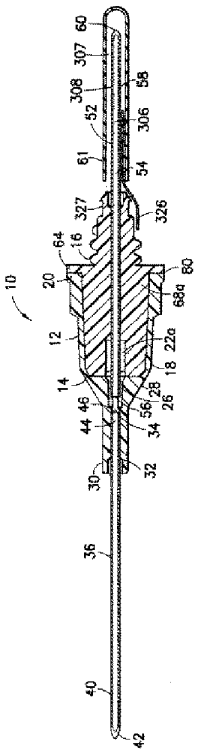
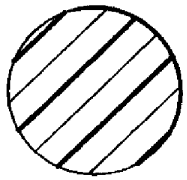
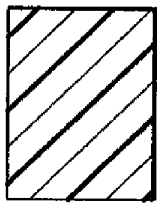
【図16】



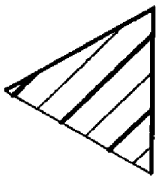
【図17】



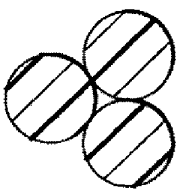
【図18】



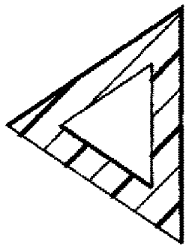
【図19】



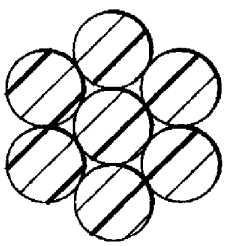
【図20】



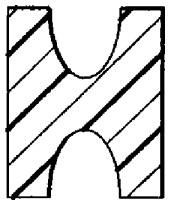
【図21】



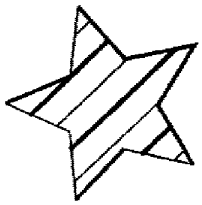
【図22】



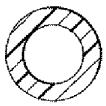
【図23】



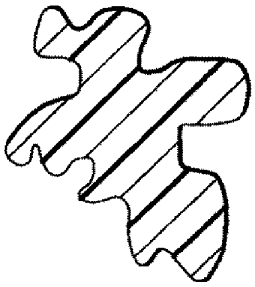
【図24】



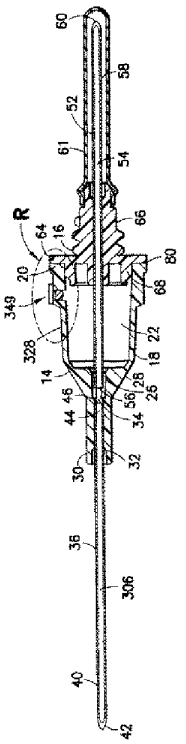
【図25】



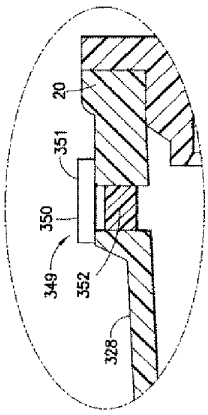
【図26】



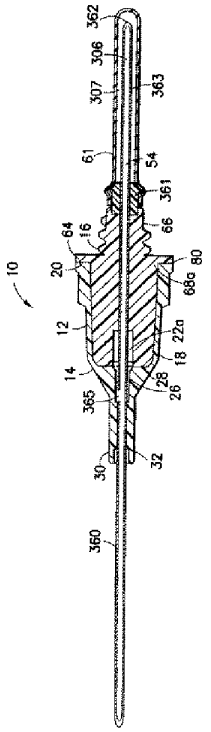
【図27A】



【図27B】



【図28】


362
306
307
363
61
54
361
64
16
66
20
80
68a
10
12
22a
18
14
28
26
365
32
30
360

(74)代理人　100088915
弁理士　阿部　和夫
(72)発明者　ハレーシュ　ナイル
アメリカ合衆国　０７０８６　ニュージャージー州　ウィーホークン　グレゴリー　アベニュー　５１８
(72)発明者　カーク　ディー．スウェンソン
アメリカ合衆国　０７００６　ニュージャージー州　ノース　コールドウェル　グランドビュー　プレイス　４２
(72)発明者　ヒュー　ティー．コンウェイ
アメリカ合衆国　０７０４４　ニュージャージー州　ベローナ　バルハラ　ウェイ　１８
(72)発明者　シー．マーク　ニュービー
アメリカ合衆国　１０９８７　ニューヨーク州　タキシード　パイン　ヒル　ロード　（番地なし）
(72)発明者　カーティス　ブロック
アメリカ合衆国　８４０７０　ユタ州　サンディー　サウス　ステート　ストリート　９４５０
(72)発明者　リチャード　レビー
アメリカ合衆国　２９１５０　サウスカロライナ州　サムター　オーク　ブルック　ブールバード　８０５
(72)発明者　ブラッドリー　ウィルキンソン
アメリカ合衆国　０７５０８　ニュージャージー州　ノース　ヘイルドン　ヒルサイド　ドライブ　３９
(72)発明者　ジェイムズ　シー．シュナイダー
アメリカ合衆国　０７４７０　ニュージャージー州　ウェイン　オーバールック　アベニュー　７０
(72)発明者　ブライアン　タウンズ
アメリカ合衆国　２１７９１　メリーランド州　ユニオン　ブリッジ　ワトソン　レーン　３７２０
(72)発明者　マイケル　イスクラ
アメリカ合衆国　０８８０７　ニュージャージー州　ブリッジウォーター　トゥロ　ファーム　ロード　１０７７
(72)発明者　ロバート　エリス
アメリカ合衆国　０７４８１　ニュージャージー州　ワイコフ　ローレル　レーン　７２０
(72)発明者　マイケル　ベネット
アメリカ合衆国　０７９０１　ニュージャージー州　サミット　マウンテン　アベニュー　２１６
(72)発明者　スチュワート　マーズデン
アメリカ合衆国　０７０４５　ニュージャージー州　モントビル　エインズレー　コート　２０
Ｆターム(参考)　4C038 TA06　UJ02
4C066 AA09　BB01　CC01　DD06　FF05　GG12　GG15　KK05　KK06

【外国語明細書】
2005349196000001.pdf

Espacenet

Bibliographic data: DE10038026 (A1) — 2001-02-22

Blood extractor for patient has extraction container with needle housing to receive retractable hollow needle to extract blood

Inventor(s):

Applicant(s): ZIERDEN PETER [DE] ± (ZIERDEN, PETER)

Classification: - **international:** ***A61B5/15;*** (IPC1-7): A61B5/15; A61M1/00
- **cooperative:** **A61B5/15003 (EP)**; **A61B5/150152 (EP)**; **A61B5/150389 (EP)**; **A61B5/150503 (EP)**; **A61B5/150656 (EP)**; **A61B5/150732 (EP)**; **A61B5/153 (EP)**; **A61B5/155 (EP)**; A61B5/150748 (EP)

Application number: DE20001038026 20000802

Priority number(s): DE20001038026 20000802 ; DE19992013417U 19990806

Also published as: DE29913417 (U1)

Abstract of DE10038026 (A1)

The blood extractor has a housing (1) with a hollow needle (10) extending through the wall of the patients blood vessel (B) to aspirate blood from it. The needle can move between a retracted position in which it is behind the surface of the housing and an extended position in which the end of the needle extends from the housing.

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 DE10038026A1

[0001]

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

[0002]

18 Such devices always comprise a hollow needle that is beveled at one end for penetrating the skin, the tissue lying between the skin and the vessel and the vessel wall, and which is usually equipped with a coupling at its other end, which is used to attach a container with a volume for receiving the blood taken .

[0003]

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

[0004]

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

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

[0005]

41 For the latter reason, it is also known to pre-evacuate the vessels that have the volume for receiving the blood taken and to seal them with a closure or

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

[0006]

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

[0007]

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

[0008]

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

[0009]

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

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

76 The risk of "wobbling" during insertion of the hollow needle is therefore significantly reduced.

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

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

[0010]

87 The means with which the hollow needle can be displaced from its retracted into its extended position preferably have an arrangement which exerts an elastic force on the hollow needle acting in the direction of the retracted towards the extended position.

90 In order to carry out the puncture, the hollow needle is then first moved into its retracted position, held in this position by suitable means, for example a locking device, and after the device has been brought to the suitable point on the body, by releasing the means, for example the locking moved to its extended position, with the tip of the hollow needle penetrating the blood vessel.

[0011]

98 In terms of its design, the arrangement for generating the elastic force can have a compression spring.

[0012]

103 However, it is also possible to generate the elastic force with the help of a compressed air reservoir or in a completely different way.

[0013]

108 The pain associated with taking blood from the patient can be further reduced if the housing of the device includes at least one internal volume for receiving the blood taken from the patient.

110 As a result of this measure, a coupling of a vessel for receiving blood taken after the puncture has been made is superfluous, so that "shaking pains" are prevented.

[0014]

115 If existing, commercially available containers are to continue to be used, an embodiment of the device according to the invention is recommended in which the housing includes an adapter arrangement for connecting at least one commercially available container for receiving the blood taken.

119 With this configuration, depending on the requirements, either a plurality of containers can be connected to the adapter at the same time or--if this is not desired or possible--a plurality of containers can also be connected one after the other.

[0015]

125 The means for sucking the blood through the interior of the hollow needle preferably include a negative pressure in the at least one interior volume compared to the outside environment.

127 This negative pressure can be generated, for example, by the inner volume being pre-evacuated and the interior of the hollow needle communicating with the inner volume in its extended position, in other words: only when the hollow needle is in the extended position is its interior connected to the pre-evacuated inner volume.

[0016]

134 However, it is also possible to provide means that only generate the negative pressure when the hollow needle is moved from its retracted to its extended position, to provide a manually or automatically actuated piston/cylinder device, or to bring about the negative pressure in any other way.

[0017]

141 Irrespective of the manner in which the negative pressure for sucking the blood is brought about, there are considerable advantages for the application if the device is designed in such a way that the negative pressure is applied to the hollow needle when it penetrates the blood vessel.

145 This measure effectively prevents painful extravascular bruising (hematoma) as a result of taking blood, which is regularly the case when blood can escape past the hollow needle from the blood vessel into the adjacent tissue during blood taking.

148 Because the suction in this preferred embodiment of the invention already exists when the hollow needle enters the blood vessel, blood that would otherwise have gotten into the tissue is also sucked out, even if the opening of the hollow needle is not completely into the vessel has penetrated or partially exited the opposite vessel wall.

152 As a further consequence, in this embodiment the "penetration depth" of the tip of the hollow needle for carrying out the blood withdrawal method does not have to be specified as precisely as hitherto, which also makes it easier for the user to take the blood.

[0018]

158 For handling the device according to the invention, it is particularly advantageous to provide the side part of the housing from which the hollow needle protrudes in its extended position with at least one contact surface via which the device is supported on the body surface of a patient during use.

162 To carry out the removal process, the device then only needs to be placed on a suitable part of the body and the displacement process of the hollow needle started.

[0019]

167 Tests have shown that the blood sampling process can be carried out particularly reliably and with little pain if the at least one contact surface is designed in such a way that when the device is supported on the body surface of the patient, the hollow needle forms an angle of between 5° and 30° with respect to the body surface in the support area - depending on the thickness of the tissue located between the vessel wall through which the hollow needle is intended to penetrate and the support surface.

[0020]

176 The device according to the invention can be used particularly variably when the at least one contact surface is designed in such a way that the angle that the hollow needle forms with the body surface during the removal process can be adjusted.

[0021]

182 In order to prevent the blood vessel intended for the removal process from being pushed away to the side when the device is put on, in a particularly preferred embodiment of the device according to the invention a recess is provided in the at least one contact surface, into which the blood vessel can at least partially bulge and thus from is positioned on the lateral boundary surfaces of the recess.

[0022]

190 If blood from a patient is used to carry out various diagnostic or

191 Therapy method required, so it is advantageous to provide a plurality of internal volumes separated from one another or an adapter arrangement for connecting a plurality of containers for receiving blood taken.

[0023]

197 The inner volumes or the containers can then optionally communicate with one another in series or also in parallel.

[0024]

202 In the drawing, exemplary embodiments of the invention are shown schematically.

203 Show it:

[0025]

207 1 shows a detail and diagrammatic view of a first exemplary embodiment of a device according to the invention in a longitudinal section, with the hollow needle being in its retracted position;

[0026]

212 FIG. 2 shows the same embodiment in the same view as in FIG. 1, but with the hollow needle being in its extended position; FIG.

[0027]

217 FIG. 3--in a detail--the same exemplary embodiment as in FIG. 1 in a partially sectional plan view (view A in FIG. 1);

[0028]

222 FIG. 4 shows another embodiment of a device according to the invention in a view corresponding to FIG. 3;

[0029]

227 5--schematically and in detail--an exemplary embodiment corresponding to FIGS. 1 to 3 of a device according to the invention during a removal process in a view in the direction of the blood vessel used for blood removal;

[0030]

233 6 - schematically - different positions of the beveled end of the hollow needle relative to the position of the blood vessel;

[0031]

238 7 shows an embodiment of a device according to the invention, which comprises a plurality of volumes communicating with one another in series for receiving blood that has been taken (schematic);

[0032]

244 8 shows an embodiment of a device according to the invention in a view corresponding to FIG

[0033]

248 9 shows an embodiment of a device according to the invention in a view corresponding to FIGS. 7 and 8, which has an adapter plate for connecting two external containers for receiving blood that has been taken.

[0034]

254 The embodiment of a device according to the invention, denoted as 100 as a whole in FIGS. 1 to 3 and shown only partially and schematically in these figures, comprises a housing 1, which in its interior has two internal volumes 3, 4 fluidically connected to one another via a channel 2 for receiving blood.

258 The housing 1 has, on its end face 5 pointing downwards in FIG. 1, a housing extension 6, the end 7 of which shown at the bottom in FIG. 1 is open.

[0035]

263 The interior 8 of the housing extension 6 serves to accommodate a hollow needle arrangement designated as a whole by 9, which essentially consists of the actual hollow needle 10 directed towards the open end 7 and a hollow needle carrier 11 serving to slidably mount the hollow needle arrangement 9 in the interior 8 of the housing extension 6 , which cooperates with the inner lateral surface 12 of the housing extension 6 at least approximately in a sealing manner.

[0036]

271 With its end face 13 facing away from the hollow needle 10 , the hollow needle carrier 11 is supported on a rigid contact surface 15 of the housing 1 via a pretensioned spiral spring 14 .

[0037]

276 A locking device 16 is used to lock the hollow needle arrangement 9 against the compressive force of the coil spring 14 in the retracted position.

[0038]

281 The hollow needle arrangement 9 has an inner channel 18 which extends from the tip 19 of the hollow needle 10 to a lateral opening 20 in the hollow needle carrier 11 .

[0039]

286 Furthermore, in the side wall of the housing extension 6 shown on the right in FIG.

[0040]

290 To move the hollow needle 10 from its retracted position shown in FIG. 1 to its extended position shown in FIG. 2, the locking device 16 is moved in such a way that the contact surface 17 is released.

293 Due to the force exerted by the spiral spring 14 on the hollow needle arrangement 9, the latter snaps down according to FIG.

295 In this position, the inner channel 18 communicates with the channel 21 via the opening 22 so that the inner volumes 3 and 4 communicate with the inner channel 18 of the hollow needle and blood can flow through the channels 18, 21 and 2 into the inner volumes 3, 4.

[0041]

301 As can also be seen from FIG.

[0042]

305 As illustrated in FIG. 6, blood can only be taken if the hollow needle 10 penetrates just deep enough into the patient's tissue that its tip does not stop before penetrating the wall of the blood vessel B (see

308 6a)), nor does the area of the hollow needle 10 which is bevelled towards the tip 19 project completely through the blood vessel B (cf.

310 Fig. 6e)).

[0043]

314 In order to be able to adapt the "penetration depth" of the tip 19 of the hollow needle 10 required for blood sampling to the individual requirements, a cuff 24 is provided on the housing extension 6, which is displaceably mounted in the direction of arrow P, with which the effective length of the housing extension 6 and thus the penetration depth the tip 19 of the hollow needle 10 can be changed.

319 The cuff 24 and the housing extension 6 can be equipped with locking means, not shown in the drawing, with which the cuff 24 can be locked in three different basic positions in which the penetration depth is adapted to the conditions usual in children, normal-weight adults or overweight adults .

[0044]

326 Extravascular bruising is also effectively prevented in end positions of the hollow needle 10 in which the tip 19 has not fully penetrated the blood vessel B (Fig. 6b)) or has partially penetrated the opposite wall of the blood vessel B (Fig. 6d)), since the negative pressure for sucking out the blood is already applied to the hollow needle as soon as it has entered the vessel.

[0045]

334 In principle, it is possible for the hollow needle 10 to pierce the blood vessel B essentially perpendicularly to its course.

336 However, such a procedure presupposes that the "penetration depth" must be predetermined almost exactly.

338 In order to avoid this, it is advisable to take the sample at an angle α between the hollow needle 10 and the blood vessel B, which is in the range between 5° and 30°.

340 For this purpose, the exemplary embodiment of the invention shown in FIGS. 1 and 2 has contact surfaces 25, through which the desired angle α is specified.

342 In the exemplary embodiments shown in the drawing, the angle α is fixed.

343 However, it is also within the scope of the invention to design the contact surfaces so variably that the angle α can be changed depending on the intended use of the device.

[0046]

348 As already described and shown again in detail in FIG. 1, a spiral spring 14 can be used to generate the force that drives the hollow needle arrangement from its retracted into its extended position.

351 However, as shown schematically in FIG. 4, it is also possible to provide a compressed air reservoir 26 between the end face 13 and the contact surface 15 or other means suitable for effecting an elastic force for propulsion.

[0047]

357 In order to prevent the vessel from which blood is to be taken from migrating laterally when the device 100 is placed on and the removal process thereby being frustrated, in a preferred embodiment of the invention a recess 27 is provided in the contact surfaces, into which the blood vessel B after the device 100 has been placed on the skin, it is at least partially pressed in and the blood vessel B is thus fixed laterally in the position required for taking blood (see Fig.

363 5).

[0048]

367 As illustrated in FIGS. 7 to 9, devices 100 according to the invention can be equipped in different ways with volumes for taking up blood that has been taken.

369 Thus, several volumes 28, 29, 30--three in FIG.

[0049]

373 It is also possible, as shown in FIG. 8, to provide inner volumes 31, 32, 33 which are arranged

parallel to one another and are correspondingly filled approximately at the same time as one another.

[0050]

379 To generate the negative pressure required for filling, the volumes 28 to 33 can be pre-evacuated, or the negative pressure required in them can take place in any other way, for example by connecting the volumes to a piston/cylinder unit, an external pump, etc.

382 In order to avoid extravascular bruising, it is only essential that the negative pressure has already been generated when the tip 19 of the hollow needle 10 penetrates into the vessel.

[0051]

387 In the exemplary embodiment shown in FIG. 9, the volumes 34, 35 provided for receiving the blood removed are arranged externally and designed as piston/cylinder units 36/37 in such a way that the pistons 36 can be displaced into the cylinder 37 by manually operable piston rods 38 .

391 To attach the piston/cylinder unit 36/37 to this device, which is designated as a whole by 200, an adapter arrangement 39 is used, from which the housing extension 206 in turn extends downward according to FIG.

394 The hollow needle arrangement 209 and the channels 202 correspond in their technical design and function to the hollow needle arrangement 9 and the channels 2 as they are described with reference to FIGS. 1 to 3 and therefore do not require any special discussion at this point.

397 Reference List

[0052]

401 The blood is taken in the device according to FIG. 9 in a manner already described with reference to FIGS. 1 to 3, whereby by pulling out the piston rods 38 into the position shown in FIG Cylinder 37 are held against the action of the negative pressure created prior to the needle propelling and penetrating the blood vessel.

1

408 Housing2 Channel3 Internal volume4 Internal volume5 Front side6 Housing extension7 End8 Interior9 Hollow needle arrangement10 Hollow needle11 Hollow needle carrier12 Inner lateral surface13 Front side14 Spiral spring15 Contact surface .16 Locking device17 Contact surface18 Inner channel19 Tip20 Opening21 Channel22 End23 Stop24 Cuff25 Contact surface26 Compressed air reservoir27 Recess28 Volume29 Volume30 Volume31 Volume32 Volume33 Volume34 volume 35 volume 36 piston 37 cylinder 38 piston rod 39 adapter assembly 40 locking projections 100 device 206 housing extension 209 hollow needle assembly 202 channels H skin B Blood vessel A view P arrow

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 DE10038026A1

1.

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

2.

24 Device according to Claim 1, characterized in that the means for displacing the hollow needle (10) from its retracted to its extended position comprise an arrangement which acts on the hollow needle (10) in a direction from the retracted to the extended position exert an acting elastic force.

3.

31 Device according to Claim 2, characterized in that the arrangement has a compression spring (14).

4.

36 Device according to Claim 2 or 3, characterized in that the arrangement has a compressed air reservoir (26).

5.

41 Device according to one of Claims 1 to 4, characterized in that the housing (1) comprises at least one internal volume (3, 4, 28-35) for receiving blood which has been removed.

6.

46 Device according to one of Claims 1 to 4, characterized in that the housing (1) comprises an adapter arrangement (39) for the connection of at least one container, the internal volume (34, 35) of which is used to hold the blood taken.

7.

52 Device according to Claim 5 or 6, characterized in that the means for sucking the blood through the interior of the hollow needles (10) comprise a negative pressure in the at least one interior volume (3, 4, 28-35) compared to the external environment.

8.

58 Device according to Claim 7, characterized in that the inner volume (3, 4, 28-35) is pre-evacuated and that the interior of the hollow needle (10) communicates with the inner volume (3, 4, 28-35) in its extended position.

9.

64 Device according to Claim 7, characterized in that means are provided which generate the negative pressure in the inner volume (3, 4, 28-35) when the hollow needle (10) is moved from its retracted to its extended position.

10.

70 Device according to Claim 9, characterized in that means for generating the negative pressure are a piston arrangement which is connected to the hollow needle (10) and which generates a negative pressure in a cylinder arrangement when the hollow needle (10) is moved into its extended position, and means which, in the extended Position of the hollow needle (10) connects the interior of the cylinder with the interior volume (3, 4, 28-35) for receiving the blood.

11.

78 Device according to one of Claims 1 to 10, characterized in that the side part of the housing (1) from which the hollow needle (10) protrudes in its extended position has at least one contact

surface (25) for supporting the device during use on the body surface of a patient.

12.

84 Device according to Claim 11, characterized in that the at least one contact surface (25) is designed in such a way that when the device is supported on the body surface of the patient, the hollow needle (10) forms an angle α to the body surface in the support area in the range between 5° and 30° includes.

13.

91 Device according to Claim 12, characterized in that the at least one contact surface (25) is designed such that the angle α between the hollow needle (10) and the body surface when the device is supported on the patient's body surface is adjustable.

14.

97 Device according to one of Claims 11 to 13, characterized in that the contact surface (25) has at least one recess (27) for fixing the blood vessel (B) used for taking blood.

15.

102 Device according to one of Claims 1 to 14, characterized in that the device comprises a plurality of separate inner volumes (3, 4, 28-33) for receiving the blood taken or an adapter arrangement (39) for connecting several containers for receiving blood taken includes.

16.

108 Device according to Claim 15, characterized in that the internal volumes (28, 29, 30) or the containers communicate with one another in series.

17.

113 Device according to Claim 15, characterized in that the inner volumes (31, 32, 33) or the containers communicate with one another in parallel.

(19) BUNDESREPUBLIK DEUTSCHLAND

DEUTSCHES PATENT- UND MARKENAMT

(12) **Offenlegungsschrift**

(10) **DE 100 38 026 A 1**

(51) Int. Cl.[7]:
A 61 B 5/15
A 61 M 1/00

(21) Aktenzeichen: 100 38 026.3
(22) Anmeldetag: 2. 8. 2000
(43) Offenlegungstag: 22. 2. 2001

DE 100 38 026 A 1

(66) Innere Priorität:
299 13 417. 2 06. 08. 1999

(71) Anmelder:
Zierden, Peter, Dr., 40764 Langenfeld, DE

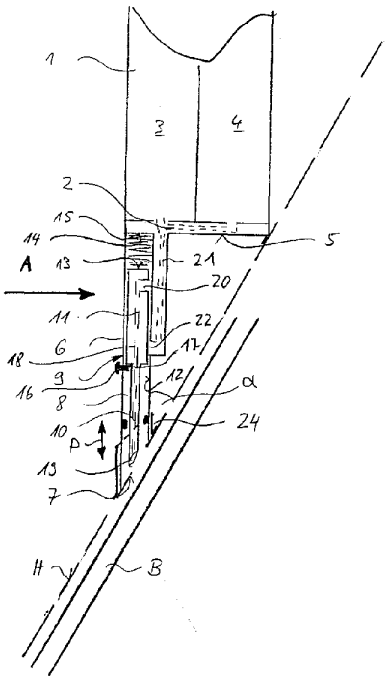
(74) Vertreter:
König · Palgen · Schumacher · Kluin, 40549 Düsseldorf

(72) Erfinder:
Erfinder wird später genannt werden

Die folgenden Angaben sind den vom Anmelder eingereichten Unterlagen entnommen

(54) Vorrichtung zur Entnahme von Blut aus einem Blutgefäß

(57) Die Vorrichtung umfaßt ein Gehäuse mit einer durch die Blutgefäßwandung ins Innere des Blutgefäßes einführbaren Hohlnadel und Mittel zum Saugen des Blutes durch das Innere der Hohlnadel.
Zwecks Blutentnahme aus einem Blutgefäß in für den Patienten weniger schmerzhafter Weise ist die Hohlnadel zwischen einer zurückgezogenen Position, in der die Hohlnadel zumindest im wesentlichen innerhalb der Außenkonturen des Gehäuses verbleibt, und einer ausgefahrenen Position, in der das in das Blutgefäß einführende Ende der Hohlnadel aus dem Gehäuse um eine Länge hervorragt, verlagerbar angeordnet. Ferner sind Mittel vorgesehen, mit denen die Hohlnadel aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist.



DE 100 38 026 A 1

Beschreibung

Die Erfindung bezieht sich auf eine Vorrichtung zur Entnahme von Blut aus einem Blutgefäß der dem Oberbegriff des Anspruchs 1 entsprechenden Art.

Derartige Vorrichtungen umfassen stets eine zur Durchdringung der Haut, des zwischen Haut und Gefäß liegenden Gewebes sowie der Gefäßwandung einenends angeschrägte Hohlnadel, die an ihrem anderen Ende meist mit einer Kupplung ausgestattet ist, welche dem Ansetzen eines ein Volumen zur Aufnahme des entnommenen Blutes aufweisenden Behälters dient.

Zur Erzeugung des zur Blutentnahme erforderlichen Soges ist es bekannt, die Behältnisse als Kolben/Zylinderanordnung auszugestalten, wobei nach erfolgtem Einstich der Hohlnadel in das Blutgefäß und Ankuppeln des Behältnisses der Kolben manuell im Sinne einer Vergrößerung des Gefäßvolumens betätigt wird.

Nachteilig ist bei dieser Vorrichtung, daß ein für den Patienten nahezu schmerzloses Einstechen der Hohlnadel in das Blutgefäß nur bei erheblichem Geschick und erheblicher Übung der den Einstich vornehmenden Person möglich ist. Weiterhin kann bei manueller Betätigung des Kolbens die Nadel in der Regel nicht vollständig ruhig gehalten werden, was dazu führt, daß die Nadel im Einstechbereich die Haut, das darunter liegende Gewebe und die Gefäßwandung dehnt oder sogar verletzt, was regelmäßig zu Schmerzbeeinträchtigungen des Patienten führt.

Aus letzterem Grunde ist es ebenfalls bekannt, die das Volumen zur Aufnahme des entnommenen Blutes aufweisenden Gefäße vorzuevakuieren und in ihrem mit der Kupplung der Hohlnadel zu verbindenden Bereich mit einer Verschluß- bzw. Ventilanordnung auszustatten, die beim Ankuppeln an die Hohlnadel geöffnet wird, so daß das zu entnehmende Blut in das Volumen des Behältnisses eingesaugt wird, ohne daß es hierzu einer zusätzlichen manuellen Betätigung der Vorrichtung bedarf.

Durch diese Maßnahme wird die Gefahr, durch die manuelle Betätigung des Kolbens hervorgerufener "Wackelschmerzen" zwar verhindert, nachteilig ist jedoch, daß das Einstechen der Hohlnadel, das anschließende Ankuppeln des vorevakuierten Gefäßes und das in häufigen Fällen notwendige Auswechseln eines vollen gegen einen leeren Behälter zur Aufnahme des entnommenen Blutes wiederum zu unerwünschten, für den Patienten schmerzhaften Bewegungen der Nadel führt.

Es ist daher die Aufgabe der Erfindung, eine Vorrichtung zu schaffen, welche eine Blutentnahme aus einem Blutgefäß in für den Patienten weniger schmerzhafter Weise ermöglicht.

Diese Aufgabe wird durch die in Anspruch 1 wiedergegebene Erfindung gelöst.

Dadurch, daß bei der erfindungsgemäßen Vorrichtung die Hohlnadel zwischen einer zurückgezogenen Position, in der die Hohlnadel zumindest im wesentlichen innerhalb der Außenkonturen des Gehäuses der Vorrichtung verbleibt, und einer ausgefahrenen Position, in der das in das Blutgefäß einzuführende Ende der Hohlnadel aus dem Gehäuse um eine bestimmte Länge hervorragt, verlagerbar angeordnet ist, und daß Mittel vorgesehen sind, mit denen die Hohlnadel aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist, ist es zum Einstechen der Nadel nicht mehr erforderlich, daß während des Einstechvorganges sowohl die Führung, als auch die Verlagerung der Nadel von der die Blutabnahme durchführenden Person bewerkstelligt werden muß. Vielmehr braucht das Gehäuse lediglich an der Stelle des Körpers, an der die Blutabnahme erfolgen soll, positioniert und anschließend die Mittel zum Ausfahren der Nadel

aktiviert zu werden. Die Gefahr des "Wackelns" während des Einstiches der Hohlnadel ist daher erheblich verringert. Da zudem die Mittel zur Verlagerung der Hohlnadel derart ausgebildet sein können, daß diese mit hoher Geschwindigkeit aus ihrer zurückgezogenen in ihre ausgefahrene Position erfolgt und damit der Einstichvorgang nur eine sehr kurze Zeit dauert, ist der mit der Blutentnahme verbundene Schmerz abermals reduziert. Weiterhin ist vorteilhaft, daß durch die hohe Eindringgeschwindigkeit der Nadel der in dem Blutgefäß zum Verhindern des Kollabierens der Gefäßwandungen beim Einstechen der Nadel erforderliche Druck der meist durch Anlegen einer Druckmanschette bewerkstelligt wird, verringert ist, wodurch das Risiko paravasaler Blutergüsse reduziert ist.

Die Mittel, mit denen die Hohlnadel aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist, weisen vorzugsweise eine Anordnung auf, die auf die Hohlnadel eine in Richtung der zurückgezogenen auf die ausgefahrene Position wirkende, elastische Kraft ausüben. Zur Durchführung des Einstiches wird die Hohlnadel dann zunächst in ihre zurückgezogene Position verlagert, in dieser durch geeignete Mittel, beispielsweise einer Verriegelungseinrichtung, gehalten, und, nachdem die Vorrichtung an die geeignete Stelle des Körpers gebracht wurde, durch Lösen der Mittel, beispielsweise der Verriegelung, in ihre ausgefahrene Position gebracht, wobei die Spitze der Hohlnadel in das Blutgefäß eindringt.

In ihrer konstruktiven Ausgestaltung kann die Anordnung zur Erzeugung der elastischen Kraft eine Druckfeder aufweisen.

Es ist jedoch ebenfalls möglich, die elastische Kraft mit Hilfe eines Druckluftreservoirs oder auch in einer gänzlich anderen Weise zu erzeugen.

Der mit der Blutentnahme für den Patienten verbundene Schmerz kann nochmals verringert werden, wenn das Gehäuse der Vorrichtung mindestens ein Innenvolumen zur Aufnahme des dem Patienten entnommenen Blutes umfaßt. Durch diese Maßnahme wird ein Ankuppeln eines Gefäßes zur Aufnahme entnommenen Blutes nach erfolgtem Einstich überflüssig, so daß "Wackelschmerzen" verhindert werden.

Sollen bereits vorhandene, handelsübliche Behälter weiterhin Verwendung finden, so empfiehlt sich eine Ausführungsform der erfindungsgemäßen Vorrichtung, bei der das Gehäuse eine Adapteranordnung zum Anschluß mindestens eines handelsüblichen Behälters zur Aufnahme entnommenen Blutes umfaßt. Durch diese Ausgestaltung können an den Adapter je nach Anforderungen entweder mehrere Behälter gleichzeitig, oder – falls dies nicht erwünscht oder möglich ist – auch mehrere Behälter nacheinander angeschlossen werden.

Die Mittel zum Saugen des Blutes durch das Innere der Hohlnadel umfassen vorzugsweise einen Unterdruck in dem mindestens einen Innenvolumen gegenüber der äußeren Umgebung. Dieser Unterdruck kann beispielsweise dadurch erzeugt werden, daß das Innenvolumen vorevakuiert ist und das Innere der Hohlnadel in ihrer ausgefahrenen Position mit dem Innenvolumen kommuniziert, mit anderen Worten: daß erst in der ausgefahrenen Position der Hohlnadel die Verbindung deren Inneren mit dem vorevakuierten Innenvolumen erfolgt.

Es ist jedoch ebenfalls möglich, Mittel vorzusehen, die den Unterdruck erst beim Verlagern der Hohlnadel aus ihrer zurückgezogenen in ihre ausgefahrene Position erzeugen, eine manuell oder automatisch betätigbare Kolben/Zylindereinrichtung vorzusehen oder den Unterdruck auf eine beliebige andere Weise zu bewerkstelligen.

Unabhängig davon, auf welche Weise der Unterdruck

zum Saugen des Blutes bewirkt wird, ergeben sich für die Anwendung erhebliche Vorteile, wenn die Vorrichtung derart ausgebildet ist, daß der Unterdruck an der Hohlnadel anliegt, wenn diese in das Blutgefäß eindringt. Durch diese Maßnahme wird nämlich wirkungsvoll verhindert, daß infolge der Blutentnahme schmerzhafte paravasale Blutergüsse (Hämatome) entstehen, was regelmäßig dann der Fall ist, wenn während der Blutentnahme Blut an der Hohlnadel vorbei aus dem Blutgefäß in das angrenzende Gewebe austreten kann. Dadurch, daß der Sog bei dieser bevorzugten Ausführungsform der Erfindung bereits beim Eindringen der Hohlnadel in das Blutgefäß besteht, wird auch Blut, was ansonsten in das Gewebe gelangt wäre, abgesaugt, und zwar selbst dann, wenn die Öffnung der Hohlnadel nicht vollständig in das Gefäß eingedrungen oder teilweise aus der gegenüberliegenden Gefäßwandung wieder ausgetreten ist. Als weitere Folge muß bei dieser Ausführungsform die "Eindringtiefe" der Spitze der Hohlnadel zur Durchführung des Blutentnahmeverfahrens nicht so exakt wie bislang vorgegeben werden, was die Blutentnahme auch dem Anwendungspersonal erleichtert.

Für die Handhabung der erfindungsgemäßen Vorrichtung ist es besonders vorteilhaft, das Seitenteil des Gehäuses, aus dem die Hohlnadel in ihrer ausgefahrenen Position herausragt, mit mindestens einer Anlagefläche zu versehen, über die sich die Vorrichtung während ihrer Verwendung auf der Körperoberfläche eines Patienten abstützt. Die Vorrichtung braucht zur Durchführung des Entnahmevorganges dann lediglich auf eine geeignete Körperstelle aufgesetzt und der Verlagervorgang der Hohlnadel in Gang gesetzt zu werden.

Versuche haben gezeigt, daß der Blutentnahmevorgang besonders zuverlässig und schmerzarm durchgeführt werden kann, wenn die mindestens eine Anlagefläche derart ausgestaltet ist, daß bei Abstützung der Vorrichtung auf der Körperoberfläche des Patienten die Hohlnadel zur Körperoberfläche im Abstützbereich einen Winkel im Bereich zwischen 5° und 30° – je nach Dicke des zwischen der Gefäßwandung, die die Hohlnadel durchdringen soll, und der Abstützfläche befindlichen Gewebes – einschließt.

Besonders variabel einsetzbar ist die erfindungsgemäße Vorrichtung dann, wenn die mindestens eine Anlagefläche derart ausgestaltet ist, daß der Winkel, den die Hohlnadel mit der Körperoberfläche während des Entnahmevorgangs einschließt, einstellbar ist.

Um zu verhindern, daß das jeweils für den Entnahmevorgang vorgesehene Blutgefäß beim Aufsetzen der Vorrichtung seitlich weggedrückt wird, ist bei einer besonders bevorzugten Ausführungsform der erfindungsgemäßen Vorrichtung eine Aussparung in der mindestens einen Anlagefläche vorgesehen, in die das Blutgefäß sich zumindest teilweise hereinwölben kann und somit von den seitlichen Begrenzungsflächen der Aussparung positioniert wird.

Wird Blut eines Patienten zur Durchführung verschiedener Diagnose- bzw. Therapieverfahren benötigt, so ist es von Vorteil, eine Mehrzahl voneinander getrennter Innenvolumina oder eine Adapteranordnung zum Anschluß mehrerer Behälter zur Aufnahme entnommenen Blutes vorzusehen.

Die Innenvolumina oder die Behälter können dann wahlweise seriell oder auch parallel miteinander kommunizieren.

In der Zeichnung sind Ausführungsbeispiele der Erfindung schematisch dargestellt. Es zeigen:

Fig. 1 – ausschnittsweise und schematisch – ein erstes Ausführungsbeispiel einer erfindungsgemäßen Vorrichtung in einem Längsschnitt, wobei sich die Hohlnadel in ihrer zurückgezogenen Position befindet;

Fig. 2 dasselbe Ausführungsbeispiel in derselben Ansicht wie in **Fig.** 1, wobei sich jedoch die Hohlnadel in ihrer ausgefahrenen Position befindet;

Fig. 3 – ausschnittsweise – dasselbe Ausführungsbeispiel wie in **Fig.** 1 in einer teilgeschnittenen Aufsicht (Ansicht A in **Fig.** 1);

Fig. 4 ein anderes Ausführungsbeispiel einer erfindungsgemäßen Vorrichtung in einer **Fig.** 3 entsprechenden Ansicht;

Fig. 5 – schematisch und ausschnittsweise – ein **Fig.** 1 bis 3 entsprechendes Ausführungsbeispiel einer erfindungsgemäßen Vorrichtung während eines Entnahmevorganges in einer Ansicht in Richtung des der Blutentnahme dienenden Blutgefäßes;

Fig. 6 – schematisch – verschiedene Positionen des abgeschrägten Endes der Hohlnadel relativ zur Lage des Blutgefäßes;

Fig. 7 eine Ausführungsform einer erfindungsgemäßen Vorrichtung, die mehrere seriell miteinander kommunizierende Volumina zur Aufnahme entnommenen Blutes umfaßt (schematisch);

Fig. 8 eine Ausführungsform einer erfindungsgemäßen Vorrichtung in einer **Fig.** 7 entsprechenden Ansicht, die mehrere parallel miteinander kommunizierende Innenvolumina zur Aufnahme entnommenen Blutes umfaßt sowie

Fig. 9 eine Ausführungsform einer erfindungsgemäßen Vorrichtung in einer **Fig.** 7 und 8 entsprechenden Ansicht, welche eine Adapterplatte zum Anschluß zweier externer Behältnisse zur Aufnahme entnommenen Bluts aufweist.

Die in den **Fig.** 1 bis 3 als Ganzes mit **100** bezeichnete, in diesen Figuren lediglich ausschnittsweise und schematisch dargestellte Ausführungsform einer erfindungsgemäßen Vorrichtung umfaßt ein Gehäuse **1**, welches in seinem Inneren zwei fluidisch über einen Kanal **2** miteinander verbundene Innenvolumina **3**, **4** zur Aufnahme entnommenen Blutes aufweist. Das Gehäuse **1** weist an seinen **Fig.** 1 nach unten weisenden Stirnseite **5** einen Gehäusefortsatz **6** auf, dessen in **Fig.** 1 unten dargestelltes Ende **7** offen ausgebildet ist.

Das Innere **8** des Gehäusefortsatzes **6** dient der Aufnahme einer als Ganzes mit 9 bezeichneten Hohlnadelanordnung, die im wesentlichen aus der zum offenen Ende **7** hin gerichteten eigentlichen Hohlnadel **10** und einem der verschiebbaren Lagerung der Hohlnadelanordnung **9** in dem Inneren **8** des Gehäusefortsatzes **6** dienenden Hohlnadelträger **11** besteht, der mit der inneren Mantelfläche **12** des Gehäusefortsatzes **6** zumindest annähernd abdichtend zusammenwirkt.

Mit seiner der Hohlnadel **10** abgewandten Stirnseite **13** stützt sich der Hohlnadelträger **11** über eine vorgespannte Spiralfeder **14** an einer starren Anlagefläche **15** des Gehäuses **1** ab.

Der Arretierung der Hohlnadelanordnung **9** gegen die Druckkraft der Spiralfeder **14** in der zurückgezogenen Position dient eine Arretiereinrichtung **16**, die in der zurückgezogenen Position der Hohlnadelanordnung **9** eine der Stirnseite **13** gegenüberliegende Anlagefläche **17** hintergreift.

Die Hohlnadelanordnung **9** weist einen Innenkanal **18** auf, der sich von der Spitze **19** der Hohlnadel **10** bis zu einer seitlichen Öffnung **20** des Hohlnadelträgers **11** erstreckt.

Ferner ist in der in **Fig.** 1 rechts dargestellten Seitenwandung des Gehäusefortsatzes **6** ein einenends in den Kanal **2** mündender Kanal **21** vorgesehen, dessen anderes Ende **22** in das Innere **8** des Gehäusefortsatzes **6** mündet.

Zur Verlagerung der Hohlnadel **10** aus ihrer in **Fig.** 1 dargestellten, zurückgezogenen Position in ihre in **Fig.** 2 dargestellte, ausgefahrene Position wird die Arretiereinrichtung **16** derart verlagert, daß die Anlagefläche **17** freigegeben wird. Durch die von der Spiralfeder **14** auf die Hohlnadelanordnung **9** ausgeübte Kraft schnellt letztere gemäß **Fig.** 2 nach unten, bis die Anlagefläche **17** an einem von der inneren Mantelfläche **12** nach innen ragenden Anschlag **23** anliegt und hierdurch der Verlagerungsweg begrenzt wird. In

dieser Position kommuniziert der Innenkanal **18** über die Öffnung **22** mit dem Kanal **21**, so daß die Innenvolumina **3** und **4** mit dem Innenkanal **18** der Hohlnadel kommunizieren und Blut durch die Kanäle **18**, **21** und **2** in die Innenvolumina **3**, **4** einströmen kann.

Wie ferner aus **Fig.** 2 ersichtlich ist, hat die Hohlnadel **10** mit ihrer Spitze **19** die Haut H im Bereich der Stelle, an der die Hohlnadel **10** in das Blutgefäß B eindringen soll, sowie eine Wandung des Blutgefäßes B durchsetzt.

Wie **Fig.** 6 veranschaulicht, ist eine Blutentnahme nur dann möglich, wenn die Hohlnadel **10** gerade so tief in das Gewebe des Patienten eindringt, daß ihre Spitze weder vor dem Durchdringen der Wandung des Blutgefäßes B zum Stillstand kommt (s. **Fig.** 6a)), noch der zur Spitze **19** hin angeschrägte Bereich der Hohlnadel **10** vollständig durch das Blutgefäß B hindurchragt (vgl. **Fig.** 6e)).

Um die zur Blutentnahme erforderliche "Eindringtiefe" der Spitze **19** der Hohlnadel **10** den individuellen Anforderungen anpassen zu können, ist an dem Gehäusefortsatz **6** eine in Richtung des Pfeiles P verschiebbar gelagerte Manschette **24** vorgesehen, mit der die wirksame Länge des Gehäusefortsatzes **6** und somit die Eindringtiefe der Spitze **19** der Hohlnadel **10** veränderbar ist. Die Manschette **24** und der Gehäusefortsatz **6** können mit in der Zeichnung nicht dargestellten Rastmitteln ausgestattet sein, mit denen sich die Manschette **24** in drei verschiedenen Grundstellungen arretieren läßt, bei denen die Eindringtiefe an die bei Kindern, normalgewichtigen Erwachsenen bzw. übergewichtigen Erwachsenen üblichen Verhältnisse angepaßt ist.

Paravasale Blutergüsse werden auch bei Endpositionen der Hohlnadel **10**, in denen die Spitze **19** nicht vollständig in das Blutgefäß B eingedrungen ist (**Fig.** 6b)) oder die gegenüberliegende Wandung des Blutgefäßes B teilweise durchdrungen hat (**Fig.** 6d)), wirksam verhindert, da der Unterdruck zum Absaugen des Blutes an der Hohlnadel bereits anliegt, sobald diese in das Gefäß eingedrungen ist.

Prinzipiell ist es zwar möglich, den Einstich der Hohlnadel **10** in das Blutgefäß B im wesentlichen senkrecht zu dessen Verlauf vorzunehmen. Eine derartige Vorgehensweise setzt jedoch voraus, daß die "Eindringtiefe" nahezu exakt vorbestimmt werden muß. Um dies zu vermeiden, empfiehlt es sich, die Entnahme unter einem Winkel α zwischen der Hohlnadel **10** und dem Blutgefäß B vorzunehmen, der im Bereich zwischen 5° und 30° liegt. Hierzu weist das in den **Fig.** 1 und 2 dargestellte Ausführungsbeispiel der Erfindung Anlageflächen **25** auf, durch die der gewünschte Winkel α vorgegeben ist. Bei den in der Zeichnung dargestellten Ausführungsbeispielen ist der Winkel α fest eingestellt. Es liegt jedoch ebenfalls im Rahmen der Erfindung, die Anlageflächen derart variabel auszugestalten, daß der Winkel α je nach vorgesehener Anwendungsweise der Vorrichtung veränderbar ist.

Wie bereits beschrieben und in **Fig.** 1 nochmals im einzelnen dargestellt, kann der Erzeugung der die Hohlnadelanordnung aus ihrer zurückgezogenen in ihre ausgefahrene Position vortreibenden Kraft eine Spiralfeder **14** dienen. Es ist – wie in **Fig.** 4 schematisch dargestellt – jedoch ebenfalls möglich, zum Vortrieb ein Druckluftreservoir **26** zwischen der Stirnseite **13** und der Anlagefläche **15** oder andere zur Bewirkung einer elastischen Kraft geeignete Mittel vorzusehen.

Um zu verhindern, daß das Gefäß, aus dem Blut entnommen werden soll, beim Aufsetzen der Vorrichtung **100** seitlich auswandert und der Entnahmevorgang hierdurch vereitelt wird, ist bei einer bevorzugten Ausführungsform der Erfindung in den Anlageflächen eine Aussparung **27** vorgesehen, in die sich das Blutgefäß B nach dem Aufsetzen der Vorrichtung **100** auf die Haut zumindest teilweise eindrückt und somit das Blutgefäß B seitlich in der für die Blutentnahme erforderlichen Position fixiert wird (s. **Fig.** 5).

Wie in den **Fig.** 7 bis 9 verdeutlicht, können erfindungsgemäße Vorrichtungen **100** in unterschiedlicher Weise mit Volumina zur Aufnahme entnommenen Blutes ausgestattet sein. So können mehrere – in **Fig.** 7 drei – Volumina **28**, **29**, **30** in dem Gehäuse **1** vorgesehen sein, die seriell miteinander kommunizieren und somit während des Entnahmevorganges nacheinander mit Blut gefüllt werden.

Ferner ist es möglich, wie in **Fig.** 8 dargestellt, parallel zueinander angeordnete Innenvolumina **31**, **32**, **33** vorzusehen, die dementsprechend etwa zeitparallel zueinander aufgefüllt werden.

Zur Erzeugung des zum Auffüllen erforderlichen Unterdrucks können die Volumina **28** bis **33** vorevakuiert sein, oder der in selbigen erforderliche Unterdruck kann auf eine beliebige andere Weise, beispielsweise durch Verbindung der Volumina mit einer Kolben/Zylindereinheit, einer externen Pumpe usw. erfolgen. Zur Vermeidung paravasaler Blutergüsse ist es lediglich wesentlich, daß der Unterdruck bereits erzeugt ist, wenn die Spitze **19** der Hohlnadel **10** in das Gefäß eindringt.

Bei dem in **Fig.** 9 dargestellten Ausführungsbeispiel sind die zur Aufnahme des entnommenen Blutes vorgesehenen Volumina **34**, **35** extern angeordnet und als Kolben/Zylindereinheiten **36/37** ausgebildet und zwar derart, daß die Kolben **36** durch manuell betätigbare Kolbenstangen **38** in den Zylinder **37** verlagerbar sind. Zur Anbringung der Kolben/Zylindereinheit **36/37** an dieser als Ganzes mit **200** bezeichneten Vorrichtung dient eine Adapteranordnung **39**, von der aus sich gemäß **Fig.** 9 wiederum nach unten der Gehäusefortsatz **206** erstreckt. Die Hohlnadelanordnung **209** und die Kanäle **202** entsprechen in ihrer technischen Ausgestaltung und Funktion der Hohlnadelanordnung **9** und den Kanälen **2**, so wie sie anhand der **Fig.** 1 bis 3 beschrieben sind und bedürfen daher an dieser Stelle keiner besonderen Erörterung.

Die Blutentnahme bei der Vorrichtung gemäß **Fig.** 9 erfolgt in einer anhand von **Fig.** 1 bis 3 bereits beschriebenen Weise, wobei durch Herausziehen der Kolbenstangen **38** in die in **Fig.** 9 dargestellte Position, in der die Kolben **36** durch Arretiervorsprünge **40** an der Innenwandung des Zylinders **37** gegen die Wirkung des Unterdrucks gehalten werden, selbiger vor dem Vorschnellen der Nadel und Eindringen in das Blutgefäß erzeugt wird.

Bezugszeichenliste

1 Gehäuse
2 Kanal
3 Innenvolumen
4 Innenvolumen
5 Stirnseite
6 Gehäusefortsatz
7 Ende
8 Inneres
9 Hohlnadelanordnung
10 Hohlnadel
11 Hohlnadelträger
12 innere Mantelfläche
13 Stirnseite
14 Spiralfeder
15 Anlagefläche
16 Arretiereinrichtung
17 Anlagefläche
18 Innenkanal
19 Spitze
20 Öffnung

21 Kanal
22 Ende
23 Anschlag
24 Manschette
25 Anlagefläche
26 Druckluftreservoir
27 Aussparung
28 Volumen
29 Volumen
30 Volumen
31 Volumen
32 Volumen
33 Volumen
34 Volumen
35 Volumen
36 Kolben
37 Zylinder
38 Kolbenstangen
39 Adapteranordnung
40 Arretiervorsprünge
100 Vorrichtung
206 Gehäusefortsatz
209 Hohlnadelanordnung
202 Kanäle
H Haut
B Blutgefäß
A Ansicht
P Pfeil

Patentansprüche

1. Vorrichtung zur Entnahme von Blut aus einem Blutgefäß (B),
mit einem Gehäuse (**1**),
mit einer durch die Blutgefäßwandung ins Innere des Blutgefäßes (B) einführbaren Hohlnadel (**10**),
und mit Mitteln zum Saugen des Bluts durch das Innere der Hohlnadel, **dadurch gekennzeichnet**,
daß die Hohlnadel (**10**) zwischen einer zurückgezogenen Position, in der die Hohlnadel (**10**) zumindest im wesentlichen innerhalb der Außenkonturen des Gehäuses verbleibt, und einer ausgefahrenen Position, in der das in das Blutgefäß (B) einzuführende Ende (**19**) der Hohlnadel (**10**) aus dem Gehäuse um eine Länge hervorragt, verlagerbar angeordnet ist, und
daß Mittel vorgesehen sind, mit denen die Hohlnadel (**10**) aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist.

2. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß die Mittel, mit denen die Hohlnadel (**10**) aus ihrer zurückgezogenen in ihre ausgefahrene Position verlagerbar ist, eine Anordnung umfassen, die auf die Hohlnadel (**10**) eine in Richtung von der zurückgezogenen auf die ausgefahrene Position wirkende, elastische Kraft ausüben.

3. Vorrichtung nach Anspruch 2, dadurch gekennzeichnet, daß die Anordnung eine Druckfeder (**14**) aufweist.

4. Vorrichtung nach Anspruch 2 oder 3, dadurch gekennzeichnet, daß die Anordnung ein Druckluftreservoir (**26**) aufweist.

5. Vorrichtung nach einem der Ansprüche 1 bis 4, dadurch gekennzeichnet, daß das Gehäuse (**1**) mindestens ein Innenvolumen (**3**, **4**, **28–35**) zur Aufnahme entnommenen Blutes umfaßt.

6. Vorrichtung nach einem der Ansprüche 1 bis 4, dadurch gekennzeichnet, daß das Gehäuse (**1**) eine Adapteranordnung (**39**) zum Anschluß mindestens eines Behälters umfaßt, dessen Innenvolumen (**34**, **35**) zur Aufnahme von entnommenem Blut dient.

7. Vorrichtung nach Anspruch 5 oder 6, dadurch gekennzeichnet, daß die Mittel zum Saugen des Blutes durch das Innere der Hohlnadeln (**10**) einen Unterdruck in dem mindestens einen Innenvolumen (**3**, **4**, **28–35**) gegenüber der äußeren Umgebung umfassen.

8. Vorrichtung nach Anspruch 7, dadurch gekennzeichnet, daß das Innenvolumen (**3**, **4**, **28–35**) vorevakuiert ist und daß das Innere der Hohlnadel (**10**) in ihrer ausgefahrenen Position mit dem Innenvolumen (**3**, **4**, **28–35**) kommuniziert.

9. Vorrichtung nach Anspruch 7, dadurch gekennzeichnet, daß Mittel vorgesehen sind, die beim Verlagern der Hohlnadel (**10**) aus ihrer zurückgezogenen in ihre ausgefahrene Position den Unterdruck in dem Innenvolumen (**3**, **4**, **28–35**) erzeugen.

10. Vorrichtung nach Anspruch 9, dadurch gekennzeichnet, daß Mittel zur Erzeugung des Unterdrucks eine mit der Hohlnadel (**10**) verbundene Kolbenanordnung, die beim Verlagern der Hohlnadel (**10**) in ihre ausgefahrene Position in einer Zylinderanordnung einen Unterdruck erzeugt, und Mittel, die in der ausgefahrenen Position der Hohlnadel (**10**) das Innere des Zylinders mit dem Innenvolumen (**3**, **4**, **28–35**) zur Aufnahme des Bluts verbindet, umfaßt.

11. Vorrichtung nach einem der Ansprüche 1 bis 10, dadurch gekennzeichnet, daß das Seitenteil des Gehäuses (**1**), aus dem die Hohlnadel (**10**) in ihrer ausgefahrenen Position herausragt, mindestens eine Anlagefläche (**25**) zur Abstützung der Vorrichtung während ihrer Verwendung auf der Körperoberfläche eines Patienten aufweist.

12. Vorrichtung nach Anspruch 11, dadurch gekennzeichnet, daß die mindestens eine Anlagefläche (**25**) derart ausgestaltet ist, daß bei Abstützung der Vorrichtung auf der Körperoberfläche des Patienten die Hohlnadel (**10**) zur Körperoberfläche im Abstützbereich einen Winkel α im Bereich zwischen 5° und 30° einschließt.

13. Vorrichtung nach Anspruch 12, dadurch gekennzeichnet, daß die mindestens eine Anlagefläche (**25**) derart ausgestaltet ist, daß der Winkel α, den die Hohlnadel (**10**) mit der Körperoberfläche bei Abstützung der Vorrichtung auf der Körperoberfläche des Patienten aufweist, einstellbar ist.

14. Vorrichtung nach einem der Ansprüche 11 bis 13, dadurch gekennzeichnet, daß die Anlagefläche (**25**) mindestens eine Aussparung (**27**) zur Fixierung des der Blutentnahme dienenden Blutgefäßes (B) aufweist.

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

16. Vorrichtung nach Anspruch 15, dadurch gekennzeichnet, daß die Innenvolumina (**28**, **29**, **30**) oder die Behälter seriell miteinander kommunizieren.

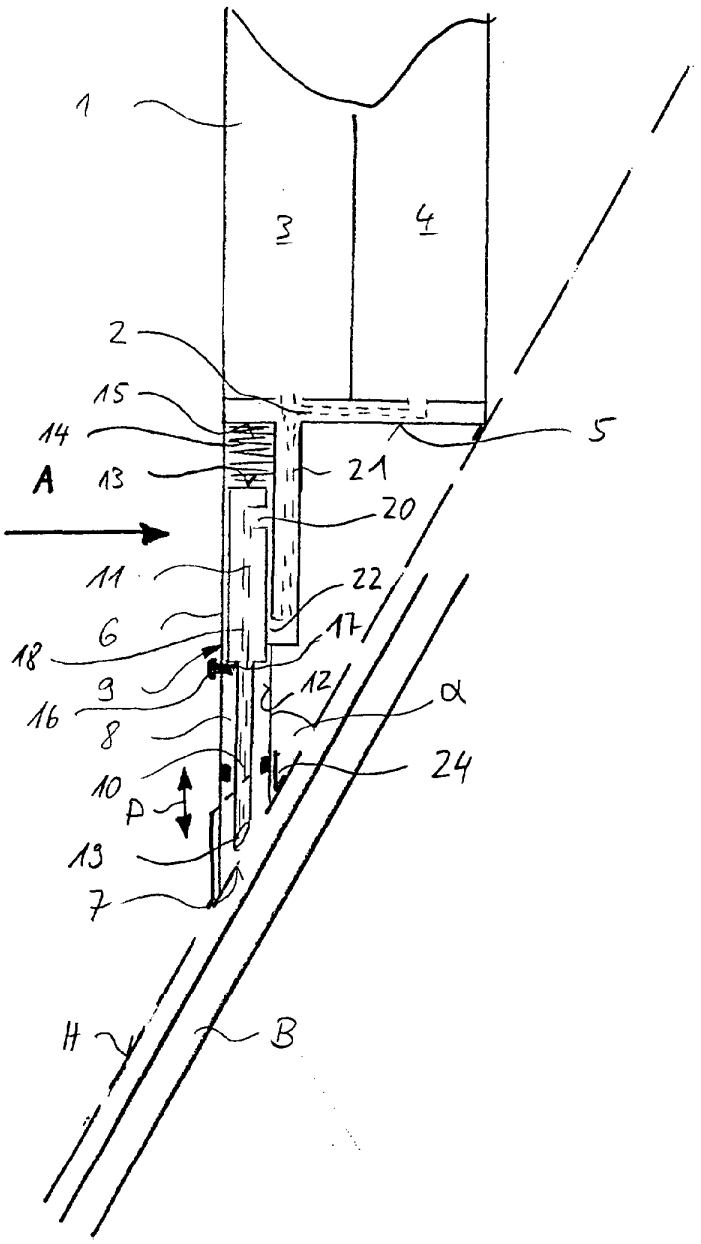
17. Vorrichtung nach Anspruch 15, dadurch gekennzeichnet, daß die Innenvolumina (**31**, **32**, **33**) oder die Behälter parallel miteinander kommunizieren.

Hierzu 6 Seite(n) Zeichnungen

- Leerseite -

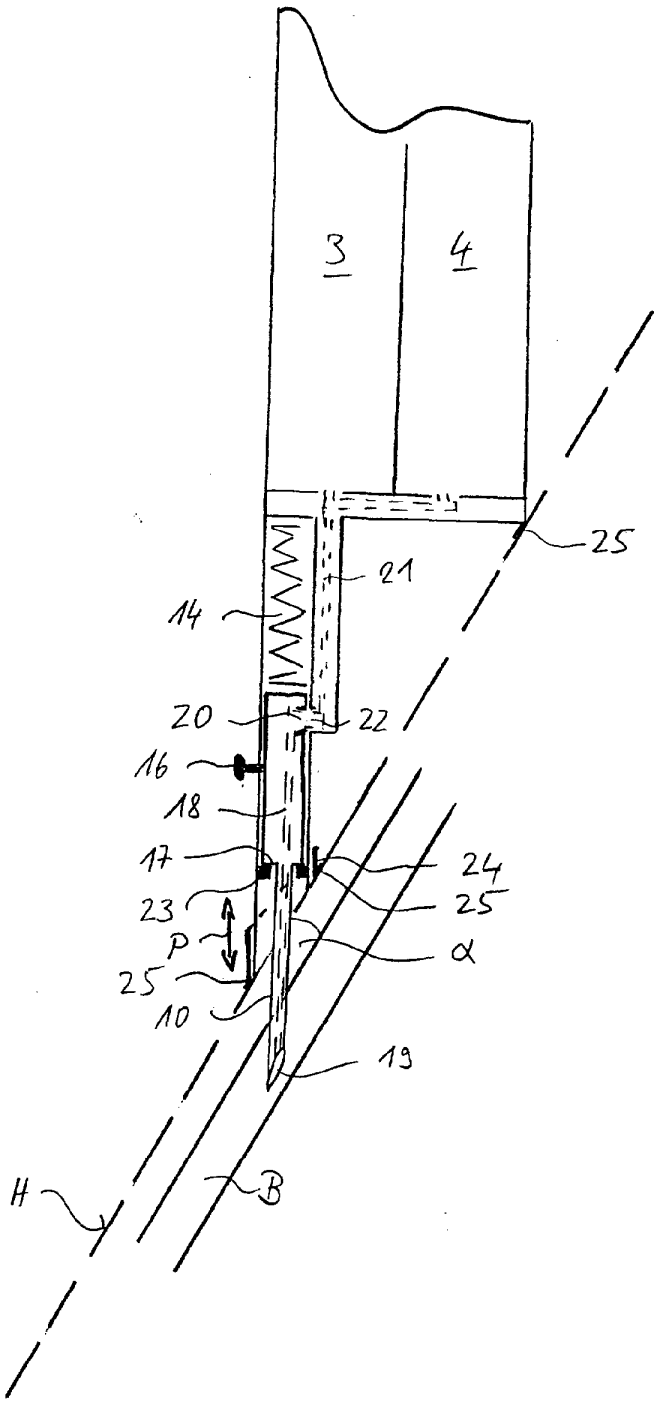
Nummer: **DE 100 38 026 A1**
Int. Cl.[7]: **A 61 B 5/15**
Offenlegungstag: 22. Februar 2001

Fig. 1



Nummer: **DE 100 38 026 A1**
Int. Cl.[7]: **A 61 B 5/15**
Offenlegungstag: 22. Februar 2001

Fig. 2



Nummer: **DE 100 38 026 A1**
Int. Cl.[7]: **A 61 B 5/15**
Offenlegungstag: 22. Februar 2001

Fig. 3

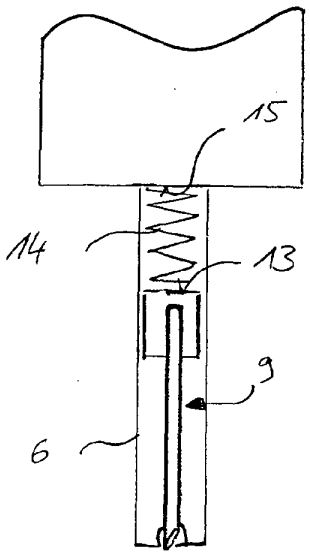
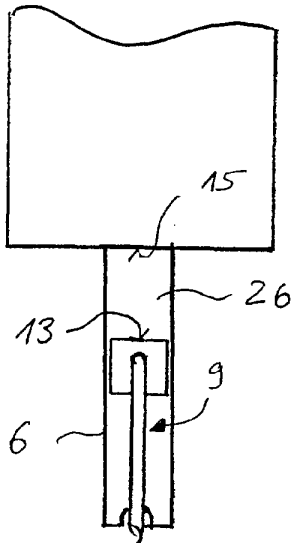


Fig. 4



Nummer: **DE 100 38 026 A1**
Int. Cl.[7]: **A 61 B 5/15**
Offenlegungstag: 22. Februar 2001

Fig. 5

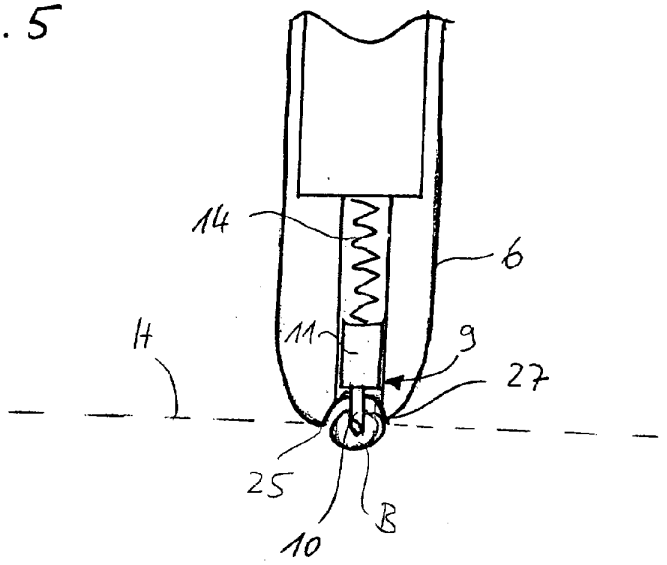
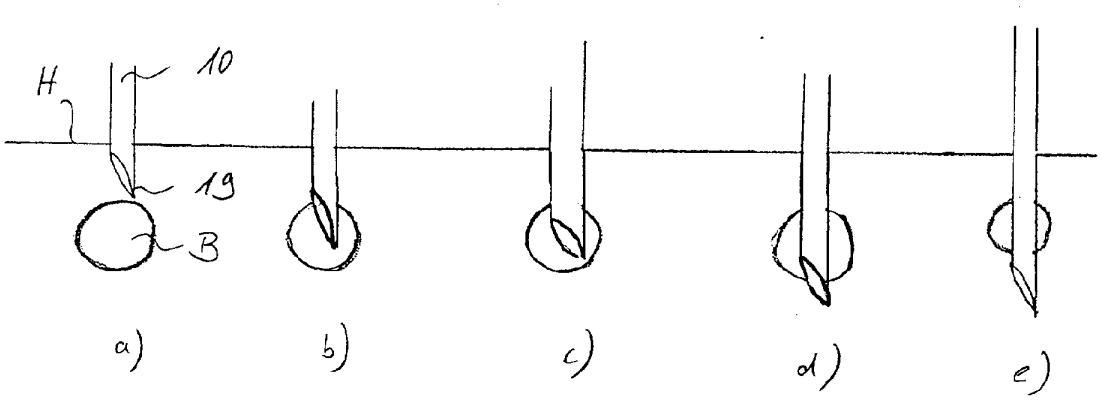


Fig. 6



Nummer: **DE 100 38 026 A1**
Int. Cl.[7]: **A 61 B 5/15**
Offenlegungstag: 22. Februar 2001

Fig. 7

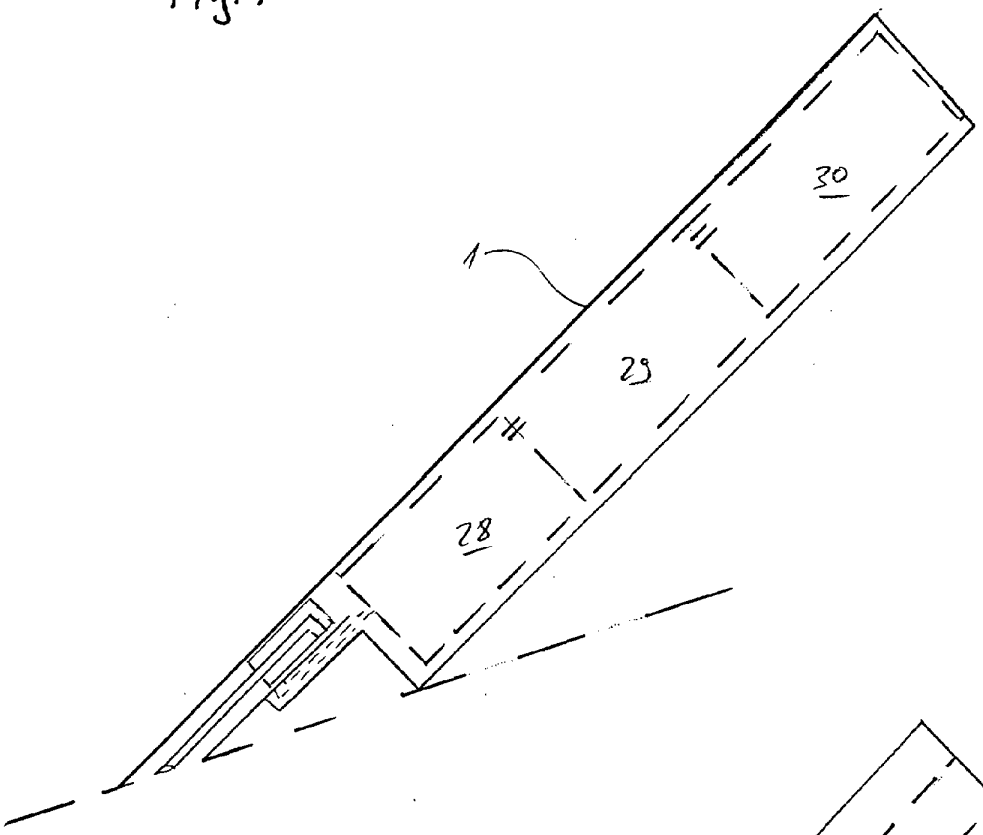
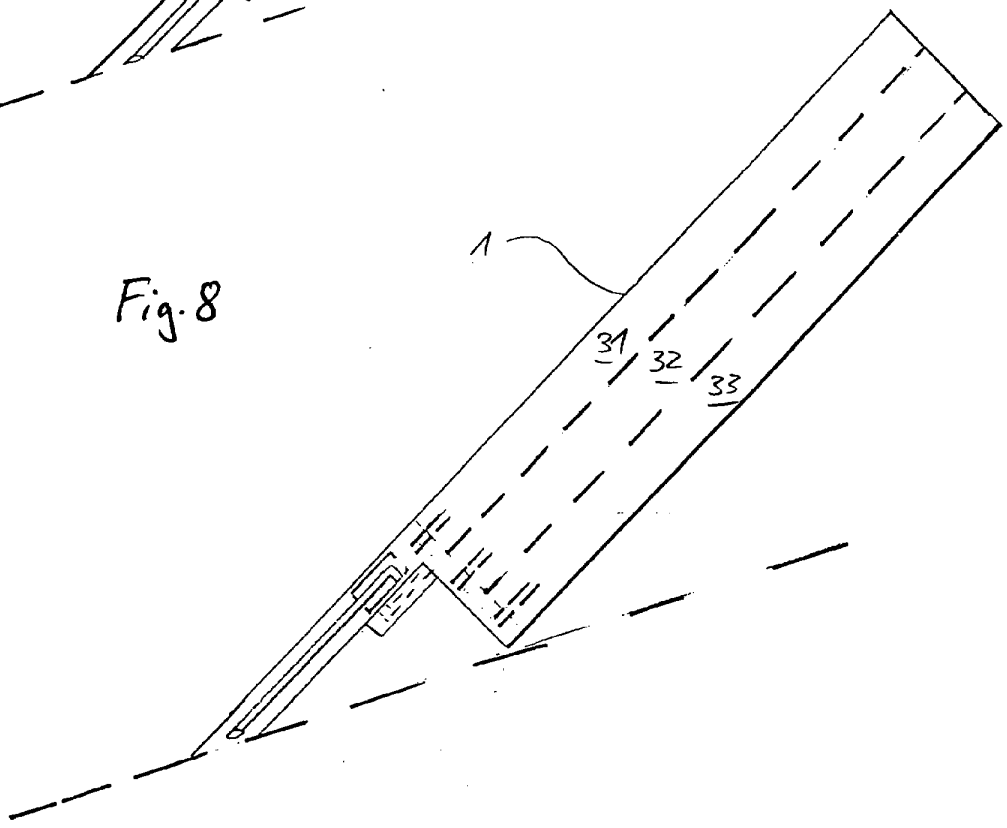


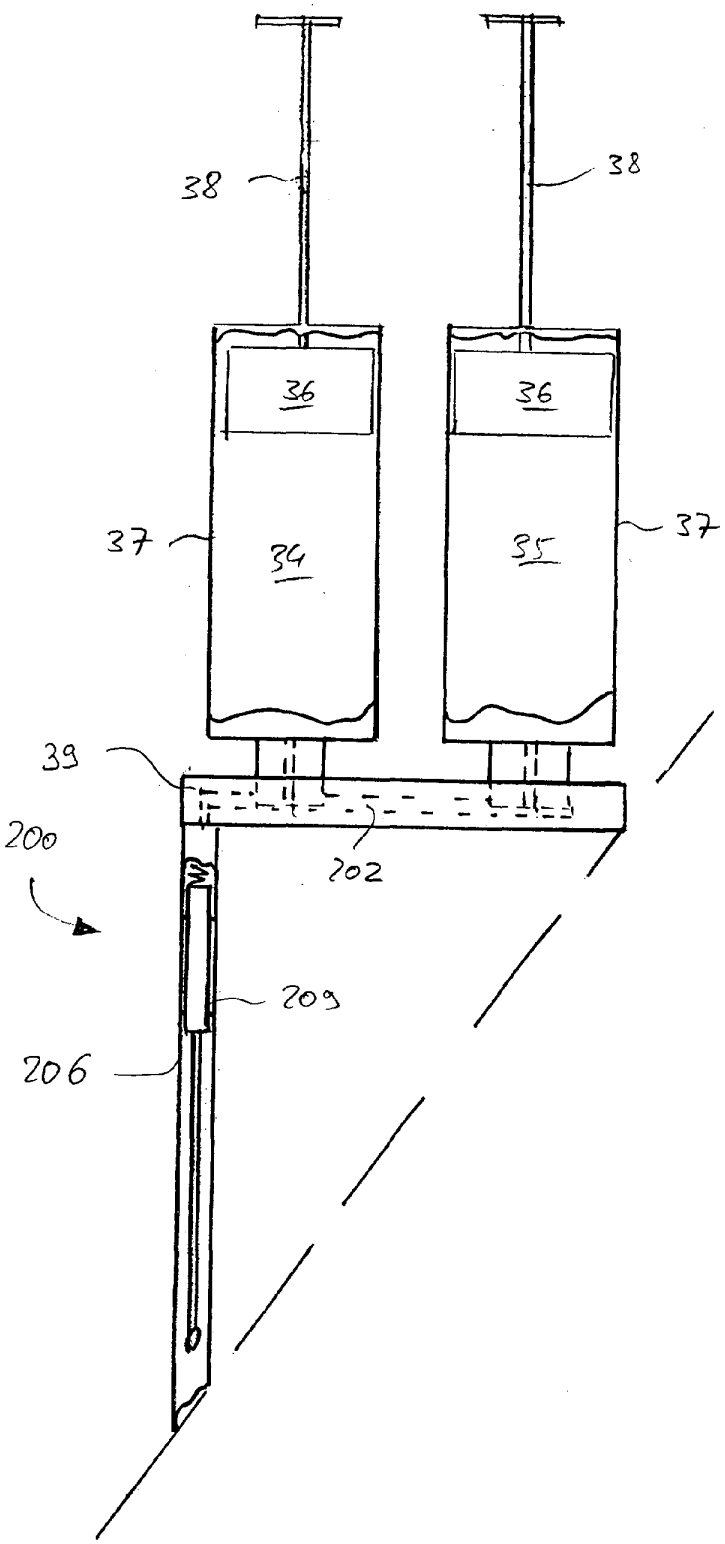
Fig. 8



002 068/115

Nummer: **DE 100 38 026 A1**
Int. Cl.[7]: **A 61 B 5/15**
Offenlegungstag: 22. Februar 2001

Fig. 9



Reduction of the risk of bacterial contamination of blood components through diversion of the first part of the donation of blood and blood components

Giancarlo Maria Liumbruno[1,2], Liviana Catalano[1], Vanessa Piccinini[1], Simonetta Pupella[1], Giuliano Grazzini[1]

[1]Centro Nazionale Sangue, Istituto Superiore di Sanità, Roma; [2]UU. OO. CC. di Immunoematologia e Medicina Trasfusionale e di Patologia Clinica, Ospedale "San Giovanni Calibita" Fatebenefratelli, Roma, Italy

Introduction

The level of safety of transfusion therapy is now very high thanks to the combination of serological methods and genomic amplification used to screen for transmissible diseases and the meticulous care with which repeat, voluntary, unpaid donors are selected[1-4].

The main risk of transfusion-related infectious diseases is currently that of bacterial sepsis[1,3-5]. The risk of bacterial contamination of blood components is, in fact, estimated to be about three orders of magnitude greater than that of post-transfusional HIV and HCV infections[5,6]; the risk of bacterial sepsis causes by the transfusion of platelets is more than two orders of magnitude greater than the risk of the same viral infections[5,6].

According to a study published in 2004[7], the year in which bacteriological screening tests for platelet units were introduced in the USA[3,8,9], the average prevalence of bacterial contamination in platelets from whole blood was 33.9/100,000 units, that of platelets from apheresis 51/100,000, while that of red cell concentrates was 2.6/100,000. The overall prevalence of bacterial contamination of units of cellular blood components was, therefore, about 1 in 3,000 donations (33.3/100,000)[7,10].

Table I reports the data on bacterial contamination of units of platelets and red blood cells derived from studies before 2003[11-19]. More recent estimates indicate that bacterial culture tests on units of platelets are positive, and confirmed as such, in about 1 in 5,000 units (20/100,000)[4]. The risk of receiving platelet concentrates contaminated by bacteria is, therefore, considerably higher than the risk of post-transfusion infection by HIV, HCV, HBV and HTLV[3,4].

Prior to the introduction of bacteriological screening tests[20], transfusion-related sepsis occurred after approximately 1 in 25,000 transfusions of platelet concentrates and 1 in 250,000 transfusions of red cells[5,7,20].

In the USA, where about 14 million units of red cells are transfused each year, in the period from 1976 to 1998, there were reports of 26 deaths due to bacterial contamination of this blood component, with an incidence, therefore, of just over one case per year[21,22]. More recently, still in the USA, analysis of data from 1998 to 2000 indicated that the incidence of fatal events was 1 case per 8,000,000 units of transfused red blood cells[23]. At the other end of the scale, the incidence of fatal events reported in New Zealand is 1 for every 104,000 units of transfused red cells[21].

According to North American studies, deaths following the transfusion of platelets are more frequent and occur after 1 in 50,000-500,000 transfusions[23,24].

Analysis of haemovigilance data from the United Kingdom, France and USA indicate that the mortality risk due to sepsis following transfusion of platelets is 1 case per 7,500-100,000 units transfused[21].

The contamination of platelets is easier and more common than that of red cells because of the storage temperature of platelets (20-24 °C), which favours the proliferation of bacteria, unlike the storage temperature of red cells, which is 2-6 °C[25,26]. Fresh-frozen plasma, precisely because of its storage conditions[25,26], is rarely contaminated by bacteria; on the other hand, this product can be contaminated during the thawing process in inadequately sterilised equipment[21].

The published mortality rates due to sepsis from bacterial contamination of transfused units of blood components vary in the different series: this is probably because of unrecognised and/or not reported cases and because of variations in the incidence in

Blood Transfus 2009; 7: 86-93 DOI 10.2450/2008.0026-08
© SIMTI Servizi Srl

Table I - Prevalence of bacterial contamination of cellular blood components recorded in studies before 2003

Type of blood component	Reference	Year of publication	Number of positive units	Number of units tested	Prevalence per 100,000 units
Platelets from whole blood	Barrett BB[11]	1993	1	4,272	23.4
	Yomtovian R[12]	1993	6	14,481	41.4
	Chiu EKW[13]	1994	10	21,503	46.5
	Blajchman MA[14]	1994	16	31,610	50.6
	Leiby DA[15]	1997	4	4,995	80.1
	Blajchman MA[16]	1997	7	10,065	69.5
Total			44	86,926	50.6
Platelets from apheresis	Blajchman MA[17]	1992	14	6,055	231.2
	Barrett BB[11]	1993	5	17,928	27.9
	Yomtovian R[12]	1993	0	2,476	0.0
	Dzieczkowski JS[18]	1995	1	5,197	19.2
	AuBuchon JP[19]	2002	1	2,678	37.3
Total			21	34,334	61.2
Red blood cell concentrates	Barrett BB[11]	1993	1	31,385	3.2
	Dzieczkowski JS[18]	1995	1	7,080	14.1
Total			2	38,465	5.2
Overall total			**67**	**159,725**	**41.9**

the context of different national epidemiological situations[21].

The aim of this review is to consider the scientific evidence supporting the efficacy of diversion of the first part of the blood collected in preventing bacterial contamination of blood components.

Source of contamination of blood components and prevention strategies

It is not always easy to identify the source of bacterial contamination of blood components. The contamination can be due to endogenous causes, such as asymptomatic bacteraemia in the donor, including transient episodes or due to exogenous causes, mainly related to contamination by transient or commensal bacterial flora present on the skin of the donor's arm or to contamination of the collection bags/kits and/or the blood component itself during the production process and/or storage[27,28]. In these latter cases, prevention is based on applying the principles of "good manufacturing practice", using sterile, closed collection systems and maintaining scrupulous hygiene of areas dedicated to the processing and storage of blood and blood components as well as the areas in which the materials used for the collection are stored.

Diversion of the first part of the blood collected is one of the interventions that can prevent the contamination of blood components caused by the introduction of skin bacteria into units of whole blood or blood components from apheresis at the time of venipuncture. Indeed, the major source of bacterial contamination is the donor's skin and disinfection, even if carried out very carefully thus reducing the bacterial load present on the superficial layers of the skin, cannot act on the deeper layers. The introduction of a needle through the skin to collect blood causes, in 65% of all cases[29], the passage of skin fragments containing live microbes or the movement of microbes from small skin flaps produced by the needle itself into the collection bags[30]. Furthermore, it is even more difficult to achieve satisfactory disinfection of a skin surface that has become irregular due to scars from previous donations[28].

The aim of diverting the first part of the blood collected into a collateral bag, used for the performance of tests of biological validation of the unit donated, is precisely that of preventing the initial flow of blood, containing microbes or skin fragments from the donor, from entering the collection bag and thus contaminating it[28,29,31,32].

Diversion of the first part of the blood

The diversion of the first 10-50 mL of donated blood, with the aim of preventing microbes or skin fragments from entering the collection bag, has been the object of

numerous studies from 1995 onwards[33-47].

Olthuis *et al.* were the first, in 1995, to demonstrate that the first 10 mL of blood, collected at the beginning of a plasmapheresis procedure with an open system, were more frequently contaminated by bacteria than were the subsequently collected 10 mL[34]; indeed, diversion of the first part of the donation guaranteed an 88% reduction in the percentage of bacterial contamination[28].

In the same year, using an experimental model, Figueroa showed that most of the bacteria (100 colony-forming units of *Staphylococcus aureus*) inoculated in the lumen of a collection needle entered the first 10 mL of fluid that it collected; this demonstrated, experimentally, that the diversion of the first 10 mL of blood collected could reduce the bacterial load of skin contaminants in the blood/blood component collected[35].

In 2000, Wagner *et al.*, also using an *in vitro* experimental model, demonstrated that diversion of the first 21-42 mL of physiological saline or whole blood reduced the load of colonies of *Staphylococcus aureus*, deliberately inoculated on the collection surface, by about 1 log[36]. This confirmed that a diversion system for the collection of samples of blood, before filling the collection bags, would be able to reduce the bacterial load in blood components subsequently produced from whole blood and, therefore, the incidence of sepsis due to cutaneous microbes.

In 2001, Cecile Bruneau's group in France published the results of a multicentre study[37] on new collection bags, specifically modified by the manufacturer (Maco Pharma, Tourcoing, France), which added two consecutive satellite bags, each containing 15 mL, to the collection line with the aim of comparing bacterial contamination between the first and second 15 mL of blood collected. The authors demonstrated that diversion of the first 15 mL reduced the bacterial contamination of the units of blood by 72% and that using the first 30 mL of blood to carry out the tests of biological validation of the units further reduced the potential bacterial load within the bags of whole blood.

Again in France, in 2002, Schneider's group obtained a 58% reduction in the contamination of platelet concentrates (PCs) from buffy coat (BC) pools by using diversion of the first part of the blood collected[38]; contemporaneously, in the Netherlands, Bos *et al.* obtained a 53% reduction of contamination of the same blood component[39].

In the same country, the use of blood bags supplied with diversion bags showed that the diversion of the first 20 mL of blood reduced the bacterial contamination of PCs from BC pools from 1% to 0.4% (- 60%)[40].

A subsequent multicentre, prospective clinical study, whose results were published in 2002 by Dirk de Korte's group from the Netherlands, demonstrated that the diversion of the first 10 mL of the donation enabled a statistically significant, 40% reduction in the percentage of contaminated whole blood units, compared to that of the standard collection without diversion[41]; consequently, there was also a statistically significant reduction (from 0.14% to 0.03% - $p<0.02$) in the frequency of staphylococcal contamination of units.

On the basis of these results in the Netherlands, since July 1, 2004, diversion of the first 20-30 mL of blood (used for validation tests of the units) has become obligatory for all whole blood and apheresis donations and this produced, on a national scale, a 59% reduction in bacterial contamination of PCs from BC pools already after 1 year[42].

In 2006, the same Dutch group published the results of another prospective, multicentre clinical study carried out between 2002 and 2003, in which they evaluated the effect of skin disinfection techniques, diversion bags, and bacterial detection tests on the contamination of more than 110,000 PCs from BC pools[43]. Diversion of the first 20-30 mL of blood was associated with a statistically significant reduction in the bacterial contamination of this blood component of 47% with the "old disinfection technique" and of 54% with the "new disinfection technique" (isopropylic alcohol 70%). Furthermore, the diversion caused a statistically significant reduction in contamination due to microbes of cutaneous origin.

More recent data from the same country, updated to 2007, but currently available only in abstract form, confirm the efficacy of the strategy adopted in 2004[44]; indeed, before diversion was obligatory, the rate of bacterial contamination among 127,797 PCs from BC pools was 0.90%, while the rate in 147,021 PCs produced after July 1, 2004, had fallen to 0.46% (- 49%). The strategy of diversion also caused:

a) a 35% reduction in the units transfused and found,

Blood Transfus 2009; 7: 86-93 DOI 10.2450/2008.0026-08

KUR-MAG-DE005077

subsequently, to be positive in culture tests;

b) a reduction (from 40% to 25%) of the frequency of contamination of red cell concentrates produced from the units from which the PCs from BC pools positive for bacterial contamination originated. The bacterial strains on which the diversion had the greatest effect were diphtheroids and coagulase-negative staphylococci.

A prospective study on units of whole blood, carried out in the United Kingdom and published in 2004 by McDonald, showed that diversion of the first 20 mL of blood produced a 47% reduction in bacterial contamination[45].

A statistically significant reduction (p = 0.005) in bacterial contamination of PCs from whole blood was also found in a Canadian study by Robillard[46], who analysed the data produced by the local haemovigilance system. In Canada the diversion of the first 40 mL of blood, introduced in February 2003, caused, in 2004, a 90% reduction in the bacterial contamination of PCs from whole blood; this result was confirmed by the data updated to the following year, in which no PCs, from either whole blood or apheresis, were found to be contaminated by bacteria[47].

In a study recently performed in the USA on bacterial contamination of platelets from apheresis[33], it was found that the bacterial contamination of PCs produced by single-needle cell separators was 47% lower than that of PCs produced by double-needle separators. The lower rate of bacterial contamination of the PCs produced by the former is explained by the different configuration of the two types of cell separators. In the double-needle separators, the sample for tests of biological validation is taken from the reinfusion line and there is not, therefore, diversion of the first amount of blood taken; in contrast, in the single-needle separators, the initial sample (40-50 mL) for haematological and biochemical investigations is taken from the collection line, thus preventing this blood from contaminating the collection kit and blood component produced.

Table II summarises the main studies on diversion, some of which are only available in abstract form, the amount of blood diverted and the percentage reduction in bacterial contamination obtained in the blood components under analysis.

Conclusions

Post-transfusion sepsis is the most common cause of death due to infectious agents[30,48].

According to data from SHOT (Serious Hazards Of Transfusion)[49], the haemovigilance system in the United Kingdom, in the period 1995-2006, there were 33 cases of post-transfusion bacterial sepsis, 29 of which (88%) were due to treatment with platelets (10 cases due to platelets from apheresis and 19 to platelets from pools) and four due to treatment with red cell concentrates. In the same period, there were no deaths due to post-transfusion infections with hepatitis viruses, HIV or HTLV-I, while eight deaths were caused by bacterial contamination of transfused

Table II - Reduction of the percentage of bacterial contamination of blood components achieved with different volumes of diversion in studies from 1995 to 2007

Reference	Year of publication	Country	Production procedure/ blood component analysed	Volume of diversion (mL)	Reduction of contamination of the blood components (%)
Olthuis H[34]	1995	The Netherlands	Plasmapheresis	10	88
Bruneau C[37]	2001	France	Whole blood	15 (+15)	72
Schneider T[38]	2002	France	PC from BC pools	Not stated	58
Bos H[39]	2002	The Netherlands	PC from BC pools	10	53
Yedema T[40]	2003	The Netherlands	PC from BC pools	20	60
de Korte D[41]	2002	The Netherlands	Whole blood	10	40
McDonald CP[45]	2004	United Kingdom	Whole blood	20	47
Robillard P[46]	2005	Canada	PC from whole blood	40	90
De Korte D[44]	2007	The Netherlands	PC from BC pools	20-30	49
Eder AF[33]	2007	USA	Platelets from apheresis	40-50	47

PC, platelet concentrates; BC, buffy coat.

platelets. This puts platelet transfusion-related sepsis alongside transfusion-related acute lung injury (TRALI) as the second most frequent cause of transfusion-related death, after post-transfusion graft-versus-host disease[48,49].

The frequency of clinical symptoms following transfusion of platelets contaminated by bacteria varies greatly; indeed, the reported range extends from a frequency of 1 case per 358 transfusions of platelets from whole blood[13], reported in a study from 1994, to the considerably lower value of 1 case per 73,000 transfusions of platelets from single donors[24], reported in a study from 2001. This latter result is completely in line with the findings of the American Red Cross[33] that, between 2004 and 2006, the residual risk of septic reactions to platelets from apheresis was 1 case per 74,807 units, and the residual risk of fatal reactions was 1 case per 498,711 units distributed.

This broad variability depends on the criteria and methods used to collect the data and is also influenced by the method used to produce the PC (from single units or pools, from BC or from platelet-rich plasma, or from apheresis) and whether strategies to divert the first part of the blood collected had been introduced[50].

The technique of diverting the first 20-40 mL of blood at the beginning of the donation of whole blood or blood components from apheresis is relatively simple and has no effect on the donor, since this is the quantity of blood that is normally taken to carry out the tests necessary for the biological validation of the unit donated.

The data from the studies analysed demonstrate the fundamental role that this modification to the collection process can have on reducing the rate of bacterial contamination of blood components: indeed, the percentage of contaminated blood components is decreased by 40-90%. The range in the reduction is probably due to differences in criteria for collecting and analysing the data and in the production processes of the blood components examined in the various studies.

In the United Kingdom, the introduction of diversion was already suggested in the SHOT report of 2002 as one of the strategies to use to reduce the risk of bacterial contamination of blood components[49]; in the same year, this measure was made obligatory in Germany[51] and other countries, including France, the Netherlands and Canada, subsequently adopted this modification of the production process of blood components[5,16,52], with manufacturers of blood bags and apheresis collection kits adapting their products to meet the circumstances. In Italy, the legislation on transfusion matters was recently integrated by Legislative Decree 208 of November 9, 2007[53]; this decree transposes Commission Directive 2005/62/EC of 30 September 2005, implementing Directive 2002/98/EC of the European Parliament and the Council as regards Community standards and specifications relating to a quality system for blood establishments, and sets out that "the procedures for collecting blood must minimise the risk of microbial contamination".

The frequency of bacterial contamination of platelets is influenced by the technique used to produce them[51]; the rate of contamination of platelets from single donors or from apheresis is significantly lower than that of PCs produced from pools. The predominant source of micro-organisms responsible for the contamination of PCs is the skin flora[51,54]. Most deaths are, however, caused by the transfusion of blood components contaminated by Gram-negative bacteria[23], predominantly of intestinal origin, responsible for asymptomatic bacteraemia in the donor, on which diversion, obviously, is not effective. The frequency of donations made during asymptomatic bacteraemia can be reduced by rigorously applying the selection criteria set out in the protocols for determining the suitability of donors of blood and blood components[55] and, during the selection process, encouraging donors to report any changes of health that occur in the period immediately after the donation[54].

Although the effect of diversion is limited to micro-organisms originating from the skin, such as coagulase-negative staphylococci, it is hoped that this strategy is applied extensively to both the collection of whole blood and apheresis collections[41,56,57].

In France[52], a statistically significant reduction in the rate of bacterial contamination of blood components was achieved through the combined action of a series of strategies aimed at preventing or reducing the initial contamination of the blood component (better skin disinfection techniques, care with regards to the personal hygiene of the staff collecting the donations, diversion, active reporting by donors of any changes in health after the donation), and the proliferation of microbes within it (meticulous control of the storage temperature of blood

Blood Transfus 2009; 7: 86-93 DOI 10.2450/2008.0026-08

KUR-MAG-DE005079

components, universal leucoreduction, separation of whole blood after 2-20 hours, transfusion of platelets stored for less than 3 days), as well as through constant improvement in scientific knowledge on the subject (production of guidelines on the management of post-transfusion bacterial infections and promotion of specific research on the subject). The implementation of these preventive measures at various stages of the production process led, at a national level, to a significant reduction in the risk of post-transfusion bacterial infection and provided results equivalent to those of other countries that privileged the use of diagnostic tests to detect bacterial contamination. The limitation of such diagnostic tests is the considerable percentage (about 50%) of false negative cultures at 24-48 hours[52,58,59]; these results are responsible for an estimated global residual risk of septic reactions of about 1/45,000 transfusions (2.2/100,000) and led, on January 29, 2008, to the premature interruption of the phase IV study, "PASSPORT" ("*Post-Approval Surveillance Study of Platelet Outcomes, Release Tested*")[60], the outcome of an agreement between Gambro BCT (Lakewood, CO, USA) and Fenwal Inc. (Lake Zurich, IL, USA). "PASSPORT" had the aim of validating the clinical use of platelets from apheresis produced by cell separators from two companies [Trima Accel, COBE Spectra (Gambro BCT) and AMICUS (Fenwal)], stored for up to 7 days and transfused after having been found to be negative for bacterial contamination according to a screening test (BacT/ALERT - bioMéricux SA, Marcy l'Etoile, France).

In conclusion, a global strategy of minimising post-transfusion bacterial infections must include the adoption of multiple preventive measures, such as those analysed in an article by George Andreau[52], as well as diagnostic tests and could also exploit pathogen inactivation methods, but remains dependent on appropriate use of transfusion therapy.

Key words: diversion volume, bacterial contamination, platelets, blood donation, blood component.

References

1) AuBuchon JP, Birkmeyer JD, Busch MP. Safety of the blood supply in the United States: opportunities and controversies. Ann Intern Med 1997; **127**: 904-9.
2) Hillyer CD, Josephson CD, Blajchman MA, et al. Bacterial contamination of blood components: risks, strategies, and regulation: joint ASH and AABB educational session in transfusion medicine. Hematology Am Soc Hematol Educ Program 2003; 575-89.
3) Stramer LS. Current risks of transfusion-transmitted agents: a review. Arch Pathol Lab Med 2007; **131**: 702-7.
4) Dodd RY. Current risk for transfusion transmitted infections. Curr Opin Hematol 2007; **14**: 671-6.
5) Blajchman MA, Beckers EAM, Dickmeiss E, et al. Bacterial detection of platelets: current problems and possible resolutions. Transfus Med Rev 2005; **19**: 259-72.
6) O'Brien SF, Yi QL, Fan W, et al. Current incidence and estimated residual risk of transfusion-transmitted infections in donations made to Canadian Blood Services. Transfusion 2007; **47**: 316-25.
7) Blajchman MA. Bacterial contamination of cellular blood components: risks, sources and control. Vox Sang 2004; **87** (Suppl 1): S98-103.
8) American Association of Blood Banks. Guidance On Implementation Of New Bacterial Reduction And Detection Standard. Bethesda, MD: AABB; August 29, 2003. Association Bulletin 03-10.
9) Alter HJ. Pathogen reduction: a precautionary principle paradigm. Transfus Med Rev 2008; **22**: 97-102.
10) Blajchman MA. Incidence and significance of the bacterial contamination of blood components. Dev Biol (Basel) 2002; **108**: 59-67.
11) Barrett BB, Anderson JW, Anderson KC. Strategies for the avoidance of bacterial contamination of blood components. Transfusion 1993; **33**: 228-33.
12) 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**: 902-9.
13) Chiu EKW, Yuen KY, Lie AKW, et al. A prospective study of symptomatic bacteremia following platelet transfusion and of its management. Transfusion 1994; **34**: 950-4.
14) 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**: 529.
15) Leiby DA, Kerr KL, Compos JM, Dodd RY. A retrospective analysis of microbial contaminants in outdated random-donor platelets from multiple sites. Transfusion 1997; **37**: 259-63.
16) Blajchman MA, Ali A, Lyn P, et al. Bacterial surveillance of platelet concentrates: quantitation of bacterial load [abstract]. Transfusion 1997; **37** (Suppl): 74S.
17) Blajchman MA, Ali AM. Bacteria in the blood supply: an overlooked issue in transfusion medicine. In: Nance SJ, editor. Blood Safety: Current Challenges, Bethesda, MD: AABB; 1992. p.213-28.
18) Dzieczkowski JS, Barrett BB, Nester D, et al. Characterization of reactions after exclusive transfusion of white cell-reduced cellular blood components. Transfusion 1995; **35**: 20-5.
19) AuBuchon JP, Cooper LK, Leach MF, et al. Experience

KUR-MAG-DE005080

Page 1390 of 5977

with universal bacterial culturing to detect contamination of apheresis platelet units in a hospital transfusion service. Transfusion 2002; **42**: 855-61.

20) Beckers EAM. Effects of bacterial testing: what risks are remaining? ISBT Science Series 2007; **2**: 30-4.

21) Brecher ME, Hay SN. Bacterial contamination of blood components. Clin Microbiol Rev 2005; **18**: 195-204.

22) Reading FC, Brecher ME. Transfusion-related bacterial sepsis. Curr Opin Hematol 2001; **8**: 380-8.

23) Kuehnert MJ, Roth VR, Haley NR, et al. Transfusion-transmitted bacterial infection in the United States, 1998 through 2000. Transfusion 2001; **41**: 1493-9.

24) Ness P, Braine H, King K, et al. Single-donor platelets reduce the risk of septic platelet transfusion reactions. Transfusion 2001; **41**: 857-61.

25) Council of Europe. Guide to the Preparation, Use and Quality Assurance of Blood Components. Recommendation No R (95) 15 on the Preparation, Use and Quality Assurance of Blood Components, 14th ed, Strasbourg, Council of Europe Press; 2008.

26) Decreto del Ministro della Salute 3 Marzo 2005. Caratteristiche e modalità per la donazione di sangue e di emocomponenti. Gazzetta Ufficiale della Repubblica Italiana n. 85, 13 Aprile 2005.

27) Vasconcelos E, Seghatchian J. Bacterial contamination in blood components and preventative strategies: an overview. Transfus Apher Sci 2001; **31**: 155-63.

28) McDonald CP. Bacterial risk reduction by improved donor arm disinfection, diversion and bacterial screening. Transfus Med 2006; **16**: 381-96.

29) Gibson T, Norris W. Skin fragments removed by injection needles. Lancet 1958; **2**: 983-5.

30) Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and interventions. Vox Sang 2004; **86**: 157-63.

31) Kojima K, Togashi T, Hasegawa K, Kawasaki H. Subcutaneous fatty tissue can stray into a blood bag [abstract]. Vox Sang 1998; **74** (Suppl 1): 1205.

32) Butchta C, Nedorost N, Regele H, et al. Skin plugs in phlebotomy puncture for blood donation. Wien Klin Wochenschr 2005; **117**: 141-4.

33) Eder AF, Kennedy JM, Dy BA, et al. Bacterial screening of apheresis platelets and the residual risk of septic transfusion reactions: the American Red Cross experience (2004-2006). Transfusion 2007; **47**: 1134-42.

34) Olthuis H, Puylaart C, Verhagen C, Valk L. Method for removal of contaminating bacteria during venapuncture [abstract]. Proceedings V Regional ISBT Congress 1995; 77.

35) Figueroa PI, Yoshimori R, Nelson E, et al. Distribution of bacteria in fluid passing through an inoculated collection needle [abstract]. Transfusion 1995; **35** (Suppl 1): 11S.

36) 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**: 335-8.

37) 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.

38) Schneider T, Tunez T, Fontaine O. Benefits of the pre-donation sampling pouch in order to reduce bacterial contamination of pooled platelet concentrates [abstract]. Vox Sang 2002; **83** (Suppl 2): 162.

39) Bos H, Yedema TH, Luten M. Reduction of the incidence on bacterial contamination by predonating drawing blood for safety tests [abstract]. Vox Sang 2002; **83** (Suppl 2): 6.

40) Yedema T, Curvers J, De Kort W, Bos H. Reduction of the incidence of bacterial contamination of thrombocyte concentrates [abstract]. Transfusion 2003; **43** (Suppl): 51A.

41) de Korte D, Marcelis JH, Verhoeven AJ, Soeterbock AM. Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections. Vox Sang 2002; **83**: 13-6.

42) de Korte D, Curvers J, Beckers E, Marcelis J. Bacterial contamination of platelet concentrates: status after implementation of diversion in the Netherlands [abstract]. Transfusion 2005; **45** (Suppl); 26A.

43) de Korte D, Curvers J, de Kort WLAM, et al. Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands. Transfusion 2006; 46: 476-85.

44) de Korte D, Curvers J, Beckers EA, Marcelis JH. 5 years bacterial screening of PC in the Netherlands [abstract]. Transfusion 2007; **47** (Suppl 3): 197A-98A.

45) McDonald CP, Roy A, Mahajan P, et al. Relative values of the interventions of diversion and improved donor-arm disinfection to reduce the bacterial risk from blood transfusion. Vox Sang 2004; **86**: 178-82.

46) Robillard P, Nawej K, Delage G. Platelet bacterial contaminations and effectiveness of diverting the first 40 mls at whole blood donation [abstract]. Transfusion 2005; **45** (Suppl): 25A.

47) Delage G, Itaj NK, Robillard P. Cumulative effect of preventive measures on incidence of bacterial infections in platelet recipients [abstract]. Transfusion 2006; **46** (Suppl 2): 33A.

48) Stainsby D, Jones H, Asher D, et al. Serious hazards of transfusion: a decade of hemovigilance in the UK. Transfus Med Rev 2006; **20**: 273-82.

49) Serious Hazards Of Transfusion (SHOT). Reports and summaries. Available at: http://www.shotuk.org/SHOT%20reports%20&%20Summaries.htm.

50) Murphy WG, Foley M, Doherty C, et al. Screening platelet concentrates for bacterial contamination: low numbers of bacteria and slow growth in contaminated units mandate an alternative approach to product safety. Vox Sang 2008; **95**: 13-9.

51) Walther-Wenke G, Doerner R, Montag T, et al. Bacterial contamination of platelet concentrates prepared by different methods: results of standardized sterility testing in Germany. Vox Sang 2006; **90**: 177-82.

52) Andreau G, Caldani C, Morel P. Reduction of septic transfusion reactions related to bacteria contamination without implementing bacteria detection. ISBT Science Series 2008; **3**: 124-32.

KUR-MAG-DE005081

Page 1391 of 5977

53) Decreto Legislativo 9 novembre 2007, n. 208. Attuazione della direttiva 2005/62/CE che applica la direttiva 2002/98/CE per quanto riguarda le norme e le specifiche comunitarie relative ad un sistema di qualità per i servizi trasfusionali. Gazzetta Ufficiale della Repubblica Italiana - Serie Generale n. 261 del 9-11-2007 - Supplemento Ordinario n. 228.

54) Rao PL, Strausbaugh LJ, Liedtke LA, et al. Bacterial infections associated with blood transfusion: experience and perspective of infectious diseases consultants. Transfusion 2007; **47**: 1206-11.

55) Decreto del Ministro della Salute 3 Marzo 2005. Protocolli per l'accertamento della idoneità del donatore di sangue e di emocomponenti. Gazzetta Ufficiale della Repubblica Italiana n. 85, 13 Aprile 2005.

56) Yomtovian R, Tomasulo P, Jacobs MR. Platelet bacterial contamination: assessing progress and identifying quandaries in a rapidly evolving field [editorial]. Transfusion 2007; **47**: 1340-6.

57) Yomtovian R. Bacterial contamination of blood: lessons from the past and road map for the future. Transfusion 2004; **44**: 450-60.

58) Benjamin RJ. Bacterial culture of apheresis platelet products and the residual risk of sepsis. ISBT Science Series 2008; **3**: 133-8.

59) Benjamin RJ, Wagner S. The residual risk of sepsis: modeling bacterial detection in a two bottle culture system and an analysis of sampling error. Transfusion 2007; **47**: 1381-9.

60) Cole B, Smith T. PASSPORT Post Approval Surveillance Study of Platelet Outcomes, Release Tested. January 29, 2008. Available at: http://www.passportstudy.com/documents/PassportLetter.pdf. Downloaded on July 7, 2008.

Received: 5 July 2008 - Revision accepted: 11 November 2008
Correspondence: Giancarlo Maria Liumbruno,
Viale Italia, 19
57126 Livorno, Italy
e-mail: giancarlo@liumbruno.it; ricerca.cns@iss.it

KUR-MAG-DE005082

Page 1392 of 5977

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 December 2013 (05.12.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/181352 A1

(51) International Patent Classification:
A61B 5/15 (2006.01) *C12M 1/00* (2006.01)
B01D 43/00 (2006.01) *C12N 5/02* (2006.01)
B01L 3/14 (2006.01) *G01N 33/49* (2006.01)

(21) International Application Number:
PCT/US2013/043289

(22) International Filing Date:
30 May 2013 (30.05.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/652,887 30 May 2012 (30.05.2012) US
13/904,691 29 May 2013 (29.05.2013) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 13/904,691 (CIP)
Filed on 29 May 2013 (29.05.2013)

(71) Applicant: **MAGNOLIA MEDICAL TECHNOLOGIES, INC.** [US/US]; 815 First Avenue, Suite 140, Seattle, Washington 98104 (US).

(72) Inventors; and

(71) Applicants : **BULLINGTON, Gregory J.** [US/US]; 5825 134th Place SE, Bellevue, Washington 98006 (US). **PATTON, Richard G.** [US/US]; 2561 Magnolia Blvd W, Seattle, Washington 98199 (US). **MIAZGA, Jay M.** [US/US]; 6025 McKinley Pl., N, Seattle, Washington 98103 (US). **GAW, Shan E.** [US/US]; 4027 Sunnyside Ave., N, Seattle, Washington 98103 (US).

(74) Agents: **CHRISTIANSEN, William T., II** et al.; COOLEY LLP, 1299 Pennsylvania Ave., Suite 700, Washington, DC 20004 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, 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, 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.

[Continued on next page]

(54) Title: FLUID DIVERSION MECHANISM FOR BODILY-FLUID SAMPLING

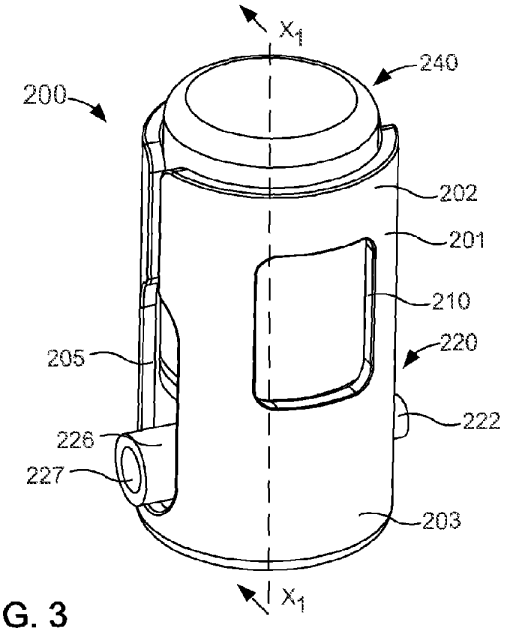


FIG. 3

(57) Abstract: An apparatus includes a housing, a fluid reservoir, a flow control mechanism, and an actuator. The housing defines an inner volume and has an inlet port that can be fluidically coupled to a patient and an outlet port. The fluid reservoir is disposed in the inner volume to receive and isolate a first volume of a bodily-fluid. The flow control mechanism is rotatable in the housing from a first configuration, in which a first lumen places the inlet port is in fluid communication with the fluid reservoir, and a second configuration, in which a second lumen places the inlet port in fluid communication with the outlet port. The actuator is configured to create a negative pressure in the fluid reservoir and is configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir.

WO 2013/181352 A1

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

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

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

— *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))*

FLUID DIVERSION MECHANISM FOR BODILY-FLUID SAMPLING

Cross-Reference to Related Applications

[1001] This application is a continuation-in-part of and claims priority to U.S. Patent Application No. 13/904,691, filed May 29, 2013, entitled "Fluid Diversion Mechanism For Bodily-Fluid Sampling," which claims priority to and the benefit of U.S. Provisional Application No. 61/652,887, filed May 30, 2012, entitled "Fluid Diversion Mechanism for Bodily-Fluid Sampling," both of which are hereby incorporated by reference in their entirety.

[1002] This application also claims priority to and the benefit of U.S. Provisional Application Serial No. 61/652,887, filed May 30, 2012, entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," the disclosure of which is hereby incorporated by reference in its entirety.

Background

[1003] The invention relates generally to the parenteral procurement of bodily-fluid samples, and more particularly to devices and methods for parenterally-procuring bodily-fluid samples with reduced contamination from microbes or other contaminants exterior to the bodily-fluid source, such as dermally-residing microbes.

[1004] Health care practitioners routinely perform various types of microbial tests on patients using parenterally-obtained bodily-fluids. Patient samples (e.g., bodily-fluids) are sometimes tested for the presence of one or more potentially undesirable microbes, such as bacteria, fungi, or yeast (e.g., Candida). Microbial testing may include incubating patient samples in one or more sterile vessels containing culture media that is conducive to microbial growth. Generally, when microbes tested for are present in the patient sample, the microbes flourish over time in the culture medium. After a pre-determined amount of time (e.g., a few hours to several days), the culture medium can be tested for the presence of the microbes. The presence of microbes in the culture medium suggests the presence of the same microbes in the patient sample which, in turn, suggests the presence of the same microbes in the bodily-fluid of the patient from which the sample was obtained. Accordingly, when microbes are determined to be present in the culture medium, the patient may be prescribed one or

more antibiotics or other treatments specifically designed to treat or otherwise remove the undesired microbes from the patient.

[1005] Patient samples, however, can sometimes become contaminated during procurement. One way in which contamination of a patient sample may occur is by the transfer of microbes from a bodily surface (e.g., dermally-residing microbes) dislodged during needle insertion into a patient and subsequently transferred to a culture medium with the patient sample. The bodily surface microbes may be dislodged either directly or via dislodged tissue fragments, hair follicles, sweat glands and other adnexal structures. The transferred microbes may thrive in the culture medium and eventually yield a positive microbial test result, thereby falsely indicating the presence of such microbes in vivo. Such inaccurate results are a concern when attempting to diagnose or treat a suspected illness or condition. For example, false positive results from microbial tests may result in the patient being unnecessarily subjected to one or more anti-microbial therapies, which may cause serious side effects to the patient including, for example, death, as well as produce an unnecessary burden and expense to the health care system.

[1006] As such, a need exists for improved bodily-fluid transfer devices and methods that reduce microbial contamination in bodily-fluid test samples.

Summary

[1007] Devices for parenterally-procuring bodily-fluid samples with reduced contamination from microbes exterior to the bodily-fluid source, such as dermally-residing microbes, are described herein. In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a fluid reservoir, a flow control mechanism, and an actuator. The housing includes a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port that is configured to be fluidically coupled to a patient and an outlet port that is configured to be fluidically coupled to a sample reservoir. The fluid reservoir is disposed within the inner volume of the housing and is configured to receive and isolate a first volume of a bodily-fluid withdrawn from the patient. The flow control mechanism defines a first lumen and a second lumen and is disposed in the housing for rotational movement from a first configuration, in which the inlet port is placed in fluid communication with the fluid reservoir such that the bodily-fluid can

flow from the inlet port, through the first lumen, and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by a user. The actuator is operably coupled to the flow control mechanism and is configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir from the patient.

Brief Description of the Drawings

[1008] FIG. 1 is a schematic illustration of a bodily-fluid transfer device according to an embodiment.

[1009] FIG. 2 is a front view of a bodily-fluid transfer device according to an embodiment.

[1010] FIG. 3 is a perspective view of the bodily-fluid transfer device of FIG. 2.

[1011] FIG. 4 is an exploded view of the bodily-fluid transfer device of FIG. 2.

[1012] FIG. 5 is a perspective view of a housing included in the bodily-fluid transfer device illustrated in FIG. 2.

[1013] FIG. 6 is a cross-sectional view of the housing illustrated in FIG. 5 taken along the line X_2-X_2.

[1014] FIG. 7 is a perspective view of a diverter included in the bodily-fluid transfer device of FIG. 2.

[1015] FIG. 8 is a cross-sectional view of the diverter illustrated in FIG. 8 taken along the line X_3-X_3.

[1016] FIG. 9 is a perspective view of a flow control mechanism included in the bodily-fluid transfer device of FIG. 2.

[1017] FIG. 10 is an exploded view of an actuator mechanism included in the bodily-fluid transfer device of FIG. 2.

[1018] FIG. 11 is a cross-sectional view of the bodily-fluid transfer device of FIG. 2 taken along the line X_1-X_1, in a first configuration.

[1019] FIG. 12 is a cross-sectional view of the bodily-fluid transfer device of FIG. 2 taken along the line X_1-X_1, in a second configuration.

[1020] FIG. 13 is a front view of a bodily-fluid transfer device according to an embodiment.

[1021] FIG. 14 is a perspective view of the bodily-fluid transfer device of FIG. 13.

[1022] FIG. 15 is an exploded view of the bodily-fluid transfer device of FIG. 13.

[1023] FIG. 16 is a cross-sectional view of a housing included in the bodily-fluid transfer device of FIG. 13 taken along the line X_5-X_5 in FIG. 14.

[1024] FIG. 17 is a cross-sectional view of the bodily-fluid transfer device taken along the line X_4-X_4 in FIG. 14, in a first configuration.

[1025] FIG. 18 is a perspective view of the bodily-fluid transfer device of FIG. 13, in a second configuration.

[1026] FIG. 19 is a cross-sectional view of the bodily-fluid transfer device of FIG. 18 taken along the line X_6-X_6.

[1027] FIG. 20 is a front view of a bodily-fluid transfer device according to an embodiment.

[1028] FIG. 21 is a perspective view of the bodily-fluid transfer device of FIG. 20.

[1029] FIG. 22 is an exploded view of the bodily-fluid transfer device of FIG. 20.

[1030] FIG. 23 is a cross-sectional view of a housing included in the bodily-fluid transfer device of FIG. 20 taken along the line X_8-X_8 in FIG. 21.

[1031] FIG. 24 is a perspective view of a first control member and a second control member included in a flow control mechanism of the bodily-fluid transfer device of FIG. 20.

[1032] FIG. 25 is a cross-sectional view of the bodily-fluid transfer device of FIG. 20 taken along the line X_7-X_7 in FIG. 21, in a first configuration.

[1033] FIG. 26 is a perspective view of the bodily-fluid transfer device of FIG. 20, in a second configuration.

[1034] FIG. 27 is a cross-sectional view of the bodily-fluid transfer device of FIG. 25 taken along the line X_9-X_9.

[1035] FIGS. 28 and 29 schematic illustrations of a bodily-fluid transfer device according to an embodiment, in a first and second configuration, respectively.

[1036] FIG. 30 is a perspective view of a bodily-fluid transfer device according to an embodiment.

[1037] FIG. 31 is an exploded perspective view of the bodily-fluid transfer device of FIG. 30.

[1038] FIG. 32 is a perspective view of a housing included in the bodily-fluid transfer device of FIG. 30.

[1039] FIG. 33 is a cross-sectional view of the housing illustrated in FIG. 32 taken along the line X_{11}-X_{11}.

[1040] FIG. 34 is a perspective view of a diverter included in the bodily-fluid transfer device of FIG. 30.

[1041] FIG. 35 is a cross-sectional view of the diverter illustrated in FIG. 34 taken along the line X_{12}-X_{12}.

[1042] FIG. 36 is a perspective view of a portion of a flow control mechanism included in the bodily-fluid transfer device of FIG. 30.

[1043] FIG. 37 is a cross-sectional view of the portion of the flow control mechanism illustrated in FIG. 36 taken along the line X_{13}-X_{13}.

[1044] FIGS. 38-41 are cross-sectional views of the bodily-fluid transfer device of FIG. 32 taken along the line X_{10}-X_{10}, in a first, second, third, and fourth configuration, respectively.

[1045] FIG. 42 is a perspective view of a bodily-fluid transfer device according to an embodiment.

[1046] FIG. 43 is an exploded perspective view of the bodily-fluid transfer device of FIG. 42.

[1047] FIG. 44 is a perspective exploded view of a flow control mechanism included in the bodily-fluid transfer device of FIG. 42.

[1048] FIGS. 45 and 46 are cross-sectional views of the bodily-fluid transfer device of FIG. 42 taken along the line X_{14}-X_{14}, in a first configuration and a second configuration, respectively.

[1049] FIG. 47 is a flowchart illustrating a method for parenterally procuring a bodily-fluid sample that is substantially free from microbes.

Detailed Description

[1050] Devices for parenterally procuring bodily-fluid samples with reduced contamination from microbes exterior to the bodily-fluid source, such as dermally-residing microbes, are described herein. In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a fluid reservoir, a flow control mechanism, and an actuator. The housing includes a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port that is configured to be fluidically coupled to a patient and an outlet port that is configured to be fluidically coupled to a sample reservoir. The fluid reservoir is disposed within the inner volume of the housing and is configured to receive and isolate a first volume of a bodily-fluid withdrawn from the patient. The flow control mechanism defines a first lumen and a second lumen and is disposed in the housing for rotational movement from a first configuration, in which the inlet port is placed in fluid communication with the fluid reservoir such that the bodily-fluid can flow from the inlet port, through the first lumen, and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port

such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by a user. The actuator is operably coupled to the flow control mechanism and is configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1051] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, an actuator, a diverter, and a flow control mechanism. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The actuator is movably disposed in the housing. The actuator includes a sealing member and a fluid reservoir defined, at least in part, by the sealing member. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by a user. The diverter is disposed in the housing and has an inlet port that is configured to be fluidically coupled to the patient, a first outlet port that is configured to be fluidically coupled to the fluid reservoir, and a second outlet port that is configured to be fluidically coupled to a sample reservoir. The flow control mechanism defines a first lumen and a second lumen. The flow control mechanism is disposed in the diverter and is rotatable from a first configuration, in which the inlet port is placed in fluid communication with the first outlet port such that bodily-fluid can flow from the inlet port, through the first lumen and to the first outlet port, to a second configuration, in which the inlet port is placed in fluid communication with the second outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the second outlet port.

[1052] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a flow control mechanism, and an actuator. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port configured to be fluidically coupled to the patient and an outlet port configured to be fluidically coupled to a sample reservoir. The flow control mechanism defines a first lumen and a second lumen. The flow control mechanism is disposed in the housing and is rotatable between a first configuration, in which the inlet port is placed in fluid communication with a fluid reservoir defined, at least in part, by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the

outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is movably disposed in the housing and is operably coupled to the flow control mechanism. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by the user. The actuator is further configured to rotate the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1053] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a seal member, a fluid reservoir, a flow control mechanism, and an actuator. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port configured to be fluidically coupled to the patient. The seal member is movably disposed in the inner volume and is configured to define, at least partially, the fluid reservoir disposed in the inner volume. The fluid reservoir is configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient. The flow control mechanism is movably disposed in the housing and is configured to move between a first configuration, in which the bodily-fluid can flow from the inlet port, through the flow control mechanism and to the fluid reservoir, to a second configuration, in which the fluid reservoir is fluidically isolated from the inlet port. The actuator is operably coupled to the seal member and the flow control mechanism. The actuator includes a spring configured to move the seal member from a first position to a second position to create a negative pressure in the fluid reservoir. The actuator is configured to move the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1054] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a housing, a flow control mechanism, and an actuator. The housing has a proximal end portion and a distal end portion and defines an inner volume therebetween. The housing has an inlet port configured to be fluidically coupled to the patient and an outlet port configured to be fluidically coupled to a sample reservoir. The flow control mechanism is disposed in the housing and includes a first control member and a second control member. The second control member defines a first lumen and a second lumen and is rotatably movable between a first configuration, in which the inlet port is placed in fluid communication with a fluid reservoir defined, at least in part, by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to

a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port. The actuator is movably disposed in the housing and is operably coupled to the flow control mechanism. The actuator is configured to create a negative pressure in the fluid reservoir when actuated by the user. The actuator is further configured to rotate the second control member from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

[1055] In some embodiments, a device for procuring bodily-fluid samples from a patient includes a diverter, a flow control mechanism, and an actuator mechanism. The diverter defines an inlet port, a first outlet port, and a second outlet port. The first outlet port is fluidically coupled to a first fluid reservoir and the second outlet port is fluidically coupled to a second reservoir, fluidically isolated from the first fluid reservoir. The flow control mechanism is configured to be disposed, at least partially within the diverter. The actuator mechanism is configured to engage the flow control mechanism to move the flow control mechanism between a first configuration, in which a flow of bodily-fluid can enter the first fluid reservoir, and a second configuration, in which a flow of bodily-fluid can enter the second fluid reservoir.

[1056] In some embodiments, a bodily-fluid transfer device can be configured to selectively divert a first, predetermined amount of a flow of a bodily-fluid to a first reservoir before permitting the flow of a second amount of the bodily-fluid into a second reservoir. In this manner, the second amount of bodily-fluid can be used for diagnostic or other testing, while the first amount of bodily-fluid, which may contain microbes from a bodily surface, is isolated from the bodily-fluid to be tested. The first amount of bodily-fluid can be subsequently used for different types of testing (e.g., CBC, other blood chemistry tests) or can be simply sequestered.

[1057] In some embodiments, a bodily-fluid transfer device is configured to automatically move from a first configuration to a second configuration, for example, without requiring an input or other action by a health care practitioner. In some embodiments, the bodily-fluid transfer device prevents bodily-fluid from flowing or otherwise being introduced into a second reservoir before at least a first amount of bodily-fluid (e.g., a predetermined amount) is first introduced into a first reservoir.

[1058] In some embodiments, a method for procuring a bodily-fluid sample using a parenteral sampling device that has a needle with a lumen and a fluid reservoir fluidically coupled to the needle includes inserting the needle of the device into a patient. The method includes establishing fluid communication between the needle and the fluid reservoir. An actuator is moved a first distance to create a negative pressure in the fluid reservoir to withdraw a predetermined volume of the bodily-fluid. The actuator is moved a second distance to engage a flow control mechanism and rotate the flow control mechanism from a first configuration to a second configuration. The first configuration is operable in allowing bodily-fluid to flow through a first flow path from the needle to the fluid reservoir and the second configuration is operable in allowing bodily-fluid to flow through a second flow path from the needle to a sample reservoir.

[1059] As used in this specification, "bodily-fluid" can include any fluid obtained from a body of a patient, including, but not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, and the like, or any combination thereof.

[1060] As used herein, the term "set" can refer to multiple features or a singular feature with multiple parts. For example, when referring to set of walls, the set of walls can be considered as one wall with distinct portions, or the set of walls can be considered as multiple walls. Similarly stated, a monolithically constructed item can include a set of walls. Such a set of walls can include, for example, multiple portions that are in discontinuous from each other. A set of walls can also be fabricated from multiple items that are produced separately and are later joined together (e.g., via a weld, an adhesive or any suitable method).

[1061] As used herein, the words "proximal" and "distal" refer to the direction closer to and away from, respectively, a user who would place the device into contact with a patient. Thus, for example, the end of a device first touching the body of the patient would be the distal end, while the opposite end of the device (e.g., the end of the device being manipulated by the user) would be the proximal end of the device.

[1062] As used herein, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, the term "an engagement surface" is intended to mean a single surface or multiple surfaces unless explicitly expressed otherwise.

[1063] FIG. 1 is a schematic illustration of a portion of a bodily-fluid transfer device 100, according to an embodiment. Generally, the bodily-fluid transfer device 100 (also referred to herein as "fluid transfer device" or "transfer device") is configured to permit the withdrawal of bodily-fluid from a patient such that a first portion or amount of the withdrawn fluid is diverted away from a second portion or amount of the withdrawn fluid that is to be used as a biological sample, such as for testing for the purpose of medical diagnosis and/or treatment. In other words, the transfer device 100 is configured to transfer a first, predetermined amount of a bodily-fluid to a first collection reservoir and a second amount of bodily-fluid to one or more bodily-fluid collection reservoirs fluidically isolated from the first collection reservoir, as described in more detail herein.

[1064] The transfer device 100 includes a diverter 120, a first reservoir 170, and a second reservoir 180, different from the first reservoir 170. The diverter 120 includes an inlet port 122 and two or more outlet ports, such as a first outlet port 124 and a second outlet port 126 shown in FIG. 1. The inlet port 122 is configured to be fluidically coupled to a medical device defining a pathway **P** for withdrawing and/or conveying the bodily-fluid from the patient to the transfer device 100. For example, the inlet port 122 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). In this manner, the diverter 120 can receive the bodily-fluid from the patient via the needle or other lumen-containing device.

[1065] The first outlet port 124 of the diverter 120 is configured to be fluidically coupled to the first reservoir 170. In some embodiments, the first reservoir 170 is monolithically formed with the first outlet port 124 and/or a portion of the diverter 120. In other embodiments, the first reservoir 170 can be mechanically and fluidically coupled to the diverter 120 via an adhesive, a resistance fit, a mechanical fastener, any number of mating recesses, a threaded coupling, and/or any other suitable coupling or combination thereof. Similarly stated, the first reservoir 170 can be physically (e.g., mechanically) coupled to the diverter 120 such that an interior volume defined by the first reservoir 170 is in fluid communication with the first outlet port 120 of the diverter 120. In still other embodiments, the first reservoir 170 can be operably coupled to the first outlet port 124 of the diverter 120 via an intervening structure (not shown in FIG. 1), such as a flexible sterile tubing. More particularly, the intervening structure can define a lumen configured to place the first reservoir 170 in fluid communication with the first outlet port 124.

[1066] The first reservoir 170 is configured to receive and contain the first, predetermined amount of the bodily-fluid. In some embodiments, the first reservoir 170 is configured to contain the first amount of the bodily-fluid such that the first amount is fluidically isolated from a second amount of the bodily-fluid (different from the first amount of bodily-fluid) that is subsequently withdrawn from the patient. The first reservoir 170 can be any suitable reservoir for containing a bodily-fluid, such as a pre-sample reservoir described in detail in U.S. Patent No. 8,197,420 ("the '420 Patent"), the disclosure of which is incorporated herein by reference in its entirety. As used in this specification, the terms "first, predetermined amount" and "first amount" describe an amount of bodily-fluid configured to be received or contained by the first reservoir 170. Furthermore, while the term "first amount" does not explicitly describe a predetermined amount, it should be understood that the first amount is the first, predetermined amount unless explicitly described differently.

[1067] The second outlet port 126 of the diverter 120 is configured to be fluidically coupled to the second reservoir 180. In some embodiments, the second reservoir 180 is monolithically formed with the second outlet port 126 and/or a portion of the diverter 120. In other embodiments, the second reservoir 180 can be mechanically coupled to the second outlet port 126 of the diverter 120 or operably coupled to the second outlet port 126 via an intervening structure (not shown in FIG. 1), such as described above with reference to the first reservoir 170. The second reservoir 180 is configured to receive and contain the second amount of the bodily-fluid. For example, the second amount of bodily-fluid can be an amount withdrawn from the patient subsequent to withdrawal of the first amount. In some embodiments, the second reservoir 180 is configured to contain the second amount of the bodily-fluid such that the second amount is fluidically isolated from the first amount of the bodily-fluid.

[1068] The second reservoir 170 can be any suitable reservoir for containing a bodily-fluid, including, for example, a sample reservoir as described in the '420 Patent incorporated by reference above. As used in this specification, the term "second amount" describes an amount of bodily-fluid configured to be received or contained by the second reservoir 180. In some embodiments, the second amount can be any suitable amount of bodily-fluid and need not be predetermined. In other embodiments, the second amount received and contained by the second reservoir 180 is a second predetermined amount.

[1069] In some embodiments, the first reservoir 170 and the second reservoir 180 can be coupled to (or formed with) the diverter 120 in a similar manner. In other embodiments, the first reservoir 170 and the second reservoir need not be similarly coupled to the diverter 120. For example, in some embodiments, the first reservoir 170 can be monolithically formed with the diverter 120 (e.g., the first outlet port 124) and the second reservoir 180 can be operably coupled to the diverter 120 (e.g., the second outlet port 126) via an intervening structure, such as a flexible sterile tubing.

[1070] As shown in FIG. 1, the transfer device 100 further includes an actuator 140 and a flow control mechanism 130 defining a first channel 138 and a second channel 139. In some embodiments, the actuator 140 can be included in or otherwise operably coupled to the diverter 120. In this manner, the actuator 140 can be configured to control a movement of the flow control mechanism 130 (e.g., between a first configuration and a second configuration). For example, the actuator 140 can be movable between a first position corresponding to the first configuration of the flow control mechanism 130, and a second position, different from the first position, corresponding to the second configuration of the flow control mechanism 130. In some embodiments, the actuator 140 is configured for uni-directional movement. For example, the actuator 140 can be moved from its first position to its second position, but cannot be moved from its second position to its first position. In this manner, the flow control mechanism 130 is prevented from being moved to its second configuration before its first configuration, thus requiring that the first amount of the bodily-fluid be directed to the first reservoir 170 and not the second reservoir 180.

[1071] The flow control mechanism 130 is configured such that when in the first configuration, the first channel 138 fluidically couples the inlet port 122 to the first outlet port 124 and when in the second configuration, the second channel 139 fluidically couples the inlet portion 122 to the second outlet port 126. In some embodiments, the actuator 140 is coupled to the flow control mechanism 130 and is configured to move the flow control mechanism 130 in a translational motion between the first configuration and the second configuration. For example, in some embodiments, the flow control mechanism 130 can be in the first configuration when the flow control mechanism 130 is in a distal position relative to the transfer device 100. In such embodiments, the actuator 140 can be actuated to move the flow control device 130 in the proximal direction to a proximal position relative to the transfer device 100, thereby placing the flow control mechanism 130 in the second

configuration. In other embodiments, the actuator 140 can be actuated to move the flow control mechanism 130 in a rotational motion between the first configuration and the second configuration.

[1072] Accordingly, when the flow control mechanism 130 is in the first configuration, the second outlet port 126 is fluidically isolated from the inlet port 122. Similarly, when the flow control mechanism 130 is in the second configuration, the first outlet port 124 is fluidically isolated from the inlet port 122. In this manner, the flow control mechanism 130 can direct, or divert the first amount of the bodily-fluid to the first reservoir 170 via the first outlet port 124 when the flow control mechanism 130 is in the first configuration and can direct, or divert the second amount of the bodily-fluid to the second reservoir 180 via the second outlet port 126 when the flow control mechanism 130 is in the second configuration.

[1073] In some embodiments, at least a portion of the actuator 140 can be operably coupled to the first reservoir 170. In this manner, the actuator 140 (or at least the portion of the actuator 140) can be configured to cause a vacuum within the first reservoir 170, thereby initiating flow of the bodily-fluid through the transfer device 100 and into the first reservoir 170 when the diverter 120 is in its first configuration. The actuator 140 can include any suitable mechanism for actuating the transfer device 100 (e.g., at least the flow control mechanism 130), such as, for example, a rotating disc, a plunger, a slide, a dial, a button, and/or any other suitable mechanism or combination thereof. Examples of suitable actuators are described in more detail herein with reference to specific embodiments.

[1074] In some embodiments, the diverter 120 is configured such that the first amount of bodily-fluid need be conveyed to the first reservoir 170 before the diverter 120 will permit the flow of the second amount of bodily-fluid to be conveyed through the diverter 120 to the second reservoir 180. In this manner, the diverter 120 can be characterized as requiring compliance by a health care practitioner regarding the collection of the first, predetermined amount (e.g., a pre-sample) prior to a collection of the second amount (e.g., a sample) of bodily-fluid. Similarly stated, the diverter 120 can be configured to prevent a health care practitioner from collecting the second amount, or the sample, of bodily-fluid into the second reservoir 180 without first diverting the first amount, or pre-sample, of bodily-fluid to the first reservoir 170. In this manner, the health care practitioner is prevented from including (whether intentionally or unintentionally) the first amount of bodily-fluid, which is more likely to contain bodily surface microbes and/or other undesirable external contaminants that

are not representative of the in vivo conditions of a patient's bodily-fluid system, in the bodily-fluid sample to be used for analysis. The forced-compliance aspect of the diverter 120 is described in more detail herein with reference to specific embodiments.

[1075] In some embodiments, the diverter 120 is configured to automatically (i.e., without requiring an input or other action by a health care practitioner or other operator of the transfer device 100) fluidically isolate the inlet port 122 from the first outlet port 124. For example, the diverter 120 can be configured such that the flow control mechanism 130 will automatically fluidically isolate the first outlet port 124 from the inlet port 122 when the first reservoir 170 has received the first, predetermined amount of bodily-fluid. As such, additional flow of bodily-fluid in excess of the first amount into the first reservoir 170 is prevented. In some embodiments, the diverter 120 is configured such that the flow control mechanism 130 automatically moves from its first configuration to its second configuration after the first amount of bodily-fluid is conveyed to the first reservoir 170.

[1076] In some embodiments, the actuator 140 can have a third position, different from the first and second positions, which corresponds to a third configuration of the flow control mechanism 130. When in the third configuration, the flow control mechanism 130 can fluidically isolate the inlet port 122 from both the first outlet port 124 and the second outlet port 126 simultaneously. Therefore, when the flow control mechanism 130 is in its third configuration, flow of bodily-fluid from the inlet port 122 to either the first reservoir 170 or the second reservoir 180 is prevented. In use, for example, the actuator 140 can be actuated to place the flow control mechanism 130 in the first configuration such that a bodily-fluid can flow from the inlet port 122 to the first reservoir 170, then moved to the second configuration such that the bodily-fluid can flow from the inlet port 122 to the second reservoir 180, then moved to the third configuration to stop the flow of bodily-fluid into and/or through the diverter 120. In some embodiments, the flow control mechanism 130 can be moved to the third configuration between the first configuration and the second configuration. In some embodiments, the flow control mechanism 130 can be in the third configuration before being moved to either of the first configuration or the second configuration.

[1077] In some embodiments, one or more portions of the transfer device 100 are disposed within a housing (not shown in FIG. 1). For example, in some embodiments, at least a portion of one or more of the diverter 120, the first reservoir 170, and the actuator 140 can be disposed within the housing. In such an embodiment, at least a portion of the actuator

140 is accessible through the housing. Examples of suitable housings are described in more detail herein with reference to specific embodiments.

[1078] Referring now to FIGS. 2-12, a transfer device 200 includes a housing 201, a diverter 220, a flow control mechanism 230, and an actuator 240. The transfer device 200 can be any suitable shape, size, or configuration. For example, while shown in FIGS. 2 and 3 as being substantially cylindrical, the transfer device 200 can be square, rectangular, polygonal, and/or any other non-cylindrical shape.

[1079] The housing 201 includes a proximal end portion 202 and a distal end portion 203. The distal end portion 203 includes a base 206 from which a set of walls 204 extend. More specifically, the walls 204 of the housing 201 define a substantially annular shape and define an inner volume 211 therebetween. The proximal end portion 202 of the housing 201 is configured to be open such that the inner volume 211 can receive at least a portion of the diverter 220, a portion of the flow control mechanism 230, and a portion of the actuator 240 (FIG. 4). Similarly stated, the housing 201 is configured to house at least the portion of the diverter 220, the portion of the flow control mechanism 230, and the portion of the actuator 240

[1080] The walls 204 of the housing 201 define a set of status windows 210 and a set of channels 205. The status windows 210 can be any suitable shape or size and are configured to allow a user to visually inspect at least a portion of the transfer device 200. While shown in FIG. 5 as including two status windows 210, in other embodiments, the housing 201 can define any number of status windows 210, such as, for example, one, three, four, or more. The channels 205 defined by the housing 201 are configured to extend from the distal end portion 203 and through the proximal end portion 202. Similarly stated, the channels 205 extend through a proximal surface of the housing 201. Said yet another way, the channels 205 are open ended at the proximal end portion 202 of the housing 201.

[1081] The housing 201 further includes a set of guide posts 207 and a set of flow control protrusions 208. While shown in FIGS. 5 and 6 as cylindrical protrusions, the guide posts 207 can be any suitable shape or size and are configured to extend from the base 206 in the proximal direction. In this manner, the guide posts 207 are configured to engage a portion of the diverter 220 and a portion of the actuator 240, as further described herein. The flow control protrusions 208 extend from the base 206 in the proximal direction and define notches

209. In this manner, the flow control protrusions 208 are configured to selectively engage the flow control mechanism 230 to move the flow control mechanism 230 between a first configuration and a second configuration, as described in further detail herein. While only one flow control protrusion 208 is shown in FIGS. 5 and 6, the housing 201 is configured to include two flow control protrusions 208. In other embodiments, the housing 201 can include any number flow control protrusions 208 such as for example, one, three, four, or more.

[1082] As shown in FIGS. 7 and 8, the diverter 220 includes a proximal end portion 228 and a distal end portion 229 and defines an inner volume 221. The inner volume 221 is configured to receive at least a portion of the flow control mechanism 230, as further described herein. The proximal end portion 228 of the diverter 220 includes a first outlet port 224 and can engage a portion of the actuator 240. The distal end portion 229 includes an inlet port 222 and a second outlet port 226. As shown in FIGS. 1 and 2, the diverter 220 is disposed within the inner volume 211 of the housing 201 such that a portion of the inlet port 222 extends through a first channel 205 defined by the walls 204 of the housing 201 and a portion of the second outlet port 226 extends through a second channel 205 opposite the first channel. While not explicitly shown in FIGS. 2-12, the distal end portion 229 of the diverter 220 is configured to engage the guide posts 207 such that lateral movement of the diverter 220 is limited. Similarly stated, the distal end portion 229 of the diverter 220 can engage the guide posts 207 of the housing 201 such that the diverter 220 is substantially limited to movement in the proximal or distal direction, relative to the housing 201, as further described herein.

[1083] The inlet port 222 included in the distal end portion 229 of the diverter 220 defines an inlet lumen 223. As shown in FIG. 8, the inlet lumen 223 is configured to be in fluid communication with the inner volume 221. Similarly stated, the inlet lumen 223 of the inlet port 222 extends through a wall defining the inner volume 221 of the diverter 220. The inlet port 222 is further configured to be fluidically coupled to a medical device (not shown) defining a fluid flow pathway for withdrawing and/or conveying the bodily-fluid from a patient to the transfer device 200. For example, the inlet port 222 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). Similarly stated, the inlet lumen 223 defined by the inlet port 222 is placed in fluid communication with a lumen defined by a lumen-containing device, when the lumen-containing device is coupled to the inlet port 222. Expanding further, when the lumen-containing device is disposed within a

portion of a body of the patient (e.g., within a vein of the patient), the inner volume 221 of the diverter 220 is placed in fluid communication with the portion of the body of the patient.

[1084] The first outlet port 224 included in the proximal end portion 228 of the diverter 220 defines a first outlet lumen 225. As shown in FIG. 8, the first outlet lumen 225 is configured to be in fluid communication with the inner volume 221 of the diverter 220 (e.g., the first outlet lumen 225 extends through the wall defining the inner volume 221). Similarly, the second outlet port 226 included in the distal end portion 229 of the diverter 220 defines a second outlet lumen 227 in fluid communication with the inner volume 221.

[1085] As shown in FIG. 9, the flow control mechanism 230 includes a first control member 231 and a second control member 235. At least a portion of the flow control mechanism 230 is configured to be disposed within the inner volume 221 defined by the diverter 220. In this manner, the flow control mechanism 230 defines a circular cross-sectional shape such that when the flow control mechanism 230 is disposed within the inner volume 221, a portion of the flow control mechanism 230 forms a friction fit with the walls of the diverter 220 defining the inner volume 221, as described in further detail herein.

[1086] The first control member 231 includes a set of activation protrusions 232 and a set of cross members 234 (only one of each is shown in FIG. 9). The activation protrusions 232 are configured to engage the flow control protrusion 208 of the housing 201. More specifically, the activation protrusions 232 can be disposed within the notch 209 defined by the flow control protrusion 208. Therefore, in use, the flow control protrusions 208 can engage the activation protrusions 232 to move the flow control mechanism 230 between a first configuration and a second configuration.

[1087] The second control member 235 defines a first lumen 238, a second lumen 239, and a set of channels 237 and is configured to be disposed, at least partially, within the first control member 231. More particularly, the first control member 231 has a first diameter D_1 and the second control member 235 has a second diameter D_2 larger than the first diameter D_1. Therefore, when the second control member 235 is disposed within the first control member 231 a portion of the second control member 235 extends beyond a surface of the first control member 231 that defines the first diameter D_1.

[1088] The channels 237 defined by the second control member 235 receive the cross members 234 of the first control member 231. The arrangement of the cross members 234

disposed within the channels 237 is such that the second control member 235 is maintained in a desired position relative to the first control member 231. In this manner, the second control member 235 is configured to move concurrently with the first control member 231 when the flow control protrusions 208 engage the activation protrusions 232 of the first control member 231. Similarly stated, the flow control mechanism 230 is moved between the first configuration and the second configuration when the first control member 231 and the second control member 235 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 230 is in the first configuration, the first lumen 238 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the first outlet lumen 225 defined by the first outlet port 224. When the flow control mechanism 230 is in the second configuration, the second lumen 239 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the second outlet lumen 227 defined by the second outlet port 226, as described in further detail herein.

[1089] As shown in FIG. 10, the actuator mechanism 240 includes an actuator housing 262, a plunger 248, a cap 255, and a spring 261. The actuator mechanism 240 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 200 between a first configuration and a second configuration, as described in further detail herein. The actuator housing 262 includes a proximal end portion 263 and a distal end portion 264 and defines an inner volume 265. The actuator housing 262 can be any suitable shape, size or configuration. For example, the actuator housing 262 can be substantially cylindrical and be configured to be disposed, at least partially, within the housing 201. The inner volume 265 is configured to receive the plunger 248, the spring 261, and at least a portion of the cap 255. The plunger 248 includes a proximal end portion 249 and a distal end portion 249 and a side wall 251. The distal end portion 250 is configured to receive the guide posts 207 of the housing 201, as described in further detail herein. The proximal end portion 249 includes a set of retention tabs 253 and can receive a portion of the spring 261. More particularly, the retention tabs 253 included in the proximal end portion 249 of the plunger 248 are configured to engage the spring 261 to removably couple the spring 261 to the plunger 248.

[1090] The side wall 251 of the plunger 248 define a set of notches 252 configured to receive a set of seal members 254. The seal members 254 can be any suitable seal members 254 such as for example, o-rings formed from any suitable elastomeric material. In this

manner, the plunger 248 is disposed within the inner volume 265 of the actuator housing 262 such that the seal members 254 define a friction fit with the inner walls (not shown in FIG. 10) that define the inner volume 265 of the actuator housing 262. Similarly stated, the seal members 254 define a fluidic seal with the inner walls of the actuator housing 262. Furthermore, the plunger 248 is disposed within the inner volume 265 such that the plunger 248 divides the inner volume 265 into a first portion 267 that is fluidically isolated from a second portion 270 (see e.g., FIGS. 11 and 12). The first portion 267 of the inner volume 265 is defined between a surface of the proximal end portion 263 of the actuator housing 262 and the proximal end portion 249 of the plunger 248. As such, the first portion 267 of the inner volume 265 is configured contain the spring 261 such that the spring 261 is in contact with the surface of the proximal end portion 263 of the actuator housing 262 and the proximal end portion 249 of the plunger 248.

[1091] The cap 255 can be any suitable shape or size and is configured to be disposed, at least partially, within the inner volume 265 of the actuator housing 262. Furthermore, the cap 255 can be formed from any suitable material. For example, in some embodiments, the cap 255 is formed from an elastomeric material such as silicone. In other embodiments, the cap 255 can be formed from any polymeric material such as, for example, rubber, vinyl, neoprene, or the like.

[1092] The cap 255 includes a proximal end portion 256 and a distal end portion 257. The proximal end portion 256 is disposed within the inner volume 265 of the actuator housing 262 such that the distal end portion 250 of the plunger 248 and the proximal end portion 256 of the cap defines the second portion 270 of the inner volume (referred to henceforth as "first reservoir") of the inner volume 265. Expanding further, the proximal end portion 256 of the cap 255 is configured to define a friction fit with the inner walls (not shown in FIG. 10) that define the inner volume 265. Similarly stated, the proximal end portion 254 defines a fluidic seal with the inner walls of the actuator housing 262. Therefore, the fluidic seal defined by the actuator housing 262 and the plunger 248 and the fluidic seal defined by the actuator housing 262 and the proximal end portion 256 of the cap 255 fluidically isolate the fluid reservoir 270 from a portion outside of the fluid reservoir 270 (i.e., the second portion of the inner volume 265).

[1093] The distal end portion 257 of the cap 255 includes a set of notches 260 configured to receive a set of protrusions 266 of the actuator housing 262 when the proximal end portion

256 is disposed within the inner volume 265. The arrangement of the notches 260 defined by the cap 255 and the protrusions 266 of the actuator housing 262 is such that the protrusions 266 form a friction fit with the walls defining the notches 260. In this manner, the protrusions 266 engage the walls defining the notches 260 to maintain the cap 255 in a desired position relative to the actuator housing 262 when the proximal end portion 256 is disposed within the inner volume 265. Moreover, the actuator mechanism 240 and the diverter 220 are disposed within the housing 201 such that the distal end portion 257 of the cap 255 is in contact with the proximal end portion 228 of the diverter 220, as described in further detail herein.

[1094] The cap 255 further defines an inlet port 258 and a set of guide post ports 259. The inlet port 258 is configured to receive a portion of the first outlet port 224 included in the diverter 220. More specifically, the inlet port 258 receives the first outlet port 224 such that the inlet port 258 form a fluidic seal with an outer surface of the first outlet port 224. Similarly, the guide post ports 259 receive a portion of the guide posts 207 of the housing 201 such that the guide post ports 259 form a fluidic seal with an outer surface of the guide posts 207. In this manner, a portion of the guide posts 207 and a portion of the first outlet port 224 are disposed within the fluid reservoir 270 defined by the actuator housing 262. Furthermore, with the portion of the first outlet port 224 disposed within the fluid reservoir 270, the fluid reservoir 270 (i.e., the second portion of the inner volume 265) is in fluid communication with the first outlet lumen 225, as described in further detail herein.

[1095] In some embodiments, the transfer device 200 can be stored in a storage configuration in which the second control member 235 of the flow control mechanism 230 fluidically isolates the inlet port 222, the first outlet port 224, and the second outlet port 226 from the inner volume 221 defined by the diverter 220. In such embodiments, first lumen 238 and the second lumen 239 are fluidically isolated from the inlet lumen 223, the first outlet lumen 225, and the second outlet lumen 227. Furthermore, the friction fit defined by the second control member 235 and the walls of the diverter 220 defining the inner volume 221 maintain the flow control mechanism 230 in the storage configuration until the flow control mechanism 230 is moved from the storage configuration.

[1096] In use, a user can engage the transfer device 200 to couple the inlet port 222 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle or, as an additional example, surgical tubing coupleable with a Luer-Lok-

type connection that allows for mating to an indwelling catheter or hub or other general vascular access device(s)/product(s). With the inlet port 222 coupled to the lumen-defining device the inlet lumen 223 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 223 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 226 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1097] With the inlet port 222 coupled to the lumen-defining device and the second outlet port 226 coupled to the external fluid reservoir, a user can place the transfer device 200 in the first configuration by applying an activation force to the actuator mechanism 240, thereby moving at least a portion of the actuator mechanism 240, the diverter 220, and the flow control mechanism 230 in the distal direction towards the first configuration, as shown by the arrow **AA** in FIG. 11. More specifically and as described above, the distal end portion 250 of the plunger 248 engages the guide posts 207 of the housing 201. The arrangement of the plunger 248 and the guide posts 207 is such that as the user applies the activation force to the actuator mechanism 240, the position of the plunger 248, relative to the housing 201, is maintained. Therefore, the activation force applied by the user moves the actuator housing 262, the cap 255, the diverter 220, and the flow control mechanism 230 in the direction of the arrow **AA**, but not the plunger 248. Thus, the distal movement of the actuator housing 262 is such that a portion of the activation force is configured to compress the spring 261, and as such, the height of the second portion 267 of the inner volume is reduced. The compression of the spring 261 is such that the spring 261 exerts a reaction force (e.g., a force of expansion) in response to the portion of the activation force compressing the spring 261. Similarly stated, the spring 261 is configured return to an expanded configuration when the activation force is removed.

[1098] The distal movement of the actuator housing 262 relative to the plunger 248 is such that the height of the fluid reservoir 270 is increased. With the fluid reservoir 270 being fluidically isolated (as described above) the increase in the height (i.e., the increase in volume) produces a negative pressure within the fluid reservoir 270. Furthermore, as the

actuator mechanism 240 is moved from the storage configuration toward the first configuration, the flow control protrusions 208 engage the activation protrusions 232 (not shown in FIG. 11) included in the first control member 231 to move the flow control mechanism 230 toward the first configuration, as indicated by the arrow **BB**. Thus, when the flow control mechanism 230 is moved to the first configuration, the first lumen 238 defined by the second control member 235 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the first outlet lumen 225 defined by the first outlet port 224.

[1099] As shown by the arrow **CC**, the inlet lumen 223 of the inlet port 222, the first lumen 238 of the second control member 235, and the first outlet lumen 225 of the first outlet port 224 define a fluid flow path such that the fluid reservoir 270 defined by the actuator housing 262 is in fluid communication with the inlet port 222. Furthermore, with the inlet port 222 coupled to the lumen-defining device the fluid reservoir 270 of the actuator housing 262 is placed in fluid communication with the portion of the patient (e.g., the vein). The negative pressure within the fluid reservoir 270 is such that the negative pressure differential introduces a suction force within the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 270 of the actuator housing 262. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes.

[1100] In some embodiments, the magnitude of the suction force can be modulated by increasing or decreasing the amount of activation force applied to the actuator mechanism 240. Excess suction force can, in some cases, collapse a patient's vein thereby cutting off sample flow. Once a vein is collapsed, one or more additional venipunctures may be required to access a non-collapsed vein. Excess suction force may also cause hemolysis at the needle tip within the vein due to excessive negative pressure. Thus, in some embodiments, it can be desirable to limit the amount of suction force (i.e., modulate the negative pressure during a blood draw) introduced to a vein to reduce, minimize, or even eliminate vein collapse and/or one potential source of hemolysis. In such embodiments, the user can reduce the amount of force applied to the actuator mechanism 240. In this manner, the reaction force exerted by the expansion of the spring 261 (e.g., as described above) is sufficient to overcome a portion of the activation force applied by the user. Thus, the spring 261 can expand to move the plunger 248 and the housing 201 in the distal direction, relative to the actuator housing 262,

thc cap 255, thc divcrtcr 220, and thc flow control mcchanism 230. Thc distal movcmcnt of the plunger 248 and housing 201 is such that the flow control protrusions 208 engage the activation protrusions 232 of the flow control mechanism 230 to move the flow control mechanism 230 towards the storage configuration. The rotation of the flow control mechanism 230 (e.g., in a direction opposite the arrow **BB**) reduces the size of the fluid pathway (e.g., an inner diameter) between the inlet lumen 223 and the first lumen 238 and the first outlet port 225 and the first lumen 238, thereby reducing the suction force introduced into the vein of the patient.

[1101] With the desired amount of bodily-fluid transferred to the fluid reservoir 270 defined by the actuator housing 262, a user can engage the transfer device 200 to move the transfer device 200 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the actuator housing 262 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 200 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 270 defined by the actuator housing 262 is in equilibrium with the pressure of the portion of thc body in which thc lumcn-dcfining dcvicc is disposcd (c.g., thc vcin). In such embodiments, the equalizing of the pressure between the second portion 176 of the inner volume 265 and the portion of the body stops the flow of the bodily-fluid into the actuator housing 262. In some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 223, the first lumen 238, the first outlet lumen 225, and the lumen-defining device.

[1102] As shown in FIG. 12, the transfer device 200 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 240 in the distal direction, as indicated by the arrow **DD**. Expanding further, the user can apply an activation force to the actuator mechanism 240 such that the actuator housing 262, the cap 255, the diverter 220, and the flow control mechanism 230 move in the distal direction. With the desired amount of the bodily-fluid disposed within the fluid reservoir 270 the volume of the fluid reservoir 270 is configured to remain constant as the actuator housing 262 and the cap 255 move relative to the plunger 248. Similarly stated, the pressure of the fluid reservoir 270 is configured to remain substantially unchanged as the transfer device 200 is moved from the first configuration to the second configuration.

[1103] As the actuator mechanism 240 is moved from the first configuration toward the second configuration, the flow control protrusions 208 engage the activation protrusions 232 (not shown in FIG. 12) included in the first control member 231 to move the flow control mechanism 230 toward the second configuration, as indicated by the arrow **EE**. Thus, when the flow control mechanism 230 is moved to the second configuration, the second lumen 239 defined by the second control member 235 is placed in fluid communication with the inlet lumen 223 defined by the inlet port 222 and the second outlet lumen 227 defined by the second outlet port 226.

[1104] As shown by the arrow **FF**, the inlet lumen 223 of the inlet port 222, the second lumen 239 of the second control member 235, and the second outlet lumen 227 of the second outlet port 226 define a fluid flow path such that the external reservoir (not shown in FIG. 12) is in fluid communication with the inlet port 222 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid is drawn into the external reservoir and is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 270 defined by the actuator housing 262. In this manner, the bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 200, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe(s)). With the desired amount of bodily-fluid contained in the external fluid reservoir, the user can remove the activation force from the actuator mechanism 240 (e.g., remove the portion of the hand engaging the actuator mechanism 240). With the removal of the activation force, the spring 261 exerts the force of expansion (described above) to move the transfer device 200 from the second configuration to the storage configuration. With the transfer device 200 in the storage configuration, the first outlet port 224 is fluidically isolated from the first lumen 238 and/or the second lumen 239 of the flow control mechanism 230. Thus, the bodily-fluid contained within the actuator housing 262 is fluidically isolated from a volume outside the actuator housing 262 and the external reservoir can be decoupled from the transfer device 200. In addition, the bodily-fluid contained within

the actuator housing 262 is isolated from the patient and the healthcare worker, and can be safely disposed of (e.g., in a biohazard materials container) in a "closed" device.

[1105] While the transfer device 200 is shown and described in FIGS. 2-12 as disposing the diverter 220 within the housing 201, in some embodiments, a transfer device can include a diverter and housing that are monolithically formed. For example, FIGS. 13-19 illustrate a transfer device 300 according to an embodiment. FIGS. 13 and 14 illustrate the transfer device 300 in a first configuration. The transfer device 300 includes a housing 301, having a diverter 320 and defining a fluid reservoir 370, a flow control mechanism 330, and an actuator 340.

[1106] The housing 301 includes a proximal end portion 302 and a distal end portion 303. The distal end portion 303 of the housing 301 includes a set of walls 304 that define a channel 305 configured to receive a distal portion 342 of the actuator 340. The walls 304 can be configured to define the channel 305 with any suitable shape, size, or configuration. For example as shown in FIG. 16, the walls 304 can be configured to further define a slot 319 in the channel 305 configured to receive an activation extension 346 included in the actuator 340 (FIG. 15). Similarly stated, the slot 319 can be configured to receive the activation extension 346 included in the distal portion 342 of the actuator 340, disposed within the channel 305, such that the activation extension 346 can pass through the walls 304 and be disposed substantially outside the channel 305, as described in further detail herein.

[1107] The walls 304 of the distal end portion 303 of the housing 301 also include a recessed surface 315 and a stop 313 (FIGS. 15 and 16). The stop 313 defines a proximal boundary of the channel 305 that can limit the movement of the actuator 340 within the channel 305. Furthermore, the stop 313 defines a passageway 314 configured to receive a portion of the actuator 340 such that the portion of the actuator 340 can extend in the proximal direction beyond the stop 313, as further described herein. The recessed surface 315 is configured to be a flat surface from which the diverter 320 can extend. Similarly stated, the diverter 320 is a set of walls configured to extend perpendicularly from the recessed surface 315. In this manner, the diverter 320 receives at least a portion of the flow control mechanism 340, as described in further detail herein. While shown and described as extending perpendicularly from the recessed surface 315, in other embodiments, the diverter 320 can extend from the recessed surface 315 at any suitable angular orientation.

[1108] As shown in FIG. 15, the proximal end portion 302 of the housing 301 includes a set of walls 318 that extend from the stop 313 in the proximal direction. In this manner, the walls 318 define a tubular shape substantially enclosed at the distal end by the stop 313 and open at the proximal end. The walls 318 define a slot 312 and an inner volume 311 configured to receive a proximal end portion 341 of the actuator 340. As further described herein, the proximal end portion 302 of the housing 301, the stop 313, and the proximal end portion 341 of the actuator 340 define a fluid reservoir 370 configured to receive and/or contain a bodily fluid.

[1109] As shown in FIG. 16, the diverter 320 includes an inlet port 322, a first outlet port 324, and a second outlet port 326, and defines an inner volume 321. The inner volume 321 is configured to receive at least a portion of the flow control mechanism 330, as further described herein. The inlet port 322 of the diverter 320 defines an inlet lumen 323. The inlet lumen 323 is configured to be in fluid communication with the inner volume 321. Similarly stated, the inlet lumen 323 of the inlet port 322 extends through a wall defining the inner volume 321 of the diverter 320.

[1110] The inlet port 322 is further configured to be fluidically coupled to a medical device (not shown) defining a fluid flow pathway for withdrawing and/or conveying the bodily-fluid from a patient to the transfer device 300. For example, the inlet port 322 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). Similarly stated, the inlet lumen 323 defined by the inlet port 322 is placed in fluid communication with a lumen defined by a lumen-containing device, when the lumen-containing device is coupled to the inlet port 322. Expanding further, when the lumen-containing device is disposed within a portion of a body of the patient (e.g., within a vein of the patient), the inner volume 321 of the diverter 320 is placed in fluid communication with the portion of the body of the patient.

[1111] The first outlet port 324 of the diverter 320 defines a first outlet lumen 325. The first outlet lumen 325 is configured to be in fluid communication with the inner volume 321 of the diverter 320 and the fluid reservoir 370 (described above). Similarly stated, the first outlet lumen 325 is configured to extend through the wall defining the inner volume 321 and through a portion of the stop 313 defining the fluid reservoir 370, thereby placing the fluid reservoir 370 in fluid communication with the inner volume 321. The second outlet port 326 of the diverter 320 defines a second outlet lumen 327 and can be coupled to an external fluid

reservoir. In this manner, the second outlet lumen 327 can extend through the wall defining the inner volume 321 to be in fluid communication with the inner volume 321 and can be fluidically coupled to the external reservoir to place the external fluid reservoir in fluid communication with the inner volume 321.

[1112] As shown in FIG. 15, the flow control mechanism 330 includes a first control member 331 and a second control member 335. At least a portion of the flow control mechanism 330 is configured to be disposed within the inner volume 321 defined by the diverter 320. In this manner, the flow control mechanism 330 defines a circular cross-sectional shape such that when the flow control mechanism 330 is disposed within the inner volume 321, a portion of the flow control mechanism 330 forms a friction fit with the walls of the diverter 320 defining the inner volume 321, as described in further detail herein.

[1113] The first control member 331 includes a set of activation protrusions 332 configured to engage a set of protrusion 347 included in the activation extension 346 of the actuator 340. Therefore, in use, the actuator 340 can engage the activation protrusions 332 to move the flow control mechanism 330 between a first configuration and a second configuration. The second control member 335 defines a first lumen 338 and a second lumen 339 and can be formed from any suitable material. For example, in some embodiments, the second control member 335 is formed from silicone. In other embodiments, the second control member 335 can be any suitable elastomer configured to deform when disposed within the inner volume 321 of the diverter. Expanding further, the second control member 335 has a diameter larger than the diameter of the inner volume 321. In the manner, the diameter of the second control member 335 is reduced when the second control member 335 is disposed within the inner volume 321. Thus, the outer surface of the second control member 335 forms a friction fit with the inner surface of the walls defining the inner volume 321.

[1114] The second control member 335 is configured to be coupled to the first control member 331. For example, in some embodiments, the first control member 331 can be coupled to the second control member 335 via a mechanical fastener and/or adhesive. In other embodiments, the first control member 331 and the second control member 335 can be coupled in any suitable manner. In this manner, the second control member 335 is configured to move concurrently with the first control member 331 when the activation extension 347 of the actuator 340 engages the activation protrusions 332 of the first control

member 331. Similarly stated, the flow control mechanism 330 is moved between the first configuration and the second configuration when the first control member 331 and the second control member 335 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 330 is in the first configuration, the first lumen 338 is placed in fluid communication with the inlet lumen 323 defined by the inlet port 322 and the first outlet lumen 325 defined by the first outlet port 324. When the flow control mechanism 330 is in the second configuration, the second lumen 339 is placed in fluid communication with the inlet lumen 323 defined by the inlet port 322 and the second outlet lumen 327 defined by the second outlet port 326, as described in further detail herein.

[1115] As described above, the actuator mechanism 340 includes the proximal end portion 341, the distal end portion 342, and an actuator arm 343 therebetween. The actuator mechanism 340 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 300 between a first configuration and a second configuration, as described in further detail herein. The proximal end portion 341 includes a plunger 348 configured to be disposed within the inner volume 311 of the housing 301. More particularly, the plunger 348 includes a seal member 354 configured to define a friction fit with the inner surface of the walls 318 defining the inner volume 311. Similarly stated, the seal member 354 defines a fluidic seal with the inner surface of the walls 318 defining the inner volume 311 such that a portion of the inner volume 311 proximal of the seal member 354 is fluidically isolated from a portion of the inner volume 311 distal of the seal member 354.

