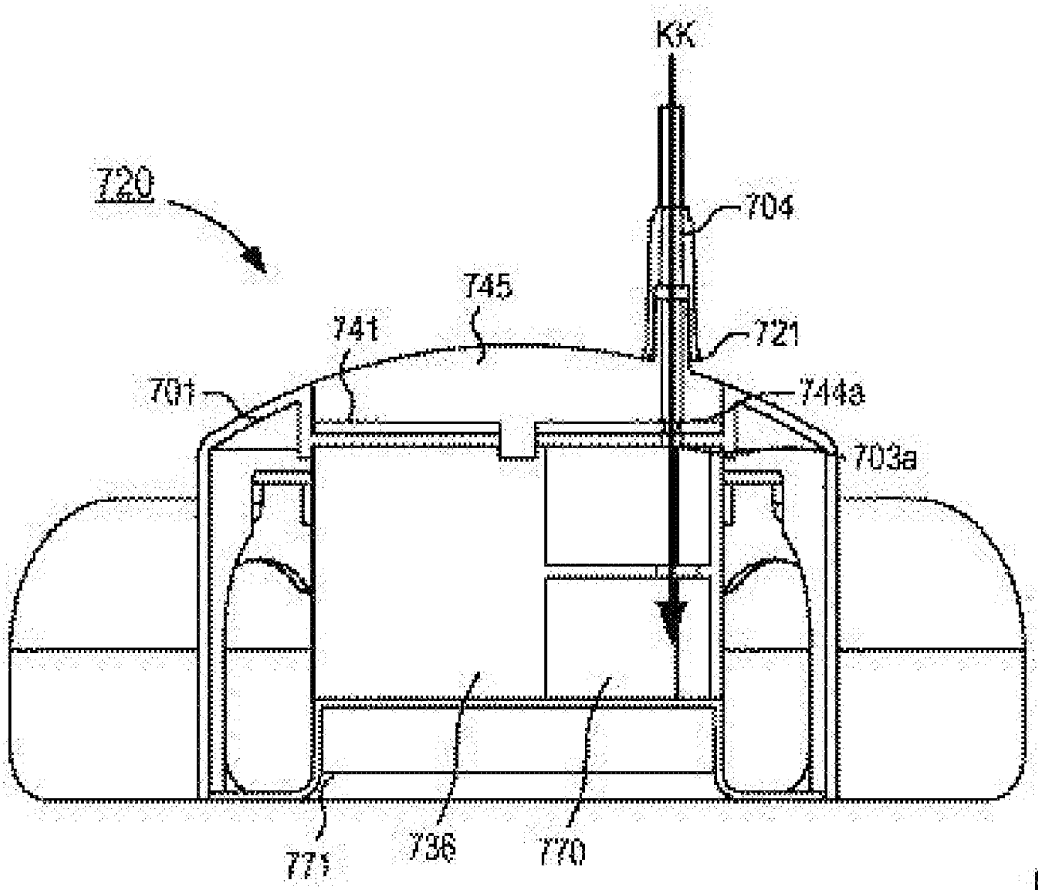


FIG. 38

[Fig.39]

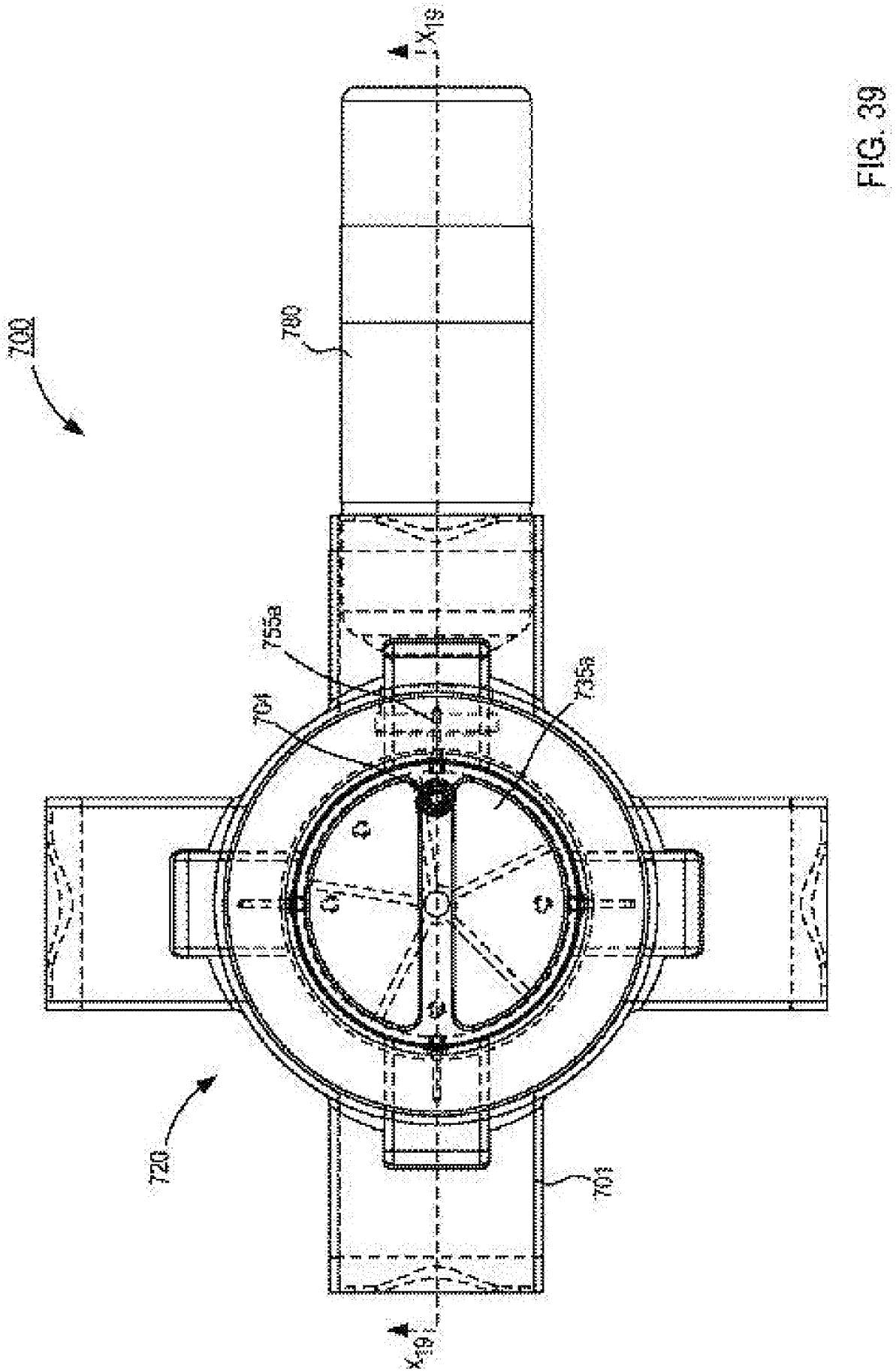


FIG. 39

[Fig. 40]

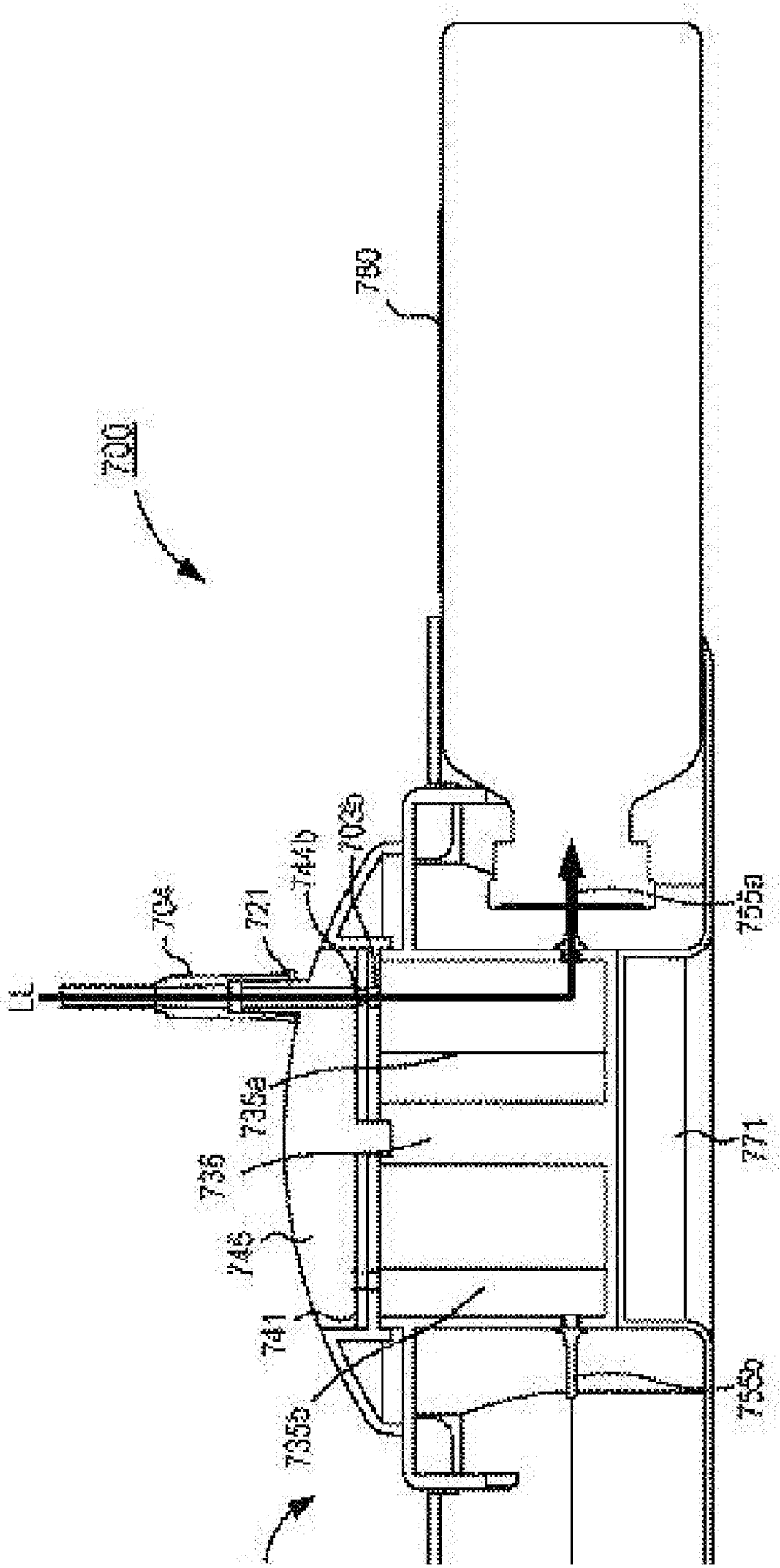
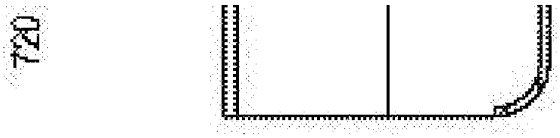
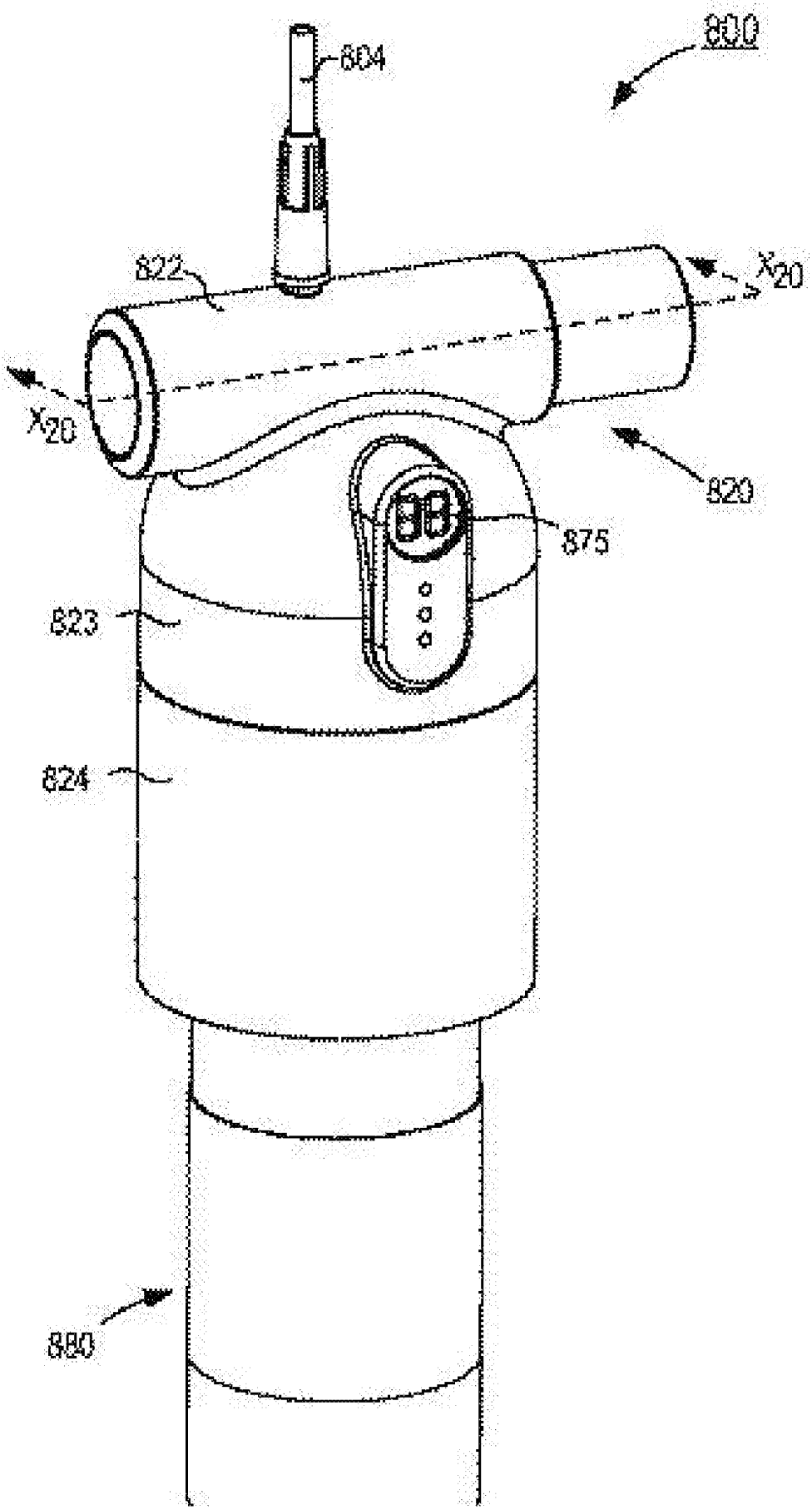


FIG. 40

[Fig. 41]




800
804
822
X20
X20
820
875
823
824
880

[Fig. 42]

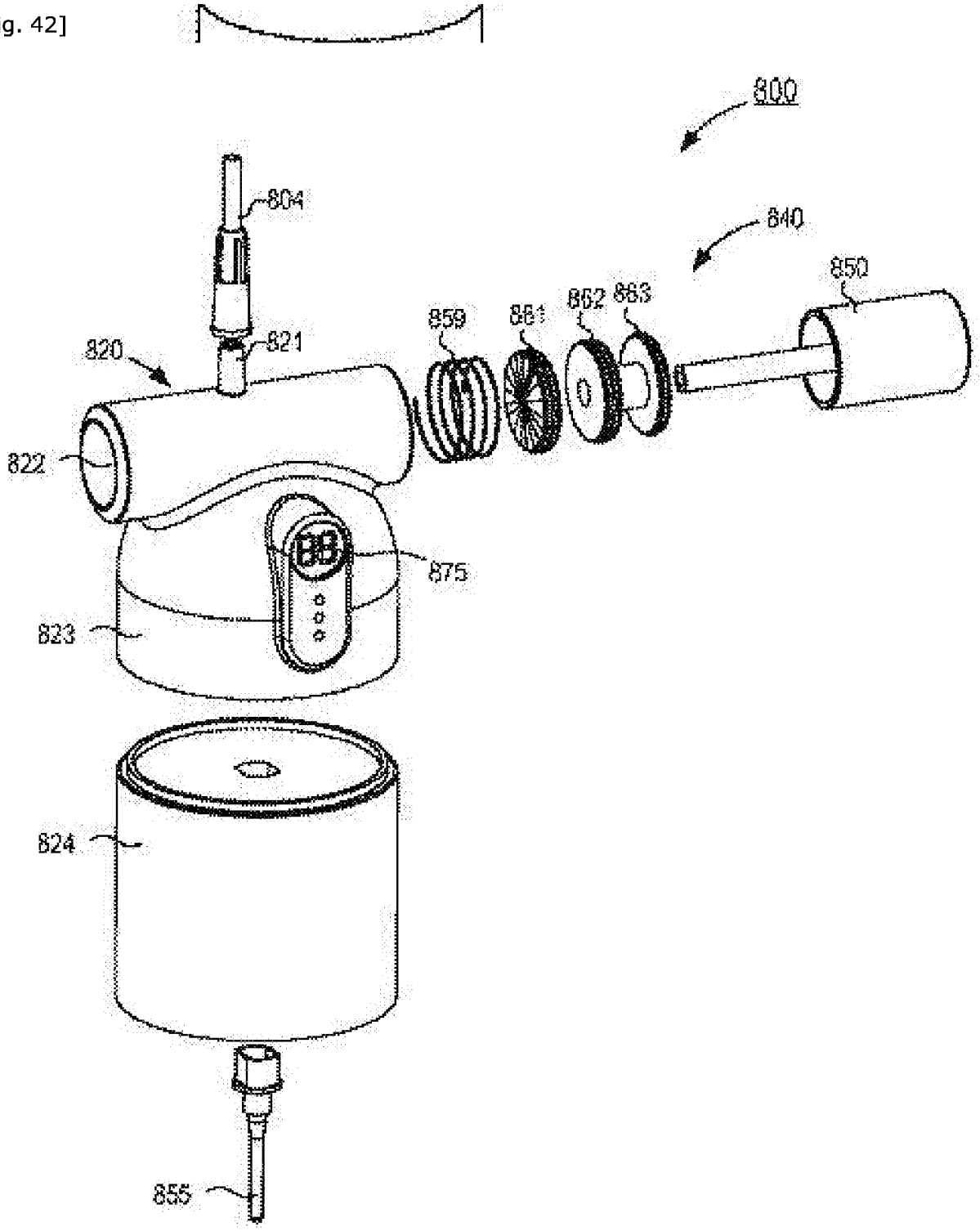
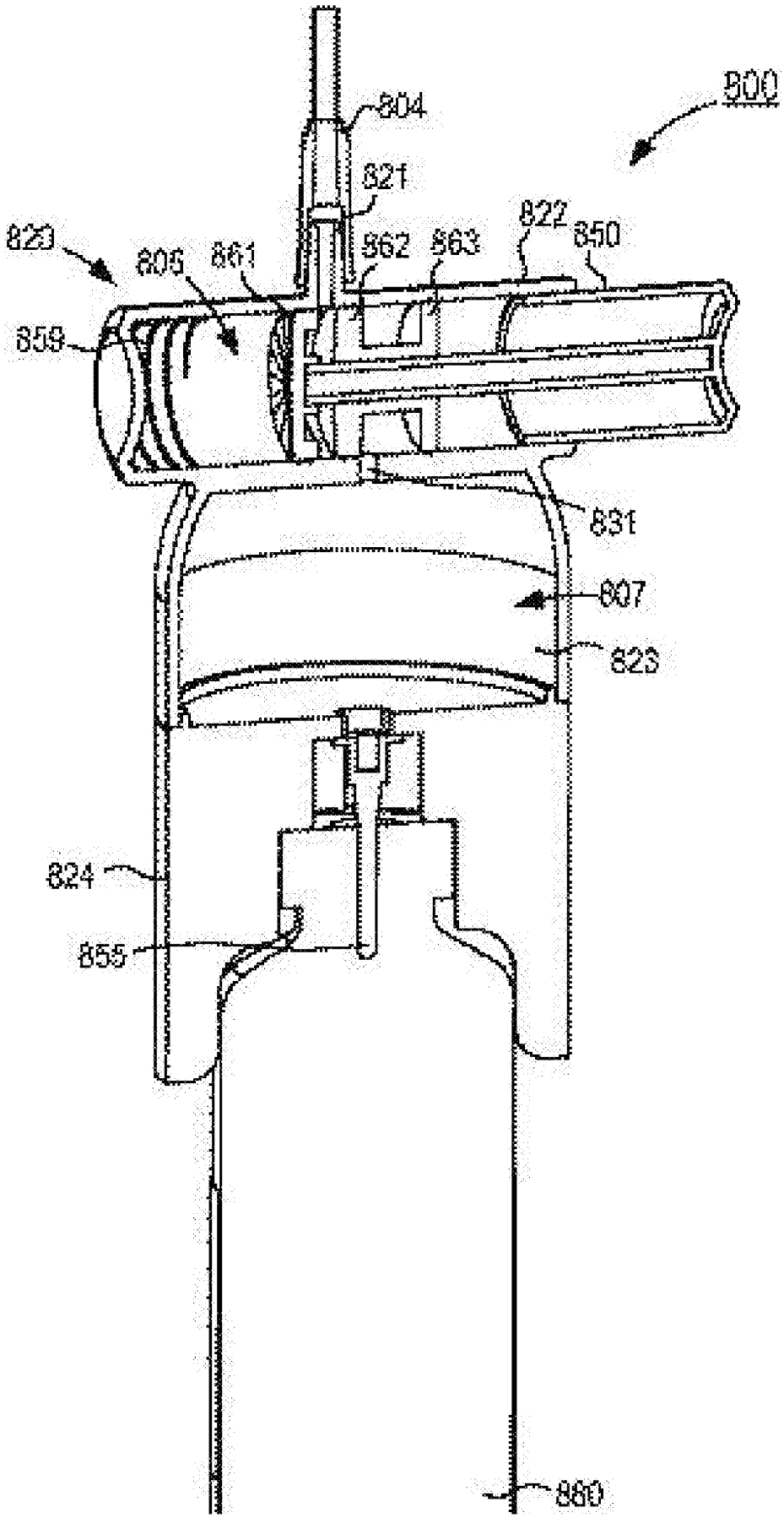


FIG. 42

[Fig. 43]


800
804
821
822
850
820
805
861
862
863
859
831
807
823
824
855
860

[Fig. 44]

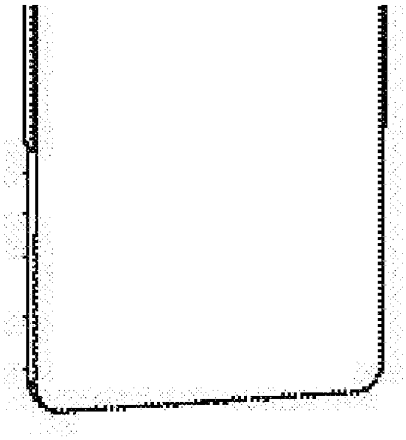
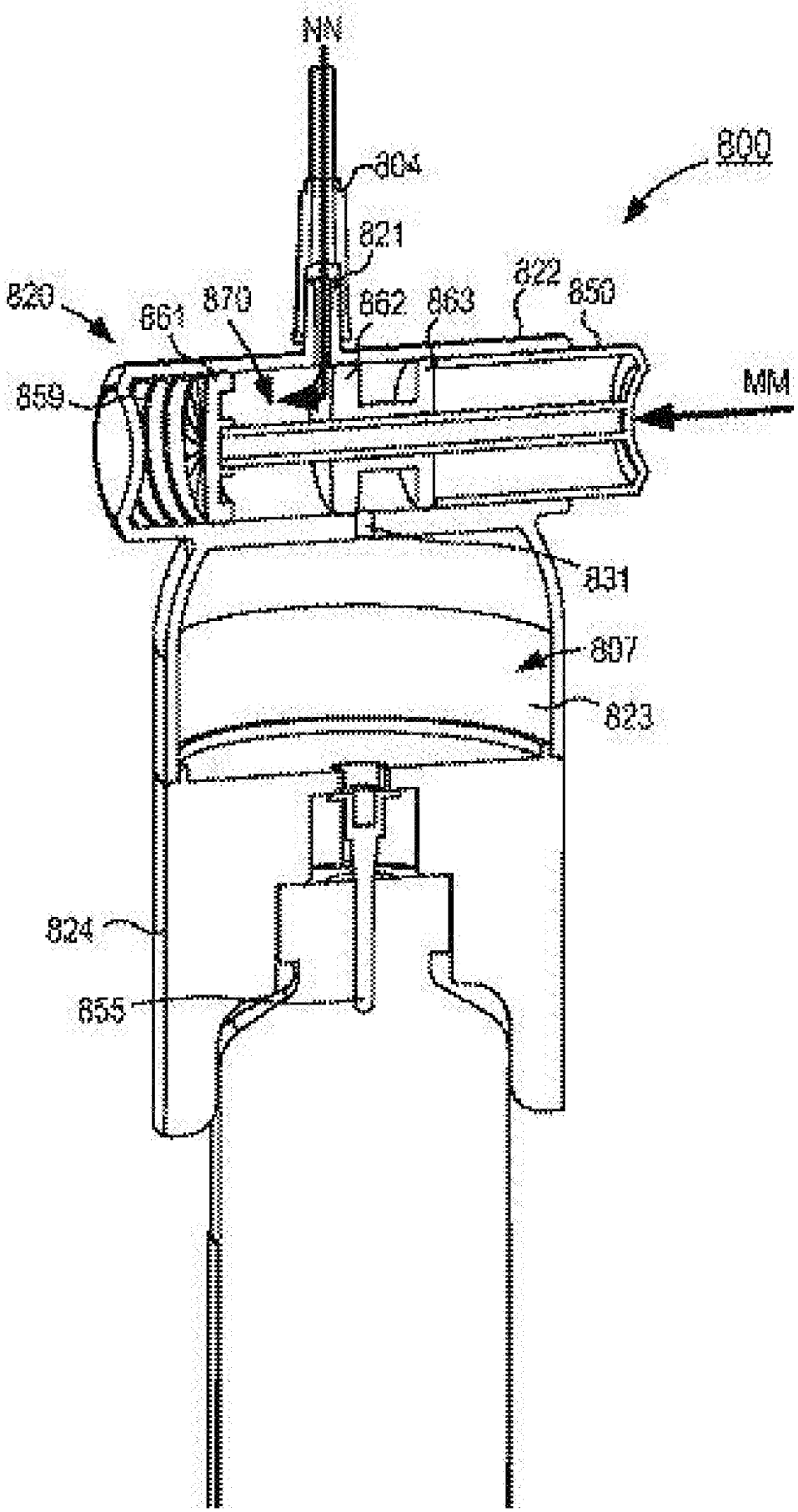


FIG. 43


NN
800
804
821
822
850
820
661
870
862
863
859
MM
831
807
823
824
855

[Fig. 45]

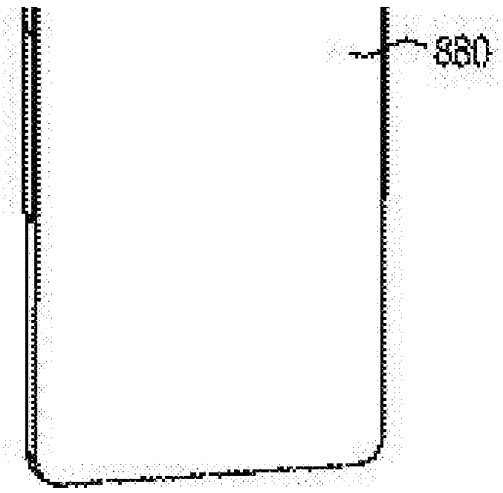
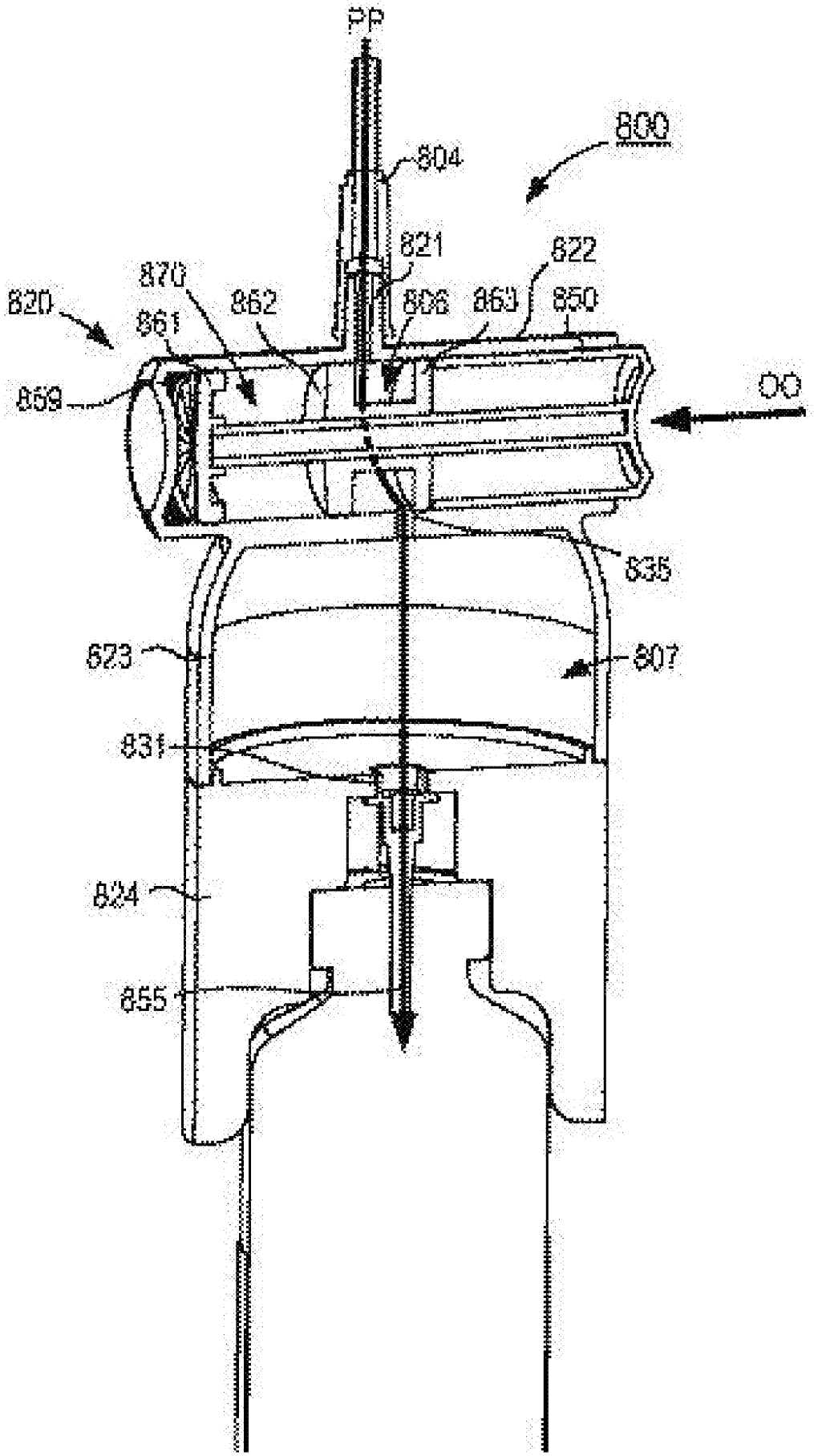


FIG. 44


PP
800
804
821
822
870
820
862
806
863
850
861
859
00
835
823
807
831
824
855

[Fig. 46]

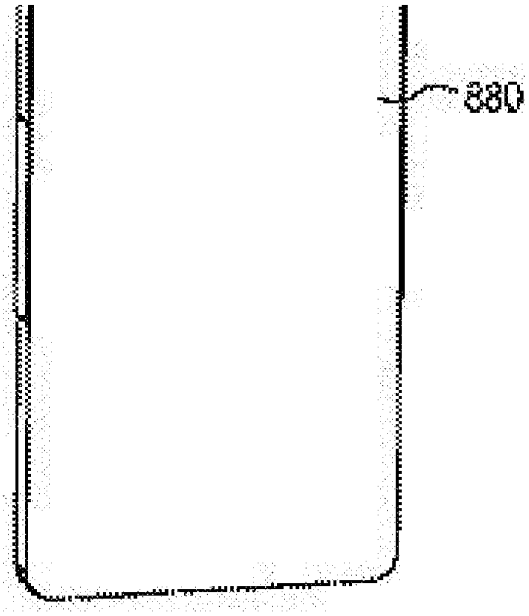
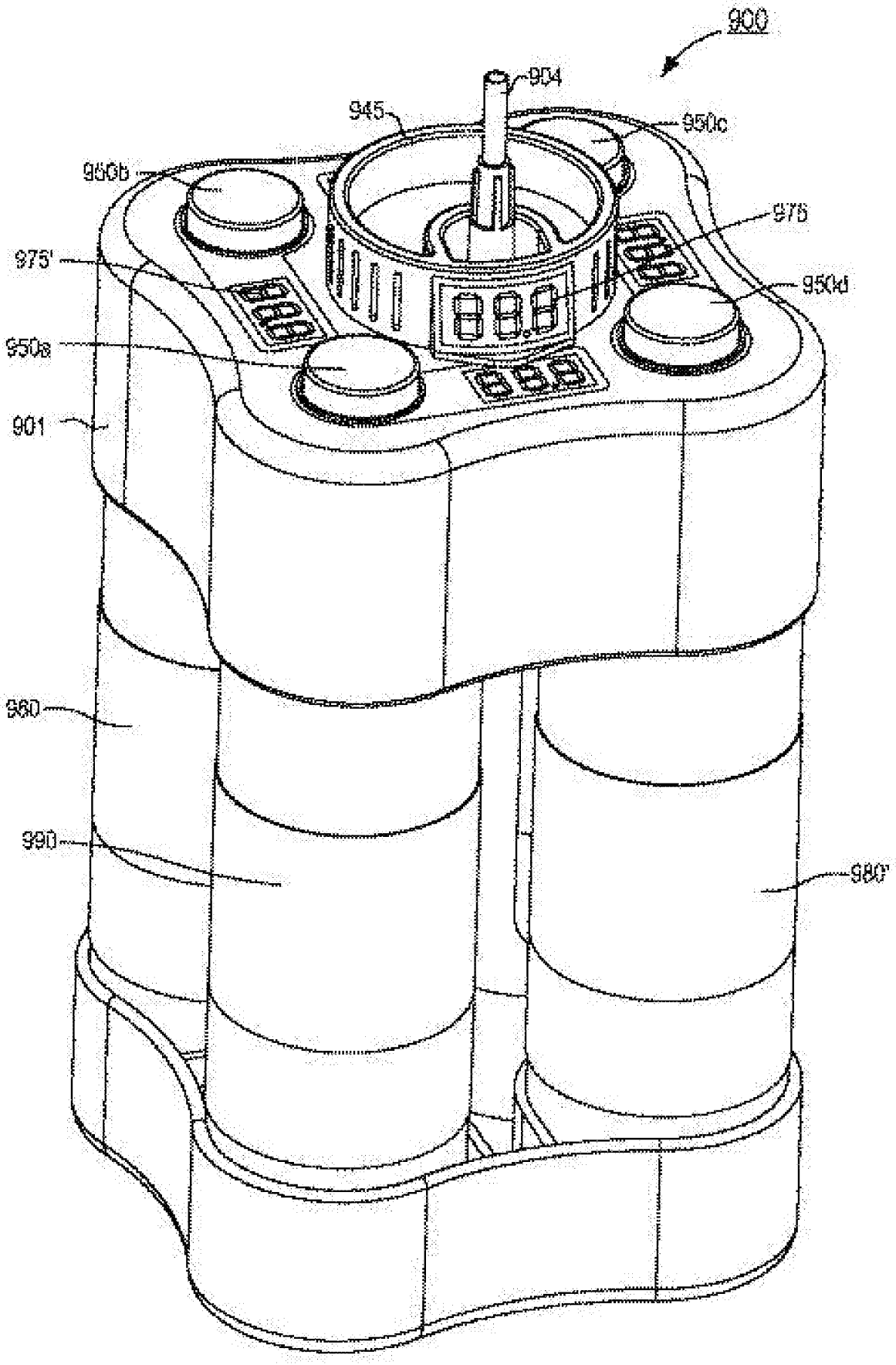
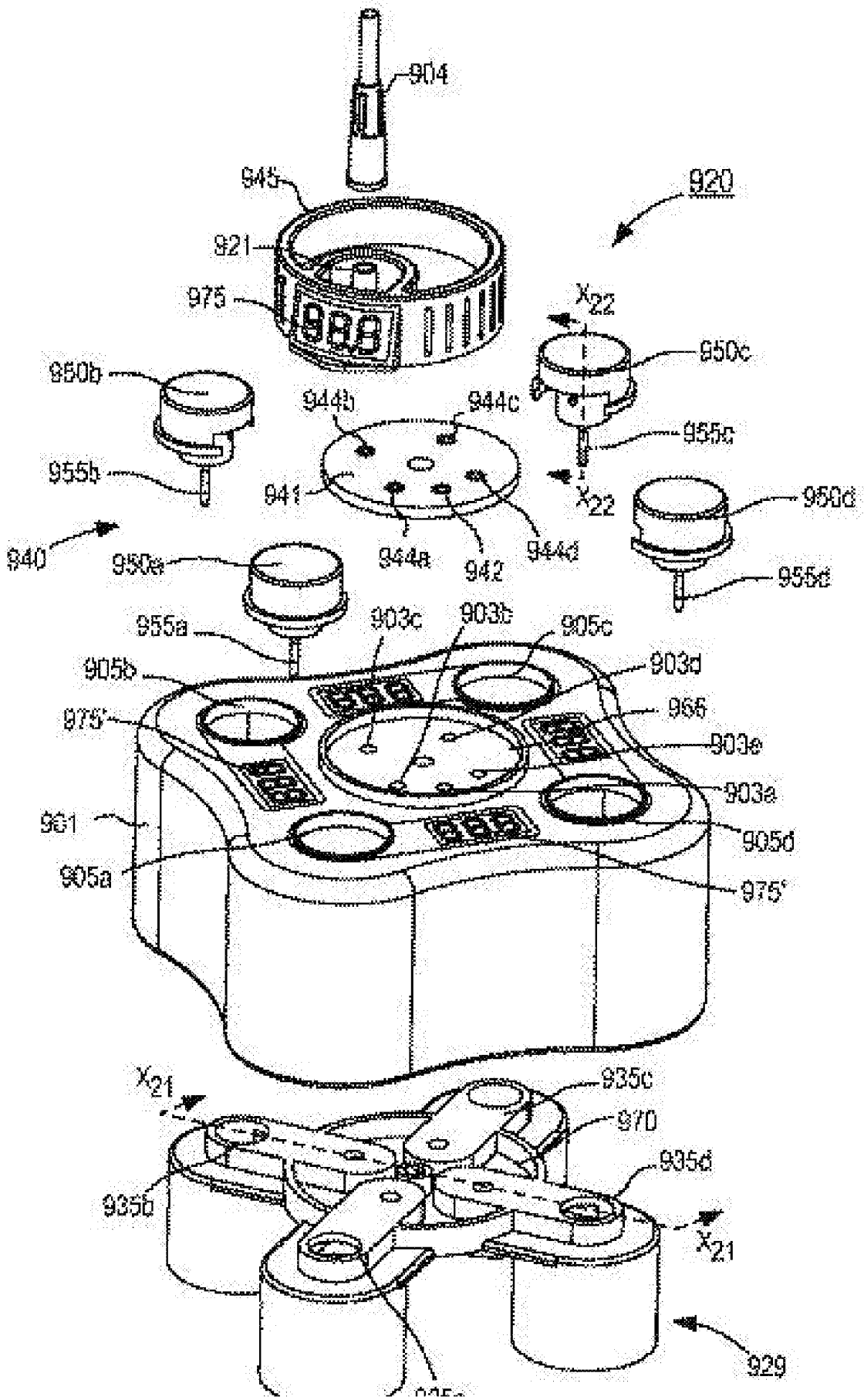


FIG. 45


900
904
945
950c
950b
975
975'
950d
950a
901
960
990
980'

[Fig. 46]




904
945
920
921
975
X22
950c
950b
944b
944c
955c
955b
941
X22
950d
940
944a
942
944d
950a
955d
955a
903c
903b
905c
905b
903d
975'
966
903e
903a
961
905d
905a
975'
X21
935c
970
935d
935b
X21
929

[Fig. 48]

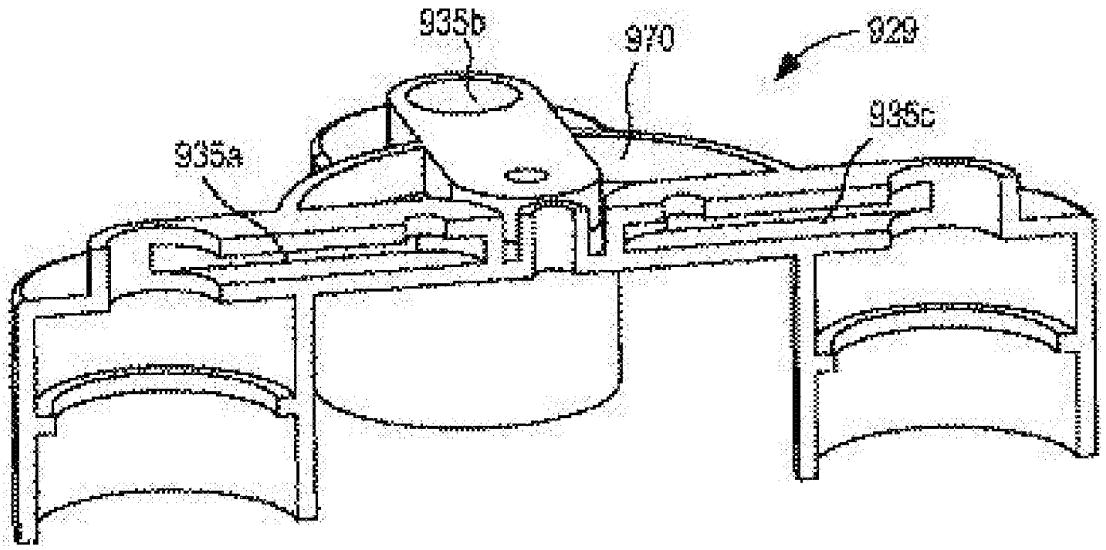


FIG. 48

[Fig. 49]

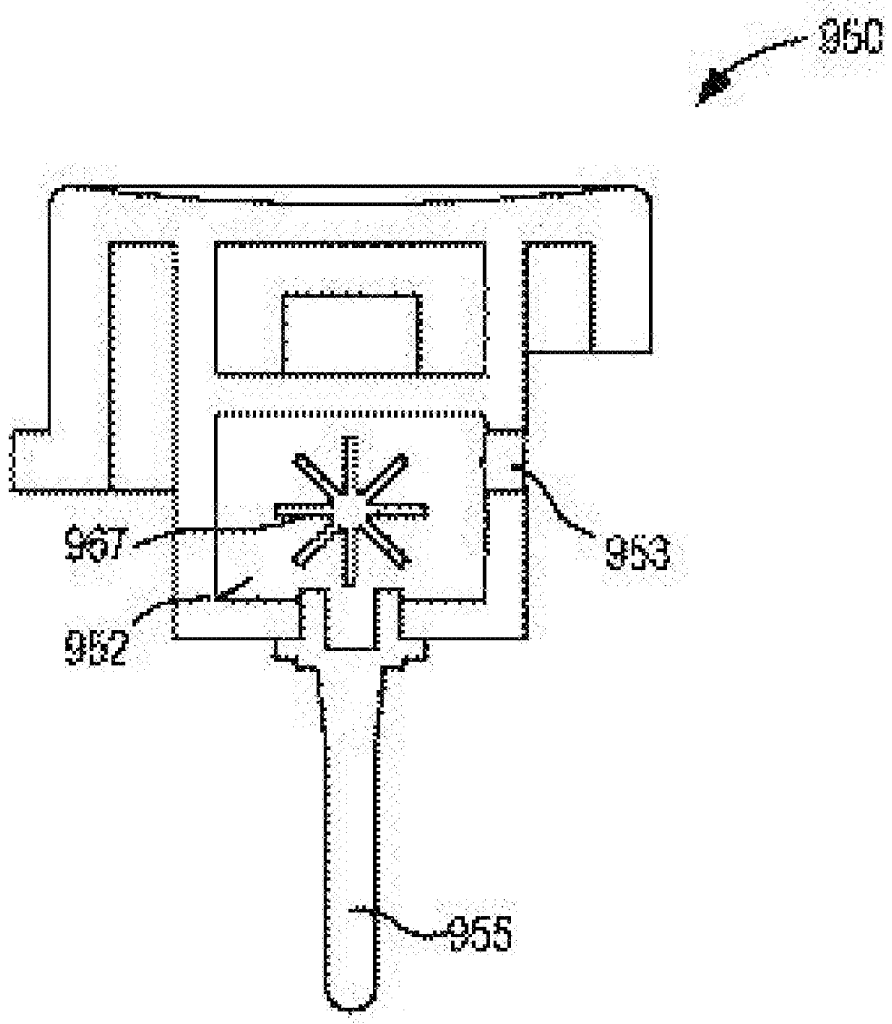


FIG. 49

[Fig. 50]

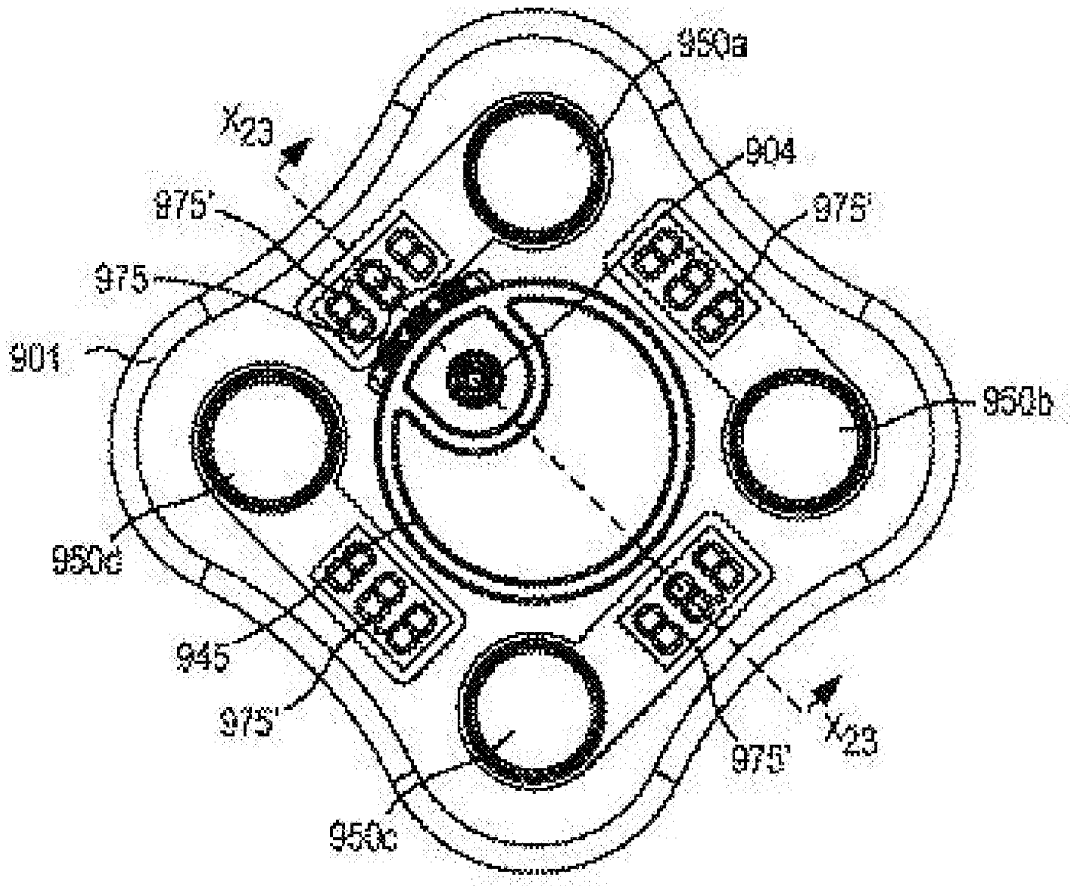


FIG. 50

[Fig. 51]

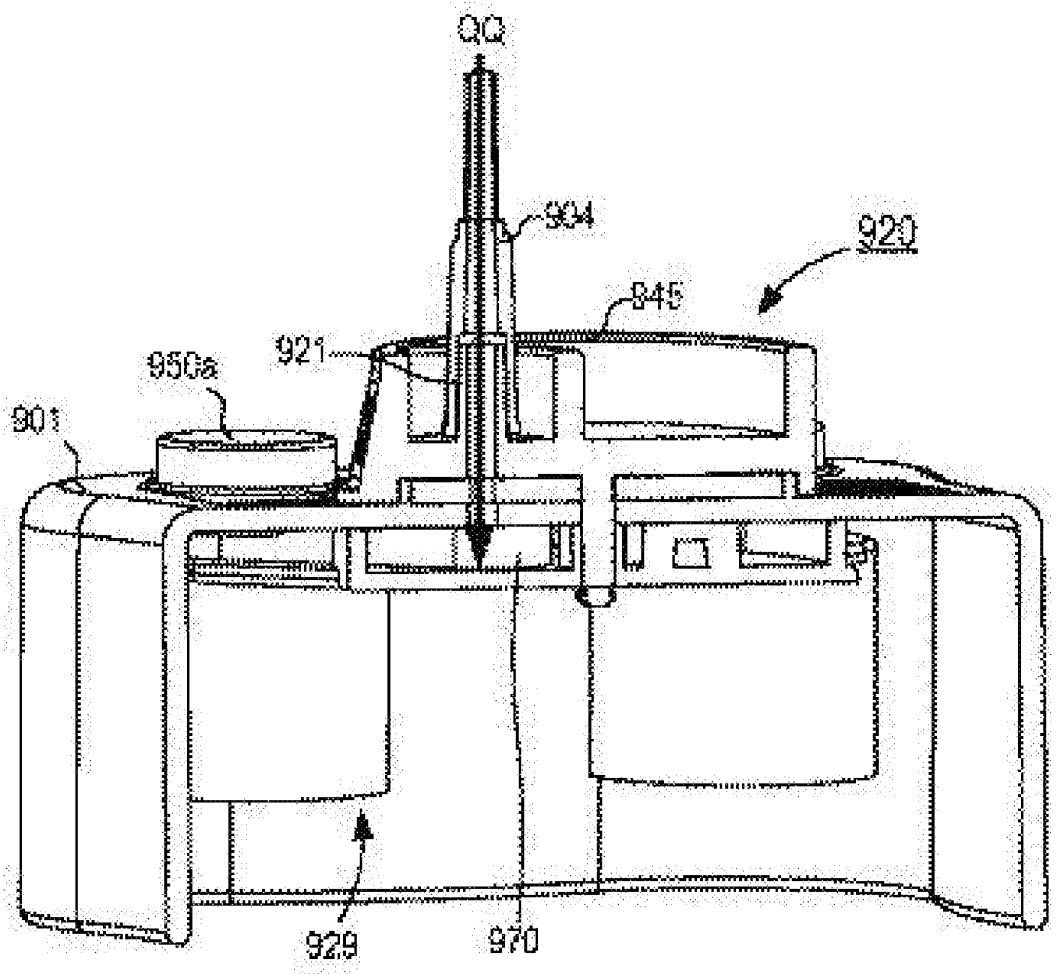


FIG. 51

[Fig. 52]

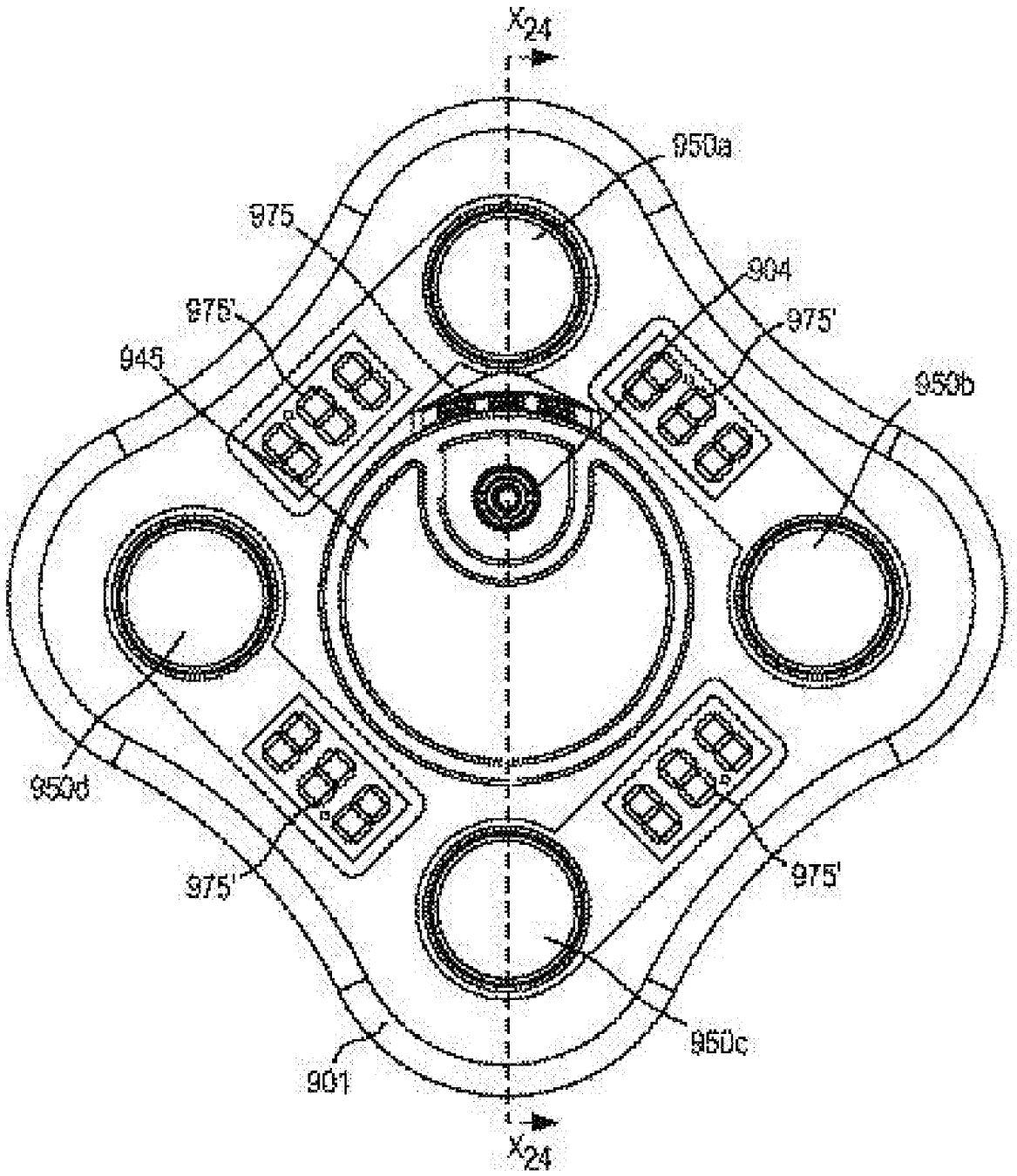
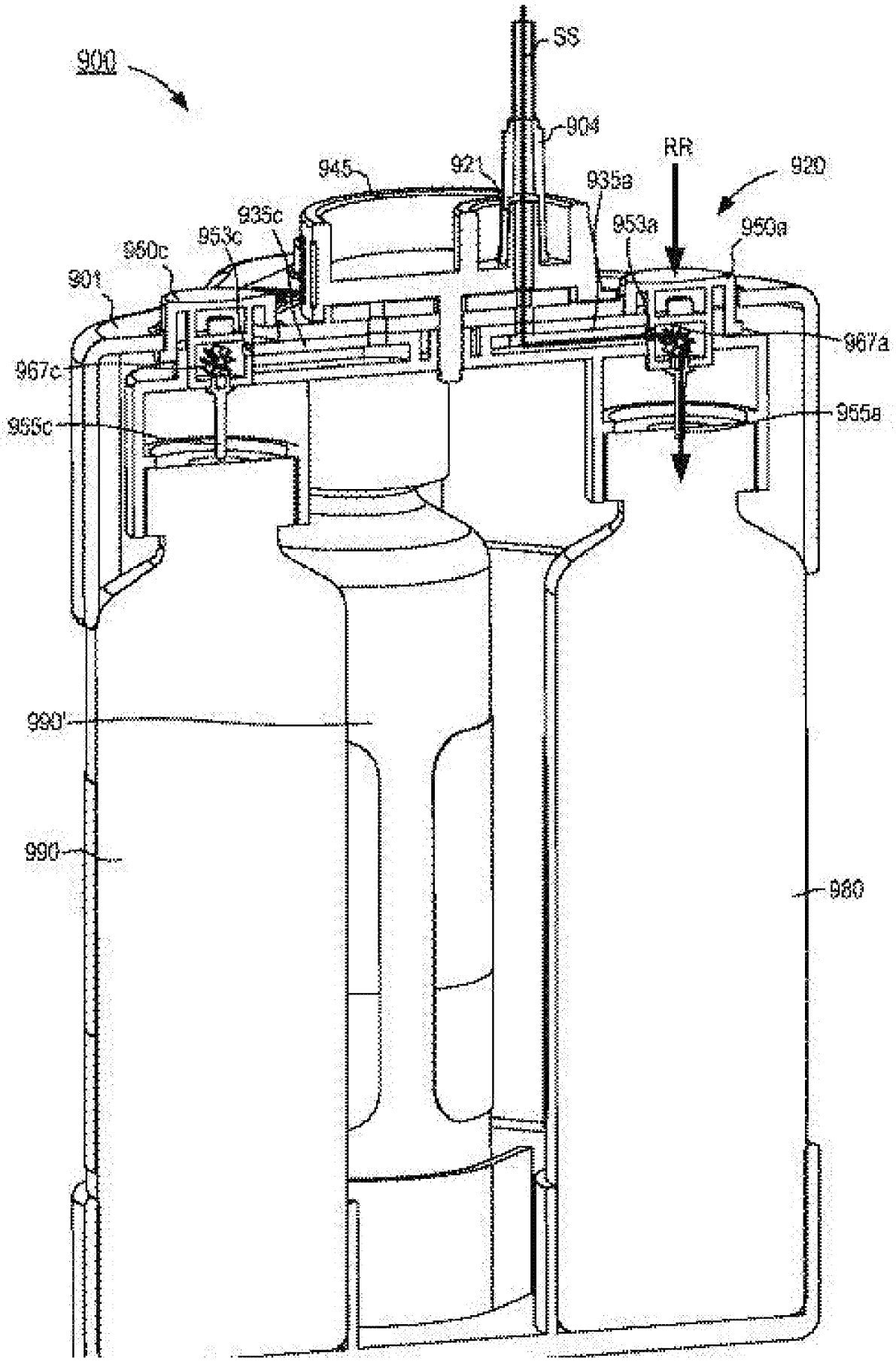
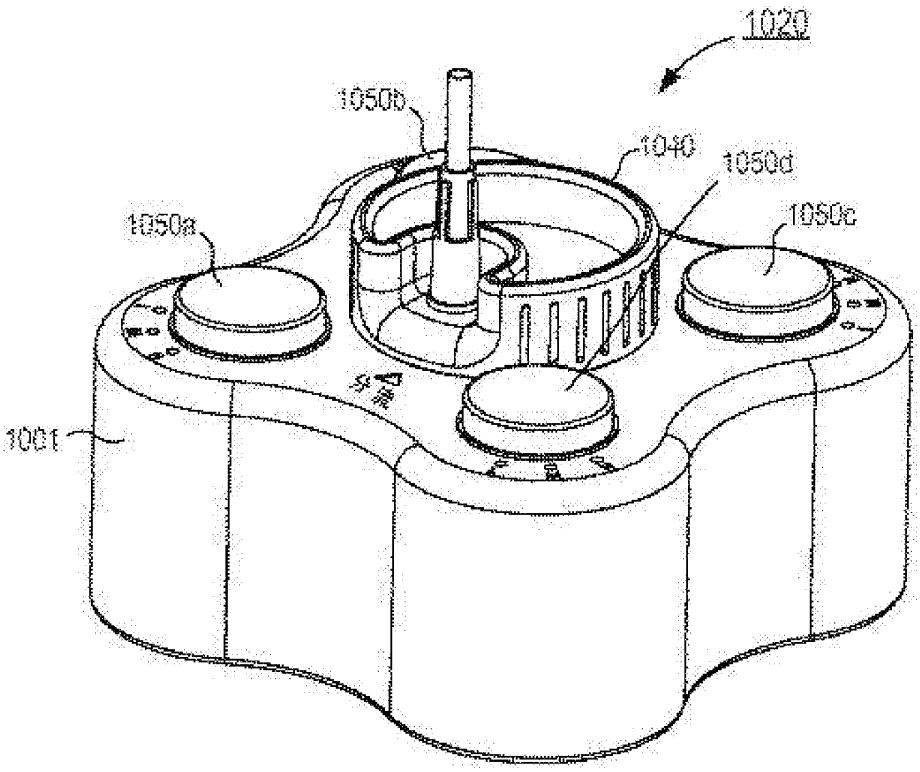


FIG. 52

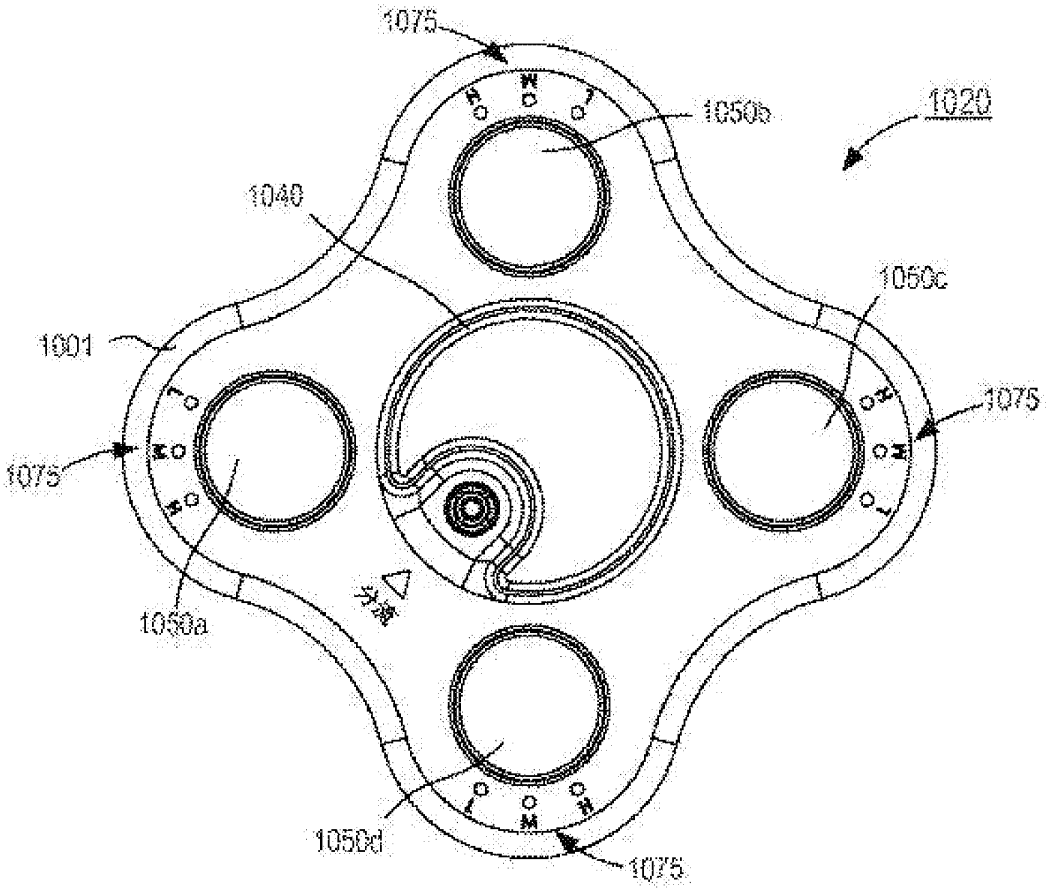
[Fig. 53]


900
SS
904
RR
920
945
921
935a
935c
953a
953c
950a
950c
901
967a
967c
955a
955c
990'
990
980

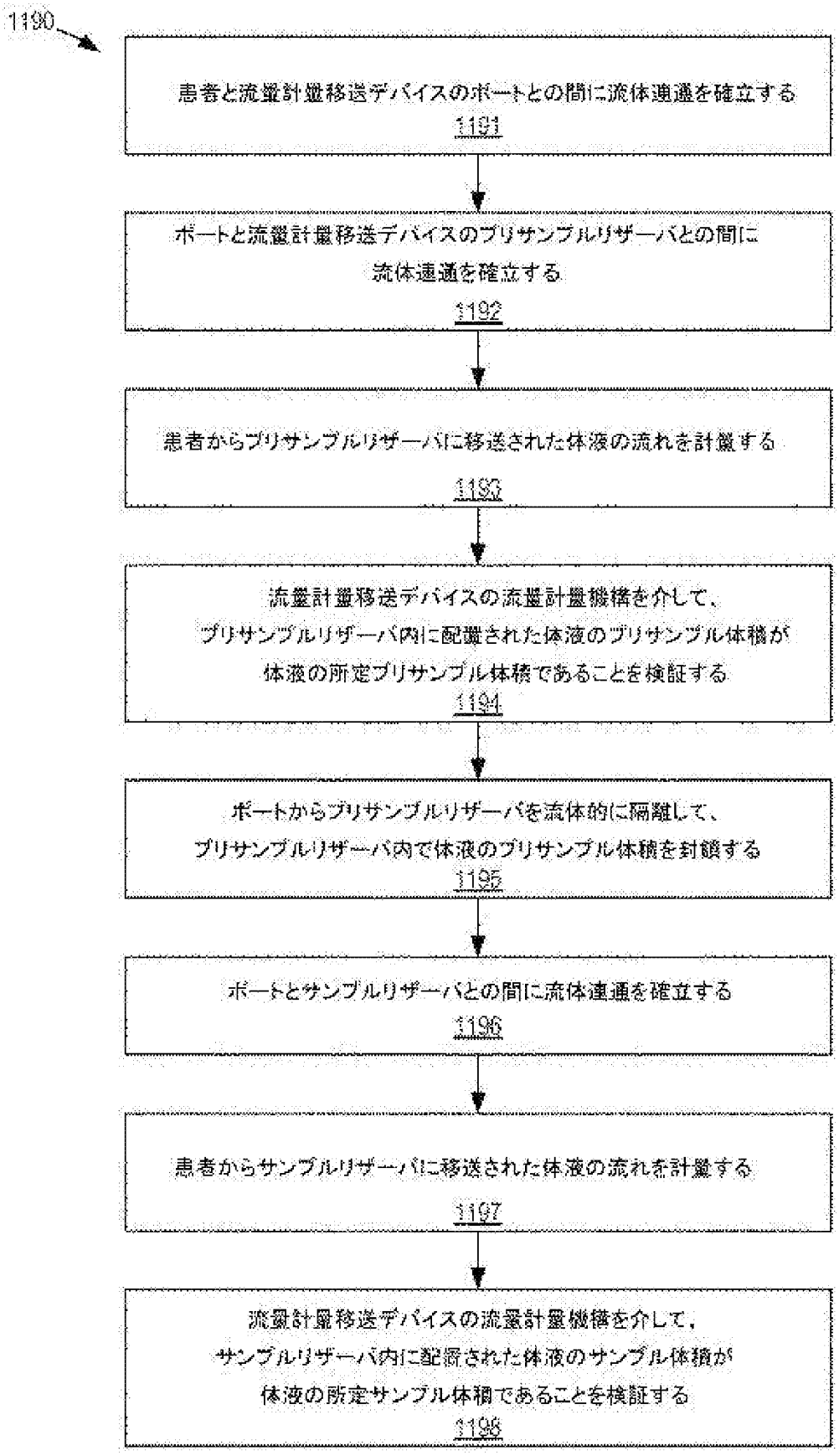
[Fig. 54]



[Fig. 55]



[Fig. 56]


1190
患者と流量計量移送デバイスのポートとの間に流体連通を確立する
1191
ポートと流量計量移送デバイスのプリサンプルリザーバとの間に
流体連通を確立する
1192
患者からプリサンプルリザーバに移送された体液の流れを計量する
1193
流量計量移送デバイスの流量計量機構を介して、
プリサンプルリザーバ内に配置された体液のプリサンプル体積が
体液の所定プリサンプル体積であることを検証する
1194
ポートからプリサンプルリザーバを流体的に隔離して、
プリサンプルリザーバ内で体液のプリサンプル体積を封鎖する
1195
ポートとサンプルリザーバとの間に流体連通を確立する
1196
患者からサンプルリザーバに移送された体液の流れを計量する
1197
流量計量移送デバイスの流量計量機構を介して、
サンプルリザーバ内に配置された体液のサンプル体積が
体液の所定サンプル体積であることを検証する
1198

search report open —

[International search report]

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/073080

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/155 (2014.01)
USPC - 600/575
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61B 5/00, 5/15, 5/153, 5/155; A61M 39/22; A61J 1/05; G01N 1/10, 1/14, 1/18 (2014.01)
USPC - 422/559; 435/294.1; 600/573, 575, 576, 577, 578; 604/248, 409

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61B 5/1405, 5/1427, 5/1438, 5/150251; A61M 39/223 (2013.01)

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X – Y	US 5,097,842 A (BONN) 24 March 1992 (24.03.1992) entire document	12, 15, 16, 18 – 1-11, 13, 14, 17, 19-29
X – Y	US 2008/0145933 A1 (PATTON) 19 June 2008 (19.06.2008) entire document	30-41 – 3, 13, 17, 22, 24, 25,
Y	US 2005/0148993 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
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
06 February 2014	18 FEB 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

drawing open

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

Magnify and Rotate

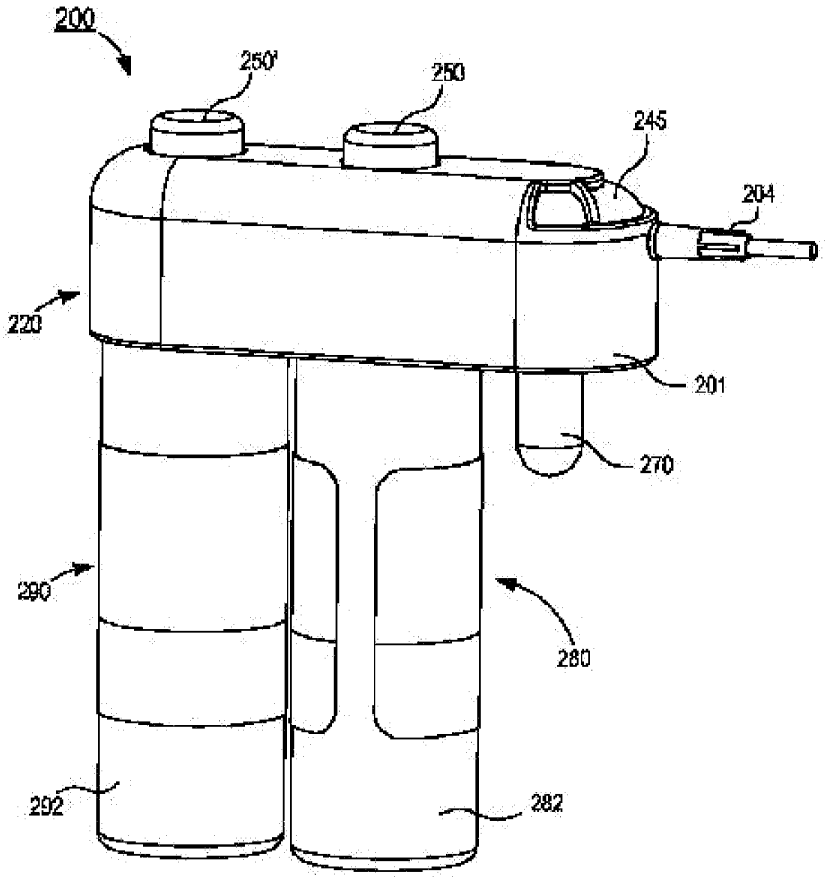


FIG. 2

Representative drawing

1 / 1 display

Copyright JPO and INPIT (P0200)

(19)日本国特許庁(JP)　(12)公表特許公報(A)　(11)特許出願公表番号
特表2016-504075
(P2016-504075A)
(43)公表日　平成28年2月12日(2016.2.12)

(51)Int.Cl.			F I			テーマコード（参考）
A61B	5/154	(2006.01)	A61B	5/14	300E	4C038
A61B	5/15	(2006.01)	A61B	5/14	300H	

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)
(86)(22)出願日　平成25年12月4日 (2013.12.4)
(85)翻訳文提出日　平成27年7月24日 (2015.7.24)
(86)国際出願番号　PCT/US2013/073080
(87)国際公開番号　WO2014/089186
(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)

(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　９８１２１，シアトル，６番　アベニュー　２００１，スイート　１６３０
(74)代理人　100079108
弁理士　稲葉　良幸
(74)代理人　100109346
弁理士　大貫　敏史
(74)代理人　100117189
弁理士　江口　昭彦
(74)代理人　100134120
弁理士　内藤　和彦

最終頁に続く

(54)【発明の名称】滅菌体液収集デバイス及び方法

(57)【要約】
装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。分流機構は、患者から体液を受け取るように内腔規定デバイスに結合可能な入口ポートと、プリサンプルリザーバに流体的に結合可能な第１出口ポートと、サンプルリザーバに流体的に結合可能な第２出口ポートと、を有する。分流機構は、第１出口ポート及び第２出口ポートをそれぞれ入口ポートに流体連通するように配置するように構成された第１流体流路及び第２流路を規定する。流量計量機構は、体液の所定体積の第１流体流路を通るプリサンプルリザーバへの流れを計量し、体液の第２体積の第２流体流路を通るサンプルリザーバへの流れを計量し、所定体積及び第２体積に関連する体積インジケータを表示するように構成される。
【選択図】図２

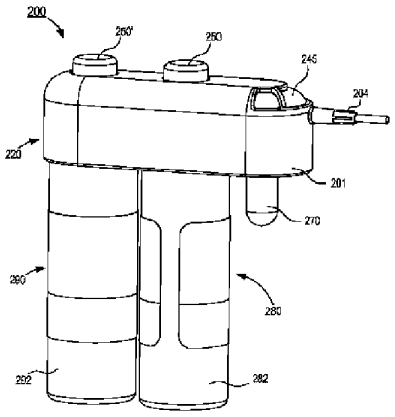


FIG. 2

【特許請求の範囲】
【請求項１】
患者から体液サンプルを取得する装置であって、
前記患者から抜き取られる体液の第１体積を受け取るように構成されたプリサンプルリザーバと、
入口ポート、第１出口ポート及び第２出口ポートを含む分流機構であって、前記入口ポートが、患者から体液を受け取るように内腔規定デバイスに結合されるように構成され、前記第１出口ポートが、前記分流機構に前記プリサンプルリザーバを流体的に結合するように構成され、前記第２出口ポートが、前記分流機構にサンプルリザーバを流体的に結合するように構成され、前記分流機構が、前記第１出口ポートを前記入口ポートに流体連通するように配置するように構成された第１流体流路と、前記第２出口ポートを前記入口ポートに流体連通するように配置するように構成された第２流体流路と、を規定する、分流機構と、
前記第１流体流路及び前記第２流体流路に流体連通する流量計量機構であって、体液の第１体積の前記第１流体流路を通る前記プリサンプルリザーバ内への流れを計量し、体液の第２体積の前記第２流体流路を通る前記サンプルリザーバ内への流れを計量するように構成され、前記第１体積及び前記第２体積に関連する体積インジケータを表示するように構成された流量計量機構と、を備える装置。
【請求項２】
前記体液の第１体積が、第１期間中に前記第１流体流路内で流れ、前記体液の第２体積が、前記第１期間の後、第２期間中に前記第２流体流路内で流れる、請求項１に記載の装置。
【請求項３】
前記体液の第１体積が、皮膚に存在する汚染物質を含み、前記体液の第２体積には、皮膚に存在する汚染物質が実質的にない、請求項１に記載の装置。
【請求項４】
前記プリサンプルリザーバが、前記分流器機構の一部によって少なくとも部分的に規定される、請求項１に記載の装置。
【請求項５】
前記体積インジケータが視覚的インジケータである、請求項１に記載の装置。
【請求項６】
前記分流機構が、前記第２出口ポートを通って移動して前記サンプルリザーバを前記第２流体流路に流体連通するように配置するように構成された可動部材を含む、請求項１に記載の装置。
【請求項７】
前記流量計量機構が、前記可動部材の一部の中に少なくとも部分的に配置される、請求項６に記載の装置。
【請求項８】
前記分流機構が、前記血液の第１体積が前記プリサンプルリザーバ内に配置されると、前記プリサンプルリザーバ及び前記第１流体流路の少なくとも一部を流体的に隔離するように構成される、請求項１に記載の装置。
【請求項９】
前記分流機構が、第２サンプルリザーバを前記分流機構に流体的に結合するように構成された第３出口ポートを含み、前記第３出口ポートを前記入口ポートに流体連通するように配置するように構成された第３流体流路を規定する、請求項１に記載の装置。
【請求項１０】
第１内腔及び第２内腔を規定する流量コントローラであって、前記第１内腔が前記第１流体流路を前記入口ポートに流体連通するように配置する第１形態と、前記第２内腔が前記第２流体流路を前記入口ポートに流体連通するように配置する第２形態との間で移動するように構成された流量コントローラをさらに備える、請求項１に記載の装置。

【請求項１１】
前記流量コントローラが、前記体液の第１体積が前記プリサンプルリザーバ内に配置された後、前記第１形態から前記第２形態に移動するように構成される、請求項１０に記載の装置。
【請求項１２】
患者から体液サンプルを取得する装置であって、
前記患者から抜き取られる体液の第１体積を受け取るように構成されたプリサンプルリザーバと、
入口ポート、第１出口ポート及び第２出口ポートを含む分流機構であって、前記入口ポートが、患者から体液を受け取るように内腔規定デバイスに結合されるように構成され、前記第１出口ポートが前記プリサンプルリザーバを前記分流機構に流体的に結合するように構成され、前記第２出口ポートが、サンプルリザーバを前記分流機構に流体的に結合するように構成される、分流機構と、
前記分流機構内に少なくとも部分的に配置された流量コントローラであって、前記流量コントローラが前記入口ポートと前記第１出口ポートとの間に流体流路の少なくとも一部を規定する第１形態と、前記流量コントローラが前記入口ポートと前記第２出口ポートとの間に流体流路の少なくとも一部を規定する第２形態との間で移動するように構成された流量コントローラと、
前記分流機構に移動可能に結合された可動部材であって、前記サンプルリザーバが前記入口ポートと前記第２出口ポートとの間の流体流路から流体的に隔離される第１形態と、前記サンプルリザーバが前記入口ポートと前記第２出口ポートとの間の前記流体流路に流体連通する第２形態との間で、前記第２出口ポートを通して移動するように構成され、前記サンプルリザーバが、前記流量コントローラがその第２形態にあり、前記可動部材がその第２形態にある時、前記患者から抜き取られる体液の第２体積を受け取るように構成される、可動部材と、を含む装置。
【請求項１３】
前記体液の第１体積が、皮膚に存在する汚染物質を含み、前記体液の第２体積には、皮膚に存在する汚染物質が実質的にない、請求項１２に記載の装置。
【請求項１４】
前記流量コントローラが、前記分流機構に対してその第１形態とその第２形態との間で回転する、請求項１２に記載の装置。
【請求項１５】
前記流量コントローラが、前記分流機構に対して線形運動で移動する、請求項１２に記載の装置。
【請求項１６】
前記流量コントローラが、その第２形態にある時に、前記プリサンプルリザーバを流体的に隔離するように構成される、請求項１２に記載の装置。
【請求項１７】
前記可動部材が、その第２形態にある時、前記サンプルリザーバの一部を穿孔するように構成された穿孔部材を含む、請求項１２に記載の装置。
【請求項１８】
前記可動部材が、前記可動部材をその第１形態で少なくとも一時的に維持するように構成された付勢部材に結合されている、請求項１２に記載の装置。
【請求項１９】
前記分流機構が、第２サンプルリザーバを前記分流機構に流体的に結合するように構成された第３出口ポートを含む、請求項１２に記載の装置。
【請求項２０】
前記可動部材が第１可動部材であり、前記装置が、
第２可動部材であって、前記第２サンプルリザーバが前記入口ポートと前記第３出口ポートとの間に規定された流体流路から流体的に隔離される第１形態と、前記第２サンプル

リザーバが前記入口ポートと前記第３出口ポートとの間に規定された前記流体流路に流体連通する第２形態との間で、前記第３出口ポートを通して移動するように構成され、前記第２サンプルリザーバが、前記流量コントローラがその第２形態にあり、前記第２可動部材がその第２形態にある時、前記患者から抜き取られる体液の第３体積を受け取るように構成される、第２可動部材をさらに含む、請求項１９に記載の装置。

【請求項２１】

患者から体液サンプルを取得する装置であって、

前記患者から抜き取られる体液の第１体積を受け取るように構成されたプリサンプルリザーバと、

ハウジング及び分配部材を含む分流機構であって、前記ハウジングが第１開口部及び第２開口部を規定し、前記第１開口部が前記プリサンプルリザーバに流体連通しており、前記分配部材が、前記ハウジング内に少なくとも部分的に配置され、かつ前記第２開口に流体連通している流体流路を規定し、前記分配部材が、前記流路に流体連通しかつサンプルリザーバに物理的にかつ流体的に結合されるように構成された結合部分を含む、分流機構と、

前記患者から体液を受け取るように内腔規定デバイスに結合されるように構成された入口ポートを含む流量コントローラであって、前記分流機構に回転可能に結合され、かつ前記入口ポートが前記第１開口部に流体連通する第１形態と、前記入口ポートが前記第２開口部に流体連通する第２形態との間で移動するように構成された流量コントローラと、を備える装置。

【請求項２２】

前記体液の第１体積が、皮膚に存在する汚染物質を含み、前記体液の第２体積には、皮膚に存在する汚染物質が実質的にない、請求項２１に記載の装置。

【請求項２３】

前記プリサンプルリザーバが、前記分配部材の一部によって少なくとも部分的に規定される、請求項２１に記載の装置。

【請求項２４】

前記結合部分が、前記サンプルリザーバの一部を穿孔して前記サンプルリザーバを前記流体流路に流体連通するように配置するように構成された穿孔部材を含む、請求項２１に記載の装置。

【請求項２５】

前記穿孔部材による前記サンプルリザーバの前記一部の前記穿孔が、前記流量コントローラがその第２形態にある時、体液の前記患者から前記入口ポート及び前記流路を通る前記サンプルリザーバ内への流れを開始する、請求項２４に記載の装置。

【請求項２６】

前記体液の第１体積が、体液の第１所定体積であり、前記流体流路が、体液の第２所定体積を受け取るように構成され、前記体液の第２所定体積がサンプル体積に関連する、請求項２１に記載の装置。

【請求項２７】

前記サンプル体積が、約１０ミリリットルと約５０ミリリットルとの間である、請求項２６に記載の装置。

【請求項２８】

前記サンプル体積が約３０ミリリットルである、請求項２６に記載の装置。

【請求項２９】

前記分流機構がシール部材を含み、前記流量コントローラが前記分流機構に結合された時に、前記シール部材が、前記流量コントローラの表面及び前記ハウジングの表面と実質的流体密封シールを形成するように、前記ハウジングと前記流量コントローラとの間に配置され、前記シール部材が第１開口部及び第２開口部を規定し、前記シール部材の前記第１開口部が、前記ハウジングの前記第１開口部と実質的に同軸であり、前記シール部材の前記第２開口部が、前記ハウジングの前記第２開口部と実質的に同軸である、請求項２１

に記載の装置。
【請求項３０】
流量計量移送デバイスを用いて患者から体液の所定サンプル体積を取得する方法であって、前記流量計量移送デバイスが、プリサンプルリザーバ及びサンプルリザーバに流体連通するように選択的に配置されるように構成された入口ポートを含む分流機構と、前記患者からの体液の前記プリサンプルリザーバへの流れ及び前記サンプルリザーバへの流れを計量するように構成された流量計量機構とを含む、方法であり、
前記患者と前記流量計量移送デバイスの前記ポートとの間に流体連通を確立するステップと、
前記ポートと前記プリサンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記プリサンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記プリサンプルリザーバ内に配置された体液のプリサンプル体積が体液の所定プリサンプル体積であることを検証するステップと、
前記プリサンプルリザーバを前記ポートから流体的に隔離して、前記プリサンプルリザーバ内で前記体液のプリサンプル体積を封鎖するステップと、
前記ポートと前記サンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記サンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記サンプルリザーバ内に配置された体液のサンプル体積が体液の所定サンプル体積であることを検証するステップと、を含む方法。
【請求項３１】
前記流量計量移送デバイスが、前記患者と前記プリサンプルリザーバとの間に流体連通が確立される第１形態と、前記患者と前記サンプルリザーバとの間に流体連通が確立される第２形態との間で移動するように構成された流量コントローラを含む、請求項３０に記載の方法。
【請求項３２】
前記体液が血液である、請求項３０に記載の方法。
【請求項３３】
前記サンプルリザーバが、好気性菌用培地又は嫌気性菌用培地のうちの少なくとも一方を含む、請求項３２に記載の方法。
【請求項３４】
前記所定プリサンプル体積が、約１ミリリットルと約１０ミリリットルとの間である、請求項３０に記載の方法。
【請求項３５】
前記所定サンプル体積が、約２０ミリリットルと約６０ミリリットルとの間である、請求項３０に記載の方法。
【請求項３６】
前記所定サンプル体積が約６０ミリリットルである、請求項３０に記載の方法。
【請求項３７】
前記サンプルリザーバが第１サンプルリザーバであり、前記サンプル体積が第１サンプル体積であり、
前記第１サンプルリザーバ内の前記第１サンプル体積が前記所定サンプル体積であることを検証した後、前記ポートと第２サンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記第２サンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記第２サンプルリザーバ内に配置された体液の第２サンプル体積が体液の前記所定サンプル体積であることを検証す

るステップと、をさらに含む、請求項３０に記載の方法。
【請求項３８】
前記第１サンプル体積及び前記第２サンプル体積が、まとめて、約２０ミリリットルと約６０ミリリットルとの間に等しい、請求項３７に記載の方法。
【請求項３９】
前記第２サンプルリザーバ内の前記第２サンプル体積が前記所定サンプル体積であることを検証した後、前記ポートと第３サンプルリザーバとの間に流体連通を確立するステップと、
前記患者から前記第３サンプルリザーバに移送された体液の流れを計量するステップと、
前記流量計量移送デバイスの前記流量計量機構を介して、前記第３サンプルリザーバ内に配置された体液の第３サンプル体積が体液の前記所定サンプル体積であることを検証するステップと、をさらに含む、請求項３７に記載の方法。
【請求項４０】
前記第１サンプル体積、前記第２サンプル体積及び前記第３サンプル体積が、まとめて、約３０ミリリットルと約６０ミリリットルとの間に等しい、請求項３９に記載の方法。
【請求項４１】
前記第１サンプル体積、前記第２サンプル体積及び前記第３サンプル体積が、まとめて、約６０ミリリットルに等しい、請求項３９に記載の方法。
【発明の詳細な説明】
【技術分野】
【０００１】
関連出願の相互参照
[1001] 本出願は、２０１２年１２月４日に出願された「滅菌体液収集デバイス及び方法（Sterile Bodily-Fluid Collection Device and Methods）」と題する米国仮特許出願第６１，７３３，１９９号に対する優先権及びその利益を主張し、その出願の開示内容は、全体として参照により本明細書に組み込まれる。
【０００２】
[1002] 本明細書に記載する実施形態は、概して体液サンプルの非経口的獲得（parenteral procurement）に関し、より詳細には、皮膚に存在する微生物等、体液源の外部の微生物又は他の汚染物質からの汚染を低減して、体液サンプルを非経口的に獲得するデバイス及び方法に関する。
【背景技術】
【０００３】
[1003] 医療従事者は、日常的に、非経口的に取得された体液を用いて患者に対してさまざまなタイプの微生物検査を行う。場合によっては、患者サンプル（例えば、体液）は、細菌、真菌又は酵母菌（例えば、カンジダ）等、１種又は複数種の望ましくない可能性がある微生物が存在するか検査される。微生物検査は、微生物増殖を促進する培地を収容する１つ又は複数の滅菌容器において患者サンプルを培養すること、リアルタイム診断及び／又は分子ＰＣＲに基づく手法を含む場合がある。一般に、こうした微生物が患者サンプルに存在する場合、それら微生物は、培地において経時的に繁殖する。可変時間（例えば数時間から数日間）の後、自動化された連続モニタリングにより、生物体の成長を検出することができる。こうした自動化モニタリングは、生物体の増殖によって生成される二酸化炭素を検出することができる。そして、培地に対して、微生物が存在するか検査することができる。培地に微生物が存在する場合、それは、患者サンプルに同じ微生物が存在することを示唆し、それはさらに、サンプルを取得した患者の体液に同じ微生物が存在することを示唆する。従って、培地に微生物が存在すると判断された場合、患者は、患者から望ましくない微生物を処置するか又は他の方法で除去するように特に設計された１種あるいは複数種の抗生物質又は他の処置が処方される可能性がある。
【０００４】

[1004] しかしながら、患者サンプルは、獲得中に汚染される可能性がり、及び／又は、他の方法で偽陽性結果が出やすい可能性がある。患者サンプルの汚染が発生する可能性がある１つの過程は、患者の体内への針の挿入中に取り除かれ後に患者サンプルとともに培地に移送された体表からの微生物（例えば、皮膚に存在する微生物）の移送による。体表微生物及び／又は他の望ましくない外部微生物は、直接、又は取り除かれた組織片、毛包、汗腺及び他の皮膚付属器構造を介して取り除かれる可能性がある。別のあり得る汚染源は、患者サンプルを抜き取る人から来る。例えば、医師、瀉血専門医、看護師等が、自身の身体（例えば、指、腕等）から患者サンプルに及び／又は患者サンプルを収容している機器に汚染物質を移送する可能性がある。さらに詳述すると、患者サンプル獲得プロセス（例えば、患者から針、針／管からサンプル容器等）の間に使用される機器及び／又はデバイスは、各々が有り得る汚染の箇所を生じさせる可能性がある複数の流体インタフェースを含むことが多い。こうした機器及び／又はデバイスの使用は、通常、さまざまなインタフェースを接続し及び／又は流体的に結合するための手作業による介入を含む。これらのインタフェースは、単一の流体的に結合されたシステムとして事前に組み立てられかつ滅菌されないため、使用者（例えば、医師、瀉血専門医等）及び／又は他の汚染源（例えば、周囲空気、病室のテーブル及びカウンタの表面の汚染物質、リネン又は衣類から移送された微生物等）を介して患者サンプルに導入される可能性がある。場合によっては、こうした汚染物質は、培地で生育し、最終的に陽性の微生物検査結果をもたらす可能性があり、それにより、体内におけるこうした微生物の存在を誤って示す。

【０００５】

[1005] 場合によっては、偽陽性結果及び／又は偽陰性結果は、患者サンプルの所定体積に起因する可能性がある。例えば、体積に影響されやすい血液培養ボトルを過充填することにより、こうした培養ボトル及び関連する自動連続モニタリング微生物検出システムの製造業者からの使用説明書及び／又は警告ラベルにおいて注記されているように、偽陽性結果に至る可能性がある。一方、別の例として、培地内における患者サンプルの体積が不十分であることにより、偽陰性結果がもたらされる可能性がある。例として、Journal of Clinical Microbiologyの２０１１年１２月号に記載された「Optimized Pathogen Detection with 30- Compared to 20-Milliliter Blood Culture Draws」と題するMayo Clinicによって行われた研究において、２０ミリリットル（ｍＬ）の患者サンプル体積により、患者サンプルに存在する菌血症の約８０％の存在を検出することができ、４０ｍＬの患者サンプル体積により、菌血症の約８８％を検出することができ、６０ｍＬの患者サンプル体積により、菌血症の約９９％を検出することができる。

【０００６】

[1006] 汚染、不十分な患者サンプル体積等の結果としてのこうした不正確な結果は、疑いのある病気又は健康状態を診断するか又は治療しようとする時に問題である。例えば、微生物検査からの偽陰性結果により、患者の病気が誤診され及び／又は治療が遅れることになる可能性があり、それによって場合によっては、患者の死に至る可能性がある。逆に、微生物検査からの偽陽性結果により、患者が１つ又は複数の抗微生物療法を不必要に受けることになる可能性があり、それにより、例えば死を含む患者の深刻な副作用が引き起こされるとともに、患者の入院の期間の延長及び／又は間違った治療に関連する他の合併症のために医療制度に対する不必要な負担及び出費がもたらされる可能性がある。さらに、これらの偽陽性結果に起因する診断撮像機器の使用はまた、コストとともに、種々の撮像処置（例えば、ＣＴスキャン）に関連する高濃度放射線の不必要な照射が長期の患者の健康に対して多くの既知の悪影響を及ぼすため、患者の安全性の観点からも問題である。

【０００７】

[1007] 従って、例えば、患者サンプル及び／又は流体インタフェースの周囲の非滅菌状態及び／又は他の外部汚染源への暴露を最小限にすることにより、体液検査サンプルにおける微生物汚染を低減する、滅菌「一体型」体液収集デバイス及び方法が必要とされている。さらに、こうした体液収集デバイスが、患者サンプルを実質的にリアルタイムに（例えば、患者のベッドわきで）獲得している医療従事者に視覚的に、計算された方法で、又

は他の方法で通信することができる、患者からサンプルリザーバ又は培地に移送された体液の体液を正確に計量し、測定し、及び／又は、他の方法で評価する手段を含むことが必要とされている。

【発明の概要】

【０００８】

[1008] 本明細書では、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体液源の外部の微生物からの汚染を低減して体液サンプルを非経口的に獲得するデバイスについて記載されている。いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、入口ポート、第１出口ポート及び第２出口ポートを含み、第１流体流路及び第２流体流路を規定している。入口ポートを、患者から体液を受け取るように内腔規定デバイスに結合することができる。第１出口ポート及び第２出口ポートは、プリサンプルリザーバ及びサンプルリザーバそれぞれを分流機構に流体的に結合するように構成されている。第１流体流路は、第１出口ポートを入口ポートに流体連通するように配置するように構成され、第２流体流路は、第２出口ポートを入口ポートに流体連通するように配置するように構成されている。流量計量機構は、第１流体流路及び第２流体流路に流体連通している。流量計量機構は、体液の第１体積の第１流体流路を通るプリサンプルリザーバ内への流れを計量し、体液の第２体積の第２流体流路を通るサンプルリザーバ内への流れを計量するように構成されている。流量計量機構は、第１体積及び第２体積に関連する体積インジケータを表示するように構成されている。

【図面の簡単な説明】

【０００９】

【図１】実施形態による体液収集デバイスの概略図である。

【図２】実施形態による体液収集デバイスの斜視図である。

【図３】図２の体液収集デバイスの組立分解斜視図である。

【図４】図２の体液収集デバイスに含まれるハウジングの図３の線X_1－X_1に沿って取り出された側断面図である。

【図５】図２の体液収集デバイスに含まれる可動部材の図３の線X_2－X_2に沿って取り出された断面図である。

【図６】図２の体液収集デバイスに含まれる流量コントローラの図３の線X_3－X_3に沿って取り出された断面図である。

【図７】図２の体液収集デバイスに含まれる流量コントローラの図３の線X_4－X_4に沿って取り出された断面図である。

【図８】第１形態にある図２の体液収集デバイスの上面図である。

【図９】第１形態にある図２の体液収集デバイスの図８の線X_5－X_5に沿って取り出された断面図である。

【図１０】第２形態にある図２の体液収集デバイスの上面図である。

【図１１】第２形態にある図２の体液収集デバイスの図１０の線X_6－X_6に沿って取り出された断面図である。

【図１２】第３形態にある図２の体液収集デバイスの図１０の線X_6－X_6に沿って取り出された断面図である。

【図１３】第４形態にある図２の体液収集デバイスの図１０の線X_6－X_6に沿って取り出された断面図である。

【図１４】実施形態による体液収集デバイスの斜視図である。

【図１５】図１４の体液収集デバイスの線X_7－X_7に沿って取り出された側断面図である。

【図１６】実施形態による体液収集デバイスの斜視図である。

【図１７】図１６の体液収集デバイスに含まれる分流機構の組立分解斜視図である。

【図１８】図１６の体液収集デバイスに含まれる分配部材の図１６の線X_8－X_8に沿っ

て取り出された側断面図である。
【図１９】第１形態にある図１６の体液収集デバイスの上面図である。
【図２０】第１形態にある図１６の一部体液収集デバイスの図１９の線X_9－X_9に沿って取り出された断面図である。
【図２１】第２形態にある図１６の体液収集デバイスの上面図である。
【図２２】第２形態にある図１６の体液収集デバイスの図２１の線X_{10}－X_{10}に沿って取り出された断面図である。
【図２３】実施形態による体液収集デバイスの斜視図である。
【図２４】第１形態にある、図２３の体液収集デバイスの一部の線X_{11}－X_{11}に沿って取り出された断面図である。
【図２５】第２形態にある、図２３の体液収集デバイスの線X_{11}－X_{11}に沿って取り出された断面図である。
【図２６】実施形態による体液収集デバイスの斜視図である。
【図２７】図２６の体液収集デバイスに含まれる分流機構の組立分解斜視図である。
【図２８】図２７の体液収集デバイスに含まれる分配部材の図２７の線X_{13}－X_{13}に沿って取り出された断面図である。
【図２９】図２６の体液収集デバイスに含まれる結合部材の図２７の線X_{14}－X_{14}に沿って取り出された断面図である。
【図３０】図２６の体液収集デバイスに含まれるダイヤルの図２７の線X_{15}－X_{15}に沿って取り出された断面図である。
【図３１】図２６の体液収集デバイスに含まれる弁の図２７の線X_{16}－X_{16}に沿って取り出された断面図である。
【図３２】第１形態にある図２６の体液収集デバイスの線X_{12}－X_{12}に沿って取り出された断面図である。
【図３３】第２形態にある図２６の体液収集デバイスの線X_{12}－X_{12}に沿って取り出された断面図である。
【図３４】実施形態による体液収集デバイスの斜視図である。
【図３５】図３４の体液収集デバイスに含まれる分流機構の組立分解斜視図である。
【図３６】図３５の分流機構に含まれる分配部材の線X_{17}－X_{17}に沿って取り出された断面図である。
【図３７】第１形態にある図３４の体液収集デバイスの一部の上面図である。
【図３８】第１形態にある図３７の一部体液収集デバイスの線X_{18}－X_{18}に沿って取り出された断面図である。
【図３９】第２形態にある図３３の体液収集デバイスの上面図である。
【図４０】第２形態にある図３３の体液収集デバイスの図３９の線X_{19}－X_{19}に沿って取り出された断面図である。
【図４１】実施形態による第１形態にある体液収集デバイスの斜視図である。
【図４２】図４１の体液収集デバイスの一部の組立分解斜視図である。
【図４３】第１形態にある図４１の体液収集デバイスの線X_{20}－X_{20}に沿って取り出された断面図である。
【図４４】第２形態にある図４１の体液収集デバイスの線X_{20}－X_{20}に沿って取り出された断面図である。
【図４５】第３形態にある図４１の体液収集デバイスの線X_{20}－X_{20}に沿って取り出された断面図である。
【図４６】実施形態による第１形態にある体液収集デバイスの斜視図である。
【図４７】図４５の体液収集デバイスの一部の組立分解斜視図である。
【図４８】図４６の体液収集デバイスに含まれる分配部材の図４７の線X_{21}－X_{21}に沿って取り出された側断面図である。
【図４９】図４６の体液収集デバイスに含まれる可動部材の図４７の線X_{22}－X_{22}に沿って取り出された側断面図である。

【図５０】第１形態にある図４６の体液収集デバイスの上面図である。
【図５１】第１形態にある図４６の一部体液収集デバイスの図５０の線$X_{23}-X_{23}$に沿って取り出された断面図である。
【図５２】第２形態にある図４６の体液収集デバイスの上面図である。
【図５３】第２形態にある図４６の体液収集デバイスの図５２の線$X_{24}-X_{24}$に沿って取り出された断面図である。
【図５４】実施形態による体液収集デバイスの斜視図である。
【図５５】図５４の体液収集デバイスの上面図である。
【図５６】実施形態による収集デバイスを用いて、汚染を低減して体液サンプルを取得する方法を示すフローチャートである。
【発明を実施するための形態】
【００１０】
[1063] 本明細書では、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体液源の外部の微生物からの汚染を低減して体液サンプルを非経口的に獲得するデバイスについて記載されている。いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量計量機構を含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、入口ポート、第１出口ポート及び第２出口ポートを含み、第１流体流路及び第２流体流路を規定している。入口ポートを、患者から体液を受け取るように内腔規定デバイスに結合することができる。第１出口ポート及び第２出口ポートは、プリサンプルリザーバ及びサンプルリザーバそれぞれを分流機構に流体的に結合するように構成されている。第１流体流路は、第１出口ポートを入口ポートに流体連通するように配置するように構成され、第２流体流路は、第２出口ポートを入口ポートに流体連通するように配置するように構成されている。流量計量機構は、第１流体流路及び第２流体流路に流体連通している。流量計量機構は、体液の第１体積の第１流体流路を通るプリサンプルリザーバ内への流れを計量し、体液の第２体積の第２流体流路を通るサンプルリザーバ内への流れを計量するように構成されている。流量計量機構は、第１体積及び第２体積に関連する体積インジケータを表示するように構成されている。
【００１１】
[1064] いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構、流量コントローラ及び可動部材を含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、入口ポート、第１出口ポート及び第２出口ポートを含む。入口ポートは、患者から体液を受け取るように内腔規定デバイスに結合可能である。第１出口ポートは、プリサンプルリザーバを分流機構に流体的に結合し、第２出口ポートは、サンプルリザーバを分流機構に流体的に結合する。流量コントローラは、分流機構内に少なくとも部分的に配置され、流量コントローラを、流量コントローラが入口ポートと第１出口ポートとの間に流体流路の少なくとも一部を規定する第１形態と、流量コントローラが入口ポートと第２出口ポートとの間に流体流路の少なくとも一部を規定する第２形態との間で移動させることができる。可動部材は、分流機構に移動可能に結合され、サンプルリザーバが入口ポートと第２出口ポートとの間の流体流路から流体的に隔離される第１形態と、サンプルリザーバが入口ポートと第２出口ポートとの間の流体流路に流体連通する第２形態との間で、第２出口ポートを通して移動可能である。サンプルリザーバは、流量コントローラがその第２形態にあり、可動部材がその第２形態にある時、患者から抜き取られる体液の第２体積を受け取るように構成されている。
【００１２】
[1065] いくつかの実施形態では、患者から体液サンプルを取得する装置は、プリサンプルリザーバ、分流機構及び流量コントローラを含む。プリサンプルリザーバは、患者から抜き取られる体液の第１体積を受け取るように構成されている。分流機構は、ハウジング及び分配部材を含む。ハウジングは、プリサンプルリザーバに流体連通している第１開口

部と第２開口部とを規定している。分配部材は、ハウジング内に少なくとも部分的に配置され、かつ第２開口に流体連通している流体流路を規定している。分配部材は、流路に流体連通しかつサンプルリザーバに物理的にかつ流体的に結合されるように構成された結合部分を含む。流量コントローラは、患者から体液を受け取るように内腔規定デバイスに結合されるように構成された入口ポートを含む。流量コントローラは、分流機構に回転可能に結合され、かつ入口ポートが第１開口部に流体連通する第１形態と、入口ポートが第２開口部に流体連通する第２形態との間で移動可能である。

【００１３】

[1066] いくつかの実施形態では、プリサンプルリザーバ及びサンプルリザーバに流体連通するように選択的に配置されるように構成された入口ポートを含む分流機構と、患者からの体液のプリサンプルリザーバへの流れ及びサンプルリザーバへの流れを計量するように構成された流量計量機構とを有する流量計量移送デバイスを用いる方法は、患者と流量計量移送デバイスの入口ポートとの間に流体連通を確立するステップを含む。そして、ポートとプリサンプルリザーバとの間に流体連通が確立される。患者からプリサンプルリザーバに移送された体液の流れが計量される。本方法は、流量計量移送デバイスの流量計量機構を介して、プリサンプルリザーバ内に配置された体液のプリサンプル体積が体液の第１プリサンプル体積であることを検証するステップを含む。プリサンプルリザーバ内にプリサンプル体積が配置された状態で、プリサンプルリザーバがポートから流体的に隔離されて、プリサンプルリザーバ内で体液のプリサンプル体積が封鎖される。プリサンプルリザーバが流体的に隔離された状態で、本方法は、ポートとサンプルリザーバとの間に流体連通を確立するステップを含む。患者からサンプルリザーバに移送された体液の流れが計量される。本方法は、流量計量移送デバイスの流量計量機構を介して、サンプルリザーバ内に配置された体液のサンプル体積が体液の第１サンプル体積であることを検証するステップを含む。

【００１４】

[1067] いくつかの実施形態では、装置は、分流機構及び流量コントローラを含む。分流機構は、入口ポート、第１出口ポート、第２出口ポート及び第３出口ポートを規定することができる。第１出口ポートは、プリサンプルリザーバに流体的に結合され、第２出口ポートは、第１サンプルリザーバに流体的に結合され、第３出口ポートは、第２サンプルリザーバに流体的に結合され、等である。流体リザーバのすべてを、互いから流体的に隔離することができる。流量コントローラはさまざまな流体チャネルを含み、流体チャネルは、指定された方向における流体移動を可能にすることができ、分流機構に動作可能に結合されるように構成され得る。使用時、分流機構が第１形態にある時、流量コントローラは、体液の流れがプリサンプルリザーバに入るのを可能にすることができる。分流機構を第２形態に移動させることができ、そこでは、流量コントローラは、体液の流れが第１サンプルリザーバに入るのを可能にすることができる。さらに、分流機構を、その後、第３形態に移動させることができ、それにより、流量コントローラは、体液の流れが第２サンプルリザーバに入るのを可能にすることができる。

【００１５】

[1068] いくつかの実施形態では、体液収集デバイスを、体液の第２体積の第１サンプルリザーバ内への流れ及び／又は体液の第３体積の第２サンプルリザーバ内への流れを可能にする前に、体液の第１の所定体積をプリサンプルリザーバに選択的に分流させるように構成することができる。このように、体液の第２体積及び／又は第３体積を、診断又は他の検査に使用することができ、一方で、体表又はサンプルを獲得する患者の外部の他の微生物源からの微生物を含む可能性がある体液の第１体積が隔離される。いくつかの実施形態では、体液収集デバイスは、行われる分析プロトコル及び／又は検査プロトコルに応じて追加のサンプルリザーバ（例えば、３、４、５、６以上）を含むことができる。

【００１６】

[1069] いくつかの実施形態では、体液収集デバイスは、体液の適切な体積が患者から収集され及び／又は所定のプリサンプルリザーバ及び／又はサンプルリザーバに移送される

のを確実にするために、流量計量を含むことができる。体液収集デバイスを、体液の計量された体積が収集された後に、流体流を自動的に分流させ及び／又は制御するように構成することができる。例えば、第１計量プリサンプル体積が収集されると、分流機構を、体液流を第１サンプルリザーバに分流させるように構成することができ、その後、第１計量サンプル体積が収集された後、分流機構を、体液流を第２サンプルリザーバに分流させるように構成することができ、等である。いくつかの実施形態では、体液収集デバイスは、例えば液晶ディスプレイ（ＬＣＤ）等の計量された体積のディスプレイを含み、どれだけの体液が各所定の個々のサンプルリザーバ内に収集されたかの視覚的指示を使用者に提供することができる。いくつかの実施形態では、カスタマイズされたプリサンプル及び／又はサンプル体積収集を可能にするように、複数のディスプレイを設けることができる。

【００１７】

[1070] 本明細書及び添付の特許請求の範囲で用いる単数形「１つの（a、an）」及び「その（the）」は、文脈に明示的に述べられていない限り、複数の指示対象を含む。従って、例えば、「（１つの）部材」という用語は、単一部材又は部材の組合せを意味するように意図され、「（１つの）材料」は、１つあるいは複数の材料又はそれらの組合せを意味するように意図されている。

【００１８】

[1071] 本明細書で用いる「体液」は、限定されないが、血液、髄液、尿、胆汁、リンパ液、唾液、滑液、漿液、胸膜液、羊水等又はそれらのあらゆる組合せを含む、患者の体内から得られるあらゆる流体を含むことができる。

【００１９】

[1072] 本明細書で用いる「第１の所定量」、「第１量」及び「第１体積」という用語は、第１リザーバ又はプリサンプルリザーバによって受け取られるか又は収容されるように構成された体液の量を述べる。「第１量」及び「第１体積」という用語は、所定量を明示的に述べないが、明示的に異なるように述べられていない限り、第１量は第１の所定量であることが理解されるべきである。

【００２０】

[1073] 本明細書で用いる「第２量」及び「第２体積」という用語は、第２リザーバ又はサンプルリザーバによって受け取られるか又は収容されるように構成された体液の量を述べる。第２量を、体液のあらゆる好適な量とすることができ、それは所定量である必要はない。逆に、そのように明示的に述べられる場合、第２リザーバ又はサンプルリザーバによって受け取られかつ収容される第２量は、第２の所定量であり得る。

【００２１】

[1074] 本明細書で用いる「組」という用語は、複数の機構又は複数の部品を含む単一の機構を指すことができる。例えば、壁の組と言う場合、壁の組を、別個の部分を含む１つの壁とみなすことができ、又は壁の組を、複数の壁とみなすことができる。同様に言えば、一体的に構成された物品は一組の壁を含むことができる。こうした一組の壁は、例えば、互いに不連続である複数の部分を含むことができる。一組の壁を、別個に製造され、後に（例えば、溶接、接着剤又はあらゆる好適な方法を介して）互いに接合される複数の物品から製造することも可能である。

【００２２】

[1075] 本明細書で用いる「近位」及び「遠位」という用語は、デバイスを患者に接触するように配置する使用者に対してそれぞれ近い方の方向及び離れる方向を指す。従って、例えば、患者の身体に最初に接触するデバイスの端部は遠位端となり、デバイスの反対側の端部（例えば、使用者が操作しているデバイスの端部）はデバイスの近位端となる。

【００２３】

[1076] 本明細書で用いる「約」、「およそ」及び「実質的に」という用語は、数値と関連して用いられる場合、そのように定義される値が名目上示されている値であることを意味するように意図されている。言い換えれば、約、およそ及び実質的にという用語は、数値に関連して用いられる場合、概して、示されている値プラスマイナス所与の許容差を含

む。例えば、場合によっては、好適な許容差は、示されている値の±１０％である可能性があり、従って、約０．５は０．４５及び０．５５を含み、約１０は９～１１を含み、約１０００は９００～１１００を含む。他の場合では、好適な許容差は、プラスマイナス示されている値の最後の有効数字の許容可能な割合であり得る。例えば、好適な許容差は、最後の有効数字の±１０％である可能性があり、従って、約１０．１は１０．０９及び１０．１１を含み、およそ２５は２４．５及び２５．５を含む。こうした変動は、製造公差又は他の実際的な考慮事項（例えば、測定器具に関連する公差、許容可能な人的ミス等）からもたらされ得る。

【００２４】

[1077] 体液の所定体積と体液の収集された体積との関係について述べる場合、それらの値は、上述したものの等の好適な許容差を含むことが理解されるべきである。例えば、体液の収集された体積が体液の所定体積と実質的に等しいと述べる場合、収集された体積及び所定体積は、名目上、好適な許容差の範囲内で等しい。場合によっては、許容差を、体液の収集された体積の意図された使用によって求めることができる。例えば、場合によっては、血液培養のアッセイは、血液の収集された体積が製造業者の（又はエビエンスに基づく最適な実践）推奨体積の１．０％から５．０％の範囲内である時、約９９％正確であり得る。例として、体液のアッセイに対する製造業者の推奨体積は、約９９％の信頼度のために、合計４本又は６本の収集ボトルが使用される場合、１本のサンプル収集ボトル当り１０ミリリットル（ｍＬ）（すなわち、総体積は４０ｍｌ～６０ｍｌ）±５％であり得る。従って、１０．５ｍＬの収集体積により、約９９％を超える信頼度での結果が提供され、１１ｍＬの収集体積により、約９９％未満の信頼度の結果が提供される。他の場合では、好適な許容差は、０．１％、０．５％、１．０％、２．０％、３．０％、４．０％、５．０％、６．０％、７．０％、８．０％、９．０％、１０．０％又はそれらの間のあらゆる分数値であり得る。さらに他の場合では、許容差は１０．０％を上回る可能性がある。従って、本明細書に記載する実施形態のいずれも、好適な許容差の範囲内で体液の流量を計量し及び／又は体液の体積を他の方法で測定するように構成されたあらゆる好適な流量測定機構及び／又はデバイスを含み及び／又はそれとともに使用することができる。さらに、流量計量機構及び／又はデバイスを、不正確な測定、人的ミス等の組合せからもたらされる可能性がある公差の蓄積を最小限にするか又はなくすように配置することができる。

【００２５】

[1078] 図１は、実施形態による体液収集デバイス１００の一部の概略図である。概して、体液収集デバイス１００（本明細書では、「流体収集デバイス」又は「収集デバイス」とも呼ぶ）は、患者から体液を抜き取ることを可能にし、その際、抜き取られた体液の第１部分又は第１量が、医療診断及び／又は治療の目的で検査されるため等、生物学的サンプルとして使用される、抜き取られた体液の第２部分あるいは体積及び／又は第３部分あるいは体積から離れるように分流されるように構成されている。言い換えれば、本明細書においてより詳細に記載するように、収集デバイス１００は、体液の第１の所定体積をプリサンプル収集リザーバに、体液の第２体積及び第３体積（又は、いくつかの実施形態では、第４、第５等）を、プリサンプルリザーバから流体的に隔離された１つ又は複数のサンプル収集リザーバ（例えば、サンプルリザーバ）に移送するように構成されている。

【００２６】

[1079] 収集デバイス１００は、分流機構１２０、流量コントローラ１４０、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０、及び第１サンプルリザーバ１８０とは異なる第２サンプルリザーバ１９０を含む。分流機構１２０は、図１に示すように、入口ポート１２１と、第１出口ポート１２５及び第２出口ポート１２６等、少なくとも２つの出口ポートとを含む。いくつかの実施形態では、分流機構１２０は、プリサンプルリザーバ及びサンプルリザーバの総数に等しい一組の出口ポートを含むことができる。例えば、収集デバイス１００が１つのプリサンプル及び４つのサンプリリザーバを有する場合、分流機構１２０は５つの出口ポートを含むことができる。いくつかの実施形態では、分流機

構１２０を、複数の形態の間の分流機構１２０の移動を容易にすることができる（図１には示さない）アクチュエータに動作可能に結合することができる。入口ポート１２１は、患者から体液を抜き取り及び／又は収集デバイス１００に輸送するための経路Ｘを規定している医療デバイスに流体的に結合されるように構成されている。例えば、入口ポート１２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。このように、分流機構１２０は、針又は他のあらゆる内腔規定デバイスを介して患者から体液を受け取ることができる。

【００２７】

[1080] 分流機構１２０の第１出口ポート１２５を、プリサンプルリザーバ１７０に流体的に結合することができる。いくつかの実施形態では、プリサンプルリザーバ１７０は、第１出口ポート１２５及び／又は分流機構１２０の一部と一体的に形成されている。他の実施形態では、プリサンプルリザーバ１７０を、接着剤、抵抗嵌め（resistance fit）、機械的締結具、あらゆる数の嵌合凹部、ねじ結合及び／又は他のあらゆる好適な結合あるいはその組合せを介して、分流機構１２０に機械的に及び／又は流体的に結合することができる。同様に言えば、プリサンプルリザーバ１７０を、分流機構１２０に物理的に（例えば、機械的に）結合することができ、それにより、プリサンプルリザーバ１７０によって規定される内部空間（volume）が分流機構１２０の第１出口ポート１２５に流体連通する。さらに他の実施形態では、プリサンプルリザーバ１７０を、可撓性滅菌管等の（図１には示さない）介在構造を介して、分流機構１２０の第１出口ポート１２５に動作可能に結合することができる。より詳細には、介在構造は、プリサンプルリザーバ１７０を、第１出口ポート１２５に流体連通するように配置するように構成された内腔を規定することができる。

【００２８】

[1081] プリサンプルリザーバ１７０は、体液の第１の所定体積を受け取りかつ収容するように構成されている。いくつかの実施形態では、プリサンプルリザーバ１７０は、体液の第１体積を、患者から後に抜き取られる（体液の第１体積と同じである場合もあれば異なる場合もある）体液の第２体積及び／又は第３体積から流体的に隔離するように収容するように構成されている。プリサンプルリザーバ１７０は、全体として参照により本明細書に組み込まれる、「汚染を低減して体液サンプルを非経口的に獲得するシステム及び方法（Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination）」と題する米国特許第８，１９７，４２０号に詳細に記載されているプリサンプルリザーバ等、体液を収容するあらゆる好適なリザーバであり得る。

【００２９】

[1082] いくつかの実施形態では、分流機構１２０の第２出口ポート１２６は、第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０に結合することができる内腔規定デバイスに流体的に結合されるように構成されている。任意選択的に、他の実施形態では、分流機構１２０の第２出口ポート１２６を、第１サンプルリザーバ１８０に結合することができ、分流機構１２０は、第２サンプルリザーバ１９０に結合された（図示せず）第３出口ポートを有することができる。いくつかの実施形態では、第１サンプルリザーバ１８０を、第２出口ポート１２６及び／又は分流機構１２０の一部と一体的に形成することができる。他の実施形態では、第１サンプルリザーバ１８０を、プリサンプルリザーバ１７０に関して上述したような介在構造を介して、第２出口ポート１２６に機械的に結合し、又は第２出口ポート１２６に動作可能に結合することができる。第１サンプルリザーバ１８０は、体液の第２体積を受け取りかつ収容するように構成されている。例えば、体液の第２体積は、第１プリサンプル体積の抜取りに続いて患者から抜き取られた量であり得る。いくつかの実施形態では、第１サンプルリザーバ１８０は、第２体積がプリサンプル体液の第１体積から流体的に隔離されるように、体液の第２体積を収容するように構成されている。

【００３０】

[1083] 第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０は、例えば、上で

参照により組み込んだ‘４２０特許に記載されているようなサンプルリザーバを含む、体液を収容するあらゆる好適な滅菌リザーバであり得る。いくつかの実施形態では、第２体積を、体液のあらゆる好適な体積とすることができ、それは所定体積である必要はない。他の実施形態では、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０への体液の移送を、第２体積が第２の所定体積であるように、計量等することができる。

【００３１】

[1084] 第２サンプルリザーバ１９０は、あらゆる好適なサンプルリザーバであり得る。いくつかの実施形態では、第２サンプルリザーバ１９０は、上述した第１サンプルリザーバ１８０と実質的に同様であり得る。第２サンプルリザーバ１９０を、上述したように、第２出口ポート１２６に流体的に結合することができる。第２出口ポート１２６の第２サンプルリザーバ１９０への流体的結合は、詳細に上述したように、第２出口ポート１２６の第１サンプルリザーバ１８０への流体的結合と実質的に同様であり得る。従って、こうした部分については、本明細書ではそれ以上詳細には記載せず、明示的に異なるように記載されていない限り、実質的に同様であるとみなすべきである。さらに、（図１には示さない）分流機構１２０の追加の出口ポート及びサンプルリザーバは、第２出口ポート１２６及び第１サンプルリザーバ１８０と実質的に同様であり得る。

【００３２】

[1085] いくつかの実施形態では、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０を、分流機構１２０に同様に結合する（又はともに形成する）ことができる。他の実施形態では、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び第２サンプルリザーバ１９０は、分流機構１２０に同様に結合される必要はない。例えば、いくつかの実施形態では、プリサンプルリザーバ１７０を、分流機構１２０（例えば、第１出口ポート１２４）と一体的に形成することができ、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０を、可撓性滅菌管又はそのあらゆる組合せ等の介在構造を介して、分流機構１２０（例えば、第２出口ポート１２６）に動作可能に結合することができる。

【００３３】

[1086] いくつかの実施形態では、収集デバイス１００は、（図１には示さない）アクチュエータと、第１流体流路１４２、第２流体流路１４４及び任意選択的に（図１には示さない）追加の流体流路を規定する流量コントローラ１４０と、をさらに含むことができる。いくつかの実施形態では、アクチュエータを、分流機構１２０に含めるか又は他の方法で動作可能に結合することができる。このように、アクチュエータを、流量コントローラ１４０内の（例えば、異なる形態の間の）流体移動を制御するように構成することができる。例えば、アクチュエータは、流量コントローラ１４０の第１形態に対応する第１位置、流量コントローラ１４０の第２形態に対応する、第１位置とは異なる第２位置等の間で移動可能であり得る。いくつかの実施形態では、アクチュエータを、単方向に移動するように構成することができる。例えば、アクチュエータを、その第１位置からその第２位置に移動させることができるが、その第２位置からその第１位置に移動させることはできない。同様に、アクチュエータを、その第２位置から第３位置に移動させることができるが、その第３位置からその第２位置に戻るように移動させることはできない。このように、流量コントローラ１４０は、その第１形態の前にその第２形態又は第３形態に移動することが防止され、従って、体液の第１量がプリサンプルリザーバ１７０に向けられ、医療診断及び／又は治療の目的での検査のため等、生物学的サンプルとして使用される抜き取られた流体の第２体積及び／又は第３体積を収容するように設計されたサンプルリザーバ１８０及び／又は１９０に向けられないことが必要である。

【００３４】

[1087] 流量コントローラ１４０は、第１形態にある時、第１流体流路１４２が入口ポート１２１を第１出口ポート１２５に流体的に結合し、第２形態にある時、第２流体流路１４４が入口ポート１２１を第２出口ポート１２６に流体的に結合するように構成されている。いくつかの実施形態では、上述したようなアクチュエータを、流量コントローラ１４

０を第１形態及び第２形態、任意選択的に第３形態又は第４形態の間で、並進運動で移動させるように構成することができる。例えば、いくつかの実施形態では、流量コントローラ１４０は、収集デバイス１００に対して遠位位置にある時に第１形態であり得る。こうした実施形態では、アクチュエータを、流量コントローラ１４０を収集デバイス１００に対して近位位置まで近位方向に移動させ、それにより流量コントローラ１３０を第２形態に配置するように作動させることができる。他の実施形態では、アクチュエータを、流量コントローラ１４０を第１形態及び第２形態又は任意選択的に第３形態あるいは第４形態の間で、回転運動で移動するように作動させることも可能である。

【００３５】

[1088] 従って、流量コントローラ１４０が第１形態にある時、第２出口ポート１２６（及び任意選択的に、サンプルリザーバに結合された追加の出口ポート）は、入口ポート１２１から流体的に隔離される。同様に、流量コントローラ１４０が第２形態にある時、第１出口ポート１２５は入口ポート１２１から流体的に隔離される。任意選択的に、流量コントローラ１４０が（図１には示さない）第３形態にある場合、第１出口ポート１２５及び第２出口ポート１２６は、入口ポート１２１から流体的に隔離される。このように、流量コントローラ１４０は、第１形態にある時、体液の第１量を、第１出口ポート１２５を介してプリサンプル流体リザーバ１７０に仕向け又は分流させることができ、第２形態にある時、体液の第２量を、第２出口ポート１２６を介して第１サンプル流体リザーバ１８０に仕向け又は分流させることができる。

【００３６】

[1089] いくつかの実施形態では、アクチュエータの少なくとも一部を、プリサンプル流体リザーバ１７０に動作可能に結合することができる。このように、アクチュエータ（又はアクチュエータの少なくとも一部）を、「プリサンプル」流体リザーバ１７０内における真空の発生を引き起こすか又は他の方法で促進し、それにより、分流機構１２０がその第１形態にある時、体液の収集デバイス１００を通りプリサンプル流体リザーバ１７０に入る流れを開始するように構成することができる。アクチュエータは、例えば、回転ディスク、プランジャ、スライド、ダイヤル、ボタン、ハンドル、レバー及び／あるいは他のあらゆる好適な機構又はそれらの組合せ等、収集デバイス１００内への体液の流れを駆動するあらゆる好適な機構を含むことができる。好適なアクチュエータの例については、本明細書において具体的な実施形態を参照してより詳細に記載する。

【００３７】

[1090] いくつかの実施形態では、分流機構１２０を、体液の第２量の流れが分流機構１２０を通って第１サンプル流体リザーバ１８０に及び／又は第２サンプル流体リザーバ１９０に輸送されるのを可能にする前に、体液の第１量をプリサンプル流体リザーバ１７０に輸送する必要があるように構成することができる。このように、分流機構１２０を、医療従事者による、体液の第２量及び／又は第３量（例えば、サンプル）を収集する前に体液の第１の所定量（例えば、プリサンプル）を収集することに関するコンプライアンスを必要とするものとして特徴付けることができる。同様に言えば、分流機構１２０を、医療従事者が、体液の第１量、すなわちプリサンプルをプリサンプルリザーバ１７０に最初に分流させることなく、体液の第２量すなわちサンプルを第１サンプル流体リザーバ１８０内に収集するのを防止するように構成することができる。このように、医療従事者は、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性がより高い体液の第１量を、分析に使用される体液サンプル内に（意図的であっても無意図的であっても）含めることが防止される。他の実施形態では、流体収集デバイス１００は、強制的コンプライアンスの特徴又は構成要素を含む必要はない。

【００３８】

[1091] いくつかの実施形態では、分流機構１２０は、第１形態、第２形態及び第３形態とは異なる（図１には示さない）第４形態を有することができる。第４形態にある時、分流機構１２０は、入口ポート１２１を、第１出口ポート１２５、第２出口ポート１２６及び任意選択的に第３出口ポートから同時に流体的に隔離することができる。従って、分流

機構１２０がその第４形態にある時、入口ポート１２１からプリサンプル流体リザーバ１７０、第１サンプル流体リザーバ１８０及び第２サンプル流体リザーバ１９０に体液が流れることが防止される。使用時、例えば、分流機構１２０を、体液が入口ポート１２１からプリサンプル流体リザーバ１７０に流れることができるように分流機構１２０を第１形態に配置するように（例えば、手動で又は自動的に）作動させ、その後、体液が入口ポート１２１から第１サンプル流体リザーバ１８０に流れることができるように第２形態まで移動させ、任意選択的に、体液が入口ポート１２１から第２サンプル流体リザーバ１９０に流れることができるように第３形態に移動させることができ、その後、体液の分流機構１２０内への及び／又はそこを通る流れを停止させるように第４形態に移動させることができる。このように、デバイスは、デバイス１００内のいかなる残留体液も汚染され及び／又は他の方法で医療従事者及び／又は患者をあり得る危険な流体にさらすことが防止されるように、有効に「ロックされ」かつ第４形態で自己完結する。この任意選択的な安全機能により、ＨＩＶ、Ｃ型肝炎等の病原体が感染している可能性がある体液サンプルへのあり得る暴露を防止することができる。

【００３９】

[1092] いくつかの実施形態では、収集デバイス１００の１つ又は複数の部分は、（図１には示さない）ハウジング内に配置されている。例えば、いくつかの実施形態では、分流機構１２０、第１プリサンプルリザーバ１７０並びにサンプルリザーバ１８０及び１９０のうちの１つ又は複数の少なくとも一部を、ハウジング内に配置することができる。こうした実施形態では、分流機構１２０の少なくとも一部は、使用者が、患者（例えば、静脈）から収集デバイス１００への体液の流れを制御するように流量コントローラ１４０を作動させることができるように、ハウジングを通してアクセス可能である。好適なハウジングの例については、本明細書において具体的な実施形態を参照してより詳細に記載する。

【００４０】

[1093] いくつかの実施形態では、収集デバイス１００は、任意選択的に、収集デバイスを通して体液の流れを計量することができる１つ又は複数の流量計量デバイスを含むことができる。例えば、流量計量デバイスは、第１流体流路１４２及び／又は第２流体流路１４４に流体連通してそこを通る体液の流れを計量することができる。他の実施形態では、流量計量デバイスは、第１ポート１２５及び／又は第２ポート１２６に流体連通し及び／又は他の方法でそこに配置されることが可能である。流量計量デバイスは、プリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０に移送されている所定体積に関連する指示を使用者に提供するように構成することができるインジケータ等（例えば、ダイヤル、ディスプレイ、色、触覚出力デバイス、ワイヤレス無線信号、Bluetooth（登録商標）無線信号等の電気信号出力デバイス）を含むことができる。いくつかの実施形態では、流量計量デバイスを、例えば、上述したもののようなアクチュエータ等に動作可能に結合することができる。こうした実施形態では、流量計量デバイスは、流量計量デバイスを通して流れた体液の所望の体積に基づいて、流量コントローラ１４０をその第１形態とその第２形態との間で移動させるようにアクチュエータを作動させるように、動作可能であり得る。従って、流量計量デバイスを用いて、体液の所望の体積がプリサンプルリザーバ１７０、第１サンプルリザーバ１８０及び／又は第２サンプルリザーバ１９０に移送され、それにより、例えば患者サンプルに対する微生物検査等において不十分な、不正確な及び／又は誤った結果を防止することができることを確実にすることができる。

【００４１】

[1094] ここで図２～図１３を参照すると、収集デバイス２００は、分流機構２２０、流量コントローラ２４０、プリサンプルリザーバ２７０、第１サンプルリザーバ２８０、及び第１サンプルリザーバ２８０とは異なる第２サンプルリザーバ２９０を含む。本明細書においてさらに記載するように、収集デバイス２００を、例えば皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出するために、第１形態、第２形態及び第３形態の間で移動させることができる。収集デ

バイス２００は、いかなる好適な形状、サイズ又は構成でもあり得る。例えば、図２～図１３ではサンプルリザーバ２８０及び／又は２９０がハウジング２０１に対して垂直に向けられているように示されているが、収集デバイス２００は、ハウジング２０１に対して平面に向けられているか又はハウジング２０１に対して円錐状に配置されている等のサンプルリザーバ２８０及び／又は２９０を有することができる。

【００４２】

[1095] 分流機構２２０は、ハウジング２０１及び可動部材２５０及び２５０’を含む。図２～図４に示すように、ハウジング２０１は、プリサンプルリザーバ２７０、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０に結合されている。ハウジング２０１は、入口ポート２２１、第１出口ポート２３０、第２出口ポート２３１、第３出口ポート２３２を含み、患者から体液を収集するための流体流路を規定することができる内部流路２３５を規定している。入口ポート２２１を、内部流路２３５に流体連通するように選択的に配置することができる。より具体的には、入口ポート２２１は、内部流路２３５に流体連通するように配置することができる入口内腔２０２を規定している。このように、入口ポート２２１は、内部流路２３５を、入口内腔２０２を介してハウジング２０１の実質的に外側の空間に流体連通するように配置することができるように、ハウジング２０１の一部から延在している。入口ポート２２１を、患者から体液を抜き取り及び／又は収集デバイス２００に輸送するための流体流路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート２２１を、アダプタ２０４を介して直接又は間接的に針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。同様に言えば、入口ポート２２１によって規定された入口内腔２０２は、内腔規定デバイスが入口ポート２２１に結合された時に内腔規定デバイスによって規定される内腔に流体連通するように配置される。さらに詳述すると、内腔規定デバイスが患者の身体の一部の中に（例えば、患者の静脈又は脊椎腔内に）配置されると、ハウジング２０１の内部流路２３５を、患者の身体のその部分に流体連通するように配置することができる。

【００４３】

[1096] ハウジング２０１によって規定される内部流路２３５は、ハウジング２０１の長さに沿って延在する中心内腔であり、それを、本明細書に記載するように静脈穿刺（体液へのアクセスを可能にするために採用される他の方法）に続いて患者の体液に流体連通するように配置することができる。内部流路２３５は、入口ポート２２１と第１出口ポート２３０、第２出口ポート２３１及び第３出口ポート２３２との間で体液を移送する流体流経路を形成する。より具体的には、内部流路２３５が（例えば、入口ポート２２１に結合された医療デバイスを介して）患者に流体連通するように配置されると、第１出口ポート２３０、第２出口ポート２３１及び第３出口ポート２３２を、内部流路２３５に流体連通するように選択的に配置して、体液がプリサンプルリザーバ２７０、第１サンプルリザーバ２８０又は第２サンプルリザーバ２９０のうちの少なくとも１つに流れ込むのを可能にすることができる。いくつかの実施形態では、体液は、体液の所定体積がプリサンプルリザーバ２７０内に収集される前に、第２出口ポート２３１及び第３出口ポート２３２に流れるのが防止される。いくつかの実施形態では、第２出口ポート２３１及び第３出口ポート２３２を、同時に内部流路２３５に流体連通するように配置することができる。いくつかの実施形態では、第２出口ポート２３１及び第３出口ポート２３２を、逐次内部流路２３５に流体連通するように配置することができる。

【００４４】

[1097] 可動部材２５０、２５０’は、使用者によって、ハウジング２０１に対して第１位置及び第２位置から作動（例えば、移動）させて、流体流を第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０内に向けるように構成されている。可動部材２５０及び２５０’は、実質的に同じであり、従って、単一の可動部材２５０に関して記載する。図５に示すように、可動部材２５０は、内部空洞２５２を規定するボス２５１と、入口ポート２５３と、第１出口ポート２５４と、内部空洞２５２に流体的に結合された内腔２５

６を規定する穿孔部材２５５とを含む。入口ポート２５３及び出口ポート２５４は、可動部材２５０の内部チャンバ２５２を規定するボス２５１の壁を通って延在している。可動部材２５０は、ボス２５１がボア２５８（図４参照）内に配置され、可動部材２５０の少なくとも一部が環状チャンバ２６０内に配置されるように、ハウジング２０１の支持体２５７（図４参照）に取り付けられるように構成されている。任意選択的に、可動部材２５０を使用者が作動させた後にその第１位置に戻すように、付勢部材２５９（例えば、ばね）を環状チャンバ２６０内に配置することができる。いくつかの実施形態では、可動部材２５０、環状チャンバ２６０、ボア２５８又はボス２５１は、使用者によって作動された後に可動部材２５０を第２位置（例えば、押下位置）で保持するように構成された機械的係止機構を含むことができる。

【００４５】

[1098] 本明細書に記載するように、第１形態では、可動部材２５０は、内部流路２３５から間隔を空けて配置されるように配置されている。こうした形態では、患者の身体の一部（例えば、静脈、脊椎腔等）とサンプルリザーバ２８０及び／又は２９０との間に、流体流路を確立することができない。言い換えれば、可動部材２５０がその第１形態にある時、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０は、ハウジング２０１によって規定される内部流路２３５から流体的に隔離される。可動部材２５０を、使用者により、可動部材２５０を第１形態から第２形態にかつ内部流路２３５と整列するように移動させるように作動させることができる。使用者によってかけられる力は、付勢部材２５９を変形させる（例えば、圧縮する）のに十分である可能性があり、それにより、穿孔部材２５５をサンプルリザーバ２８０及び／又は２９０内に挿入することができる。第２形態では、入口ポート２５３及び出口ポート２５４は、内部流路２３５と実質的に位置合せされて、内部空洞２５２を内部流路２３５に流体連通するように配置する。従って、可動部材２５０が第２形態にある場合、内部流路２３５と、内部空洞２５２と、穿孔部材２５５の内腔２５６と、サンプルリザーバ２８０との間に流体流経路が確立される。言い換えれば、こうした形態では、本明細書においてさらに詳細に記載するように、体液は、患者（例えば、静脈、脊椎腔等）から分流機構２２０を通って、第１サンプルリザーバ２８０及び／又は第２サンプルリザーバ２９０内に流れ込むことができる。

【００４６】

[1099] プリサンプルリザーバ２７０は、例えば、単回使用使い捨て収集チューブ、真空による収集チューブ等、体液を収容するあらゆる好適なリザーバであり得る。プリサンプルリザーバ２７０は、収集デバイス２００の第１出口ポート２３０に（直接、又は滅菌可撓性管等の介在構造を介して）あらゆる好適な方法で流体的に結合されるように構成されている。例えば、いくつかの実施形態では、プリサンプルリザーバ２７０の一部は、第１出口ポート２３０の一部の中に摩擦嵌めを形成することができる。他の実施形態では、プリサンプルリザーバ２７０を、ねじ結合、接着剤、スナップフィット、機械的締結具及び／又は他のあらゆる好適な結合方法を介して、第１出口ポート２３０に結合することができる。いくつかの実施形態では、プリサンプルリザーバ２７０を、ハウジング２０１と一体的に形成することができる。プリサンプルリザーバ２７０を、体液を、真空吸引を介して入口ポート２２１から出口ポート２３０を通りプリサンプルリザーバ２７０に引き込むのを可能にすることができる負圧状態（真空状態）を（プリサンプルリザーバ２７０の）内部で維持するように構成することができる。プリサンプルリザーバ２７０は、体液の第１量を収容するように構成されており、そこでは、体液の第１量は所定量であることも未定量であることも可能であり、それにより、体液の第１量は、患者から後に抜き取られる体液の第２量及び／又は第３量から流体的に隔離される。

【００４７】

[1100] サンプルリザーバ２８０及び／又は２９０は、単回使用使い捨て収集チューブ、真空による収集チューブ、上記参照により本明細書に組み込まれる‘４２０特許に記載されているようなサンプルリザーバ等を含む、体液を収容するあらゆる好適なリザーバであり得る。いくつかの実施形態では、サンプルリザーバ２８０及び／又は２９０は、例えば

Vacutainer（登録商標）等、既知のサンプル容器と実質的に同様であるか又は同じであり得る。サンプルリザーバ２８０及び２９０は、それぞれサンプル容器２８２及び２９２を含み、それぞれ真空シール２８４及び２９４を含む。真空シール２８４又は２９４は、サンプル容器２８２又は２９２それぞれ内部に、真空吸引を介して内部流路２３５からサンプル容器２８２又は２９２それぞれに体液が引き込まれるのを可能にすることができる負圧状態（真空状態）を維持する。サンプル容器２８０及び／又は２９０を、収集デバイス２００の第２出口ポート２３１及び第３出口ポート２３２それぞれに（直接、又は滅菌可撓管等の介在構造を介して）あらゆる好適な方法で流体的に結合されるように構成することができる。サンプルリザーバ２８０及び／又は２９０を、出口ポート２３１及び／又は２３２に流体連通するように配置するように、出口ポート２３１及び／又は２３２に対して移動させることができる。サンプルリザーバ２８０及び２９０を、体液の第２量又は第３量を収容するように構成することができる。体液の第２量又は第３量は、所定量であることも未定量であることも可能であり、それにより、体液の第２量又は第３量は、患者から抜き取られる体液の第１量から流体的に隔離される。いくつかの構成では、サンプルリザーバ２８０及び／又は２９０を、プリサンプルリザーバ２７０と同様にハウジング２０１と一体的に形成することによって収集デバイス２００に結合することができ、従って、それらについてはここでは詳細に記載しない。場合によっては、サンプルリザーバ２８０及び／又は２９０を透明とすることができ、それにより、使用者は、サンプルリザーバ２８０及び／又は２９０内への体液の流れを確認するように視覚的フィードバックを得ることができる。

【００４８】

[1101] いくつかの実施形態では、サンプルリザーバ２８０及び２９０と分流機構２２０（及び／又はサンプルリザーバ２８０及び２９０以外の収集デバイス２００の部分）とは、独立して形成され（例えば、一体的に形成されず）例えば製造プロセス中に合わせて結合される。場合によっては、サンプルリザーバ２８０及び２９０を、実質的に滅菌又は密封環境（例えば、エチレンオキシド等で充填された環境）で分流機構２２０に結合することができる。従って、サンプルリザーバ２８０及び２９０と分流機構２２０との間のインタフェースは、使用前に実質的に滅菌される。さらに、収集デバイス２００を、サンプルリザーバ２８０及び２９０と分流機構２２０との間に実質的滅菌インタフェースを維持するため等、事前組立式に輸送及び／又は保管することができる。

【００４９】

[1102] 図６及び図７に示すように、流量コントローラ２４０は、第１部材２４１及び第２部材２４５を含む。第１部材２４１は、ハウジング２０１の凹部２６６（例えば、図４を参照）内に配置されるように構成され、第１部材２４１を、例えば、チタン、グラファイト、熱分解炭素、ポリエステル、ポリカーボネート、ポリウレタン、エラストマー材料等、生体適合性であるあらゆる材料から作製することができる。いくつかの実施形態では、第２部材２４５は、第１部材２４１を第１形態から第２形態に移動させるアクチュエータとしての役割を果たす。より具体的には、第１部材２４１が凹部２６６内に配置されると、第２部材２４５を、第１位置と第２位置との間で移動させて、流量コントローラ２４０を第１形態と第２形態との間で移動させることができる。いくつかの実施形態では、ハウジング２０１は、第２部材２４５のその第１位置からその第２位置への移動を選択的に制限することができる。いくつかの実施形態では、ハウジング２０１を、第２位置に移動した第２部材２４５の移動を防止するように構成することができる。言い換えれば、ハウジング２０１は、第２部材２４５が第２位置から第１位置に戻るように移動するのを防止する係止機構を含むことができる。第２部材２４５及び／又はハウジング２０１はまた、第２部材２４５の正確な位置決めを確実にするように視覚的フィードバック又は触覚フィードバックを提供する機械的戻り止め及び／又は他のインジケータを含むことも可能である。

【００５０】

[1103] 第１部材２４１は、静脈穿刺（及び／又は患者の体液にアクセスする他の方法）

に続いて流体流を方向付ける複数のチャネルを含むことができる。例えば、図６及び図７に示すように、第１部材２４１は第１流路２４２及び第２流路２４４を含む。第２部材２４５が第１位置にある時（例えば、図８及び図９を参照）、流量コントローラ２４０は第１形態に配置され、第１流路２４２は、入口ポート２２１を内部流路２３５から流体的に隔離しながら、入口ポート２２１と第１出口ポート２３０との間に流体連通を確立する。第２部材２４５が第２位置にある時（例えば、図１０～図１３を参照）、流量コントローラ２４０は第２形態に配置され、第２流路２４４は、入口ポート２２１を第１出口ポート２３０から流体的に隔離しながら、入口ポート２２１と内部流路２３５との間に流体連通を確立する。患者と収集デバイス２００との間で流体流をさらに方向付ける／隔離するように、追加の第１部材２４１の流路及び／又は流量コントローラ２４０の形態に対応する追加の第２部材２４５の位置を含めることができる。例えば、第２部材２４５は、患者と収集デバイス２００との間の流体流を全体的に実質的に防止する、流量コントローラ２４０の第３形態に対応する第３位置を有することができる。言い換えれば、いくつかの実施形態では、すべての体液サンプルが患者から取り出された後に、収集デバイス２００内のサンプルを外部環境から実質的に封止するように、ダイヤルを第３位置に移動させることができる。

【００５１】

[1104] 動作時、収集デバイス２００を使用して、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質からの汚染を低減して、患者から体液（例えば、血液）を収集することができる。例えば、収集デバイス２００の入口ポート２２１は、アダプタ２０４を介して針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合される。静脈穿刺（又は他の体液アクセス方法）に続いて、第２部材２４５を、図８及び図９に示すように第１位置に達するまで回転させる。別法として、第２部材２４５を第１位置に事前設定することができ、収集デバイス２００を、プリサンプルリザーバ２７０内の真空及び収集デバイス２００の無菌状態を保持するように他の方法で封止することができる。例えば、入口ポート２２１及び／又はアダプタ２０４は、収集デバイス２００が針又は他の内腔規定デバイスに結合された時に開放される弁を含むことができる。

【００５２】

[1105] 上述したように、第２部材２４５が第１位置にある時、流量コントローラ２４０は第１形態に配置され、第１部材２４１の第１流路２４２は、入口ポート２２１を内部流路２３５から流体的に隔離しながら、入口ポート２２１と第１出口ポート２３０との間に流体連通を確立する。さらに、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０は、第１形態では入口ポート２２１から流体的に隔離され、図９において矢印ＡＡによって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ２７０との間に流体流路が規定される。上述したように、プリサンプルリザーバ２７０並びにサンプルリザーバ２８０及び２９０等、収集デバイス２００で使用される流体リザーバを、負圧（すなわち、収集デバイス２００が体液を抜き取るために使用されている身体の部分の流体圧力未満の圧力）を規定し、それにより、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ２７０との間に流体連通が確立されると、プリサンプルリザーバ２７０内の負圧により、プリサンプルリザーバ２７０と患者の身体のその部分との間の圧力差によってプリサンプルリザーバ２７０内に体液が引き込まれるようになる。この第１形態では、流量コントローラ２４０はまた、プリサンプルリザーバ２７０を内部流路２３５から流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、（例えば）静脈穿刺の直後にプリサンプルリザーバ２７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス２００を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の検査のために収集され使用される体液サンプルの後続する量を汚染しないようにすることができる。

【００５３】

[1106] プリサンプルリザーバ２７０内における体液プリサンプルの体積の収集に続いて

、第２部材２４５を、図１０及び図１１に示すような第２位置に達するまで、回転させることができる。第２部材２４５が第２位置にある時、流量コントローラ２４０は第２形態に配置され、第１部材２４１の第２流路２４４は、第１出口ポート２３０（すなわち、プリサンプルリザーバ２７０）を入口ポート２２１から流体的に隔離しながら、入口ポート２２１と内部流路２３５との間に流体連通を確立する。言い換えれば、第２形態では、流量コントローラ２４０は、図１１において矢印ＢＢによって示すように第２流路２４４を介して、患者の身体の一部（例えば、静脈）と内部流路２３５との間に流体流路を確立する。

【００５４】

[1107] 流量コントローラ２４０が第２形態にある状態で、可動部材２５０及び／又は２５０’を使用者が第１位置から第２位置に作動させて（すなわち、押下して）、患者の身体の一部（例えば静脈）と第１サンプルリザーバ２８０及び／又は第２サンプルリザーバ２９０との間に流体連通を確立することができる。より具体的には、可動部材２５０は、その第１位置からその第２形態に移動して、図１２において矢印ＣＣによって示すように、穿孔部材２５５が第１サンプルリザーバ２８０の真空シール２８４に穴をあけサンプル容器２８２内部に配置されことが可能であるように、穿孔部材２５５が出口ポート２３１を通過するようにする。第２位置にある時、可動部材２５０の入口ポート２５３及び出口ポート２５４は、内部流路２３５と実質的に位置合せされかつそれに流体連通し、それにより、体液が、内部流路２３５から可動部材２５０の内部空洞２５２内に、かつ穿孔部材２５５の内腔２５６から出て第１サンプルリザーバ２８０内に流れることができる。サンプルリザーバ２８０（例えば、真空又は負圧）と内部流路２３５との圧力差により、体液がサンプルリザーバ２８０内に引き込まれる。言い換えれば、第２形態では、図１２において矢印ＤＤによって示すように、可動部材２５０は、内部流路２３５と第１サンプルリザーバ２８０との間に流体流路を確立する。第１サンプルリザーバ２８０に体液の所望の量（例えば、第２量）が収集されると、使用者は、可動部材２５０を解放して、付勢部材２５９がボタンをその第１位置に戻るように移動させるのを可能にすることができる。可動部材２５０がその第１位置に戻ると、穿孔部材２５５は第１サンプルリザーバ２８０から取り除かれ、シール２８４（例えば、自己封止膜（self sealing septum））が、第１サンプルリザーバ２８０を内部流路２３５から流体的に隔離する。

【００５５】

[1108] 同様に、流量コントローラ２４０が第２形態にある間、図１３において矢印ＥＥによって示すように、可動部材２５０’を、使用者がその第１位置から第２位置に作動させる（押下する）ことができる。このように、上述した可動部材２５０及び第１サンプルリザーバ２８０と同様の方法で、患者の身体の一部（例えば、静脈）と第２サンプルリザーバ２９０との間に（出口ポート２３２を介して）流体連通が確立される。言い換えれば、第２形態では、可動部材２５０’は、図１３において矢印ＦＦによって示すように、内部流路２３５と第２サンプルリザーバ２９０との間に流体流路を確立する。第２サンプルリザーバ２９０内に体液の所望の量（例えば、第３量）が収集されると、使用者は、可動部材２５０’を解放して、付勢部材２５９’がボタン２５０’をその第１位置に戻るように移動させるのを可能にすることができる。逐次プロセスであるものとして示しかつ記載しているが、充填の順序及び／又は順序付けは必ずしも必要ではない（すなわち、サンプルリザーバ２８０は、必ずしもサンプルリザーバ２９０より前に充填されなくてもよい、等）。言い換えれば、流量コントローラ２４０が第２形態に移動すると、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０（及び任意の追加のサンプルリザーバ）を、あらゆる順序で、同じ時点で（例えば、同時に）及び／又は一部が重なる時間間隔で充填することができる。例えば、使用者は、第１サンプルリザーバ２８０への充填を開始することができ、その後、第１サンプルリザーバ２８０が部分的に充填された後、使用者は、可動部材２５０’を押下して、第１サンプルリザーバ２８０が充填を終了している間に、第２サンプルリザーバ２９０への充填を開始するようにすることができる。さらに、サンプルリザーバ２８０及び／又は２９０内に収集された体液の体積の調整を、可動部材２

５０及び／又は２５０’を繰り返し作動させる（挿入する）ことによって可能にすることができる。上述したように、第２部材２４５は、流量コントローラ２４０の第３形態に対応する第３位置を有することができ、それにより、患者と収集デバイス２００との間の流体流を全体的に実質的に防止して、収集デバイス２００内のサンプルを外部環境から実質的に封止することができる。

【００５６】

[1109] 図２～図１３には示さないが、収集デバイス２００は、プリサンプルリザーバ２７０、第１サンプルリザーバ２８０及び／又は第２サンプルリザーバ２９０に移送される体液の体積を計量するように構成することができる流量計量デバイス等を含むことができる。例えば、いくつかの実施形態では、流量コントローラ２４０の第１部材２４１は、第１流路２４２及び第２流路２４４に流体連通している流量計量デバイスを含むことができる。他の実施形態では、流量計量デバイスを、可動部材２５０及び／又は２５０’の内部空洞２５２内に配置することができる。従って、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０に移送されかつその中に配置される体液サンプルの体積を、各サンプルリザーバ２８０及び２９０内に配置される体液サンプルの体積が例えば１０ｍＬ、２０ｍＬ、３０ｍＬ等の所定体積であるように、計量し及び／又は制御することができる。

【００５７】

[1110] 収集デバイス２００は、第１サンプルリザーバ２８０及び第２サンプルリザーバ２９０を含むものとして示されかつ記載されているが、他の実施形態では、あらゆる数のプリサンプルリザーバ及び／又はサンプルリザーバを含むことができる。例えば、図１４及び図１５は、実施形態による収集デバイス３００を示す。図示するように、収集デバイス３００のいくつかの態様は、図２～図１３を参照して上述した収集デバイス２００の対応する態様に実質的に同様であり得る。従って、同様の態様については本明細書ではそれ以上詳細には記載しない。

【００５８】

[1111] 図１４及び図１５に示すように、収集デバイス３００は、分流機構３２０、流量コントローラ３４０、プリサンプルリザーバ３７０、第１サンプルリザーバ３８０、第２サンプルリザーバ３８０’、第３サンプルリザーバ３９０及び第４サンプルリザーバ３９０’を含む。プリサンプルリザーバ３７０は、詳細に上述したプリサンプルリザーバ２７０と実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、詳細に上述したサンプルリザーバ２８０及び２９０と実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、実質的に同じ形状及びサイズを有することができ、例えば、実質的に同じ培地を含むことができる。他の実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、実質的に同じ形状及びサイズを有することができ、好気性菌用培地又は嫌気性菌用培地のうちの一方を含むことができる。例えば、いくつかの実施形態では、第１サンプルリザーバ３８０及び第３サンプルリザーバ３９０は好気性菌用培地を含むことができ、第２サンプルリザーバ３８０’及び第４サンプルリザーバ３９０’は嫌気性菌用培地を含むことができる。他の実施形態では、サンプルリザーバ３８０、３８０’、３９０及び３９０’は、各々、好気性菌用培地又は嫌気性菌用培地をあらゆる配置又は組合せで含むことができる。

【００５９】

[1112] 分流機構３２０は、ハウジング３０１と一組の可動部材３５０、３５０’、３５０’’及び３５０’’’とを含む。可動部材３５０、３５０’、３５０’’及び３５０’’’は、例えば、図５を参照して上述した可動部材２５０と実質的に同様である。従って、可動部材３５０、３５０’、３５０’’及び３５０’’’を、サンプルリザーバ３８０、３８０’、３９０及び３９０’それぞれに流体連通して配置されるように、ハウジング３０１に対して第１位置と第２位置との間で移動させることができる。ハウジング３０１は、入口ポート３２１と、プリサンプルリザーバ３７０に流体連通するように配置されるように構成された第１出口ポート３３０と、第１サンプルリザーバ３８０に流体連通する

ように配置されるように構成された第２出口ポート３３１と、第２サンプルリザーバ３８０’に流体連通するように配置されるように構成された第３出口ポート３３２と、第３サンプルリザーバ３９０’に流体連通するように配置されるように構成された第４出口ポート３３３と、第４サンプルリザーバ３９０’に流体連通するように配置されるように構成された第５出口ポート３３４とを含む。さらに、ハウジング３０１は、ハウジング２０１の内部流路２３５に関して上述したものと同様の方法で、入口ポート３２１並びに出口ポート３３１、３３２、３３３及び３３４に流体連通するように選択的に配置することができる内部流路３３５を規定している。

【００６０】

[1113] 流量コントローラ３４０は、例えば、図６～図１３を参照して上述した流量コントローラ２４０と実質的に同様である。従って、流量コントローラ３４０を、第１形態と第２形態との間で回転させて、患者とプリサンプルリザーバ３７０又はサンプルリザーバ３８０、３８０’、３９０及び３９０’との間に流体流路の一部を選択的に規定することができる。このように、使用者は、図８～図１３において収集デバイス２００に関して上述したものと同様の方法で、収集デバイス３００を操作することができる。従って、体液の第１体積をプリサンプルリザーバ３７０に移送しかつその中に配置することができ、体液の後続する体積を、サンプルリザーバ３８０、３８０’、３９０及び３９０’に移送しかつその中に配置することができる。

【００６１】

[1114] 図１６～図２２は、実施形態による収集デバイス４００を示す。収集デバイス４００は、分流機構４２０、流量コントローラ４４０並びにサンプルリザーバ４８０、４８０’、４９０及び４９０’を含む。本明細書においてさらに記載するように、収集デバイス４００を、第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス４００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、図１６～図２２において、サンプルリザーバ４８０、４８０’、４９０及び４９０’がハウジング４０１に対して垂直に向けられて示されているが、収集デバイス４００は、ハウジング４０１に対してあらゆる好適な平面において向けられ、又はハウジング４０１に対して円錐状に配置される等のサンプルリザーバ４８０、４８０’、４９０及び４９０’を有することができる。

【００６２】

[1115] サンプルリザーバ４８０、４８０’、４９０及び４９０’は、収集デバイス２００のサンプルリザーバ２８０及び／又は２９０と形態及び機能が実質的に同様であるか又は同じであり、従って、本明細書では詳細には記載しない。上述したように、サンプルリザーバ４８０、４８０’、４９０及び４９０’は、吸引を介して患者からサンプルリザーバ４８０、４８０’、４９０及び４９０’に体液を引き込むのを可能にすることができる負圧状態（真空状態）を維持する。いくつかの実施形態では、サンプルリザーバ４８０及び４８０’を好気性菌用培養ボトルとすることができ、サンプルリザーバ４９０及び４９０’を嫌気性菌用培養ボトルとすることができ、収集デバイス４００を用いて、１回の静脈穿刺から複数の好気性菌用血液培養サンプル及び複数の嫌気性菌用血液培養サンプルを収集することができる。本明細書においてさらに詳細に記載するように、サンプルリザーバ４８０、４８０’、４９０及び４９０’を、各々、体液サンプルのある体積を受け取るように分流機構４２０の少なくとも一部に流体連通するように配置することができる。体液サンプルの体積は、所定量でも未定量であり得る。さらに、サンプルリザーバ４８０、４８０’、４９０、４９０’内に体液の所望の体積が配置されると、本明細書においてさらに詳細に記載するように、各サンプルリザーバ４８０、４８０’、４９０及び４９０’を、分流機構４２０の少なくとも一部から流体的に隔離することができる。

【００６３】

[1116] 分流機構４２０は、ハウジング４０１及び分配部材４２９を含む。分流機構４２０のハウジング４０１は、分配部材４２９に物理的にかつ流体的に結合され、患者から体

液を収集する一組の流体流経路を提供し及び／又は規定している。ハウジング４０１は、凹部４６６及び一組の出口開口部４０３を規定している。凹部４６６は、本明細書においてさらに詳細に記載するように、流量コントローラ４４０に含まれるシール部材４４１を受け入れるように構成されている。出口開口部４０３の組は、各々が、分配部材４２９の異なる部分に流体連通している異なる流体流路を規定するように構成されている、第１出口開口部４０３ａ、第２出口開口部４０３ｂ、第３出口開口部４０３ｃ、第４出口開口部４０３ｄ及び第５出口開口部４０３ｅを含む。より具体的には、分配部材４２９は、第１出口開口部４０３ａに流体連通しているプリサンプルリザーバ４７０の少なくとも一部と、第２出口開口部４０３ｂに流体連通している第１流路４３５ａ、第３出口開口部４０３に流体連通している第２流路４３５ｂ、第４出口開口部４０３ｄに流体連通している第３流路４３５ｃ及び第５出口開口部４０３ｅに流体連通している第４流路４３５とを規定し及び／又は形成している。

【００６４】

[1117] 図１７及び図１８に示すように、分配部材４２９は、プリサンプルリザーバ４７０の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ４７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。ハウジング４０１の第１出口開口部４０３ａを、プリサンプルリザーバ４７０が患者から体液の流れを受け取るのを可能にするように、プリサンプルリザーバ４７０の開放部分と実質的に位置合せすることができる。例えば、プリサンプルリザーバ４７０は、体液の第１量又は第１体積を受け取りかつ収容することができ、ここで、体液の第１量は、所定量でも未定量でもあり得る。さらに、分流機構４２０の配置を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ４７０が流路４３５ａ、４３５ｂ、４３５ｃ及び４３５ｄ並びに／又は患者から抜き取られた体液の後続する体積から流体的に隔離して維持されるというものとすることができる。プリサンプルリザーバ２７０及び３７０を、負圧を維持するものとして上述しているが、プリサンプルリザーバ４７０は、負圧状態（真空状態）を維持せず、従って、例えば重力等の他の機構を用いて、体液をプリサンプルリザーバ４７０内に引き込むことができる。

【００６５】

[1118] 流路４３５ａ～４３５ｄは、分配部材４２９の中心から放射状に延在し、各流路４３５ａ、４３５ｂ、４３５ｃ及び４３５ｄがプリサンプルリザーバ４７０及び他の流路から流体的に隔離されるように配置されている。このように、流路４３５ａ、４３５ｂ、４３５ｃ及び４３５ｄは、出口開口部４０３ｂ、４０３ｃ、４０３ｄ及び４０３ｅそれぞれと実質的に位置合せされる第１端部と第２端部との間で流体流路を方向付け及び／又は他の方法で規定することができる。図１７及び図１８に示すように、分配部材４２９は、第１流路４３５ａの第２端部に配置された第１出口ポート４３１と、第２流路４３５ｂの第２端部に配置された第２出口ポート４３２と、第３流路４３５ｃの第２端部に配置された第３出口ポート４３３と、第４流路４３５ｄの第２端部に配置された第４出口ポート４３４とを規定している。さらに、分配部材４２９は、第１穿孔部材４５５ａ、第２穿孔部材４５５ｂ、第３穿孔部材４５５ｃ及び第４穿孔部材４５５ｄを含み、それらは、第１出口ポート４３１、第２出口ポート４３２、第３出口ポート４３３及び第４出口ポート４３４それぞれに、物理的にかつ流体的に結合されている。従って、本明細書においてさらに詳細に記載するように、穿孔部材４５５ａ～３５５ｄを用いて、サンプルリザーバ４８０、４８０’、４９０及び４９０’の真空シールに穴をあけることができ、それにより、体液の流れを開始することができる。図１７及び図１８には示さないが、サンプルリザーバ４８０、４８０’、４９０及び４９０’を、サンプルリザーバ４８０、４８０’、４９０及び４９０’が出口ポート４３１、４３２、４３３及び４３４それぞれに流体連通するように配置されるのを可能にすることができるあらゆる好適な方法で、分配部材４２９の一部に（直接、又は滅菌可撓性管等の介在構造を介して）物理的に結合することができる。

【００６６】

[1119] 流量コントローラ４４０は、ダイヤル４４５及びシール部材４４１を含む。シー

ル部材４４１は、ハウジング４０１の凹部４６６内に配置される（例えば、図２０を参照）。より詳細には、流量コントローラ４４０を、シール部材４４１が凹部４６６を規定するハウジング４０１の表面とダイヤル４４５の表面との間にかつそれらと接触して配置されるように、ハウジング４０１に結合することができる。さらに、シール部材４４１は、本明細書においてさらに詳細に記載するように、流量コントローラ４４０がハウジング４０１に結合された時、シール部材４４１が、ダイヤル４４５の表面及び凹部４６６を規定するハウジング４０１の表面と実質的流体密封シールを形成するような、サイズ及び形状を有することができる。シール部材４４１を、例えば、シリコーン、ポリ乳酸、ポリグリコール酸、ポリ乳酸－グリコール酸共重合体（ＰＬＧＡ）、ポリ酸無水物、ポリオルトエステル、ポリエーテルエステル、ポリカプロラクトン、ポリエステルアミド、ポリ（酪酸）、ポリ（吉草酸）、ポリウレタン、ナイロン、ポリエステル、ポリカーボネート、ポリアクリレート、エチレンービニルアセテート及び他のアシル置換セルロースアセテートのポリマー、ポリスチレン、ポリ塩化ビニル、ポリフッ化ビニル、ポリ（ビニルイミダゾール）、クロロスルホネートポリオレフィン、ポリエチレンオキシド並びに／又はそれらの混合物及びコポリマー等、生体適合性であるあらゆる材料から作製することができる。

【００６７】

[1120] 図１７に示すように、シール部材４４１は、静脈穿刺（又は体液にアクセスする他の方法）に続いて体液の流れを方向付けることができる一組の開口部４４４を規定している。例えば、シール部材４４１によって規定される一組の開口部４４４は、第１開口部４４４ａ、第２開口部４４４ｂ、第３開口部４４４ｃ、第４開口部４４４ｄ及び第５開口部４４４ｅを含む。シール部材４４１の配置は、シール部材４４１が凹部４４６内に配置された時、第１開口部４４４ａ、第２開口部４４４ｂ、第３開口部４４４ｃ、第４開口部４４４ｄ及び第５開口部４４４ｅが、ハウジング４０１の第１出口開口部４０３ａ、第２出口開口部４０３ｂ、第３出口開口部４０３ｃ、第４出口開口部４０３ｄ及び第５出口開口部４０３ｅそれぞれと実質的に位置合せされる、というものである。

【００６８】

[1121] 流量コントローラ４４０のダイヤル４４５は、ハウジング４０１に回転可能に結合され、かつハウジング４０１に対する第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル４４５は、内腔４０２を規定する入口ポート４２１を含む。入口ポート４２１を、患者の体内から体液を抜き取り及び／又は収集デバイス４００に輸送するための流体流経路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート４２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に直接又はアダプタ４０４を介して間接的に流体的に結合することができる。同様に言えば、入口ポート４２１によって規定される入口内腔４０２は、内腔規定デバイスが入口ポート４２１に結合された時、内腔規定デバイスによって規定される内腔に流体連通するように配置される。このように、入口ポート４２１を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ４７０、第１サンプルリザーバ４８０、第２サンプルリザーバ４８０’、第３サンプルリザーバ４９０及び第４サンプルリザーバ４９０’を、患者に流体連通するように選択的に配置するように構成することができる。

【００６９】

[1122] 上述したように、ダイヤル４４５は、第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル４４５が第１位置にある時、流量コントローラ４４０は第１形態で配置され、入口ポート４２１を、シール部材４４１の第１開口部４４４ａ及びハウジング４０１の第１出口開口部４０３ａと実質的に位置合せすることができる。このように、シール部材４４１の第１開口部４４４ａは、入口ポート４２１を出口開口部４０３ｂ、４０３ｃ、４０３ｄ及び４０３ｅから流体的に隔離し、それにより入口ポート４２１を流路４３５ａ～３３５ｄから流体的に隔離しながら、入口ポート４２１と第１出口開口部４０３ａとの間に流体連通を確立する。第１出口ポート４０３ａがプリサンプルリザーバ４７０の開放部分と位置合せされると、第１開口部４４４ａ及び第１出

口開口部４０３ａは、入口ポート４２１とプリサンプルリザーバ４７０との間に流体連通を確立する。ダイヤル４４５が第２位置まで回転した（又は駆動された）時、流量コントローラ４４０は第２形態に配置され、第２出口開口部４４４ｂは、入口ポート４２１を出口開口部４０３ａ、４０３ｃ、４０３ｄ及び４０３ｅから流体的に隔離しながら、入口ポート４２１と第２出口開口部４０３ｂとの間に流体連通を確立する。第２出口開口部４０３ｂが第１流路４３５ａの第１端部と位置合せされると、第２開口部４４４ｂ及び第２出口開口部４０３ｂは、入口ポート４２１と第１流路４３５ａとの間に流体連通を確立する。

【００７０】

[1123] 収集デバイス４００は、ダイヤル４４５が第３位置、第４位置及び第５位置まで回転した時、同様に作用する。従って、入口内腔４０２が（例えば、入口ポート４２１に結合された医療デバイスを介して）患者に流体連通するように配置されると、第１出口ポート４３０、第２出口ポート４３１、第３出口ポート４３２、第４出口ポート４３３及び第５出口ポート４３４を、入口内腔４０２に流体連通するように選択的に配置して、体液のすべてがプリサンプルリザーバ４７０のうちの少なくとも１つ、又はサンプルリザーバ４８０、４８０’４９０及び４９０’のうちの１つあるいは複数に流れ込むのを可能にすることができる。いくつかの実施形態では、患者と収集デバイス４００との間で流体流をさらに方向付け／隔離するために、追加のシール出口開口部及び／又は流量コントローラ４４０の形態に対応する追加のダイヤル４４５の位置を含めることができる。例えば、ダイヤル４４５は、患者と収集デバイス４００との間の流体流を全体として実質的に防止する、流量コントローラ４４０の第６形態に対応する第６位置を有することができる。言い換えれば、いくつかの実施形態では、すべての体液サンプルが患者から取り出された後、収集デバイス４００内のサンプルを外部環境から実質的にシールするようにダイヤル４４５を第６位置に移動させることができる。

【００７１】

[1124] いくつかの実施形態では、プリサンプルリザーバ４７０内に体液の所定体積が収集される後まで、体液は、サンプルリザーバに関連する出口ポート（例えば、出口ポート４３１～４３４）に流れるのが防止される。いくつかの実施形態では、サンプルリザーバに関連する出口ポート（例えば、出口ポート４３１～４３４）を、逐次的にのみ、入口内腔４０２に流体連通するように配置することができる（例えば、出口ポート４３１は、出口ポート４３２の前に入口内腔４０２に流体連通しなければならない、等）。いくつかの実施形態では、後続するサンプルリザーバに関連する出口ポート（例えば、出口ポート４３２～４３４）を、体液の確定された体積が収集された後にのみ、入口内腔４０２に流体連通するように配置することができる。いくつかの実施形態では、サンプルリザーバに関連する出口ポート（例えば、出口ポート４３１～４３４）を、いかなる順序の優先もなくあらゆるランダムな方法で入口内腔４０２に流体連通するように配置することができる（例えば、出口ポート４３４は、出口ポート４３１の前に入口内腔４０２に流体連通することができ、出口ポート４３２は、出口ポート４３３の前に入口内腔４０２に流体連通することができる等）。

【００７２】

[1125] いくつかの実施形態では、ハウジング４０１は、ダイヤル４４５のその第１位置からその第２位置、第３位置、第４位置及び第５位置への移動を選択的に制限することができる。いくつかの実施形態では、ハウジング４０１を、第５位置まで移動したダイヤル４４５の移動を防止するように構成することができる。言い換えれば、ハウジング４０１は、ダイヤル４４５が第５位置から第１位置に戻るように移動するのを防止する係止機構を含むことができる。ダイヤル４４５及び／又はハウジング４０１は又はウジング４０１の出口開口部４０３ａ～４０３ｅに対するダイヤル４４５の正確な位置決めを確実にするように視覚的フィードバック又は触覚フィードバックを提供する、機械的戻り止め及び／又は他のインジケータを含むことも可能である。

【００７３】

[1126] 動作時、収集デバイス４００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス４００の入口ポート４２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は体液にアクセスする他の方法）に続いて、図１９及び図２０に示すように、ダイヤル４４５が第１位置に達するまで駆動される（又は回される）。別法として、ダイヤル４４５を第１位置に事前設定することができ、収集デバイス４００を、収集デバイス４００の無菌状態を維持するように他の方法で封止することができる。例えば、入口ポート４２１は、収集デバイス４００が針又は他の内腔規定デバイスに結合されると開放する弁を含むことができる。

【００７４】

[1127] 上述したように、ダイヤル４４５が第１位置にある時、流量コントローラ４４０は第１形態に配置され、シール部材４４１の第１開口部４４４ａは、入口ポート４２１を４つの流路４３５ａ～３３５ｄから流体的に隔離しながら、（ハウジング４０１内に含まれる）入口ポート４２１と第１出口ポート４３０との間で流体連通を確立する。さらに、サンプルリザーバ４８０、４８０’、４９０及び４９０’は、第１形態では入口ポート４２１から流体的に隔離されており、図２０において矢印ＧＧによって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ４７０との間に、流体流路が規定される。この第１形態では、体液は、患者の身体のその部分から入口ポート４２１の入口内腔４０２、シール部材４４１の第１開口部４４４ａ、第１出口ポート４３０を通り、プリサンプルリザーバ４７０内に（例えば、重力、真空等により）流れ込む。第１形態では、流量コントローラ４４０はまた、プリサンプルリザーバ４７０を流路４３５ａ～３３５ｄから流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ４７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス４００を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の試験に対して収集され使用される体液サンプルの後続する量を汚染しないようにすることができる。

【００７５】

[1128] プリサンプルリザーバ４７０内への体液プリサンプルの収集に続き、図２１及び図２２に示すように、ダイヤル４４５を、第２位置に達するまで作動させる（回転させる）ことができる。ダイヤル４４５が第２位置にある時、流量コントローラ４４０は第２形態に配置され、シール部材４４１の第２開口部４４４ｂは、プリサンプルリザーバ４７０を入口ポート４２１から流体的に隔離しながら、入口ポート４２１と流路４３５ａとの間に流体連通を確立する。言い換えれば、第２形態では、図２２において矢印ＨＨによって示すように、流量コントローラ４４０は、患者の身体の一部（例えば、静脈）と流路４３５ａとの間に流体流路を確立する。流量コントローラ４４０が第２形態にある状態で、サンプルリザーバ４８０を、使用者が、第１形態から第２形態に作動させて（例えば、穿孔部材４５５ａを押して）患者の身体の一部（例えば、静脈）と第１サンプルリザーバ４８０との間に流体連通を確立することができる。

【００７６】

[1129] 上述したように、サンプルリザーバ４８０を第２形態に移動させることにより、穿孔部材４５５ａが、サンプルリザーバ４８０の真空シールに穴をあけでサンプルリザーバ４８０の内側に配置される。この第２形態では、患者の身体の一部（例えば、静脈）が、サンプルリザーバ４８０内の負圧状態（真空）によるサンプルリザーバ４８０からの真空吸引力にさらされる。サンプルリザーバ４８０（例えば、真空又は負圧）と患者の身体のその部分との圧力差により、サンプルリザーバ４８０内に体液が引き込まれる。体液は、患者の身体のその部分から、入口ポート４２１の入口内腔４０２、シール部材４４１の第２開口部４４４ｂ、ハウジング４０１の第２出口開口部４０３ｂを通って、第１流路４３５ａ内に流れ込む。真空吸引により、体液の流れが第１流路４３５ａを通って、第２出口ポート４３１及び穿孔部材４５５ａを介してサンプルリザーバ４８０内に引き込まれる

。言い換えれば、第２形態では、流量コントローラ４４０は、入口ポート４２１とサンプルリザーバ４８０との間に流体流路を確立する。サンプルリザーバ４８０内に体液の所望の量（例えば、第２量）が収集されると、使用者は、流量コントローラ４４０を第３位置まで作動させ（回転させ）、及び／又はサンプルリザーバ４８０をその第１形態に戻るように移動させて、第１サンプルリザーバ４８０を流路４３５ａから隔離することができる。サンプルリザーバ４８０が第１形態に戻ると、穿孔部材４５５ａはサンプルリザーバ４８０から取り除かれ、サンプルリザーバ４８０のシール（例えば、自己封止膜）が、第１サンプルリザーバ４８０を流路４３５ａから隔離する。他のサンプルリザーバの充填は、流量コントローラ４４０が第３形態、第４形態及び第５形態それぞれに配置されて同様に行われる。

【００７７】

[1130] 充填の順序及び／又は順序付けは必ずしも必要ではない（すなわち、サンプルリザーバ４８０は必ずしもサンプルリザーバ４９０の前に充填されなくてもよい等）ことに留意されたい。言い換えれば、第１サンプルリザーバ４８０及び第２サンプルリザーバ４９０（及び任意の追加のサンプルリザーバ）をあらゆる順序で充填することができる。例えば、使用者は、第１サンプルリザーバ４８０の充填を開始することができ、その後、第１サンプルリザーバ４８０が部分的に充填された後、使用者は第２サンプルリザーバ４９０を充填することができる。さらに、サンプルリザーバ４８０及び／又は４９０内に収集された体液の体積の調整を、サンプルリザーバ４８０及び／又は４９０の繰り返される充填によって可能とすることができる。しかしながら、他の実施形態では、充填の順序を、体液の指定された量が第１リザーバ内に配置されたことが確認されるまで、第２サンプルリザーバにアクセスすることができない等のように、機械的に操作することができる。上述したように、ダイヤル４４５は、患者と収集デバイス４００との間の流体流を全体として実質的に防止して、収集デバイス４００内のサンプルを外部環境から実質的に封止することができる、流量コントローラ４４０の第６形態に対する第６位置を有することができる。

【００７８】

[1131] 収集デバイス４００を、４つのサンプルリザーバの組（例えば、第１サンプルリザーバ４８０、第２サンプルリザーバ４８０’、第３リザーバ４９０及び第４リザーバ４９０’）を含み及び／又はそれらに他の方法で結合しているものとして上に示し記載しているが、他の実施形態では、収集デバイスは、あらゆる好適な数のサンプルリザーバを含むことができ及び／又はそれらに結合され得る。例えば、図２３～図２５は、実施形態による収集デバイス５００を示す。図示するように、収集デバイス５００のいくつかの態様は、図１６～図２２を参照して上述した収集デバイス５００の対応する態様と実質的に同様であり得る。従って、同様の態様については本明細書ではそれ以上詳細には記載しない。

【００７９】

[1132] 収集デバイス５００は、分流機構５２０、流量コントローラ５４０、第１サンプルリザーバ５８０及び第２サンプルリザーバ５９０を含む。サンプルリザーバ５８０及び５９０は、詳細に上述したサンプルリザーバと実質的に同様であり得る。いくつかの実施形態では、サンプルリザーバ５８０及び５９０は、実質的に同じ形状及びサイズを有することができ、実質的に同じ培地を含むことができる。他の実施形態では、サンプルリザーバ５８０及び５９０は、実質的に同じ形状及びサイズを有することができ、好気性菌用培地又は嫌気性菌用培地のうちの一方を含むことができる。さらに他の実施形態では、第１サンプルリザーバ５８０は、第２サンプルリザーバ５９０のサイズより実質的に大きい第１サイズを有することができる。

【００８０】

[1133] 図２４及び図２５に示すように、分流機構５２０は、ハウジング５０１及び分配部材５２９を含む。分流機構５２０のハウジング５０１は、分配部材５２９に物理的にかつ流体的に結合されており、患者から体液を収集する一組の流体流経路を提供し及び／又

は規定している。ハウジング４０１に関して上述したように、ハウジング５０１は、凹部と、第１出口開口部５０３ａ、第２出口開口部５０３ｂ及び第３出口開口部５０３ｃとを規定することができる。凹部は、詳細に上述したように、流量コントローラ５４０に含まれるシール部材５４１を受け入れるように構成されている。第１出口開口部５０３ａ、第２出口開口部５０３ｂ及び第３出口開口部５０３ｃは、ハウジング４０１によって規定された第１出口開口部４０３ａ、第２出口開口部４０３ｂ及び第３出口開口部４０３ｃそれぞれと形態及び機能が実質的に同様であり得る。同様に、分配部材５２９は、分流部材４２９に含まれるプリサンプルリザーバ４７０、第１流路４３５ａ及び第２流路４３５ｂと実質的に同様である、プリサンプルリザーバ４７０、第１流路４３５ａ及び第２流路４３５ｂを規定している。従って、分流機構４２０に関して上述したように、プリサンプルリザーバ５７０は、第１出口開口部５０３ａに流体連通しており、第１流路５３５ａは、第２出口開口部５０３ｂに流体連通しており、第２流路５３５ｂは、第３出口開口部５０３ｃに流体連通している。図２５に示すように、分配部材５２９は、第１流路５３５ａ及び第１穿孔部材５５５ａに流体連通している第１出口ポート５３１と、第２流路５３５ｂ及び第２穿孔部材５５５ｂに流体連通している第２出口ポート５３２とを規定している。上述したように、穿孔部材５５５ａ及び５５５ｂを用いて、本明細書においてさらに詳細に記載するように、サンプルリザーバ５８０及び５９０の真空シールに穴をあけることができ、それにより、体液の流れを開始することができる。

【００８１】

[1134] 流量コントローラ５４０は、ダイヤル５４５及びシール部材５４１を含む。シール部材５４１は、上述したように、ハウジング５０１の凹部内に配置される。このように、流量コントローラ５４０がハウジング５０１に結合されると、シール部材５４１は、ダイヤル５４５の表面及び凹部を規定するハウジング５０１の表面と実質的流体密封シールを形成する。図２４及び図２５に示すように、シール部材５４１は、シール部材４４１に関して詳細に上述したように、第１出口開口部５０３ａ、第２出口開口部５０３ｂ及び第３出口開口部５０３ｃそれぞれと実質的に位置合せされる、第１開口部５４４ａ、第２開口部５４４ｂ及び第３開口部５４４ｃを規定している。

【００８２】

[1135] 流量コントローラ５４０のダイヤル５４５は、ハウジング５０１に結合されるのに好適なサイズを有していながら、ダイヤル４４５と形態及び機能が実質的に同様であり得る。従って、ダイヤル５４５を、ハウジング５０１に回転可能に結合し、ハウジング５０１に対して第１位置、第２位置及び第３位置の間で移動可能とすることができる。ダイヤル５４５は、内腔５０２を規定する入口ポート５２１を含み、入口ポート５２１を、患者から体液を抜き取り及び／又は収集デバイス５００に輸送するための流体流経路を規定する医療デバイス（図示せず）に流体的に結合することができる。このように、入口ポート５２１を、プリサンプルリザーバ５７０、第１サンプルリザーバ５８０及び第２サンプルリザーバ５９０を選択的に配置するように構成することができる。より詳細には、ダイヤル５４５が第１位置にある時、流量コントローラ５４０は第１形態に配置され、入口ポート５２１は、シール部材５４１の第１開口部５４４ａ及びハウジング５０１の第１出口開口部５０３ａと実質的に位置合せされる。このように、収集デバイス４００に関して詳細に上述したように、シール部材５４１の第１開口部５４４ａは、入口ポート５２１と第１出口開口部５０３ａとの間に流体連通を確立し、従って、入口ポート５２１を、プリサンプルリザーバ５７０に流体連通するように配置する。同様に、ダイヤル５４５が第２位置まで回される（又は駆動される）と、流量コントローラ５４０は第２形態に配置され、第２出口開口部５４４ｂは、入口ポート５２１と第２出口開口部５０３ｂ、従って第１流路５３５ａとの間に流体連通を確立し、ダイヤル５４５が第３位置まで回されると、流量コントローラ５４０は第３形態に配置され、第３出口開口部５４４ｃは、入口ポート５２１と第３出口開口部５０３ｃ、従って第２流路５３５ａとの間に流体連通を確立する。このように、収集デバイス４００に関して詳細に上述したように、収集デバイス５００を、プリサンプル５７０に体液の第１体積を移送するために使用し、その後、第１サンプルリ

ザーバ５８０及び第２サンプルリザーバ５９０それぞれに体液の第２体積及び第３体積を移送するために使用することができる。

【００８３】

[1136] 図２６～図３３は、実施形態による収集デバイス６００を示す。収集デバイス６００は、分流機構６２０、流量コントローラ６４０並びにサンプルリザーバ６８０、６８０’、６９０及び６９０’を含む。本明細書においてさらに記載するように、収集デバイス６００を、第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的ない体液の流れを送出することができる。収集デバイス６００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス６００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００及び／又は５００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が同様であり得る。従って、こうした同様の態様及び／又は部分については、本明細書ではそれ以上詳細には記載しない。例として、いくつかの実施形態では、収集デバイス６００のサンプルリザーバ６８０、６８０’、６９０及び６９０’は、図１６～図２２の収集デバイス４００に含まれるサンプルリザーバ４８０、４８０’、４９０及び４９０’それぞれと形態及び／又は機能が実質的に同様であり及び／又は同じであり得る。

【００８４】

[1137] 分流機構６２０は、分配部材６２９並びに一組の結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄを含む（例えば、図２７を参照）。分配部材６２９は、結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄに流体連通しており、患者から体液を収集する一組の流体流経路を提供し及び／又は規定するように構成されている。図２７及び図２８に示すように、分配部材６２９は、プリサンプルリザーバ６７０に流体連通している第１出口ポート６３０と、第１結合部材６３７ａに流体連通している第２出口ポート６３１と、第２結合部分６３７ｂに流体連通している第３出口ポート６３２と、第３結合部分６３７ｃに流体連通している第４出口ポート６３３と、第４結合部分６３７ｄに流体連通している第５出口ポート６３４とを規定し及び／又は形成している。

【００８５】

[1138] 図２８に示すように、分配部材６２９は、プリサンプルリザーバ６７０の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ６７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。例えば、プリサンプルリザーバ６７０は、患者から体液の第１量又は第１体積を受け取りかつ収容することができ、そこでは、体液の第１量は所定量でも未定量でもあり得る。さらに、分流機構６２０及び流量コントローラ６４０の配置は、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ６７０が結合部分６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄ並びに／又は患者から抜き取られる体液の後続する体積から流体的に隔離されて維持されるというものであり得る。このように、出口ポート６３１、６３２、６３３及び６３４は、本明細書においてさらに詳細に記載するように、流量コントローラ６４０と結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄそれぞれとの間に流体流路を方向付け及び／又は他の方法で規定することができる。いくつかの実施形態では、第１出口ポート６３０及びプリサンプルリザーバ６７０の配置は、プリサンプルリザーバ４７０及び／又は５７０と形態及び機能が実質的に同様であり得る。従って、プリサンプルリザーバ６７０について、本明細書ではそれ以上詳細には記載しない。

【００８６】

[1139] 図２９に示すように、第１結合部材６３７ａは、穿孔部材６５５ａに流体的に結合されている流路６３８ａを規定している。上述したように、結合部材６３７ａを、分配部材６２９に物理的にかつ流体的に結合することができる。例えば、流路６３８ａは、分配部材の第２出口ポート６３１の一部を受け入れて、結合部材６３７ａをそれに物理的にかつ流体的に結合することができる。いくつかの実施形態では、第２出口ポート６３１の表面は、流路６３８ａを規定する結合部分６３７ａの内面と実質的流体密封シール（例え

ば、実質的気密シールを形成することができる摩擦嵌め）を形成することができる。結合部分６３７ａの穿孔部材６５５ａは、図１６～図２２の収集デバイス４００に含まれる穿孔部材４５５ａと形態及び機能が実質的に同様であり得る。従って、穿孔部材６５５ａについては本明細書ではそれ以上記載しない。第２結合部材６３７ｂ、第３結合部材６３７ｃ及び第４結合部材６３７ｄは同様に配置される。従って、第２結合部材６３７ｂ、第３結合部材６３７ｃ及び第４結合部材６３７ｄは各々、穿孔部材６５５ｂ、６５５ｃ及び６５５ｄそれぞれを含み、各々、流路６３８ｂ、６３８ｃ及び６３８ｄそれぞれを規定している。本明細書においてさらに詳細に記載するように、第１結合部材６３７ａ、第２結合部材６３７ｂ、第３結合部材６３７ｃ及び第４結合部材６３７ｄを用いて、分流機構６２０を、第１サンプルリザーバ６８０、第２サンプルリザーバ６８０’、第３サンプルリザーバ６９０及び第４サンプルリザーバ６９０’それぞれに流体連通するように選択的に配置することができる。

【００８７】

[1140] 図３０及び図３１に示すように、流量コントローラ６４０は、ダイヤル６４５及びシール部材６４１を含む。流量コントローラ６４０のダイヤル６４５は、分配部材６２９内に回転可能に配置され（図３２及び図３３を参照）、第１位置、第２位置、第３位置及び第４位置の間で移動可能である。ダイヤル６４５は、各々が内部空間６４６に流体連通している入口ポート６２１、第１出口ポート６４７及び第２出口ポート６４８を含む（例えば、図３０を参照）。内部空間６４６は、本明細書においてさらに詳細に記載するように、シール部材６４１の一部を受け入れるように構成されている。入口ポート６２１を、患者から体液を抜き取り及び／又は収集デバイス６００に輸送するための流体流経路を規定する（図示せず）医療デバイスに流体的に結合することができる。例えば、入口ポート６２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に直接又はアダプタ６０４（例えば、図２６及び図２７を参照）を介して間接的に流体的に結合することができる。第１出口ポート６４７は、プリサンプルリザーバ６７０に流体連通している。例えば、第１出口ポート６４７を、分配部材６２９の第１出口ポート６３０内に回転可能に配置することができる。ダイヤル６４５が、その第１位置、第２位置、第３位置及び第４位置にそれぞれある時、第２出口ポート６４８を、第２出口ポート６３１、第３出口ポート６３２、第４出口ポート６３３及び第５出口ポート６３４に流体連通するように選択的に配置することができる。このように、本明細書においてさらに詳細に記載するように、ダイヤル６４５の内部空間６４６を、プリサンプルリザーバ６７０、第１サンプルリザーバ６８０、第２サンプルリザーバ６８０’、第３サンプルリザーバ６９０及び第４サンプルリザーバ６９０’に流体連通するように選択的に配置することができる。

【００８８】

[1141] 流量コントローラ６４０のシール部材６４１の少なくとも一部が、ダイヤル６４５の内部空間６４６内に回転可能に配置され、第１位置と第２位置との間で移動可能である。さらに、シール部材６４１は、シール部材６４１の外面が、内部空間６４６の少なくとも一部を規定するダイヤル６４５の内面と実質的流体密封シールを形成するようなサイズ及び形状を有することができる。図３１に示すように、シール部材６４１は、第１流路６４２及び第２流路６４４を規定している。シール部材６４１が内部空間６４６内でその第１位置にある時、流路６４２は、入口ポート６２１を第２出口ポート６４８から流体的に隔離しながら、入口ポート６２１と第１出口ポート６４７との間に流体連通を確立する。同様に、シール部材６４１が内部空間６４６内でその第２位置にある時、第２流路６４４は、入口ポート６２１を第１出口ポート６４７から流体的に隔離しながら、入口ポート６２１と第２出口ポート６４８との間に流体連通を確立する。収集デバイス６００は、ダイヤル６４５が分配部材６２９内で第２位置、第３位置及び第４位置まで回転する時に同様に作用する。従って、入口ポート６２１が（例えば、入口ポート６２１及び／又はアダプタ６０４に結合された医療デバイスを介して）患者に流体連通するように配置されると、分配部材６２９の第１出口ポート６３０、第２出口ポート６３１、第３出口ポート６３２、第４出口ポート６３３及び第５出口ポート６３４を、入口ポート６２１に流体連通す

るように選択的に配置して、体液がプリサンプルリザーバ６７０、第１サンプルリザーバ６８０、第２サンプルリザーバ６８０’、第３サンプルリザーバ６９０及び第４サンプルリザーバ６９０’それぞれの中に流れ込むのを可能にすることができる。

【００８９】

[1142] 動作時、収集デバイス６００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス６００の入口ポート６２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は体液にアクセスする他の方法）に続き、図３２に示すように、シール部材をその第１位置になるまで作動（又は回転）させることができる。別法として、シール部材６４１を第１位置に事前設定することができ、収集デバイス６００を、収集デバイス６００の無菌状態を維持するように他の方法で封止することができる。シール部材６４１がその第１位置にある時、流量コントローラ６４０は、入口ポート６２１を結合部材６３７ａ、６３７ｂ、６３７ｃ及び６３７ｄから流体的に隔離しながら、入口ポート６２１と分配部材６２９の第１出口ポート６３０との間に流体連通を確立する。従って、図３２において矢印ＩＩによって示すように、収集デバイス４００に関して上述したものと同様の方法で、体液を、患者から入口ポート６２１、第１流路６４２、ダイヤル６４５の第１出口ポート６４７、分配部材６２９の第１出口ポート６３０を介してプリサンプルリザーバ６７０内に移送することができる。

【００９０】

[1143] プリサンプルリザーバ６７０内における体液プリサンプルの収集に続いて、シール部材６４１をダイヤル６４５に対してその第１位置からその第２位置に作動させる（回転させる）ことができる。同様に、図３３に示すように、ダイヤル６４５を、それが分配部材６２９に対して第２位置に達するまで作動させる（又は回転させる）ことができる。シール部材６４１及びダイヤル６４５がその第２位置にある時、流量コントローラ６４０は第２形態に配置され、シール部材６４１の第２流路６４４は、プリサンプルリザーバ６７０を入口ポート６２１から流体的に隔離しながら、入口ポート６２１と第１結合部材６３７ａの流路６３８ａとの間に流体連通を確立する。流量コントローラ６４０が第２形態にある状態で、サンプルリザーバ６８０を、使用者によりその第１形態から第２形態に作動させて（例えば、穿孔部材６５５ａを押して）、患者の身体の一部（例えば、静脈）と第１サンプルリザーバ６８０との間に流体連通を確立することができる。詳細に上述したように、サンプルリザーバ６８０を第２形態に移動させることにより、穿孔部材６５５ａが、サンプルリザーバ６８０の真空シールに穴をあけてサンプルリザーバ６８０の内側に配置される。この第２形態では、患者の身体のその部分（例えば、静脈）が、サンプルリザーバ６８０内の負圧状態（真空）のためにサンプルリザーバ６８０からの真空吸引力にさらされる。従って、図３３において矢印ＪＪによって示すように、体液を、患者の身体のその部分から入口ポート６２１、第２流路６４４、第２出口ポート６３１及び流路６３８ａ並びに第１結合部材６３７ａの穿孔部材６５５ａを通って第１サンプルリザーバ６８０内に強制的に流すことができる。

【００９１】

[1144] サンプルリザーバ６８０内に体液の所望の体積（例えば、第２量）が収集されると、使用者は、流量コントローラ６４０を第３位置まで作動させ（回転させ）及び／又はサンプルリザーバ６８０をその第１形態に戻るように移動させて、第１サンプルリザーバ６８０を第２流路６４４から隔離することができる。サンプルリザーバ６８０が第１形態に戻ると、穿孔部材６５５ａは、サンプルリザーバ６８０から取り除かれ、サンプルリザーバ６８０のシール（例えば、自己封止膜）が、第１サンプルリザーバ６８０を流路６３５ａから流体的に隔離する。他のサンプルリザーバの充填は、流量コントローラ６４０が第３形態、第４形態及び第５形態それぞれに配置されている状態で同様に行われる。

【００９２】

[1145] 図３４～図４０は、実施形態による収集デバイス７００を示す。収集デバイス７００は、分流機構７２０、流量コントローラ７４０並びにサンプルリザーバ７８０及び７

９０を含む（４つのサンプルリザーバに対してホルダが存在するが、明確にするために図では２つのサンプルリザーバのみが含まれており、収集デバイス７００の一部として、追加のサンプルリザーバ（例えば、第５、第６等）を含めることができる）。本明細書においてさらに記載するように、収集デバイス７００を第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス７００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス７００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００、５００及び／又は６００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／又は部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス７００のサンプルリザーバ７８０及び７９０は、図１６～図２２の収集デバイス４００に含まれるサンプルリザーバ４８０及び４９０それぞれと形態及び機能が実質的に同様及び／又は同じであり得る。

【００９３】

[1146] 分流機構７２０は、ハウジング７０１、分配部材７２９及びベースプレート７７１を含む。収集デバイス４００に関して上述したように、ハウジング７０１は、各々、分配部材７２９の異なる部分に流体連通しているように構成されている、第１出口開口部７０３ａ、第２で出口開口部７０３ｂ、第３出口開口部７０３ｃ、第４出口開口部７０３ｄ及び第５出口開口部７０３ｅを規定している。より具体的には、分配部材７２９は、第１出口開口部７０３ａに流体連通しているプリサンプルリザーバ７７０の少なくとも一部と、第２出口開口部７０３ｂに流体連通している第１流体チャンバ７３５ａ、第３出口開口部７０３ｂに流体連通している第２流体チャンバ７３５ｂ、第４出口開口部７０３ｄに流体連通している第３流体チャンバ７３５ｃ、第５出口開口部７０３ｅに流体連通している第４流体チャンバ７３５ｄとを規定し及び／又は形成している。さらに、本明細書においてさらに記載するように、ハウジング７０１は、流量コントローラ７４０の少なくとも一部を移動可能に受け入れるように構成された凹部７６６を規定している。

【００９４】

[1147] 図３６に示すように、分配部材７２９は、プリサンプルリザーバ７７０の少なくとも一部を形成するチャンバ又は空間を規定している。プリサンプルリザーバ７７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。ハウジング７０１の第１出口開口部７０３ａを、詳細に上述したように、プリサンプルリザーバ７７０が患者から体液の流れを受け取ることができるように、プリサンプルリザーバ７７０の開放部分と実質的に位置合せすることができる。さらに詳述すると、分配部材７２９は一組の壁７３６を含み、それらは、例えば、分配部材７２９の内部空間を互いに流体的に隔離されている部分及び／又は空間に分割することができる。例えば、図３６に示すように、一組の壁７３６は、分配部材７２９の内部空間を、プリサンプルリザーバ７７０、第１流体チャンバ７３５ａ、第２流体チャンバ７３５ｂ、第３流体チャンバ７３５ｃ及び第４流体チャンバ７３５ｄに分割することができる。いくつかの実施形態では、壁７３６は、プリサンプルリザーバ７７０及び流体チャンバ７３５ａ～７３５ｄを等しく規定し及び／又は形成することができる。他の実施形態では、プリサンプルリザーバ７７０は、流体チャンバ７３５ａ～７３５ｄによって規定される空間とは異なる空間を規定することができる。

【００９５】

[1148] 分配部材７２９は、第１流体チャンバ７３５ａ、第２流体チャンバ７３５ｂ、第３流体チャンバ７３５ｃ及び第４流体チャンバ７３５ｄそれぞれに流体連通している、第１穿孔部材７５５ａ、第２穿孔部材７５５ｂ、第３穿孔部材７５５ｃ及び第４穿孔部材７５５ｄをさらに含む。従って、穿孔部材７５５ａ～３５５ｄを用いて、本明細書においてさらに詳細に記載するように、サンプルリザーバ７８０及び７９０（並びに図３４～図４０には示さない対応するサンプルリザーバ）に穴をあけることができ、それにより、体液の流れを開始することができる。

【００９６】

[1149] 収集デバイス７００の流量コントローラ７４０は、ダイヤル７４５及びシール部材７４１を含む。シール部材７４１は、ハウジング７０１の凹部７６６内に配置される（例えば、図３８及び図４０を参照）。より詳細には、シール部材７４１が、凹部７６６を規定するハウジング７０１の表面とダイヤル７４５の表面との間にかつそれらと接触して配置されるように、流量コントローラ７４０をハウジング７０１に結合することができる。シール部材７４１を、詳細に上述したように、ダイヤル７４５の表面及び凹部７６６を規定するハウジング７０１の表面と実質的流体密封シールを形成するように構成することができる。図３５に示すように、シール部材７４１は、第１開口部７４４ａ、第２開口部７４４ｂ、第３開口部７４４ｃ、第４開口部７４４ｄ及び第５開口部７４４ｅを規定している。シール部材７４１の配置は、シール部材７４１が凹部７６６内に配置された時、第１開口部７４４ａ、第２開口部７４４ｂ、第３開口部７４４ｃ、第４開口部７４４ｄ及び第５開口部７４４ｅが、ハウジング７０１の第１出口開口部７０３ａ、第２出口開口部７０３ｂ、第３出口開口部７０３ｃ、第４出口開口部７０３ｄ及び第５出口開口部７０３ｅそれぞれと実質的に位置合せされる、というものである。

【００９７】

[1150] 流量コントローラ７４０のダイヤル７４５は、ハウジング７０１に回転可能に結合され、ハウジング７０１に対して第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル７４５は入口ポート７２１を含み、入口ポート７２１を、患者から体液を抜き取り及び／又は収集デバイス７００に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ７０４を介して間接的に）流体的に結合することができる。このように、入口ポート７２１を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ７７０、第１サンプルリザーバ７８０、第２サンプルリザーバ７８０’、第３サンプルリザーバ７９０及び第４サンプルリザーバ７９０’を患者に流体連通するように選択的に配置するように構成することができる。ダイヤル７４５が第１位置にある時、流量コントローラ７４０は第１形態に配置され、入口ポート７２１を、シール部材７４１の第１開口部７４４ａ及びハウジング７０１の第１出口開口部７０３ａと実質的に位置合せすることができる。このように、シール部材７４１の第１開口部７４４ａは、入口ポート７２１を出口開口部７０３ｂ、７０３ｃ、７０３ｄ及び７０３ｅから流体的に隔離し、それにより入口ポート７２１を流体チャンバ７３５ａ～３３５ｄから流体的に隔離しながら、入口ポート７２１と第１出口開口部７０３ａとの間に流体連通を確立する。ダイヤル７４５が第２位置まで回される（又は駆動される）と、流量コントローラ７４０は第２形態に配置され、第２出口開口部７４４ｂは、入口ポート７２１をプリサンプルリザーバ７７０及び流体チャンバ７３５ｂ～７３５ｄから流体的に隔離しながら、入口ポート７２１と第２出口開口部７０３ｂとの間に流体連通を確立する。収集デバイス７００は、ダイヤル７４５が第３位置、第４位置及び第５位置まで回される時、同様に作用する。従って、入口ポート７２１が（例えば、入口ポート７２１に結合された医療デビスを介して）患者に流体連通するように配置されると、体液のすべてがプリサンプルリザーバ７７０、第１サンプルリザーバ７８０又は第２サンプルリザーバ７９０（又はそれらに結合された他の任意の流体リザーバ）内に流れ込むことができるように、第１出口開口部７０３ａ、第２出口開口部７０３ｂ、第３出口開口部７０３ｃ、第４出口開口部７０３ｄ及び第５出口開口部７０３ｅを入口ポート７２１に流体連通するように選択的に配置することができる。

【００９８】

[1151] いくつかの実施形態では、ハウジング７０１は、ダイヤル７４５のその第１位置からその第２位置、第３位置、第４位置及び第５位置への移動を選択的に制限することができる。いくつかの他の実施形態では、ハウジング７０１を、第５位置まで移動したダイヤルの移動を防止するように構成することができる。言い換えれば、ハウジング７０１は、ダイヤル７４５が第５位置から第１位置に戻るように移動するのを防止する係止機構を含むことができる。この特徴により、流量チャンバ７３５ａ～７３５ｄ並びに／又はサン

プルリザーバ７８０及び７９０内に収集された体液が（表面に結合された微生物及び／又は他の望ましくない外部汚染物質を含むリスクが高い）プリサンプルリザーバ７７０内に収容された体液から汚染されるリスクを低減することができる。この係止機構により、医療従事者を、ＨＩＶ、Ｃ型肝炎等を含む可能性がある患者サンプル内の血液媒介病原体にさらされることから保護することも可能である。ダイヤル７４５及び／又はハウジング７０１は又はウジング７０１における出口ポート７０３ａ及び出口開口部７０３ａ～７０３ｄに対するダイヤル７４５の正確な位置合せを確実にするように視覚的フィードバック又は触覚フィードバックを提供する、機械的戻り止め及び／又は他のインジケータも含むことができる。

【００９９】

[1152] 図１６～図２２に示す収集デバイス４００の実施形態と同様に、収集デバイス７００は、分配部材７２９内に収容されるチャンバであるプリサンプルリザーバ７７０を含む。プリサンプルリザーバ７７０は、例えば、血液、血漿、尿等の体液を収容することができる。プリサンプルリザーバ７７０は、（ハウジング７０１内に位置する）収集デバイス７００の第１出口ポート７０３ａに流体的に結合されるように構成されている。収集デバイス７００の動作中、流量コントローラ７４０が第１位置にある時、体液は、患者の身体の一部（例えば、静脈）から、入口ポート７２１を介して、プリサンプルリザーバ７７０、シール部材７４１内に位置するプリサンプルリザーバ７４４ａ用の開口部及び第１出口ポート７０３ａ内に引き込まれる。プリサンプルリザーバ７７０は、患者から抜き取られる流体の第１量を収容するように構成され、そこでは、体液の第１量は、所定量であることも未定量であることも可能であり、それにより、体液の第１量は、患者から後に抜き取られる体液の第２量及び／又は第３量及び／又は第４量及び／又は第５量から流体的に隔離される。

【０１００】

[1153] 動作時、収集デバイス７００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス７００の入口ポート７２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺に続き、図３７及び図３８に示すように、ダイヤル７４５が第１位置に達するまで回される。別法として、上述したように、ダイヤル７４５を第１位置で事前設定することができ、収集デバイス７００の無菌状態を維持するように、収集デバイス７００を他の方法で封止することができる。ダイヤル７４５が第１位置にある状態で、流量コントローラ７４０は第１形態に配置され、シール部材７４１の第１出口開口部７４４ａは、入口ポート７２１を４つのサンプル流路７３５ａ～７３５ｄから流体的に隔離しながら、（ハウジング７０１内に含まれる）入口ポート７２１と第１出口ポート７４１との間に流体連通を確立する。この第１形態では、体液は、図３８において矢印ＫＫによって示すように、患者の身体のその部分から、入口ポート７２１、シール部材７４１の第１出口開口部７４４ａ、ハウジング７０１の第１出口ポート７０３ａを通って、分配部材７７０によって規定されたプリサンプルリザーバ７７０内に流れ込む。従って、詳細に上述したように、体液の第１量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ７７０内に受け取り、後続するサンプルから隔離することができる。

【０１０１】

[1154] プリサンプルリザーバ７７０内における体液プリサンプルの収集に続き、ダイヤル７４５を、図３９及び図４０に示すように第２位置に達するまで作動させる（又は回転させる）ことができる。ダイヤル７４５が第２位置にある時、流量コントローラ７４０は第２形態に配置され、シール部材７４１の第２出口開口部７４４ａは、プリサンプルリザーバ７７０を入口ポート７２１から流体的に隔離しながら、入口ポート７２１と第１流体チャンバ７３５ａとの間に流体連通を確立する。第１流体チャンバ７３５ａに体液が充填されると、流量コントローラ７４０を第３位置に移動させて、第１流路７３５ａを外部環境から隔離し封止することができる。さらに、サンプルリザーバ７８０を第１形態から第２形態に作動させて、体液を第１流体チャンバ７３５ａからサンプルリザーバ７８０に移

送することができる。例えば、サンプルリザーバ７８０を使用者が又は自動的に第１形態から第２形態に作動させて（穿孔部材７５５ａを押して）、患者の身体の一部（例えば、静脈）とサンプルリザーバ７８０との間に流体連通を確立することができる。上述したように、サンプルリザーバ７８０を第２形態まで移動させることにより、穿孔部材７５５ａがサンプルリザーバ７８０の真空シールに穴をあけ、サンプルリザーバ７８０の内側に配置される。第２形態では、患者の身体のその部分（例えば、静脈）は、幾つかの実施形態ではサンプルリザーバ７８０内部に存在する負圧状態（真空）によりサンプルリザーバ７８０からの真空吸引にさらされる。従って、図４０において矢印ＬＬによって示すように、体液は、患者の身体のその部分から、入口ポート７２１、シール部材７４１の第２出口開口部７４４ｂ、ハウジング７０１の第２出口開口部７０３ｂ、第２流体チャンバ７３５ｂを通って第１サンプルリザーバ７８０内に流れ込む。

【０１０２】

[1155] サンプルリザーバ７８０内に体液の所望の量（例えば、第２量）が収集されると、使用者は、流量コントローラ７４０を第３位置まで作動させ（回転させ）及び／又はサンプルリザーバ７８０をその第１形態に戻るように移動させて、第１サンプルリザーバ７８０を入口ポート７２１から隔離することができる。サンプルリザーバ７８０が第１形態に戻ると、穿孔部材７５５ａはサンプルリザーバ７８０から取り除かれ、サンプルリザーバ７８０のシール（例えば、自己封止膜）が、第１サンプルリザーバ７８０を第２流体チャンバ７３５ｂ及び外部環境から流体的に隔離する。他のサンプルリザーバの充填は、流量コントローラ７４０が第３形態、第４形態及び第５形態それぞれにある状態で同じ方法で行われる。

【０１０３】

[1156] いくつかの実施形態では、収集デバイス７００を、分配部材７２９内で異なる流体チャンバ７３５ａ～７３５ｄを分離する一組の壁７３６が存在しないように構成することができる（図１６における詳細な断面図を参照）。こうした実施形態では、分配部材７２９は、プリサンプルリザーバ７７０と結合された流体チャンバ７３５との間で分割される（すなわち、流体チャンバは、壁７３６によって４つの別個の部分に分離されない）。こうした実施形態では、使用者は、ダイヤル７４５を第２位置、第３位置、第４位置又は第５位置のいずれかに作動（回転）させることによって、一度に４つのサンプルリザーバすべてを充填することができる。

【０１０４】

[1157] 本明細書に記載する実施形態のうちのいずれも、例えば、プリサンプルリザーバ及び／又はサンプルリザーバ内への体液の流れを計量する（例えば、定量化する）ために使用することができる計量デバイスと使用することができる。場合によっては、検査標準実施により、充填体積が臨床医及び／又は瀉血専門医によって視覚的に判断され従って人的ミスを受けやすいという事実により、体液（例えば、血液試料）の正確な接種体積との一貫したコンプライアンスが確保されない。血液収集ボトルの体積インジケータは、保持されている時に読み取ることが困難であり、収集ボトルは引込み処置の間、直立して保持されないという事実が、患者から受け取られた体液サンプルの不正確な体積の要因となる可能性がある。サンプル体積が不十分である（例えば、製造業者の推奨未満である）ことにより、培養検査の感度が低下し、偽陰性結果に至る可能性がある。さらに、所定タイプの検査供給品及び装置（例えば、Franklin Lakes、NJのBecton Dickinson等の製造業者によって生成される自動微生物検出システムと使用するように設計された血液培養ボトル）に対する概要資料及び使用説明書において指示されているように、製造業者の推奨を上回る充填体積は、偽陽性をもたらす可能性がある。従って、流量計量及び体積表示機能により、検査技師及び／又は医療従事者（例えば、瀉血専門医）は、サンプルがいかに処理される必要があるかに応じて、サンプルリザーバをインキュベータに又は他の研究室検査機器内に配置する前に各個々のサンプルリザーバ内に収集される体液の体積を確認することができる。検査技師及び／又は瀉血専門医はまた、結果が受け取られる時に臨床医が評価するための正確な体積情報を（例えば、診療記録、データベース、スプレッドシート等に

）記録することも可能であり、それにより、偽陰性結果及び／又は偽陽性結果の誤った解釈の可能性を低減するのに役立つ。

【０１０５】

[1158] 例として、図４１～図４５は、１つ又は複数の計量デバイスを含むことができる収集デバイス８００を示す。収集デバイス８００は、分流機構８２０、流量コントローラ８４０、ディスプレイ８７５及びサンプルリザーバ８８０を含む。本明細書においてさらに記載するように、収集デバイス８００を第１形態、第２形態及び第３形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス８００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス６００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００、５００、６００及び／又は７００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／又は部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス８００のサンプルリザーバ８８０は、図１６～図２２の収集デバイス４００に含まれるサンプルリザーバ４８０と形態及び機能が実質的に同様であり及び／又は同じであり得る。

【０１０６】

[1159] 図４１～図４３に示すように、分流機構８２０は、アクチュエータ部分８２２（例えば、第１部分）、中間部分８２３（例えば、第２部分）及び結合部分８２４（例えば、第３部分）を含む。分流機構８２０のアクチュエータ部分８２２は、内部空間８０６を規定する一組のアクチュエータ壁を含む実質的に円筒状である。より具体的には、アクチュエータ部分８２２は、実質的に閉鎖されている第１端部と、内部空間８０６へのアクセスを可能にするように実質的に開放されている、第１端部と反対側の第２端部とを含む。このように、アクチュエータ部分８２２は、本明細書においてさらに詳細に記載するように、流量コントローラ８４０の少なくとも一部を移動可能に受け入れることができる。アクチュエータ部分８２２は、入口ポート８２１及び出口ポート８３１をさらに含む。入口ポート８２１を、詳細に上述したように、患者から体液を抜き取り及び／又は収集デバイス８００に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ８０４を介して間接的に）流体的に結合することができる。

【０１０７】

[1160] アクチュエータ部分８２２の出口ポート８３１は、アクチュエータ部分８２２の内部空間８０６の一部を、中間部分８２３によって規定される内部空間８０７に流体連通するように選択的に配置することができる。図４３に示すように、中間部分８２３は、アクチュエータ部分８２２と結合部分８２４との間に配置されている。図４１～図４５には示さないが、中間部分８２３は、例えばサンプルリザーバ８８０に移送される体液の体積を計量するように構成することができる計量デバイスを含むことができる。例えば、いくつかの実施形態では、流量計量デバイスを出口ポート８３１に流体的に結合して、そこを通る体液の流れを計量することができる。図４１及び図４２に示すように、中間部分８２３はディスプレイ８７５を含み、ディスプレイ８７５は、例えば、出口ポート８３１を通って流れた体液の体積に関連する視覚的インジケータ及び／又は情報を使用者に提供することができる。他の実施形態では、流量計量デバイスを、分流機構８２０内の又はそれに沿った他のあらゆる好適な位置に配置することができる。

【０１０８】

[1161] 結合部分８２４を、中間部分８２３に物理的にかつ流体的に結合することができる。例えば、いくつかの実施形態では、結合部分８２４を、中間部分８２３の内部空間８０７内に部分的に配置し、それに、摩擦嵌め、圧入、スナップフィット、ねじ結合、接着剤等を介して少なくとも一時的に結合することができる。結合部分８２４は、詳細に上述したように、サンプルリザーバ８８０の一部を受け入れるように構成されており、サンプルリザーバ８８０の真空シールに穴をあけ、それにより体液の流れを開始することができるように使用することができる穿孔部材８５５を含む。

【０１０９】

[1162] 収集デバイス８００の流量コントローラ８４０は、アクチュエータ部分８２２によって規定された内部空間８０６内に少なくとも部分的に配置され、第１形態、第２形態及び第３形態の間で移動可能である。図４２及び図４３に示すように、流量コントローラ８４０は、第１シール部材８６１、第２シール部材８６２及び第３シール部材８６３を有する可動部材８５０と、付勢部材８５９（例えば、ばね等）とを含む。シール部材８６１、８６２及び８６３は、内部空間８０６を規定するアクチュエータ部分８２２の内面と接触している。従って、本明細書においてさらに詳細に記載するように、シール部材８６１、８６２及び８６３は各々、例えばアクチュエータ部分８２２の内部空間８０６を流体的に隔離された部分に分割することができる内面と、実質的流体密封シールを形成することができる。

【０１１０】

[1163] 可動部材８５０は、内部空間８０６内で第１位置、第２位置及び第３位置の間で移動可能である。可動部材８５０の配置は、可動部材８５０がその第１位置、第２位置及び第３位置の間で移動する際に、シール部材８６１、８６２及び８６３が内部空間８０６内で選択的に移動する、というものであり得る。より具体的には、可動部材８５０がその第１位置、第２位置及び第３位置の間で移動する際、第１シール部材８６１を可動部材８５０と同時に移動させることができる。第２シール部材８６２及び第３シール部材８６３を、互いに固定して結合し（例えば、互いに固定距離で配置し）、可動部材８５０の一部の周囲に摺動可能に配置することができ、それにより、可動部材８５０は、第２シール部材８６２及び第３シール部材８６３がアクチュエータ部分８２２に対して実質的固定位置にあり続ける間に、その第１位置（例えば、図４３を参照）からその第２位置（例えば、図４４を参照）に移動することを可能にすることができる。例えば、可動部材８５０がその第１位置と第２位置との間で移動する際、第２シール部材８６２及び第３シール部材８６３は、実質的固定位置にあり続けることができ、それにより、入口ポート８２１は第２シール部材８６２の第１側に配置され、出口ポート８３１は、第２シール部材８６２の第１側とは反対側の第２側に配置される。従って、本明細書においてさらに詳細に記載するように、可動部材８５０がその第１位置（図４３）及びその第２位置（図４４）にある時、入口ポート８２１は、第１シール部材８６１と第２シール部材８６２との間に規定された内部空間８０６の部分に流体連通しており、出口ポートは、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分に流体連通している。

【０１１１】

[1164] 流量コントローラ８４０の配置は、可動部材８５０がその第１位置からその第２位置に移動した時に、第１シール部材８６１が第２シール部材８６２及び第３シール部材８６３に対して移動する、というものであり得る。第２シール部材８６２に対する第１シール部材８６１の移動により、それらの間に規定された空間が拡大することが可能であり、それにより、プリサンプルリザーバ８７０を形成し及び／又は他の方法で規定することができる。さらに、シール部材８６１及び８６２がアクチュエータ部分８２２の内面と実質的流体密封シールを形成していることにより、第１シール部材８６１と第２シール部材８６２との間に規定されたプリサンプルリザーバ８７０は、内部空間８０６の他の部分から流体的に隔離される。従って、可動部材８５０がその第１位置からその第２位置に移動する時、入口ポート８２１はプリサンプルリザーバ８７０に流体連通することができる。可動部材８５０がその第２位置（例えば、図４４を参照）からその第３位置（例えば、図４５を参照）まで移動する時、可動部材８５０の一部は第３シール部材８６３と接触して、内部空間８０６内で第１シール部材８６１、第２シール部材８６２及び第３シール部材８６３を実質的に同時に移動させることができる。従って、本明細書においてさらに詳細に記載するように、入口ポート８２１及び出口ポート８３１の両方が、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分に流体連通するように、第２シール部材８６２を入口ポート８２１に対して移動させることができる。

【０１１２】

[1165] 動作時、収集デバイス８００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス８００の入口ポート８２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。入口ポート８２１が内腔規定デバイスに結合された状態で、流量コントローラ８４０をその第１形態からその第２形態に移動させることができる。このように、使用者は、図４４において矢印ＭＭによって示すように、可動部材８５０をその第１位置からその第２位置に移動させるように力をかけることができる。上述したように、第１シール部材８６１は、可動部材８５０と同時に移動し、それによって、第１シール部材８６１と第２シール部材８６２との間に規定された空間が拡大し、それにより、プリサンプルリザーバ８７０が形成され及び／又は規定される。第１シール部材８６１及び第２シール部材８６２が、内部空間８０６を規定するアクチュエータ部分８２２の内面と実質的流体密封シールを形成していることにより、第１シール部材８６１と第２シール部材８６２との間の容積の増大によって、プリサンプリリザーバ８７０内に負圧がもたらされる。従って、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ８７０との間に（例えば、図４４における入口ポート８２１を介して）流体連通が確立されると、図４４において矢印ＮＮによって示すように、プリサンプルリザーバ８７０と患者の身体のその部分との間の負圧の差により、入口ポート８２１を通してプリサンプルリザーバ８７０内に体液が引き込まれる。この第１形態では、流量コントローラ８４０はまた、プリサンプルリザーバ８７０を出口ポート８３１から流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、（例えば）静脈穿刺の直後にプリサンプルリザーバ８７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス８００を用いて、体表微生物及び／又は他の望ましくない外部汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の検査のために収集されかつ使用される体液サンプルの後続する量を汚染するのを防止することができる。いくつかの実施形態では、計量デバイスは、プリサンプルリザーバ８７０内に配置された体液の体積を計量し、その体積に関連する値をディスプレイ８７５に提示することができる。

【０１１３】

[1166] プリサンプルリザーバ８７０内における体液プリサンプルの体積の収集に続き、図４５において矢印ＯＯによって示すように、可動部材８５０をその第２位置からその第３位置に移動させて、流量コントローラを第３形態に配置することができる。上述したように、可動部材８５０がその第２位置からその第３位置に移動すると、可動部材８５０の部分は、第３シール部材８６３と接触するように配置される。従って、可動部材８５０は、内部空間８０６内で、第１シール部材８６１、第２シール部材８６２及び第３シール部材８６３を実質的に同時に移動させる。従って、入口ポート８２１及び出口ポート８３１両方が、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分に流体連通するように、第２シール部材８６２を、入口ポート８２１に対して移動させることができる。さらに、体液の体積がプリサンプルリザーバ８７０内で流体的に隔離されているため、第２シール部材８６２及び第３シール部材８６３の第１シール部材８６１の方向における移動が制限される（すなわち、体液は実質的に非圧縮性流体である）。このように、体液のプリサンプル体積は、プリサンプルリザーバ８７０内で封鎖（sequester）され、第２シール部材８６２と第３シール部材８６３との間に規定された空間は、入口ポート８２１と出口ポート８３１との間に流体流路を規定する。さらに、流量コントローラ８４０の配置は、その第３形態にある時、第１シール部材８６１が付勢部材８５９と接触するように配置され、使用者により可動部材８５０にかけられる力の少なくとも一部が、付勢部材８５９を変形させ、圧縮し、屈曲させ及び／又は他の方法で再構成するように動作可能である、というものである。従って、付勢部材８５９は、本明細書においてさらに詳細に記載するように、第１シール部材８６１に対して、流量コントローラ８４０のその第２形態からその第３形態への移動に抵抗する反力を及ぼすことができる。

【０１１４】

[1167] 詳細に上述したように、穿孔部材８５５が、サンプルリザーバ８８０の真空シー

ルに穴をあけてサンプルリザーバ内部に配置されるように、サンプルリザーバ８８０を収集デバイス８００に対して配置することができる。サンプルリザーバ８８０（例えば、真空又は負圧）と身体のその部分との間の圧力差により、体液がサンプルリザーバ８８０内に引き込まれる。言い換えれば、第２形態では、流量コントローラ８４０及び分流機構８２０は、図４５において矢印ＰＰによって示すように、体液を、患者から、入口ポート８２１、第２シール部材８６２と第３シール部材８６３との間に規定された内部空間８０６の部分、及びアクチュエータ部分８２２の出口ポート８３１を通って、中間部分８２３及び結合部分８２４の穿孔部材８５５を通って、サンプルリザーバ８８０内に引き込むことができるように、流体流路を確立する。上述したように、（図示せず）計量デバイスが、例えば出口ポート８３１を通して移送される体液の体積を計量することができ、体液の体積に関連する値をディスプレイ８７５に提示することができる。

【０１１５】

[1168] サンプルリザーバ８８０内に体液の所望の体積（例えば、第２量）が収集されると、使用者は、可動部材８５０にかけられた力を取り除き及び／又は低減することができ、それにより、付勢部材８５９が、第１シール部材８６１及び可動部材８５０をそれらの第３位置からそれらの第２位置に向かって移動させることができる。さらに、プリサンプルリザーバ８７０内に配置された体液が実質的に非圧縮性であることにより、第１シール部材８６１の移動が、体液の体積を通して力を移送し、第２シール部材８６２及び第３シール部材８６３をそれらの第３位置からそれらの第２位置に向かって移動させる。いくつかの実施形態では、付勢部材８５９は、第２シール部材８６２をアクチュエータ部分８２２に対して例えば入口ポート８２１を実質的に遮断することができる第４位置に移動させるように作用可能であり得る力を、第１シール部材８６１にかけることができる。従って、入口ポート８２１を、アクチュエータ部分８２２の内部空間８０６から流体的に隔離することができる。さらに、穿孔部材８５５をサンプルリザーバ８８０から取り除くことができ、シール（例えば、自己封止膜）が、体液サンプルをサンプルリザーバ８８０の外側の空間から流体的に隔離することができる。後続するサンプルリザーバの充填を、穿孔部材８５５をサンプルリザーバ内に配置し、流量コントローラ８４０を第３形態まで移動させて体液が患者からサンプルリザーバに流れるのを可能にすることによって、同様に行うことができる。

【０１１６】

[1169] 図４６～図５３は、実施形態による収集デバイス９００を示す。収集デバイス９００は、分流機構９２０、流量コントローラ９４０及びサンプルリザーバ９８０、９８０’、９９０及び９９０’を含む。本明細書においてさらに記載するように、収集デバイス９００を、第１形態、第２形態、第３形態、第４形態及び第５形態の間で移動させて、例えば、皮膚に存在する微生物及び／又は他の望ましくない外部汚染物質等、体外の微生物が実質的にない体液の流れを送出することができる。収集デバイス９００は、あらゆる好適な形状、サイズ又は構成であり得る。例えば、収集デバイス９００の態様及び／又は部分は、上述した収集デバイス１００、２００、３００、４００、５００、６００、７００及び／又は８００のいずれかの対応する態様及び／又は部分と形態及び／又は機能が実質的に同様であり得る。従って、こうした同様の態様及び／部分については、本明細書ではそれ以上詳細に記載しない。例として、いくつかの実施形態では、収集デバイス９００のサンプルリザーバ９８０、９８０’、９９０及び９９０’は、図２６～図３３の収集デバイス６００に含まれる、サンプルリザーバ６８０、６８０’、６９０及び６９０’と形態及び機能が実質的に同様であり及び／又は同じであり得る。

【０１１７】

[1170] 分流機構９２０は、ハウジング９０１、分配部材９２９並びに可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄを含む。ハウジング９０１は、分配部材９２９に物理的にかつ流体的に結合されており、患者から体液を収集する一組の流体流経路を提供し及び／又は規定している。ハウジング９０１は、本明細書においてさらに詳細に記載するように、流量計量デバイスに含め及び／又は他の方法で（例えば、電気的に及び／又は機械

的に）結合することができる一組のディスプレイ９７５’（例えば、液晶ディスプレイ（ＬＣＤ）等）を含む。ハウジング９０１は、凹部９６６、出口開口部９０３ａ、９０３ｂ、９０３ｃ、９０３ｄ、９０３ｅ及び（本明細書において「開口」とも呼ぶ）可動部材開口９５０ａ、９５０ｂ、９５０ｃ、９５０ｄを規定している。凹部９６６は、本明細書においてさらに詳細に記載するように、流量コントローラ９４０に含まれるシール部材９４１を受け入れるように構成されている。第１出口開口部９０３ａ、第２出口開口部９０３ｂ、第３出口開口部９０３ｃ、第４出口開口部９０３ｄ及び第５出口開口部９０３ｅは、各々、分配部材９２９の異なる部分に流体連通している異なる流体流路を規定するように構成されている。より具体的には、分配部材９２９は、第１出口開口部９０３ａに流体連通しているプリサンプルリザーバ９７０の少なくとも一部と、第２出口開口部９０３ｂに流体連通している第１流路９３５ａ、第３出口開口部９０３ｂに流体連通している第２流路９３５ｂ、第４出口開口部９０３ｄに流体連通している第３流路９３５ｃ、第５出口開口部９０３ｅに流体連通している第４流路９３５とを規定し及び／又は形成している。

【０１１８】

[1171] 図４７及び図４８に示すように、分配部材９２９は、プリサンプルリザーバ９７０の少なくとも一部を規定するチャンバ又は空間を規定している。プリサンプルリザーバ９７０は、例えば、血液、血漿、尿等の体液を収容するように構成されている。図１６～図２２においてプリサンプルリザーバ４７０に関して詳細に上述したように、プリサンプルリザーバ９７０が患者から体液の流れを受け取るのを可能にするように、ハウジング９０１の第１出口開口部９０３ａを、プリサンプルリザーバ９７０の開放部分と実質的に位置合せすることができる。流路９３５ａ～９３５ｄは、分配部材９２９の中心から放射状に延在し、各流路９３５ａ、９３５ｂ、９３５ｃ及び９３５ｄがプリサンプルリザーバ９７０及び他の流路から流体的に隔離されるように配置されている。このように、流路９３５ａ、９３５ｂ、９３５ｃ及び９３５ｄは、出口開口部９０３ｂ、９０３ｃ、９３０ｄ及び９０３ｅそれぞれと実質的に位置合せされた開口を規定する第１端部と、可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄそれぞれを受け入れるように構成された開口又はポートを規定する第２端部との間で、流体流路を方向付け及び／又は他の方法で規定することができる。図４７及び図４８において、分配部材９２９は、実質的に閉鎖されている流路９３５ａ～９３５ｄを含むものとして示されているが、他の実施形態では、図１７及び図１８の分配部材４２９に関して上に示しかつ記載したように、流路９３５ａ～９３５ｄを実質的に開放することができる。従って、収集デバイス９００の分配部材９２９は、収集デバイス４００の分配部材４２９と実質的に同様に機能することができる。

【０１１９】

[1172] 可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄは、ハウジング９０１の開口９０５ａ、９０５ｂ、９０５ｃ及び９０５ｄそれぞれと、分配部材９２９の第２端部によって規定される対応する開口とに移動可能に配置される。図４６～図５３には示さないが、いくつかの実施形態では、可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄを、収集デバイス２００の可動部材２５０及び２５０’に関して詳細に上述したように、付勢部材等に動作可能に結合することができる。このように、可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄを、使用者が、ハウジング９０１及び分配部材９２９に対して第１位置及び第２位置から作動させ（移動させ）て、流体流を第１サンプルリザーバ９８０、第２流体リザーバ９８０’、第３流体リザーバ９９０及び第４サンプルリザーバ９９０’それぞれの中に仕向けることができる。可動部材９５０ａ、９５０ｂ、９５０ｃ及び９５０ｄは、実質的に同じであり、従って、図４９において単一の可動部材９５０に関して記載する。さらに、可動部材９５０のいくつかの部分は、上述した可動部材２５０及び３５０と実質的に同様であり得る。従って、可動部材９５０のいくつかの部分については、本明細書においてそれ以上詳細に説明しない。可動部材９５０は、入口ポート９５３及び穿孔部材９５５に流体連通している内部空洞９５２を規定している。穿孔部材は、詳細に上述したものと実質的に同様である。入口ポート９５３は、一組の壁を通して延在し、一組の壁は、可動部材９５０の内部空間９５２を対応する流路９３５ａ、９３５ｂ、９３５ｃ

又は９３５ｄに流体連通するように選択的に配置するように内部チャンバ９５２を規定している。

【０１２０】

[1173] 図４９に示すように、可動部材９５０は、内部空間９５２内に回転可能に配置されかつ入口ポート９５３と実質的に直接流体連通している流量制御機構９６７を含む。流量計量機構９６７は、例えば、一組のスポーク又はフィンを含むことができるホイール等であり得る。このように、体液は、可動部材９５０の入口ポート９５３に入り、流量計量デバイス９６７を通過して流れることができ、それにより、流量計量デバイス９６７が可動部材９５０に対して回転することができる。従って、流量計量デバイス９６７の回転の特徴は、可動部材９５０の内部空間９５２に移送される体液の体積、体積流量等を求める際に使用可能であり得る。図４６～図５３には示さないが、可動部材９５０の流量制御機構９６７は、ハウジング９０１のディスプレイ９７５’に動作可能に結合される。従って、体液が、例えばサンプルリザーバ９８０、９８０’、９９０及び／又は９９０’に移送される際、体液の流れに関連する体積情報をディスプレイ９７５’に提示することができる。このように、使用者は、患者から体液サンプルを収集するように収集デバイス９００を操作することができ、例えばサンプルリザーバ９８０に移送される体液サンプルの正確な体積を求めるためにディスプレイ９７５’の少なくとも１つを視覚化することができる。

【０１２１】

[1174] 収集デバイス９００の流量コントローラ９４０は、ダイヤル９４５及びシール部材９４１を含む。シール部材９４１は、ハウジング９０１の凹部９６６内に配置される。より詳細には、シール部材９４１が、凹部９６６を規定するハウジング９０１の表面とダイヤル９４５の表面との間にかつそれらと接触するように配置されるように、流量コントローラ９４０をハウジング９０１に結合することができる。本明細書において詳細に記載するように、シール部材９４１を、ダイヤル９４５の表面及び凹部９６６を規定するハウジング９０１の表面と実質的流体密封シールを形成するように構成することができる。図４７に示すように、シール部材９４１は、第１開口部９４４ａ、第２開口部９４４ｂ、第３開口部９４４ｃ、第４開口部９４４ｄ及び第５開口部９４４ｅを規定している。シール部材９４１の配置は、シール部材９４１が凹部９６６内に配置されると、第１開口部９４４ａ、第２開口部９４４ｂ、第３開口部９４４ｃ、第４開口部９４４ｄ及び第５開口部９４４ｅが、ハウジング９０１の第１出口開口部９０３ａ、第２出口開口部９０３ｂ、第３出口開口部９０３ｃ、第４出口開口部９０３ｄ及び第５出口開口部９０３ｅそれぞれと実質的に位置合せされる、というものである。