[1116] The actuator arm 343 is configured to extend from the proximal end portion 341 of the actuator 340 through the passageway 314 defined by the stop 313. Therefore, as described above, the distal end portion 342 of the actuator 340 is disposed on a distal side of the stop 313. More specifically, the distal end portion 342 includes an engagement portion 344 and the activation portion 346. The engagement portion 344 and at least a portion (e.g., a distal portion) of the actuator arm 343 are configured to be disposed within the channel 305 such that the activation portion 346 can extend through the slot 319, as described above. In this manner, a user can engage the engagement portion 344 to move the actuator 340 in a distal direction between a first configuration and a second configuration, as further described herein.

[1117] In some embodiments, the transfer device 300 can be stored in the first configuration in which the first lumen 338 of the second control member 335 is in fluid communication with the inlet port 322 and the first outlet port 324. In such embodiments, the friction fit defined by the second control member 335 and the walls of the diverter 320 defining the inner volume 321 maintain the flow control mechanism 330 in the first configuration until the actuator 340 moves the flow control mechanism 330 to the second configuration.

[1118] In use, a user can engage the transfer device 300 to couple the inlet port 322 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. With the inlet port 322 coupled to the lumen-defining device the inlet lumen 323 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 323 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 326 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA blood culture collection bottle with media specifically designed to facilitate the growth of certain types of microbes (e.g., aerobic media/broth and/or aerobic media/broth), manufactured by BIOMERIEUX, INC.

[1119] With the inlet port 322 coupled to the lumen-defining device and the second outlet port 326 coupled to the external fluid reservoir, a user can begin the transfer of a bodily-fluid by applying an activation force to the engagement portion 344 of the actuator 340, thereby moving the actuator 340 the distal direction, as shown by the arrow **GG** in FIG. 17. More specifically and as described above, the plunger 348 engages the inner surface of the walls 318 defining the inner volume 311 such that the volume of the fluid reservoir 370 is increased (e.g., as defined by the plunger 348, the walls 318 of the housing 301 and the stop 313). With the fluid reservoir 370 being fluidically isolated (as described above) from a volume on the proximal side of the seal member 354, the increase in the volume of the fluid reservoir 370 produces a negative pressure within the fluid reservoir 370. Moreover, with the flow control mechanism 330 in the first configuration, negative pressure differential introduces a suction force within the first lumen 338, the inlet lumen 323, and the first outlet lumen 325.

[1120] As shown by the arrow **HH**, the inlet lumen 323 of the inlet port 322, the first lumen 338 of the second control member 335, and the first outlet lumen 325 of the first outlet port 324 define a fluid flow path such that the second portion 376 of the inner volume 373 defined by the fluid reservoir 370 is in fluid communication with the inlet port 322. Furthermore, with the inlet port 322 coupled to the lumen-defining device the fluid reservoir 370 is in fluid communication with the portion of the patient (e.g., the vein) and at least a portion of the suction force is introduced to the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 370. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes dislodged during the insertion of the lumen-defining device.

[1121] In some embodiments, the magnitude of the suction force can be modulated by moving the actuator 340 in the proximal or distal direction. For example, in some embodiments, it can be desirable to limit the amount of suction force introduced to a vein. In such embodiments, the user can move the actuator 340 in the proximal direction (e.g., the direction of the arrow **II** in FIG. 18) such the activation extension 346 can engage the protrusions 332 of the first control member 331. In this manner, the protrusions 347 included in the activation extension 346 can mesh with the protrusions 332 of the first control member 331 to rotate the first control member 331 in the direction of the arrow **JJ**. The rotation of the flow control mechanism 330 (e.g., in a direction opposite the arrow **JJ**) reduces the size of the fluid pathway (e.g., an inner diameter) between the inlet lumen 323 and the first lumen 338 and the first outlet port 325 and the first lumen 338, thereby reducing the suction force introduced into the vein of the patient.

[1122] With the desired amount of bodily-fluid transferred to the fluid reservoir 370, a user can engage the transfer device 300 to move the transfer device 300 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the fluid reservoir 370 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 300 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 370 is equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein). In such embodiments, the equalizing of the pressure between the fluid reservoir 370 and the portion of the body stops the flow of the bodily-fluid into the fluid reservoir 370. In

some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 323, the first lumen 338, the first outlet lumen 325, and the lumen-defining device.

[1123] As shown in FIG. 18, the transfer device 300 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 340 in the distal direction, as indicated by the arrow **II**. As the actuator mechanism 340 is moved from the first configuration toward the second configuration, the protrusions 347 of the activation extension 346 further engage the activation protrusions 332 included in the first control member 331 to move the flow control mechanism 330 to the second configuration, as indicated by the arrow **KK** in FIG. 19. In this manner, the flow control mechanism 330 is moved to the second configuration, and the first lumen 238 is fluidically isolated from the inlet lumen 223 and the first outlet lumen 225. In addition, the second lumen 339 defined by the second control member 335 is placed in fluid communication with the inlet lumen 323 defined by the inlet port 322 and the second outlet lumen 327 defined by the second outlet port 326.

[1124] As shown by the arrow **LL**, the inlet lumen 323 of the inlet port 322, the second lumen 339 of the second control member 335, and the second outlet lumen 327 of the second outlet port 326 define a fluid flow path such that the external reservoir (not shown in FIG. 19) is in fluid communication with the inlet port 322 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid is drawn into the external reservoir and is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 370.

[1125] The bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 300, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe). In some embodiments, with the desired amount of bodily-fluid contained in the external fluid reservoir, the user can further move the actuator 340 in the proximal direction to place the

transfer device 300 in a third configuration. In such embodiments, the actuator 340 can be moved in the proximal direction such that the engagement portion 344 and/or the activation extension 346 contact the stop 313, thereby limiting further proximal movement of the actuator 340. In this configuration, the actuator 340 can place the flow control mechanism 330 in a third configuration configured to fluidically isolate the first lumen 338 and the second lumen 339 from the inlet lumen 323, the first outlet lumen 325, and the second outlet lumen 327. Thus, the bodily-fluid contained within the fluid reservoir 370 is fluidically isolated from a volume outside the fluid reservoir 370 and the external reservoir can be decoupled from the transfer device 300.

[1126] While the transfer device 300 is shown and described in FIGS. 13-19 as being configured to actuated by continual user influence (e.g., the user manually moves the actuator 340 in the proximal direction), in some embodiments, a transfer device need not require continual user influence. For example, FIGS. 20-26 illustrate a transfer device 400 according to an embodiment. FIGS. 20 and 21 illustrate the transfer device 400 in a first configuration. The transfer device 400 includes a housing 401, having a diverter 420 and defining a fluid reservoir 470, a flow control mechanism 430, and an actuator mechanism 440.

[1127] The housing 401 includes a proximal end portion 402 and a distal end portion 403. The distal end portion 403 of the housing 401 includes a set of walls 404 having a recessed portion 415 and a stop 413 (FIGS. 22 and 23). The stop 413 defines a distal boundary of the recessed portion 415 and defines a passageway 414. The passageway 414 is configured to receive an activation extension 346 included in the actuator mechanism 440 such that the activation extension 346 extends through the stop 413, as further described herein. The recessed portion 415 includes a substantially flat surface from which the diverter 420 can extend (FIG. 22). Similarly stated, the diverter 420 is a set of walls configured to extend perpendicularly from the surface of the recessed portion 415. In this manner, the diverter 420 receives at least a portion of the flow control mechanism 430, as described in further detail herein. While shown and described as extending perpendicularly from the surface of the recessed portion 415, in other embodiments, the diverter 420 can extend from the surface at any suitable angular orientation.

[1128] The proximal end portion 402 of the housing 401 includes a set of walls 418 that extend from the stop 413 in the proximal direction. In this manner, the walls 418 define a tubular shape substantially enclosed at the distal end by the stop 413 and open at the proximal

end. The proximal end portion 402 of the housing 401 can be formed from any suitable material. For example, in some embodiments, the proximal end portion 402 can be formed from a relatively flexible material. In such embodiments, the proximal end portion 402 can be configured to deform (e.g., bend, compress, or otherwise reconfigure) under a given force, as described in further detail herein. As shown in FIG. 23, the walls 418 include shoulder 416 and retention tabs 417 and define an inner volume 411 configured to receive a portion of the actuator mechanism 440. As further described herein, the proximal end portion 402 of the housing 401, the stop 413, and a portion of the actuator mechanism 440 define a fluid reservoir 470 configured to receive and/or contain a bodily fluid.

[1129] As shown in FIG. 23, the diverter 420 includes an inlet port 422, a first outlet port 424, and a second outlet port 426, and defines an inner volume 421. The inner volume 421 is configured to receive at least a portion of the flow control mechanism 430, as further described herein. The inlet port 422 of the diverter 420 defines an inlet lumen 423. The inlet lumen 423 is configured to be in fluid communication with the inner volume 421. Similarly stated, the inlet lumen 423 of the inlet port 422 extends through a wall defining the inner volume 421 of the diverter 420.

[1130] The inlet port 422 is further configured to be fluidically coupled to a medical device (not shown) defining a fluid flow pathway for withdrawing and/or conveying the bodily-fluid from a patient to the transfer device 400. For example, the inlet port 422 can be fluidically coupled to a needle or other lumen-containing device (e.g., flexible sterile tubing). Similarly stated, the inlet lumen 423 defined by the inlet port 422 is placed in fluid communication with a lumen defined by a lumen-containing device, when the lumen-containing device is coupled to the inlet port 422. Expanding further, when the lumen-containing device is disposed within a portion of a body of the patient (e.g., within a vein of the patient), the inner volume 421 of the diverter 420 is placed in fluid communication with the portion of the body of the patient.

[1131] The first outlet port 424 of the diverter 420 defines a first outlet lumen 425. The first outlet lumen 425 is configured to be in fluid communication with the inner volume 421 of the diverter 420 and the fluid reservoir 470 (described above). Similarly stated, the first outlet lumen 425 is configured to extend through the wall defining the inner volume 421 and through a portion of the stop 413 defining the fluid reservoir 470, thereby placing the fluid reservoir 470 in fluid communication with the inner volume 421. The second outlet port 426

of the diverter 420 defines a second outlet lumen 427 and is configured to be coupled to an external fluid reservoir. In this manner, the second outlet lumen 427 can extend through the wall defining the inner volume 421 to be in fluid communication with the inner volume 421 and can be fluidically coupled to the external reservoir to place the external fluid reservoir in fluid communication with the inner volume 421.

[1132] As shown in FIG. 24, the flow control mechanism 430 includes a first control member 431 and a second control member 435. At least a portion of the flow control mechanism 430 is configured to be disposed within the inner volume 421 defined by the diverter 420. In this manner, the flow control mechanism 430 defines a circular cross-sectional shape such that when the flow control mechanism 430 is disposed within the inner volume 421, a portion of the flow control mechanism 430 forms a friction fit with the walls of the diverter 420 defining the inner volume 421, as described in further detail herein.

[1133] The first control member 431 includes an activation protrusion 432 and engagement protrusions 433. The activation protrusion 432 is configured to engage a protrusion 447 included in the activation extension 446 of the actuator mechanism 440. Therefore, in use, the actuator mechanism 440 can engage the activation protrusion 432 to move the flow control mechanism 430 between a first configuration and a second configuration. The second control member 435 defines a first lumen 438, a second lumen 439, and a set of grooves 437. The second control member 435 can be formed from any suitable material such as, for example, silicone. In other embodiments, the second control member 435 can be any suitable elastomer configured to deform when disposed within the inner volume 421 of the diverter. Expanding further, the second control member 435 has a diameter larger than the diameter of the inner volume 421. In the manner, the diameter of the second control member 435 is reduced when the second control member 435 is disposed within the inner volume 421. Thus, the outer surface of the second control member 435 forms a friction fit with the inner surface of the walls defining the inner volume 421.

[1134] The grooves 437 defined by the second control member 435 are configured to receive the engagement protrusions 433. In this manner, the first control member 431 can selectively engage the second control member 435 such that the second control member 435 is moved concurrently with the first control member 431 when the activation extension 447 of the actuator mechanism 440 engages the activation protrusion 432 of the first control member 431. Similarly stated, the flow control mechanism 430 is moved between the first

configuration and the second configuration when the first control member 431 and the second control member 435 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 430 is in the first configuration, the first lumen 438 is placed in fluid communication with the inlet lumen 423 defined by the inlet port 422 and the first outlet lumen 425 defined by the first outlet port 424. When the flow control mechanism 430 is in the second configuration, the second lumen 439 is placed in fluid communication with the inlet lumen 423 defined by the inlet port 422 and the second outlet lumen 427 defined by the second outlet port 426, as described in further detail herein.

[1135] As shown in FIGS. 22 and 25, the actuator mechanism 440 includes an engagement member 444, the activation extension 446, a plunger 448, and a spring 461. The engagement member 444 is configured to be coupled to the distal end portion 403 of the housing 401. In this manner, the housing 401 and the engagement member 444 house the flow control mechanism 430 and at least a portion of the diverter 420. The engagement member 444 includes a throttling button 445. The throttling button 445 is configured such that when engaged by a user, the throttling button 445 interacts with the flow control mechanism 430 to modulate the movement of the flow control mechanism 440, as described in further detail herein.

[1136] The plunger 448 includes a proximal end portion 449 and a distal end portion 450 and is configured to be disposed within the inner volume 411 defined by the housing 401. The proximal end portion 449 of the plunger 448 is configured to selectively engage the retention protrusions 417 included in the housing 401. The plunger 448 further includes a sealing member 454 disposed at the distal end portion 450. The seal member 454 is configured to define a friction fit with the inner surface of the walls 418 defining the inner volume 411. Similarly stated, the seal member 454 defines a fluidic seal with the inner surface of the walls 418 defining the inner volume 411 such that a portion of the inner volume 411 proximal of the seal member 454 is fluidically isolated from a portion of the inner volume 411 distal of the seal member 454.

[1137] The spring 461 includes a proximal end portion 462 and a distal end portion 463 and is configured to circumscribe the plunger 448. Similarly stated, the plunger 448 is disposed within the spring 461 when the spring 461 and the plunger 448 are disposed within the housing 401. Furthermore, when disposed within the inner volume 411, the distal end portion 463 of the spring 461 is configured to engage the shoulder 416 of the housing 401

and the proximal end portion 462 is configured to engage the proximal end portion 449 of the plunger 448. In this manner, the spring 461, when urged to move from a first (compressed) configuration to a second (expanded) configuration, is configured to move the plunger 448 in the proximal direction, as described in further detail herein.

[1138] The activation extension 446 can be any suitable size, shape, or configuration. For example, as shown in FIG. 22, the activation extension 446 can be a flexible tether formed from, for example, nylon. In this manner, the activation extension 446 can be substantially flexible in a lateral direction and substantially rigid in an axial direction. Similarly stated, in some embodiments, the activation extension 446 is configured to bend, twist, conform, and/or otherwise reconfigure without stretching. Said yet another way, the length of the activation extension 446 is configured to remain substantially unchanged as the activation extension 446 is bent or otherwise reconfigured.

[1139] The activation extension 446 is configured to be coupled to the distal end portion 450 of the plunger 448. More specifically, a proximal end portion of the activation extension 446 is disposed within the inner volume 411 of the housing 401 and is coupled to the plunger 448 and a distal end portion of the activation extension 446 passes through the stop 413 and is disposed within the recessed portion 415 of the housing 401. In this manner, the activation extension 446 is configured engage the activation protrusion 432 of the first control member 431 to move the flow control mechanism 430 between the first configuration and the second configuration, as described in further detail herein.

[1140] In some embodiments, the transfer device 400 can be stored in a storage configuration in which the second control member 435 of the flow control mechanism 430 fluidically isolates the inlet port 422, the first outlet port 424, and the second outlet port 426 from the inner volume 421 defined by the diverter 420. In such embodiments, first lumen 438 and the second lumen 439 are fluidically isolated from the inlet lumen 423, the first outlet lumen 425, and the second outlet lumen 427. Furthermore, the friction fit defined by the second control member 435 and the walls of the diverter 420 defining the inner volume 421 maintain the flow control mechanism 430 in the storage configuration until the flow control mechanism 430 is moved from the storage configuration.

[1141] In use, a user can engage the transfer device 400 to couple the inlet port 422 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a

butterfly needle. With the inlet port 422 coupled to the lumen-defining device the inlet lumen 423 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 423 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 426 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1142] With the inlet port 422 coupled to the lumen-defining device and the second outlet port 426 coupled to the external fluid reservoir, a user can begin a transfer of a bodily-fluid by applying an activation force to the transfer device 400. More specifically, the user can introduce an activation force to the proximal end portion 402 of the housing 401 by squeezing, for example, the sides of the proximal end portion 402 such that the proximal end portion 402 deforms in response to the activation force, as described above. Thus, the proximal end portion 402 is urged (in response to the activation force) to reconfigure such that the retention tabs 417 are removed from contact with the proximal end portion 449 of the plunger 448. Expanding further, the retention tabs 417 are configured to apply a reaction force to the proximal end portion 449 of the plunger 448 in response to an expansion force exerted by the spring 461, thereby maintaining the spring 461 in the compressed configuration. With the retention tabs 417 removed from contact with the plunger 448 and with the distal end portion 463 of the spring 461 in contact with the shoulder 416 of the housing 401, the proximal end portion 462 of the spring 462 expands to move the plunger 448 in the direction of the arrow **MM** in FIG. 25.

[1143] As described above, the plunger 448 engages the inner surface of the walls 418 defining the inner volume 411 such that the volume of the fluid reservoir 470 is increased (e.g., as defined by the plunger 448, the walls 418 of the housing 401 and the stop 413). With the fluid reservoir 470 being fluidically isolated (as described above) from a volume on the proximal side of the seal member 454, the increase in the volume of the fluid reservoir 470 produces a negative pressure within the fluid reservoir 470. Moreover, movement of the plunger 448 in the proximal direction is such that the activation extension 446 is moved in the proximal direction. In this manner, the protrusion 447 of the activation extension 446

engages the protrusion 432 of the first control member 431 to move the flow control mechanism 430 from the storage configuration to the first configuration, as indicated by the arrow **NN**. With the flow control mechanism 430 in the first configuration, the negative pressure of the fluid reservoir 470 introduces a suction force within the first lumen 438, the inlet lumen 423, and the first outlet lumen 425.

[1144] As shown by the arrow **OO**, the inlet lumen 423 of the inlet port 422, the first lumen 438 of the second control member 435, and the first outlet lumen 425 of the first outlet port 424 define a fluid flow path such that the second portion 476 of the inner volume 473 defined by the fluid reservoir 470 is in fluid communication with the inlet port 422. Furthermore, with the inlet port 422 coupled to the lumen-defining device the fluid reservoir 470 is in fluid communication with the portion of the patient (e.g., the vein) and at least a portion of the suction force is introduced to the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 470. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes dislodged during the insertion of the lumen-defining device.

[1145] In some embodiments, the rate of expansion of the spring 461 can be modulated by engaging the throttling button 445 included in the engagement portion 444 of the actuator mechanism 440. For example, in some embodiments, it can be desirable to limit the amount of suction force introduced to a vein. In such embodiments, the user can exert a force on the throttling button 445 such that the throttling button 445 is moved to engage the flow control mechanism 430. In this manner, the throttling button 445 can increase the friction between, for example, the second control member 435 and the walls defining the inner volume 421 of the diverter. Thus, the increase in friction between the second control member 435 and the walls defining the inner volume 411 resist the force exerted by the activation extension 446, thereby slowing the rate of expansion of the spring. In this manner, the reduction of pressure (e.g., the increase in negative pressure) of the fluid reservoir 470 can be controlled to maintain a desired pressure differential between the vein and the fluid reservoir 470 and limit the suction force introduced to the vein.

[1146] In some embodiments, the user can depress the throttling button 445 to maintain the transfer device 400 in the first configuration. With the desired amount of bodily-fluid transferred to the fluid reservoir 470, a user can disengage the throttling button 445 to disengage the throttling button 445 from the flow control mechanism 430. In this manner,

the friction between the second control member 435 and the walls defining the inner volume 411 is reduced and the force of expansion exerted by the spring is sufficient to again overcome the friction between the second control member 435 and the walls defining the inner volume 411. Therefore, the transfer device 400 is moved 400 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above).

[1147] In some embodiments, the desired amount of bodily-fluid transferred to the fluid reservoir 470 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 400 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 470 is equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein). In such embodiments, the equalizing of the pressure between the fluid reservoir 470 and the portion of the body stops the flow of the bodily-fluid into the fluid reservoir 470. In some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 423, the first lumen 438, the first outlet lumen 425, and the lumen-defining device.

[1148] As described above, the transfer device 400 is moved from the first configuration to the second configuration by further moving the plunger 448 in the distal direction. As the plunger 448 is moved from the first configuration toward the second configuration, the protrusions 447 of the activation extension 446 further engage the activation protrusions 432 included in the first control member 431 to move the flow control mechanism 430 to the second configuration, as indicated by the arrow **PP** in FIG. 26. In this manner, the flow control mechanism 430 is moved to the second configuration, and the first lumen 438 is fluidically isolated from the inlet lumen 423 and the first outlet lumen 425. In addition, the second lumen 439 defined by the second control member 435 is placed in fluid communication with the inlet lumen 423 defined by the inlet port 422 and the second outlet lumen 427 defined by the second outlet port 426.

[1149] As shown by the arrow **QQ** in FIG. 27, the inlet lumen 423 of the inlet port 422, the second lumen 439 of the second control member 435, and the second outlet lumen 427 of the second outlet port 426 define a fluid flow path such that the external reservoir (not shown in FIG. 19) is in fluid communication with the inlet port 422 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative

pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. In some embodiments, the user can engage throttling button 445 to again increase the friction between the second control member 435 and the walls defining the inner volume 411. In this manner, further expansion of the spring 461 is limited and a desired amount of bodily-fluid can be drawn into the external reservoir such that the desired amount of bodily fluid is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 470.

[1150] The bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally-residing microbes, microbes within a lumen defined by the transfer device 400, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe). In some embodiments, with the desired amount of bodily-fluid contained in the external fluid reservoir, the user can disengage the throttling button 445 such that the transfer device returns to the storage configuration. As described above, in this configuration the actuator mechanism 440 can place the flow control mechanism 430 in a third configuration configured to fluidically isolate the first lumen 438 and the second lumen 439 from the inlet lumen 423, the first outlet lumen 425, and the second outlet lumen 427. Thus, the bodily-fluid contained within the fluid reservoir 470 is fluidically isolated from a volume outside the fluid reservoir 470 and the external reservoir can be decoupled from the transfer device 400.

[1151] While the transfer device 400 is described above with reference to FIGS. 20-27 as being stored in a storage configuration, in some embodiments, a transfer device can be stored in a first configuration (e.g., defining a flow path between an inlet port and a fluid reservoir). For example, FIGS. 28 and 29 illustrate a transfer device 500 according to an embodiment. In some embodiments, aspects of the transfer device 500 can be substantially similar to corresponding aspects of the transfer device 200. In this manner, details of certain aspects are not described in further detail herein and it should be understood that such aspects are substantially similar in form or function to the corresponding aspects.

[1152] The transfer device 500 includes a housing 501, a diverter 520, a flow control mechanism 530, and an actuator 540. The housing 501 includes a proximal end portion 502 and a distal end portion 503. The proximal end portion 502 defines an inner volume configured to receive at least a portion of the actuator mechanism 540, as described in further

detail herein. The distal end portion 503 of the housing 501 includes the diverter 520. Similarly stated, the diverter 520 is monolithically formed with the distal end portion 503 of the housing 501. The diverter 520 receives at least a portion of the flow control mechanism 530, as described in further detail herein.

[1153] As shown in FIG. 28, the diverter 520 includes an inlet port 522, a first outlet port 524, and a second outlet port 526, and defines an inner volume 521. The inner volume 521 is configured to receive at least a portion of the flow control mechanism 530, as further described herein. The inlet port 522 of the diverter 520 defines an inlet lumen 523. The inlet lumen 523 is configured to be in fluid communication with the inner volume 521. Similarly stated, the inlet lumen 523 of the inlet port 522 extends through a wall defining the inner volume 521 of the diverter 520.

[1154] The flow control mechanism 530 includes a first control member 531 and a second control member 535. At least a portion of the flow control mechanism 530 is configured to be disposed within the inner volume 521 defined by the diverter 520. In this manner, the flow control mechanism 530 defines a circular cross-sectional shape such that when the flow control mechanism 530 is disposed within the inner volume 521, a portion of the flow control mechanism 530 forms a friction fit with the walls of the diverter 520 defining the inner volume 521, as described further detail herein.

[1155] The first control member 53 is configured to engage an activation extension 546 of the actuator mechanism 540 and move between a first configuration and a second configuration. The second control member 535 defines a first lumen 538 and a second lumen 539and is configured to be coupled to the first control member 531. Therefore, the second control member 535 is configured to move concurrently with the first control member 531 when the activation extension 546 engages the first control member 531. Similarly stated, the flow control mechanism 530 is moved between the first configuration and the second configuration when the first control member 531 and the second control member 535 are moved between the first configuration and the second configuration, respectively. Furthermore, when the flow control mechanism 530 is in the first configuration, the first lumen 538 is placed in fluid communication with the inlet lumen 523 defined by the inlet port 522 and the first outlet lumen 525 defined by the first outlet port 524. When the flow control mechanism 530 is in the second configuration, the second lumen 539 is placed in fluid

communication with the inlet lumen 523 defined by the inlet port 522 and the second outlet lumen 527 defined by the second outlet port 526, as described in further detail herein.

[1156] The actuator mechanism 540 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 500 between a first configuration and a second configuration, as described in further detail herein. The actuator mechanism 540 includes a plunger 548 and the activation extension 546. The plunger 548 includes a proximal end portion 549, a distal end portion 550, and an engagement portion 544 and is configured to be disposed, at least partially within the inner volume 511 of the housing 501. The engagement portion 544 is configured to extend in the distal direction from the proximal end portion 549 of the plunger 548. In this manner, the engagement portion 544 can be engaged by a user to move the actuator mechanism 540 between the first configuration and the second configuration, as described in further detail herein.

[1157] The distal end portion 550 of the plunger 548 includes a seal member 554 configured to define a friction fit with the inner surface of the walls defining the inner volume 511. Similarly stated, the seal member 554 defines a fluidic seal with the inner surface of the walls defining the inner volume 511 such that a portion of the inner volume 511 proximal of the seal member 554 is fluidically isolated from a portion of the inner volume 511 distal of the seal member 554. Furthermore, the portion of the inner volume 511 distal of the seal member 554 defines a fluid reservoir 570. Similarly stated, the fluid reservoir 570 defined by the walls defining the inner volume 511 and the seal member 554 of the plunger 548.

[1158] The activation extension 546 includes a protrusion 547 configured to selectively engage the proximal end portion 549 of the plunger 548. In this manner, the proximal end portion 549 of the plunger 548 can move the activation extension 546 when the plunger 548 moves from a first configuration to a second configuration, as further described herein.

[1159] As described above, the transfer device 500 is stored in the first configuration in which the first lumen 538 of the second control member 535 is in fluid communication with the inlet port 522 and the first outlet port 524. In such embodiments, the friction fit defined by the second control member 535 and the walls of the diverter 520 defining the inner volume 521 maintain the flow control mechanism 530 in the first configuration until the actuator 540 moves the flow control mechanism 530 to the second configuration.

[1160] In use, a user can engage the transfer device 500 to couple the inlet port 522 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. With the inlet port 522 coupled to the lumen-defining device the inlet lumen 523 is placed in fluid communication with the lumen defined by the lumen-defining device. Furthermore, the distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thus, the inlet lumen 523 is in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 526 can be coupled to an external fluid reservoir (not shown).

[1161] With the inlet port 522 coupled to the lumen-defining device and the second outlet port 526 coupled to the external fluid reservoir, a user can begin the transfer of a bodily-fluid by applying an activation force to the engagement portion 544 of the actuator 540, thereby moving the plunger 548 in the distal direction, as shown by the arrow **RR** in FIG. 28. More specifically and as described above, the plunger 548 engages the inner surface of the walls defining the inner volume 511 such that the volume of the fluid reservoir 570 is increased (e.g., as defined by the plunger 548 and the housing 501). With the fluid reservoir 570 being fluidically isolated (as described above) from a volume on the proximal side of the seal member 554, the increase in the volume of the fluid reservoir 570 produces a negative pressure within the fluid reservoir 570. Moreover, with the flow control mechanism 530 in the first configuration, negative pressure differential introduces a suction force within the first lumen 538, the inlet lumen 523, and the first outlet lumen 525.

[1162] As shown by the arrow **SS**, the inlet lumen 523 of the inlet port 522, the first lumen 538 of the second control member 535, and the first outlet lumen 525 of the first outlet port 524 define a fluid flow path such that the second portion 576 of the inner volume 573 defined by the fluid reservoir 570 is in fluid communication with the inlet port 522. Furthermore, with the inlet port 522 coupled to the lumen-defining device the fluid reservoir 570 is in fluid communication with the portion of the patient (e.g., the vein) and at least a portion of the suction force is introduced to the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 570. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes dislodged during the insertion of the lumen-defining device.

[1163] As shown in FIG. 28, the actuator mechanism 540 is configured such that the proximal end portion 549 of the plunger 548 is spaced apart from the protrusion 547 of the

activation extension 546. In this manner, the plunger 548 can move in the proximal direction without engaging the protrusion 547 of the activation extension 546. Thus, the plunger 548 can move to introduce the change of the volume in the fluid reservoir 570 without the activation extension 546 moving the first control member 531 from the first configuration toward the second configuration. Therefore, the transfer device 500 can be stored in the first configuration, as described above.

[1164] With a desired amount of bodily-fluid transferred to the fluid reservoir 570, a user can move the transfer device 500 from the first configuration to the second configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the fluid reservoir 570 is a predetermined amount of fluid. For example, in some embodiments, the transfer device 500 can be configured to transfer bodily-fluid until the pressure within the fluid reservoir 570 is equilibrium with the pressure of the portion of the body in which the lumen-defining device is disposed (e.g., the vein). In such embodiments, the equalizing of the pressure between the fluid reservoir 570 and the portion of the body stops the flow of the bodily-fluid into the fluid reservoir 570. In some embodiments, the predetermined amount of bodily-fluid (e.g., volume) is at least equal to the combined volume of the inlet lumen 523, the first lumen 538, the first outlet lumen 525, and the lumen-defining device.

[1165] As shown in FIG. 29, the transfer device 500 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 540 in the distal direction, as indicated by the arrow **TT**. As the actuator mechanism 540 is moved from the first configuration toward the second configuration, the protrusions 547 of the activation extension 546 is engaged by the proximal end portion 549 of the plunger 548 such that the activation extension 546 is moved in the direction **TT**. Furthermore, the proximal motion of the activation extension 546 moves the first control member 331 and places the flow control mechanism 530 in the second configuration, as indicated by the arrow **UU**. In this manner, the first lumen 538 is fluidically isolated from the inlet lumen 523 and the first outlet lumen 525. In addition, the second lumen 539 defined by the second control member 535 is placed in fluid communication with the inlet lumen 523 defined by the inlet port 522 and the second outlet lumen 527 defined by the second outlet port 526.

[1166] As shown by the arrow **VV**, the inlet lumen 523 of the inlet port 522, the second lumen 539 of the second control member 535, and the second outlet lumen 527 of the second

outlet port 526 define a fluid flow path such that the external reservoir (not shown in FIGS. 28 and 29) is in fluid communication with the inlet port 522 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid is drawn into the external reservoir and is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 570.

[1167] The bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 500, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe). As described above, the bodily-fluid contained within the fluid reservoir 570 is fluidically isolated from a volume outside the fluid reservoir 570 and the external reservoir can be decoupled from the transfer device 500.

[1168] While some embodiments described above include a flow control mechanism that can be rotated to control the flow of a bodily-fluid (e.g., the flow rate) and/or to control the amount of negative pressure within a fluid reservoir, in other embodiments, bodily-fluid transfer device can include any suitable device, mechanism, and/or assembly that can control, at least partially, a flow of bodily-fluid (e.g., the flow rate of the bodily-fluid). For example, FIGS. 30-41 illustrate a transfer device 600 according to an embodiment. The transfer device 600 includes a housing 601, a diverter 620, a flow control mechanism 630, and adjustment mechanism 685, and an actuator 640. The transfer device 600 can be any suitable shape, size, or configuration. For example, the transfer device 600 can have a shape and size that is substantially similar to the transfer device 200 described above with reference to FIGS. 2-12. As such, portions of the transfer device 600 can be substantially similar in form and/or function to corresponding portions of the transfer device 200 of FIGS. 2-12. Thus, aspects of the transfer device 600 are not described in further detail herein.

[1169] The housing 601 of the transfer device 600 includes a proximal end portion 602 and a distal end portion 603. The distal end portion 603 includes a base 606 from which a set of walls 604 extend. The walls 604 of the housing 601 define a substantially annular shape

and define an inner volume 611 between the proximal end portion 602 and the distal end portion 603. The proximal end portion 602 of the housing 601 is open to receive at least a portion of the diverter 620, a portion of the flow control mechanism 630, and a portion of the actuator 640 within the inner volume 611 (see e.g., FIG. 31). The walls 604 of the housing 601 define a set of status windows 610 and a set of channels 605. The status windows 610 and the channels 605 can be any suitable shape or size. For example, the status windows 610 and the channels 605 can be substantially similar in form and function to the status windows 210 and the channels 205 of the transfer device 200.

[1170] As shown in FIGS. 32 and 33, the housing 601 includes a set of guide posts 607 and a set of flow control protrusions 608 and defines a passageway 614. The guide posts 607 engage a portion of the diverter 620 and a portion of the actuator 640, as further described herein. The flow control protrusions 608 extend from the base 606 in the proximal direction and can be arranged to selectively engage a portion of the flow control mechanism 630 to move the flow control mechanism 630 between a first configuration and a second configuration, as described in further detail herein. While only one flow control protrusion 608 is shown in FIGS. 32 and 33, the housing 601 can include, for example, two flow control protrusions 608 that are disposed adjacent to a guide post 607. As shown in FIG. 33, the passageway 614 extends through the base 606 and can be arranged to receive a portion of the flow control mechanism 630, as described in further detail herein.

[1171] As shown in FIG. 31, the actuator mechanism 640 includes the actuator housing 662, a plunger 648, and a cap 655. The actuator mechanism 640 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 600 between a first configuration and a second configuration, as described in further detail herein. The actuator housing 662 includes a proximal end portion 663 and a distal end portion 664 and defines an inner volume 665. The inner volume 665 of the actuator housing 662 receives the plunger 648 and at least a portion of the cap 655. The plunger 648 includes a set of seal member 654 that can form a friction fit with an inner surface (not shown in FIG. 31) of the actuator housing 662 that defines the inner volume 665 of the actuator housing 662. Thus, the plunger 648 can be configured to divide the inner volume 665 into a first portion 667 that is fluidically isolated from a second portion 670 (also referred to herein as "fluid reservoir"). The cap 655 defines an inlet port 658 and a set of guide post ports 659. The inlet port 658 receives a portion of a first outlet port 624 of the diverter 620. The guide

post ports 659 movably receive the guide posts 607 of the housing 601 to allow the guide posts 607 to be in contact with the plunger 648. In this manner, the actuator housing 662, the plunger 648, and the cap 655 of the actuator mechanism 640 can be substantially similar to or the same as the actuator housing 262, the plunger 248, and the cap 255, respectively, of the actuator mechanism 640 included in the transfer device 200 described above with reference to FIGS. 2-12. Thus, aspects of the actuator housing 662, the plunger 648, and the cap 655 are not described in further detail herein. As shown in FIG. 31, the actuator mechanism 640 can differ from the actuator mechanism 240 in that the actuator mechanism 640 does not include a spring such as the spring 261 of the actuator mechanism 240. In other embodiments, however, the actuator mechanism 640 can include a spring that is substantially similar to the spring 261.

[1172] As shown in FIGS. 34 and 35, the diverter 620 of the transfer device 600 includes a proximal end portion 628 and a distal end portion 629 and defines an inner volume 621. The inner volume 621 can receive at least a portion of the flow control mechanism 630, as described above with reference to the transfer device 200. The proximal end portion 628 of the diverter 620 includes a first outlet port 624. The distal end portion 629 includes an inlet port 622 and a second outlet port 626. The diverter 620 is movably disposed within the inner volume 611 of the housing 601 such that a portion of the inlet port 622 extends through a first channel 605 defined by the walls 604 of the housing 601 and a portion of the second outlet port 626 extends through a second channel 605 opposite the first channel (see e.g., FIG. 30). While not explicitly shown in FIGS. 30-41, the distal end portion 629 of the diverter 620 can engage the guide posts 607 to limit, for example, lateral movement of the diverter 620 as the diverter 620 is moved in the inner volume 611. Similarly stated, the guide posts 607 of the housing 601 can engage the diverter 620 to substantially limit its movement to a proximal direction or distal direction relative to the housing 601, as further described herein.

[1173] As shown in FIG. 35, the inlet port 622, the first outlet port 624, and the second outlet port 626 define an inlet lumen 623, a first outlet lumen 625, and a second outlet lumen 627, respectively, that are each in fluid communication with the inner volume 621. The inlet port 622 can be fluidically coupled to a needle or other lumen-containing device (not shown in FIGS. 30-41) that can be disposed within a portion of a body of the patient (e.g., within a vein of the patient), the first outlet port 624 can be fluidically coupled to a portion of the actuator 640, and the second outlet port 626 can be fluidically coupled to an external

reservoir (e.g., a sample reservoir not shown in FIGS. 30-41). In this manner, the diverter 620 can be arranged to selectively place the portion of the actuator 640 or the external reservoir in fluid communication with the portion of the body via the inlet port 622 and the first outlet port 624 or via the inlet port 622 and the second outlet port 626, respectively. As shown in FIG. 35, the diverter 620 also defines an opening 689 that can receive a portion of the flow control mechanism 630, as described in further detail herein.

[1174] As shown in FIGS. 36 and 37, the flow control mechanism 630 includes a first activation mechanism 631A, a second activation mechanism 631B, a control member 635, and an adjustment mechanism 685. At least a portion of the flow control mechanism 630 is configured to be disposed within the inner volume 621 defined by the diverter 620. More specifically, the flow control mechanism 630 has a circular cross-sectional shape such that when the flow control mechanism 630 is disposed in the inner volume 621, a portion of the control member 635 forms a friction fit with the walls of the diverter 620 defining the inner volume 621, as described in further detail herein. Although not shown in FIGS. 30-41, the flow control mechanism 630 can be arranged within the inner volume 611 of the housing 601 and the inner volume 621 of the diverter 620 such that the first activation mechanism 631A and the second activation mechanism 631B are disposed adjacent to and in contact with the control member 635. More specifically, the first activation mechanism 631A and the second activation mechanism 631B can be in frictional contact with the control mechanism 635. In other embodiments, the first activation mechanism 631A and the second activation mechanism 631B can be coupled to the control member 635 via a mechanical fastener and/or an adhesive. In this manner, the first activation mechanism 631A and the second activation mechanism 631B can be moved concurrently to move the control member 635, as described in further detail herein.

[1175] The first activation mechanism 631A and the second activation mechanism 631B include a set of engagement members 634A and 634B, respectively (although only one engagement member 634B is shown in FIG. 36, the second activation mechanism 631B is arranged in similar manner as the first activation mechanism 631A). The engagement members 634A and 634B are configured to engage the flow control protrusion 608 of the housing 601. For example, the diverter 620 and the flow control mechanism 630 can be moved within the inner volume 611 of the housing 601 to place the engagement members 634A and 634B in contact with the flow control protrusions 608. Moreover, once the

engagement members 634A and 634B are placed in contact with the flow control protrusions 608, further movement of the diverter 620 and the flow control mechanism 630 can rotate the flow control mechanism 630 relative to the diverter 620 between a first configuration and a second configuration, as described in further detail herein.

[1176] As shown in FIG. 37, the control member 635 defines a first lumen 638, a second lumen 639, and a set of channels 637. The channels 637 can be configured to receive a portion of the adjustment mechanism 685, as described in further detail herein. The flow control mechanism 630 can be arranged such that when in its first configuration, the first lumen 638 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the first outlet lumen 625 defined by the first outlet port 624. Similarly, when the flow control mechanism 630 is in the second configuration, the second lumen 639 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the second outlet lumen 627 defined by the second outlet port 626. Therefore, the flow control mechanism 630 can be rotated relative to the diverter 620 to selectively place the first outlet port 624 or the second outlet port 626 in fluid communication with the inlet port 622.

[1177] The adjustment mechanism 685 includes a dial 686 and an adjustment member 688 (see e.g., FIG. 31). In some embodiments, the adjustment member 688 can be, for example, a screw or the like. As shown in FIG. 30, the adjustment mechanism 685 can be disposed adjacent to the base 606 of the housing 601. More specifically, the dial 686 includes a receiving portion 686A that can be inserted into the passageway 614 defined by the base 606. In this manner, a coupler 687 (e.g., a retaining ring or the like) can be positioned about the receiving portion 686 to limit movement of the dial 686 relative to the base 606. For example, the coupler 687 can be configured to limit translational movement of the dial 686 relative to the base 606 while allowing rotational movement of the dial 686 relative to the base 606. The adjustment mechanism 685 can be arranged such that at least a portion of the adjustment member 688 is movably disposed in the opening 689 defined by the diverter 620. For example, the adjustment member 688 and a set of walls defining the opening 689 of the diverter 620 can define a threaded coupling. Thus, the adjustment member 688 can be rotated relative to the diverter 620 and, as such, the adjustment member 688 can be moved in a translation motion (e.g., proximal or distal direction) relative to the diverter 620. For example, a portion of the adjustment member 688 (e.g., a head of a bolt or screw) can be disposed within the receiving portion 686A of the dial 686 such that as the dial

686 is rotated relative to the housing 601, the adjustment member 688 is rotated relative to the diverter 620. Moreover, a portion of the adjustment member 688 can be disposed within one of the channels 637 of the control member 635. As such, the adjustment mechanism 685 can be manipulated to advance the adjustment member 688 relative to the diverter 620 to place the adjustment member 688 in contact with an engagement surface 636 of the control member 635 (see e.g., FIG. 37). In this manner, the movement of the adjustment member 688 can exert a force on the engagement surface 636 that can be sufficient to deform, bend, or otherwise reconfigure a wall of the control member 635 defining either the first lumen 638 or the second lumen 639, as described in further detail herein.

[1178] In some embodiments, the transfer device 600 can be stored in a storage configuration (e.g., a first configuration) in which the control member 635 of the flow control mechanism 630 fluidically isolates the inlet port 622, the first outlet port 624, and the second outlet port 626 from the inner volume 621 defined by the diverter 620. In such embodiments, first lumen 638 and the second lumen 639 are fluidically isolated from the inlet lumen 623, the first outlet lumen 625, and the second outlet lumen 627, as shown in FIG. 38. Furthermore, the friction fit defined by the control member 635 and the walls of the diverter 620 defining the inner volume 621 maintain the flow control mechanism 630 in the storage configuration until the flow control mechanism 630 is moved from the storage configuration.

[1179] In use, a user can manipulate the transfer device 600 to couple the inlet port 622 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. The distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thereby placing the inlet lumen 623 in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 626 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1180] With the inlet port 622 coupled to the lumen-defining device and the second outlet port 626 coupled to the external fluid reservoir, a user can move the transfer device 600 from the first configuration to a second configuration by applying an activation force to the actuator mechanism 640. In this manner, at least a portion of the actuator mechanism 640, the diverter 620, and the flow control mechanism 630 are moved in the distal direction

toward the second configuration, as indicated by the arrow **WW** in FIG. 39. More specifically and as described above, the arrangement of the plunger 648 and the guide posts 607 is such that as the user applies the activation force to the actuator mechanism 640, the position of the plunger 648, relative to the housing 601, is maintained. Therefore, the activation force applied by the user moves the actuator housing 662, the cap 655, the diverter 620, and the flow control mechanism 630 in the direction of the arrow **WW**, but not the plunger 648. The distal movement of the actuator housing 662 is such that the height of the first portion 667 of the inner volume 665 is reduced and the height of the fluid reservoir 670 is increased. With the fluid reservoir 670 being fluidically isolated (as described above) the increase in the height (i.e., the increase in volume) produces a negative pressure within the fluid reservoir 670. Said another way, the movement of the plunger 648 increases the volume of the fluid reservoir 670, which, in turn, produces a negative pressure therein.

[1181] As the actuator mechanism 640 is moved from the storage configuration toward the first configuration, the flow control protrusions 608 engage the engagement members 634A and 634B of the first activation mechanism 631A and the second activation member 631B, respectively, (not shown in FIG. 39) to move the flow control mechanism 630 toward the first configuration, as indicated by the arrow **XX** in FIG. 39. Thus, when the flow control mechanism 630 is moved to its first configuration, the first lumen 638 defined by the control member 635 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the first outlet lumen 625 defined by the first outlet port 624. As indicated by the arrow **YY** in FIG. 39, the inlet lumen 623 of the inlet port 622, the first lumen 638 of the control member 635, and the first outlet lumen 625 of the first outlet port 624 define a fluid flow path such that the fluid reservoir 670 defined by the actuator housing 662 is placed in fluid communication with the inlet port 622. Thus, the negative pressure within the fluid reservoir 670 is such that the negative pressure differential introduces a suction force within the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 670 of the actuator housing 662, as indicated by the arrow **YY**. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes. In some instances, the magnitude of the suction force can be modulated by increasing or decreasing the amount of activation force applied to the actuator mechanism 640. In this manner, the change in the volume of the fluid reservoir 670 can be modulated such that a desired amount of a suction force is exerted within the vein of the patient.

[1182] With the desired amount of bodily-fluid transferred to the fluid reservoir 670 defined by the actuator housing 662, a user can manipulate the transfer device 600 to move the transfer device 600 from the second configuration to the third configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the actuator housing 662 is a predetermined amount of fluid, as described in detail above.

[1183] The transfer device 600 can be moved from the second configuration to the third configuration by further moving the actuator mechanism 640 in the distal direction, as indicated by the arrow **ZZ** in FIG. 40. Expanding further, the user can apply an activation force to the actuator mechanism 640 such that the actuator housing 662, the cap 655, the diverter 620, and the flow control mechanism 630 move in the distal direction. With the desired amount of the bodily-fluid disposed within the fluid reservoir 670 the volume of the fluid reservoir 670 is configured to remain constant as the actuator housing 662 and the cap 655 move relative to the plunger 648. Similarly stated, the pressure of the fluid reservoir 670 is configured to remain substantially unchanged as the transfer device 600 is moved from the first configuration to the second configuration. As the actuator mechanism 640 is moved from its first configuration toward its second configuration, the flow control protrusions 608 engage the engagement members 634A and 634B to rotate the flow control mechanism 630 toward the second configuration, as indicated by the arrow **AAA**. Thus, when the flow control mechanism 630 is moved to its second configuration, the second lumen 639 defined by the control member 635 is placed in fluid communication with the inlet lumen 623 defined by the inlet port 622 and the second outlet lumen 627 defined by the second outlet port 626.

[1184] As shown by the arrow **BBB**, the inlet lumen 623 of the inlet port 622, the second lumen 639 of the control member 635, and the second outlet lumen 627 of the second outlet port 626 define a fluid flow path such that the external reservoir (not shown in FIG. 40) is in fluid communication with the inlet port 622 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid can be drawn into the external reservoir that is fluidically isolated from the first,

predetermined amount of bodily-fluid contained within the fluid reservoir 670 defined by the actuator housing 662. In this manner, the bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 600, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe).

[1185] In some instances, it may be desirable to limit and/or modulate the amount of a suction force exerted on the vein of the patient and/or a flow rate of the bodily-fluid. In such instances, the user can manipulate the adjustment mechanism 685 to move the adjustment member 688 relative to the control member 635. For example, the distal movement of the diverter 620 relative to the housing 601 is such that a portion of the adjustment member 688 is disposed in the receiving portion 686A of the dial 686. In this manner, the dial 686 can be rotated to advance the adjustment member 688 relative to the control member 635, as indicated by the arrow **CCC** in FIG. 41. Thus, the adjustment member 688 can be moved into contact with the engagement surface 636 to deform a portion of the control member 635 defining the second lumen 639. As such, the wall of the control member 635 constricts the second lumen 639 (e.g., reduces a diameter of at least a portion of the second lumen 639), thereby reducing the suction force exerted within the vein and/or slowing the rate at which the bodily-fluid flows within the second lumen 639. In some embodiments, the dial 686 can be rotated in alternating directions to alternately move the adjustment member 688 in the proximal direction and the distal direction. In this manner, the flow of the bodily-fluid can be, for example, pulsed or the like. In this manner, bodily-fluid that is substantially free from microbes (e.g., dermally residing microbes or the like) can flow with a desired set of characteristics into the external reservoir.

[1186] While the transfer device 200 is described above with reference to FIGS. 2-12 as including a linear spring 261 (e.g., a compression spring), in other embodiments, a transfer device can include any suitable spring that can be configured to modulate, change, and/or control a negative pressure within a fluid reservoir and/or a flow rate of a bodily-fluid. For example, FIGS. 42-47 illustrate a transfer device 700 according to another embodiment. The transfer device 700 includes a housing 701, a diverter 720, a flow control mechanism 730, and adjustment mechanism 785, and an actuator 740. The transfer device 700 can be any suitable shape, size, or configuration. For example, portions of the transfer device 700 can be

substantially similar to or the same as corresponding portions of the transfer device 200 (described above with reference to FIGS. 2-12) and/or the transfer device 600 (described above with reference to FIGS. 30-41). As such, aspects of the transfer device 700 of the transfer device 700 are not described in further detail herein.

[1187] The housing 701 of the transfer device 700 includes a proximal end portion 702 and a distal end portion 703. The distal end portion 703 includes a base 706 from which a set of walls 704 extend. The walls 704 of the housing 701 define a substantially annular shape and define an inner volume 711 between the proximal end portion 702 and the distal end portion 703. The proximal end portion 702 of the housing 701 is open to receive at least a portion of the diverter 720, a portion of the flow control mechanism 730, and a portion of the actuator 740 within the inner volume 711 (see e.g., FIG. 31). The walls 704 of the housing 701 define a set of status windows 710 and a set of channels 705. The status windows 710 and the channels 705 can be any suitable shape or size. For example, the status windows 710 and the channels 705 can be substantially similar in form and function to the status windows 210 and the channels 205 of the transfer device 200. The housing 701 includes a set of guide posts 707 and a set of flow control protrusions (not shown in FIGS. 43-46). In this manner, the housing 701 can function similarly to the housing 601 included in the transfer device 600 described above.

[1188] As shown in FIG. 31, the actuator mechanism 740 includes the actuator housing 762, a plunger 748, and a cap 755. The actuator mechanism 740 is configured to move between a first configuration and a second configuration, thereby moving the transfer device 700 between a first configuration and a second configuration, as described in further detail herein. The actuator housing 762 includes a proximal end portion 763 and a distal end portion 764 and defines an inner volume 765. The inner volume 765 of the actuator housing 762 receives the plunger 748 and at least a portion of the cap 755. As such, the actuator mechanism 740 can be substantially similar in form and function as the actuator mechanism 640 included in the transfer device 600 described above with reference to FIGS. 30-41. Thus, the plunger 748 can be disposed in the actuator housing 762 to divide the inner volume 765 into a first portion 767 and a second portion 770 (also referred to herein as "fluid reservoir").

[1189] As shown in FIGS. 43, the diverter 720 of the transfer device 700 includes an inlet port 722, a first outlet port 724, and a second outlet port 726 and defines an inner volume 721. The inner volume 721 can receive at least a portion of the flow control mechanism 730,

as described above with reference to the transfer device 200. The diverter 720 is movably disposed within the inner volume 711 of the housing 701 such that a portion of the inlet port 722 extends through a first channel 705 defined by the walls 704 of the housing 701 and a portion of the second outlet port 726 extends through a second channel 705 opposite the first channel (see e.g., FIG. 42). While not explicitly shown in FIGS. 42-46, the distal end portion 729 of the diverter 720 can engage the guide posts 707 to limit, for example, lateral movement of the diverter 720 as the diverter 720 is moved in the inner volume 711. Similarly stated, the guide posts 707 of the housing 701 can engage the diverter 720 to substantially limit its movement to a proximal direction or distal direction relative to the housing 701, as further described herein.

[1190] The inlet port 722, the first outlet port 724, and the second outlet port 726 define an inlet lumen 723, a first outlet lumen 725, and a second outlet lumen 727, respectively, that are each in fluid communication with the inner volume 721 (see e.g., FIGS. 45 and 46). The inlet port 722 can be fluidically coupled to a needle or other lumen-containing device (not shown in FIGS. 30-41) that can be disposed within a portion of a body of the patient (e.g., within a vein of the patient), the first outlet port 724 can be fluidically coupled to a portion of the actuator 740, and the second outlet port 726 can be fluidically coupled to an external reservoir (e.g., a sample reservoir not shown in FIGS. 30-41). In this manner, the diverter 720 can be arranged to selectively place the portion of the actuator 740 or the external reservoir in fluid communication with the portion of the body via the inlet port 722 and the first outlet port 724 or via the inlet port 722 and the second outlet port 726, respectively.

[1191] As shown in FIG. 44, the flow control mechanism 730 includes a first activation mechanism 731A, a second activation mechanism 731B, a control member 735, a first torsion spring 761A, and a second torsion spring 761B. At least a portion of the flow control mechanism 730 is configured to be disposed within the inner volume 721 defined by the diverter 720, as described above. Although not shown in FIGS. 42-46, the flow control mechanism 730 can be arranged within the inner volume 711 of the housing 701 and the inner volume 721 of the diverter 720 such that the first activation mechanism 731A and the second activation mechanism 731B are disposed adjacent to and in contact with the control member 735. More specifically, the first activation mechanism 731A and the second activation mechanism 731B can be in frictional contact with the control mechanism 735. In other embodiments, the first activation mechanism 731A and the second activation

mechanism 731B can be coupled to the control member 735 via a mechanical fastener and/or an adhesive. In this manner, the first activation mechanism 731A and the second activation mechanism 731B can be moved concurrently to move the control member 735, as described in further detail herein.

[1192] The first activation mechanism 731A and the second activation mechanism 731B include a set of engagement members 734A and 734B, respectively (although only one engagement member 734B is shown in FIG. 36, the second activation mechanism 731B is arranged in similar manner as the first activation mechanism 731A). The engagement members 734A and 734B are configured to engage the flow control protrusion 708 of the housing 701, as described with reference to the transfer device 600 of FIGS. 30-41. In use, once the engagement members 734A and 734B are placed in contact with the flow control protrusions 708, further movement of the diverter 720 and the flow control mechanism 730 can rotate the flow control mechanism 730 relative to the diverter 720 between a first configuration and a second configuration. As such, the torsion springs 761A and 761B can be moved from a first configuration having a substantially smaller potential energy to a second configuration having a substantially larger potential energy. In other words, the rotational movement of the flow control mechanism 730 relative to the diverter 720 can transfer the torsion springs 761A and 761B to a configuration having a larger potential energy than the potential energy prior to the rotation of the flow control mechanism 730 relative to the diverter 720, as described in further detail herein.

[1193] As shown in FIG. 44, the control member 735 defines a first lumen 738, a second lumen 739. The flow control mechanism 730 can be arranged such that when in its first configuration, the first lumen 738 is placed in fluid communication with the inlet lumen 723 defined by the inlet port 722 and the first outlet lumen 725 defined by the first outlet port 724. Similarly, when the flow control mechanism 730 is in the second configuration, the second lumen 739 is placed in fluid communication with the inlet lumen 723 defined by the inlet port 722 and the second outlet lumen 727 defined by the second outlet port 726. Therefore, the flow control mechanism 730 can be rotated relative to the diverter 720 to selectively place the first outlet port 724 or the second outlet port 726 in fluid communication with the inlet port 722.

[1194] In some embodiments, the transfer device 700 can be stored in a storage configuration in which the control member 735 of the flow control mechanism 730 fluidically

isolates the inlet port 722, the first outlet port 724, and the second outlet port 726 from the inner volume 721 defined by the diverter 720. In such embodiments, first lumen 738 and the second lumen 739 are fluidically isolated from the inlet lumen 723, the first outlet lumen 725, and the second outlet lumen 727. Furthermore, the friction fit defined by the control member 735 and the walls of the diverter 720 defining the inner volume 721 maintain the flow control mechanism 730 in the storage configuration until the flow control mechanism 730 is moved from the storage configuration.

[1195] In use, a user can manipulate the transfer device 700 to couple the inlet port 722 to a proximal end portion of a lumen-defining device (not shown) such as, for example, a butterfly needle. The distal end portion of the lumen-defining device can be disposed within a portion of the body of a patient (e.g., a vein), thereby placing the inlet lumen 723 in fluid communication with the portion of the body of the patient. In a similar manner, the second outlet port 726 can be coupled to an external fluid reservoir (not shown). The external fluid reservoir can be any suitable reservoir. For example, in some embodiments, the external fluid reservoir can be a BacT/ALERT® SN or a BacT/ALERT® FA, manufactured by BIOMERIEUX, INC.

[1196] With the inlet port 722 coupled to the lumen-defining device and the second outlet port 726 coupled to the external fluid reservoir, a user can move the transfer device 700 from the first configuration to a second configuration by applying an activation force to the actuator mechanism 740. In this manner, at least a portion of the actuator mechanism 740, the diverter 720, and the flow control mechanism 730 are moved in the distal direction toward the second configuration, as indicated by the arrow **DDD** in FIG. 45. More specifically and as described above, the distal movement of the actuator housing 762 is such that a height of the first portion 767 of the inner volume 765 is reduced and a height of the fluid reservoir 770 is increased. With the fluid reservoir 770 being fluidically isolated (as described above) the increase in the height (i.e., the increase in volume) produces a negative pressure within the fluid reservoir 770. Said another way, the movement of the plunger 748 increases the volume of the fluid reservoir 770, which, in turn, produces a negative pressure therein.

[1197] As shown in FIG. 45, when the flow control mechanism 730 is moved to its first configuration (e.g., from a storage configuration), the first lumen 738 defined by the control member 735 is placed in fluid communication with the inlet lumen 723 defined by the inlet

port 722 and the first outlet lumen 725 defined by the first outlet port 724. As indicated by the arrow **EEE** in FIG. 45, the inlet lumen 723 of the inlet port 722, the first lumen 738 of the control member 735, and the first outlet lumen 725 of the first outlet port 724 define a fluid flow path such that the fluid reservoir 770 defined by the actuator housing 762 is placed in fluid communication with the inlet port 722. Thus, the negative pressure within the fluid reservoir 770 is such that the negative pressure differential introduces a suction force within the portion of the patient. In this manner, a bodily-fluid is drawn into the fluid reservoir 770 of the actuator housing 762, as indicated by the arrow **EEE**. In some embodiments, the bodily-fluid can contain undesirable microbes such as, for example, dermally-residing microbes.

[1198] In some instances, the magnitude of the suction force can be modulated by increasing or decreasing the amount of activation force applied to the actuator mechanism 740. More specifically and as described above, the rotational movement of the flow control mechanism 730 can increase the potential energy of the torsion springs 761A and 761B (not shown in FIG. 45). For example, in some embodiments, an end portion of the torsion springs 761A and 761B can be placed in contact with the flow control protrusions 708 to substantially limit the movement of the end portion of the torsion springs 761A and 761B. Thus, the rotational movement of the first activation mechanism 731A and the second activation mechanism 731B rotates a second end portion of the torsion springs 761A and 761B, respectively, relative to the end portion in contact with the flow control protrusions 708, thereby changing the potential energy of the torsion springs 761A and 761B. In this manner, the torsion springs 761A and 761B can exert a reaction force that can resist the activation force applied to the user on the actuator mechanism 740. Therefore, by reducing the activation force, the flow control mechanism 730 can rotate relative to the diverter 720 to change the alignment of the first lumen 738 of the control member 735 relative to the inlet lumen 723 and the first outlet lumen 725 of the diverter 720. As such, the negative pressure within the fluid reservoir 770 can be reduced and/or otherwise changed.

[1199] With the desired amount of bodily-fluid transferred to the fluid reservoir 770 defined by the actuator housing 762, a user can manipulate the transfer device 700 to move the transfer device 700 from the second configuration to the third configuration, wherein a flow of bodily-fluid is transferred to the external reservoir (e.g., such as those described above). In some embodiments, the desired amount of bodily-fluid transferred to the actuator

housing 762 is a predetermined amount of fluid, as described in detail above. The transfer device 700 can be moved from the first configuration to the second configuration by further moving the actuator mechanism 740 in the distal direction, as indicated by the arrow **FFF** in FIG. 46. Expanding further, the user can apply an activation force to the actuator mechanism 740 such that the actuator housing 762, the cap 755, the diverter 720, and the flow control mechanism 730 move in the distal direction. As the actuator mechanism 740 is moved from its first configuration toward its second configuration, the flow control protrusions 708 engage the engagement members 734A and 734B to rotate the flow control mechanism 730 toward the second configuration, as indicated by the arrow **GGG**. Thus, when the flow control mechanism 730 is moved to its second configuration, the second lumen 739 defined by the control member 735 is placed in fluid communication with the inlet lumen 723 defined by the inlet port 722 and the second outlet lumen 727 defined by the second outlet port 726.

[1200] As shown by the arrow **HHH** in FIG. 46, the inlet lumen 723 of the inlet port 722, the second lumen 739 of the control member 735, and the second outlet lumen 727 of the second outlet port 726 define a fluid flow path such that the external reservoir (not shown in FIG. 46) is in fluid communication with the inlet port 722 and, therefore, the portion of the patient (e.g., the vein). Furthermore, the external reservoir is configured to define a negative pressure (e.g., the known external reservoirs referred to herein are vessels defining a negative pressure). The negative pressure within the external reservoir is such that the negative pressure differential between the external reservoir and the portion of the body of the patient introduces a suction force within the portion of the patient. Therefore, a desired amount of bodily-fluid can be drawn into the external reservoir that is fluidically isolated from the first, predetermined amount of bodily-fluid contained within the fluid reservoir 770 defined by the actuator housing 762. In this manner, the bodily-fluid contained in the external reservoir is substantially free from microbes generally found outside of the portion of the patient (e.g., dermally residing microbes, microbes within a lumen defined by the transfer device 700, microbes within the lumen defined by the lumen defining device, and/or any other undesirable microbe).

[1201] In some instances, it may be desirable to limit and/or modulate the amount of a suction force exerted on the vein of the patient and/or a flow rate of the bodily-fluid. In such instances, the user can decrease the activation force applied to the actuator mechanism 740. In this manner, the torsion springs 761A and 761B can exert a force that is operable in

rotating the control member 735 relative to the diverter 720. Thus, the flow control mechanism 730 can rotate relative to the diverter 720 to change the alignment of the first lumen 738 of the control member 735 relative to the inlet lumen 723 and the first outlet lumen 725 of the diverter 720. As such, the negative pressure within the fluid reservoir 770 can be reduced, modulated, pulsed and/or otherwise changed.

[1202] Referring now to FIG. 47, a flowchart illustrates a method 1000 for parenterally procuring a bodily-fluid sample that is substantially free from microbes. In some embodiments, the method 1000 includes inserting a needle of a parenteral sampling device into a patient, at 1001. In some embodiments, the parenteral sampling device can be, for example, a fluid transfer device such as those described herein. As such, the parenteral sampling device (also referred to herein as "device") can include at least the needle, an actuator, a flow control mechanism, and a fluid reservoir. As described above with reference to the transfer devices 100, 200, 300, 400, 500, 600, and/or 700, the device can be configured to selectively place the needle in fluid communication with the fluid reservoir.

[1203] The method 1000 includes establishing fluid communication between the needle and the fluid reservoir, at 1002. For example, in some embodiments, the device can be in a storage configuration prior to use in which the needle is fluidically isolated from the fluid reservoir. Therefore, in use, the device can be manipulated to define a fluid flow path between the needle and the fluid reservoir. In some embodiments, for example, the device can be manipulated to arrange the flow control mechanism included in the device in a first configuration such that the flow control mechanism defines at least a portion of the fluid flow path. For example, the flow control mechanism can be substantially similar to the flow control mechanism 230 included in the transfer device 200 described above with reference to FIGS. 2-12.

[1204] With the flow path defined between the needle and the fluid reservoir, an actuator is moved a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid, at 1003. For example, in some embodiments, a user can exert an activation force on the actuator to move the actuator relative to a portion of the device. In such embodiments, the actuator can include a plunger or the like that can be disposed within a portion of the actuator and arranged such that the plunger defines, at least partially, the fluid reservoir. Thus, when the activation force is applied to the actuator, the actuator can move relative to the plunger such that a negative pressure is produced within the

fluid reservoir. In this manner, a bodily-fluid can flow through a first flow path from the needle to the fluid reservoir (e.g., via a lumen defined by the flow control mechanism). In some instances, the negative pressure in the fluid reservoir can be reduced, for example, by reducing the activation force applied to the actuator and/or releasing the actuator, at 1004. For example, in some embodiments, the actuator can include a spring and/or any other suitable device, mechanism, or member that can be operable in constricting at least a portion of the fluid flow path. The negative pressure in a subsequent sample reservoir can also be reduced, for example, by apply an activation force to the actuator, at 1004, as described herein.

[1205] The method 1000 includes moving the actuator a second distance to engage the flow control mechanism to move the flow control mechanism between the first configuration and a second configuration that is operable in allowing bodily-fluid to flow through a second flow path from the needle to a sample reservoir, at 1005. For example, in some embodiments, by moving the actuator the second distance, the flow control mechanism is rotated such that a lumen defined therein defines at least a portion of the second fluid flow path. In this manner, bodily-fluid can flow through the second flow path to be disposed within the sample reservoir. In some embodiments, the collection and/or the isolation of a first volume of the bodily-fluid can reduce and/or eliminate, for example, an amount of microbes (e.g., dermally-residing microbes, other undesirable external contaminants, or the like) in the sample volume.

[1206] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Where methods and steps described above indicate certain events occurring in certain order, those of ordinary skill in the art having the benefit of this disclosure would recognize that the ordering of certain steps may be modified and that such modifications are in accordance with the variations of the invention. Additionally, certain of the steps may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above. Additionally, certain steps may be partially completed and/or omitted before proceeding to subsequent steps.

[1207] While various embodiments have been particularly shown and described, various changes in form and details may be made. Although various embodiments have been described as having particular features and/or combinations of components, other

embodiments are possible having any combination or sub-combination of any features and/or components from any of the embodiments described herein. For example, while the not shown in FIGS. 28 and 29, in some embodiments, the transfer device 500 can include a throttling button, similar in form and function to the throttling button 445 included in the transfer device 400. By way of another example, although not shown in FIGS. 30-41, in some embodiments, the transfer device 600 can include one or more springs such as, for example, the spring 261 of the transfer device and/or the torsion springs 761A and 761B of the transfer device 700.

[1208] The specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different than the embodiments shown, while still providing the functions as described herein. More specifically, the size and shape of the various components can be specifically selected for a desired rate of bodily-fluid flow into a fluid reservoir.

Claims

1. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient, and an outlet port configured to be fluidically coupled to a sample reservoir;

a fluid reservoir disposed in the inner volume and configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient;

a flow control mechanism disposed in the housing and defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement from a first configuration, in which the inlet port is placed in fluid communication with the fluid reservoir such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port; and

an actuator operably coupled to the flow control mechanism and configured to create a negative pressure in the fluid reservoir when actuated by a user, the actuator further configured to rotate the flow control mechanism from the first configuration to the second configuration after the first volume of bodily-fluid is received in the fluid reservoir from the patient.

2. The device of claim 1, wherein the actuator is further configured to move a first distance to create the negative pressure in the fluid reservoir when actuated by a user.

3. The device of claim 2, wherein the actuator is further configured to move a second distance to rotate the flow control mechanism from the first configuration to the second configuration.

4. The device of claim 1, wherein the actuator is configured to move in a first direction to create the negative pressure in the fluid reservoir, and to move in a second direction to reduce the negative pressure created in the fluid reservoir from movement in the first direction.

5. The device of claim 1, wherein the actuator is configured to allow the user to modulate the negative pressure created in the fluid reservoir.

6. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween;

an actuator movably disposed in the housing, the actuator including a sealing member and a fluid reservoir defined at least in part by the sealing member, the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user;

a diverter disposed in the housing, the diverter having an inlet port configured to be fluidically coupled to the patient, a first outlet port configured to be fluidically coupleable to the fluid reservoir, and a second outlet port configured to be fluidically coupled to a sample reservoir; and

a flow control mechanism disposed in the diverter and defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement between a first configuration, in which the inlet port is placed in fluid communication with the first outlet port such that bodily-fluid can flow from the inlet port, through the first lumen and to the first outlet port, to a second configuration, in which the inlet port is placed in fluid communication with the second outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the second outlet port.

7. The device of claim 6, wherein the actuator is further configured to rotate the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

8. The device of claim 7, wherein the actuator is configured to move a first distance to create the negative pressure in the fluid reservoir, and to move a second distance to rotate the flow control mechanism from the first configuration to the second configuration, when actuated by a user.

9. The device of claim 6, wherein the actuator is configured to move in a first direction to create the negative pressure in the fluid reservoir, and to move in a second direction to

reduce the negative pressure created in the fluid reservoir from movement in the first direction.

10. The device of claim 6, wherein the actuator further includes a plunger operably coupled to the sealing member.

11. The device of claim 10, wherein the actuator further includes a spring operably coupled to the plunger, the spring configured to compress in response to an activation force when the actuator is actuated by a user.

12. The device of claim 11, wherein the spring is configured to expand and exert a reaction force when the activation force is removed.

13. The device of claim 12, wherein the spring is configured to allow the user to modulate the negative pressure created in the fluid reservoir.

14. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient, and an outlet port configured to be fluidically coupled to a sample reservoir;

a flow control mechanism disposed in the housing and defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement between a first configuration, in which the inlet port is placed in fluid communication with a fluid reservoir defined at least in part by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port; and

an actuator movably disposed in the housing and operably coupled to the flow control mechanism, the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user, the actuator further configured to rotate the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

15. The device of claim 14, wherein the actuator includes an activation mechanism configured to rotate the flow control mechanism from the first configuration to the second configuration.

16. The device of claim 15, wherein the activation mechanism includes a first set of protrusions and the flow control mechanism includes a second set of protrusions, the first set of protrusions configured to operably engage the second set of protrusions to rotate the flow control mechanism from the first configuration to the second configuration.

17. The device of claim 14, wherein the actuator is further configured to create the negative pressure in the fluid reservoir when the actuator is moved from a first position to a second position by the user.

18. The device of claims 17, wherein the actuator is further configured to rotate the flow control mechanism from the first configuration to the second configuration when the actuator is moved from the second position to a third position by the user.

19. The device of claim 18, wherein the actuator includes an activation mechanism and the flow control mechanism includes a set of protrusions, the activation mechanism configured to operably engage the set of protrusions to rotate the flow control mechanism from the first configuration to the second configuration when the actuator is moved from the second position to a third position by the user.

20. A device for procuring bodily-fluid samples from a patient, the device comprising:

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

a seal member movably disposed in the inner volume;

a fluid reservoir disposed in the inner volume and at least partially defined by the seal member, the fluid reservoir configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient;

a flow control mechanism movably disposed in the housing, the flow control mechanism configured to move between a first configuration, in which the bodily-fluid can flow from the inlet port, through the flow control mechanism and to the fluid reservoir, and a

second configuration, in which the fluid reservoir is fluidically isolated from the inlet port; and

an actuator operably coupled to the seal member and to the flow control mechanism, the actuator including a spring configured to move the seal member from a first position to a second position to create a negative pressure in the fluid reservoir, the actuator further configured to move the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

21. The device of claim 20, further comprising:

a throttling button operably coupled to the actuator and configured to modulate the rate at which the spring moves the seal member from the first position to the second position based on user manipulation of the throttling button.

22. The device of claim 20, wherein the flow control mechanism includes a first control member and a second control member, the second control member defining a first lumen and a second lumen, the flow control mechanism configured for rotational movement between the first configuration in which the inlet port is placed in fluid communication with the fluid reservoir such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with a sample reservoir such that the bodily-fluid can flow from the inlet, through the second lumen and to the sample reservoir.

23. The device of claim 22, wherein the first control member includes a protrusion movably disposed in a grove defined by the second control member, the protrusion configured to move in the grove as the spring moves the seal member from the first position to the second position.

24. The device of claim 23, wherein the protrusion is configured to rotate the second control member when the spring moves the seal member from the second position to a third position.

25. A device for procuring bodily-fluid samples from a patient, the device comprising:

a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient, and an outlet port configured to be fluidically coupled to a sample reservoir;

a flow control mechanism disposed in the housing, the flow control mechanism including a first control member and a second control member, the second control member defining a first lumen and a second lumen and configured for rotational movement between a first configuration in which the inlet port is placed in fluid communication with a fluid reservoir defined at least in part by the housing such that bodily-fluid can flow from the inlet port, through the first lumen and to the fluid reservoir, to a second configuration, in which the inlet port is placed in fluid communication with the outlet port such that the bodily-fluid can flow from the inlet, through the second lumen and to the outlet port; and

an actuator movably disposed in the housing and operably coupled to the first control member, the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user, the actuator further configured to rotate the second control member from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

26. The device of claim 25, wherein the actuator includes an activation mechanism operably coupled to the first control member and configured to rotate the second control member from the first configuration to the second configuration.

27. The device of claim 25, wherein the actuator is further configured to create the negative pressure in the fluid reservoir when the actuator is moved from a first position to a second position by the user.

28. The device of claims 27, wherein the actuator is further configured to rotate the second control member from the first configuration to the second configuration when the actuator is moved from the second position to a third position by the user.

29. The device of claim 28, further comprising:

an activation mechanism coupled to the first control member, the activation mechanism including a protrusion configured to operably engage the actuator when the actuator is moved from the second position to a third position by the user.

30. A method for procuring bodily-fluid samples using a parenteral sampling device, the device including a needle having a lumen configured for insertion into the patient, and a fluid reservoir fluidically coupleable to the needle, the method comprising:

inserting the needle of the device into the patient;

establishing fluid communication between the needle and the fluid reservoir;

moving an actuator a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid;

moving the actuator a second distance to engage a flow control mechanism and rotate the flow control mechanism from a first configuration to a second configuration, the first configuration operable to allow bodily-fluid to flow through a first flow path from the needle to the fluid reservoir, the second configuration operable to allow bodily-fluid to flow through a second flow path from the needle to a sample reservoir.

31. The method of claim 30, wherein moving the actuator the first distance includes applying an activation force to the actuator in a first direction.

32. The method of claim 31, wherein releasing the activation force allows the actuator to move in a second direction opposite the first direction, to reduce the negative pressure created in the fluid reservoir.

33. The method of claim 30, further comprising:

moving the actuator a third distance to reduce the flow rate of bodily-fluid through the second flow path to the sample reservoir in the second configuration.

34. The method of claim 33, further comprising:

moving the actuator a third distance to engage a control member and deform the second flow path reduce the flow rate of bodily-fluid through the
second flow path to the sample reservoir in the second configuration.

35. A method for procuring bodily-fluid samples using a parenteral sampling device, the device including a needle having a lumen configured for insertion into the patient, and a fluid reservoir fluidically coupleable to the needle, the method comprising:

inserting the needle of the device into the patient;

establishing fluid communication between the needle and the fluid reservoir;

applying a first activation force to an actuator to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid;

reducing the first activation force applied to the actuator to reduce the negative pressure created in the fluid reservoir; and

applying a second activation force to the actuator to engage a flow control mechanism and move the flow control mechanism from a first configuration to a second configuration, the first configuration operable to allow bodily-fluid to flow through a first flow path from the needle to the fluid reservoir, the second configuration operable to allow bodily-fluid to flow through a second flow path from the needle to a sample reservoir.

36. The method of claim 35, wherein the first activation force moves the actuator a first distance in a first direction to create the negative pressure in the fluid reservoir.

37. The method of claim 36, wherein reducing the first activation force allows the actuator to move in a second direction opposite the first direction, to reduce the negative pressure created in the fluid reservoir.

38. The method of claim 35, wherein the second activation force moves the actuator a second distance in the first direction to move the flow control mechanism from the first configuration to the second configuration.

39. The method of claim 35, further comprising:

applying a third activation force to reduce the flow rate of bodily-fluid through the second flow path to the sample reservoir in the second configuration.

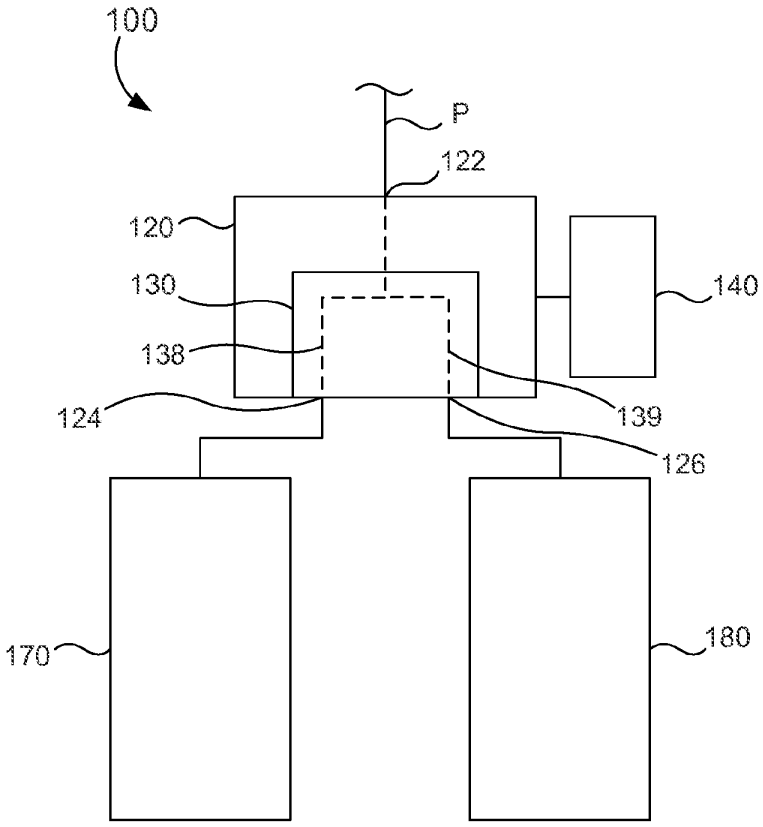


FIG. 1

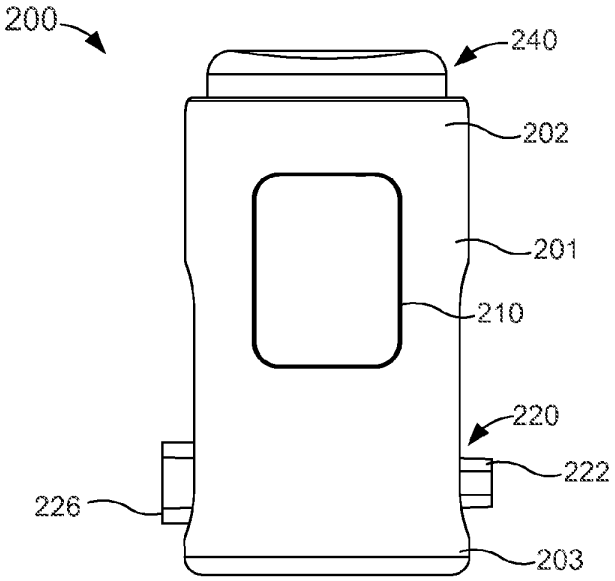

200
240
202
201
210
220
222
226
203

FIG. 2

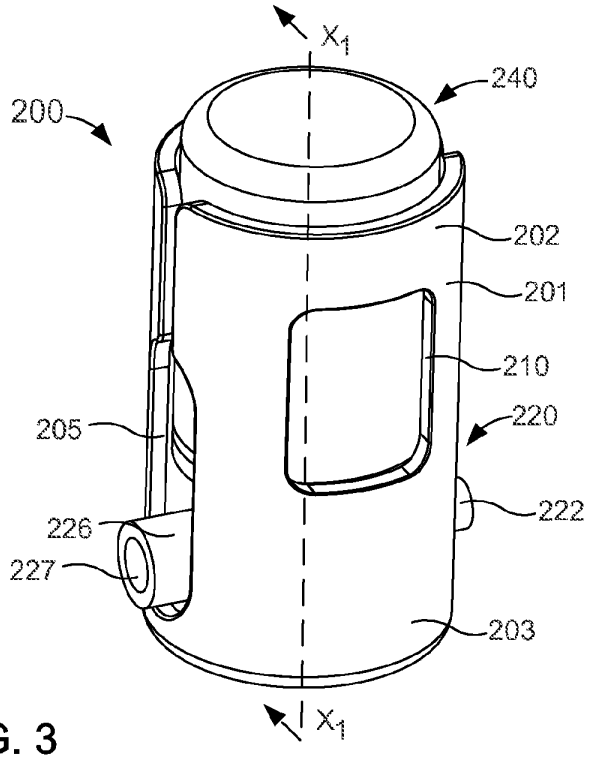

X1
200
240
202
201
210
205
220
222
226
227
203
X1

FIG. 3

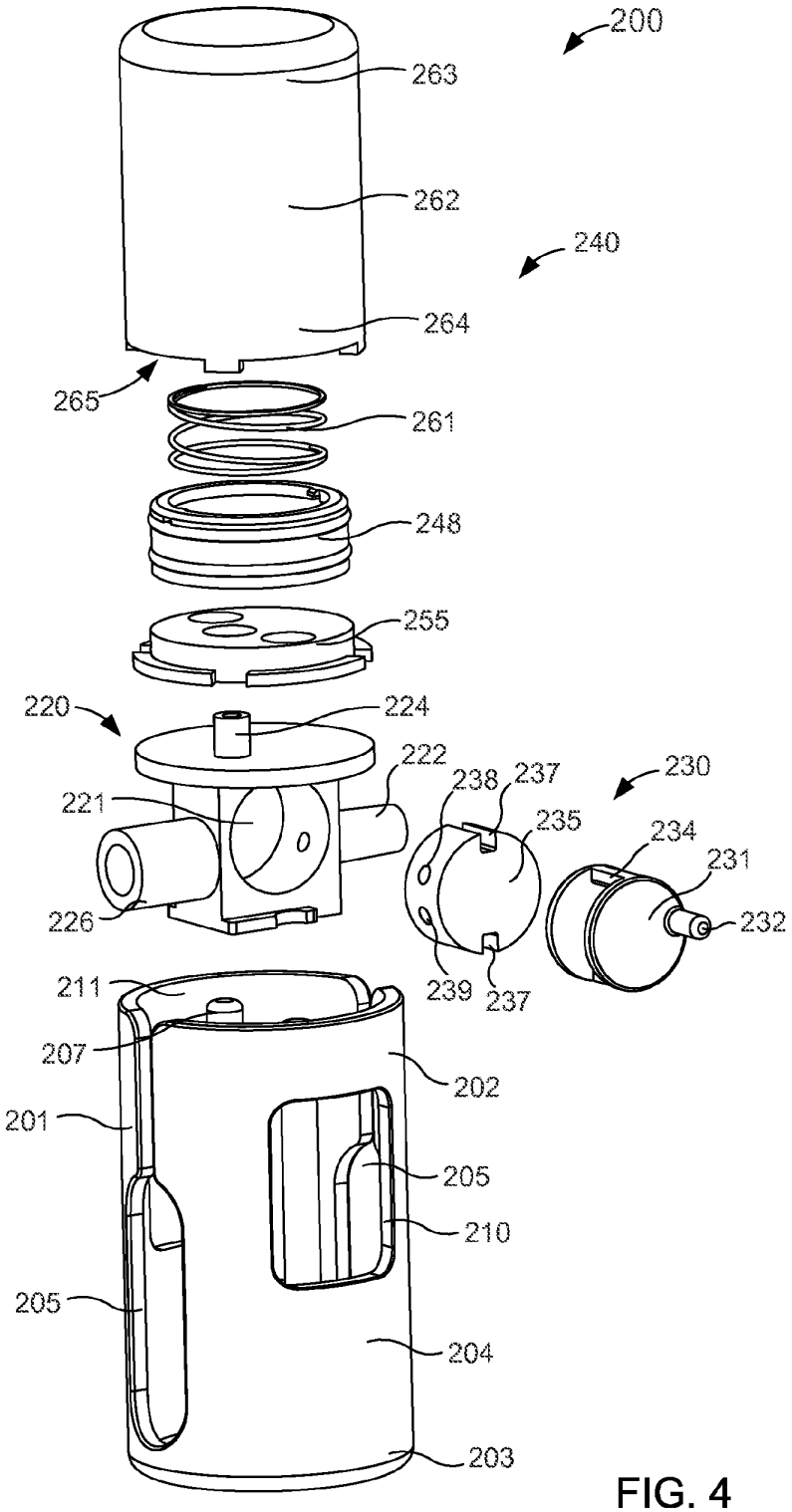

200
263
262
240
264
265
261
248
255
220
224
222
221
238
237
230
235
234
231
232
226
239
237
211
207
202
201
205
210
205
204
203

FIG. 4

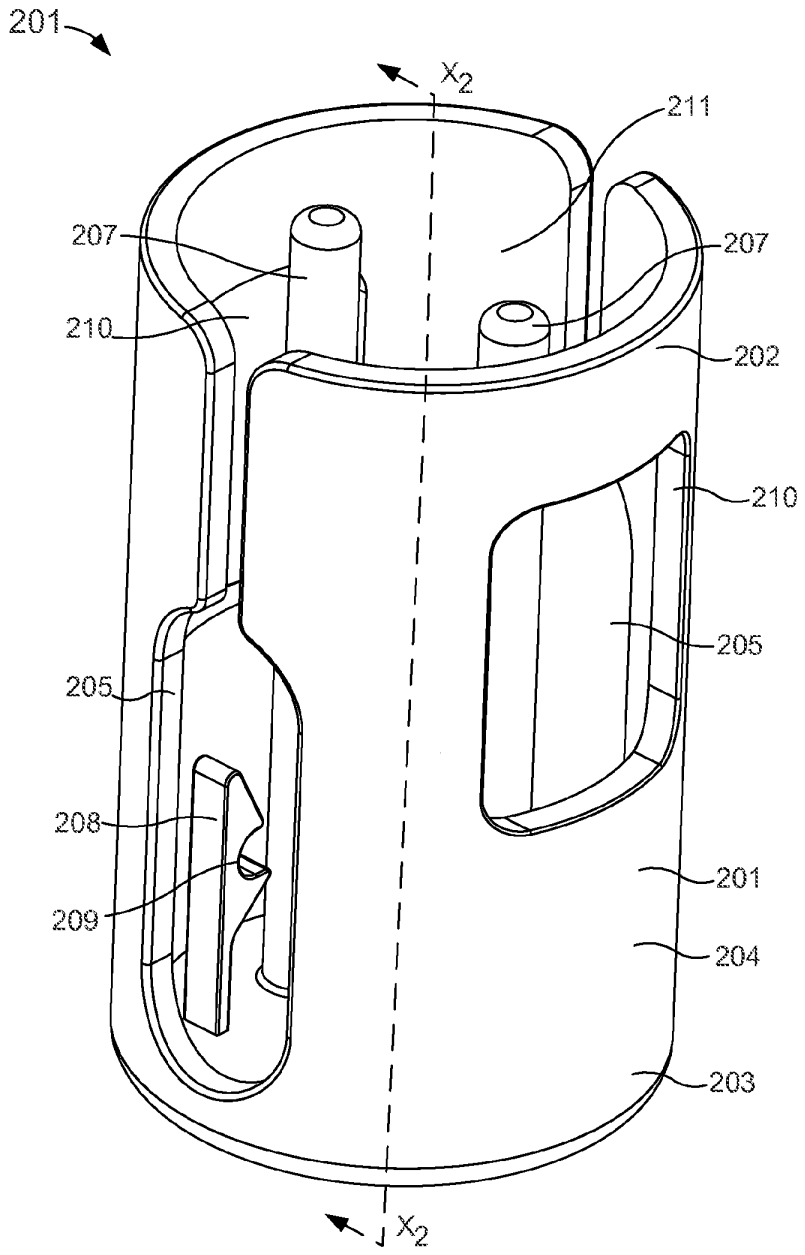


FIG. 5

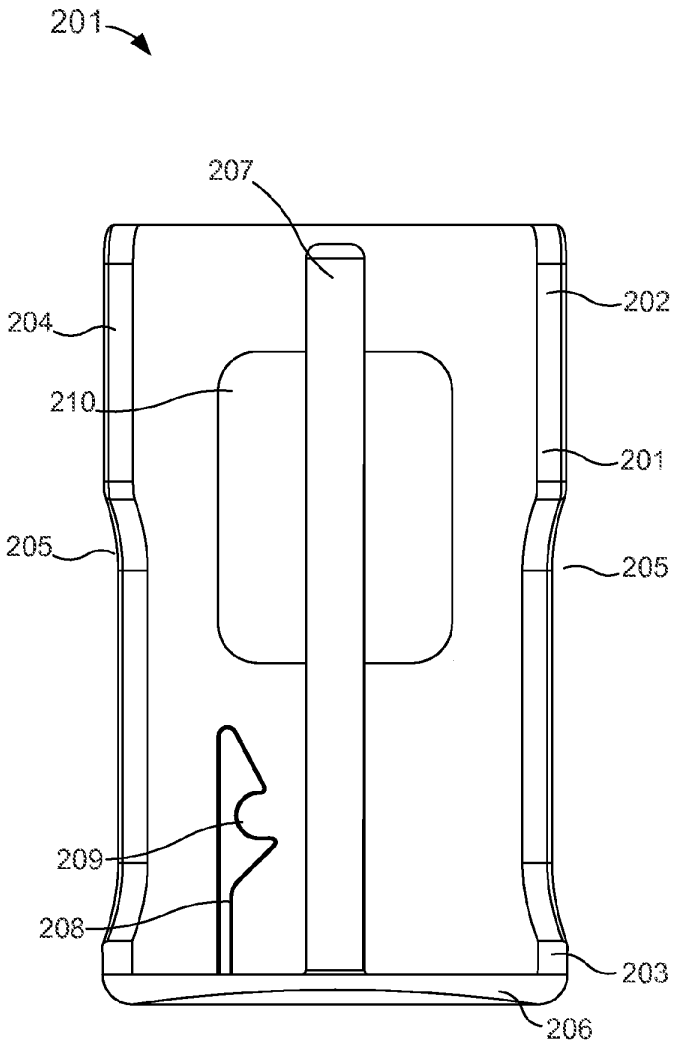


FIG. 6

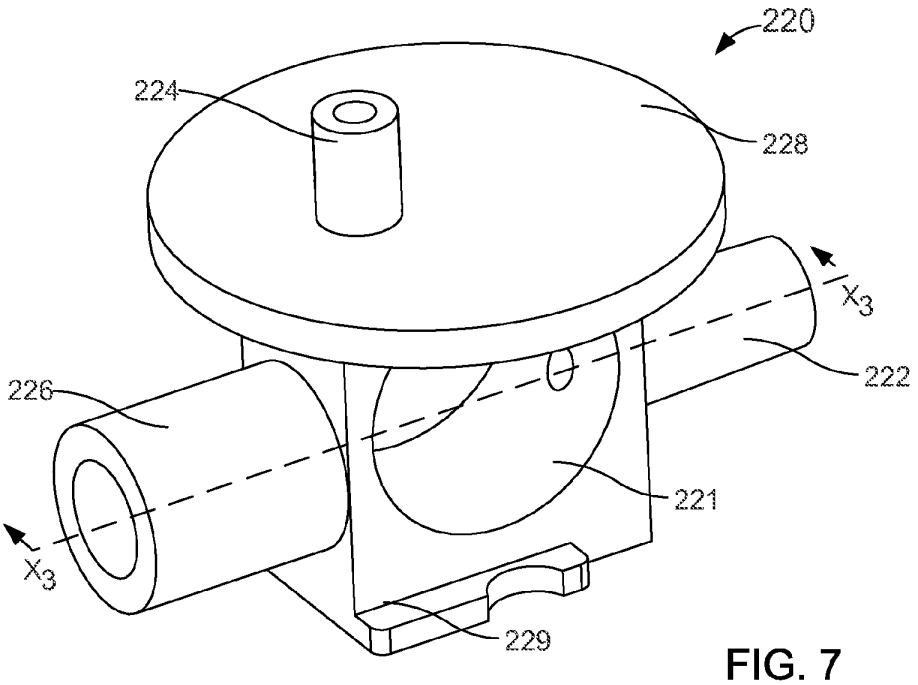

220
224
228
X_3
222
226
221
X_3
229

FIG. 7

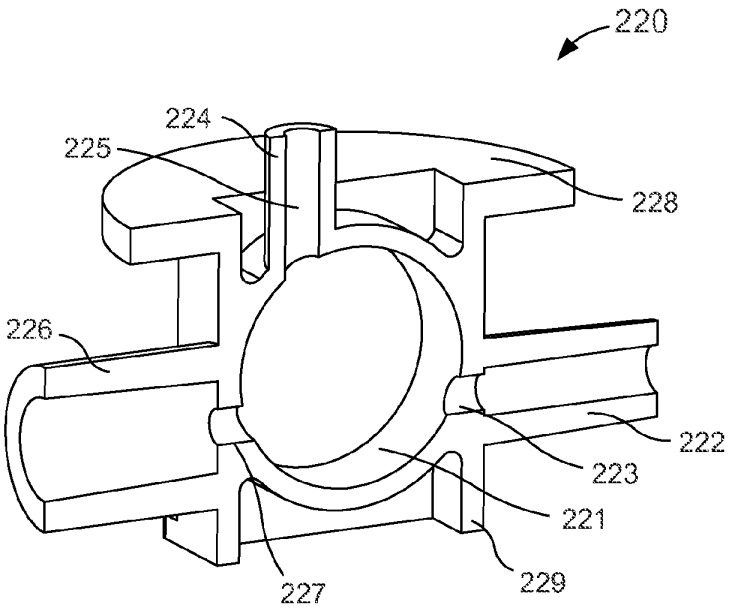

220
224
225
228
226
222
223
221
227
229

FIG. 8

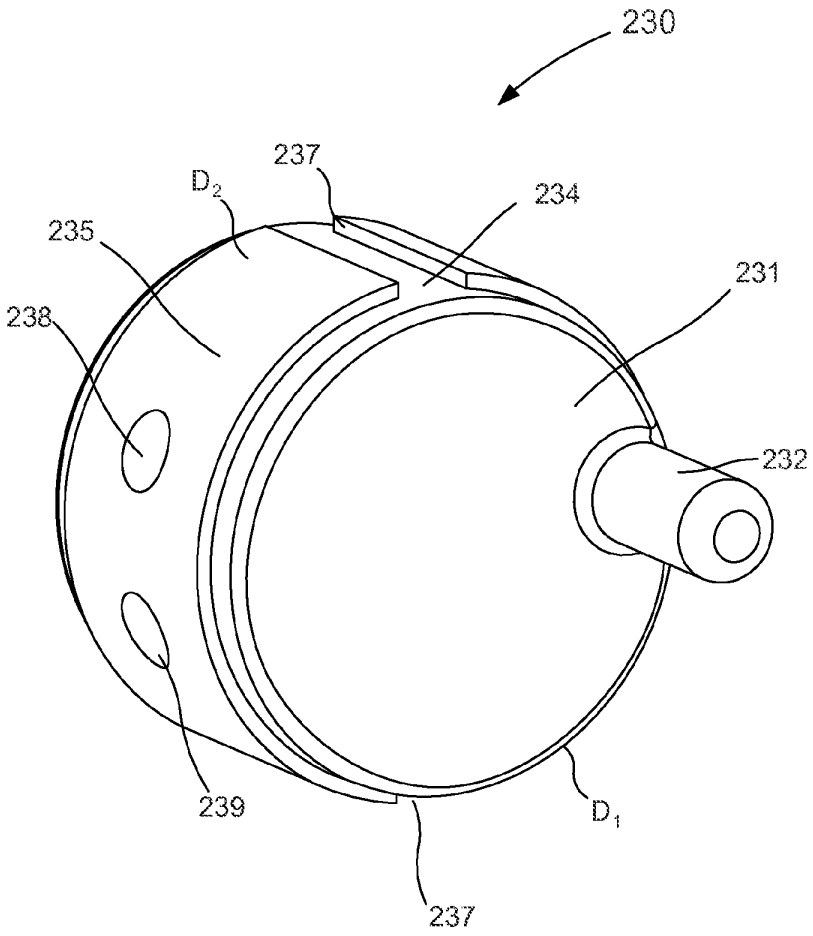


FIG. 9

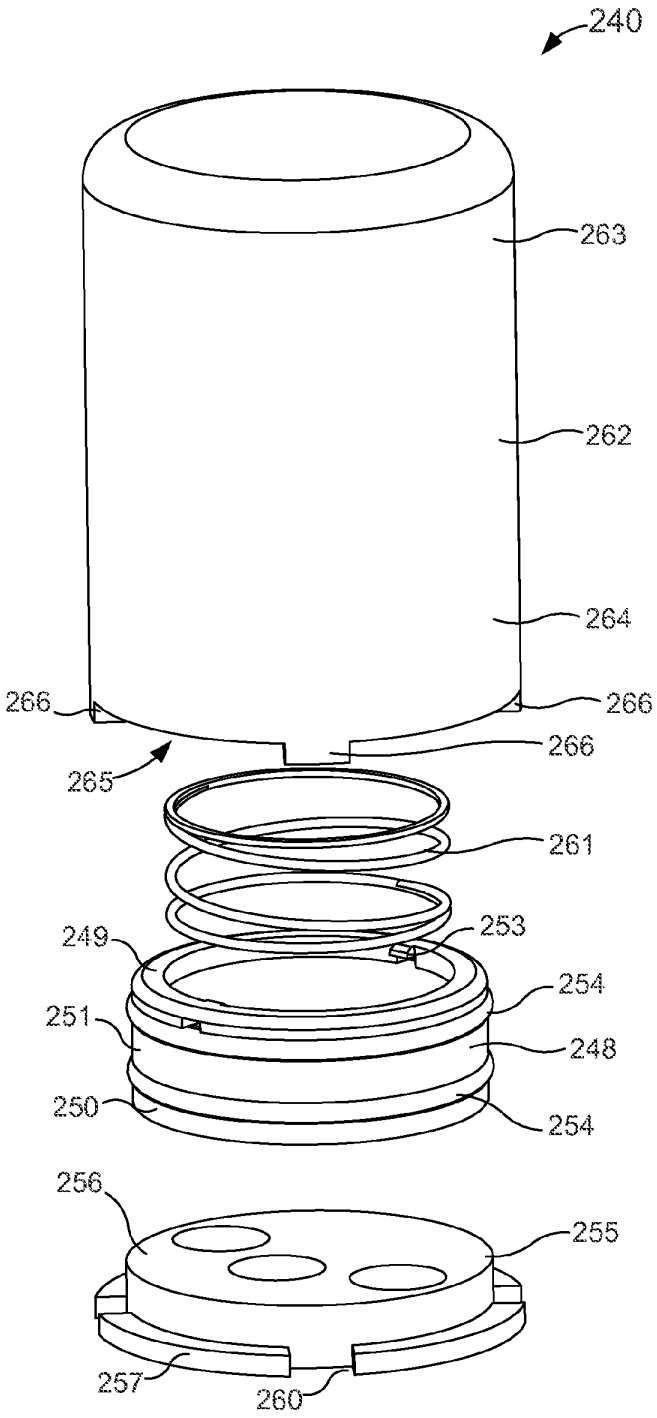

240
263
262
264
266
266
266
265
261
249
253
254
251
248
250
254
256
255
257
260

FIG. 10

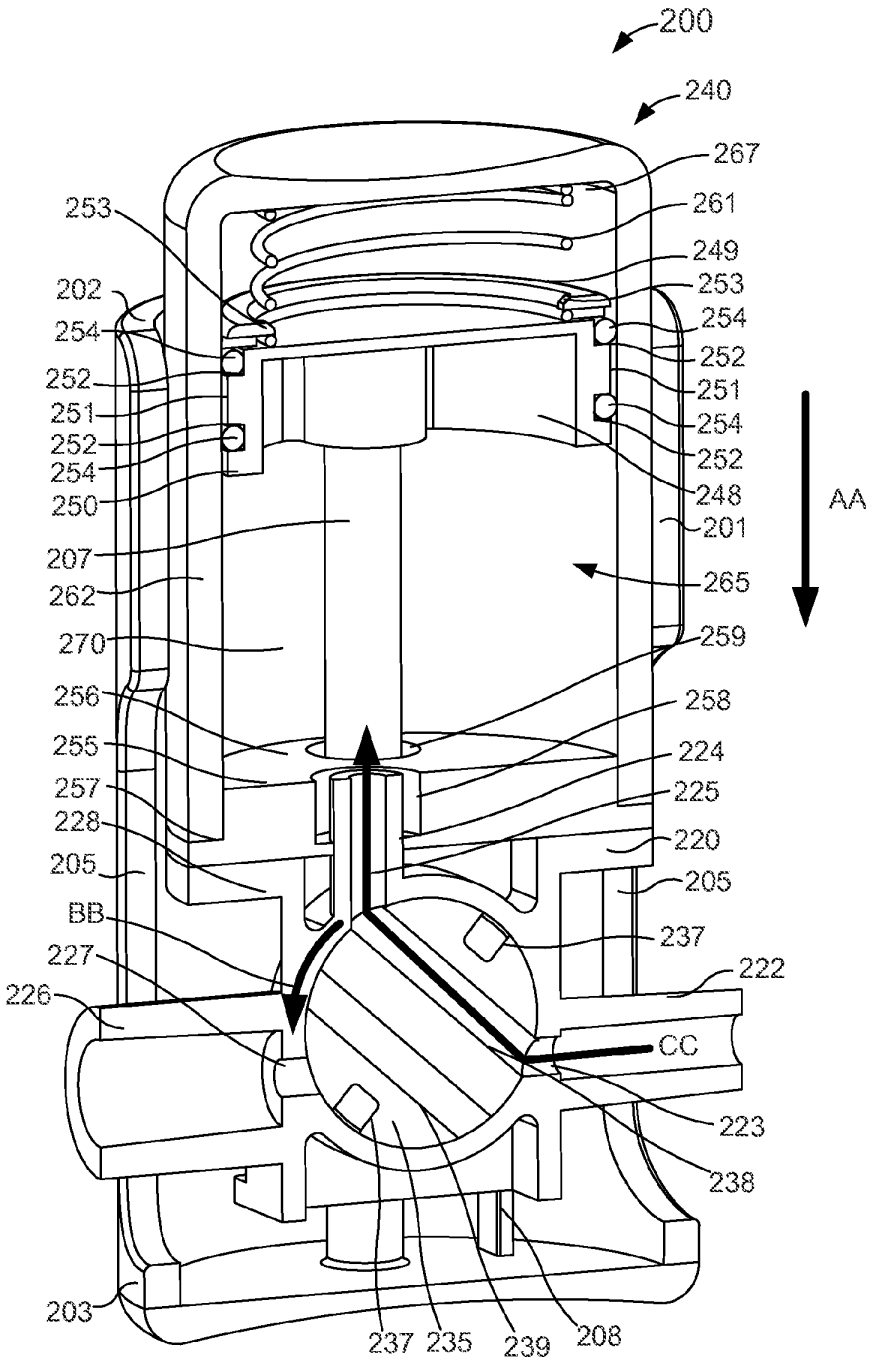

200
240
267
253
261
249
202
253
254
254
252
252
251
251
254
252
254
252
248
AA
250
201
207
265
262
259
270
258
256
224
255
225
257
220
228
205
205
BB
237
227
222
226
CC
223
238
203
237
235
239
208

FIG. 11

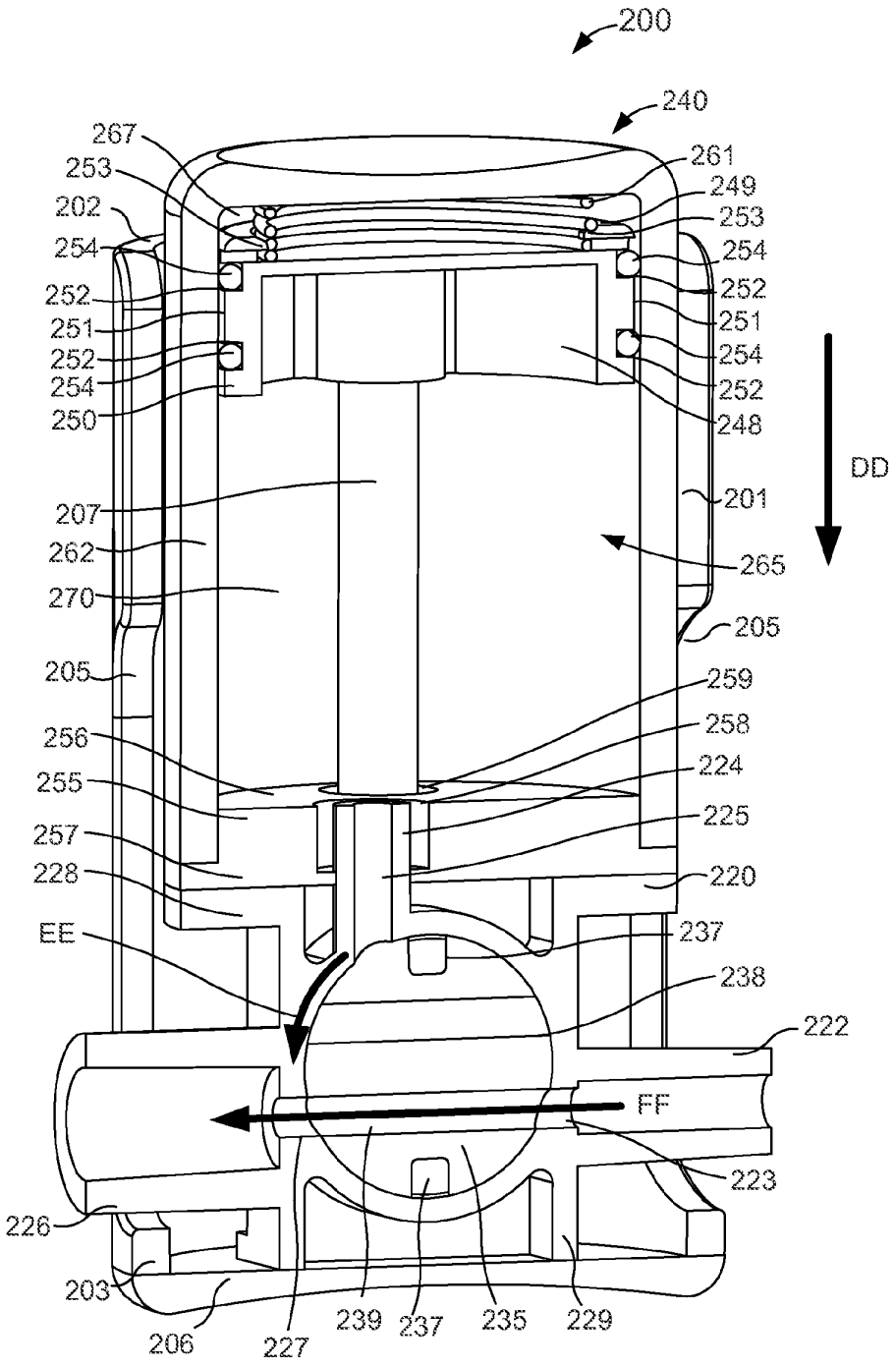

200
240
267
253
202
254
252
251
252
254
250
207
262
270
205
256
255
257
228
EE
261
249
253
254
252
251
254
252
248
DD
201
265
205
259
258
224
225
220
237
238
222
FF
223
226
203
206
227
239
237
235
229

FIG. 12

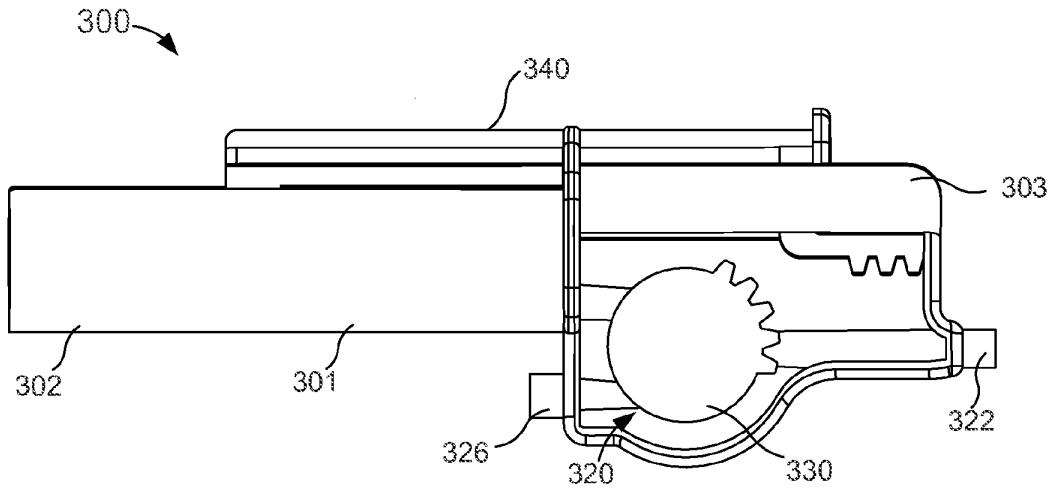

300
340
303
302
301
322
326
320
330

FIG. 13

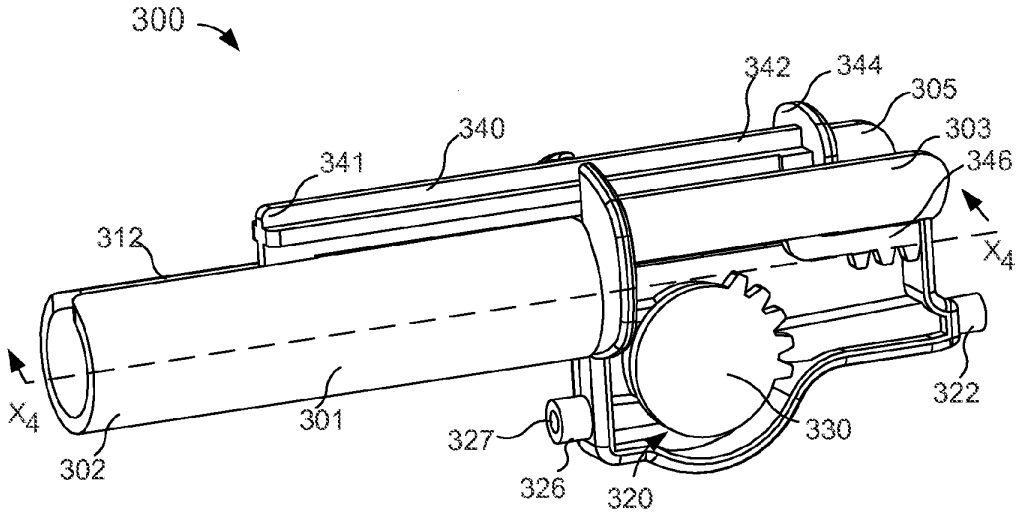

300
342
344
305
340
303
341
346
312
X4
X4
301
322
327
330
302
326
320

FIG. 14

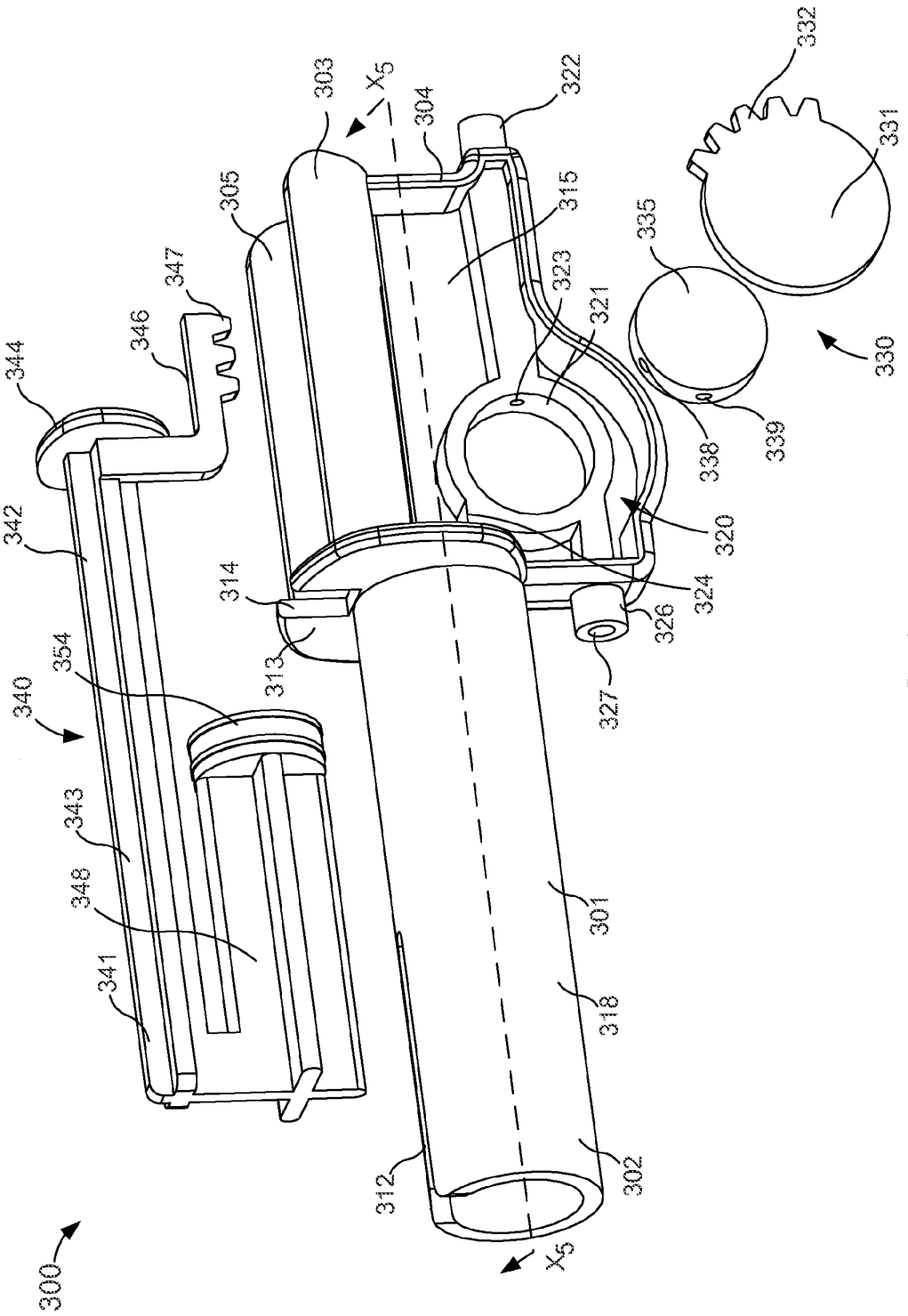

300
301
302
303
304
305
312
313
314
315
318
320
321
322
323
324
326
327
330
331
332
335
338
339
340
341
342
343
344
346
347
348
354
X_5
X_5

FIG. 15

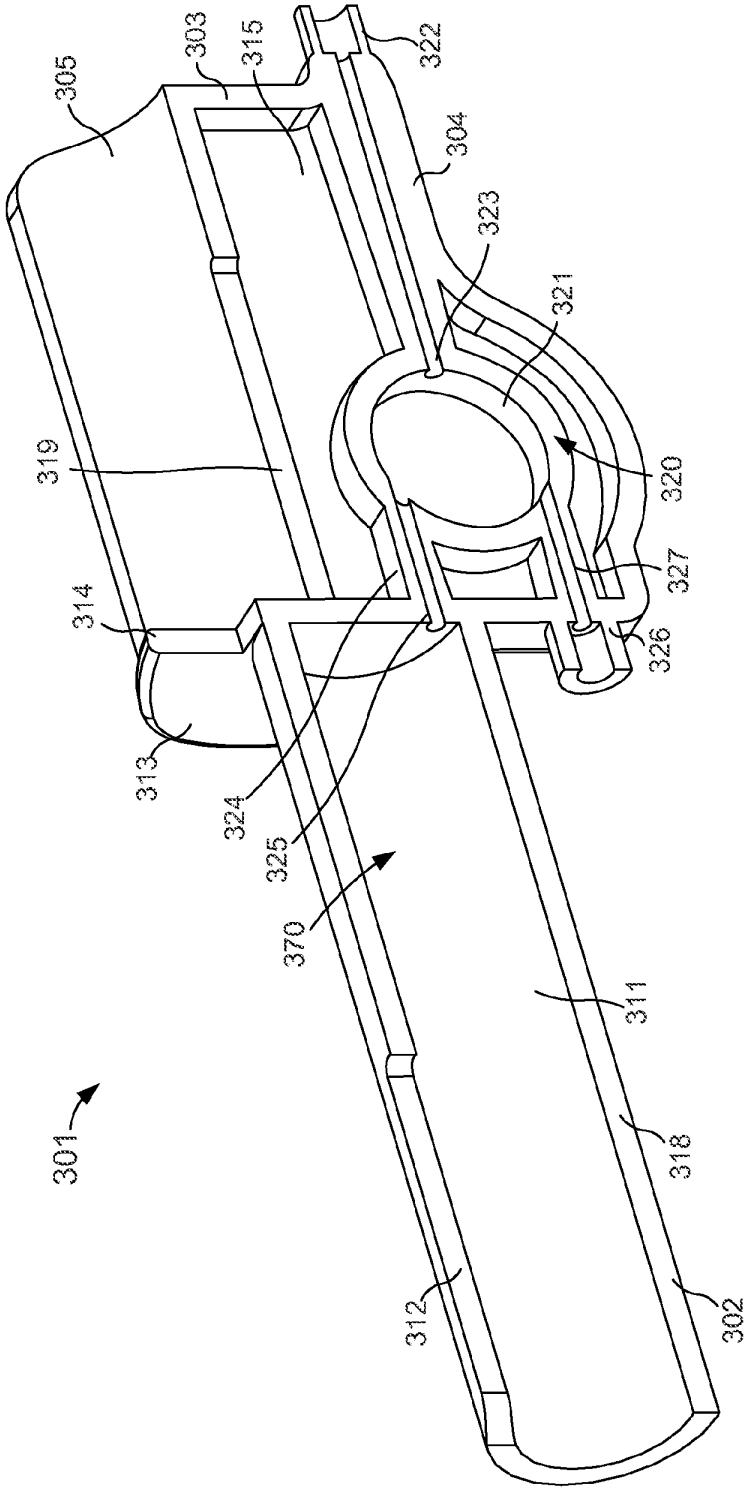

305
303
315
322
304
323
321
319
320
314
327
326
313
324
325
370
311
301
318
312
302

FIG. 16

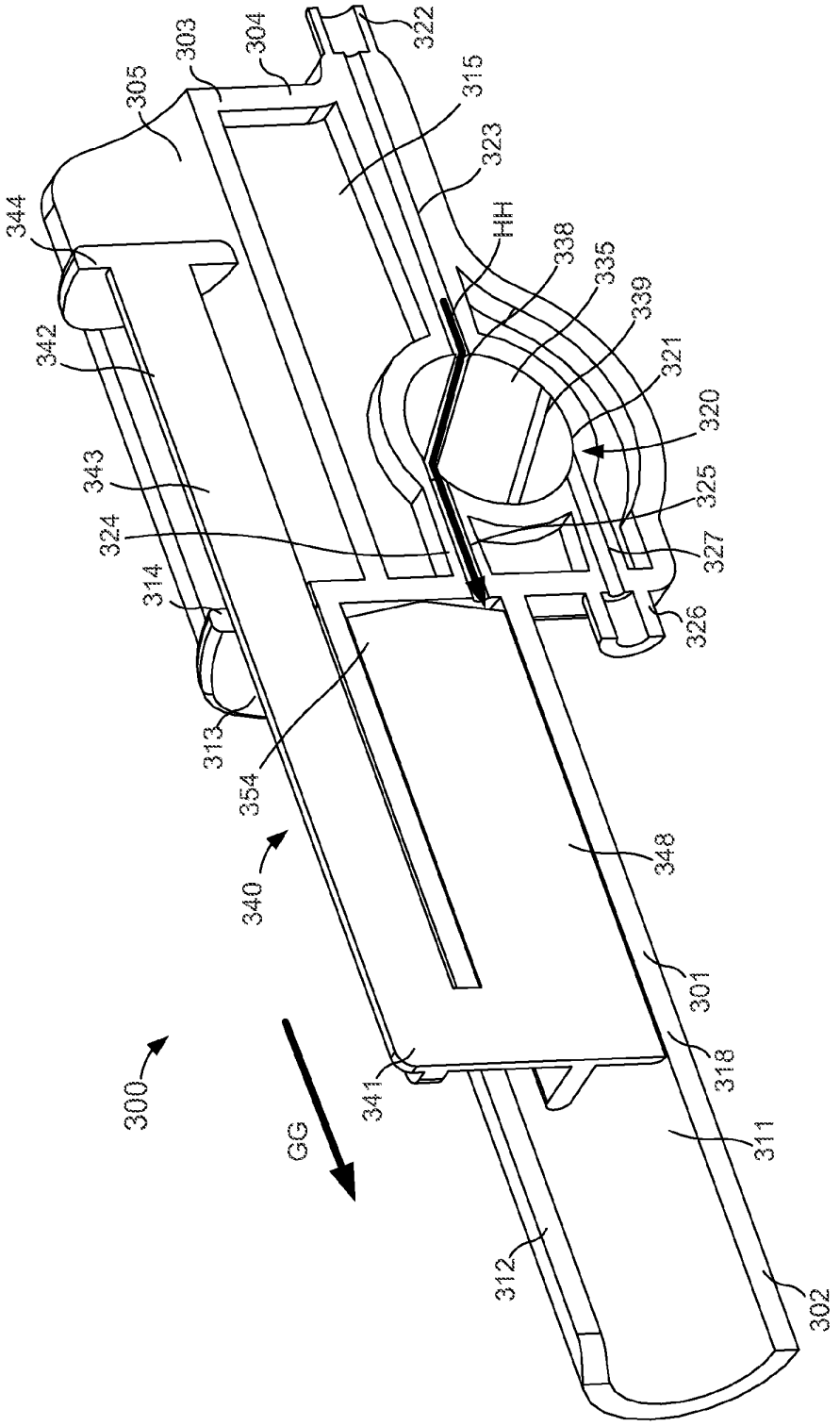

322
304
303
305
315
323
344
HH
338
335
339
342
321
320
343
325
324
327
314
326
313
354
340
348
301
318
300
GG
341
311
312
302

FIG. 17

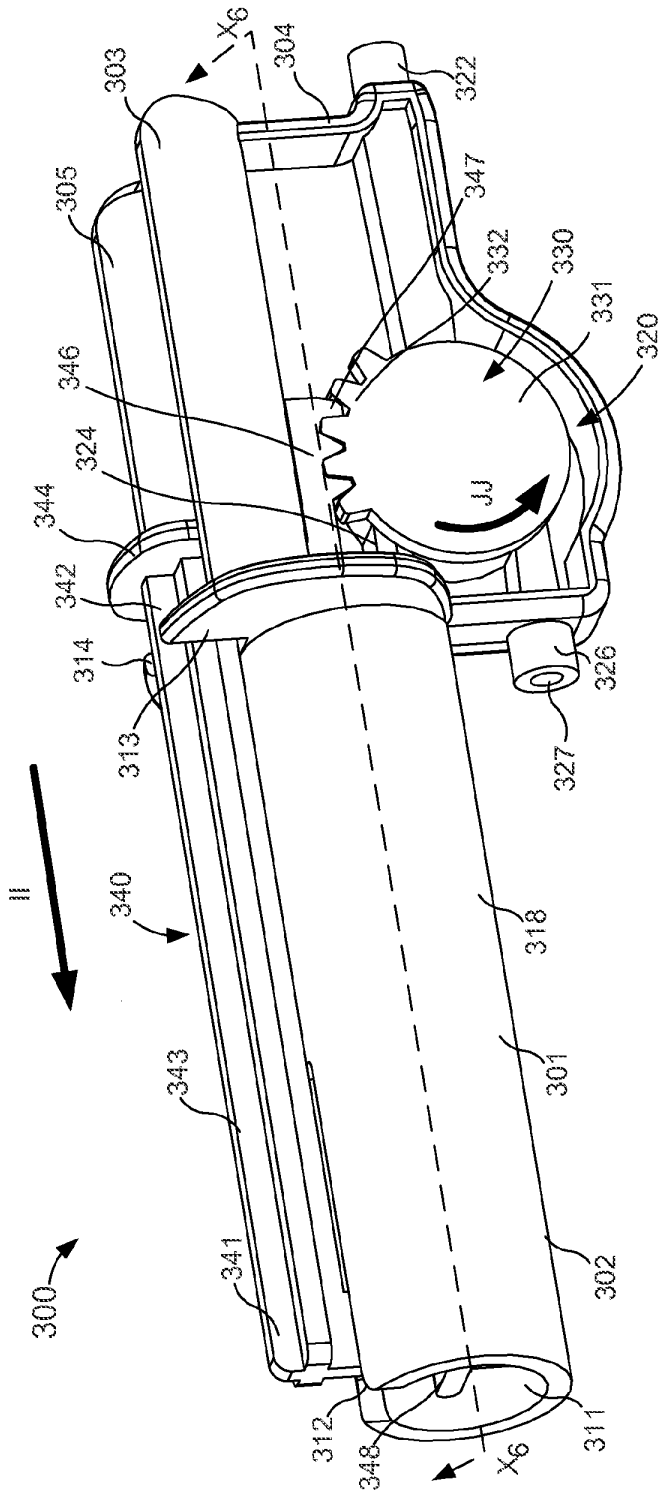

X6
303
304
322
305
347
332
330
331
320
346
324
JJ
344
342
314
313
326
327
II
340
318
343
301
341
302
300
312
348
311
X6

FIG. 18

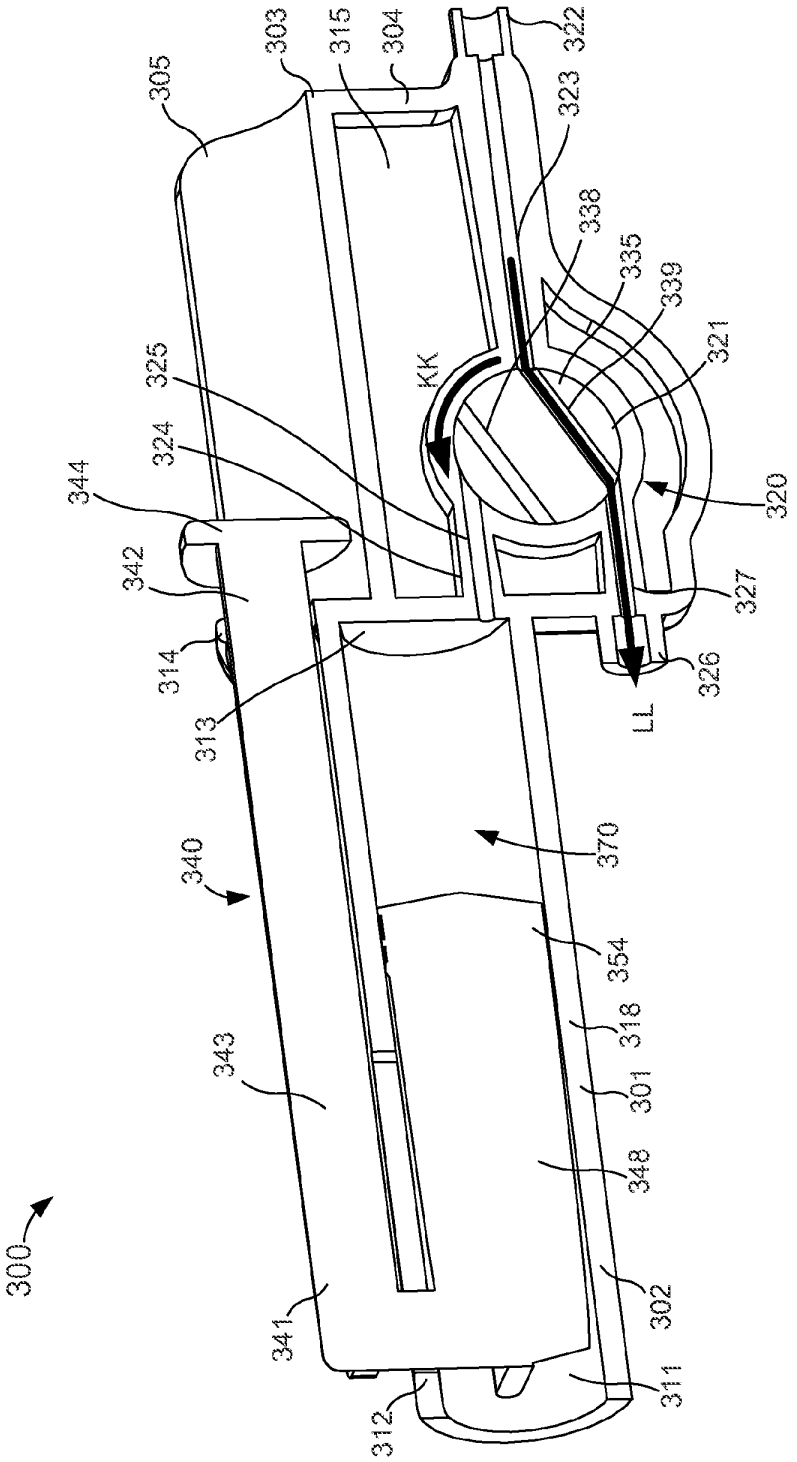

300
305
303
315
304
322
323
338
335
339
321
325
324
344
342
314
313
KK
LL
320
327
326
340
370
354
318
301
348
343
341
302
311
312

FIG. 19

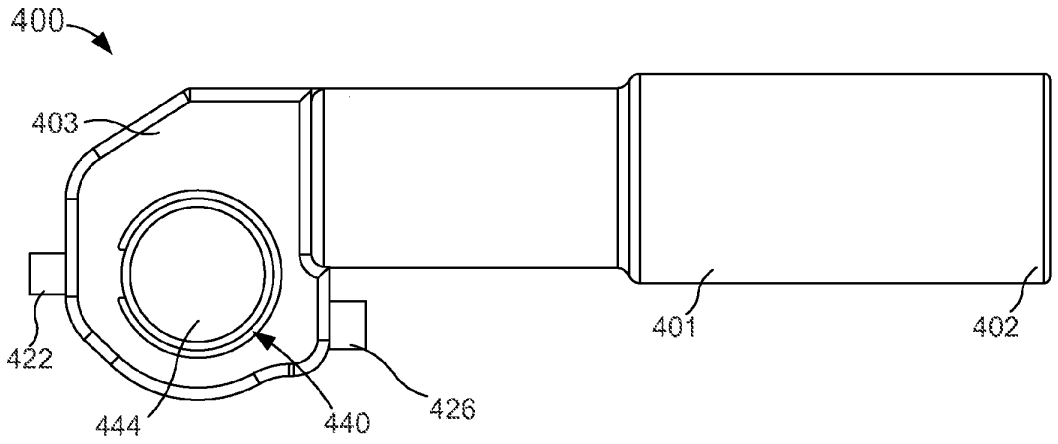

400
403
422
444
440
426
401
402

FIG. 20

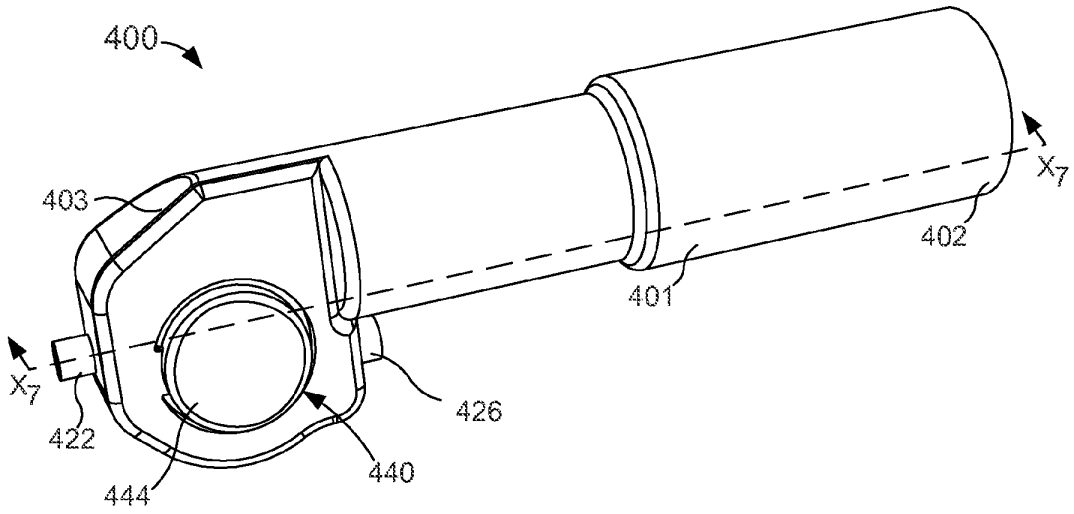

400
403
422
444
440
426
401
402
X7
X7

FIG. 21

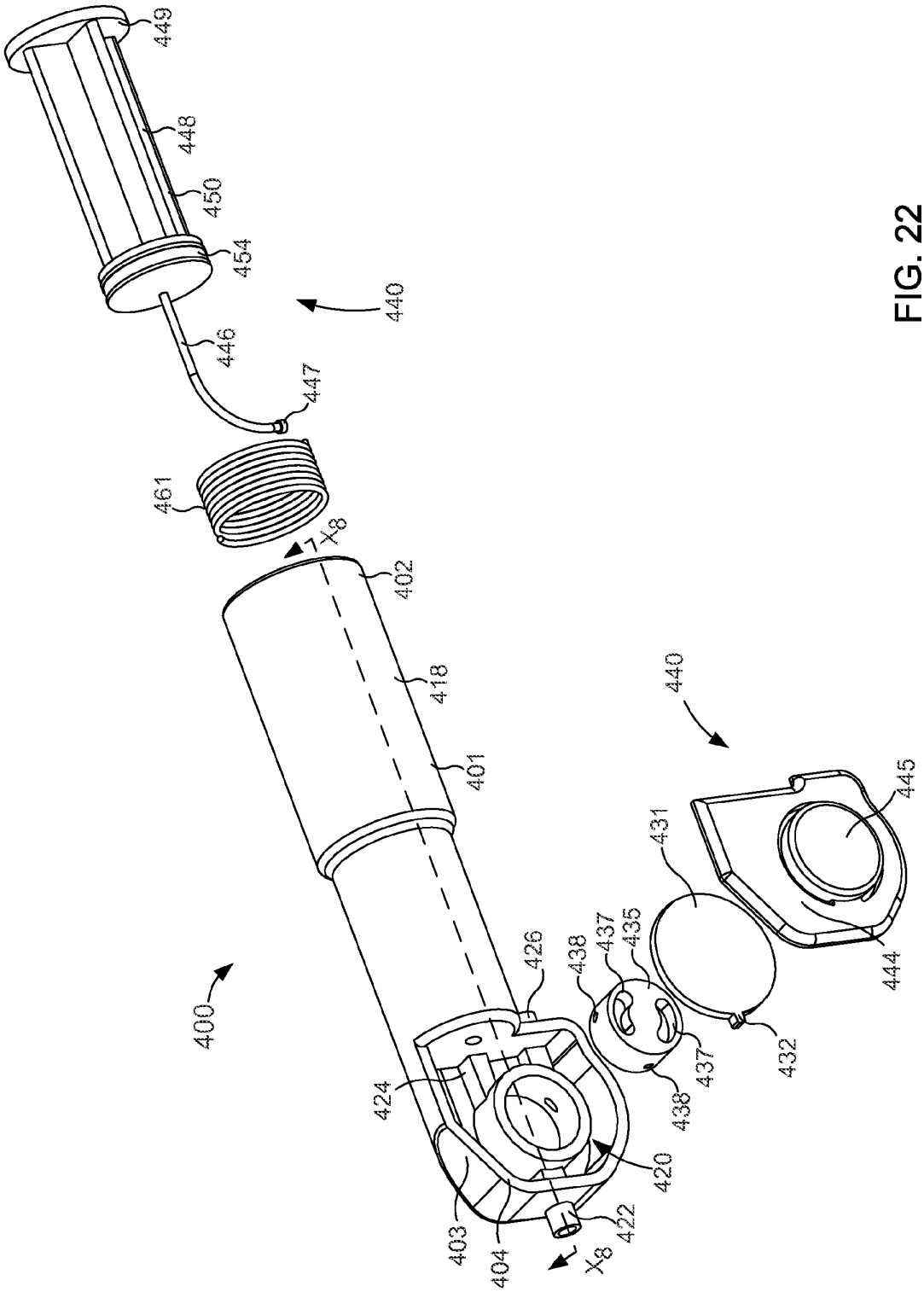

449
448
450
454
440
446
447
461
X8
402
418
401
440
445
431
426
438
437
435
400
424
437
438
432
444
420
422
403
404
X8

FIG. 22

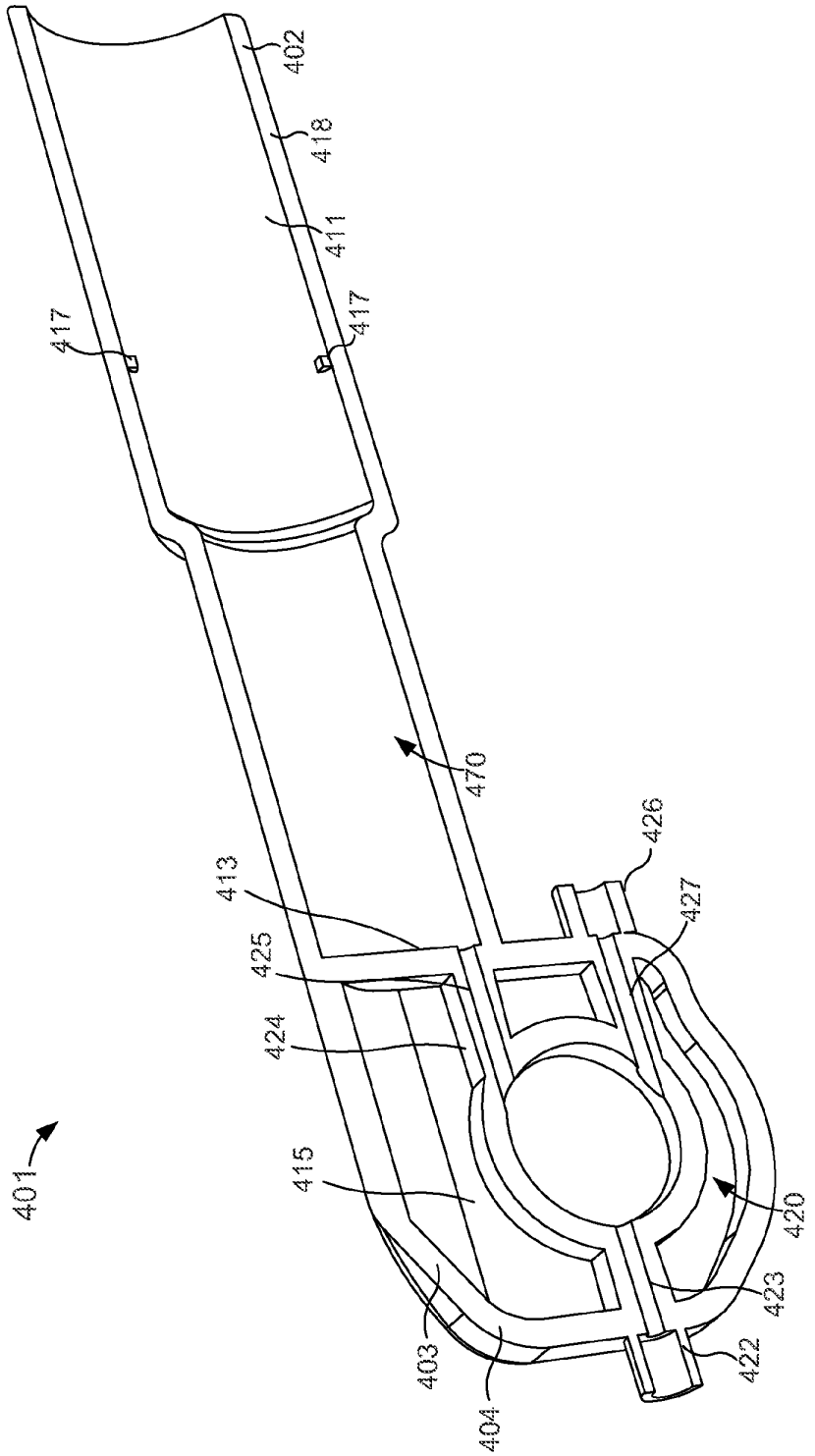

402
418
411
417
417
470
426
427
413
425
424
401
415
420
423
422
403
404

FIG. 23

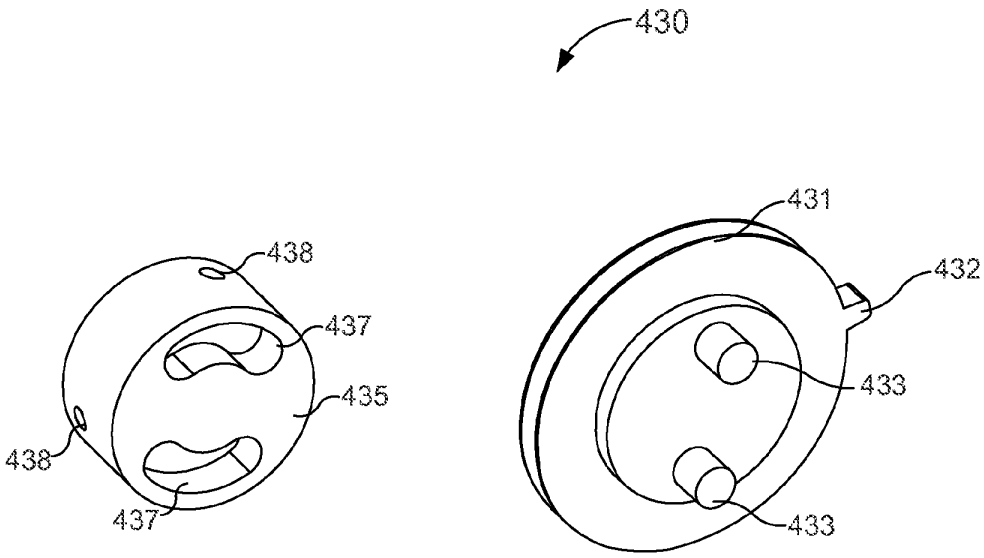


FIG. 24

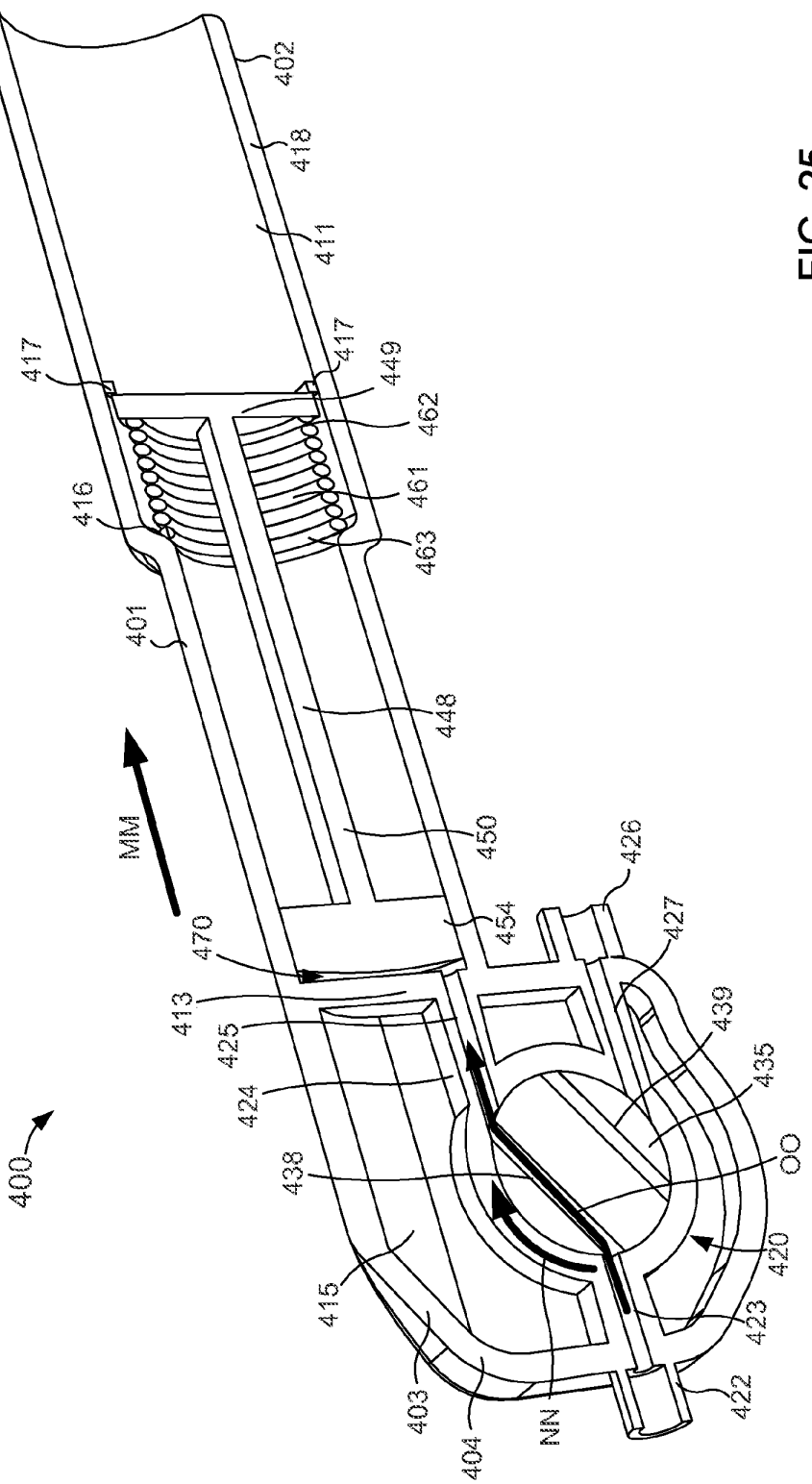

400
402
418
411
417
417
449
462
461
463
416
401
448
450
426
427
454
470
413
425
424
438
439
435
OO
420
423
422
415
403
404
NN
MM

FIG. 25

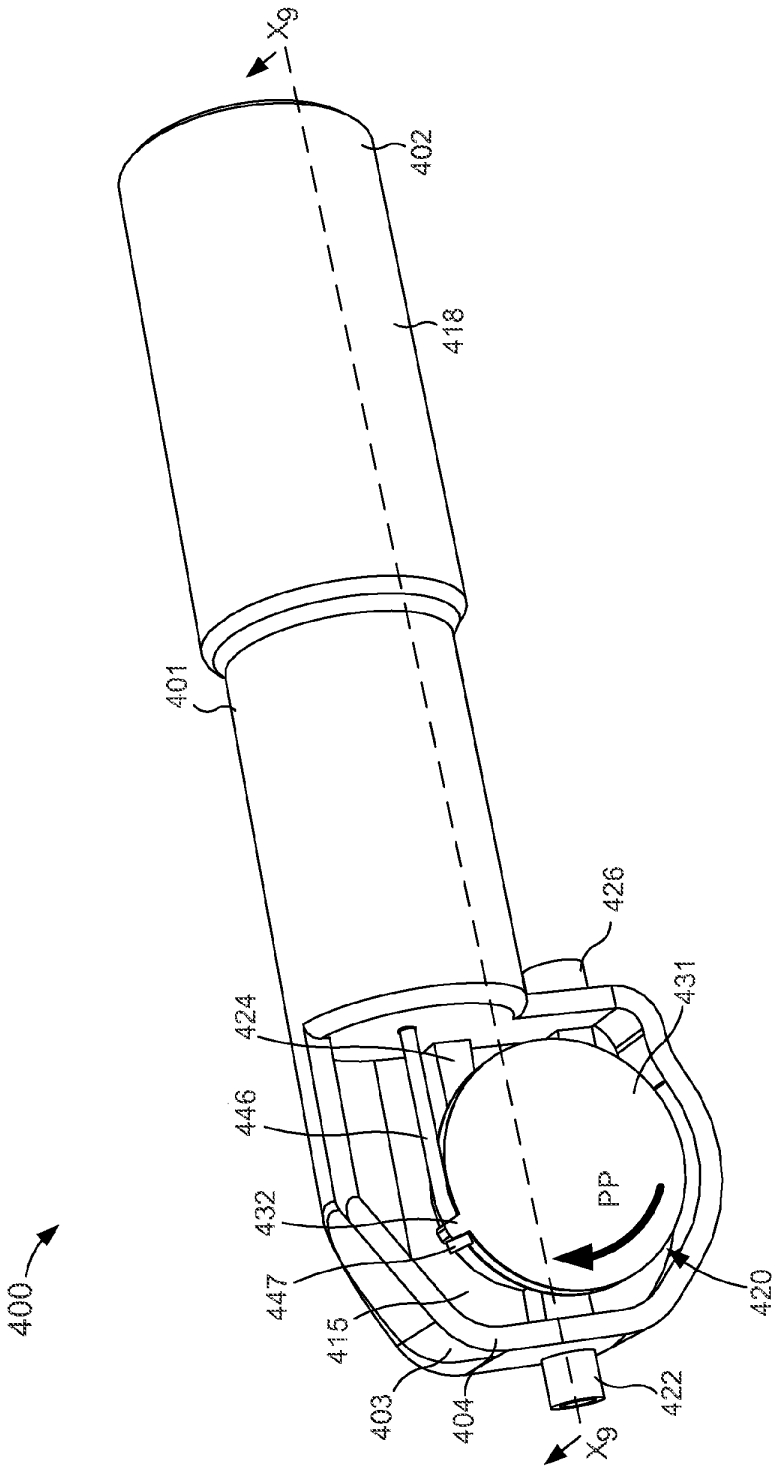

X9
402
418
401
426
431
424
446
432
447
415
403
404
PP
420
422
X9
400

FIG. 26

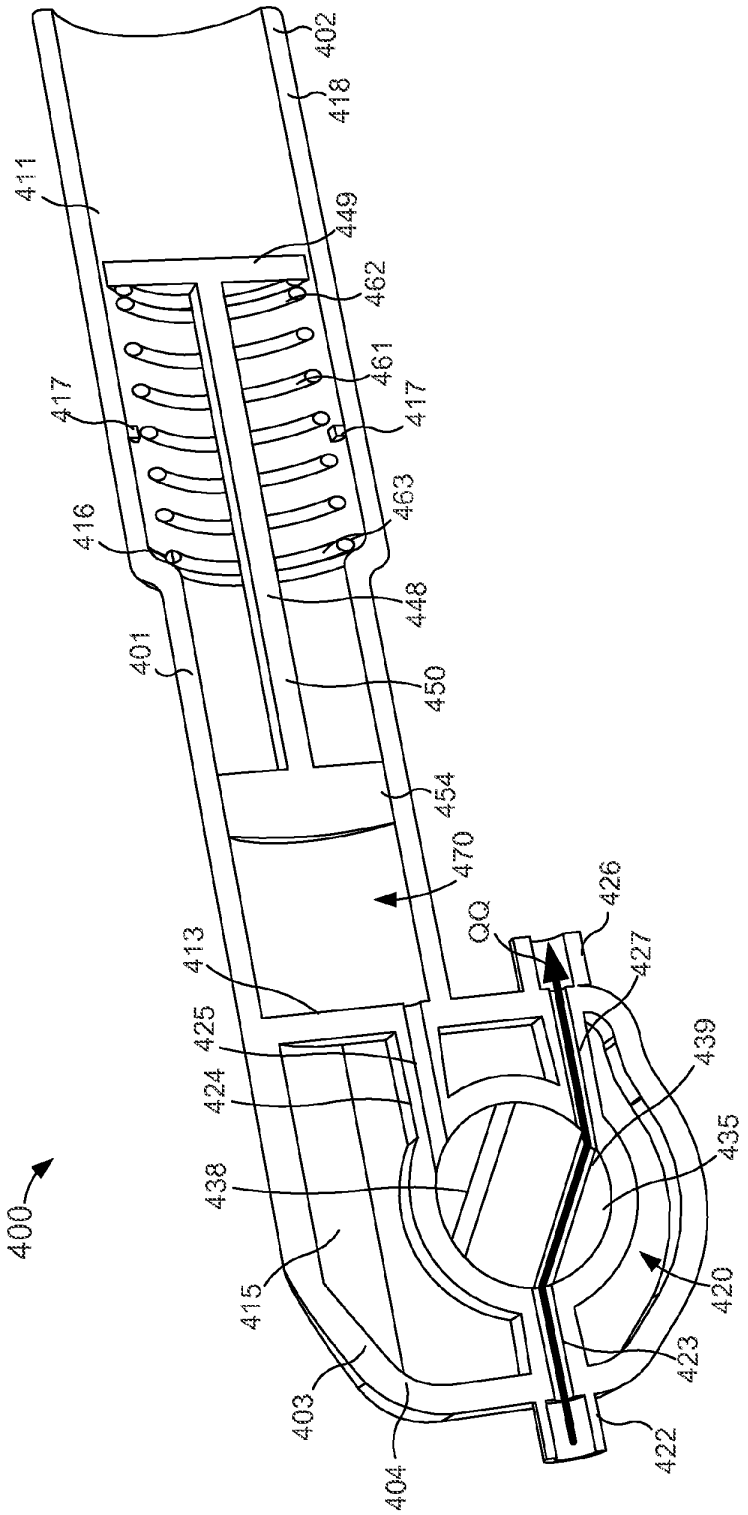

400
401
402
403
404
411
413
415
416
417
417
418
420
422
423
424
425
426
427
435
438
439
448
449
450
454
461
462
463
470
QQ

FIG. 27

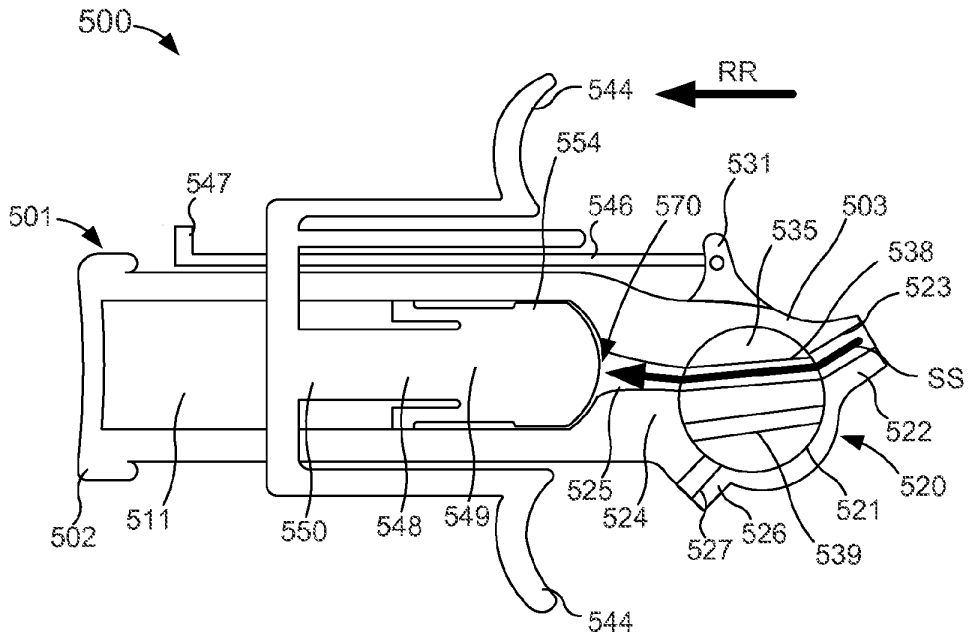

500
544
RR
554
531
547
501
546
570
503
535
538
523
SS
522
520
521
525
524
527
526
539
502
511
550
548
549
544

FIG. 28

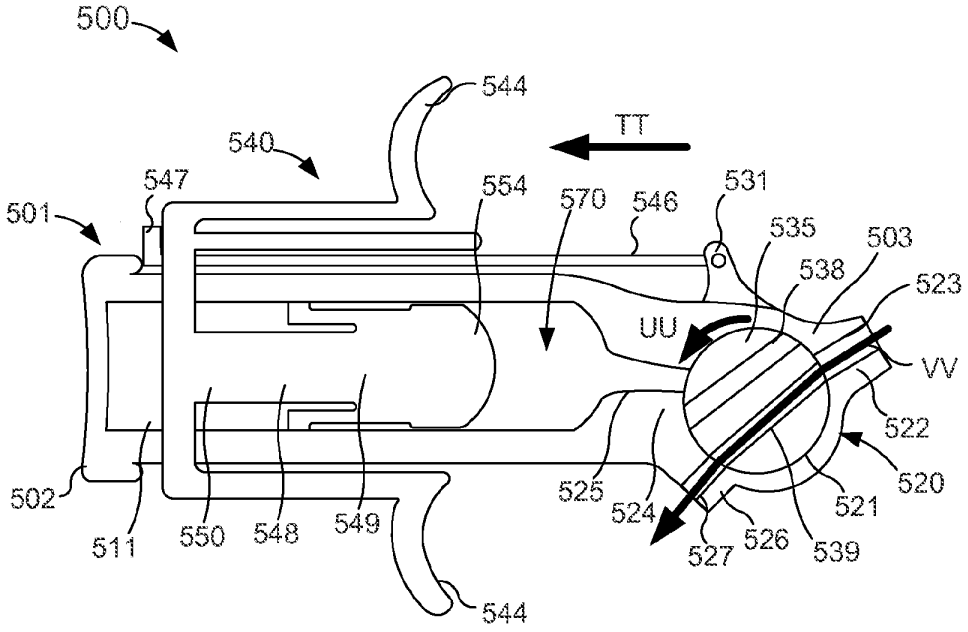

500
544
TT
540
547
554
570
546
531
501
535
503
538
523
UU
VV
522
520
521
525
524
527
526
539
502
511
550
548
549
544

FIG. 29

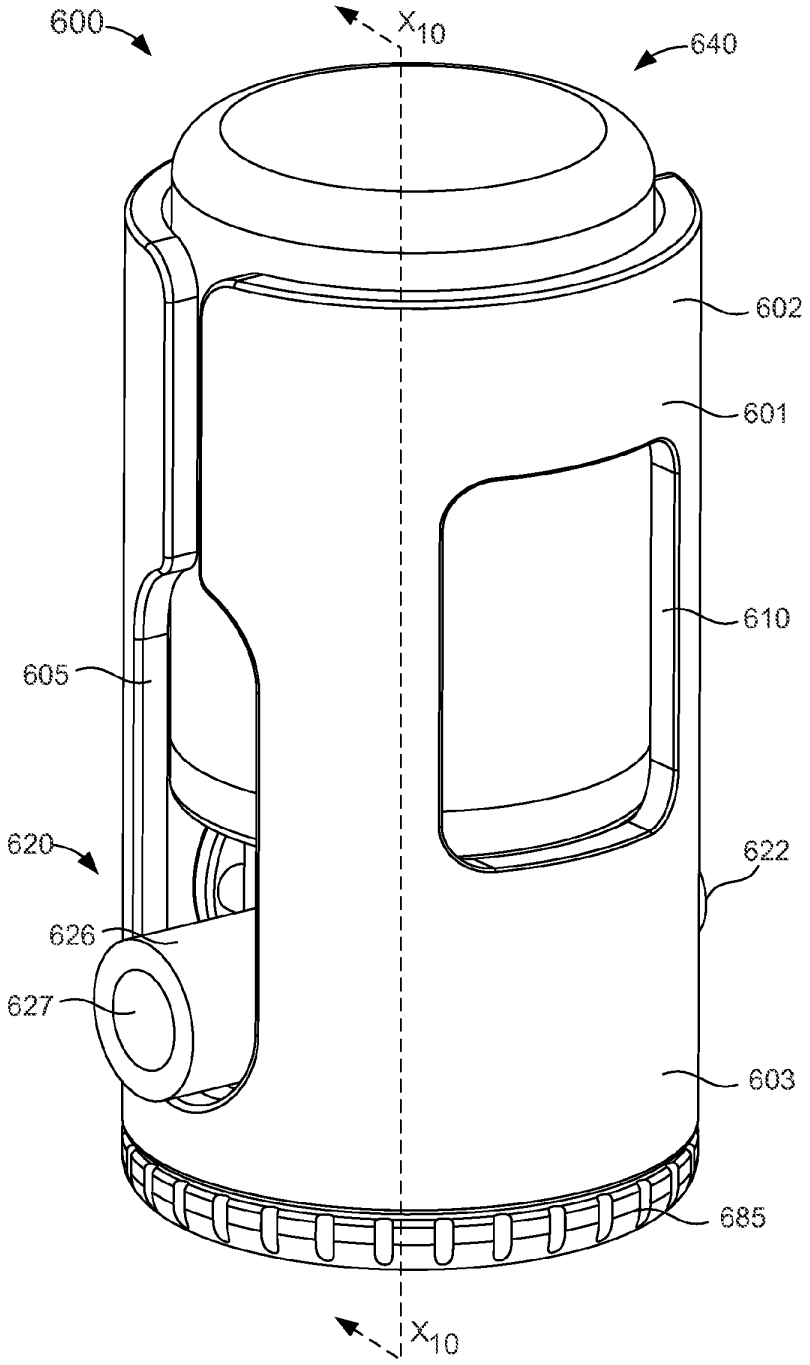


FIG. 30

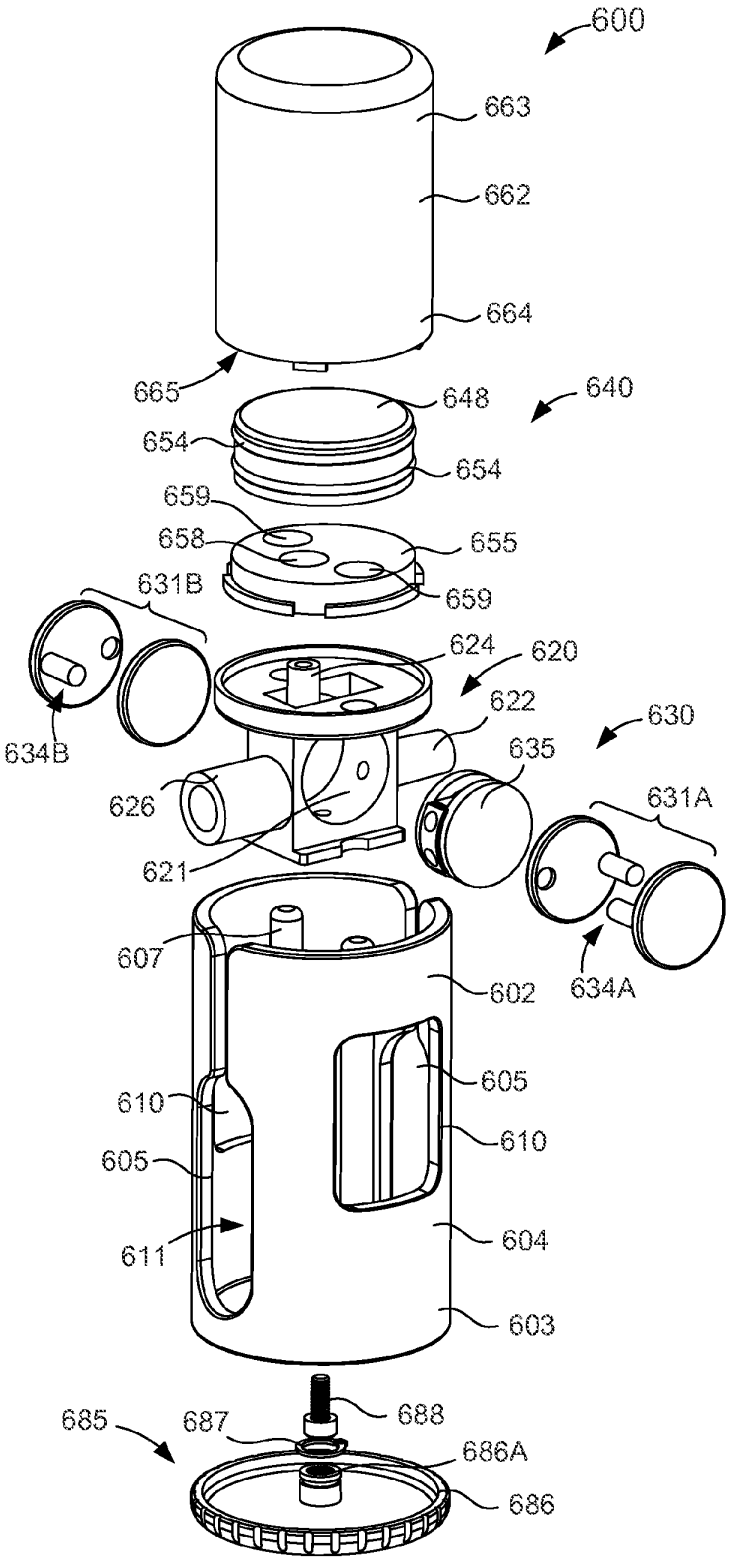

600
663
662
664
665
648
640
654
654
659
658
655
659
631B
624
620
622
630
634B
635
626
631A
621
607
602
634A
605
610
610
605
604
611
603
685
687
688
686A
686

FIG. 31

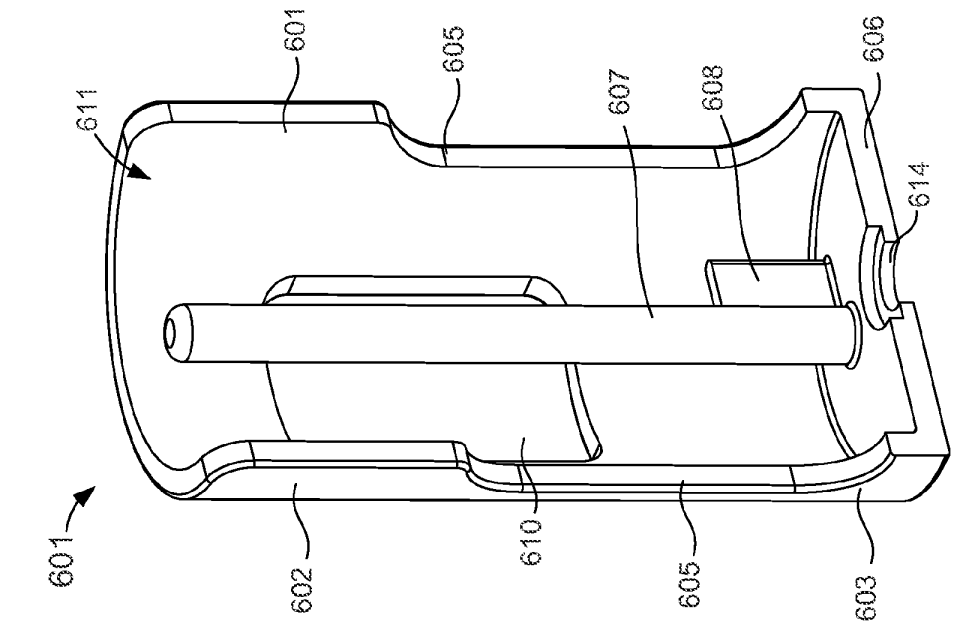

601
605
607
608
606
611
614
601
602
610
605
603

FIG. 33

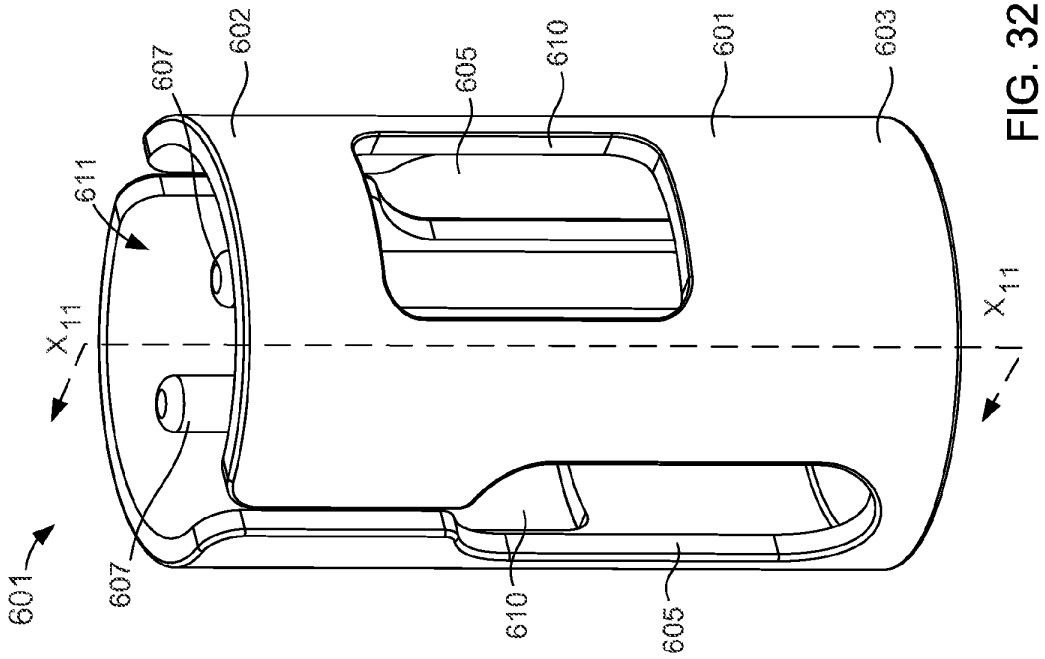

607
602
605
610
601
603
611
X11
X11
601
607
610
605

FIG. 32

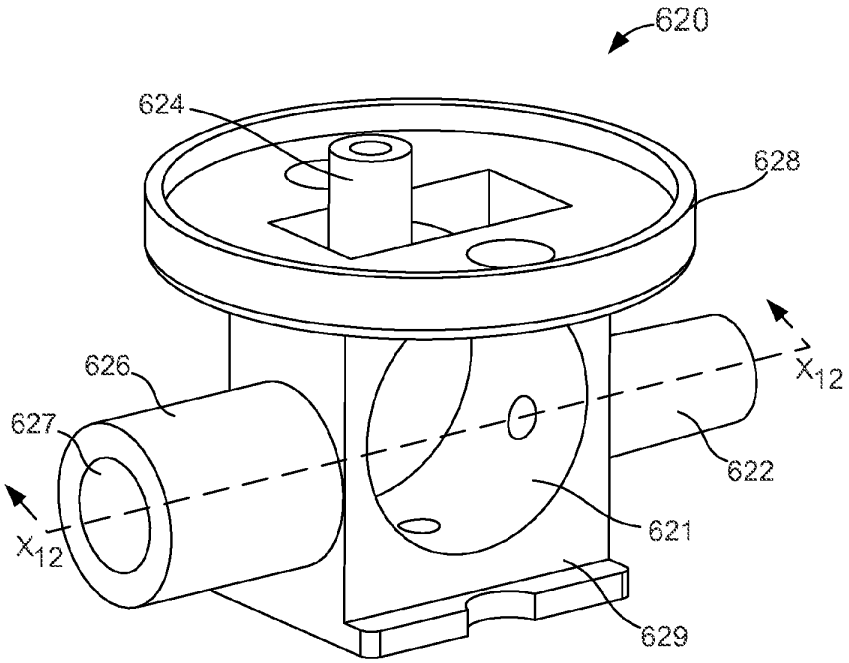

620
624
628
626
627
X_{12}
622
621
X_{12}
629

FIG. 34

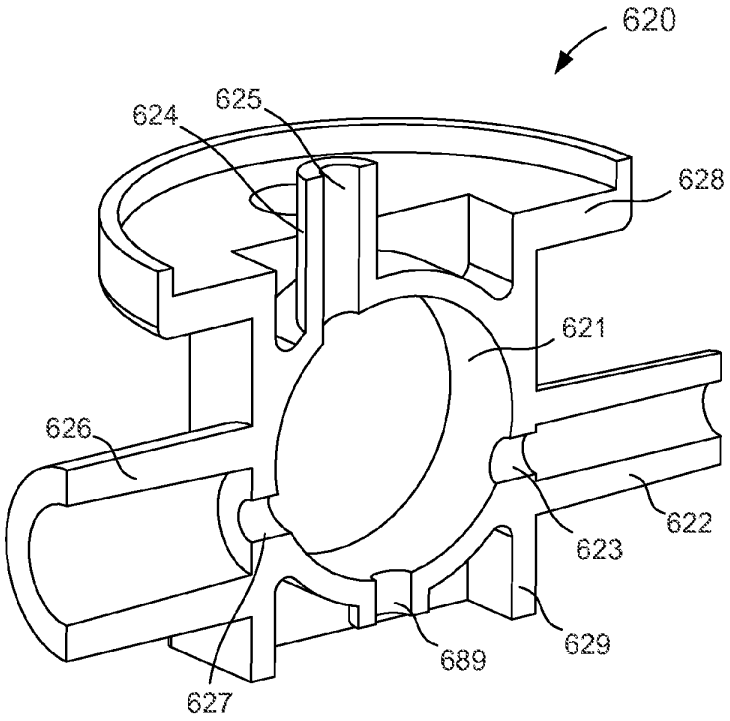

620
624
625
628
621
626
622
623
629
689
627

FIG. 35

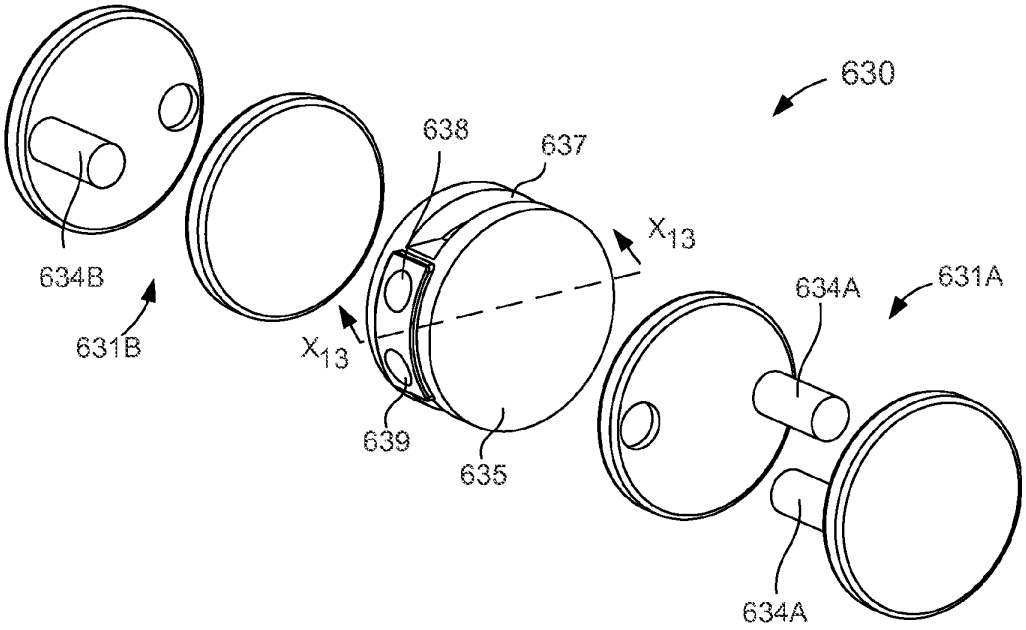

630
638
637
X_{13}
634B
631B
X_{13}
639
635
634A
631A
634A

FIG. 36

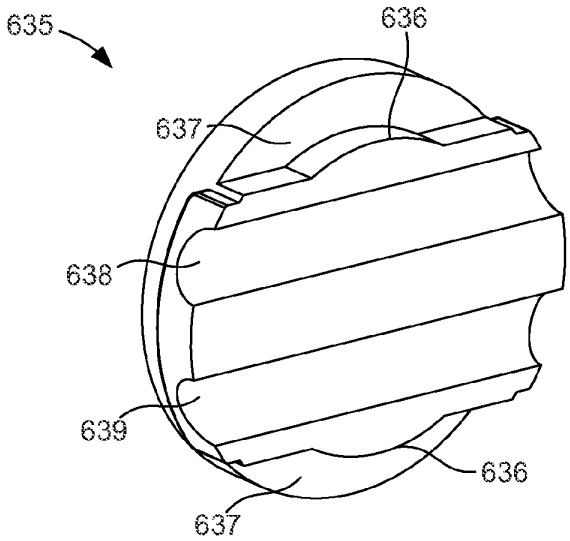

635
636
637
638
639
636
637

FIG. 37

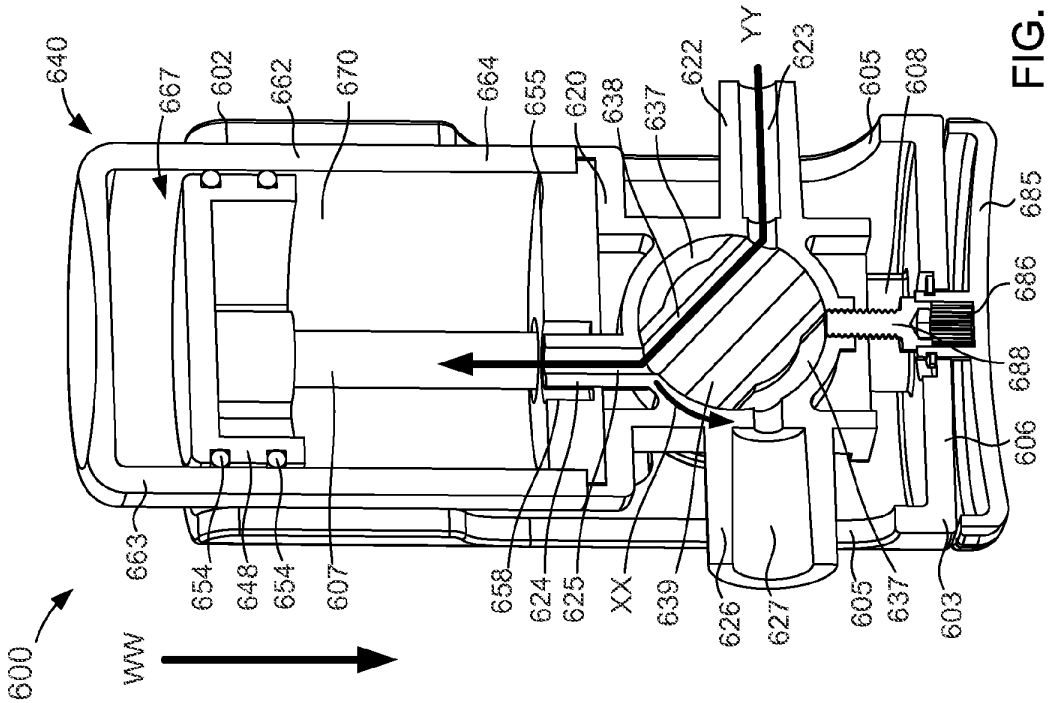

640
667
602
662
670
664
655
620
638
637
622
623
YY
605
608
685
686
688
606
603
637
605
627
626
639
XX
625
624
658
607
654
648
654
663
WW
600

FIG. 39

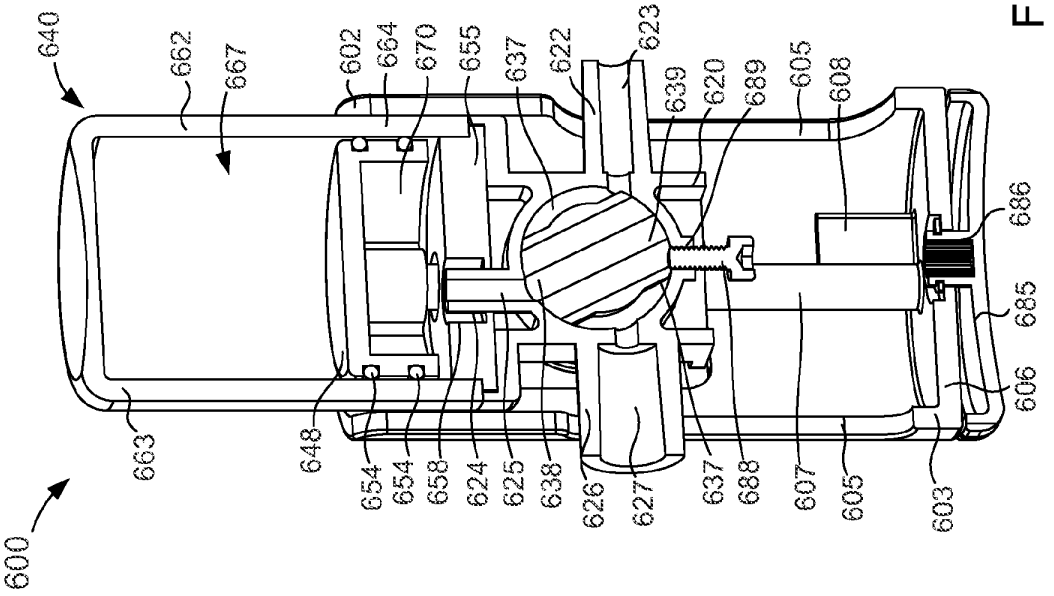

640
662
667
602
664
670
655
637
622
623
639
620
689
605
608
686
685
606
603
637
688
607
605
626
627
624
625
638
658
654
654
648
663
600

FIG. 38

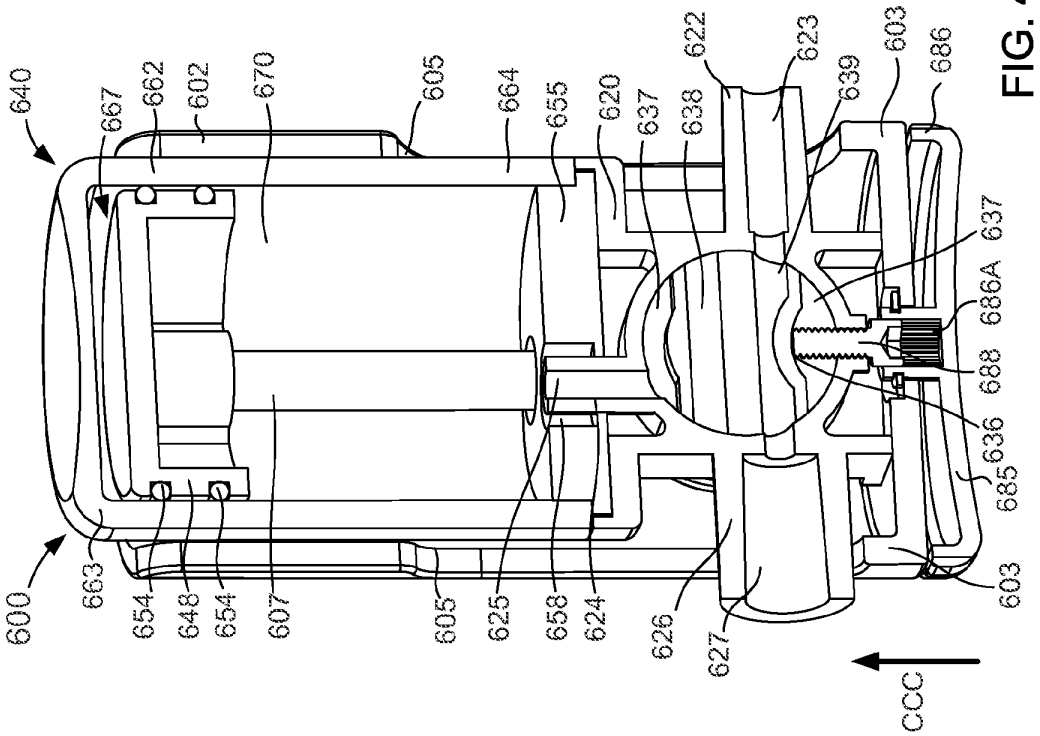

640
667
662
602
670
605
664
655
620
637
638
622
623
639
603
686
637
686A
688
636
685
603
600
663
654
648
654
607
605
625
658
624
626
627
CCC

FIG. 41

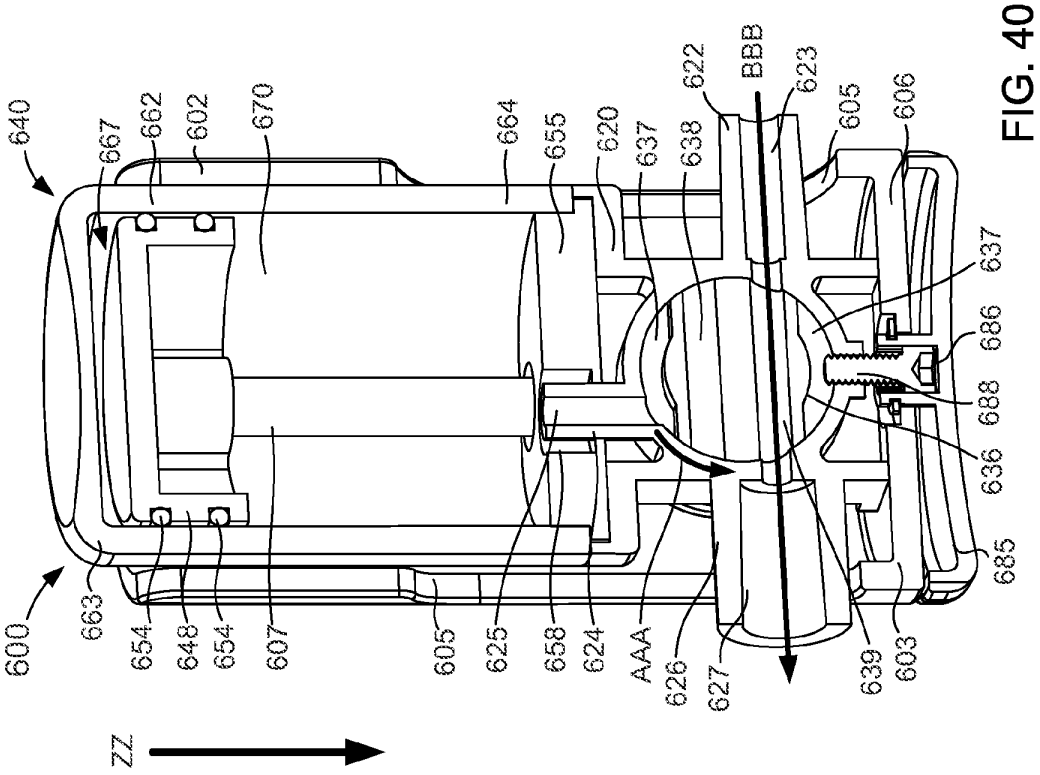

640
667
662
602
670
664
655
620
637
638
622
BBB
623
605
606
637
686
688
636
685
600
663
654
648
654
607
605
625
658
624
AAA
626
627
639
603
ZZ

FIG. 40

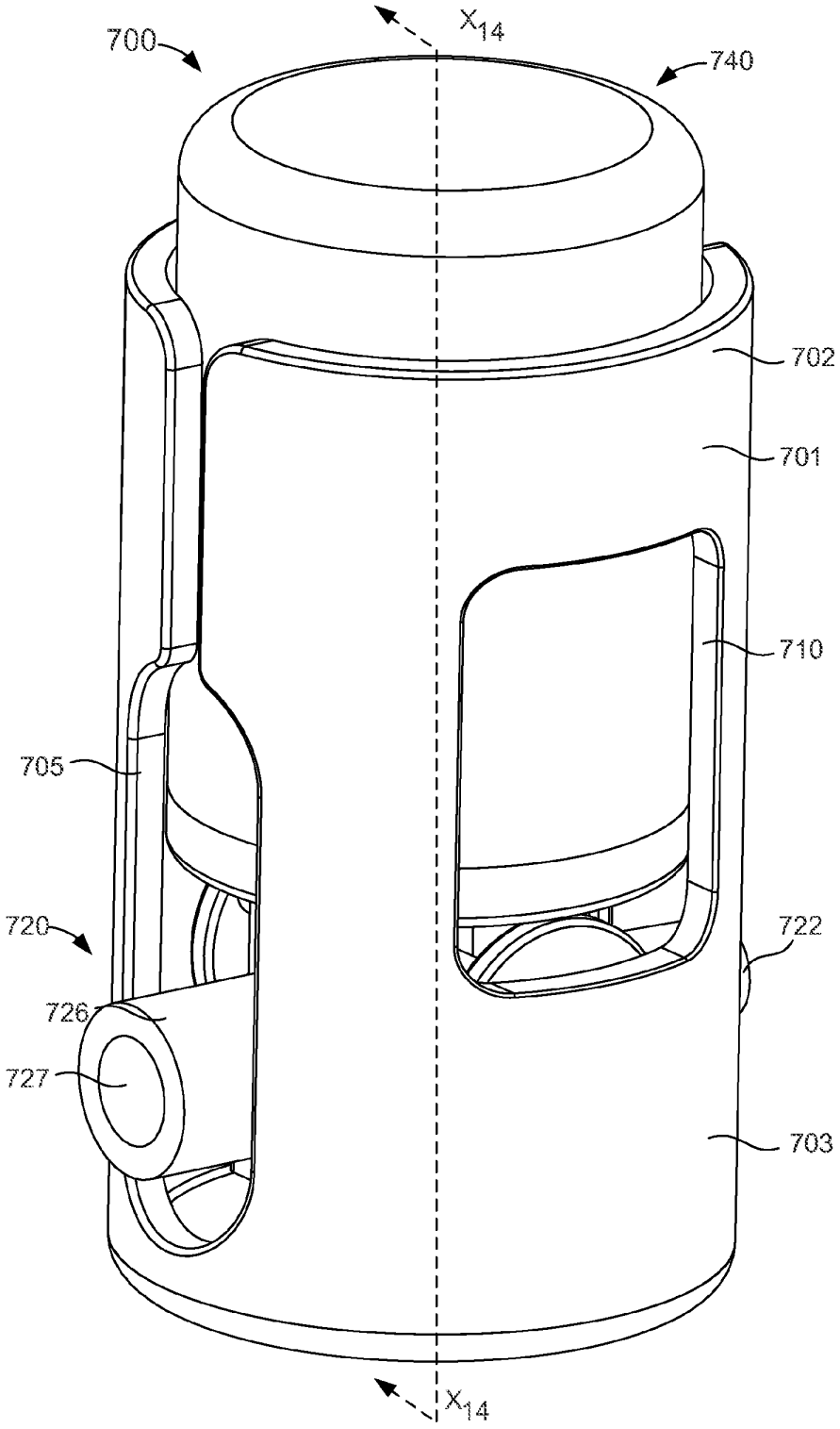


FIG. 42

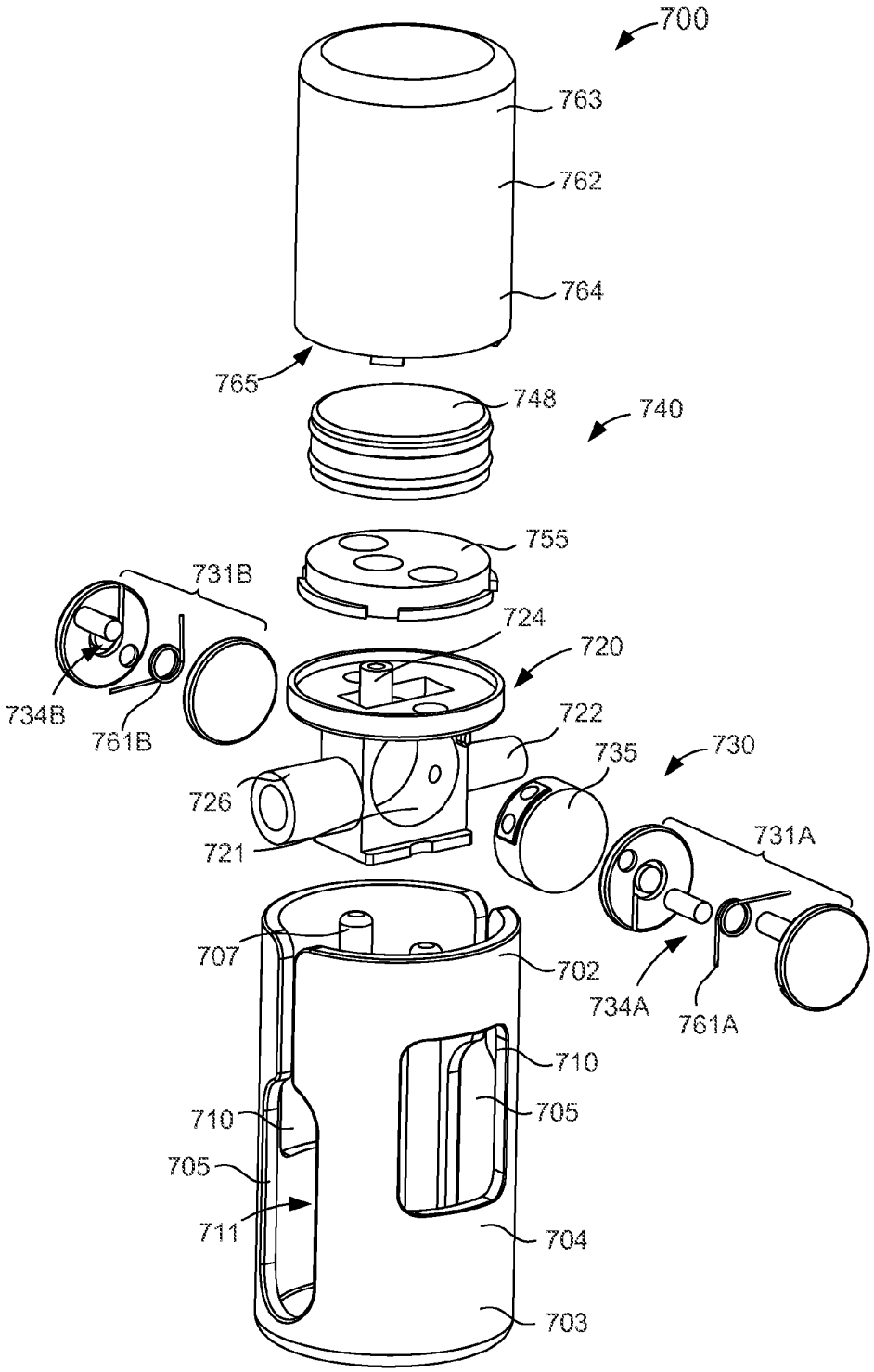

700
763
762
764
765
748
740
755
731B
724
720
734B
761B
722
735
730
726
721
731A
707
702
734A
761A
710
705
710
705
711
704
703

FIG. 43

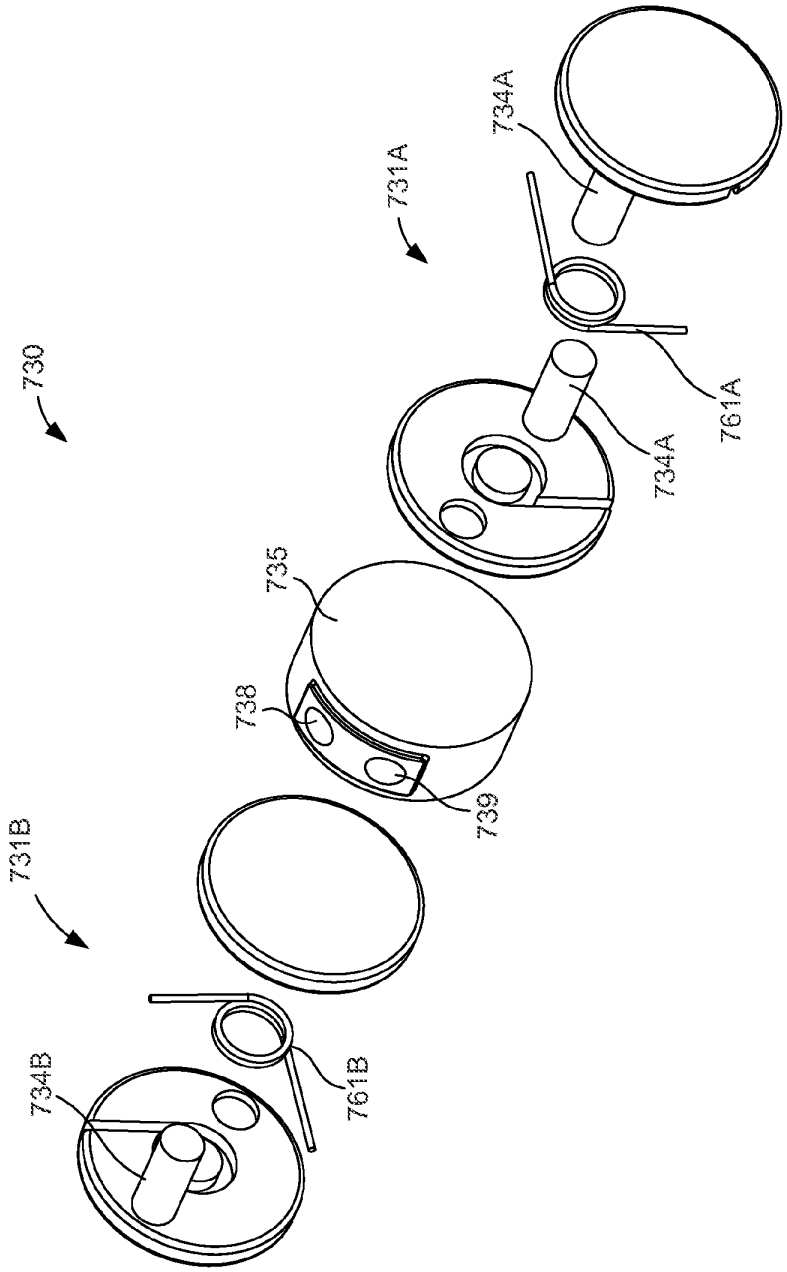


FIG. 44

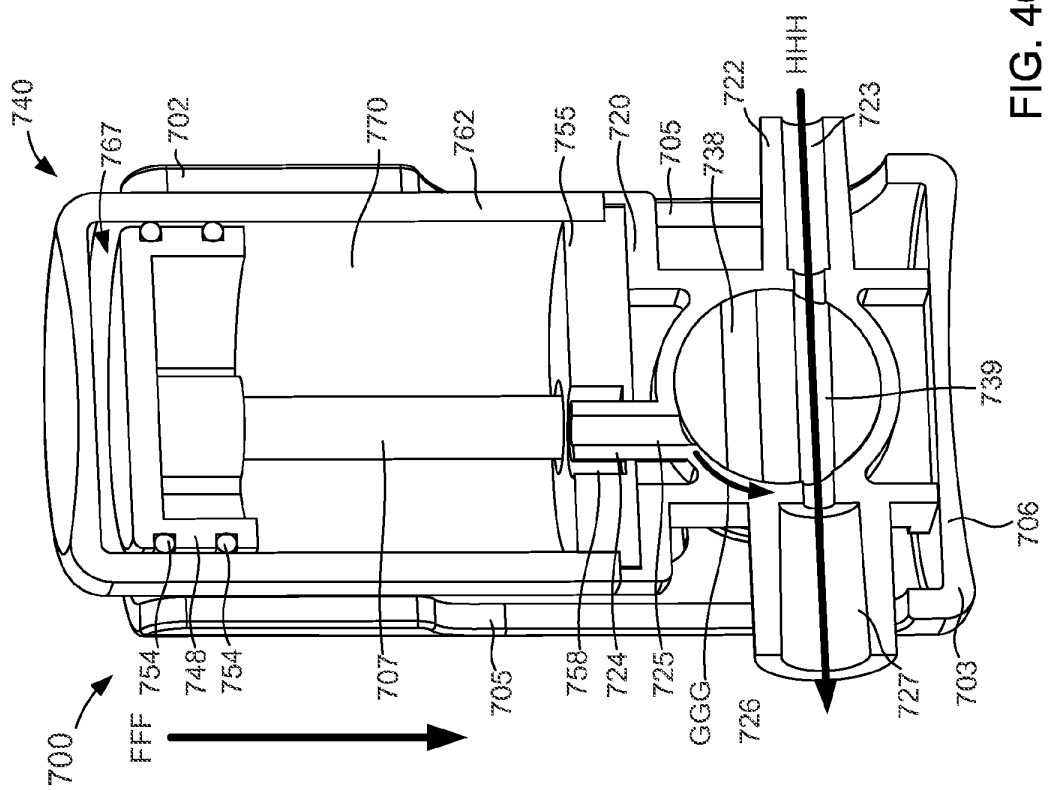

740
767
702
770
762
755
720
705
738
722
HHH
723
739
706
754
748
754
707
705
758
724
725
GGG
726
727
703
FFF
700

FIG. 46

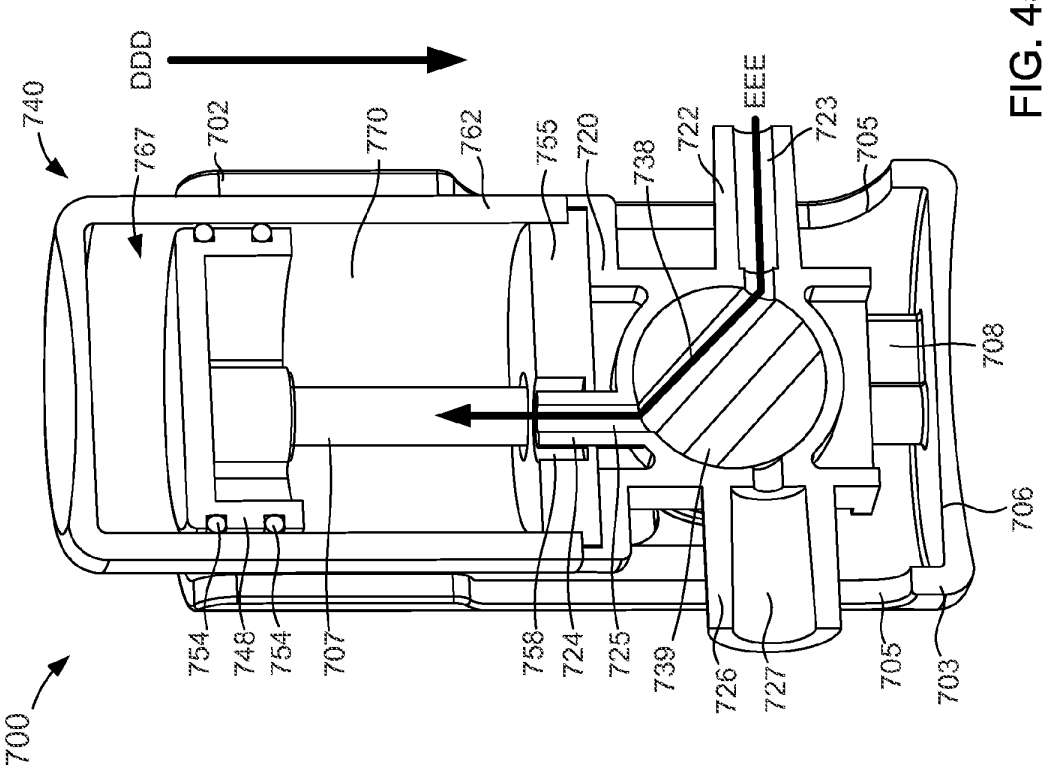

740
DDD
767
702
770
762
755
720
738
722
EEE
723
705
708
706
754
748
754
707
758
724
725
739
726
727
705
703
700

FIG. 45

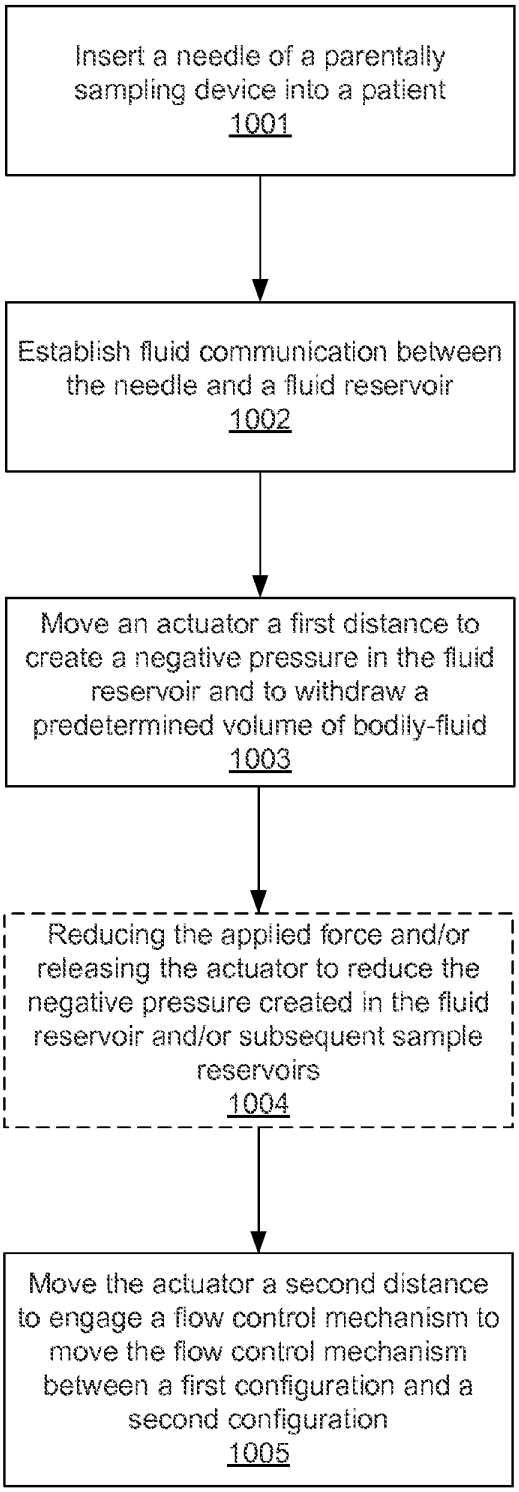

Insert a needle of a parentally sampling device into a patient
1001
Establish fluid communication between the needle and a fluid reservoir
1002
Move an actuator a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid
1003
Reducing the applied force and/or releasing the actuator to reduce the negative pressure created in the fluid reservoir and/or subsequent sample reservoirs
1004
Move the actuator a second distance to engage a flow control mechanism to move the flow control mechanism between a first configuration and a second configuration
1005

FIG. 47

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US13/43289

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B5/15; B01D43/00; B01L3/14; C12M1/00; C12N5/02; G01N33/49 (2013.01)
USPC - 210/516, 789; 422/918, 533; 600/573, 576, 579; 604/30, 33, 248
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): A61B5/15; B01D43/00; B01L3/14; C12M1/00; C12N5/02; G01N33/49 (2013.01)
USPC: 210/516, 789; 422/918, 533; 600/573, 576, 579; 604/30, 33, 248

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Public Patent Application Information Retrieval (PAIR); Google/Google Scholar; DialogPro; Pubmed/Medline: negative pressure, vacuum, contamination, sterile, low valve, rotating, actuator, inlet, outlet, reservoir, housing, body fluid, blood, semen, urine, sample, collection, specimen, assay, medical, diversion

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4425235 A (CORNELL, WD et al.) January 10, 1984; figures 1-4; column 2, lines 56-67; column 3, lines 1-11, 18-36; column 4, lines 26-67; column 5, lines 1-13, 25-57	1-5, 14-19, 25-34
Y	US 2012/0095367 A1 (PATTON, RG) April 19, 2012; paragraphs [0041]-[0044]; claims 33, 38-41	1-5, 14-19, 25-34
Y	US 2008/0108954 A1 (MATHIAS, JM et al.) May 8, 2008; figures 6a-b; paragraph [0064]	16, 19, 29
E, X	US 2013/0116599 A1 (BULLINGTON, GJ et al.) May 9, 2013; figures 2-3; paragraphs [0037], [0068]-[0069]	1, 14, 25, 30

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

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

Date of the actual completion of the international search	Date of mailing of the international search report
16 October 2013 (16.10.2013)	24 OCT 2013
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US13/43289

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

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

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

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

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

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

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

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

Group I: Claims 1-5, 14-19 and 25-34 are directed toward a device and method for procuring bodily-fluid samples from a patient comprising an outlet port configured to be fluidically coupled to a sample reservoir; the fluid reservoir disposed in the inner volume and configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient.

Group II: Claims 6-13 are directed toward a device for procuring bodily-fluid samples from a patient, the device comprising: a diverter.

Group III: Claims 20-24 are directed toward device for procuring bodily-fluid samples from a patient, the device comprising: a seal member.

-***-Continued Within the Next Supplemental Box-***-

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

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

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

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-5, 14-19 and 25-34

Remark on Protest

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

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

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US13/43289

-***-Continued from Box No. III: Observations where unity of invention is lacking-***-

Group IV: Claims 35-39 are directed toward a method for procuring bodily-fluid samples using a parenteral sampling device, the device including a needle having a lumen configured for insertion into the patient, and a fluid reservoir fluidically coupleable to the needle, the method comprising: a first and second activation force.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I include an outlet port configured to be fluidically coupled to a sample reservoir; a fluid reservoir disposed in the inner volume and configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient; moving an actuator a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid; moving the actuator a second distance to engage a flow control mechanism and rotate the flow control mechanism from a first configuration to a second configuration, the first configuration operable to allow bodily-fluid to flow through a first flow path from the needle to the fluid reservoir, the second configuration operable to allow bodily-fluid to flow through a second flow path from the needle to a sample reservoir, which are not present in Groups II-IV; the special technical features of Group II include a diverter disposed in the housing, the diverter having an inlet port configured to be fluidically coupled to the patient, a first outlet port configured to be fluidically coupleable to the fluid reservoir, and a second outlet port configured to be fluidically coupled to a sample reservoir, which are not present in Groups I and III-IV; the special technical features of Group III include a seal member movably disposed in the inner volume; a fluid reservoir disposed in the inner volume and at least partially defined by the seal member, the fluid reservoir configured to receive and isolate a first volume of bodily-fluid withdrawn from the patient, which are not present in Groups I-II and IV; the special technical features of Group IV include applying a first activation force to an actuator; reducing the first activation force applied to the actuator to reduce the negative pressure created in the fluid reservoir; and applying a second activation force to the actuator, which are not present in Groups I-III.

The common technical features of Groups I-III are a housing including a proximal end portion and a distal end portion and defining an inner volume therebetween, the housing having an inlet port configured to be fluidically coupled to the patient; the actuator configured to create a negative pressure in the fluid reservoir when actuated by a user; a flow control mechanism movably disposed in the housing, the flow control mechanism configured to move between a first configuration, in which the bodily-fluid can flow from the inlet port, through the flow control mechanism and to the fluid reservoir, and a second configuration, in which the fluid reservoir is fluidically isolated from the inlet port; create a negative pressure in the fluid reservoir, the actuator further configured to move the flow control mechanism from the first configuration to the second configuration after a first volume of bodily-fluid is received in the fluid reservoir from the patient.

The common technical features of Groups I and II further include an actuator movably disposed in the housing.

These common technical features are disclosed by the Cornell reference. Cornell discloses an actuator movably disposed in the housing (chamber 14 is a fluid reservoir configured to receive whole blood; figures 1-4; column 4, lines 26-37).

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups I and II lack unity.

The common technical features of Groups I and III further include an actuator operably coupled to the flow control mechanism.

These common technical features are disclosed by the Cornell reference. Cornell discloses an actuator operably coupled to the flow control mechanism (chamber 14 is a fluid reservoir configured to receive whole blood; figures 1-4; column 4, lines 26-37).

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups I and III lack unity.

The common technical features of Groups I and IV further include inserting the needle of the device into the patient; establishing fluid communication between the needle and the fluid reservoir.

These common technical features are disclosed by the Cornell reference. Cornell discloses inserting the needle of the device into the patient (distal end of cannula is inserted into vein of patient; column 4, lines 26-37); establishing fluid communication between the needle and the fluid reservoir (whole blood flows into container; column 4, lines 26-37).

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups I and IV lack unity.

The common technical features of Groups II and III further include a sealing member and a fluid reservoir defined at least in part by the sealing member.

These common technical features are disclosed by the Cornell reference. Cornell discloses a sealing member and a fluid reservoir defined at least in part by the sealing member (stopper 20 serves as a seal and is pierceable by a cannula which can be coupled to a patient; column 3, lines 1-11),

Since the common technical features are previously disclosed by the Cornell reference, the common features are not special and so Groups II and III lack unity.

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :		(11) International Publication Number:	WO 92/16144
A61B 5/14	A1	(43) International Publication Date:	1 October 1992 (01.10.92)

(21) International Application Number: PCT/AU92/00105

(22) International Filing Date: 10 March 1992 (10.03.92)

(30) Priority data:
PK 5140 15 March 1991 (15.03.91) AU

(71) Applicant *(for all designated States except US)*: GOLDSPILL PTY. LTD. [AU/AU]; 8 Eagle Street, Alderley, QLD 4051 (AU).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)* : ROBB, Darryl, Gordon [AU/AU]; 10 Chapple Lane, Gympie, QLD 4570 (AU).

(74) Agent: F.B. Rice & Co.; 28A Montague Street, Balmain, NSW 2041 (AU).

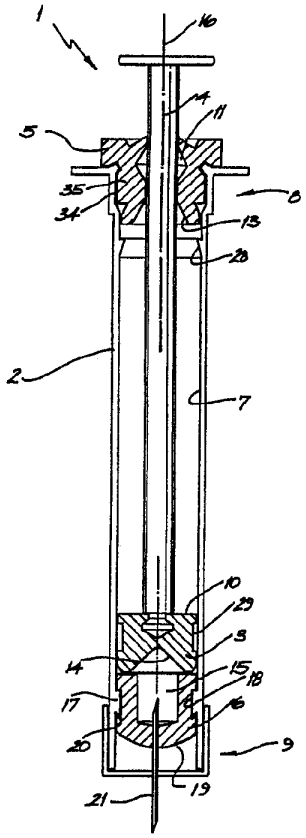
(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European patent), NO, PL, RO, RU, SD, SE, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent), US.

Published
With international search report.

(54) Title: BODY FLUID EXTRACTION DEVICE

(57) Abstract

A device (1) for extracting body fluid in which depression of a plunger (4) into a tubular body (2) during a preparatory stroke creates a pressure reduction in a first chamber (12). After the preparatory stroke, the pressure reduction in the first chamber (12) exerts a force on a piston (3) to cause it to move and thereby to draw body fluid into a second chamber (15). The rate of extraction of the body fluid is governed by a frictional force on the plunger (4) which can be controlled by a cam arrangement (5).



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	**FI**	Finland	**ML**	Mali
AU	Australia	**FR**	France	**MN**	Mongolia
BB	Barbados	**GA**	Gabon	**MR**	Mauritania
BE	Belgium	**GB**	United Kingdom	**MW**	Malawi
BF	Burkina Faso	**GN**	Guinea	**NL**	Netherlands
BG	Bulgaria	**GR**	Greece	**NO**	Norway
BJ	Benin	**HU**	Hungary	**PL**	Poland
BR	Brazil	**IE**	Ireland	**RO**	Romania
CA	Canada	**IT**	Italy	**RU**	Russian Federation
CF	Central African Republic	**JP**	Japan	**SD**	Sudan
CG	Congo	**KP**	Democratic People's Republic of Korea	**SE**	Sweden
CH	Switzerland			**SN**	Senegal
CI	Côte d'Ivoire	**KR**	Republic of Korea	**SU**	Soviet Union
CM	Cameroon	**LI**	Liechtenstein	**TD**	Chad
CS	Czechoslovakia	**LK**	Sri Lanka	**TG**	Togo
DE	Germany	**LU**	Luxembourg	**US**	United States of America
DK	Denmark	**MC**	Monaco		
ES	Spain	**MG**	Madagascar		

BODY FLUID EXTRACTION DEVICE

Field of the Invention

The present invention relates to devices for extracting body fluid, and more particularly to a device for extracting body fluid in which a pressure reduction is created by depression of a piston into a tubular body, and the pressure reduction so created is used to draw fluid into the tubular body.

Background

A conventional apparatus for extracting a body fluid, such as blood from a patient, usually comprises a cannula and an evacuated vial which is sealed with a rubber-like membrane. It is common practice to extract the body fluid by inserting a first end of the cannula into a part of the patient's body which contains the body fluid, followed by piercing the rubber-like membrane with a second end of the cannula. Body fluid is then drawn through the cannula into the evacuated vial.

A first disadvantage of the conventional apparatus for body fluid extraction is that the rate of flow of body fluid into the evacuated vial cannot be accurately and easily controlled, but depends on such parameters as the diameter of the cannula and the pressure inside the evacuated tube. In the case of blood extraction, it is desirable to control the rate of extraction, especially from weak patients, to avoid causing the patient's blood vessels to collapse.

A second disadvantage of the conventional apparatus for body fluid extraction is that it is potentially hazardous. In order that they may have sufficient strength to sustain a required low internal pressure, the evacuated vials are usually constructed from glass. However, this presents a potential hazard because glass vials can be shattered easily to expose sharp edges which can cut workers or technicians. This can be especially

dangerous when the vials contain hazardous substances such as blood infected with viruses.

A third disadvantage of the conventional apparatus for body fluid extraction is that it requires the maintenance of a stock of evacuated vials. Over time, the low pressures in such vials may degrade such that the vials may not be effective in receiving body fluid.

A fourth disadvantage of the conventional apparatus for body fluid extraction is that the evacuated vial cannot be pre-filled easily and accurately to predetermined levels with such fluids as anticoagulants or agents for separating red and white blood cells.

A fifth disadvantage of the conventional apparatus for body fluid extraction is that, once the body fluid is extracted, withdrawal of a sample of the body fluid from the evacuated vial for analysis can be difficult or dangerous. To withdraw a sample from the conventional apparatus, one end of the evacuated vial is usually removed, and the sample is sucked into a pipette. This can lead to spread of disease.

Summary of the Invention

In preferred embodiments the present invention overcomes at least some of the above deficiencies of conventional body fluid extraction devices.

According to one broad form of the invention, there is provided a device for extracting body fluid having a syringe-type construction. The device includes a tubular body having a proximal end, a distal end, and a bore.

A piston is disposed within the bore. The piston has a proximal face, a distal face, and an outer face which is in slidable contact with the bore.

A plunger, which has a shank, is mounted slidably at the proximal end of the tubular body and removably attached to the proximal face of the piston for pushing the piston from the proximal end of the tubular body

towards the distal end of the tubular body during a preparatory stroke in which external pressure is applied to the plunger.

A sealing means is used to seal the shank slidably to the proximal end of the tubular body so as to form a first chamber defined by the bore, the shaft, the proximal face of the piston and the distal face of the sealing means. A pressure reduction is formed in the first chamber during the preparatory stroke of the plunger.

Closure means are provided to close the distal end of the tubular body so as to form a second chamber defined by the bore, the distal face of the piston and the closure means. The closure means is adapted to cooperate with filling means which places the body fluid in communication with the second chamber.

After the preparatory stroke when external pressure is removed from the plunger, the pressure reduction in the first chamber causes the piston to move towards the proximal end of the tubular body and to draw the body fluid into the second chamber.

The rate of extraction of body fluid is preferably made controllable by providing a cam arrangement in which rotation of the sealing means causes a variation of a frictional force on the plunger. Non-circular cross sections are preferably provided on a lip at the proximal end of the tubular body and to a groove around an outer surface of the sealing means which engages with the lip. The sealing means can be rotated within the lip about an axis of rotation. The sealing means is constructed from a compressible elastic material such that, during rotation, its motion relative to the lip, combined with the non-circular cross sections, causes a variation in an internal pressure in the compressible elastic material. The magnitude of the internal pressure is determined by an angle of rotation of the sealing means relative to the

lip. The shaft of the plunger passes through a hole in the sealing means so that the internal pressure is communicated as a controllable pressure of the sealing means on the shaft. This results in a controllable frictional force between the sealing means and the shaft, and this retards the rate of movement of the plunger, the rate of movement of the piston, and the rate of body fluid extraction.

In a preferred embodiment of the invention a bung is situated within the bore between the piston and the distal end of the tubular body and constitutes the closure means. The bung has an outer wall which is in slidable contact with the bore, so as to form the second chamber defined by the bore, the distal face of the piston, and the bung. At the end of the preparatory stroke, an arresting means retains the bung at the distal end of the tubular body.

In the abovementioned preferred embodiment, the arresting means which retains the bung at the distal end of the tubular body preferably comprises a circumferential rib around the bore and a circumferential groove around the outer wall of the bung. The bung is constructed from an elastic material and has a distal surface with a generally convex shape so that, during the preparatory stroke, the distal surface passes the circumferential rib. At the end of the preparatory stroke, the circumferential rib is substantially aligned with the circumferential groove. The circumferential rib has a cross section with an acute edge proximate the distal end of the tubular body. The acute edge engages with the circumferential groove so as to impede the movement of the bung towards the proximal end of the tubular body, and thus acts to retain the bung at the distal end of the tubular body.

In this way, a body fluid extraction device is

provided in which the rate of body fluid extraction can be controlled easily and accurately. In addition, the body fluid extraction device can be constructed from a plastic-like material so that hazards due to shattering of evacuated vials are eliminated. Further, the pressure reduction in the first chamber need only be created immediately before the device is to be used; thus avoiding the problems due to loss of low pressure in the evacuated vial. The device can be pre-filled easily and accurately to predetermined levels with fluids such as anticoagulant agents. Finally, samples containing precise amounts of body fluid can be withdrawn from the body fluid extraction device because a cannula can be fitted to the distal end of the tubular body, and the fluid can be expelled from the device in the same way that fluids can be expelled from a hypodermic syringe.

Brief Description of the Drawings

The invention will now be further described with reference to the accompanying drawings in which:

Fig. 1 is a longitudinal section of a body fluid extraction device in accordance with a preferred embodiment of the invention in which the device is shown before use;

Fig. 2 is a longitudinal section of the body fluid extraction device of Fig. 1 in which the device is shown at the end of a preparatory stroke;

Fig. 3 is a longitudinal section of the body fluid extraction device of Fig. 1 in which the device is shown after body fluid has been extracted;

Fig. 4 is an end view of a sealing means adapted to fit into a proximal end of the body fluid extraction device of Fig. 1, viewed from the proximal end of the device;

Fig. 5 is an end view of the body fluid extraction device of Fig. 1, viewed from the proximal end of the

device;

Fig. 6 is a longitudinal sectional view of a needle like device which can be utilised in the withdrawal of body fluid from the body fluid extraction device; and

Fig. 7 is a longitudinal section of a body fluid extraction device according to a second embodiment of the invention in which the device is shown before use.

Detailed Description of the Preferred Embodiment

Figs. 1 to 3 show an illustrative embodiment of the body fluid extraction device 1 which comprises syringe-like tubular body 2, piston 3, plunger 4, sealing means 5, and bung 6. Bore 7 is situated inside tubular body 2 and extends from proximal end 8 to distal end 9. Bore 7, piston 3, plunger 4, and bung 6 all have longitudinal axes which are substantially coincident.

Piston 3 is disposed within tubular body 2 in slidable contact with bore 7 and is shaped so as to form a substantially air-tight seal against bore 7.

Plunger 4 is removably attached to proximal face 10 of piston 3 and extends out of proximal end 8 of tubular body 2 through hole 11 in sealing means 5.

Sealing means 5 forms substantially air-tight seals against bore 7 and plunger 4. In addition circular lip 23 surrounding the proximal end of body 2 is sealingly engaged by groove 22 in sealing means 5. Plunger 4 can slide through hole 11 while retaining a substantially air-tight seal with sealing means 5.

First chamber 12 is defined by proximal face 10 of piston 3, bore 7, plunger 4, and face 13 of sealing means 5. The position of piston 3 relative to proximal end 8 defines a volume of first chamber 12.

Bung 6 is disposed within tubular body 2 in slidable contact with bore 7 between distal face 14 of piston 3 and distal end 9 of tubular body 2. Bung 6 is shaped so as to form a substantially air-tight seal against bore 7.

Distal face 14 of piston 3, tubular body 2, and bung 6 define second chamber 15 in which body fluid is to be collected and temporarily stored and into which anti-coagulants and other reagents may be pre-filled.

Fig. 1 shows body fluid extraction device 1 in a state before use. In this state, proximal face 10 of piston 3 is close to sealing means 5 so that the volume of first chamber 12 is small.

Body fluid extraction device 1 is prepared for use by a preparatory stroke in which external pressure is applied to plunger 4 along longitudinal axis 16 of tubular body 2 to cause plunger 4, piston 3, and bung 6 to move away from proximal end 8 toward distal end 9.

During the preparatory stroke, the movement of piston 3 causes the volume of first chamber 12 to increase. Because sealing means 5 forms substantially air-tight seals with tubular body 2 and plunger 4, substantially no air enters first chamber 12, and so the increase of the volume of that chamber causes a pressure decrease there.

At, or close to, the end of the preparatory stroke, plunger 4, piston 3, and bung 6 reach the position shown in Fig. 2. At this position, an arresting means impedes the movement of bung 6 so that it cannot move freely back toward proximal end 8.

Preferably, the arresting means comprises circumferential rib 17 around bore 7 and circumferential groove 18 around the outer wall of bung 6. Bung 6 is constructed from an elastic material and has a distal surface 19 with a generally convex shape so that, during the preparatory stroke, distal surface 19 passes circumferential rib 17. At the end of the preparatory stroke, circumferential rib 17 is substantially aligned with circumferential groove 18. Circumferential rib 17 has a cross section with an acute edge 20 proximate distal

end 9 of tubular body 2. Acute edge 20 engages with circumferential groove 18 so as to impede the movement of bung 6 back towards proximal end 8 of tubular body 2, and thus acts to retain bung 6 at distal end 9.

With the device in the state illustrated in Fig. 2, a filling means allows body fluid such as blood to be brought into fluid contact with second chamber 15. Preferably, the filling means comprises cannula 21 as shown in Figs. 2 and 3. When distal end 9 is brought into contact with cannula 21, bung 6 is pierced; thus preparing a path for body fluid to flow into second chamber 15.

After the preparatory stroke, external pressure is removed from plunger 4. The pressure reduction in first chamber 12 exerts an attractive force on proximal face 10 of piston 3 to cause it to move toward proximal end 8 and away from distal end 9. This movement of piston 3, together with the arrested position of bung 6, creates a pressure reduction in second chamber 15 which causes body fluid to be drawn into that chamber.

As second chamber 15 fills with body fluid, piston 3 and plunger 4 move away from distal end 9 toward proximal end 8. When piston 3 reaches a position sufficiently close to proximal end 8, the body fluid extraction ceases. At this point, the cannula 21 may be removed, and plunger 4 may be removed from piston 3. In this way, second chamber 15 forms a substantially sealed container for holding body fluid.

The rate of extraction of body fluid can be controlled, for example, by governing the rate at which plunger 4 (and hence piston 3) are allowed to move back towards proximal end 8. In the preferred embodiment, this rate is governed by a cam arrangement which can be used to adjust a frictional force exerted on plunger 4 by sealing means 5.

As illustrated in Figs. 4 and 5, such a frictional

force can be rendered adjustable by providing on sealing means 5 a body portion 35 having a non-circular outer cross section, and a similar non-circular inner cross section to a portion 34 of the tubular body 2 proximal end 8 of tubular body 2. Body portion 35 has a large dimension 24 and a small dimension 25. Similarly, portion 34 of the tubular body has a large dimension 26 and a small dimension 30.

Sealing means 5 is constructed from a compressible elastic material such that any attempt to deform its outer surface results in a variation of an internal pressure within the compressible elastic material. Plunger 4 passes through hole 11 in sealing means 5 so that the internal pressure is communicated as a pressure of sealing means 5 on plunger 4. This results in a frictional force between sealing means 5 and plunger 4 which retards its rate of movement.

Sealing means 5 can be rotated within portion 34 of the tubular body 2 about longitudinal axis 16. When sealing means 5 is rotated relative to portion 34 of tubular body 2 such that large dimensions 26 and 24 are substantially collinear. The internal pressure in sealing means 5 is a minimum. However, when sealing means 5 is rotated relative to portion 34 of tubular body 2 such that large dimension 26 is substantially collinear with small dimension 30, the internal pressure in sealing means 5 is a maximum.

Thus, by varying an angle of rotation of sealing means 5 relative to tubular body 2, a user of the device can control the amount of pressure exerted by sealing means 5 on plunger 4. This results in a controllable frictional force between sealing means 5 and plunger 4 which controllably retards the rate of movement of plunger 4, the rate of movement of piston 3, and the rate of body fluid extraction.

After body fluid extraction device 1 is filled, as illustrated in Fig. 3, cannula 21 and plunger 4 can be removed to form a substantially sealed container in which body fluid can be stored.

Samples of body fluid can be withdrawn from body fluid collection device 1 using several methods. A first method comprises the steps of inserting a needle, cannula or similar device through bung 6 into second chamber 15 containing the body fluid, attaching a plunger to proximal face 10 of piston 3, and applying external pressure along longitudinal axis 16 so as to move piston 3 towards distal end 9 and to expel body fluid through the cannula. Circumferential rib 17 around bore 7 is provided with acute edge 20 to engage with circumferential groove 18 around the outer surface of bung 6 to ensure that the insertion of a cannula or the like through bung 6 does not cause the bung to move into bore 7 toward proximal end 8, but instead causes acute edge 20 to further engage with circumferential groove 18. Preferably, acute angle 20 is thirty degrees.

Fig 6 shows a preferred form of a needle-like device 27 for insertion through bung 6 to allow withdrawal of body fluid from second chamber 15. Device 27 is circular in cross-section and has a bore 28 extending axially through it. A first end portion 29 of device 27 is of narrow external diameter and is sharpened to point 31. Second end portion 32 is frustoconical in shape. An annular ridge 33 is formed between first and second end portions 29 and 32. In use first end portion is pushed through bung 6. The body fluid in second chamber 15 may be expressed through bore 28 by depressing plunger 4 and thus piston 13. This form of device has the advantage that after communication has been established with the contents of the second chamber 15 there are no sharp edges projecting from device 1 on which a user could be cut.

A second method of withdrawing a sample of body fluid from body fluid extraction device 1, for which method piston 3 is constructed from a penetrable material, comprises the steps of inserting a cannula attached to a suitable sampling device such as a hypodermic syringe through hole 11 in sealing means 5 and through piston 3 into second chamber 15, and to withdraw body fluid into the sampling device. Circumferential ledge 28 around bore 7 engages with circumferential slot 29 around the outer surface of piston 3 to ensure that the insertion of the cannula through piston 3 does not cause that piston to move into bore 7 toward distal end 9.

Before use, body fluid extraction device 1 can be operated as a hypodermic syringe to pre-fill tubular body 2 with fluids such as anticoagulants or agents for separating red and white blood cells.

Fig. 7 shows a fluid or blood extracting device quite similar to that of the device shown in Fig. 1 but includes a plug 114 which is screwed, by screw thread 116, into sealing engagement with end 93 of body 91 at the tapered matching surfaces 115. Plug 114 also provides an air seal about plunger 96 at cylindrical region 114.

Plug 114 frictionally grips plunger 96 at cylindrical portion 117, the frictional grip being adjustable by way of adjusting the screw pressure applied to plug 114. Tight screw pressure applied to plug 114 results in tapered surfaces 115 radially compressing the volume of plug 114 that surrounds portion 117, thus increasing the frictional grip between plug 114 and plunger 96. By reducing the screw force applied to plug 114, but not so much as to violate the seal at surfaces 115, the radial pressure applied to surface portion 117 is reduced and the frictional grip reduced.

In the arrangement of Fig. 7 engagement portion 98 of plunger 96 comprises a cylindrical boss separated from the

remainder of plunger 96 by a groove. Engagement portion 98 is resiliently gripped by piston head 95 which is made of rubber or some similar elastomeric material.

Immediately before use the device is in the configuration as illustrated in Fig. 7. Cap 112 is removed and a suitable cannular inserted into sleeve 111. Piston head 95 is then pressed fully down to end 94, by applying pressure to handle 97. By virtue of the seal applied by plug 114 at surface area 118 with plunger 96 and at surfaces 115 with body 91, a substantially evacuated volume is formed between piston head 95 and plug 114.

With piston head 95 fully depressed to end 94, the cannular is inserted into the appropriate vessel and by releasing the pressure applied to handle 97, the evacuated volume behind piston head 95 will retract piston head 5 back toward end 93 and thus allow the collection of the blood sample within the device. The speed of retraction of piston head 95 can be adjusted by adjusting the screw tensioning of plug 114. Thus the device will provide a smooth rate of retraction of piston head 95 at an adjustable speed.

Plug 114 will serve to prevent the complete removal of piston head 95, after removal of the cannular the cap 112 is replaced over sleeve 111, and the sample of blood or other fluid, is now ready for safe and convenient transportation or storage.

CLAIMS:-

1. A device for extracting body fluid comprising:
a tubular body having a proximal end, a distal end, and a bore;

a piston disposed within the bore, the piston having a proximal face, a distal face, and an outer face, the outer face being in slidable contact with the bore;

a plunger mounted slidably at the proximal end of the tubular body and removably attached to the proximal face of the piston for pushing the piston from the proximal end of the tubular body towards the distal end of the tubular body during a preparatory stroke in which an external pressure is applied to the plunger, the plunger having a shank;

sealing means for slidably sealing the proximal end of the tubular body to the shank of the plunger so as to form a first chamber defined by the bore, the shaft, the sealing means, and the proximal face of the piston, so that a pressure reduction is formed in the first chamber during the preparatory stroke of the plunger;

closure means to close the distal end of the tubular body so as to form a second chamber defined by the bore, the distal face of the piston and the closure means;

the closure means is adapted to cooperate with filling means for placing the body fluid in fluid communication with the second chamber so that, after the external pressure is removed from the plunger, the pressure reduction in the first chamber causes the piston to move towards the proximal end of the tubular body and to draw body fluid into the second chamber.

2. A device for extracting body fluid as claimed in claim 1 in which the closure means comprises

a bung situated within the bore between the piston and the distal end of the tubular body, the bung having an outer wall in slidable contact with the bore, so as to

form the second chamber defined by the bore, the distal face of the piston, and the bung and in which arresting means are provided for retaining the bung at the distal end of the tubular body after the preparatory stroke;

3. A device for extracting body fluid as claimed in claim 1 or claim 2 wherein the sealing means is constructed from a compressible elastic material, the shaft of the plunger passes through a hole in the sealing means, and the device for extracting body fluid includes a cam arrangement which comprises:

a first cam means for creating a controllable deformation of the sealing means; and

a second cam means for cooperating with the first cam means to create the controllable deformation of the sealing means, the second cam means being rotatably engaged with the first cam means such that relative rotation of the second cam means with respect to the first cam means causes the controllable deformation of the sealing means and a corresponding controllable internal pressure in the compressible elastic material, thereby creating a controllable frictional force to be applied to the shaft of the plunger to enable the body fluid to be extracted at a controllable rate.

4. A device for extracting body fluid as claimed in claim 3 in which the first cam means has a non-circular inner cross section and the second cam means has a non-circular outer cross section.

5. A device for extracting body fluid as claimed in claim 4 wherein the first cam means comprises a lip at the proximal end of the tubular body.

6. A device for extracting body fluid as recited in claim 4 wherein the second cam means comprises a groove around an outer surface of the sealing means.

7. A device for extracting body fluid as recited in claim 2 wherein the bung is constructed from an elastic

material and has a distal surface with a generally convex shape and the arresting means comprises:

a circumferential rib around the bore proximate the distal end of the tubular body; and

a circumferential groove around the outer wall of bung so that, at the end of the preparatory stroke, the circumferential rib is substantially aligned with the circumferential groove so as to impede a movement of the bung towards the proximal end of the tubular body.

8. A device for extracting body fluid as claimed in claim 5 wherein the circumferential rib has an acute edge proximate the distal end of the tubular body.

9. A device for extracting body fluid as claimed in claim 1 wherein the device includes filling means comprising a needle, cannula or similar device which is removably attached to the distal end of the tubular body.

10. A device for extracting body fluid as claimed in claim 1 wherein the piston is constructed from a penetrable material and samples of body fluid may be withdrawn by inserting a cannula through the piston.

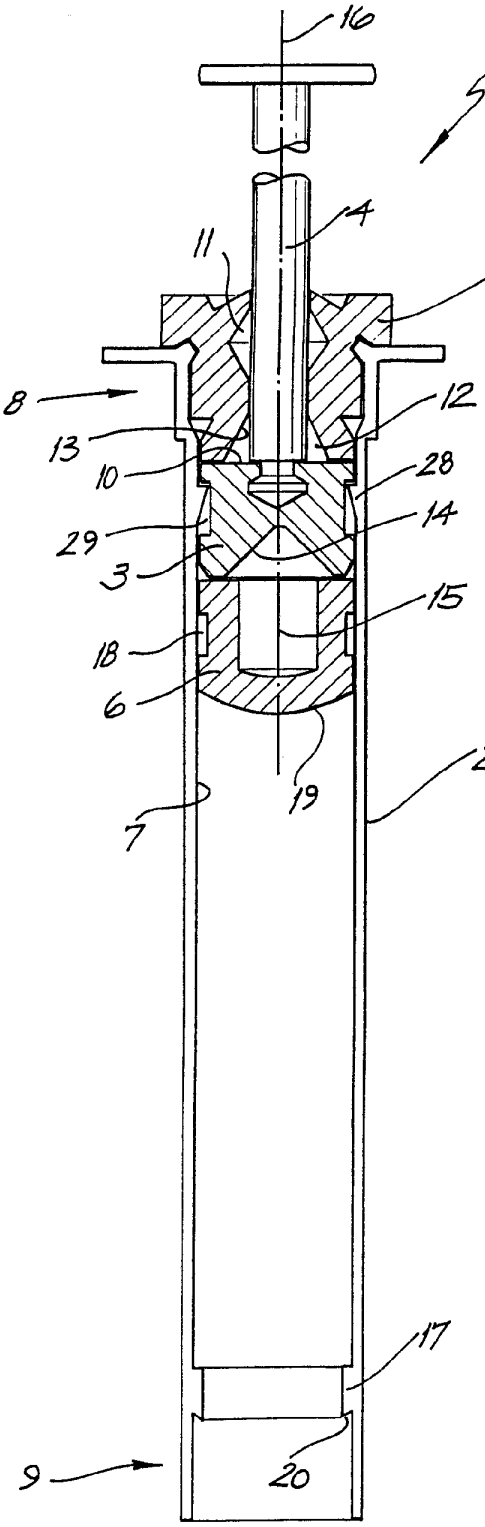

16
1
4
11
5
8
12
13
10
28
29
14
3
15
18
6
19
2
7
17
9
20

FIG. 1

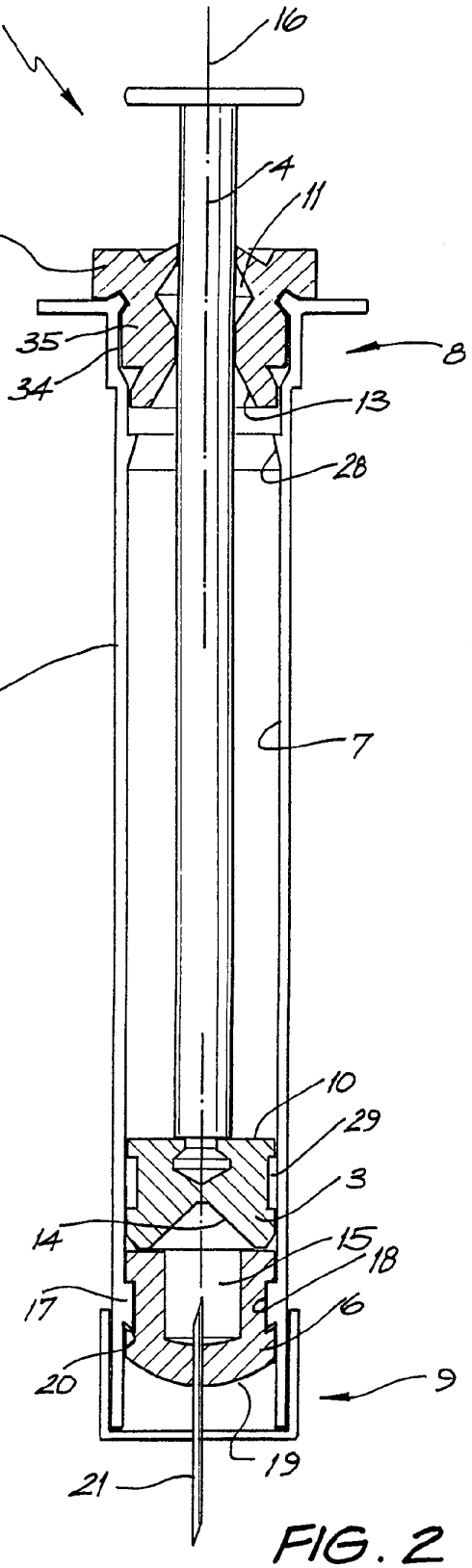

16
4
11
35
34
8
13
28
2
7
10
29
3
14
15
18
17
16
20
9
19
21

FIG. 2

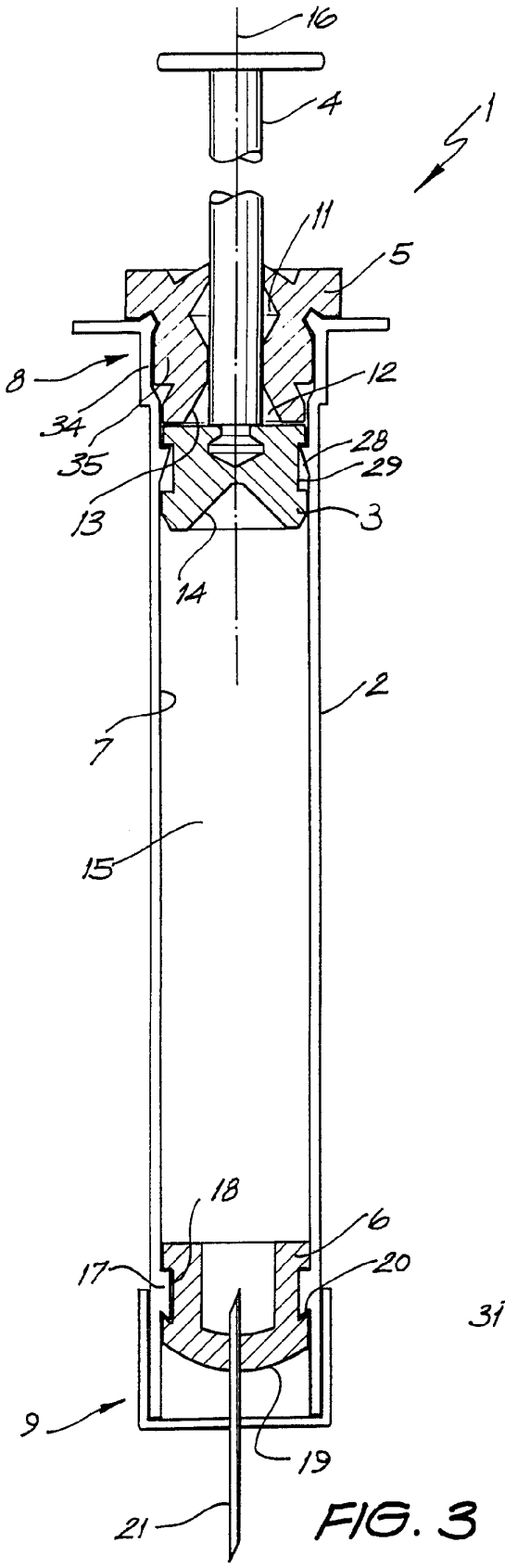


FIG. 3

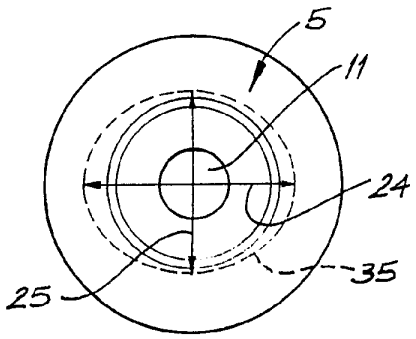


FIG. 4

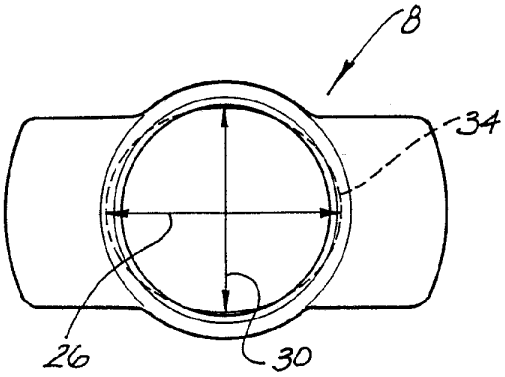


FIG. 5

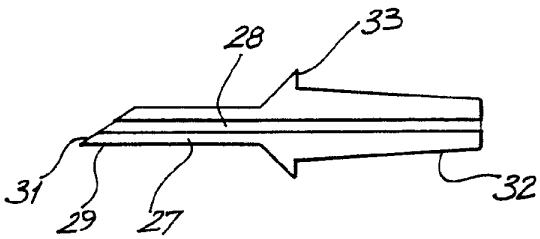


FIG. 6

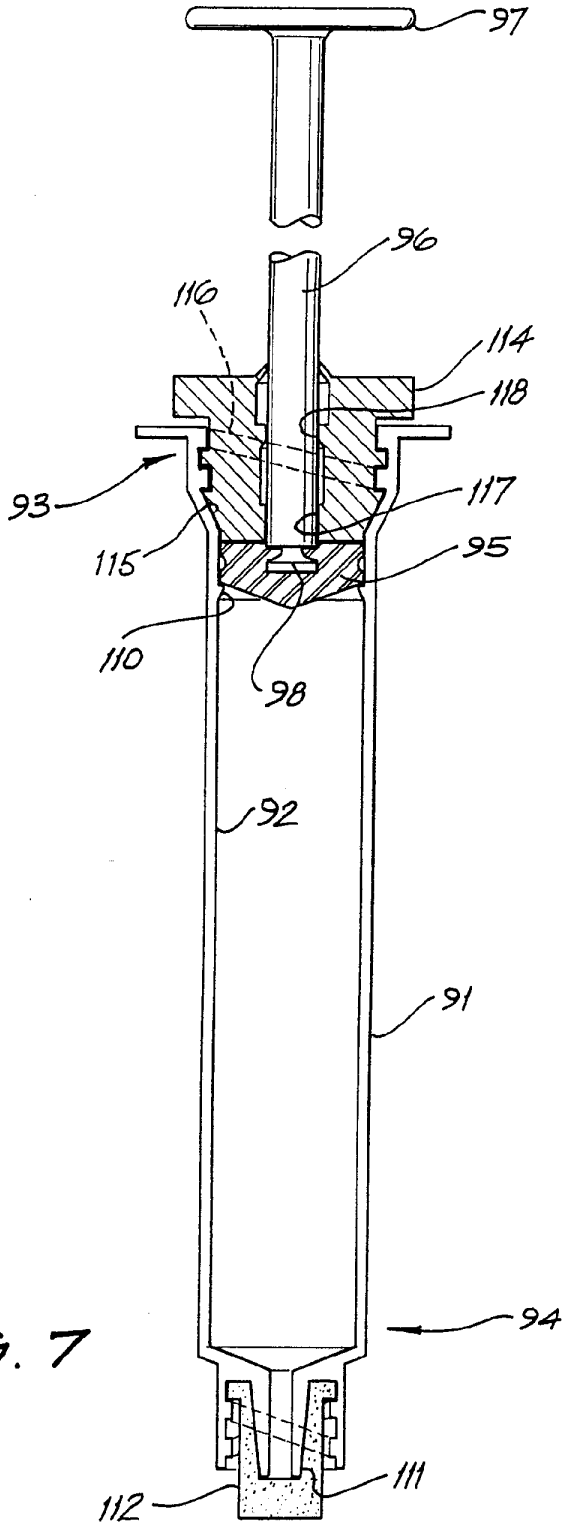


FIG. 7

INTERNATIONAL SEARCH REPORT

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent classification (IPC) or to both National Classification and IPC
Int. Cl.[5] A61B 5/14

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC	A61B 5/14

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

AU:IPC as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category*	Citation of Document, [11] with indication, where appropriate of the relevant passages [12]	Relevant to Claim No [13]
X,Y	EP,A,0279956 (VAN-TEC INCORPORATED) 31 August 1988 (31.08.88) See whole document, particularly claim 1.	(1,9-10)
Y	US,A,4361155 (ANASTASIO) 30 November 1982 (30.11.82) See column 3, lines 40-45.	(9)
Y	US,A,3930492 (HATSUNO et al) 6 January 1976 (06.01.76) See column 2.	(9-10)
A	US,A,4041934 (GENESE) 16 August 1977 (16.08.77)	

(continued)

* Special categories of cited documents : [10]

"A" Document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" doocument whioh 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 t the international filing date but later than the priority date claimed

"T" Later document published after the international filing date or priority date and not in oonflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step
"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

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
22 May 1992 (22.05.92)	2 June 1992 (02.06.92)
International Searching Authority	**Signature of Authorized Officer**
AUSTRALIAN PATENT OFFICE	A HENDRICKSON

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

A	US,A,4215702 (AYER) 5 August 1980 (05.08.80)	A US,A,4215702
A	US,A,4257426 (BAILEY) 24 March 1981 (24.03.81)	
A	GB,A,2218076 (BATES) 8 November 1989 (08.11,89)	

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

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

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

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

3. ☐ Claim numbers ..., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4a

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

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

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. ☐ No required additional search fees were timely paid by the applicant. Consaquently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL APPLICATION NO. PCT/AU 92/00105

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report	Patent Family Member	
US 4361155		
EP 279956	JP 63246145	US 4766908
US 3930492		

END OF ANNEX

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference KURIN7PCT		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US20/26276	International filing date *(day/month/year)* 01 April 2020 (01.04.2020)	(Earliest) Priority Date *(day/month/year)* 01 April 2019 (01.04.2019)
Applicant Bobby E. Rogers		

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

This international search report consists of a total of 2 sheets.

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

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

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

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

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

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

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 1A

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

Pending processing

Form PCT/ISA/210 (first sheet) (July 2019)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US20/26276

A. CLASSIFICATION OF SUBJECT MATTER

IPC - G01N 1/10, 1/02; A61B 5/15 (2020.01)

CPC - G01N 1/10, 1/02; B01L 3/0203

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2018/0271425 A1 (KURIN, INC.) 27 September 2018; abstract; figures 24A-24D; paragraphs [0066], [0096], [0144]-[0148]	1-10, 14-18 -- 11-13, 19-20
Y	GB 1 3786 02 A (AYERS, WA) 02 May 1974; page 5, lines 34-95; figures 4, 6	11-12, 19-20
Y	US 2014/0112841 A1 (SCHOEN, C) 24 April 2014; abstract; paragraph [0035]	13
A	WO 2019/055487 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 21 March 2019; paragraphs [1071], [1080]; figures 2-5	13
P, X	WO 2019/232196 A1 (MAGNOLIA MEDICAL TECHNOLOGIES, INC.) 05 December 2019; entire document	1, 6, 14

Online processing

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

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

Date of the actual completion of the international search	Date of mailing of the international search report
25 June 2020 (25.06.2020)	16 JUL 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/210 (second sheet) (July 2019)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: James Scott Nolan
P.O. Box 371710
San Diego, California 92110
United States of America

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	16 JUL 2020

Applicant's or agent's file reference	FOR FURTHER ACTION
KURIN7PCT	See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US20/26276	01 April 2020 (01.04.2020)	01 April 2019 (01.04.2019)

International Patent Classification (IPC) or both national classification and IPC
IPC - G01N 1/10, 1/02; A61B 5/15 (2020.01)
CPC - G01N 1/10, 1/02; B01L 3/0203

Applicant
Bobby E. Rogers

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

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

2. **FURTHER ACTION**

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

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

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

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	25 June 2020 (25.06.2020)	Shane Thomas PCT Help Desk Telephone No. 571-272-4300

Form PCT/ISA/237 (cover sheet) (revised January 2019)

Undergoing Processing

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US20/26276

Box No. I Basis of this opinion

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

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

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

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

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

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

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

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

b. ☐ furnished together with the international application under PCT Rule 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:

Pending processing

Form PCT/ISA/237 (Box No. I) (revised January 2019)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US20/26276

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

1. Statement

Novelty (N)	Claims	4, 9, 11-13, 18-20	YES
	Claims	1-3, 5-8, 10, 14-17	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-20	NO
Industrial applicability (IA)	Claims	1-20	YES
	Claims	NONE	NO

2. Citations and explanations:

Claims 1-3, 5-8, 10, and 14-17 lack novelty under PCT Article 33(2) as being anticipated by US 2018/0271425 Al to Kurin, Inc. (hereafter 'Kurin')

As per claim 1, Kurin discloses a fluid sample optimization device for optimizing a fluid sample collected by a fluid collection device from a fluid source, a first portion of the fluid sample potentially having contaminants (sample optimization systems that reduce or eliminate contaminates in collected blood samples by including a blood sequestration device; abstract), the fluid sample optimization device comprising: an inlet configured to connect with the fluid source (blood sequestration device 2408 includes an inlet port 2412; figure 24B; paragraph [0146]); an outlet configured to connect with the fluid collection device (blood sequestration device 2408 includes an outlet port 2414; figure 24B; paragraph [0146]); a sample path connected between the inlet and the outlet (a blood sample channel 2422; figure 24C; paragraph [0147]); and a contaminant containment reservoir connected between the inlet and the outlet (blood sequestration chamber 2418; figure 24B; paragraph [0147]), the contaminant containment reservoir having an air permeable fluid resistor proximate the outlet (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]), the contaminant containment reservoir being arranged to receive, when a pressure differential is applied between the inlet and the outlet, a first portion of the fluid sample from the fluid source to displace air therein through the air permeable fluid resistor and the outlet (upon drawing of blood by way of a syringe or Vacutainer (pressure differential is applied) initial aliquot of blood flows into the blood sequestration chamber 2418 displacing air through blood barrier 2420 (air permeable fluid) and the outlet; figures 24B-24C; paragraph [0148]), such that upon receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir, subsequent portions of the fluid sample can be conveyed by the sample path from the inlet to the outlet when subsequent pressure differentials are applied between the inlet and the outlet (the blood in the sequestration chamber 2418 forces the inner chamber housing to the second position allowing one or more apertures 2424 to open to create a pathway from the inlet port 2412 to the blood sampling channel 2422, bypassing and/or flowing around the blood sequestration chamber 2418 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraph [0148]).

As per claim 2, Kurin discloses the fluid sample optimization device in accordance with claim 1, and Kurin further discloses comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the contaminant containment reservoir (blood sequestration device 2408 houses the inlet, the outlet, the sample path, and the contaminant containment reservoir; figures 24B-24D; paragraph [0147]).

As per claim 3, Kurin discloses the fluid sample optimization device in accordance with claim 1, and Kurin further discloses wherein the air permeable fluid resistor (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]) includes a material that seals upon contact with the first portion of the fluid sample (the term "air permeable blood barrier" is formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid; paragraph [0066]).

As per claim5, Kurin discloses the fluid sample optimization device in accordance with claim 1, and Kurin further discloses wherein each pressure differential is provided by a vacuum pressure provided by the fluid collection device (in a blood sample under vacuum pressure or force through the conduit 2006 [2406] from the patient needle 2402 using a syringe or Vacutainer; figure 24B; paragraphs [0144], [0148]).

-***-Continued Within the Next Supplemental Box-***-

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US20/26276

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO 2019/232196 A1	05/12/2019	30/05/2019	31/05/2018

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Pending processing

Form PCT/ISA/237 (Box No. VI) (revised January 2019)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US20/26276

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

-***-Continued from Box V: Citations and Explanations-***-

As per claim 6, Kurin discloses a fluid sample optimization device for optimizing a fluid sample collected by a fluid collection device from a fluid source, a first portion of the fluid sample potentially having contaminants (sample optimization systems that reduce or eliminate contaminates in collected blood samples by including a blood sequestration device; abstract), the fluid sample optimization device comprising: an inlet configured to connect with the fluid source (blood sequestration device 2408 includes an inlet port 2412, for blood sample; figure 24B; paragraph [0146]); an outlet configured to connect with the fluid collection device (blood sequestration device 2408 includes an outlet port 2414 for blood sample; figure 24B; paragraph [0146]); a sample path connected between the inlet and the outlet (a blood sample channel 2422; figure 24C; paragraph [0147]), the sample path further having a resistive plug that is configured to inhibit at least a part of the first portion of the fluid sample and the contaminants from entering the sample path (in the first position one or more apertures 2424 are closed to flow blood into sequestration chamber 2418 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraphs [0147]-[0148]); and a contaminant containment reservoir connected between the inlet and the outlet (blood sequestration chamber 2418; figure 24B; paragraph [0147]), the contaminant containment reservoir further having an air permeable fluid resistor proximate the outlet (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]), the contaminant containment reservoir being arranged to receive, when a pressure differential is applied between the inlet and the outlet, the first portion of the fluid sample from the fluid source to displace air therein through the air permeable fluid resistor and the outlet (upon drawing of blood by way of a syringe or Vacutainer (pressure differential is applied) initial aliquot of blood flows into the blood sequestration chamber 2418 displacing air through blood barrier 2420 (air permeable fluid) and the outlet; figures 24B-24C; paragraph [0148]), such that upon receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir, subsequent portions of the fluid sample can be forced through the resistive plug and conveyed by the sample path from the inlet to the outlet when subsequent pressure differentials are applied between the inlet and the outlet (the blood in the sequestration chamber 2418 forces the inner chamber housing to the second position allowing one or more apertures 2424 to open to create a pathway from the inlet port 2412 to the blood sampling channel 2422, bypassing and/or flowing around the blood sequestration chamber 2418 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraph [0148]).

As per claim 7, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin further discloses further comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the contaminant containment reservoir (blood sequestration device 2408 houses the inlet, the outlet, the sample path, and the contaminant containment reservoir; figures 24B-24D; paragraph [0147]).

As per claim 8, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin further discloses wherein the air permeable fluid resistor (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]) includes a material that seals upon contact with the first portion of the fluid sample (the term "air permeable blood barrier" is formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid; paragraph [0066]).

As per claim 10, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin further discloses wherein each pressure differential is provided by a vacuum pressure provided by the fluid collection device (in a blood sample under vacuum pressure or force through the conduit 2006 [2406] from the patient needle 2402 using a syringe or Vacutainer; figure 24B; paragraphs [0144], [0148]).

As per claim 14. A fluid sample optimization device for optimizing a fluid sample, a first portion of the fluid sample potentially having contaminants (sample optimization systems that reduce or eliminate contaminates in collected blood samples by including a blood sequestration device; abstract), the fluid sample optimization device comprising: an inlet (blood sequestration device 2408 includes an inlet port 2412; figure 24B; paragraph [0146]); an outlet (blood sequestration device 2408 includes an outlet port 2414; figure 24B; paragraph [0146]); a sample path connected between the inlet and the outlet (a blood sample channel 2422; figure 24C; paragraph [0147]); and a contaminant containment reservoir connected between the inlet and the outlet (blood sequestration chamber 2418; figure 24B; paragraph [0147]), the contaminant containment reservoir having an air permeable fluid resistor proximate the outlet (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]), the contaminant containment reservoir being arranged to receive, when a pressure differential is applied between the inlet and the outlet, a first portion of the fluid sample to displace air therein through the air permeable fluid resistor and the outlet (upon drawing of blood by way of a syringe or Vacutainer (pressure differential is applied) initial aliquot of blood flows into the blood sequestration chamber 2418 displacing air through blood barrier 2420 (air permeable fluid) and the outlet; figures 24B-24C; paragraph [0148]), such that upon receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir, subsequent portions of the fluid sample can be conveyed by the sample path from the inlet to the outlet when subsequent pressure differentials are applied between the inlet and the outlet (the blood in the sequestration chamber 2418 forces the inner chamber housing to the second position allowing one or more apertures 2424 to open to create a pathway from the inlet port 2412 to the blood sampling channel 2422, bypassing and/or flowing around the blood sequestration chamber 2418 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraph [0148]).

-***-Continued Within the Next Supplemental Box-***-

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US20/26276

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:

-***-Continued from Previous Supplemental Box-***-

As per claim 15, Kurin discloses the fluid sample optimization device in accordance with claim 14, and Kurin further discloses wherein the sample path further includes a resistive plug that is configured to inhibit at least a part of the first portion of the fluid sample and the contaminants from entering the sample path during receipt of the first portion of the fluid sample and containment of the contaminants in the contaminant containment reservoir (in the first position one or more apertures 2424 are closed to flow blood into sequestration chamber 2418 (still under pressure from a syringe or Vacutainer); figures 24B-24D; paragraphs [0147]-[0148]).

As per claim 16, Kurin discloses the fluid sample optimization device in accordance with claim 14, and Kurin further discloses further comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the contaminant containment reservoir (blood sequestration device 2408 houses the inlet, the outlet, the sample path, and the contaminant containment reservoir; figures 24B-24D; paragraph [0147]).

As per claim 17, Kurin discloses the fluid sample optimization device in accordance with claim 14, and Kurin further discloses wherein the air permeable fluid resistor (blood sequestration chamber 2418 includes an air permeable blood barrier 2420 at a distal end of the blood sequestration chamber 2418, near outlet 2414; figure 24B; paragraph [0147]) includes a material that seals upon contact with the first portion of the fluid sample (the term "air permeable blood barrier" is formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid; paragraph [0066]).

Claims 4, 9, 18 lack an inventive step under PCT Article 33(3) as being obvious over Kurin,

As per claim 4, Kurin discloses the fluid sample optimization device in accordance with claim 1, but Kurin does not disclose, in the first embodiment, wherein the contaminant containment reservoir includes a tortuous path. In a different embodiment, Kurin further discloses wherein the contaminant containment reservoir includes a tortuous path (a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of im1er conduit 2620; figures 26C-26D; paragraph [0154]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of the first embodiment of Kurin to provide wherein the contaminant containment reservoir includes a tortuous path, as taught by the second embodiment of Kurin, in order to provide an associated amount of the sequestered fluid (paragraph [0096]).

As per claim 9, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin does not disclose, in the first embodiment, wherein the contaminant containment reservoir includes a tortuous path. In a different embodiment, Kurin further discloses wherein the contaminant containment reservoir includes a tortuous path (a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of im1er conduit 2620; figures 26C-26D; paragraph [0154]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of the first embodiment of Kurin to provide wherein the contaminant containment reservoir includes a tortuous path, as taught by the second embodiment of Kurin, in order to provide an associated amount of the sequestered fluid (paragraph [0096]).

As per claim 18, Kurin discloses the fluid sample optimization device in accordance with claim 14, but Kurin does not disclose, in the first embodiment, wherein the contaminant containment reservoir includes a tortuous path. In a different embodiment, Kurin further discloses wherein the contaminant containment reservoir includes a tortuous path (a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of im1er conduit 2620; figures 26C-26D; paragraph [0154]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of the first embodiment of Kurin to provide wherein the contaminant containment reservoir includes a tortuous path, as taught by the second embodiment of Kurin, in order to provide an associated amount of the sequestered fluid (paragraph [0096]).

Claims 11-12, 19-20 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of GB 1378602 A (AYERS).

As per claim 11, Kurin discloses the fluid sample optimization device in accordance with claim 6, but Kurin does not disclose wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials. Ayers discloses a resistive plug includes a film that is pierceable by a first of a subsequent pressure differentials (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

-***-Continued Within the Next Supplemental Box-***-

Claims Not Examined

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US20/26276

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:

-***-Continued from Previous Supplemental Box-***-

As per claim 12, Kurin and Ayers, in combination, disclose the fluid sample optimization device in accordance with claim 11, but Kurin does not disclose wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film. Ayers discloses a resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

As per claim 19, Kurin discloses the fluid sample optimization device in accordance with claim 15, but Kurin does not disclose wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials. Ayers discloses a resistive plug includes a film that is pierceable by a first of a subsequent pressure differentials (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug includes a film that is pierceable by a first of the subsequent pressure differentials, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

As per claim 20, Kurin and Ayers, in combination, disclose the fluid sample optimization device in accordance with claim 19, but Kurin does not disclose wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film. Ayers discloses a resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film (when blood fills chamber 26, the cannula is pushed (pressure differential) through stopper 41 to allow blood flow into tube 39; page 5, lines 34-60; figures 4, 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug further includes a piercing member configured to pierce the film when the first of the subsequent pressure differentials is exerted on an opposite side of the film, as taught by Ayers, in order to provide enable sealing until the sample is desired; (Ayers: page 5, lines 68-95).

Claim 13 lacks an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 2014/0112841 Al to Schoen, et al. (hereafter 'Schoen') as evidenced by WO 2019/055487 Al to Magnolia Medical Technologies (hereafter 'Magnolia').

As per claim 13, Kurin discloses the fluid sample optimization device in accordance with claim 6, and Kurin discloses the use of mesh for resistive plugs (barriers are made from mesh or filter material; paragraph [0066]), but Kurin does not disclose wherein the resistive plug includes a mesh with a dissolvable material that dissolves upon contact with a first of the subsequent portions of the fluid sample. Schoen discloses a resistive plug includes a mesh with a dissolvable material that dissolves upon contact with a first of the subsequent portions of the fluid sample (water-soluble membrane (mesh) used for temporarily retaining a liquid in a holding chamber, where the membrane dissolves after a certain amount of time; abstract; paragraph [0035]). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kurin to provide wherein the resistive plug includes a mesh with a dissolvable material that dissolves upon contact with a first of the subsequent portions of the fluid sample, as taught by Schoen, as evidenced by Magnolia that discloses an actuator that changes a sample device from sequestration to flow through upon dissolving (Magnolia: actuator 250, used to change sample flow from sequestration to flow through, is transitioned by a change of configuration such as dissolving; paragraphs [1071], [1080]; figures 2-5).

Claims 1-20 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.

Pending Processing

Form PCT/ISA/237 (Supplemental Box) (revised January 2019)

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
KURIN4PCT		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 20/23617	19 March 2020 (19.03.2020)	13 March 2020 (13.03.2020)
Applicant KURIN, INC.		

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

This international search report consists of a total of 2 sheets.

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

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

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

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

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

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

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 35

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☒ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

Pending processing

Form PCT/ISA/210 (first sheet) (July 2019)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/23617

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61B 5/15, A61B 5/153, A61B 5/154, A61B 5/157 (2020.01)

CPC - A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2018/0177445 A1 (Kurin, Inc.) 28 June 2018 (28.06.2018), entire document	1-4, 10-12, 18 --- 5-9, 13-17, 19-20
Y	US 4,349,035 A (Thomas et al.) 14 September 1982 (14.09.1982), entire document	5-6, 8-9, 13-14, 16-17, 19-20
Y	US 5,401,262 A (Karwoski et al.) 28 March 1995 (28.03.1995), entire document	5, 7, 13, 15
A	US 2018/0271425 A1 (Kurin, Inc.) 27 September 2018 (27.09.2018), entire document	1-20
A	US 2018/0353117 A1 (Magnolia Medical Technologies, Inc.) 13 December 2018 (13.12.2018), entire document	1-20

Document being processed

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

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

Date of the actual completion of the international search	Date of mailing of the international search report
07 JUNE 2020	19 JUN 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/210 (second sheet) (July 2019)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: JAMES SCOTT NOLAN
P.O. BOX 371710
SAN DIEGO, CA 92110

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	19 JUN 2020

Applicant's or agent's file reference	FOR FURTHER ACTION
KURIN4PCT	See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 20/23617	19 March 2020 (19.03.2020)	13 March 2020 (13.03.2020)

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

IPC - A61B 5/15, A61B 5/153, A61B 5/154, A61B 5/157 (2020.01)

CPC - A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946

Applicant KURIN, INC.

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

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

2. **FURTHER ACTION**

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

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

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

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	07 JUNE 2020	Lee Young PCT Help Desk Telephone No. 571-272-4300

Form PCT/ISA/237 (cover sheet) (revised January 2019)

International Processing

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 20/23617

Box No. I Basis of this opinion

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

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

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

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

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

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

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

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

b. ☐ furnished together with the international application under PCT Rule 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:

Pending processing

Form PCT/ISA/237 (Box No. I) (revised January 2019)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 20/23617

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

1. Statement

Novelty (N)	Claims	5-9, 13-20	YES
	Claims	1-4, 10-12	NO
Inventive step (IS)	Claims	none	YES
	Claims	1-20	NO
Industrial applicability (IA)	Claims	1-20	YES
	Claims	none	NO

2. Citations and explanations:

Claims 1-4 and 10-12 lack novelty under PCT Article 33(2) as being anticipated by US 2018/0177445 A1 to Kurin, Inc. (hereinafter Kurin).

Regarding claim 1, Kurin teaches a blood sequestration device (see fig. 30A-G; para [0156]) comprising; an inlet path (fig. 30A see inlet path 3002; para [0156]); an outlet path (fig. 30A see outlet path 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first portion of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A-D see vent 3010; para [0161]; para [0163]-[0165]), the junction being configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, it is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see para[0156], [0160]-[0161], [0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first amount of blood is received by the sequestration chamber (para [0160]-[0170]).

Regarding claim 2, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction is angled from the inlet path toward the sequestration chamber (fig. 30A; fig. 17A see junction 3007 is angled from the inlet path to the sequestration chamber; para [0160]) .

Regarding claim 3, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction has a cross-sectional area that is smaller than a cross-sectional area of the inlet path (fig. 30A; fig. 17A see junction 3007 has a cross-sectional area closest to the inlet path that is smaller than a cross-sectional area of the inlet path below where it meets the junction; para [0160]).

Regarding claim 4, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction has a cross-sectional area that is larger than a cross-sectional area of the inlet path (fig. 30A; fig. 17A see junction 3007 has a cross-sectional area near the sequestration chamber 3008 that is larger than a cross-sectional area of the inlet path where the inlet path opens to the junction; para [0160]; para [0163] junction cross-sectional area widens towards the sequestration chamber to direct blood).

Regarding claim 10, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the vent includes two or more vent apertures (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060] air permeable blood barrier may comprise a mesh, a mesh inherently comprises two or more vent apertures).

Regarding claim 11, Kurin teaches a blood sequestration device (see fig. 30A-G; para [0156]) comprising; a housing (fig. 30A see housing 3001; para [0161]) having in inlet port (fig. 30A see inlet path 3002 has port opening in housing 3001; para [0156; para [0161]) and an outlet port (fig. 30A see outlet path 3004 has outlet opening in housing 3001; para [0159]; para [0161]), the housing containing: an inlet path connected to the inlet port (fig. 30A see inlet path 3002; para [0156]); an outlet path connected with the outlet port (fig. 30A see outlet path 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first amount of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A see vent 3010; para [0161]; para [0163]-[0165]), the vent further being further configured to close upon the sequestration chamber being filled with the first portion of blood (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060]; para [0160]-[0170]), the junction being configured to inhibit a return of the first portion of blood out of the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, is is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see also para[0156],[0160]-[0161],[0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first portion of blood is received by the sequestration chamber (para [0160]-[0170]).

-*-Continued in Supplemental Box-*-

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 20/23617

Box No. VIII Certain observations on the international application

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

Regarding claim 18, the claim language is confusing and lacks clarity. Specifically, the recitation "the patient needle and the sample needle", lack proper antecedent basis. In order to give meaning to this claim and to give proper antecedent basis, based on the specification (para [0063]), this recitation has been interpreted as the following: "and a blood sequestration device connected along the blood sampling pathway between a patient needle and a sample needle, wherein the venipunture apparatus includes the patient needle and the reservoir includes the sample needle".

Pending processing

Form PCT/ISA/237 (Box No. VIII) (revised January 2019)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
-*-Box V.2 - Citations and Explanations-*-

Regarding claim 12, Kurin teaches the blood sequestration device in accordance with claim 11, wherein the vent further comprises a closure mechanism that inhibits air from reentering the sequestration chamber after it has been displaced (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060]).

Claim 18 lacks an inventive step under PCT Article 33(3) as being obvious over Kurin.

Regarding claim 18, Kurin teaches a blood sample optimization system (fig. 30A-G; para [0156]) comprising: a blood sampling system (para [0156]) comprising: a venipuncture apparatus configured for venipuncture of a patient to access a sample of blood of a patient (para [0156] inlet port 3002 with opening connects to patient needle, needle is a suitable venipuncture apparatus); a blood sampling pathway connected with the venipuncture apparatus for conveying the sample of blood (fig. 30A see system 3000 comprises blood sampling pathway from inlet 3002 to outlet 3004 through sampling channel 3006; para [0156]); and a reservoir (fig. 30A see reservoir 3004; para [0158]); and a blood sequestration device connected along the blood sampling pathway between a patient needle and the reservoir (see fig. 30A-G; para [0156]), wherein the venipunture apparatus includes the patient needle (para [0156] inlet port 3002 with opening connects to patient needle), the blood sequestration device comprising: an inlet path connected with the patient needle (fig. 30A see inlet path 3002; para [0156]); an outlet path connected with the reservoir (fig. 30A see outlet path through outlet reservoir 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first portion of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A see vent 3010; para [0161]; para [0163]-[0165]), the junction being configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, is is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see para[0156], [0160]-[0161], [0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first amount of blood is received by the sequestration chamber (para [0160]-[0170]); but Kurin does not explicitly teach wherein the reservoir is configured for receiving an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood, nor wherein reservoir and connected outlet path comprise a sample needle. However, in another embodiment, Kurin teaches a sample needle at an outlet path of a blood sample collection device facilitates connection to an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood (fig. 1 see sample needle 5; para [0065]; see fig. 7). Combining embodiments is within the ordinary skill of a person within the art. Accordingly, it would have been obvious to a person having ordinary skill in the art to have provided a sample needle such that the reservoir is configured for receiving an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood in order to provide blood collection means with the blood sampling device.

Claims 5-6, 8-9, 13-14, 16-17 and 19-20 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 4,349,035 A to Thomas et al. (hereinafter Thomas).

Regarding claim 5, Kurin teaches the blood sequestration device in accordance with claim 1, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, ln 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, ln 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, ln 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, ln 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 6, Kurin in view of Thomas teaches the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a conical baffle having a tapered end directed toward the sequestration chamber (see Thomas fig. 4-5 passive structure tapers to a point towards chamber, thus restricting flow; see column 5, ln 13 -17).

Regarding claim 8, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a divider wall extending across a cross-section of the junction (see Thomas fig. 4-5 divider wall 25; column 6, ln 7-13).

-*-Continued in next Supplemental Box-*-

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 20/23617

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:
-*-Supplemental Box - Box V.2 - Citations and Explanations-*-

Regarding claim 9, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a flow director extending from an inner surface of the junction (see Thomas fig. 4-5 valve 22 is a flow director; column 4, ln 23-38; column 5, ln 13-17), the flow director being configured to control a flow of blood (see Thomas column 4, ln 23-28 flow director valve 22 controls flow by directing into chamber 21 and preventing backflow).

Regarding claim 13, Kurin teaches the blood sequestration device in accordance with claim 11, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, ln 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, ln 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, ln 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, ln 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 14, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a conical baffle having a tapered end directed toward the sequestration chamber (see Thomas fig. 4-5 passive structure tapers to a point towards chamber, thus restricting flow; see column 5, ln 13 -17).

Regarding claim 16 Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a divider wall extending across a cross-section of the junction. (see Thomas fig. 4-5 divider wall 25; column 6, ln 7-13).

Regarding claim 17 Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a flow director extending from an inner surface of the junction (see Thomas fig. 4-5 valve 22 is a flow director; column 4, ln 23-38; column 5, ln 13-17), the flow director being configured to control a flow of blood (see Thomas column 4, ln 23-28 flow director valve 22 controls flow by directing into chamber 21 and preventing backflow).

Regarding claim 19, Kurin teaches the blood sample optimization system in accordance with claim 18, but does not explicitly teach wherein the junction of the blood sequestration device includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, ln 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, ln 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, ln 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, ln 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 20, Kurin in view of Thomas teach the blood sample optimization system in accordance with claim 19, and Kurin modified by Thomas further teaches wherein the one or more passive structures includes a wall extending from an inner surface of the junction to control a flow of the first portion of blood (see Thomas fig. 4-5 divider wall 25; column 6, ln 7-13).

-*-Continued in next Supplemental Box-*-

Pending (Continued)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
-*-Supplemental Box - Box V.2 - Citations and Explanations-*-

Claim 5, 7 and 13, 15 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 5,401,262 A to Karwoski et al. (hereinafter Karwoski).

Regarding claim 5, Kurin teaches the blood sequestration device in accordance with claim 1, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Karwoski teaches a blood collection device (see fig. 1; column 4, ln 20-40). Karwoski further teaches wherein a pathway of the blood collection devices includes one or more passive structures configured to inhibit a return to an inlet path of any of a sample of blood (fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, ln 1-24; column 21, ln 55-65). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structures as taught by Karwoski in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 7, Kurin in view of Karwoski teach the blood sequestration device in accordance with claim 5, and Kurin modified by Karwoski further teaches wherein the one or more passive structures include two or more staggered baffles extending from an inner surface of the junction (Karwoski fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, ln 1-24; column 21, ln 55-65).

Regarding claim 13, Kurin teaches the blood sequestration device in accordance with claim 11, wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Karwoski teaches a blood collection device (see fig. 1; column 4, ln 20-40). Karwoski further teaches wherein a pathway of the blood collection devices includes one or more passive structures configured to inhibit a return to an inlet path of any of a sample of blood (fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, ln 1-24; column 21, ln 55-65). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structures as taught by Karwoski in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 15, Kurin in view of Karwoski teach the blood sequestration device in accordance with claim 13, and Kurin modified by Karwoski further teaches wherein the one or more passive structures include two or more staggered baffles extending from an inner surface of the junction (Karwoski fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, ln 1-24; column 21, ln 55-65).

Claims 1-20 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used by industry.

Pending processing

Form PCT/ISA/237 (Supplemental Box) (revised January 2019)

SEARCH HISTORY

Application Number	PCT/US 20/23617
Search Conducted By	EAW
Search Approved By	SCL

CPC/IPC Classifications Searched	IPC(8): A61B 5/15, A61B 5/153, A61B 5/154, A61B5/157 (2020.01) CPC: A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946
Date Conducted	7 June 2020 (07.06.2020)

Documentation Searched	IPC(8): A61B 5/15, A61B 5/153, A61B 5/154, A61B5/157 (2020.01) CPC: (keyword limited; see below)
Search Terms Used	baffle*, prevent*, inhibit*, back*, return*, sequestration*, flow*, blood*, sample*, restrict*
Date Conducted	7 June 2020 (07.06.2020)

Electronic Database Searched	PatBase
Files Searched	Full-text: AU BE BR CA CH CN DE DK EP ES FI FR GB IN JP KR SE TH TW US WO Bibliographic: (European) AT BA BE BG CH CS CY CZ DD DK EE ES FI GE GR HR HU IE IS IT LT LU LV MC MD MT NL NO PL PT RO RS SE SI SK SM TR UA YU (Asia) EA GC HK ID IL IN KZ MN MY PH RU SG SU TH TJ TW UZ VN (North America) CA CR CU DO GT HN MX NI PA SV TT (South America) AR BR CL CO EC PE UY (Australasia) AU NZ (Africa) AP DZ EG KE MA MW OA ZA ZM ZW
Date Conducted	7 June 2020 (07.06.2020)
Search Logic:	

Search 1: PA=(Kurin inc) (Results 5)
Search 2: PN=(US2018/0177445) (Results 1)
Search 3: ctb 2 or ctf 2 (Results 5)
Search 4: CPC=(A61B5/15003) (Results 2650)
Search 5: 4 and ft=(baffle%) (Results 36)
Search 6: 4 and ft=((prevent* or inhibit*) near (back* or return*)) (Results 226)
Search 7: 6 and ft=(sequestration) (Results 3)
Search 8: 6 and ft=(flow*) (Results 182)
Search 9: IPC=(A61B5/15 or A61B5/153 or A61B5/154 or A61B5/157) (Results 13750)
Search 10: CPC=(A61B5/15003 or A61B5/150213 or A61B5/150251 or A61B5/150992 or A61B5/150206 or A61B5/150221 or A61B5/150946) (Results 3410)
Search 11: 9 or 10 (Results 14204)
Search 12: 11 and ft=(sequestration) (Results 32)
Search 13: 11 and ft=((prevent* or inhibit*) near (back* or return*)) (Results 535)
Search 14: 13 and ft=(blood* near sample*) (Results 335)
Search 15: 14 not 8 (Results 198)
Search 16: ft=(sequestration* and baffle* and blood*) (Results 170)
Search 17: 16 not (14 or 8) (Results 170)
Search 18: ft=(blood* and sequestration* and (restrict* near flow*)) (Results 176)

Electronic Database Searched	Google
Files Searched	Patents
Date Conducted	7 June 2020 (07.06.2020)

Search Logic:

blood sampling sequestration device prevent backflow

blood sampling sequestration device baffle directs flow

blood sampling collection device prevent backflow

blood sampling device valve restricts backflow controls flow

blood sequestration junction prevents backflow blood sequestration junction flow restriction

Electronic Database Searched	Google
Files Searched	Web
Date Conducted	7 June 2020 (07.06.2020)
Search Logic:	
blood sampling sequestration device prevent backflow blood sampling sequestration device baffle directs flow blood sampling collection device prevent backflow blood sampling device valve restricts backflow controls flow blood sequestration junction prevents backflow blood sequestration junction flow restriction	

UNITED STATES
PATENT AND TRADEMARK OFFICE

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

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/783,088	**08/26/2024 08:23:36 PM Z ET**	**069366-0580418_KUR2C06US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2051	FILED BY	Trent Tercenio
PATENT CENTER #	66924990	FILING DATE	07/24/2024
CUSTOMER #	27500	FIRST NAMED INVENTOR	Bobby E. ROGERS
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Benjamin Hudson

Documents

TOTAL DOCUMENTS: 100

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0580418_KUR2C06US-A-Foreign-008-FOR.pdf	21	Foreign Reference	885 KB
069366-0580418_KUR2C06US-A-Foreign-005-FOR.pdf	13	Foreign Reference	970 KB
069366-0580418_KUR2C06US-A-Foreign-009-FOR.pdf	65	Foreign Reference	2627 KB
069366-0580418_KUR2C06US-A-Foreign-010-FOR.pdf	91	Foreign Reference	2911 KB
069366-0580418_KUR2C06US-A-	186	Foreign Reference	2958 KB

Foreign-011-FOR.pdf			
069366-0580418_KUR2C06US-A-Foreign-007-FOR.pdf	92	Foreign Reference	5068 KB
069366-0580418_KUR2C06US-A-Foreign-012-FOR.pdf	126	Foreign Reference	4117 KB
069366-0580418_KUR2C06US-A-Foreign-006-FOR.pdf	132	Foreign Reference	6913 KB
069366-0580418_KUR2C06US-A-Foreign-013-FOR.pdf	71	Foreign Reference	4563 KB
069366-0580418_KUR2C06US-A-Foreign-018-FOR.pdf	14	Foreign Reference	1784 KB
069366-0580418_KUR2C06US-A-Foreign-015-FOR.pdf	74	Foreign Reference	4560 KB
069366-0580418_KUR2C06US-A-Foreign-014-FOR.pdf	101	Foreign Reference	5095 KB
069366-0580418_KUR2C06US-A-Foreign-019-FOR.pdf	40	Foreign Reference	2708 KB
069366-0580418_KUR2C06US-A-Foreign-016-FOR.pdf	158	Foreign Reference	5951 KB
069366-0580418_KUR2C06US-A-Foreign-022-FOR.pdf	27	Foreign Reference	2373 KB
069366-0580418_KUR2C06US-A-Foreign-023-FOR.pdf	16	Foreign Reference	453 KB
069366-0580418_KUR2C06US-A-Foreign-021-FOR.pdf	55	Foreign Reference	4401 KB
069366-0580418_KUR2C06US-A-Foreign-026-FOR.pdf	92	Foreign Reference	2890 KB

069366-0580418_KUR2C06US-A-Foreign-025-FOR.pdf	84	Foreign Reference	3373 KB
069366-0580418_KUR2C06US-A-Foreign-020-FOR.pdf	206	Foreign Reference	6968 KB
069366-0580418_KUR2C06US-A-Foreign-017-FOR.pdf	168	Foreign Reference	7949 KB
069366-0580418_KUR2C06US-A-Foreign-024-FOR.pdf	112	Foreign Reference	5078 KB
069366-0580418_KUR2C06US-A-Foreign-028-FOR.pdf	21	Foreign Reference	1635 KB
069366-0580418_KUR2C06US-A-Foreign-029-FOR.pdf	19	Foreign Reference	1762 KB
069366-0580418_KUR2C06US-A-Foreign-027-FOR.pdf	123	Foreign Reference	4097 KB
069366-0580418_KUR2C06US-A-Foreign-033-FOR.pdf	45	Foreign Reference	2277 KB
069366-0580418_KUR2C06US-A-Foreign-034-FOR.pdf	26	Foreign Reference	1739 KB
069366-0580418_KUR2C06US-A-Foreign-037-FOR.pdf	10	Foreign Reference	281 KB
069366-0580418_KUR2C06US-A-Foreign-032-FOR.pdf	47	Foreign Reference	3472 KB
069366-0580418_KUR2C06US-A-Foreign-036-FOR.pdf	91	Foreign Reference	3103 KB
069366-0580418_KUR2C06US-A-Foreign-038-FOR.pdf	15	Foreign Reference	425 KB
069366-0580418_KUR2C06US-A-	26	Foreign Reference	685 KB

Foreign-039-FOR.pdf			
069366-0580418_KUR2C06US-A-Foreign-035-FOR.pdf	20	Foreign Reference	1801 KB
069366-0580418_KUR2C06US-A-Foreign-041-FOR.pdf	32	Foreign Reference	1020 KB
069366-0580418_KUR2C06US-A-Foreign-030-FOR.pdf	126	Foreign Reference	6357 KB
069366-0580418_KUR2C06US-A-Foreign-031-FOR.pdf	82	Foreign Reference	5401 KB
069366-0580418_KUR2C06US-A-Foreign-040-FOR.pdf	45	Foreign Reference	970 KB
069366-0580418_KUR2C06US-A-Foreign-042-FOR.pdf	33	Foreign Reference	1024 KB
069366-0580418_KUR2C06US-A-Foreign-043-FOR.pdf	31	Foreign Reference	1081 KB
069366-0580418_KUR2C06US-A-Foreign-048-FOR.pdf	4	Foreign Reference	197 KB
069366-0580418_KUR2C06US-A-Foreign-045-FOR.pdf	8	Foreign Reference	510 KB
069366-0580418_KUR2C06US-A-Foreign-047-FOR.pdf	23	Foreign Reference	941 KB
069366-0580418_KUR2C06US-A-NPL-002-Other.pdf	9	Non Patent Literature	556 KB
069366-0580418_KUR2C06US-A-Foreign-050-FOR.pdf	17	Foreign Reference	512 KB
069366-0580418_KUR2C06US-A-NPL-001-Other.pdf	6	Non Patent Literature	316 KB

069366-0580418_KUR2C06US-A-Foreign-049-FOR.pdf	15	Foreign Reference	1987 KB
069366-0580418_KUR2C06US-A-NPL-006-Other.pdf	4	Non Patent Literature	111 KB
069366-0580418_KUR2C06US-A-Foreign-046-FOR.pdf	61	Foreign Reference	2472 KB
069366-0580418_KUR2C06US-A-Foreign-044-FOR.pdf	53	Foreign Reference	3547 KB
069366-0580418_KUR2C06US-A-NPL-008-Other.pdf	3	Non Patent Literature	109 KB
069366-0580418_KUR2C06US-A-NPL-007.pdf	11	Non Patent Literature	397 KB
069366-0580418_KUR2C06US-A-NPL-005-Other.pdf	11	Non Patent Literature	783 KB
069366-0580418_KUR2C06US-A-NPL-012-Other.pdf	6	Non Patent Literature	159 KB
069366-0580418_KUR2C06US-A-NPL-009-Other.pdf	12	Non Patent Literature	621 KB
069366-0580418_KUR2C06US-A-NPL-010-Other.pdf	12	Non Patent Literature	386 KB
069366-0580418_KUR2C06US-A-NPL-013-Other.pdf	8	Non Patent Literature	216 KB
069366-0580418_KUR2C06US-A-NPL-011-Other.pdf	9	Non Patent Literature	268 KB
069366-0580418_KUR2C06US-A-NPL-016-Other.pdf	13	Non Patent Literature	358 KB
069366-0580418_KUR2C06US-A-	5	Non Patent Literature	218 KB

NPL-014-Other.pdf			
069366-0580418_KUR2C06US-A-NPL-017.pdf	20	Non Patent Literature	130 KB
069366-0580418_KUR2C06US-A-NPL-015-Other.pdf	9	Non Patent Literature	267 KB
069366-0580418_KUR2C06US-A-NPL-004-Other.pdf	125	Non Patent Literature	4474 KB
069366-0580418_KUR2C06US-A-NPL-018.pdf	15	Non Patent Literature	1026 KB
069366-0580418_KUR2C06US-A-NPL-019.pdf	4	Non Patent Literature	1168 KB
069366-0580418_KUR2C06US-A-NPL-020.pdf	10	Non Patent Literature	2225 KB
069366-0580418_KUR2C06US-A-NPL-024.pdf	11	Non Patent Literature	1731 KB
069366-0580418_KUR2C06US-A-NPL-022.pdf	15	Non Patent Literature	2902 KB
069366-0580418_KUR2C06US-A-NPL-021.pdf	3	Non Patent Literature	2923 KB
069366-0580418_KUR2C06US-A-NPL-027.pdf	5	Non Patent Literature	601 KB
069366-0580418_KUR2C06US-A-NPL-028.pdf	4	Non Patent Literature	324 KB
069366-0580418_KUR2C06US-A-NPL-023.pdf	6	Non Patent Literature	4234 KB
069366-0580418_KUR2C06US-A-NPL-030.pdf	5	Non Patent Literature	403 KB

069366-0580418_KUR2C06US-A-NPL-031.pdf	2	Non Patent Literature	122 KB
069366-0580418_KUR2C06US-A-NPL-034.pdf	1	Non Patent Literature	82 KB
069366-0580418_KUR2C06US-A-NPL-003.pdf	131	Non Patent Literature	12245 KB
069366-0580418_KUR2C06US-A-NPL-033.pdf	8	Non Patent Literature	653 KB
069366-0580418_KUR2C06US-A-NPL-032.pdf	10	Non Patent Literature	1685 KB
069366-0580418_KUR2C06US-A-NPL-035.pdf	3	Non Patent Literature	458 KB
069366-0580418_KUR2C06US-A-NPL-029.pdf	4	Non Patent Literature	5178 KB
069366-0580418_KUR2C06US-A-NPL-038.pdf	9	Non Patent Literature	861 KB
069366-0580418_KUR2C06US-A-NPL-036.pdf	15	Non Patent Literature	2065 KB
069366-0580418_KUR2C06US-A-NPL-040.pdf	4	Non Patent Literature	703 KB
069366-0580418_KUR2C06US-A-NPL-025.pdf	7	Non Patent Literature	9814 KB
069366-0580418_KUR2C06US-A-NPL-042.pdf	7	Non Patent Literature	732 KB
069366-0580418_KUR2C06US-A-NPL-041.pdf	19	Non Patent Literature	2135 KB
069366-0580418_KUR2C06US-A-	4	Non Patent Literature	1377 KB

NPL-043.pdf			
069366-0580418_KUR2C06US-A-NPL-037.pdf	4	Non Patent Literature	6178 KB
069366-0580418_KUR2C06US-A-NPL-046.pdf	2	Non Patent Literature	776 KB
069366-0580418_KUR2C06US-A-NPL-047.pdf	3	Non Patent Literature	221 KB
069366-0580418_KUR2C06US-A-NPL-045.pdf	4	Non Patent Literature	1526 KB
069366-0580418_KUR2C06US-A-NPL-048.pdf	3	Non Patent Literature	310 KB
069366-0580418_KUR2C06US-A-NPL-026.pdf	9	Non Patent Literature	14484 KB
069366-0580418_KUR2C06US-A-NPL-044.pdf	3	Non Patent Literature	2668 KB
069366-0580418_KUR2C06US-A-NPL-039.pdf	3	Non Patent Literature	3889 KB
069366-0580418_KUR2C06US_Transmittal-Letter.pdf	1	Transmittal Letter	493 KB
069366-0580418_KUR2C06US-A-Foreign-001-FOR.pdf	31	Foreign Reference	1175 KB
069366-0580418_KUR2C06US-A-Foreign-003-FOR.pdf	32	Foreign Reference	2090 KB
069366-0580418_KUR2C06US-A-Foreign-002-FOR.pdf	44	Foreign Reference	2593 KB
069366-0580418_KUR2C06US-A-NPL-050.pdf	8	Non Patent Literature	4918 KB

069366-0580418_KUR2C06US_PTO_IDS-Form-A.pdf	31	Information Disclosure Statement (IDS) Form (SB08)	1280 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
069366-0580418_KUR2C06US-A-Foreign-008-FOR.pdf	5210BEA64627F998AC1C600DB796F1C2B3C2943BB325F9A870A56CCCD52EE58A8A8FE55FE34322E2C354947B36972552D172D4DE5BA1DC1B73BB30CBD0883302
069366-0580418_KUR2C06US-A-Foreign-005-FOR.pdf	87EDCC7278AAC006CF10943F43A5CF82EFA46A0601739943A21A7D15AE77B375D9E43A2C41CC99A1272FF960E746998DFE6F94D7FA00344652C75146DB0E2CBA
069366-0580418_KUR2C06US-A-Foreign-009-FOR.pdf	1EBB8E4DADD362DD741BCF95839AF2123E42EB41C7C29A782C87033AA8A98233C3E8176B7A87D9C740AF92CC3F3561EEB4DA39CBEFF35779C591A8AE8965E2EE
069366-0580418_KUR2C06US-A-Foreign-010-FOR.pdf	D72D2DB3A053FC6D60F516B5B4D9F9A607B832CDEDE6A1F3D691BAB540B628D9CFB957386951395696E2129911426BE44FDF6D93FDB284FDDB35E17009666DC1
069366-0580418_KUR2C06US-A-Foreign-011-FOR.pdf	7622BCCF59819EE8118D4EF0CD1F3285A80E48A757656A9052FC7F3F9D97F0893C944CD2419C178E2E738156F4AE0D9A8974A7C00A48C61D606FD63A124A5BA3
069366-0580418_KUR2C06US-A-Foreign-007-FOR.pdf	36B6FB543AF414B82B0BA1111A98340E067C76CF8AF602DA348CEDC14D9C86ABEB52583D31258E2D83DD44225BF42678CF53B22BA65811F64E6C38BB63F6CE35
069366-0580418_KUR2C06US-A-Foreign-012-FOR.pdf	17678AA39876788EC4B8FD3F7298D94DD773893A987D48878300612355D974F91E358804FBAB831A0773ABF33ABEAC704AF60F149FE0349CDDE1659C3A766692
069366-0580418_KUR2C06US-A-Foreign-006-FOR.pdf	901471A7661028AFD4FCDE344F7D1277D7E94EF0CA8B339DCCB6E71E9BAB78ABECB24A3BA37A0733D850B86F5393C10676E90E8D2F18BA6B6AC036CD66293AFB
069366-0580418_KUR2C06US-A-Foreign-013-FOR.pdf	D853F48E2ECF75741957DFD065C5A7BBE56FA4AF168BF391D7703E1A470819E3BA99FE7E76D45FEE895E43437FEA04099F2E7B84CDA933FEE35DD08262682AEC
069366-0580418_KUR2C06US-A-Foreign-018-FOR.pdf	D0B1AEE2D4F69E32A3ADDC034618879B973313C163EB79A14C087FDF110F8B3683FE0133D95245C6327B4D9D229C8DE719E72DCCCC2282996219BBE30620DD88
069366-0580418_KUR2C06US-A-Foreign-015-FOR.pdf	D38E2BE6001DDFCE3F3936F8BAD530467915EEFF51CCBA1934198AB61C9C068D0A320A76E5781660F04C2B0D70D35660DADCEFCB647CF93DB7404A1C178024F1

069366-0580418_KUR2C06US-A-Foreign-014-FOR.pdf	07C97CF2DDA1F8441F6119A580F651DE2CEEEB6000522DD7102E8D3914EC1B13D19295C675666838B2B92EEA699B47381A344779DDBE5C5F3C889C5E4A8C61EF
069366-0580418_KUR2C06US-A-Foreign-019-FOR.pdf	396EBA3701CD0F9855E3D0BA9E1C27DE12429323B8ADFE7B2EA5ADC80EC19F687BE5B0919111A1C869E527597664F5FB0DFA7B9C97AC41A760076100DA16EEBF
069366-0580418_KUR2C06US-A-Foreign-016-FOR.pdf	184A1C5FEB5A980F0527CC834DB59EC33D97AA8B16EF4D661BEDA9A8FBB29D607818450F4E30E8CF16F90E4F0DD006A5BC22E7641C84996985A9F38A3EE215DF
069366-0580418_KUR2C06US-A-Foreign-022-FOR.pdf	21279E3BADE85D345EE15DCE7F32BF4B019E455223CDD77DB1ED1013A4812054F9AE43701FA762C76653D8BE6CAA0D424B74D472F627CC83494D6FD2EA7BBC99
069366-0580418_KUR2C06US-A-Foreign-023-FOR.pdf	DE238943278425773B30B48915816C28AB605BE2CFBC3782001C2912CBED662E79CF185F6940DAADD1D73C0055F414265D8CC2260327D361CF28C7A108A9EE03
069366-0580418_KUR2C06US-A-Foreign-021-FOR.pdf	71CCD917BF6EC08BA5BB4EDC32D77DFF090FC63744CE9FFE7E7F9788567CDD52334842C6A710BEDCA96DED62E626E3315F217E4B6CCBACC4317AB207651A1C6B
069366-0580418_KUR2C06US-A-Foreign-026-FOR.pdf	1EB85065C421EBBA51DDFA7839396E292862D1D5849FABA6522F74652FB4CABCD4908E6DC4FD7700CA34F1D47F70AE54EF2F09A3BB4BABC82A1D12DC25D0ACA2
069366-0580418_KUR2C06US-A-Foreign-025-FOR.pdf	D7428BB62CC61C66EE26965E0E2D2FD801D2486A684C16AC77E74B8216ED398C0489CCE951BA5D4A5A6537C57A076D08393E04ED81342D32702B447A88FA1934
069366-0580418_KUR2C06US-A-Foreign-020-FOR.pdf	2CE228DF7C266894160BC0C16D180CF2BD7378B863ED2A3320A57D019BA7A297FBB500FFF9C0A11CD3F6DCCFEC9F974B6641CE576F19304883701E6E4ADEE10C
069366-0580418_KUR2C06US-A-Foreign-017-FOR.pdf	281A361C6D1625BC6DE0AF756EDFB7C0CB01365EAE9DA613BDB2F463CFE6F3AA74408A24AFBA80F272F41AAC573040800846097A9640CC75E419976F5663D632
069366-0580418_KUR2C06US-A-Foreign-024-FOR.pdf	976828016715EDB56B1AE8B1D805C3B7033DD9B538C590BCA5EF86AADF5519AE4E3F33A0E409F5F8169243A17CD4F51C44596757C7379F73AFAA9EAF4EE1CE77
069366-0580418_KUR2C06US-A-Foreign-028-FOR.pdf	9EDD1C2564954F27FF4AB56BE093DA35182B84134C7E733631143899584365EBFB138B0C68AE1A7CB86D9F44D8C465B25BD4B03B55296D81C40B3D2809CF84C3
069366-0580418_KUR2C06US-A-Foreign-029-FOR.pdf	BC0F71A7D6E4672B812459C11F6FC7D99C128705328261C733880EB8FE52BA4F87720C2527D5A37F787C90936AF489419D524E95970DC66F3939CE7E3FBF3A40
069366-0580418_KUR2C06US-A-	C88D531E70366EC7238F99D4A8354548FEFF69194989B382E4FF86105DCDA59DBEEAE46B0AABEA1569A010F498A2A05FB7

Foreign-027-FOR.pdf	E0F6F93342D584E35153EE38A76737
069366-0580418_KUR2C06US-A-Foreign-033-FOR.pdf	C203BFDEDDC4BE384CEC12DA781B51CC426545975D46E2D16E6AD3D60F5FC539FF63E6223B66162D0E487374530BA17346C1159D4E80DCCF93F25A11FA13DECB
069366-0580418_KUR2C06US-A-Foreign-034-FOR.pdf	7D0078A65D6A3FC255D1F5D34D44B255BDF84FFCFC5EE56B8385A915CD7AA599791E53CC5CB8A2DDFBF12966C576564710714FBD9D307CC37FE6A0E1C1230512
069366-0580418_KUR2C06US-A-Foreign-037-FOR.pdf	A0DF74CCE0B654E92D0995FF644CA1B5E52D8C165576A3ED2383FFD382BDFD3FE3A44F7BF7715C732D25690C7262C398A8642DF1EF93C8044DED8B9B32B6923C
069366-0580418_KUR2C06US-A-Foreign-032-FOR.pdf	71036FB7EA56146A950DA60257BC3897BF98F2C4BB45624FA487717FB613C6F1F5CEC5406F696075BA6B978931590BC102DAF5DB1C44E29D1065F4F32D55E843
069366-0580418_KUR2C06US-A-Foreign-036-FOR.pdf	FDF6C3D37C2E613AC1718F79C5EADDD8D786F4FBD22AB126F8C660F2FA1145990FC8D16393C00D2F4F2B9B29E1E4ABA59EF038762A4F296008399261F7C098D1
069366-0580418_KUR2C06US-A-Foreign-038-FOR.pdf	4E9FF8C03AC091D8F719681E6D831B46CED2AA646B60469A7826EA09191BDE3CCCE1E7BF3130BB091D903590AD193B0AE883C9F06FF61793B3AE62AE81933141
069366-0580418_KUR2C06US-A-Foreign-039-FOR.pdf	CB604BB65B71D6F1E1254405211590E54985C4C320FDD9664CDA2C98605757E5C4EE71BDFE8F588C2E8BDFA8FF60CC0E813252AC940691925597636AB4957751
069366-0580418_KUR2C06US-A-Foreign-035-FOR.pdf	40F2BBD14E9BA45D1A31405DFD91478F835A7791E82B4CB492600075289C54E0D5F3A56FE963E0E887422E799C001D1D3426BD3491984B166AB2C308454FF14B
069366-0580418_KUR2C06US-A-Foreign-041-FOR.pdf	26B2DA0BA46413B6735A443198C39E1C98C066227D9C7BB5E312279C2FCE7E9B5A32234C0B08BD2F05540FA9439554EC63BB265A1BF38110AFB0BE4DF90C2637
069366-0580418_KUR2C06US-A-Foreign-030-FOR.pdf	2F7621BE9D1627CB09B24998AA7E651C7D86DA0A3A786D2A5734D75D6ADD3DD7FDD7552F2F9626F49C694AD81D76EB34B782AAE14DE2F4904645EB214DF38FDF
069366-0580418_KUR2C06US-A-Foreign-031-FOR.pdf	2141B7BE4FDB9351D87DED9C31FBEDB428FE561D4E008C1CD8908EE189BCF69EDAF49261985F77204943D07B53AFD7610B1912178E54B6224B66AED81496F315
069366-0580418_KUR2C06US-A-Foreign-040-FOR.pdf	C20B62EB04BEDF0C9FA458CDF6E28FF2A1DAABA7588D51D5569762E6AC6C6084226857D676BEE89DBBC354C67A19E64142DE2C513E29FBE5A27890455827FB17
069366-0580418_KUR2C06US-A-Foreign-042-FOR.pdf	875C32978076E2B2E2B5AE7AB89CCF8D787329C7C78E36FA6CE880CF3265997F07498D62C063957FED3897D51E4E058D8C5823BA4ECA29DD0759C463CE726ABD

069366-0580418_KUR2C06US-A-Foreign-043-FOR.pdf	0F37B5CACFACAEB00A0DA7C4B909FDD19B2A8E2697D0BEADB4E40FAD7B0E62D4623F0E06F56709A8D12FE305226359BF1BF48EA1590F8E005D6D88B8BF406A95
069366-0580418_KUR2C06US-A-Foreign-048-FOR.pdf	213B535ED8BF93E83B19B977F1251A66F75D10706EF518CCEA75AB51A56B33A3C5715D47C4339857C93650195FB0CFA773C8F0BA8ED66F379CB6804FDDC03B2B
069366-0580418_KUR2C06US-A-Foreign-045-FOR.pdf	7A2C0DB4BBA8536C9A1FC354DD8650DE93E9AABF2A6F5A6CA493B3A767999C27E0431C880FDD1371B48F89892BA007E12DC041BA2A3B0F6DFEB50E33CFE6DD44
069366-0580418_KUR2C06US-A-Foreign-047-FOR.pdf	9E68510863D5C044B805222671E8A3536275772D930FC061CD3E3F112896C3232F8F5B35CAC1E15699FBB32BC1049921F769AE97C26697799013FDC7FADD8F4A
069366-0580418_KUR2C06US-A-NPL-002-Other.pdf	DC45A321E10E3A4EBA16E7711F6FC68893CD979D4536C6AD0E70AA9EAF5A3828FC7EFAA3577F9E243E629E0D5A87646B2154167D7ED22088A216D2FBF42BC52D
069366-0580418_KUR2C06US-A-Foreign-050-FOR.pdf	E826181EFFCBAAC0439EB9004E12769EAA3A9CA1445F10B7150DECBFEE18CDDE9294533E73DC5CE6913B4C3FFE4C81AC1DF27B663B98C3E1A98519840AEDECEF
069366-0580418_KUR2C06US-A-NPL-001-Other.pdf	D68229DD310382F9DE5E7625F7FC66AB0BBBC265BA862DAFC7AFA7AEE019B8B3C653934E95D5CE8F82C2F3F40F7D9B99EC70AB64D6BD3B008C42BD149EF7958D
069366-0580418_KUR2C06US-A-Foreign-049-FOR.pdf	54318CC74348A8E82A8697BA0279DC13B73653BFDF5799B6BD8B13234FD320A1464C5774834D498E72A1552F692ED5B9F6E6F7F2EB690EACA765D58C60F9D1C2
069366-0580418_KUR2C06US-A-NPL-006-Other.pdf	74282D8B209E7D1D40DC68AE92015300C2BD7C168E3998A1265ADA0CFCA488CDC74320F9CB265DE33A49665C714EE5269A9A032A3E1849FE53B708EA60A29CA9
069366-0580418_KUR2C06US-A-Foreign-046-FOR.pdf	0614C2370DBAB62349F1778D23A96510FB1E5A4E22B53D7DC9C704B8497FD46BB5CBD0D63F7F5C9484ED3BD26D8081C5ACA87C34962D3C393A559ECED2054A7E
069366-0580418_KUR2C06US-A-Foreign-044-FOR.pdf	34B418733B3E5CEC305FCE700E6E8529CE1CD72A74969275870390D4CE81674424EC0196505B0B5085A044B886C67C39B856FA8D85662559789B9E5C95016789
069366-0580418_KUR2C06US-A-NPL-008-Other.pdf	491C076ECB3EE19D457FC60982F940696BFEE721F9712537E22A4726379A331CB744406CD4752D0CDE20200A016CE1A575BEA3E00A62B9896450436BCAB082DA
069366-0580418_KUR2C06US-A-NPL-007.pdf	97D1E9B0E98E597A3BD84E36144094DDCEF37F48F78E982D9617EAC4FA0FF00F7C581C64C816ACAF64AF594CCC976ABE3A3BA027B827F7368135F0121D1A353F
069366-0580418_KUR2C06US-A-NPL-	14A100B4E5B6CCFC34736648E1EC63B258B8C4898C10DF08ABDBDDBC6C28842AB3939AEDEAAD59507DE5BFBE5091A45

005-Other.pdf	2ECCCA76EC65A501F976D7E823C0355C7
069366-0580418_KUR2C06US-A-NPL-012-Other.pdf	90CA2CAFB662499E6703D096DF2C2D6F7A14D570DC0022B22DA3CCFA1E532050DFC77FAD158269D405DAA664F52BEAFC972DF7438395C5F341F34084A45A11E3
069366-0580418_KUR2C06US-A-NPL-009-Other.pdf	432E2C442E62A55E5C9B4D58EBEF3D5DEAF6362B79F2400198588034D4BFC2B1ABE4653A22A5B6965D4B7FB053C65E4B45AEE609C48288066FE1200DCF56247D
069366-0580418_KUR2C06US-A-NPL-010-Other.pdf	D7E4B8C4415238C3B188F994260373C88428C766DC2497028023532 3A551BA64B13B71E8F9539D0BF9D3074E9A1BE4484E0A4F655878D6BF5D7C8C3CC0E1796D
069366-0580418_KUR2C06US-A-NPL-013-Other.pdf	3C2CF238B3A826241646A8D676BE42BFDE4E4A3CBF82914852AE55111CA0AE0184C8316F984735AA227CCC74330849444F371DF896467762F42C12BF02C39C6A
069366-0580418_KUR2C06US-A-NPL-011-Other.pdf	BCD3256DF3EA015400F62092A9A99A99D66227228B02C80D753FEEF77BBA76DA11A1A3C0011BFEE8B6E370C6B10F4BAA7A255919B7D97696759B325FFA254B9C
069366-0580418_KUR2C06US-A-NPL-016-Other.pdf	A65E6F7E2BE0324E9238616F4591E1CA69A97F0365028C71C48801D77CC04D11A9F274FEB4A52B7873D9CB30D0D8338EF10619D73F3A9EE6B64132CA05AB1CD7
069366-0580418_KUR2C06US-A-NPL-014-Other.pdf	2F26534813F83E771CF43094EDC2F8CD7371E33722B45CD1C14ED3B44D77C0AD2620C014DF5BB3D5B0FD1F2073AEB57051CD4CE6BCE9F7E47256892A41A4C3B4
069366-0580418_KUR2C06US-A-NPL-017.pdf	9E746126990C48ACA437052D5CFA58E5EAD0EEEBB40AC2A1E7D579B4EA8734AD54B8668D383FA9593DC5EB0E18E365AF172AFF82DDFA4593DAB421F4EBD17702
069366-0580418_KUR2C06US-A-NPL-015-Other.pdf	FAA865C7F871CFA50EE98B84BA88D678A493D789E3021E54ED0492FC4344E3ADFC6BF74800B734525463F87C98B8CDEE2B0D5878C60F0BABFCCB0E6D89240929
069366-0580418_KUR2C06US-A-NPL-004-Other.pdf	9686060D214B99D554C7476EE16C982D32C08B025D85AADC13E5BF42FDE7E092E3D70255123E8867588083AB14BB7B23F64A5B8FFDD1308542AE295B35E4F1C7
069366-0580418_KUR2C06US-A-NPL-018.pdf	E543315FCAF99C2C8854DA566DBE7467940B98FF8031843460936D0C6FEAC698FD8575E0743E761526BB18D69F1572ABBC8AD52EA22B6D0007E378E376ED0A4C
069366-0580418_KUR2C06US-A-NPL-019.pdf	8C2E19995218C84266FE091D6FCA5794D56E53C936483E140DE8D4B3270D7C0504E6DCC30B7AD564E13AEF72DD4E4F071703C5CB3C023295AC365843FE155E8F
069366-0580418_KUR2C06US-A-NPL-020.pdf	42DA89AF75935079F1E35BC60D19237E96A8D1A1BCCAD418CC1894B748F3B167BB0FF6AE0DD4F79A4B2D50B8D8F44FE86F8F67B51526B60B18E78A107F16338D

069366-0580418_KUR2C06US-A-NPL-024.pdf	CCF5A85D5C7C63A2B1CDBB9BEFE0C5417B199C9522CBBF2A2B349E2C2D2761873010512681B4E4C25F8728A0D3DCAC70D02862615CD0503E192C0215D79F02EC
069366-0580418_KUR2C06US-A-NPL-022.pdf	EC3DEDEBB59C089D0327A5B34E0EA63F52572ABBBDCEAD0DF88321E98C752608B441591325AA22D0A0D0043281ACAABD661C7AE6D547DCA529BD4B540809DE9E
069366-0580418_KUR2C06US-A-NPL-021.pdf	3DC23A30CF410E12F0E293A5FC0F8FF952FFB4992C14C95D20E112107033E7CA7AAA72EE6CF5EA07DFE182E16CE7D6A0D2142FAE5CB1422D4F0DA3A1E943F054
069366-0580418_KUR2C06US-A-NPL-027.pdf	4AFB3B6C095CBEB8733F2A3DECDEEBFDE39281473AEBF6447EF920E829DE6F78ECDBD7C030781AA25A6D62FA6F79BF55CF6461D512BCB81878B1047AACA3AF05
069366-0580418_KUR2C06US-A-NPL-028.pdf	00C864FA0F9FF9AA6AE873F97D8334028457852203A383CEEE063CC604F79792FE2C1A7F777385AC4F10D4E661A530EE063B8464E0C0082F409EB92066BAFC1C
069366-0580418_KUR2C06US-A-NPL-023.pdf	CC245297C4220864352BC146922CCE14EB69868155695BE32512EC06AE179533ABA4B9BB4C9BDD76C34D4420182CFA21F5FCB00591D94BCF4EB99502C978A7AE
069366-0580418_KUR2C06US-A-NPL-030.pdf	25EF3F95EBE28062B6AAD2E790980960B726C0125A987898E0BD0FB6CC8839413228B2123412F622E5A2A10BDD5F8B479DC6B3F625D548B060B9E2B745B767BC
069366-0580418_KUR2C06US-A-NPL-031.pdf	1DD33BE1F660F7962DC5F6C8905C12294A18D8C841BB1CFC122EDBF25BADF1A2E8184A931488466875F29C094EB9D35E7B5921AC2CE63256B66775C2C2F889D9
069366-0580418_KUR2C06US-A-NPL-034.pdf	F7E63222894F5478B4FFB547E0AC6DEBC053F3F52EFADE54008331A6A085D0C2992B22D50AA4480315A30AF6C14C4E5124441FCE3A7631D797B8060B8CC9E1C7
069366-0580418_KUR2C06US-A-NPL-003.pdf	737D87F678BD178C8F7D17AB0542E3DAB2E158C9A19921F28ACDE9ADFCBD69AB85AE8F1294EBA1E72B4C75049F4D143C37AF75BE48A8FD04D69047C326ABF959
069366-0580418_KUR2C06US-A-NPL-033.pdf	E05A59CAFD7FFB9A28BA51F74FBBF73EEA949069F2454A323F516FEEA8083FE07C856959DC2D3568DEB14CFC2FBE11F998B3830B66C8CA20755850062F97C210
069366-0580418_KUR2C06US-A-NPL-032.pdf	C84488FC62B0FA5637670202FCBA7BC3D1E7D921A8AFB5FFC4708631E6B367C75DE1C652E7920952AFFDF894245BB2450AA74E605E580C3ED452AD9B9431C6B9
069366-0580418_KUR2C06US-A-NPL-035.pdf	67661C0FA48D8E54DE4FD850BF145CF7F49C49532A2B9FF73496EC0FF81180B25D984D8E0F0B9C0B60B4F4AB370ACB6A646B264193AA3C62A80BBD3DC03CD27F
069366-0580418_KUR2C06US-A-NPL-	FD5B5446212F8950DA194D104C121A43FDFB6CFFD5F174C775BB4A5A5A8BCF3D4AE1310FC5F79A51D68AD4365DDCBA23

029.pdf	5B0E2E671B190B52B5E0E509BBB44446
069366-0580418_KUR2C06US-A-NPL-038.pdf	361A6894546BF22C1A2BC1248DE1AB8E050E0CDDC0B9FD40E6D76DB700C2864DE2104D70DF8D7663D71F7143E2AE50C6ECDD831A6AAC08465191876F507C3A88
069366-0580418_KUR2C06US-A-NPL-036.pdf	52DDAA67B1E86D5B60F7B3F37870A517B7CFF06D6673528807AD59F45EA3B8439D1A0BAE7FD6749EB3A7D57EEEED28EC1B671132C88194940A2F0FBB42F11F75
069366-0580418_KUR2C06US-A-NPL-040.pdf	0B1193A0B722DFE0633873E47C2199E1E4A567E7D046B9C74F500E5BA8363D57D19560743B49AC4EB6AF3B2DDD58D176CC6A13F831156B5864FCA0ACECBEC06A
069366-0580418_KUR2C06US-A-NPL-025.pdf	87DE1EB677333F251344672861AD75AF87D11C494C0F469DF6565489270656313 2B5FC4E0A8AF74987FE97FF3B77FA83E032FE4A297CC488B7BF765E1AE62BD1
069366-0580418_KUR2C06US-A-NPL-042.pdf	9C9137C719C8D2648E38022F99E7FF4384BA2036ECD83FD2BB40E148AD9E6C20EEB9678C8A06AC0361753E84E7A2F22BBCABF7DF682124F60B32F4EFD070DFA7
069366-0580418_KUR2C06US-A-NPL-041.pdf	3D8D00506512ECF4F632CD82E1ABD05B605EDD181C55B6F5B9DF97EFF995D9D7ED5DA8245EFA616F18083EB4C8D2BD225ADBBF165D577255C5C05DDBD50AEE24
069366-0580418_KUR2C06US-A-NPL-043.pdf	89AD11F8524CAF449489D1C7B4C6AE90D560B36CA5B4A13907AC2767277D9810CF8FB770D66DB559866953E6088E7C681F2E34B13017B8E8A7948E5CEAABDB6D
069366-0580418_KUR2C06US-A-NPL-037.pdf	AC238C6D6ED9CD2FFDA33083CA12816C563EA5920D2ADEE7B432E27E462FE9E1FCFC8CC8B3DCFDA77DFB543B54B5FE79BBBC71D226B225232C61D35D8FF83DD1
069366-0580418_KUR2C06US-A-NPL-046.pdf	5BDE00F43AF6D9F9D9D3A661688ECE6F405F03F094B0155BBEB58EA7FE3554BFFAA450E6BF61E7FE83E1FBC6F8D96A4A64DF3DFDCDBF9A668C3BC88BAB579334
069366-0580418_KUR2C06US-A-NPL-047.pdf	4561DE8E2BE88692727D104B8B516466D7783132BDEB00892D9B8DB9E86306954995F63A92B70FABAB3FF41ED9A04CD9E9AFA4FA30DF118484235A3A0264E151
069366-0580418_KUR2C06US-A-NPL-045.pdf	58960B5C010BAED038BDB4B9C1830FC3C5E257F277154194398F61F257989358009D3788D3A866C1F1F54B57BFF8BE17653E2DD0E5307ECC3AB9D33AC1EDADD4
069366-0580418_KUR2C06US-A-NPL-048.pdf	1574A0ADF9554876D678515D72E9850BDB0CC5149BF4AD045BC39F9EF515F37547AB10FDA1880E3034C6BEC768FFCB2F6F9693C748B094BC5A57CB08E680049A
069366-0580418_KUR2C06US-A-NPL-026.pdf	00B0A7347DF98C2D64E7380EFF4893DD5DB33CEBCC8B64D8477D82FFEB10E9E9E6829D009838D1E36D0809FDECE52D5E5D1BBCC150E118D96B465CF9082382F7

069366-0580418_KUR2C06US-A-NPL-044.pdf	860F6B690511135366834A648B3E333E3B8298D7CBF176A29BA942287474BBBF519A09B427D020F0E4554A93E8C6F370B2DB64BC5D9D6E14B89AEB6818305866
069366-0580418_KUR2C06US-A-NPL-039.pdf	9F50D12FA91D47183447A27D48A4A0F7C9103D9326800DB0E032673C02DBCB86ADBFD7D2735DF682C24E1E3C67A8F8183A237C18D4AC9933A4B3B8DDDB4DE487
069366-0580418_KUR2C06US_Transmittal-Letter.pdf	CCE386BC89A767012D40BBA7E3C09101F7A4CE361BA5F9FAAC91C143D52439B463FA8F8F21562F0A73F9890205117A4C1F65D23D1D9CCE06DF23E9EDB8D6B6DC
069366-0580418_KUR2C06US-A-Foreign-001-FOR.pdf	ED4F3FF402283E9C49CFC3DED3A9F965FEB97EF051765B096712A4F881AE67B17B49731C308BC999F6E44A4ADB7004ACE81D44B1F9B8C7D0772F6FAFA1776867
069366-0580418_KUR2C06US-A-Foreign-003-FOR.pdf	764B190421CD735AD6512390DF99AF3DA4EA905F4A9D5428E9FB3379D51464C02845B890A8F63F29B060B35BD47F7AF9B62A499674B3AC184C372F2557E3022F
069366-0580418_KUR2C06US-A-Foreign-002-FOR.pdf	728A788D4B37FD12BE15D5EE6503E706D36289E3FFD1F4A2433592AFC3816E33A6D5EC400B2D946E5F58F98DD1344F679BE7F90F386CB76FBD82E4CCC4189533
069366-0580418_KUR2C06US-A-NPL-050.pdf	C6AFB655240F76C3B32C300992A94F305D313740DDB42DB6F61A3E09208B9FA5E58C3E6860238A9D9E88143F32A34A8CB0A5FC2536E675037AC9CD79B6490C96
069366-0580418_KUR2C06US_PTO_IDS-Form-A.pdf	3BA39822C24F451733142C07233822A065A280FE9BB77F07AB1D535D7EA8225F02944DA0C54831D378D26BDE816F64870F61821DDE08F9A165DA49099D01243E

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.

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. 62/318,194, entitled "Blood Sample Optimization System and Blood Contaminant Isolation Apparatus and Method," filed herein, the disclosure of which is incorporated herein by reference in its entirety. shall be included in the Bacteremia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteremia with clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteremia 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 in hospitals or other health care facilities, and
catheters and venipunctures are sources of contamination as potential carriers of these pathogens.

[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 arterial 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 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 .