【０１２２】

[1175] 流量コントローラ９４０のダイヤル９４５は、ハウジング９０１に回転可能に結合され、ハウジング９０１に対して第１位置、第２位置、第３位置、第４位置及び第５位置の間で移動可能である。ダイヤル９４５は入口ポート９２１を含み、入口ポート９２１を、患者から体液を抜き取り及び／又は収集デバイス９００に輸送するための流体流経路を規定する医療デバイスに（直接又はアダプタ９０４を介して間接的に）流体的に結合することができる。このように、入口ポート９２１を、本明細書においてさらに詳細に記載するように、プリサンプルリザーバ９７０、第１サンプルリザーバ９８０、第２サンプルリザーバ９８０’、第３サンプルリザーバ９９０及び第４サンプルリザーバ９９０’を患者に流体連通するように選択的に配置するように構成することができる。ダイヤル９４５を、収集デバイス４００のダイヤル４４５に関して上述したものと実質的に同様な方法で、第１位置、第２位置、第３位置、第４位置及び第５位置を通して回転するように構成することができ、従って、それについては本明細書においてそれ以上詳細に記載しない。

【０１２３】

[1176] 図示するように、ダイヤル９４５は、体液の流れに関連する体積情報を提示するように構成することができるディスプレイ９７５をさらに含むことができる。例えば、図４６～図５３には示さないが、ダイヤルは、可動部材９５０に含まれる流量計量デバイス

９６７等、流量計量デバイス等を含むことができる。このように、流量計量デバイスは、例えば入口ポート９２１を通る体液の流れを計量することができ、入口ポート９２１を通る体液の流れに関連する体積情報がダイヤル９４５のディスプレイ９７５に提示されるように、ディスプレイ９７５に動作可能に結合され得る。

【０１２４】

[1177] 動作時、収集デバイス９００を用いて、汚染を低減して患者から体液（例えば、血液、血漿、尿等）を収集することができる。例えば、収集デバイス９００の入口ポート９２１を、針又は他の内腔規定デバイス（例えば、可撓性滅菌管）に流体的に結合することができる。静脈穿刺（又は、体液にアクセスする他の方法）に続き、図５０及び図５１に示すように、ダイヤル９４５は、第１位置に達するまで駆動される（又は回される）。別法として、ダイヤル９４５を第１位置に事前設定することができ、収集デバイス９００の無菌状態を維持するように、収集デバイス９００を他の方法で封止することができる。

【０１２５】

[1178] 上述したように、ダイヤル９４５が第１位置にある時、流量コントローラ９４０は第１形態に配置され、シール部材９４１の第１開口部９４４ａは、入口ポート９２１を４つの流路９３５ａ～３３５ｄから流体的に隔離しながら、（ハウジング９０１内に含まれる）入口ポート９２１と第１出口ポート９３０との間に流体連通を確立する。さらに、サンプルリザーバ９８０、９８０’、９９０及び９９０’は、第１形態では入口ポート９２１から流体的に隔離されており、図５１において矢印ＱＱによって示すように、患者の身体の一部（例えば、静脈）とプリサンプルリザーバ９７０との間に、流体流路が規定される。この第１形態では、体液は、（例えば、重力、真空等により）、患者の身体のその部分から、入口ポート９２１、シール部材９４１の第１開口部９４４ａ、ハウジング９０１の第１出口ポート９０３ａを通って、プリサンプルリザーバ９７０内に流れ込む。第１形態では、流量コントローラ９４０はまた、流路９３５ａ～９３５ｄからプリサンプルリザーバ９７０を流体的に隔離する。従って、体液の第１量（所定量又は未定量）を、静脈穿刺の直後にプリサンプルリザーバ９７０内に受け取り、後続するサンプルから隔離することができる。このように、収集デバイス９００を用いて、体表微生物及び／又は他の望ましくない汚染物質を含む可能性が最も高い体液の第１量が、診断又は汚染物質によって影響を受ける可能性がある他の検査に対して収集されかつ使用される体液サンプルの後続する量を汚染しないようにすることができる。さらに、ディスプレイ９７５は、例えば、プリサンプルリザーバ９７０に移送される体液の体積に関連する、（図示せず）流量制御機構から受け取られる情報を提示することができる。従って、体液の正確な体積を、プリサンプルリザーバに移送し、かつその中で流体的に隔離することができる。

【０１２６】

[1179] プリサンプルリザーバ９７０内における体液プリサンプルの収集に続き、図５２及び図５３に示すように、ダイヤル９４５を、第２位置に達するまで作動させる（又は回転させる）ことができる。ダイヤル９４５が第２位置にある時、流量コントローラ９４０は第２形態に配置され、シール部材９４１の第２開口部９４４ｂは、プリサンプルリザーバ９７０を入口ポート９２１から流体的に隔離しながら、入口ポート９２１と流路９３５ａとの間に流体連通を確立する。流量コントローラ９４０が第２形態にある状態で、可動部材９５０ａを、使用者が第１位置から第２位置に作動させて（すなわち押下して）、患者（例えば、静脈）と第１サンプルリザーバ８８０との間に流体連通を確立することができる。より具体的には、図５３において矢印ＲＲによって示すように、可動部材９５０は、その第１位置からその第２位置に移動して、穿孔部材９５５が、第１サンプルリザーバ９８０の真空シールを通過して第１サンプルリザーバ９８０内に配置されるようにする。

【０１２７】

[1180] 第２位置にある間、可動部材９５０の入口ポート９５３は、第１流路９３５ａと実質的に位置合せされかつ流体連通し、それにより、体液が、第１流路９３５ａから稼働部材９５０の内部空洞９５２内に入り、穿孔部材９５５から出て第１サンプルリザーバ９８０に入るように流れることができる。サンプルリザーバ９８０（例えば、真空又は負圧

）と第１流路９３５ａとの圧力差により、サンプルリザーバ９８０内に体液が引き込まれる。言い換えれば、第２形態では、図５３において矢印ＳＳによって示すように、流量コントローラ９４０及び可動部材９５０ａは、ダイヤル９４５の入口ポート９２１と第１サンプルリザーバ９８０との間に流体流路を確立する。さらに、体液の可動部材９５０ａを通る流れにより、可動部材９５０に対して流量計量機構９６７が回転する。従って、流量計量機構９６７の回転は、サンプルリザーバ９８０に移送される体液サンプルの体積を求める際に使用可能であり得る。さらに、ディスプレイ９７５’は、例えば、サンプルリザーバ９８０に移送される体液の体積に関連する、流量制御機構９６７から受け取られる情報を提示することができる。従って、体液の正確な体積をサンプルリザーバ９８０に移送することができる。例えば、場合によっては、収集デバイス９００を用いて、第１サンプルリザーバ９８０、第２サンプルリザーバ９８０’及び第３サンプルリザーバ９９０の各々に２０ｍＬの３つのサンプル体積を収集する（すなわち、合計６０ｍＬのサンプル体積が収集される）ことができる。

【０１２８】

[1181] 第１サンプルリザーバ９８０内に体液の所望の体積（例えば、第２量）が収集されると、使用者は、可動部材９５０を解放して、（図示せず）付勢部材がその第１位置に戻るように移動するのを可能にすることができる。可動部材９５０がその第１位置に戻ると、穿孔部材９５５は、第１サンプルリザーバ９８０から取り除かれ、シール（例えば、自己封止膜）が、第１サンプルリザーバ９８０を内部流路９３５から流体的に隔離する。収集デバイス９００を用いて、ダイヤル９４５をその第３位置、第４位置及び第５位置までそれぞれ回転させることにより、第２サンプル体積を第２サンプルリザーバ９８０’に、第３サンプル体積を第３サンプルリザーバ９９０に、第４サンプル体積を第４サンプルリザーバ９９０’に、同様に移送することができる。

【０１２９】

[1182] 場合によっては、体液収集デバイス９００により、臨床医及び／又は瀉血専門医は、体液収集デバイス９００を収容するパッケージを開封し、（分配部材９２９を含む）ハウジング９０１のみを取り出し、ハウジング９０１を患者のベッドわきに持って行くことができる。臨床医及び／又は瀉血専門医は、あらゆる標準化技法を用いて患者の身体の一部（例えば、静脈）に対して静脈穿刺を行う（又は、患者の体液にアクセスする他のあらゆる方法を採用する）ことができる。静脈穿刺に続き、臨床医及び／又は瀉血専門医は、すべてのサンプルに対して必要な総血液体積を収集することができる。例えば、臨床医及び／又は瀉血専門医は、２．５ｍＬプリサンプル分流体積及び４つのサンプルリザーバの各々に対して１０ｍＬサンプル体積を収集することができ、それにより、収集された体液（例えば、血液）は合計４２．５ｍＬになる。体液の所望の量の収集に続き、皮下注射針を患者の身体のその部分（例えば、静脈）から取り除くことができ、臨床医及び／又は瀉血専門医は、（体液を収容している）ハウジング９０１を、膜頂部がハウジング９０１の形状に一致するカスタムトレイ内に事前に配置された状態で、４パック（又は２パック）の事前滅菌されたサンプルリザーバの上に配置することができる。サンプルリザーバのこうした事前滅菌されたパックを使用することにより、臨床医は、滅菌剤を用いてサンプルリザーバの頂部を「拭く」プロセスステップを行う必要がなく、それにより、例えば、リザーバ頂部の滅菌が不適切及び／又は不十分である場合に、汚染の可能性が低減する。そして、臨床医及び／又は瀉血専門医は、体液を含むサンプルリザーバの自動接種を正確な体積制御で起動させることができる。いくつかの実施形態では、サンプルリザーバの接種が完了した後、各個々のサンプルリザーバに対して体積情報が表示されているデバイス９００全体を、分析のために研究室に送ることができる。他の実施形態では、サンプルリザーバ９８０及び／又は９９０を個々に取り除き、分析のために研究室に送ることができる。

【０１３０】

[1183] 収集デバイス９００を、図４６～図５３を参照して、収集デバイスの一部を通して移送される体液の体積に関する体積データを提示することができる一組のディスプレイ

９７５及び９７５’を含むものとして示し記載しているが、他の実施形態では、収集デバイスは、あらゆる好適な出力インジケータを有するあらゆる好適な流量計量機構を含むことができる。例えば、図５４及び図５５は、実施形態による分流機構１０２０及び流量コントローラ１０４０を示す。分流機構１０２０及び流量コントローラ１０４０は、分流機構９２０及び流量コントローラ９４０それぞれと形態及び機能が実質的に同様であり得る。従って、同様の部分については本明細書ではそれ以上記載しない。しかしながら、分流機構１０２０及び流量コントローラ１０４０は、一組のディスプレイ１０７５の配置が異なる可能性がある。例えば、分流機構１０２０は、可動部材９５０に関して上述したよう、各々が流量計量機構を含むことができる一組の可動部材１０５０ａ、１０５０ｂ、１０５０ｃ及び１０５０ｄを移動可能に受け入れるように構成されるハウジング１００１を含む。従って、可動部材１０５０ａ、１０５０ｂ、１０５０ｃ及び１０５０ｄを用いて、それらを通して移送される体液の正確な体積を求めることができる。図５５に示すように、ハウジング１００１のディスプレイ１０７５は、小さい体積（例えば、５ｍＬ）の第１照明、中間の体積（例えば、２０ｍＬ）に関連する第２照明、及び許容可能な及び／又は大きい体積（例えば、４０ｍＬ）に関連する第３照明を含む３つの照明の組を含むことができる。このように、体液の流れが流量コントローラ１０４０及び分流機構１０２０を通して、例えば第１可動部材１０５０ａ内に移送される際、その中に含まれる流量計量機構は、信号等をディスプレイに送信することができ、ディスプレイは、可動部材１０５０を通して移送される体液の体積に従って第１照明、第２照明及び／又は第３照明を点灯するように動作可能である。

【０１３１】

[1184] 他の実施形態では、可動部材１０５０ａ、１０５０ｂ、１０５０ｃ及び１０５０ｄを、ハウジング１００１に対して第１位置から第２位置、第３位置又は第４位置に移動させることができる。こうした実施形態では、それらの位置を、例えば、サンプルリザーバに移送される体液の意図された体積に関連付けることができる。例えば、いくつかの実施形態では、使用者は、可動部材１０５０ａをその第１位置からその第２位置に作動させる（例えば、移動させる）ことができる。こうした実施形態では、第２位置を、例えば、サンプルリザーバに移送される体液の小さい体積（例えば、１０ｍＬ）に関連付けることができる。いくつかの実施形態では、ハウジング１００１及び／又は可動部材１０５０ａは、サンプルの低い体積量がサンプルリザーバに移送されるまで、可動部材１０５０ａを第２位置で一時的に保持することができる、戻り止め、ロック、留め具、突起、凹部等を含むことができる。さらに、第２位置に配置されると、ディスプレイ１０７５を、サンプルリザーバに移送される体液の事前設定された体積を使用者に示すように、小さい体積に関連する第１照明を照明するように構成することができる。体液の所望の体積がサンプルリザーバに移送されかつその中で流体的に隔離されると、分流機構１０２０を、可動部材１０５０ａをその第１位置に自動的に戻すように構成することができる。このように、分流機構１０２０及び流量コントローラ１０４０を、あらゆる数のサンプルリザーバに物理的にかつ流体的に結合し、各サンプルリザーバに体液の正確な体積を移送するように使用することができる。

【０１３２】

[1185] 図５６は、流量計量移送デバイスを用いて患者から体液の所定サンプル体積を取得する方法１１９０を示すフローチャートである。流量計量移送デバイスは、（本明細書において「収集デバイス」とも呼ぶ）本明細書に記載する移送デバイスのいずれでもあり得る。例として、いくつかの実施形態では、移送デバイスは、図４６～図５３を参照して上述した収集デバイス９００であり得る。従って、移送デバイスは、患者に流体連通するように選択的に配置されるように構成された入口ポートと、プリサンプルリザーバ及びサンプルリザーバと、患者からプリサンプルリザーバへの体液の流れ及びサンプルリザーバへの体液の流れを計量するように構成された流量計量機構とを含むことができる。方法１１９０は、１１９１において、患者と流量計量移送デバイスのポートとの間に流体連通を確立することを含む。例えば、ポートを針又は他の内腔規定デバイス（例えば、可撓性滅

菌管）に流体的に結合することができ、針又は他の内腔規定デバイスを、患者の体内に挿入することができる（例えば、静脈穿刺事象又は体液にアクセスする他の方法）。

【０１３３】

[1186] ポートが患者に流体連通している状態で、１１９２において、ポートとプリサンプルリザーバとの間の流体連通を確立する。いくつかの実施形態では、流量計量移送デバイスは流量コントローラ等（例えば、収集デバイス９００に含まれる流量コントローラ９４０等）を含むことができ、それを、ポートとプリサンプルリザーバとの間に流体連通を確立する位置（例えば、第１位置）まで作動させ及び／又は操作する（例えば、回転させる）ことができる。いくつかの実施形態では、流量コントローラの作動により、流量コントローラ及び分流機構は、ポートとプリサンプルリザーバとの間の流体流路の少なくとも一部をまとめて規定するようにすることができる。いくつかの実施形態では、プリサンプルリザーバは、患者からプリサンプルリザーバへの体液の流れを開始することができる負圧等を含むことができる。他の実施形態では、体液の流れを、他のあらゆる好適な方法（例えば、重力等）で開始することができる。

【０１３４】

[1187] １１９３において、患者からプリサンプルリザーバに移送された体液の流れを計量する。例えば、いくつかの実施形態では、ポートは、（例えば、収集デバイス９００の流量制御機構９６７に関して上述したものと同様の方法で）ポートを通過する体液の流れを計量することができる流量制御機構を含むことができる。従って、体液のプリサンプル体積がプリサンプルリザーバに移送される。方法１１９０は、１１９４において、流量計量移送デバイスの流量計量機構を介して、プリサンプルリザーバ内に配置された体液のプリサンプル体積が体液の所定プリサンプル体積であることを検証することを含む。例えば、流量計量機構は、ディスプレイ等（例えば、収集デバイス９００のディスプレイ９７５及び／又は９７５’）を含むことができ、及び／又はディスプレイ等に動作可能に結合され得る。流量計量機構を、上述したように、ディスプレイに体積情報を提示するように構成することができる。

【０１３５】

[1188] プリサンプルリザーバ内に体液のプリサンプル体積が配置されると、１１９５において、プリサンプルリザーバをポートから流体的に隔離して、プリサンプルリザーバ内で体液のプリサンプル体積を封鎖する。例えば、場合によっては、流量コントローラ及び／又は分流機構を、第１位置及び／又は第１形態から第２位置及び／又は第２形態に作動させる（又は回転させる）ことができる。流量コントローラ及び／又は分流機構が第２形態にある場合、プリサンプルリザーバは、プリサンプルリザーバの外部の空間から流体的に隔離される。いくつかの実施形態では、流量コントローラ及び／又は分流機構がその第２位置及び／又は第２形態に駆動されると、１１９６において、ポートとサンプルリザーバとの間に流体連通を確立する。例えば、いくつかの実施形態では、流量計量移送デバイスは、サンプルリザーバの一部（例えば、膜等）を穿孔するように構成された穿孔部材を含むことができる、可動部材（例えば可動部材９５０）等を含むことができる。従って、流量コントローラ及び／又は分流機構がその第２位置及び／又は第２形態にある時、サンプルリザーバのその部分の穿孔により、サンプルリザーバがポートに流体連通するように配置される。上述したように、サンプルリザーバは、例えば、患者からサンプルリザーバへの体液の流れを開始することができる負圧等を含むことができる。

【０１３６】

[1189] １１９７において、患者からプリサンプルリザーバに移送された体液の流れを計量する。例えば、上述したように、ポートは、（例えば、収集デバイス９００の流量制御機構９６７に関して上述したものと同様の方法で）ポートを通過する体液の流れを計量することができる流量制御機構を含むことができる。いくつかの実施形態では、流量制御機構を、例えば、図４９の可動部材９５０等の可動部材等に含めることができる。従って、体液のサンプル体積がサンプルリザーバに移送される。方法１１９０は、１１９８において、流量計量移送デバイスの流量計量機構を介して、サンプルリザーバ内に配置された体

液のサンプル体積が体積の所定サンプル体積であることを検証することを含む。例えば、上述したように、ディスプレイ等を、体積情報を提示するように構成することができる。

【０１３７】

[1190] このように、例えば外部に存在する微生物を含む可能性がある、体液の所定プリサンプル体積が収集される。例えば、いくつかの実施形態では、所定プリサンプル体積は、約０．１ｍＬ、約０．３ｍＬ、約０．５ｍＬ、約１．０ｍＬ、約２．０ｍＬ、約３．０ｍＬ、約４．０ｍＬ、約５．０ｍＬ、約１０ｍＬ、約２０ｍＬ、約５０ｍＬ及び／又はそれらの間のあらゆる体積あるいは体積の分数値であり得る。他の実施形態では、プリサンプル体積は、５０ｍＬを超えるか又は０．１ｍＬであり得る。他の実施形態では、所定プリサンプル体積は、約２ｍＬと約５ｍＬとの間であり得る。一実施形態では、所定プリサンプル体積は約３ｍＬであり得る。さらに、所定プリサンプル体積を収集することにより、１つ又は複数のサンプルリザーバ内に配置された所定サンプル体積に、外部に存在する微生物が実質的にないようにすることができる。いくつかの実施形態では、所定サンプル体積は、１０ｍＬと６０ｍＬとの間であり得る。他の実施形態では、所定サンプル体積は、３０ｍＬと６０ｍＬとの間であり得る。さらに他の実施形態では、所定サンプル体積は６０ｍＬであり得る。体液のサンプル体積を単一のサンプルリザーバに移送するものとして上述したが、他の実施形態では、流量計量移送デバイスを用いて、所定サンプル体積を２つ以上のサンプルリザーバに移送することができる。例えば、いくつかの実施形態では、上述したように、体液の所定プリサンプル体積を、プリサンプルリザーバに収集しかつその中で流体的に隔離することができる。プリサンプル体積が流体的に隔離されている状態で、流量計量移送デバイスを用いて、所定サンプル体積を第１サンプルリザーバに、所定サンプル体積を第２サンプルリザーバに、所定サンプル体積を第３サンプルリザーバに移送することができる。こうした場合、所定サンプル体積を例えば２０ｍＬにすることができ、それにより、第１リザーバ、第２リザーバ及び第３リザーバ内に配置される総サンプル体積は６０ｍＬとなる。

【０１３８】

[1191] 本明細書に記載した体液収集デバイスのさまざまな実施形態により、１回の静脈穿刺から２つ（又はそれより多く）の組の体液（例えば、血液）サンプルを収集するのを可能にすることができる。現標準治療では、いくつかの検査（例えば、血液培養）を、（例えば、２回の別個の静脈穿刺を介して、カテーテル＋静脈穿刺及び／又はそれらの組合せを介して）サンプルを別個の独立した体液アクセス点から獲得して行うように求められている。本明細書に記載する実施形態により、単一の体液アクセス点（例えば、静脈穿刺）から所定の診断検査（例えば、血液培養検査）のための複数のサンプルの獲得を容易にすることができ、それにより、これらのサンプルの獲得に必要な静脈穿刺の年間の数を１／２低減させることができる。これは、患者及び医療従事者両方に同様に有利である。静脈穿刺（及び／又は他の血液アクセス処置）の数が低減することにより、大幅に、医療従事者に対する針刺し損傷のリスクを低減させ、これらの処置からもたらされる患者に関連する合併症（例えば、血腫、血栓症、静脈炎、感染症等）を低減させることができる。さらに、体液アクセス処置（例えば、静脈穿刺）の数を低減させることにより、これらの処置に関連する供給品の利用、労力及び廃棄物が低減する。医療制度によって実現されるコストの削減は、重要であり、より効率的な資源の消費とともに、治療計画の展開及び実施を通知するより正確な患者診断をもたらすサンプルの完全性の改善のために患者の転帰の改善を促進する機会を示す。体液収集デバイスはまた、収集後分析からの偽陽性の発生も大幅に低減させる。本明細書に記載する体液収集デバイスはまた、体液収集プロセスを効率化し、手作業によるステップ及び「接触点」の数を低減させ、それにより外部汚染の機会を低減させることも可能である。本明細書に記載するデバイスはまた、検査技師及び／又は瀉血専門医に対する針刺し損傷及び感染のリスクを最小限にすることができる。

【０１３９】

[1192] いくつかの実施形態では、本明細書に記載した体液収集デバイス（例えば、１００、２００、３００、４００、５００、６００、７００、８００及び９００）は、消毒飽

和材料（例えば、ハウジング４０１）を含み及び／又はそれから部分的に形成され得る。現標準は、医療従事者が個々の消毒材料（例えば、イソプロピルアルコール綿棒）を個々のサンプルリザーバ（例えば、４８０、４８０’、４９０及び４９０’）の頂部に配置することに依存する。このプロトコルとのコンプライアンスを確保するために、（例えば）デバイス４００は、デバイス４００内に配置された消毒材料を含むことができ、それにより、図１６に示すように、ハウジング４０１が４パック（又は２パック）のボトルの頂部に配置された時、ハウジング４０１及びサンプルリザーバ４８０、４８０’、４９０、４９０’の頂部からの最初の接触点は、消毒材料である。このように、サンプルリザーバ４８０、４８０’、４９０、４９０’の頂部は、体液がサンプルリザーバ内に接種される前に適切な消毒が適用されることが保証される。

【０１４０】

[1193] さまざまな実施形態について特に示し記載したが、形態及び詳細のさまざまな変更を行うことができる。例えば、ダイヤル４４５（アクチュエータ）を、図１９～図２２を参照して、単一方向に回転するものとして示し記載しているが、他の実施形態では、ダイヤル４４５（アクチュエータ）を、第１方向と第１方向とは反対の第２方向とに回転させることができる。こうした実施形態では、第２方向における回転を、収集デバイスを、あらゆる数の形態を通して移動させるように構成することができる。他の実施形態では、アクチュエータの第２方向における回転を制限することができる。いくつかの実施形態では、ダイヤルは、患者から受け取られる体液の第１体積（すなわち、汚染されたサンプル）を流体的に隔離するように機械的止め具又はロックを含むことができる。言い換えれば、第１リザーバ（プリサンプルリザーバ）に体液の所定体積が充填され、使用者が、追加のサンプルの引込みを開始するようにダイヤル（アクチュエータ）を回転させると、ダイヤル（アクチュエータ）を、（プリサンプルリザーバ内に収容された）第１サンプル体積との流体連通を確立するように戻るように移動させることはできない。

【０１４１】

[1194] いくつかの実施形態について上述したが、それらは、限定としてではなく単に例として提示されていることが理解されるべきである。さまざまな実施形態を、特定の特徴及び／又は構成要素の組合せを含むものとして記載したが、本明細書に記載した実施形態のいずれかからのいずれの特徴及び／又は構成要素のいかなるコンビネーション又はサブコンビネーションを有する他の実施形態が可能である。例えば、図３４～図４０を参照して、収集デバイス７００を、第１形態、第２形態、第３形態、第４形態又は第５形態を有するものとして示し記載しているが、他の実施形態では、本明細書に記載した収集デバイスは、それより多いか又は少ない形態を有することができる。さらに、収集デバイス２００を、図２～図１３を参照して、プリサンプルリザーバ２７０として真空による収集チューブを有するものとして示し記載しているが、他の実施形態では、収集デバイス２００は、分配部材４２９内に収容されたチャンバであるプリサンプルリザーバ４７０を含む、図１６～図２２に提示した実施形態の収集デバイス４００に類似するハウジング２０１内に収容されたチャンバを有することができ、その逆も可能である。

【０１４２】

[1195] さまざまな構成要素の具体的な構成を変更することも可能である。例えば、さまざまな構成要素のサイズ及び具体的な形状は、依然として本明細書に記載するような機能を提供しながら、図示する実施形態とは異なり得る。より具体的には、さまざまな構成要素のサイズ及び形状を、体液流の流体リザーバ内への所望の流量に対して具体的に選択することができる。例えば、図４９において流量計量機構９６７を特に示すが、本明細書に記載した収集デバイスのいずれも、あらゆる好適な流量計量機構とともに使用することができる。例えば、いくつかの実施形態では、収集デバイスは、流量計量機構、及び／又は、例えば、圧力センサ、電圧センサ、光センサ、速度センサ、流量計、歪みゲージ、弁、タービン、浮き、変位分析、密度分析、重量分析、光学分析、超音波分析、熱分析、ドップラ分析、電磁場（ｅｍｆ）分析、反射分析、障害物分析、面積分析、ベンチュリ分析、コリオリ分析、視覚分析並びに／又は他のあらゆる好適なセンサ、分析及び／あるいは計

算（例えば、一例としてボイルの法則、理想気体法則、力計算（力＝質量×加速度）等を適用し及び／又は使用する）等、体液の体積特徴を測定するように構成された、他のあらゆる機構、デバイス又は方法を含むことができる。

【図１】

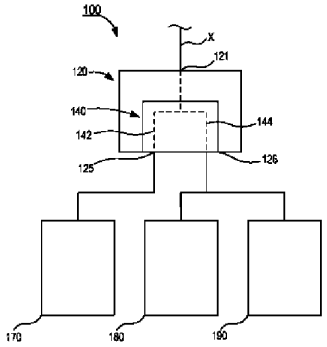


FIG. 1

【図２】

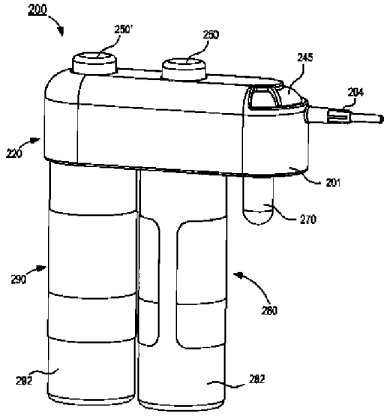


FIG. 2

【図３】

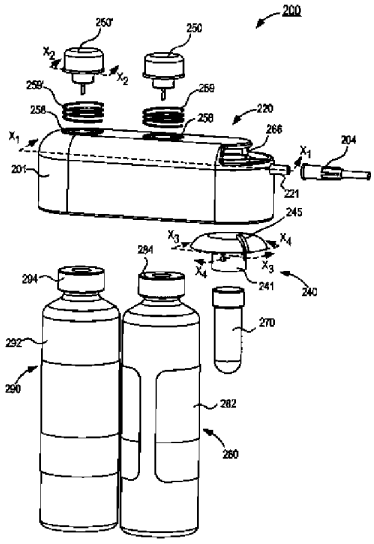


FIG. 3

【図４】

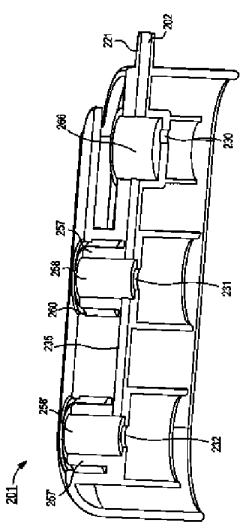


FIG. 4

【図５】

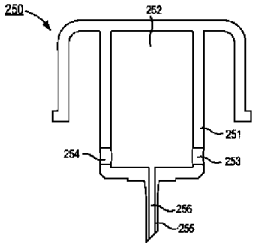


FIG. 5

【図６】

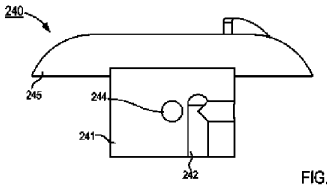


FIG. 6

【図７】

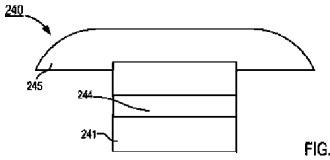


FIG. 7

【図８】

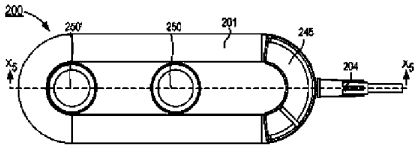


FIG. 8

【図９】

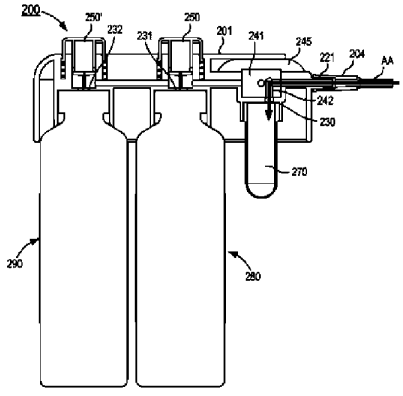


FIG. 9

【図１０】

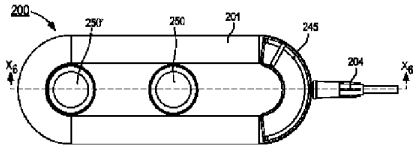


FIG. 10

【図１１】

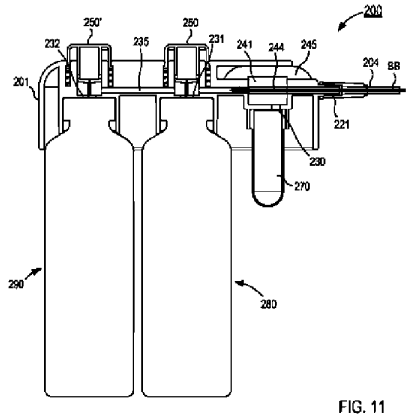


FIG. 11

【図１２】

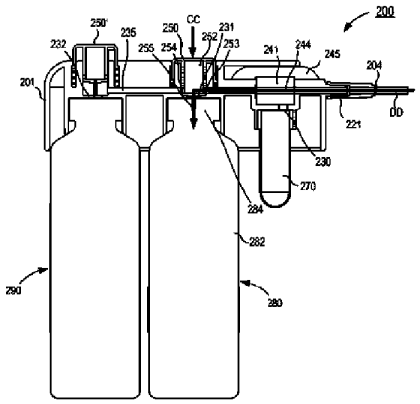


FIG. 12

【図１３】

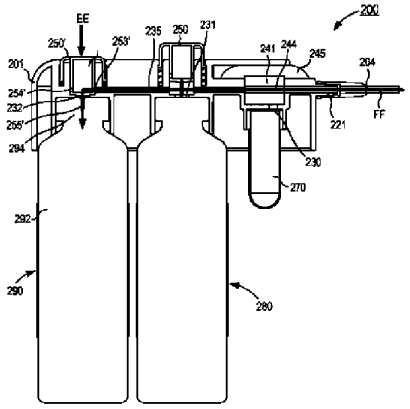


FIG. 13

【図１４】

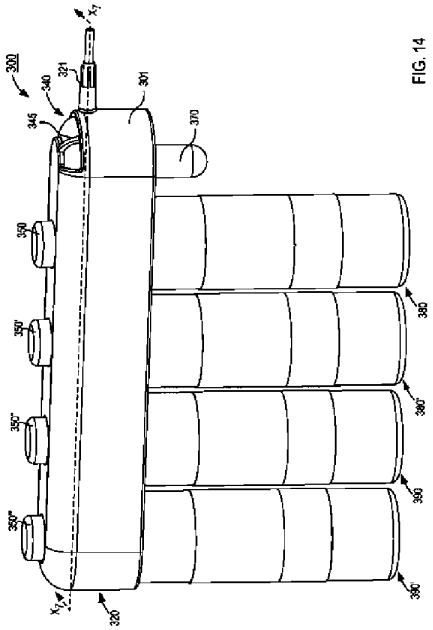


FIG. 14

【図１５】

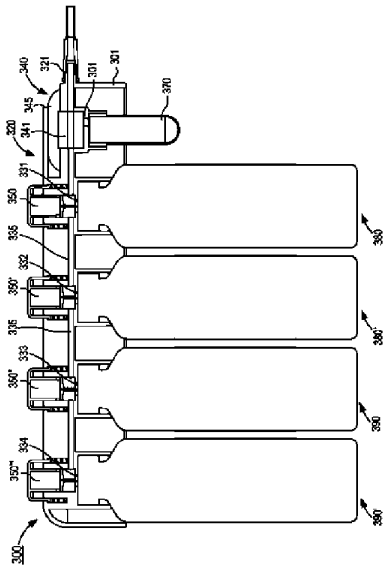


FIG. 15

【図１６】

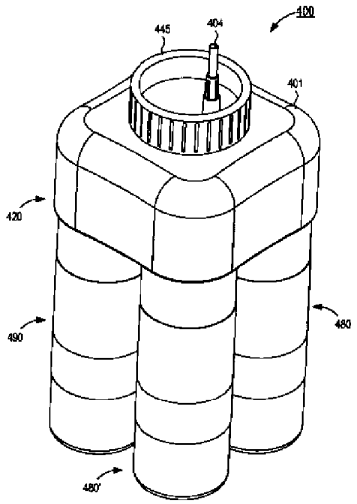


FIG. 16

【図１７】

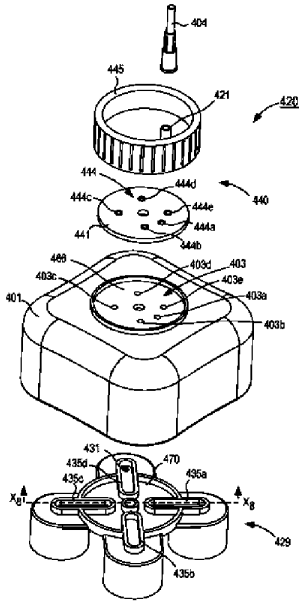


FIG. 17

【図１８】

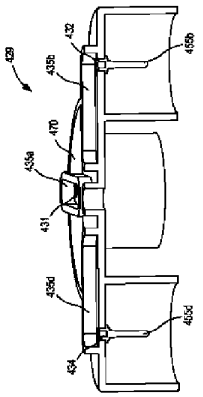


FIG. 18

【図１９】

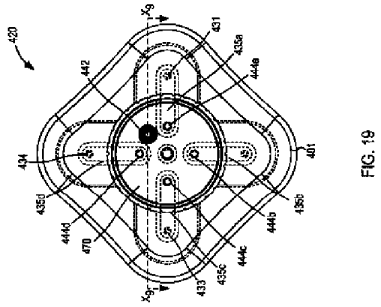


FIG. 19

【図２０】

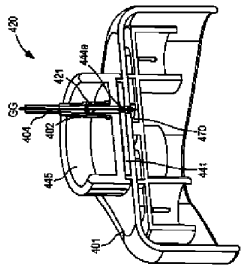


FIG. 20

【図２１】

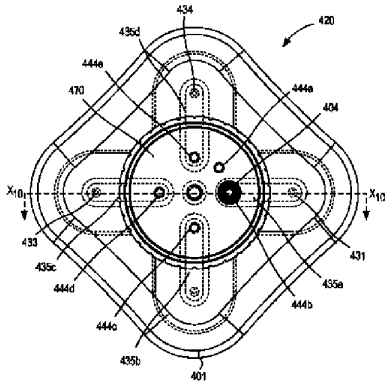


FIG. 21

【図２２】

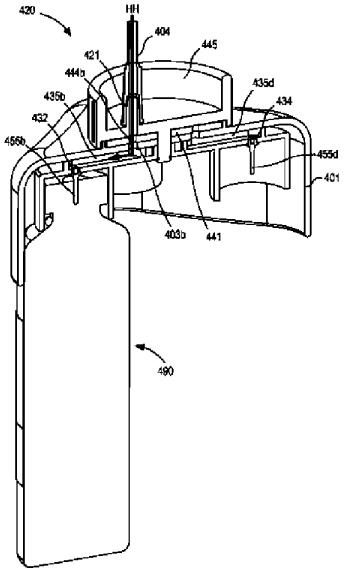


FIG. 22

【図２３】

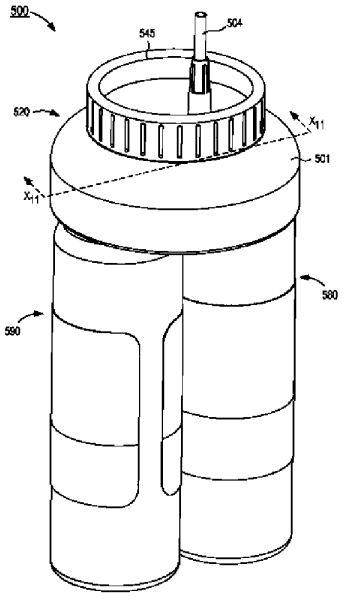


FIG. 23

【図２４】

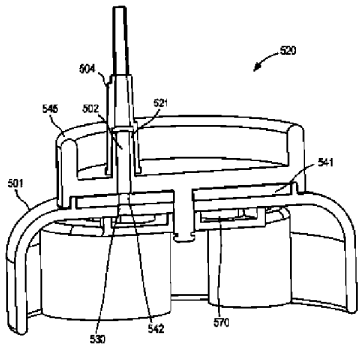


FIG. 24

【図２５】

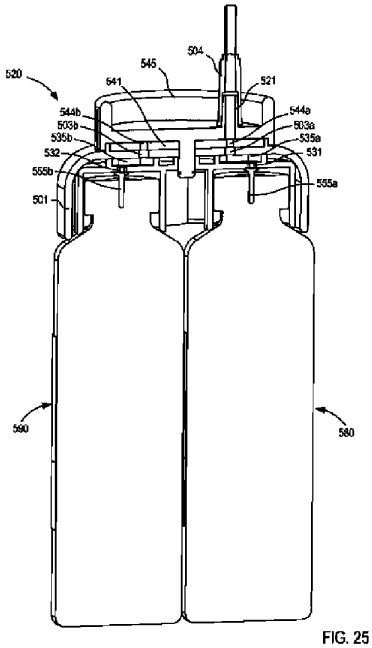


FIG. 25

【図２６】

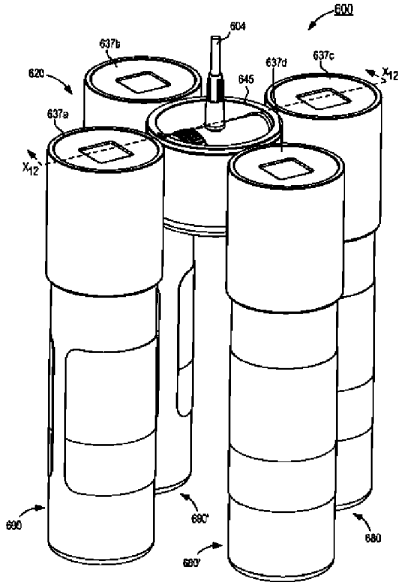


FIG. 26

【図２７】

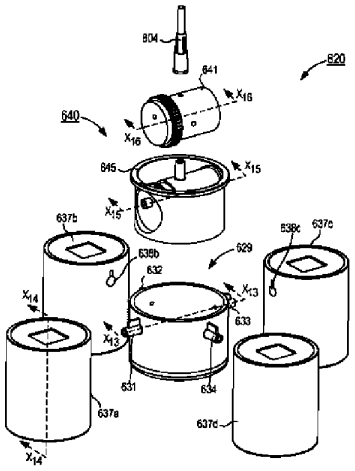


FIG. 27

【図２８】

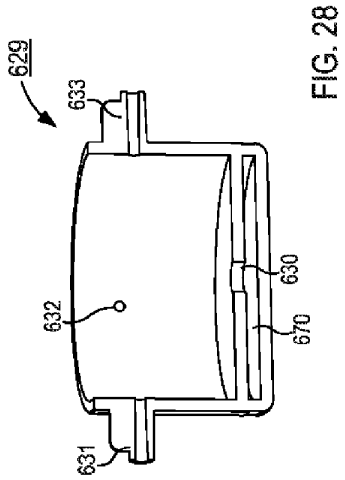


FIG. 28

【図２９】

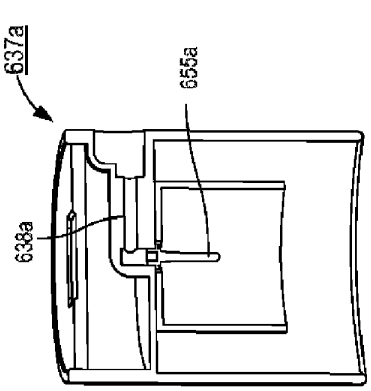


FIG. 29

【図３０】

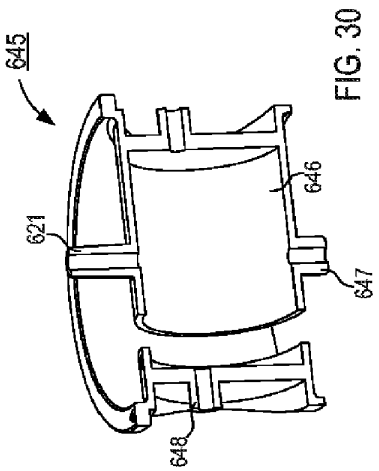


FIG. 30

【図３１】

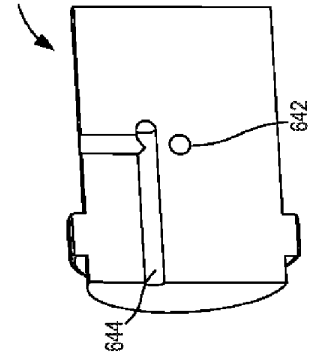


FIG. 31

【図３２】

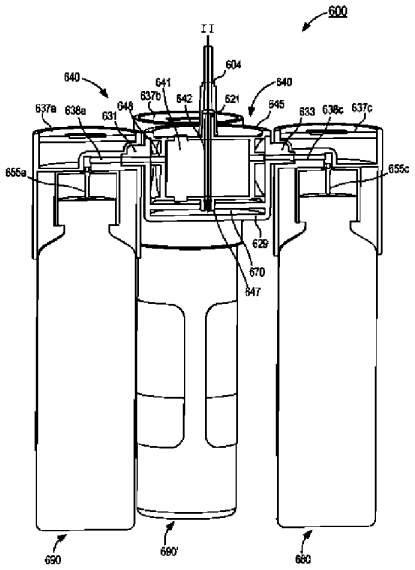


FIG. 32

【図３３】

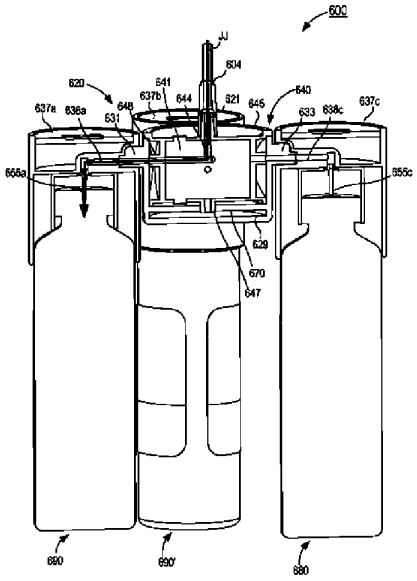


FIG. 33

【図３４】

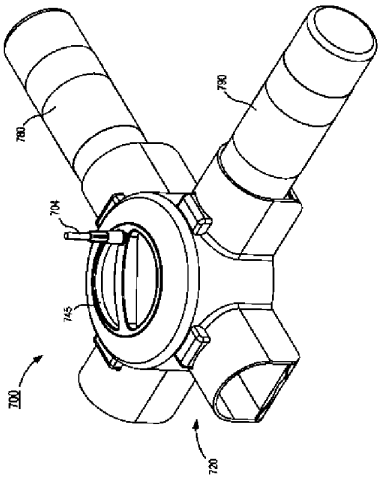


FIG. 34

【図３５】

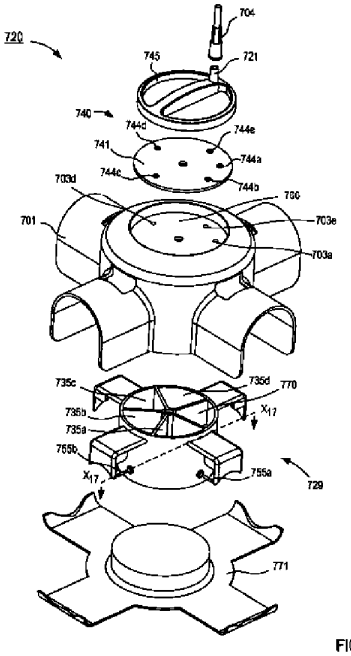


FIG. 35

【図３６】

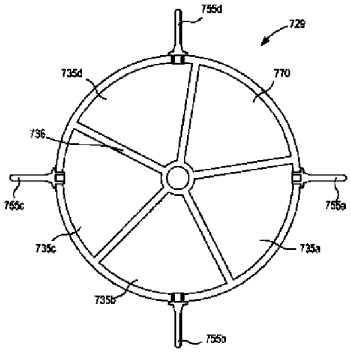


FIG. 36

【図３７】

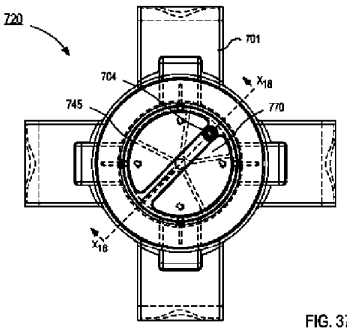


FIG. 37

【図３８】

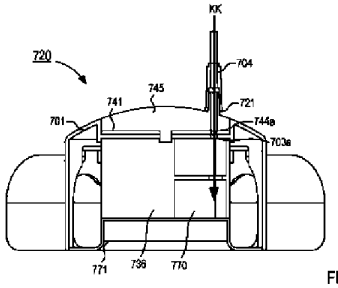


FIG. 38

【図３９】

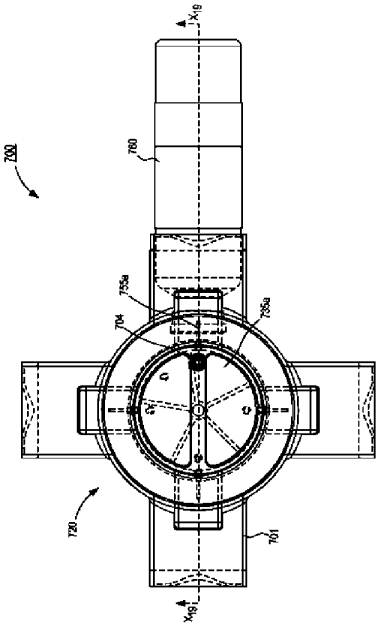


FIG. 39

【図４０】

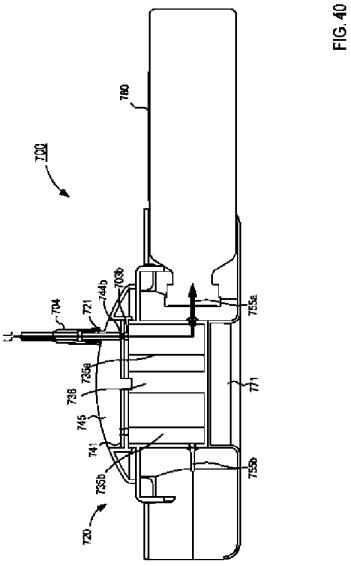


FIG. 40

【図４１】

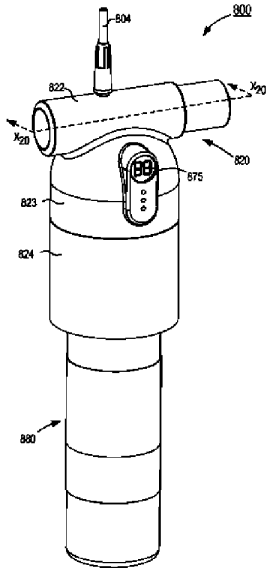


FIG. 41

【図４２】

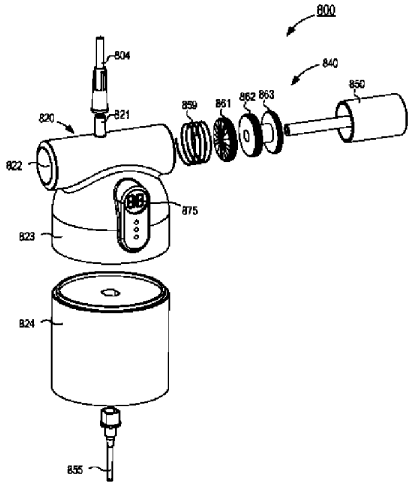


FIG. 42

【図４３】

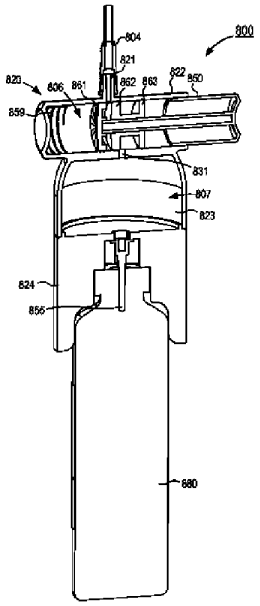


FIG. 43

【図４４】

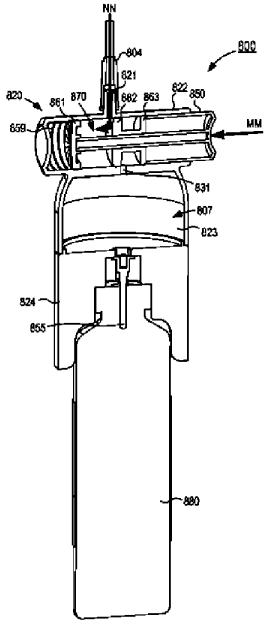


FIG. 44

【図４５】

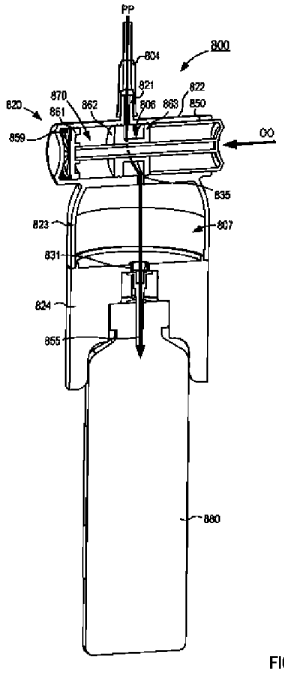


FIG. 45

【図４６】

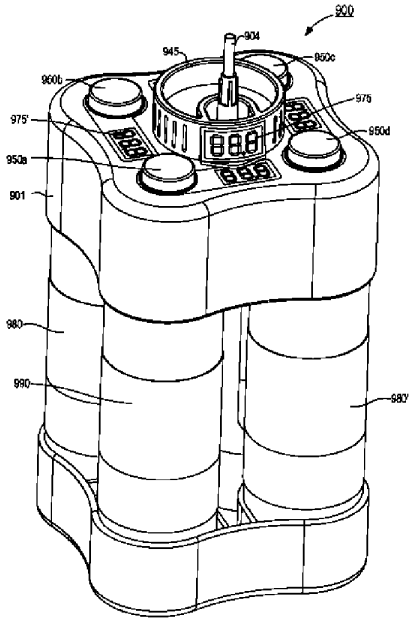


FIG. 46

【図４７】

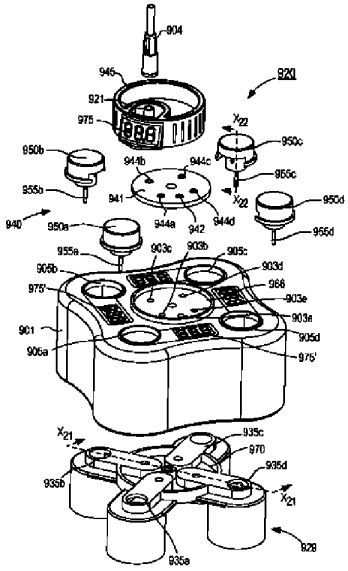


FIG. 47

【図４８】

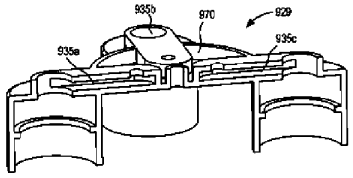


FIG. 48

【図４９】

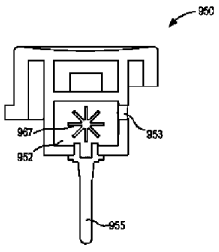


FIG. 49

【図５０】

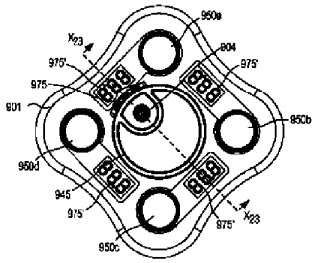


FIG. 50

【図５１】

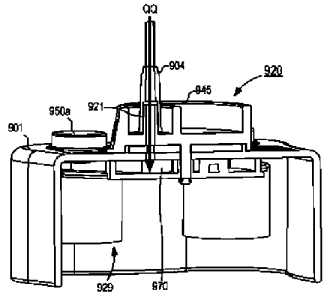


FIG. 51

【図５２】

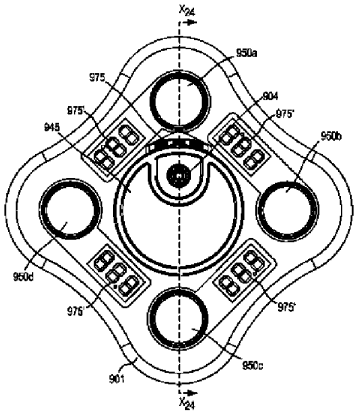


FIG. 52

【図５３】

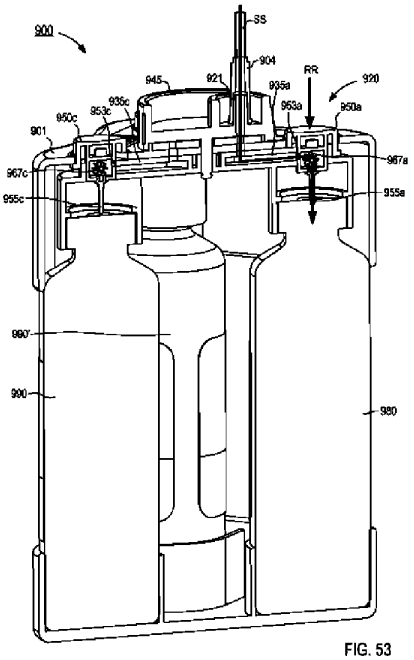
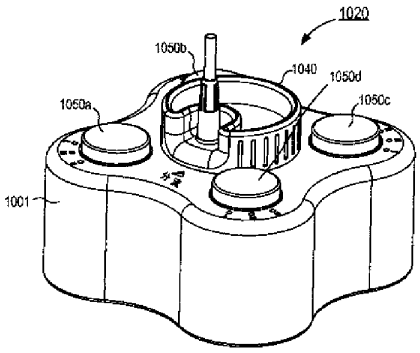
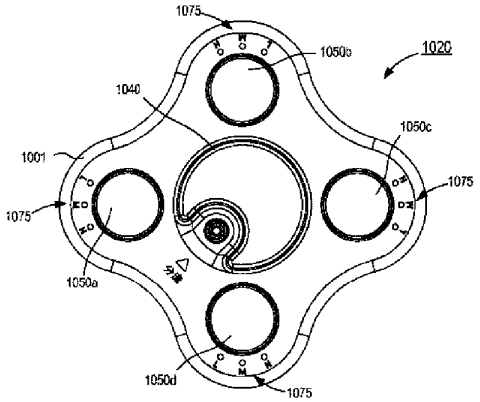


FIG. 53

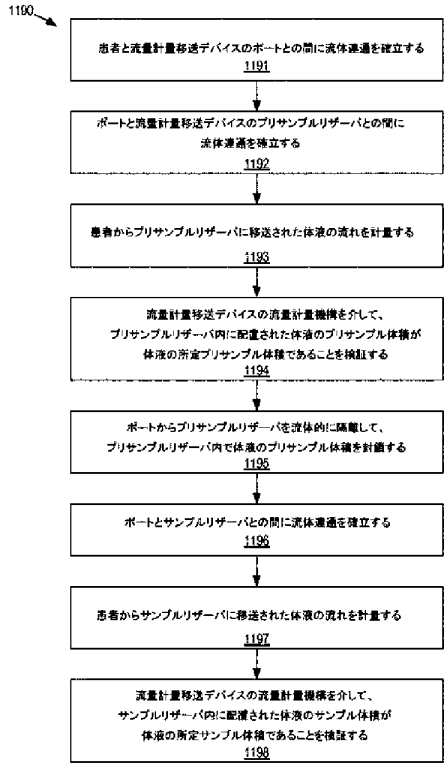
【図５４】



【図５５】



【図５６】


1190
患者と流量計量移送デバイスのポートとの間に流体連通を確立する
1191
ポートと流量計量移送デバイスのプリサンプルリザーバとの間に
流体連通を確立する
1192
患者からプリサンプルリザーバに移送された体液の流れを計量する
1193
流量計量移送デバイスの流量計量機構を介して、
プリサンプルリザーバ内に配置された体液のプリサンプル体積が
体液の所定プリサンプル体積であることを検証する
1194
ポートからプリサンプルリザーバを流体的に隔離して、
プリサンプルリザーバ内で体液のプリサンプル体積を封鎖する
1195
ポートとサンプルリザーバとの間に流体連通を確立する
1196
患者からサンプルリザーバに移送された体液の流れを計量する
1197
流量計量移送デバイスの流量計量機構を介して、
サンプルリザーバ内に配置された体液のサンプル体積が
体液の所定サンプル体積であることを検証する
1198

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/073060

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/155 (2014.01)
USPC - 600/575
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61B 5/00, 5/15, 5/153, 5/155; A61M 39/22; A61J 1/05; G01N 1/10, 1/14, 1/18 (2014.01)
USPC - 422/559; 435/294.1; 600/573, 575, 576, 577, 578; 604/248, 409

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61B 5/1405, 5/1427, 5/1438, 5/150251; A61M 39/223 (2013.01)

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X – Y	US 5,097,842 A (BONN) 24 March 1992 (24.03.1992) entire document	12, 15, 16, 18 – 1-11, 13, 14, 17, 19-29
X – Y	US 2008/0145933 A1 (PATTON) 19 June 2008 (19.06.2008) entire document	30-41 – 3, 13, 17, 22, 24, 25,
Y	US 2005/0148893 A1 (MATHIAS et al) 07 July 2005 (07.07.2005) entire document	1-11
Y	WO 2005/068011 A1 (MEHLHORN) 28 July 2005 (28.06.2005) entire document	14, 21-29
Y	US 3,848,581 A (CINQUALBRE et al) 19 November 1974 (19.11.1974) entire document	9, 19, 20

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

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

Date of the actual completion of the international search	Date of mailing of the international search report
06 February 2014	18 FEB 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

フロントページの続き

(81)指定国 AP(BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), EA(AM, AZ, BY, KG, KZ, RU, TJ, TM), EP(AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OA(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG), AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US

(72)発明者 バリントン，グレゴリー，ジェイ.
アメリカ合衆国，ワシントン州 ９８１０４，ベルビュー，１３４番 プレイス サウスイースト ５８２５
(72)発明者 パットン，リチャード ジー.，エム.，ディー.
アメリカ合衆国，ワシントン州 ９８１９９，シアトル，マグノリア ブールバード ウェスト ２５６１
(72)発明者 ガウ，シャン，イー.
アメリカ合衆国，ワシントン州 ９８１０３，シアトル，サニーサイド アベニュー ノース ４０２７

Ｆターム(参考) 4C038 TA01 UA10 UB07

Received 6.24.05 | Revisions Received 7.26.05 | Accepted 7.27.05

Bacterial Contamination of Platelets for Transfusion: Recent Advances and Issues

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

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

DOI: 10.1309/167948JY25TMY611

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

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

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

Estimates of Prevalence and Incidence

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

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

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

Sources of Bacterial Contamination

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

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

Downloaded from https://academic.oup.com/labmed/article-abstract/36/12/767/2657241 by guest on 07 April 2019

KUR-MAG-DE005185

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

An Open Letter to the Blood Community and AABB Standard 5.1.5.1

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

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

Clinical Relevance

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

Table 1_Description of Tests Capable of Detecting Bacteria

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

Adapted from Reference 22.

Downloaded from https://academic.oup.com/labmed/article-abstract/36/12/767/2557341 by guest on 07 April 2019

KUR-MAG-DE005186

Strategies for the Mitigation of Contaminated Blood Products

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

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

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

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

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

Residual Risk in "Tested" Components

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

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

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

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

Downloaded from https://academic.oup.com/labmed/article-abstract/36/12/767/2557341 by guest on 07 April 2019

KUR-MAG-DE005187

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.

1. Kuehnert MJ. Transfusion-transmitted bacterial infection in the United States, 1998 through 2000. Transfusion. 2001;41:1493-1499.
2. Halpin TJ, Moore W, Waterman SH, et al. Red Blood Cell Transfusions Contaminated with *Yersinia enterocolitica* — United States, 1991-1996, and Initiation of a National Study to Detect Bacteria-Associated Transfusion Reactions. MMWR. CDC, Editor. 1997.
3. Hillyer CD. Bacterial contamination of blood components: risks, strategies, and regulation: joint ASH and AABB educational session in transfusion medicine. Hematology. 2003:575-589.
4. Jacobs MR, Palavecino E, Yomtovian R. Don't bug me: the problem of bacterial contamination of blood components—challenges and solutions. Transfusion. 2001;41:1331-1334.
5. Goodnough LT, Shander A, Brecher ME. Transfusion medicine: Looking to the future. Lancet. 2003;361:161-169.
6. Association Bulletin #96-6: Bacterial contamination of blood components. 1996, AABB Faxnet, No.94, Bethesda, MD: American Association of Blood Banks.
7. Dykstra A, Jacobs J, Yamtovian R. Prospective microbiologic surveillance (PMS) of random donor platelets (RDP)and single donor apheresis platelets (SDP). Transfusion. 1998;38:104S.
8. Ness P. Single-donor platelets reduce the risk of septic platelet transfusion reactions. Transfusion. 2001;41:857-861.
9. Yomtovian R. A prospective microbiologic surveillance program to detect and prevent the transfusion of bacterially contaminated platelets. *Transfusion*. 1993;33:902-909.
10. Dodd R. Adverse consequence of blood transfusion: quantitative risk estimates, in blood supply: risks, perceptions and prospects for the future, S. Nance, Editor. Bethesda, MD: AABB; 1994:1-24.
11. Blajchman MA. Incidence and significance of the bacterial contamination of blood components. *Develop Biolog*. 2002;108:59-67.
12. Goldman M, Blajchman MA. Blood product-associated bacterial sepsis. *Transfusion Medicine Reviews*. 1991;5:73-83.
13. Roth VR. Evaluation of a reporting system for bacterial contamination of blood components in the United States. *Transfusion*. 2001;41:1486-1492.
14. Williamson LM. Serious hazards of transfusion (SHOT) initiative: analysis of the first two annual reports.[see comment]. *BMJ*. 1999;319:16-19.
15. Perez P. Determinants of transfusion-associated bacterial contamination: results of the French BACTHEM Case-Control Study. *Transfusion*. 2001;41:862-872.
16. Fang CT, Chambers LA, Kennedy JM, et al. Detection of bacterial contamination in apheresis platelet products: American red cross experience, 2004.
17. Burns KHWerch JB. Bacterial contamination of platelet units: a case report and literature survey with review of upcoming american association of blood banks requirements. *Arch Pathol Lab Med*. 2004;128:279-281.
18. Haimowitz MD, Hernandez LA, Herron RM, Jr. A blood donor with bacteraemia. *Lancet*. 2005;365:1596.
19. Jafari M. Salmonella sepsis caused by a platelet transfusion from a donor with a pet snake. *NEJM*. 2002;347:1075-1078.
20. Grossman BJ. Screening blood donors for gastrointestinal illness: a strategy to eliminate carriers of *Yersinia enterocolitica*. *Transfusion*. 1991;31:500-501.
21. Brecher ME, AuBuchon J,Yomtovian R, et al. 2002. (letter).
22. Brecher ME, Hay SN. Bacterial contamination of blood components. *Clin Microbiol Rev*. 2005;18:195-204.
23. Brecher ME. Growth of bacteria in inoculated platelets: Implications for bacteria detection and the extension of platelet storage. Transfusion. 2000;40:1308-1312.
24. te Boekhorst PA. Clinical significance of bacteriologic screening in platelet concentrates. *Transfusion*. 2005;45:514-519.
25. Blajchman MA, Goldman M, Baeza F. Improving the bacteriological safety of platelet transfusions. *Transfusion Medicine Reviews*. 2004;18:11-24.
26. Larsen CP, Ezdigini F, Hermansen NO, et al. Six years' experience of using the BacT/ALERT system to screen all platelet concentrates and additional testing of outdated platelet concentrates to estimate the frequency of false-negative results. *Vox Sanguinis*. 2005;88:93-97.
27. Arendt A, Koch JCE, Rolfs R, et al. Fatal bacterial infections associated with platelet transfusion-United States, 2004 [From the Centers for Disease Control and Prevention: Morbidity and Mortality Weekly Report]. *JAMA*. 2005;293:2586-2591.
28. Allain JP, Bianco C, Blachjman MA, et al. Protecting the blood supply from emerging pathogens: the role of pathogen inactivation. *Transfusion Medicine Reviews*. 2005;19:110-126.
29. Holme S, McAlister MB, Ortolano, GA, et al. Strategies for the mitigation of contaminated blood products. *Transfusion*. 2005;45:984-993.

Downloaded from https://academic.oup.com/labmed/article-abstract/36/12/767/2557344 by guest on 07 April 2019

KUR-MAG-DE005188

J-PlatPat 特許情報プラットフォーム English close

Literature display help

< 1 / 1 display >

Patent 6643474

publication Document unit PDF progress information OPD search key URLs

Display format of the document display screen:

text display PDF display

primary literature

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Patent publication (B2)
(11) [Patent number] Patent No. 6643474 (P6643474)
(24) [Registration date] Reiwa 2 January 8, 2020 (2020.1.8)
(45) [Issue date] February 12, 2020 (2020.2.12)
(54) [Title of the invention] Blood sample optimization system and blood isolation device
(51) [International Patent Classification]
A61B 5/15 (2006.01)
A61B 5/154 (2006.01)
[FI]
A61B 5/15 200
A61B 5/154 200
[Number of Claims] 16
[Total Number of Pages] 39
(21) [Application No.] Patent application 2018-523384 (P2018-523384)
(86) (22) [Application date] July 22, 2016 (2016.7.22)
(65) [Publication number] Special table 2018-525191 (P2018-525191A) (43) [Publication d

e] September 6, 2018 (2018.9.6) (86) [International application number] PCT/US2016/043709 (87) [International publication number] WO2017/019552 (87) [International publication Date] February 2, 2017 (2017.2.2)

[Date of request for examination] May 20, 2019 (2019.5.20)
(31) [Priority claim number] 62/238,636
(32) [Priority date] October 7, 2015 (2015.10.7)
(33) [Country/region or organization claiming priority] United States (US)
(31) [Priority claim number] 62/318,194
(32) [Priority date] April 4, 2016 (2016.4.4)
(33) [Priority claiming country/region or organization] United States (US)
(31) [Priority claim number] 62/196,797
(32) [Priority date] July 24, 2015 (2015.7.24)
(33) [Priority Country/Territory or Organization] United States (US)
(31) [Priority claim number] 15/140,448
(32) [Priority date] April 27, 2016 (2016.4.27)
(33) [Priority claim Country/region or organization] United States (US)
(31) [Priority claim number] 15/140,443
(32) [Priority date] April 27, 2016 (2016.4.27)
(33) [Priority claim country/ Region or institution] United States (US)
[Application subject to accelerated examination]
(73) [Patent holder]
[Identification number] 518026730
[Name] Klin Inc.
(74) [Agent]
[Identification number] 100083806
[Patent attorney]]
[Name] Hidekazu Miyoshi
(74) [Agent]
[Identification number] 100095500
[Patent attorney]
[Name] Masakazu Ito
(74) [Agent]
[Identification number] 100111235 [
Patent attorney]
[Name or name] Yuko Hara

(74) [Agent]
[Identification number] 100195257
[Patent Attorney]
[Name] Kazushi Obuchi
(72) [Inventor]
[Name] Rogers, Bobby
(72) [Inventor]
[Name] Kan, Gino
(72) [Inventor]
[Name] Detrov, John
[Examiner] Hirokatsu Shimizu

(56) [Reference]
[Reference] Japanese Patent Application Laid-Open No. 58-025146 (JP, A) [Reference] Japanese Patent Application Laid-Open No. 58-067238 (JP, A) [Reference] Japanese Patent Application Laid- Open No. 2012-016496 (JP, A) [Reference] JP-A-57-089869 (JP, A) [Reference] National Publication of International Patent Application No. 09-504726 (JP, A) [Reference] JP-A-02-224742 (JP, A) [Reference] United States Patent No. 04207870 (US, A)

(58) [Investigated field] (Int.Cl., DB name)
A61B 5/153-5/154

The scope of the claims open —

(57) [Claims]
[Claim 1]
A blood sample optimization system, a blood
collection system,
a patient configured for venipuncture of a patient to allow withdrawal of a patient blood sample. a needle,
a blood collection path connected to said patient needle and configured to carry said blood sample, and a
sample configured to receive an evacuated blood collection tube for collecting and contain

g a subsequent portion of said blood sample. a blood isolation
device
connected along the blood collection path between the patient needle and the sample needl e, the inlet port
configured to receive the blood sample
; An isolation chamber connected to the inlet port and having a vent including an air perme able blood barrier for receiving said initial volume of blood sample and isolating at least a first portion of said initial volume of blood sample. a configured isolation chamber and a samplin g flow path having a proximal end connected to the inlet port and configured to receive a s ubsequent portion of the blood sample; the passageway and the inlet port are connected to th e blood sample

bypassing the isolation chamber and a first portion of the blood sample isolated in the isolatio n chamber and connecting the subsequent portion of the blood sample to the distal end of the sampling channel. an outlet port configured to direct a subsequent portion of the blood sampl e into the evacuated blood collection tube, the inlet port, the outlet port, the isolation chambe r and
the
blood sample optimization system, further comprising a housing containing and defining a sa mpling flow path; and a blood isolation device .
2.
The isolation chamber of the blood isolation device is at ambient air pressure, and wherein t he isolation chamber receives a first portion of the blood sample by patient blood pressure ov ercoming the ambient air pressure within the isolation chamber. 2. The blood sample optimiza tion system of claim 1. 3. The blood of claim 2, wherein said sample needle includes a seal p ierced by said evacuated blood collection tube to open access to said patient needle via said bl ood collection path and said sampling flow path
.
Sample optimization system.
4. The
blood isolation device of claim 3, wherein said sampling channel of said blood isolation devic e permits a subsequent portion of said blood sample to enter said inlet port under vacuum pre ssure by said evacuated blood collection tube opening said sample needle. blood sample opti mization system.
5.
The blood sample optimization system of claim 1, wherein said air permeable blood barrier o f said blood isolation device comprises an air permeable material that seals upon contact wit

blood.

[Claim 6]

3. The blood sample optimization system of Claim 1, wherein the blood collection path of the blood collection system comprises a tube.

7. A

patient needle configured to enable removal of a blood sample from a patient and a sealed s ample needle, wherein the sample needle is unsealed and the blood sample adapted to be re moved from the patient. a blood isolation device connected to a blood collection system comp rising a sample needle adapted to receive an evacuated blood collection tube

for receiving a blood sample from a patient connected to said patient needle; an isolation ch amber having a configured inlet port,

an outlet port connected to the inlet port, and

a vent connected to the inlet port and including an air permeable blood barrier, wherein the sample needle is connected to the vacuum an isolation chamber configured to receive and isol ate a first portion of the blood sample before it is opened by a blood vessel; and a proximal e nd connected to the inlet port for receiving subsequent portions of the blood sample

. a sampling channel configured to receive said isolation chamber

,

said sampling channel and said inlet port are adapted to receive said blood sample with subs equent portions of said blood sample isolated within said isolation chamber and said isolation chamber. and to direct subsequent portions of the blood sample to the outlet port connected t o the distal end of the sampling channel, said inlet port, said outlet

port , a blood isolation device, further comprising a housing containing and defining said isol ation chamber and said sampling channel.

[Claim 8]

8. The blood isolation device of claim 7, wherein the isolation chamber is at ambient air pres sure and the isolation chamber receives an initial portion of the blood sample by patient blood pressure overcoming the ambient air pressure within the isolation chamber.

[Claim 9]

8. The blood isolation device of Claim 7, wherein the air permeable blood barrier comprises a n air permeable material that seals upon contact with blood.

10.

The blood isolation device of claim 7, wherein said isolation chamber includes an isolation ch annel defined within said housing.

11.

A blood sample optimization system, a blood

collection system, comprising:

a patient needle configured for venipuncture of a patient to enable withdrawal of a patient blood sample; and a patient

needle connected to the patient needle. a blood collection system comprising: a blood colle ction path configured to carry said blood sample; and a sample needle

configured to receive an evacuated blood collection tube for withdrawing and containing a s ubsequent portion of said blood sample; A blood isolation device connected along the blood co llection path between a patient needle and the sample needle, the inlet port configured to rec eive the blood sample, and a sample needle of the inlet port and the blood collection syste m . and an isolation chamber having a vent connected to the inlet port and including an air permeable blood barrier for receiving the initial volume of the blood sample and for removi ng the initial volume of the blood sample. an isolation chamber configured to isolate at least a first portion ;

a sampling channel having a proximal end connected to said inlet port and configured to re ceive a subsequent portion of said blood sample, said isolation chamber, said sampling channe l and said inlet port being connected to said blood
sample

; allowing a subsequent portion of the blood sample to bypass the isolation chamber and a first portion of the blood sample isolated within the isolation chamber and directing the subse quent portion of the blood sample to a distal end of the sampling channel; and a blood isolatio n device configured to direct the outlet port connected to a

blood vessel and further comprising a housing containing and defining the inlet port, the ou tlet port, the isolation chamber and the sampling flow path.
Sample optimization system.
12.
The isolation chamber of the blood isolation device is at ambient air pressure, and wherein t he isolation chamber receives a first portion of the blood sample by patient blood pressure ov ercoming the ambient air pressure within the isolation chamber. 12. The blood sample optimiz ation system according to 11.
13.
The blood sample optimization system of claim 11, wherein said sample needle includes a se al pierced by said evacuated blood collection tube to open access to said patient needle via sai d blood collection pathway.
14.
The blood sample optimization system of claim 11, wherein said air permeable blood barrier of said blood isolation device comprises an air permeable material that seals upon contact wit h blood.

15.

The blood sample optimization system of claim 11, wherein said isolation chamber includes a n isolation flow path defined within said housing.

[Claim 16]

12. The blood sample optimization system of Claim 11, wherein the blood collection path of t he blood collection system includes a tube.

detailed description open —

[Detailed description of the invention]

[Background art]

CROSS

-REFERENCE TO RELATED APPLICATIONS

This application is based on US Nonprovisional Application Serial No. 15/140,443, entitled "B lood Sample Optimization System and Blood Contaminant Isolation Apparatus and Method," fil ed April 27, 2016. and U.S. nonprovisional application Ser. and both of these U.S. nonprovisio nal applications are U.S. Provisional Patent Application Serial No. 62/196,797, entitled "Blood Culture Improvement Systems and Methods," filed on Jul. 24, 2015, dated Oct. 7, 2015; U.S. Provisional Application No. 62/238,636, entitled "Blood Isolation System for Clean Blood Colle ction," filed on April 4, 2016, and "Blood Sample Optimization System and Blood Contaminant Isolation Device and No. 62/318,194 entitled "Methods", the disclosure of which is hereby inc orporated by reference in its entirety.

Bacteremia

is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteremia wit h clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bactere mia and sepsis are associated with high mortality, hospitalization incidence and length of stay and associated costs. Many bacteremia, sepsis, fungemia, and other pathogens do occur withi n hospitals or other medical facilities, and catheters and venipunctures are sources of contami nation as potential carriers of these pathogens.

[0003]

Blood cultures are the standard test used to detect microbial pathogens associated with bact eremia and sepsis in the blood of patients. The term blood culture refers to a single venipunct ure from a peripheral site or central or arterial line in which blood is inoculated into one or mo re blood culture bottles or vessels. One bottle is considered one blood culture and two or mor e are considered a set. Multiple sets are obtained from multiple venipunctures and are associa ted with different sites in the patient.

[0004]

Although these methods enable microbial identification and susceptibility testing, which are important factors in the management of sepsis, their lack of rapid results and low sensitivity to nasty pathogens pose challenges for improvement. This has led to the development of refined systems and adjunctive molecular or proteomics tests.

[0005]

The collection of blood samples for blood culture is an important component of modern patient care, both positively impacting patient outcome by providing an accurate diagnosis and eliminating unnecessary antimicrobial therapy. It can also adversely affect outcomes by prolonging morbidity, lengthening hospital stays, and increasing costs.

One

consequence of blood culture collection is contamination. Contamination of blood cultures can lead to false positive culture results and/or significantly increased healthcare-related costs. Sources of blood culture contamination include inadequate skin disinfection, inadequate collection tube disinfection, and contamination of the initial blood draw, which can skew results.

[0007]

Blood culture collection kits generally include "butterfly" sets, infusion sets, or other types of venipuncture devices provided by companies such as BD, Smith, and B.Brown, as well as aerobic and anaerobic blood culture bottles. Consists of a bottle and A variety of different bottles are also available depending on inspection requirements. These bottles are specially designed to optimize the collection of both aerobic and anaerobic organisms. In conventional kits, the bottle used is commonly known as a "vacutainer", which is used to create a vacuum inside the tube to facilitate the collection of a predetermined amount of liquid, such as blood. A blood collection tube formed from a sterile glass or plastic tube with a lid that is evacuated to a vacuum.

[0008]

False positive blood cultures are generally the result of poor sampling techniques. They cause antibiotics to be used when they are not needed, increasing hospital costs and patient anxiety. Blood cultures are taken from a needle prick into the skin, after which a Vacutainer® is attached to take a sample of blood. Contamination can result from improper or incomplete disinfection of the puncture site and the surrounding skin area. It can also result from the piercing of the skin by the needle during insertion, which draws pierced skin cells and associated contaminants into the sample.

[0009]

Blood flow through a hypodermic needle is laminar, which causes a flow velocity gradient across the flow tube when a pressure drop is applied across the hypodermic needle. Strong aspiration of blood or use of a very small hypodermic needle can cause lysis and release of potassium from red blood cells, thereby making the blood sample abnormal.

[0010]

In another example, some patients have delicate veins that are subject to pressure drops or vacuums, such as those exerted by the plunger of a syringe that is withdrawn too rapidly, esp ecially for the patient's condition. can collapse under Such venous collapse is dangerous and v ery difficult to control because such a condition cannot be known in advance. Various strateg ies have been implemented to reduce the contamination rate of blood cultures, such as staff t raining in sterile collection techniques, feedback on contamination rates, and the introduction of blood culture collection kits

.

Skin antisepsis can reduce contamination concerns, but more than 20% of skin microbes are l ocated deep in the dermis and are not affected by antisepsis. Changing needles prior to bottle inoculation is not recommended as it increases the risk of needlestick injuries without reducin g contamination rates.

[0012]

Some conventional systems and techniques for reducing contamination of blood cultures inv olve discarding the initial aliquot of blood drawn from central venous catheters, venous punctu res and other vascular access systems. However, these systems either require the user to me chanically manipulate the intravascular device or require a complex series of steps that are dif ficult to ensure.

SUMMARY OF THE INVENTION

[

0013]

The present specification presents systems and methods for reducing blood culture contamin ation, cell lysis, and venous collapse. In some implementations, the systems and methods can eliminate variability in user disinfection and also eliminate the risk of skin cells entering blood culture samples. The systems and methods disclosed herein potentially indicate when to attac h a Vacutainer® or other blood collection device (i.e., a syringe) to obtain a contaminant-free blood sample. , does not require changes to existing clinical processes. In some implementat ions of the systems and methods disclosed herein, blood sampling is accomplished passively t hrough the use of the patient's own blood pressure, thereby reducing the risk of venous collap se and reducing current practice

.

eliminates further user steps beyond The system and method can be adapted to suit short-pat h direct puncture or butterfly venipuncture systems. It can also be used with samples taken t hrough a catheter. Means

for Solving the Problems

In one aspect, a blood isolation device is presented. A blood isolation device includes an inlet port and an outlet port. The blood isolation device further includes an isolation chamber conne cted to the inlet port, the isolation chamber having a vent including an air permeable blood b

rrier. The blood isolation device has a proximal end connected with the inlet port and a distal e nd connected with the outlet port, a sampling channel
further includes

[0016]

In another aspect, a blood isolation device is described that is connected to a blood collectio n path. The blood collection path has a patient needle and a sample collection device. The blo od isolation device includes an entry port connected to the patient needle and an isolation cha mber connected to the entry port, the isolation chamber having a vent including an air perme able blood barrier. The blood isolation device further includes a sampling channel having a pro ximal end connected to the inlet port, and an outlet port connected to the distal end of the sa mpling channel and the sample collection device.

[0017]

In yet another aspect, a blood isolation device is described that interfaces with a blood collec tion system. The blood collection system includes a patient needle for allowing a blood sample to be drawn from a patient and a sample needle that is sealed and adapted to receive an evac uated blood collection tube. A blood isolation device includes an inlet port connected to a patie nt needle for receiving a blood sample from a patient. A blood isolation device is an isolation c hamber connected to an inlet port and having a vent containing an air permeable blood barrie r for receiving and receiving an initial portion of a blood sample before the sample needle is o pened by an evacuated blood collection tube. Further includes an isolating isolation chamber. The blood isolation device further includes a sampling channel having a proximal end connect ed to the inlet port for carrying a subsequent portion of the blood sample when the sample ne edle is opened by the evacuated blood collection tube. The blood isolation device further inclu des an exit port connected with the distal end of the sampling channel for carrying subsequen t portions of the blood sample to the sample needle.

[0018]

In yet another aspect, a blood sample optimization system is disclosed and described. The bl ood sample optimization system includes a blood collection system for enabling and obtaining one or more samples of a patient's blood and false positive identification of pathogens in the p atient's blood that may have been contaminated by the venipuncture process. a blood isolatio n device for receiving and isolating an initial portion of one or more samples of the patient's bl ood that may result in

A

blood collection system includes a patient needle configured for venipuncture of a patient to enable withdrawal of a sample of the patient's blood, a blood collection channel connected to t he patient needle for carrying the blood sample, and a blood sample. and a sample needle co nfigured to receive an evacuated blood collection container for collecting and containing a sub sequent portion of the blood sample.

[0020]

In yet another aspect, a blood isolation device is disclosed and described. In some implementations, a blood isolation device can include an inlet port, an outlet port connected to the inlet port, and an isolation chamber connected to the inlet port. The isolation chamber can have a vent containing an air permeable blood barrier.

[0021]

A blood isolation device is connected along the blood collection path between the patient needle and the sample needle and includes an entry port for receiving the blood sample. A blood isolation device is an isolation chamber connected with an inlet port for receiving an initial volume of blood sample and includes an air permeable blood barrier to isolate at least a first portion of the initial volume of blood sample. Further includes an isolation chamber having a vent. The blood isolation device is a sampling channel having a proximal end connected with the inlet port, the isolation chamber isolating at least a first portion of a first volume of blood sample and a subsequent volume of blood sample into the evacuated blood collection container. It further includes a sampling channel that carries to. The blood isolation device further includes an outlet port connected to the distal end of the sampling channel for outputting a subsequent volume of the blood sample. The details of one or more embodiments are set forth in the accompanying drawings and the description below

.

Other features and advantages will be apparent from the specification and drawings, and from the claims.

[Brief description of the drawing]

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

1 shows a blood sample optimization system; FIG.

FIG. 2 shows a blood sample optimization system according to an alternative implementation;

FIG. 3 shows a blood sample optimization system according to another alternative implementation;

FIG. 4 shows a blood sample optimization system according to another alternative implementation;

FIG. 5 shows a blood sample optimization system according to another alternative implementation;

FIG. 6 shows a blood sample optimization system according to an alternative implementation;

FIG. 7 is a flowchart of a method for optimizing blood culture quality;

FIG. 8A illustrates a blood isolation system for non-contaminated blood collection, according to some implementations;

FIG. 8B illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 8C illustrates a blood isolation system for clean blood collection, according to some imp

mentations;

FIG. 8D illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 8E illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 9 shows a path splitter for use in a blood sequestration system;

FIG. 10A shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10B shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10C shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10D shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 11A shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11B shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11C shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11D shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11E shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 12A shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation;

12B shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation; FIG.

FIG. 12C shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation;

FIG. 12D shows a blood sample optimization system including a blood isolation device according to yet another alternative implementation;

FIG. 13A shows blood sample optimization system 1300 according to yet another alternative implementation.

FIG. 13B shows blood sample optimization system 1300 according to yet another alternative implementation.

FIG. 13C shows blood sample optimization system 1300 according to yet another alternative implementation.

FIG. 13D shows blood sample optimization system 1300 according to yet another alternative

mplementation.

FIG. 14A illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14B illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14C shows yet another implementation of a blood collection system that isolates contami nants in the initial aliquot or sample to reduce false positives in blood cultures or tests perfor med on patient blood samples.

FIG. 14D illustrates yet another implementation of a blood collection system that isolates cont aminants in the initial aliquot or sample to reduce false positives in blood cultures or tests per formed on patient blood samples.

FIG. 14E further illustrates a blood collection system that isolates contaminants of an initial ali quot or sample to reduce false positives in blood cultures or tests performed on patient blood samples.

Show another implementation.

15A-B illustrate a blood isolation device and method of using the same according to yet anoth er implementation.

15B illustrates a blood isolation device and method of using the same according to yet anothe r implementation; FIG.

FIG. 15C illustrates a blood isolation device and method of using the same according to yet an other implementation;

FIG. 15D illustrates a blood isolation device and method of using the same according to yet an other implementation;

FIG. 15E illustrates a blood isolation device and method of using the same according to yet an other implementation;

Figure 15F illustrates a blood isolation device and method of using the same according to yet another implementation;

FIG. 15G shows a blood isolation device and method of using the same according to yet anoth er implementation;

FIG. 16A shows a blood isolation device according to yet another implementation;

16B shows a blood isolation device according to yet another implementation; FIG.

16C shows a blood isolation device according to yet another implementation; FIG.

16D shows a blood isolation device according to yet another implementation; FIG.

Figure 17A shows a lower member of a housing for a blood isolation device;

Figure 17B shows a lower member of a housing for a blood isolation device;

Figure 17C shows a lower member of a housing for a blood isolation device;

Figure 17D shows a lower member of a housing for a blood isolation device;

Figure 17E shows a lower member of a housing for a blood isolation device;
Figure 18A shows a top member of a housing for a blood isolation device;
Figure 18B shows a top member of a housing for a blood isolation device;
Figure 18C shows a top member of a housing for a blood isolation device;
Figure 18D shows a top member of a housing for a blood isolation device;
Figure 18E shows a top member of a housing for a blood isolation device;
Figure 18F shows a top member of a housing for a blood isolation device;
Figure 19A shows a blood isolation device having an upper member that mates with a lower member.
Figure 19B shows a blood isolation device having an upper member that mates with a lower member.
FIG. 20 shows a blood sample optimization system including a blood sequestration device;
Figure 21 shows a non-vented blood isolation device using a wicking material chamber.
Figure 22A shows the material composition of a filter for isolating blood in an isolation chamb er of a blood isolation device;
Figure 22B shows the material composition of a filter for isolating blood in an isolation chamb er of a blood isolation device;
FIG. 23A shows another implementation of a blood isolation device using vacuum force from a blood collection device;
Figure 23B shows another implementation of a blood isolation device using vacuum force from a blood collection device. Like numbers in the various drawings indicate like elements.
DETAILED DESCRIPTION OF THE INVENTION
[0024]

The present specification provides a blood sample optimization system that reduces or elimin ates contaminants in a blood sample taken, thereby reducing or eliminating false positive read ings in blood cultures or other tests of the blood sample taken. and methods. In some implem entations, the blood sample optimization system includes a patient needle for vascular access to the patient's bloodstream and a blood collection container such as a vacutainer or evacuate d blood collection tube or other and a blood isolation device positioned between the patient ne edle and the sample needle. The blood isolation device includes an isolation chamber for isolat ing a first aliquot of blood that may be contaminated, and after the first aliquot of blood is isol ated in the isolation chamber, the blood is isolated between the patient needle and the sample needle. A sampling flow path bypassing the isolation chamber for carrying potentially unconta minated blood may also be included.

FIG .

1 shows a blood sample optimization system according to some implementations. The syste m includes a patient needle 1 for puncturing the patient's skin to access the patient's vein and intravenous blood therein. The system may include a resealable boot 10, a luer actuated valv e, or another sampling interface.

or with a sample needle (i.e., a Vacutainer®, etc.) that can be housed within the device and i nitially sealed by a resealable boot 10, a luer-actuated valve, or another collection interface or device. It further includes a resealably sealed needle) 5 for. The resealable boot 10 can be pus hed by or around the sample needle 5 by using a Vacutainer® bottle (not shown) for collectin g the patient's blood. The system can further include a low volume chamber 30 leading to the sample needle 5, but also includes a hole or one or more channels 45 leading to the isolation chamber 55 formed by the housing 50. FIG. Isolation chamber 55 includes chambers, chann els, passages for receiving and holding an initial aliquot of patient blood, which can be of a pr edetermined or measured volume, depending on the volume of isolation chamber 55

.

, locks, or other structures. Initial blood draws generally contain or are more susceptible to co ntain microorganisms or other pathogens that cause bacteremia and sepsis than subsequent blood draws. The isolation chamber 55 can be contained within a rigid housing, can be a conta iner formed in or defined by the housing itself, or can be realized as a tube or lumen. Isolation chamber 55 can have a predetermined volume, regardless of how it is formed and implement ed. In some implementations, the predetermined volume is based on the volume of the patien t needle, i.e., ranges from a volume less than the volume of the patient needle to any volume to a volume greater than 20 times the volume of the patient needle. can be done. The predet ermined volume of isolation chamber 55 can also be set to conserve or minimize the amount of blood that is isolated and disposed of.

[0027]

Isolation chamber 55 may be formed, contained, or housed within chamber housing 50 and may be made of plastic, rubber, steel, aluminum, or other suitable material. For example, isol ation chamber 55 can be formed from flexible tubing or other elastomeric material. The isolati on chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the is olation chamber 55 . As used herein, the term "air permeable blood barrier" means an air per meable but substantially blood impermeable substance, material or structure. Representative examples are hydrophobic membranes and hydrophobic coatings, hydrophilic membranes or h ydrophilic coatings in combination with hydrophobic membranes or coatings, meshes, filters, mechanical valves, antimicrobial materials, or isolation chamber 55 is blood. Any other means capable of expelling air from the isolation chamber 55 when filled with air may be included. In various exemplary embodiments, the air permeable blood barrier can be formed by one or mo re materials that allow air to pass through until it contacts liquid, such materials being air per meable. and/or completely or partially sealed to prevent or block the passage of liquids. In ot her words, the material forms an air permeable barrier prior to contact with the liquid. After c ontact with liquid, the material substantially or completely prevents further passage of air an d/or liquid.

[0028]

Holes or channels 45 can be of any desired length, cross-sectional shape or size and/or can

be formed away from low volume chamber 30 at any desired angle or orientation. The hole or channel 45 may also include a one-way flap or valve 60 that retains the first aliquot of blood s ample within the isolation chamber 55 . In some particular implementations, hole or channel 45 may include a "duckbill" valve or flapper valve 60 or the like for unidirectional blood flow fr om low volume chamber 30 to isolation chamber 55 . Air permeable blood barrier 20 may also be constructed of a material that allows air to escape but seals upon contact with blood, there by not allowing outside air to enter isolation chamber 55 . This seal eliminates the need for va lves.

Valve 60

can be any type of valve or opening/closing mechanism. The chamber 30 is designed to retai n substantially no residual blood and retains a specific volume or percentage of blood in the is olation chamber.

It can be configured to hold or pass through the member 55 . Similarly, the isolation chamber 55 may also include any type of coating, such as an antimicrobial coating, or a coating that as sists in identifying and/or diagnosing components of the isolated primary blood draw. Housin gs 50 and 40 may be formed from any suitable material, including plastics such as acrylonitril e butadiene styrene (ABS) or other thermoplastic or polymeric materials, rubber, steel, or alu minum

.

The air permeable blood barrier 20 is activated upon contact with blood from the first draw or when the expulsion of air is stopped, or upon any combination of events and blood in the isola tion chamber 55, color A donator or other signaling mechanism may be included. The air per meable barrier can also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents inadvertent or premature sealing of the filter by external fluid sources, spl ashes, and the like. The isolation chamber 55 can also be translucent or transparent to allow t he user to visually confirm that the chamber has been filled.

[0031]

FIG. 2 shows a blood sample optimization system according to some alternative implementa tions. In the implementation shown in FIG. 2, an isolation chamber 55 or waste chamber surr ounds the patient needle 1 and an open-ended cuff or housing is connected to the waste cha mber and surrounds the sample needle housing base and housing. The patient needle 1 and t he sample needle 5 are connected to each other by a boot 56 which forms a continuous blood collection flow path therethrough. Boot 56 includes a single hole or channel leading from the b lood collection channel to isolation chamber 55 . The device can include multiple holes or chan nels in other implementations. Each hole or channel can include a one-way valve and can be s ized and adapted for a predetermined amount of blood flow.

Isolation

chamber 55 contains an air permeable blood barrier. The filter may further include sensors o r indicators, respectively, for sensing and/or indicating when a predetermined volume of bloc

has been collected in the isolation chamber 55 . The instructions alert the user to attach an ev acuated blood collection tube or bottle, such as a Vacutainer®, to the sample needle 5 . The h ousing for isolation chamber 55 can be of any size or shape and can include any type of mater ial to define an interior space or volume within the housing. The interior space is initially filled with air only, but can also be coated with agents or substances such as decontamination agen ts, coagulants, and the like. When the evacuated blood collection tube is attached to the samp le needle 5, blood automatically flows into the patient needle 1, through the blood collection c hannel and the sample needle 5 into the bottle. The sample needle 5 is covered by a resealabl e boot, coating or membrane that seals the sample needle when no blood collection bottle is a ttached to the sample needle.

[0033]

FIG. 3 shows a blood sample optimization system according to some alternative implementa tions. In the illustrated implementation, sample needle 5 is surrounded by a resealable boot o r membrane and is also connected to patient needle 1 . A blood flow path is formed through t he sample needle and the patient needle. The connection between the sample needle and the patient needle includes a 'T' or 'Y' connector 102 that includes a flow path, port or opening lea ding from the main blood flow path to the isolation chamber 104 .

The T or Y connector 102 includes a

flap or one-way valve and has holes sized and adapted for a predetermined flow rate of bloo d. The isolation chamber 104 can be formed from a tube or formed by a rigid housing and is i nitially filled with air. The isolation chamber 104 receives blood flowing out of the patient auto matically, ie, under pressure due to the patient's own blood pressure. The isolation chamber 1 04 preferably includes an air permeable blood barrier 106 at the distal end of the tube formin g the isolation chamber 104 and connected at the proximal end to the T or Y connector 102 . The T or Y connector 102 can branch at any desired angle for most efficient blood flow and to minimize or eliminate mixing of the initial aliquot of blood with the main blood sample. Minimi ze the interface between the openings and channels and the main blood channel

can be configured to In some alternative implementations, the sample needle can be attache d to any length of tubing whose opposite end is connected to a T or Y connector 102, as show n in FIG

.

can be done. The isolation chamber 104 can be of any shape or volume so long as the initial a liquot contains a predetermined amount of blood sample. The T or Y connector 102 can also in clude openings or channels parallel to the main blood flow channel. The air permeable blood b arrier may further include an indicator 107 or other mechanism to indicate when a predetermi ned amount of blood has been collected in the isolation chamber or when the released air has reached a certain threshold, i.e. zero. . The tube can also include a clip 109 that can be used t o pinch and prevent fluid flow through the tube. Once the air permeable blood barrier and pr imary chamber are sealed, the first aliquot of blood is confined to the isolation chamber 104

nd a vacuum blood collection tube, such as a Vacutainer® bottle, is attached to the sample ne edle to obtain a sample

.

5 is attached. The blood collection tube can be removed and the sample needle 5 resealed. An y number of subsequent blood collection tubes can be attached for additional blood draws or s amples. When all blood draws are completed, the system is discarded, leaving the first aliquot of blood trapped in isolation chamber 104 .

FIG.

5 shows a blood sample optimization system according to some alternative implementations. In the illustrated implementation, the sample needle 5 is connected by tubing to the patient n eedle. A "T" or "Y" connector 120 is added at any desired location along the tube to include an opening, port or flow path leading to isolation chamber 204, substantially as described above.

[0038]

FIG. 6 illustrates a blood sample optimization system according to some alternative impleme ntations in which an isolation chamber 304 configured as the primary collection flow path rece ives the first aliquot of blood and is provided adjacent to the blood collection flow path. show. The isolation chamber 304 can surround the blood collection channel, patient needle 1 and/or sample needle 5 . The primary collection channel may include T or Y connectors 120, or other types of openings or channels. The isolation chamber 304 includes an air permeable blood bar rier and, as described above, may also include an indicator of contact with fluid such as blood.

In some implementations, either or both of the patient needle 1 or the sample needle 5 can be replaced with luer lock male or luer lock female connectors

.

However, in various implementations, the connector at the sample needle end of the blood sa mple optimization system is first sealed and the first aliquot is transferred to an isolation cha mber pressurized with ambient air pressure and containing the air outlet of the air permeable blood barrier. Allows blood to be diverted. In this way, the system passively and automatically uses the patient's own blood pressure to overcome the ambient air pressure in the isolation c hamber, force air through the air permeable blood barrier, and replace the air in the isolation c hamber with blood.

[0040]

FIG. 7 is a flowchart of an exemplary method for optimizing blood culture quality. At 702, a c linician inserts a needle into a patient's vein. At 704, blood flows into the isolation chamber, fo rcing air within the isolation chamber out of the isolation chamber through the air permeable blood barrier. In some implementations, the volume of the isolation chamber is from less than 0.1 cubic centimeters (cc) to 5 cubic centimeters (cc) or more. The isolation chamber is sized and adapted to collect a second portion of the blood sample and other subsequent portions or a first portion of the blood sample that is more susceptible to contamination than subsequent collections. The isolation chamber has an air permeable blood barrier through which air can

e expelled by the blood expelled from the patient's veins so that such blood can be placed in a vacutainer for receiving and storing blood samples. ® or other bottle, it necessarily and auto matically flows into the isolation chamber before being drawn into or otherwise entering the b ottle.

As the isolation chamber fills, blood collects or otherwise contacts an air permeable blood ba rrier that blocks or prevents blood from passing through . At 706, once the blood contacts the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is closed and air no longer flows out or in. At 708, the clinician is provided an indication or can view the full chamber indicating that an evacuated blood collection tube, such as a Vacutainer ®, can be attached. The indicator may include visibility of the primary chamber to see if the p rimary chamber is full, eg, a blood barrier that changes color, or other indicator. Since the fill t ime of the isolation chamber may be substantially instantaneous, such an indication, if presen t, may simply be that the isolation chamber is filled. Before the evacuated blood collection tu be is attached, communication between the needle, the sampling channel, and the isolation c hamber is restricted by the sealing of the isolation chamber's blood barrier, thus allowing air t o re-enter the system through isolation

.

do not. Sealing of the communication path is accomplished by mechanical twisting or other ac tion, small hole or tortuous path, obviating the need for a separate valve or mechanical action or manipulation by the clinician. At 710, the evacuated blood collection tube is removed, a self -sealing membrane seals the sample needle, and at 712, a further subsequent evacuated bloo d collection tube can be attached. At 714, once the sample has been taken, the device is rem oved from the patient and discarded.

[0043]

Figures 8A-8E show an exemplary blood sample optimization system 800 for non-contaminat ed blood collection, according to some implementations. Blood sample optimization system 80 0 includes an entry port 802 that can be connected to tubing, a patient needle (or both), or ot her vascular or venous access device, and a first exit to isolation chamber tubing 806 and sa mple collection tubing. a path splitter 804 with a second exit to 808; One or both of isolation c hamber tube 806 and sample collection tube 808 can be formed from tubing. In some implem entations, isolation chamber tube 806 is sized to accommodate a specific amount of initial blo od sample. A sample collection tube 808 receives a blood sample once the isolation chamber t ube 806 is filled. The sample collection tube 808 can be connected to a Vacutainer® base or h ousing 810, or other blood sample collection device. Blood isolation system 800 further inclu des blood isolation device 812, which includes housing 818, shown in more detail in FIGS

.

or connected at either end to a non-contaminated sample collection tube 808 . The sampling f low path 820 can be curved through the housing 818 to better secure and stabilize the hous

g 818 in position along the clean sample collection tube 808 .

[0045]

Blood isolation device 812 further includes an isolation chamber 822 or other chamber conne cted with isolation chamber tube 806 . Isolation chamber 822 terminates in air permeable blo od barrier 824 . The air permeable blood barrier 824 can also include a coloring agent that ch anges to a different color upon full contact with blood as an indicator that a blood sample (i. e., non-contaminated blood sample) can be properly taken. . Other indicators such as small li ghts, sound generating mechanisms, etc. can be used. In some implementations, the air per meable blood barrier is positioned perpendicular to the orientation of isolation chamber 822, b ut may be positioned at any distance or orientation to conserve space and materials used for housing 818. be able to. Housing 818 and its contents can be formed from any rigid or semi-ri gid material or range of materials.

FIG.

9 illustrates a path splitter for use in, for example, blood sequestration systems such as thos e shown in FIGS. 8A-8E.

900 is shown. Path splitter 900 includes inlet port 902 , main conduit outlet port 904 and isola tion channel outlet port 906 . The entry port 902 can be connected to a main tube that is also connected to the patient needle system or directly to the patient needle. The main line outlet port 904 can be connected to a main line tube to a blood collection system, such as a Vacutai ner® base or housing, or directly to such a blood collection system. The isolation channel outl et port 906 can be connected to an isolation tube for receiving and isolating the first sample o f blood up to a measured volume or predetermined threshold. Alternatively, the isolation flow path outlet port 906 can connect to the isolation chamber. The isolation channel outlet port 90 6 is preferably angled from 20 to 70 degrees from the main conduit outlet port 904 while the main conduit outlet port 904 is preferably in line with the inlet port 902 . Once an initial blood sample of predetermined volume has been isolated in an isolation tube or isolation chamber a ccording to the mechanisms and techniques described herein, subsequent blood samples can f low into inlet port 902 and pass unobstructed. It flows out directly from the main conduit outl et port 904 . 10A-10D show blood isolation device 1000 according to another implementatio n

.

Blood isolation device 1000 includes inlet port 1002 , main outlet port 1004 , and isolation flo w port 1006 . Entry port 1002 can be connected with a patient needle or associated tubing. T he main exit port 1004 can be connected to a blood sampling device such as a Vacutainer®, a ssociated tubing, or a luer-actuated valve. An isolation flow port 1006 separates from the mai n exit port 1004 into an isolation chamber 1008 . In some implementations, isolation chamber 1008 is formed as a spiral channel within housing or other container 1001 .

[0048]

Isolation chamber 1008 is connected at its distal end to air permeable blood barrier 1010, s

bstantially as described above. Air within the isolation chamber 1008 is expelled by the first al iquot of blood directed into the isolation flow path port 1006 through the air permeable blood barrier 1010 . Once the isolation chamber 1008 is filled, further blood draws through the main exit port 1004 are accomplished and these samples are clean.

11A -

11E show blood isolation device 1100 according to another alternative implementation. Bloo d isolation device 1100 includes an inlet port 1102 similar to the inlet ports described above, a main outlet port 1104 and an isolation flow port 1106 separate from main outlet port 1104 and inlet port 1102 . The isolation flow port is connected to isolation chamber 1108 . In the i mplementation shown in FIGS. 11A-11E, the blood isolation device includes a base member 1 101 having a flow path therein that functions as an isolation chamber 1108 . The flow path ca n be formed as a tortuous path through the base member 1101 while the base member 1101 is shaped and shaped to rest on the patient's limb. A portion of isolation chamber 1108 may protrude from or near the top surface of the base member just prior to exiting air permeable blood barrier 1110 to serve as blood isolation indicator 1109

.

Indicator 1109 can be made of a transparent material or a material that changes color when i n contact with blood.

[0051]

In some implementations, the blood isolation device 1100 can include a blood collection devi ce 1120, such as a normally closed needle, Vacutainer® shield, or other collection device. Blo od collection device 1120 may be manufactured and sold with blood isolation device 1100 for efficiency and convenience so that the initial aliquot of blood that may be contaminated by the patient needle insertion process can be isolated. can. Accordingly, the blood collection device 1120 can collect and ensure a clean blood sample so as to reduce the risk of false positive tes ts.

[0052]

Figures 12A-12D show a blood sample optimization system 1200 according to yet another al ternative implementation. System 1200 includes a blood isolation device 1202 for attachment to a blood collection device 1204, such as a Vacutainer® or other collection and sampling devi ce. Blood isolation device 1202 receives an initial aliquot or volume of blood before a Vacutain er® container or vial is attached to the collection needle of blood collection device 1204 and t ransfers that initial aliquot or volume to blood isolation device 1202 . Constructed and arrange d to isolate within the isolation channel.

[0053]

In some implementations, the blood isolation device 1202 can include an inlet port 1212, a main outlet port, and an isolation flow path port. Entry port 1212 can be connected to a patie nt needle or associated tubing. The main exit port 1214 is a normally closed needle or needle to allow connection with other collection devices such as evacuated blood collection containe

or vacutainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be co nnected to a device. The isolation flow port separates the isolation chamber 1218 from the ma in exit port.

[0054]

In some implementations, isolation chamber 1218 is formed as a channel within the body of isolation device 1202 . The isolation chamber 1218 can be a tortuous channel, such as a U-sh aped channel, an S-shaped channel, a spiral channel, or any other tortuous channel. Isolation device 1202 can include a housing or other enclosure and one or more channels formed therei n. As shown in FIGS. 12A and 12B, isolation device 1202 includes body 1206 and cap 1208 . One or more cavities or channels are formed in the body 1206, and the cavities or channels ar e further formed with one or more arms 1210 extending from the cap 1208, the one or more arms 1210 extending from the cavities or channels of the body 1206. A primary collection por t and a main outlet port are formed against the flow path.

[0055]

Figures 13A-13D illustrate a blood sample optimization system 1300 according to yet anothe r alternative implementation. System 1300 includes a blood isolation device 1302 for attachm ent to a blood collection device 1304, such as a Vacutainer® or other body fluid collection and sampling device. Blood isolation device 1302 receives an initial aliquot or volume of blood and receives that initial aliquot or volume of blood or other bodily fluid before a Vacutainer® conta iner or vial is attached to the collection needle of blood collection device 1304 . within the isol ation channel of the blood isolation device 1302 .

[0056]

Blood isolation device 1302 includes housing 1301 having inlet port 1314 , main outlet port 1312 , and isolation flow path port 1316 . Entry port 1314 can be connected to a patient need le or associated tubing. The main exit port 1312 is a normally closed needle or needle to allow connection with other collection devices such as evacuated blood collection containers or vacu tainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be connecte d to a device. An isolation flow port 1316 separates from the main inlet port 1314 into an isol ation chamber 1318 . In the embodiment shown in FIGS. 13A-13D, isolation chamber 1318 i s formed as a cavity or chamber within housing 1301 or is formed by walls defining housing 1 301

.

The isolation chamber 1318 is a tortuous flow path such as a U-shaped flow path, an S-shape d flow path, a spiral flow path, or any other tortuous flow path defined by the cooperation and connection of the housing 1301 and the cap 1307. There can be and the cap 1307 can include protrusions 1305 that provide one or more walls or directors for the tortuous flow path within the isolation chamber 1318 . Projections 1305 from cap 1307 can be straight or curved, can b e embedded with various channels, openings or grooves, and can extend from cap 1307 at an y angle or orientation. can be done. isolation chamber 13

When the cap 1307 is connected with the housing 1301 to complete the formation of 18 , the protrusions 1305 form at least a portion of the tortuous flow path and the isolation flow forme d by the tortuous flow path within the isolation chamber 1318 . Isolate the first aliquot or volu me of blood or other bodily fluid in the tract.

Isolation chamber 1318

includes air permeable blood barrier 1310 substantially as described above. Air within the iso lation chamber 1318 is expelled through the air permeable blood barrier 1310 by the first aliq uot of blood supplied into the isolation chamber 1318 by the patient's blood pressure. Once th e isolation chamber 1318 has been filled and the air within the isolation chamber 1318 has be en expelled, a force such as a vacuum or other pressure such as provided by a blood sampling device such as a Vacutainer® is applied to the next aliquot or Until a volume of blood or fluid has been provided to withdraw, the patient's blood pressure is insufficient to drive or provide additional blood to blood isolation device 1302 , particularly outlet port 1312 . Further blood d raws can be taken through the main exit port 1312 and these samples are not contaminated a s any contaminants are sequestered in the isolation chamber 1318 along with the first aliquot of blood.

[0059]

Figures 14A-14E illustrate yet another implementation of a blood collection system 1400 that sequesters contaminants in an initial aliquot or sample to reduce false positives in blood cultur es or tests performed on patient blood samples. Blood collection system 1400 includes a bloo d isolation device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutain er® or the like. Blood isolation device 1401 includes an entry port 1402 that can be connecte d to a patient needle that is inserted into the patient's vasculature for access to and collection of a blood sample. Inlet port 1402 may also be connected to a tube or other conduit that is al so connected to a patient needle.

Inlet port 1402

defines an opening to blood isolation device 1401, which opening can be of the same cross-s ectional dimensions as a tube or other conduit connected to the patient needle or the patient needle itself. For example, the opening can be circular with a diameter of about 0.045 inch (1. 143 mm), but may be from 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm) or more. can have a diameter of Blood isolation device 1401 further includes an exit port 1404 that defines an ope ning from blood isolation device 1401 and to blood sampling device 1403 . Exit port 1404 can also be connected to a tube or other conduit that is also connected to blood isolation device 1 403 . The exit port 1404 has a connector device such as an unthreaded interference or glue jo int for attachment to a variety of devices including, but not limited to, threaded caps, luer con nectors (male or female), tubing, and the like. can further include

[0061]

Blood isolation device 1401 further includes a sampling channel 1406 between inlet port 14

2 and outlet port 1404, which functions as a blood sample path once the first aliquot of blood has been isolated. Sampling channel 1406 can be a channel or conduit of any size, shape or c onfiguration. In some implementations, sampling channel 1406 has a cross-sectional area sub stantially similar to the opening of inlet port 1402 . In other implementations, sampling chann el 1406 can gradually widen from inlet port 1402 to outlet port 1404 .

Blood isolation device 1401 further includes isolation chamber 1408 , which

is connected to and separated from sampling channel 1406 at any location between inlet por t 1402 and outlet port 1404 . redirected, but preferably connected to the proximal end of sam pling channel 1406 near inlet port 1402 and from the proximal end.

separated or diverted from the The isolation chamber 1408 is initially maintained at atmosphe ric pressure and includes an air outlet 1412 at or near the distal end of the isolation chamber 1408 opposite the turning point from the sampling channel 1406 . Air outlet 1412 includes air permeable blood barrier 1412 . The air permeable blood barrier 1412 can be covered with a p rotective cover 1416, as shown in FIG. 14B. The protective cover 1416 can be sized and confi gured to prevent a user from touching the air permeable blood barrier 1412 with their fingers or other external instruments while still allowing the patient's own blood pressure to pressure the isolation chamber 1408. Allowing air to exit the air permeable blood barrier 1412 as the ai r is forced out of the isolation chamber by forcing blood into it. Protective cover 1416 can also be configured to block or prevent accidental exposure of the air permeable blood barrier to su rrounding fluids or droplets. This can be done in a variety of mechanical ways including, but n ot limited to, adding a hydrophobic membrane to the protective cover. As shown in FIGS. 14 C and 14D, the sampling channel 1406 may be cylindrical or frusto-conical in shape from a sm aller diameter to a larger diameter to minimize the possibility of lysing red blood cells

.

can. Similarly, the sampling channel 1406 is formed with a minimal amount or no sharp bends or sharp angles that could lyse red blood cells. Sampling channel 1406 splits near inlet port 1 402 through diverting path 1409 into isolation chamber 1408 . Diversion pathway 1409 can h ave any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least a portion of inlet port 1402 .

[0064]

In some implementations, sampling channel 1406 and isolation chamber 1408 are formed b y grooves, channels, locks or other pathways formed in housing 1414 . Housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a lowe r member that sealably mates with the upper member. One or both of the lower and upper m embers can include a sampling channel 1406 and an isolation chamber 1408 as well as a dive rting passageway 1409 , an inlet port 1402 and an outlet port 1404 . In some other implemen tations, one or more of diverting path 1409 , inlet port 1402 , and/or outlet port 1404 are at l east partially closed by a cap member connected to either end of housing 1414 . can be forme d in In some implementations, the upper and lower members and the cap member can be co

nected together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the lik e. In other implementations, some or all of the interior surfaces of the diversion pathway 140 9 and/or the isolation chamber 1408 can be coated or filled with agents or substances such as decontamination agents, coagulants, and the like. For example, when the sequestration cham ber 1408 fills and the first aliquot of blood returns to the diverting path 1409, the final volume of sequestered blood clots, creating a barrier between the sequestration chamber 1408 and th e sampling channel 1406. As such, turning path 1409 may be provided with a coagulant. 15 A-15G show a blood isolation device 1500. FIG

.

The blood isolation device 1500 includes a needle or needle that is normally closed to allow co nnection with other collection devices such as evacuated blood collection containers or vacutai ners, associated tubing, luer connectors, syringes, luer actuated valves, and the like. It can b e connected to a device.

[0066]

Blood isolation device 1500 includes an entry port 1502 that can be connected to a patient n eedle that is inserted into the patient's vasculature for access to and collection of a blood sam ple. Entry port 1502 can also be connected to a tube or other conduit that is also connected t o a patient needle. Entry port 1502 defines an opening to blood isolation device 1500, which o pening can be of the same cross-sectional dimensions as a tube or other conduit connected to the patient needle or the patient needle itself. For example, the opening has a diameter of ap proximately 0.045 inches (1.143 mm).

It can be circular, but can have a diameter of 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm) or more. Inlet port 1502 may also include a sealed or fluid tight connector or connection such a s a threaded or luer fitting or the like

.

In some implementations, a tube or other conduit that is coupled to the patient needle can be integrated with the entry port 1502, such as by co-molding, gluing, laser welding, or heat bon ding the parts together. This allows the blood isolation device 1500 to be manufactured and s old as a single unit with the patient needle, eliminating the need to connect the patient needle to the blood isolation device 1500 during blood draw or sampling.

Blood isolation device 1500 further includes an exit port 1504 that

defines an opening from blood isolation device 1500 and to the blood sampling device. Exit p ort 1504 may also be connected to a tube or other conduit that is also connected to a blood is olation device and may include a sealed or fluid tight connector or connection such as a threa ded or luer fitting. Thus, as noted above, the blood isolation device 1500 is manufactured and sold as a single unit with the patient needle and/or tubing and blood sample collection device such that the patient needle and blood sample collection device are connected to blood isolati on during blood collection or sampling. The need to connect to device 1500 can be eliminated.

[0069]

Blood isolation device 1500 further includes a sampling channel 1506 between inlet port 150 2 and outlet port 1504, which functions as a blood sample path once the first aliquot of blood has been isolated. Sampling channel 1506 can be a channel or conduit of any size, shape, or c onfiguration. In some implementations, sampling channel 1506 has a cross-sectional area sub stantially similar to the opening of inlet port 1502 . In other implementations, sampling chann el 1506 can gradually diverge from inlet port 1502 to outlet port 1504 .

Blood isolation device 1500 further includes isolation chamber 1508 , which

is connected to and separated from sampling channel 1506 at any location between inlet por t 1502 and outlet port 1504 . Although diverted, it is preferably connected to and disconnecte d or diverted from the proximal end of sampling channel 1506 near inlet port 1502 . In some i mplementations, the diversion channel includes a Y-junction. The isolation chamber 1508 is pr eferably maintained at atmospheric pressure and includes a vent 1510 at or near the distal en d of the isolation chamber 1508 . Vent 1510 includes air permeable blood barrier 1512 . FIG. 15C shows blood isolation device 1500 with isolation chamber 1508 filled with an initial aliquo t or sample of blood from a patient.

[0071]

Air permeable blood barrier 1512 can be covered with protective cover 1516 . The protective cover 1516 can be sized and configured to prevent a user from touching the air permeable blo od barrier 1512 with their fingers or other external instruments while still allowing the patien t's own blood pressure to pressure the isolation chamber 1508. Allowing air to exit the air per meable blood barrier 1512 as the air is forced out of the isolation chamber by forcing blood int o it. The protective cover 1516 can be configured to block or prevent accidental exposure of t he filter to ambient fluids or splashes. This can be done in a variety of mechanical ways, inclu ding but not limited to adding a hydrophobic membrane to the protective cover.

FIG.

15B is a perspective view of blood isolation device 1500 from the top of housing 1501 includi ng outlet port 1504 and vent 1510 of blood isolation device 1500 and sampling channel 1506 before the sample collection device is activated. The first aliquot of blood is separated while th e is empty.

Filling the separation chamber 1508 is shown. Figure 15G is a perspective view of the blood is olation device 1500 from the bottom of the housing 1501 and the exit port 1504 of the blood i solation device 1500, showing the initial flow while the sampling channel 1506 is empty befor e the sample collection device is activated. An aliquot of blood is shown filling the isolation ch amber 1508 . FIG. 15C is another perspective view of blood isolation device 1500 from the to p of housing 1501, including inlet port 1502 and vent 1510 of blood isolation device 1500, wit h the isolated blood substantially remaining within isolation chamber 1508. FIG. Blood is draw n through sampling channel 1506 during the period of time.

FIG .

15D is a cross-sectional view of blood isolation device 1500 according to some implementat

ons, showing housing 1501 defining sampling channel 1506 and isolation chamber 1508 . 15E and 15F illustrate various form factors of housings for blood isolation devices according to one or more implementations described herein. Isolation chamber 1508 can have a larger cross-sectional area than sampling channel 1506, and the cross-sectional area or length can be conf igured such that a predetermined or specific blood volume is isolated or locked

.

can. The sampling channel 1506 can be sized to fit tubing for either or both the patient needle tubing or the blood collection device tubing.

[0075]

Housing 1501 can be formed from multiple pieces or a single unitary piece. In some implem entations, as shown in FIG. 15D, housing 1501 includes an upper member 1520 and a lower member 1522 that mate with each other, one or both of which may be formed by, for exampl e, an injection molding process or by etching, cutting, cutting, or molding. It has grooves, cha nnels, locks, conduits or other pathways pre-formed by perforations or the like. The upper me mber 1520 may be attached by any mating or connecting mechanism, such as using laser wel ding, thermal bonding, ultrasonic welding, adhesives, screws, rivets, bolts, etc., or latches, gr ooves, tongues, pins, flanges. Other mating mechanisms, such as, can connect with lower me mber 1522 . In some implementations, the upper member 1520 can include grooves, chann els, locks, conduits or other pathways, while the lower member 1522 is the upper member 15 20, as shown in FIG. 15D

.

A protrusion 1524 sized and adapted to fit into at least one of a groove, channel, lock or other pathway may be included. Protrusions 1524 can provide surface features such as partial groov es or partial channels, for example, to complete the formation of either sampling channel 150 6 and/or isolation chamber 1508 . In some implementations, the protrusions 1524 can be for med with one or more slanted sides or faces to fit more snugly within corresponding grooves, channels, locks or other pathways. In still other implementations, both the upper member 15 20 and the lower member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524 .

[0077]

In some implementations, sampling channel 1506 and isolation chamber 1508 are formed b y grooves, channels, locks or other pathways formed in housing 1501 . Housing 1501 can be made of any suitable material including rubber, plastic, metal or other material. Housing 1501 can be formed from a transparent or translucent material, or from an opaque or non-transluce nt material. In other implementations, the housing 1501 can be largely opaque or non-transp arent, but the housing surfaces immediately adjacent the sampling channel 1506 and/or the i solation chamber 1508 are transparent or translucent and initially A visual cue or sign that the sequestration chamber 1508 is filled to the required or desired degree and/or the sequestered blood is then released while a clean blood sample is drawn through the sampling channel 15

6. Provide visual cues or signs to remain isolated.

give to the artist. Other visual cues or signs of isolation include, but are not limited to, contact, penetration, or partial penetration of blood, the air permeable blood barrier 1512 turning a different color; Color-coded tabs or indicators at any location along or adjacent to the isolation chamber, audible, vibratory, or other signals may be included. After venipuncture with a patient needle (not shown), which can collect many pathogens from the patient's skin, the patient's own blood pressure overcomes the atmospheric pressure in isolation chamber 1508 to form air permeable blood barrier 1512

.

As the air in the isolation chamber 1508 is expelled through, the initial volume of the patient's blood with these pathogens enters the blood isolation device 1500 inlet port 1502 and flows into the isolation chamber 1508 by following the path of least resistance. . The patient's blood pressure is not sufficient to overcome the rising air pressure within the sealed sampling channel 1506 . Ultimately, an isolation chamber 1508 of predetermined volume is filled with blood that drives air out through an air permeable blood barrier 1512 . When blood impinges on the air permeable blood barrier, the blood interacts with the material of air permeable blood barrier 1512 to completely or partially seal vent 1510 . A signal or indication can be provided that the practitioner can now utilize the VACUTAINER® capsule or other blood sampling device to obtain the next volume of the patient's blood for sampling. The blood in the isolation chamber 1508 is now effectively isolated within the isolation chamber.

[0079]

Upon filling the blood isolation channel 1508, and prior to use of a Vacutainer® or other blood sampling device, the patient's blood pressure causes compression of the air in the sampling channel 1506 and possibly a small amount of blood. It moves past the turning point into the isolation chamber 1508 into the sampling channel 1506 and queues clean blood to be drawn through the sampling channel 1506 .

Figures 16-19

show yet another implementation of a blood isolation device. 16A-16D are connected between a blood sample collection device such as an evacuated blood collection container such as a Vacutainer® (not shown) and a patient needle (not shown) and/or associated tubing. 16 shows a blood isolation device 1600 that can be used. Figure 17 shows the lower member of the blood isolation device and Figure 18 shows the upper member of the blood isolation device, the upper and lower members interfitting to provide an inlet port as described in more detail below. Ports, exit ports, isolation chambers and sampling channels can be formed. Figures 19A and 19B show the upper and lower members mating together. It should be appreciated that FIGS. 16-19 show one exemplary method of constructing the blood isolation devices described herein and that other forms of construction are possible.

[0081]

16A-16D, blood isolation device 1600 includes an entry port 1602 that can be connected to

patient needle that is inserted into a patient's vasculature for access and collection of a blood sample. Inlet port 1602 can also be connected to a tube or other conduit that is also connecte d to a patient needle. Entry port 1602 defines an opening to blood isolation device 1600, whic h opening can be of the same cross-sectional dimensions as a tube or other conduit connecte d to the patient needle or the patient needle itself. For example, the opening can be circular w ith a diameter of about 0.045 inch (1.143 mm), but may be from 0.01 inch (0.254 mm) to 0. 2 inch (5.08 mm) or more. can have a diameter of

Inlet port 1602

may also include a sealed or fluid tight connector or connection such as a threaded or luer fit ting or the like. In some implementations, a tube or other conduit coupled to the patient need le can be integrated with the entry port 1602, such as by co-molding, gluing, laser welding, or heat bonding the parts together. Blood isolation device 1600 is thereby manufactured and sol d as a single unit along with the patient needle and/or tubing,

The need to connect the patient needle to the blood isolation device 1600 during blood draw o r sampling can be eliminated.

Blood isolation device 1600 further includes an exit port 1604 that

defines an opening from blood isolation device 1600 and to the blood sampling device. Exit p ort 1604 may also be connected to a tube or other conduit that is also connected to a blood is olation device and may include a sealed or fluid tight connector or connection such as a threa ded or luer fitting. Thus, as noted above, the blood isolation device 1600 is manufactured and sold as a single unit along with the patient needle and/or tubing and blood sample collection d evice such that the patient needle and blood sample collection device are connected to blood i solation during blood collection or sampling. The need to connect to device 1600 can be elimin ated.

[0084]

Blood isolation device 1600 is connected to sampling channel 1606 between inlet port 1602 and outlet port 1604, and at any location between inlet port 1602 and outlet port 1604, and s ampling channel 1606. and an isolation chamber 1608 that is isolated or diverted from. Sampl ing channel 1606 functions as a blood collection path once the first aliquot of blood is sequest ered in sequestration chamber 1608 . Sampling channel 1606 can be a channel or conduit of a ny size, shape or configuration. In some implementations, sampling channel 1606 has a cross -sectional area substantially similar to the opening of inlet port 1602 . In other implementatio ns, sampling channel 1606 can gradually widen from inlet port 1602 to outlet port 1604 . The isolation chamber 1608 widens toward the path of the isolation channel so that blood first atte mpts to enter the reservoir as opposed to entering the smaller diameter of the sampling chan nel 1606, as shown in more detail in FIGS. It can have a larger cross-section to form a reserv oir. In some exemplary implementations, the diversion between sampling channel 1606 and i solation chamber 1608 is accomplished by diversion junction 1607

.

Turning junction 1607 can be substantially Y-shaped, T-shaped, or U-shaped. In some preferr ed exemplary implementations, redirection junction 1607 is configured such that flow from inl et port 1602 is preferentially directed into isolation chamber 1608, as shown in FIGS. 17A-17 B. The isolation chamber 1608 can also include or form a bend or ramp to move the initial blo od flow toward and into the isolation chamber 1608 .

[0086]

The isolation chamber 1608 is preferably maintained at atmospheric pressure and includes a vent 1610 at or near the distal end of the isolation chamber 1608 . Vent 1610 can include an air permeable blood barrier 1612 as described above. Blood isolation device 1600 can includ e a housing 1601 that can be formed from multiple pieces or a single unitary piece

.

In some implementations, as shown in FIGS. 17A-17D and 18A-18F, housing 1601 includes an upper member 1620 and a lower member 1622 that fit together. Blood isolation device 1600 i ncludes a gasket or other sealing member (not shown) such that when upper member 1620 is mechanically attached to lower member 1622, the junction therebetween is sealed by the gas ket or sealing member. can also include 17A-17D show the lower member 1622 of the housing for the blood isolation device 1600. FIG. The lower member 1622 includes pre-formed groove s, channels, locks, conduits, such as by an injection molding process or by etching, cutting, dr illing, etc., to form the sampling channels 1606, the isolation chambers 1608, and the turning junctions 1607. or other routes.

Isolation chamber 1608

prevents blood from entering the smaller diameter of sampling channel 1606 .

, can have a larger cross-section than the sampling channel 1606 so as to preferentially move into the isolation chamber first.

FIGS.

18A-18F may be attached by any mating or connecting mechanism such as using laser weldi ng, thermal bonding, gluing, screws, rivets, bolts, etc., or latches, grooves, tongues, pins, flan ges. Upper member 1620 is shown connectable with lower member 1622 by other mating me chanisms such as. Top member 1620 can include some or all of grooves, channels, locks, con duits or other pathways to form sampling channels 1606 , isolation chambers 1608 and turnin g junctions 1607 . In still other implementations, both upper member 1620 and lower membe r 1622 can include grooves, channels, locks or other pathways.

[0090]

In some implementations, sampling channel 1606 and isolation chamber 1608 are formed b y grooves, channels, locks or other pathways formed in housing 1601 . Housing 1601 can be made of rubber, plastic, metal or any other suitable material. Housing 1601 can be formed fro m a transparent or translucent material, or from an opaque or non-translucent material. In ot her implementations, housing 1601 can be largely opaque or non-translucent, but housing sur faces directly adjacent sampling channel 1606 and/or isolation chamber 1608 can be transpa

ent or translucent. There may be first a visual cue or sign that the isolation chamber 1608 is fi lled to the required or desired degree, and/or a subsequent isolation while a clean blood samp le is taken through the sampling channel 1606. Gives the practitioner a visual cue or sign that the sequestered blood remains sequestered. Other visual cues or signs of isolation include, bu t are not limited to, contact, penetration, or partial penetration of blood, causing the air perm eable blood barrier 1612 to turn a different color; Color-coded tabs or indicators at any locatio n along or adjacent to the isolation chamber, audible, vibratory, or other signals may be includ ed.

[0091]

The air permeable blood barrier 1612 can be covered or surrounded by a protective member 1616, as shown in FIGS. 18A-18F. Protective member 1616 can be sized and configured to pre vent a user from touching air permeable blood barrier 1612 with their fingers or other externa l instruments, while still allowing air to be expelled from isolation chamber 1608. Occasionally allow air to exit the air permeable blood barrier 1612 . In some implementations, protective member 1616 includes protrusions that extend from the top surface of top member 1620 up a nd around air permeable blood barrier 1612 . The protective cover 1616 can be configured to block or prevent accidental exposure of the filter to ambient fluids or splashes. This can be do ne in a variety of mechanical ways, including but not limited to adding a hydrophobic membra ne to the protective cover. In use, blood isolation device 1600 includes sampling channel 160 6 and isolation chamber 1608

.

Both pathways are initially filled with air at atmospheric pressure, but the sampling channel 1 606 is initially sealed by a Vacutainer® or other such sealed blood collection device at the outl et port 1604. , the isolation chamber 1608 terminates in a vent 1610 to the atmosphere that i ncludes an air permeable blood barrier 1612 .

[0093]

After venipuncture with a patient needle (not shown), which can collect many pathogens fro m the patient's skin, an initial volume of the patient's blood with these pathogens passes thro ugh inlet port 1602 of blood isolation device 1600 . do. This initial volume of potentially conta minated blood preferentially enters isolation chamber 1608 by finding the path of least resista nce. The patient's own blood pressure overcomes the atmospheric pressure in the vented isol ation chamber 1608 and expels the air in the isolation chamber 1608 through the air permeab le blood barrier 1612, while the air pressure builds up in the sealed sampling channel 1606. is insufficient to overcome the various exemplary

In some embodiments, isolation chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome the eff ects of gravity regardless of the orientation of the blood isolation device. can.

Ultimately

, the isolation chamber 1608 fills with blood that drives air out through the air permeable b

od barrier 1612 . When blood contacts the air permeable blood barrier, the blood interacts wit h the material of air permeable blood barrier 1612 to completely or partially seal vent 1610 . A signal or indication can be provided that the practitioner can now utilize the Vacutainer® or other blood collection device. Upon filling blood isolation channel 1608 and prior to use of a Vacutainer® or other blood sampling device, the patient's blood pressure causes compression of air within sampling channel 1606, possibly a small amount

.

of blood moves past the turning point into sampling channel 1606 , queuing clean blood to be drawn through sampling channel 1506 .

FIG .

19A is a side view of blood isolation device 1600 and FIG. 19B is a cross-sectional view of bl ood isolation device 1600 showing upper member 1620 mating with lower member 1622 .

[0097]

FIG. 20 illustrates a patient needle 2002 for vascular access to a patient's bloodstream, a blo od sample collection device 2004 that facilitates the collection of one or more blood samples, and the patient needle 2002 and blood sample collection device 2004. A blood sample optimiz ation system 2000 is shown including a conduit 2006 providing a fluid connection between. In some implementations, the blood sample collection device 2004 includes a protective shield th at includes a sealed collection needle such that once a sealed vacuum container is placed on t he collection needle and the container is pierced once by the collection needle, the patient nee dle is exposed to the patient needle. A blood sample is drawn from 2002 through conduit 200 6 with vacuum pressure or force.

Blood sample optimization system 2000

further includes a blood isolation device 2008 located at any point on conduit 2006 between patient needle 2002 and blood sampling device 2004, as described herein. .

FIG.

21 shows a non-vented blood isolation device 2100 that uses wicking material chambers. Blo od isolation device 2100 includes a housing 2101 having a sampling channel 2104 at least par tially surrounded or abutted by an isolation chamber 2102 filled with wicking material. A first aliquot of blood is drawn from the patient needle into the sampling channel 2104 where it im mediately escapes into the wicking material of the isolation chamber 2102 . The wicking mate rial and/or isolation chamber 2102 is filled with a predetermined volume such that subsequent or subsequent blood draws flow past the wicking material and through the sampling channel 2 104 directly to a sampling device such as a vacutainer. Dimensioned and adapted to receive a nd retain blood. The wicking material can include substances such as solidifying agents, decon taminating agents, or other additives.

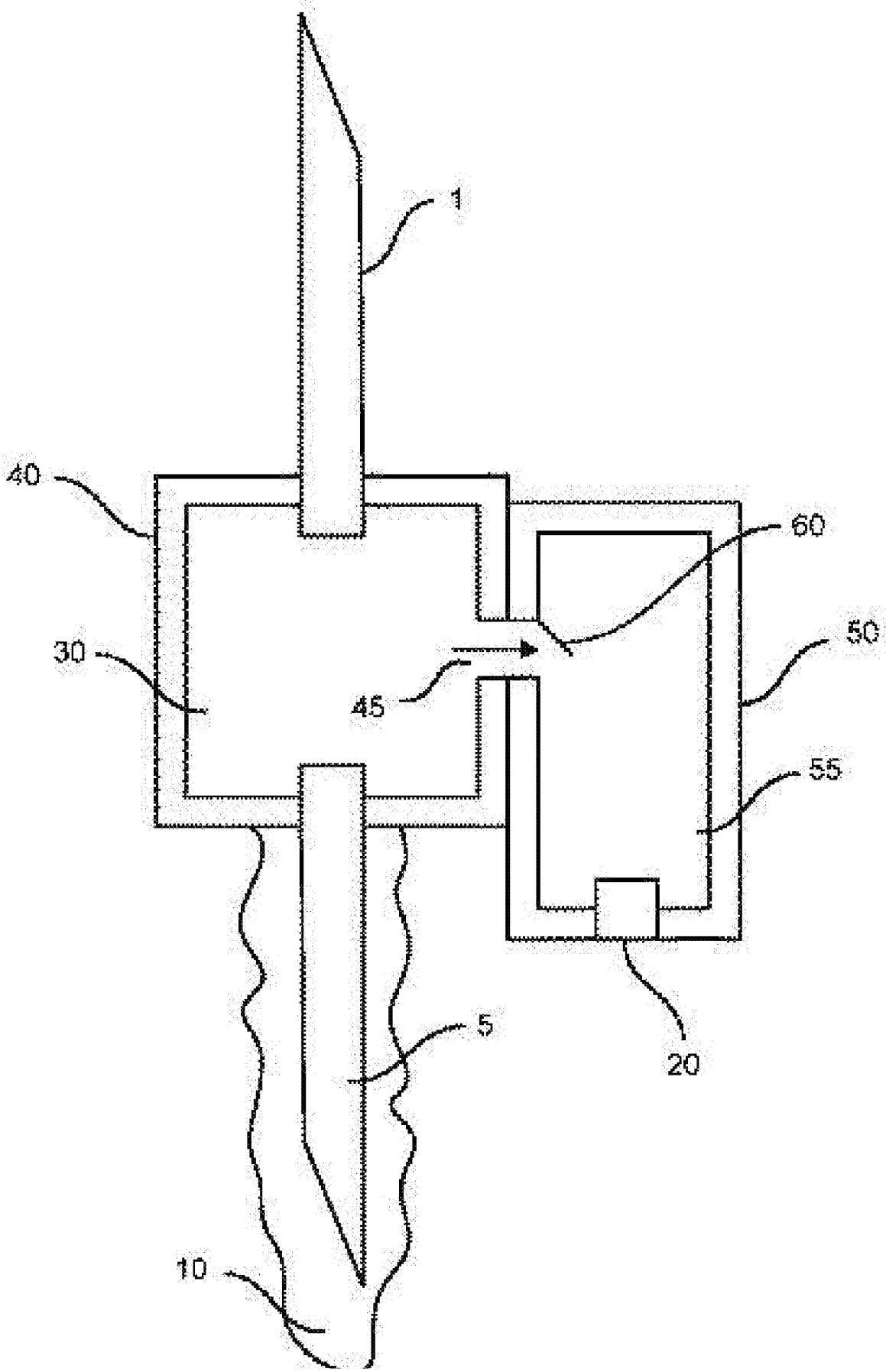
[0100]

As described herein, air permeable blood barriers can be made using a wide variety of differ ent structures and materials. As shown in Figures 22A and 22B, an air permeable blood barr

r 2202 of a blood isolation device 2200 can include a polymeric bead matrix 2204 that has be en treated to render at least some of the beads hydrophilic. Air permeable blood barrier 2202 further comprises a self-sealing material 2206 such as carboxymethylcellulose (CMC) or cellul ose gum, or other sealing material. Air permeable blood barrier 2202 may further include void s 2208 that allow air flow prior to or during partial contact with a fluid such as blood. Self-seal ing material 2206 expands upon contact with fluid, as shown in FIG. 22B.
Tightens to close void 2208, occluding air flow through void 2208, and completely or partially sealing. Figures 23A and 23B show an entry port 2302 for connection with a patient needle, an exit port 2304 for connection with a blood sampling device, an isolation chamber 2306, an isolation chamber 2306, and a contaminant to be isolated
.
23 shows yet another implementation of the blood isolation device 2300 having a sampling ch annel 2308 that bypasses the isolation chamber 2306 once the isolation chamber is filled to th e first aliquot of blood that may be present. Isolation chamber 2306 includes a hydrophobic pl ug 2312 at the distal end of isolation chamber 2306 furthest from inlet port 2302 . A vacuum or other suction force applied from outlet port 2304, such as from a Vacutainer®, draws blood into inlet port 2302 and directly into isolation chamber 2306, where the first aliquot of blood i s removed. Contacting the hydrophobic plug 2312, the first aliquot of blood is returned to the sequestration chamber 2306 where it is sequestered. A small amount of blood can enter samp ling channel 2308 which is initially closed by valve 2308 . When valve 2308 is released, a subs equent volume of blood, under additional vacuum or other force, flows into inlet port 2302, by passes isolation chamber 2306, and through sampling channel 2308 to outlet port 2304. flow towards and sent to the collection device. Sampling channel 2308 can have any suitable geo metry and can be formed from plastic tubing or any other suitable material
.
Valve 2308 can be a clip or other enclosing device to pinch, deflect, bend, or otherwise close t he sampling channel before the first aliquot of blood is sequestered in sequestration chamber 2306 . can.
[0103]
While various embodiments have been described in detail above, other modifications are pos sible. Other embodiments may be within the scope of the following claims.

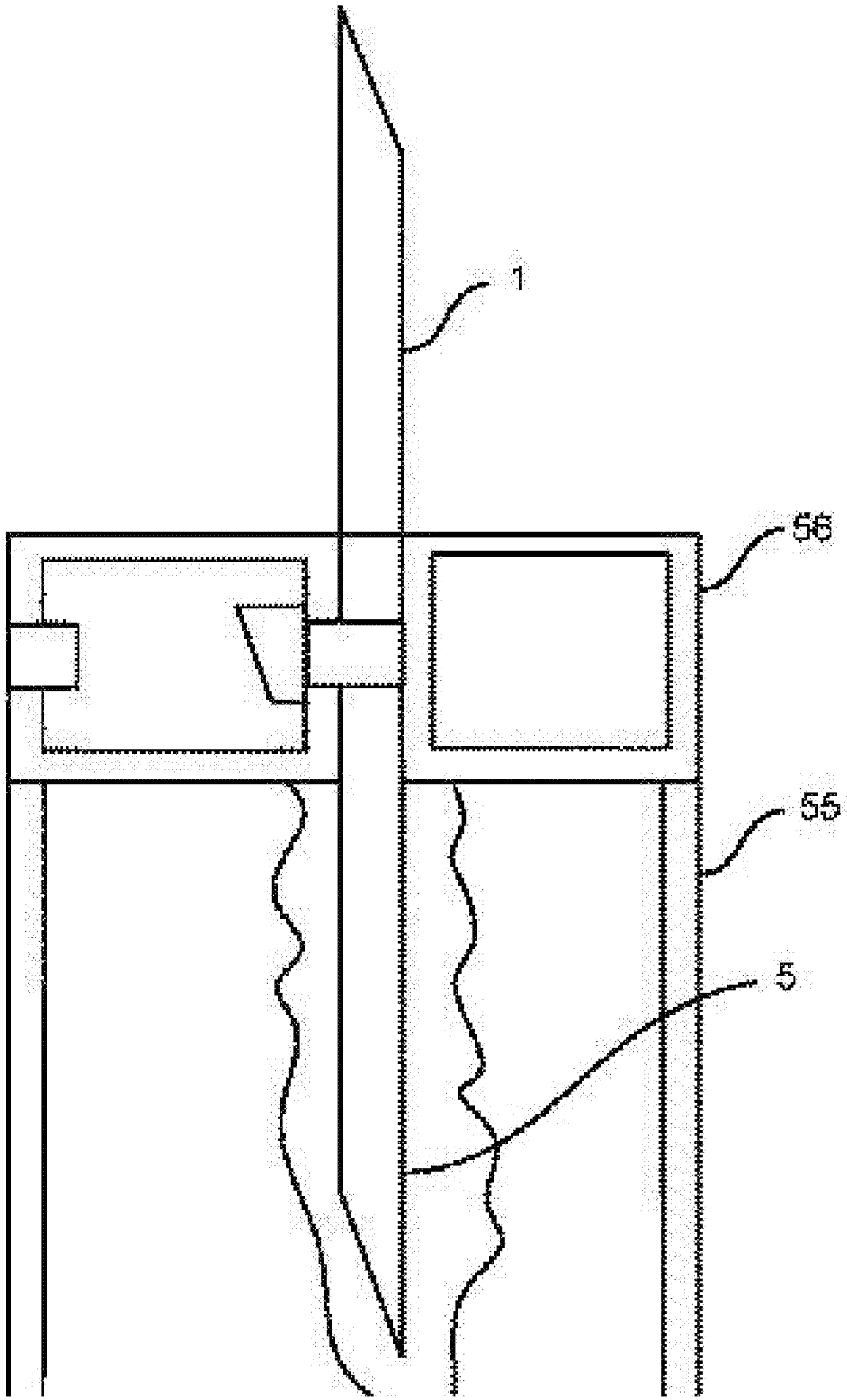
drawing open —

[Fig. 1]


1
40
60
30
50
45
55
5
20
10

[Figure 2]

FIG. 1


1
56
55
5

[Figure 3]

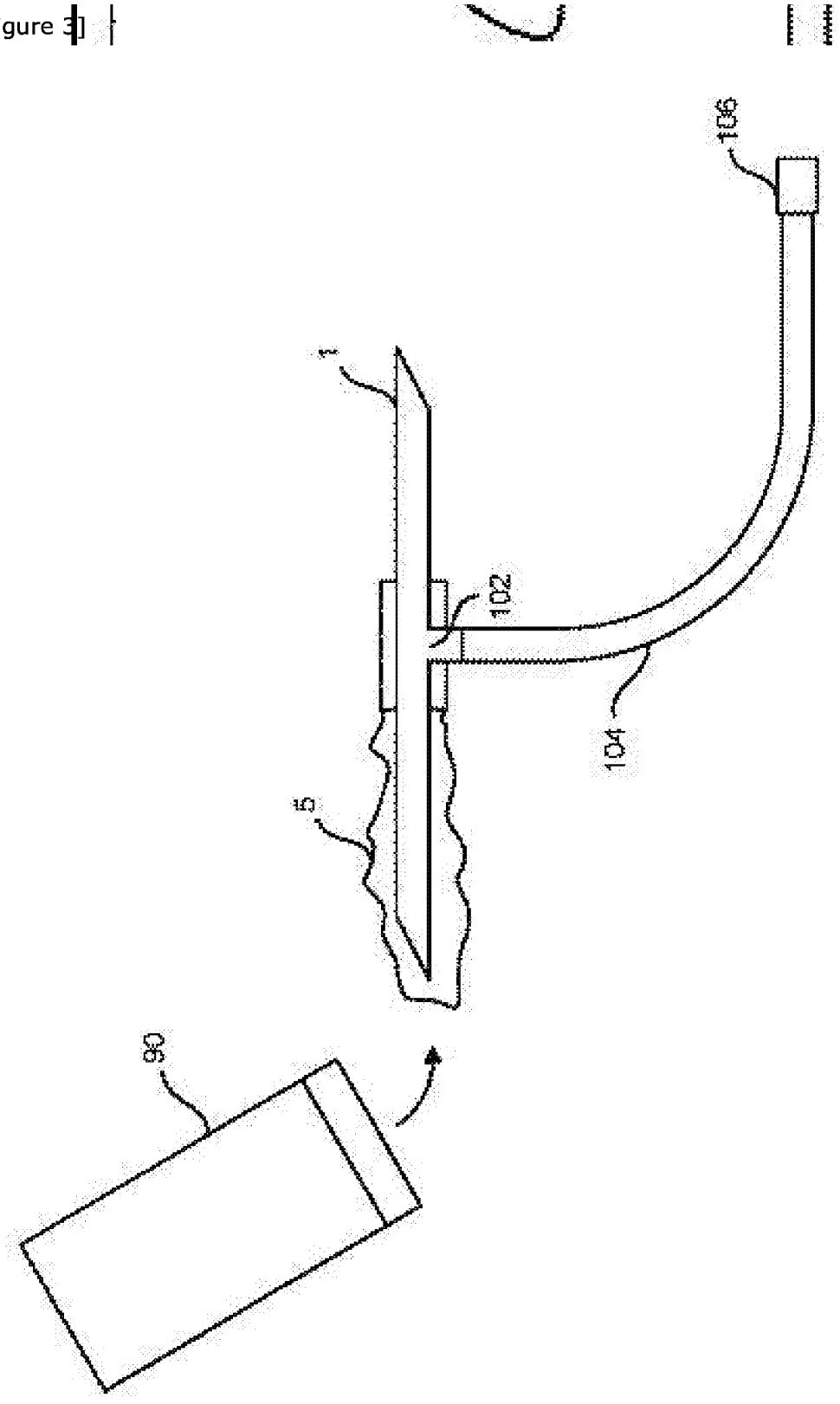


FIG. 3

[Figure 4]

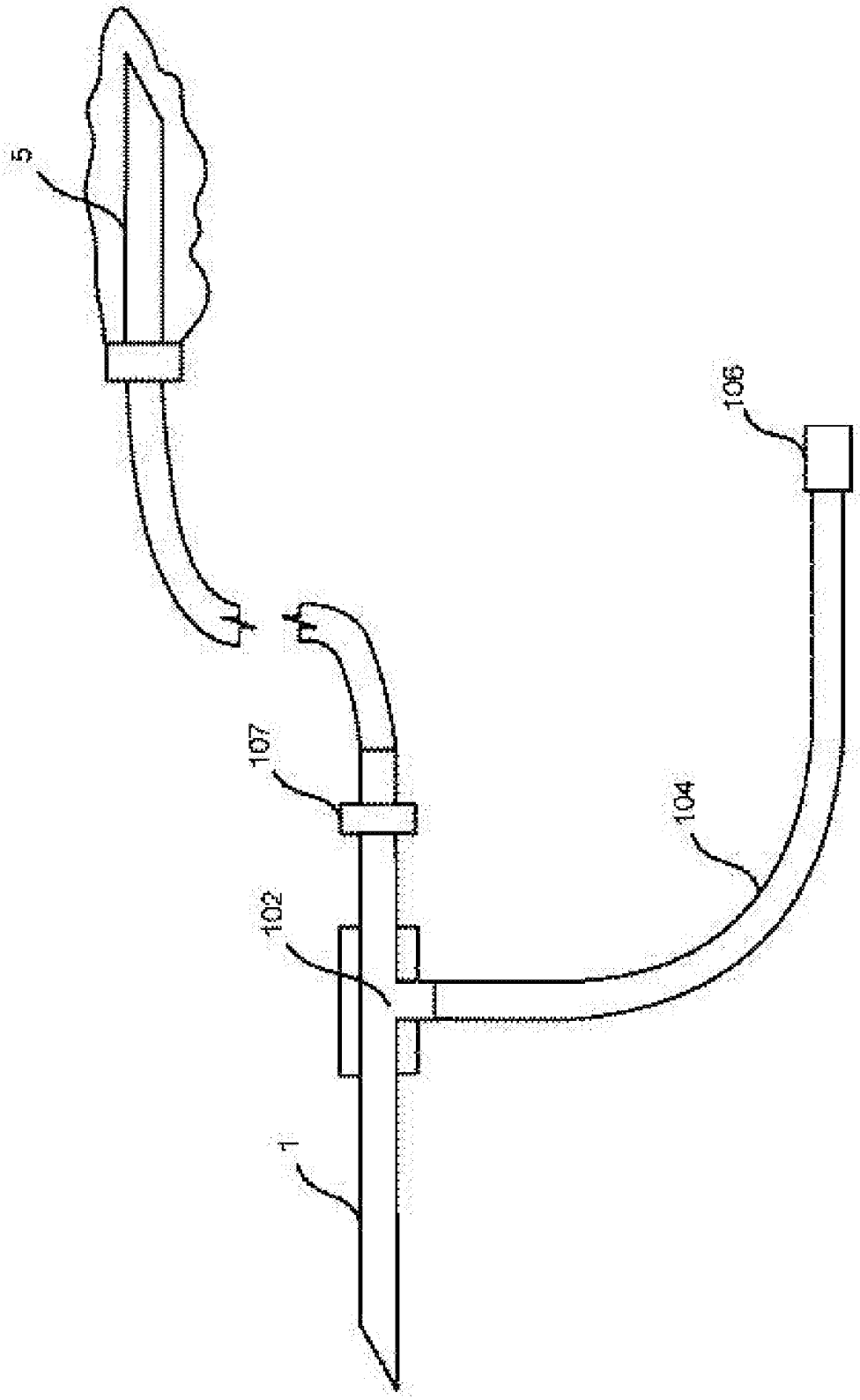


FIG. 4

[Figure 5]

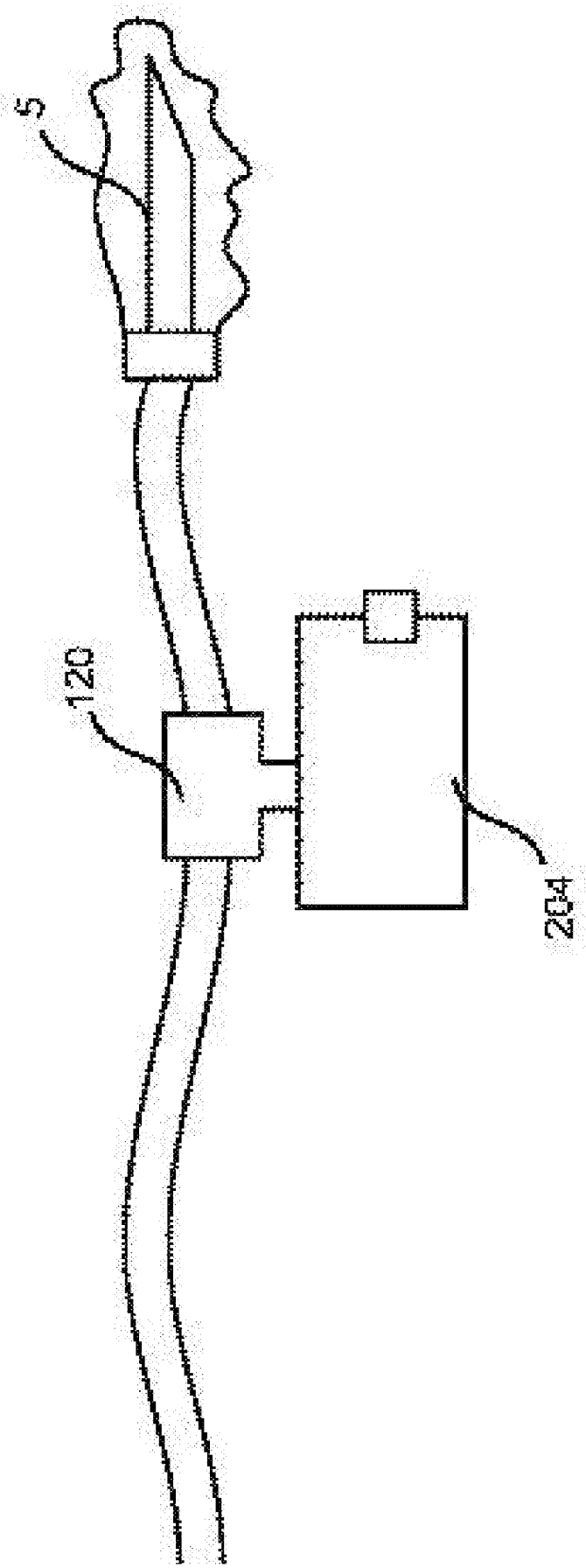
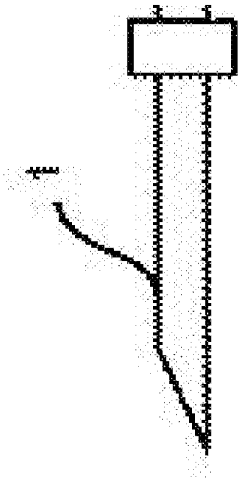


FIG. 5

[Fig. 6]



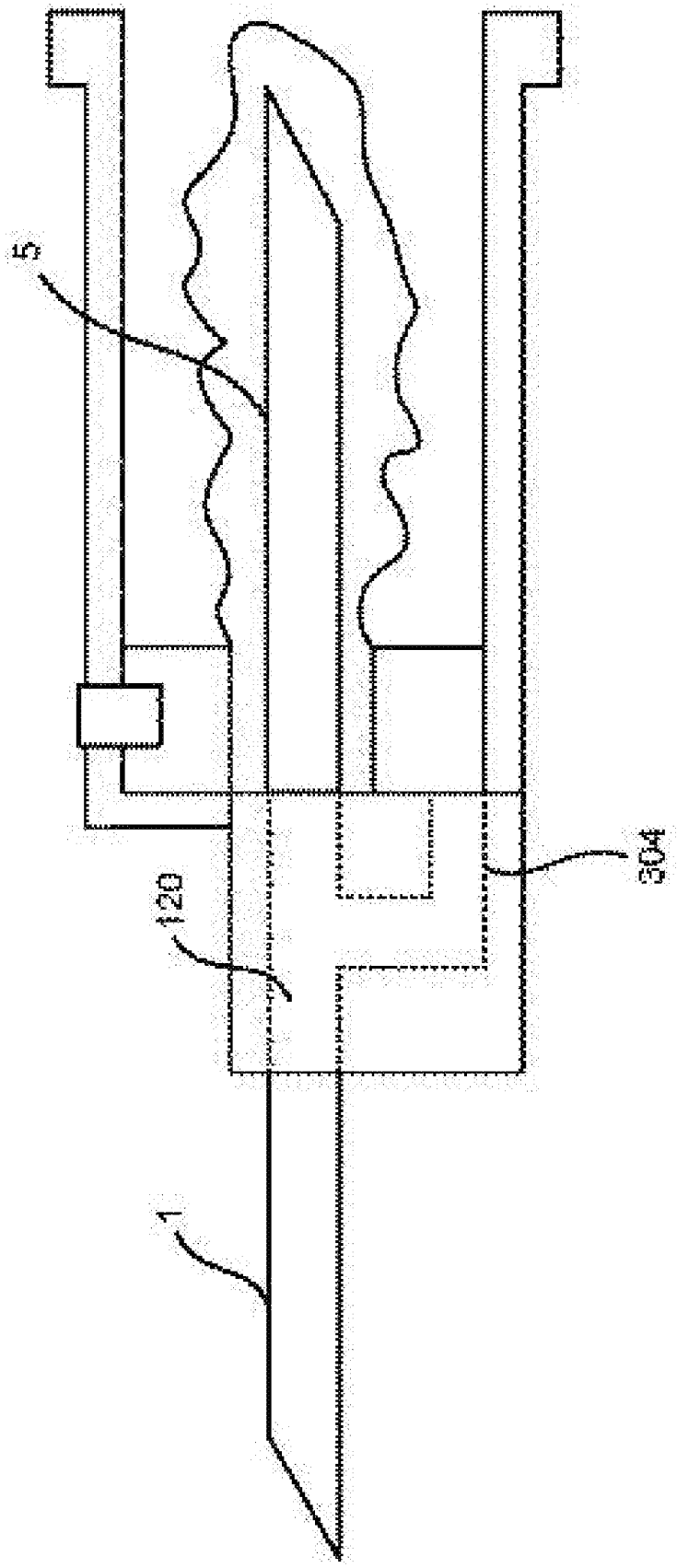


FIG. 6

[Fig. 7]

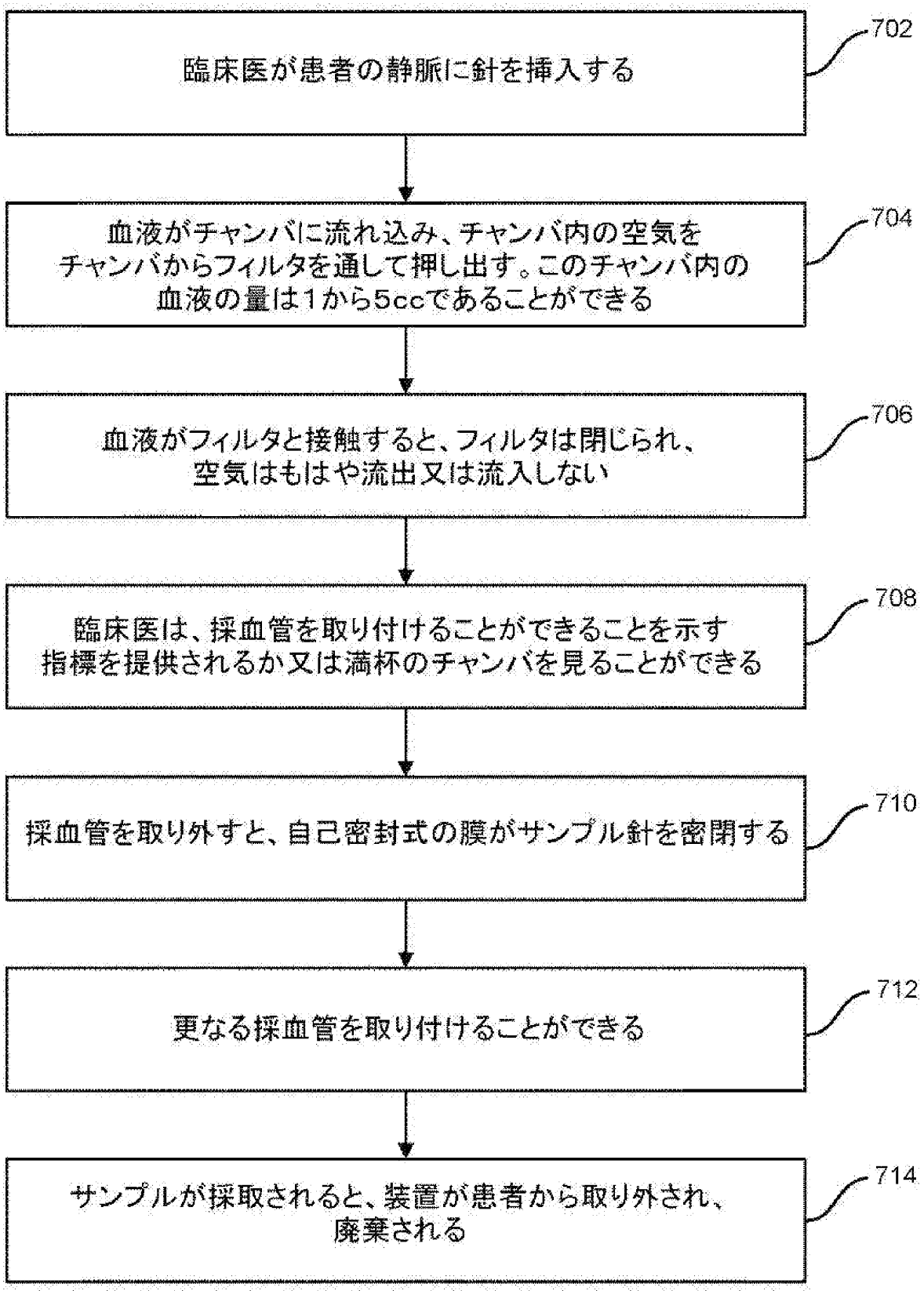
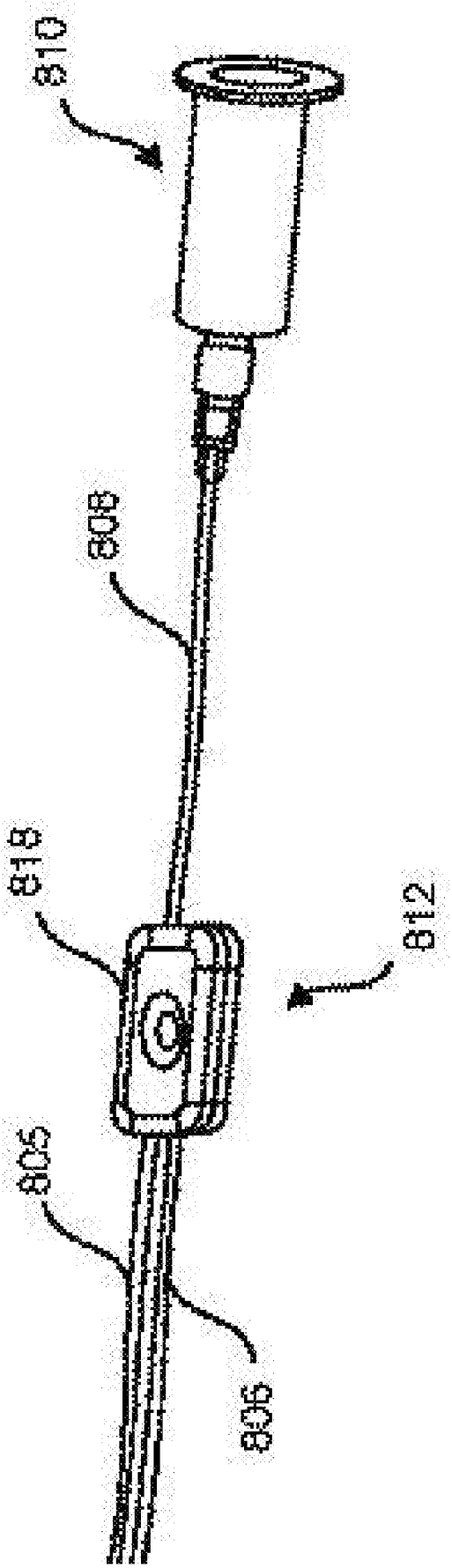

臨床医が患者の静脈に針を挿入する
702
血液がチャンバに流れ込み、チャンバ内の空気を
チャンバからフィルタを通して押し出す。このチャンバ内の
血液の量は1から5ccであることができる
704
血液がフィルタと接触すると、フィルタは閉じられ、
空気はもはや流出又は流入しない
706
臨床医は、採血管を取り付けることができることを示す
指標を提供されるか又は満杯のチャンバを見ることができる
708
採血管を取り外すと、自己密封式の膜がサンプル針を密閉する
710
更なる採血管を取り付けることができる
712
サンプルが採取されると、装置が患者から取り外され、
廃棄される
714

FIG. 7

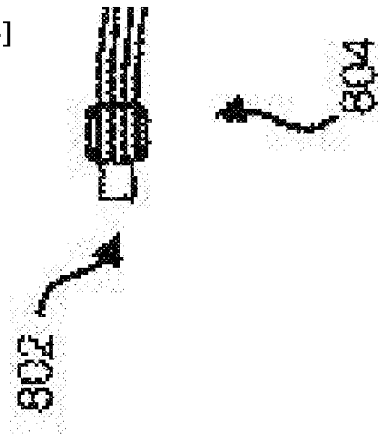
[Fig. 8A]



803

FIG. 8A

[Fig. 8B]



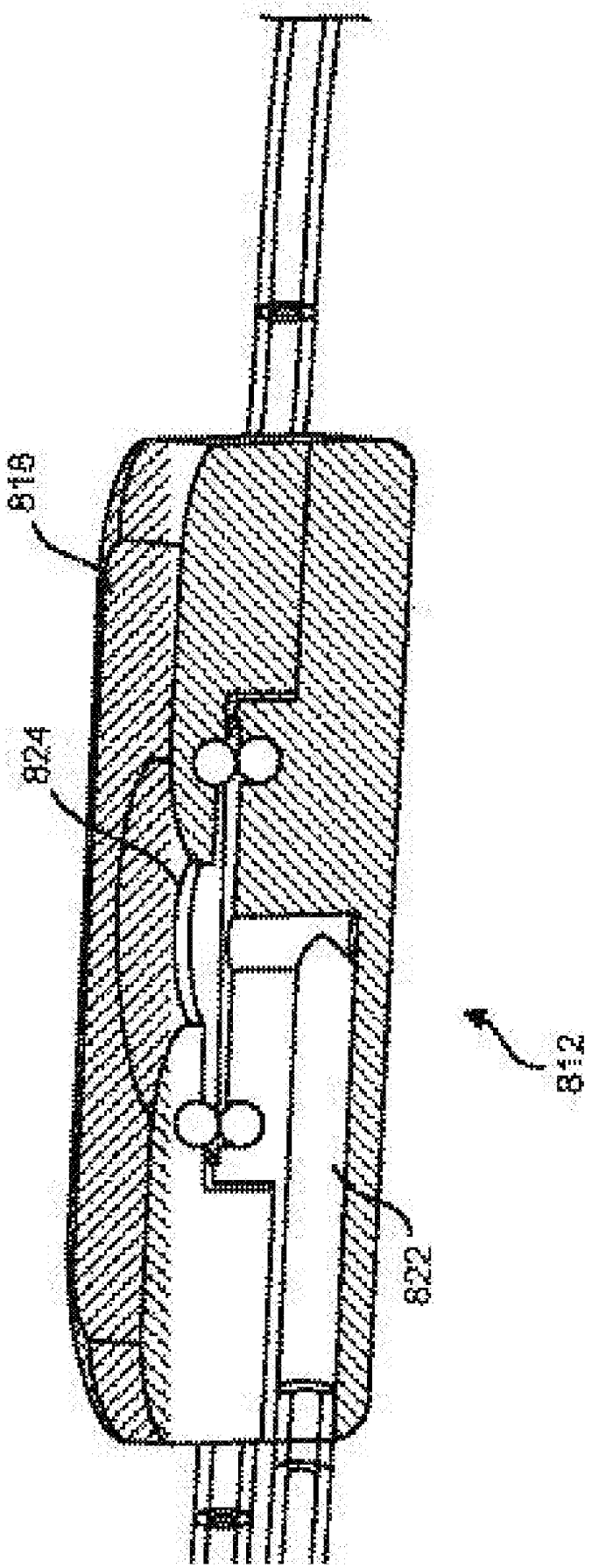
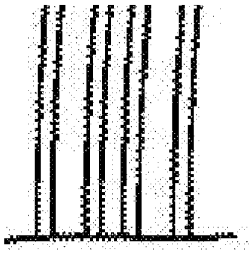


FIG. 8B

[Fig. 8C]



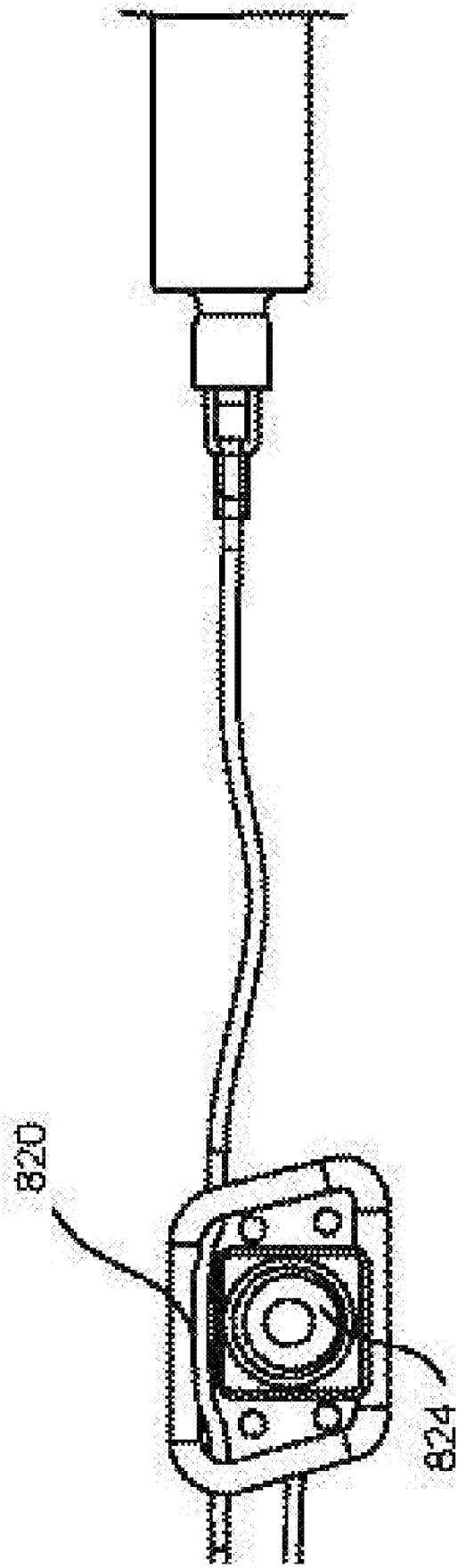
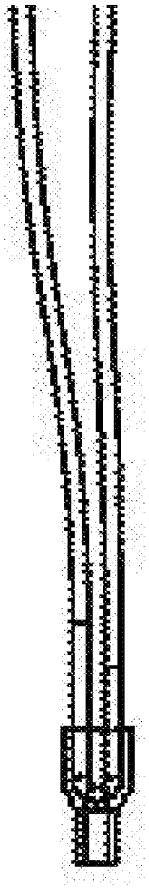


FIG. 8C

[Fig. 8D]



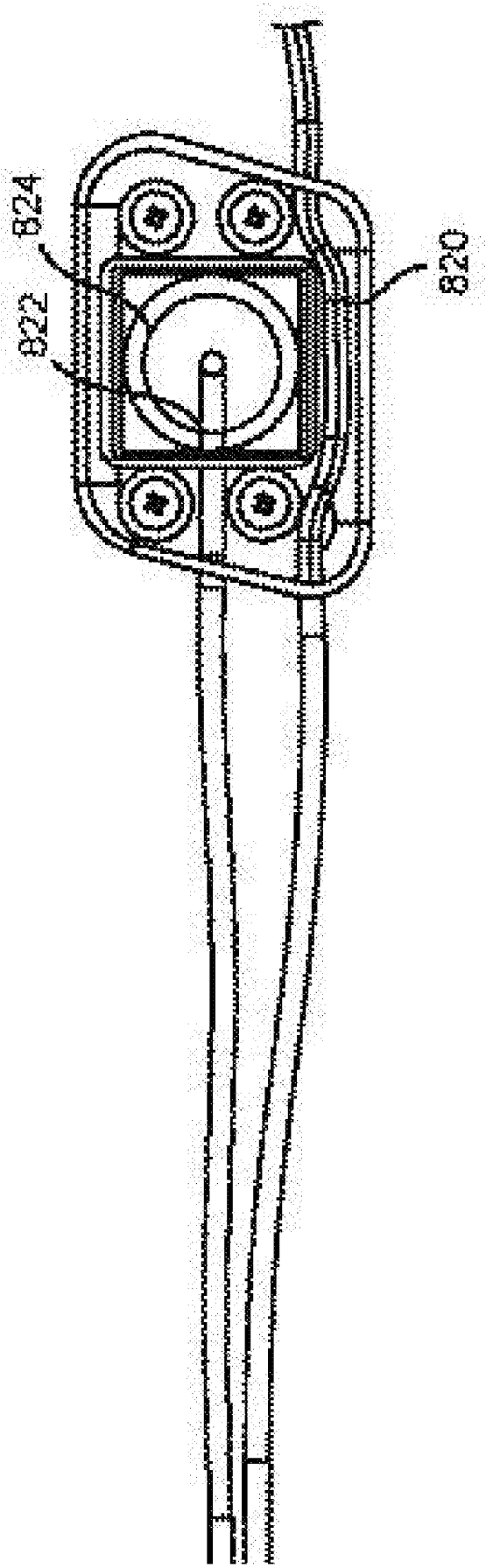
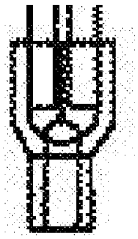


FIG. 8D

[Fig. 8E]



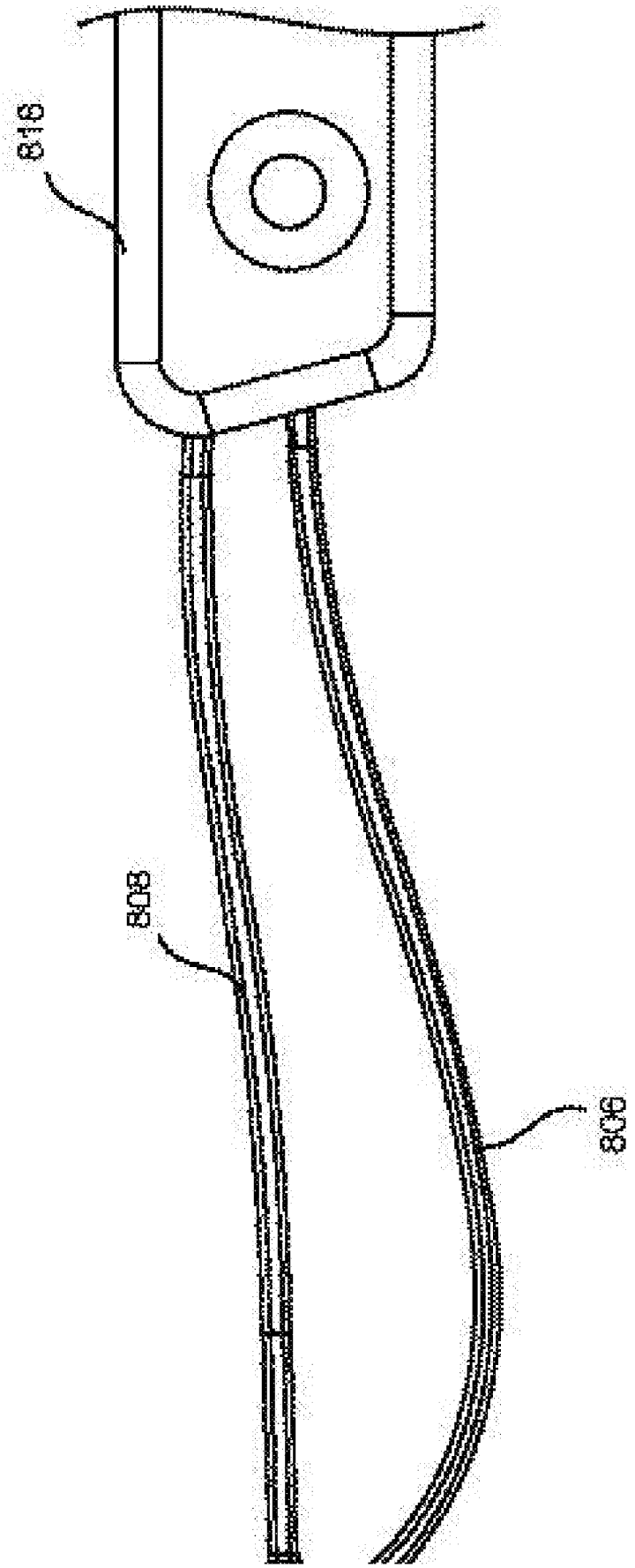
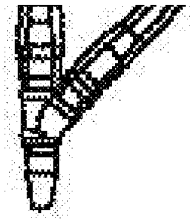


FIG. 8E

[Fig. 9]



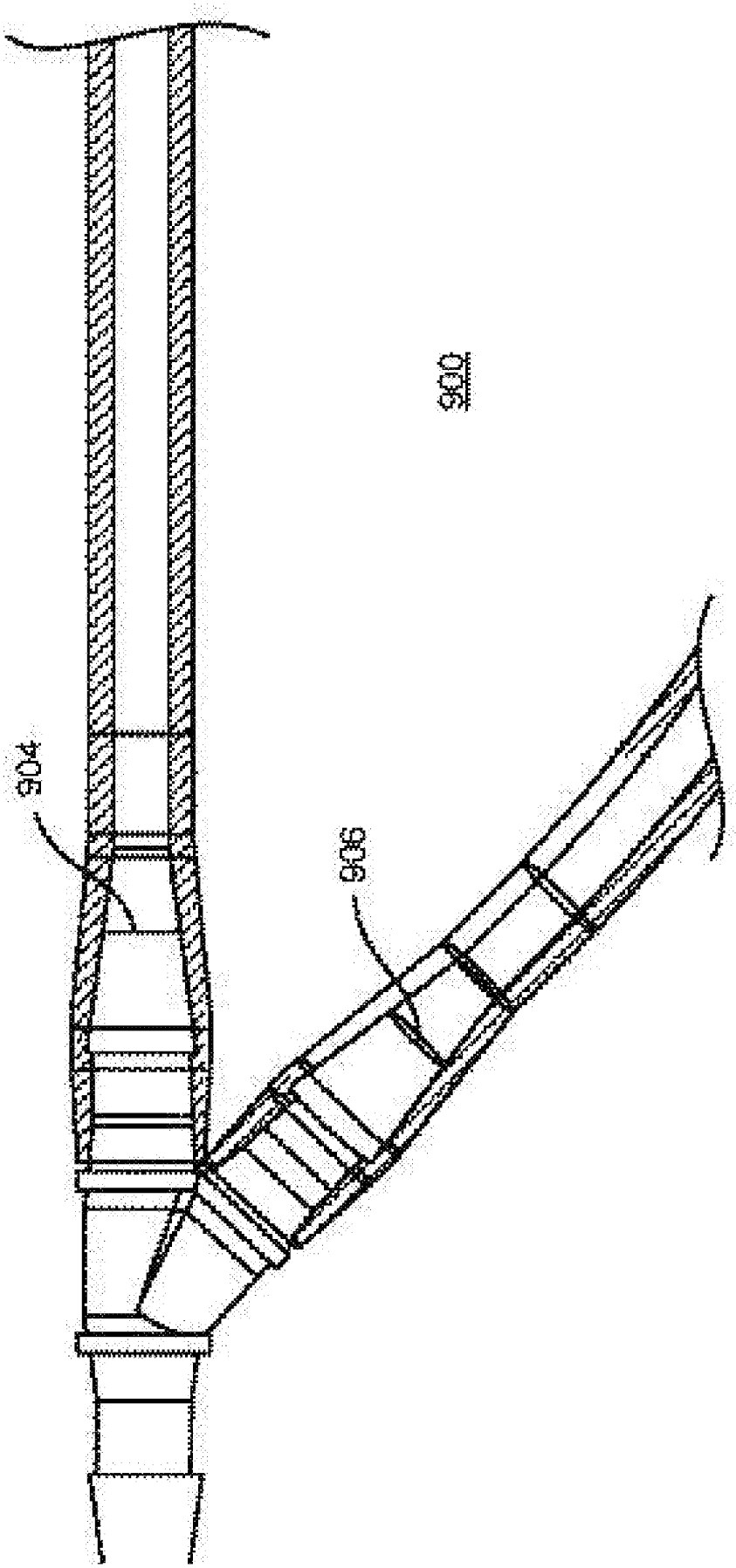


FIG. 9

[Fig. 10A]

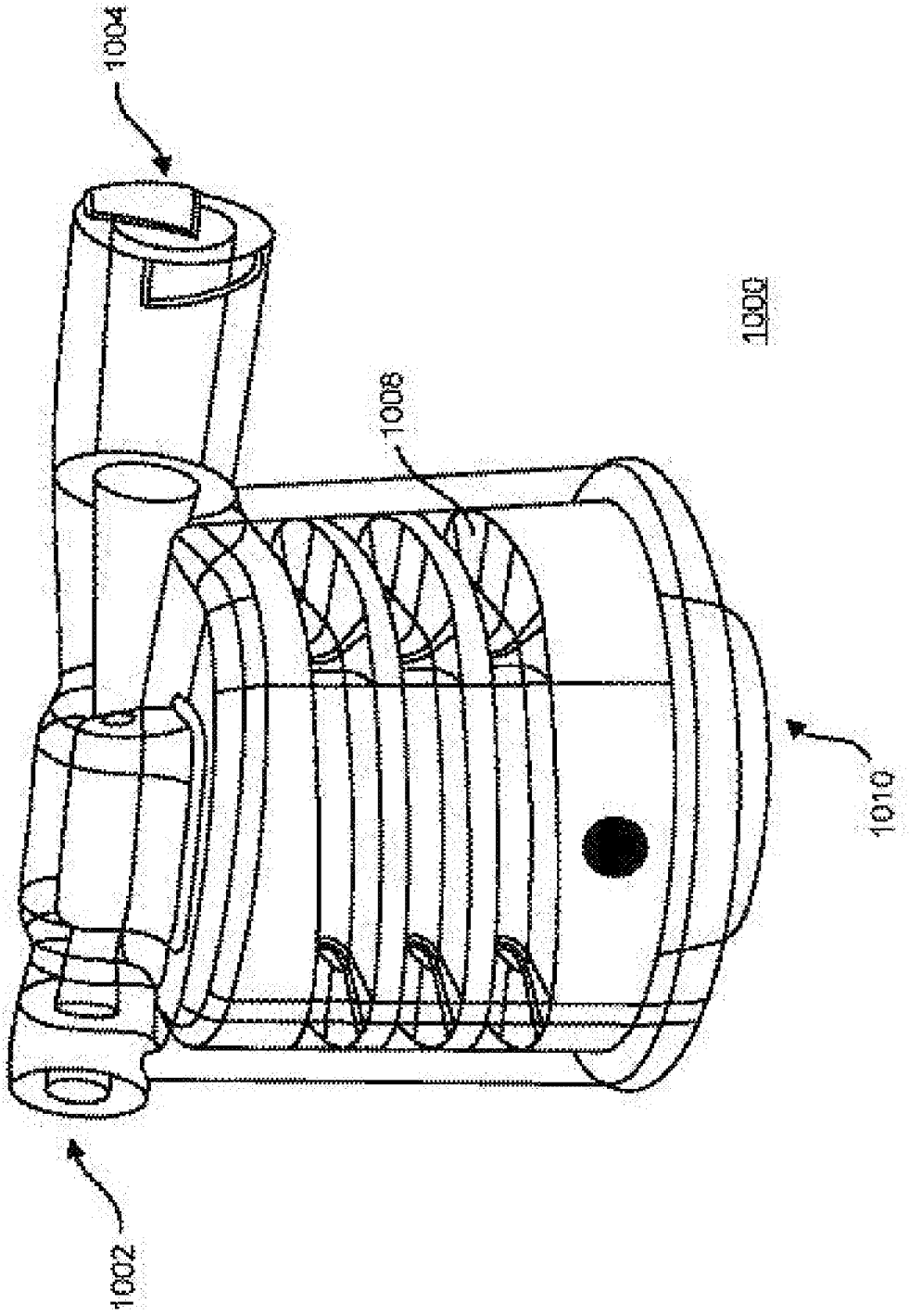


FIG. 10A

[Fig. 10B]

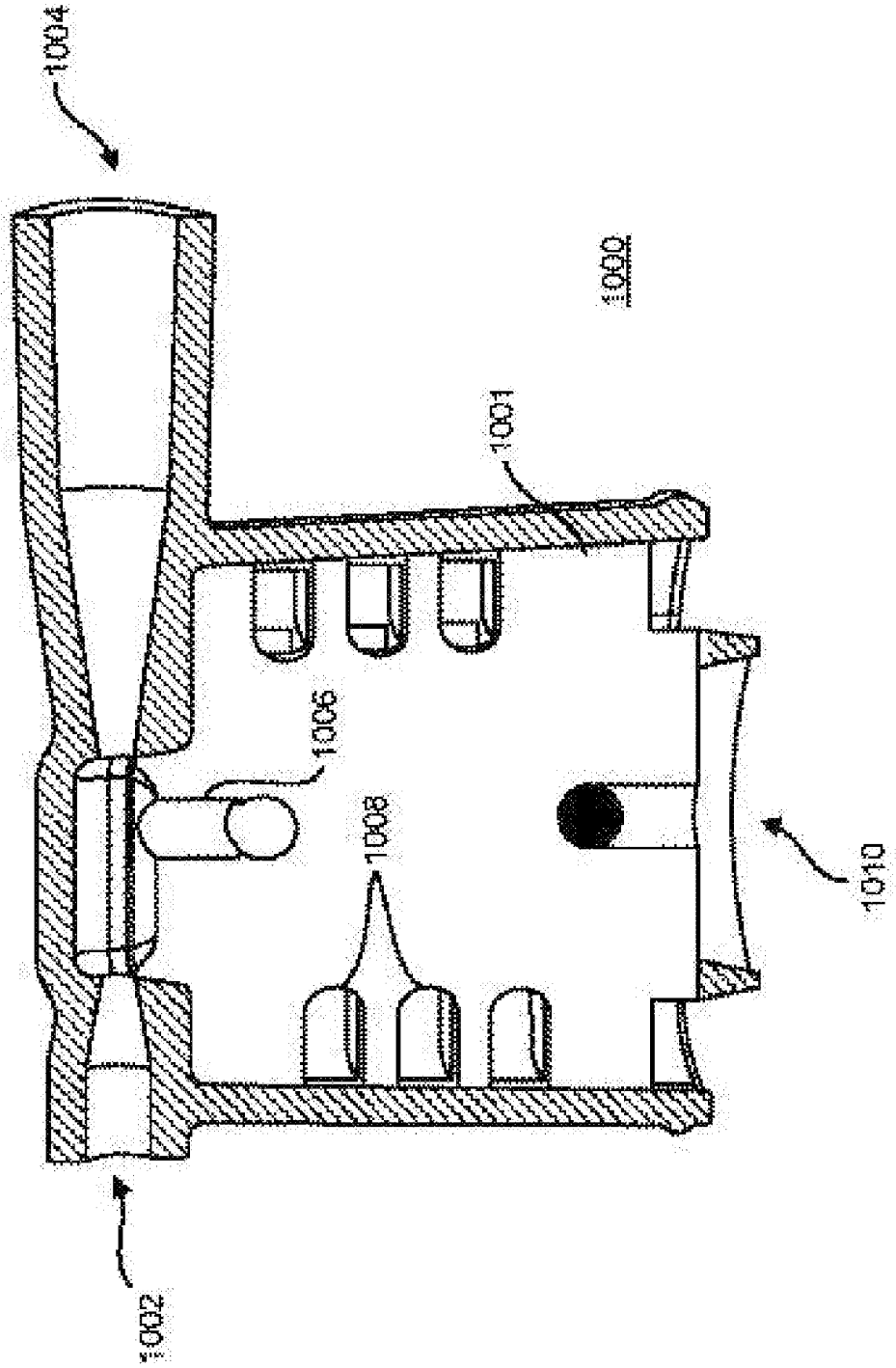
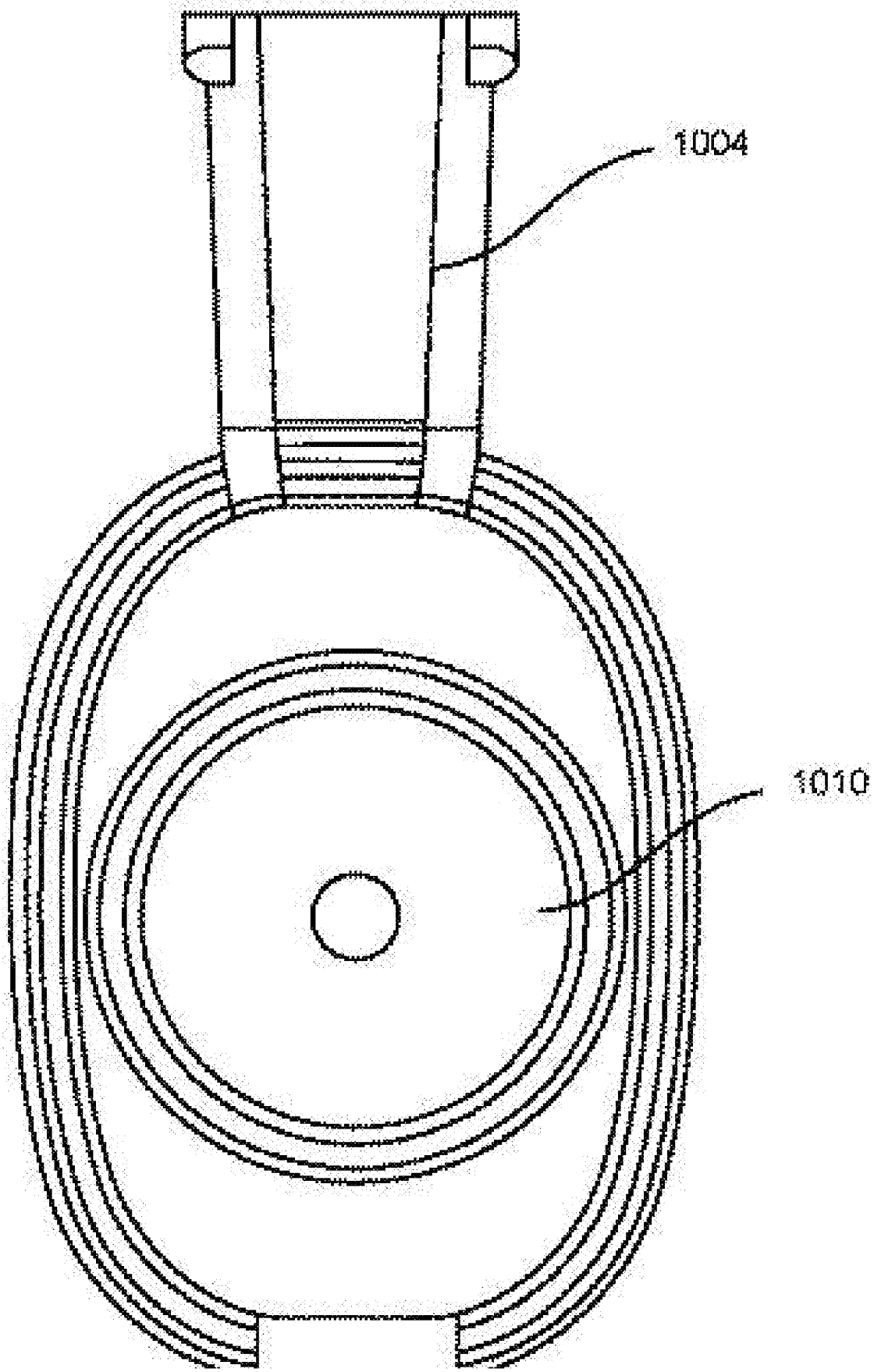


FIG. 10B

[Fig. 10C]


1004
1010

[Fig. 10D]

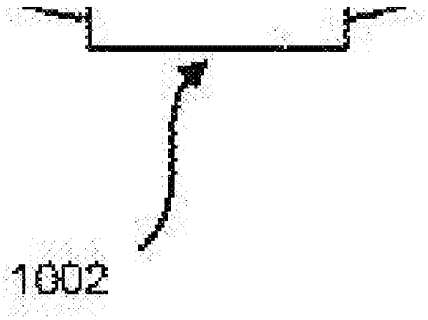
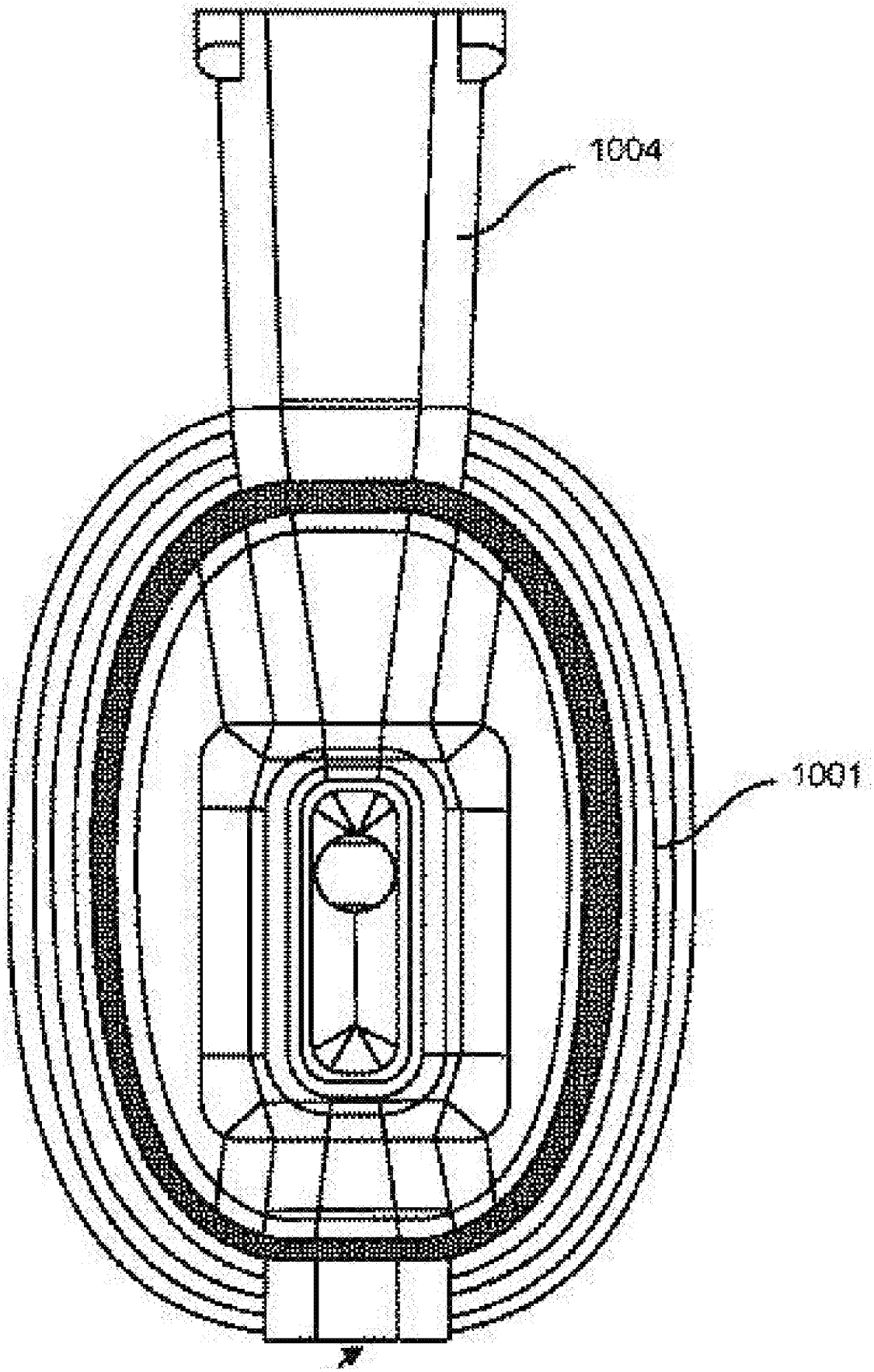


FIG. 10C


1004
1001

[Fig. 11A]

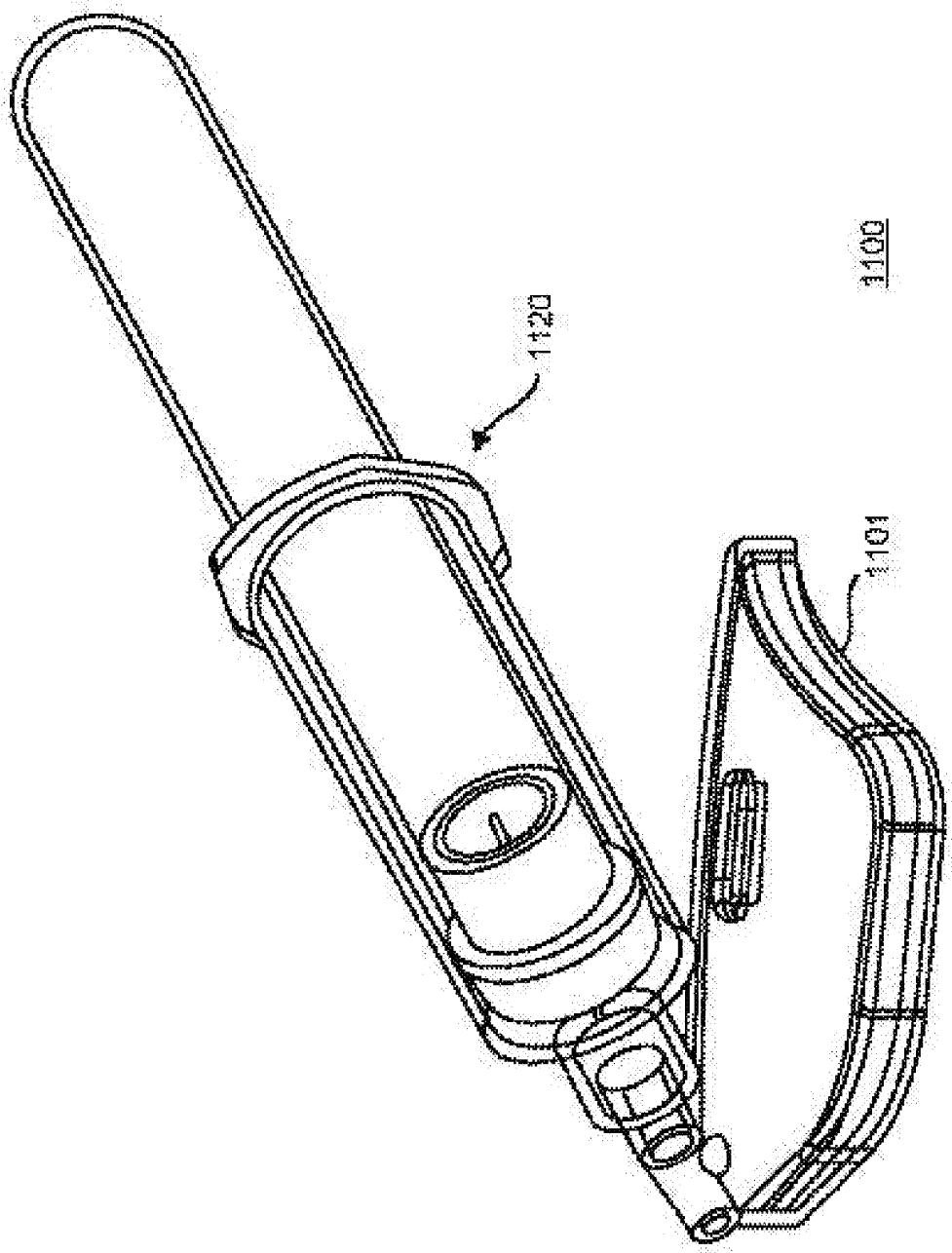


FIG. 11A

[Fig. 11B]

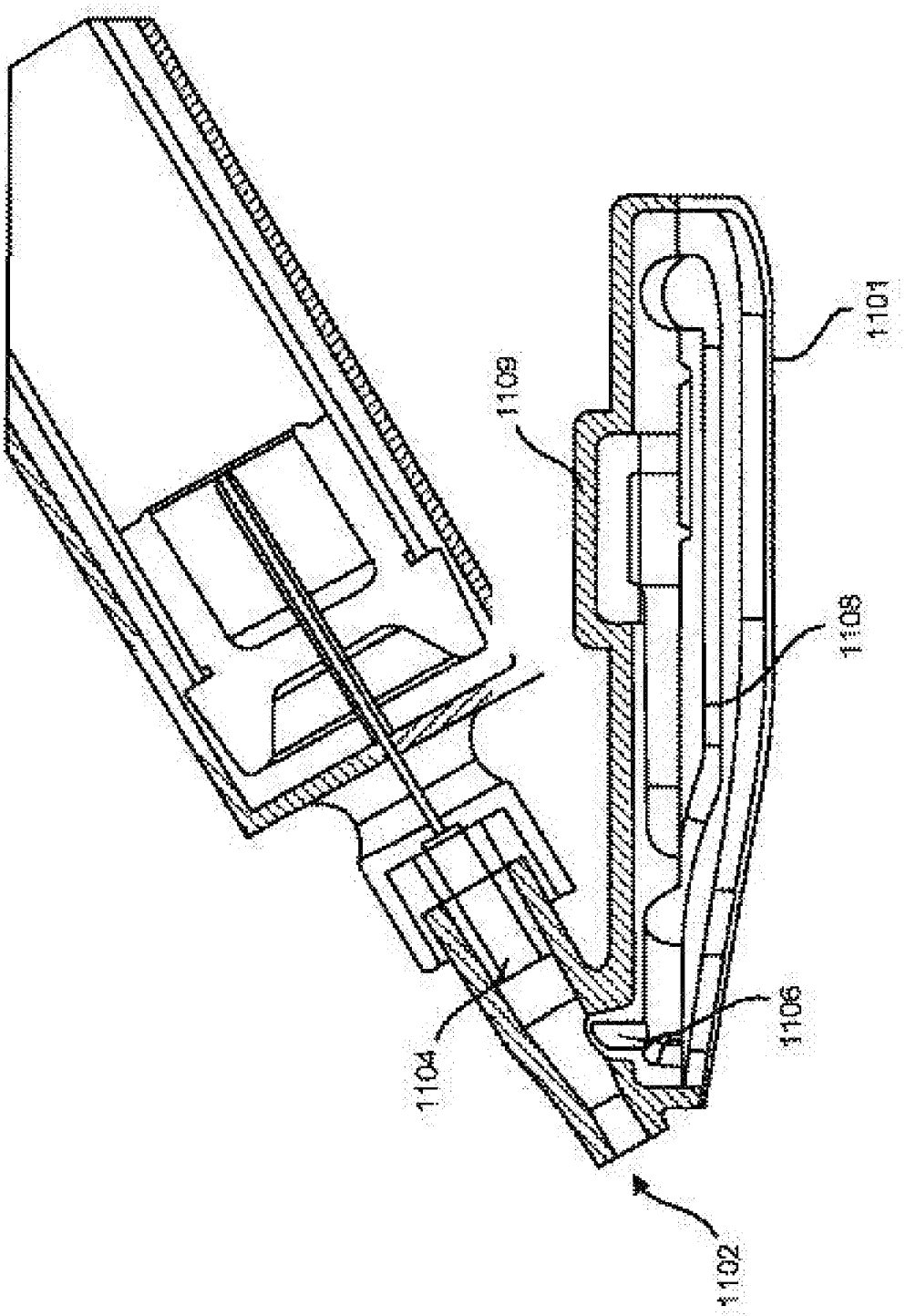
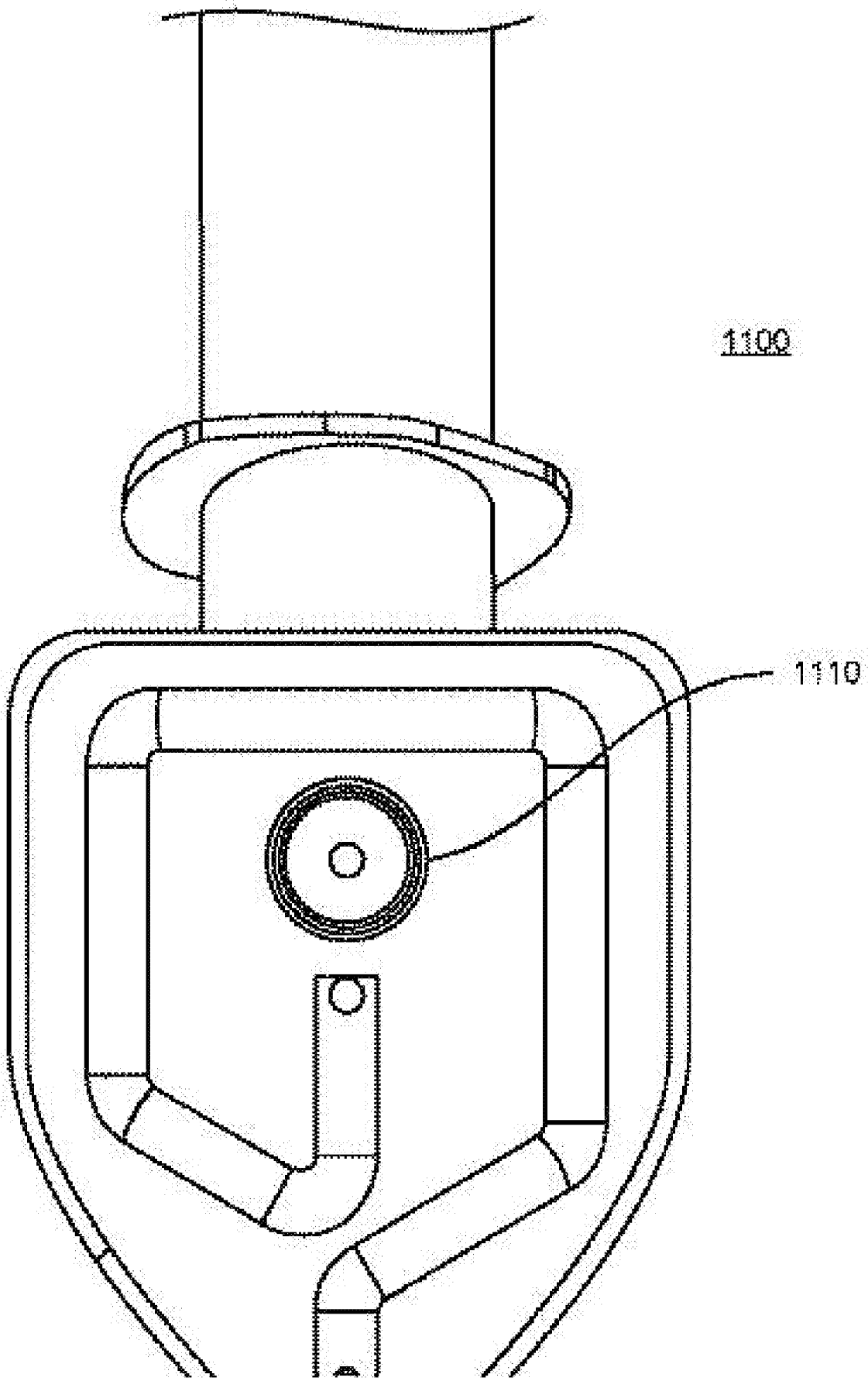


FIG. 11B

[Fig. 11C]


1100
1110

[Fig. 11D]

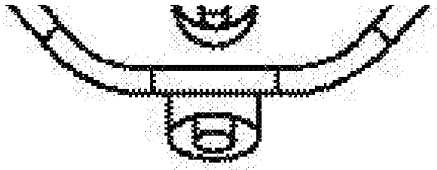
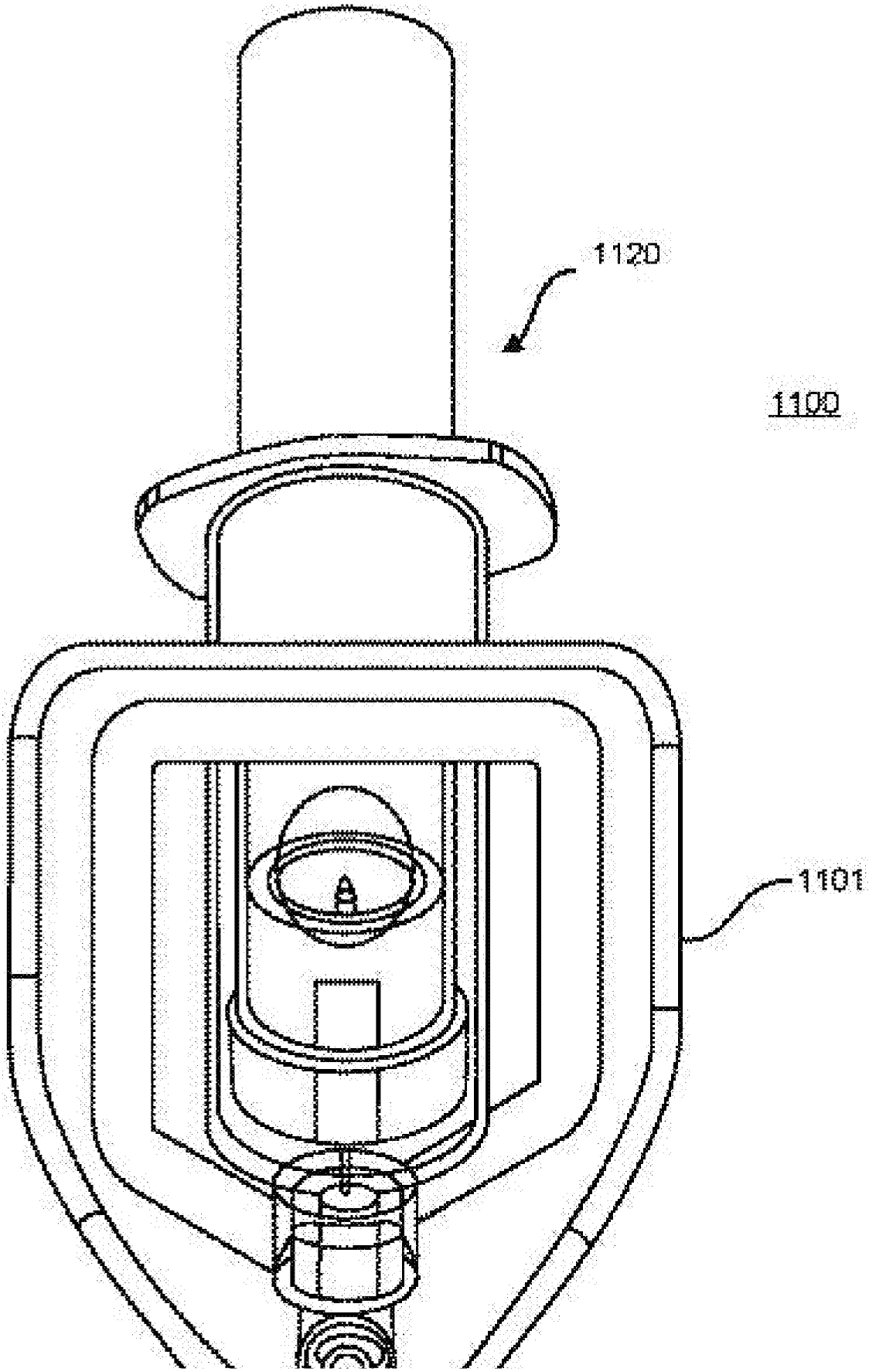


FIG. 11C


1120
1100
1101

[Fig. 11E]

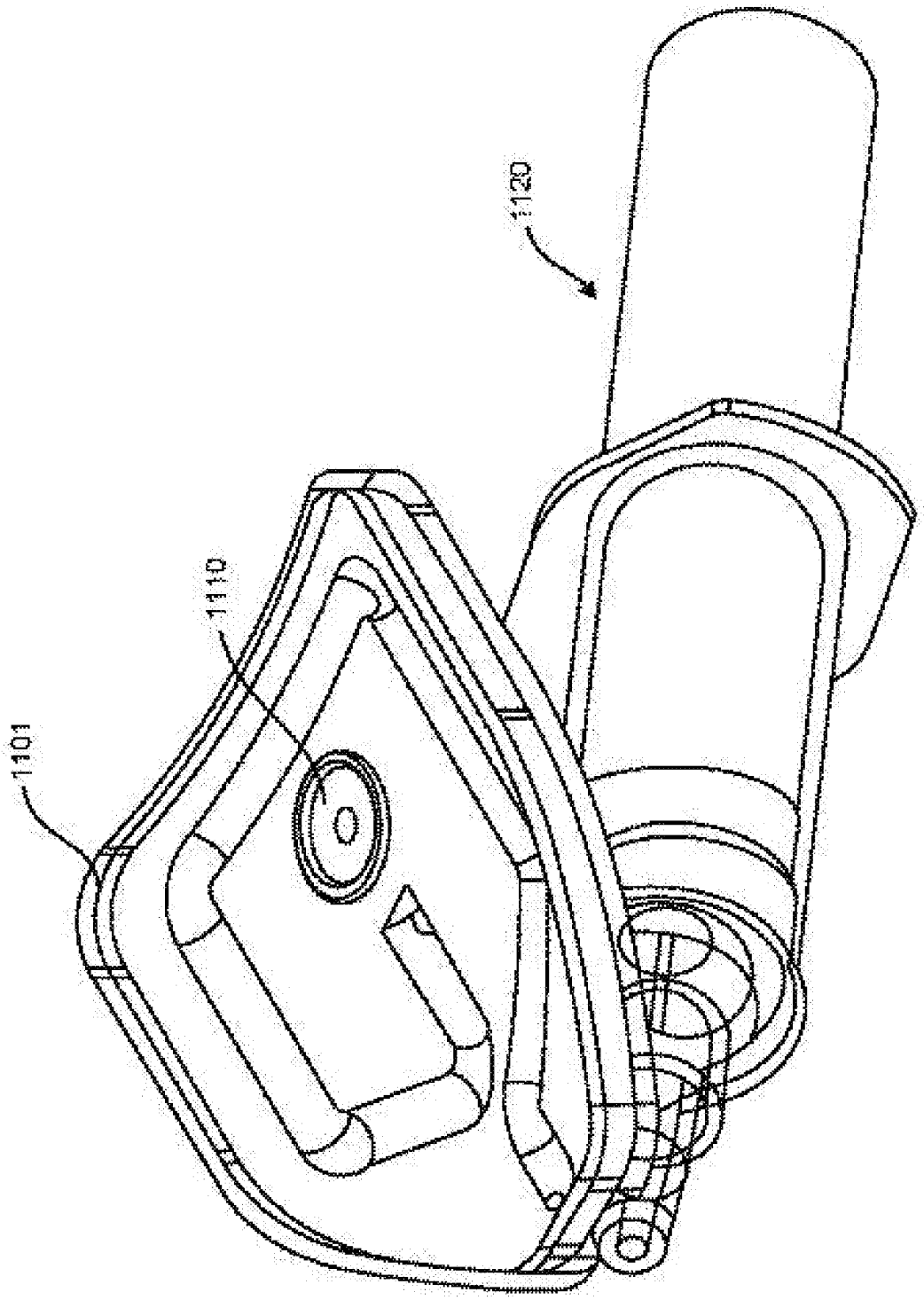


FIG. 11E

[Fig. 12A]

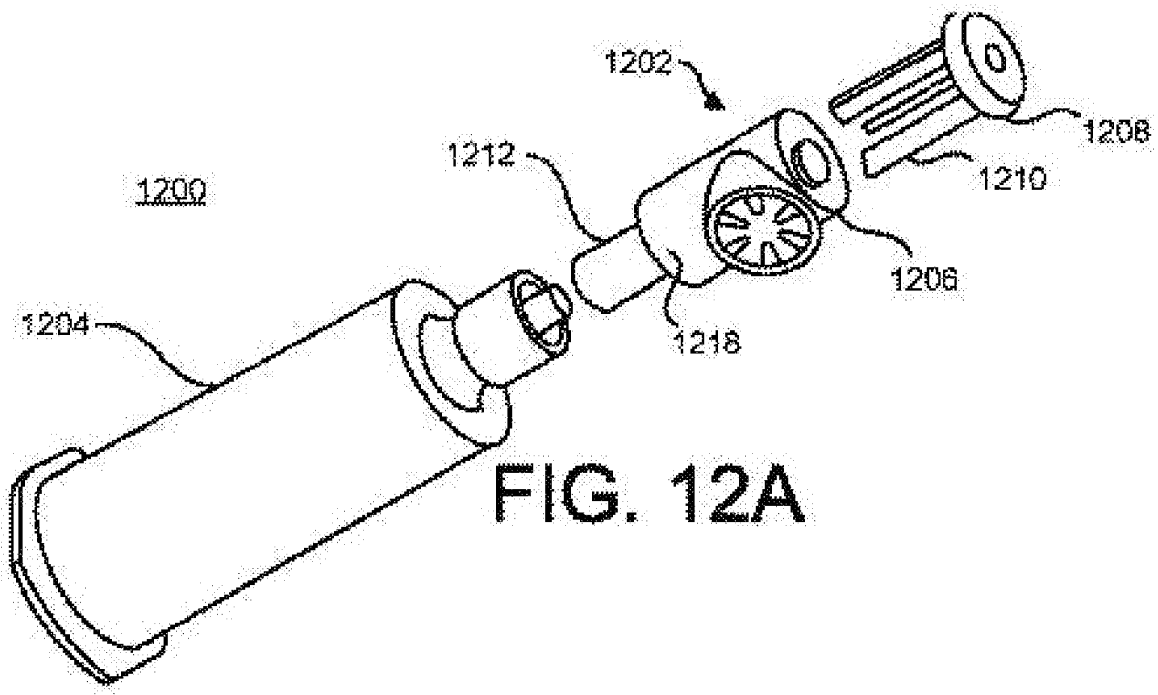


FIG. 12A

[Fig. 12B]

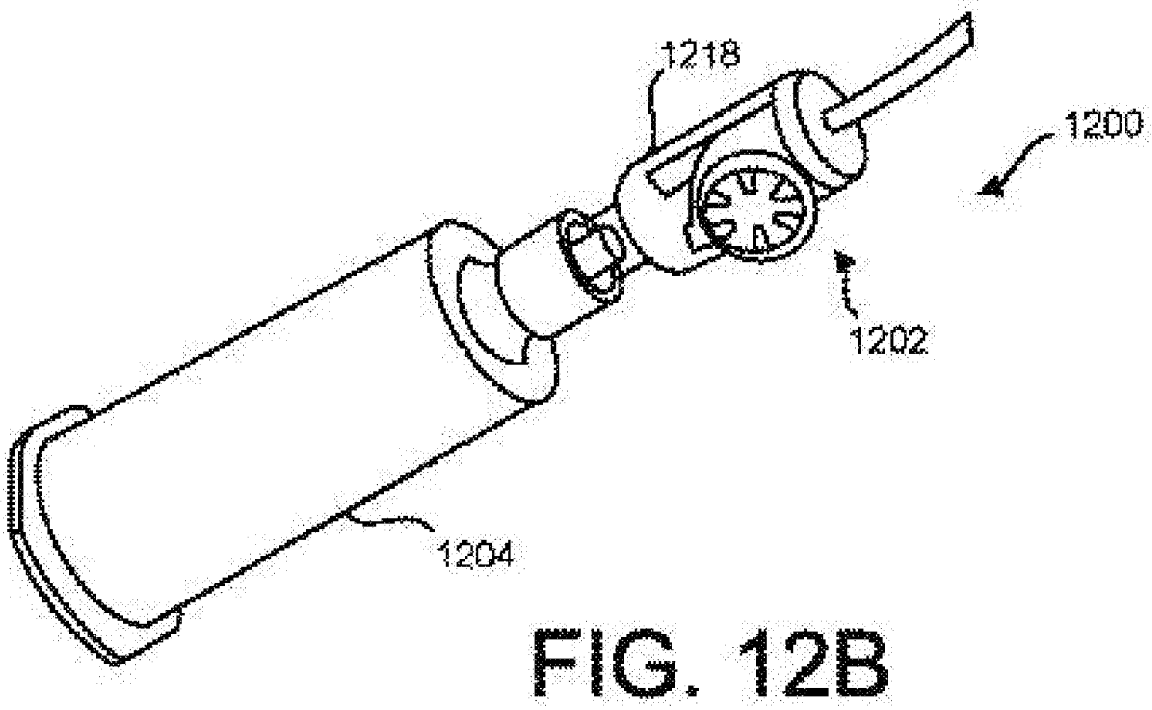


FIG. 12B

[Fig. 12C]

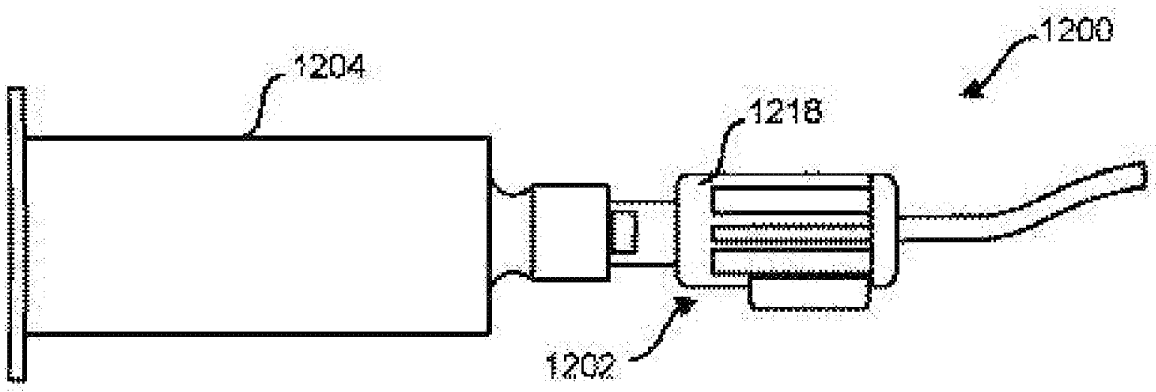


FIG. 12C

[Fig. 12D]

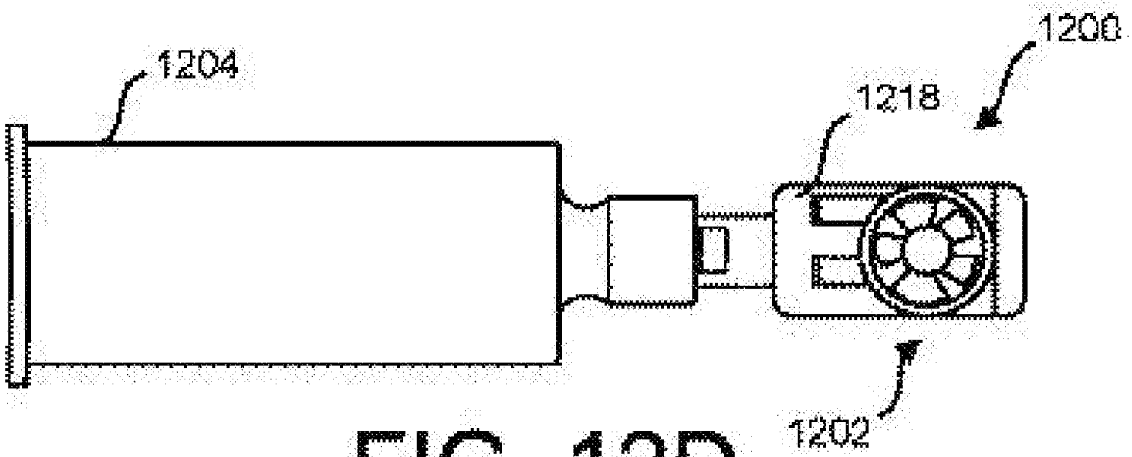


FIG. 12D

[Fig. 13A]

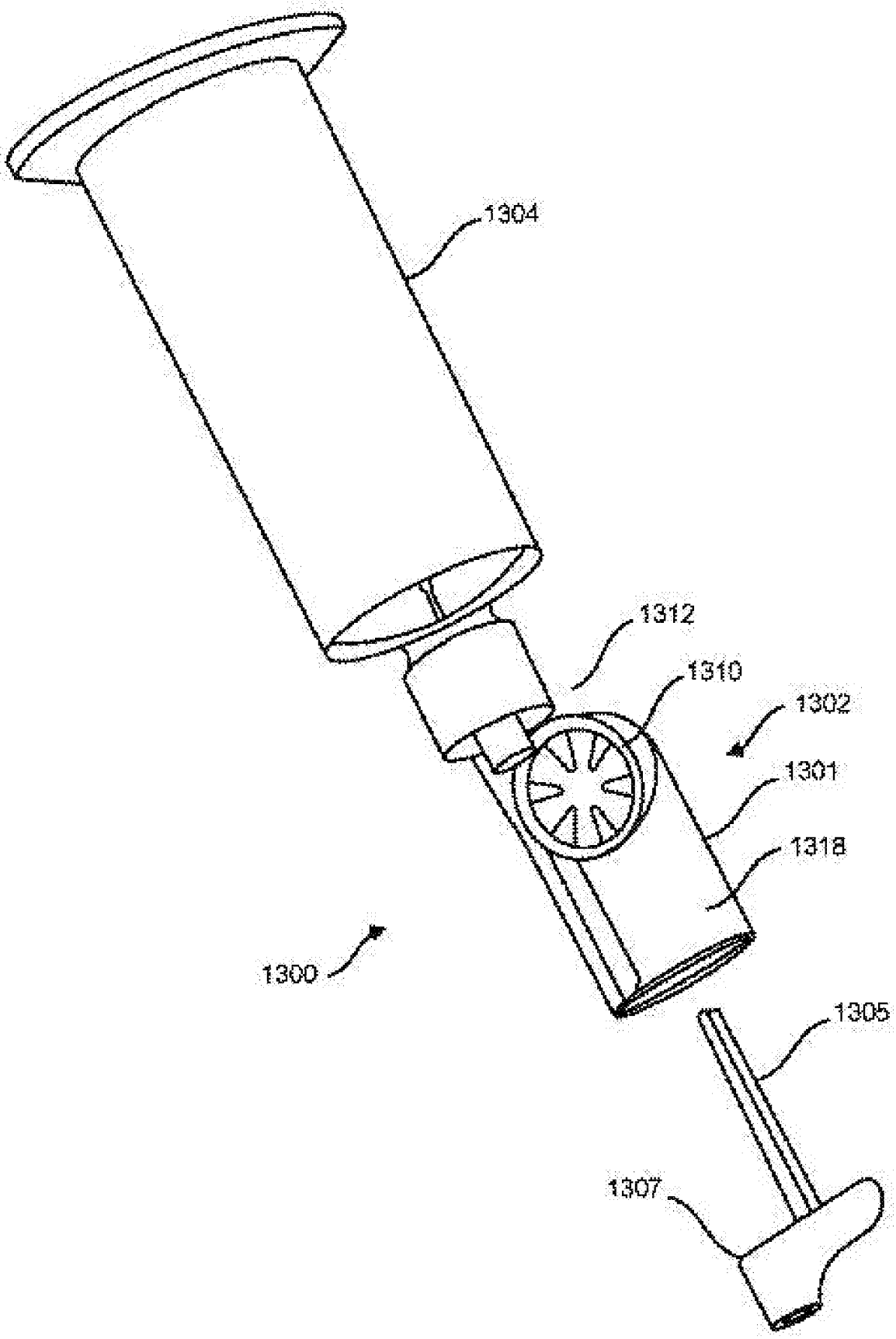


FIG. 13A

[Fig. 13B]