[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 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 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 allow air to re-enter
the system . Sealing of the communication path is accomplished by mechanical twisting or other
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 blood collection tube
can be attached. At 714, once the sample has been taken, the device is removed from the patient 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 or 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 is 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 . Blood 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 pathway or is connected at either end with a clean sample collection tube 808 . The sampling flow path 820 can be curved through the housing 818 to better secure and stabilize the housing 818 in position along the clean sample collection tube 808 . Blood isolation device 812 further includes 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]

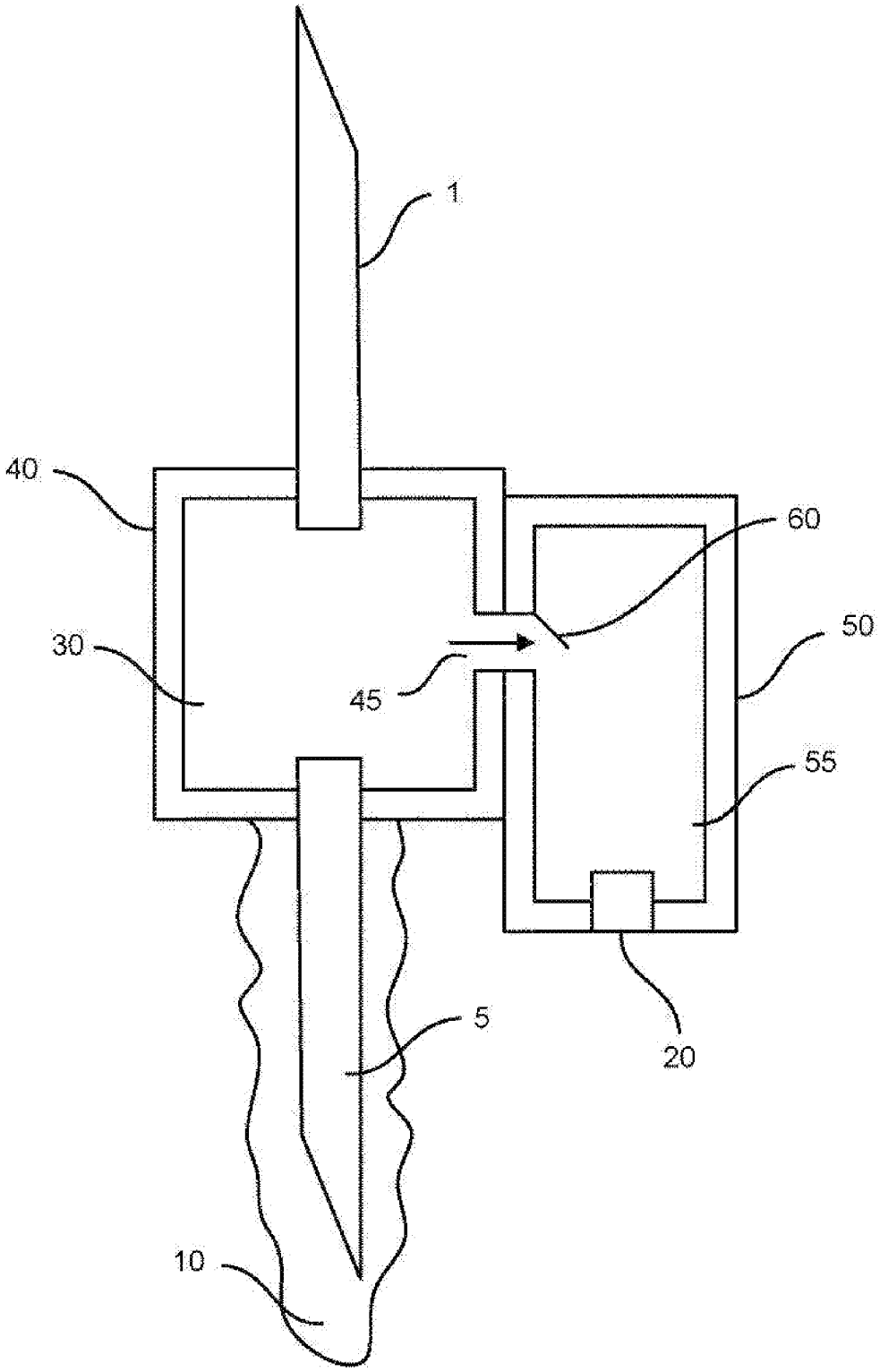


FIG. 1

[Figure 2]



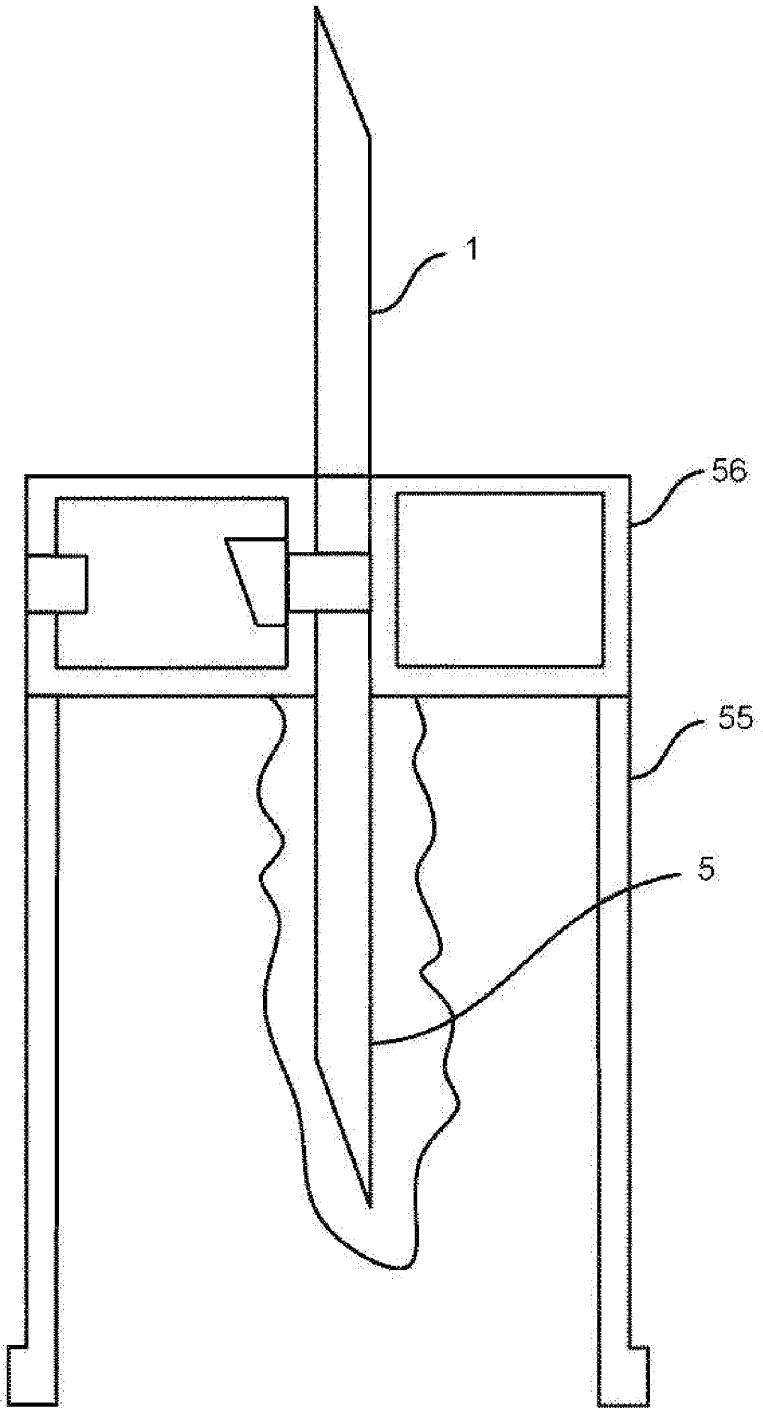


FIG. 2

[Figure 3]

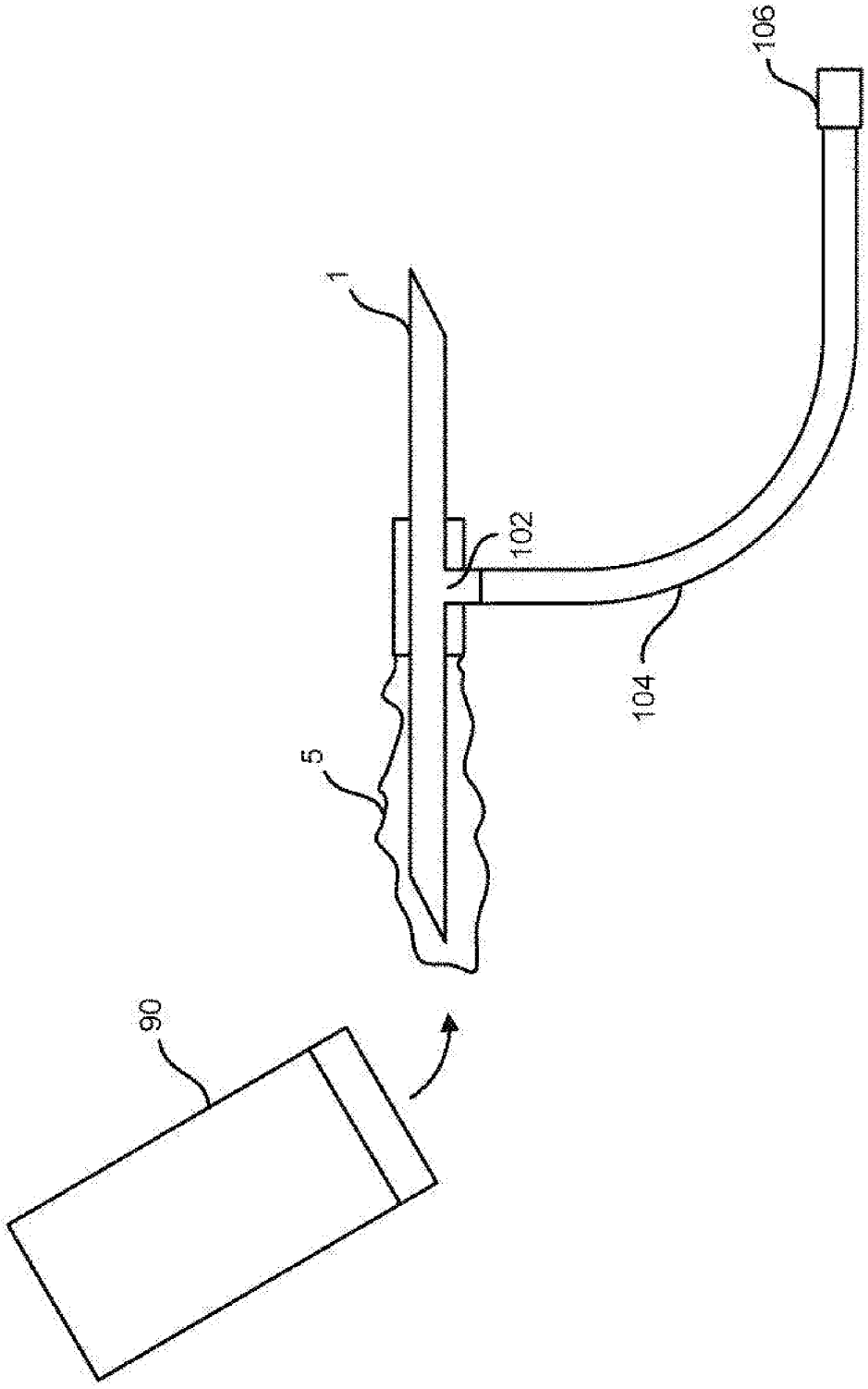


FIG. 3

[Figure 4]

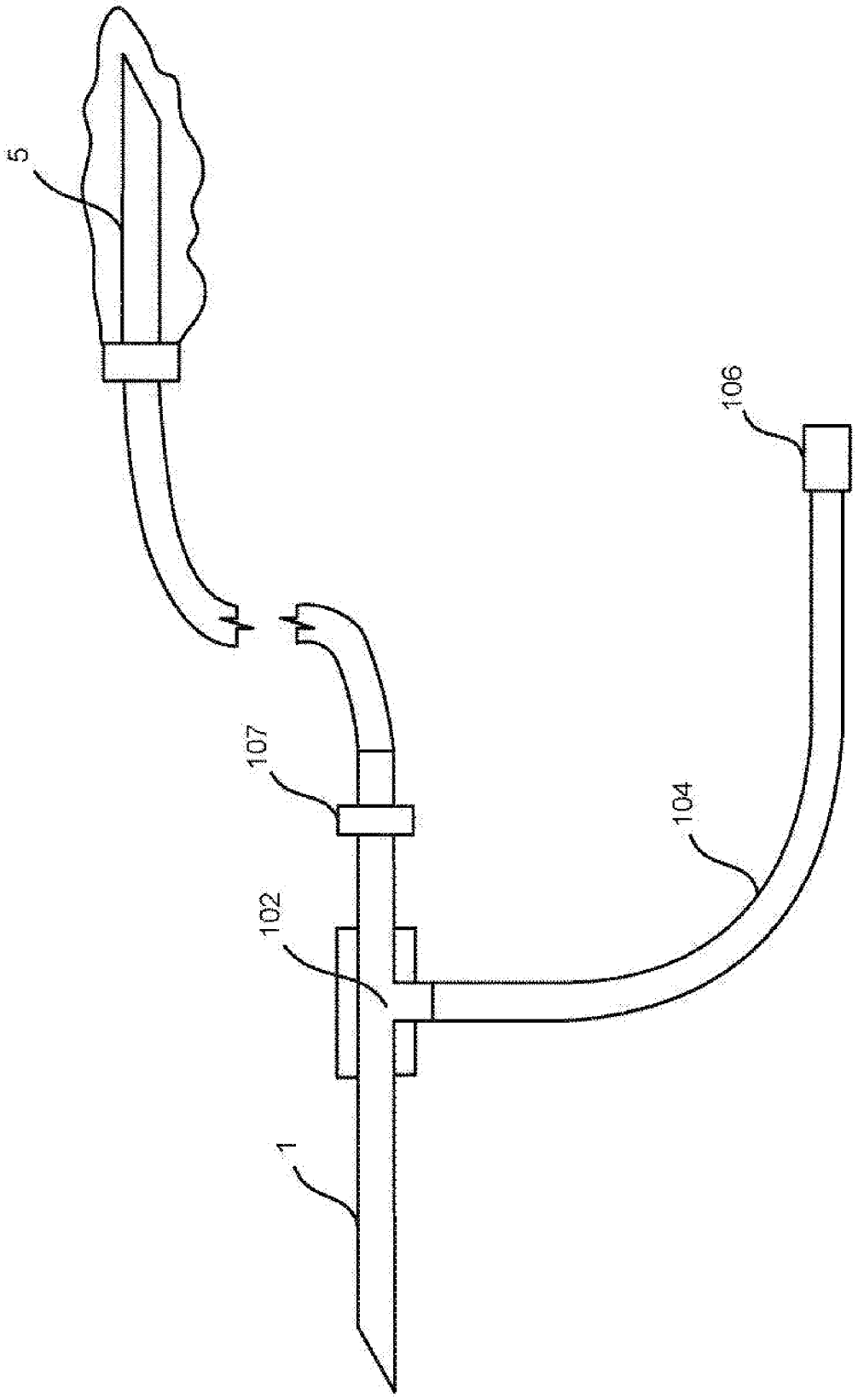


FIG. 4

[Figure 5]

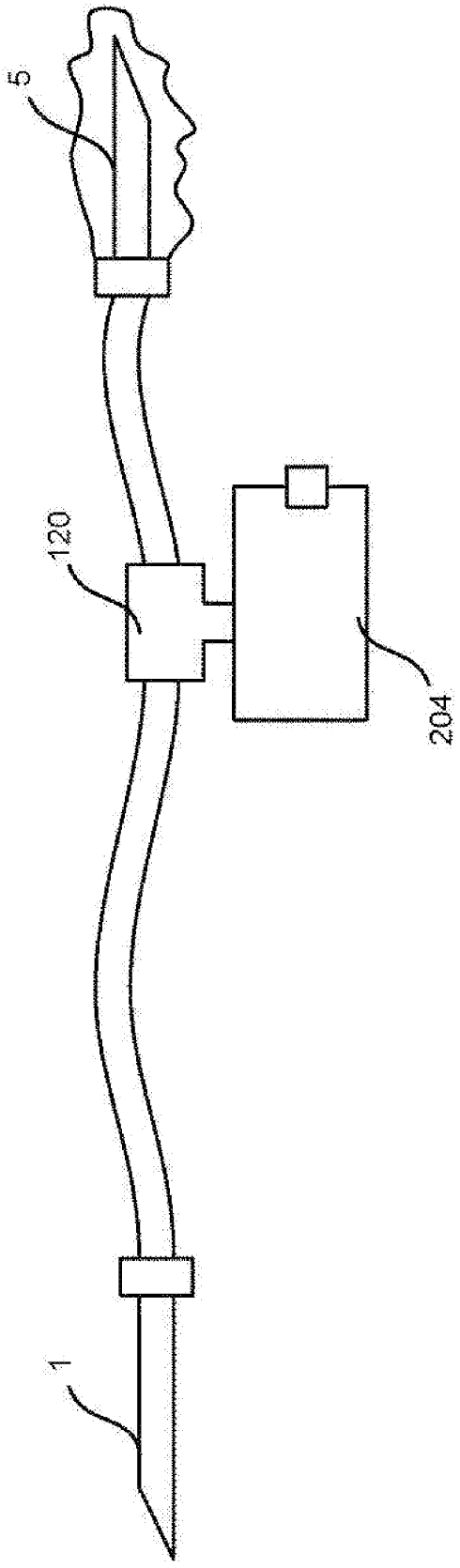


FIG. 5

[Fig. 6]

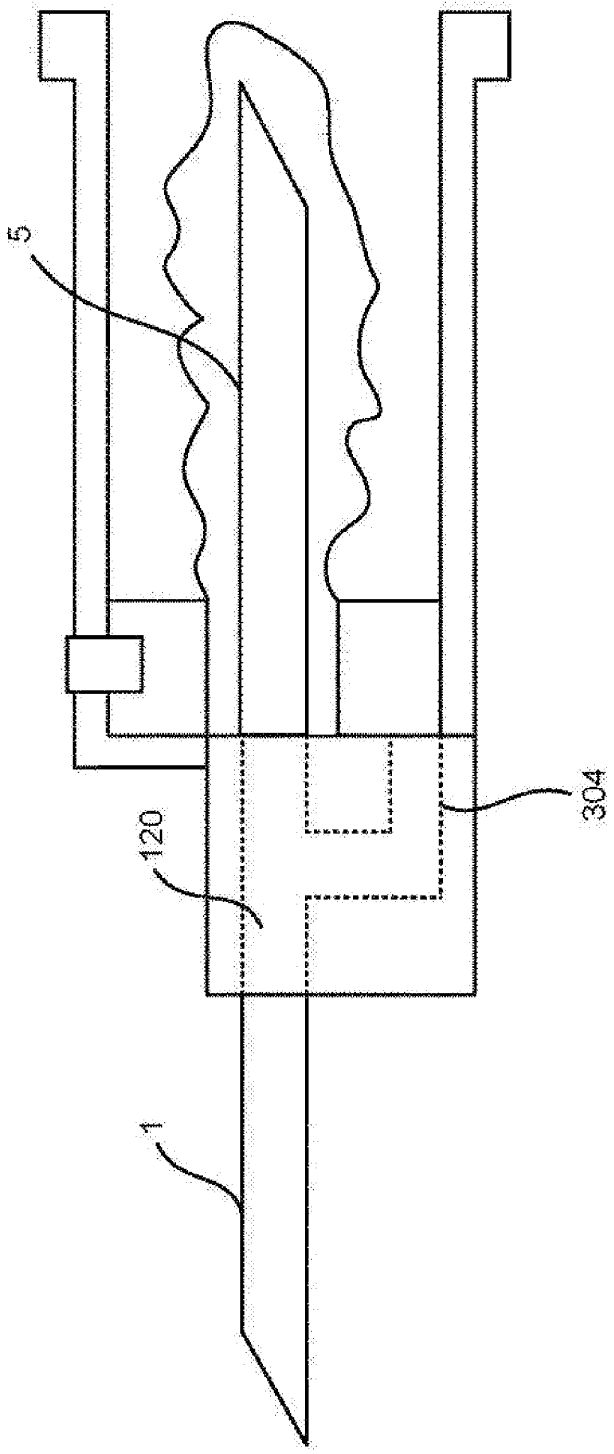


FIG. 6

[Fig. 7]

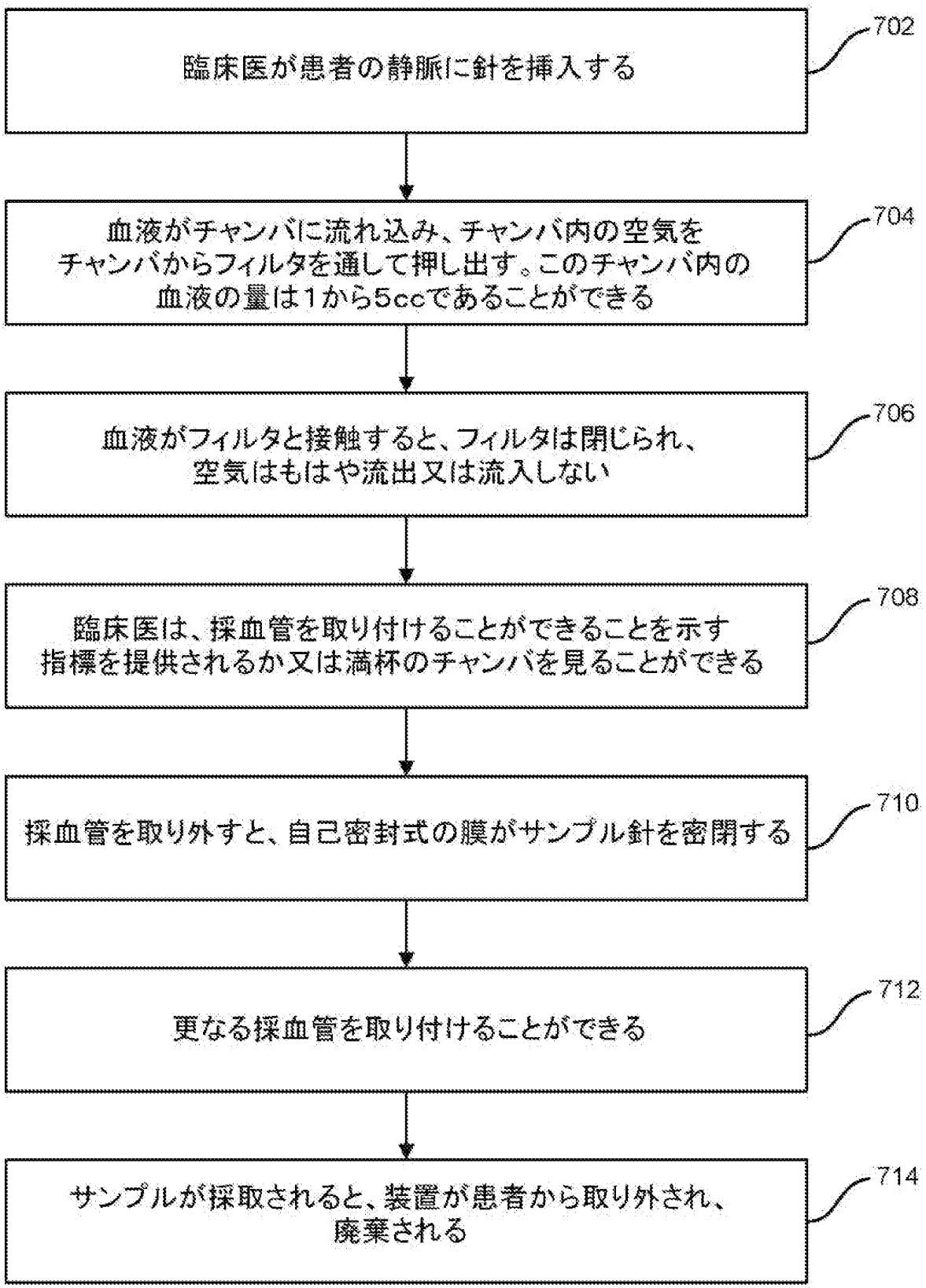

臨床医が患者の静脈に針を挿入する
702
血液がチャンバに流れ込み、チャンバ内の空気を
チャンバからフィルタを通して押し出す。このチャンバ内の
血液の量は1から5ccであることができる
704
血液がフィルタと接触すると、フィルタは閉じられ、
空気はもはや流出又は流入しない
706
臨床医は、採血管を取り付けることができることを示す
指標を提供されるか又は満杯のチャンバを見ることができる
708
採血管を取り外すと、自己密封式の膜がサンプル針を密閉する
710
更なる採血管を取り付けることができる
712
サンプルが採取されると、装置が患者から取り外され、
廃棄される
714

FIG. 7

[Fig. 8A]

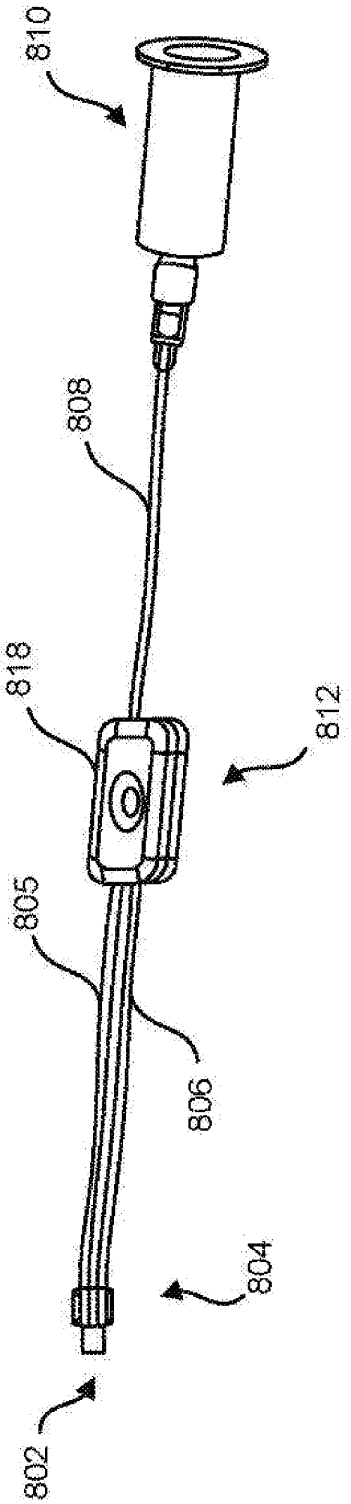


FIG. 8A

[Fig. 8B]

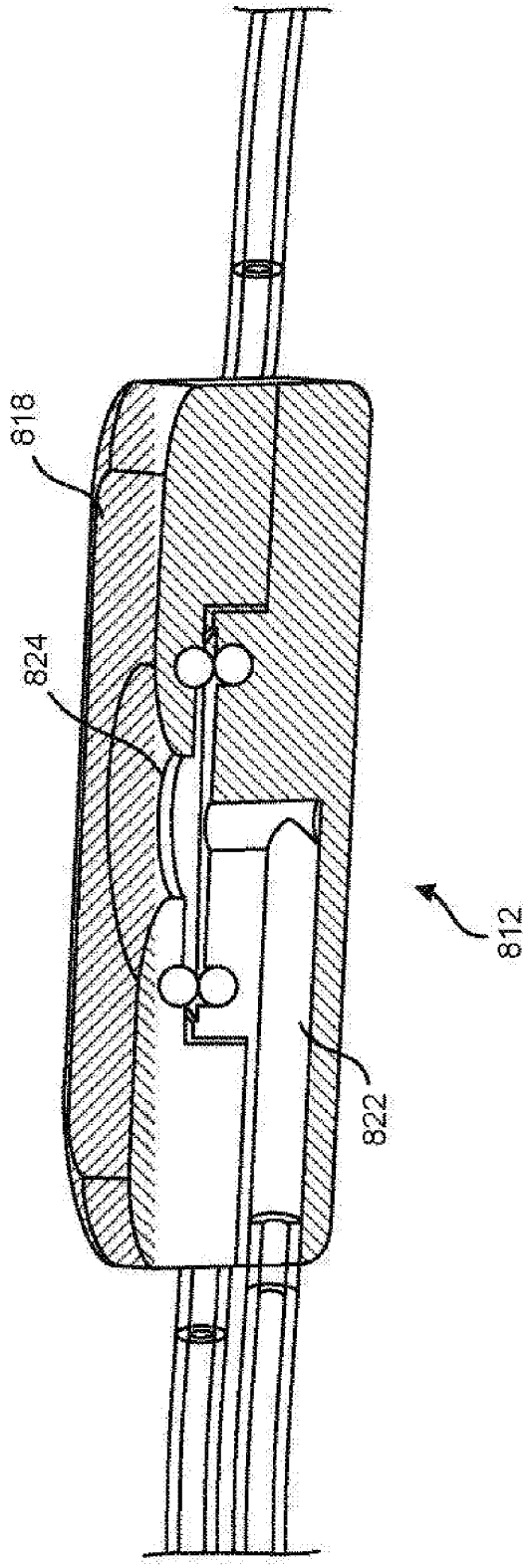


FIG. 8B

[Fig. 8C]

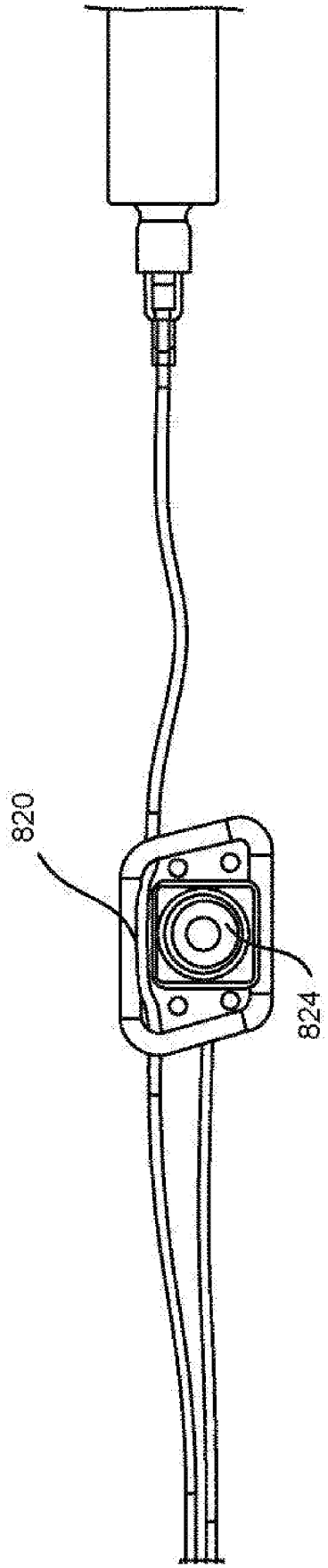


FIG. 8C

[Fig. 8D]



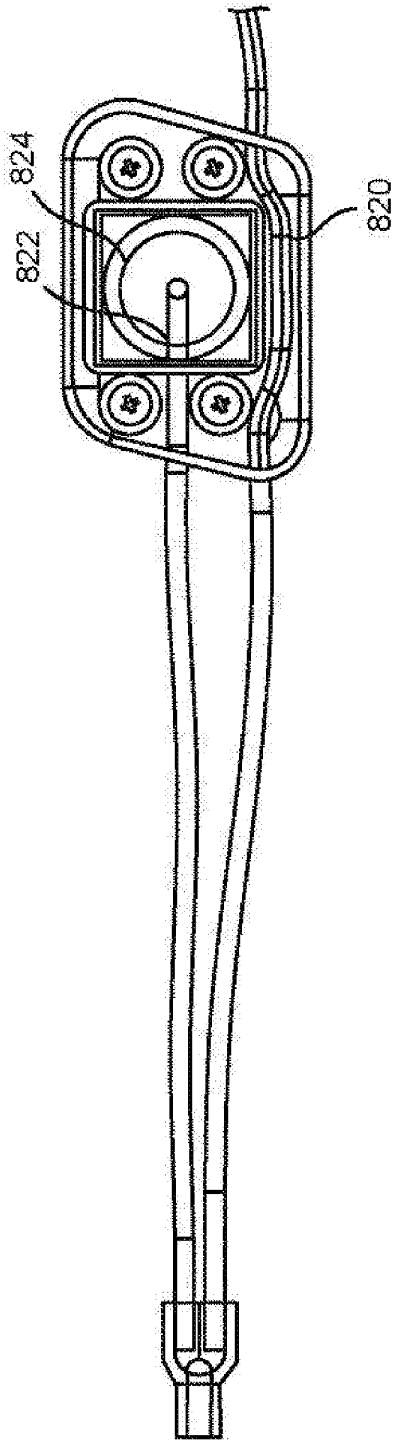


FIG. 8D

[Fig. 8E]

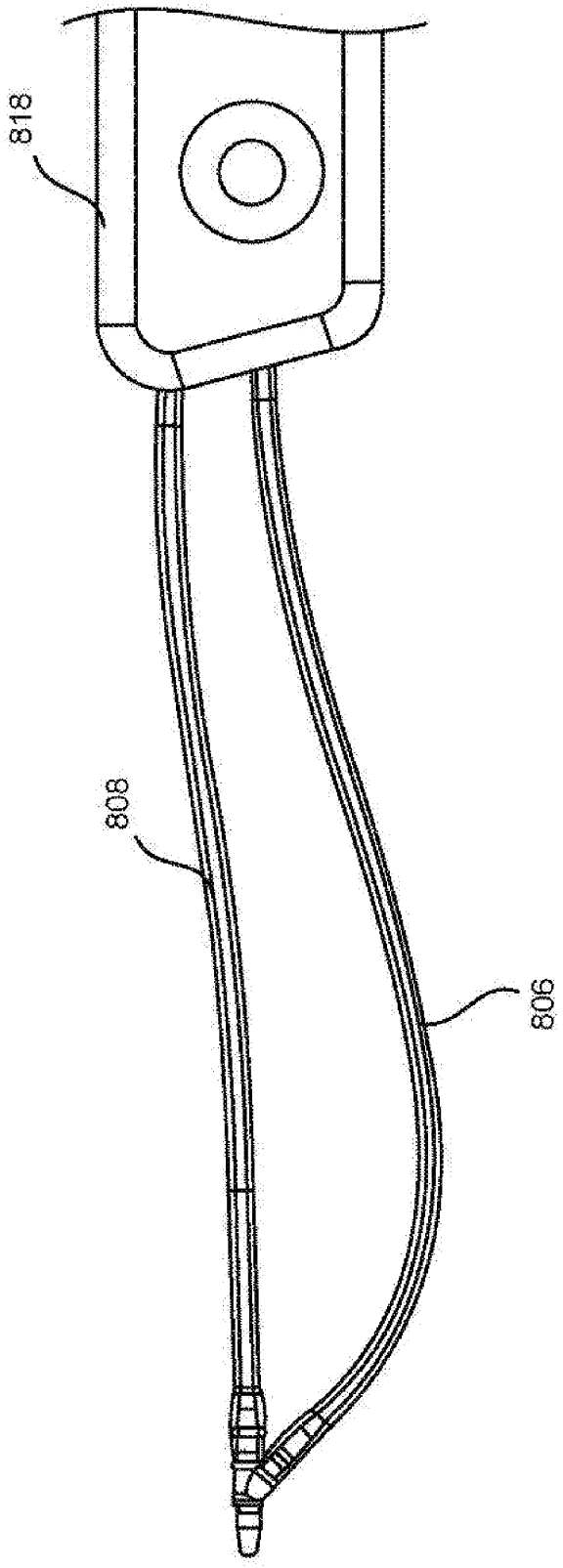


FIG. 8E

[Fig. 9]

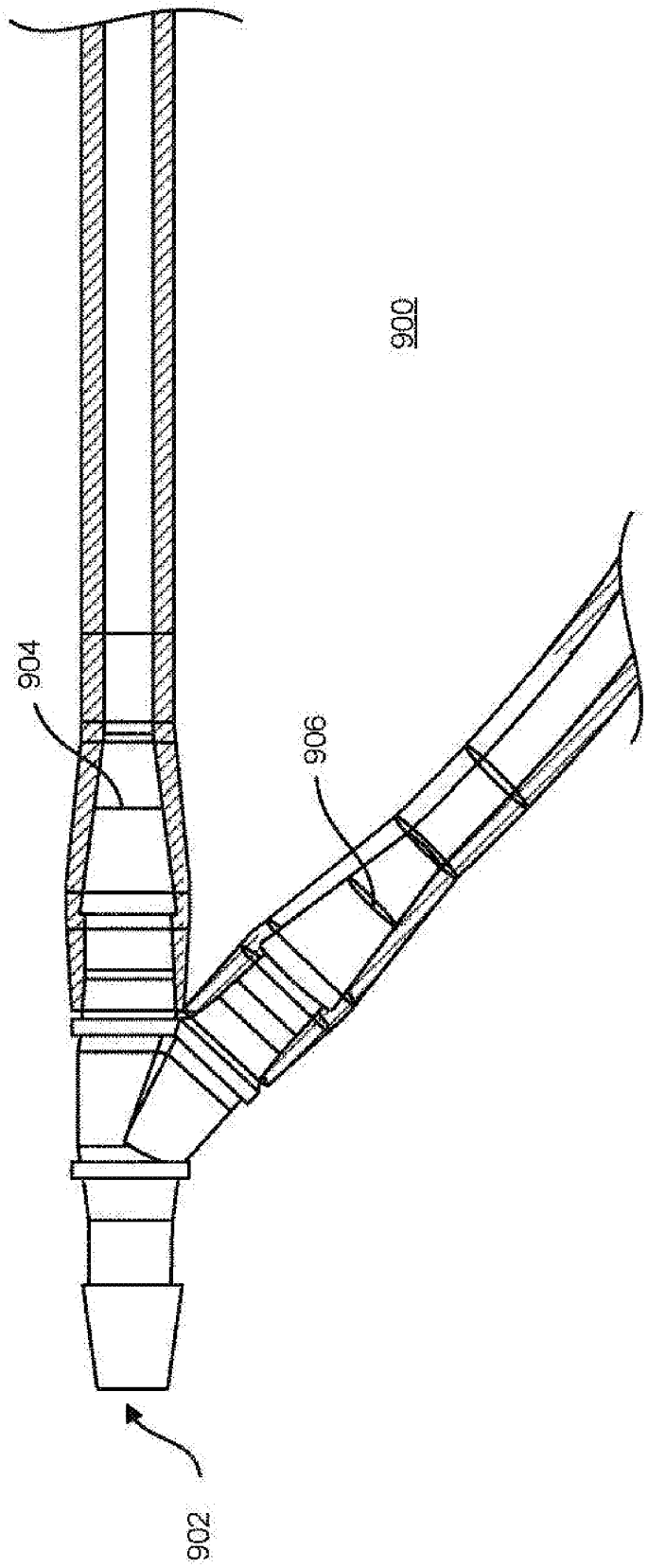


FIG. 9

[Fig. 10A]

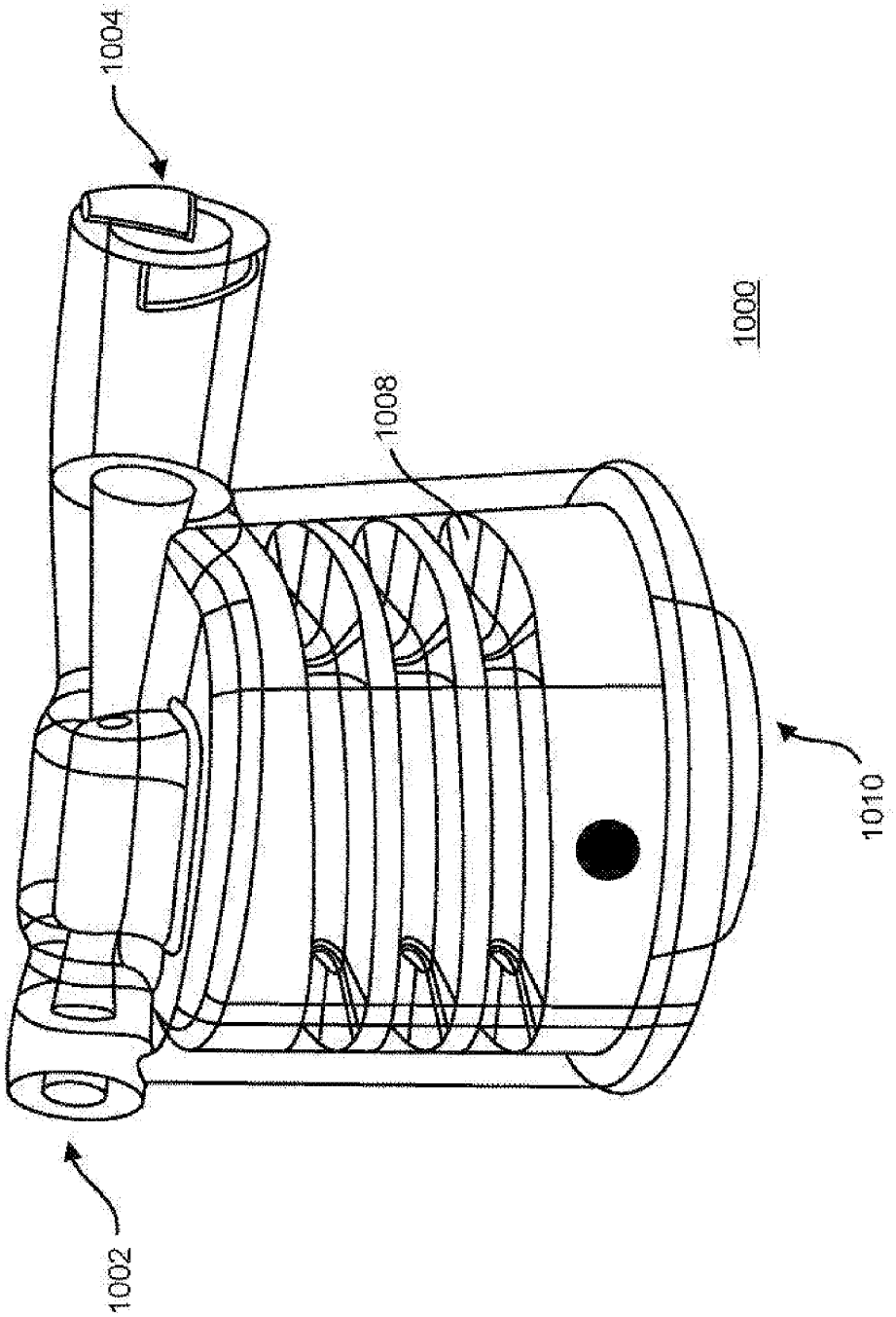


FIG. 10A

[Fig. 10B]

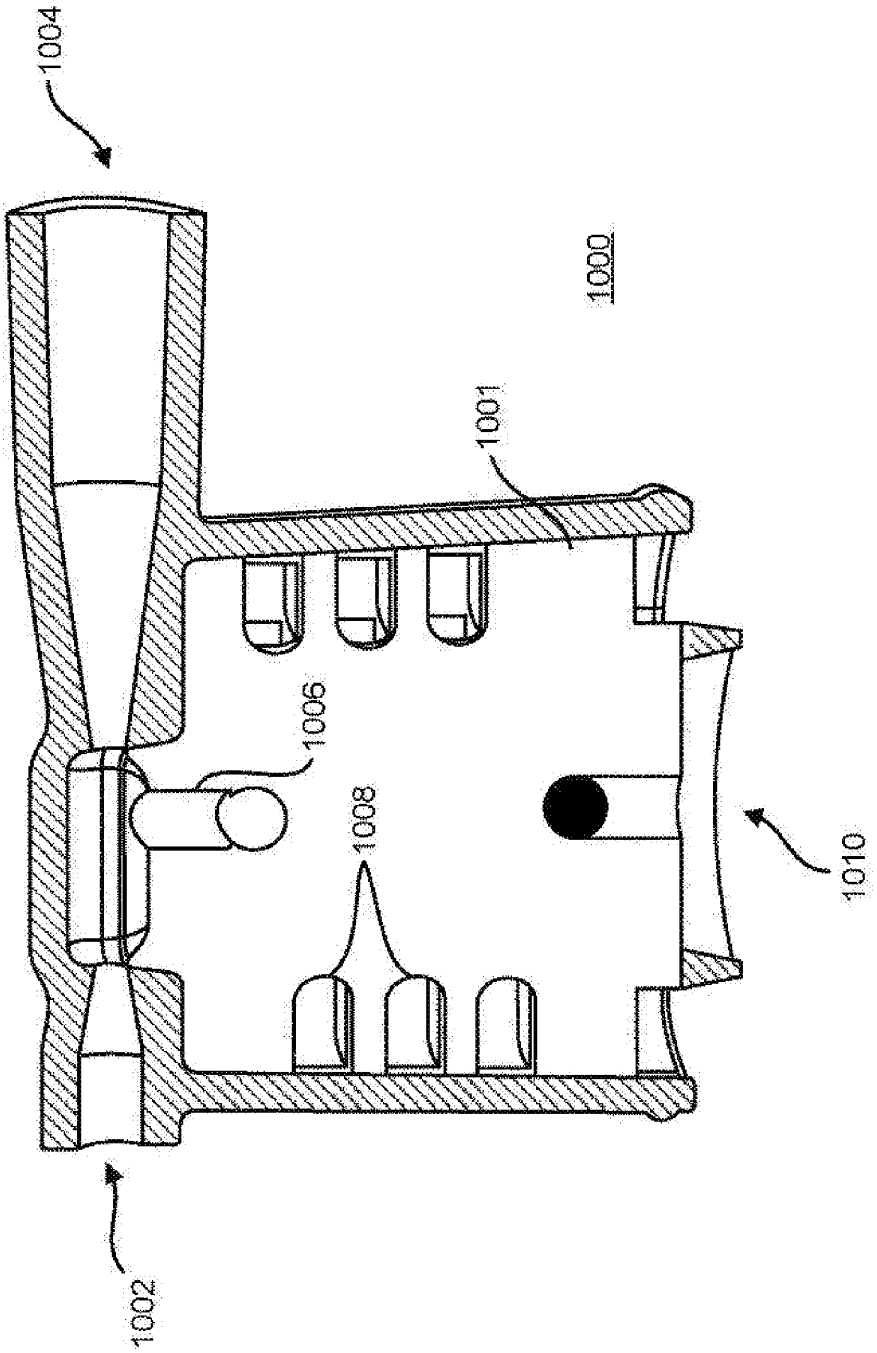


FIG. 10B

[Fig. 10C]

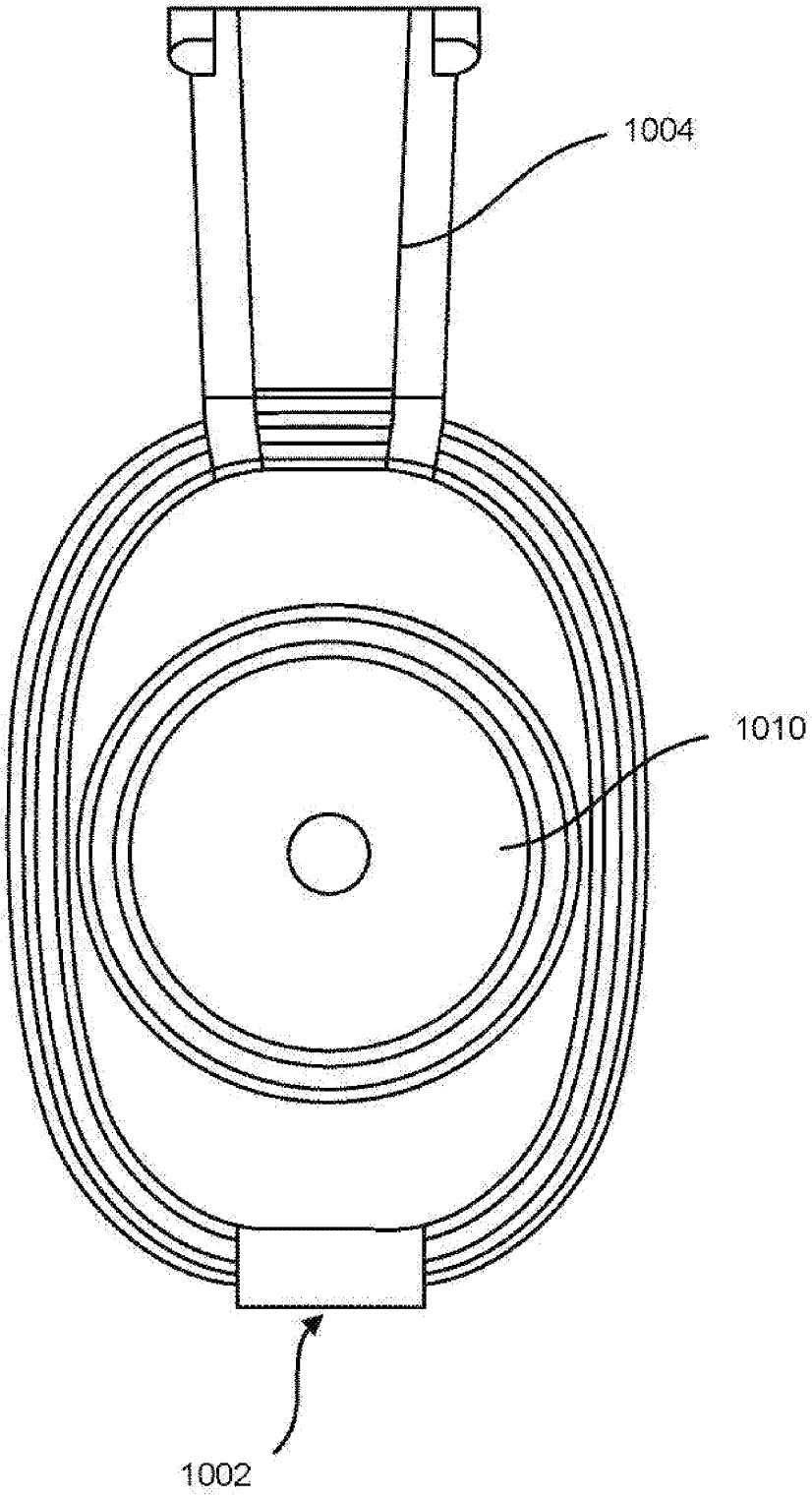
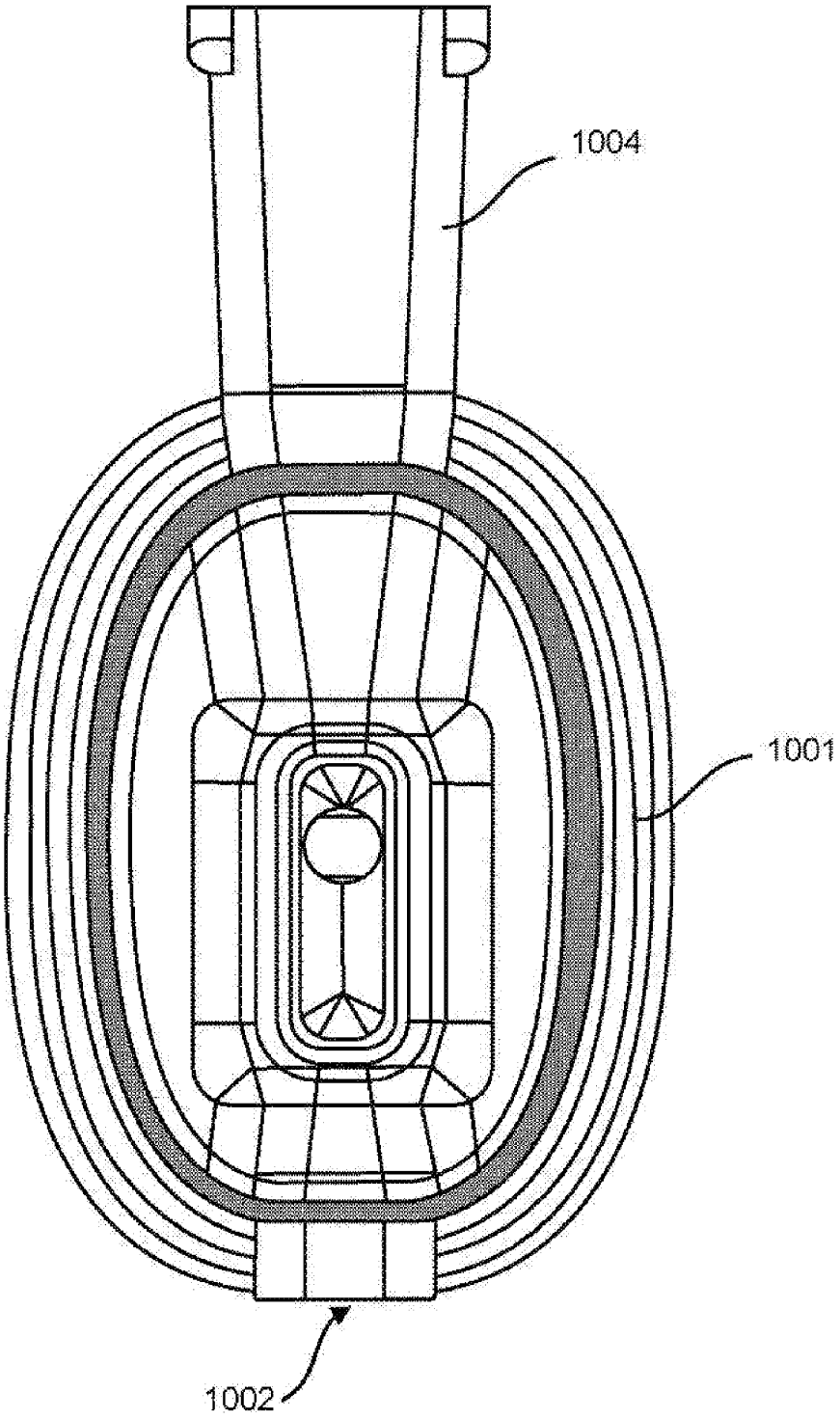


FIG. 10C

[Fig. 10D]




1004
1001
1002

[Fig. 11A]

FIG. 10D

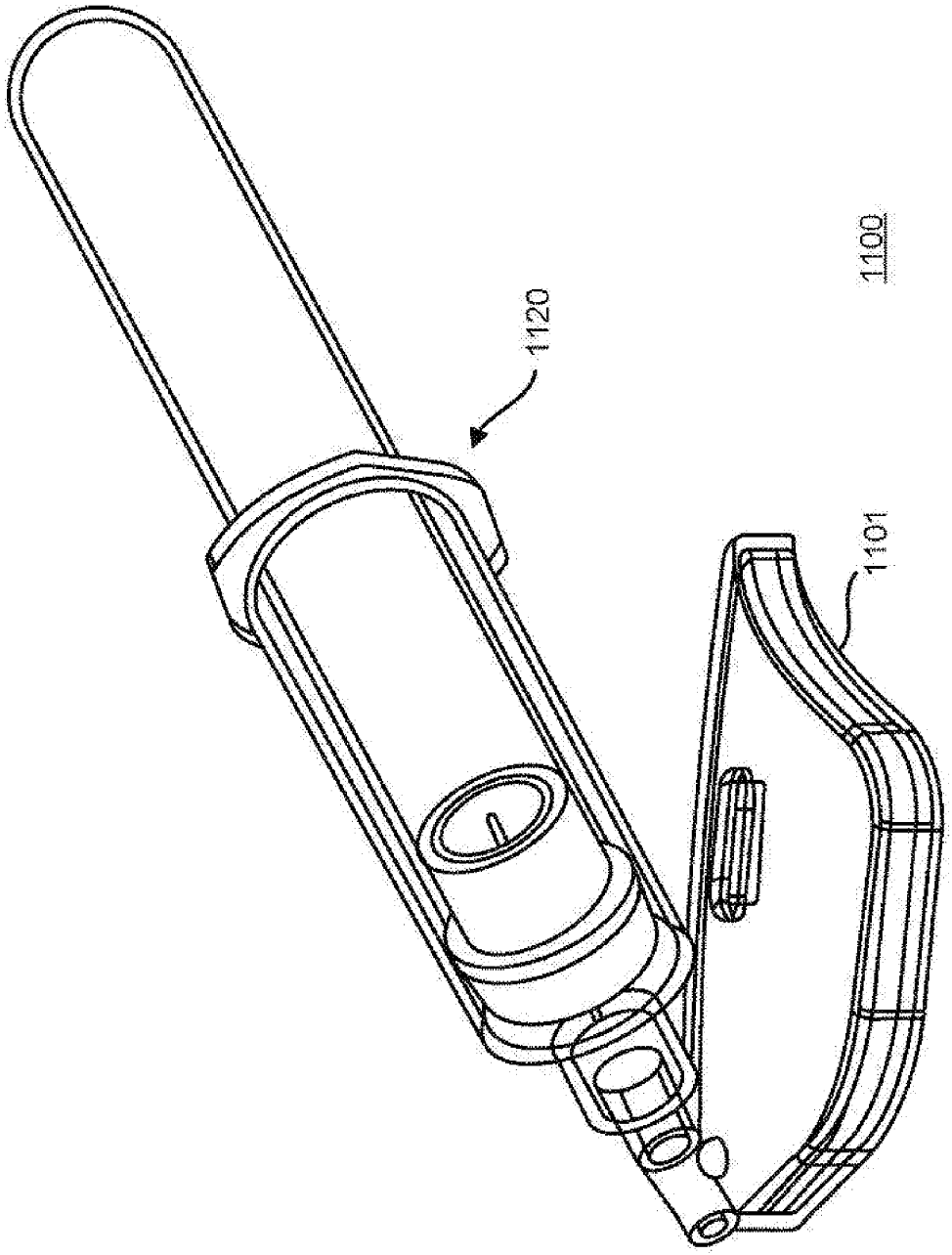


FIG. 11A

[Fig. 11B]

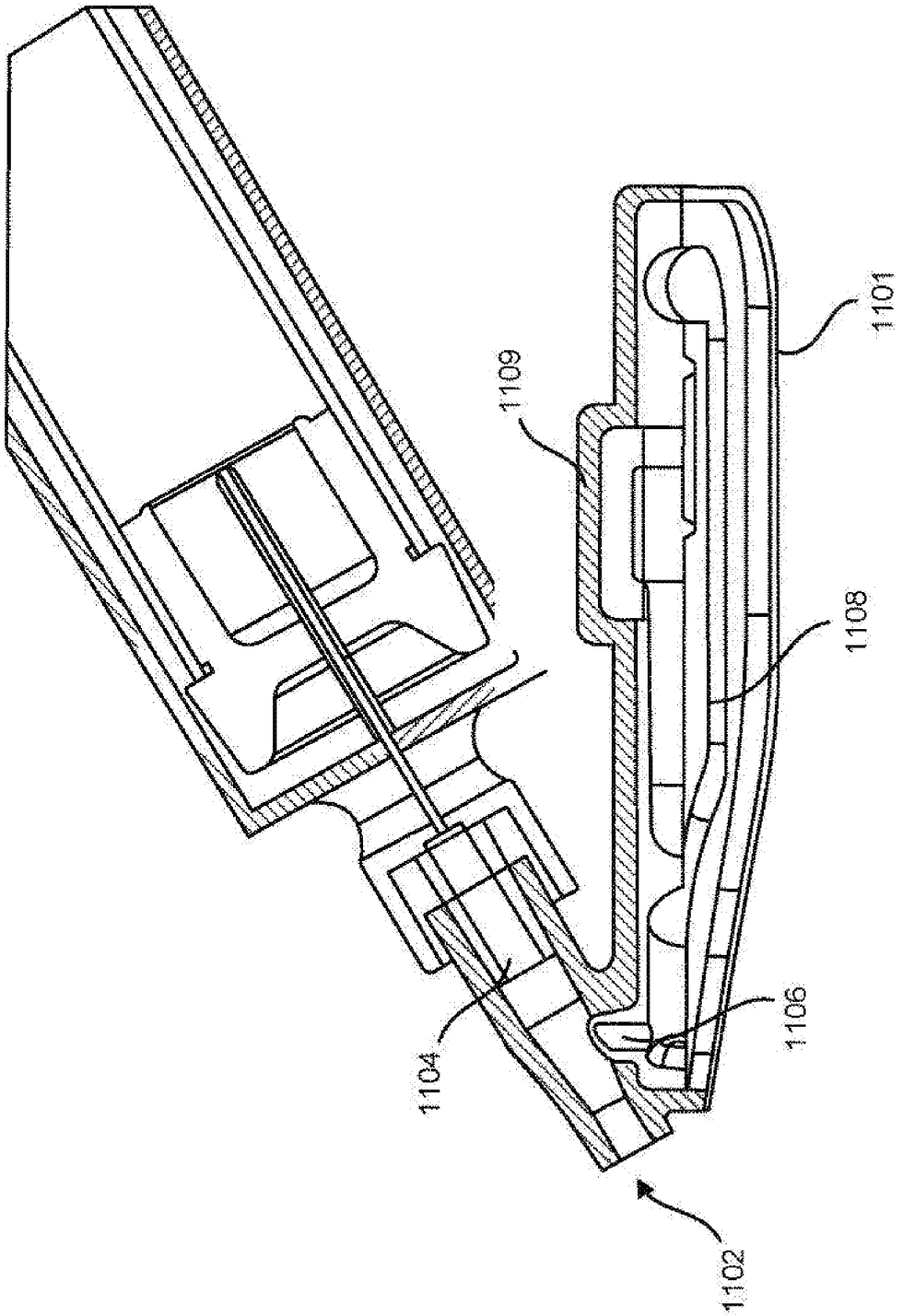
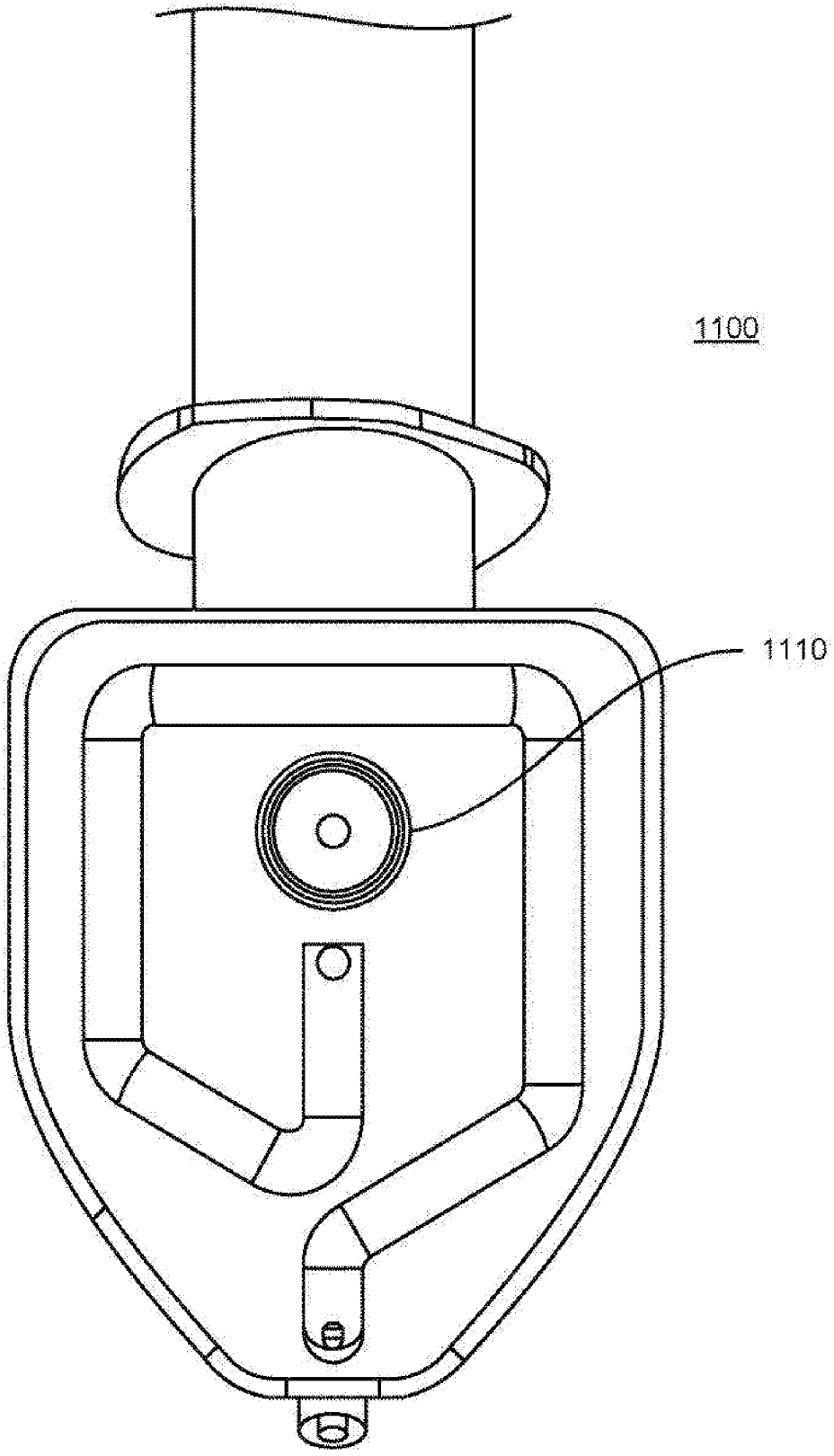


FIG. 11B

[Fig. 11C]


1100
1110

[Fig. 11D]

FIG. 11C

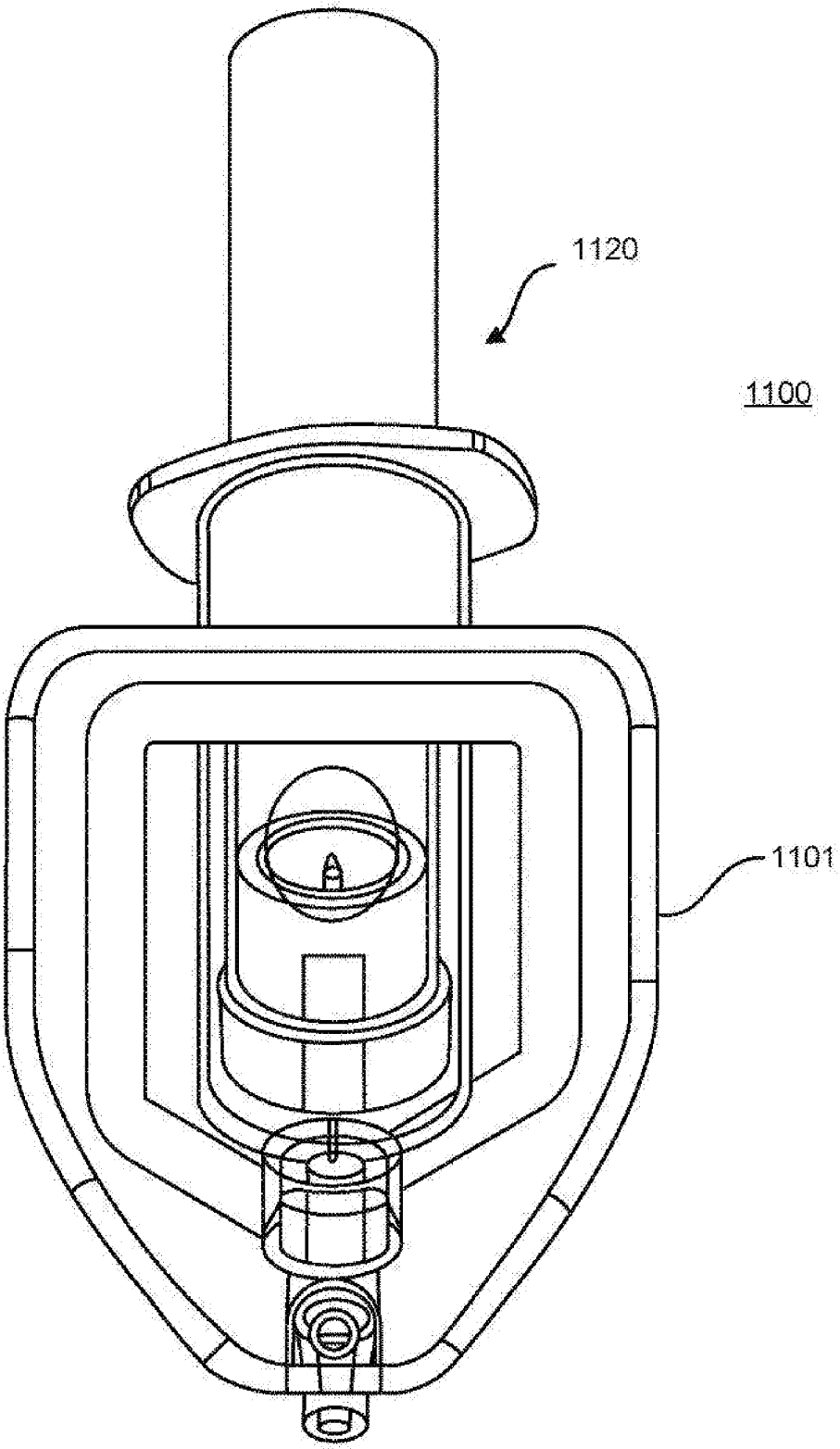


FIG. 11D

[Fig. 11E]

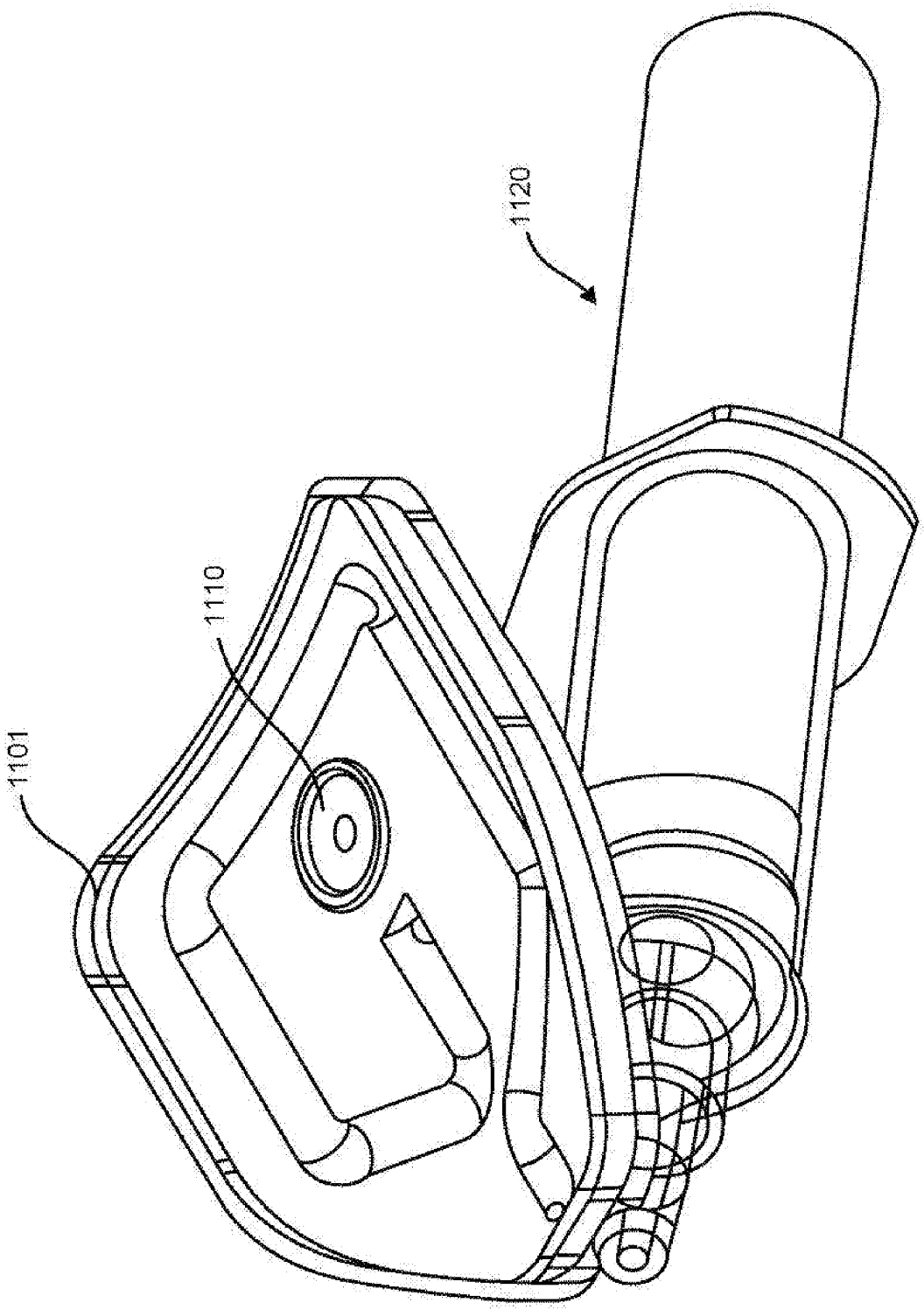


FIG. 11E

[Fig. 12A]

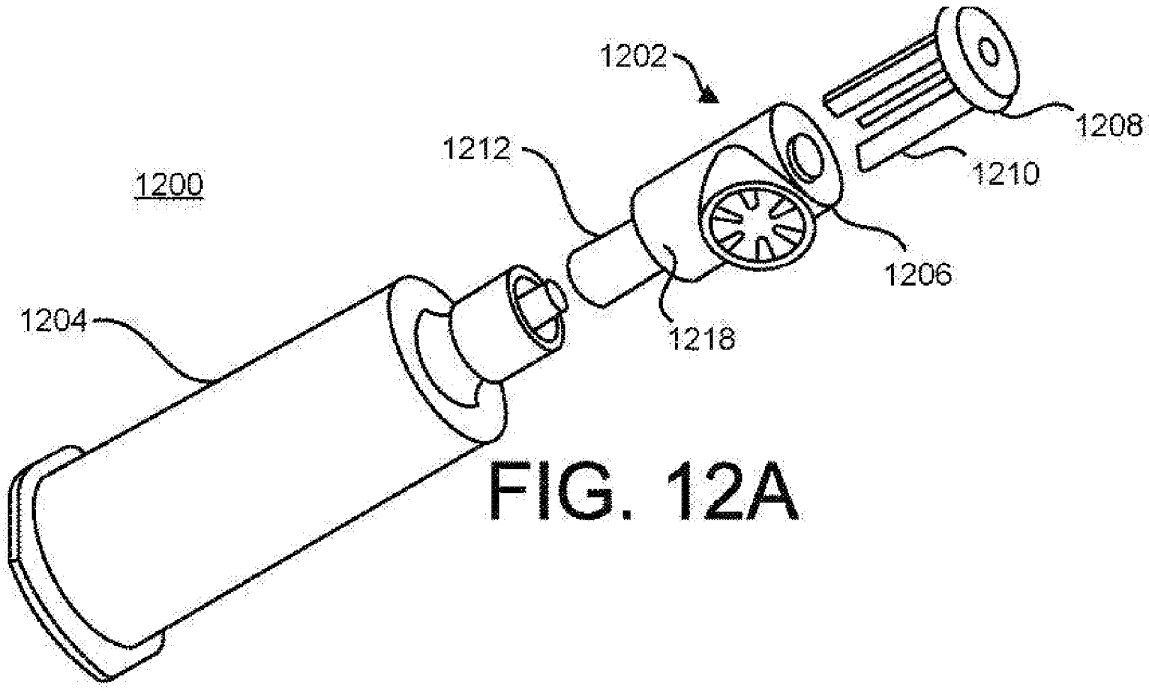


FIG. 12A

[Fig. 12B]

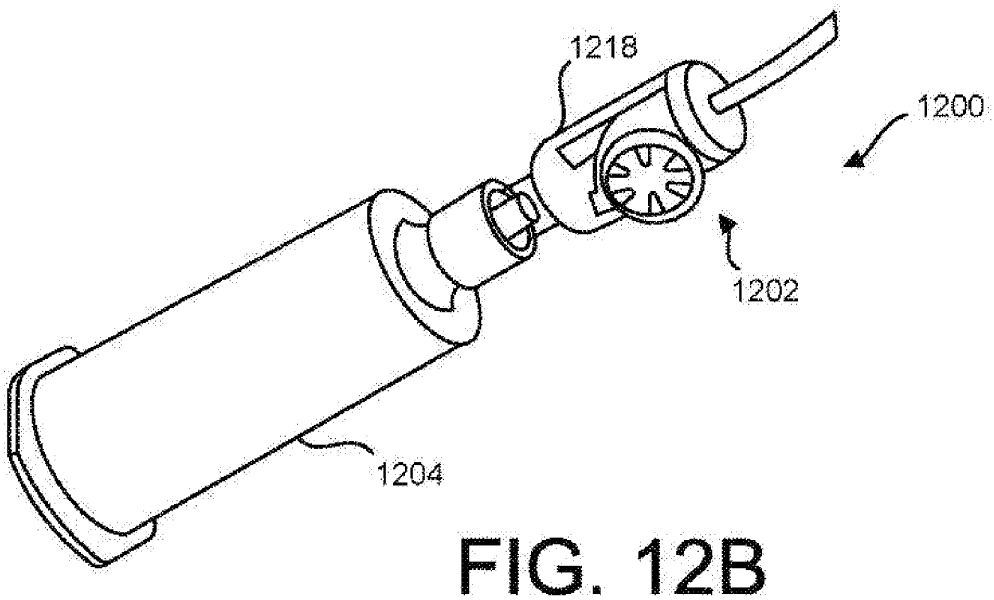


FIG. 12B

[Fig. 12C]

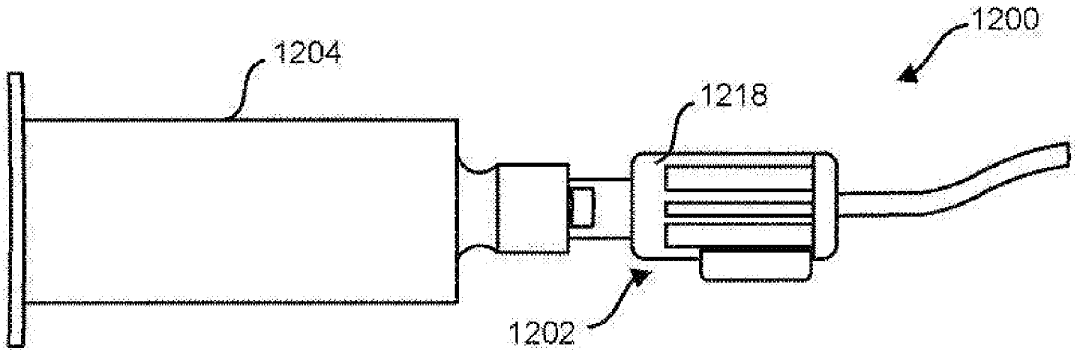


FIG. 12C

[Fig. 12D]

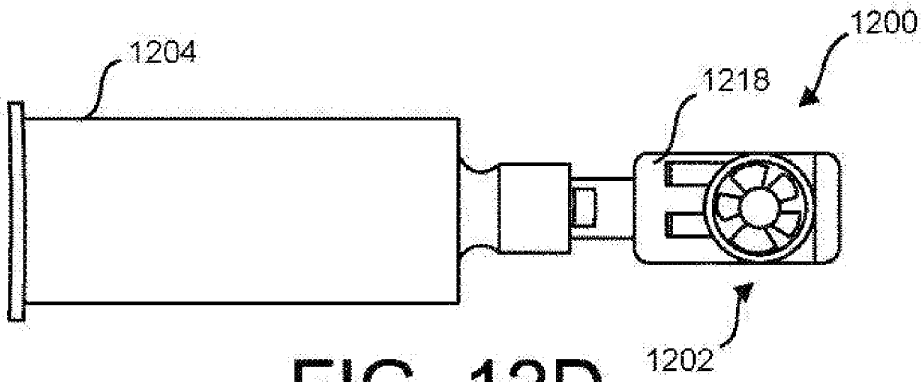


FIG. 12D

[Fig. 13A]

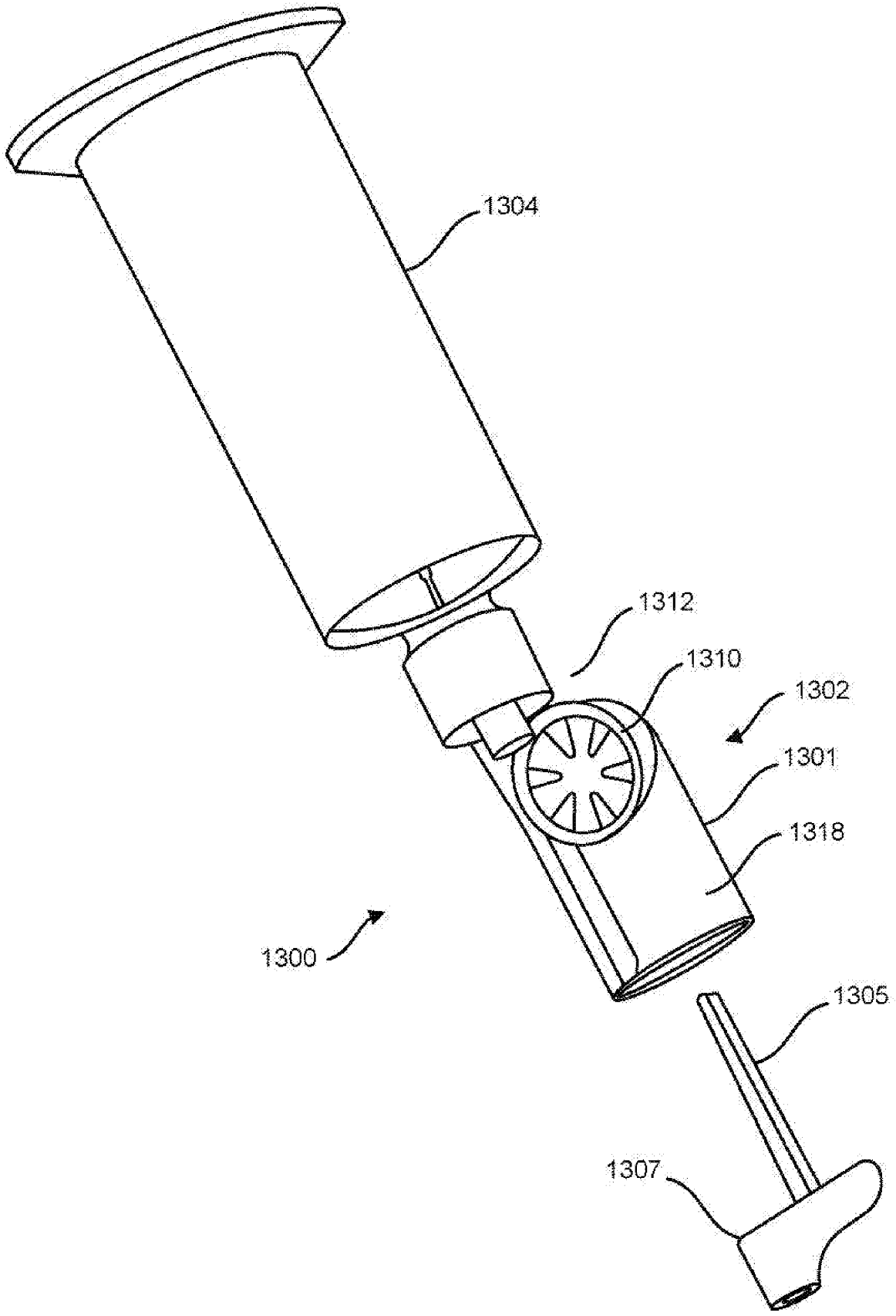


FIG. 13A

[Fig. 13B]

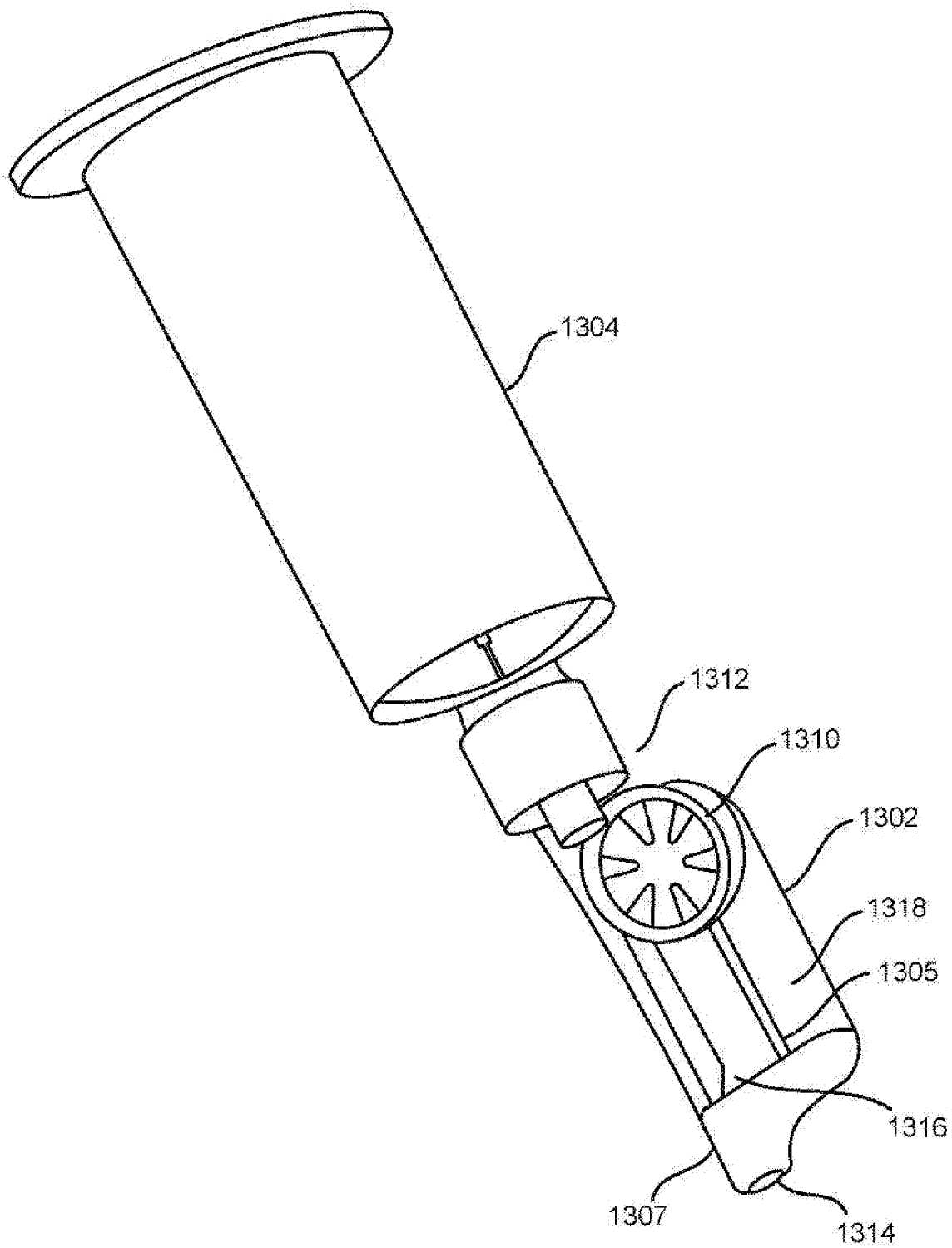


FIG. 13B

[Fig. 13C]

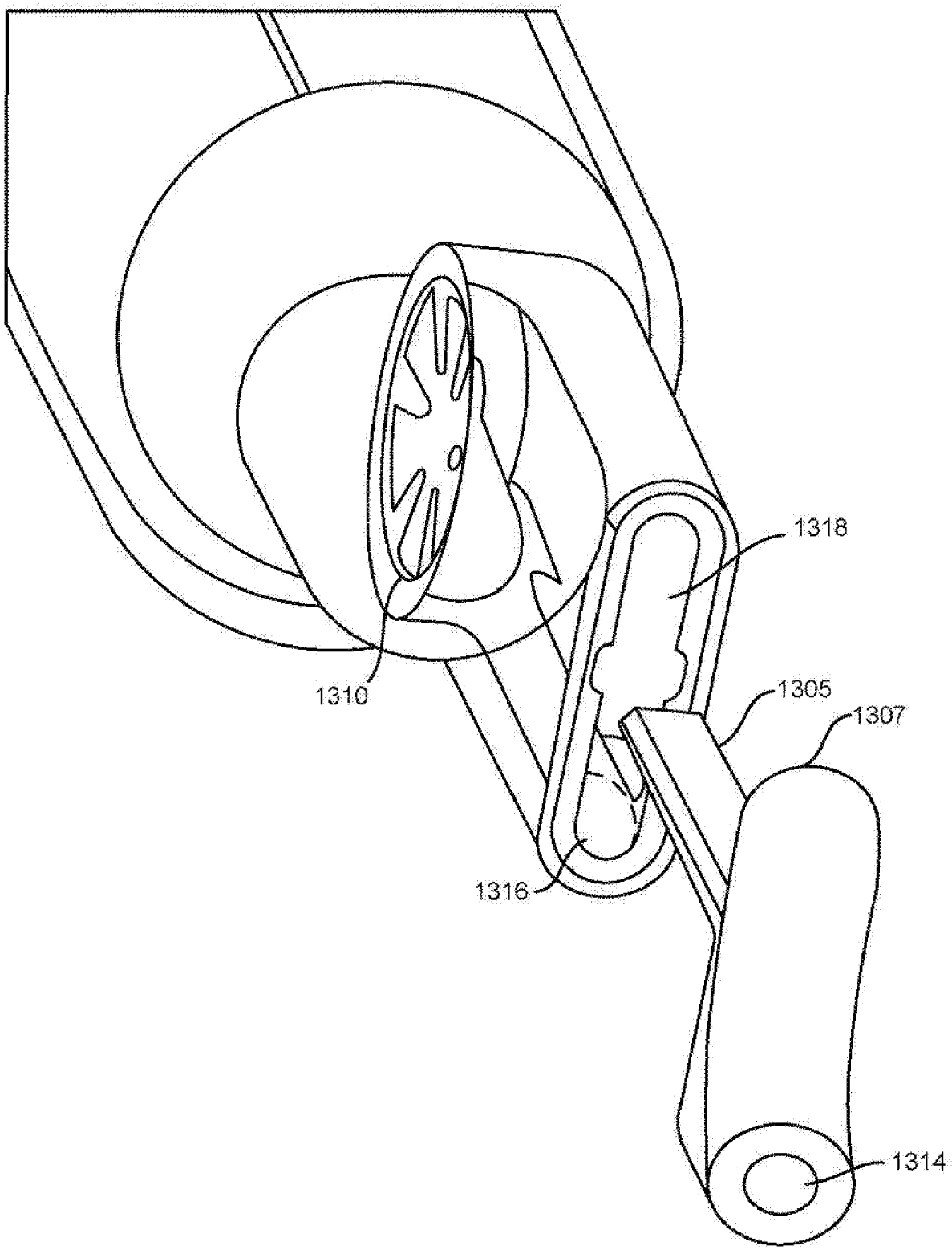
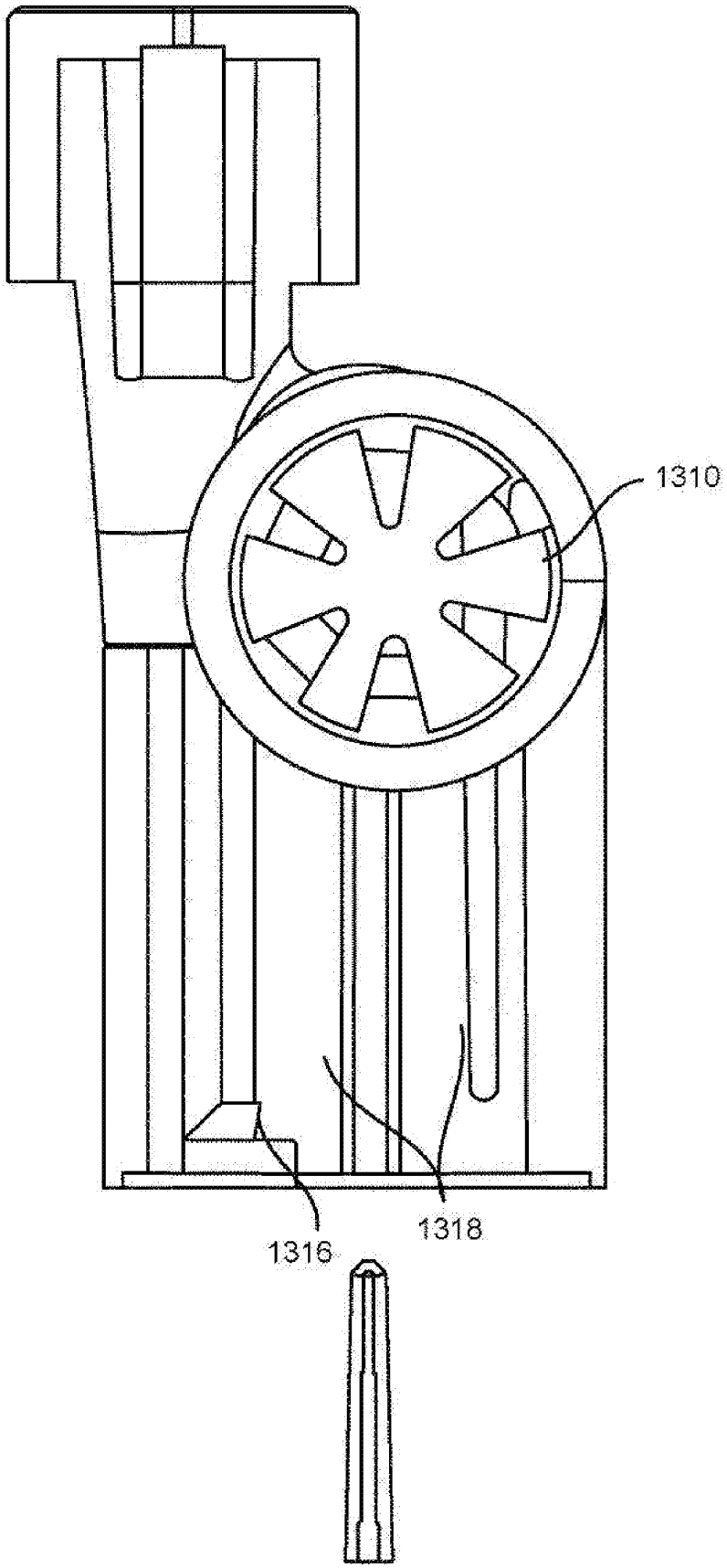


FIG. 13C

[Fig. 13D]


1310
1316
1318

[Fig. 14A]

FIG. 13D

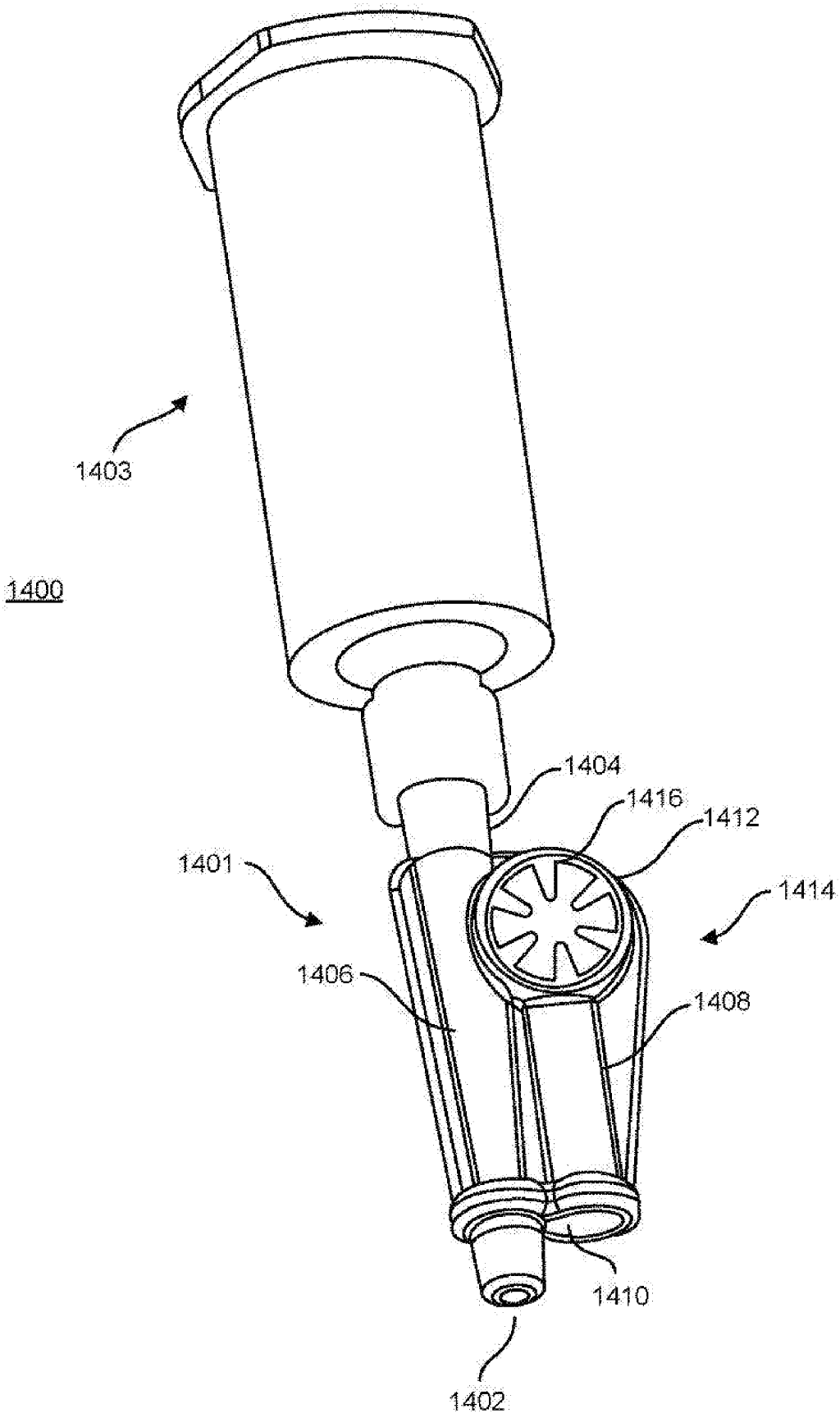
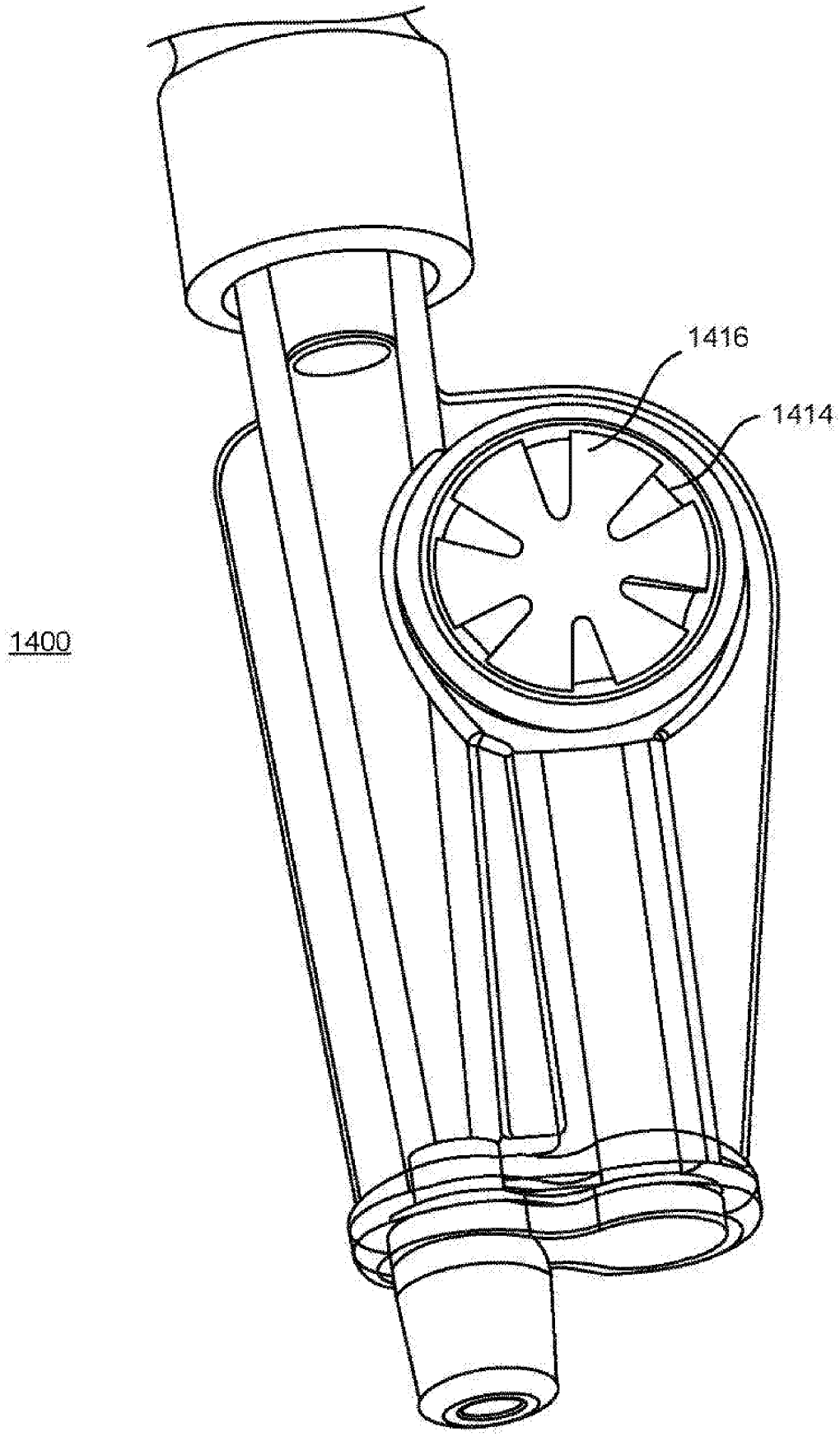


FIG. 14A

[Fig. 14B]


1400
1416
1414

[Fig. 14C]

FIG. 14B

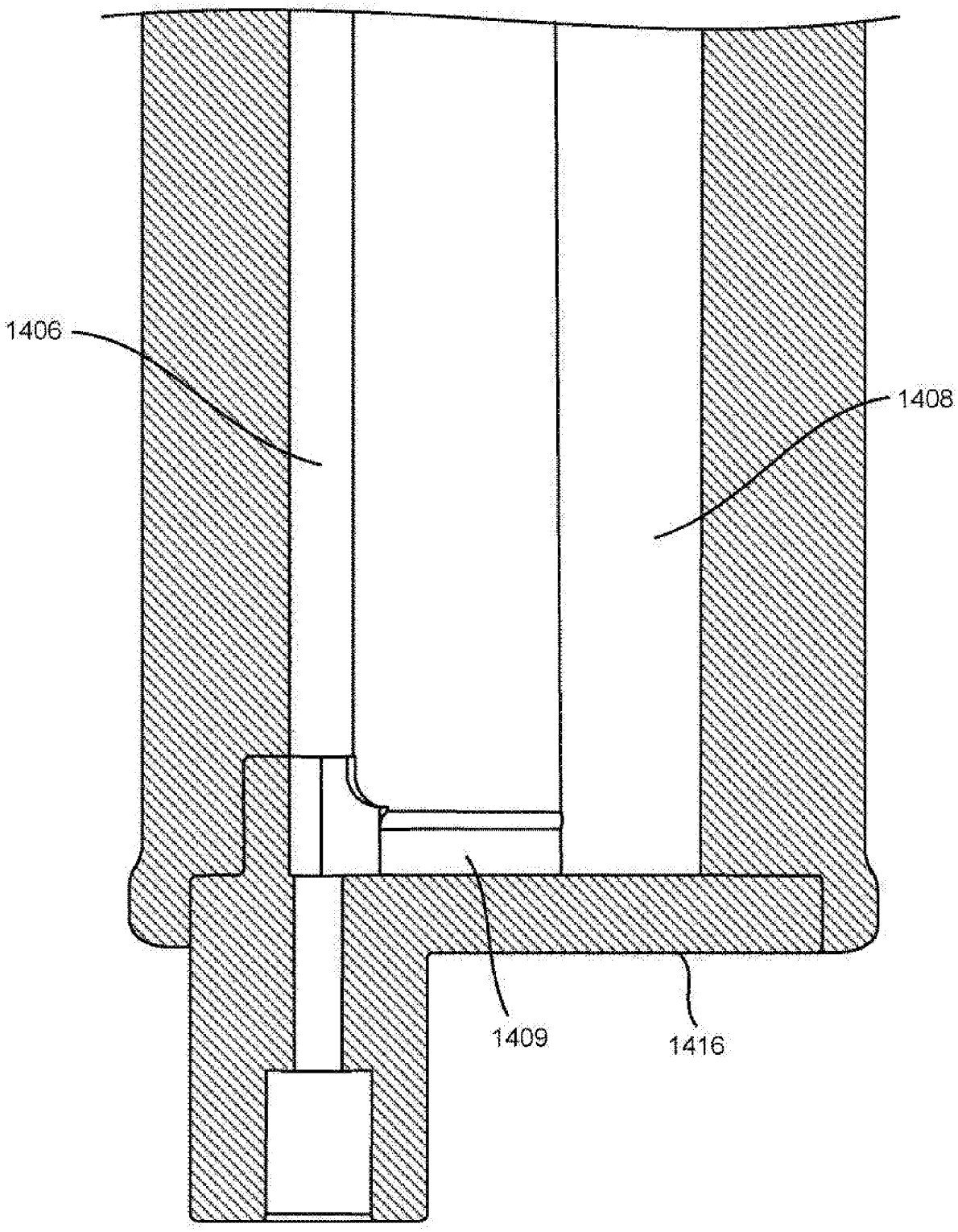
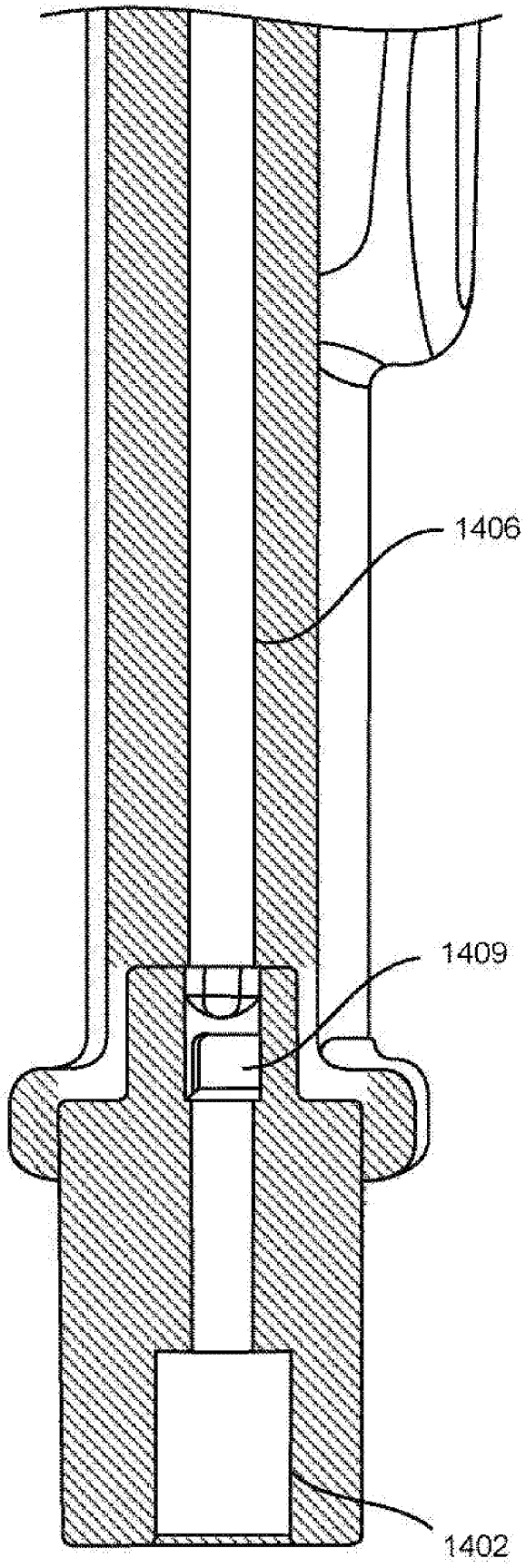


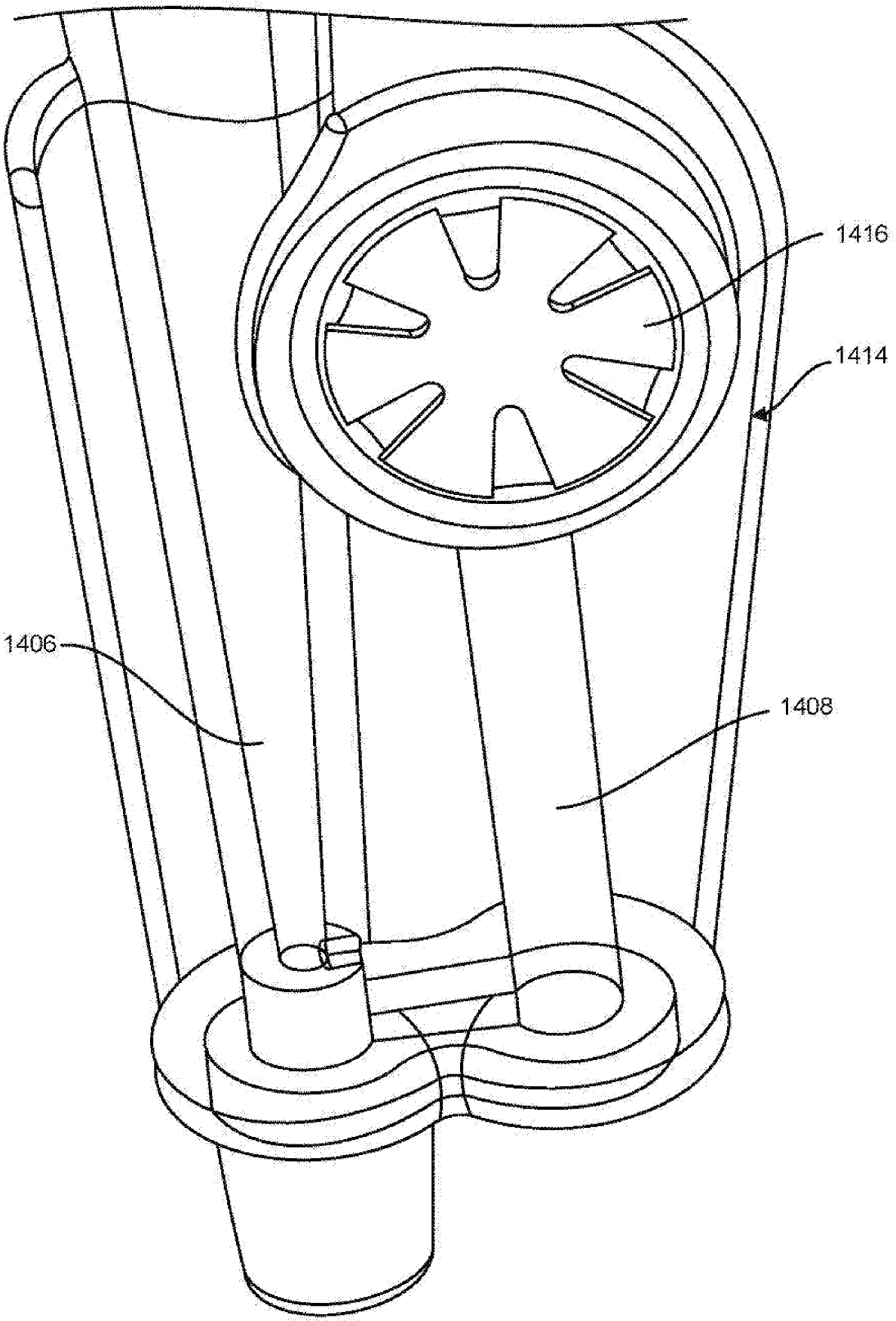
FIG. 14C

[Fig. 14D]


1406
1409
1402

[Fig. 14E]

FIG. 14D


1416
1414
1406
1408

[Fig. 15A]

FIG. 14E

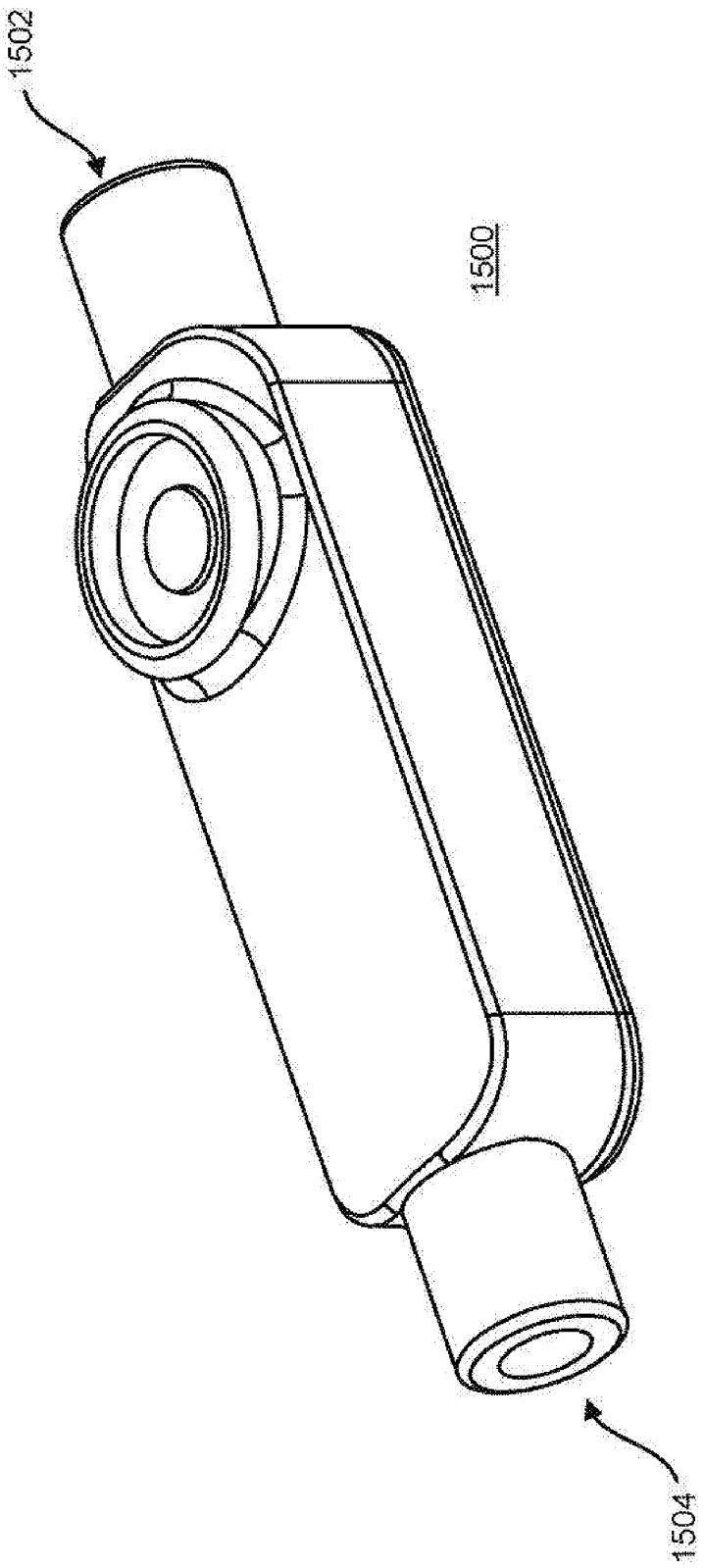


FIG. 15A

[Fig. 15B]

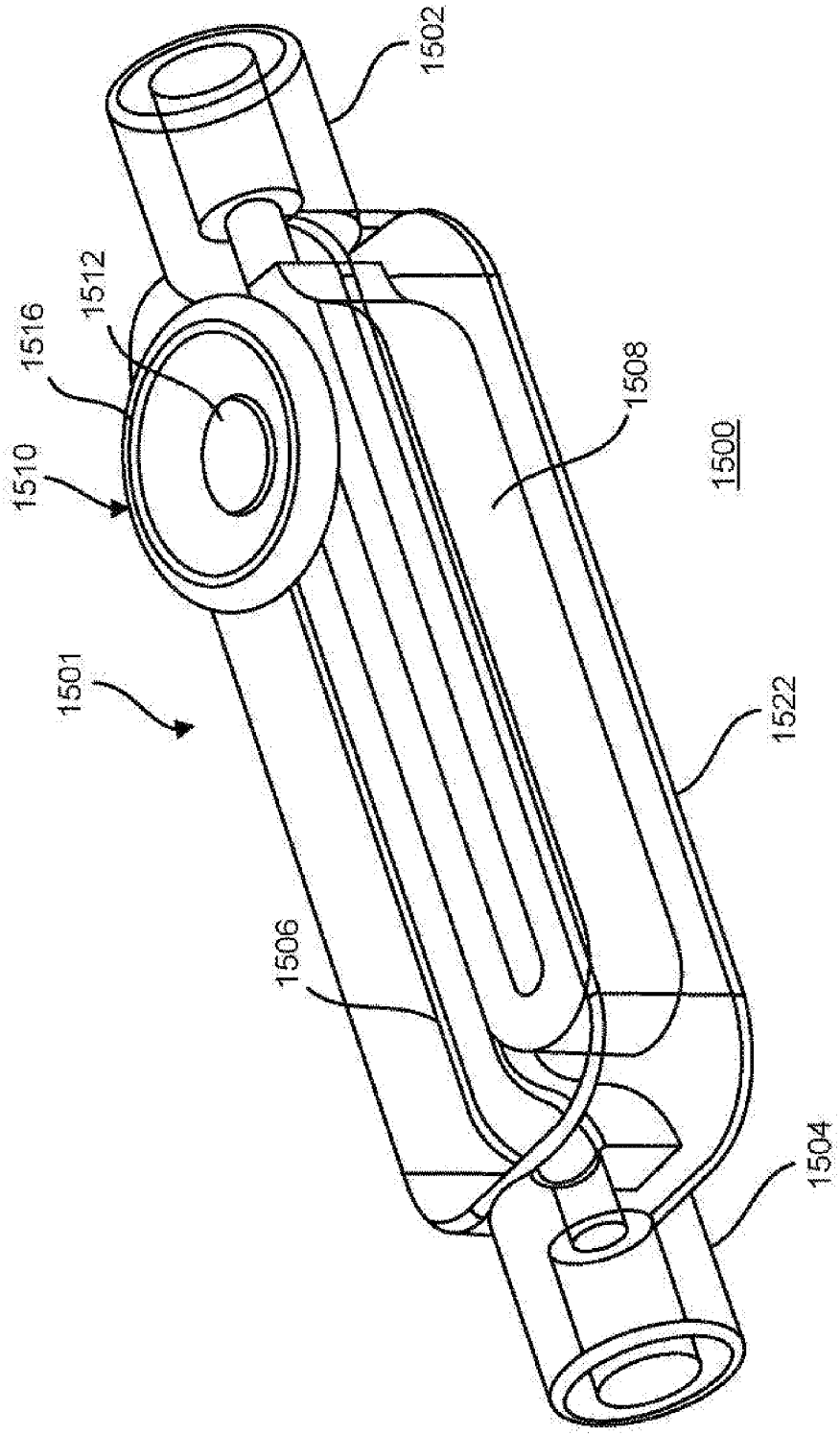


FIG. 15B

[Fig. 15C]

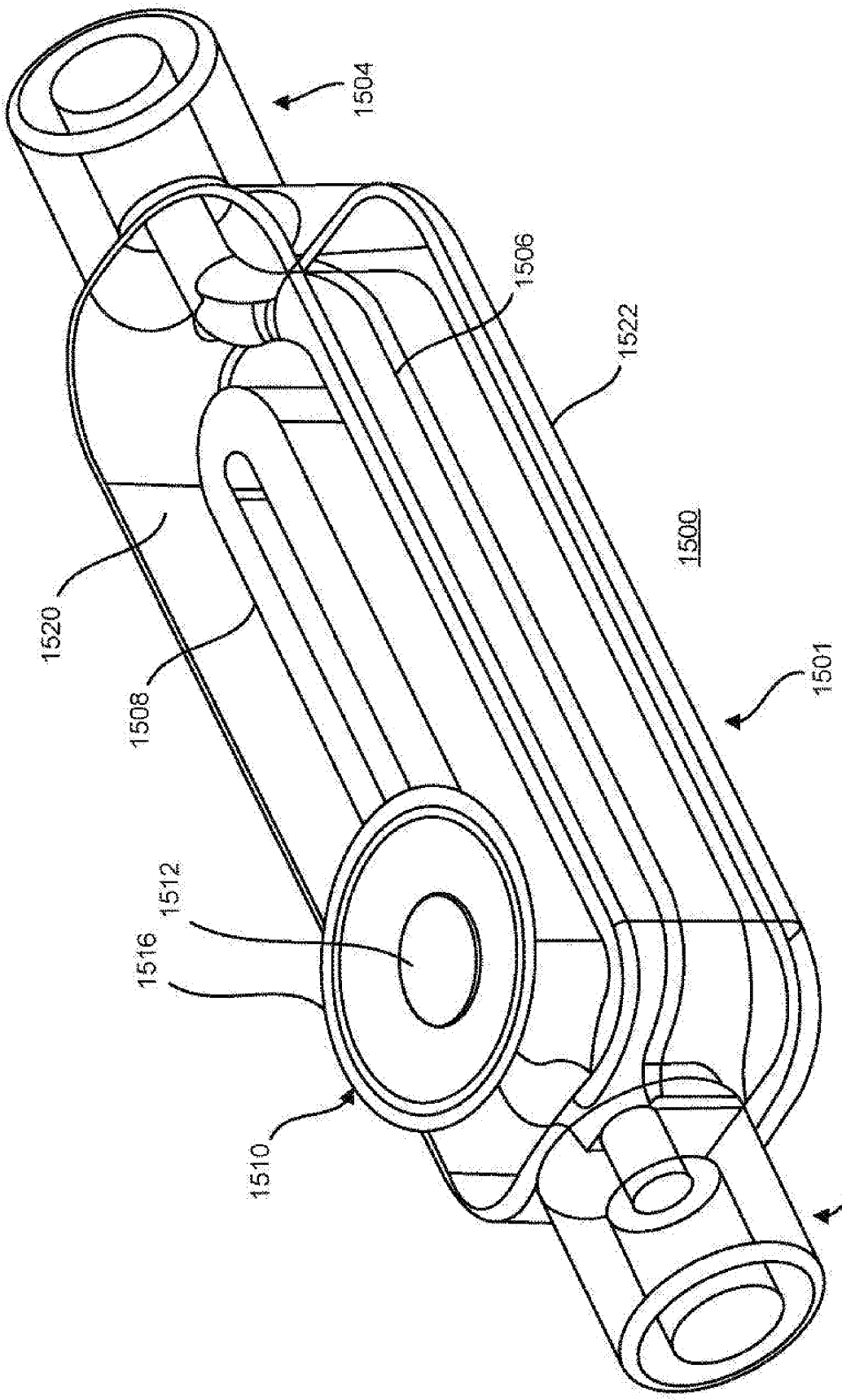


FIG. 15C

[Fig. 15D]

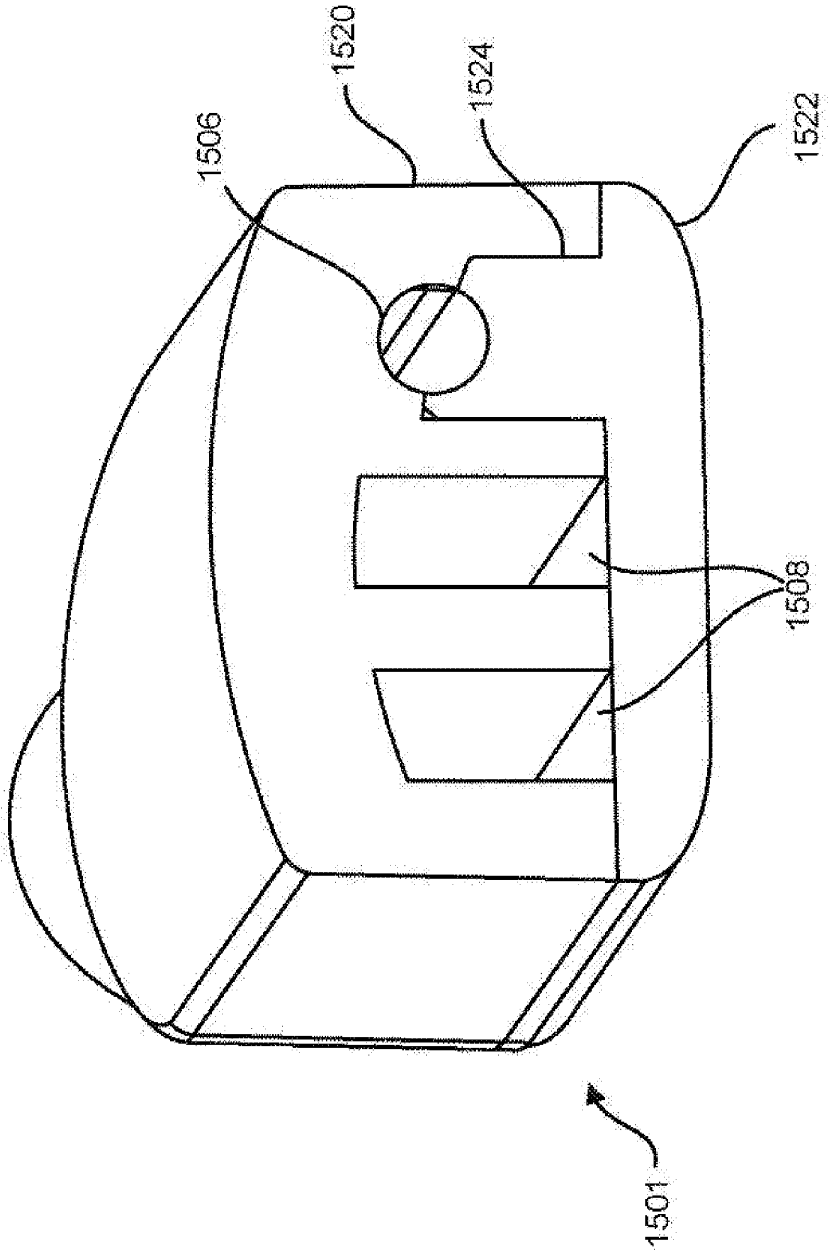


FIG. 15D

[Fig. 15E]

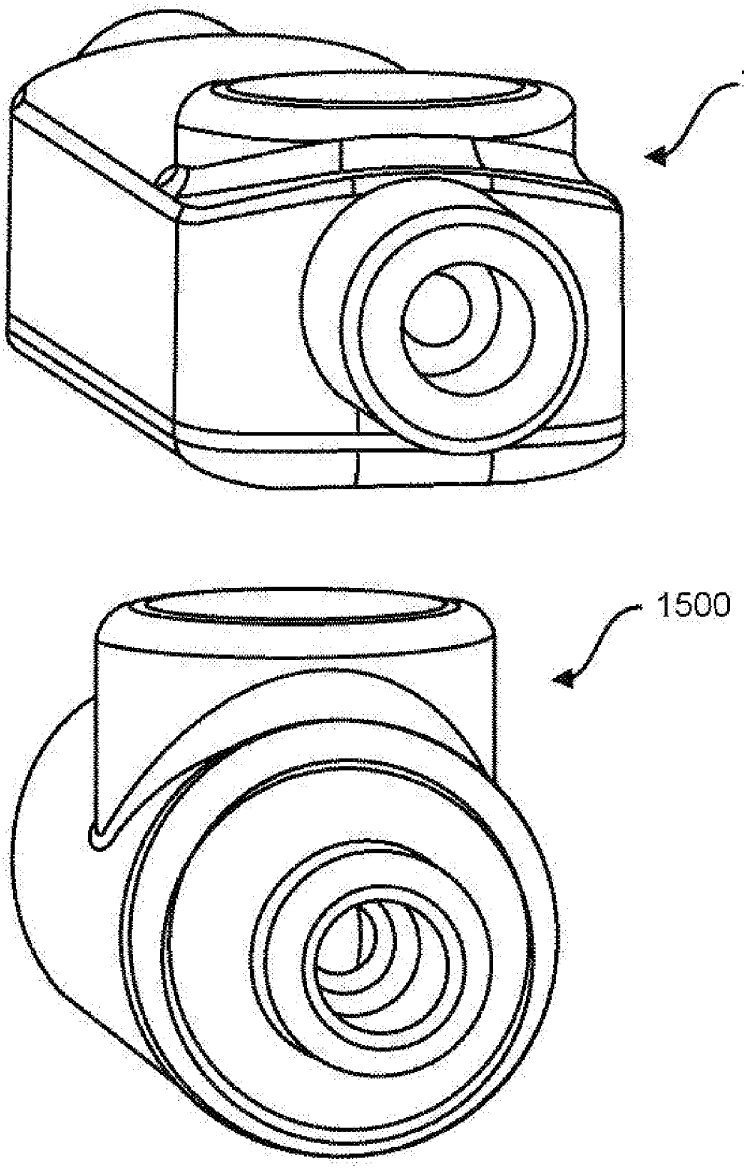


FIG. 15E

[Fig. 15F]

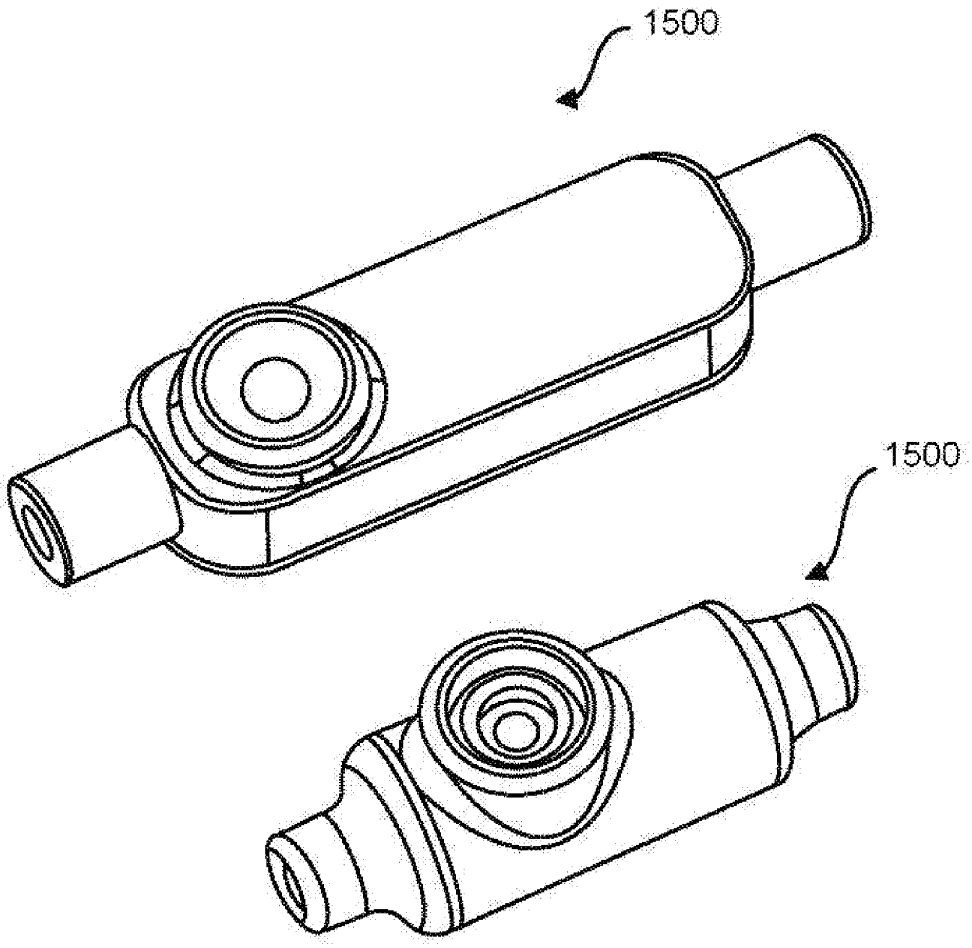


FIG. 15F

[Fig. 15G]

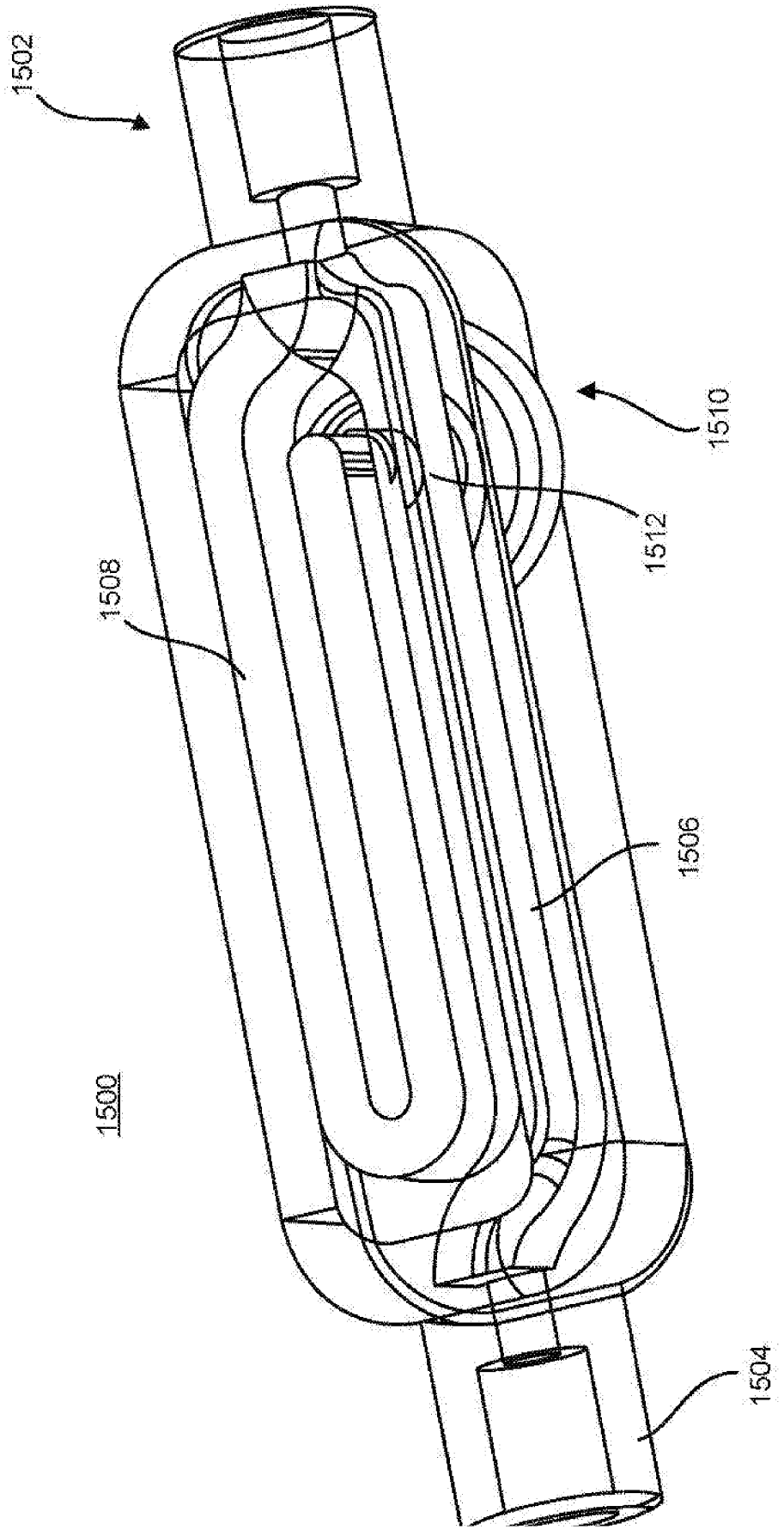


FIG. 15G

[Fig. 16A]

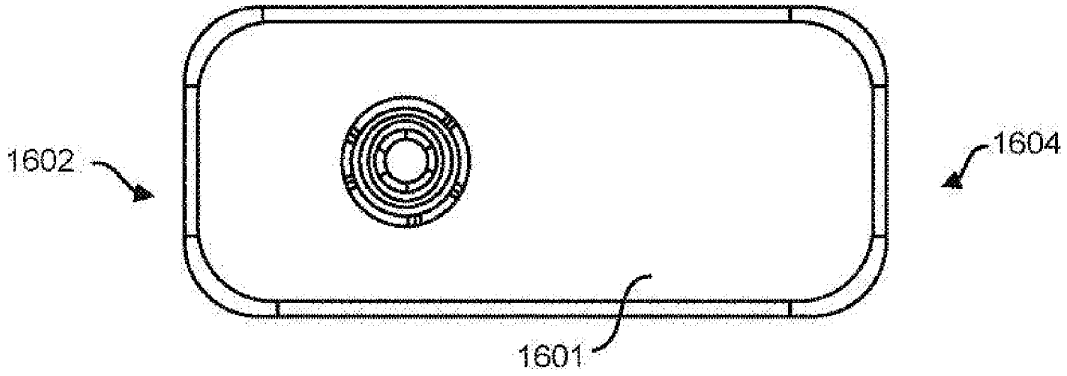


FIG. 16A

[Fig. 16B]

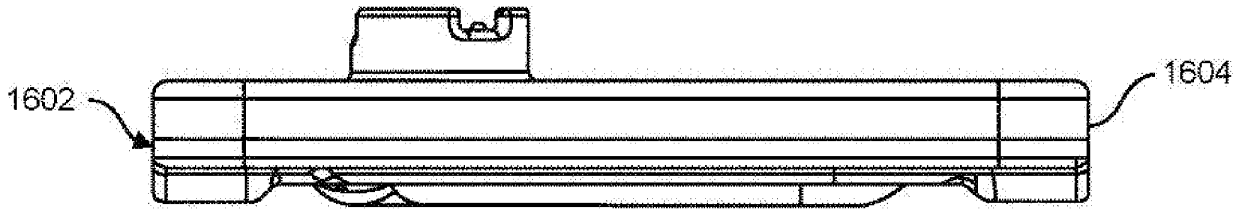


FIG. 16B

[Fig. 16C]

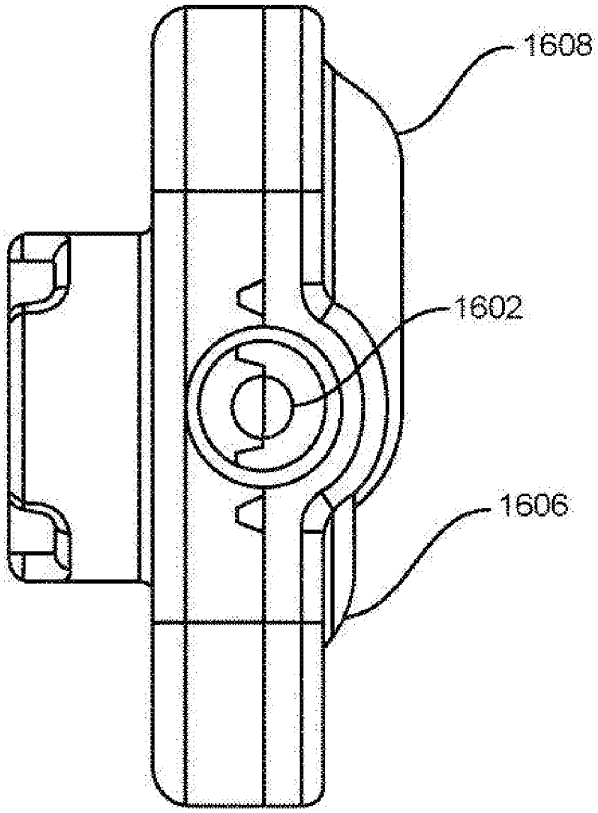


FIG. 16C

[Fig. 16D]

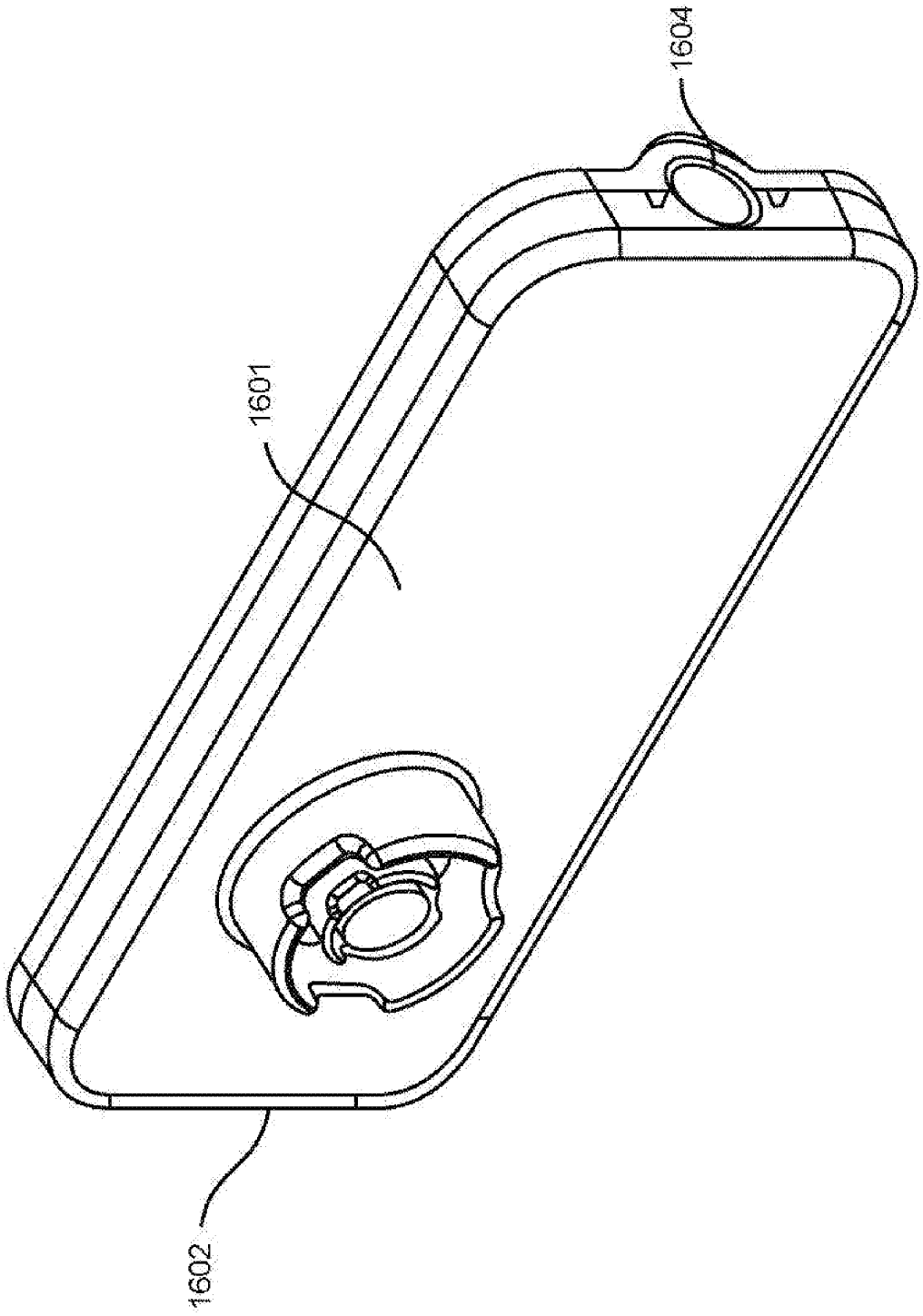


FIG. 16D

[Fig. 17A]

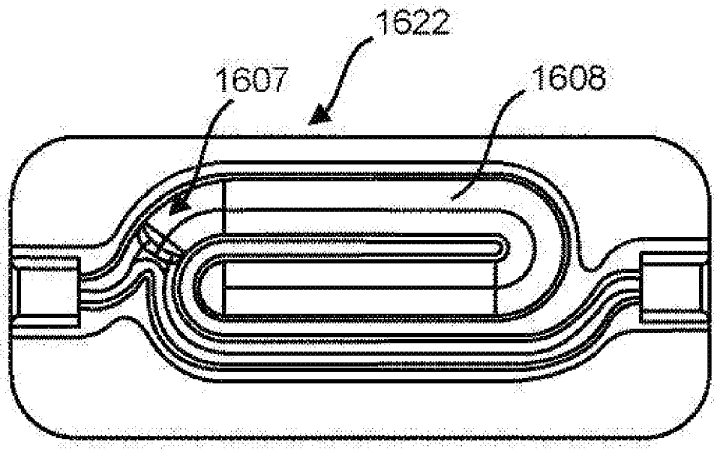


FIG. 17A

[Fig. 17B]

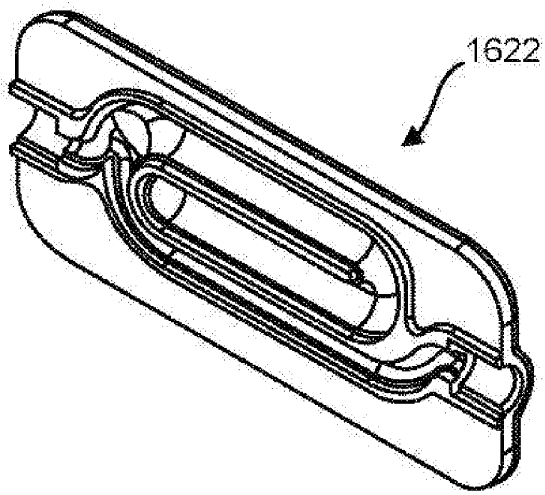


FIG. 17B

[Fig. 17C]

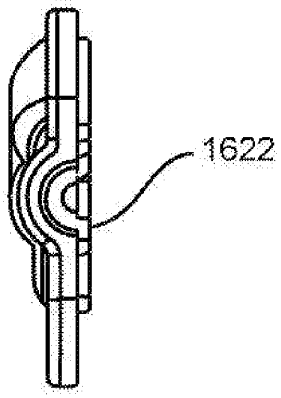


FIG. 17C

[Fig. 17D]

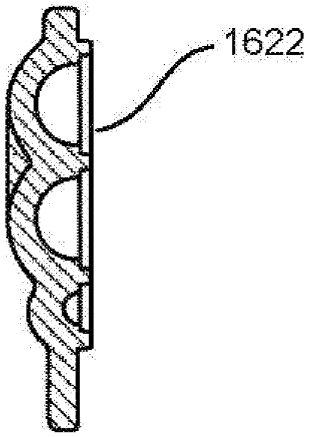


FIG. 17D

[Fig. 17E]

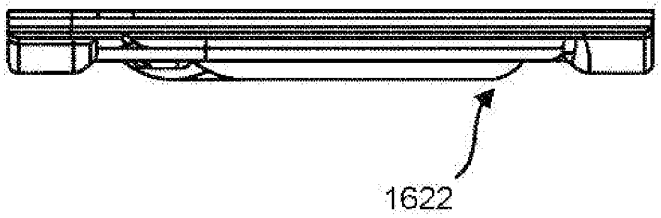


FIG. 17E

[Fig. 18A]

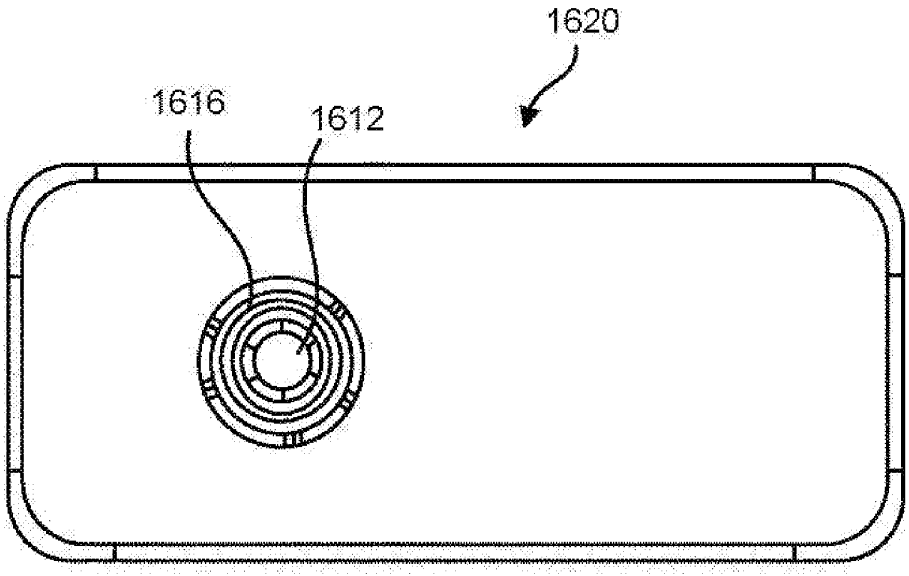


FIG. 18A

[Fig. 18B]

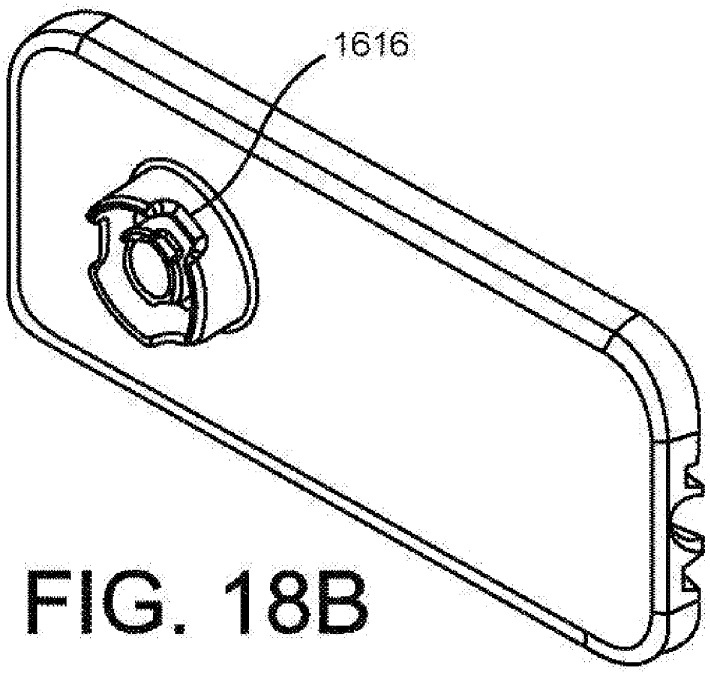


FIG. 18B

[Fig. 18C]

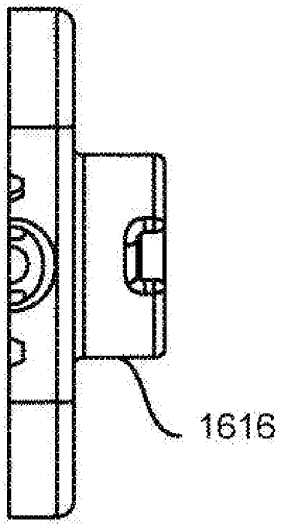


FIG. 18C

[Fig. 18D]

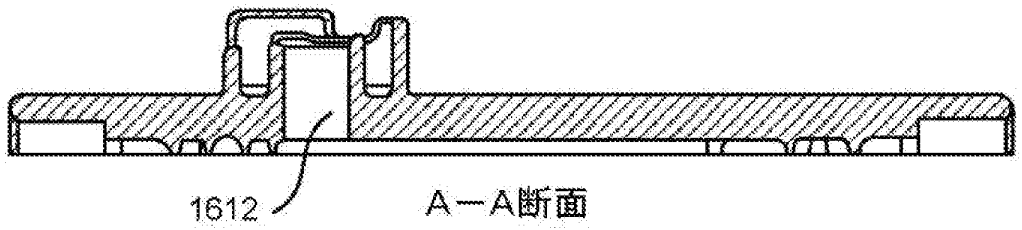


FIG. 18D

[Fig. 18E]

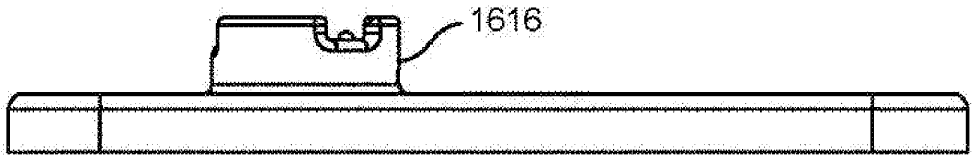


FIG. 18E

[Fig. 18F]

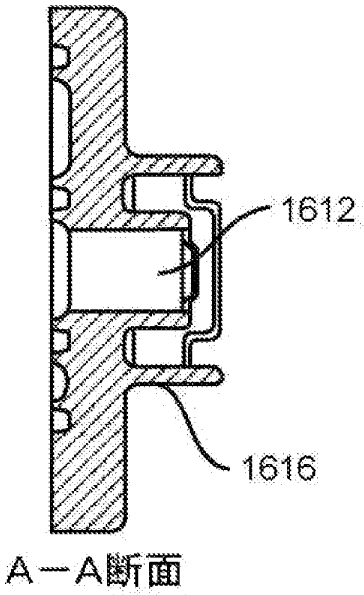


FIG. 18F

[Fig. 19A]

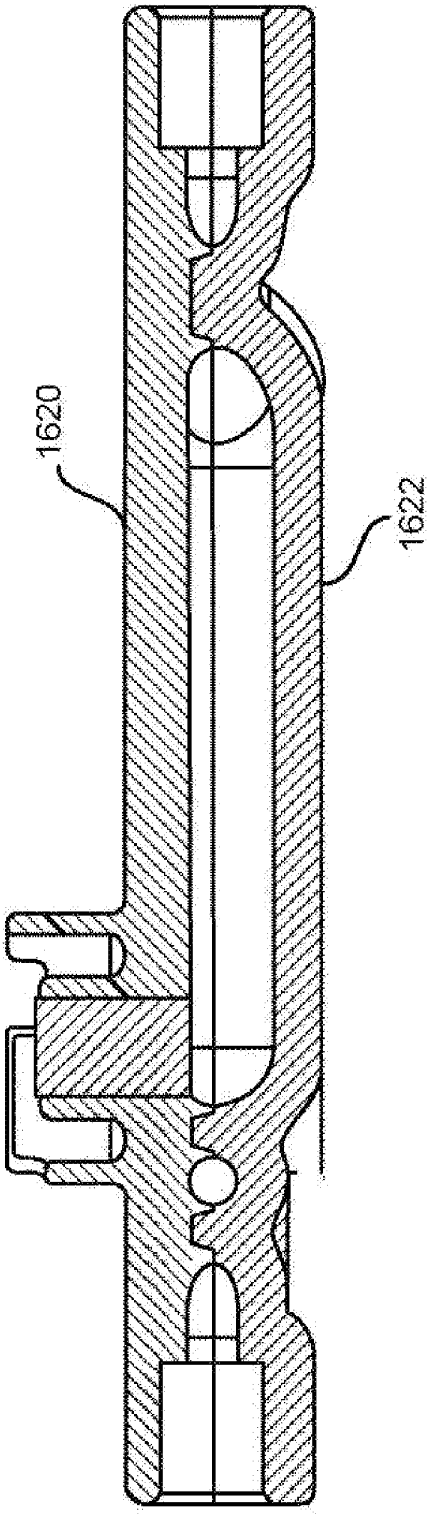


FIG. 19A

[Fig. 19B]

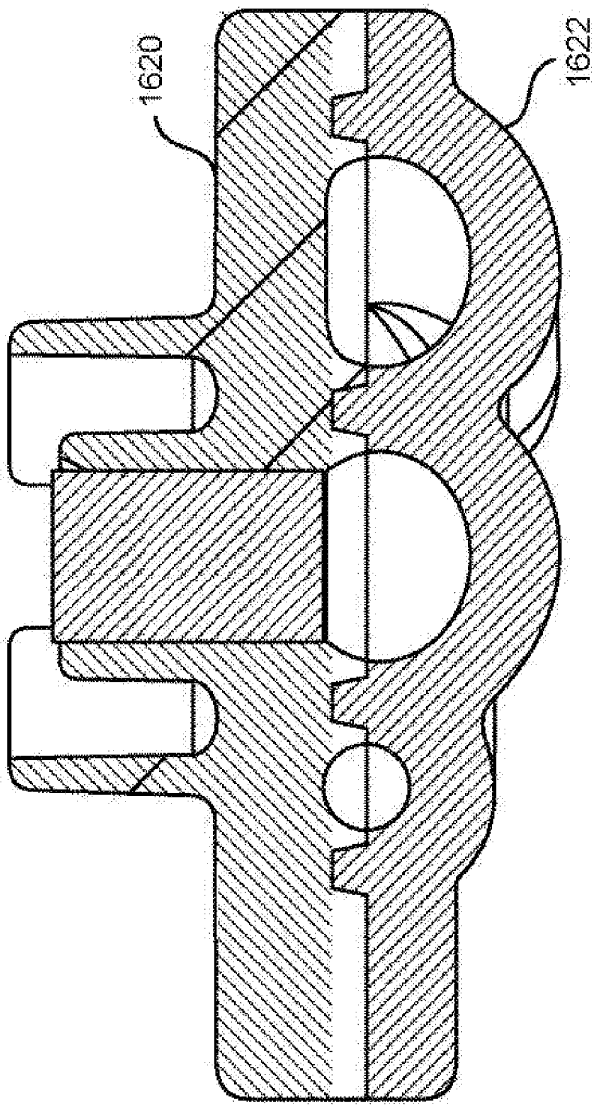


FIG. 19B

[Fig. 20]

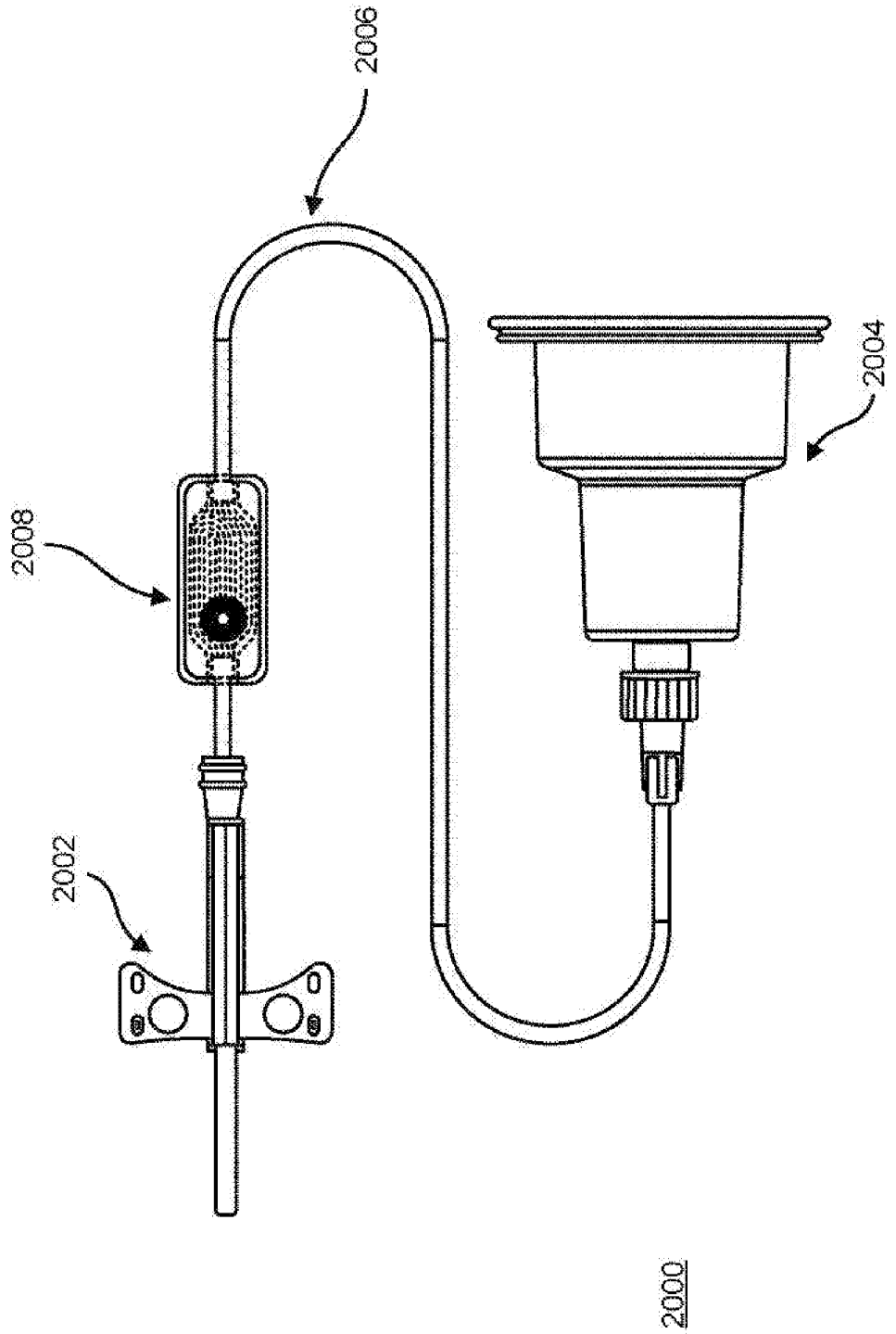


FIG. 20

[Fig. 21]

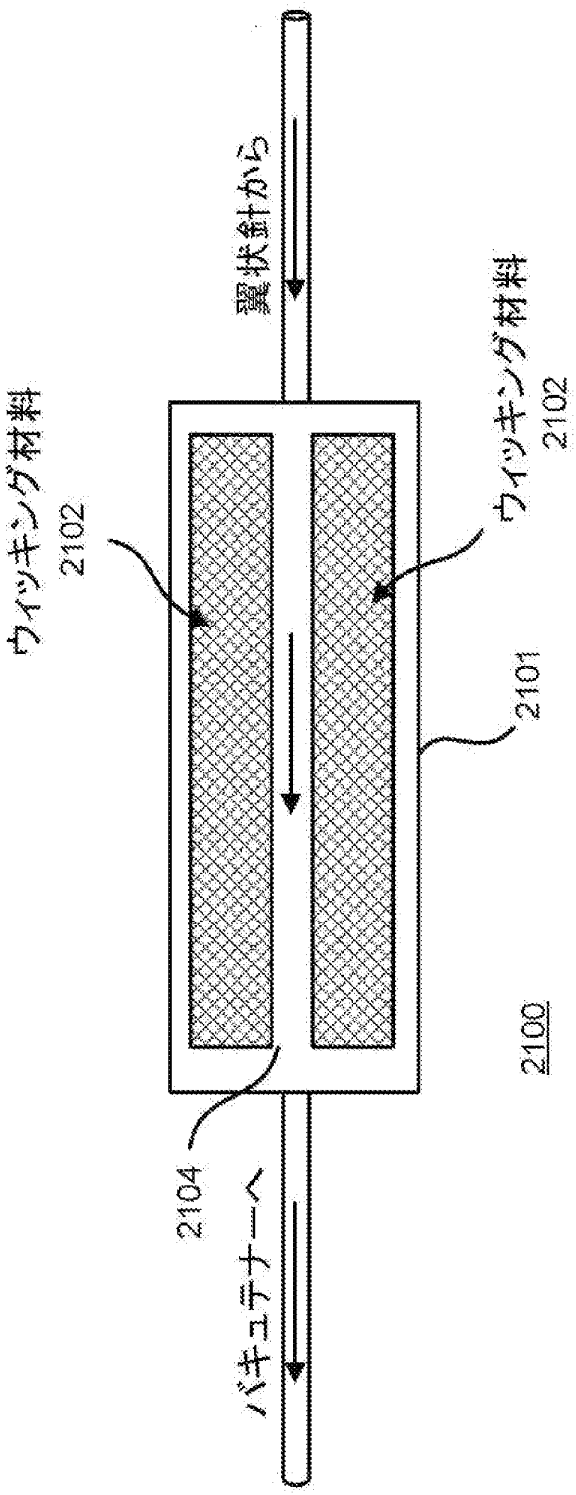


FIG. 21

[Fig. 22A]

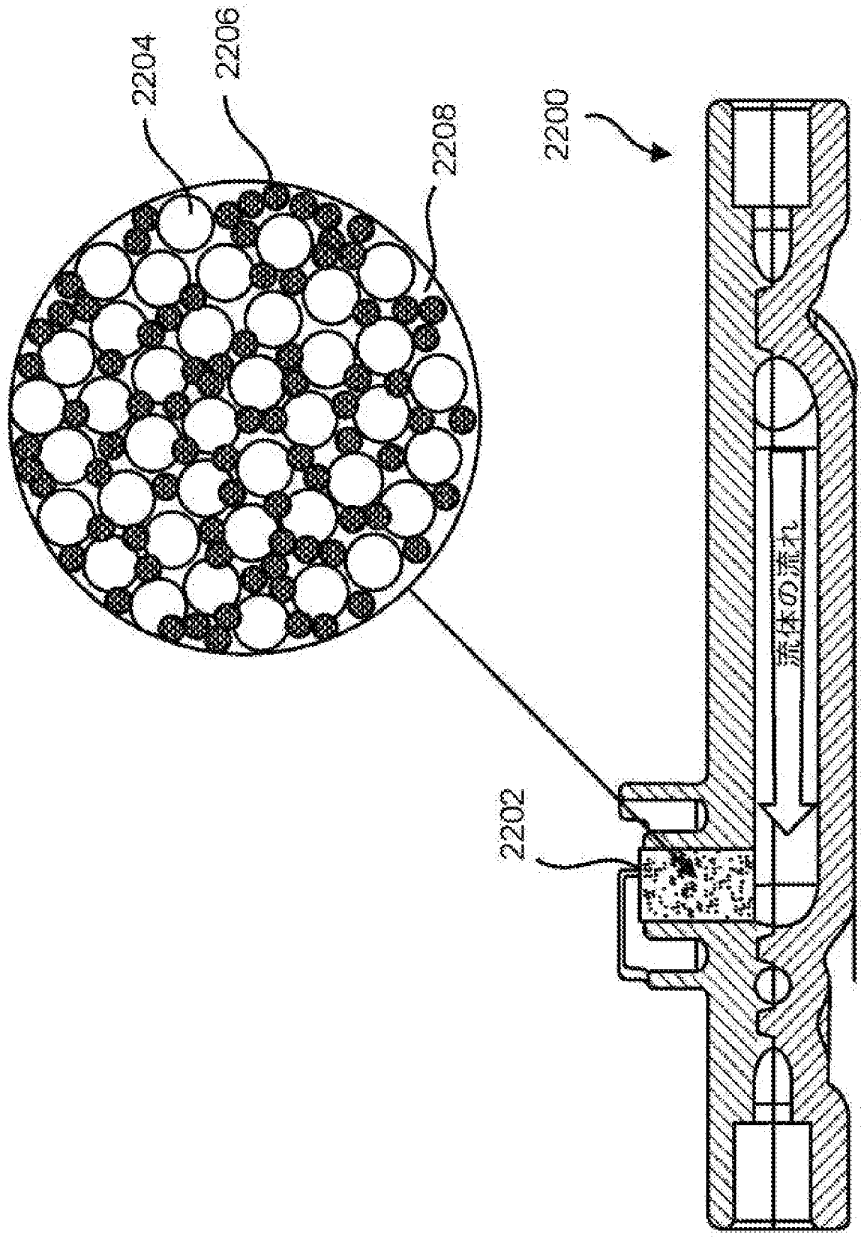


FIG. 22A

[Fig. 22B]