FIG. 13A

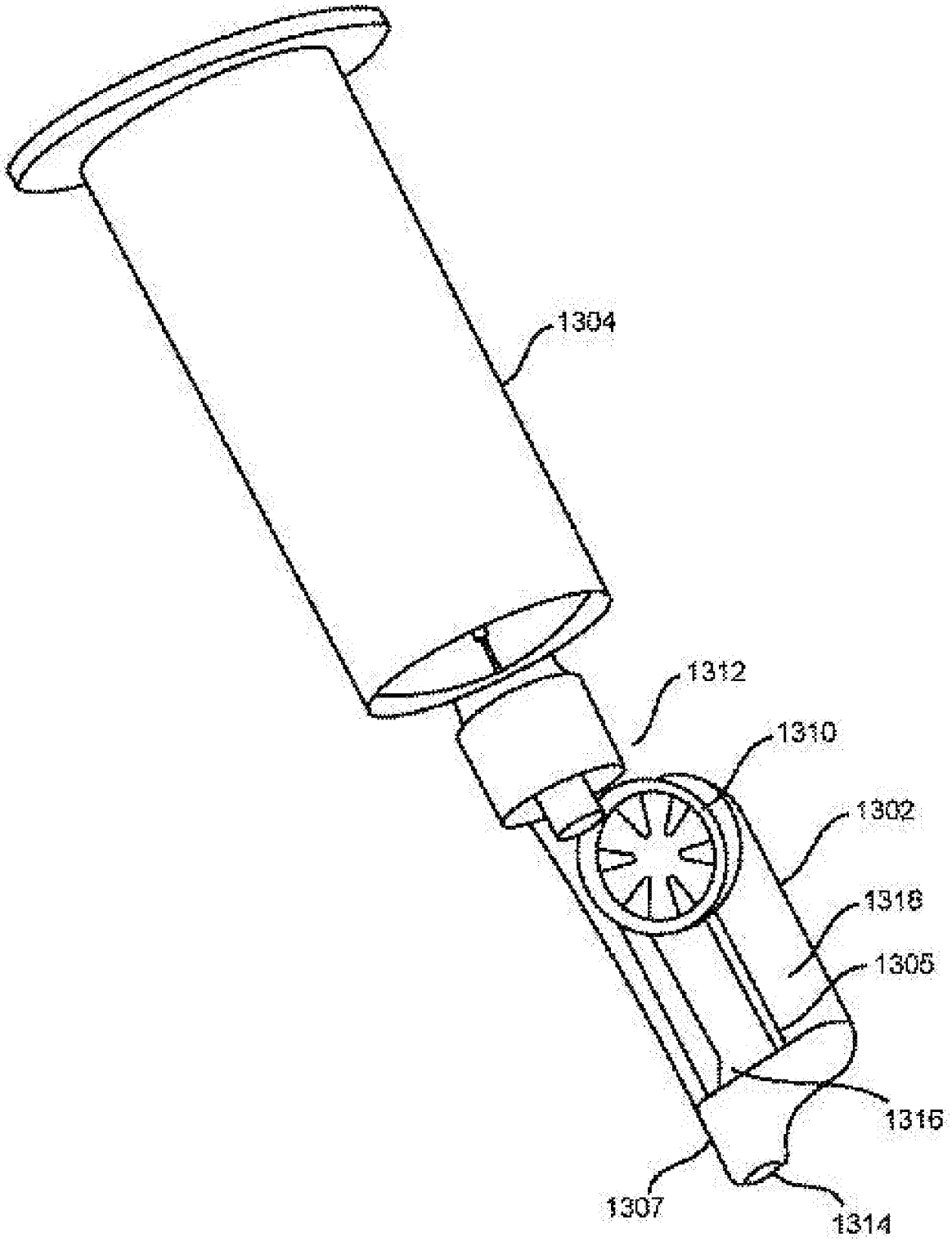


FIG. 13B

[Fig. 13C]

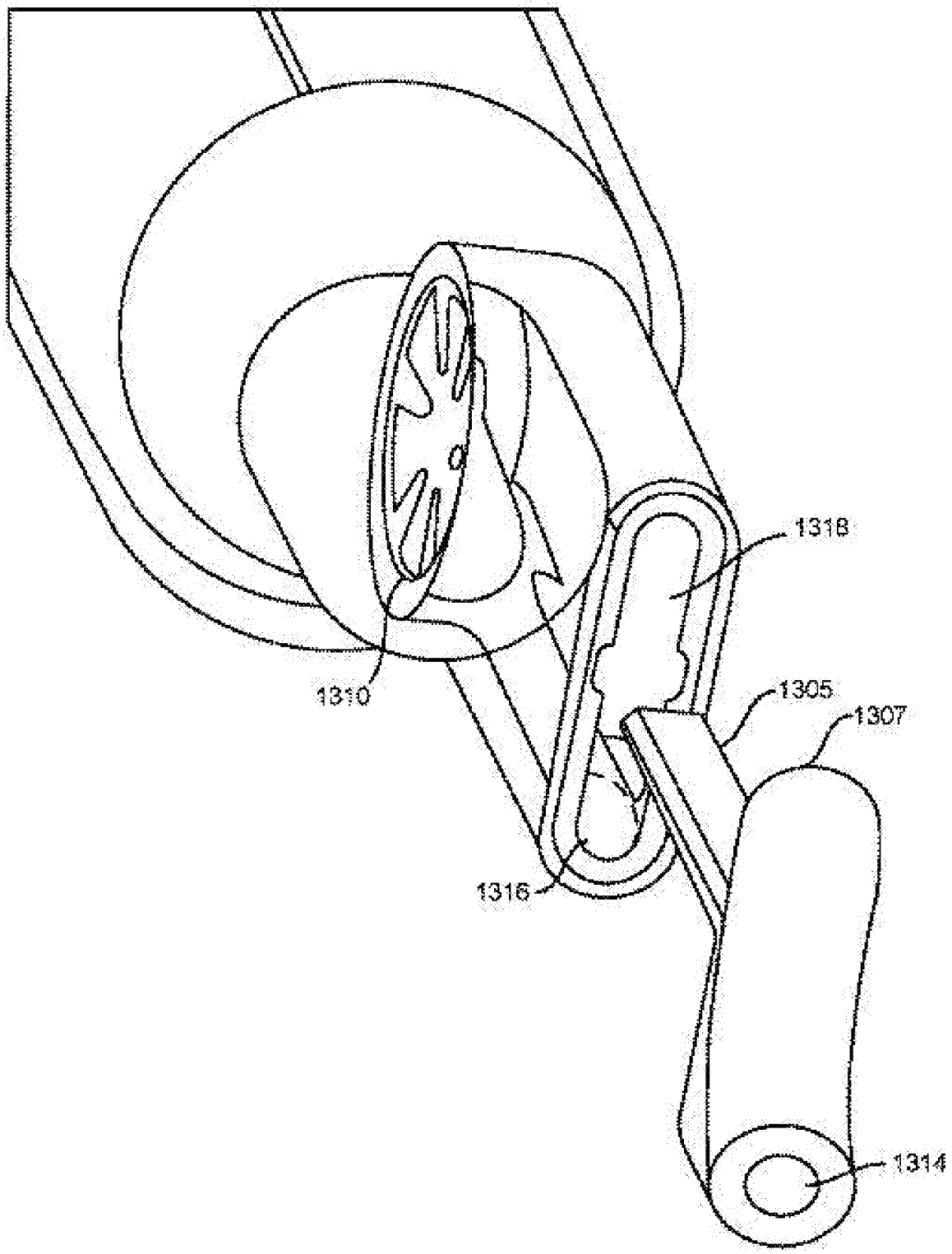
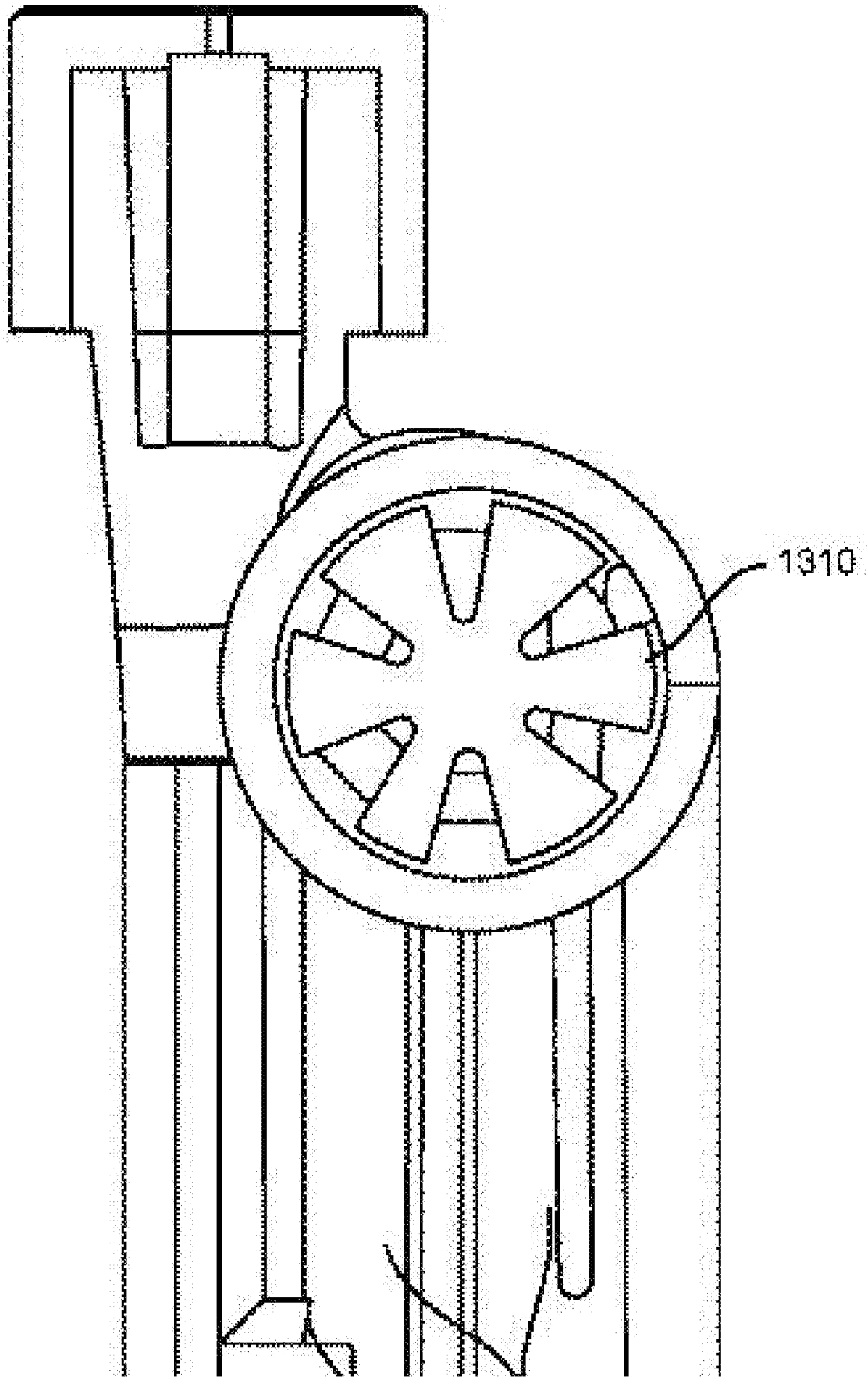


FIG. 13C

[Fig. 13D]


1310

[Fig. 14A]

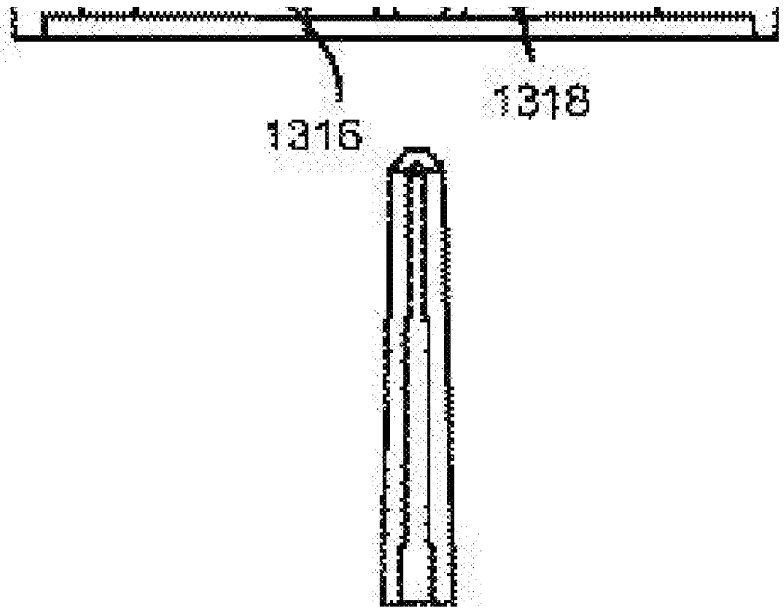
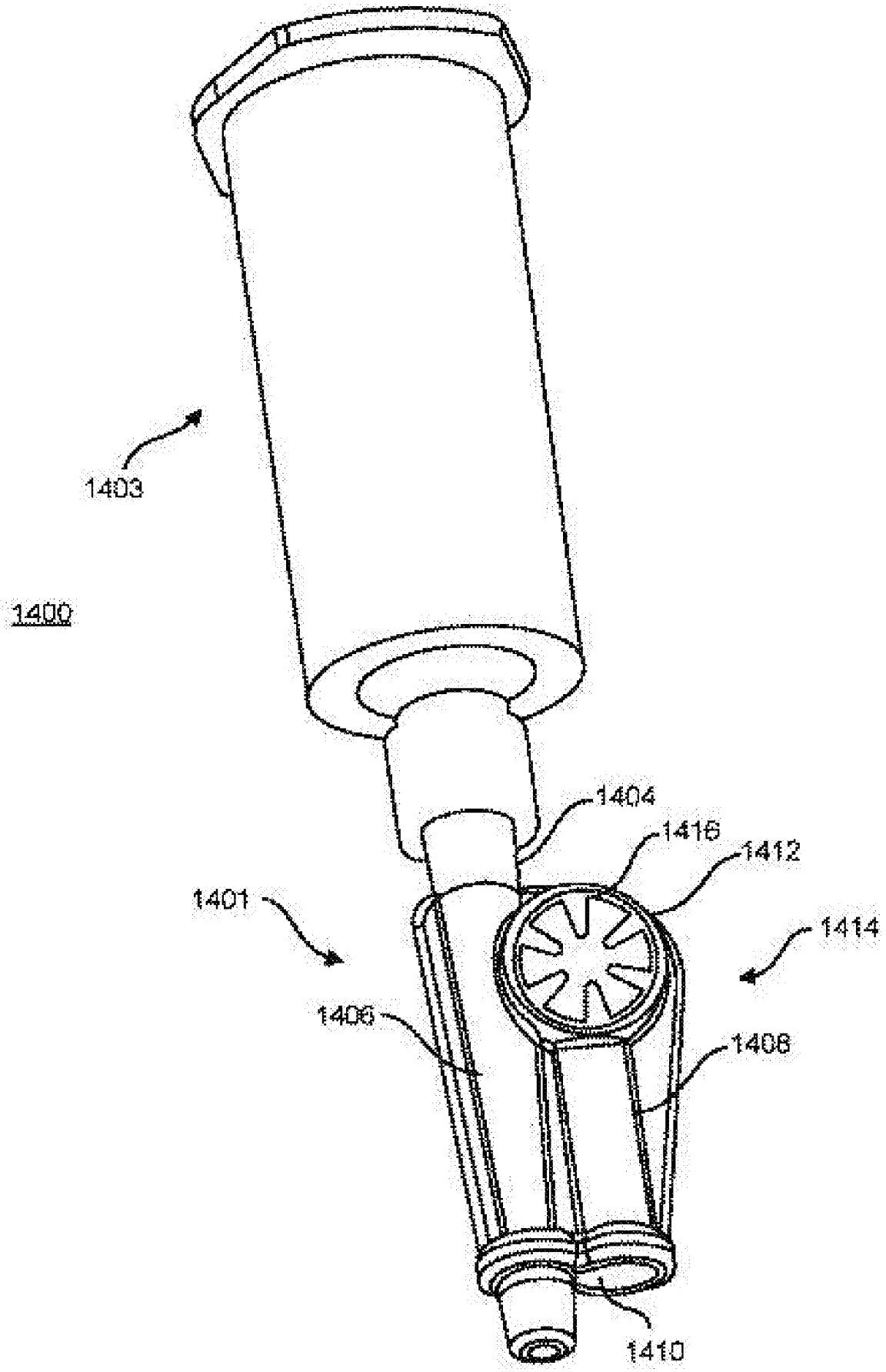


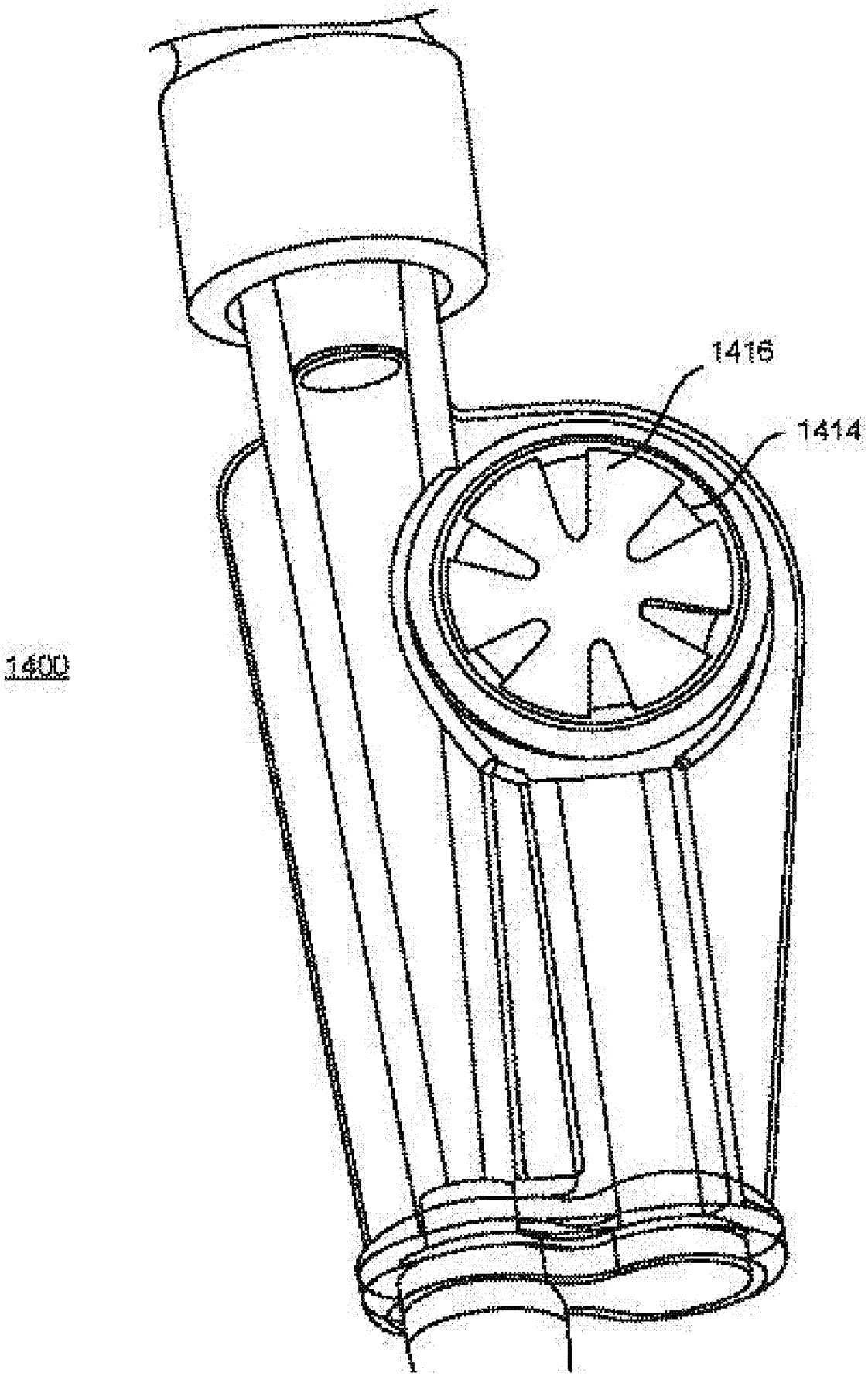
FIG. 13D


1403
1400
1404
1416
1412
1401
1414
1406
1408
1410

[Fig. 14B]



FIG. 14A


1416
1414
1400

[Fig. 14C]



FIG. 14B

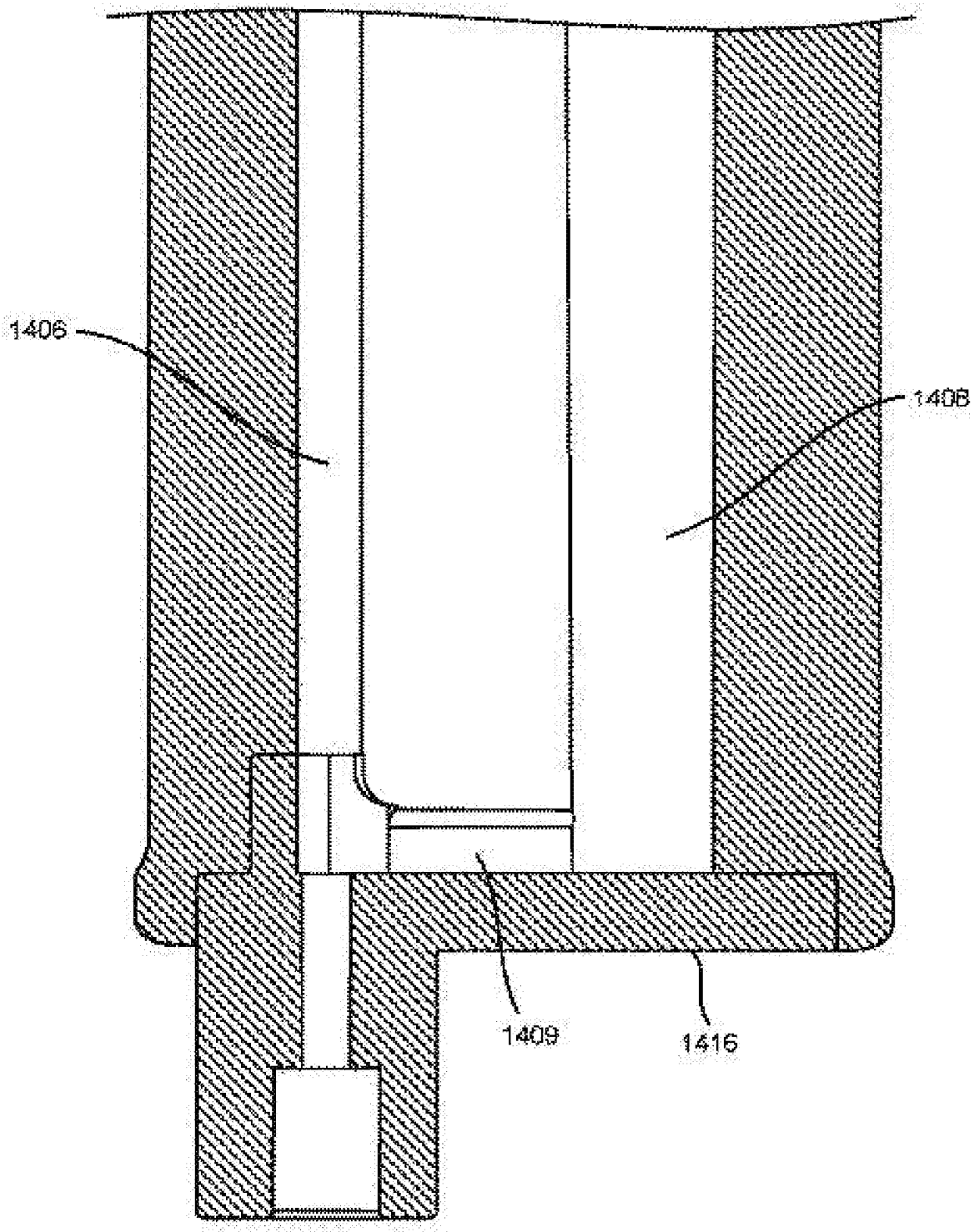
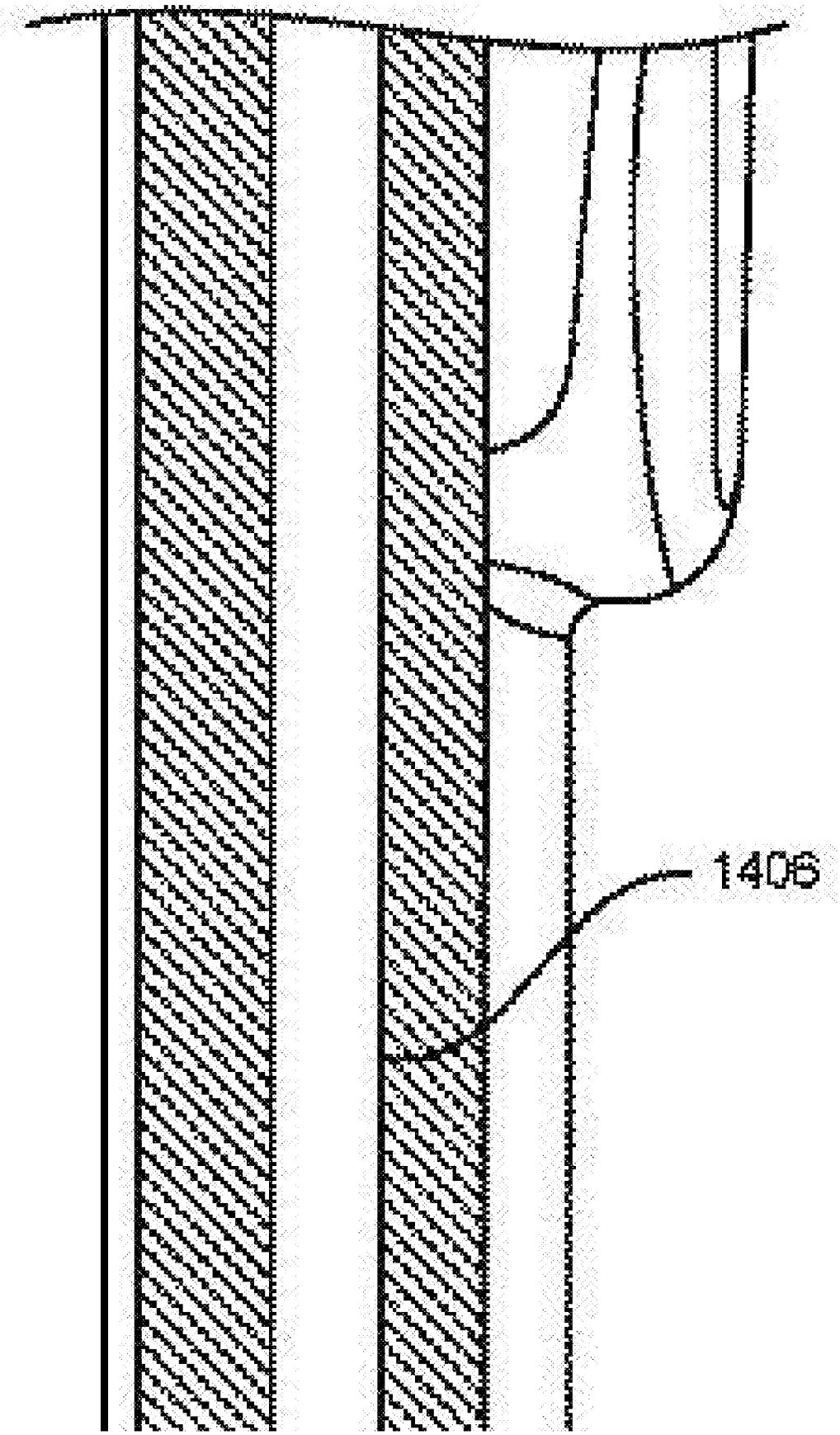


FIG. 14C

[Fig. 14D]


1406

[Fig. 14E]

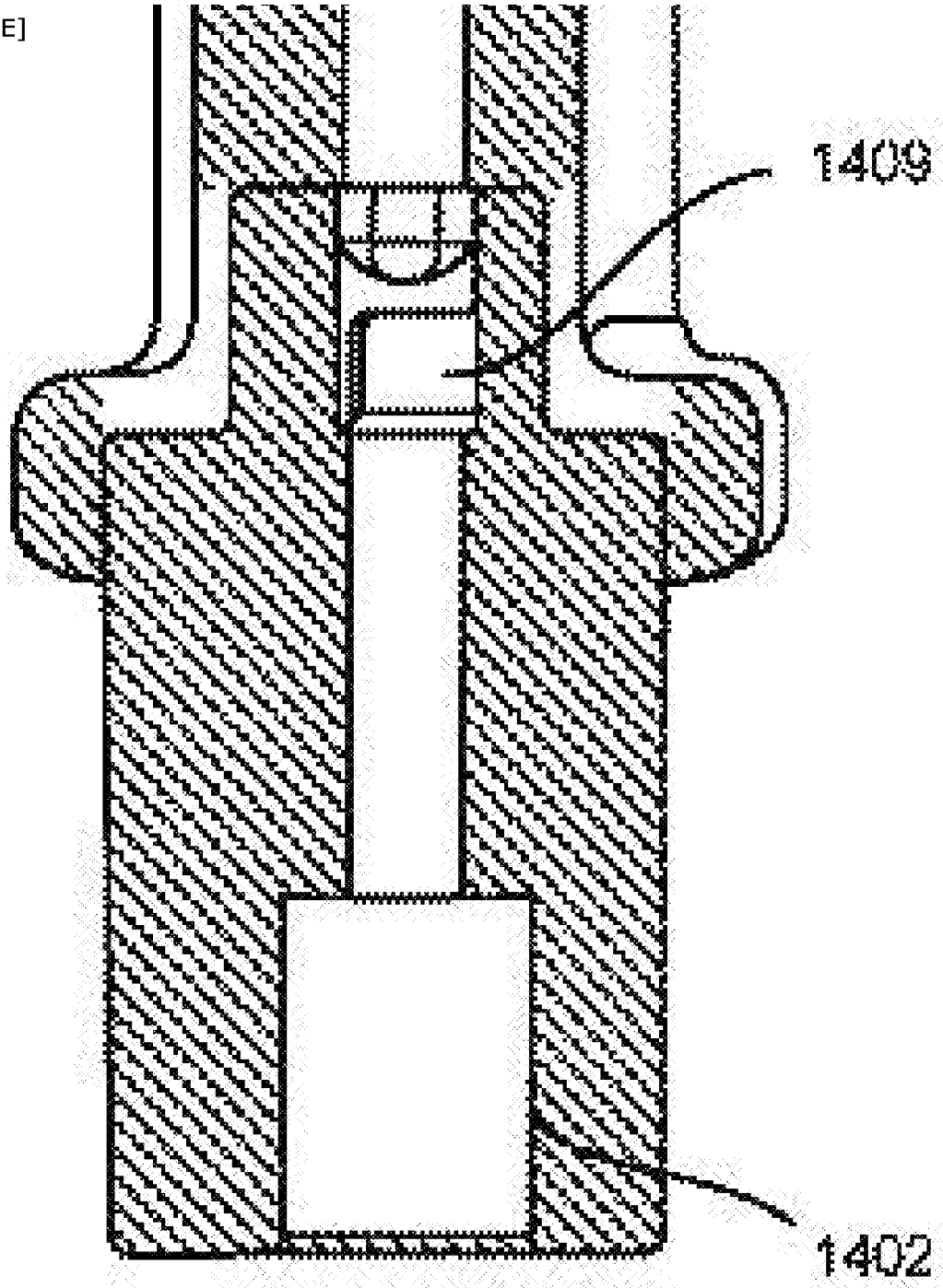


FIG. 14D

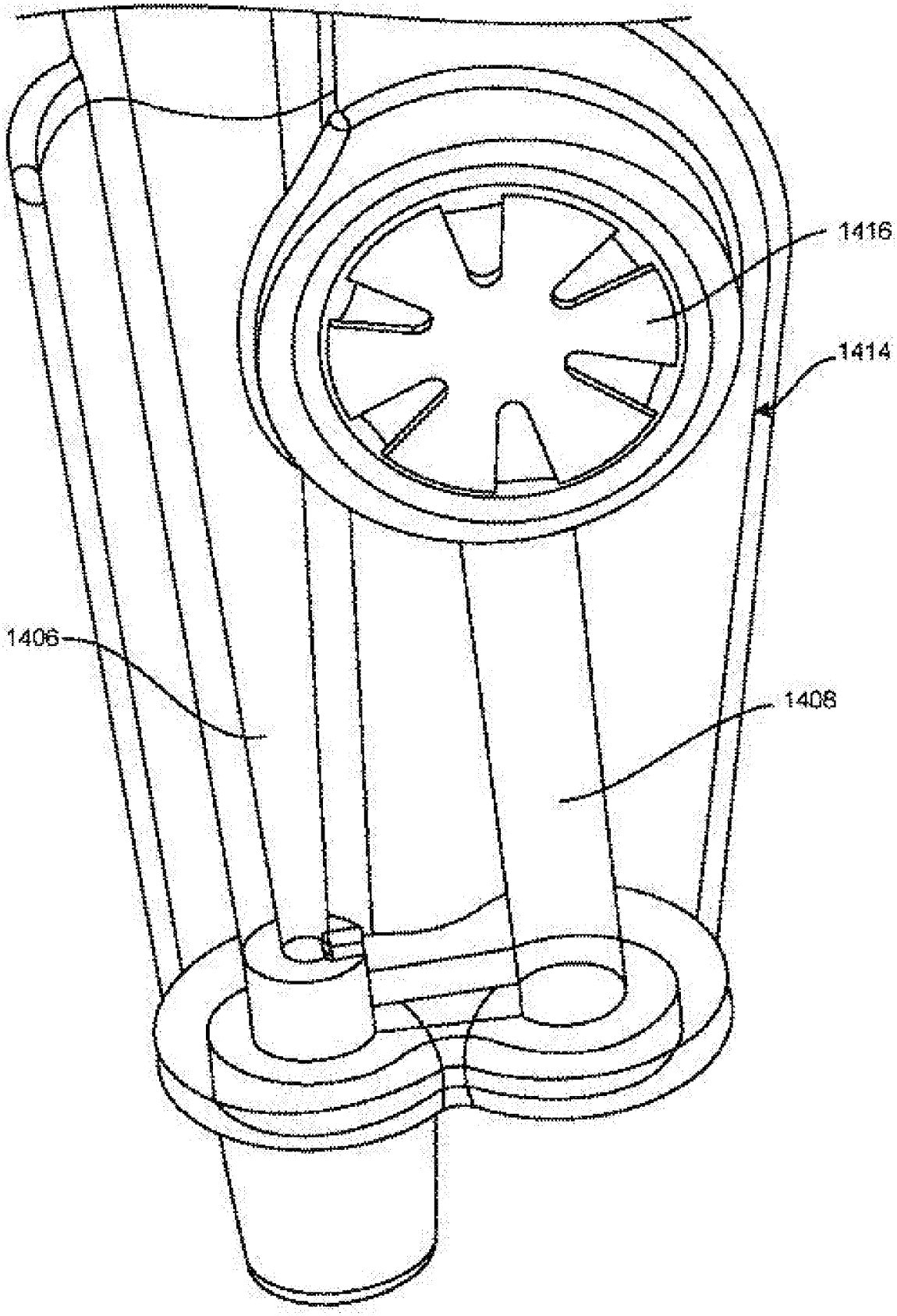


FIG. 14E

[Fig. 15A]

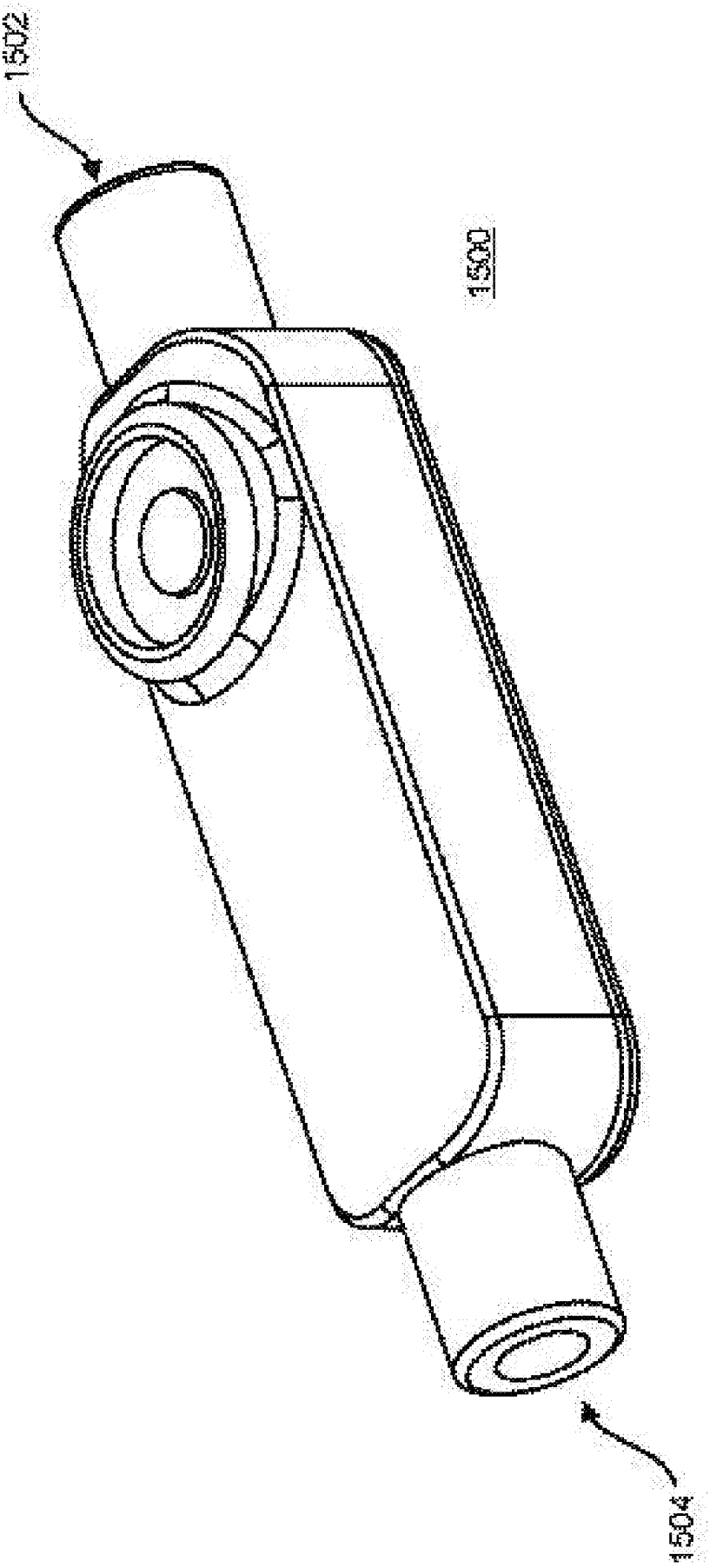


FIG. 15A

[Fig. 15B]

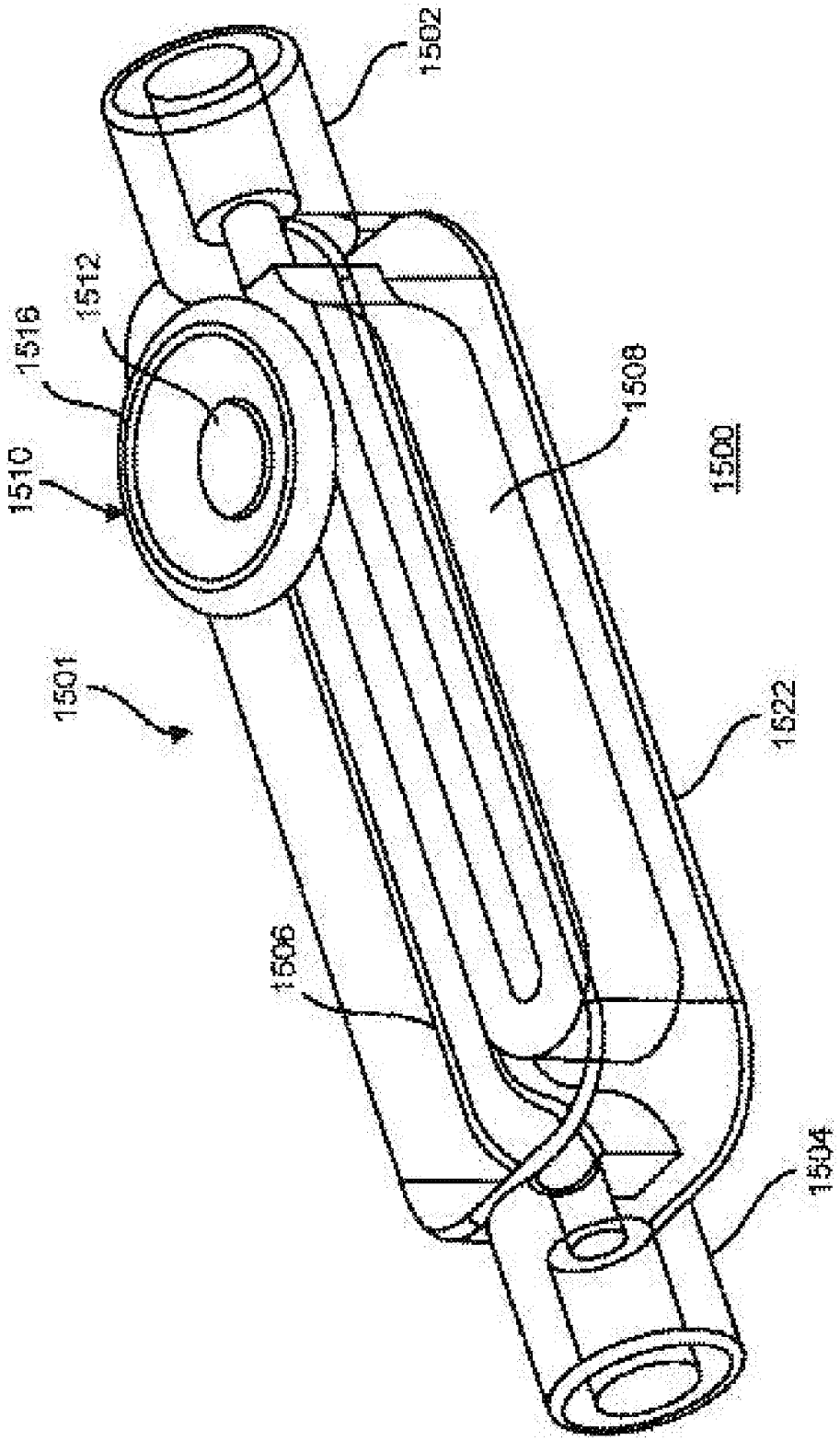


FIG. 15B

[Fig. 15C]

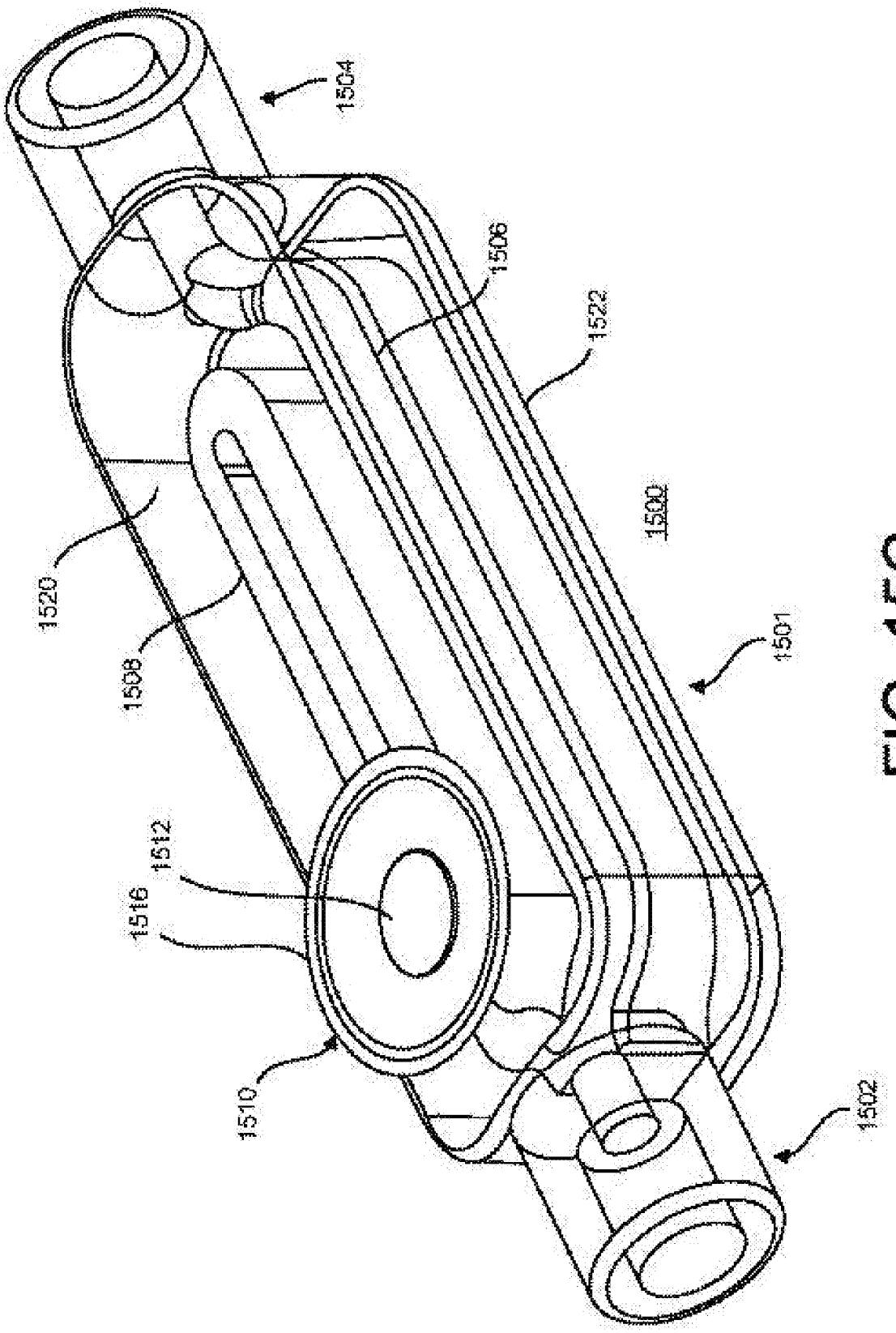


FIG. 15C

[Fig. 15D]

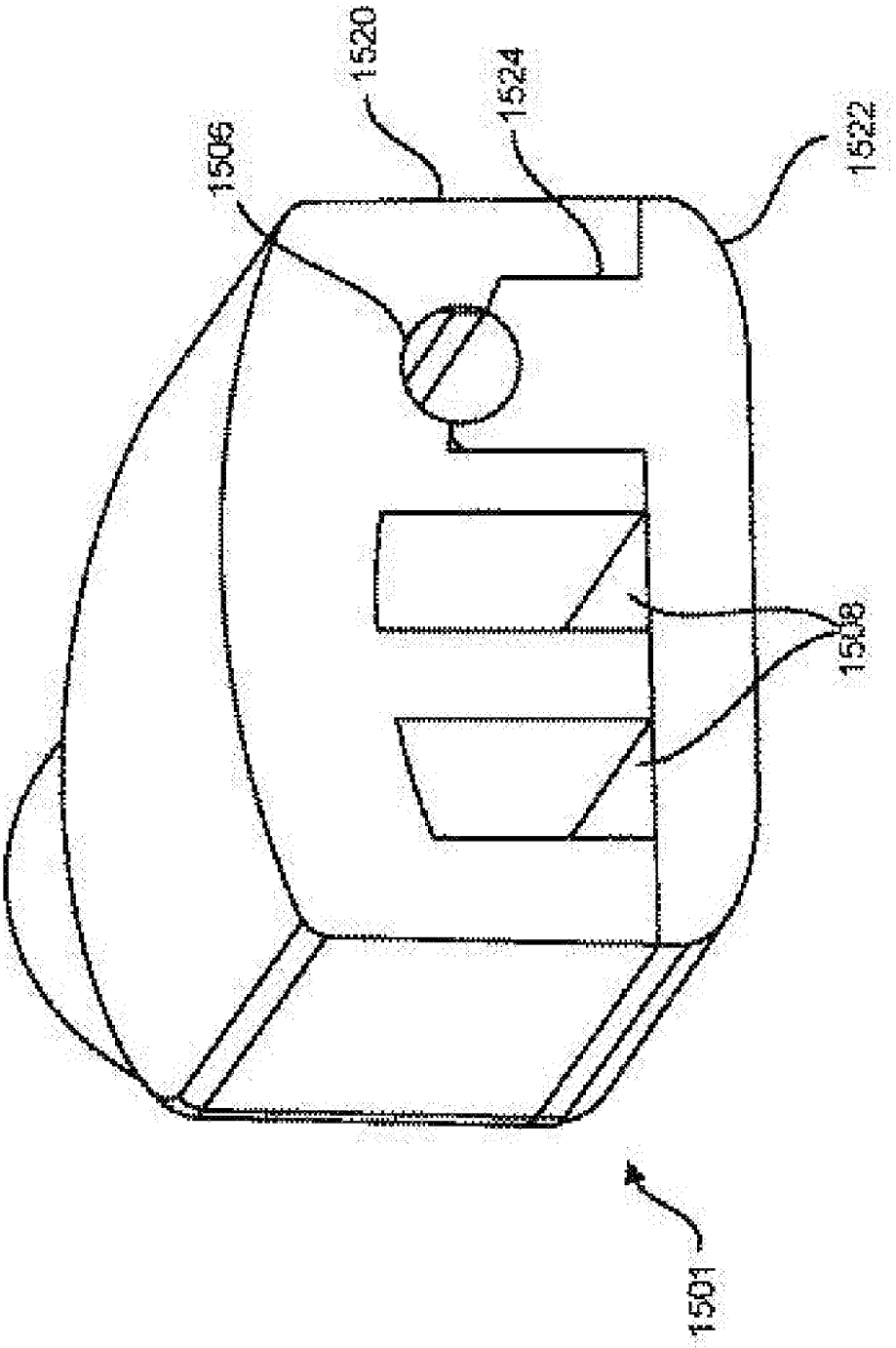


FIG. 15D

[Fig. 15E]

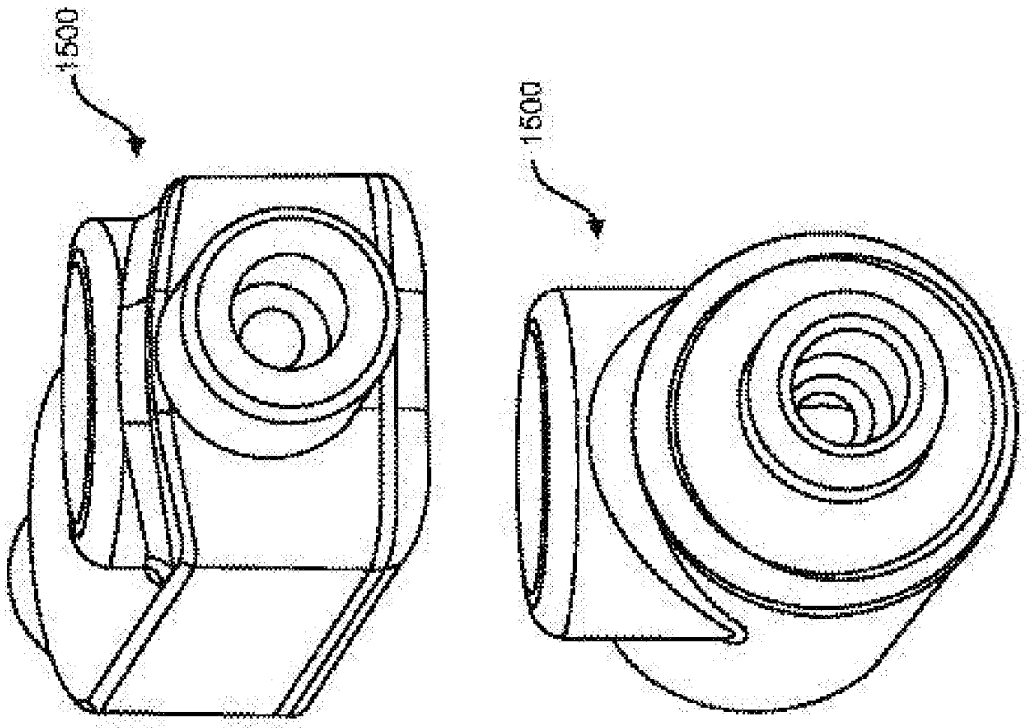


FIG. 15E

[Fig. 15F]

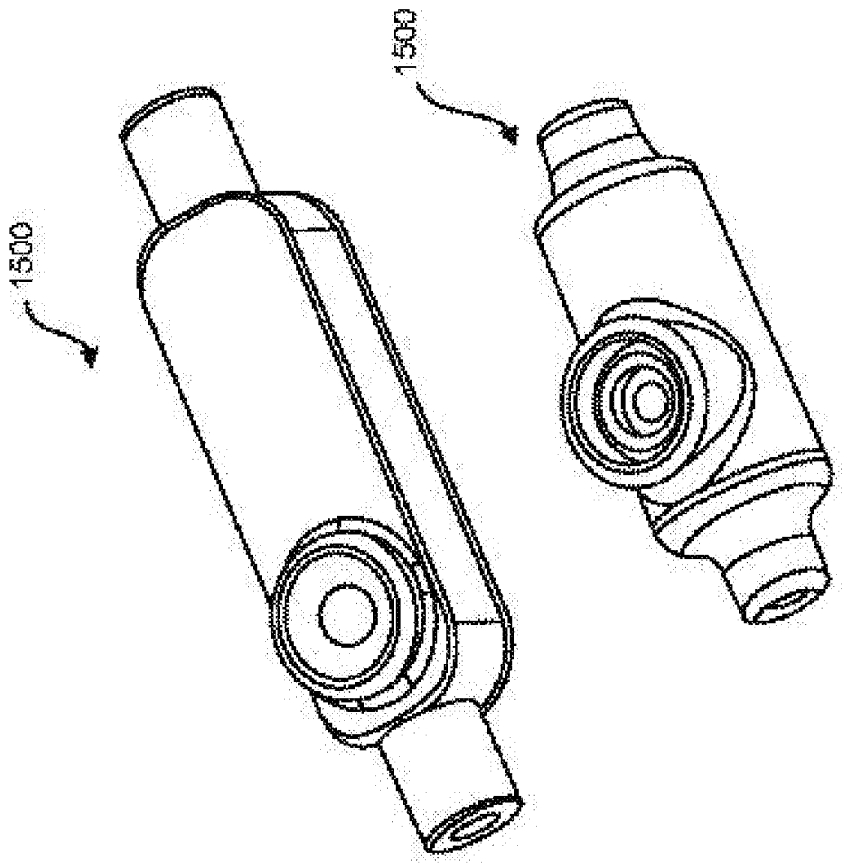


FIG. 15F

[Fig. 15G]

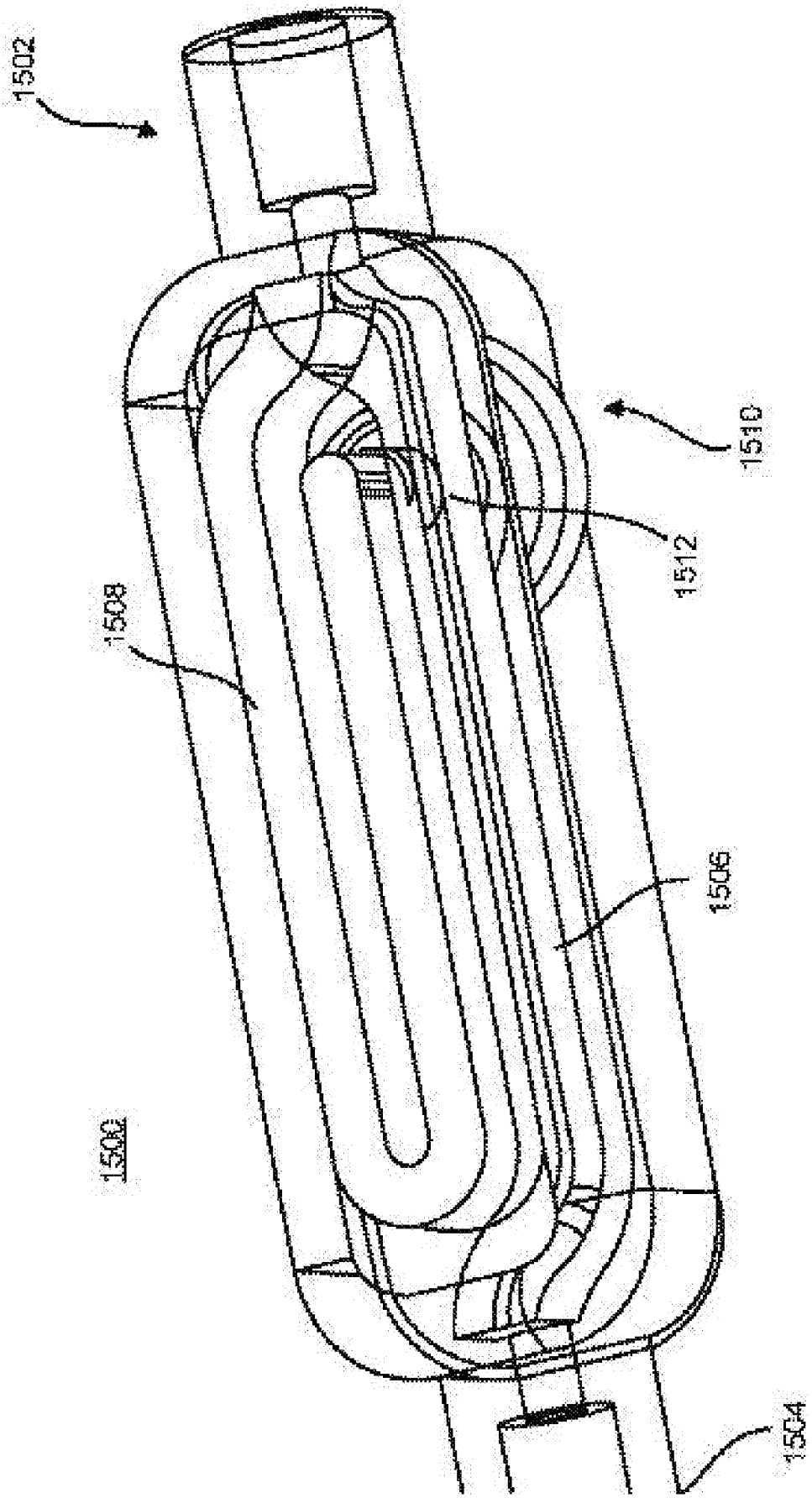


FIG. 15G

[Fig. 16A]



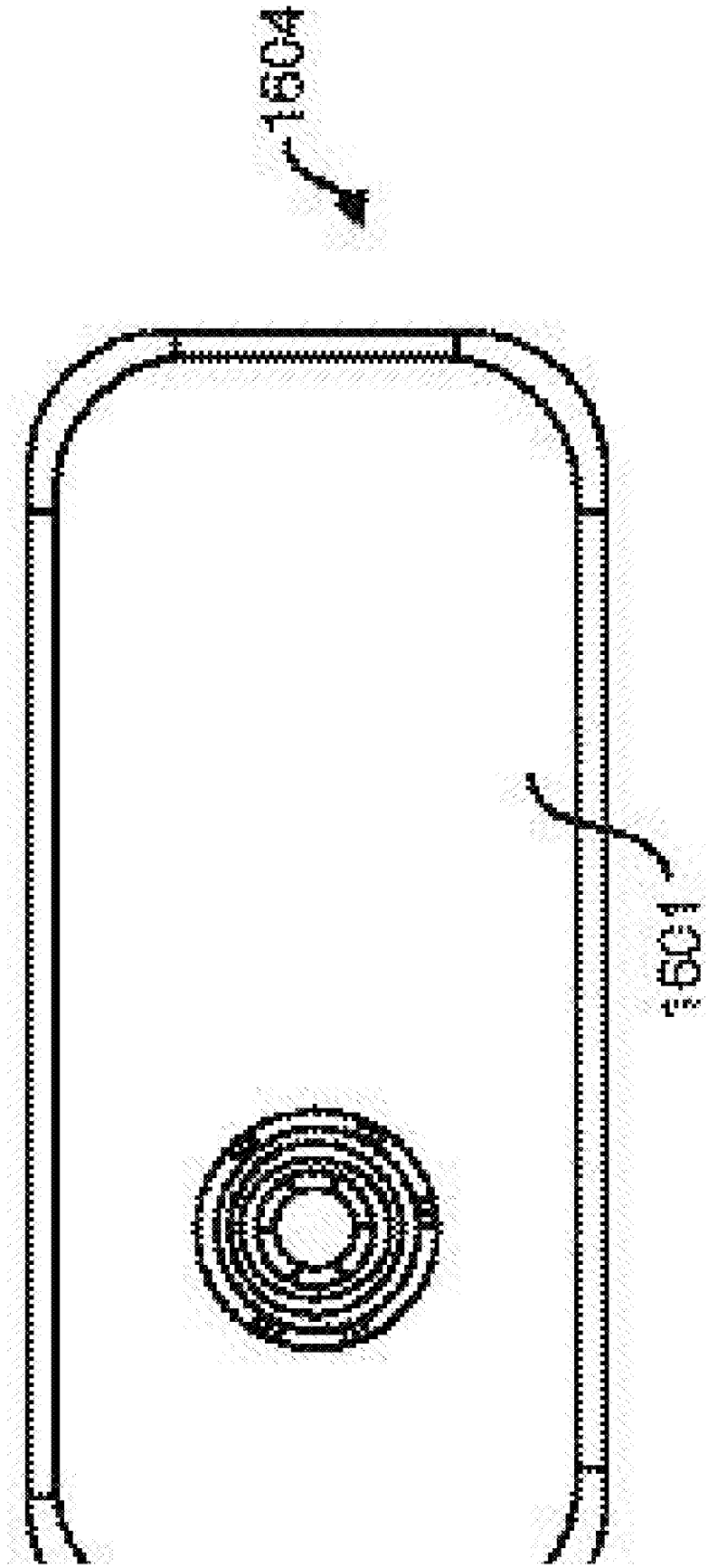
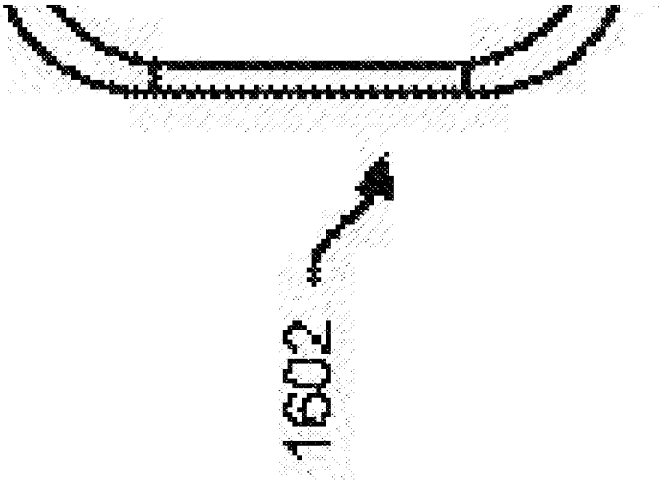
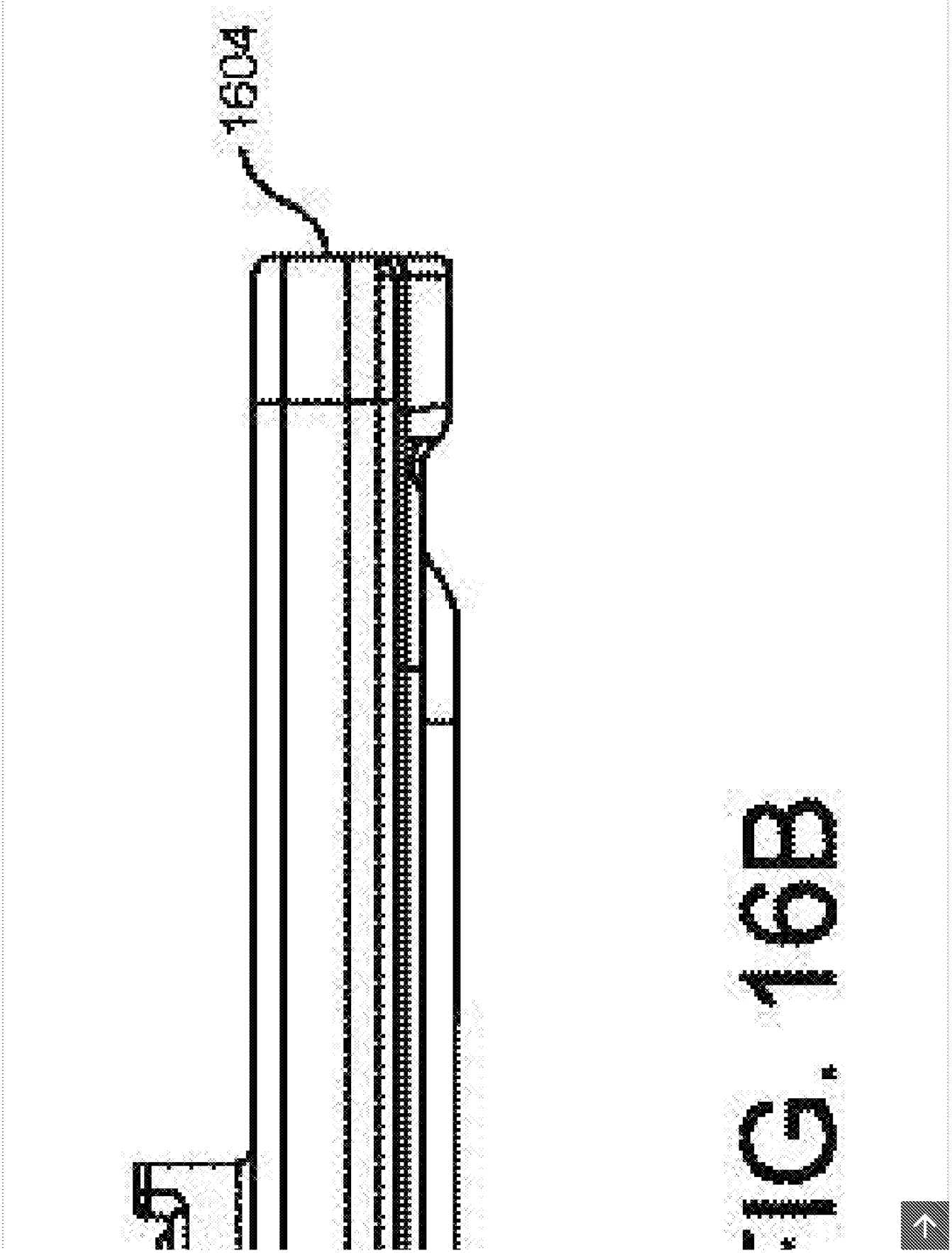


FIG. 16A

[Fig. 16B]




160a
160
160b

[Fig. 16C]

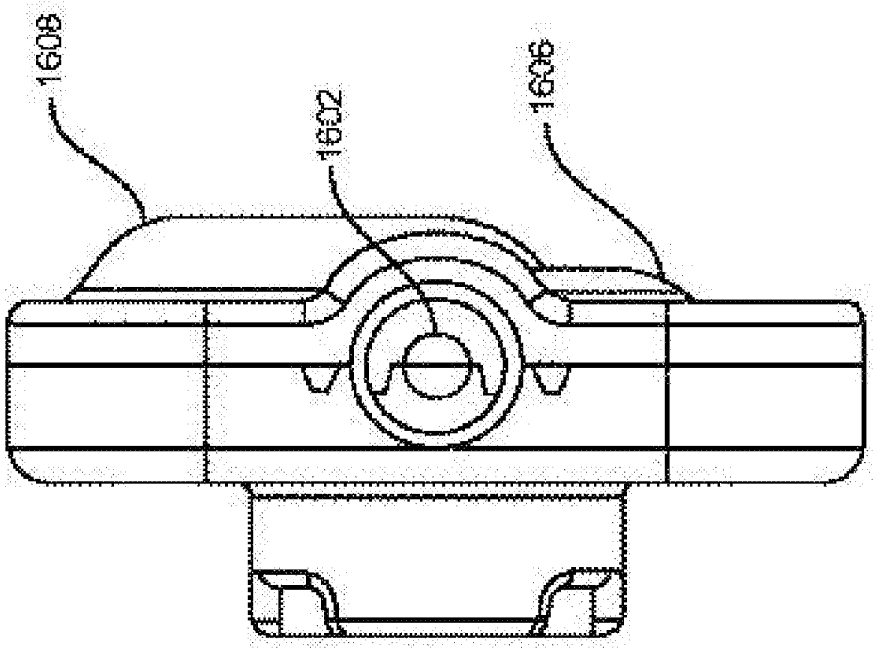
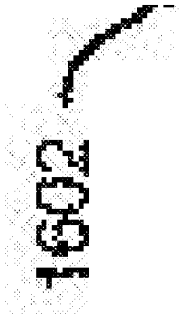


FIG. 16C

[Fig. 16D]



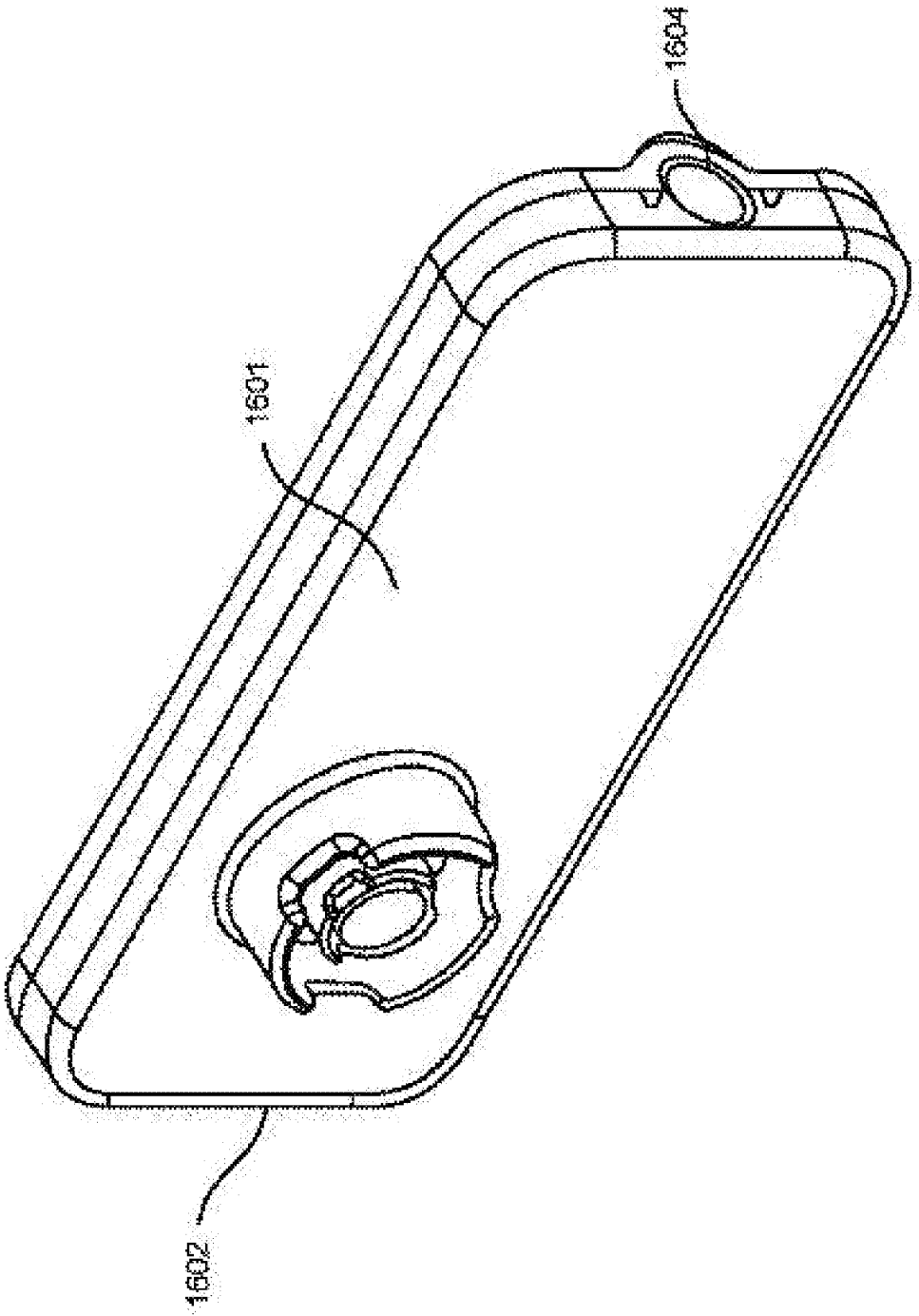


FIG. 16D

[Fig. 17A]

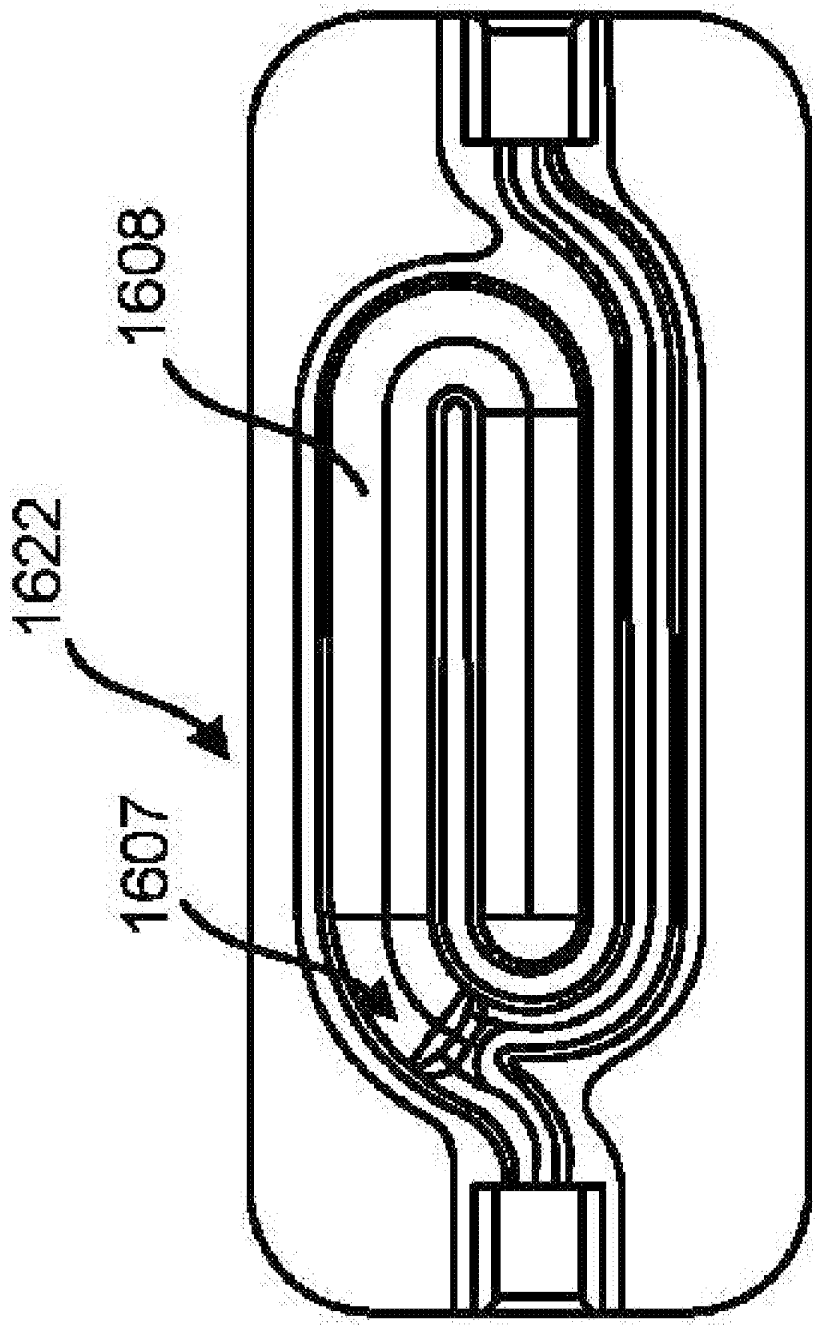


FIG. 17A

[Fig. 17B]

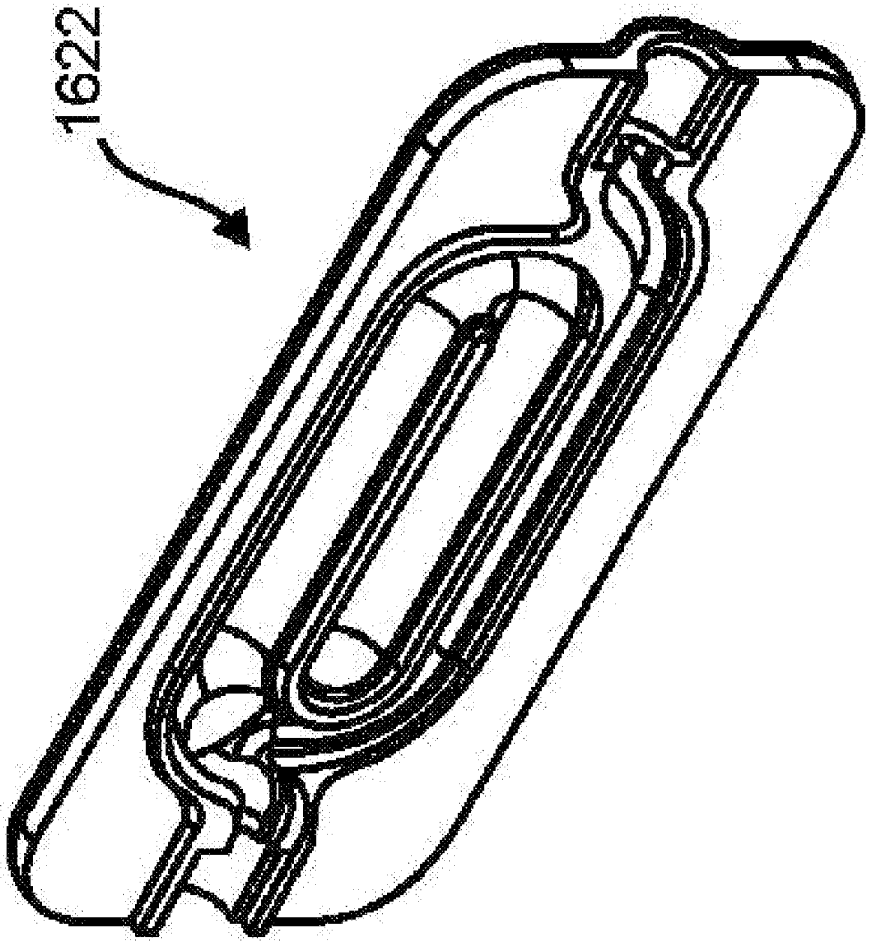


FIG. 17B

[Fig. 17C]

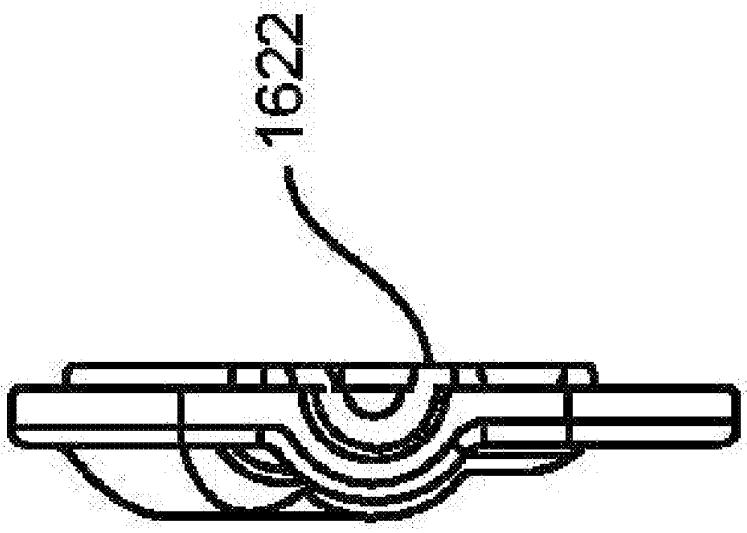


FIG. 17C

[Fig. 17D]

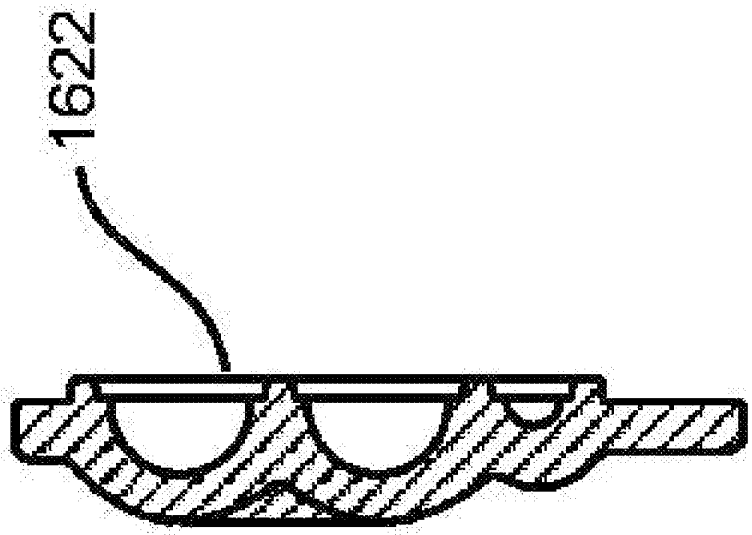


FIG. 17D

[Fig. 17E]



FIG. 17E

[Fig. 18A]

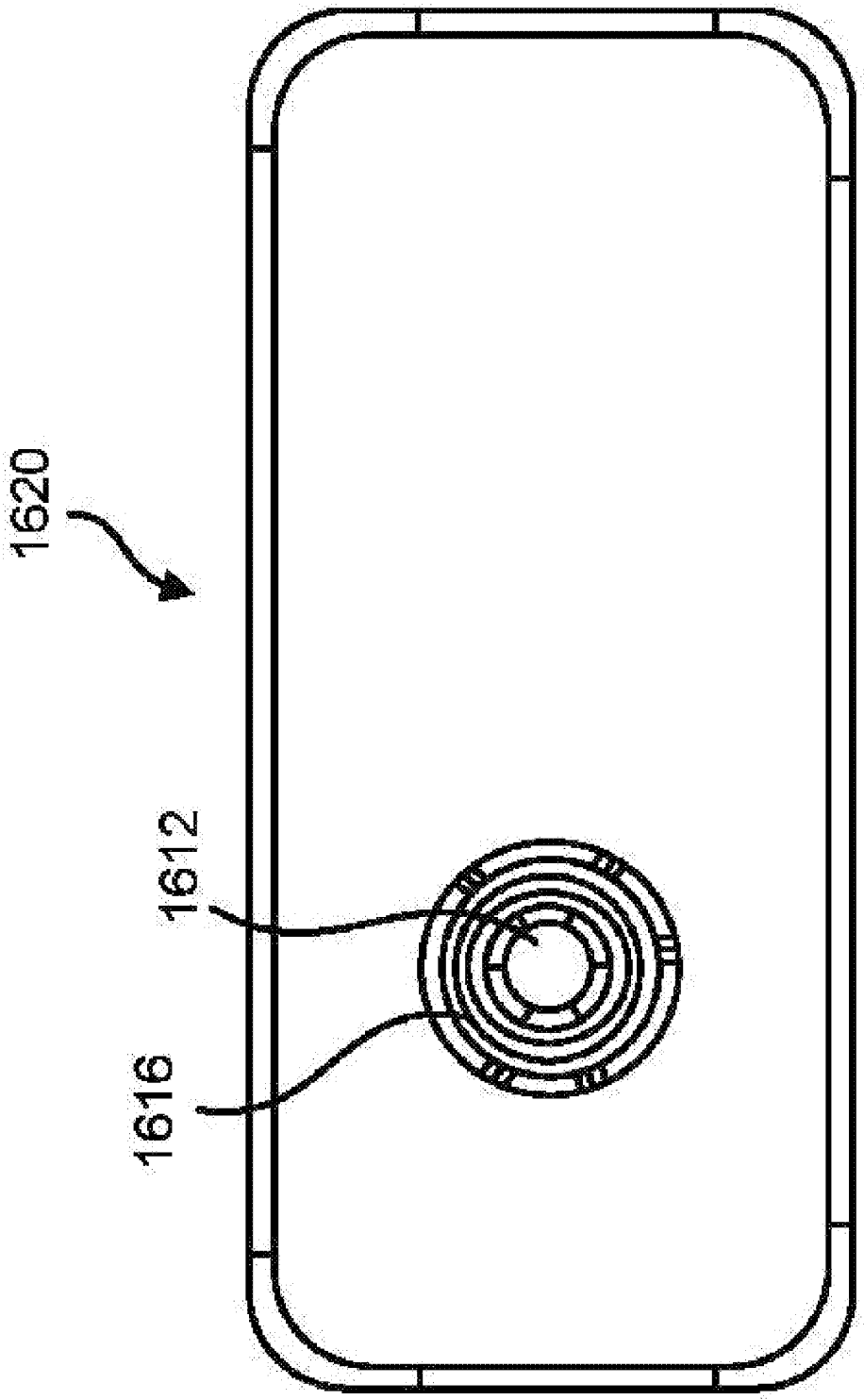


FIG. 18A

[Fig. 18B]

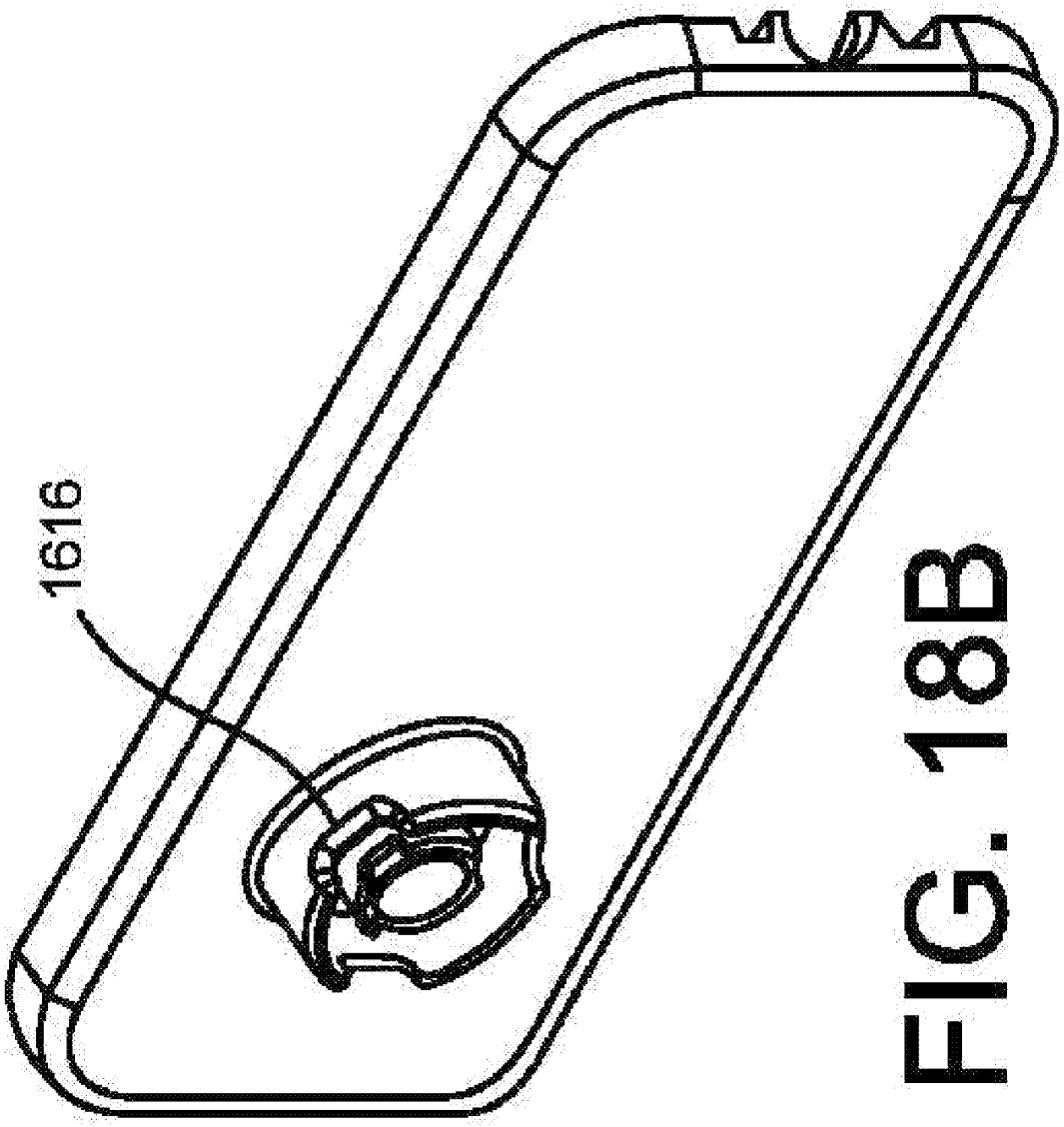


FIG. 18B

[Fig. 18C]

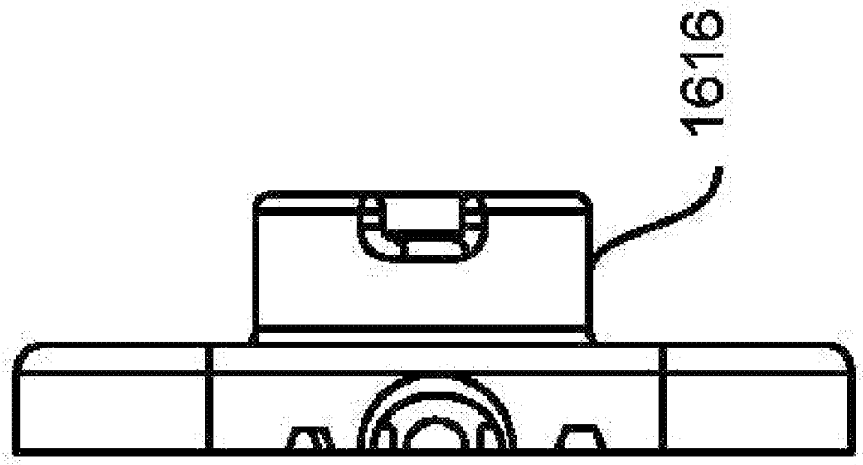


FIG. 18C

[Fig. 18D]

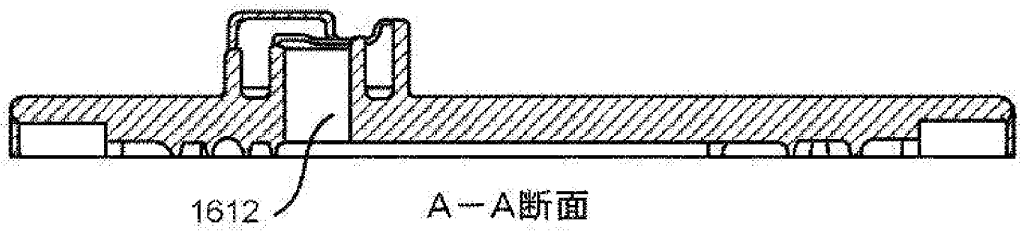


FIG. 18D

[Fig. 18E]

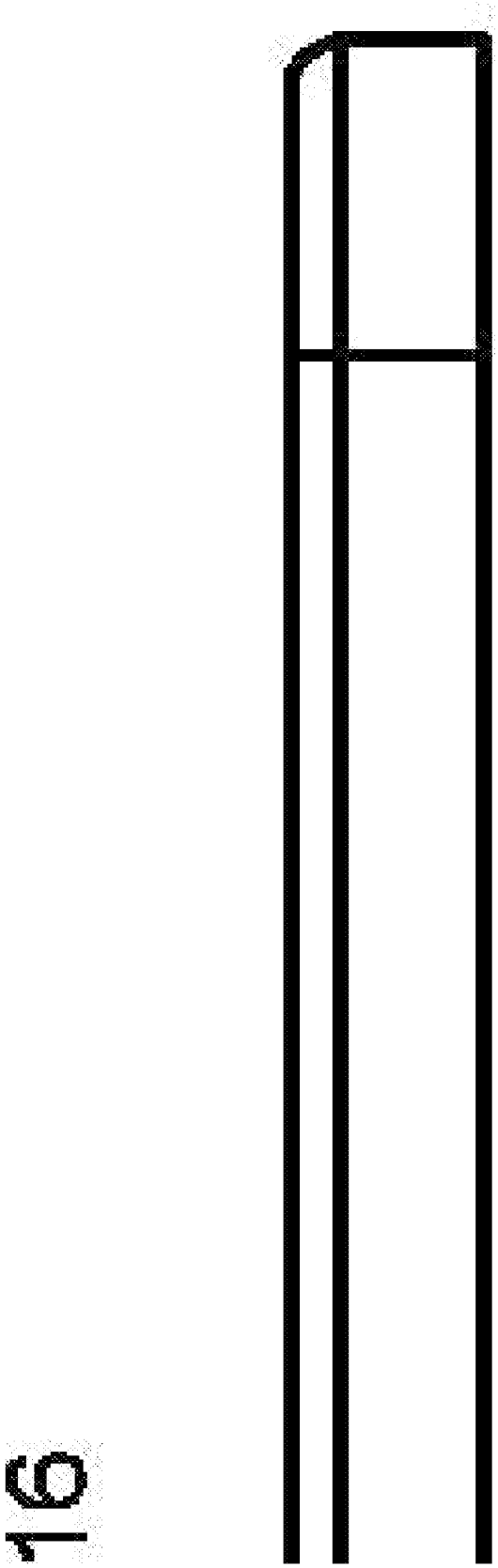
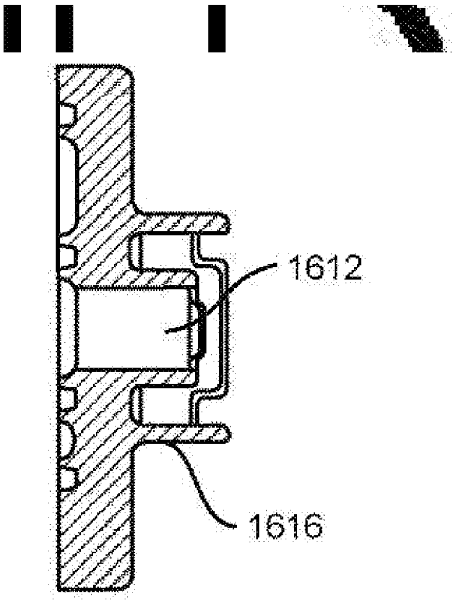


図6

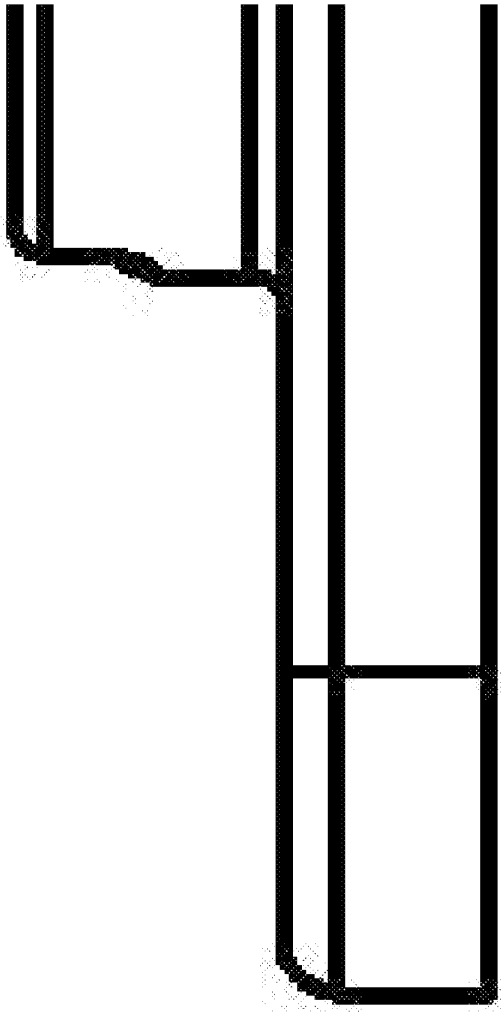
[Fig. 18F]



A－A断面

FIG. 18F

[Fig. 19A]



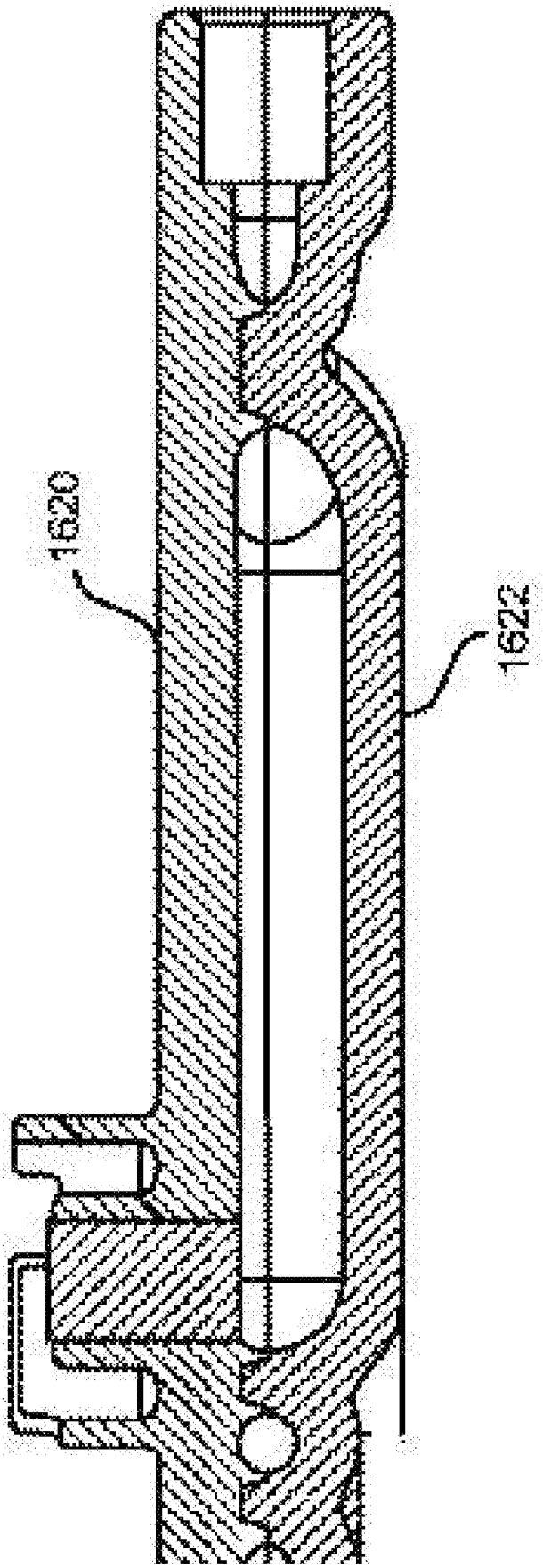


FIG. 19A

[Fig. 19B]

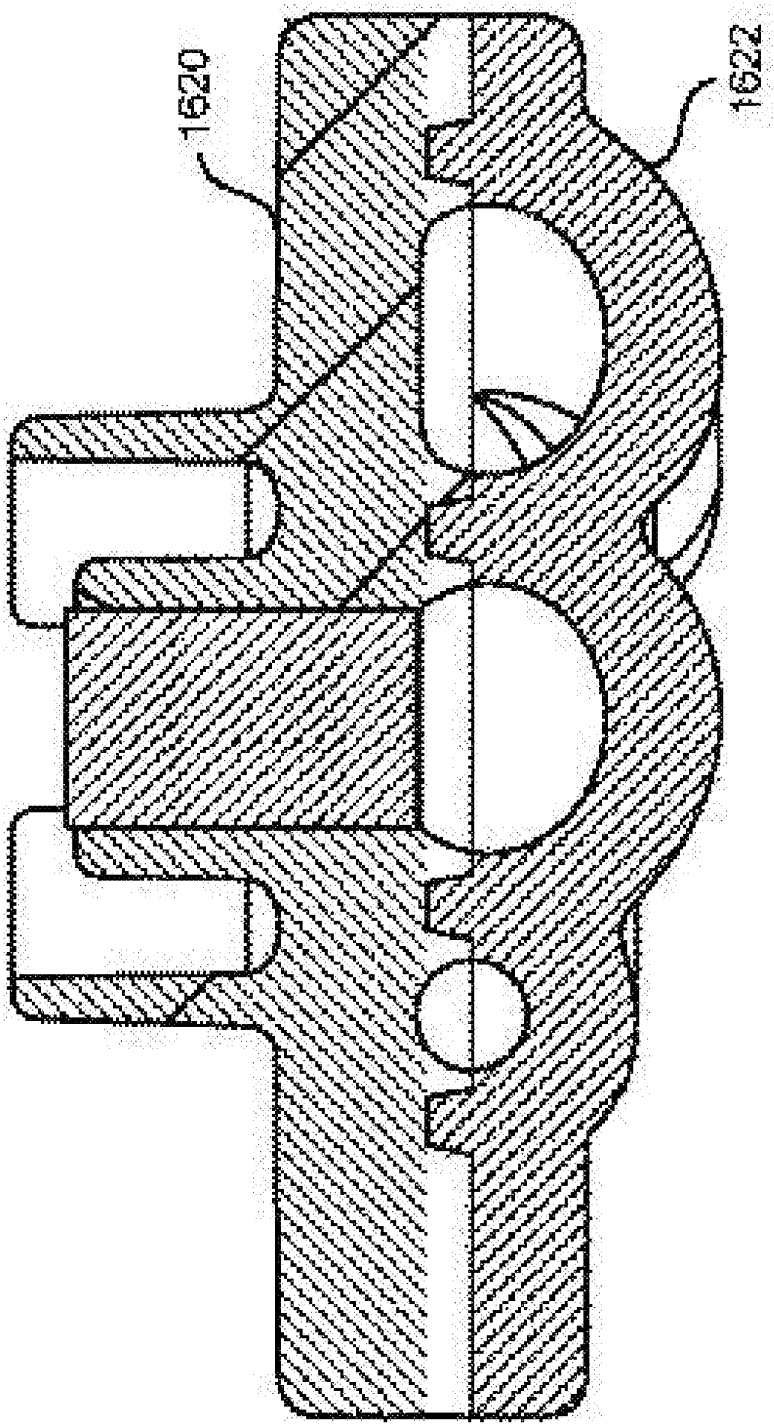


FIG. 19B

[Fig. 20]

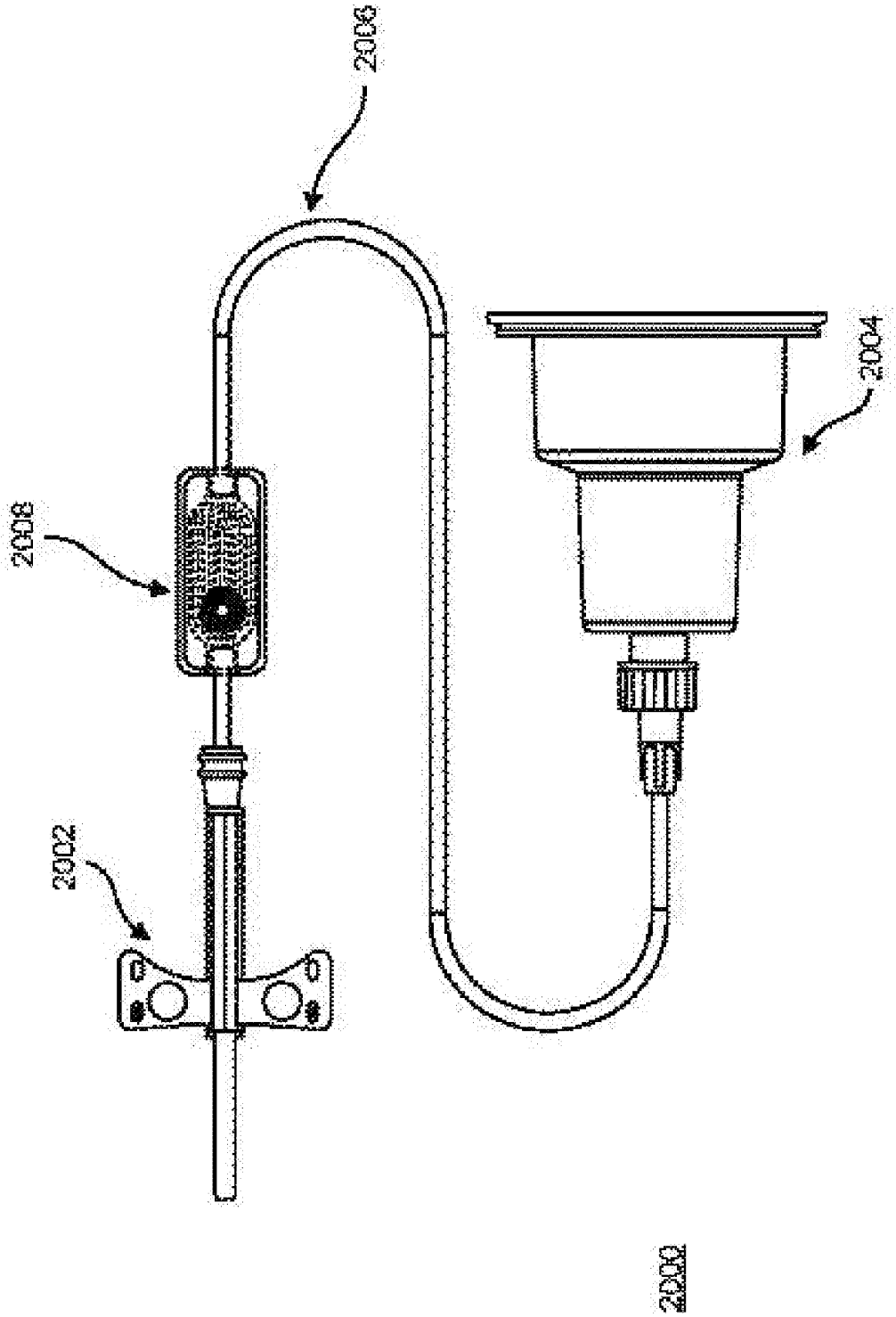


FIG. 20

[Fig. 21]

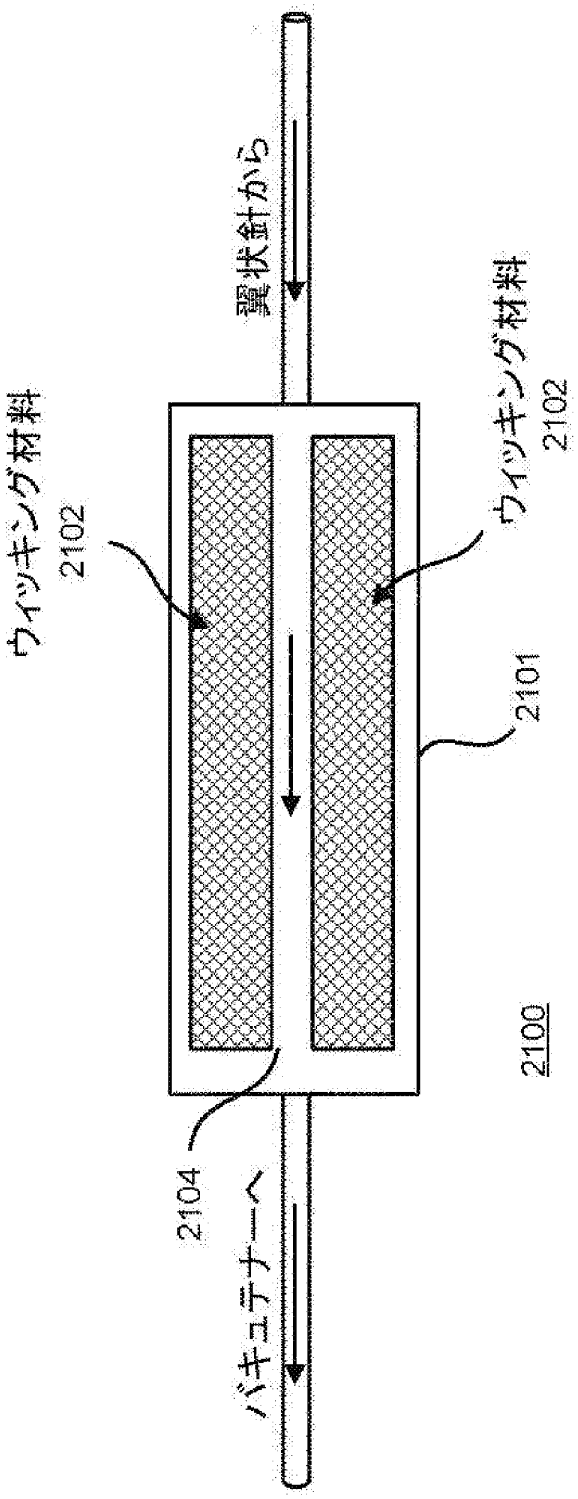


FIG. 21

[Fig. 22A]

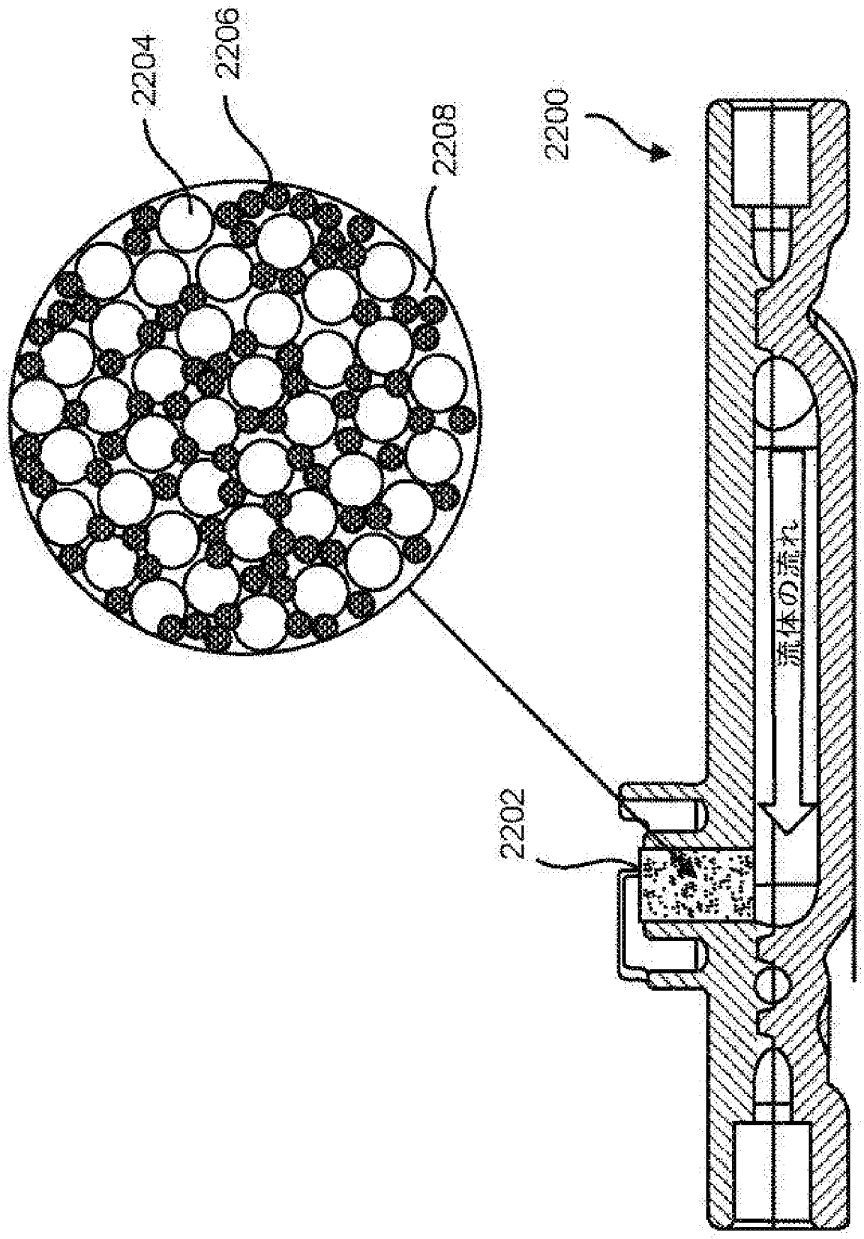


FIG. 22A

[Fig. 22B]

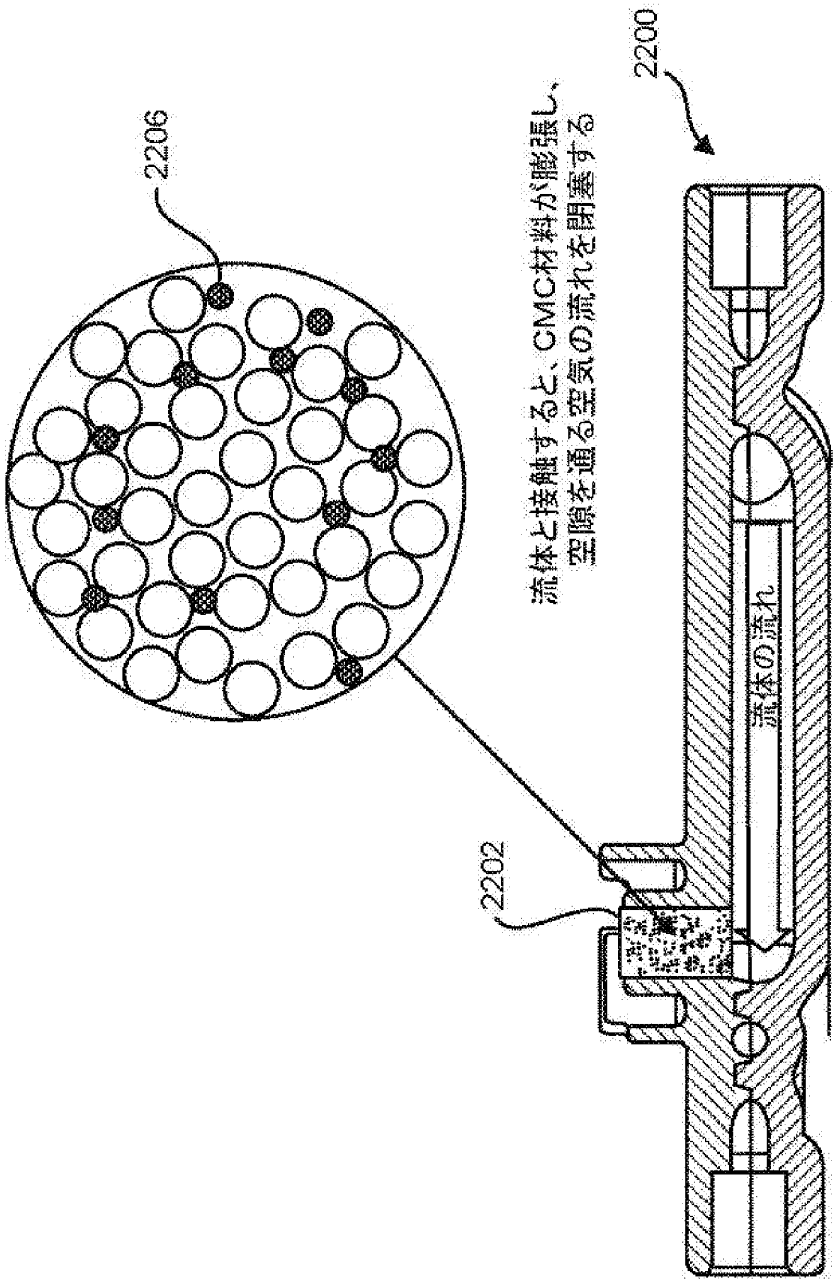


FIG. 22B

[Fig. 23A]

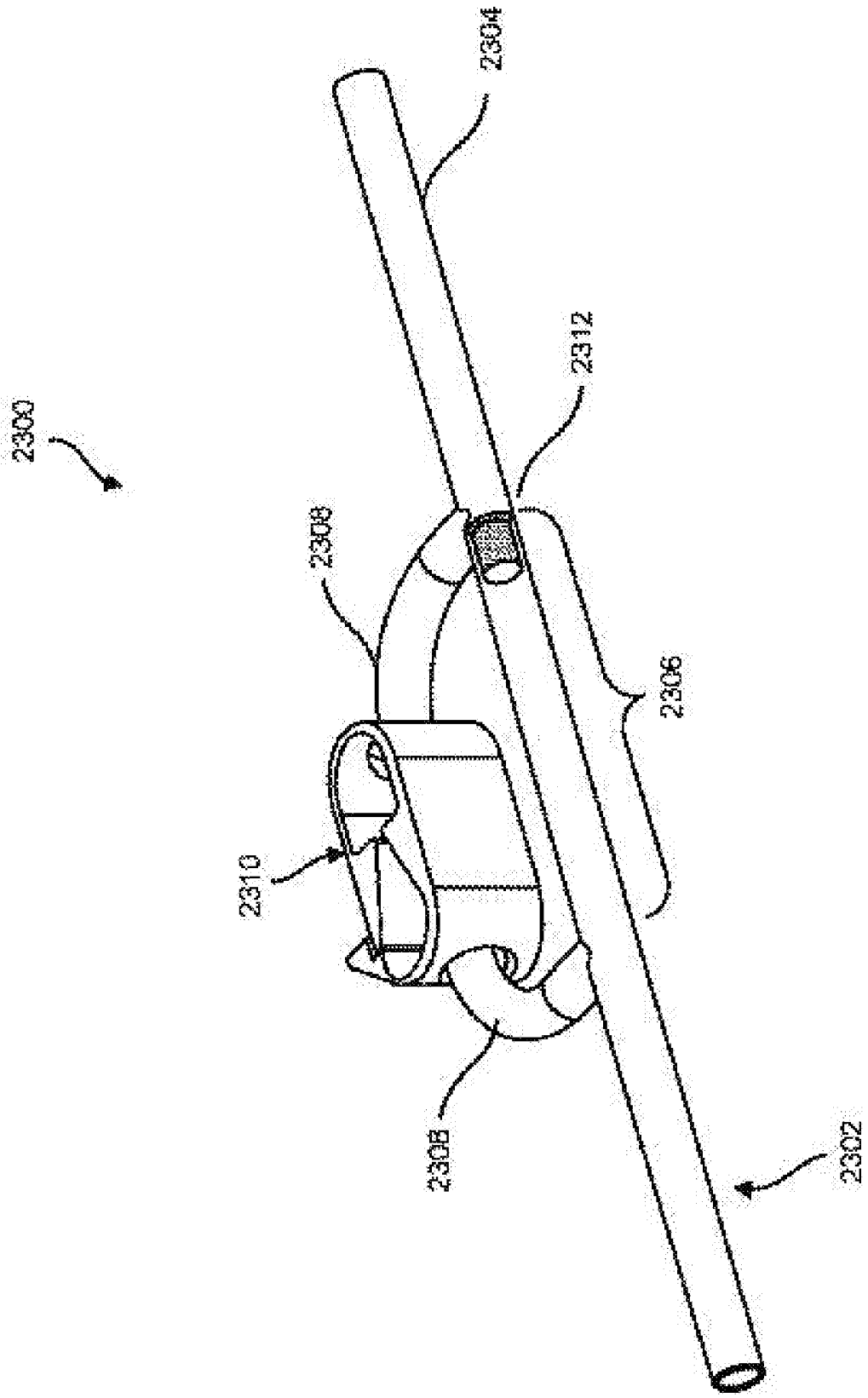


FIG. 23A

[Fig. 23B]

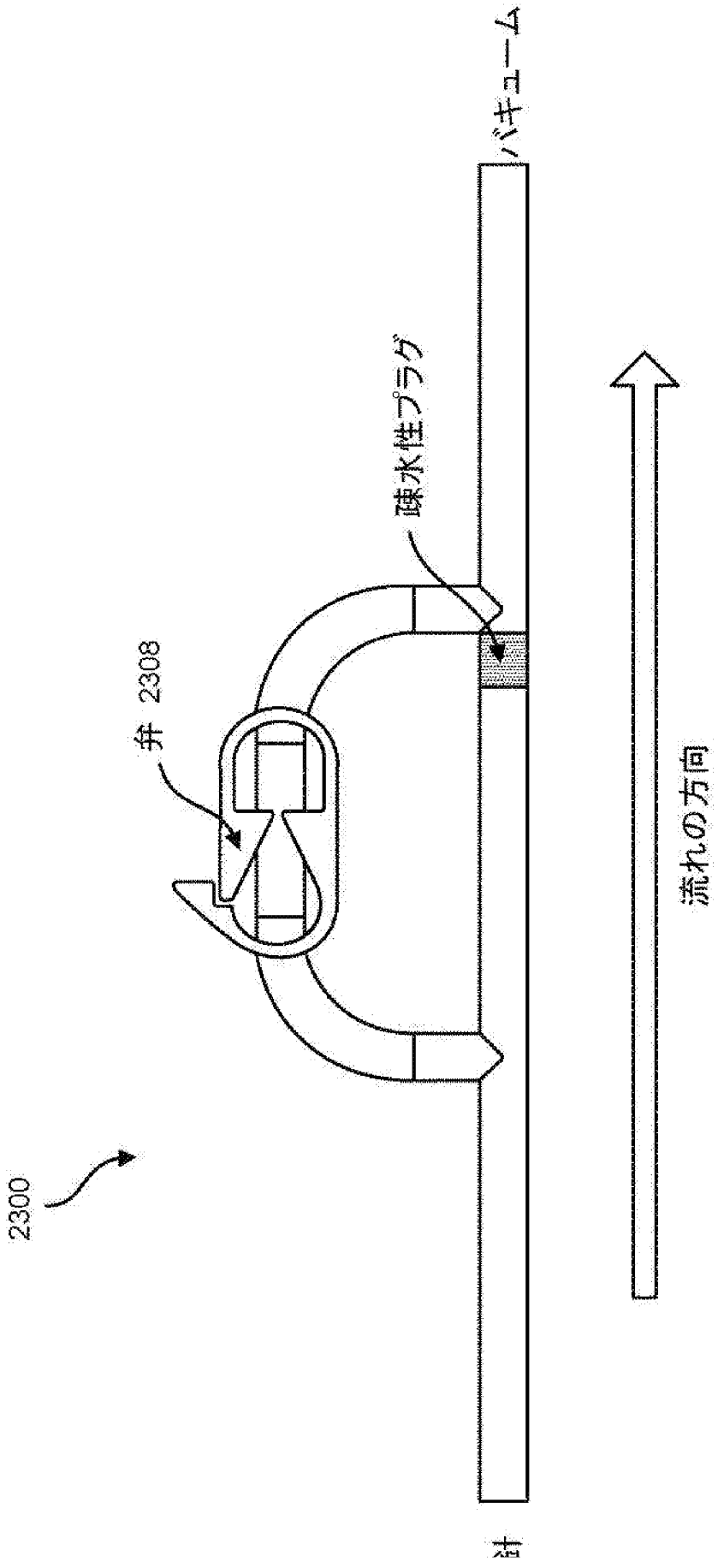


FIG. 23B

drawing open

1 2 3 Four Five 6 7 8A 8B 8C ...

Magnify and Rotate

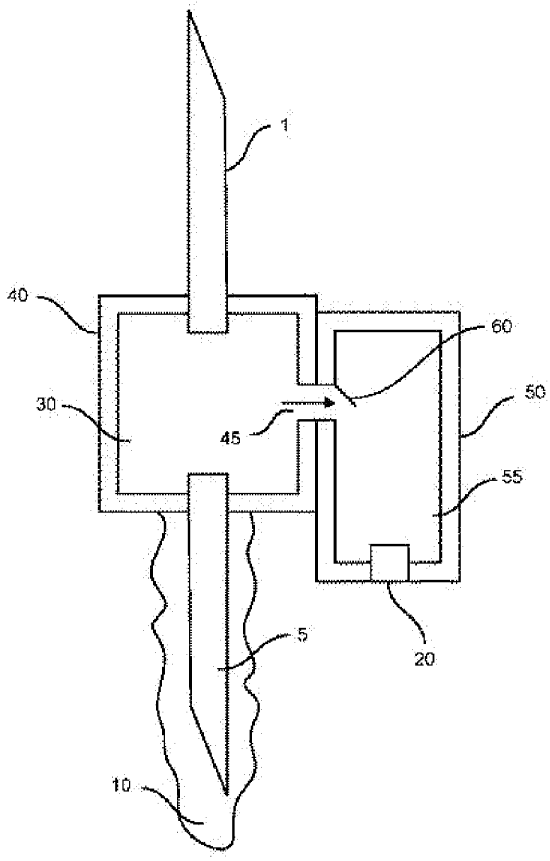


FIG. 1

Figure 1

1 / 1 display

Copyright JPO and INPIT

Espacenet

Bibliographic data: JP6643474 (B2) — 2020-02-12

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Inventor(s): ロジャーズ、 ボビー, ; カン、 ジーノ, ; デトロフ、 ジョン

Applicant(s): クリン インコーポレイテッド

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

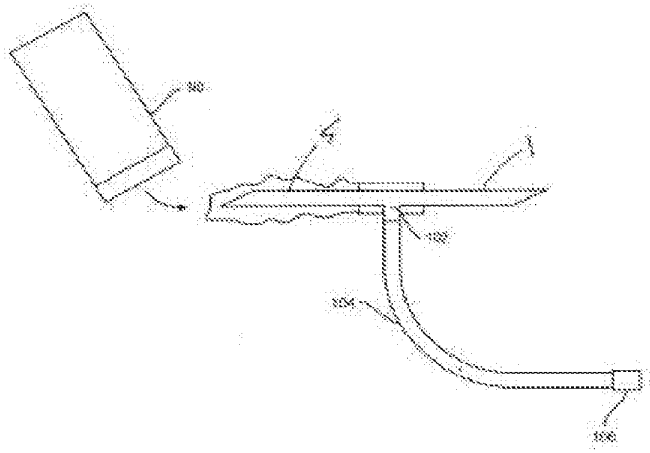
Application number: JP20180523384 20160722 Global Dossier

Priority number(s): US201562238636P 20151007 ; US201662318194P 20160404 ; US201562196797P 20150724 ; US201615140448 20160427 ; US201615140443 20160427 ; WO2016US43709 20160722

Also published as: AU2016297849 (A1) CA2993646 (A1) EP3324845 (A1) EP3324845 (B1) EP3622890 (A1) more

Abstract not available for JP6643474 (B2)
Abstract of corresponding document: US2017020427 (A1)

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



(19)日本国特許庁(JP)　(12)特　許　公　報(B2)　(11)特許番号
特許第6643474号
(P6643474)
(45)発行日　令和2年2月12日(2020.2.12)　(24)登録日　令和2年1月8日(2020.1.8)

(51)Int.Cl.　　F I
A61B 5/15 (2006.01)　A61B 5/15 200
A61B 5/154 (2006.01)　A61B 5/154 200

請求項の数 16　(全 39 頁)

(21)出願番号　特願2018-523384(P2018-523384)
(86)(22)出願日　平成28年7月22日(2016.7.22)
(65)公表番号　特表2018-525191(P2018-525191A)
(43)公表日　平成30年9月6日(2018.9.6)
(86)国際出願番号　PCT/US2016/043709
(87)国際公開番号　WO2017/019552
(87)国際公開日　平成29年2月2日(2017.2.2)
審査請求日　令和1年5月20日(2019.5.20)
(31)優先権主張番号　62/238,636
(32)優先日　平成27年10月7日(2015.10.7)
(33)優先権主張国・地域又は機関
米国(US)
(31)優先権主張番号　62/318,194
(32)優先日　平成28年4月4日(2016.4.4)
(33)優先権主張国・地域又は機関
米国(US)

(73)特許権者　518026730
クリン　インコーポレイテッド
アメリカ合衆国　９２１３１　カリフォルニア州　サンディエゴ　スクリップス　ポーウェイ　パークウェイ　１０７５５　ナンバー　２５７
(74)代理人　100083806
弁理士　三好　秀和
(74)代理人　100095500
弁理士　伊藤　正和
(74)代理人　100111235
弁理士　原　裕子
(74)代理人　100195257
弁理士　大渕　一志

最終頁に続く

(54)【発明の名称】血液サンプル最適化システム及び血液隔離装置

(57)【特許請求の範囲】
【請求項１】
血液サンプル最適化システムであって、
採血システムであって、
患者の血液サンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、
前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と、
前記血液サンプルの後続の部分を採取しかつ収容するために真空採血管を受け入れるように構成されたサンプル針と
を含む採血システムと、
前記患者針と前記サンプル針との間に前記採血経路に沿って接続された血液隔離装置であって、
前記血液サンプルを受け入れるように構成された入口ポートと、
前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記血液サンプルの最初の量を受け入れかつ前記血液サンプルの最初の量の少なくとも最初の部分を隔離するように構成された隔離チャンバと、
前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と
を含み、
前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプル

の後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された出口ポートに向かわせるように構成され、前記出口ポートは、前記血液サンプルの後続の部分を前記真空採血管に排出するように構成され、

前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置と

を含む、血液サンプル最適化システム。

【請求項２】

前記血液隔離装置の前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項１に記載の血液サンプル最適化システム。

【請求項３】

前記サンプル針は、前記採血経路及び前記サンプリング流路を介した前記患者針へのアクセスを開くために前記真空採血管によって穿孔されるシールを含む、請求項２に記載の血液サンプル最適化システム。

【請求項４】

前記血液隔離装置の前記サンプリング流路は、前記サンプル針を開封する前記真空採血管によって真空圧力下で前記血液サンプルの後続部分を前記入口ポートに進入させる、請求項３に記載の血液サンプル最適化システム。

【請求項５】

前記血液隔離装置の前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項１に記載の血液サンプル最適化システム。

【請求項６】

前記採血システムの前記採血経路はチューブを含む、請求項１に記載の血液サンプル最適化システム。

【請求項７】

患者から血液サンプルを取り出せるようにするように構成された患者針と、密封されたサンプル針であって、前記サンプル針を開封しかつ取り出せるようにされた血液サンプルを患者から採取するために真空採血管を受け入れるように適合されたサンプル針とを含む血液採取システムに接続された血液隔離装置であって、

前記患者針に接続され、患者からの血液サンプルを受け入れるように構成されたた入口ポートと、

前記入口ポートに接続された出口ポートと、

前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記サンプル針が前記真空採血管によって開封される前に前記血液サンプルの最初の部分を受け入れかつ隔離するように構成された隔離チャンバと、

前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と

を含み、

前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された前記出口ポートに向かわせるように構成され、

前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置。

【請求項８】

前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項７に記載の血液隔離装置。

【請求項９】

前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項７に記載の血液隔離装置。
【請求項１０】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項７に記載の血液隔離装置。
【請求項１１】
血液サンプル最適化システムであって、
採血システムであって、
患者の血液サンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、
前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と、
前記血液サンプルの後続の部分を採取しかつ収容するために真空採血管を受け入れるように構成されたサンプル針と
を含む採血システムと、
前記患者針と前記サンプル針との間に前記採血経路に沿って接続された血液隔離装置であって、
前記血液サンプルを受け入れるように構成された入口ポートと、
前記入口ポート及び前記採血システムのサンプル針に接続された出口ポートと、
前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記血液サンプルの最初の量を受け入れかつ前記血液サンプルの最初の量の少なくとも最初の部分を隔離するように構成された隔離チャンバと、
前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と
を含み、
前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された前記出口ポートに向かわせるように構成され、
前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置と
を含む、血液サンプル最適化システム。
【請求項１２】
前記血液隔離装置の前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項１１に記載の血液サンプル最適化システム。
【請求項１３】
前記サンプル針は、前記採血経路を介した前記患者針へのアクセスを開くために前記真空採血管によって穿孔されるシールを含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１４】
前記血液隔離装置の前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１５】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１６】
前記採血システムの前記採血経路はチューブを含む、請求項１１に記載の血液サンプル最適化システム。
【発明の詳細な説明】
【背景技術】

【０００１】
関連出願との相互参照
本出願は、２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４３号及び２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４８号の優先権の利益を主張するものであり、これらの米国非仮出願の両方が２０１５年７月２４日に出願された「血液培養改良システム及び方法」と題する米国仮特許出願第６２／１９６，７９７号、２０１５年１０月７日に出願された「非汚染採血用の血液隔離システム」と題する米国仮出願第６２／２３８，６３６号、及び２０１６年４月４日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国仮特許出願第６２／３１８，１９４号の優先権を主張しており、これらの開示はその全体が参照により本明細書に含まれるものとする。
【０００２】
菌血症は、血液中に微生物が存在することである。一方、敗血症は、発熱、頻脈、頻呼吸及び低血圧などの臨床症状及び臨床兆候がある場合の菌血症である。菌血症及び敗血症は、高い死亡率、入院発生率及び入院期間と関連する費用の増加とを伴う。多くの菌血症、敗血症、真菌血症及び他の病原体が実際に病院又は他の医療施設内で発生し、カテーテル及び静脈穿刺がこれらの病原体の潜在的なキャリアとしての汚染源である。
【０００３】
血液培養は、患者の血液中の菌血症及び敗血症に関連する微生物病原体を検出するのに使用される標準検査である。血液培養という用語は、血液が１つ以上の血液培養ボトル又は容器に接種される、末梢部位又は中心ライン又は動脈ラインからの１回の静脈穿刺を指す。１つのボトルが１つの血液培養と見なされ、２つ以上がセットと見なされる。複数のセットは複数の静脈穿刺から得られ、患者の異なる部位に関連する。
【０００４】
これらの方法は、敗血症を管理する上で重要な要素である微生物同定及び感受性検査を可能にするが、迅速な結果が得られないことと厄介な病原体に対する感度が低いことが、改良されたシステムの開発及び補助的な分子検査又はプロテオミクス検査につながっている。
【０００５】
血液培養を行うための血液サンプルの採取は、現代の患者ケアの重要な要素であり、正確な診断を提供することによって患者の結果に良い影響を与えることも、不必要な抗菌療法を長引かせ、入院期間を長くし、コストを増加させることによって結果に悪影響を与えることもある。
【０００６】
血液培養の採取の１つの結果は、汚染である。血液培養の汚染は、偽陽性の培養結果及び／又は医療関連コストの著しい増加につながる可能性がある。血液培養の汚染の原因は、不適切な皮膚消毒、不適切な採取管の消毒、最初の採血の汚染を含み、これらは結果を歪める可能性がある。
【０００７】
血液培養採取キットは、一般に、ＢＤ、スミス、ビー・ブラウンなどの会社によって提供される「バタフライ」セット、輸液セット、又は他のタイプの静脈穿刺装置と、好気性血液培養ボトル及び嫌気性血液培養ボトルとで構成される。様々な異なるボトルも検査要件に応じて利用可能である。これらのボトルは、好気性生物と嫌気性生物の両方の回収を最適化するように特別に設計されている。従来のキットでは、使用されるボトルは一般に「バキュテナー（登録商標）」として知られており、これは、所定の量の血液などの液体の採取を容易にするべく管の内部に真空を作り出すために排気される蓋を備える滅菌ガラス管又は滅菌プラスチック管から形成される採血管である。
【０００８】

偽陽性の血液培養は、一般的に、不十分なサンプリング技術の結果である。それらは、必要でないときに抗生物質を使用させ、病院費及び患者の不安を増大させる。血液培養は、皮膚内への針刺しから採取され、その後で血液のサンプルを取り込むためにバキュテナー（登録商標）が取り付けられる。汚染は、穿刺部位及びその周辺の皮膚領域の不適切又は不完全な消毒によって生じ得る。それはまた、挿入中の針による皮膚のくりぬきから、くりぬかれた皮膚細胞と関連する汚染物質とがサンプル中に引き込まれることで生じることもある。

【０００９】

皮下注射針を通る血流は層流であり、このため、皮下注射針に圧力降下が加えられるときに流管にわたって流速勾配が発生する。血液を強く吸引するか又は非常に小さな皮下注射針を使用すると、溶解及び赤血球からのカリウムの放出が起こり、それにより血液サンプルが異常になる可能性がある。

【００１０】

他の例では、一部の患者は繊細な静脈を有し、繊細な静脈は、特に患者の状態に対してあまりにも急速に引き出される注射器のプランジャによって加えられるような圧力低下又は真空の下で崩壊し得る。このような状態は事前に知ることが不可能であるため、このような静脈崩壊は危険であり、制御することは非常に困難である。

【００１１】

血液培養の汚染率を低下させるために、例えば、無歯採取技術に関するスタッフの訓練、汚染率に関するフィードバック、及び血液培養採取キットの導入など、様々な戦略が実施されている。皮膚消毒は汚染の心配を減らすことができるが、２０％以上の皮膚の微生物は真皮の深部に位置し、消毒の影響を受けない。ボトル接種の前に針を交換することは、汚染率を低下させることなく針刺し損傷を受ける危険性を高めるので推奨されない。

【００１２】

血液培養の汚染を低減するための一部の従来のシステム及び技術は、中心静脈カテーテル、静脈穿刺及び他の血管アクセスシステムから採取された最初のアリコートの血液を捨てることを含む。しかしながら、これらのシステムは、ユーザーが血管内装置を機械的に操作することを必要とするか又は確実にすることが困難な複雑な一連のステップを踏むこと必要とする。

【発明の概要】

【発明が解決しようとする課題】

【００１３】

本明細書は、血液培養の汚染、細胞の溶解、及び静脈崩壊を低減するためのシステム及び方法を提示する。一部の実施では、システム及び方法は、ユーザーの消毒のばらつきをなくし、また皮膚細胞が血液培養サンプルに入り込む危険性をなくすこともできる。本明細書に開示されたシステム及び方法は、汚染物質のない血液サンプルを採取するためにバキュテナー（登録商標）又は他の採血装置（すなわち、注射器）をいつ取り付けるべきかを潜在的に示す以外は、既存の臨床プロセスの変更を必要としない。

【００１４】

本明細書に開示されたシステム及び方法の一部の実施では、採血は、患者自身の血圧の使用によって受動的に成し遂げられ、それによって静脈崩壊の危険性を低減し、現行の実務を超える更なるユーザーのステップを排除する。システム及び方法は、短経路の直接刺し又はバタフライ静脈穿刺システムに適合するように適用されることができる。カテーテルを通して採取されたサンプルと共に使用されることもできる。

【課題を解決するための手段】

【００１５】

一態様では、血液隔離装置が提示されている。血液隔離装置は、入口ポートと出口ポートとを含む。血液隔離装置は、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端と、出口ポートと接続される遠位端とを有する、サンプリング流路

を更に含む。

【００１６】

別の態様では、採血経路と接続される血液隔離装置が記載されている。採血経路は、患者針とサンプル採取装置とを有する。血液隔離装置は、患者針と接続される入口ポートと、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバとを含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路と、サンプリング流路の遠位端及びサンプル採取装置と接続される出口ポートとを更に含む。

【００１７】

更に別の態様では、採血システムと接続される血液隔離装置が記載されている。採血システムは、患者から血液サンプルを取り出せるようにするための患者針と、密封され且つ真空採血管を受け入れるように適合されたサンプル針とを含む。血液隔離装置は、患者からの血液サンプルを受け入れるために患者針と接続される入口ポートを含む。血液隔離装置は、入口ポートと接続され且つ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、サンプル針が真空採血管によって開封されるより前に血液サンプルの最初の部分を受け入れ且つ隔離する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、真空採血管によってサンプル針が開封されると血液サンプルの後続の部分を運ぶサンプリング流路を更に含む。血液隔離装置は、血液サンプルの後続の部分をサンプル針に運ぶためにサンプリング流路の遠位端と接続される出口ポートを更に含む。

【００１８】

更に別の態様では、血液サンプル最適化システムが開示され、記載されている。血液サンプル最適化システムは、患者の血液の１つ以上のサンプルを取り出せるようにし且つ得るための採血システムと、静脈穿刺プロセスによって汚染されている恐れがあり且つ患者の血液中の病原体の偽陽性同定をもたらす可能性がある患者の血液の１つ以上のサンプルの最初の部分を受け入れ且つ隔離するための血液隔離装置とを含む。

【００１９】

採血システムは、患者の血液のサンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、血液サンプルを運ぶために患者針と接続される採血経路と、血液サンプルの後続の部分を採取し且つ収容するために真空採血容器を受け入れるように構成されたサンプル針とを含む。

【００２０】

更に別の態様では、血液隔離装置が開示され、記載されている。一部の実施では、血液隔離装置は、入口ポートと、入口ポートと接続される出口ポートと、入口ポートと接続される隔離チャンバとを含むことができる。隔離チャンバは、空気透過性血液バリアを含む通気口を有することができる。

【００２１】

血液隔離装置は、患者針とサンプル針との間で採血経路に沿って接続され、血液サンプルを受け入れるための入口ポートを含む。血液隔離装置は、血液サンプルの最初の量を受け入れるために入口ポートと接続される隔離チャンバであって、血液サンプルの最初の量の少なくとも最初の部分を隔離するために空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、隔離チャンバが血液サンプルの最初の量の少なくとも最初の部分を隔離すると血液サンプルの後続の量を真空採血容器に運ぶサンプリング流路を更に含む。血液隔離装置は、サンプリング流路の遠位端と接続される出口ポートであって、血液サンプルの後続の量を出力する出口ポートを更に含む。

【００２２】

１つ以上の実施形態の詳細が、添付の図面及び以下の説明に記載されている。他の特徴及び利点は、明細書及び図面並びに特許請求の範囲から明らかになるであろう。

【図面の簡単な説明】

【００２３】
以下、これら及び他の態様について、以下の図面を参照して詳細に説明する。
【図１】血液サンプル最適化システムを示す。
【図２】代替的な実施に従う血液サンプル最適化システムを示す。
【図３】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図４】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図５】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図６】代替的な実施に従う血液サンプル最適化システムを示す。
【図７】血液培養の質を最適化するための方法のフローチャートである。
【図８Ａ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｂ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｃ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｄ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｅ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図９】血液隔離システムに用いる経路スプリッタを示す。
【図１０Ａ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｂ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｃ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｄ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ａ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｂ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｃ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｄ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｅ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１２Ａ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｂ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｃ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｄ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１３Ａ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｂ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｃ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｄ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１４Ａ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｂ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｃ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｄ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｅ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に

別の実施を示す。
【図１５Ａ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｂ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｃ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｄ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｅ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｆ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｇ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１６Ａ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｂ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｃ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｄ】更に別の実施に従う血液隔離装置を示す。
【図１７Ａ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｂ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｃ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｄ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｅ】血液隔離装置用のハウジングの下部部材を示す。
【図１８Ａ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｂ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｃ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｄ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｅ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｆ】血液隔離装置用のハウジングの上部部材を示す。
【図１９Ａ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図１９Ｂ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図２０】血液隔離装置を含む血液サンプル最適化システムを示す。
【図２１】ウィッキング材料チャンバを使用する通気口付きでない血液隔離装置を示す。
【図２２Ａ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２２Ｂ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２３Ａ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。
【図２３Ｂ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。　様々な図面における同様の符号は同様の要素を示す。
【発明を実施するための形態】
【００２４】
本明細書は、採取される血液サンプル中の汚染物質を低減又は排除し、その結果、採取される血液サンプルの血液培養又は他の検査における偽陽性の判断を減少又は排除する血液サンプル最適化システム及び方法を記載している。一部の実施では、血液サンプル最適化システムは、患者の血流への血管アクセスのための患者針と、バキュテナー（登録商標）のような真空採血容器又は真空採血管などの採血容器か又は他のサンプリング装置に血液サンプルを供給するためのサンプル針と、患者針とサンプル針との間に位置する血液隔離装置とを含む。血液隔離装置は、汚染されている可能性のある最初のアリコートの血液を隔離するための隔離チャンバを含み、最初のアリコートの血液が隔離チャンバ内に隔離された後に患者針とサンプル針との間の汚染されていない可能性のある血液を運ぶために隔離チャンバを迂回するサンプリング流路を更に含むことができる。
【００２５】
図１は、一部の実施に従う血液サンプル最適化システムを示す。システムは、患者の皮膚を穿刺してその中の患者の静脈及び静脈内の血液にアクセスするための患者針１を含む。システムは、再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース

又は装置内に収容され且つ再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース又は装置によって当初は密封されていることができる、サンプル針（すなわち、バキュテナー（登録商標）などと共に使用するための再密封可能に密封された針）５を更に含む。再密封可能なブーツ１０は、患者の血液を採取するためのバキュテナー（登録商標）ボトル（図示せず）を用いることによって、サンプル針５のそばに又はサンプル針５の周りに押し付けることができる。システムは、サンプル針５に通じる低容量チャンバ３０を更に含むことができるが、ハウジング５０によって形成される隔離チャンバ５５に通じる穴又は１つ以上の流路４５も含む。

【００２６】

隔離チャンバ５５は、隔離チャンバ５５の容積に応じて、所定の又は測定された量であることができる、患者の血液の最初のアリコートを受け入れ且つ保持するためのチャンバ、流路、通路、ロック、又は他の構造である。最初の採血は、一般的に、後続の採血に比べて菌血症及び敗血症を引き起こす微生物又は他の病原体を含有しているか又はより含有の影響を受けやすい。隔離チャンバ５５は、硬いハウジング内に収容されるか、ハウジング自体に形成され又はハウジング自体によって画定された容器であることができ、或いはチューブ又は内腔として実現されることができる。隔離チャンバ５５は、どのように形成され且つ実施されるかにかかわらず、所定の容積を有することができる。一部の実施では、所定の容積は、患者針の容積に基づくこと、すなわち、患者針の容積よりも少ない容積から任意の容積から患者針の容積の２０倍以上大きい容積までの範囲であることができる。隔離チャンバ５５の所定の容積は、隔離され且つ処分される血液の量を節約又は最小化するように設定されることもできる。

【００２７】

隔離チャンバ５５は、チャンバハウジング５０内に形成、包含、又は収容されることができ、プラスチック、ゴム、鋼、アルミニウム又は他の適切な材料で作られることができる。例えば、隔離チャンバ５５は、可撓性チューブ又は他のエラストマー材料から形成されることができる。隔離チャンバ５５は、空気が隔離チャンバ５５から出ることを可能にする空気透過性血液バリア２０を更に含む。本明細書で使用される「空気透過性血液バリア」という用語は、空気透過性であるが実質的に血液不透過性の物質、材料又は構造体を意味する。代表的な例は、疎水性膜及び疎水性コーティング、疎水性膜又は疎水性コーティングと組み合わせた親水性膜又は親水性コーティング、メッシュ、フィルタ、機械的弁、抗菌性材料、又は隔離チャンバ５５が血液で満たされるときに隔離チャンバ５５から空気を追い出すことができる他の任意の手段を含むことができる。様々な例示的な実施形態において、空気透過性血液バリアは、空気が液体と接触するまで通過することを可能にする１つ以上の材料によって形成されることができ、このような材料は、空気及び／又は液体の通過を防止又は阻止するために完全に又は部分的に密封される。言い換えれば、液体との接触より前に、材料は空気透過性のバリアを形成している。液体との接触後、材料は、空気及び／又は液体の更なる通過を実質的に又は完全に防止する。

【００２８】

穴又は流路４５は、任意の所望の長さ、断面形状又はサイズであることができ、且つ／又は任意の所望の角度又は向きで低容量チャンバ３０から離れるように形成されることができる。穴又は流路４５はまた、最初のアリコートの血液サンプルを隔離チャンバ５５内に保持する一方向フラップ又は一方向弁６０を含むことができる。一部の特定の実施では、穴又は流路４５は、低容量チャンバ３０から隔離チャンバ５５への一方向の血液の流れのための「ダックビル」弁又はフラッパ弁６０などを含むことができる。空気透過性血液バリア２０は、空気が出ることを可能にするが血液と接触すると密封する材料で構成することもでき、それによって外気が隔離チャンバ５５に入ることを許容しない。この密封は弁を不要にする。

【００２９】

弁６０は、任意のタイプの弁又は開閉機構であることができる。チャンバ３０は、実質的に残留血液を保持しないように設計されており、特定の容積又は割合の血液を隔離チャ

ンバ５５に保持し又は通過させるように構成することができる。同様に、隔離チャンバ５５は、抗菌コーティングのような任意のタイプのコーティング、又は隔離された最初の採血の成分の同定及び／又は診断を支援するコーティングも含むことができる。

【００３０】

ハウジング５０及び４０は、アクリロニトリルブタジエンスチレン（ＡＢＳ）又は他の熱可塑性材料又はポリマー材料などのプラスチック、ゴム、鋼、又はアルミニウムを含む任意の適切な材料から形成されることができる。空気透過性血液バリア２０は、最初の採血による血液と接触すると又は空気の追い出しが停止されたときに、又は事象と隔離チャンバ５５内の血液との任意の組み合わせの場合に活性化される、色提供物質又は他の信号伝達機構を含むことができる。空気透過性のバリアはまた、外部流体源、しぶき等によるフィルタの不注意による又は早過ぎる密封を阻止又は防止する疎水性膜又はカバーなどの外層を含むことができる。隔離チャンバ５５はまた、チャンバが充填されたことをユーザーが視覚的に確認することを可能にするために半透明又は透明であることができる。

【００３１】

図２は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図２に示す実施では、隔離チャンバ５５又は廃棄チャンバが患者針１を取り囲み、端部が開放されたカフ又はハウジングが廃棄チャンバと接続され、サンプル針ハウジングベース及びハウジングを取り囲んでいる。患者針１とサンプル針５とは、ブーツ５６によって互いと接続されており、ブーツ５６は、それを貫通する連続的な採血流路を形成している。ブーツ５６は、採血流路から隔離チャンバ５５に通じる単一の穴又は流路を含む。装置は、他の実施では、複数の穴又は流路を含むことができる。各穴又は流路は、一方向弁を含むことができ、所定の量の血流のために寸法設定され且つ適合されることができる。

【００３２】

隔離チャンバ５５は、空気透過性血液バリアを含む。フィルタは、所定容積の血液が隔離チャンバ５５に集められたときに、それぞれ、感知及び／又は指示するためのセンサ又は指標を更に含むことができる。その指示は、バキュテナー（登録商標）などの真空採血管又はボトルをサンプル針５に取り付けるようにユーザーに警告する。隔離チャンバ５５用のハウジングは、任意のサイズ又は形状であることができ、ハウジング内の内部空間又は容積を画定するために任意のタイプの材料を含むことができる。内部空間は、最初は空気のみで満たされているが、汚染除去剤、凝固剤などの薬剤又は物質でコーティングされることもできる。真空採血管がサンプル針５に取り付けられると、血液は自動的に患者針１に、採血流路及びサンプル針５を通ってボトルに流入する。サンプル針５は、採血ボトルがサンプル針に取り付けられていないときにサンプル針を密封する再密封可能なブーツ、コーティング又は膜によって覆われている。

【００３３】

図３は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図示の実施では、サンプル針５は、再密封可能なブーツ又は膜によって取り囲まれ、更に患者針１と接続される。サンプル針及び患者針を通って血液流路が形成される。サンプル針と患者針との間の接続は、主血液流路から隔離チャンバ１０４へと導く流路、ポート又は開口部を含む「Ｔ」又は「Ｙ」コネクタ１０２を含む。

【００３４】

Ｔ又はＹコネクタ１０２は、フラップ又は一方向弁を含み、所定の流量の血液のために寸法設定され且つ適合された穴を有する。隔離チャンバ１０４は、チューブから形成され又は硬いハウジングによって形成されることができ、最初は空気で満たされている。隔離チャンバ１０４は、自動的に、すなわち、患者自身の血圧による圧力下で患者から流出する血液を受け入れる。隔離チャンバ１０４は、好ましくは隔離チャンバ１０４を形成し且つ近位端がＴ又はＹコネクタ１０２に接続されたチューブの遠位端に、空気透過性血液バリア１０６を含む。Ｔ又はＹコネクタ１０２は、最も効率的な血流のために任意の所望の角度で分岐することができ、最初のアリコートの血液と主要な採血サンプルとの混合を最小限に抑え又は排除するために、開口部及び流路と主血液流路との間の接合部分を最小化

するように形成されることができる。

【００３５】

一部の代替的な実施では、サンプル針は、図４に示すように、その反対側の端部がＴ又はＹコネクタ１０２と接続している任意の長さのチューブに取り付けられることができる。隔離チャンバ１０４は、最初のアリコートに所定量の血液サンプルを含む限り、任意の形状又は容積であることができる。Ｔ又はＹコネクタ１０２はまた、主血液流路に対して平行な開口部又は流路を含むことができる。空気透過性血液バリアは、所定量の血液が隔離チャンバに集められたとき、又は放出される空気が特定の閾値、すなわちゼロに達したときを示す指標１０７又は他の機構を更に含むことができる。チューブはまた、挟んでチューブを通る流体の流れを防止するのに使用することができるクリップ１０９を含むことができる。

【００３６】

空気透過性血液バリア及び一次チャンバが密封されると、最初のアリコートの血液が隔離チャンバ１０４に閉じ込められ、サンプルを得るためにバキュテナー（登録商標）ボトルのような真空採血管がサンプル針５に取り付けられる。採血管は取り外すことができ、サンプル針５は再密封される。更なる採血又はサンプルのために、任意の数の後続の採血管を取り付けることができる。全ての採血が完了すると、最初のアリコートの血液が隔離チャンバ１０４に閉じ込められたまま、システムは廃棄される。

【００３７】

図５は、一部の代替的な実施に従う血液サンプル最適化システムを示す。図示の実施では、サンプル針５が患者針とチューブによって接続されている。「Ｔ」又は「Ｙ」コネクタ１２０が、チューブに沿って任意の所望の位置に追加され、実質的に上記のように、隔離チャンバ２０４に通じる開口部、ポート又は流路を含む。

【００３８】

図６は、一次採取流路として形成された隔離チャンバ３０４が最初のアリコートの血液を受け入れ、採血流路に隣接して設けられている、一部の代替的な実施に従う血液サンプル最適化システムを示す。隔離チャンバ３０４は、採血流路、患者針１及び／又はサンプル針５を取り囲むことができる。一次採取流路は、Ｔ又はＹコネクタ１２０、又は他のタイプの開口部又は流路を含むことができる。隔離チャンバ３０４は空気透過性血液バリアを含み、上記のように、血液などの流体が接触したことの指標を含むこともできる。

【００３９】

一部の実施では、患者針１又はサンプル針５のいずれか又は両方をルアーロック雄コネクタ又はルアーロック雌コネクタで置き換えることができる。しかしながら、様々な実施で、血液サンプル最適化システムのサンプル針端部にあるコネクタを最初に密封し、周囲空気圧で加圧され且つ空気透過性血液バリアの空気出口を含む隔離チャンバへ最初のアリコートの血液をそらすことを可能にする。このようにして、システムは受動的且つ自動的に患者自身の血圧を用いて隔離チャンバの周囲空気圧に打ち勝ち、空気透過性血液バリアを通して空気を押し出し、隔離チャンバ内の空気を血液に置き換える。

【００４０】

図７は、血液培養の質を最適化するための例示的な方法のフローチャートである。７０２において、臨床医が患者の静脈に針を挿入する。７０４において、血液が隔離チャンバに流れ込み、隔離チャンバ内の空気を隔離チャンバから空気透過性血液バリアを通して押し出す。一部の実施では、隔離チャンバの容積は、０．１立方センチメートル（ｃｃ）未満から５立方センチメートル（ｃｃ）以上である。隔離チャンバは、血液サンプルの第２部分及び他の後続の部分又は後続の採取よりも汚染しやすい血液サンプルの第１部分を採取するように寸法設定され且つ適合されている。隔離チャンバは空気透過性血液バリアを有し、この血液バリアを通して空気を患者の静脈から押し出された血液で追い出すことができるので、このような血液は、血液サンプルを受け入れ且つ保管するためのバキュテナー（登録商標）又は他のボトルに引き込まれるか又は他の方法で入る前に、必然的に且つ自動的に隔離チャンバに流入する。

【００４１】
隔離チャンバがいっぱいになると、血液は、血液が通過するのを阻止又は防止する空気透過性血液バリアに集まるか、さもなければ接触する。７０６において、血液が空気透過性血液バリアの全内部表面積と接触すると、空気透過性血液バリアは閉じられ、空気はもはや流出又は流入しない。７０８において、臨床医は、バキュテナー（登録商標）などの真空採血管を取り付けることができることを示す指標を提供されるか又は満杯のチャンバを見ることができる。指標は、一次チャンバがいっぱいであるか否かを確認するための一次チャンバの可視性、例えば、色を変える血液バリア、又は他の指標を含むことができる。隔離チャンバの充填時間は、実質的に瞬間的であり得るので、このような指標は、存在する場合、隔離チャンバが満たされているというだけである可能性がある。

【００４２】
真空採血管が取り付けられる前、針、サンプリング流路、及び隔離チャンバの間の連通は、隔離チャンバの血液バリアの密封によって制限され、従って隔離によって空気がシステムに再び入ることを可能にしない。連通経路の密封は、機械的にねじること又は他の動作、小さな穴又は曲がりくねった経路によって達成され、臨床医による別個の弁又は機械的な動作又は操作の必要性をなくす。７１０において、真空採血管を取り外すと、自己密封式の膜がサンプル針を密封し、７１２で、更なる後続の真空採血管を取り付けることができる。７１４において、サンプルが採取されると、装置が患者から取り外され、廃棄される。

【００４３】
図８Ａ～８Ｅは、一部の実施に従う、非汚染採血用の例示的な血液サンプル最適化システム８００を示す。血液サンプル最適化システム８００は、チューブ、患者針（又は両方）、又は他の血管又は静脈アクセス装置に接続されることができる入口ポート８０２と、隔離チャンバチューブ８０６への第１出口とサンプル採取チューブ８０８への第２出口とを有する経路スプリッタ８０４とを含む。隔離チャンバチューブ８０６及びサンプル採取チューブ８０８の一方又は両方は、チューブから形成されることができる。一部の実施では、隔離チャンバチューブ８０６は、特定の量の当初血液サンプルを収容するように寸法設定される。サンプル採取チューブ８０８は、ひとたび隔離チャンバチューブ８０６が満たされると、血液サンプルを受け入れる。サンプル採取チューブ８０８は、バキュテナー（登録商標）ベース又はハウジング８１０、又は他の血液サンプル採取装置に接続されることができる。

【００４４】
血液隔離システム８００は血液隔離装置８１２を更に含み、血液隔離装置８１２は、図８Ｂ～８Ｄにより詳細に示すようにハウジング８１８を含み、ハウジング８１８は、非汚染サンプル採取チューブ８０８用の経路を画定するか又はいずれかの端部が非汚染サンプル採取チューブ８０８と接続されるサンプリング流路８２０を含む。サンプリング流路８２０は、非汚染サンプル採取チューブ８０８に沿った位置でハウジング８１８をより良好に固定し且つ安定させるように、ハウジング８１８を通って曲線状であることができる。

【００４５】
血液隔離装置８１２は、隔離チャンバチューブ８０６と接続される隔離チャンバ８２２又は他のチャンバを更に含む。隔離チャンバ８２２は、空気透過性血液バリア８２４で終端している。空気透過性血液バリア８２４はまた、血液サンプル（すなわち、非汚染血液サンプル）の正式な採取を開始することができる指標として、血液との完全な接触時に異なる色に変わる着色剤を含むことができる。小さい光、音発生機構などの他の指標を使用することができる。一部の実施では、空気透過性血液バリアは、隔離チャンバ８２２の方向から直角に配置されているが、ハウジング８１８に使用される空間及び材料を節約するために任意の距離又は向きに配置されることができる。ハウジング８１８及びその内容物は、任意の剛性材料又は半剛性材料又は一連の材料から形成されることができる。

【００４６】
図９は、例えば、図８Ａ～８Ｅに示すような血液隔離システムに用いる経路スプリッタ

９００を示す。経路スプリッタ９００は、入口ポート９０２と、主管路出口ポート９０４と、隔離流路出口ポート９０６とを含む。入口ポート９０２は、同様に患者針システムに接続される主チューブに、又は直接患者針に接続されることができる。主管路出口ポート９０４は、バキュテナー（登録商標）ベース又はハウジングなどの採血システムへの主管路チューブに、又は直接そのような採血システムに接続されることができる。隔離流路出口ポート９０６は、測定された量又は所定の閾値まで血液の第１サンプルを受け入れ且つ隔離するための隔離チューブに接続されることができる。代わりに、隔離流路出口ポート９０６は、隔離チャンバに接続することができる。隔離流路出口ポート９０６は、好ましくは、主管路出口ポート９０４から２０～７０度の角度に曲げられ、一方、主管路出口ポート９０４は、好ましくは、入口ポート９０２と一直線である。所定の量の最初の血液サンプルが、本明細書に記載された機構及び技術に従って隔離チューブ又は隔離チャンバ内に隔離されると、後続の血液サンプルは、入口ポート９０２に流入し、障害物なしで主管路出口ポート９０４から直接流出する。

【００４７】

図１０Ａ～１０Ｄは、別の実施に従う血液隔離装置１０００を示す。血液隔離装置１０００は、入口ポート１００２と、主出口ポート１００４と、隔離流路ポート１００６とを含む。入口ポート１００２は、患者針又は関連するチューブと接続されることができる。主出口ポート１００４は、バキュテナー（登録商標）、関連するチューブ、又はルアー作動弁などの血液サンプル採取装置に接続されることができる。隔離流路ポート１００６は、主出口ポート１００４から隔離チャンバ１００８に分離する。一部の実施では、隔離チャンバ１００８は、ハウジング又は他の容器１００１内に螺旋流路として形成される。

【００４８】

隔離チャンバ１００８は、実質的に上記のように、遠位端が空気透過性血液バリア１０１０に接続される。隔離チャンバ１００８内の空気は、空気透過性血液バリア１０１０を通して、隔離流路ポート１００６内に案内される最初のアリコートの血液によって追い出される。ひとたび隔離チャンバ１００８が満たされると、主出口ポート１００４を通る更なる採血が成し遂げられ、これらのサンプルは汚染されていない。

【００４９】

図１１Ａ～１１Ｅは、他の代替的な実施に従う血液隔離装置１１００を示す。血液隔離装置１１００は、上述の入口ポートと同様の入口ポート１１０２と、主出口ポート１１０４と、主出口ポート１１０４及び入口ポート１１０２から分離する隔離流路ポート１１０６とを含む。隔離流路ポートは、隔離チャンバ１１０８に接続されている。図１１Ａ～１１Ｅに示す実施では、血液隔離装置は、隔離チャンバ１１０８として機能する流路を内部に有するベース部材１１０１を含む。流路は、ベース部材１１０１を通る曲がりくねった経路として形成されることができ、一方、ベース部材１１０１は、患者の四肢に載るように成形され且つ形成される。

【００５０】

隔離チャンバ１１０８の一部は、血液隔離指標１１０９として機能するように、空気透過性血液バリア１１１０に出る直前に、ベース部材から又はベース部材の上面付近に突出することができる。指標１１０９は、透明な材料、又は血液と接触すると変色する材料で形成されることができる。

【００５１】

一部の実施では、血液隔離装置１１００は、常時閉じている針、バキュテナー（登録商標）シールド又は他の採取装置などの採血装置１１２０を含むことができる。採血装置１１２０は、患者針の挿入プロセスによって汚染される恐れがある最初のアリコートの血液を隔離することができるように、効率及び利便性のために血液隔離装置１１００と共に製造及び販売されることができる。従って、採血装置１１２０は、偽陽性の検査のリスクを低減するように非汚染血液サンプルを採取し且つ非汚染サンプルを確実にすることができる。

【００５２】

図１２Ａ～１２Ｄは、更に他の代替的な実施に従う血液サンプル最適化システム１２００を示す。システム１２００は、バキュテナー（登録商標）又は他の採取及びサンプリング装置のような採血装置１２０４に取り付けるための血液隔離装置１２０２を含む。血液隔離装置１２０２は、バキュテナー（登録商標）容器又はバイアルが採血装置１２０４の採取針に取り付けられる前に、最初のアリコート又は量の血液を受け入れ、且つその最初のアリコート又は量を血液隔離装置１２０２の隔離流路内に隔離するように、構成され且つ配置されている。

【００５３】

一部の実施では、血液隔離装置１２０２は、入口ポート１２１２と、主出口ポートと、隔離流路ポートとを含むことができる。入口ポート１２１２は、患者針又は関連するチューブに接続されることができる。主出口ポート１２１４は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁との接続を可能にするために、常時閉じている針又は装置に接続されることができる。隔離流路ポートは、主出口ポートから隔離チャンバ１２１８に分離する。

【００５４】

一部の実施では、隔離チャンバ１２１８は、隔離装置１２０２の本体内の流路として形成される。隔離チャンバ１２１８は、Ｕ字形流路、Ｓ字形流路、螺旋流路、又は任意の他の曲がりくねった流路などの曲がりくねった流路であることができる。隔離装置１２０２は、ハウジング又は他の収容体、及びその中に形成された１つ以上の流路を含むことができる。図１２Ａ及び１２Ｂに示すように、隔離装置１２０２は、本体１２０６とキャップ１２０８とを含む。本体１２０６には１つ以上の空洞又は流路が形成され、空洞又は流路にはキャップ１２０８から延びる１つ以上のアーム１２１０が更に形成され、１つ以上のアーム１２１０は、本体１２０６の空洞又は流路に当接して一次採取ポート及び主出口ポートを形成している。

【００５５】

図１３Ａ～１３Ｄは、更に他の代替的な実施に従う血液サンプル最適化システム１３００を示す。システム１３００は、バキュテナー（登録商標）又は他の体液採取及びサンプリング装置などの採血装置１３０４に取り付けるための血液隔離装置１３０２を含む。血液隔離装置１３０２は、バキュテナー（登録商標）容器又はバイアルが採血装置１３０４の採取針に取り付けられる前に、最初のアリコート又は量の血液を受け入れ、且つその最初のアリコート又は量の血液又は他の体液を血液隔離装置１３０２の隔離流路内に隔離するように、構成され且つ配置されている。

【００５６】

血液隔離装置１３０２は、入口ポート１３１４と、主出口ポート１３１２と、隔離流路ポート１３１６とを有するハウジング１３０１を含む。入口ポート１３１４は、患者針又は関連するチューブに接続されることができる。主出口ポート１３１２は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁との接続を可能にするために、常時閉じている針又は装置に接続されることができる。隔離流路ポート１３１６は、主入口ポート１３１４から隔離チャンバ１３１８に分離する。

【００５７】

図１３Ａ～１３Ｄに示す実施例では、隔離チャンバ１３１８は、ハウジング１３０１内の空洞又はチャンバとして形成され、又はハウジング１３０１を画定する壁によって形成される。隔離チャンバ１３１８は、Ｕ字形流路、Ｓ字形流路、螺旋流路などの曲がりくねった流路、又はハウジング１３０１とキャップ１３０７との協働及び接続によって画定される任意の他の曲がりくねった流路であることができ、キャップ１３０７は、隔離チャンバ１３１８内の曲がりくねった流路のための１つ以上の壁又はディレクタを提供する突出部１３０５を含むことができる。キャップ１３０７からの突出部１３０５は、真っ直ぐであるか湾曲していることができ、様々な流路、開口部又は溝が埋め込まれていることができ、キャップ１３０７から任意の角度又は向きで延びることができる。隔離チャンバ１３

１８の形成を完了するためにキャップ１３０７がハウジング１３０１と接続されると、突出部１３０５は曲がりくねった流路の少なくとも一部を形成し、隔離チャンバ１３１８内に曲がりくねった流路によって形成される隔離流路に最初のアリコート又は量の血液又は他の体液を隔離する。

【００５８】

隔離チャンバ１３１８は、実質的に上記のように空気透過性血液バリア１３１０を含む。隔離チャンバ１３１８内の空気は、患者の血圧によって隔離チャンバ１３１８内に供給される最初のアリコートの血液によって空気透過性血液バリア１３１０を通して追い出される。隔離チャンバ１３１８が満たされ、隔離チャンバ１３１８内の空気が追い出されると、バキュテナー（登録商標）のような血液サンプル採取装置によって提供されるような真空又は他の圧力のような力が次のアリコート又は量の血液又は体液を引き抜くために提供されるまで、患者の血圧は、血液隔離装置１３０２、特に、出口ポート１３１２に更なる血液を追い込み又は提供するのには不十分である。主出口ポート１３１２を通して更なる採血を行うことができ、あらゆる汚染物質が最初のアリコートの血液と共に隔離チャンバ１３１８内に隔離されているので、これらのサンプルは汚染されない。

【００５９】

図１４Ａ～１４Ｅは、患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システム１４００の更に別の実施を示す。採血システム１４００は、血液サンプル採取装置１４０３と患者針（図示せず）との間に接続されることができる血液隔離装置１４０１を含む。血液サンプル採取装置１４０３は、バキュテナー（登録商標）などであることができる。血液隔離装置１４０１は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１４０２を含む。入口ポート１４０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。

【００６０】

入口ポート１４０２は、血液隔離装置１４０１への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有する円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。血液隔離装置１４０１は、血液隔離装置１４０１から及び血液サンプル採取装置１４０３への開口部を画定する出口ポート１４０４を更に含む。出口ポート１４０４は、同様に血液隔離装置１４０３と接続されるチューブ又は他の導管と接続されることもできる。出口ポート１４０４は、ねじ付きキャップ、ルアーコネクタ（雄型又は雌型）、チューブなどを含むがそれらに限定されない様々な装置の取り付け用のねじが切られていない締め代又は接着継手などのコネクタ装置を更に含むことができる。

【００６１】

血液隔離装置１４０１は、入口ポート１４０２と出口ポート１４０４との間にサンプリング流路１４０６を更に含み、サンプリング流路１４０６は、最初のアリコートの血液が隔離されると血液サンプル経路として機能する。サンプリング流路１４０６は、任意のサイズ、形状又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１４０６は、入口ポート１４０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１４０６は、入口ポート１４０２から出口ポート１４０４まで徐々に広がることができる。

【００６２】

血液隔離装置１４０１は隔離チャンバ１４０８を更に含み、隔離チャンバ１４０８は、入口ポート１４０２と出口ポート１４０４との間の任意の位置でサンプリング流路１４０６に接続され且つサンプリング流路１４０６から分離又は方向転換されるが、好ましくは入口ポート１４０２の近くのサンプリング流路１４０６の近位端に接続され且つ近位端か

ら分離又は方向転換される。隔離チャンバ１４０８は、最初は大気圧に維持され、サンプリング流路１４０６からの方向転換点と反対側の隔離チャンバ１４０８の遠位端又はその近傍に空気出口１４１２を含む。空気出口１４１２は、空気透過性血液バリア１４１２を含む。図１４Ｂに示すように、空気透過性血液バリア１４１２は、保護カバー１４１６で覆われていることができる。保護カバー１４１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１４１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも患者自身の血圧によって隔離チャンバ１４０８内に強制的に血液が供給されることによって空気が隔離チャンバから追い出されるときに空気が空気透過性血液バリア１４１２から出ることを可能にする。また、保護カバー１４１６は、空気透過性血液バリアが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００６３】

図１４Ｃ及び１４Ｄに示すように、サンプリング流路１４０６は、赤血球を溶解する可能性を最小限に抑えるために、より小さい直径からより大きい直径になる円筒形又は円錐台形であることができる。同様に、サンプリング流路１４０６は、赤血球を溶解する可能性がある急カーブ又は鋭角が最小限の量で又はなしで形成される。サンプリング流路１４０６は、方向転換経路１４０９を通して入口ポート１４０２の近くで隔離チャンバ１４０８へと分離する。方向転換経路１４０９は、任意の断面形状又はサイズを有することができるが、好ましくは、入口ポート１４０２の少なくとも一部の断面形状と同様である。

【００６４】

一部の実施では、サンプリング流路１４０６及び隔離チャンバ１４０８は、ハウジング１４１４に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１４１４は、プラスチック、金属又は他の剛性又は半剛性材料で作られることができる。ハウジング１４１４は、上部部材と密封可能に嵌合する下部部材を有することができる。下部部材及び上部部材の一方又は両方は、サンプリング流路１４０６及び隔離チャンバ１４０８、並びに方向転換経路１４０９、入口ポート１４０２、及び出口ポート１４０４を含むことができる。一部の他の実施態様では、方向転換経路１４０９、入口ポート１４０２、及び／又は出口ポート１４０４のうちの１つ以上が、ハウジング１４１４のいずれかの端部に接続されるキャップ部材によって少なくとも部分的に形成されることができる。一部の実施では、上部部材及び下部部材、並びにキャップ部材は、レーザ溶接、ヒートシール、接着、スナップ止め、ねじ止め、ボルト止めなどによって互いに連結されることができる。他の実施では、方向転換経路１４０９及び／又は隔離チャンバ１４０８の内面の一部又は全部が、汚染除去剤、凝固剤などの薬剤又は物質でコーティング又は充填されることができる。例えば、隔離チャンバ１４０８が満たされて最初のアリコートの血液が方向転換経路１４０９に戻るとき、隔離された血液の最後の量が凝固し、隔離チャンバ１４０８とサンプリング流路１４０６との間に障壁を作り出すように、方向転換経路１４０９に凝固剤を設けることができる。

【００６５】

図１５Ａ～１５Ｇは、血液隔離装置１５００を示す。血液隔離装置１５００は、真空採血容器又はバキュテナー（登録商標）などの他の採取装置、関連するチューブ、ルアーコネクタ、注射器、ルアー作動弁などとの接続を可能にするために常時閉じている針又は装置に接続されることができる。

【００６６】

血液隔離装置１５００は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１５０２を含む。入口ポート１５０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。入口ポート１５０２は、血液隔離装置１５００への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有す

る円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。

【００６７】

入口ポート１５０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封のコネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザ溶接、又は熱接合などによって、入口ポート１５０２と一体化されることができる。これによって、血液隔離装置１５００は、患者針と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針を血液隔離装置１５００に接続する必要性をなくすことができる。

【００６８】

血液隔離装置１５００は、血液隔離装置１５００から及び血液サンプル採取装置への開口部を画定する出口ポート１５０４を更に含む。出口ポート１５０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１５００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１５００に接続する必要性をなくすことができる。

【００６９】

血液隔離装置１５００は、入口ポート１５０２と出口ポート１５０４との間にサンプリング流路１５０６を更に含み、サンプリング流路１５０６は、最初のアリコートの血液が隔離されると血液サンプル経路として機能する。サンプリング流路１５０６は、任意のサイズ、形状、又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１５０６は、入口ポート１５０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１５０６は、入口ポート１５０２から出口ポート１５０４まで徐々に広がることができる。

【００７０】

血液隔離装置１５００は隔離チャンバ１５０８を更に含み、隔離チャンバ１５０８は、入口ポート１５０２と出口ポート１５０４との間の任意の位置でサンプリング流路１５０６に接続され且つサンプリング流路１５０６から分離又は方向転換されるが、好ましくは入口ポート１５０２の近くのサンプリング流路１５０６の近位端に接続され且つ近位端から分離又は方向転換される。一部の実施では、分水路はＹ字路を含む。隔離チャンバ１５０８は、好ましくは大気圧に維持され、隔離チャンバ１５０８の遠位端又はその近傍に通気口１５１０を含む。通気口１５１０は、空気透過性血液バリア１５１２を含む。図１５Ｃは、隔離チャンバ１５０８が患者からの血液の最初のアリコート又はサンプルで満たされた血液隔離装置１５００を示す。

【００７１】

空気透過性血液バリア１５１２は、保護カバー１５１６で覆されていることができる。保護カバー１５１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１５１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも患者自身の血圧によって隔離チャンバ１５０８内に強制的に血液が供給されることによって空気が隔離チャンバから追い出されるときに空気が空気透過性血液バリア１５１２から出ることを可能にする。保護カバー１５１６は、フィルタが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００７２】

図１５Ｂは、血液隔離装置１５００の出口ポート１５０４及び通気口１５１０を含むハウジング１５０１の上面からの血液隔離装置１５００の斜視図であり、サンプル採取装置が起動される前、サンプリング流路１５０６が空である間に最初のアリコートの血液が隔

離チャンバ１５０８を満たすことを示す。図１５Ｇは、血液隔離装置１５００の出口ポート１５０４及びハウジング１５０１の底面からの血液隔離装置１５００の斜視図であり、サンプル採取装置が起動される前、サンプリング流路１５０６が空である間に最初のアリコートの血液が隔離チャンバ１５０８を満たすことを示す。図１５Ｃは、血液隔離装置１５００の入口ポート１５０２及び通気口１５１０を含むハウジング１５０１の上面からの血液隔離装置１５００の別の斜視図であり、隔離された血液は実質的に隔離チャンバ１５０８内にとどまっている間に血液がサンプリング流路１５０６を通って採取されることを示す。

【００７３】

図１５Ｄは、一部の実施に従う血液隔離装置１５００の断面図であり、サンプリング流路１５０６及び隔離チャンバ１５０８を画定するハウジング１５０１を示す。図１５Ｅ及び１５Ｆは、本明細書に記載される１つ以上の実施に従う血液隔離装置用のハウジングの様々なフォームファクタを示す。

【００７４】

隔離チャンバ１５０８は、サンプリング流路１５０６よりも大きい断面積を有することができ、断面積又は長さは、所定の又は特定の血液量が隔離又はロックされるように構成されることができる。サンプリング流路１５０６は、患者針のチューブ又は採血装置のチューブのいずれか又は両方のためのチューブに適合するように寸法設定されることができる。

【００７５】

ハウジング１５０１は、複数の部品又は単一の一体部品から形成されることができる。一部の実施では、図１５Ｄに示すように、ハウジング１５０１は、互いに嵌合する上部部材１５２０と下部部材１５２２とを含み、それらの一方又は両方は、例えば、射出成形プロセスによって又はエッチング、切削、穿孔などによって予め形成された溝、流路、ロック、導管又は他の経路を有する。上部部材１５２０は、レーザ溶接、熱接合、超音波溶接、接着、ねじ、リベット、ボルトなどを使用することなどの任意の嵌合又は接続機構によって、又はラッチ、溝、舌状部、ピン、フランジなどの他の嵌合機構によって、下部部材１５２２と接続されることができる。

【００７６】

一部の実施では、図１５Ｄに示すように、上部部材１５２０は、溝、流路、ロック、導管又は他の経路を含むことができ、一方、下部部材１５２２は、上部部材１５２０の溝、流路、ロック又は他の経路のうちの少なくとも１つに嵌合するように寸法設定され且つ適合された突出部１５２４を含むことができる。突出部１５２４は、例えば、サンプリング流路１５０６及び／又は隔離チャンバ１５０８のいずれかの形成を完了させるために、部分的な溝又は部分的な流路などの表面特徴を提供することができる。一部の実施では、突出部１５２４は、対応する溝、流路、ロック又は他の経路内によりぴったりと嵌合するために、１つ以上の傾斜した側面又は面を形成されることができる。更に他の実施では、上部部材１５２０と下部部材の両方が、溝、流路、ロック又は他の経路、並びに１つ以上の突出部１５２４を含むことができる。

【００７７】

一部の実施では、サンプリング流路１５０６及び隔離チャンバ１５０８は、ハウジング１５０１に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１５０１は、ゴム、プラスチック、金属又は他の材料を含む任意の適切な材料で作られることができる。ハウジング１５０１は、透明又は半透明の材料から、又は不透明又は非半透明の材料から形成されることができる。他の実施では、ハウジング１５０１は、大部分が不透明又は非透明であることができるが、サンプリング流路１５０６及び／又は隔離チャンバ１５０８に直接隣接するハウジング表面は、透明又は半透明であり、最初に隔離チャンバ１５０８が必要又は所望の程度まで満たされているという視覚的な合図又はサイン、及び／又は、次に汚染されていない血液サンプルがサンプリング流路１５０６を通して採取される間、隔離された血液が隔離されたままであるという視覚的な合図又はサインを施

術者に与える。隔離の他の視覚的な合図又はサインは、以下に限定されるものではないが、血液の接触、浸透、又は部分的な浸透で空気透過性血液バリア１５１２が異なる色に変わること、隔離チャンバに沿った又は隔離チャンバに隣接する任意の位置にある色分けされたタブ又は指標、可聴信号、振動信号、又は他の信号を含むことができる。

【００７８】

患者の皮膚から多数の病原体を集める可能性がある患者針（図示せず）による静脈穿刺の後、患者自身の血圧が隔離チャンバ１５０８内の大気圧に打ち勝って空気透過性血液バリア１５１２を通して隔離チャンバ１５０８内の空気を追い出すので、これらの病原体を有する患者の血液の最初の量が、血液隔離装置１５００入口ポート１５０２に入り、最も抵抗の少ない経路をたどることによって隔離チャンバ１５０８に流入する。患者の血圧は、密封されたサンプリング流路１５０６内で高まっている空気圧に打ち勝つのに十分ではない。最終的に、所定の容積を有する隔離チャンバ１５０８は、空気透過性血液バリア１５１２を通して空気を追い出す血液で満たされる。血液が空気透過性血液バリアに衝突すると、血液は空気透過性血液バリア１５１２の材料と相互作用して、通気口１５１０を完全に又は部分的に密封する。施術者がいまやバキュテナー（登録商標）カプセル又は他の血液サンプル採取装置を利用してサンプリングのために患者の血液の次の量を得ることができるという信号又は表示を提供することができる。隔離チャンバ１５０８内の血液は、このとき隔離チャンバ内で事実上隔離されている。

【００７９】

血液隔離経路１５０８を満たすと、バキュテナー（登録商標）又は他の血液サンプル採取装置の使用より前に、患者の血圧は、サンプリング流路１５０６内の空気の圧縮を引き起こし、場合によっては少量の血液が隔離チャンバ１５０８への方向転換点を過ぎてサンプリング流路１５０６に移動し、サンプリング流路１５０６を通して採取される汚染されていない血液を待ち行列に入れる。

【００８０】

図１６～１９は、血液隔離装置の更に別の実施を示す。図１６Ａ～１６Ｄは、バキュテナー（登録商標）（図示せず）のような真空採血容器のような血液サンプル採取装置と患者針（図示せず）及び／又は関連するチューブとの間に接続されることができる血液隔離装置１６００を示す。図１７は、血液隔離装置の下部部材を示し、図１８は、血液隔離装置の上部部材を示し、上部部材及び下部部材は、以下でより詳しく説明するように、相互に嵌合して、入口ポート、出口ポート、隔離チャンバ及びサンプリング流路を形成することができる。図１９Ａ及び１９Ｂは、互いに嵌合する上部部材及び下部部材を示す。図１６～１９は本明細書に記載される血液隔離装置を構成する１つの例示的な方法を示しており、他の形態の構成も可能であることを理解されたい。

【００８１】

図１６Ａ～１６Ｄを参照すると、血液隔離装置１６００は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１６０２を含む。入口ポート１６０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。入口ポート１６０２は、血液隔離装置１６００への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有する円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。

【００８２】

入口ポート１６０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封コネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザー溶接、又は熱接合などによって、入口ポート１６０２と一体化されることができる。これによって、血液隔離装置１６００は、患者針及び／又はチューブと共に単一ユニットとして製造及び販売され、

採血又はサンプリングの際に患者針を血液隔離装置１６００に接続する必要性をなくすことができる。

【００８３】

血液隔離装置１６００は、血液隔離装置１６００から及び血液サンプル採取装置への開口部を画定する出口ポート１６０４を更に含む。出口ポート１６０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１６００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１６００に接続する必要性をなくすことができる。

【００８４】

血液隔離装置１６００は、入口ポート１６０２と出口ポート１６０４との間のサンプリング流路１６０６と、入口ポート１６０２と出口ポート１６０４との間の任意の位置でサンプリング流路１６０６に接続され且つサンプリング流路１６０６から分離又は方向転換される隔離チャンバ１６０８とを更に含む。サンプリング流路１６０６は、最初のアリコートの血液が隔離チャンバ１６０８内に隔離されると、採血経路として機能する。サンプリング流路１６０６は、任意のサイズ、形状又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１６０６は、入口ポート１６０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１６０６は、入口ポート１６０２から出口ポート１６０４まで徐々に広がることができる。隔離チャンバ１６０８は、図１７及び１９により詳しく示すように、血液がサンプリング流路１６０６のより小さい直径に入るのに対して、まずリザーバに入ろうとするように、隔離流路の経路に向かって大きいリザーバを形成するべくより大きい断面を有することができる。

【００８５】

一部の例示的な実施では、サンプリング流路１６０６と隔離チャンバ１６０８との間の方向転換は、方向転換分岐点１６０７によって行われる。方向転換分岐点１６０７は、実質的にＹ字形、Ｔ字形、又はＵ字形であることができる。一部の好ましい例示的な実施では、図１７Ａ～１７Ｂに示すように、方向転換分岐点１６０７は、入口ポート１６０２からの流れが優先的に隔離チャンバ１６０８に向けられるように構成される。隔離チャンバ１６０８はまた、最初の血液流を隔離チャンバ１６０８に向かって且つ隔離チャンバ１６０８内に移動させるための湾曲部又は傾斜路を含むか又は形成することができる。

【００８６】

隔離チャンバ１６０８は、好ましくは大気圧に維持され、隔離チャンバ１６０８の遠位端又はその近傍に通気口１６１０を含む。通気口１６１０は、上記のように空気透過性血液バリア１６１２を含むことができる。

【００８７】

血液隔離装置１６００は、複数の部品又は単一の一体部品から形成されることができるハウジング１６０１を含むことができる。一部の実施では、図１７Ａ～１７Ｄ及び図１８Ａ～１８Ｆに示すように、ハウジング１６０１は、互いに嵌合する上部部材１６２０と下部部材１６２２とを含む。血液隔離装置１６００は、上部部材１６２０が下部部材１６２２に機械的に取り付けられたときに、両者の間の接合部分がガスケット又は密封部材によって密封されるように、ガスケット又は他の密封部材（図示せず）を含むこともできる。図１７Ａ～１７Ｄは、血液隔離装置１６００用のハウジングの下部部材１６２２を示す。下部部材１６２２は、サンプリング流路１６０６、隔離チャンバ１６０８、及び方向転換分岐点１６０７を形成するために、射出成形プロセスによって又はエッチング、切削、穿孔などによって予め形成された溝、流路、ロック、導管又は他の経路を含むことができる。

【００８８】

隔離チャンバ１６０８は、血液がサンプリング流路１６０６のより小さい直径に入るの

に対して、まず隔離チャンバ内に優先的に移動するように、サンプリング流路１６０６よりも大きい断面を有することができる。

【００８９】

図１８Ａ～１８Ｆは、レーザ溶接、熱接合、接着、ねじ、リベット、ボルトなどを使用することなどの任意の嵌合又は接続機構によって、又はラッチ、溝、舌状部、ピン、フランジなどの他の嵌合機構によって、下部部材１６２２と接続可能な上部部材１６２０を示す。上部部材１６２０は、サンプリング流路１６０６、隔離チャンバ１６０８、及び方向転換分岐点１６０７を形成するために、溝、流路、ロック、導管又は他の経路の一部又はすべてを含むことができる。更に他の実施では、上部部材１６２０と下部部材１６２２の両方が、溝、流路、ロック又は他の経路を含むことができる。

【００９０】

一部の実施では、サンプリング流路１６０６及び隔離チャンバ１６０８は、ハウジング１６０１に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１６０１は、ゴム、プラスチック、金属又は任意の他の適切な材料で作られることができる。ハウジング１６０１は、透明又は半透明の材料から、又は不透明又は非半透明の材料から形成されることができる。他の実施では、ハウジング１６０１は、大部分が不透明又は非半透明であることができるが、サンプリング流路１６０６及び／又は隔離チャンバ１６０８に直接隣接するハウジング表面は、透明又は半透明であることができ、最初に隔離チャンバ１６０８が必要又は所望の程度まで満たされているという視覚的な合図又はサイン、及び／又は、次に汚染されていない血液サンプルがサンプリング流路１６０６を通して採取される間、隔離された血液が隔離されたままであるという視覚的な合図又はサインを施術者に与える。隔離の他の視覚的な合図又はサインは、以下に限定されるものではないが、血液の接触、浸透、又は部分的な浸透で空気透過性血液バリア１６１２が異なる色に変わること、隔離チャンバに沿った又は隔離チャンバに隣接する任意の位置にある色分けされたタブ又は指標、可聴信号、振動信号、又は他の信号を含むことができる。

【００９１】

図１８Ａ～１８Ｆに示すように、空気透過性血液バリア１６１２は、保護部材１６１６で覆われているか又は保護部材１６１６によって包囲されていることができる。保護部材１６１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１６１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも空気が隔離チャンバ１６０８から追い出されるときに空気が空気透過性血液バリア１６１２から出ることを可能にする。一部の実施では、保護部材１６１６は、上部部材１６２０の上面から上に空気透過性血液バリア１６１２の周りに延びる突出部を含む。保護カバー１６１６は、フィルタが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００９２】

使用時、血液隔離装置１６００は、サンプリング流路１６０６と隔離チャンバ１６０８とを含む。両方の経路が、最初は大気圧で空気を充填されているが、サンプリング流路１６０６は、最初はバキュテナー（登録商標）又は他のこのような密封された採血装置によって密封されている出口ポート１６０４に向けられ、隔離チャンバ１６０８は、空気透過性血液バリア１６１２を含む大気への通気口１６１０で終端している。

【００９３】

患者の皮膚から多数の病原体を集める可能性がある患者針（図示せず）による静脈穿刺の後、これらの病原体を有する患者の血液の最初の量が、血液隔離装置１６００の入口ポート１６０２を通過する。この汚染されている可能性のある血液の最初の量は、最も抵抗の少ない経路を見出すことによって、隔離チャンバ１６０８に優先的に流入する。患者自身の血圧は、通気口付きの隔離チャンバ１６０８内の大気圧に打ち勝ち、空気透過性血液バリア１６１２を通して隔離チャンバ１６０８内の空気を追い出すが、密封されたサンプリング流路１６０６内で高まっている空気圧に打ち勝つには不十分である。様々な例示的

な実施形態では、隔離チャンバ１６０８及びサンプリング流路１６０６は、患者の血圧によって生じた力が、血液隔離装置の向きに関わらず、重力の影響に打ち勝つのに十分であるように構成されることができる。

【００９４】

最終的に、隔離チャンバ１６０８は、空気透過性血液バリア１６１２を通して空気を追い出す血液で満たされる。血液が空気透過性血液バリアと接触すると、血液は空気透過性血液バリア１６１２の材料と相互作用して通気口１６１０を完全に又は部分的に密封する。施術者がいまやバキュテナー（登録商標）又は他の採血装置を利用することができるという信号又は表示を提供することができる。

【００９５】

血液隔離経路１６０８を満たすと、バキュテナー（登録商標）又は他の血液サンプル採取装置の使用より前に、患者の血圧は、サンプリング流路１６０６内の空気の圧縮を引き起こし、場合によっては少量の血液が方向転換点を過ぎてサンプリング流路１６０６に移動しサンプリング流路１５０６を通して採取される汚染されていない血液を待ち行列に入れる。

【００９６】

図１９Ａは、血液隔離装置１６００の側面図であり、図１９Ｂは、血液隔離装置１６００の断面図であり、下部部材１６２２と嵌合する上部部材１６２０を示す。

【００９７】

図２０は、患者の血流への血管アクセスのための患者針２００２と、１つ以上の血液サンプルの採取を容易にする血液サンプル採取装置２００４と、患者針２００２と血液サンプル採取装置２００４との間の流体接続を提供する導管２００６とを含む血液サンプル最適化システム２０００を示す。一部の実施では、血液サンプル採取装置２００４は、密封された採取針を含む保護シールドを含み、採取針に密封された真空容器が置かれ、容器は採取針によって一度穿孔されると、患者針２００２から導管２００６を通して真空圧力又は真空力で血液サンプルを吸い込む。

【００９８】

血液サンプル最適化システム２０００は、本明細書で説明するように、患者針２００２と血液サンプル採取装置２００４との間の導管２００６上の任意の点に位置する血液隔離装置２００８を更に含む。

【００９９】

図２１は、ウィッキング材料チャンバを使用する通気口付きでない血液隔離装置２１００を示す。血液隔離装置２１００は、ウィッキング材料で満たされた隔離チャンバ２１０２によって少なくとも部分的に囲まれ又は当接されるサンプリング流路２１０４を有するハウジング２１０１を含む。最初のアリコートの血液が患者針からサンプリング流路２１０４に引き込まれ、サンプリング流路２１０４において隔離チャンバ２１０２のウィッキング材料の中に直ちに逃がされる。ウィッキング材料及び／又は隔離チャンバ２１０２は、後続の又はそれ以降の採血がウィッキング材料を通り過ぎ、サンプリング流路２１０４を通って直接バキュテナー（登録商標）などのサンプリング装置に流れるように、所定量の血液を受け入れ且つ保持するように寸法設定され且つ適合されている。ウィッキング材料は、固化剤、汚染除去剤、又は他の添加剤などの物質を含むことができる。

【０１００】

本明細書に記載されるように、空気透過性血液バリアは、多種多様な異なる構造及び材料を用いて作られることができる。図２２Ａ及び２２Ｂに示すように、血液隔離装置２２００の空気透過性血液バリア２２０２は、少なくとも一部のビーズが親水性になるように処理されたポリマービーズマトリックス２２０４を含むことができる。空気透過性血液バリア２２０２は、カルボキシメチルセルロース（ＣＭＣ）又はセルロースガムなどの自己密封材料２２０６、又は他の密封材料を更に含む。空気透過性血液バリア２２０２は、血液などの流体との接触前又は部分接触中の空気の流れを可能にする空隙２２０８を更に含むことができる。図２２Ｂに示すように、流体と接触すると、自己密封材料２２０６が膨

張して空隙２２０８を閉鎖し、空隙２２０８を通る空気の流れを閉塞し、完全に又は部分的に密封する。

【０１０１】

図２３Ａ及び２３Ｂは、患者針と接続するための入口ポート２３０２と、血液サンプル採取装置と接続するための出口ポート２３０４と、隔離チャンバ２３０６と、隔離チャンバ２３０６と、隔離するべき汚染されている可能性のある血液の最初のアリコートまで隔離チャンバが満たされると隔離チャンバ２３０６を迂回するサンプリング流路２３０８とを有する、血液隔離装置２３００の更に別の実施を示している。隔離チャンバ２３０６は、入口ポート２３０２から最も遠い隔離チャンバ２３０６の遠位端に疎水性プラグ２３１２を含む。バキュテナー（登録商標）などからのような、出口ポート２３０４から加えられる真空力又は他の吸引力は、血液を入口ポート２３０２内に、そして隔離チャンバ２３０６内に直接吸い込み、そこで最初のアリコートの血液が疎水性プラグ２３１２に接触し、最初のアリコートの血液を隔離チャンバ２３０６に戻してそこで隔離させる。少量の血液が、最初は弁２３０８によって閉鎖されているサンプリング流路２３０８に入ることができる。弁２３０８が解放されると、真空の更なる力又は他の力の下で、後続の量の血液が入口ポート２３０２に流れ、隔離チャンバ２３０６を迂回し、サンプリング流路２３０８を通り抜けて出口ポート２３０４に向かって流れ、採取装置に送られる。

【０１０２】

サンプリング流路２３０８は、任意の適切な幾何学的形状を有することができ、プラスチックチューブ又は任意の他の適切な材料から形成されることができる。弁２３０８は、最初のアリコートの血液が隔離チャンバ２３０６内に隔離される前にサンプリング流路を挟み、脇へそらし、曲げ、又は他の方法で閉じるためにクリップ又は他の包囲装置であることができる。

【０１０３】

様々な実施形態を上記で詳細に説明してきたが、他の変更も可能である。他の実施形態は、添付の特許請求の範囲内に含まれ得る。

【図１】

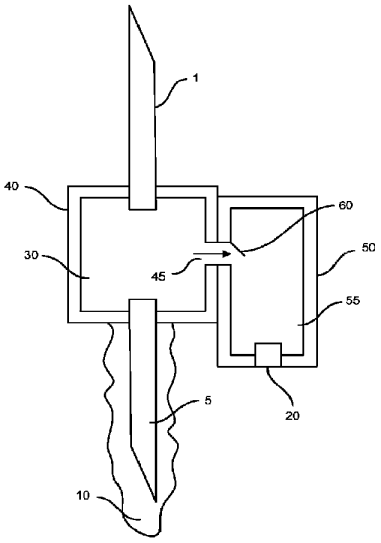


FIG. 1

【図２】

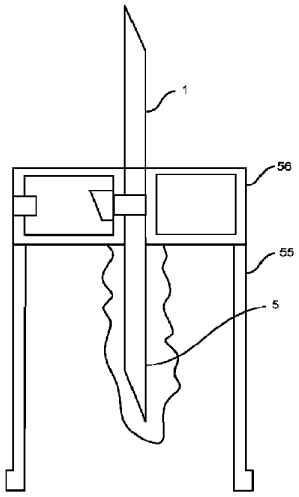


FIG. 2

【図３】

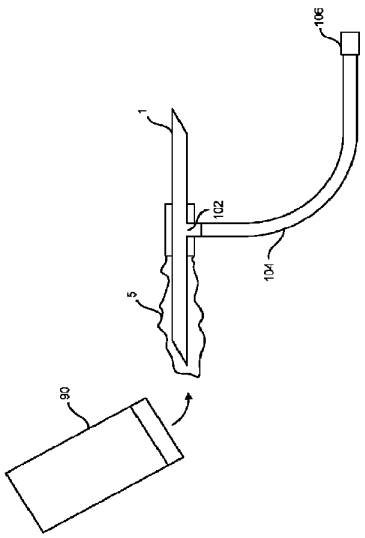


FIG. 3

【図４】

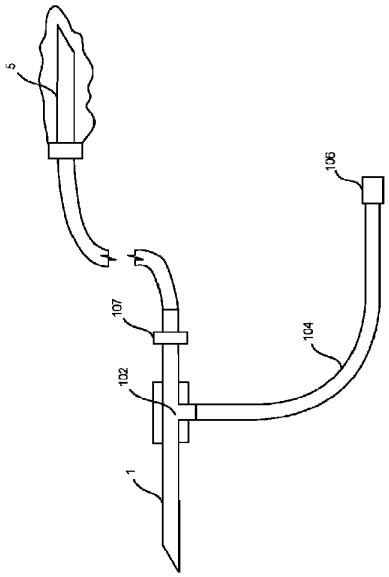


FIG. 4

【図５】

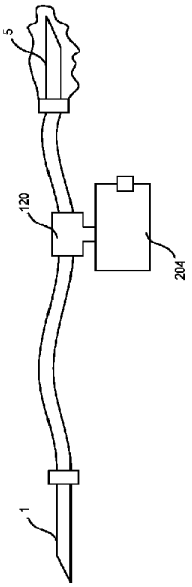


FIG. 5

【図６】

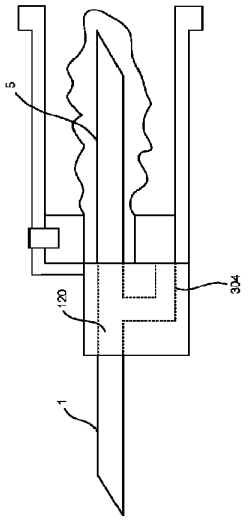


FIG. 6

【図７】

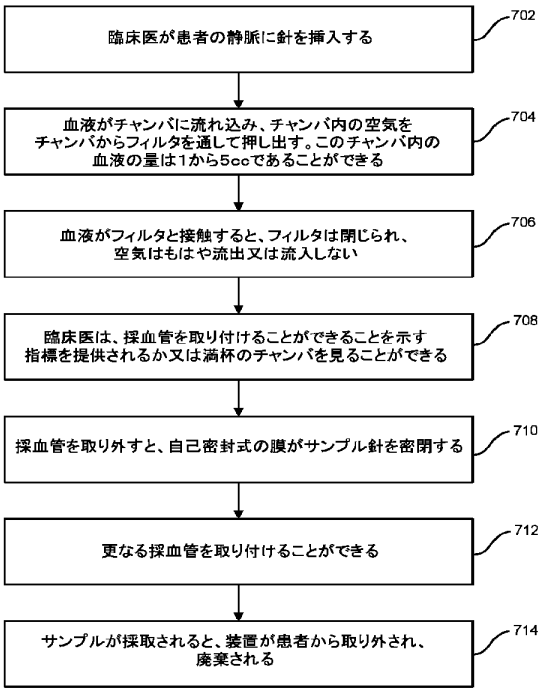


FIG. 7

【図８Ａ】

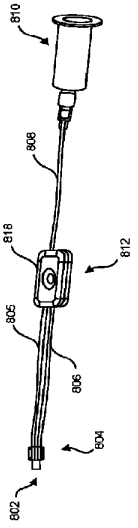


FIG. 8A

【図８Ｂ】

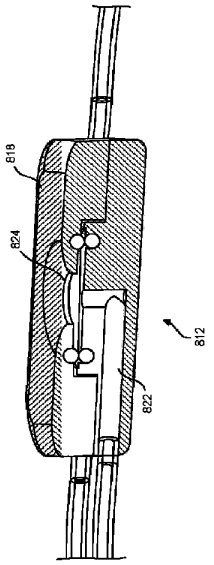


FIG. 8B

【図８Ｃ】

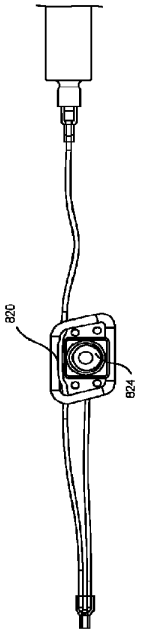


FIG. 8C

【図８Ｄ】

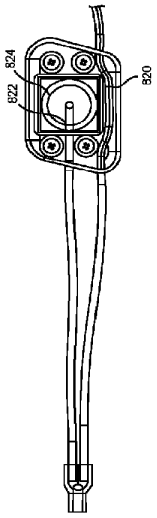


FIG. 8D

【図８Ｅ】

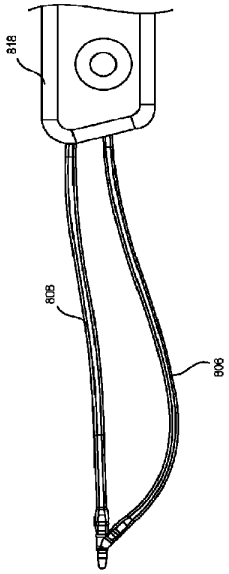


FIG. 8E

【図９】

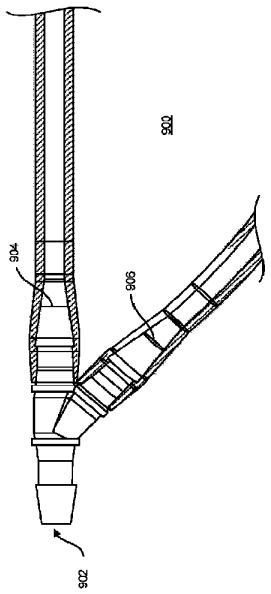


FIG. 9

【図１０Ａ】

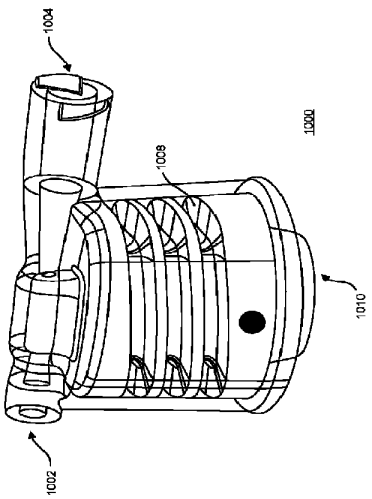


FIG. 10A

【図１０Ｂ】

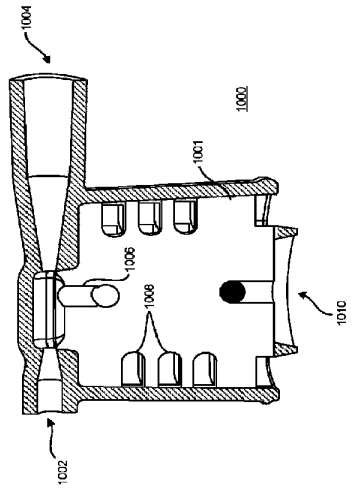


FIG. 10B

【図１０Ｃ】

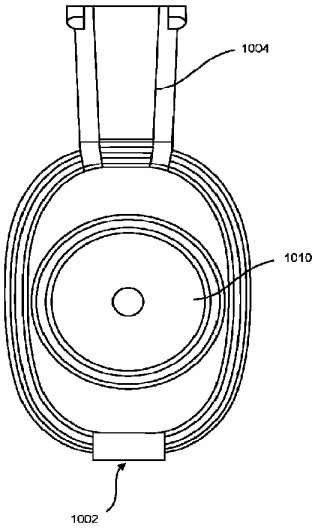


FIG. 10C

【図１０Ｄ】

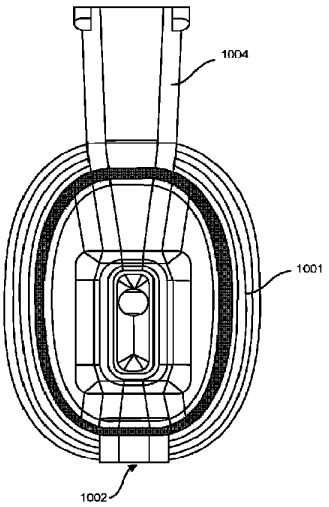


FIG. 10D

【図１１Ａ】

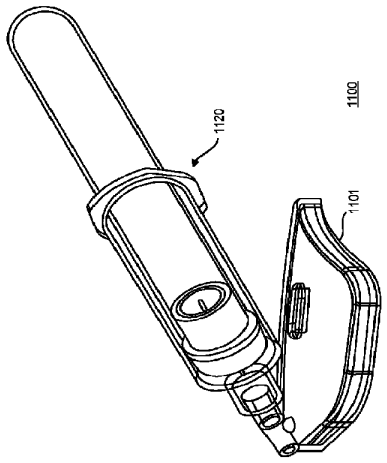


FIG. 11A

【図１１Ｂ】

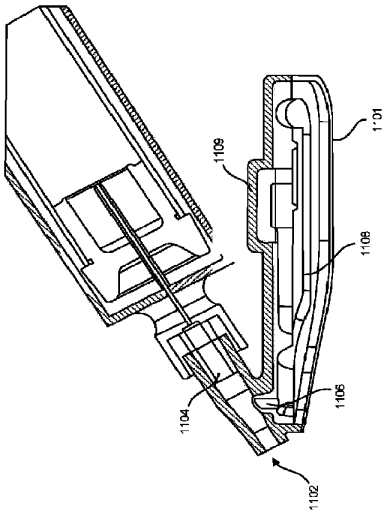


FIG. 11B

【図１１Ｃ】

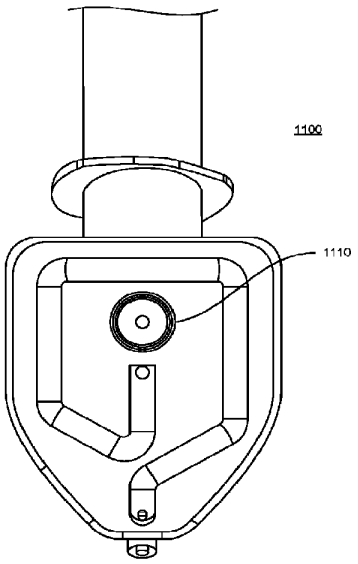


FIG. 11C

【図１１Ｄ】

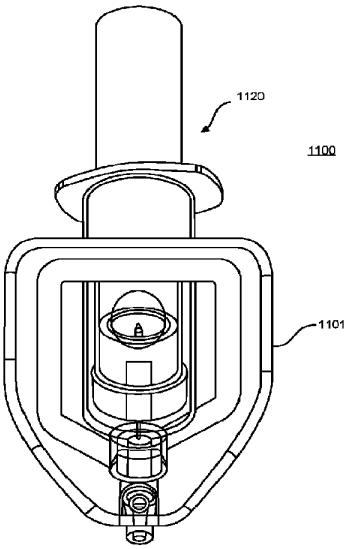


FIG. 11D

【図１１Ｅ】

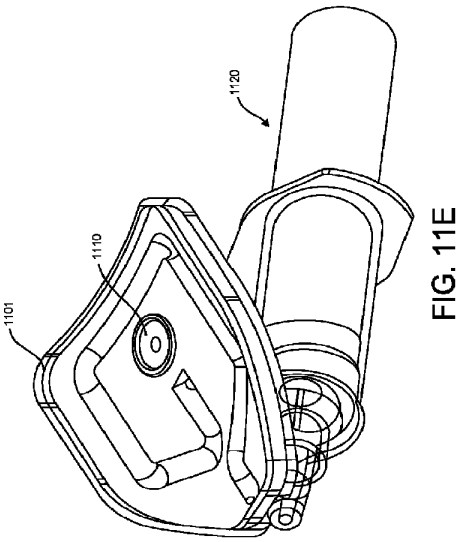


FIG. 11E

【図１２Ａ】

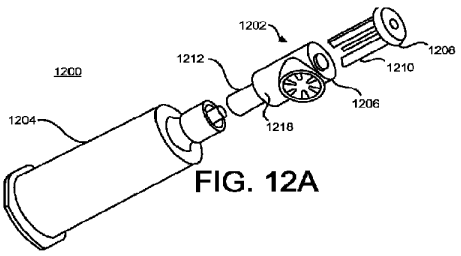


FIG. 12A

【図１２Ｂ】

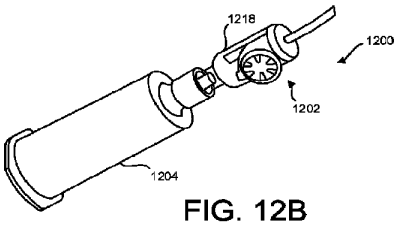


FIG. 12B

【図１２Ｃ】

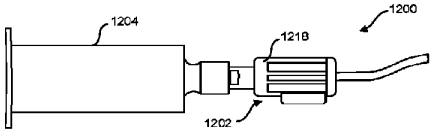


FIG. 12C

【図１２Ｄ】

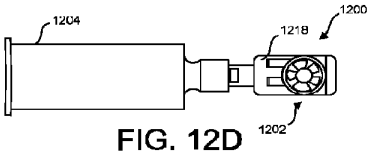


FIG. 12D

【図１３Ａ】

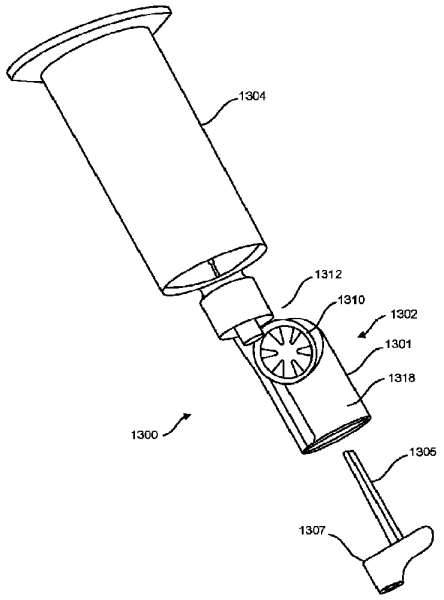


FIG. 13A

【図１３Ｂ】

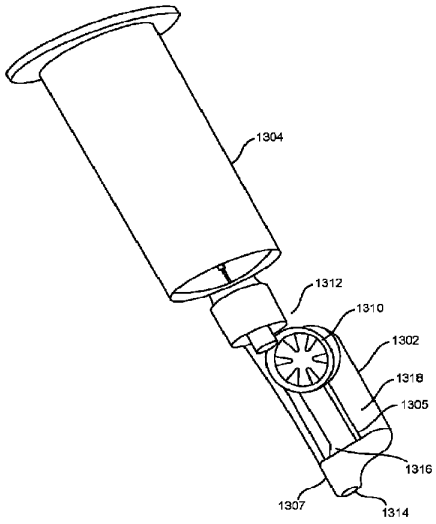


FIG. 13B

【図１３Ｃ】

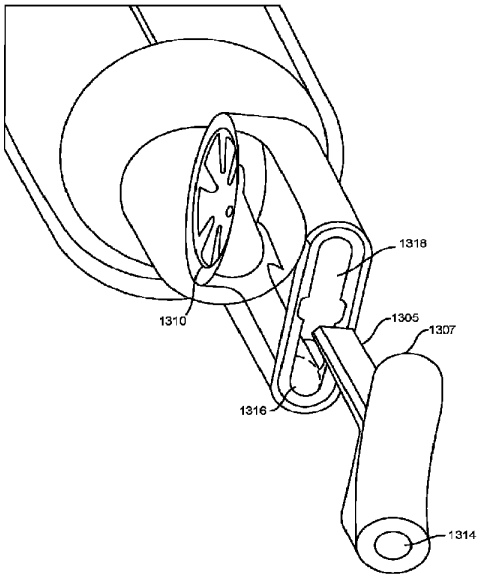


FIG. 13C

【図１３Ｄ】

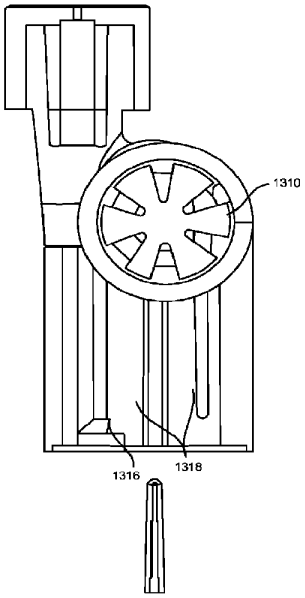


FIG. 13D

【図１４Ａ】

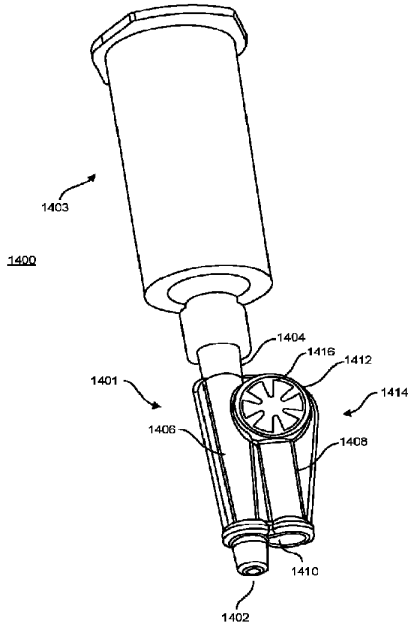


FIG. 14A

【図１４Ｂ】

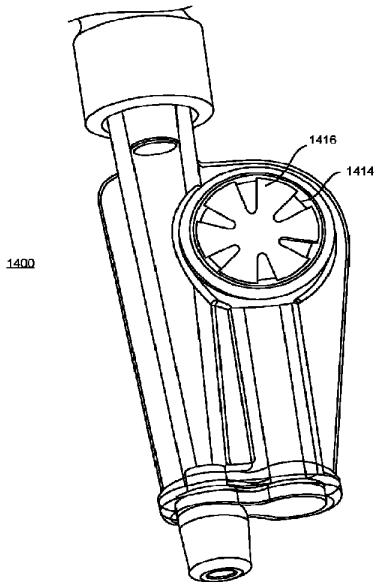


FIG. 14B

【図１４Ｃ】

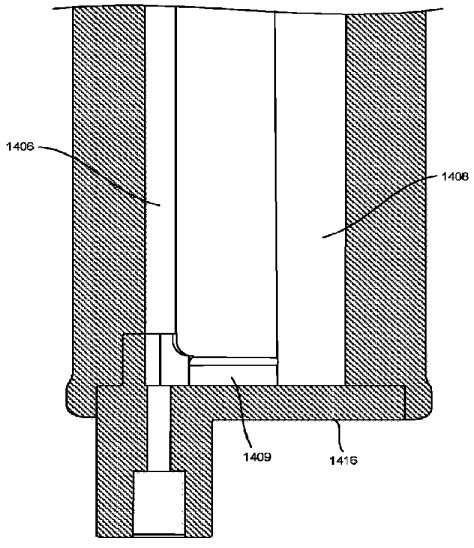


FIG. 14C

【図１４Ｄ】

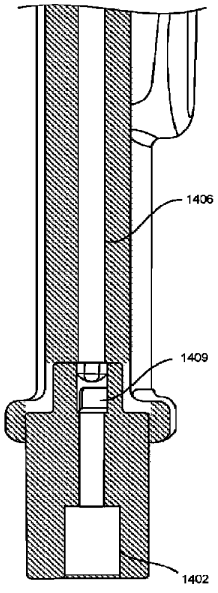


FIG. 14D

【図１４Ｅ】

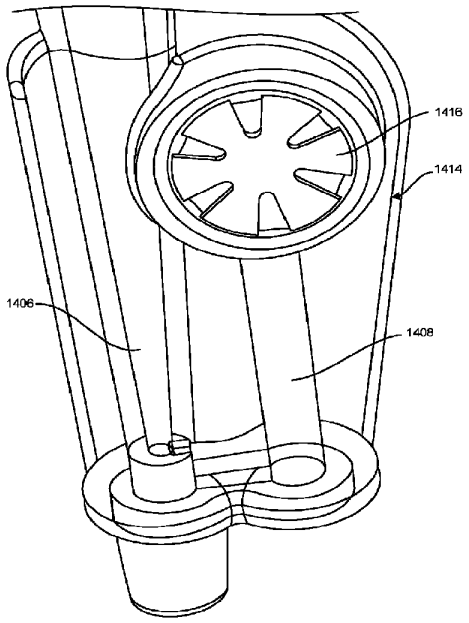


FIG. 14E

【図１５Ａ】

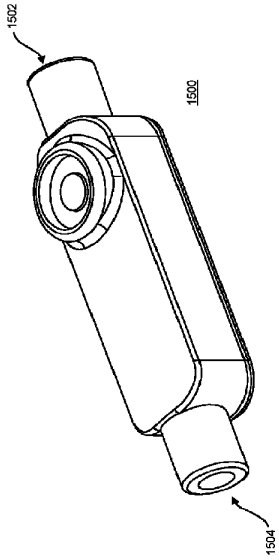


FIG. 15A

【図１５Ｂ】

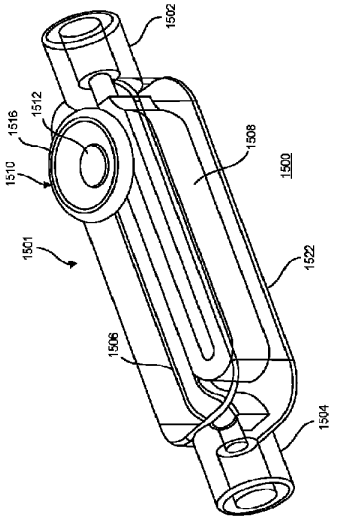


FIG. 15B

【図１５Ｃ】

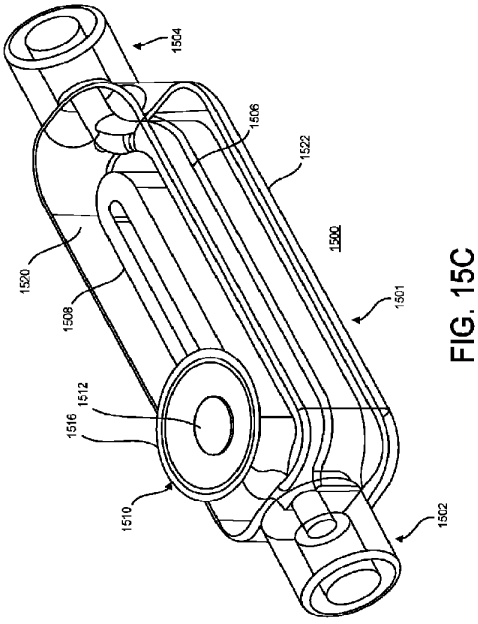


FIG. 15C

【図１５Ｄ】

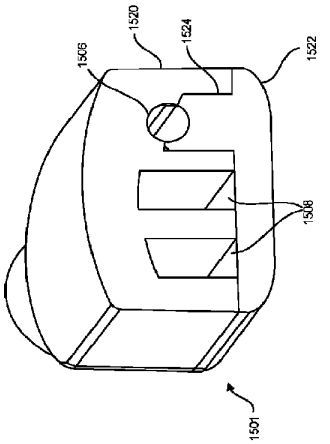


FIG. 15D

【図１５Ｅ】

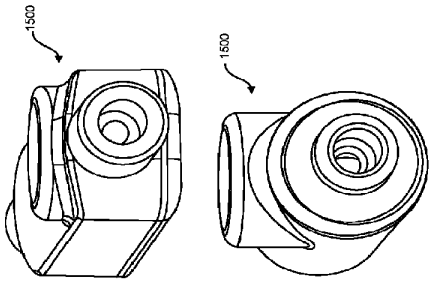


FIG. 15E

【図１５Ｆ】

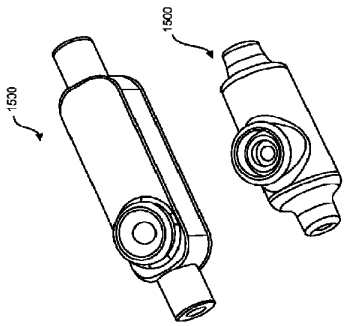


FIG. 15F

【図１５Ｇ】

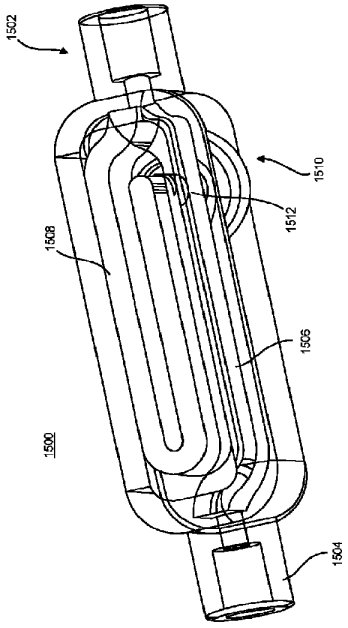


FIG. 15G

【図１６Ａ】

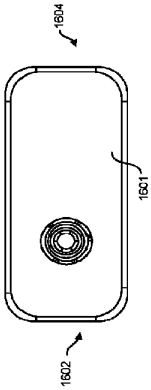


FIG. 16A

【図１６Ｂ】

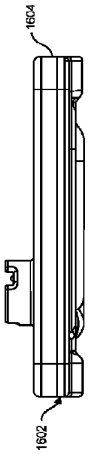


FIG. 16B

【図１６Ｃ】

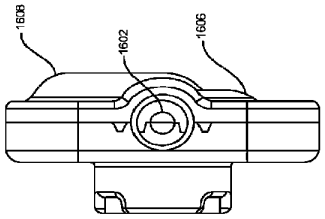


FIG. 16C

【図１６Ｄ】

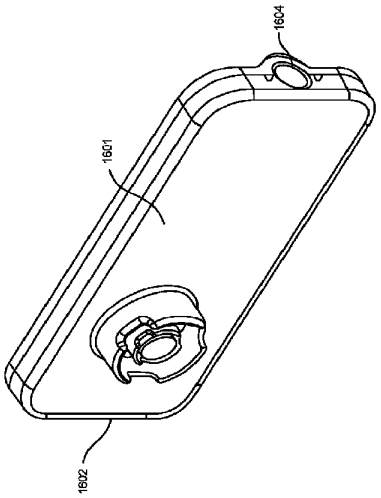


FIG. 16D

【図１７Ａ】

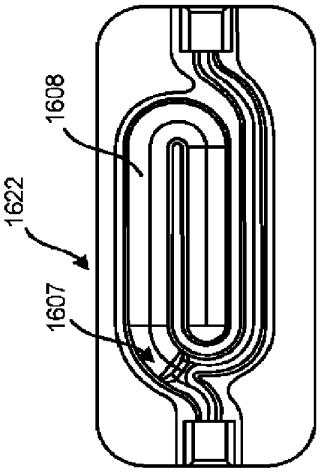


FIG. 17A

【図１７Ｂ】

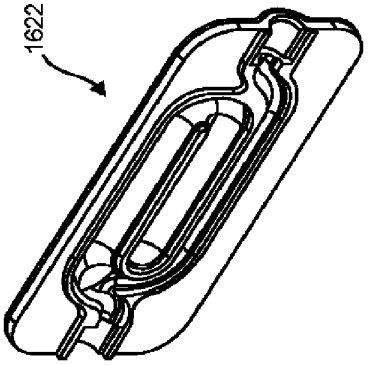


FIG. 17B

【図１７Ｃ】

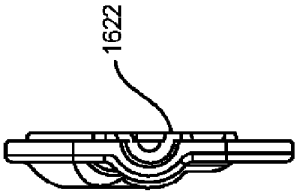


FIG. 17C

【図１７Ｄ】

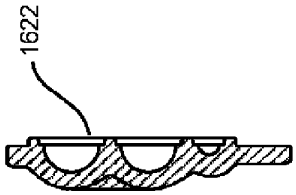


FIG. 17D

【図１７Ｅ】

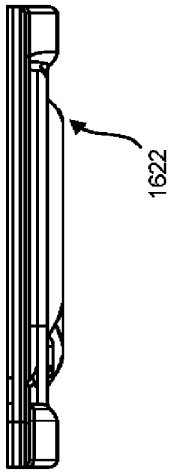


FIG. 17E

【図１８Ａ】

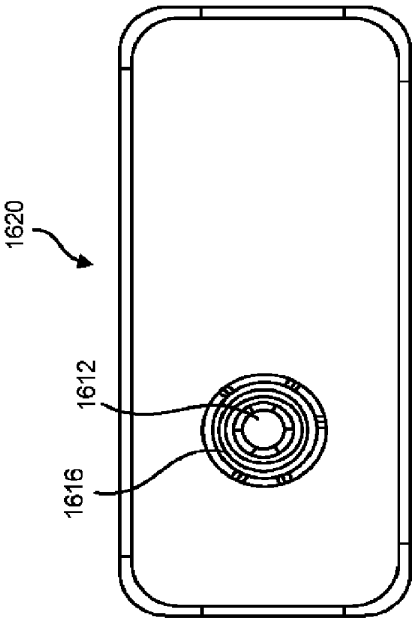


FIG. 18A

【図１８Ｂ】

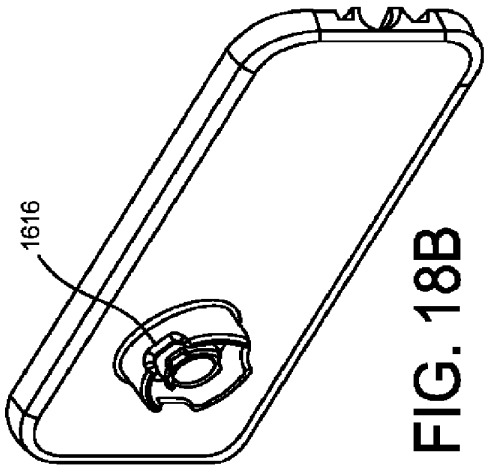


FIG. 18B

【図１８Ｃ】

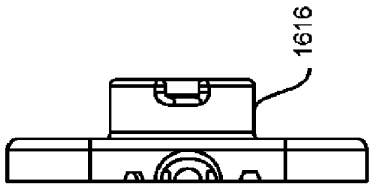


FIG. 18C

【図１８Ｄ】

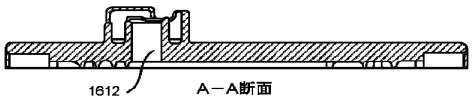


FIG. 18D

【図１８Ｅ】

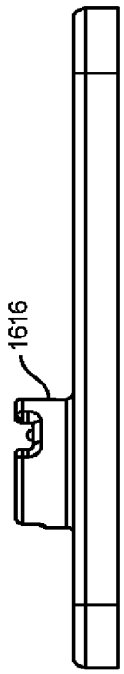


FIG. 18E

【図１８Ｆ】

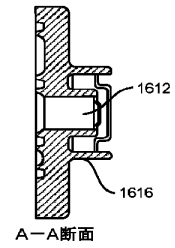


FIG. 18F

【図１９Ａ】

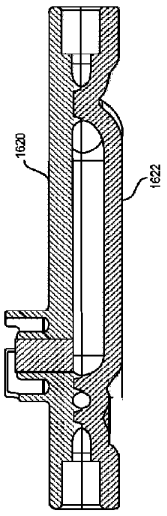


FIG. 19A

【図１９Ｂ】

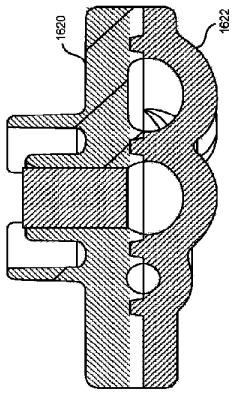


FIG. 19B

【図２０】

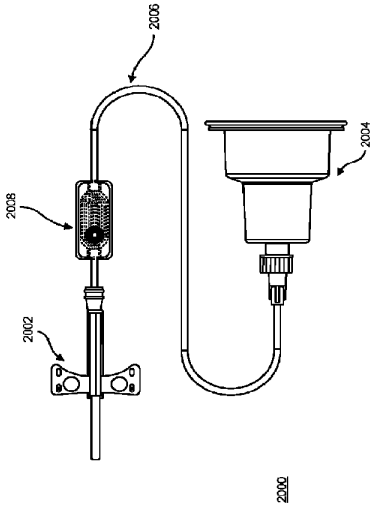


FIG. 20

【図２１】

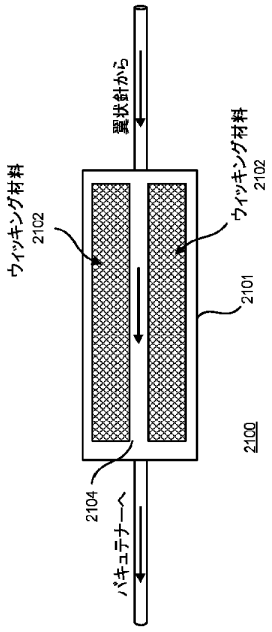


FIG. 21

【図２２Ａ】

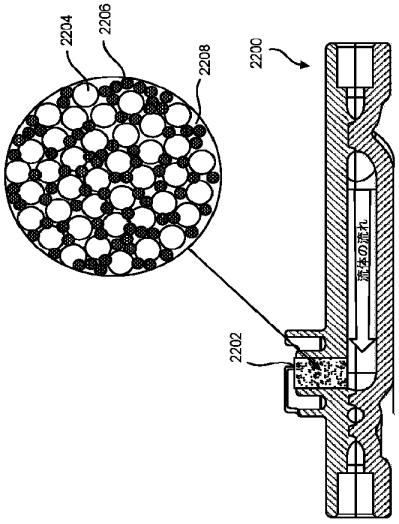


FIG. 22A

【図２２Ｂ】

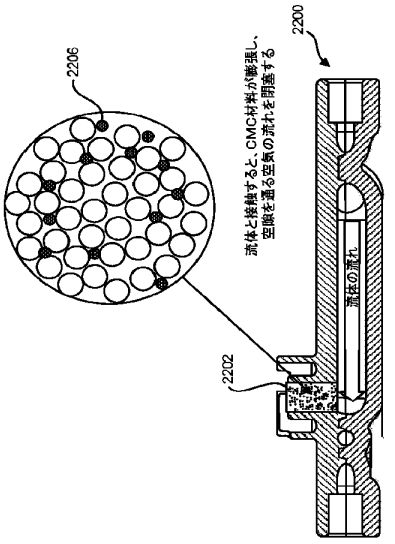


FIG. 22B

【図２３Ａ】

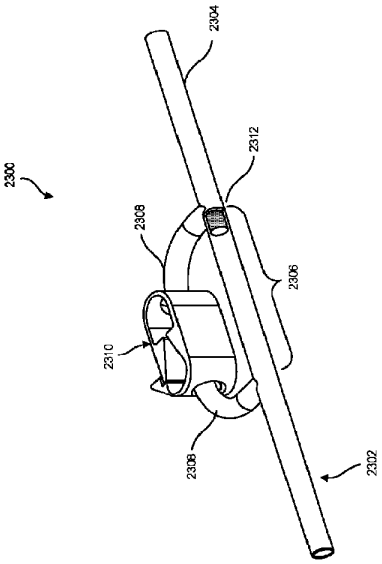


FIG. 23A

【図２３Ｂ】

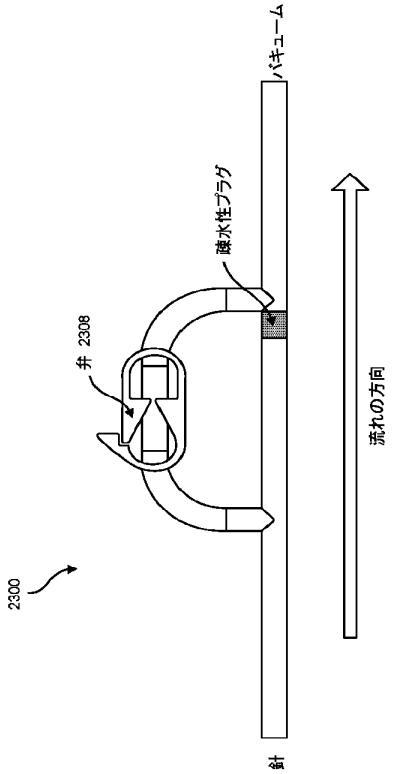


FIG. 23B

フロントページの続き

(31)優先権主張番号 62/196,797
(32)優先日 平成27年7月24日(2015.7.24)
(33)優先権主張国・地域又は機関
米国(US)
(31)優先権主張番号 15/140,448
(32)優先日 平成28年4月27日(2016.4.27)
(33)優先権主張国・地域又は機関
米国(US)
(31)優先権主張番号 15/140,443
(32)優先日 平成28年4月27日(2016.4.27)
(33)優先権主張国・地域又は機関
米国(US)

早期審査対象出願

(72)発明者 ロジャーズ、 ボビー
アメリカ合衆国 ９２１３１ カリフォルニア州 サンディエゴ スクリップス ポーウェイ パークウェイ １０７５５ ナンバー ２５７
(72)発明者 カン、 ジーノ
アメリカ合衆国 ９２１３１ カリフォルニア州 サンディエゴ スクリップス ポーウェイ パークウェイ １０７５５ ナンバー ２５７
(72)発明者 デトロフ、 ジョン
アメリカ合衆国 ９２１３１ カリフォルニア州 サンディエゴ スクリップス ポーウェイ パークウェイ １０７５５ ナンバー ２５７

審査官 清水 裕勝

(56)参考文献 特開昭５８－０２５１４６（ＪＰ，Ａ）
特開昭５８－０６７２３８（ＪＰ，Ａ）
特開２０１２－０１６４９６（ＪＰ，Ａ）
特開昭５７－０８９８６９（ＪＰ，Ａ）
特表平０９－５０４７２６（ＪＰ，Ａ）
特開平０２－２２４７４２（ＪＰ，Ａ）
米国特許第０４２０７８７０（ＵＳ，Ａ）

(58)調査した分野(Int.Cl.，ＤＢ名)
Ａ６１Ｂ ５／１５３－５／１５４

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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

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

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

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

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. [ ] **Certain claims were found unsearchable** (See Box No. II)
3. [ ] **Unity of invention is lacking** (see Box No III)
4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:
5. With regard to the **abstract,**
   [ ] the text is approved as submitted by the applicant
   [X] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority
6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 15C
      [X] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (January 2015)

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

Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61B5/153 A61B5/154
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHEL LLOYD [US]; BR) 29 December 2011 (2011-12-29)	1-5, 7-13, 15-20
A	paragraph [0070] figure 15 abstract	6,14
A	US 2009/227953 A1 (TAN CHEE LEONG [SG] ET AL) 10 September 2009 (2009-09-10) the whole document	1-20
A	JP H08 257018 A (NISSHO KK) 8 October 1996 (1996-10-08) abstract; figures	1-20

-/--

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Schultz, Ottmar

2

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

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18	1-20

2

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2016/043709

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011162772 A1	29-12-2011	NONE	
US 2009227953 A1	10-09-2009	US 2009227953 A1	10-09-2009
		US 2010262038 A1	14-10-2010
		US 2012330187 A1	27-12-2012
JP H08257018 A	08-10-1996	NONE	
US 4416290 A	22-11-1983	NONE	
US 3648684 A	14-03-1972	NONE	
EP 1665986 A1	07-06-2006	BR PI0505336 A	11-07-2006
		EP 1665986 A1	07-06-2006
		JP 4914601 B2	11-04-2012
		JP 2006150083 A	15-06-2006
		US 2006129064 A1	15-06-2006
US 4056101 A	01-11-1977	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015

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

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

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

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

FOR FURTHER ACTION
See paragraph 2 below

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

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

Applicant
CALLIOPE SOLUTIONS, INC.

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

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

2. **FURTHER ACTION**

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

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

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

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

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

Box No. I Basis of the opinion

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

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

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

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

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

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

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

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

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

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

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

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

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

5. Additional comments:

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

1. Statement

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

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

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

see separate sheet

Box No. VIII Certain observations on the international application

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

see separate sheet

+++++

Reference is made to the following document:

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

+++++

Re Item V

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

+++++

1 INDEPENDENT CLAIMS 1, 8, 17

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

+++++

Re Item VII

Certain defects in the international application

+++++

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

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

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

+++++

Re Item VIII

Certain observations on the international application

+++++

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

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

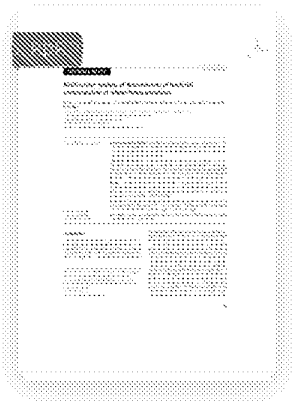
The technical features and the related definitions of the blood sampling pathway can therefore not be used to render the subject-matter of claim 8 either novel or inventive.

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

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

+++++

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations



Multivariate analysis of determinants of bacterial contamination of whole-blood donations

Vox Sanguinis, 2002

Luc Noel P. Perez Paul Pérez

or download with email

Vox Sanguinis (2002) 82, 55–60
© 2002 Blackwell Science

ORIGINAL PAPER

Multivariate analysis of determinants of bacterial contamination of whole-blood donations

P. Perez[1], C. Bruneau[2], M. Chassaigne[2], L. R. Salmi[1], L. Noel[3], P. Allouch[3], A. Audurier[2], C. Gulian[4], G. Janus[5], G. Boulard[3] & P. de Micco[4]

[1]Institut de Santé publique, d'Epidémiologie et de Développement, Université Victor Segalen Bordeaux 2, Bordeaux, France
[2]EFS Centre-Atlantique and Faculté de Médecine, Université de Tours, Tours, France
[3]Hôpital Mignot and EFS Île-de-France, Versailles, France
[4]EFS Alpes-Méditerranée, Marseille, France
[5]Centre de Transfusion Sanguine des Armées Jean Julliard, Clamart, France

Vox Sanguinis

Background and Objectives Introduction of bacteria into blood components at the collection stage seems to be a frequent occurrence. We therefore assessed determinants of bacterial contamination of whole-blood donations to gain insight into contamination mechanisms and direct prevention.

Materials and Methods A cross-sectional study was carried out on donors accepted for whole-blood donation in four French blood banks. Each blood bank used its own two-stage procedure for phlebotomy site preparation. Contamination was identified by culturing two 15-ml samples (collected aseptically at the outset of donation) in a BacT/Alert 240® system. Determinants were assessed by logistic regression analysis.

Results Bacterial contamination, mainly by skin flora, occurred in 76 (2·2%) out of 3385 donations. Significant determinants were as follows: the blood bank (odds ratio (OR) range = 3·0–5·6, $P < 0·001$); lack of repetition of scrub (OR = 2·7, $P = 0·032$); and donor age > 35 years (OR = 1·8, $P = 0·036$).

Conclusion Systematic scrub repetition should be implemented to reduce bacterial contamination by skin flora at the collection stage. Further research is required to clarify the role of different antiseptic agents and of donor age.

Received: 14 May 2001, revised: 16 October 2001, accepted: 25 October 2001

Key words: adverse effects, bacterial infections, blood donors, blood transfusion, logistic models, prevention, risk factors.

DOWNLOAD

Introduction

Transfusion-associated bacterial contamination (TABC) is a potentially serious transfusion adverse event, reported to be responsible for 10% of transfusion-related fatalities reported in the USA from 1976 to 1999 [1], and for 22% in France from 1994 to 1999 [2]. TABC was considered by the United States National Institute of Health to be a real priority for improving transfusion safety [3] and has been recently acknowledged as the most frequent transfusion-transmitted infection [4].

The most effective measures for preventing TABC would be systematic culture of every blood component or the application of bacterial inactivation steps during manufacture. However, bacterial inactivation methods are still under development [5], and techniques currently available for aseptic sampling and culture of cellular blood components may need further validation [6]. Other possible interventions may be aimed at avoiding or reducing the introduction of bacteria from all possible sources [7]. Contamination sources are rarely found, but that most frequently reported is the blood donor [7,8]. Bacteria may come from the bloodstream of infected but asymptomatic donors, or from the donor skin [8]. Despite well-conducted antisepsis, high concentrations of bacteria

Correspondence: Paul Perez, MD, PhD, Unité de Soutien Méthodologique à la Recherche Clinique et Epidémiologique du Centre Hospitalier Universitaire de Bordeaux, Unité INSERM 330, Case 11, Université V. Segalen Bordeaux 2, 146 Léo-Saignat, 33076 Bordeaux Cedex, France
Tel.: (33) 5 57 57 14 42
Fax: (33) 5 57 57 15 78
E-mail: Paul.Perez@isped.u-bordeaux2.fr

may remain on the skin surface [9,10]. Moreover, a core of deeper skin layers, which might not be adequately disinfected, may enter the needle during collection and introduce bacteria into the donation [7]. Pilot studies have reported that 0·3–0·6% of whole-blood donations are contaminated by bacteria, probably of skin origin [11,12].

Research on factors contributing to bacterial contamination at the collection stage may help to identify contamination mechanisms and consequently lead to the development of new interventions to improve the safety of blood transfusion. Possible factors favouring bacterial multiplication might include a high ambient temperature (leading to sweating) and poor skin hygiene. In addition, factors leading to a higher possibility of unintentional inclusion of bacteria from the phlebotomy site might be important; these factors include: skin lesions (because of their possible infectious origin); hairs (because hair follicles, rich in bacteria, may be touched by the needle); and scars (already reported to contain higher concentrations of bacteria than healthy skin) [13].

The objective of our study was to assess determinants associated with bacterial contamination of whole-blood donations.

Subjects and methods

Data collection

This cross-sectional study was nested in a study implemented to assess the efficacy of diverting the first 15 ml of blood collection to reduce bacterial contamination of whole-blood donations [14]. The study was carried out from March to December 1997 in four French volunteer blood banks: Etablissement Français du Sang (EFS) Centre-Atlantique (Tours); Centre de Transfusion Sanguine des Armées Jean Julliard (Clamart); EFS Alpes-Méditerranée (Marseille); and EFS Île-de-France (Versailles). To culture blood samples on the day of donation, collection sites were selected if they collected whole-blood donations in the morning. Donors were included if they had been accepted for donation after a medical selection complying with French regulations [15] and had given their informed consent to participate.

The phlebotomy site was prepared according to a two-stage procedure complying with the French Blood Agency recommendations [16]. This involved preparation of an area of skin of ≈ 3·5 cm in all directions around the intended phlebotomy site. The site was then scrubbed with a gauze pad soaked with an antiseptic or detergent agent (the regulations recommend that this stage is to be repeated 'if needed'). The second stage involved application of an antiseptic agent compatible with the one used in the first stage. The skin was then allowed to dry for the time recommended by the manufacturer of the antiseptic agent. Different antiseptic agents were used by each of the participating blood banks. However, all of the blood banks used the same agent for both stages of skin preparation. The scrub duration was 5–10 seconds. Application times were 5–10 seconds in all blood banks except in blood bank 4 where the second gauze pad soaked with antiseptic was left on the intended phlebotomy site for 30 seconds before being used to wipe the site. Drying times after application varied according to the antiseptic agent used: more than 15–20 seconds for iodine tincture in blood bank 1; more than 30 s for Hibisprint® (chlorhexidine) in blood bank 2; and 1 min for non-alcoholic Betadine® (povidone-iodine) in blood bank 3. Blood bank 4 used Bisseptine® (chlorhexidine, benzalkonium chloride, benzylic alcohol) and did not recommend any drying time. An additional drying time of 30 seconds between stages 1 and 2 was applied in blood bank 2.

The age and gender of the donor, the time since the last meal (as stated by the donor), and the site, date and hour of collection, were recorded by the physician. The skin at the phlebotomy site was carefully inspected by the nurse who recorded the presence of hairs, scars from previous phlebotomies, or skin lesions less than 10 cm away from the phlebotomy site. The requirement to repeat the scrub stage when the first gauze pad was dirty, and the ease of phlebotomy, were also recorded.

Blood was collected into standard Maco Pharma packs (Maco Pharma, Tourcoing, France), specially equipped with two small sample bags into which the first (S1) and second (S2) 15 ml of donation were aseptically collected, before blood was allowed to enter the unit bag. At the end of donation, the two sample bags were separated from the rest of the pack by double welding, placed into an isothermal box and brought to the bacteriology laboratory within 6 h.

Bacteriological methods

Samples were cultured in a BacT/Alert® 240 automated system (Organon Teknika, Durham, NC). Each sample bag was equipped with a needle allowing direct inoculation through the rubber cap of an anaerobic then an aerobic FAN culture bottle. Bottles were incubated in the BacT/Alert® for 7 days at 35 °C, according to the manufacturer's instructions.

A sample from each bottle detected as positive was subcultured onto trypticase–soy 5% blood agar (for aerobic culture) and onto Columbia blood agar (for anaerobic culture), both at 37 °C. When a subculture was positive, bacteria were identified according to standard microbiological methods and stored. A donation was defined as contaminated with bacteria if at least one aerobic or anaerobic bottle inoculated with S1 or S2 was culture positive.

The correct functioning of the automated culture systems was verified by inoculation and incubation of positive controls in the same conditions as study samples. One out of four strains was cultured each week in each centre, alternately: *Staphyloccocus aureus* CIP 53·156 (American Type Culture Collection [ATCC] 6538P; ATCC, Rockville, MD), *Clostridium sporogenes* CIP 79·03 (ATCC 19404), *Propionibacterium*

KUR-MAG-DE005597

5/17/2019 (PDF) Multivariate analysis of determinants of bacterial contamination of whole-blood donations | Luc Noel - Academia.edu

DOWNLOAD

acnes CIP 53·117T (ATCC 6919) and *Pseudomonas aeruginosa* CIP 76·110 (ATCC 27853). Bottles were expected to be culture positive within 10–24 h, depending on the strain of bacteria used. The rate of secondary contamination related to handling or inoculation was estimated by culturing the anticoagulant from 189 S1 and 189 S2 sample bags which were not used for donation, but which were transported, inoculated and incubated under the same experimental conditions as the study samples.

Data management and analysis

For each donation, information regarding blood collection was recorded on a report form. Culture results were recorded on a separate form at the laboratory and transferred to the corresponding donation form. Data were entered in each centre on the EPI INFO software (6·04b French version, January 1997, ENSP – Epiconcept) and files were transmitted to the Institut de Santé Publique, d'Epidémiologie et de Développement (Université Victor Segalen Bordeaux 2). Donations were excluded from analysis if clots or welding problems were reported during collection or inoculation, or if the blood volumes collected in S1 or S2 or inoculated in FAN bottles, were less than 5 ml.

The bacterial contamination rates of donations were estimated by the proportion of donations for which S1 or S2 was culture positive and its exact binomial 95% confidence intervals (95% CI). Comparisons were based upon standard tests [17]. The association between a variable and donation contamination was estimated by the odds ratio (OR) [18]. To analyse the simultaneous effect of several variables on the risk of contamination, a logistic regression model was used [19]. All variables were included in the multivariate model, regardless of their association with bacterial contamination in univariate analysis. A stepwise backward procedure was used to remove variables that were less significantly associated with donation contamination, according to Wald or the likelihood ratio test [19]. Statistical analysis was conducted using the STATA software (Stata 5·0; Stata Corporation, College Station, TX).

Results

Study population

Among 3441 whole-blood donations, collected from March through December 1997, 56 (1·6%) were excluded because of clots, welding problems or insufficient collection or culture volumes. Most donations were collected during mobile sessions (premises, 50%; vehicle, 37%), and before 14·00 h (99·4%); the time since the last meal was less than 3 h in 60·4% of the donors. A high percentage of the donors were male (73·3%) and their median age was 39 years (first quartile: 27 years; third quartile: 48 years). The presence of hairs at the phlebotomy site was reported in 29·5% of men and 2·0% of women; skin lesions close to the phlebotomy site were present in 2·3% of donors; and scars were present in 14·3% (minor signs, 10·6%; multiple scars, 2·9%; dimpled skin, 0·7%). The scrub stage of antisepsis was repeated in 8·5% of donations, and phlebotomy was reported as easy in 43·3%.

Bacteriological results

All positive controls were detected by the automated culture system. One negative control out of 378 (0·26%) was culture positive for coagulase negative staphylococci (CNS).

Seventy-nine bacteria were cultured from samples originating from 76 donations. The most common bacterial species were Gram-positive cocci, which accounted for 81% of the bacterial species and were mostly CNS (66%). Gram-positive bacilli, mostly Bacillus species and *P. acnes*, accounted for 14%, and Gram-negative bacilli for 5%, of species.

The overall prevalence rate of bacterial contamination was 2·2% (95% CI: 1·8–2·8%).

Determinants of bacterial contamination

In the univariate analysis, characteristics significantly associated with bacterial contamination were the blood bank, period of collection, time since last meal, donor age and the presence of hairs at the phlebotomy site (Table 1). As the rate of contamination was more than twofold higher when donors were > 35 years, this characteristic was used as a binary variable.

Characteristics significantly associated with bacterial contamination in the final multivariate model were the blood bank, a donor age > 35 years and the lack of repetition of the antisepsis scrub stage (Table 1).

Discussion

Our study confirmed the high frequency of bacterial contamination of whole-blood donations and revealed a strong protective role of repeating the antisepsis scrub stage. Other main determinants were the collecting blood bank and donor age. Contaminating bacteria, isolated after culture, were most likely to have a skin origin.

Our estimation of bacterial contamination rates of blood donations is higher than those previously reported in whole-blood units, but consistent with those of the first few ml collected [20] and with blood-culture contamination rates reported in clinical settings, where the same mechanisms may be implicated [21,22].

The major influence of the collecting blood bank may be related to the agent used for antisepsis. The risk of bacterial contamination was the highest in the blood bank using non-alcoholic povidone-iodine. This is consistent with studies

© 2002 Blackwell Science Ltd.

Table 1 Univariate (3385 donations) and multivariate (3227 donations) analysis of associations between whole-blood donation characteristics and bacterial contamination in four French blood banks, March–December 1997

	Univariate analysis		Multivariate analysis (final model)	

https://www.academia.edu/10154576/Multivariate_analysis_of_determinants_of_bacterial_contamination_of_whole-blood_donations 3/6

KUR-MAG-DE005598

Page 3462 of 4132

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

DOWNLOAD

1	1·59	2·71		2·05 (0·66–6·37)	
2	0·59	Ref.[d]		Ref.[d] (Ref.[d])	
3	3·92	6·87	< 0·001	5·63 (1·92–16·48)	0·0002
4	2·42	4·18		3·56 (1·16–10·91)	
Collection site					
Mobile session (premises)	2·74	1·58			
Mobile session (truck)	1·75	Ref.[d]	0·15		
Blood bank premises	1·77	1·01			
Period of collection					
March to May	1·59	Ref.[d]		Ref.[d] (Ref.[d])	
June to September	1·89	1·19	0·03	0·87 (0·41–1·86)	0·091
October to December	3·32	2·13		1·53 (0·70–3·36)	
Time since last meal (19 missing data)					
0 to 59 min	1·74	Ref.[d]		Ref.[d] (Ref.[d])	
1 h to 1 h 59 min	3·16	1·96		1·95 (0·87–4·36)	
2 h to 2 h 59 min	1·52	0·87	0·02	1·01 (0·43–2·37)	0·052
3 h to 3 h 59 min	1·57	0·90		1·01 (0·42–2·43)	
4 h or more	3·53	2·06		2·22 (0·98–5·02)	
Donor gender					
Male	2·14	Ref.[d]			
Female	2·55	1·20	0·47		
Donor age > 35 years					
No	1·43	Ref.[d]		Ref.[d] (Ref.[d])	
Yes	2·82	2.00	0·008	1·77 (1·02–3·07)	0·036
Phlebotomy site features					
Hairs (14 missing data)					
None	1·98	Ref.[d]		Ref.[d] (Ref.[d])	
Yes	3·21	1·64	0·05	1·51 (0·90–2·54)	0·125
Skin lesions (98 missing data)					
None	2·31	Ref.[d]			
Yes	2·60	1·13	0·87		
Scars					
None	2·31	Ref.[d]			
Minor signs	1·39	0·60			
Multiple scars	3·03	1·32	0·60		
Dimpled skin	4·00	1·76			
Scrub stage repeated (30 missing data)					
Yes	1·40	Ref.[d]		Ref.[d] (Ref.[d])	
No	2·35	1·68	0·32	2·72 (0·96–7·73)	0·032
Easiness of phlebotomy (29 missing data)					
Yes	1·72	Ref.[d]			
No	2·68	1·57	0·07		

[a]χ^2 or Fisher's exact test.
[b]CI: confidence interval of odds ratio (OR).
[c]Likelihood ratio test.
[d]Reference category for OR estimation.

© 2002 Blackwell Science Ltd.

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

DOWNLOAD

KUR-MAG-DE005600

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

DOWNLOAD

About Press Blog People Papers Job Board Advertise We're Hiring! Help Center
Find new research papers in: Physics Chemistry Biology Health Sciences Ecology Earth Sciences Cognitive Science Mathematics Computer Science
Terms Privacy Copyright Academia ©2019

Transfus Med Hemother. 2011 Aug; 38(4): 255–258.
Published online 2011 Jul 15. doi: 10.1159/000330474

PMCID: PMC3190222
PMID: 22016668

Language: English | Español

Interventions Implemented to Reduce the Risk of Transmission of Bacteria by Transfusion in the English National Blood Service

Carl P. McDonald*

NHS Blood and Transplant, London, UK

*Dr. Carl P. McDonald, NHS Blood and Transplant, Colindale Avenue, Colindale London NW9 5BG, UK, Tel. +44 208 957 27-22, Fax -26, carl.mcdonald@nhsbt.nhs.uk

Received: 2011 Jun 14; Accepted: 2011 Jun 30.

Copyright © 2011 by S. Karger GmbH, Freiburg

Abstract

Summary

Background

Bacterial contamination remains a significant problem in transfusion medicine. A National Health Service Blood and Transplant (NHSBT) study and surveillance data indicated skin commensals derived from the skin of the donor are the major contaminants of blood components. NHSBT therefore explored two interventions: improved donor arm disinfection and diversion.

Methods

Improved donor arm disinfection: Commercial and in-house methods of disinfection were evaluated. Swabs of the venepuncture site were taken before and after disinfection and the reduction in bioburden determined. Diversion: Special collection bags were manufactured to allow the initial volume of blood to flow into a pouch, representing the diversion pouch and then the next flow of blood into another pouch representing the collection bag. Pouches were screened for the presence of bacteria. The reduction in bacterial contamination was then determined.

Results

A two-step commercial procedure (Donor Prep Kit; DPK) consisting of 70% isopropyl alcohol followed by tincture of iodine was shown to be a best practice procedure (2-min procedure). A 99.79% reduction was obtained, and this method was 10 times more effective than current practice at that time. The DPK was shown in a field trial to increase donor waiting time. A second study was initiated to find a more rapid procedure. ChloraPrep®, consisting of 2% chlorhexidine gluconate and 70% isopropyl alcohol, was shown to have equivalent disinfection efficiency as the DPK, but only took 1 min to perform. In 2006, ChloraPrep was introduced as the national method of donor arm disinfection. Diversion was shown to give a 47% reduction in contamination and was introduced nationally in 2002.

Conclusion

Improved donor arm disinfection and diversion are effective, low-cost interventions, but do not eliminate all bacterial transmissions. In 2011, bacterial screening of platelet components was introduced by NHSBT to further increase the safety of the blood supply.

KeyWords: Bacterial contamination, Blood donation, Blood safety, Haemovigilance, Platelet concentrates, Transfusion reaction, Transfusion risks, Transfusion-associated infectious Bacteria, Diversion, Disinfection

Introduction

Since the 1970s, the risk of viral transmission by transfusion has been markedly reduced [1]. Transmission of bacteria by transfusion is not a new problem, having been reported nearly 70 years ago [2, 3]. In the mid 1990s, the attention of the blood community was drawn to bacterial transmissions due to case reports in the literature and the establishment of haemovigilance systems. In 1995 the U.K. Serious Hazards of Transfusion (SHOT) voluntary surveillance system was established, reporting that between 1995 and 2001 bacterial transmissions accounted for 64% (21/33) of microbial transmissions [4]. In this period in the UK, 85% (6/7) of microbial fatalities reported to SHOT were due to transmission of bacteria by transfusion. Platelet concentrates accounted for 81% (17/21) of these transmissions.

From 1994 to 1998, the French haemovigilance surveillance system (a mandatory requirement under French law), attributed 18 deaths (four occurring in 1997) to blood components contaminated with bacteria [5, 6]. Between 1994 and 1999, bacterial transmissions comprised 22% of total transfusion-associated fatalities [7]. Transmission of bacteria by transfusion was reported to the haemovigilance surveillance system as the most frequently identified cause of death [5].

In the USA, from 1985 to 1989 bacterial contamination was second only to haemolytic reactions as the most frequent reported cause of mortality, accounting for over 10% (77/694) of transfusion fatalities [8]. From 2001 to 2003, the transmission of bacteria by transfusion accounted for 37 deaths, amounting to 14.1% of all transfusion fatalities [9].

A National Health Service Blood and Transplant (NHSBT) retrospective monitoring study was established in 1995 to determine the bacterial contamination rate in blood components using an automated microbial detection system [10, 11]. The study was also used to determine the effectiveness of any interventions implemented to reduce bacterial contamination.

Data from this study and SHOT surveillance data indicated that the vast majority of organisms that contaminate blood components are skin commensals derived from the skin of the donor at venepuncture. NHSBT therefore explored two interventions:

– improved donor arm disinfection,
– diversion.

Material and Methods

Improved Donor Arm Disinfection

A study was undertaken to determine the effectiveness of in-house and commercial disinfection protocols [12]. Swabbing of the venepuncture site was performed before and after disinfection. Swabs were inoculated onto agar plates, and the reduction in bioburden pre and post disinfection was determined. A second study was undertaken to derive a disinfection procedure that would only take 1 min to perform [13].

Diversion

In 1995, Olbuis et al. [14] proposed that diversion of the initial volume of blood donation from the collection bag had the potential to dramatically reduce bacterial contamination. The rationale behind this is that (as previously mentioned) the major source of bacterial contamination of blood components occurs at the collection stage, due to inadequate donor arm disinfection and/or a small core of skin entering the collection bag from coring by the phlebotomy needle. Re-direction of the initial flow of blood from the collection bag into a pouch or side arm would thus reduce the risk of bacterial contamination of the donation contents.

Special collection bags were manufactured for a study to determine the effectiveness of diversion [15]. These bags consisted of two sampling pouches attached to the standard collection bag configuration. At donation, blood was made to flow initially into pouch P1, which represented a diversion pouch. Pouch P1 was then closed causing the blood to flow into pouch P2, which acted as a representative sample of the collection bag post diversion. P2 was then closed, and blood was

diverted into the collection bag as in a routine donation. The pouches were sampled and inoculated into culture bottles and incubated on an automated microbial detection system for 7 days. Any bacteria that grew were sub-cultured and identified.

Results

Improved Donor Arm Disinfection

The Donor Prep Kit (DPK) (Ecolab (formerly Medi-Flex), Leadwood, KS, USA) was shown to be a best-practice technique, consisting of an initial application of isopropyl alcohol and tincture of iodine. The procedure took 2 min, with an application time of 30 s and drying time of 30 s for each disinfectant. A percentage reduction of 99.79% ($\log_{10}$ reduction 2.67%) was obtained compared with 78.2% ($\log_{10}$ reduction 1.31%) for the then current method, 0.5% chlorhexidine isopropyl alcohol wipe (Guardpack, Chelmsford, Essex, UK) [12].

The DPK was implemented for apheresis platelet donations in July 2001, and the reduction in the bacterial contamination rate of time-expired platelet donations was shown to be 57% [16]. Previously an experimental study predicted a 57% reduction in contamination [15]. A 67% reduction in clinically apparent cases of bacterial transmission following transfusion of NHSBT blood donations reported to SHOT was observed [17]. In the period 1997 to 2000 prior to implementation, 6 clinical cases (including 2 deaths) were reported. After the introduction of the DPK at apheresis clinics in the 4-year period from July 2001 to 2005, only 2 clinically apparent reactions from transfusion of platelet concentrates manufactured by NHSBT have been reported.

An extensive field evaluation of the use of the DPK procedure has been undertaken at mobile blood donor sessions. It was however, deemed inappropriate for routine use by NHSBT because it would increase donor waiting times. This was due to the additional 3 min that was required with the DPK compared with the routine method in use at that time. The NHSBT National Bacteriology Laboratory (NBL) was therefore tasked with identifying a disinfection procedure that was of comparable disinfection efficacy as the DPK, but was only 1 min in duration.

The ChloraPrep® disinfection method (CareFusion Ltd, Reigate, UK), consisting of a 30-second application of 70% isopropyl alcohol and 2% chlorhexidine gluconate with a 30-second drying time was shown to give equivalent disinfection efficiency as the DPK [13]. In 2006, ChloraPrep was implemented throughout NHSBT for both routine and apheresis donations.

Diversion

A 47% reduction in bacterially contaminated blood donations was observed in our study on the effectiveness of diversion [15]. On the basis of this study, diversion was implemented nationally in 2002. Monitoring data derived from testing outdated platelet concentrates showed a 66% reduction in contamination [16]. Prior to the implementation of diversion in the 3-year period 1999 to 2001, there were 11 clinically apparent cases from NHSBT-produced pooled platelet concentrates (n = 9) and red cell units (n = 2). After the implementation of diversion in the 3-year period 2003 to 2005, there were only 2 reports of clinically apparent transmission of bacteria by transfusion, a reduction of 82% [17].

The NHSBT diversion study also indicated that diversion, together with improved donor arm disinfection, would reduce bacterial contamination by approximately 77% [15].

Discussion

Donor arm disinfection is the first physical intervention applied to prevent microbial contamination of a blood donation. Many blood services have now validated and implemented best-practice procedures [18, 19]. In Canada the DPK system was shown to be a best-practice procedure, a finding confirmed by our studies [20]. Studies in the USA and Canada with the ChloraPrep disinfection device have confirmed the findings of NHSBT [21, 22]. This device has been adopted for use in these countries. Since the work of NHSBT, the evidence-based practice in Infection Control Guidelines Version 2 (epic 2) for National Health Service hospitals in England recommend "a single patient use application of alcoholic chlorhexidine gluconate solution, preferably 2% chlorhexidine in 70% isopropyl alcohol" for central venous access device decontamination [23].

The NHSBT diversion study indicated that a 47% reduction in bacterial contamination would be obtained, although a greater reduction of 66% was observed in the outdated platelet study, and clinically apparent transmissions were reduced by as much as 82%. Studies in the Netherlands by de Korte et al. [24] and by Ohlbius et al. [11] showed a 40% and 82% reduction respectively. Brunead et al. [25] in France reported a 72% and Benjamin et al. in the USA a 54% reduction in bacterial contamination [26]. Diversion has now been widely adopted by blood services.

Improved donor arm disinfection and diversion have been shown to be highly effective, relatively low-cost interventions for reducing the transmission of bacteria by transfusion. An NHSBT study indicated that improved donor arm disinfection in conjunction with diversion would reduce bacterial contamination by approximately 77% [27]. Residual contamination levels of blood units after the introduction of diversion may be in the order of 30–80% [23, 28].

Since 2006, improved donor arm disinfection and diversion have been used for all NHSBT donations. In the period of SHOT haemovigilance 2006–2009, bacterial transmission was reported from 10 NHSBT donations which resulted in 4 deaths [29]. In November 2005 in the UK, it became mandatory to report adverse transfusion reactions, which resulted in an increase in bacterial investigations, revealing more cases of transmission. In 2011, in view of this data, NHSBT implemented bacterial screening of platelet concentrates to further increase the safety of the blood supply.

Disclosure Statement

The author declared no conflicts of interest.

Acknowledgements

The author would like to thank Tracy Ward, Siobhan Ancliff, and Professor Barbara for assistance in preparation of this manuscript.

References

1. Soldan K, Davison K, Dow B. Estimates of the frequency of HBV, HCV, and HIV infectious donations entering the blood supply in the United Kingdom, 1996 to 2003. Euro Surveill. 2005;10:17–19. [PubMed] [Google Scholar]

2. Novak M. Preservation of stored blood with sulfonilamide. JAMA. 1939;113:2227–2229. [Google Scholar]

3. Strumia MM, McGraw B. Frozen and dried plasma for civil and military use. JAMA. 1941;116:2378–2382. [Google Scholar]

4. Asher D, Atterbury C L J, Chapman C, Cohen H, Jones H, Love E M, Norfolk D R, Revill J, Soldan K, Todd A, Williamson LM; on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2008/2009 Annual SHOT Report. www.shotuksorg.co.uk/uploads/2010/05/SHOT-Report-BMH.pdf

5. Debets J, Noel L, Allen J-P, Erette C, Sari F, Mai M, Cosson A. The French haemovigilance system. Vox Sang. 1999;77:77–81. [PubMed] [Google Scholar]

6. Morel PC. Bacterial Contamination of Platelets Workshop. Washington DC: FDA; 1990. The French Experience in the Prevention of Transfusion Incidents due to Bacterial Contamination. [Google Scholar]

7. Morel P: Bacterial Contamination of Platelets Workshop, Bethesda. www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/UCM062892.pdf

8. Center for Biologics Evaluation and Research: Workshop on Bacterial Contamination of Platelets, Bethesda. 1999. www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/UCM062892.pdf

9. Goldman M, Webert KE, Arnold DM. Proceedings of a consensus conference: towards an understanding of TRALI. Transfus Med Rev. 2005;19:3–31. [PubMed] [Google Scholar]

10. McDonald CP, Roy A, Lowe P, Robbins S, Hartley S, Barbara JA. Evaluation of the BacT/Alert automated blood culture system for detecting bacteria and measuring their growth kinetics in leucodepleted and non-leucodepleted platelet concentrates. Vox Sang. 2001;81:154–160. [PubMed] [Google Scholar]

11. McDonald CP, Rogers A, Cox M, Smith R, Roy A, Robbins S, Hartley S, Barbara JA, Rothenberg S, Stutzman L, Widders G. Evaluation of the 3D BacT/ALERT automated culture system for the detection of microbial contamination of platelet concentrates. Transfus Med. 2002;12:303–309. [PubMed] [Google Scholar]

12. McDonald CP, Lowe P, Roy A, Robbins S, Hartley S, Barrison JE, Slupecki A, Verlander N, Barbara JA. Evaluation of donor arm disinfection techniques. Vox Sang. 2001;80:135–141. [PubMed] [Google Scholar]

13. McDonald C, McGuane S, Thomas I, Hartley S, Robbins S, Roy A, Verlander N, Barbara J. a novel rapid and effective donor arm disinfection method. Transfusion. 2010;50:53–58. [PubMed] [Google Scholar]

14. Olthuis H, Peylaert C, Verhagen C, Valk L: Method for removal of contamination bacteria during venepuncture. Presented at the 5th International Society of Blood Transfusion Regional Congress, Venice, Italy July 2–5, 1995.

15. McDonald CP, Roy A, Mahajan P, Smith R, Chariett A, Barbara JA. Relative values of the interventions of diversion and improved donor-arm disinfection to reduce the bacterial risk from blood transfusion. Vox Sang. 2004;86:178–182. [PubMed] [Google Scholar]

16. McDonald C, Colvin I, Biggs C, Goodband K, Barden G, McGuane S. Do diversion and improved donor arm disinfection reduce bacterial contamination in platelet concentrates. Transfusion. 2005;45:56A. (Abstract). [Google Scholar]

17. Stainsby D, Jones H, Cohen H, Asher A, Atterbury C, Boocieelli A, Brant L, Chapman CE, Knowles S, Milkins C, Norfolk DR; on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2005 Annual SHOT Report. www.shotuk.org/wp-content/uploads/2011/03/SHOT-report-2005.pdf.

18. Wong PY, Colville VL, White V, Walker HM, Morris RA. Validation and assessment of a blood-donor arm disinfectant containing chlorhexidine and alcohol. Transfusion. 2004;44:1238–1242. [PubMed] [Google Scholar]

19. Lee CK, Ho PL, Chan NK, Mak A, Hong J, Liu CK. Impact of donor arm skin disinfection on the bacterial contamination rate of platelet concentrates. Vox Sang. 2002;83:264–268. [PubMed] [Google Scholar]

20. Goldman M, Roy G, Brochette N, Decary F, Massicotte L, Delage G. Evaluation of donor skin disinfection methods. Transfusion. 1997;37:309–312. [PubMed] [Google Scholar]

21. Ramirez-Arcos S, Goldman M. Skin disinfection methods: prospective evaluation and postimplementation results. Transfusion. 2010;50:59–64. [PubMed] [Google Scholar]

22. Benjamin RJ, Dy B, Warren R, Lischka M, Eder AF. Skin disinfection with a single-step 2% chlorhexidine swab is more effective than a two-step povidone-iodine method in preventing bacterial contamination of apheresis platelets. Transfusion. 2011;51:531–538. [PubMed] [Google Scholar]

23. Pratt RJ, Pellowe CM, Wilson JA, Loveday HP, Harper PJ, Jones SR, McDougall C, Wilcox MH, epic2: National evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. J Hosp Infect. 2007;65(suppl 1):S1–64. [PubMed] [Google Scholar]

24. de Korte D, Marcelis JH, Verhoeven AJ, Soeterboek AM. Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections. Vox Sang. 2002;83:13–16. [PubMed] [Google Scholar]

25. Bruneau C, Perez P, Chassaigne M, Allonch P, Audurier A, Gutian C, Janas G, Boulard G, De Micco P, Saint LR, Noel L. Efficacy of a new collection procedure for preventing bacterial contamination of whole-blood donations. Transfusion. 2001;41:74–81. [PubMed] [Google Scholar]

26. Benjamin RJ, Kline L, Dy BA, Kennedy J, Pisciotto P, Sapatnekar S, Mercado R, Eder AF. Bacterial contamination of whole-blood-derived platelets: the introduction of sample diversion and prestorage pooling with culture testing in the American Red Cross. Transfusion. 2008;48:2348–2355. [PubMed] [Google Scholar]

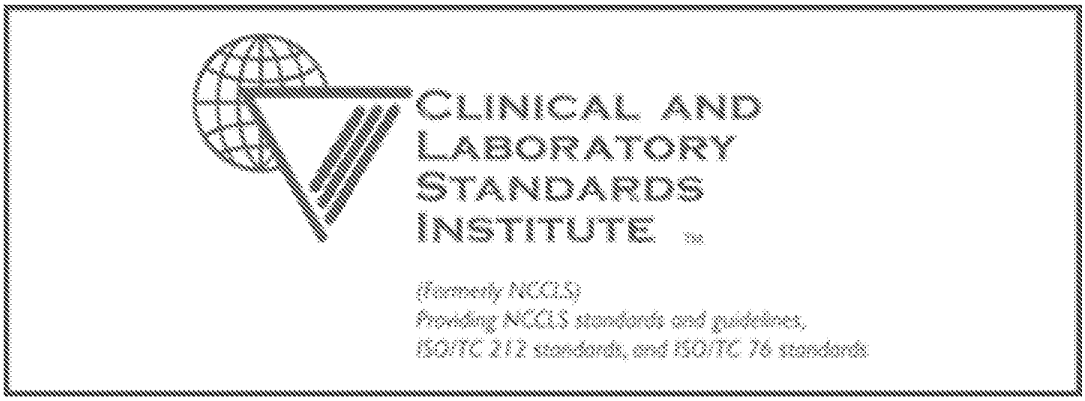
27. McDonald CP, Roy A, Mahajan P, Smith R, Chariett A, Barbara JA. Relative values of the interventions of diversion and improved donor-arm disinfection to reduce the bacterial risk from blood transfusion. Vox Sang. 2004;86:178–182. [PubMed] [Google Scholar]

28. Taylor C (ed). Cohen H, Mold D, Jones M, Davies T, Mistry H, Batt J, Asher D, Cawley C, Chaffe B, Chapman C, Gray A; on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group: The 2009 Annual SHOT report. www.shotuk.org/wp-content/uploads/2010/07/SHOTR09.pdf

Articles from Transfusion Medicine and Hemotherapy are provided here courtesy of **Karger Publishers**

H3-A5
Vol. 23 No. 32
Replaces H3-A4
Vol. 18 No. 7

Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition



This document provides procedures for the collection of diagnostic specimens by venipuncture, including line draws, blood culture collection, and venipuncture in children.

A standard for global application developed through the NCCLS consensus process.

NCCLS

NCCLS...

Serving the World's Medical Science Community Through Voluntary Consensus

NCCLS is an international, interdisciplinary, nonprofit, standards-developing, and educational organization that promotes the development and use of voluntary consensus standards and guidelines within the healthcare community. It is recognized worldwide for the application of its unique consensus process in the development of standards and guidelines for patient testing and related healthcare issues. NCCLS is based on the principle that consensus is an effective and cost-effective way to improve patient testing and healthcare services.

In addition to developing and promoting the use of voluntary consensus standards and guidelines, NCCLS provides an open and unbiased forum to address critical issues affecting the quality of patient testing and health care.

PUBLICATIONS

An NCCLS document is published as a standard, guideline, or committee report.

Standard A document developed through the consensus process that clearly identifies specific, essential requirements for materials, methods, or practices for use in an unmodified form. A standard may, in addition, contain discretionary elements, which are clearly identified.

Guideline A document developed through the consensus process describing criteria for a general operating practice, procedure, or material for voluntary use. A guideline may be used as written or modified by the user to fit specific needs.

Report A document that has not been subjected to consensus review and is released by the Board of Directors.

CONSENSUS PROCESS

The NCCLS voluntary consensus process is a protocol establishing formal criteria for:

- the authorization of a project
- the development and open review of documents
- the revision of documents in response to comments by users
- the acceptance of a document as a consensus standard or guideline.

Most NCCLS documents are subject to two levels of consensus—"proposed" and "approved." Depending on the need for field evaluation or data collection, documents may also be made available for review at an intermediate (i.e., "tentative") consensus level.

Proposed An NCCLS consensus document undergoes the first stage of review by the healthcare community as a proposed standard or guideline. The document should receive a wide and thorough technical review, including an overall review of its scope, approach, and utility, and a line-by-line review of its technical and editorial content.

Tentative A tentative standard or guideline is made available for review and comment only when a recommended method has a well-defined need for a field evaluation or when a recommended protocol requires that specific data be collected. It should be reviewed to ensure its utility.

Approved An approved standard or guideline has achieved consensus within the healthcare community. It should be reviewed to assess the utility of the final document, to ensure attainment of consensus (i.e., that comments on earlier versions have been satisfactorily addressed), and to identify the need for additional consensus documents.

NCCLS standards and guidelines represent a consensus opinion on good practices and reflect the substantial agreement by materially affected, competent, and interested parties obtained by following NCCLS's established consensus procedures. Provisions in NCCLS standards and guidelines may be more or less stringent than applicable regulations. Consequently, conformance to this voluntary consensus document does not relieve the user of responsibility for compliance with applicable regulations.

COMMENTS

The comments of users are essential to the consensus process. Anyone may submit a comment, and all comments are addressed, according to the consensus process, by the NCCLS committee that wrote the document. All comments, including those that result in a change to the document when published at the next consensus level and those that do not result in a change, are responded to by the committee in an appendix to the document. Readers are strongly encouraged to comment in any form and at any time on any NCCLS document. Address comments to the NCCLS Executive Offices, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

VOLUNTEER PARTICIPATION

Healthcare professionals in all specialties are urged to volunteer for participation in NCCLS projects. Please contact the NCCLS Executive Offices for additional information on committee participation.

H3-A5
ISBN 1-56238-515-1
Volume 23 Number 32 ISSN 0273-3099

Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition

Charles F. Arkin, M.D.
J. David Bessman, M.D.
Roger R. Calam, Ph.D., DABCC
Dennis J Ernst, M.T.(ASCP)
Gary T. Parish
Diane I. Szamosi, M.A., M.T.(ASCP), SH
David J. Warunek, Ph.D.
Joan D. Wiseman, M.T.(ASCP)CT

Abstract

H3-A5—*Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition* provides a descriptive, stepwise procedure for the collection of diagnostic blood specimens by venipuncture. Special considerations for venipuncture in children, line draws, blood culture collection, and venipuncture in isolation situations are included.

NCCLS. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition*. NCCLS document H3-A5 (ISBN 1-56238-515-1). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2003.

THE NCCLS consensus process, which is the mechanism for moving a document through two or more levels of review by the healthcare community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of NCCLS documents. Current editions are listed in the *NCCLS Catalog*, which is distributed to member organizations, and to nonmembers on request. If your organization is not a member and would like to become one, and to request a copy of the *NCCLS Catalog*, contact the NCCLS Executive Offices. Telephone: 610.688.0100; Fax: 610.688.0700; E-Mail: exoffice@nccls.org; Website: www.nccls.org



This publication is protected by copyright. No part of it may be reproduced, stored in a retrieval system, transmitted, or made available in any form or by any means (electronic, mechanical, photocopying, recording, or otherwise) without prior written permission from NCCLS, except as stated below.

NCCLS hereby grants permission to reproduce limited portions of this publication for use in laboratory procedure manuals at a single site, for interlibrary loan, or for use in educational programs provided that multiple copies of such reproduction shall include the following notice, be distributed without charge, and, in no event, contain more than 20% of the document's text.

> Reproduced with permission, from NCCLS publication H3-A5—*Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition* (ISBN 1-56238-515-1). Copies of the current edition may be obtained from NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA.

Permission to reproduce or otherwise use the text of this document to an extent that exceeds the exemptions granted here or under the Copyright Law must be obtained from NCCLS by written request. To request such permission, address inquiries to the Executive Director, NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA.

Copyright ©2003. The National Committee for Clinical Laboratory Standards.

Suggested Citation

(NCCLS. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition.* NCCLS document H3-A5 [ISBN 1-56238-515-1]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2003.)

Proposed Standard
August 1977

Tentative Standard
February 1979

Approved Standard
March 1980

Approved Standard—Second Edition
April 1984

Approved Standard—Third Edition
July 1991

Approved Standard—Fourth Edition
June 1998

Approved Standard—Fifth Edition
December 2003

ISBN 1-56238-515-1
ISSN 0273-3099

Committee Membership

Area Committee on Hematology

Charles F. Arkin, M.D.
Chairholder
Lahey Clinic
Burlington, Massachusetts

Bruce H. Davis, M.D.
Vice-Chairholder
Maine Medical Center Research Institute
Scarborough, Maine

J. David Bessman, M.D.
University of Texas Medical Branch
Galveston, Texas

Berend Houwen, M.D., Ph.D.
Beckman Coulter, Inc.
Brea, California

Frank M. LaDuca, Ph.D.
International Technidyne Corporation
Edison, New Jersey

Ginette Y. Michaud, M.D.
FDA Center for Devices/Rad. Health
Rockville, Maryland

Onno W. van Assendelft, M.D., Ph.D.
Centers for Disease Control and Prevention
Atlanta, Georgia

Advisors

Dorothy M. Adcock, M.D.
Esoterix Coagulation
Aurora, Colorado

Sheila Clover, CPT (ASCP) (NCA)
Phlebotomy West
Brentwood, California

Dennis J. Ernst, M.T.(ASCP)
Center for Phlebotomy Education
Ramsey, Indiana

J. Heinrich Joist, M.D., Ph.D.
St. Louis University Health Science Center
St. Louis, Missouri

John A. Koepke, M.D.
Durham, North Carolina

Francis Lacombe, M.D., Ph.D.
Laboratoire d'Hematologie
Pessac, France

Samuel J. Machin, MB, Ch.B, FRCPath
The University College London Hospital
London, United Kingdom

Richard A. Marlar, Ph.D.
Denver VA Medical Center
Denver, Colorado

Diane L. Szamosi, M.A.,M.T.(ASCP)SH
Greiner Bio-One, VACUETTE North America, Inc.
Monroe, North Carolina

Luc Van Hove, M.D., Ph.D.
Abbott Laboratories
Abbott Park, Illinois

Staff

Tracy A. Dooley, M.L.T.(ASCP)
Staff Liaison
NCCLS
Wayne, Pennsylvania

David E. Sterry, M.T.(ASCP)
Project Manager
NCCLS
Wayne, Pennsylvania

Donna M. Wilhelm
Editor
NCCLS
Wayne, Pennsylvania

Melissa A. Lewis
Assistant Editor
NCCLS
Wayne, Pennsylvania

Acknowledgement

NCCLS gratefully acknowledges the working group for their help in preparing the approved-level, fifth edition of this standard.

Charles F. Arkin, M.D.
Lahey Clinic

J. David Bessman, M.D.
University of Texas Medical Branch

Roger R. Calam, Ph.D., DABCC
St. John Hospital

Dennis J. Ernst, M.T.(ASCP)
Center for Phlebotomy Education

Gary T. Parish
Sarstedt, Inc.

Diane I. Szamosi, M.A., M.T.(ASCP), SH
Greiner Bio-One, VACUETTE North America, Inc.

David J. Warunek, Ph.D., M.B.A.
BD VACUTAINER Systems

Joan D. Wiseman, M.T.(ASCP), CT
Consultant
Bernardsville, New Jersey

KUR-MAG-DE005088

Contents

Abstract i

Committee Membership iii

Foreword vii

1 Scope 1

2 Introduction 1

3 Standard Precautions 1

4 Definitions 1

5 Factors That Affect Laboratory Values 2

6 Facilities 2

6.1 Venipuncture Chairs 2
6.2 Hospital Area 3

7 Supplies 3

7.1 Utility Carts 3
7.2 Blood Collecting Trays 3
7.3 Gloves 3
7.4 Needles and Holders 4
7.5 Sterile Syringes 4
7.6 Venous Blood Collection Tubes 4
7.7 Tourniquets 4
7.8 Antiseptics 5
7.9 Gauze Pads 5
7.10 Puncture-Resistant Disposal Container 5
7.11 Ice 5
7.12 Adhesive Bandages 5
7.13 Warming Devices 5
7.14 Test Reference Manual 5

8 Venipuncture Procedure 5

8.1 Step 1: Prepare Accession Order 6
8.2 Step 2: Approach and Identify the Patient 6
8.3 Step 3: Verify Patient Diet Restrictions and Latex Sensitivity 8
8.4 Step 4: Assemble Supplies 8
8.5 Step 5: Position Patient 9
8.6 Step 6: Apply Tourniquet 10
8.7 Step 7: Put on Gloves 13
8.8 Step 8: Cleanse Venipuncture Site 13
8.9 Step 9: Perform Venipuncture 13
8.10 Step 10: Order of Draw 17
8.11 Step 11: Release the Tourniquet 17
8.12 Step 12: Place the Gauze Pad 17
8.13 Step 13: Remove and Dispose of the Needle 18
8.14 Step 14: Bandage the Arm 18

Contents (Continued)

8.15 Step 15: Label Blood Collection Tubes and Record Time of Collection 18
8.16 Step 16: Chill the Specimen 19
8.17 Step 17: Send Blood Collection Tubes to the Proper Laboratories 19

9 Venipuncture in Children and Difficult Collections 19

9.1 Procedure 19
9.2 Equipment 19

10 Additional Considerations 19

10.1 Monitoring Blood Volume Collected 19
10.2 Hematoma 20
10.3 Hemolysis 20

11 Special Situations 20

11.1 Timed Intervals 20
11.2 Specific Collection Techniques 20
11.3 Indwelling Lines or VADs 21
11.4 Heparin or Saline Locks 22
11.5 Fistula 22
11.6 Intravenous Fluids 22
11.7 Isolation 23
11.8 Emergency Situations 24

References 26

Summary of Comments and Subcommittee Responses 27

Summary of Delegate Comments and Working Group Responses 28

The Quality System Approach 34

Related NCCLS Publications 35

KUR-MAG-DE005090

Foreword

The errors that can occur during the collection and handling of blood specimens are potentially numerous (e.g., inaccurate identification of specimens, specimen hemolysis, the improper handling of anticoagulants, the formation of hematomas, hemoconcentration). Standards for venipuncture can reduce or alleviate many of these errors in much the same way that quality control standards have reduced errors within the laboratory.

Reducing errors during blood collecting will result in biologically representative specimens that are comparable from one institution to another. A well-planned, attractive environment in which to perform venipunctures will reduce patient anxiety and increase the efficiency and accuracy of the phlebotomist. Phlebotomists need a complete assortment of equipment at their fingertips so they can judiciously select the most appropriate materials for each patient. Standards governing the processing of paperwork will reduce errors and save time. Without question, a comprehensive training program is needed to produce efficient, well-trained phlebotomists. Finally, standards for the actual venipuncture procedure are needed to help eliminate the many errors that can occur during blood collection. Biologically representative specimens for laboratory testing will be obtained if national venipuncture standards are used.

Various comments received on the previous edition of this standard have been reviewed and incorporated where appropriate. All comments and the subcommittee's responses are summarized at the end of the document.

This document replaces the fourth edition approved standard, H3-A4, which was published in 1998. Several changes have been made in this edition; chief among them is the revised order of draw (Section 8.10.2), which reflects the increased use of plastic blood collection tubes. This standard also contains revised recommendations regarding collection of blood specimens in relation to intravenous sites (Section 11.6). The recommendations regarding the collection of coagulation specimens (Section 8.10.3) have been revised for consistency with NCCLS document H21—*Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays.*

Key Words

Accession, blood specimen, phlebotomist, sample, venipuncture

KUR-MAG-DE005091

KUR-MAG-DE005092

Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition

1 Scope[a]

This document establishes criteria for the correct collection of blood specimens by venipuncture. These procedures are intended to be a suitable model for adoption by all healthcare providers responsible for the collection and handling of blood specimens in both outpatient and inpatient settings.

2 Introduction

Since 1977, NCCLS has progressively recognized the quality requirement that significant attention be directed towards the preanalytical components of laboratory testing, specifically, the correct collection and handling of blood specimens. Highly sophisticated testing technology cannot produce a good result from a poor specimen. Proper specimen collection and handling are of the utmost importance because significant errors occur in the preanalytical phase of laboratory testing.[1]

Preanalytical errors have the potential to be numerous: incorrect patient ID, incorrect order-of-draw, incorrect use of additive tubes, labeling errors, incorrect timing of collection, clerical errors, etc. Standard procedures and protocols are intended to prevent these problems and protect patient results quality.

3 Standard Precautions

Because it is often impossible to know what might be infectious, all human blood specimens are to be treated as infectious and handled according to "standard precautions." Standard precautions are guidelines that combine the major features of "universal precautions and body substance isolation" practices. Standard precautions cover the transmission of any pathogen and thus are more comprehensive than universal precautions which are intended to apply only to transmission of blood-borne pathogens. Standard precaution and universal precaution guidelines are available from the U.S. Centers for Disease Control and Prevention (*Guideline for Isolation Precautions in Hospitals*. Infection Control and Hospital Epidemiology. CDC. 1996;Vol 17;1:53-80), (MMWR 1987;36[suppl 2S]2S-18S), and (MMWR 1988;37:377-382, 387-388). For specific precautions for preventing the laboratory transmission of blood-borne infection from laboratory instruments and materials and for recommendations for the management of blood-borne exposure, refer to the most current edition of NCCLS document M29—*Protection of Laboratory Workers from Occupationally Acquired Infections.*

4 Definitions

In the context of this publication, the terms listed below are defined as follows:

Accession – The steps required to ensure that a specific patient specimen and the accompanying documentation are unmistakably identified as referring to a specific person.

Angle of insertion – The angle formed by the surface of the arm and the needle entering the arm.

[a] This standard reflects recent revisions to OSHA's Blood Borne Pathogens Standard (29 CFR 1910.1030). Therefore, all references to needles/winged blood collection sets indicate sharps with engineered safety features. This also encompasses safety accessories used in combination with conventional needles.

©NCCLS. All rights reserved.

KUR-MAG-DE005093

(Patient) sample – A sample taken from the patient specimen and used to obtain information by means of a specific laboratory test.

(Patient) specimen – The discrete portion of a body fluid or tissue taken for examination, study, or analysis of one or more quantities or characteristics to determine the character of the whole.

Pre-evacuation – The creation of a vacuum (in a collection tube), induced by either the manufacturer or by the user immediately before a liquid specimen is taken.

Vascular access device (VAD) – A device inserted into a vein or artery to allow access to the circulatory system for the administration of intravenous fluids and/or medications.

Venipuncture – The puncture of a vein for surgical, or therapeutic, purposes, or for collecting blood specimens for analysis.

5 Factors That Affect Laboratory Values

Interpretation of laboratory data has assumed new importance and attracted increased attention with both more frequent testing and multiple testing. The increased use of laboratories predictably yields abnormal unsolicited data that requires interpretation and may lead to costly, unproductive, and unnecessary sequential testing. Even when an analytical procedure has been performed correctly and precisely, variables can affect the test result. Knowledge of these variables and standardization of laboratory testing procedures are essential for correct interpretation and optimal use of the data.

Major causes of "laboratory error" can be related to nonanalytical factors such as specimen collection, handling, and transport. Nonbiological factors—such as patient misidentification, and biological factors—such as patient posture and the time a specimen is drawn, all contribute to the total "laboratory error."

Physiological factors that influence results include age, activity, bed rest, food ingestion, alcohol ingestion, menstrual cycle, obesity, oral contraceptives, posture, pregnancy, race, gender, smoking, and time of day. All biological phenomena exhibit rhythms, with the circadian rhythm (the change in a 24-hour period) being the most important to laboratory testing. Many factors with documented effects on laboratory values have been published.[2-6]

6 Facilities

The venipuncture should be performed in a clean, quiet, and private environment. Reasonably soundproof rooms for pediatric patients should be considered.

The room should have facilities to allow the phlebotomist to wash his/her hands between patients. Washing with soap and running water is recommended; however, any standard detergent product acceptable to personnel may be used. In settings where water is not available, alcohol-based gels or liquids, hand-wipe towelettes, and cleansing foams can be used.[b]

6.1 Venipuncture Chairs

Venipuncture chairs should be designed for the maximum comfort and safety of the patient. Consideration should be given to the ergonomic comfort plus easy accessibility to the patient for the phlebotomist. Both armrests of the chairs should be adjustable so that the best venipuncture position for

[b] In the U.S., employees must wash their hands with soap and running water as soon as feasible thereafter.

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

each patient can be achieved. The chair should have a safety device to prevent patients from falling if feeling faint.

6.2 Hospital Area

A central venipuncture area should be designed to include the following features.

6.2.1 Central Desk

The central desk is a location for a telephone system used to handle emergency request calls, facilities for processing daily and future requests, and a paging system for contacting the phlebotomist who is collecting specimens outside of the central area.

6.2.2 Cart Area

The cart area is constructed to allow easy access to the supplies.

6.2.3 Storage Area

The storage area should be large enough to accommodate the necessary supplies.

6.2.4 Counter Space

Counter space should be adequate for efficient sorting and dispatching of specimens.

6.2.5 Sampling Time Recorder

The sampling time recorder (i.e., time stampers, bar codes, or information system) should be located for convenient time recording of venipuncture paperwork.

7 Supplies

The following supplies should be available at any location where venipunctures are performed routinely.

7.1 Utility Carts

Utility carts, designed to roll smoothly and silently over all types of surfaces, may be useful. The phlebotomist may also find it very useful to have a specially designed rack on the top shelf for storing supplies.

7.2 Blood Collecting Trays

Blood collecting trays or carts may be used. The trays should be lightweight and easy to handle with enough space and compartments for the various supplies that are needed.

7.3 Gloves

Latex, vinyl, or nitrile gloves provide barrier protection. Disposable latex, vinyl, or nitrile gloves are available from hospital suppliers.

©NCCLS. All rights reserved.

Some workers may develop dermatitis from wearing latex gloves for long periods of time. These workers should experiment with nitrile, polyethylene or other gloves of various composition or gloves without powdered lubricant or they may wear cotton gloves under latex or plastic gloves.

Severe hypersensitivity has been reported and cases of anaphylactic shock have occurred. In such hypersensitive individuals, latex gloves must be avoided.

7.4 Needles and Holders

Needles/holders should be compatible with the tubes selected for use. For more information on venous blood collection tubes and additives, refer to the most current edition of NCCLS document H1—*Evacuated Tubes and Additives for Blood Specimen Collection.*

Needles and winged blood collection sets are individually color-coded according to their respective gauge sizes. The gauge number indicates the size of the needle. A large gauge number indicates a small needle, while a small gauge number indicates a large needle. The sizes for venipuncture range from 19 through 23. Needles must always be sterile.

In order to prevent potential worker exposure, the needle safety feature should be activated immediately after specimen collection and discarded without disassembly into a sharps container.[c]

7.5 Sterile Syringes

In general, venipuncture using a needle and syringe should be avoided for safety reasons; however, it may be suitable under some circumstances to have sterile syringes of the appropriate size available.

7.6 Venous Blood Collection Tubes

Venous blood collection tubes are manufactured to withdraw a predetermined volume of blood. At present, venous blood collection tubes used in venipuncture are designated sterile. It is recommended that information regarding the venous blood collection tubes selected for general use be clearly displayed in venipuncture areas for easy reference. Similar information should also be made available to all personnel who collect blood. Instructions furnished in the package insert by the manufacturer of venous blood collection tubes and needles should be available. (See also the most current version of NCCLS document H1—*Evacuated Tubes and Additives for Blood Specimen Collection* for information on venous blood collection tubes.)

7.7 Tourniquets

Tourniquets or products for use as tourniquets should be available. Examples include:

- Single-use disposable tourniquet, preferably latex-free.
- Blood pressure cuff inflated to 40 mmHg.
- Rubber/fabric-type tourniquets with closure tape, plastic clip, buckle, or similar type of fastening.

Tourniquets must be discarded immediately when contaminated with blood or body fluids or must be discarded if contamination is suspected.

[c] In the U.S., refer to OSHA's Bloodborne Pathogens Standard (29 CFR 1910.1030), the safe practice of phlebotomy and blood tube holder use (CPL2-2.9 at XIII.D.5).

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

KUR-MAG-DE005096

7.8 Antiseptics

Antiseptics for skin preparation are necessary. The following are some examples:

- Isopropyl or ethyl alcohol: 70%
- 1 to 10% povidone-iodine as swab sticks or chlorhexidine gluconate for blood cultures[7] (see Section 8.8.2).
- Nonalcohol-based cleanser for blood alcohol specimens (e.g., chlorhexidine).

7.9 Gauze Pads

Small prepackaged gauze pads, (i.e., 2 x 2 in or 3 x 3 in [5.0 x 5.0 cm or 7.5 x 7.5 cm]) should be available. Cotton balls are not recommended because of the possibility of dislodging the platelet plug at the venipuncture site.

7.10 Puncture-Resistant Disposal Container

An approved puncture-resistant disposal container that is compliant with OSHA regulations must be available.

7.11 Ice

Ice or refrigerant should be available.

7.12 Adhesive Bandages

Adhesive bandages and/or gauze pads should be available. Hypoallergenic adhesives should also be available.

7.13 Warming Devices

Warming devices may be used to increase blood flow.

7.14 Test Reference Manual

A test manual which explains which tube is to be used, that also indicates minimum volume requirements, special handling, and precautions to be taken should be consulted.

8 Venipuncture Procedure

The venipuncture procedure is complex and requires both knowledge and skill (refer to Sections 8.1 to 8.17 for detailed information on the procedure). When drawing a blood specimen, the trained phlebotomist must:

Step 1. Prepare accession order.
Step 2. Approach and identify the patient.
Step 3. Verify patient's diet restrictions, as appropriate, and inquire if patient has a latex sensitivity. Select appropriate gloves and tourniquet.
Step 4. Assemble necessary supplies and select appropriate tubes according to test requests.
Step 5. Position the patient.
Step 6. Apply the tourniquet, ensure the patient's hand is closed, and select the vein site.
Step 7. Put on gloves.

©NCCLS. All rights reserved.

KUR-MAG-DE005097

Step 8. Cleanse the venipuncture site.
Step 9. Perform venipuncture; once blood flow begins, request patient to open hand.
Step 10. Use the correct order of draw.
Step 11. Release and remove the tourniquet.
Step 12. Place the gauze pad over the puncture site.
Step 13. Remove the needle, activating any safety feature according to manufacturers' instructions.
Step 14. Apply pressure to the site, making sure bleeding has stopped, and then bandage the arm.
Step 15. Label the tubes and record the time of collection.
Step 16. Chill the specimen (if required).
Step 17. Send properly labeled blood collection tubes to the appropriate laboratories.

8.1 Step 1: Prepare Accession Order

Each request for a blood specimen must be accessioned to identify all paperwork and supplies associated with each patient. An organized system will ensure prompt and accurate processing of the various forms required when performing a venipuncture and analyzing the results. Record all information on the test request form.

8.1.1 Information for Test Request Form

The following information should be included:

- The patient's name and age from identification plate
- An identification number
- The date and time the specimen is to be obtained
- An accessioning number
- The doctor's name
- The department or location for which the work is being done
- Other information as needed (e.g., special comments: intravenous site, sampling site if other than arm).

8.2 Step 2: Approach and Identify the Patient

The phlebotomist should identify himself or herself, establish a rapport, and gain the patient's confidence. Information given to the patient regarding the testing to be performed and specimen to be drawn must be in accordance with institutional policy. The phlebotomist must **NOT** perform blood collection against the patient's or guardian's consent. Instead, report the patient's objections to the physician's/nurse's station.

8.2.1 Identify Patient

Identification of the patient is crucial. The phlebotomist must ensure that the blood specimen is being drawn from the individual designated on the request form. The phlebotomist must not rely on a bed tag, or on charts or records placed on the bed, nearby tables, or equipment. The following steps are a suggested sequence for ensuring patient identification, regardless of the clinical setting.

8.2.2 Patient Who Is Conscious

The suggested sequence of steps for a patient who is conscious:

(1) Ask outpatients to give full name, address, identification number, and/or birth date.

(2) Compare this information with the information on the request form.

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

(3) Ask inpatients for the same information and compare this information with the information on the request form and the patient's identification bracelet, which must be attached to the patient.

(4) Report any discrepancy, however minor, to the responsible person in the area (as determined by institutional policy) and have the patient identified by name and identification number before drawing any specimen.

8.2.3 Patient Who Is Semiconscious, Comatose, or Sleeping

The phlebotomist must take special care when drawing blood from semiconscious, comatose, or sleeping patients to anticipate any unexpected movements or jerks either while introducing the needle, or while it is in place in the arm. Sleeping patients should be awakened before drawing blood. A gauze pad should be readily available and the tourniquet quickly released in the event the needle is violently removed or repositioned. If the needle accidentally goes much deeper into the arm, the phlebotomist must inform the doctor's/nurse's station. If unable to identify the patient, then contact the nurse or physician.

8.2.4 Patient Who Is Unconscious, Too Young, Mentally Incompetent, or Does Not Speak the Language of the Phlebotomist

In any of these circumstances, the phlebotomist should follow this suggested sequence of steps:

(1) Ask the nurse, a relative, or a friend to identify the patient by name, address, identification number, and/or birth date. If unable to identify the patient, then contact the nurse or physician.

(2) Compare these data with the information on the request form and the patient's identification bracelet, which must be attached to the patient.

(3) Report any discrepancy, however minor, to the responsible person in the area (as determined by institutional policy) and have the patient identified by name and identification number before drawing any specimen.

8.2.5 Procedure for Identifying Unidentified Emergency Patients

Identification standards established by the American Association of Blood Banks (AABB) provide clear guidelines for unidentified emergency patients.[8]

The patient must be positively identified when the blood specimen is collected. The unidentified emergency patient should be given some temporary but clear designation until positive identification can be made. For a person who cannot be identified immediately, it is necessary to:

- Assign a master identification number (temporary) to the patient in accord with institutional policy.
- Select the appropriate test request forms and record with master identification number.
- Complete the necessary labels either by hand or by computer and apply the labels to the test request forms and specimens.
- When a permanent identification number is assigned to the patient, make sure the temporary identification number is cross-referenced to the permanent number to ensure correct identification and correlation of patient and test result information.

©NCCLS. All rights reserved.

KUR-MAG-DE005099

In all cases, the name and permanent or temporary identification designation must be attached to the patient's body either by wristband or some similar device. Except in the case of isolation patients, bed labels must not be used in place of wristbands.

8.2.6 Physician Relationship

The physician has priority with the patient. The phlebotomist should not enter the room without permission while the physician or nurse is consulting with the patient. If the order is stat or the specimen is a "timed" specimen, the phlebotomist should request permission to draw the blood specimen.

8.3 Step 3: Verify Patient Diet Restrictions and Latex Sensitivity

Some tests require the patient to fast and/or eliminate certain foods from the diet before the blood is drawn. Time and diet restrictions vary according to the test. Such restrictions are necessary to ensure accurate test results.

The procedure for holding meals and notifying appropriate personnel that the patient has been drawn should be according to institutional policy.

Please refer to Section 7.3 for information regarding latex sensitivity to gloves and to Section 7.7 for tourniquets.

8.4 Step 4: Assemble Supplies

8.4.1 Supplies[d]

It is important that phlebotomy devices used reflect the most current local and regional safety regulations.[9]

Inspect all supplies for possible defects and applicable expiration dates. The following supplies should be available at any location where venipunctures are performed routinely:

- Blood collection tubes/blood culture bottles
- Needle
- Single-use tube/needle holder
- Syringe
- Syringe transfer device
- A tourniquet
- Alcohol prep pads
- 1 to 10% povidone-iodine pads, tincture iodine, or chlorhexidine compounds if blood culture is to be drawn
- Nonalcohol-based cleanser if blood alcohol is to be drawn
- Gauze pads, adhesive bandages, or tape (including hypoallergenic adhesives)
- Gloves
- Sharps container, consistent with OSHA regulations

8.4.2 Needles

The phlebotomist must select the appropriate needle gauge based on the physical characteristics of the vein, location of the vein, and the volume of blood to be drawn.

[d] In the U.S., OSHA mandates the use of engineering and work practice controls that eliminate occupational exposure or reduce it to the lowest feasible extent (e.g., safety needles, shielded needle devices, etc.).

 ©NCCLS. All rights reserved.

8.4.3 Syringes

The plunger must be moved within the barrel of the syringe to show syringe and needle patency and freedom of plunger movement.

8.4.4 System

The phlebotomist must select the appropriate blood collection system according to the patient's physical characteristics.

8.4.4.1 Venous Blood Collection Systems

When venous blood collection tubes are used, the phlebotomist must:

- Select the correct types and sizes of venous blood collection tubes. (Color-coded closures and labels make it easy to perform this step.)
- Apply a label to each of the necessary tubes and all test forms immediately after blood specimen has been drawn
- Refer to institutional policy.

All tubes should be labeled immediately *after* the blood specimen has been drawn. The completed label must be attached to the tube before leaving the side of the patient, and there must be a mechanism to identify the person who drew the blood.[8] If preprinted labels are not available, complete patient information can be handwritten on the tube label. This procedure eliminates the possibility of mixing up the blood specimens.

It is recommended that blood specimens be collected by venipuncture using a blood collection system that collects the blood directly into tubes. (For greater detail on venous blood collection tubes and additives, refer to the most current edition of NCCLS document H1—*Evacuated Tubes and Additives for Blood Specimen Collection.)* If the components are from different manufacturers, they should be checked to ensure compatibility.

8.4.4.2 Plastic Syringe

In general, the use of a syringe and needle should be avoided for safety reasons. If a syringe is used, a safety syringe shielded transfer device should be used to transfer blood to the appropriate venous blood collection tube.

8.4.4.3 Blood Collection Set

The blood collection set (i.e., winged blood collection set) is described in Section 9.2.

8.5 Step 5: Position Patient

8.5.1 Procedure for Seating Patient

(1) Ask the patient to be seated comfortably in a chair suitable for venipuncture. The chair should have arms to provide support and prevent falls if the patient loses consciousness. Chairs without arms do not provide adequate support for the arm or protect fainting patients from falls.

©NCCLS. All rights reserved.

(2) Have the patient position his/her arm on the slanting armrest and extend the arm to form a straight line from the shoulder to the wrist. The arm should be supported firmly by the armrest and should not be significantly bent at the elbow. A slight bend may be important in avoiding hyperextension of the arm.

8.5.2 Procedure for Having Patient Lie Down

(1) Ask the patient to lie on his/her back in a comfortable position.

(2) If additional support is needed, place a pillow under the arm from which the specimen is being drawn.

(3) Have the patient extend his/her arm to form a straight line from the shoulder to the wrist.

8.5.3 Foreign Objects in Mouth

No food or liquid, chewing gum, or thermometer should be in the patient's mouth at the time the specimen is drawn.

8.6 Step 6: Apply Tourniquet

A tourniquet is used to increase venous filling. This makes the veins more prominent and easier to enter. (See Section 7.7).

8.6.1 Precautions When Using a Tourniquet

Tourniquet application for preliminary vein selection should not exceed one minute as localized stasis with hemoconcentration and infiltration of blood into tissue can occur. This may result in erroneously high values for all protein-based analytes, packed cell volume, and other cellular elements. If the patient has a skin problem, the tourniquet should be applied over the patient's gown or a piece of gauze pad or paper tissue should be used so that the skin is not pinched.

8.6.2 Tourniquet Location

Wrap the tourniquet around the arm 3 to 4 inches (7.5 to 10.0 cm) above the venipuncture site.

8.6.3 Blood Pressure Cuff

If a blood pressure cuff is used as a tourniquet, inflate it to 40 mm Hg.

8.6.4 Ensure Patient's Hand Is Closed

The veins become more prominent and easier to enter when the patient forms a fist. There must not be vigorous hand exercise ("pumping"). Vigorous hand pumping can cause changes in the concentration of certain analytes in the blood.

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

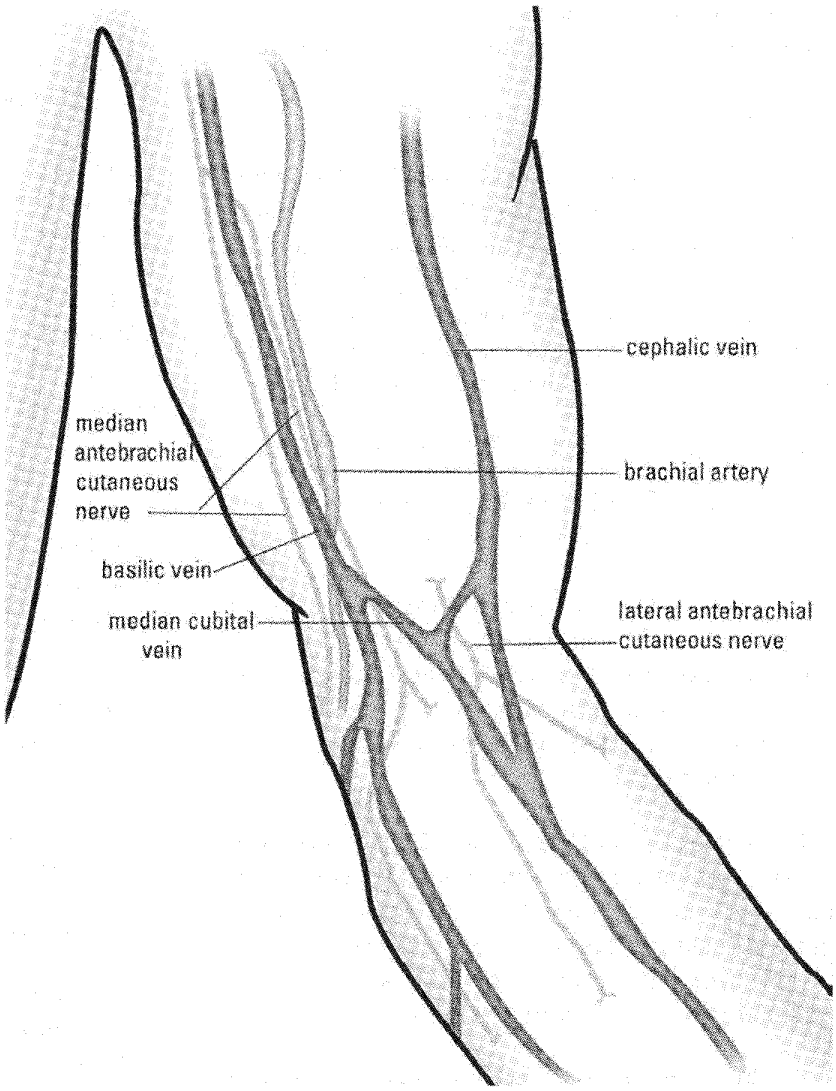


Figure 1. Superficial Veins of the Anterior Surface of the Upper Extremity (From Ernst DJ, Ernst C. Phlebotomy tools of the trade: Part 2—Surveying the antecubital area. *Home Healthcare Nurse.* 2002;20:402-403. Reprinted with permission from Lippincott Williams & Wilkins.)

8.6.5 Select Vein

Refer to Figure 1 for a description of the superficial veins of the anterior surface of the upper extremity.

8.6.5.1 Caution

It is important to select the vein carefully for blood collection because the veins also provide an avenue of entry for transfusion, infusion, and therapeutic agents. Because the brachial artery passes through the antecubital area, caution must be exercised to avoid the artery. If, during the procedure, arterial puncture is suspected, direct forceful pressure must be applied to the puncture site for a minimum of five minutes upon removal of the needle or until active bleeding has ceased. The nursing staff and physician are to be notified immediately thereafter.

©*NCCLS. All rights reserved.*

8.6.6 Preferred Veins

Arterial punctures should not be considered as an alternative to venipuncture for difficult draws. If this appears to be the only alternative, consult with the physician.

Although the larger and fuller median cubital and cephalic veins (see Figure 1) are used most frequently, veins on the back of the hand are also acceptable for venipuncture. Veins on the underside of the wrist must not be used.

Draws to the median cubital veins are preferred because they are typically closer to the surface of the skin, more stationary, less painful upon needle insertion, and less likely to injure nerves if needle placement is not accurate. Attempt to locate the median cubital vein on either arm before considering alternative veins. Due to the proximity of the basilic vein to the brachial artery and the median nerve, this vein should only be considered if no other vein is more prominent. Above all, phlebotomists should be aware of the potential for injury associated with each vein and select the vein that brings the greatest degree of confidence of being accessed successfully without risking nerve or arterial involvement. (See Figure 1.)

Alternative sites such as ankles or lower extremities must not be used without the permission of the physician because of the potential for significant medical complications (e.g., phlebitis, thrombosis, tissue necrosis, etc.)[10-12]

8.6.7 Factors in Site Selection

8.6.7.1 Extensive Scarring

Healed burn areas are to be avoided.

8.6.7.2 Mastectomy

A physician must be consulted before drawing blood from the side on which a mastectomy was performed because of the potential for complications due to lymphostasis.

8.6.7.3 Hematoma

Specimens collected through a hematoma area may cause erroneous test results. Phlebotomy must not be performed on any size hematoma. If another vein site is not available, the specimen is collected distal to the hematoma.

8.6.7.4 Intravenous Therapy

Preferably, specimens should not be collected from an arm with an intravenous site. (See Section 11.6).[13]

8.6.7.5 Cannula, Fistula, Vascular Graft

A cannulated arm is used only after consulting the attending physician.

8.6.8 Procedure for Vein Selection

8.6.8.1 Locating Veins

To locate veins, it is necessary to palpate and trace the path of veins several times with the index finger. Unlike veins, arteries pulsate, are more elastic, and have a thick wall. Thrombosed veins lack resilience,

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

feel cord-like, roll easily, and should not be used. A tourniquet must be used to aid in the selection of a vein site unless specific tests require tourniquets not be used (e.g., lactate). If a tourniquet must be applied for the preliminary vein selection, it should be released and reapplied after two minutes.

8.7 Step 7: Put on Gloves

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.

8.8 Step 8: Cleanse Venipuncture Site

The puncture site must be cleansed to prevent microbiological contamination of either the patient or the specimen.

8.8.1 Cleansing Method for Venipuncture

(1) Use a gauze pad with 70% isopropyl alcohol solution, or a commercially prepared alcohol pad.

(2) Cleanse the site with a circular motion from the center to the periphery.

(3) *Allow the area to air dry* to prevent hemolysis of the specimen and to prevent the patient from experiencing a burning sensation when the venipuncture is performed.

8.8.2 For Blood Culture Collection

For blood cultures, it is necessary to carefully disinfect the venipuncture site. Chlorhexidine gluconate is recommended for infants two months and older and patients with iodine sensitivity. Cleanse the site with 70% alcohol, then swab concentrically, starting at the middle of the site with a 1 to 10% povidone-iodine solution (0.1 to 1% available iodine) or chlorhexidine gluconate. Allow the site to air dry, then remove the iodine or chlorhexidine from the skin with alcohol.[8]

When specimens are obtained for blood cultures, disinfect the culture bottle stopper according to the manufacturer's instructions.

8.8.3 Touching the Site After Cleansing

If the venipuncture proves difficult and the vein must be touched again to draw blood, the site should be cleansed again.

8.9 Step 9: Perform Venipuncture

8.9.1 Venipuncture Procedure When Venous Blood Collection Tubes Are Used

There are several different blood collection systems available that collect blood samples using different principles. For example, there are evacuated tube systems and systems that have a flexible/dual collection technique that employ either a vacuum—user evacuates the tube immediately prior to use referred to as pre-evacuation—or aspiration principle of collection. For the proper venipuncture technique using the blood collection system selected refer to the manufacturers' instructions for use.

(1) If pre-evacuation is required, and the blood collection tubes are not evacuated by the manufacturer, evacuate the tubes immediately prior to use according to the manufacturer's instructions.

KUR-MAG-DE005105

(2) If not preassembled by the manufacturer, thread the appropriate needle into the holder until it is secure.

(3) When drawing blood for cultures, wipe the stopper with a suitable antiseptic solution. Make certain the stopper is dry before performing the venipuncture.

(4) Make sure the patient's arm or other venipuncture site is in a downward position to prevent reflux or "backflow."

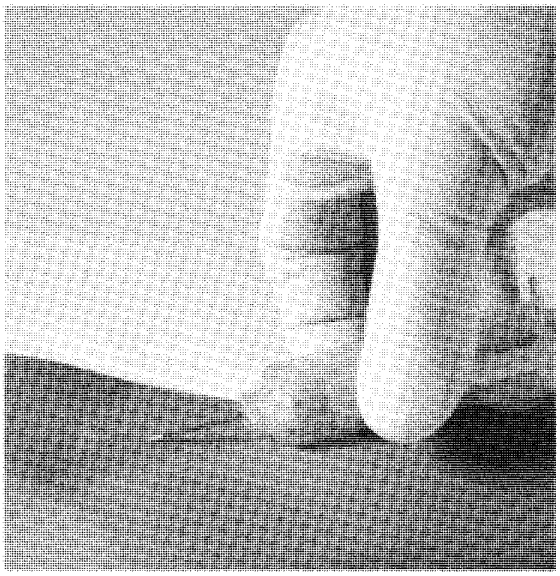


Figure 2. Proper Angle of Insertion (Figure contributed by the Center for Phlebotomy Education, Inc.)

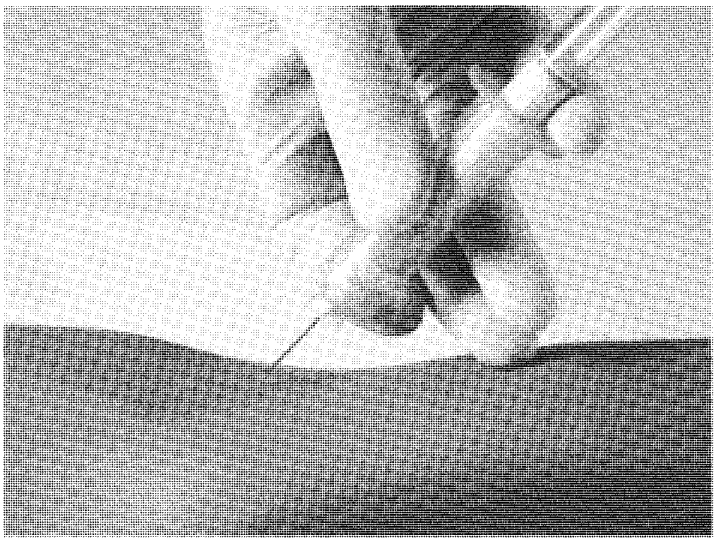


Figure 3. Improper Angle of Insertion (Figure contributed by the Center for Phlebotomy Education, Inc.)

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

(5) Prior to venipuncture, if required, assemble the tube to the needle/holder according to the manufacturer's instructions.

(6) Hold the patient's arm firmly distal to the intended puncture site. The phlebotomist's thumb should be used to draw the skin taut. This anchors the vein. The thumb should be 1 to 2 inches (2.5 to 5.0 cm) below the venipuncture site.

(7) To prepare the patient, inform him or her that the venipuncture is about to occur. **NOTE:** From this point on, be prepared to react to a sudden and unexpected loss of consciousness.

(8) With the bevel up, puncture the vein with the needle at an angle of insertion of 30 degrees or less (See Figure 2). Keeping the needle as stable as possible in the vein, push/connect the first tube onto the needle. Maintain the tube below the site when the needle is in the vein.

(9) Release the tourniquet as soon as possible after the blood begins to flow. Do not change the position of the tube until it is removed from the needle. During the collection, do not allow the contents of the tube to contact the closure. Movement of the blood back and forth in the tube can cause reflux into the venous system and possible adverse patient reaction.

(10) Allow the tube to fill until the vacuum is exhausted and blood flow ceases. For tubes that contain additives, this will ensure there is a correct ratio of blood to additive.

NOTE: For systems that collect blood using an aspiration principle of collection rather than a vacuum, gently pull back on the piston rod until the piston reaches the base of the tube. This will ensure there is a correct ratio of blood to additive.

(11) When the blood ceases to flow, remove/disconnect the tube from the needle/holder. The sleeve re-covers the needlepoint that pierces the tube closure, stopping blood flow until the next tube is inserted/connected to the needle/holder. To obtain additional specimens, insert/connect the next tube to the needle/holder and repeat the collection procedure. Always remove the last tube collected from the needle/holder prior to withdrawing the needle from the vein. If only one tube is collected this must be removed prior to withdrawing the needle from the vein.

(12) Immediately after drawing each tube that contains an additive mix the blood gently and thoroughly by inverting the tube five to ten times. To avoid hemolysis, do not mix vigorously. For tubes that have been drawn using an aspiration principle, lock the piston into the base of the tube and snap off the piston rod after mixing.

8.9.2 Venipuncture Procedure Using Needle and Syringe

In general, venipuncture using a needle and syringe should be avoided for safety reasons. If conditions require a syringe draw, the following procedure is recommended:

(1) Assemble the needle and syringe.

(2) Hold the patient's arm firmly distal to the intended puncture site. The phlebotomist's thumb should be used to draw the skin taut. This anchors the vein. The phlebotomist's thumb should be 1 or 2 inches (2.5 cm or 5.0 cm) below the venipuncture site.

(3) Prepare the patient by informing him or her that the venipuncture is about to occur.

(4) With the bevel up, puncture the vein with the needle at an angle of insertion of 30 degrees or less (see Figure 2).

©NCCLS. All rights reserved.

(5) Keeping the needle as stable as possible in the vein, slowly withdraw the desired amount of blood.

(6) Release the tourniquet as soon as possible, after the blood begins to flow.

8.9.3 Fill the Tubes If Syringe and Needle Are Used

Syringe method of drawing venous blood is not recommended since it is much safer and easier to use a closed, venous blood collection tube system. If it is necessary to use a syringe, proceed with the following recommendations to transfer the blood from a syringe to a blood collection tube:

- Use the same "order of draw" as for a venous blood collection tube system (see Section 8.10.2).
- Rubber stoppers should not be removed from venous blood collection tubes to transfer blood to multiple tubes.
- 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.
- The stopper is pierced with the needle and the tube is allowed to fill (without applying any pressure to the plunger) until flow ceases. This technique helps to maintain the correct ratio of blood to additive if an additive tube is being used.
- Mix additive tubes by inversion.

8.9.4 Blood Specimen That Cannot Be Obtained

When a blood specimen cannot be obtained, it may be necessary to:

- 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 never be attempted in an effort to access the basilic vein, since nerves and the brachial artery are in close proximity.
- Try another tube to ensure the tube selected is not defective.
- 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.

8.9.5 Ensure Patient's Hand Is Open

Opening the patient's hand reduces the amount of venous pressure as muscles relax. The patient must not be allowed to pump the hand.

An NCCLS global consensus standard. ©NCCLS. All rights reserved.

8.10 Step 10: Order of Draw

8.10.1 Additive Tubes

Gel separator tubes with clotting activators or anticoagulants are classified as additive tubes.[14] (For further information, refer to the most current edition of NCCLS document H18— *Procedures for the Handling and Processing of Blood Specimens*). These tubes should be drawn after the coagulation tube (blue stopper) and before other additive tubes (green, lavender, gray). All additive tubes should have a complete draw (see Section 8.9.1[10]).

8.10.2 Glass and Plastic Venous Blood Collection Tubes

The following order-of-draw is recommended when drawing multiple specimens for clinical laboratory testing during a single venipuncture. Its purpose is to avoid possible test result error due to cross contamination from tube additives.[15] This procedure should be followed for both glass and plastic venous blood collection tubes.

(1) Blood culture tube
(2) Coagulation tube (e.g., blue closure)
(3) Serum tube with or without clot activator, with or without gel (e.g., red closure)
(4) Heparin tube with or without gel plasma separator (e.g., green closure)
(5) EDTA (e.g., lavender closure)
(6) Glycolytic inhibitor (e.g., gray closure)

NOTE: 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 non-additive serum tubes may be drawn before the coagulation tube.

NOTE: When using a winged blood collection set for venipuncture and a coagulation tube is the first tube to be drawn, a discard tube should be drawn first. The discard tube must be used to fill the blood collection tubing dead space and to assure maintenance of the proper anticoagulant/blood ratio and need not be completely filled. The discard tube should be a nonadditive or a coagulation tube.

8.10.3 Coagulation Testing

Studies have shown that the PT (INR) and APTT results are not affected if tested on the first tube drawn.[16-18] Since it is not known whether other coagulation testing is affected, it may be advisable to draw a second tube for other coagulation assays. When a syringe system is used and a large specimen is taken, part of the blood from the second syringe should be used for the coagulation specimen. In the case of any unexplained abnormal coagulation test result, a new specimen should be obtained and the test repeated. If heparin contamination is suspected, the test should be repeated after the specimen is treated with a method that removes or neutralizes heparin. For more detailed descriptions of collection for coagulation testing, see the most current edition of NCCLS document H21—*Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays*.

8.11 Step 11: Release the Tourniquet

Release the tourniquet as soon as possible after the blood begins to flow.

8.12 Step 12: Place the Gauze Pad

A clean gauze pad should be placed lightly over the venipuncture site. Cotton balls are not recommended because of the possibility of dislodging the platelet plug at the venipuncture site.

KUR-MAG-DE005109

8.13 Step 13: Remove and Dispose of the Needle

Remove the needle and activate the safety mechanism according to the device manufacturer's instructions. Safely dispose of the unit into an easily accessible sharps container, consistent with OSHA regulations. 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. Phlebotomists should anticipate a loss of consciousness and be prepared to react according to institutional policy. The use of ammonia inhalants may be associated with untoward effects and is not recommended. (See Section 11.8.1).

8.14 Step 14: Bandage the Arm

8.14.1 Normal Conditions

Under normal conditions, the phlebotomist should:

(1) Place the gauze pad over the site, continuing mild pressure.

(2) Check that bleeding has ceased, observe for hematoma, and apply an adhesive or gauze bandage over the venipuncture site. It is recommended that hypoallergenic adhesives be available.

(3) Tell patient to leave the bandage on for at least 15 minutes.

8.14.2 Continued Bleeding

The phlebotomist should watch for excessive bleeding. If a hematoma develops or bleeding persists longer than five minutes, a nurse should be alerted so that the attending physician can be notified. Pressure, applied with a gauze pad, must continue at the site as long as necessary to stop the bleeding. Wrap a gauze bandage tightly around the arm to keep the pad in place and tell the patient to leave the bandage on the site for at least 15 minutes.

8.15 Step 15: Label Blood Collection Tubes and Record Time of Collection

The patient and the patient's blood specimen must be positively identified at the time of collection. Blood specimens must be obtained in tubes identified with a firmly attached label bearing at least the following:

- The patient's first and last names
- An identification number
- The date
- The time (as required, e.g., therapeutic drug monitoring)
- The identification of the person collecting specimen.

The completed label must be attached to the tube before leaving the side of the patient, and there must be a mechanism to identify the person who drew the blood.[8] Alternatively, the manufacturer's tube label can be inscribed with the patient's complete information. Blood bank specimens must be labeled according to the standards set by the American Association of Blood Banks (AABB).

If an encoded (bar code) label is used, attach the label according to established institutional policy.

A permanent record is needed by the physician who must know exactly when each specimen was drawn to correlate the results with any change in the patient's condition. The laboratory also must document the

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

time when the specimen was collected. If unable to obtain specimens, a record of the reasons and initials of the venipuncturist are necessary.

8.16 Step 16: Chill the Specimen (This is done only for certain specimens.)

Some tests require that blood specimens be cooled immediately following the venipuncture to slow down metabolic processes which may alter some test results. For more information on blood specimen handling and processing, see the most current edition of NCCLS document H18—*Procedures for the Handling and Processing of Blood Specimens*.

Examples of tests requiring chilling the specimen are:[19]

- Gastrin
- Ammonia
- Lactic acid
- Catecholamines
- pH/blood gas
- Parathyroid hormone (PTH).

8.17 Step 17: Send Blood Collection Tubes to the Proper Laboratories

Appropriately labeled blood collection tubes should be sent to appropriate laboratories designated to perform the required testing procedures. (See Section 8.15 for recommendations for labeling of tubes.)

9 Venipuncture in Children and Difficult Collections

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. For information on skin puncture blood collection, refer to the most current edition of NCCLS document H4—*Procedures and Devices for the Collection of Diagnostic Blood Specimens by Skin Puncture.*

9.1 Procedure

Except where indicated below, the procedure for venipuncture of adults as described in Section 8 should be followed for pediatric venipuncture.

9.2 Equipment

Venipunctures should be performed using equipment that can help to reduce the stress exerted on a vein to prevent vascular collapse. Examples include a venous blood collection system with a 22- to 23-gauge needle, or a 22- to 23-gauge (winged) blood collection set with attached tubing and venous blood collection tube holder. For pediatric patients, through the age of 16, larger gauge needles may be appropriate.

10 Additional Considerations

10.1 Monitoring Blood Volume Collected

It is recommended that a mechanism be in place to monitor the amount of blood drawn for pediatric and critically ill patients to avoid phlebotomy-induced anemia.

©NCCLS. All rights reserved.

10.2 Hematoma

To prevent a hematoma when performing a venipuncture, the phlebotomist should:

- Make sure the needle fully penetrates the uppermost wall of the vein (partial penetration may allow blood to leak into the soft tissue surrounding the vein by way of the needle bevel).
- Remove the tourniquet before removing the needle.
- Use the major superficial veins.
- Hold the venous blood collection assembly still while collecting the specimen.
- Before bandaging, ensure that the puncture to the vein has sealed by observing for hematoma formation after pressure is released.
- Apply a small amount of pressure to the area with the gauze pad when bandaging the arm.

10.3 Hemolysis

To prevent hemolysis when performing a venipuncture, the phlebotomist should:

- After cleansing, allow the venipuncture site to air dry.
- Never draw blood through a hematoma.
- If using a syringe, make sure the needle is fitted securely on a syringe to avoid frothing.
- When using a syringe and needle, avoid drawing the plunger back too forcibly.
- Gently invert the blood collection tube to mix additive specimens as recommended by the manufacturer.

11 Special Situations

11.1 Timed Intervals

Some specimens must be drawn at timed intervals because of medications, fasting requirements, and/or biological variations (circadian rhythm). It is important that collection of specimens for timed tests be obtained at the precisely specified interval. Directions should be given to the venipuncture team to obtain these specimens accurately.

11.1.1 Examples of Tests Requiring Timed Specimens

- Tolerance tests (e.g., two-hour postprandial glucose and three-hour glucose tolerance test), cortisol
- Therapy monitoring (e.g., prothrombin time, APTT, digoxin, and other drugs)

11.1.2 Documentation

For therapeutic drug monitoring, the dose of the medication and the time of the last dose given, as well as the time of the specimen collection, should be recorded accurately on the request slip.

11.2 Specific Collection Techniques

11.2.1 Blood Alcohol

When drawing a blood specimen for alcohol testing, a nonalcohol-based cleanser should be used to cleanse the venipuncture site (e.g., soap). (See the most current edition of NCCLS document T/DM6—*Blood Alcohol Testing in the Clinical Laboratory* for further information.)

An NCCLS global consensus standard. ©NCCLS. All rights reserved.

KUR-MAG-DE005112

11.2.2 Legal Specimens

Appropriate chain-of-custody procedure should be followed. (See NCCLS document T/DM6—*Blood Alcohol Testing in the Clinical Laboratory*.)

11.2.3 Blood Culture Specimens

There are time and temperature requirements to be followed in collection, transport and storage of specimens for blood culture. In addition, there are variations in the volume of blood needed for culture. In general, adult blood cultures require 10 to 20 mL/set and infant blood cultures are done on 1 to 2 mL/set.[7] Please refer to the manufacturer's instructions for specific blood volume requirements. These requirements may vary considerably depending on the device.

11.2.4 Trace Elements

For collection of blood for trace elements testing (e.g., zinc) special, metal-free collection containers should be used. (See the most current edition of NCCLS document C38—*Control of Preanalytical Variation in Trace Element Determinations*, for more information.)

11.2.5 Immunohematology Specimens

Gel separator tubes must not be used for immunohematology specimens.[8] It is important to refer to manufacturer's package inserts for collection tubes and for test methods for other possible gel tube application limitations.

11.3 Indwelling Lines or VADs

A line is a piece of tubing inserted into a patient's vein or artery for administering fluids and medications, monitoring pressures, and obtaining blood samples for diagnostic tests. Without complete, thorough and documented training, it is not recommended that phlebotomists draw blood from indwelling cardiovascular (arterial, central venous) or umbilical lines. Institutional policy should be followed.

NOTE: Under certain circumstances, blood specimens for clinical laboratory testing may be drawn from a vascular access device (VAD) using a blood collection system or a syringe. When obtaining a blood specimen from a VAD, the components of the blood collection system (VAD, connecting device, syringe, needle, and collection device) should be checked to ensure compatibility to avoid air leaks, which may cause hemolysis and incorrect draw volumes. Collection of the blood through lines that have been previously flushed with heparin should be avoided, if possible. If the blood must be drawn through a VAD, possible heparin contamination and specimen dilution should be considered. The line should be flushed with 5 mL of saline, and the first 5 mL of blood or six dead space volumes of the VAD discarded.

11.3.1 Potential Error

Obtaining blood specimens from indwelling lines or VADs may be a problem and a potential source of test error because of incomplete flushing of collection site resulting in contamination and/or dilution of the specimen contributing to inaccurate results.[20-22]

11.3.2 Flushing Lines

Because it is normal practice to flush lines with a solution to reduce the risk of thrombosis, lines must be cleared of this fluid before blood specimens can be drawn for diagnostic testing. An adequate amount of blood must be withdrawn from the line and discarded before drawing a specimen to ensure that the actual specimen is not diluted or contaminated with the flush solution. Discard volume is dependent on the dead

©*NCCLS. All rights reserved.*

KUR-MAG-DE005113

space volume of the particular line. Discarding two times the dead-space volume is recommended for noncoagulation testing, and 5 mL or six times the dead-space volume for coagulation tests.[20,23-25] (For additional information, please refer to the most current edition of NCCLS document H21—*Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays.*) See the "NOTE" in Section 11.3 for specific recommendations for coagulation testing specimens with line draws.

11.4 Heparin or Saline Locks

An indwelling winged infusion set can be successfully left in a vein from 36 to 48 hours for intravenous administration of medication or as a vein source to obtain a blood specimen. This procedure, known as a "heparin or saline lock," has become more common in hospitals to "save" veins for therapeutic use and also to cause less trauma to the patient. With this system, it is not necessary to keep the vein open with a continuous intravenous infusion, thus allowing the patient more comfort and mobility.

11.5 Fistula

A fistula is an artificial shunt connection done by a surgical procedure to fuse the vein and artery together. It is used for dialysis only.

An arm with a fistula should not be used routinely for blood drawing. When possible, specimens should be drawn from the opposite arm. Care must be taken of the fistula, as it is permanent.

11.6 Intravenous Fluids

Skin puncture is recommended when venous access is not readily available. (See the most current edition of NCCLS document H4—*Procedures and Devices for the Collection of Diagnostic Blood Specimens by Skin Puncture* for more information.)

When an intravenous fluid (including transfused blood products) is being administered in a patient's arm, blood should not be drawn from that arm if at all possible. Test results from this blood may be erroneous and thus misleading to the physician.

Satisfactory specimens may be drawn distal to the intravenous infusion site. If this is not possible, a specimen may be obtained from a proximal site.[13,26] However, it has been shown that blood drawn proximal to the intravenous site can be contaminated with the fluid being administered. Facilities should establish their own policy. The collection procedure is as follows:

(1) Ask the responsible caregiver for the intravenous infusion to be turned off for at least two minutes before venipuncture. Care should be taken to ensure that the flow has been completely discontinued.

(2) Apply the tourniquet. When drawing distal to the intravenous infusion site, apply the tourniquet between the intravenous and the intended venipuncture site.

(3) Perform the venipuncture.

It must be documented that the venipuncture was performed proximal or distal to an infusion site and from which arm.

An NCCLS global consensus standard. ©NCCLS. All rights reserved.

KUR-MAG-DE005114

11.7 Isolation

Patients are isolated to prevent disease from spreading to other patients, visitors, or employees.[27] Some hospitals may also provide a different, protective isolation for patients who could be placed at increased risk from outside contamination.

11.7.1 Isolation Systems

Each hospital determines the system which best provides for their particular mix of patients, visitors, and employees. In most cases, a color-coded card placed just outside the patient's room describes the type of isolation and the precautions to be taken by those entering the room. It is important to understand and use the appropriate precautions.

11.7.1.1 Types of Isolation

Recent guidance emphasizes two tiers of infection control precautions[27]:

- standard, to be used for all patients, and
- transmission-based.

There are three types of transmission based isolation precautions[23]:

- airborne,
- droplet, and
- contact.

Hospitals have protocols for isolation procedures available through their infection control practitioner, infection control committee, or hospital epidemiologist. The example given in Sections 11.7.1.2 through 11.7.2 is an example of such a protocol. Some hospitals may provide for disinfection, dedication or disposal of equipment used in isolation rooms.

11.7.1.2 Clean Area

Gowns, gloves, masks, etc., are kept in a clean area. In some hospitals, a stand containing these supplies is kept outside the room. The new modern hospital often has an anteroom which serves as the "clean area." Here, the person entering the room can gown and apply other protective barriers as necessary before entering the patient's room. Doctors' suit coats, jackets, and other apparel are left here.

11.7.2 Isolation Room

11.7.2.1 Procedures to Follow Before Entering the Isolation Room

(1) Read the isolation sign on the door. It will explain the type of isolation, protective clothing to be worn, and the procedure to follow. Follow these instructions carefully.

(2) Check the orders and assemble an adequate amount of necessary equipment for the patient.

NOTE: Any supplies taken into the room must be left there, or discarded.

(3) Never take trays into the isolation room.

©NCCLS. All rights reserved.

11.7.2.2 Procedures to Follow in an Isolation Room

(1) Place paper towels on the table and place the equipment on one or two towels that have been spread open.

(2) Wash hands.

(3) Put on gloves.

(4) Obtain blood specimens in the usual manner, avoiding any unnecessary contact with the patient and bed.

(5) After mixing, place the filled tubes on a clean paper towel.

(6) Dispose of blood collection assembly into an easily accessible, approved puncture resistant disposal container, consistent with OSHA regulations, according to institutional policy.

NOTE: Recapping of needle is not recommended. (See the most current edition of NCCLS publication M29—*Protection of Laboratory Workers from Occupationally Acquired Infections*.)

(7) Dispose of the tourniquet in the proper container.

(8) Remove gown and gloves and dispose of them in the proper container.

(9) Wash hands.

(10) Turn off the faucet with a clean paper towel so that hands are not contaminated.

(11) Pick up the tubes from the paper towel and clean the outside of the tube with 1:10 dilution of bleach. Place tubes in a secondary container, which will contain the specimen if the primary container breaks or leaks in transit to the laboratory. A plastic bag with a sealable, leakproof closure can be used.

(12) If blood smears were made, place the smears on two clean paper towels. When ready to leave, wrap the smears and tubes in the top paper towel and discard the bottom paper towel and place in a secondary container.

11.7.3 Exposure

The phlebotomist must immediately report an accidental needlestick or contamination of a break in the skin by blood or excreta to a supervisor, and follow institutional guidelines. (See also NCCLS document M29—*Protection of Laboratory Workers from Occupationally Acquired Infections*.)

11.8 Emergency Situations

At least one member of available on-site healthcare personnel should have extensive first aid training, including special training in cardiopulmonary resuscitation, so that medical attention can be given to a needy patient while the physician on call is en route. This individual should be identified to phlebotomists. Emergency numbers should be posted in phlebotomy drawing areas.

11.8.1 Syncope (Fainting) or Unexpected Nonresponsiveness

The procedure for dealing with a patient who has fainted or is unexpectedly nonresponsive is to:

 An NCCLS global consensus standard. ©NCCLS. All rights reserved.

KUR-MAG-DE005116

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

New Closed IV Catheter System

A. VAN ZUNDERT

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

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

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

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

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

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

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

A. van Zundert, M.D., Ph.D., F.R.C.A., Catharina Hospital – Brabant Medical School, Eindhoven, The Netherlands.
Correspondence address : Prof. dr. A. van Zundert, Department of Anesthesiology, ICU & Pain Therapy, Catharina Hospital – Brabant Medical School, Michelangelolaan 2, Eindhoven, 5623 EJ, The Netherlands. E-mail : zundert@jae.nl.

KUR-MAG-DE003906

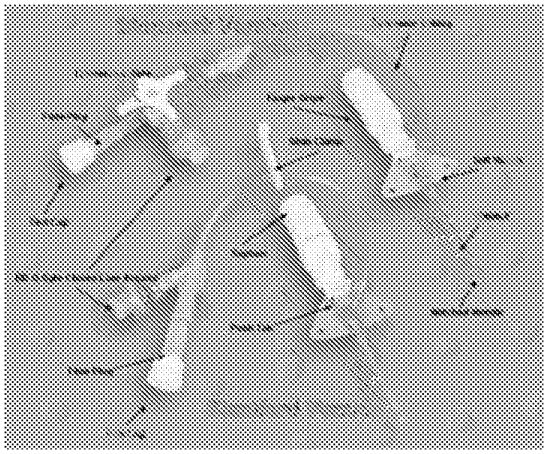


Fig. 1. — The new integrated completely closed IV catheter system (BD Nexiva™). Shown are two versions : the top one has a three-way valve to which the Q-Syte™ is attached ; the bottom one, with the Q-Syte™ closed Luer Lok access. Both devives have a flow plug for venting out the air during insertion.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

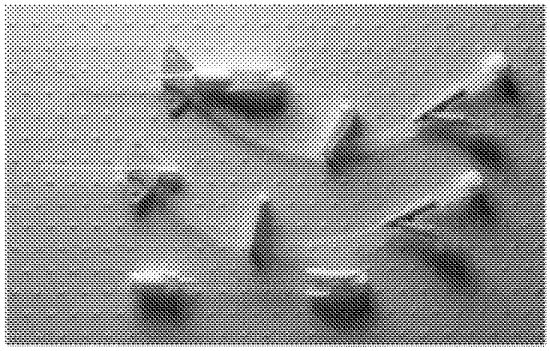


Fig. 2. — Non-activated (top) and activated (bottom) versions of the BD Nexiva™.
The white portion (catheter body) is used for gripping the device. Once inserted into the vein, the catheter body is withdrawn completely and the needle is automatically sheathed (see lower picture), thus protecting from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

Table 1

Characteristics of IV needles

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

Table 2

Advantages of new IV cannula over previous IV catheters

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

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

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

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

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

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

KUR-MAG-DE003907

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.

References

1. Peters J. L., Fisher C., Mehtar S., *Intravenous stopcocks and injection ports (letter)*, Lancet, **II**, 701-702, 1980.
2. Oberhammer E. P., *Contamination of injection ports on intravenous cannulae (letter)*, Lancet, **II**, 1027-1028, 1980.
3. Pilsworth R., *Risk from cannulae used to maintain intravenous access* (letter), Br. Med. J., **282**, 222-223, 1981.
4. Gaukroger P. B., Roberts J. G., Manners T. A., *Infusion thrombophlebitis : A prospective comparison of 645 vialon and teflon cannulae in anaesthetic and postoperative use*, Anesth. Intens. Care, **16**, 265-271, 1988.
5. Jaquot C., Fauvage B., Bru J. P., Croize J., Calop J., *Effect of type of material on thrombophlebitis risk with peripheral venous catheters*, Ann. Fr. Anaesth. Reanim., **8**, 3-7, 1989.
6. McKee J. M., Shell J. A., Warren T. A., Campbell V. P., *Complications of intravenous therapy : A randomised prospective study – vialon vs teflon*, J. Intraven. Nurs., **129**, 288-295, 1989.

KUR-MAG-DE003908

Bibliographic data: DE10243129 (A1) — 2004-04-01

Multiple compartment blood collecting device for collecting blood from small animals such as dogs and cats comprises a cannula, blood receiving vessels and tubes connected to the rear end of the cannula

Inventor(s): WEIS GERMAN [DE] ± (WEIS, GERMAN)

Applicant(s): RITTER GMBH [DE] ± (RITTER GMBH)

Classification: **- international:** ***A61B5/155; A61D1/00;*** (IPC1-7): A61B5/15; A61J1/20

- cooperative: A61B5/15003 (EP); A61B5/150351 (EP); A61B5/150389 (EP); A61B5/150503 (EP); A61B5/15074 (EP); A61B5/154 (EP); A61D1/00 (EP)

Application number: DE20021043129 20020918

Priority number(s): DE20021043129 20020918

Abstract of DE10243129 (A1)

Multiple compartment blood collecting device comprises a cannula (1), blood receiving vessels (7, 8, 9), and tubes (2, 3, 4, 5, 6) connected to the rear end of the cannula with their branches connected to the blood receiving vessels. Preferred Features: Each blood receiving vessel is closed by a semi-permeable stopper (10) through which air can pass and the blood collected can not. The stopper are made from an air-permeable stopper body and a semi-permeable membrane formed on its inner side. Each branch of the tube has a hollow needle penetrating the stopper.

Patent Translate
Powered by EPO and Google

Notice

This translation is machine-generated. It cannot be guaranteed that it is intelligible, accurate, complete, reliable or fit for specific purposes. Critical decisions, such as commercially relevant or financial decisions, should not be based on machine-translation output.

DESCRIPTION DE10243129A1

[0001]

13 The invention relates to a multiple blood collection device for use in smaller animals such as cats, dogs and the like, or for similar applications where only limited amounts of blood are available, for example in small children.

[0002]

19 Multiple blood sampling, i.e. filling several tubes with blood, is required for various examination methods. For example, one tube of untreated blood is required for standard analyses. For blood count and cell tests as well as for HbA1 you need a collection tube coated with EDTA, for coagulation tests you need a tube that has been mixed with citrate, etc.

[0003]

26 Known multiple blood collection systems are designed for adult humans.

27 They consist of a cannula that is inserted into the vein once and then several blood collection tubes can be coupled to the cannula in order to be filled. In the case of animals, a simple cannula, open at the back, is usually used, to which the blood collection tubes, which are also open and to be filled, are simply held out until they are sufficiently filled.

[0004]

34 These known systems are not very suitable for smaller animals such as cats, for example, where only a limited amount of blood is available.

36 If the front leg of the cat is tied off to take blood, the blood accumulates and shoots out violently when a cannula is inserted due to the pressure that has built up. When using an open system,

blood is often splattered, which is then lost and can also occur when the tubes are changed blood are lost. In addition, the first tube fills up very quickly and possibly overflows, and there is then no longer enough blood for a second and possibly a third tube.

[0005]

44 The object of the invention is to create a multiple blood sampling device that is particularly suitable for applications where only a limited amount of blood is available.

[0006]

49 According to the invention, this object is achieved by the multiple blood sampling device specified in claim 1 .

51 Advantageous configurations of the invention are the subject matter of the dependent claims.

[0007]

55 The multiple blood collection device according to the invention embodies a closed or quasi-closed system which avoids the above-mentioned problems of the conventional systems which are unsuitable for the purposes under discussion here.

58 In the blood collection device according to the invention, a cannula is connected via a branching hose to a plurality of blood collection tubes, which are filled at the same time.

60 Even if there is a strong flow of blood at the beginning, this is then distributed evenly over the connected tubes, so that the required number of sufficiently filled tubes are available without loss of blood drawn.

[0008]

66 The device according to the invention can be realized in several versions, for example with two tubes or with three tubes, in order to take account of the cases in which only two tubes of blood or in which three tubes of blood are required.

69 It is also possible, for example with a device comprising three tubes, to take blood from only two tubes by pinching off the hose branch to the third tube.

[0009]

74 Further details and advantageous refinements of the invention are described in more detail below using an exemplary embodiment with reference to the attached drawing.

[0010]

79 The drawing shows a schematic representation of a multiple blood sampling device according to

the invention.

[0011]

84 The multiple blood sampling device according to the invention shown in the drawing has a cannula 1, which is shown only schematically.

86 Its rear end is connected to three blood collection vessels 7 , 8 , 9 via a hose 2 which branches at a junction 3 into three branch hoses 4 , 5 , 6 in the exemplary embodiment.

[0012]

91 The blood collection vessels 7 , 8 , 9 can each be closed by a semi-permeable stopper 10 .

92 Such plugs are known per se.

93 They are permeable to air, so if blood enters the tube, air can escape through the stopper, but they seal up on contact with liquid so that blood cannot escape.

95 Such plugs can also consist of an air-permeable plug body and a semi-permeable membrane formed on the inside thereof.

97 The ends of the branch hoses can be connected to hollow needles that are inserted into the respective stopper 10 .

99 Since such stoppers are also self-sealing, each blood withdrawal vessel can be removed from the hollow needle after it has been filled, with the stopper closing itself automatically.

[0013]

104 As an alternative to this, each blood collection vessel can also be provided with a cap which has an air outlet opening.

106 This can be closed, for example with a cap, or it can be designed as a small piece of tubing that can be closed with a clamp.

[0014]

111 During use, the three blood collection vessels fill evenly after the cannula has been inserted into the vein.

113 If, in individual cases, only two of the three blood collection vessels are to be filled, the branch hose of the third vessel can be pinched off with a clamp, or where caps with a closable ventilation opening are used for the blood collection vessels, the ventilation opening can be closed, with the result that vessel also no blood enters.

117 By closing the ventilation opening, the further inflow of blood can also be terminated when the desired filling quantity is reached in one vessel, while other vessels continue to be filled.

[0015]

122 It is also possible to design the branch in such a way that access to a blood collection vessel that is not required can be blocked there.

[0016]

127 For frequently occurring applications, for example for filling two vessels or for filling three vessels, versions of the device with branching of the tube 2 into only two vessels or, as in the exemplary embodiment, into three vessels can preferably be kept ready.

Patent Translate
Powered by EPO and Google

Notice

This translation is machine-generated. It cannot be guaranteed that it is intelligible, accurate, complete, reliable or fit for specific purposes. Critical decisions, such as commercially relevant or financial decisions, should not be based on machine-translation output.

CLAIMS DE10243129A1

1.

13 Multiple blood collection device, consisting of a cannula (1), at least two blood collection vessels (7 , 8 , 9), and a hose connection (2 , 3 , 4 , 5 , 6), the branches of which are each connected to one of the blood collection vessels (7 , 8 , 9).

16 Blood collection apparatus according to claim 1, wherein each blood collection vessel (7, 8, 9) is closed with a semi-permeable plug (10) which allows air to escape but blocks the escape of liquid and through which the respective branch of the tubing connection passes.

19 A blood collection device according to claim 2, wherein said semi-permeable plug consists of an air-permeable plug body and a semi-permeable membrane formed on the inside thereof

21 Blood collection device according to claim 2 or 3, wherein each branch of the hose connection has a hollow needle penetrating the stopper (10), and wherein the stopper is self-closing after the hollow needle has been withdrawn.

24 Blood collection device according to one of claims 1 to 4, wherein the hose connection has a branch piece (3) which is connected via a hose (2) to the cannula (1) and connected to three branch hoses (4, 5, 6) connected to the blood collection vessels .

27 A blood collection device according to claim 5, wherein the branch piece (3) has a mechanism for selectively shutting off one of the branch tubes.

2.

32 A sheet of drawings follows

(19) Bundesrepublik Deutschland
Deutsches Patent- und Markenamt

(10) **DE 102 43 129 A1** 2004.04.01

(12) # Offenlegungsschrift

(21) Aktenzeichen: **102 43 129.9**
(22) Anmeldetag: **18.09.2002**
(43) Offenlegungstag: **01.04.2004**

(51) Int Cl.[7]: **A61B 5/15**
A61J 1/20

(71) Anmelder:
Ritter GmbH, 86830 Schwabmünchen, DE

(74) Vertreter:
Fleuchaus & Gallo, 86152 Augsburg

(72) Erfinder:
Weis, German, Dr., 86199 Augsburg, DE

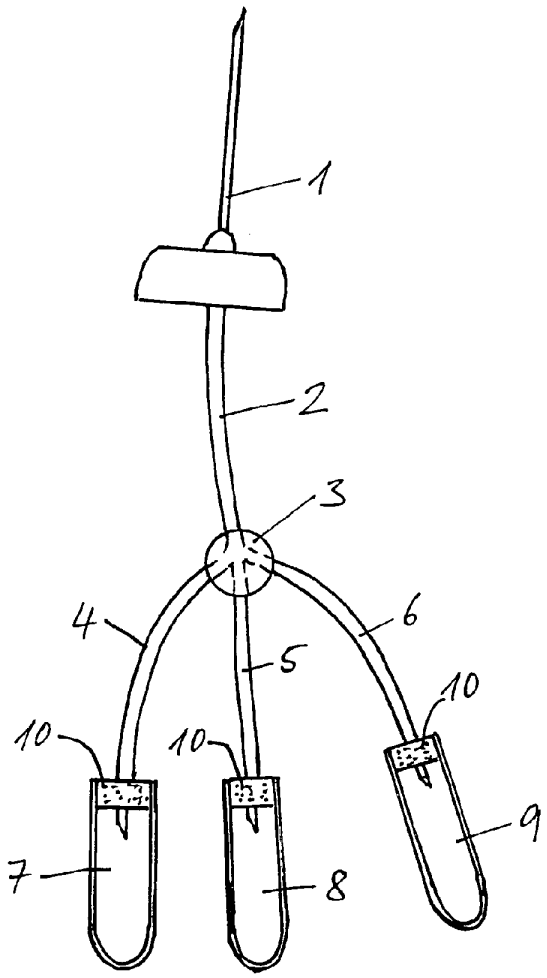
(56) Für die Beurteilung der Patentfähigkeit in Betracht zu ziehende Druckschriften:
DE 40 32 274 A1
US 58 82 318 A
US 55 07 299 A
WO 97/45 055 A1

Die folgenden Angaben sind den vom Anmelder eingereichten Unterlagen entnommen

Rechercheantrag gemäß § 43 Abs. 1 Satz 1 PatG ist gestellt.

(54) Bezeichnung: **Mehrfachblutentnahmegerät für Kleintiere und ähnliche Anwendungen**

(57) Zusammenfassung: Mehrfachblutentnahmegerät mit einer Kanüle, die über eine sich verzweigende Schlauchverbindung (2, 3, 4, 5, 69 mit einer Mehrzahl von Blutentnahmegefäßen (7, 8, 9) verbunden ist.



Beschreibung

[0001] Die Erfindung betrifft ein Mehrfachblutentnahmegerät zur Verwendung bei kleineren Tieren wie Katzen, Hunden und dergleichen, oder auch für ähnliche Anwendungen, wo nur begrenzte Blutmengen zur Verfügung stehen, also zum Beispiel bei Kleinkindern.

Stand der Technik

[0002] Eine Mehrfachblutentnahme, das heißt das Füllen mehrerer Röhrchen mit Blut, ist bei verschiedenen Untersuchungsmethoden erforderlich. So benötigt man ein Röhrchen unbehandeltes Blut für Standardanalysen. Für Blutbild- und Zelluntersuchungen sowie für HbA1 benötigt man ein mit EDTA beschichtetes Entnahmeröhrchen, für Gerinnungsuntersuchungen benötigt man ein Röhrchen, das mit Zitrat versetzt ist, usw.

[0003] Bekannte Mehrfachblutentnahmesysteme sind für erwachsene Menschen ausgelegt. Sie bestehen aus einer Kanüle, die einmal in die Vene eingestochen wird, und dann können mehrere Blutentnahmeröhrchen nacheinander zum Füllen mit der Kanüle gekuppelt werden. Bei Tieren wird meist eine einfache, hinten offene Kanüle verwendet, an die einfach die ebenfalls offenen, zu füllenden Blutentnahmeröhrchen hingehalten werden, bis sie genügend gefüllt sind.

[0004] Bei kleineren Tieren wie beispielsweise Katzen, wo nur eine begrenzte Blutmenge zur Verfügung steht, sind diese bekannten Systeme wenig geeignet. Wird der Katze zur Blutentnahme der Vorderlauf abgebunden staut sich das Blut und schießt beim Einstechen einer Kanüle aufgrund des aufgebauten Drucks erst einmal heftig heraus, wobei bei Verwenden eines offenen Systems oftmals Blut verspritzt wird, das dann verloren ist, und auch beim Wechseln der Röhrchen kann Blut verloren gehen. Außerdem läuft dadurch das erste Röhrchen sehr schnell voll und womöglich über, und für ein zweites und eventuell ein drittes Röhrchen ist dann nicht mehr genügend Blut vorhanden.

Aufgabenstellung

[0005] Aufgabe der Erfindung ist es, ein Mehrfachblutentnahmegerät zu schaffen, das sich besonders bei Anwendungsfällen eignet, wo nur eine begrenzte Blutmenge zur Verfügung steht.

[0006] Diese Aufgabe wird gemäß der Erfindung durch das im Anspruch 1 angegebene Mehrfachblutentnahmegerät gelöst. Vorteilhafte Ausgestaltungen der Erfindung sind Gegenstand der Unteransprüche.

[0007] Das erfindungsgemäße Mehrfachblutentnahmegerät verkörpert ein geschlossenes oder quasi-geschlossenes System, das die oben erwähnten Probleme der herkömmlichen, für die hier in Rede stehenden Anwendungszwecke ungeeigneten Systeme vermeidet. Bei dem erfindungsgemäßen Blutentnahmegerät ist eine Kanüle über einen sich verzweigenden Schlauch mit einer Mehrzahl von Blutentnahmeröhrchen verbunden, die gleichzeitig befillt werden. Auch bei anfänglich stark hereinschießendem Blut verteilt sich dieses dann gleichmäßig auf die angeschlossenen Röhrchen, so daß ohne Verlust von entnommenem Blut ausreichend befiillte Röhrchen in der erforderlichen Anzahl zur Verfügung stehen.

[0008] Das erfindungsgemäße Gerät kann in mehreren Versionen, beispielsweise mit zwei Röhrchen oder mit drei Röhrchen realisiert werden, um den Fällen Rechnung zu tragen, in denen nur zwei Röhrchen Blut oder in denen drei Röhrchen Blut benötigt werden. Es ist auch möglich, beispielsweise mit einem drei Röhrchen umfassenden Gerät nur zwei Röhrchen Blut zu entnehmen, indem der Schlauchzweig zum dritten Röhrchen abgeklemmt wird.

[0009] Weitere Einzelheiten und vorteilhafte Ausgestaltungen der Erfindung werden nachstehend anhand eines Ausführungsbeispiels unter Bezugnahme auf die anliegende Zeichnung mehr im einzelnen beschrieben.

Ausführungsbeispiel

[0010] Die Zeichnung zeigt in schematischer Darstellung ein Mehrfachblutentnahmegerät nach der Erfindung.

[0011] Das in der Zeichnung dargestellte erfindungsgemäße Mehrfachblutentnahmegerät weist eine Kanüle **1** auf, die nur schematisch dargestellt ist. Ihr rückwärtiges Ende ist über einen Schlauch **2** der sich an einer Verzweigung **3** in beim Ausführungsbeispiel drei Zweigschläuche **4**, **5**, **6** verzweigt, mit drei Blutentnahmegefäßen **7**, **8**, **9** verbunden.

[0012] Die Blutentnahmegefäße **7**, **8**, **9** können jeweils durch einen halbdurchlässigen Stopfen **10** verschlossen sein. Solche Stopfen sind an sich bekannt. Sie sind luftdurchlässig, so daß beim Eintritt von Blut in das Röhrchen Luft durch den Stopfen entweichen kann, aber sie verschließen sich bei Kontakt mit Flüssigkeit, so daß kein Blut austreten kann. Solche Stopfen können auch aus einem luftdurchlässigen Stopfenkörper und einer an dessen Innenseite gebildeten halbdurchlässigen Membran bestehen. Die Enden der Zweigschläuche können dabei mit Hohlnadeln verbunden sein, die in den jeweiligen Stopfen **10** eingestochen sind. Da solche Stopfen auch selbstverschließend sind, kann jedes Blutentnahmegefäß nach dem Füllen von der Hohlnadel abgezogen werden, wobei der Stopfen sich selbsttätig verschließt.

[0013] Alternativ dazu kann jedes Blutentnahmegefäß auch mit einer Kappe versehen sein, die eine Luftaustrittsöffnung hat. Diese kann verschließbar sein, beispielsweise mit einem Hütchen, oder sie kann als kleines Schlauchstück ausgebildet sein, das mit einer Klemme verschließbar ist.

[0014] Im Gebrauch füllen sich die drei Blutentnahmegefäße nach dem Einstechen der Kanüle in die Vene gleichmäßig. Sollen im Einzelfall nur zwei von den drei Blutentnahmegefäßen befüllt werden, kann der Zweigschlauch des dritten Gefäßes mit einer Klemme abgequetscht werden, oder wo bei den Blutentnahmegefäßen Kappen mit verschließbarer Entlüfteöffnung verwendet werden, kann die Entlüfteöffnung geschlossen werden, mit der Folge, daß dann in dieses Gefäß ebenfalls kein Blut eintritt. Durch verschließen der Entlüfteöffnung kann auch bei Erreichen der gewünschten Füllmenge in einem Gefäß der weitere Blutzutritt beendet werden, während andere Gefäße noch weiter befüllt werden.

[0015] Es ist auch möglich, die Verzweigung so auszubilden, daß dort wahlweise der Zutritt zu einem nicht benötigten Blutentnahmegefäß gesperrt werden kann.

[0016] Für häufig auftretende Anwendungsfälle, beispielsweise zum Befüllen von zwei Gefäßen oder zum Befüllen von drei Gefäßen, können vorzugsweise Versionen des Geräts mit Verzweigung des Schlauchs **2** auf nur zwei Gefäße oder, wie beim Ausführungsbeispiel, auf drei Gefäße bereitgehalten werden.

Patentansprüche

1. Mehrfachblutentnahmegerät, bestehend aus einer Kanüle (**1**), mindestens zwei Blutentnahmegefäßen (**7**, **8**, **9**), und einer mit dem rückwärtigen Ende der Kanüle verbundenen und sich in eine der Anzahl der Blutentnahmegefäße entsprechenden Anzahl von Zweigen verzweigenden Schlauchverbindung (**2**, **3**, **4**, **5**, **6**), deren Zweige mit jeweils einem der Blutentnahmegefäße (**7**, **8**, **9**) verbunden sind.

2. Blutentnahmegerät nach Anspruch 1, wobei jedes Blutentnahmegefäß (**7**, **8**, **9**) mit einem halbdurchlässigen Stopfen (**10**) verschlossen ist, der Luft austreten läßt, aber den Austritt von Flüssigkeit sperrt und durch welchen der jeweilige Zweig der Schlauchverbindung hindurchverläuft.

3. Blutentnahmegerät nach Anspruch 2, wobei der halbdurchlässige Stopfen aus einem luftdurchlässigen Stopfenkörper und einer an dessen Innenseite gebildeten halbdurchlässigen Membran besteht

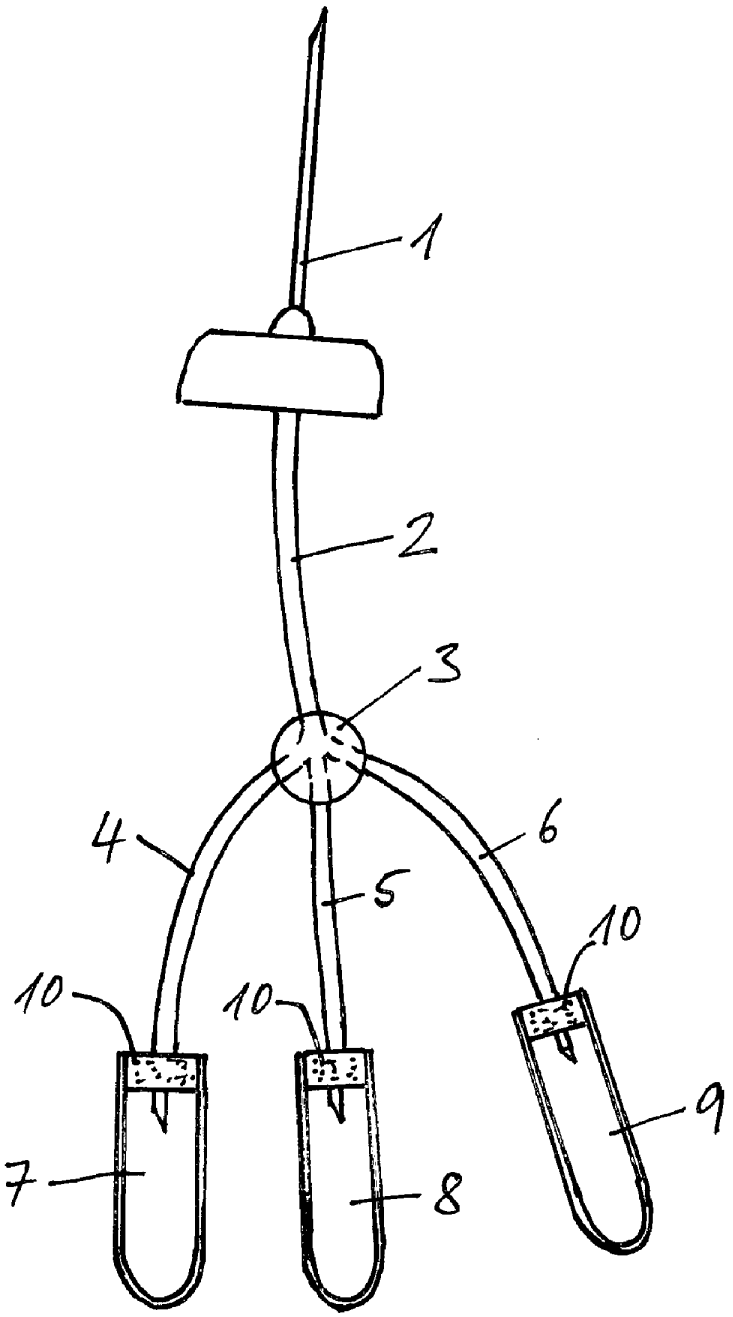
4. Blutentnahmegerät nach Anspruch 2 oder 3, wobei jeder Zweig der Schlauchverbindung eine den Stopfen (**10**) durchdringende Hohlnadel aufweist, und wobei der Stopfen nach Herausziehen der Hohlnadel selbstschließend ist.

5. Blutentnahmegerät nach einem der Ansprüche 1 bis 4, wobei die Schlauchverbindung ein Verzweigungsstück (**3**) aufweist, das über einen Schlauch (**2**) mit der Kanüle (**1**) verbunden und mit drei mit den Blutentnahmegefäßen verbundenen Zweigschläuchen (**4**, **5**, **6**) verbunden ist.

6. Blutentnahmegerät nach Anspruch 5, wobei das Verzweigungsstück (**3**) einen Mechanismus zum wahlweisen Absperren eines der Zweigschläuche aufweist.

Es folgt ein Blatt Zeichnungen

Anhängende Zeichnungen



J-PlatPat 特許情報プラットフォーム English close

Literature display help

Patent 5867238

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

Display format of the document display screen:

(●) text display ( ) PDF display

primary literature

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Patent gazette (B2)
(11) [Patent number] Patent No. 5867238 (P5867238)
(24) [Registration date] 2016 January 15 (2016.1.15)
(45) [Issue date] February 24, 2016 (2016.2.24)
(54) [Title of the invention] Auto scaling method, auto scaling program and computer node
(51) [International Patent Classification]
G06F 9/50 (2006.01)
[FI]
G06F 9/46 462A
[Number of Claims] 6
[Total Number of Pages] 22
(21) [Application Number] Patent Application 2012-78501 (P2012-78501)
(22) [Application date] March 30, 2012 (2012.3.30)
(65) [Publication number] JP 2013-210683 (P2013-210683A) (43) [Publication date] October 10, 2013 (2013.10.10) [Date of request for examination] January 6, 2015 (2015.1.6) (73) [Patent holder] [Identification number] 000005223 [Name] Fujitsu Limited (74) [Agent] [Identi

fication Number] 100111822 [Patent Attorney] [Name] Akihiko Watabe

(74) [Agent]
[Identification number] 100119161
[Patent attorney]
[Name] Keiko Shigehisa
(72) [Inventor]
[Name] Kiyonobu Sato
(72) [Inventor]
[Name] Kazumi Shinozaki
(72) [Inventor]
[Name] Hiroaki Kubota
[Examiner] Yukio Tanaka
(56) [Reference]
[Reference] JP-A-2009-265778 (JP, A) [Reference] JP-A-2008-015958 (JP, A) (58)) [Investigated field] (Int.Cl., DB name) G06F 9/50

The scope of the claims open ---

(57) [Claims]
[Claim 1] In a system that distributes and executes
requested processing to a plurality of virtualized
computer nodes, a computer node that manages tasks executed in the system comprises: When a processing request with a specified delivery date is received, the management information stored in the storage unit for managing the tasks executed by the computer nodes of the system is referred to, and the task of the processing request is assigned to the computer node.

A simulation is performed, and

the simulation of the assignment shows that there is no computer node that can complete th e processing of the task of the processing request within the delivery date, and even if anothe r computer node moves the task that can complete the processing within the delivery date, th e processing will be performed. An auto-scaling method characterized by executing a proces s of increasing the number of computer nodes in the system when it is determined that a com puter node capable of completing the processing of the requested task within the deadline can not be prepared. 2. The computer node that manages the task further refers to the manag ement information and executes a simulation of moving a task running on one computer node to another computer node, and simulating the movement of the task . If it is determined tha t a computer node that does not have a task to be executed can be prepared by moving tasks that can be completed within the deadline on other computer nodes, the other computer node s can also complete the processing within the deadline. move the task,

2. The autoscaling method of claim 1, further comprising removing from the system compu ter nodes that have no tasks to execute .

3.

The computer node that manages the tasks further

moves tasks that can be completed by other computer nodes within the delivery date by sim ulating the movement so that the number of tasks to be executed is equal to or less than a pr edetermined number. If it is determined that a computer node can be prepared to meet the pr ocessing request, tasks that can be completed within the deadline are moved to other comput er nodes, and computer

nodes with a predetermined number or less of tasks to be executed are assigned to the proc essing request task.

3. The auto-scaling method according to claim 2, further comprising executing a process of s etting the object to be excluded from allocation .

4.

In the process of adding a computer node to the system, the task of the processing request can be completed within the deadline even if the setting of the computer node set to be exclu ded from the assignment of the task of the processing request is cancelled.

4. The autoscaling method according to claim 3, further comprising adding a computer node to said system when it is determined that a computer node capable of completing processing cannot be prepared.

5. In a system that distributes and executes

requested processing to a plurality of virtualized computer nodes, a computer node that manages tasks executed in the system includes:

When a processing request with a specified delivery date is received, the management information stored in the storage unit for managing the tasks executed by the computer nodes of the system is referred to, and the task of the processing request is assigned to the computer node. A simulation is performed, and

the simulation of the assignment shows that there is no computer node that can complete the processing of the task of the processing request within the delivery date, and even if another computer node moves the task that can complete the processing within the delivery date, the processing will be performed. An auto-scaling program for increasing the number of computer nodes in the system when it is determined that a computer node capable of completing the processing of the requested task within the deadline cannot be prepared. 6. In a system comprising a plurality of virtualized computer nodes, a computer node that manages tasks executed in the system, and management information that manages the tasks executed by the computer nodes in the system a storage unit, a schedule processing unit that, when receiving a processing request with a specified delivery date, refers to the management information and executes a simulation that allocates the task of the processing request to a computer node ; , Even if there is no computer node that can complete the processing of the task of the processing request within the delivery date, and even if another computer node moves the task that can complete the processing of the task within the delivery date, the processing of the task of the processing request can be completed within the delivery date. If it is determined that a sufficient computer node cannot be prepared, the system

A computer node, comprising: a scale-out processing unit that executes processing for increasing the number of computer nodes.

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to an autoscaling method, an autoscaling

program, and computer nodes for controlling the number of computer nodes provided in a system. [Background technology]

[0002]

In a conventional on-premise system, the resource amount of the system was fixed, and therefore it was not possible to accept processing requests from clients exceeding the resource amount of the system.

[0003]

On the other hand, in a system using cloud computing, which has been developed in recent years, the amount of resources possessed by the system can be changed dynamically. Therefore, even if the amount of system resource consumption exceeds the available resources of the system by executing the processing requested by the client, requests from the client can be accepted by dynamically increasing the system resources. It becomes possible.

As a technique for increasing or decreasing such system resources, there is a technique called scale-up/scale-down for increasing or

decreasing the amount of resources of virtualized computer nodes in the system. However, increasing the resources of virtualized computer nodes is limited by the amount of physical machine resources.

Another

technique for increasing or decreasing system resources is called scale-out/scale-shrink, which increases or decreases the number of computer nodes in the system. With this technology, there is no limit to the amount of physical machine resources when increasing the amount of system resources. There is also a technology called autoscaling that automatically scales out and scales down according to the resource consumption rate of the system.

[0006]

In a distributed batch system, when a new batch process is requested, the batch process being executed by a certain processing server is transferred to another server, and the new batch process is executed by the server that is ready for processing. There is known a technique for managing deadlines for batch processing by doing so.

[Patent Document] [Patent

Document 1] Japanese Unexamined Patent Application Publication No. 2002-342098 [Summary of the Invention] [Problems to be Solved by the Invention] When auto-scaling is performed according to the resource consumption rate, unnecessary computer nodes may be added due to scale-out, and processing being executed by the system may be forcibly interrupted due to incorrect scale-shrink. In cloud computing, when pay-as-you-go billing is performed according to the number of computer nodes, useless scale-out may result in unnecessary billing. [0009] In one aspect, the object of the present invention is to provide a technique that enables

the operation of a system with good billing efficiency. [0010] In one aspect, an autoscaling method distributes requested processing to a plurality of virtualized

In a system in which execution is distributed to computer nodes, when a computer node that manages tasks to be executed in the system receives a processing request with a specified de livery date, the computer node that is stored in the storage unit is referring to management in formation for managing tasks to be executed, executing a simulation of allocating the task of t he processing request to a computer node; Furthermore, even if a task that can be completed within the deadline is moved to another computer node, a computer node that can complete t he processing of the requested task within the deadline is used.
If it is determined that the number of computer nodes in the system cannot be increased, pro cessing is executed to increase the number of computer nodes in the syste
m. EFFECTS OF THE INVENTION [0011] According to one a spect, it is possible to operate a system with good billing efficiency. BRIEF DESCRIPTION OF T HE DRAWINGS [0012] FIG. 1 is a diagram explaining a problem of a system realized on-premi ses; FIG. 2 is a diagram explaining a problem of a system realized by cloud computing; FIG. 3 is a diagram showing a configuration example of a system according to this embodiment; FIG. 4 is a diagram showing an example of functional configuration of each node according to the e mbodiment; FIG. 5 is a diagram showing an example of a virtual machine system that implem ents a node according to this embodiment; FIG. 6 is a diagram illustrating an example of a si mulation of assignment of processing-requested tasks by a scheduler in a master node accord ing to the present embodiment; FIG. 7 is a diagram illustrating an example of a simulation of assignment of processing request tasks by a schedule processing unit in a master node accord ing to the present embodiment; FIG. 8 is a diagram illustrating an example of a simulation of assignment of processing request tasks by a schedule processing unit in a master node accord ing to the present embodiment; FIG. 9 is a diagram illustrating an example of a simulation of assignment of processing request tasks by a schedule processing unit in a master node accord ing to the present embodiment;

FIG. 10 is a diagram illustrating an example of a task migration simulation by a rescheduling processor in a master node according to the embodiment;
FIG. 11 is a diagram illustrating an example of a task movement simulation by a rescheduling processor in a master node according to the embodiment;
12A and 12B are diagrams for explaining an example of lock setting for a slave node by a resc heduling processor in a master node according to the present embodiment; FIG.
13A and 13B are diagrams for explaining an example of lock setting for a slave node by a resc heduling processor in a master node according to the present embodiment; FIG.
14A and 14B are diagrams illustrating an example of unlocking of a slave node by a schedule processing unit in the master node according to the present embodiment; FIG.
FIG. 15 is a processing flowchart when a processing request is accepted by the master node a ccording to the embodiment;
16 is a processing flowchart when a processing request is received by the master node accord ing to the embodiment; FIG.
FIG. 17 is a flowchart of rescheduling by the master node according to the embodiment; BEST MODE FOR CARRYING OUT THE INVENTION The present embodiment will be described belo w with reference to the drawings. [0014] FIG. 1 is a diagram for explaining problems of a sy stem implemented on-premise. In the example shown in FIG. 1, the vertical length of a grap hic representing a task indicates the resource consumption of the task, and the horizontal len gth indicates the processing time of the task. In the example shown in FIG. 1, the vertical axi s of the graph indicates the resource consumption of the system, and the horizontal axis indic ates the passage of time. t0 _

~ t 3 indicates the times at equal intervals.

[0016]

In an on-premise system, the amount of resources that the system has is fixed. That is, it is not possible to process resource consumption that exceeds the amount of resources that the system has in advance. In the example shown in Figure 1, the System Resources line represents the amount of resources the system has.

indicate. For example, in FIG. 1A, it is assumed that the processing requests for tasks #1 to #4 are issued to the system at approximately the same

time t0 . At this time, the system starts processing in the order in which the processing requests are accepted, here in the order of task #1, task #2, task #3, and task #4. However, as shown in FIG. 1A, when the processing of task #3 is started, the resource consumption of the system reaches the amount of resources that the system has, and the processing of task #4 cannot be started. will not be able to accept processing requests for The example shown in FIG .

1B is an example of a scheduling system. In a scheduling system, the task processing time is estimated at the time a processing request is received, and even if there are no available resources at the time the processing request is generated, the task of the processing request that is received after the completion of other tasks in progress. Schedule tasks to execute For example, it is assumed that the deadline for processing task #4, which is finally accepted, is time t3 . As shown in FIG. 1B, the processing end time of task #3, which has the earliest processing end time, is t1, so if task #4 is scheduled after task #3, the processing end time of task #4 is is t3 , and the deadline is met. In this case, the processing request for task #4 can be accepted by the system. [0020]

However, in the example shown in FIG. 1(C), if task #4 is scheduled after task #2, which has the earliest processing end time, the processing end time of task #4 will exceed t3, and the deadline will not be met . In this case, the processing request for task #4 is not accepted by the system. On-premises systems may not be able to accept processing requests even after scheduling. Cloud computing technology exists at the opposite end of such on-premise technology

.

The amount of system resources realized by cloud computing is variable. In cloud computing, each computer node provided in the system is realized by, for example, a virtual machine (VM)

.

In the following description, the computer nodes included in the system are simply referred to as nodes. In cloud computing, there is, for example, a scale-up/scale-down technique as a t echnique for changing the amount of system resources

.

Scaling up is a technique for increasing the resource amount of a node. Also, scaling down is a technique to reduce the resource amount of a node. By using scale-up technology, for exam ple, even if a task with a new processing request cannot be executed in time with the current resources, by increasing the amount of node resources, the new processing request can be ful filled. Be able to complete tasks on time.

[0024]

However, since the resources that can be scaled up are limited to the resources of the physic al machines that implement the nodes, which are virtual machines, there is a limit to how mu ch nodes can be scaled up. In addition, usually multiple virtual machine nodes are arranged o n one physical machine, and if there is no surplus after allocating the resources of the physica l machine to each node, it can be specified without reducing the performance of other nodes. It becomes impossible to increase the performance of the nodes of For example, in a multi-te nant environment, multiple tenants' virtual machines are running on a single physical machin e, and in order to increase the resource amount of one tenant's virtual machine, it is possible to reduce the resource amount of other tenants. cannot be done easily. Therefore, even if scal e-up techniques are used, the required processing

Not all tasks can be executed with a guaranteed delivery date. In cloud computing, there is a scale-out/scale-shrink technique in addition to the scale-up/scale-down technique as a tech nique for changing the amount of system resources

.

Scale-out is a technique for adding nodes to a system. Scale shrink is a technique for removin g nodes from a system. By using scale-out technology, it is almost certain that all requested p rocessing tasks can be executed with a guaranteed delivery date.

[0026]

However, in the world of cloud computing, the service usage fee is normally based on a pay-as-you-go system, and as the number of nodes provided in the system increases due to scale-out, the service usage fee increases.

FIG.

2 is a diagram for explaining problems of a system realized by cloud computing.

In the example shown in FIG. 2, the

vertical length of a graphic representing a task indicates the resource consumption of the tas k, and the horizontal length indicates the processing time of the task. In the example shown i n FIG. 2, the vertical axis of the graph indicates the total amount of resource consumption of the nodes that make up the system, and the horizontal axis indicates the passage of time. t_0 to t_3 indicate times at equal intervals. In the example shown in FIG. 2, the system resource li

ne indicates the total amount of resources possessed by the nodes that make up the system.

[0029]

In FIG. 2A, it is assumed that the system initially has three nodes VM#1 to VM#3. Here, it is assumed that the processing requests of task #1 to task #4 are issued to the system at approximately the same time t0 . At this time, in the system, tasks are assigned to the nodes in the order in which the processing requests are accepted, here in the order of task #1, task #2, task #3, and task #4, and processing is started. However, as shown in FIG. 2A, when task #3 is assigned to node VM#3, the resource consumption of all nodes in the system becomes the upper limit, and task #4 can be assigned. node disappears. At this time, as shown in FIG. 2A, for example, the system is scaled out and a VM#4 node is added to the system

.

As shown in FIG. 2A, by adding a VM#4 node to the system by scale-out, the processing of the requested task #4 can be executed. For example, in cloud computing, as a service of an IaaS (Infrastructure as a Service) vendor that provides infrastructure such as virtual machines and networks as a service, it automatically scales out when the resource consumption rate of the system exceeds a predetermined level. There is service. In cloud computing, the technology for automatically expanding/reducing the system is also called autoscaling. Here, it is assumed that the deadline for processing task #4 is

time t3 . As shown in FIG. 2A, the processing end time of task #3, which has the earliest processing end time, is t 1

Therefore, if task #4 is scheduled after task #3, the processing end time of task #4 will be t 3, and the deadline will be met . If task scheduling can be performed in this way, it is possible to execute the processing of task #4 in time for the delivery date without increasing the number of nodes for VM #4 due to scale-out

.

. However, such a judgment cannot be made just by looking at resource consumption as in the case of the IaaS service described above. As mentioned above, in cloud computing, the usage fee increases as the number of nodes increases. I have a request.

[0033]

Further, in order to suppress useless node usage charges, a scale shrink is performed on a node that is determined not to be in operation in the system, and the node is removed from the system. For example, in cloud computing, as a service of an IaaS vendor, when the CPU (Central Processing Unit) usage rate of a node falls below a predetermined level, task processing is not performed at the node and only middleware such as the OS operates. There is a service that automatically scales and shrinks if it judges that it is not.

[0034]

However, even if the resource consumption of a node is low, it does not necessarily mean that the requested task is not being processed. For example, in the example shown in FIG. 2B, in the node of VM#3, the amount of resource consumption is drastically reduced after the proc

essing of task #3 is completed. However, in the example shown in FIG. 2B, in the node of VM #3, task #4, which consumes less resources, is being executed in parallel with task #3. If the node of VM#3 is scale-shrinked at the same time as the processing of task #3 ends, the proce ssing of task #4 will be forcibly terminated. In this way, if scale shrinkage is determined just b y looking at resource consumption as in the above-mentioned IaaS vendor service, for exampl e, task #4 shown in FIG. It is possible to accidentally remove a running node.

[0035]

The auto-scaling technique according to the present embodiment for solving such problems will be described below.

FIG.

3 is a diagram showing a configuration example of a system according to this embodiment.

[0037]

In this embodiment, the system 100 shown in FIG. 3 is assumed to be a computer system c omposed of virtual machine nodes provided from the IaaS side in cloud computing. The syste m 100 distributes and executes the processing requested by the client 200 over a plurality of nodes. The system 100 and the client 200 are connected by a network 300 such as a LAN (Lo cal Area Network) or the Internet. The system 100 comprises a master node 110 and slave no des 120 .

The master node 110 receives processing requests from the client 200 , assigns

tasks to each slave node 120 , and manages tasks to be executed in the system 100 . Note t hat the master node 110 according to this embodiment performs auto-scaling processing such as scale-out and scale-shrink of the slave node 120 . Note that the master node 110 may be o ne of the slave nodes 120 at the same time.

The slave node 120 is a computer node that

executes tasks requested by the master node 110 . The slave node 120 is capable of parallel processing of multiple tasks. The slave node 120 is added to the system 100 or deleted from t he system 100 by autoscaling processing. For example, in FIG. 3, when the slave node 120a #a and the slave node 120b #b are executing task processing, if there is a processing request that cannot be executed by those slave nodes 120, #c A slave node 120 c is added to system 100 . Also, for example, when there are no more tasks to be executed by the #c slave node 1 20c, the #c slave node 120c is deleted from the system 100 .

[0040]

The client 200 is a computer having a high-level application that requests the system 100 to execute processing provided by the system 100 . In the example shown in FIG. 1, the client 2 00 is an external device of the system 100.

Node 200 may be a node within system 100 .

FIG.

4 is a diagram showing an example of the functional configuration of each node according to this embodiment.

The master

node 110 comprises a client communication section 111 , a schedule processing section 112 , a schedule information storage section 113 , a scale-out processing section 114 , a slave co mmunication section 115 , a rescheduling processing section 116 and a scale shrink processin g section 117 .

[0043]

The client communication unit 111 receives a processing request from the client 200 . If the processing of the received request is executable within the system 100, the client communicat ion unit 111 passes it to the schedule processing unit 112. FIG. If the processing of the receiv ed request cannot be processed within the system 100, the client communication unit 111 res ponds to that effect to the client 200. FIG. Processes that cannot be executed within the syste m 100 include, for example, application processes that are not present in the slave node 120 and large-scale processes that cannot be completed by the slave node 120 of one virtual mac hine by the due date. The technique of distributing and executing large-scale processing on a plurality of nodes is outside the scope of the technique according to the present embodiment, and will not be described here. The client communication unit 111 notifies the client 200 of th e processing result received from the slave node 120 . When the client communication unit 1 11 receives a processing request with a specified delivery date, the schedule processing unit 1 12 refers to the management information stored in the schedule information storage unit 113 and slaves the task of the processing request

.

Run the simulation assigned to node 120 .

[0045]

The schedule information storage unit 113 is a management information storage unit for ma naging tasks executed by the slave nodes 120 provided in the system 100 . The management information stored in the schedule information storage unit 113 records schedules of tasks to be executed by all the slave nodes 120 .

More

specifically, the schedule processing unit 112 first detects the slave node 120 that can compl ete the processing of the received processing request within the specified delivery date in the current state. Here, the schedule processing unit 112 not only selects the slave nodes 120 tha t can immediately execute the processing, but also the slave nodes 120 that can complete the processing within the deadline even if the processing request task is executed after the proces sing of other tasks is completed. To detect. The schedule processing unit 112 selects the slave node 120 to which the task of the processing request is to be assigned from among the slave nodes 120 detected here. Note that the locked slave node 120 is excluded from detection her e. In the present embodiment, locking refers to setting the slave node 120 as a non-allocation target for the task of the processing request.

[0047]

In the current state, if there is no slave node 120 that can complete the processing of the requested task within the deadline, the schedule processing unit 112 detects a task that can complete the processing within the deadline even if the task is moved to another slave node 120. . By moving the detected task, the schedule processing unit 112 determines whether or not the slave node 120 capable of completing the processing of the requested task within the delivery date can be prepared. If it is determined that by moving the task, the slave node 120 capable of completing the processing of the task requested by the deadline can be prepared, the schedule processing unit 112 performs the process of moving the task to another slave node 120 as follows: It is executed via the slave communication unit 115 . The task may be moved by, for example, stopping the processing of the task at the source slave node 120 and restarting it at the destination slave node 120. A method of transferring data to the destination slave node 120 may also be used. In this embodiment, the task is moved by a method of restarting the processing of the task in the destination slave node 120 . Schedule processing unit 11
In step 2, the slave node 120 that has become free due to the movement of the task is determined as the target slave node 120 to which the task of the processing request is to be assigned. If the schedule processing unit 112 cannot prepare a slave node 120 capable of completing the processing of the requested task within the delivery date even if the task is moved, the schedule processing unit 112 unlocks the locked slave node 120 if any

.

For example, it is determined whether the processing of the requested task can be completed within the deadline. When it is determined that the processing of the requested task can be completed within the due date by unlocking, the schedule processing unit 112 unlocks the locked slave node 120 . The schedule processing unit 112 determines the unlocked slave node 120 as the target slave node 120 to which the task of the processing request is to be assigned.

[0049]

If the slave node 120 to which the task of the processing request is to be assigned is not found in the processing up to this point, the schedule processing unit 112 determines that the slave node 120 should be added to the system 100 by scale-out.

The scale-out processing unit 114 performs processing for

adding computer nodes to the system 100 by scale-out. More specifically, the scale-out processing unit 114 accesses the management computer on the IaaS side using an interface prepared by the IaaS side and requests scale-out to the own system 100 .

[0051]

The slave communication unit 115 communicates with the slave node 120 . For example, the slave communication unit 115 requests the slave node 120 to which the task of the received processing request is to be assigned to process the task. The slave communication unit 115 also receives the processing result of the requested task from the slave node 120 as a response. When a task is moved, the slave communication unit 115 notifies the source slave node 120 of the stop of the task, and notifies the destination slave node 120 of the execution of the task.

. The rescheduling processing unit 116, for example, periodically refers to the management information stored in the schedule information storage unit 113, and targets slave nodes 120 that do not have tasks to be executed

. The rescheduling processing unit 116 also refers to the management information stored in the schedule information storage unit 113 and executes a simulation of migrating a task running on a certain slave node 120 to another slave node 120 . . The rescheduling processing unit 116 detects tasks that can be completed within the deadline even if they are moved to another slave node 120 . [0054]

The rescheduling processing unit 116 determines whether or not the slave node 120 having no task to be executed can be prepared by moving the detected task. If it is determined that a slave node 120 that does not have a task to be executed can be prepared by moving the task, the rescheduling processing unit 116 transfers the task to another slave node 120 via the slave communication unit 115. to run. The movement of tasks is the same as in the case of the schedule processing unit 112 described above. The rescheduling unit 116 targets the slave node 120, which no longer has tasks to be executed due to the movement of tasks, for scale shrink.

The rescheduling processing unit 116 also determines whether or not it is possible to prepare a slave node 120 in which the number of tasks to be executed is equal to or less than a predetermined number by moving the detected tasks. If it is determined that a slave node 120 can be prepared in which the number of tasks to be executed by task movement is equal to or less than a predetermined number, the rescheduling processing unit 116 performs the process of moving the corresponding task to another slave node 120 via slave communication. 115. Reschedule processing part

116 sets a lock on the slave node 120 for which the number of tasks to be executed due to task movement is equal to or less than a predetermined number. As a general rule, the locked slave node 120 is not assigned a task with a new processing request, so it becomes the target of scale shrink after the processing of the remaining tasks is completed. The scale shrink processing unit 117 performs processing for deleting the target slave node 120 from the system 100 by scale shrink

.

More specifically, the scale shrink processing unit 117 uses an interface prepared by the IaaS side to access the management computer on the IaaS side and request scale shrinking of the target slave node 120 . The slave node 120 has a master communication section 121 and an application 122

.

As shown in FIG. 4, the slave node 120 can run multiple types of applications 122a, b, . When the task of the processing request is assigned, the task processing is executed by the applicati on 122 corresponding to the processing request.

[0058]

The master communication unit 121 communicates with the master node 110 . For example, the master communication unit 121 receives a task execution request or a stop request from t he master node 110, and performs processing for starting or stopping task execution. Further, when task processing is completed, the master communication unit 121 returns a processing r esult response to the master node 110 .

FIG.

5 is a diagram showing an example of a virtual machine system that implements a node acc ording to this embodiment.

[0060]

The virtual machine system shown in FIG. 5 is, for example, a system in which one or more virtual machines operate on one physical machine. In the example of the virtual machine syst em shown in FIG. 5, a plurality of virtual machines 30 including a master node 110 and slave nodes 120 are operating using the resources of the computer 10, which is a physical machine, such as the CPU 11 and memory 12. . In the virtual machine system shown in FIG. 5, the ma ster node 110 and slave nodes 120 are realized by the same physical machine, but in a cloud computing environment, the master node 110 and each slave node 120 are different. It is ofte n implemented on a physical machine.

In the virtual machine system shown in FIG .

5, the hypervisor 20 is software that implements a virtual environment using the computer 1 0 . A virtual machine 30 including the master node 110 and slave node 120 can be constructe d on the hypervisor 20 . The computer 10, which implements the master node 110 and slave node 120 shown in FIG

.

, an input device 16, an output device 17, and other hardware. The storage device 13 is, for e xample, an external storage device such as a HDD (Hard Disk Drive) or an auxiliary storage d evice. The medium reading/writing device 15 is, for example, a CD-R (Compact Disc Recordab le) drive or a DVD-R (Digital Versatile Disc Recordable) drive. The input device 16 is, for exam ple, a keyboard/mouse. The output device 17 is, for example, a display device such as a displ ay. Note that the hardware configuration of the computer 10 can be arbitrarily designed as re quired.

The master node 110, slave node 120, and functional units provided in each node shown in F IG. 4 can be realized by hardware such as the CPU 11 and memory 12 provided in the comput er 10, and software programs . A program executable by the computer 10

The gram is stored in the storage device 13, for example, read out to the memory 12 when ex

ecuted, and executed by the CPU 11. FIG.

The computer 10

can also read a program directly from a portable recording medium and execute processing according to the program. The computer 10 can also execute processing according to the received program every time the program is transferred from the server computer. Furthermore, this program can be recorded in a computer-readable recording medium.

Processing by the master node 110 according to this embodiment will now be described using a

more specific example.

FIGS.

6 to 9 are diagrams for explaining an example of a simulation of assignment of processing request tasks by the schedule processor in the master node of this embodiment.

FIG .

6A shows an example of notation of tasks. In FIG. 6A, solid figures represent task processing. The vertical length of the figure indicating task processing indicates the resource consumption of the task, and the horizontal length indicates the processing time of the task. Also, in FIG. 6A, the right end of the outline figure indicates the due date of the task. The due date is the deadline for completing the processing of the task designated by the client 200 . In the following description, all tasks are represented as shown in FIG. 6(A).

FIG . 6B shows the time t_0

from the client 200. shows the schedule of tasks executed by the slave nodes 120a and 120b included in the system 100 when a processing request is received. As shown in FIG. 6(B), the system 100 has two slave nodes 120 at this time: #a slave node 120a and #b slave node 120b. Note that the schedule information storage unit 113 stores management information in which the schedule of tasks executed by the slave nodes 120 included in the system 100 is converted into data, for example, as shown in the graph of FIG. 6B. In FIG. 6B, the vertical axis of the graph indicates the amount of resources consumed by the slave node, and the horizontal axis indicates the passage of time. t_{-1} to t_3 indicate times at equal intervals.

FIG. 6C

is a diagram showing the task X of the processing request received from the client 200 at time t_0 . As shown in FIG. 6(C), the processing of the processing request task X is indicated by hatching so as to be distinguished from other tasks. As shown in FIG. 6C, the due date of time t3 is specified for task X of the processing request .

[0070]

Note that there are many well-known techniques for estimating the task processing time and resource consumption, such as methods based on past results and theoretical methods, so a detailed description is omitted here. Estimation of the processing time of a task differs depending on the target processing of the task. For example, the image processing time is affected by the image file size. Processing using a database is affected by the number of accesses to th

e database. As for the resource consumption of a task, for example, if a value is determined f or each application 122 that processes the task, that value can be used. The resource consum ption amount may be inquired of the slave node 120 . In addition, various well-known techniq ues can be used.

In the master node 110 , when the schedule processing unit 112 receives a processing reques t, it

first verifies whether the task of the processing request can be assigned to the slave node 1 20 under the current circumstances.

FIG .

7(A) shows the execution of the process request task X at #a so that the process execution i s started at time t0 .

An example of verification assigned to a slave node 120a is shown. Also, FIG. 7B shows an ex ample of verification in which the task X of the processing request is assigned to the #b slave node 120b so as to start processing execution at time t0 . In either case, the resource consum ption of the node exceeds the resource limit of the node, so the verification result is NG.

FIG. 7C

shows an example of verification in which task X requesting processing is scheduled after tas k A#1 executed by slave node 120a of #a, which finishes processing the earliest, is complete d. In this case, the verification result is NG because the processing end time of the processing request task X exceeds the due date t3 . Next, the schedule processing unit 112 performs ver ification to move a task whose processing can be completed by the due date even if the task i s restarted with another task

.

As shown in FIG. 8A, task B#3 executed by the #b slave node 120b can be moved to the #a s lave node 120a in terms of resource consumption. Processing can be completed by the due da te even if the system is restarted. FIG. 8(B) shows an example of verification in which the pro cessing request task X is assigned to the #b slave node 120b whose resource consumption ha s decreased due to the movement of the tasks shown in FIG. 8(A). Even if the task is moved, the resource consumption of the node exceeds the resource limit of the node, so the verificati on result is NG.

[0075]

Since there is no other locked slave node 120 , the schedule processing unit 112 determines that the slave node 120 will be added by the scale-out processing by the scale-out processing unit 114 . FIG. 9 shows a state in which the task X requesting processing is assigned to the # c slave node 120 c added by the scale-out processing unit 114 . As described above, the ma ster node 110 according to the present embodiment performs verification including scheduling in the current state of the slave node 120, and furthermore, even if verification including task migration is performed, the task can be completed within the deadline

.

Scale out only if the task of the processing request cannot be assigned so that the processing is finished. As a result, useless scale-out can be suppressed, so that the system 100 can be o perated efficiently without unnecessary billing.

10 and 11 are diagrams for explaining an

example of task movement simulation by the rescheduling processor in the master node of t his embodiment.

FIG .

10 shows the schedule of tasks executed by the slave nodes 120a, 120b, and 120c of the sy stem 100 at time t0 . As shown in FIG. 10, at this point, the system 100 has three slave node s 120: #a slave node 120a, #b slave node 120b, and #c slave node 120c.

[0079]

First, in the master node 110, the rescheduling processing unit 116 periodically refers to the schedule information storage unit 113 to check whether there is a slave node 120 that has no task to be executed. As shown in FIG. 10, all the slave nodes 120 are executing processing at this point, so there is no slave node 120 that has no task to execute. At this time, the resched uling processing unit 116 determines that there is no slave node 120 that can be scaled down as it is.

Next, the rescheduling processing unit 116 performs verification to move the task that can be completed by the due date even if it

is restarted by another task.

FIG. 11A

shows an example of verification in which task B#1 executed by slave node 120b of #b is re started by slave node 120a of #a. As shown in Figure 11(A), the task

If B#1 is restarted by another slave node 120, the processing end time will exceed the deliver y date t2 , so the verification result will be NG. The rescheduling unit 116 determines that it is not possi ble to move the task and perform scale shrinking on the #b slave node 120b.

FIG. 11B

shows an example of verification in which task C#1 executed by slave node 120c of #c is res tarted by slave node 120a of #a. As shown in FIG. 11B, task C#1 can be completed by the de adline t3 even if the slave node 120a of #a is restarted. Furthermore, when task C#1 is move d to the slave node 120a of #a, there is no task to be executed by the slave node 120c of #C, so scale shrinking can be performed on the slave node 120c of #C. The rescheduling unit 11 6 instructs the #C slave node 120c to stop task C#1 and the #A slave node 120a to execute t ask C#1 via the slave communication unit 115

.

do. Since there are no more tasks to be executed by the #C slave node 120c, the reschedulin g unit 116 targets the #C slave node 120c for scale shrink. The scale shrink processing unit 1 17 executes scale shrink processing for the #C slave node 120c.

[0084]

In this way, the master node 110 according to the present embodiment actively creates slave nodes 120 that do not have tasks to be executed by moving tasks to other slave nodes 120, and executes scale shrink. As a result, it is possible to positively delete useless slave nodes 120, so that it is possible to operate the system 100 efficiently without unnecessary billing. 12 and 13 are diagrams for explaining an example of setting a lock on a slave node by the rescheduling processor in the master node of this embodiment
. FIG . 12 shows the schedule of tasks executed by the slave nodes 120a and 120b of the system 100 at time t0 . As shown in FIG. 12, the system 100 has two slave nodes 120 at this time: #a slave node 120a and #b slave node 120b. In the master node 110, when the slave node 120 that has no tasks to be executed cannot be prepared even if the tasks are moved, the rescheduling processing unit 116 reduces the number of tasks to be executed by moving the tasks to a predetermined number or less. Verifies whether the slave node 120 can be prepared. For example, the predetermined number is 1 here. FIG. 13A shows an example of verification in which task B#2 executed by the #b slave node 120b is restarted by the #a slave node 120a. As shown in FIG. 13(A), task B#2 has a deadline of t 3 even if the slave node 120a of #a is restarted.

Processing can be completed by Even if task B#1 executed by slave node 120b of #b is to be restarted by slave node 120a of #a, task B#1 will be moved because the processing end time will exceed the due date t2 . Can not.
Assuming that task B#2 is
moved to #a slave node 120a, as shown in FIG. . At this time, the rescheduling processing unit 116 instructs the #B slave node 120b to stop the task B#2 and instructs the #A slave node 120a to execute the task B#2 via the slave communication unit 115. do.

Also, as shown in FIG. 13(B), a lock is set for the slave node 120b of #b, for which the only task to be executed is B#1 . Information on the slave node 120 that has set the lock is recorded in a storage unit such as the schedule information storage unit 113 that can be accessed by the schedule processing unit 112 . As a general rule, the #b slave node 120b is not assigned a new processing request task. can be deleted. As described above, the master node 110 according to the present embodiment moves tasks to other slave nodes 120, actively creates slave nodes 120 with fewer tasks to be executed, and creates new slave nodes 120 for those slave nodes 120
.

Suppress task allocation for processing requests. As a result, the environment of the system 1 00 becomes an environment where it is easy to create slave nodes 120 that do not have tasks to be executed, and it is possible to positively delete useless slave nodes 120, so it is efficient to avoid unnecessary billing. Operation of the system 100 becomes possible.

FIG.

14 is a diagram for explaining an example of unlocking a slave node by the schedule process ing unit in the master node of this embodiment.

[0093]

Here, it is assumed that the system 100 receives a processing request for task X shown in FI G. 6(C) from the client 200 in the state shown in FIG. 13(B). At this time, the schedule proces sing unit 112 attempts to allocate the processing request task X to the unlocked #a slave nod e 120a as shown in FIG. Cannot be allocated because it would exceed the resource limit. Furt hermore, there is no other slave node 120 to which the task can be transferred. At this time, the schedule processing unit 112 verifies whether or not task X requested by the slave node 1 20b of #b can be completed by the due date by unlocking the locked slave node 120b of #b .

do. As shown in FIG. 14B, the slave node 120b of #b can complete the processing of the task X of the processing request by the due date. is released, and the task X of the processing req uest is assigned to the #b slave node 120b.

As described above, the slave node 120 that is locked is assigned

a task requesting processing only when the task requesting processing cannot be assigned t o another slave node 120 . As a result, it is possible to suppress the occurrence of scale-out w hile maintaining an environment that facilitates scale-shrinking to the very limit, so that the s ystem 100 can be operated efficiently without unnecessary billing.

The master node 110 according to this embodiment gives the highest priority to completing ta sk processing within the deadline, so the system 100

always maintains the minimum processing performance.

[0097]

15 and 16 are processing flowcharts when the master node of this embodiment accepts a pr ocessing request. In the master node 110, the client communication section 111 receives a processing request from a client (step S10)

.

A delivery date is specified in the processing request received here. The client communication unit 111 determines whether the processing request can be accepted (step S11). If the proce ssing request is not acceptable (NO in step S11), the client

The communication unit 111 responds to the client that the processing request cannot be acc epted (step S12), and terminates the processing. If the processing request can be accepted (YES in step S11), the schedule processing unit 112 refers to the management information in the schedule information storage unit 113 and performs a simulation of allocating the task of t

he processing request to the current slave node 120

.

(step S13). Here, for example, verification including scheduling is performed as shown in FIG. The

schedule processing unit 112 determines whether or not it is possible to allocate the task of the processing request to the current slave node 120 (step S14). If the task of the processing request can be assigned (YES in step S14), the schedule processing unit 112 determines the s lave node 120 to which the task of the processing request is assigned (step S15). The slave c ommunication unit 115 requests the determined slave node 120 to process the task of the pro cessing request (step S22).

If it is not possible to assign the task of the processing request (NO in step S14), the schedule processing unit

112 refers to the management information in the schedule information storage unit 113, mo ves the existing task, and A simulation of assigning tasks is performed (step S16). Here, for e xample, as shown in FIG. 8, if there is an existing task that can be completed within the deliv ery date even if it is moved to another slave node 120 and re-executed, the existing task is m oved and resource It is verified whether the task of the processing request can be assigned to the slave node 120 that has become free.

[0102]

The schedule processing unit 112 determines whether it is possible to allocate the task of th e processing request by moving the existing task (step S17). If the task of the processing req uest can be assigned (YES in step S17), the schedule processing unit 112 moves the correspo nding existing task (step S18). More specifically, the schedule processing unit 112 requests, vi a the slave communication unit 115, the slave node 120 from which the existing task is move d to stop the task. Also, the schedule processing unit 112 requests the slave node 120 to whic h the existing task is moved to execute the task via the slave communication unit 115 . The sl ave communication unit 115 requests the slave node 120, whose resource becomes available due to the migration of the existing task, to process the requested task (step S22).

If it is not possible to allocate the task of the processing request (NO in step S17), the schedu le processing unit 112 determines that there is a locked slave node 120 ,

and if the slave node 120 is unlocked, It is determined whether or not the task of the proces sing request can be assigned (step S19). If the lock is released and it becomes possible to all ocate the task of the processing request (YES in step S19), the schedule processing unit 112 unlocks the locked slave node 120 (step S20). The slave communication unit 115 requests the unlocked slave node 120 to process the requested task (step S22). This case is the case show n in the example of FIG.

[0104]

If there is no locked slave node 120 or if it is not possible to allocate the processing request task even if the lock is released (NO in step S19), the scale-out processing unit 114 executes

scale-out processing (step S21). A slave node 120 is added to the system 100 by scale-out. T he slave communication unit 115 requests the added slave node 120 to process the requested task (step S22). This case is the case shown in the example of FIG. The slave communicatio n unit 115 receives a processing result response to the processing request from the slave nod e 120

.

is received (step S23), the client communication unit 111 transmits the response to the client (step S24).

FIG.

17 is a flow chart of rescheduling by the master node of this embodiment. In the master no de 110, the rescheduling processing section 116 starts this processing at a predetermined tim ing

. The rescheduling processing unit 116 refers to the management information in the schedul e information storage unit 113 and determines whether there is a slave node 120 that current ly has no task to be executed (step S30). If there is a slave node 120 that does not have a ta sk to be executed (YES in step S30), the scale shrink processing unit 117 executes scale shrin k processing for that slave node 120 (step S31). The scale shrink removes the slave node 120 from the system 100 . The rescheduling processing unit 116 refers to the management infor mation in the schedule information storage unit 113 and performs a task migration simulation (step S32). Here, for example, as shown in FIG. 11, if there is a task that can be completed w ithin the deadline even if it is moved to another slave node 120 and re-executed, there is no t ask to move and execute the task. It is verified whether the slave node 120 can be created. F or example, as shown in FIG. 13, if there is a task that can be completed within the deadline even if it is moved to another slave node 120 and re-executed, a predetermined number of ta sks are moved and executed. It is verified whether the following slave nodes 120 can be gene rated. [0110]

The rescheduling unit 116 determines whether it is possible to generate a slave node 120 th at does not have a task to be executed by moving the task, that is, whether it is possible to m ove the task and perform scale shrinking (step S33). If scale shrinking becomes possible by m oving the task (YES in step S33), the rescheduling processor 116 moves the task (step S34). More specifically, the rescheduling processing unit 116 requests the slave node 120 from whic h the task is moved to stop the task via the slave communication unit 115 . Also, the resched

uling processing unit 116 requests the slave node 120 to which the task is moved to execute t he task via the slave communication unit 115 . The scale shrink processing unit 117 executes scale shrink processing for the slave node 120 that has no tasks to be executed due to the mo vement of the tasks (step S35). The scale shrink removes the slave node 120 from the syste m 100 . If scale shrinking is not possible even after the task is moved (NO in step S33), the rescheduling processing unit 116 determines that there is a slave node 120 where the number of tasks to be executed by moving the task is less than the predetermined number

.

It is determined whether or not (step S36). If there is no slave node 120 whose number of tas ks to be executed is equal to or less than the predetermined number even after the task is mo ved (NO in step S36), the rescheduling processing unit 116 ends the process.

[0112]

If there is a slave node 120 in which the number of tasks to be executed by migrating tasks i s equal to or less than the predetermined number (YES in step S36), the rescheduling process ing unit 116 migrates the tasks (step S37). More specifically, the rescheduling processing unit 116 requests the slave node 120 from which the task is moved to stop the task via the slave c ommunication unit 115 . Also, the rescheduling processing unit 116 requests the slave node 1 20 to which the task is moved to execute the task via the slave communication unit 115 . The rescheduling processing unit 116 locks the slave node 120 for which the number of tasks to b e executed by moving tasks is less than a predetermined number.

is set (step S38). If all tasks remaining without being unlocked are processed, the slave node 120 to which the lock is set becomes the target of scale shrink in subsequent steps S30 and S 31.

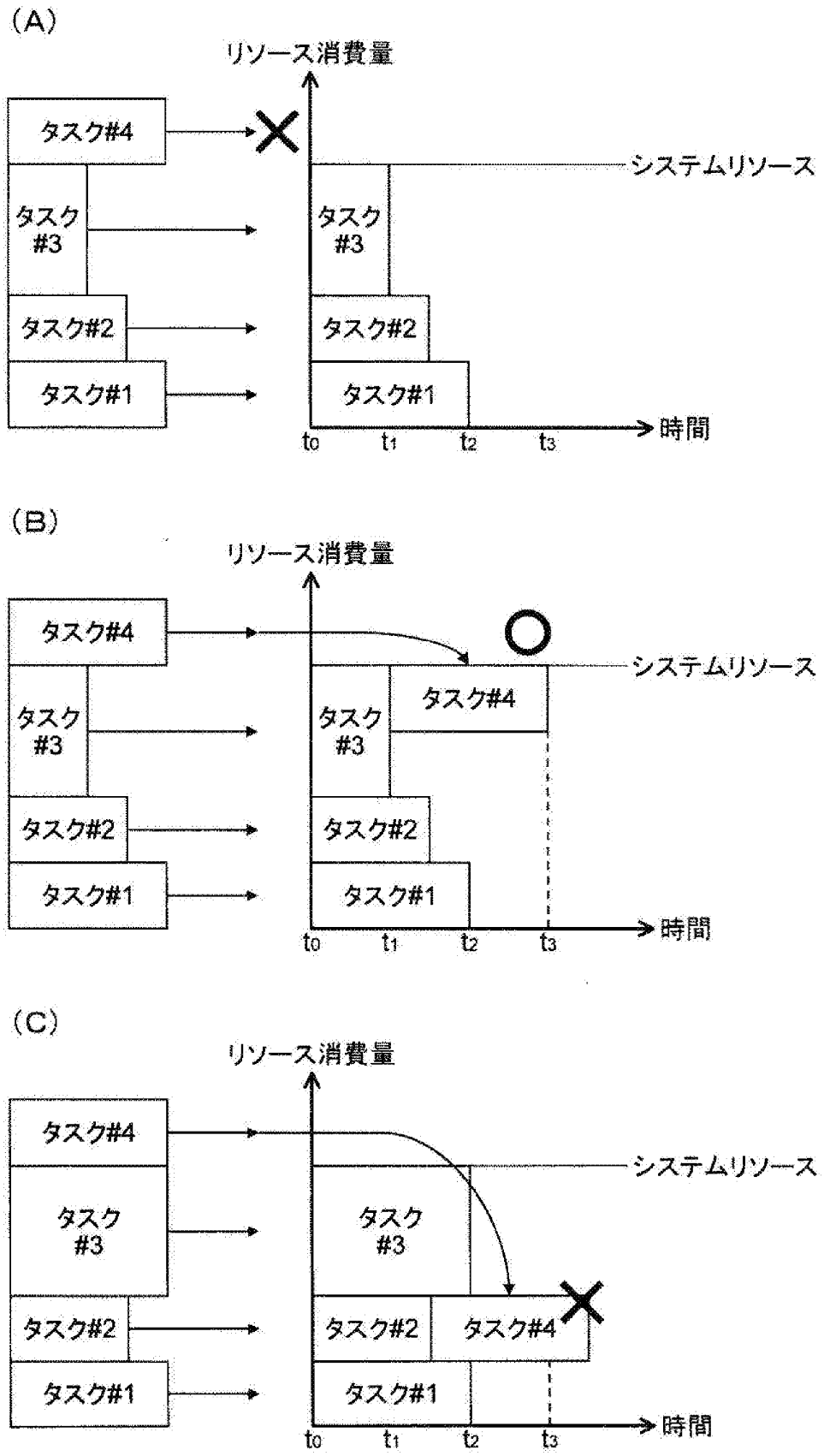
Although the present embodiment has been described above

, it is a matter of course that the present invention can be modified in various ways within th e spirit and scope of the invention. 100

System 110 Master node 111 Client communication unit 112 Schedule processing unit 113 Schedule information storage unit 114 Scale-out processing unit 115 Slave communic ation unit 116 Reschedule processing unit 117 Scale shrink processing unit 120 Slave nod e 121 Master Communication unit 122 Application 200 Client 300 Network

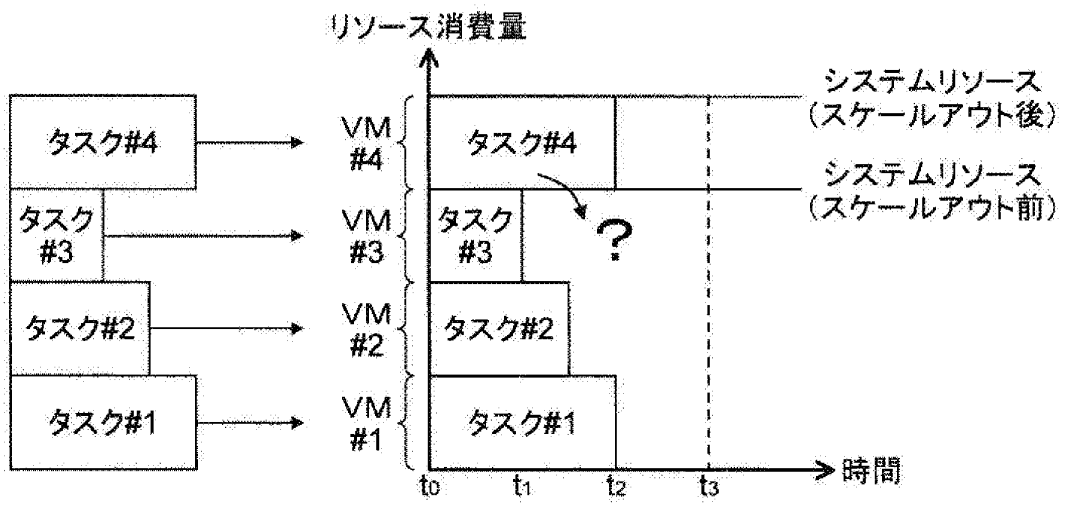
drawing open —

[Fig. 1]

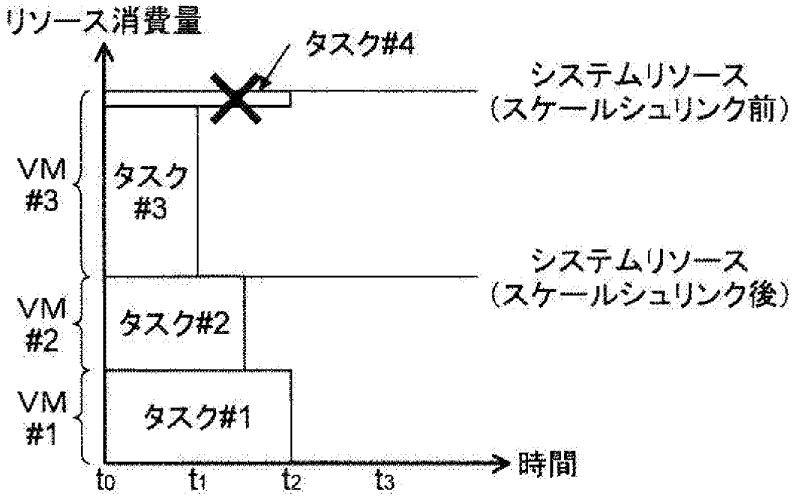

(A)
リソース消費量
タスク#4
タスク#3
タスク#2
タスク#1
システムリソース
タスク#3
タスク#2
タスク#1
時間
t0
t1
t2
t3
(B)
リソース消費量
タスク#4
タスク#3
タスク#2
タスク#1
システムリソース
タスク#4
タスク#3
タスク#2
タスク#1
時間
t0
t1
t2
t3
(C)
リソース消費量
タスク#4
タスク#3
タスク#2
タスク#1
システムリソース
タスク#3
タスク#2
タスク#4
タスク#1
時間
t0
t1
t2
t3

[Figure 2]

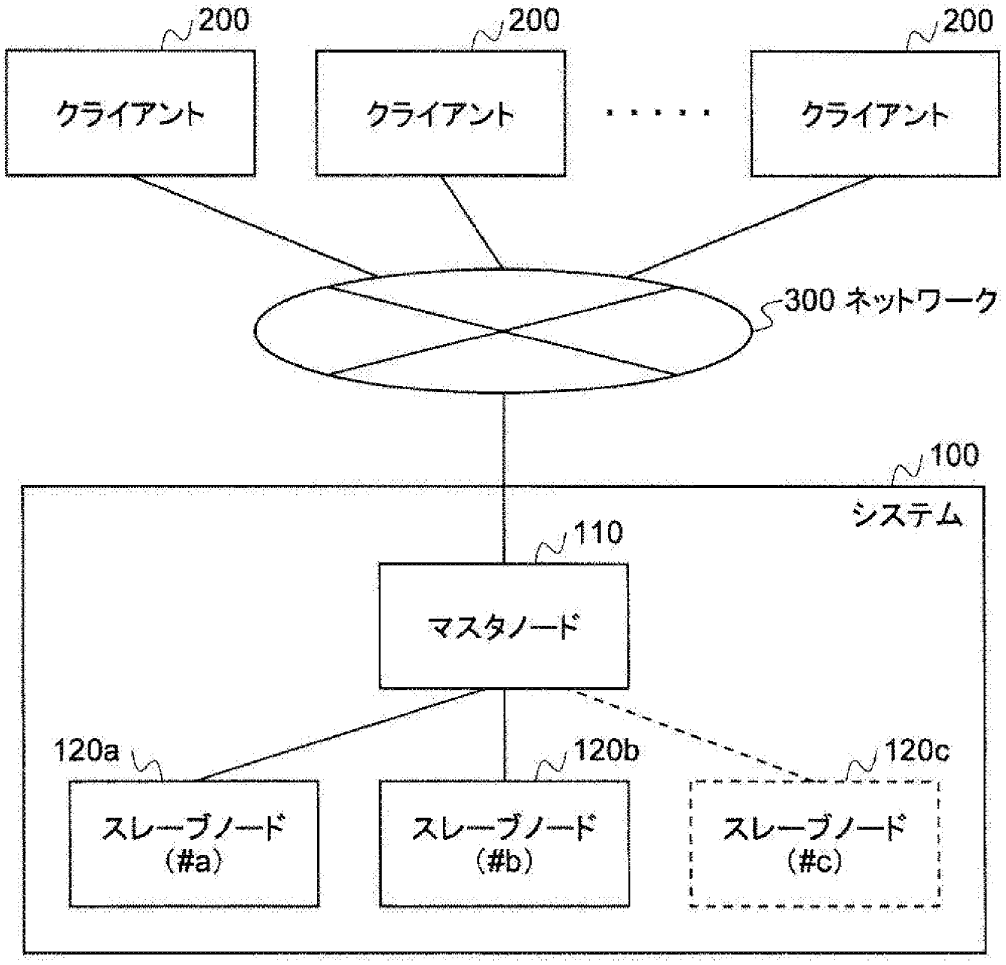
（A）


リソース消費量
タスク#4
タスク
#3
タスク#2
タスク#1
VM
#4
VM
#3
VM
#2
VM
#1
タスク#4
タスク
#3
?
タスク#2
タスク#1
システムリソース
（スケールアウト後）
システムリソース
（スケールアウト前）
時間
t0
t1
t2
t3

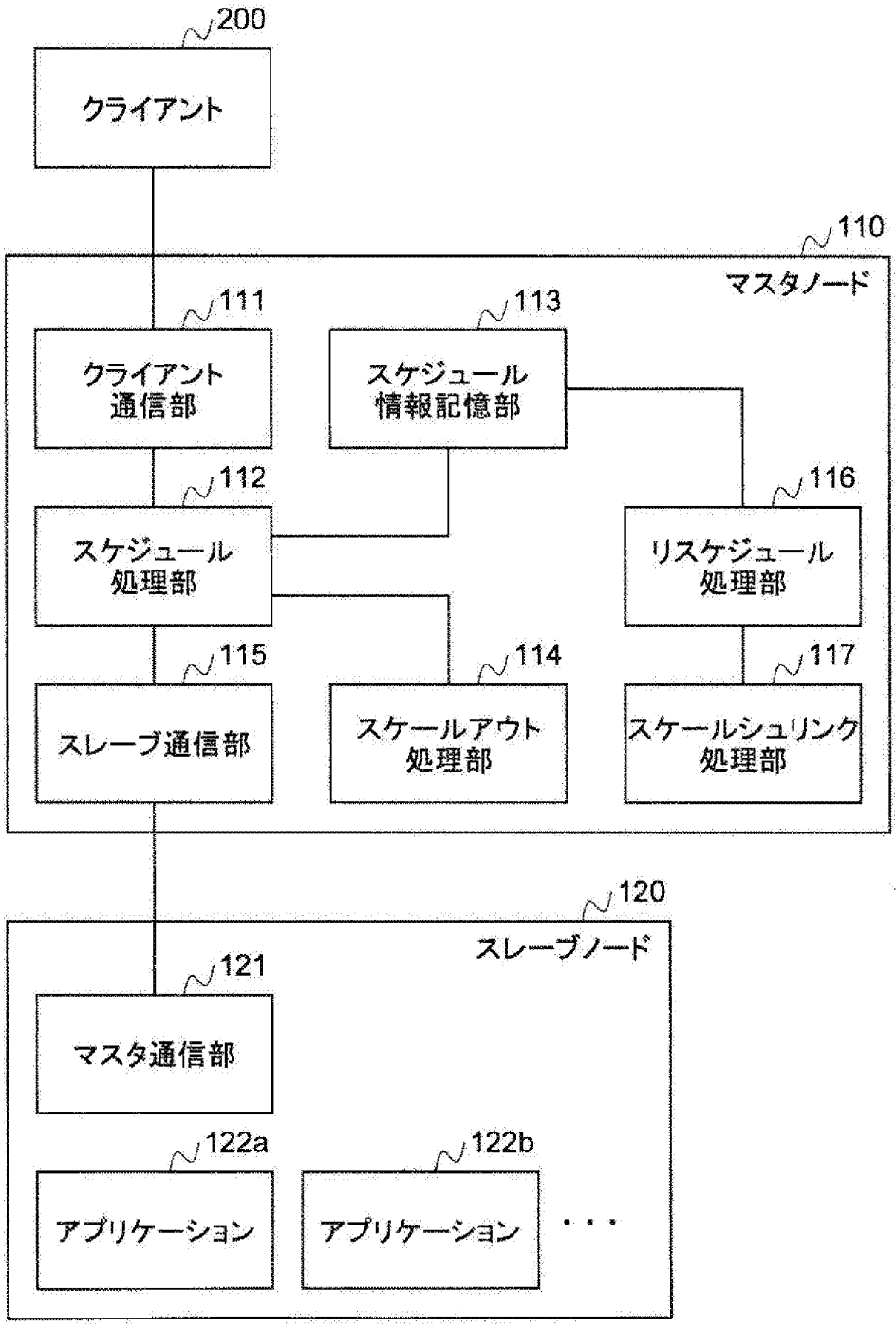
（B）


リソース消費量
タスク#4
システムリソース
（スケールシュリンク前）
VM
#3
タスク
#3
システムリソース
（スケールシュリンク後）
VM
#2
タスク#2
VM
#1
タスク#1
時間
t0
t1
t2
t3

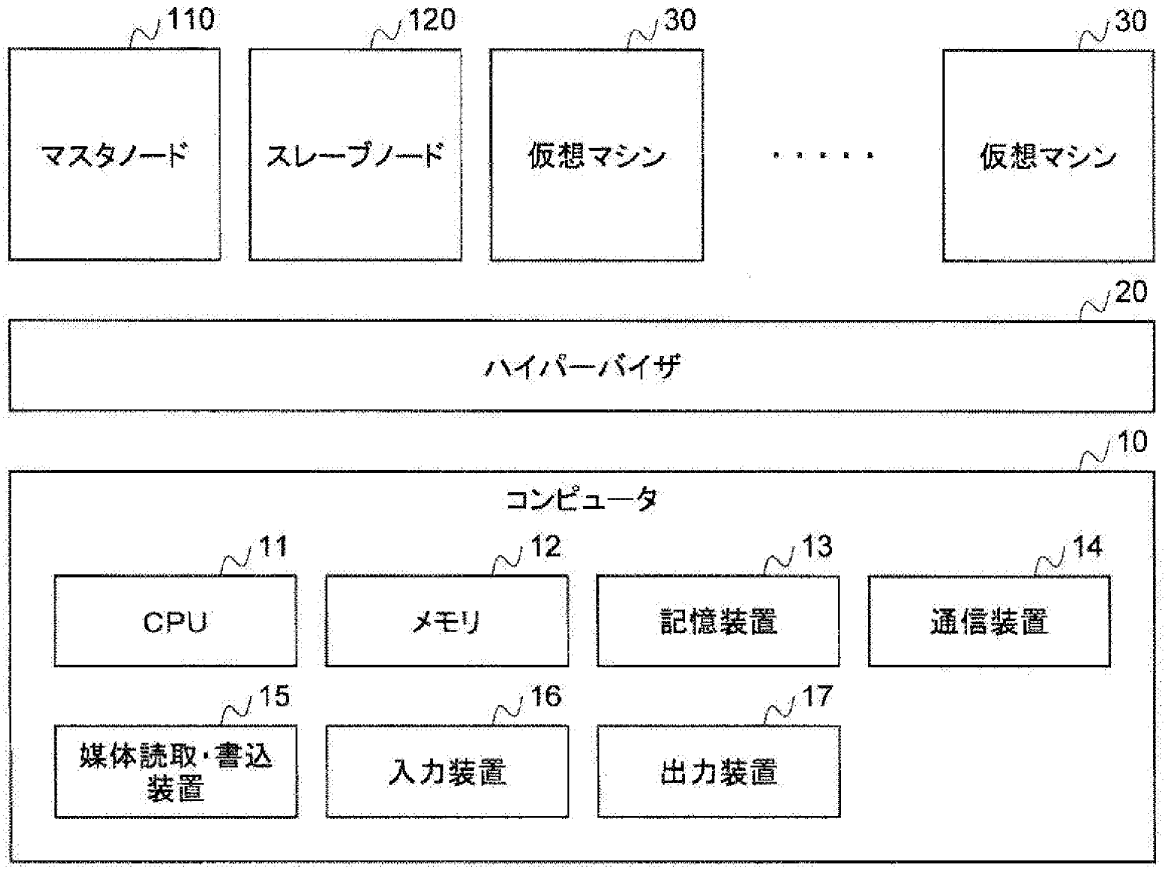
[Figure 3]


200
クライアント
200
クライアント
・・・・・
200
クライアント
300 ネットワーク
100
システム
110
マスタノード
120a
スレーブノード
(#a)
120b
スレーブノード
(#b)
120c
スレーブノード
(#c)

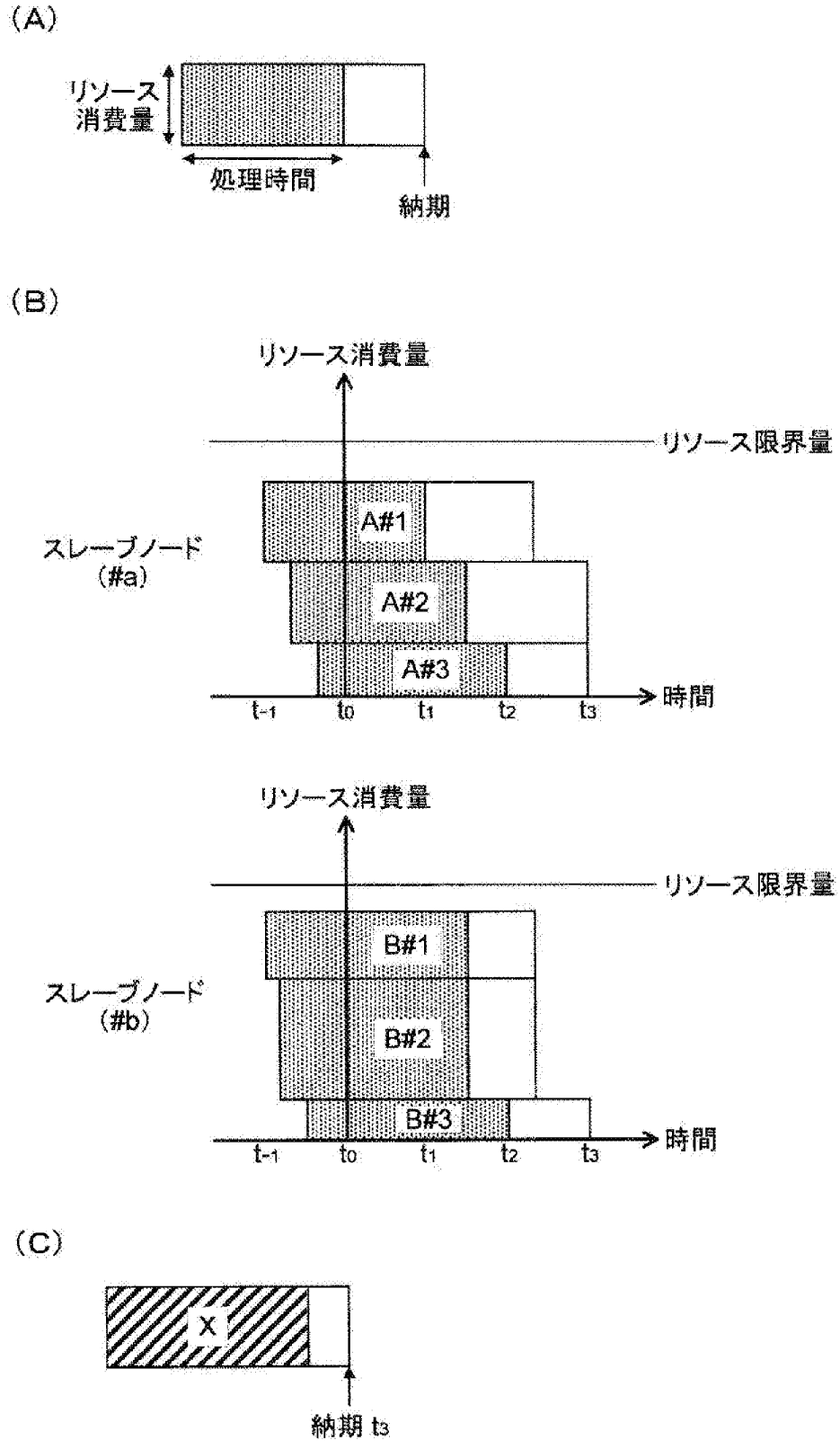
[Figure 4]


200
クライアント
110
マスタノード
111
クライアント
通信部
113
スケジュール
情報記憶部
112
スケジュール
処理部
116
リスケジュール
処理部
115
スレーブ通信部
114
スケールアウト
処理部
117
スケールシュリンク
処理部
120
スレーブノード
121
マスタ通信部
122a
アプリケーション
122b
アプリケーション
・・・

[Figure 5]

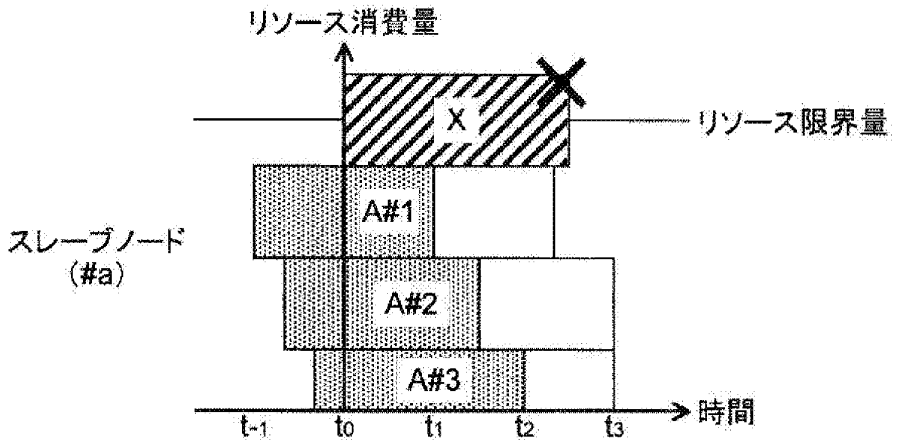

110
120
30
30
マスタノード
スレーブノード
仮想マシン
・・・・・
仮想マシン
20
ハイパーバイザ
10
コンピュータ
11
12
13
14
CPU
メモリ
記憶装置
通信装置
15
16
17
媒体読取・書込装置
入力装置
出力装置

[Fig. 6]

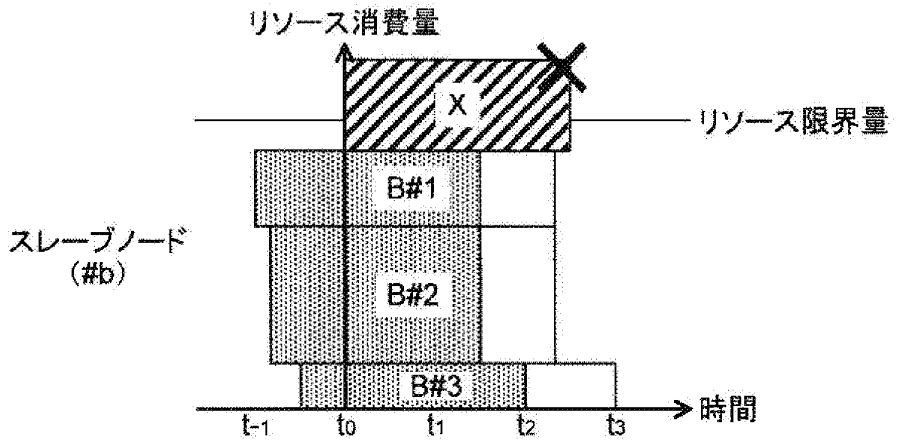

(A)
リソース
消費量
処理時間
納期
(B)
リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
t-1
t0
t1
t2
t3
(C)
X
納期 t3

[Fig. 7]

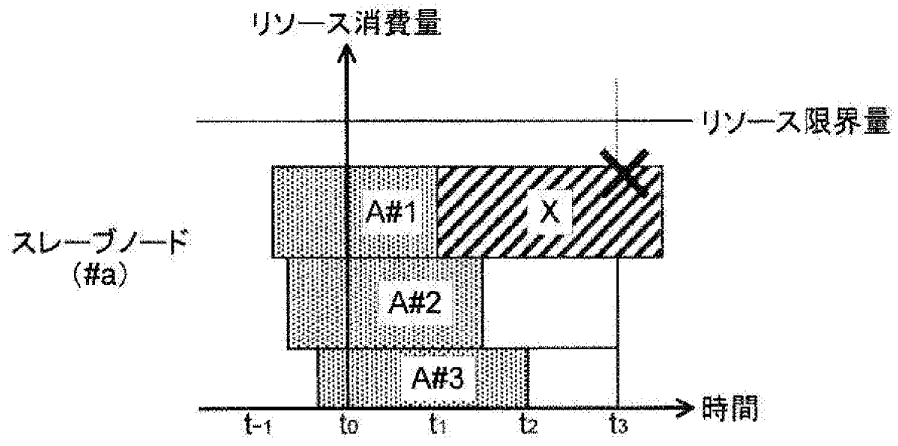
（A）


リソース消費量
X
リソース限界量
スレーブノード
（#a）
A#1
A#2
A#3
時間
t-1
t0
t1
t2
t3

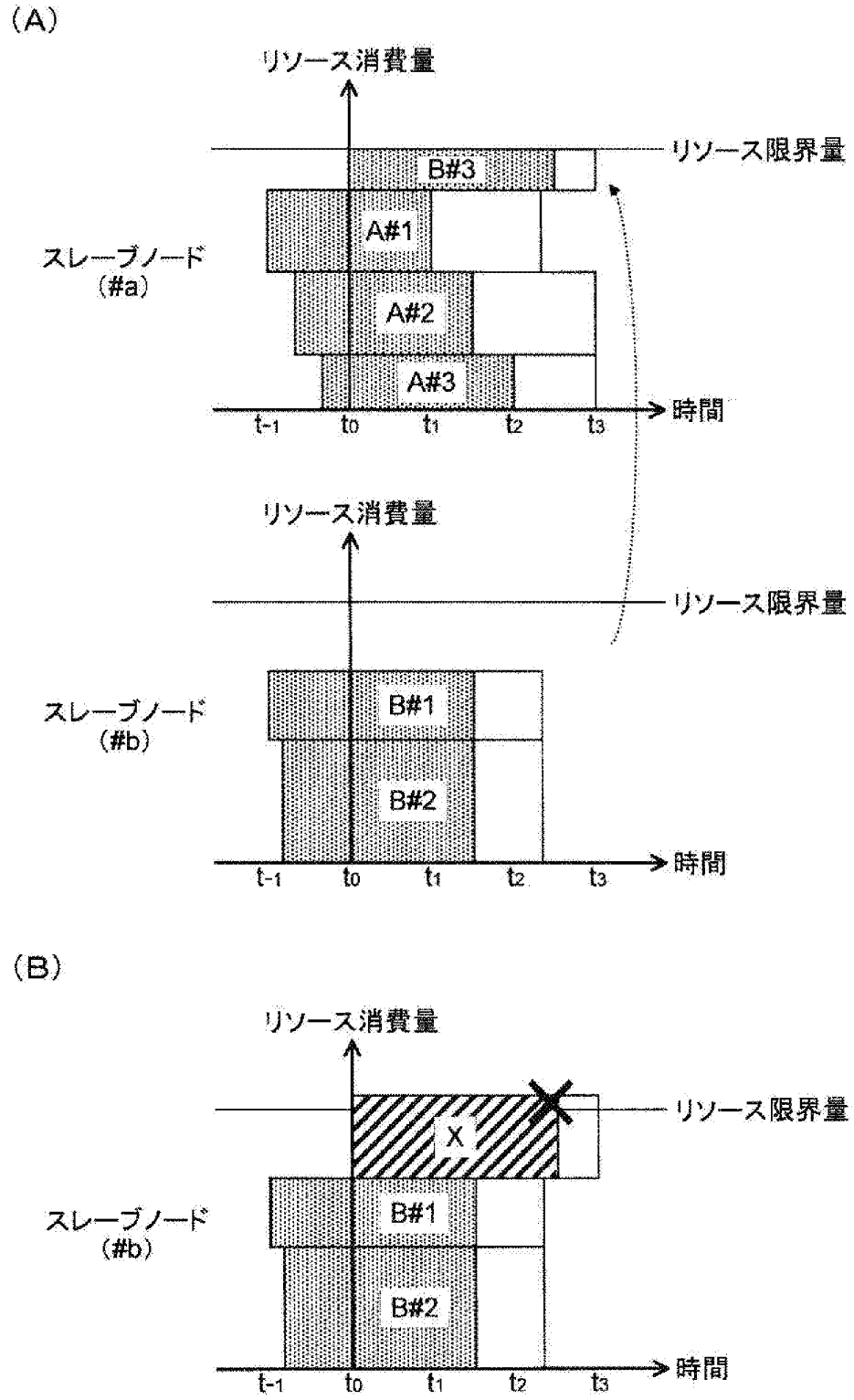
（B）


リソース消費量
X
リソース限界量
スレーブノード
（#b）
B#1
B#2
B#3
時間
t-1
t0
t1
t2
t3

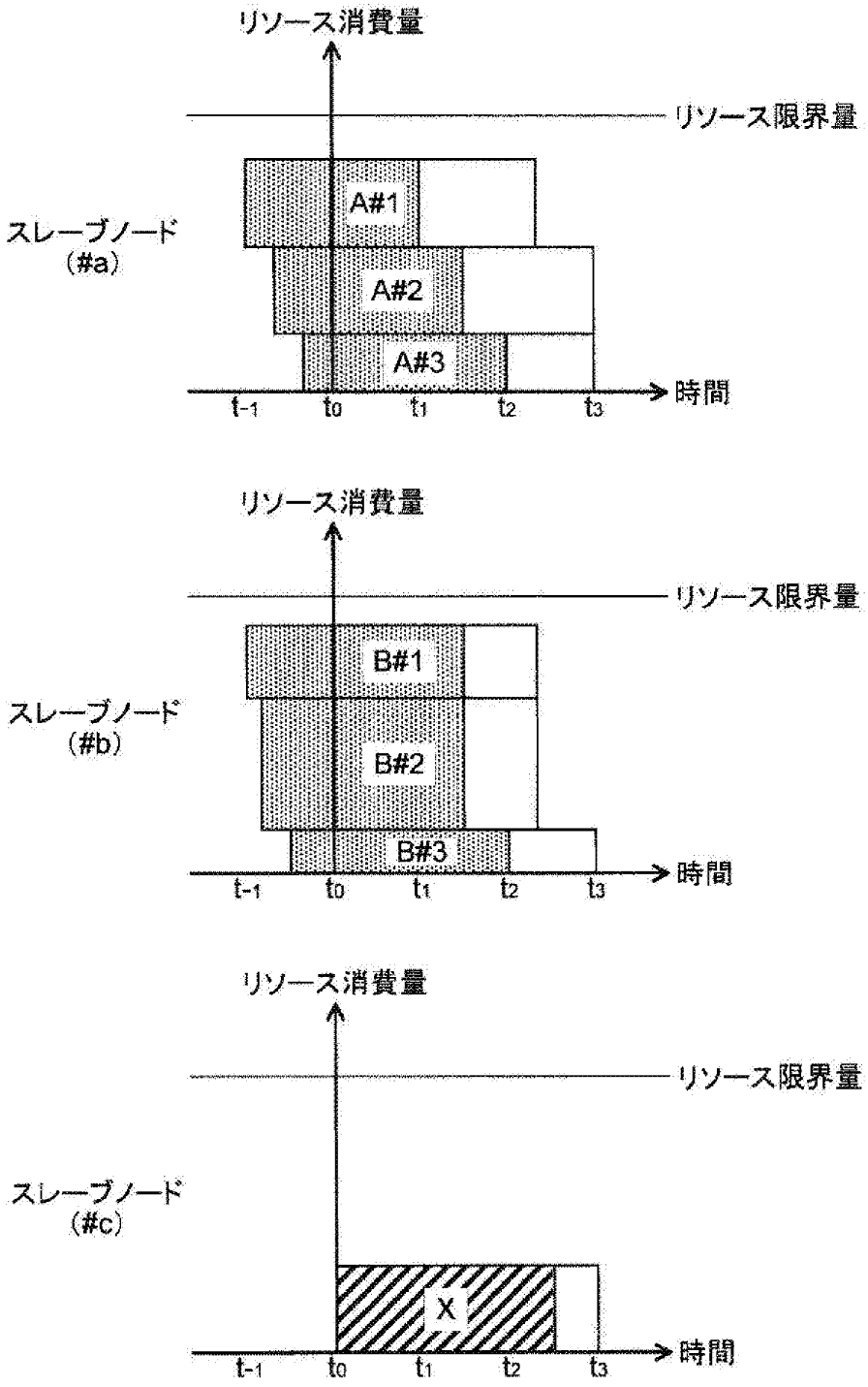
（C）


リソース消費量
リソース限界量
スレーブノード
（#a）
A#1
X
A#2
A#3
時間
t-1
t0
t1
t2
t3

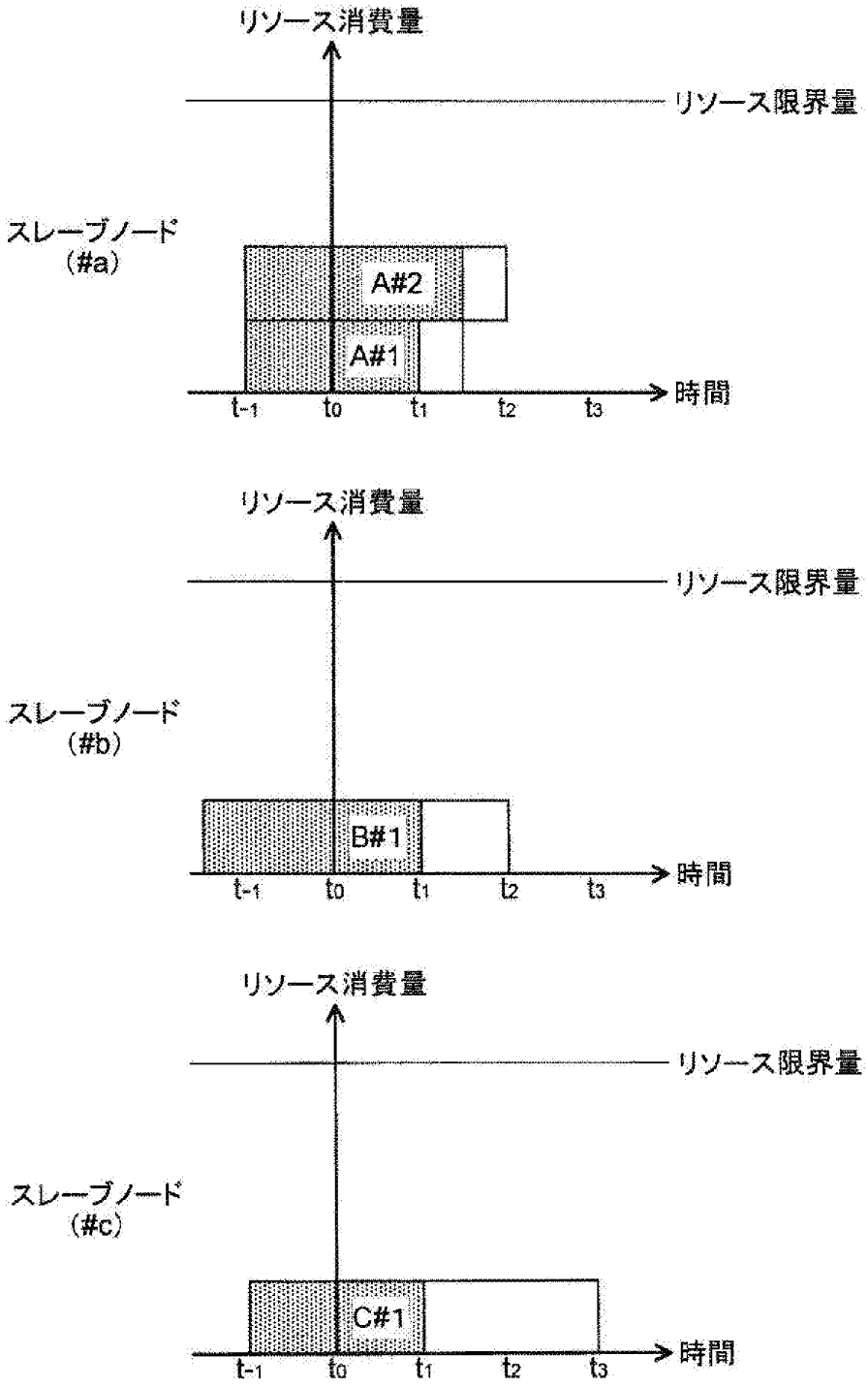
[Fig. 8]


(A)
リソース消費量
リソース限界量
B#3
A#1
スレーブノード
(#a)
A#2
A#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
時間
t-1
t0
t1
t2
t3
(B)
リソース消費量
リソース限界量
X
スレーブノード
(#b)
B#1
B#2
時間
t-1
t0
t1
t2
t3

[Fig. 9]

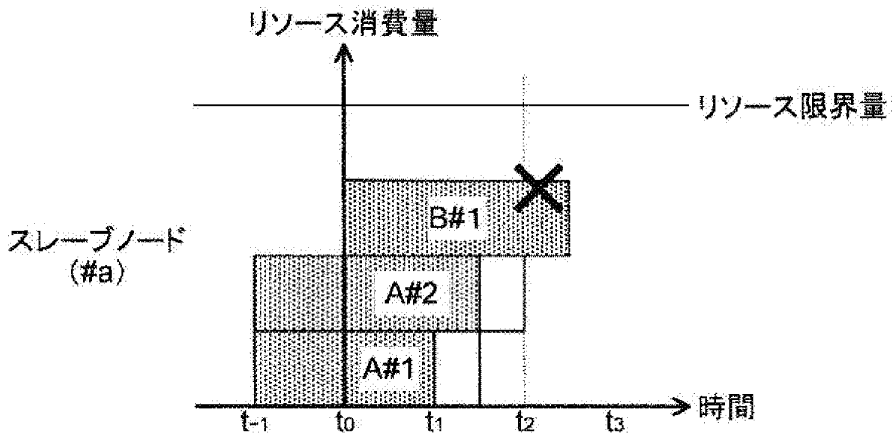

リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#c)
X
時間
t-1
t0
t1
t2
t3

[Fig. 10]

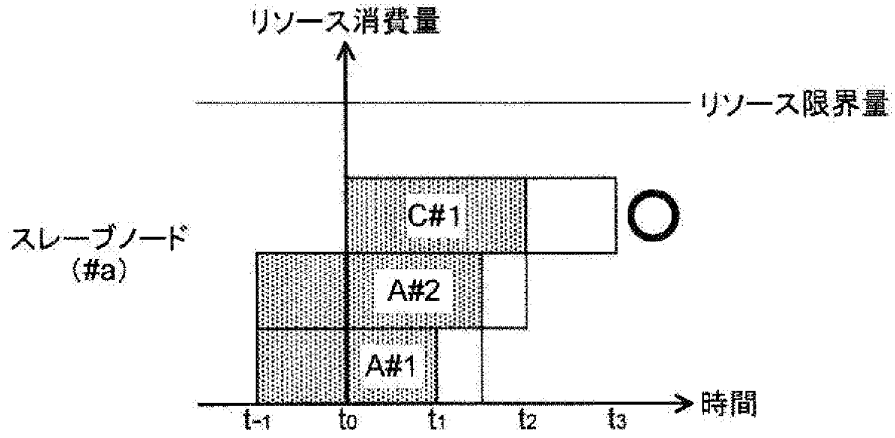

リソース消費量
リソース限界量
スレーブノード
(#a)
A#2
A#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#c)
C#1
時間
t-1
t0
t1
t2
t3

[Fig. 11]

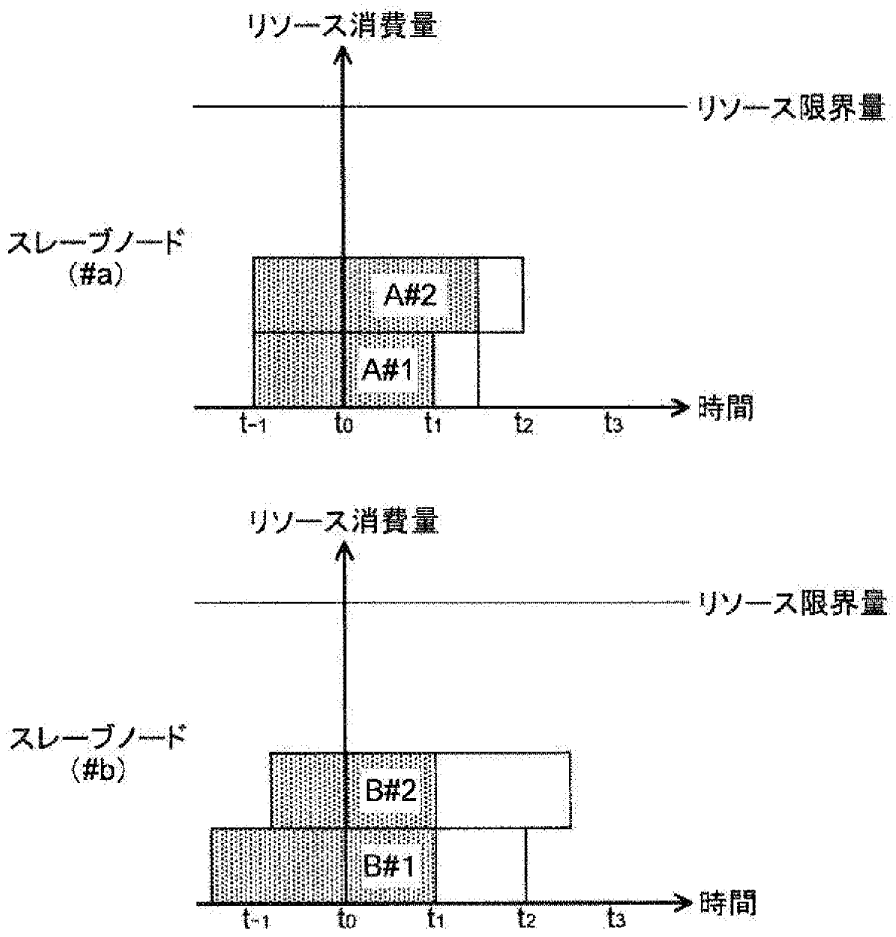
（A）


リソース消費量
リソース限界量
スレーブノード
（#a）
B#1
A#2
A#1
時間
t-1
t0
t1
t2
t3

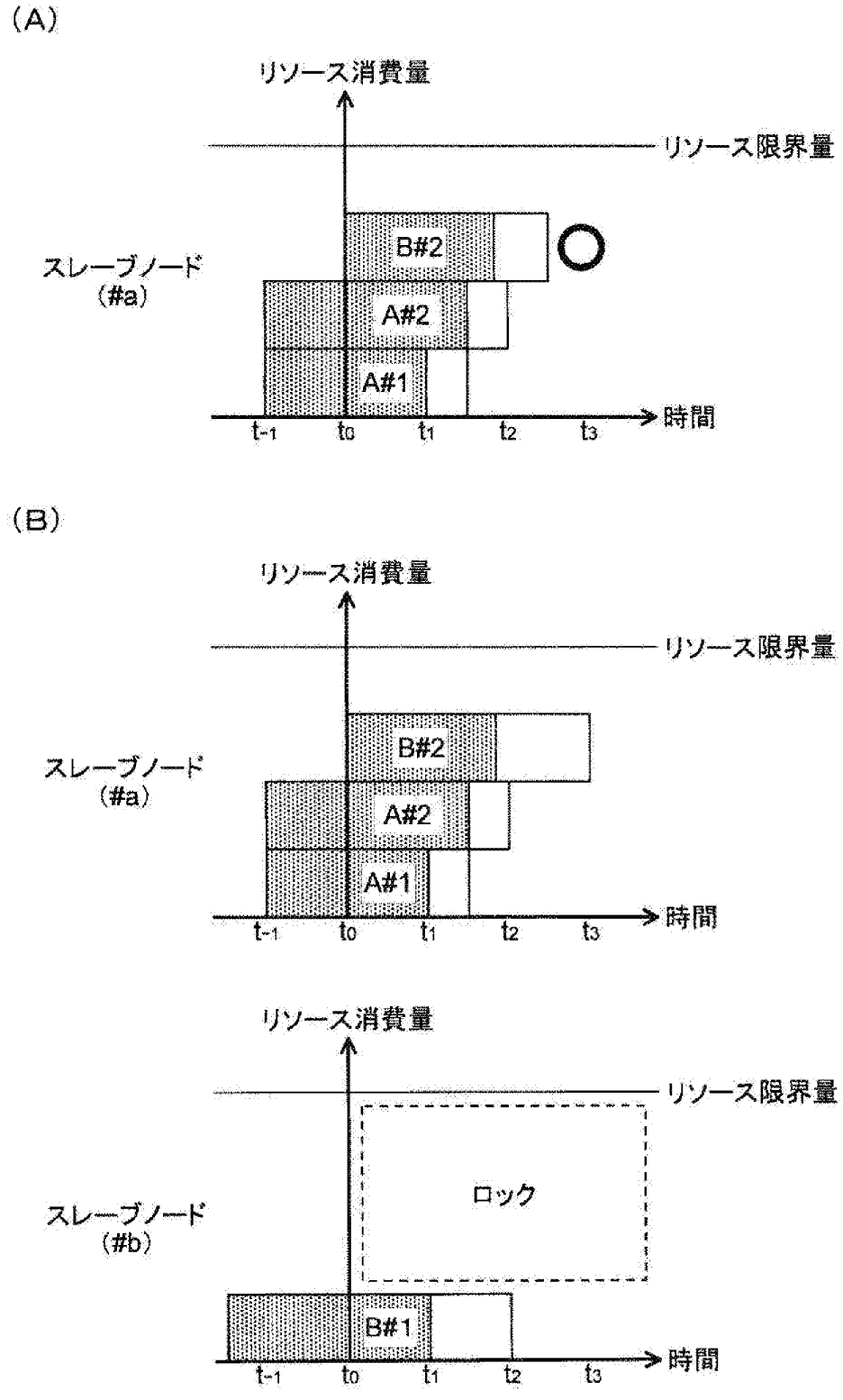
（B）


リソース消費量
リソース限界量
スレーブノード
（#a）
C#1
A#2
A#1
時間
t-1
t0
t1
t2
t3

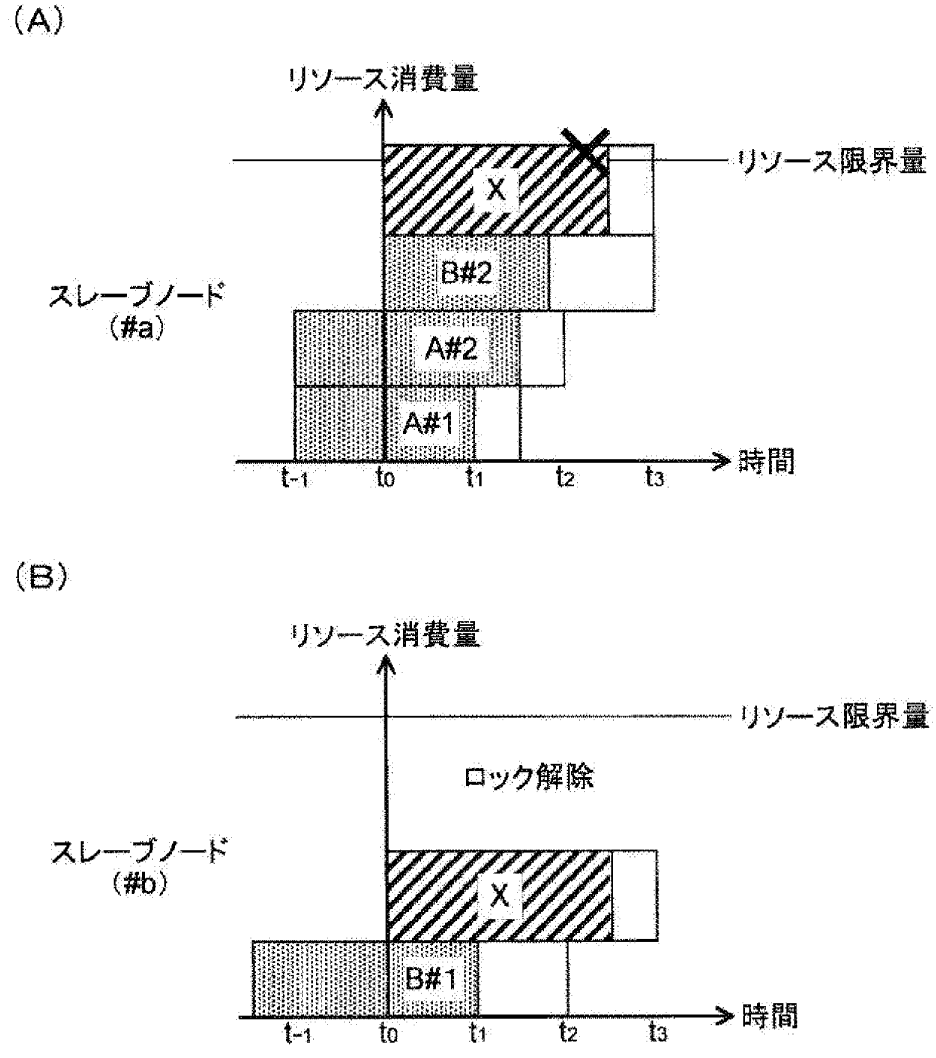
[Fig. 12]


リソース消費量
リソース限界量
スレーブノード
(#a)
A#2
A#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#2
B#1
時間
t-1
t0
t1
t2
t3

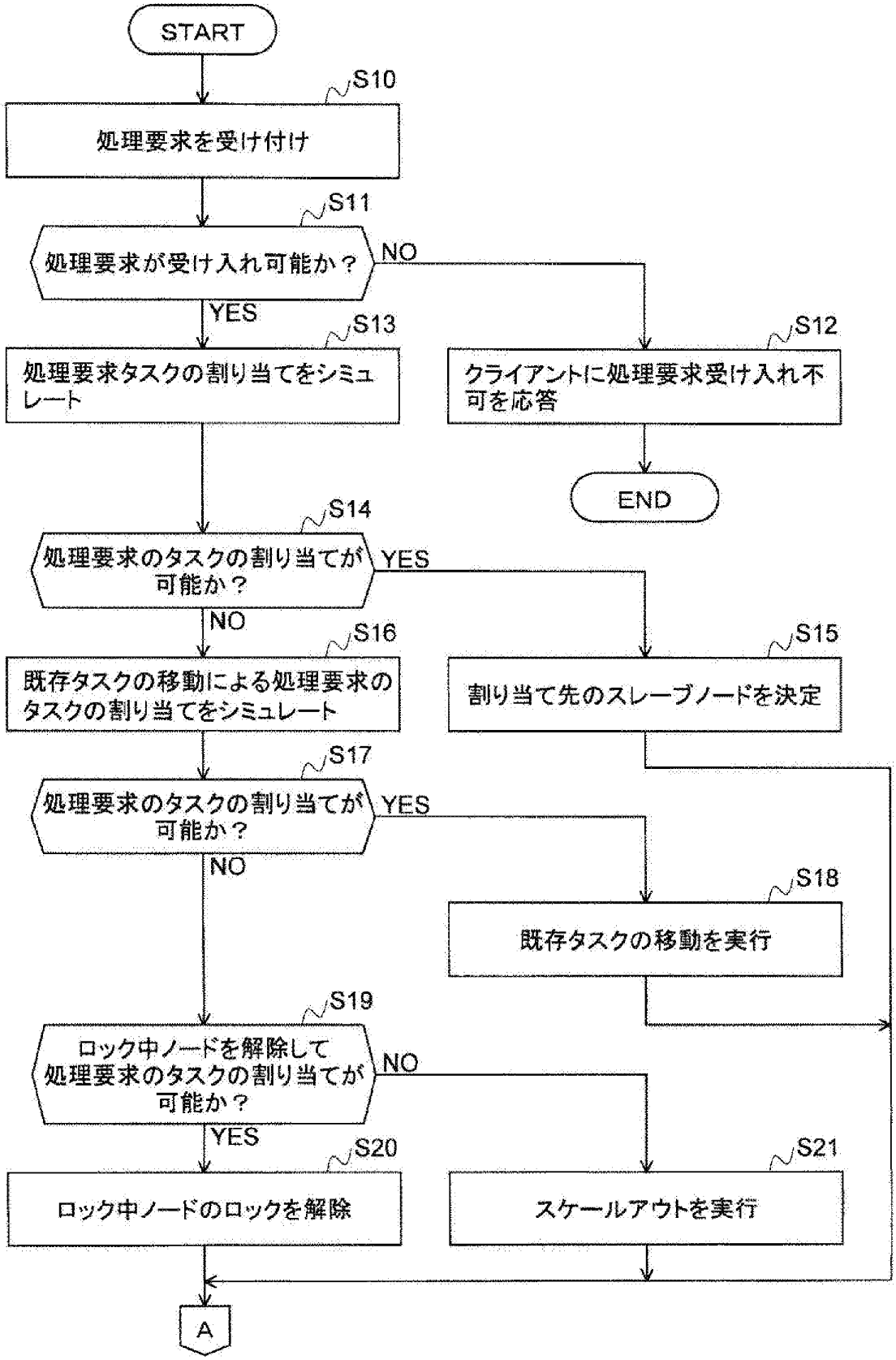
[Fig. 13]


(A)
リソース消費量
リソース限界量
スレーブノード
(#a)
B#2
A#2
A#1
時間
t-1
t0
t1
t2
t3
(B)
リソース消費量
リソース限界量
スレーブノード
(#a)
B#2
A#2
A#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
ロック
B#1
時間
t-1
t0
t1
t2
t3

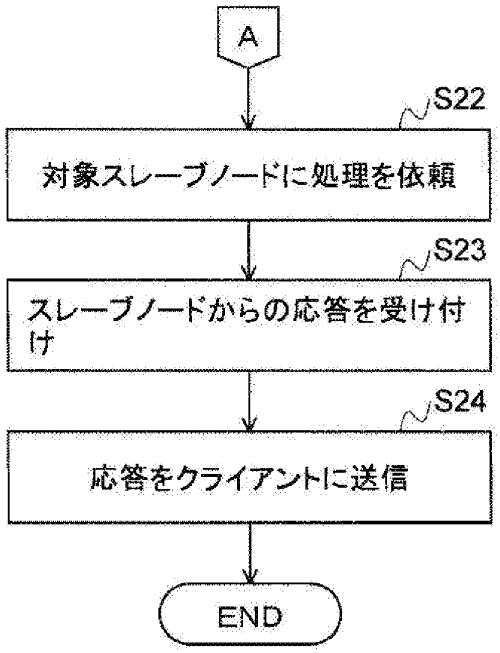
[Fig. 14]


(A)
リソース消費量
リソース限界量
X
B#2
スレーブノード
(#a)
A#2
A#1
時間
t-1
t0
t1
t2
t3
(B)
リソース消費量
リソース限界量
ロック解除
スレーブノード
(#b)
X
B#1
時間
t-1
t0
t1
t2
t3

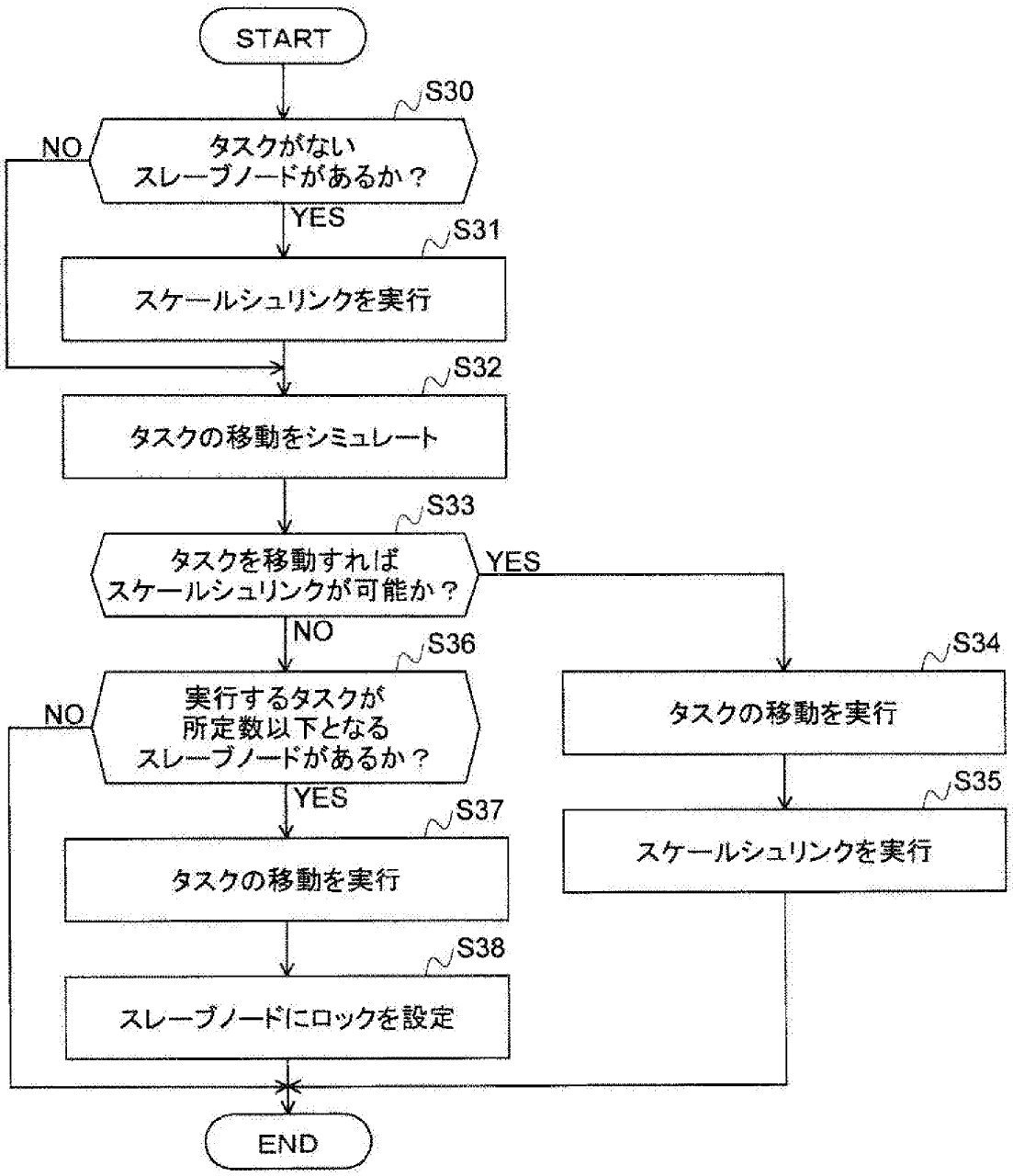
[Fig. 15]


START
S10
処理要求を受け付け
S11
処理要求が受け入れ可能か？
NO
YES
S13
処理要求タスクの割り当てをシミュレート
S12
クライアントに処理要求受け入れ不可を応答
END
S14
処理要求のタスクの割り当てが可能か？
YES
NO
S16
既存タスクの移動による処理要求のタスクの割り当てをシミュレート
S15
割り当て先のスレーブノードを決定
S17
処理要求のタスクの割り当てが可能か？
YES
NO
S18
既存タスクの移動を実行
S19
ロック中ノードを解除して処理要求のタスクの割り当てが可能か？
NO
YES
S20
ロック中ノードのロックを解除
S21
スケールアウトを実行
A

[Fig. 16]


A
S22
対象スレーブノードに処理を依頼
S23
スレーブノードからの応答を受け付け
S24
応答をクライアントに送信
END

[Fig. 17]


START
S30
タスクがない
スレーブノードがあるか？
NO
YES
S31
スケールシュリンクを実行
S32
タスクの移動をシミュレート
S33
タスクを移動すれば
スケールシュリンクが可能か？
YES
NO
S34
タスクの移動を実行
S35
スケールシュリンクを実行
S36
実行するタスクが
所定数以下となる
スレーブノードがあるか？
NO
YES
S37
タスクの移動を実行
S38
スレーブノードにロックを設定
END

drawing open

1 2 3 Four Five 6 7 8 9 Ten ...