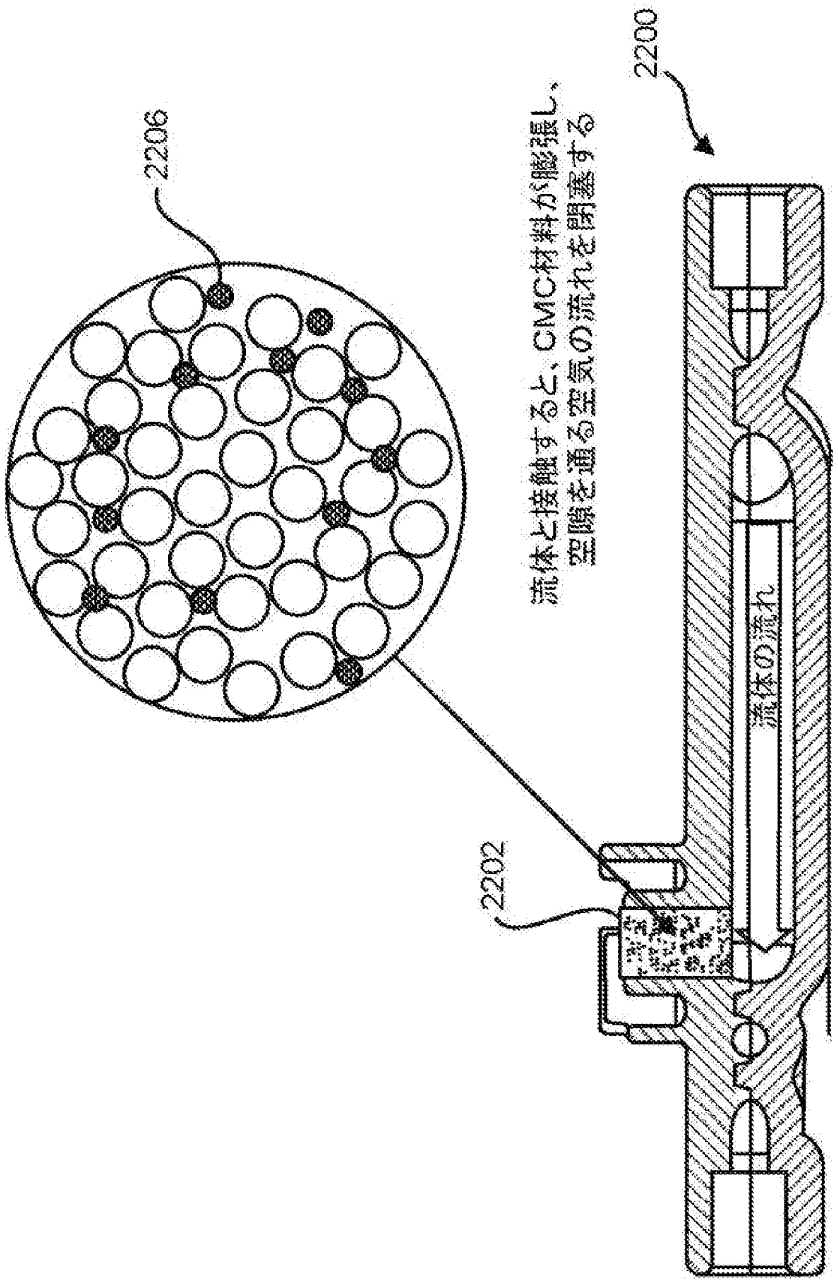


FIG. 22B

[Fig. 23A]

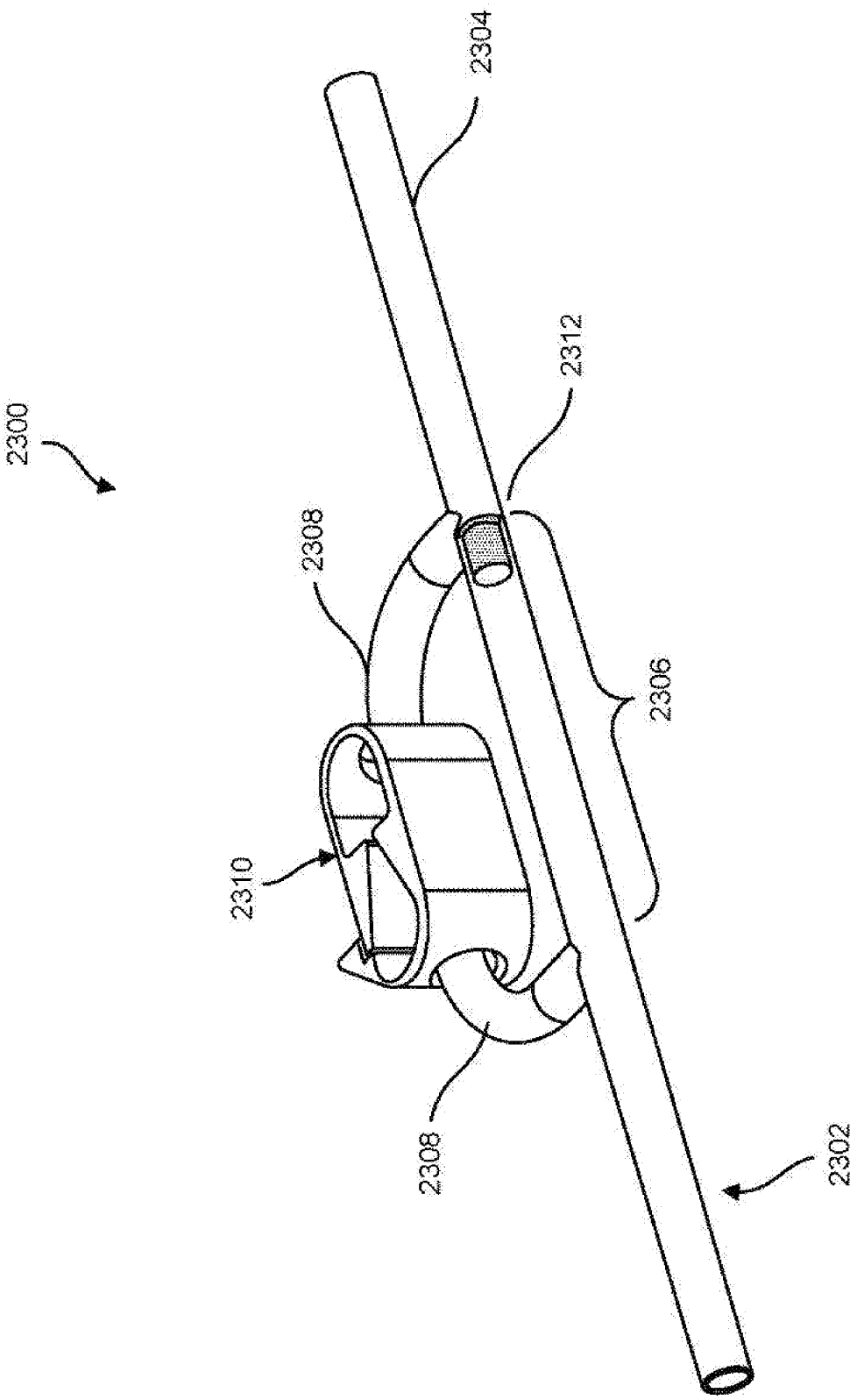


FIG. 23A

[Fig. 23B]

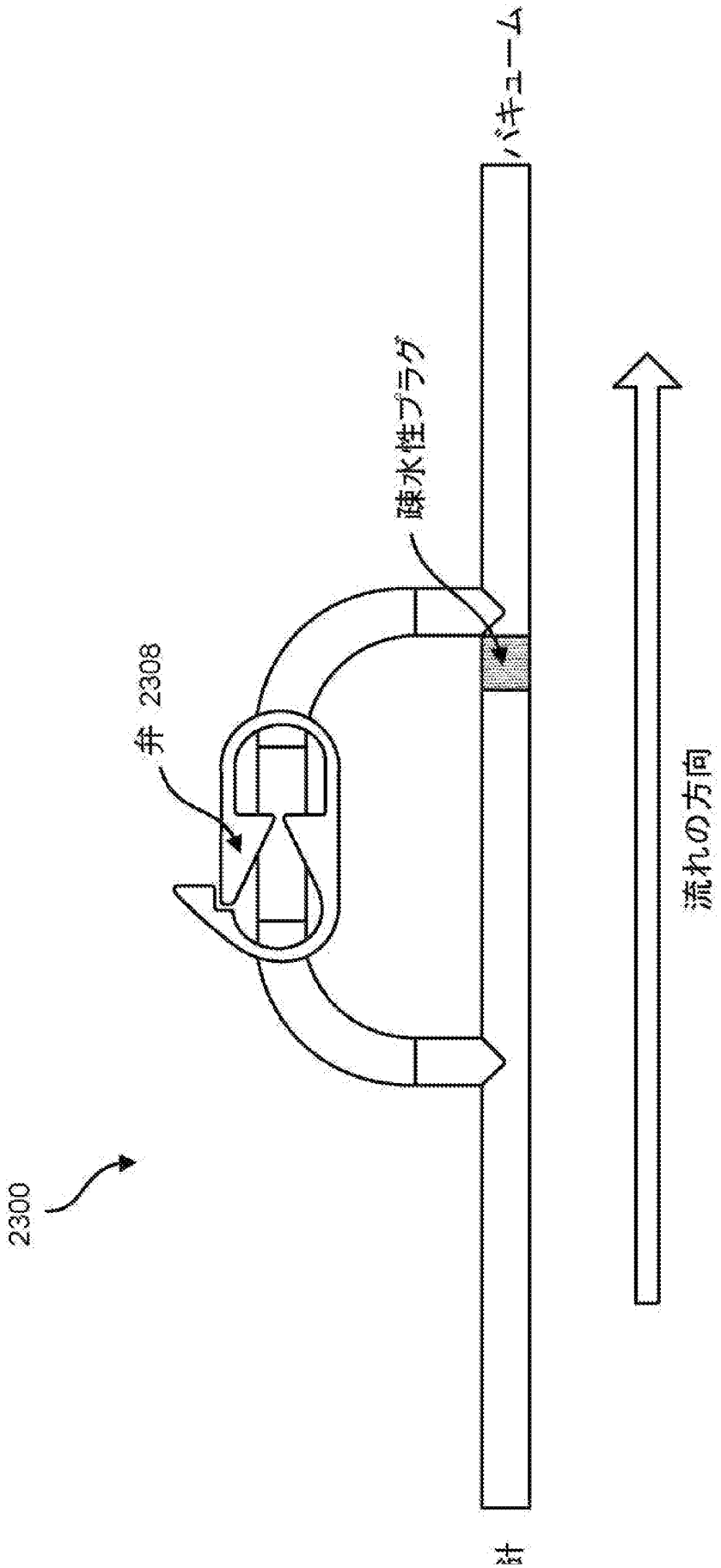


FIG. 23B

drawing open

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

Magnify and Rotate

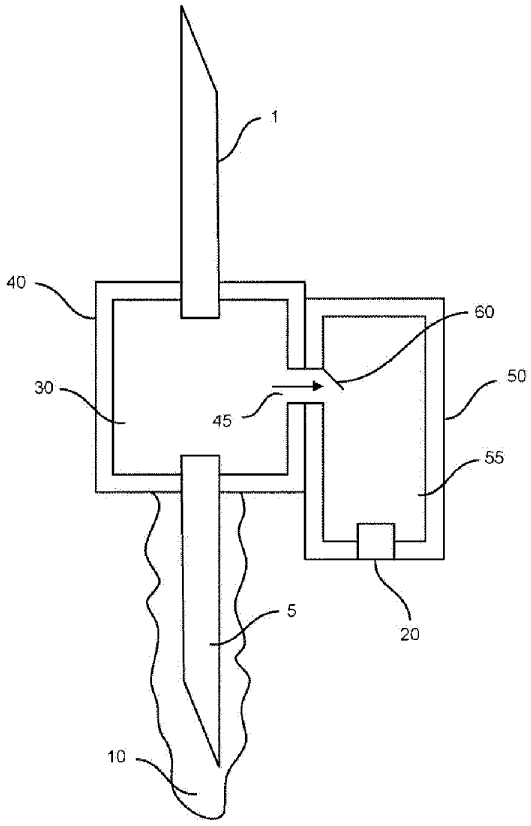


FIG. 1

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】

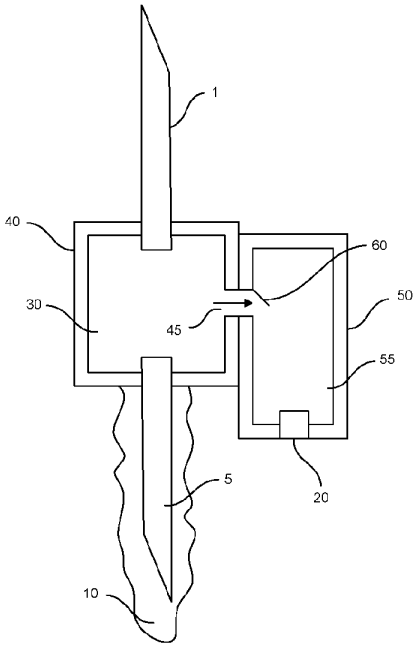


FIG. 1

【図２】

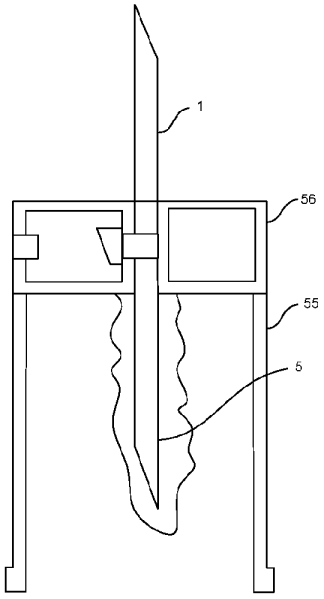


FIG. 2

【図３】

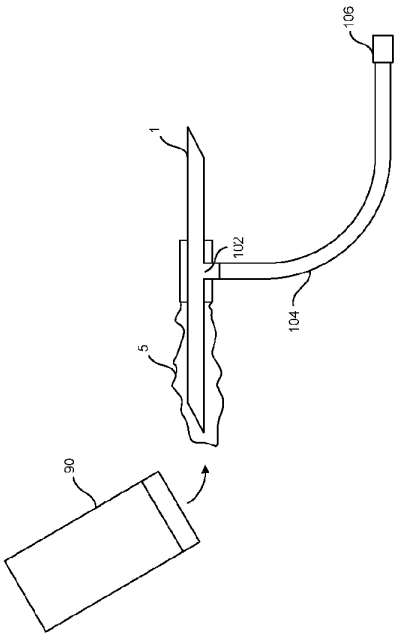


FIG. 3

【図４】

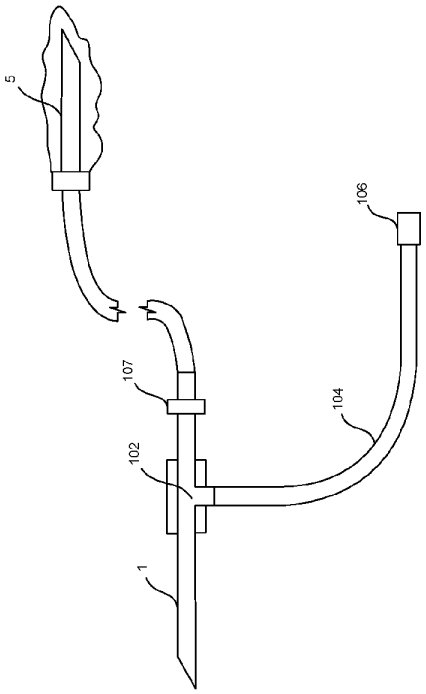


FIG. 4

【図５】

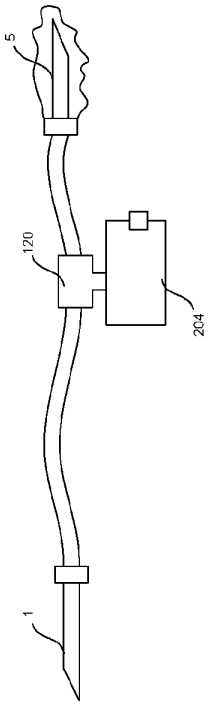


FIG. 5

【図６】

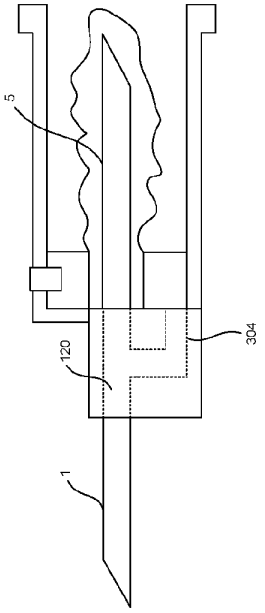


FIG. 6

【図７】

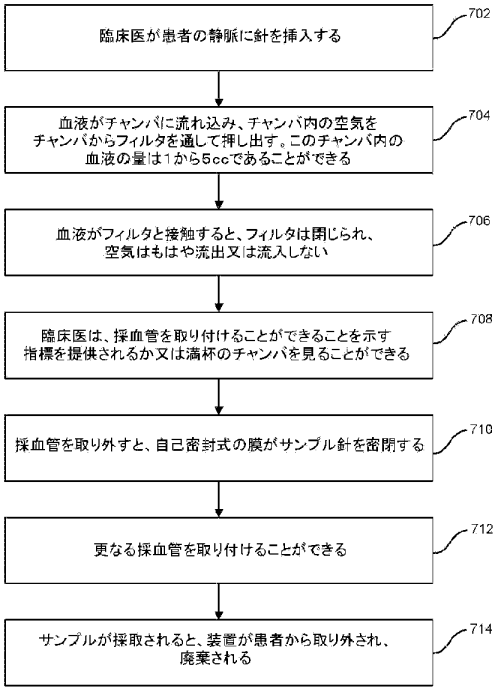


FIG. 7

【図８Ａ】

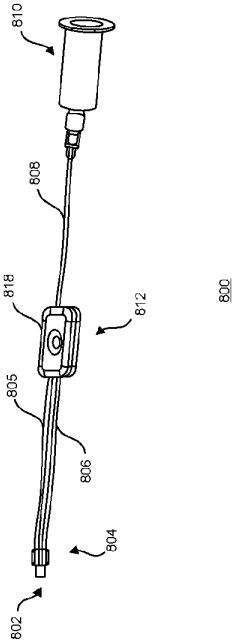


FIG. 8A

【図８Ｂ】

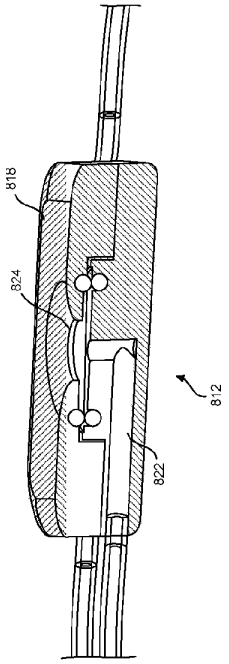


FIG. 8B

【図８Ｃ】

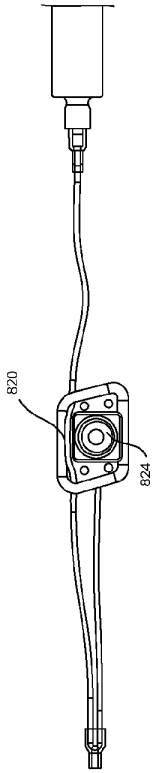


FIG. 8C

【図８Ｄ】

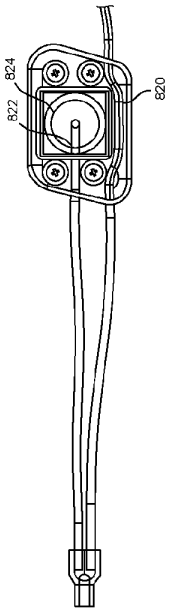


FIG. 8D

【図８Ｅ】

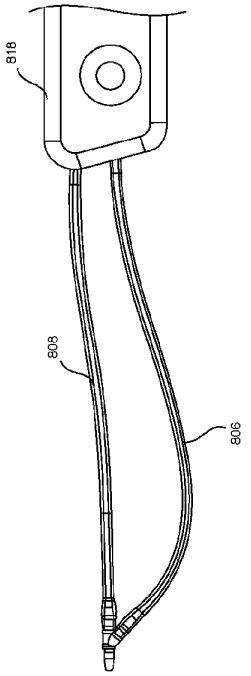


FIG. 8E

【図９】

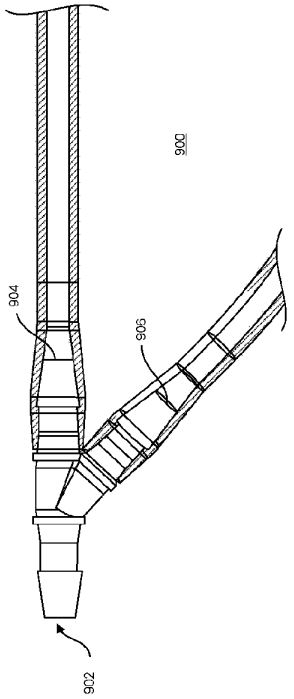


FIG. 9

【図１０Ａ】

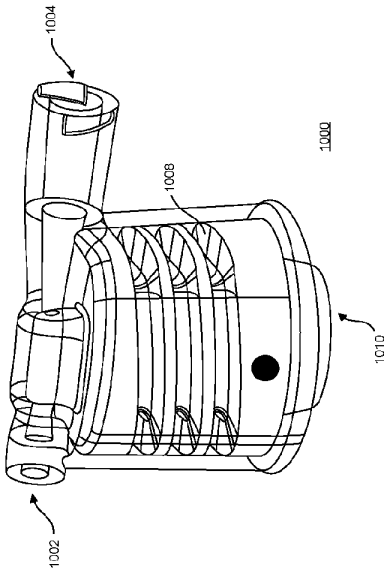


FIG. 10A

【図１０Ｂ】

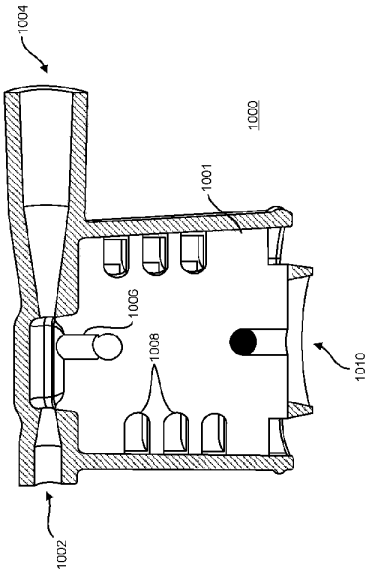


FIG. 10B

【図１０Ｃ】

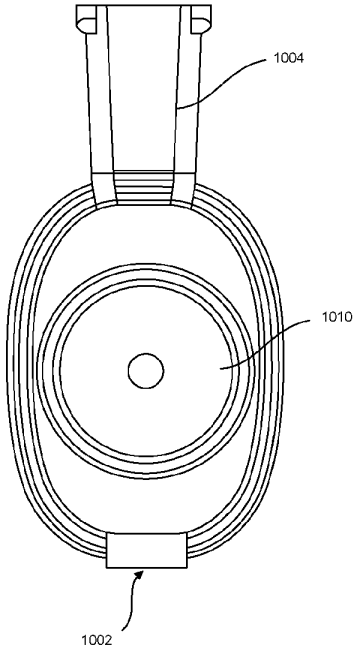


FIG. 10C

【図１０Ｄ】

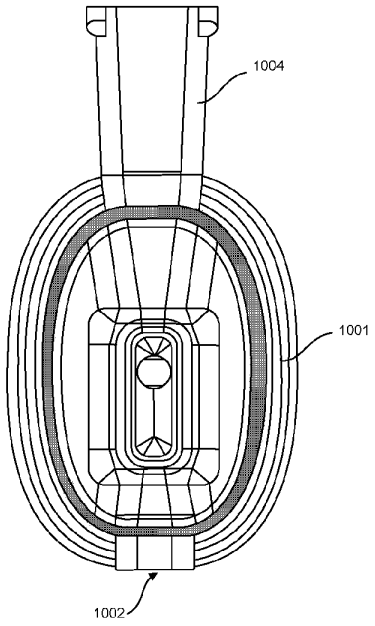


FIG. 10D

【図１１Ａ】

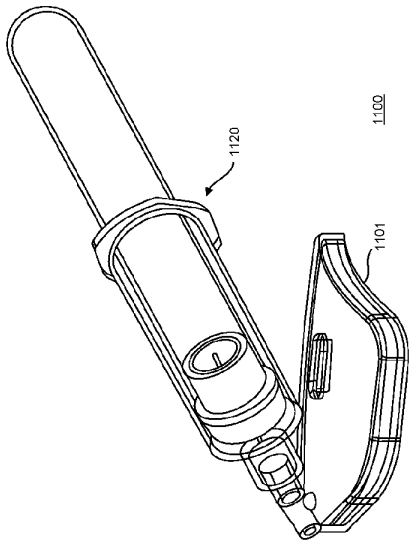


FIG. 11A

【図１１Ｂ】

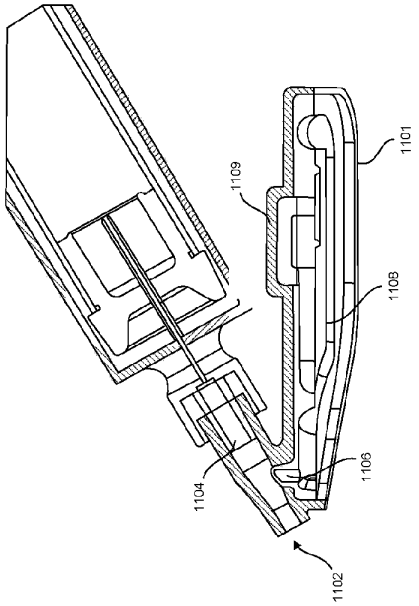


FIG. 11B

【図１１Ｃ】

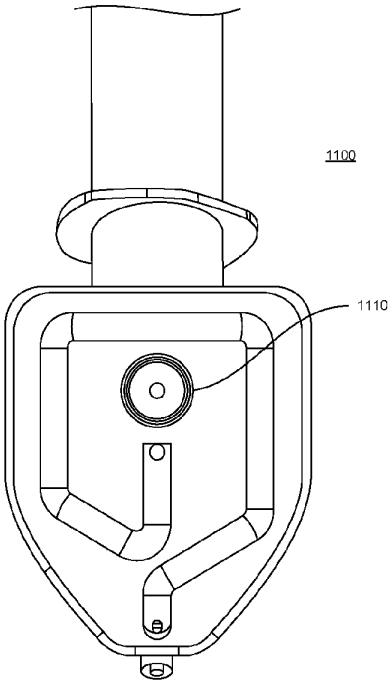


FIG. 11C

【図１１Ｄ】

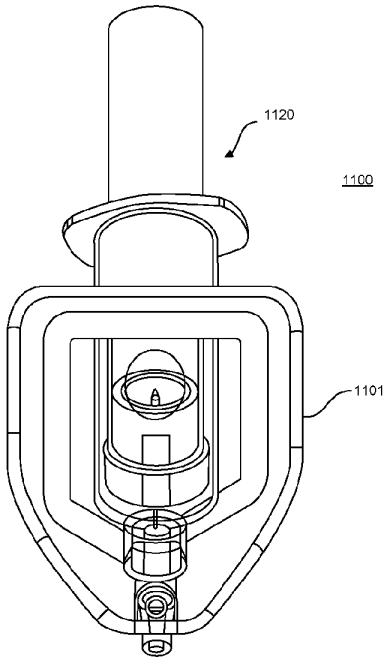


FIG. 11D

【図１１Ｅ】

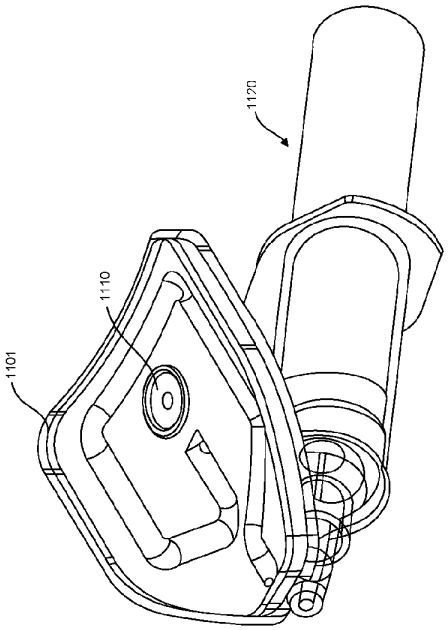


FIG. 11E

【図１２Ａ】

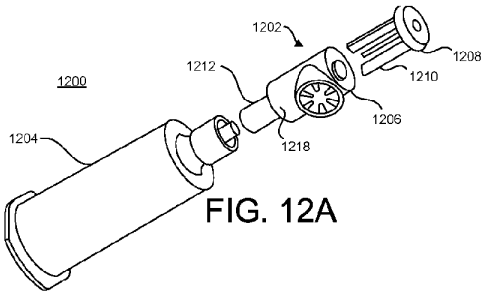


FIG. 12A

【図１２Ｂ】

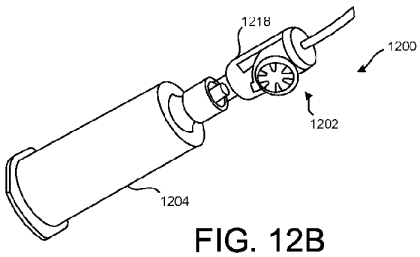


FIG. 12B

【図１２Ｃ】

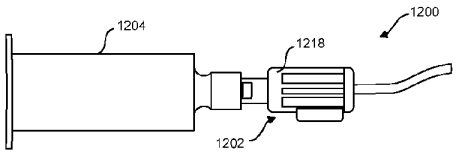


FIG. 12C

【図１２Ｄ】

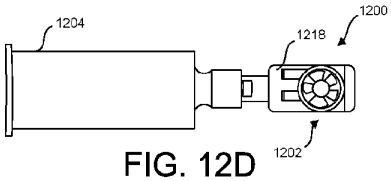


FIG. 12D

【図１３Ａ】

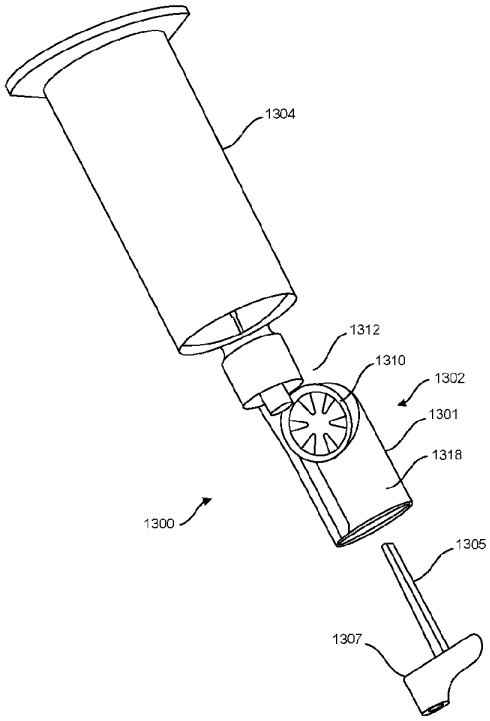


FIG. 13A

【図１３Ｂ】

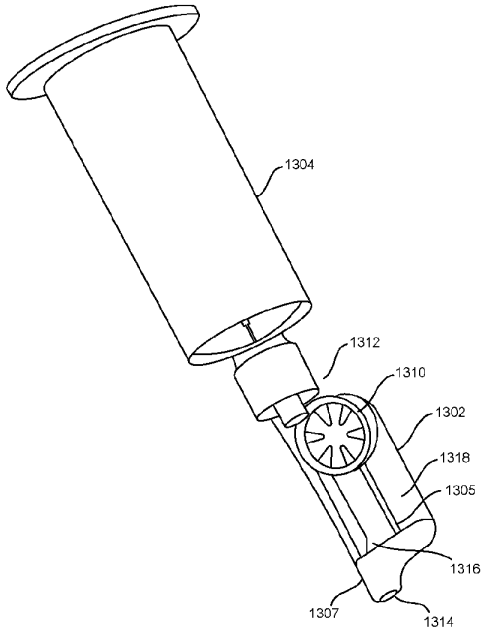


FIG. 13B

【図１３Ｃ】

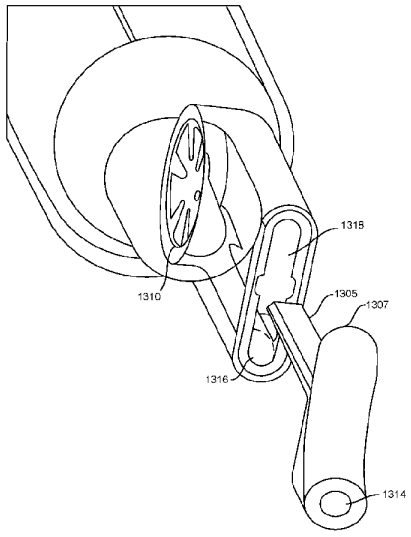


FIG. 13C

【図１３Ｄ】

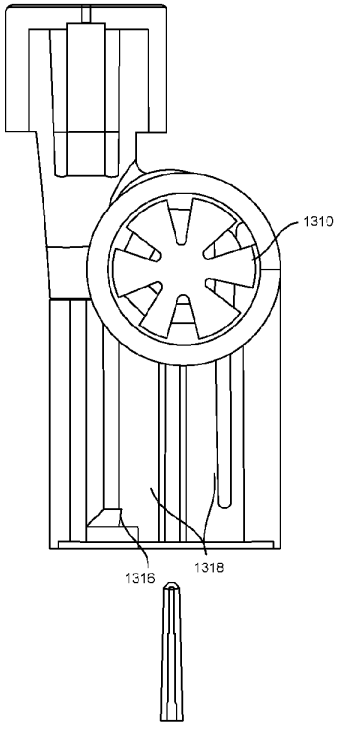


FIG. 13D

【図１４Ａ】

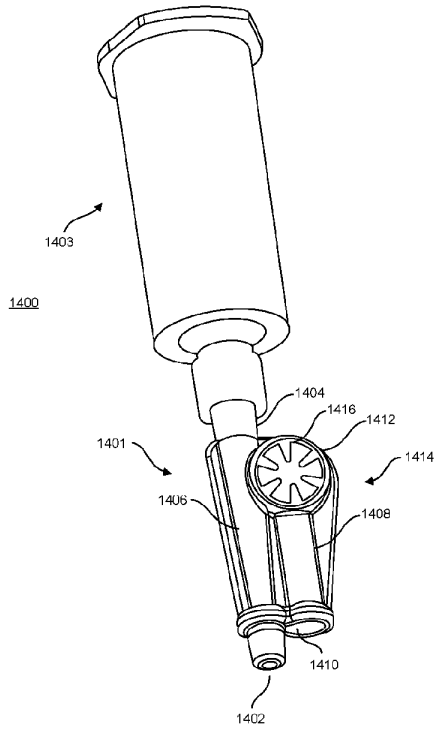


FIG. 14A

【図１４Ｂ】

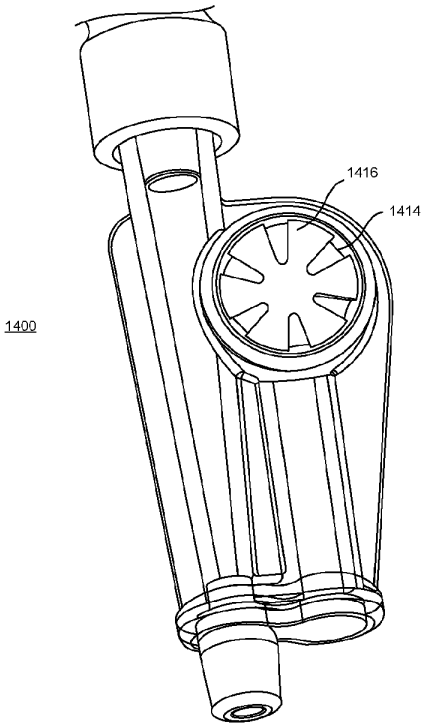


FIG. 14B

【図１４Ｃ】

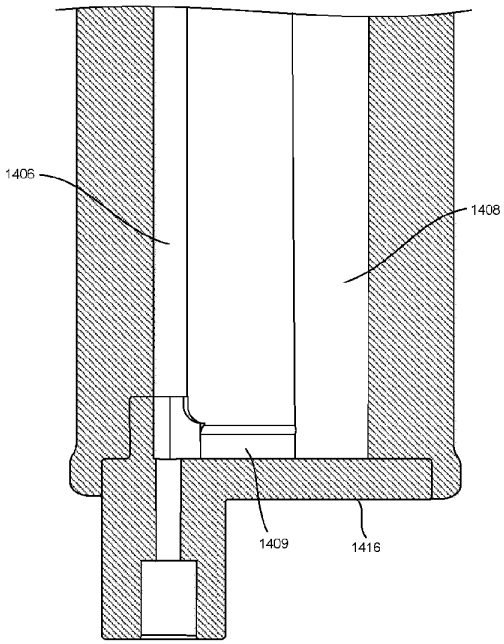


FIG. 14C

【図１４Ｄ】

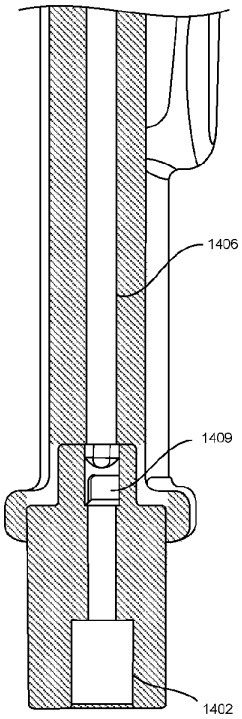


FIG. 14D

【図１４Ｅ】

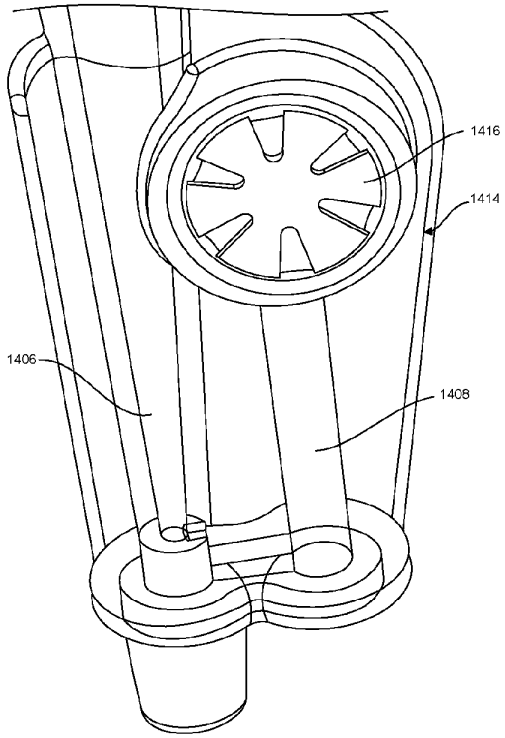


FIG. 14E

【図１５Ａ】

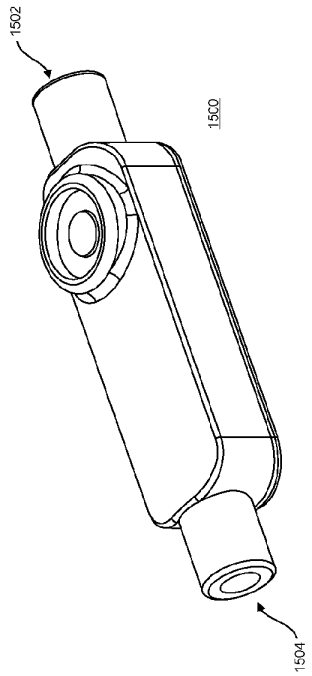


FIG. 15A

【図１５Ｂ】

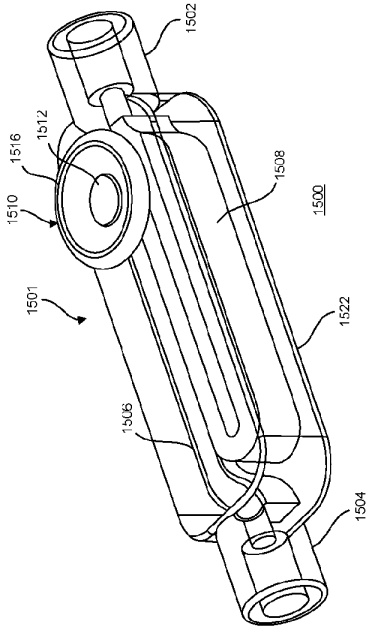


FIG. 15B

【図１５Ｃ】

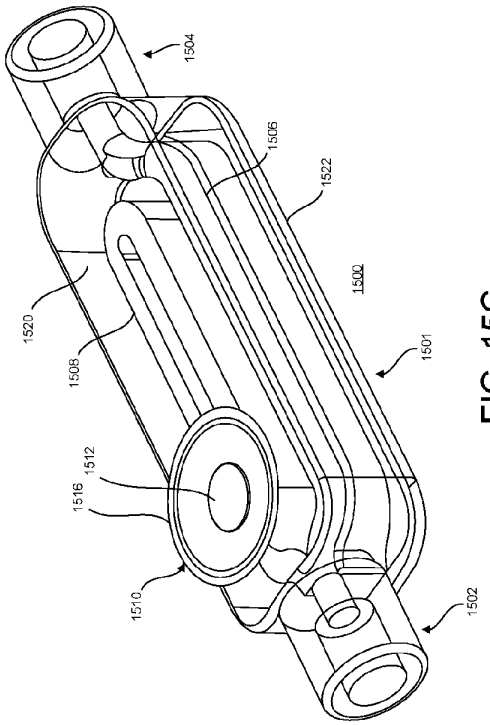


FIG. 15C

【図１５Ｄ】

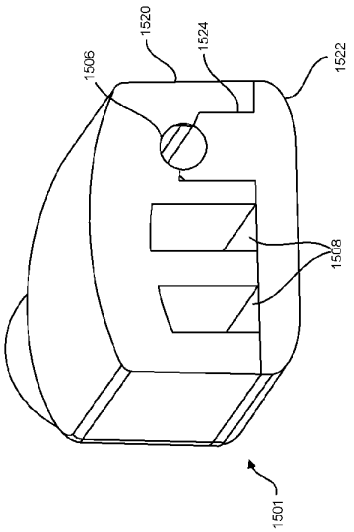


FIG. 15D

【図１５Ｅ】

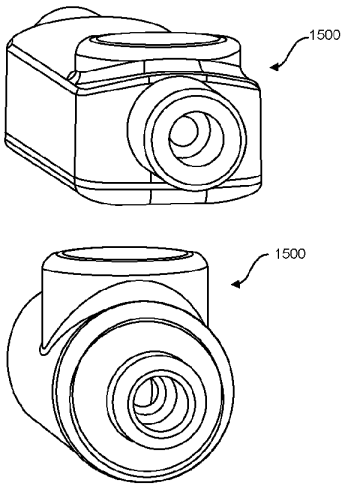


FIG. 15E

【図１５Ｆ】

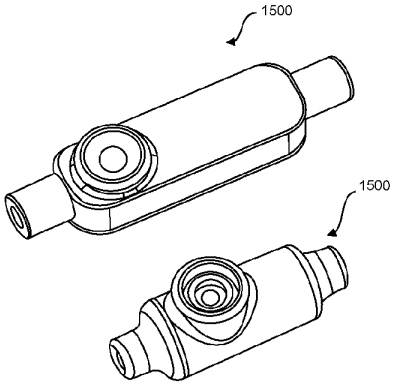


FIG. 15F

【図１５Ｇ】

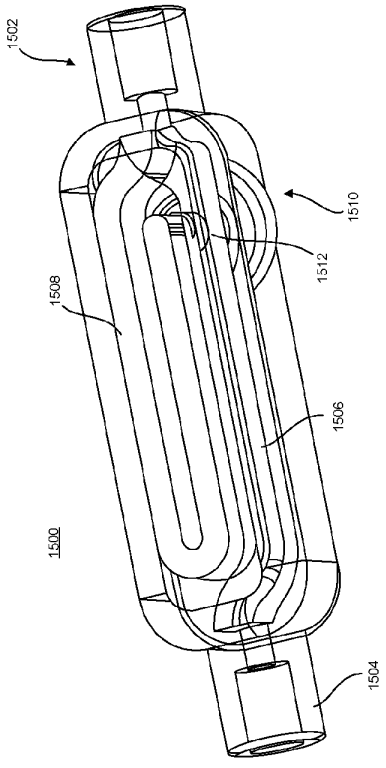


FIG. 15G

【図１６Ａ】

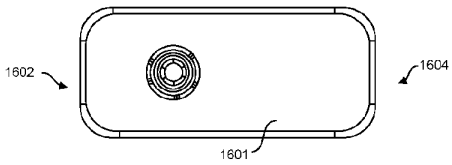


FIG. 16A

【図１６Ｂ】

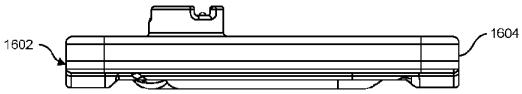


FIG. 16B

【図１６Ｃ】

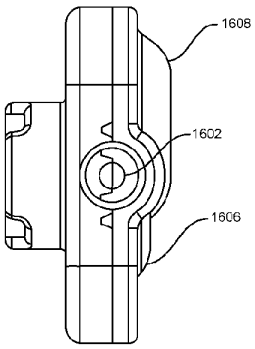


FIG. 16C

【図１６Ｄ】

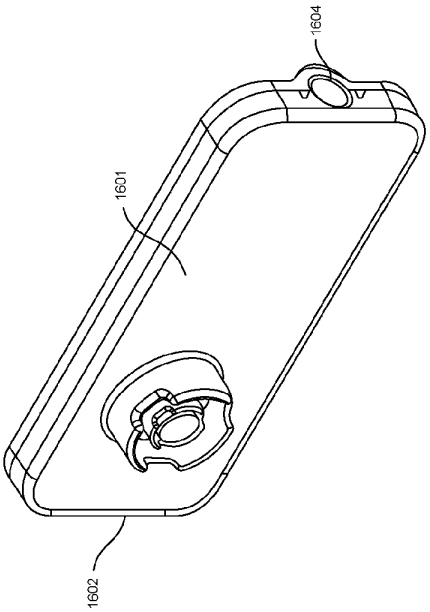


FIG. 16D

【図１７Ａ】

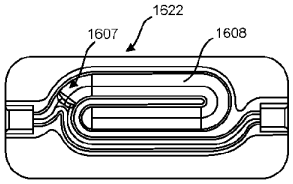


FIG. 17A

【図１７Ｂ】

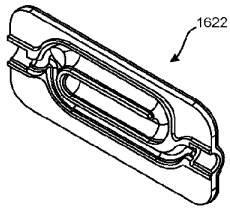


FIG. 17B

【図１７Ｃ】

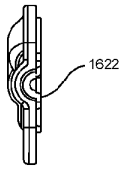


FIG. 17C

【図１７Ｄ】

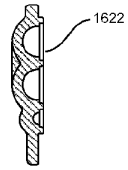


FIG. 17D

【図１７Ｅ】



FIG. 17E

【図１８Ａ】

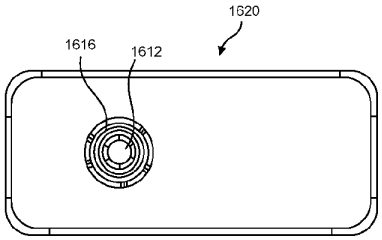


FIG. 18A

【図１８Ｂ】

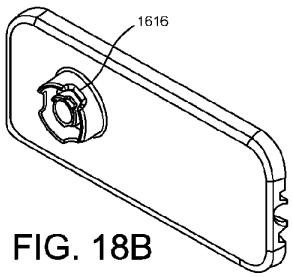


FIG. 18B

【図１８Ｃ】

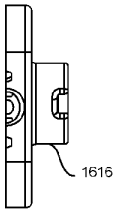


FIG. 18C

【図１８Ｄ】

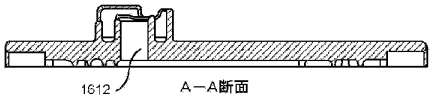


FIG. 18D

【図１８Ｅ】

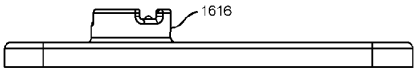


FIG. 18E

【図１８Ｆ】

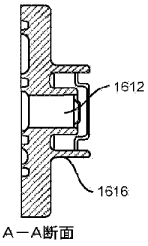


FIG. 18F

【図１９Ａ】

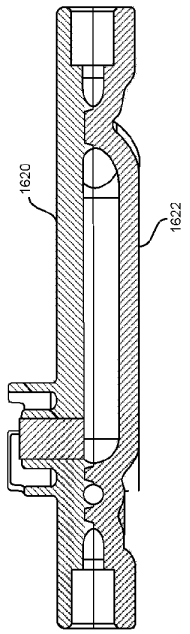


FIG. 19A

【図１９Ｂ】

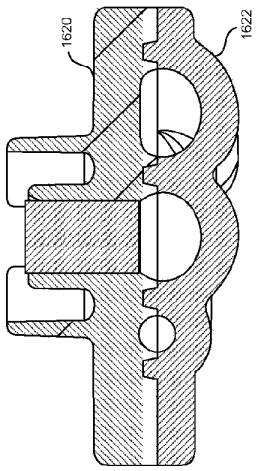


FIG. 19B

【図２０】

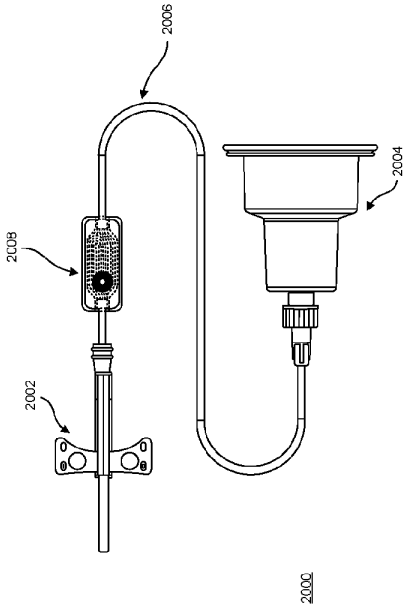


FIG. 20

【図２１】

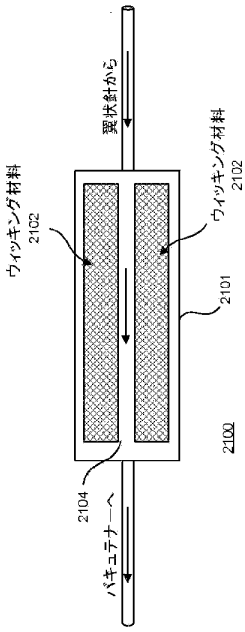


FIG. 21

【図２２Ａ】

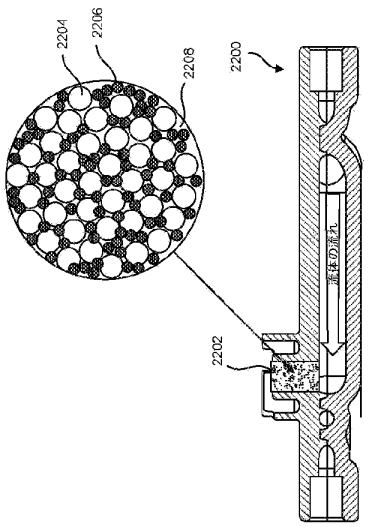


FIG. 22A

【図２２Ｂ】

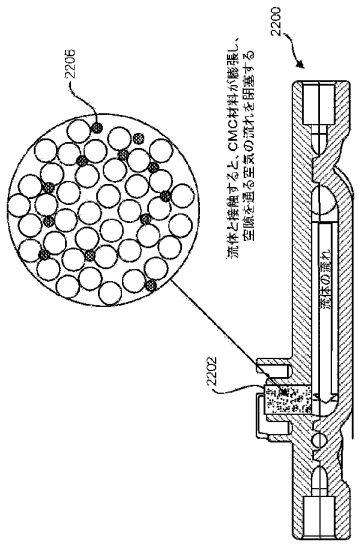


FIG. 22B

【図２３Ａ】

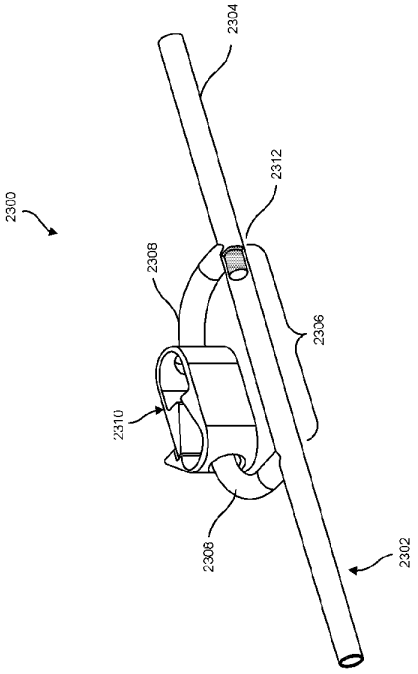


FIG. 23A

【図２３Ｂ】

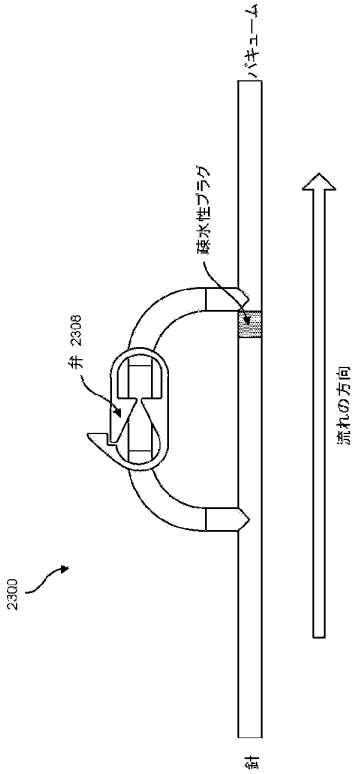


FIG. 23B

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

Bibliographic data: WO2018125929 (A1) — 2018-07-05

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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

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

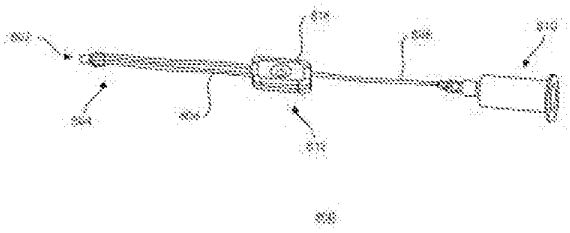
Classification: **- international:** ***A61B5/15; A61B5/153; A61B5/154; A61B5/157***
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150221 (US); A61B5/150251 (EP, US); A61B5/150274 (EP, US); A61B5/150351 (US); A61B5/150755 (US); A61B5/150786 (US); A61B5/150946 (US); A61B5/150992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

Application number: WO2017US68569 20171227 Global Dossier

Priority number(s): US201662439426P 20161227

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

Abstract of WO2018125929 (A1)



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

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

(19) World Intellectual Property Organization
International Bureau

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

WIPO | PCT

(10) International Publication Number
WO 2018/125929 A1

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

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

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

(25) Filing Language: English

(26) Publication Language: English

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

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

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

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

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

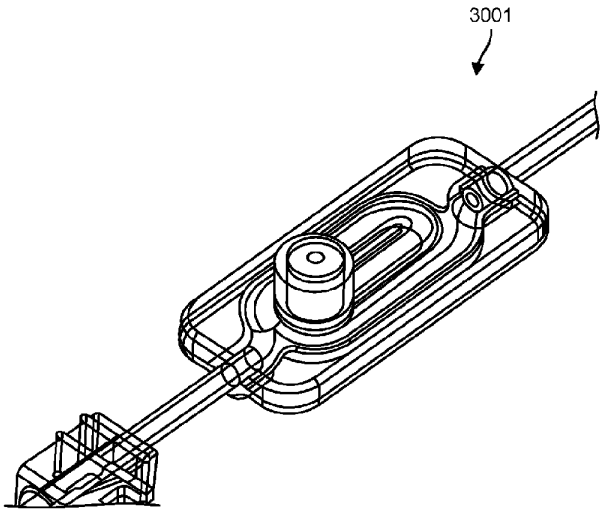


FIG. 30B

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

WO 2018/125929 A1

[Continued on next page]

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

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

Published:

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

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

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

BACKGROUND

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

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

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

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

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

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

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

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

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

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

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

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

SUMMARY

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

BRIEF DESCRIPTION OF THE DRAWINGS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

DETAILED DESCRIPTION

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

[00144] FIGS. 25A – D show a blood optimization system 2500 and blood sequestration device 2502, formed substantially as described in FIGS. 15, 16, 17, 18 and 19, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2520. Air initially in the blood sequestration chamber 2520 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2520. The air venting mechanism includes an air permeable blood barrier 2506, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2520.

[00145] The air venting mechanism includes an inner wall 2516 that at least partially circumscribes or surrounds the air permeable blood barrier 2506, and an outer wall 2504 spaced apart from the inner wall 2516. The outer wall 2504 can have one or more air vents 2514 formed therein. The outer wall 2504 extends higher upward than the inner wall 2516, such that a lid 2510, such as a cap, plug, cover, etc., can be attached to the outer wall 2504 and be displaced by a small distance from the top of the inner wall 2516. A seal 2508 in the form of a silicone wafer, or other elastomeric material, fits within the outer wall 2504 to cover the air permeable blood barrier 2506 and abut the top of the inner wall 2516. The seal 2508 covers and seals the air permeable blood barrier 2506 and inhibits air from entering the blood sequestration chamber 2520 through the air permeable blood barrier 2506. A fulcrum 2512 on an underside of the lid 2510 allows the seal 2508 to flexibly disconnect from the top of the inner wall 2516 when pushed by air displaced from the blood sequestration chamber 2520, to allow air to vent from the air permeable blood barrier 2506 and through the one or more air vents 2514 in the outer wall 2504.

[00146] FIG. 26A – E illustrate a blood sample optimization system 2600 that includes a patient needle 2602 for vascular access to a patient's bloodstream, a blood sample collection device 2604 to facilitate the collecting of one or more blood samples for blood testing or blood cultures, and a conduit 2606 providing a fluid connection between the patient needle 2602 and the blood sample collection device 2604. The conduit 2606 can include flexible tubing. In preferred implementations, the blood sample collection device 2604 includes a protective shield 2605 that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the

collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2602.

[00147] The blood sample optimization system 2600 further includes a blood sequestration device 2608, located at any point on the conduit 2606 between the patient needle 2602 and the blood sample collection device 2604. The location of the blood sequestration device 2608 can be based on a length of the conduit between the blood sequestration device 2608 and the patient needle 2602, and the associated volume that length provides.

[00148] The blood sequestration device 2608 includes an inlet port 2612 for being connected to the conduit 2606 toward the patient needle 2602, and an outlet port 2614 for being connected to the conduit 2606 toward the blood sample collection device 2604. The blood sequestration device 2608 includes an outer housing 2616 and an inner housing 2617, both having a cylindrical form, and being connected concentrically. The outer housing 2616 includes an outer wall 2618 and an inner conduit 2620 that defines a blood sampling channel 2622 to convey blood through the conduit 2606 to the blood sampling device 2604. The inner housing 2617 fits snugly between the inner conduit 2620 and the outer wall 2618 of the outer housing, and is rotatable in relation to the outer housing 2616. The fit between the outer housing 2616 and the inner housing 2617 can be a friction fit that maintains the housings in a particular position. The inner housing 2617 defines a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of inner conduit 2620 of the outer housing 2616, and which terminates at an air vent 2628 having an air permeable blood barrier, as shown in FIG. 26E.

[00149] The blood sequestration chamber 2624 is connected with the blood sampling channel 2622 via diversion junction 2624 formed in the inner conduit 2620, when the blood sequestration device in a first state, illustrated in FIG. 26C. The protective shield 2606 on the collection needle 2604 provides a block for air or blood, enabling a diversion of an initial aliquot of blood into the blood sequestration chamber 2624 as the patient's blood pressure overcomes the ambient air pressure in the blood sequestration channel 2624 to displace air therefrom through air vent 2628.

[00150] When the inner housing 2617 is rotated relative to the outer housing 2616, or vice versa, to a second state, as illustrated in FIG. 26D, the blood sequestration chamber 2624 is shut off from diversion junction 2624, enabling a direct path from the patient needle through the conduit 2606 to the collection needle 2604, via blood sampling channel 2622. The outer housing 2616 and/or inner housing 2617 can include ridges or grooves formed within a portion of their surfaces, to facilitate relative rotation from the first state to the second state.

[00151] FIGS. 27A – D illustrate a blood optimization system 2700 and blood sequestration device 2702, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, and 25, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2720. Air initially in the blood sequestration chamber 2720 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2720. The air venting mechanism includes an air permeable blood barrier 2706, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2720.

[00152] The air venting mechanism includes an inner wall 2716 that at least partially circumscribes or surrounds the air permeable blood barrier 2706, and an outer wall 2704 spaced apart from the inner wall 2716. A cap 2722 is positioned on the air venting mechanism, preferably by having a lower cap wall 2728 that fits between the inner wall 2716 and the outer wall 2704 of the air venting mechanism, and frictionally abutting either the the inner wall 2716 or the outer wall 2704 or both. The cap 2722 further includes one or more vent holes 2724 or slits, apertures, openings, or the like, which extend through an upper surface of the cap 2722 around a downwardly extending plug 2726. The plug 2726 is sized and adapted to fit snugly within the space defined by inner wall 2716.

[00153] In a first position, as illustrated in FIG. 27C, the cap 2722 is extended from the air venting mechanism to allow air from the blood sequestration chamber 2720 to exit through the air permeable blood barrier 2706 and through the one or more vent holes 2724. Once the air from the blood sequestration chamber 2720 has been displaced, i.e., when the blood sequestration chamber 2720 is filled with the first aliquot of potentially tainted blood from the patient, then the cap 2722 can be pushed down on the air venting

mechanism in a second position as shown in FIG. 27D, so that the plug 2726 fits within the inner wall 2716 over the air permeable blood barrier 2706 to seal the air venting mechanism. In either the first position or the second position, the cap 2722 protects the air permeable blood barrier 2706 from outside air or from being touched by a user.

[00154] FIGS. 28A – F illustrate a blood optimization system 2800 and blood sequestration device 2802, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but utilizing a multi-layered filter, and in some implementations, a filter with trapped reactive material, for an air permeable blood barrier. As shown in FIGS. 28C and D, an air permeable blood barrier 2803 includes a first layer 2804 of an air permeable but blood impermeable material, and a second layer 2806 that includes a reactive material, such as a hydrophobic material, for repelling blood while still allowing air to pass through both layers. As shown in FIGS. 28E and F, the air permeable blood barrier 2803 can include any number of layers, such as a third layer 2808 formed of the same air permeable but blood impermeable material as first layer 2804, while a second layer 2806 includes trapped or embedded blood reactive material.

[00155] FIGS. 29A – C illustrate a blood optimization system 2900 and blood sequestration device 2902, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but in which a blood sequestration chamber 2904 is at least partially filled with a blood-absorptive material 2906. The blood-absorptive material 2906 can act as a wicking material to further draw in blood to be sequestered upon venipuncture of the patient, and prior to use of a blood drawing device such as a Vacutainer™ or a syringe, or the like.

[00156] FIGS. 30A – G illustrate a blood optimization system 3000 and blood sequestration device 3002, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26. The blood sequestration device 3000 includes an inlet port 3002 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 3002 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 3002 defines an opening into the blood sequestration device 3000, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the

opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00157] The inlet port 3002 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 3002, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 3000 at the time of blood draw or sampling.

[00158] The blood sequestration device 3000 further includes an outlet port 3004, which defines an opening out of the blood sequestration device 3000 and to the blood sample collection device. The outlet port 3004 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 3000 at the time of blood draw or sampling.

[00159] The blood sequestration device 3000 further includes a sampling channel 3006 between the inlet port 3002 and the outlet port 3004, and a sequestration chamber 3008 that is connected to and split off or diverted from the sampling channel 3006 at any point between the inlet port 3002 and the outlet port 3004. The sampling channel 3006 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 3008. The sampling channel 3006 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 3006 has a substantially similar cross sectional area as the opening of the inlet port 3002. In other implementations, the sampling channel 3006 can gradually widen from the inlet port 3002 to the outlet port 3004. The sequestration chamber 3008 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the

blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 3006.

[00160] In some exemplary implementations, the diversion between the sampling channel 3006 and the sequestration chamber 3008 is by diverter junction 3007. Diverter junction 3007 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008. The sequestration chamber 3008 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 3008.

[00161] The sequestration chamber 3008 is preferably maintained at atmospheric pressure, and includes a vent 3010 at or near a distal end of the sequestration chamber 3008. The vent 3010 may include an air permeable blood barrier 3012 as described above.

[00162] The blood sequestration device 3000 can include a housing 3001 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated FIG. 30F, the housing 3001 includes a top member 3020 and a bottom member 3022 that are mated together. The blood sequestration device 3000 can also include a gasket or other sealing member (not shown) so that when the top member 3020 is mechanically attached with the bottom member 3022, the interface between the two is sealed by the gasket or sealing member. The bottom member 3022 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 3006, the sequestration chamber 3008, and diverter junction 3007.

[00163] The sequestration chamber 3008 may have a larger cross section than the sampling channel 3006 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 3006.

[00164] In some implementations, the sampling channel 3006 and the sequestration chamber 3008 are formed by grooves, channels, locks or other pathways formed in housing 3001. The housing 3001 can be made of rubber, plastic, metal or any other suitable material. The housing 3001 can be formed of a clear or translucent material, or

of an opaque or non-translucent material. In other implementations, the housing 3001 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 3006 and/or the sequestration chamber 3008 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 3008 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 3006. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 3012 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00165] The air permeable blood barrier 3012 can be covered with, or surrounded by, a cap 3032. The cap 3032 can be sized and configured to inhibit a user from touching the air permeable blood barrier 3012 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 3012 as the air is displaced from the sequestration chamber 3008. The cap 3032 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00166] The air venting mechanism includes a wall 3030 that at least partially circumscribes or surrounds the air permeable blood barrier 3012. The wall 3030 can have one or more air vents formed therein. The cap 3032 covers wall 3030 and can be snapped, glued, or otherwise attached in place. A seal 3017 in the form of a silicone wafer, or other elastomeric material, fits within the wall 3030 to cover the air permeable blood barrier 3012 and abut the top of the wall 3030. The seal 3017 covers and seals the air permeable blood barrier 3012 and inhibits air from entering the blood sequestration chamber 3008 through the air permeable blood barrier 3012. A fulcrum 3012 on an underside of the cap 3032 allows the seal 3008 to flexibly disconnect from the top of the inner wall 3016 when pushed by air displaced from the blood sequestration chamber 3008, to allow air to vent from the air permeable blood barrier 3012 and through the one or more air vents in the wall 3030 and/or cap 3032.

[00167] In use, the blood sequestration device 3000 includes a sampling channel 3006 and a sequestration chamber 3008. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 3006 is directed to an outlet port 3004 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 3008 terminates at a vent 3010 to atmosphere that includes an air permeable blood barrier 3012.

[00168] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through inlet port 3002 of blood sequestration device 3000. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 3008 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 3008 to displace air therein through the air permeable blood barrier 3012, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 3006. In various exemplary embodiments, the sequestration chamber 3008 and sampling channel 3006 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00169] Eventually, the sequestration chamber 3008 fills with blood that displaces air through the air permeable blood barrier 3012. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 3012 material to completely or partially seal the vent 3010. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00170] Upon filling the blood sequestration pathway 3008 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 3006, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 3006, queuing up the uncontaminated blood to be drawn through the sampling channel 3006.

[00171] In yet another aspect, the blood sequestration chamber and/or blood sampling channel, or other component, of any of the implementations described herein,

can provide a visually discernable warning or result in a component adapted for operative fluid communication with the flash chamber of an introducer for an intravenous catheter into a blood vessel of a patient. The device and method provides a visually discernable alert when blood from the patient communicates with a test component reactive to communicated blood plasma, to visually change. The reaction with the blood or the plasma occurs depending on one or a plurality of reagents positioned therein configured to test for blood contents, substances or threshold high or low levels thereof, to visually change in appearance upon a result.

[00172] In yet other aspects, the blood sequestration chamber and/or blood sampling channel can be sized and adapted to provide a particular volumetric flow of blood, either during the sequestration process and/or the sampling process.

[00173] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

CLAIMS

1. A blood sequestration device comprising;

an inlet port;

an outlet port;

a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

the sequestration chamber, the sampling channel and the junction being sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

2. The blood sequestration device in accordance with claim 1, further comprising a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

3. The blood sequestration device in accordance with claim 1, wherein the vent further includes an inner wall within the outer wall and that contains the air permeable blood barrier.

4. The blood sequestration device in accordance with claim 1, wherein the one-way seal is positioned over the inner wall and within the outer wall of the vent.

5. The blood sequestration device in accordance with claim 4, wherein the cap includes an inner surface that faces the air permeable blood barrier, the

inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

6. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a sealing material that seals the vent upon contact with blood.

7. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

8. A blood sequestration and sampling system comprising;

a blood sampling pathway having a patient needle on a proximal end and a sample collection device on a distal end; and

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

an inlet port coupled with the blood sampling pathway toward the patient needle;

an outlet port coupled with the blood sampling pathway toward the sample collection device;

a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

the sequestration chamber, the sampling channel and the junction being sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the

first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

9. The blood sequestration system in accordance with claim 8, wherein the blood sequestration device further comprises a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

10. The blood sequestration system in accordance with claim 8, wherein the vent of the blood sequestration device further includes an inner wall within the outer wall and that contains the air permeable blood barrier.

11. The blood sequestration system in accordance with claim 8, wherein the one-way seal of the vent is positioned over the inner wall and within the outer wall of the vent.

12. The blood sequestration system in accordance with claim 11, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

13. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a sealing material that seals the vent upon contact with blood.

14. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

15. A blood sequestration device comprising;

an inlet port;

an outlet port;

a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

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

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

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

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

19. The blood sequestration device in accordance with claim 18, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

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

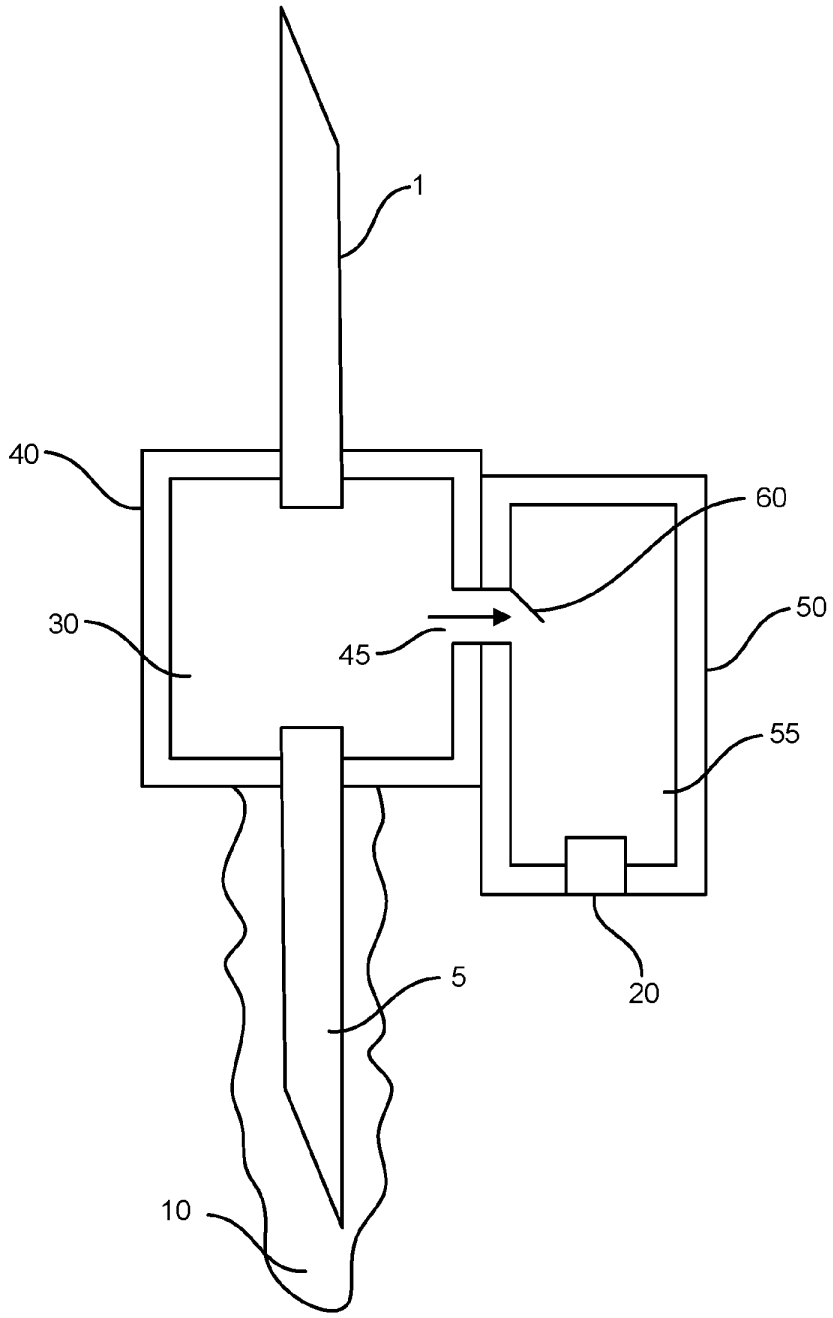


FIG. 1

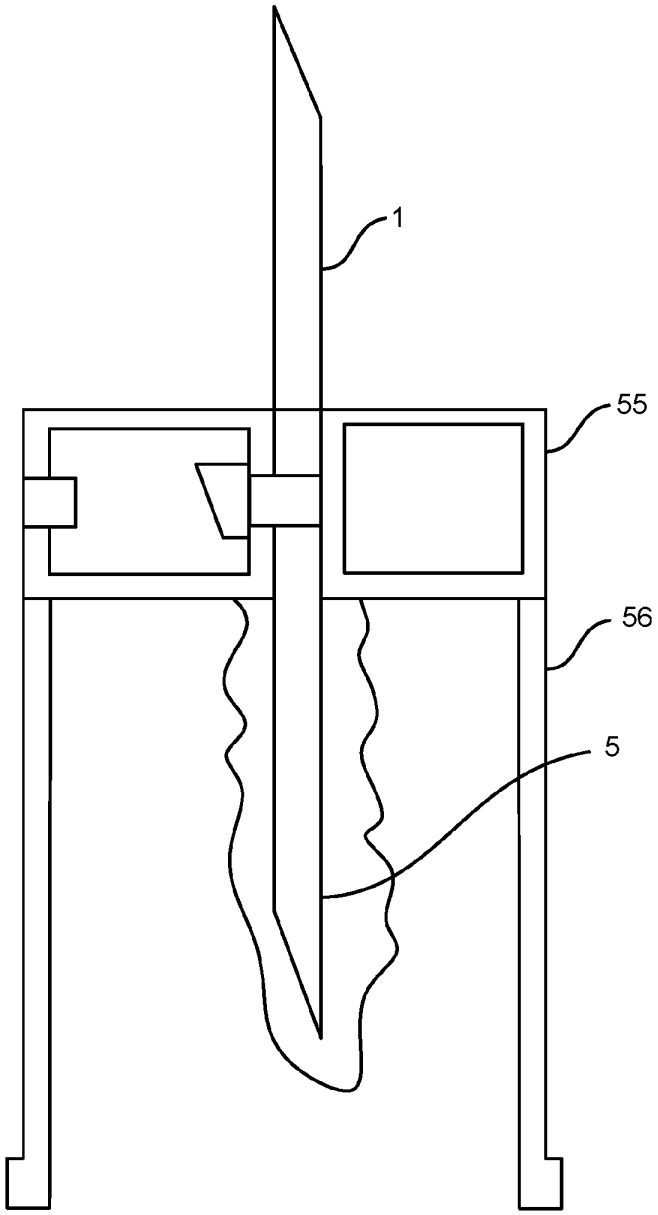


FIG. 2

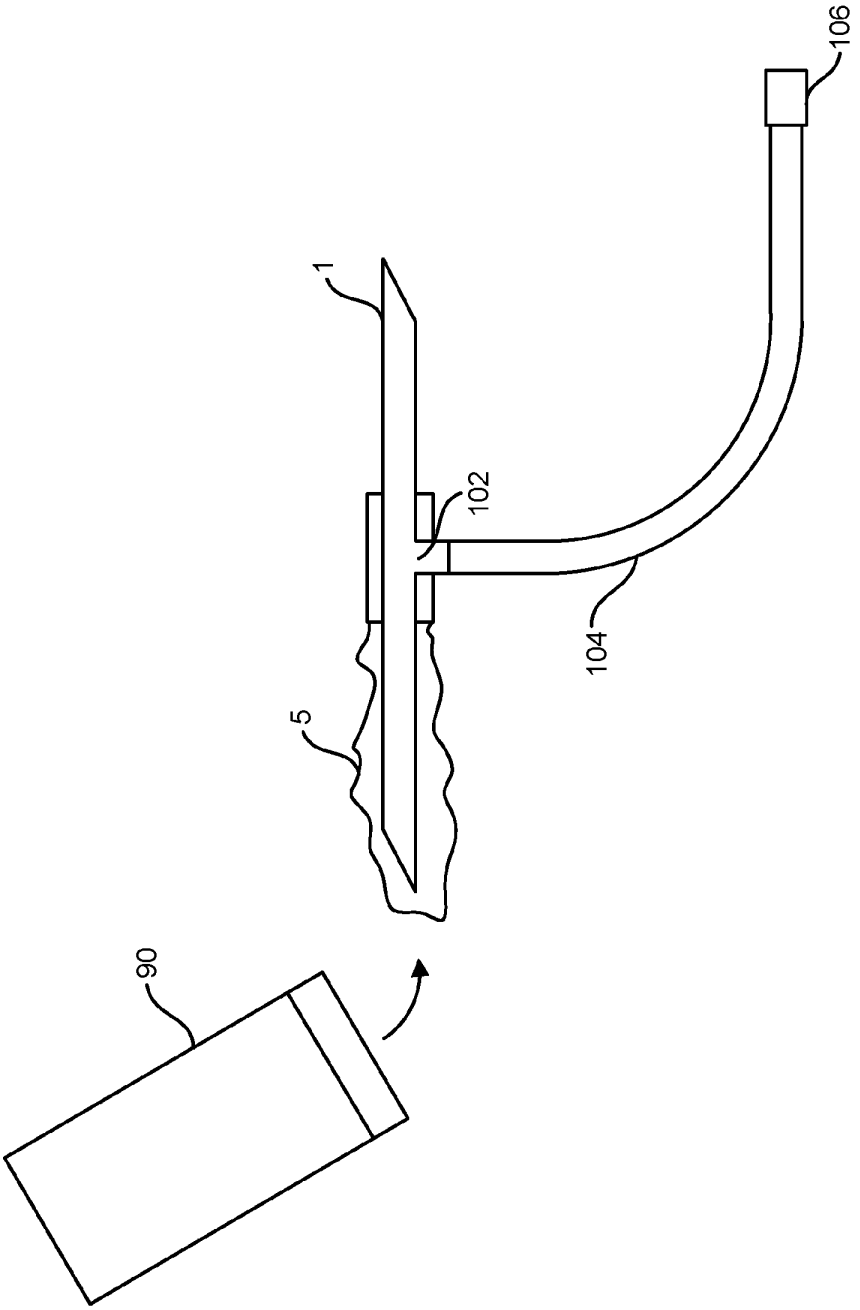


FIG. 3

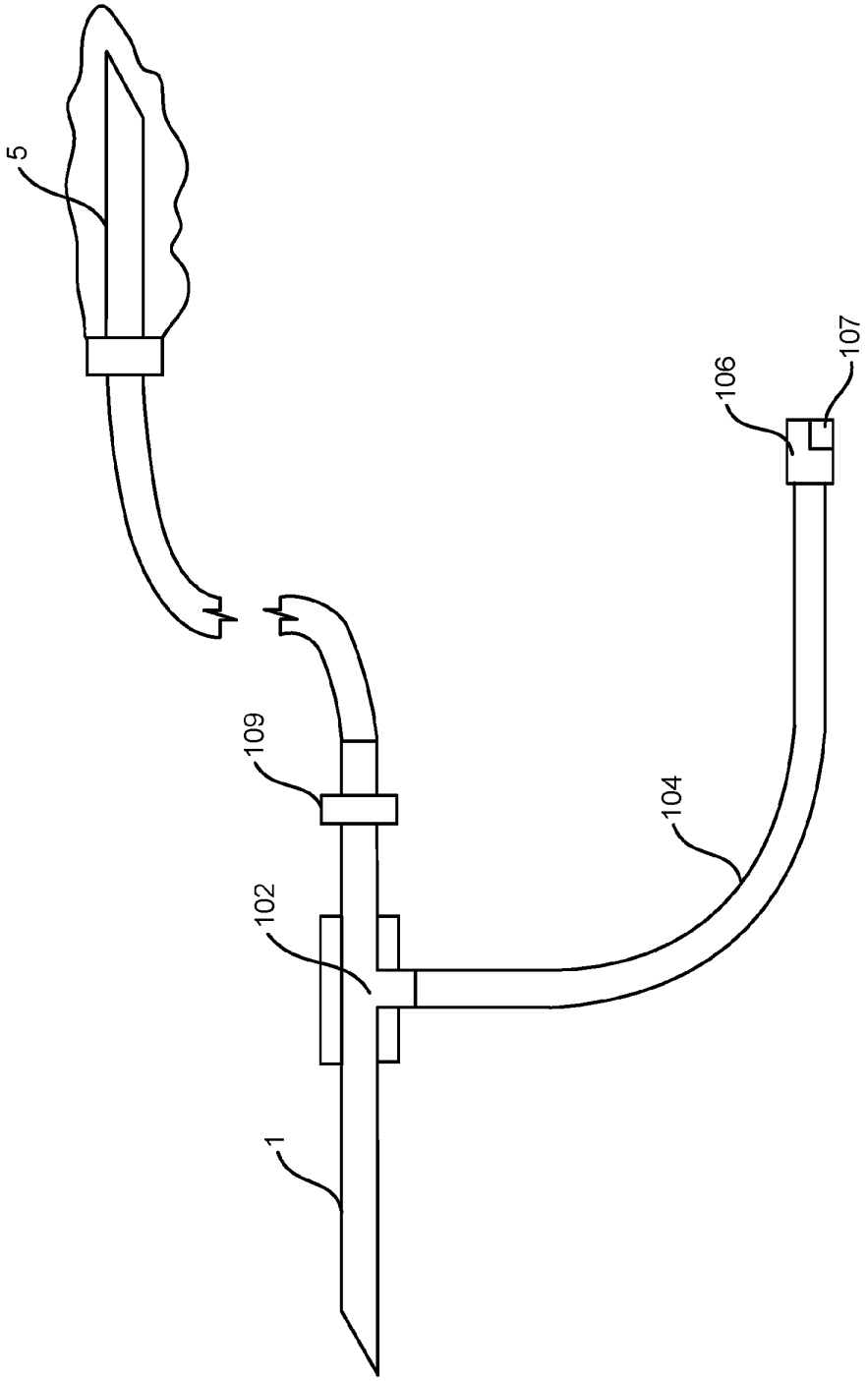


FIG. 4

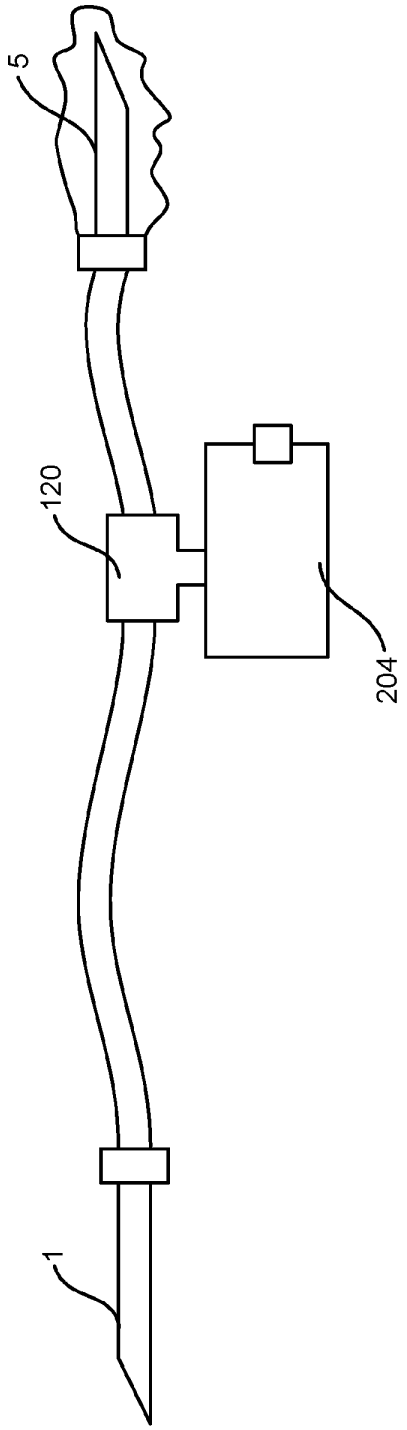


FIG. 5

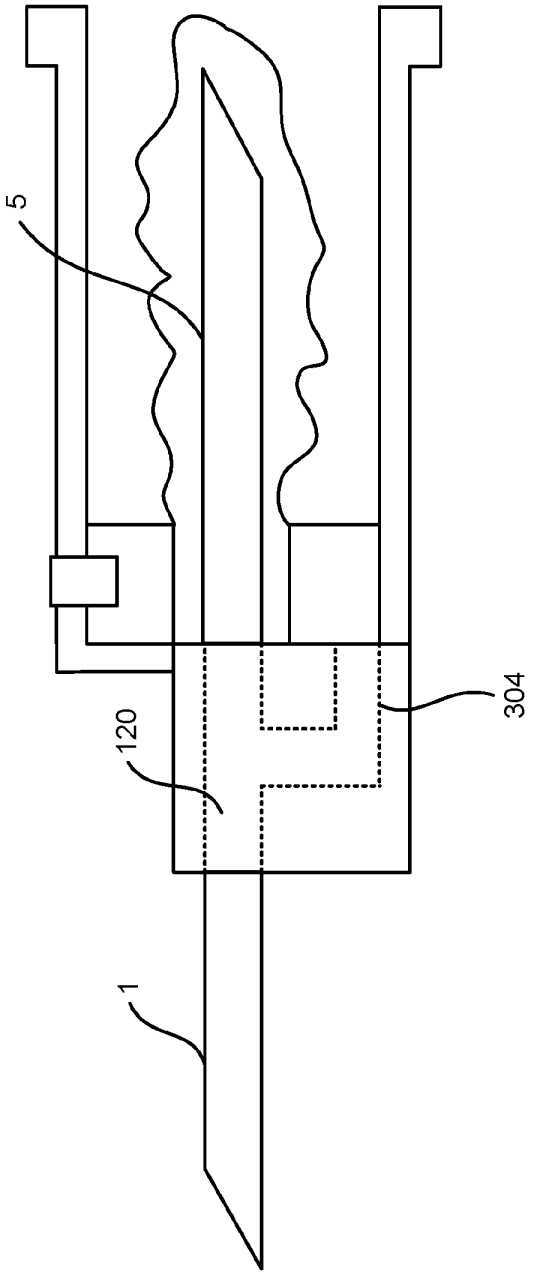


FIG. 6

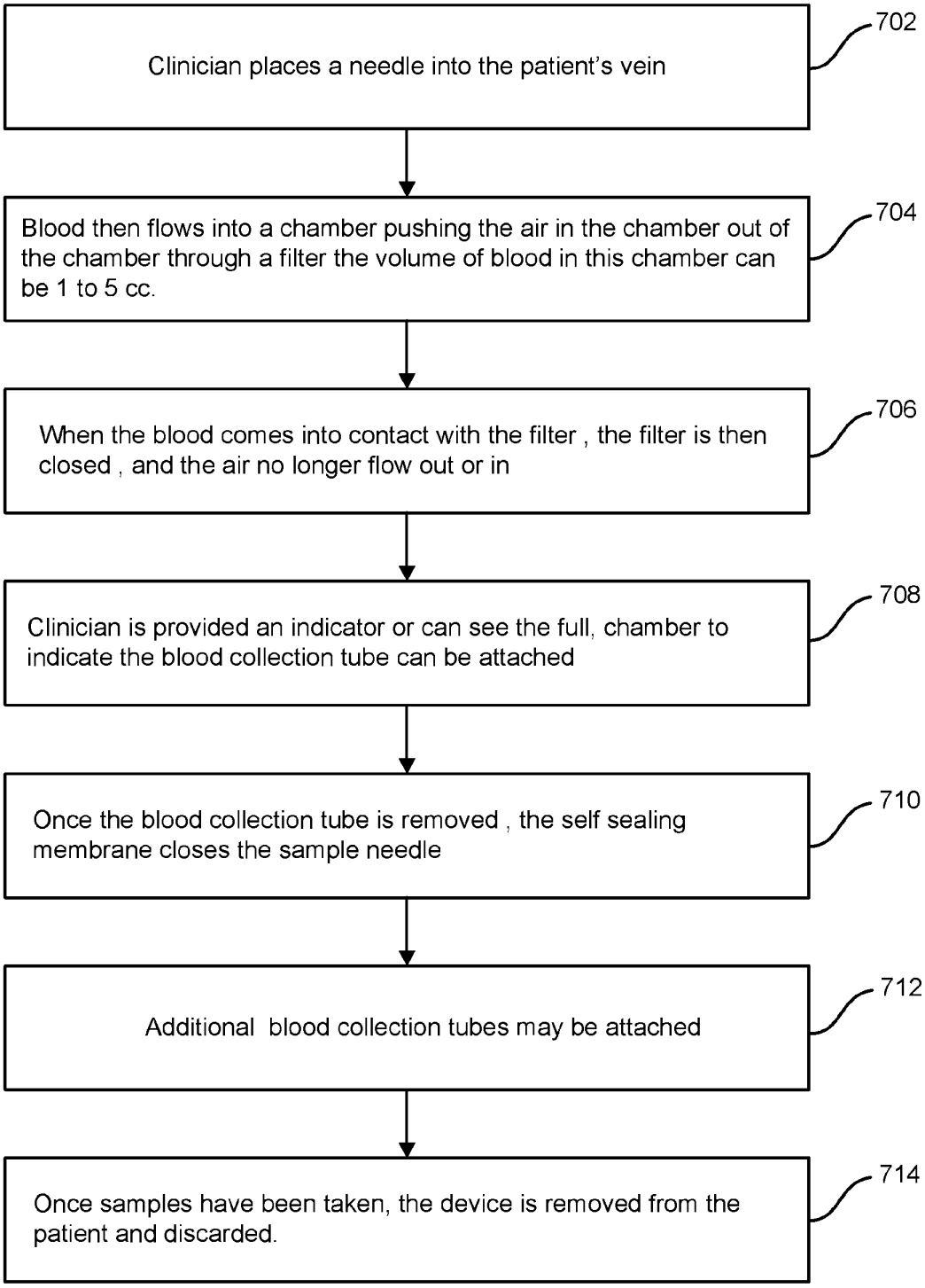

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air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