Magnify and Rotate

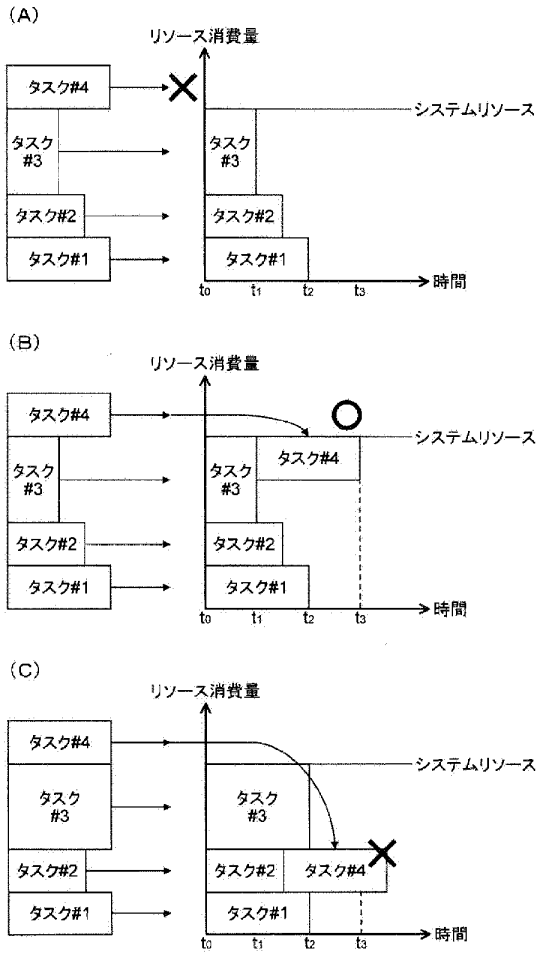


Figure 1

1 / 1 display

Copyright JPO and INPIT (P0200)

Espacenet

Bibliographic data: JP5867238 (B2) — 2016-02-24

AUTOSCALING METHOD, AUTOSCALING PROGRAM AND COMPUTER NODE

Inventor(s): SATO KIYONOBU, ; SHINOZAKI KAZUMI, ; KUBOTA HIROAKI, ; 佐藤 清伸, ; 篠崎 和美, ; 久保田 博昭

Applicant(s): FUJITSU LTD, ; 富士通株式会社

Classification: **- international:** ***G06F9/50***
- cooperative:

Application number: JP20120078501 20120330 Global Dossier

Priority number(s): JP20120078501 20120330

Also published as: JP2013210683 (A)

Abstract of JP2013210683 (A)

PROBLEM TO BE SOLVED: To provide a technology for allowing application of a system with excellent efficiency of charging.SOLUTION: A master node 110 manages tasks to be executed by the respective slave nodes 120. A schedule information storage part 113 stores management information for managing the tasks to be executed by the respective slave nodes 120. A schedule processing part 112 verifies whether or not there is a slave node 120 capable of terminating processing of a task of a processing request in a delivery. In addition, the schedule processing part 112 verifies whether or not a computer node capable of terminating processing of the task of the processing request can be prepared in the delivery when a task whose processing can be terminated even by other computer nodes is moved. As results of verification, when both are negative, a scale out processing part 114 increases the slave nodes 120 by scale out.

(19)日本国特許庁(JP)　(12)特　許　公　報(B2)　(11)特許番号
特許第5867238号
(P5867238)
(45)発行日　平成28年2月24日(2016.2.24)　(24)登録日　平成28年1月15日(2016.1.15)

(51)Int.Cl.　F I
G06F 9/50 (2006.01)　G06F 9/46 462A

請求項の数 6　(全 22 頁)

(21)出願番号　特願2012-78501(P2012-78501)
(22)出願日　平成24年3月30日(2012.3.30)
(65)公開番号　特開2013-210683(P2013-210683A)
(43)公開日　平成25年10月10日(2013.10.10)
審査請求日　平成27年1月6日(2015.1.6)

(73)特許権者　000005223
富士通株式会社
神奈川県川崎市中原区上小田中４丁目１番１号
(74)代理人　100111822
弁理士　渡部　章彦
(74)代理人　100119161
弁理士　重久　啓子
(72)発明者　佐藤　清伸
神奈川県川崎市中原区上小田中４丁目１番１号　富士通株式会社内
(72)発明者　篠崎　和美
神奈川県川崎市中原区上小田中４丁目１番１号　富士通株式会社内

最終頁に続く

(54)【発明の名称】オートスケーリング方法，オートスケーリングプログラムおよびコンピュータノード

(57)【特許請求の範囲】
【請求項１】
要求された処理を複数の仮想化されたコンピュータノードに分散して実行するシステムにおいて，該システムで実行するタスクの管理を行うコンピュータノードが，
納期が指定された処理要求を受け付けた際に，記憶部に記憶された，前記システムが備えるコンピュータノードが実行するタスクを管理する管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行し，
前記割り当てのシミュレーションにより，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムのコンピュータノードの数を増加する処理を実行する
ことを特徴とするオートスケーリング方法。
【請求項２】
前記タスクの管理を行うコンピュータノードが，さらに，
前記管理情報を参照して，あるコンピュータノードで動作するタスクを，他のコンピュータノードに移動するシミュレーションを実行し，
前記移動のシミュレーションにより，他のコンピュータノードでも納期内に処理終了可能なタスクを移動して，実行するタスクがないコンピュータノードを用意できると判定された場合に，該他のコンピュータノードでも納期内に処理終了可能なタスクを移動し，

実行するタスクがないコンピュータノードを前記システムから削除する処理とを実行する
ことを特徴とする請求項１に記載のオートスケーリング方法。
【請求項３】
前記タスクの管理を行うコンピュータノードが，さらに，
前記移動のシミュレーションにより，他のコンピュータノードでも納期内に処理終了可能なタスクを移動して，実行するタスクの数が所定数以下となるコンピュータノードを用意できると判定された場合に，該他のコンピュータノードでも納期内に処理終了可能なタスクを移動し，
実行するタスクの数が所定数以下のコンピュータノードを処理要求のタスクの割り当て対象外に設定する処理を実行する
ことを特徴する請求項２に記載のオートスケーリング方法。
【請求項４】
前記システムにコンピュータノードを増設する処理では，さらに，前記処理要求のタスクの割り当て対象外に設定されたコンピュータノードの設定を解除しても，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムにコンピュータノードを増設する
ことを特徴とする請求項３に記載のオートスケーリング方法。
【請求項５】
要求された処理を複数の仮想化されたコンピュータノードに分散して実行するシステムにおいて，該システムで実行するタスクの管理を行うコンピュータノードに，
納期が指定された処理要求を受け付けた際に，記憶部に記憶された，前記システムが備えるコンピュータノードが実行するタスクを管理する管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行し，
前記割り当てのシミュレーションにより，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムのコンピュータノードの数を増加する
処理を実行させるためのオートスケーリングプログラム。
【請求項６】
複数の仮想化されたコンピュータノードを備えるシステムにおいて，該システムで実行されるタスクの管理を行うコンピュータノードであって，
前記システムが備えるコンピュータノードが実行するタスクを管理する管理情報の記憶部と，
納期が指定された処理要求を受け付けた際に，前記管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行するスケジュール処理部と，
前記スケジュール処理部により，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムのコンピュータノードの数を増加する処理を実行するスケールアウト処理部とを備える
ことを特徴とするコンピュータノード。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は，システムが備えるコンピュータノード数を制御するオートスケーリング方法，オートスケーリングプログラムおよびコンピュータノードに関するものである。
【背景技術】

【０００２】
従来のオンプレミスのシステムでは，システムが持つリソース量が固定であったので，そのシステムが持つリソース量を超えて，クライアントからの処理要求を受け付けることができなかった。
【０００３】
これに対して，近年発展しているクラウドコンピューティングを利用したシステムでは，システムが持つリソース量を動的に変更可能である。そのため，クライアントから要求される処理を実行することによってシステムのリソース消費量がシステムが持つリソース量を超えてしまうような場合でも，システムのリソースを動的に増やすことで，クライアントからの要求を受け付け可能となる。
【０００４】
このようなシステムのリソースを増減する技術として，システムにおける仮想化されたコンピュータノードのリソース量を増減するスケールアップ・スケールダウンと呼ばれる技術がある。しかし，仮想化されたコンピュータノードのリソースの増加には，物理マシンのリソース量の限界がある。
【０００５】
システムのリソースを増減する別の技術として，システムにおけるコンピュータノードの数を増減するスケールアウト・スケールシュリンクと呼ばれる技術がある。この技術では，システムのリソース量の増加に，物理マシンのリソース量の限界がない。システムのリソース消費率に応じて自動でスケールアウト・スケールシュリンクを行う，オートスケーリングと呼ばれる技術もある。
【０００６】
なお，分散バッチシステムにおいて，新たなバッチ処理が要求された際に，ある処理サーバで実行中のバッチ処理を他のサーバに移行し，処理可能となったサーバで新しいバッチ処理を実行することで，バッチ処理のデッドラインを管理する技術が知られている。
【先行技術文献】
【特許文献】
【０００７】
【特許文献１】特開２００２－３４２０９８号公報
【発明の概要】
【発明が解決しようとする課題】
【０００８】
しかし，上述のように，システムのリソース消費率に応じてオートスケーリングを行うと，スケールアウトによって無駄なコンピュータノードが増設されたり，誤ったスケールシュリンクによってシステムが実行中の処理が強制的に中断される場合がある。クラウドコンピューティングにおいて，コンピュータノードの数に応じた従量課金が行われる場合には，無駄なスケールアウトによって無駄な課金が発生してしまう場合がある。
【０００９】
一側面では，本発明は，課金の効率がよいシステムの運用が可能となる技術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】
【００１０】
１態様では，オートスケーリング方法では，要求された処理を複数の仮想化されたコンピュータノードに分散して実行するシステムにおいて，該システムで実行するタスクの管理を行うコンピュータノードが，納期が指定された処理要求を受け付けた際に，記憶部に記憶されたシステムが備えるコンピュータノードが実行するタスクを管理する管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行し，割り当てのシミュレーションにより，処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても処理要求のタスクを納期内に処理終了可能なコンピュータノードを用

意できないと判定された場合に，システムのコンピュータノードの数を増加する処理を実行する。

【発明の効果】

【００１１】

１態様では，課金の効率がよいシステムの運用が可能となる。

【図面の簡単な説明】

【００１２】

【図１】オンプレミスで実現されるシステムの課題を説明する図である。

【図２】クラウドコンピューティングで実現されるシステムの課題を説明する図である。

【図３】本実施の形態によるシステムの構成例を示す図である。

【図４】本実施の形態による各ノードの機能構成例を示す図である。

【図５】本実施の形態によるノードを実現する仮想マシンシステムの例を示す図である。

【図６】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図７】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図８】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図９】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図１０】本実施の形態のマスタノードにおけるリスケジュール処理部によるタスクの移動シミュレーションの例を説明する図である。

【図１１】本実施の形態のマスタノードにおけるリスケジュール処理部によるタスクの移動シミュレーションの例を説明する図である。

【図１２】本実施の形態のマスタノードにおけるリスケジュール処理部によるスレーブノードにロック設定を行う例を説明する図である。

【図１３】本実施の形態のマスタノードにおけるリスケジュール処理部によるスレーブノードにロック設定を行う例を説明する図である。

【図１４】本実施の形態のマスタノードにおけるスケジュール処理部によるスレーブノードのロック解除を行う例を説明する図である。

【図１５】本実施の形態のマスタノードによる処理要求受け付け時の処理フローチャートである。

【図１６】本実施の形態のマスタノードによる処理要求受け付け時の処理フローチャートである。

【図１７】本実施の形態のマスタノードによるリスケジュールの処理フローチャートである。

【発明を実施するための形態】

【００１３】

以下，本実施の形態について，図を用いて説明する。

【００１４】

図１は，オンプレミスで実現されるシステムの課題を説明する図である。

【００１５】

図１に示す例において，タスクを示す図形の縦の長さは該タスクのリソース消費量を示し，横の長さは該タスクの処理時間を示す。また，図１に示す例において，グラフの縦軸はシステムのリソース消費量を示し，横軸は時間の経過を示す。t_0 ～ t_3 は，等間隔の時刻を示す。

【００１６】

オンプレミスのシステムでは，システムが持つリソースの量は固定となる。すなわち，あらかじめシステムが持つリソース量を超えたリソース消費量の処理を行うことはできない。図１に示す例において，システムリソースのラインは，システムが持つリソースの量

を示す。

【００１７】

例えば，図１（Ａ）において，システムに対して，タスク＃１～タスク＃４の処理要求が，ほぼ同時刻 t_0 にあったものとする。このとき，システムは，処理要求を受け付けた順，ここではタスク＃１，タスク＃２，タスク＃３，タスク＃４の順に処理を開始する。しかし，図１（Ａ）に示すように，タスク＃３の処理を開始したところで，システムのリソース消費量がシステムが持つリソース量に達してタスク＃４の処理を開始できない状態となり，タスク＃４の処理要求を受け付けられなくなる。

【００１８】

図１（Ｂ）に示す例は，スケジューリングを行うシステムの例である。スケジューリングを行うシステムでは，処理要求を受け付けた時点でタスクの処理時間を見積もり，処理要求が発生した時点でリソースに空きがなくても，実行中の他のタスクの終了後に受け付けた処理要求のタスクを実行するように，タスクのスケジューリングを行う。

【００１９】

例えば，最後に受け付けるタスク＃４の処理の納期が，時刻 t_3 であるものとする。図１（Ｂ）に示すように，最も処理終了時刻が早いタスク＃３の処理終了時刻が t_1 であるので，タスク＃４をタスク＃３の後にスケジュールすれば，タスク＃４の処理終了時刻は t_3 となり，納期に間に合う。この場合，タスク＃４の処理要求は，システムで受け付け可能となる。

【００２０】

ところが，図１（Ｃ）に示す例では，最も処理終了時刻が早いタスク＃２の後にタスク＃４をスケジュールすると，タスク＃４の処理終了時刻は t_3 を超えてしまい，納期に間に合わない。この場合，タスク＃４の処理要求は，システムで受け付けられない。オンプレミスのシステムでは，スケジューリングを行っても，処理要求を受け付けできない場合がある。

【００２１】

このようなオンプレミスの技術の対極に存在するのが，クラウドコンピューティングの技術である。クラウドコンピューティングによって実現されるシステムのリソース量は，可変となる。

【００２２】

クラウドコンピューティングでは，システムが備える各コンピュータノードが，例えば仮想マシン（ＶＭ：Virtual Machine ）で実現される。なお，以下では，システムが備えるコンピュータノードを，単にノードとも呼ぶ。

【００２３】

クラウドコンピューティングにおいて，システムのリソース量を変更する技術として，例えば，スケールアップ・スケールダウンの技術がある。スケールアップは，ノードのリソース量を増加させる技術である。また，スケールダウンは，ノードのリソース量を減少させる技術である。スケールアップの技術を利用すれば，例えば，現状のリソースでは新たな処理要求のタスクを実行しても納期に間に合わないような場合でも，ノードのリソース量を増加させることで，新たな処理要求のタスクを納期に間に合うように実行できるようになる。

【００２４】

しかし，スケールアップ可能なリソースは，仮想マシンであるノードを実現する物理マシンのリソースが上限となるため，ノードのスケールアップには限界がある。また，通常は１つの物理マシン上に複数の仮想マシンのノードが配置されており，物理マシンのリソースを各ノードに配分しきって余剰がない場合には，他のノードの性能を下げることなく特定のノードの性能を上げることは不可能となる。例えば，マルチテナントの環境では，１つの物理マシン上で複数のテナントの仮想マシンを動作することになり，あるテナントの仮想マシンのリソース量を増やすために，他のテナントのリソース量を減らすといったことは，簡単にはできない。よって，スケールアップの技術を用いても，要求された処理

のタスクをすべて納期を保証して実行できるわけではない。

【００２５】

クラウドコンピューティングにおいて，システムのリソース量を変更する技術として，スケールアップ・スケールダウンの技術以外に，スケールアウト・スケールシュリンクの技術がある。スケールアウトは，システムにノードを増設する技術である。スケールシュリンクは，システムからノードを撤去する技術である。スケールアウトの技術を用いれば，ほぼ確実に要求された処理のタスクをすべて納期を保証して実行できるようになる。

【００２６】

ただし，クラウドコンピューティングの世界では，通常はサービス使用料金が従量制となっており，スケールアウトによってシステムが備えるノードの数が増加するにつれて，サービスの使用料金が増えてしまう。

【００２７】

図２は，クラウドコンピューティングで実現されるシステムの課題を説明する図である。

【００２８】

図２に示す例において，タスクを示す図形の縦の長さは該タスクのリソース消費量を示し，横の長さは該タスクの処理時間を示す。また，図２に示す例において，グラフの縦軸はシステムを構成するノードのリソース消費量の合計を示し，横軸は時間の経過を示す。t_0 ～ t_3 は，等間隔の時刻を示す。図２に示す例において，システムリソースのラインは，システムを構成するノードが持つリソースの量の合計を示す。

【００２９】

図２（Ａ）において，システムは，当初，ＶＭ＃１～ＶＭ＃３の３つのノードを備えているものとする。ここで，システムに対して，タスク＃１～タスク＃４の処理要求が，ほぼ同時刻 t_0 にあったものとする。このとき，システムでは，処理要求を受け付けた順，ここではタスク＃１，タスク＃２，タスク＃３，タスク＃４の順に，ノードにタスクが割り当てられ，処理が開始される。しかし，図２（Ａ）に示すように，ＶＭ＃３のノードにタスク＃３の処理を割り当てたところで，システムのすべてのノードのリソース消費量が上限となり，タスク＃４の処理を割り当て可能なノードがなくなる。

【００３０】

このとき，例えば図２（Ａ）に示すように，システムではスケールアウトが行われ，ＶＭ＃４のノードがシステムに増設される。図２（Ａ）に示すように，スケールアウトによってＶＭ＃４のノードがシステムに増設されることで，要求されたタスク＃４の処理が実行可能となる。例えば，クラウドコンピューティングにおいて，仮想マシンやネットワークなどのインフラをサービスとして提供するＩａａＳ（Infrastructure as a Service）ベンダのサービスとして，システムのリソース消費率が所定以上となったときに自動でスケールアウトを行うサービスがある。クラウドコンピューティングにおいて，自動でシステムの拡張／縮小を行う技術は，オートスケーリングとも呼ばれる。

【００３１】

ここで，タスク＃４の処理の納期が時刻 t_3 であるものとする。図２（Ａ）に示すように，最も処理終了時刻が早いタスク＃３の処理終了時刻が t_1 であるので，タスク＃４をタスク＃３の後にスケジュールすれば，タスク＃４の処理終了時刻は t_3 となり，納期に間に合う。

【００３２】

このように，タスクのスケジューリングを行うことができれば，スケールアウトによりＶＭ＃４のノードを増設しなくても，納期に間に合うようにタスク＃４の処理を実行することが可能であった。しかし，このような判断は，上述のＩａａＳのサービスのようにリソース消費を見ただけではできない。上述したように，クラウドコンピューティングでは，ノードが増えるごとに使用料金が増えるため，ノードを増設しなくても納期に間に合うようにタスクの処理を実行できるのであれば，ノードを増設したくないという要望がある。

【００３３】
また，無駄なノードの使用料金を抑えるために，システムで運用されていないと判断されるノードに対するスケールシュリンクが行われ，該ノードがシステムから撤去される。例えば，クラウドコンピューティングにおいて，ＩａａＳベンダのサービスとして，ノードのＣＰＵ（Central Processing Unit ）使用率が所定以下となったときに，該ノードではタスクの処理が行われておらずＯＳなどのミドルウェアしか動作していないと判断し，自動でスケールシュリンクを行うサービスがある。
【００３４】
だだし，ノードのリソース消費量が少ないからといって，必ずしも要求されたタスクの処理が行われていないとは限らない。たとえば，図２（Ｂ）に示す例において，ＶＭ＃３のノードでは，タスク＃３の処理が終了すると，リソース消費量が極端に減ってしまう。しかし，図２（Ｂ）に示す例において，ＶＭ＃３のノードでは，タスク＃３と並列にリソース消費量が少ないタスク＃４が実行されている。タスク＃３の処理の終了と同時にＶＭ＃３のノードに対するスケールシュリンクが行われると，タスク＃４の処理が強制終了されてしまう。このように，上述のＩａａＳベンダのサービスのようにリソース消費を見ただけでスケールシュリンクを判断すると，例えば，図２（Ｂ）に示すタスク＃４のようにリソース消費量が少ないタスクの処理を実行中であるノードを，誤って撤去してしまう可能性がある。
【００３５】
以下では，このような問題の解決を図った本実施の形態によるオートスケーリングの技術を説明する。
【００３６】
図３は，本実施の形態によるシステムの構成例を示す図である。
【００３７】
本実施の形態において，図３に示すシステム１００は，クラウドコンピューティングにおいて，ＩａａＳ側から提供される仮想マシンのノードから構成されるコンピュータシステムであるものとする。システム１００は，クライアント２００から要求された処理を，複数のノードで分散して実行する。システム１００とクライアント２００とは，ＬＡＮ（Local Area Network）やインターネットなどのネットワーク３００で接続されている。システム１００は，マスタノード１１０，スレーブノード１２０を備える。
【００３８】
マスタノード１１０は，クライアント２００からの処理要求を受け付け，各スレーブノード１２０に対するタスクの割り当てや，システム１００で実行するタスクの管理を行う。なお，本実施の形態によるマスタノード１１０は，スレーブノード１２０のスケールアウトやスケールシュリンクなどのオートスケーリングの処理を行う。なお，マスタノード１１０が，同時にスレーブノード１２０の１つであってもよい。
【００３９】
スレーブノード１２０は，マスタノード１１０から割り当てられた処理要求のタスクを実行するコンピュータノードである。スレーブノード１２０は，複数のタスクの並列処理が可能である。スレーブノード１２０は，オートスケーリングの処理によって，システム１００に増設，またはシステム１００から削除される。例えば，図３において，＃ａのスレーブノード１２０ａと＃ｂのスレーブノード１２０ｂがタスクの処理を実行している場合に，それらのスレーブノード１２０で実行しきれない処理要求があれば，＃ｃのスレーブノード１２０ｃがシステム１００に増設される。また，たとえば，＃ｃのスレーブノード１２０ｃが実行するタスクがなくなれば，＃ｃのスレーブノード１２０ｃがシステム１００から削除される。
【００４０】
クライアント２００は，システム１００に対して，システム１００が提供する処理の実行要求を行う上位アプリケーションを有するコンピュータである。なお，図１に示す例では，クライアント２００がシステム１００外部の装置となっているが，例えばクライアン

ト２００がシステム１００内部のノードであってもよい。

【００４１】

図４は，本実施の形態による各ノードの機能構成例を示す図である。

【００４２】

マスタノード１１０は，クライアント通信部１１１，スケジュール処理部１１２，スケジュール情報記憶部１１３，スケールアウト処理部１１４，スレーブ通信部１１５，リスケジュール処理部１１６，スケールシュリンク処理部１１７を備える。

【００４３】

クライアント通信部１１１は，クライアント２００からの処理要求を受け付ける。クライアント通信部１１１は，受け付けた要求の処理がシステム１００内で実行可能なものであれば，スケジュール処理部１１２に渡す。クライアント通信部１１１は，受け付けた要求の処理がシステム１００内で処理実行不可能なものであれば，その旨をクライアント２００に応答する。システム１００内で処理実行不可能な処理は，例えばスレーブノード１２０にないアプリケーションの処理や，１仮想マシンのスレーブノード１２０では納期までに終了できない大規模な処理などである。大規模な処理を，複数のノードで分散して実行する技術については，本実施の形態による技術の範囲外であるので，ここでは説明を行わない。クライアント通信部１１１は，スレーブノード１２０から受け取った処理結果をクライアント２００に通知する。

【００４４】

スケジュール処理部１１２は，クライアント通信部１１１が納期が指定された処理要求を受け付けた際に，スケジュール情報記憶部１１３に記憶された管理情報を参照して，該処理要求のタスクをスレーブノード１２０に割り当てるシミュレーションを実行する。

【００４５】

スケジュール情報記憶部１１３は，システム１００が備えるスレーブノード１２０が実行するタスクを管理する管理情報の記憶部である。スケジュール情報記憶部１１３に記憶された管理情報には，すべてのスレーブノード１２０で実行するタスクのスケジュールが記録されている。

【００４６】

より具体的には，スケジュール処理部１１２は，まず，現行の状態で，受け付けた処理要求のタスクを，指定された納期内に処理終了可能なスレーブノード１２０の検出を行う。ここでは，スケジュール処理部１１２は，即時に処理実行可能なスレーブノード１２０だけではなく，他のタスクの処理終了後に処理要求のタスクを実行しても，納期内に処理終了可能なスレーブノード１２０も検出する。スケジュール処理部１１２は，ここで検出されたスレーブノード１２０から，処理要求のタスクを割り当てるスレーブノード１２０を選択する。なお，ここでは，ロック中のスレーブノード１２０については，検出の対象外とする。本実施の形態において，ロックは，スレーブノード１２０を，処理要求のタスクの割り当て対象外に設定することをいう。

【００４７】

スケジュール処理部１１２は，現行の状態で処理要求のタスクを納期内に処理終了可能なスレーブノード１２０がなければ，他のスレーブノード１２０に移動しても納期内に処理終了可能なタスクを検出する。スケジュール処理部１１２は，検出されたタスクを移動することで，処理要求のタスクを納期内に処理終了可能なスレーブノード１２０を用意できるかを判定する。タスクを移動することで処理要求のタスクを納期内に処理終了可能なスレーブノード１２０を用意できると判定される場合，スケジュール処理部１１２は，該当タスクを他のスレーブノード１２０に移動する処理を，スレーブ通信部１１５を介して実行する。タスクの移動は，例えば該タスクの処理を移動元のスレーブノード１２０で停止し，移動先のスレーブノード１２０で再起動させる方法でもよいし，移動元のスレーブノード１２０における該タスクの実行中のイメージデータを移動先のスレーブノード１２０に転送する方法でもよい。本実施の形態では，該タスクの処理を移動先のスレーブノード１２０で再起動させる方法でタスクの移動を行うものとする。スケジュール処理部１１

２は，タスクの移動により空きができたスレーブノード１２０を，処理要求のタスクを割り当てる対象のスレーブノード１２０に決定する。

【００４８】

スケジュール処理部１１２は，タスクを移動しても処理要求のタスクを納期内に処理終了可能なスレーブノード１２０を用意できない場合，ロック中のスレーブノード１２０があれば，そのロックを解除すれば，処理要求のタスクを納期内に処理終了可能であるかを判定する。ロック解除により，処理要求のタスクを納期内に処理終了可能となると判定される場合には，スケジュール処理部１１２は，ロック中のスレーブノード１２０のロックを解除する。スケジュール処理部１１２は，ロックを解除したスレーブノード１２０を，処理要求のタスクを割り当てる対象のスレーブノード１２０に決定する。

【００４９】

スケジュール処理部１１２は，ここまでの処理で，処理要求のタスクを割り当てる対象のスレーブノード１２０が見つけられなかった場合，スケールアウトにより，システム１００にスレーブノード１２０を増設すると判断する。

【００５０】

スケールアウト処理部１１４は，スケールアウトによって，システム１００にコンピュータノードを増設する処理を行う。より具体的には，スケールアウト処理部１１４は，ＩａａＳ側で用意しているインタフェースを用いて，ＩａａＳ側の管理コンピュータにアクセスし，自システム１００へのスケールアウトを要求する。

【００５１】

スレーブ通信部１１５は，スレーブノード１２０との通信を行う。例えば，スレーブ通信部１１５は，受け付けた処理要求のタスクを割り当てる対象のスレーブノード１２０に対して，該タスクの処理を依頼する。また，スレーブ通信部１１５は，スレーブノード１２０から，依頼したタスクの処理結果を応答として受け付ける。また，スレーブ通信部１１５は，タスクの移動が行われる際に，移動元のスレーブノード１２０に対して該当タスクの停止を通知し，移動先のスレーブノード１２０に対して該当タスクの実行を通知する。

【００５２】

リスケジュール処理部１１６は，例えば定期的に，スケジュール情報記憶部１１３に記憶された管理情報を参照し，実行するタスクがないスレーブノード１２０を，スケールシュリンクの対象とする。

【００５３】

また，リスケジュール処理部１１６は，スケジュール情報記憶部１１３に記憶された管理情報を参照して，あるスレーブノード１２０で動作するタスクを，他のスレーブノード１２０に移動するシミュレーションを実行する。リスケジュール処理部１１６は，他のスレーブノード１２０に移動しても納期内に処理終了可能なタスクを検出する。

【００５４】

リスケジュール処理部１１６は，検出されたタスクを移動することで，実行するタスクがないスレーブノード１２０を用意できるかを判定する。タスクを移動することで実行するタスクがないスレーブノード１２０を用意できると判定される場合，リスケジュール処理部１１６は，該当タスクを他のスレーブノード１２０に移動する処理を，スレーブ通信部１１５を介して実行する。タスクの移動については，上述のスケジュール処理部１１２の場合と同様である。リスケジュール処理部１１６は，タスクの移動により実行するタスクがなくなったスレーブノード１２０を，スケールシュリンクの対象とする。

【００５５】

また，リスケジュール処理部１１６は，検出されたタスクを移動することで，実行するタスクの数が所定数以下となるスレーブノード１２０を用意できるかを判定する。タスクの移動により実行するタスクの数が所定数以下となるスレーブノード１２０を用意できると判定される場合，リスケジュール処理部１１６は，該当タスクを他のスレーブノード１２０に移動する処理を，スレーブ通信部１１５を介して実行する。リスケジュール処理部

１１６は，タスクの移動により実行するタスクの数が所定数以下となるスレーブノード１２０にロックを設定する。ロック中のスレーブノード１２０には，原則として新たな処理要求のタスクが割り当てられないので，残ったタスクの処理が終了した後で，スケールシュリンクの対象となる。

【００５６】

スケールシュリンク処理部１１７は，スケールシュリンクによって，対象のスレーブノード１２０をシステム１００から削除する処理を行う。より具体的には，スケールシュリンク処理部１１７は，ＩａａＳ側で用意しているインタフェースを用いて，ＩａａＳ側の管理コンピュータにアクセスし，対象スレーブノード１２０のスケールシュリンクを要求する。

【００５７】

スレーブノード１２０は，マスタ通信部１２１，アプリケーション１２２を備える。図４に示すように，スレーブノード１２０では，複数種類のアプリケーション１２２ａ，ｂ，... を稼働することが可能である。処理要求のタスクが割り当てられた際には，該処理要求に対応するアプリケーション１２２によって，タスクの処理が実行される。

【００５８】

マスタ通信部１２１は，マスタノード１１０との通信を行う。例えば，マスタ通信部１２１は，マスタノード１１０からタスクの実行要求や停止要求を受け付け，タスクの実行開始または実行停止の処理を行う。また，タスクの処理が終了した場合には，マスタ通信部１２１は，マスタノード１１０に処理結果の応答を返す。

【００５９】

図５は，本実施の形態によるノードを実現する仮想マシンシステムの例を示す図である。

【００６０】

図５に示す仮想マシンシステムは，例えば，１台の物理マシン上で１または複数台の仮想マシンが動作するシステムである。図５に示す仮想マシンシステムの例では，ＣＰＵ１１やメモリ１２などの，物理マシンであるコンピュータ１０の資源を利用して，マスタノード１１０やスレーブノード１２０を含む複数の仮想マシン３０が動作している。なお，図５に示す仮想マシンシステムでは，マスタノード１１０とスレーブノード１２０とが同じ物理マシンで実現されているが，クラウドコンピューティングの環境では，マスタノード１１０や，各スレーブノード１２０が，それぞれ異なる物理マシンで実現されることも多い。

【００６１】

図５に示す仮想マシンシステムにおいて，ハイパーバイザ２０は，コンピュータ１０を利用した仮想化環境を実現するソフトウェアである。マスタノード１１０やスレーブノード１２０を含む仮想マシン３０は，ハイパーバイザ２０上に構築可能である。

【００６２】

図４に示すマスタノード１１０，スレーブノード１２０を仮想マシンで実現するコンピュータ１０は，例えば，ＣＰＵ１１，主記憶となるメモリ１２，記憶装置１３，通信装置１４，媒体読取・書込装置１５，入力装置１６，出力装置１７等のハードウェアを備える。記憶装置１３は，例えばＨＤＤ（Hard Disk Drive ）等の外部記憶装置や，補助記憶装置などである。媒体読取・書込装置１５は，例えばＣＤ－Ｒ（Compact Disc Recordable ）ドライブやＤＶＤ－Ｒ（Digital Versatile Disc Recordable ）ドライブなどである。入力装置１６は，例えばキーボード・マウスなどである。出力装置１７は，例えばディスプレイ等の表示装置などである。なお，コンピュータ１０のハードウェア構成は，必要に応じて任意の設計が可能である。

【００６３】

図４に示すマスタノード１１０，スレーブノード１２０および各ノードが備える機能部は，コンピュータ１０が備えるＣＰＵ１１，メモリ１２等のハードウェアと，ソフトウェアプログラムとによって実現することが可能である。コンピュータ１０が実行可能なプロ

グラムは，例えば，記憶装置１３に記憶され，その実行時にメモリ１２に読み出され，ＣＰＵ１１により実行される。

【００６４】

コンピュータ１０は，可搬型記録媒体から直接プログラムを読み取り，そのプログラムに従った処理を実行することもできる。また，コンピュータ１０は，サーバコンピュータからプログラムが転送されるごとに，逐次，受け取ったプログラムに従った処理を実行することもできる。さらに，このプログラムは，コンピュータで読み取り可能な記録媒体に記録しておくことができる。

【００６５】

以下，本実施の形態によるマスタノード１１０による処理について，より具体的な例を用いて説明する。

【００６６】

図６～図９は，本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【００６７】

図６（Ａ）は，タスクの表記の例を示す。図６（Ａ）において，塗り潰しされた図形が，タスクの処理を表す。タスクの処理を示す図形の縦の長さは該タスクのリソース消費量を示し，横の長さは該タスクの処理時間を示す。また，図６（Ａ）において，白抜き図形の右端は，該タスクの納期を示す。納期は，クライアント２００に指定されたタスクの処理を終了する期限である。以下の説明において，タスクについてはすべて図６（Ａ）に示す通りの表記が行われる。

【００６８】

図６（Ｂ）は，クライアント２００から時刻t_0に処理要求を受け付けた時点における，システム１００が備える各スレーブノード１２０ａ，ｂが実行するタスクのスケジュールを示す。図６（Ｂ）に示すように，この時点でシステム１００が備えるスレーブノード１２０は，＃ａのスレーブノード１２０ａと＃ｂのスレーブノード１２０ｂの２つである。なお，スケジュール情報記憶部１１３には，例えば図６（Ｂ）のグラフに示すようなシステム１００が備えるスレーブノード１２０が実行するタスクのスケジュールをデータ化した管理情報が記憶されている。図６（Ｂ）において，グラフの縦軸はスレーブノードのリソース消費量を示し，横軸は時間の経過を示す。t_{-1}～t_3は，等間隔の時刻を示す。

【００６９】

図６（Ｃ）は，時刻t_0の時点でクライアント２００から受け付けた処理要求のタスクＸを示す図形である。図６（Ｃ）に示すように，処理要求のタスクＸの処理については，他のタスクと区別がつくように，ハッチングで表されている。図６（Ｃ）に示すように，処理要求のタスクＸについては，時刻t_3の納期が指定されている。

【００７０】

なお，タスクの処理時間やリソース消費量の推定については，過去の実績から求める方法や理論的に求める方法などで多数の周知技術が存在するので，ここでは詳細な説明を省略する。タスクの処理時間の推定は，タスクが対象とする処理によって異なる。例えば画像の処理の処理時間については，画像ファイルサイズの影響を受ける。データベースを用いた処理では，データベースへのアクセス回数の影響を受ける。また，タスクのリソース消費量については，例えば，タスクの処理を行うアプリケーション１２２ごとに値が決まっている場合にはその値を用いることができる。スレーブノード１２０にリソース消費量を問い合わせるようにしてもよい。その他，様々な周知技術の利用が可能である。

【００７１】

マスタノード１１０において，スケジュール処理部１１２は，処理要求を受け付けると，まず，現状で，処理要求のタスクをスレーブノード１２０に割り当て可能であるかを検証する。

【００７２】

図７（Ａ）は，処理要求のタスクＸを，時刻t_0に処理実行を開始するように，＃ａの

スレーブノード１２０ａに対して割り当てした検証の例を示す。また，図７（Ｂ）は，処理要求のタスクＸを，時刻t_0に処理実行を開始するように，＃ｂのスレーブノード１２０ｂに対して割り当てした検証の例を示す。いずれも，ノードのリソース消費量が，ノードのリソース限界量を超えてしまうため，検証結果はＮＧとなる。

【００７３】

図７（Ｃ）は，最も早く処理が終了する，＃ａのスレーブノード１２０ａが実行するタスクＡ＃１の処理終了後に，処理要求のタスクＸをスケジュールした検証の例を示す。この場合，処理要求のタスクＸの処理終了時刻が納期t_3を超えてしまうため，検証結果はＮＧとなる。

【００７４】

次に，スケジュール処理部１１２は，他のタスクで再起動しても納期までに処理終了可能なタスクを移動する検証を行う。図８（Ａ）に示すように，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃３は，リソース消費量の面でも＃ａのスレーブノード１２０ａに移動可能であり，＃ａのスレーブノード１２０ａで再起動しても納期までに処理終了可能である。図８（Ｂ）は，図８（Ａ）に示すタスクの移動によってリソース消費量が減った＃ｂのスレーブノード１２０ｂに対して，処理要求のタスクＸを割り当てした検証の例を示す。タスクの移動を行っても，ノードのリソース消費量が，ノードのリソース限界量を超えてしまうため，検証結果はＮＧとなる。

【００７５】

他にロック中のスレーブノード１２０が存在しないので，スケジュール処理部１１２は，スケールアウト処理部１１４によるスケールアウトの処理でスレーブノード１２０を増設すると判断する。図９は，スケールアウト処理部１１４によって増設された＃ｃのスレーブノード１２０ｃに，処理要求のタスクＸが割り当てられた状態を示す。

【００７６】

このように，本実施の形態によるマスタノード１１０は，現状のスレーブノード１２０の状態でスケジューリングを含めた検証を行っても，さらにタスクの移動を行う検証を行っても，納期内に処理が終了するように処理要求のタスクを割り当てできない場合にのみ，スケールアウトを実行する。これにより，無駄なスケールアウトを抑制できるので，無駄な課金が発生しない，効率がよいシステム１００の運用が可能となる。

【００７７】

図１０，図１１は，本実施の形態のマスタノードにおけるリスケジュール処理部によるタスクの移動シミュレーションの例を説明する図である。

【００７８】

図１０は，時刻t_0の時点での，システム１００が備える各スレーブノード１２０ａ，ｂ，ｃが実行するタスクのスケジュールを示す。図１０に示すように，この時点でシステム１００が備えるスレーブノード１２０は，＃ａのスレーブノード１２０ａと，＃ｂのスレーブノード１２０ｂと，＃ｃのスレーブノード１２０ｃの３つである。

【００７９】

まず，マスタノード１１０において，リスケジュール処理部１１６は，定期的にスケジュール情報記憶部１１３を参照して，実行するタスクがないスレーブノード１２０があるかをチェックする。図１０に示すように，この時点では，すべてのスレーブノード１２０が処理を実行しているので，実行するタスクがないスレーブノード１２０はない。このとき，リスケジュール処理部１１６は，現状のままでスケールシュリンクできるスレーブノード１２０はないと判断する。

【００８０】

次に，リスケジュール処理部１１６は，他のタスクで再起動しても納期までに処理終了可能なタスクを移動する検証を行う。

【００８１】

図１１（Ａ）は，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃１を，＃ａのスレーブノード１２０ａで再起動する検証の例を示す。図１１（Ａ）に示すように，タスク

Ｂ＃１を他のスレーブノード１２０で再起動すると，処理の終了時刻が納期t_2を超えてしまうため，検証結果はＮＧとなる。リスケジュール処理部１１６は，タスクを移動して＃ｂのスレーブノード１２０ｂに対してスケールシュリンクを行うことはできないと判断する。

【００８２】

図１１（Ｂ）は，＃ｃのスレーブノード１２０ｃが実行するタスクＣ＃１を，＃ａのスレーブノード１２０ａで再起動する検証の例を示す。図１１（Ｂ）に示すように，タスクＣ＃１は，＃ａのスレーブノード１２０ａで再起動しても納期t_3までに処理終了可能である。さらに，タスクＣ＃１を＃ａのスレーブノード１２０ａに移動すると，＃Ｃのスレーブノード１２０ｃが実行するタスクがなくなるため，＃Ｃのスレーブノード１２０ｃに対してスケールシュリンクを行うことが可能である。

【００８３】

リスケジュール処理部１１６は，スレーブ通信部１１５を介して，＃Ｃのスレーブノード１２０ｃにタスクＣ＃１の停止を指示し，＃Ａのスレーブノード１２０ａにタスクＣ＃１の実行を指示する。＃Ｃのスレーブノード１２０ｃが実行するタスクがなくなるので，リスケジュール処理部１１６は，＃Ｃのスレーブノード１２０ｃをスケールシュリンクの対象とする。スケールシュリンク処理部１１７は，＃Ｃのスレーブノード１２０ｃに対するスケールシュリンクの処理を実行する。

【００８４】

このように，本実施の形態によるマスタノード１１０は，他のスレーブノード１２０にタスクを移動することで，実行するタスクがないスレーブノード１２０を積極的に作り，スケールシュリンクを実行する。これにより，無駄なスレーブノード１２０を積極的に削除することが可能となるので，無駄な課金が発生しない効率がよいシステム１００の運用が可能となる。

【００８５】

図１２，図１３は，本実施の形態のマスタノードにおけるリスケジュール処理部によるスレーブノードにロック設定を行う例を説明する図である。

【００８６】

図１２は，時刻t_0の時点での，システム１００が備える各スレーブノード１２０ａ，ｂが実行するタスクのスケジュールを示す。図１２に示すように，この時点でシステム１００が備えるスレーブノード１２０は，＃ａのスレーブノード１２０ａと＃ｂのスレーブノード１２０ｂの２つである。

【００８７】

マスタノード１１０において，リスケジュール処理部１１６は，タスクを移動しても実行するタスクがないスレーブノード１２０が用意できない場合に，タスクを移動することで実行するタスクの数が所定数以下となるスレーブノード１２０を用意できるかを検証する。例えば，ここでは，所定数を１とする。

【００８８】

図１３（Ａ）は，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃２を，＃ａのスレーブノード１２０ａで再起動する検証の例を示す。図１３（Ａ）に示すように，タスクＢ＃２は，＃ａのスレーブノード１２０ａで再起動しても納期t_3までに処理終了可能である。なお，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃１を，＃ａのスレーブノード１２０ａで再起動しようとしても，処理の終了時刻が納期t_2を超えてしまうため，タスクＢ＃１は移動できない。

【００８９】

タスクＢ＃２を＃ａのスレーブノード１２０ａに移動したとすると，図１３（Ｂ）に示すように，＃ｂのスレーブノード１２０ｂは，実行するタスクの数が所定数１以下となる。このとき，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，＃Ｂのスレーブノード１２０ｂにタスクＢ＃２の停止を指示し，＃Ａのスレーブノード１２０ａにタスクＢ＃２の実行を指示する。

【００９０】
また，図１３（Ｂ）に示すように，実行するタスクがＢ＃１のみとなった＃ｂのスレーブノード１２０ｂに，ロックを設定する。なお，ロックを設定したスレーブノード１２０の情報は，スケジュール情報記憶部１１３など，スケジュール処理部１１２がアクセス可能な記憶部に記録しておく。これで，＃ｂのスレーブノード１２０ｂには，原則として，新規の処理要求のタスクが割り当てされないので，残っている＃Ｂ１のタスクの終了後に，スケールシュリンク処理部１１７によって，＃ｂのスレーブノード１２０ｂを削除することができる。
【００９１】
このように，本実施の形態によるマスタノード１１０は，他のスレーブノード１２０にタスクを移動して，実行するタスクが少ないスレーブノード１２０を積極的に作り，そのスレーブノード１２０に対する新規の処理要求のタスクの割り当てを抑制する。これにより，システム１００の環境が，実行するタスクがないスレーブノード１２０ができやすい環境となり，無駄なスレーブノード１２０を積極的に削除することが可能となるので，無駄な課金が発生しない効率がよいシステム１００の運用が可能となる。
【００９２】
図１４は，本実施の形態のマスタノードにおけるスケジュール処理部によるスレーブノードのロック解除を行う例を説明する図である。
【００９３】
ここで，システム１００が，図１３（Ｂ）に示す状態で，クライアント２００から，図６（Ｃ）に示すタスクＸの処理要求を受けたものとする。このとき，スケジュール処理部１１２は，処理要求のタスクＸを，図１４（Ａ）に示すようにロックされていない＃ａのスレーブノード１２０ａに割り当てしようとするが，ノードのリソース消費量がノードのリソース限界量を超えてしまうため，割り当てできない。さらに，他にタスクを移動できる相手先のスレーブノード１２０もない。
【００９４】
このとき，スケジュール処理部１１２は，ロック中の＃ｂのスレーブノード１２０ｂのロックを解除すれば，＃ｂのスレーブノード１２０ｂで処理要求のタスクＸが納期までに処理終了可能かを検証する。図１４（Ｂ）に示すように，＃ｂのスレーブノード１２０ｂで処理要求のタスクＸが納期までに処理終了可能であるので，スケジュール処理部１１２は，ロック中の＃ｂのスレーブノード１２０ｂのロックを解除し，＃ｂのスレーブノード１２０ｂに処理要求のタスクＸを割り当てる。
【００９５】
このように，ロック中のスレーブノード１２０には，他のスレーブノード１２０に処理要求のタスクを割り当てできない場合にのみ，処理要求のタスクの割り当てが行われる。これにより，スケールシュリンクを実行しやすい環境をギリギリまで維持しながら，スケールアウトの発生を抑制できるので，無駄な課金が発生しない効率がよいシステム１００の運用が可能となる。
【００９６】
なお，本実施の形態によるマスタノード１１０は，納期内にタスクの処理が終了することを最優先としているので，システム１００では常に最低限の処理性能が維持されている。
【００９７】
図１５，図１６は，本実施の形態のマスタノードによる処理要求受け付け時の処理フローチャートである。
【００９８】
マスタノード１１０において，クライアント通信部１１１は，クライアントから処理要求を受け付ける（ステップＳ１０）。ここで受け付ける処理要求には，納期が指定されている。クライアント通信部１１１は，処理要求が受け入れ可能かを判定する（ステップＳ１１）。処理要求が受け入れ可能でなければ（ステップＳ１１のＮＯ），クライアント通

信部１１１は，クライアントに処理要求の受け入れが不可能である旨を応答し（ステップＳ１２），処理を終了する。

【００９９】

処理要求が受け入れ可能であれば（ステップＳ１１のＹＥＳ），スケジュール処理部１１２は，スケジュール情報記憶部１１３の管理情報を参照し，現状のスレーブノード１２０に処理要求のタスクを割り当てるシミュレーションを行う（ステップＳ１３）。ここでは，例えば，図７に示すようにスケジューリングを含めた検証が行われる。

【０１００】

スケジュール処理部１１２は，現状のスレーブノード１２０に対する処理要求のタスクの割り当てが可能かを判定する（ステップＳ１４）。処理要求のタスクの割り当てが可能であれば（ステップＳ１４のＹＥＳ），スケジュール処理部１１２は，処理要求のタスクを割り当てる先のスレーブノード１２０を決定する（ステップＳ１５）。スレーブ通信部１１５は，決定されたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。

【０１０１】

処理要求のタスクの割り当てが可能でなければ（ステップＳ１４のＮＯ），スケジュール処理部１１２は，スケジュール情報記憶部１１３の管理情報を参照し，既存のタスクを移動して，処理要求のタスクを割り当てるシミュレーションを行う（ステップＳ１６）。ここでは，例えば，図８に示すように，他のスレーブノード１２０に移動して再実行しても納期内に処理を終了可能な既存のタスクがある場合に，その既存タスクを移動してリソースに空きができたスレーブノード１２０に処理要求のタスクを割り当てることができるかが検証される。

【０１０２】

スケジュール処理部１１２は，既存タスクを移動して処理要求のタスクの割り当てが可能となるかを判定する（ステップＳ１７）。処理要求のタスクの割り当てが可能となれば（ステップＳ１７のＹＥＳ），スケジュール処理部１１２は，該当既存タスクの移動を実行する（ステップＳ１８）。より具体的には，スケジュール処理部１１２は，スレーブ通信部１１５を介して，既存タスクの移動元のスレーブノード１２０に該タスクの停止を依頼する。また，スケジュール処理部１１２は，スレーブ通信部１１５を介して，既存タスクの移動先のスレーブノード１２０に該タスクの実行を依頼する。スレーブ通信部１１５は，既存タスクの移動によりリソースに空きができたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。

【０１０３】

処理要求のタスクの割り当てが可能とならなければ（ステップＳ１７のＮＯ），スケジュール処理部１１２は，ロック中のスレーブノード１２０が存在して，該スレーブノード１２０のロックを解除すれば，処理要求のタスクの割り当てが可能となるかを判定する（ステップＳ１９）。ロックを解除して処理要求のタスクの割り当てが可能となれば（ステップＳ１９のＹＥＳ），スケジュール処理部１１２は，ロック中のスレーブノード１２０のロックを解除する（ステップＳ２０）。スレーブ通信部１１５は，ロックが解除されたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。このケースは，図１４の例に示されるケースである。

【０１０４】

ロック中のスレーブノード１２０がないか，ロックを解除しても処理要求のタスクの割り当てが可能とならなければ（ステップＳ１９のＮＯ），スケールアウト処理部１１４は，スケールアウトの処理を実行する（ステップＳ２１）。スケールアウトにより，システム１００にスレーブノード１２０が増設される。スレーブ通信部１１５は，増設されたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。このケースは，図９の例に示されるケースである。

【０１０５】

スレーブ通信部１１５が，スレーブノード１２０から処理要求に対する処理結果の応答

を受け付けると（ステップＳ２３），クライアント通信部１１１は，その応答をクライアントに送信する（ステップＳ２４）。

【０１０６】

図１７は，本実施の形態のマスタノードによるリスケジュールの処理フローチャートである。

【０１０７】

マスタノード１１０において，リスケジュール処理部１１６は，所定のタイミングで本処理を開始する。

【０１０８】

リスケジュール処理部１１６は，スケジュール情報記憶部１１３の管理情報を参照し，現状で実行するタスクがないスレーブノード１２０があるかを判定する（ステップＳ３０）。実行するタスクがないスレーブノード１２０があれば（ステップＳ３０のＹＥＳ），スケールシュリンク処理部１１７は，該当スレーブノード１２０に対するスケールシュリンクの処理を実行する（ステップＳ３１）。スケールシュリンクにより，システム１００からスレーブノード１２０が削除される。

【０１０９】

リスケジュール処理部１１６は，スケジュール情報記憶部１１３の管理情報を参照し，タスクを移動するシミュレーションを行う（ステップＳ３２）。ここでは，例えば図１１に示すように，他のスレーブノード１２０に移動して再実行しても納期内に処理を終了可能なタスクがある場合に，そのタスクを移動して実行するタスクがないスレーブノード１２０を生成できるかが検証される。また，例えば図１３に示すように，他のスレーブノード１２０に移動して再実行しても納期内に処理を終了可能なタスクがある場合に，そのタスクを移動して実行するタスクが所定数以下となるスレーブノード１２０を生成できるかが検証される。

【０１１０】

リスケジュール処理部１１６は，タスクを移動して実行するタスクがないスレーブノード１２０を生成できるか，すなわちタスクを移動してスケールシュリンクが可能となるかを判定する（ステップＳ３３）。タスクを移動してスケールシュリンクが可能となれば（ステップＳ３３のＹＥＳ），リスケジュール処理部１１６は，該当タスクの移動を実行する（ステップＳ３４）。より具体的には，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動元のスレーブノード１２０に該タスクの停止を依頼する。また，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動先のスレーブノード１２０に該タスクの実行を依頼する。スケールシュリンク処理部１１７は，タスクの移動により実行するタスクがなくなったスレーブノード１２０に対するスケールシュリンクの処理を実行する（ステップＳ３５）。スケールシュリンクにより，システム１００からスレーブノード１２０が削除される。

【０１１１】

タスクを移動してもスケールシュリンクが可能とならなければ（ステップＳ３３のＮＯ），リスケジュール処理部１１６は，タスクを移動して実行するタスクが所定数以下となるスレーブノード１２０があるかを判定する（ステップＳ３６）。タスクを移動しても実行するタスクが所定数以下となるスレーブノード１２０がなければ（ステップＳ３６のＮＯ），リスケジュール処理部１１６は，処理を終了する。

【０１１２】

タスクを移動して実行するタスクが所定数以下となるスレーブノード１２０があれば（ステップＳ３６のＹＥＳ），リスケジュール処理部１１６は，該当タスクの移動を実行する（ステップＳ３７）。より具体的には，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動元のスレーブノード１２０に該タスクの停止を依頼する。また，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動先のスレーブノード１２０に該タスクの実行を依頼する。リスケジュール処理部１１６は，タスクを移動して実行するタスクが所定数以下となったスレーブノード１２０にロック

を設定する（ステップＳ３８）。このまま，ロックが解除されずに残ったタスクの処理がすべて終了すれば，ロックが設定されたスレーブノード１２０は，その後のステップＳ３０，Ｓ３１の処理でスケールシュリンクの対象となる。

【０１１３】

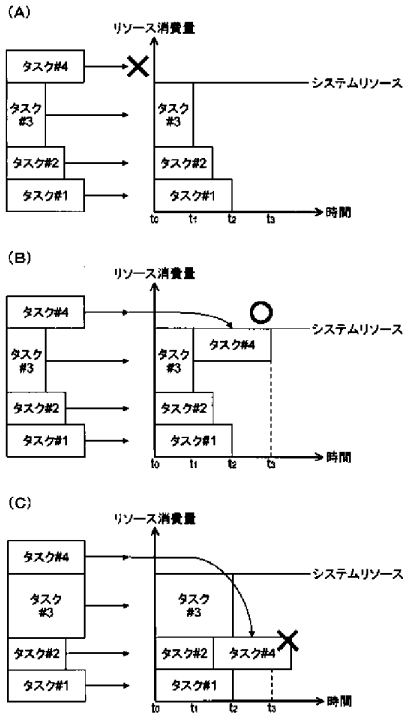
以上，本実施の形態について説明したが，本発明はその主旨の範囲において種々の変形が可能であることは当然である。

【符号の説明】

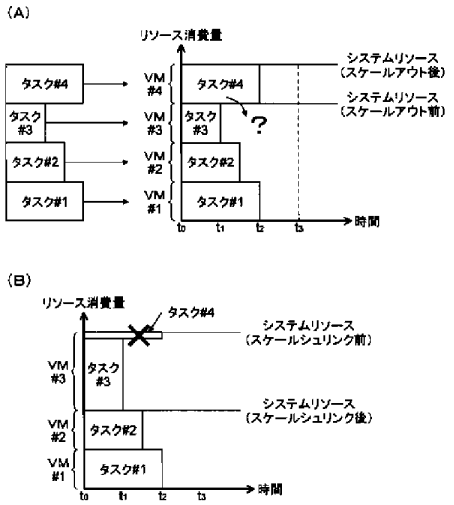
【０１１４】

１００　システム
１１０　マスタノード
１１１　クライアント通信部
１１２　スケジュール処理部
１１３　スケジュール情報記憶部
１１４　スケールアウト処理部
１１５　スレーブ通信部
１１６　リスケジュール処理部
１１７　スケールシュリンク処理部
１２０　スレーブノード
１２１　マスタ通信部
１２２　アプリケーション
２００　クライアント
３００　ネットワーク

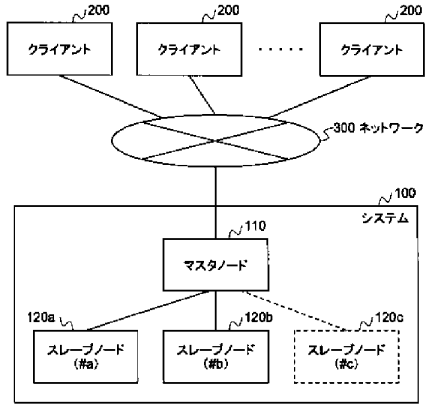
【図１】



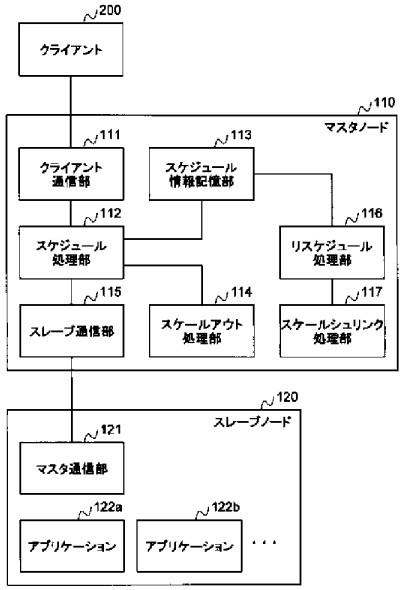
【図２】



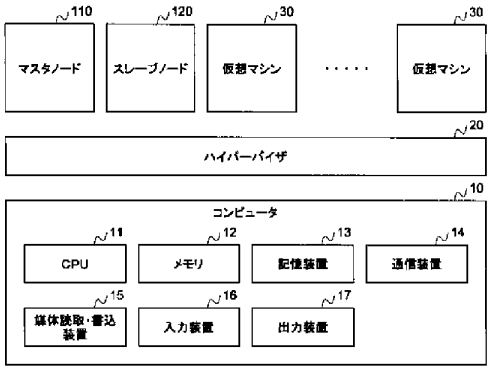
【図３】


200
クライアント
200
クライアント
200
クライアント
300 ネットワーク
100
システム
110
マスタノード
120a
スレーブノード
(#a)
120b
スレーブノード
(#b)
120c
スレーブノード
(#c)

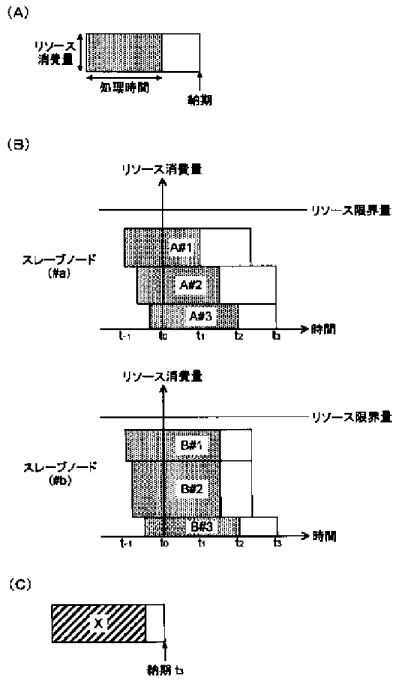
【図４】


200
クライアント
110
マスタノード
111
クライアント
通信部
113
スケジュール
情報記憶部
112
スケジュール
処理部
116
リスケジュール
処理部
115
スレーブ通信部
114
スケールアウト
処理部
117
スケールシュリンク
処理部
120
スレーブノード
121
マスタ通信部
122a
アプリケーション
122b
アプリケーション

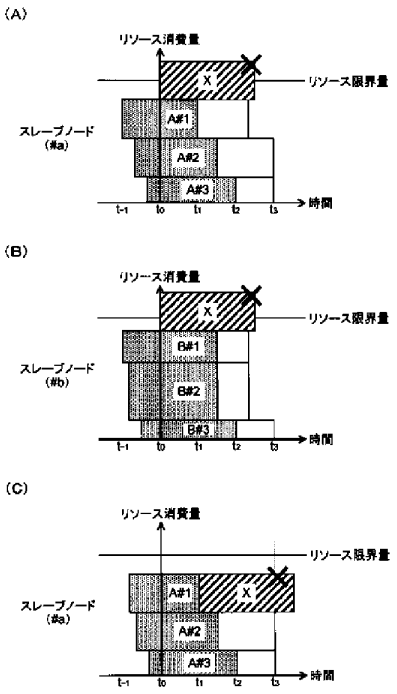
【図５】


110
マスタノード
120
スレーブノード
30
仮想マシン
30
仮想マシン
20
ハイパーバイザ
10
コンピュータ
11
CPU
12
メモリ
13
記憶装置
14
通信装置
15
媒体読取・書込
装置
16
入力装置
17
出力装置

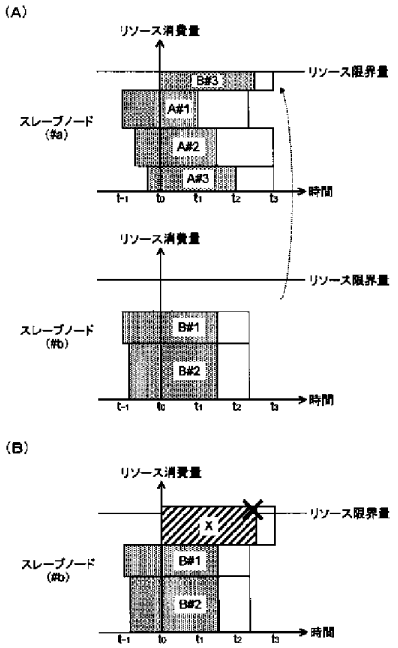
【図６】


(A)
リソース
消費量
処理時間
納期
(B)
リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
(C)
X
納期 b

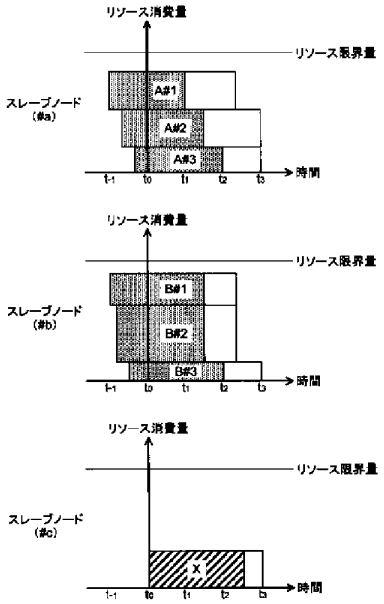
【図７】


(A)
リソース消費量
リソース限界量
X
スレーブノード
(#a)
A#1
A#2
A#3
時間
(B)
リソース消費量
リソース限界量
X
スレーブノード
(#b)
B#1
B#2
B#3
時間
(C)
リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
X
A#2
A#3
時間

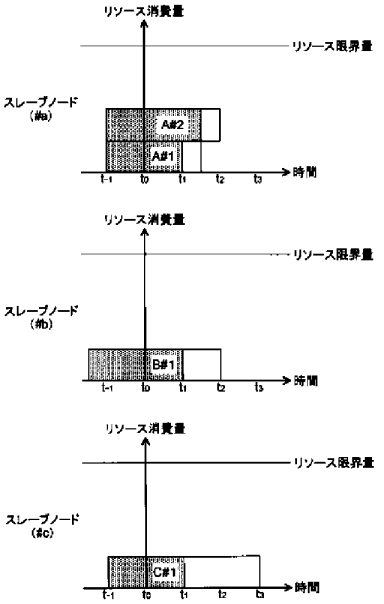
【図８】


(A)
リソース消費量
リソース限界量
B#3
スレーブノード
(#a)
A#1
A#2
A#3
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
時間
(B)
リソース消費量
リソース限界量
X
スレーブノード
(#b)
B#1
B#2
時間

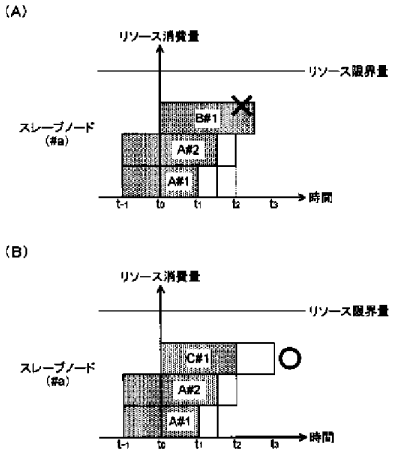
【図９】


リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
リソース消費量
リソース限界量
スレーブノード
(#c)
X
時間

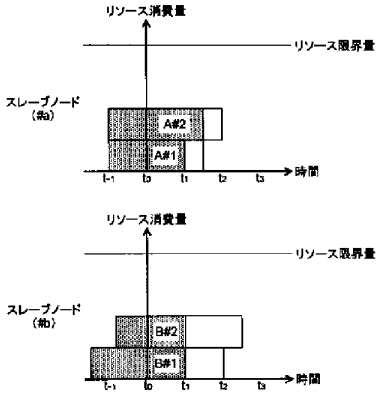
【図１０】


リソース消費量
リソース限界量
スレーブノード
(#a)
A#2
A#1
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
時間
リソース消費量
リソース限界量
スレーブノード
(#c)
C#1
時間

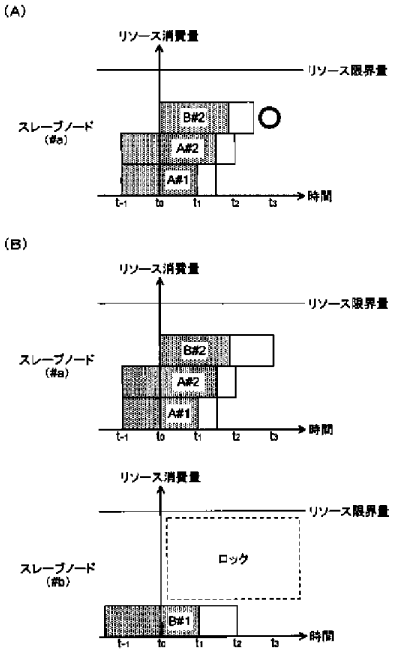
【図１１】



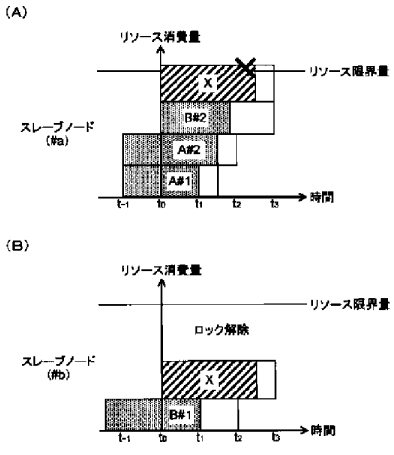
【図１２】



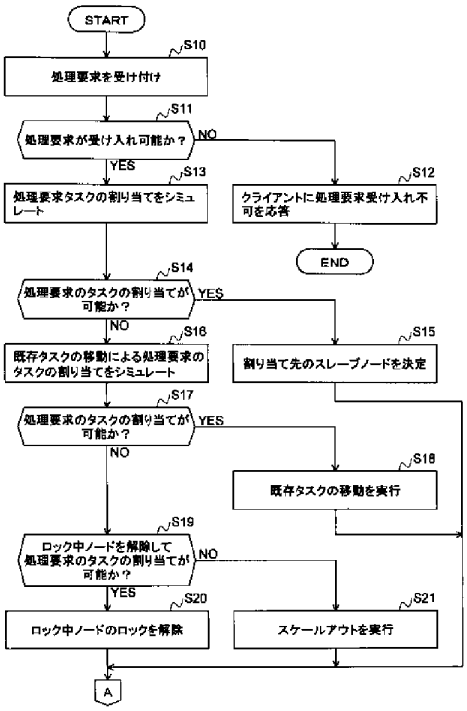
【図１３】



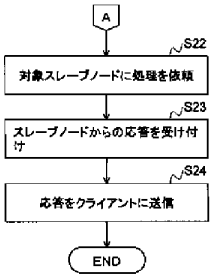
【図１４】



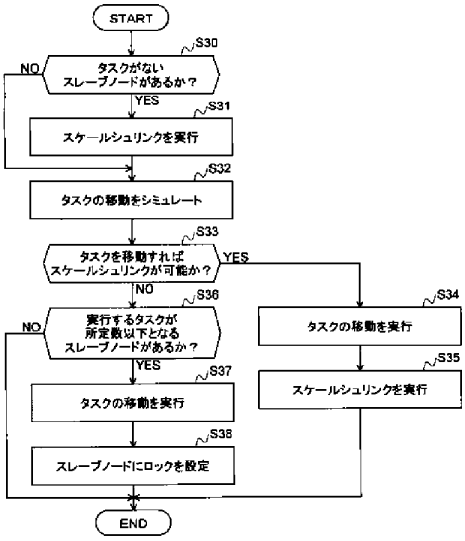
【図１５】


START
S10
処理要求を受け付け
S11
処理要求が受け入れ可能か？
NO
YES
S12
クライアントに処理要求受け入れ不可を応答
END
S13
処理要求タスクの割り当てをシミュレート
S14
処理要求のタスクの割り当てが可能か？
YES
NO
S15
割り当て先のスレーブノードを決定
S16
既存タスクの移動による処理要求のタスクの割り当てをシミュレート
S17
処理要求のタスクの割り当てが可能か？
YES
NO
S18
既存タスクの移動を実行
S19
ロック中ノードを解除して処理要求のタスクの割り当てが可能か？
NO
YES
S20
ロック中ノードのロックを解除
S21
スケールアウトを実行
A

【図１６】


A
S22
対象スレーブノードに処理を依頼
S23
スレーブノードからの応答を受け付け
S24
応答をクライアントに送信
END

【図１７】


START
S30
タスクがないスレーブノードがあるか？
NO
YES
S31
スケールシュリンクを実行
S32
タスクの移動をシミュレート
S33
タスクを移動すればスケールシュリンクが可能か？
YES
NO
S34
タスクの移動を実行
S35
スケールシュリンクを実行
S36
実行するタスクが所定数以下となるスレーブノードがあるか？
NO
YES
S37
タスクの移動を実行
S38
スレーブノードにロックを設定
END

フロントページの続き

(72)発明者 久保田 博昭
神奈川県川崎市中原区上小田中４丁目１番１号 富士通株式会社内

審査官 田中 幸雄

(56)参考文献 特開２００９－２６５７７８（ＪＰ，Ａ）
特開２００８－０１５９５８（ＪＰ，Ａ）

(58)調査した分野(Int.Cl.，ＤＢ名)
Ｇ０６Ｆ ９／５０

Check for updates



Bacterial Contamination of Blood Components: Risks, Strategies, and Regulation

Joint ASH and AABB Educational Session in Transfusion Medicine

*Christopher D. Hillyer, Cassandra D. Josephson, Morris A. Blajchman, Jaroslav G. Vostal, Jay S. Epstein, and Jesse L. Goodman**

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

Bacterial contamination of transfusion products, especially platelets, is a longstanding problem that has been partially controlled through modern phlebotomy practices, refrigeration of red cells, freezing of plasma and improved materials for transfusion product collection and storage. Bacterial contamination of platelet products has been acknowledged as the most frequent infectious risk from transfusion occurring in approximately 1 of 2,000-3,000 whole-blood derived, random donor platelets, and apheresis-derived, single donor platelets. In the US, bacterial contamination is considered the second most common cause of death overall from transfusion (after clerical errors) with mortality rates ranging from 1:20,000 to 1:85,000 donor exposures. Estimates of severe morbidity and mortality range from 100 to 150 transfused individuals each year.

Concern over the magnitude and clinical relevance of this issue culminated in an open letter calling for the "blood collection community to immediately initiate a program for detecting the presence of bacteria in units of platelets." Thereafter, the American Association of Blood Banks (AABB) proposed new standards to help mitigate transfusion of units that were contaminated with bacteria. Adopted with a final implementation date of March 1, 2004, the AABB Standard reads "*The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components.*"

This Joint ASH and AABB Educational Session reviews the risks, testing strategies, and regulatory approaches regarding bacterial contamination of blood components to aid in preparing practitioners of hematology and transfusion medicine in understanding the background and clinical relevance of this clinically important issue and in considering the approaches currently available for its mitigation, as well as their implementation.

In this chapter, Drs. Hillyer and Josephson review the background and significance of bacterial contamination, as well as address the definitions, conceptions and limitations of the terms *risk, safe* and *safety*. They then describe current transfusion risks including non-infectious serious hazards of transfusion, and current and emerging viral risks. In the body of the text, Dr. Blajchman reviews the prevalence of bacterial contamination in cellular blood components in detail with current references to a variety of important studies. He then describes the signs and symptoms of transfusion-associated sepsis and the sources of the bacterial contamination for cellular blood products including donor bacteremia, and contamination during whole blood collection and of the collection pack. This is followed by strategies to decrease the transfusion-associated morbidity/mortality risk of contaminated cellular blood products

* Christopher D. Hillyer, MD, Emory University School of Medicine, Atlanta, GA
Cassandra D. Josephson, MD, Emory University School of Medicine, Atlanta, GA
Morris A. Blajchman, MD, FRCP(C), McMaster University and Canadian Blood Services, Hamilton, Ontario, Canada
Jaroslav G. Vostal, MD, PhD, Center for Biologics Evaluation and Research, FDA
Jay S. Epstein, MD, Center for Biologics Evaluation and Research, FDA
Jesse L. Goodman, MD, MPH, Center for Biologics Evaluation and Research, FDA

including improving donor skin disinfection, removal of first aliquot of donor blood, pre-transfusion detection of bacteria, reducing recipient exposure, and pathogen reduction/inactivation. In the final sections, Drs. Vostal, Epstein and Goodman describe the regulations and regulatory approaches critical to the appropriate implementation of a bacterial contamination screening and limitation program including their and/or the FDA's input on prevention of bacterial contamination, bacterial proliferation, and detection of bacteria in transfusion products. This is followed by a discussion of sampling strategy for detection of bacteria in a transfusion product, as well as the current approval process for bacterial detection devices, trials recommended under "actual clinical use" conditions, pathogen reduction technologies, and bacterial detection and the extension of platelet storage.

Bacterial contamination of transfusion products, especially platelets, is a longstanding problem that has been partially controlled through modern phlebotomy practices, refrigeration of red cells, freezing of plasma, and improved materials for transfusion product collection and storage. Indeed, bacterial contamination of platelet products has been acknowledged as the most frequent *infectious risk* from transfusion occurring in approximately 1 of 2,000–3,000 whole-blood derived, random donor platelets (hereafter RDP), and apheresis-derived, single donor platelets (hereafter SDP)[1-4] (see below). In the US, bacterial contamination is considered the second most common cause of death overall from transfusion (after clerical errors) with mortality rates for platelet-related sepsis ranging from 1:20,000 to 1:85,000 donor exposures.[5] Estimates of severe morbidity and mortality range from 100 to 150 transfused individuals each year.[6,7]

To address this problem, the US Food and Drug Administration (FDA) has sponsored scientific workshops to highlight and clarify relevant issues and to promote the development of technologic interventions.[8-10] Additionally, the Centers for Disease Control and Prevention (CDC) conducted a nationwide surveillance study on bacterial contamination in blood products.[11] Many publications (detailed later in this chapter) have added important data attempting to determine and define the true clinical effect of bacterial contamination of blood components, and a similar number of publications have offered data as to the ability of a variety of methods to detect and limit this contamination.

Concern over the magnitude and clinical relevance of this issue culminated in an open letter calling for the "blood collection community to immediately initiate a program for detecting the presence of bacteria in units of platelets" (see http://www.cbbsweb.org/bacterial risk.pdf). Thereafter, the American Association of Blood Banks (AABB), after publication of a number of Association Bulletins (see AB 96-06[3] at www.AABB.org), proposed new standards (December 2002) to help mitigate transfusion of units that were contaminated with bacteria. Adopted with a final implementation date of March 1, 2004, AABB Standard 5.1.5.1. now reads:

> **5.1.5.1** *The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components. Standard 5.6.2 applies. [Arm Prep]*

Thus, this Joint ASH and AABB Educational Session was conceived to review the risks, testing strategies, and regulatory approaches regarding bacterial contamination of blood components; to aid in preparing practitioners of hematology and transfusion medicine in understanding the background and clinical relevance of this important issue; and to consider the approaches currently available for its mitigation as well as their implementation.

Background and Significance

Whereas the risk of transfusion related transmission of viral diseases such as human immunodeficiency virus (HIV) and hepatitis has steadily decreased over the last 40 years, the risk of transmission of bacteria has remained about the same. Thus, due to our success with viral pathogens, bacterial contamination now has the dubious distinction of being the most common infectious risk from transfusion and has become a matter of increasing concern and attention.[12,13] Recent studies of platelets have suggested a bacterial contamination rate of about 1 per 1–3,000 units, clinical sepsis in about 1 per 20,000 transfusions and related fatality in about 1 per 60,000 transfusions[5,14,15] (reviewed in detail below). The fatality risk from bacterially contaminated red blood cells (RBCs) is much lower, about 1 per 500,000.[15]

Despite this longstanding, persistent infectious risk of transfusion, it has been tolerated by some as an "acceptable risk." However, with the significant risk reduction of transfusion-transmitted diseases attributable to viruses such as HIV, hepatitis C virus (HCV), and hepatitis B virus (HBV), the magnitude and relative importance of platelet-induced sepsis has moved to the forefront of blood supply safety.[16] In order to appreci-

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

ate the significance of the relative importance of bacterial contamination of platelets, a perspective on the safety of the nation's blood supply is necessary.

Risk

There are approximately 30 million units of blood and blood products transfused each year in the US, and perhaps an equal number internationally. The American public, the medical profession, and the government hold the transfusion of these units to the highest standards of safety.[17] Indeed, the blood supply in the US has been described as "safer than ever relative to known risks," however, "the usual notions of safety do not necessarily apply where transfusion is concerned."[17] The CDC, the AABB, and the American Red Cross[18] have echoed these statements.

In the early 1980s, the incidence of transfusion transmitted (TT) HIV was greater than 1 case per 1,000 units in some locales, whereas the current incidence of TT-HIV is less than 1 case per 2 million screened and tested units;[19] some authorities have posited that this risk may actually be closer to 1 in 5 million screened and tested units especially if there is widespread implementation of "single unit" nucleic acid testing (NAT). Similar improvements have been made for HBV and HCV, two TT-viruses carrying significant morbidity and mortality (**Figure 1**).[20] Despite these improvements, many experts argue that the potential US blood recipient demands a "zero-risk" blood supply. Unfortunately, even for HIV in 2002, this goal has not been achieved as there were two reported cases of persons allegedly contracting HIV through transfusion and subsequently suing the blood supplier. In one case, a $100 million dollar negligence lawsuit has been filed. Additionally, a number of "emerging pathogens" still exist, as does the transfusion transmission of pathogens for which testing is not required. Thus, how safe the blood supply is becomes difficult to quantitate and by some criteria the risks to the blood recipient would be considered "very low" to "negligible" (see **Table 1**).[21]

Safe and safety

The word "safe" has been defined as free from "harm or risk" or "secure from danger, harm, or evil." However, safety is a more subjective term emanating from one's understanding and perspective, as well as the amount of control one has in determining the chance of the adverse outcome occurring. Thus, while the risk of dying in a car accident significantly exceeds the risk of dying from TT-infectious disease, the latter has elements of increased dread and less control and therefore has an increasingly fear-filled association. The Paling Perspective Scale[22] provides several examples of risks with which the public is "comfortable" (see **Figure 2**) and allows comparison to the risk of TT-HIV (< 1:2M) and bacterial contamination (see discussion of risk estimates below). Indeed, research has shown that patients, and the majority of the population, have a very poor understanding of risk. It is worthwhile to compare the risk of death from influenza, cigarette smoking, motorcycle riding, or lightning with the risk of dying or acquiring variant Creutzfeldt-Jakob disease (vCJD) though there

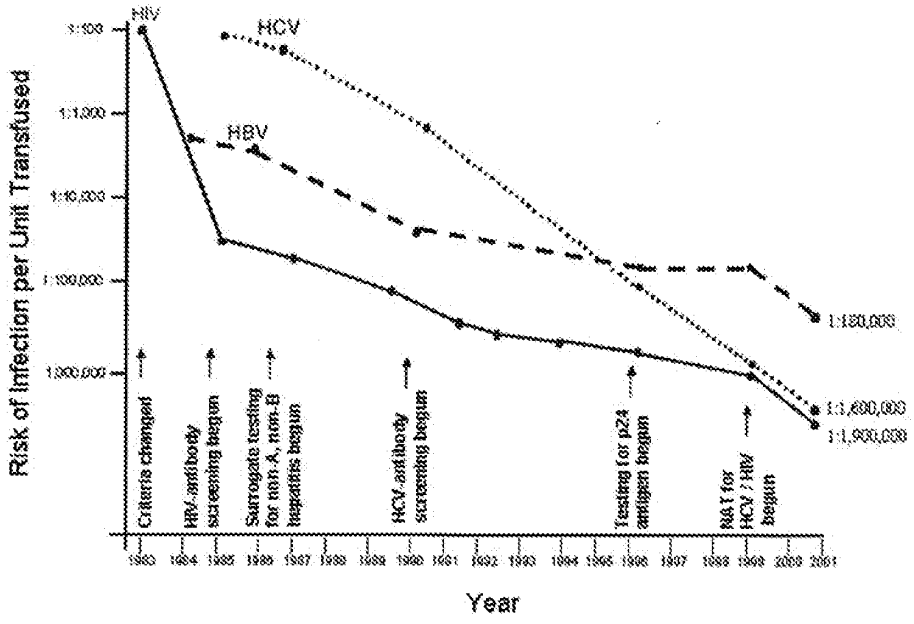


Figure 1. New test implementation and declining risk of viral infections from transfusion.[20]

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; NAT, nucleic acid testing.

Modified by M.P. Busch from table in AuBuchon JP, Birkmeyer JD, Busch MP. Safety of the Blood Supply in the United States: Opportunities and Controversies. Ann Intern Med. 1997;127:904-909 and used with permission.

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

Table 1. Risk of an individual dying (D) in 1 year or developing an adverse response (A).[21]

Term Used	Risk Range	Example	Risk Estimate
High	> 1:100	(A) Transmission to susceptible household contacts of measles and chickenpox	1:1–1:2
		(A) Transmission of HIV from mother to child (Europe)	1:6
Moderate	1:100–1:1,000	(D) Smoking 10 cigarettes per day	1:200
		(D) All natural causes, age 40	1:850
Low	1:1,000–1:10,000	(D) All kinds of violence	1:3,300
		(D) Influenza	1:5,000
		(D) Accident on road	1:8,000
Very low	1:10,000–1:100,000	(D) Leukemia	1:12,000
		(D) Playing soccer	1:25,000
		(D) Accident at work	1:43,000
Minimal	1:100,000–1:1,000,000	(D) Accident on railway	1:500,000
Negligible	< 1:1,000,000	(D) Hit by lightning	1:1,000,000
		(D) Release of radiation by nuclear power station	1:10,000,000

have been no known TT-cases of vCJD, although animal models support the possibility that vCJD may be transfusion-transmitted.[23]

Transfusion risks

It is vital to consider the other risks of transfusion such as those termed non-infectious serious hazards of transfusion (often termed NiSHOTs; see **Table 2**) which dramatically outweigh the residual risk of TT-infectious diseases.[24] However, the agents that are known to be transfusion transmitted, and those that "might be" are described in **Table 3**, for it is only upon this backdrop that a decision can be made on the relative value of new technologies and their ability to abrogate the agents,

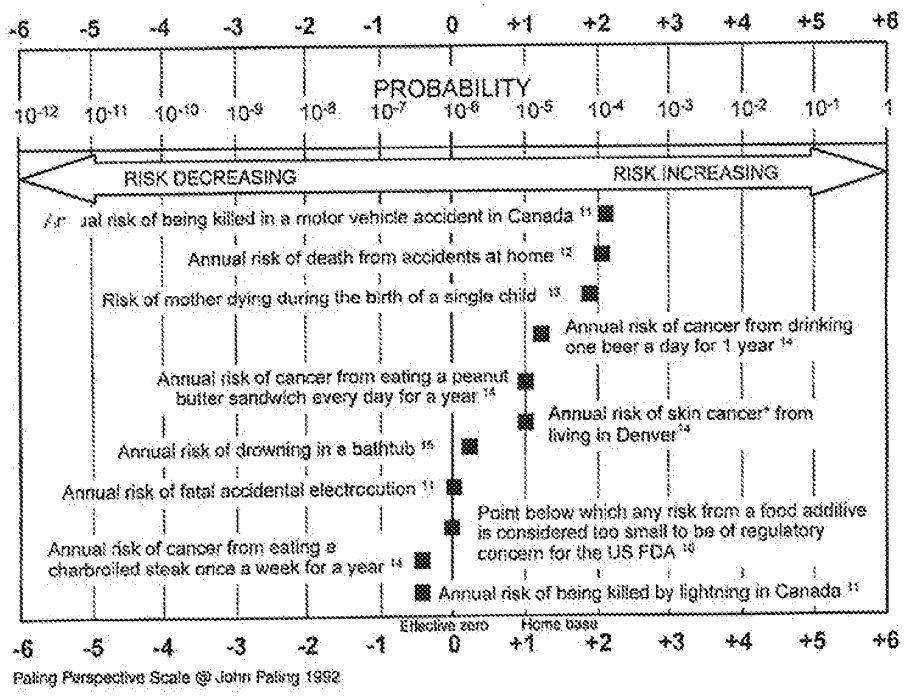


Figure 2. Risks with which the public is comfortable.

The numbers denoting references in this figure are those from the primary article and are not notations of the references found at the conclusion of this chapter.

Abbreviations: FDA, Food and Drug Administration.[22]

Reprinted with permission from Lee DH, Paling JE, Blajchman MA. A new tool for communicating transfusion risk information. Transfusion. 1998;38:184-188.

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

Table 2. Noninfectious serious hazards of transfusion (NiSHOTs).[24]

- Mistransfusion and ABO/Rh incompatible transfusion
- Cardiopulmonary toxicity
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated graft-versus-host disease (TA-GVHD)
- Metabolic derangements in pediatric and massive transfusion
- Undertransfusion

Table 4. Criteria for transfusion transmission of viruses and other infectious agents.[25]

1. There must be an asymptomatic, viremic phase in the blood donor.
2. Virus viability must be maintained during storage.
3. There must be a seronegative recipient population.
4. The agent must be capable of inducing disease.

including bacterial contamination of platelet products.

Typically, four elements are required for an infectious disease–causing agent to be transmitted by transfusion and the criteria are listed in **Table 4**.[25] However, despite many possible agents that can be transmitted by transfusion, units are regularly tested only for HIV, HCV, HBV, HTLV, and *Treponema pallidum*. Donor demographics may bring changes in risk level of transfusion-transmitted agents and affect future choices for routine screening. For example, the incidence of malaria and Chagas disease seems to be rising due to increasing travel to endemic areas, climate changes, and immigration.

Clinical relevance

The unique aspect of most bacterial species when compared to viral pathogens is that they can readily proliferate in the nutrient-rich blood product environment during storage. This is particularly true in platelet products that are stored at room temperature, rather than in the cold. It is estimated that the level of contamination at the time of collection is generally relatively low, probably on the order of 1–10 colony forming units/mL or less.[26] Once the product is contaminated, the inoculated bacterial seed can proliferate within hours to reach levels of 10^6/mL or greater. Such quantities of bacteria infused with the transfusion product over a short period of time can cause bacteremia that may progress to sepsis and death. The outcome of a contaminated transfusion is highly dependent on the amount of bacteria transfused, the type of bacteria and its pathogenicity for humans, the rate of transfusion, and the clinical status of the recipient. Immunosuppressed patients and older individuals with poor nutritional status will be the most susceptible population. However, even healthy individuals can have a rapidly fatal outcome when transfused with a large load of endotoxin-producing Gram-negative bacteria.

Thus, there is significant concern about, and demand for, a "safe" or "safer" blood supply in order to provide the best and safest patient care. This, in turn, has the public, government, and blood suppliers' attention keenly focused on preventing bacterial contamination of platelets and subsequent sepsis due to platelet transfusions. This risk has become "unacceptable" in a climate where the blood supply remains "the safest that it has ever been."

Table 3. Agents and their likelihood of transfusion transmission in qualitative terms.

Agent	Transfusion Transmission
Parasites	
Malaria	Rare cases
Babesia	Occasional cases, endemic
T. cruzii	Occasional cases, US
T. gondii	Rare cases
Leishmania	Rare cases (< 5 worldwide)
Bacteria	
Contaminants	Approximately 1:3,000 platelet units
Specific Agents	
T. pallidum	Rare cases
B. burgdorferi	No known cases
E. chaffeensis	No known cases
E. cytophagophilia	One possible case
R. rickettsii	One reported case
Viruses	
HIV	Rare cases
HCV	Rare cases
HBV	Occasional cases
HTLV	Rare cases
CMV	Occurs, threat to specific pts
EBV	Occurs, threat to specific pts
B19	Occurs, threat to specific pts
HAV	Rare cases
HGV	Occurs, not a threat to pts
TTV	Occurs, not a threat to pts
Sen-V	Occurs, not a threat to pts
HHV-8	No known cases
WNV	Several cases reported
Enterovirus	Known donor viremia
Prions	
CJD	No known cases
vCJD	No known cases*

* Animal models support the possibility that this agent may be able to be transmitted by transfusion

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; HBV, hepatitis B virus; HTLV, human T-cell lymphotrophic virus; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HAV, hepatitis A virus; HGV, hepatitis G virus; TTV, transfusion-transmitted virus; HHV-8, human herpes virus–8; WNV, West Nile virus; CJD, Creutzfeld-Jakob disease; vCJD, variant CJD.

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

Table 5. Summary of the available prospective studies evaluating the prevalence of bacterial contamination in whole blood–derived platelets, apheresis platelets, and red blood cell units.

Blood Produce Type	Reference	Positives per Number of Units Tested	Contamination Prevalence per 100,000 Units
WB-plts	Morrow et al[32]	6 per 74,598	8
WB-plts	Barrett et al[33]	1 per 4,272	23
WB-plts	Yomtovian et al[34]	6 per 15,705	38
WB-plts	Chiu et al[35]	10 per 21,503	46
WB-plts	Blajchman et al[36]	16 per 31,610	51
WB-plts	Leiby et al[37]	4 per 4,995	80
WB-plts	Blajchman et al[38]	7 per 10,065	70
A-plts	Morrow et al[32]	1 per 9,519	5
A-plts	Blajchman et al[31]	14 per 6,055	230
A-plts	Barrett et al[33]	5 per 17,928	28
A-plts	Yomtovian et al[34]	0 per 2,476	0
A-plts	Dzieczkowski et al[39]	1 per 5,197	19
A-plts	Aubuchon et al[40]	1 per 2,678	37
RBCs	Barrett et al[33]	1 per 31,385	3
RBCs	Dzieczkowski et al[39]	1 per 7,080	0
Overall	*n* = 15	89 per 274,379	32.4*

* 95% confidence intervals 25.6 to 39.1

Abbreviations: A-plts, apheresis platelets; WB-plts, whole blood–derived platelets; RBCs, red blood cells; *n*, number of studies.

Prevalence of Bacterial Contamination in Cellular Blood Components

The contamination of RBCs and platelets with bacteria occurs relatively frequently.[12,15,27-31] However, the available prevalence data vary considerably from one study to the next. The data from the available prospective studies evaluating frequency of bacterial contamination of blood components are summarized in **Table 5**. The mean prevalence of bacterial contamination in whole blood–derived, RDP platelets is 33.9 per 100,000 units and for apheresis-derived, SDP platelet units is 51.0 per 100,000 units. For RBCs it is 2.6 per 100,000 units. The overall cellular blood product contamination prevalence from all of the data shown in **Table 5** is 32.4 per 100,000 units. This translates into an approximate rate of 1 bacterially contaminated cellular blood product unit per 3,000 cellular blood product units released.

In contradistinction to the available data on the bacterial contamination of cellular blood products (RBCs and platelets), the frequency of clinically apparent septic transfusion events or reactions due to such contaminated products is considerably lower. The available data on the prevalence of transfusion-associated septic events is summarized in **Table 6**. It should be noted that these summaries report only the more severe or potentially life threatening septic reactions. It is likely, therefore, that these reports represent only one end of the clinical spectrum of transfusion-associated septic transfusion reactions. Moreover, it is very likely that even severe and even fatal septic transfusion reactions go unrecognized as being transfusion-associated. Thus, the actual prevalence of septic transfusion reactions may be considerably higher than reported, due to the observational bias that occurs. For all of these reasons, it has been very difficult to determine the true morbidity and mortality risk of transfusing bacterially contaminated cellular blood products.

The variation in the reported prevalence of clinical events is shown clearly in **Table 6**. This table enumerates the risk of septic clinical events per million units transfused from 3 published studies: (1) the BaCon Study from the US, (2) the Hémovigilance system in France, and (3) the Johns Hopkins Hospital, which reports a 10-year follow-up of platelet transfusion episodes detected in that institution.[11,41,5] From the data in **Table 6**, it is impossible to define a specific prevalence of clinical transfusion-associated septic events, except to say that they probably occur with a frequency of 1 per approximately 25,000 platelet units transfused, and 1 per approximately 250,000 RBC units transfused. This latter estimate excludes the data from the BaCon study (1:5 million), as this study was likely limited by an underestimation bias.[11]

It is important to note that transfusion-associated septic reactions due to bacterially contaminated cellular blood products often go unrecognized as such, because of the high frequency of febrile non-hemolytic transfusion reactions

Table 6. Prevalence of transfusion-associated septic reactions per million (10^6) apheresis platelets, whole blood–derived platelets, and red blood cell units transfused.[17-19]

Study	Country	A-Plts	WB-Plts	Case Fatality Rate - Plts	RBCs	Case Fatality Rate - RBCs
Perez et al[41]	France	31.8	71.8	31.3%	5.8	24.0%
Kuehnert et al[11]	US	9.9	10.6	20.7%	0.2	60.0%
Ness et al[5]	US	74.5	67.0	17.4%	ND	ND

Abbreviations: A-plts; apheresis platelets; WB-plts, whole blood–derived platelets; RBCs, red blood cells; ND, not determined.

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

(FNHTR) that occur following the transfusion of cellular blood products, particularly following platelet transfusions. For platelets, the FNHTR rate may be as high as 15% per unit transfused, whereas for RBCs the FNHTR rate is less than 1% per RBC unit transfused. As the symptoms of septic transfusion reactions often mimic those occurring with FNHTRs, many apparently mild septic transfusion reactions may not be recognized as such. Moreover, most of the organisms isolated from contaminated platelet and RBC units tend to be skin-associated organisms (i.e., Gram-positive cocci), which are not usually implicated in RBC-associated septic transfusion reactions, and are often considered contaminants related to procedure of taking the sample for culture (i.e., a false positive).

Signs and Symptoms of Transfusion-Associated Sepsis

The transfusion of a contaminated cellular blood product unit may be associated with variable signs and symptoms. As indicated above, not all contaminated blood products cause symptoms in the recipient; in fact, it appears that many do not.[28] The initial signs and symptoms, when they occur, include fever and chills, which usually begin shortly after (within 2 hours) the start of the transfusion. Subsequent signs may include: hypotension, nausea, vomiting, diarrhea, oliguria, and shock. Other potential presenting symptoms include: respiratory symptoms (dyspnea, wheezing, and/or cough) and bleeding due to the consequence of endotoxin-induced disseminated intravascular coagulation. It is important to note that a majority of septic transfusion reactions associated with contaminated RBCs usually occur with units that have been stored for more than 21 days, whereas septic reactions associated with contaminated platelets usually occur with units that have been stored for 3 days or more.[28]

The clinical severity of a transfusion-associated septic reaction can vary considerably, depending on: (1) the species of bacteria present in the blood product unit, with Gram-negative organisms tending to cause more severe reactions, due to the presence of endotoxin often elaborated by such organisms; (2) the total number of bacteria infused or present in the cellular blood product unit infused to a recipient; (3) the rate of propagation of the bacteria present; and (4) recipient characteristics, such as underlying disease, leukocyte count, the status of the immune system, and whether the recipient is receiving concomitant antibiotic therapy.

Sources of the Bacterial Contamination for Cellular Blood Products

Possible mechanisms of the bacterial contamination of blood components include: donor bacteremia, contamination during the whole blood collection procedure, contamination of the collection pack, and contamination during the blood processing procedure.

Donor bacteremia

Blood donors with an asymptomatic bacteremia or who are in the recovery phase of a bacterial infection, may have transient bacteremic episodes and still qualify as a blood donor. Approximately 30 cases of *Yersinia enterocolitica* sepsis associated with RBC transfusion have been reported in the literature. This Gram-negative bacillus may cause enterocolitis, characterized by diarrhea, low-grade fever, and abdominal pain in the donor. Symptoms may be very mild and asymptomatic cases have been documented. In cases of transfusion-associated *Yersinia enterocolitica* septicemia reported to the CDC, approximately 75% of the implicated blood donors recalled having had diarrhea in the days preceding or following their blood donation, on retrospective questioning.[42] Transfusion-associated *Yersinia enterocolitica* sepsis varies markedly from country to country, with an estimated incidence of 1 per 65,000 transfusions in New Zealand to 1 per 500,000 transfusions in the US.[43,44] It is important to note that *Yersinia*-related sepsis is very episodic. Thus, over longer time intervals, the rates in these two countries might be different.

Bacteremia of short duration may also occur following dental manipulation such as tooth extraction, the use of gum irrigation devices, and even tooth brushing. A case of transfusion-associated *Staphylococcus aureus* platelet contamination has been documented, likely the result of a bacteremia in a blood donor who had undergone the repair of a tooth 3 hours before the donation.[45]

Contamination during whole blood collection

Contamination at the time of blood collection is the major cause of bacterial contamination of platelet units. The majority of organisms present in both culture studies and case reports of platelet-associated sepsis is usually normal skin flora as it may be virtually impossible to totally decontaminate human skin. Blood culture results show an incidence of positive cultures, ranging from 2% to 6% after the cleansing of the skin.[46] In addition, it has been postulated that a small core of skin may enter the phlebotomy needle at the time of donation and that viable bacteria remain associated with the deep layers of skin, in spite of adequate skin disinfection.[47] In the presence of a scarred phlebotomy site, surface cultures may be negative, while blood cultures are positive.[48] Organisms not part of the normal skin flora may colonize on the skin and be associated with a septic transfusion reaction. A recent report of a fatal reaction due to *Clostridium perfringens* was linked to a

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

donor who frequently changed his infant children's diapers. This organism, as well as other species, normally part of fecal flora, grew in arm swab cultures from the implicated donor.[49] Although not linked to episodes of bacterial contamination of blood products, skin disinfection materials including swab sticks containing iodine or alcohol have been reported to be contaminated by various bacterial species.[28]

Contamination of the collection pack

Leaky seals, damaged tubing, or micro-punctures in collection bags have been linked to episodes of bacterial sepsis.[50] Regularly, blood packs used to collect donor blood have been found to have micro-punctures, possibly leading to the bacterial contamination of a cellular blood product.[28] Moreover, it has been reported that blood packs in the absence of any defects may be heavily contaminated. A report published in 1999 reported 6 patients who developed septicemia with *Serratia marcescens*, following transfusions with red cells or platelets.[51] This outbreak was traced to the heavy contamination of the exterior of blood packs. Upon investigation, 0.73% of blood bags from the same lot of packs grew the same ribotype of *Serratia marcescens*. It was postulated that the bacteria probably entered the blood bag at the time of blood donation, either by suction into the needle or due to contamination of the phlebotomist's hands and subsequently the donor's skin.[51]

Strategies to Decrease the Transfusion-Associated Morbidity/Mortality Risk of Contaminated Cellular Blood Products

A variety of strategies have evolved in recent years in an attempt to decrease the morbidity and mortality risk associated with transfusion-associated bacteremic and septic episodes. These measures are aimed at reducing the risk of the transfusion of cellular blood product units that are contaminated with bacteria by: (1) reducing recipient exposure; (2) avoiding contamination (i.e., improved donor screening or better skin disinfection); (3) optimizing blood component processing and storage; and (4) implementing tests and procedures that can be used to detect the presence of bacteria in blood product units.[28] These approaches are summarized in **Table 7**.

Improving donor skin disinfection

Because most of the bacteria isolated from contaminated blood products are normal skin flora, optimal disinfection of donor venesection sites may significantly reduce the bacterial contamination of blood products.[52,53] Recent studies exploring blood culture contamination rates of blood products have demonstrated that both the quality of the antiseptic used and/or the mode of application of the antiseptic can influence the efficacy of skin disinfection. Thus, one possibility of reducing the prevalence of blood product bacterial contamination might be to improve donor skin disinfection.

Removal of first aliquot of donor blood

Even if skin disinfection is optimal, bacteria may be introduced into the blood container by means of a skin core, which is often taken inadvertently when the blood collection needle enters the skin.[31] This has been reported to occur in approximately 65% of all venepunctures.[47] Recently, studies have suggested that when a needle tip is contaminated, the majority of the contaminating bacteria can be detected in the first few millimeters of blood passing through the venepuncture needle. Several recent studies suggest that the diversion of the initial 15 to 30 mL of whole blood from the main container might be associated with reduced risk of bacterial contamination.[54-56] Several blood bag manufacturers have developed plastic software to accommodate such an option. Several countries, including Canada, have recently introduced this intervention to try to reduce the rate of transfusion-associated sepsis.

Pretransfusion detection of bacteria

The pretransfusion detection of bacteria is an important potential method to reduce the risk of transfusion-associated bacteremia and septic reactions. However, no single

Table 7. Proposed strategies to reduce transfusion-associated septic risk.

A. Reducing risk of blood product contamination:
   1. Improved donor screening.
   2. Improved venepuncture site disinfection.
   3. Removal of first aliquot of donor blood.

B. Optimizing blood component processing and storage:
   1. Optimize storage temperature.
   2. Limit storage time.
   3. Universal leukocyte reduction.

C. Reduce recipient exposure to blood donors:
   1. Optimize transfusion indications.
   2. Reduce transfusion triggers for RBCs and platelets.
   3. Increase use of apheresis-derived products.

D. Pretransfusion bacterial detection:
   1. Visual inspection of components before issue.
   2. Direct staining for bacteria.
   3. Bacterial ribosomal assays.
   4. Assays for bacterial endotoxin.
   5. NAT for bacterial DNA.
   6. Measure CO_2 production by bacteria.
   7. Measure O_2 consumption by bacteria.
   8. Direct bacterial culture (manual or automated).

E. Implement pathogen reduction methodology when available.

Abbreviations: NAT, nucleic acid test; RBCs, red blood cell units.

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

currently available laboratory technique is ideal.[15] Pretransfusion detection of bacteria is much more complex than traditional transmissible disease testing, because the amount of bacteria present in a particular cellular blood component usually changes over time. Moreover, because the initial inoculum is usually very small (less than 10 organisms per mL) even a very sensitive technique will miss some contaminated units, if the testing is performed very soon after blood collection.[15]

Automated blood culture methods are being used currently in some European and US centers to test buffy-coat platelets or apheresis platelet concentrates for the presence of bacterial contamination. Because of the larger volume of these products, a 10-mL sample can be used for bacterial culture, substantially improving the sensitivity of detection. Various protocols are in use to culture platelet units: this can be done either shortly after component production, or only for platelet units that have not been transfused by day 3 of storage. A quarantine period of 24–48 hours after inoculation into a culture tube is used in some European centers, prior to issuing such platelet units. In several European countries, the regulatory authorities have accepted the extension of the platelet shelf life to 7 days, for platelet units on which bacterial cultures have been performed. Reduced platelet outdating appears to offset the cost of such bacterial testing.[40]

Because the number of bacteria present in a contaminated blood unit increases over time of storage, less sensitive methods potentially can be used in the hospital blood bank to perform bacterial screening prior to transfusion. Relatively rapid methods of bacterial detection, such as Gram-staining or the detection of metabolic changes, are being used. However, screening with such low sensitivity methods may be inadequate to prevent some transfusion-associated septic reactions.[7]

Reducing recipient exposure

One approach that has not been extensively utilized in an attempt to prevent transfusion-associated bacterial contamination is to reduce recipient exposure. In this regard, it would be possible to reduce transfusion-associated septic events by reducing transfusion triggers. Recent studies for both the use of allogeneic RBCs as well as prophylactic platelet transfusions have suggested that reduced transfusion triggers do not endanger recipients. One suggested approach to reducing the risk of transfusion-associated sepsis due to contaminated platelets is to use apheresis platelets in preference to pools of whole blood-derived platelets.[5] The universal use of apheresis platelets would significantly reduce recipient exposure to contaminated blood products by a factor of 5. Five is the number of whole blood-derived platelet units usually used per platelet transfusion episode to an adult recipient. Finally, attention should be paid to optimizing transfusion indications. Audits of cellular blood transfusion use have regularly indicated that cellular blood products are often prescribed inappropriately. The reduction of such inappropriate use of cellular blood products should significantly reduce the incidence of transfusion-associated septic reactions.

Pathogen inactivation

Over the past 10 years, a number of photodynamic or photochemical methods have been reported that could lead to the reduction of viruses, bacteria, and protozoa that are present in cellular blood products.[15] These pathogen reduction devices include: the use of a combination of a psoralen and ultraviolet A (UVA) light; riboflavin and visible light; ultraviolet B irradiation; and the addition of methylene blue or phthalocyanines with visible light.[57-60] With regard to the bacterial inactivation of contaminated platelet concentrates, Lin et al reported that the novel psoralen amotosalen (S-59), combined with UVA light exposure has effective bacterial inactivation capability.[61] Thus, a combination of 150 μmol/L of the psoralen S-59 and 3 joules/cm UVA light result in significant bacterial reduction of contaminated apheresis platelets, as well as whole blood–derived platelets. Such methodologies are undergoing regulatory review in both North America and Western Europe.

Regulation and Regulatory Approaches

Prevention of bacterial contamination

Several approaches have been instituted by the transfusion community and the FDA to help minimize the chances of bacterial contamination of transfusion products at the time of collection. However, the improvement of collection techniques cannot prevent product contamination when the source is occult bacteremia in the donor; this risk may potentially be reduced by more careful and specific questioning of donors to identify recent medical procedures or symptoms that could indicate the onset of an infectious process. For sources of contamination associated with the collection method, steps can be taken that are more likely to decrease the risk.

An obvious first step is more effective sterilization of the phlebotomy site. The FDA has publicly discussed education about proper application of disinfectants and the problems with scar tissue.[62] More effective disinfectants have been recommended to sterilize the collection sites and the use of ineffective disinfectants, such as green soap, have been discouraged.[62] However, a careful review of the literature by FDA revealed that certain skin disinfection procedures using isopropyl

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

alcohol followed by tincture of iodine that have been thought to be superior to those using povodone iodine actually are comparably effective in studies using hospitalized patients.[62] Sterilization of the skin surface also has limits when the phlebotomy needle cores out a skin plug as it passes through the skin. This inherently nonsterile skin plug can be carried into and seed the collected blood.

Recently, two studies have suggested that diversion of the initially collected blood to a separate container (referred to as a diversion pouch) away from the rest of the collected product that is to be used in transfusion could reduce the contamination rate. In a European study of actual transfusion products, diverting the first 15 mL of whole blood appeared to reduce the contamination rate of the final container.[63] Similar findings were also shown in an artificial model of blood collection.[56] The diversion pouch approach, using two recently FDA approved collection systems, is now being adopted by many blood centers as a way to lower the contamination risk. However, the ability of initial aliquot diversion to prevent clinical cases of transfusion-associated sepsis has not, as yet, been reported. It is important to note that this approach will only reduce the level of skin contaminants in blood products.

Prevention of bacterial proliferation—Refrigeration of platelets?

For red cells that are stored at 4°C, bacterial growth is slow and limited to a few psychrophilic bacteria such as *Yersinia enterocolitica*, *Pseudomonas* species and *Serratia liquefaciens*.[64] In comparison, platelets are stored at room temperature and provide a good medium for growth of both Gram-negative and Gram-positive bacteria. For most bacterial species, growth in platelet units can occur, rapidly reaching log phase within 24-48 hours.[12,26] An exception is the common skin contaminant, *Staphylococcus epidermidis* which is a slower growing organism and usually reaches the log phase in 48–72 hours. Since this and similar organisms account for a large proportion of the bacterial species found to contaminate blood units, such slower growth characteristics need to be considered when optimizing sampling strategies for bacterial detection.[65]

Rapid proliferation of bacteria during storage of transfusion products could be decreased if cold temperatures were used. For red cells, this is generally a standard practice and reduces the growth of most bacterial species and the risk of transfusion related sepsis. On the other hand, platelets do not maintain adequate function when stored at cold temperatures. Even relatively short exposures to cold are associated with irreversible changes in platelets that significantly decrease their ability to remain in circulation.[66] Attempts to understand the basis of the temperature sensitivity of platelets have only recently been productive.

A new study has suggested that platelets may respond to cold by clustering of GpIb on their surface which is then recognized by macrophages as a signal for clearance.[67] Better understanding of the molecular changes in platelet physiology after cold exposure could lead to alternate storage conditions that would allow cold temperature storage and a reduction of bacterial proliferation while preserving platelet function and viability. Evaluation of novel storage conditions would involve in vitro experiments to demonstrate that the platelets have not been extensively activated or damaged by the conditions. Since in vitro tests have a poor predictive value for clinical performance of platelets, the gold standard for platelet evaluation remains the recovery and survival of radiolabeled transfused platelets.[68] Platelets, collected from a single donor by apheresis, are divided into two products and stored under either conventional or novel conditions. At the end of storage a small portion of the cells is labeled with either ^{51}Cr or ^{111}In and the radiolabeled cells are reinfused into the original donor. Serial blood samples are then taken to monitor clearance of the cells from circulation. The double label allows for a direct comparison of the same platelets stored under different conditions in the same recipient.

Detection of bacteria in transfusion products

Ultimately, the reduction of bacterial contamination of transfusion products will require routine testing of the products for the presence of bacteria. Attempts to detect bacteria in transfusion products have spanned the range of simple to highly sophisticated state-of-the-art methodologies. On the low tech side, changes in the appearance of the product, such as platelet swirling or the color of the red cell units, have been utilized but with low specificity and sensitivity.[69] Other tests such as determining pH or glucose levels, or direct bacterial staining with Gram's stain or acridine orange have similarly not been very useful due to relatively low sensitivity when compared with bacterial concentrations that can cause sepsis. Tests with bacteria-specific nucleic acid probes or fluorescent dyes or antibodies are currently being developed.[70,71] However, the most useful detection systems currently available appear to be automated, culture-based methods similar to what has been used for clinical detection of bacteremia in blood cultures obtained from patients.[65]

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

Sampling strategy for detection of bacteria in a transfusion product

Currently utilized platelet products are either random donor or apheresis units. Both types of units may be stored individually for up to 5 days at room temperature. Approximately 4–6 random donor units are pooled prior to transfusion to achieve a transfusion product with sufficient platelet content. The major factor in sampling either a random donor unit or an apheresis unit is the difference in volume. A typical apheresis unit contains approximately 200–250 mL while the random donor unit contains only 45–55 mL. Thus, the volume of the sample taken for bacterial detection can have a significant impact on the amount of product left for transfusion, particularly for random donor units. On the other hand, a larger sample volume increases sensitivity and thus a balance has to be reached to optimize sensitivity and minimize the impact on the product.

The timing of sampling is highly dependent on the method of detection. For culture-based methods, the product sample is inoculated into a container (bottle or bag) that allows for bacterial growth. Usually this occurs at 37°C and in the presence of sodium polysulfone (SPS), a bacteria growth-potentiating substance, that allows the bacteria to grow faster in the device than in the transfusion product. As the bacteria proliferate in the device, there is a fixed amount of time before a positive signal can be detected. The time to detection, dependent on the initial inoculum and the growth characteristic of the bacteria, is usually 24-48 hours when employing currently available detection methods. Because of this time required, the ideal sampling time for culture-based devices is as early as possible in the storage period so that a test-based decision about the clinical usefulness of the product can be made prior to its use. However, since the level of contamination at the time of collection is low and bacteria could be missed by a sampling error (especially with a low sample volume) at the beginning of storage, a certain amount of presampling storage time is usually allowed for the bacteria to begin to proliferate in the product. For platelets this is usually 24–48 hours.

The length of this presampling incubation period also depends on the sensitivity of the detection device. A more sensitive device can utilize a sample collected earlier in the product storage period while a less sensitive device would require a sample that contains more bacteria as occurs later in storage. The sampling strategy can be altered for a detection method that detects bacteria in real time. These approaches utilize probes, antibodies or nucleic acid–based detection system and can produce an answer within hours of sampling. The sensitivity of culture-based assays should be in the range of 10–100 CFU/mL and the sensitivity of methods that could be used at the point of transfusion would most likely be in the range of 100–1000 CFU/mL.[26]

Current approval process for bacterial detection devices

The FDA has encouraged manufacturers to submit applications for devices that will detect bacteria in transfusion products. The most urgent need is for bacterial screening of platelet products. Two devices have recently been cleared by the FDA for use in quality control monitoring of the platelet collection process that, in the past, was performed by manual culture (BioMeriuex, Inc. BK 000042; Pall Corp. BK 020014). The current devices allow sampling of the platelet product and automation of the quality control culture process. One device detects bacteria based on elaboration of CO_2 in the sample culture, while the other detects a decrease in pO_2. *However, these devices have not yet been specifically approved for use in release of platelets for transfusion because the effectiveness of the devices to detect bacterial contamination in the clinical setting has not been established.*

For the quality control indication, the validation was based on in vitro "spiking" experiments. A unit of platelets, either whole blood–derived, random donor, or apheresis-derived, single donor, was deliberately contaminated with a known amount of a single bacterial species. The unit was then repeatedly sampled 10 times and each time the sample was inoculated into the device. Thus, 10 separate readings were performed by the device for each bacterial species. The manufacturers were encouraged to validate their devices for as many bacterial species as possible and a list of the most common relevant bacteria was agreed on based on literature search, FDA advisory committee input and public workshops input.[10,65]

Trials recommended under "actual clinical use" conditions

The FDA has proposed that validation of bacterial detection devices for release of platelets for transfusion would require a field trial of the device under actual clinical use conditions.[62] The design of such a trial would be to obtain a sample for bacterial detection by a culture-based device early in the storage period. A second sample would then be taken at the end of the storage period or at the time of release of platelets. The results of both cultures would be compared to determine if the first culture was predictive of the result of the second culture. If the unit is contaminated at collection, then the bacteria will have time to grow between the first and second sampling. The bacterial load

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

should be higher and detection of bacteria should be easier at the second sampling.

The needed studies should demonstrate that a sample taken early in the storage period and screened by the automatic culture device is predictive of the culture results up to the time of outdate of the product. Although some aspects of the study could be modeled in vitro it is not clear what is the expected level of bacterial contamination under actual clinical conditions, whether the devices will have sufficient sensitivity or whether sampling errors may occur when low levels of bacteria are present early in the storage period. In addition, such studies will also demonstrate the false positive rate and rate of contamination, if any, from bacteria introduced by sampling and inoculation procedures.[72] An excessive false positive rate would lead to an unnecessarily high discard rate for transfusion products.

Such issues raise the level of safety and efficacy concerns for devices intended for release of blood products for transfusion and are the basis for the current FDA practice of requesting clinical or field study data prior to approval of the devices. The field trials of the bacterial detection devices could be combined, under an IND or IDE application, with an extension of storage to day 7 or with pre storage pooling, allowing some costs to potentially be offset by savings from decreasing platelet product loss due to expiration and/or from pre storage leukoreduction of a pool instead of individual units.

Pathogen reduction technologies

As an additional measure of safety, transfusion products could potentially be treated with a pathogen reduction process to decrease or eliminate pathogens, including bacteria, which were not detected by testing. Methods are being developed that allow selective targeting of pathogens in blood products. The selectivity is based on absence of nucleic acids in platelets and red cells. A chemical compound is added to the transfusion product that interacts with the nucleic acids of pathogens and, upon spontaneous or light energy–induced activation, cross links nucleic acids and prevents their transcription and replication. Efficacy of these methods is usually established by in vitro studies where various pathogens are "spiked" into a platelet or red cell unit and then treated using the pathogen reduction methodology. The efficacy of these treatments should be in the range of 6–10 log reduction of common bacterial pathogens.[10]

However, from an FDA perspective, evaluation of the safety aspects of these methods is more complex and challenging. It includes assessment of possible damage caused by the treatment to the transfusion product (including functionality and survival of transfused cells) and evaluation of the potential toxicities of any residual chemicals to the recipients of the product. In fact, concerns about the safety of these products may arise because of mutagenicity of some of the chemical agents employed and thus their potential to be carcinogenic and genotoxic. In addition, the reactions of the chemical agent(s) with plasma and cellular proteins and lipids can create novel chemical entities that may have unexpected toxicities and increased immunogenicity when administered to certain patient populations. Because of the uncertainties that surround the treated products, even after extensive preclinical and clinical evaluation, it is likely that postmarketing studies will be needed to identify any low frequency adverse events associated with their use in a broader patient population. Another issue is whether the therapeutic efficacy of the treated transfusion products has been fully preserved after treatment with the pathogen reduction process. This is again being evaluated both in vitro and in Phase 2 and 3 clinical trials designed to follow efficacy endpoints, such as hemostasis in the case of platelet transfusions.

The final analysis of the documented and theoretical risks of the pathogen reduction process to the recipient of treated transfusion products will need to be weighed against the risk of the transfusion-transmitted diseases they could prevent, a risk which currently is relatively low. Thus, the clinical use of these products will ultimately depend on the appropriate risk benefit analysis for proposed uses and upon the data submitted for evaluation.

Transfusion product substitutes

The risk of transmitting pathogens by transfusion has been a major driving force for the development of manufactured substitutes for transfusion products. Such products would ideally be free of pathogens, have a long shelf life and may also not present the requirement of having to be serologically typed for each recipient. However, initial results of efforts to engineer red cells or platelets have so far fallen short of matching the natural cells. For example, initial efforts using the hemoglobin molecule to carry oxygen has been associated with a variety of toxicity issues.[73] Additional research and clinical testing will need to be done to fully evaluate and, hopefully, realize the potential of these types of products.

Bacterial detection and the extension of platelet storage

Increased risk of bacterial contamination has been the major concern regarding prestorage pooling of platelets and extension of platelet storage beyond the currently allowed 5 days. For pooled platelets it has been demonstrated that a platelet pool created by combining

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

1 contaminated unit with 3–4 other units permits greater levels of bacteria at stationary phase.[74] Until 1986, platelets could be stored for up to 7 days at room temperature. However, due to concerns over a rise in clinically significant transfusion-associated infections from an increased bacterial load at the end of an extended storage period, this was shortened to 5 days on the advice of an FDA scientific advisory committee.

Returning to platelet storage beyond 5 days and allowing prestorage pooling of platelets would require an appropriately validated effective bacterial detection system. Such validation would involve in vitro testing with pooled products and a field trial in a clinical setting. In addition to bacterial detection the storage conditions for pooled platelets and platelets stored beyond 5 days will need to be validated to demonstrate that platelet quality is preserved under these conditions.[75] Use of FDA-approved sterile connection devices otherwise allows pooling and sampling of platelets without introducing bacterial contamination through the pooling process itself.[62]

Regulatory summary

Bacterial contamination of transfusion products, especially platelets, is a significant clinical problem with multiple causes. Based on recognition of this issue, the FDA and the blood industry have taken steps to improve control of bacterial contamination at multiple steps during blood collection and processing. Dealing effectively with this problem will involve continued and enhanced education of phlebotomy, technical, nursing, and medical staff with regard to sources of contamination and the importance of the problem. Using approved products and procedures, blood collection centers can implement practices that may decrease bacterial contamination, including better skin disinfection, collection of blood with a diversion pouch set, testing for bacteria, and, potentially, the use of safe and effective pathogen reduction technologies if and when available. Promising technologies for bacterial detection appear to be close at hand and offer significant potential to screen out contaminated units. The FDA and the blood community share a common goal that increased efforts focused on the problem of bacterial contamination will be translated into successes comparable to those we have already achieved in decreasing risks from most transfusion transmitted viral diseases.

Concluding Comments

Septic transfusion reactions associated with the use of contaminated blood products remain a very significant adverse event. Nonetheless, clear-cut approaches to reduce the frequency of such events are appearing. A wide variety of measures have been proposed in order to reduce the frequency of transfusion-associated septic reactions and many of these measures are being actively investigated, and in some countries being instituted.[15,76] Thus, the potential reduction in the risk of transfusion-associated septic reactions is a realistic possibility in the foreseeable future.

References

1. Jacobs MR, Palavecino E, Yamotovian R. Don't bug me: The problem of bacterial contamination of blood components—challenges and solutions. Transfusion. 2001;41:1131-1134.
2. Goodnough LT, Shander A, Brecher ME. Transfusion medicine: looking to the future. Lancet. 2003;361:161-169.
3. Association Bulletin #96-6: Bacterial contamination of blood components. AABB Faxnet, No. 294, American Association of Blood Banks, Bethesda, MD 1996.
4. Dykstra A, Jacobs J, Yamtovian R. Prospective microbiologic surveillance (PMS) of random donor (RDP) and single donor apheresis platelets (SDP). Transfusion. 1998;38:104S.
5. Ness PM, Braine HG, King K, et al. Single donor platelets reduce the risk of septic transfusion reactions. Transfusion. 2001;41:857-861.
6. Yomtovian R, Lazarus HM, Goodnough LT, et al. A prospective microbiologic surveillance program to detect and prevent the transfusion of bacterially contaminated platelets. Transfusion. 1993;33:902-909.
7. Dodd RY. Adverse consequence of blood transfusion: quantitative risk estimates. In: Nance ST, ed. Blood supply: risks, perceptions and prospects for the future. Bethesda, MD: American Association of Blood Banks; 1994:1-24.
8. Klein HG, Dodd RY, Ness PM, Fratantoni JA, Nemo GJ. Current status of microbial contamination of blood components: summary of a conference. Transfusion. 1997;37:95-101.
9. FDA workshop. Bacterial Contamination of Platelets. 1999. Available at: http://www.fda.gov/cber/minutes/bact092499.pdf. Accessed 7/20/03.
10. FDA workshop. Safety and Efficacy of Methods for Reducing Pathogens in Cellular Blood Products Used in Transfusion. 2002; Available at: http://www.fda.gov/cber/minutes/pathtrans080702.pdf.
11. Kuehnert MJ, Roth VR, Haley NR, et al. Transfusion-transmitted bacterial infection in the United States, 1998 through 2000. Transfusion. 2001;41:1493-1499.
12. Blajchman MA. Bacterial contamination and proliferation during the storage of cellular blood products. Vox Sang. 1998;74:155-159.
13. Dodd RY. Bacterial contamination and transfusion safety: experience in the United States. Transfus Clin Biol. 2003;10:6-9.
14. Brecher ME, Hay SN. The role of bacterial testing of cellular blood products in light of new pathogen inactivation technologies. Blood Therapies Med. 2003;3:49-55.
15. Blajchman MA. Incidence and significance of the bacterial contamination of blood components. Dev Biol. 2002;108:59-67.
16. Association Bulletin #02-8: Update on Bacterial Contamination of Platelet Units. American Association of Blood Banks, Bethesda, MD 2002.
17. AdvaMed. Ensuring blood safety and availability in the U.S.: technological advances, cost, and challenges to payment. Lewin Group. Transfusion (Suppl). 2003; 43:41S-46S.
18. American Red Cross: Blood Safety and Availability. 2002;

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

Available at: http://www.redcross.org/services/biomed/blood/supply/intro.html. Accessed 7/20/03.
19. Dodd RY, Notari EP, Stramer SL. Current prevalence and incidence of infectious disease markers and estimated window-period risk in the American Red Cross blood donor population. Transfusion. 2002;42:975-979.
20. AuBuchon JP, Birkmeyer JD, Busch MP. Safety of the Blood Supply in the United States: Opportunities and Controversies. Ann Intern Med. 1997;127:904-909.
21. Calman KC. Cancer: science and society and the communication of risk. BMJ. 1996; 313:799-802.
22. Lee DH, Paling JE, Blajchman MA. A new tool for communicating transfusion risk information. Transfusion. 1998;38:184-188.
23. Hunter N, Foster J, Chong A, et al. Transmission of prion diseases by blood transfusion. J Gen Virol. 2002;83:2907-2914.
24. Association Bulletin #01-4: Non-infectious Serious Hazards of Transfusion—NiSHOTs. American Association of Blood Banks; Bethesda, MD 2001.
25. Hillyer CD, Lankford KV, Roback JD, Gillespie TW, Silberstein LE. Transfusion of the HIV-seropositive patient: immunomodulation, viral reactivation, and limiting exposure to EBV (HHV-4), CMV (HHV-5), and HHV-6, 7, and 8. Transfus Med Rev. 1999;13:1-17.
26. Brecher ME, Holland PV, Pineda AA, Tegtmeier GE, Yomtovian R. Growth of bacteria in inoculated platelets: implications for bacteria detection and the extension of platelet storage. Transfusion. 2000;40:1308-1312.
27. Borden CW, Hall WH. Fatal transfusion reactions from massive bacterial contamination of blood. N Engl J Med. 1951;245:760-765.
28. Goldman M, Blajchman MA. Bacterial contamination. In: Popovsky M, ed. Transfusion Reactions. 2nd ed. Bethesda, MD: AABB; 2001:133-159.
29. Sazama K. Reports of 355 transfusion-associated deaths: 1976 through 1985. Transfusion. 1990;30:583-590.
30. Honig CL, Bove JR. Transfusion-associated fatalities: Review of Bureau of Biologics reports 1976-1978. Transfusion. 1980;20:653-661.
31. Blajchman MA, Ali AM. Bacteria in the blood supply: An overlooked issue in transfusion medicine. In: Nance, SJ, ed. Blood Safety: Current Challenges. Bethesda, MD: AABB; 1992: 213-228.
32. Morrow JF, Braine HG, Kickler TS, et al. Septic reactions to platelet transfusions. JAMA. 1991;266:555-558.
33. Barrett BB, Anderson JW, Anderson KC. Strategies for the avoidance of bacterial contamination of blood components. Transfusion. 1993;133:228-233.
34. Yomtovian R, Lazarus HM, Goodnough LT, et al. A prospective microbiologic surveillance program to detect and prevent the transfusion of bacterially contaminated platelets. Transfusion. 1993;33:902-909.
35. Chiu EKW, Yuen KY, Lie AKW, et al. A prospective study on symptomatic bacteremia from platelet transfusion and its management. Transfusion. 1994;34:950-965
36. Blajchman MA, Ali A, Lyn P, et al. A prospective study to determine the frequency of bacterial contamination in random donor platelet concentrates [abstract]. Blood. 1994;84(suppl):529.
37. Leiby DA, Kerr KL, Compos JM, Dodd RY. A prospective analysis of microbial contaminants in outdated random-donor platelets from multiple sites. Transfusion. 1997;37:259-263.
38. Blajchman MA, Ali A, Lyn P, et al. Bacterial surveillance of platelet concentrates: quantitation of bacterial load. [Abstract]. Transfusion. 1997;37(suppl):74S.
39. Dzieczkowski JS, Barrett BB, Nester D, et al. Characterization of reactions after exclusive transfusion of while cell-reduced cellular blood components. Transfusion. 1995;35:20-25.
40. Aubuchon JP, Cooper LK, Leach MF, et al. Experience with universal bacterial culturing to detect contamination of apheresis platelet units in a hospital transfusion service. Transfusion. 2002;42:855-861.
41. Perez P, Salmi LR, Follea G, et al. Determinants of transfusion-associated bacterial contamination: Results of the French BACTHEM Case-Control Study. Transfusion. 2001;41:862-872.
42. Grossman BJ. Kollins P, Lau PM, et al. Screening blood donors for gastrointestinal illness: a strategy to eliminate carriers of *Yersinia enterocolitica*. Transfusion. 1991;31:500-501.
43. Theakston EP, Morris AJ, Streat SJ, et al. Transfusion-transmitted *Yersinia enterocolitica* infection in New Zealand. Aust N Z J Med 1997; 127:62-67.
44. Beresford AM. Transfusion reaction due to *Yersinia enterocolitica* and review of other reported cases. Pathology. 1995;27:133-135.
45. Goldman M, Blajchman MA. Blood product-associated bacterial sepsis. Transfus Med Rev. 1991;5:73-83.
46. Schifman RB, Pindur A. The effect of skin disinfection materials on reducing blood culture contamination. Am J Clin Pathol. 1993;99:536-538.
47. Gibson T and Norris W. Skin fragments removed by injection needles. Lancet. 1958;2:983-985.
48. Anderson KC, Lew MA, Gorgone BC, et al. Transfusion-related sepsis after prolonged platelet storage. Am J Med. 1986;81:405-411.
49. McDonald CP, Hartley S, Orchard K, et al. Fatal *Clostridium perfringens* sepsis from a pooled platelet transfusion. Trans Med. 1998;8:19-22.
50. Hogman CF, Engstrand L. Serious bacterial complications from blood components–how do they occur? Trans Med. 1998;8:1-3.
51. Hogman CF, Fritz H, Sandberg L. Posttransfuion *Serratia marcescens* septicemia. Transfusion. 1993;33:189-191.
52. Goldman M, Roy G, Frechette N, et al. Evaluation of donor skin disinfection methods. Transfusion. 1997;37:309-312.
53. McDonald CP, Lowe P, Roy A, et al. Evaluation of donor arm disinfection techniques. Vox Sang. 2001;80:135-141.
54. Bruneau C, Perez P, Chassaigne M et al. Efficacy of a new collection procedure for preventing bacterial contamination of whole-blood donations. Transfusion. 2001;41:74-81.
55. de Korte D, Marcelis JH, Soeterboek AM. Determination of the degree of bacterial contamination of whole-blood collections using an automated microbe-detection system. Transfusion. 2001;41:815-818.
56. Wagner SJ, Robinette D, Friedman LI, Miripol J. Diversion of initial blood flow to prevent whole-blood contamination by skin surface bacteria: an in vitro model. Transfusion. 2000;40:335-338.
57. Ben-Hur E, Moor ACE, Margolis-Nunno H, et al. The photodecontamination of cellular blood components: Mechanisms and use of photosensitization in transfusion medicine. Transfus Med Rev. 1997;10:15-22.
58. Corash L. Inactivation of viruses, bacteria, protozoa, and leukocytes in platelet concentrates: Current research perspectives. Transfus Med Rev. 1999;13:18-30.
59. Chapman J. Progress in improving the pathogen safety of red cell concentrates. Vox Sang. 2000;78(suppl 2):203-204.
60. Goodrich RP. The use of riboflavin for the inactivation of

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

pathogens in blood products. Vox Sang. 2000;78(suppl 2):211-215.
61. Lin L, Cook DN, Wiesehahn GP et al. Photochemical inactivation of viruses and bacteria in platelet concentrates by use of a novel psoralen and long-wavelength ultraviolet light. Transfusion. 1997;37:423-435.
62. FDA Blood Products Advisory Committee, December. 2002. Available at: http://www.fda.gov/ohrms/dockets/ac/02/transcripts/3913t1.rtf. 7/20/03
63. de Korte D, Marcelis JH, Verhoeven AJ, Soeterboek AM. Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections. Vox Sang. 2002;83:13-16.
64. Kopko PM, Holland PV. Mechanisms of severe transfusion reactions. Transfusion Clin Bio. 2001;8:278-281.
65. Brecher ME, Means N, Jere CS, Heath DG, Rothenberg SJ, Stutzman LC. Evaluation of an automated culture system for detecting bacterial contamination of platelets: an analysis with 15 contaminating organisms. Transfusion. 2001;41:477-482.
66. Vostal JG, Mondoro TH. Liquid cold storage of platelets: a revitalized possible alternative for limiting bacterial contamination of platelet products. Trans Med Rev. 1997;11:286-295.
67. Hoffmeister KM, Felbinger TW, Falet H, et al. The clearance mechanism of chilled blood platelets. Cell. 2003;112:87-97.
68. FDA draft guidance. For platelet testing and evaluation of platelet substitutes. 1999; Available at: http://www.fda.gov/cber/gdlns/platelet.htm. 7/20/03
69. Wagner SJ, Robinette D. Evaluation of swirling, pH, and glucose tests for the detection of bacterial contamination in platelet concentrates. Transfusion. 1996;36:989-993.
70. Brecher ME, Wong EC, Chen SE, Vampola C, Rocco RM. Antibiotic-labeled probes and microvolume fluorimetry for the rapid detection of bacterial contamination in platelet components: a preliminary report. Transfusion. 2000;40:411-413.
71. Brecher ME, Hogan JJ, Boothe G, et al. Platelet bacterial contamination and the use of a chemiluminescence-linked universal bacterial ribosomal RNA gene probe. Transfusion. 1994;34:750-755.
72. AuBuchon JP, Cooper LK, Leach MF, Zuaro DE, Schwartzman JD. Experience with universal bacterial culturing to detect contamination of apheresis platelet units in a hospital transfusion service. Transfusion. 2002;42:809-811.
73. Winslow RM. Current status of blood substitute research: towards a new paradigm. J Intern Med. 2003;253:508-517.
74. Wagner SJ, Moroff G, Katz AJ, Friedman LI. Comparison of bacteria growth in single and pooled platelet concentrates after deliberate inoculation and storage. Transfusion. 1995;35:298-302.
75. FDA Blood Products Advisory Committee, March. 2003. Available at: http://www.fda.gov/ohrms/dockets/ac/03/transcripts/3940t1.htm. 7/20/03
76. Engelfriet CP, Reesink HW, Blajchman MA, et al. International Forum: Bacterial contamination of blood components. Vox Sang. 2000;78:59-67.

Downloaded from http://ashpublications.org/hematology/article-pdf/2003/1/575/1713810/575_589a.pdf by guest on 08 March 2023

BD

BD Saf-T-Intima™ closed IV cat



BD Saf-T-Intima™ closed IV catheter system

The BD Saf-T-Intima™ closed IV catheter system incorporates preattached extension tubing to help support reduction in blood exposure.

About

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

Configure Accept

A removable PRN adapter allows the use of an ISO-compliant needleless connector.

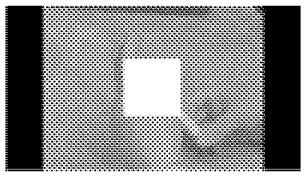
Closed system

Preattached extension tubing offers a closed system to minimize blood exposure during catheter insertion.

BD Vialon™ biomaterial

The system is constructed with BD Vialon biomaterial, a proprietary catheter material that softens in the vein.

Related Videos



BD Saf-T-Intima™ Closed IV Catheter...

Related Products



BD Nexiva™ closed IV catheter system



BD Nexiva™ Diffusics™ closed IV catheter system

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

Configure Accept

Do you like this? Share it:

Contact Sales

Contact Support

DOWNLOADS

BD Saf-T-Intima™ directions for use

BD Saf-T-Intima™ points to practice in-service material

IV catheters/devices brochure

RESOURCES

Infusion Resource Library

Notes

* Compared to a nontapered tip

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

Configure Accept

Video gallery

CLINICAL EXCELLENCE

Case studies

Events

Webcasts

Training

SUPPORT

Technical support

Product security and privacy

Live chat

Customer portals

Alerts and notices

Electronic Instructions for Use

© 2019 BD. All rights reserved. Unless otherwise noted, BD, the BD Logo and all other trademark are property of Becton, Dickinson and Company.

Privacy Policy | Terms of Use | Cookie Options

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

Configure Accept

The Clinical Significance of Positive Blood Cultures in the 1990s: A Prospective Comprehensive Evaluation of the Microbiology, Epidemiology, and Outcome of Bacteremia and Fungemia in Adults

Melvin P. Weinstein, Michael L. Towns, Seth M. Quartey, Stanley Mirrett, Larry G. Reimer, Giovanni Parmigiani, and L. Barth Reller

From the Departments of Medicine and Pathology, University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School, New Brunswick, New Jersey; Clinical Microbiology Laboratory, Duke University Medical Center, Departments of Medicine and Pathology, Duke University School of Medicine, and Institute of Statistics and Decision Sciences, Duke University, Durham, North Carolina; and Departments of Pathology and Medicine, Salt Lake City Veterans Administration Medical Center and University of Utah Medical School, Salt Lake City, Utah

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 19 April 2019

To assess changes since the mid-1970s, we reviewed 843 episodes of positive blood cultures in 707 patients with septicemia. The five most common pathogens were *Staphylococcus aureus, Escherichia coli,* coagulase-negative staphylococci (CNS), *Klebsiella pneumoniae,* and *Enterococcus* species. Although CNS were isolated most often, only 12.4% were clinically significant. Half of all episodes were nosocomial, and a quarter had no recognized source. Leading identifiable sources included intravenous catheters, the respiratory and genitourinary tracts, and intraabdominal foci. Septicemia-associated mortality was 17.5%. Patients who received appropriate antimicrobial therapy throughout the course of infection had the lowest mortality (13.3%). Multivariate analysis showed that age (relative risk [RR], 1.80), microorganism (RR, 2.27), source of infection (RR, 2.86), predisposing factors (RR, 1.98), blood pressure (RR, 2.29), body temperature (RR, 2.04), and therapy (RR, 2.72) independently influenced outcome. Bloodstream infections in the 1990s are notable for the increased importance of CNS as both contaminants and pathogens, the proportionate increase in fungi and decrease in anaerobes as pathogens, the emergence of *Mycobacterium avium* complex as an important cause of bacteremia in patients with advanced human immunodeficiency virus infection, and the reduction in mortality associated with infection.

The presence of living microorganisms in blood has substantial clinical importance. From the diagnostic standpoint, a positive blood culture yielding a clinically important microorganism represents either failure of host defenses to contain an infection at its primary focus or failure of the physician to effectively eradicate, drain, excise, or otherwise remove that focus of infection. The presence of bacteremia or fungemia also is an indicator of disseminated infection and, as such, generally indicates a poorer prognosis than that associated with localized disease. A positive blood culture, however, is not always clinically significant, since contamination may occur or the positive result might represent the transient and self-limited presence of microorganisms in the blood [1].

Our current understanding of the clinical significance of positive blood cultures has been enhanced by studies reported over several decades [2–21]. In recent years there have been many changes in medical practice, influenced in part by technologic advances and in part by the increased incidence of diseases not recognized previously. Just a few examples include the more frequent use of invasive or prosthetic devices; the increase in solid-organ and bone marrow transplantation as well as improvements in posttransplantation medical management; the introduction of HIV infection and AIDS as a scourge on late 20th century society; and therapeutic advances in the form of improved imaging techniques, less invasive methods of draining pus from closed spaces, and availability of broader spectrum antiinfective therapy.

We therefore undertook a comprehensive analysis of positive blood cultures in the 1990s. As a template for this project, we used an earlier review of bacteremia and fungemia [10, 11] authored by two of the current investigators (M.P.W. and L.B.R.). Although the earlier work has been widely recognized, the aforementioned changes in medicine and its practice argued for the need to reevaluate the clinical and prognostic importance of positive blood cultures. The primary goal of this study, therefore, was to determine the current microbiology, epidemiology, and prognostic importance of positive blood cultures, with special reference to similarities with and differences from the earlier reports from our group [10, 11, 22, 23].

Materials and Methods

For a 12-month period, February 1992 through January 1993, all inpatients ≥18 years of age with culture-positive blood

Received 4 April 1996; revised 27 September 1996.

Reprints or correspondence: Dr. Melvin P. Weinstein, UMDNJ–Robert Wood Johnson Medical School, 1 Robert Wood Johnson Place, New Brunswick, New Jersey 08903-0019.

Clinical Infectious Diseases 1997;24:584–602
© 1997 by The University of Chicago. All rights reserved.
1058–4838/97/2404–0009$02.00

KUR-MAG-DE005275

were evaluated at Duke University Medical Center (DUMC), in Durham, NC; Robert Wood Johnson University Hospital (RWJUH), in New Brunswick, NJ; and the Salt Lake City Veterans Administration Medical Center (SLCVAMC), in Salt Lake City. Each patient was observed prospectively from the time the blood culture became positive, unless the patient had been discharged or had died before review of the hospital records by one of the investigators, in which case the review of the medical record was retrospective. Charts were evaluated according to the method of Feinstein et al. [24, 25], such that if the presence or absence of a particular finding was not clearly indicated, that case was excluded from analysis for that finding.

During the study period, 20 mL or more of blood was obtained for each culture and inoculated into media for processing on the BACTEC NR660 (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) or BacT/Alert (Organon Teknika, Durham, NC) blood culture system or both systems at all three centers. Blood was obtained at the bedside by house officers, medical students, or other trained health care personnel (nurses, phlebotomists, etc.) using 70% isopropyl alcohol and then 10% povidone-iodine. Although most of the blood culture specimens were obtained by peripheral venipuncture, it was not possible to determine specifically which ones were obtained in this manner and which were obtained through access devices.

Bottles were transported to the laboratory and incubated until flagged as positive or for 7 days in either BACTEC nonradiometric instruments (NR6 and NR7 bottles) or BacT/Alert continuous-monitoring instruments (BacT/Alert aerobic and anaerobic bottles). Broth from positive bottles was gram-stained and subcultured with use of standard techniques [26]. Susceptibility testing of isolates was done according to guidelines established by the National Committee on Clinical Laboratory Standards [27, 28].

All information obtained from patients' records was recorded on data worksheets and then transferred to a database software program for analysis.

Definitions

Definitions for this study for the most part were identical to those of Weinstein et al. [10, 11]. Only a few will be detailed here. New or modified definitions also will be detailed.

True septicemia vs. contamination. Each positive blood culture was assessed critically by one of the investigators, each an infectious disease physician. All isolates were categorized as true-positives, contaminants, or of unknown clinical significance. The categorical decision was made after the following factors were taken into account: the patient's clinical history, physical findings, body temperature at the time of the blood culture, leukocyte count and differential cell counts, number of positive blood cultures out of the total number performed, results of cultures of specimens from other sites, imaging results, histopathologic findings, and clinical course and response to therapy. If the clinical significance of the positive culture was not clear on the basis of the available information, the isolate was categorized as being of unknown significance.

Episode. An episode of bacteremia, fungemia, or mycobacteremia was defined by the first positive blood culture in a series or by any new positive blood culture result that occurred >48 hours after the previous positive result, unless it was clear to the investigator that the new positive culture was part of the same episode. For example, a positive blood culture for *Staphylococcus aureus* on the fifth day of antibiotic therapy for *S. aureus* endocarditis was considered part of the original bacteremic episode.

Community- vs. hospital-acquired septicemia. Each episode was classified as either community- or hospital-acquired septicemia, according to guidelines of the Centers for Disease Control and Prevention [29]. Septicemia in nursing home patients with positive blood cultures was always classified as hospital-acquired, whereas that in patients transferred from other outside facilities was classified according to their total period of hospitalization at both institutions.

Antimicrobial Therapy

Data on antimicrobial therapy were obtained at four chronologic points for each episode. These points were as follows: (1) at the time the first positive blood culture specimen was obtained, (2) after the blood culture was performed but before positive culture results were reported (i.e., empirical therapy), (3) after the blood culture was reported to be positive and gram-stained smear results were made known to the primary physician(s) but before organism identification and susceptibility test results were available, and (4) after organism identification and susceptibility test results were reported to the physicians.

Therapy was assessed critically at each time point on the basis of the clinical information available (time points 1–3) or the identification of the isolate and susceptibility test results (time point 4).

Treatment was judged to be the first choice if it was in accordance with the recommendations of a standard reference for antimicrobial therapy [30] and an alternative choice if the etiologic microorganism(s) was (were) susceptible to the agent administered but that agent was not considered the first choice. For purposes of judging the adequacy of therapy, both first-choice and alternative-choice agents were considered appropriate. Therapy was designated as the wrong choice if the causative microorganism was resistant to the antibiotic given. Superfluous therapy was defined as either the administration of unnecessary antibiotics in addition to a first- or alternative-choice agent or the administration of antibiotics for contaminant isolates. Ineffective or superfluous agents given for infections elsewhere in the body were recorded separately.

If a patient died before susceptibility results became available, that fact was recorded. When no therapy was given after the report of a positive blood culture to the physician, one of

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

three assessments was made: (1) appropriate, if the isolate was a contaminant; (2) appropriate, if the episode was judged to represent true but transient bacteremia or fungemia that resolved spontaneously without adversely affecting the patient; or (3) inappropriate, if the culture represented true sepsis and the patient's status deteriorated because of the infection.

Outcome

The outcome of each episode was categorized as follows. The patient was (1) discharged alive, (2) alive but still hospitalized 30 days or longer after the onset of bacteremia or fungemia, (3) dead from causes attributable to the septicemic episode, or (4) dead from causes unrelated to septicemia. For the purposes of this study, mortality is termed associated or nonassociated in the subsequent text and tables.

Statistical Methods

For univariate analyses, statistical significance was calculated with the χ^2 test as described by O'Brien and Shampo [31]. The multivariate analysis and the resulting significance calculations were based on the logistic regression model [32], as implemented by the function "glm" in the statistical package S+ [33].

Results

During the study period, 1,585 blood culture–positive episodes occurred in 1,267 patients and yielded 1,844 microorganisms. Nine hundred forty-four microorganisms were isolated from 707 patients who had 843 episodes of true bacteremia or fungemia. There were 658 contaminant episodes and 84 episodes of unknown clinical significance.

Microbiological Features

The microorganisms isolated from positive blood cultures and the frequency with which they caused true bacteremia or fungemia are shown in table 1. The most common isolates from blood were coagulase-negative staphylococci. *S. aureus* was the microorganism most frequently causing true bacteremia; 87.2% of isolates were judged clinically significant. In contrast, only 12.4% of the coagulase-negative staphylococci were clinically significant, but they ranked as the third most frequent cause of bacteremia by virtue of their high prevalence.

Given the frequency with which coagulase-negative staphylococci were isolated from blood and the difficulty in determining their clinical significance, we analyzed *Staphylococcus epidermidis* isolates on the basis of the number of culture sets positive vs. the number of sets performed for each episode. The results are shown in table 2. When only a single culture set yielded *S. epidermidis,* the culture result almost always was judged to be of indeterminate significance or to represent contamination. When all of two or three culture sets yielded *S. epidermidis,* the isolates usually were judged clinically significant, but a substantial minority were of unknown (i.e., indeterminate) significance.

Whereas pneumococci always represented real infection, enterococcal isolates did so only 70% of the time, and viridans streptococci more often were contaminants (49%) than clinically significant isolates (38%) (table 1). Among the gram-negative aerobic and facultative bacteria, *Escherichia coli* was the most common isolate, and this microorganism was second only to *S. aureus* as a cause of septicemia. Overall, the Enterobacteriaceae and *Pseudomonas aeruginosa* represented true bacteremia >95% of the time when isolated.

Anaerobic bacteria were not common blood pathogens, accounting for only 3.9% of clinically important isolates. The isolation of a member of the *Bacteroides fragilis* group, however, almost always indicated true bacteremia (89%). *Clostridium perfringens* usually represented contamination when isolated from the blood, whereas the isolation of other *Clostridium* species usually represented true bacteremia.

Yeasts were relatively common isolates from blood cultures and almost always represented true fungemia when detected (91.7%). These organisms were present as clinically important pathogens almost twice as often as anaerobic bacteria, and *Candida albicans* ranked among the top 10 microorganisms causing septicemia. All mycobacteria and all but one *Cryptococcus neoformans* isolate were isolated from HIV-infected patients.

Of the 843 episodes of bacteremia and fungemia, 764 (90.6%) were unimicrobial and 79 (9.4%) were polymicrobial. Two microorganisms were isolated in 57 (72.2%) of the polymicrobial episodes, and ⩾3 microorganisms were isolated in 22 episodes (27.8%).

Epidemiological Features

Age and sex. Patients ranged in age from 17 to 103 years (mean, 56.2 years). Patients with HIV infection were younger (mean age, 36.9 years). Four hundred ninety of the episodes (58.1%) occurred in men. Ninety-nine percent of the episodes at the SLCVAMC, vs. 54% at both DUMC and RWJUH, were in men.

Community- vs. hospital-acquired infection. Of the 843 episodes, 404 (47.9%) were of community-acquired infection and 439 (52.1%) were of nosocomial infection. The microorganisms isolated in these episodes, categorized according to place of acquisition, are shown in table 3. Microorganisms more often associated with nosocomial acquisition were coagulase-negative staphylococci, enterococci, Enterobacteriaceae other than *E. coli, P. aeruginosa, Clostridium* species, *Bacteroides* species, and yeasts other than *C. neoformans.* A somewhat surprising finding was that nearly 40% of *P. aeruginosa* bacteremias were community-acquired.

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

KUR-MAG-DE005277

Table 1. Microorganisms isolated from blood of patients at Duke University Medical Center, Robert Wood Johnson University Hospital, and the Salt Lake City VA Medical Center, February 1992 through January 1993.

Microorganism (no. of isolates)	No. (%) of isolates per indicated category		
	True pathogen	Contaminant	Unknown
Aerobic and facultative bacteria			
Gram-positive			
Staphylococcus aureus (204)	178 (87.2)	13 (6.4)	13 (6.4)
Coagulase-negative staphylococci (703)	87 (12.4)	575 (81.9)	41 (5.8)
Enterococcus species (93)	65 (69.9)	15 (16.1)	13 (14.0)
Viridans streptococci (71)	27 (38.0)	35 (49.3)	9 (12.7)
Streptococcus pneumoniae (34)	34 (100)	0	0
Group A streptococci (3)	3 (100)	0	0
Group B streptococci (15)	10 (66.7)	3 (20.0)	2 (13.3)
Other streptococci (13)	8 (61.5)	3 (23.1)	2 (15.4)
Bacillus species (12)	1 (8.3)	11 (91.7)	0
Corynebacterium species (53)	1 (1.9)	51 (96.2)	1 (1.9)
Listeria monocytogenes (2)	1 (50.0)	0	1 (50.0)
Lactobacillus species (15)	6 (54.5)	2 (18.2)	3 (27.3)
Other gram-positive bacteria (15)	2 (13.3)	12 (80)	1 (6.7)
Gram-negative			
Escherichia coli (143)	142 (99.3)	0	1 (0.7)
Klebsiella pneumoniae (65)	65 (100)	0	0
Enterobacter cloacae (25)	25 (100)	0	0
Serratia marcescens (22)	22 (100)	0	0
Proteus mirabilis (16)	16 (100)	0	0
Other Enterobacteriaceae (45)	41 (91)	1 (2.2)	3 (6.7)
Pseudomonas aeruginosa (55)	53 (96.4)	1 (1.8)	1 (1.8)
Pseudomonas species (8)	6 (75)	0	2 (25)
Stenotrophomonas maltophilia (7)	5 (71.4)	0	2 (28.6)
Acinetobacter baumanii (16)	13 (81.2)	1 (6.2)	2 (12.5)
Haemophilus influenzae (3)	3 (100)	0	0
Other gram-negative bacteria (16)	10 (62.5)	3 (18.8)	3 (18.8)
Anaerobic bacteria			
Clostridium perfringens (13)	3 (23.1)	10 (76.9)	0
Clostridium species (15)	12 (80)	3 (20)	0
Propionibacterium species (48)	0	48 (100)	0
Other gram-positive anaerobic bacteria (7)	4 (57.1)	2 (28.6)	1 (14.3)
Bacteroides fragilis group (18)	16 (88.9)	0	2 (11.1)
Other gram-negative anaerobic bacteria (5)	2 (40)	2 (40)	1 (20)
Yeasts and fungi			
Candida albicans (30)	27 (90)	0	3 (10)
Other *Candida* species (15)	15 (100)	0	0
Cryptococcus neoformans (8)	8 (100)	0	0
Torulopsis glabrata (15)	14 (93.3)	0	1 (6.7)
Other yeasts and fungi (4)	2 (50)	1 (25)	1 (25)
Mycobacteria			
Mycobacterium avium complex (16)	16 (100)	0	0
M. tuberculosis (1)	1 (100)	0	0
All microorganisms (1,844)	944 (51.2)	791 (42.9)	109 (5.9)

Hospital service. Six hundred twenty of the 843 bacteremic and fungemic episodes (73.5%) occurred in patients hospitalized on the medical services of our institutions. Patients hospitalized on the nontransplantation surgical services accounted for 21.3% of total episodes, with the remaining 5.2% of episodes distributed among the transplantation surgery, obstetric and gynecologic services, and emergency and outpatient departments. Pneumococcal bacteremia, not surprisingly, was seen almost exclusively in patients on the medical service.

Proportionately, enterococcal and pseudomonas bacteremias were twofold more common on the general and transplantation surgical services than on the medical service. Indeed, *P. aeruginosa* accounted for only 4.4% of septicemias on the medical service. Fungemia was proportionately most common on the

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

Table 2. Clinical significance of *Staphylococcus epidermidis* isolates (unimicrobial episodes only).

No. of culture sets		Clinical significance: no. (%) of isolates		
Positive	Performed	Significant	Contaminant	Indeterminate
1	1	0	33 (97.1)	1 (2.9)
1	2	3 (2.2)	129 (94.8)	4 (3.0)
2	2	18 (60.0)	1 (3.3)	11 (36.7)
1	3	0	2 (100)	0
2	3	3 (75.0)	0	1 (25)
3	3	4 (100)	0	0

transplantation surgical service, accounting for nearly 25% of septicemic episodes. Anaerobic bacteremia, which was uncommon in general, was seen most frequently in patients on the general surgery service (6.6% of episodes) and obstetric and gynecologic service (11.1% of episodes).

Sources of infection. The sources of bacteremia and fungemia were identifiable in 627 (74.4%) of episodes and are listed in table 4. Intravenous catheters were the most common primary foci for septicemia. Despite the availability of increasingly sophisticated imaging techniques, the sources for nearly one-fourth of episodes could not be determined.

The relationship between microorganism and sources of unimicrobial bacteremia and fungemia are presented in table 5, which also delineates those episodes confirmed by cultures of specimens other than blood or by clinical evidence. The majority of *S. aureus* and coagulase-negative staphylococcal bacteremias were associated with intravascular devices. Not surprisingly, pneumococcal bacteremia was most often associated with pneumonia, but in 7 of 34 episodes (20.6%) a primary source could not be determined. Among the Enterobacteriaceae, primary foci of infection below the diaphragm predominated (table 5), as would be expected given the normal habitat of these bacteria. In contrast, the most common focus for bacteremia due to *P. aeruginosa* was the respiratory tract, which was the focus more than twice as frequently as the next most common focus, the genitourinary tract.

Several microorganisms or microorganism groups were associated at a particularly high frequency with bacteremia or fungemia in which a primary focus for infection could not be determined. These included the viridans streptococci (44.4%), *Enterobacter cloacae* (58.3%), *Klebsiella pneumoniae* (33.3%), *Candida* species (37.5%), *Torulopsis glabrata* (41.7%), and *Mycobacterium avium* complex (100%). All of the *E. cloacae* bacteremias and many of the fungemias and *K. pneumoniae* bacteremias with unknown sources occurred in patients with underlying malignancies.

Table 3. Community-acquired and hospital-acquired microorganisms and major microorganism groups involved in episodes of bacteremia and fungemia.

	No. (%) of isolates per place of acquisition of infection	
Microorganisms	Community	Hospital
Staphylococcus aureus	90 (50.6)	88 (49.4)
Coagulase-negative staphylococci	27 (31.0)	60 (69.0)
Streptococcus pneumoniae	31 (91.2)	3 (8.8)
Other streptococci	32 (68.1)	15 (31.9)
Enterococcus species	15 (23.1)	50 (76.9)
Escherichia coli	87 (61.3)	55 (38.7)
Other Enterobacteriaceae	61 (36.1)	108 (63.9)
Pseudomonas aeruginosa	21 (39.6)	32 (60.4)
Other nonfermentative gram-negative rods	16 (51.6)	15 (49.4)
Clostridium species	5 (33.3)	10 (66.7)
Bacteroides species	7 (38.9)	11 (61.1)
Candida species	7 (16.7)	35 (83.8)
Cryptococcus neoformans	8 (100)	0
Torulopsis glabrata	2 (14.3)	12 (85.7)
Mycobacterium avium complex	16 (100)	0

Clinical Observations

In order to determine whether certain indicators might assist in assessing the clinical significance of positive blood cultures, we examined the relationship between positive cultures and the peripheral leukocyte count, absolute neutrophil count, blood pressure, and body temperature at the time the first positive blood culture specimen was obtained for a given episode. We also examined the relationship between each of these variables and the microorganisms isolated from true positive cultures. In addition, we critically assessed the antimicrobial therapy as described in the Materials and Methods section.

Leukocyte count and absolute neutrophil count. Patients with culture-positive blood and a peripheral leukocyte count of $<4{,}000/\mu L$ or $\geq 20{,}000/\mu L$ were significantly more likely

Table 4. Sources of bacteremia and fungemia.

	No. of episodes confirmed by		
Source	Culture	Clinical evidence	Total no. (%) of episodes
Intravascular catheter	29	97	161 (19.1)
Genitourinary tract	115	28	147 (17.4)
Respiratory tract	56	46	104 (12.3)
Bowel and peritoneum	22	21	45 (5.3)
Biliary tract	9	21	33 (3.9)
Intraabdominal abscess	9	15	24 (2.8)
Skin	11	29	42 (5.0)
Bone and joint	11	5	16 (2.0)
Surgical wound	7	2	11 (1.3)
Other	25	18	44 (5.2)
Unknown	0	0	216 (25.6)

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

Table 5. Sources and confirmatory evidence for episodes of unimicrobial bacteremia and fungemia, according to microorganism.

Microorganism(s) (no. of episodes)	No. of sources confirmed by		Common source(s) (no. of episodes)*
	Culture	Clinical evidence	
Staphylococcus aureus (159)	56	74	IV (56), skin (19), respiratory (18), bone/joint (10)
Coagulase-negative staphylococci (73)	16	45	IV (59), skin (5)
Streptococcus pneumoniae (34)	5	22	Respiratory (26)
Group B streptococci (8)	4	3	Skin (3), GU (3)
Viridans group streptococci (24)	3	10	Respiratory (3), skin (2)
Enterococcus species (38)	13	9	GU (15), IV (3)
Escherichia coli (116)	70	30	GU (67), biliary (11), peritoneal (10)
Klebsiella pneumoniae (48)	15	15	Biliary (10), GU (8), peritoneal (5)
Enterobacter cloacae (12)	3	2	Biliary (2), respiratory (2)
Serratia marcescens (20)	11	6	GU (4), respiratory (4), IV (3)
Proteus mirabilis (13)	10	2	GU (9)
Pseudomonas aeruginosa (48)	25	12	Respiratory (19), GU (9)
Acinetobacter baumanii (12)	4	0	Respiratory (3)
Bacteroides fragilis group (9)	3	4	Abscess (6)
Candida albicans (21)	7	2	IV (5), peritoneal (2)
Candida tropicalis (7)	1	4	IV (1), GU (1), peritoneal (1)
Torulopsis glabrata (12)	1	4	GU (4)
Mycobacterium avium (15)	0	0	No sources identified

NOTE. The list of microorganisms includes all those isolated ≥5 times as causes of unimicrobial bacteremia or fungemia.

* Abscess = intraabdominal abscess; GU = genitourinary tract; IV = intravascular device; respiratory = respiratory tract.

($P < .001$) to have true bacteremia or fungemia episodes (62.5% and 60.3%, respectively) than contaminant episodes when compared with patients who had peripheral leukocyte counts between 4,000 and 19,999/μL (proportion of true bacteremias, 49.2%). Similarly, patients with absolute neutropenia were significantly more likely ($P < .001$) than nonneutropenic patients to have a positive blood culture represent true bacteremia or fungemia (70.2% vs. 51.4% of positive cultures, respectively).

The distribution of microorganisms causing septicemia in neutropenic and nonneutropenic patients is shown in table 6. Neutropenic patients were significantly less likely to have bacteremia due to *S. aureus* ($P < .0001$; RR, 0.33) but were significantly more likely to have fungemia ($P < .01$; RR, 1.81) and polymicrobial bacteremia ($P < .0001$; RR, 2.63) than were nonneutropenic individuals.

Blood pressure. Approximately 14% of patients were hypotensive at the time the first positive blood culture specimen was obtained. The positive blood cultures of these patients were more likely to represent true bacteremia than were positive blood cultures of patients with normal blood pressure at the time cultures were performed (72.7% vs. 51.1% of positive cultures, respectively; $P < .0001$). The distribution of microorganisms causing bacteremia and fungemia in these patients is shown in table 7. There were no statistically significant differences in microorganisms or microorganism groups in hypotensive vs. normotensive patients. However, polymicrobial episodes occurred significantly more often in hypotensive patients than in patients whose blood pressure was normal at the time of blood culture ($P < .05$; RR, 1.58).

Temperature. Cultures of patients who were hypothermic (temperature, <36°C) or who had marked fever (temperature, ≥40°C) were more likely to be true-positives (67.7% and 69.6% of positive cultures, respectively) than were those of patients whose temperatures were normal (39.2% of positive cultures) or moderately elevated (55.9% of positive cultures) at the time the positive blood culture specimen was obtained.

Endocarditis. Of 31 episodes (in 31 patients) of endocarditis, 11 were due to *S. aureus,* 10 to viridans streptococci, and 3 to enterococci. All episodes were unimicrobial; 30 of the 31 were due to gram-positive bacteria, and one was caused by *K. pneumoniae.* Twenty-one patients presented following <1 week of symptoms, 8 following 1–3 weeks of symptoms, and 2 following >3 weeks of symptoms. Seven of 11 patients with endocarditis due to *S. aureus* and 7 of 10 patients with endocarditis caused by viridans streptococci presented following <1 week of symptoms.

Antibiotic therapy. Of the 1,585 episodes of positive blood cultures, 454 (28.6%) involved patients receiving antimicrobial agents at the time the first positive blood culture specimen was obtained. The proportion of patients who were receiving antibiotics was the same regardless of whether growth repre-

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

Table 6. Microorganisms recovered from and types of episodes in patients with bacteremia and fungemia, according to absolute neutrophil count.

Variable	No. (%) of isolates from patients with indicated neutrophil count	
	<1,000/μL	≥1,000/μL
Microorganisms		
Staphylococcus aureus	9 (6.0)*	169 (21.1)*
Coagulase-negative staphylococci	12 (8.1)	75 (9.4)
Streptococci	9 (6.0)	78 (9.7)
Enterococcus species	13 (8.7)	52 (6.5)
Enterobacteriaceae	58 (38.9)	253 (31.6)
Pseudomonas aeruginosa	11 (7.4)	42 (5.2)
Other nonfermentative gram-negative rods	2 (1.3)	29 (3.6)
Anaerobic bacteria	9 (6.1)	29 (3.6)
Yeasts and fungi	17 (12.1)†	48 (6.0)†
Type of episode: total no. (%)		
Unimicrobial	96 (69.6)	668 (87.4)
Polymicrobial	24 (30.4)*	55 (12.6)*

* $P < .0001$.
† $P < .01$.

sented true bacteremia or contamination. Of the 843 episodes of true bacteremia or fungemia, 71 (8.4%) occurred in patients who were receiving therapy that was effective against the microorganism(s) that grew in the blood culture. This proportion was the same at all three hospitals (range, 8.0%–9.1%).

Appropriate antimicrobial therapy was administered to a substantial majority of patients at all of the time points assessed. Excluding the 48 patients who died prior to the availability of susceptibility test results, 620 of 795 patients (78%) received appropriate therapy at all time points. In addition, 111 patients (14%) were given appropriate therapy after susceptibility test results were available, regardless of whether they had received inappropriate empirical therapy at an earlier time point.

Patients with unimicrobial septicemia were more likely than those with polymicrobial septicemia to be treated with appropriate therapy, especially after susceptibility test results were available (92.7% vs. 83.6%, respectively). At all time points assessed, medical patients were somewhat more likely than surgical patients to receive appropriate therapy. Among medical patients, the proportion who received appropriate therapy at the different time points ranged from 89.4% to 91.0%, versus a range of 83.0% to 87.1% among surgical patients.

After susceptibility test results were available, approximately one-quarter of all patients were receiving antimicrobial agents judged to be superfluous for the infecting microorganism(s) and clinical setting. Twenty-six patients (3.3%) were receiving agents to which their infecting organisms were resistant in vitro, and nine patients (1.1%) received no antimicrobials despite a clinical setting that should have mandated therapeutic intervention.

Outcome and Factors Influencing Prognosis

One hundred forty-eight patients (17.5%) died of causes directly or indirectly attributable to an episode of septicemia (associated mortality). Five hundred thirty-five patients (63.5%) were discharged alive, 118 (14.0%) were alive but remained hospitalized 30 days after onset of the septicemic episode, and 42 (5.0%) died from causes that were judged by the investigators not to be associated with the bacteremia or fungemia. There were no significant differences in mortality at the three collaborating hospitals.

Univariate Analyses

Age and sex. The effect of age on outcome of bacteremia and fungemia was assessed according to the decade of life of the infected patients. As shown in figure 1, septicemia-associated mortality gradually increased with age and was especially notable after the age of 70 years. The infection-associated mortality for septicemic patients over 70 years of age was 24.2% compared with 15.2% for patients 70 years of age or less. In comparison with other patients, the relative risks of death from bacteremia and fungemia for patients between 71 and 80 years of age and >80 years of age were 2.58 and 3.4, respectively. There were no significant differences in infection-associated mortality between septicemic men and women.

Hospital service. The septicemia-associated mortality rates ranged from zero among obstetric and gynecologic patients to 19% and 23% among medical and cardiovascular surgery patients, respectively. However, none of the differences in mortality, when sorted according to hospital service, were statistically significant.

Table 7. Microorganisms recovered from and types of episodes in hypotensive and normotensive patients with bacteremia and fungemia.

Variable	No. (%) of isolates from patients with indicated blood pressure status	
	Hypotensive	Normotensive
Microorganism		
Staphylococcus aureus	21 (16.0)	157 (19.3)
Coagulase-negative staphylococci	6 (4.6)	81 (10.0)
Streptococcus pneumoniae	8 (6.1)	26 (3.2)
Other streptococci	6 (4.6)	41 (5.0)
Enterococcus species	13 (10.0)	52 (6.4)
Enterobacteriaceae	46 (35.1)	265 (32.6)
Pseudomonas aeruginosa	7 (5.3)	46 (5.7)
Other nonfermentative gram-negative rods	1 (0.8)	30 (3.7)
Anaerobic bacteria	5 (3.8)	33 (4.1)
Yeasts and fungi	12 (9.2)	54 (6.6)
Type of episode: total no. (%)		
Unimicrobial	96 (85.7)	668 (91.4)
Polymicrobial	16 (14.3)*	63 (8.6)*

* $P < .05$.

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

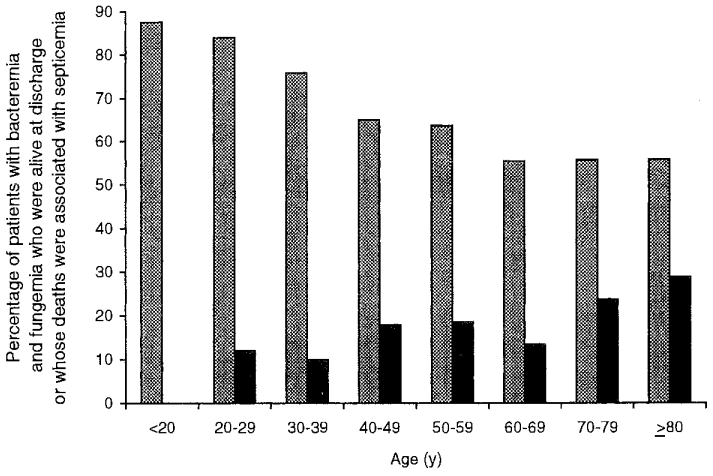


Figure 1. Outcome of bacteremia or fungemia, according to age group of patients (▩ = alive at discharge; ■ = death, associated with septicemia).

Place of acquisition of bacteremia and fungemia. Patients who developed bacteremia or fungemia during the course of hospitalization had an infection-associated mortality rate of 20.3%, vs. 14.6% for patients with community-acquired disease. The relative risk of death associated with nosocomial septicemia was 1.39 ($P < .05$).

Table 8. Associated mortality in episodes of bacteremia and fungemia and relative risk of death, as related to etiologic microorganisms in unimicrobial episodes and to the type of episode.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Microorganisms		
Staphylococcus aureus	19/159 (11.9)	2.18
Coagulase-negative staphylococci	4/73 (5.5)*	1.0
Streptococcus pneumoniae	6/34 (17.6)	3.22
Other streptococci	5/38 (13.1)	2.40
Enterococcus species	5/38 (13.1)	2.40
Other gram-positive aerobic bacteria	1/9 (11.1)	2.03
Escherichia coli	14/116 (12.1)	2.20
Other Enterobacteriaceae	31/125 (24.8)†	4.53
Pseudomonas aeruginosa	8/48 (16.7)	3.04
Other nonfermentative gram-negative rods	3/25 (12.0)	2.19
Other gram-negative aerobic bacteria	0/6	0.04
Gram-negative anaerobic bacteria	2/14 (14.3)	2.61
Gram-positive anaerobic bacteria	2/8 (25.0)	3.65
Yeasts and fungi	19/53 (35.8)‡	6.54
Mycobacteria	2/16 (12.5)	2.28
Type of episode		
Unimicrobial	120/764 (15.7)	1.0
Polymicrobial	27/79 (34.2)‡	2.16

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Microorganism. The microorganism isolated and type of bacteremia or fungemia (i.e., unimicrobial or polymicrobial) influenced outcome (table 8). Among the common etiologic agents of bacteremia and fungemia, the lowest associated mortality occurred with coagulase-negative staphylococci (5.5%) and the highest with yeasts and fungi (35.8%). Infection-associated mortality was lower with gram-positive unimicrobial bacteremia (11.1%) than with gram-negative bacteremia (17.6%), anaerobic bacteremia (18.2%), or fungemia (35.8%).

The mortality associated with pneumococcal bacteremia was greater than that associated with enterococcal or *S. aureus* bacteremia (table 8). Also noteworthy was the mortality rate with *P. aeruginosa* bacteremia, which was less than that with bacteremia due to enteric gram-negative rods other than *E. coli* (table 8). The mortality associated with polymicrobial bacteremia was more than twice that associated with unimicrobial episodes.

Table 9. Associated mortality in episodes of bacteremia and fungemia, according to source of infection.

Source of infection	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Intravascular catheter	12/161 (7.4)*	1.0
Genitourinary tract	16/147 (10.8)†	1.46
Respiratory tract	26/104 (25.0)†	3.35
Bowel and peritoneum	23/45 (51.1)‡	6.86
Biliary tract	4/33 (12.1)	1.63
Intraabdominal abscess	3/24 (12.5)	1.68
Skin	6/42 (14.3)	1.92
Bone and joint	1/16 (6.25)	0.84
Surgical wound	0/11	0.01
Other	3/44 (6.8)	0.91
Unknown	54/216 (25.0)*	3.35

* $P < .01$.
† $P < .05$.
‡ $P < .001$.

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

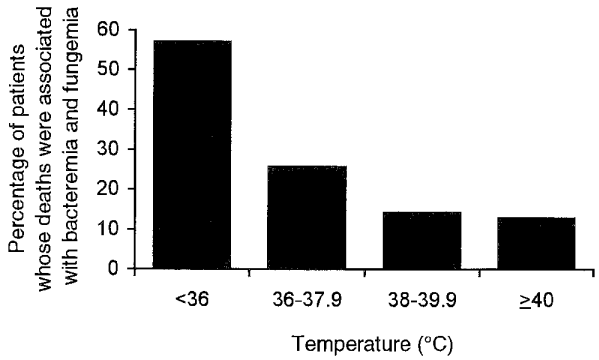


Figure 2. Septicemia-associated mortality as related to temperature of patients at the time the first positive blood culture specimen was obtained.

Source of infection. The outcome of bacteremia and fungemia was affected by the primary source of infection (table 9). For risk factor analysis, we assigned a risk of 1.0 to septicemia associated with iv catheters in order to maintain consistency with our earlier work [11]. Significantly increased septicemia-associated mortality and relative risk of death occurred with respiratory tract sources ($P < .05$), with bowel and peritoneal sources ($P < .01$), and when a primary focus of infection could not be found ($P < .05$).

Body temperature. The mortality associated with bacteremia and fungemia was inversely related to the body temperature of patients at the time the first positive blood culture specimen was obtained (figure 2). Risk factor analysis showed significantly increased mortality ($P < .05$) among the patients who were hypothermic at the onset of septicemia.

Blood pressure. Septic shock, as evidenced by the presence of hypotension at the time the first positive blood culture specimen was obtained, was associated with increased mortality. Table 10 reveals that this relationship was a virtually uniform finding, regardless of the etiologic microorganism or the type of septic episode.

Leukocyte count and absolute neutrophil count. The relationship between septicemia-associated mortality and total leukocyte count or absolute neutrophil count is shown in table 11. Patients who had leukocyte counts of $<4{,}000/\mu L$ or $\geq 20{,}000/\mu L$ had a twofold increase in relative risk of death from septicemia. Patients with absolute neutropenia had a significantly increased relative risk of death in comparison with that for nonneutropenic patients.

Predisposing factors. The influence of predisposing factors on the outcome of septicemia was analyzed both when individual factors were present alone and when multiple factors were present (table 12). Nearly one-quarter of the patients had no predisposing factors, and these patients had the lowest septicemia-associated mortality (8.2%; RR, 1.0). The greatest mortality was associated with moderate renal failure (61.5%; RR, 7.54).

Table 10. Associated mortality in episodes of bacteremia and fungemia, as related to etiologic microorganism in unimicrobial episodes, type of episode, and blood pressure status at the time of onset of septicemia.

Variable	Associated mortality: no. (%) of deaths per no. of episodes in indicated group	
	Hypotensive	Normotensive
Microorganisms		
Staphylococcus aureus	5/18 (27.8)*	14/141 (9.9)*
Coagulase-negative staphylococci	1/4 (25)	3/69 (4.3)
Streptococcus pneumoniae	1/8 (12.5)	5/26 (19.2)
Other streptococci	1/3 (33.3)	3/35 (8.6)
Enterococcus species	1/5 (20)	4/33 (12.1)
Escherichia coli	4/13 (30.8)*	10/103 (9.7)*
Other Enterobacteriaceae	12/23 (52.2)†	19/104 (18.3)*
Pseudomonas aeruginosa	3/6 (50)*	5/42 (11.9)*
Other nonfermentative gram-negative rods	0/1	3/28 (10.7)
Anaerobic bacteria	1/2 (50)	3/24 (12.5)
Yeasts and fungi	5/7 (71.4)*	14/46 (30.4)*
Type of episode		
Unimicrobial	35/96 (36.4)‡	85/668 (12.7)
Polymicrobial	10/16 (62.5)†	17/63 (27.0)

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Although the relative risk of death was high in the presence of severe renal failure and biopsy-proven cirrhosis, statistical significance was not achieved because of the relative infrequency of each of these predisposing factors as the sole underlying problem. Not surprisingly, there was a direct relationship between septicemia-associated mortality and the number of predisposing factors present. Thus, mortality was greater among the patients with multiple predisposing factors than among patients with only a single factor.

Table 11. Associated mortality in episodes of bacteremia and fungemia, as related to leukocyte count and absolute neutrophil count.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Total leukocyte count (per μL)		
$<4{,}000$	42/177 (23.7)	2.11*
4,000–10,999	28/249 (11.2)	1.0
11,000–19,999	48/293 (16.4)	1.46
20,000–49,999	27/115 (23.5)	2.09*
$\geq 50{,}000$	2/8 (25)	2.22
Absolute neutrophil count (per μL)		
$<1{,}000$	31/120 (25.8)	1.58*
$\geq 1{,}000$	115/702 (16.4)	1.0

* $P < .05$.

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/336162 by guest on 16 April 2019

Table 12. Influence of predisposing factors on associated mortality in episodes of bacteremia and fungemia.

Factor(s)	Associated mortality: no. (%) of deaths* per no. of episodes	Relative risk of death
None	16/196 (8.2)	1.0
Hematologic malignancy	14/70 (20.0)	2.45†
Other neoplasm	27/150 (18.0)	2.20†
Corticosteroids	3/28 (10.7)	1.31
AIDS	11/51 (21.6)	2.64†
Trauma	1/11 (9.1)	1.11
Recent surgery	7/49 (14.3)	1.75
Diabetes mellitus	6/59 (10.2)	1.25
Creatinine level, 2–5 mg/dL	16/26 (61.5)	7.54‡
Creatinine level, >5 mg/dL	4/16 (25)	3.06
Cirrhosis	2/6 (33.3)	4.08
One factor	91/477 (19.1)	2.34†
Two or more factors	41/168 (24.4)	2.99†

* No. of deaths among patients in whom listed predisposing factor was the only one present.
† $P < .05$.
‡ $P < .01$.

Antibiotic and other therapy. The mortality associated with bacteremia and fungemia clearly was affected by the type of antimicrobial therapy administered (table 13). The great majority (78%) of patients received appropriate therapy at all three time points at which assessments were made, and this group of patients had the lowest septicemia-associated mortality. Patients who received inappropriate empirical therapy but whose physicians administered appropriate therapy once the blood culture was reported to be positive also had low mortality. By contrast, among the small group of patients who received inappropriate therapy at all three time points, three of nine (33%) died of causes attributable to sepsis.

Indeed, the data shown in table 13 clearly indicate that septicemia-associated mortality increased in proportion to the duration of inappropriate antimicrobial therapy. Since our definition of appropriate empirical therapy allowed for the possibility that the organism(s) grown in blood culture might not be susceptible to the agents given, we also assessed outcome in terms of whether the infecting organisms were susceptible to therapy being administered at each time point. The results of this analysis were very similar; that is, associated mortality was lowest (9.8%) when the organism was susceptible at all three time points and also was low (12.6%) when patients received effective antimicrobial therapy after blood cultures were reported to be positive.

When mortality following the availability of susceptibility test results was analyzed alone, the mortality rates when first-choice or alternative-choice agents were given were identical (8.3%), but the rate was 24% when superfluous therapy was given. Since superfluous therapy included at least one agent with in vitro activity against the infecting microorganism, other factors that may have influenced outcome were assessed. Patients receiving superfluous therapy were twofold to threefold more likely to have absolute granulocytopenia, fungemia, or polymicrobial episodes than were patients who received first-choice or alternative-choice agents.

The removal, excision, or drainage of a primary focus of infection, if feasible, often has a salutary effect on the outcome of septicemia. Therefore, we assessed outcome when such therapeutic maneuvers were undertaken. The results confirmed the beneficial effect of these interventions. Among patients who survived until susceptibility test results were available, associated mortality was 6.2% (14 of 224) when an infected focus was excised, drained, or removed, vs. 15.6% (87 of 557) when no additional interventions were (or could be) undertaken ($P < .001$). Among patients with catheter-associated bacteremia or fungemia, removal of the catheter was associated with death due to septicemia in only 3.9%.

Table 13. Associated mortality in episodes of bacteremia and fungemia, as related to appropriateness of antimicrobial therapy at different time points during septicemia.

Assessment of therapy at indicated time point*				
Initial empirical therapy	After culture reported positive	After susceptibility results available	Associated mortality: no. (%) of deaths per no. of patients	RR
A	A	A	65/620 (10.5)	1.0
I	A	A	6/45 (13.3)	1.27
A	I	A	7/35 (20.0)	1.91
A	A	I	7/35 (20.0)	1.91
I	I	A	8/31 (25.8)	2.46
A	I	I	4/14 (28.6)	2.73
I	A	I	0/2	0.05
I	I	I	3/9 (33.3)	3.18

* A = appropriate; I = inappropriate. Therapy was considered appropriate after susceptibility test results became available if the microorganism(s) were susceptible (on the basis of in vitro testing) to at least one agent administered, whereas therapy was considered appropriate at the earlier time points it if was appropriate for the clinical situation.

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

Multivariate Analysis

Based on the results of univariate analysis, high- and low-risk categories were established for each variable assessed. When there was more than one high-risk component for a variable (e.g., microorganism, source, or predisposing factor), these components were grouped and assigned a univariate relative risk for the purpose of multivariate analysis. Then, with use of logistic regression, the relative risk of death was determined for each variable in the presence of all others.

The results of this analysis are shown in table 14. Those variables associated with a significantly increased risk of death in multivariate analysis were advanced age (>70 years); isolation of fungi or Enterobacteriaceae other than *E. coli;* a primary source of infection in the respiratory tract, bowel, or peritoneum or that was unknown; underlying malignancy, AIDS, or renal failure; shock, as manifested by hypotension; inability to mount a febrile response to sepsis; and inappropriate antibiotic therapy at two or more of the time points assessed.

Discussion

It was our hypothesis that the many changes in medicine since the mid-1970s, when two of us and other investigators [10, 11] comprehensively reviewed a large series of patients with bacteremia and fungemia, would lead to substantive changes in the microbiology, epidemiology, and clinical and prognostic significance of positive blood cultures in the 1990s. Indeed, the more aggressive and widespread use of prosthetic materials and intravascular devices, the occurrence of syndromes such as AIDS not known 2 decades ago, and therapeutic advances in imaging, interventional radiology, and antimicrobial therapy virtually ensured the presence of important differences and underscored the need for this update.

In order to best compare the differences and similarities of bacteremia and fungemia in the 1990s versus the mid-1970s, we used definitions, including clinical and diagnostic criteria, that were similar to those in our earlier work [10, 11]. However, we performed this study prospectively, gathering data concurrently on patients with culture-positive blood, to better assess the ways in which physicians used laboratory results for therapeutic decisions.

Laboratory Observations

True septicemia vs. contamination. The observations from this study suggest that contaminants in blood cultures are more frequent in the 1990s than they were 2 decades ago. Of 1,582 positive blood culture episodes in the current study, 656 (41.5%) were judged to represent contamination and another 84 (5.3%) were of indeterminate significance. Thus, only about half of all positive blood cultures represented true bloodstream infection. These findings contrast markedly with the observations in our earlier study, in which approximately one-third of all positive blood cultures represented contamination [10].

There are several possible explanations for these findings. One is the increasing use of central, long-term intravascular catheters (e.g., Hickman and Broviac) and the utilization of these access devices for the purpose of obtaining blood for culture. Access ports from intravascular devices may be more difficult to sterilize than skin at venipuncture sites, thereby resulting in increased contamination rates; at least one study has documented increased contamination rates when blood culture specimens are obtained from central lines [34].

Although physicians may believe they are benefiting their patients by obtaining blood culture specimens from catheters (i.e., saving patients from needlesticks), they actually may be doing a disservice, since culture contaminants (false-positives)

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/430162 by guest on 10 April 2019

Table 14. Comparison of univariate and multivariate analysis of factors affecting risk of death in patients with bacteremia and fungemia.

Variable	Univariate high risk	Univariate RR	Multivariate RR
Age	>70 y	1.88	1.80*
Place of acquisition	Hospital	1.39	1.12
Microorganisms	Fungi and Enterobacteriaceae other than *E. coli*	5.13	2.27†
Type of episode	Polymicrobial	2.16	1.55
Source of infection	Respiratory tract, bowel, peritoneum, or unknown	2.56	2.86†
Predisposing factor	Malignancy, AIDS, or renal failure	1.92	1.98†
Blood pressure	Hypotension	2.85	2.29†
Leukocyte count	<4,000/μL or >20,000/μL	1.67	1.24
Absolute neutrophil count	<1,000/μL	1.58	0.65
Body temperature	Absence of fever (<37.9°C)	2.06	2.04†
Antibiotic therapy	Inappropriate at ≥2 time points	2.32	2.72†

* $P < .05$.
† $P < .01$.

KUR-MAG-DE005285

cultures) have been shown to result in longer hospitalizations and increased costs to patients and institutions [35].

A second possible reason for the increased incidence of contaminants is blood culture technique. Although several recent studies have indicated that the current single-needle technique for obtaining blood and inoculating cultures is not associated with increased rates of contamination [14, 36, 37], Spitalnic et al. [38], in a meta-analysis, have suggested otherwise. Alternatively, it may be that in institutions such as ours, in which house officers and medical students obtain the majority of blood culture specimens, failure to apply antiseptic solutions (usually iodophors and alcohol) properly and to let them exert their antimicrobial effect over 1–2 minutes as recommended results in increased contamination.

Possible remedies include use of blood culture teams from the laboratory's phlebotomy service, which seems unlikely in the managed care era, or the development and use of potentially more effective antiseptic skin preparation materials (e.g., 2% iodine tincture) before blood sampling. A final possible explanation for increased rates of contamination of blood cultures could be that newer blood culture systems and media are more sensitive and capable of detecting the few viable skin bacteria that might remain after appropriate antiseptic preparation.

Of the 843 septicemias, a source was confirmed by culture in 294 (34.9%) and by clinical evidence in 282 (33.4%). Of the remaining 267 episodes, at least two blood cultures were positive for the same microorganism in 181 (67.8%; 21.5% of total septicemias). Thus, there was objective evidence of true infection in 757 of the 843 episodes (89.8%), an observation that is remarkably similar to that in our earlier study [10]. This finding is important clinically, since it suggests that, despite increased rates of contamination of blood cultures, in the great majority of instances physicians should be able to determine with some confidence whether a positive blood culture represents significant infection.

Nevertheless, positive blood cultures yielding coagulase-negative staphylococci may present great interpretative difficulties, even when more than one culture set is positive. For example, Zaidi et al. [39] have found that coagulase-negative staphylococci with identical species designations, serotypes, and antibiograms recovered from the blood of infants sometimes represented different strains when the isolates were analyzed by molecular typing techniques. Similarly, even when both of two blood cultures yielded *S. epidermidis* of the same biotype in the current study, we were frequently not certain of the isolates' clinical significance (table 2).

Patterns of positive blood cultures. In our earlier study [10], we noted different patterns of blood culture positivity in patients with endocarditis, those with true septicemia that was not due to endocarditis, and those with contaminant isolates. Similar observations were made in this study. Thus, in patients with endocarditis, a disease characterized by continuous seeding of blood from the infected heart valve, all blood cultures obtained in a series were positive.

By contrast, for patients with septicemia not due to endocarditis, most but not all blood cultures obtained in a series were positive, a finding consistent with the understanding that bloodstream infection in such patients may be short-lived or intermittent (abscesses). For patients whose blood cultures were contaminated, an initial positive culture in a series virtually always was followed by negative cultures. When a subsequent culture was positive, it usually was positive with a different microorganism (e.g., *S. epidermidis* followed by a diphtheroid).

The proportion of patients with polymicrobial septicemia in this study (79 of 843; 9.4%) is consistent with findings in earlier studies, in which frequencies of polymicrobial bacteremia ranged from 6% to 18% [10, 17, 40–43].

Epidemiological Observations

Place of acquisition of septicemia. At our institutions the proportions of episodes that were of community-acquired septicemia and hospital-acquired septicemia were nearly equal (48% vs. 52%). This observation contrasts with the results of our earlier study at the University of Colorado hospitals, in which nearly two-thirds of episodes were nosocomial [10]. The difference may relate not only to patient-population variability [44, 45] but also to changes in health care, particularly shorter lengths of stay in the 1990s than those of 2 decades ago, as well as outpatient surgery and chemotherapy.

In contrast to the relative equivalence of community- and hospital-acquired septicemic episodes overall, there were important differences with regard to individual microorganisms. For example, 91% of pneumococcal bacteremias and all mycobacteremias and cryptococcemias were community-acquired. These observations are consistent with prior reports (on pneumococci) and with our understanding of the epidemiology of infections due to these microorganisms [10, 44, 46]. However, nosocomial pneumococcal bacteremia can occur and may be relatively common in institutions with longer patient stays [47, 48].

Fungemia, enterococcal bacteremia, and coagulase-negative staphylococcal bacteremia disproportionately were nosocomial in origin (table 3). The observations for fungi and enterococci were virtually identical to those in our earlier studies of bacteremia [10] and probably relate to the fact that infection with these microorganisms tend to occur in more debilitated patients. The predominance of hospital-acquired coagulase-negative staphylococcal bacteremia is explained by the current use of long-term indwelling central and peripheral catheters as well as other prosthetic devices, the ubiquity of these bacteria as normal skin flora, and the ability of these relatively avirulent microorganisms to adhere to the surfaces of biomaterials.

P. aeruginosa bacteremia usually occurs as a nosocomial infection. In the current study, *P. aeruginosa* bacteremia was community-acquired in 39.6% of episodes, compared with 17% in our earlier study. The explanation for this difference in the epidemiology of *P. aeruginosa* bacteremia may be related in

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

KUR-MAG-DE005286

part to the prevalence of HIV infection. In bacteremic patients known to be infected with HIV, *P. aeruginosa* was the third most frequently isolated pathogen, and in seven of 11 episodes in these patients, bacteremia was community-acquired. Several recent reports have documented similar findings in patients with HIV infections [49–51].

Hospital service. The overwhelming majority of bloodstream infections in this series occurred in patients hospitalized on either the medical services (73.6%) or nontransplantation surgical services (21.3%), an observation similar to that in our previous report [10] in which 54.6% of episodes occurred in medical patients and 27.2% of episodes occurred in surgical patients.

The current study also confirmed the rarity of *P. aeruginosa* bacteremia in medical patients (4.4% of episodes), the absence of enterococcal bacteremias in obstetrical and gynecologic patients, the high proportion of fungemias in transplantation patients (23.1% of episodes), and the proportionately increased frequency of anaerobic bacteremia in patients hospitalized on the surgical and gynecologic services (6.6% and 11.1% of episodes, respectively).

Sources of septicemia. Onc of the striking findings in the currcnt scries in comparison with our earlier work [10] was the ascendancy of intravascular catheters as an important source of bloodstream infections. Whereas only 3% of episodes were catheter-related in the previous study, iv catheters were the source of 19% of the episodes in the current series. The increasing importance of intravascular catheters also was noted by Mylotte et al. [47], who examined nosocomial bacteremia between 1979 and 1987; in that study, the proportion of episodes associated with intravascular devices increased from 6% (1979) to 19% (1987). During a similar time period, the proportion of bloodstream infections due to intravascular devices at a university hospital in Berlin was consistently ~16% [19].

The inability to determine the focus of bacteremia and fungemia remains a vexing problem. Despite substantial advances in diagnostic imaging over the past 2 decades, 26% of the septicemic episodes in this series, compared with 31% in our earlier study [10], had no discernible focus. Leibovici and colleagues [20] noted similar results; 23% of episodes during 1988 and 1989 at their university hospital in Israel were of unknown origin.

Since episodes with unknown foci are associated with increased mortality ([11, 20] and present study), improved methods for determining the primary site of infection in septicemic patients clearly are needed. Microorganisms from unknown foci commonly are assumed to have a gut mucosal source. The organisms associated highly with an unknown source in this study (e.g., *E. cloacae, K. pneumoniae, Candida* species, *T. glabrata,* viridans streptococci, and *M. avium* complex) support this hypothesis.

When we examined the sources of septicemia according to each microorganism or microorganism group (table 5), there were several noteworthy observations. For example, in the years since our previous study, the proportion of *S. aureus* bacteremias associated with intravascular catheters has nearly doubled, from 20% to 35%. Respiratory and skin sources remained important primary foci for staphylococcal bacteremia. The recent report by Roberts and colleagues [18] confirmed the importance of intravascular and pulmonary foci for staphylococcal bacteremia. In addition, in the current study and in the report by Roberts et al. [18], respiratory foci for klebsiella bacteremia were considerably less prominent than we observed previously [10]; intraabdominal and genitourinary sources now predominate. In contrast to the findings of Roberts et al., who found enterococcal bacteremia most commonly to have wound sources [18], our patients most often had genitourinary tract foci.

Epidemiology of septicemia in neutropenic patients. The differences in the microbiology of bacteremia and fungemia in neutropenic patients compared with nonneutropenic patients (table 6) stand in contrast with the observations in our earlier report [10]. In the present series bacteremia due to *S. aureus* was significantly less common and fungemia significantly more common in neutropenic than nonneutropenic patients, whereas there were no such differences noted in the previous study. However, in both series, polymicrobial episodes were more frequent in granulocytopenic patients.

A study of bacteremia and fungemia in granulocytopenic patients during 1985 and 1986 at the University of Colorado Health Sciences Center [52], which was the site of our earlier study, showed both similarities to and differences from the distributions of microorganisms in the 1975–1977 review [10] and the current one. For example, in the study by Ehni et al. [52], fungemias were proportionately less common (2%, vs. 11% [10] and 12% [current study]) and *P. aeruginosa* bacteremias were more common (27%, vs. 9% [10] and 7% [current study]). However, the proportionate frequency of bacteremias due to Enterobacteriaceae was similar in all three studies.

In the study by Ehni and colleagues [52] and the present report, bacteremia due to *S. aureus* accounted for ~5% of episodes in neutropenic patients, whereas in the 1975–1977 review [10], 13% of episodes in neutropenic patients were caused by *S. aureus.* Finally, the increasing importance of bacteremia due to coagulase-negative staphylococci in neutropenic patients was evident in the study of Ehni et al. [52] and in the current one (14% and 8% of episodes in neutropenic patients, respectively). In our earlier review, coagulase-negative staphylococcal bacteremia was sufficiently uncommon in granulocytopenic patients that it did not merit mention [10].

A possible explanation for the higher rates of fungemia currently includes the extensive use of more effective antipseudomonal β-lactam drugs such as piperacillin, ceftazidime, and imipenem. Although their early and empirical use may decrease mortality owing to *P. aeruginosa* infection, their prolonged pressure on normal gut flora is associated with overgrowth of yeasts and increased risk of subsequent fungemia [53]. The relative importance of coagulase-negative staphylococci presently probably relates to the common and prolonged use of

Downloaded from http://academic.oup.com/cid/article-abstract/24/4/584/391652 by guest on 10 April 2019

central iv catheters and the resistance of this group of organisms to commonly used antimicrobial agents.

Epidemiology of septicemia in hypotensive patients. Septic shock most frequently has been associated with gram-negative bacteremia. Indeed, in our earlier review [10], aerobic or facultative gram-negative rods accounted for 53% of the isolates from hypotensive patients. In the current series, however, whereas we observed that aerobic or facultative gram-negative rods continued to be common etiologic agents of septic shock, they were isolated less frequently than in the past (43% of isolates). *S. aureus* was detected twice as frequently in hypotensive patients in the current series (16%, vs. 7% in the earlier series), and anaerobic bacteria were detected substantially less often in hypotensive patients (4%, vs. 11% in the earlier series). In both series, hypotensive patients were twice as likely as normotensive patients to have polymicrobial bacteremia ([10] and table 7).

Clinical and Prognostic Observations

Our observations suggest that the mortality associated with bacteremia and fungemia appears to have decreased during the past 2 decades. However, this conclusion may not be applicable widely and should be interpreted with caution. Indeed, the differences in patient population as well as the prospective nature of the current study vs. our retrospective earlier review [11] limited the ability to make direct comparisons with the previous work. Nonetheless, mortality attributable to septicemia in this study was markedly less than in the 1975–1977 study (17.5% vs. 31%, respectively). Moreover, Geerdes et al. [19] recently reported that between 1979 and 1989, mortality from septicemia at a university hospital in Berlin decreased from 34% to 21%.

Crude mortality has varied substantially in recent reports of bacteremic patients, ranging from 16% at a Swedish university hospital from 1973 to 1980 [54] to >40% among patients with nosocomial bacteremia from 1981 to 1983 at a university hospital in the United States [55] and with gram-negative bacteremia at a Turkish university hospital from 1983–1989 [21]. By comparison, crude mortality among septicemic patients at the University of Colorado during 1975–1977 was 42% [11], vs. 22.5% in this study (patients were followed for a maximum of 30 days after detection of bacteremia). Most comparable to our data are the observations of Roberts and colleagues, who recently reported a 30-day mortality of 27% among bacteremic patients studied during 1984–1987 in western Canada [18].

Age and sex. Numerous reports have emphasized the importance of advanced age as an unfavorable prognostic factor in septicemic patients [11, 15, 18, 21, 54, 55]. In contrast to our earlier data, which showed a statistically significant increase in mortality due to septicemia after age 40 years [11], in this series significantly increased mortality occurred after age 70 years. No differences in mortality according to sex were evident in this study or in a recent report from a Swedish university hospital [54].

Place of acquisition of bacteremia and fungemia. Nosocomial septicemias historically have been associated with substantially higher mortality than community-acquired septicemias [9, 11, 44]. In the current series and in another recent report [21], however, the evidence suggests that the increase in mortality associated with hospital-acquired bacteremia and fungemia may be less dramatic than reported in the past. Uzun et al. [21] noted crude mortality of 46% in episodes of nosocomial bacteremia vs. 37% in those of community-acquired bacteremia. In this series, associated mortality due to nosocomial septicemia was 20.3%, vs. 14.6% due to community-acquired septicemia.

Microorganisms. Many studies have looked at the mortality rates with bloodstream infections due to individual microorganisms; some have focused only on certain patient populations. Unfortunately, definitions of mortality in the various reports have not been uniform: some have evaluated total (or crude) mortality, others have evaluated only septic deaths (those judged to be directly related to septicemia), and still others have addressed mortality judged directly or indirectly attributable to septicemia. Furthermore, not all studies have indicated clearly whether mortality rates have been calculated on the basis of unimicrobial episodes, thereby excluding the confounding variable of concomitant bacteremia with other microorganisms. These differences make direct comparisons of mortality in other reports problematic, and the comments that follow should be interpreted accordingly.

The lower mortality overall from bacteremia in this series compared with that noted in our earlier work [11] was reflected in the mortality rates associated with individual microorganisms or groups thereof (table 8). Several comparisons and contrasts with regard to etiologic microorganisms deserve emphasis.

Fungemia, which was associated with more than a sixfold increased risk of death in the earlier series [11], also carried a sixfold increased relative risk of death in the present study (table 8). Overall mortality associated with fungemia, however, was lower in the current series than in our earlier report [11], and the associated mortality in this series was somewhat less (36%) than that due to candida and torulopsis fungemias (44%) in Detroit in the mid-1980s [56].

Among episodes of polymicrobial septicemia, for which the directly related mortality was 35% in the earlier series [11], the associated mortality in this series was 34% and the risk of death was significantly increased compared with that in unimicrobial episodes. The mortality associated with polymicrobial bacteremia in the recent report by Cooper et al. [17] was remarkably similar to the observations in our earlier and current series.

In our earlier review, the mortality directly related to pneumococcal bacteremia was 15% (crude mortality, 22%), vs. 17.6% associated mortality in this series. Data from other recent reports are consistent with these findings [57, 58]. These data

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

KUR-MAG-DE005288

provide impressive evidence that there has been little change in the outcome of *Streptococcus pneumoniae* bacteremia since the classic studies of Austrian and Gold >3 decades ago [59].

By contrast, the dramatically increased risk of death from bacteremia due to *P. aeruginosa* in our earlier report (RR, 6.84) was moderated in this study (RR, 3.04). The mortality associated with pseudomonas bacteremia was 16.7%, compared with 36% for deaths directly due to bacteremia in the earlier review [11]. Two studies examining pseudomonas bacteremia during the early 1980s revealed case fatality rates attributable to sepsis of 41% and 48% [60, 61]. Thus, our data suggest the possibility that the outcome of bacteremia due to *P. aeruginosa* may have improved over the past decade.

Mortality from bacteremia due to gram-positive organisms also was lower in the current study than in the prior review [11]. In the case of *S. aureus,* septicemia-associated mortality in the current series was 11.9%, compared with crude mortality of 33% and directly related mortality of 9% in the earlier series. By comparison, in the recent report from Lautenschlager et al. [62] encompassing the years 1980–1986 in Basel, Switzerland, total mortality was 34% and directly related mortality was 20%.

Coagulase-negative staphylococcal bacteremia had the lowest attributable mortality of all microorganism groups in the current study (5.5%); case-fatality rates were somewhat higher during the mid-1980s: 13.6% at the University of Iowa Hospital [63] and 18% at a large hospital in Spain [64]. The mortality associated with enterococcal bacteremia was 13% in this series, considerably lower than the crude or directly related mortality (45% and 27%, respectively) in our earlier series [11], despite the presence of vancomycin-resistant enterococci at both RWJUH and DUMC during the current study period. By comparison, reports based on data from the 1980s have described case fatality rates associated with enterococcal bacteremia varying from 12% to 51% [65–67].

Several studies have recently provided data on the outcome of bacteremia due to members of the family Enterobacteriaceae. Mortality due to *E. coli* bacteremia appears to be lower now than 2 decades ago. In our earlier report [11], 41% of patients died of causes directly related to bacteremia, compared with an associated mortality of 10.3% in this study.

Grandsen et al. [68] prospectively evaluated *E. coli* bacteremia in London from 1969 through 1987 and noted a case-fatality rate of 20.7%; approximately half the deaths were judged to be directly related to sepsis. Similarly, the recent review by Roberts and colleagues [18] noted that the 30-day mortality due to *E. coli* bacteremia was 21.5%. Mortality associated with *K. pneumoniae* bacteremia has ranged from 14.6% in the current study to 37% (crude mortality) in another recent report [69]. Korvick et al. [70] reported 19% mortality at 14 days in a recent multicenter study of 230 patients with klebsiella bacteremia.

Mortality associated with serratia bacteremia was 30% among our patients; by contrast, Saito and colleagues [71] reported a mortality rate of 23% in cancer patients between 1982 and 1987. In the present series, associated mortality among 12 patients with *E. cloacae* bacteremia was 8.3%, compared with crude mortality of 24% in a recent multicenter study of 129 patients with enterobacter (all species) bacteremia [72]. The attributable mortality between 1980 and 1992 among patients with *Proteus mirabilis* bacteremia was 25.6% in a recent report [73], remarkably similar to the bacteremia-associated mortality of 23.1% in this series.

Source of infection. As in our earlier study [11], the mortality associated with bacteremia was increased when the primary focus of infection was either unknown or at a site that was difficult to treat, such as the respiratory tract or the bowel and peritoneum. Similarly, when the primary focus of infection could be removed or drained easily (e.g., the genitourinary tract), the mortality was reduced (table 9). The higher mortality in septicemia with an unknown primary focus of infection also has been noted by others [19–21].

Body temperature. The current study confirmed the observations made in our earlier report [11], namely, that the inability of a patient to mount a febrile response to septicemia is a poor prognostic sign (figure 2). This relationship has been noted by others [9, 74, 75] but could not be confirmed in a study designed to examine independent predictors of mortality associated with bloodstream infections [55]. Kluger [76] and Roberts [77] have each recently presented information to support the premise that the presence of physiologically elevated body temperature is beneficial.

Blood pressure. The well-known association between hypotension as a marker for septic shock and poor outcome was again confirmed during this study. This association was noted not only in prior studies [9, 11, 74] but also in more recent reports [18–21]. Compared with data in our earlier review [11], the incremental risk of death when hypotension was present was greater in the current series than was noted previously (RR, 2.8 vs. 2.0).

Total leukocyte count and absolute neutrophil count. Infection-associated mortality and relative risk of death from bacteremia were increased among patients with leukopenia and absolute granulocytopenia, as in our earlier study [11]. In addition, in this study mortality was increased also among patients with total leukocyte counts $\geq 20{,}000/\mu L$. Recent studies in varied patient groups have provided similar observations [17, 60].

Predisposing factors. For consistency and to enable accurate comparisons of risk associated with various underlying conditions that may affect mortality among patients with bacteremia and fungemia, we used the same criteria and definitions as in our earlier review [11] and included HIV infection and AIDS, neither of which were known at the time the earlier study was undertaken. Moreover, the risk associated with each factor was judged when that condition was the only one present (table 12).

As in the earlier study [11], increased risk of death in bacteremia was associated with the presence of malignancies and

Downloaded from https://academic.oup.com/clinids/article-abstract/24/4/584/366969 by guest on 20 August 2019

biopsy-proven hepatic cirrhosis. In contrast with our earlier observations, the presence of moderate renal failure (serum creatinine level, 2.0–5.0 mg/dL) but not severe renal failure (serum creatinine level, >5 mg/dL) was associated with increased mortality among bacteremic patients.

Although this observation may seem paradoxical, we interpret the results to suggest that patients with chronic renal failure probably were undergoing dialysis and therefore had stable albeit poor renal function, whereas those with moderate renal failure were more likely to have acute deterioration of function and greater metabolic instability which, in turn, was associated with a greater likelihood of a poor outcome. Finally, the presence of AIDS was associated with an increased risk of death associated with bacteremia or fungemia.

Antibiotic and other therapy. Intuitively, one would expect that administration of antimicrobial agents active in vitro against the infecting microorganism(s) would be associated with improved prognosis. Our prior study and others [11, 78, 79] have supported this assumption, and the current study again confirmed the principle (table 13). By assessing therapy at several different time points, we hoped to determine that degree to which appropriate treatment affected outcome at each stage.

One might have expected, for example, that appropriate therapy given early (empirical therapy time point) would be associated with lower attributable mortality than would appropriate therapy delayed until after susceptibility test results were available to the physician. Indeed, this was the case. As is evident in table 13, the lowest attributable mortality occurred among those patients who received appropriate therapy throughout the course of their septicemic episodes (10.4%). Prompt initiation of appropriate therapy by physicians after notification of a positive blood culture also was associated with low mortality (13.3%). If appropriate therapy was not initiated until after susceptibility test results were available, mortality was 25.8%.

Why 60 (7.6%) of 791 septicemic patients received inappropriate therapy even after the identification and antibiotic susceptibilities of infecting microorganisms were reported is uncertain (table 13). Antibiotic misuse has been studied by others. In one report [80], the most common form of misuse in bacteremic patients was the administration of superfluous agents, a finding that corroborates our observations. In another study [81], multivariate analysis showed that four clinical variables (i.e., nosocomial bacteremia, recent prior antibiotic therapy, nursing home residence, and central iv catheters) and four microorganisms (i.e., *Candida, Acinetobacter, Enterococcus,* and *Pseudomonas* species) were independently associated with inappropriate antimicrobial therapy. Our data also showed that the use of inappropriate therapy was more likely to occur on the surgical services.

A fundamental principle in the management of bloodstream infections has always been that eradication of the primary source of infection is a necessary component of the therapeutic regimen. Thus, removal, drainage, or excision of an infected focus, when possible, should result in an improved prognosis. Both the current study and our prior report [11] provide support for this principle. Indeed, in the current study, infection-associated mortality among patients who had a primary focus that was excised, drained, or removed was less than one-third that among patients who did not have these interventions (6.2% vs. 22.0%, respectively).

Multivariate Analysis of Factors Influencing Prognosis

As in the earlier review by our group [11], we subjected each of the variables that were associated with an increased risk of death in univariate analyses to multivariate analysis (table 14). In the earlier report, seven variables were independently associated with an increased risk of death; all but one were confirmed in the current study. These included advanced age, microorganism, source of infection, predisposing factors, hypotension, and absence of fever. Nosocomial acquisition of bacteremia was not an independent predictor of death in the current study, in contrast to the observations in the earlier report.

In our earlier report we were unable to include antimicrobial therapy in the multivariate analysis. Inclusion of therapy was possible in this study and confirmed the importance of administering appropriate antimicrobial agents.

Although advanced age again was an independent predictor of poor prognosis, the increased risk statistically was greatest after age 70 years in the current study, compared with age >40 years in the earlier series. Septicemia caused by a high-risk microorganism also was again an independent risk factor in multivariate analysis, but there were some changes in the individual microorganisms associated with a high risk of death. In the earlier report there was increased risk with gram-negative rods generally, whereas in the current study increased risk was observed only with Enterobacteriaceae other than *E. coli.*

The reasons for this difference are not readily apparent. Speculation might focus on greater resistance to antimicrobial agents among these strains than among *E. coli.* In contrast to the results of the earlier series, enterococcal bacteremia was not associated with increased risk in the current study. However, fungemia was confirmed to be associated with poor prognosis, in concordance with our earlier observations.

Primary foci of infection in the respiratory tract, bowel, or peritoneum and septicemia from an unknown source again were shown to be independent predictors of poor prognosis. However, primary foci in abscesses, skin, and surgical wounds, each of which was associated with an increased risk of death in the earlier series, were not associated independently with increased risk in the present study.

As in the earlier study, the presence of underlying diseases associated with high risk in univariate analysis was an independent predictor of increased mortality in the multivariate analysis. The underlying diseases associated with high risk were somewhat different from those in the earlier report and included AIDS, a syndrome that was unknown at the time of the earlier

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/439162 by guest on 10 April 2019

KUR-MAG-DE005290

review; renal failure, which was not a high-risk factor in the prior study; and malignancies, which were high-risk factors in the earlier study.

Comparative Features of Bacteremia and Fungemia in the 1970s and 1990s

During the past 20 years, numerous changes have occurred in medicine and health care. Nevertheless, several fundamental aspects of bloodstream infections have remained constant. Major examples include the continued frequency with which *S. aureus* and *E. coli* are causative agents of bacteremia; the importance of the respiratory tract, genitourinary tract, and bowel as primary foci; the association between gram-negative or polymicrobial bacteremia and septic shock; and the importance of advanced age, difficult-to-eradicate or unknown sources, malignancies and renal failure, hypotension, and absence of fever as independent predictors of a poor outcome (table 15).

The differences noted in the 1990s provide cause for concern but perhaps also for optimism (table 15). The increased proportion of blood isolates representing contamination is of concern, especially in an environment that mandates cost-effective care. The frequency of coagulase-negative staphylococcal isolation particularly is problematic, since it often is difficult for clinicians to determine the clinical significance of these bacteria. The decrease in anaerobic bacteremia and proportionate increase in fungemia have prompted some authorities to recommend changes in routine blood culture techniques [82].

Table 15. Major similarities and differences in positive blood cultures, 1975–1977 [10, 11] and 1992–1993.

Similarities	• *Staphylococcus aureus* and *Escherichia coli* most frequent etiologic agents
	• Importance of respiratory tract, genitourinary tract, and bowel as primary foci
	• Association of gram-negative and polymicrobial bacteremia with septic shock
	• Importance of age, source of infection, predisposing factors, hypotension, and absence of fever as independent predictors of poor outcome
Differences	• Increased importance of iv catheters as source of septicemia
	• Increased proportion of isolates representing contamination
	• Increased isolation of coagulase-negative staphylococci, both as contaminants and as pathogens
	• Increased frequency of *Pseudomonas aeruginosa* as a community-acquired pathogen
	• Emergence of *M. avium* complex as cause of bloodstream infection in HIV-infected patients
	• Proportionate increase in fungemia and decrease in anaerobic bacteremia
	• Decreased mortality

The most frequent source of bloodstream infections has become the intravenous catheter, and it may be expected that prosthetic materials and devices will continue to be important sources of infection. HIV infection and AIDS have allowed *M. avium* complex to become a bloodstream pathogen, and the increased frequency of community-acquired *P. aeruginosa* bacteremia also seems to be associated with HIV-infected patients [49–51].

The most optimistic finding with regard to bacteremia and fungemia in the 1990s is that mortality associated with these serious infections has decreased. The reasons for this improved outcome are not fully explained but could be related to earlier detection with use of modern blood culture systems; more sophisticated imaging methods that better elucidate primary foci of infection; the frequency of infections emanating from easily removed (iv catheters) or drained (genitourinary tract) foci; and improved antimicrobial agents and use thereof by clinicians.

Although we have shown that mortality is lower than it was 2 decades ago, bacteremia and fungemia remain serious syndromes with substantial risk. Moreover, the combination of an aging population, improved survival among immunocompromised patients and those with organ transplants, and the emergence of β-lactam-drug-resistant gram-positive and gram-negative bacteria as well as vancomycin-resistant enterococci (and possibly staphylococci in the future) [83], will continue to challenge all who care for patients with bloodstream infections.

Downloaded from https://academic.oup.com/clinids/article-abstract/24/4/582/432992 by guest on 10 April 2019

References

1. Everett ED, Hirschmann JV. Transient bacteremia and endocarditis prophylaxis: a review. Medicine (Baltimore) **1977**;56:61–77.
2. McCabe WR, Jackson GG. Gram-negative bacteremia. I. Etiology and ecology. Arch Intern Med **1962**;110:847–55.
3. McCabe WR, Jackson GG. Gram-negative bacteremia. II. Clinical, laboratory, and therapeutic observations. Arch Intern Med **1962**;110:856–64.
4. DuPont HL, Spink WW. Infections due to gram-negative organisms: an analysis of 860 patients with bacteremia at the University of Minnesota Medical Center, 1958–1966. Medicine (Baltimore) **1969**;48:307–32.
5. MacGregor RR, Beaty HN. Evaluation of positive blood cultures: guidelines for early differentiation of contaminated from valid positive cultures. Arch Intern Med **1972**;130:84–7.
6. Winchester PD, Todd JK, Roe MH. Bacteremia in hospitalized children. Am J Dis Child **1977**;131:753–8.
7. Singer C, Kaplan MH, Armstrong D. Bacteremia and fungemia complicating neoplastic disease: a study of 364 cases. Am J Med **1977**;62:731–42.
8. Kreger BE, Craven DE, Carling PC, McCabe WR. Gram-negative bacteremia. III. Reassessment of etiology, epidemiology and ecology in 612 patients. Am J Med **1980**;68:332–43.
9. Kreger BE, Craven DE, McCabe WR. Gram-negative bacteremia. IV. Re-evaluation of clinical features and treatment in 612 patients. Am J Med **1980**;68:344–55.
10. Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. Rev Infect Dis **1983**;5:35–53.
11. Weinstein MP, Murphy JR, Reller LB, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500

episodes of bacteremia and fungemia in adults. II. Clinical observations, with special reference to factors influencing prognosis. Rev Infect Dis **1983**;5:54–70.
12. Whimbey E, Kiehn TE, Brannon P, Blevins A, Armstrong D. Bacteremia and fungemia in patients with neoplastic disease. Am J Med **1987**;82: 723–30.
13. Whimbey E, Gold JWM, Polsky B, et al. Bacteremia and fungemia in patients with the acquired immunodeficiency syndrome. Ann Intern Med **1986**;104:511–4.
14. Krumholz HM, Sande MA, Lo B. Community-acquired bacteremia in patients with acquired immunodeficiency syndrome: clinical presentation, bacteriology, and outcome. Am J Med **1989**;86:776–9.
15. Gatell JM, Trilla A, Latorre X, et al. Nosocomial bacteremia in a large Spanish teaching hospital: analysis of factors influencing prognosis. Rev Infect Dis **1988**;10:203–10.
16. Aronson MD, Bor DH. Blood cultures. Ann Intern Med **1987**;106: 246–53.
17. Cooper GS, Havlir DS, Shlaes DM, Salata RA. Polymicrobial bacteremia in the late 1980s: predictors of outcome and review of the literature. Medicine (Baltimore) **1990**;69:114–23.
18. Roberts FJ, Geere IW, Coldman A. A three-year study of positive blood cultures, with emphasis on prognosis. Rev Infect Dis **1991**;13:34–46.
19. Geerdes HF, Ziegler D, Lode H, et al. Septicemia in 980 patients at a university hospital in Berlin: prospective studies during 4 selected years between 1979 and 1989. Clin Infect Dis **1992**;15:991–1002.
20. Leibovici L, Konisberger H, Pitlik SD, Samra Z, Drucker M. Bacteremia and fungemia of unknown origin in adults. Clin Infect Dis **1992**;14: 436–43.
21. Uzun Ö, Akalin HE, Hayran M, Ünal S. Factors influencing prognosis in bacteremia due to gram-negative organisms: evaluation of 448 episodes in a Turkish university hospital. Clin Infect Dis **1992**;15:866–73.
22. Weinstein MP, Reller LB. Clinical importance of "breakthrough" bacteremia. Am J Med **1984**;76:175–80.
23. Weinstein MP, Reller LB, Murphy JR. Clinical importance of polymicrobial bacteremia. Diagn Microbiol Infect Dis **1986**;5:185–96.
24. Feinstein AR, Pritchett JA, Schimpff CR. The epidemiology of cancer therapy. III. The management of imperfect data. Arch Intern Med **1969**; 123:448–61.
25. Feinstein AR, Pritchett JA, Schimpff CR. The epidemiology of cancer therapy. IV. The extraction of data from medical records. Arch Intern Med **1969**;123:571–90.
26. Balows A, Hausler WJ Jr, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of clinical microbiology. 5th ed. Washington, DC: American Society for Microbiology, **1991.**
27. National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial disk susceptibility tests. 4th ed. Approved standard. NCCLS document M2-A4. Villanova, Pennsylvania: National Committee for Clinical Laboratory Standards, **1990.**
28. National Committee for Clinical Laboratory Standards. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. 2nd ed. Approved standard. NCCLS document M7-A2. Villanova, Pennsylvania: National Committee for Clinical Laboratory Standards, **1990.**
29. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control **1988**;16:128–40.
30. Abramowicz M, ed. The choice of antibacterial drugs. Med Lett **1992**;34: 49–56.
31. O'Brien PC, Shampo MA. Statistics for clinicians. 8. Comparing two proportions: the relative deviate test and chi-square equivalent. Mayo Clin Proc **1981**;56:513–5.
32. McCullagh P, Nelder FRS. Generalized linear models. 2nd ed. London: Chapman and Hall, **1989.**
33. Hastie TJ, Pregibon D. Generalized linear models. In: Chambers JM, Hastie TJ, eds. Statistical models in S. Pacific Grove, California: Wadsworth and Brooks/Cole, **1992**:195–248.
34. Bryant JK, Strand CL. Reliability of blood cultures collected from intravascular catheter versus venipuncture. Am J Clin Pathol **1987**;88:113–6.
35. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization: the true consequences of false-positive results. JAMA **1991**; 265:365–9.
36. Isaacman DJ, Karasic RB. Utility of collecting blood cultures through newly inserted intravenous catheters. Pediatr Infect Dis J **1990**;9: 815–8.
37. Leisure MK, Moore DM, Schwartzman JD, Hayden GF, Donowitz LG. Changing the needle when inoculating blood cultures: a no-benefit and high-risk procedure. JAMA **1990**;264:2111–2.
38. Spitalnic SJ, Woolard RH, Mermel LA. The significance of changing needles when inoculating blood cultures: a meta-analysis. Clin Infect Dis **1995**;21:1103–6.
39. Zaidi AKM, Harrell LJ, Rost JR, Reller LB. Assessment of similarity among coagulase-negative staphylococci from sequential blood cultures of neonates and children by pulsed-field gel electrophoresis. J Infect Dis **1996**;174:1010–4.
40. Hermans PE, Washington JA II. Polymicrobial bacteremia. Ann Intern Med **1970**;73:387–92.
41. Roselle GA, Watanakunakorn C. Polymicrobial bacteremia. JAMA **1979**; 242:2411–3.
42. Kiani D, Quinn EL, Burch KH, Madhavan T, Saravolatz LD, Neblett TR. The increasing importance of polymicrobial bacteremia. JAMA **1979**; 242:1044–7.
43. Elting LS, Bodey GP, Fainstein V. Polymicrobial septicemia in the cancer patient. Medicine (Baltimore) **1986**;65:218–25.
44. McGowan JE Jr, Barnes MW, Finland M. Bacteremia at Boston City Hospital: occurrence and mortality during 12 selected years (1935–1972), with special reference to hospital-acquired cases. J Infect Dis **1975**;132:316–35.
45. Scheckler WE. Septicemia in a community hospital: 1970 through 1973. JAMA **1977**;237:1938–41.
46. Eykyn SJ, Gransden WR, Phillips I. The causative organisms of septicaemia and their epidemiology. J Antimicrob Chemother **1990**;25(suppl C):41–58.
47. Mylotte JM, White D, McDermott C, Hodan C. Nosocomial bloodstream infection at a veterans hospital, 1979 to 1987. Infect Control Hosp Epidemiol **1989**;10:455–64.
48. Alvarez S, Guarderas J, Shell CG, Holtsclaw-Berk S, Berk SL. Nosocomial pneumococcal bacteremia. Arch Intern Med **1986**;146:1509–12.
49. Kielhofner M, Atmar RL, Hamill RJ, Musher DM. Life-threatening *Pseudomonas aeruginosa* infections in patients with human immunodeficiency virus infection. Clin Infect Dis **1992**;14:403–11.
50. Fichtenbaum CJ, Woeltje KF, Powderly WG. Serious *Pseudomonas aeruginosa* infections in patients infected with human immunodeficiency virus: a case-control study. Clin Infect Dis **1994**;19:417–22.
51. Mendelson MH, Gurtman A, Szabo S, et al. *Pseudomonas aeruginosa* bacteremia in patients with AIDS. Clin Infect Dis **1994**;18:886–95.
52. Ehni WF, Reller LB, Ellison RT III. Bacteremia in granulocytopenic patients in a tertiary-care general hospital. Rev Infect Dis **1991**;13: 613–9.
53. Hiemenz JW, Pizzo PA. New developments in the etiology, diagnosis, treatment and prevention of infectious complications in patients with leukemia. In: Bloomfield CD, ed. Chronic and acute leukemias in adults. Boston: Martinus Nijhoff, **1985**:283–337.
54. Julander I. Septicemia and endocarditis, 1965–1980, in a Swedish university hospital for infectious diseases. Infection **1987**;15:177–83.
55. Miller PJ, Wenzel RP. Etiologic organisms as independent predictors of death and morbidity associated with bloodstream infections. J Infect Dis **1987**;156:471–7.
56. Komshian SV, Uwaydah AK, Sobel JD, Crane LR. Fungemia caused by *Candida* species and *Torulopsis glabrata* in the hospitalized patient: frequency, characteristics, and evaluation of factors influencing outcome. Rev Infect Dis **1989**;11:379–90.

Downloaded from https://academic.oup.com/cid/article-abstract/24/4/584/433162 by guest on 10 April 2019

57. Breiman RF, Spika JS, Navarro VJ, Darden PM, Darby CP. Pneumococcal bacteremia in Charleston County, South Carolina: a decade later. Arch Intern Med **1990**;150:1401–5.
58. Afessa B, Greaves WL, Frederick WR. Pneumococcal bacteremia in adults: a 14-year experience in an inner-city university hospital. Clin Infect Dis **1995**;21:345–51.
59. Austrian R, Gold J. Pneumococcal bacteremia with especial reference to bacteremic pneumococcal pneumonia. Ann Intern Med **1964**;60: 759–76.
60. Gallagher PG, Watanakunakorn C. Pseudomonas bacteremia in a community teaching hospital, 1980–1984. Rev Infect Dis **1989**;11:846–52.
61. Hilf M, Yu VL, Sharp J, Zuravleff JJ, Korvick JA, Muder RR. Antibiotic therapy for *Pseudomonas aeruginosa* bacteremia: outcome correlations in a prospective study of 200 patients. Am J Med **1989**;87:540–6.
62. Lautenschlager S, Herzog C, Zimmerli W. Course and outcome of bacteremia due to *Staphylococcus aureus:* evaluation of different clinical case definitions. Clin Infect Dis **1993**;16:567–73.
63. Martin MA, Pfaller MA, Wenzel RP. Coagulase-negative staphylococcal bacteremia: mortality and hospital stay. Ann Intern Med **1989**;110: 9–16.
64. Fidalgo S, Vázquez F, Mendoza MC, Pérez F, Méndez FJ. Bacteremia due to *Staphylococcus epidermidis:* microbiologic, epidemiologic, clinical, and prognostic features. Rev Infect Dis **1990**;12:520–8.
65. Maki DG, Agger WA. Enterococcal bacteremia: clinical features, the risk of endocarditis, and management. Medicine (Baltimore) **1988**;67: 248–69.
66. Gullberg RM, Homann SR, Phair JP. Enterococcal bacteremia: analysis of 75 episodes. Rev Infect Dis **1989**;11:74–85.
67. Hoge CW, Adams J, Buchanan B, Sears SD. Enterococcal bacteremia: to treat or not to treat, a reappraisal. Rev Infect Dis **1991**;13:600–5.
68. Gransden WR, Eykyn SJ, Phillips I, Rowe B. Bacteremia due to *Escherichia coli:* a study of 861 episodes. Rev Infect Dis **1990**;12:1008–18.
69. Watanakunakorn C, Jura J. Klebsiella bacteremia: a review of 196 episodes during a decade (1980–1989). Scand J Infect Dis **1991**;23:399–405.
70. Korvick JA, Bryan CS, Farber B, et al. Prospective observational study of *Klebsiella* bacteremia in 230 patients: outcome for antibiotic combinations versus monotherapy. Antimicrob Agents Chemother **1992**;36: 2639–44.
71. Saito H, Elting L, Bodey GP, Berkey P. Serratia bacteremia: review of 118 cases. Rev Infect Dis **1989**;11:912–20.
72. Chow JW, Fine MJ, Shlaes DM, et al. *Enterobacter* bacteremia: clinical features and emergence of antibiotic resistance during therapy. Ann Intern Med **1991**;115:585–90.
73. Watanakunakorn C, Perni SC. *Proteus mirabilis* bacteremia: a review of 176 cases during 1980–1992. Scand J Infect Dis **1994**;26:361–7.
74. Bryant RE, Hood AF, Hood CE, Koenig MG. Factors affecting mortality of gram-negative rod bacteremia. Arch Intern Med **1971**;127: 120–8.
75. Montgomerie JZ, Ota JK. Klebsiella bacteremia. Arch Intern Med **1980**; 140:525–7.
76. Kluger MJ. The adaptive value of fever. In: Mackowiak P, ed. Fever: basic mechanisms and management. New York: Raven Press, **1991**: 105–24.
77. Roberts NJ Jr. The immunological consequences of fever. In: Mackowiak P, ed. Fever: basic mechanisms and management. New York: Raven Press, **1991**:125–42.
78. Setia U, Gross PA. Bacteremia in a community hospital: spectrum and mortality. Arch Intern Med **1977**;137:1698–701.
79. Gross PA, Barrett TL, Dellinger EP, et al. Quality standard for the treatment of bacteremia. Clin Infect Dis **1994**;18:428–30.
80. Dunagan WC, Woodward RS, Medoff G, et al. Antibiotic misuse in two clinical situations: positive blood culture and administration of aminoglycosides. Rev Infect Dis **1991**;13:405–12.
81. Leibovici L, Konisberger H, Pitlik SD, Samra Z, Drucker M. Patients at risk for inappropriate antibiotic treatment of bacteraemia. J Intern Med **1992**;231:371–4.
82. Morris AJ, Wilson ML, Mirrett S, Reller LB. Rationale for selective use of anaerobic blood cultures. J Clin Microbiol **1993**;31:2110–3.
83. Edmond MB, Wenzel RP, Pasculle AW. Vancomycin-resistant *Staphylococcus aureus:* perspectives on measures needed for control. Ann Intern Med **1996**;124:329–34.

Downloaded from https://academic.oup.com/clinids/article-abstract/24/4/584/439162 by guest on 10 April 2019

PCT WORLD INTELLECTUAL PROPE
International Bu

INTERNATIONAL APPLICATION PUBLISHED UNDER WO 9605875A1

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

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

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

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

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

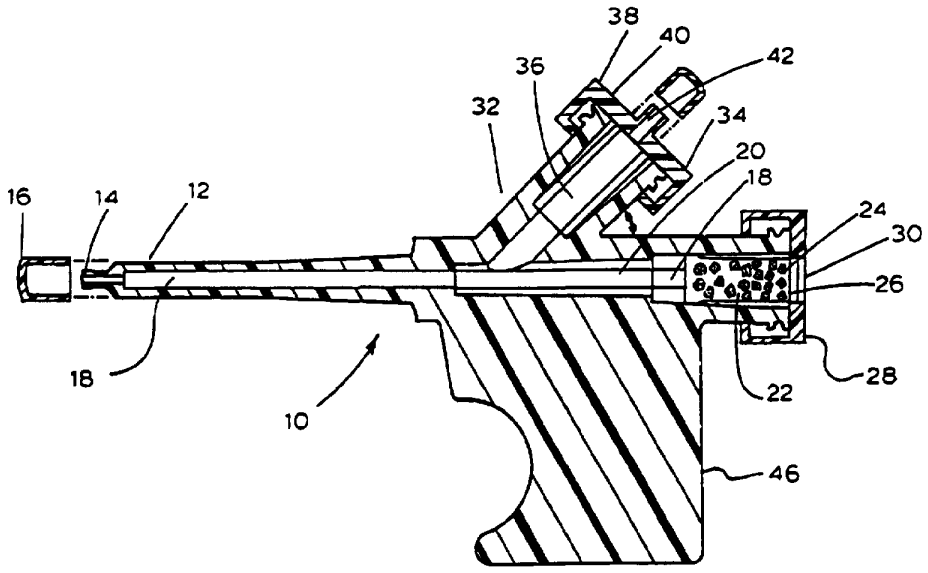
(72) Inventors: DESECKI, Vincent, C.; 28420 West Big Hollow Road, Ingleside, IL 60041 (US). BROWNE, Glennie; 944 Hidden Lake Drive, Buffalo Grove, IL 60089 (US).

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

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

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

(54) Title: CLOSED SYSTEM BLOOD SAMPLING DEVICE



(57) Abstract

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

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	**GB**	United Kingdom	**MR**	Mauritania
AU	Australia	**GE**	Georgia	**MW**	Malawi
BB	Barbados	**GN**	Guinea	**NE**	Niger
BE	Belgium	**GR**	Greece	**NL**	Netherlands
BF	Burkina Faso	**HU**	Hungary	**NO**	Norway
BG	Bulgaria	**IE**	Ireland	**NZ**	New Zealand
BJ	Benin	**IT**	Italy	**PL**	Poland
BR	Brazil	**JP**	Japan	**PT**	Portugal
BY	Belarus	**KE**	Kenya	**RO**	Romania
CA	Canada	**KG**	Kyrgystan	**RU**	Russian Federation
CF	Central African Republic	**KP**	Democratic People's Republic of Korea	**SD**	Sudan
CG	Congo			**SE**	Sweden
CH	Switzerland	**KR**	Republic of Korea	**SI**	Slovenia
CI	Côte d'Ivoire	**KZ**	Kazakhstan	**SK**	Slovakia
CM	Cameroon	**LI**	Liechtenstein	**SN**	Senegal
CN	China	**LK**	Sri Lanka	**TD**	Chad
CS	Czechoslovakia	**LU**	Luxembourg	**TG**	Togo
CZ	Czech Republic	**LV**	Latvia	**TJ**	Tajikistan
DE	Germany	**MC**	Monaco	**TT**	Trinidad and Tobago
DK	Denmark	**MD**	Republic of Moldova	**UA**	Ukraine
ES	Spain	**MG**	Madagascar	**US**	United States of America
FI	Finland	**ML**	Mali	**UZ**	Uzbekistan
FR	France	**MN**	Mongolia	**VN**	Viet Nam
GA	Gabon				

CLOSED SYSTEM BLOOD SAMPLING DEVICE

FIELD OF THE INVENTION

The invention relates to closed system blood sampling devices.

BACKGROUND OF THE INVENTION

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

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

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

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

THE DRAWINGS

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

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

In the drawings, like parts have like numbers.

THE INVENTION

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

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

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

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

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

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

DETAILED DESCRIPTION OF THE INVENTION

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

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

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

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

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

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

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

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

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

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

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

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

WE CLAIM:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

c. discarding the closed system blood sampling device

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

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

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

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

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

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

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

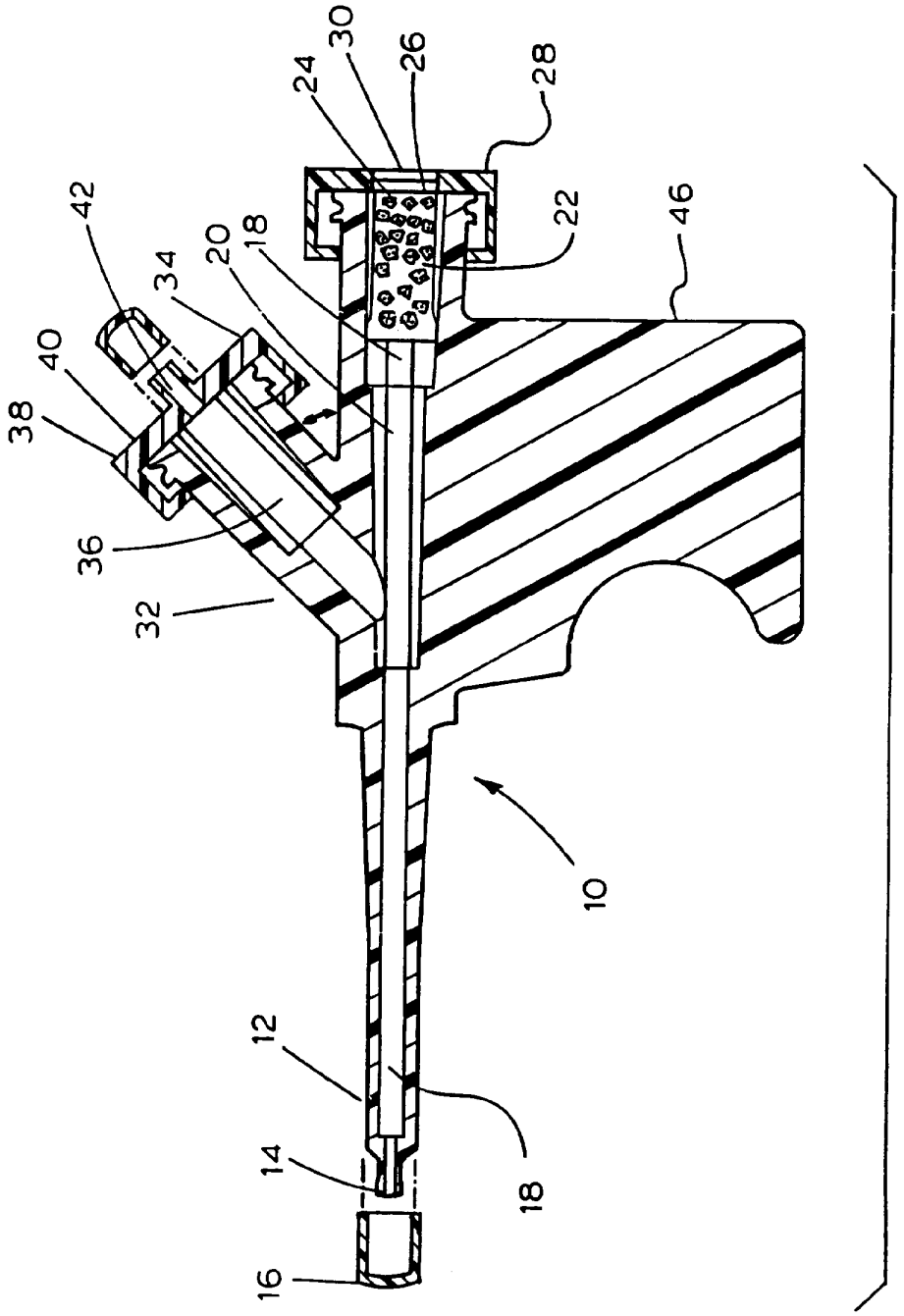


FIG. 1

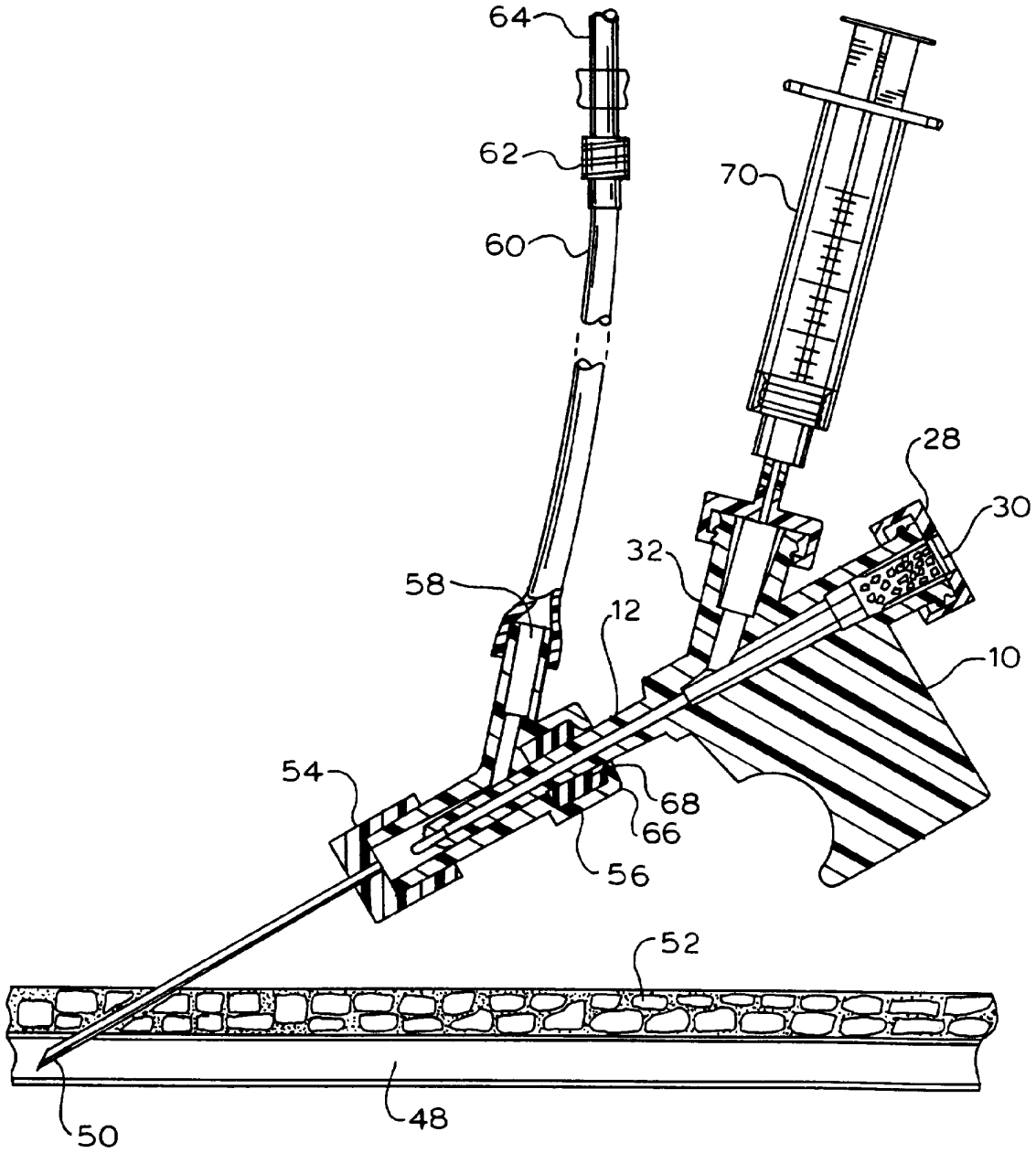


FIG. 2

SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/10702

A. CLASSIFICATION OF SUBJECT MATTER

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

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

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

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

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

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

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 June 2010 (03.06.2010)

PCT

(10) International Publication Number
WO 2010/062734 A1

(51) International Patent Classification:
A61F 13/02 (2006.01) *A61P 7/04* (2006.01)
A61L 15/44 (2006.01)

(21) International Application Number:
PCT/US2009/063049

(22) International Filing Date:
3 November 2009 (03.11.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/110,698 3 November 2008 (03.11.2008) US
61/234,773 18 August 2009 (18.08.2009) US

(71) Applicants *(for all designated States except US)*: **UNIVERSITY OF MARYLAND, BALTIMORE** [US/US]; 520 West Lombard Street, Baltimore, Maryland 21201 (US). **UNIVERSITY OF MARYLAND, COLLEGE PARK** [US/US]; Office of Technology Commercialization, 0133 Cole Student Activities Bldg., College Park, Maryland 20742 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CASEY, Brendan, J.** [US/US]; 9540 Rhode Island Avenue, College Park, Maryland 20740 (US). **KOFINAS, Peter** [US/US]; 5809 Nicholson Lane, #610, North Bethesda, Maryland 20852 (US). **BEHRENS, Adam** [US/US]; 3608 Toddsbury Lane, Olney, Maryland 20832 (US). **SNYDER, Trevor, A.** [US/US]; c/o UNIVERSITY OF MARYLAND, BALTIMORE, 520 West Lombard Street, Baltimore, Maryland 21201 (US). **GRIFFITH, Bartley, P.** [US/US]; c/o UNIVERSITY OF MARYLAND, BALTIMORE, 520 West Lombard Street, Baltimore, Maryland 21201 (US).

(74) Agents: **IYER, Chid, S.** et al.; Sughrue Mion, PLLC, 2100 Pennsylvania Ave., N.W., Suite 800, Washington, District of Columbia 20037-3213 (US).

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

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

Published:

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

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

(54) Title: BLOOD COAGULATION INDUCING POLYMER HYDROGEL

(57) Abstract: The present application is drawn to a synthetic, polymer hydrogel-based material, which is able to actively induce the body's natural hemostatic coagulation process in blood or acellular plasma. The present invention provides the development of a primary amine containing polymer hydrogel capable of inducing blood coagulation and delivering therapeutics for hemostatic or wound care applications, and a method of forming such a primary amine containing polymer hydrogel capable of inducing the blood coagulation process. The primary amine containing polymer hydrogel is able to achieve the same end result as biological-based hemostatics, without the innate risk of disease transmission or immunological response, and at a fraction of the price. Furthermore, due to its inherent hydrogel-based design the material has the capability of arresting blood loss while simultaneously delivering therapeutics in a controlled manner, potentially revolutionizing the way in which wounds are treated.

WO 2010/062734 A1

BLOOD COAGULATION INDUCING POLYMER HYDROGEL

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional applications Serial Nos. 61/110,698, filed November 3, 2008 and 61/234,773, filed August 18, 2009, which are incorporated in their entireties by reference herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] This invention was made with government support under CTS0640778 awarded by the National Science Foundation. The U.S. Government has certain rights in this invention.

TECHNICAL FIELD

[0003] The present invention relates to a polymer material capable of actively inducing the blood coagulation cascade while simultaneously delivering therapeutics in a controlled manner for application in the wound care field.

BACKGROUND

[0004] Technology capable of effectively controlling traumatic hemorrhaging does not exist. As a result, millions of people around the world are dying every year. Over 3,000,000 worldwide, 156,000 in the U.S. alone, die from trauma related injuries each year. Half will die before they reach the hospital, and 80% will die within 24 hours of hospital admission. Uncontrolled hemorrhaging, or blood loss, accounts for almost half of these deaths. Moreover, on the battlefield an astounding 85% of military mortalities are due to blood loss, a statistic that has remained mostly unchanged since the Vietnam War. Army medics, emergency medical technicians (E.M.T.) personnel, and other various emergency responders need a product capable of providing rapid and effective hemostasis until they can get their patients to the operating room. Once at the operating room, hemostatic products are still crucial to surgeons who must control bleeding to maintain the stability of their patient.

[0005] Current products are either exorbitantly expensive, ineffective, and/or have adverse side effects. There is a clear need for a hemostatic product which is inexpensive,

effective, with little to no adverse side effects and medics, emergency responders, and surgeons are all looking for a solution. Furthermore, there is currently no existing product or material on the market with the capability of providing rapid hemostasis along with simultaneous drug delivery. A product which could effectively stop blood loss while simultaneously delivering potentially life-saving therapeutics such as adrenaline or insulin in a regulated manner would have a multitude of applications from the battlefield to the operating room.

[0006] Death may occur in minutes after a traumatic injury due to blood loss. The body has natural mechanisms to control hemorrhaging yet these processes may be insufficient in cases of excessive hemorrhaging, defective due to medical conditions such as hemophilia, or compromised due to adverse effects of medication like Coumadin. The natural hemostatic response is not adequate to control major hemorrhaging due to traumatic injury, which is the main reason why such injuries, if gone untreated, are typically fatal. Administration of biologically derived blood products to augment the native hemostatic response and to maintain adequate oxygen delivery to the brain and vital organs, carries significant risks including disease transmission, infection, pulmonary dysfunction, and immune response. Furthermore, many people have deficiencies within their hemostatic response i.e. hemophilia, which prevent them from adequately stopping blood loss. Millions of people around the world suffer from bleeding disorders, and are unable to clot blood effetively. Current treatments are typically limited to clotting factor (Factor VIII, Factor II) replacement therapies, which are typically painful and exorbitantly expensive. There is a clear need for an inexpensive, painless alternative to current treatments. Whether the injury overwhelms the body's clotting response or the native response is deficient or compromised, an inexpensive, synthetic material which has the ability to induce clotting effectively, while simultaneously delivering therapeutics would undoubtedly revolutionize the way in which wounds are treated.

[0007] The field of hemostatic agents and materials has expanded dramatically within the last decade. This considerable expansion and evolution of the field, throughout the last decade has also been accompanied by tremendous diversification resulting in a multitude of hemostatic products now available on the market, each with their own advantages and disadvantages. The hemostatic products currently available on the market today are either biological-based or synthetic-based. Biological-based hemostatics are comprised of animal or "animal derived" substrates which are able to initiate, amplify, and/or assist the natural

coagulation response. Although they have excellent hemostatic effects and work via the promotion of the body's natural responses, they are incredibly expensive (up to $500 per application) and carry risks of disease infection and severe immunological response. Synthetic hemostatic agents are typically less expensive and immune inert yet often fail to effectively induce the coagulation cascade. Such synthetic agents are mainly designed to be mere physical obstructions to impede blood flow while providing a scaffold for the coagulation process to occur. A purely synthetic, polymer-based hydrogel material capable of effectively inducing the body's natural coagulation response has enormous potential within the field. Such a material is unique to the market in that it could be used to effectively stop bleeding while simultaneously delivering necessary therapeutics to a wound site.

SUMMARY OF THE INVENTION

[0008] The inventors of the present application have developed a purely synthetic, polymer hydrogel-based material, which is able to actively induce the body's natural hemostatic coagulation process in blood or acellular plasma. There is currently no polymer hydrogel-based, synthetic hemostatic agent with the capability of inducing the formation of a natural hemostatic matrix in the absence of platelets or blood cells. Since the material is able to induce the formation of a natural hemostatic plug in the absence of platelets or cells, it has enormous potential as a hemostatic agent in surgery, to treat trauma victims, and especially for patients with platelet disorders. The material is able to achieve the same end result as biological-based hemostatics, without the innate risk of disease transmission or immunological response, and at a fraction of the price. Furthermore, due to its inherent hydrogel-based design the material has the capability of arresting blood loss while simultaneously delivering therapeutics in a controlled manner, potentially revolutionizing the way in which wounds are treated.

[0009] The blood coagulation cascade may be activated via two distinct routes, the tissue factor pathway and the intrinsic pathway, also known as the contact activation pathway. Both pathways eventually result in the activation of a common pathway, which leads to the formation of a fibrin-based hemostatic clot Our research has shown that a material is able to induce the formation of fibrin via the tissue pathway factor Specifically, a positively charged polymer network with adequate mechanical rigidity is capable of efficiently and effectively inducing the activation of FVII, which in turn leads to the activation of the common pathway and subsequent fibrin formation. Furthermore, the material is able to induce the activation of

FVII irrespective of calcium or platelets which are typically vital cofactors of the process.

[0010] In one aspect, the present invention provides a cross-linked primary amine containing polymer hydrogel capable of inducing blood coagulation, and subsequent fibrin clot formation, while simultaneously delivering therapeutics in a controlled or regulated manner for wound care applications.

[0011] In another aspect the present invention is able to induce coagulation in Factor XII, XI, IX, VIII, and V deficient blood plasma.

[0012] In another aspect the present invention is capable of inducing the activation of FVII irrespective of calcium and platelets.

[0013] In another aspect, the present invention provides a method of forming the specific type of cross-linked primary amine containing polymer hydrogel in order to effectively induce blood coagulation: (a) adding either a primary amine containing monomer or primary amine containing polymer with a pKa greater than 7.4 thereby being positively charged within a plasma or blood environment (pH 7.4); (b) addition of additional monomers different from the initial primary amine containing monomer; (c) forming a polymer matrix by initiating polymerization of monomer units into polymer strand; (d) cross-linking the polymer strands to produce a polymeric mesh network.

[0014] In other aspects, the present invention provides various uses for a polymer hydrogel capable of inducing blood coagulation and delivering therapeutics in a controlled manner, in the health care field.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] **Figure 1: Coagulate complex formed by optimal hydrogel after immersion in citrated plasma.** Typical coagulate complex (fibrin-hydrogel complex) formed after rotating the optimal hydrogel in human plasma (4 % w/v sodium citrate) for 18 hours.

[0016] **Figure 2: Characterization images (H&E, IHC, ESEM) of coagulate complex formed by optimal hydrogel after immersion in citrated plasma.** (**A**) H&E stained micrograph image of coagulate complex. Polymer hydrogel appears as lighter, smoother material on right side of the micrograph while fibrin appears as the darker, rougher material on the left side of them micrograph. (**B**) IHC stained micrograph image of coagulate complex. (**C**) ESEM surface image of the coagulate complex.

[0017] **Figure 3: Optimization experiment.** Experiment aimed to investigate the dependence of fibrin formation on various compositional factors including total monomer

concentration (acrylamide + APM + BIS), positive electrostatic charge (APM), and cross-linker ratio (acrylamide:APM:BIS). Acrylamide concentration is located on the horizontal axis while APM concentration is on the vertical axis. BIS concentration is also indicated on the horizontal axis and is kept constant for each respective acrylamide concentration. The amount of fibrin formation induced by each composition was visually scored from 0 (no fibrin formation) to 10 (substantial fibrin formation). All samples were run in triplicate.

[0018] Figure 4. Factor deficient and factor inhibited plasma experiment. Optimal hydrogel composition tested in various factor deficient and factor inhibited plasmas. The resulting fibrin formation was visually scored from 0 (no fibrin formation) to 10 (substantial fibrin formation) and graphed accordingly. All samples were run in triplicate.

[0019] Figure 5: Kinetic biological mechanism experiments. Factor VIIa concentration (**A**), calcium concentration (**B**) , and TFPI activity (**C**) was measured in human plasma containing various hydrogel compositions at 30, 90, and 180 minutes (left axis: bar graph). The amount of fibrin formation was also rated for each composition at each time point (right axis: line graph). Data is representative of an average and corresponding standard deviation (error bar) of three (n=3) separate sample trials. Asterisk (*) indicates duplicate sample point.

[0020] Figure 6: Dynamic mechanical analysis. Dynamic mechanical analysis of three compositions used in the kinetic biological mechanism experiments (FVIIa, calcium, TFPI) ranging from high APM, low acrylamide and BIS content (composition A) to low APM, high acrylamide and BIS content (composition F). Spectra for sample compositions C and F are shifted vertically to avoid overlapping of data.

[0021] Figure 7: Fresh sheep blood experiment. 250 mg of our hydrogel material (**A**) compared to a control (**B**). Clotting time of blood with material was dramatically decreased (~45 seconds) compared to control (~10 minutes).

[0022] Figure 8: Prototype images. (**A**) Computer generated graphic of prototype used in animal experiment. (**B**) Actual prototype used in animal trial.

[0023] Figure 9: Animal trial. (**A**) Image of lung at time of incision, before hydrogel was applied. (**B**) Image of the incision site after the hydrogel prototype bandage was applied for approximately 2 minutes.

[0024] Figure 10: Stained lung section of incision site. Micrograph of hematoxylin and eosin (H&E) stained section of incision site after hydrogel material was applied for two minutes.

DETAILED DESCRIPTION OF THE INVENTION

[0025] A reference to an element by the indefinite article "a" or "an" does not exclude the possibility that more than one of the element is present. Rather, the article "a" or "an" is intended to mean one or more (or at least one) unless the text expressly indicates otherwise. The terms "first," "second," and so on, when referring to an element, are not intended to suggest a location or ordering of the elements. Rather, the terms are used as labels to facilitate discussion and distinguish elements from one another.

[0026] The foregoing description and examples have been set forth merely to illustrate the invention and are not intended to be limiting. Each of the disclosed aspects and embodiments of the present invention may be considered individually or in combination with other aspects, embodiments, and variations of the invention. Modifications of the disclosed embodiments incorporating the spirit and substance of the invention may occur to persons skilled in the art and such modifications are within the scope of the present invention.

[0027] The present invention provides the development of a primary amine containing polymer hydrogel capable of inducing blood coagulation and delivering therapeutics for hemostatic or wound care applications. Various therapeutics intended to be delivered include but are not limited to ester or amide based anesthetics such as Novocain or Lidocain, antibiotics such as erythromycin or bacitracin, vasoconstrictors such as adrenaline, and pain relievers or anti-inflammatory medicines such as topricin, acetaminophen, or ibuprofen. The hydrogel may be designed in order to deliver the drugs in various ways including based on a swelling change, a change in pH, or via the introduction of a magnetic or electric field.

[0028] The present invention provides the development of a primary amine containing polymer hydrogel capable of inducing blood coagulation and delivering other hemostatic agents for hemostatic or wound care applications, including biological-based hemostatic agents and non biological-based hemostatic agents.

[0029] Biological-based hemostatics contain, incorporate, or are derived from biological substrates, i.e. proteins, or cells. They can further be subdivided into the type of biological substrates incorporated into the system including collagen, thrombin, fibrin, albumin, and/or platelets.

[0030] Collagen is the main protein of connective tissue in mammals, including the skin, bones, ligaments, and tendons making up about 30% of the total protein in the body. In addition to providing structural integrity for the animal body, including all organs, collagen also activates the contact activation pathway of the coagulation cascade. Due to collagen's

ability to induce coagulation, along with the fact that is it naturally occurring, makes it an ideal choice for a hemostatic agent. Collagen is typically incorporated into the products via gelatin or microfibrillar form. Gelatin is an irreversibly hydrolyzed form of collagen and may be prepared as a powder, sponge, sheet, film or foam. Gelatin products are typically pliable, easy to handle, and relatively inert. When placed in soft tissue gelatin products typically absorb in 4 to 6 weeks, yet when applied to bleeding nasal, rectal or vaginal mucosa, will liquefy in approximately 2 to 5 days. The product Gelfoam (Pfizer, New York, NY), first introduced in 1945, is produced from purified pork skin gelatin granules. The foam swells up to 45 times its original dry weight and 200% of its initial volume.

[0031] Microfibrillar collagen is the predominant form used in modern hemostatic products. The collagen network acts as a framework which aggregates clotting factors, platelets, along with various coagulative and adhesive proteins to facilitate clot formation. Furthermore, the collagen fibrils are able to efficiently activate the contact activation coagulation pathway. The product is typically formed into various products including powder (shredded fibrils), sheets, and sponges. Market examples include Ultrafoam and Avitene (Davol Inc., Cranston, RI), Instat (Johnson & Johnson, Langhorne, PA), Helistat and Helitene (Integra LifeSciences, Plainsboro, NJ), Collatape/CollaCote/CollaPlug (Integra Lifesciences Corporation, Plainsboro, NJ), Collastat and Collatene (Xemax, Napa, CA).

[0032] Collagen-based hemostatic products are easily removable, cause little aggravation to the wound site, and can be very effective hemostats (especially relative to cellulose or gelatin hemostats). Disadvantages of collagen products include their prohibitive high price (around $150 per dressing), poor biodegradability, inherent risk of antigenicity, low solubility (difficult to make concentrated solutions), and handling difficulties since the products will irreversibly adhere to any hydrated surface.

[0033] Thrombin is the central activating enzyme of the common coagulation pathway. Thrombin circulates within the blood in its precursor, or zymogen form, prothrombin. Prothrombin is specifically cleaved to produce the enzyme thrombin. The main role of thrombin in the coagulation pathway is to convert fibrinogen into fibrin, which in turn is covalently cross-linked to produce a hemostatic plug. Thrombin-based products are typically sold in liquid or powder form and include Thrombostat (ParkeDavis, Ann Arbor, MI), Thrombin-JMI (King Pharmaceuticals, Briston, TN), and Quixil (Omrix Biopharmaceuticals Ltd, Tel Hashomer, Israel). There are also several combination products which include Evicel

(Johnson & Johnson, Langhorne, PA) which is a combination of thrombin and fibrin used mainly as a tissue sealant, along with FloSeal (Baxter Healthcare Corporation, Westlake Village, CA) and SurgiFlow which are both hybrid products composed of bovine or porcine gelatin and thrombin.

[0034] Thrombin-based products take advantage of the natural physiologic coagulation response by augmenting, amplifying, and assisting the process. Advantages of these products include low risk of foreign body or inflammatory reactions, firm attachment to wound bed, and its excellent hemostatic effect, specifically with patients that have platelet dysfunctions. Another advantage of thrombin is the versatility that the product may be applied, in powder or liquid (spray on) form. Disadvantages of these products include their often prohibitive high price ($75-$300 per application), difficulty of use including the inconvenience of premixing preparation, along with the risk of intravenous introduction which may result in intravascular clotting.

[0035] Fibrin is a fibrillar protein which is polymerized and cross-linked to form a mesh network, typically at the site of an injury after the induction of the coagulation cascade. The mesh network, incorporative of other various proteins and platelets, forms a hemostatic plug to prevent continuous or further blood loss. Fibrin is activated from its inert zymogen, fibrinogen, by thrombin. Fibrin is in turn polymerized and covalently cross-linked by another coagulation factor, known as Factor XIIIa. Due to its natural mechanical hemostatic role fibrin has been commercially used to control blood flow since the early 1900s. Most fibrin glues or fibrin sealants are derived from human and bovine proteins. The product is typically sold in the form of a dual syringe. The first syringe compartment contains the matrix and matrix stabilizing components including fibrinogen, factor XIII, fibronectin, and fibrinolysis inhibitors. The second syringe compartment contains the activating agent, typically thrombin and calcium chloride. At the time of application, the contents of both syringes are ejected, combining to activate fibrin matrix formation which typically takes a matter of seconds to set and approximately 5 to 10 days to degrade or absorb into the body. Various fibrin sealants on the market include Tiseel (Baxter HealthCare Corporation, Westlake Village, CA), FibRx (CryoLife Inc., Kennesaw, GA), Crosseel (Johnson & Johnson, Langhorne, PA), Hemaseel (Haemacure Corporation, Montreal, Quebec), Beriplast P (Aventis Behring, King of Prussia, PA), and Bolheal (Kaketsuken, Kumamoto, Japan).

[0036] Fibrin-based hemostatics or tissue sealants are fast-acting, composed of native coagulative factors, are biodegradable, do not promote inflammation or tissue necrosis, have diverse applications, and are particularly useful in patients with coagulation deficiencies such as hemophilia or von Willebrand's disease. Major disadvantages of fibrin-based hemostatics include their often prohibitive price ($100- $300/mL), their fragile nature, and difficulty of handling and application.

[0037] Other prominent biological-based hemostatic products include those composed of covalently cross-linked protein networks such as BioGlue (Cryolife, Kennewsaw, GA), along with products which incorporate platelets such as Costasis, marketed as Vitagel (Orthovita, Malvern, PA). BioGlue is comprised of bovine serum albumin, and various other proteins, cross-linked with glutaraldehyde to form a rigid, insoluble matrix. The reaction occurs spontaneously upon the introduction of glutaraldehyde to the protein mixture, and requires no external factors such as coagulation factors. Disadvantages of the product include the high price ($300-$425/5 ml application), mediocre hemostatic effect, necessity of a dry environment for application, the toxic effects associated with tissue exposure to glutaraldehyde, and risk of immune reactions associated with glutaraldehyde-based products.

[0038] Costasis is a combination product combining bovine collagen and the patient's own platelets. The collagen within the product promotes the initiation of the contact activation pathway of the coagulation cascade. The presence of platelets in such a product improves overall clot strength and supplies various growth factors which facilitate tissue regeneration. Disadvantages include high price ($100- $150/mL) and difficultly of application.

[0039] Non biological-based, or synthetic, hemostatic agents are defined as any products which do not incorporate biological materials, or more specifically animal derived components. Synthetic hemostatics are typically cheaper, easier to use, and easier to apply relative to their biological counterparts. Furthermore, synthetic hemostatics have no innate antigenicity, rarely induce immune responses or inflammatory reactions, and are inherently free of disease vectors." The main classes of synthetic hemostatics include cyanoacrylates, polysaccharides (e.g. oxidized cellulose, N-acetyl glucosamine), synthetic polymers, and mineral/metal based.

[0040] Cyanoacrylates are liquids that rapidly polymerize. These products create a tight seal between tissues, obstructing blood flow. Cyanoacrylates are categorized upon their

length. Shorter chain cyanoacrylates (ethyl cyanoacrylates) are typically quicker to absorb yet more toxic relative to intermediate (butyl cyanoacrylates) or longer chain cyanoacrylates (octyl cyanoacrylates). Due to their inherent high toxicity few hemostatic products composed of short chain cyanoacrylates have reached the market. There is however some research supporting the efficacy of Krazy Glue (ethyl-2-cyanoacrylate, Elmer's, Columbus, OH) for cutaneous wound closure. Cohera Medical Corporation is currently in the process of developing a butyl cyanoacrylate (isobutyl-2-cyanoacrylate), marketed as TissuGlu (Cohera Medical Inc., Pittsburgh, PA). Furthermore, there are currently several octyl acrylate-based hemostatic products that are FDA-approved for skin closure which include Dermabond (Ethicon, Somerville, NJ) and Band-Aid Liquid Bandage (Johnson & Johnson, Langhore, PA).

[0041] Cyanoacrylates are typically nonreactive, do not promote infection, are rapidly curing, and are only moderately expensive. Disadvantages of cyanoacrylates and cyanoacrylate-based hemostatics include difficulty of application due to their highly adhesive nature, and risk of tissue neurotoxicity, fibrosis and inflammatory reactions.

[0042] The two main polysaccharides used as hemostatics today are oxidized cellulose and poly-N-acetyl glucosamine. The hemostatic effects of certain polysaccharides, specifically oxidized cellulose and N-acetyl glucosamine, have been known since the early twentieth century. Oxidized cellulose is derived from plant fiber, which is in turn oxidized in the presence of nitrogen dioxide to form cellulosic acid. Oxidized cellulose activates the coagulation cascade (contact activation pathway) and accelerates thrombin generation within the body. Furthermore, the polysaccharide meshwork serves as a physical framework for coagulation to occur, with moderate absorbent properties. Oxidized cellulose products on the market today include Oxycel (Becton Dickinson, Franklin Lakes, NJ), Celox (Medtrade Products Ltd., Crewe, England), Surgicel (Ethicon Incorporation), and BloodStop (LifeScience PLUS, Inc., Santa Clara, CA).

[0043] Cellulose-based hemostatics are relatively easy to handle, fully absorbable and biodegradable (over 1 to 6 weeks), relatively inexpensive, and have antibacterial properties. The major drawback of these products is the risk of foreign body reactions. Furthermore, these products have only moderate coagulation-inducing capability and therefore are reserved as an adjunct to the natural response rather than a synthetic replacement.

[0044] Poly-N-acetyl glucosamine, also known as chitin or chitosan, is a complex polysaccharide produced by fermenting microalgal cultures. The hemostatic effects of poly-N-acetyl glucosamine are believed to be a result of the attraction and binding of circulating blood cells. The positive charges on the polymer attract the negatively charged erythrocytes, to help seal the clot. Poly-N-acetyl glucosamine also has vasospasm effects. Poly-N-acetyl glucosamine products include HemCon (HemCon Inc., Portland, OR), TraumaDex (Medafor, Minneapolis, MN), SyvekPatch (Marine Polymer Technologies Inc., Danvers, MA), Clo-Sur P.A.D. (Scion Cardio-Vascular, Miami, FL), and Chito-Seal (Abbott Vascular Devices, Redwood, City, CA).1

[0045] Advantages of poly-N-acetyl glucosamine dressings include their ease of application, robustness, and lack of toxicity. Disadvantages include the high cost ($100 per unit), and variability of efficacy between batches.

[0046] Most polymer-based hemostatics are designed to provide a mechanical tissue sealant. The majority of products on the market today are composed of polyethylene glycol (PEG) which are applied and polymerized at the wound site. The polymer is typically cross-linked with itself or with a primer to yield a robust framework stopping blow flow and sealing tissue. Most PEG products undergo biodegradation in approximately 30 days. PEG products include Coseal (Baxter Healthcare Corporation, Westlake Village, CA) and AdvaSeal-S (Genzyme Corporation, Cambridge, MA). PEG-based hemostatics or tissue sealants are typically non inflammatory, do not induce immune response, and are biodegradable. Drawbacks include difficulty of application and high price ($400/application).

[0047] Pro QR Powder (Biolife, Sarasota, FL) is another polymer-based hemostatic on the market today. Pro QR is a combination product of a hydrophilic polymer and a potassium iron oxyacid salt. The polymer is absorptive of blood flow, promoting the formation of a natural blood clot while the potassium salt component releases iron which complexes with proteins and activates hemostatic channels. The product is inexpensive, nontoxic, easily stored, flexible, stops bleeding rapidly, and is available over the counter. The main drawback of the product is its awkward application.

[0048] The final class of non-biological, or synthetic, hemostatics includes those which incorporate metal salts or minerals such as zinc, iron, silver nitrate, or aluminum chloride. Although this class of hemostatics are typically easy to use, cost-effective, and provide adequate hemostatic effects their toxic side effects limit their appeal.

[0049] Zinc paste was first used to fix tissue after surgery in the early 1940s. Zinc paste solutions have impressive hemostatic abilities but are rarely used do to their harmful side effects including pain and toxicity of the site. Monsel's solution is a 20% ferric subsulfate solution, which is believed to occlude vessels via protein precipitation. Monsel's solution is easy to obtain, cost-effective, and resistant to bacterial contamination. Major disadvantages include its caustic and toxic nature which may promote melanocyte activity, increased erythema, dermal fibrosis, and reepithelialization. Silver nitrate is typically used as a 10% solution and coagulates blood through protein precipitation. Silver nitrate is cost-effective, easy to use, and has potent antibacterial properties. Disadvantages include its severe tissue toxicity, risk of permanent skin discoloration, and the painful burning sensation experienced upon application. Aluminum chloride has modest hemostatic properties and is prepared in concentrations of 20% to 40% in water, alcohol, ether, or glycerol. Its mechanism of action is thought to be caused by the hydrolysis of the salt, resulting in the generation of hydrogen chloride which causes vasoconstriction, and can assist in the activation of the extrinsic coagulation pathway. Aluminum chloride is cost effective, easy to use, and may be stored at room temperature. Side effects of its use include painful paresthesias, tissue irritation, and reepithelialization. Aluminum chloride solutions are marketed as Drysol and Xerac AC (person-Covey, Dallas, TX).I

[0050] A small subclass of hemostatics is based upon various mixtures of minerals. Zeolite is a granular mixture of silicon, aluminum, sodium, and magnesium derived from lava rock. When coming into contact with blood the mixture absorbs water, concentrating platelets and coagulation factors within the wound, accelerating the clotting process. QuikClot (Z-Medica, Wallingford, CT) and WoundStat (TraumaCure, Bethesda, MD) are two main products based upon a zeolite mixture. Zeolite is inexpensive, easy to manufacture, clots fairly quickly, robust under various conditions, and is fairly immunological inert. The main drawback of the formulation is the risk of thermal injury associated with use.

[0051] A hydrogel is generically defined as an insoluble, cross-linked network of polymer chains which swells in an aqueous environment. A hydrogel may be chemically cross-linked through covalent bonds or physically cross-linked through entanglements or non-covalent interactions. Due to their unique properties hydrogels have been used in various pharmaceutical and biomedical applications. Since it is possible to create hydrogel constructs with specific degradative and swelling characteristics their potential for tissue engineering

and artificial implantation is immense. Furthermore, because hydrogels can be engineered with "smart" swelling behavior based on time, pH, ionic concentration, electrical, or magnetic stimuli they have been used with incredible success as drug delivery systems.

[0052] A cationic, acrylamide-based hydrogel has been developed which exhibits unique and potent coagulation-inducing effects upon the interaction with blood or acellular plasma. The hydrogel is composed of acrylamide, N-(3-Aminopropy)methacrylamide hydrochloride, and cross-linked with N-N'- methylenebisacrylamide. Upon interaction with acellular plasma the hydrogel initiates the coagulation cascade which results in the formation of a natural, fibrin-based hemostatic matrix (Figure 1). The stained microscopic images clearly show two distinct materials; the polymer hydrogel, which appears smooth and glassy on the right side of each image and a fibrin layer, which surrounds the polymer hydrogel located on the left side of each image.

[0053] In one aspect, the present invention provides a specific method of forming such a primary amine containing polymer hydrogel capable of inducing the blood coagulation process. In one embodiment, the primary amine monomer may be a strong base (wherein its ability to exhibit a positive charge is largely pH independent). In another embodiment, the primary amine monomer may be a weak base (wherein its ability to exhibit a positive charge is largely pH dependent). In yet another embodiment, the primary amine monomer is a weak base with a pKa above 7.4 and is able to exhibit a strong positive charge at the pH of blood and plasma (~7.4).

[0054] The method involves mixing at least one monomer with a primary amine group, along with desired other monomers, different from the initial primary amine containing monomer in a solvent, specifically an aqueous solvent. The polymer hydrogel is formed by polymerizing the monomers and cross-linking either after or during the polymerization process. Preferably, the polymer hydrogel is cross-linked in such a way so as to ensure the creation of pockets within the hydrogel which are incredibly dense with primary amine functionality. These dense pockets of positive electrostatic charge are able to induce coagulation through a Factor VII dependent mechanism. Without being bound to any specific theory, it is believed that that hydrogel acts as a catalyst activating and enhancing the functioning of Factor VII along with the Factor VII-tissue factor complex. Research has shown that this phenomenon is dependent on positive electrostatic charge and the mechanical rigidity of the hydrogel formed. That is to say, the primary amine monomer, within the hydrogel, should be positively charged at the pH of blood and/or plasma, 7.4. Therefore, if

the monomer is a weak base it preferably has a pKa of at least 7.4, more preferably at least 8, and even more preferably, at least 8.5, to ensure the predominant majority of the monomers are hydrogenated bearing a positive charge. Furthermore, as stated previously the amine monomer containing polymer strand must be sufficiently cross-linked to create an appropriately rigid material.

[0055] In certain embodiments, the monomer units are capable of exhibiting an electrostatic charge in an aqueous solution. In particular the primary amine containing monomer is able to exhibit a positive electrostatic in a salt buffered, aqueous environment of pH 7.4 (blood/plasma). In some cases, the contributing monomer units may be acidic or basic, which under the appropriate pH conditions, exhibit a negative or positive electrostatic charge, respectively. The acid/base monomer units may have varying levels of acidity/basicity, which will determine the extent to which the monomer units will be present in the anionic/cationic form at the pH level of the aqueous solution. With respect to acidic monomer units, the monomer unit may be a strong acid (in which its ability to exhibit a negative charge is largely pH independent) or a weak acid (in which its ability to exhibit a negative charge is pH dependent respect to basic monomer units), the monomer unit may be a strong base (in which its ability to exhibit a positive charge is largely pH independent) or a weak base (in which its ability to exhibit a positive charge is pH dependent).

[0056] In certain embodiments, the monomer units used are able to exhibit marked morphological or structural changes based on certain stimuli such as pH, electric field, magnetic field, or temperature for regulated drug delivery applications. In some cases the contributing monomer units may be basic, which under the appropriate pH conditions, exhibit a positive electrostatic charge. The base monomer units may have varying levels of basicity, which will determine the extent to which the monomer units will be present in the cationic form at the pH level of the aqueous solution. The monomer unit may be a strong base (in which its ability to exhibit a positive charge is largely pH independent) or a weak base (in which its ability to exhibit a positive charge is pH dependent).

[0057] In some cases the contributing monomers may be electrically sensitive, that is, the monomer is able to exhibit a structural phase change upon introduction to an electrical field. Examples of such monomers include vinyl alcohol, diallyldimethylammonium chloride, and acrylic acid.

[0058] In some cases the contributing monomers may able to exhibit a marked morphological or structural change based upon temperature. An example of such a

temperature sensitive monomer is N-isopropylacrylamide. The monomer may be used to produce a temperature-sensitive hydrogel for regulated release or rather for a hydrogel capable of inducing coagulation in a temperature dependent manner.

[0059] Examples of primary amine containing monomers include but are not limited to allylamine, N-3-aminopropyl methacrylamide (APM), and N-2-aminoethyl methacrylamide (AEMA). Examples of monomer units that are strong bases include those having ammonium groups, such as 3-acrylamidopropyl trimethylammonium chloride (AMPTAC). The monomer units may also be neutral monomers exhibiting no electrostatic charge in the solution. Examples of such monomers include acrylamide (Am), N-tertbutylacrylamide (NTBAAm), N-isopropylacrylamide (NIPAAm), and N,N'-dimethylacrylamide (DMAAm).

[0060] Polymerization of the monomer units can be achieved using any of various techniques known in the art, including chemical processes (e.g., using free-radical initiators and/or catalysts), photochemical processes (e.g., exposure to UV-irradiation), or electrochemical processes. Likewise, cross-linking can be achieved using any of various techniques known in the art, including the addition of a cross-linking agent to the solution. In some cases, polymerization may be effected by the addition of ammonium persulfate (APS) as the polymerization initiator and N,N,N',N'-tetramethylethylenediamene (TEMED) as the catalyst. In some cases, the cross-linking agent is a difunctional monomer, N,N'-methylenebisacrylamide (BIS), epichlorohydrin (EPI), genipin, glutaraldehyde, or ethylene glycol diglycidyl ether (EDGE). Biodegradable cross-linkers such as ethylene glycol dimethacrylate and ethylene glycol diacrylate may also be used as the cross-linking agent. The biodegradable polymers are capable of undergoing hydrolytic cleavage in vivo. Polymerization and cross-linking may take place simultaneously or sequentially in any order. As such, the polymerization initiator, catalyst, and/or cross-linking agent may be added to the solution simultaneously or sequentially in any order.

[0061] Upon polymerization (and cross-linking, in some cases) of the monomer units, a polymer matrix is formed. The amount of cross-linker used (ratio of cross-linker monomer:total remaining functional monomers) determines the mesh size of the gel network. If a polymer hydrogel composed of a primary amine containing monomer is cross-linked appropriately the material, is capable of inducing the blood coagulation pathway, in a factor VII-tissue factor dependent manner. The ability of the polymer hydrogel to induce coagulation is dependent mainly on mechanical rigidity, i.e. cross-link density, and the primary amine functionality on the main chain polymer backbone. It should be noted that

experiments were conducted using the non-cross-linked amine containing polymers, and they were unable to induce coagulation.

[0062] In certain embodiments, the polymer hydrogel is able to induce clotting in platelet deficient plasma. In other embodiments, the polymer hydrogel is able to induce clotting in Factor XII, XI, Factor IX, or Factor VIII-deficient plasma.

[0063] In a specific aspect the invention details the production of a multi-component material consisting of two different compositions of polymeric hydrogels – one for use in any internal hemostatic application, and one for use in any external hemostatic application.

[0064] In another aspect, an embodiment of the present invention provides a polymeric material comprising a cross-linked polymer matrix having a cavity, highly dense in primary amine functionality capable of inducing the blood coagulation pathway. This polymeric hydrogel may be synthesized using any of various techniques, including those described above.

[0065] The cavity may have a geometry (including its size and shape) which is capable of aiding in the activation process. Geometry of the cavity, along with density of electrostatic functional groups within the cavity, is determined, in part, by the amount of cross-linker used in the process.

[0066] The created polymeric hydrogel, depending on the specific concentration of primary amine monomers and corresponding cross-link density may have varying degrees of inducing the blood coagulation cascade, as shown in Figure 6 herein. In a specific embodiment, the optimum concentration for the APM, acrylamide, BIS hydrogel is between 1.5-2 M of APM and 1.5-2 M of acrylamide cross-linked at between 5:1 and 7:1 (acrylamide:BIS). In another specific embodiment (blood optimization) the optimum composition is approximately 2.73 M of APM, .27 M of acrylamide, and .056 M BIS.

[0067] The ability of the hydrogel to initiate blood coagulation in the absence of cells offers a potentially substantial advantage over other hemostatic approaches. In particular these polymers may offer treatment alternatives for patients experiencing platelet-related disorders for which there are no accepted treatment methods available. Another desirable characteristic of the materials, depicted in Figure 1 herein, is their ability to swell in plasma. In practice this would allow the polymers to apply pressure (tamponade) at the site of action, which also aids in reducing blood loss. Furthermore, because of this characteristic swelling in plasma, the hydrogel may be designed in order to administer therapeutics in a controlled and regulated manner.

EXAMPLES

[0068] In one experiment, a randomized copolymer composed of acrylamide and APM, initiated with a 7.5% weight percent solution of TEMED (20 μL/1 mL) and a 15% weight percent solution of APS (20 μL/1 mL), and cross-linked with BIS, was produced. Figure 3 depicts an optimization chart where 156 different polymer compositions, each cross-linked at three different ratios, were tested in citrated human plasma, and rated accordingly their ability to produce a clot. As shown the optimal concentration for inducing coagulation lies between 1.5-2 M of acrylamide and 1.5-2 M of APM, each at its highest cross-link density (maximal amount soluble). The primary amine-containing hydrogel is able to induce the blood coagulation cascade resulting in the formation of a fibrin clot. Figure 1 depicts the ability of the material to induce a fibrin based clot in human plasma (4% sodium citrate). The hydrogel shown is composed of 1.5 M acrylamide 1.5 M APM and cross-linked with .3 M BIS (acrylamide:BIS ratio = 5:1).

[0069] Figure 2 shows micrographs of the coagulate complex (fibrin-hydrogel complex) after hematoxlyin and eosin (H&E) staining, immunohistochemical (IHC) staining, along with an image of the complex obtained using an environmental scanning electron microscope.

[0070] Figure 4 shows the ability of the optimized hydrogel (1.5 M acrylamide, 1.5 M APM< and .3 M BIS) to induce fibrin formation in a variety of factor deficient and factor inhibited plasmas.

[0071] Figure 5 shows the ability of the optimized hydrogel to induce the activation of FVII (5C).

[0072] Figure 6 shows that the optimized hydrogel is not in fact a homogenous network but rather is made up of several mechanically distinct regions.

[0073] Experimentation in human and sheep blood produced an optimum composition consisting of .27 M of acrylamide and 2.73 M of APM and .056 M (acrylamide:BIS ratio= 5:1). [Composition 2]

[0074] The effectiveness of the primary amine-containing hydrogel in hemostatic clot formation was assessed. Blood was drawn from a live adult sheep and added immediately to a vial containing a small amount of the primary amine-containing hydrogel (Figure 7A) and an empty vial (Figure 7B), used as a control. The material was able to induce the formation of a robust clot within seconds of blood contact, compared to the control which took

approximately 10 minutes. Furthermore, the mechanical integrity of the clot produced was dramatically superior to that of the control.

[0075] The primary amine-containing hydrogel was also effective in inducing hemostatic clot formation in vivo. A primary amine-containing hydrogel, consisting of 0.27 M acrylamide, 2.73 M N-3-aminopropyl methacrylamide (APM), and 0.054 M N-N'-methylene bisacrylamide (BIS), placed on a 4x4 inch gauze bandage (a prototype of the presently claimed invention, shown in Figure 8), was administered to inhibit bleeding from an incision introduced into a live sheep lung. The hydrogel was able to successfully stop bleeding from the induced lung incision in approximately 2 minutes. Figure 9 shows an image of the site immediately after the surgeon made the incision (Figure 9A) along with an image of the incision site after the hydrogel based prototype was applied for 2 minutes (Figure 9B). Initial post operative analysis showed that the material was able to induce fibrin formation at the incision causing a natural suturing process, and thus sealing the tissue preventing blood loss. Hematoxylin and eosin stained sections of the incision site confirmed that the material was able to induce the rapid formation of a natural, fibrous-based hemostatic suture, as shown in Figure 10.

INDUSTRIAL APPLICABILITY

[0076] The polymer hydrogel created of the present invention may have various uses. Such uses include a bandage for trauma related injuries or a surgical gauze for use in the operating rooms. In terms of the bandage the hydrogel would be incorporated into a filtered bandage, similar to that of a Band-Aid®, which would then be applied to the wound in order to prevent blood loss and deliver necessary therapeutics. In terms of the surgical gauze the hydrogel would be incorporated into a filtered gauze-like material for use by surgeons to control blood loss during surgery.

[0077] Notably, the bandage application of the hydrogel is novel in the sense that there is no other synthetic polymer, hydrogel material capable of inducing blood clotting while simultaneously delivering therapeutics. Furthermore, the hydrogel functions in Factor VIII and Factor IX deficient plasma, a functionality which should revolutionize wound care for people suffering from hemophilia.

CLAIMS

We claim:

1. A cross-linked polymer, comprising cross-links between at least two monomer backbones, wherein at least one monomer comprises a primary, secondary, tertiary or quaternary amine with a pKa of at least 7.4, and capable of displaying a positive electrostatic charge at the pH of blood or plasma (7.4), and wherein the polymer is capable of activating the blood coagulation cascade by inducing fibrin formation.

2. The polymer of claim 1, wherein said at least one monomer is selected from the group consisting of N-3-aminopropyl methacrylamide, allylamine, and a primary-amine containing monomer capable of displaying a positive electrostatic charge at the pH of blood or plasma (7.4).

3. The polymer of claim 1, wherein at least one of the monomer backbones is acrylamide, or a derivative thereof.

4. A hydrogel comprising the polymer of claim 1, wherein the monomer backbones are cross-linked with cross-linkers selected from the group consisting of N-N'-methylene bisacrylamide, N-N'-bisacrylylcystamine, bisacrylyl piperazine, ethylene glycol diglycidyl ether, epichlorohydrin, N-N'-diallyltartardiamide, ethylene glycol dimethacrylate and ethylene glycol diacrylate.

5. The hydrogel of claim 4, wherein the primary amine is allylamine and the cross-linker is either ethylene glycol diglycidyl ether or epichlorohydrin.

6. The hydrogel of claim 4, therein the monomer backbones are cross-linked with cross-linkers selected from the group consisting of ethylene glycol dimethacrylate and ethylene glycol diacrylate.

7. The polymer of claim 1, wherein the primary amine containing monomer is N-3-aminopropyl methacrylamide (APM), the co-monomer is acrylamide, and the cross-linker is N-N'-methylene bisacrylamide (BIS).

8. The hydrogel of claim 4, wherein said hydrogel consists of 1.5 M acrylamide, 1.5 M N-3-aminopropyl methacrylamide (APM), and 0.3 M N-N'-methylene bisacrylamide (BIS).

9. The polymer of claim 7, wherein said hydrogel consists of 0.27 M acrylamide, 2.73 M N-3-aminopropyl methacrylamide (APM), and 0.054 M N-N'-methylene bisacrylamide (BIS).

10. The hydrogel of claim 4, wherein said hydrogel consists of 1.5 M acrylamide, 1.5 M N-3-aminopropyl methacrylamide (APM), and 0.3 M N-N'-methylene bisacrylamide (BIS).

11. The hydrogel of claim 4, further comprising one or more pharmaceutical active ingredients selected from the group consisting of Novocain, Lidocain, erythromycin, bacitracin, adrenaline, topricin, acetaminophen, ibuprofen, and a hemostatic agent.

12. A method of forming the hydrogel of claim 4, comprising:

adding the monomer backbone comprising a primary amine to the aqueous solution, wherein the first monomer unit exhibits an electrostatic positive charge in the aqueous solution at pH of 7.4 (pH of blood or plasma);

adding a second monomer backbone to the aqueous solution, wherein the second monomer backbone is different from the first monomer unit;

forming the cross-linked polymer using a cross-linking agent, wherein the step of forming polymer comprises polymerizing the monomer backbone.

13. The method of claim 12, wherein the second monomer backbone is neutral or exhibits an electrostatic charge opposite to that of the first monomer backbone.

14. The method of claim 12, wherein the first monomer backbone is added before the second monomer backbone is added.

15. The method of claim 12, wherein the second monomer backbone is added before the first monomer backbone.

16. The method of claim 12, wherein the first and second monomer backbone are added simultaneously to the aqueous solution.

17. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 4.

18. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 5.

19. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 6.

20. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 8.

21. A kit for inducing hemostatic clot formation, comprising the polymeric hydrogel of claim 10.

22. A method of treating trauma-induced hemorrhage, comprising administering the hydrogel of any of Claims 4-6, 8, 10 and 11 to a subject in need thereof.

23. A method of treating internal hemorrhaging, comprising administering the hydrogel of any of Claims 4-6, 8, 10 and 11 to a subject in need thereof.

24. A method of treating hemorrhaging during surgical operations, comprising administering the hydrogel of any of Claims 4-6, 8, 10 and 11 to a subject in need thereof.

25. The method of any one of Claims 22-24, wherein said hydrogel is administered on a material selected from the group consisting of a bandage, gauze, tape and adhesive wound dressing.

FIG. 1

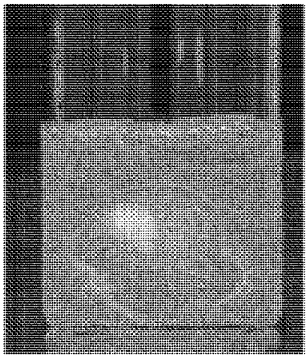
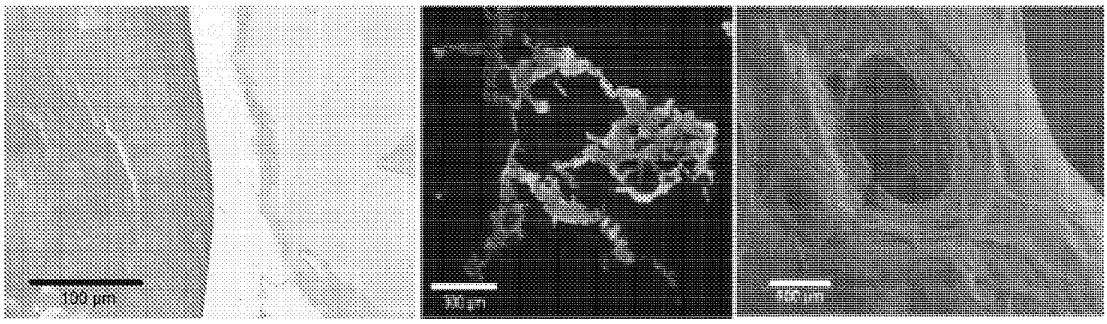


FIG. 2



a b c

FIG. 3

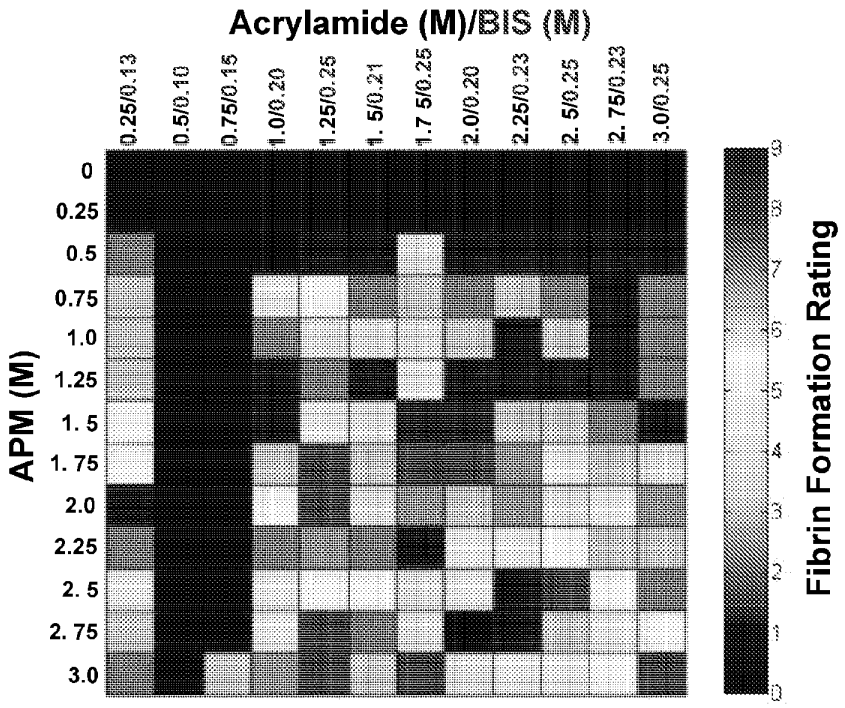

Acrylamide (M)/BIS (M)
0.25/0.13
0.5/0.10
0.75/0.15
1.0/0.20
1.25/0.25
1. 5/0.21
1.7 5/0.25
2.0/0.20
2.25/0.23
2. 5/0.25
2. 75/0.23
3.0/0.25
APM (M)
0
0.25
0.5
0.75
1.0
1.25
1. 5
1. 75
2.0
2.25
2. 5
2. 75
3.0
Fibrin Formation Rating

FIG. 4

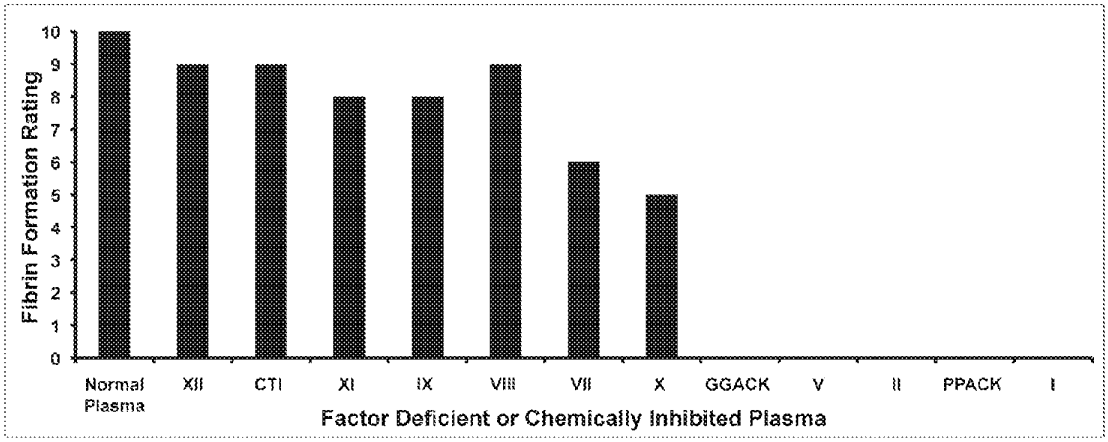

Fibrin Formation Rating
10
9
8
7
6
5
4
3
2
1
0
Normal Plasma
XII
CTI
XI
IX
VIII
VII
X
GGACK
V
II
PPACK
I
Factor Deficient or Chemically Inhibited Plasma

FIG. 5

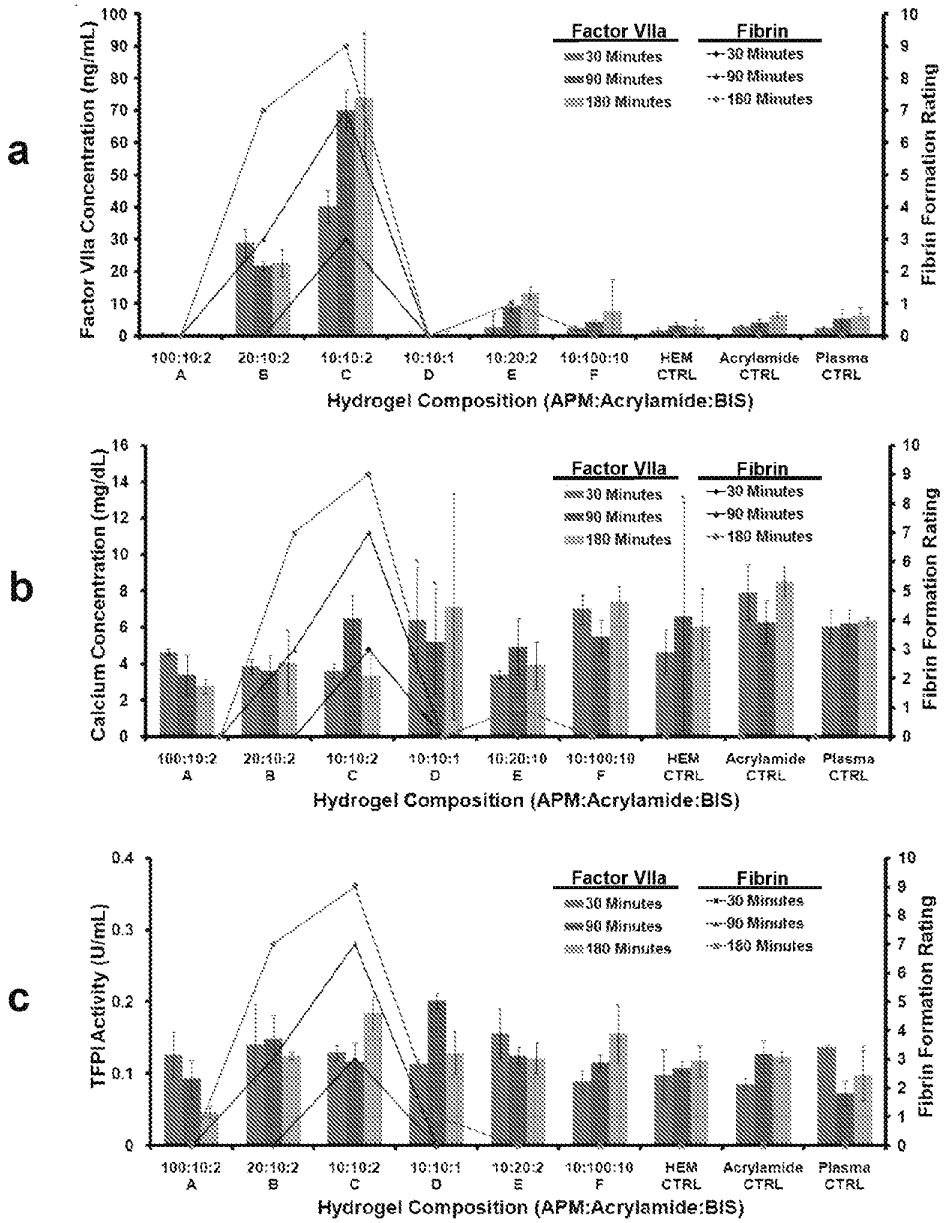

a
Factor VIIa Concentration (ng/mL)
Fibrin Formation Rating
Factor VIIa
30 Minutes
90 Minutes
180 Minutes
Fibrin
30 Minutes
90 Minutes
180 Minutes
100:10:2 A
20:10:2 B
10:10:2 C
10:10:1 D
10:20:2 E
10:100:10 F
HEM CTRL
Acrylamide CTRL
Plasma CTRL
Hydrogel Composition (APM:Acrylamide:BIS)
b
Calcium Concentration (mg/dL)
Fibrin Formation Rating
Factor VIIa
30 Minutes
90 Minutes
180 Minutes
Fibrin
30 Minutes
90 Minutes
180 Minutes
100:10:2 A
20:10:2 B
10:10:2 C
10:10:1 D
10:20:10 E
10:100:10 F
HEM CTRL
Acrylamide CTRL
Plasma CTRL
Hydrogel Composition (APM:Acrylamide:BIS)
c
TFPI Activity (U/mL)
Fibrin Formation Rating
Factor VIIa
30 Minutes
90 Minutes
180 Minutes
Fibrin
30 Minutes
90 Minutes
180 Minutes
100:10:2 A
20:10:2 B
10:10:2 C
10:10:1 D
10:20:2 E
10:100:10 F
HEM CTRL
Acrylamide CTRL
Plasma CTRL
Hydrogel Composition (APM:Acrylamide:BIS)

FIG. 6

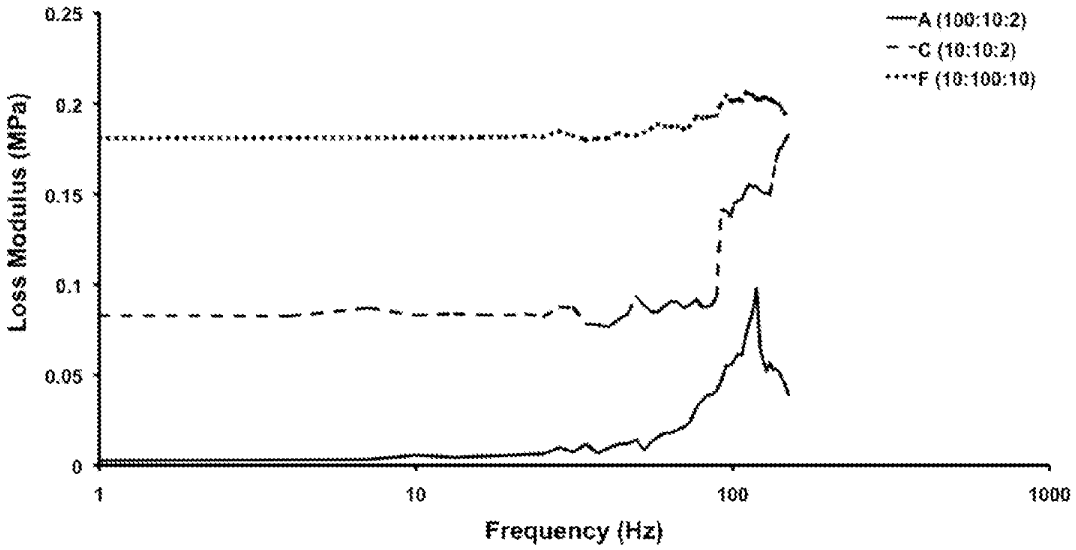

A (100:10:2)
C (10:10:2)
F (10:100:10)
Loss Modulus (MPa)
0.25
0.2
0.15
0.1
0.05
0
1
10
100
1000
Frequency (Hz)

FIG. 7

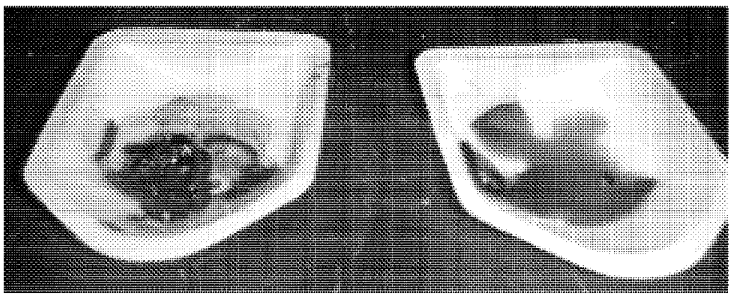
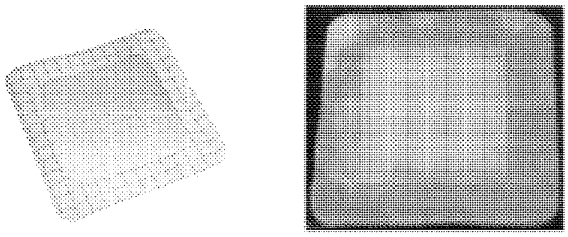
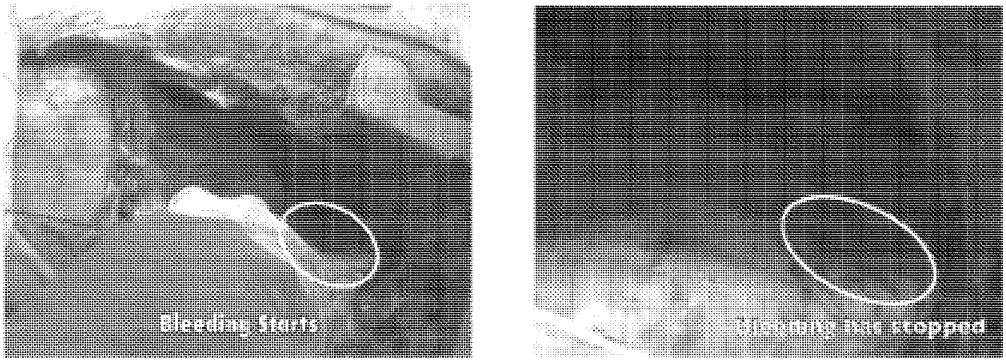

A
B

FIG. 8



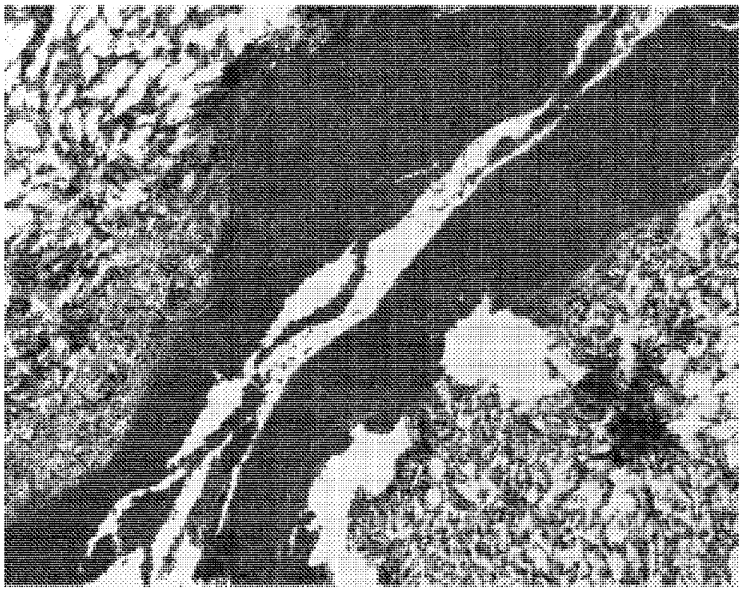
A B

FIG. 9



A B

FIG. 10



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/063049

A. CLASSIFICATION OF SUBJECT MATTER

A61F 13/02(2006.01)i, A61L 15/44(2006.01)i, A61P 7/04(2006.01)i

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61F 13/02; A61K 31/785; A61K 9/14; A61K 9/16; A61K 9/50; B01D 21/26

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models
(Chinese Patents and application for patent)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: coagulation, polymer, crosslink, hydrogel

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007-0237742 A1 (GARRET FIGULY et al.) 11 October 2007 See whole pages.	1-21
A	US 2003-0215519 A1 (ALEXANDER SCHWARZ et al.) 20 November 2003 See whole pages.	1-21
A	US 5648100 A1 (BOSCHETTI; EGISTO et al.) 15 July 1997 See whole pages.	1-21
A	US 4994192 A1 (CORIN; ALAN F. et al.) 19 February 1991 See whole pages.	1-21

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

☒ See patent family annex.

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

Date of the actual completion of the international search	Date of mailing of the international search report
31 MARCH 2010 (31.03.2010)	**01 APRIL 2010 (01.04.2010)**

Name and mailing address of the ISA/KR
Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea
Facsimile No. 82-42-472-7140

Authorized officer
LEE, Dong Won
Telephone No. 82-42-481-5549

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/063049

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 22-25
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 22-25 pertain to methods for treatment of the human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required addtional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2009/063049

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2007-0237742 A1	11.10.2007	None	
US 2003-0215519 A1	20.11.2003	AU 2003-239374 A1	11.11.2003
		WO 03-094930 A1	20.11.2003
US 5648100 A1	15.07.1997	CA 2110290 C	05.02.2002
		EP 0588875 A1	30.03.1994
		EP 0588875 A4	03.08.1994
		EP 0588875 B1	09.04.1997
		JP 03-509858 B2	09.01.2004
		KR 10-1994-0700869 A	22.04.1994
		US 5635215 A1	03.06.1997
		WO 92-21327 A1	10.12.1992
US 4994192 A1	19.02.1991	EP 0438192 A1	24.07.1991
		JP 06-249849 A	09.09.1994
		KR 10-1991-0014707 A	31.08.1991

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Japanese Patent Application Laid-Open No. 58-025146

Registration Gazette | public notice | Document unit PDF | progress information | OPD | search key | URLs

Display format of the document display screen:
text display PDF display
primary literature

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Unexamined patent publication (A)
(11) [Publication number] JP-A-58-25146
(43) [Published date] 1983 (1983) February 15
(54) [Title of Invention] Blood vessel puncture display type multi-sample needle assembly
(51) [International Patent Classification 5th edition]
A61B 5/14
[FI]
A61B 5/14
[Request for examination] Yes
[Total number of pages] 9
(21) [Application number] Japanese Patent Application Showa 57-126629
(22) [Filing date] July 20, 1982
(31) [Priority claim number] 284894
(32) [Priority date] July 20, 1981
(33) [Country claiming priority] United States of America (US)
(71) [Applicant]

[Identification number] 999999999
[Name] Becton, Ditzkinson & Company
(72)) [Inventor]
[Name] Josef Kaufmann
(74) [Agent]
[Name] Kyozo Yuasa

wrap up close

(57) [Abstract] Since this gazette is application data before electronic filing, abstract data is n ot recorded.

The scope of the claims open

[Claims]
1. A multi-sample needle assembly capable of recognizing a vascular puncture when collecting blood from a patient, the assembly having a front end, a rear end and an internal chamber, th e chamber being translucent surrounding at least the chamber for user perception. a first pun cture needle in fluid communication with the chamber and extending outwardly from the front end and insertable into the patient; and a first puncture needle in fluid communication with th e chamber and outwardly from the rear end. a second puncture needle extending outward an d penetrating into the vacuum container for blood sample collection; an air permeable blood i mpermeable porous plug positioned within the lumen of a second needle in the space between said transverse holes; and a second puncture. a resilient slidable valve mounted on the outsid e of the needle in a closed position covering at least one of said lateral holes to prevent blood from flowing out of said second puncture needle, said valve being slidable to an open position. means, in the open position, for allowing blood to flow out of a lateral hole near said chamber and return to the second needle through the other lateral hole, whereby blood is collected fro m the second needle; A sample needle assembly with a blood vessel puncture indicator, chara cterized by:
2. 3. The assembly of claim 1, wherein said valve is a sleeve in airtight slidable contact over t he second puncture needle.
3. 3. An assembly as claimed in claim 2, wherein said sleeve covers the lateral hole near said chamber in airtight contact under unforced conditions.
4. 3. The assembly according to claim 2, wherein said sleeve includes an inner diameter porti on that fits over the outer diameter of the second puncture needle and covers at least one of t

he lateral holes in airtight contact.

5. The means for permitting blood flow includes a cavity formed in the sleeve and having a di ameter greater than the fitting diameter, the length of the cavity extending inwardly toward th e trailing end of the sleeve. ToWhen slid, the lateral holes are covered so that blood flows fro m the lateral hole closer to the chamber, through the cavity, back through the other lateral hol e, bypassing the plug, and continuing through the second puncture needle. 5. An assembly as claimed in claim 4 for collecting blood.

6. 6. The assembly of claim 5, wherein the cavity-free portion of said sleeve is compressible a gainst said trailing end during inward sliding of the sleeve.

7. 7. The assembly of claim 6, wherein the compressible portion of the sleeve is a peripheral wall thinner than the portion of the sleeve containing the cavity.

8. 6. An assembly according to claim 2 or 5, wherein said sleeve is made of an elastomeric m aterial.

9. 2. The assembly according to claim 1, wherein said first and second puncture needles are c oupled within said chamber, and both puncture needles communicate with said chamber throu gh a common lateral hole.

10. 3. The assembly of claim 1, wherein said porous plug is made of sintered polyethylene.

11. 2. An assembly according to claim 1, including means for connecting a holder for a vacuu m vessel to said housing.

12. 12. An assembly according to claim 11, comprising a holder for a vacuum vessel connecte d to said housing.

13. A multi-sample needle assembly for collecting a fluid sample from a source, comprising a housing having a chamber therein and a first piercing needle in fluid communication with the chamber for insertion into the fluid source and fluid passing through the chamber. a second pu ncture needle that feeds a collection device through a piercing device; a device mounted withi n the lumen of the second piercing needle that permits gas and liquid to pass through the sec ond piercing needle; and a device for operatively collecting fluid from the second puncture ne edle by diverting the fluid away from the impermeable device.

14. The device for operatively collecting liquid has a lateral hole passing laterally between the second puncture needle liquid flow blocker and the chamber, and is attached to the second pu ncture needle and covers the lateral hole in the closed position. and a resiliently movable valv e that prevents fluid from flowing out of the second puncture needle, and when said valve is moved to an open position, said lateral hole is opened to allow fluid to flow out through said la teral hole. 14. The assembly of claim 13 collected.

15. 14. The assembly according to claim 13, wherein said first and second puncture needles a re integrally formed to form one puncture needle device, and a common lateral hole communi cating with said chamber is provided.

16. A multi-sample needle assembly capable of recognizing a vascular puncture when collectin g blood from a patient, the assembly having a front end, a rear end and an internal chamber

which is translucent to allow the assembly user to view the chamber. a housing; a first piercin g needle in fluid communication with the chamber and extending outwardly from the front end and insertable into a patient; a second puncture needle penetrating into the vacuum container for sample collection; an air permeable blood impermeable porous plug positioned within the l umen of the second puncture needle in the space between the transverse holes; and a sleeve made of elastic slidable elastomer that covers at least one of the lateral holes in air-tight cont act to prevent outflow of blood from the second puncture needle in the stationary mounting p osition, and the inner diameter of the sleeve is the same as that of the second puncture needl e. The airtight contact is caused as a fit on the outer diameter, the sleeve is provided with a c avity having an inner diameter larger than the fitting inner diameter, the cavity is long enough to cover both lateral holes, and the sleeve is directed toward the rear end. Sliding to the open position, the cavity covers both lateral holes, blood flows out from the lateral hole near the ch amber bypassing the plug, enters the cavity, returns through the other lateral hole, and passe s through the second puncture needle. Generating a continuous flow to allow collection, chara cterized in that the non-cavity portion of the sleeve is compressible towards the trailing end w hen the sleeve is slid during collection of blood from the second puncture needle. A multi-sam ple needle assembly with a vessel puncture indicator.

detailed description open —

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a needle assembly for collecting fluids from a patient or the li ke, and more particularly to collecting multiple samples of blood from a patient in multiple eva cuated tubes to prevent blood leakage when changing tubes. More particularly, it relates to a needle assembly having a device for indicating that the needle assembly has entered a patien t's blood vessel.

It is now standard practice to collect multiple samples of fluid, such as blood, from a patient i n a single procedure. Once the needle is inserted into the patient's blood vessel, the evacuate d blood collection tube is then inserted into the holder. A holder is configured to connect to th e needle and accommodate the vacuum tube. The needle remains inserted in the patient's ves sel as each filled tube is removed from the holder. Various valves are currently in use to preve nt blood from flowing out of the holder during removal of a filled tube and insertion of the nex t evacuated tube for subsequent sample collection. An elastomeric sleeve surrounding the inn er needle is commonly used as this valve. Although the valve for this multi-sample needle ass embly has the required functionality, various ways to improve this device are being explored. Additionally, it would be desirable to provide a mechanism by which the user of the multi-sam

ple needle assembly can perceive when the intravenous needle has entered the patient's bloo d vessel. Blood flow within the collection device is often minimal due to difficulty in locating th e vessel or other reasons when collecting blood from the patient. In this case, it is most desira ble to be able to rapidly determine that an intravascular insertion is made and blood flows into the needle assembly. When this determination has been made and the endovascular puncture has been performed, an evacuated blood collection container is inserted into the collection de vice during a single collection procedure by well-known techniques for multiple sample collecti on.

A problem that arises during the vascular puncture process is air pockets. This is found in vari ous needle assemblies used for multi-sample blood collection. When a vascular puncture is pe rformed and a vacuum blood collection container has not yet been attached to the other end o f the needle device, pockets of air may prevent blood from flowing into the needle assembly. T hat is, the pocket remains within the needle assembly under steady atmospheric pressure. Th erefore, even if a vascular puncture is performed, venous pressure may not allow blood to flo w through the intravascular needle and into the collection device, and if a vacuum blood conta iner is attached, the vacuum force will be sufficient within the needle assembly. Acts as a forc e of attraction. As recognized by the inventors in US Pat. No. 4,207,870, this air block proble m prevents blood from flowing through the blood immersion needle to a point visible to the us er. The device of this patent combines a porous evacuation device with a bypass valve throug h which air within the needle assembly escapes during the initial stages of the blood collection procedure. This evacuation device prevents the outflow of blood.

Kaufman, U.S. patent application Ser. No. 160.781, entitled "Multi-Sample Needle With Vascul ar Puncture Indicator," filed Jun. 18, 1980, shows a different type of needle device wherein an air-permeable blood-impermeable porosity is present within the actuation valve. use the plug. U.S. Pat. No. 4,207,870 and the Kaufman invention are preferred as a combination one-way v alve and air exclusion device, but are subject to further improvement. The present invention i mproves upon this device so that air is evacuated from the needle assembly and blood can flo w directly into the needle assembly by evacuating the air.

A multi-sample needle assembly according to the present invention is useful for collecting liqui d samples from a liquid supply. The needle assembly has a housing with a chamber and a pun cture needle device in communication with the chamber. The piercing needle device includes a first piercing needle that inserts into a fluid supply and a second piercing needle that delivers f luid through a chamber to a collection device. A device is provided within the lumen of the sec ond puncture needle that allows gas and liquid to pass through the second puncture needle. A device is provided for shunting the liquid flow preventer to the needle assembly to operatively collect liquid from the second puncture needle.

In accordance with a preferred embodiment of the present invention, a housing is provided wi th a front end, a rear end and an interior chamber. The housing surrounds at least the chamb er and is translucent so that a user of the assembly can view the chamber. A first puncture ne

edle extends outwardly from the forward end for insertion into the patient. A second piercing needle extends outwardly from the rear end to be penetrable into an evacuated blood collectio n container for blood sample collection. Two lateral holes are formed in the lateral side of the outward extension of the second puncture needle, and the lateral holes communicate with the lumen of the second puncture needle. An air permeable liquid impermeable porous plug is ins erted into the space between the lateral holes of the lumen of the second puncture needle. A r esilient slidable valve is provided on the outer surface of the second puncture needle to cover one lateral hole in the stationary position of the closed position of the valve to prevent blood f rom flowing out of the second puncture needle. The valve is slidable to an open position, allow ing blood to flow out of a lateral port near the chamber and into a secondMeans are provided f or returning through the lateral hole and blood is collected from the second puncture needle. Structurally, the multi-sample needle assembly of the present invention is significantly differe nt from devices for the same purpose. In particular, the present invention mounts the anti-flo w device directly into the second puncture needle. One or more lateral holes are provided in t he second puncture needle to allow fluid such as blood to bypass the fluid impermeable plug. According to a preferred embodiment, a slidable sleeve valve is associated with the lateral por t to control liquid flow bypassing the liquid impermeable plug. Known devices place liquid-imp ermeable members in the chamber. There are no valves or liquid-impermeable plugs in the ch amber with the configuration of the present invention. Thus, the user can easily see blood ent ering the chamber during the vascular puncture procedure. By using a gas permeable plug me mber in the second puncture needle, air is evacuated from within the assembly as blood enter s the chamber, eliminating the problem of air blocking in the absence of a gas permeable me mber. Of particular advantage, during a multi-sample blood collection procedure, the present i nvention prevents blood leakage during blood collection container changes while the needle as sembly remains inserted into the patient. The present invention provides automatic blood flow control to prevent blood leakage from the chamber after the filled blood collection container is removed from the assembly.

Embodiments and drawings illustrating the invention will now be described. The following desc riptions of various embodiments are illustrative of the principles of the invention and are not i ntended to limit the invention.

FIG. 1 shows a multi-sample needle assembly 10 according to a preferred embodiment of the invention. The basic outer members of needle assembly 10 include a housing 12, a first punct ure needle 14 for insertion into the patient, a second puncture needle 15 at the opposite end of housing 12, and a second puncture needle. The needle punctures the vacuum vessel 16 to collect a blood sample. The housing 12 has a threaded portion 18 adjacent the second piercin g needle 15 to which internal threads 20 at the front end of the container holder 19 are threa ded to attach the holder 19 . The vacuum container 16 is slid into the holder 19 and the secon d puncture needle 15 penetrates the penetrable stopper 21 at the front end of the container 1 6 . Multi-sample blood collection device schemes of the type described above are well known.

2 and 4 show details of the needle assembly 10. FIG. The housing 12 has a front end 24 and a rear end 25, and in the preferred embodiment the ends are manufactured as separate piece s to facilitate replacement of parts and to allow for chambering within the housing. Front end 24 is preferably cylindrical with a large bore extending inwardly through a portion of the body. This hole becomes the chamber 28 in the housing 12 after assembly. A small hole 29 is forme d in the rear end and is sized to fit the puncture needle 14 . The puncture needle 14 is inserte d into the hole 29, the inner end slightly entering the chamber 28 and communicating with th e chamber. The tip of puncture needle 14 protrudes outward from end 25 . After positioning th e puncture needle, it can be secured by adhesive or the like.

The front end 24 of the housing is formed with a number of proximal ribs 31 to surround the o utwardly extending piercing needle. A needle shield, not shown, normally surrounds the outw ard extension of the puncture needle and likewise has internal ribs. Engagement ribs between the needle shield and the needle assembly facilitate the user's insertion and removal of the ne edle assembly into and out of the tube holder. A portion 34 of the front end surrounding the c hamber 18 is smooth and preferably translucent or transparent to allow the user to see inside the housing. In many cases the entire front end and preferably the rear end are also made of translucent or transparent material to facilitate manufacturing and minimize the variety of ma terials used. A translucent rigid synthetic resin is the most preferred material. There may also be various sealed windows, ports, etc. for the user to view into the room. Such a window or p ort is sealed to prevent leakage of blood entering chamber 28 when the needle enters the ves sel. An annular flange 35 is provided at the front end 24 to form a surface for joining the two parts of the housing during assembly. Both portions of the housing are secured using any desi red securing means, such as adhesive.

The rear end 25 is provided with a short projection 36 to give it a generally cylindrical shape. This projecting portion serves as a reinforcing portion for supporting the inner end of the seco nd puncture needle 15 in this embodiment. The end opposite the rear end is formed with exte rnal threads 18 as previously described to provide a connection to the tube holder. A bore 38 extends through the rear end of the housing. the hole is sized to receive the diameter of the s econd puncture needle 15, the inner end 39 of the second puncture needle projecting into the chamber 28;It is in fluid communication with chamber 28 when the front and rear ends are joi ned. The second puncture needle 15 is fixed in the hole 38 with an adhesive or the like. A larg e hole 40 extends a short dimension into rear end 25 and communicates with hole 38 . A slee ve valve 41 is slidable around the outward extension of the second puncture needle 15 . The s leeve valve 41 has a thick wall portion 42, a thin wall portion 42 and a flange 45 at the end of the thin wall portion. The sleeve valve is positioned so that the flange 45 and thin walled porti on slide into the bore 40 and the flange 45 contacts the inner wall of the rear end of the housi ng. Furthermore, a cavity portion 46 is provided in the thick wall portion 42 . The inner diame ter of the sleeve valve 41 is fitted to the outer diameter of the second puncture needle 15 exc ept for the cavity portion. The inner diameter of the cavity 46 is larger than the inner diamete

r of the sleeve and larger than the outer diameter of the puncture needle. Functional differenc es between the two inner diameters will be made clear in the instructions for use below.

As shown in FIG. 4, two holes 48 and 50 are provided in the side wall of the outward extensio n of the second puncture needle 15 . At steady state, the resilient sleeve valve 41 covers the holes 48,50. Both holes can be covered by the tight-fitting inner diameter of the sleeve, but it is preferred to cover only the hole 48 near the chamber in the housing. The sleeve valve 41 m akes an airtight contact over the bore 48 in the steady position. At the same time cavity 46 su rrounds hole 50 and the valve is not in hermetic contact with hole 50 .

A gas-permeable, liquid-impermeable porous member 52 is placed within the lumen 51 of the second puncture needle 15 . In a preferred embodiment, this member is an air permeable, blo od impermeable, porous plug. A plug 52 is placed in the space between holes 48,50. Blood pa ssing through the second puncture needle 15 is therefore blocked by the blood impermeable p roperties of the porous plug 52 and blood does not flow out of the tip of the second puncture needle. The air permeable properties of the porous plug 52 allow air within the chamber 28 an d within the second needle to flow freely and out the tip of the second needle.

An annular flange 54 is provided at the rear end of the housing to facilitate joining the rear an d front ends of the housing. To ensure the required fluid flow within the housing, an elastomer ic ring 55 is interposed between the flanges 35, 54 in the example shown. When assembling t he front and rear ends, the flanges 35, 54 are fixed by a required fixing means such as an ad hesive.

The sleeve valve 41 is compressible toward the rear end 25 when a thin walled portion 44 slid es the valve as described below. The thick walled portion of the sleeve valve 41 has a cavity 4 6 and is not axially compressed like the thin walled portion. Further, the cavity 46 is of a lengt h that communicates both bores 48, 50 together when the sleeve valve is slid inward toward t he rearward end. Various materials can be used to manufacture the sleeve valve, but elastom eric materials are preferred.

For the porous plug 52, a porous material, such as sintered polyethylene, having an average p ore size of about 10 microns.

Before explaining the operation of the present invention, another embodiment of the puncture needle is shown in FIG. In the illustrated example, the multiple sample needle assembly 60 ha s elements similar to those shown in FIG. 2, and has similar characteristics, so that similar ele ments are indicated by the same reference numerals with the suffix a. In the embodiment of FIG. 2, separate front and rear puncture needles are used, but in the example of FIG. 3, a sin gle puncture needle 61, preferably a single puncture needle 61, is passed through the housing 12a. First puncture needle portion 14a extends outwardly from front end 24a. The second pun cture needle portion 15a extends outward from the rear end portion 25a. A common fluid outl et hole 62 is formed in the central portion of the puncture needle 61 and communicates with t he chamber 28a. In the example of FIG. 3, blood flows through the lateral hole 62 and fills th e chamber 28a when the sleeve valve is closed. This provides a visual indication to the user th

at the vascular puncture has been successfully performed.

FIG. 5 shows the needle assembly 10 or 60 of the present invention connected to the multi-sa mple holder 19. FIG. A puncture needle 14 extending from a front end 24 is inserted into the patient P during a vessel puncture procedure. At this time the needle assembly is at steady re st and the sleeve valve is in fluid tight contact over the lateral bore 48 . At steady venous pres sure, blood from the patient is forced into the puncture needle 14 and into the chamber 28 th rough the front end 24 of the housing. Incoming blood expels air that was originally in chamb er 28 through porous plug 52 . Plug 52 is air permeable, blood impermeableis sex. Air exits th e open end of the second puncture needle. Blood flows through the first puncture needle 14 a nd fills the chamber 28 through the internal opening 30 shown in FIG. 2 or the transverse hol e 62 shown in FIG. At least front end 24 or a portion thereof, such as wall 34, is translucent s o that a user of the needle assembly can perceive if blood has entered chamber 28. FIG. If th e user sees blood in the chamber, it is an indication that a vascular puncture has been perfor med. Conversely, if the puncture needle 14 is inserted into the patient and no blood is visible within the chamber 28, this indicates an inadequate vessel puncture. This feature eliminates t he need for the user to attach the evacuated blood collection container to the second punctur e needle 15 in the holder 19 until viewing the vascular puncture indication. Since the blood im permeable plug 52 and the sleeve valve 41 prevent blood flow from the second needle, no blo od will flow from the second needle. When the user is satisfied with the vessel puncture, evac uated blood collection container 16 is slid into holder 19 and second puncture needle 15 penet rates penetrable stopper 21 . This combination is shown in FIG.

FIG. 6 shows the evacuated blood collection container 16 fully inserted into the holder 19, the second puncture needle 15 penetrating the penetrable stopper 21 and the tip entering the blo od collection container ready to supply blood. . A resilient sleeve valve 41 slides along the out er surface of the puncture needle and is compressed against the trailing end 25 when the pun cture needle 15 penetrates the penetrable stopper 21 . An enlarged view of the compressed sl eeve valve 41 is shown in FIG. As shown, the thin walled portion 44 is compressed in an accor dion fashion within the bore 40 and pressed against the rear end of the needle assembly. The thick wall portion 42 is not compressed or folded against it, but simply slides toward the rear end portion 25 . Due to the sliding of the thick wall portion 42, the cavity 46 is above both lat eral holes 48 and 50, and neither hole becomes a liquid impermeable block. As a result, the bl ood in the second puncture needle 15, which was blocked by the blood-impermeable plug 52, is supplied around this obstacle. That is, blood flows through lateral hole 48, cavity 46, and by passes plug 52, as shown in FIG. Blood flows continuously from the cavity through the lateral hole 50 and back into the lumen 51 of the second puncture needle. Blood that exits the open end of the second puncture needle is collected in a blood collection container.

Once blood fills the blood collection container, the filled container is removed from holder 19 w hile needle 14 remains punctured within the patient's blood vessel. Removal of the blood colle ction container simultaneously removes the compressive force against the slidable sleeve 41 a

nd the sleeve slides outward back to the position shown in FIG. This position is the valve close d position and prevents blood from flowing out of the second puncture needle 15 . This sleeve valve movement automatically prevents blood from flowing out of the second puncture needl e. In particular, no blood leakage occurs between exchanges of the evacuated blood collection container. Blood therefore flows from the patient's vessel into chamber 28, the next blood coll ection container is inserted into the holder, and the inward compression movement of the slid able valve is repeated as described above. Once the multi-sample blood collection is complet e, the puncture needle 14 is removed from the patient and the entire needle assembly discard ed.

Various modifications are possible for the present invention. The embodiment shown in Figure s 8 and 9 prevents blood from flowing out of the puncture needle during valve closure and allo ws air to pass through for evacuation purposes. In the embodiment of FIG. 8, the multiple sa mple needle assembly 70 is largely similar to the previous embodiment, except that the pierci ng needle 71 pierces the penetrable stopper 72 of the blood collection container and leaves on ly one side hole 74. prepare. The location of this lateral hole at the puncture needle 71 is signi ficantly away from the rear end 75 of the needle assembly and close to the open end 76 of th e puncture needle. A gas-permeable, liquid-impermeable, porous plug 78 is positioned within the lumen 79 between the transverse bore 74 and the open end 76 . Sleeve valve 80 is subst antially similar to sleeve valve 41 previously described, but is somewhat longer to contact cro ssbore 74 in a fluid impermeable manner. Further, sleeve valve 80 does not require the cavity noted for sleeve valve 41 described above. Furthermore, although the sleeve valve 80 is provi ded with the thick wall portion 81 and the thin wall portion 82 in the illustrated example, this i s a suitable example, and the thickness of the sleeve may be uniform throughout.

When the sleeve 80 is in the closed position of FIG. 8, air in the needle assembly flows throug h the air permeable plug 78 and blood does not pass through the plug. Furthermore, the sleev e 80 effectively closes the lateral hole 74 so that no blood escapes. FIG. 9 shows the compres sed position of sleeve valve 80 and is similar to FIG. Needle 71 penetratesA puncture is made in the possible stopper 72 and the lateral hole 74 is in the blood collection container. The sleev e valve 80 is slid and compressed toward the rear end 75 of the needle assembly. Since the la teral hole 74 is exposed, blood in the lumen 79 flows through the lateral hole 74 directly into t he blood collection container. As shown in FIG. 9, blood bypasses plug 78 and diverts to latera l hole 74 and does not flow out the open end of the puncture needle. Once the blood collectio n container is full, the container is removed from the holder and the sleeve valve 80 is slid ba ck to the position shown in FIG. This prevents blood from flowing out of the puncture needle b etween exchanges of the blood collection container.

As noted above, a multi-sample needle assembly according to the present invention controls t he flow of liquids, such as blood, therethrough. To prevent blood from leaking out of the asse mbly during exchange of blood collection containers between multiple sample collection proce sses. Additionally, the present invention provides a visual indication to the user so that they c

an immediately recognize when the vessel has been punctured for blood collection. The above characteristics contribute to the efficient use of the needle assembly for multiple sample collec tion.

Brief description of the drawing open —

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of the multiple sample needle assembly, evacuated vessel holder and evacuated blood collection vessel of the present invention used to collect blood from a pat ient; FIG. FIG. 3 is an enlarged cross-sectional view of the multi-sample needle assembly take n along line 2-2, FIG. 3 is an enlarged cross-sectional view showing another embodiment of th e multi-sample needle assembly, and FIG. FIG. 5 is an enlarged cross-sectional view showing the valve portion in a normally closed position for blocking the blood flow of the patient; FIG. FIG. 7 is an enlarged cross-sectional view showing the valve in the open position and blood flo wing through the puncture needle; FIG. 8 is another embodiment of the present invention sho wn in FIG. 4 and FIG. 9 is a sectional view showing a similar valve closed position, and FIG. 9 is a sectional view showing the valve open position of the embodiment of FIG.

Reference Signs List 10 Multi-sample needle assembly

12 Housings

14, 15 Puncture needle

16 Vacuum blood collection container

19 Container holder 24

Front end

25 Rear end

28 Chamber

41 Sleeve valve

42 Thick wall portion

44 Thin Wall portion

46... Cavities

48, 50... Lateral hole

52... Porous plug

Copyright JPO and INPIT (P0200)

⑲ 日本国特許庁（JP）　　⑪ 特許出願公開

⑫ 公開特許公報（A）　　昭58—25146

⑤1Int. Cl.³　識別記号　庁内整理番号　⑬公開　昭和58年(1983) 2月15日
A 61 B 5/14　6530—4C

発明の数　3
審査請求　未請求

（全 9 頁）

⑤4血管穿刺表示器付き多サンプル針組立体

⑳特　願　昭57—126629
㉒出　願　昭57(1982) 7月20日
優先権主張　㉜1981年7月20日㉝米国(US)
㉛284894

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

明　細　書

1.〔発明の名称〕

血管穿刺表示器付き多サンプル針組立体

2.〔特許請求の範囲〕

1. 患者から血液を収集する時に血管穿刺を認識し得る多サンプル針組立体であつて、前端部と後端部と内部の室とを有し少なくとも室を囲んで半透明として使用者が室を認識し得るようにしたハウジングと、上記室に流体連通し上記前端部から外方に延長して患者内に挿入可能の第1の穿刺針と、上記室に流体連通して上記後端部から外方に延長し血液サンプル収集用の真空容器内に貫通させる第2の穿刺針と、第2の穿刺針の上記外方延長部の側部に形成し第2の穿刺針の内腔に連通させた2個の互に離間した横孔と、第2の穿刺針の内腔内に上記両横孔間のスペースの位置とした空気透過性血液不透過性の多孔性プラグと、第2の穿刺針の外側に取付け閉位置では上記両横孔の少なくとも一方を覆つて血液が第2の穿刺針から流出するのを防ぐ弾性の滑動可能の弁とを備え、上記弁は開位置に滑動可能とし、開位置では血液が上記室に近い横孔から流出して他方の横孔から第2の穿刺針に戻ることを可能にする手段を有し、これによつて血液が第2の穿刺針から収集されることを特徴とする血管穿刺表示器付きサンプル針組立体。

2. 前記弁は気密に滑動可能に第2の穿刺針上に接触するスリーブである特許請求の範囲第1項記載の組立体。

3. 前記スリーブは力を受けない条件で前記室に近い横孔を気密接触によつて覆う特許請求の範囲第2項記載の組立体。

4. 前記スリーブには第2の穿刺針の外径に嵌合して少なくとも一方の横孔を気密接触によつて覆う内径部分を含む特許請求の範囲第2項記載の組立体。

5. 前記血液流を可能にする手段には前記スリーブ内に形成して前記嵌合直径より大きな直径を有するキヤビテイーを含み、上記キヤビテイーの長さは前記スリーブが前記後端部に向けて内方に

滑動した時に前記両横孔を覆うようにし、これによつて血液は上記室に近い横孔から上記キャビテイを経て他方の横孔から戻つて前記プラグをバイパスして第2の穿刺針を通る連続流と血液収集とを行なう特許請求の範囲第4項記載の組立体。

6. 前記スリーブのキャビテイを含まない一部がスリーブの内方滑動間前記後端部に圧縮可能である特許請求の範囲第5項記載の組立体。

7. 前記スリーブの圧縮可能部分はスリーブのキャビテイーを含む部分より薄い周壁である特許請求の範囲第6項記載の組立体。

8. 前記スリーブはエラストマー材料製である特許請求の範囲第2項又は第5項記載の組立体。

9. 前記第1，第2の穿刺針を前記室内で結合し、両穿刺針は上記室に共通横孔によつて連通する特許請求の範囲第1項記載の組立体。

10. 前記多孔性プラグは焼結ポリエチレン製である特許請求の範囲第1項記載の組立体。

11. 前記ハウジングには真空容器用のホルダーを連結する手段を含む特許請求の範囲第1項記載の組立体。

12. 前記ハウジングに連結する真空容器用のホルダを備える特許請求の範囲第11項記載の組立体。

13. 供給源から液サンプルを収集するための多サンプル針組立体であつて、内部に室を有するハウジングと、上記室に流体連通し液供給源内に挿入する第1の穿刺針と液を室を通つて収集装置に供給する第2の穿刺針とを含む穿刺針装置と、第2の穿刺針の内腔内に取付け第2の穿刺針から液を通さずガスを通す装置と、上記液流を通さない装置を離れて液を分流することによつて第2の穿刺針から液を作動的に収集する装置とを備えることを特徴とする多サンプル針組立体。

14. 前記液を作動的に収集する装置には前記第2の穿刺針の液流防止装置と室との間で側面を通す横孔と、第2の穿刺針に取付け閉位置では上記横孔を覆つて液が第2の穿刺針から流出するのを防ぐ弾性の可動の弁とを含み、上記弁が開位置に動いた時は上記横孔を開放して液が横孔を通つて流出して収集される特許請求の範囲第13項記載の組立体。

15. 前記第1，第2の穿刺針を一体形成して1本の穿刺針装置とし、上記室に連通した共通横孔を設ける特許請求の範囲第13項記載の組立体。

16. 患者から血液を収集する時に血管穿刺を認識し得る多サンプル針組立体であつて、前端部と後端部と内部の室とを有し組立体使用者が室を見得るようにした半透明ハウジングと、上記室に流体連通し上記前端部から外方に延長して患者内に挿入可能の第1の穿刺針と、上記室に流体連通して上記後端部から外方に延長し血液サンプル収集用の真空容器内に貫通させる第2の穿刺針と、第2の穿刺針の上記外方延長部の側部に形成し第2の穿刺針の内腔に連通させた2個の互に離間した横孔と、第2の穿刺針の内腔内に上記両横孔間のスペースの位置とした空気透過性血液不透過性の多孔性のプラグと、第2の穿刺針の外面に取付け定常位置では上記両横孔の少なくとも一方を気密接触で覆つて第2の穿刺針から血液の流出を防ぐ弾性滑動可能エラストマー製のスリーブとを備え、上記スリーブの内径を第2の穿刺針の外径に嵌合として上記気密の接触を生じさせ、上記スリーブに上記嵌合内径より大きな内径のキャビテイを設け、上記キャビテイは両横孔を覆い得る長さとし、上記スリーブは後端部に向けて開位置に滑動して上記キャビテイーが両横孔を覆い血液は上記プラグをバイパスとして室に近い横孔から流出してキャビテイーに入り他方の横孔を通つて戻り第2の穿刺針を通る連続流を生じて収集を可能にし、上記スリーブのキャビテイーを含まない部分を第2の穿刺針からの血液収集間スリーブが滑動した時に後端部に向けて圧縮可能とすることを特徴とする血管穿刺表示器付き多サンプル針組立体。

3.〔発明の詳細な説明〕

本発明は患者等から液を収集する針組立体に関し、特に患者からの血液の複数のサンプルを複数の真空管内に収集し、管を交換する際に血液の漏洩がなく、針組立体が患者の血管内に入つたことを表示する装置を有する針組立体に関する。

患者から液例えば血液の複数のサンプルを収集する場合に1回の手順で行なうことは現在では標準の手法である。針が患者の血管内に挿入されれば、次に真空血液収集管をホルダーに挿入する。ホルダーは針に接続し、真空管を収容する構成である。各充填した管をホルダーから取外す時に針は患者の血管内に挿入された状態を保つ。充填した管を取外し次のサンプル収集のための次の真空管を挿入する間にホルダーから血液が流出するのを防ぐ各種の弁が現用されている。内側針を囲むエラストマーのスリーブが通常はこの弁として使用される。この多サンプル針組立体用の弁は所要の機能を有するが、この装置の改良のための各種方途が探求されている。

更に、静脈内針が患者の血管に入つた時に多サンプル針組立体の使用者が認識し得る機構を設けることが望ましい。患者から血液を収集する時に血管の位置を探すことの困難又は他の理由によつて収集装置内の血流が最小であることが多い。この場合、血管内挿入が行なわれ、血液が針組立体内に流入することを急速に定め得ることが最も望ましい。この決定が行なわれ、血管内穿刺が行なわれた時に、真空血液収集容器を多サンプル収集の周知の技法によつて1回の収集手順間に収集装置内に挿入する。

血管穿刺過程間に生ずる問題として、空気のポケットがある。これは多サンプル血液収集に使用する各種針組立体に見られる。血管穿刺を行ない、針装置の他端に真空血液収集容器がまだ取付けてない時は、エアのポケットのため血液は針組立体内に流れないことがある。即ち、ポケットは定常大気圧下では針組立体内に残る。それ故、血管穿刺が行なわれていても、静脈圧では血液は血管内針を通つて収集装置内に流入しないことがあり、真空血液収容容器が取付けられれば真空力は針組立体内に十分な吸引力を作用する。米国特許第4.207.870号での発明者の認識では、このエアブロックの問題によつて、血液は使用者の見得る点まで血液内針を流れることを防止される。この特許の装置では多孔性排気装置をバイパス弁に組合せ、針組立体内のエアが血液収集手順の最初の段階で排気装置を通つて流出する。この排気装置は血液の流出を防ぐ。

1980年6月18日出願のカウフマンの米国特許願第160.781号、"血管穿刺表示器付き多サンプル針"には異なる型式の針装置を示し、作動弁内に空気透過血液不透過多孔性プラグを使用する。

米国特許第4.207.870号及びカウフマンの発明は一方弁と空気排除装置との組合せとして好適であるが更に改良の余地がある。本発明はこの装置を改良して空気を針組立体から排出し、血液はエアの排出によつて直に針組立体内に流入可能とするようにする。

本発明による多サンプル針組立体は液供給源から液サンプルを収集するために有効である。この針組立体には室を有するハウジングと、室に連通した穿刺針装置とを有する。この穿刺針装置には液供給源内に挿入する第1の穿刺針と、液を室を経て収集装置に供給する第2の穿刺針とを含む。第2の穿刺針の内腔内に、第2の穿刺針内を液を通さずガスを通す装置を設ける。針組立体に液流防止装置を分流して液を第2の穿刺針から作動的に収集する装置を設ける。

本発明の好適な実施例によつて、ハウジングに前端部と、後端部と、内部の室とを設ける。ハウジングは少なくとも室を囲んで半透明とし、組立体使用者が室を見得るようにする。第1の穿刺針は前端部から外方に延長して患者内に挿入可能とする。第2の穿刺針は後端部から外方に延長して血液サンプル収集用の真空血液収集容器に貫入可能とする。第2の穿刺針の外方延長部の側面に2個の互に離間した横孔を形成し、横孔は第2の穿刺針の内腔に連通させる。第2の穿刺針の内腔の両横孔間のスペースに空気透過性液不透過性の多孔性プラグを挿入する。第2の穿刺針の外面に弾性の滑動可能の弁を設け、弁の閉位置とした定常位置で一方の横孔を覆つて血液が第2の穿刺針から流出するのを防ぐ。この弁は開位置に滑動可能とし、血液が室に近い横孔から流出して第2の

横孔を通つて戻る手段を設け、血液が第２の穿刺針から収集される。

構造的に本発明の多サンプル針組立体は同じ目的の装置とは著しく異なる。特に本発明は液流防止装置を直接第２の穿刺針内に取付ける。第２の穿刺針に１個以上の横孔を設けて、血液等の液は液不透過性プラグをバイパスして流れる。好適な実施例によつて、滑動可能のスリーブ弁を横孔に組合せ、液不透過プラグをバイパスする液流を制御する。既知の装置では液不透過性部材を室内に置く。本発明の構成によつて室内には弁又は液不透過性プラグがない。このため、使用者は血管穿刺手順間に室に流入する血液を容易に見られる。第２の穿刺針内にガス透過性プラグ部材を使用することによつて、血液が室に流入する時に空気は組立体内から排出され、ガス透過性部材がない時のエアブロックの問題は生じない。特に有利な点は、多サンプル血液収集手順間、本発明は血液収集容器交換間に血液の漏洩を防ぎ、この間針組立体は患者に挿入された状態にある。本発明は自動血流制御を行ない、充填した血液収集容器を組立体から外した後に室からの血液漏洩を防ぐ。

本発明を例示とした実施例並びに図面について説明する。以下各種の実施例についての説明は本発明の原理についての例示であり、発明を限定するものではない。

第１図は本発明の好適な実施例による多サンプル針組立体１０を示す。針組立体１０の基本的外側部材にはハウジング１２と、患者内に挿入する第１の穿刺針１４と、ハウジング１２の反対側端部の第２の穿刺針１５とを含み、第２の穿刺針は真空容器１６に穿刺して血液サンプルを収集する。ハウジング１２は第２の穿刺針１５に近接したねじ部１８を有し、容器ホルダー１９の前端の内ねじ２０をねじこんでホルダー１９を取付ける。真空容器１６をホルダー１９内に滑動させ、第２の穿刺針１５は容器１６の前端の貫通可能ストッパ２１を貫通する。上述の型式の多サンプル血液収集装置概要は周知である。

第２，４図は針組立体１０の詳細を示す。ハウジング１２は前端部２４と後端部２５とを有し、好適な例では両端部を別部材として製造し、部品交換を容易にすると共にハウジング内に室を形成するのを可能にする。前端部２４は好適な例では円筒形とし大きな穴部が内方に本体の一部内を延長する。この穴部は組立後にハウジング１２内の室２８となる。後端部内に小さな穴部２９を形成しほゞ穿刺針１４を嵌合する寸法とする。穿刺針１４は穴部２９内に挿入し、内方端は僅に室２８内に入り、室に連通する。穿刺針１４の尖端は端部２５から外方に突出する。穿刺針の位置ぎめ後接着剤等によつて固着できる。

ハウジングの前端部２４に多数の表手方向のリブ３１を形成して外方に延長する穿刺針を囲む。図示しない針シールドが通常穿刺針の外方延長部を囲み、同様に内部リブを有する。針シールドと針組立体との間の係合リブによつて使用者は針組立体を管ホルダーに対する収納取出が容易になる。室１８を囲む前端部の一部３４は平滑で好適な例で半透明又は透明とし、使用者がハウジング内を見得るようにする。多くの場合は前端部全部、できれば後端部も半透明又は透明材料製とし、製造を容易にし、使用材料の種類を最小にする。半透明剛性合成樹脂が最も好適な材料である。使用者が室内を見るための各種のシールした窓、ポート等とすることもできる。この種窓又はポートをシールし、針が血管内に入つた時に室２８に入る血液が漏洩しないようにする。前端部２４に環状フランジ３５を設けてハウジングの２部分を組立に際して接合する面を形成する。所要の固着手段、例えば接着剤等を使用してハウジングの両部分を固着する。

後端部２５には短い突出部３６を設け、ほゞ円筒形とする。この突出部はこの実施例では第２の穿刺針１５の内方端の支持の補強部とする。後端部の反対側端部には外ねじ１８を前述の通りに形成して管ホルダに対する連結装置とする。穴部38がハウジングの後端部内を延長する。この穴部の寸法は第２の穿刺針１５の直径を受ける寸法とし、第２の穿刺針の内方端３９は室２８内に突出し、

前後端部を結合した時に室２８に液連通する。第２の穿刺針１５は穴部３８内に接着剤等によつて固着する。大きな穴部４０が後端部２５内に短い寸法だけ延長し、穴部３８に連通する。第２の穿刺針１５の外方延長部を囲んでスリーブ弁４１を滑動可能とする。スリーブ弁４１は厚壁部４２と薄壁部４２と薄壁部の端部のフランジ４５とを有する。このスリーブ弁はフランジ４５と薄壁部とが穴部４０内に滑動して入り、フランジ４５がハウジングの後端部の内壁に接触する位置とする。更に厚壁部４２にキヤビテイ部４６を設ける。スリーブ弁４１の内径はキヤビテイ部を除いて第２の穿刺針１５の外径に嵌合させる。キヤビテイ46の内径はスリーブの内径より大とし、穿刺針の外径よりも大とする。両内径の機能上の差は後述の使用説明で明らかにする。

第４図に示す通り、第２の穿刺針１５の外方延長部側壁に２個の孔48，50を設ける。弾性スリーブ弁４１の定常条件では孔48，50を覆う。両孔共にスリーブの緊密な嵌合の内径で覆うこともできるがハウジング内の室に近い孔４８のみを覆うのが好適である。スリーブ弁４１は定常位置で孔４８上に気密接触を行なう。同時にキヤビテイ４６は孔５０を囲み、弁は孔５０に対して気密接触でない。

第２の穿刺針１５の内腔５１内にガス透過性液不透過性の多孔性部材５２を置く。好適な例で、この部材は空気透過性血液不透過性の多孔性プラグとする。プラグ５２は孔48，50間のスペースに置く。それ故、第２の穿刺針１５を通る血液は多孔性プラグ５２の血液不透過特性によつて妨害され、第２の穿刺針の尖端から血液が流出しない。多孔性プラグ５２の空気透過特性によつて室２８内及び第２の穿刺針内のエアは自由に流れて第２の穿刺針の尖端から流出する。

ハウジングの後端部と前端部の接合を容易にするために、環状フランジ５４をハウジングの後端部に設ける。ハウジング内の所要の流体流を確実にするために、エラストマーのリング５５を図示の例ではフランジ35，54間に介挿する。前端部と後端部との組合せに際してフランジ35，54を所要の固着手段、例えば接着剤等によつて固着する。

スリーブ弁４１は薄壁部４４が後述する通り弁を滑動させた時に後端部２５に向けて圧縮可能とする。スリーブ弁４１の厚壁部はキヤビテイ-46を有し、薄壁部のように軸線方向には圧縮されない。更にキヤビテイ－４６はスリーブ弁を後端部に向けて内方に滑動した時に両孔48，50を共に連通する長さとする。スリーブ弁を製造するには各種の材料を使用できるがエラストマー材料が好適である。

多孔性プラグ５２に関しては、多孔性材料、例えば焼結ポリエチレンの平均孔径約１０ミクロンの材料とする。

本発明の作動説明の前に穿刺針の他の実施例を第３図に示す。図示の例では多サンプル針組立体６０は第２図に示したと同様の素子を有し、同様の特性を有するため、同じ符号に添字αを付して同様の素子を示す。第２図の実施例では前後別の穿刺針を使用したが第３図の例では１本の、好適な例では一体の穿刺針６１をハウジング１２α内を貫通させる。第１の穿刺針部分14αは前端部24αから外方に延長させる。第２の穿刺針部15αは後端部25αから外方に延長させる。共通流体出口孔６２は穿刺針６１の中央部に形成して室28αに連通させる。第３図の例では血液は横孔６２を通つてスリーブ弁が閉鎖した時に室28α内に充満する。これによつて使用者は血管穿刺が有効に行なわれたことを知る目視表示となる。

第５図は本発明針組立体１０又は６０が多サンプルホルダー１９に接続された状態を示す。前端部２４から延長する穿刺針１４が血管穿刺手順間に患者P内に挿入される。この時に針組立体は定常静止状態にあり、スリーブ弁は横孔４８上に液不通過接触となる。定常静脈圧では患者からの血液は穿刺針１４内に押出されてハウジングの前端部２４を経て室２８に入る。流入血液は最初に室２８内にあつた空気を多孔性プラグ５２を通つて排出する。プラグ５２は空気透過性、血液不透過

性である。空気は第２の穿刺針の開放端から出る。血液は第１の穿刺針１４を通つて流れ第２図に示す内部開口３０又は第３図に示す横孔６２を経て室２８に充満する。少なくとも前端部２４又はその一部例えば壁部３４が半透明であるため、針組立体の使用者は血液が室２８に流入すれば認識できる。使用者が室内の血液を見れば、血管穿刺が行なわれた表示となる。反対に、穿刺針１４を患者内に穿刺しても室２８内の血液が見えなければ、血管穿刺が不十分であることを示す。この特性によつて、使用者は血管穿刺の表示を見るまではホルダー１９内の第２の穿刺針１５に真空血液収集容器を取付ける必要はない。血液不透過プラグ52とスリーブ弁４１とが第２の穿刺針からの血液流を防ぐため、第２の穿刺針から血液が流れることはない。使用者が血管穿刺に満足すれば、真空血液収集容器１６をホルダー１９内に滑動させて第２の穿刺針１５は貫通可能ストツパ２１を貫通する。この組合せを第６図に示す。

第６図は真空血液収集容器１６をホルダー１９内に完全に挿入し、第２の穿刺針１５は貫通可能ストツパ２１を貫通して先端部が血液収集容器内に入り血液を供給する状態にある。穿刺針１５が貫通可能ストツパ２１を貫通する時に弾性のスリーブ弁４１は穿刺針の外面に沿つて滑動し、後端部２５に圧縮される。圧縮されたスリーブ弁４１の拡大図を第７図に示す。図示の通り、薄壁部44は穴部４０内でアコーデイオン状に圧縮されて針組立体の後端部に押圧される。厚壁部４２はこれに対して圧縮又は畳まれず、単に後端部２５に向けて滑動する。厚壁部４２の滑動によつてキヤビテイー４６は両横孔４８，５０上となり、何れの孔も液を通さないブロックとならない。この結果、第２の穿刺針１５内の血液は血液不透過性プラグ５２によつてブロックされていたが、この障害物を廻つて供給される。即ち、第７図に示す通り、血液は横孔４８，キヤビテイー４６を通つて流れ、プラグ５２をバイパスする。血液はキヤビテイーから横孔５０を経て第２の穿刺針の内腔５１に戻つて連続流となる。第２の穿刺針の開放端を流出した血液は血液収集容器内に収集される。

血液が血液収集容器内に充満すれば、充満した容器はホルダー１９から取外し、この間穿刺針14は患者の血管内に穿刺された状態を保つ。血液収集容器を取外せば同時に滑動可能スリーブ４１に対する圧縮力もなくなり、スリーブは外方に滑動して第４図の位置に戻る。この位置は弁閉鎖位置であり、第２の穿刺針１５からの血液流出を防ぐ。このスリーブ弁の動きは自動的に血液が第２の穿刺針から流出するのを防ぐ。特に真空血液収集容器の交換間は血液の漏洩が生ずることはない。それ故、血液は患者の血管から室２８に流れ、次の血液収集容器がホルダーに挿入され、滑動可能の弁の内方圧縮運動が上述の通りに繰返される。多サンプル血液の収集が終れば、穿刺針１４を患者から取外し、全部の針組立体を廃棄する。

本発明は各種の変型が可能である。第８，９図に示す実施例は弁閉鎖の間は穿刺針からの血液の流出を防ぎ、空気は通過して排気目的を達する。第８図の実施例では多サンプル針組立体７０は大部分前の実施例と同様であるが、穿刺針７１は血液収集容器の貫通可能ストツパ７２を穿刺し、１個のみの横孔７４を設ける。この横孔の穿刺針71での位置は針組立体の後端部７５から著しく離れ、穿刺針の開放端７６に近い。ガス透過性液不透過性の多孔性プラグ７８を内腔７９内の横孔７４と開放端７６との間とする。スリーブ弁８０は前述のスリーブ弁４１とほゞ同様であるがいくらか長くして横孔７４を液不通過に接触する。更にスリーブ弁８０には前述のスリーブ弁４１に記したキヤビテイーを必要としない。更に、スリーブ弁80は図示の例では厚壁部８１と薄壁部８２とを設けたが、好適な例示であり、スリーブの厚さは全体を均等とすることもできる。

スリーブ８０が第８図の位置即ち閉位置にある時は針組立体内のエアは空気透過性プラグ７８を通つて流れ、血液はプラグを通らない。更に、スリーブ８０が有効に横孔７４を閉鎖するため、血液は流出しない。第９図はスリーブ弁８０の圧縮位置を示し、第７図と同様である。針７１は貫通

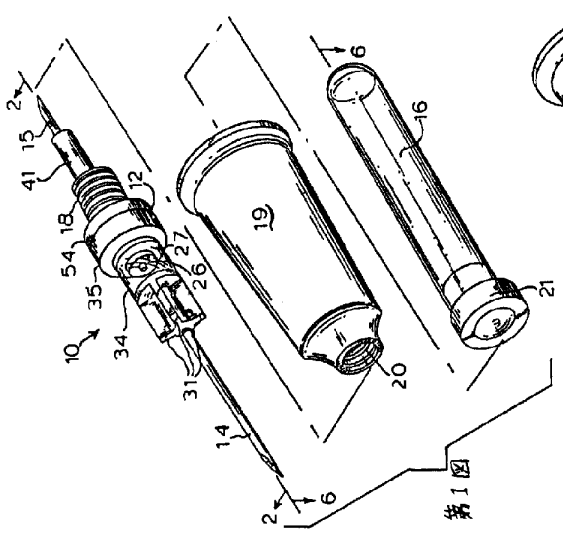
可能ストッパ７２内に穿刺し、横孔７４は血液収集容器内にある。スリーブ弁８０は滑動して針組立体の後端部７５に向けて圧縮される。横孔７４が露出したため、内腔７９内の血液は横孔７４を通つて直接血液収集容器内に流出する。第９図に示す通り、血液はプラグ７８を通らずに分流して横孔７４に流れ、穿刺針の開放端からは流れない。血液収集容器が充満すれば容器はホルダーから取外し、スリーブ弁８０は滑動して第８図に示す位置に戻る。これによつて血液収集容器の交換間に血液が穿刺針から流出するのを防ぐ。

上述した通り、本発明による多サンプル針組立体は中を通る血液等の液の流れを制御する。多サンプル収集過程間の血液収集容器の交換の間に血液が組立体外に漏洩するのを防ぐ。更に、本発明は使用者に対する目視表示を行ない、血液収集のために血管内に穿刺された時に直に認識し得る。上述の特性は針組立体を多サンプル収集用として有効に使用するために貢献する。

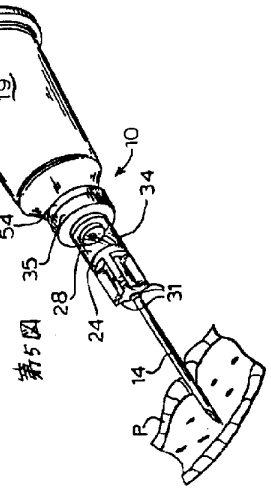
4.〔図面の簡単な説明〕

第１図は本発明の多サンプル針組立体と真空容器のホルダーと真空血液収集容器とを患者からの血液収集に使用する斜視図、第２図は第１図の２－２線に沿う多サンプル針組立体の拡大断面図、第３図は多サンプル針組立体の他の実施例を示す拡大断面図、第４図は第２図又は第３図の実施例の血流を遮断する定常閉位置とした弁部分を示す拡大断面図、第５図はホルダを連結した針組立体を患者に穿刺した斜視図、第６図は第１図の６－６線に沿い各部の使用間の組立状態を示す断面図、第７図は弁が開位置であり血液が穿刺針を流れる拡大断面図、第８図は本発明の別の実施例の第４図と同様の弁閉鎖位置を示す断面図、第９図は第８図の実施例の弁開位置を示す断面図である。

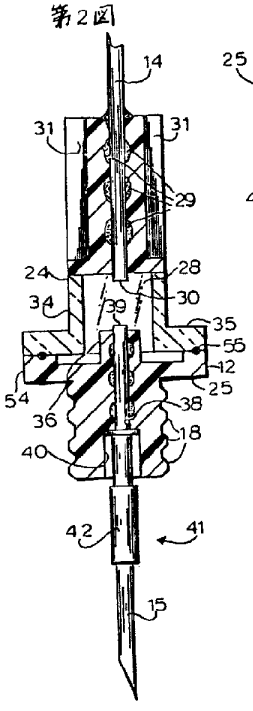
１０ … 多サンプル針組立体
１２ … ハウジング
１４，１５ … 穿刺針
１６ … 真空血液収集容器
１９ … 容器ホルダー
２４ … 前端部
２５ … 後端部
２８ … 室
４１ … スリーブ弁
４２ … 厚壁部
４４ … 薄壁部
４６ … キャビティー
４８，５０ … 横孔
５２ … 多孔性プラグ



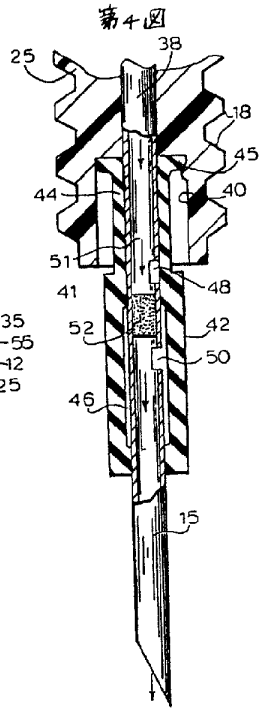
第1図



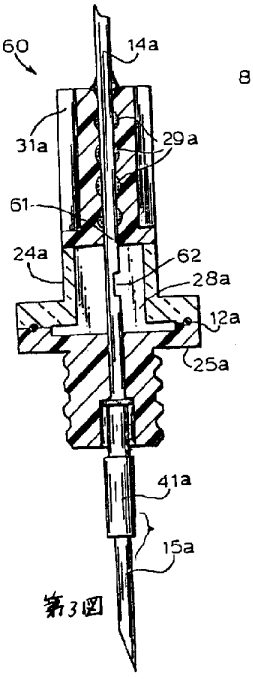
第5図



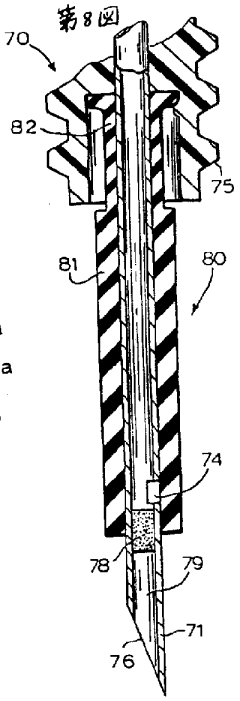
第2図



第4図

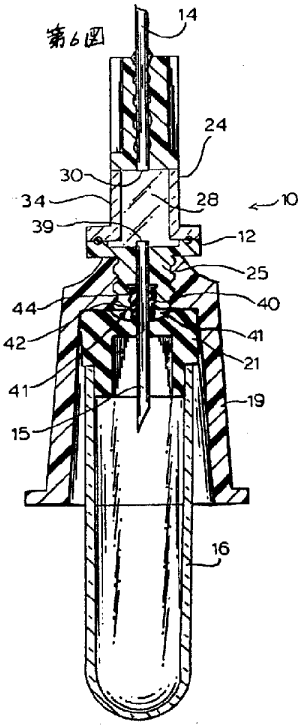


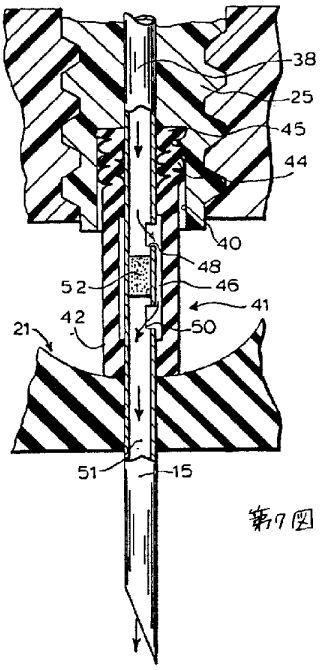
第3図



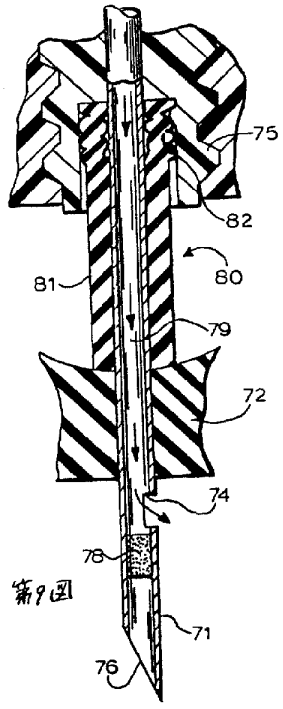
第8図

第6図


14
24
30
34
28
10
39
12
25
44
40
42
41
21
41
19
15
16


38
25
45
44
40
48
52
46
41
42
50
21
51
15

第7図


75
82
80
81
79
72
74
78
71
76

第9図

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Japanese Patent Application Laid-Open No. 02-224742

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

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

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] JP-A-2-224742
(43) [Published date] 1990 (1990) September 6
(54) [Title of invention] Improved blood sampling device
(51) [International patent classification 5th edition]
A61B 5/14 300 H
A61M 1/02 370
[FI]
A61B 5/14 300 H
A61M 1/02 370
[Request for examination] Unclaimed
[Total number of pages] 10
(21) [Application number] Japanese Patent Application Hei 1-338039
(22) [Filing date] December 26, 1989
(31)) [Priority claim number] 292490
(32) [Priority date] December 30, 1988
(33) [Priority claim country] United States of America (US)

(71) [Applicant]
[Identification number] 999999999
[Name] Spacelabs Inc.
(72) [Inventor]
[Name] John A. R. Cater
(74) [Agent]
[Name] Minoru Nakamura (7 others)

wrap up close —

(57) [Abstract] Since this gazette is application data before electronic filing, abstract data is n ot recorded.

The scope of the claims open —

Claims:
(1) In a coupling used by medical personnel in drawing and storing blood from a patient to ins ert the needle of the needle assembly into the patient to draw the blood sample, the coupling comprises first
and an elongated hollow shaft having a second end; and a
first portion of the shaft fixedly connecting the needle assembly to the shaft so that blood dra wn by the needle can be delivered to the shaft. and an adapter sleeve attached to a second e nd of said shaft for
connecting said shaft to a blood storage means,
for communicating blood received by said shaft; an opening connected to said shaft between an adapter sleeve and said connecting member and communicating with said connecting mem ber.
(2) The coupling of claim 1, further comprising means for blocking blood flow and exhausting air trapped within said shaft.
(3) intermediate the opening and the adapter sleeve, wherein the means for evacuating air re stricts blood flow from the shaft to the adapter sleeve while permitting air flow from the shaft to the adapter sleeve; 3. A coupling according to claim 2, comprising flow control means locat ed within said shaft of.
(4) The coupling of Claim 3, wherein said flow control means comprises a microporous hydrop hobic plug.
(5) The coupling of claim (4) further comprising needle guide means for guiding a needle coup

led to blood reservoir means through said plug and for coaxially fitting said needle with said s haft.

(6) The cup according to (2), further comprising blood storage means for temporarily storing a portion of blood drawn from a patient, said blood storage means being sealably connectable to said opening. ring.

(7) The coupling of claim (6), wherein said blood storage means comprises a syringe.

(8) Further comprising valve means fixedly positioned intermediate said opening and said shaf t for enabling selective communication between said shaft and said opening. coupling.

(9) The coupling of claim 2, further comprising means for sealing said opening.

(10) In a blood collection device used by medical personnel to withdraw and store a blood sa mple from a patient, needle means adapted to be inserted into the patient to withdraw the blo od

sample

; coupling means for connecting the means to the blood storage means,

said coupling means having first and second openings;and adapted to direct blood from said n eedle means to said first and second openings.

(11) The coupling of claim 10, further comprising means for blocking blood flow to exhaust air trapped within said coupling means.

(12) the means for evacuating air restricts blood flow from the needle means to the first openi ng while permitting air flow from the needle means to the first opening; 12. The blood collecti on device of claim 11, comprising flow control means positioned within said coupling means b etween said first and second openings.

(13) The blood collection device of Claim 12, wherein said flow control means comprises a mic roporous hydrophobic plug.

(14) The blood collection device of (13) further comprising needle guide means for guiding a n eedle coupled to blood reservoir means through said plug and coaxial with said coupling mean s.

(15) The method according to (14), further comprising blood storage means for temporarily st oring a portion of the blood drawn from the patient, said blood storage means being sealingly connectable to said second opening. A blood collection device as described.

(16) The blood collection device of (12), wherein said blood storage means comprises a syring e.

(17) The blood collection device of (12) further comprising means for sealing said second ope ning.

(18) further comprising valve means disposed intermediate said needle means and said secon d opening for enabling selective communication between said needle means and said second opening. The blood sampling device according to (12).

(19) said needle means is an elongate needle for insertion into a patient and leading from sai d needle to said coupling means;

13. The blood collection device of claim 12, comprising: a tube, said tube being generally tran sparent so that medical personnel can see blood being directed therethrough.

(20) A blood collection device for use by medical personnel in drawing and collecting blood sa mples from a patient, comprising needle means for drawing blood from a patient and coupling means for selectively connecting blood reservoir means to

said

needle means. wherein

said coupling means is secured to said needle means, said coupling means being positioned b etween said first opening and said needle means and a first opening for receiving blood storag e means; a hollow shaft, said coupling means further comprising a second opening for receivi ng blood storage means, said second opening being connected to said first opening and said n eedle; Mounted on the shaft between means,

the blood sampling device restricts the flow of blood from the shaft to the first opening, but re stricts the flow of blood from the shaft to the first opening.The blood collection device further comprising a flow control device located within the shaft intermediate the first and second ope nings to allow gas flow to the first opening.

(21) further comprising blood storage means for temporarily storing a portion of blood, said bl ood storage means being sealed to said second opening for receiving blood delivered from sai d needle means to said shaft; 21. A blood collection device according to claim 20, adapted for coupling.

(22) said blood storage means comprises a syringe having a blood storage chamber and a plu nger located within said blood storage chamber, said syringe sealing said blood storage chamb er to said second opening; 22. A blood collection device according to claim 21, further compri sing means for connecting with.

(23) The blood collection device of Claim 20, wherein said flow control means comprises a mic roporous hydrophobic plug.

(24) further comprising blood storage means for storing a blood sample, said blood storage m eans being sealingly attachable to said first opening for insertion through said plug, thereby 2 4. A blood collection device according to claim 23, comprising a needle adapted to lead blood f rom the shaft to said blood storage means.

(25) guiding means located within said shaft between said plug and said first opening for guidi ng said needle of said blood storage means through said plug and making said needle coaxial with said shaft; 25. The blood collection device of claim 24, further comprising:

(26) within said shaft between said flow control means and said first opening for guiding a ne edle coupled to said blood storage means through said flow control means and coaxial with sai d shaft; 21. A blood collection device according to claim 20, further comprising guide means l ocated at the .

(27) The blood collection device of Claim 20, further comprising valve means for selectively all owing communication between said shaft and said second opening.

(28) said needle means comprises a needle for insertion into a patient to withdraw a blood sa mple and an elongated tube for guiding blood withdrawn from a patient to said coupling mean s, said tube being flexible

; 21. A blood collection device according to claim 20, and wherein the blood being conducted by said tube is generally transparent so as to be visible to medical personnel.

(29) further comprising a syringe having a blood storage chamber and a plunger positioned wi thin the blood storage chamber, the syringe having means for sealingly connecting the blood s torage chamber to the second opening; 29. A blood collection device according to claim 28, fu rther comprising.

(30) The blood collection device of (11) further comprising cap means for sealing said second opening.

(31) in drawing and collecting a blood sample from a patientA blood collection device for use by medical personnel comprising a

first elongated needle member having an insertion end and an attachment end, said insertion end adapted for insertion into a patient, said first needle member comprising: has a coaxial p assageway for carrying blood drawn from a patient from the insertion end to the attachment e nd and includes a

needle receiving end, a mating end, and from the needle receiving end to the mating end. an d said mounting of said first needle member

such that blood drawn from a patient is conveyed by said first needle member to said first fe male connector. means for fixedly and sealingly connecting an end to a receiving end of said fi rst female connector; a

mating end; a mounting end; and a coaxial extending from said mating end to said mounting end. further comprising a first male connector having a passageway, wherein the mating end of the first male connector is adapted to receive blood conveyed to the first female connector by the first male connector;

first and second ends and a passage extending from the first end to the second end sealingly mated to the mating end of the first female connector; and wherein the first end of the tube i s connected to the attachment end of the first male connector such that blood received by the first male connector is carried by the tube. sealingly attached to the portion, the tube being fl exible and generally transparent so that blood received by the tube is visible to medical perso nnel;

Further comprising a coupling having an elongated hollow shaft and a connecting member att ached to a first end of said shaft, said coupling securing a second end of said tube to said cou pling. to sealably connect to a second end of the shaft, thereby conveying blood received by t he tube to the coupling, the coupling being attached to a second end of the shaft connecting t he shaft to blood storage means. and the coupling is fixedly attached to the shaft between the adapter sleeve and the connecting member such that blood received by the coupling flows int o and out of the second female connector. a plug communicatively further comprising a secon

d female connector in communication with said connecting member and
positioned within said shaft of said coupling between said second female connector and said a dapter sleeve; wherein said plug is adapted to allow gas to escape from said shaft to effectivel y block blood flow from said shaft to said adapter sleeve.
(32) a second needle member having an insertion end, a connecting end, a coaxial passagewa y extending from said insertion end to said connecting end, and a vacutainer means for storin g blood drawn from a patient
; The vacutainer means is fixedly attached to the second needle member, the adapter sleeve i s positioned such that the vacutainer means is press fit into the adapter sleeve, and the secon d 32. A blood collection device according to claim 31, wherein a needle member is configured to be inserted through said plug, thereby conveying blood received by said shaft of said coupli ng to said vacutainer means.
(33) located within said coupling between said plug and said adapter sleeve for guiding said s econd needle member to insert said second needle member into said plug coaxial with said co upling; 33. A blood collection device according to claim 32, further comprising a needle guide means for receiving the blood.
(34) needle guide means located within said coupling between said plug and said adapter slee ve for guiding a needle coupled to blood storage means for coaxial insertion of said needle int o said coupling; 32. The blood collection device of claim 31, further comprising:
(35) further comprising cap means adapted to engage said second female connector and ther eby seal said second female connector to prevent blood from flowing out of said second femal e connector; A blood sampling device according to claim (31).
(36) Further comprising a syringe for temporarily storing blood, said syringe having a blood st orage chamber and a plunger located within said blood storage chamber, said syringe being in communication with said blood storage means. (31) adapted to mate with said second female connector such that blood received by said coupling is stored within said syringe.
(37) located within said coupling between said plug and said adapter sleeve for guiding said s econd needle member to insert said second needle member into said plug coaxial with said co upling; 37. A blood collection device according to claim 36, further comprising a needle guide means for receiving the blood.
(38) a second needle member having an insertion end, a connecting end, a coaxial passagewa y extending from said insertion end to said connecting end, and a vacutainer means for storin g blood drawn from a patient
; The vacutainer means is fixedly attached to the second needle member, the adapter sleeve i s positioned such that the vacutainer means is press fit into the adapter sleeve, and the secon d A needle member is configured to be inserted through said plug, thereby carrying blood rec eived by said shaft of said coupling to said vacutainer means.38. The blood collection device o f claim 37.
(39) The blood collection of claim (37) further comprising first, second and third cap means re

spectively sealing said first needle means, said second female connector and said adapter slee ve. Device.

(40) The blood collection device of claim (31) further comprising valve means coupled to said second female connector for selectively communicating between said second female connector and said shaft.

(41) needle means for withdrawing blood from a patient

and

temporarily storing a first blood portion withdrawn from the patient in a blood collection devic e used by medical personnel to withdraw and store a blood sample from a patient; syringe me ans and

coupling means sealingly connecting said needle means to said syringe means, said coupling means including flow control means for venting air trapped within said needle means and said coupling means. said coupling means further comprising adapter means adapted to receive bl ood storage means and direct blood to said coupling means for storage; A blood collection dev ice wherein the means are further configured to return said first blood portion to the patient.

(42) said coupling means comprises a coupling having an elongated hollow shaft, said couplin g means attached to a first end of said shaft fixedly connecting said needle means to said cou pling; further comprising a connecting member, said adapter means being attached to a secon d end of said shaft, said coupling receiving said syringe means, said shaft between said adapt er means and said connecting member; 42. A blood collection device according to claim 41, fu rther comprising a connecting member fixedly attached to.

(43) The blood collection device of Claim 42, wherein said flow control means comprises a plu g positioned within said shaft of said coupling between said connecting member and said adap ter means.

(44) The blood collection device of Claim 43, wherein said plug comprises a microporous hydr ophobic plug.

(45) said needle means comprises a needle for insertion into a patient to withdraw a blood sa mple and an elongated tube for conducting blood withdrawn from the patient to said coupling, said tube being flexible; 44. A blood collection device according to claim 43, and wherein bloo d being conducted by said tube is generally transparent so as to be visible to medical personn el.

(46) drawing a first blood portion from the patient to fill the blood collection device while evac uating the air trapped in the blood collection device so that the anaerobic sample is not conta minated with air trapped in the blood collection means; An anaerobic sample is taken from th e patient after generally evacuating the trapped air from the blood collection device.A method of drawing

an anaerobic blood sample from a patient comprising the step of drawing a sample of blood fr om a patient.

(47) temporarily storing the first blood portion after drawing the first blood portion and

returning the first blood portion to the patient after drawing the anaerobic blood sample
; The method of claim (46), further comprising:
(48) withdrawing the first blood portion
further comprises coupling a coupling to a syringe, the coupling sealably coupled to a needle assembly; inserting
the
needle assembly into a patient and coupling the inserted needle assembly and the coupling so that blood is directed through the needle assembly and into the coupling with the syringe atta ched
; evacuating trapped air,
connecting a vacutainer needle of a vacutainer to said vented coupling, said vacutainer needle being in communication with said inserted needle assembly, and a cup with said vacutainer at tached
.
48. The method of claim (47), comprising withdrawing said first blood portion from a ring into said syringe .
(49) wherein withdrawing the anaerobic blood sample comprises establishing blood flow betw een the needle assembly and the vacutainer after the first blood portion has been withdrawn; The method described in .
(50) The method of claim (48), wherein withdrawing the first blood portion into the syringe co mprises allowing blood to flow freely under the pressure of the patient's heart.

detailed description open —

Description:
INDUSTRIAL APPLICABILITY
The present invention is directed to apparatus for taking a blood sample from a patient, and i n particular to apparatus for obtaining a blood sample from a patient in which the partial pres sure of gas within the sample is such that the blood pressure in the patient's body is An impro ved blood collection device is directed to receiving a blood sample so as to approximately equ al the gas partial pressure therein.
(PRIOR ART)
In the medical field, it is necessary to determine the in vivo gaseous equilibrium in the blood of a patient.
A medical worker will typically be concerned with the partial pressures of oxygen and carbon d ioxide. They may also be concerned with ionic species whose activity is related to the gas bala

nce in the blood, such as hydrogen ions and calcium ions.

In order for a blood sample to be valid for gas-in-blood analysis, the sample must be under a naerobic conditions, i.e., to prevent fluctuations in the partial pressure of the gas to be tested (when the blood is outside the patient's body). Must be collected to avoid exposure to gas.The major commercially available blood collection devices that must be present are largely unsatis factory in ensuring the integrity of anaerobic blood collection. An example of a conventional d evice uses a syringe and a vented plunger, where the syringe is removed from the patient unti l the correct blood volume is obtained from the patient by pulling on the vented plunger from no void in the barrel. Slowly withdraw the blood into the barrel of the However, these devices allow some exposure of the blood sample to the atmosphere. Some amount of ambient air will be contained within the barrel before the plunger moves. Thus, the initial portion of blood is e xposed to these gases, thereby changing the partial pressure of the gases contained in this ini tial sample. No means are provided for discarding the first portion of the drawn blood, so the entire sample would be contaminated.

Further, no means are provided to protect the medical personnel of the device against acciden tal bursting or exposure to contaminated blood during the course of the procedure when using the aforementioned device.

Other devices, such as the Becton and Dickenson Vacutainer and vacutainer attachments, hav e shown improved properties to protect medical personnel from exposure to drawn blood. Ho wever, these devices also. It allows some exposure of the first part of the blood sample to the atmosphere.

In addition to the shortcomings of the prior art described above, blood collection devices that provide means for flushing, i.e., injecting, for example, nutrients, medications, etc., into the b lood stream while permitting the collection of an anaerobic blood sample are currently lackin g. not known where.

Accordingly, it is desirable to provide a device for drawing an anaerobic blood sample from a p atient, and it is further desirable to provide a device for drawing a blood sample that can also inject a liquid into the patient's blood stream, i.e., a puncture. It is further desirable to provid e such a device that allows repeated blood sampling without the need for additional needle pl acement, and during scheduled interval sampling, i.e., between other subsequent blood sampl ings. It would be desirable to provide a device for drawing blood samples that can be left in th e patient.

OBJECTS OF THE INVENTION

It is therefore an object of the present invention to provide a blood collection device for drawi ng an anaerobic blood sample from a patient.

It is also an object of the present invention to provide a blood collection device that can withd raw an initial contaminated blood sample portion and maintain complete anaerobicity in the re maining sample.

It is a further object of the present invention to provide a blood collection device that can inje

ct an external liquid into the patient's blood stream.

It is a further object of the present invention to provide a blood sampling device that allows re peated blood sampling without the need for additional puncture or needle placement.

Yet another object of the present invention is to provide a blood collection device that can be l eft on the patient between scheduled intervals of collection, ie, other subsequent blood collect ions.

These and other objects of the present invention are met by providing a coupling for use by m edical personnel when drawing blood from a patient and storing it, which coupling draws the b lood sample. The coupling is particularly adapted for use with a needle assembly for injecting a needle into a patient. A coupling fixedly

connects the elongated hollow shaft and the needle assembly to the shaft for withdrawal by th e needle. a connecting member attached to the first end of the shaft that delivers blood to the shaft, and a coupling attached to the second end of the shaft that connects the shaft to variou s blood storage means. The adapter sleeve further comprises an opening coupled to the shaft intermediate the adapter sleeve and the connecting member, the opening being in communica tion with the opening such that blood received in the shaft communicates with the opening. In another embodiment

of the present invention, a device is provided for blocking blood flow and venting air trapped i n the shaft, particularly flow control means, such as microporous A hydrophobic plug is locate d in the shaft intermediate the opening and the adapter sleeve to restrict blood flow from the shaft to the adapter sleeve while allowing air flow from the shaft to the adapter sleeve. 6 In a nother embodiment of the invention, a valve is provided intermediate the shaft and the openi ng to allow selective communication between the shaft and the opening.

Other embodiments of the invention are particularly pointed out and distinctly claimed in the c laims. The invention, however, as to organization and method of implementation, will best be understood from the following detailed description when read with the accompanying drawing s in which: FIG.

DETAILED DESCRIPTION OF THE INVENTION

A cross-sectional view showing the improved blood collection device of the present invention i s provided in FIG. The blood sampling device comprises an elongated needle 100 having an in sertion end 102 adapted for insertion into a patient's blood stream (artery or vein). Needle 10 0 further has an attachment end 104 attached to first connecting member 106 via cylindrical seal 108 . As is well known in the art, meter 100- has a coaxial passageway extending from in sertion end 102 to attachment end 104 that conducts blood withdrawn from the patient to firs t connecting member 106. As shown in FIG.

Cylindrical seal 10B has a central opening 110 in which mounting end 104 of needle 100 is fix edly mounted. Additionally, the cylindrical seal 108 isIt is fixedly attached to needle receiving end 112 of member 106 . The second connecting member 114 has a mating end 116 adapted to mate with the mating end 118 of the first connecting member 106 so that it is received by

the first connecting member. rice field. Blood from leaflet 100 is directed to second connecting member 114 via mating joints 116,118.

First end 120 of tube 122 is sealingly attached to attachment end 124 of second connecting m ember 114 . A tube 122 is provided for carrying blood withdrawn from the patient through tub e 100 to coupling 126 . Tubing 122 allows the needle to be easily inserted into the patient's bl oodstream and, after insertion, the coupling 126 can be disengaged by medical personnel wit hout undue movement of the total 100 and causing discomfort to the patient. Preferably, the t ube 122 is flexible so as to be operable, and preferably transparent so that the medical perso nnel can visually observe the blood drawn from the patient.

The combination of needle 100, first connecting member 106, second connecting member 11 4, and tube 122 constitutes a needle assembly, readily available from needles, connecting me mbers, and tubes well known in the art. Can be assembled. - By way of example, the first and second connecting members 106 and 114 consist of male and female Luer connectors, as is w ell known in the art.

A coupling 126 is provided for connecting the second end 128 of the tube with each of the firs t and second blood storage means 130 and 132 . To this end, coupling 126 has a connecting member 134 with a central opening that receives second end 128 of tube 122 . Connecting m ember 134 is integrally connected to elongated hollow shaft 136 such that blood delivered to coupling 126 by tube 122 is received within shaft 136 . Adapter sleeve 138 is integrally conne cted to shaft 136 at the end opposite to the end to which connecting member 134 is connecte d. Adapter sleeve 138 is in communication with shaft 136 and is provided for receiving second blood storage means 132, as will be described more fully below.

Coupling 126 further includes an opening 140 integrally connected to shaft 136 intermediate a dapter sleeve 138 and connecting member 134 .

An opening 140 is provided for connecting first blood storage means 130 to shaft 136 of coupl ing 126 . A passageway 162 is provided in shaft 136 proximate opening 140 such that openin g 140 communicates with connecting member 134 . Accordingly, blood delivered to coupling 1 26 by tube 122 is conveyed via adapter sleeve 138 and opening 140 to first and second blood storage means 130 and 132 for storage.

Coupling 126 also has a plug 142 disposed within the shaft between adapter sleeve 138 and o pening 140 . Plug 142 is a fluid flow, e.g., porous plug, venting air trapped within connecting members 106, 114, tube 122, shaft 136, and opening 140 during the early stages of a blood c ollection procedure. It consists of control means. The plug 142 is thus adapted to restrict bloo d flow from the shaft 136 to the adapter sleeve 138 and allow air flow from the shaft to the a dapter sleeve. 142 consists of a microporous, hydrophobic plug, well known in the art. Howev er, those skilled in the art will appreciate that other liquid flow control means may be used in place of the preferred microporous hydrophobic plug 142 .

As previously mentioned, opening 140 is adapted to receive first blood storage means 130 .

A cap 144 is engageable with opening 140 to seal the opening from inadvertent blood loss, w

hich often occurs when first blood storage means 130 is not connected to coupling 126 . Howe ver, in normal operation, cap 144 is removed from opening 140 and connects first blood stora ge means 130 thereto.

In a preferred embodiment of the present invention, the first blood storage means 130 compri ses a syringe of the type having a blood storage chamber 146 and a plunger 148 positioned w ithin the blood storage chamber 146 .

As is well known, in operation, plunger 148 is slowly withdrawn from blood storage chamber 1 46 so that blood enters the chamber. Blood storage means 130 further comprises connection means 150 for connecting blood storage means 130 to opening 140 . In a preferred embodim ent of the invention, opening 140 and connecting member 150 each comprise male and femal e luer connectors. However, it will be apparent to those skilled in the art that other connector members may be provided to sealingly connect first blood storage means 130 to coupling 126 .

In operation, the cap 144 is removed from the opening 140 and the blood reservoir means 13 0 is connected thereto.The blood is then withdrawn, or preferably allowed to flow freely under the pressure of the patient's heart. Meter 100 is inserted into the patient's blood stream so as to be able and delivered to shaft 136 via connecting members 106 , 114 and tubing 122 . Air trapped within connecting members 106, 114, tube 122, shaft 136 and opening 140 is displac ed by the patient's blood entering the flow passageway and vented through porous plug 142, as previously described. .

A first portion of the blood that is withdrawn or flows under cardiac pressure from the patient is exposed to trapped air before being ventilated.As it is exposed, it is generally contaminated and therefore not suitable for anaerobic blood sampling.

This first blood portion is thus withdrawn from the coupling 126 into the blood storage means 130 for temporary storage, while the anaerobic blood sample passes through the second bloo d storage means 132. to be received. After the anaerobic blood sample is received, the blood temporarily stored in blood storage means 130 is discarded or returned to the patient via tube 122 and meter 100 .

A second blood storage means 132 is connected to the coupling 126 via an adapter sleeve 13 8 for withdrawing an anaerobic blood sample. The second blood storage means 132 may com prise a Becton Dickenson vacutainer well known in the art. Blood storage means 132 has a blo od storage chamber 152 for receiving an anaerobic blood sample drawn from the patient. are doing. Needle 154 is sealingly connected to needle hub 156 and their assembly is connected t o blood storage chamber 152 via a compatible coupling 158 (commonly referred to as a vacut ainer adapter). Hermetically connected. Needle 154 has a seal to prevent communication with blood storage chamber 152, as is well known in the art. Additionally, as is well known in the a rt, blood storage chamber 152 is evacuated so as not to contain air that contaminates blood d rawn from the patient.

A compatible coupling 158 provides means for removing the seal from needle 154 in order to

place needle 154 in communication with blood storage chamber 152 .

Adapter sleeve 138 has an internal adapter chamber 160 sized to snugly receive needle hub 1 56 . The length of adapter sleeve 138 and the position of plug 142 within shaft 136 is such th at blood reservoir 132 is fully inserted into adapter sleeve 138 and needle 154 passes through passageway 162 and second end 128 of tube 122 through plug 142 . is selected to lie betwee n A needle guide 164 is positioned within coupling 126 between adapter sleeve 138 and plug 142 to allow a needle to be inserted into coupling 126 coaxially with shaft 136 . Needle guide 164 receives needle 154 during insertion of blood reservoir 132 into coupling 126 and guides t he needle prior to needle insertion into plug 142 so that the needle is coaxial with shaft 136 . provided for positioning.

In operation, blood reservoir means 130 is connected to coupling 126 via opening 140 as prev iously described for collecting an anaerobic blood sample. The meter 100 is inserted into the p atient's bloodstream and air trapped inside the meter 100, connectors 106, 114, tubing 122 a nd coupling 126 is evacuated through plug 142 as previously described.Total 154 of blood stor age means 132 is then inserted through plug 142 and into coupling 126 so that it lies beyond passageway 162 near tube 122 . The contaminated air of the blood sample is removed so that any fraction of contaminated air that accumulates within needle 154 is exhausted through plu g 142, i.e., removed from coupling 126 prior to receiving the anaerobic blood sample. It is des irable to insert gauge 154 into coupling 126 prior to storing the portion in storage means 130 .

After the soot 154 is properly inserted into the coupling 126, the first portion of contaminated blood is drawn from the coupling 126 into the blood storage means 130 for temporary storag e. At this time, the seal on needle 154 is removed by compatible coupling 158, as is well kno wn in the art, so that the anaerobic blood sample is directed to blood reservoir 152. FIG.

To ensure that substantially all of the blood directed to blood storage chamber 152 is blood re ceived from tube 122 and not blood received from blood storage chamber 146 of blood storag e means 130, total 154 is connected to passageway 162. and tube 122 and near second end 128 of tube 122 in coupling 126 in shaft 136 .

In an alternative embodiment of the present invention, when receiving an anaerobic blood sa mple, a valve capable of substantially isolating a contaminated blood sample stored in blood s torage means 130 from shaft 136 during operation; Alternatively, it may be desirable to provi de other selective coupling means.

In addition to the cap 144, a plurality of caps or other sealing means may be provided for posi tioning the total 100 to seal the chamber 160 of the adapter sleeve 138, as is common in the medical industry.

Although only some of the preferred embodiments of the novel blood collection device have b een described in detail herein, many modifications and variations will become readily apparent to those skilled in the art without the true scope and spirit of the invention. It is the intent of t he appended claims to cover all such improvements and modifications that fall within the scop

e of the claims.

Brief description of the drawing open —

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a cross-sectional view of one of the improved blood collection devices of the pre sent invention.

100 Needle

106 First connecting member

114 Second connecting member

122 Tube

126 Coupling

130.132 Blood reservoir Means

134 ... Connection member

136 ... Shaft

138 ·

140 ·

142,

144,

146.

148

154

Adapter sleeve

opening

plug

cam

blood storage chamber plunger

needle



Copyright JPO and INPIT

(P0200)

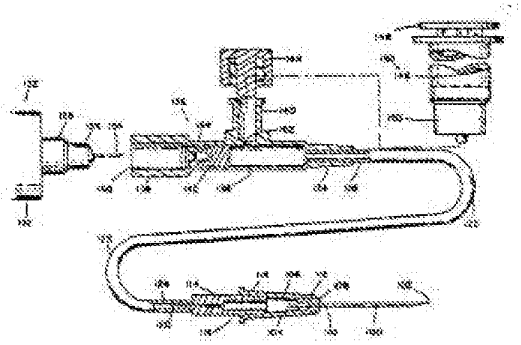
Espacenet

Bibliographic data: JPH02224742 (A) — 1990-09-06

IMPROVED BLOOD SAMPLER

Inventor(s):	JIYON EI AARU KEITAA ± (JIYON EI AARU KEITAA)
Applicant(s):	SPACELABS INC ± (SPACELABS INC)
Classification:	**- international:** ***A61B5/15; A61B5/155; A61M1/02;*** (IPC1-7): A61B5/14; A61M1/02 **- cooperative:** **A61B5/15003 (EP, US); A61B5/150992 (EP, US)**
Application number:	JP19890338039 19891226
Priority number(s):	US19880292490 19881230
Also published as:	CA2002175 (A1) EP0376168 (A2) EP0376168 (A3) US5046509 (A)

Abstract of JPH02224742 (A)



PURPOSE: To keep completely anaerobic of the residual a blood sample, with the first sampled portion of contaminated blood removed, by fixedly coupling a slender hollow shaft and a needle assembly together, with a joint member mounted to the first end of a shaft and an adapter sleeve to the second end. CONSTITUTION: Coupling 126 has joint member 134 which receives the second end 128 of tube 122. Adapter sleeve 138 is connected integrally to shaft 136 at an opposite end of the end to which the joint member 134 is connected. The adapter sleeve 138 communicates with the shaft 136 and receives second blood storage means 132. The coupling 126 has further opening 140 which is joined integrally to the shaft 136 between the adapter sleeve 138 and joint member 134. The blood delivered to the coupling 126 through tube 122 is transferred to the first and second blood storage means 130, 132 respectively for storage therein via the adapter sleeve 138 and opening 140.

⑲日本国特許庁(JP)　⑪特許出願公開

⑫公開特許公報(A)　平2-224742

⑤Int. Cl.[5]	識別記号	庁内整理番号
A 61 B 5/14	300 H	7831-4C
A 61 M 1/02	370	7180-4C

⑬公開　平成2年(1990)9月6日

審査請求　未請求　請求項の数 50　(全10頁)

⑤④発明の名称　改良された血液採取装置

⑳特　願　平1-338039

㉒出　願　平1(1989)12月26日

優先権主張　㉜1988年12月30日㉝米国(US)㉛292490

⑦②発明者　ジョン エイ アール ケイター　アメリカ合衆国 カリフォルニア州 92704 サンタ アナ ウエスト サン ローレンゾー 2037

⑦①出願人　スペイスラブズ インコーポレーテッド　アメリカ合衆国 ワシントン州 98073-9713 レッドモンド ワンハンドレッドアンドフィフテイス アベニュー ノースイースト 4200

⑦④代理人　弁理士 中村 稔　外7名

明　細　書

1.発明の名称　改良された血液採取装置

2.特許請求の範囲

(1) 患者から血液を抜き取って貯蔵する際に医療作業員によって使用され、血液サンプルを抜き取るために針組立体の針を患者に挿入する、カップリングにおいて、

第1及び第2の端部を有する細長い中空シャフトと、

前記針組立体を前記シャフトに固定して連結し、それによって、前記針によって引き抜かれた血液を前記シャフトに送ることができる、前記シャフトの第1の端部に取り付けられた接続部材と、

前記シャフトを血液貯蔵手段に接続する、前記シャフトの第2の端部に取り付けられたアダプタースリーブと、

前記シャフトによって受け入れられた血液を連通させるため、前記アダプタースリーブと前記接続部材との間の前記シャフトに連結されて前記接続部材に連通している開口部と、から成るカップリング。

(2) 血液の流れを遮断して、前記シャフト内にたまった空気を排気する手段をさらに備える請求項(1)に記載のカップリング。

(3) 前記空気を排気する手段が、前記シャフトから前記アダプタースリーブへの空気の流れを可能にしつつ、シャフトからアダプタースリーブへの血液の流れを制限する、前記開口部と前記アダプタースリーブとの中間の前記シャフト内に位置している流れ制御手段から成る請求項(2)に記載のカップリング。

(4) 前記流れ制御手段が、微孔質疎水性プラグから成る請求項(3)に記載のカップリング。

(5) 血液貯蔵手段に結合している針を前記プラグを通して案内し、前記針を前記シャフトと同軸にする針案内手段をさらに備える請求項(4)に記載のカップリング。

(6) 患者から抜き取った血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記開口部に密封して連結可能である請求項(2)に記載のカップリング。

(7) 前記血液貯蔵手段が、注射器から成る請求項(6)に記載のカップリング。

(8) 前記シャフトと前記開口部との間の選択的な連通を可能にする、前記開口部と前記シャフトの中間に固定して配置されているバルブ手段をさらに備える請求項(2)に記載のカップリング。

(9) 前記開口部を密封する手段をさらに備える請求項(2)に記載のカップリング。

(10)患者から血液サンプルを抜き取って貯蔵するために医療作業員によって使用される血液採取装置において、

血液サンプルを抜き取るために、患者に挿入されるように適合している針手段と、

前記針手段を血液貯蔵手段に連結させるカップリング手段とを備え、

前記カップリング手段は、第1及び第2の開口部を有しており、前記針手段からの血液を前記第1及び第2の開口部に導くようになっている血液採取装置。

(11)血液の流れを遮断して、前記カップリング手段内にたまった空気を排気する手段をさらに備える請求項(10)に記載のカップリング。

(12)前記空気を排気する手段が、前記針手段から前記第1の開口部への空気の流れを可能にしつつ、前記針手段から前記第1の開口部への血液の流れを制限する、前記第1及び第2の開口部の間の前記カップリング手段内に位置している流れ制御手段から成る請求項(11)に記載の血液採取装置。

(13)前記流れ制御手段が、微孔質疎水性プラグから成る請求項(12)に記載の血液採取装置。

(14)血液貯蔵手段に結合している針を前記プラグを通して案内し、前記カップリング手段と同軸になる針案内手段をさらに備える請求項(13)に記載の血液採取装置。

(15)患者から抜き取った血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記第2の開口部に密封して連結可能である請求項(14)に記載の血液採取装置。

(16)前記血液貯蔵手段が、注射器から成る請求項(12)に記載の血液採取装置。

(17)前記第2の開口部を密封する手段をさらに備える請求項(12)に記載の血液採取装置。

(18)前記針手段と前記第2の開口部との間の選択的な連通を可能にする、前記針手段と前記第2の開口部の中間に配置されているバルブ手段をさらに備える請求項(12)に記載の血液採取装置。

(19)前記針手段が、患者に挿入する針と、前記針から前記カップリング手段へ導く、細長いチューブと、から成り、前記チューブは、医療作業員が導かれている血液を前記チューブを通して見ることができるように、概ね透明である請求項(12)に記載の血液採取装置。

(20)患者から血液サンプルを抜き取って集める際に医療作業員が使用する血液採取装置において、

患者から血液を抜き取る針手段と、

前記針手段に血液貯蔵手段を選択的に連結するカップリング手段と、を備え、

前記カップリング手段は前記針手段に固定されており、前記カップリング手段は、血液貯蔵手段を受け入れる第1の開口部と、前記第1の開口部と前記針手段との間にある中空のシャフトとを有しており、前記カップリング手段は、血液貯蔵手段を受け入れる第2の開口部をさらに備えており、前記第2の開口部は、前記第1の開口部と前記針手段の間の前記シャフトに取り付けられており、

前記血液採取装置は、前記シャフトから前記第1の開口部への血液の流れを制限するが、前記シャフトから前記第1の開口部への気体の流れを可能にする、前記第1及び第2の開口部の中間の前記シャフト内部に位置している流れ制御装置をさらに備える血液採取装置。

(21)血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記針手段から前記シャフトへ送られた血液を受け入れる、前記第2の開口部へ密封して連結されるようになっている請求項(20)に記載の血液採取装置。

(22)前記血液貯蔵手段が、血液貯蔵チャンバーと前記血液貯蔵チャンバー内に位置しているプラ

ンジャーとを有する注射器から成り、前記注射器は、前記血液貯蔵チャンバーを前記第２の開口部へ密封して連結する手段をさらに有している請求項(21)に記載の血液採取装置。

(23)前記流れ制御手段が、微孔質疎水性プラグから成る請求項(20)に記載の血液採取装置。

(24)血液サンプルを貯蔵する血液貯蔵手段をさらに有しており、前記血液貯蔵手段は、前記第１の開口部に密封して取り付け自在であって、前記プラグを通して挿入し、それによって、前記シャフトから前記血液貯蔵手段へ血液を導くようになっている針を有している請求項(23)に記載の血液採取装置。

(25)前記プラグを通して前記血液貯蔵手段の前記針を案内し、前記針を前記シャフトと同軸にする、前記プラグと前記第１の開口部との間の前記シャフト内に位置している案内手段をさらに備えている請求項(24)に記載の血液採取装置。

(26)前記流れ制御手段を通して前記血液貯蔵手段に結合している針を案内し、前記針を前記シャフトと同軸にする、前記流れ制御手段と前記第１の開口部との間の前記シャフト内に位置している案内手段をさらに備えている請求項(20)に記載の血液採取装置。

(27)前記シャフトと前記第２の開口部との間を選択的に連通できるように、バルブ手段をさらに備える請求項(20)に記載の血液採取装置。

(28)前記針手段が、血液サンプルを抜き取るために患者に挿入する針と、患者から抜き取られた血液を前記カップリング手段へ導く細長いチューブとを有し、前記チューブは可撓性を有し、かつ、前記チューブによって導かれている血液が医療作業員に見えるように概ね透明である請求項(20)に記載の血液採取装置。

(29)血液貯蔵チャンバーと該血液貯蔵チャンバー内に位置しているプランジャーとを有する注射器をさらに備え、前記注射器は、前記血液貯蔵チャンバーを前記第２の開口部へ密封して連結する手段をさらに備えている請求項(28)に記載の血液採取装置。

(30)前記第２の開口部を密封するキャップ手段をさらに備える請求項(11)に記載の血液採取装置。

(31)患者から血液サンプルを抜き取って集める際に医療作業員が使用する血液採取装置において、

挿入端部と取り付け端部を有する第１の細長い針部材を備え、前記挿入端部が患者に挿入するようになっており、前記第１の針部材が患者から抜き取られた血液を前記挿入端部から前記取付端部へ運ぶ同軸通路を有しており、

針受け入れ端部と、嵌合端部と、前記針受け入れ端部から前記嵌合端部へ延びる同軸通路と、を有する第１の雌コネクターと、

患者から抜き取られた血液が前記第１の針部材によって前記第１の雌コネクターに運ばれるように、前記第１の針部材の前記取り付け端部を前記第１の雌コネクターの受け入れ端部に固定してかつ密封自在に連結する手段と、

嵌合端部と、取り付け端部と、前記嵌合端部から前記取り付け端部へ延びる同軸通路を有する第１の雄コネクターをさらに備え、前記第１の雄コネクターの前記嵌合端部は、前記第１の雌コネクターへ運ばれた血液が前記第１の雄コネクターによって受け入れられるように、前記第１の雄コネクターの前記嵌合端部に密封自在に嵌合されており、

第１及び第２の端部と、前記第１の端部から前記第２の端部へ延びている通路とを有する細長いチューブをさらに備え、前記チューブの前記第１の端部は、前記第１の雄コネクターによって受け入れられた血液が前記チューブによって送られるように、前記第１の雄コネクターの前記取り付け端部に密封自在に取り付けられており、前記チューブは、可撓性を有し、かつ、前記チューブによって受け入れられた血液が医療作業員に見えるように概ね透明であり、

細長い中空のシャフトと、前記シャフトの第１の端部に取り付けられている接続部材とを有するカップリングをさらに備え、前記カップリングは、前記チューブの第２の端部を前記カップリングに固定して密封自在に連結し、それによって、前記チューブによって受け入れられた

血液を前記カップリングに送り、前記カップリングは、前記シャフトを血液貯蔵手段に接続する、前記シャフトの第２の端部に取り付けられたアダプタースリーブをさらに有し、前記カップリングは、前記アダプタースリーブと前記接続部材との間の前記シャフトに固定して取り付けられて、前記カップリングによって受け入れられた血液が前記第２の雌コネクターと連通するように、前記接続部材と連通している第２の雌コネクターをさらに有し、

前記第２の雌コネクターと前記アダプタースリーブとの間の前記カップリングの前記シャフト内に位置しているプラグをさらに備え、前記プラグは、気体を前記シャフトから逃がして前記シャフトから前記アダプタースリーブへ血液流れを有効に遮断するようになっている血液採取装置。

(32)挿入端部と、連結端部と、前記挿入端部から前記連結端部へ延びる同軸通路とを有する第２の針部材と、

患者から抜き取られた血液を貯蔵するバキュティナー手段とをさらに備え、前記バキュティナー手段は、前記第２の針部材に固定して取り付けられ、前記アダプタースリーブは、前記バキュティナー手段が前記アダプタースリーブの中へ圧入されるように、かつ、前記第２の針部材が前記プラグを通して挿入され、それによって前記カップリングの前記シャフトによって受け入れられた血液を前記バキュティナー手段へ運ぶように、形成されている請求項(31)に記載の血液採取装置。

(33)前記第２の針部材を案内して前記第２の針部材を前記カップリングと同軸の前記プラグへ挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(32)に記載の血液採取装置。

(34)血液貯蔵手段に結合している針を案内して前記針を前記カップリングへ同軸に挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(31)に記載の血液採取装置。

(35)前記第２の雌コネクターに係合しそれによって前記第２の雌コネクターから血液が流出するのを防止すべく前記第２の雌コネクターを密封するようになっているキャップ手段をさらに備える請求項(31)に記載の血液採取装置。

(36)一時的に血液を貯蔵する注射器をさらに備え、前記注射器は、血液貯蔵チャンバーと該血液貯蔵チャンバー内に位置するプランジャーとを有し、前記注射器は、前記血液貯蔵手段と連通していて、前記カップリングによって受け入れられた血液が前記注射器内に貯蔵されるように、前記第２の雌コネクターと嵌合するようになっている請求項(31)に記載の血液採取装置。

(37)前記第２の針部材を案内して前記第２の針部材を前記カップリングと同軸の前記プラグへ挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(36)に記載の血液採取装置。

(38)挿入端部と、連結端部と、前記挿入端部から前記連結端部へ延びる同軸通路とを有する第２の針部材と、

患者から抜き取られた血液を貯蔵するバキュティナー手段とをさらに備え、前記バキュティナー手段は、前記第２の針部材に固定して取り付けられ、前記アダプタースリーブは、前記バキュティナー手段が前記アダプタースリーブの中へ圧入されるように、かつ、前記第２の針部材が前記プラグを通して挿入され、それによって前記カップリングの前記シャフトによって受け入れられた血液を前記バキュティナー手段へ運ぶように、形成されている請求項(37)に記載の血液採取装置。

(39)前記第１の針手段、前記第２の雌コネクター、及び前記アダプタースリーブを各々密封する、第１、第２及び第３のキャップ手段をさらに備える請求項(37)に記載の血液採取装置。

(40)前記第２の雌コネクターと前記シャフトとの間を選択的に連通する、前記第２の雌コネクターに連結されたバルブ手段をさらに備える請求項(31)に記載の血液採取装置。

(41)患者から血液サンプルを抜き取って貯蔵するために、医療作業員が使用する血液採取装置において、

患者から血液を抜き取る針手段と、

患者から抜き取った第1の血液部分を一時的に貯蔵する注射器手段と、

前記針手段を前記注射器手段へ密封自在に連結するカップリング手段とを備え、前記カップリング手段は、前記針手段と前記カップリング手段内にたまった空気を排気する流れ制御手段を有しており、前記カップリング手段は、血液貯蔵手段を受け入れて前記カップリング手段へ貯蔵のために血液を導くようになっているアダプター手段をさらに有しており、前記注射器手段と前記カップリング手段は、前記第1の血液部分を患者に戻すようにさらになっている血液採取装置。

(42)前記カップリング手段が、細長い中空シャフトを有するカップリングを備え、前記カップリング手段が、前記カップリングへ前記針手段を固定して連結する、前記シャフトの第1の端部に取り付けた接続部材をさらに有し、前記アダプター手段は、前記シャフトの第2の端部に取り付けられており、前記カップリングは、前記注射器手段を受け入れる、前記アダプター手段と前記接続部材との間の前記シャフトに固定して取り付けた接続部材をさらに有している請求項(41)に記載の血液採取装置。

(43)前記流れ制御手段が、前記接続部材と前記アダプター手段との間の前記カップリングの前記シャフト内に位置しているプラグから成る請求項(42)に記載の血液採取装置。

(44)前記プラグが微孔質疎水性プラグから成る請求項(43)に記載の血液採取装置。

(45)前記針手段が、血液サンプルを抜き取るために患者に挿入する針と、患者から抜き取られた血液を前記カップリングへ導く、細長いチューブとを有し、前記チューブは可撓性を有し、かつ、前記チューブによって導かれている血液が医療作業員に見えるように概ね透明である請求項(43)に記載の血液採取装置。

(46)前記血液採取装置にたまった空気を排気しながら患者から第1の血液部分を抜き取って前記血液採取装置を満たし、嫌気性サンプルが前記血液採取手段にたまった空気に汚染されないように、前記血液採取装置にたまった空気を概ね排気した後、患者から嫌気性サンプルを抜き取る、

ステップから成る患者から嫌気性血液サンプルを抜き取る方法。

(47)前記第1の血液部分を抜き取った後に、前記第1の血液部分を一時的に貯蔵し、

前記嫌気性血液サンプルを抜き取った後に、前記第1の血液部分を患者に戻す、

ステップをさらに含む請求項(46)に記載の方法。

(48)前記第1の血液部分を抜き取るステップが、

注射器にカップリングを連結するステップをさらに含み、前記カップリングは針組立体に密封自在に連結されており、

さらに、前記第1の血液部分を抜き取るステップが、

血液が前記針組立体を介して前記注射器を取り付けたカップリングの中に導かれるように、患者に前記針組立体を挿入し、

前記挿入された針組立体とカップリング内にたまった空気を排気し、

バキュティナーのバキュティナー針を前記通気されたカップリングに接続して、前記バキュティナー針を前記挿入された針組立体と連通させ、

前記バキュティナーを取り付けたカップリングから前記第1の血液部分を前記注射器の中に抜き取る、

ステップを含んでいる請求項(47)に記載の方法。

(49)前記嫌気性血液サンプルを抜き取るステップが、前記第1の血液部分が抜き取られた後で前記針組立体と前記バキュティナーとの間に血液の流れをつくるステップから成る請求項(48)に記載の方法。

(50)前記第1の血液部分を前記注射器へ抜き取るステップが、患者の心臓の圧力下で自由に血液

を流すステップから成る請求項(48)に記載の方法。

3.発明の詳細な説明

(産業上の利用分野)

本発明は、患者から血液サンプルを採取する装置に向けられたものであり、特に、サンプル内の気体分圧が、患者の生体内における血液内の気体分圧とほぼ等しくなるように、血液サンプルを受け取ることができる、改良された血液採取装置に向けられたものである。

(従来技術)

医療分野では、患者の血液内の、生体内における気体の平衡状態を決定することが必要である。医療作業員は、代表的には、酸素と二酸化炭素の分圧を気にかけるであろう。彼らは、また、例えば水素イオンやカルシウムイオンのような、活性が血液中の気体平衡に関連してくるイオンの種を気にかけるであろう。

血液サンプルを血液中の気体分析のために有効なものにするには、サンプルは、嫌気条件で、すなわち、検査すべき気体の分圧に変動が生ずるのを防止すべく血液が患者の体外の気体にさらされないように、採取されなければならない。現在市販されて利用できる主要な血液採取装置は、嫌気血液採取の完全性を保証しているという点では、概ね妥当であるとはいえない。従来装置の例としては、注射器及びベント式プランジャーが使用されており、バレル内の空隙がない状態からベント式プランジャーを引っ張ることによって、患者から正確な血液体積が得られるまで、患者から注射器のバレルの中に血液をゆっくりと抜き取る。しかしながら、これらの装置は、血液サンプルが外気にさらされるのをある程度許している。プランジャーが移動する前に、ある程度の外気量はバレル内に含有されるであろう。従って、血液の最初の部分はこれらの気体にさらされ、それによって、この最初のサンプルに含有している気体の分圧が変化する。抜き取られた血液のうち最初の部分を捨てる手段は提供されておらず、そのため、全サンプルが汚染されるであろう。

さらに、前述した装置を用いる際に、装置の医療作業員を、作業の途中で汚染された血液の偶発的な破裂や暴露に対して保護する手段も提供されていない。

ベクトンディケンソン(Becton and Dickenson)のバキュテイナー(Vacutainer)及びバキュテイナー付属装置のような他の装置は、抜き取られた血液に対する暴露から医療作業員を保護する、改良された特性を示している。しかしながら、これらの装置もまた、外気に対する血液サンプルの最初の部分の暴露を、ある程度許容してしまう。

前述した従来技術の欠点に加えて、嫌気性血液サンプルの採取を可能にしつつ、流し込み、すなわち血液の流れの中へ、例えば栄養剤や薬等を注入する手段を備える血液採取装置は、現在のところ知られていない。

従って、患者から嫌気性血液サンプルを抜き取る装置を提供することが望ましい。さらに、液体を患者の血液の流れに注入することもできる、血液サンプルを抜き取る装置を提供することがさらに望ましい。穿刺、すなわち針の配置を追加して行う必要のない、繰り返して血液を採取できる、前記装置を提供することがさらに望ましい。また、予定された区間の採取、すなわち他の引き続いて行なわれる血液の採取の間、患者に残してお

くことができる、血液サンプルを抜き取る装置を提供することが望ましい。

(発明の目的)

それゆえ、本発明の目的は、患者から嫌気性血液サンプルを抜き取る血液採取装置を提供することである。

また、本発明の目的は、最初の汚染された血液のサンプル部分を抜き取って、残りのサンプルにおける完全な嫌気性を維持できる、血液採取装置を提供することである。

さらに、本発明の目的は、外部の液体を患者の血液の流れの中に注入できる血液採取装置を提供することである。

さらに、本発明の目的は、穿刺、すなわち針の配置を追加して行なう必要のない、繰り返して血液を採取できる血液採取装置を提供することである。

さらに、本発明の別の目的は、予定された区間の採取、すなわち他の引き続いて行なわれる血液採取の間、患者に残しておくことができる血液採取装置を提供することである。

本発明の、これら及び他の目的は、患者から血液を抜き取ってこれを貯蔵するときに、医療作業員が使用するカップリングを提供することによって、かなえられる。このカップリングは、血液サンプルを引き出すべく、患者に針を注入する針組立体とともに使用するために、特に利用される。カップリングは、細長い中空シャフトと、針組立体を該シャフトに固定的に連結し、針によって引き出された血液をシャフトに送る、シャフトの第1の端部に取り付けられる接続部材と、から成る。カップリングは、シャフトを様々な血液貯蔵手段に接続する、シャフトの第2の端部に取りつけられたアダプタースリーブをさらに備えている。開口部が、アダプタースリーブと接続部材との中間のシャフトに連結されており、シャフトに受け入れられた血液がその開口部と連通するように、その開口部は、接続部材と連通している。

本発明の別の実施例では、血液の流れを遮断してシャフトにたまった空気を通気する装置が提提される。特に、流れ制御手段、例えば、微孔質の疎水性プラグが、シャフトからアダプタースリーブへの空気の流れを可能にしつつ、シャフトからアダプタースリーブへの血液の流れを制限するため、開口部とアダプタースリーブとの中間のシャフト内に位置している。本発明の他の実施例では、シャフトと開口部との選択的な連通を可能にするバルブが、シャフトと開口部との中間に設けられる。

本発明の他の実施例は、特許請求の範囲で特に示され、明瞭に請求される。しかしながら、本発明は、実施の構成や方法に関する限り、添付図面を参照して次の詳細な説明を読むことから最も良く理解できるであろう。

(実施例)

本発明の改良された血液採取装置を示す断面図が第1図に提供されている。血液採取装置は、患者の血液流れ(動脈あるいは静脈)内に挿入するようになった挿入端部102を有する細長い針100を備えている。針100は、さらに、円筒シール108を介して第1の接続部材106に取り付けられている取り付け端部104を有している。当業界で周知のように、針100は、患者から引き出された血液を第1の接続部材106へ導く、挿入端部102から取り付け端部104へ延びる同軸通路を有している。

円筒シール108は、内部に針100の取り付け端部104が固定して取り付けられている中央開口部110を有している。さらに、円筒シール108は、第1の接続部材106の針受け入れ端部112へ固定して取り付けられている。第2の接続部材114は、第1の接続部材106の嵌合端部118と嵌合するようになった嵌合端部116を有しており、その結果、第1の接続部材によって受け入れられた、針100からの血液は、嵌合接合116、118を介して第2の接続部材114に導かれる。

チューブ122の第1の端部120が、第2の接続部材114の取り付け端部124に密封して取り付けられている。チューブ122は、患者から引き出された血液を針100を介してカップリング126へ運ぶために設けられている。チューブ122は、針を患者の血液流れに容易に挿入可能であり、さらに、挿入後、針100に無用な動

きを与えて患者に不快感を生ぜしめることなく、医療作業員がカップリング１２６を操作可能となるように、可撓性であるのが好ましい。さらに、チューブ１２２は、医療作業員が患者から引き出された血液を視覚で観察できるように、透明であるのが好ましい。

針１００と、第１の接続部材１０６と、第２の接続部材１１４と、チューブ１２２との組合わせは、針組立体を構成し、当業界で周知の針、接続部材、及びチューブから容易に組立て可能である。一例として、第１及び第２の接続部材１０６及び１１４は、当業界で周知のように、雄及び雌のルエル(Luer)コネクターから成る。

カップリング１２６は、チューブの第２の端部１２８を、第１及び第２の血液貯蔵手段１３０及び１３２の各々と接続するために設けられている。この目的のために、カップリング１２６は、チューブ１２２の第２の端部１２８を受け入れる中央開口部を有する接続部材１３４を有している。接続部材１３４は、チューブ１２２によってカップリング１２６に送られる血液がシャフト１３６の内部に受け入れられるように、細長い中空シャフト１３６に一体に接続される。アダプタースリーブ１３８は、接続部材１３４が接続されている端部と反対側の端部でシャフト１３６に一体に接続されている。アダプタースリーブ１３８は、シャフト１３６と連通しており、後で完全に説明するように、第２の血液貯蔵手段１３２を受け入れるために設けられる。

カップリング１２６は、さらに、アダプタースリーブ１３８と接続部材１３４との中間のシャフト１３６に一体に接続されている開口部１４０を、さらに有している。開口部１４０は、第１の血液貯蔵手段１３０をカップリング１２６のシャフト１３６へ接続するために設けられる。通路１６２は、開口部１４０が接続部材１３４と連通するように、開口部１４０に近接してシャフト１３６に設けられている。従って、チューブ１２２によってカップリング１２６に送られてきた血液は、貯蔵のため、アダプタースリーブ１３８及び開口部１４０を経由して第１及び第２の血液貯蔵手段１３０及び１３２へ運ばれる。

カップリング１２６は、また、アダプタースリーブ１３８と開口部１４０との間のシャフト内に配置されたプラグ１４２を有している。プラグ１４２は、血液採取作業の初期の段階の間に、接続部材１０６、１１４、チューブ１２２、シャフト１３６、及び開口部１４０内にたまった空気を排気する、例えば、多孔質プラグのような液体流れ制御手段から成る。従って、プラグ１４２は、シャフト１３６からアダプタースリーブ１３８への血液の流れを制限して、シャフトからアダプタースリーブへの空気の流れを可能にするようになっている。本発明の好ましい実施例では、プラグ１４２は、当業界で周知の、微孔質の疎水性プラグから成る。しかしながら、他の液体流れ制御手段が、好ましい微孔質疎水性プラグ１４２の代わりに、用いることができることは、当業者には明らかであろう。

前述したように、開口部１４０は、第１の血液貯蔵手段１３０を受け入れるようになっている。キャップ１４４は、第１の血液貯蔵手段１３０がカップリング１２６に接続されていないときに、しばしばおこる不注意な血液損失から開口部を密封するため、開口部１４０と係合可能である。しかしながら、通常作業では、キャップ１４４は、開口部１４０から取り除かれ、そこに第１の血液貯蔵手段１３０を接続している。

本発明の好ましい実施例では、第１の血液貯蔵手段１３０は、血液貯蔵チャンバー１４６と、その血液貯蔵チャンバー１４６内に配置されたプランジャー１４８を有する形式の注射器から成る。周知のように、操作の際には、プランジャー１４８は、血液がチャンバー内に入るように、血液貯蔵チャンバー１４６からゆっくりと引き出される。血液貯蔵手段１３０は、さらに、血液貯蔵手段１３０を開口部１４０に接続するため、接続手段１５０を備えている。本発明の好ましい実施例では、開口部１４０と接続部材１５０は、各々、雄雌のルエルコネクターから成る。しかしながら、他のコネクター部材が第１の血液貯蔵手段１３０をカップリング１２６に密封して接続するために提供されることは、当業者には明らかであろう。

操作の際は、キャップ１４４は、開口部１４０から取り除かれて、そこに血液貯蔵手段１３０が接続される。次いで、血液が引き出され、あるいは好ましくは患者の心臓の圧力下で自由に流れることができるように、かつ、接続部材１０６、１１４及びチューブ１２２を介して、シャフト１３６に送られるように、患者の血液流れの中に針１００が挿入される。接続部材１０６、１１４、チューブ１２２、シャフト１３６及び開口部１４０内にたまった空気は、前述したように、流れ通路に入った患者の血液によって、置換され、多孔質プラグ１４２を介して通気される。引き出され、あるいは患者からの心臓の圧力下で流れる血液の第１の部分は、通気される前に、たまった空気にさらされるので、概ね汚染されており、それゆえ、嫌気性血液採取に適していない。従って、この第１の血液の部分は、一時的に貯蔵するために、血液貯蔵手段１３０の中へカップリング１２６から引き出され、一方、嫌気性血液サンプルは、第２の血液貯蔵手段１３２を介して受取られる。嫌気性血液サンプルが受取られた後、血液貯蔵手段１３０内に一時的に貯蔵された血液は、捨てられ、あるいは、チューブ１２２及び針１００を介して患者に戻される。

嫌気性血液サンプルを引き出すため、第２の血液貯蔵手段１３２がアダプタースリーブ１３８を介してカップリング１２６に接続されている。第２の血液貯蔵手段１３２は、当業界で周知のベクトン・ディケンソン・バキュティナーから成っていてもよい。血液貯蔵手段１３２は、患者から抜き取られた嫌気性血液サンプルを受け入れる血液貯蔵チャンバー１５２を有している。針１５４は、針ハブ１５６に密封して接続されており、それらの組立体は、適合性を有するカップリング１５８（普通は、バキュテイナーアダプターとして言及されている）を介して血液貯蔵チャンバー１５２に密封して接続されている。当業界で周知のように、針１５４は、血液貯蔵チャンバー１５２と連通することを防止するため、シールを有している。さらに、当業界で周知のように、血液貯蔵チャンバー１５２は、患者から抜き取られた血液を汚染する空気を含まないようにするため、排気されている。適合性を有するカップリング１５８は、針１５４を血液貯蔵チャンバー１５２と連通させて配置するため、針１５４からシールを取り除く手段を備えている。

アダプタースリーブ１３８は、針ハブ１５６をきちんと受け入れるような径でできた内部アダプターチャンバー１６０を有している。アダプタースリーブ１３８の長さとシャフト１３６内のプラグ１４２の位置は、血液貯蔵手段１３２がアダプタースリーブ１３８に完全に挿入され、針１５４がプラグ１４２を通って通路１６２とチューブ１２２の第２の端部１２８との間に位置するように、選択される。針がシャフト１３６と同軸になるようにカップリング１２６内に挿入されることを可能とするため、針ガイド１６４がアダプタースリーブ１３８とプラグ１４２との間のカップリング１２６内に配置されている。針ガイド１６４は、カップリング１２６内への血液貯蔵手段１３２の挿入の間、針１５４を受け入れて、かつ、針がシャフト１３６と同軸となるように、プラグ１４２への針の挿入前に針を位置決めするために、設けられている。

操作の際は、嫌気性血液サンプルを集めるために、血液貯蔵手段１３０が、前述した開口部１４０を介してカップリング１２６に連結される。針１００が患者の血液流れの中に挿入され、針１００、コネクター１０６、１１４、チューブ１２２及びカップリング１２６の内部にたまった空気が前述したようにプラグ１４２を介して排気される。次いで、血液貯蔵手段１３２の針１５４が、チューブ１２２の近傍の通路１６２を越えて位置するように、プラグ１４２を通してカップリング１２６内に挿入される。針１５４内にたまった汚染空気のどんなにわずかの部分でもプラグ１４２を介して排気されるように、すなわち、嫌気性血液サンプルを受け入れる前にカップリング１２６から取り除かれるように、血液サンプルの汚染された部分を貯蔵手段１３０内に貯蔵する前に、針１５４をカップリング１２６へ挿入することが望ましい。

針１５４がカップリング１２６内に適当に挿入された後、汚染された血液の第１の部分はカップ

リング１２６から一時貯蔵のため血液貯蔵手段１３０へ引き出される。このとき、針１５４のシールは、嫌気性血液サンプルが血液貯蔵１５２へ導かれるように、当業界で周知のように、適合性カップリング１５８によって除去される。血液貯蔵チャンバー１５２へ導かれた血液のほぼ全部がチューブ１２２から受け取った血液であって、血液貯蔵手段１３０の血液貯蔵チャンバー１４６から受け取った血液ではないようにするために、針１５４は、通路１６２とチューブ１２２との中間でかつ、チューブ１２２の第２の端部１２８の近傍の、シャフト１３６内のカップリング１２６内に位置していることが好ましい。

本発明の代わりの実施例では、嫌気性血液サンプルを受け取っているとき、血液貯蔵手段１３０内に貯蔵された汚染された血液サンプルを、操作中に、シャフト１３６からほぼ隔離することができるバルブ、あるいは他の選択性カップリング手段を備えることが望ましい。

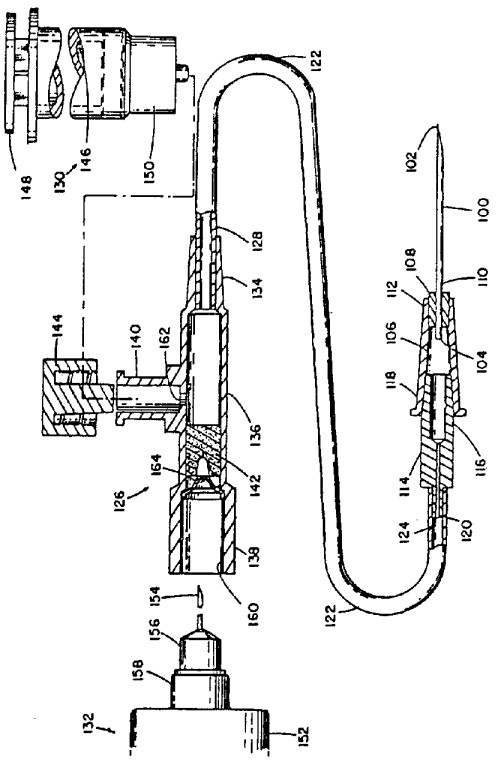
医療業界では普通となっているように、キャップ１４４に加えて、複数のキャップあるいは他のシール手段が、針１００に配置してアダプタースリーブ１３８のチャンバー１６０を密封するために設けられてもよい。

新規な血液採取装置の好ましい実施例のいくつかのみをここで詳細に説明したが、当業者には、多くの改良や変更が容易に明らかとなるであろう。本発明の真の範囲及び精神に入るこのようなすべての改良や変更を包含することが、特許請求の範囲の趣旨である。

4.図面の簡単な説明

第１図は、本発明の改良された血液採取装置の断面図を示す。

１００・・・・・針
１０６・・・・・第１の接続部材
１１４・・・・・第２の接続部材
１２２・・・・・チューブ
１２６・・・・・カップリング
１３０、１３２・血液貯蔵手段
１３４・・・・・接続部材
１３６・・・・・シャフト
１３８・・・・・アダプタースリーブ
１４０・・・・・開口部
１４２・・・・・プラグ
１４４・・・・・キャップ
１４６、１５２・血液貯蔵チャンバー
１４８・・・・・プランジャー
１５４・・・・・針



Espacenet

Bibliographic data: WO2011162772 (A1) — 2011-12-29

BLOOD DRAWING DEVICE WITH FLASH DETECTION

Inventor(s): FISCHEL LLOYD [US]; BROWN LEROY [US] ± (FISCHEL, LLOYD, ; BROWN, LEROY)

Applicant(s): CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHEL LLOYD [US]; BROWN LEROY [US] ± (CLEARVIEW PATIENT SAFETY TECHNOLOGIES, LLC, ; FISCHEL, LLOYD, ; BROWN, LEROY)

Classification: **- international:** ***A61M5/36***
- cooperative: **A61B5/15003 (EP); A61B5/150213 (EP); A61B5/150389 (EP); A61B5/150496 (EP); A61B5/150572 (EP); A61B5/150732 (EP); A61B5/15074 (EP); A61B5/150992 (EP); A61B5/1545 (EP);** A61B5/150473 (EP)

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.

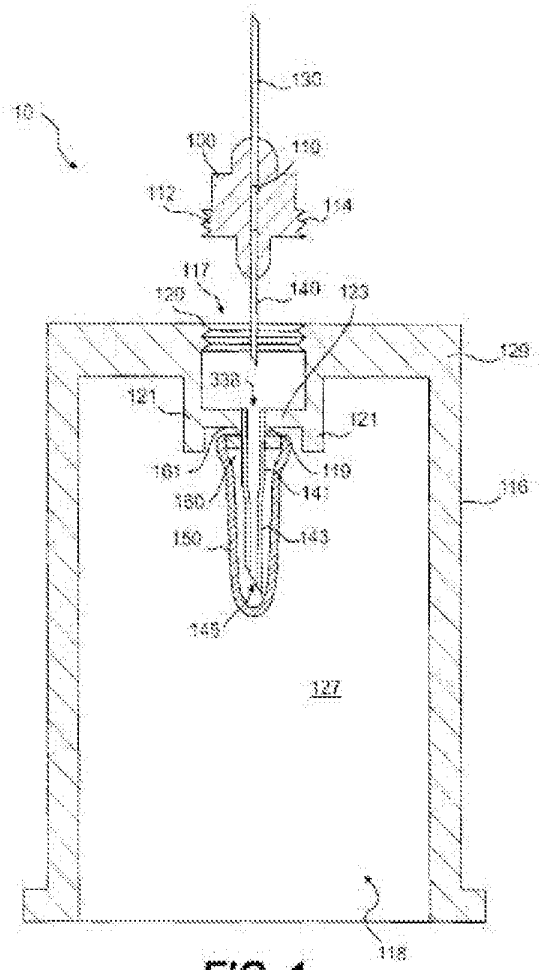

10
130
100
110
112
114
117
120
140
123
125
338
121
121
160
110
141
116
150
143
145
127
118

FIG. 1

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 December 2011 (29.12.2011)

PCT

(10) International Publication Number
WO 2011/162772 A1

(51) International Patent Classification:
A61M 5/36 (2006.01)

(21) International Application Number:
PCT/US2010/040030

(22) International Filing Date:
25 June 2010 (25.06.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
12/822,931 24 June 2010 (24.06.2010) US

(71) Applicant *(for all designated States except US)*: **CLEARVIEW PATIENT SAFETY TECHNOLOGIES, LLC** [US/US]; 20 N. Lanikai Place, Haiku, HI 96708 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **FISCHEL, Lloyd** [US/US]; 20 N. Lanikai Place, Haiku, HI 96708 (US). **BROWN, Leroy** [US/US]; 9393 River Oaks Lane, Orangevale, CA 95662 (US).

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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK,

[Continued on next page]

(54) Title: BLOOD DRAWING DEVICE WITH FLASH DETECTION

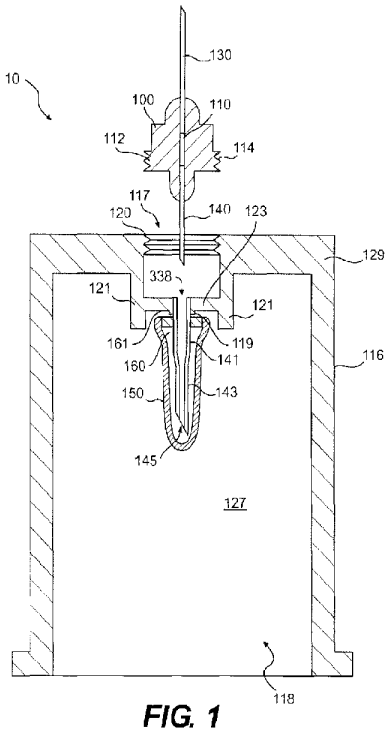


FIG. 1

(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.

WO 2011/162772 A1

SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

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

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 ninteenth 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, hydrophyllic/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/hydrophyllic 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).