FIG. 7

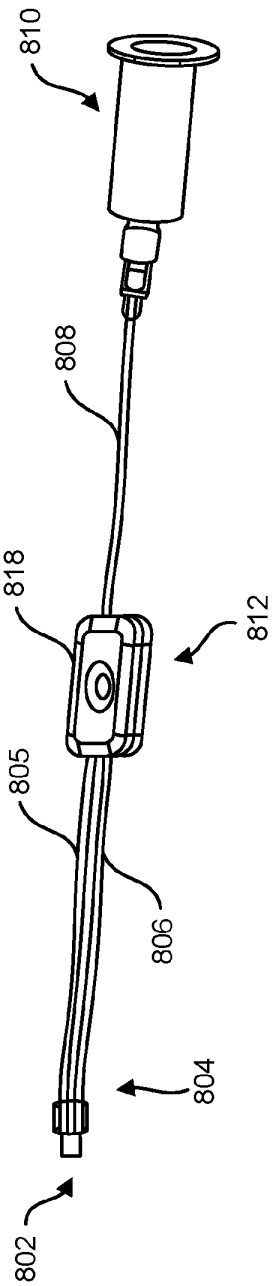


FIG. 8A

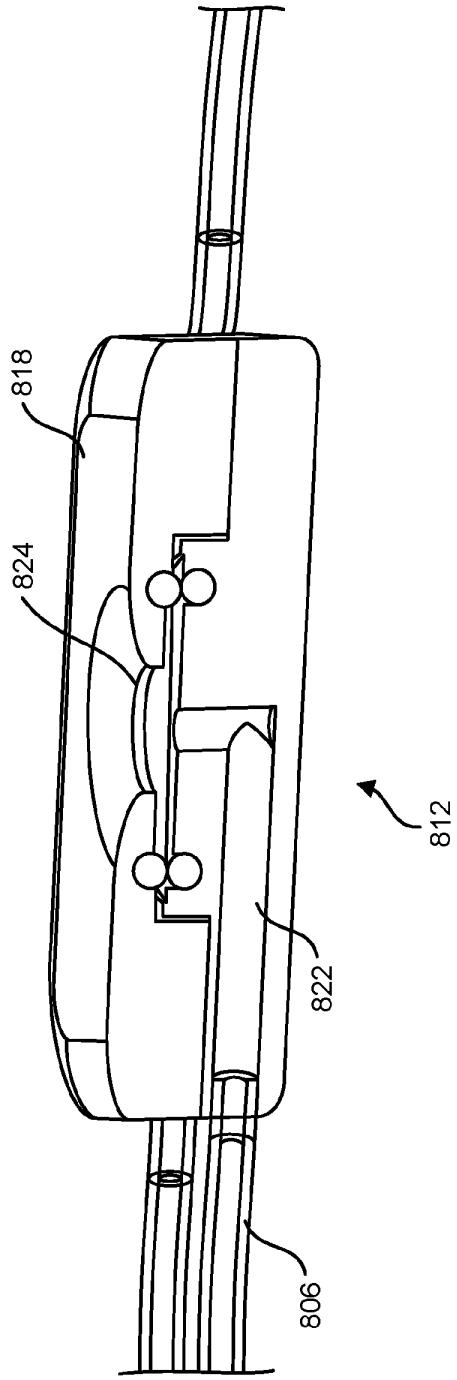


FIG. 8B

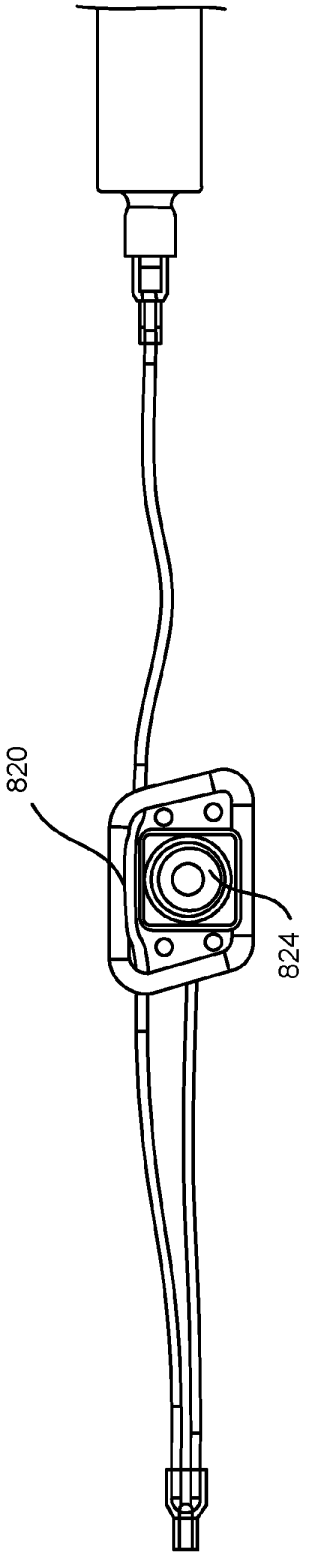


FIG. 8C

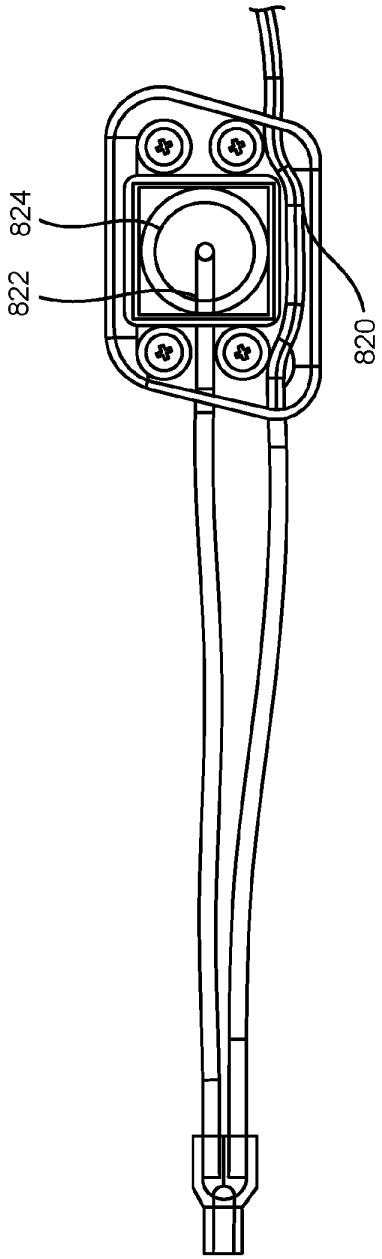


FIG. 8D

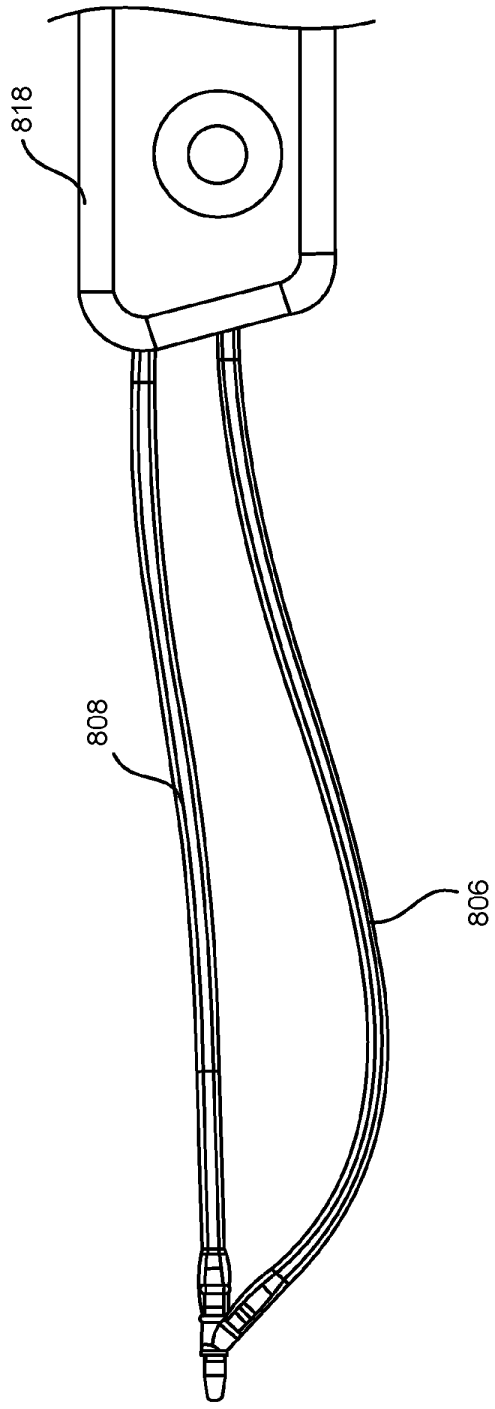


FIG. 8E

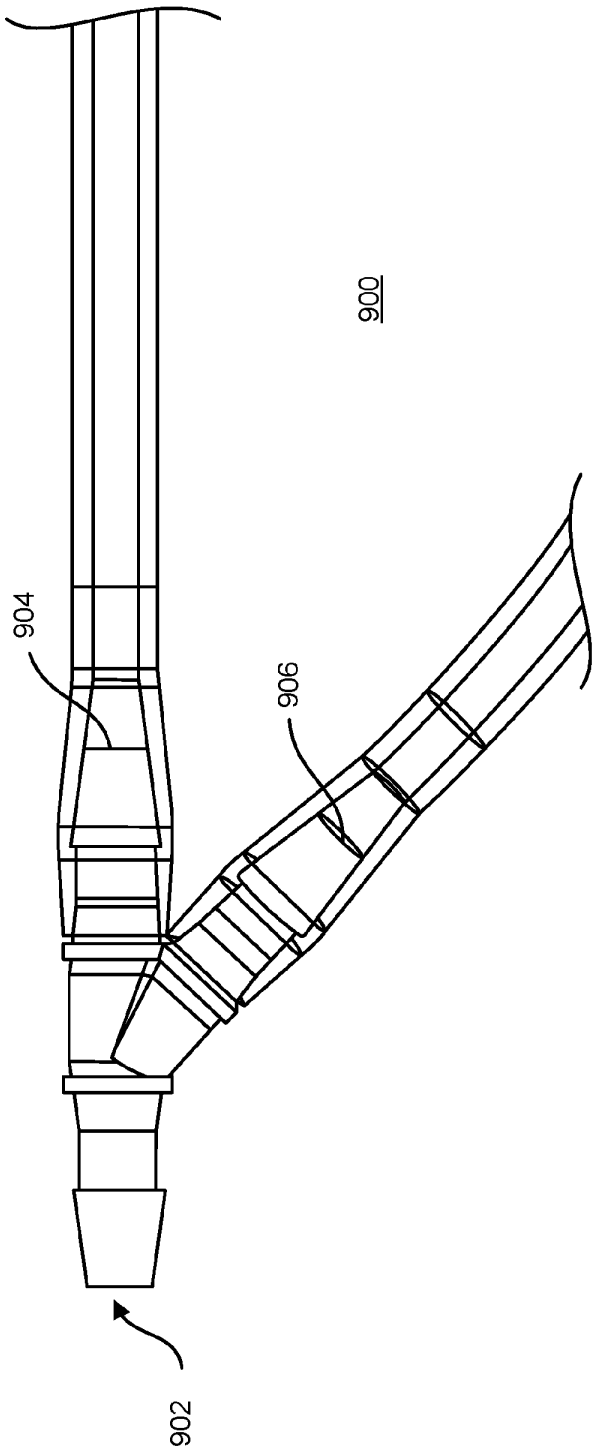


FIG. 9

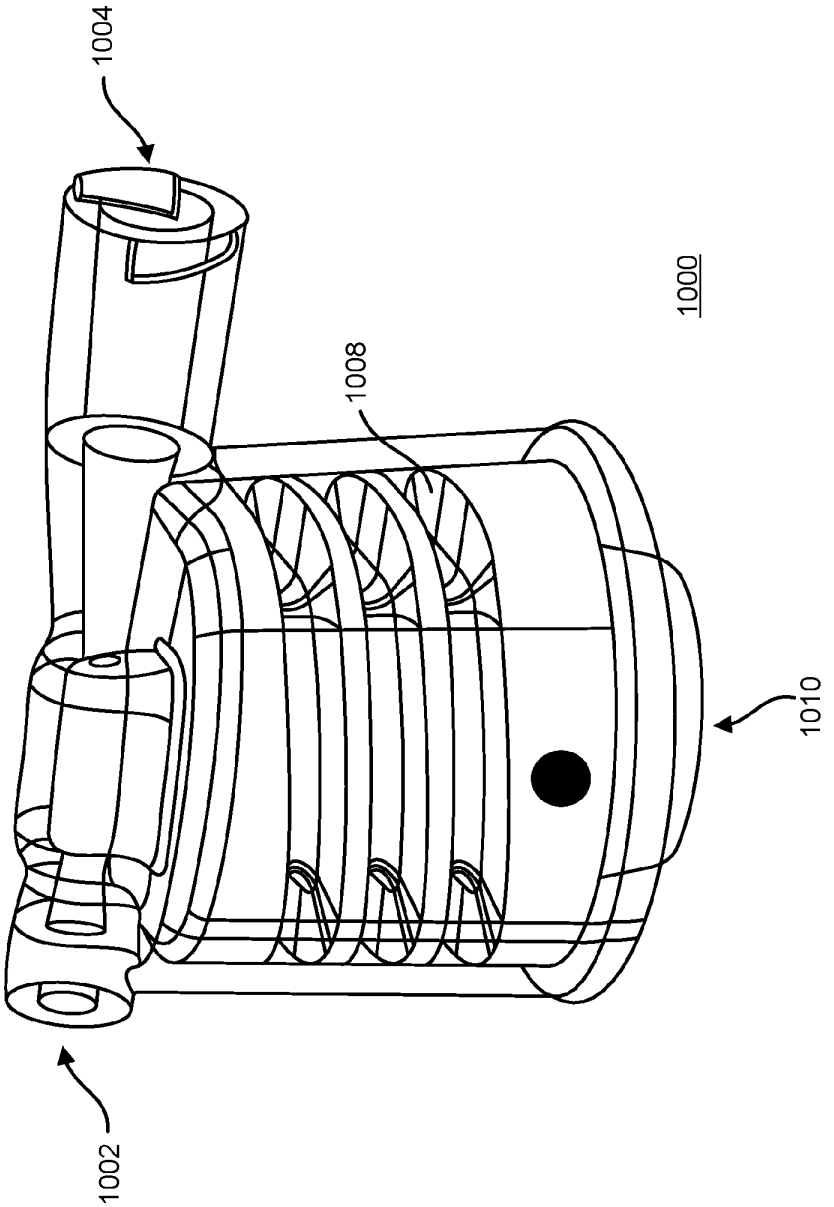


FIG. 10A

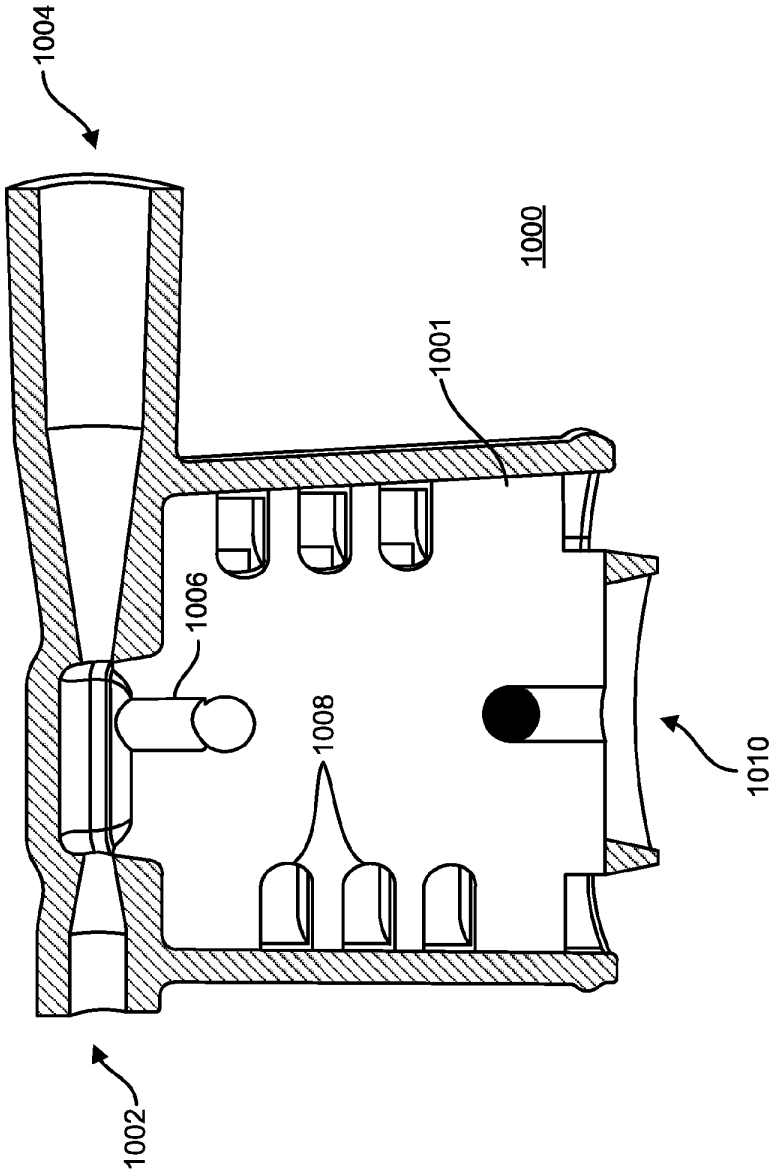


FIG. 10B

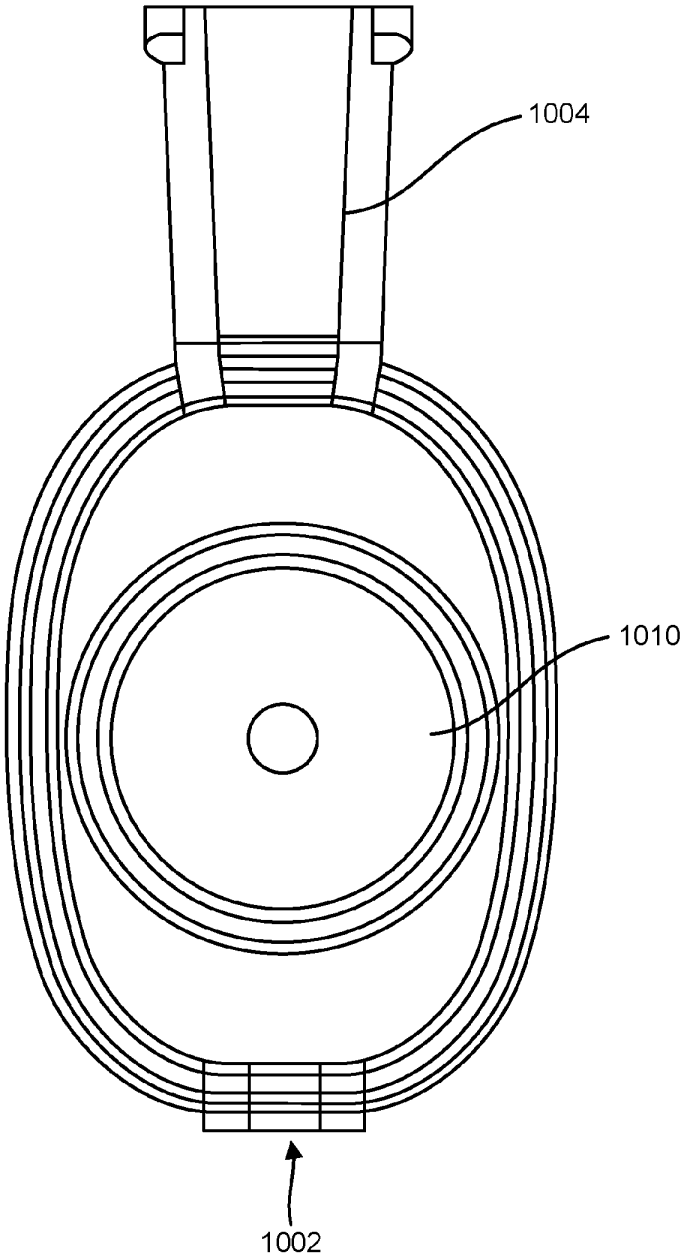


FIG. 10C

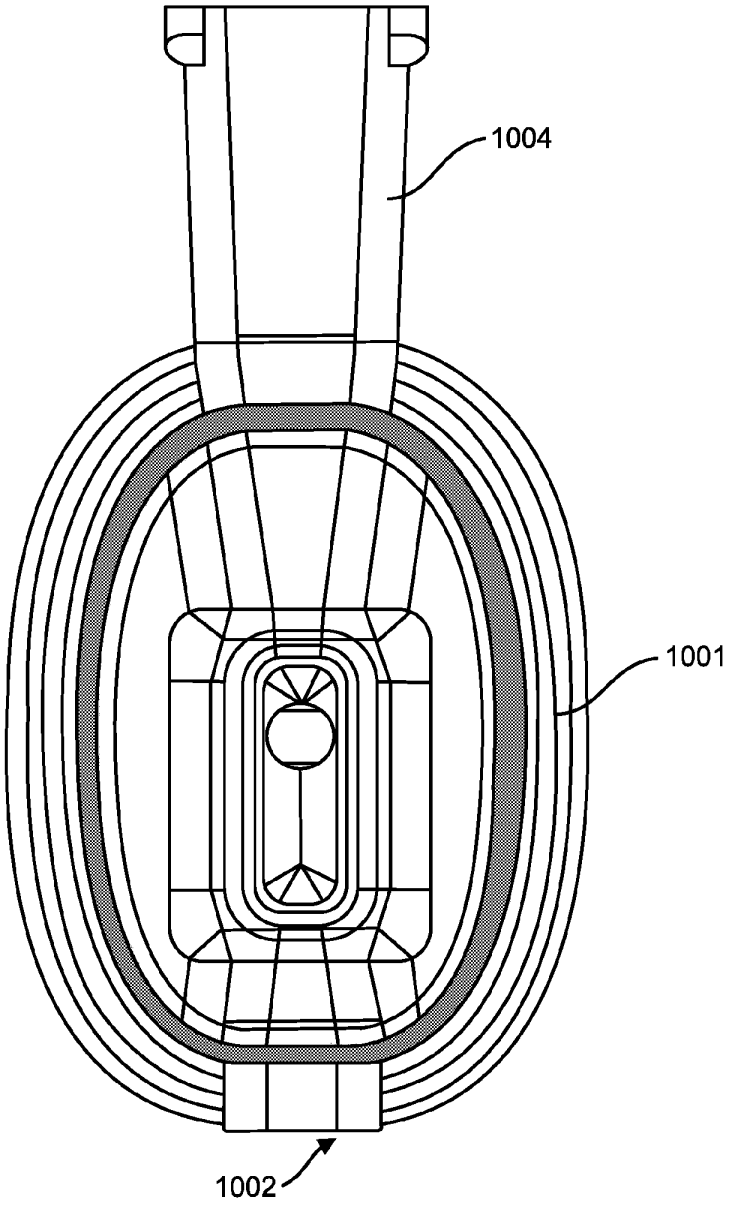


FIG. 10D

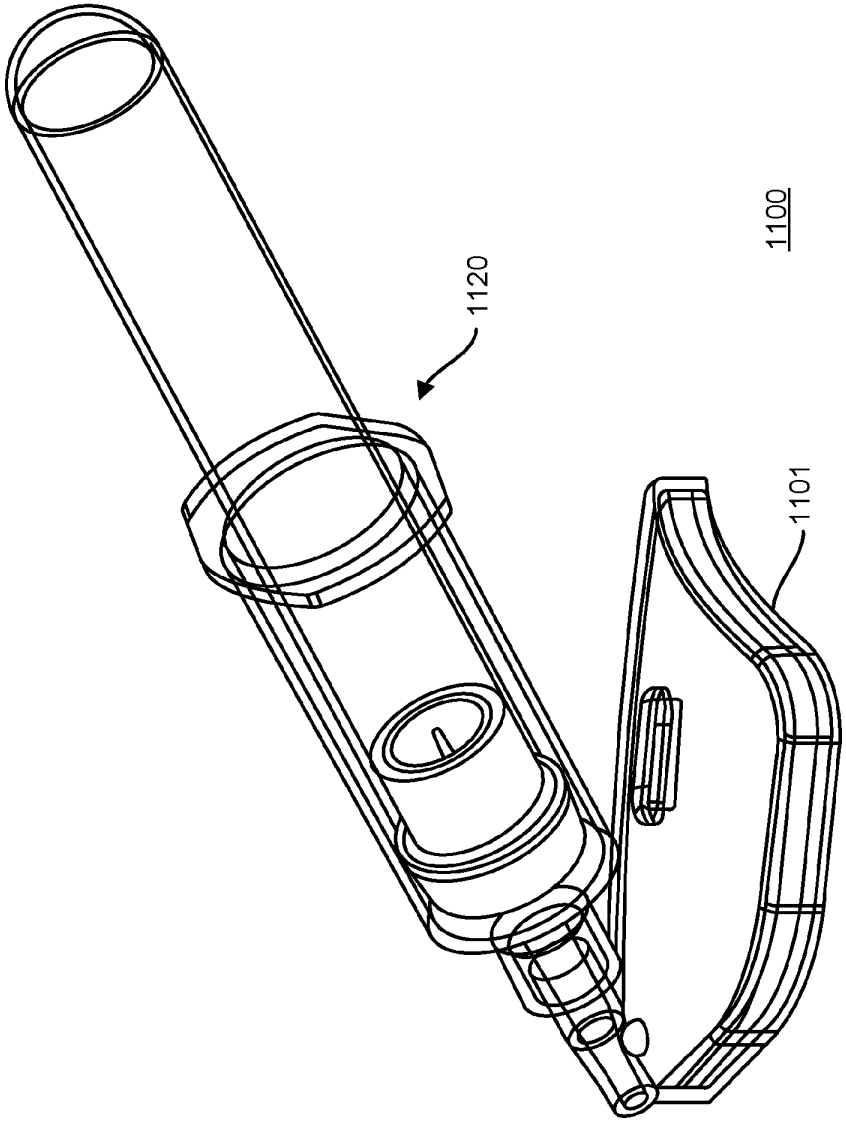


FIG. 11A

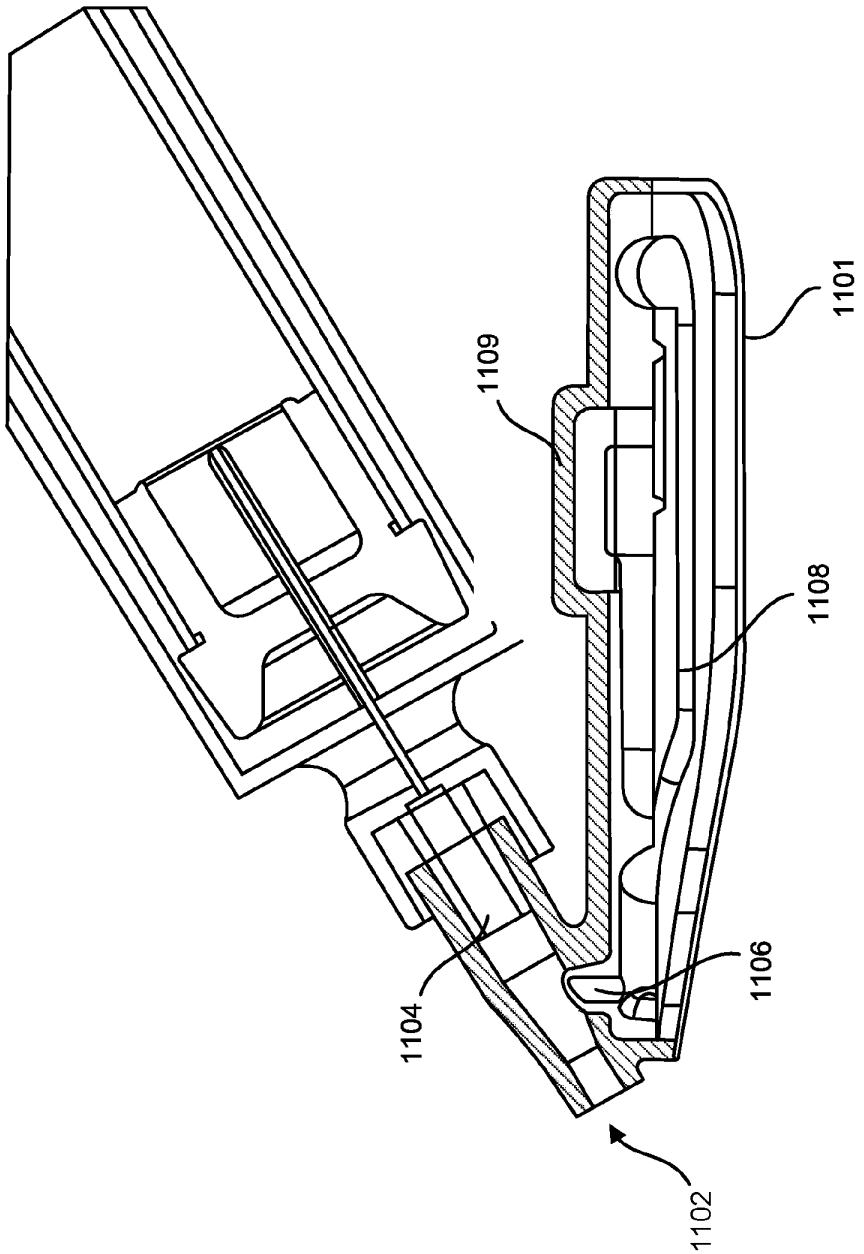


FIG. 11B

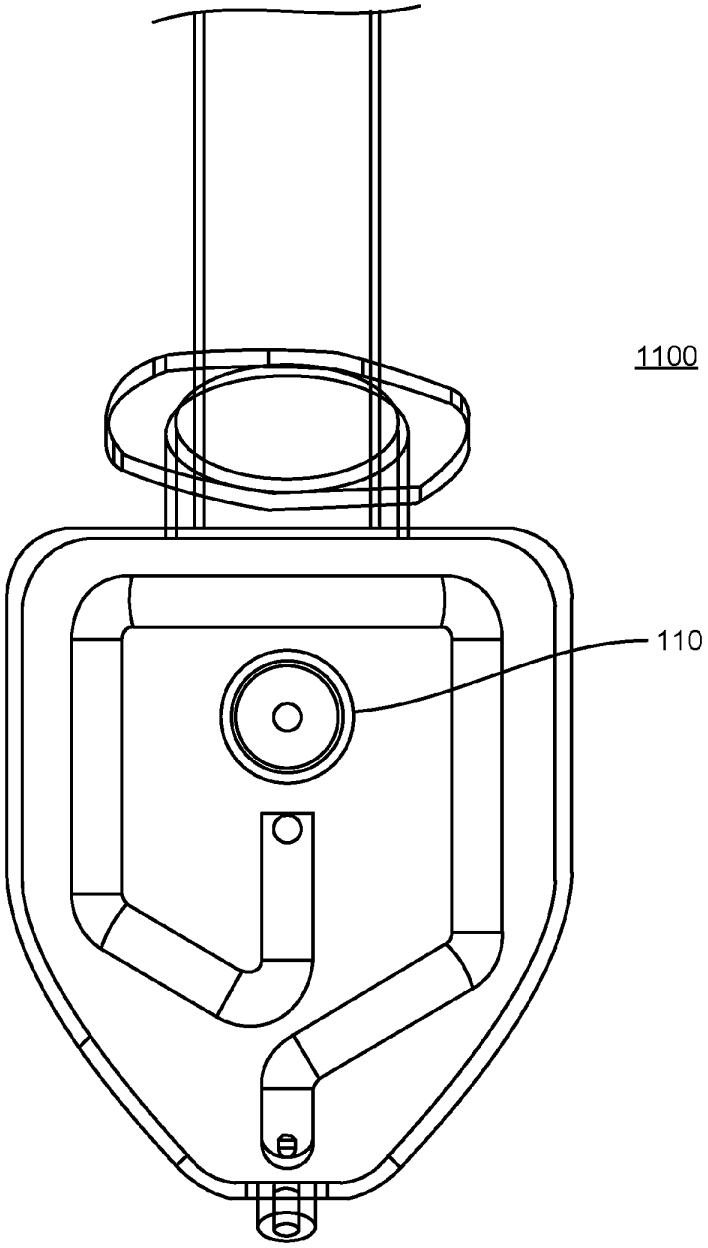


FIG. 11C

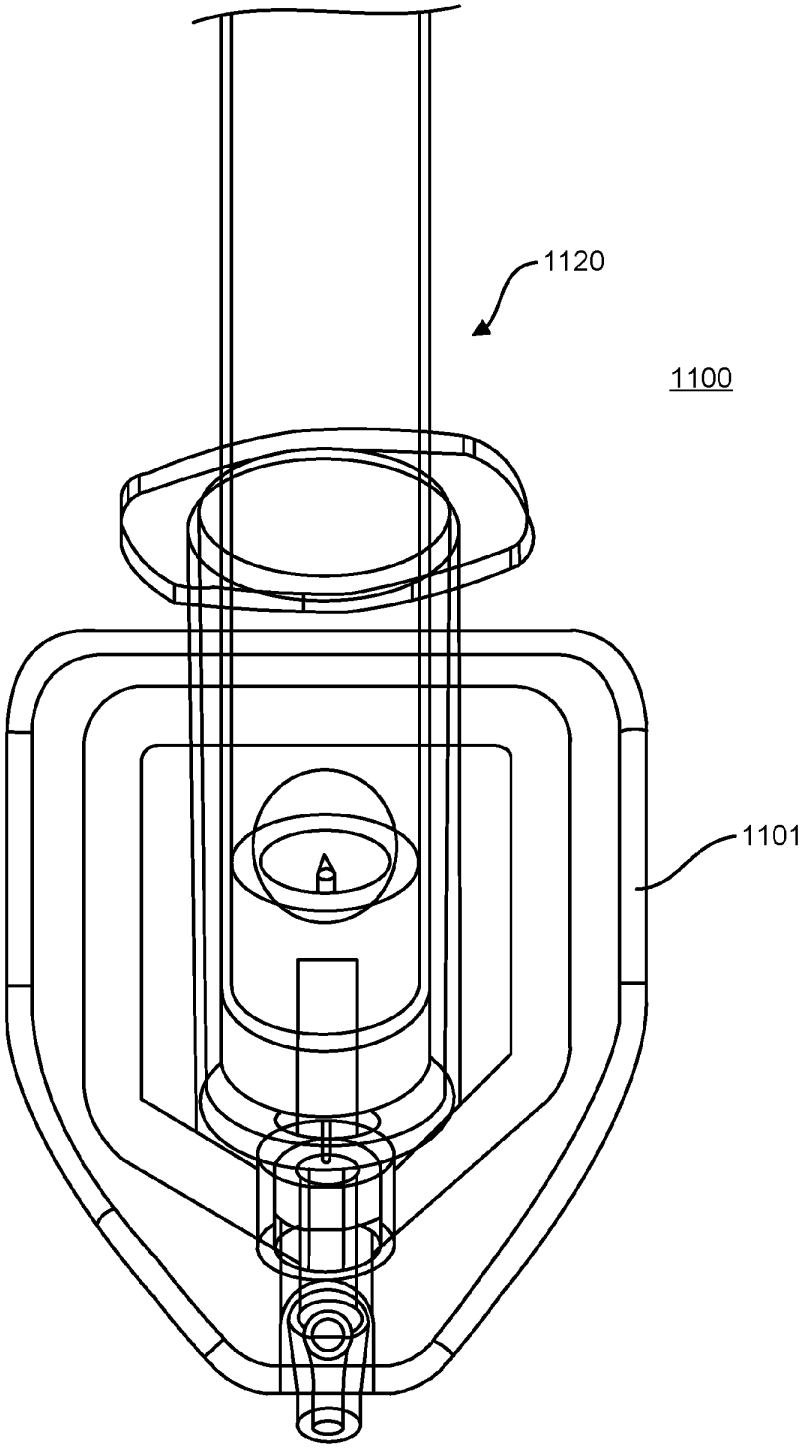


FIG. 11D

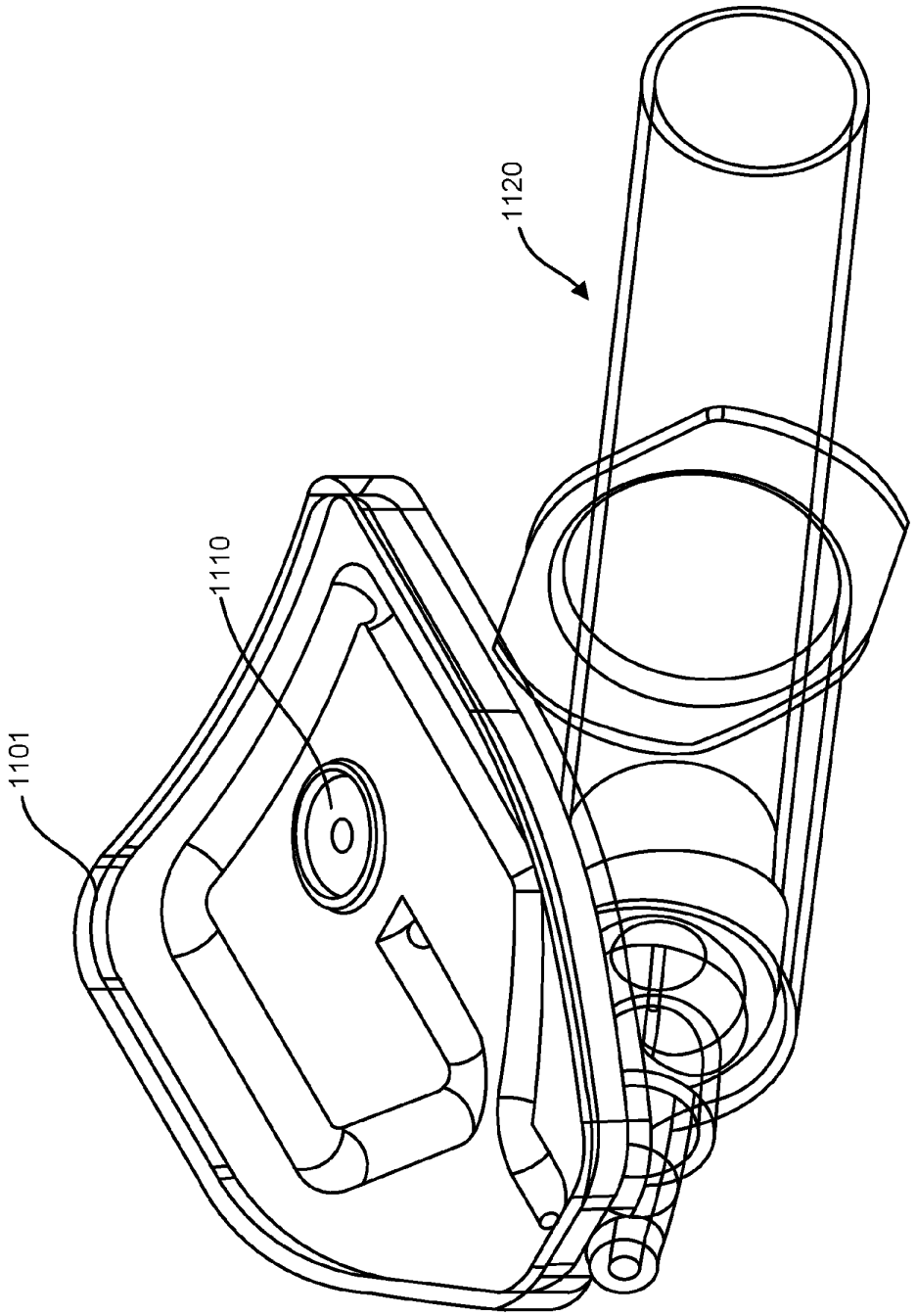


FIG. 11E

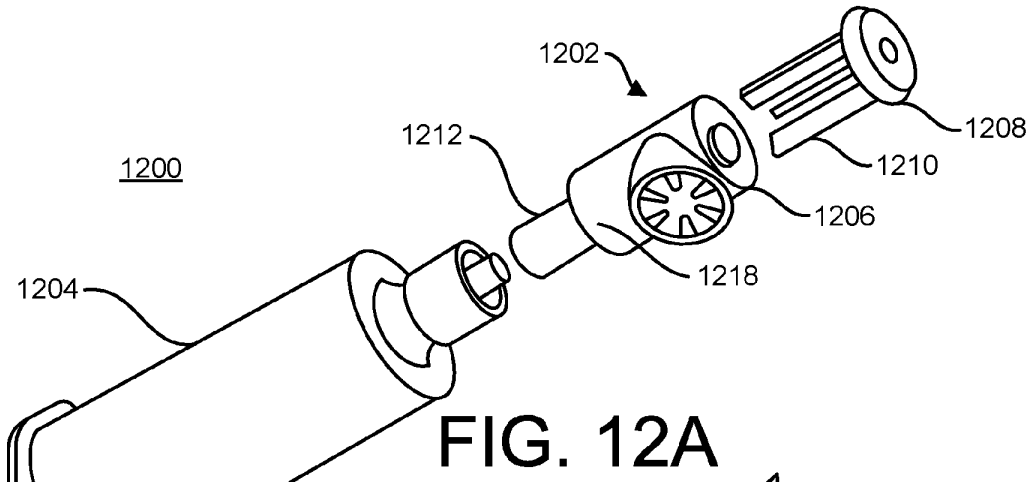


FIG. 12A

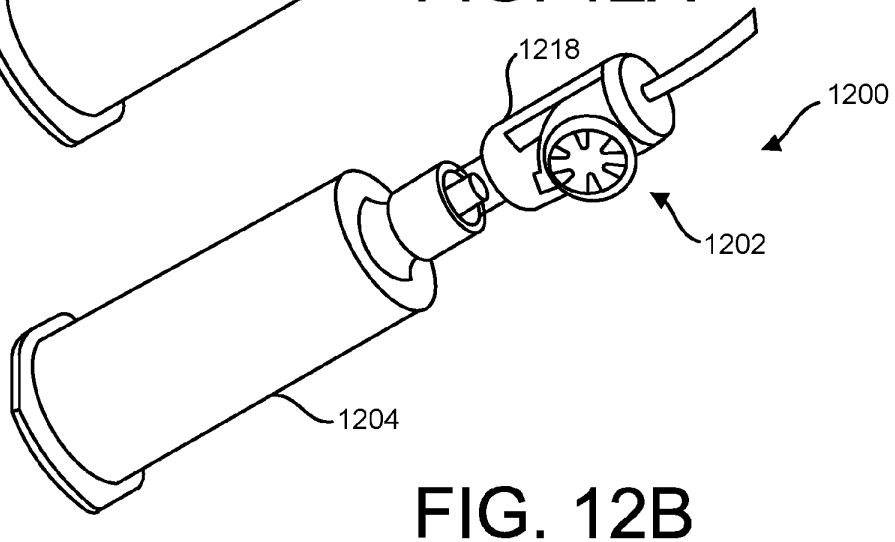


FIG. 12B

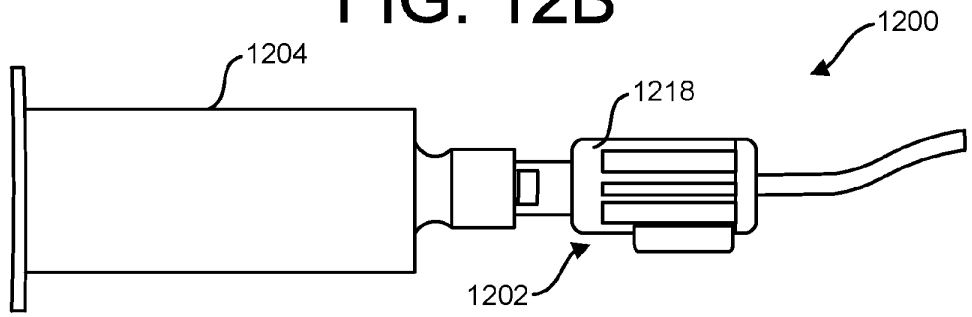


FIG. 12C

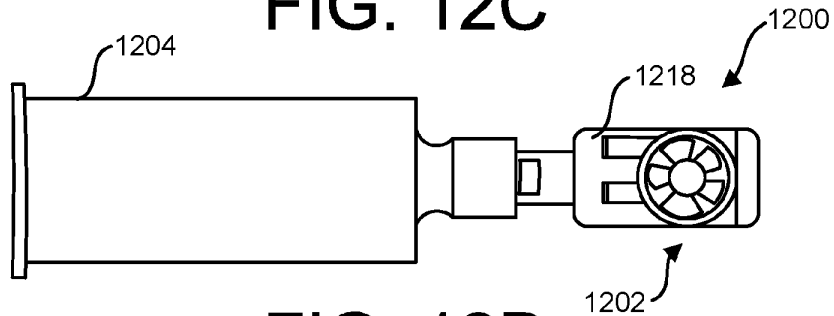


FIG. 12D

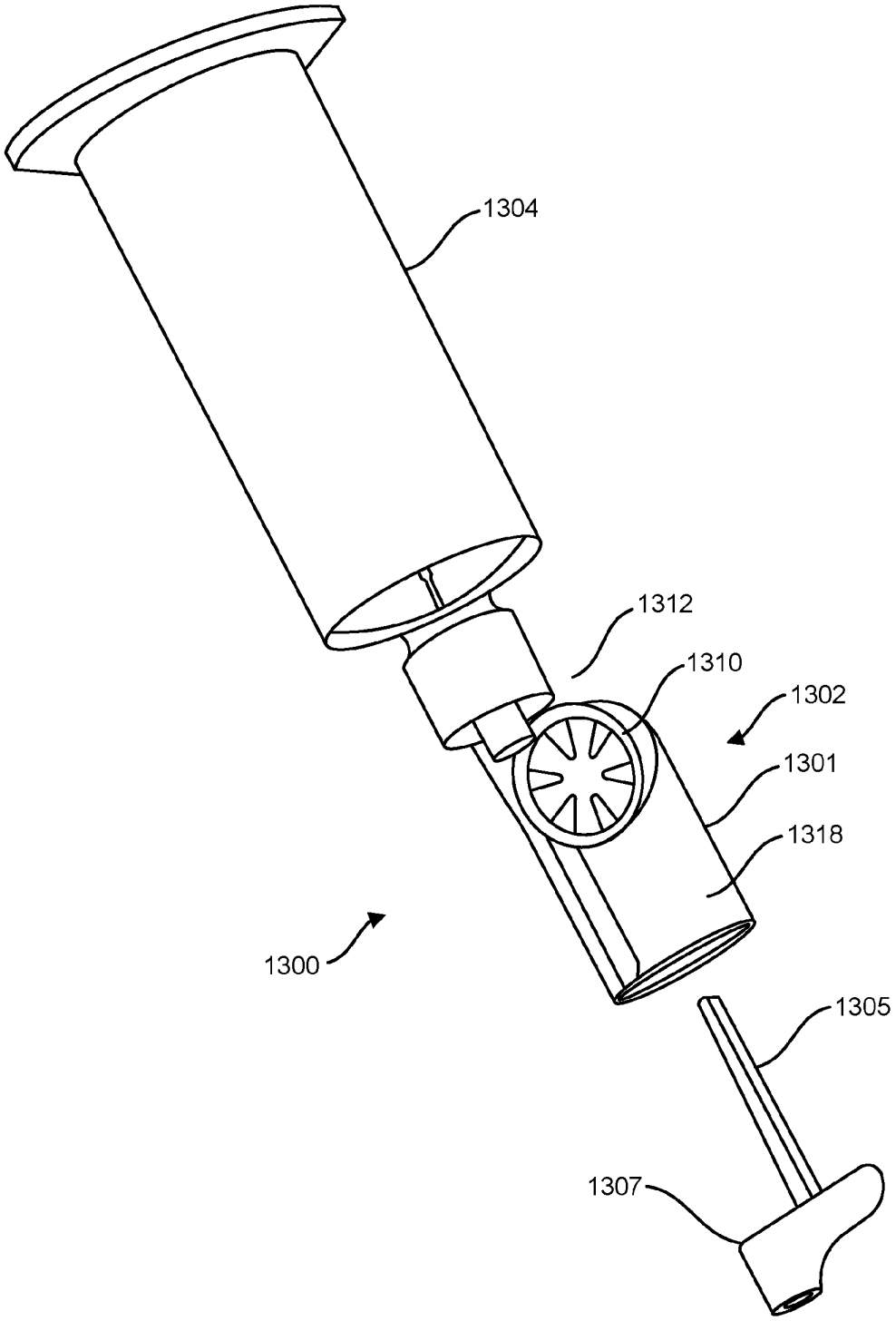


FIG. 13A

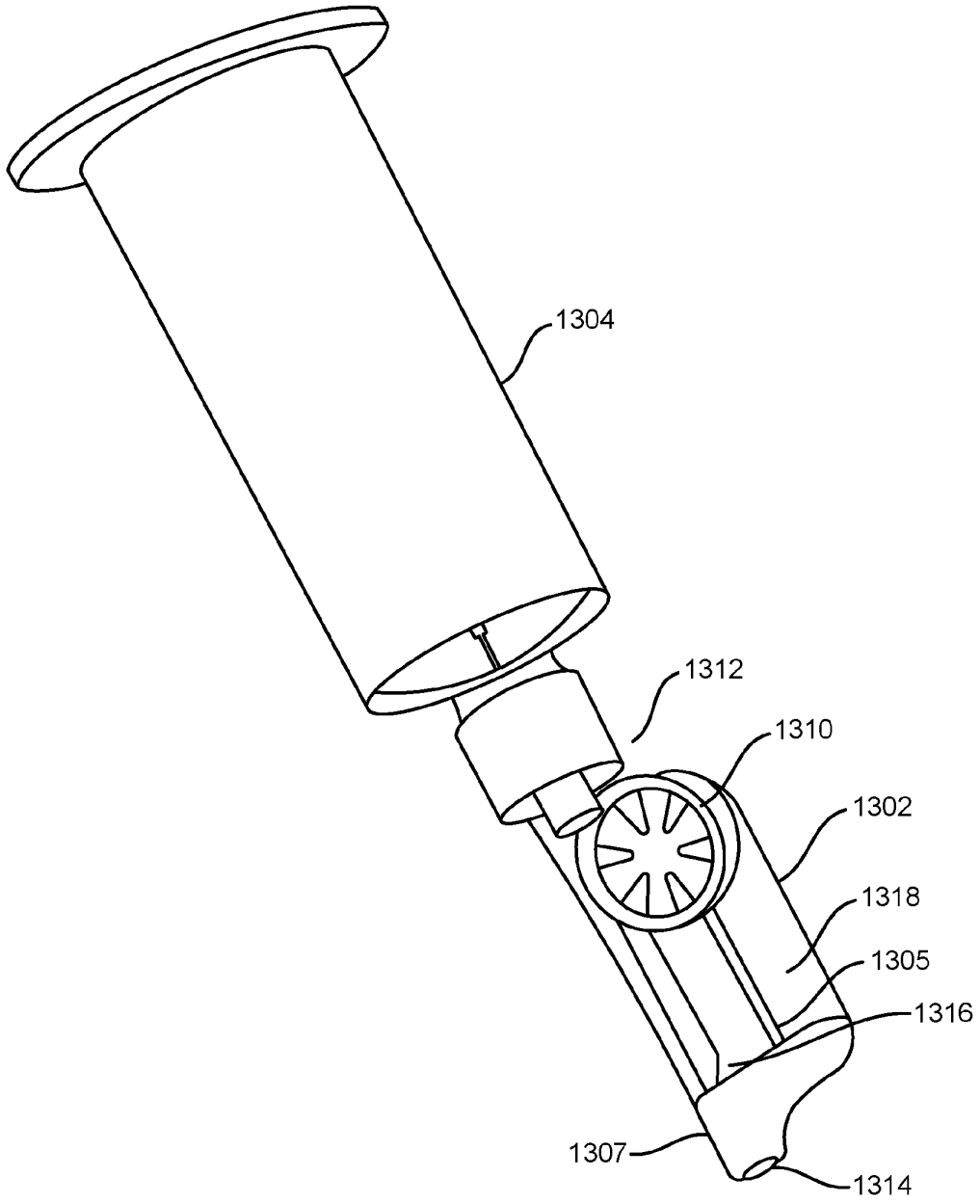


FIG. 13B

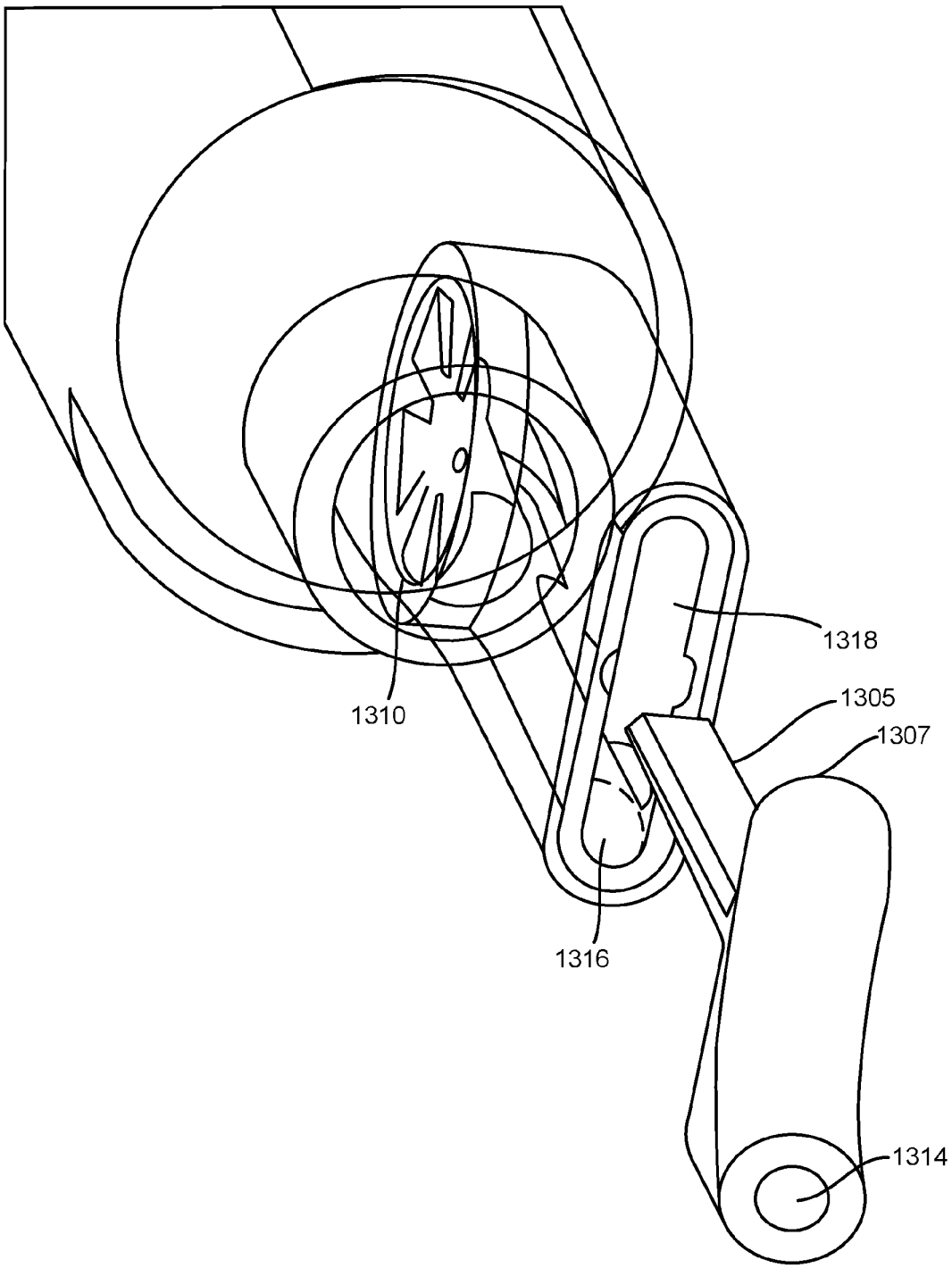


FIG. 13C

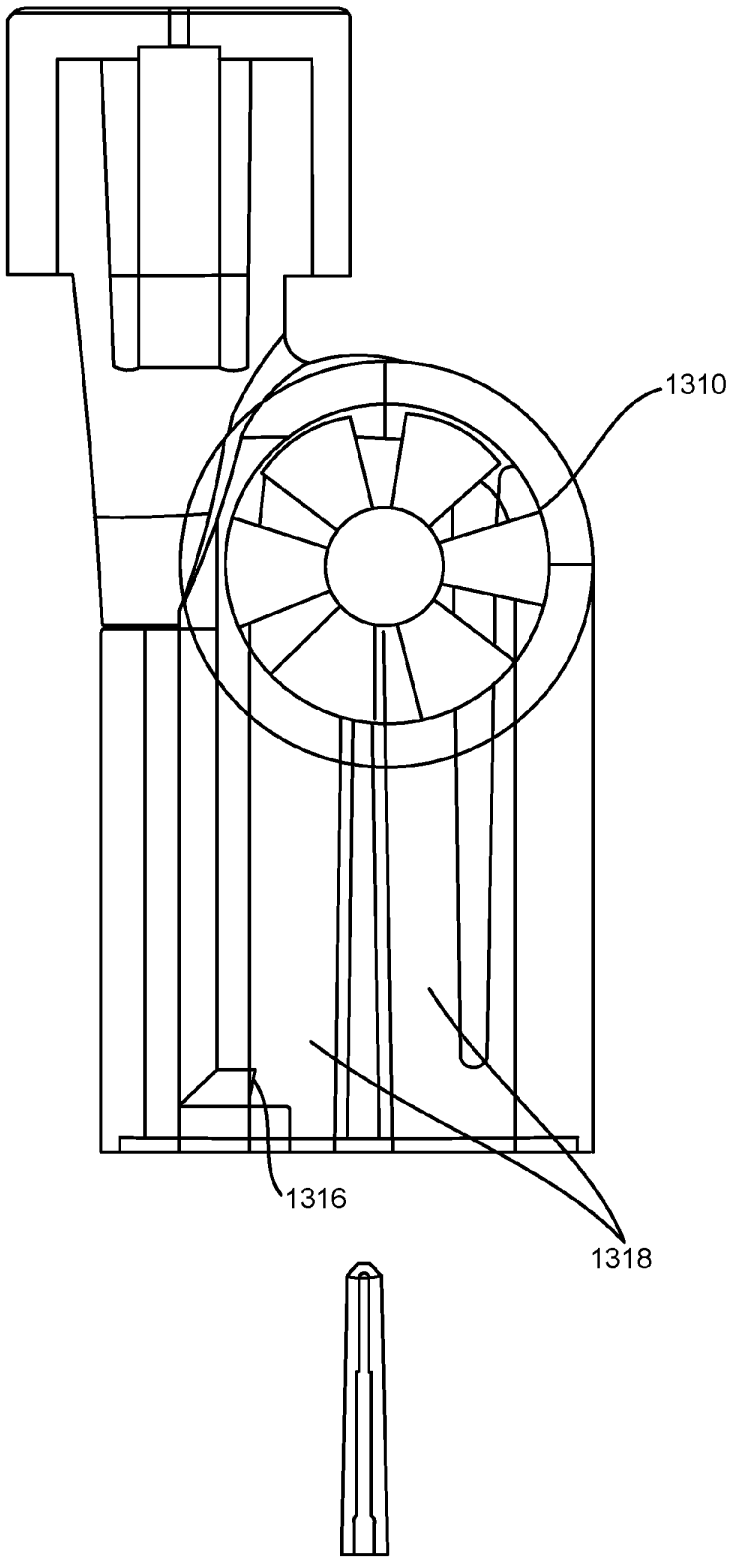


FIG. 13D

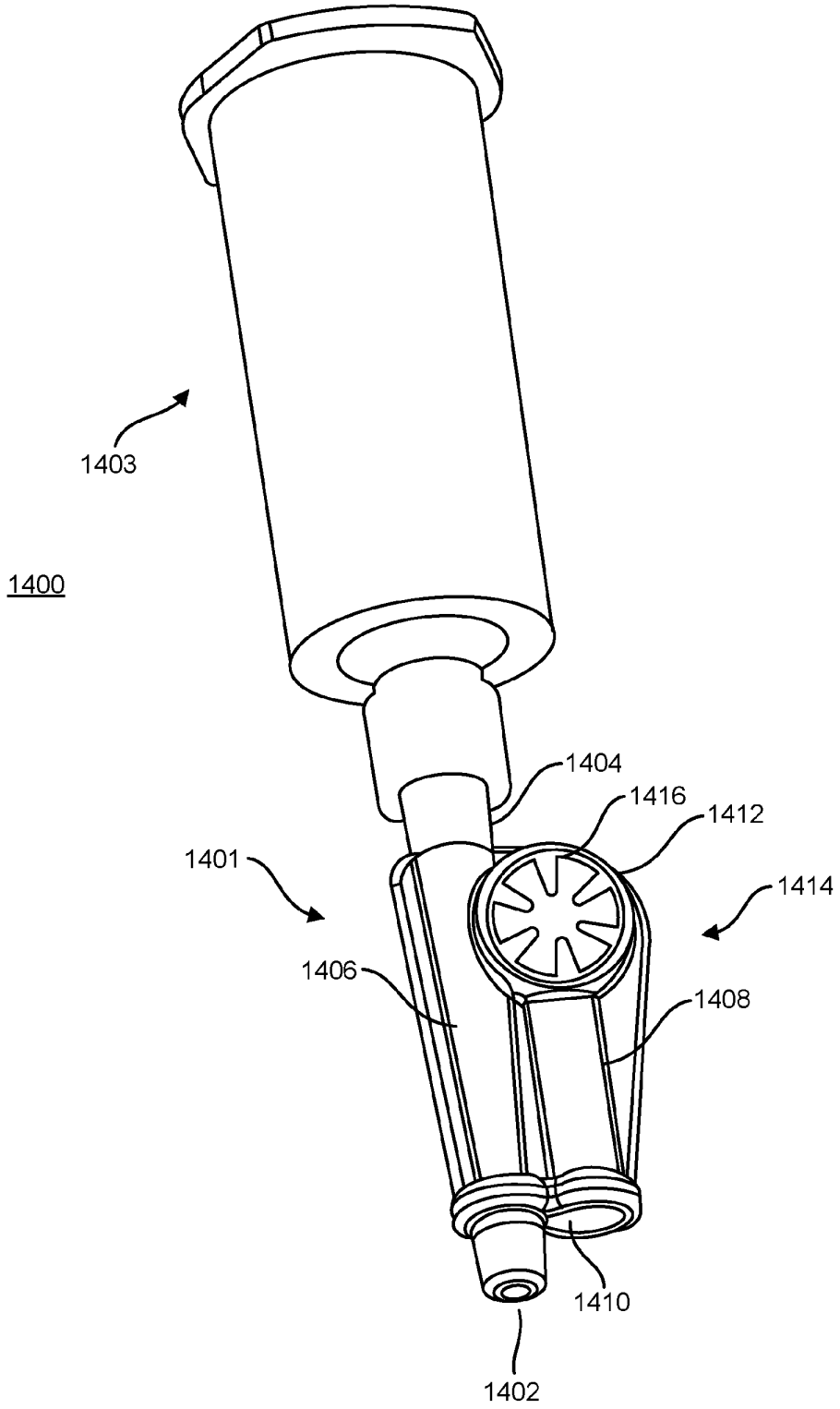


FIG. 14A

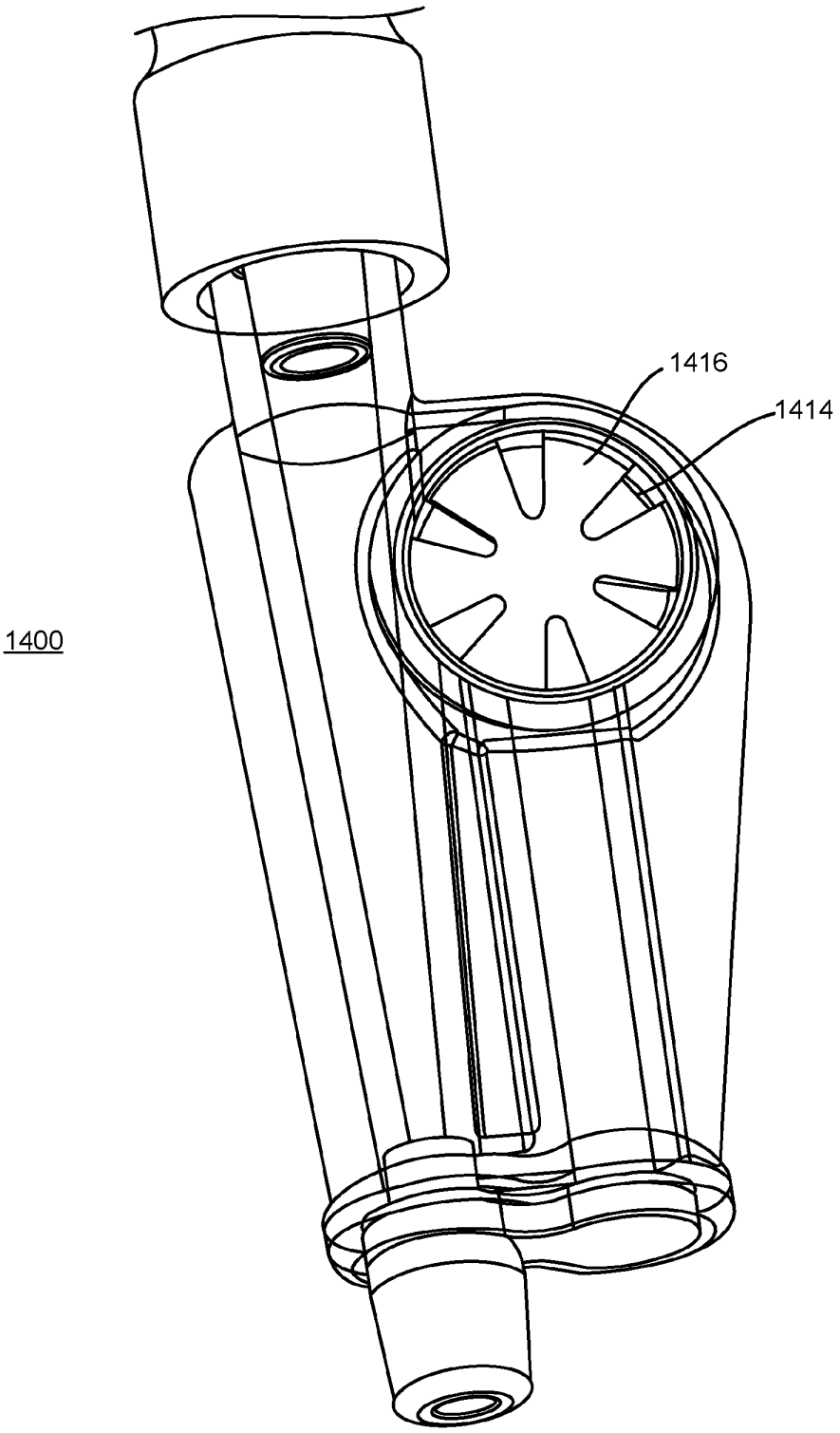


FIG. 14B

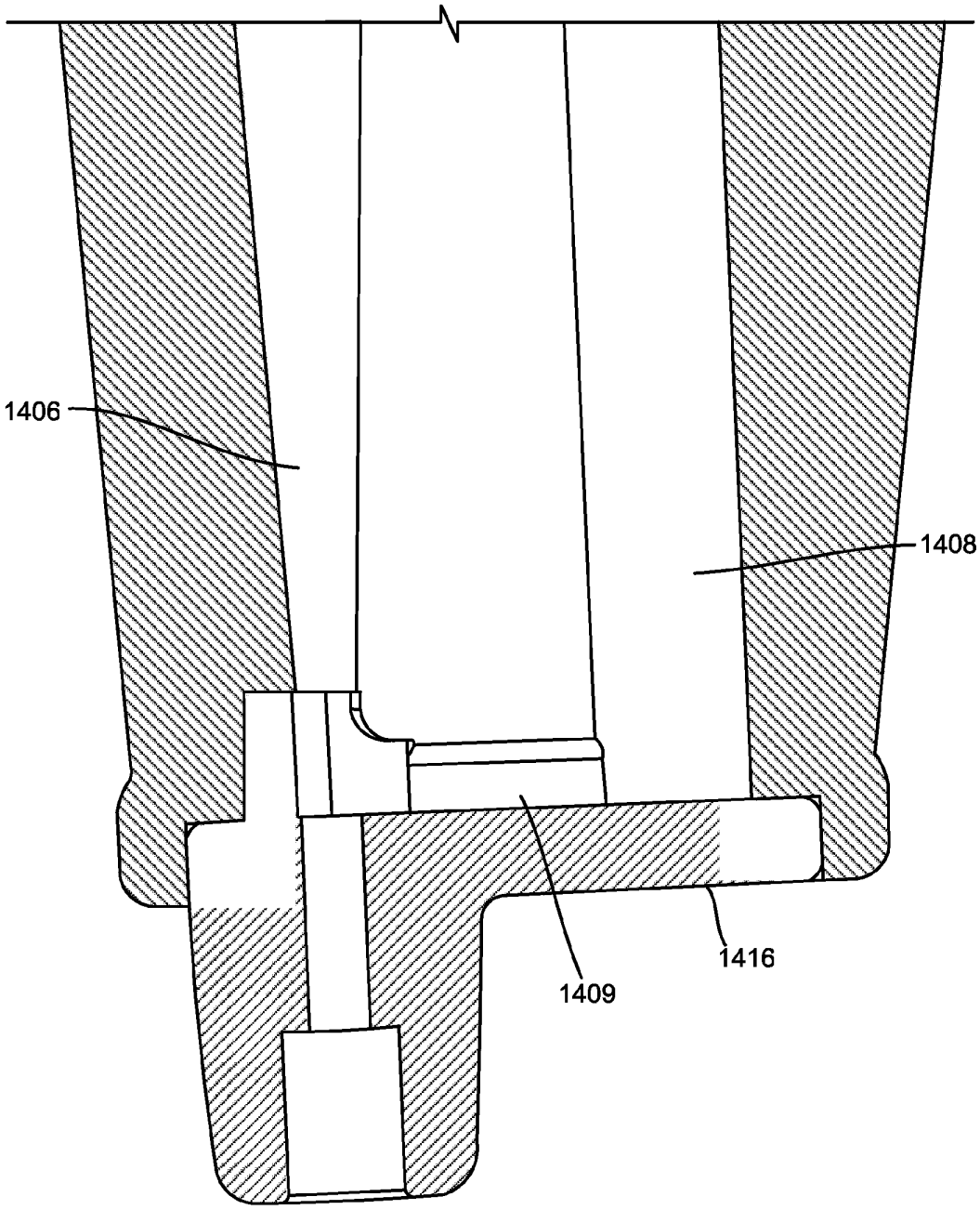


FIG. 14C

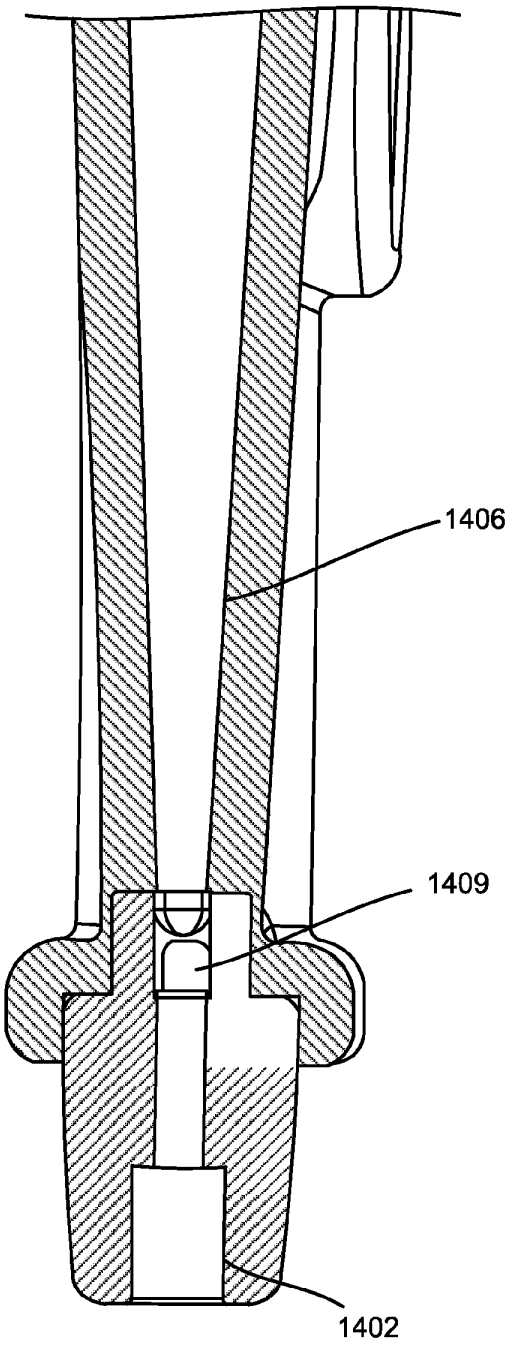


FIG. 14D

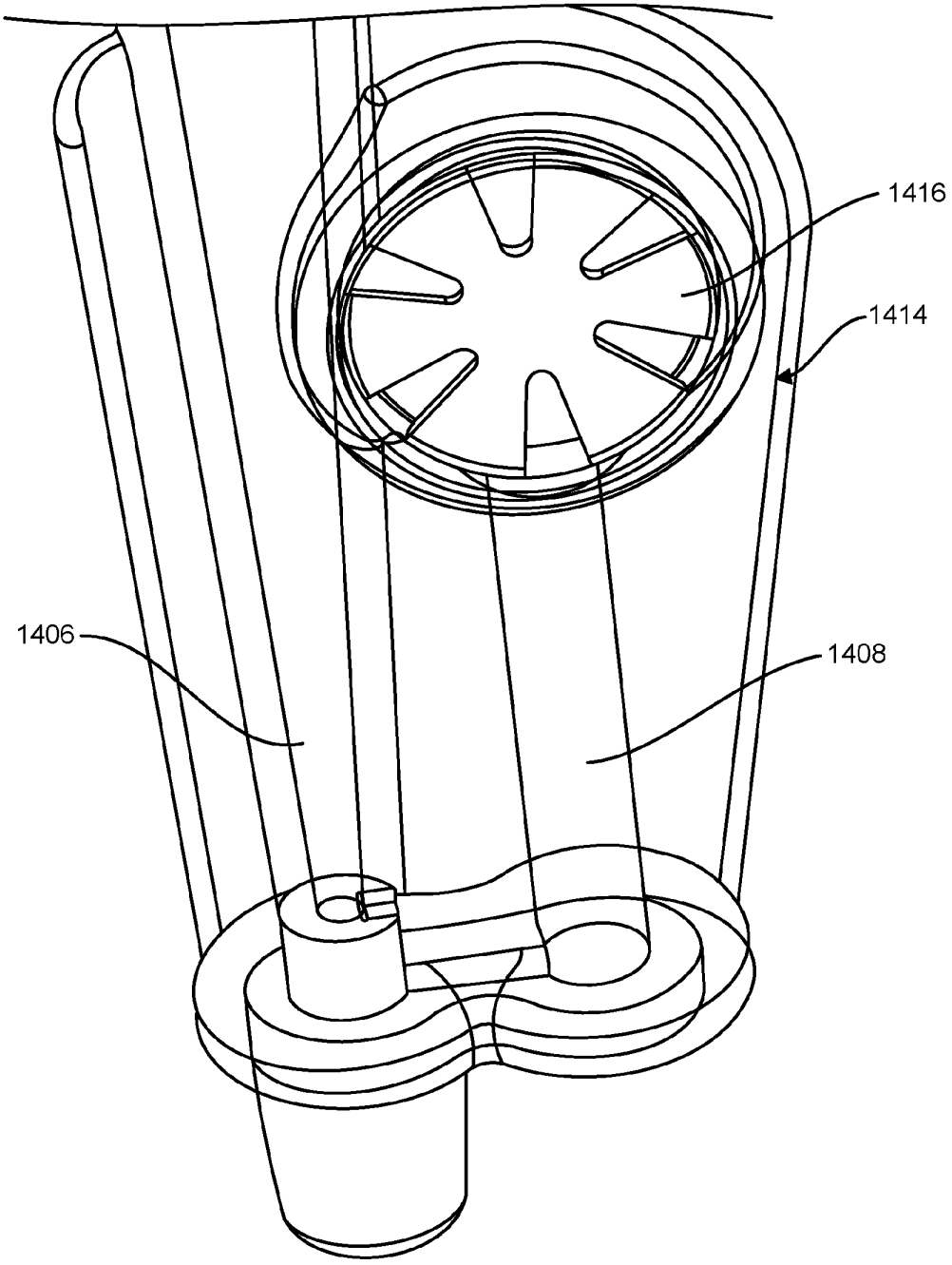


FIG. 14E

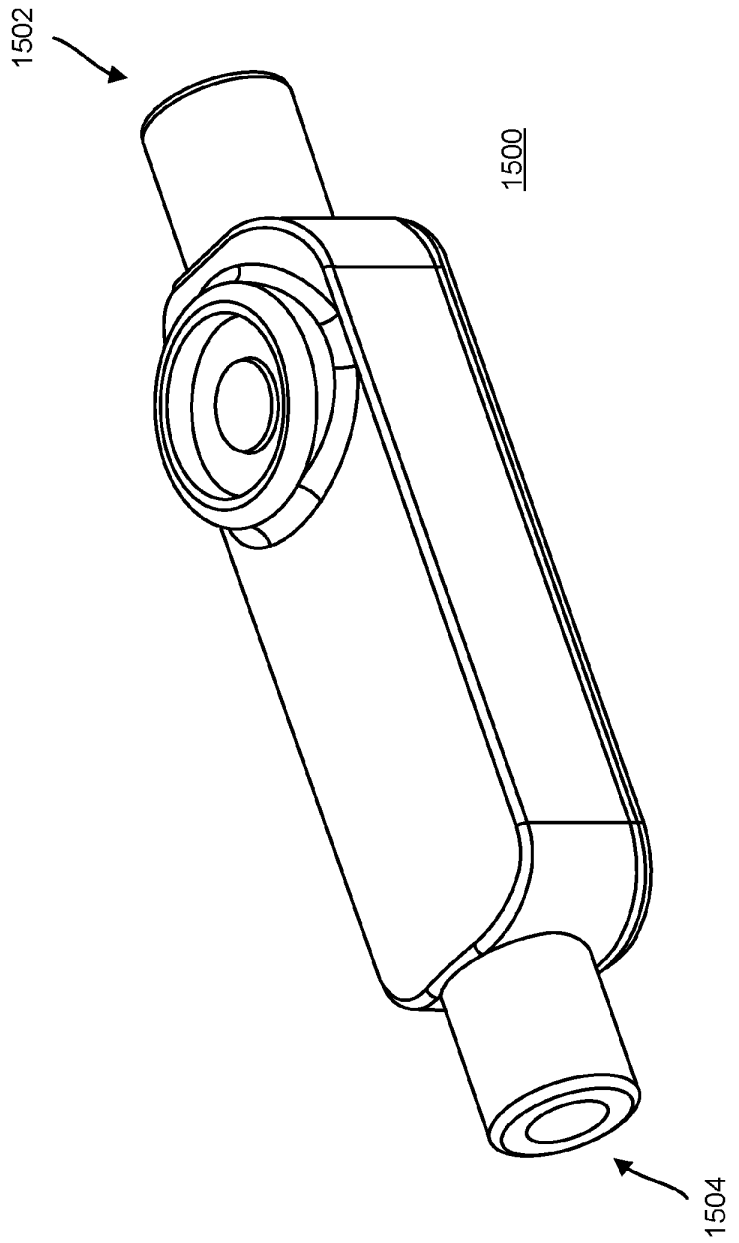


FIG. 15A

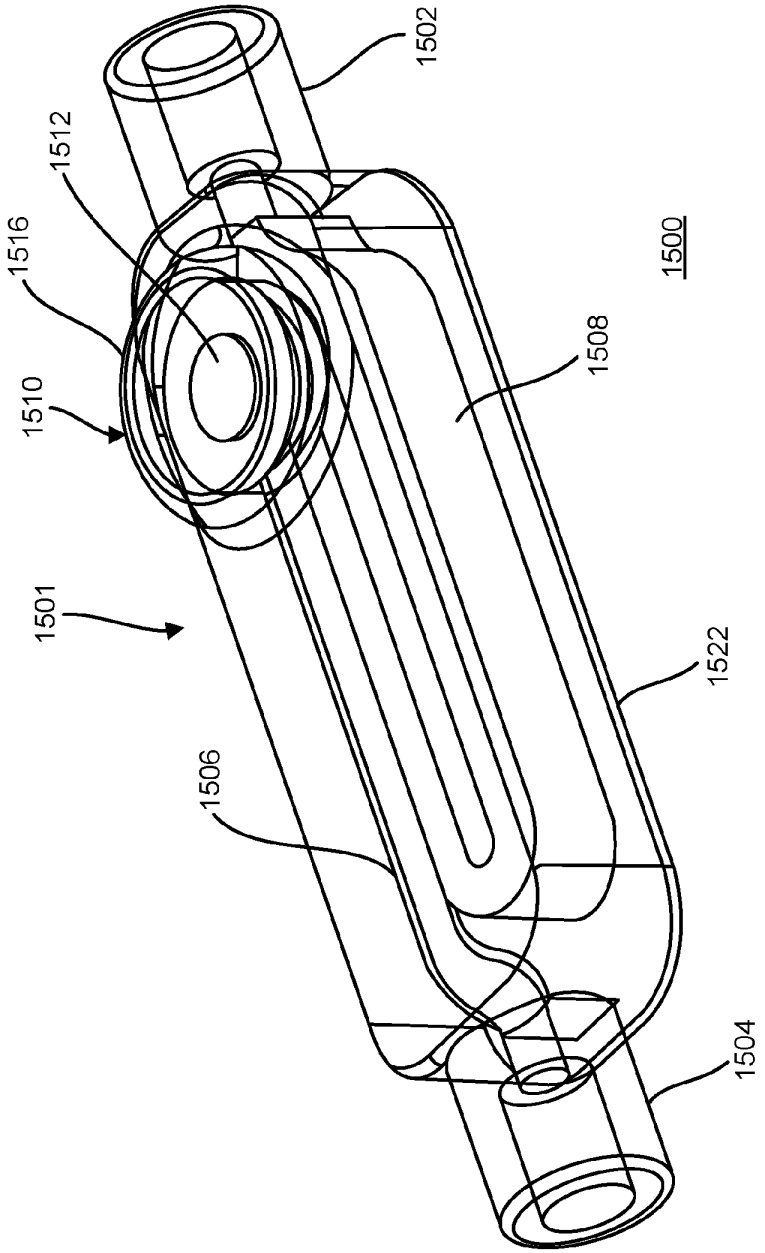


FIG. 15B

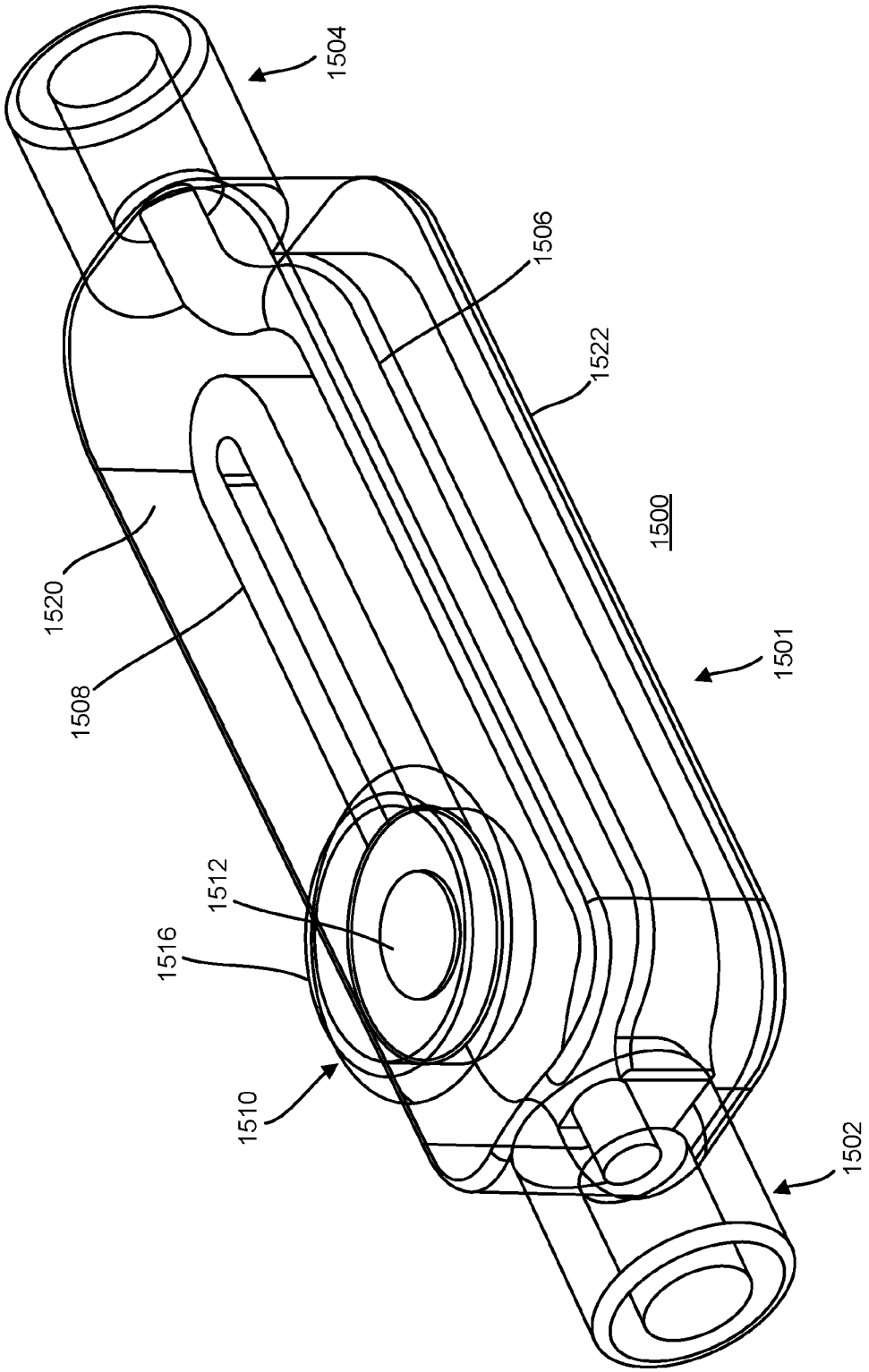


FIG. 15C

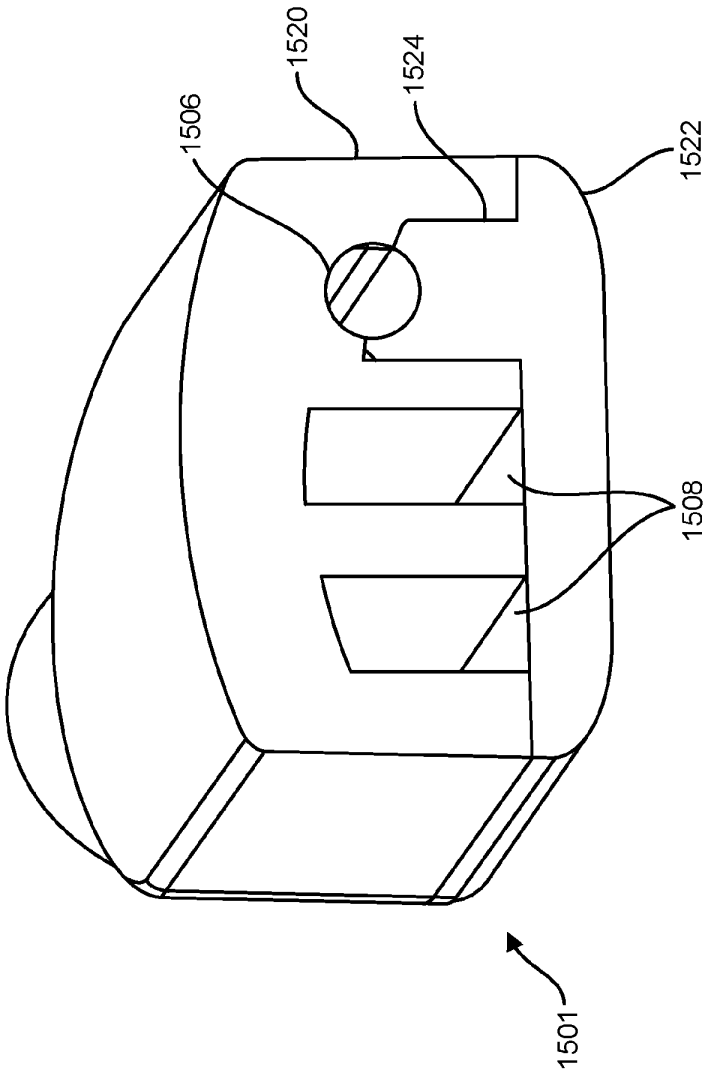


FIG. 15D

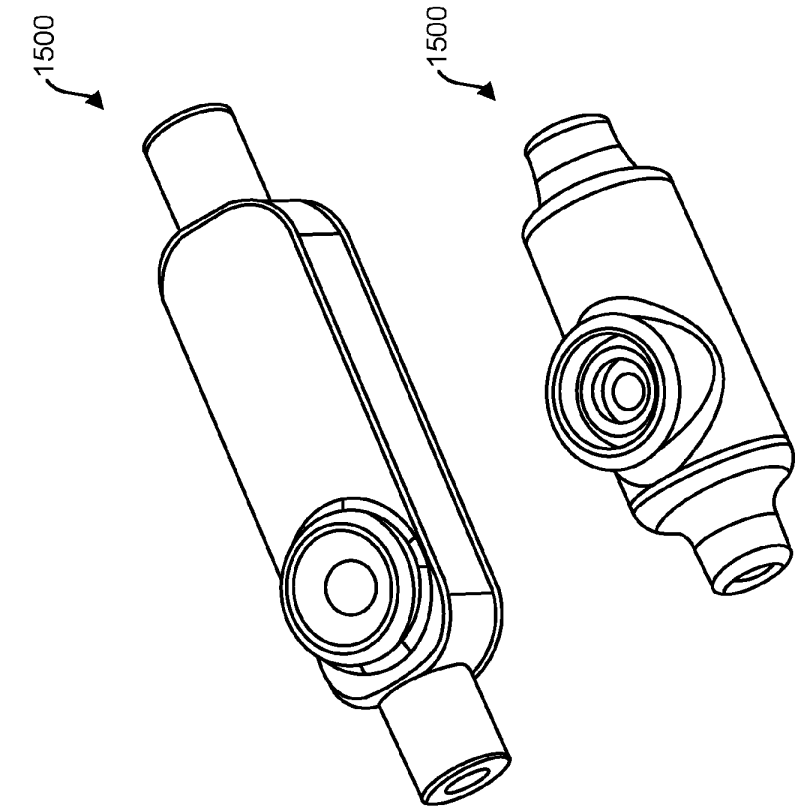


FIG. 15F

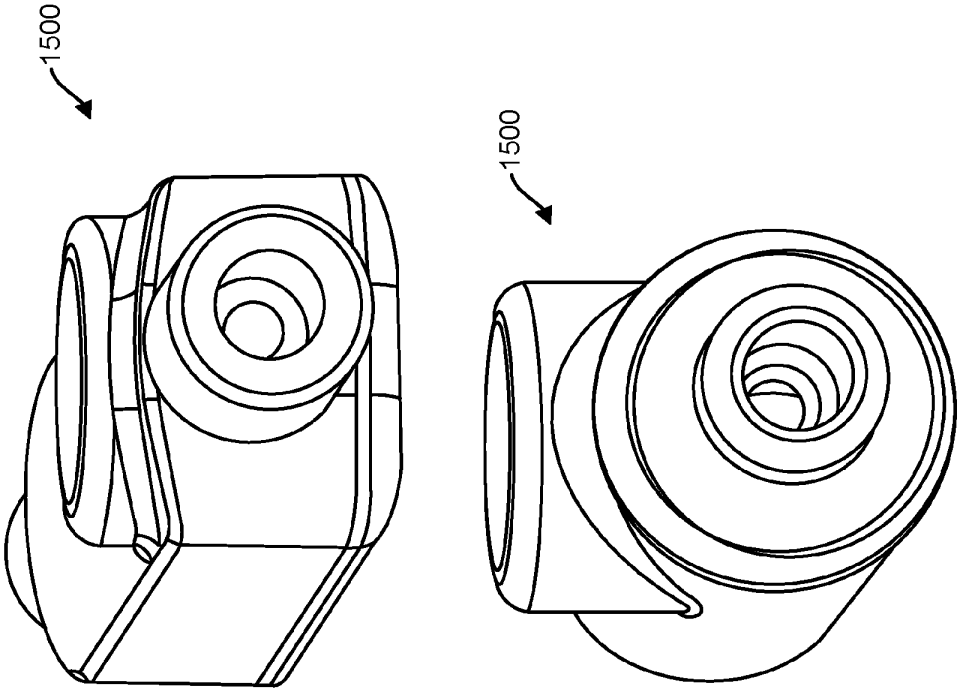


FIG. 15E

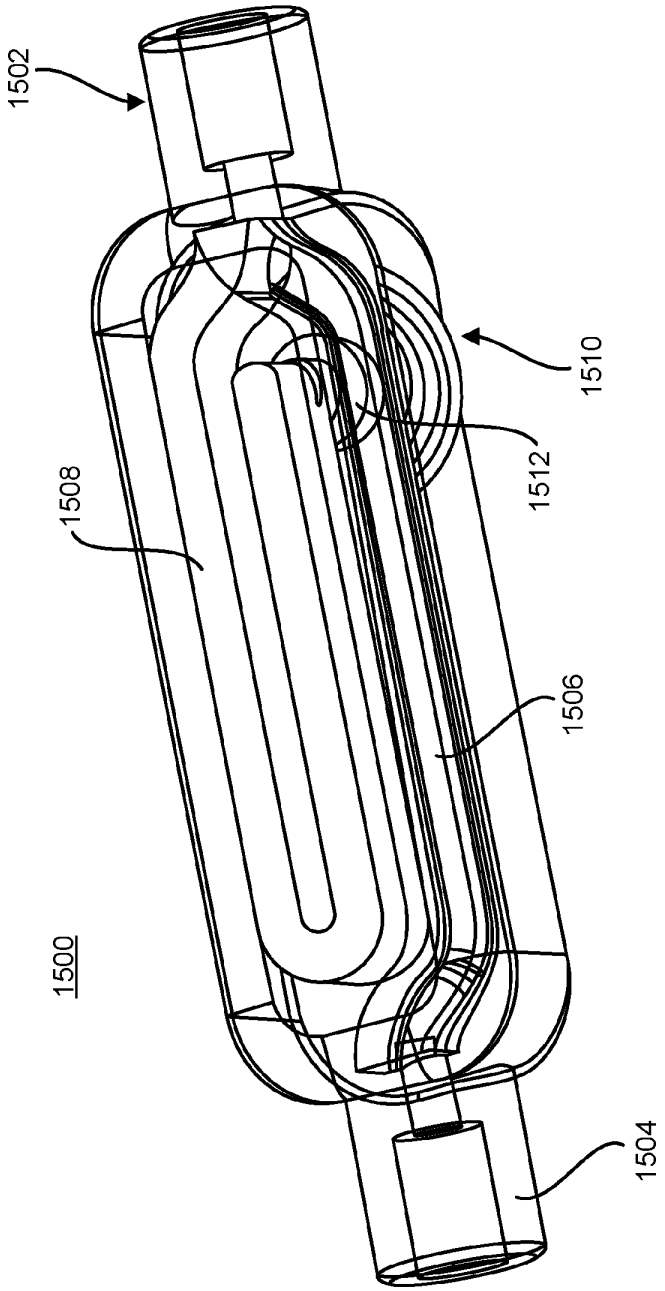


FIG. 15G

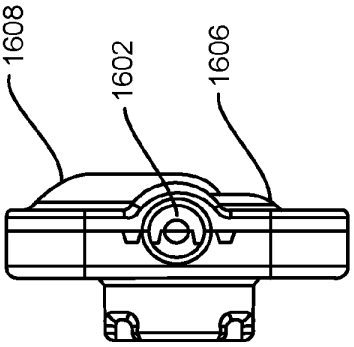


FIG. 16C

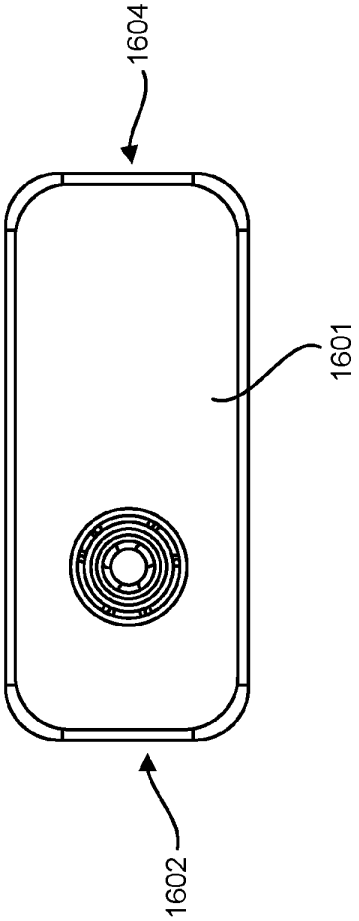


FIG. 16A

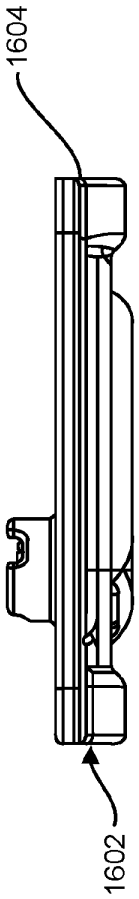


FIG. 16B

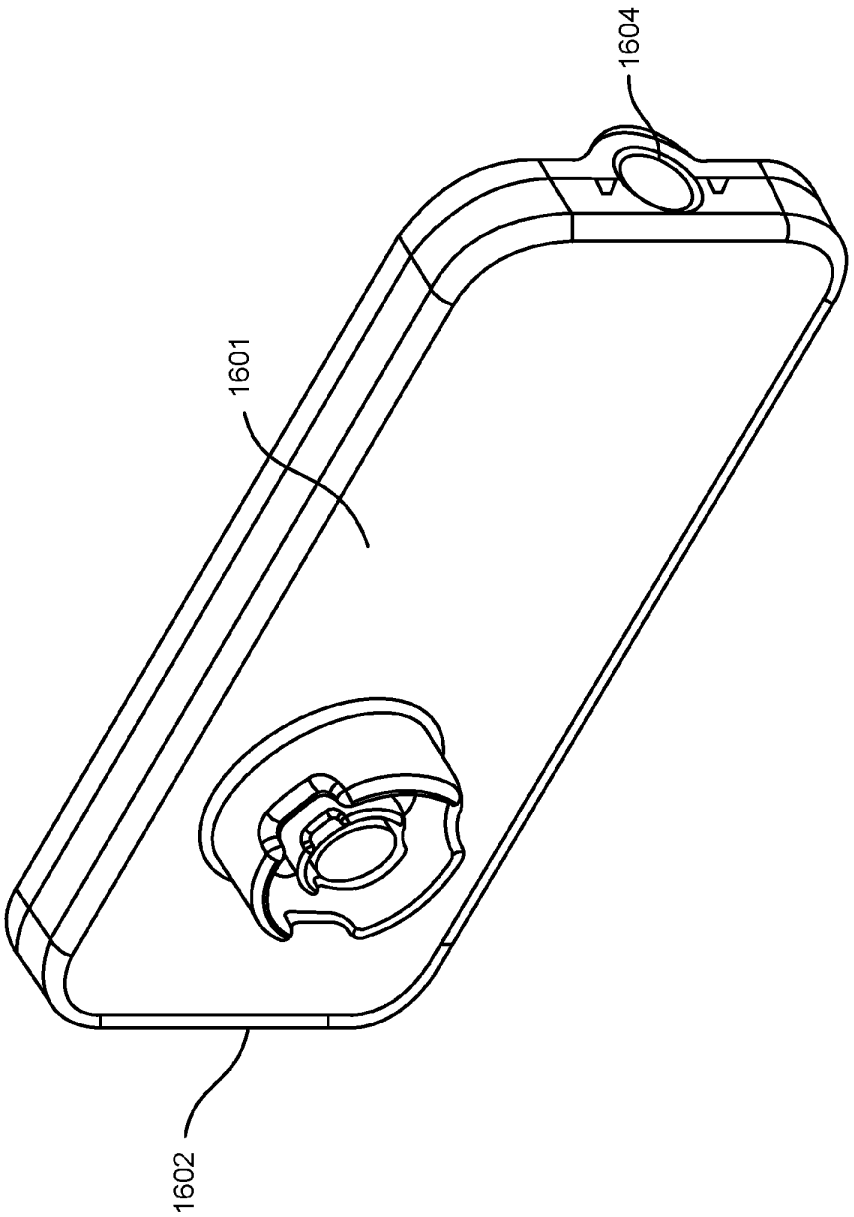


FIG. 16D

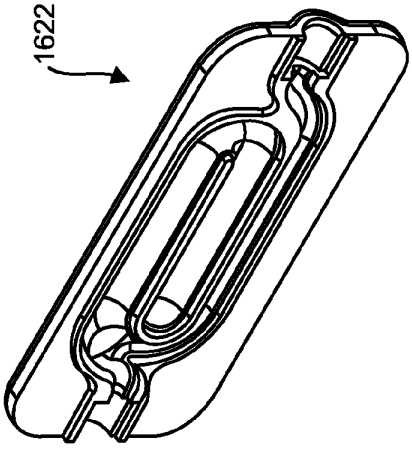


FIG. 17B



FIG. 17E

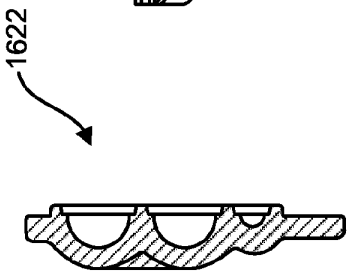


FIG. 17D

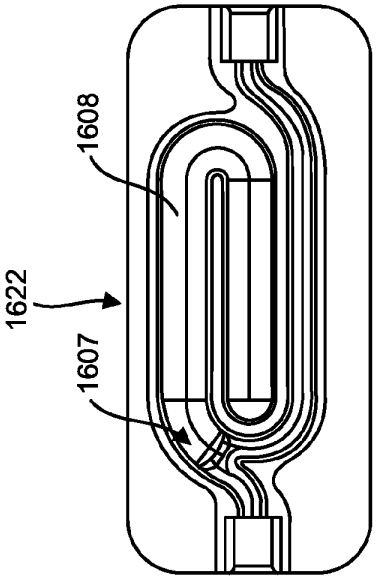


FIG. 17A

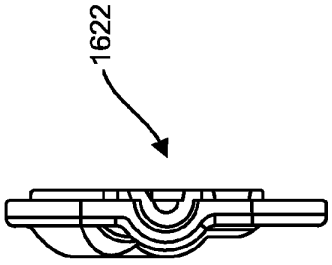


FIG. 17C

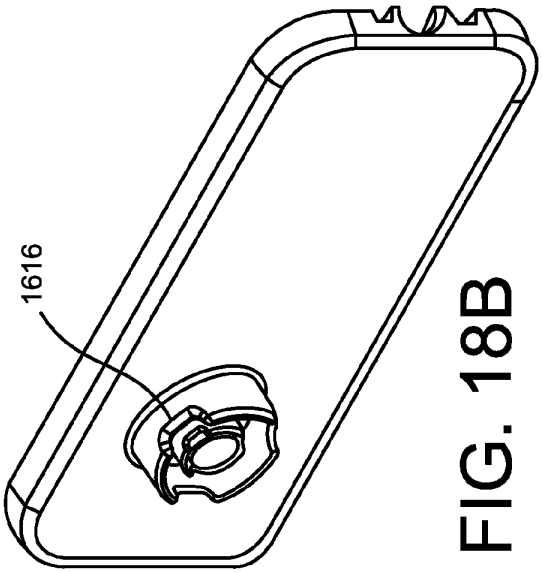


FIG. 18B

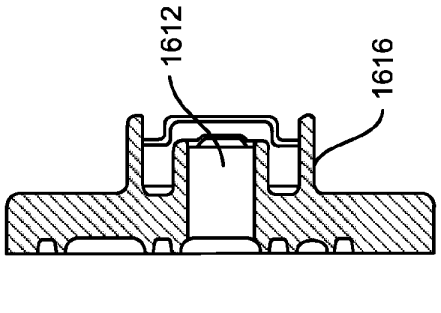


FIG. 18F

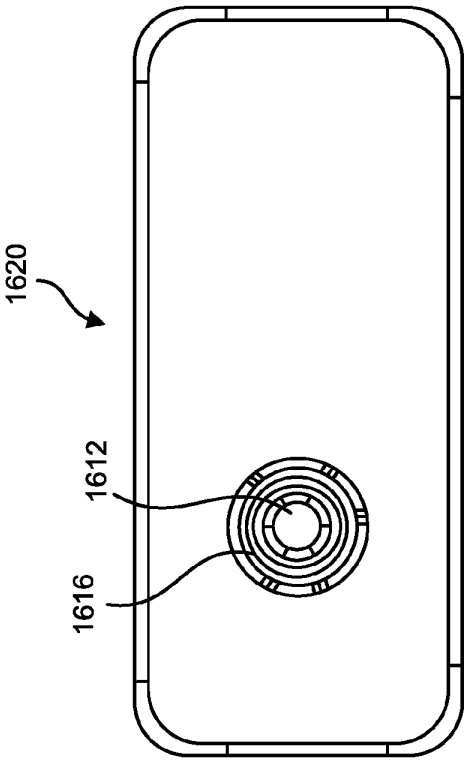


FIG. 18A

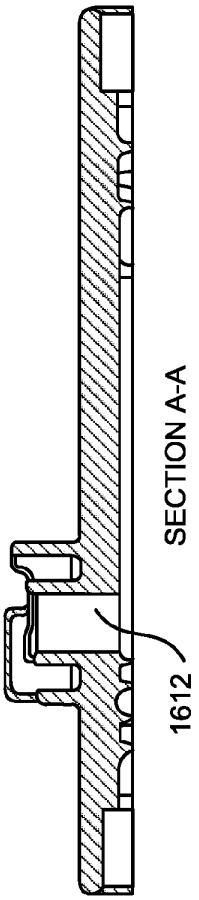


FIG. 18D

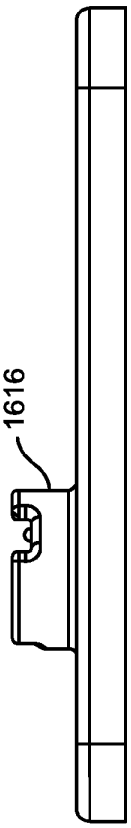


FIG. 18E

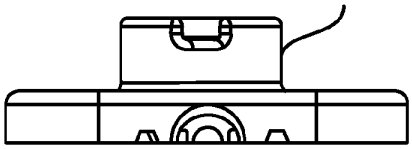


FIG. 18C

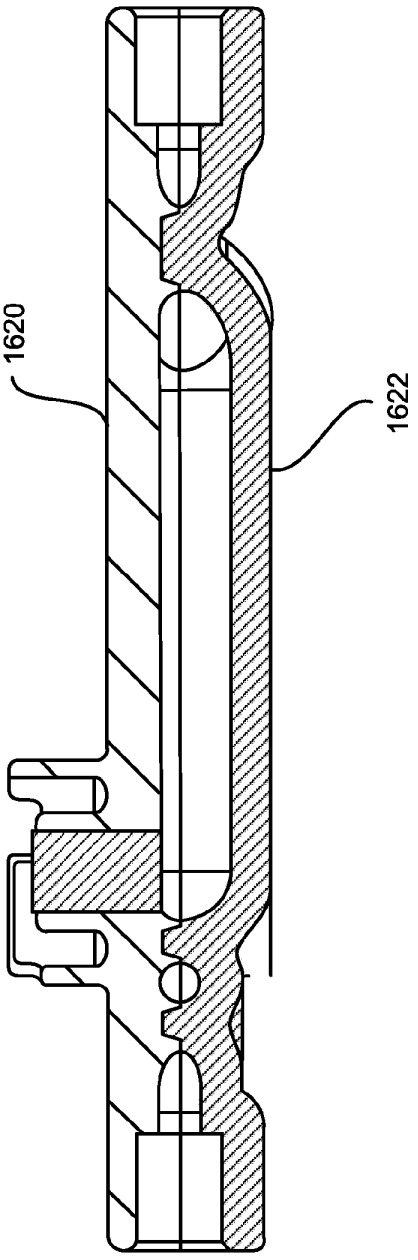


FIG. 19A

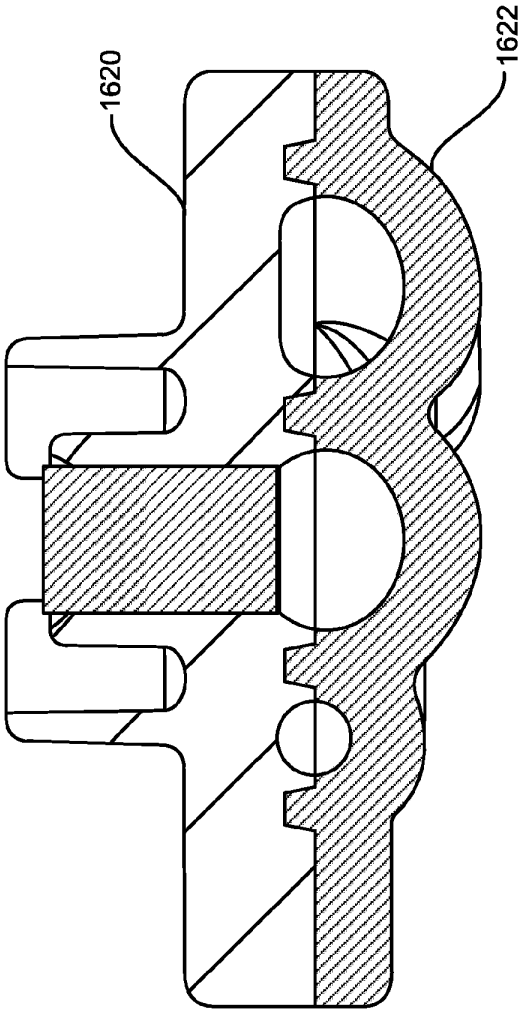


FIG. 19B

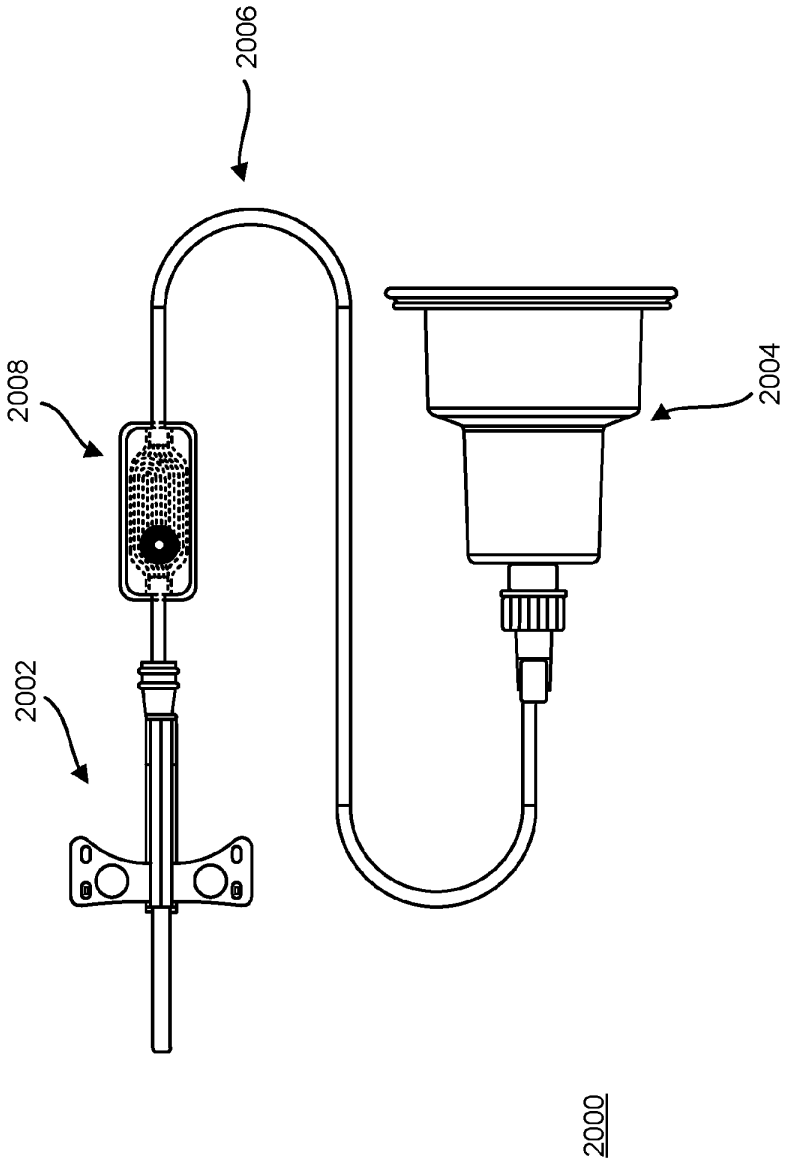


FIG. 20

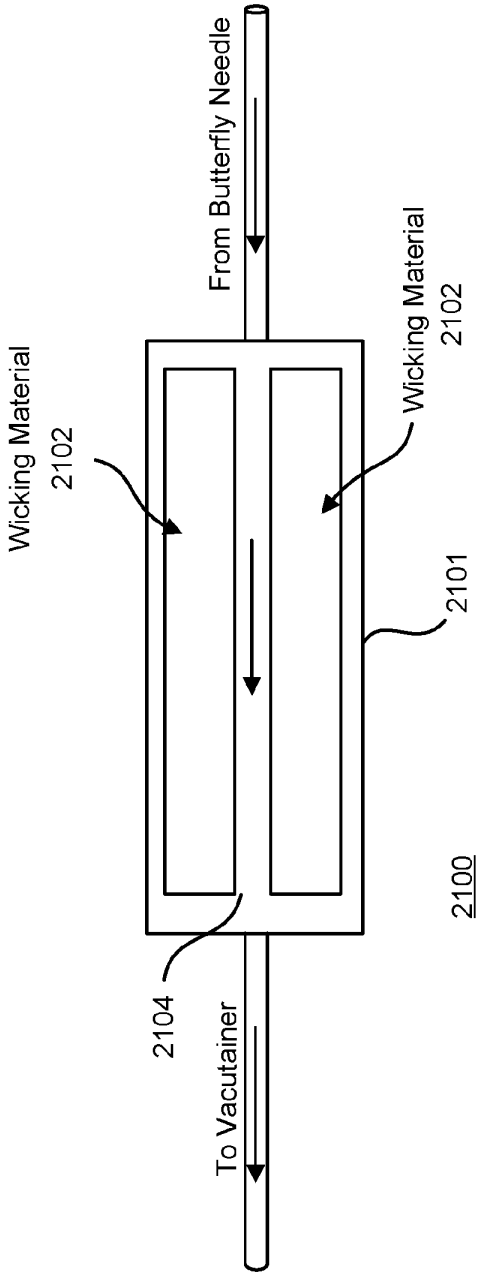

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

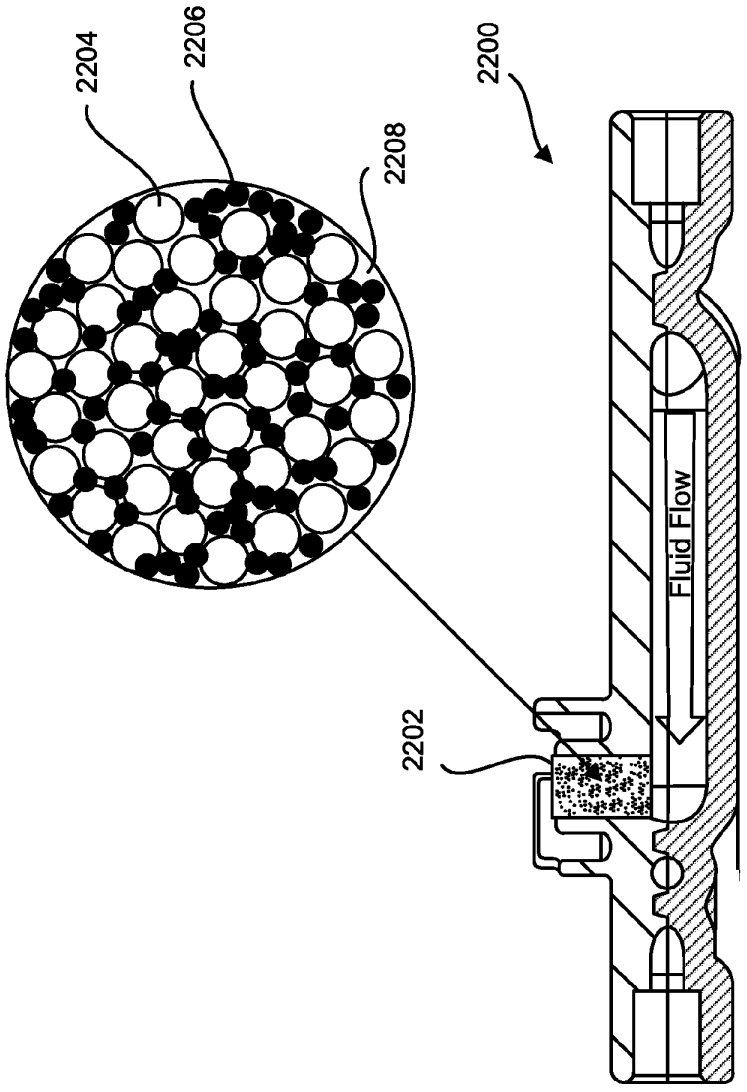


FIG. 22A

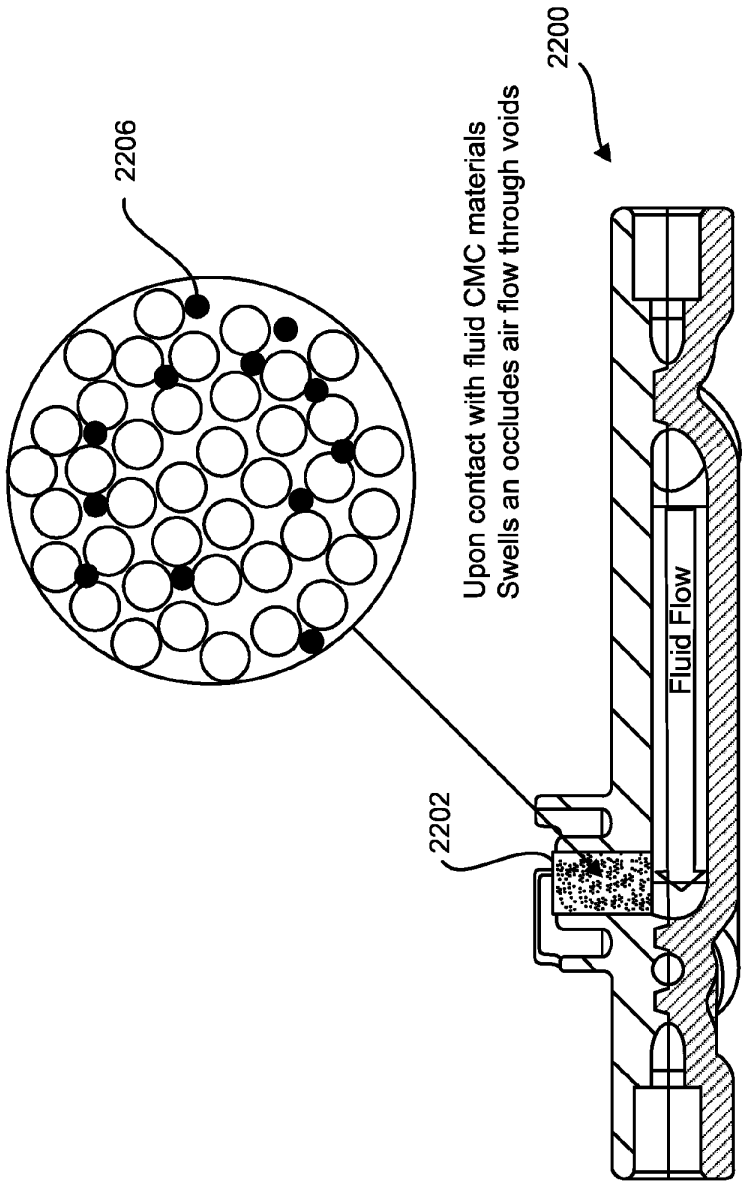

2200
2206
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

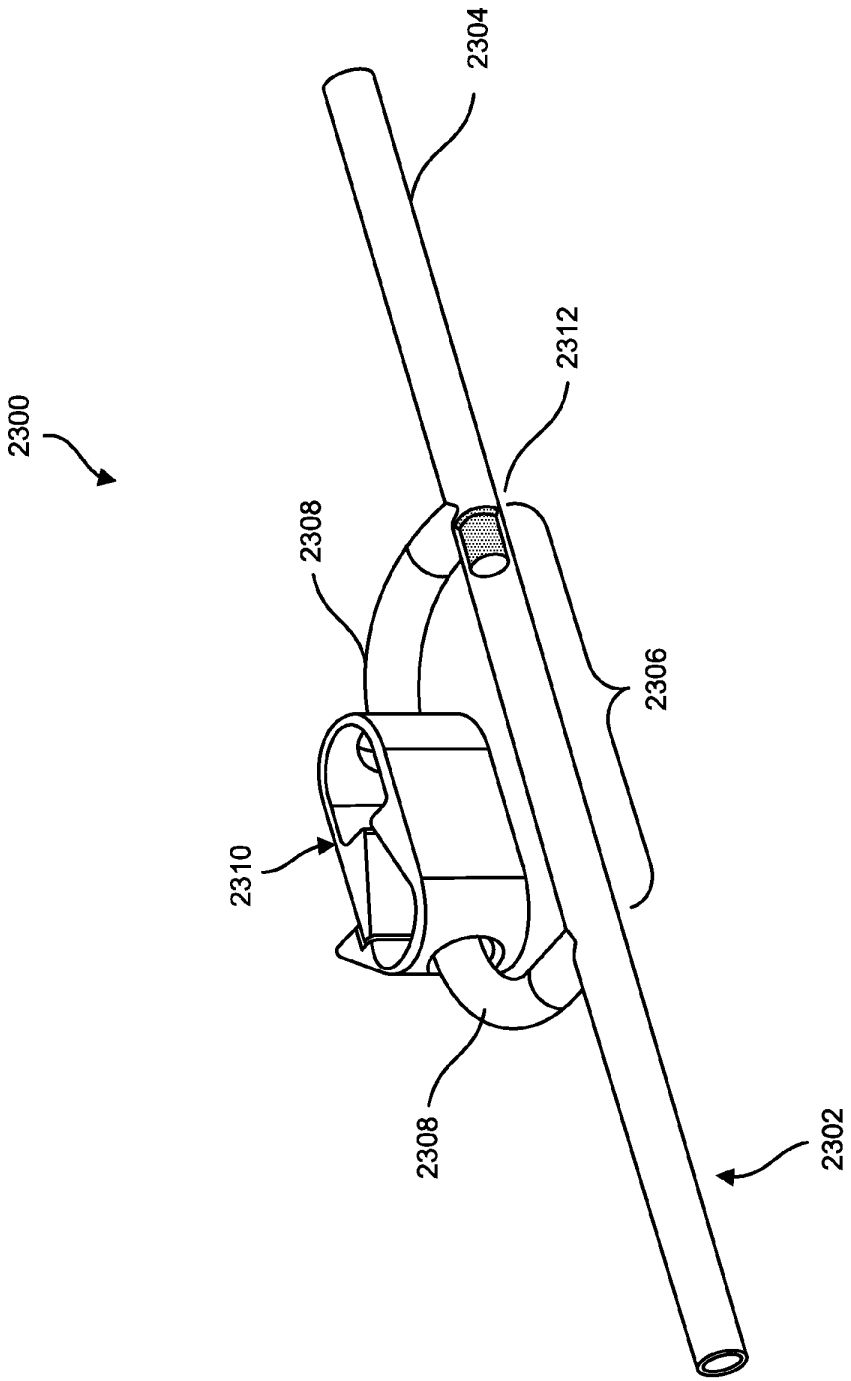


FIG. 23A

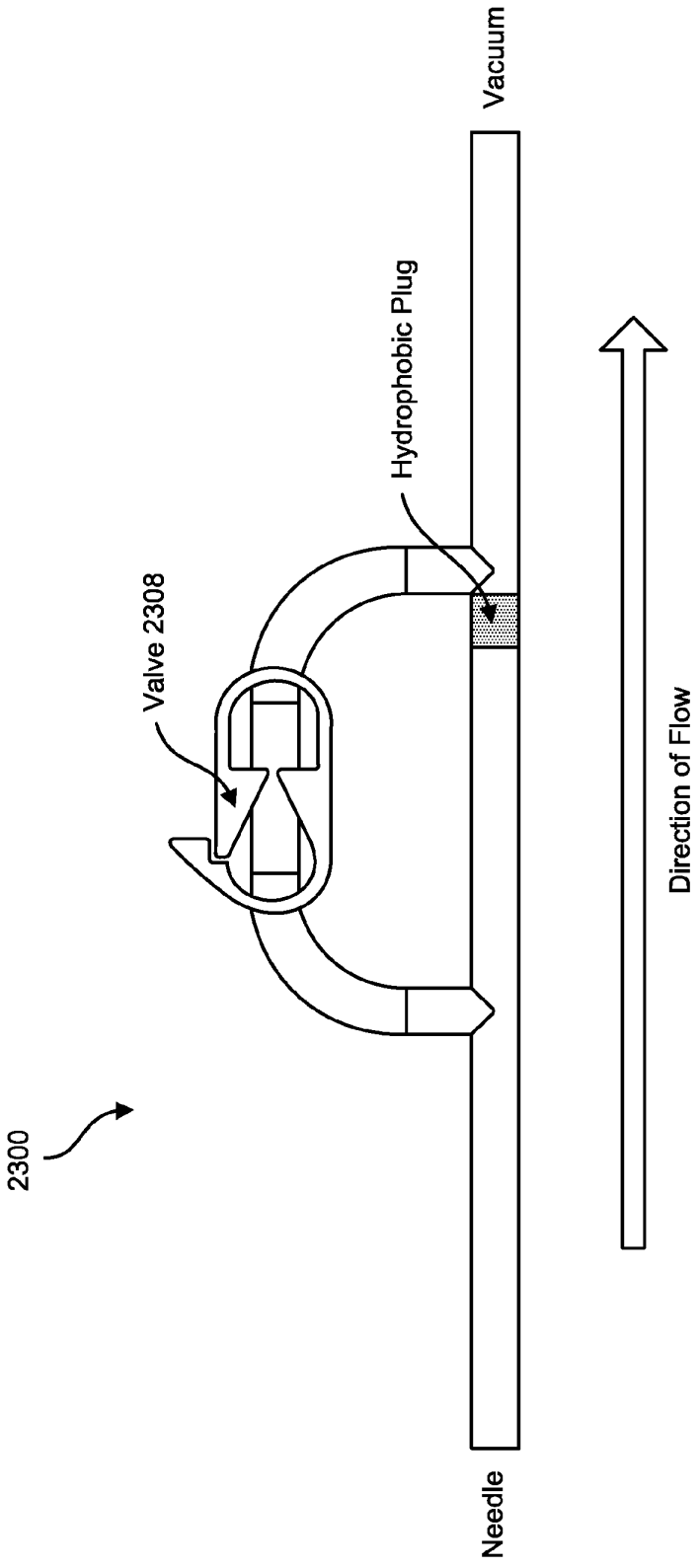

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

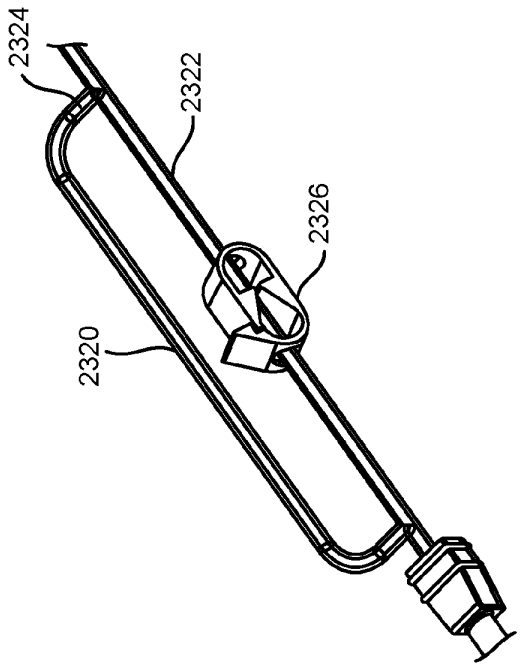


FIG. 23D

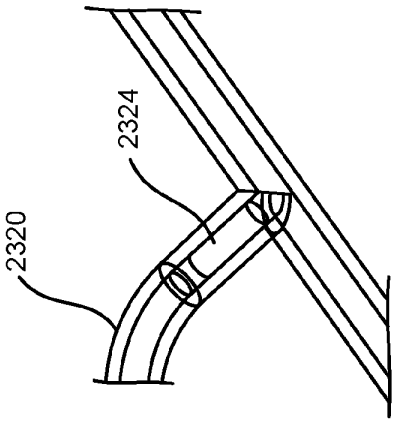


FIG. 23E

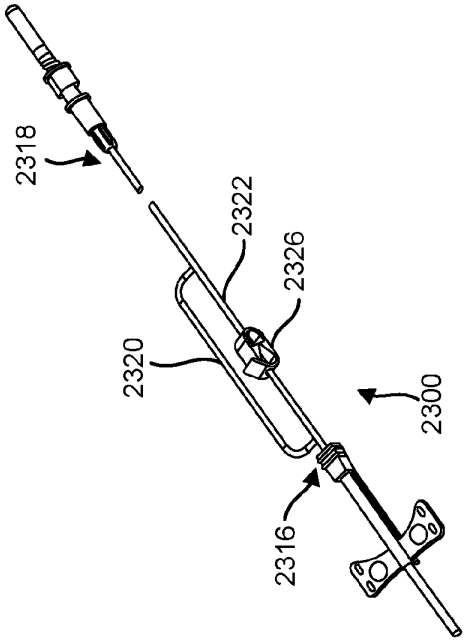


FIG. 23C

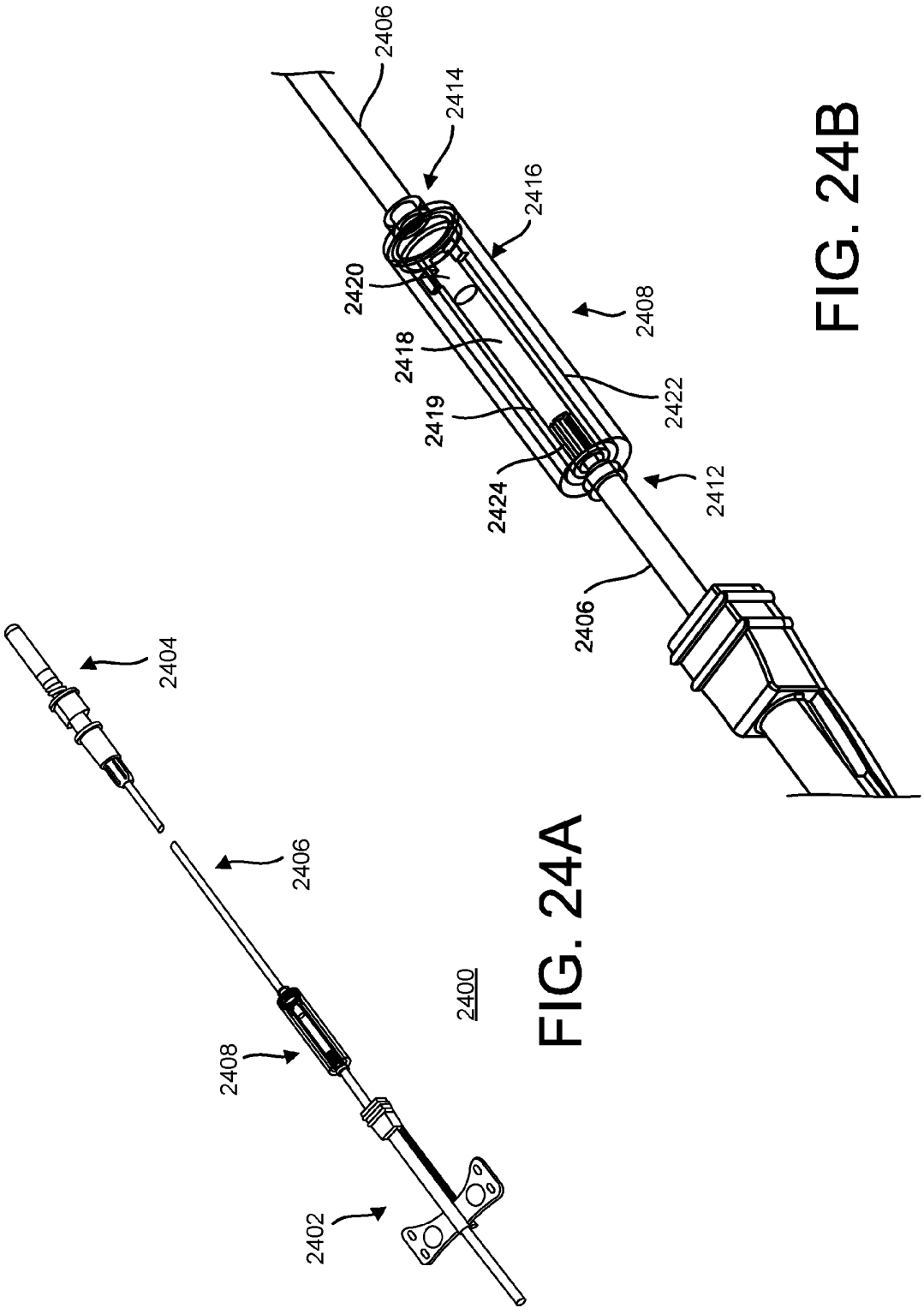


FIG. 24B

FIG. 24A

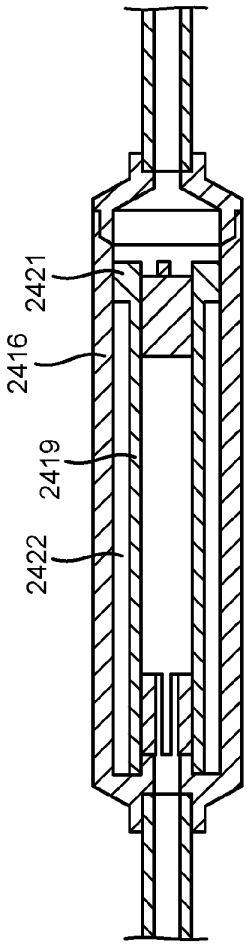


FIG. 24C

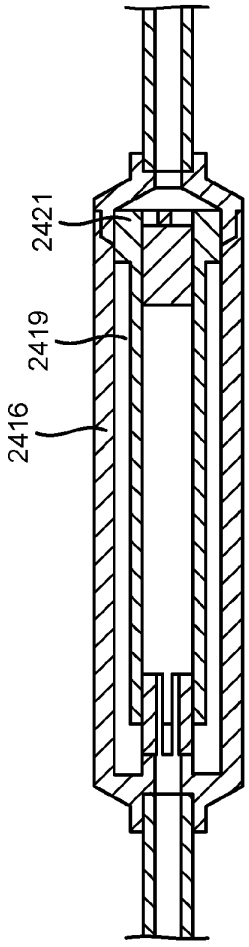


FIG. 24D

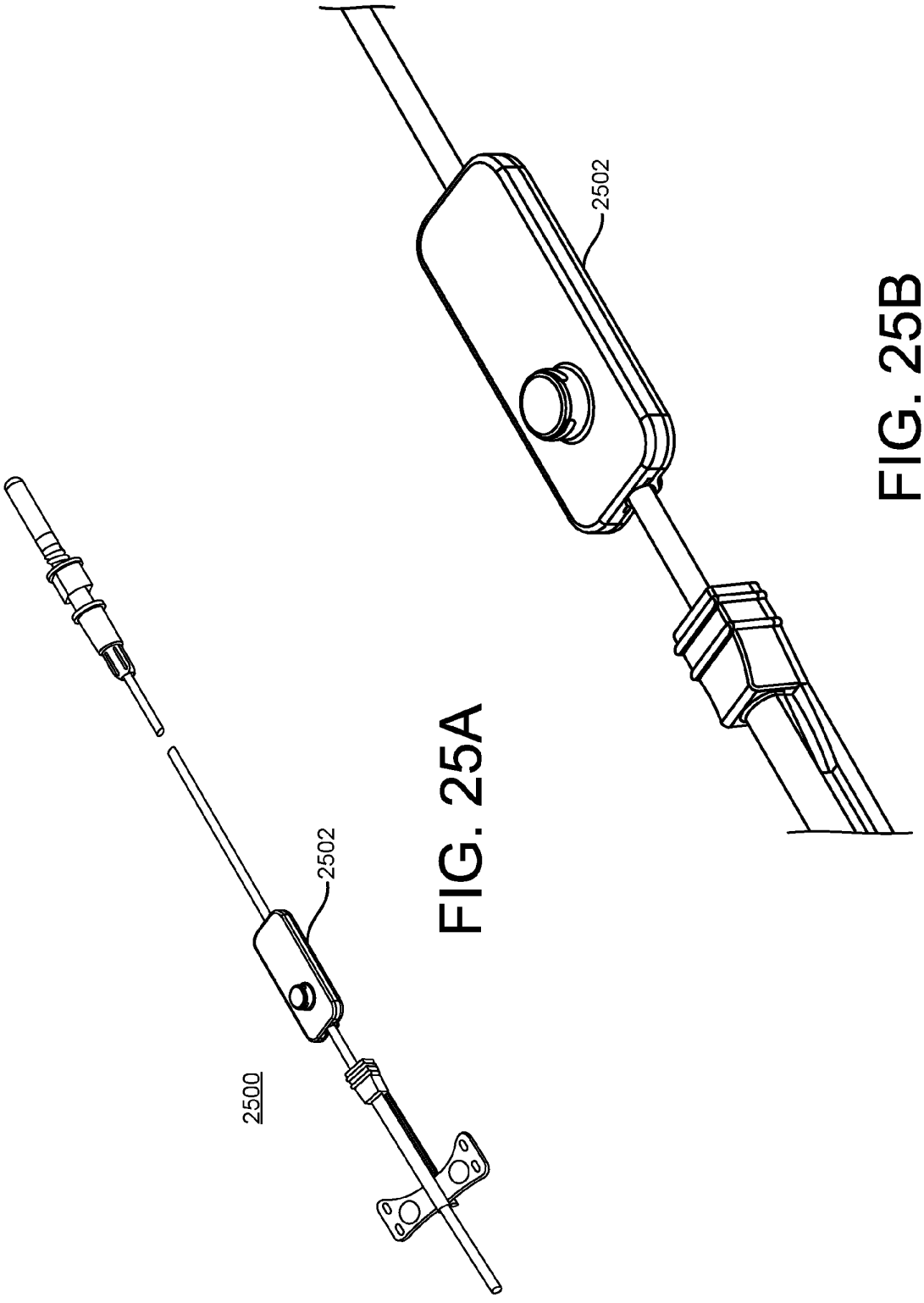


FIG. 25A

FIG. 25B

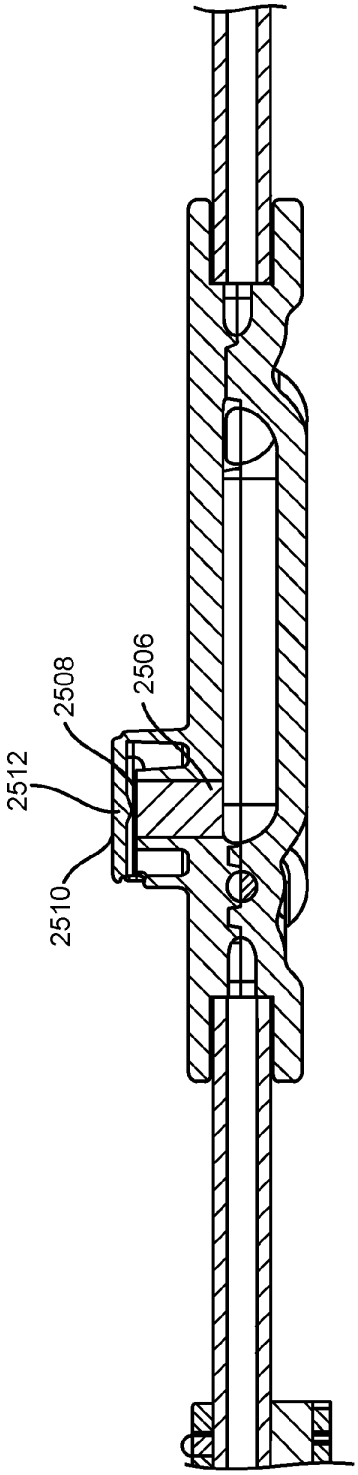


FIG. 25C

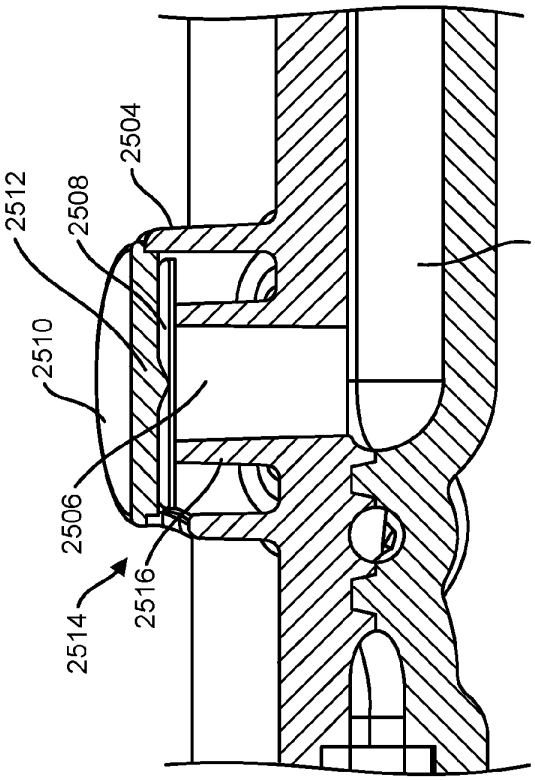


FIG. 25D

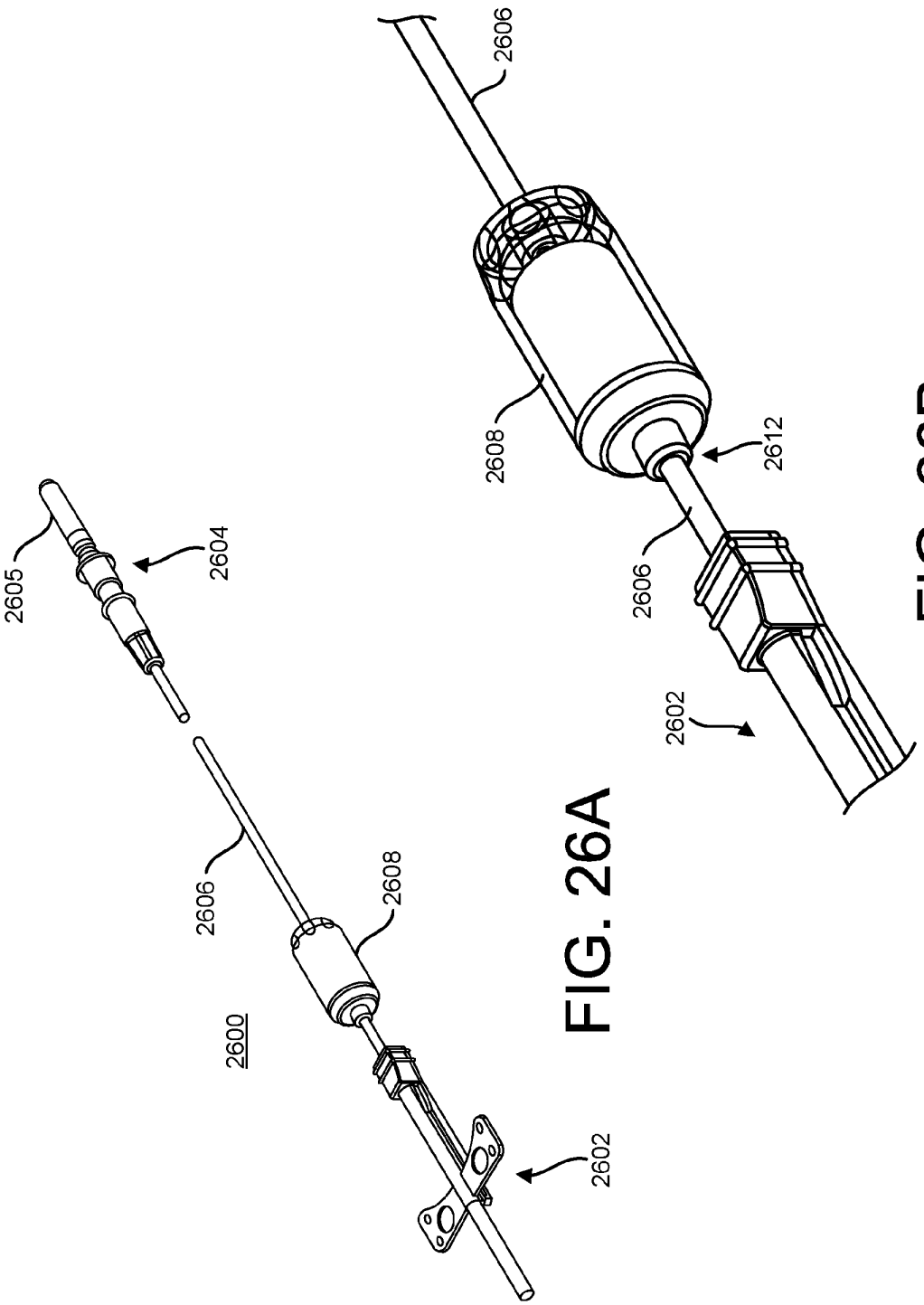


FIG. 26A

FIG. 26B

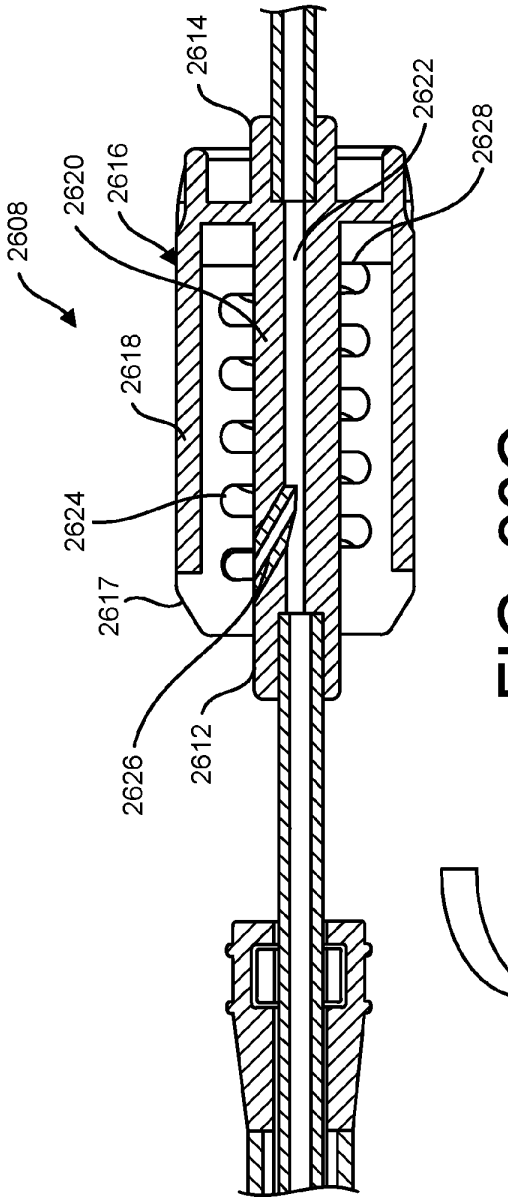


FIG. 26C

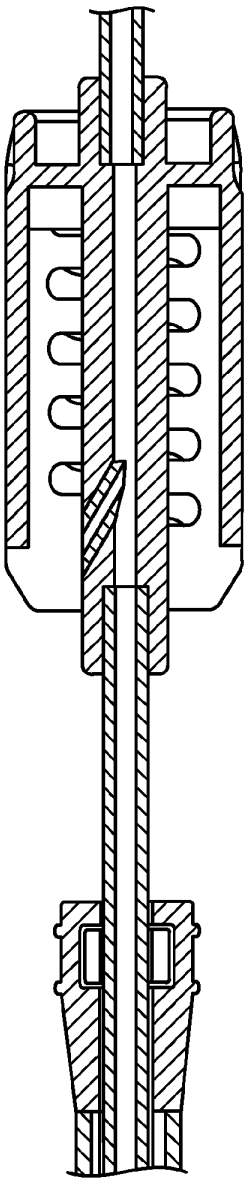


FIG. 26D

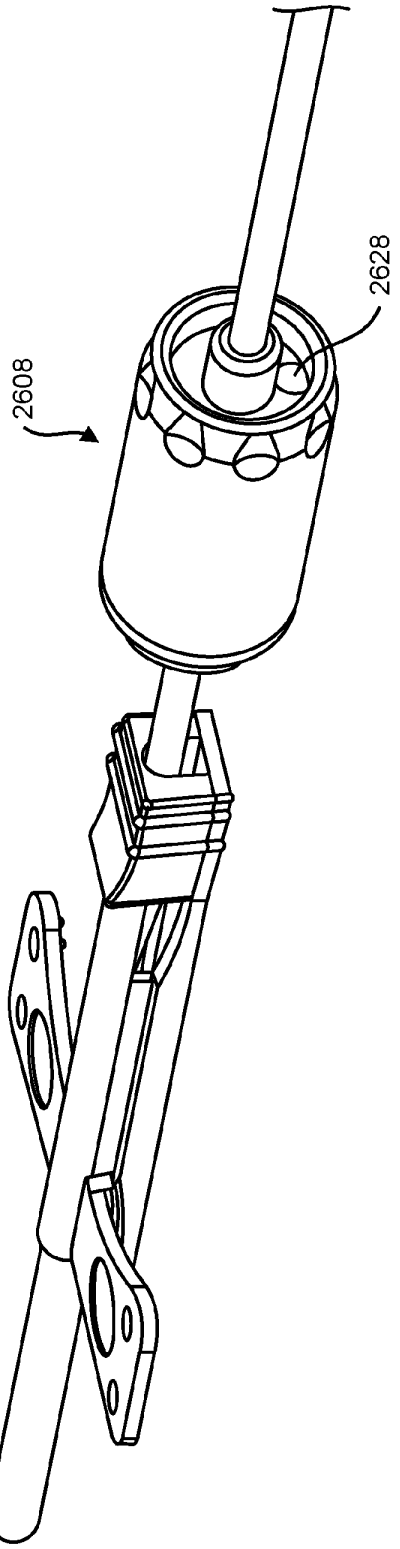


FIG. 26E

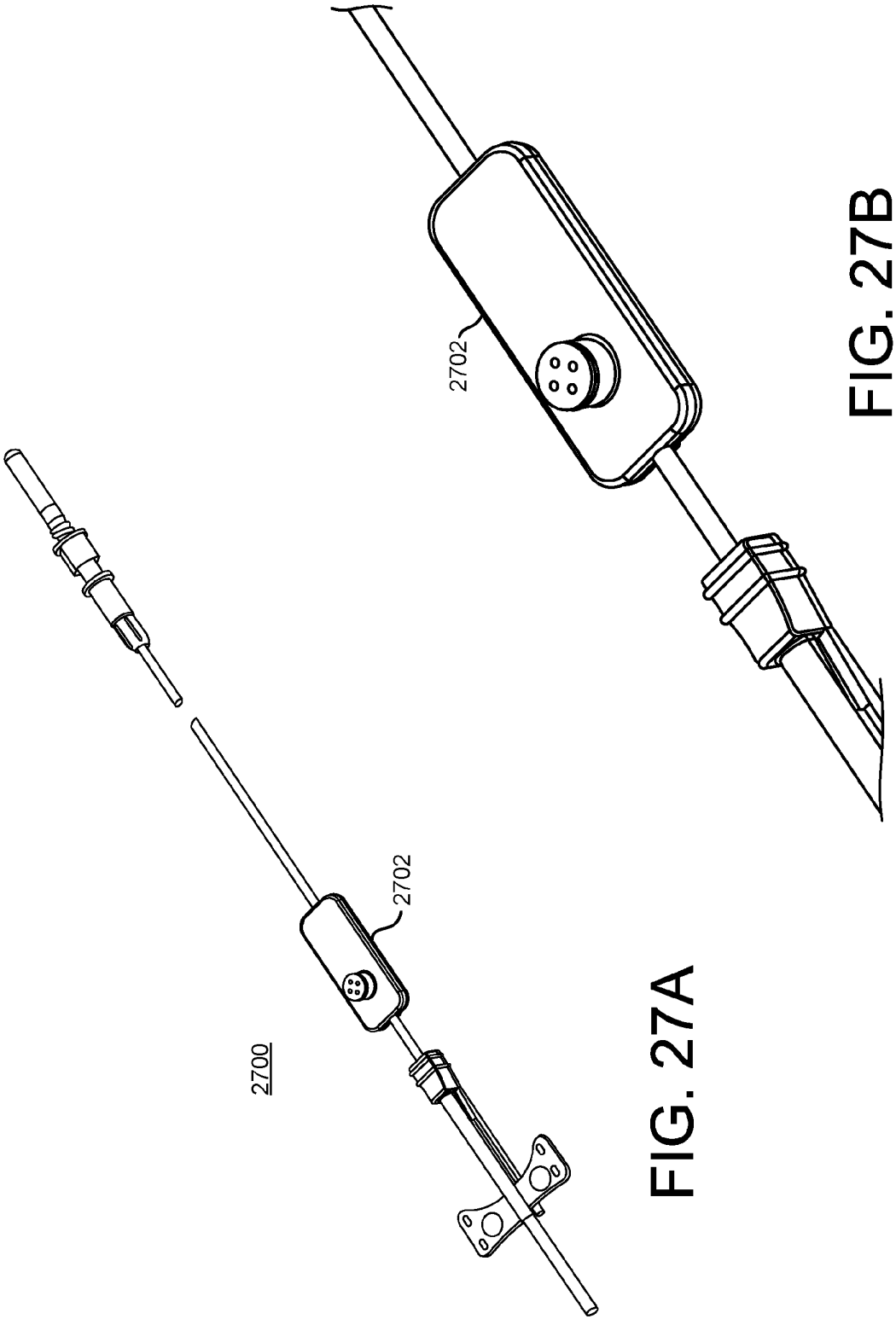


FIG. 27A

FIG. 27B

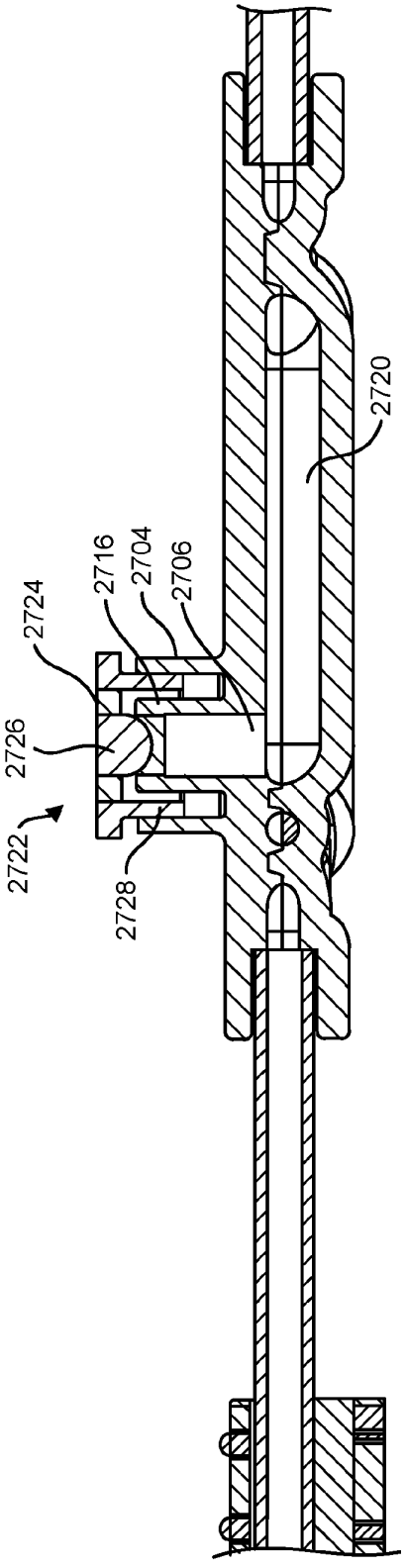


FIG. 27C

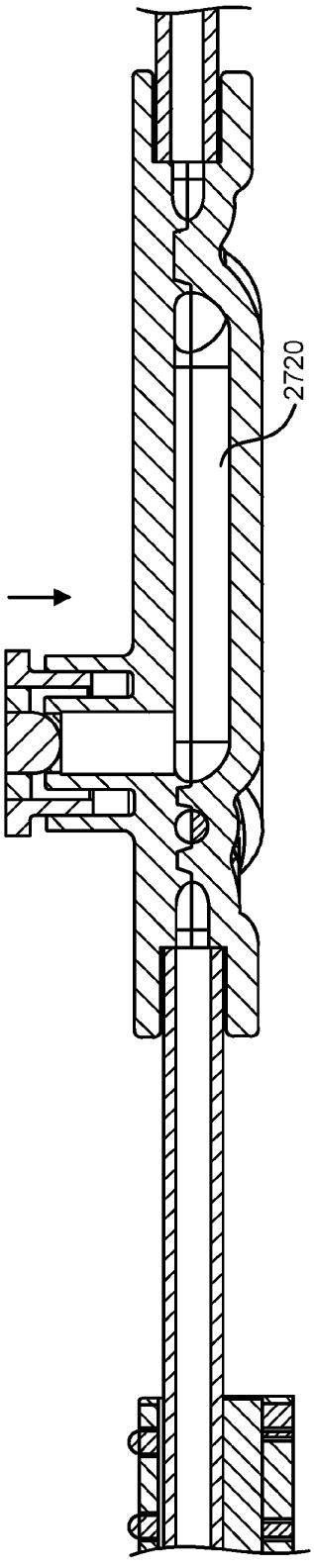


FIG. 27D

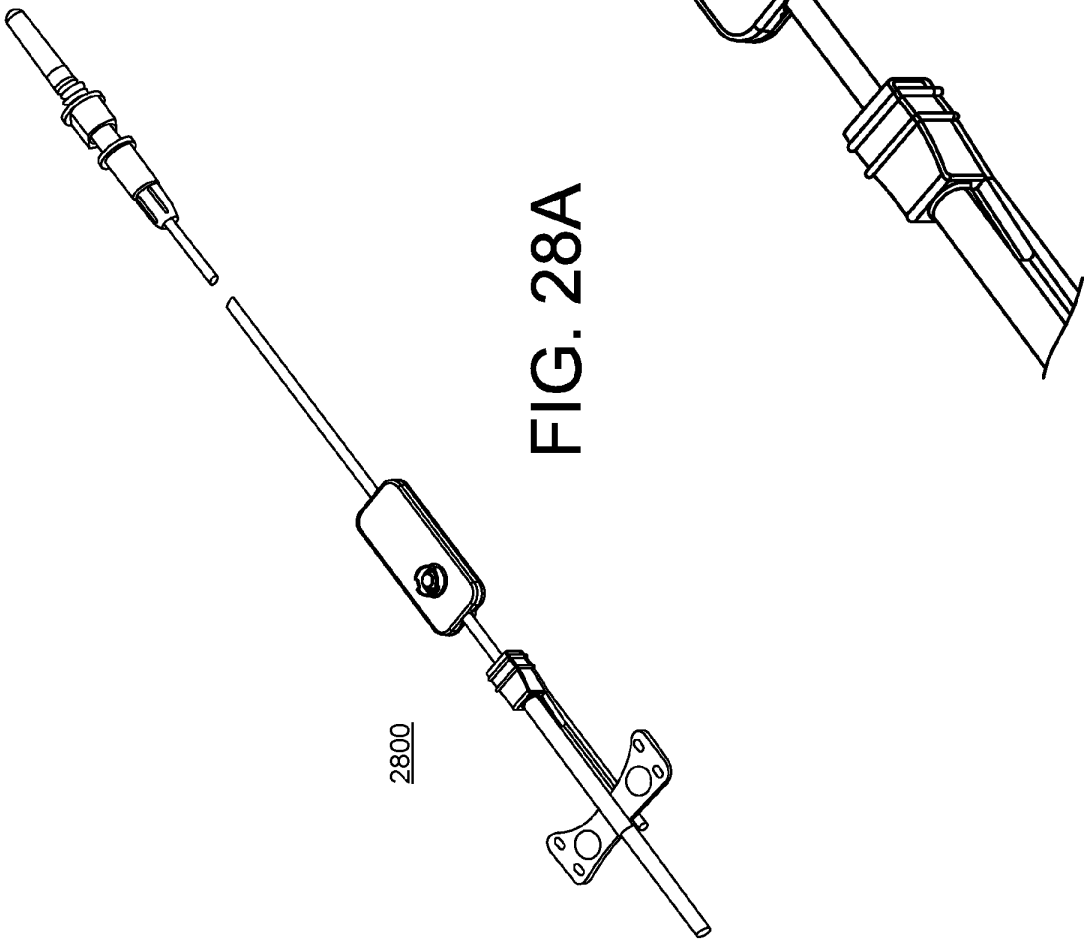


FIG. 28B

FIG. 28A

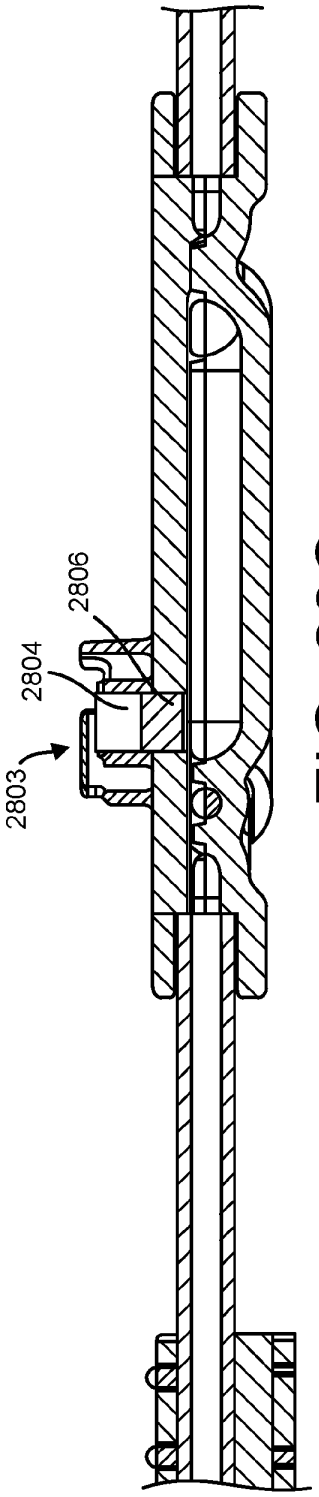


FIG. 28C

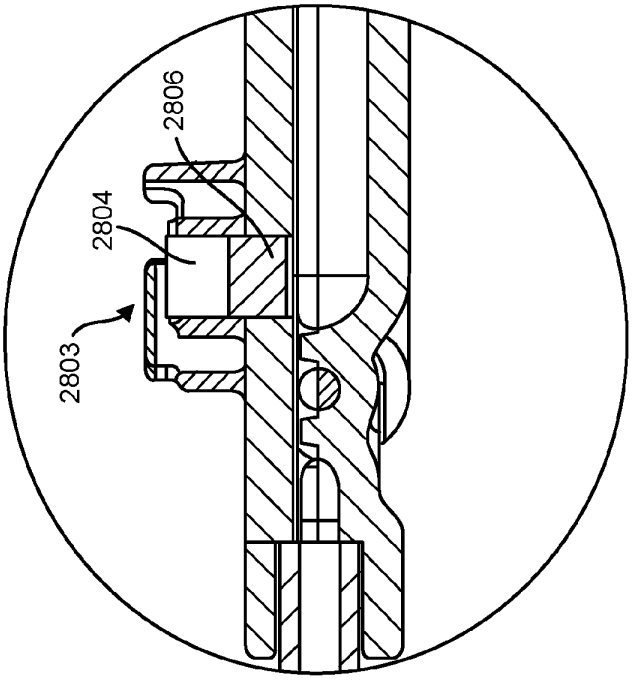


FIG. 28D

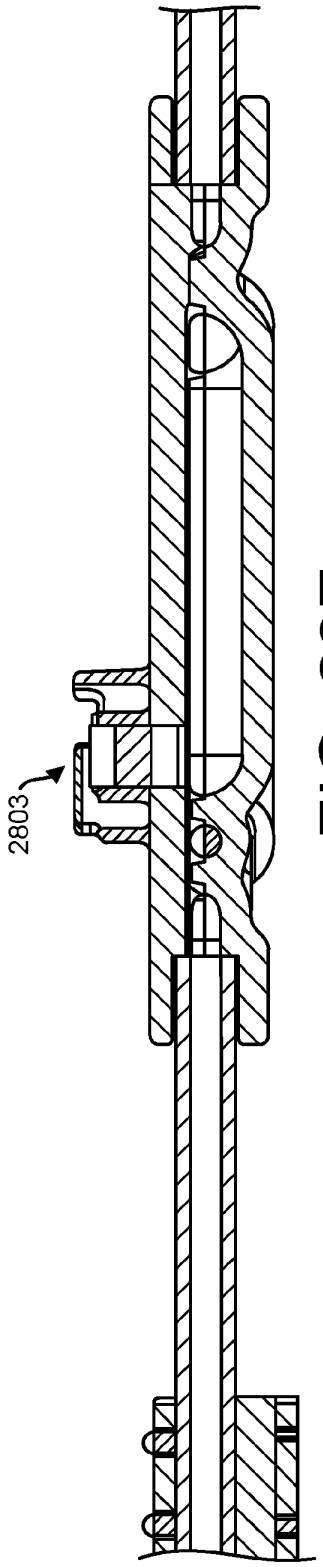


FIG. 28E

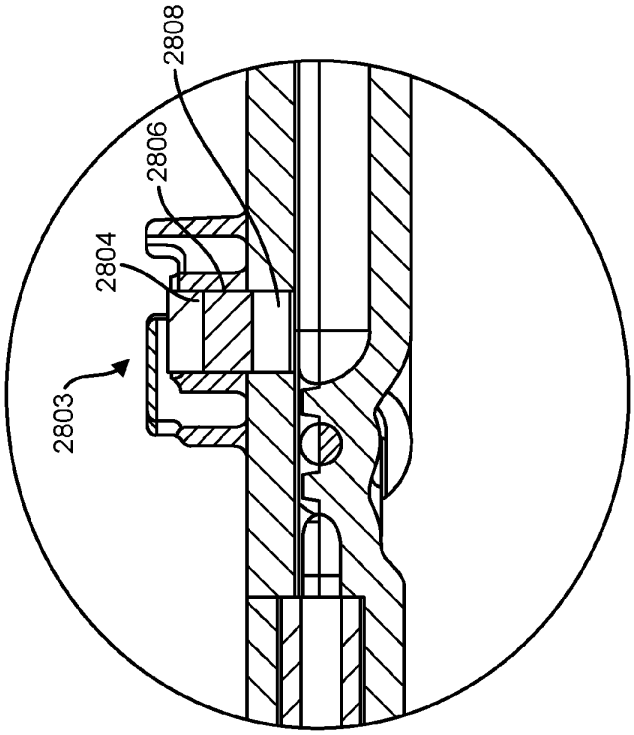


FIG. 28F

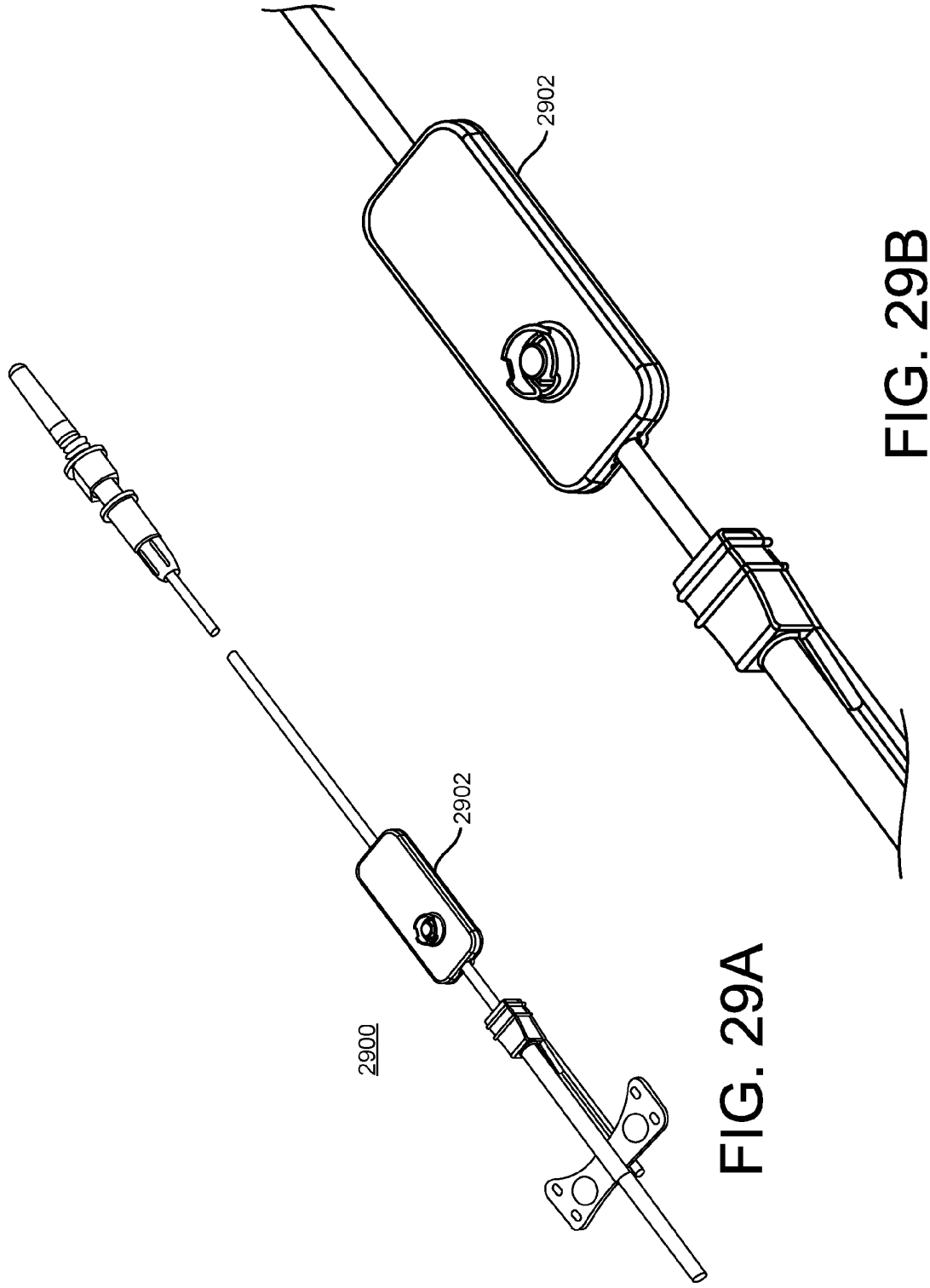


FIG. 29B

FIG. 29A

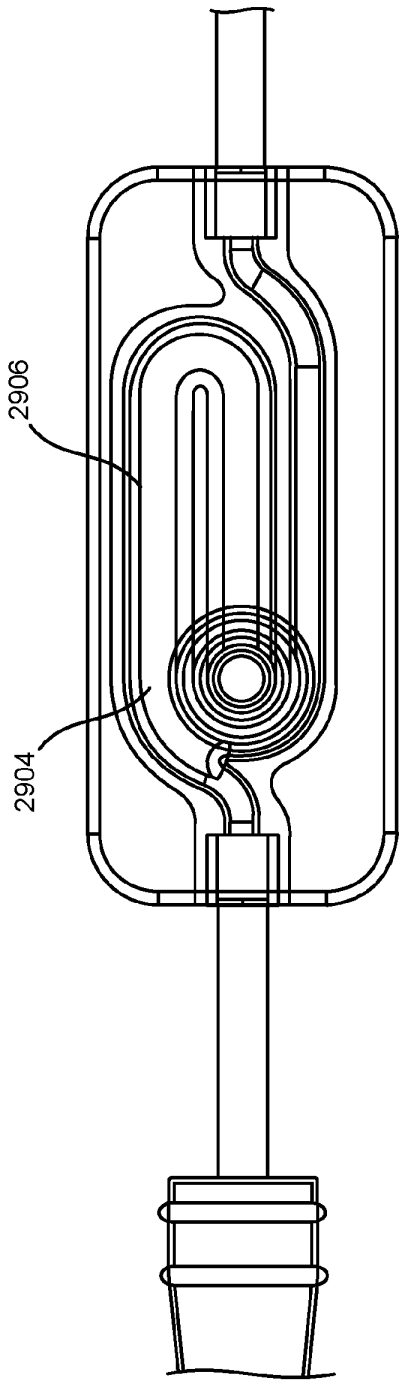


FIG. 29C

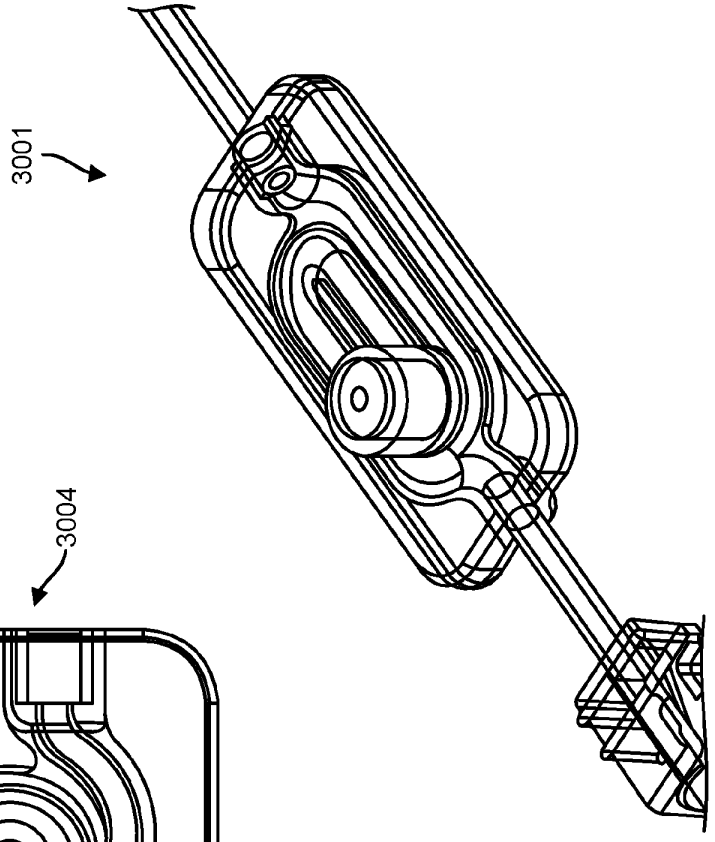


FIG. 30B

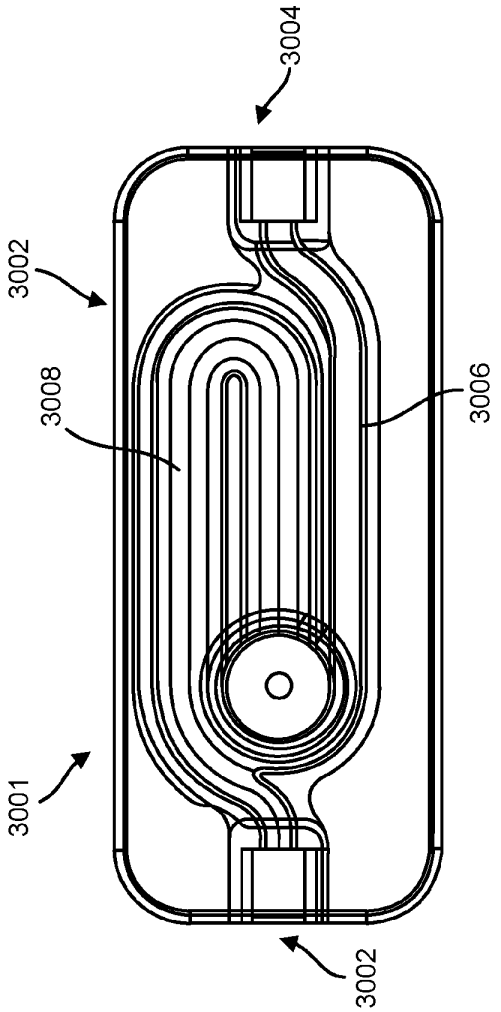


FIG. 30A

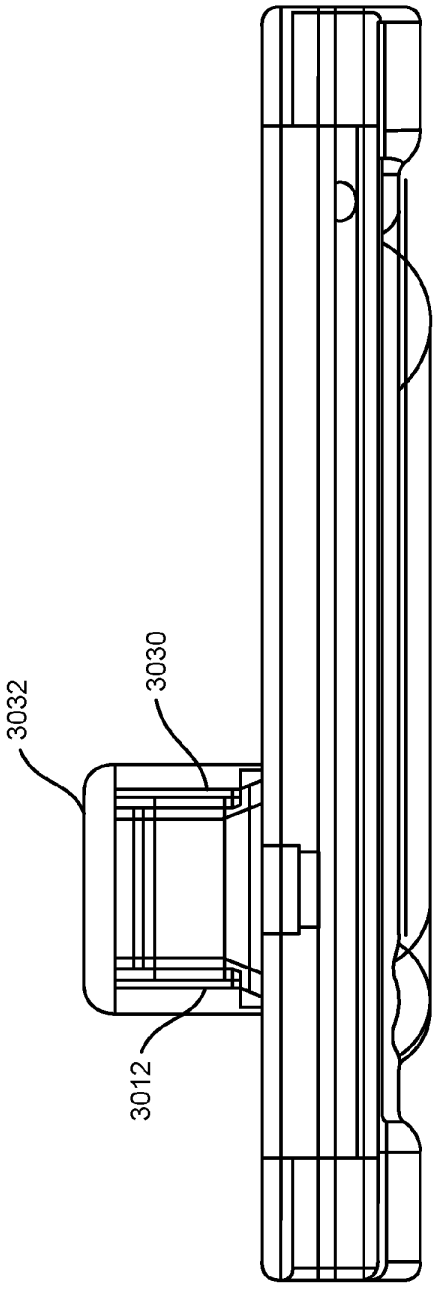


FIG. 30C

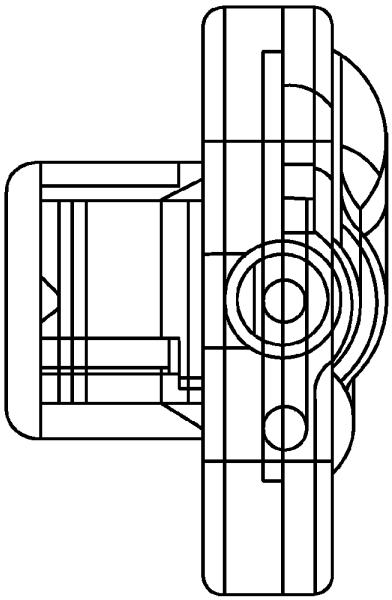


FIG. 30D

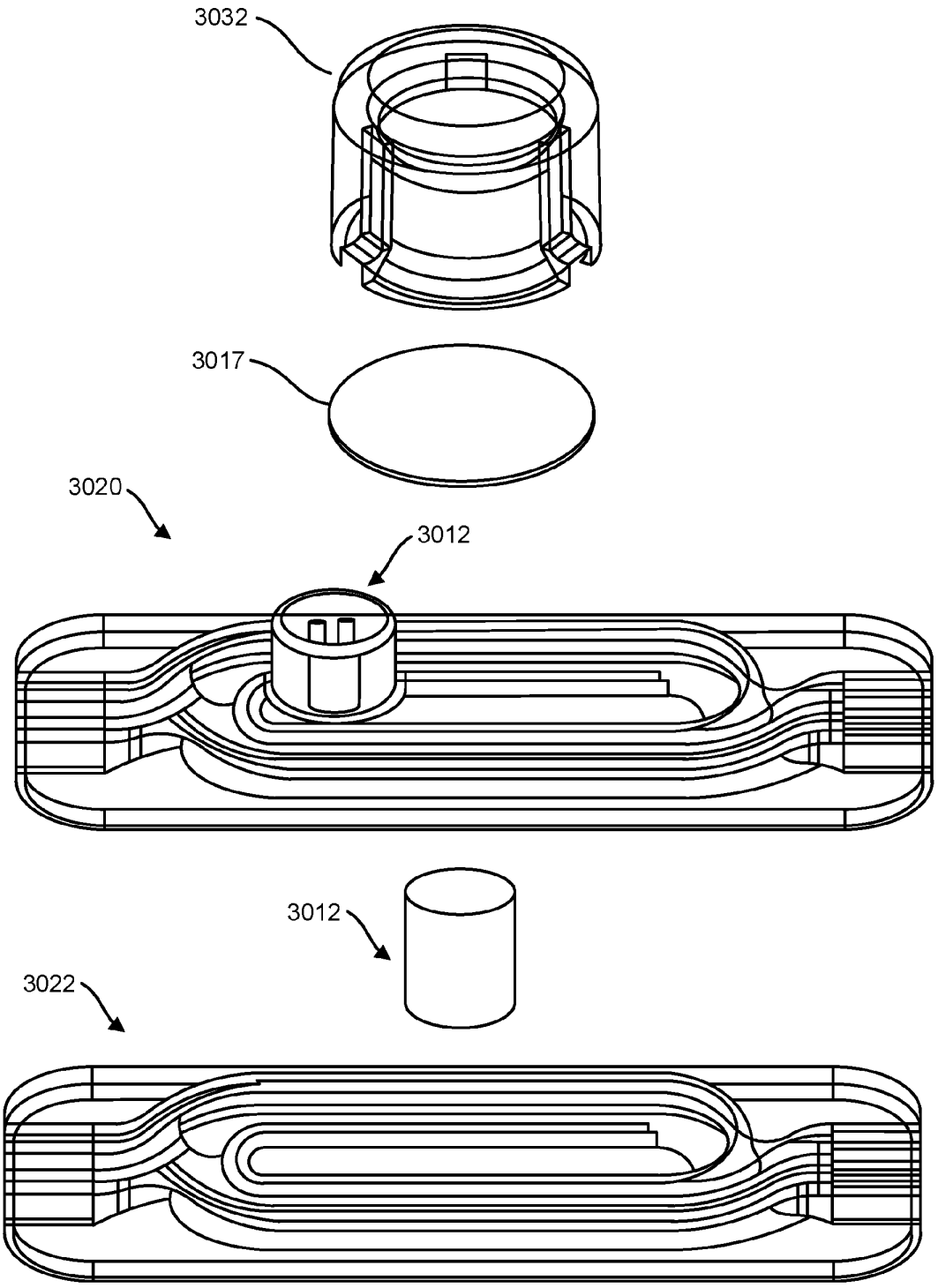


FIG. 30E

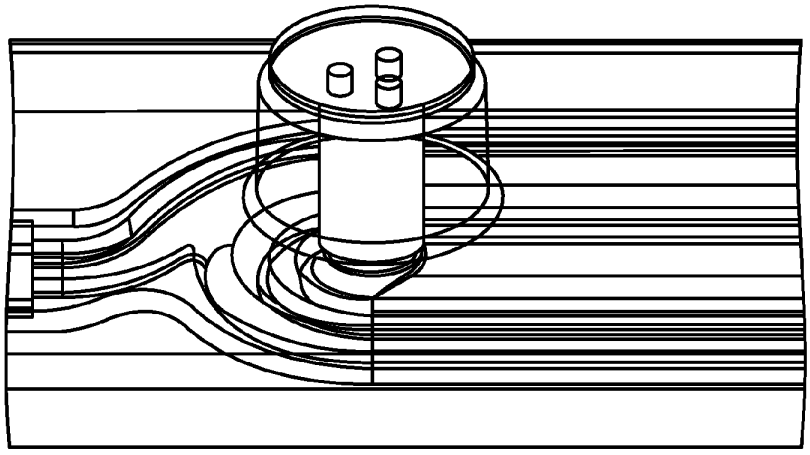


FIG. 30F

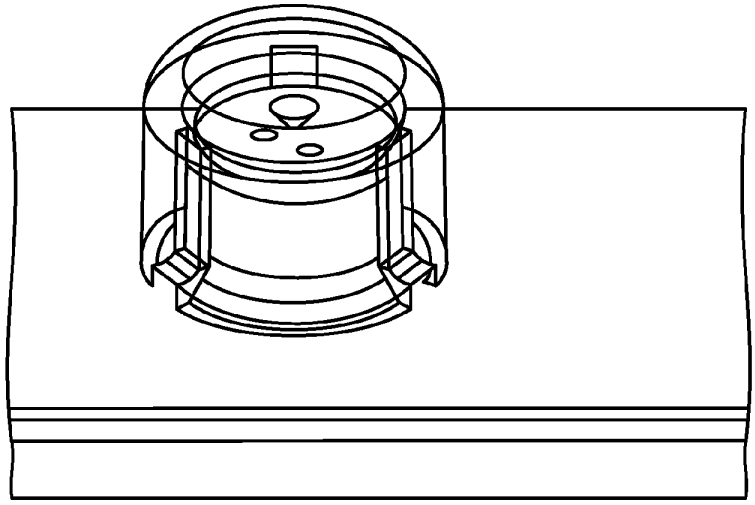


FIG. 30G

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/068569

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/039348 A1 (BULLINGTON GREGORY J [US] ET AL) 6 February 2014 (2014-02-06) the whole document	1-20
A	US 2014/107564 A1 (BULLINGTON GREGORY J [US] ET AL) 17 April 2014 (2014-04-17) the whole document	1-20
A	US 4 813 433 A (DOWNEY JOHN M [US]) 21 March 1989 (1989-03-21) the whole document	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) abstract paragraph [0048] - paragraph [0075]; figures 2-12	1-20

-/--

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Nielsen, Michael

1

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

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/068569

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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

1

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/068569

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014039348 A1	06-02-2014	US 2014039348 A1	06-02-2014
		US 2016113560 A1	28-04-2016
		WO 2014022275 A1	06-02-2014
US 2014107564 A1	17-04-2014	EP 2906269 A1	19-08-2015
		US 2014107564 A1	17-04-2014
		US 2015367069 A1	24-12-2015
		WO 2014058945 A1	17-04-2014
US 4813433 A	21-03-1989	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015
WO 2013181352 A1	05-12-2013	AU 2013267448 A1	18-12-2014
		AU 2017216493 A1	07-09-2017
		CA 2875118 A1	05-12-2013
		CN 104902817 A	09-09-2015
		CN 107736901 A	27-02-2018
		EP 2854643 A1	08-04-2015
		EP 3173021 A1	31-05-2017
		JP 6242386 B2	06-12-2017
		JP 2015519145 A	09-07-2015
		JP 2018034009 A	08-03-2018
		US 2014155781 A1	05-06-2014
		US 2015351679 A1	10-12-2015
		WO 2013181352 A1	05-12-2013

Europäisches Patentamt
European Patent Office
Office européen des brevets

European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840

Formalities Officer
Name: Schulze, Cornelia
Tel: +49 30 25901 - 701
or call
+31 (0)70 340 45 00

Substantive Examiner
Name: Schultz, Ottmar
Tel: +49 30 25901 - 566

Thum, Bernhard
Wuesthoff & Wuesthoff
Patentanwälte PartG mbB
Schweigerstraße 2
81541 München
ALLEMAGNE

WUESTHOFF & WUESTHOFF
Patentanwälte PartG mbB
06. Nov. 2018
RECEIVED

Application No.	Ref.	Date
16 747 682.9 - 1132	EPA-142 451	31.10.2018
Applicant: KURIN, INC.		

Basis 28.02./gedRo
WL 06.12.18 ✓
WV 28.01.19 ✓ voll 103

Communication pursuant to Article 94(3) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(2) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 126(2) and 131(2) and (4) EPC. One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (R. 50(1) EPC).

If filing amendments, you must identify them and indicate the basis for them in the application as filed. Failure to meet either requirement may lead to a communication from the Examining Division requesting that you correct this deficiency (R. 137(4) EPC).

In case you withdraw the application within the above-mentioned period, the examination fee will be refunded at a rate of 50% (Art. 11 (b) RFees).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Art. 94(4) EPC).

Registered letter
EPO Form 2001 11.16TRI

Schultz, Ottmar
Primary Examiner
For the Examining Division

Enclosure(s): 1 page/s reasons (Form 2906)

Registered letter
EPO Form 2001 11.16 TRI

The examination is being carried out on the **following application documents**

Description, Pages

1-33 as published

Claims, Numbers

1-20 as published

Drawings, Sheets

1/50-50/50 as published

+++++

An International Preliminary Report on Patentability has already been drawn up for the present application in accordance with the PCT. The deficiencies mentioned in that report give rise to objections under the corresponding provisions of the EPC.

+++++

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 50828-501001WO	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2016/043709	International filing date *(day/month/year)* 22 July 2016 (22.07.2016)	Priority date *(day/month/year)* 24 July 2015 (24.07.2015)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant KURIN, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	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 Article 35(2) with regard to novelty, inventive step or 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

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 30 January 2018 (30.01.2018)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Lingfei Bai e-mail: pct.team2@wipo.int

Form PCT/IB/373 (January 2004)

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.

+++++

Letter to the Editor

Quality control of bacterial contamination of blood components: the feasibility of diversion system testing

Marcello Napolitano, Giulia Micciulli, Emilio Leone

Centro Trasfusionale, Ospedale Civile di Castrovillari, Cosenza, Italia

Quality controls and retrospective investigations indicate that the majority of bacterial strains isolated from platelet concentrates (PC) derives from bacterial flora contaminating the skin[1,2], while about 50% of cases of bacterial contamination of red cell concentrates (RCC) are caused by transitory episodes of asymptomatic bacteraemia in the donor[3]. For the recipient, the risk of receiving PC contaminated by bacteria is 10-1,000 higher than the combined risk of receiving product contaminated by viruses such as HBV, HCV and HIV. The available epidemiological data show that 1: 2-3,000 PC can be contaminated by bacteria and that the risk of severe sepsis is about 1 case for every 1:50,000 platelet transfusions[1]. The risk of severe sepsis from transfusion of RCC is estimated to be about 1:500,000[4]. In the United States bacterial contamination of blood components is the second cause, after human error, of transfusion-related deaths[2].

The recognized preventive measures include: careful selection of the donor in order to avoid periods of possible bacteraemia (recent dental procedures or diarrhoea), scrupulous disinfection of the venipuncture site with appropriate disinfectants not contaminated by bacteria, diversion – for diagnostic purposes – of the first millilitres of donated blood. Widespread use of pathogen inactivation is currently only available for plasma. Assessment of microbiological contamination of blood components by automated culture systems is increasing and is the subject of considerable debate.

Received: 30 April 2004 - Revision accepted: 31 May 2004
Correspondence:
Dott. Marcello Napolitano
Centro Trasfusionale
Ospedale Civile
Viale del Lavoro
87012 Castrovillari (CS), Italia
E-mail: manop@libero.it

Microbiological cultures of blood components have two aims: to avoid assigning contaminated blood components and to control the quality of the process of producing the blood components themselves. Given the low prevalence of potentially contaminated blood components, preventive bacteriological screening should include all blood components produced: this is an onerous and demanding strategy. Again, in consideration of the low prevalence of contamination, the efficacy of the bacteriological controls on samples can be challenged. Nevertheless, statistically and epidemiologically interesting results can be obtained from co-operation among centres which share the same investigation methods and aims.

We analyzed the technical feasibility of a study on microbiological contamination, using a simple system of diversion into a satellite bag, which allows the blood component to be sampled without compromising its clinical usefulness.

The system allows samples of the contents of the primary bag to be analysed, so the results are applicable to all the blood components produced by fractionating that unit of whole blood, or to conserve the satellite bag in the same conditions as those of the blood component to test, thus exactly reproducing the times and methods of storing the component.

Triple or quadruple bags with SAG-M are used. After having carried out the fractionation and having detached the plasma bag, the SAG-M is allowed to flow into the bag with the red blood cells. After mixing, about 20 mL of the product are allowed to flow into the bag containing SAG-M. This bag is then destined fro sampling for microbiological tests.

We used this system to investigate microbial contamination of RCC. The satellite bags were stored in the blood bank in the same conditions as those used for

the RCC to be transfused. The samples were taken in a sterile environment, under a laminar flow hood, on day + 16 of storage (this being the mean time of use of RCC in our centre) and on day + 42 (expiry date). The cultures were carried out with the MiniVITAL system (BioMerieux SA, Marcy- l'Etoile, France).

The presence of aerobic and anaerobic bacteria and mycetes was investigated. The sampling was carried out using two blood culture bottles with 5 mL of sample in each bottle. Overall, 340 cultures were set up for 170 units of RCC. One blood culture was positive for *Micrococcus spp.*, a saprophytic skin contaminant, weakly pathogenic for humans. This positive culture was found in the group of samples taken on day + 42. Our results, indicating a higher than expected percentage of contamination, support the fact that the most prevalent type of contamination is that from the skin; the data are also of interest with the aim of controlling the production process of blood components[5]. It goes without saying that the number of investigations carried out is too low to attribute any statistical significance to the results.

We believe that it would be worthwhile building a multicentre collaboration on the basis of our methodological approach and in the light of our results.

References

1) Blajchman MA, Goldman M, Baeza F. Improving the bacteriological safety of platelet transfusion. Transf Med Rev 2004; **18**: 11-24.

2) Hillery CD, Josephson CD, Blajchman MA, et. al. Bacterial contamination of blood components: risks, strategies, and regulation. Hematology (Am Soc Hematol Educ Program) 2003; **i**: 575-89.

3) Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and intervention. Vox Sang 2004; **86**: 157-63.

4) Blajchman MA. Incidence and significance of the bacterial contamination of blood components. Dev Biol (Basel) 2002; **108**: 59-67.

5) McDonald CP, Roy A, Mahaian P, et. al. Relative values of the intervention of diversion and improved donor-arm disinfection to reduce the bacterial risk from blood transfusion. Vox Sang 2004; **86**: 178-82.

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

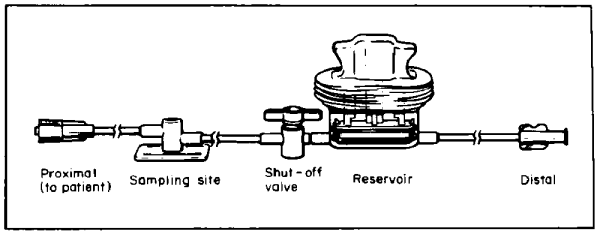


Fig. 1. Baxter venous/arterial blood management protection system (VAMPTM).

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

Original Article

Quality of Processed Blood for Autotransfusion

Gerald Shulman, MD

University of Texas Medical Branch, Galveston, Texas

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

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

ABSTRACT

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

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

KUR-MAG-DE005189

Page 1870 of 5977

INTRODUCTION

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

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

MATERIALS AND METHODS

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

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

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

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

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

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

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

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

KUR-MAG-DE005190

Page 1871 of 5977

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

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

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

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

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

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

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

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

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

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

STATISTICS

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

RESULTS

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

KUR-MAG-DE005191

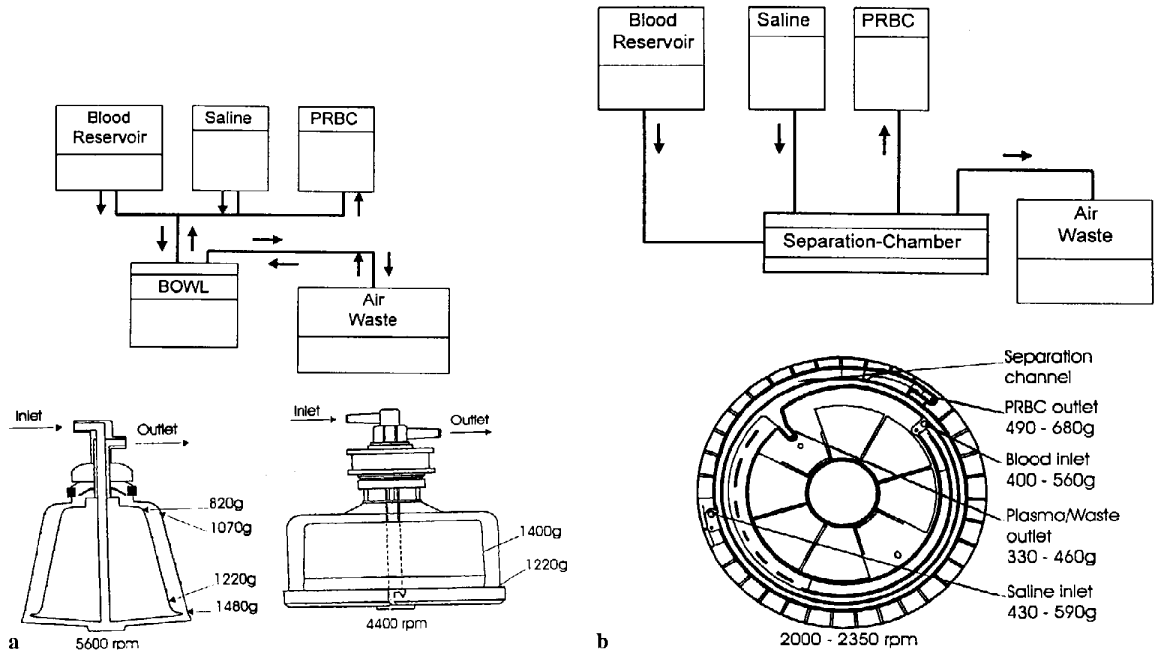


Figure 1: Diagrammatic representations of the flow in systems devised for intraoperative autologous transfusion in (a) discontinuous and (b) continuous flow procedures.

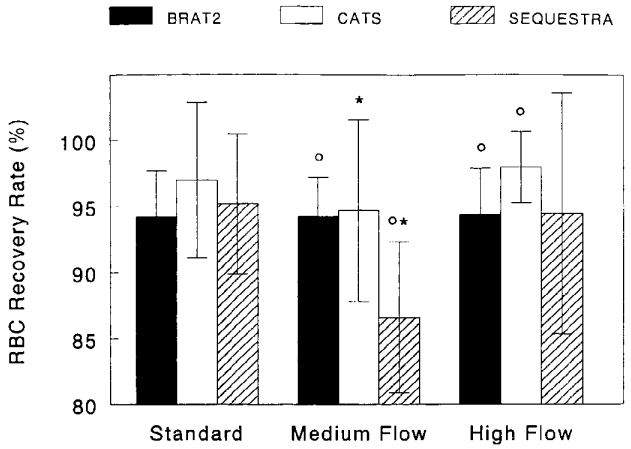


Figure 2: Mean red blood cell recovery rates ± standard deviations for three replicate processing runs using three autotransfusion devices in three programs; ° * = $p < .05$; $N = 9$.

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

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

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

KUR-MAG-DE005192

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

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

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

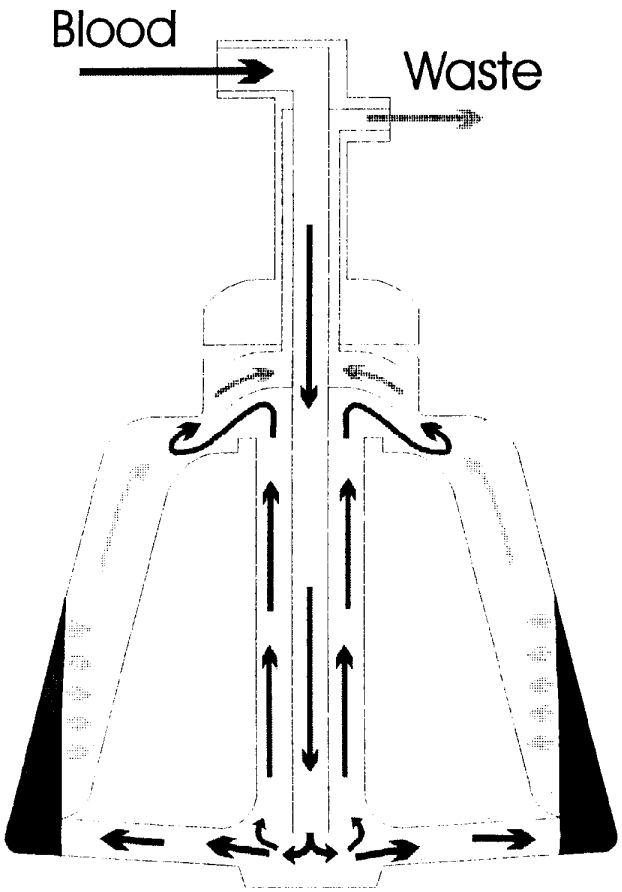


Figure 3: Processing with the conical centrifuge bowl at high flow rates showing red cell loss to waste, presumably due to pressure buildup.

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

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

DISCUSSION

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

KUR-MAG-DE005193

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

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

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

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

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

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

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

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

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

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

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

KUR-MAG-DE005194

Page 1875 of 5977

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

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

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

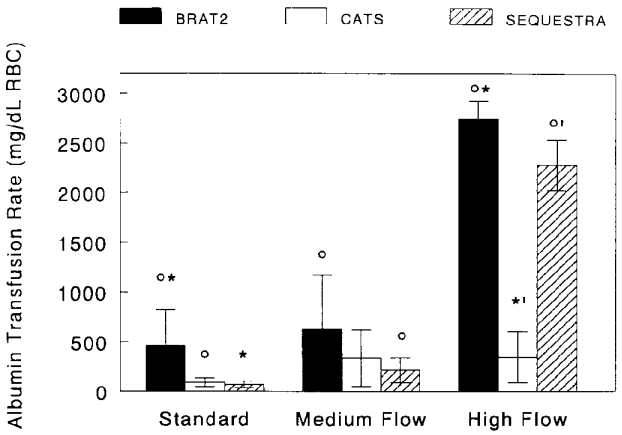


Figure 4: Mean holding bag supernatant albumin transfusion rates ± standard deviations (mg/dL/RCM) for three replicate processing runs using three autotransfusion devices in three programs; ° * = $p < .05$; $N = 9$.

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

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

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

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

KUR-MAG-DE005195

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

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

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

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

REFERENCES

1. Holleufer RF, von Bormann B. Comparative study of the Fresenius CATS and the Dideco Autotrans autotransfusion systems in vascular surgery. In: World Apheresis Association 6th International Congress, 1996, Abstract Book. Scientific Press, Florence, Italy.
2. Walpoth BH, Eggensperger N, Walpoth-Aslan BN, et al. Qualitative assessment of blood washing with the continuous autologous transfusion system (CATS). Int J Artif Organs. 1997;20:234–239.
3. Florio G, Valbonesi M, Lercari G, et al. The Fresenius continuous autotransfusion system (CATS): Preliminary studies and application. Int J Artif Organs. 1996;19:431–434.
4. Breitinger D, Frick U, Mauermann K, et al. Maschinelle intraoperative Autotransfusion (MAT): Qualitative untersuchung Verschiedener Programme eines Kontinuierlichem Autotransfusionsverfahrens. A I N S. 1998;33 Suppl 3;FP-D 205.6.
5. Booke M, Fingerhut D, Greis A, et al. Intraoperative autotransfusion—A clinical study of two different blood pro-

KUR-MAG-DE005196

Page 1877 of 5977

cessing techniques. Infusionther Transfusionsmed. 1997; 24:190–336.
6. Lorentz A, Waibel H, Becker P. Qualitatskontrollen bei zwei maschinellen autotransfusiongeraten (CATS/Cell-Saver V). Haematologie, Munchen, Sympomed. 1997;16.
7. Mertzlufft F, Bergum G, Seyfert UT. Maschinelle intraoperative Autotransfusion (MAT): Untersuchung zur qualitat verschiedener Autotransfusionssysteme. Anaesthesist. 1996;45;Suppl 2: FV 1313.
8. Van Slyke DD, Phillips RA, Dole VP, et al. Calculation of hemoglobin from blood specific gravities. J Biol Chem. 1950;183:349.
9. von Finck M, Schmidt R, Schneider W, et al. The quality of retransfused autologous red cells. Investigation on the elimination of plasma haemoglobin, osmotic fragility and survival rate of retransfused red cells. Anaesthesist. 1986; 35:686–692.
10. Pipa A, Petersen J, Hergert M. Maschinelle Autotransfusion: Vergleich gewaschener erythrozytenkonzentrate mit biochemischen, haematologischen, und mikroskopischen verfahren. Haematologie, Munchen, Sympomed. 1997.
11. Schleinzer W, Singbartl G. Intraoperative Autotransfusion mit einem neuen Kontinuierlichen Autotransfusionssystem (Fresenius CATS). Haematologie, Munchen, Sympomed. 1996;5:6–9.
12. Santrach PJ, Willis EA, Mathison BA, et al. Performance characteristics of a modified centrifuge bowl for blood salvage. Transfusion. 1998;38, Suppl:77S.
13. Santrach PJ, Willis EA, Mathison BA, et al. Potassium removal as a measure of processing efficiency in blood salvage. Transfusion. 1998;38, Suppl:79S.

KUR-MAG-DE005197

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

(11) Veröffentlichungsnummer:
(11) Publication number: **EP 2 593 169 A0**
(11) Numéro de publication:

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

WO 2012/009459 (Art. 153(3) EPÜ).

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

WO 2012/009459 (Art. 153(3) EPC).

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

WO 2012/009459 (art. 153(3) CBE).

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 January 2012 (19.01.2012)

PCT

(10) International Publication Number
WO 2012/009459 A1

(51) International Patent Classification:
A61M 25/06 (2006.01) *A61B 5/153* (2006.01)

(21) International Application Number:
PCT/US2011/043892

(22) International Filing Date:
13 July 2011 (13.07.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/364,535 15 July 2010 (15.07.2010) US
13/181,265 12 July 2011 (12.07.2011) US

(71) Applicant *(for all designated States except US)*: **BECTON, DICKINSON AND COMPANY** [US/US]; 1 Becton Drive, Mail Code 110, Franklin Lakes, NJ 07417-1880 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **BURKHOLZ, Jonathan Karl** [US/US]; 3610 Hermes Drive, Salt Lake City, UT 84124 (US). **HOANG, Minh Quang** [US/US]; 7954 English Oaks Cove, Sandy, UT 84093 (US).

(74) Agents: **HIGHET, David W.** et al.; Becton, Dickinson and Company, 1 Becton Drive, Mail Code 110, Franklin Lakes, NJ 07417-1880 (US).

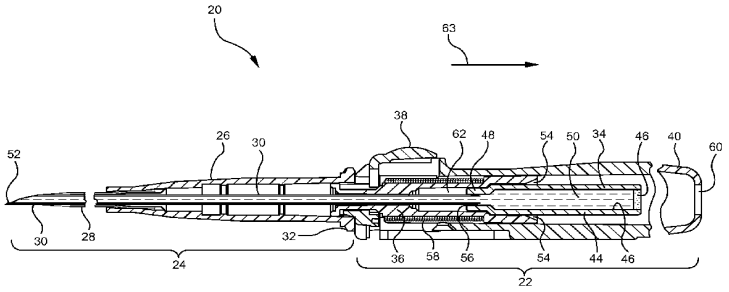
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, 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, RS, 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))*

(54) **Title**: A REMOVABLE FLASH CHAMBER

FIG. 2



(57) **Abstract**: A needle hub (36) and catheter assembly are (20) disclosed herein. The needle hub includes an introducer needle (30) having a lumen extending therethrough. A needle hub is coupled to a proximal end of the introducer needle. A flash chamber (34) is removably coupled to the needle hub or the introducer needle. An interior of the flash chamber is in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub or the introducer needle. As such, the flash chamber can collect a sample of blood that can be accessed when the flash chamber is removed. In some instances, the blood can also be dispensed from the flash chamber into a test strip (70) or other testing device.

WO 2012/009459 A1

A REMOVABLE FLASH CHAMBER

BACKGROUND

[0001] The present disclosure relates to venting air and blood sampling with vascular access devices. Blood sampling is a common health care procedure involving the withdrawal of at least a drop of blood from a patient. Blood samples are commonly taken from hospitalized, homecare, and emergency room patients either by finger stick, heel stick, or venipuncture. Once collected, blood samples are analyzed via one or more blood test levels.

[0002] Blood tests determine the physiological and biochemical states of the patient, such as disease, mineral content, drug effectiveness, and organ function. Blood tests may be performed in a laboratory, a distance away from the location of the patient, or performed at the point of care, near the location of the patient. One example of point of care blood testing is the routine testing of a patient's blood glucose levels. This involves the extraction of blood via a finger stick and the mechanical collection of blood into a diagnostic cartridge. Thereafter the diagnostic cartridge analyzes the blood sample and provides the clinician a reading of the patient's blood glucose level. Other devices are available which analyze blood gas electrolyte levels, lithium levels, ionized calcium levels. Furthermore, some point-of-care devices identify markers for acute coronary syndrome (ACS) and deep vein thrombosis/pulmonary embolism (DVT/PE).

[0003] Blood testing is frequently necessary prior to surgery or other medical procedures. For example, there are indications that diabetes contributes to an increase risk of Surgical Site Infection (SSI). Accordingly some guidelines suggest that diabetes is one characteristic that may influence the development of SSI. As such, preoperative blood glucose control is deemed a possible SSI risk reduction measure. Testing of creatine-based estimated glomerular filtration rate (GFR) can also be useful prior to some medical procedures. In February 2002, The National Kidney Foundation published that GFR is the best overall indicator of kidney function. The demonstration of normal kidney function may be important prior to a patient obtaining a contrast enhanced CT scan, which can have significant impact on the kidneys. Despite these needs, blood diagnosis is typically done at remote labs, which do not produce immediate results.

[0004] Furthermore, despite the rapid advancement in point of care testing and diagnostics, blood sampling techniques have remained relatively unchanged. Blood samples are frequently drawn using hypodermic needles or vacuum tubes coupled to a proximal end

of a needle or a catheter assembly. In some instances, clinicians collect blood from a catheter assembly using a needle and syringe that is inserted into the catheter to withdraw blood from a patient through the inserted catheter. These procedures utilize needles and vacuum tubes as intermediate devices from which the collected blood sample is typically withdrawn prior to testing. These processes are thus device intensive, utilizing multiple devices in the process of obtaining, preparing, and testing blood samples. Furthermore, each device required adds time and cost to the testing process. Accordingly, there is a need for more efficient blood sampling and testing devices and methods.

SUMMARY

[0005] The present invention has been developed in response to problems and needs in the art that have not yet been fully resolved by currently available blood sampling devices and methods. Thus, these devices and methods are developed to efficiently collect a blood sample from a flash chamber that is removably coupled to the proximal end of an introducer needle. Since blood is already collected in this chamber, the use of this blood can avoid the need for a separate blood sampling procedures and devices, which can decrease the cost and time of blood diagnosis. Once removed, blood can be dispensed from the flash chamber into a point-of-care diagnostic device, for prompt test results, which can enable time-sensitive health information, such as the risk of diabetes or impaired kidney function to be more quickly and easily acquired. Furthermore, the flash chamber can be sized to accommodate the desired blood sample. As such, the flash chamber can be enlarged, which increases the flashback visualization period.

[0006] In one aspect of the invention, a needle hub comprises: an introducer needle having a lumen extending therethrough; a needle hub coupled to a proximal end of the introducer needle; and a flash chamber removably coupled to the needle hub, an interior of the flash chamber being in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub.

[0007] Implementation may include one or more of the following features. A portion of the flash chamber can be compressible. The flash chamber can comprise: a chamber body defining an internal cavity; and an air permeable membrane coupled to the chamber body and in fluid communication with the internal cavity. The internal cavity of the chamber body of the flash chamber can have in an internal volume between about 0.1 mL to about 10 mL. The flash chamber can be press fit into the needle hub or introducer needle. The flash chamber can be screwed onto the needle hub. The flash chamber can be selectively coupled to the needle hub or the introducer needle via a keyed connection. The flash chamber can be

selectively coupled to the needle hub or the introducer needle via a breakable connection. The flash chamber can be a breakable ampoule.

[0008] In another aspect of the invention, a catheter assembly comprises: an introducer needle having a lumen extending therethrough; a needle hub coupled to a proximal end of the introducer needle; a flash chamber selectively coupled to the needle hub or the introducer needle, an interior of the flash chamber being in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub, the flash chamber having an air permeable membrane and a distal connector portion; the chamber body defining an internal cavity, the chamber body having at least a compressible portion that decreases the internal volume of the internal cavity when compressed; the air permeable membrane coupled to the chamber body and in fluid communication with the internal cavity; and the distal connector portion of the chamber body for selectively coupling to the needle hub.

[0009] Implementation may include one or more of the following features. At least a portion of the flash chamber can be compressible. The flash chamber can have an internal volume between about 0.1 mL to about 10 mL. The flash chamber can be press fit into the needle hub or introducer needle. The flash chamber can be screwed onto the needle hub. The flash chamber can be selectively coupled to the needle hub or the introducer needle via a breakable connection, the breakable connection including at least one scored line and a stress riser. The flash chamber is a breakable ampoule.

[0010] In another aspect of the invention, a method for providing a removable flash chamber of a catheter assembly, the method comprising: providing a catheter assembly having a needle hub, the needle hub having an introducer needle coupled thereto; providing an introducer needle coupled to the needle hub, the introducer needle having a lumen extending therethrough; and providing a flash chamber removably coupled to the needle hub, an interior of the flash chamber being in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub.

[0011] Implementation may include one or more of the following features. The method may further comprise providing at least a single compressible portion of the flash chamber for selectively ejecting blood within the flash chamber from therefrom. The method may further comprise providing an inner cavity within a body of the flash chamber having an internal volume about 0.1 mL to 10 mL. The flash chamber can have a distal connector portion, the distal connector portion having at least one of a press fit connector, screw threads, a keyed connection, and a breakable connection.

[0012] These and other features and advantages of the present invention may be incorporated into certain embodiments of the invention and will become more fully apparent from the following description and appended claims, or may be learned by the practice of the invention as set forth hereinafter. The present invention does not require that all the advantageous features and all the advantages described herein be incorporated into every embodiment of the invention.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

[0013] In order that the manner in which the above-recited and other features and advantages of the invention are obtained will be readily understood, a more particular description of the invention briefly described above will be rendered by reference to specific embodiments thereof which are illustrated in the appended drawings. These drawings depict only typical embodiments of the invention and are not therefore to be considered to limit the scope of the invention.

[0014] Figure 1 illustrates a perspective view of a catheter assembly with a removable flash chamber, according to some embodiments.

[0015] Figure 2 illustrates a cross-section view of a catheter assembly of Figure 1 taken along line 2-2, according to some embodiments.

[0016] Figure 3 illustrates a cross-section view of a catheter assembly with a removable flash chamber after the introducer needle has been withdrawn from the catheter, according to some embodiments.

[0017] Figure 4 illustrates a perspective view of a catheter assembly with a removable flash chamber that has been removed therefrom, according to some embodiments.

[0018] Figure 5 illustrates a perspective view of a removable flash chamber dispensing a sample of blood on a blood test strip, according to some embodiments.

[0019] Figure 6 illustrates a cross-section view of a proximal portion of a catheter assembly with a removable flash chamber, according to some embodiments.

[0020] Figure 7 illustrates a cross-section view of a proximal portion of another catheter assembly with a removable flash chamber, according to some embodiments.

[0021] Figure 8 illustrates a perspective view of a keyed connection between a flash chamber and a needle hub or safety barrel, according to some embodiments.

[0022] Figure 9 illustrates a cross-section view of a removable flash chamber, according to some embodiments.

DETAILED DESCRIPTION OF THE INVENTION

[0023] Embodiments of the present invention can be understood by reference to the drawings, wherein like reference numbers indicate identical or functionally similar elements. It will be readily understood that the components of the present invention, as generally described and illustrated in the figures herein, could be arranged and designed in a wide variety of different configurations. Thus, the following more detailed description, as represented in the figures, is not intended to limit the scope of the invention as claimed, but is merely representative of presently preferred embodiments of the invention.

[0024] Reference will now be made to Figure 1, which illustrates a catheter assembly 20 that can be used to access the vascular system of a patient, such as the BD Insyte (TM) Autoguard (TM) from Beckton, Dickinson and Company, Inc. (as shown), the BD Protect IV (TM) also from Beckton, Dickinson and Company, Inc., and the Medikit Z5 from Medikit Company Inc. The catheter assembly 20 can include various other configurations. The catheter assembly 20 generally includes a catheter adapter 24 and a needle assembly 22. The catheter adapter 24 is inserted into a patient to establish fluid communication with the patient's vasculature, and may be used to infuse fluids therethrough. The needle assembly 22 includes an introducer needle 30 that is used to assist the catheter assembly 24 to be accurately placed into the vasculature of the patient. After the catheter assembly 24 is properly placed, the needle assembly 22 is removed and uncoupled from the catheter assembly 24.

[0025] The needle assembly 22 includes a generally rigid introducer needle 30 that provides structural support to the flexible or semi-flexible catheter 28 of the catheter assembly 24. In a pre-use position, the introducer needle 30 is inserted through the catheter 28, as shown. During infusion or other such procedures the introducer needle 30 and catheter 28 are inserted through the skin of a patient and advanced into the vasculature of a patient. Once the catheter 28 is properly placed, the introducer needle 30 is removed from the catheter 28.

[0026] As shown in Figure 1, the catheter adapter 24 includes a catheter hub 26 that is coupled to a catheter 28 that extends distally from the distal end of the catheter hub 26. The catheter hub 26 includes an inner lumen that extends therethrough and provides fluid communication to an inner lumen of the catheter 28. In some configurations, the catheter hub 26 also includes a proximal connector 32, such as a threaded luer connector, that can connect to a needle assembly 22 or other vascular access device.

[0027] The needle assembly 22 includes an introducer needle 30 that extends through the catheter assembly 20 in a pre-insertion state. The introducer needle 30 is coupled to a needle hub 36 at its proximal end. In some embodiments, as shown, the needle hub 36 is disposed within a safety barrel 40 that shields the introducer needle 30 after it is withdrawn from the patient and out of the catheter adapter 24. In the illustrated embodiment, the introducer needle 30 is withdrawn, via a spring force, from the catheter adapter 24 when a user presses a button 38 of the needle assembly 22. The button 38 releases a fastener that holds the introducer needle 30 in place, permitting it to be withdrawn proximally through the catheter 28 and catheter hub 26 into the safety barrel 40.

[0028] With continued reference to Figure 1, in some embodiments, a flash chamber (also known as "flashback chamber") 34 is coupled to the needle hub 36 or directly to the proximal end of the introducer needle 30. The flash chamber 34 can receive blood therein from the introducer needle 30. In some configurations, the flash chamber 34 is transparent or semi-transparent such that a user can view blood flowing into the flash chamber 34 from the introducer needle 30.

[0029] In some catheter placement procedures, flashback occurs when blood from within the vasculature of a patient enters into the catheter 28 and/or introducer needle 30 of the catheter assembly 20. In some instances, the catheter 28 is transparent or semi-transparent such that the clinician can recognize blood flowing through the catheter 28 after the introducer needle 30 has entered the patient's vascular. To provide an extended flashback period that may enable a clinician to verify that the catheter 28 has entered and remains properly placed. In some embodiments, the catheter hub 26 and/or the needle assembly 22 can include a flash chamber 34. A flash chamber 34 of the needle assembly 22 can be in fluid communication with the introducer needle 30 so that blood flowing through the introducer needle 30 enters into the flash chamber 34. The size of the flash chamber 34 can be varied so that the length of time required to fill the chamber provides the clinician adequate time to properly position the catheter 28. As mentioned, once the catheter 28 is properly placed, the introducer needle 30 can be withdrawn from the catheter 28.

[0030] After the needle assembly 22 is uncoupled from the catheter adapter 24, the sample of blood within the flash chamber 34 can be use for diagnosis. In some embodiments, the flash chamber 34 can be selectively uncoupled from the needle assembly 22 so that the blood therein can be accessed and tested. Thus, in some embodiments, there is a means for extracting the blood from the flash chamber 34. This means can include compressing at least a portion of the flash chamber 34 to dispense blood therefrom. This means can also include

breaking the flash chamber 34, sucking or wicking blood from the flash chamber 34, or otherwise removing the blood therefrom.

[0031] In some embodiments, the flash chamber 34 extends through a proximal opening 60 in the safety barrel 40 after the needle is withdrawn from the catheter adapter 24. Thus, the flash chamber 34 can be larger, with an increased internal volume, than it could be without a proximal opening 60. In some configurations, the flash chamber 34 has in an internal volume between about 0.1 mL to 10 mL. In other configurations, the flash chamber 34 has in an internal volume between about 0.5 mL to 7 mL. In other configurations, the flash chamber 34 has in an internal volume between about 1 mL to 3 mL. In other configurations, the flash chamber 34 has in an internal volume greater or less than the listed volumes. The larger internal volume of the flash chamber 34 can provide longer flashback indication periods. As such, a clinician can have more time to place and ensure proper placement of the catheter 28.

[0032] Reference will now be made to Figure 2, which depicts a cross section of the catheter assembly 20 of Figure 1 taken along line 2-2. This figure depicts at least some of the inner components of the catheter adapter 24 and needle assembly 22. For simplicity, the catheter hub 26 is depicted as having few features or components therein. However, it will be understood that the catheter hub 26 can include various known components and features, such as a valve, blood control valve, inner ridges, or other known elements.

[0033] As shown in Figure 2, in some embodiments, the needle assembly 22 includes a needle hub 36 coupled to an introducer needle 30, a spring 58, and a removable flash chamber 34. These components can be at least partially disposed within a safety barrel 40 that prevents blood and needle exposure after the introducer needle 30 is drawn into the safety barrel 40. A cross section of the button 38 and its related components shows how the button 38, when depressed, disengages the needle hub 36, which is then moved proximally 62 under the force of the spring 58. The spring 58 is positioned between the safety barrel 40 and the needle hub 36, so that when the button 38 is depressed it releases its mechanical energy, uncompresses, and forces the needle hub 36 proximally 62. In some instances, the spring 58 is a compression spring that stored energy when compressed. In some configurations, the flash chamber 34 is disposed on the proximal end of the needle hub 36, and the flash chamber 34 extends at least partially out of a proximal opening 60 in the safety barrel 40 as it moves to the proximal end of the safety barrel 40. The tip of the introducer needle 30 can be drawn into the safety barrel 40 as the needle hub 36 is forced proximally 63. This movement draws the introducer needle 30 and its tip into a shielded position, within the covering and the

containment of the safety barrel 40, which can serve as a shield between the introducer needle 30 and the clinician to prevent needle stick injuries and blood contamination.

[0034] In some instances, in the shielded position as shown in Figure 3, the introducer needle 30 is safely contained within the safety barrel 40 while the flash chamber 34 extends at least partly out of a proximal opening 60 of the safety barrel 40. In some embodiments, the proximal opening 60 is shaped and sized to conform quite closely to the outer geometry of the flash chamber 34 so as to minimize any spacing therebetween that might otherwise provide room for blood flow of blood within the safety barrel 40. In the shielded position, a proximal portion of the flash chamber 34 can be accessed by a clinician and selectively uncoupled from the needle hub 36. Depending on the type of coupling between the flash chamber 34 and the needle hub 36 or introducer needle 30, the clinician will pull and/or twist, or otherwise manipulate the flash chamber 34 to uncouple it from the needle hub 36. In some configurations, the flash chamber 34 is directly coupled to the needle hub 36 and the introducer needle 30, as shown in Figure 2. In some configurations, the flash chamber 34 is indirectly coupled to the needle hub 36 and directly coupled to the introducer needle 30, which is directly coupled to the needle hub 36. In other configurations, the flash chamber 34 is indirectly coupled to the needle 30 and directly coupled to the needle hub 36, which is directly coupled to the introducer needle 30, as shown in Figure 6.

[0035] Referring again to Figure 2, in some embodiments, the flash chamber 34 is removably or selectively coupled to the needle hub 36. This removable coupling can have various configurations, such as a press-fit coupling, a threaded screw-on coupling, a keyed connection, a breakable connection, and other various types of removable couplings. As shown, the flash chamber 34 is press fit within an inner bore 62 of the needle hub 36. Also shown, the introducer needle 30 is press fit within the flash chamber 34. In some embodiments, only one of these press-fit couplings is used, rather than both. In a press-fit coupling, the inner geometry of the inner bore 62 approximates and may be approximately equal to or slightly smaller than the outer geometry of the chamber body 44 of the flash chamber 34. Additionally or alternatively, the inner surface of the inner bore 62 can include one or more inward protrusions 54 that press against the outer surface of the chamber body 44 to provide pressure between these components. In other embodiments, the outer surface of the chamber body of the flash chamber 34 includes one or more outward protrusions that press against the inner surface of the inner bore 62 to provide pressure between these components.

[0036] In some embodiments, flash chamber 34 includes a distal connector portion 48 of the chamber body 44 for selectively coupling to the needle hub 36. As shown in Figure 2, this distal connector portion 48 includes the distal portion of the chamber body 44, which has an outer geometry that is press fit into the needle hub 36 and over the proximal end of the introducer needle 30. In other embodiments, the distal connector portion 48 includes a threaded member used to screw the flash chamber 34 into the needle hub 36. In some embodiments, the distal connector portion 48 includes a keyed connection that mates with a keyed portion of the needle hub 36, as shown in Figure 8. In some embodiments, the distal connector portion 48 includes a breakable connection having, for example, a scored line and/or a stress riser.

[0037] In some embodiments, the flash chamber 34 includes a membrane 46 that is air permeable, through which air from within the introducer needle 30 passes. In some embodiments, the membrane 46 is hydrophobic so that it does not permit blood to pass through it. In such embodiments, blood 50 entering the introducer needle 30 forces air out the membrane 46 as it enters the introducer needle 30 and fills the introducer needle 30 and the flash chamber 34 to the membrane 46. At this point, blood 50 ceases to flow into the introducer needle 30.

[0038] In some embodiments, the membrane 46 is both air permeable and hydrophobic, to permit air, but not blood 50 to pass therethrough. In other embodiments, the membrane 46 is hydrophilic. The membrane 46 can include various materials and components that provide these properties. For example, in some embodiments, the membrane 46 includes glass, polyethylene terephthalate (PET), a microfiber material, and/or other synthetic material made of high-density polyethylene fibers, such as TYVEK® material from DuPont. Other such materials and components can also be used as a layer of the membrane 46 or as the entire membrane 46 to enable the membrane 46 to be hydrophobic, hydrophilic, and/or air permeable, according to some configurations.

[0039] In some embodiments, the flash chamber 34 is configured to retain blood 50 as it is withdrawn from the needle hub 36 to prevent blood spills and blood contamination. Thus, in some configurations, a distal opening 56 of the flash chamber 34 is shaped and sized to retain blood 50. Blood retention within the internal cavity 66 is governed, at least in part, by the inner perimeter of the distal opening 56, the surface tension of blood 50, and the force on the blood 50 to flow out of the distal opening 56. Accordingly, the inner perimeter of the distal opening 56 can be designed so that blood 50 is retained within the internal cavity 66 when the

force of the blood 50 to flow out of the distal opening 56 is within a certain range, but permit at least some blood to flow out when the pressure on the blood 50 exceeds this range.

[0040] For example, in some embodiments, when the distal opening 56 is circular, an inner perimeter of less than or equal to approximately 2.0 mm, and a diameter of less than or equal to approximately 0.6 mm, permits the retention of blood 50 within the internal cavity 66 against approximately the force of gravity. When the force on the blood 50 is greater than the force of gravity some blood 50 can flow out of the distal opening 56. Similarly, a circular distal opening 56 with a diameter of about 0.3 mm may retain blood 50 therein against forces stronger than gravity, such as bumping, jarring, and movement of the filled flash chamber 34. When the distal opening 56 has a very small inner perimeter, the force required to expel blood 50 will be very large.

[0041] In some embodiments, the distal opening 56 has a inner perimeter greater than or equal to about 0.3 mm, which when the distal opening 56 is a circular opening, corresponds to a diameter of about 0.1 mm. Thus, in some configurations, the distal opening 56 has an inner perimeter between about 0.3 mm to about 2.0 mm. In some configurations, the distal opening 56 is approximately circular and has a diameter between about 0.1 mm to about 0.6 mm. In other embodiments, the distal lumen opening 58 is non-circular.

[0042] Reference will now be made to Figure 3, which depicts the needle assembly 22 in the shielded position, with the spring 58 released to a decompressed state, which has forced the needle hub 36 to the proximal end of the safety barrel 40 and the flash chamber 34 at least partially out of the proximal opening 60 of the safety barrel 40. The internal cavity 66 of the flash chamber 34 is filled at least partially with blood 50. In this shielded position, the proximal portion of the chamber body 44 can be gripped and selectively decoupled from the needle hub 36. In this manner, the blood 50 sample within the flash chamber 34 can be used for diagnosis.

[0043] As shown in Figure 4, flash chamber 34 is decoupled from the needle assembly 22. This flash chamber 34 can now be used as a storage vial of blood 50 as it is transported to a testing facility. Additionally, the blood 50 sample within the flash chamber 34 can be immediately used for point-of-care blood diagnostic testing.

[0044] Reference will now be made to Figure 5, which depicts the flash chamber 34 dispensing blood 50 onto a blood test strip 70. The test strip 70 can be used to test for glucose, creatine, cystatin C test, or other such test at the point of care, the location of the patient. Such diagnosis can provide rapid diagnostic results at the point of care, without the need to withdraw a blood 50 sample via a syringe, vacuum tube, or other traditional device.

In some instances, the blood 50 can be dispensed into a diagnostic test device that performs diagnostic testing on the blood. In other instances, the blood 50 can be dispensed from the flash chamber 34 into a sterile vial or tube, such as a in-vitro test tube that is taken to a medical laboratory for testing.

[0045] The chamber body 44 of the flash chamber 34 can have various embodiments that can facilitate the dispensing blood 50 from the flash chamber 34. In some embodiments, at least a portion of the chamber body 44 is compressible to at least a small degree. When compressed, such as in an inward direction 72, the internal volume of the internal cavity 66 of the flash chamber 34 decreases, increasing the internal pressure of the internal cavity 66, and dispensing a sample of blood 50 from the distal opening 56. In some embodiments, the flash chamber 34 is rigid or semi-rigid. In some embodiments, only a portion of the flash chamber 34 is compressible. The compressible portion can be located and designed so that it does not compress during normal removal of the flash chamber 34 from the needle hub 36. In other embodiments, the chamber body 44 of the flash chamber 34 is a breakable ampoule, which when broken, dispenses blood 50 therefrom. In some embodiments, the distal opening 56 of the flash chamber 34 is shaped and sized so that a clinician can wick blood 50 therefrom using a test strip 70 or other device.

[0046] Reference will now be made to Figure 6, which depicts another embodiment of a connection between the needle hub 36 and the flash chamber 34. As shown, in some embodiments, the needle hub 36 includes a valve 80 that can prevent blood 50 from spilling out of the proximal opening 60 of the inner bore 62 of the needle hub 36 when the flash chamber 34 is removed therefrom. In some configurations, the valve 80 is flexible and selectively opens upon insertion of the flash chamber 34 therein. In some embodiments, the valve 80 is made of an elastomeric material, such as silicon rubber or the like. The valve 80 can selectively close and seal when the flash chamber 34 is removed therefrom. The valve 80 can provide a fluid tight connection between the flash chamber 34 and the valve 80 when the flash chamber 34 is inserted therein. As shown, in some embodiments, the flash chamber 34 can coupled directly into the valve 80 with a press fit connection. As further shown, in some embodiments, the flash chamber 34 is not coupled to, nor does it contact, the introducer needle 30.

[0047] As shown, in some embodiments, the valve 80 includes a connection portion 90 that is coupled to the inner surface of the needle hub 36 and a barrier portion 82. The barrier portion 82 spans a cross section of inner bore 62 to seal the inner bore 62 upon removal of the flash chamber 34. The barrier portion 82 can include a hole or slit that selectively open and

closes. The slit can be a straight slit, a Y-shaped slit, or a cross-shaped slit. The barrier portion 82 can also include an inward facing duckbill shape that at least partially can prevent the slit from opening in response to proximally oriented internal pressure on the valve 80. The valve 80 can retain the flash chamber 34 within the needle hub 36 until a threshold force is applied proximally 63 on the flash chamber. In some embodiments, the flash chamber 34 is retained in the needle hub 36 with a breakable connection 92, which breaks when a threshold force is applied proximally 63 on the flash chamber 34. The breakable connection 92 can be made of a breakable material. The breakable connection 92 can also have a scored line 94 and/or a stress riser that facilitates breaking at that point.

[0048] Referring still to Figure 6, in some embodiments, the needle hub 36 includes a latch member 86 that extends distally from the needle hub 36. The latch member 86 permits the needle hub 36 to be is drawn proximally 62 and distally within the safety barrel 40 until the latch member 86 is drawn proximally passed an inward ridge 84. The inward ridge 84 can have a steep proximal face 92 that restricts the latch member's 86 distal movement. As such, the latch member 86 and the inward ridge 84 can prevent the needle hub 34 from advancing the introducer needle 30 out the safety barrel 40. The shape and configuration of the latch member 86 and the inward ridge can be adjusted, anticipated, and/or changed. Furthermore, other such means for limiting the needle hub's 36 distal movement can be incorporated into the needle assembly 22.

[0049] Figure 9 depicts another embodiment of a flash chamber 34 that can be used with the valve 80 and needle hub 36 of Figure 6. This flash chamber 34 includes a distal connector portion 48 that includes a narrow nose extension 130. The narrow nose extension 130 can pierce through the valve 80 and allows for effective resealing of the valve 80 after the removal of the flash chamber 34.

[0050] Reference will now be made to Figure 7, which depicts yet another embodiment of a connection between the needle hub 36 and the flash chamber 34. As shown, flash chamber 34 is removably coupled to the needle hub 36. The distal connector portion 48 of the flash chamber 34 includes an annular flange 102 that extends outwardly from the flash chamber 34. This distal connector portion 48 is positioned within proximal portion of the inner bore 62 of the needle hub 36. A valve 80 is located within this proximal portion of the inner bore 62. The valve 80 includes an inner cavity 108 that receives the distal connector portion 48 therein. The annular flange 102 of the distal connector portion 48 is interlocked within an inner groove 100 of the valve 80. The valve 80 is disposed within a distal region 110 of the inner cavity 108. The valve 80 and/or the flash chamber 34 can longitudinally within this

distal region 110. This distal region is terminated at its distal end with an inward flange 104 of the needle hub 36. This inward flange 104 prevents the annular flange 102 of the flash chamber 34 from being withdrawn from the needle hub 36 until a threshold force is applied to the flash chamber 34. When a threshold force pulls the flash chamber 34, the proximal movement of the annular flange 102 forces the valve 80 and the inward flange 104 to flex outwardly into the space 106 between the needle hub 36 and the safety barrel 40. The characteristics, shapes, dimensions, and properties of the needle hub 36 and the valve 80 can be designed to require a certain threshold force that will allow a user to easily remove the flash chamber 34, while preventing the flash chamber 34 from falling out when it is slightly jarred, bumped, or touched.

[0051] In other embodiments, the flash chamber 34 is screwed onto the needle hub 36. As shown, the annular flange 102 can be angled to form one or more male threaded connectors and the inner groove 100 of the valve 80 and/or the inward flange 104 of the needle hub 36 can form a female threaded connector. Thus configured, the flash chamber 34 can be screwed into the needle hub 36. To remove the flash chamber 34 it can be unscrewed from the needle hub 36.

[0052] As shown in Figure 8, in some embodiments, the flash chamber 34 is connected to the needle hub 36 via a keyed connection. The distal connector portion 48 can include a one or more keyed connector components 120 that mates with keyed connector components 122 in the proximal opening 60 of the safety barrel 40 and/or the needle hub 36. For example, in some instances, the keyed distal connector portion 48 is inserted into the keyed safety barrel 40 and/or the needle hub 36 in a distal direction 124. When fully inserted, the flash chamber 34 can be rotated, for example in a clockwise direction 126, to lock it in place. To remove the flash chamber 34, the clinician rotates the flash chamber 34 in a counter-clockwise direction and withdraws the flash chamber 34 in the proximal direction 63. In addition to the connections between the flash chamber 34 and the needle hub 36 described herein, other such connecting means for connecting the flash chamber 34 to the needle hub 36 can be incorporated into the catheter assembly 20.

[0053] From the foregoing, it will be seen that the present devices and methods efficiently collect a blood sample from a flash chamber that is removably coupled to the proximal end of an introducer needle. Since blood is already collected in this chamber, the use of this blood can avoid the need for a separate blood sampling procedure. Once removed, blood can be dispensed from the flash chamber into a point-of care diagnostic device, for rapid, prompt test results, which can enable time-sensitive health information, such as the risk of diabetes or

impaired kidney function to be more quickly and easily acquired. Furthermore, the flash chamber can be sized for accommodate the needed blood sample. As such, the flash chamber can be enlarged, which increases the flashback visualization period.

[0054] The present invention may be embodied in other specific forms without departing from its structures, methods, or other essential characteristics as broadly described herein and claimed hereinafter. The described embodiments are to be considered in all respects only as illustrative, and not restrictive. The scope of the invention is, therefore, indicated by the appended claims, rather than by the foregoing description. All changes that come within the meaning and range of equivalency of the claims are to be embraced within their scope.

CLAIMS

1. A needle hub comprising:

an introducer needle having a lumen extending therethrough;

a needle hub coupled to a proximal end of the introducer needle; and

a flash chamber removably coupled to the needle hub, an interior of the flash chamber being in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub.

2. The catheter assembly of claim 1, wherein at least a portion of the flash chamber is compressible.

3. The catheter assembly of claim 1, wherein the flash chamber comprises:

a chamber body defining an internal cavity; and

an air permeable membrane coupled to the chamber body and in fluid communication with the internal cavity.

4. The catheter assembly of claim 3, wherein the internal cavity of the chamber body of the flash chamber has in an internal volume between about 0.1 mL to about 10 mL.

5. The catheter assembly of claim 1, wherein the flash chamber is press fit into the needle hub or introducer needle.

6. The catheter assembly of claim 1, wherein the flash chamber is screwed onto the needle hub.

7. The catheter assembly of claim 1, wherein the flash chamber is selectively coupled to the needle hub or the introducer needle via a keyed connection.

8. The catheter assembly of claim 1, wherein the flash chamber is selectively coupled to the needle hub or the introducer needle via a breakable connection.

9. The catheter assembly of claim 1, wherein the flash chamber is a breakable ampoule.

10. A catheter assembly comprising:

an introducer needle having a lumen extending therethrough;

a needle hub coupled to a proximal end of the introducer needle;

a flash chamber selectively coupled to the needle hub or the introducer needle, an interior of the flash chamber being in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub, the flash chamber having an air permeable membrane and a distal connector portion;

the chamber body defining an internal cavity, the chamber body having at least a compressible portion that decreases the internal volume of the internal cavity when compressed;

the air permeable membrane coupled to the chamber body and in fluid communication with the internal cavity; and

the distal connector portion of the chamber body for selectively coupling to the needle hub.

11. The catheter assembly of claim 10, wherein at least a portion of the flash chamber is compressible.

12. The catheter assembly of claim 10, wherein the flash chamber has in an internal volume between about 0.1 mL to 10 mL.

13. The catheter assembly of claim 10, wherein the flash chamber is press fit into the needle hub or introducer needle.

14. The catheter assembly of claim 10, wherein the flash chamber is screwed onto the needle hub.

15. The catheter assembly of claim 10, wherein the flash chamber is selectively coupled to the needle hub or the introducer needle via a breakable connection, the breakable connection including at least one scored line and a stress riser.

16. The catheter assembly of claim 10, wherein the flash chamber is a breakable ampoule.

17. A method for providing a removable flash chamber of a catheter assembly, the method comprising:

providing a catheter assembly having a needle hub, the needle hub having an introducer needle coupled thereto;

providing an introducer needle coupled to the needle hub, the introducer needle having a lumen extending therethrough;

providing a flash chamber removably coupled to the needle hub, an interior of the flash chamber being in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub.

18. The method of claim 17, further comprising providing at least a single compressible portion of the flash chamber for selectively ejecting blood within the flash chamber from therefrom.

19. The method of claim 18, providing an inner cavity within a body of the flash chamber having an internal volume about 0.1 mL to 10 mL.

20. The method of claim 19, wherein the flash chamber has a distal connector portion, the distal connector portion having at least one of a press fit connector, screw threads, a keyed connection, and a breakable connection.

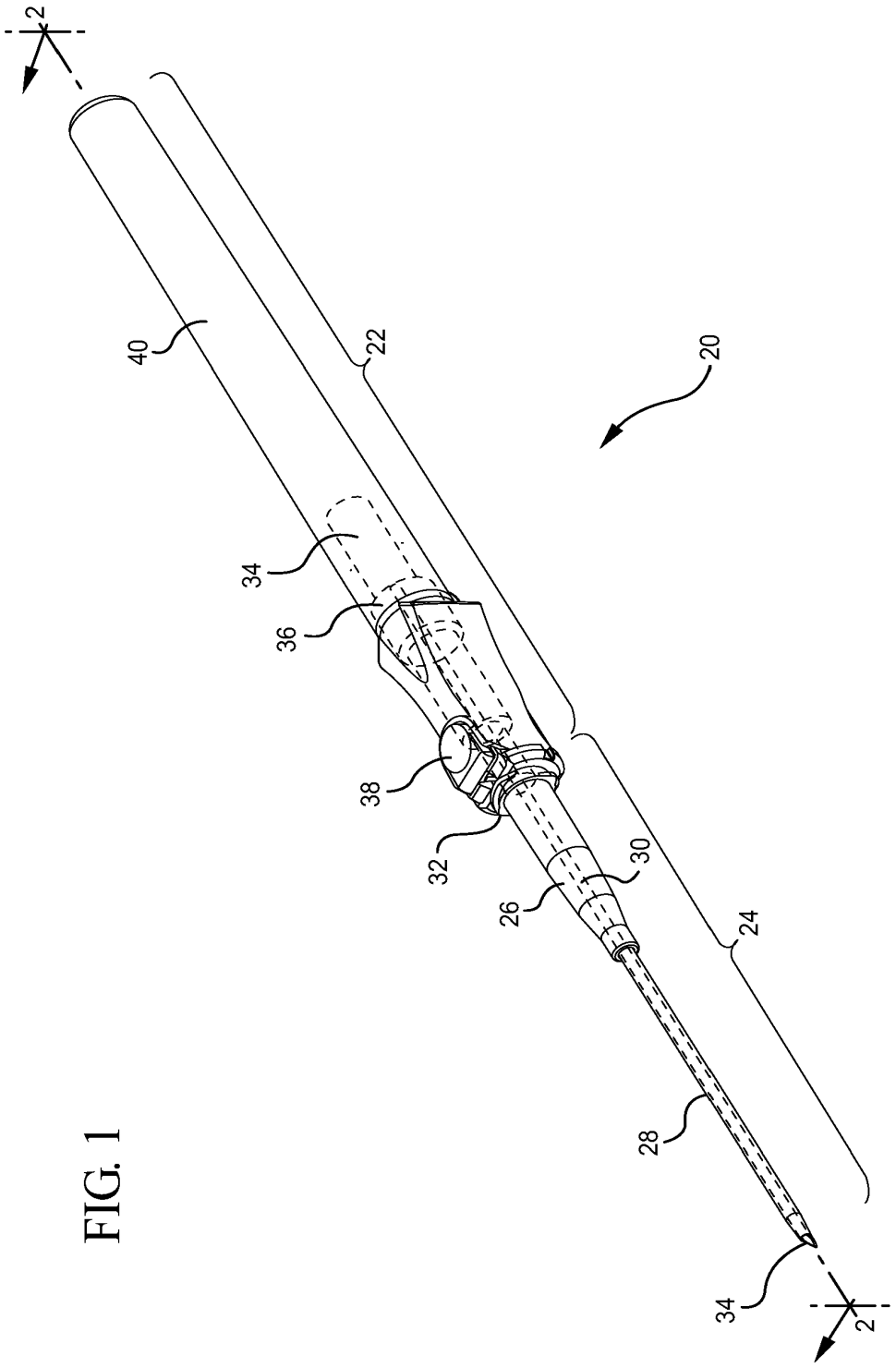


FIG. 1

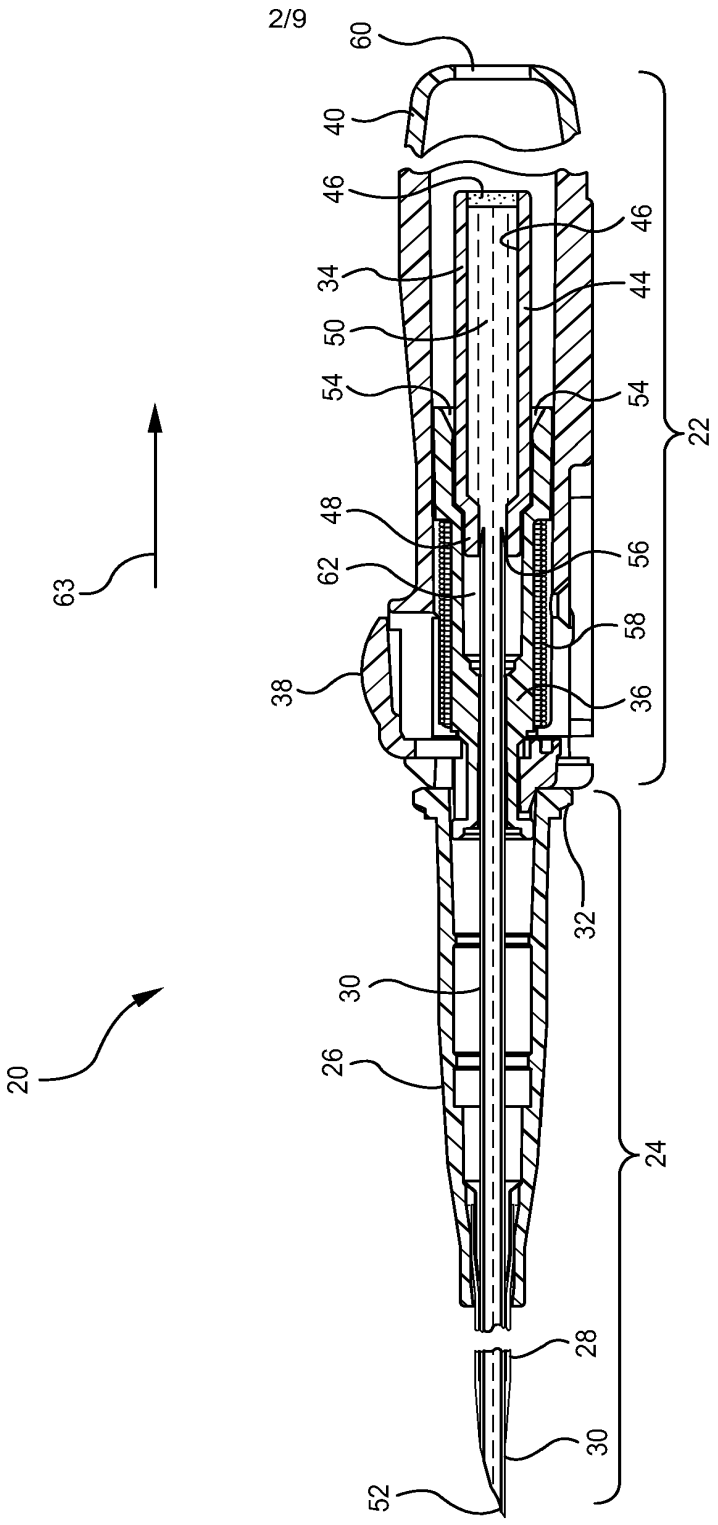

60
40
46
46
34
44
50
54
54
22
48
56
62
58
38
36
32
30
26
24
28
30
52
63
20

FIG. 2

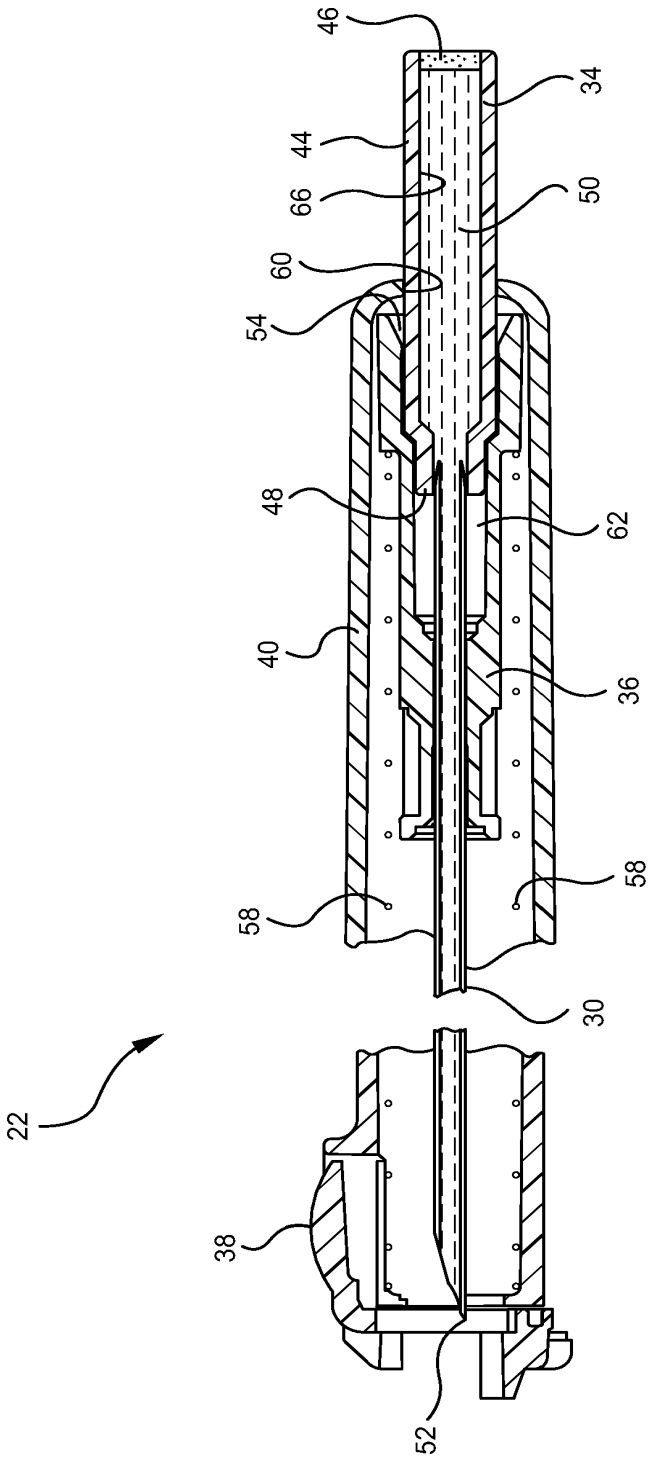


FIG. 3

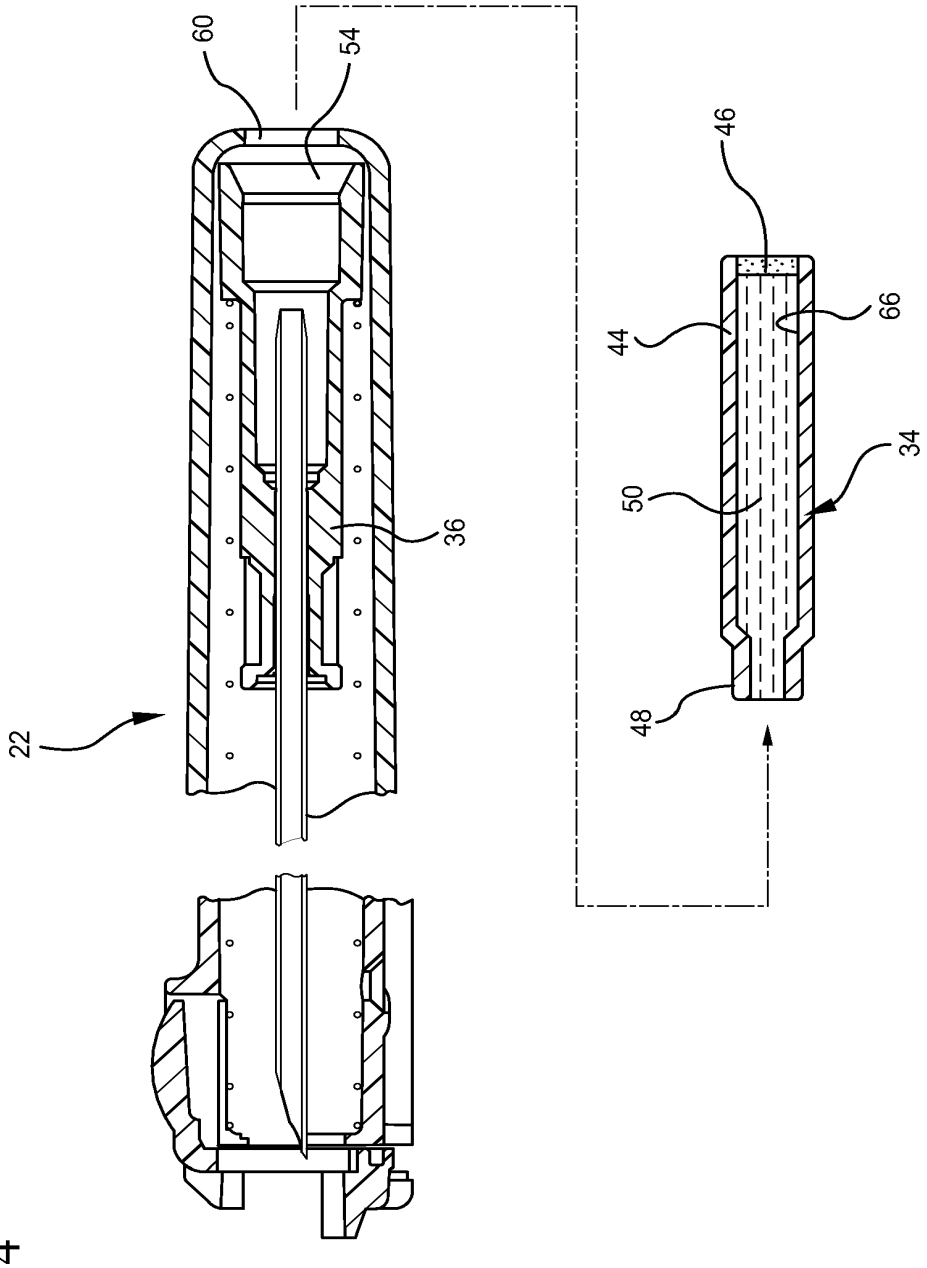


FIG. 4

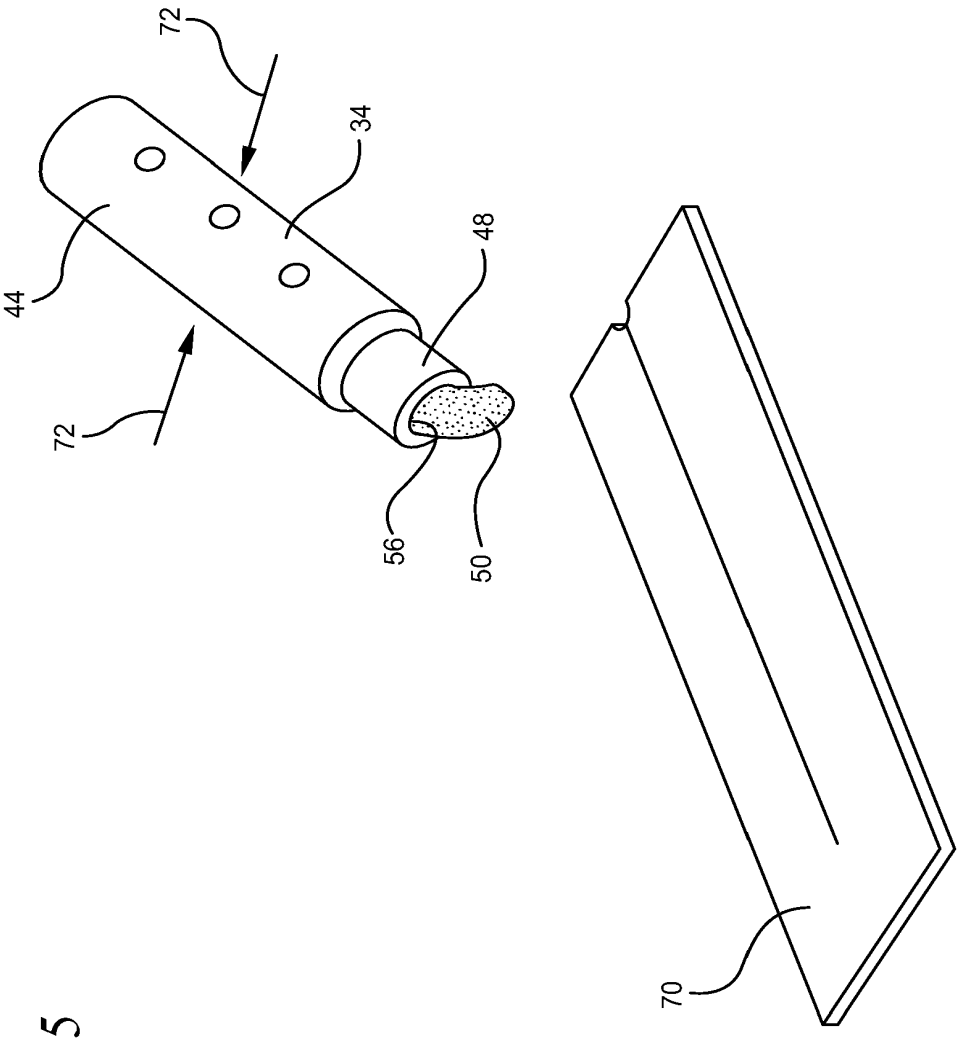


FIG. 5

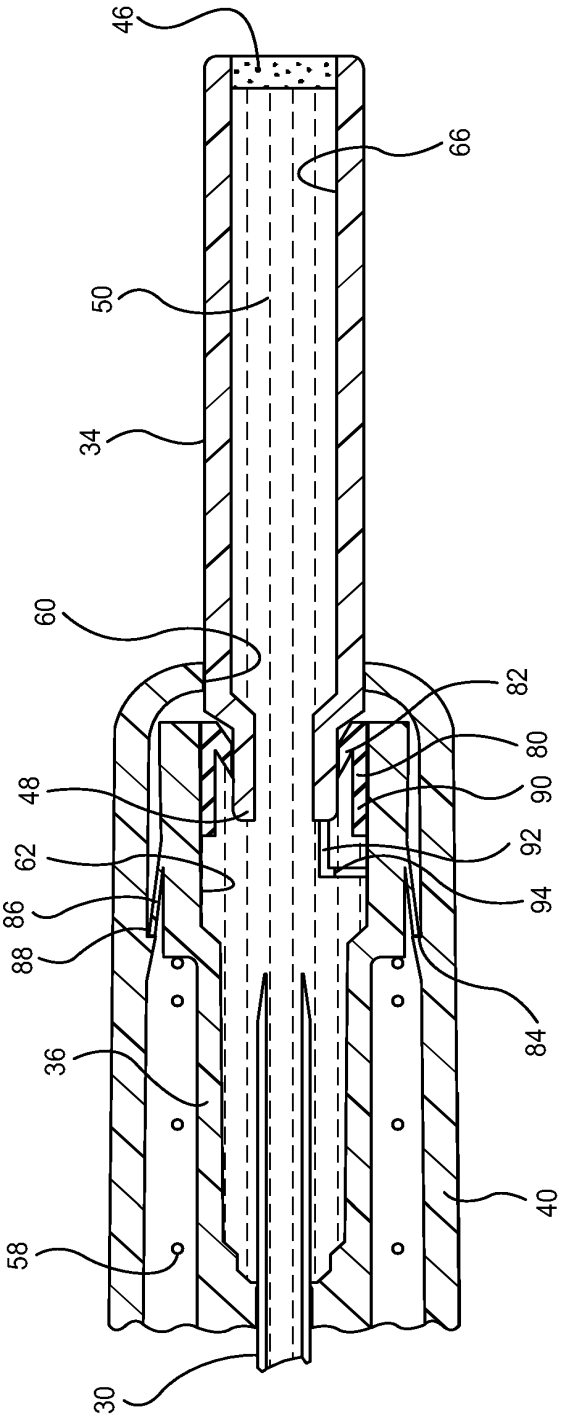


FIG. 6

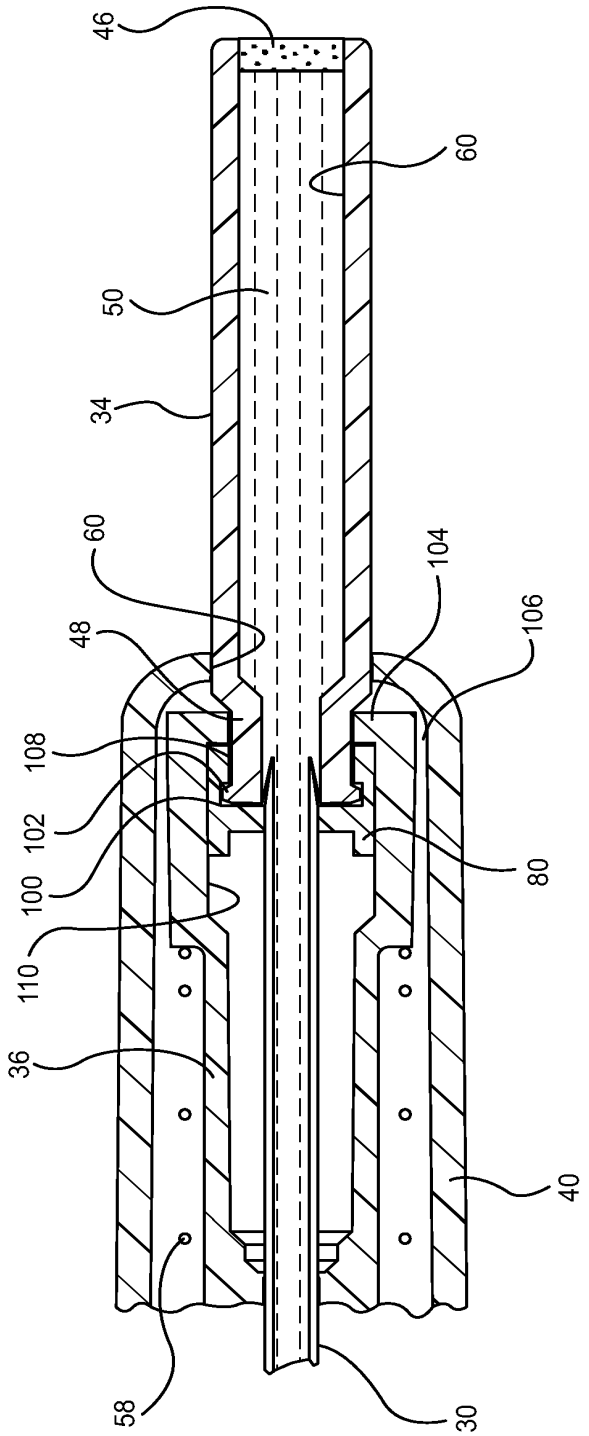


FIG. 7

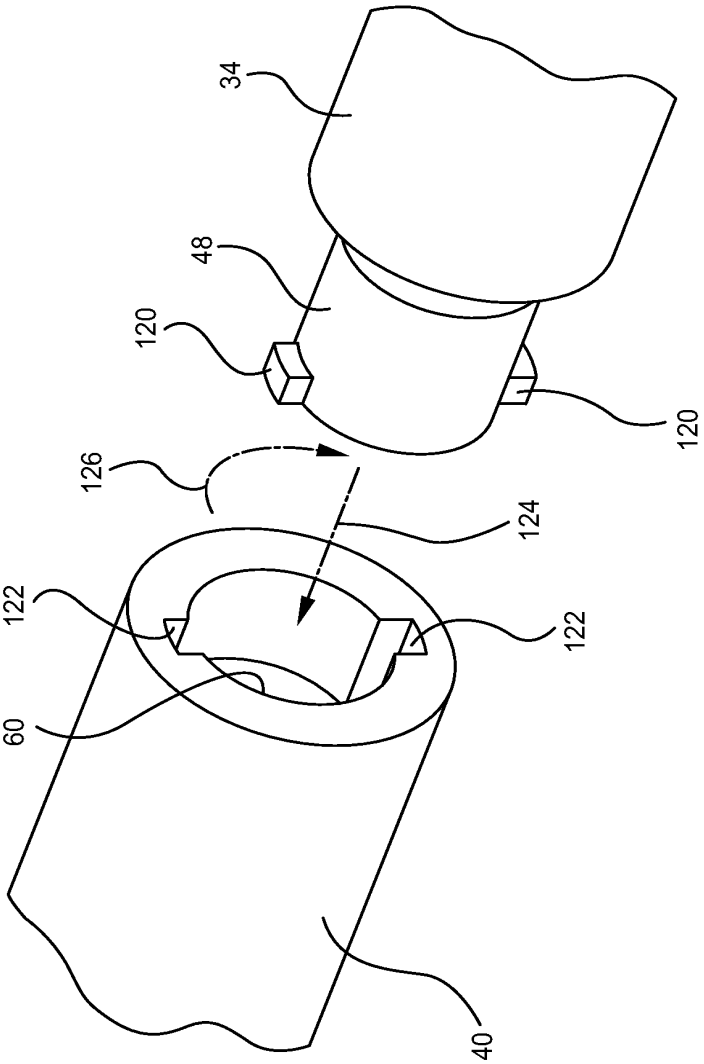


FIG. 8

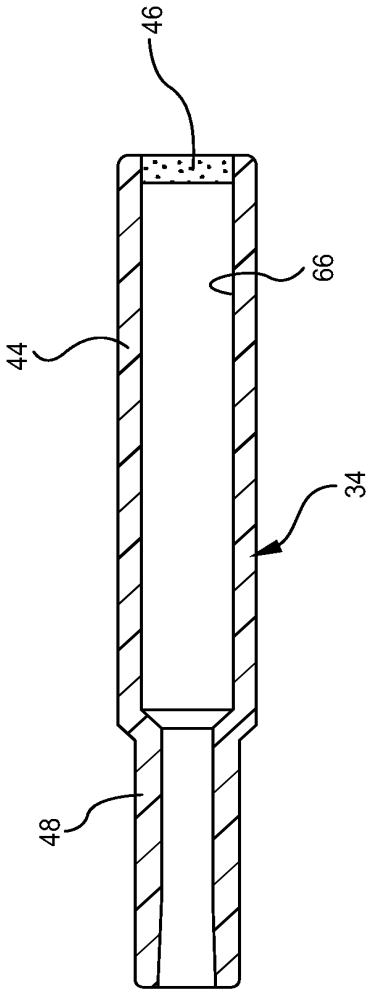


FIG. 9

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2011/043892

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M25/06 A61B5/153
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)
A61M A61B

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, 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	EP 1 884 257 A1 (SHUE MING-JENG [TW]; HUANG DEBORAH [TW]; SHUE PHILLIP [TW]) 6 February 2008 (2008-02-06)	1,2,4-9, 17-20
Y	figures 3, 4, 30-35, 41-46 paragraph [0019] paragraph [0039] - paragraph [0041]	3,10-16
X	WO 01/12254 A1 (BECTON DICKINSON CO [US]) 22 February 2001 (2001-02-22)	1,3-9,17
Y	figures 1-6	3,10-16
A	page 4, line 4 - line 7 page 4, line 10 - page 6, line 16 page 6, line 19 - line 29	2,18-20
A	EP 0 812 601 A2 (BECTON DICKINSON CO [US]) 17 December 1997 (1997-12-17) column 3, line 35 - column 5, line 55; figures 1-6	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 document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 August 2011	31/08/2011

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	Przykutta, Andreas

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2011/043892

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

A needle hub (36) and catheter assembly are (20) disclosed herein. The needle hub includes an introducer needle (30) having a lumen extending therethrough. A needle hub is coupled to a proximal end of the introducer needle. A flash chamber (34) is removably coupled to the needle hub or the introducer needle. An interior of the flash chamber is in fluid communication with the lumen of the introducer needle when the flash chamber is coupled to the needle hub or the introducer needle. As such, the flash chamber can collect a sample of blood that can be accessed when the flash chamber is removed. In some instances, the blood can also be dispensed from the flash chamber into a test strip (70) or other testing device.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2011/043892

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 2007/191777 A1 (KING ALAN D [US]) 16 August 2007 (2007-08-16) paragraph [0015] - paragraph [0026]; figures 1-5 -----	1-20

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2011/043892

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 1884257 A1	06-02-2008	NONE	
WO 0112254 A1	22-02-2001	AU 6537300 A	13-03-2001
		US 6273874 B1	14-08-2001
EP 0812601 A2	17-12-1997	CA 2206215 A1	10-12-1997
		JP 3023953 B2	21-03-2000
		JP 10052498 A	24-02-1998
		US 5824001 A	20-10-1998
US 2007191777 A1	16-08-2007	AT 434463 T	15-07-2009
		AU 2006338197 A1	23-08-2007
		CA 2642680 A1	23-08-2007
		EP 1984057 A1	29-10-2008
		ES 2327679 T3	02-11-2009
		JP 2009526602 A	23-07-2009
		WO 2007094841 A1	23-08-2007

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

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
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

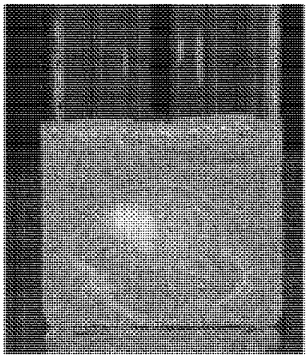
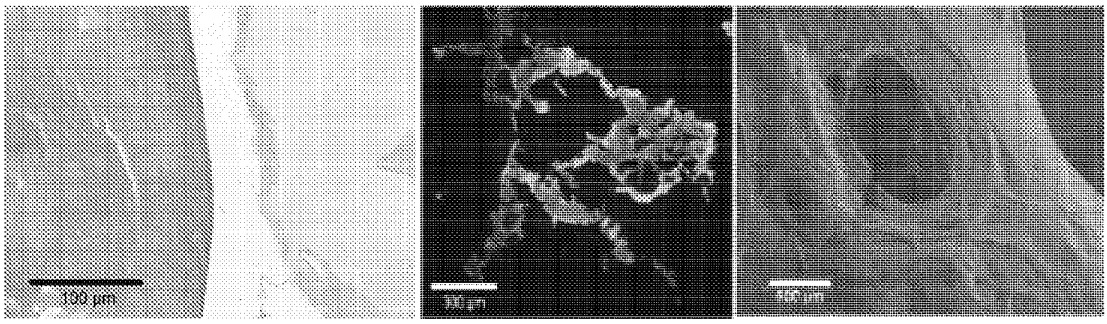


FIG. 2



a b c

FIG. 3

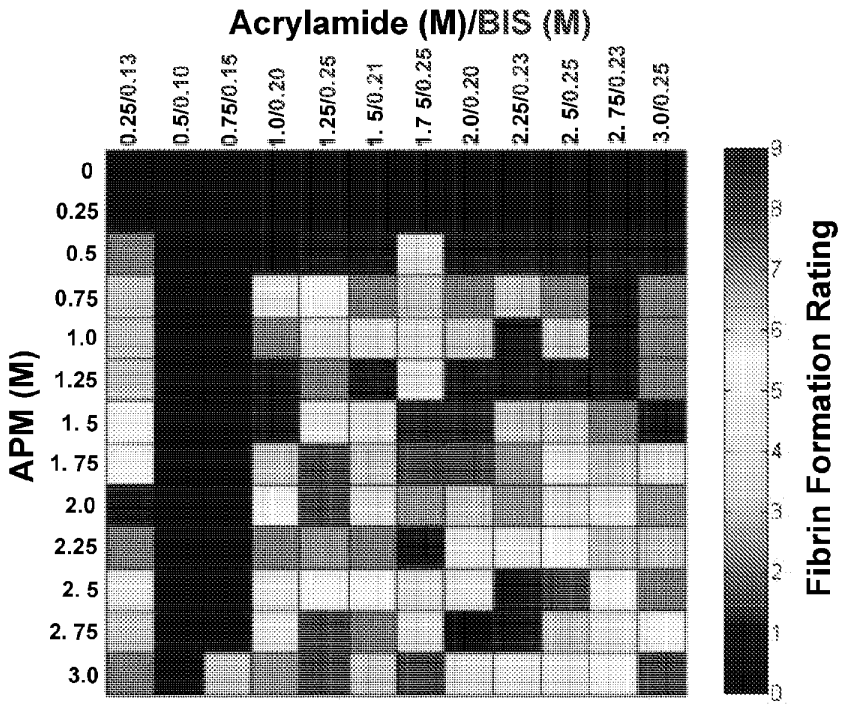

Acrylamide (M)/BIS (M)
0.25/0.13
0.5/0.10
0.75/0.15
1.0/0.20
1.25/0.25
1. 5/0.21
1.7 5/0.25
2.0/0.20
2.25/0.23
2. 5/0.25
2. 75/0.23
3.0/0.25
APM (M)
0
0.25
0.5
0.75
1.0
1.25
1. 5
1. 75
2.0
2.25
2. 5
2. 75
3.0
Fibrin Formation Rating

FIG. 4

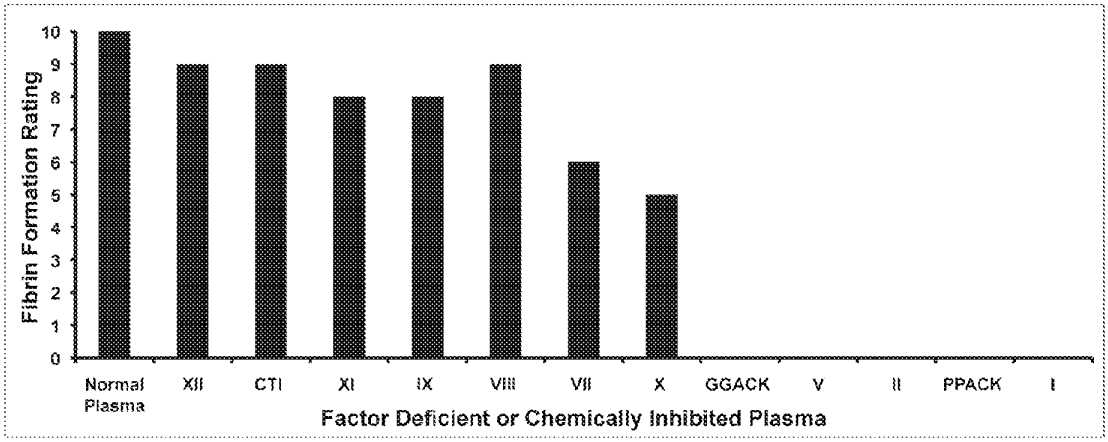

Fibrin Formation Rating
10
9
8
7
6
5
4
3
2
1
0
Normal Plasma
XII
CTI
XI
IX
VIII
VII
X
GGACK
V
II
PPACK
I
Factor Deficient or Chemically Inhibited Plasma

FIG. 5

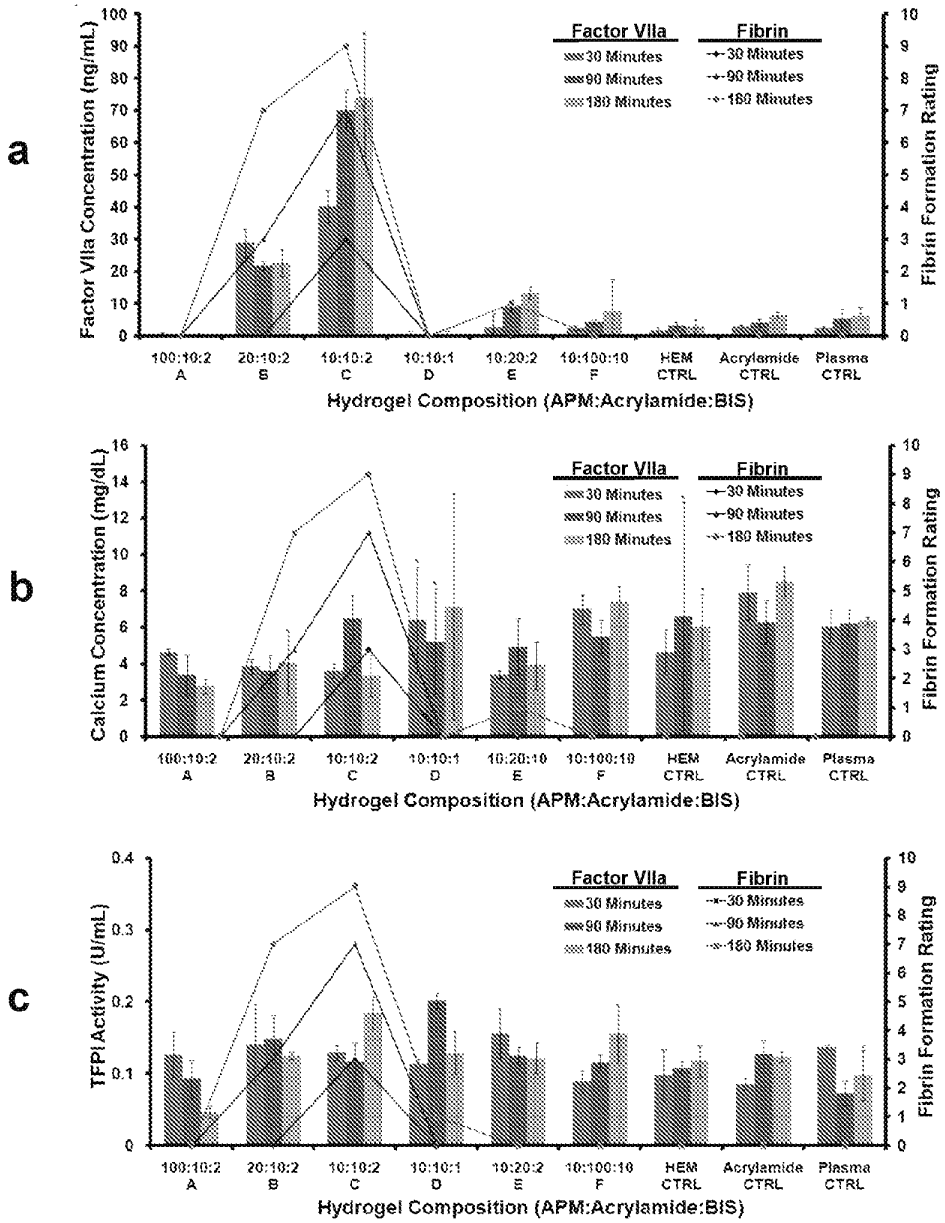

a
Factor VIIa Concentration (ng/mL)
Fibrin Formation Rating
Factor VIIa
30 Minutes
90 Minutes
180 Minutes
Fibrin
30 Minutes
90 Minutes
180 Minutes
100:10:2 A
20:10:2 B
10:10:2 C
10:10:1 D
10:20:2 E
10:100:10 F
HEM CTRL
Acrylamide CTRL
Plasma CTRL
Hydrogel Composition (APM:Acrylamide:BIS)
b
Calcium Concentration (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

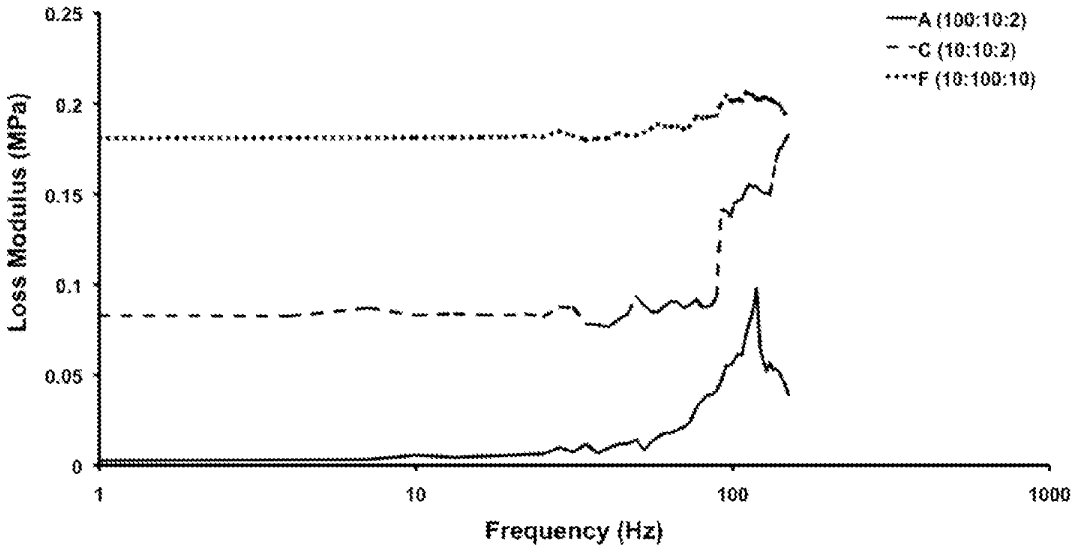

A (100:10:2)
C (10:10:2)
F (10:100:10)
Loss Modulus (MPa)
0.25
0.2
0.15
0.1
0.05
0
1
10
100
1000
Frequency (Hz)

FIG. 7

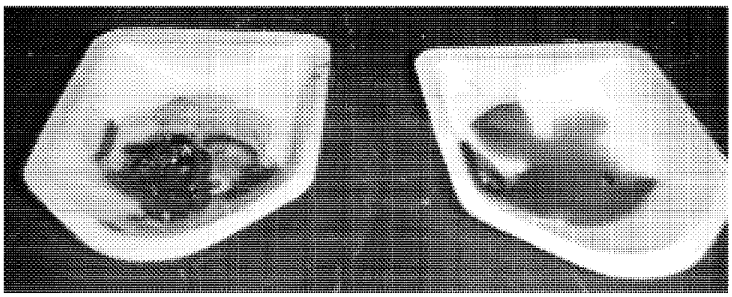
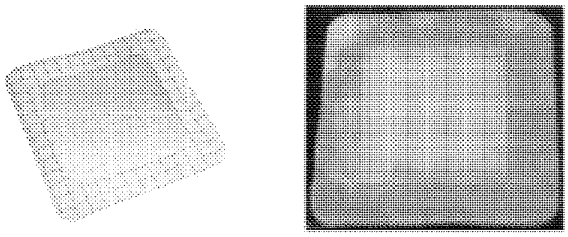
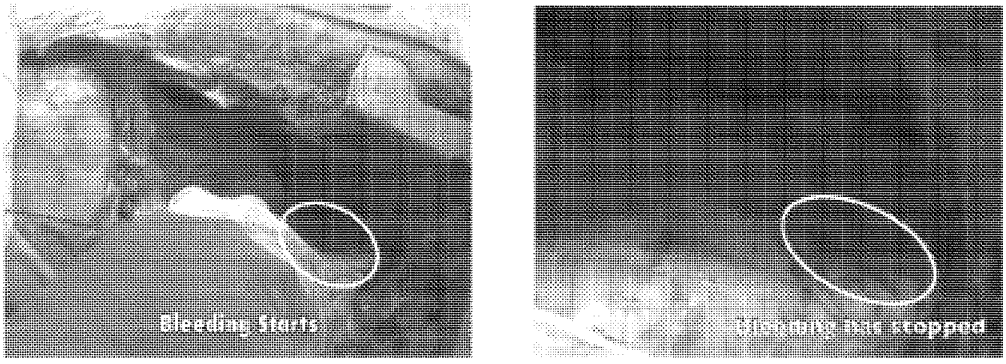

A
B

FIG. 8



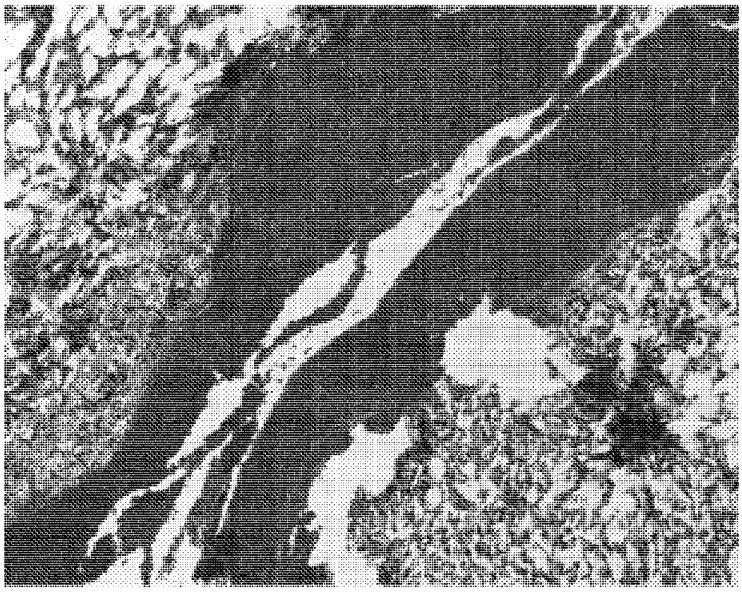
A B

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ィ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ィ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ィ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ィを設け、上記キャビティ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ィ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ィ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ィ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ピテイー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，キヤピテイー46を通つて流れ、プラグ５２をバイパスする。血液はキヤピテイーから横孔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に記したキヤピ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

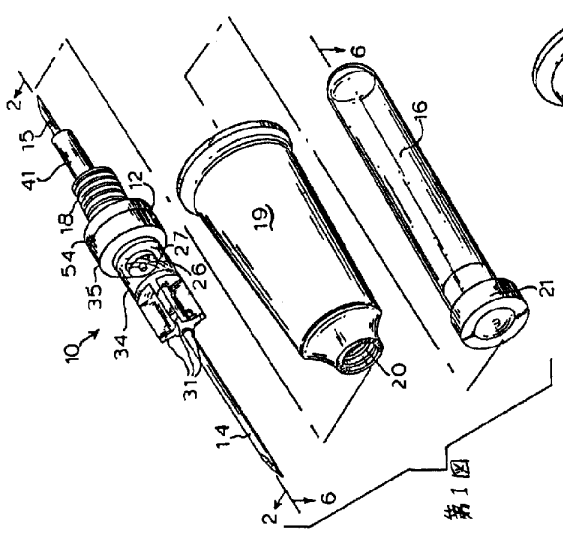
可能ストッパ７２内に穿刺し、横孔７４は血液収集容器内にある。スリーブ弁８０は滑動して針組立体の後端部７５に向けて圧縮される。横孔７４が露出したため、内腔７９内の血液は横孔７４を通つて直接血液収集容器内に流出する。第９図に示す通り、血液はプラグ７８を通らずに分流して横孔７４に流れ、穿刺針の開放端からは流れない。血液収集容器が充満すれば容器はホルダーから取外し、スリーブ弁８０は滑動して第８図に示す位置に戻る。これによつて血液収集容器の交換間に血液が穿刺針から流出するのを防ぐ。

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。

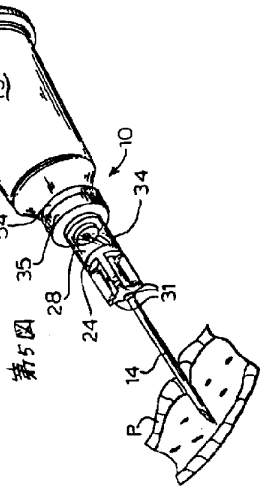
4.〔図面の簡単な説明〕

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。

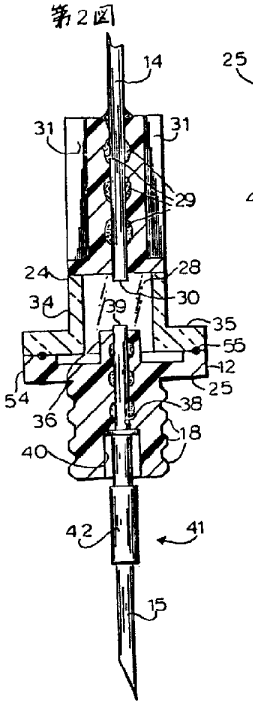
１０…多サンプル針組立体
１２…ハウジング
１４，１５…穿刺針
１６…真空血液収集容器
１９…容器ホルダー
２４…前端部
２５…後端部
２８…室
４１…スリーブ弁
４２…厚壁部
４４…薄壁部
４６…キャビティー
４８，５０…横孔
５２…多孔性プラグ



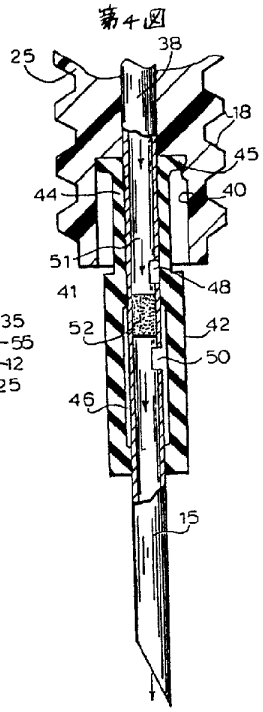
第1図



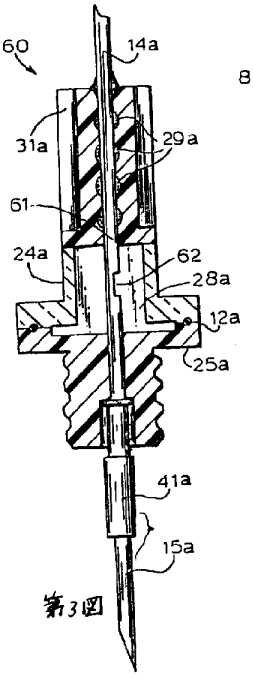
第5図



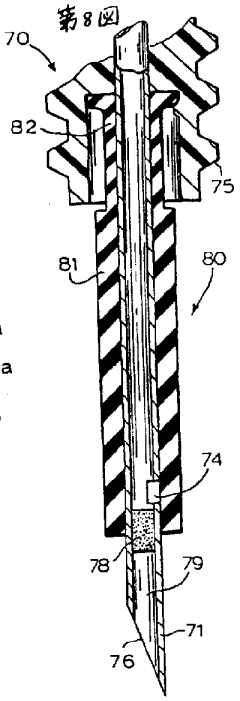
第2図



第4図

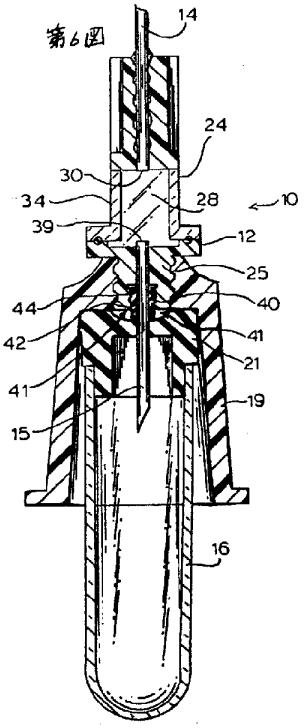


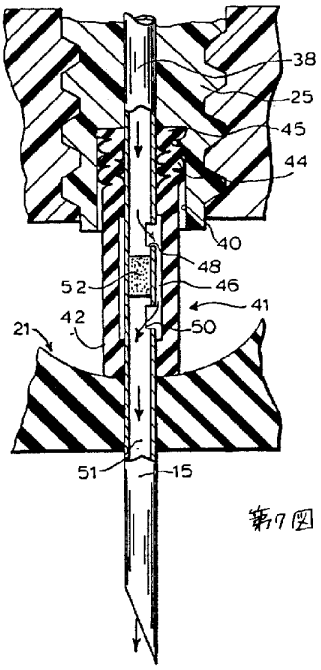
第3図



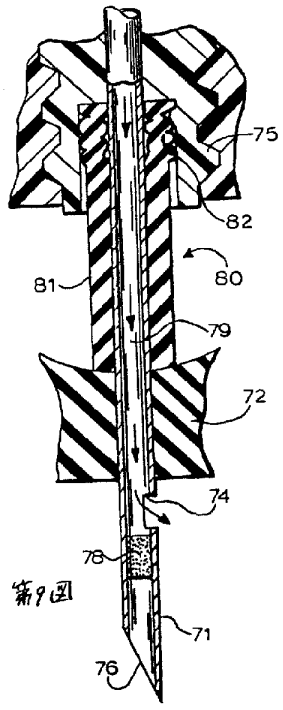
第8図

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

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

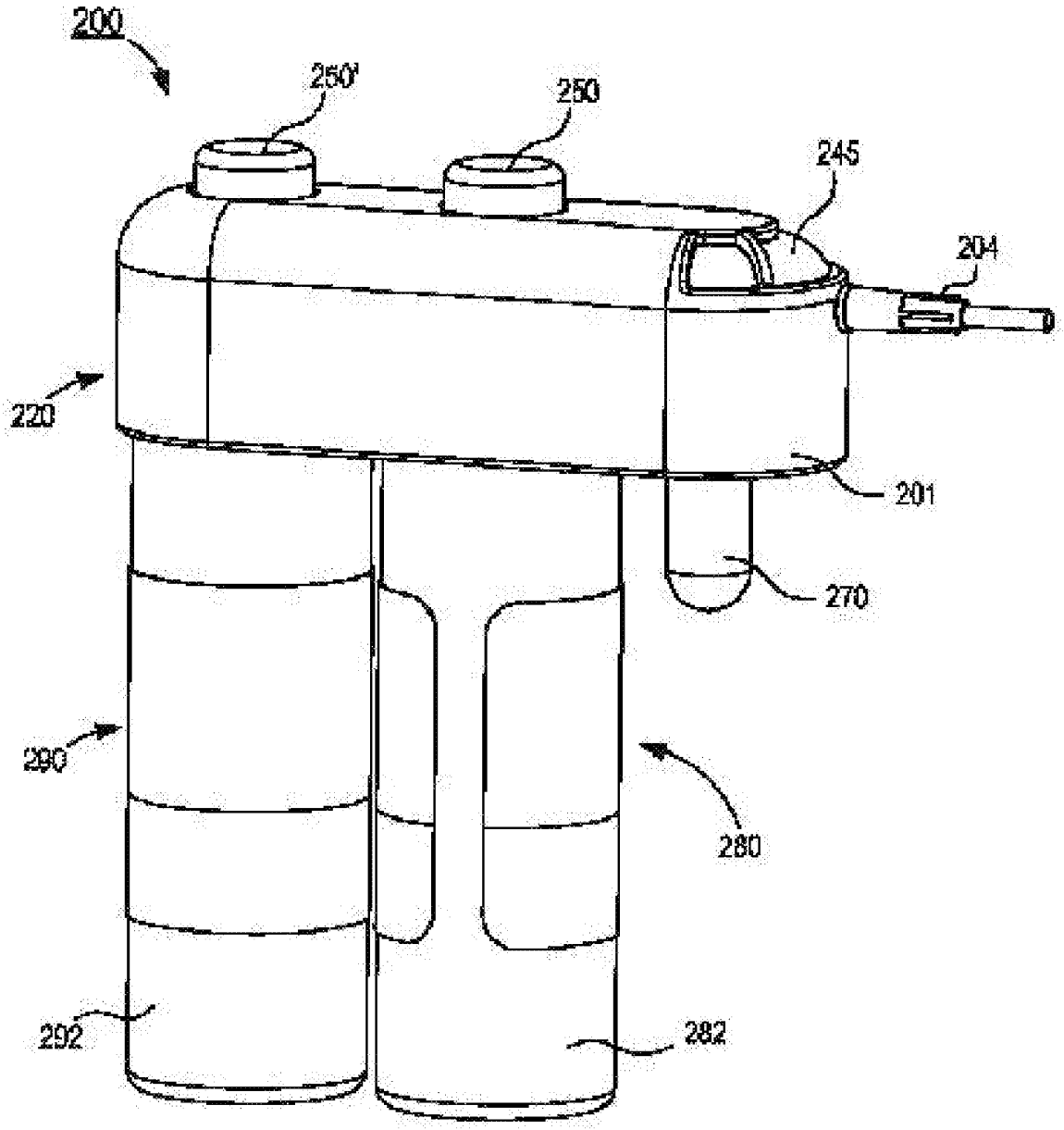


FIG. 2

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 collection device of FIG. 26;

31 is a cross-sectional view taken along line X 16 -X 16 of FIG. 27 of the valve included in the bodily fluid collection device of FIG. 26;

32 is a cross-sectional view taken along line X 12 -X 12 of the bodily fluid collection device of FIG. 26 in the first configuration; FIG.

33 is a cross-sectional view taken along line X 12 -X 12 of the bodily fluid collection device of FIG. 26 in a second configuration; FIG.

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

35 is an exploded perspective view of a flow diverting mechanism included in the bodily fluid collection device of FIG. 34; FIG.

36 is a cross-sectional view taken along line X 17 -X 17 of a distribution member included in the flow diverting mechanism of FIG. 35; FIG.

37 is a top view of a portion of the bodily fluid collection device of FIG. 34 in a first configuration; FIG.

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

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

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

of Figure 39 of the body fluid collection device of Figure 33 in a second configuration ; 41 is a perspective view of a bodily fluid collection device in a first configuration according to embodiments; FIG. 42 is an exploded perspective view of a portion of the bodily fluid collection device of FIG. 41; FIG. 43 is a cross-sectional view taken along line X 20 -X 20 of the bodily fluid collection device of FIG. 41 in the first configuration; FIG. Figure 44 is a cross-sectional view taken along line X20 - X20 of the bodily fluid collection device of Figure 41 in a second configuration ; Figure 45 is a cross-sectional view taken along line X20 - X20 of the body fluid collection device of Figure 41 in a third configuration ; Figure 46 is a perspective view of a bodily fluid collection device in a first configuration according to an embodiment; 47 is an exploded perspective view of a portion of the bodily fluid collection device of FIG. 45; FIG. 48 shows the distribution member included in the bodily fluid collection device of FIG. 46, line X of FIG. 47. FIG.

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

49 is a side sectional view taken along line X 22 -X 22 of FIG. 47 of a movable member included in the 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 flow of the second volume of bodily fluid is transported through the flow diverter mechanism 120 to the first sample fluid reservoir 180 and/or to the second sample fluid reservoir 190. can be configured such that a first volume of bodily fluid needs to be transported to the pre-sample fluid reservoir 170 before allowing for . In this manner, the flow diverting mechanism 120 can be used by a healthcare professional to collect a first predetermined amount of bodily fluid (e.g., a pre-sample) before collecting a second amount and/or a third amount of bodily fluid (e.g., a sample). can be characterized as requiring compliance with respect to Similarly, the flow diverter mechanism 120 can be used by a medical practitioner to transfer a second volume of bodily fluid, i.e., a sample, into a first sample fluid reservoir without first diverting the first volume of bodily fluid, i.e., a pre-sample, into a pre-sample reservoir 170. It can be configured to prevent collection within 180 . In this manner, a healthcare professional may (intentionally or not) add a first volume of bodily fluid that is more likely to contain surface microbes and/or other undesirable external contaminants into the bodily fluid sample used for analysis. (either unintentionally or unintentionally). In other embodiments, the fluid collection device 100 need not include mandatory compliance features or components.

[1091

] In some embodiments, the flow diverter mechanism 120 can have a fourth configuration (not shown in FIG. 1) that is different from the first, second, and third configurations. When in the fourth configuration, the flow diverter mechanism 120 can simultaneously fluidly isolate the inlet port 121 from the first outlet port 125, the second outlet port 126 and, optionally, the third outlet port. Therefore, the shunting

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

[0039]

[1092] In some embodiments, one or more portions of the collection device 100 are disposed

within a housing (not shown in FIG. 1). For example, in some embodiments, at least a portion of one or more of flow diverting mechanism 120, first pre-sample reservoir 170 and sample reservoirs 180 and 190 can be disposed within the housing. In such embodiments, at least a portion of the flow diverter mechanism 120 is configured so that the user can activate the flow controller 140 to control the flow of bodily fluid from the patient (e.g., vein) to the collection device 100. Accessible through the housing. Examples of suitable housings are described in more detail herein with reference to specific embodiments.

[0040]

[1093] In some embodiments, the collection device 100 can optionally include one or more flow metering devices that can meter the flow of bodily fluid through the collection device. For example, a flow metering device can be in fluid communication with the first fluid flow path 142 and/or the second fluid flow path 144 to meter the flow of bodily fluid therethrough. In other embodiments, a flow metering device can be in fluid communication with and/or otherwise disposed in first port 125 and/or second port 126 . The flow metering device can be configured to provide the user with an indication related to the predetermined volume being transferred to the pre-sample reservoir 170, the first sample reservoir 180 and/or the second sample reservoir 190, such as an indicator (For example, electrical signal output devices such as dials, displays, colors, tactile output devices, wireless radio signals, Bluetooth radio signals, etc.). In some embodiments, a flow metering device can be operably coupled to an actuator, such as, for example, those described above. In such embodiments, the flow metering device operates an actuator to move flow controller 140 between its first configuration and its second configuration based on the desired volume of bodily fluid that has flowed through the flow metering device. may be operable as such. Thus, using the flow metering device, a desired volume of bodily fluid is transferred to the pre-sample reservoir 170, the first sample reservoir 180 and/or the second sample reservoir 190, thereby providing an insufficient volume, such as in microbiological testing, for example on patient samples. can ensure that incorrect and/or erroneous results can be prevented.

[0041]

[1094] Referring now to FIGS. Includes reservoir 290 . As further described herein, the collection device 200 is used to deliver a bodily fluid stream that is substantially free of extracorporeal microbes, such as microbes present on the skin and/or other undesirable external contaminants. It can be moved between a first configuration, a second configuration and a third configuration. collection de

Vise 200 may be of any suitable shape, size or configuration. For example, while sample reservoirs 280 and/or 290 are shown oriented perpendicular to housing 201 in FIGS. 2-13, collection device 200 is oriented planar to housing 201. It can have sample reservoirs 280 and/or 290, such as or arranged conically with respect to housing 201 .

[0042]

[1095] The flow diverter mechanism 220 includes a housing 201 and movable members 250 a

nd 250'. As shown in FIGS. 2-4, housing 201 is coupled to pre-sample reservoir 270 , first 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 partic ularly, coupling flow controller 440 to housing 401 such that seal member 441 is positioned be tween and in contact with the surface of housing 401 defining recess 466 and the surface of di al 445 . can be done. In addition, seal member 441 may be positioned against the surface of housing 401 defining dial 445 and recess 466 when flow controller 440 is coupled to housing 401, as described in further detail herein. can be sized and shaped to form a substantially flui d-tight seal with. The sealing member 441 is made of, for example, silicone, polylactic acid, p olyglycolic acid, polylactic-co-glycolic acid (PLGA), polyanhydride, polyorthoester, polyetherest er, polycaprolactone, polyesteramide, poly(butyric acid).), poly(valeric acid), polyurethanes, nylons, polyesters, polycarbonates, polyacrylates, polymers of ethylene-vinyl acetate and othe r acyl-substituted cellulose acetates, polystyrene, polyvinyl chloride, polyvinyl fluoride, poly(vi nylimidazole), chloro It can be made from any material that is biocompatible, such as sulfonat e polyolefins, polyethylene oxides and/or mixtures and copolymers thereof.

[0067]

[1120] As shown in FIG. 17, the sealing member 441 defines a set of openings 444 through w hich the flow of bodily fluids can be directed following venipuncture (or other method of acces sing bodily fluids). . For example, the set of openings 444 defined by the seal member 441 inc ludes a first opening 444a, a second opening 444b, a third opening 444c, a fourth opening 44 4d and a fifth opening 444e. The arrangement of the sealing member 441 is such that when t he sealing member 441 is arranged in the recess 446, the first opening 444a, the second ope ning 444b, the third opening 444c, the fourth opening 444d, and the fifth opening 444e are , t he first outlet opening 403a, the second outlet opening 403b, the third outlet opening 403c, t he fourth outlet opening 403d and the fifth outlet opening 403e of the housing 401, respectiv ely. is.

[0068]

[1121] The dial 445 of the flow controller 440 is rotatably coupled to the housing 401 and is movable between a first position, a second position, a third position, a fourth position and a fif th position relative to the housing 401. . Dial 445 includes an entry port 421 that defines lume n 402 . Inlet port 421 can be fluidly coupled to a medical device (not shown) that defines a flu id flow path for withdrawing and/or transporting bodily fluid from the patient's body to collecti on device 400 . For example, entry port 421 can be fluidly coupled to a needle or other lumen defining device (eg, flexible sterile tubing) either directly or indirectly via adapter 404 . Simila rly, inlet lumen 402 defined by inlet port 421 is arranged to be in fluid communication with th e lumen defined by the lumen-defining device when the lumen-defining device is coupled to in let port 421 . be. Inlet port 421 thus connects to pre-sample reservoir 470, first sample reser voir 480, second sample reservoir 480', third sample reservoir 490 and fourth sample reservoi r 490, as described in further detail herein. ' can be configured to be selectively placed in 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]

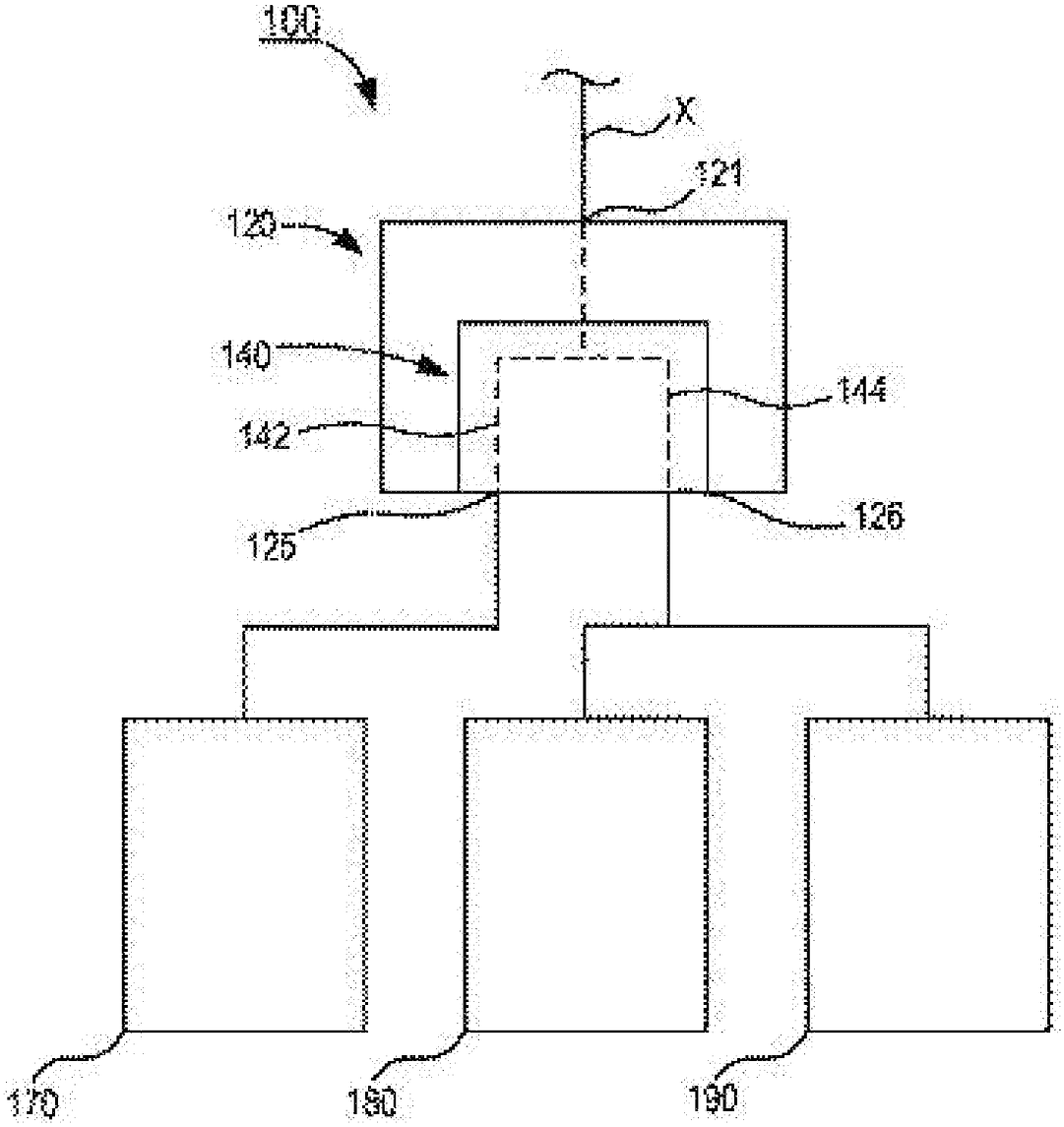


FIG. 1

[Figure 2]

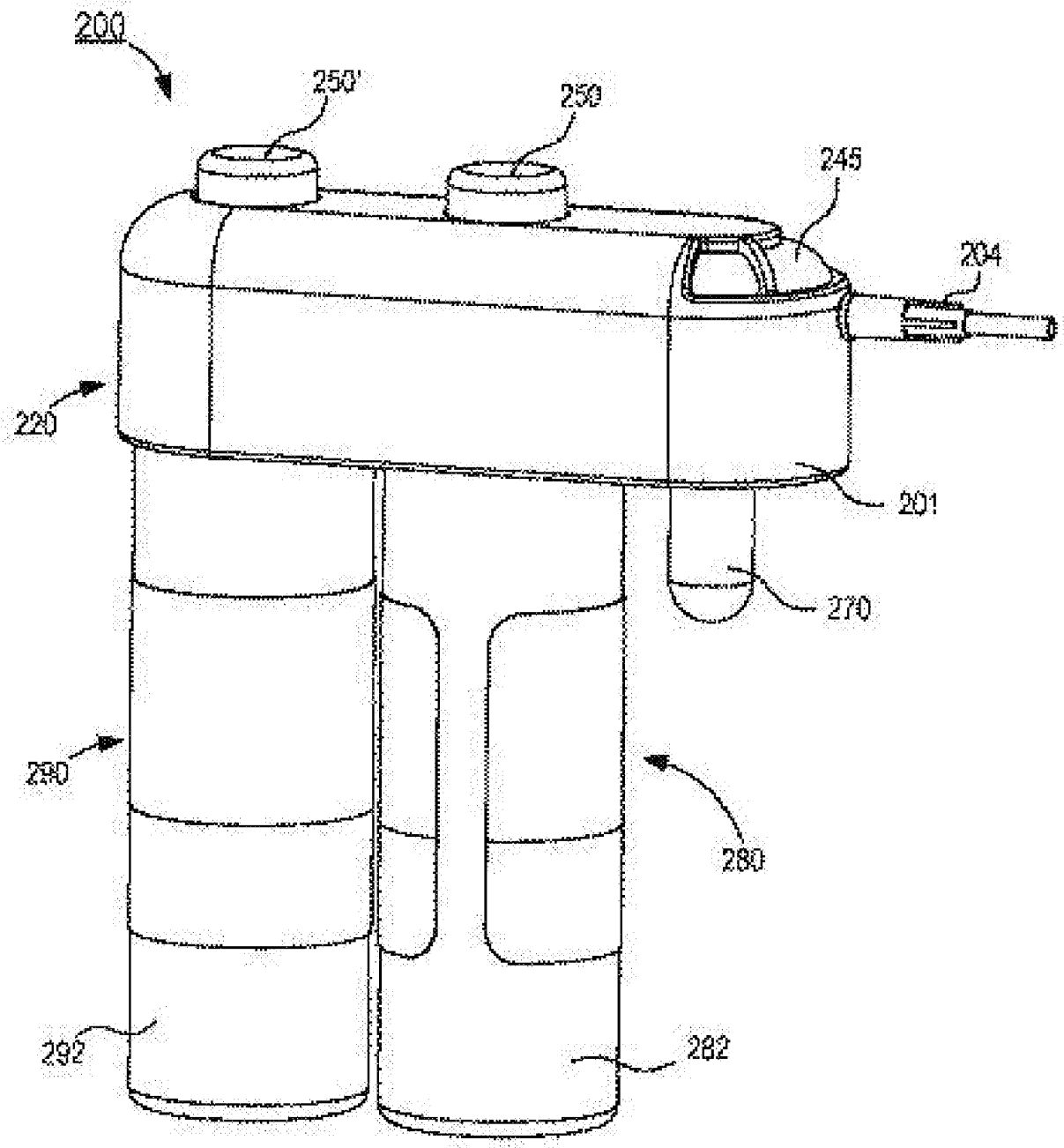
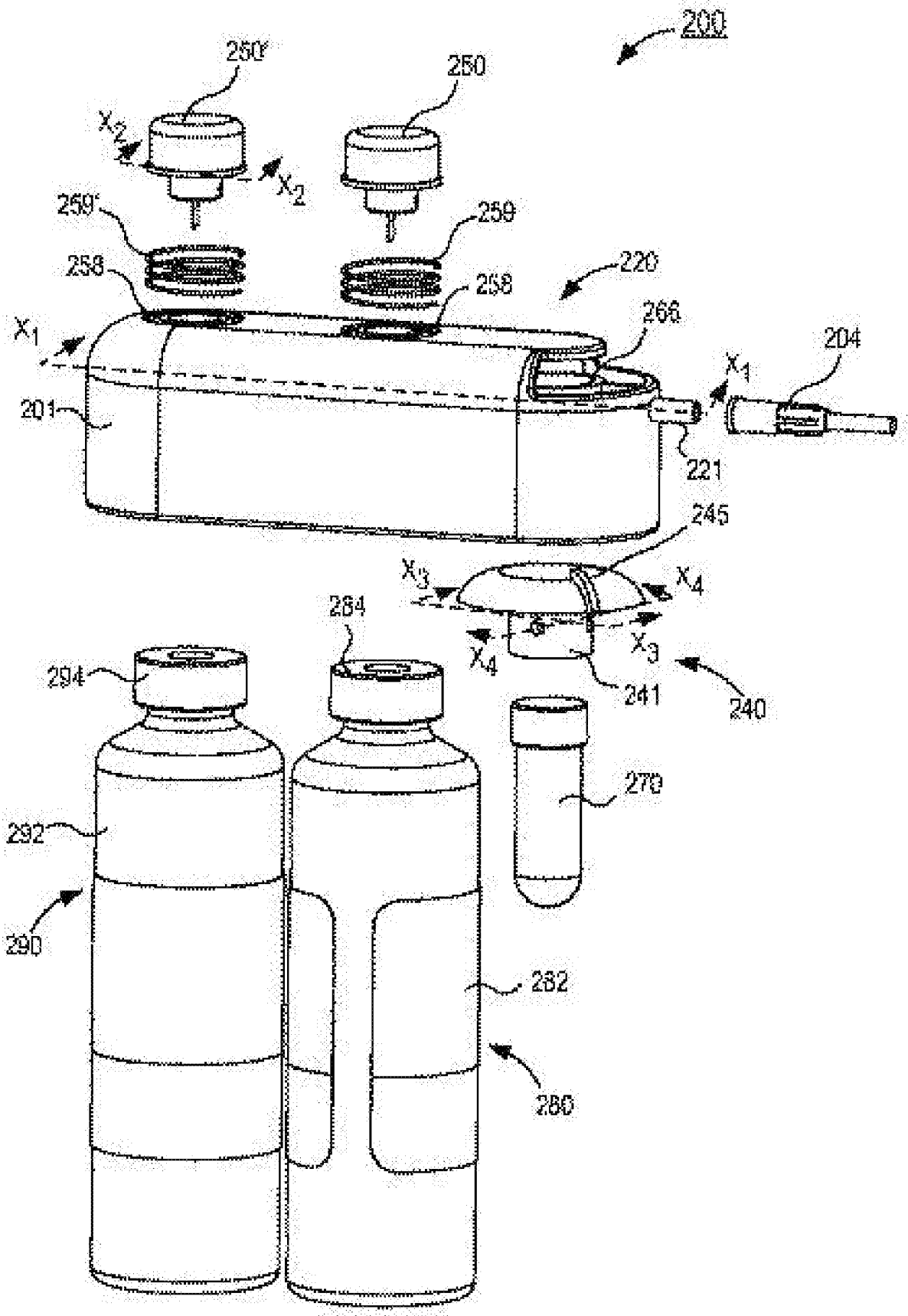


FIG. 2

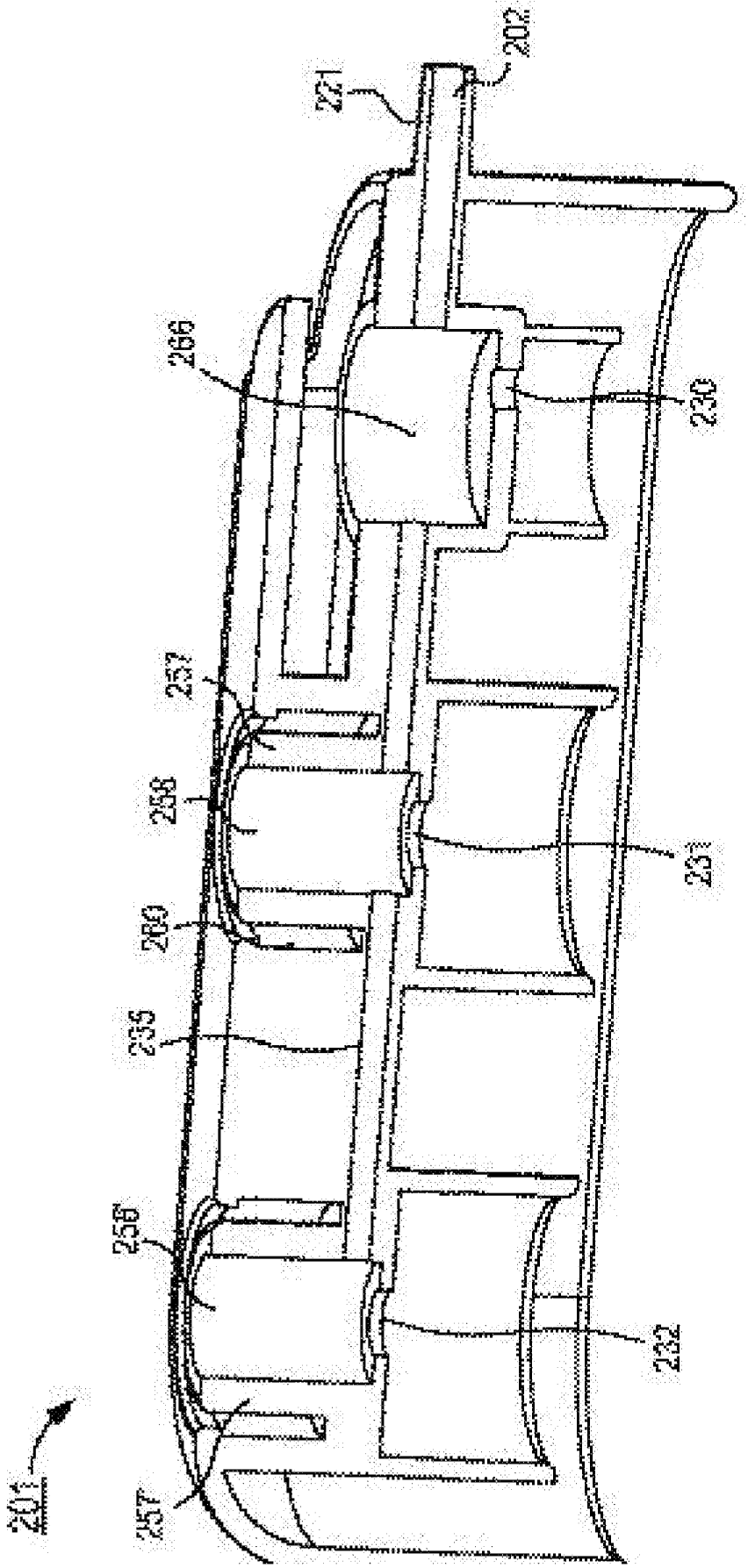
[Figure 3]


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]

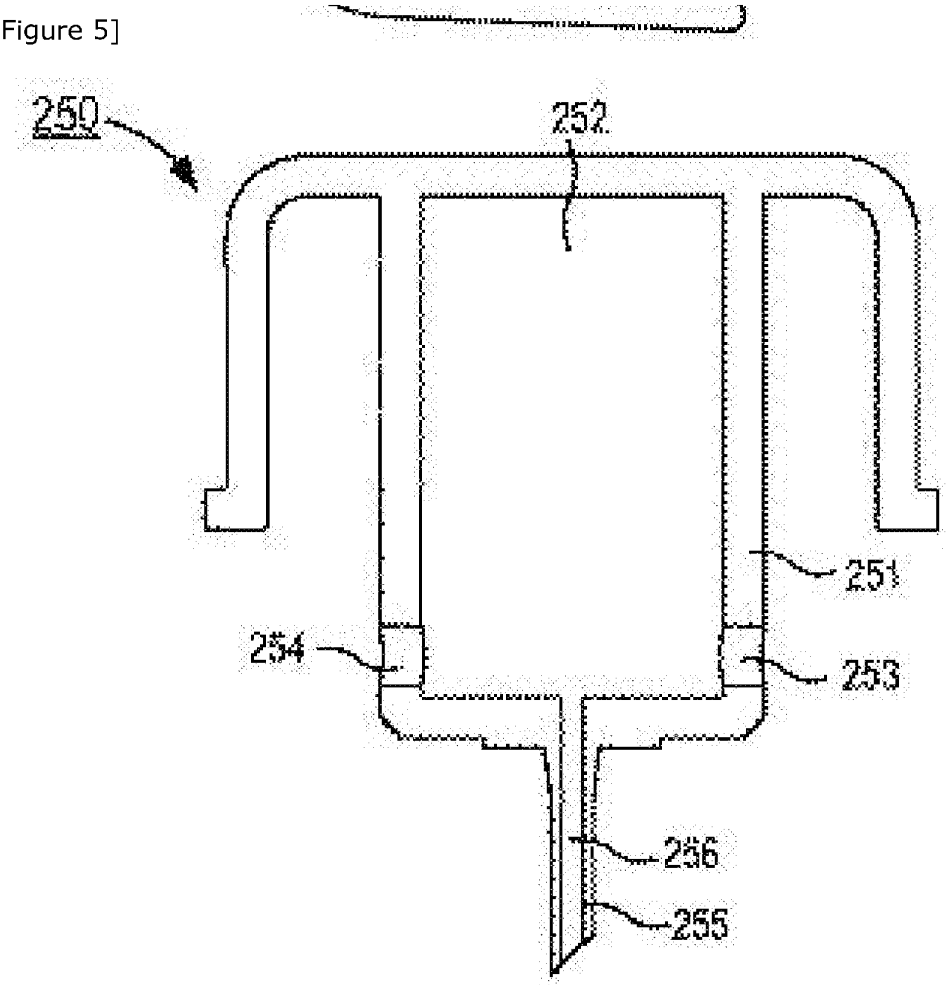


FIG. 5

[Fig. 6]

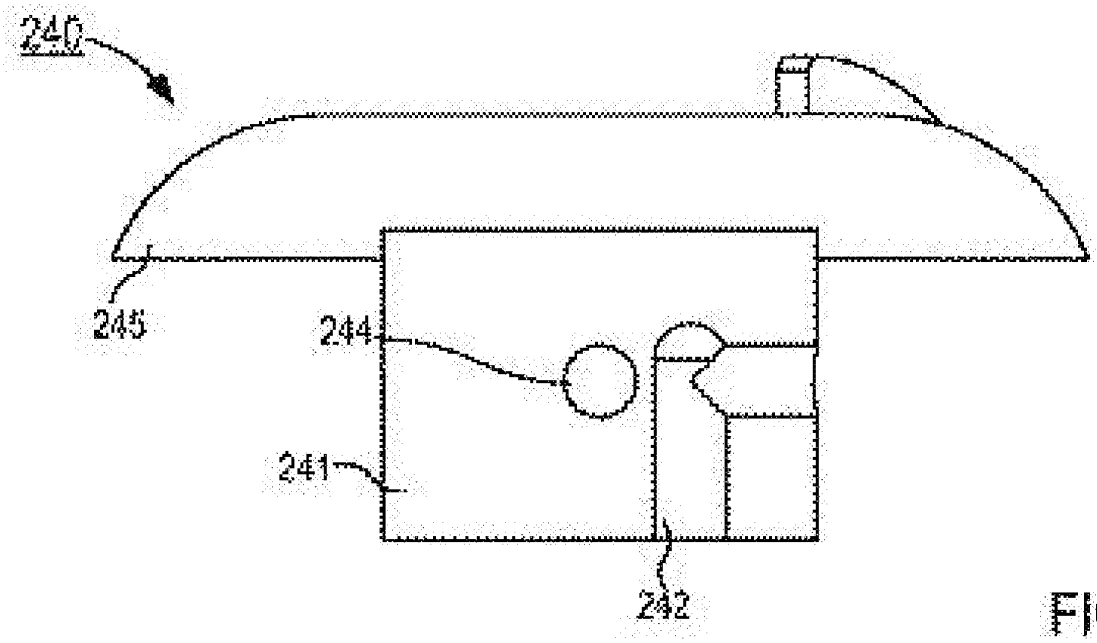


FIG. 6

[Fig. 7]

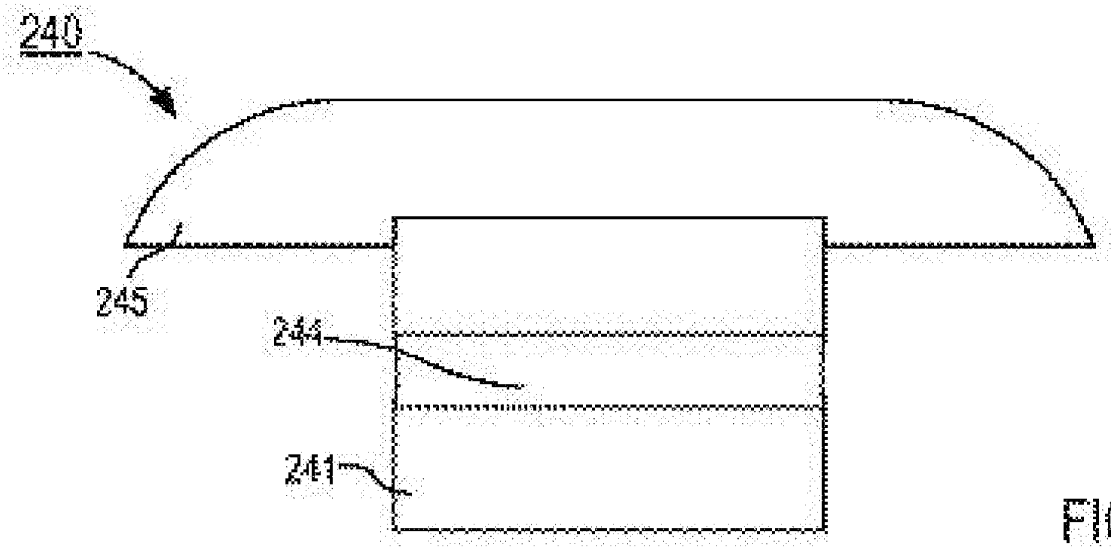


FIG. 7

[Fig. 8]

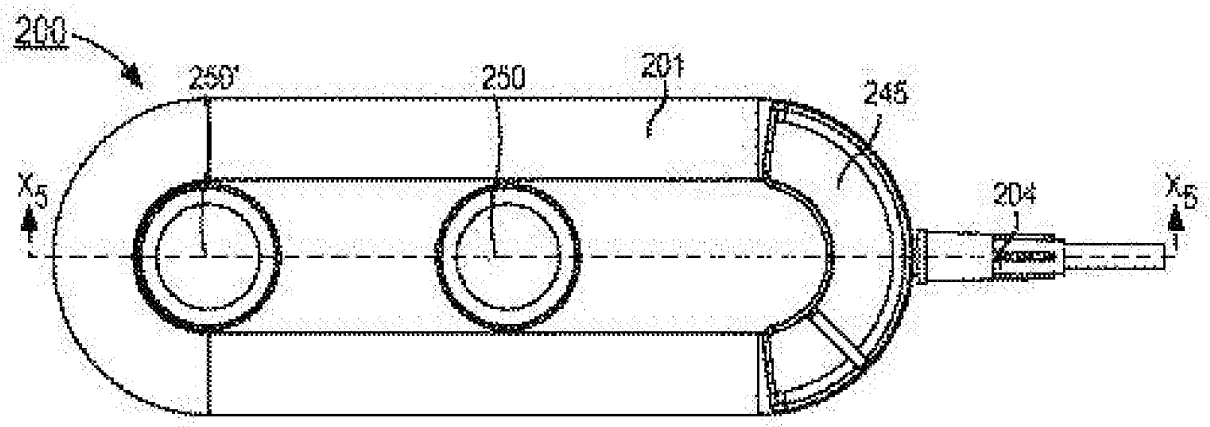


FIG. 8

[Fig. 9]

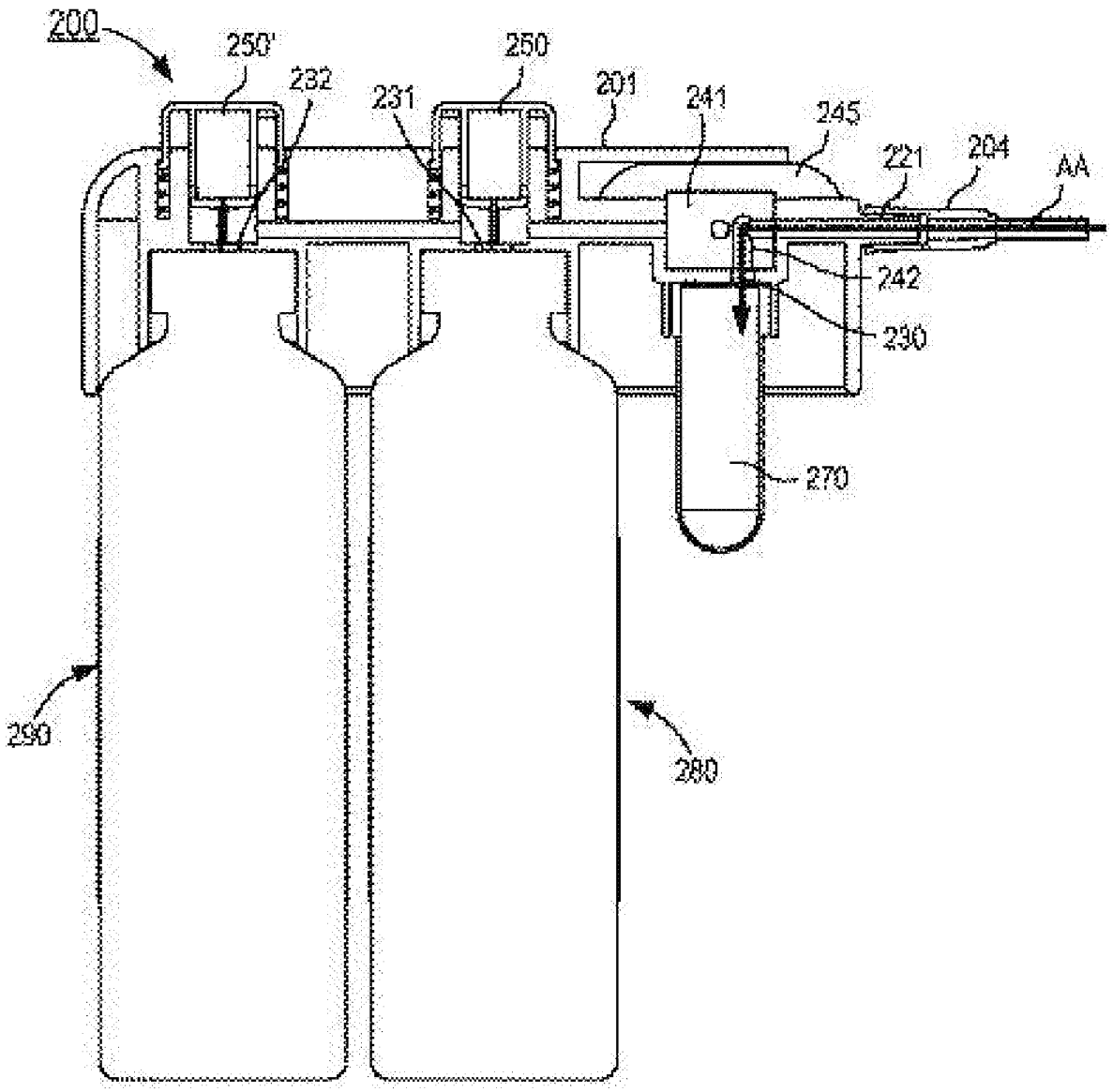


FIG. 9

[Fig. 10]

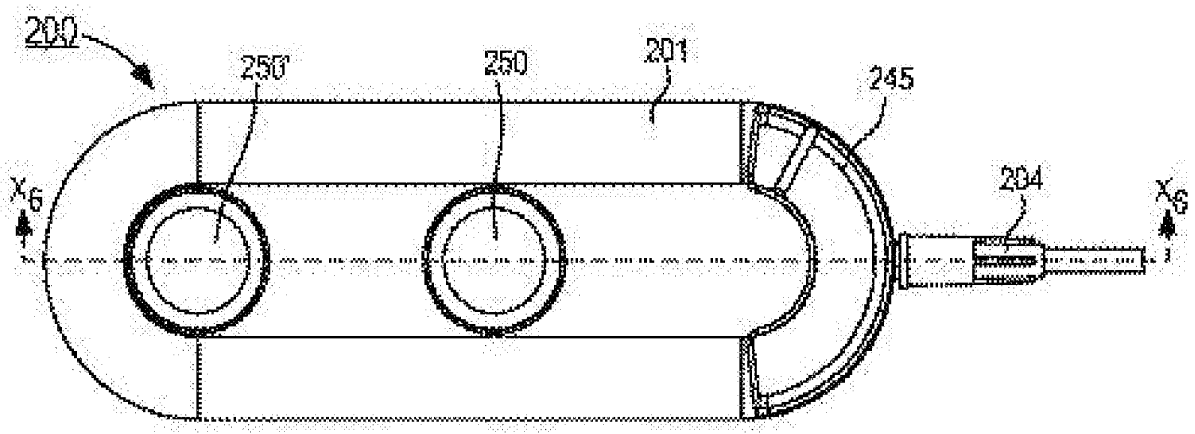


FIG. 10

[Fig. 11]

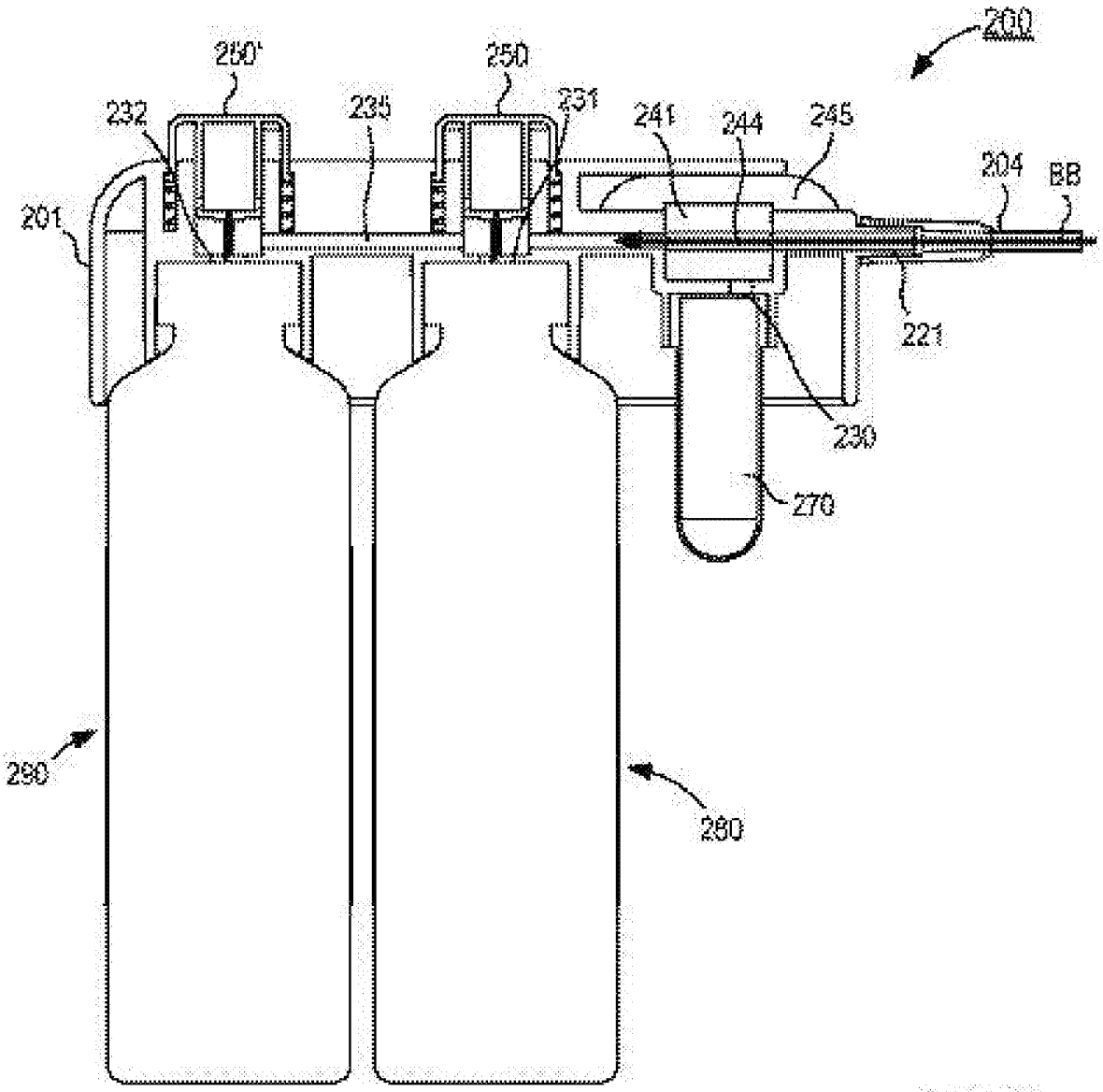

200
250'
250
232
235
231
241
244
245
204
BB
201
221
230
270
280
280

FIG. 11

[Fig. 12]

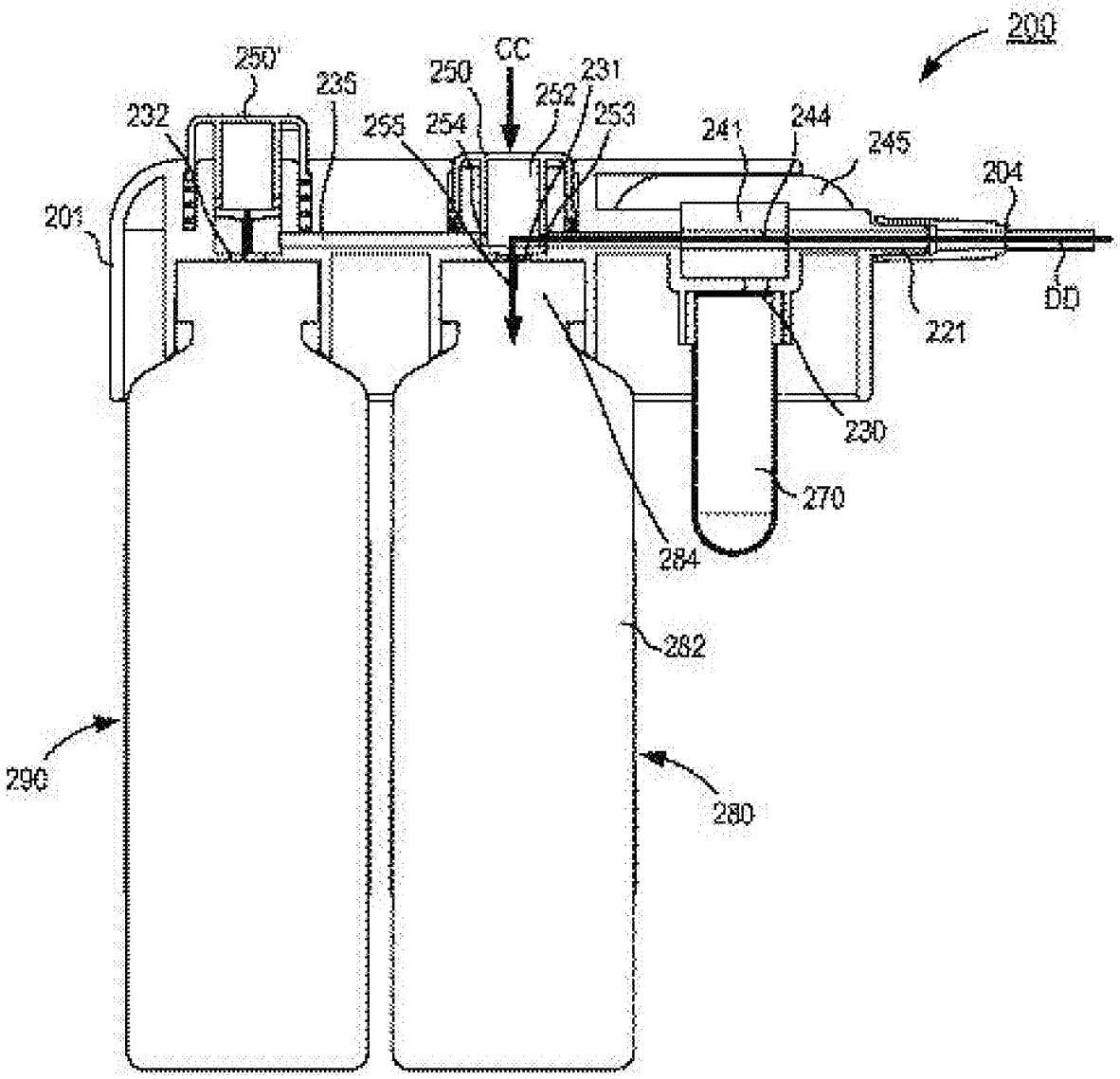

200
250'
236
250
CC
231
232
255
254
252
253
241
244
245
204
201
DD
221
230
270
284
282
290
280

FIG. 12

[Fig. 13]

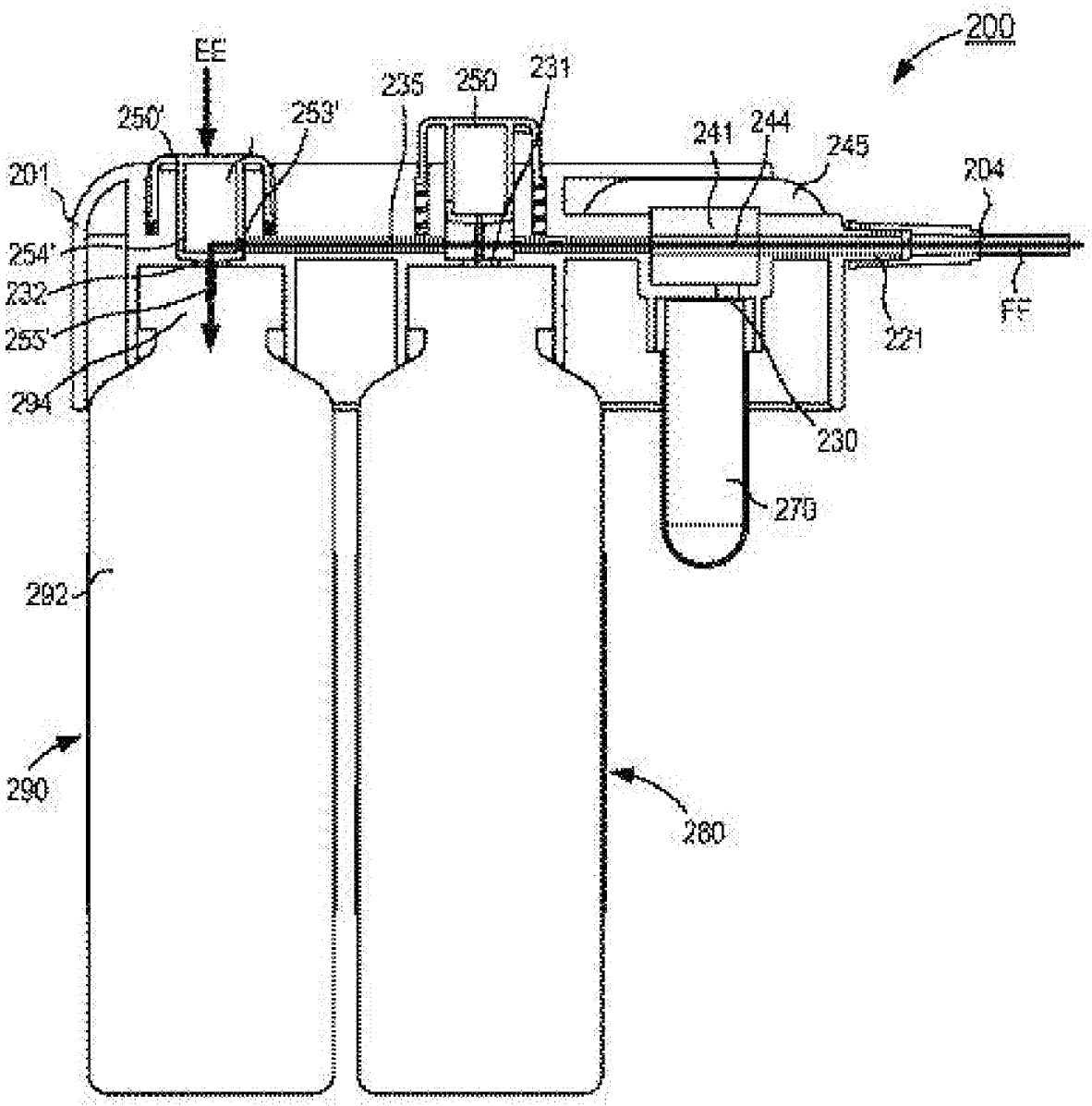

200
EE
250'
253'
235
250
231
241
244
245
204
201
254'
232
255'
294
221
FF
230
270
292
290
280

FIG. 13

[Fig. 14]

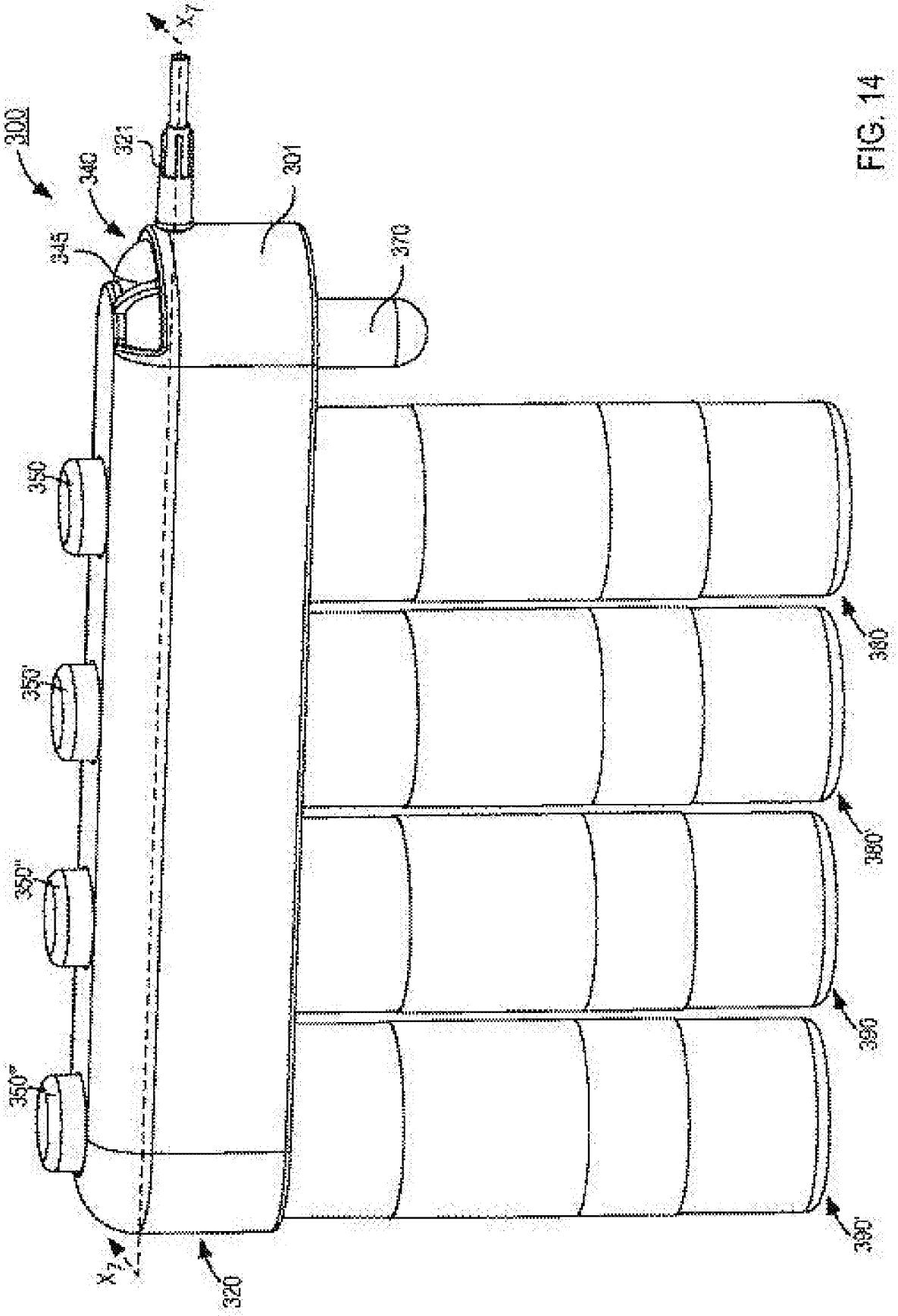
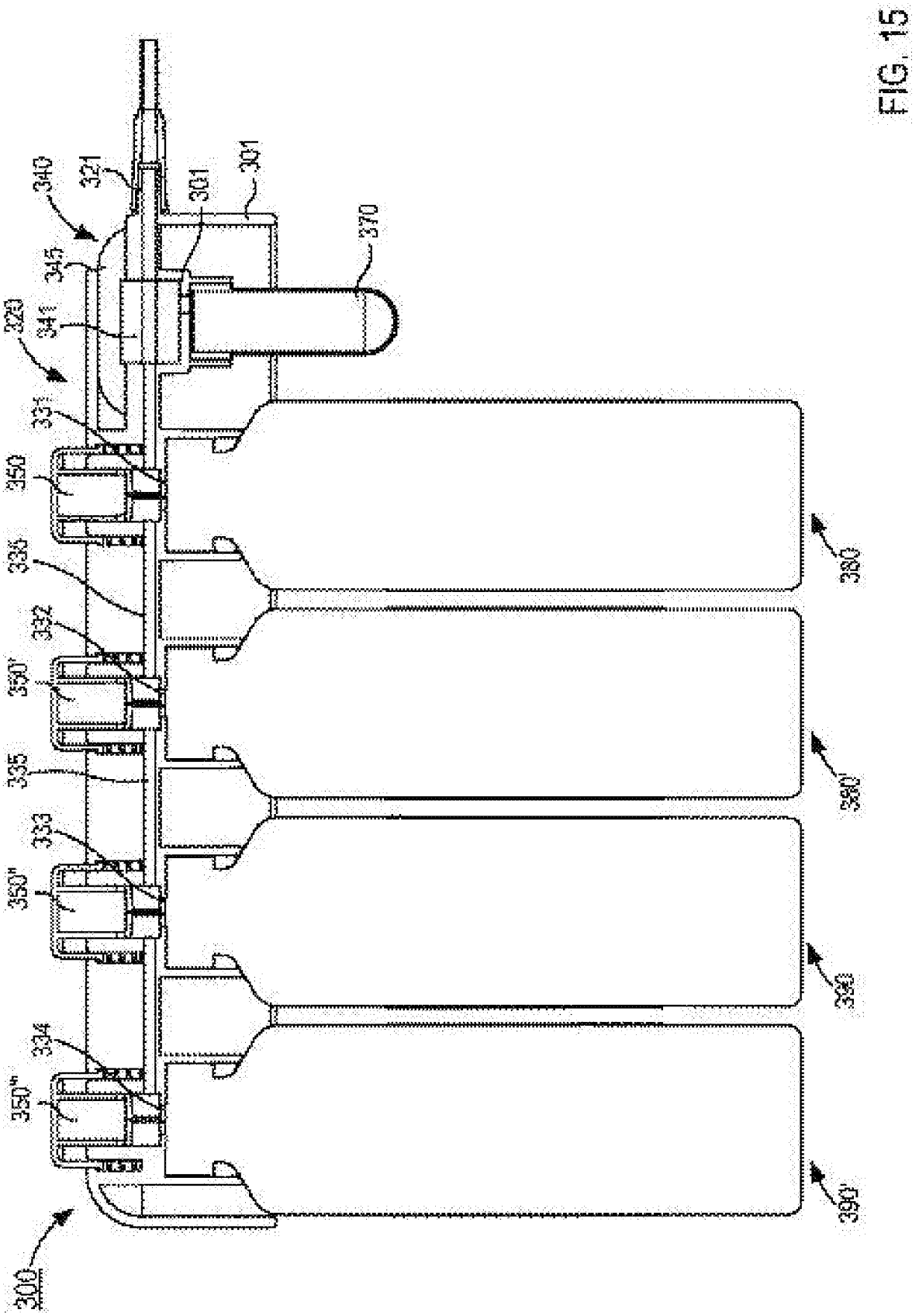
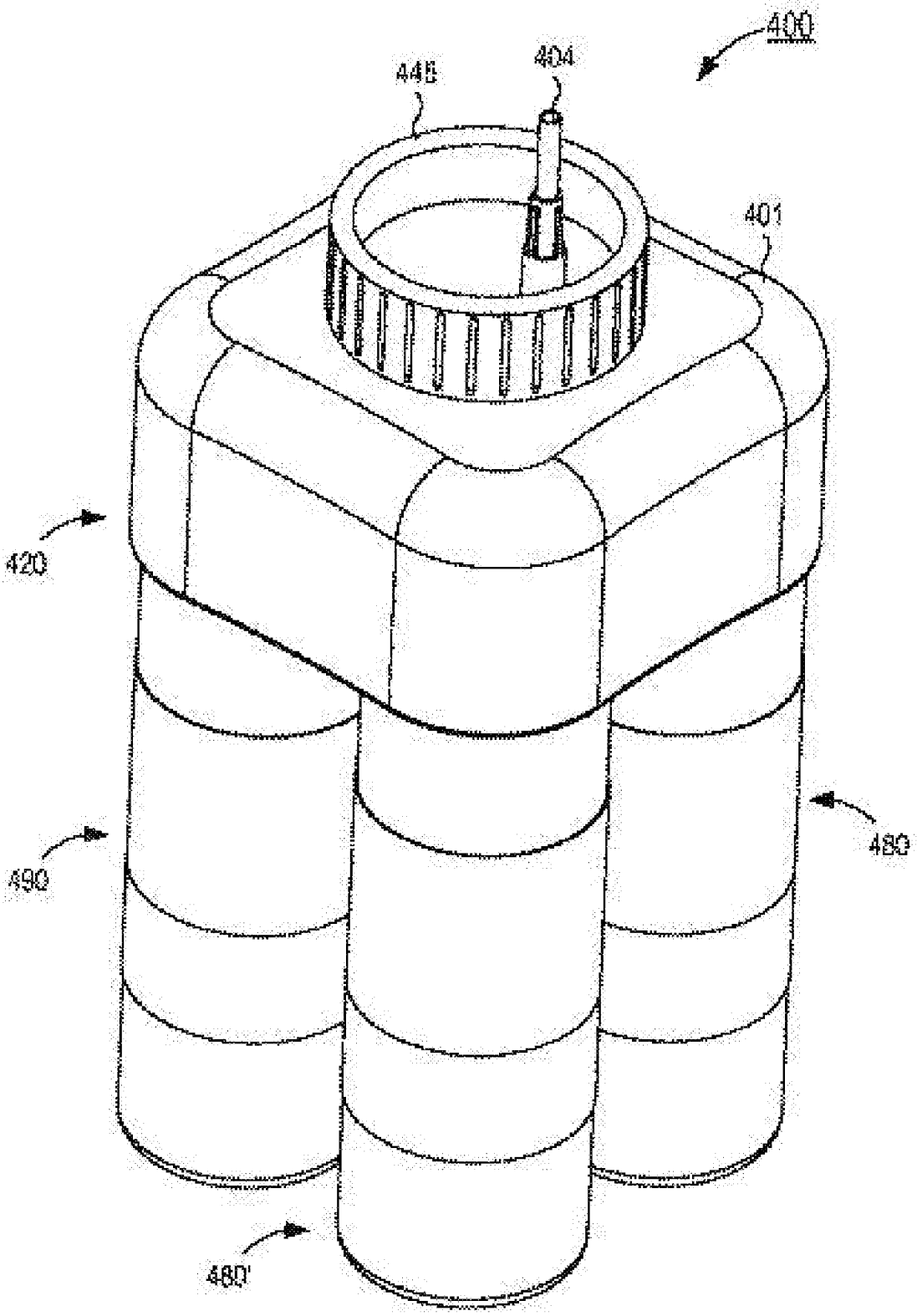

300
321
340
345
301
370
350
350'
350"
350"
360
360'
350
380'
320
X_1
X_2
Z_2

FIG. 14

[Fig. 15]

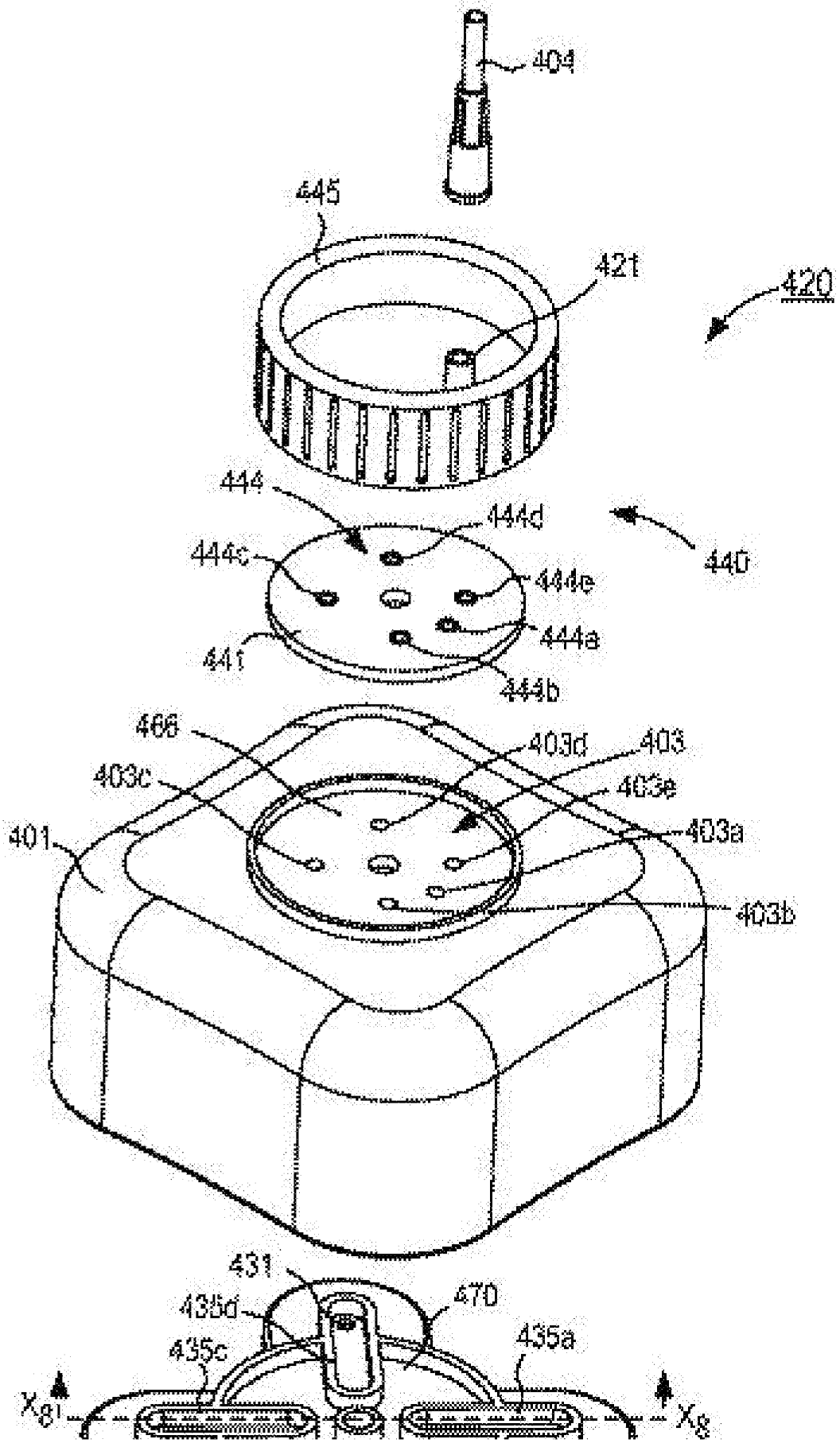

FIG. 15
340
321
301
301
370
345
343
223
333
350
335
332
350'
335
333
350"
334
350"
300
380
380'
380
390'

[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]

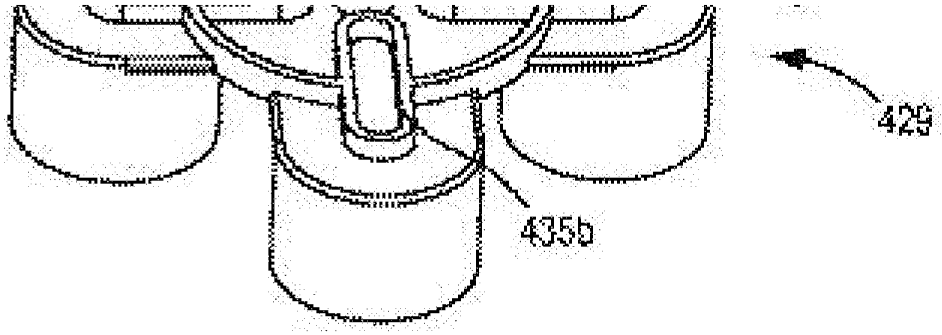


FIG. 17

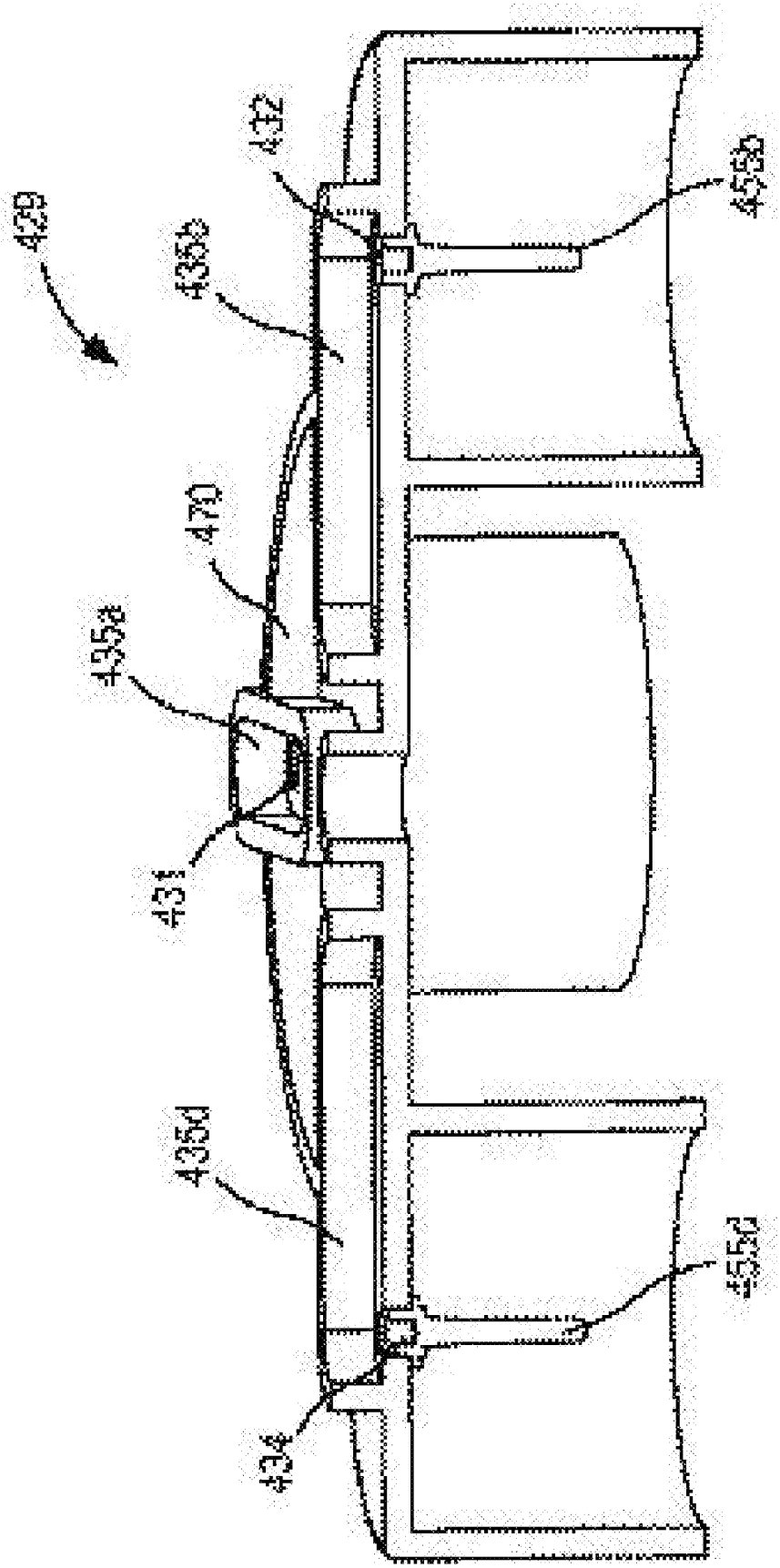


FIG. 18

[Fig. 19]

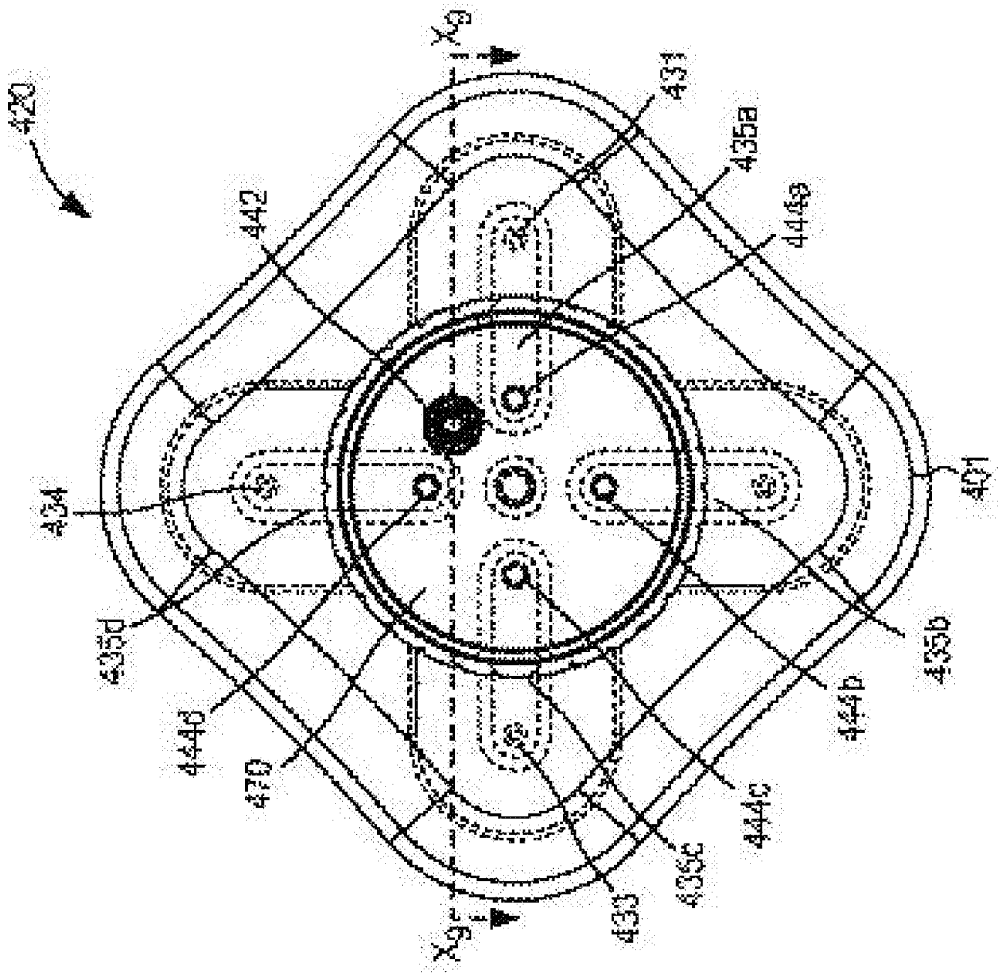


FIG. 19

[Fig. 20]

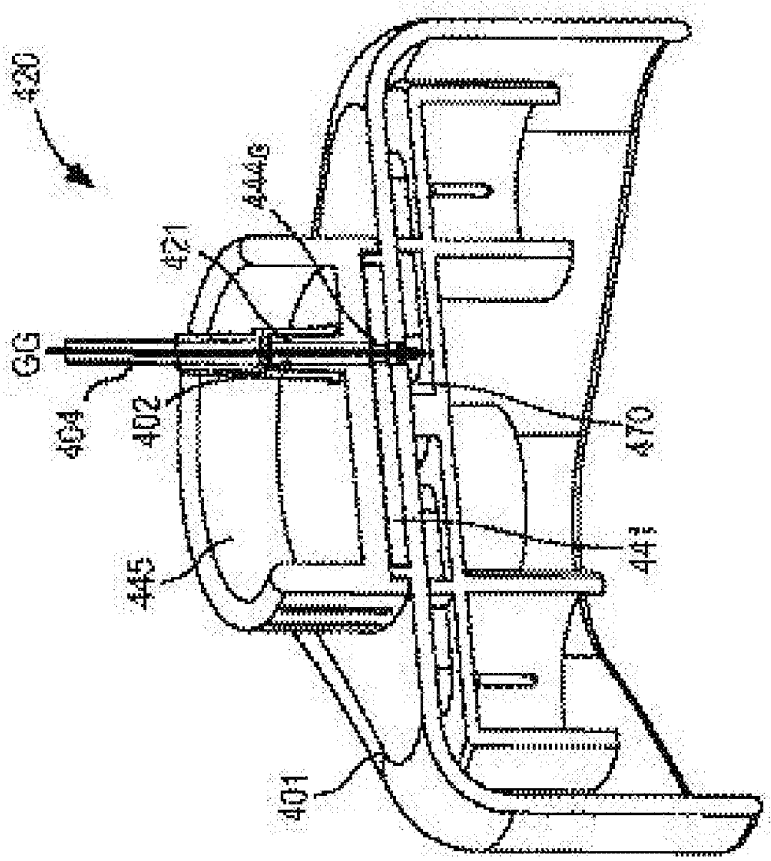


FIG. 20

[Fig. 21]

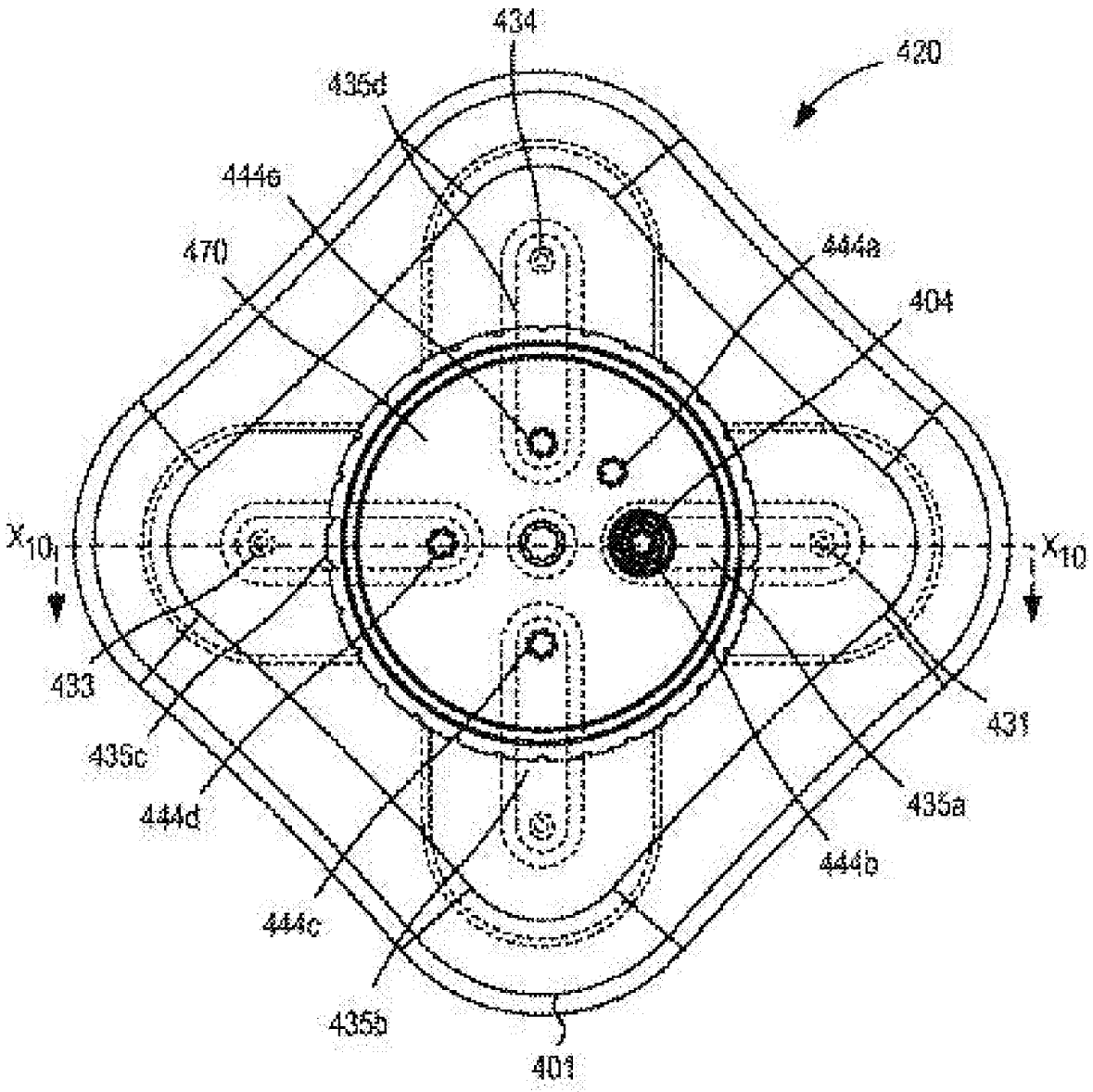
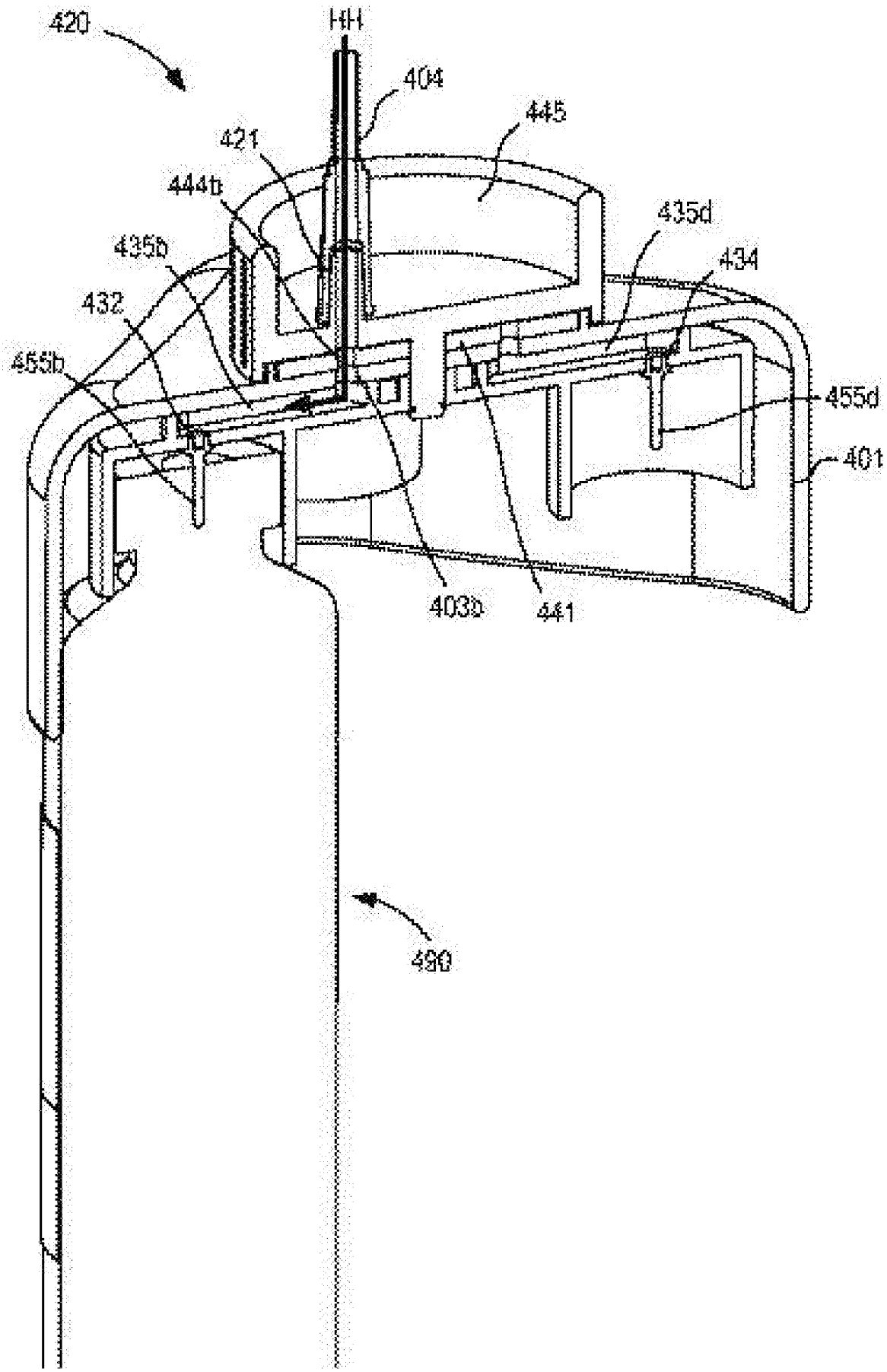

434
420
435d
444e
470
444a
404
X_{10}
X_{10}
433
439c
444d
431
435a
444b
444c
435b
401

FIG. 21

[Fig. 22]


420
HH
404
445
421
444b
435d
435b
434
432
455b
455d
401
403b
441
490

[Fig.23]

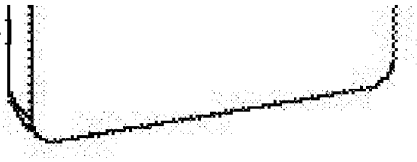
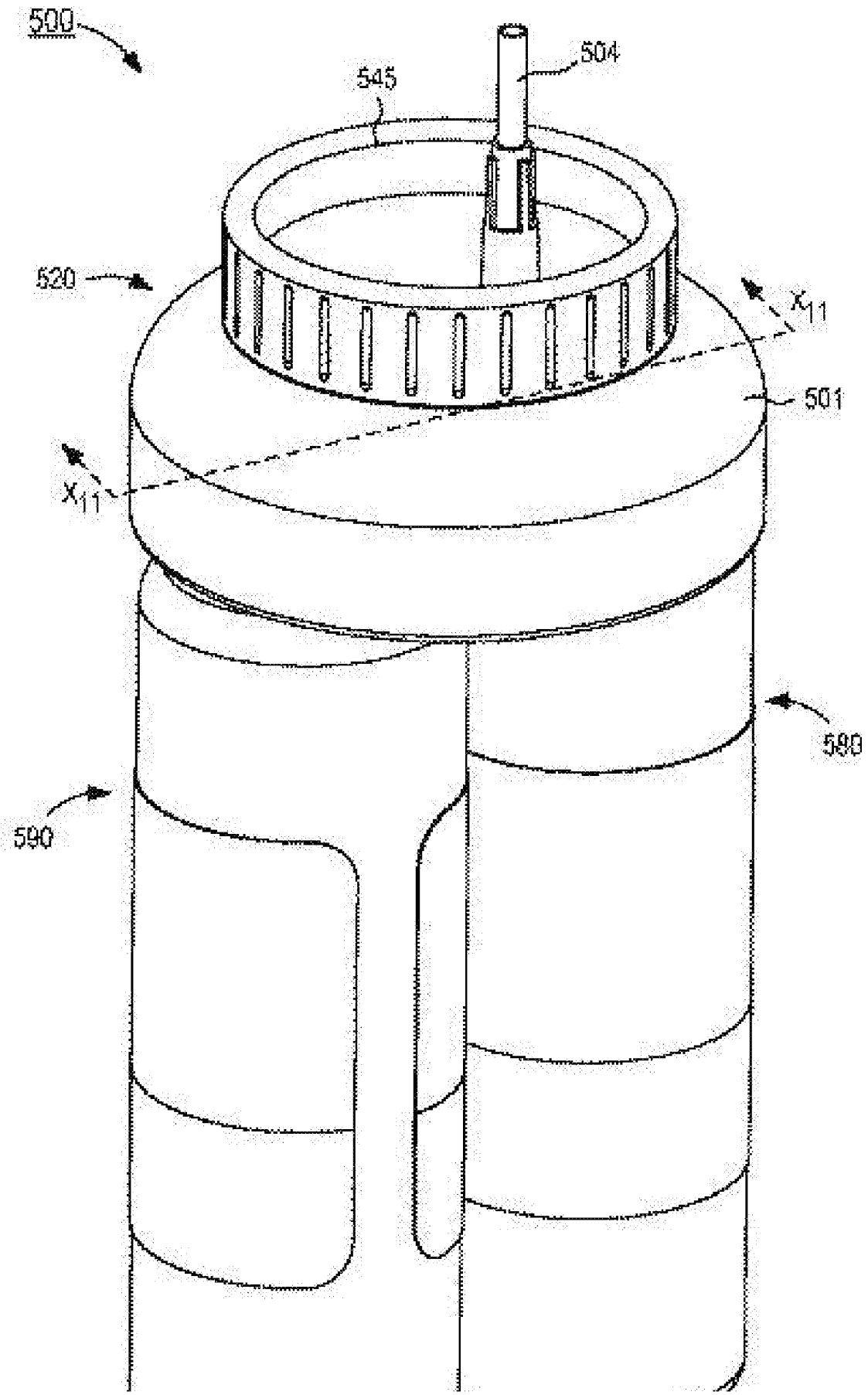


FIG. 22


500
504
545
520
X_{11}
501
X_{11}
590
590

[Fig.24]

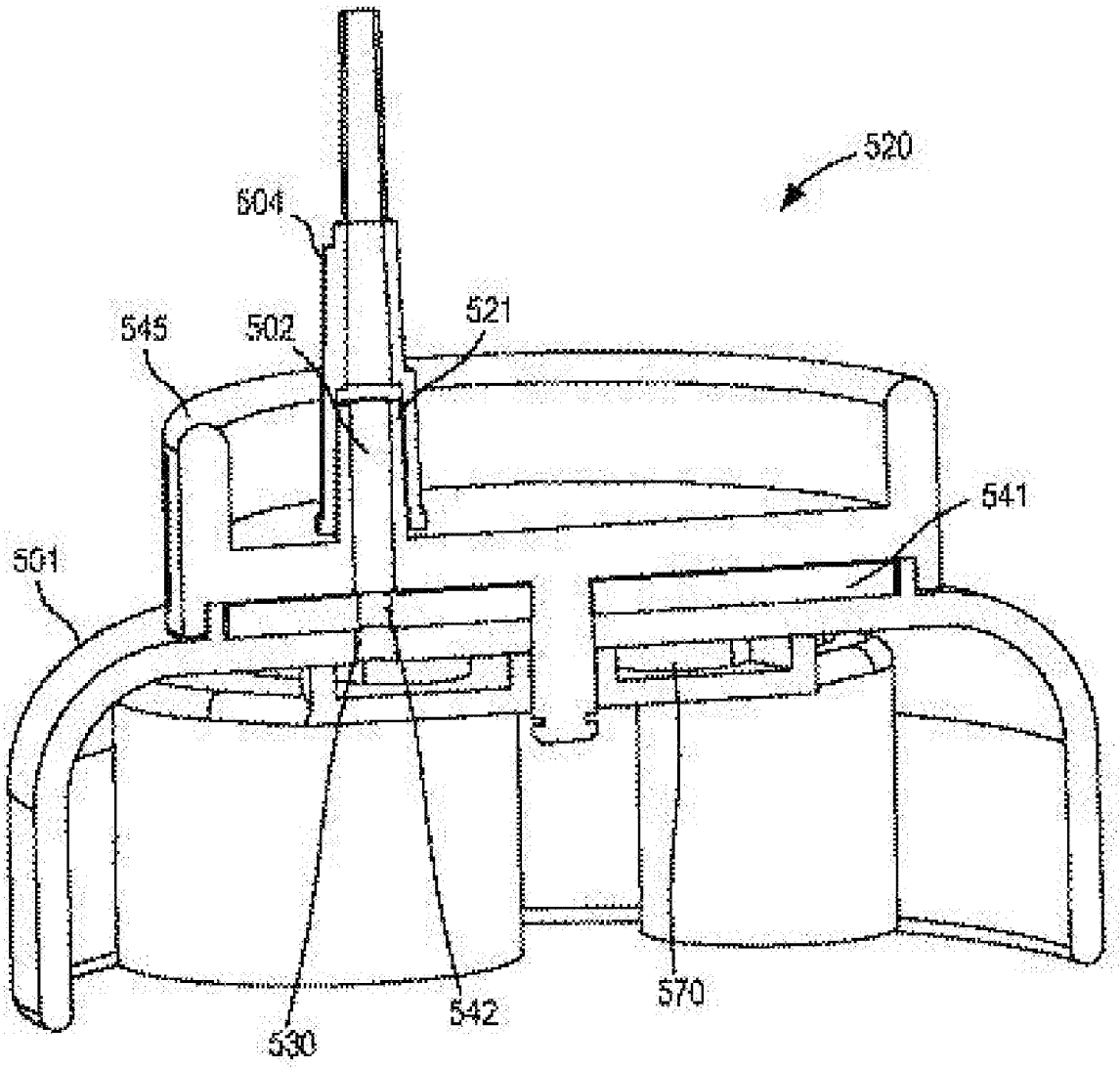
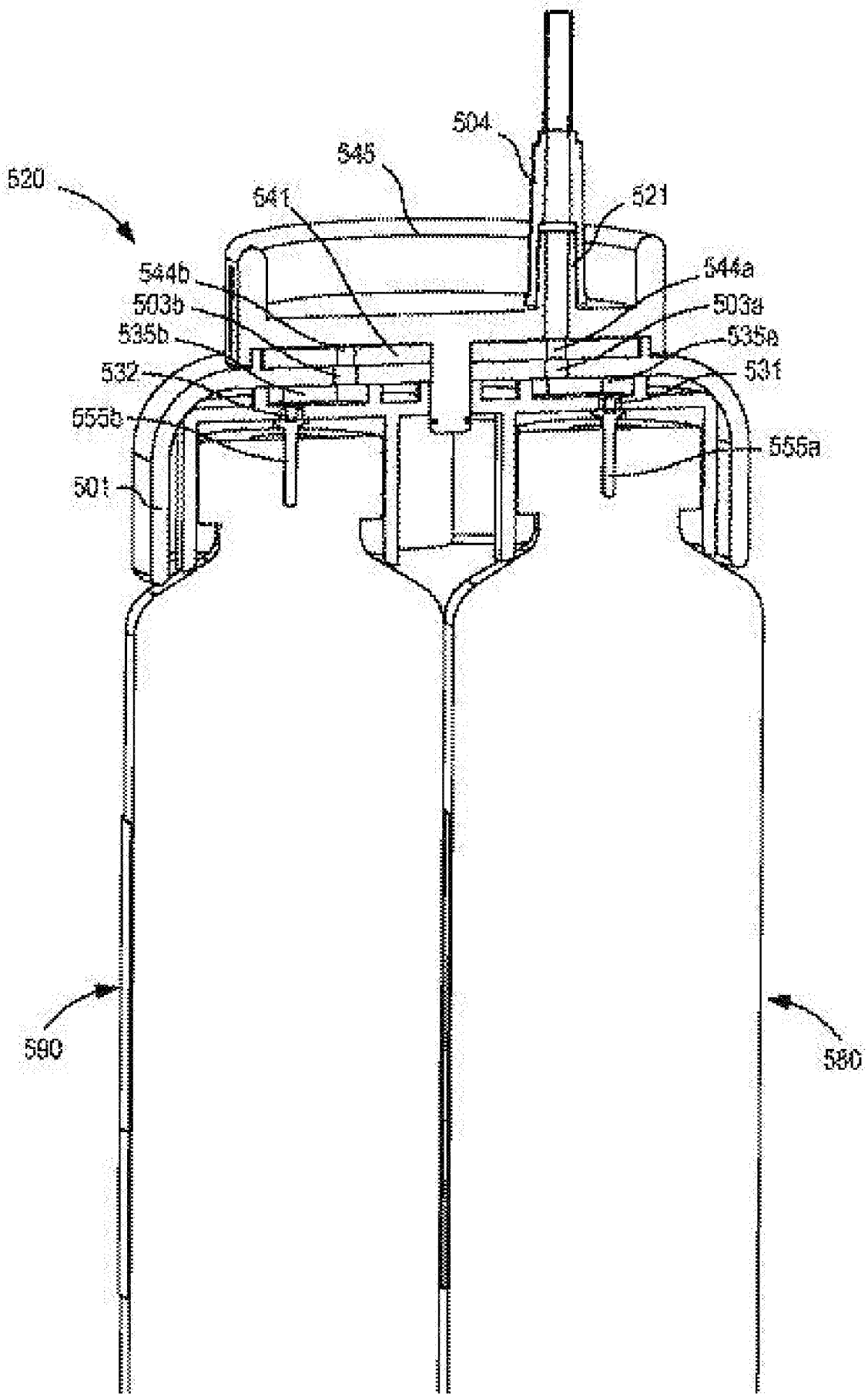


FIG. 24

[Fig.25]


504
545
520
541
521
544b
544a
503b
503a
535b
535a
532
531
555b
555a
501
590
580

[Fig.26]

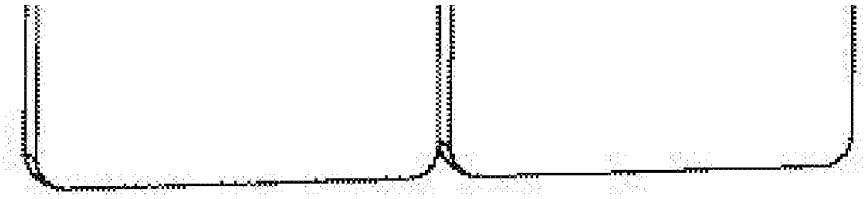
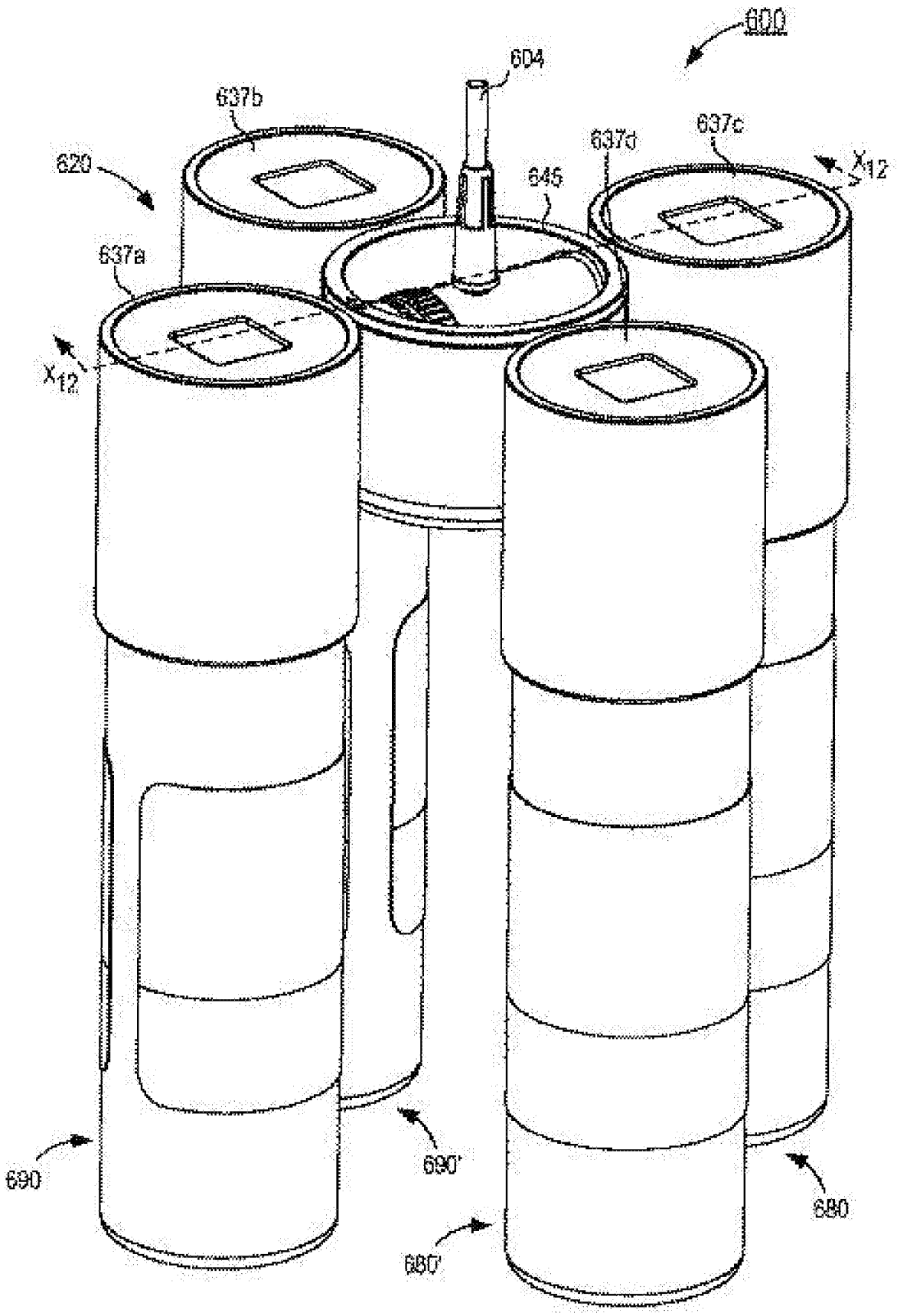