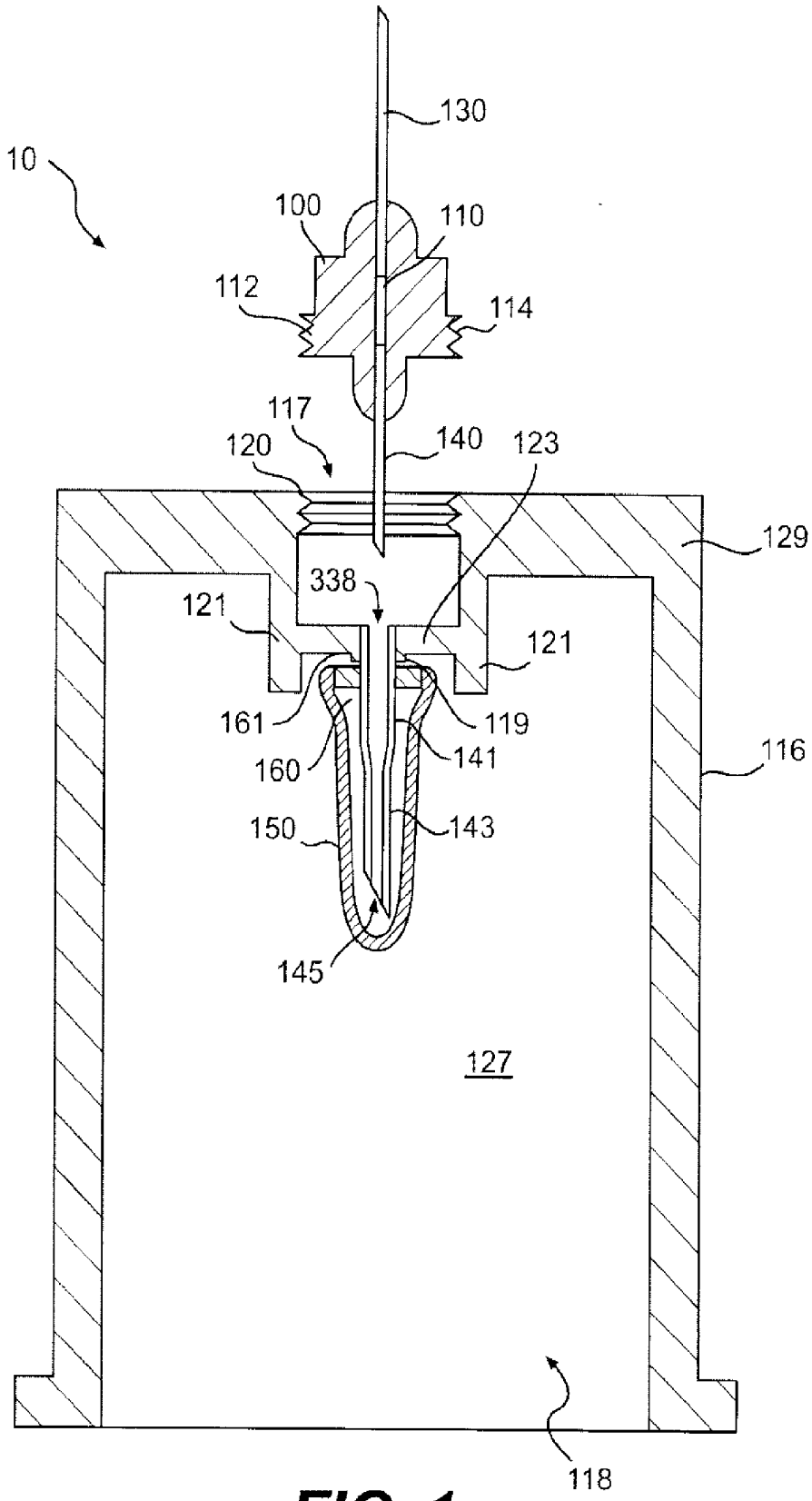

10
130
100
110
112
114
117
120
140
123
129
338
121
121
161
119
160
141
150
143
145
116
127
118

FIG. 1

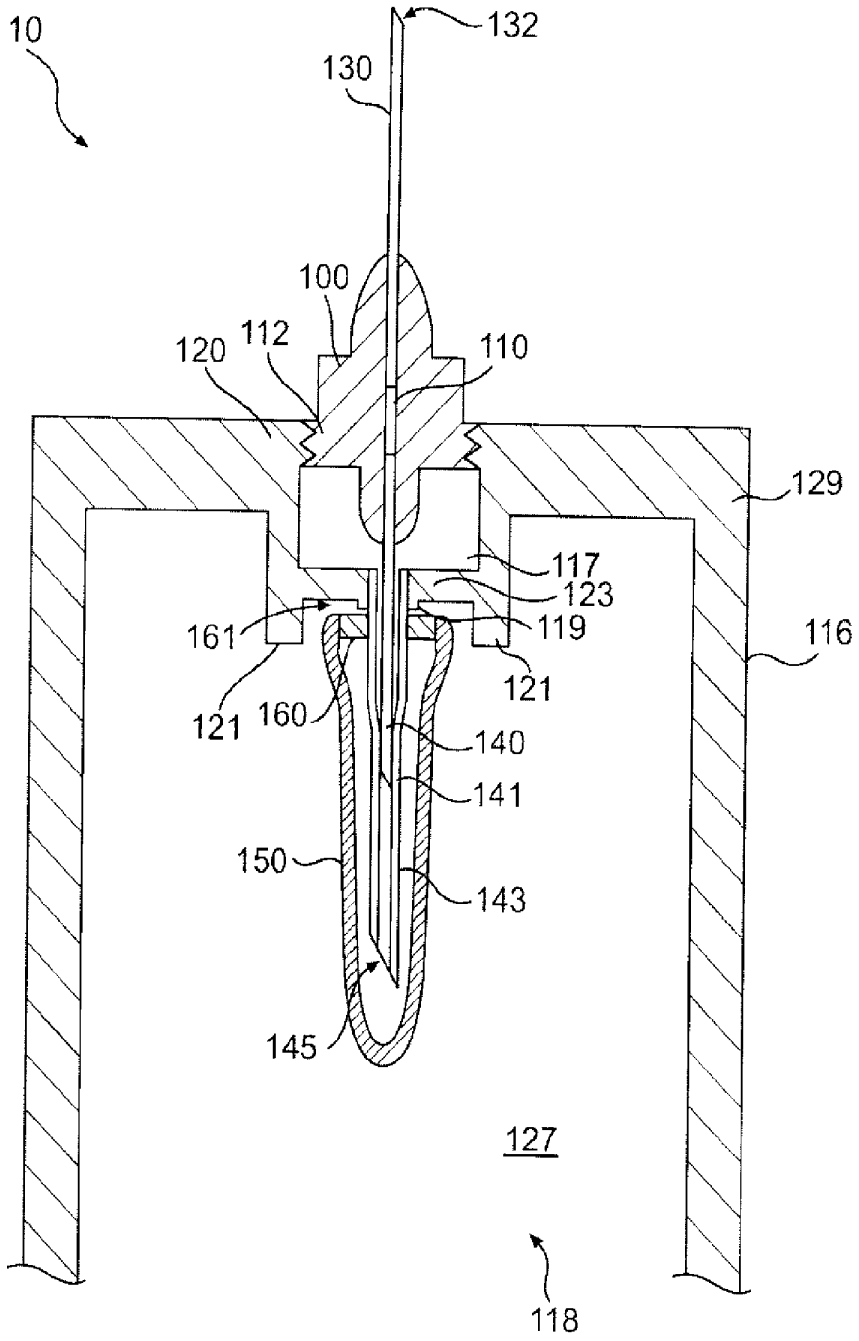

10
132
130
100
120
112
110
129
117
123
161
119
116
121
121
160
140
141
150
143
145
127
118

FIG. 2

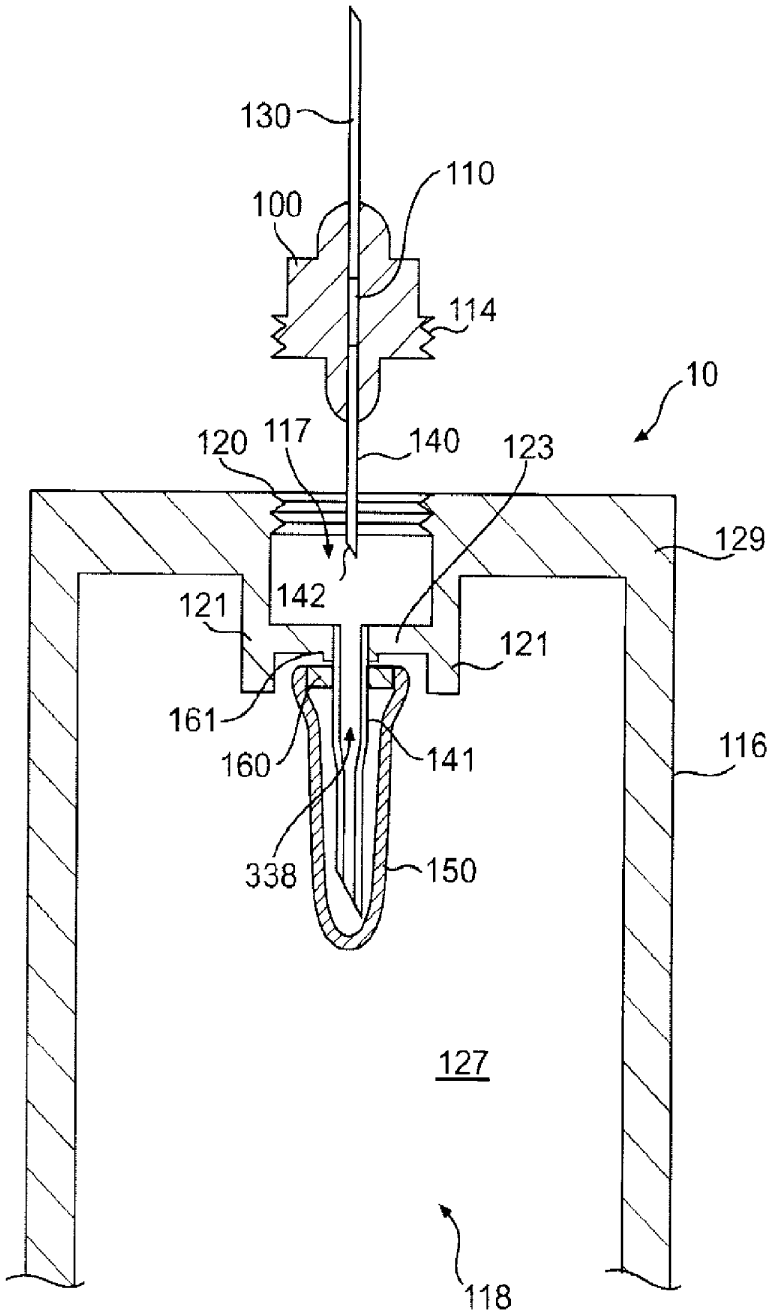


FIG. 3

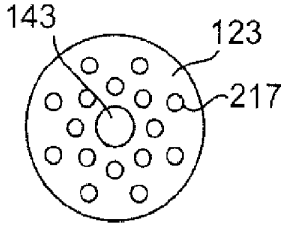


FIG. 4

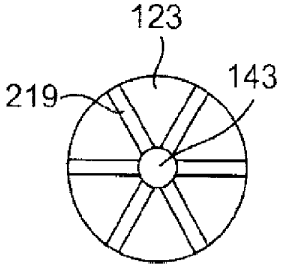


FIG. 5

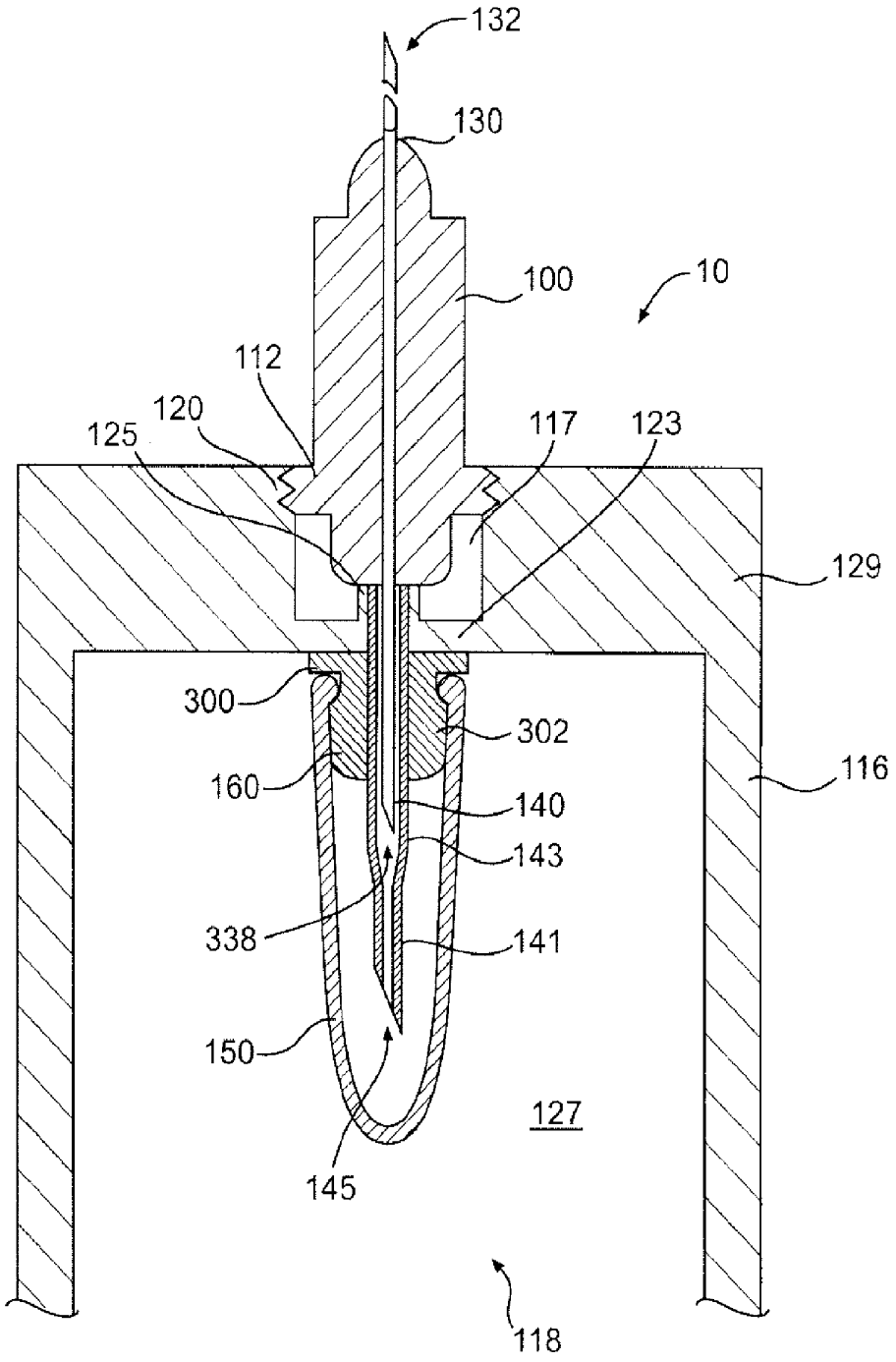

132
130
100
10
112
120
125
117
123
129
300
302
160
116
140
143
338
141
150
127
145
118

FIG. 6

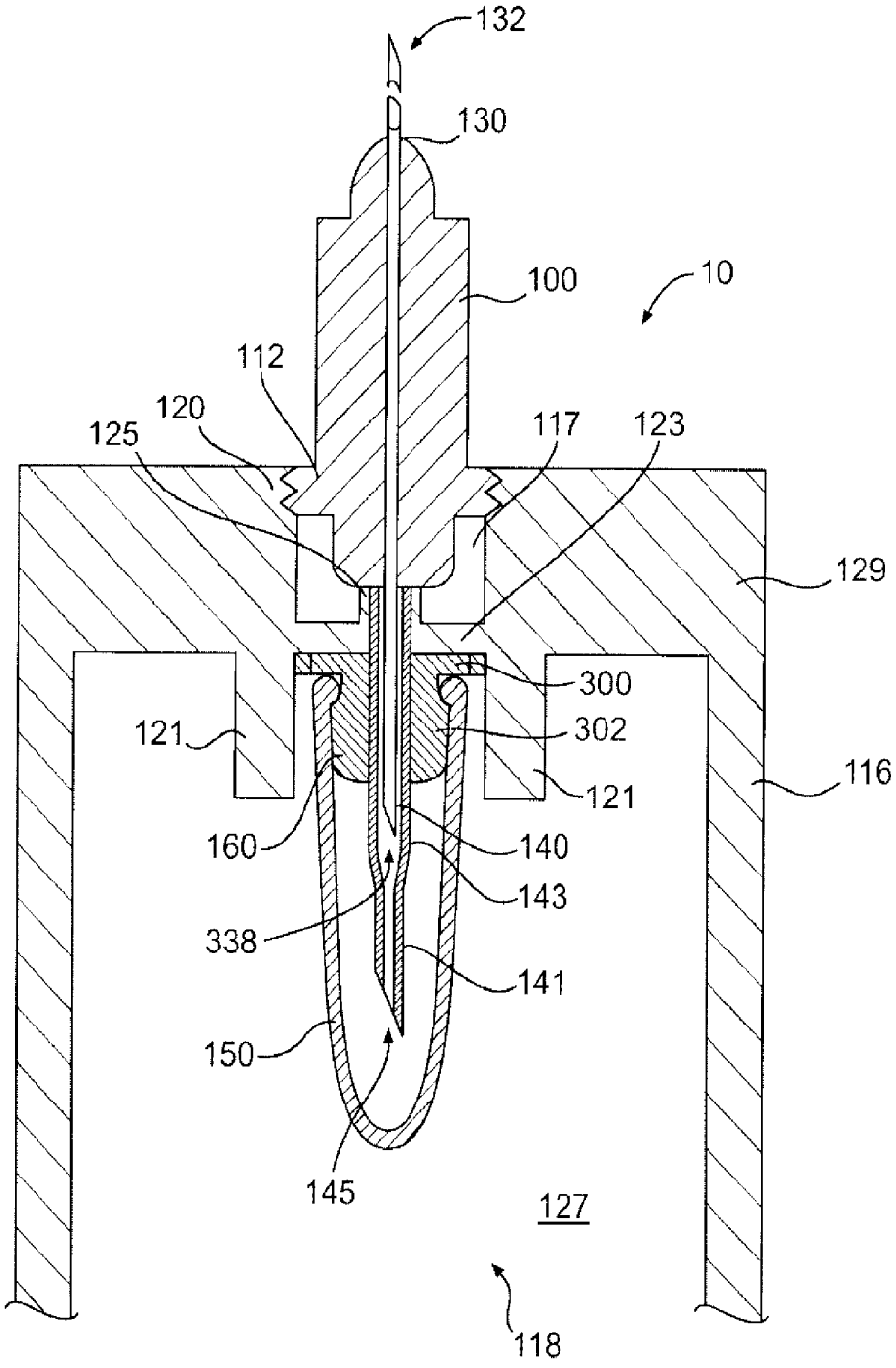

132
130
100
10
112
120
125
117
123
129
300
121
302
121
116
160
140
143
338
141
150
145
127
118

FIG. 7

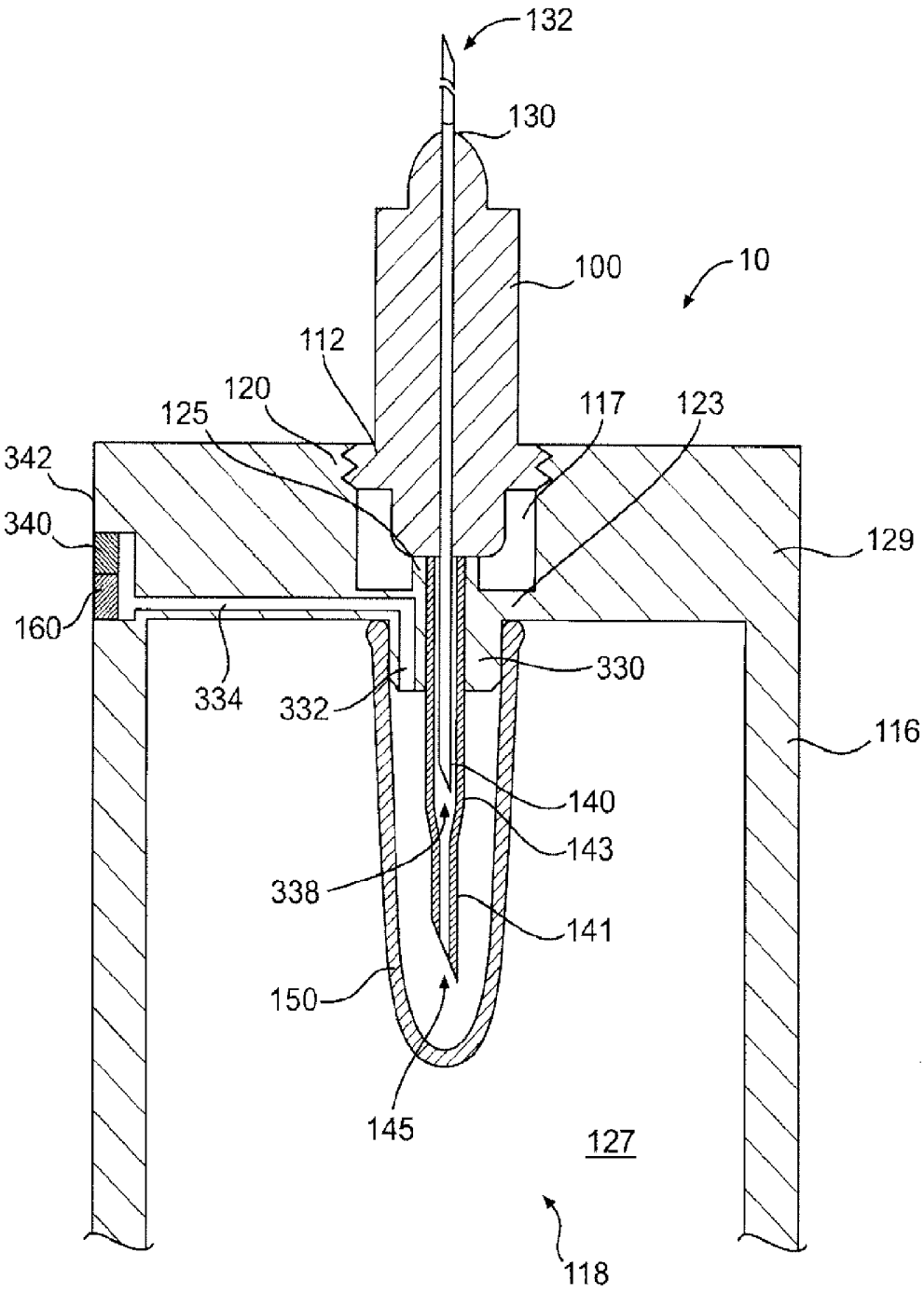

132
130
100
10
112
120
125
117
123
342
340
129
160
334
332
330
116
140
143
338
141
150
145
127
118

FIG. 8

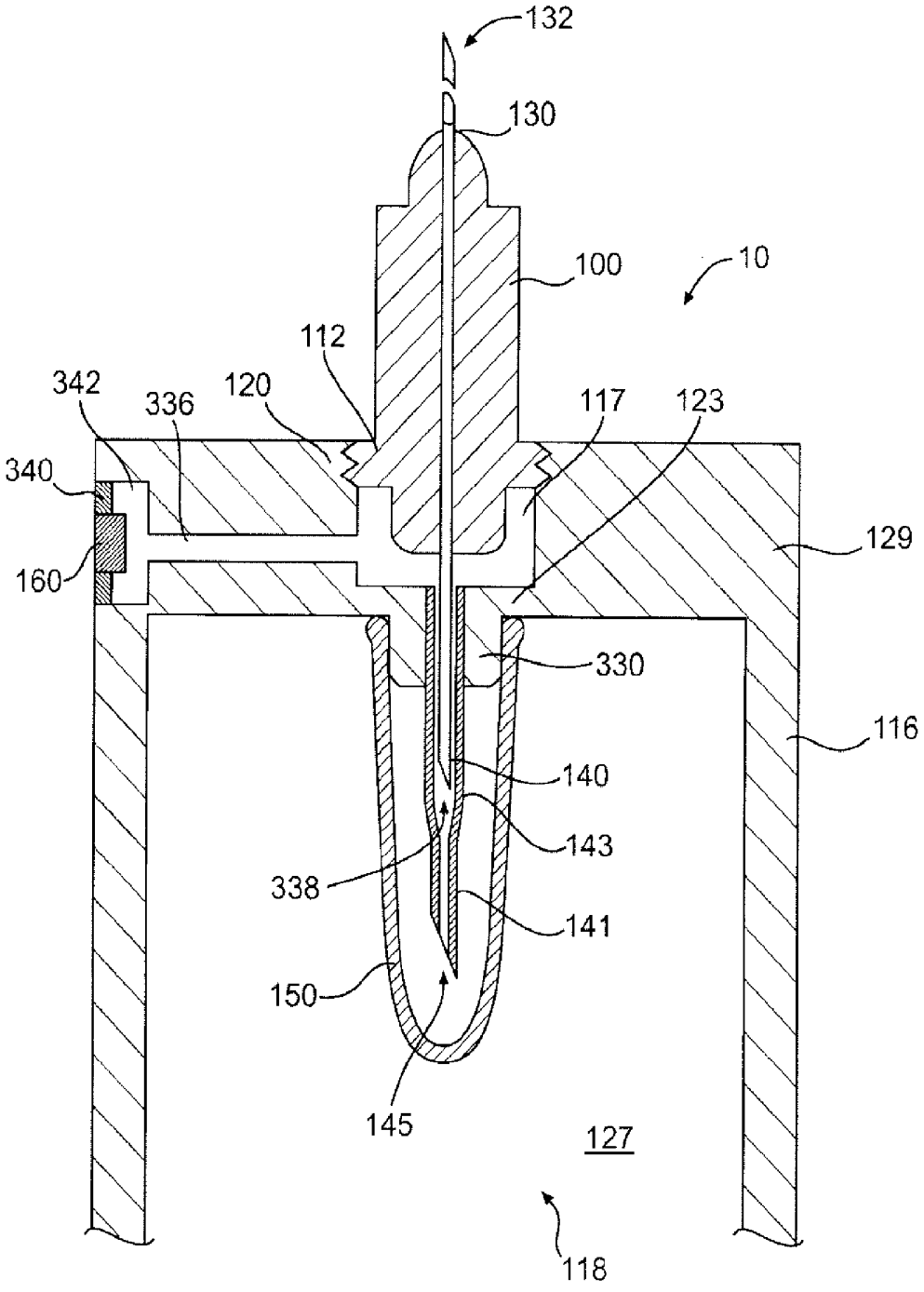

132
130
100
10
112
342
336
120
117
123
340
129
160
330
116
140
143
338
141
150
145
127
118

FIG. 9

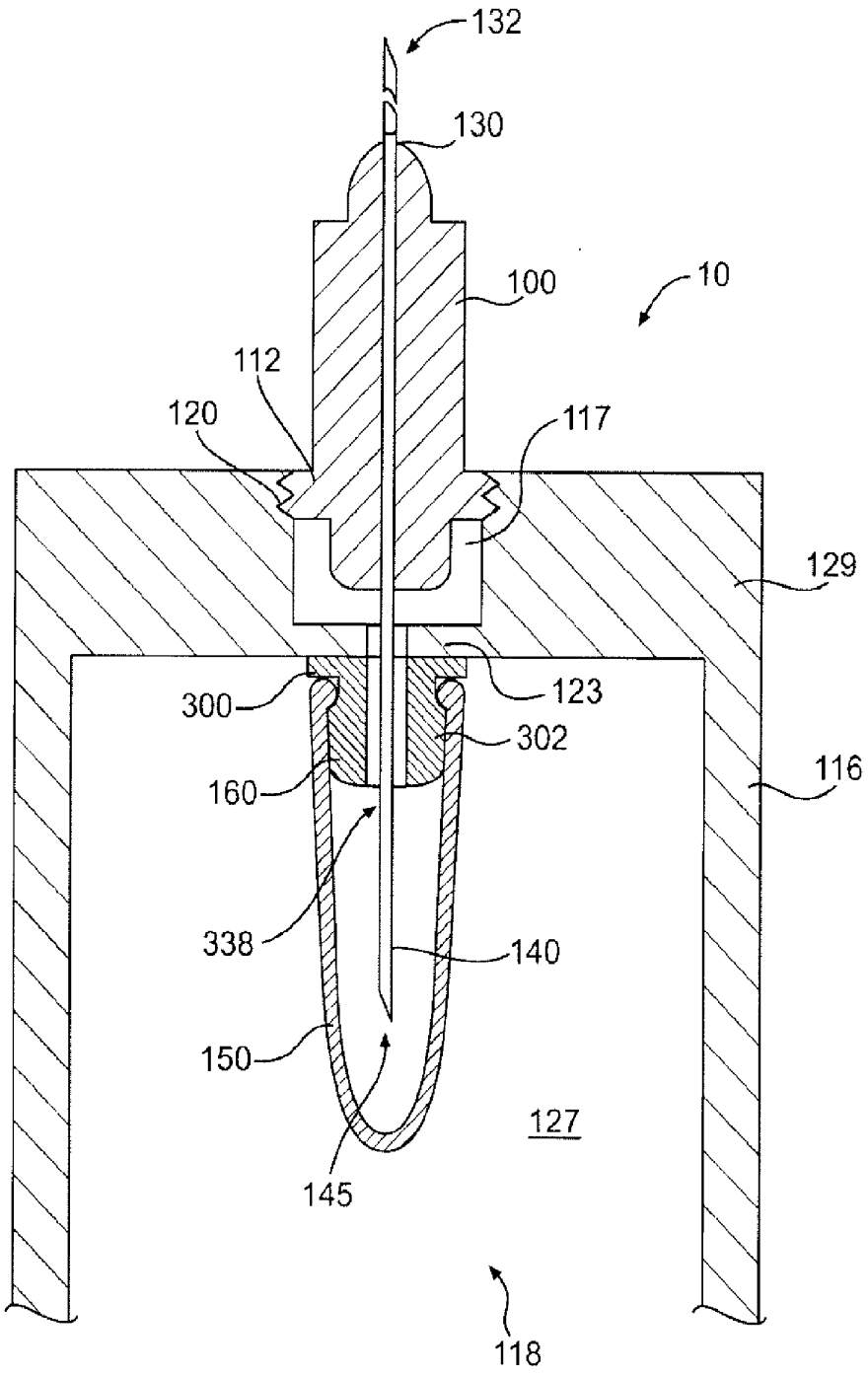

132
130
100
10
112
120
117
129
123
300
302
116
160
338
140
150
127
145
118

FIG. 10

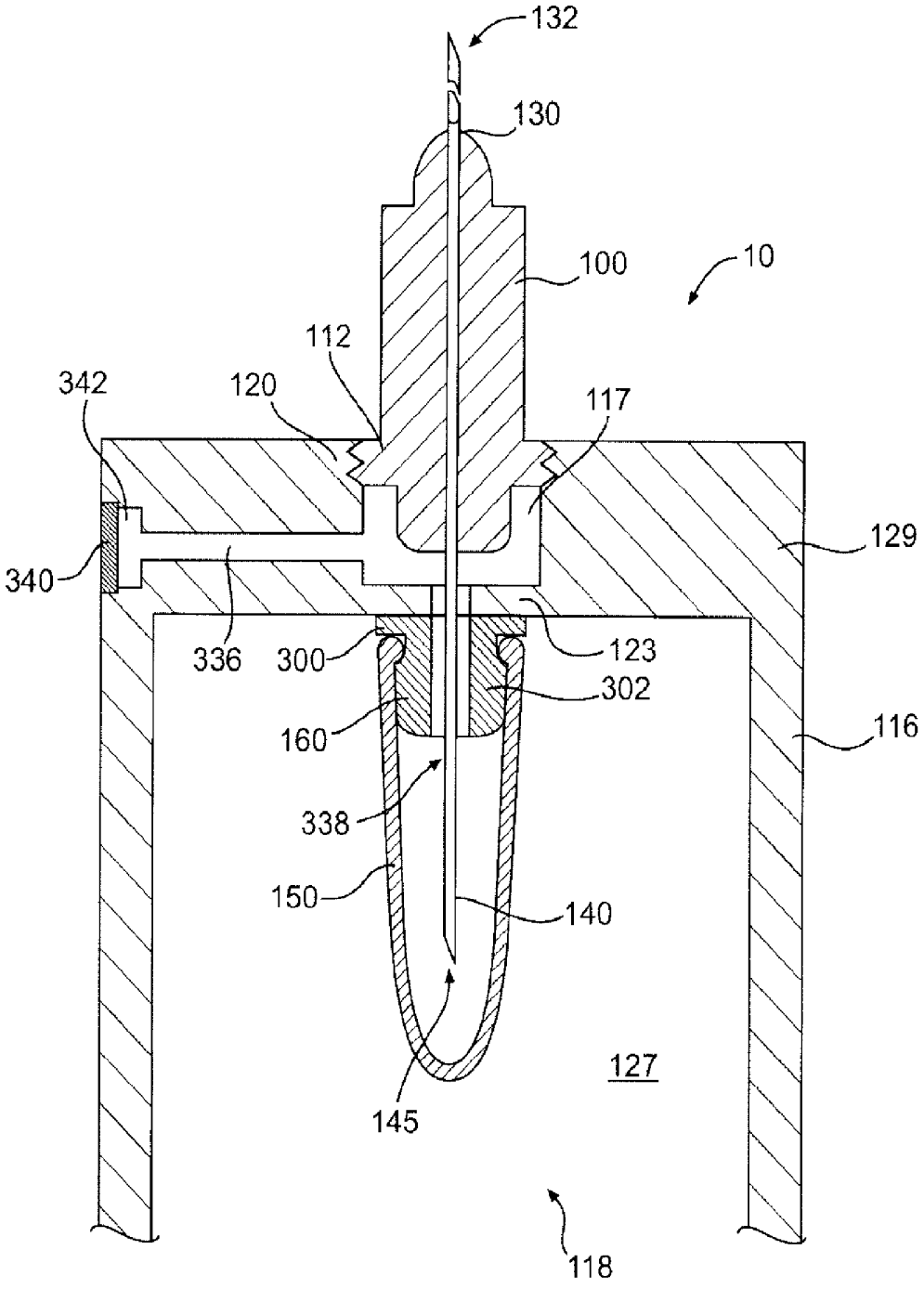

132
130
100
10
112
342
120
117
129
340
336
300
123
302
160
116
338
150
140
127
145
118

FIG. 11

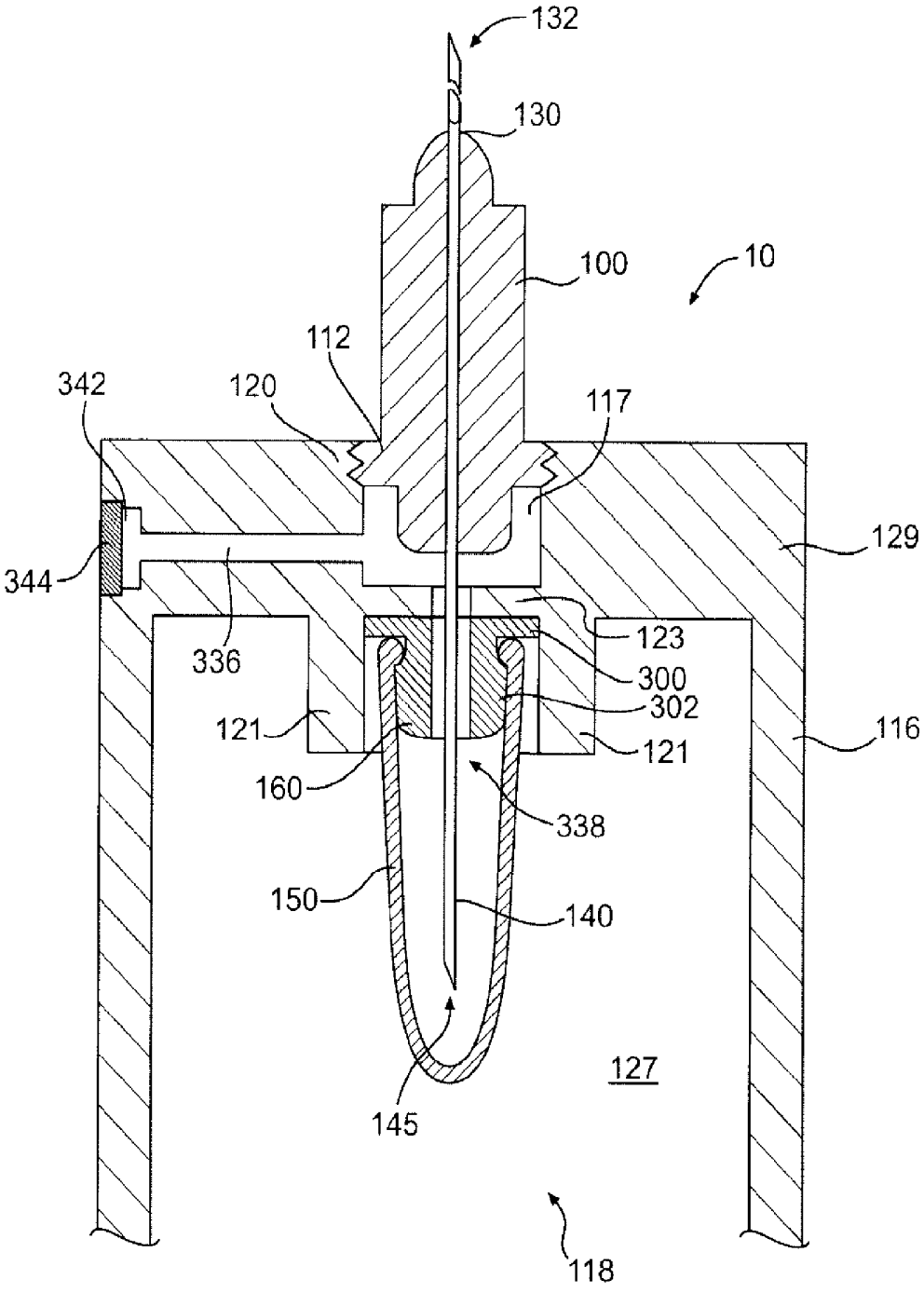

132
130
100
10
112
342
120
117
129
344
336
123
300
302
121
116
121
160
338
150
140
127
145
118

FIG. 12

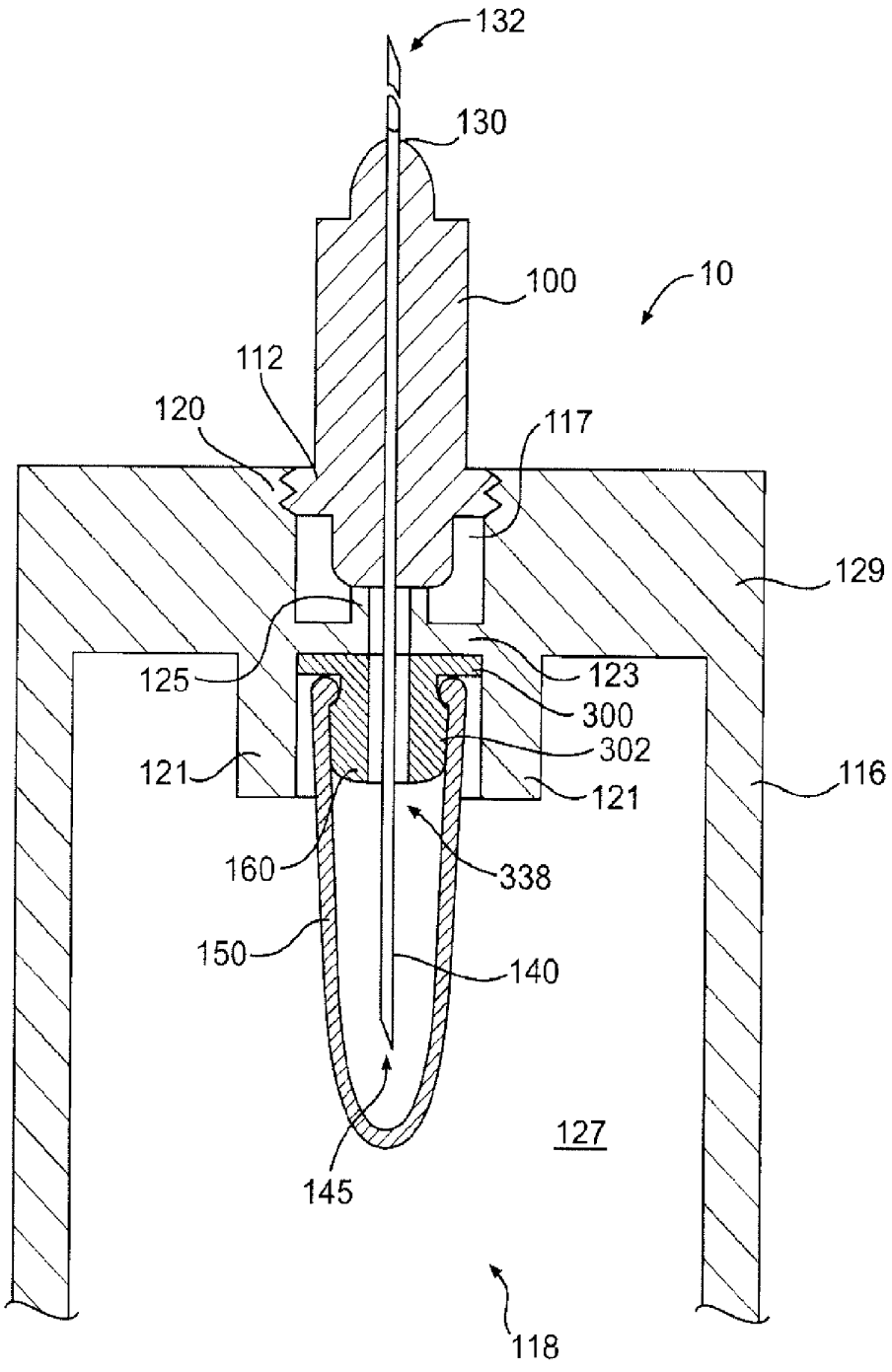

132
130
100
10
112
120
117
129
125
123
300
302
121
121
116
160
338
150
140
127
145
118

FIG. 13

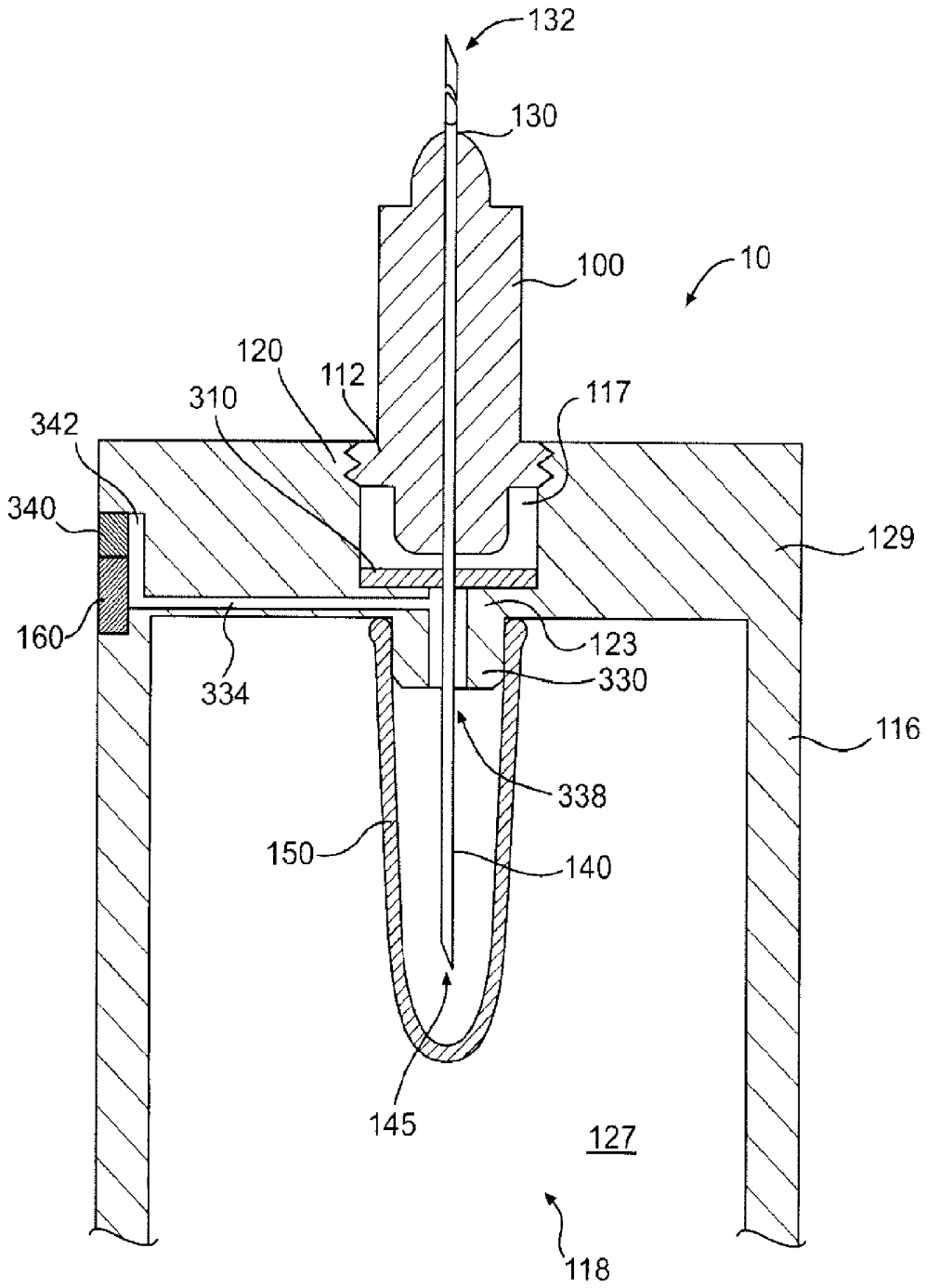

132
130
100
10
120
112
310
117
342
340
129
160
123
334
330
116
338
150
140
145
127
118

FIG. 14

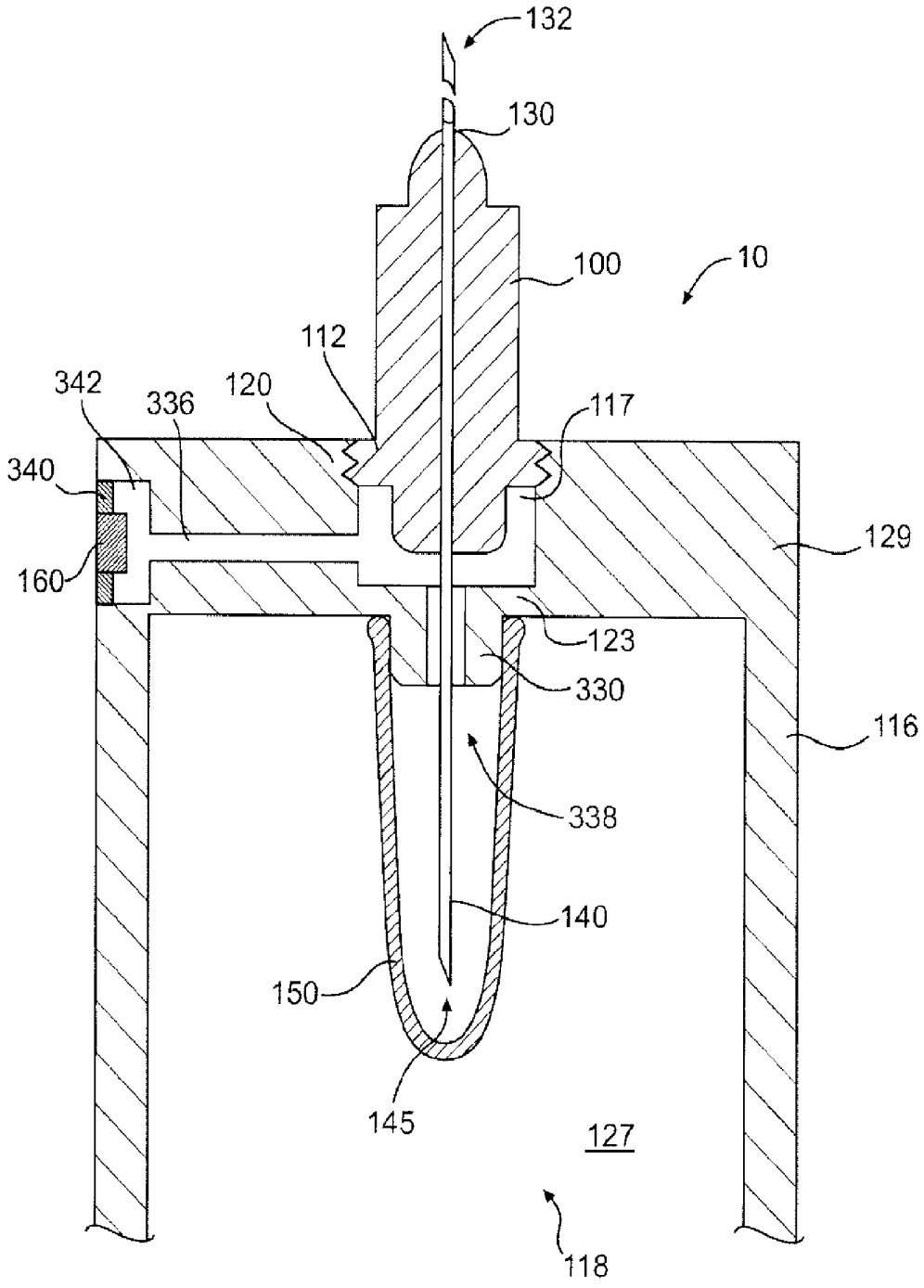

132
130
100
10
112
342
336
120
117
340
160
129
123
330
116
338
140
150
145
127
118

FIG. 15

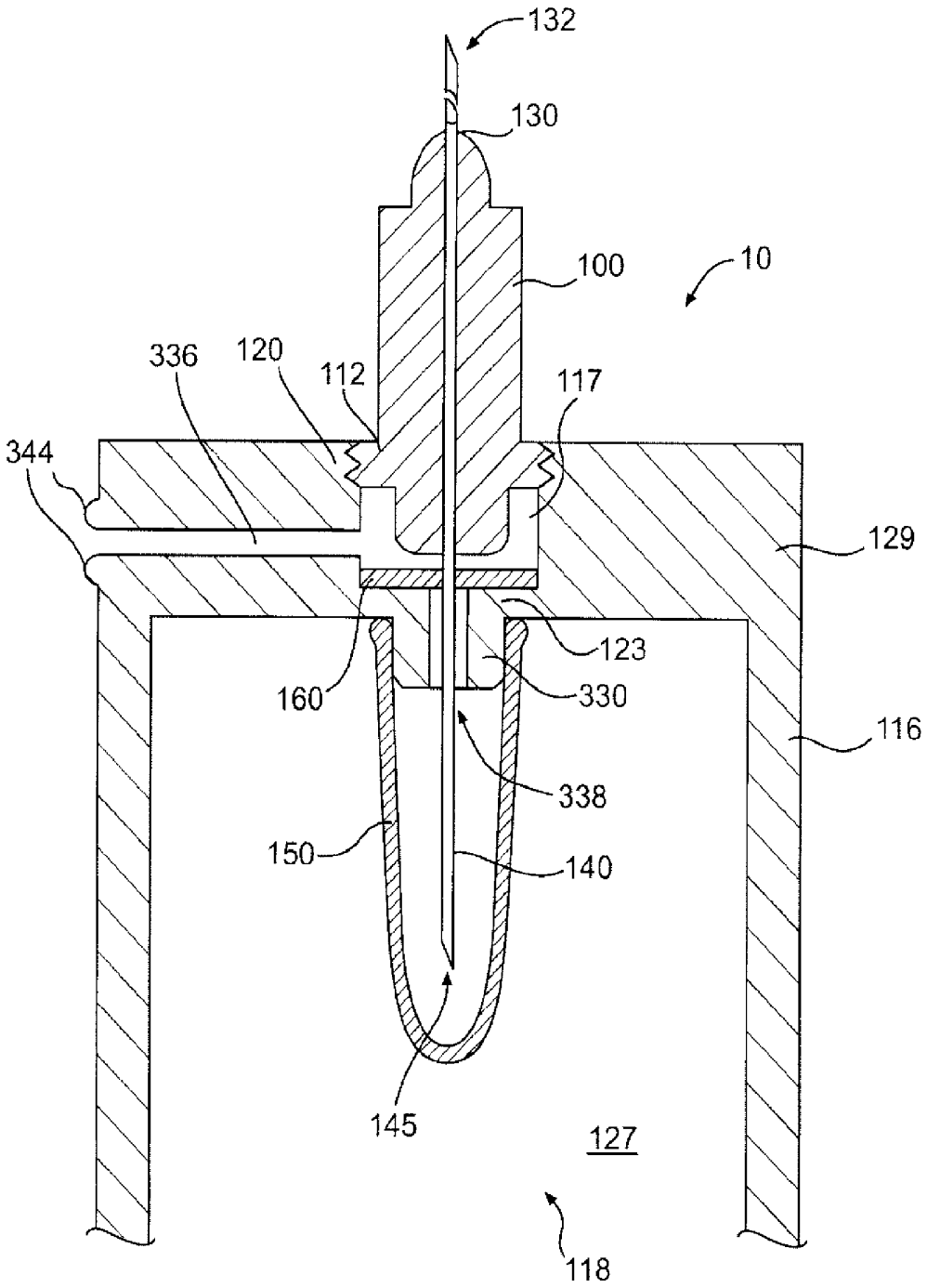

132
130
100
10
336
120
112
117
344
129
123
160
330
116
338
150
140
145
127
118

FIG. 16

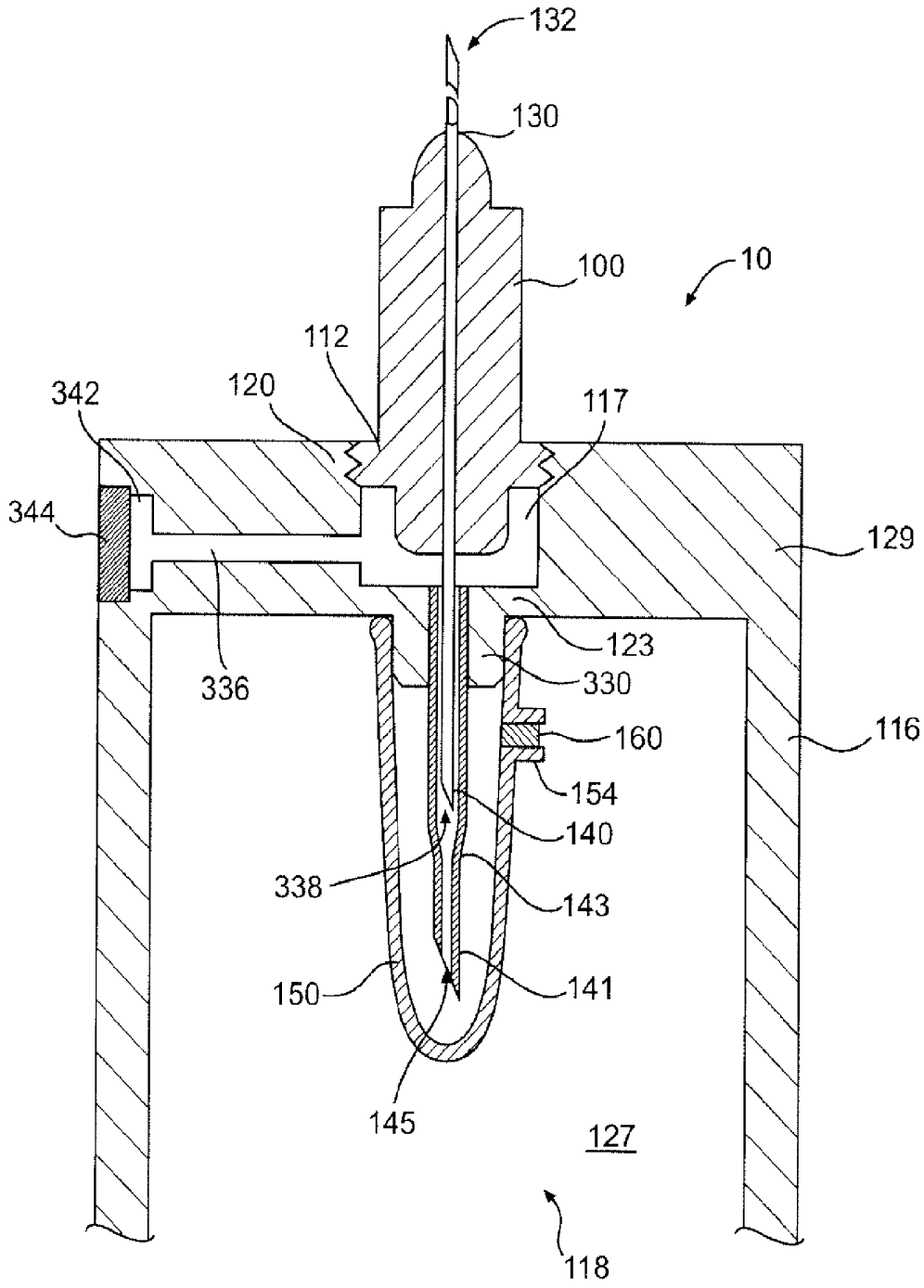

132
130
100
10
112
120
342
117
344
129
123
336
330
160
116
154
140
338
143
150
141
145
127
118

FIG. 17

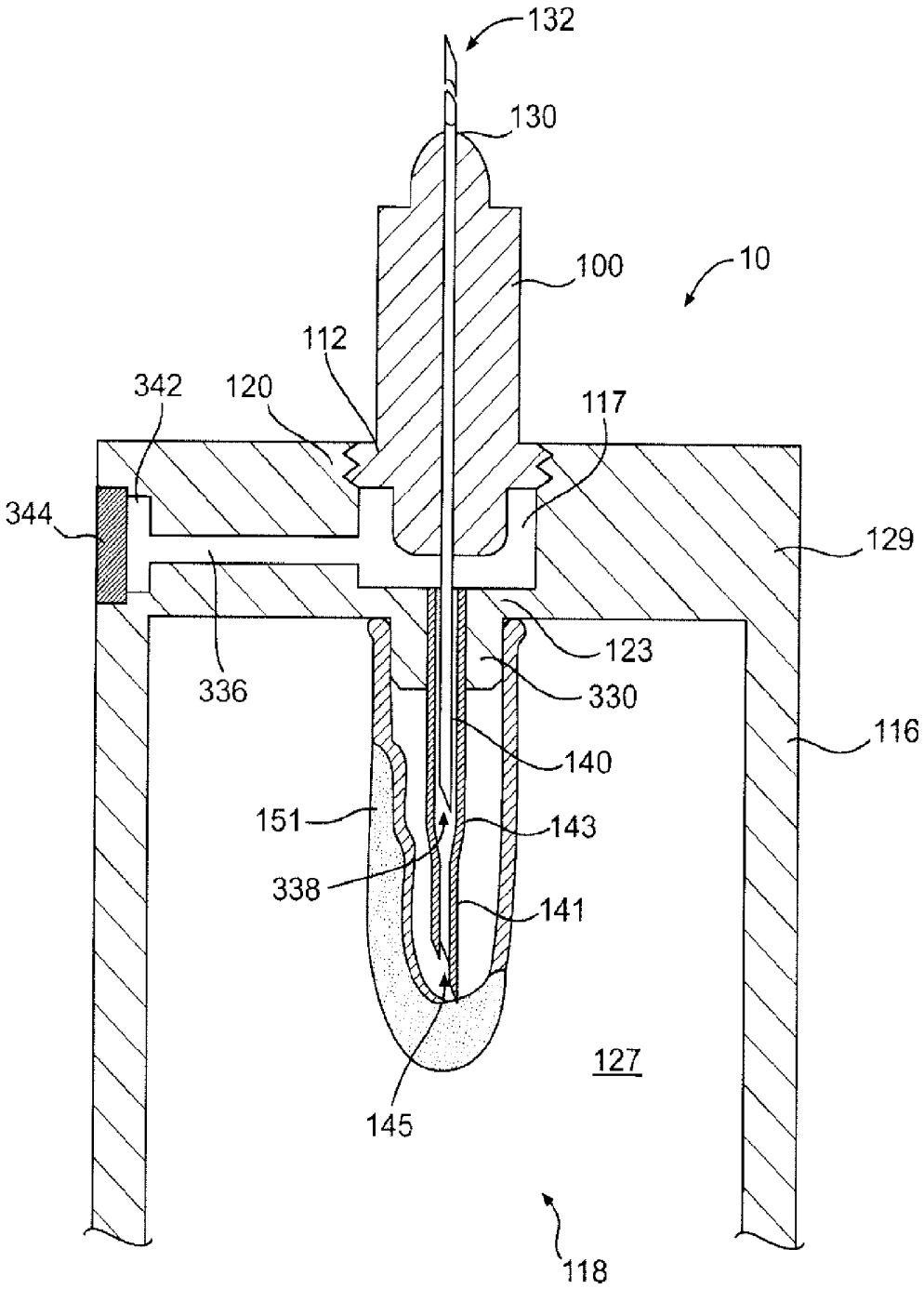

132
130
100
10
112
342
120
117
344
129
123
336
330
116
140
151
143
338
141
127
145
118

FIG. 18

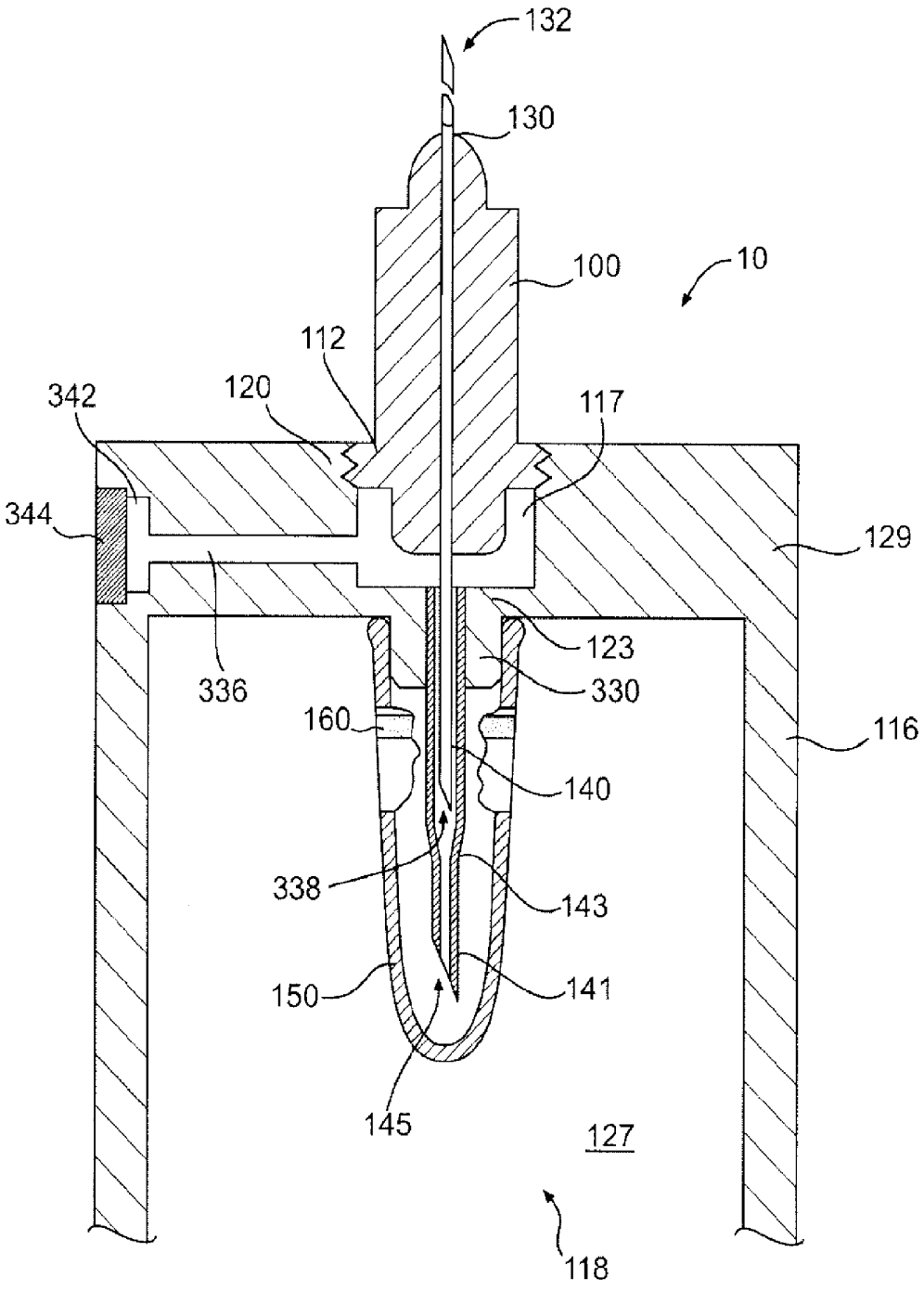

132
130
100
10
112
120
342
117
344
129
336
123
330
160
116
140
338
143
150
141
145
127
118

FIG. 19

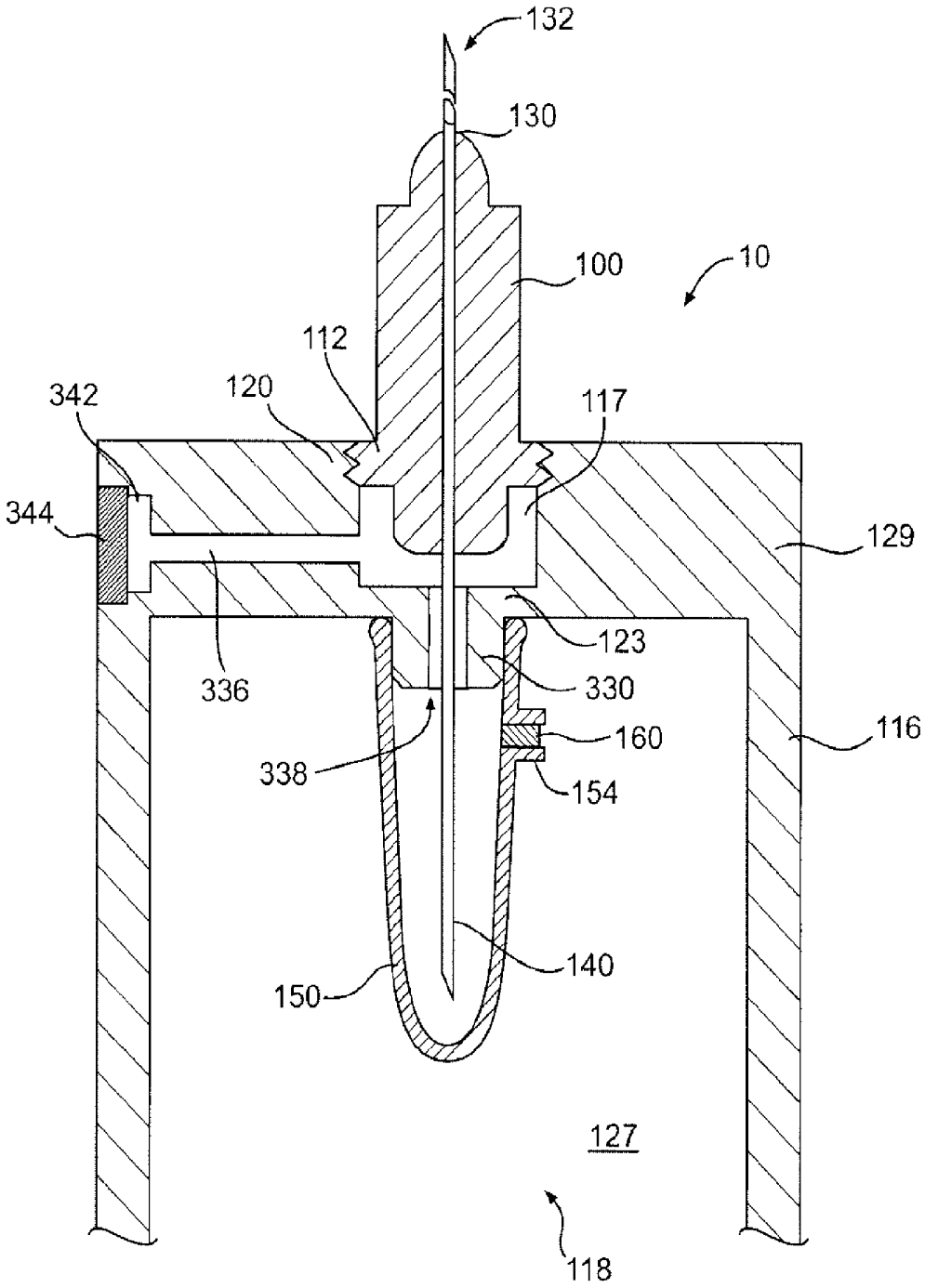

132
130
100
10
112
120
342
117
344
129
123
336
330
160
116
338
154
140
150
127
118

FIG. 20

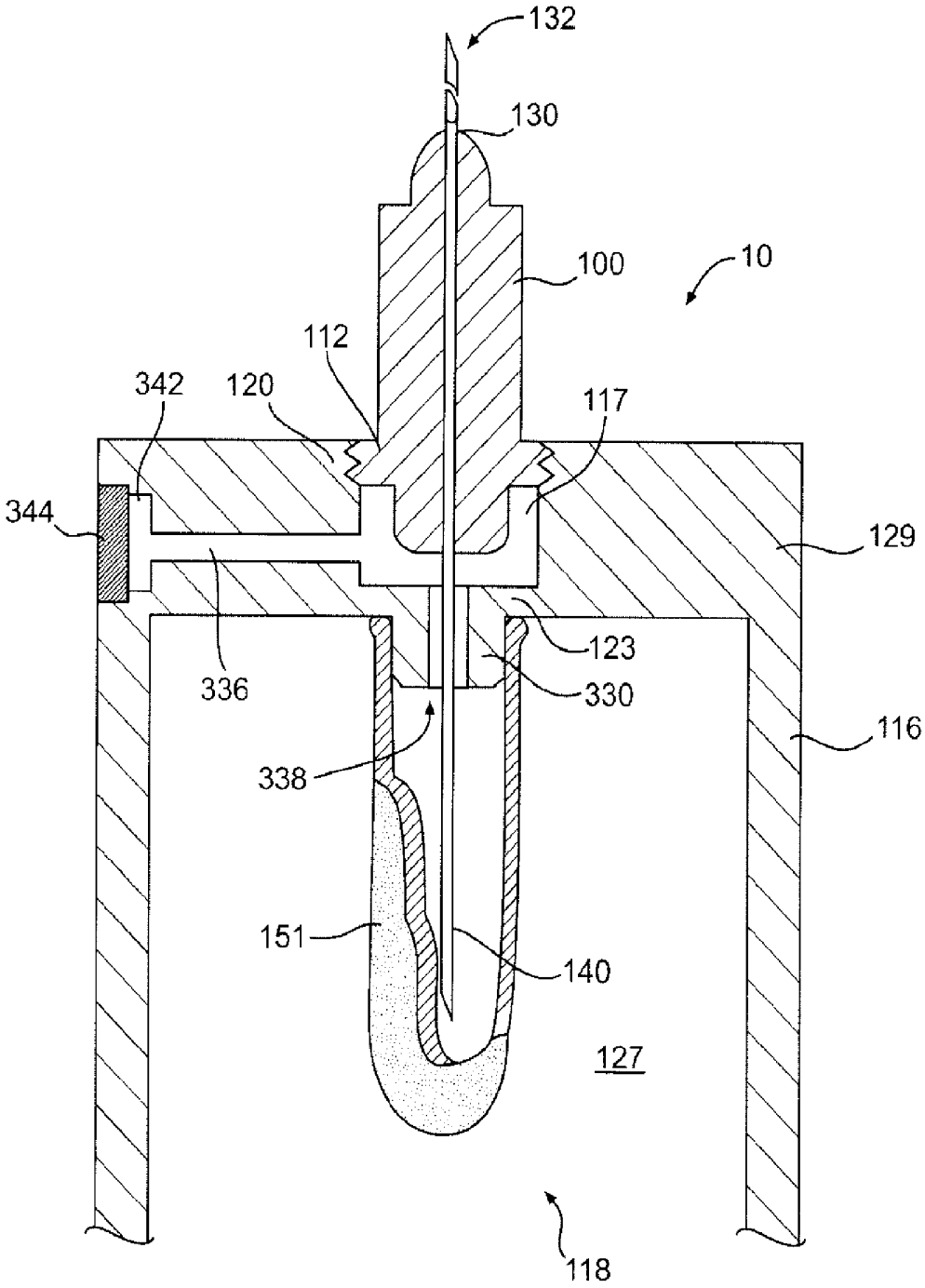

132
130
100
10
112
342
120
117
344
129
123
336
330
116
338
151
140
127
118

FIG. 21

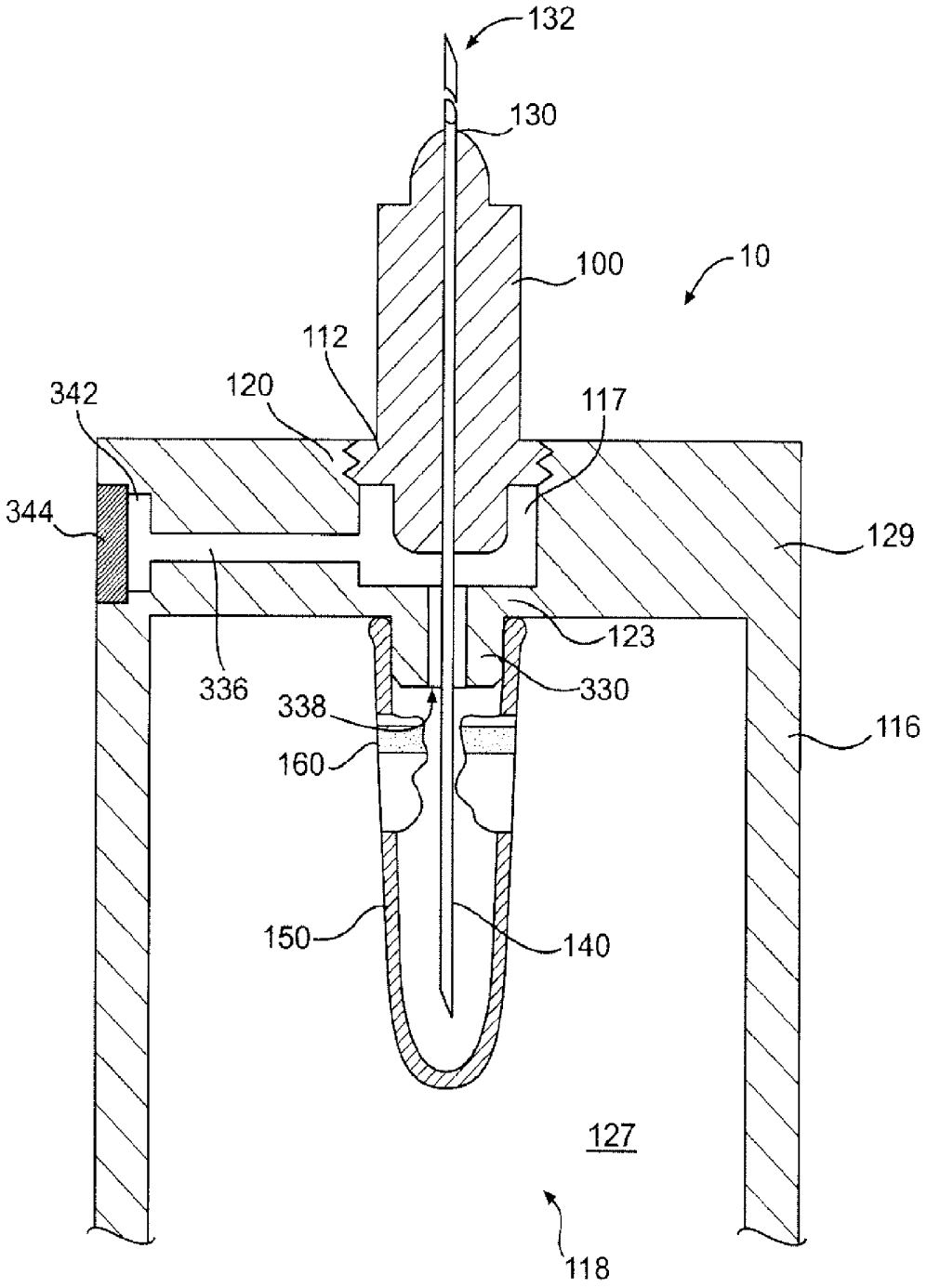

132
130
100
10
112
120
342
117
344
129
123
336
330
338
116
160
150
140
127
118

FIG. 22

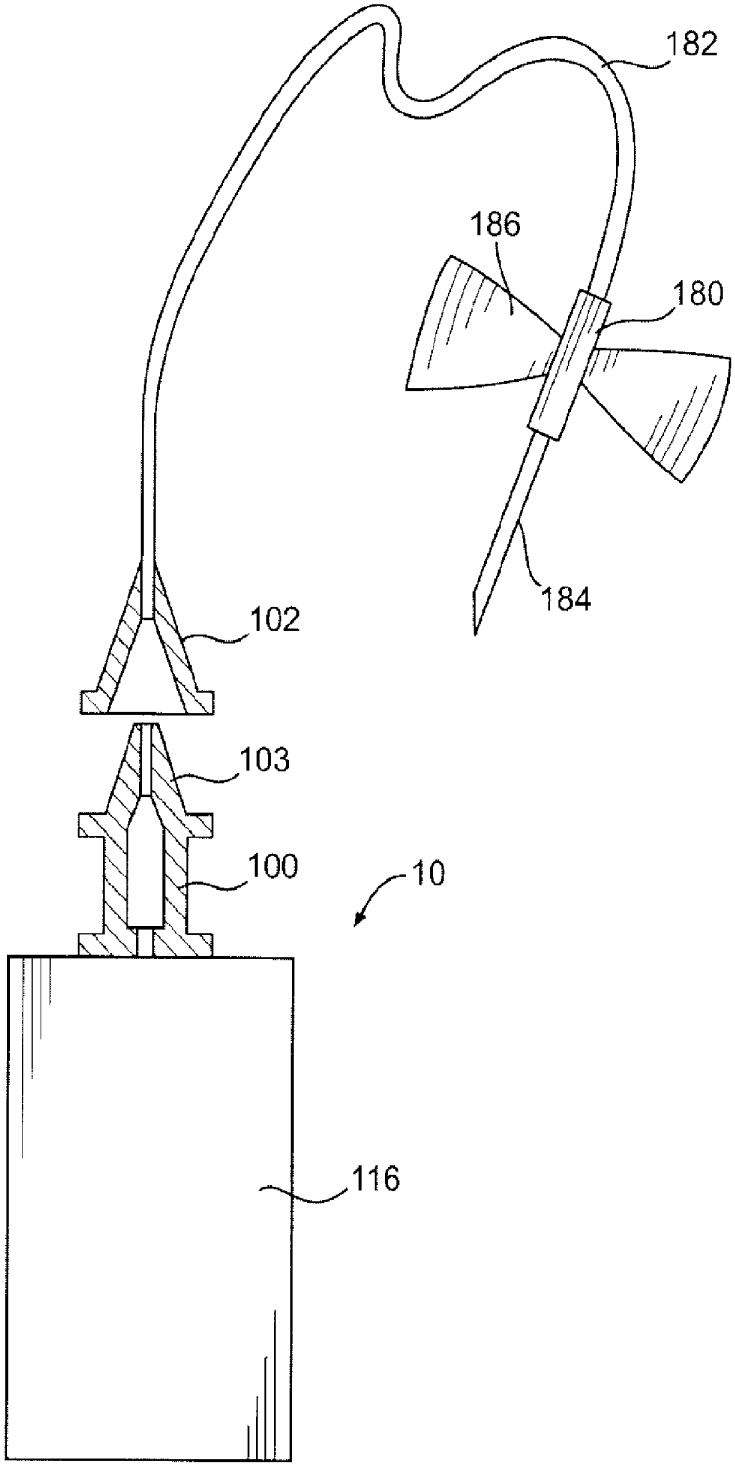


FIG. 23

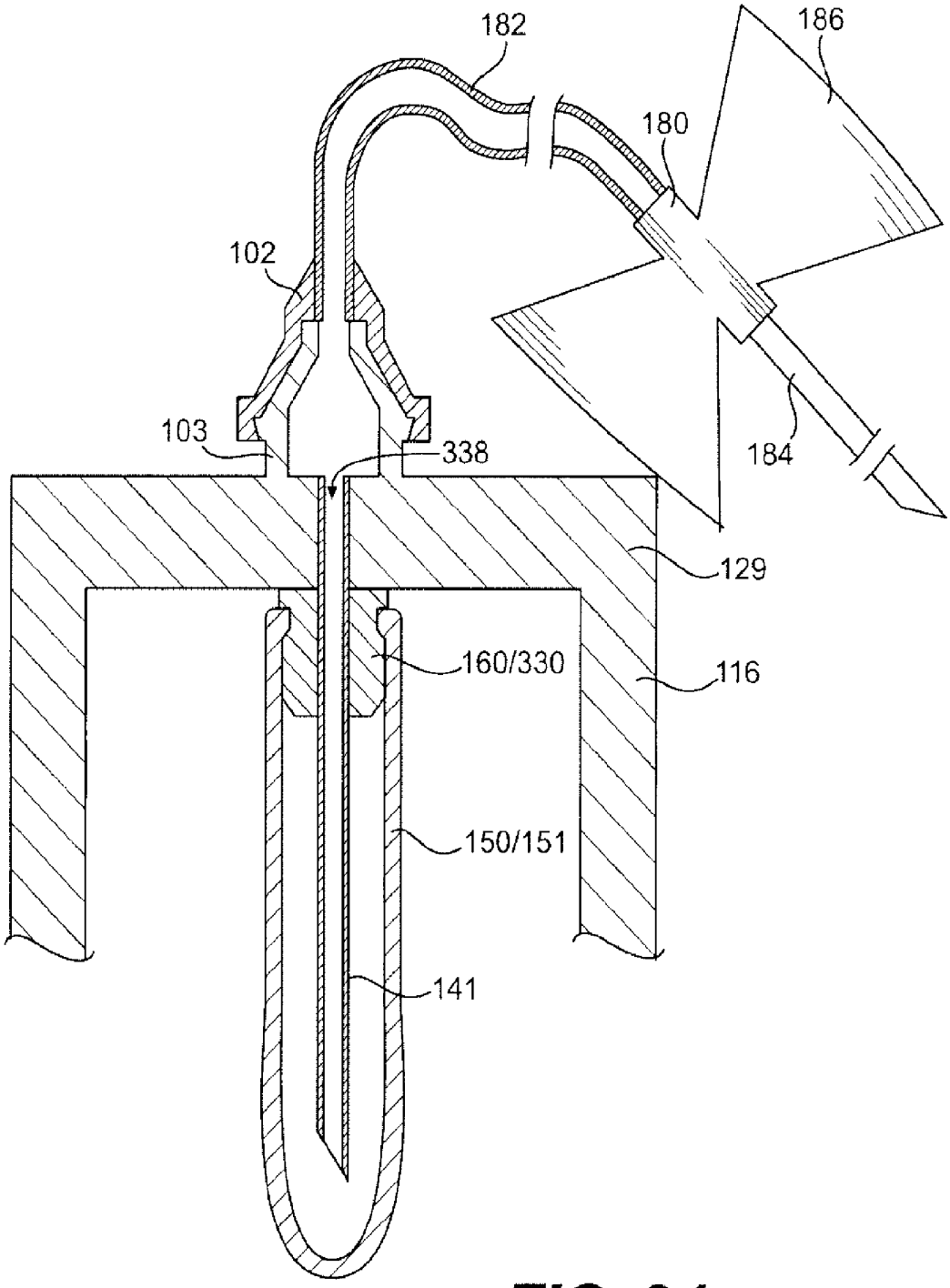


FIG. 24

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

Date of the actual completion of the international search	Date of mailing of the international search report
12 August 2010	30 AUG 2010
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

JP 2012-016496

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

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

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] JP 2012-16496 (P2012-16496A)
(43) [Published date] January 26, 2012 (2012.1.26)
(54) [Title of Invention] Sampling Port
(51) [International Patent Classification]
A61B 5/15 (2006.01)
A61B 5/154 (2006.01)
A61M 39/02 (2006.01)
[FI]
A61B 5/14 300Z
A61B 5/14 300E
A61M 5/14 459P
[Request for examination] Unclaimed
[Number of claims] 5
[Application form] OL
[Total number of pages] 12

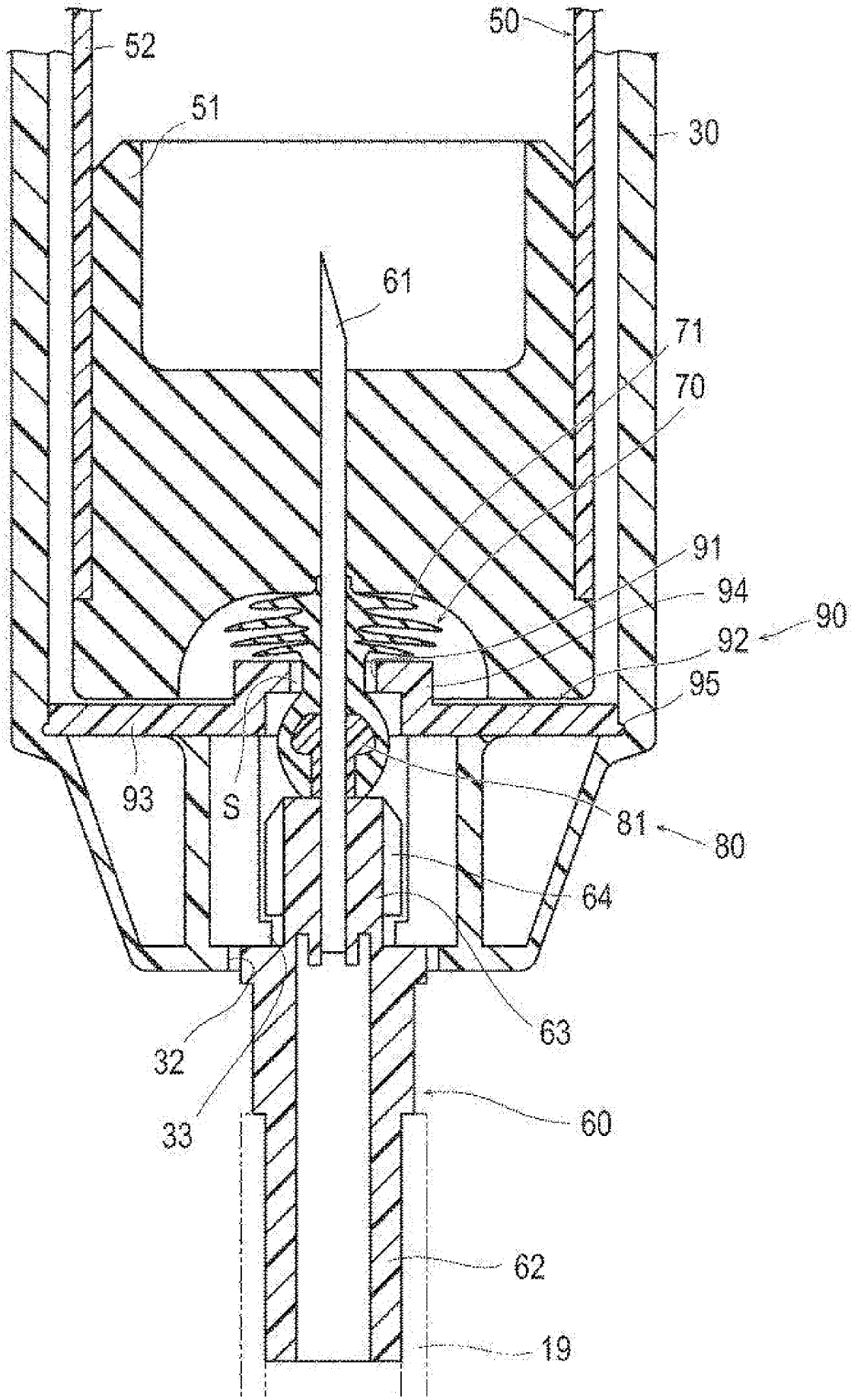
(21) [Application number] Patent Application 2010-156165 (P2010-156165)
(22) [Filing Date] July 8, 2010 (2010.7.8)
(71) [Applicant]
[Identification Number] 000109543
[Name] Terumo Corporation
(74) [Agent]
[Identification number] 110000671
[Name] Hatta International Patent Business Corporation
(72) [Inventor]
[Name] Masahide Murakoshi
(72) [Inventor]
[Name] Masahiro Akiyama
(72) [Inventor]
[Name] Aya Hayakawa
[Theme code (reference)]
4C038
4C066
[F term (reference)]
4C038TA01
4C038TA10
4C038UA10
4C038UB07
4C038UF03
4C038UF11
4C038UF14 4C066 AA07
4C066BB10 4C066FF05 4C066JJ08

wrap up close

(57) [Summary]
[Problem] To hold a rubber cap on a needle assembly even when the rubber cap is elastically contracted and wrinkled as a hollow needle is passed through a rubber plug of a blood collecti on tube. To provide a sampling port capable of maintaining force and sufficiently preventing le akage of blood.

A sampling port (20) includes a main body (30) formed with an opening (31) for inserting a bl ood collection tube (50) having a rubber plug (51), a hollow needle (61) that can be freely ins erted into the rubber plug of the blood collection tube, and a hollow needle. a needle assembl y 60 attached to the main body, comprising a hub 64 supporting the proximal end of the need le, an elastic rubber cap 70 covering the hollow needle, and a holding portion 80 holding the r ubber cap; A through hole 91 through which a hollow needle covered with a rubber cap penetr ates is provided, and wrinkles 71 generated by elastic contraction of the rubber cap accompan ying insertion of the hollow needle into the rubber stopper are suppressed from reaching the holding portion. and a plate 92 as a suppressing member 90 .

[Selection drawing] Fig. 4


50
52
51
30
61
71
70
91
94
90
92
95
93
S
81
80
64
63
32
33
60
62
19



The scope of the claims open

What is claimed is

: 1.

A main body having an opening for inserting a blood collection tube having a rubber stopper, a hollow

needle that can be inserted through the rubber stopper of the blood collection tube, and the hollow needle. a hub for supporting the proximal end of the hollow needle; an elastic rubber c ap placed on the hollow needle; and a holding portion for holding the rubber cap

. A through hole is provided through which the hollow needle covered with a rubber cap pen etrates, and wrinkles generated by elastic contraction of the rubber cap as the hollow needle i s inserted into the rubber plug reach the holding portion. and a suppression member that sup presses the sampling port.

2.

The main body is rotatably attached to the needle assembly,

the suppressing member is fixed to the main body, and between the through hole and the ru bber cap, 2. The sampling port of claim 1, having clearance to allow rotation of said body porti on.

3.

The main body has a cylindrical shape, and

the suppressing member has a disk shape and includes a projection projecting toward the op ening of the main body. 3. The sampling port of claim 2.

4.

The sampling port according to any one of claims 1 to 3, wherein a ring-shaped projection pr otruding radially outward is provided on the outer peripheral edge of said suppressing membe r.

[Claim 5]

The main body portion is made of a resin material that shrinks more than the resin material forming the suppressing member when heat is applied, and the suppressing member is shrun k to the main body portion by applying heat for sterilization. A sampling port according to any one of claims 1 to 4, fixed with respect to

detailed description open

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to sampling ports for holding blood collec tion tubes. 2. Description of the Related Art When blood is collected using a blood collection tube with a rubber stopper, a sampling port for holding the blood collection tube is used (see Patent Document 1). The sampling port has a main body with an opening for inserting a blood collection tube, and a needle assembly having a hollow needle that can be freely inserted into the rubber stopper of the blood collection tube is attached to the main body. there is The hollo w needle is covered with an elastic rubber cap to prevent leakage of blood. [0003] As the bl ood collection tube is inserted into the body of the sampling port and the hollow needle is pas sed through the rubber plug, the rubber cap is elastically contracted and wrinkled to expose t he hollow needle. The exposed hollow needle is used to collect blood into a collection tube. W hen the blood collection tube is pulled out after blood collection, the rubber cap elastically stre tches from the contracted state as if smoothing the wrinkles, and restores to the state where i t covers the hollow needle again. This prevents leakage of blood from the hollow needle. The r ubber cap is held on the needle assembly by, for example, fitting the root portion to the needl e assembly. [Prior Art Document] [Patent Document] [Patent Document 1] Japanese Patent A pplication Laid-Open No. 2002-291724 [Summary of the Invention]

[0005] However, when the hollow needle is passed

through the rubber plug of the blood collection tube, the wrinkles caused by the elastic contr action of the rubber cap may reach the base of the rubber cap. There is In such a case, the ro ot portion of the rubber cap swells, weakening the holding force for holding the rubber cap to the needle assembly. For this reason, if the tip of the rubber cap is biting into the small inserti on hole of the rubber stopper of the blood collection tube, the rubber cap will be pulled togeth er when the blood collection tube is pulled out, and the position of the rubber cap will be affec ted. There is a risk that the blood will not be sufficiently prevented from leaking.

[0006]

The present invention was made in order to solve the above-mentioned problems associated with the prior art. When a hollow needle is passed through a rubber plug of a blood collection tube, the rubber cap is elastically contracted and wrinkled. It is an object of the present inven tion to provide a sampling port capable of maintaining a holding force for holding a rubber cap to a needle assembly even when the needle assembly is closed, thereby sufficiently preventin g leakage of blood. [0007] A sampling port of the present
invention for achieving the above objects comprises a main body having an opening for inser ting a blood collection tube having a rubber stopper, and the blood collection tube . a hollow needle that can be freely inserted into the rubber plug of the above, a hub that supports the b ase end of the hollow needle, an elastic rubber cap that covers the hollow needle, and a holdi ng portion that holds the rubber cap a needle assembly attached to the main body, and a thro ugh hole through which the hollow needle covered with the rubber cap passes, wherein the r ubber cap is elastic as the hollow needle is inserted into the rubber plug and a suppressing m ember that suppresses wrinkles generated by the contraction from reaching the holding portio n.

[0008] The suppressing

member suppresses wrinkles generated by elastic contraction of the rubber cap as the hollo w needle is passed through the rubber stopper of the blood collection tube from reaching the holding portion. , the rubber cap does not swell at the holding part, and the holding force for holding the rubber cap to the needle assembly does not weaken. Therefore, even if the rubber cap is pulled together when the blood collection tube is pulled out after blood collection, the p osition of the rubber cap will not be displaced, and blood leakage can be sufficiently prevente d. Thus, even if the rubber cap is elastically contracted and wrinkled as the hollow needle is p assed through the rubber plug of the blood collection tube, the holding force for holding the ru bber cap to the needle assembly can be maintained, Thus, a sampling port that can sufficientl y prevent blood leakage can be provided.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009]

FIG. 1 is a block diagram showing a blood bag system incorporating a sampling port;
2 is a perspective view showing the initial blood bag shown in FIG. 1 and a sampling port; FI G.
FIG. 3 is a cross-sectional view showing essential parts of a sampling port before a blood colle ction tube is inserted;

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

5(A) is a perspective view showing a plate as a suppressing member, FIG. 5(B) is a cross-sect ional view along line 5B-5B in FIG. 5(A), and FIG. It is sectional drawing which expands and s hows 5C part of FIG.5(B).

6A and 6B are cross-sectional views showing how a plate as a suppressing member is fixed to the main body; FIG.

FIG. 7A is a conceptual diagram for explaining the action of the present embodiment, and FI G. 7B is a conceptual diagram for explaining the action in the case of contrast without a plate;

8A to 8D are cross-sectional views showing modified examples of the plate; FIG.

9A and 9B are plan views showing further modifications of the plate; FIG.

DETAILED DESCRIPTION OF THE INVENTION Embodiments of the present invention will now

be described with reference to the accompanying drawings. In the description of the drawing s, the same elements are denoted by the same reference numerals, and overlapping descripti ons are omitted. Also, the dimensional ratios in the drawings are exaggerated for convenience of explanation, and may differ from the actual ratios.

Referring to FIG .

1, the illustrated blood bag system 10 removes the initial flow (initial blood flow) of the colle cted blood when collecting blood, and uses the initial blood flow as test blood. It is a blood coll ection device. Bacteria present on and under the skin enter along with the skin fragments at t he time of puncture, so the initial blood flow is removed. A blood bag system 10 includes a b lood collecting needle 11, a blood bag 12 containing blood collected through the blood collecti ng needle 11, a blood collecting tube 13 connecting the blood collecting needle 11 and the blo od bag 12, and a blood collecting tube

.

13, an initial blood flow bag 16 communicating with the blood collection tube 13 via a branch t ube 15 connected to the branch connector 14, and a sampling port 20 connected to the end of the initial blood flow bag 16. ,have. The branch connector 14 is provided with a sealing memb er 17 that seals communication with the blood bag 12 . The sealing member 17 seals the com munication with the blood bag 12 until the collection of the initial blood flow into the initial blo od bag 16 is completed. The branch tube 15 is provided with a clamp member 18 that blocks blood flow to the initial blood bag 16 . After collecting the initial blood flow, the clamp membe r 18 clamps the branch tube 15 to block the blood flow to the initial blood bag 16 . After that, the sealing member 17 is opened to start collecting blood into the blood bag 12 .

[0013]

FIG. 2 shows a state in which the initial blood contained in the initial blood bag 16 is collecte d as test blood. A sampling port 20 is connected to a blood extraction tube 19 connected to a n initial blood bag 16 . A lid member 40 that opens and closes the opening 31 is rotatably con

nected to the sampling port 20 via a hinge 41 . When collecting the initial blood contained in t he initial blood bag 16 as test blood, a reduced-pressure blood collection tube 50 (correspondi ng to a blood collection tube) having a rubber plug 51 is inserted into the sampling port 20 thr ough the opening 31 .

A reduced

-pressure blood collection tube 50 is an instrument for collecting the initial blood that is stor ed in the initial blood bag 16 . The vacuum blood collection tube 50 has a blood collection tub e body 52 and a rubber plug 51 fitted into the opening of the blood collection tube body 52 . T he vacuum blood collection tube 50 is in a vacuum or a reduced pressure state. When the vac uum blood collection tube 50 is connected to the sampling port 20 , the rubber stopper 51 is p ierced by the hollow needle 61 . As a result, the inside of the vacuum blood collection tube 50 and the blood extraction tube 19 are communicated, and the initial blood flow from the blood extraction tube 19 is collected in the vacuum blood collection tube 50 .

[0015]

With reference to FIGS. 3 and 4, the sampling port 20 according to the embodiment is gener ally composed of a body portion 30 formed with an opening 31 for inserting a blood collection tube 50 having a rubber stopper 51, a blood collection tube A hollow needle 61 that can be fre ely inserted into the rubber plug 51 of 50, a hub 64 that supports the base end of the hollow needle 61, an elastic rubber cap 70 that covers the hollow needle 61, and a holder that holds the rubber cap 70. and a needle assembly 60 attached to the body portion 30 with a portion 8 0 . The sampling port 20 further suppresses wrinkles 71 (see FIG. 4) caused by elastic contra ction of the rubber cap 70 as the hollow needle 61 is inserted into the rubber plug 51 from rea ching the holding portion 80. It has a member 90 . The suppressing member 90 has a throug h hole 91 through which the hollow needle 61 covered with the rubber cap 70 passes. 3 and 4, the upper side in the drawings is defined as the "upper side" of each member, and the lowe r side in the drawings is defined as the "lower side" of each member. Details are given below.

The body portion 30 has a cylindrical shape and has a tapered shape on the lower side

.

The main body 30 has

, an insertion port 32 for inserting the needle assembly 60, and an engaging portion 33 for pr eventing the inserted needle assembly 60 from coming off.

Body

portion 30 is rotatably attached to needle assembly 60 . By making it rotatable, the body po rtion 30 can be rotated with respect to the needle assembly 60 to easily finely adjust the posit ion of the lid member 40 with respect to the initial blood flow bag 16 . A needle assembly 60 includes a hollow needle 61 having a sharp tip at its tip, a connecting portion 62 connected to the blood extraction tube 19, a boss portion 63 holding the proximal end portion of the hollow needle 61

,

have. The hub 64 is provided so as to protrude radially outward from the boss portion 63 . Th e needle assembly 60 is attached to the body portion 30 with the hub 64 overcoming the locki ng portion 33 when it is inserted into the insertion port 32 of the body portion 30 . The upper end of the hub 64 in the figure is formed into an inclined surface so that it can easily get over the engaging portion 33 when it is inserted. In order to pivotally attach the body portion 30 t o the needle assembly 60, the clearance between the connecting portion 62 of the needle ass embly 60 and the receptacle 32 of the body portion 30 and the outer circumference of the hu b 64

are

and the body portion 30 are adjusted. As the blood collection tube 50 is inserted into the ma in body 30 and the hollow needle 61 is passed through the rubber stopper 51, the rubber cap 70 is elastically contracted to form wrinkles 71, thereby exposing the hollow needle 61

.

Let When the blood collection tube 50 is pulled out, the rubber cap 70 is elastically stretched f rom the shrunk state so as to smooth out the wrinkles 71, and restores to the state where it c overs the hollow needle 61 again. This prevents blood from leaking from the hollow needle 61

.

[0021]

The holding portion 80 includes a lock member 81 through which the hollow needle 61 is ins erted and which is attached to the boss portion 63 of the needle assembly 60 . The locking m ember 81 has an undercut shape in which the base end side of the hollow needle 61 has a sm aller diameter than the tip end side. The undercut shape of the locking member 81 holds the r ubber cap 70 .

5(A) and 5(B), restraining member 90 includes a disk -

shaped flat plate portion 93 fitted in main body portion 30 and a center portion of flat plate portion 93 protruding upward. It consists of a plate 92 with a projection 94 . A through-hole 9 1 through which the hollow needle 61 with the rubber cap 70 is attached is formed in the conv ex portion 94 . As shown in FIG. 5C , a ring-shaped projection 95 projecting radially outward i s provided integrally with the flat plate portion 93 on the outer peripheral edge of the flat plat e portion 93 . 3 and 4, the plate 92 is mounted inside the main body 30 at a position above t he lock member 81 forming the holding portion 80. As shown in FIG

.

As the blood collection tube 50 is inserted into the main body 30 and the hollow needle 61 is passed through the rubber stopper 51, the rubber cap 70 is elastically contracted to form wrin kles 71, thereby exposing the hollow needle 61. . A clearance S between the through hole 91 of the plate 92 and the rubber cap 70 is relatively small. Therefore, the plate 92 prevents the wrinkles 71 generated by the elastic contraction of the rubber cap 70 from reaching the holdin g portion 80 (FIG. 4).

[0024]

As described above, the body portion 30 is rotatably attached to the needle assembly 60 . A clearance S is provided between the through hole 91 of the plate 92 fixed to the main body 30 and the rubber cap 70 to allow the main body 30 to rotate. By setting the clearance S to a di mension that does not hinder the rotation of the main body 30, the rotational position of the main body 30 with respect to the needle assembly 60, the position of the lid member 40 with respect to the initial blood bag 16, and the like can be easily finely adjusted. becomes possibl e.

By providing the plate 92 with the protrusions 94, it is possible to increase the area of the ru bber cap 70 in the longitudinal direction that is not affected by the wrinkles 71. As shown in F IG . As a result, a decrease in holding force for holding the rubber cap 70 to the needle assem bly 60 can be further suppressed. Even if the arrangement position of the plate 92 is shifted u pward from the position shown in FIG. 4, the area in the longitudinal direction of the rubber c ap 70 that is not affected by the wrinkles 71 can be increased. However, in this case, since th e position of the blood collection tube 50 is also shifted upward, it may be necessary to slightl y increase the longitudinal dimension of the main body 30 . Therefore, by providing the plate 92 with the convex portion 94 projecting toward the opening 31 side of the body portion 30, while maintaining the length of the body portion 30 in the longitudinal direction, It is possible to secure a sufficient holding force for holding the rubber cap 70 to the needle assembly 60 b y increasing the area not affected by the wrinkles 71 .

[0026]

The material of the main body 30, the cover member 40, the needle assembly 60 excluding t he hollow needle 61, the holding part 80, and the plate 92 is not particularly limited, but exa mples thereof include polycarbonate, polyethylene, polypropylene, ethylene- Examples include polyolefins such as vinyl acetate copolymers and modified polyolefins. The material of the ho llow needle 61 is not particularly limited, but examples include various metal materials such a s stainless steel, aluminum or aluminum alloys, titanium or titanium alloys, superelastic alloys such as Ni--Ti alloys, polyphenylene sulfide, and the like

.

and various hard resin materials.

[0028]

The material constituting the rubber cap 70 is not particularly limited, but examples include natural rubber, isoprene rubber, butadiene rubber, styrene-butadiene rubber, nitrile rubber, chl oroprene rubber, butyl rubber, acrylic rubber, ethylene-propylene rubber, hydrin rubber, Variou s rubber materials such as urethane rubber, silicone rubber, and fluororubber can be used.

FIGS.

6A and 6B show how the plate 92 is fixed to the body portion 30. FIG. In this embodiment, t he body portion 30 is made of a resin material that shrinks more than the resin material formi ng the plate 92 when heat is applied. This is because the plate 92 can be fixed to the body po

rtion 30 by applying heat for sterilization. More specifically, as shown in FIG. 6A, before heat is applied, the inner diameter of the main body 30 is relatively large, and the ring-shaped proj ection 95 of the plate 92 bites into the main body 30 by a small amount

.

I'm in. Since the plate 92 can be inserted into the main body 30 relatively easily, the assembl y work of the plate 92 can be easily performed.

Then ,

as shown in FIG. 6(B), when heat is applied for sterilization, for example, in a high-pressure steam sterilization method (autoclave), the main body 30 shrinks more than the plate 92 doe s. As a result, the ring-shaped protrusion 95 of the plate 92 further bites into the body portion 30 , and the plate 92 can be easily fixed to the body portion 30 . As an example of a combin ation of resin materials as described above, for example, polypropylene can be used as the m olding material for the main body 30 and polycarbonate can be used as the molding material f or the plate 92

. [0033]

The operation of this embodiment will be described. When collecting blood, the blood collec tion tube 50 is inserted into the body portion 30 of the sampling port 20, and is hollow

.

A needle 61 is passed through the rubber stopper 51 . As the hollow needle 61 is inserted thr ough the rubber stopper 51, the rubber cap 70 is elastically contracted to form wrinkles 71, th ereby exposing the hollow needle 61. As shown in FIG. Referring to FIG. 7B, in the case of c ontrast without plate 92, rubber cap 170 is elastically closed as hollow needle 161 is inserted i nto rubber plug 51 of blood collection tube 50

.

Wrinkles 171 caused by shrinking may reach the base of the rubber cap 170 . In such a case, the base portion of rubber cap 170 swells, and the holding force for holding rubber cap 170 to needle assembly 160 is weakened. Therefore, when the blood collection tube 50 is pulled out, the rubber cap 170 may be pulled together, and the position of the rubber cap 170 may be dis placed, resulting in insufficient prevention of blood leakage. On the other hand, referring to FIGS. 4 and 7A, in the present embodiment, the plate 92 is positioned above the locking mem ber 81 forming the holding portion 80, and the main

body

It is installed inside the part 30 . This plate 92 prevents wrinkles 71 generated by elastic contr action of the rubber cap 70 as the hollow needle 61 is inserted into the rubber plug 51 of the blood collection tube 50 from reaching the locking member 81 . Since the rubber cap 70 does not swell at the portion of the lock member 81, the holding force for holding the rubber cap 7

0 to the needle assembly 60 is not weakened.

[0037]

The exposed hollow needle 61 is inserted through the rubber stopper 51 and blood is collected into the blood collection tube 50 . When the blood collection tube 50 is pulled out after blood collection, the rubber cap 70 elastically expands from the shrunk state so as to smooth out the wrinkles 71 and restores to the state where it covers the hollow needle 61 again. This prevents blood from leaking from the hollow needle 61 . The rubber cap 70 is held by the needle assembly 60 at the locking member 81 .

When the tip of the rubber cap 70 bites into the

minute insertion hole of the rubber stopper 51 of the blood collection tube 50 and the blood collection tube 50 is pulled out, the rubber cap 70 is pulled together. However, since the portion of the locking member 81 is not affected by the wrinkles 71, the holding force remains set at the initial stage. Therefore, the rubber cap 70 does not come off from the hollow needle 61 and the blood collection tube 50 is released from biting into the rubber plug 51 . As a result, the position of the rubber cap 70 is not displaced, and blood leakage can be sufficiently prevented.

As described

above, even if the rubber cap 70 is elastically contracted as the hollow needle 61 is inserted into the rubber stopper 51 of the blood collection tube 50 and wrinkles 71 are generated, the rubber cap 70 is attached to the needle assembly 60. It is possible to provide the sampling port 20 which can maintain a holding force for holding and thereby sufficiently prevent leakage of blood. Main body 30 is rotatably attached to needle assembly 60 , plate 92 is fixed to main body 30 , and main body 30 is positioned between through hole 91 and rubber cap 70

.

Since there is a clearance S that allows rotation, it is possible to easily finely adjust the rotation position of the main body 30 with respect to the needle assembly 60 .

[0041]

In addition, since the plate 92 has a convex portion 94 that protrudes toward the opening 31 side of the body portion 30, the longitudinal length of the rubber cap 70 is increased while maintaining the length of the body portion 30 in the longitudinal direction. It is possible to secure a sufficient holding force for holding the rubber cap 70 to the needle assembly 60 by enlarging the area that is not affected by the wrinkles 71 . In addition, since the ring-shaped projection 95 projecting radially outward is provided on the outer peripheral edge of the plate 92, the plate 92 is attached to the body portion 30 so that the ring-shaped projection 95 bites into the body portion 30 by a small amount

.

It can be inserted into the plate 30, and the assembly work of the plate 92 can be easily performed.

becomes possible. The main body 30 is made of a resin material that shrinks more than the

resin material forming the plate 92 when heat is applied

.

Since it is fixed to the body portion 30, the plate 92 can be relatively easily inserted into the b ody portion 30 before heat is applied, and the plate 92 can be easily assembled. On the other hand, when heat is applied for sterilization, the body portion 30 contracts more than the plate 92 . This makes it possible to easily fix the plate 92 to the body portion 30 .

(

Modified Example of Plate)

The plate has a through hole 91 through which the hollow needle 61 with the rubber cap 70 attached passes. As long as wrinkles 71 generated by elastic contraction of 70 are prevented f rom reaching holding portion 80, the shape can be modified as appropriate.

For example, referring to FIG. 8, a plate 92a (FIG. 8A) in which

a projection 94 smoothly protrudes from a flat plate portion 93, a plate 92b with a thicker ov erall thickness and a flat upper surface, 92c (FIGS. 8B and 8C), and a cap-shaped plate 92d (FIG. 8D) that covers the holding portion 80 without covering the entire bottom surface of the main body portion 30 can be exemplified. Further, referring to FIG. 9, a plate 92e (FIG. 9A) i n which the flat plate portion 93 is not formed with the through portion, and a plate 92f (FIG. 9A) in which the flat plate portion 93 is formed with the through portion 96 are provided

.

(B)).

(

Other modifications)

Although the lock member 81 having an undercut shape has been exemplified as the holding portion 80 that holds the rubber cap 70, the holding portion 80 is not limited to this case. The holding part 80 can be appropriately modified as long as it has a function of preventing the ru bber cap 70 from coming off and holding it in the needle assembly 60 . For example, the holdi ng part 80 uses a form in which the rubber cap 70 is adhered to the hollow needle 61 with an adhesive to hold it, a form in which the rubber cap 70 is held by being fused to the hollow nee dle 61 by ultrasonic fusion, or a clip. For example, a configuration in which the rubber cap 70 i s held on the hollow needle 61 by fitting is exemplified. These holding portions 80 may be use d alone, or may be a holding portion 80 in which two or more types are combined.

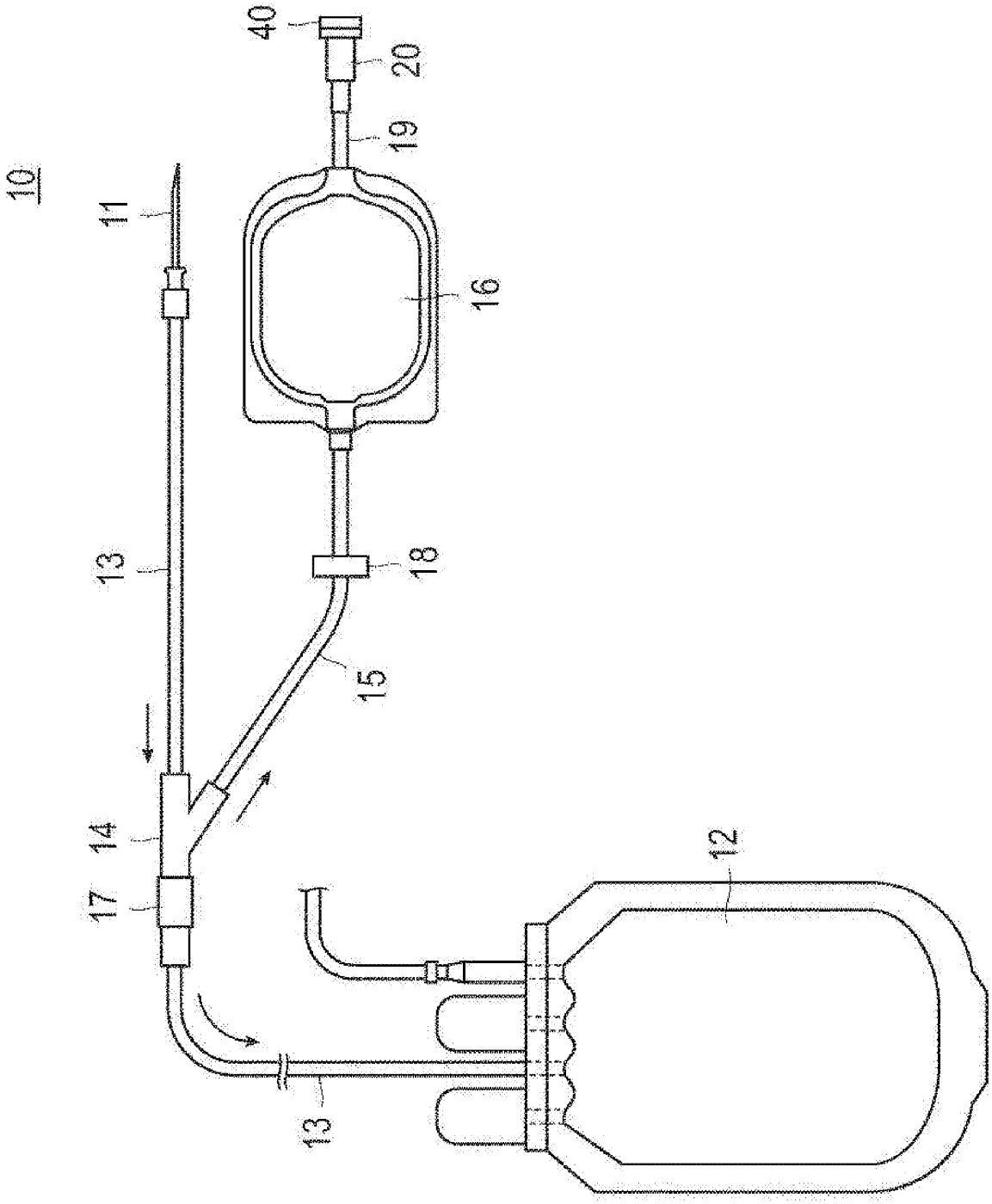
20 sampling port 30 main body 31 opening 50 vacuum

blood collection tube (collection tube) 51 rubber plug 60 needle assembly 61 hollow needle 64 hub 70 rubber cap 71 wrinkles 80 holding part 81 locking member 90 suppressing member 91 through hole 92 plate (suppressing member);

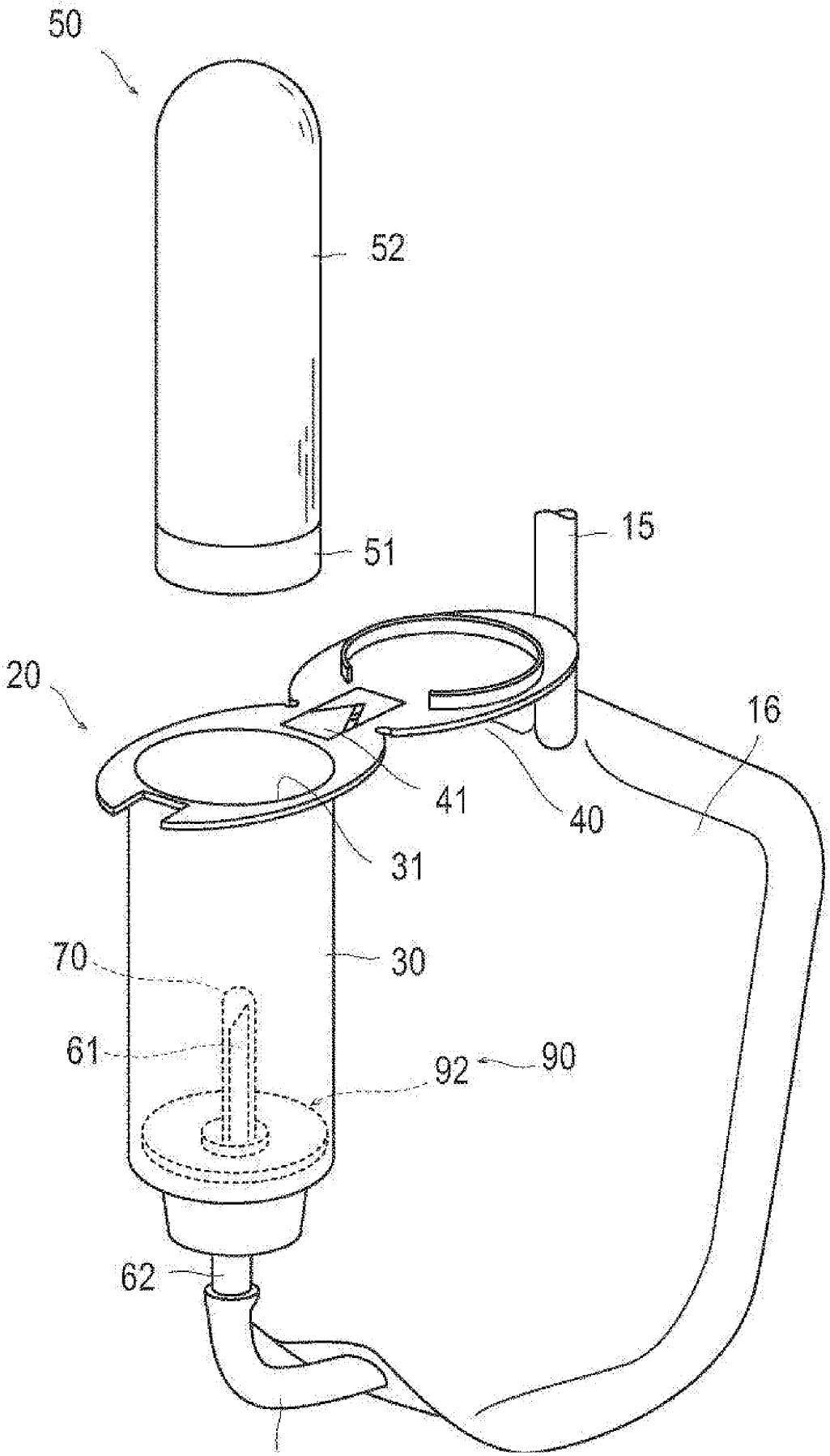
93 flat plate portion,
94 convex portion,
95 ring-shaped projection,
S clearance.

drawing open —

[Fig. 1]

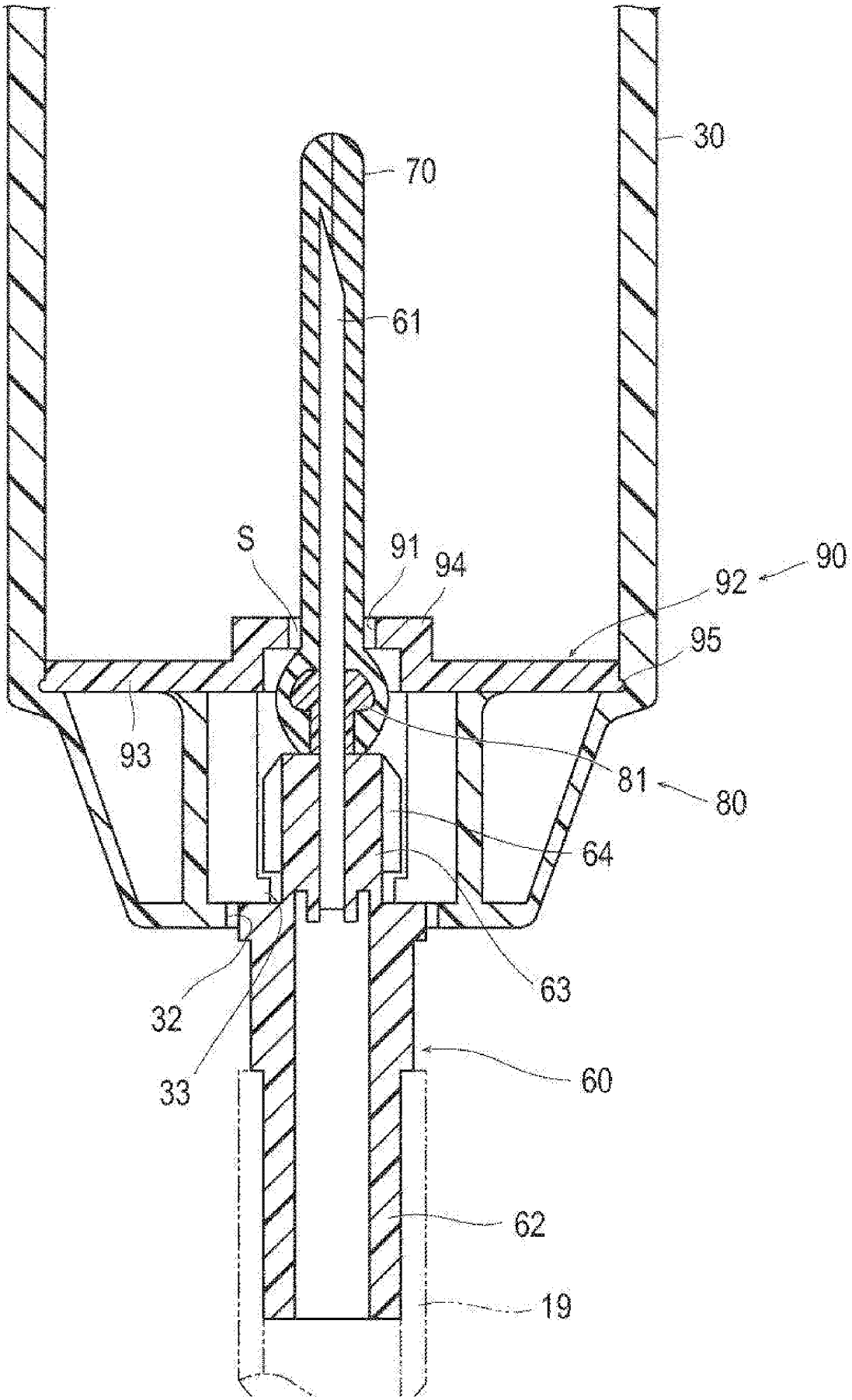


[Figure 2]

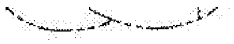

50
52
51
15
20
16
41
40
31
70
30
61
92
90
62

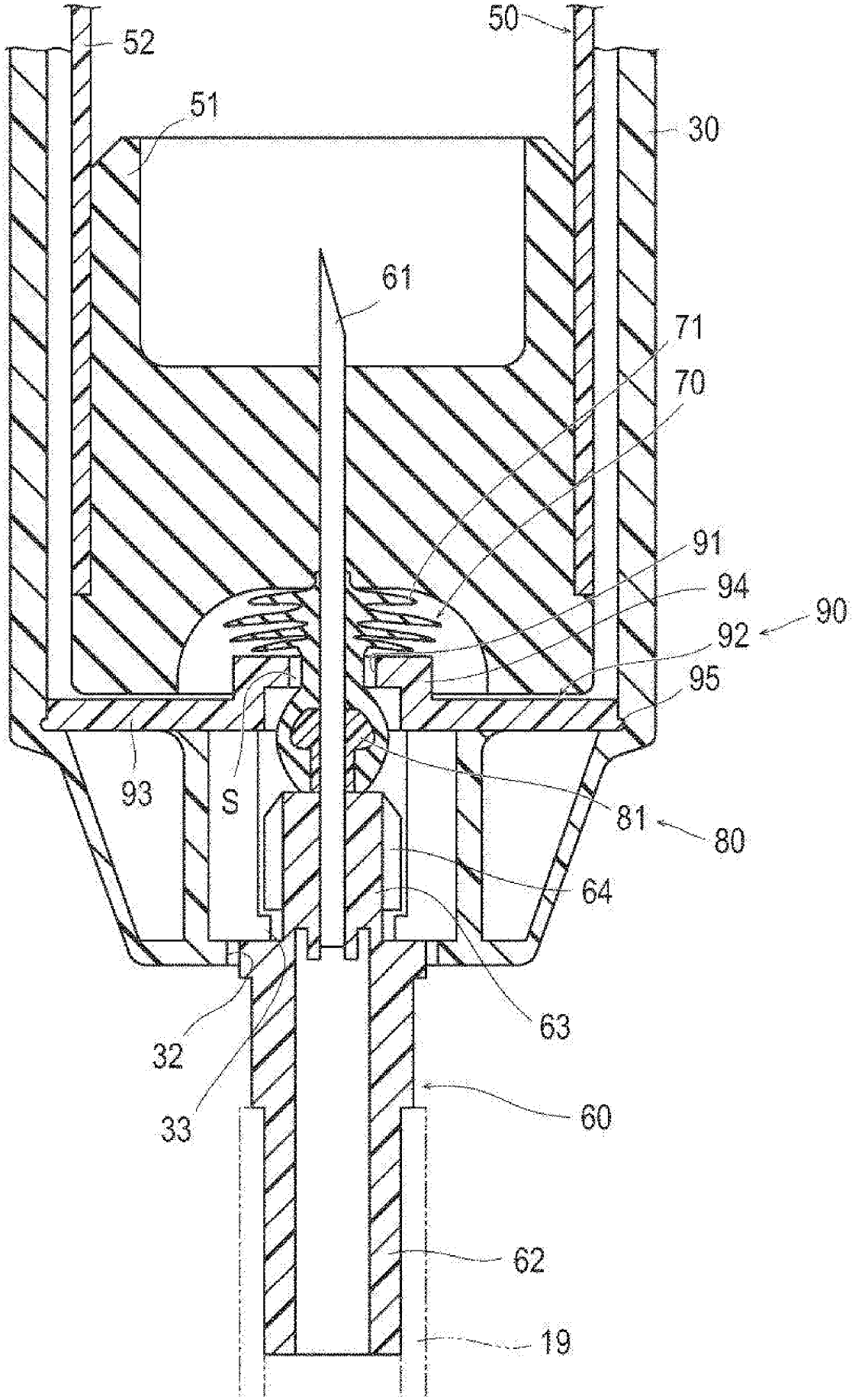
[Figure 3]




30
70
61
S
91
94
90
92
95
93
81
80
64
63
32
33
60
62
19

[Figure 4]

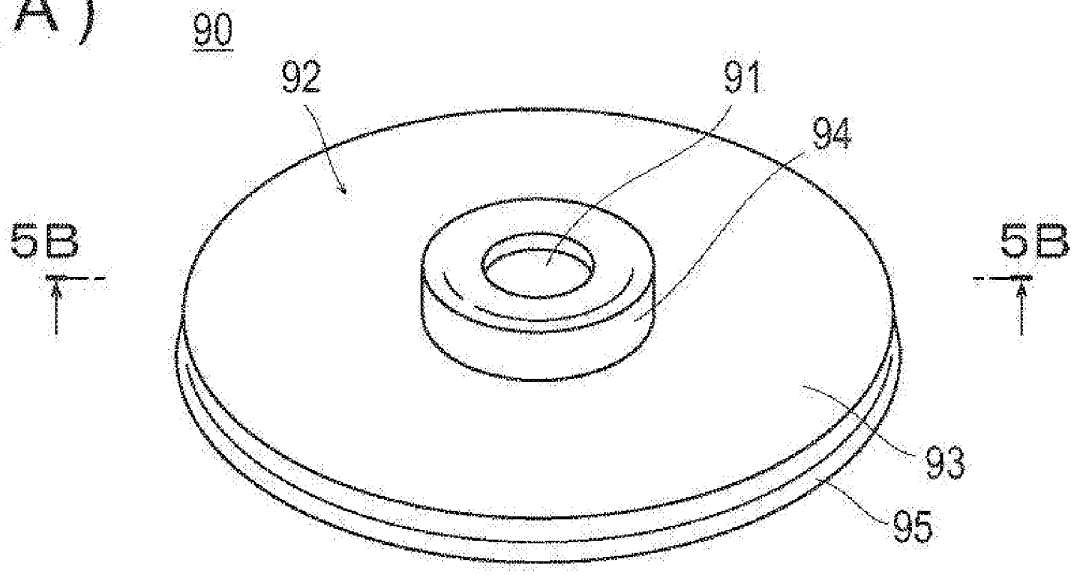



50
52
51
30
61
71
70
91
94
90
92
95
93
S
81
80
64
63
32
33
60
62
19

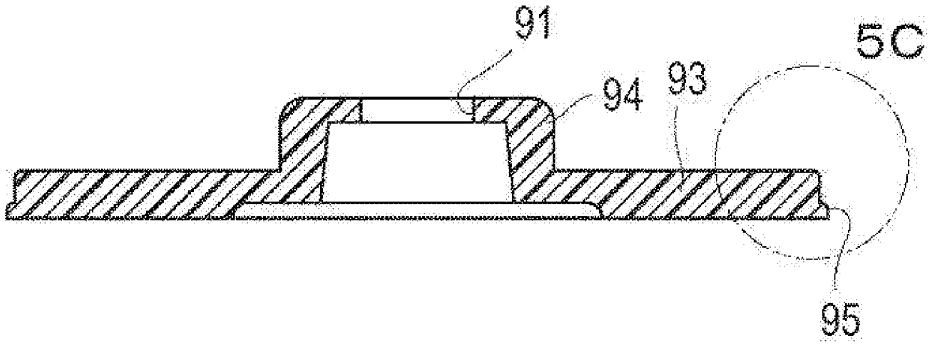
[Figure 5]



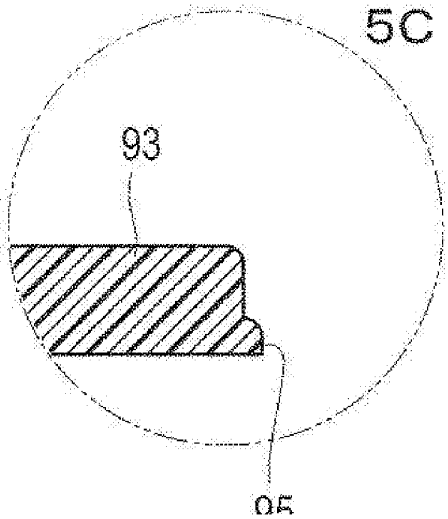
(A)



(B)

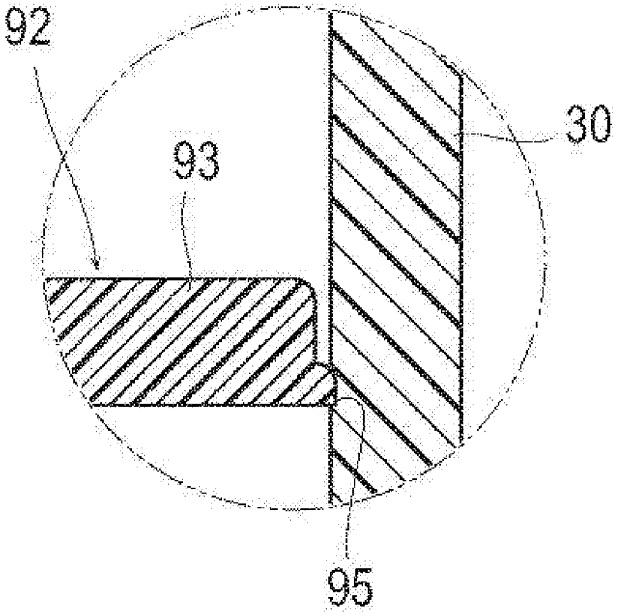


(C)

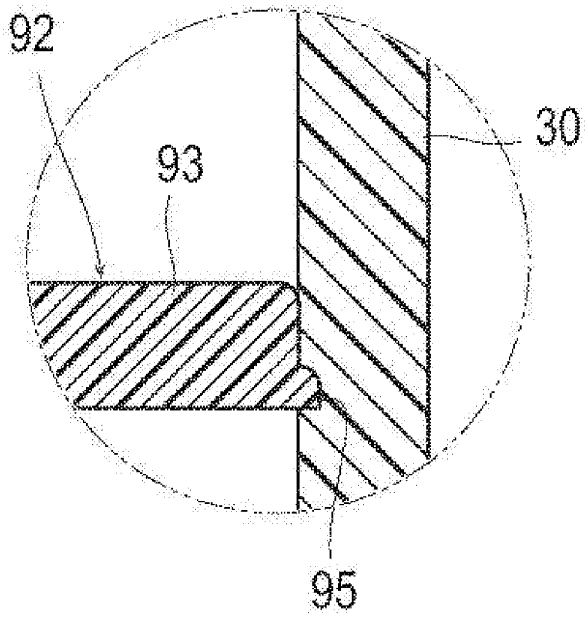


[Fig. 6]

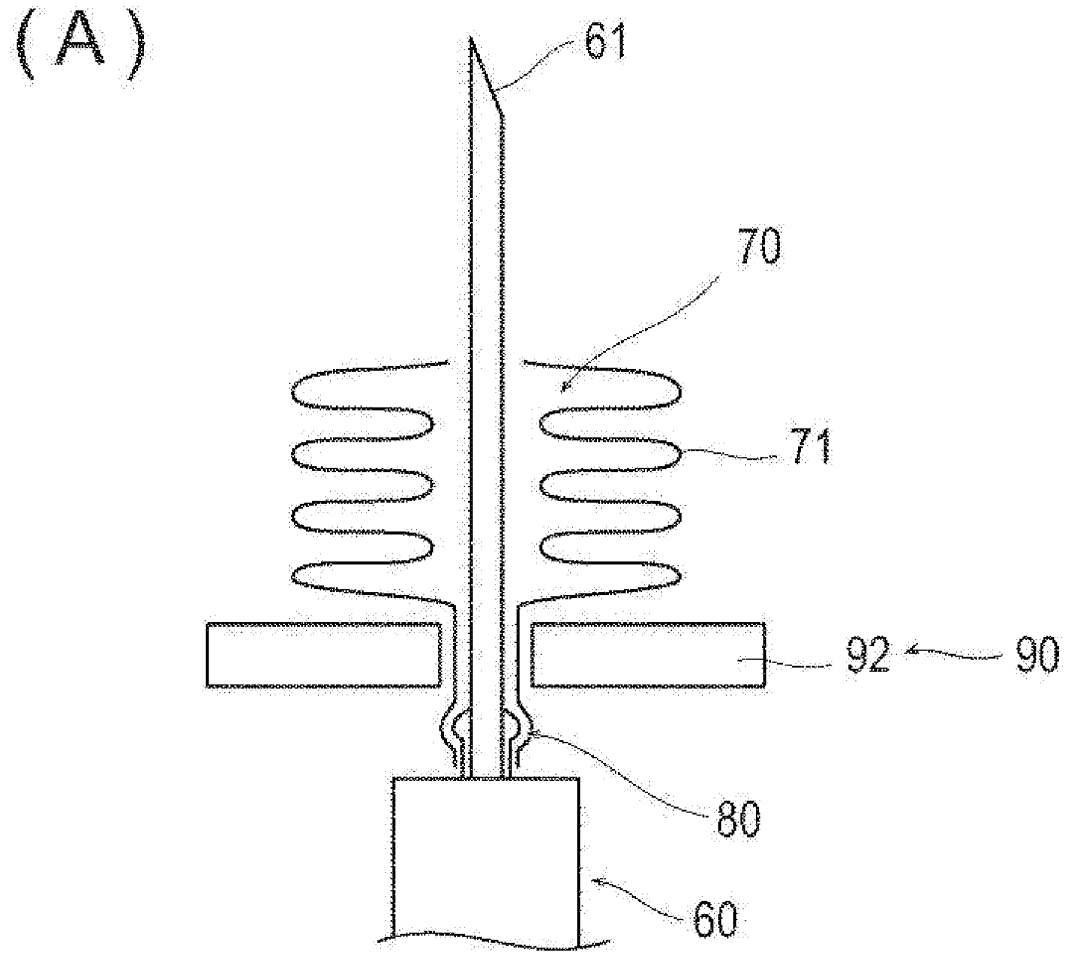
(A)

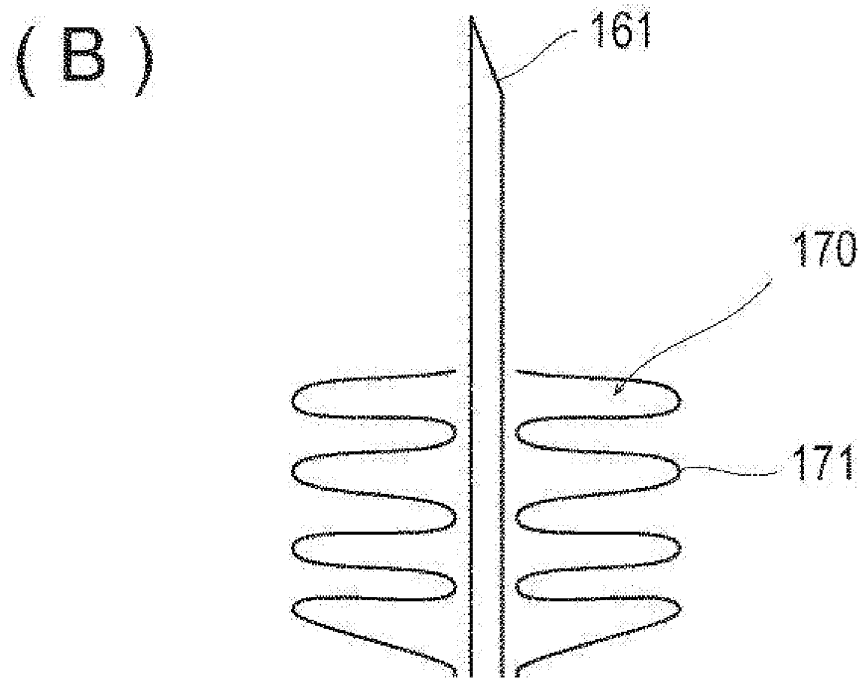


(B)

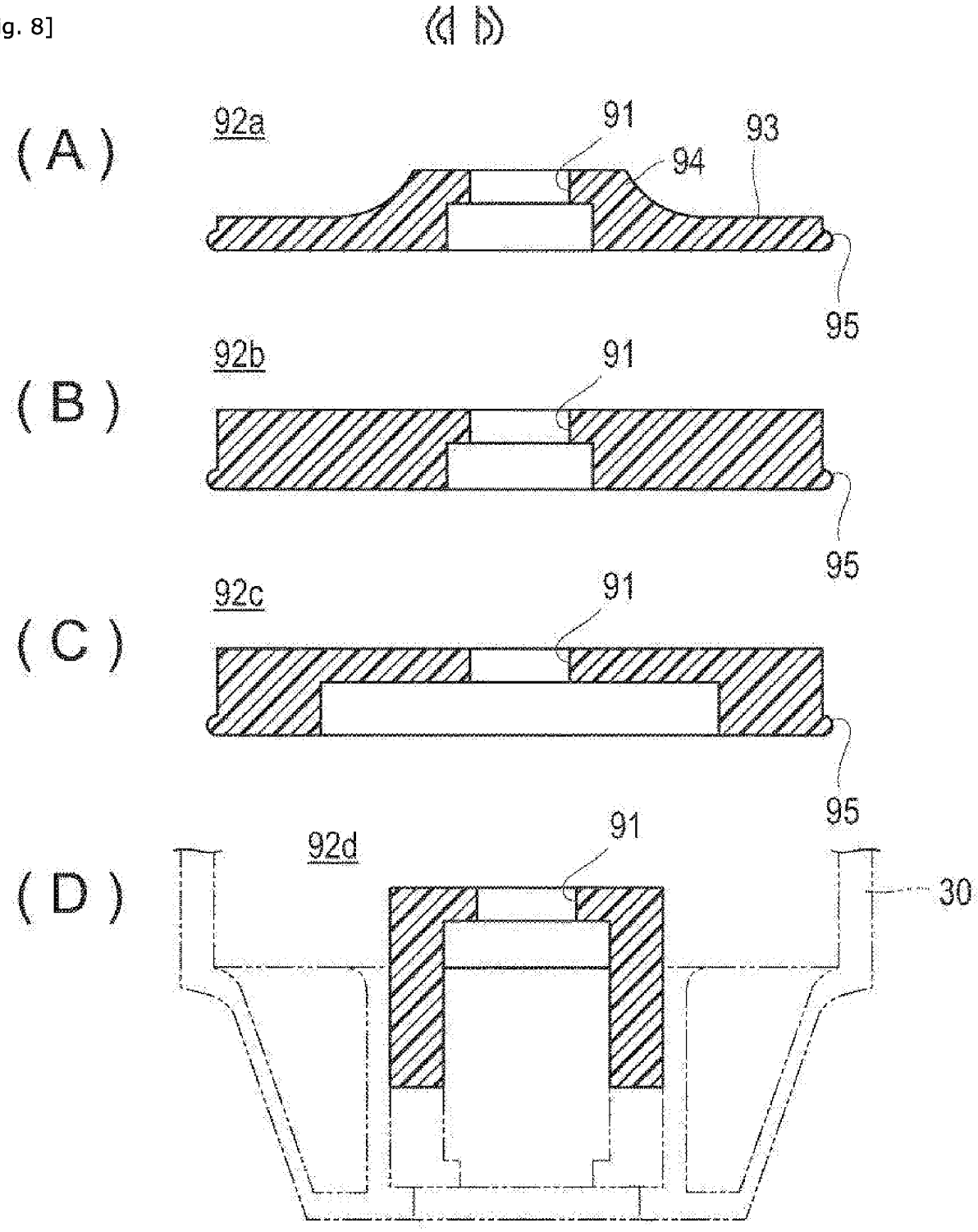


[Fig. 7]

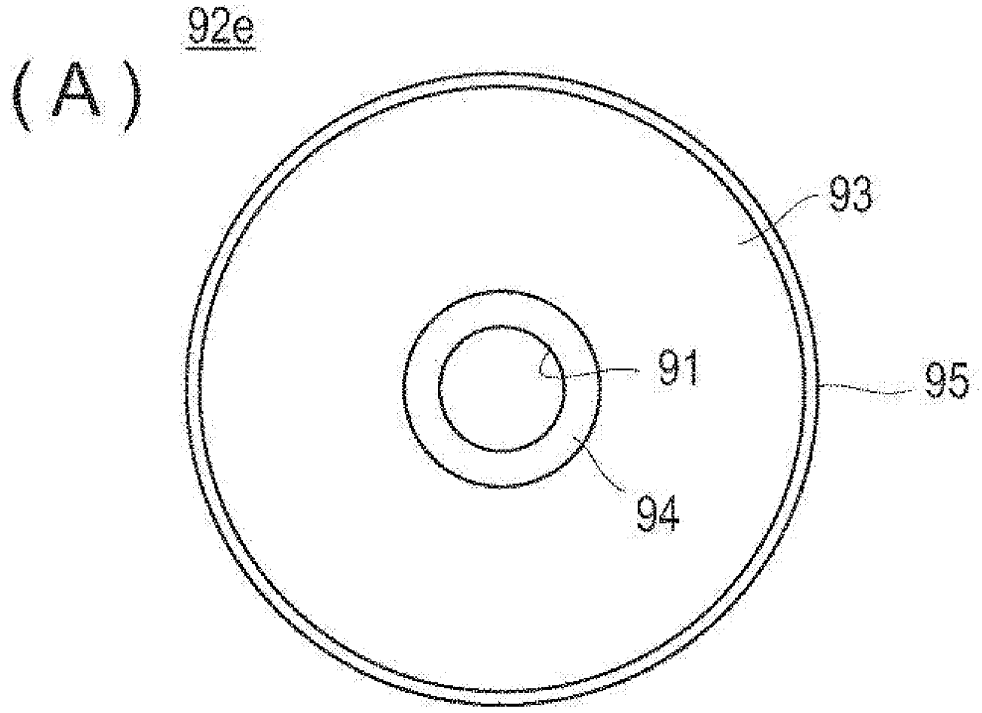

(A)
61
70
71
92
90
80
60

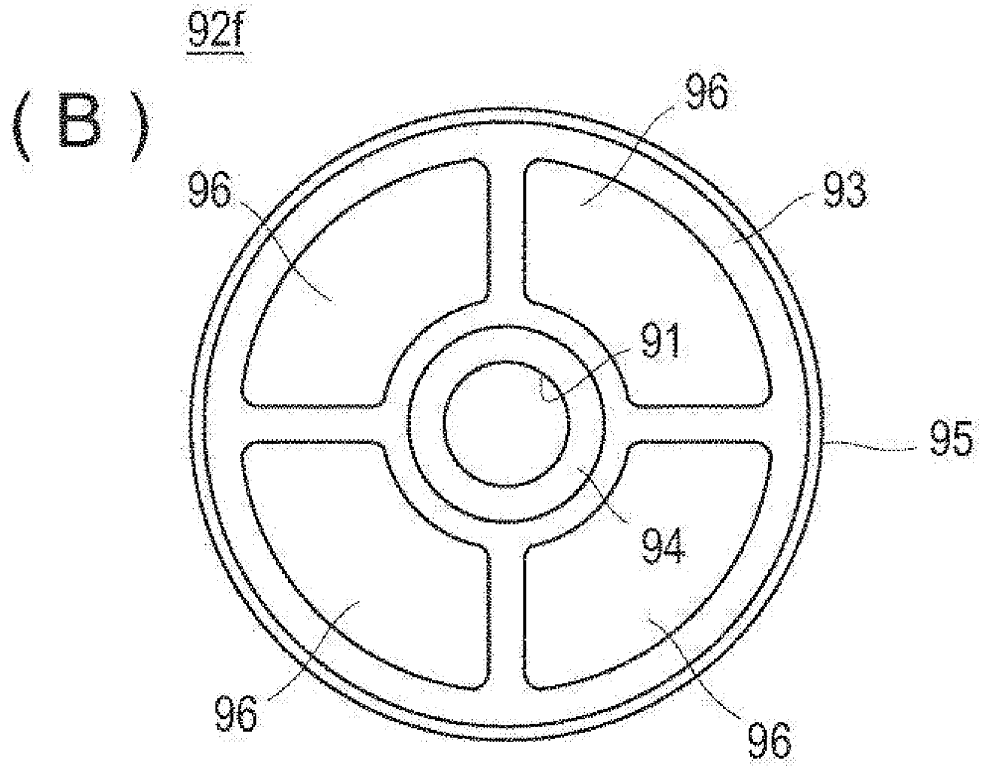

(B)
161
170
171

[Fig. 8]



[Fig. 9]

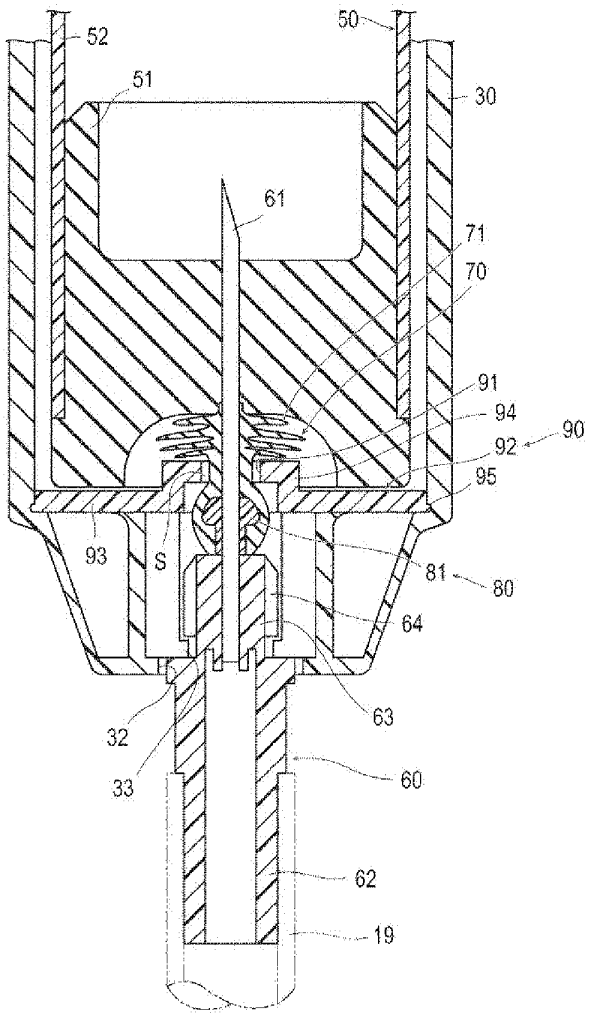

92e
(A)
93
91
95
94


92f
(B)
96
96
93
91
95
94
96
96

drawing open

Representative drawing 1 2 3 Four Five 6 7 8 9

Magnify and Rotate



Representative drawing

1 / 1 display

Copyright JPO and INPIT (P0200)

(19)日本国特許庁(JP)　(12)公開特許公報(A)　(11)特許出願公開番号
特開2012-16496
(P2012-16496A)
(43)公開日　平成24年1月26日(2012.1.26)

(51)Int.Cl.		F I			テーマコード（参考）
A61B 5/15	***(2006.01)***	A61B	5/14	300Z	4C038
A61B 5/154	***(2006.01)***	A61B	5/14	300E	4C066
A61M 39/02	*(2006.01)*	A61M	5/14	459P	

審査請求 未請求　請求項の数 5　OL　（全 12 頁）

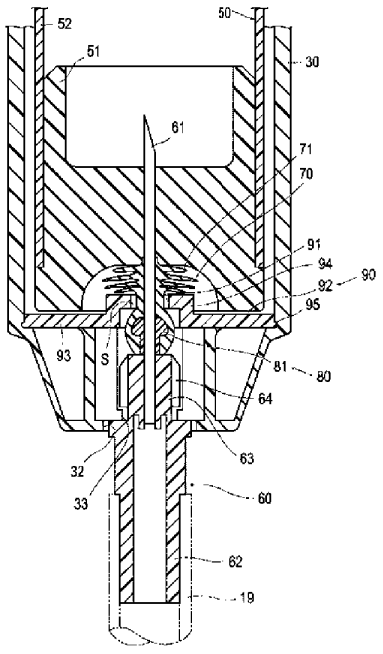
(21)出願番号　特願2010-156165 (P2010-156165)
(22)出願日　平成22年7月8日 (2010.7.8)

(71)出願人　000109543
テルモ株式会社
東京都渋谷区幡ヶ谷２丁目４４番１号
(74)代理人　110000671
八田国際特許業務法人
(72)発明者　村越　正英
静岡県富士宮市三園平８１８　テルモ株式会社内
(72)発明者　秋山　真洋
静岡県富士宮市三園平８１８　テルモ株式会社内
(72)発明者　早川　彩
静岡県富士宮市三園平８１８　テルモ株式会社内

最終頁に続く

(54)【発明の名称】サンプリングポート

(57)【要約】
【課題】採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められて皺が生じても、ゴムキャップを針組立体に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポートを提供する。
【解決手段】サンプリングポート２０は、ゴム栓５１を備える採血管５０を挿入するための開口部３１が形成された本体部３０と、採血管のゴム栓に挿通自在な中空針６１と、中空針の基端部を支持するハブ６４と、中空針に被せられた弾性を有するゴムキャップ７０と、ゴムキャップを保持する保持部８０と、を備え、本体部に取り付けられた針組立体６０と、ゴムキャップが被せられた中空針が貫通する貫通孔９１を備え、ゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められることによって生じる皺７１が保持部に達することを抑制する抑制部材９０としてのプレート９２と、を有している。
【選択図】図４



【特許請求の範囲】
【請求項１】
ゴム栓を備える採血管を挿入するための開口部が形成された本体部と、
前記採血管の前記ゴム栓に挿通自在な中空針と、前記中空針の基端部を支持するハブと、前記中空針に被せられた弾性を有するゴムキャップと、前記ゴムキャップを保持する保持部と、を備え、前記本体部に取り付けられた針組立体と、
前記ゴムキャップが被せられた前記中空針が貫通する貫通孔を備え、前記ゴム栓への前記中空針の挿通に伴って前記ゴムキャップが弾性的に縮められることによって生じる皺が前記保持部に達することを抑制する抑制部材と、を有することを特徴とするサンプリングポート。
【請求項２】
前記本体部は、前記針組立体に対して回動自在に取り付けられ、
前記抑制部材は、前記本体部に固定されており、前記貫通孔と前記ゴムキャップとの間に、前記本体部の回動を許容するクリアランスを有する、請求項１に記載のサンプリングポート。
【請求項３】
前記本体部は、円筒形状であり、
前記抑制部材は、円盤形状であり、前記本体部の前記開口部の側に向けて突出する凸部を備えている、請求項１または請求項２に記載のサンプリングポート。
【請求項４】
前記抑制部材の外周縁には、径方向外方に突出するリング状突起が設けられている、請求項１～３のいずれか１つに記載のサンプリングポート。
【請求項５】
前記本体部は、熱を印加したときに前記抑制部材を形成する樹脂材料よりも大きく収縮する樹脂材料から形成されており、滅菌のための熱を印加することによって、前記抑制部材を前記本体部に対して固定する、請求項１～４のいずれか１つに記載のサンプリングポート。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、採血管を保持するサンプリングポートに関する。
【背景技術】
【０００２】
ゴム栓を備える採血管を用いて採血するときには、採血管を保持するサンプリングポートが使用される（特許文献１を参照）。サンプリングポートは、採血管を挿入するための開口部が形成された本体部を有し、この本体部には、採血管のゴム栓に挿通自在な中空針を備えた針組立体が取り付けられている。中空針には、血液の漏洩を防止するために、弾性を有するゴムキャップが被せられている。
【０００３】
サンプリングポートの本体部に採血管を挿入し、中空針をゴム栓に挿通させるのに伴って、ゴムキャップは、弾性的に縮められて皺を生じながら中空針を露出させる。露出した中空針は、採血管に採血する。採血後に採血管を引き抜くと、ゴムキャップは、縮んだ状態から、皺を伸ばすように弾性的に伸び、中空針に再び被せられる状態まで復元する。これによって、中空針からの血液の漏洩を防止する。ゴムキャップは、例えば根元部分を針組立体に密着させることによって、針組立体に保持されている。
【先行技術文献】
【特許文献】
【０００４】
【特許文献１】特開２００２－２９１７２４
【発明の概要】

【発明が解決しようとする課題】
【０００５】
しかしながら、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められることによって生じる皺が、ゴムキャップの根元部に達することがある。このような場合には、ゴムキャップの根元部が膨らんでしまい、ゴムキャップを針組立体に保持するための保持力が弱くなる。このため、採血管のゴム栓の微小な挿通孔にゴムキャップの先端部が食い込んでいるような場合においては、採血管を引き抜くときにゴムキャップが一緒に引っ張られてしまい、ゴムキャップの位置などがずれてしまい、血液の漏洩の防止が不十分になる虞がある。
【０００６】
本発明は、上記従来技術に伴う課題を解決するためになされたものであり、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められて皺が生じても、ゴムキャップを針組立体に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポートを提供することを目的とする。
【課題を解決するための手段】
【０００７】
上記目的を達成するための本発明のサンプリングポートは、ゴム栓を備える採血管を挿入するための開口部が形成された本体部と、
前記採血管の前記ゴム栓に挿通自在な中空針と、前記中空針の基端部を支持するハブと、前記中空針に被せられた弾性を有するゴムキャップと、前記ゴムキャップを保持する保持部と、を備え、前記本体部に取り付けられた針組立体と、
前記ゴムキャップが被せられた前記中空針が貫通する貫通孔を備え、前記ゴム栓への前記中空針の挿通に伴って前記ゴムキャップが弾性的に縮められることによって生じる皺が前記保持部に達することを抑制する抑制部材と、を有している。
【発明の効果】
【０００８】
抑制部材によって、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められることによって生じる皺が保持部に達することが抑制されているので、保持部の部分でゴムキャップが膨らむことがなく、ゴムキャップを針組立体に保持するための保持力が弱くならない。このため、採血後に採血管を引き抜くときにゴムキャップが一緒に引っ張られてしまっても、ゴムキャップの位置などがずれることがなく、血液の漏洩を十分に防止することが可能となる。このように、採血管のゴム栓への中空針の挿通に伴ってゴムキャップが弾性的に縮められて皺が生じても、ゴムキャップを針組立体に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポートを提供できる。
【図面の簡単な説明】
【０００９】
【図１】サンプリングポートが組み込まれた血液バッグシステムを示す構成図である。
【図２】図１に示される初流血バッグと、サンプリングポートとを示す斜視図である。
【図３】採血管を挿入する前のサンプリングポートの要部を示す断面図である。
【図４】採血管を挿入した後のサンプリングポートの要部を示す断面図である。
【図５】図５（Ａ）は、抑制部材としてのプレートを示す斜視図、図５（Ｂ）は、図５（Ａ）の５Ｂ－５Ｂ線に沿う断面図、図５（Ｃ）は、図５（Ｂ）の５Ｃ部分を拡大して示す断面図である。
【図６】図６（Ａ）（Ｂ）は、抑制部材としてのプレートを本体部に対して固定する様子を示す断面図である。
【図７】図７（Ａ）は、本実施形態の作用の説明に供する概念図、図７（Ｂ）は、プレートを設けていない対比例の場合の作用の説明に供する概念図である。
【図８】図８（Ａ）～（Ｄ）は、プレートの改変例を示す断面図である。
【図９】図９（Ａ）（Ｂ）は、プレートのさらなる改変例を示す平面図である。

【発明を実施するための形態】
【００１０】
以下、添付した図面を参照しながら、本発明の実施形態を説明する。なお、図面の説明において同一の要素には同一の符号を付し、重複する説明を省略する。また、図面の寸法比率は、説明の都合上誇張されており、実際の比率とは異なる場合がある。
【００１１】
図１を参照して、図示する血液バッグシステム１０は、血液を採取する際に、採取された血液の初流（初流血）を除去し、その初流血を検査用血液として利用する採血器具である。皮膚上や皮下に存在する細菌が穿刺時の皮膚のかけらとともに侵入するため、初流血を除去している。
【００１２】
血液バッグシステム１０は、採血針１１と、採血針１１を介して採取された血液を収納する血液バッグ１２と、採血針１１と血液バッグ１２とを連通する採血チューブ１３と、採血チューブ１３の途中に配置した分岐コネクタ１４と、分岐コネクタ１４に接続した分岐チューブ１５を介して採血チューブ１３に連通する初流血バッグ１６と、初流血バッグ１６の端部に接続されたサンプリングポート２０と、を有している。分岐コネクタ１４には血液バッグ１２への連通を封止する封止部材１７が設けられている。初流血バッグ１６への初流血の採血が終わるまで、封止部材１７は血液バッグ１２への連通を封止している。分岐チューブ１５には、初流血バッグ１６への血流を遮断するクランプ部材１８が設けられている。初流血の採血が終わると、クランプ部材１８によって分岐チューブ１５をクランプし、初流血バッグ１６への血流が遮断される。その後、封止部材１７を開放し、血液バッグ１２への採血を開始する。
【００１３】
図２には、初流血バッグ１６に収納した初流血を検査用血液として回収するときの状態が示されている。初流血バッグ１６に接続された血液取出チューブ１９にサンプリングポート２０が接続されている。サンプリングポート２０には、開口部３１を開閉する蓋部材４０がヒンジ４１を介して回動自在に接続されている。初流血バッグ１６に収納した初流血を検査用血液として回収するときには、ゴム栓５１を備える減圧採血管５０（採血管に相当する）が開口部３１からサンプリングポート２０内に挿入される。
【００１４】
減圧採血管５０は、初流血バッグ１６内に貯留された初流血を採取するための器具である。この減圧採血管５０は、採血管本体５２と、この採血管本体５２の開口に嵌め込まれているゴム栓５１と、を有している。減圧採血管５０内は、真空または減圧状態になっている。減圧採血管５０は、サンプリングポート２０に接続されたとき、ゴム栓５１が中空針６１によって刺通される。これによって、減圧採血管５０内と血液取出チューブ１９とが連通し、当該血液取出チューブ１９からの初流血が減圧採血管５０に回収される。
【００１５】
図３および図４を参照して、実施形態に係るサンプリングポート２０は、概説すれば、ゴム栓５１を備える採血管５０を挿入するための開口部３１が形成された本体部３０と、採血管５０のゴム栓５１に挿通自在な中空針６１と、中空針６１の基端部を支持するハブ６４と、中空針６１に被せられた弾性を有するゴムキャップ７０と、ゴムキャップ７０を保持する保持部８０と、を備え、本体部３０に取り付けられた針組立体６０と、を有している。サンプリングポート２０はさらに、ゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められることによって生じる皺７１（図４を参照）が保持部８０に達することを抑制する抑制部材９０を有している。抑制部材９０は、ゴムキャップ７０が被せられた中空針６１が貫通する貫通孔９１を備えている。なお、図３および図４において図中上側を各部材における「上部側」とし、図中下側を各部材における「下部側」とする。以下詳述する。
【００１６】
本体部３０は、円筒形状を有し、下部側は先細りの形状を有している。本体部３０には

、針組立体６０を差し込むための差込口３２と、差し込まれた針組立体６０の抜けを防止する係止部３３とが設けられている。

【００１７】

本体部３０は、針組立体６０に対して回動自在に取り付けられている。回動自在にすることによって、本体部３０を針組立体６０に対して回動させて、初流血バッグ１６に対する蓋部材４０の位置などを簡単に微調整することができる。

【００１８】

針組立体６０は、先端に鋭利な針先を有する中空針６１と、血液取出チューブ１９に接続される接続部６２と、中空針６１の基端部を保持するボス部６３と、を有している。ハブ６４は、ボス部６３の径方向外方へ突出するように設けている。針組立体６０は、本体部３０の差込口３２に差し込むときにハブ６４が係止部３３を乗り越えて、本体部３０に取り付けられる。ハブ６４の図中上端は、差し込むときに係止部３３を乗り越え易いように傾斜面に形成されている。

【００１９】

本体部３０を針組立体６０に対して回動自在に取り付けるために、針組立体６０の接続部６２と本体部３０の差込口３２との間のクリアランス、およびハブ６４の外周と本体部３０との間のクリアランスの寸法が調整されている。

【００２０】

ゴムキャップ７０は、本体部３０に採血管５０を挿入させ、中空針６１をゴム栓５１に挿通させるのに伴って、弾性的に縮められて皺７１を生じながら中空針６１を露出させる。採血管５０を引き抜くと、ゴムキャップ７０は、縮んだ状態から、皺７１を伸ばすように弾性的に伸び、中空針６１に再び被せられる状態まで復元する。これによって、中空針６１からの血液の漏洩を防止する。

【００２１】

保持部８０は、中空針６１が挿通されるとともに針組立体６０のボス部６３に取り付けられたロック部材８１から構成されている。ロック部材８１は、中空針６１の基端部側が先端側よりも小径部となったアンダーカット形状を有している。ロック部材８１におけるアンダーカット形状によって、ゴムキャップ７０を保持している。

【００２２】

図５（Ａ）（Ｂ）を参照して、抑制部材９０は、本体部３０内に嵌り込む円盤形状の平板部９３と、平板部９３の中央部分において上部側に向けて突出する凸部９４とを有するプレート９２から構成されている。凸部９４に、ゴムキャップ７０が取り付けられた中空針６１が貫通する貫通孔９１が形成されている。図５（Ｃ）に示すように、平板部９３の外周縁には、径方向外方に突出するリング状突起９５が、平板部９３と一体的に設けられている。

【００２３】

図３および図４を再び参照して、プレート９２は、保持部８０をなすロック部材８１よりも上部側の位置において、本体部３０内に取り付けられている。本体部３０に採血管５０を挿入し、中空針６１をゴム栓５１に挿通させるのに伴って、ゴムキャップ７０は、弾性的に縮められて皺７１を生じながら中空針６１を露出させている。プレート９２の貫通孔９１とゴムキャップ７０との間のクリアランスＳは比較的小さい。したがって、プレート９２によって、ゴムキャップ７０が弾性的に縮められることによって生じる皺７１が保持部８０に達することが抑制される（図４）。

【００２４】

前述のように本体部３０は、針組立体６０に対して回動自在に取り付けられている。そして、本体部３０に固定されたプレート９２の貫通孔９１とゴムキャップ７０との間に、本体部３０の回動を許容するクリアランスＳを設定してある。クリアランスＳを本体部３０の回動を阻害しない寸法に設定することによって、針組立体６０に対する本体部３０の回動位置や、初流血バッグ１６に対する蓋部材４０の位置などを簡単に微調整することが可能となる。

【００２５】
プレート９２に凸部９４を備えさせることによって、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくすることができる。その結果、ゴムキャップ７０を針組立体６０に保持するための保持力の低下をより一層抑えることができる。プレート９２の配置位置を図４に示される位置から上部側にずらしても、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくすることができる。但し、この場合には、採血管５０の位置も上部側にずれるため、本体部３０の長手方向の長さ寸法を若干大きくする必要が生じる場合がある。したがって、プレート９２に本体部３０の開口部３１の側に向けて突出する凸部９４を備えさせることによって、本体部３０の長手方向の長さを維持したまま、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくして、ゴムキャップ７０を針組立体６０に保持するための十分な保持力を確保することが可能となる。

【００２６】
本体部３０、蓋部材４０、中空針６１を除いた針組立体６０、保持部８０、およびプレート９２の構成材料としては、特に限定されないが、例えば、ポリカーボネート、ポリエチレン、ポリプロピレン、エチレン－酢酸ビニル共重合体等のポリオレフィン、変性ポリオレフィンが挙げられる。

【００２７】
中空針６１の構成材料としては、特に限定されないが、例えば、ステンレス鋼、アルミニウムまたはアルミニウム合金、チタンまたはチタン合金、Ｎｉ－Ｔｉ合金等の超弾性合金等の各種金属材料、ポリフェニレンサルファイド等の各種硬質樹脂材料等が挙げられる。

【００２８】
また、ゴムキャップ７０の構成材料としては、特に限定されないが、例えば、天然ゴム、イソプレンゴム、ブタジエンゴム、スチレン－ブタジエンゴム、ニトリルゴム、クロロプレンゴム、ブチルゴム、アクリルゴム、エチレン－プロピレンゴム、ヒドリンゴム、ウレタンゴム、シリコーンゴム、フッ素ゴムのような各種ゴム材料が挙げられる。

【００２９】
図６（Ａ）（Ｂ）に、プレート９２を本体部３０に対して固定する様子が示される。本実施形態においては、本体部３０は、熱を印加したときにプレート９２を形成する樹脂材料よりも大きく収縮する樹脂材料から形成してある。滅菌のための熱を印加することによって、プレート９２を本体部３０に対して固定することができるからである。

【００３０】
さらに詳しくは、図６（Ａ）に示すように、熱を印加する前では、本体部３０の内径が比較的大きく、プレート９２のリング状突起９５が若干寸法だけ本体部３０に食い込んでいる。プレート９２を比較的簡単に本体部３０内に挿入できることから、プレート９２の組み込み作業を行いやすい。

【００３１】
そして、図６（Ｂ）に示すように、滅菌のために行われる例えば高圧蒸気滅菌法（オートクレーブ）における熱を印加すると、本体部３０がプレート９２よりも大きく収縮する。これによって、プレート９２のリング状突起９５が本体部３０にさらに食い込み、プレート９２を本体部３０に対して簡単に固定することができる。

【００３２】
上記のような樹脂材料の組み合わせ例として、例えば、本体部３０の成形材料としてポリプロピレンを適用し、プレート９２の成形材料としてポリカーボネートを適用することができる。

【００３３】
本実施形態の作用を説明する。

【００３４】
採血するときには、サンプリングポート２０の本体部３０に採血管５０を挿入し、中空

針６１をゴム栓５１に挿通させる。ゴム栓５１に中空針６１が挿通するのに伴って、ゴムキャップ７０は、弾性的に縮められて皺７１を生じながら中空針６１を露出させる。

【００３５】

図７（Ｂ）を参照して、プレート９２を設けていない対比例の場合には、採血管５０のゴム栓５１への中空針１６１の挿通に伴ってゴムキャップ１７０が弾性的に縮められることによって生じる皺１７１が、ゴムキャップ１７０の根元部に達することがある。このような場合には、ゴムキャップ１７０の根元部が膨らんでしまい、ゴムキャップ１７０を針組立体１６０に保持するための保持力が弱くなる。このため、採血管５０を引き抜くときにゴムキャップ１７０が一緒に引っ張られてしまい、ゴムキャップ１７０の位置などがずれてしまい、血液の漏洩の防止が不十分になる虞がある。

【００３６】

これに対して、図４および図７（Ａ）を参照して、本実施形態にあっては、プレート９２を、保持部８０をなすロック部材８１よりも上部側の位置において、本体部３０内に取り付けている。このプレート９２によって、採血管５０のゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められることによって生じる皺７１がロック部材８１に達することが抑制される。ロック部材８１の部分でゴムキャップ７０が膨らむことがないので、ゴムキャップ７０を針組立体６０に保持するための保持力が弱くならない。

【００３７】

露出した中空針６１は、ゴム栓５１に挿通されて、採血管５０に採血する。採血後に採血管５０を引き抜くと、ゴムキャップ７０は、縮んだ状態から、皺７１を伸ばすように弾性的に伸び、中空針６１に再び被せられる状態まで復元する。これによって、中空針６１からの血液の漏洩を防止する。ゴムキャップ７０は、ロック部材８１の部分で針組立体６０に保持されている。

【００３８】

採血管５０のゴム栓５１の微小な挿通孔にゴムキャップ７０の先端部が食い込んだ状態で採血管５０を引き抜くと、ゴムキャップ７０が一緒に引っ張られる。しかし、ロック部材８１の部分は皺７１の影響を受けていないので、保持力は初期に設定したままである。このため、ゴムキャップ７０は、中空針６１から抜けずに、採血管５０のゴム栓５１への食い込みが解除される。これによって、ゴムキャップ７０の位置などがずれることがなく、血液の漏洩を十分に防止することが可能となる。

【００３９】

このように、採血管５０のゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められて皺７１が生じても、ゴムキャップ７０を針組立体６０に保持するための保持力を維持でき、もって、血液の漏洩を十分に防止し得るサンプリングポート２０を提供できる。

【００４０】

また、本体部３０は針組立体６０に対して回動自在に取り付けられ、プレート９２は本体部３０に固定されており、貫通孔９１とゴムキャップ７０との間に本体部３０の回動を許容するクリアランスＳを有するため、針組立体６０に対する本体部３０の回動位置などを簡単に微調整することが可能となる。

【００４１】

また、プレート９２は、本体部３０の開口部３１の側に向けて突出する凸部９４を備えているため、本体部３０の長手方向の長さを維持したまま、ゴムキャップ７０の長手方向のうち皺７１の影響を受けない範囲を大きくして、ゴムキャップ７０を針組立体６０に保持するための十分な保持力を確保することが可能となる。

【００４２】

また、プレート９２の外周縁に径方向外方に突出するリング状突起９５を設けているため、リング状突起９５を若干寸法だけ本体部３０に食い込ませるようにしてプレート９２を本体部３０内に挿入させることができ、簡単にプレート９２の組み込み作業を行うこと

が可能となる。

【００４３】

また、本体部３０は、熱を印加したときにプレート９２を形成する樹脂材料よりも大きく収縮する樹脂材料から形成されており、滅菌のための熱を印加することによって、プレート９２を本体部３０に対して固定するため、熱を印加する前ではプレート９２を比較的簡単に本体部３０内に挿入でき、プレート９２の組み込み作業を行いやすい。一方、滅菌のための熱を印加すると、本体部３０がプレート９２よりも大きく収縮する。これによって、プレート９２を本体部３０に対して簡単に固定することができる。

【００４４】

（プレートの改変例）

プレートは、ゴムキャップ７０が取り付けられた中空針６１が貫通する貫通孔９１を備え、採血管５０のゴム栓５１への中空針６１の挿通に伴ってゴムキャップ７０が弾性的に縮められることによって生じる皺７１が保持部８０に達することを抑制する限りにおいて適宜の形状に改変することができる。

【００４５】

例えば、図８を参照して、凸部９４を平板部９３から滑らかに突出させたプレート９２ａ（図８（Ａ））、全体の厚みを厚くし上面を平坦面としたプレート９２ｂ、９２ｃ（図８（Ｂ）（Ｃ））、本体部３０の底面全体を覆わずに保持部８０に被せるようなキャップ形状を有するプレート９２ｄ（図８（Ｄ））などを例示することができる。

【００４６】

また、図９を参照して、平板部９３に貫通部を形成しないタイプのプレート９２ｅ（図９（Ａ））、平板部９３に貫通部９６を形成したタイプのプレート９２ｆ（図９（Ｂ））とすることもできる。

【００４７】

（その他の改変例）

ゴムキャップ７０を保持する保持部８０として、アンダーカット形状を有するロック部材８１を例示したが、保持部８０はこの場合に限定されるものではない。保持部８０は、針組立体６０に設けられゴムキャップ７０の抜けを防止して保持する機能を有している限りにおいて適宜改変することができる。例えば、保持部８０は、接着剤によってゴムキャップ７０を中空針６１に接着させて保持する形態、超音波融着によってゴムキャップ７０を中空針６１に融着させて保持する形態、クリップなどを用いた嵌め込みによってゴムキャップ７０を中空針６１に保持する形態などを例示することができる。これらの保持部８０を単独で用いてもよいし、２種以上を組み合わせた保持部８０であってもよい。

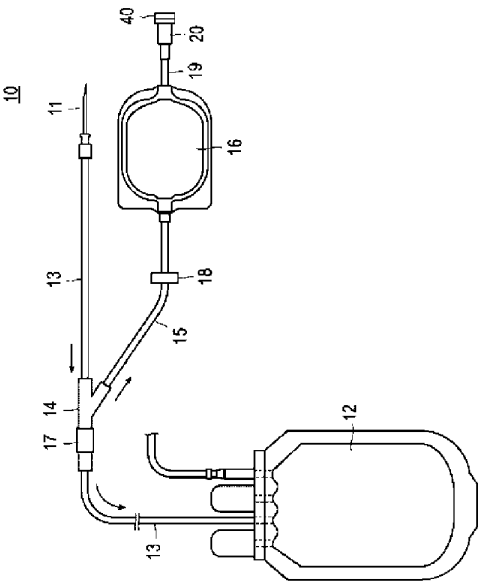
【符号の説明】

【００４８】

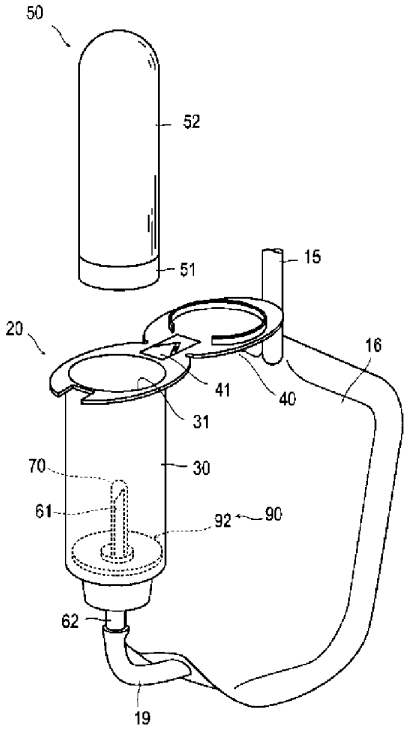
２０　サンプリングポート、
３０　本体部、
３１　開口部、
５０　減圧採血管（採血管）、
５１　ゴム栓、
６０　針組立体、
６１　中空針、
６４　ハブ、
７０　ゴムキャップ、
７１　皺、
８０　保持部、
８１　ロック部材、
９０　抑制部材、
９１　貫通孔、
９２　プレート（抑制部材）、

９３　　平板部、
９４　　凸部、
９５　　リング状突起、
Ｓ　　クリアランス。

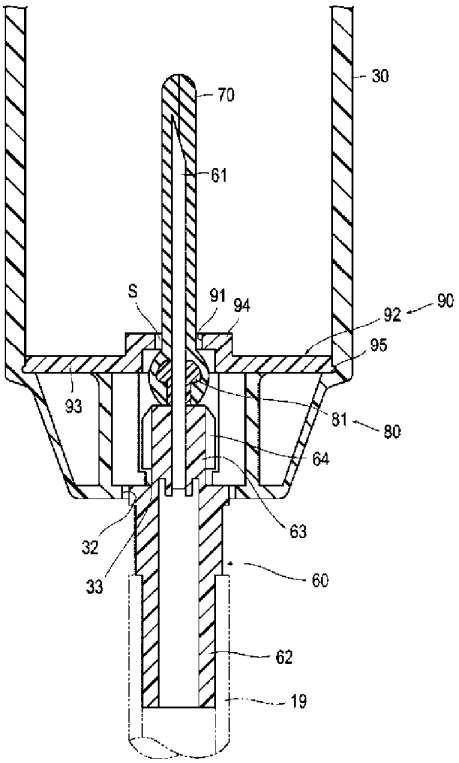
【図１】



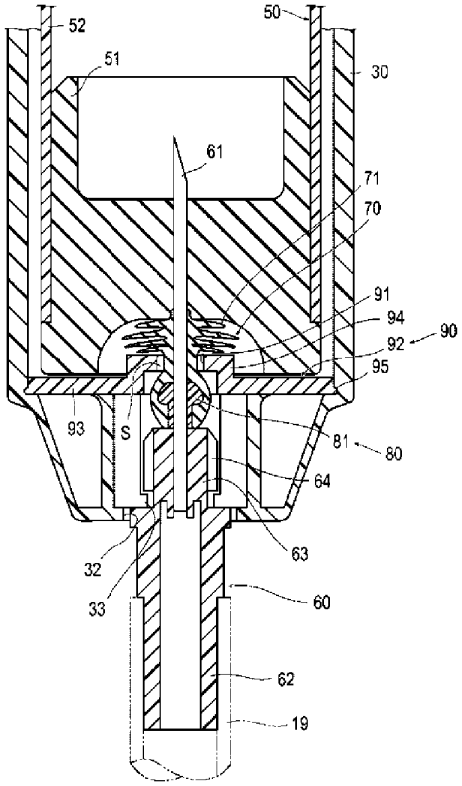
【図２】



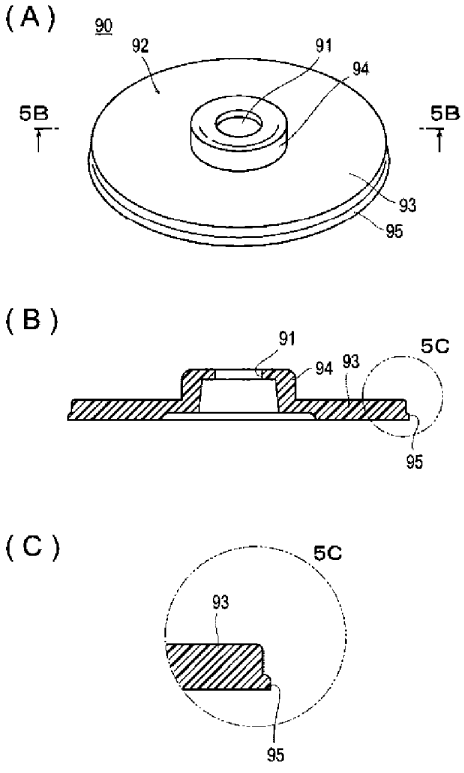
【図３】


70
30
61
S
91
94
92
90
95
93
81
80
64
63
32
33
60
62
19

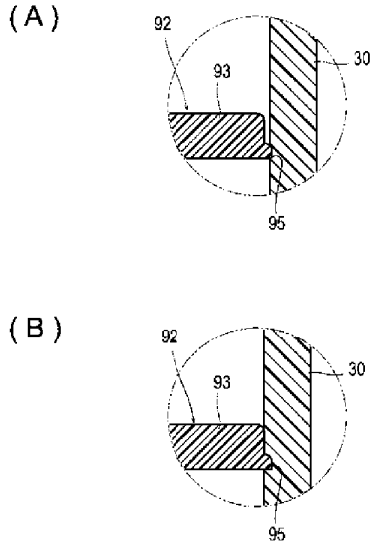
【図４】


52
50
51
30
61
71
70
91
94
92
90
95
93
S
81
80
64
63
32
33
60
62
19

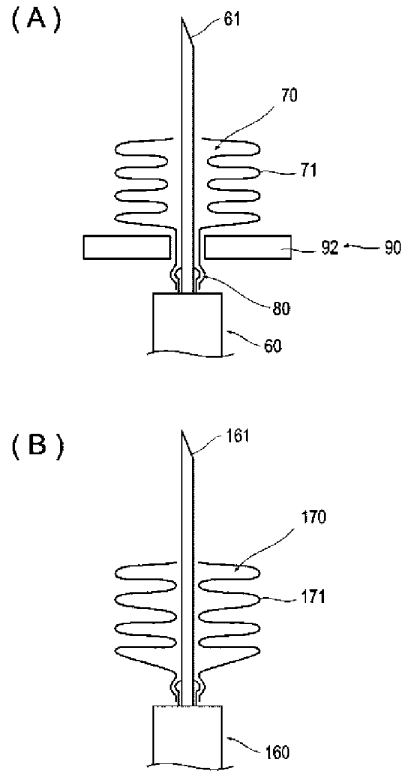
【図５】


(A)
90
92
91
94
5B
5B
93
95
(B)
91
94
93
5C
95
(C)
5C
93
95

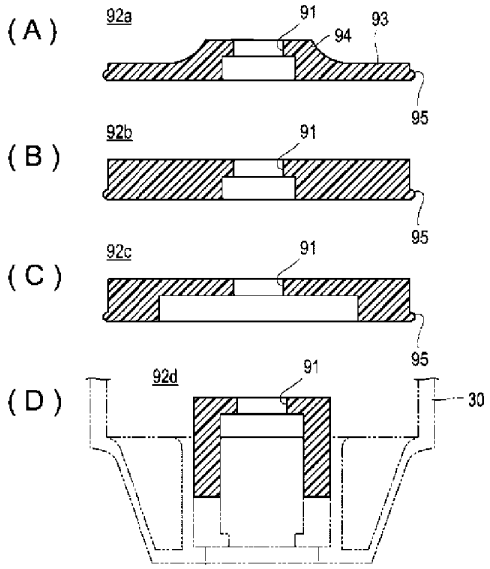
【図６】


(A)
92
30
93
95
(B)
92
30
93
95

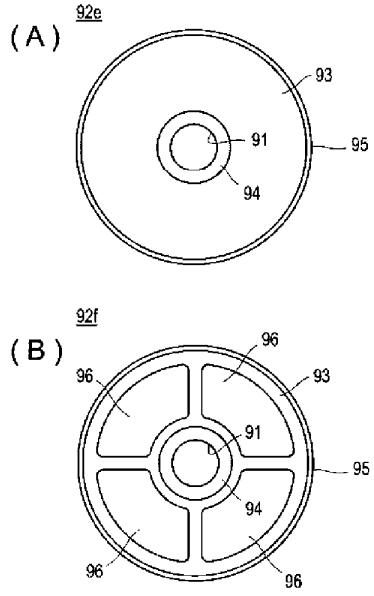
【図７】


(A)
61
70
71
92
90
80
60
(B)
161
170
171
160

【図８】


(A)
92a
91
94
93
95
(B)
92b
91
95
(C)
92c
91
95
(D)
92d
91
30

【図９】


(A)
92e
93
91
95
94
(B)
92f
96
96
93
91
95
94
96
96

フロントページの続き

Ｆターム(参考) 4C038 TA01 TA10 UA10 UB07 UF03 UF11 UF14
4C066 AA07 BB10 FF05 JJ08

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Special table 2019-534792

Registration Gazette Document unit PDF progress information OPD search key URLs

Display format of the document display screen:
text display PDF display
primary literature

bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] Special table 2019-534792 (P2019-534792A)
(43) [Publication date] December 5, 2019 (2019.12.5)
(54) [Title of invention] Cooling of rolls in rolling stands
(51) [International patent classification]
B21B 27/10 (2006.01)
[FI]
B21B 27/10 A
B21B 27/10 C
B21B 27/10 D
[Request for examination] Yes
[Request for preliminary examination] Not yet requested
[Total number of pages] 21
(21
) 22) [Filing date] October 12, 2017 (2017.10.12)
(85) [Translation submission date] June 13, 2019 (2019.6.13)

(86) [International application number] PCT/ EP2017/076000
(87) [International publication number] WO2018/073086 (87) [International publication date] April 26, 2018 (2018.4.26) (31) [Priority claim number] 16194099.4 (32) [Priority date] October 17, 2016 (2016.10.17) (33) [Country/region or organization claiming priority] European Patent Office (EP)

(81) [Designated countries/regions] AP (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), EA (AM, AZ, BY, KG, KZ, RU, TJ, TM), EP (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR ,HU,IE,IS,IT,LT,LU,LV,MC,MK,MT,NL,NO,PL,PT,RO,RS,SE,SI,SK,SM,TR),OA(BF,BJ, CF,CG,CI,CM,GA,GN,GQ,GW,KM,ML,MR,NE,SN,TD,TG),AE,AG,AL,AM,AO,AT,AU,AZ,BA,BB , BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES ,FI,GB,GD,GE,GH,GM,GT,HN,HR,HU,ID,IL,IN,IR,IS,JO,JP,KE,KG,KH,KN,KP,KR,KW,KZ ,LA,LC,LK,LR,LS,LU,LY,MA,MD,ME,MG,MK,MN,MW,MX,MY,MZ,NA,NG,NI,NO,NZ,OM,PA,PE ,PG,PH,PL,PT,QA,RO,RS,RU,RW,SA,SC,SD,SE,SG,SK,SL,SM,ST,SV,SY,TH,TJ,TM,TN,TR , TT

(71) [Applicant]
[Identification number] 515153152
[Name] Primetals Technologies Austria GmbH
(74) [Agent]
[Identification number] 100133400 [
Patent attorney]
[Name] Tatsuhiko Abe
(74) [Agent]
[Identification number] 100110364
[Patent Attorney]
[Name] Shinya Sanehiro
(72) [Inventor]
[Name] Alois Seilinger
(72) [Inventor]
[Name] Erich Orpits
(72) [Inventor]
[Name] Lucas Pichler

wrap up close

(57) [Summary]

The present invention relates to a cooling device (7) for cooling the rolls (5) of the rolling sta nd (1). The cooling device (7) comprises cooling beams (13) for receiving and discharging coo lant. The cooling beam (13) has a plurality of full jet nozzles (21) arranged on the discharge si de (19) of said cooling beam (13), said side facing the roll (5).) extending parallel to the roll axis (17). A jet of coolant with a substantially constant jet diameter can be sprayed through e ach of the full jet nozzles from the cooling beam (13) towards the roll (5) in the discharge dire ction (23).

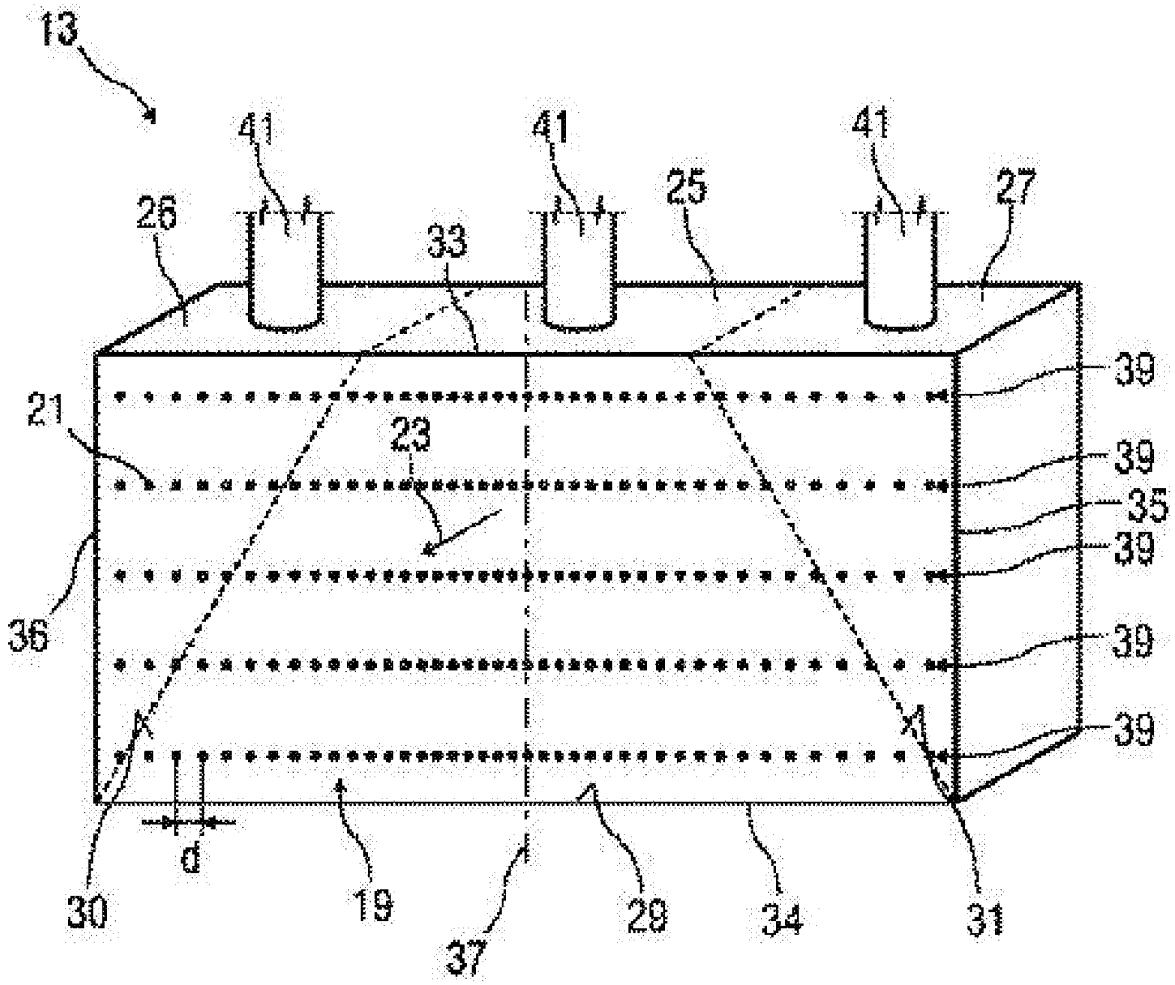


FIG 2

The scope of the claims open

We claim:

1.

A cooling device (7) for cooling rolls (5) of a rolling stand (1) comprising cooling bars (13) fo r receiving and discharging a coolant. wherein

said cooling rod (13) has a plurality of full jet nozzles (21) arranged on a discharge side (19) of said cooling rod (13), said discharge side facing a roll (5). , extending parallel to the roll axi s (17) of said roll (5) and sending coolant jets of substantially constant jet diameter through e ach of the full jet nozzles from said cooling rods (13) to said roll. A cooling device (7) capable of discharging in a discharge direction (23) towards (5).

2.

The cooling rod (13) is divided into at least two mutually separated coolant chambers (25-2 7) for receiving coolant, each coolant chamber (25-27) comprising: Corresponding sub-region s (29-31) of said discharge side (19) of said cooling rod (13) where a plurality of full-jet nozzl es (21) are arranged, through each of said full-jet nozzles (21), coolant Cooling device (7) acc ording to claim 1, characterized in that a jet can be discharged from the coolant chamber (25-27) towards the roll (5).

3.

A first coolant chamber (25) corresponds to a first partial area (29) of said discharge side (1 9) of said cooling rod (13), said first partial area (29)) is mirror symmetrical with respect to t he centerline (37) of the discharge side (19) of the cooling rod (13), the axis being perpendic ular to the roll axis (17). 3. Cooling device (7) according to claim 2.

[Claim 4]

characterized in that the extent of the first sub-region (29) parallel to the center line (37) va ries along the direction of said roll axis (17) and is greatest along said center line (37). A cooli ng device (7) according to claim 2 or 3, wherein

5.

A cooling device (7) according to any one of claims 2 to 4, characterized in that the first part ial area (29) is polygonal.

6.

Each coolant chamber (25-27) is connected to a coolant supply line (41) for supplying coola nt into said coolant chamber (25-27), said coolant supply line (41) opens into said coolant cha mber (25-27) substantially perpendicular to said discharge direction (23) of said coolant. A co oling device (7) according to claim 1.

7.

The amount of coolant supplied into the coolant chambers (25-27) is controlled independentl y of each other by respective control valves (43) and/or respective pumps (45). A cooling devi ce (7) according to any one of claims 2 to 6, characterized in that it is capable of

8. A

system according to any one of claims 2 to 7, characterized by an automated system for con trolling the amount of coolant fed into the coolant chamber (25-27). Cooling device (7).

9.

Characterized in that the nozzle spacing (d) of full jet nozzles (21) adjacent to each other al ong a direction parallel to said roll axis (17) varies along said direction. A cooling device (7) a ccording to any one of claims 1 to 8.

[Claim 10]

10. Cooling device (7) according to claim 9, characterized in that said nozzle spacing (d) is n arrowest in a central region of said discharge side (19) of said cooling rod (13).

11.

The nozzle spacing (d) is between about 25 mm and about 50 mm.

Cooling device (7) according to claim 9 or 10.

12. The method

according to any one of claims 1 to 11, characterized in that said full jet nozzles (21) are arr anged in a plurality of mutually parallel nozzle rows (39). A cooling device (7) as described.

13.

Characterized in that said cooling rod (13) has a nozzle opening for each full jet nozzle (21) to which said full jet nozzle (21) is detachably fixed. A cooling device (7) according to any one of claims 1 to 12.

14.

A wiper (15) for wiping coolant from said roll (5), characterized by a wiper (15) which can be pivoted together with said cooling rod (13). A cooling device (7) according to any one of claim s 1 to 13.

15. A

rolling stand (1) with rolls (5) and two cooling devices (7) each designed as claimed in any o ne of claims 1 to 13. A rolling stand (1), wherein said two cooling devices (7) are arranged on either side of said rolls (5).

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to a cooling device for cooling the rolls of a rolling stand. BACKGROUND OF THE INVENTION Rolling stands for rolling rolling stock hav e rolls which are cooled with a cooling liquid, generally cooling water. [0003] US Pat. No. 6,2 00,000 discloses a stiff, concave shell that allows low-pressure cooling liquid to be applied to t he rolls of a rolling stand. [0004] US Pat. No. 6,200,000 discloses fluid cooling of the work r

olls of a roll stand by means of movable, articulated cooling shells. In this case, the cooling liq uid is applied mainly at low pressure using the cooling shell, but in addition the cooling liquid i s applied at high pressure to produce a sufficient cooling effect. [0005] US Pat. No. 5,300,00 9 discloses a cooling device for cooling the work rolls of a rolling stand, which device comprise s a fixed spray that is slightly narrower than the narrowest strip produced using the relevant r olling stand. It has axially displaceable spray bars for cooling only those portions of the work r olls which have bars and which correspond to the width of the strip being rolled at the time. [0006] US Pat. No. 6,200,403 discloses a method for cooling the work rolls of a rolling stan d, in which cooling water is sprayed onto the work rolls at low pressure rather than high press ure, but at the same time, The range that can be used is widened. [0007]

US Pat. No. 5,300,003 discloses a spray bar for cooling rolled stock, the spray bar extending transversely to the direction of travel of the rolled stock and having a central region and two e dge regions. , the cooling medium can be supplied to each of them separately.
[0008]
[Patent Document 1] US Patent Application Publication No. 2010/0089112 [Patent Document 2] German Patent Application Publication No. 102009053074

[Patent Document 3] JP-A-6-170420 [Patent Document 4] JP-A-59-156506 [Patent Document 5] International Publication No. 2014/170139 [Outline of the Invention] [Problems to be Solve d by the Invention] [SUMMARY OF THE INVENTION It is a principal object of the present inv ention to identify an improved cooling device for cooling the rolls of a rolling stand. [0010] Ac cording to the invention , this object is achieved by the features of claim 1 . Advantageous embodiments of the invention form the subject matter of the dependent claims . A cooling de

vice according to the invention for cooling the rolls of a rolling stand comprises cooling rods f or receiving and discharging coolant. The cooling rod has a plurality of full jet nozzles located on the discharge side of the cooling rod, said side facing the roll and extending parallel to the roll axis of the roll. A coolant jet of coolant of substantially constant jet diameter can be disch arged through each full jet nozzle from the cooling rod toward the roll in the discharge directi on. [0013]

A full jet nozzle shall mean a nozzle capable of delivering a substantially straight jet of coola nt with a substantially constant jet diameter. By virtue of the concentrated coolant discharge, the full jet nozzle produces a higher roll impact pressure at the same coolant pressure at the c ooling rod than the conventionally used fan jet nozzle. Due to the large amount of coolant app lied throughout, there is always a specific coolant film, typically a few millimeters to a few cen timeters thick, by impinging coolant jets for good heat dissipation. Since this film should be p enetrated as completely as possible, a higher impact pressure has a direct positive effect on t he cooling action at the roll surface. Thanks to the high impact pressure of the coolant jets on the rolls produced by the full-jet nozzles, the coolant pressure in the cooling rods can be signif icantly reduced compared to when fan-jet nozzles are used, thereby increasing the cooling sys tem It is advantageous to be able to significantly reduce the energy consumption and operatin g costs of

[0014]

Since the coolant is discharged through a full-jet nozzle, the distance from the roll to the spr ay bar is also less critical over a wider range and therefore does not have to be adapted to the roll diameter. Thus, for example, a substantially straight coolant jet can cool the roll surface to be cooled at distances between 50 mm and 500 mm without any significant change in the coo ling effect of the coolant jet.

[0015]

Since the reduction in coolant pressure is also associated with reduced loading and conseque nt wear on the nozzles, this also results in reduced maintenance costs as a result of reduced c oolant pressure in the cooling rods, which Another advantage of using a full jet nozzle.

[0016]

In one embodiment of the invention, it is envisioned that the cooling rod is divided into at le ast two mutually separated coolant chambers for receiving coolant. Each coolant chamber cor responds to a sub-region of the discharge side of the cooling rod with a plurality of full-jet noz zles arranged through each of the full-jet nozzles to discharge a coolant jet from the coolant c hamber toward the roll. can. Dividing the cooling rod into a plurality of mutually separated co olant chambers corresponding to different subregions of the discharge side of the cooling rod controls the coolant pressure in the subregions independently of each other, resulting in It is a dvantageous to be able to control the cooling effect of the subregions independently of each o ther by controlling the coolant flow rate delivered by the . Thereby, depending on the position, the roll

It is advantageous to be able to influence the cooling and ensure that the more strongly heate d areas of the roll surface, for example the central area of the roll surface, are cooled more st rongly than the less intensely heated areas. . A development of the above-described embodi ment of the invention is that the first coolant chamber corresponds to a first partial area of th e discharge side of the cooling rod, the first partial area being the discharge side of the coolin g rod

.

is assumed to be mirror-symmetrical about the centerline of the roll, and its axis is perpendic ular to the roll axis. For example, the extent of the first subregion parallel to the centerline va ries along the direction of the roll axis and is greatest along the centerline. For example, the fi rst partial area is polygonal. Embodiments in which the first sub-region is mirror-symmetrical about the center line take into account the fact that the rolls are generally also heated symme trically about the center line. The fact that the extent of the first subregion parallel to the cent er line varies along the direction of the roll axis and has a maximum extent along the center li ne means that the roll is generally heated most strongly at the center and the heating of the r oll decreases towards the edge region. A corresponding configuration of the first subregion th us makes it possible to adapt the cooling of the rolls to the position-dependent thermal load o f the rolls by means of the first subregions.

[0018]

In another embodiment of the invention, each coolant chamber is connected to a coolant sup ply line for supplying coolant into the coolant chamber, the coolant supply line supplying coola nt into the coolant chamber. It is assumed that the opening is substantially perpendicular to t he ejection direction of the . The coolant supply lines opening into the cooling rods substantial ly perpendicular to the direction of discharge allow for a substantially uniform coolant pressur e distribution in each coolant chamber. Advantageously, the pressure gradient between the ful

l jet nozzle near the opening and the full jet nozzle away from the opening is thereby eliminat ed.

[0019]

Another embodiment of the invention envisions that the amount of coolant supplied into the coolant chambers can be controlled independently of each other by respective control valves a nd/or respective pumps. This allows the cooling effectiveness of the coolant jets discharged fr om the individual coolant chambers to be controlled independently of each other, as described above. If, for example, a conventional coolant supply system present at any given time can be used in the relevant rolling system, for example a water supply system that normally delivers cooling water at a pressure of 4 bar, the control It is particularly advantageous to control the amount of coolant by means of a valve. In this case, complex and expensive pressure boost s ystems can be dispensed with for roll cooling. By controlling the amount of coolant by the pu mps, if appropriate in conjunction with control valves, individual pumps can be turned off or t urned on during breaks between rolling or in the case of rolling operations requiring only a lo w cooling capacity. Power can be lowered, thereby reducing energy consumption. Another e mbodiment of the present invention contemplates an automated system for controlling the a mount of coolant supplied into the coolant chamber

.

Thereby, it is advantageous to be able to automatically control the volumetric flow rate of the coolant discharged from the coolant chamber onto the roll in order to adapt the volumetric flo w rate to the temperature distribution of the roll surface. In this case, the amount of coolant s upplied into the coolant chamber is preferably controlled by an automated system through co ntrolling the control valves and/or pumps mentioned above.

[0021]

In another embodiment of the invention, it is envisaged that the nozzle spacing of full jet no zzles adjacent to each other along a direction parallel to the roll axis varies along said directio n. In this case, the nozzle spacing is preferably the narrowest in the central region of the disc harge side of the cooling rod. For example, the nozzle spacing along the direction parallel to t he roll axis is between about 25mm and about 50mm. These embodiments of the present inve ntion also allow the nozzle spacing along the direction parallel to the roll axis to be varied acc ording to the position-dependent thermal load of the roll surface, so that the placement of the full-jet nozzles can also be adapted to this thermal load. can. The minimum nozzle spacing in the central region of the discharge side of the cooling rods takes into account the fact that the central region of the roll surface generally experiences the greatest heat load.

Another

embodiment of the present invention envisions that the full jet nozzles are arranged in parall el rows of nozzles. Advantageously, this allows the coolant to be applied to the roll over a wid er area and evenly as the roll rotates.

Another

embodiment of the invention envisions that the cooling rod has a nozzle opening for each full jet nozzle to which the full jet nozzle is removably secured. Advantageously, this embodiment of the present invention allows for easy replacement of defective jet nozzles.

In another embodiment of the invention, a wiper is provided for wiping coolant from the roll, and the wiper and cooling bar can be pivoted together. For example, wipers direct excess coolant to the rolled stock and/or to the roll nip where the rolled stock is guided between two rolls to reduce friction between the rolled stock and the rolls. It is advantageous to be able to prevent the lubricant from washing away. Advantageously, the ability to pivot the wiper and cooling rods together obviates the need for additional equipment to move the cooling rods. In this case, the advantages of using full-jet nozzles already mentioned above are also in effect here. That is, by using a full-jet nozzle, the distance between the spray bar and the roll becomes less critical over a wider range and therefore no longer needs to be adapted to the roll diameter. Furthermore, the present invention is also particularly suitable as a retrofit to existing rolling systems with wipers, for example only conventional high pressure spray rods need to be replaced with cooling rods according to the invention.

[0025]

The rolling stand according to the invention comprises rolls and two cooling devices according to the invention, the two cooling devices being arranged on opposite sides of the rolls. The advantages of the rolling stand according to the invention result from the advantages of the cooling device according to the invention already mentioned above.

The above-described properties, features, and advantages of the present invention, as well as the manner in which they are achieved, will become clearer and will be clearly understood.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027]

FIG. 1 is a schematic view of a rolling stand with cooling device;

2 is a schematic perspective view of a first exemplary embodiment of a cooling rod; FIG.

3 shows the volumetric flow rate of coolant delivered by the cooling rods shown in FIG. 2 as a function of position; FIG.

FIG. 4 is a discharge side view of a second exemplary embodiment of a cooling rod;

FIG. 5 is a discharge side view of a third exemplary embodiment of a cooling rod;

FIG. 6 is a discharge side view of a fourth exemplary embodiment of a cooling rod;

FIG. 7 is a view of the discharge side of the fifth exemplary embodiment of the cooling rod;

FIG. 8 is a view of the discharge side of the sixth exemplary embodiment of the cooling rod;

FIG. 9 is a view of the discharge side of the seventh exemplary embodiment of the cooling rod;

FIG. 10 is a discharge side view of an eighth exemplary embodiment of a cooling rod;

FIG. 11 is a discharge side view of a ninth exemplary embodiment of a cooling rod;

FIG. 12 is a discharge side view of a tenth exemplary embodiment of a cooling rod;

[Mode for carrying out the invention]

[0028]

In all drawings, the same parts are provided with the same reference numerals.

[0029]

FIG. 1 is a schematic diagram of a rolling stand 1 for rolling a rolling stock 3. FIG. The rolling stand 1 comprises two rolls 5 designed as work rolls and two cooling devices 7 for each roll 5 , said devices being arranged on either side of the rolls 5 . The rolls 5 are spaced apart by a r oll nip 9 and pass the rolling stock 3 through the roll nip 9 in the rolling direction 11 to form t he rolled stock 3 . Each cooling device 7 comprises cooling bars 13 and wipers 15 . Each cool ing rod 13 is designed to receive and discharge coolant

.

For discharging the coolant, the cooling rod 13 has a plurality of full jet nozzles 21 arranged o n the discharge side 19 of the cooling rod 13, said side facing the respective roll 5 and the roll of the roll 5. A coolant jet extending parallel to axis 17 and having a substantially constant jet diameter can be discharged in discharge direction 23 from cooling rod 13 towards roll 5 throu gh each of the full-jet nozzles. Coolant may be supplied into the cooling rods 13 via coolant su pply lines 41, the amount of coolant supplied into the cooling rods 13 being controlled by a co ntrol valve 43 and/or a frequency controlled pump 45, for example. can be controlled by A co olant is, for example, water. Each wiper 15 is designed to wipe coolant from the respective r oll 5 and can be pivoted toward and away from the roll 5

.

The cooling rods 13 and wipers 15 of each cooling device 7 are fixed to the pivoting device of the cooling device 7 , thus pivoting the cooling rods 13 and wipers 15 together toward and aw ay from the rolls 5 . Preferably, it can be moved.

[0032]

FIG. 2 is a schematic perspective view of a first exemplary embodiment of cooling rods 13 fo r delivering coolant to rolls 5. As shown in FIG. The cooling rod 13 is divided into three mutual ly separated coolant chambers 25-27 to receive coolant. Each coolant chamber 25-27 corresp onds to a sub-region 29-31 of the discharge side 19 in which a plurality of full jet nozzles 21 a re arranged to roll coolant jets from the coolant chambers 25-27 through each of the full jet n ozzles. 5 can be discharged in the discharge direction 23 . The discharge side 19 is rectangula r with two longitudinal sides 33 , 34 parallel to the roll axis 17 and two lateral sides 35 , 36 pe rpendicular to the roll axis 17 . The first coolant chamber 25 corresponds to a first partial ar ea 29 of the discharge side 19 of the cooling rod 13 forming the central area of the discharge side 19

.

The first partial region 29 is mirror-symmetrical to the centerline 37 of the discharge side 19 o f the cooling rod 13, said axis being perpendicular to the roll axis 17 and arranged on the first longitudinal side 33. It is a trapezoid with four vertices and two vertices each located at the e

ndpoint of the second longitudinal side 34 .

[0034]

The full jet nozzles 21 are arranged on the discharge side surface 19 in a plurality of nozzle r ows 39 each extending parallel to the roll axis 17 . In this case, the nozzle spacing d between the adjacent full jet nozzles 21 of each nozzle row 39 varies symmetrically with respect to the center line 37, so that the nozzle spacing d is is narrowest at and widens towards the edge re gion of the outlet side 19, for example parabolically. In the exemplary embodiment shown in F IG. 2, the nozzle spacing d is twice as large at the ends of each nozzle row 39 as it is at the c enter of the nozzle row 39 . The nozzle spacing d varies, for example, between 25mm and 50 mm. The nozzle rows 39 extend substantially evenly over the entire extent of the discharge si de 19 and thus produce a relatively uniform cooling effect on the roll surface of the roll 5 . A further development of the exemplary embodiment shown in FIG. 2 envisions arranging the n ozzle rows 39 staggered with respect to each other, so that the full jet nozzles 21 of the vario us nozzle rows 39 are arranged in

roll

It is not arranged along a direction perpendicular to the axis 17. A "cooling channel" extends perpendicular to the row of nozzles 39 where no coolant is ejected onto the roll 5, resulting in a reduced cooling effect, but this "cooling channel" can be avoided. so that the nozzle row 39 has a particularly uniform

Advantageously, a good cooling effect is achieved. Furthermore, the full jet nozzles 21 very c lose to or on the boundary between two adjacent sub-regions 29-31 in FIG

.

Displaced with respect to the arrangement, they are arranged to fall into one of the adjacent s ub-regions 29-31, which subdivide into the coolant chambers 25-27 inside the cooling tube 13 by the separating plate such a boundary line. because it extends along Each full jet nozzle 2 1 is removably attached to the nozzle opening of the cooling rod 13, for example by a threade d joint

.

Each full jet nozzle 21 has a minimum diameter nozzle cross-section of, for example, about 4 mm. Each coolant chamber 25-27 is connected to a coolant supply line 41 for supplying cool ant into the coolant chambers 25-27

.

, it is open substantially perpendicular to the discharge direction 23 of the coolant. The cross-sections of the coolant supply lines 41 each have a diameter of, for example, between 100 m m and 150 mm. The amount of coolant supplied into coolant chambers 25-27 via coolant su pply line 41 is controlled by respective control valves 43 (not shown in FIG. 2) and/or respecti ve pumps

.

can be controlled independently of each other by 45 (not shown in FIG. 2). Advantageously, t

his allows the amount of coolant discharged from the coolant chambers 25-27 to be adapted t o different heat loads in different regions of the roll surface.

FIG . 3 shows, by way of example, the volume flow rate V_1 of three coolants discharged from the cooling rod 13 shown in FIG. , V_2 , V_3 as a function o f the position y along the direction parallel to the roll axis 17 . Here, the volumetric flows V_1 , V_2 , V_3 are expressed as a percentage of the rated flow.

The rated flow is the first volumetric flow V_1 at the center position y_m . A first volumetric flow rate V_1 occur s when coolant is fed into all three coolant chambers 25-27 at the same specified pressure rat ing for all coolant chambers 25-27. The first volume flow rate V_1 has a parabolic shape with a maximum at the central position y_m and decreases from the central position y_m towards the two end regions to half the value of the central position y_m Become. The reason for this shap e of the first volumetric flow rate V1 is that from the center of the nozzle row 39 to the two en ds, the nozzle spacing d of the full jet nozzles 21 along the nozzle row 39 doubles . , a parabo lic increase in the nozzle spacing d is assumed. Second volumetric flow rate V_2 supplies coolant into the first coolant chamber 25 at a coolant pressure of approximately twic e the rated pressure and into the other two coolant chambers 26, at a coolant pressure of app roximately half the rated pressure. 27 when supplied to each of them. The third volume flow rate V3 supplies coolant into the first coolant chamber 25 at a coolant pressure approximately h alf the rated pressure and supplies coolant at a coolant pressure approximately twice the rate d pressure . into each of the other two coolant chambers 26, 27. FIG . 3 illustrates the volumetric flow ra tes V_1 , V_2 , V_3 with different patterns of dependence on position y along the direction par allel to the roll axis 17 at different coolant pressures in the coolant chambers 25-27. , so that the volume flows V_1 , V_2 , V_3 discharged from the cooling rods 13 can be adapted to the te mperature distribution of the roll surfaces. The coolant pressure in each coolant chamber 25 - 27 is set by a respective control valve 43 and/or a respective pump 45 . FIGS. 4-12 each sh ow the discharge side 19 of another exemplary embodiment of the cooling rod 13. FIG. these differs from the exemplary embodiment shown in FIG. 2 only in the shape and number of the coolant chambers 25-27 and the corresponding partial areas 29-31 of the discharge side 19. F IG. As in the exemplary embodiment shown in FIG. 2, the full jet nozzles 21 are each arrange d in a plurality of nozzle rows 39, with the nozzle spacing d in each case extending from the c enter along it to the two ends. increase towards the part. Therefore, the full jet nozzle 21 of Fi

gures 4-12 will not be described here again. Due to the distribution of the full jet nozzles 21 o n the discharge side 19 similar to the exemplary embodiment shown in FIG. 2, each of the ex emplary embodiments shown in FIGS. V_1 , V_2 , V_3 can be produced. Like the exemplary e mbodiment shown in FIG. 2, the exemplary embodiments shown in FIGS. 4-10 each correspo nd to three coolant chambers 25-27 and a discharge side 19

.

It has partial regions 29-31. Similar to the exemplary embodiment shown in FIG. 2, the first s ubregion 29 is mirror-symmetrical about the centerline 37 of the discharge side 19 of the cool ing rod 13, perpendicular to the roll axis 17, and the other The two partial areas 30 , 31 adjoi n the first partial area 29 and on different sides of the centerline 37 .

FIG.

4 shows that the first partial area 29 is trapezoidal with two vertices located on the first long itudinal side 33 and two vertices located on the second longitudinal side 34 . 1 illustrates an e xemplary embodiment;

[0048]

FIG. 5 shows that the first partial region 29 has one vertex arranged at the intersection of th e centerline 37 and the first longitudinal side 33 and two corners arranged at the end of the s econd longitudinal side 34 . 2 shows an exemplary embodiment that is a triangle with four ver tices.

FIG.

6 shows that the first partial area 29 has one vertex located at the intersection of the centerl ine 37 and the first longitudinal side 33 and two corners located at the second longitudinal sid e 34 . 2 shows an exemplary embodiment that is a triangle with four vertices.

FIG .

7 shows an exemplary embodiment in which the first partial area 29 is a rectangle with verti ces located on the longitudinal sides 33,34. In this exemplary embodiment, no coolant is disc harged via the two outer partial regions 30 , 31 , so that the discharge of coolant can only occ ur from the central region of the discharge side 19 . This exemplary embodiment is therefore particularly suitable for rolling rolling blanks 3 of different widths.

FIG .

8 shows that the second partial area 30 and the third partial area 31 each have a vertex on t he first longitudinal side 33 and a vertex located at one end of the first longitudinal side 33. , and vertices located on the lateral sides 35, 36. FIG.

FIG.

9 shows that the first partial region 29 has two vertices on the first longitudinal side 33 and t wo vertices located at the ends of the second longitudinal side 34, respectively. Figure 10 sho ws an exemplary embodiment that is a hexagon with vertices on its short sides 35,36.

[0053]

FIG. 10 shows that the first partial regions 29 are arranged at one vertex arranged at the int

ersection of the centerline 37 and the first longitudinal side 33 and at the end of the second lo ngitudinal side 34 respectively. An exemplary embodiment is shown that is a pentagon with t wo vertices and one vertex on each of the short sides 35,36. The exemplary embodiments s hown in FIGS. 11 and 12 each have two coolant chambers 25 , 26 and corresponding subregi ons 29 , 30 of the discharge side 19

.

Both partial regions 29 are mirror-symmetrical with respect to a centerline 37 of the discharg e side 19 of the cooling rod 13 perpendicular to the roll axis 17 .

FIG .

11 shows that the first partial area 29 is triangular with one vertex located at the centerline 37 and two vertices located at the ends of the second longitudinal sides 34 respectively. show s an exemplary embodiment

.

FIG.

12 shows that the first partial area 29 has one vertex located on the centerline 37 and two v ertices located respectively at the ends of the second longitudinal sides 34 and each short edg e. 4 shows an exemplary embodiment that is a pentagon with vertices on hand sides 35,36.

Although the present invention has been illustrated and described in more detail by way of p referred exemplary embodiments, the present invention is not limited to the disclosed exampl es, and a person skilled in the art can fully understand the scope of protection of the present i nvention

.

Other variations can be obtained from these without exceeding.

[Description of Symbols]

1

Rolling stand

3 Rolling material, rolling material

5 Roll

7 Cooling device

9 Roll gap

11 Rolling direction 13

Cooling bar

15 Wiper

17 Roll shaft

19 Discharge side surface

21 Full jet nozzle

23 Discharge direction

25-27 Cooling Agent chambers

29 to 31 Partial areas

33, 34 Longitudinal sides

35, 36 Short side

37 Center line

39 Nozzle row

41 Coolant supply line

43 Control valve

45 Pump

d Nozzle spacing

drawing open —

[Fig. 1]

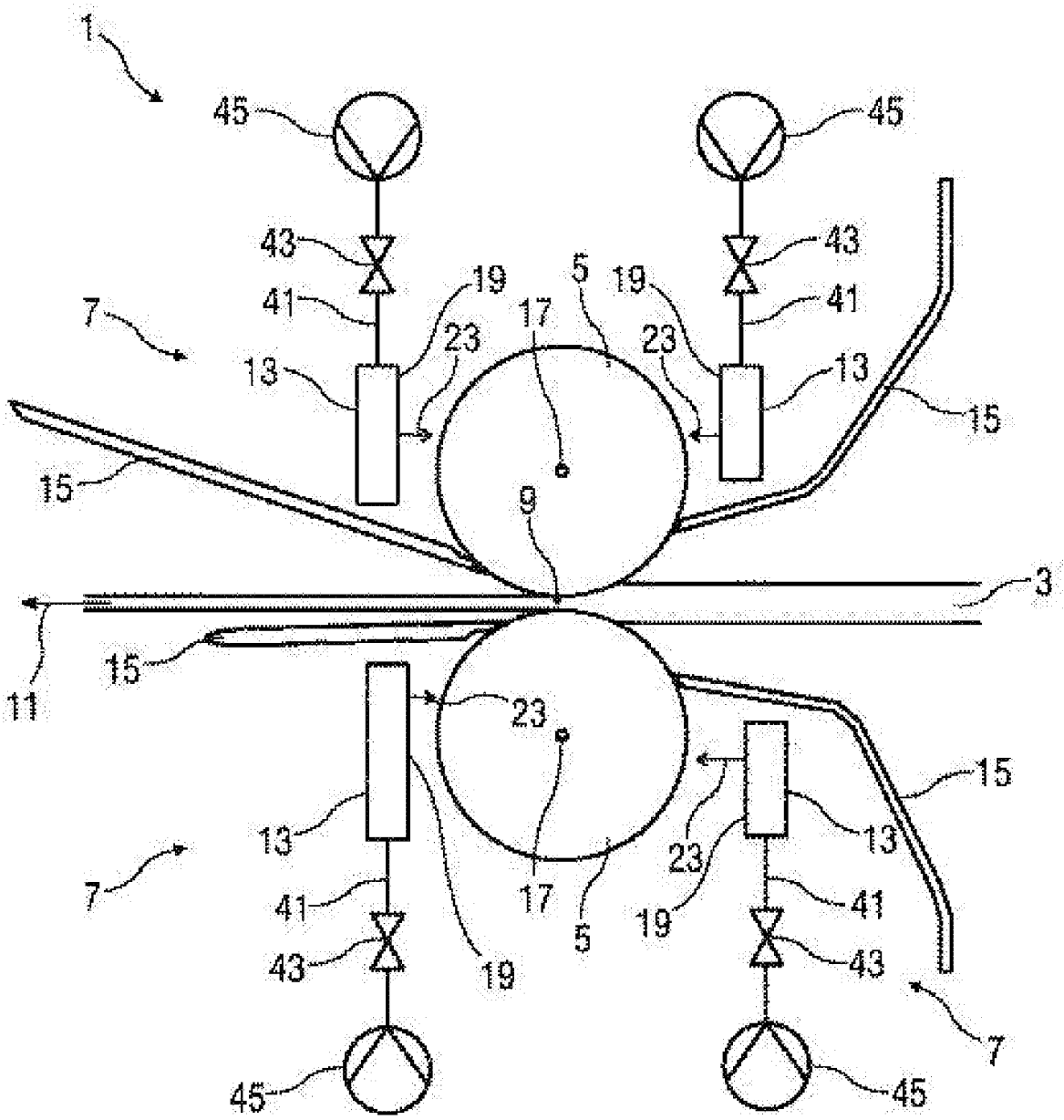


FIG 1

[Figure 2]

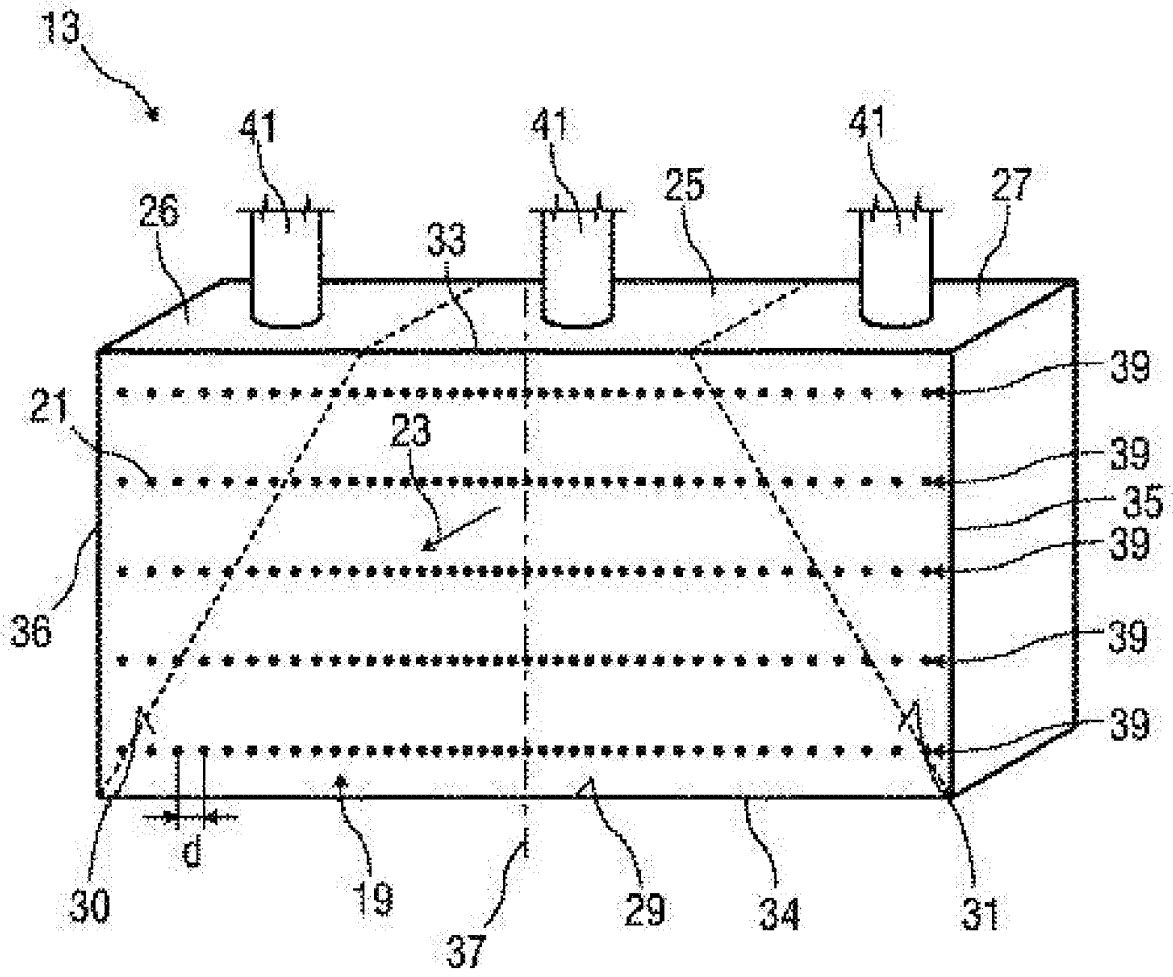


FIG 2

[Figure 3]

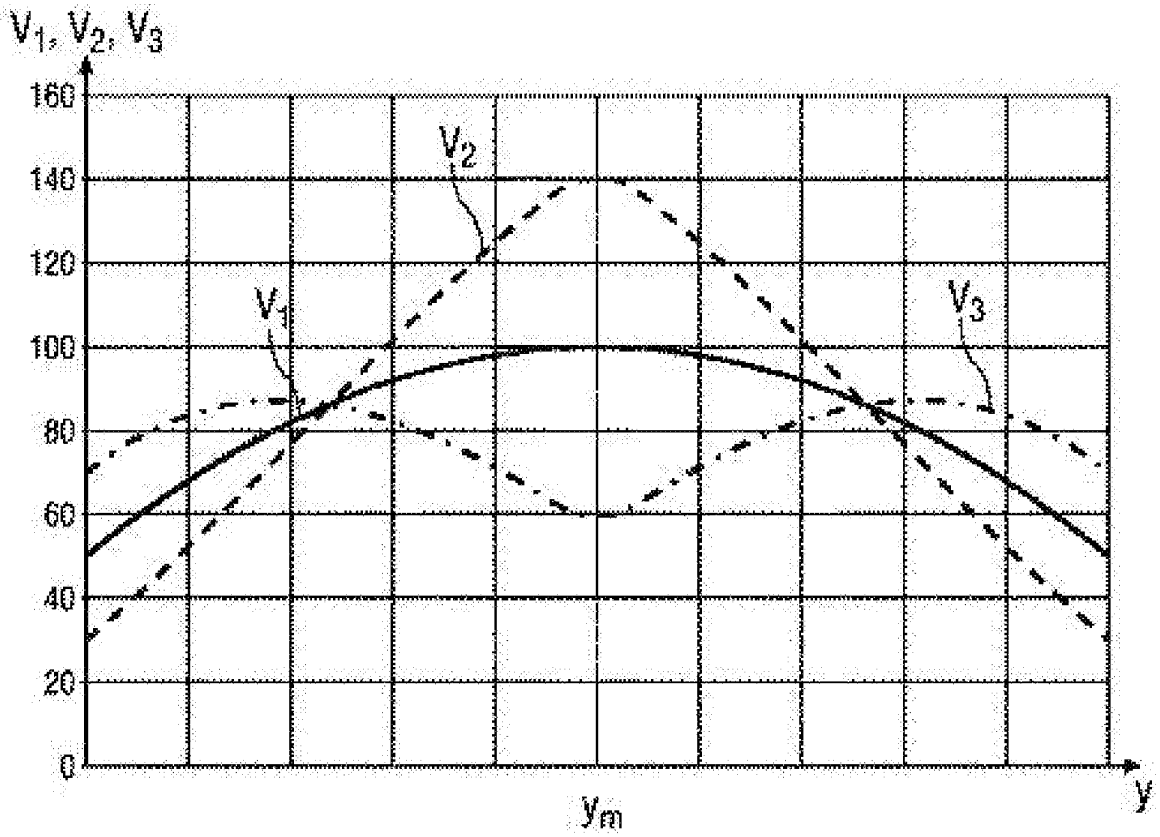


FIG 3

[Figure 4]

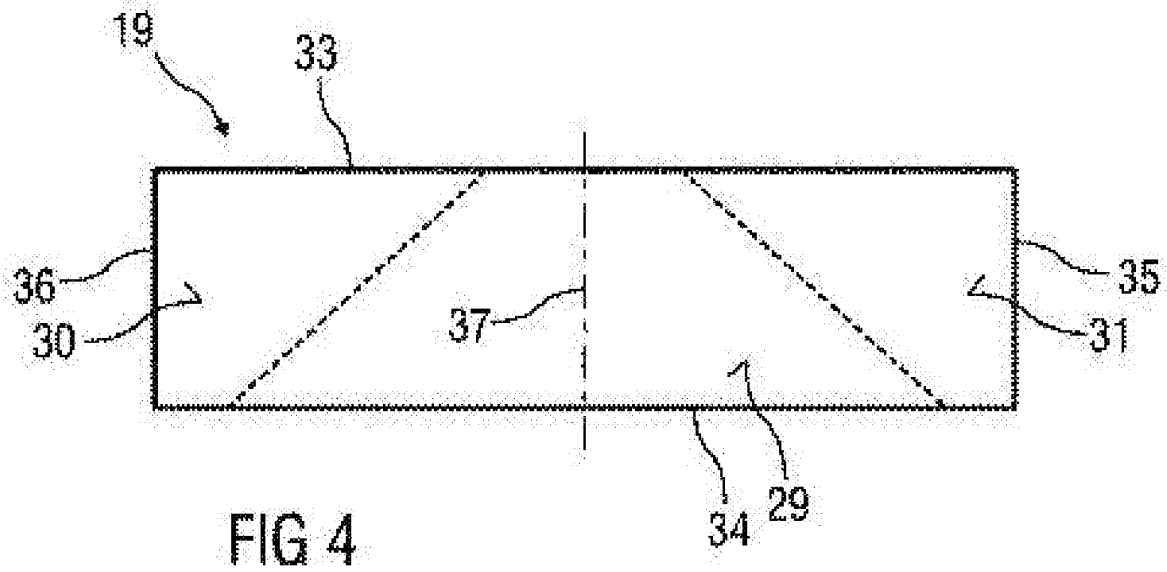


FIG 4

[Figure 5]

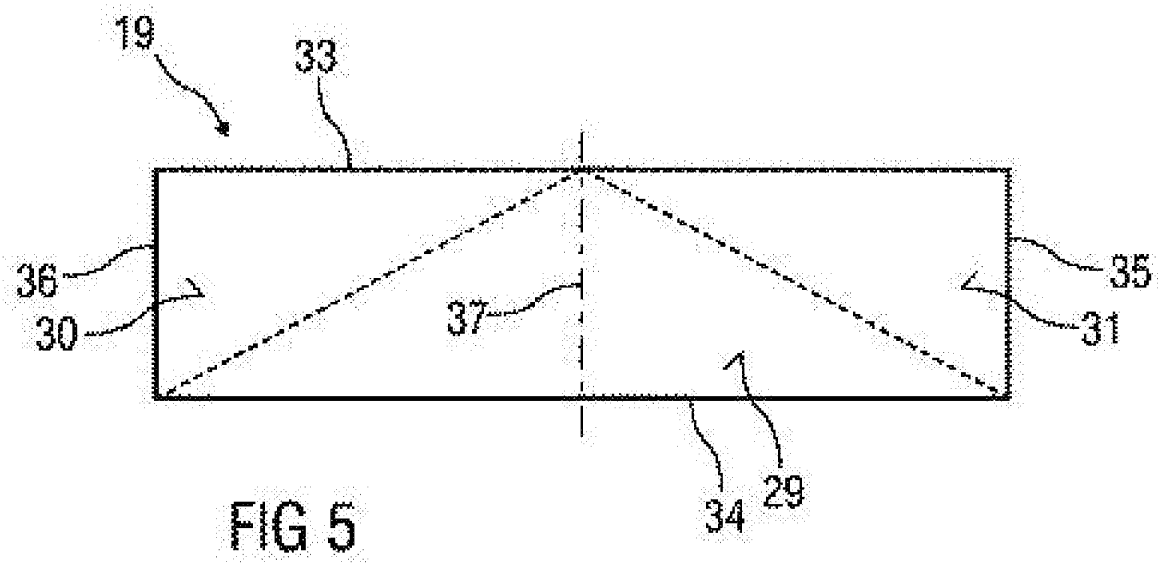


FIG 5

[Fig. 6]

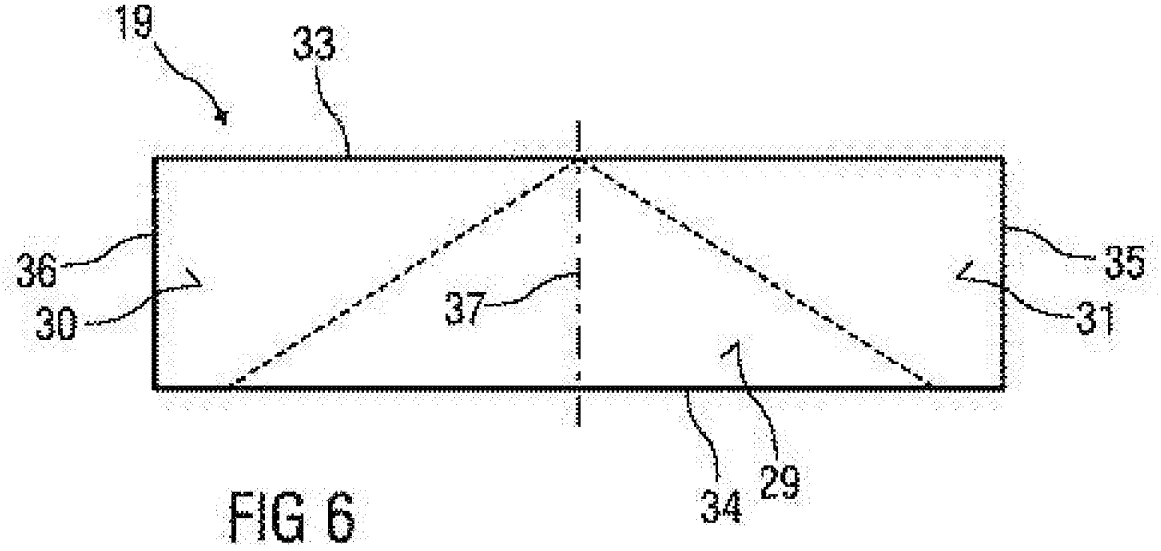


FIG 6

[Fig. 7]

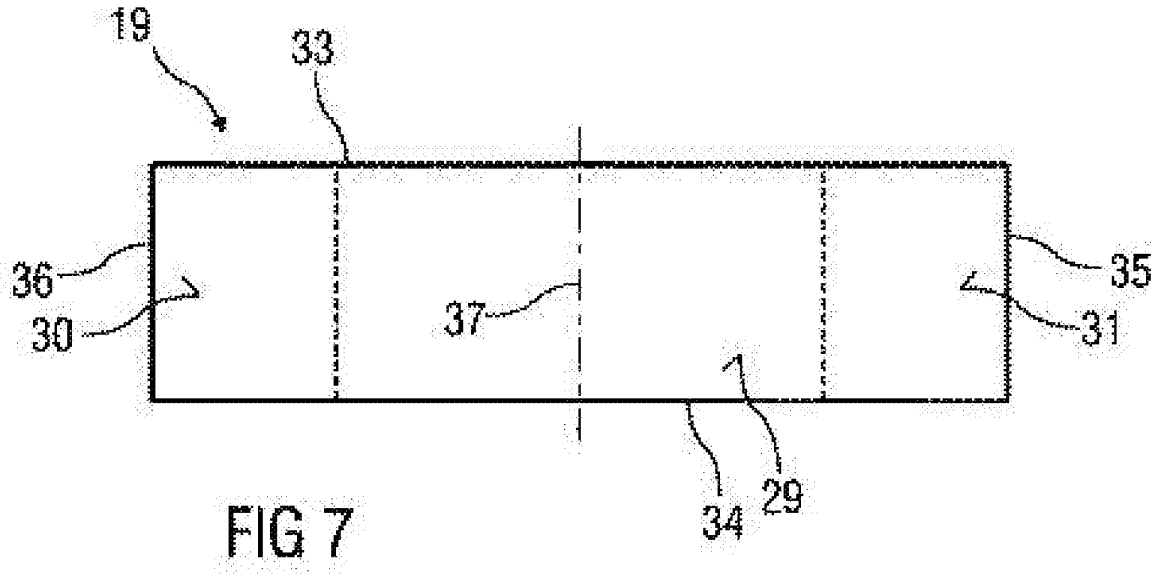


FIG 7

[Fig. 8]

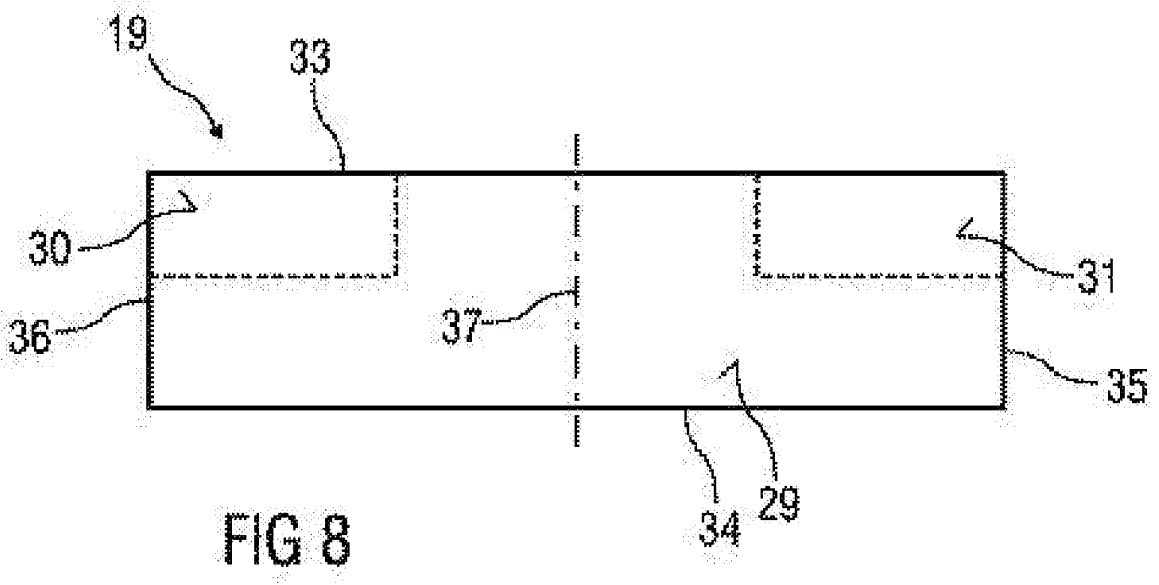


FIG 8

[Fig. 9]

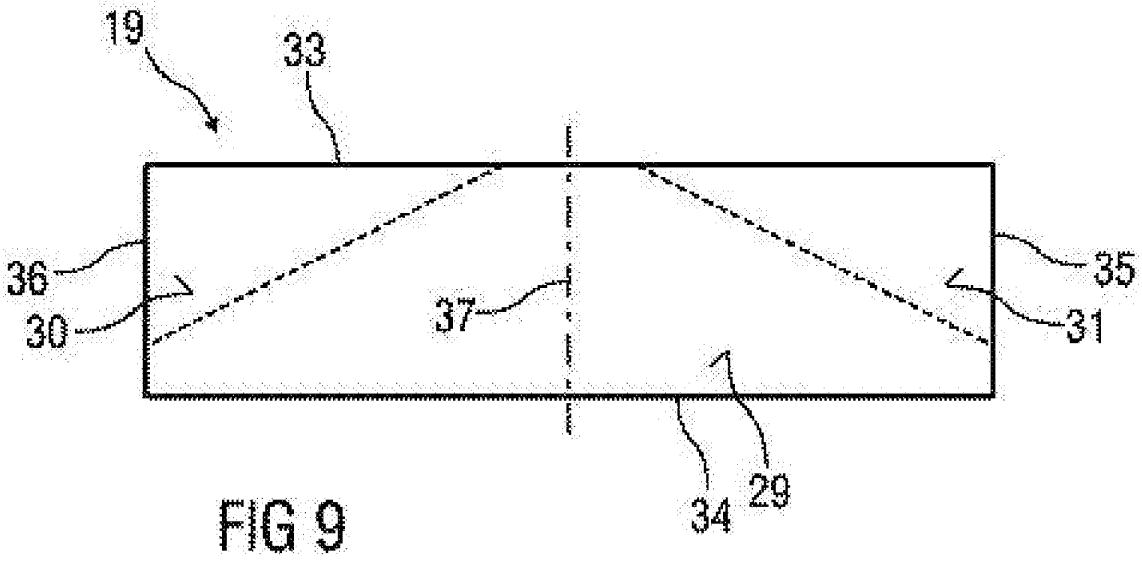


FIG 9

[Fig. 10]

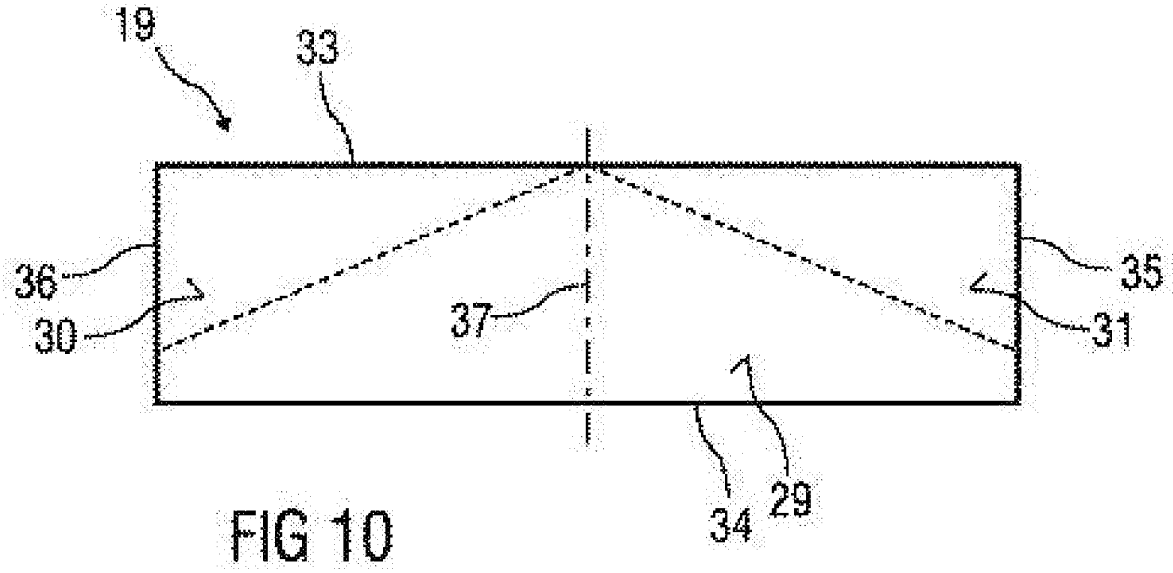


FIG 10

[Fig. 11]

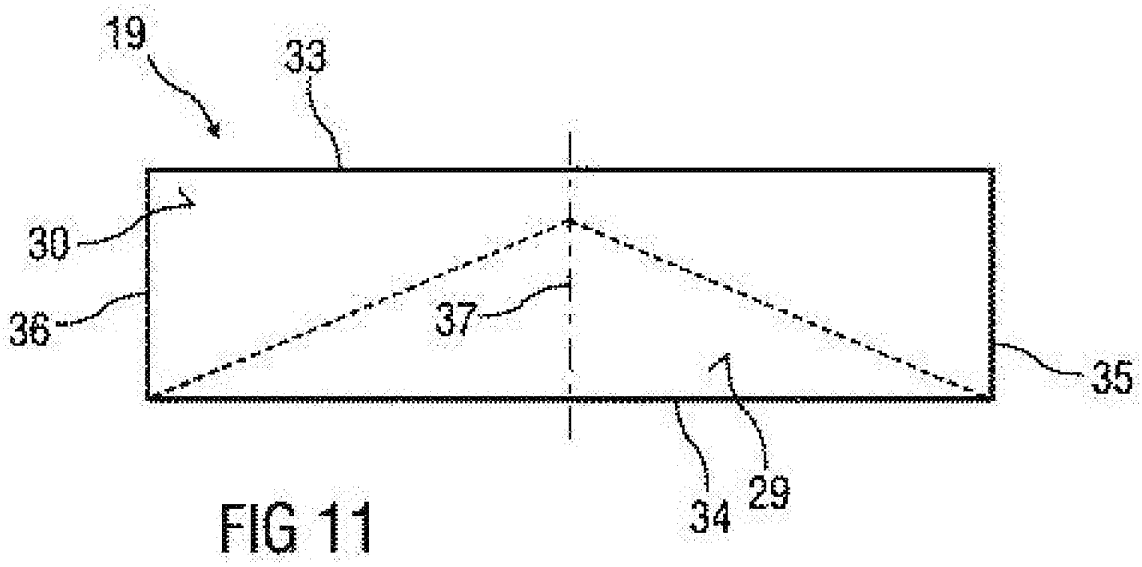


FIG 11

[Fig. 12]

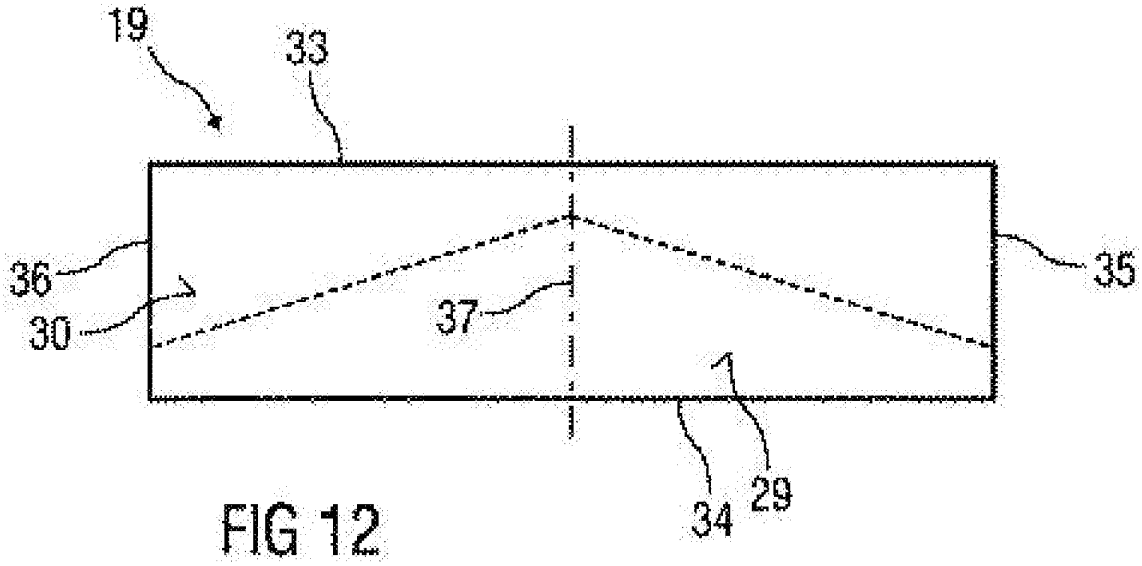


FIG 12

search report open

[International search report]

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/076000

A. CLASSIFICATION OF SUBJECT MATTER
INV. B21B27/10
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B21B

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31 August 2000 (2000-08-31)	1,15
Y	page 5, paragraph 3 - page 7, paragraph 3	2-5
X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11 December 2008 (2008-12-11)	1,15
Y	page 3, line 20 - page 4, line 12; figures 1,2	2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22 October 2014 (2014-10-22) paragraph [0017] - paragraph [0027]; figures 1-3	2-5
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6 August 2015 (2015-08-06) page 4, line 8 - line 17	1

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

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 January 2018	06/03/2018

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Frisch, Ulrich

2

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-5, 15

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

The International Searching Authority has found that the international application contains multiple (groups of) inventions, as follows:

1. Claims 1-5, 15

Cooling device for cooling a roller, wherein two coolant chambers are provided which are separated from each other.

---

2. Claims 1, 6-8

Cooling device for cooling a roller, wherein the feed/control of the coolant is further defined.

---

3. Claims 1, 9-13

Cooling device for cooling a roller, wherein the distance of the nozzles is defined.

---

4. Claims 1, 14

Cooling device for cooling a roller, wherein an additional stripper is defined.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2017/076000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

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

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
INV. B21B27/10
ADD.

Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
B21B

Recherchierte, aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, WPI Data

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31. August 2000 (2000-08-31)	1,15
Y	Seite 5, Absatz 3 - Seite 7, Absatz 3	2-5
X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11. Dezember 2008 (2008-12-11)	1,15
Y	Seite 3, Zeile 20 - Seite 4, Zeile 12; Abbildungen 1,2	2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22. Oktober 2014 (2014-10-22) Absatz [0017] - Absatz [0027]; Abbildungen 1-3	2-5
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6. August 2015 (2015-08-06) Seite 4, Zeile 8 - Zeile 17	1

☐ Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen ☒ Siehe Anhang Patentfamilie

* Besondere Kategorien von angegebenen Veröffentlichungen :
"A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist
"E" frühere Anmeldung oder Patent, die bzw. das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist
"L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Rechercherenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt)
"O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausstellung oder andere Maßnahmen bezieht
"P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist
"T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist
"X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann allein aufgrund dieser Veröffentlichung nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden
"Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist
"&" Veröffentlichung, die Mitglied derselben Patentfamilie ist

Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
11. Januar 2018	06/03/2018

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Frisch, Ulrich

2

Formblatt PCT/ISA/210 (Blatt 2) (April 2005)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

Feld Nr. II Bemerkungen zu den Ansprüchen, die sich als nicht recherchierbar erwiesen haben (Fortsetzung von Punkt 2 auf Blatt 1)

Gemäß Artikel 17(2)a) wurde aus folgenden Gründen für bestimmte Ansprüche kein internationaler Recherchenbericht erstellt:

1. ☐ Ansprüche Nr.
weil sie sich auf Gegenstände beziehen, zu deren Recherche diese Behörde nicht verpflichtet ist, nämlich

2. ☐ Ansprüche Nr.
weil sie sich auf Teile der internationalen Anmeldung beziehen, die den vorgeschriebenen Anforderungen so wenig entsprechen, dass eine sinnvolle internationale Recherche nicht durchgeführt werden kann, nämlich

3. ☐ Ansprüche Nr.
weil es sich dabei um abhängige Ansprüche handelt, die nicht entsprechend Satz 2 und 3 der Regel 6.4 a) abgefasst sind.

Feld Nr. III Bemerkungen bei mangelnder Einheitlichkeit der Erfindung (Fortsetzung von Punkt 3 auf Blatt 1)

Diese Internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere Erfindungen enthält:

siehe Zusatzblatt

1. ☐ Da der Anmelder alle erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht auf alle recherchierbaren Ansprüche.

2. ☐ Da für alle recherchierbaren Ansprüche die Recherche ohne einen Arbeitsaufwand durchgeführt werden konnte, der zusätzliche Recherchengebühr gerechtfertigt hätte, hat die Behörde nicht zur Zahlung solcher Gebühren aufgefordert.

3. ☐ Da der Anmelder nur einige der erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht nur auf die Ansprüche, für die Gebühren entrichtet worden sind, nämlich auf die Ansprüche Nr.

4. ☒ Der Anmelder hat die erforderlichen zusätzlichen Recherchengebühren nicht rechtzeitig entrichtet. Dieser internationale Recherchenbericht beschränkt sich daher auf die in den Ansprüchen zuerst erwähnte Erfindung; diese ist in folgenden Ansprüchen erfasst:
1-5, 15

Bemerkungen hinsichtlich eines Widerspruchs

☐ Der Anmelder hat die zusätzlichen Recherchengebühren unter Widerspruch entrichtet und die gegebenenfalls erforderliche Widerspruchsgebühr gezahlt.

☐ Die zusätzlichen Recherchengebühren wurden vom Anmelder unter Widerspruch gezahlt, jedoch wurde die entsprechende Widerspruchsgebühr nicht innerhalb der in der Aufforderung angegebenen Frist entrichtet.

☐ Die Zahlung der zusätzlichen Recherchengebühren erfolgte ohne Widerspruch.

Formblatt PCT/ISA/210 (Fortsetzung von Blatt 1 (2)) (April 2005)

Internationales Aktenzeichen PCT/ EP2017/ 076000

WEITERE ANGABEN **PCT/ISA/** 210

Die internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere (Gruppen von) Erfindungen enthält, nämlich:

1. Ansprüche: 1-5, 15

   Kühlvorrichtung zur Kühlung einer Walze, wobei zwei voneinander getrennte Kühlmittelkammern vorgesehen sind.

   ---

2. Ansprüche: 1, 6-8

   Kühlvorrichtung zur Kühlung einer Walze, wobei die Zuleitung / Steuerung des Kühlmittels weiter definiert wird.

   ---

3. Ansprüche: 1, 9-13

   Kühlvorrichtung zur Kühlung einer Walze, wobei der Abstand der Düsen definiert wird.

   ---

4. Ansprüche: 1, 14

   Kühlvorrichtung zur Kühlung einer Walze, wobei ein zusätzlicher Abstreifer definiert wird

   ---

INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
PCT/EP2017/076000

Im Recherchenbericht angeführtes Patentdokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie	Datum der Veröffentlichung
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

Formblatt PCT/ISA/210 (Anhang Patentfamilie) (April 2005)

drawing open

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

Magnify and Rotate

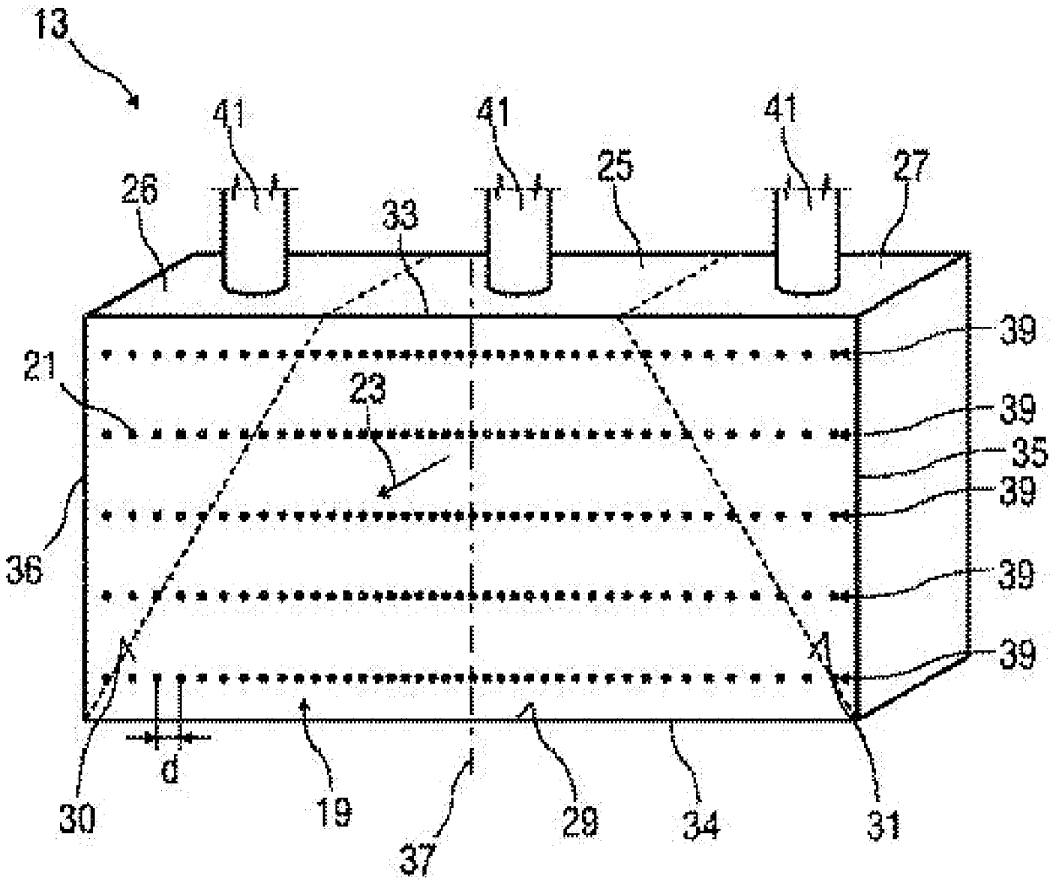


FIG 2

Representative drawing

1 / 1 display

Copyright JPO and INPIT (P0200)

Patent Translate
Powered by EPO and Google

Notice

This translation is machine-generated. It cannot be guaranteed that it is intelligible, accurate, complete, reliable or fit for specific purposes. Critical decisions, such as commercially relevant or financial decisions, should not be based on machine-translation output.

ABSTRACT JP2019534792A

[0001]

The present invention relates to a cooling device (7) for cooling the rolls (5) of the rolling stand (1). The cooling device (7) comprises cooling beams (13) for receiving and discharging coolant. The cooling beam (13) has a plurality of full jet nozzles (21) arranged on the discharge side (19) of said cooling beam (13), said side facing the roll (5).) parallel to the roll axis (17). A jet of coolant with a substantially constant jet diameter can be sprayed through each of the full jet nozzles from the cooling beam (13) towards the roll (5) in the discharge direction (23).



(19)日本国特許庁(JP)　(12)公表特許公報(A)　(11)特許出願公表番号
特表2019-534792
(P2019-534792A)
(43)公表日　令和1年12月5日(2019.12.5)

(51)Int.Cl.		F I			テーマコード（参考）
B21B 27/10	(2006.01)	B21B	27/10	A	
		B21B	27/10	C	
		B21B	27/10	D	

審査請求 有　予備審査請求 未請求　（全 21 頁）

(21)出願番号　特願2019-520550 (P2019-520550)
(86)(22)出願日　平成29年10月12日 (2017.10.12)
(85)翻訳文提出日　令和1年6月13日 (2019.6.13)
(86)国際出願番号　PCT/EP2017/076000
(87)国際公開番号　WO2018/073086
(87)国際公開日　平成30年4月26日 (2018.4.26)
(31)優先権主張番号　16194099.4
(32)優先日　平成28年10月17日 (2016.10.17)
(33)優先権主張国・地域又は機関
欧州特許庁 (EP)

(71)出願人　515153152
プライメタルズ・テクノロジーズ・オーストリア・ゲーエムベーハー
オーストリア・４０３１・リンツ・ツームシュトラーセ・４４
(74)代理人　100133400
弁理士　阿部　達彦
(74)代理人　100110364
弁理士　実広　信哉
(72)発明者　アロイス・ザイリンガー
オーストリア・４０４０・リンツ・ハーゼルグラーベンヴェーク・１７
(72)発明者　エリッヒ・オービッツ
オーストリア・７１２３・メンヒーホフ・アンガーガッセ・４６

最終頁に続く

(54)【発明の名称】圧延スタンドのロールの冷却

【要約】
本発明は、圧延スタンド　のロール　を冷却するための冷却装置　に関する。冷却装置　は、冷却剤を受け入れて吐出するための冷却ビーム　を備える。冷却ビーム　は、前記冷却ビーム　の吐出側面　に配置された複数のフルジェットノズル　を有し、前記側面は、ロール　に面してロール　のロール軸　に平行に延在する。ほぼ一定のジェット径を有する冷却剤のジェットを、フルジェットノズルのそれぞれを通して、冷却ビーム　からロール　に向けて吐出方向　に噴霧することができる。

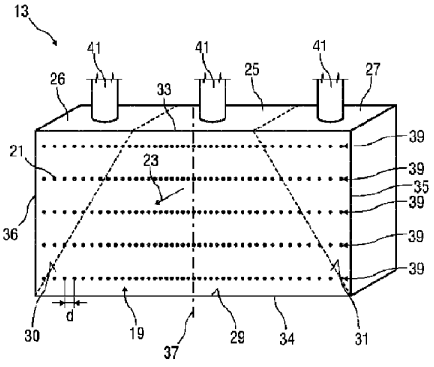


FIG 2

【特許請求の範囲】
【請求項１】
冷却剤を受け入れて吐出するための冷却棒（１３）を備えた、圧延スタンド（１）のロール（５）を冷却するための冷却装置（７）であって、
前記冷却棒（１３）が、前記冷却棒（１３）の吐出側面（１９）に配置された複数のフルジェットノズル（２１）を有し、前記吐出側面が、ロール（５）に面して前記ロール（５）のロール軸（１７）に平行に延在し、ほぼ一定のジェット径の冷却剤の冷却剤ジェットを、フルジェットノズルのそれぞれを通して、前記冷却棒（１３）から前記ロール（５）に向けて吐出方向（２３）に吐出することができる、冷却装置（７）。
【請求項２】
前記冷却棒（１３）が、冷却剤を受け入れるための、相互に分離した少なくとも２つの冷却剤室（２５～２７）に分割され、各冷却剤室（２５～２７）が、複数のフルジェットノズル（２１）が配置された前記冷却棒（１３）の前記吐出側面（１９）の部分領域（２９～３１）に対応し、前記フルジェットノズル（２１）のそれぞれを通して、冷却剤ジェットを前記冷却剤室（２５～２７）から前記ロール（５）に向けて吐出することができることを特徴とする、請求項１に記載の冷却装置（７）。
【請求項３】
第１の冷却剤室（２５）が、前記冷却棒（１３）の前記吐出側面（１９）の第１の部分領域（２９）に対応し、前記第１の部分領域（２９）が、前記冷却棒（１３）の前記吐出側面（１９）の中心線（３７）に対して鏡面対称であり、軸が前記ロール軸（１７）に垂直であることを特徴とする、請求項２に記載の冷却装置（７）。
【請求項４】
中心線（３７）に並行する第１の部分領域（２９）の範囲が、前記ロール軸（１７）の方向に沿って変化し、前記中心線（３７）に沿って最大であることを特徴とする、請求項２または３に記載の冷却装置（７）。
【請求項５】
第１の部分領域（２９）が多角形であることを特徴とする、請求項２から４のいずれか一項に記載の冷却装置（７）。
【請求項６】
各冷却剤室（２５～２７）が、前記冷却剤室（２５～２７）内に冷却剤を供給するための冷却剤供給ライン（４１）に接続され、前記冷却剤供給ライン（４１）が、前記冷却剤室（２５～２７）内に、前記冷却剤の前記吐出方向（２３）に実質的に垂直に開口していることを特徴とする、請求項２から５のいずれか一項に記載の冷却装置（７）。
【請求項７】
前記冷却剤室（２５～２７）内に供給される前記冷却剤の量を、それぞれの制御弁（４３）、および／または、それぞれのポンプ（４５）によって互いに独立して制御することができることを特徴とする、請求項２から６のいずれか一項に記載の冷却装置（７）。
【請求項８】
前記冷却剤室（２５～２７）内に供給される前記冷却剤の量を制御するための自動化システムによって特徴付けられた、請求項２から７のいずれか一項に記載の冷却装置（７）。
【請求項９】
前記ロール軸（１７）に平行な方向に沿って相互に隣り合うフルジェットノズル（２１）のノズル間隔（ｄ）が、前記方向に沿って変化していることを特徴とする、請求項１から８のいずれか一項に記載の冷却装置（７）。
【請求項１０】
前記ノズル間隔（ｄ）が、前記冷却棒（１３）の前記吐出側面（１９）の中央領域において最も狭いことを特徴とする、請求項９に記載の冷却装置（７）。
【請求項１１】
前記ノズル間隔（ｄ）が、約２５ｍｍから約５０ｍｍの間であることを特徴とする、請

求項９または１０に記載の冷却装置（７）。
【請求項１２】
前記フルジェットノズル（２１）が、相互に平行な複数のノズル列（３９）になるように配置されていることを特徴とする、請求項１から１１のいずれか一項に記載の冷却装置（７）。
【請求項１３】
前記冷却棒（１３）が、前記フルジェットノズル（２１）が取り外し可能に固定された、各フルジェットノズル（２１）のためのノズル開口を有していることを特徴とする、請求項１から１２のいずれか一項に記載の冷却装置（７）。
【請求項１４】
前記ロール（５）から冷却乳をぬぐい取るためのワイパ（１５）であって、前記冷却棒（１３）と一緒に枢動させることができるワイパ（１５）によって特徴付けられた、請求項１から１３のいずれか一項に記載の冷却装置（７）。
【請求項１５】
ロール（５）と、請求項１から１３のいずれか一項に記載されたようにそれぞれ設計された２つの冷却装置（７）と、を備えた圧延スタンド（１）であって、前記２つの冷却装置（７）が、前記ロール（５）の両側に配置されている、圧延スタンド（１）。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は、圧延スタンドのロールを冷却するための冷却装置に関する。
【背景技術】
【０００２】
圧延素材を圧延するための圧延スタンドは、冷却液体、一般的には冷却水を用いて冷却されるロールを有する。
【０００３】
特許文献１には、低圧の冷却液体を圧延スタンドのロールにかけることができる、剛性の高い凹状のシェルが開示されている。
【０００４】
特許文献２には、移動可能な関節式冷却シェルによる圧延スタンドのワークロールの流動冷却が開示されている。この場合、冷却液体は、冷却シェルを用いて主として低圧でかけられるが、さらに、冷却液体は、高圧でかけられて十分な冷却効果を生じる。
【０００５】
特許文献３には、圧延スタンドのワークロールを冷却するための冷却装置が開示されており、この装置は、関係する圧延スタンドを用いて生産される最も狭い片よりもやや狭い固定スプレー棒を有し、そのときに圧延されている片の幅に対応するワークロールのこれらの部分のみを冷却するための、軸方向に移動可能なスプレー棒を有する。
【０００６】
特許文献４には、圧延スタンドのワークロールを冷却するための方法が開示されており、この方法では、冷却水が、高圧ではなく低圧でワークロールに噴霧されるが、同時に、かけられる範囲が広くされている。
【０００７】
特許文献５には、圧延材を冷却するためのスプレー棒が開示されており、このスプレー棒は、圧延材の移動方向に横断して延在し、中央領域および２つの縁領域を有して、冷却媒体をそれらのそれぞれに別々に供給することができる。
【先行技術文献】
【特許文献】
【０００８】
【特許文献１】米国特許出願公開第　　号
【特許文献２】独国特許出願公開第　　号

【特許文献３】特開平　　号
【特許文献４】特開昭　　号
【特許文献５】国際公開第　　号
【発明の概要】
【発明が解決しようとする課題】
【０００９】
圧延スタンドのロールを冷却するための改善された冷却装置を特定することが本発明の基本的な目的である。
【課題を解決するための手段】
【００１０】
本発明によれば、この目的は、請求項　の特徴によって達成される。
【００１１】
本発明の有利な実施形態は、従属請求項の主題を形成する。
【００１２】
圧延スタンドのロールを冷却するための本発明による冷却装置は、冷却剤を受け入れて吐出するための冷却棒を備える。冷却棒は、冷却棒の吐出側面に配置された複数のフルジェットノズルを有し、前記側面は、ロールに面してロールのロール軸に平行に延在する。ほぼ一定のジェット径の冷却剤の冷却剤ジェットを、各フルジェットノズルを通して、冷却棒からロールに向けて吐出方向に吐出することができる。
【００１３】
フルジェットノズルとは、ほぼ一定のジェット径で実質的に直線状の冷却剤ジェットを吐出することができるノズルを意味するものとする。冷却剤を集中させて吐出するおかげで、フルジェットノズルは、従来使用されてきたファンジェットノズルよりも、冷却棒での同じ冷却剤圧力でより高いロールへの衝撃圧を生じる。全体にかけられた大量の冷却剤の量により、典型的には、数ミリメートルから数センチメートルの厚さの特定の冷却剤膜が常にあり、良好な放熱のために冷却剤ジェットを衝突させることによって、この膜はできるだけ完全に貫通されるべきであるので、より高い衝撃圧は、ロール表面での冷却作用に直接良い効果を生じる。フルジェットノズルによって生じた、ロールへの冷却剤ジェットの高い衝撃圧のおかげで、冷却棒の冷却剤圧力は、ファンジェットノズルを使用した場合に比べて大きく下げることができ、それによって、冷却装置のＴネルギー消費および運用コストを大きく下げることができることは有利である。
【００１４】
冷却剤はフルジェットノズルを通って吐出されるので、ロールからスプレー棒までの間隔はさらに、広い範囲にわたってそれほど重要ではなくなり、したがって、ロール直径に適合させる必要はない。したがって、例えば、実質的に直進する冷却剤ジェットによって、冷却剤ジェットの冷却効果に何ら大きな変化もなしに、　　から　　の間の距離で、冷却されるべきロール表面を冷却することができる。
【００１５】
冷却剤圧力の低下はまた、負荷の低減、その結果としてノズルの摩耗の低減に関係するので、これもまた、冷却棒の冷却剤圧力の低下の結果、保守費用が低減され、これがフルジェットノズルの使用の別の利点である。
【００１６】
本発明の一実施形態では、冷却棒が、冷却剤を受け入れるための、相互に分離した少なくとも　つの冷却剤室に分割されることが想定されている。各冷却剤室は、複数のフルジェットノズルが配置された冷却棒の吐出側面の部分領域に対応し、フルジェットノズルのそれぞれを通して、冷却剤ジェットを冷却剤室からロールに向けて吐出することができる。冷却棒の吐出側面の異なる部分領域に対応する、相互に分離した複数の冷却剤室に、冷却棒を分割すると、互いに独立して、部分領域の冷却剤圧力を制御し、その結果、部分領域によって吐出される冷却剤流量を制御することによって、部分領域の冷却効果を互いに独立して制御することができることは有利である。それによって、位置に応じてロールの

冷却に影響を与えることが可能となり、ロール表面のより強く加熱された領域、例えば、ロール表面の中央領域を、それほど強く加熱されていない領域よりも確実に強く冷却することができることは有利である。

【００１７】

本発明の上記の実施形態の展開としては、第 の冷却剤室が、冷却棒の吐出側面の第 の部分領域に対応し、第 の部分領域が、冷却棒の吐出側面の中心線に対して鏡面対称であり、その軸がロール軸に垂直であることが想定されている。例えば、中心線に並行する第 の部分領域の範囲は、ロール軸の方向に沿って変化し、中心線に沿って最大である。例えば、第 の部分領域は多角形である。第 の部分領域が中心線に対して鏡面対称の実施形態は、ロールが概ね同様に、中心線に対して対称的に加熱されるという事実を考慮している。中心線に並行する第 の部分領域の範囲がロール軸の方向に沿って変化し、中心線に沿って最大範囲を有することは、ロールが、一般に、中心において最も強く加熱され、ロールの加熱が縁領域に向けて減少するという事実を考慮している。したがって、これに対応した第 の部分領域の構成は、第 の部分領域によって、位置に依存したロールの熱負荷にロールの冷却を適合させることを可能にする。

【００１８】

本発明の別の実施形態では、各冷却剤室が、冷却剤室内に冷却剤を供給するための冷却剤供給ラインに接続され、冷却剤供給ラインが、冷却剤室内に、冷却剤の吐出方向に実質的に垂直に開口していることが想定されている。冷却剤供給ラインが、冷却棒内に、吐出方向に実質的に垂直に開口していることによって、各冷却剤室内の冷却剤の圧力分布をほとんど均一にすることができる。それによって、開口近くのフルジェットノズルと開口から離れたノルジェットノズルとの間の圧力勾配がなくなることは有利である。

【００１９】

本発明の別の実施形態では、冷却剤室内に供給される冷却剤の量を、それぞれの制御弁、および／または、それぞれのポンプによって互いに独立して制御することができることが想定されている。これによって、上記のように、個々の冷却剤室から吐出される冷却剤ジェットの冷却効果を互いに独立して制御することができる。例えば、通常、 の圧力で冷却水を送出する水供給システムなどの、例えば、いかなるときにも存在する従来の冷却剤供給システムを、関連する圧延システムにおいて使用することができる場合には、制御弁によって冷却剤の量を制御することが特に有利である。この場合、ロール冷却をするために複雑で高価な昇圧システム無しで済ますことができる。適当であれば、制御弁と共に、ポンプによって冷却剤の量を制御することによって、圧延間の休止時、または、低い冷却能力しか必要でない圧延作業の場合に、個々のポンプを止める、またはポンプの動力を下げることができ、それによって、エネルギー消費を低減することができる。

【００２０】

本発明の別の実施形態では、冷却剤室内に供給される冷却剤の量を制御するための自動化システムが想定されている。それによって、体積流量をロール表面の温度分布に適合させるために、冷却剤室からロールに吐出される冷却剤の体積流量を自動的に制御することができることは有利である。この場合、冷却剤室内に供給される冷却剤の量は、上記の制御弁および／またはポンプを制御することを通じて、自動化システムによって制御されることが好ましい。

【００２１】

本発明の別の実施形態では、ロール軸に平行な方向に沿って相互に隣り合うフルジェットノズルのノズル間隔が前記方向に沿って変化していることが想定されている。この場合、ノズル間隔は、冷却棒の吐出側面の中央領域において最も狭いことが好ましい。例えば、ロール軸に平行な方向に沿うノズル間隔は、約 から約 の間である。本発明のこれらの実施形態によって、また、ロール軸に平行な方向に沿うノズル間隔が位置に依存したロール表面の熱負荷に従って変えられるので、フルジェットノズルの配置をこの熱負荷に適合させることもできる。最小のノズル間隔が冷却棒の吐出側面の中央領域にあるのは、ロール表面の中央領域が一般に、最大の熱負荷を受けるという事実を考慮している。

【００２２】
本発明の別の実施形態では、フルジェットノズルが、相互に平行な複数のノズル列になるように配置されていることが想定されている。これによって、冷却剤をより広い範囲にわたって、かつ、ロールが回転することと併せて、均一にロールにかけることができることは有利である。
【００２３】
本発明の別の実施形態では、冷却棒が、フルジェットノズルが取り外し可能に固定された、各フルジェットノズルのためのノズル開口を有していることが想定されている。本発明のこの実施形態によって、不良なジェットノズルを容易に交換することができることは有利である。
【００２４】
本発明の別の実施形態では、ロールから冷却剤をぬぐい取るためのワイパが提供され、ワイパと冷却棒を一緒に枢動させることができる。例えば、ワイパによって、過剰な冷却剤が、圧延材に、および／または、圧延材が つのロール間を案内されるロール間隙に導かれて、圧延材とロールとの間の摩擦を低減するための潤滑剤を洗い流すことを防ぐことができることは有利である。ワイパと冷却棒が一緒に枢動することができることによって、冷却棒を動かすための追加の装置の必要が除かれることは有利である。この場合、上記ですでに言及したフルジェットノズルを使用する利点は、この場合にもまた効果がある。すなわち、フルジェットノズルを使用することによって、スプレー棒とロールとの間の距離は、広い範囲にわたってそれほど重要ではなくなり、したがって、ロール直径に適合させる必要がなくなる。さらに、本発明はまた、ワイパを有する既存の圧延システムに対しては改造策として特に適しており、例えば、従来の高圧スプレー棒のみを本発明による冷却棒に交換するだけでよい。
【００２５】
本発明による圧延スタンドは、ロール、および本発明による つの冷却装置を備え、 つの冷却装置は、ロールの反対側に配置される。本発明による圧延スタンドの利点は、上記ですでに言及した、本発明による冷却装置の利点から生じる。
【００２６】
この発明の上記の特性、特徴、および利点、ならびにこれらを達成する態様は、図面と併せてより詳細に説明される例示的な実施形態の以下の説明と関連して、より明確かつ明瞭に理解されるであろう。
【図面の簡単な説明】
【００２７】
【図１】冷却装置を有する圧延スタンドの概略図である。
【図２】冷却棒の第 の例示的な実施形態の概略斜視図である。
【図３】図 に示した冷却棒によって吐出される冷却剤の体積流量を位置の関数として示した図である。
【図４】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図５】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図６】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図７】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図８】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図９】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図１０】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図１１】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【図１２】冷却棒の第 の例示的な実施形態の吐出側面の図である。
【発明を実施するための形態】
【００２８】
すべての図面で、同じ部品には同じ参照符号が付けられている。
【００２９】

図 は、圧延素材 を圧延するための圧延スタンド の概略図である。圧延スタンド は、ワークロールとして設計された つのロール 、および各ロール に対して つの冷却装置 を備え、前記装置は、ロール の両側に配置されている。ロール は、ロール間隙 だけ間隔を置いて配置され、圧延材 を形成するために、圧延素材 をロール間隙 に圧延方向 に通す。各冷却装置 は、冷却棒 およびワイパ を備える。

【００３０】

各冷却棒 は、冷却剤を受け入れて吐出するように設計されている。冷却剤を吐出するために、冷却棒 は、冷却棒 の吐出側面 に配置された複数のフルジェットノズル を有し、前記側面は、それぞれのロール に面してロール のロール軸 に平行に延在し、ほぼ一定のジェット径の冷却剤ジェットを、フルジェットノズルのそれぞれを通して、冷却棒 からロール に向けて吐出方向 に吐出することができる。冷却剤は、冷却剤供給ライン を経て冷却棒 内に供給することができ、冷却棒 内に供給される冷却剤の量は、制御弁 、および／または、例えば周波数制御のポンプ によって制御することができる。冷却剤は、例えば、水である。

【００３１】

各ワイパ は、それぞれのロール から冷却剤をぬぐい取るように設計され、ロール に向かうように、またこれから離れるように枢動させることができる。各冷却装置 の冷却棒 およびワイパ は、冷却装置 の枢動装置に固定され、したがって、冷却棒 およびワイパ をロール に向かうように、またロール から離れるように一緒に枢動させることができることが好ましい。

【００３２】

図 は、ロール に冷却剤を吐出するための冷却棒 の第 の例示的な実施形態の概略斜視図である。冷却棒 は、相互に分離した つの冷却剤室 ～ に分割されて、冷却剤を受け入れる。各冷却剤室 ～ は、複数のフルジェットノズル が配置された吐出側面 の部分領域 ～ に対応し、冷却剤ジェットを冷却剤室 ～ からフルジェットノズルのそれぞれを通してロール に向けて吐出方向 に吐出することができる。吐出側面 は、ロール軸 に平行な つの長手方向辺 、 、およびロール軸 に垂直な つの短手方向辺 、 を有する長方形である。

【００３３】

第 の冷却剤室 は、吐出側面 の中央領域を形成する、冷却棒 の吐出側面 の第 の部分領域 に対応する。第 の部分領域 は、冷却棒 の吐出側面 の中心線 に対して鏡面対称であり、前記軸はロール軸 に垂直であり、第 の長手方向辺 に配置された つの頂点と、第 の長手方向辺 の端点にそれぞれ配置された つの頂点とを有する台形である。

【００３４】

フルジェットノズル は、それぞれがロール軸 に平行に延在する複数のノズル列 になって、吐出側面 に配置されている。この場合、各ノズル列 の相互に隣り合うフルジェットノズル のノズル間隔ｄは、中心線 に対して対称的に変化しており、その結果、ノズル間隔ｄは、吐出側面 の中央領域において最も狭く、吐出側面 の縁領域に向かって、例えば、放物線状に広くなっている。図 に示した例示的な実施形態では、ノズル間隔ｄは、各ノズル列 の端部ではノズル列 の中心での間隔の 倍大きくなっている。ノズル間隔ｄは、例えば、 から の間を変化する。ノズル列 は、吐出側面 の全範囲にわたって実質的に等間隔に延在し、したがって、ロール のロール表面に比較的均一な冷却効果を生じる。

【００３５】

図 に示した例示的な実施形態のさらなる展開としては、ノズル列 を互いに対してずらして配置することが想定され、したがって、様々なノズル列 のフルジェットノズル が、ロール軸 に垂直な方向に沿って配置されてはいない。「冷却チャネル」は、ノズル列 に垂直に延在して、そこでは、ロール に冷却剤が吐出されず、その結果、冷却効果が低下するが、この「冷却チャネル」を避けることができるので、ノズル列 の特に均一

な冷却効果が達成されることは有利である。
【００３６】
さらに、図 の隣り合う つの部分領域 ～ 間の境界線に非常に近い、または境界線上にあるフルジェットノズル は、完全に省かれるか、または、図 に示した配置に対してずらされて、隣接した部分領域 ～ の つに入るように配置され、それは分離板による冷却筒 の内部の冷却剤室 ～ への細分がこのような境界線に沿って延在するからである。
【００３７】
各フルジェットノズル は、冷却棒 のノズル開口に、例えば、ねじ込み継手によって取り外し可能に取り付けられる。フルジェットノズル はそれぞれ、例えば、約 の最小直径のノズル断面を有する。
【００３８】
各冷却剤室 ～ は、冷却剤室 ～ 内に冷却剤を供給するための冷却剤供給ライン に接続され、冷却剤供給ライン は、冷却剤室 ～ 内に、冷却剤の吐出方向 に実質的に垂直に開口している。冷却剤供給ライン の断面はそれぞれ、例えば、 からの間の直径を有する。
【００３９】
冷却剤供給ライン を経て冷却剤室 ～ 内に供給される冷却剤の量を、それぞれの制御弁 図 には示されていない 、および／または、それぞれのポンプ 図 には示されていない によって互いに独立して制御することができる。これによって、冷却剤室 ～ から吐出される冷却剤の量を、ロール表面の様々な領域の異なる熱負荷に対して適合させることができることは有利である。
【００４０】
図 は、一例として、図 に示した冷却棒 から吐出される つの冷却剤の体積流量 、 、 を、ロール軸 に平行な方向に沿う位置ｙの関数として示す。ここで、体積流量 、 、 は定格流量に対する比率で示されている。
【００４１】
定格流量は、中央位置ｙにおける第 の体積流量 である。第 の体積流量 は、冷却剤が、すべての冷却剤室 ～ に対して同じ与定の定格圧力で、すべての つの冷却剤室 ～ 内に供給された場合に生じる。第 の体積流量 は、中央位置ｙで最大となる放物線の形状を有し、中央位置ｙから つの端部領域に向かって減少して、中央位置ｙの値の半分になる。第 の体積流量 がこのような形状になる理由は、ノズル列 の中心から２つの端部へ、ノズル列 に沿うフルジェットノズル のノズル間隔ｄが 倍になるからであり、ノズル間隔ｄの放物線状の増大が仮定される。
【００４２】
第 の体積流量 は、定格圧力のほぼ 倍の冷却剤圧力で冷却剤を第 の冷却剤室 内に供給し、定格圧力のほぼ半分の冷却剤圧力で冷却剤を他の つの冷却剤室 、 内のそれぞれに供給した場合に生じる。
【００４３】
第 の体積流量 は、定格圧力のほぼ半分の冷却剤圧力で冷却剤を第 の冷却剤室 内に供給し、定格圧力のほぼ 倍の冷却剤圧力で冷却剤を他の つの冷却剤室 、 内のそれぞれに供給した場合に生じる。
【００４４】
図 は、ロール軸 に平行な方向に沿う位置ｙへの依存性が異なるパターンを有する体積流量 、 、 を、冷却剤室 ～ の異なる冷却剤圧力によって生じさせることができ、その結果、冷却棒 から吐出される体積流量 、 、 を、ロール表面の温度分布に適合させることができることを示している。各冷却剤室 ～ の冷却剤圧力は、それぞれの制御弁 および／またはそれぞれのポンプ によって設定される。
【００４５】
図 ～図 はそれぞれ、冷却棒 の別の例示的な実施形態の吐出側面 を示す。これら

の例示的な実施形態は、図 に示した例示的な実施形態とは、冷却剤室 ～ 、およびそれに対応する吐出側面 の部分領域 ～ の形状および数だけが異なる。図 に示した例示的な実施形態のように、フルジェットノズル はそれぞれ、複数のノズル列 になるように配置され、それぞれの場合のノズル間隔ｄは、それに沿って中央から つの端部に向かって増大する。したがって、図 ～図 のフルジェットノズル はここでまた説明することはしない。吐出側面 のフルジェットノズル の、図 に示した例示的な実施形態と同様な分布によって、図 ～図 に示される例示的な実施形態のそれぞれで、図 と同様な体積流量 、 、 を生じさせることができる。

【００４６】

図 に示した例示的な実施形態のように、図 ～図 に示した例示的な実施形態はそれぞれ、 つの冷却剤室 ～ 、および吐出側面 にそれに対応する部分領域 ～ を有する。図 に示した例示的な実施形態と同様に、第 の部分領域 は、冷却棒 の吐出側面 の、ロール軸 に垂直な中心線 に対して鏡面対称であり、他の つの部分領域 、 は、第 の部分領域 と中心線 の異なる側で隣接する。

【００４７】

図 は、第 の部分領域 が、第 の長手方向辺 に配置された つの頂点と、第 の長手方向辺 に配置された つの頂点とを有する台形である例示的な実施形態を示す。

【００４８】

図 は、第 の部分領域 が、中心線 と第 の長手方向辺 との交点に配置された つの頂点と、第 の長手方向辺 の端部に配置された つの頂点とを有する三角形である例示な実施形態を示す。

【００４９】

図 は、第 の部分領域 が、中心線 と第 の長手方向辺 との交点に配置された つの頂点と、第 の長手方向辺 に配置された つの頂点とを有する三角形である例示的な実形態を示す。

【００５０】

図 は、第 の部分領域 が、頂点が長手方向辺 、 に配置された長方形である例示的な実施形態を示す。この例示的な実施形態では、 つの外側の部分領域 、 を経て冷却剤を吐出しないので、冷却剤の吐出を吐出側面 の中央領域からのみ生じさせることができる。したがって、この例示的な実施形態は、異なる幅の圧延素材 を圧延するのに特に適している。

【００５１】

図 は、第 の部分領域 および第 の部分領域 がそれぞれ、第 の長手方向辺 上の頂点と、第 の長手方向辺 の一端に配置された頂点と、短手方向辺 、 に配置された頂点とを有する長方形である例示的な実施形態を示す。

【００５２】

図 は、第 の部分領域 が、第 の長手方向辺 上の つの頂点と、第 の長手方向辺 の端部にそれぞれ配置された つの頂点と、それぞれの短手方向辺 、 上の頂点とを有する六角形である例示的な実施形態を示す。

【００５３】

図 は、第 の部分領域 が、中心線 と第 の長手方向辺 との交点に配置された つの頂点と、第 の長手方向辺 の端部にそれぞれ配置された つの頂点と、それぞれの短手方向辺 、 上の つの頂点とを有する五角形である例示的な実施形態を示す。

【００５４】

図 および図 に示した例示的な実施形態はそれぞれ、 つの冷却剤室 、 、およびそれに対応する、吐出側面 の部分領域 、 を有する。両方の部分領域 は、冷却棒 の吐出側面 の、ロール軸 に垂直な中心線 に対して鏡面対称である。

【００５５】

図 は、第 の部分領域 が、中心線 に配置された つの頂点と、第 の長手方向辺 の端部にそれぞれ配置された つの頂点とを有する三角形である例示的な実施形態を示す

。
【００５６】
図　は、第　の部分領域　が、中心線　に配置された　つの頂点と、第　の長手方向辺　の端部にそれぞれ配置された　つの頂点と、それぞれの短手方向辺　、　上の頂点とを有する五角形である例示的な実施形態を示す。
【００５７】
本発明を、好ましい例示的な実施形態によって、より詳細に例示および説明したが、本発明は、開示した例に限定されるものではなく、当業者は、本発明の保護の範囲を超えずにこれらから他の変形を得ることができる。
【符号の説明】
【００５８】
圧延スタンド
圧延素材、圧延材
ロール
冷却装置
ロール間隙
圧延方向
冷却棒
ワイパ
ロール軸
吐出側面
ノルジェットノズル
吐出方向
～　冷却剤室
～　部分領域
、　長手方向辺
、　短手方向辺
中心線
ノズル列
冷却剤供給ライン
制御弁
ポンプ
ノズル間隔

【図１】

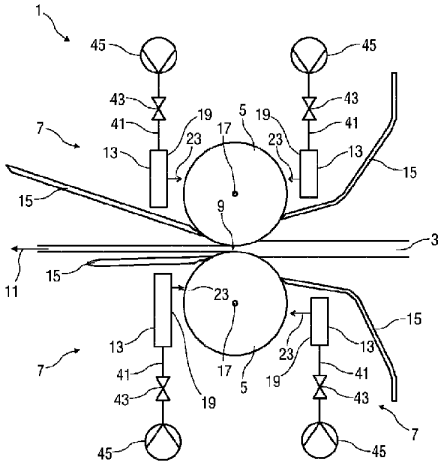


FIG 1

【図２】

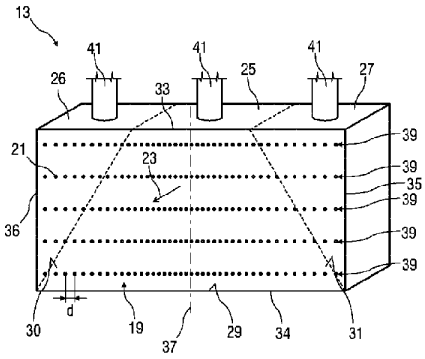


FIG 2

【図３】

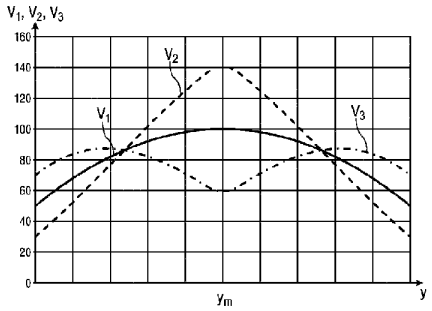


FIG 3

【図４】

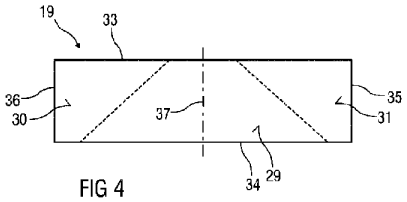


FIG 4

【図５】

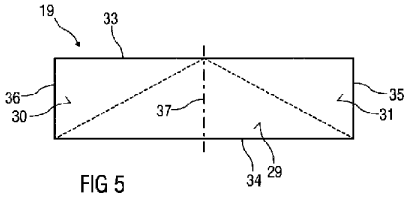


FIG 5

【図６】

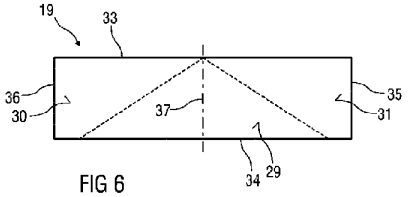


FIG 6

【図７】

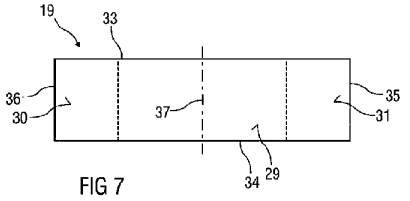


FIG 7

【図８】

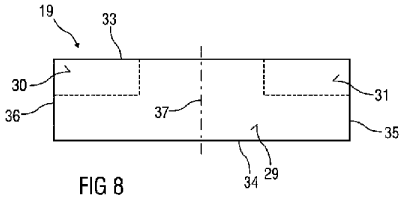


FIG 8

【図９】

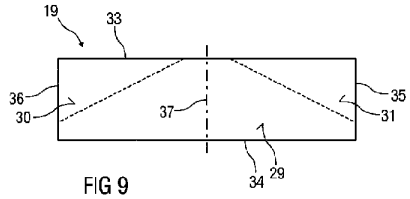


FIG 9

【図１０】

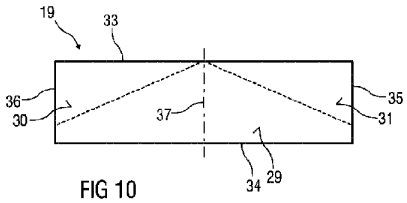


FIG 10

【図１１】

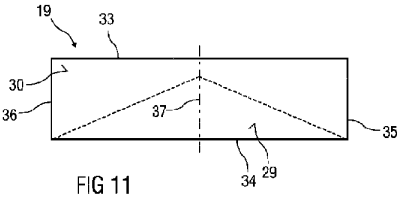


FIG 11

【図１２】

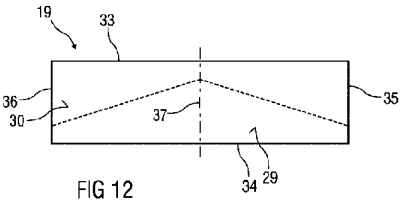


FIG 12

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/076000

A. CLASSIFICATION OF SUBJECT MATTER
INV. B21B27/10
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B21B

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31 August 2000 (2000-08-31)	1,15
Y	page 5, paragraph 3 - page 7, paragraph 3	2-5
X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11 December 2008 (2008-12-11)	1,15
Y	page 3, line 20 - page 4, line 12; figures 1,2	2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22 October 2014 (2014-10-22) paragraph [0017] - paragraph [0027]; figures 1-3	2-5
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6 August 2015 (2015-08-06) page 4, line 8 - line 17	1

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

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 January 2018	06/03/2018

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016	Frisch, Ulrich

2

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-5, 15

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

The International Searching Authority has found that the international application contains multiple (groups of) inventions, as follows:

1. Claims 1-5, 15

Cooling device for cooling a roller, wherein two coolant chambers are provided which are separated from each other.

---

2. Claims 1, 6-8

Cooling device for cooling a roller, wherein the feed/control of the coolant is further defined.

---

3. Claims 1, 9-13

Cooling device for cooling a roller, wherein the distance of the nozzles is defined.

---

4. Claims 1, 14

Cooling device for cooling a roller, wherein an additional stripper is defined.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2017/076000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

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

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
INV. B21B27/10
ADD.

Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
B21B

Recherchierte, aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, WPI Data

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31. August 2000 (2000-08-31)	1,15
Y	Seite 5, Absatz 3 - Seite 7, Absatz 3	2-5

X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11. Dezember 2008 (2008-12-11)	1,15
Y	Seite 3, Zeile 20 - Seite 4, Zeile 12; Abbildungen 1,2	2-5

Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22. Oktober 2014 (2014-10-22) Absatz [0017] - Absatz [0027]; Abbildungen 1-3	2-5

A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6. August 2015 (2015-08-06) Seite 4, Zeile 8 - Zeile 17	1

☐ Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen ☒ Siehe Anhang Patentfamilie

* Besondere Kategorien von angegebenen Veröffentlichungen :
"A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist
"E" frühere Anmeldung oder Patent, die bzw. das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist
"L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Recherchenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt)
"O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausstellung oder andere Maßnahmen bezieht
"P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist
"T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist
"X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann allein aufgrund dieser Veröffentlichung nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden
"Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist
"&" Veröffentlichung, die Mitglied derselben Patentfamilie ist

Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
11. Januar 2018	06/03/2018

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Frisch, Ulrich

2

Formblatt PCT/ISA/210 (Blatt 2) (April 2005)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

Feld Nr. II Bemerkungen zu den Ansprüchen, die sich als nicht recherchierbar erwiesen haben (Fortsetzung von Punkt 2 auf Blatt 1)

Gemäß Artikel 17(2)a) wurde aus folgenden Gründen für bestimmte Ansprüche kein internationaler Recherchenbericht erstellt:

1. ☐ Ansprüche Nr.
weil sie sich auf Gegenstände beziehen, zu deren Recherche diese Behörde nicht verpflichtet ist, nämlich

2. ☐ Ansprüche Nr.
weil sie sich auf Teile der internationalen Anmeldung beziehen, die den vorgeschriebenen Anforderungen so wenig entsprechen, dass eine sinnvolle internationale Recherche nicht durchgeführt werden kann, nämlich

3. ☐ Ansprüche Nr.
weil es sich dabei um abhängige Ansprüche handelt, die nicht entsprechend Satz 2 und 3 der Regel 6.4 a) abgefasst sind.

Feld Nr. III Bemerkungen bei mangelnder Einheitlichkeit der Erfindung (Fortsetzung von Punkt 3 auf Blatt 1)

Diese Internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere Erfindungen enthält:

siehe Zusatzblatt

1. ☐ Da der Anmelder alle erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht auf alle recherchierbaren Ansprüche.

2. ☐ Da für alle recherchierbaren Ansprüche die Recherche ohne einen Arbeitsaufwand durchgeführt werden konnte, der zusätzliche Recherchengebühr gerechtfertigt hätte, hat die Behörde nicht zur Zahlung solcher Gebühren aufgefordert.

3. ☐ Da der Anmelder nur einige der erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht nur auf die Ansprüche, für die Gebühren entrichtet worden sind, nämlich auf die Ansprüche Nr.

4. ☒ Der Anmelder hat die erforderlichen zusätzlichen Recherchengebühren nicht rechtzeitig entrichtet. Dieser internationale Recherchenbericht beschränkt sich daher auf die in den Ansprüchen zuerst erwähnte Erfindung; diese ist in folgenden Ansprüchen erfasst:
1-5, 15

Bemerkungen hinsichtlich eines Widerspruchs

☐ Der Anmelder hat die zusätzlichen Recherchengebühren unter Widerspruch entrichtet und die gegebenenfalls erforderliche Widerspruchsgebühr gezahlt.

☐ Die zusätzlichen Recherchengebühren wurden vom Anmelder unter Widerspruch gezahlt, jedoch wurde die entsprechende Widerspruchsgebühr nicht innerhalb der in der Aufforderung angegebenen Frist entrichtet.

☐ Die Zahlung der zusätzlichen Recherchengebühren erfolgte ohne Widerspruch.

WEITERE ANGABEN PCT/ISA/ 210

Die internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere (Gruppen von) Erfindungen enthält, nämlich:

1. Ansprüche: 1-5, 15

   Kühlvorrichtung zur Kühlung einer Walze, wobei zwei voneinander getrennte Kühlmittelkammern vorgesehen sind.

   ---

2. Ansprüche: 1, 6-8

   Kühlvorrichtung zur Kühlung einer Walze, wobei die Zuleitung / Steuerung des Kühlmittels weiter definiert wird.

   ---

3. Ansprüche: 1, 9-13

   Kühlvorrichtung zur Kühlung einer Walze, wobei der Abstand der Düsen definiert wird.

   ---

4. Ansprüche: 1, 14

   Kühlvorrichtung zur Kühlung einer Walze, wobei ein zusätzlicher Abstreifer definiert wird

   ---

INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
PCT/EP2017/076000

Im Recherchenbericht angeführtes Patentdokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie	Datum der Veröffentlichung
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR PI0812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

Formblatt PCT/ISA/210 (Anhang Patentfamilie) (April 2005)

フロントページの続き

指定国・地域

発明者　ルーカス・ピヒラー
オーストリア・４０４０・リンツ・シュトライムリングヴェーク・７

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

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

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

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

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

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

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

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

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

CERTIFICATION STATEMENT

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

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

OR

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

See attached certification statement.

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

☒ A certification statement is not submitted herewith.

SIGNATURE

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

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-05-16
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

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

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

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

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

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

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

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

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

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

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

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

INFORMATION DISCLOSURE STATEMENT BY APPLICANT		
	Application Number	17538990
	Filing Date	11/30/2021
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Client Number	069366
Page 1 of 1	**Matter Number**	0572201_KUR2C03US

GENERAL

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

Although the information submitted herewith may be "material" to the Examiner's consideration of the subject application, this submission is not intended to constitute an admission that such information is "prior art" as to the claimed invention.

In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

TIMING

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

CERTIFICATION STATEMENT

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

FEE

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

ADDITIONAL COMMENTS

SIGNATURE

Signature	/ Benjamin F. Hudson /	**Date**	2023-05-16
Name	Benjamin F. Hudson	**Registration Number**	71,474

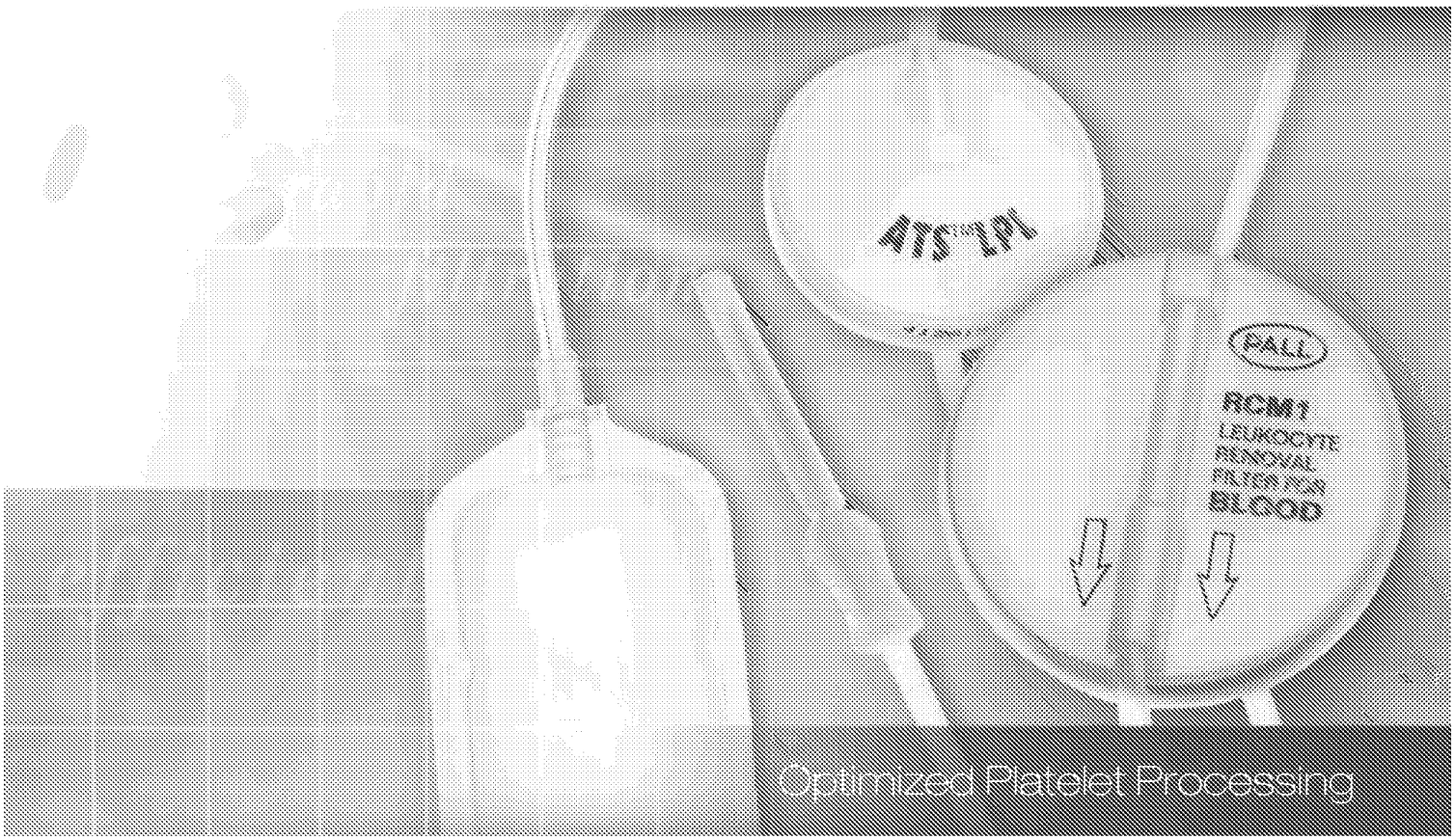
SyncIDS.com

PALL Medical

www.pall.com/medical

Leukotrap® Filtration Systems for Whole Blood Derived Platelets

Leukotrap RC PL and Leukotrap PL Systems



Better Blood, Better Care.℠

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.

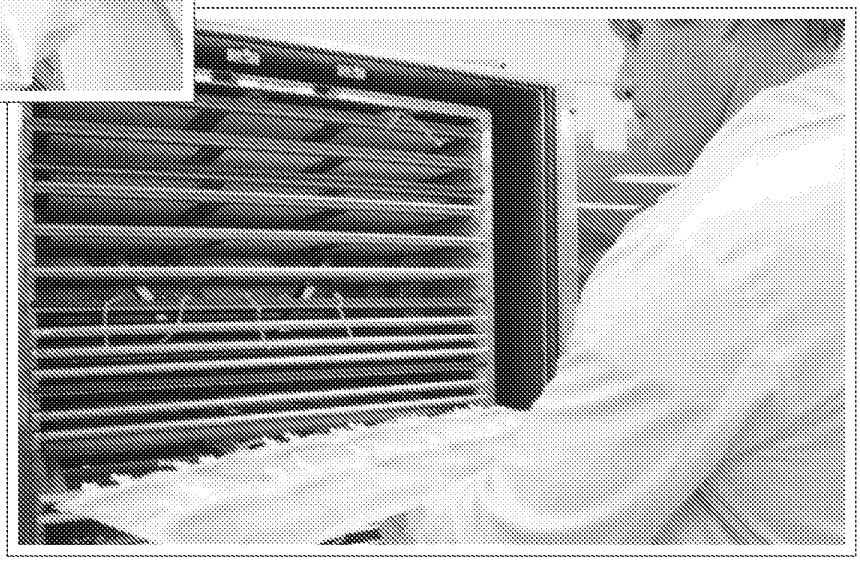
Leukotrap PL System produces leukocyte reduced platelets and plasma.

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

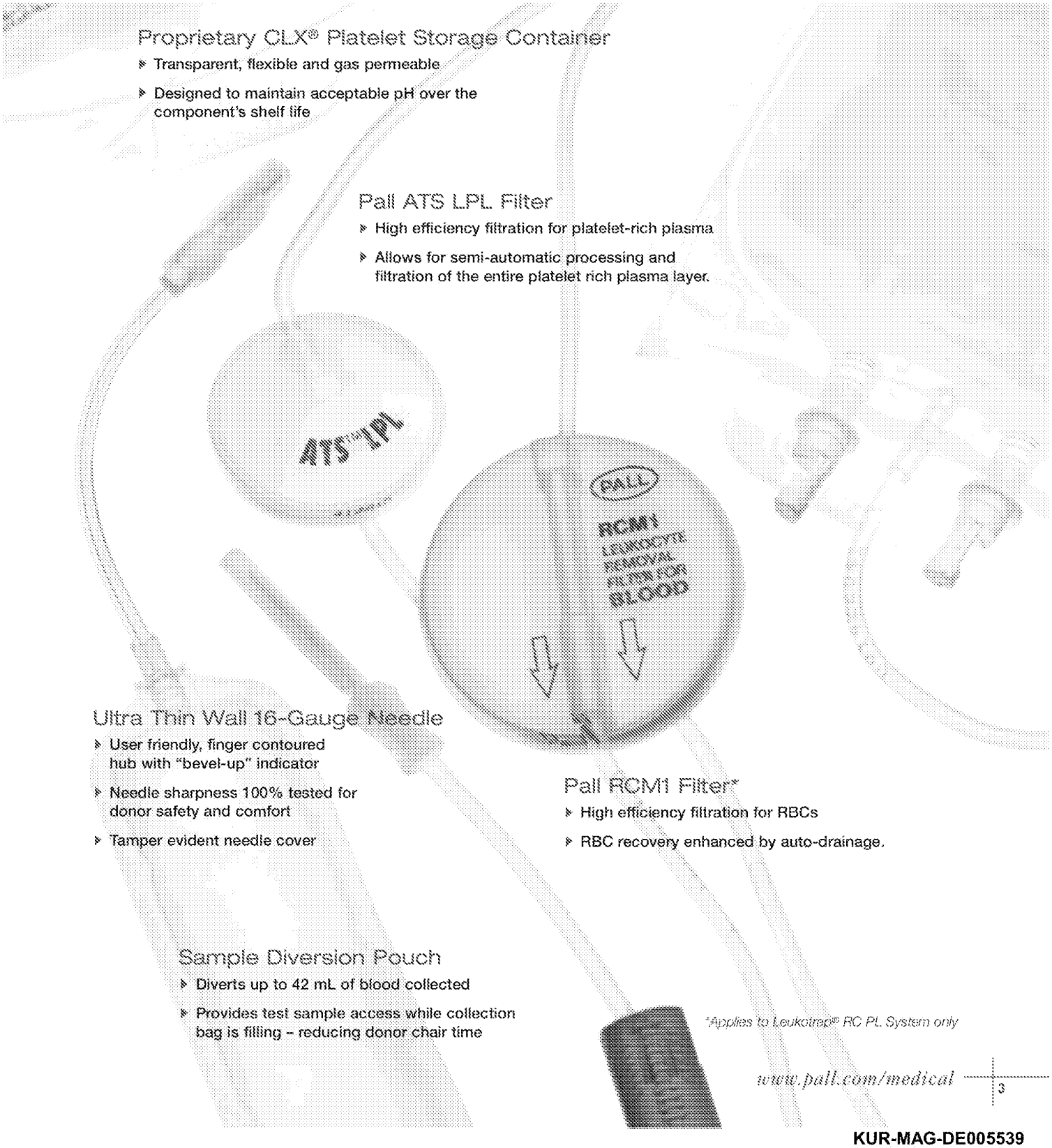
Makes cGMP compliance easier than ever.

- 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

Pall RCM1 Filter*

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

Sample Diversion Pouch

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

*Applies to Leukotrap® RC PL System only

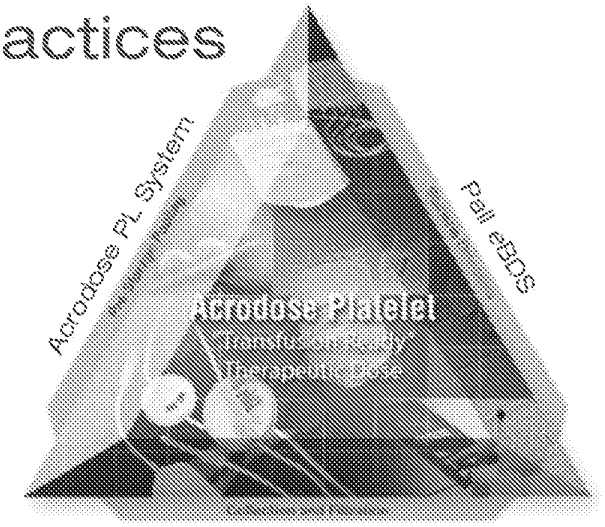
www.pall.com/medical

KUR-MAG-DE005539

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 mL[1]
- 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



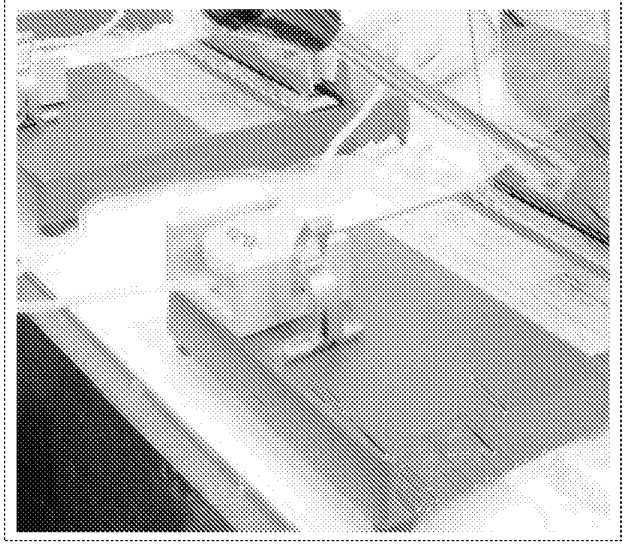
Leukotrap RC PL and
Leukotrap PL Systems

Collection and Filtration

Pall Sample Diversion Pouch



Leukotrap RC PL or
Leukotrap PL System



1 Automatically divert initial blood with the Pall Sample Diversion Pouch

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.

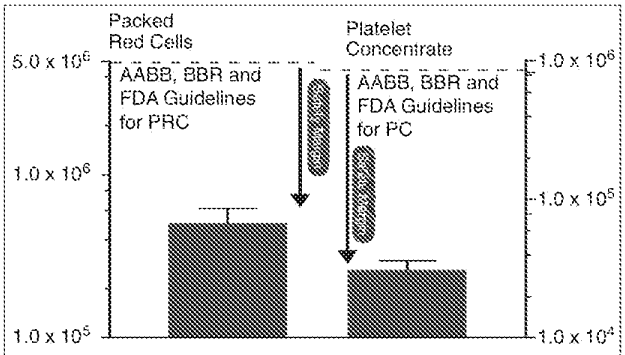
Pall eBDS and Pall Data



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



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

Figure 1

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

Data from actual field use.

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

Greater QC Assurance of Platelet Recovery Requirements

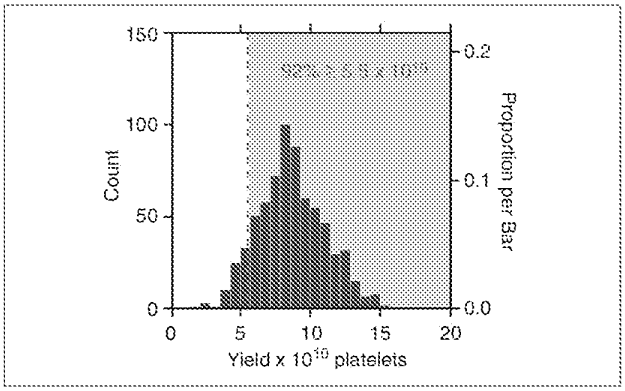


Figure 2

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

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

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

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

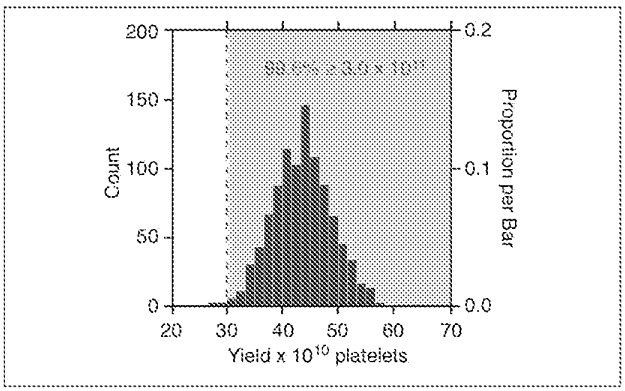


Figure 3

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

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

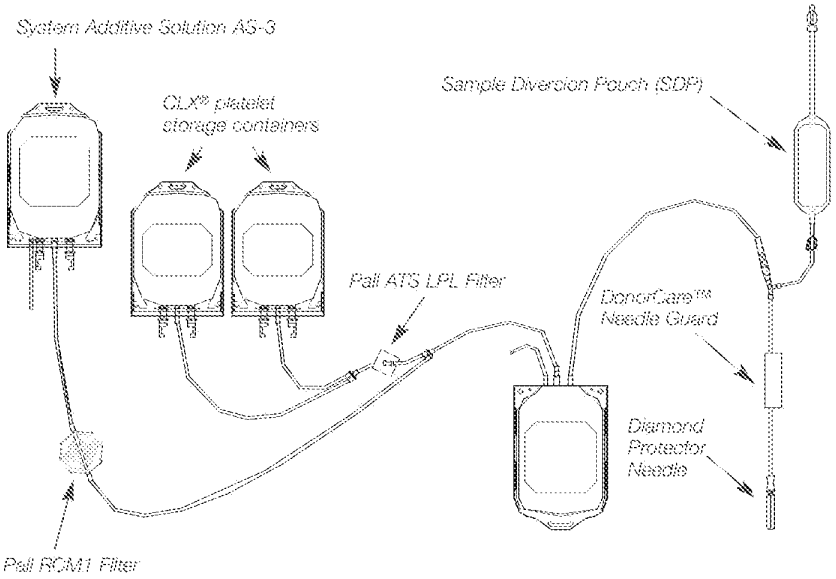
Mean platelet yield with a pool of 5 = 4.3 x 10^{11} with a standard deviation of 5.3 x 10^{10} platelets.

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

PALL Medical

KUR-MAG-DE005542

Leukotrap® RC PL System

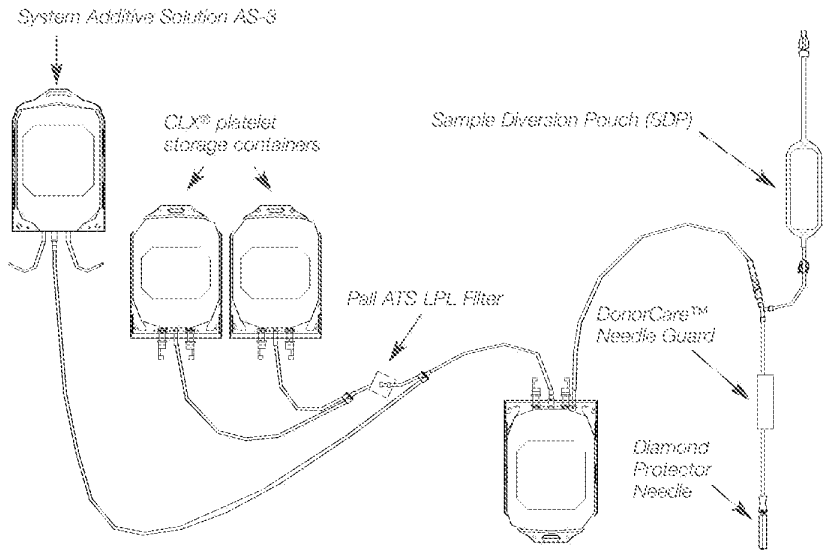


Ordering Information*

Leukotrap RC PL System

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

Leukotrap PL System

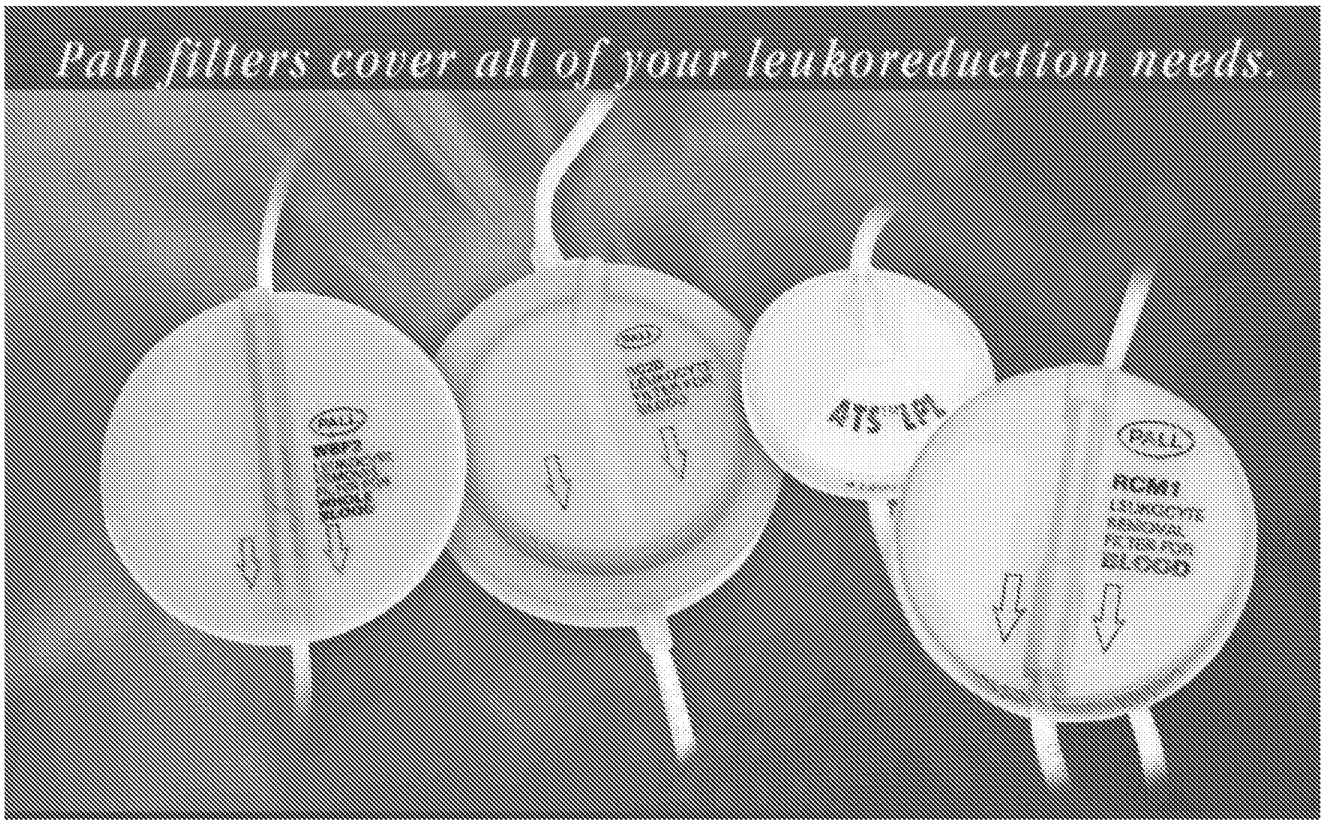


Ordering Information*

Leukotrap PL System

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

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



References

1 Bruneau C, Perez P, Chassaigne M, Allouch P, Audurier A, Gulian C, Janus G, Boulard G, De Micco P, Salmi LR, Noel L. Efficacy of a new collection procedure for preventing bacterial contamination of whole-blood donations. Transfusion 41:74-81, 2001.

2 Hogman CF, Gone J, Hambraeus A, et al. The role of leukocytes in the transmission of Yersinia enterocolitica with blood components. Transfusion 32: 654-657, 1992.

3 Kim DM, Brecher ME, Bland LA, et al. Prestorage removal of Yersinia enterocolitica from red cells with white cell-reducing filters. Transfusion 32: 658-662, 1992.

4 Wenz B, Burns ER, Freundlich LF. Prevention of growth of Yersinia enterocolitica in blood by polyester fiber filtration. Transfusion 32: 663-666, 1992.

5 Standard 5.1.5.1 - Standards for Blood Banks and Transfusion Services, AABB 21st Edition, 2002.

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

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

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

PALL Medical

United States
2200 Northern Boulevard
East Hills, NY 11548-1289

800 645 6576 toll free phone (USA)
516 484 5400 phone
516 484 6668 fax

www.pall.com

International Offices
Pall Corporation has offices and plants throughout the world in locations such as: Argentina, Australia, Austria, Belgium, Brazil, Canada, China, France, Germany, Hong Kong, India, Indonesia, Ireland, Italy, Japan, Korea, Malaysia, Mexico, the Netherlands, New Zealand, Norway, Poland, Puerto Rico, Russia, Singapore, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, the United Kingdom, the United States and Venezuela. Distributors in all major industrial areas of the world.

The information provided in this literature was reviewed for accuracy at the time of publication. Product data may be subject to change without notice. For current information consult your local Pall distributor or contact Pall directly.

© 2005, Pall Corporation. Pall, PALL, and Leukotrap, CLY and Nutrikal are trademarks of Pall Corporation. ® indicates a Pall trademark registered in the USA. DonorCare is a trademark owned by Noble House Group Pty Ltd, Australia and used under license by ITL Corporation Pty Ltd. *Better Blood. Better Care.*SM is a service mark of Pall Corporation.

*Better Blood. Better Care.*SM

9.05, AN, GN05.1242 FN XXXXX

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

DISC REMOVAL

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

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

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

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

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

SUMMARY

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

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

G. A. MAYER, M.D.,† *Kingston, Ont.*

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

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

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

---

*Read before the Annual Meeting of the Canadian Physiological Society, Toronto, October 23, 1954.

Aided by a grant from the Canadian Life Insurance Officers Association.

†Research Assistant, Department of Medicine, Queen's University, Kingston, Ontario.

KUR-MAG-DE005529

Canad. M. A. J.
June 15, 1955, vol. 72

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

KUR-MAG-DE005530

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

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

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

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

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

ACCURACY OF THE METHOD

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

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

NORMAL VALUES

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

SUMMARY

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

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

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

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

REFERENCES

1. LEE, R. I. AND WHITE, P. D.: *Am. J. M. Sc.*, **145**: 495, 1913.
2. QUICK, A. J., HONORATO, C. R. AND STEFANINI, M.: *Blood*, **3**: 1120, 1948.
3. JAQUES, L. B. *et al.*: *Canad. M. A. J.*, **55**: 26, 1946.
4. ALLEN, G. W. AND ATTYAH, A. M.: *J. Lab. & Clin. Med.*, **41**: 767, 1953.
5. MARGULIES, H. AND BARKER, N. W.: *Am. J. M. Sc.*, **218**: 42, 1949.
6. LOSNER, S. AND VOLK, B. W.: *Am. J. M. Sc.*, **226**: 61, 1953.
7. WHITTAKER, J.: *Canad. M. A. J.*, **52**: 185, 1945.
8. FOWLER, N. O.: *J. Clin. Invest.*, **28**: 671, 1949.
9. PICHOTKA, J. AND REICHEL, H.: *Am. J. Physiol.*, **162**: 632, 1950.

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.

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/538,990	**05/16/2023 04:23:02 PM ET**	**069366-0572201_KUR2C03US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	3420	FILED BY	Trent Tercenio
PATENT CENTER #	62078044	FILING DATE	11/30/2021
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 6

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0572201_KUR2C03US-B-NPL-003.pdf	3	Non Patent Literature	225 KB
069366-0572201_KUR2C03US-A-NPL-050.pdf	3	Non Patent Literature	310 KB
069366-0572201_KUR2C03US-B-NPL-002.pdf	8	Non Patent Literature	4918 KB
069366-0572201_KUR2C03US-B-	5	Non Patent Literature	7065 KB

NPL-001.pdf			
069366-0572201_KUR2C03US_PTO_IDS-Form-B.pdf	4	Information Disclosure Statement (IDS) Form (SB08)	1029 KB
069366-0572201_KUR2C03US_Transmittal-Letter.pdf	1	Transmittal Letter	497 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-0572201_KUR2C03US-B-NPL-003.pdf	4845D9C9B8E1D227954B09848282BAD98734BAA46835DEEBDBA6DA3C2307CFB01622003E57BD77C3B014529C291A0BA338BB2CEB71F6E572FBD01BE8990C7A38
069366-0572201_KUR2C03US-A-NPL-050.pdf	1574A0ADF9554876D678515D72E9850BDB0CC5149BF4AD045BC39F9EF515F37547AB10FDA1880E3034C6BEC768FFCB2F6F9693C748B094BC5A57CB08E680049A
069366-0572201_KUR2C03US-B-NPL-002.pdf	C6AFB655240F76C3B32C300992A94F305D313740DDB42DB6F61A3E09208B9FA5E58C3E6860238A9D9E88143F32A34A8CB0A5FC2536E675037AC9CD79B6490C96
069366-0572201_KUR2C03US-B-NPL-001.pdf	C2AC22C21DDF22356324DE1908A437F001030F01724034F2DBA52B22C70AF7594A74AB21D73726D6B72ECC6E7314598F8415A49003968A3E8ABD716124EF386D
069366-0572201_KUR2C03US_PTO_IDS-Form-B.pdf	7EE87B793330BD063C01E3030EA7CCDE4E21630893DE722217955D7541FE3E1E7514CA367F7A4DFEE35266BE6D42FD3A05A7D3442F6F7B47B19C4F399D9D32EC
069366-0572201_KUR2C03US_Transmittal-Letter.pdf	6F31AE32020C351783964EB2FF52AF2FE6F7D13882C1537D354AE4EC4FDB466561D33324D69DF26642848F0BE3C42417B48A02D9658978F715830B93B477F900

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

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

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

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

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

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

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

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

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

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

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

MATERIALS AND METHODS

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

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

Downloaded from http://jcm.asm.org/ on August 20, 2019 by guest

KUR-MAG-DE005532

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

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

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

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

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

RESULTS

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

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

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

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

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

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

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

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

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

Downloaded from http://jcm.asm.org/ on August 20, 2019 by guest

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

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

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

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

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

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

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

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

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

DISCUSSION

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

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

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

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

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

Downloaded from http://jcm.asm.org/ on August 20, 2019 by guest

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

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

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

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

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

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

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

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

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

Downloaded from http://jcm.asm.org/ on August 20, 2019 by guest

KUR-MAG-DE005535

ACKNOWLEDGMENTS

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

REFERENCES

1. **Auckenthaler, R., P. Rohner, G. Verschraegen, D. Bernard, G. Claeys, M. S. Sha'®, M. Stevens, and G. Schuster.** 1994. Kontinuierlich messende Blutkultursysteme. *In* European Congress of Clinical Microbiology and Infectious Diseases, Seville, Spain (März 1993).
2. **Fontanals, D., I. Stafelin, I. Pons, D. Mariscal, and M. Torra.** 1996. Evaluation of the performance of BacT/Alert and VITAL blood culture systems for diagnosis of bacteremia. Poster 16/17 at the Seventh National Congress of the Spanish Society for Infectious Diseases and Clinical Microbiology, Torremolinos, Spain.
3. **Hardy, D. J., B. B. Hulbert, and P. C. Migneault.** 1992. Time to detection of positive BacT/Alert blood cultures and lack of need for routine subculture of 5- to 7-day negative cultures. J. Clin. Microbiol. **30**:2743±2745.
4. **Jorgensen, J. H., S. Mirrett, L. C. McDonald, P. R. Murray, M. P. Weinstein, J. Fune, C. W. Trippy, M. Masterson, and L. B. Reller.** 1997. Controlled clinical laboratory comparison of BACTEC Plus Aerobic/F Resin medium with BacT/Alert aerobic FAN medium for detection of bacteremia and fungemia. J. Clin. Microbiol. **35**:53±58.
5. **Morris, A. J., M. L. Wilson, S. Mirrett, and L. B. Reller.** 1993. Rationale for selective use of anaerobic blood cultures. J. Clin. Microbiol. **31**:2110±2113.
6. **Pittet, D.** 1997. Nosocomial bloodstream infections. *In* R. P. Wenzel (ed.), Prevention and control of nosocomial infections, 3rd ed. The Williams & Wilkins Co., Baltimore, Md.
7. **Pittet, D., N. Li, R. F. Woolson, and R. P. Wenzel.** 1997. Microbiological factors influencing the outcome of nosocomial bloodstream infections: a 6-year validated, population-based model. Clin. Infect. Dis. **24**:1068±1078.
8. **Pohlman, J. K., B. A. Kirkley, K. A. Easley, B. A. Basille, and J. A. Washington.** 1995. Controlled clinical evaluation of BACTEC Plus Aerobic/F and BacT/Alert aerobic FAN bottles for detection of bloodstream infections. J. Clin. Microbiol. **33**:2856±2858.
9. **Riest, G., H.-J. Linde, and P. M. Shah.** 1997. Comparison of BacT/Alert and Bactec NR 860 blood culture systems in a laboratory not continuously staffed. Clin. Microbiol. Infect. **3**:345±351.
10. **Roberts, F. J., L. W. Geere, and A. Coldman.** 1991. A three-year study of positive blood cultures, with emphasis on prognosis. Rev. Infect. Dis. **13**:34±46.
11. **Rohner, P., B. Pepey, and R. Auckenthaler.** 1995. Comparison of BacT/Alert with signal blood culture systems. J. Clin. Microbiol. **33**:313±317.
12. **Shigei, J. T., J. A. Shimabukuro, M. T. Pezzlo, L. M. de la Maza, and E. M. Peterson.** 1995. Value of terminal subcultures for blood cultures monitored by BACTEC 9240. J. Clin. Microbiol. **33**:1385±1388.
13. **Smith, J. A., E. A. Bryce, J. H. Ngui-Yen, and F. J. Roberts.** 1995. Comparison of BACTEC 9240 and BacT/Alert blood culture systems in an adult hospital. J. Clin. Microbiol. **33**:1905±1908.
14. **Snyder, J. W., and S. K. Lude.** 1996. Comparison of BacT/Alert FAN medium with BACTEC NR660 Plus 26A medium. J. Clin. Microbiol. **34**:1327±1329.
15. **Weinstein, M. P.** 1996. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. Clin. Infect. Dis. **23**:40±46.
16. **Weinstein, M. P., L. B. Reller, J. R. Murphy, and K. A. Lichtenstein.** 1983. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. Rev. Infect. Dis. **5**:35±53.
17. **Weinstein, M. P., S. Mirrett, M. L. Wilson, L. G. Reimer, and L. B. Reller.** 1994. Controlled evaluation of 5 versus 10 milliliters of blood cultured in aerobic BacT/Alert blood culture bottles. J. Clin. Microbiol. **32**:2103±2106.
18. **Widmer, A. F.** 1997. Intravenous-related infections. *In* R. P. Wenzel (ed.), Prevention and control of nosocomial infections, 3rd ed. The Williams & Wilkins Co., Baltimore, Md.
19. **Wilson, M. L., M. P. Weinstein, L. G. Reimer, S. Mirrett, and L. B. Reller.** 1992. Controlled comparison of BacT/Alert and BACTEC 660/730 nonradiometric blood culture systems. J. Clin. Microbiol. **30**:323±329.
20. **Wilson, M. L., T. E. Davis, S. Mirrett, J. Reynolds, D. Fuller, S. D. Allen, K. K. Flint, F. Koontz, and L. B. Reller.** 1993. Controlled comparison of the BACTEC high-blood-volume fungal medium, BACTEC Plus 26 aerobic blood culture bottle, and 10-milliliter Isolator blood culture system for detection of fungemia and bacteremia. J. Clin. Microbiol. **31**:865±871.

Downloaded from http://jcm.asm.org/ on August 20, 2019 by guest

THE AMERICAN JOURNAL OF CLINICAL PATHOLOGY
Vol. 39, No. 3, pp. 321-323 March, 1963
Copyright © 1963 by The Williams & Wilkins Co.
Printed in U.S.A.

Reprinted from TECHNICAL BULLETIN OF THE
REGISTRY OF MEDICAL TECHNOLOGISTS
Vol. 33, No. 2, February, 1963, pp. 29-31

THE STANDARD CLOTTING TIME

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

GEORGE F. MEISSNER, M.D., AND CONSTANCE M. MOEHRING, B.S.

Rhode Island Hospital, Providence, Rhode Island, and Tufts University School of Medicine, Boston, Massachusetts

Downloaded from https://academic.oup.com/ajcp/article-abstract/39/3_ts/321/4821791 by wai@turnerboyd.com on 26 August 2019

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

MATERIALS AND METHODS

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

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

Received, July 2, 1962; revision received, September 14; accepted for publication November 14.

Dr. Meissner is Associate Pathologist at the Rhode Island Hospital, and Assistant Professor at Tufts University Medical School. Mrs. Moehring is Medical Technologist at the Rhode Island Hospital.

KUR-MAG-DE005545

RESULTS

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

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

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

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

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

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

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

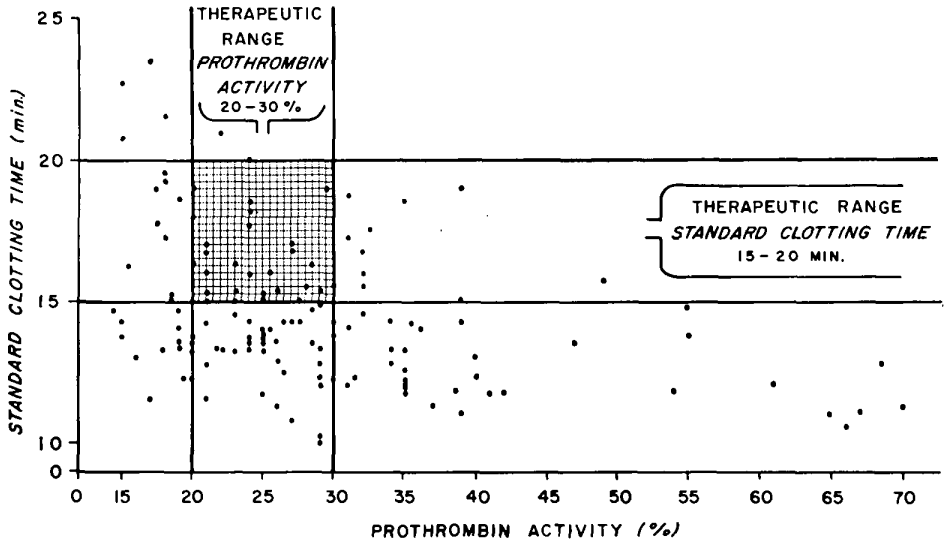


FIG. 1. A scattergram of the standard clotting time (min.) and prothrombin activity (per cent) of 139 determinations on 36 patients being treated with anticoagulants. Except for the *cross-hatched area*, there is no consistent correlation between the 2 tests.

Downloaded from https://academic.oup.com/ajcp/article-abstract/39/3_ts/321/4821791 by wai@turnerboyd.com on 26 August 2019

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

COMMENTS

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

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

SUMMARY

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

SUMMARIO IN INTERLINGUA

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

REFERENCES

1. Mayer, G. A.: Method for reliable determination of clotting time in whole blood. Canad. M. A. J., **72:** 927–929, 1955.
2. Mayer, G. A.: Standard clotting time. J. Lab. & Clin. Med., **49:** 938–944, 1957.
3. Mayer, G. A., and Connell, W. F.: Effect of bishydroxycoumarin (Dicumarol) on clotting time of whole blood. J. A. M. A., **161:** 806–811, 1956.
4. McMillan, C. W.: Manual of the Coagulation Laboratory of Children's Medical Center. Boston, 1960.
5. Meissner, G. F., and Moehring, C. M.: Synthetic estrogens in treatment of atherosclerosis. (A study of prostatic cancer patients.) Arch. Int. Med., **110:** 467–471, 1962
6. Rapaport, S. I., and Ames, S. A.: Relation between levels of plasma thromboplastin component (PTC) and prothrombin times by the P & P and Quick methods in patients receiving Warfarin. New England J. Med., **267:** 125–130, 1962.
7. Roberts, L. N., and Mason, G. P.: A clinical assessment of anticoagulant control. Canad. M. A. J., **85:** 831–835, 1961.

Downloaded from https://academic.oup.com/ajcp/article-abstract/39/3_ts/321/4821791 by wai@turnerboyd.com on 26 August 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

27500 7590 10/04/2023

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

EXAMINER	
ABOUELELA, MAY A	

ART UNIT	PAPER NUMBER
3791	

NOTIFICATION DATE	DELIVERY MODE
10/04/2023	ELECTRONIC

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

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

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

Docket_IP@pillsburylaw.com

Office Action Summary	Application No. 17/538,990	Applicant(s) ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	AIA (FITF) Status Yes

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

Period for Reply

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

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

Status

1)☑ Responsive to communication(s) filed on 11/30/2021.

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

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

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

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

Disposition of Claims*

5) ☑ Claim(s) 1-20 is/are pending in the application.

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

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-20 is/are rejected.

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

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

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

Application Papers

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

11)☑ The drawing(s) filed on 11/30/2011 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

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

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

Priority under 35 U.S.C. § 119

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

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

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

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

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

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

Attachment(s)

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

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

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

4) ☐ Other: _____.

Notice of Pre-AIA or AIA Status

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

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 05/16/2023. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

3. Claim 1 is objected to because of the following informalities: the phrase “blood” in lines 8 and 10 should be amended to read –the blood--. Appropriate correction is required.

4. Claim 1 is objected to because of the following informalities: the phrase “the junction being sized” in lines 7-8 should be amended to read –wherein the junction being sized--. Appropriate correction is required.

5. Claim 2 is objected to because of the following informalities: the phrase “blood” in line 3 should be amended to read –the blood--. Appropriate correction is required.

6. Claim 11 is objected to because of the following informalities: the phrase "an curved channel" in line 2 should be amended to read –the curved channel--. Appropriate correction is required.

7. Claim 12 is objected to because of the following informalities: the phrase "an air permeable blood barrier" in line 2 should be amended to read –the air permeable blood barrier--. Appropriate correction is required.

8. Claim 13 is objected to because of the following informalities: the phrase "the chamber" in line 9 should be amended to read –wherein the chamber--. Appropriate correction is required.

9. Claim 13 is objected to because of the following informalities: the phrase "bodily fluid" in lines 9-10, 12 and 13 should be amended to read –the bodily fluid--. Appropriate correction is required.

10. Claim 13 is objected to because of the following informalities: the phrase "from the inlet to bypass the chamber" in line 13 should be amended to read –to be directed from the inlet to bypass the chamber--. Appropriate correction is required.

11. Claim 16 is objected to because of the following informalities: the phrase "bodily fluid" in line 3 should be amended to read –the bodily fluid--. Appropriate correction is required.

Claim Interpretation

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

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

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

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

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

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

(A) the claim limitation uses the term "means" or "step" or a term used as a substitute for "means" that is a generic placeholder (also called a nonce term or a non-structural term having no specific structural meaning) for performing the claimed function;

(B) the term "means" or "step" or the generic placeholder is modified by functional language, typically, but not always linked by the transition word "for" (e.g.,

"means for") or another linking word or phrase, such as "configured to" or "so that"; and

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

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

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

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

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

Limitation "junction" in claims 1, 6 and 13, the claims does not recite enough structure that corresponds to the claimed "junction", the specification disclose (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, par.0109) which can be interpreted as the structure that corresponds to the claimed "junction".

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

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

claimed function); or (2) present a sufficient showing that the claim limitation(s) recite(s) sufficient structure to perform the claimed function so as to avoid it/them being interpreted under 35 U.S.C. 112(f) or pre-AIA 35 U.S.C. 112, sixth paragraph.

Claim Rejections - 35 USC § 112

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

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

Claims 1-12 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

14. Claim 1 recites the limitation "the patient" in line2. There is insufficient antecedent basis for this limitation in the claim.

15. Claim 6 recites the limitation "the blood control device" in line 2. There is insufficient antecedent basis for this limitation in the claim.

16. Claim 6 recites the limitation "the sequestration chamber" in line 10. There is insufficient antecedent basis for this limitation in the claim. Examiner respectfully notes that the phrase “the sequestration chamber” is also recite in claim 7.

17. Claim 8 recites the limitation "the blood sampling pathway" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

18. Claim 9 recites the limitation "the blood sampling pathway" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

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

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

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

Claims 1-20 are non-provisionally rejected on the ground of statutory double patenting as being unpatentable over claims 1-20 of U.S Patent Application No.11311219, claims 1-16 of U.S Patent Application No. 9820682, claims 1-23 of U.S Patent Application No.10143412, and claims 1-26 of U.S Patent Application No.11185266.

Also, claim 1-20 are provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 1-20 of U.S pending Application No.17/730118, and claims 1-18 and 20 of U.S pending Application No.17/094692.

Although the claims at issue are not identical, they are not patentably distinct from each other because the U.S Patent applications, pending applications and the instance application are claiming a common subject matter including: a blood sample device comprising; an inlet, an outlet; a chamber having a vent that includes an air permeable blood barrier; a sampling channel; and a junction connected between the inlet, the

chamber and the sampling channel, wherein the junction being sized and configured such that a first portion of blood conveyed from the patient flows into the chamber to displace air therein through the air permeable blood barrier, and such that a second portion of blood is allowed to bypass the chamber and the first portion of blood at least temporarily contained therein to be directed into the sampling channel toward the outlet.

Conclusion

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

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

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JACQUELINE CHENG can be reached on 5712725596. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and

https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MAY A ABOUELELA/
Primary Examiner, Art Unit 3791

Notice of References Cited	Application/Control No. 17/538,990	Applicant(s)/Patent Under Reexamination ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	Page 1 of 4

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20080319346-A1	12-2008	Crawford; Jamieson	A61B5/150656	600/576
*	B	US-4412548-A	11-1983	Hoch; Louis	A61B5/150213	600/577
*	C	US-5222502-A	06-1993	Kurose; Katsutoshi	A61B5/150732	600/584
*	D	US-5520193-A	05-1996	Suzuki; Issei	A61B5/1545	604/126
*	E	US-20100057004-A1	03-2010	Christensen; Kelly D.	A61M39/22	604/122
*	F	US-20070088279-A1	04-2007	Shue; Ming-Jeng	A61M25/0693	604/168.01
*	G	US-20080145933-A1	06-2008	Patton; Richard G.	A61B5/154	435/379
*	H	US-20040054333-A1	03-2004	Theeuwes, Felix	A61M5/14276	604/248
*	I	US-9022951-B2	05-2015	Bullington; Gregory	A61B5/150221	600/576
*	J	US-6569117-B1	05-2003	Ziv; David	A61M39/02	604/246
*	K	US-3741197-A	06-1973	Sanz; Manuel C.	A61B5/150267	600/583
*	L	US-20100010372-A1	01-2010	BROWN; LEROY R.	A61B5/15003	600/573
*	M	US-8603009-B2	12-2013	Tan; Alvin Chee Leong	A61B5/150251	600/573

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Notice of References Cited	Application/Control No. 17/538,990	Applicant(s)/Patent Under Reexamination ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	Page 2 of 4

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-4207870-A	06-1980	Eldridge; William N.	A61B5/150732	604/167.03
*	B	US-20080167577-A1	07-2008	Weilbacher; Eugene E.	A61B5/1545	600/576
*	C	US-20080086085-A1	04-2008	Brown; Leroy R.	A61B5/150389	604/122
*	D	US-9877675-B2	01-2018	Baid; Rishi	A61B5/150389	1/1
*	E	US-4444203-A	04-1984	Engelman; Allan	A61B5/150496	600/576
*	F	US-20070083162-A1	04-2007	O'Reagan; James	A61M39/26	604/167.03
*	G	US-6398743-B1	06-2002	Halseth; Thor R.	A61B5/15003	604/164.12
*	H	US-9022950-B2	05-2015	Bullington; Gregory	A61B5/150251	600/576
*	I	US-9155495-B2	10-2015	Bullington; Gregory J.	A61B5/1405	1/1
*	J	US-20160008579-A1	01-2016	Burkholz; Jonathan Karl	A61M5/158	604/164.08
*	K	US-20120016266-A1	01-2012	Burkholz; Jonathan Karl	A61B5/150992	600/581
*	L	US-4436098-A	03-1984	Kaufman; Joseph	A61B5/1545	604/199
*	M	US-20130317391-A1	11-2013	Bullington; Gregory J.	A61B5/15003	600/578

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Notice of References Cited	Application/Control No. 17/538,990	Applicant(s)/Patent Under Reexamination ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	Page 3 of 4

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-9138572-B2	09-2015	Zeytoonian; Paul	A61M39/26	1/1
*	B	US-8568371-B2	10-2013	Siopes; William	A61M39/06	251/903
*	C	US-8540663-B2	09-2013	Davey; Christopher T.	A61M1/30	604/93.01
*	D	US-8523826-B2	09-2013	Layton, Jr.; Russell K.	A61M39/16	604/533
*	E	US-20160174888-A1	06-2016	Berthier; Erwin	A61B5/150503	600/573
*	F	US-8197420-B2	06-2012	Patton; Richard G.	A61B5/150503	600/573
*	G	US-4057050-A	11-1977	Sarstedt; Walter	A61B5/150351	604/125
*	H	US-20050240161-A1	10-2005	Crawford, Jamieson William McLean	A61B5/150572	604/264
*	I	US-20040147855-A1	07-2004	Marsden, Stewart	A61B5/150496	600/576
*	J	US-8864684-B2	10-2014	Bullington; Gregory J.	A61B10/0048	600/576
*	K	US-8535241-B2	09-2013	Bullington; Gregory	A61B5/150946	604/249
*	L	US-20040073171-A1	04-2004	Rogers, Bobby E.	A61M39/26	604/164.13
*	M	US-20050004524-A1	01-2005	Newby, C. Mark	A61B5/150648	604/164.08

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Notice of References Cited	Application/Control No. 17/538,990	Applicant(s)/Patent Under Reexamination ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	Page 4 of 4

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20030105414-A1	06-2003	Leong, Alvin Tan Chee	A61B5/15003	600/576
*	B	US-5749857-A	05-1998	Cuppy; Michael J.	A61M25/0606	604/161
*	C	US-9060724-B2	06-2015	Bullington; Gregory J.	A61B5/150099	1/1
*	D	US-9204864-B2	12-2015	Bullington; Gregory J.	A61B10/0096	1/1
*	E	US-20020004647-A1	01-2002	Leong, Alvin Tan Chee	A61B5/1545	604/168.01
*	F	US-3817240-A	06-1974	Ayres; Waldemar A.	A61B5/150221	600/584
*	G	US-3874367-A	04-1975	Ayres; Waldemar A.	A61B5/15003	600/577
*	H	US-3886930-A	06-1975	Ryan; George R.	A61B5/15003	600/584
*	I	US-4106497-A	08-1978	Percarpio; Edward P.	A61B5/150389	600/579
*	J	US-4154229-A	05-1979	Nugent; Edward L.	A61B5/150473	600/577
*	K	US-20150359473-A1	12-2015	Garrett; Chad	A61B5/157	600/309
*	L	US-20150314105-A1	11-2015	GASPARYAN; Levon	A61M5/427	604/117
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/538,990	ROGERS et al.
	Examiner	Art Unit
	MAY A ABOUELELA	3791

CPC - Searched*		
Symbol	Date	Examiner
A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068	07/05/2023	MA

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

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

Search Notes		
Search Notes	Date	Examiner
text search, inventor name search, class/subclass search	07/05/2023	MA

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

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/538,990	ROGERS et al.
	Examiner	**Art Unit**
	MAY A ABOUELELA	3791

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

CLAIMS

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

CLAIM		DATE								
Final	Original	07/05/2023								
	1	✓								
	2	✓								
	3	✓								
	4	✓								
	5	✓								
	6	✓								
	7	✓								
	8	✓								
	9	✓								
	10	✓								
	11	✓								
	12	✓								
	13	✓								
	14	✓								
	15	✓								
	16	✓								
	17	✓								
	18	✓								
	19	✓								
	20	✓								

PE2E SEARCH - Search History (Prior Art)

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

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

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

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

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

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

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

		| "5450856" | "5462534" | "5485854" | "5486163" | "5490841" | "5496281" | "5509907" | "5520193" | "5533984" | "5542932" | "5584816" | "5599313" | "5599318" | "5603699" | "5632732" | "5643219" | "5662617" | "5665075" | "5669889" | "5693022" | "5697914" | "5702369" | "5733265" | "5755701" | "5807351" | "5830190" | "5836920" | "5885249" | "5893844" | "5913846" | "5984895" | "5993426" | "6059737" | "6077244" | "6077253" | "6080137" | "6096006" | "6110160" | "6120482" | "6156010" | "6190370" | "6261263" | "6511439" | "6533760" | "6964658" | "7160267" | "RE31086").PN. OR ("7615033").URPN.					
L102	215	L101 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:51 PM
L103	1347	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:11 PM
L104	17	L103 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L105	19	("2009/0312711").URPN.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L106	11	("2007/0106220").URPN.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L107	288967	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L108	6321	L107 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L109	121	L108 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:17 PM
L110	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:31 PM
L111	6	L110 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:31 PM
L113	71	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:31 PM
L114	0	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:38 PM

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

		| "D604838" | "D604839" | "D605287" | "RE35539" | "RE43473").PN. OR ("9615783").URPN.					
L342	115	("20020193748" | "20030093009" | "20030105414" | "20030220614" | "20030229315" | "20040059302" | "20040092872" | "20040193120" | "20050004524" | "20050065482" | "20050124944" | "20050187493" | "20050245868" | "20050245869" | "20050245870" | "20050245879" | "20050245885" | "20060036219" | "20060224122" | "20070106220" | "20070106224" | "20070167914" | "20080086085" | "20080177202" | "20080319345" | "20080319346" | "20090204026" | "20100262038" | "4106497" | "4207870" | "4305406" | "4572210" | "4573976" | "4641663" | "4795443" | "4840619" | "4894055" | "4900307" | "4994046" | "5015241" | "5195985" | "5215534" | "5222502" | "5242417" | "5246428" | "5256153" | "5295970" | "5303713" | "5312372" | "5336199" | "5348544" | "5356392" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5599313" | "5662617" | "5665075" | "5672161" | "5676658" | "5702369" | "5704920" | "5733265" | "5755522" | "5957892" | "5984899" | "6149629" | "6224576" | "6254575" | "6261263" | "6298541" | "6344032" | "6436086" | "6440104" | "6524277" | "6533760" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"6592556" | "6623456" | "6635032" | "6648855" | "6695819" | "6699217" | "6712792" | "6780169" | "6837877" | "6869415" | "6984223" | "7001363" | "7128726" | "7147624" | "7160267" | "7163526" | "7223258" | "7226432" | "7396343" | "7428773" | "7537581" | "7766879" | "D422700" | "D442280" | "D604836" | "D604837" | "D604838" | "D604839" | "D605287").PN. OR ("8603009").URPN.					
L343	148	("20020193748" | "20030105414" | "20030229315" | "20040059302" | "20040092872" | "20050004524" | "20050187493" | "20050245868" | "20050245869" | "20050245870" | "20050245885" | "20060036219" | "20070106220" | "20070167914" | "20080086085" | "20080177202" | "4106497" | "4207870" | "4305406" | "4573976" | "4641663" | "4795443" | "4840619" | "4894055" | "4900307" | "4994046" | "5015241" | "5195985" | "5215534" | "5222502" | "5242417" | "5256153" | "5295970" | "5303713" | "5312372" | "5336199" | "5348544" | "5356392" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5672161" | "5676658" | "5702369" | "5704920" | "5755522" | "5984899" | "6149629" | "6261263" | "6298541" | "6436086" | "6440104" | "6524277" | "6533760" | "6592556" | "6623456" | "6635032" | "6648855" | "6699217" | "6712792" | "6780169" | "6837877" | "6869415" | "6984223" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"7001363" | "7128726" | "7147624" | "7160267" | "7163526" | "7223258" | "7226432" | "7396343" | "7428773" | "D422700" | "D442280").PN. OR ("7766879").URPN.					
L344	41	("2735430" | "2798487" | "3187749" | "3240209" | "3585984" | "3817240" | "4166450" | "4207870" | "4295477" | "4312362").PN. OR ("4436098").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:22 PM
L345	163	L341 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:22 PM
L346	163	L345 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:23 PM
L347	22	("2005/0283093").URPN.	(USPAT)	OR	ON	ON	2021/07/08 04:23 PM
L348	163	L345 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L349	163	L348 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L350	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/08 04:37 PM
L351	1363	L350 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:37 PM
L352	1346	L351 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L353	136	L352 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L354	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:41 PM
L355	711	L354 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L356	699	L355 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L357	123	L356 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L358	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:44 PM
L359	277	L358 and ((blood or fluid$4) near4 (sequest$5 or sampl$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM

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

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

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

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

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

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

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

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

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

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

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

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

		OR membrane OR permeab$4 OR vent$4))					
L491	204	482 AND (hous$4 SAME (inlet AND outlet AND channel))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:29 PM
L492	118	491 AND (hous$4 near5 ((top OR upper) AND (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:33 PM
L493	1	489 AND (hous$4 near5 ((top OR upper) AND (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L494	0	489 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L495	27	492 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L496	172	484 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:41 PM
L497	113	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/07/05 01:58 PM
L498	26	497 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 01:58 PM
L499	4	15/855439	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 03:12 PM
L500	48306	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT;	OR	ON	ON	2023/07/05 03:36 PM

			IBM_TDB)				
L501	5081	500 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 03:36 PM
L502	3947	501 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 03:37 PM
L503	1069	502 AND (air near5 (filter$4 OR material$4 OR membrane OR permeab$4 OR vent$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 03:37 PM
L504	3871	501 AND ((blood OR fluid$4 OR urine) near5(divert$4 OR direct$4 OR flow$4 OR bypass$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:18 PM
L505	3030	501 AND ((blood OR fluid$4 OR urine) near5(divert$4 OR direct$4 OR flow$4 OR bypass$4 OR allow$4)) SAME (channel$4 OR chamber OR junct$4 OR inlet OR outlet OR path$4 OR contain$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:20 PM
L506	921	503 AND ((blood OR fluid$4 OR urine) near5(divert$4 OR direct$4 OR flow$4 OR bypass$4 OR allow$4)) SAME (channel$4 OR chamber OR junct$4 OR inlet OR outlet OR path$4 OR contain$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:20 PM

PE2E SEARCH - Search History (Interference)

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

		sequest$5).clm.					
N249	4	(blood and fluid$4 and inlet and outlet and port and reservoir and allow$4 and initial$4 and sequest$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N250	495	(blood and fluid$4 and allow$4 and initial$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N251	107	(blood and fluid$4 and allow$4 and initial$4 and subsequent$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N283	9	((blood or fluid$4) and sequestrat$4 and chamber and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N284	530	((blood or fluid$4) and chamber and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N285	84	((blood or fluid$4) and chamber and cap and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:32 PM
N365	6	(port and sequest$5 and junction and chamber and sampl$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:49 PM
N366	9	(blood AND fluid$4 AND inlet AND outlet AND junct$4 AND inhibit$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:31 PM
N367	84	((blood OR fluid$4) AND chamber AND sampl$4 AND junction AND (inhibit$4 OR prevent$4)).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:36 PM
N368	25	(blood AND chamber AND sampl$4 AND junction AND inlet AND outlet AND port AND first).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:48 PM
N369	4	(blood AND chamber AND sampl$4 AND junction AND inlet AND outlet AND port AND first AND hous$4 AND subsequent).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:49 PM
N370	64902	"465" AND housing	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:50 PM
N371	6	(inlet AND outlet AND junct$4 AND channel	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:51 PM

		AND sampl$4 AND fluid$4 AND vent AND air AND permeab$4).clm.					
N372	167	(inlet AND outlet AND junct$4 AND channel AND sampl$4 AND fluid$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:52 PM
N373	23	(inlet AND outlet AND junct$4 AND channel AND sampl$4 AND fluid$4 AND bypass$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:53 PM

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17538990
Filing Date	2021-11-30
First Named Inventor	Bobby E. ROGERS
Art Unit	OPAP
Examiner Name	CENTRAL, DOCKET
Attorney Docket Number	069366-0572201_KUR2C03US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

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

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

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

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

EXAMINER SIGNATURE

Examiner Signature	/MAY A ABOUELELA/	Date Considered	07/05/2023

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

CERTIFICATION STATEMENT

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

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

OR

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

See attached certification statement.

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

☒ A certification statement is not submitted herewith.

SIGNATURE

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

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-05-16
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

Privacy Act Statement

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

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

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

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

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

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

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

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

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

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	17538990
Filing Date	2021-11-30
First Named Inventor	Bobby E. ROGERS
Art Unit	OPAP
Examiner Name	CENTRAL, DOCKET
Attorney Docket Number	069366-0572201_KUR2C03US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5200325		1993-04-06	BLATT JOEL M	
	2	5432084		1995-07-11	BRUBAKER DANIEL B	
	3	5972294		1999-10-26	SMITH JOHN L	
	4	6187347		2001-02-13	PATTERSON JAMES A	
	5	6599474		2003-07-29	EVTODIENKO VLADIMIR	
	6	8197420		2012-06-12	PATTON RICHARD G	
	7	8535241		2013-09-17	BULLINGTON GREGORY	
	8	9060724		2015-06-23	BULLINGTON GREGORY J	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	9	9155495		2015-10-13	BULLINGTON GREGORY J	
	10	4412548		1983-11-01	HOCH LOUIS	
	11	5222502		1993-06-29	KUROSE KATSUTOSHI	
	12	5520193		1996-05-28	SUZUKI ISSEI	
	13	9022951		2015-05-05	BULLINGTON GREGORY	
	14	6569117		2003-05-27	ZIV DAVID	
	15	3741197		1973-06-26	SANZ M	
	16	8603009		2013-12-10	TAN ALVIN CHEE LEONG	
	17	4207870		1980-06-17	ELDRIDGE WILLIAM N	
	18	9877675		2018-01-30	BAID RISHI	
	19	4444203		1984-04-24	ENGELMAN ALLAN	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	20	6398743		2002-06-04	HALSETH THOR R	
	21	9022950		2015-05-05	BULLINGTON GREGORY	
	22	4436098		1984-03-13	KAUFMAN JOSEPH	
	23	9138572		2015-09-22	ZEYTOONIAN PAUL	
	24	8568371		2013-10-29	SIOPES WILLIAM	
	25	8540663		2013-09-24	DAVEY CHRISTOPHER T	
	26	8523826		2013-09-03	LAYTON JR RUSSELL K	
	27	4057050		1977-11-08	SARSTEDT WALTER	
	28	8864684		2014-10-21	BULLINGTON GREGORY J	
	29	5749857		1998-05-12	CUPPY MICHAEL J	
	30	9204864		2015-12-08	BULLINGTON GREGORY J	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	31	3874367		1975-04-01	AYRES WALDEMAR A	
	32	3886930		1975-06-03	RYAN GEORGE R	
	33	4106497		1978-08-15	PERCARPIO EDWARD P	
	34	4154229		1979-05-15	NUGENT EDWARD L	
	35	4980297		1990-12-25	HAYNES JOHN L	
	36	9820682		2017-11-21	ROGERS BOBBY E	
	37	10010282		2018-07-03	ROGERS BOBBY E	
	38	10143412		2018-12-04	ROGERS BOBBY E	
	39	11185266		2021-11-30	ROGERS BOBBY E	
	40	10827964		2020-11-10	ROGERS BOBBY E	
	41	11311219		2022-04-26	ROGERS BOBBY E	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	42	3817240		1974-06-18	AYRES W	
	43	3648684		1972-03-14	BARNWELL CLEORA W	
	44	4056101		1977-11-01	GEISSLER ULRICH C	
	45	4416290		1983-11-22	LUTKOWSKI LAWRENCE	
	46	8070725		2011-12-06	CHRISTENSEN KELLY D	
	47	4349035		1982-09-14	THOMAS JOSEPH J	
	48	4813433		1989-03-21	DOWNEY JOHN M	
	49	5401262		1995-03-28	KARWOSKI THEODORE	
	50	3859998		1975-01-14	THOMAS JOSEPH JOHN	
	51	4373535		1983-02-15	MARTELL MICHAEL D	
	52	4690154		1987-09-01	WOODFORD TIMOTHY	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	53	5097842		1992-03-24	BONN GINA B	
	54	5865803		1999-02-02	MAJOR MIKLOS	
	55	5873841		1999-02-23	BRANNON JAMES K	
	56	6013037		2000-01-11	BRANNON JAMES K	
	57	6913580		2005-07-05	STONE BENJAMIN CURTIS	
	58	11213232		2022-01-04	IVOSEVIC MILAN	
	59	6626884		2003-09-30	DILLON JAGMOHANBIR SINGH	
	60	4904240		1990-02-27	HOOVER ROCKLIN L	
	61	4673386		1987-06-16	GORDON MARK G	
	62	7461671		2008-12-09	EHWALD RUDOLF	
	63	6506182		2003-01-14	ESTABROOK BRIAN K	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	64	3382865		1968-05-14	WORRALL JR ASHTON L	
	65	3848579		1974-11-19	VILLA REAL A	
	66	6106509		2000-08-22	LOUBSER PAUL G	
	67	3494352		1970-02-10	RUSSO RONALD D	
	68	6224561		2001-05-01	SWENDSON DAVID L	
	69	7055401		2006-06-06	PRYBELLA JOHN R	
	70	5135489		1992-08-04	JEPSON STEVEN C	
	71	5811658		1998-09-22	VAN DRIEL MICHAEL R	
	72	3604410		1971-09-14	WHITACRE GARY L	
	73	5772608		1998-06-30	DHAS V VARAPRABHU	
	74	4150089		1979-04-17	LINET MICHAEL S	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	75	4257416		1981-03-24	PRAGER DAVID	
	76	4193400		1980-03-18	LOVELESS JAMES C	
	77	6843775		2005-01-18	HYUN DONGCHUL D	
	78	7666166		2010-02-23	EMMERT MICHAEL	
	79	7479131		2009-01-20	MATHIAS JEAN-MARIE	
	80	8377040		2013-02-19	BURKHOLZ JONATHAN KARL	
	81	5417673		1995-05-23	GORDON MARK G	
	82	6638252		2003-10-28	MOULTON WILLIAM G	
	83	3945380		1976-03-23	DABNEY WILLIAM C	
	84	5100394		1992-03-31	DUDAR THOMAS E	
	85	8827958		2014-09-09	BIERMAN STEVEN F	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	86	8574203		2013-11-05	STOUT MARTY L	
	87	6860871		2005-03-01	KURACINA THOMAS C	
	88	6945948		2005-09-20	BAINBRIDGE MARLENE	
	89	7306736		2007-12-11	COLLINS GREGORY R	
	90	5691486		1997-11-25	BEHRINGER BRUCE E	
	91	5980830		1999-11-09	SAVAGE DOUGLAS ROBERT	
	92	5045185		1991-09-03	OHNAKA YUKIHIRO	
	93	5632906		1997-05-27	ISHIDA NOBORU	
	94	6695004		2004-02-24	RAYBUCK JOHN L	
	95	6733433		2004-05-11	FELL CLAUDE	
	96	7241281		2007-07-10	COELHO PHILIP H	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	97	8349254		2013-01-08	HOSHINO YOSHITERU	
	98	5439450		1995-08-08	HAEDT LORI E	
	99	6905483		2005-06-14	NEWBY C MARK	
	100	5431811		1995-07-11	TUSINI ANDREA	
	101	6736783		2004-05-18	BLAKE KEVIN R	
	102	7052603		2006-05-30	SCHICK KARL G	
	103	3835835		1974-09-17	THOMPSON R	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20010044615		2001-11-22	AMANO YOSHIKAZU	
	2	20030082074		2003-05-01	JURIK FRANKLIN A	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	3	20030185707		2003-10-02	IWAKI YOSHIHIDE	
	4	20040116830		2004-06-17	TRUDEAU WILLIAM M	
	5	20090299253		2009-12-03	HURSEY FRANCIS X	
	6	20130158506		2013-06-20	HARRIS ADRIENNE ROSE	
	7	20150246352		2015-09-03	BULLINGTON GREGORY J	
	8	20150342510		2015-12-03	BULLINGTON GREGORY J	
	9	20160361006		2016-12-15	BULLINGTON GREGORY J	
	10	20170065733		2017-03-09	BULLINGTON GREGORY J	
	11	20180140240		2018-05-24	BULLINGTON GREGORY J	
	12	20140112841		2014-04-24	SCHOEN CHRISTIAN	
	13	20180271425		2018-09-27	ROGERS BOBBY E	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	14	20080319346		2008-12-25	CRAWFORD JAMIESON	
	15	20100057004		2010-03-04	CHRISTENSEN KELLY D	
	16	20070088279		2007-04-19	SHUE MING-JENG	
	17	20080145933		2008-06-19	PATTON RICHARD G	
	18	20040054333		2004-03-18	THEEUWES FELIX	
	19	20100010372		2010-01-14	BROWN LEROY R	
	20	20080167577		2008-07-10	WEILBACHER EUGENE E	
	21	20080086085		2008-04-10	BROWN LEROY R	
	22	20070083162		2007-04-12	O'REAGAN JAMES	
	23	20160008579		2016-01-14	BURKHOLZ JONATHAN KARL	
	24	20120016266		2012-01-19	BURKHOLZ JONATHAN KARL	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	25	20130317391		2013-11-28	BULLINGTON GREGORY J	
	26	20160174888		2016-06-23	BERTHIER ERWIN	
	27	20050240161		2005-10-27	CRAWFORD JAMIESON W M	
	28	20040147855		2004-07-29	MARSDEN STEWART	
	29	20040073171		2004-04-15	ROGERS BOBBY E	
	30	20050004524		2005-01-06	NEWBY C MARK	
	31	20030105414		2003-06-05	LEONG ALVIN TAN CHEE	
	32	20020004647		2002-01-10	LEONG ALVIN TAN CHEE	
	33	20140155781		2014-06-05	BULLINGTON GREGORY J	
	34	20030208151		2003-11-06	KRAUS MENACHEM	
	35	20090227953		2009-09-10	TAN CHEE LEONG	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	36	20170020428		2017-01-26	ROGERS BOBBY E	
	37	20170020427		2017-01-26	ROGERS BOBBY E	
	38	20050005635		2005-01-13	LE METAIS MARC	
	39	20050007524		2005-01-13	LUO FANG-CHEN	
	40	20140039348		2014-02-06	BULLINGTON GREGORY J	
	41	20140107564		2014-04-17	BULLINGTON GREGORY J	
	42	20140155782		2014-06-05	BULLINGTON GREGORY J	
	43	20140276578		2014-09-18	BULLINGTON GREGORY J	
	44	20160017488		2016-01-21	KOBAYASHI MASAYUKI	
	45	20180177445		2018-06-28	ROGERS BOBBY E	
	46	20180353117		2018-12-13	BULLINGTON GREGORY J	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	47	20190159711		2019-05-30	ROGERS BOBBY E	
	48	20050245885		2005-11-03	BROWN LEROY	
	49	20110306899		2011-12-15	BROWN LEROY R	
	50	20130116599		2013-05-09	BULLINGTON GREGORY J	
	51	20050273019		2005-12-08	CONWAY HUGH	
	52	20150351678		2015-12-10	BULLINGTON GREGORY	
	53	20220160271		2022-05-26	IVOSEVIC MILAN	
	54	20050161112		2005-07-28	EHWALD RUDOLF	
	55	20070119508		2007-05-31	WEST RICHARD L	
	56	20220304600		2022-09-29	HAMMER JEREMY	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17538990
Filing Date	2021-11-30
First Named Inventor	Bobby E. ROGERS
Art Unit	OPAP
Examiner Name	CENTRAL, DOCKET
Attorney Docket Number	069366-0572201_KUR2C03US

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2593169A1	EP		2013-05-22	BECTON DICKINSON CO		
	2	2009131273A	JP		2009-06-18	CSL BEHRING GMBH		X
	3	2010062734A1	WO		2010-06-03	UNIV MARYLAND		☐
	4	2013082301A1	WO		2013-06-06	TELEFLEX MEDICAL INC		☐
	5	1378602A	GB		1974-12-27	BECTON DICKINSON CO		☐
	6	2019055487A1	WO		2019-03-21	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	7	2019232196A1	WO		2019-12-05	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	8	H08257018	JP		1996-10-08	NISSHO KK		☒
	9	1665986	EP		2006-06-07	BECTON DICKINSON CO		☐
	10	2011162772A1	WO		2011-12-29	CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC		☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	11	2993646	CA		2017-02-02	KURIN INC		☒
	12	3324845A1	EP		2018-05-30	KURIN INC		☐
	13	3562397A1	EP		2019-11-06	KURIN INC		☐
	14	3622890A1	EP		2020-03-18	KURIN INC		☐
	15	5789869B2	JP		2015-10-07	TOHO ENGINEERING KK,		☒
	16	5867238B2	JP		2016-02-24	FUJITSU LTD,		☒
	17	6643474B2	JP		2020-02-12	クリン インコーポレイテッド		☒
	18	6734490	JP		2020-08-05	クリン インコーポレイテッド		☒
	19	2001000424	JP		2001-01-09	NISSHO KK		☒
	20	2012016496A	JP		2012-01-26	TERUMO CORP		☒
	21	2016504075	JP		2016-02-12	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		☒

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	22	2019534792A	JP		2019-12-05	プライメタルズ・テクノロジーズ・オーストリア・ゲーエムベーハー		☒
	23	H09504726A	JP		1997-05-13	BAXTER INT		☒
	24	9605875A1	WO		1996-02-29	BAXTER INT		☐
	25	2013181352A1	WO		2013-12-05	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	26	2014058945	WO		2014-04-17	BULLINGTON GREGORY J		☐
	27	2017019552A1	WO		2017-02-02	KURIN INC		☐
	28	2018125929A1	WO		2018-07-05	KURIN INC		☐
	29	S5825146A	JP		1983-02-15	BECTON DICKINSON CO		☒
	30	S5867238A	JP		1983-04-21	BECTON DICKINSON CO		☒
	31	5643474	JP		2014-12-17	ヴェロシス，インク.		☒
	32	5825146B2	JP		2015-12-02	JVC KENWOOD CORP,		☒

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	33	2020000340A	JP		2020-01-09	TOSHO INC		☒
	34	2013240628	JP		2013-12-05	COVIDIEN LP		☒
	35	H02224742	JP		1990-09-06	SPACELABS INC		☒
	36	S5789869	JP		1982-06-04	BECTON DICKINSON CO		☒
	37	2005349196	JP		2005-12-22	BECTON DICKINSON CO		☒
	38	10243129	DE		2004-04-01	RITTER GMBH		☒
	39	7203008	DE		1972-05-10	IMMUNO AG FUER CHEM-MED PROD		☒
	40	10038026	DE		2001-02-22	ZIERDEN PETER		☒
	41	29913417	DE		2000-12-28	ZIERDEN PETER		☐
	42	10134913	DE		2003-02-20	HIBERNA AG		☒
	43	10134913C2	DE		2003-06-26	HIBERNA AG		☒

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	44	2541494	DE		1977-03-31	GUERRA LUIS A		☒
	45	2008101025	WO		2008-08-21	EDWARDS LIFESCIENCES CORP		☐
	46	0448795A2	EP		1991-10-02	BECTON DICKINSON CO		☐
	47	2007033319A1	WO		2007-03-22	EDWARDS LIFESCIENCES CORP		☐
	48	199216144	WO		1992-10-01	GOLDSPILL PTY. LTD.		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
	1	International Search Report and Written Opinion dated Nov. 5, 2015, for PCT application No. PCT/US2015/035870. 6 pages.	
	2	International Search Report and VVritten Opinion dated 16 July 2020 for PCT application no. PCT/US2020/026276. 9 pages.	
	3	Bullington, et al., Systems and Methods for Sample Collection with Reduced Hemolysis, Exhibit H in U.S. Appl. No. 62/517,681, dated Jun. 9, 2017, 131 pages.	
	4	Communication Under Rule 71(3) EPC dated Apr. 22, 2020 for EP application No. 17840467.9. 125 pages.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	5	European Patent Application No. EP19200766.4 extended European Search Report dated Dec. 2, 2019, 11 pages.	
	6	European Patent Office, Extended European Search Report for European Patent Application 20197213.0-1132, dated Dec. 9, 2020, 6 pages.	
	7	European Patent Office; Communication pursuant to Article 94(3) EPC; dated Oct. 31, 2018; 11 pages.	
	8	Examination Report No. 1 dated Apr. 29, 2020, for Australian Patent Application No. 2016297849. 3 pages.	
	9	International Search Report and Written Opinion dated Jun. 19, 2020, for PCT application No. PCTUS2020/023617. 12 pages.	
	10	European Patent Office, International Search Report and Written Opinion for PCT/US16/43709, dated Oct. 19, 2016, 14 pages.	
	11	International Search Report/Written Opinion for PCT/US17/68569 dated Apr. 25, 2018. 9 pages.	
	12	European Patent Office, International Search Report/Written Opinion for PCT/US17/068569 dated Apr. 25, 2018, 9 pages.	
	13	International Search Report and Written Opinion for PCT/US16/43709, Dated October 19,2016. 13 pages.	
	14	Retractable Techs., Inc. v. Becton Dickinson & Co., CA No. 2:07-CV-250, Claim Construction Order (E.D. Tex., Jan. 20, 2009). 20 pages.	
	15	Hillyer, Christopher D., et al. "Bacterial Contamination of Blodd Components: Risks, Strategies and Regulation," Hematology, 2003, pp. 575-589.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	16	De Korte, Dirk, et al. "Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections." Vox sanguinis 83.1 (2002): 13-16.	
	17	Brecher, Mark E., et al. "Bacterial contamination of blood components." Clinical microbiology reviews 18.1 (2005): 195-204.	
	18	Van Zundert, Adrien. "New closed IV catheter system." Acta Anæsthesiologica Belgica 56.3 (2005): 283-285.	
	19	Hall, Keri K., et al. "Updated review of blood culture contamination." Clinical microbiology reviews 19.4 (2006): 788-802.	
	20	Li, Yiwen, et al. "Direct labeling and visualization of blood vessels with lipophilic carbocyanine dye DiI." Nature protocols 3.11 (2008): 1703-1708.	
	21	Page, Catherine, et al. "Blood conservation devices in critical care: a narrative review." Annals of intensive care 3 (2013): 1-6.	
	22	Abbott Point of Care, Cartridge and Test Information, Art: 714258-01O; Rev. Date: 15-Aug-16, 1-6 pages.	
	23	Zimmon, David S. et al. "Effect of portal venous blood flow diversion on portal pressure." The Journal of Clinical Investigation 65.6 (1980): 1388-1397.	
	24	Patton, Richard G., et al. "Innovation for reducing blood culture contamination: initial specimen diversion technique." Journal of clinical microbiology 48.12 (2010): 4501-4503.	
	25	Tang, Menglin, et al. "Closed blood conservation device for reducing catheter-related infections in children after cardiac surgery." Critical Care Nurse 34.5 (2014): 53-60.	
	26	Ernst, Dennis J. et al. "NCCLS simplifies the order of draw: a brief history." MLO: medical laboratory observer 36.5 (2004): 1-5 pages.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	27	Gottlieb, T. "Hazards of bacterial contamination of blood products." Anaesthesia and intensive care 21.1 (1993): 20-23.	
	28	Norberg, Alonna, et al. "Contamination rates of blood cultures obtained by dedicated phlebotomy vs intravenous catheter." Jama 289.6 (2003): 726-729.	
	29	Quilici, Nathalie, et al. "Differential quantitative blood cultures in the diagnosis of catheter-related sepsis in intensive care units." Clinical infectious diseases 25.5 (1997): 1066-1070.	
	30	Napolitano, Marcello, et al. "Quality control of bacterial contamination of blood components: the feasibility of diversion system testing." Blood Transfus 2 (2004): 231-232.	
	31	De Korte, Dirk, et al. "Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands." Transfusion 46.3 (2006): 476-485.	
	32	Liumbruno, Giancarlo Maria, et al. "Reduction of the risk of bacterial contamination of blood components through diversion of the first part of the donation of blood and blood components." Blood Transfusion 7.2 (2009): 86.	
	33	NCCLS. Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition. H3-A5, Vol. 23, No. 32. Replaces H3-A4; Vol. 18, No. 7. 1-52 pages. http://demo.nextlab.ir/Organization/Documents/CLSI-Standards/CLSI-H3-A5.aspx	
	34	Challiner, A., et al. "Venous/arterial blood management protection system." Anaesthesia 47.2 (1992): 169-169.	
	35	Murphy, Michael F. "Better Blood Transfusion." Journal of the Intensive Care Society 4.3 (2003): 78-80.	
	36	Palavecino, Elizabeth L., et al. "Detecting bacterial contamination in platelet products." Clinical laboratory 52.9-10 (2006): 443-456.	
	37	Sheppard, Chelsea A., et al. "Bacterial contamination of platelets for transfusion: recent advances and issues." Laboratory Medicine 36.12 (2005): 767-770.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	38	Shulman, Gerald. "Quality of processed blood for autotransfusion." JOURNAL OF EXTRACORPOREAL TECHNOLOGY 32.1 (2000): 11-19.	
	39	Weinbaum, Fredric I., et al. "Doing it right the first time: quality improvement and the contaminant blood culture." Journal of Clinical Microbiology 35.3 (1997): 563-565.	
	40	Weinstein, Melvin P. "Blood culture contamination: persisting problems and partial progress." Journal of clinical microbiology 41.6 (2003): 2275-2278.	
	41	Weinstein, Melvin P., et al. "The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults." Clinical Infectious Diseases 24.4 (1997): 584-602.	
	42	Weinstein, Melvin P. "Current blood culture methods and systems: clinical concepts, technology, and interpretation of results." Clinical infectious diseases 23.1 (1996): 40-46.	
	43	Closed IV, BD Saf-T-Intima. "Catheter System, Becton, Dickinson and Company, Brochure." Retrieved from the Internet (August 23, 2019). 4 pages.	
	44	Perez, P., et al. "Multivariate analysis of determinants of bacterial contamination of whole-blood donations." Vox Sanguinis 82.2 (2002): 55-60.	
	45	McDonald, Carl P. "Interventions implemented to reduce the risk of transmission of bacteria by transfusion in the English National Blood Service." Transfusion Medicine and Hemotherapy 38.4 (2011): 255-258.	
	46	Lifesciences, Edwards. "Conservation. Safety. Simplicity. Edwards VAMP and VAMP Jr. Systems." (2002). 4 pages.	
	47	Sheppard, et al., Bacterial Contamination of Platelets for Transfusion: Recent Advances and Issues, LABMEDICINE, Vol. 36, No. 12, Dec. 2005 ("Sheppard 2005").	
	48	BD Diagnostics, "Venous Blood Collection, BD Vacutainer Passive Shielding Blood Collection Needle " literature (2005) 2 pages.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	49	Barnard, Dorothy R., et al. "Fibronectin (cold insoluble globulin) in the neonate," The Journal of Pediatrics, Vol. 102, Issue 3, March 1983, Pages 453-455.

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

EXAMINER SIGNATURE

Examiner Signature	/MAY A ABOUELELA/	Date Considered	07/05/2023

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

CERTIFICATION STATEMENT

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

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

OR

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

See attached certification statement.

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

☒ A certification statement is not submitted herewith.

SIGNATURE

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

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-05-16
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

Privacy Act Statement

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

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

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

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

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

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

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

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

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

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

Bibliographic Data

Application No: 17/538,990

Foreign Priority claimed: ○ Yes ◉ No

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

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

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

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
11/30/2021	600	3791	069366-0572201_KUR2C03US
RULE			

APPLICANTS

Kurin, Inc., San Diego, CA, UNITED STATES

INVENTORS

Bobby E. ROGERS, Park City, UT, UNITED STATES

Gino KANG, Irvine, CA, UNITED STATES

John DETLOFF, San Diego, CA, UNITED STATES

CONTINUING DATA

This application is a CON of 16208559 12/04/2018 PAT 11185266

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

15994559 is a CON of 15140448 04/27/2016 PAT 10010282

15140448 has PRO of 62318194 04/04/2016

15140448 has PRO of 62238636 10/07/2015

15140448 has PRO of 62196797 07/24/2015

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

12/09/2021

**** SMALL ENTITY ****

STATE OR COUNTRY

UNITED STATES

ADDRESS

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)

ATTENTION: DOCKETING DEPARTMENT

P.O BOX 10500

McLean, VA 22102
UNITED STATES

FILING FEE RECEIVED

$830

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

Wed Oct 04 05:12:22 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

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

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

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

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

Application	Document	Mailroom Date	Attorney Docket No.
17538990	CTNF	10/04/2023	069366-0572201_KUR2C03US
17538990	892	10/04/2023	069366-0572201_KUR2C03US
17538990	1449	10/04/2023	069366-0572201_KUR2C03US
17538990	1449	10/04/2023	069366-0572201_KUR2C03US

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

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

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

Sincerely,

The Patent Center Team

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

TERMINAL DISCLAIMER TO OBVIATE A PROVISIONAL DOUBLE PATENTING REJECTION OVER A PENDING "REFERENCE" APPLICATION

APPLICATION #	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET #
17538990	11/30/2021	Bobby ROGERS	069366-0572201_KUR2C03US

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

☑ Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action

☑ This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

Owner	Percent interest
Kurin, Inc.	100%
Total	100%

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending reference Application Number(s)

Application #	Filing Date

as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent

granted on the reference application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.
In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term of any patent granted on said reference application, "as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application," in the event that any such patent granted on the pending reference application: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s)

Patent #
9820682
10143412
11185266

as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.
In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later:
- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.



Terminal disclaimer fee under 37 CFR 1.20(d) included with Electronic Terminal Disclaimer request.

Applicant claims the following entity status:
Small

I hereby declare that all statements made herein of my own knowledge are true and that all statemnts made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I certify, in accordance with 37 CFR 1.4(d)(4) that I am: An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application

Signature	Name	Registration #
/Ben Hudson/	Benjamin Hudson	71474

---

* Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner). Form PTO/SB/96 may be used for making this certification. See MPEP 324.

UNITED STATES
PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

APPROVAL LETTER

APPLICATION #	FILING DATE	APPLICANT/PATENT UNDER REEXAMINATION
17/538,990	11/30/2021	Bobby ROGERS

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Electronic terminal disclaimer filed on 12/20/2023

☑ Approved

This patent is subject to a Terminal Disclaimer

Approved / Disapproved by: Electronic Terminal Disclaimer automatically approved

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/538,990	**12/20/2023 05:00:45 PM Z ET**	**069366-0572201_KUR2C03US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	3420	FILED BY	Trent Tercenio
PATENT CENTER #	63688999	FILING DATE	11/30/2021
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
petition-request.pdf	3	Terminal Disclaimer-Filed (Electronic)	49 KB
grantLetter.pdf	1	Terminal Disclaimer-Electronic-Approved	19 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
petition-request.pdf	8FE2C23FB46A46B431F87565754BC627034E96C2243B2E587A DE0E55356D62855D361D698680E77B5C5C89BBE5362A8FA24

	9C1BF05ABD049D51F0F6C62565B07
grantLetter.pdf	AA4113DD5B338D7812EDEDF9F837B082AF5B908E3BE6FA3A EF89E6086770F6E57C47F78DD567801943687B08A7827BB7C1 00C2CCFB1E29F92169A23B5495C40F

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/538,990	12/20/2023 05:00:45 PM Z ET	069366-0572201_KUR2C03US

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	3420	FILED BY	Trent Tercenio
PATENT CENTER #	63688999	AUTHORIZED BY	Benjamin Hudson
CUSTOMER #	27500	FILING DATE	11/30/2021
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Bobby E. ROGERS

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 033975	E2023BJH01218925	Benjamin Hudson

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2814	STATUTORY DISCLAIMER, INCLUDING TERMINAL DISCLAIMER	170.00	1	170.00
			TOTAL AMOUNT:	$170.00

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

INFORMATION DISCLOSURE STATEMENT BY APPLICANT		
	Application Number	17538990
	Filing Date	11/30/2021
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Client Number	069366
Page 1 of 1	**Matter Number**	0572201_KUR2C03US

GENERAL

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

Although the information submitted herewith may be "material" to the Examiner's consideration of the subject application, this submission is not intended to constitute an admission that such information is "prior art" as to the claimed invention, nor is it intended to constitute an admission that such information is "analogous prior art".

In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

TIMING

In accordance with 37 CFR 1.97(c), this Information Disclosure Statement is being filed after the period specified in 37 CFR 1.97(b) and before the mailing date of a Final Action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an Action that otherwise closes prosecution in the application.

CERTIFICATION STATEMENT

No certification statement is required. This Information Disclosure Statement is being filed in accordance with 37 CFR 1.97(c) and is accompanied by the fee set forth in 37 CFR 1.17(p).

FEE

This Information Disclosure Statement is being filed in accordance with 37 CFR 1.97(c), and is not accompanied by one of the certification statements of 37 CFR 1.97(e). Therefore, this Information Disclosure Statement is subject to the $104 (small entity) fee set forth in 37 CFR 1.17(p).

ADDITIONAL COMMENTS

SIGNATURE

Signature	/Benjamin F. Hudson/	**Date**	2023-12-20
Name	Benjamin F. Hudson	**Registration Number**	71,474

SyncIDS.com

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

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

U.S.PATENTS						Remove
Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4416291		1983-11-22	KAUFMAN JOSEPH	
	2	10299713		2019-05-28	PATTON RICHARD G	
	3	10265007		2019-04-23	BULLINGTON GREGORY	
	4	11395612		2022-07-26	BULLINGTON GREGORY J	
	5	10881343		2021-01-05	BULLINGTON GREGORY J	
	6	10596315		2020-03-24	BULLINGTON GREGORY J	
	7	11660030		2023-05-30	BULLINGTON GREGORY J	
	8	11259727		2022-03-01	BULLINGTON GREGORY J	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	9	11737693		2023-08-29	BULLINGTON GREGORY J	
	10	11439332		2022-09-13	BULLINGTON GREGORY J	
	11	11589843		2023-02-28	BULLINGTON GREGORY J	
	12	11612340		2023-03-28	BULLINGTON GREGORY J	
	13	11234626		2022-02-01	BULLINGTON GREGORY J	
	14	10624977		2020-04-21	BULLINGTON GREGORY J	
	15	11653863		2023-05-23	BULLINGTON GREGORY J	
	16	11419531		2022-08-23	BULLINGTON GREGORY J	
	17	11786155		2023-10-17	BULLINGTON GREGORY J	
	18	11789017		2023-10-17	BULLINGTON GREGORY J	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20220151525		2022-05-19	BULLINGTON GREGORY J	
	2	20220151527		2022-05-19	BULLINGTON GREGORY J	
	3	20200289039		2020-09-17	BULLINGTON GREGORY J	
	4	20210275068		2021-09-09	MIAZGA JAY M	
	5	20220304664		2022-09-29	HAMMER JEREMY	
	6	20160073937		2016-03-17	BURKHOLZ JONATHAN KARL	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

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

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

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

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

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

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

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

CERTIFICATION STATEMENT

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

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

OR

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

☐ See attached certification statement.

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

☒ A certification statement is not submitted herewith.

SIGNATURE

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

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-12-20
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

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

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

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

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

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

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

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

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

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

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

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Bobby E. Rogers, et al. **Confirmation No:** 3420

Application No.: 17/538,990 **Art Unit:** 3791

Filed: November 30, 2021 **Examiner:** May A. Abouelela

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

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO NON-FINAL OFFICE ACTION

Dear Examiner Abouelela:

This reply is responsive to the Non-Final Office Action mailed October 4, 2023, in the above-referenced matter (hereinafter "the Office Action"). Reconsideration and allowance of the application is requested in view of the following:

Listing of Claims beginning on page 2.

Remarks beginning on page 7.

LISTING OF CLAIMS

This listing of claims replaces all prior versions of claims in the application:

1. (Currently Amended) A blood sample control device comprising[[;]]:

an inlet configured to receive blood from [[the]] a patient;

an outlet;

a chamber connected with the inlet and having a vent that includes an air permeable blood barrier; ~~and~~

a sampling channel having a distal end connected with the outlet; and

a junction connected between the inlet, the chamber and the sampling channel, wherein the junction ~~being~~ is sized and configured such that a first portion of the blood conveyed from the patient flows into the chamber to displace air therein through the air permeable blood barrier, and such that a second portion of blood is allowed to bypass the chamber and the first portion of the blood at least temporarily contained therein to be directed into the sampling channel toward the outlet.

2. (Currently Amended) The blood ~~sequestration~~ sample control device in accordance with claim 1, wherein the air permeable blood barrier includes an air permeable material that at least partially seals upon contact with the blood.

3. (Currently Amended) The blood ~~sequestration~~ sample control device in accordance with claim 1, further comprising a housing that defines at least a part of each of the inlet, the outlet, the chamber, and the sampling channel.

4. (Currently Amended) The blood ~~sequestration~~ sample control device in accordance with claim 3, wherein the chamber includes a control channel defined in the housing.

5. (Currently Amended) The blood ~~sequestration~~ sample control device in accordance with claim 2, 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, the outlet, the chamber, and the sampling channel.

6. (Currently Amended) A bodily fluid control device connected along a fluid sampling pathway that includes a patient needle or catheter and a sample collection device, the ~~blood~~ bodily fluid control device comprising:

an inlet connected with the patient needle or catheter;

an outlet connected with the sample collection device;

a diversion chamber having a vent that includes an air permeable blood barrier; ~~and~~

a sampling channel having a distal end connected with the outlet; and

each of the diversion chamber and the sampling channel being connected with the inlet via a junction that is sized and configured such that a first portion of the bodily fluid flows into the ~~sequestration~~ diversion chamber to displace air therein through the air permeable blood barrier, and such that a second portion of the bodily fluid bypasses the diversion chamber and the first portion of the bodily fluid therein to be directed into the sampling channel toward the outlet and the sample collection device.

7. (Currently Amended) The bodily fluid control device in accordance with claim 6, further comprising a housing that at least partially houses and defines the inlet, the outlet, the ~~sequestration~~ diversion chamber, and the sampling channel.

8. (Currently Amended) The bodily fluid control device in accordance with claim 6, wherein the inlet is connected with the patient needle or catheter via a first portion of the ~~blood~~ sampling channel ~~pathway~~.

9. (Currently Amended) The bodily fluid control device in accordance with claim 6, wherein the outlet is connected with the sample collection device via a second portion of the ~~blood~~ sampling channel ~~pathway~~.

10. (Original) The bodily fluid control device in accordance with claim 6, wherein the air permeable blood barrier includes an air permeable material that at least partially seals upon contact with blood.

11. (Currently Amended) The bodily fluid control device in accordance with claim 7, wherein the diversion chamber includes [[an]] a curved channel defined in the housing.

12. (Currently Amended) The bodily fluid control device in accordance with claim 11, wherein the curved channel has a proximal end connected with the inlet, and a distal end having the vent comprising [[an]] the air permeable blood barrier.

13. (Currently Amended) A bodily fluid control device comprising;

an inlet;

a junction connected with the inlet;

an outlet;

a chamber connected with the inlet via the junction, the chamber having a vent that includes an air permeable bodily fluid barrier that at least partially seals upon contact with a first portion of ~~the~~ bodily fluid; ~~and~~

a housing that houses and defines the inlet, the outlet, and the chamber[[,]]; and

wherein the chamber and the junction being configured to direct the first portion of the bodily fluid from the inlet into the chamber toward the air permeable bodily fluid barrier and to displace air in the chamber, whereupon at least partially sealing of the air permeable bodily fluid barrier enables at least temporary containment of the first portion of the bodily fluid in the chamber, and enables a second portion of the bodily fluid from the inlet to bypass the chamber via the junction and be directed toward the outlet.

14. (Original) The bodily fluid control device in accordance with claim 13, wherein the air permeable bodily fluid barrier includes an air permeable material that seals upon contact with the bodily fluid.

15. (Original) The bodily fluid control device in accordance with claim 13, wherein the chamber includes a channel defined in the housing.

16. (Currently Amended) The bodily fluid control device in accordance with claim 13, further comprising a sampling pathway connected with the inlet via the junction, and wherein the sampling pathway conveys the second portion of the bodily fluid from the inlet to the outlet.

17. (Original) The bodily fluid control device in accordance with claim 13, 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, the outlet, and the chamber.

18. (Original) The bodily fluid control device in accordance with claim 13, further comprising a sampling channel having a proximal end connected with the junction and a distal end connected with the outlet.

19. (Currently Amended) The ~~blood~~ bodily fluid control device in accordance with claim 16, 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, the outlet, the chamber, and the sampling pathway.

20. (Currently Amended) The ~~blood~~ bodily fluid control device in accordance with claim 18, 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, the outlet, the chamber, and the sampling channel, and wherein proximate the junction the chamber has a cross-section that is larger than a cross-section of the sampling channel.

REMARKS

Claim Summary: Prior to this response, Claims 1-20 were pending. Claims 1-9, 12, 13, 16, 19, and 20 are amended. After entry of this response, Claims 1-20 will be pending. No new matter is added with this amendment. Reconsideration and allowance of the current application are requested in light of the following remarks.

Summary of Rejections: The Office objects to Claims 1, 2, 11, 12, 13, and 16. The Office interprets Claims 1, 6, and 13 under 35 U.S.C. § 112(f). The Office rejects Claims 1-20 on the grounds of statutory double patenting over claims 1-20 of U.S. Patent No. 11,311,219, claims 1-16 of U.S. Patent No. 9,820,682, claims 1-23 of U.S. Patent No. 10,143,412, and claims 1-26 of U.S. Patent Application No. 11,185,266; and claims 1-20 are provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 1-20 of U.S. pending Application No.17/730,118, and claims 1-18 and 20 of U.S. pending Application No. 17/094,692. The Office has rejected Claims 1-12 under 35 U.S.C. §112(b) as allegedly being indefinite.

No Change in Scope of Claims: The Office is respectfully reminded that the scope of at least one claim has remained unchanged in this Response. If new grounds of rejection for an unchanged claim are presented in a subsequent action, per MPEP§706.07(a), that subsequent action cannot properly be made final.

Request for Interview: The present response is believed to be sufficient to overcome the pending rejections. However, if this paper is not deemed sufficient to result in a notice of allowance, or if any remaining issues can be more efficiently handled by telephone, the Examiner is respectfully requested to contact the undersigned by either phone or e-mail to

schedule an interview at a mutually convenient time.

Claim objections

The applicant does not acquiesce to the basis of the many claim objections in the Office Action, however, amendments are being made to obviate these objections in order to further prosecution.

Claim 1 – corrections have been made to address the informalities.

Claim 2 – corrections have been made to address the informalities.

Claim 11 – has been amended to improve form, but the element "curved channel" is first introduced in this claim and so is presently stated as "a curved channel" rather than the requested "the curved channel."

Claim 12 – corrections have been made to address the informalities.

Claim 13 – corrections have been made to address the informalities.

However, Item 10 in the Office action requests the Claim 13 phrase "from the inlet to bypass the chamber" to be amended to read "to be directed from the inlet to bypass the chamber." Applicant respectfully suggests that this amendment is not needed because this portion is grammatically apparatus written. The claim's reciting of "to be directed" is not needed because this part already contains a verb "to bypass."

Claim 16 – appropriate corrections have been made to address the informalities.

Rejections for Non-Statutory Double Patenting

The Office rejects Claims 1-20 on the grounds of statutory double patenting over claims 1-20 of U.S. Patent No. 11,311,219, claims 1-16 of U.S. Patent No. 9,820,682, claims 1-23 of U.S. Patent No. 10,143,412, and claims 1-26 of U.S. Patent Application No. 11,185,266; and

claims 1-20 are provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 1-20 of U.S. pending Application No.17/730,118, and claims 1-18 and 20 of U.S. pending Application No. 17/094,692.

Applicant notes that the Office Action referred to U.S. 11,311,219, U.S. 9,820,682, U.S. 10,143,412, and U.S. 11,185,266 as patent applications, but these are issued patents.

Applicant also notes that the Office Action referred to the double patenting rejections over the '219, '682, '412, and '266 patents as being "statutory" double patenting rejections. However, because the claims are not identical (as also acknowledged in the Office Action) it is believed that the Office Action contained a typographical error and meant to say "non-statutory."

In order to further prosecution of the present application and obtain allowance of the pending claims, Applicant submits herewith a terminal disclaimer to overcome the rejections over parent patents U.S. 9,820,682, U.S. 10,143,412, and U.S. 11,185,266. In so doing, Applicant does not indicate agreement with the propriety of the rejections.

Please note that there are three cited patents/applications that Applicant believes do not require a terminal disclaimer. Similar double patenting rejections were withdrawn in sister application U.S. 18/113,710. The instant application has a filing date of April 27, 2016 based on the filing date of the oldest non-provisional parent application (now U.S. 10,010,282) and predates the effective filing date of U.S. 11,311,219 (December 27, 2016 for its U.S. provisional application 62/439,426). Thus, the instant application will expire prior to the '219 patent and therefore the double patenting rejection over the '219 patent is moot. This also applies to the '219's pending child application (U.S. 17/730,118), which also has a later filing date than the instant application. The double patenting rejection over U.S. pending Application No. 17/094,692 is similarly moot because the '692 application has a later filing date of February 10,

2017 and the instant application will similarly expire prior to the '692 application and therefore the double patenting rejection over the '692 application is also moot. As such, the instant response does not include a terminal disclaimer to overcome double-patenting rejections over the '219 patent and the '118 and '692 applications.

Claim interpretation under 35 U.S.C. §112(f)

The Office Action alleges that Claims 1, 6, and 13 should be interpreted under 35 U.S.C. §112(f) as allegedly reciting functional language without sufficient structure to perform the recited function. Applicant respectfully disagrees.

At the outset, Applicant notes that sister application U.S. 18/113,710 (now U.S. 11,832,944) was examined by the instant Examiner and the term "junction" was initially alleged to need interpretation under § 112(f). However, the interpretation was apparently not maintained in view of Applicant's rebuttal. Likewise, the term "junction" in the instant application should not be interpreted under § 112(f). For completeness of response, Applicant's prior arguments against the interpretation of the term "junction" are reproduced below from the sister application.

MPEP § 2181 (I) (A) states that a term denotes structure (and therefore should not be interpreted under § 112(f)) when the specification provides sufficient description informing one of skill in the art that it denotes structure:

> "To determine whether a word, term, or phrase coupled with a function denotes structure, examiners may check whether: (1) **the specification provides a description sufficient to inform one of ordinary skill in the art that the term denotes structure**...."

In this case, the present specification clearly indicates that the term "junction" is a term that denotes structure. See, e.g., Paragraph [0109]:

> "... junction 1607 may be substantially **Y-shaped, T-shaped, or U-shaped**."

When something is described as having a shape, it is a structure, not a function.

For at least these reasons, withdrawal of the pending interpretations under §112(f) is respectfully requested.

Rejections under 35 U.S.C. §112(b) (indefiniteness)

The Office Action rejects Claims 1, 6, 8, and 9 as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. The Office Action stated that certain limitations of those claims lacked antecedent basis. Appropriate corrections have been made with this response and withdrawal of the pending rejections under §112(b) is respectfully requested.

CONCLUSION

On the basis of the foregoing remarks and/or amendments, allowance of the pending claims is respectfully requested. It is believed that all the pending rejections have been addressed in this paper. However, failure to address a specific rejection, issue or comment, does not signify agreement with or concession of that rejection, issue or comment. In addition, because any arguments made above are not intended to be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper.

No additional fees are believed to be due, however the Commissioner is authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account 033975, Reference No. 069366-0572201_KUR2C03US. If there are any questions regarding this submission, the Examiner is encouraged to contact the undersigned at the telephone number

provided below.

Respectfully submitted,
PILLSBURY WINTHROP SHAW PITTMAN LLP

Date: December 20, 2023 By: /Ben Hudson/
Benjamin F. Hudson, Ph.D.
Reg. No. 71,474

PO BOX 10500
McLean, Virginia 22102
Telephone: (858) 509-4000
Customer No. 27500

4868-8868-2628.v1

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/538,990	**12/20/2023 05:27:32 PM Z ET**	**069366-0572201_KUR2C03US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	3420	FILED BY	Trent Tercenio
PATENT CENTER #	63688797	FILING DATE	11/30/2021
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0572201_KUR2C03US Response to Non-Final Office Action rcvd 04OCT2023-APP.TEXT.docx	12	Application body structured text document	42 KB
Warning: Text decorations have been removed. Bookmarks were found and have been removed. All artifacts (SmartArt, Drawings, Charts, etc) have been replaced with images.			
069366-0572201_KUR2C03US_Transmittal-Letter.pdf	1	Transmittal Letter	493 KB
069366-	6	Information Disclosure	1019 KB

0572201_KUR2C03US_PTO_IDS-Form.pdf	Statement (IDS) Form (SB08)

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-0572201_KUR2C03US Response to Non-Final Office Action rcvd 04OCT2023-APP.TEXT.docx	97BD56A174F3D52E48F567E8D90868EF676F7849A0CA8BF178DB6D8D75BA6C1A0869592D5F1ACDB4206FA682417B72C4FED5947C9D3D9F7918217C8C00FF5FEB
069366-0572201_KUR2C03US_Transmittal-Letter.pdf	2C923639C2912665220858 4D8EEDC1250E7343EA341B4F2C024E72360E792B2D851CE06198CBCC0C03B99DE60B2DB5B1D3C6D0C61F3044F7A5F808A7D51698B3
069366-0572201_KUR2C03US_PTO_IDS-Form.pdf	96191F7D76D6704837404FE40414A48137B063E7329333DDBD4BCD93275049C8FC47D49A1F2E4964B4F0DBD8F0A2CCFFA75CB94A66E8170A827EDEC812EF3E46

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/538,990	12/20/2023 05:27:32 PM Z ET	069366-0572201_KUR2C03US

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	3420	FILED BY	Trent Tercenio
PATENT CENTER #	63688797	AUTHORIZED BY	Benjamin Hudson
CUSTOMER #	27500	FILING DATE	11/30/2021
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Bobby E. ROGERS

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 033975	E2023BJH28036016	Trent Tercenio

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2806	SUBMISSION OF AN INFORMATION DISCLOSURE STATEMENT	104.00	1	104.00
			TOTAL AMOUNT:	$104.00

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 17/538,990	Filing Date 11/30/2021	☐ To be Mailed

ENTITY: ☐ LARGE ☑ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $50 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $240 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT	12/20/2023	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 20	Minus	** 20	= 0		x $40 =	0
	Independent (37 CFR 1.16(h))	* 3	Minus	*** 3	= 0		x $192 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

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

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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

NOTICE OF ALLOWANCE AND FEE(S) DUE

27500 7590 01/17/2024

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

EXAMINER	
ABOUELELA, MAY A	
ART UNIT	PAPER NUMBER
3791	

DATE MAILED: 01/17/2024

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

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

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	04/17/2024

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27500 7590 01/17/2024
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

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

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	04/17/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
ABOUELELA, MAY A	3791	600-573000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via the USPTO patent electronic filing system ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

❑ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

❑ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

27500 7590 01/17/2024

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

EXAMINER	
ABOUELELA, MAY A	

ART UNIT	PAPER NUMBER
3791	

DATE MAILED: 01/17/2024

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/ owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).
https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to:

1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;
2) a federal, state, local, or international agency, in response to its request;
3) a contractor of the USPTO having need for the information in order to perform a contract;
4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;
5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c));
9) the Office of Personnel Management (OPM) for personnel research purposes; and
10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Notice of Allowability	Application No. 17/538,990	Applicant(s) ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	AIA (FITF) Status Yes

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

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 12/20/2023.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

3. ☑ The allowed claim(s) is/are 1-20 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

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

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☑ Interview Summary (PTO-413), Paper No./Mail Date. 10/08/2024.
5. ☑ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/MAY A ABOUELELA/
Primary Examiner, Art Unit 3791

Notice of Pre-AIA or AIA Status

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

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 12/20/2023. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Terminal Disclaimer

3. The terminal disclaimer filed on 12/20/2023 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S Patent Applications No. 9820682, 10143412 and 11185266 has been reviewed and is accepted. The terminal disclaimer has been recorded.

EXAMINER'S AMENDMENT

4. Authorization for this examiner's amendment was given in an interview with BEN HUDSON on 01/08/2024.

Claim 5 should be amended as follow:

5. (Currently Amended) The blood sample control device in accordance with claim **3** ~~2~~, 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, the outlet, the chamber, and the sampling channel.

Claim 10 should be amended as follow:

10. (**Currently Amended**) The bodily fluid control device in accordance with claim 6, wherein the air permeable blood barrier includes an air permeable material that at least partially seals upon contact with **the bodily fluid** ~~blood~~.

Claim 13 should be amended as follow:

13. (Currently Amended) A bodily fluid control device comprising;

an inlet;

a junction connected with the inlet;

an outlet;

a chamber connected with the inlet via the junction, the chamber having a vent that includes an air permeable bodily fluid barrier that at least partially seals upon contact with a first portion of bodily fluid;

a housing that houses and defines the inlet, the outlet, and the chamber; and

wherein the chamber and the junction **are** ~~being~~ configured to direct the first portion of the bodily fluid from the inlet into the chamber toward the air permeable bodily fluid barrier and to displace air in the chamber, whereupon at least partially sealing of the air permeable bodily fluid barrier enables at least temporary containment of the first portion of the bodily fluid in the chamber, and enables a second portion of the bodily fluid from the inlet to bypass the chamber via the junction and be directed toward the outlet.

Allowable Subject Matter

5. Claims 1-20 are allowed.

6. The following is an examiner's statement of reasons for allowance: the most pertinent prior art Eldridge et al (U.S 4,207,870) teaches a blood sample device for sampling blood conveyed from a patient, the blood device comprising; an inlet port configured to receive the blood conveyed from the patient; an outlet port; a chamber; and a sampling channel having a distal end connected with the outlet port; a junction connected between the inlet port, the chamber and the sampling channel, the junction being sized and configured such that a first portion of blood conveyed from the patient flows into the chamber to displace air therein through the air permeable blood barrier and to be sequestered in the chamber.

The prior art does not teach, disclose and/or fairly suggest the chamber having a vent that includes an air permeable blood barrier, and wherein the junction is configured to allow a second portion of blood to bypass the chamber and the first portion of blood sequestered therein to be directed into the sampling channel toward the outlet port.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

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

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

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JACQUELINE CHENG can be reached on 5712725596. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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

/MAY A ABOUELELA/
Primary Examiner, Art Unit 3791

Examiner-Initiated Interview Summary	**Application No.** 17/538,990	**Applicant(s)** ROGERS et al.		
	Examiner MAY A ABOUELELA	**Art Unit** 3791	**AIA (First Inventor to File) Status** Yes	**Page** 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	**Title**	**Type**
MAY A ABOUELELA	Primary Examiner	Telephonic
BEN HUDSON	Attorney of Record	

Date of Interview: 08 January 2024

Issues Discussed:

35 U.S.C. 112

Applicant and Examiner discussed the claims set mailed on 12/20/2023. Applicant and Examiner discussed the claim language with respect to the applied prior art and the disclosure. Applicant and Examiner discussed proposed claim amendments represented by the Examiner to overcome 112 rejection for claims 5, 10 and 13. The Applicant has authorized the Examiner to amend the claims.

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	

Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04
Please further see:
MPEP 713.04
Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b)
37 CFR § 1.2 Business to be transacted in writing

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/538,990	ROGERS et al.
	Examiner	**Art Unit**
	MAY A ABOUELELA	3791

CPC						
Symbol					**Type**	**Version**
A61B	/	5	/	150992	F	2013-01-01
A61M	/	39	/	04	I	2013-01-01
A61B	/	5	/	150221	I	2013-01-01
A61B	/	5	/	15003	I	2013-01-01
A61B	/	5	/	150213	I	2013-01-01
A61B	/	5	/	150389	I	2013-01-01
A61B	/	5	/	150473	I	2013-01-01
A61B	/	5	/	150572	I	2013-01-01
A61B	/	5	/	154	I	2013-01-01
A61B	/	5	/	153	I	2013-01-01
A61M	/	39	/	0693	I	2013-01-01
A61M	/	2039	/	0202	A	2013-01-01
A61M	/	2039	/	068	A	2013-01-01
A61M	/	2039	/	0633	A	2013-01-01

CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
	/		/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	20	
/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	08 January 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	15C

U.S. Patent and Trademark Office — Part of Paper No.: 20240108

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/538,990	ROGERS et al.
	Examiner	**Art Unit**
	MAY A ABOUELELA	3791

INTERNATIONAL CLASSIFICATION					
CLAIMED					
A61B	/	5	/	00	

NON-CLAIMED					
	/		/		

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					

NONE (Assistant Examiner) (Date)	**Total Claims Allowed:** 20	
/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791 (Primary Examiner) 08 January 2024 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 15C

U.S. Patent and Trademark Office Part of Paper No.: 20240108

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/538,990	ROGERS et al.
	Examiner	**Art Unit**
	MAY A ABOUELELA	3791

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

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		10		19										
	2		11		20										
	3		12												
	4		13												
	5		14												
	6		15												
	7		16												
	8		17												
	9		18												

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 20	
/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791 (Primary Examiner)	08 January 2024 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 15C

U.S. Patent and Trademark Office Part of Paper No.: 20240108

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/538,990	ROGERS et al.
	Examiner	**Art Unit**
	MAY A ABOUELELA	3791

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

CLAIMS

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

CLAIM		DATE								
Final	Original	07/05/2023	01/08/2024							
	1	✓	=							
	2	✓	=							
	3	✓	=							
	4	✓	=							
	5	✓	=							
	6	✓	=							
	7	✓	=							
	8	✓	=							
	9	✓	=							
	10	✓	=							
	11	✓	=							
	12	✓	=							
	13	✓	=							
	14	✓	=							
	15	✓	=							
	16	✓	=							
	17	✓	=							
	18	✓	=							
	19	✓	=							
	20	✓	=							

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/538,990	ROGERS et al.
	Examiner	Art Unit
	MAY A ABOUELELA	3791

CPC - Searched*		
Symbol	**Date**	**Examiner**
A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068	07/05/2023	MA
updated as above	01/08/2024	MA

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

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

Search Notes		
Search Notes	**Date**	**Examiner**
text search, inventor name search, class/subclass search	07/05/2023	MA
updated as above	01/08/2024	MA

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
as above		01/08/2024	MA

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	

Bibliographic Data

Application No: 17/538,990

Foreign Priority claimed: ○ Yes ◉ No

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

Verified and Acknowledged: /MAY A ABOUELELA/ (Examiner's Signature) | M.A.A (Initials)

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

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
11/30/2021	600	3791	069366-0572201_KUR2C03US
RULE			

APPLICANTS

Kurin, Inc., San Diego, CA, UNITED STATES

INVENTORS

Bobby E. ROGERS, Park City, UT, UNITED STATES

Gino KANG, Irvine, CA, UNITED STATES

John DETLOFF, San Diego, CA, UNITED STATES

CONTINUING DATA

This application is a CON of 16208559 12/04/2018 PAT 11185266

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

15994559 is a CON of 15140448 04/27/2016 PAT 10010282

15140448 has PRO of 62318194 04/04/2016

15140448 has PRO of 62238636 10/07/2015

15140448 has PRO of 62196797 07/24/2015

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

12/09/2021

**** SMALL ENTITY ****

STATE OR COUNTRY

UNITED STATES

ADDRESS

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)

ATTENTION: DOCKETING DEPARTMENT

P.O BOX 10500

McLean, VA 22102
UNITED STATES

FILING FEE RECEIVED

$830

PE2E SEARCH - Search History (Prior Art)

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

		"6387086" | "6403381" | "6692479" | "6746420" | "6913580" | "7044941" | "7087047").PN. OR ("8197420").URPN.					
L11	2	L10 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:44 PM
L12	77	("0453322" | "0577682" | "0729011" | "1074965" | "1110189" | "1450016" | "1521890" | "2218899" | "2688325" | "2895773" | "3176595" | "3214069" | "3236268" | "3263874" | "3486503" | "3577980" | "3754644" | "3794221" | "3834387" | "3855997" | "3937211" | "3958570").PN. OR ("4057050").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:47 PM
L13	852	L4 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L14	46	L10 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L15	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:29 PM
L16	1	("20130317391").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:42 PM
L17	1254	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:43 PM
L18	1070	L17 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 06:43 PM
L19	265030	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:09 PM
L20	5653	L19 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L21	207	L20 and (seal near4 air)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L22	23	"2004087258"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 08:59 PM
L23	1	("20050004524").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 08:23 PM

L24	1	("20030105414").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 08:24 PM
L25	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 08:26 PM
L26	13	("20040073171"|"20040147855"|"20050240161"|"20130317391"|"20160174888"|"4057050"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8864684"|"9138572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 08:39 PM
L27	1	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 09:43 PM
L28	0	("4and(bloodnear4air)").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 10:01 PM
L29	3	L26 and (blood near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:01 PM
L30	6	L26 and vent$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:02 PM
L31	5	("2013/0317391").URPN.	(USPAT)	OR	OFF	OFF	2017/04/11 10:06 PM
L32	48	("2005/0004524").URPN.	(USPAT)	OR	OFF	OFF	2017/04/11 10:17 PM
L33	1	("20120170037").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/12 04:11 PM
L34	1	("6139540").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:52 PM
L35	1	("20040116878").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:54 PM
L36	1	("20100152752").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:16 PM
L37	1	("6395003").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:20 PM
L38	5	("2013/0317391").URPN.	(USPAT)	OR	OFF	OFF	2017/04/13 01:43 PM
L39	1	("4444203").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:44 PM
L40	1	("20020004647").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:48 PM
L41	1	("3817240").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L42	1	("3874367").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L43	1	("3886930").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:58 PM
L44	1	("4106497").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM
L45	1	("4154229").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM

L46	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:00 PM
L47	292	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2017/04/13 02:01 PM
L48	1	("4412548").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:04 PM
L49	1	("5222502").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:11 PM
L50	1	("5520193").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:15 PM
L51	1	("20100057004").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:16 PM
L52	1	("20070088279").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:29 PM
L53	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/04/13 03:29 PM
L54	13	L53 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 03:52 PM
L55	1255	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 04:23 PM
L56	4	L55 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:23 PM
L57	272301	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L58	5898	L57 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L59	114	L58 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:29 PM
L60	2	("2007/0088279").URPN.	(USPAT)	OR	OFF	OFF	2017/04/13 05:58 PM
L61	1	("6358217").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/21 02:02 PM
L62	6	("2002/0004647").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 12:48 PM
L63	2	("14493796").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:21 PM
L64	2	("14494208").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:23 PM
L65	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/27 01:28 PM
L66	1	("20080145933").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:51 PM
L67	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 01:55 PM

L68	1	("20040054333").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:59 PM
L69	1	("20120109034").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:37 PM
L70	1	("20100228206").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:39 PM
L71	3	("2010/0228206").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 02:47 PM
L72	66	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:41 PM
L73	4	L72 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:42 PM
L74	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:58 PM
L75	845	L74 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:58 PM
L76	9	L75 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L77	86	("2007/0083162").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L78	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:59 PM
L79	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 02:04 PM
L80	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 02:20 PM
L81	1071	L80 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:20 PM
L82	78	L81 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:21 PM
L83	282596	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L84	6183	L83 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L85	387	L84 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:01 PM
L86	362	L85 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:02 PM
L87	12	("2005/0010189").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 04:03 PM
L88	1363	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:04 PM
L89	74	L88 and (blood near4 (sequest$5 or	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:05 PM

		sampl$4))					
L90	21	("3965910" | "3996923" | "4131127" | "4301811" | "4450854" | "4506691" | "4819684" | "5147333" | "5393035" | "5636975").PN. OR ("6569117").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2017/09/28 04:09 PM
L91	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:12 PM
L92	18	L91 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:12 PM
L93	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/28 04:13 PM
L95	67	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:23 PM
L96	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:25 PM
L97	4	L96 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:25 PM
L98	3	L97 and (blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:26 PM
L99	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:50 PM
L100	13	L99 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:50 PM
L101	255	("1779451" | "2004050" | "2700385" | "2836942" | "2854976" | "2953243" | "3021942" | "3073307" | "3074542" | "3255873" | "3294231" | "3323523" | "3329146" | "3333682" | "3367488" | "3382865" | "3485239" | "3537452" | "3585984" | "3610240" | "3658061" | "3664879" | "3817240" | "3828775" | "3859998" | "3874367" | "3886930" | "3890971" | "3904033" | "3934722" | "3968876" | "4106497" | "4108175" | "4113090" | "4139009" | "4154229" | "4166450" | "4175008" | "4193400" | "4207870" | "4269186" | "4300678" | "4312362" | "4317445" | "4340068" | "4375849" | "4398544" | "4409990" | "4412548" | "4416290" | "4416291" | "4418703"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/01/09 04:51 PM

		| "4430082" | "4436098" | "4444203" | "4592744" | "4634428" | "4643722" | "4659330" | "4664249" | "4664654" | "4671408" | "4679571" | "4681567" | "4695274" | "4702738" | "4723943" | "4728320" | "4728321" | "4731059" | "4735311" | "4735618" | "4737144" | "4738663" | "4743233" | "4746008" | "4747836" | "4747837" | "4772272" | "4778453" | "4781697" | "4782841" | "4788986" | "4790828" | "4793484" | "4795432" | "4795443" | "4801295" | "4804372" | "4813426" | "4816022" | "4816024" | "4819659" | "4820277" | "4826490" | "4826491" | "4838871" | "4842587" | "4844089" | "4846796" | "4850968" | "4850976" | "4850977" | "4850978" | "4850994" | "4850996" | "4858607" | "4863434" | "4863435" | "4863436" | "4865592" | "4867746" | "4872552" | "4874383" | "4874384" | "4883469" | "4886072" | "4886503" | "4888001" | "4892107" | "4892521" | "4894052" | "4900309" | "4909791" | "4909792").PN. OR ("4921096" | "4927018" | "4944397" | "4966591" | "4971068" | "4976699" | "4982842" | "5011475" | "5011479" | "5030207" | "5032116" | "5033476" | "5055102" | "5069225" | "5078693" | "5078698" | "5092845" | "5112327" | "5116325" | "5120319" | "5122121" | "5135509" | "5137518" | "5139489" | "5151089" | "5154285" | "5181523" | "5188611" | "5197954" | "5201794" | "5207653" | "5217025" | "5222502" | "5232454" | "5232455" | "5242411" | "5242417" | "5277311" | "5290246" | "5295969" | "5303713" | "5306259"					

		| "5312369" | "5401251" | "5405332" | "5423765" | "5450856" | "5462534" | "5485854" | "5486163" | "5490841" | "5496281" | "5509907" | "5520193" | "5533984" | "5542932" | "5584816" | "5599313" | "5599318" | "5603699" | "5632732" | "5643219" | "5662617" | "5665075" | "5669889" | "5693022" | "5697914" | "5702369" | "5733265" | "5755701" | "5807351" | "5830190" | "5836920" | "5885249" | "5893844" | "5913846" | "5984895" | "5993426" | "6059737" | "6077244" | "6077253" | "6080137" | "6096006" | "6110160" | "6120482" | "6156010" | "6190370" | "6261263" | "6511439" | "6533760" | "6964658" | "7160267" | "RE31086").PN. OR ("7615033").URPN.					
L102	215	L101 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:51 PM
L103	1347	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:11 PM
L104	17	L103 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L105	19	("2009/0312711").URPN.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L106	11	("2007/0106220").URPN.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L107	288967	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L108	6321	L107 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L109	121	L108 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:17 PM
L110	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:31 PM
L111	6	L110 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:31 PM
L113	71	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:31 PM
L114	0	("15140443").PN.	(US-PGPUB; USPAT;	OR	OFF	OFF	2018/07/24

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

		"20040147855" | "20050004524" | "20050240161" | "20050245885" | "20050281713" | "20060287639" | "20080108954" | "20080145933" | "2707953" | "3013557" | "3098016" | "3382865" | "3405706" | "3494351" | "3577980" | "3648684" | "3848579" | "3937211" | "4057050" | "4133863" | "4166450" | "4340067" | "4370987" | "4444203" | "4459997" | "4509534" | "4657160" | "4676256" | "4865583" | "4890627" | "4988339" | "5009847" | "5097842" | "5108927" | "5122129" | "5269317" | "5330464" | "5360011" | "5429610" | "5450856" | "5507299" | "5577513" | "5762633" | "5865812" | "5882318" | "5922551" | "6016712" | "6057105" | "6159164" | "6210909" | "6364890" | "6387086" | "6403381" | "6626884" | "6692479" | "6746420" | "6913580" | "7044941" | "7087047" | "7335188" | "7744573" | "8197420" | "8231546" | "8337418").PN. OR ("8535241").URPN.					
L134	307	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:47 PM
L135	23	("4166450").PN. OR ("4412548").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L136	307	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L137	4	("2007/0088279").URPN.	(USPAT)	OR	ON	ON	2018/07/24 02:48 PM
L138	1	(14/990763).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 02:58 PM
L139	9	(blood and sequest$5 and junction and first	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 03:07 PM

		and portion and sampl$4).clm.					
L140	1	(15/287421).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/25 09:39 PM
L141	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/26 11:56 AM
L142	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:24 PM
L143	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:25 PM
L144	34	("20020004647"|"20030105414"|"20040054333"|"20040073171"|"20040147855"|"20050004524"|"20050240161"|"20070088279"|"20080145933"|"20100057004"|"20130317391"|"20160174888"|"3817240"|"3874367"|"3886930"|"4057050"|"4106497"|"4154229"|"4207870"|"4412548"|"5222502"|"5520193"|"5749857"|"6569117"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8864684"|"9022951"|"9060724"|"9138572"|"9204864").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 05:53 PM
L145	272	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("STROUP") near3 ("David")) OR (("COCHRAN") near3 ("Jonas")) OR (("DEPTALA") near3 ("Arthur")) OR (("DETLOFF") near3 ("John")) OR (("POGUE") near3 ("Lonnie")) OR (("MACOWSKI") near3 ("Brian")) OR (("GARRETT") near3 ("Chad"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/07 05:57 PM
L146	9	L145 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 05:58 PM
L147	34	("20020004647"|"20030105414"|"20040054333"|"20040073171"|"20040147855"|"20050004524"|"20050240161"|"20070088279"|"200801459	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 06:26 PM

		33"|"20100057004"|"20130317391"|"20160174888"|"3817240"|"3874367"|"3886930"|"4057050"|"4106497"|"4154229"|"4207870"|"4412548"|"5222502"|"5520193"|"5749857"|"6569117"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8864684"|"9022951"|"9060724"|"9138572"|"9204864").PN.					
L148	5	L147 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 06:29 PM
L149	6	("2010/0057004").URPN.	(USPAT)	OR	ON	ON	2019/11/07 06:40 PM
L150	0	L149 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:20 PM
L151	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:21 PM
L152	4	L151 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L153	1766	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:21 PM
L154	13	L153 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L155	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:22 PM
L156	48	L155 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:22 PM
L157	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L158	17	L157 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:43 PM
L159	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L160	6	L159 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L161	333030	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L162	6981	L161 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L163	139	L162 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L164	117	L163 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:45 PM
L165	1	L146 and (enclos$3	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07

		near4 mechanism)					07:51 PM
L166	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/08 04:57 PM
L167	1	(15/139716).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/11 12:09 PM
L168	1	(15/520430).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 11:02 AM
L169	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:11 PM
L170	1	("20120253321").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:13 PM
L171	1	(15/861959).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:14 PM
L172	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 02:17 PM
L173	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:14 PM
L174	1	("20080167577").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:19 PM
L175	4	("2008/0167577").URPN.	(USPAT)	OR	ON	ON	2019/12/09 03:30 PM
L176	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:31 PM
L177	39	(US-20040073171-$ or US-20160174888-$ or US-20050240161-$ or US-20040147855-$ or US-20130317391-$ or US-20050004524-$ or US-20030105414-$ or US-20020004647-$ or US-20100057004-$ or US-20070088279-$ or US-20080145933-$ or US-20040054333-$ or US-20100010372-$ or US-20080319346-$ or US-20080167577-$).did. or (US-9138572-$ or US-8568371-$ or US-8540663-$ or US-8523826-$ or US-8197420-$ or US-4057050-$ or US-8864684-$ or US-8535241-$ or US-5749857-$ or US-9060724-$ or US-9204864-$ or US-3817240-$ or US-3874367-$ or US-3886930-$ or US-4106497-$ or US-4154229-$ or US-	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:37 PM

		4207870-$ or US-4412548-$ or US-5222502-$ or US-5520193-$ or US-9022951-$ or US-6569117-$ or US-3741197-$ or US-8603009-$).did.					
L178	8	("20040054333"|"8197420"|"9855001"|"9861306"|"10045724"|"10028687"|"8337418"|"10028689").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:42 PM
L179	100	("20020002349" | "20020183651" | "20030055381" | "20040010228" | "20040054333" | "20040147855" | "20050004524" | "20050240161" | "20050245885" | "20050281713" | "20060287639" | "2707953" | "3013557" | "3098016" | "3382865" | "3405706" | "3494351" | "3577980" | "3648684" | "3848579" | "3937211" | "4057050" | "4133863" | "4166450" | "4340067" | "4370987" | "4444203" | "4459997" | "4509534" | "4676256" | "4865583" | "4890627" | "4988339" | "5009847" | "5097842" | "5108927" | "5122129" | "5269317" | "5360011" | "5429610" | "5450856" | "5507299" | "5577513" | "5762633" | "5882318" | "5922551" | "6016712" | "6057105" | "6159164" | "6210909" | "6364890" | "6387086" | "6403381" | "6692479" | "6746420" | "6913580" | "7044941" | "7087047").PN. OR ("8197420").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 03:43 PM
L180	70	L179 and (blood near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 03:43 PM
L181	43	L180 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 03:44 PM
L182	270	((("BULLINGTON")	(US-PGPUB; USPAT;	OR	ON	ON	2019/12/09

		near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR (("GAW") near3 ("Shan"))).INV.	USOCR; EPO; JPO; DERWENT)				04:13 PM
L183	335813	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L184	7259	L183 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L185	325	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 04:33 PM
L186	594	L184 and (flash$6 and seal$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L187	476	L186 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L188	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:14 PM
L189	1123	L188 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L190	1013	L189 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L191	10	L190 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:16 PM
L192	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:23 PM
L193	1143	L192 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L194	1038	L193 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L195	3	L194 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L196	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:24 PM
L197	618	L196 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L198	557	L197 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L199	1	(15/854273).APP.	(US-PGPUB; USPAT;	OR	OFF	OFF	2019/12/09

			USOCR)				05:25 PM
L200	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:31 PM
L201	219	L200 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:33 PM
L202	199	L201 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:33 PM
L203	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:36 PM
L204	44	L203 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:37 PM
L205	1	(15/508871).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/10 11:58 AM
L206	342199	(blood near4 (sequest$5 or sampl$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/03/16 12:53 PM
L207	4239	L206 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:53 PM
L208	146	L207 and ((vent$4 near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:54 PM
L209	101	L208 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:55 PM
L210	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:38 PM
L211	1123	L210 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:38 PM
L212	1013	L211 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L213	22	L212 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L214	108	("20020193748" | "20030093009" | "20030105414" | "20030220614" | "20030229315" | "20040059302" | "20040092872" | "20040193120" | "20050004524" | "20050065482" | "20050124944" | "20050187493" | "20050245868" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 01:46 PM

		"20050245869" | "20050245870" | "20050245879" | "20050245885" | "20060036219" | "20060224122" | "20070106220" | "20070106224" | "20070167914" | "20080086085" | "20080177202" | "20080319345" | "20080319346" | "20090204026" | "20100262038" | "4106497" | "4207870" | "4305406" | "4572210" | "4573976" | "4641663" | "4795443" | "4840619" | "4894055" | "4900307" | "4994046" | "5015241" | "5195985" | "5215534" | "5222502" | "5242417" | "5246428" | "5256153" | "5295970" | "5303713" | "5312372" | "5336199" | "5348544" | "5356392" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5599313" | "5662617" | "5665075" | "5672161" | "5676658" | "5702369" | "5704920" | "5733265" | "5755522" | "5957892" | "5984899" | "6149629" | "6224576" | "6254575" | "6261263" | "6298541" | "6344032" | "6436086" | "6440104" | "6524277" | "6533760" | "6592556" | "6623456" | "6635032" | "6648855" | "6695819" | "6699217" | "6712792" | "6780169" | "6837877" | "6869415" | "6984223" | "7001363" | "7128726" | "7147624" | "7160267" | "7163526" | "7223258" | "7226432" | "7396343" | "7428773" | "7537581" | "7766879" | "D422700" | "D442280" | "D604836" | "D604837" | "D604838" | "D604839" | "D605287").PN. OR ("8603009").URPN.					

L215	26	L214 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:47 PM
L216	27	("2008/0319346").URPN.	(USPAT)	OR	ON	ON	2020/03/16 01:47 PM
L217	23	("2003/0105414").URPN.	(USPAT)	OR	ON	ON	2020/03/16 01:48 PM
L218	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:52 PM
L219	1143	L218 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L220	25	L219 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L221	353695	((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:54 PM
L222	3643	L221 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L223	1926	L222 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L224	785	L223 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:56 PM
L225	7046	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 02:32 PM
L226	14	L225 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:35 PM
L227	1352	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:36 PM
L228	135	L227 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L229	19	L228 and (((vent$4 or open$5 or hole or aperture) near4 air) and flash$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L230	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:47 PM
L231	3	L230 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:47 PM
L232	19	("2008/0145933").URPN.	(USPAT)	OR	ON	ON	2020/03/16 02:48 PM
L233	795	(600/576).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16

							02:58 PM
L234	71	L233 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:58 PM
L235	57	L234 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:59 PM
L236	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 03:12 PM
L237	11	L236 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:12 PM
L238	45	("20040054333"|"20050240161"|"4412548"|"5749857"|"8197420"|"9855001"|"9861306"|"20020004647"|"20100057004"|"3741197"|"20040073171"|"3874367"|"4057050"|"4106497"|"8197420"|"8535241"|"8540663"|"8603009"|"8864684"|"10045724"|"3817240"|"10028687"|"20030105414"|"5222502"|"5520193"|"6569117"|"8568371"|"20040147855"|"20070088279"|"20080145933"|"20100010372"|"3886930"|"8523826"|"9060724"|"9204864"|"8337418"|"20050004524"|"20080167577"|"20080319346"|"20130317391"|"4154229"|"9022951"|"10028689"|"20160174888"|"4207870"|"9138572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:13 PM
L239	6	("2008/0167577").URPN.	(USPAT)	OR	ON	ON	2020/03/16 03:13 PM
L240	118	("3500828" | "3670729" | "3714945" | "3977400" | "3994293" | "3995619" | "4106491" | "4200096" | "4468224" | "4531987" | "4549554" | "4735215" | "4828548" | "4874373" | "4893635" | "4894052" | "4907599" | "4944308" | "4994042" | "5129884" | "5400798").PN. OR ("5749857").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 03:15 PM
L241	6	("2008/0167577").URPN.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 03:15 PM
L242	274	((("BULLINGTON") near3 ("Gregory")) OR	(US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	ON	2020/03/16 03:25 PM

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

L262	1	("3648684").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L263	1	("4056101").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L264	329	(600/577).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/06/10 06:39 PM
L265	11	L264 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:39 PM
L266	29	("2008/0319346").URPN.	(USPAT)	OR	ON	ON	2020/06/10 06:40 PM
L267	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:40 PM
L268	72	L267 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:40 PM
L269	1767	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:44 PM
L270	31	L269 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:45 PM
L271	77	("4676249" | "4787891" | "4850960" | "4874382" | "4886067" | "4886500" | "4900307" | "4904242" | "4917102" | "4950252" | "4955862" | "5046508" | "5116353" | "5125718" | "5129884" | "5163911" | "5217435" | "5290244" | "5295974" | "5314503" | "5318585" | "5330432" | "5360410" | "5366441" | "5376075" | "5395337" | "5531692" | "5695475" | "5695479" | "5702367" | "5735813" | "5749857" | "5788654" | "5800395" | "5846226" | "5871470" | "5882342" | "5919172" | "5935108" | "5935113" | "5989220" | "6050976" | "6077244" | "6099504" | "6126641" | "6162195").PN. OR ("6398743").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/06/10 06:46 PM
L272	18	L271 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:46 PM
L273	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:48 PM
L274	7050	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:49 PM

L275	14	L274 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:49 PM
L276	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:51 PM
L277	7	L276 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:51 PM
L278	1368	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:52 PM
L279	135	L278 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:52 PM
L280	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 07:08 PM
L281	3	L280 and ((blood or fluid$4) near4 (sequest$5 or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 07:08 PM
L282	20	("2008/0145933").URPN.	(USPAT)	OR	ON	ON	2020/06/10 07:08 PM
L286	1	("10045704").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 08:56 PM
L287	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:16 PM
L288	1	("10010282").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:17 PM
L289	100	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/01 09:17 PM
L290	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:36 PM
L291	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:39 PM
L292	180	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/03/02 12:19 PM
L293	11	L292 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 12:20 PM
L294	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:47 PM
L295	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:49 PM
L296	1	("20020048170").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:36 PM
L297	1	("20040174525").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:49 PM
L298	1	("10045704").PN.	(US-PGPUB; USPAT;	OR	OFF	OFF	2021/03/02

			USOCR)				03:09 PM
L299	27321	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/153 or A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/03/02 03:17 PM
L300	4594	L299 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:27 PM
L301	3762	L300 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:28 PM
L302	257	L301 and (air near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L303	420	L301 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L304	1	("20110167658").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 03:30 PM
L305	5	("2015/0306288").URPN.	(USPAT)	OR	ON	ON	2021/03/02 04:15 PM
L306	1	(16/208559).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 04:32 PM
L307	2	("2009/0043225").URPN.	(USPAT)	OR	ON	ON	2021/03/02 04:49 PM
L308	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/03/02 05:00 PM
L309	1363	L308 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:00 PM
L310	73	L309 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L311	73	L310 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L312	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:34 PM
L313	711	L312 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L314	58	L313 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L315	58	L314 and	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02

		@ad<"20150724"					05:34 PM
L316	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:42 PM
L317	277	L316 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:42 PM
L318	20	L317 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:43 PM
L319	336	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/03/02 05:44 PM
L320	210	L319 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L321	196	L320 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L322	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:48 PM
L323	1208	L322 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L324	73	L323 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L325	73	L324 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:49 PM
L326	1368	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:59 PM
L327	271	L326 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L328	10	L327 and ((air or gas$4) near4 permeab$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L329	268	L327 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L330	182	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/07/08 02:22 PM
L331	27660	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/153 or	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/07/08 03:27 PM

		A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc.					
L332	4684	L331 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:28 PM
L333	3769	L332 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L334	579	L333 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L335	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:54 PM
L336	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:56 PM
L337	337	("2913000" | "3817240" | "3859998" | "3864979" | "4016879" | "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:19 PM
L338	211	L337 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L339	196	L338 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L340	37	L339 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L341	221	("20010021827" | "20020004650" | "20020055716" | "20020072715" | "20020103464" | "20020103465" | "20020107488" | "20020151856" | "20020193748" | "20030028171" | "20030036730" | "20030050608" | "20030055385" | "20030078544" | "20030093009" | "20030105414" | "20030114797" | "20030120222" | "20030176842" | "20030181873" | "20030191438" | "20030199827" | "20030216687" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"20030220614" | "20030229315" | "20030229316" | "20040024370" | "20040059302" | "20040092872" | "20040102740" | "20040111068" | "20040193120" | "20040204681" | "20040210197" | "20050004524" | "20050059936" | "20050065482" | "20050124944" | "20050165353" | "20050187493" | "20050228345" | "20050245868" | "20050245869" | "20050245870" | "20050245879" | "20050245885" | "20050283093" | "20060015073" | "20060036217" | "20060036219" | "20060079847" | "20060129064" | "20060189934" | "20060189936" | "20060224122" | "20060270947" | "20060276756" | "20070021724" | "20070027430" | "20070106220" | "20070106224" | "20070167914" | "20070282275" | "20080015513" | "20080086085" | "20080177202" | "20080221528" | "20080269691" | "20080306452" | "20080319345" | "20080319346" | "20090204026" | "20090227896" | "20100063455" | "20100191189" | "20100262038" | "20110118674" | "4106497" | "4207870" | "4305406" | "4572210" | "4573976" | "4641663" | "4795443" | "4813426" |				

		"4840619" | "4887998" | "4894055" | "4900307" | "4923477" | "4994046" | "5015241" | "5195985" | "5215534" | "5219333" | "5222502" | "5242417" | "5246428" | "5256153").PN. OR ("5295970" | "5295975" | "5303713" | "5312372" | "5318547" | "5336199" | "5344408" | "5348544" | "5356392" | "5389085" | "5403286" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5549558" | "5595566" | "5599313" | "5607402" | "5662617" | "5665075" | "5669889" | "5672161" | "5676658" | "5681295" | "5685855" | "5687740" | "5688241" | "5695474" | "5702369" | "5704920" | "5718239" | "5733265" | "5755522" | "5769826" | "5795336" | "5879337" | "5893845" | "5910130" | "5921964" | "5957892" | "5984899" | "6149629" | "6171284" | "6183445" | "6224576" | "6254575" | "6261263" | "6261265" | "6298541" | "6344032" | "6419658" | "6436086" | "6440104" | "6471677" | "6475191" | "6485469" | "6524277" | "6533760" | "6554807" | "6575939" | "6592556" | "6623456" | "6623461" | "6635032" | "6641555" | "6648855" | "6648856" | "6659983" | "6695819" | "6699217" | "6712792" | "6716199" | "6761704" | "6773419" | "6780169" | "6805689" | "6811545" | "6835190" | "6837877" | "6846302" | "6860872" | "6869415" | "6905483" | "6918891" | "6958054" | "6974423" | "6984223" | "6997913" | "7001363" | "7083600" | "7101355" | "7128726" | "7147624" | "7160267" | "7163526" | "7201740" | "7211065" | "7223258"				

		| "7226432" | "7361159" | "7396343" | "7428773" | "7524308" | "7537581" | "7670320" | "7727190" | "7766879" | "7938808" | "8066679" | "8282605" | "8795198" | "D422700" | "D442280" | "D604836" | "D604837" | "D604838" | "D604839" | "D605287" | "RE35539" | "RE43473").PN. OR ("9615783").URPN.					
L342	115	("20020193748" | "20030093009" | "20030105414" | "20030220614" | "20030229315" | "20040059302" | "20040092872" | "20040193120" | "20050004524" | "20050065482" | "20050124944" | "20050187493" | "20050245868" | "20050245869" | "20050245870" | "20050245879" | "20050245885" | "20060036219" | "20060224122" | "20070106220" | "20070106224" | "20070167914" | "20080086085" | "20080177202" | "20080319345" | "20080319346" | "20090204026" | "20100262038" | "4106497" | "4207870" | "4305406" | "4572210" | "4573976" | "4641663" | "4795443" | "4840619" | "4894055" | "4900307" | "4994046" | "5015241" | "5195985" | "5215534" | "5222502" | "5242417" | "5246428" | "5256153" | "5295970" | "5303713" | "5312372" | "5336199" | "5348544" | "5356392" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5599313" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"5662617" | "5665075" | "5672161" | "5676658" | "5702369" | "5704920" | "5733265" | "5755522" | "5957892" | "5984899" | "6149629" | "6224576" | "6254575" | "6261263" | "6298541" | "6344032" | "6436086" | "6440104" | "6524277" | "6533760" | "6592556" | "6623456" | "6635032" | "6648855" | "6695819" | "6699217" | "6712792" | "6780169" | "6837877" | "6869415" | "6984223" | "7001363" | "7128726" | "7147624" | "7160267" | "7163526" | "7223258" | "7226432" | "7396343" | "7428773" | "7537581" | "7766879" | "D422700" | "D442280" | "D604836" | "D604837" | "D604838" | "D604839" | "D605287").PN. OR ("8603009").URPN.					
L343	148	("20020193748" | "20030105414" | "20030229315" | "20040059302" | "20040092872" | "20050004524" | "20050187493" | "20050245868" | "20050245869" | "20050245870" | "20050245885" | "20060036219" | "20070106220" | "20070167914" | "20080086085" | "20080177202" | "4106497" | "4207870" | "4305406" | "4573976" | "4641663" | "4795443" | "4840619" | "4894055" | "4900307" | "4994046" | "5015241" | "5195985" | "5215534" | "5222502" | "5242417" | "5256153" | "5295970" | "5303713" | "5312372" | "5336199" | "5348544" | "5356392" | "5411492" | "5439449" | "5466223" | "5501675" | "5542932" | "5672161" |	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"5676658" | "5702369" | "5704920" | "5755522" | "5984899" | "6149629" | "6261263" | "6298541" | "6436086" | "6440104" | "6524277" | "6533760" | "6592556" | "6623456" | "6635032" | "6648855" | "6699217" | "6712792" | "6780169" | "6837877" | "6869415" | "6984223" | "7001363" | "7128726" | "7147624" | "7160267" | "7163526" | "7223258" | "7226432" | "7396343" | "7428773" | "D422700" | "D442280").PN. OR ("7766879").URPN.					
L344	41	("2735430" | "2798487" | "3187749" | "3240209" | "3585984" | "3817240" | "4166450" | "4207870" | "4295477" | "4312362").PN. OR ("4436098").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:22 PM
L345	163	L341 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:22 PM
L346	163	L345 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:23 PM
L347	22	("2005/0283093").URPN.	(USPAT)	OR	ON	ON	2021/07/08 04:23 PM
L348	163	L345 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L349	163	L348 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L350	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/08 04:37 PM
L351	1363	L350 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:37 PM
L352	1346	L351 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L353	136	L352 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L354	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:41 PM
L355	711	L354 and ((blood or fluid$4) near4 (sequest$5 or sampl$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM

		or flash$4 or collect$4))					
L356	699	L355 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L357	123	L356 and (vent$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L358	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:44 PM
L359	277	L358 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM
L360	260	L359 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM
L361	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:46 PM
L362	1208	L361 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:46 PM
L363	1194	L362 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L364	1194	L363 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L366	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:05 PM
L367	319	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR (("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/02/02 03:14 PM
L368	1	(16/376745).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:35 PM
L369	190	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 03:36 PM
L370	2	(15/140448).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:41 PM
L371	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L372	1	("9060725").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L373	1	("9060724").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:43 PM
L374	1	("9022950").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L375	1	("9022951").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L376	1	("10292633").PN.	(US-PGPUB; USPAT;	OR	OFF	OFF	2022/02/02

			USOCR)				03:46 PM
L377	1	("10433779").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:47 PM
L378	1	("10436554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:48 PM
L379	1	("10736554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L380	1	("10912506").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L381	1	("10010282").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L382	1	(16/376745).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:50 PM
L383	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:51 PM
L384	276	(600/579).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:52 PM
L385	204	L384 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 03:53 PM
L386	37427	(A61B5/150221 or A61B5/15003 or A61B5/150236 or A61B5/150244 or A61B5/150251 or A61B5/150389 or A61B5/150503 or A61B5/150992 or A61B5/153 or A61B5/155 or A61B10/0048 or A61B10/0051 or A61B10/007 or A61B2010/0061 or A61B2010/0077 or A61B2010/008).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 04:35 PM
L387	7279	L386 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L388	4442	L387 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L389	874	L388 and (seal$4 near4 (member or mechanism$4 or vent$4 or elastic$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:38 PM
L390	26	("2008/0145933").URPN.	(USPAT)	OR	ON	ON	2022/02/02 04:52 PM
L391	44	("2008/0319346").URPN.	(USPAT)	OR	ON	ON	2022/02/02 04:59 PM
L392	385	L386 and ((blood or fluid) near4 (seal$4 near4 (member or	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM

		mechanism$4 or vent$4 or elastic$4)))					
L393	171	L392 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM
L394	355	(604/103).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 05:52 PM
L395	7	L394 and ((blood or fluid) near4 (seal$4 near4 (member or mechanism$4 or vent$4 or elastic$4)))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:52 PM
L396	1	(16/328127).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/03 12:00 PM
L397	0	"1020130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L398	8	"20130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L399	14	"2013021595"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:18 PM
L400	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/04 07:10 PM
L401	1	(15/746656).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/05 11:48 AM
L402	0	(17/388440).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/07 09:34 AM
L403	1	("20050048465").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2022/02/07 09:34 AM
L404	196	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:08 PM
L405	16	L404 and (blood near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L406	16	L404 and ((blood or chamber) near4 sequest$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L407	16	L406 and (junct$4 or bypass$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L408	16	L406 and junct$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L409	22445	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:54 PM

		A61B5/150572 or A61B5/154 or A61B5/15074).cpc.					
L410	4525	L409 and ((blood or fluid$4) near4 (sequest$5 or sampl$4 or flash$4 or collect$4 or flush$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:55 PM
L411	3810	L410 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:56 PM
L412	820	L411 and ((vent$4 or open$4 or apertur$4) near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:57 PM
L413	22445	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 05:51 PM
L414	4603	L413 and ((blood or fluid$4 or chamber) same (sequest$5 or sampl$4 or flash$4 or collect$4 or flush$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:51 PM
L415	511	L414 and ((junct$4 or bypass$4 or divert$4) near4 (blood or fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:52 PM
L416	355	L415 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:53 PM
L417	1	(16/819033).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:10 PM
L418	1	(17/094692).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L419	1	(17/538990).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L420	1	("11311219").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:27 PM
L421	1	("11185266").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:30 PM
L422	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:31 PM
L423	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:32 PM
L424	252	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS,	OR	OFF	OFF	2022/10/13 01:41 PM

			IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L425	38	424 AND (closur$4 OR enclos$4)	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 01:42 PM
L426	42781	(A61B5/150213 OR A61B5/15003 OR A61B5/150221 OR A61B5/150251 OR A61B5/150732 OR A61B5/15074 OR A61B5/150992 OR A61B5/153 OR A61B5/150389 OR A61B5/150503).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/13 01:47 PM
L427	5205	426 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 01:50 PM
L428	4803	427 AND ((blood OR fluid$4) near4 (sequest$5 OR sampl$4 OR flash$4 OR collect$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 01:51 PM
L429	519	428 AND ((closur$4 OR enclos$4 OR pug$4) near5 (vent OR open$4 OR air))	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 01:54 PM
L430	169	"5749857"	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 02:14 PM
L431	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 02:14 PM
L432	346	427 AND ((junct$4 OR bypass$4 OR divert$4) near4 (blood OR fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 02:18 PM
L433	186	("3500828" | "3670729" | "3714945" | "3977400" | "3994293" | "3995619" | "4106491" | "4200096" | "4468224" | "4531987" | "4549554" | "4735215" | "4828548" | "4874373" | "4893635" | "4894052" | "4907599" | "4944308" | "4994042" | "5129884"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/10/13 02:32 PM

		| "5400798").pn. OR ("5749857").urpn. AND (PGPB | USPT | USOC).dbnm.					
L434	124	433 AND ((blood OR fluid$4) near4 (sequest$5 OR sampl$4 OR flash$4 OR collect$4 OR optimiz$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 02:34 PM
L435	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 02:34 PM
L436	1	17/138056	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/19 11:35 AM
L437	253	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/11/16 03:25 PM
L438	39	437 AND (closur$4 OR enclos$4)	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 03:25 PM
L439	35391	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/154 OR A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/11/16 03:46 PM
L440	4100	439 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:48 PM
L441	3875	440 AND ((blood OR fluid$4 OR urine) SAME (sequest$5 OR sampl$4 OR flash$4 OR collect$4 OR	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:49 PM

		optimiz$5))					
L442	368	441 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:50 PM
L443	7	"10827964"	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 04:13 PM
L444	1	16/819033	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 04:48 PM
L445	359	"4207870"	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 05:07 PM
L446	1	("4207870").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 05:07 PM
L447	3814	440 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flash$4 OR collect$4 OR optimiz$5))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:17 PM
L448	366	447 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:17 PM
L449	89	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 01:13 PM
L450	24	449 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5or flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:14 PM
L451	24	449 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:14 PM
L452	6634	(A61B5/150213 OR A61B5/15003 OR A61B5/150221 OR A61B5/150251 OR A61B5/150732 OR A61B5/15074 OR A61B5/150992 OR A61B5/153 OR A61B5/150389 OR A61B5/150503).cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 01:32 PM
L453	5326	452 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:32 PM
L454	4928	453 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:32 PM

		OR collect$4 OR optimiz$5 OR flash$4))					
L455	371	454 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:33 PM
L456	11	("2016/0361006").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:03 PM
L457	1	17/094692	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 03:11 PM
L458	49	("20020004647"|"20030105414"|"20040054333"|"20040073171"|"20040147855"|"20050004524"|"20050240161"|"20070083162"|"20070088279"|"20080086085"|"20080145933"|"20080167577"|"20080319346"|"20100010372"|"20100057004"|"20120016266"|"20130317391"|"20160008579"|"20160174888"|"3741197"|"3817240"|"3874367"|"3886930"|"4057050"|"4106497"|"4154229"|"4207870"|"4412548"|"4436098"|"4444203"|"5222502"|"5520193"|"5749857"|"6398743"|"6569117"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8603009"|"8864684"|"9022950"|"9022951"|"9060724"|"9138572"|"9155495"|"9204864"|"9877675").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 03:18 PM
L459	13	458 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:18 PM
L460	155	("2707953" | "2992974" | "3013557" | "3098016" | "3382865" | "3405706" | "3494351" | "3577980" | "3635798" | "3648684" | "3848579" | "3890203" | "3937211" | "4057050" | "4133863" | "4166450" | "4340067" | "4370987" | "4425235" | "4444203" | "4459997" | "4509534" | "4657160" | "4676256" | "4865583" | "4890627"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:21 PM

		| "4988339" | "5009847" | "5097842" | "5108927" | "5122129" | "5269317" | "5330464" | "5360011" | "5429610" | "5450856" | "5454786" | "5485854" | "5507299" | "5577513" | "5762633" | "5865812" | "5882318" | "5922551" | "6016712" | "6057105" | "6159164" | "6210909" | "6328726" | "6364890" | "6387086" | "6403381" | "6520948" | "6626884" | "6692479" | "6716187" | "6746420" | "6913580" | "7044941" | "7087047" | "7335188" | "7384416" | "7744573" | "8197420" | "8231546" | "8337418" | "8535241" | "8647286" | "8864684" | "8876734" | "20020002349" | "20020183651" | "20030055381" | "20030208151" | "20040010228" | "20040054283" | "20040054333" | "20040147855" | "20050004524" | "20050240161" | "20050245885" | "20050281713" | "20060287639" | "20080108954" | "20080145933" | "20100152681" | "20120095367" | "20120215131" | "20130079604" | "20130116599" | "20130317391" | "20140081172").pn. OR ("9060724").urpn. AND (PGPB | USPT | USOC).dbnm.					
L461	31	("2008/0145933").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:30 PM
L462	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 03:46 PM
L463	13	459 AND ((junct$4 OR bypass$4 OR divert$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:47 PM

L464	4994	453 AND ((blood OR fluid$4 OR urine OR semen) SAME (sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:58 PM
L465	968	464 AND ((junct$4 OR bypass$4 OR diver$5) SAME (blood OR fluid OR urine OR semen))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:59 PM
L466	707	465 AND housing	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:50 PM
L467	2911	464 AND ((blood OR fluid$4 OR urine OR semen) near5 (first OR second OR subsequent$4 OR bypass))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L468	2954	464 AND ((blood OR fluid$4 OR urine OR semen) near5 (first OR second OR subsequent$4 OR convey$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L469	2891	464 AND ((blood OR fluid$4 OR urine OR semen) near5 (first OR second OR subsequent$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L470	790	469 AND ((junct$4 OR bypass$4 OR diver$5) SAME (blood OR fluid OR urine OR semen))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:53 PM
L471	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 12:35 PM
L472	164	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2023/05/08 02:18 PM
L473	1	("4207870").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:23 PM
L474	1	("10827964").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08

							03:31 PM
L475	1	("11311219").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:32 PM
L476	1	"17094692"	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:34 PM
L477	2	"17730118"	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:34 PM
L478	1	("10012828").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:36 PM
L479	1	("10010282").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:36 PM
L480	48138	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/05/08 03:59 PM
L481	5081	480 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 04:15 PM
L482	3947	481 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 04:17 PM
L483	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 04:17 PM
L484	1069	482 AND (air near5 (filter$4 OR material$4 OR membrane OR permeab$4 OR vent$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 04:32 PM
L485	203	("3500828" | "3670729" | "3714945" | "3977400" | "3994293" | "3995619" | "4106491" | "4200096" | "4468224" | "4531987" | "4549554" | "4735215" | "4828548" | "4874373" | "4893635" | "4894052" | "4907599" | "4944308" | "4994042" | "5129884" | "5400798").pn. OR ("5749857").urpn. AND	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/05/08 04:51 PM

		(PGPB | USPT | USOC).dbnm.					
L486	606	484 AND ((pressure OR vacuum) near5 (draw OR forc$4 OR withdraw OR flow$4)) SAME (blood OR fluid)	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 05:32 PM
L487	24	("2010/0057004").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/05/08 05:35 PM
L488	3	487 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 05:55 PM
L489	49	((US-20080319346-A1 OR US-20100057004-A1 OR US-20070088279-A1 OR US-20080145933-A1 OR US-20040054333-A1 OR US-20100010372-A1 OR US-20080167577-A1 OR US-20080086085-A1 OR US-20070083162-A1 OR US-20160008579-A1 OR US-20120016266-A1 OR US-20130317391-A1 OR US-20160174888-A1 OR US-20050240161-A1 OR US-20040147855-A1 OR US-20040073171-A1 OR US-20050004524-A1 OR US-20030105414-A1 OR US-20020004647-A1).did. AND PGPB.dbnm.) OR ((US-4412548-A OR US-5222502-A OR US-5520193-A OR US-9022951-B2 OR US-6569117-B1 OR US-3741197-A OR US-8603009-B2 OR US-4207870-A OR US-9877675-B2 OR US-4444203-A OR US-6398743-B1 OR US-9022950-B2 OR US-9155495-B2 OR US-4436098-A OR US-9138572-B2 OR US-8568371-B2 OR US-	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/05/08 06:07 PM

		8523826-B2 OR US-8197420-B2 OR US-4057050-A OR US-8864684-B2 OR US-8535241-B2 OR US-5749857-A OR US-9060724-B2 OR US-9204864-B2 OR US-3817240-A OR US-3874367-A OR US-3886930-A OR US-4106497-A OR US-4154229-A).did. AND USPT.dbnm.)					
L490	25	489 AND (air near5 (filter$4 OR material$4 OR membrane OR permeab$4 OR vent$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:07 PM
L491	204	482 AND (hous$4 SAME (inlet AND outlet AND channel))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:29 PM
L492	118	491 AND (hous$4 near5 ((top OR upper) AND (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:33 PM
L493	1	489 AND (hous$4 near5 ((top OR upper) AND (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L494	0	489 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L495	27	492 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L496	172	484 AND (hous$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:41 PM
L497	113	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/07/05 01:58 PM
L498	26	497 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 01:58 PM

L499	4	15/855439	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 03:12 PM
L500	48306	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/07/05 03:36 PM
L501	5081	500 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 03:36 PM
L502	3947	501 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 03:37 PM
L503	1069	502 AND (air near5 (filter$4 OR material$4 OR membrane OR permeab$4 OR vent$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 03:37 PM
L504	3871	501 AND ((blood OR fluid$4 OR urine) near5(divert$4 OR direct$4 OR flow$4 OR bypass$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:18 PM
L505	3030	501 AND ((blood OR fluid$4 OR urine) near5(divert$4 OR direct$4 OR flow$4 OR bypass$4 OR allow$4)) SAME (channel$4 OR chamber OR junct$4 OR inlet OR outlet OR path$4 OR contain$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:20 PM
L506	921	503 AND ((blood OR fluid$4 OR urine) near5(divert$4 OR direct$4 OR flow$4 OR bypass$4 OR allow$4)) SAME (channel$4 OR chamber OR junct$4 OR inlet OR outlet OR path$4 OR contain$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:20 PM
L507	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05

							06:04 PM
L508	1	16/961875	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 08:21 PM
L509	7	"20070148624"	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 01:02 PM
L510	43469	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO)	OR	ON	ON	2023/08/31 01:28 PM
L511	5081	510 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/31 01:32 PM
L512	3947	511 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/31 01:32 PM
L513	2653	512 AND ((blood OR fluid$4 OR urine) near5(divert$4 OR direct$4 OR flow$4 OR bypass$4 OR allow$4)) SAME (channel$4 OR chamber OR junct$4 OR inlet OR outlet OR path$4 OR contain$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/31 01:32 PM
L514	921	513 AND (air near5 (filter$4 OR material$4 OR membrane OR permeab$4 OR vent$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 01:33 PM
L515	1	18/113710	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 02:05 PM
L516	372	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR (("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/11/20 02:30 PM
L517	172	516 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/11/20 02:41 PM

		sampl$4 OR flush$4 OR collect$4 OR optimiz$5 OR flash$4 OR divert$4 OR bypass$4))					
L518	165	516 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR flush$4 OR optimiz$5 OR flash$4 OR divert$4 OR bypass$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/11/20 02:42 PM
L519	165	516 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR flush$4 OR optimiz$5 OR flash$4 OR diver$5 OR bypass$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/11/20 02:42 PM
L520	1	("11395612").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:43 PM
L521	1	("11395611").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:45 PM
L522	1	("10292633").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:46 PM
L523	1	("9022950").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:52 PM
L524	11	"10736554"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:55 PM
L525	1	("10736554").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:55 PM
L526	1	("10912506").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:55 PM
L527	1	("10010282").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:56 PM
L528	1	("9820682").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 02:58 PM
L529	67080	(A61B5/150221 OR A61B5/15003 OR A61B5/150236 OR A61B5/150244 OR A61B5/150251 OR A61B5/150389 OR A61B5/150503 OR A61B5/150992 OR A61B5/153 OR A61B5/155 OR A61B10/0048 OR A61B10/0051 OR A61B10/007 OR A61B2010/0061 OR A61B2010/0077 OR A61B2010/008).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/11/20 03:05 PM
L530	1791	529 AND ((blood OR fluid$4 OR urine)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/11/20 03:05 PM

		near5(sequest$5 OR flush$4 OR optimiz$5 OR flash$4 OR diver$5 OR bypass$4))					
L531	322	530 AND (flow$4 OR control$4 OR divert$4 OR mechanism) near5 rotat$4	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 03:07 PM
L532	420	530 AND (flow$4 OR control$4 OR divert$4 OR mechanism OR valve) near5 rotat$4	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 03:07 PM
L533	0	("2021/0128037").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/11/20 03:39 PM
L534	1267	530 AND (flow$4 OR control$4 OR divert$4 OR mechanism OR valve) near5 (chamber OR reservoir OR hous$4 OR container)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 03:56 PM
L535	1142	530 AND (flow$4 OR control$4 OR divert$4 OR mechanism OR valve) near5 (chamber OR reservoir OR container)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 03:56 PM
L536	1	17/863605	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 04:48 PM
L537	1	("10292633").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 05:19 PM
L538	505	530 AND (flow$4 OR control$4 OR divert$4 OR mechanism OR valve) near5 (multiple OR pluarlit$4 OR first OR second) near5 (lumen OR channel OR path$4)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/20 05:25 PM
L539	8	"20080077183"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 01:29 PM
L540	1	15/933356	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 01:47 PM
L541	7	("20060074354"|"20080077183"|"20100131454"|"20140228714"|"20150196247"|"20200129380"|"9974476").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:08 PM
L542	6	541 AND (suck$4 near5 pressure)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:09 PM
L543	146297	(A61B5/4542 OR A61B5/7242 OR A61B5/7246 OR	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY,	OR	ON	ON	2023/11/21 02:17 PM

		A61B5/7257 OR A61B5/7267 OR A61B5/7282 OR A61B2503/045 OR A61B2562/0247 OR A61B5/038 OR A61B5/002).cpc.	CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L544	16368	543 AND @ad<"20170322"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:17 PM
L545	15	544 AND (determin$4 OR measur$4 OR detect$4 OR process$4) near5(suck$4 near5 pressure)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:18 PM
L546	120	544 AND (determin$4 OR measur$4 OR detect$4 OR process$4 OR estimat$4) near5((suck$4 OR feed$4) near5 pressure)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:20 PM
L547	15	544 AND (determin$4 OR measur$4 OR detect$4 OR process$4 OR estimat$4) near5((suck$4) near5 pressure)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:20 PM
L548	1868	(determin$4 OR measur$4 OR detect$4 OR process$4 OR estimat$4) near5(suck$4 near5 pressure)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:27 PM
L549	1387	548 AND @ad<"20170322"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:27 PM
L550	48	(determin$4 OR measur$4 OR detect$4 OR process$4 OR estimat$4) near5(suck$4 near5 pressure) AND (nutrit$4 SAME feed$4)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:34 PM
L551	39	550 AND (baseline OR threshold OR predetermin$4)	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:35 PM
L552	16	"20150011874"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 02:55 PM
L553	5	"20140288398"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21

							02:55 PM
L554	6	"20140120531"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 03:01 PM
L555	1	("9060724").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 03:45 PM
L556	1	("10433779").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 03:49 PM
L557	12	"10736554"	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 03:50 PM
L558	1	("10912506").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 03:54 PM
L559	0	18/381369	(US-PGPUB; USPAT)	OR	ON	ON	2023/11/21 05:01 PM
L560	21	(Artificial Intelligence) More like doc: US-10912506-B2 Text: (US-20200359951-A1 OR US-11395611-B2 OR US-20220071533-A1 OR US-20180116577-A1 OR US-11395612-B2 OR US-20220079482-A1 OR US-10736554-B2 OR US-10433779-B2 OR US-20150351679-A1 OR US-20140155781-A1 OR US-9060724-B2 OR US-20150011910-A1 OR US-9022951-B2 OR US-20210361206-A1 OR US-20150011911-A1 OR US-9022950-B2 OR US-20150257691-A1 OR US-20200060595-A1 OR US-10292633-B2 OR US-20230172502-A1).did.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/11/21 07:16 PM
L561	0	("10912506").urpn. AND (PGPB | USPT | USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/11/21 07:16 PM
L562	273	("2707953" | "2992974" | "3013557" | "3098016" | "3382865" | "3405706" | "3467095" | "3494351" | "3494352" | "3577980" | "3604410" | "3635798" | "3648684" | "3730168" | "3741197" | "3777773" | "3803810" | "3817240" | "3834372" | "3835835" | "3848579" | "3848581"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/11/21 07:16 PM

		| "3874367" | "3886930" | "3890203" | "3890968" | "3937211" | "3945380" | "3978846" | "4056101" | "4057050" | "4063460" | "4077395" | "4106497" | "4133863" | "4150089" | "4154229" | "4166450" | "4190426" | "4193400" | "4207870" | "4212308" | "4238207" | "4257416" | "4275730" | "4298358" | "4340067" | "4340068" | "4349035" | "4370987" | "4398544" | "4412548" | "4416290" | "4425235" | "4444203" | "4459997" | "4509534" | "4608996" | "4654027" | "4657027" | "4657160" | "4673386" | "4676256" | "4679571" | "4705497" | "4714461" | "4772273" | "4865583" | "4879098" | "4886072" | "4890627" | "4904240" | "4980297" | "4988339" | "5009847" | "5027827" | "5032116" | "5045185" | "5066284" | "5084034" | "5097842" | "5100394" | "5108927" | "5116323" | "5122129" | "5135489" | "5222502" | "5269317" | "5330464" | "5417673" | "5431811" | "5439450" | "5450856" | "5466228" | "5472605" | "5485854" | "5507299" | "5520193" | "5575777" | "5603700" | "5632906" | "5649912" | "5691486" | "5749857" | "5772608" | "5811658" | "5824001" | "5865812" | "5871699" | "5911705" | "5961472" | "5971956" | "5980830" | "6001307" | "6010633" | "6106509" | "6210909" | "6224561" | "6325975" | "6328726" | "6364890" | "6387086" | "6403381" | "6506182" | "6520948" | "6569117" | "6626884" | "6638252" | "6648835" | "6692479" | "6695004" | "6716187" | "6733433" | "6736783" | "6746420" | "6843775" | "6860871" | "6905483"					

		| "6913580" | "6945948" | "7044941" | "7052603" | "7055401" | "7087047" | "7141097" | "7241281" | "7306736" | "7314452" | "7316662" | "7335188" | "7384416" | "7461671" | "7479131" | "7614857" | "7615033" | "7618407" | "7648491" | "7666166" | "7744573" | "7766879" | "8070725" | "8197420" | "8231546" | "8337418" | "8349254" | "8377040" | "8382712" | "8383044" | "8412300" | "8523826" | "8535241" | "8540663" | "8568371" | "8574203" | "8603009" | "8647286" | "8795198" | "8827958" | "8864684" | "8876734" | "9022950" | "9022951" | "D731643" | "9060724" | "9060725" | "9138572" | "9149576" | "9155495" | "9204864" | "9314201" | "9855001" | "9855002" | "9855386" | "9861306" | "9872645" | "9877675" | "9895092" | "9950084" | "9999383" | "10028687" | "10028689" | "10045724" | "10251590" | "10736554" | "20010039058" | "20020002349" | "20020004647" | "20020183651" | "20020193751" | "20030013991" | "20030055381" | "20030069543" | "20030105414" | "20030208151" | "20040009542" | "20040010228" | "20040054283" | "20040054333" | "20040127816" | "20040147855" | "20050004524" | "20050148993" | "20050161112" | "20050199077" | "20050240161" | "20050245885" |				

		"20050273019" | "20050281713" | "20060251622" | "20060287639" | "20070088279" | "20070100250" | "20070119508" | "20070287948" | "20080086085" | "20080108954" | "20080167577" | "20080185056" | "20080319346" | "20090050213" | "20090306601" | "20100010372" | "20100042048" | "20100057004" | "20100094171" | "20100152681" | "20100268118" | "20110306899" | "20120035540" | "20120265099" | "20120265128" | "20140066880" | "20150018715" | "20150342510" | "20150351679" | "20160174888" | "20160213294" | "20170071519" | "20180160958" | "20180353117" | "20190076074" | "20190175087" | "20200060595" | "20200060596").pn. OR ("10912506").urpn. AND (PGPB | USPT | USOC).dbnm.					
L563	303	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/01/08 02:52 PM

L564	26	563 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR flush$4 OR optimiz$5 OR flash$4 OR diver$5 OR bypass$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2024/01/08 02:55 PM
L565	33645	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/01/08 03:06 PM
L566	5091	565 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2024/01/08 03:09 PM
L567	1014	566 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR flush$4 OR optimiz$5 OR flash$4 OR diver$5 OR bypass$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2024/01/08 03:09 PM
L568	828	567 AND (flow$4 OR control$4 OR divert$4 OR mechanism OR valve OR junct$4) near5 (chamber OR reservoir OR container OR hous$4 OR inlet OR outlet OR channel OR port)	(US-PGPUB; USPAT)	OR	ON	ON	2024/01/08 03:15 PM
L569	51	("20020004647"|"20030105414"|"20040054333"|"20040073171"|"20040147855"|"20050004524"|"20050240161"|"20070083162"|"20070088279"|"20080086085"|"20080145933"|"20080167577"|"20080319346"|"20100010372"|"20100057004"|"20120016266"|"20130317391"|"20150314105"|"20150359473"|"20160008579"|"20160174888"|"3741197"|"3817240"|"3874367"|"3886930"|"4057050"|"4106497"|"4154229"|"4207870"|"4412548"|"443609	(US-PGPUB; USPAT)	OR	ON	ON	2024/01/08 03:40 PM

		8"|"4444203"|"5222502"|"5520193"|"5749857"|"6398743"|"6569117"|"8197420"|"8523826"|"8535241"|"8540663"|"8568371"|"8603009"|"8864684"|"9022950"|"9022951"|"9060724"|"9138572"|"9155495"|"9204864"|"9877675").PN.					
L570	35	569 AND ((blood OR fluid$4 OR urine) near5(sequest$5 OR flush$4 OR optimiz$5 OR flash$4 OR diver$5 OR bypass$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2024/01/08 03:40 PM
L571	353	567 AND (air near5 (filter$4 OR material$4 OR membrane OR permeab$4 OR vent$4))	(US-PGPUB; USPAT)	OR	ON	ON	2024/01/08 04:09 PM
L572	3	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2024/01/08 04:12 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N94	1	(port and sequest$5 and junction and chamber and sampl$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:15 PM
N112	3	(port and sequest$5 and chamber and sampl$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:39 PM
N248	4	(blood and fluid$4 and inlet and outlet and port and reservoir and allow and initial$4 and sequest$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N249	4	(blood and fluid$4 and inlet and outlet and port and reservoir and allow$4 and initial$4 and sequest$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N250	495	(blood and fluid$4 and allow$4 and initial$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N251	107	(blood and fluid$4 and allow$4 and initial$4 and subsequent$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N283	9	((blood or fluid$4) and	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10

		sequestrat$4 and chamber and sampl$4 and vent$4 and air$4).clm.					06:31 PM
N284	530	((blood or fluid$4) and chamber and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N285	84	((blood or fluid$4) and chamber and cap and sampl$4 and vent$4 and air$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:32 PM
N365	6	(port and sequest$5 and junction and chamber and sampl$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:49 PM
N366	9	(blood AND fluid$4 AND inlet AND outlet AND junct$4 AND inhibit$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:31 PM
N367	84	((blood OR fluid$4) AND chamber AND sampl$4 AND junction AND (inhibit$4 OR prevent$4)).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:36 PM
N368	25	(blood AND chamber AND sampl$4 AND junction AND inlet AND outlet AND port AND first).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:48 PM
N369	4	(blood AND chamber AND sampl$4 AND junction AND inlet AND outlet AND port AND first AND hous$4 AND subsequent).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:49 PM
N370	64902	"465" AND housing	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:50 PM
N371	6	(inlet AND outlet AND junct$4 AND channel AND sampl$4 AND fluid$4 AND vent AND air AND permeab$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:51 PM
N372	167	(inlet AND outlet AND junct$4 AND channel AND sampl$4 AND fluid$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:52 PM
N373	23	(inlet AND outlet AND junct$4 AND channel AND sampl$4 AND fluid$4 AND bypass$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:53 PM

N374	33	(inlet AND outlet AND chamber AND blood AND sampl$4 AND bypass).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 02:35 PM
N375	18	(inlet AND outlet AND chamber AND blood AND sampl$4 AND bypass AND air AND permeable).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 02:36 PM
N376	14	(inlet AND outlet AND chamber AND (blood OR fluid OR urine) AND sampl$4 AND bypass AND air AND permeable AND junct$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2024/01/08 04:24 PM
N377	14	(inlet AND outlet AND chamber AND (blood OR fluid OR urine) AND sampl$4 AND bypass AND air AND permeable AND junct$4 AND channel).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2024/01/08 04:25 PM
N378	14	(inlet AND outlet AND chamber AND (blood OR fluid OR urine) AND sampl$4 AND bypass AND air AND permeable AND junct$4 AND channel AND vent).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2024/01/08 04:25 PM

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4416291		1983-11-22	KAUFMAN JOSEPH	
	2	10299713		2019-05-28	PATTON RICHARD G	
	3	10265007		2019-04-23	BULLINGTON GREGORY	
	4	11395612		2022-07-26	BULLINGTON GREGORY J	
	5	10881343		2021-01-05	BULLINGTON GREGORY J	
	6	10596315		2020-03-24	BULLINGTON GREGORY J	
	7	11660030		2023-05-30	BULLINGTON GREGORY J	
	8	11259727		2022-03-01	BULLINGTON GREGORY J	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	9	11737693		2023-08-29	BULLINGTON GREGORY J	
	10	11439332		2022-09-13	BULLINGTON GREGORY J	
	11	11589843		2023-02-28	BULLINGTON GREGORY J	
	12	11612340		2023-03-28	BULLINGTON GREGORY J	
	13	11234626		2022-02-01	BULLINGTON GREGORY J	
	14	10624977		2020-04-21	BULLINGTON GREGORY J	
	15	11653863		2023-05-23	BULLINGTON GREGORY J	
	16	11419531		2022-08-23	BULLINGTON GREGORY J	
	17	11786155		2023-10-17	BULLINGTON GREGORY J	
	18	11789017		2023-10-17	BULLINGTON GREGORY J	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

EFS Web 2.1.18

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20220151525		2022-05-19	BULLINGTON GREGORY J	
	2	20220151527		2022-05-19	BULLINGTON GREGORY J	
	3	20200289039		2020-09-17	BULLINGTON GREGORY J	
	4	20210275068		2021-09-09	MIAZGA JAY M	
	5	20220304664		2022-09-29	HAMMER JEREMY	
	6	20160073937		2016-03-17	BURKHOLZ JONATHAN KARL	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

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

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

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

EXAMINER SIGNATURE

Examiner Signature	/MAY A ABOUELELA/	Date Considered	01/08/2024

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

CERTIFICATION STATEMENT

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

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

OR

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

☐ See attached certification statement.

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

☒ A certification statement is not submitted herewith.

SIGNATURE

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

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-12-20
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

Privacy Act Statement

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

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

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

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

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

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

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

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

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

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

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

Wed Jan 17 05:08:43 EST 2024

Dear Patent Center Customer:

Correspondence Address:

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

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

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

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

Application	Document	Mailroom Date	Attorney Docket No.
17538990	NOA	01/17/2024	069366-0572201_KUR2C03US
17538990	EXIN	01/17/2024	069366-0572201_KUR2C03US
17538990	1449	01/17/2024	069366-0572201_KUR2C03US

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

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

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

Sincerely,

The Patent Center Team

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27500 7590 01/17/2024
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or format drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

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

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	04/17/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
ABOUELELA, MAY A	3791	600-573000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Pillsbury Winthrop Shaw Pittman LLP
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Kurin, Inc.
(B) RESIDENCE: (CITY and STATE OR COUNTRY): San Diego, CA

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☒ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

☒ Electronic Payment via the USPTO patent electronic filing system ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. 033975

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

☐ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

☐ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Ben Hudson/ Date March 19, 2024

Typed or printed name Benjamin F. Hudson Registration No. 71474

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/538,990	**03/19/2024 02:35:43 PM Z ET**	**069366-0572201_KUR2C03US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	3420	FILED BY	Trent Tercenio
PATENT CENTER #	64724210	FILING DATE	11/30/2021
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0572201_KUR2C03US_Comments_on_reasons_for_allowance-LET.-LET..docx	2	Miscellaneous Incoming Letter	32 KB
069366-0572201_KUR2C03US_ISSUE_FEE_PYMT.pdf	1	Issue Fee Payment (PTO-85B)	988 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-	0F38551BB28811736CE5DC436908EC7C67ECD0AD38C4B205

0572201_KUR2C03US_Comments_on_reasons_for_allowance-LET.-LET..docx	3935F87895EC4F8955A8159AFA19B4656B2A873FBA5C6BB1E7DF62284F22B81FC25FF1D83929375E
069366-0572201_KUR2C03US_ISSUE_FEE_PYMT.pdf	2F68FA5F6CA6A40F8D32009D95000EFE85D3200C649892EB9E0E689CDE6D37AD297803B6AFAB596A7213D3AFB623F17A725DA4F7FEB728EB262DD55F7A4CB43F

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/538,990	**03/19/2024 02:35:43 PM Z ET**	**069366-0572201_KUR2C03US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	3420	FILED BY	Trent Tercenio
PATENT CENTER #	64724210	AUTHORIZED BY	Benjamin Hudson
CUSTOMER #	27500	FILING DATE	11/30/2021
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Bobby E. ROGERS

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 033975	**E20243IE36598116**	**Trent Tercenio**

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2501	UTILITY ISSUE FEE	480.00	1	480.00
			TOTAL AMOUNT:	**$480.00**

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

New Applications Under 35 U.S.C. 111

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

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

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage

submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Bobby E. Rogers

Confirmation No: 3420

Application No.: 17/538,990

Art Unit: 3791

Filed: November 30, 2021

Examiner: May A. Abouelela

For: Blood Sample Optimization System and Blood Contaminant Sequestration Device and Method

Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

COMMENTS ON EXAMINER'S STATEMENT OF REASONS FOR ALLOWANCE

Applicant thanks Examiner Abouelela for the Notice of Allowance and the Examiner's efforts in examining the above-referenced application.

Applicant received the Examiner's "Statement Of Reasons For Allowance" (hereafter the "Statement") along with the Notice and wishes to note that entry of this Statement should not be construed as Applicant necessarily agreeing with or acquiescing to the reasons stated therein.

Applicant recognizes that, in accordance with MPEP § 1302.14, the Statement need not set forth all of the details as to why claims are allowed and, respectfully, Applicant does not concede that the Statement contains the only reasons for which the pending claims are allowable. Each of the claims stands on its own merits and is patentable because of the combination it recites and not because of the presence or absence of any one particular element.

CONCLUSION

It is believed that no fees are due in connection with the filing of this paper. In the event that it is determined that fees are due, however, the Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account 033975, Reference No. 069366-0572201_KUR2C03US.

Respectfully submitted,
PILLSBURY WINTHROP SHAW PITTMAN LLP

Date: March 19, 2024 By: /Ben Hudson/
Benjamin F. Hudson, Ph.D.
Reg. No. 71,474

PO Box 10500
McLean, Virginia 22102
Telephone: (858) 509-4000
Customer No. 27500

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	04/23/2024	11963769	069366-0572201_KUR2C03US	3420

27500 7590 04/03/2024

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

ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at https://patentcenter.uspto.gov/. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at https://certifiedcopycenter.uspto.gov/index.html. The Certified Copy Center may be reached at (800)972-6382.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 247 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (https://patentcenter.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional inventors):

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

APPLICANT(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional applicants):

Kurin, Inc., San Diego, CA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

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

Thu Apr 04 05:22:10 EDT 2024

Dear Patent Center Customer:

Correspondence Address:

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

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

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

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

Application	Document	Mailroom Date	Attorney Docket No.
17538990	ISSUE.NTF	04/03/2024	069366-0572201_KUR2C03US

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

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

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

Sincerely,

The Patent Center Team

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

27500 7590 04/23/2024

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

EXAMINER	
ABOUELELA, MAY A	

ART UNIT	PAPER NUMBER
3791	

NOTIFICATION DATE	DELIVERY MODE
04/23/2024	ELECTRONIC

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

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

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

Docket_IP@pillsburylaw.com

PTOL-90A (Rev. 04/07)

APPLICATION NO.	ISSUE DATE	PATENT NO.
17/538,990	23-Apr-2024	11963769

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
McLean, VA 22102

EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at https://patentcenter.uspto.gov

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit https://www.uspto.gov/electronicgrants

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

Tue Apr 23 07:21:46 EDT 2024

Dear Patent Center Customer:

Correspondence Address:

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

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

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

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

Application	Patent	Document	Mailroom Date	Attorney Docket No.
17538990	11963769	EGRANT.NTF	04/23/2024	069366-0572201_KUR2C03US

To examine your eGrant and eCofC online, please access Patent Center then search using the listed application or patent number. To download your eGrant, click on the eGrant and eCofC link on the left-hand menu or select the “Download eGrant” link on the Application data page. To download your eCofC, click on the eGrant and eCofC link on the left-hand menu.

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

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

Sincerely,

The Patent Center Team