FIG. 25


600
604
637b
637d
637c
620
645
637a
X12
X12
690
690'
680
680'

[Fig.27]

FIG. 26

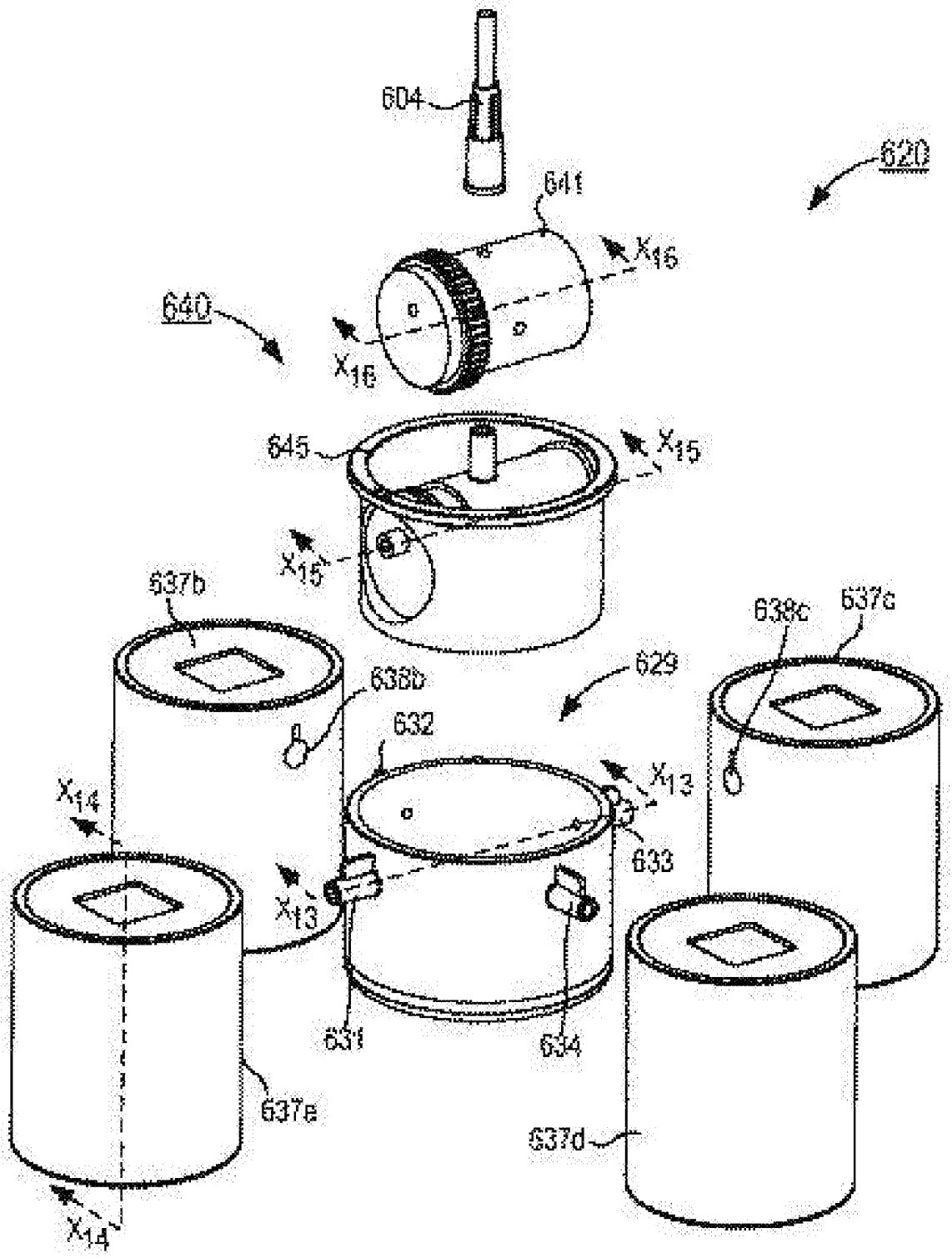

604
620
641
X_{16}
640
X_{16}
645
X_{15}
X_{15}
637b
638c
637c
638b
629
632
X_{14}
X_{13}
633
X_{13}
631
634
637e
637d
X_{14}

FIG. 27

[Fig.28]

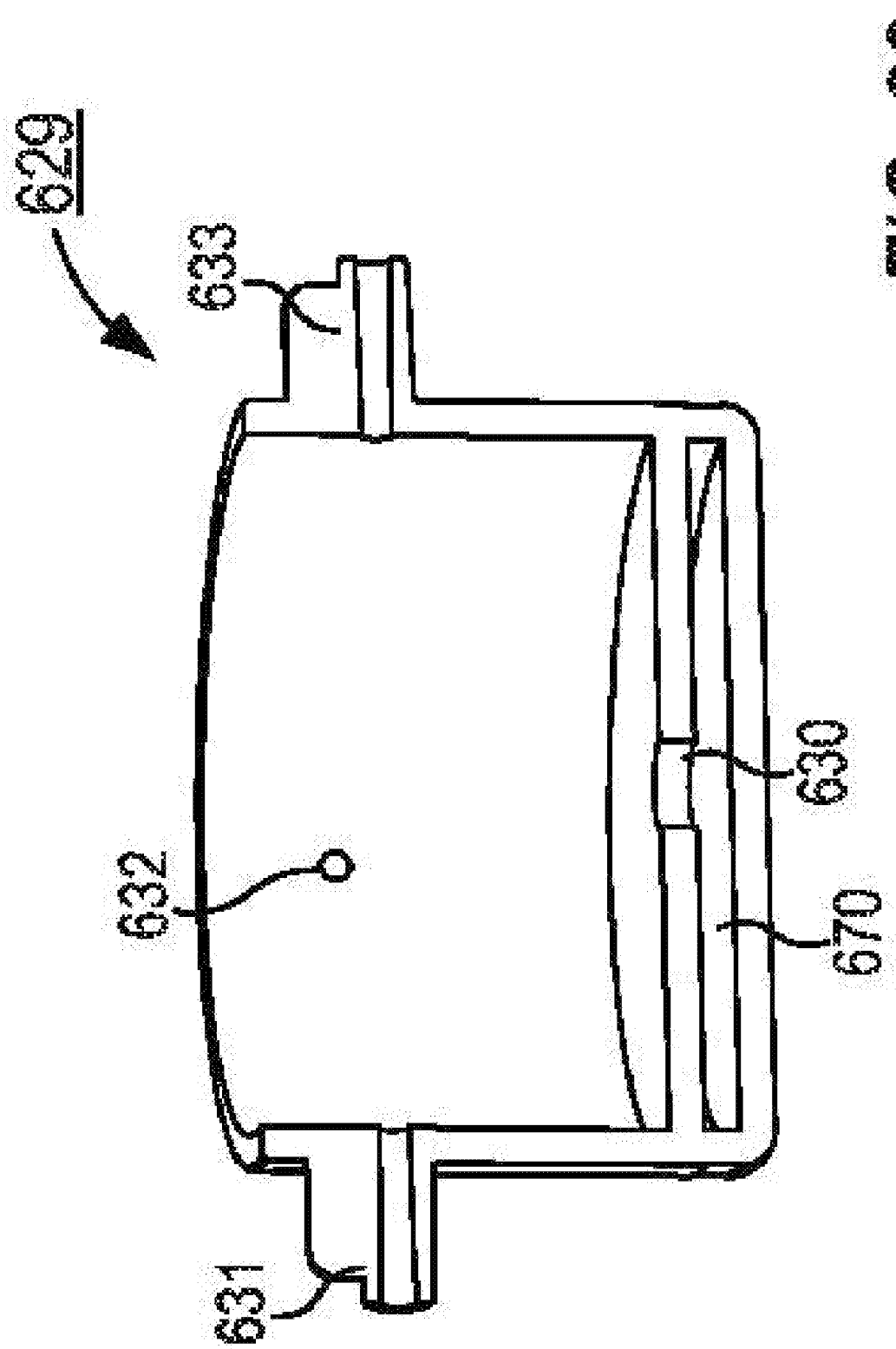


FIG. 28

[Fig.29]

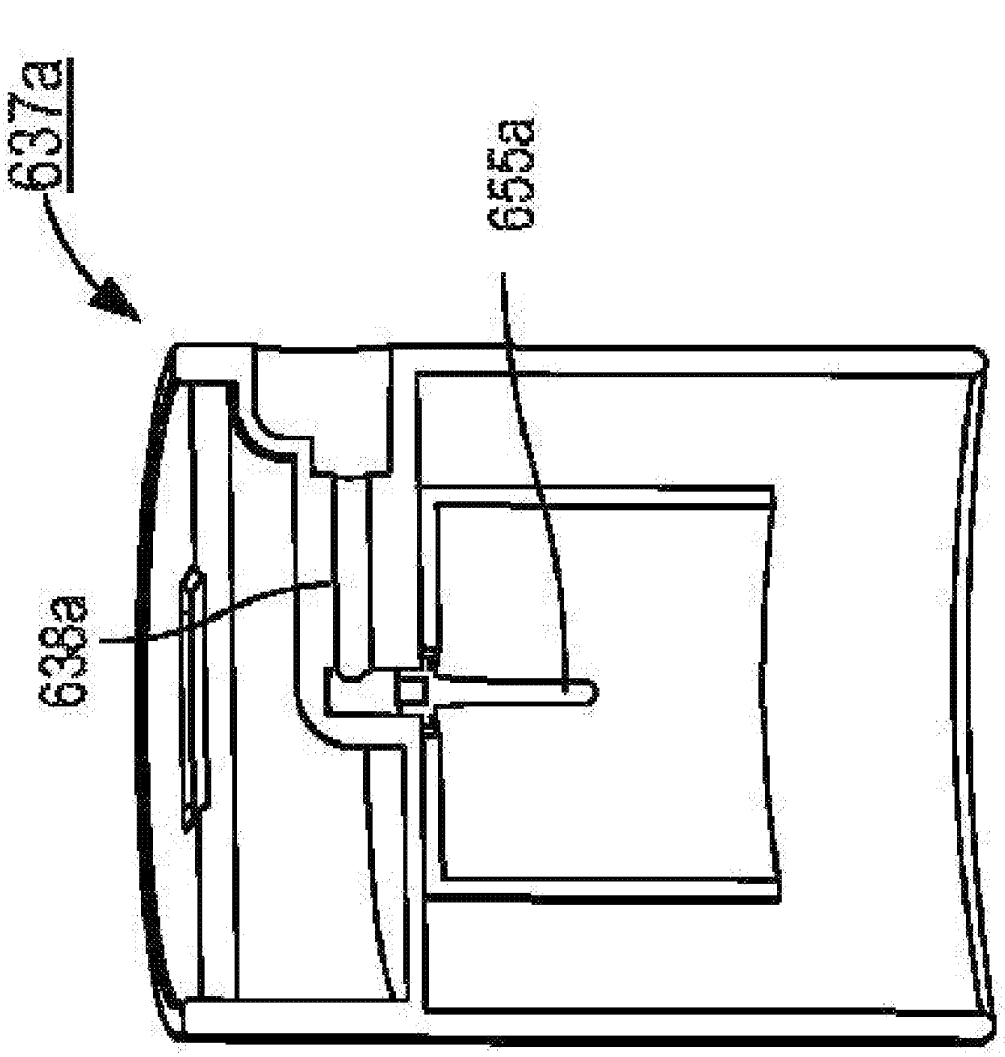
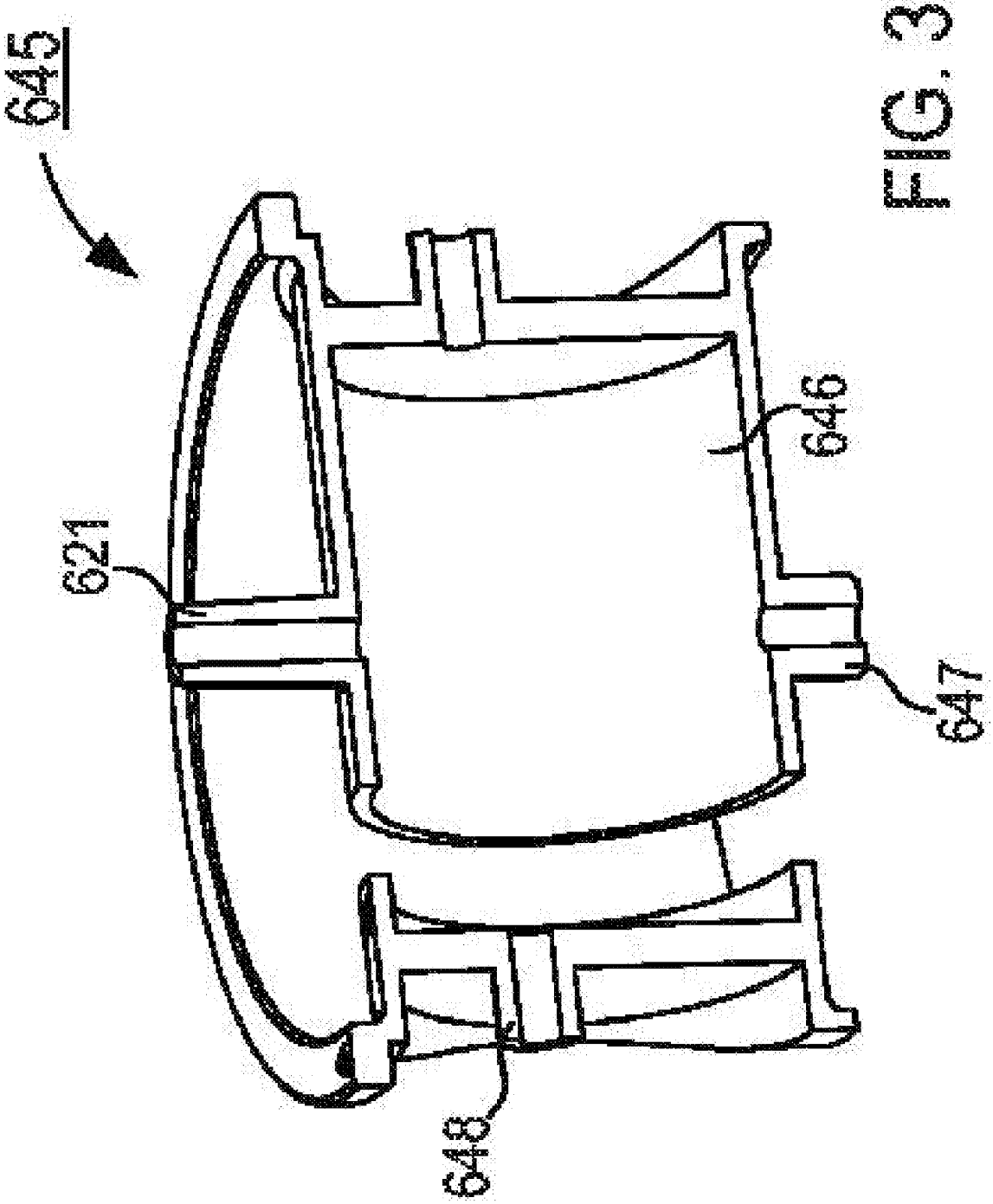


FIG. 29

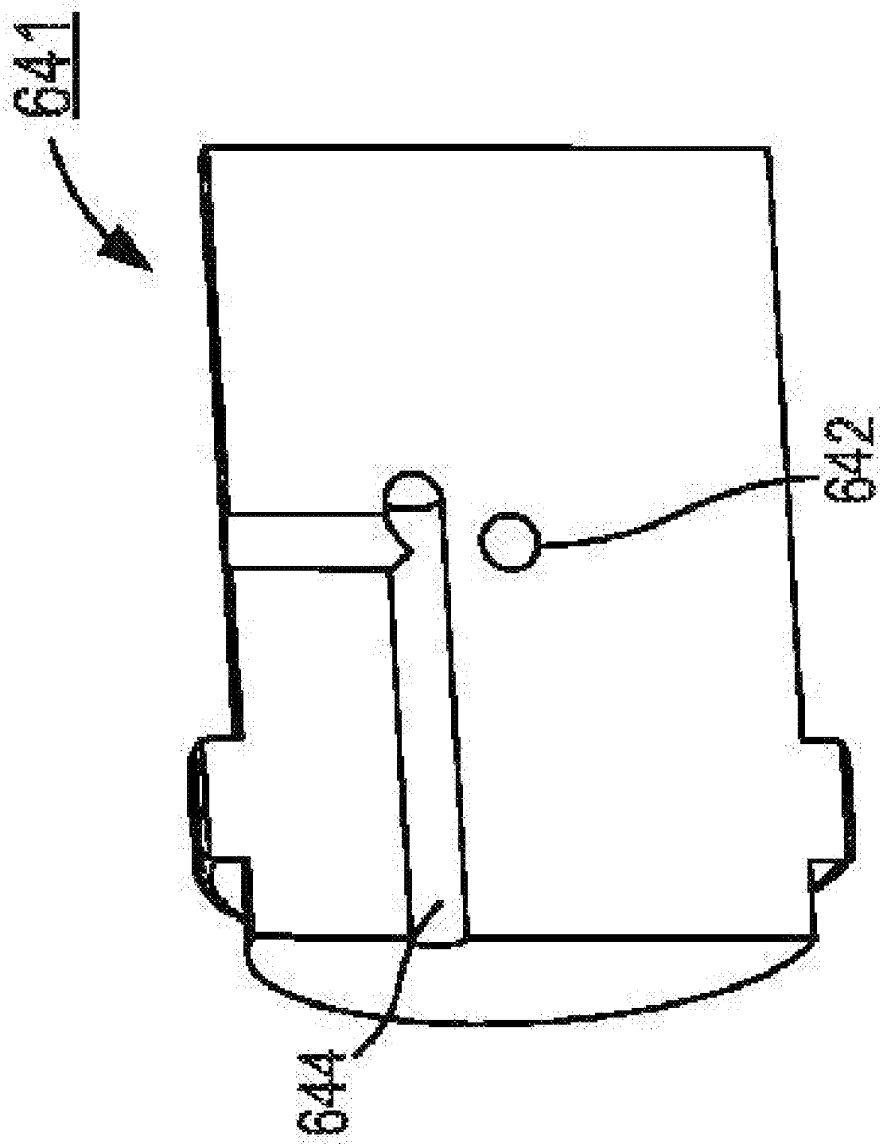
[Fig. 30]

FIG. 30



[Fig. 31]

FIG. 31



[Fig. 32]

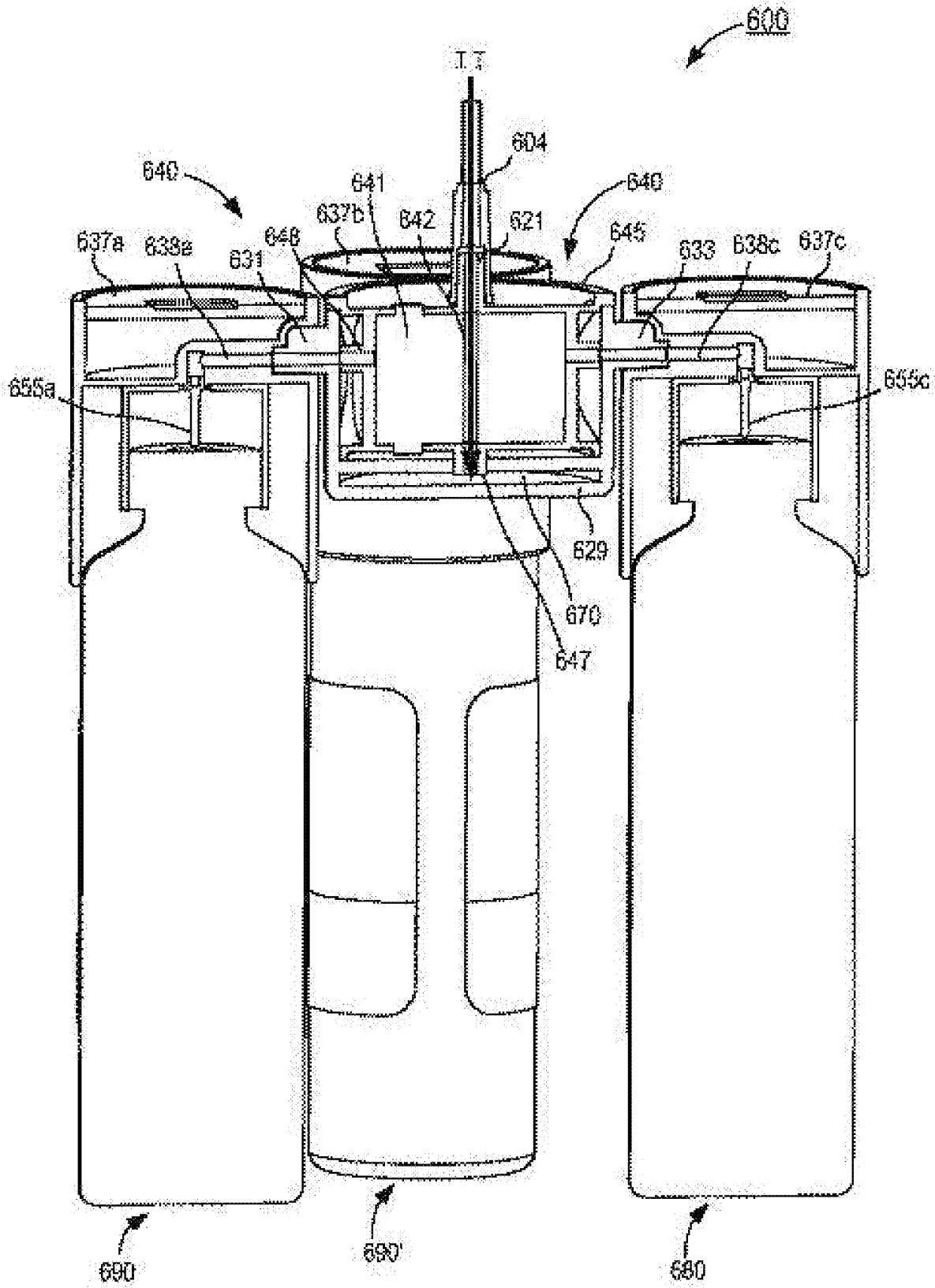

600
I
I
604
640
641
637b
642
621
640
645
637a
638a
631
648
633
638c
637c
655a
655c
629
670
647
690
690'
680

FIG. 32

[Fig. 33]

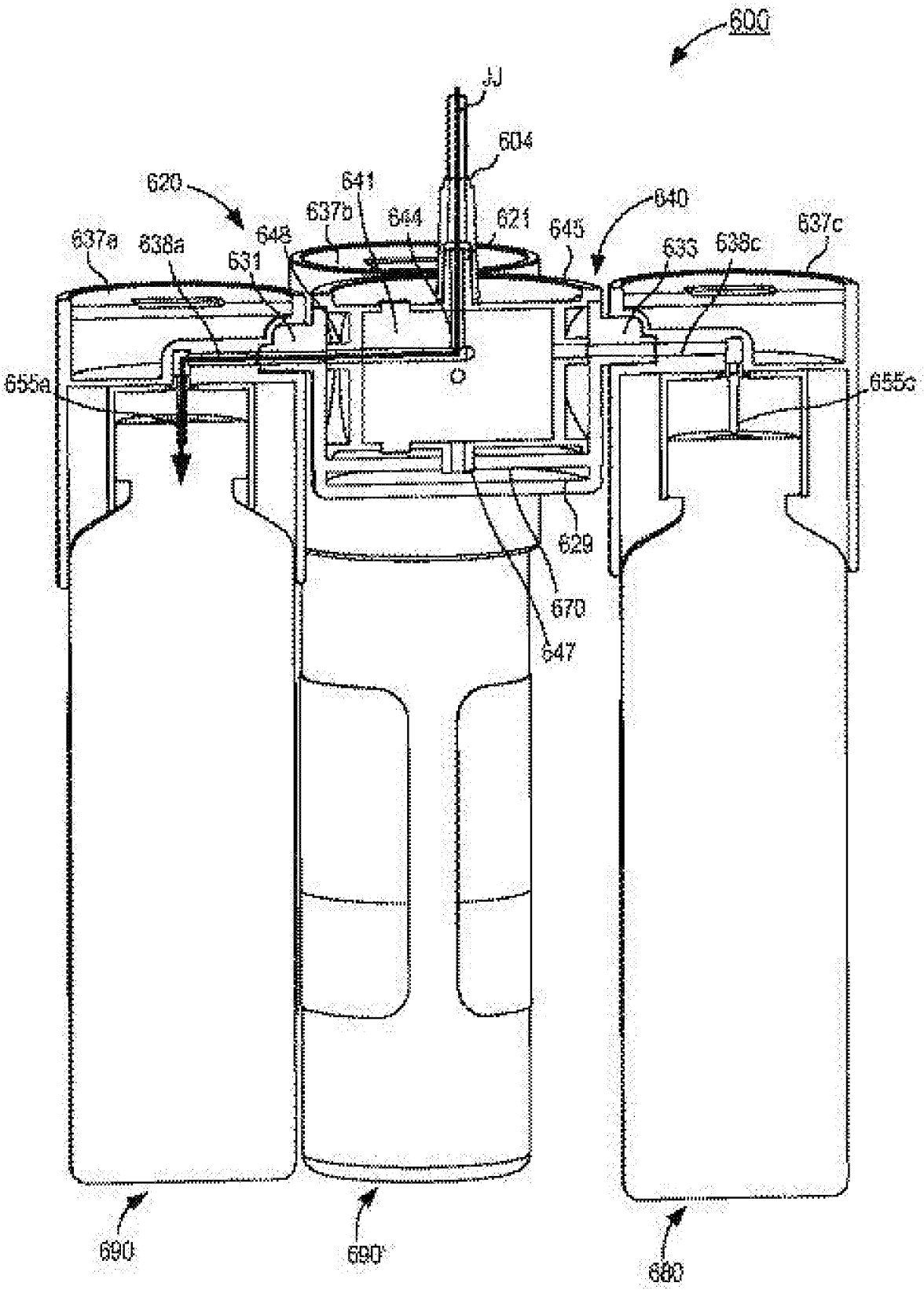

600
JJ
604
620
641
637b
644
621
645
640
637a
638a
648
631
633
638c
637c
655a
655c
629
670
647
690
690'
680

FIG. 33

[Fig. 34]

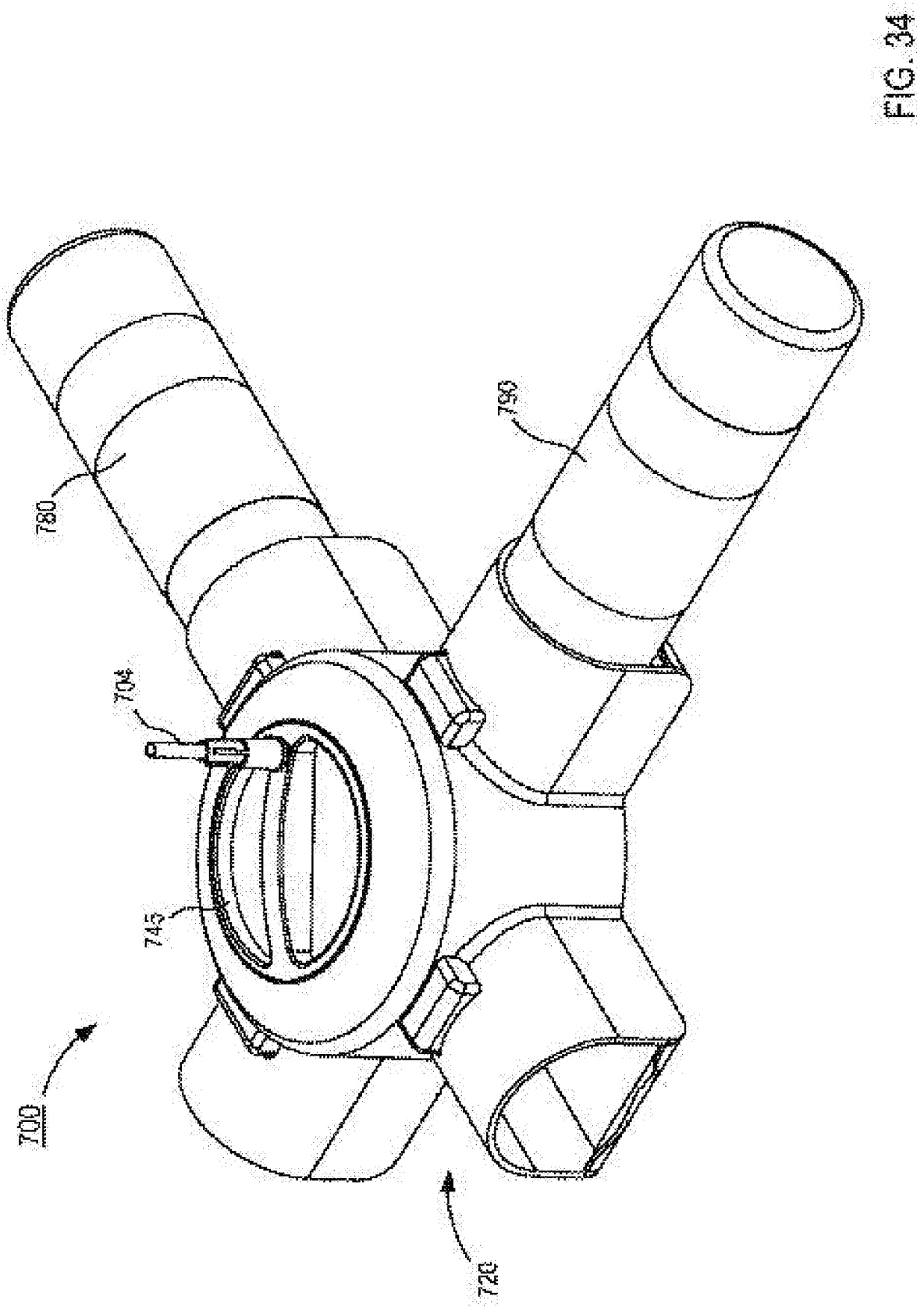
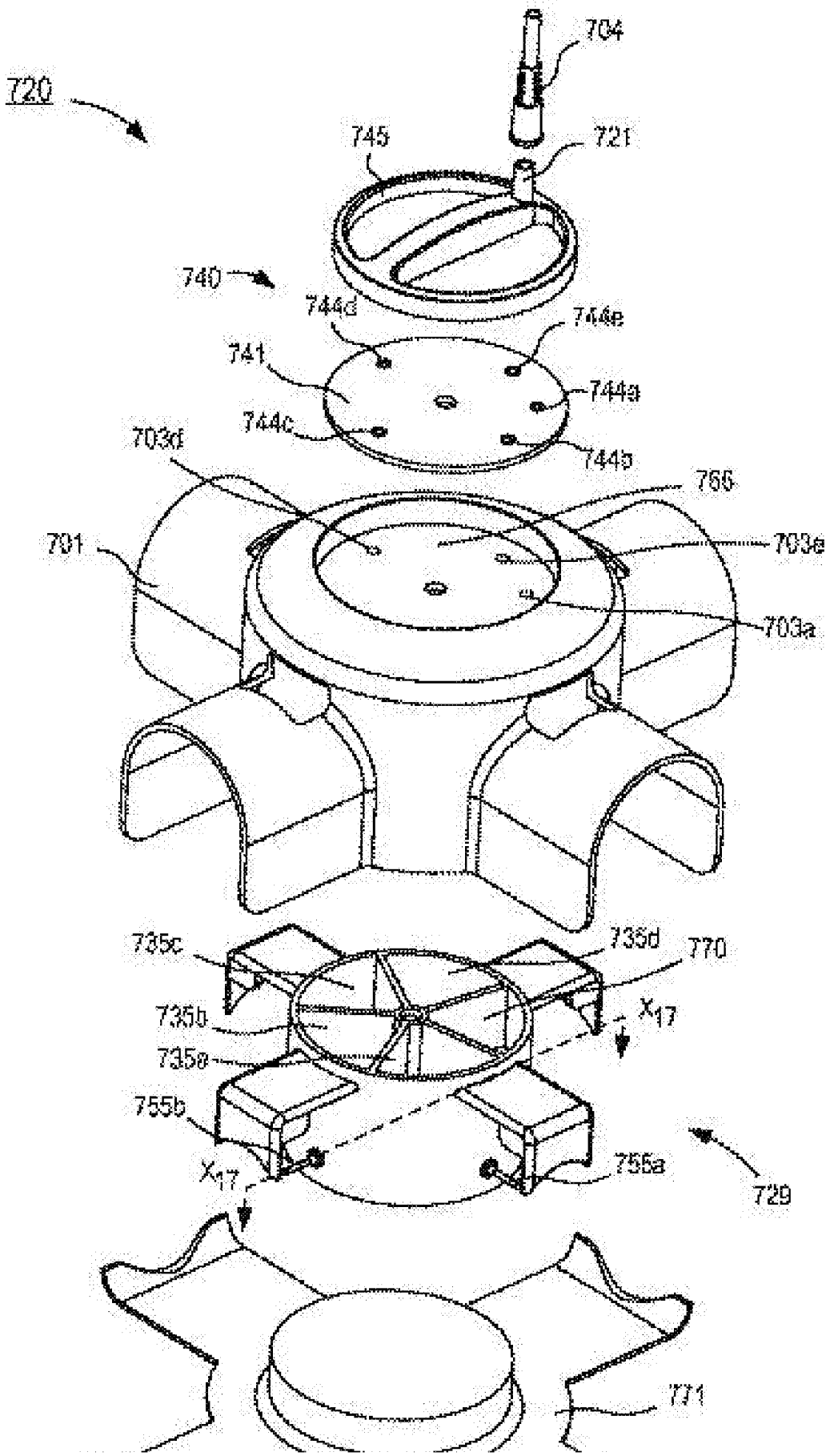


FIG. 34

[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]

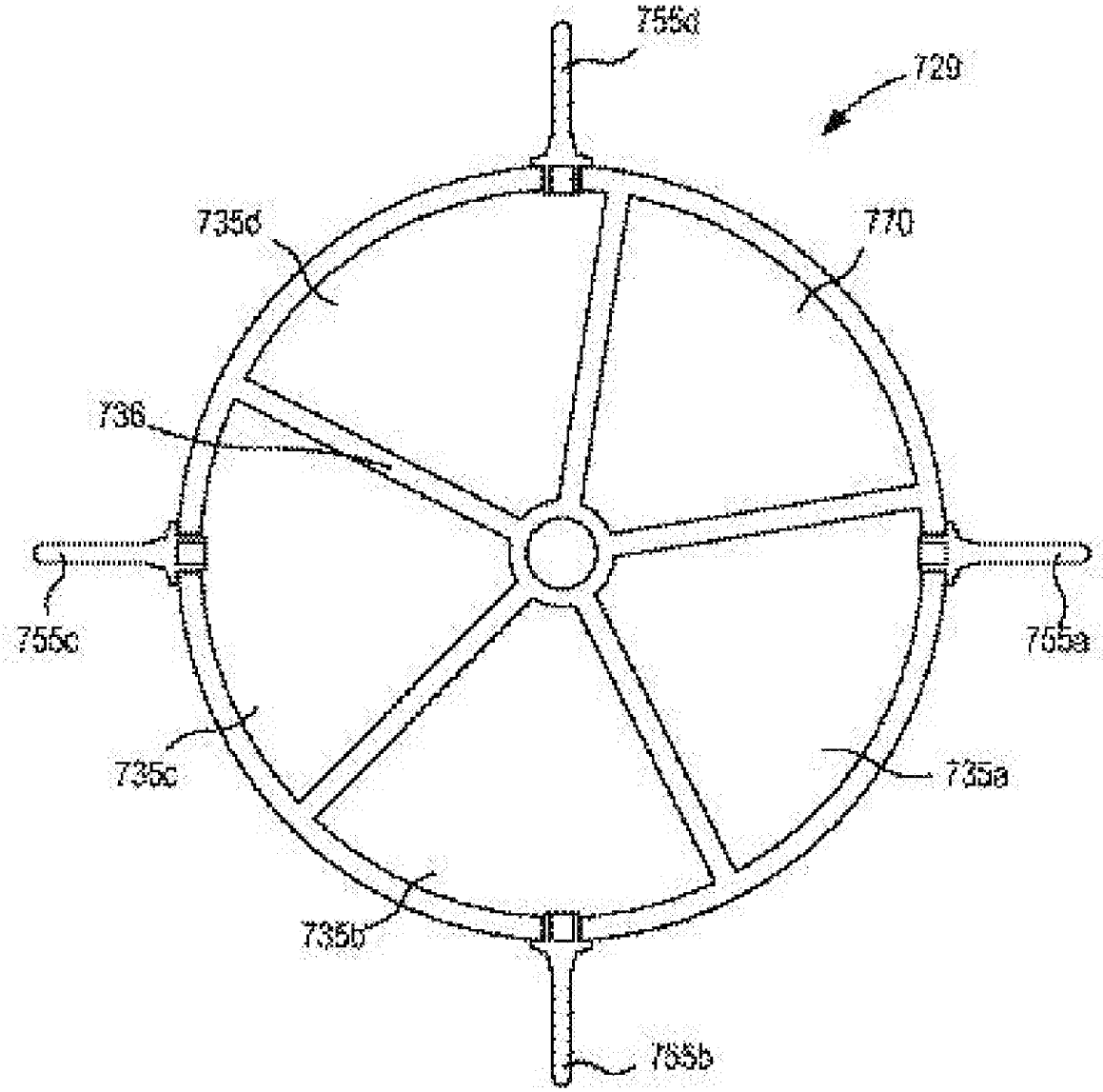


FIG. 36

[Fig. 37]

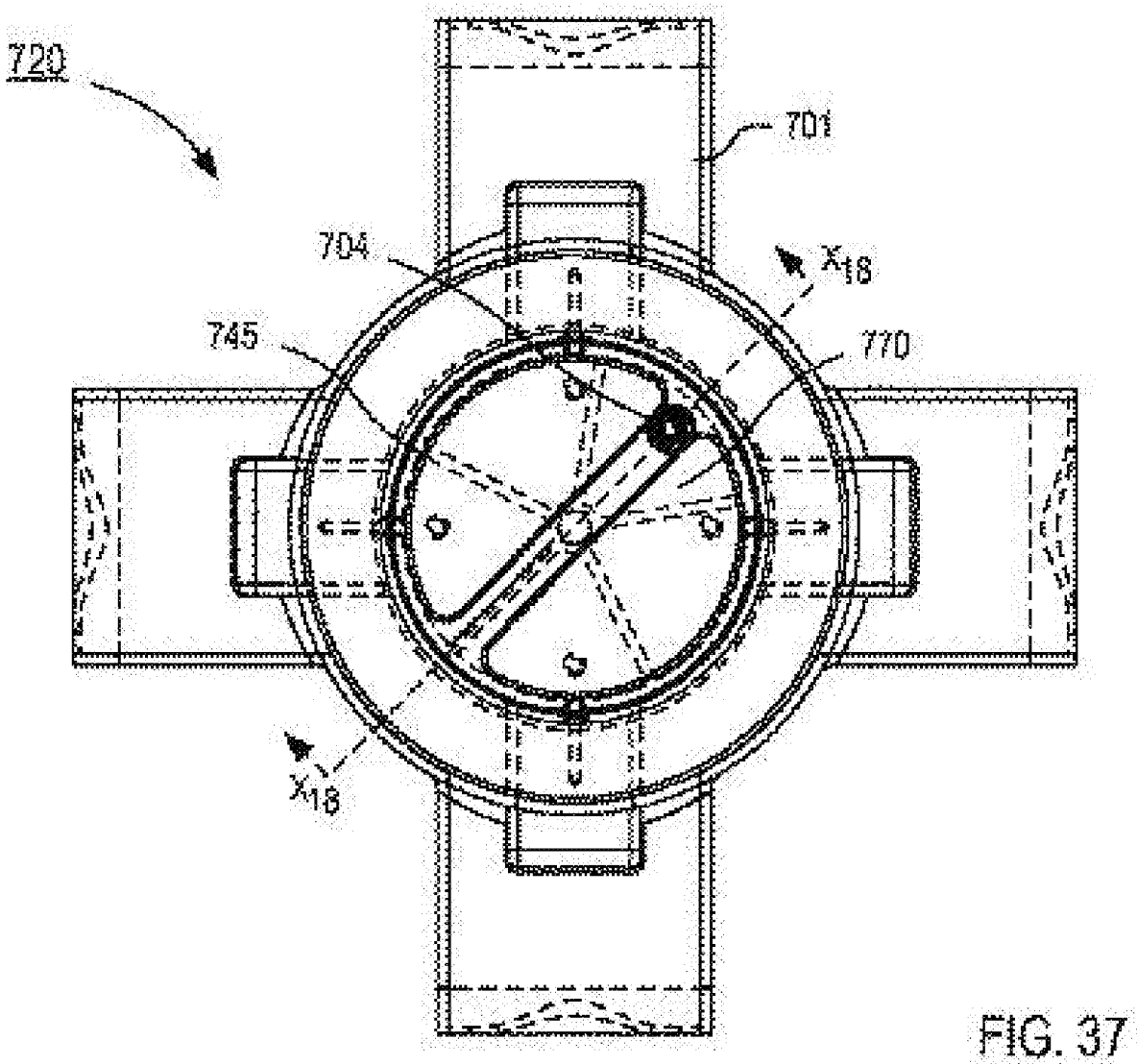


FIG. 37

[Fig. 38]

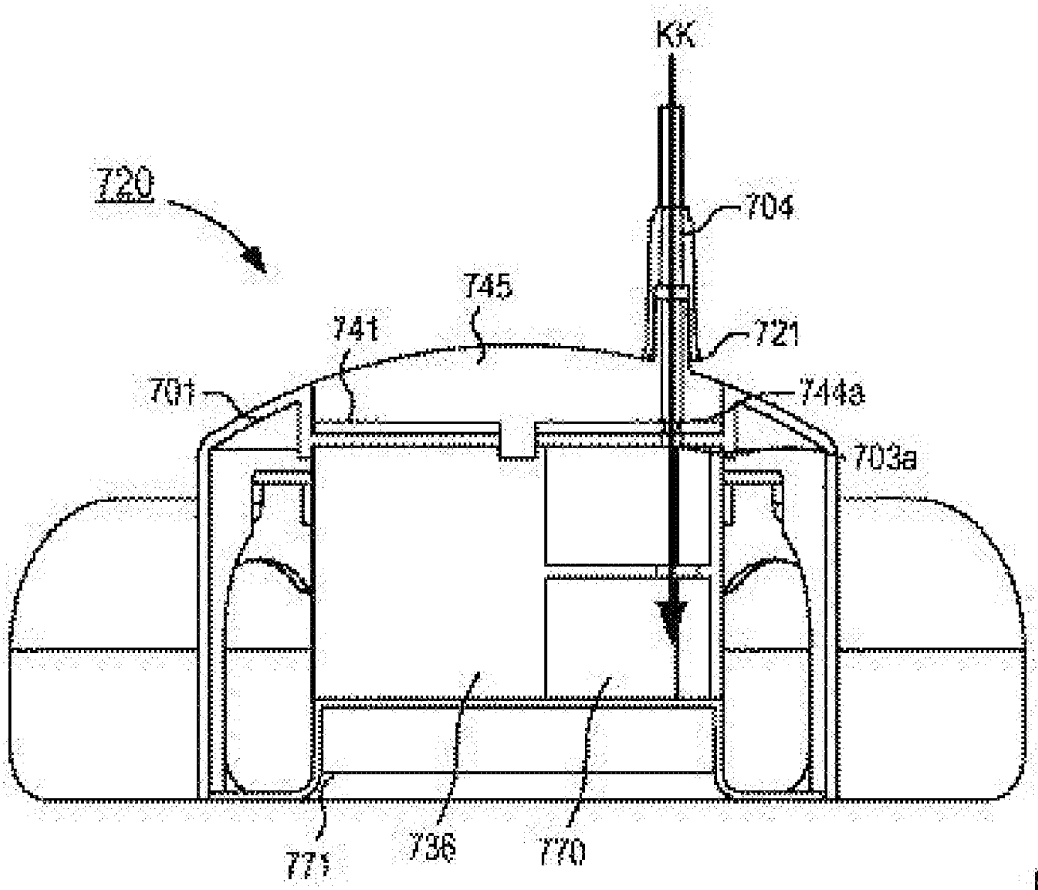


FIG. 38

[Fig.39]

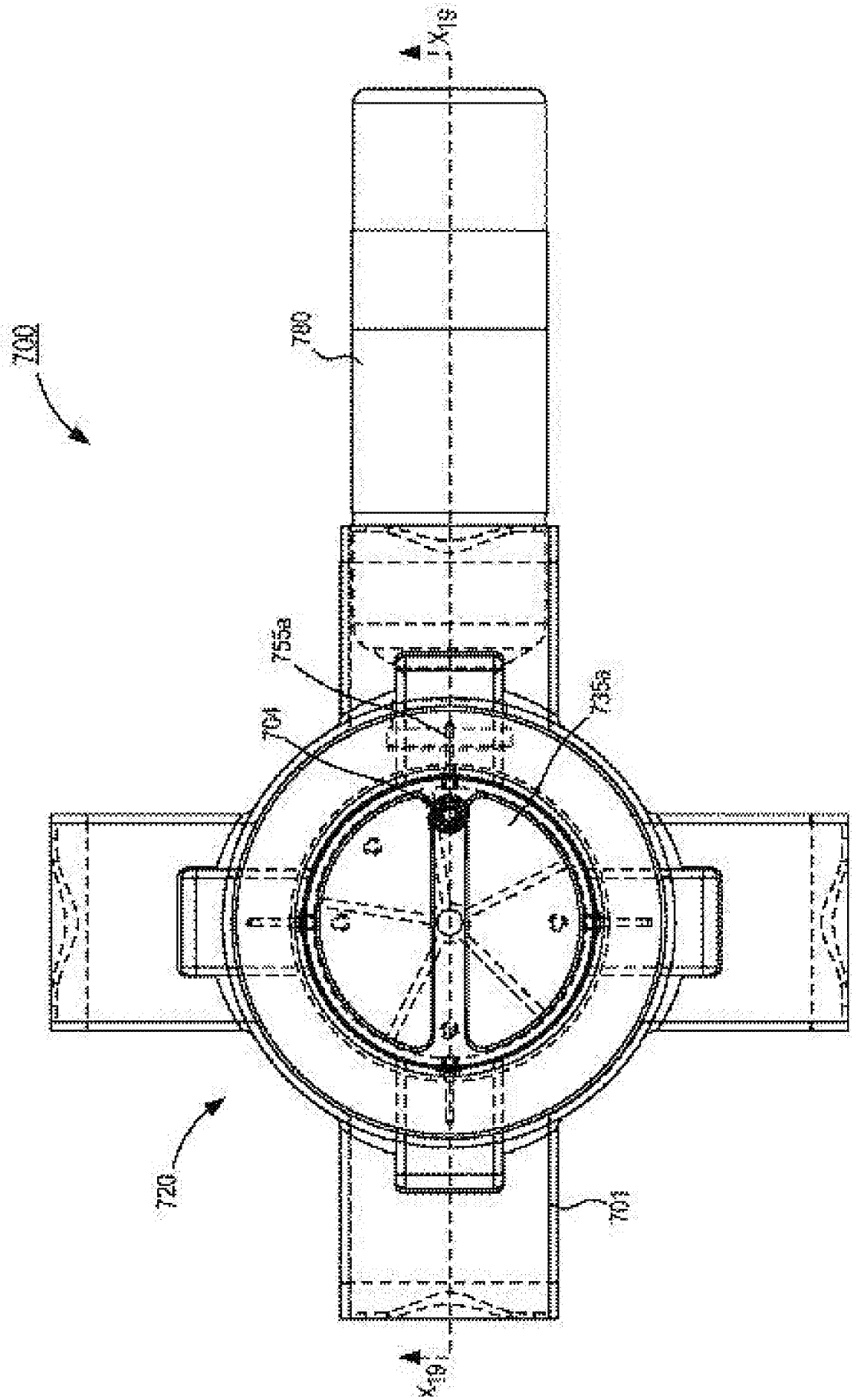


FIG. 39

[Fig. 40]

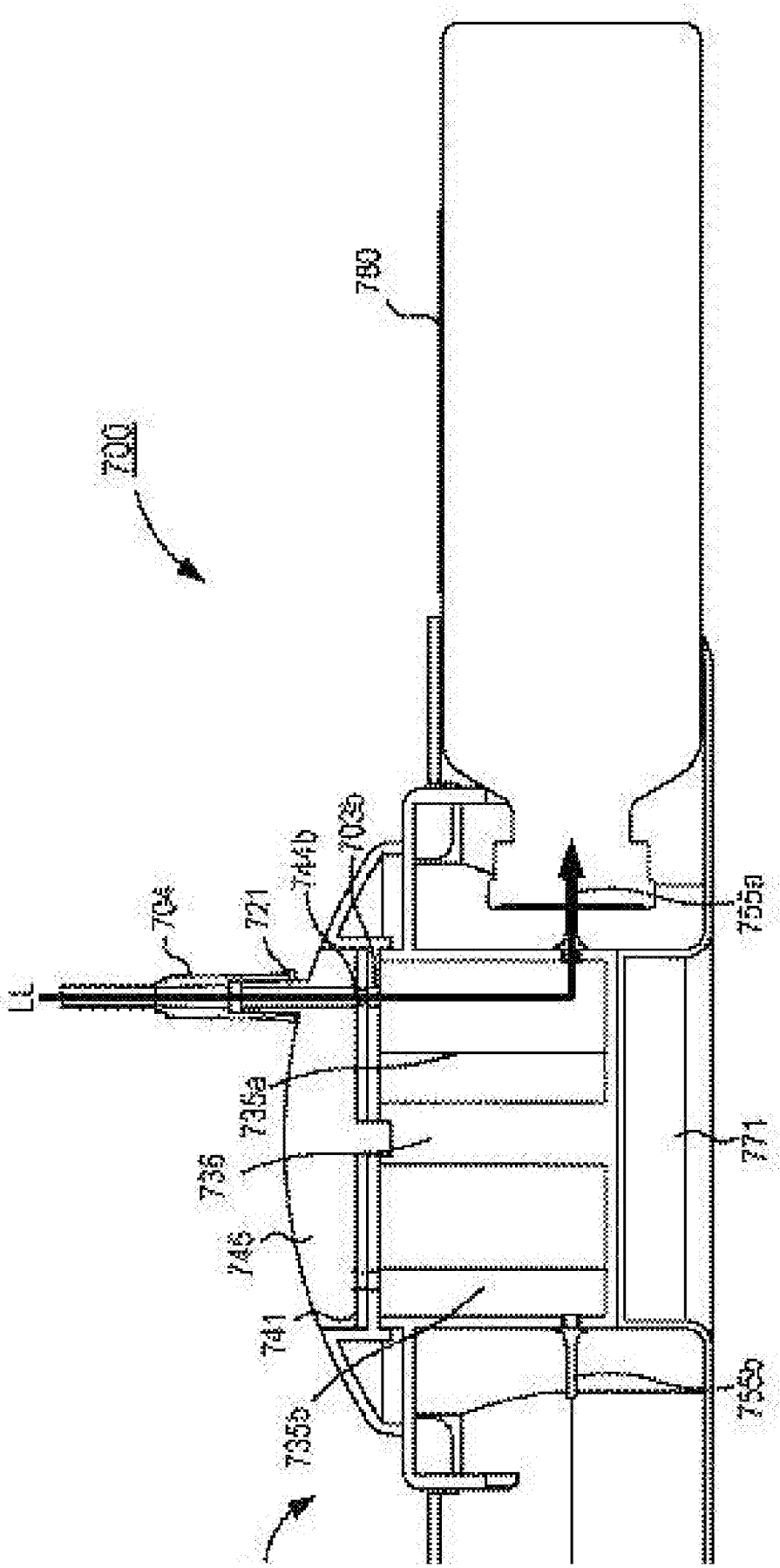
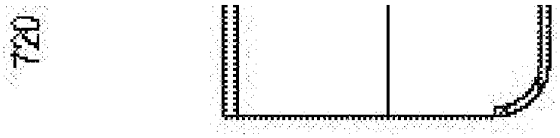
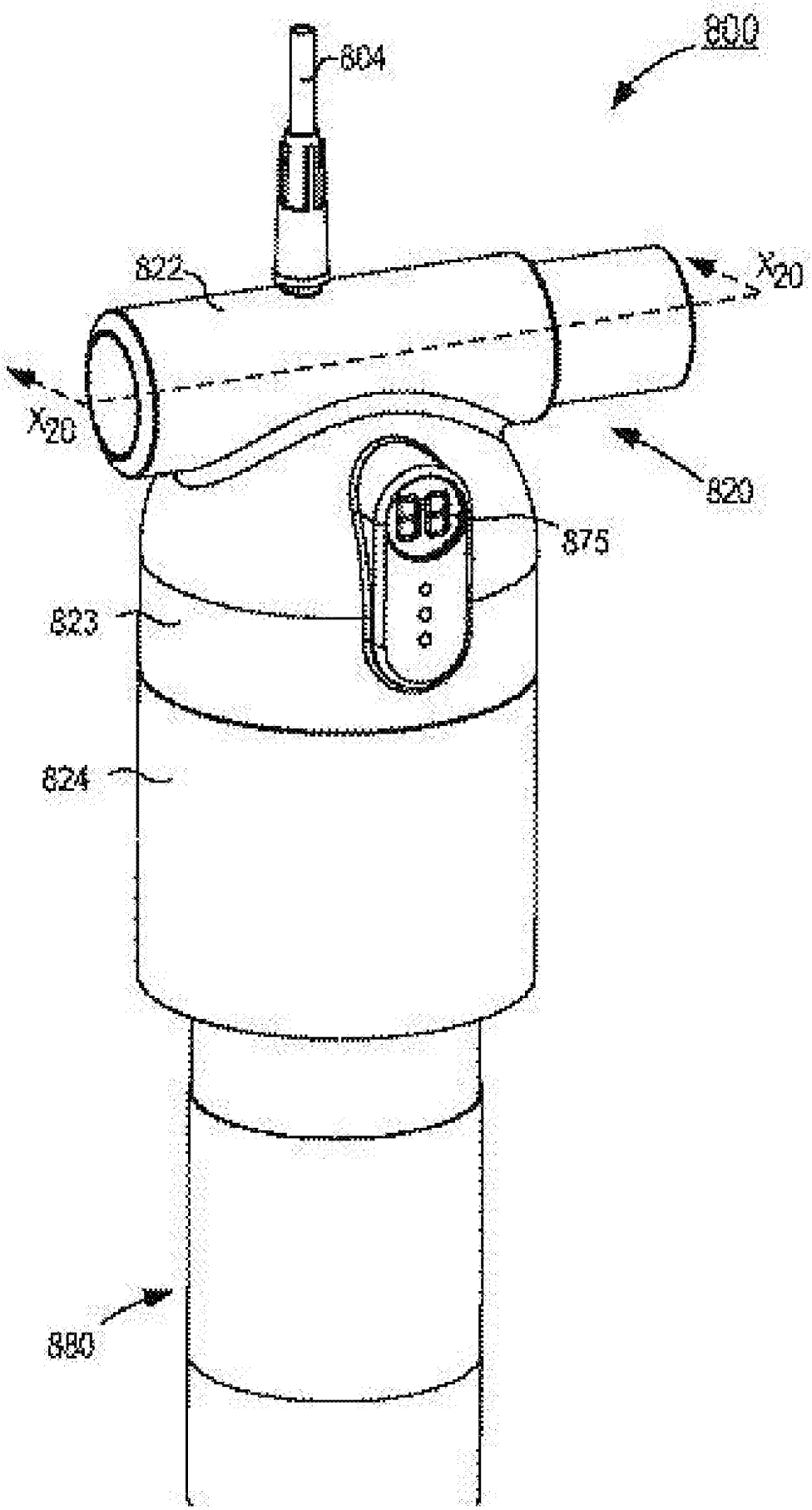

700
793
LL
704
721
744b
703a
755a
735a
735
746
741
735b
771
755b

FIG. 40

[Fig. 41]




800
804
822
X20
X20
820
875
823
824
880

[Fig. 42]

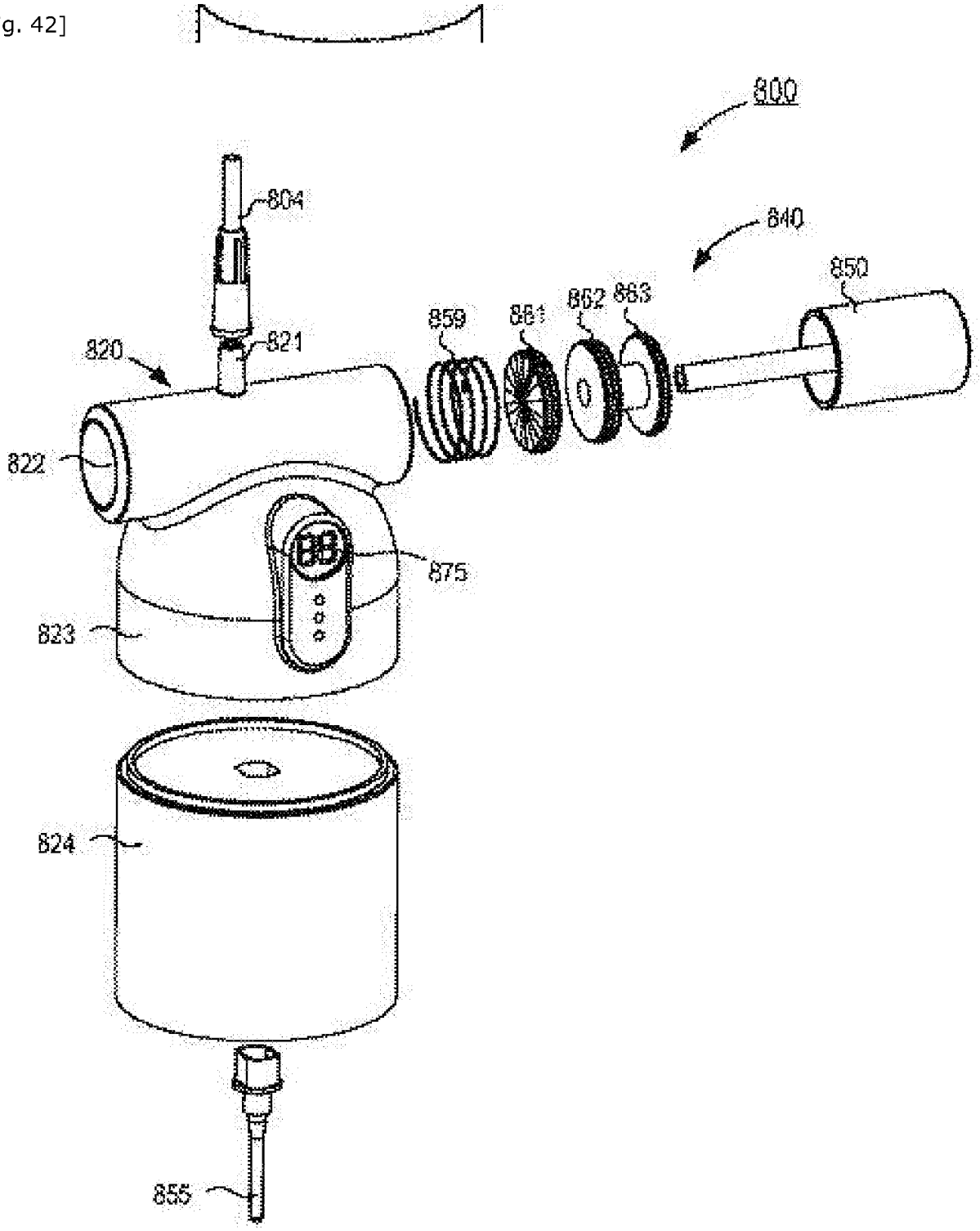
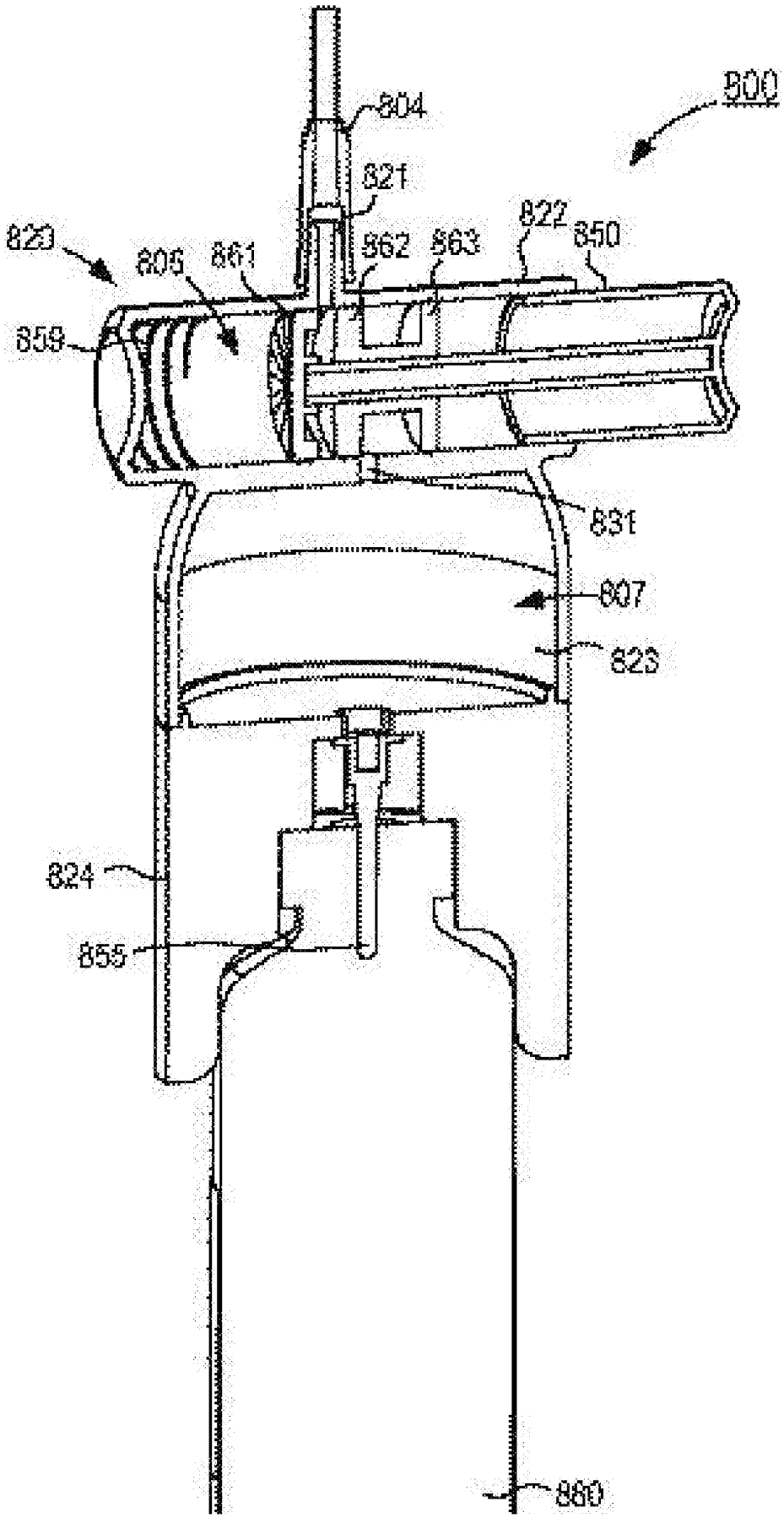


FIG. 42

[Fig. 43]


800
804
821
822
850
820
805
861
862
863
859
831
807
823
824
855
860

[Fig. 44]

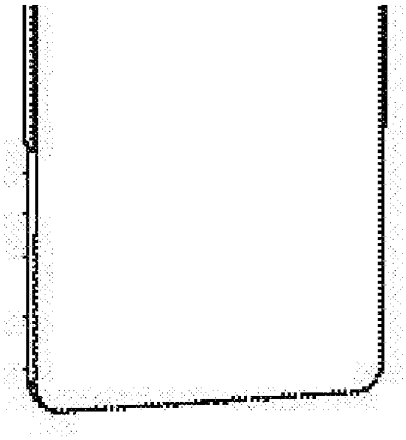
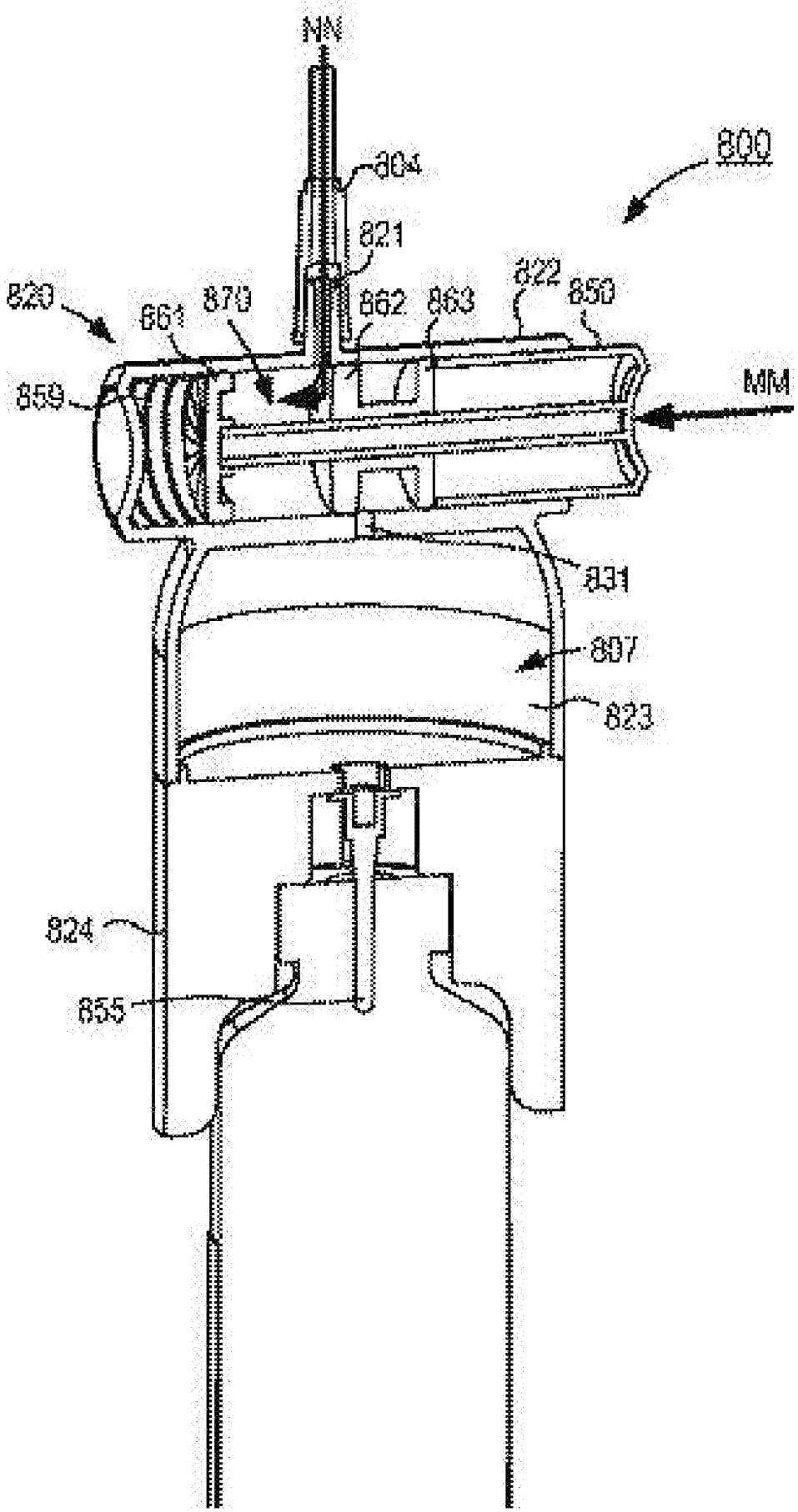


FIG. 43


NN
800
804
821
822
850
820
661
870
862
863
859
MM
831
807
823
824
855

[Fig. 45]

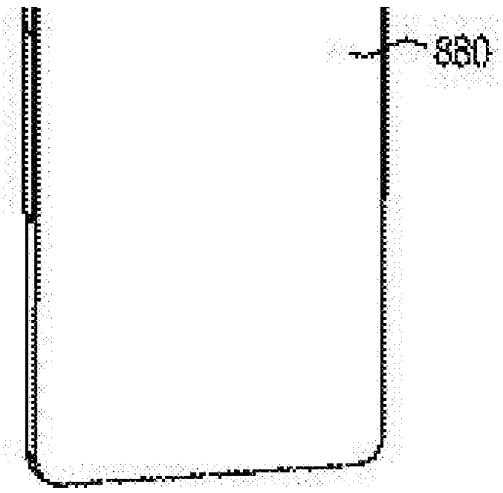
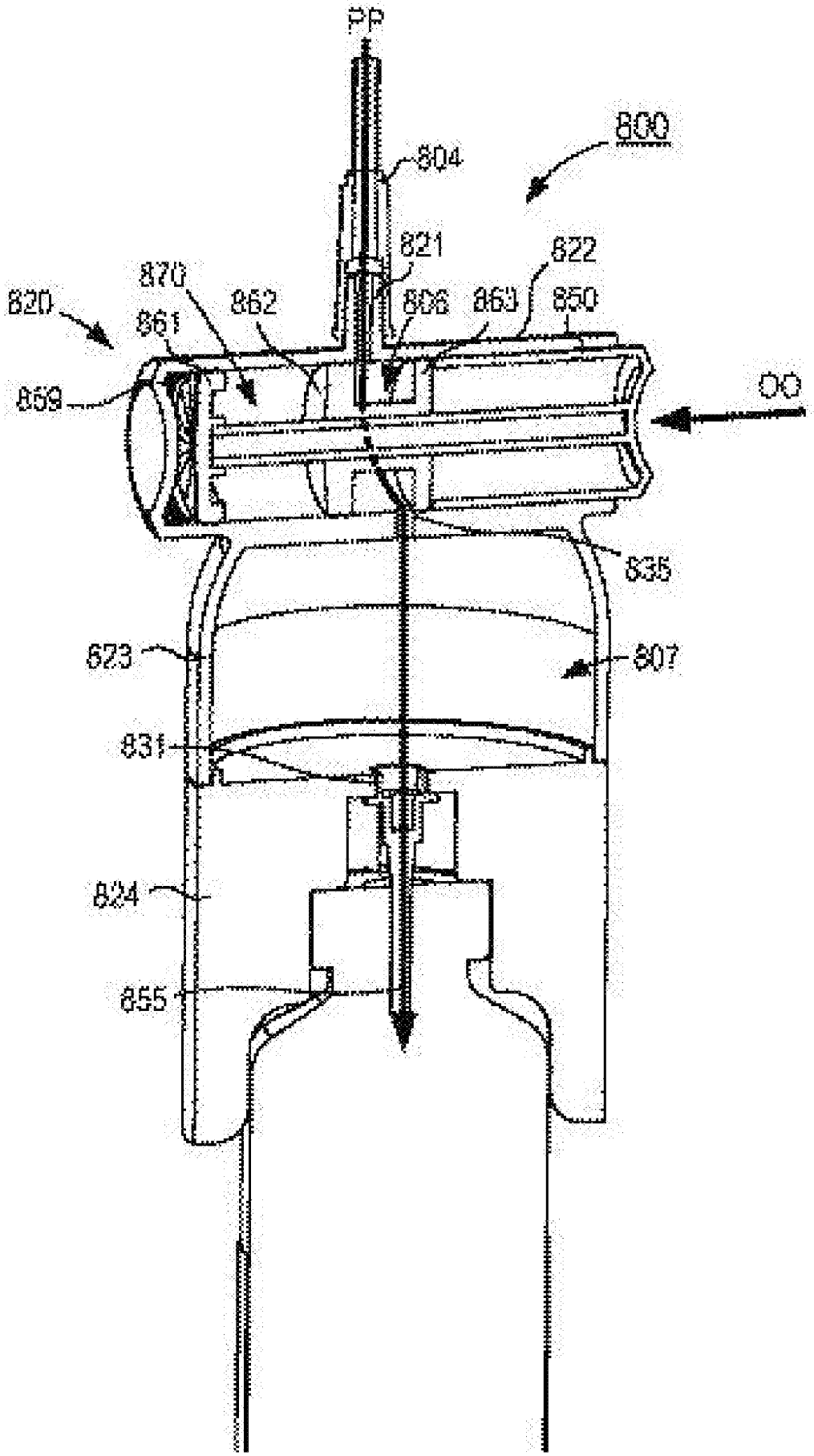


FIG. 44


PP
800
804
821
822
870
820
862
806
863
850
861
859
00
835
823
807
831
824
855

[Fig. 46]

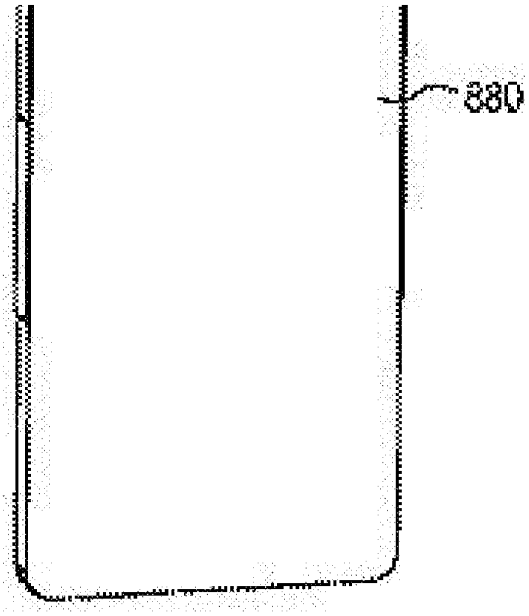
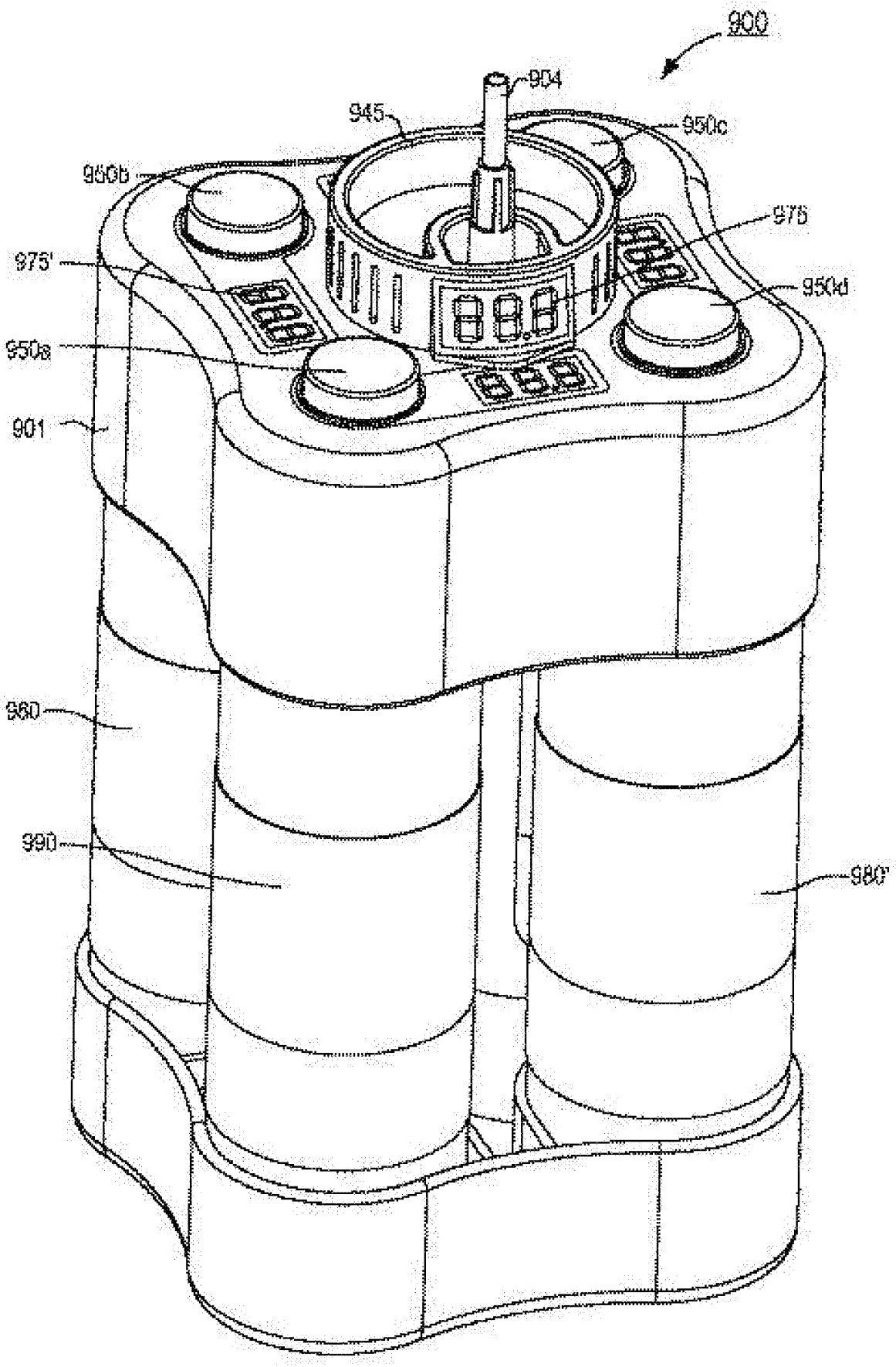
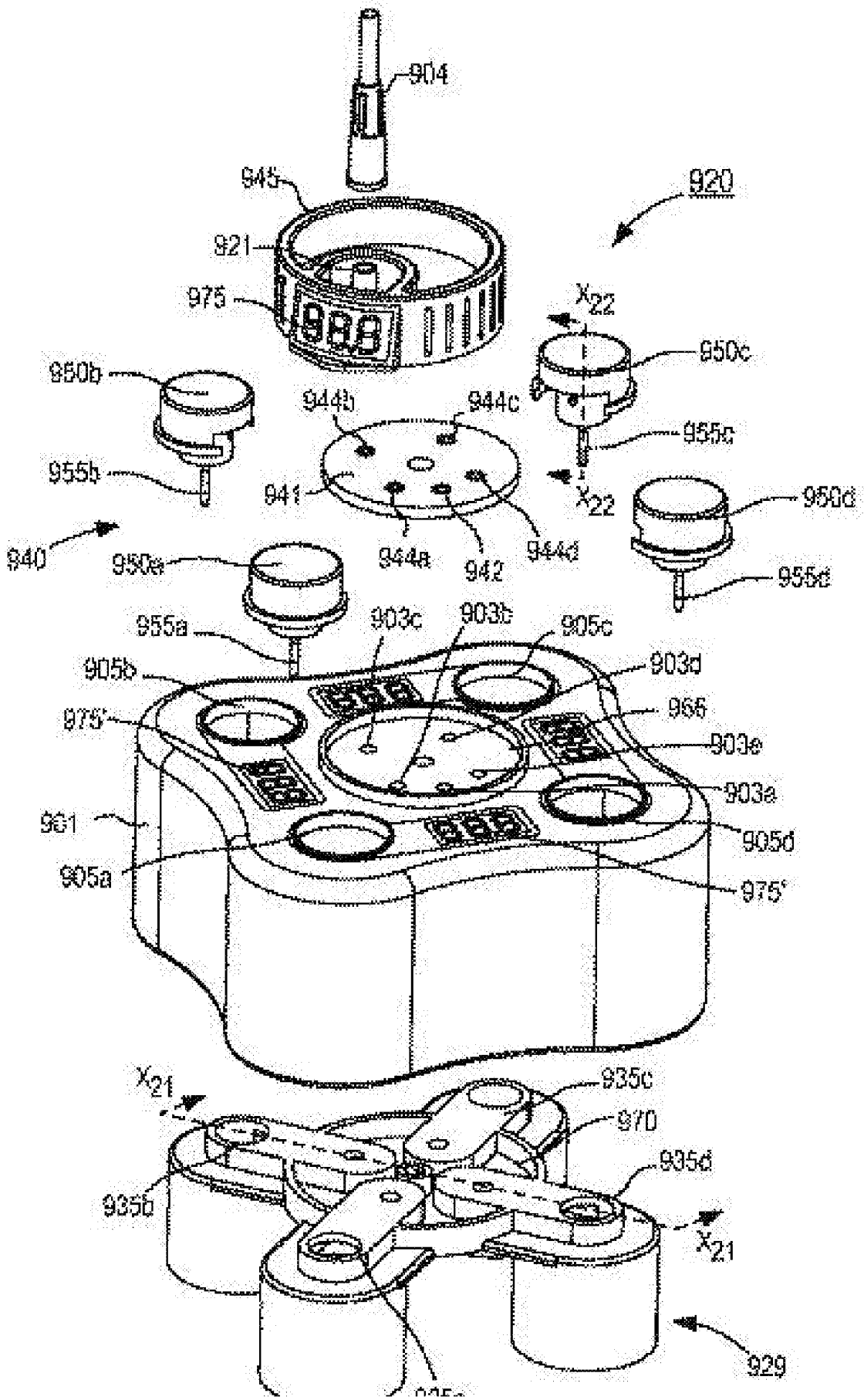


FIG. 45


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]

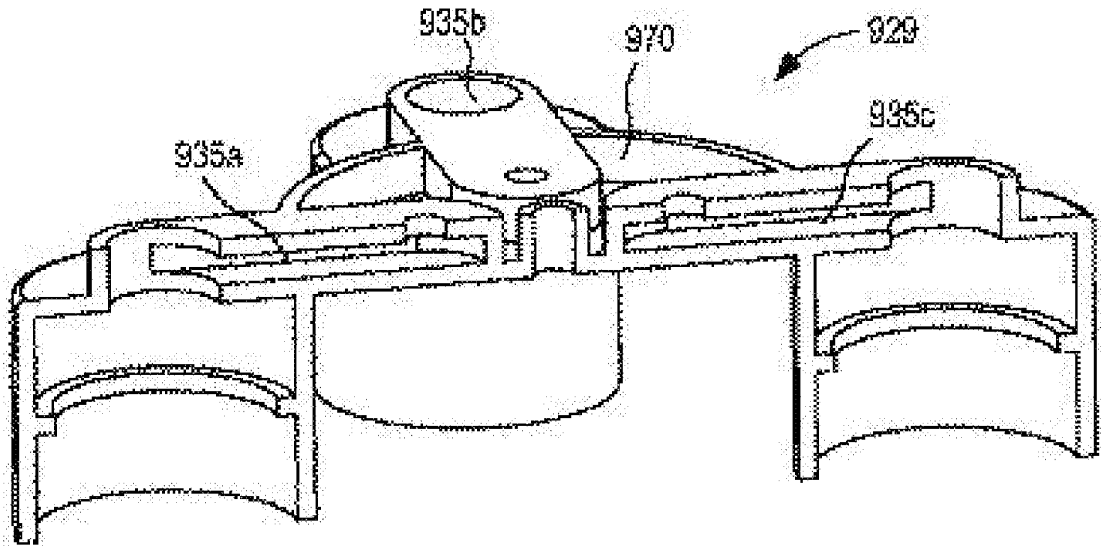


FIG. 48

[Fig. 49]

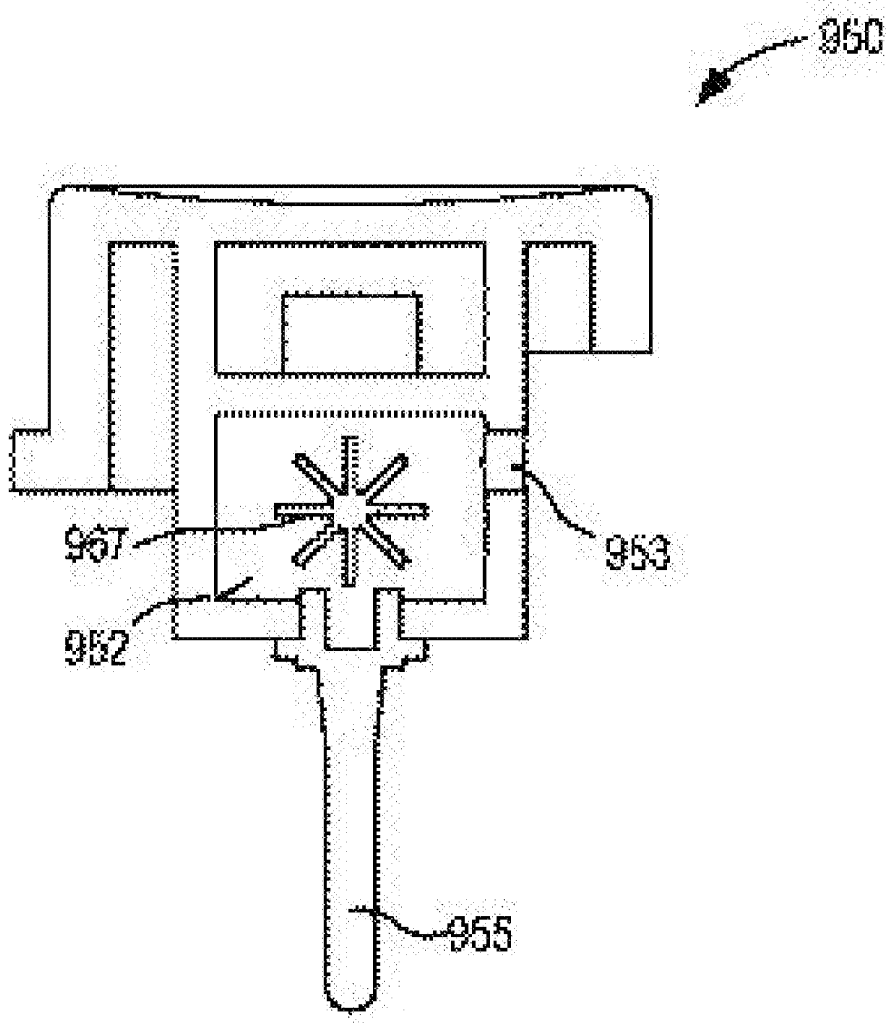


FIG. 49

[Fig. 50]

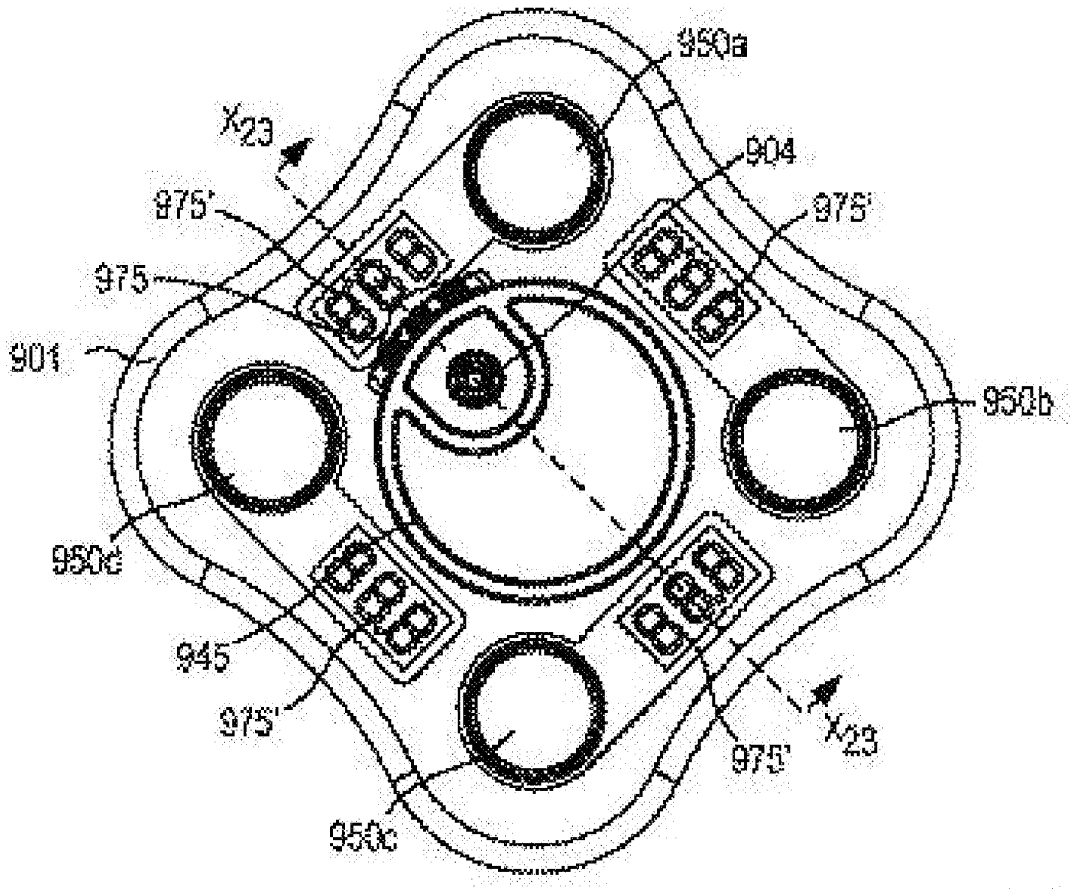


FIG. 50

[Fig. 51]

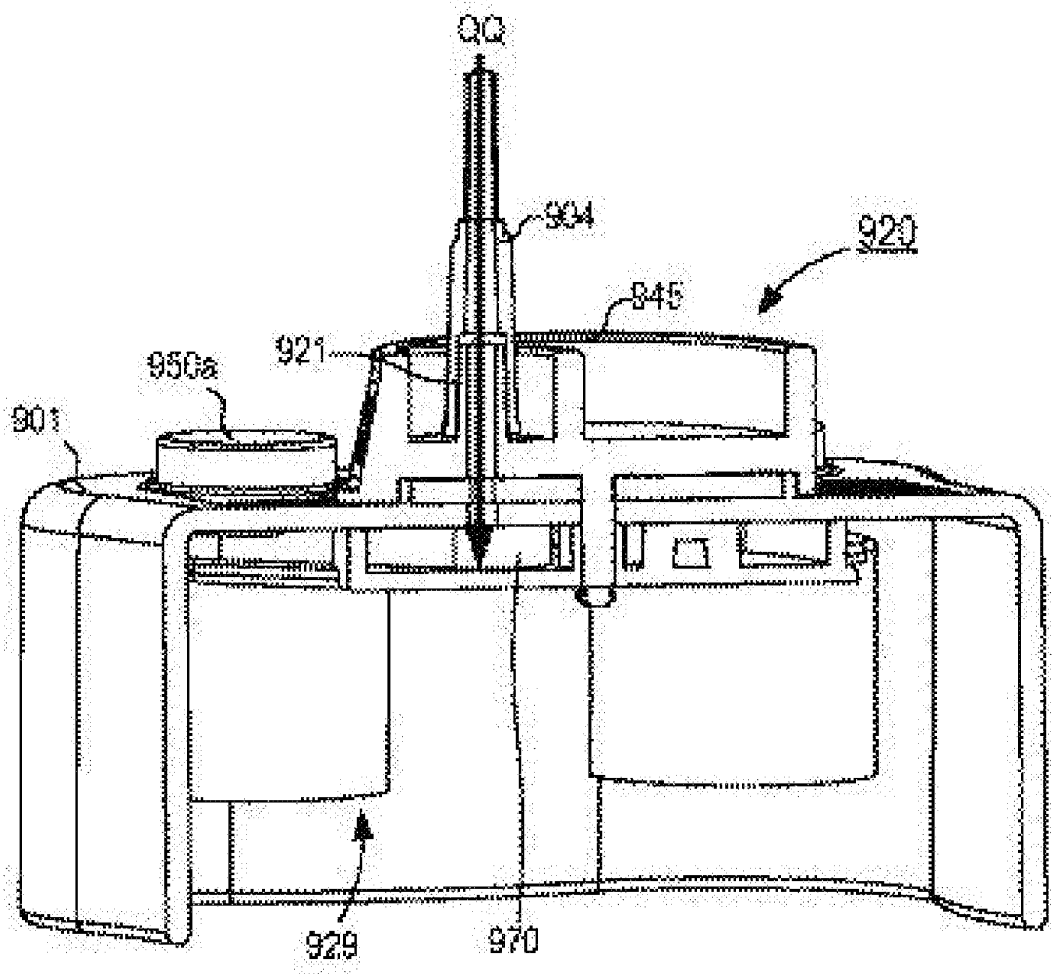


FIG. 51

[Fig. 52]

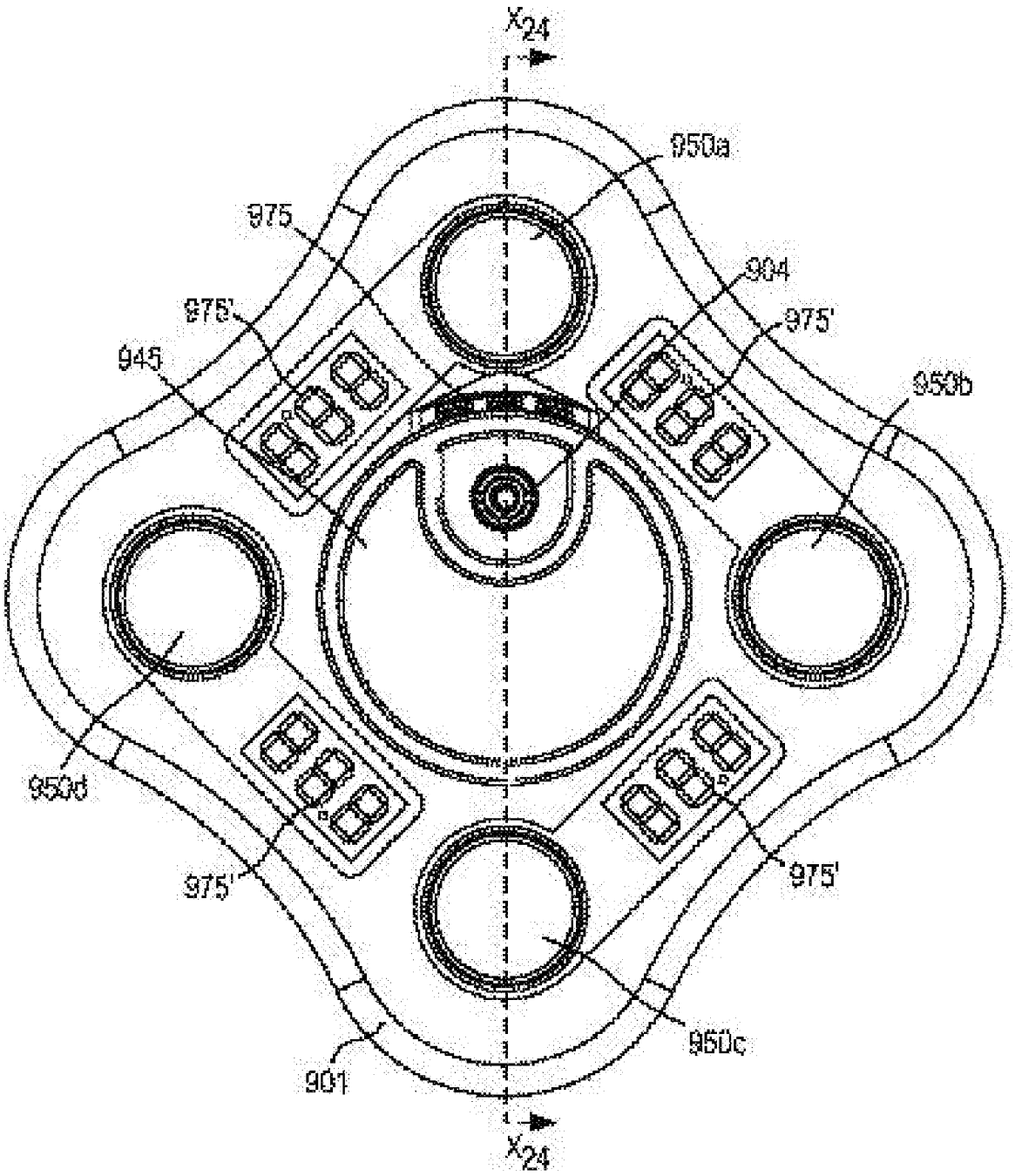
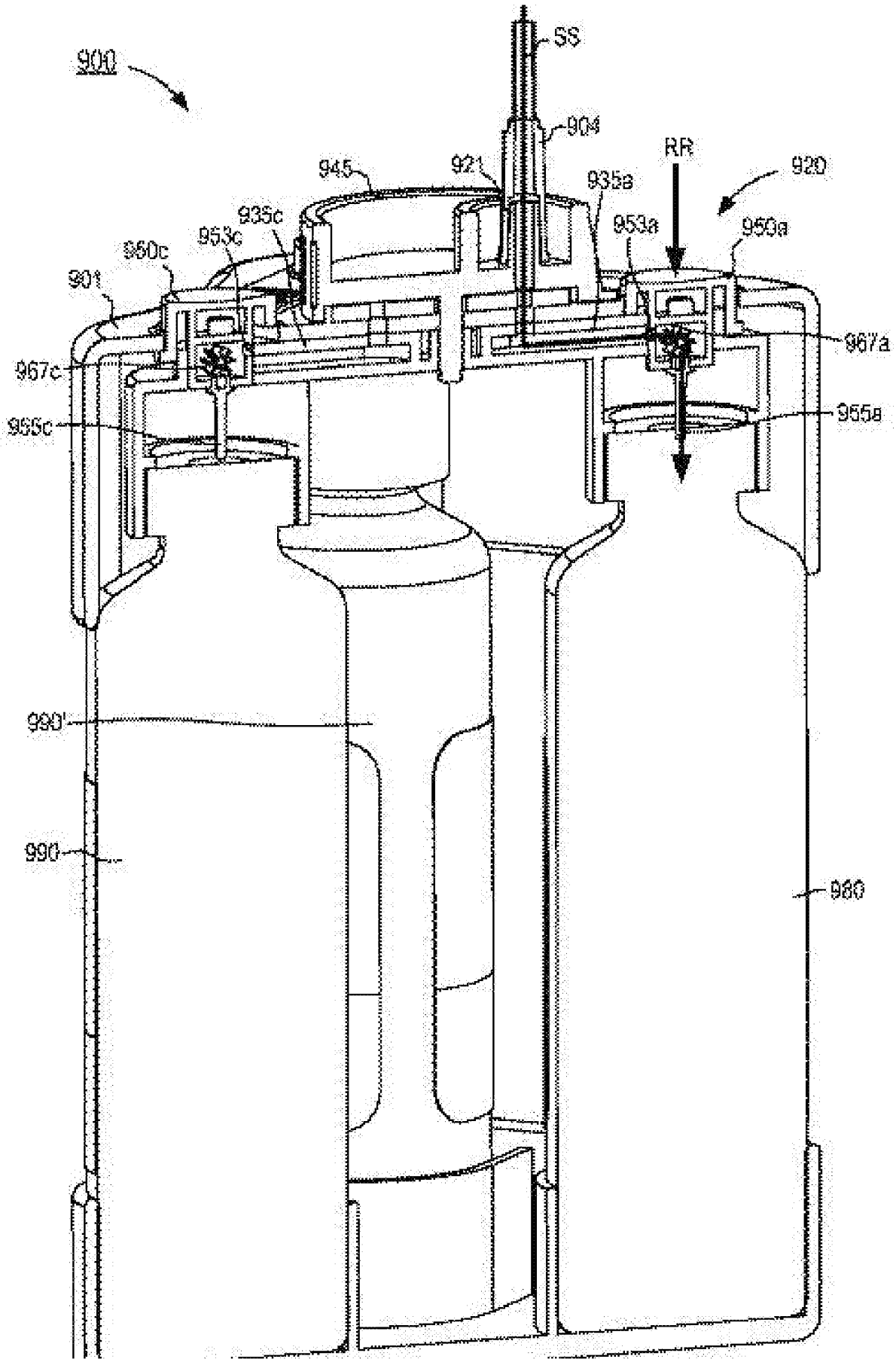
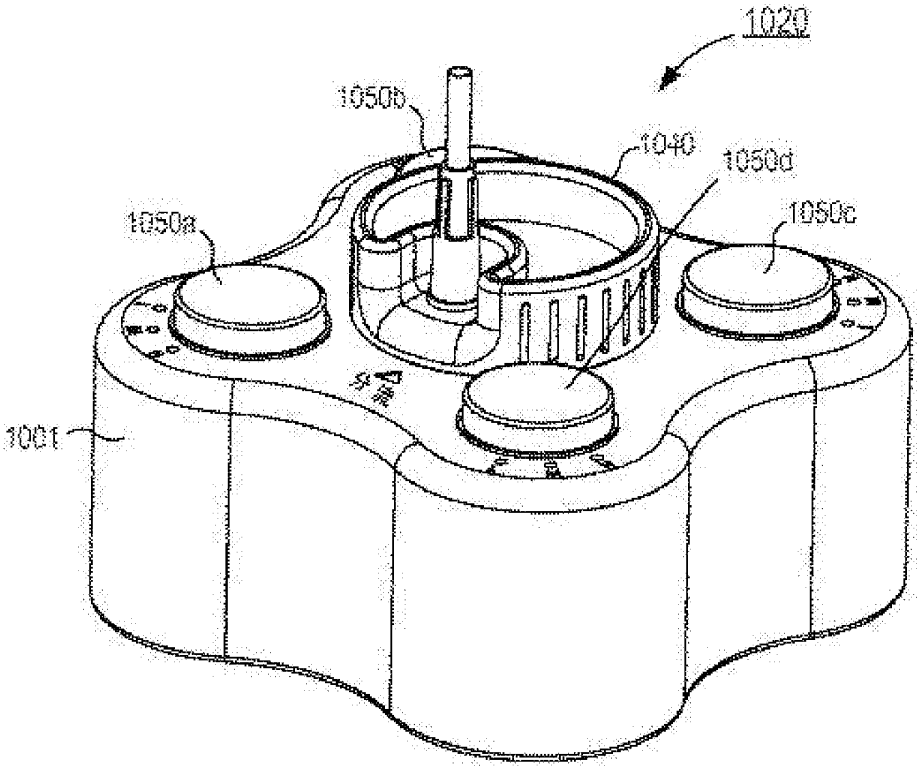


FIG. 52

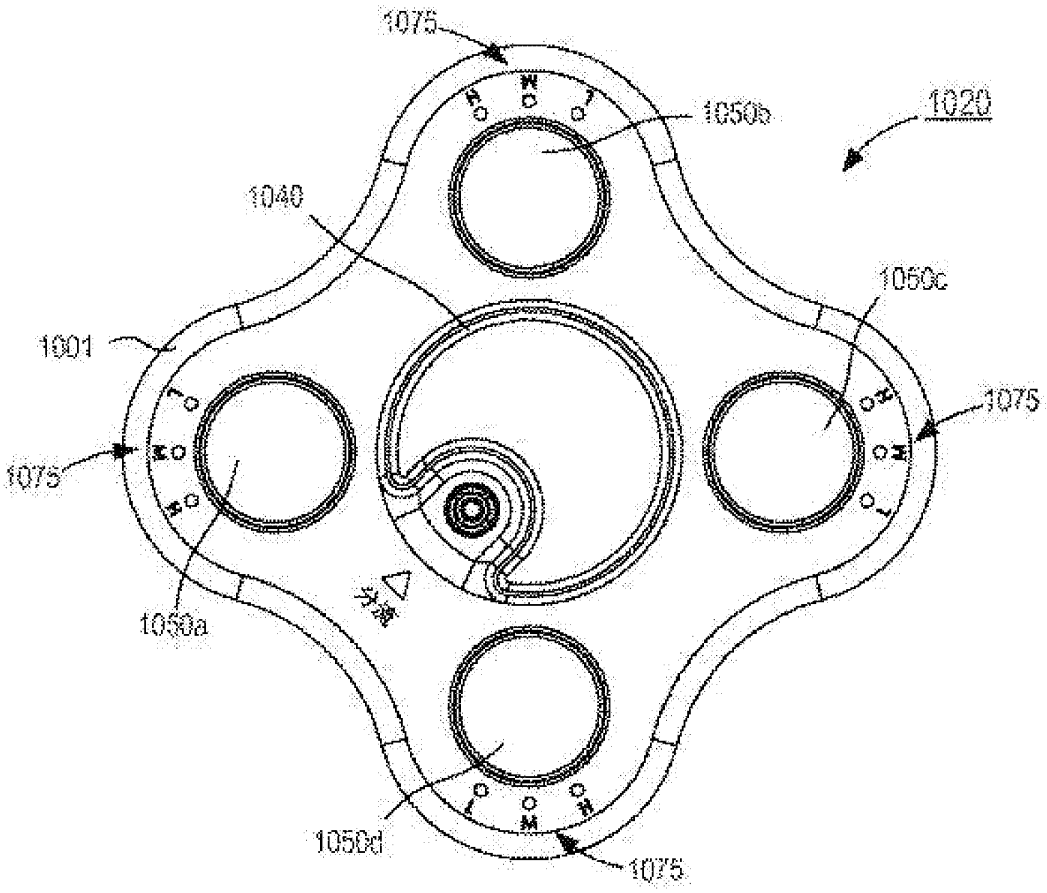
[Fig. 53]


900
SS
904
RR
920
945
921
935a
935c
953a
953c
950a
950c
901
967a
967c
955a
955c
990'
990
980

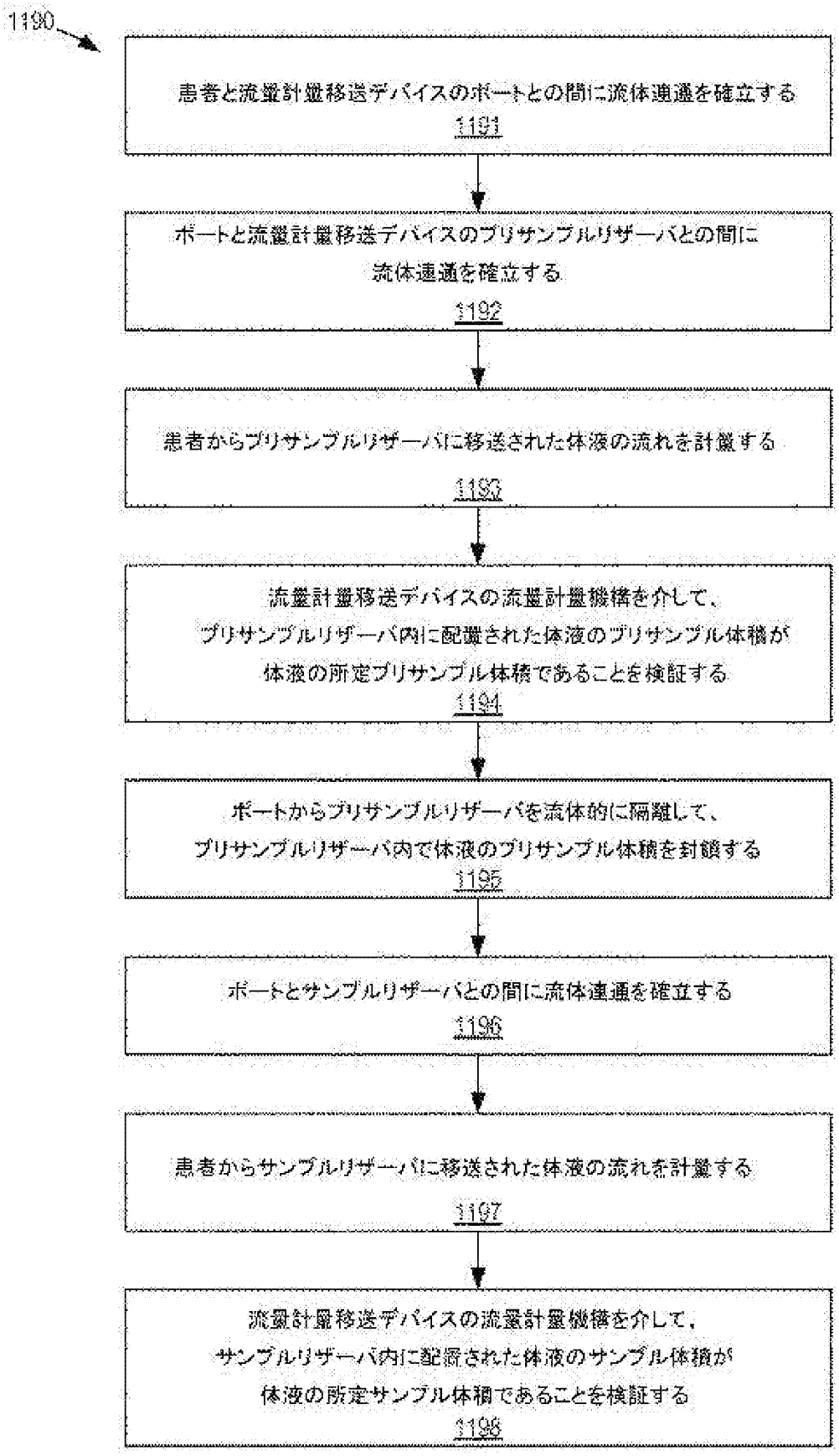
[Fig. 54]



[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	US 5,097,842 A (BONN) 24 March 1992 (24.03.1992) entire document	12, 15, 16, 18
Y		1-11, 13, 14, 17, 19-29
X	US 2008/0145933 A1 (PATTON) 19 June 2008 (19.06.2008) entire document	30-41
Y		3, 13, 17, 22, 24, 25,
Y	US 2005/0148993 A1 (MATHIAS et al) 07 July 2005 (07.07.2005) entire document	1-11
Y	WO 2005/068011 A1 (MEHLHORN) 28 July 2005 (28.06.2005) entire document	14, 21-29
Y	US 3,848,581 A (CINQUALBRE et al) 19 November 1974 (19.11.1974) entire document	9, 19, 20

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

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

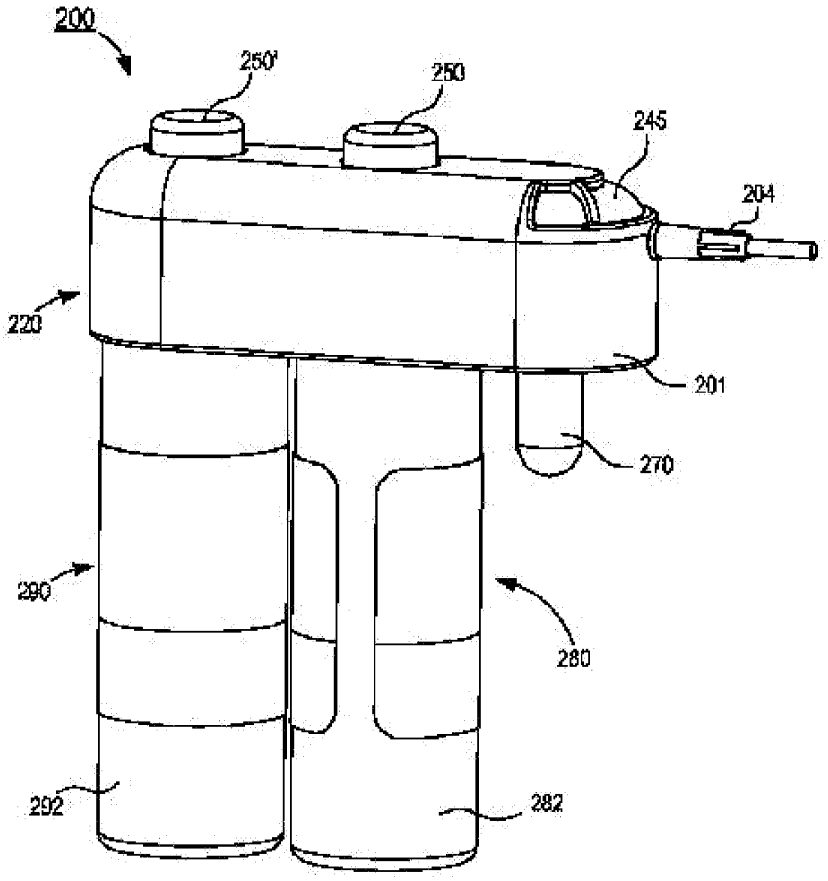


FIG. 2

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

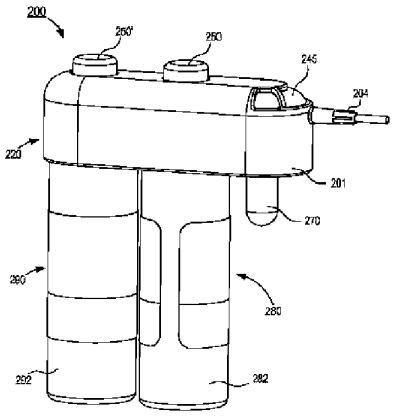


FIG. 2

【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】

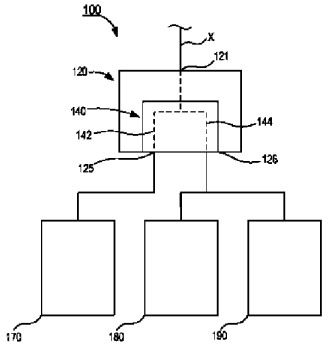


FIG. 1

【図２】

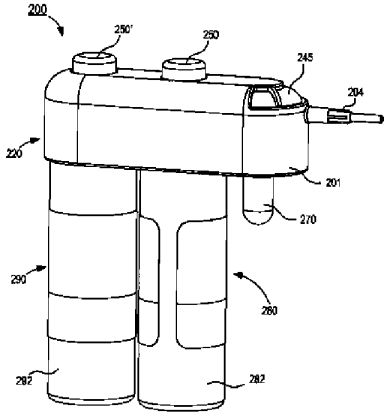


FIG. 2

【図３】

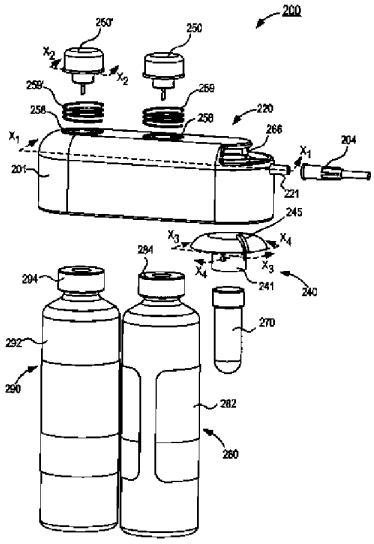


FIG. 3

【図４】

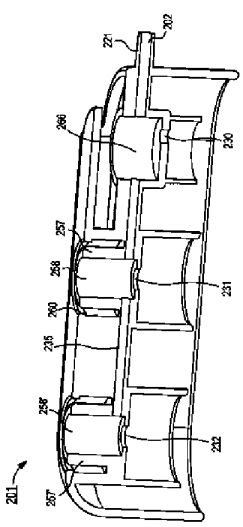


FIG. 4

【図５】

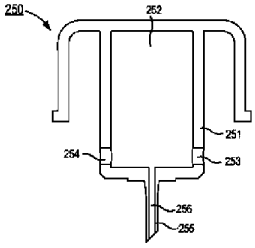


FIG. 5

【図６】

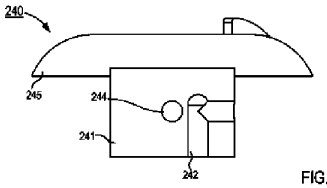


FIG. 6

【図７】

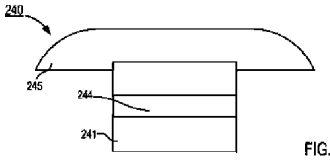


FIG. 7

【図８】

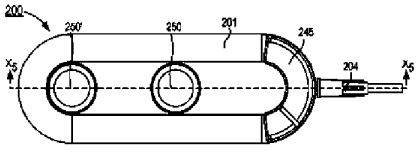


FIG. 8

【図９】

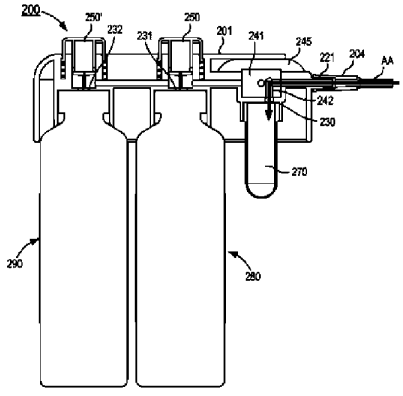


FIG. 9

【図１０】

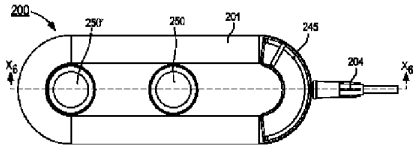


FIG. 10

【図１１】

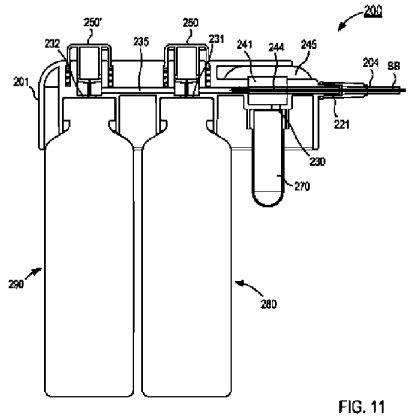


FIG. 11

【図１２】

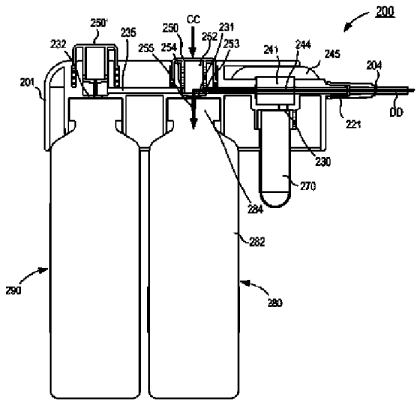


FIG. 12

【図１３】

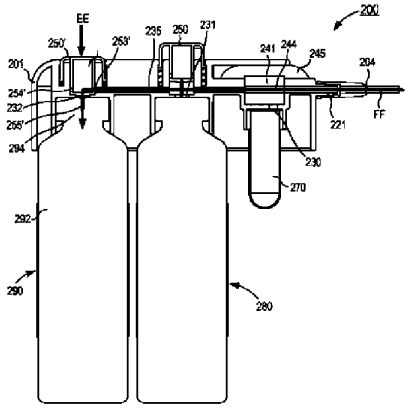


FIG. 13

【図１４】

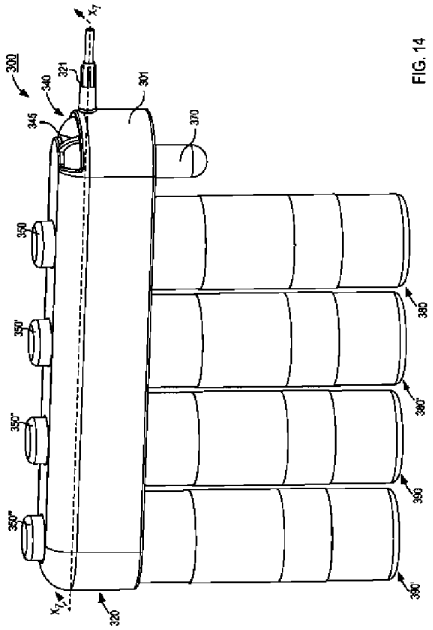


FIG. 14

【図１５】

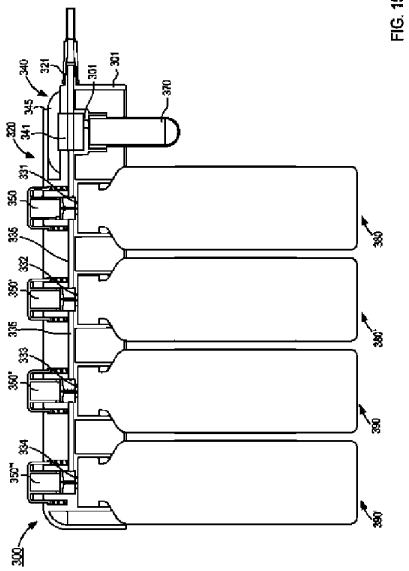


FIG. 15

【図１６】

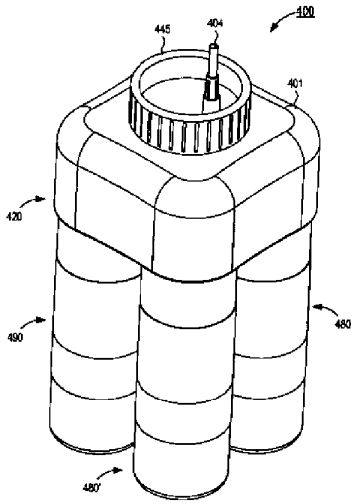


FIG. 16

【図１７】

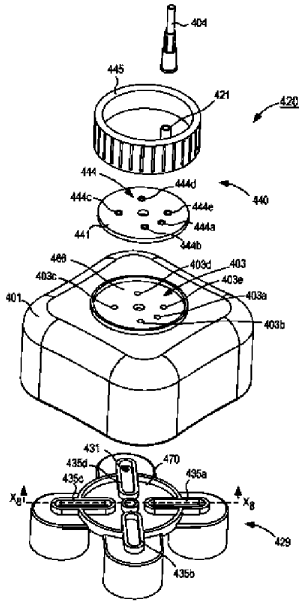


FIG. 17

【図１８】

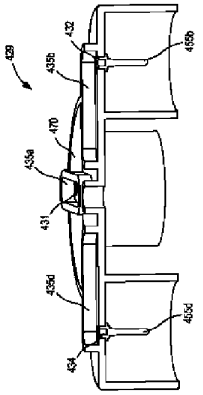


FIG. 18

【図１９】

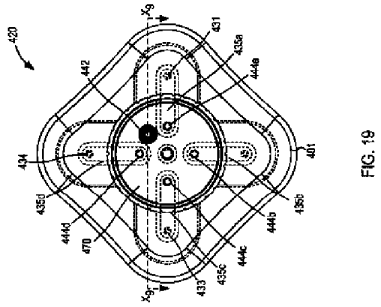


FIG. 19

【図２０】

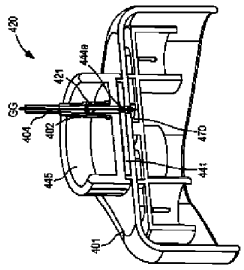


FIG. 20

【図２１】

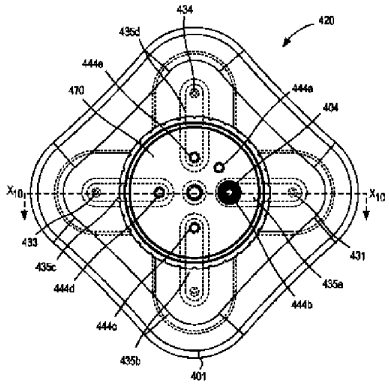


FIG. 21

【図２２】

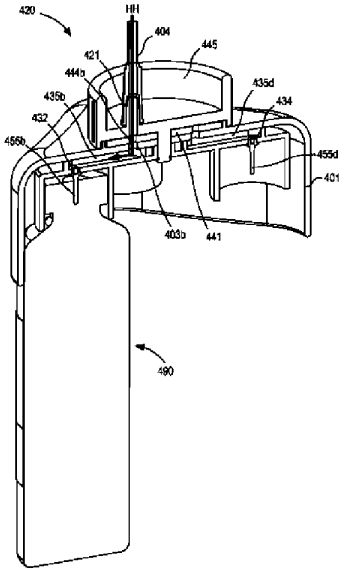


FIG. 22

【図２３】

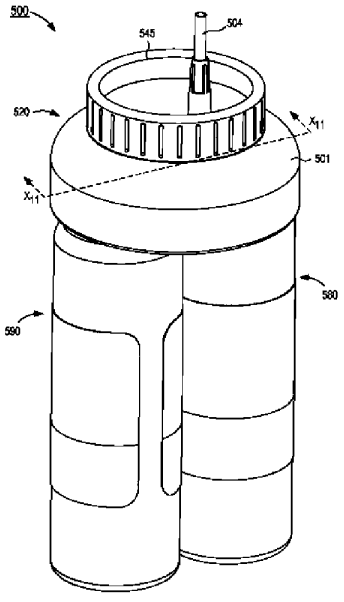


FIG. 23

【図２４】

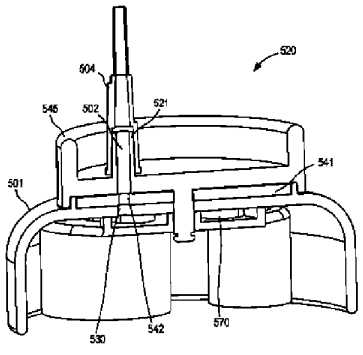


FIG. 24

【図２５】

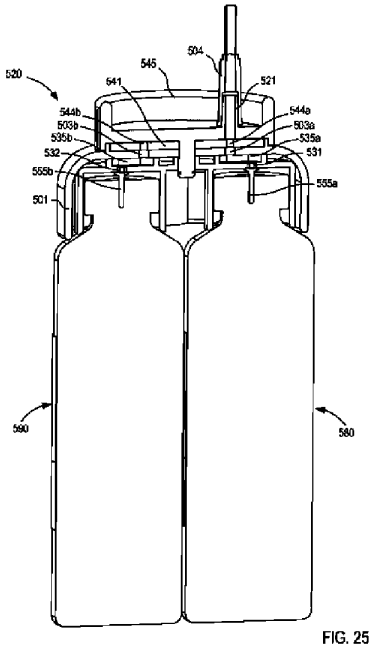


FIG. 25

【図２６】

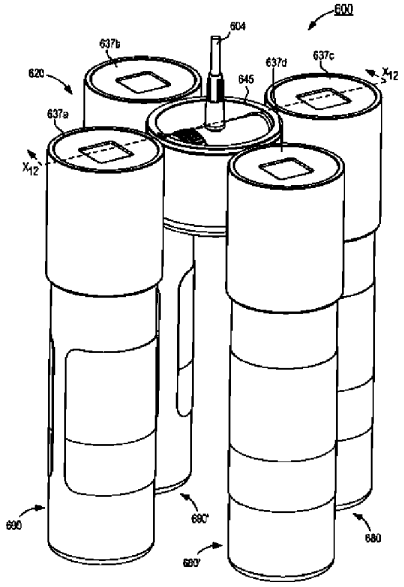


FIG. 26

【図２７】

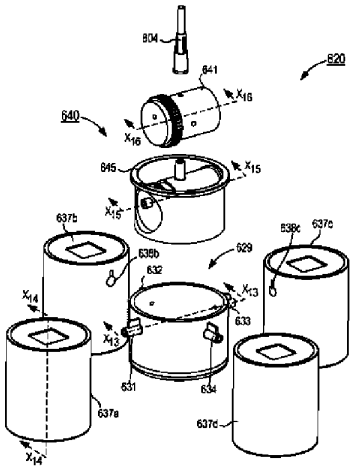


FIG. 27

【図２８】

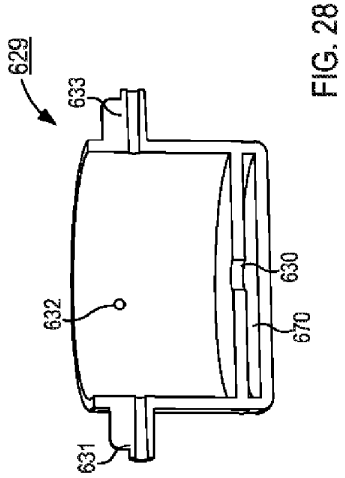


FIG. 28

【図２９】

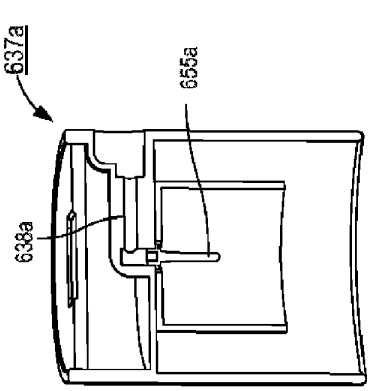


FIG. 29

【図３０】

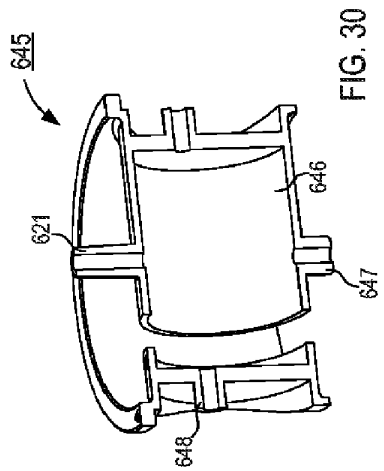


FIG. 30

【図３１】

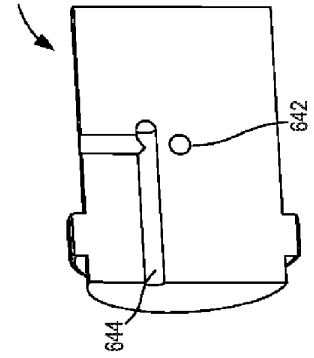


FIG. 31

【図３２】

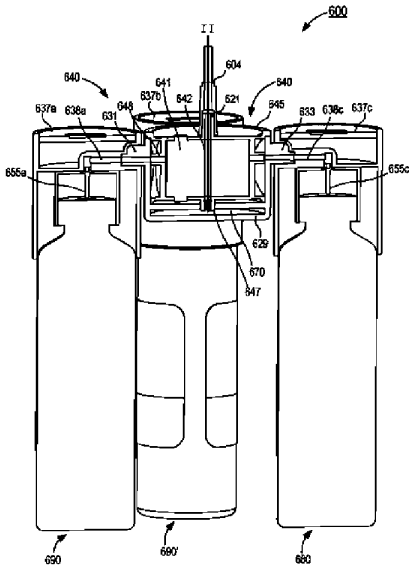


FIG. 32

【図３３】

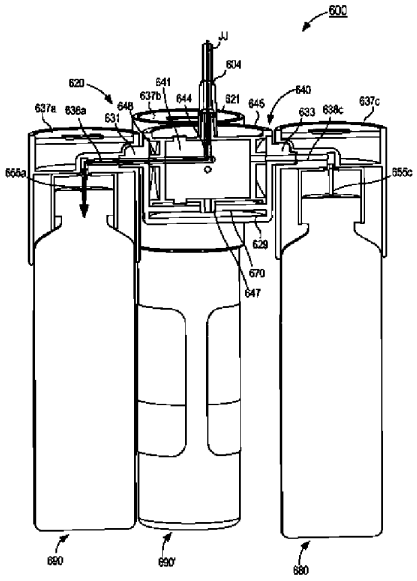


FIG. 33

【図３４】

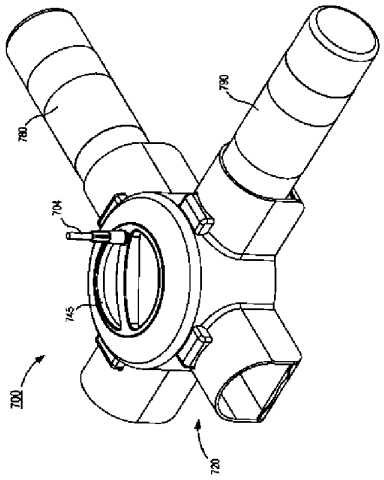


FIG. 34

【図３５】

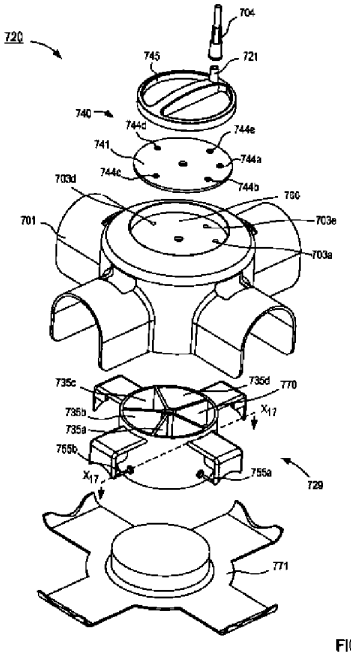


FIG. 35

【図３６】

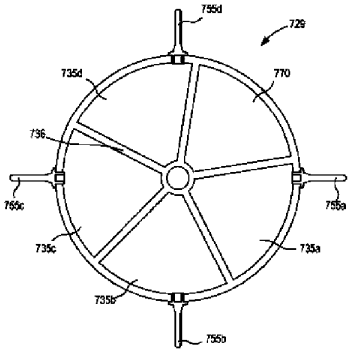


FIG. 36

【図３７】

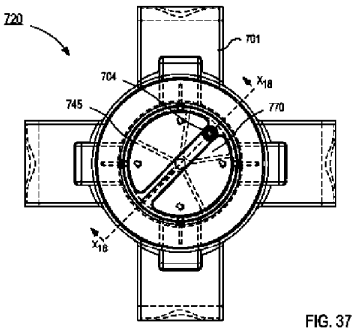


FIG. 37

【図３８】

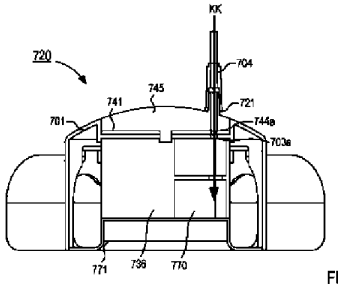


FIG. 38

【図３９】

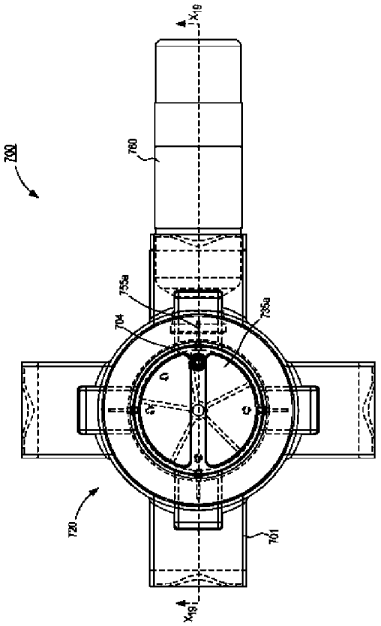


FIG. 39

【図４０】

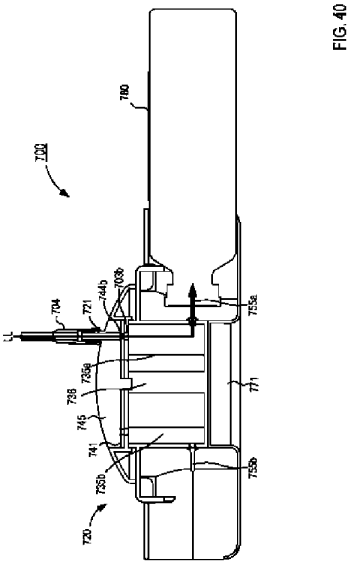


FIG. 40

【図４１】

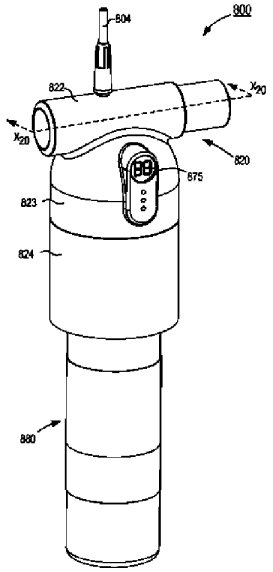


FIG. 41

【図４２】

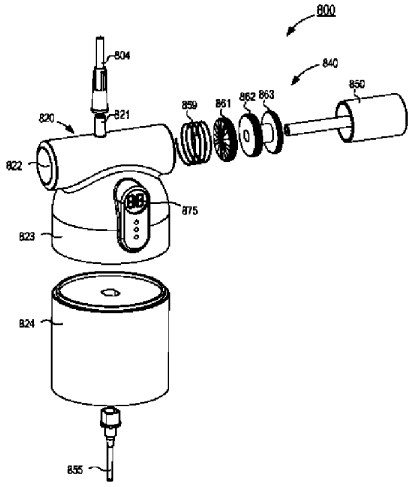


FIG. 42

【図４３】

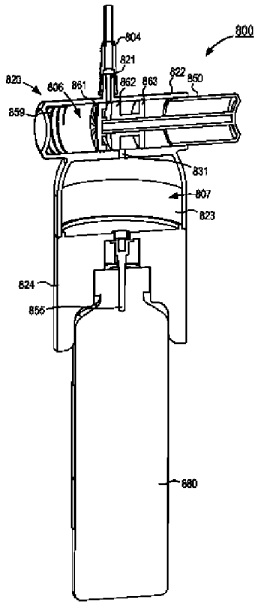


FIG. 43

【図４４】

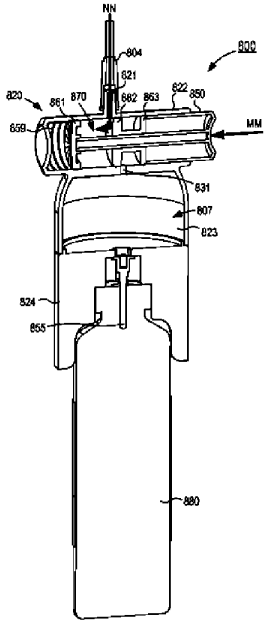


FIG. 44

【図４５】

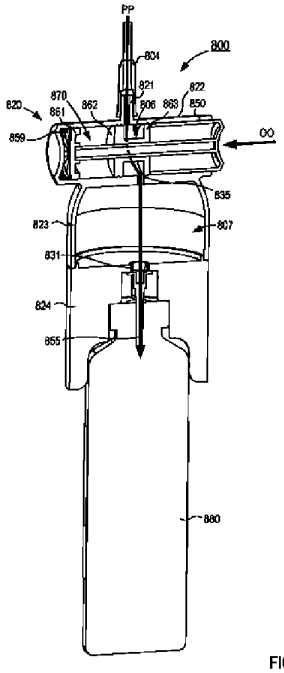


FIG. 45

【図４６】

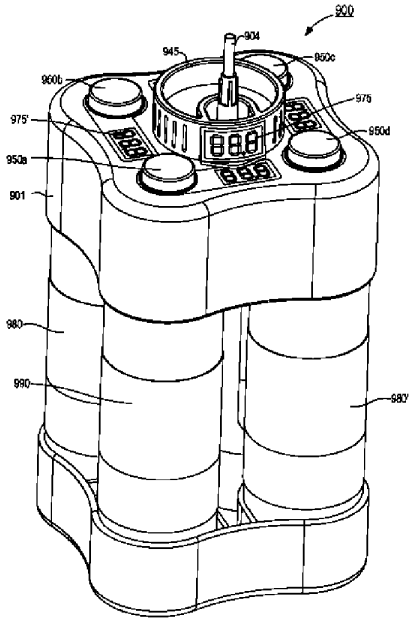


FIG. 46

【図４７】

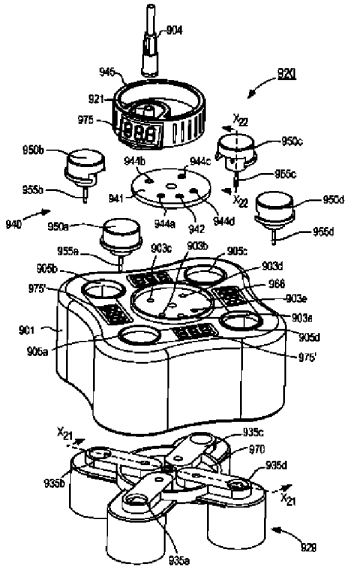


FIG. 47

【図４８】

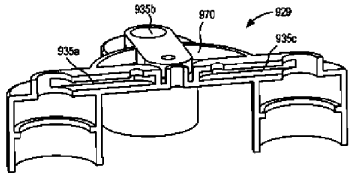


FIG. 48

【図４９】

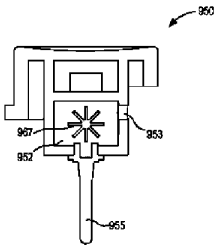


FIG. 49

【図５０】

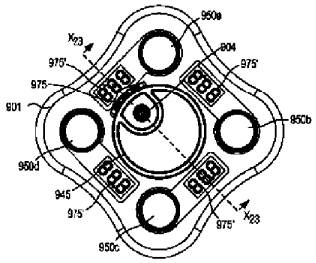


FIG. 50

【図５１】

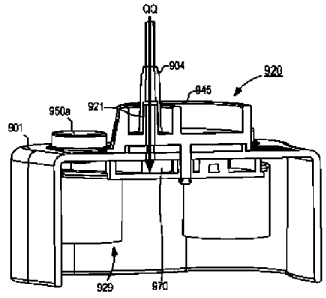


FIG. 51

【図５２】

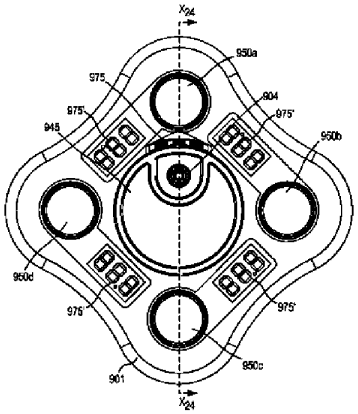


FIG. 52

【図５３】

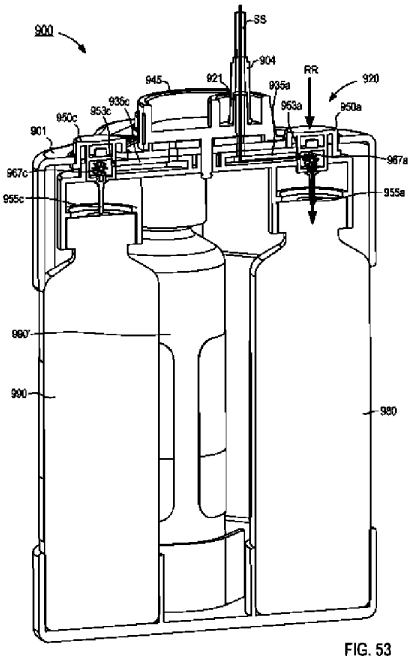
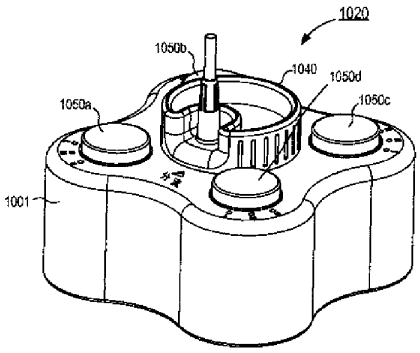
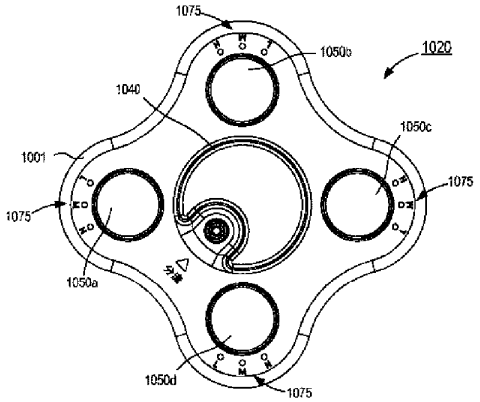


FIG. 53

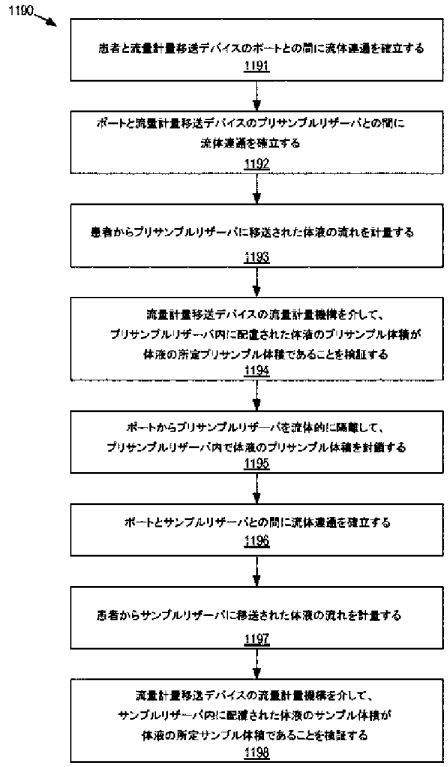
【図５４】



【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

Espacenet

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

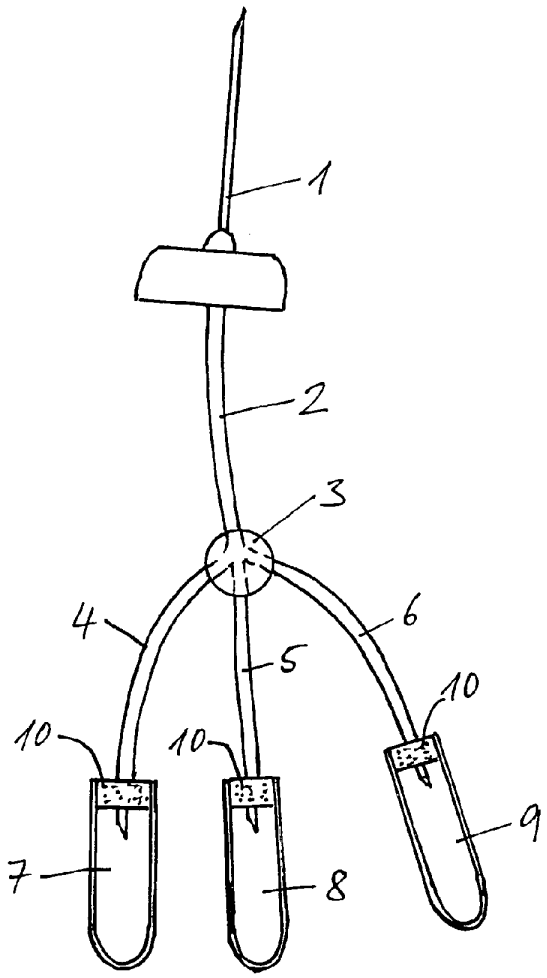
(56) Für die Beurteilung der Patentfähigkeit in Betracht zu ziehende Druckschriften:
DE 40 32 274 A1
US 58 82 318 A
US 55 07 299 A
WO 97/45 055 A1

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

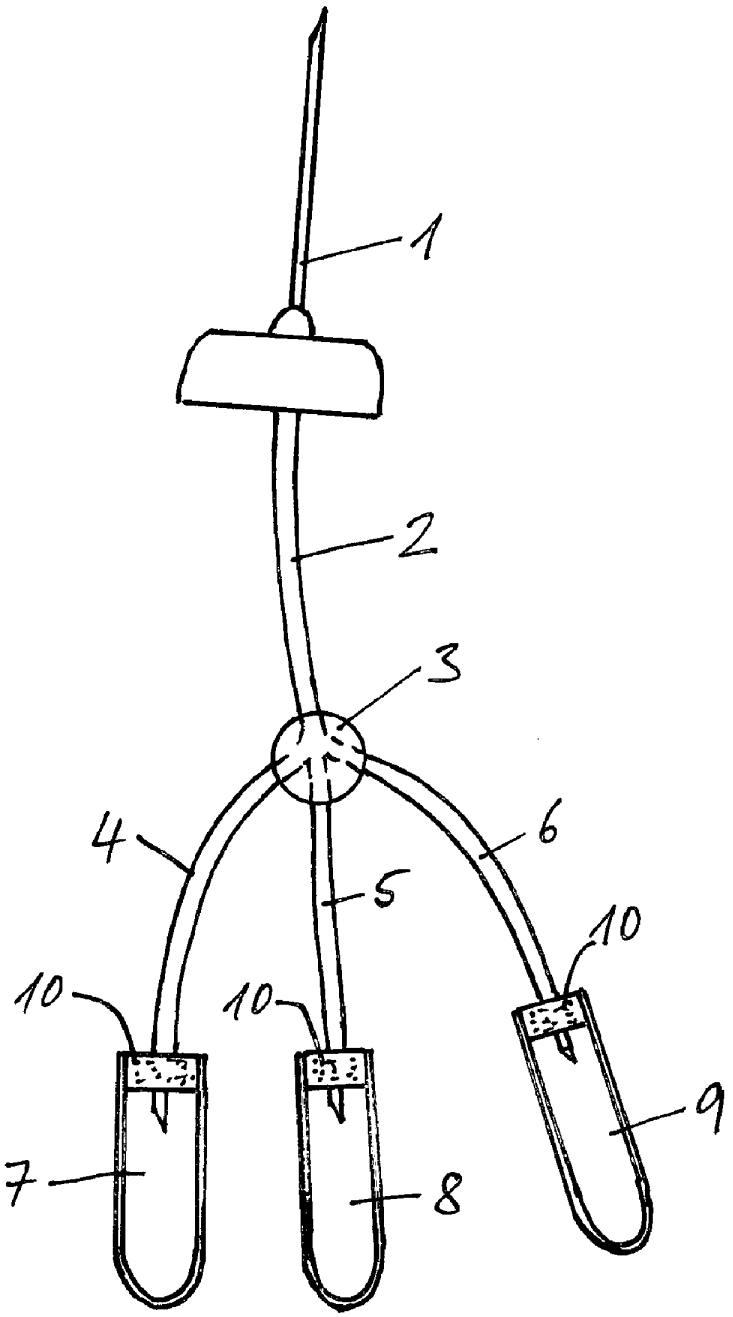
4. Blutentnahmegerät nach Anspruch 2 oder 3, wobei jeder Zweig der Schlauchverbindung eine den Stopfen (**10**) durchdringende Hohlnadel aufweist, und wobei der Stopfen nach Herausziehen der Hohlnadel selbstschließend ist.

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



Europäisches Patentamt
European Patent Office
Office européen des brevets

European Patent Office
80298 MUNICH
GERMANY

Questions about this communication ?
Contact Customer Services at www.epo.org/contact

Thum, Bernhard
Wuesthoff & Wuesthoff
Patentanwälte PartG mbB
Schweigerstraße 2
81541 München
ALLEMAGNE

Date
09.12.20

Reference	Application No./Patent No.
EPA-150 670	20197213.0 - 1132
Applicant/Proprietor	
Kurin, Inc.	

Communication

The extended European search report is enclosed.

The extended European search report includes, pursuant to Rule 62 EPC, the European search report (R. 61 EPC) or the partial European search report/ declaration of no search (R. 63 EPC) and the European search opinion.

Copies of documents cited in the European search report are attached.

☑ 0 additional set(s) of copies of such documents is (are) enclosed as well.

The following have been approved:

☐ Abstract ☐ Title

☑ The Abstract was modified and the definitive text is attached to this communication.

The following figure(s) will be published together with the abstract: 30B

Refund of search fee
If applicable under Article 9 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.

Should you wish to further prosecute this application in the examination phase, your attention is drawn to the provisions of Rule 70a EPC. An invitation to respond to the extended European search report will be issued once the date of publication of the European search report has been mentioned in the European Patent Bulletin (R. 69(1), R. 70(2) EPC).

Europäisches Patentamt • European Patent Office • Office européen des brevets

Europäisches Patentamt
European Patent Office
Office européen des brevets

European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840

Application No.: 20 197 213.0

The application and the invention to which it relates seem to meet the requirements of the EPC. Upon presence of a valid request for examination and consideration by the examining division, a communication under Rule 71(3) EPC may be issued.

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 20 19 7213

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	US 2014/039348 A1 (BULLINGTON GREGORY J [US] ET AL) 6 February 2014 (2014-02-06) * the whole document *	1-7	INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157
A	US 2014/107564 A1 (BULLINGTON GREGORY J [US] ET AL) 17 April 2014 (2014-04-17) * the whole document *	1-7	
A	US 4 813 433 A (DOWNEY JOHN M [US]) 21 March 1989 (1989-03-21) * the whole document *	1-7	
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) * abstract * * paragraph [0048] - paragraph [0075]; figures 2-12 *	1-7	
A	WO 2013/181352 A1 (MAGNOLIA MEDICAL TECHNOLOGIES INC [US]; BULLINGTON GREGORY J [US]; PAT) 5 December 2013 (2013-12-05) * abstract * * paragraph [1090]; figures 11,12 *	1-7	TECHNICAL FIELDS SEARCHED (IPC) A61B

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Berlin	19 November 2020	Nielsen, Michael

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

1

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 20 19 7213

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

19-11-2020

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014039348 A1	06-02-2014	US 2014039348 A1	06-02-2014
		US 2016113560 A1	28-04-2016
		WO 2014022275 A1	06-02-2014
US 2014107564 A1	17-04-2014	EP 2906269 A1	19-08-2015
		EP 3318295 A1	09-05-2018
		US 2014107564 A1	17-04-2014
		US 2015367069 A1	24-12-2015
		US 2018177943 A1	28-06-2018
		US 2019151536 A1	23-05-2019
		WO 2014058945 A1	17-04-2014
US 4813433 A	21-03-1989	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015
		US 2018092584 A1	05-04-2018
		US 2019209066 A1	11-07-2019
WO 2013181352 A1	05-12-2013	AU 2013267448 A1	18-12-2014
		AU 2017216493 A1	07-09-2017
		AU 2019204941 A1	25-07-2019
		AU 2020213415 A1	27-08-2020
		CA 2875118 A1	05-12-2013
		CN 104902817 A	09-09-2015
		CN 107736901 A	27-02-2018
		EP 2854643 A1	08-04-2015
		EP 3173021 A1	31-05-2017
		EP 3549522 A1	09-10-2019
		JP 6242386 B2	06-12-2017
		JP 6695314 B2	20-05-2020
		JP 2015519145 A	09-07-2015
		JP 2018034009 A	08-03-2018
		JP 2020121167 A	13-08-2020
		US 2014155781 A1	05-06-2014
		US 2015351679 A1	10-12-2015
		US 2018116577 A1	03-05-2018
		US 2020359951 A1	19-11-2020
		WO 2013181352 A1	05-12-2013

EPO FORM P0459

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

CLINICAL MICROBIOLOGY REVIEWS, Oct. 2006, p. 788–802 Vol. 19, No. 4
0893-8512/06/$08.00+0 doi:10.1128/CMR.00062-05
Copyright © 2006, American Society for Microbiology. All Rights Reserved.

Updated Review of Blood Culture Contamination

Keri K. Hall[1]* and Jason A. Lyman[2]

Division of Infectious Diseases and International Health, Department of Internal Medicine,[1] and Division of Clinical Informatics, Department of Public Health Sciences,[2] University of Virginia School of Medicine, Charlottesville, Virginia 22908

INTRODUCTION 788
Prevalence and Significance 788
DETECTION OF CONTAMINATED BLOOD CULTURES 789
Identity of Organism 789
Number of Positive Blood Culture Sets 790
Number of Positive Blood Culture Bottles within a Blood Culture Set 792
Time to Growth (Time to Positivity) 792
Quantity of Growth per Culture Bottle 793
Clinical and Laboratory Clues 793
Source of Cultures (Catheter Drawn versus Percutaneous) 793
Role of Information Technology: Automated Classification of Positive Blood Cultures 794
PREVENTING CONTAMINATION 795
Skin Preparation 795
Culture Bottle Preparation 796
Single Needle versus Double Needle 796
Obtaining Cultures Percutaneously instead of via Vascular Catheters 796
Phlebotomy Team 796
Commercial Blood Culture Collection Kits 797
SUPPORTING OPTIMAL USE OF BLOOD CULTURES 797
Clinical Prediction Models 797
Population Studies of Bacteremia Prevalence 798
BLOOD CULTURE CONTAMINATION IN THE PEDIATRIC POPULATION 798
CONCLUSION 799
REFERENCES 799

INTRODUCTION

The blood culture represents a critical tool for the health care professional as a means of detecting the dangerous presence of living organisms in the bloodstream. A positive blood culture can suggest a definitive diagnosis, enable the targeting of therapy against the specific organism(s) in question, and provide prognostic value (22). Like any test, however, false-positive results can limit the utility of this important tool. In blood cultures, false positives arise due to contamination, which occurs when organisms that are not actually present in a blood sample are grown in culture. Contaminated cultures have been recognized as a troublesome issue for decades and continue to be a source of frustration for clinical and laboratory personnel alike. Faced with a positive blood culture result, clinicians must determine whether the organism represents a clinically significant infection associated with great risk of morbidity and mortality or a false-positive result of no clinical consequence. Further complicating the issue in recent years is the increasing use of central venous catheters (CVC) and other indwelling vascular access devices (5, 90). Interpretation of culture results for patients with these devices in place is particularly challenging because while these individuals are at increased risk for bacteremia, such results may also indicate culture contamination or colonization of the line. The clinical uncertainty associated with the interpretation of ambiguous culture results is costly, as has been demonstrated in a number of studies of both adult and pediatric patients (13, 115, 125, 138).

Prevalence and Significance

While target rates for contamination have been set at 2 to 3% (30, 131), actual rates seem to vary widely between institutions, from as little as 0.6% to over 6% (13, 64, 67, 82, 89, 112, 113, 125, 131, 150). The College of American Pathologists (CAP) Q-Probes quality improvement study involved the prospective examination of 497,134 blood culture specimens from 640 U.S. health care institutions (113). While the median adult inpatient contamination rate was 2.5%, some organizations had a rate of less than 1.0%, while for other organizations, more than 5.0% of their blood cultures were contaminated. More recently, the CAP Q-Tracks study found an overall median contamination rate of 2.92% for data collected from 356 institutions from 1999 to 2003. There is also some evidence to suggest that in recent decades, these rates have been on the increase (150), although the Q-Tracks study found no increase over the 4-year time frame for their data. The suggested reasons for this increase include technological advances that allow the detection of smaller quantities of living microorganisms in the blood, the increased use of indwelling catheters for the

* Corresponding author. Mailing address: P.O. Box 800473, Department of Infection Control, University of Virginia Health System, Charlottesville, VA 22908. Phone: (434) 924-0260. Fax: (434) 924-1225. E-mail: kkh2n@virginia.edu.

KUR-MAG-DE003920

Page 2183 of 5977

TABLE 1. Addressing the challenge of blood culture contamination

Approach	Rationale
Detecting contaminants	Given that contamination can likely never be eliminated, having reliable factors to help identify true positives vs false positives is critical for patient management and population-based surveillance
Prevention	Reducing contamination rates will improve the specificity of the blood culture and result in a higher PPV, resulting in a significantly more useful test
Supporting optimal use of blood cultures	Reducing the use of blood cultures in patients with a very low likelihood of bacteremia will result in a higher PPV and reduced costs associated with contamination; pretest probability of bacteremia can be estimated using population-based studies of disease prevalence or clinical prediction rules

provision of therapy, and changes in phlebotomy practices to minimize the risk of needlestick injuries (151).

The financial impact of blood culture contamination has been described in a number of studies (13, 35, 125, 145). Bates et al. found that contaminant results, compared with true-negative results, were independently associated with increased subsequent laboratory charges (20% increase) and intravenous antibiotic charges (39% increase) (13). In a subsequent prospective study focused on blood culture contamination caused by coagulase-negative staphylococci, Souvenir et al. reported that almost half of the patients with a false-positive result were treated with antibiotics, often with vancomycin (125). According to their estimates, the additional costs associated with this unnecessary treatment were approximately $1,000 per patient. Other investigators focused on the consequences of contaminated cultures in pediatric populations (115, 138). Segal and Chamberlain estimated that the additional charges associated with contaminated cultures in 85 children aged 3 to 36 months who were evaluated in an emergency department and believed to be at risk for occult bacteremia totaled $78,904, the majority of which was due to subsequent hospital admission (115). In a retrospective study of 9,959 blood cultures performed in children aged 1 month to 18 years, Thuler et al. found that 26% of children with false-positive cultures who were initially evaluated as outpatients were subsequently admitted to the hospital on the basis of initial culture results (138). Measured in costs or charges, there is compelling evidence that the financial impact of blood culture contamination is significant.

Given these excessive costs, how can we address the problem of contaminated blood cultures? There has been significant effort in recent years to attempt to identify ways of preventing contamination in the first place. In addition, investigators have studied factors that help distinguish true positives from false positives. Since a major consequence of contaminated cultures is a lower positive predictive value (PPV) for the blood culture test, and the pretest probability of bacteremia is a key determinant of PPV (6), there have been increasing endeavors to discourage the utilization of blood cultures in patients at very low risk for this disease. For example, clinical bacteremia prediction rules have been developed and studied to help guide clinical decision-making in the use and interpretation of blood cultures and the initiation of empirical antibiotic therapy. In addition, population-based studies of bacteremia prevalence for specific patient groups have been performed in the past decade. Such information, while not completely individualized to a given patient, provides a rough estimate of pretest probability for bacteremia. In summary, the challenge of blood culture contamination can be addressed by at least three different avenues of approach, as summarized in Table 1.

In the last decade, significant progress has been made in each of these three broad areas. New evidence for measures to reduce contamination rates is emerging, and we are becoming better able to ascertain bacteremia risk at both the individual and patient population levels. In addition, much has been learned about how to accurately distinguish between true bacteremia and contamination. In this review, we provide an updated analysis of this important, complex topic with special attention paid to each of these areas. We also highlight specific challenges associated with blood culture contamination in the pediatric population, although an in-depth analysis is beyond the scope of our review.

DETECTION OF CONTAMINATED BLOOD CULTURES

Despite its limitations, the blood culture remains the "gold standard" for the detection of bacteremia. An accurate interpretation of culture results is critical not only from the perspective of individual patient care but also from the standpoint of hospital epidemiology and public health. The tracking and reporting of nosocomial infections and monitoring of bloodstream infection rates are both essential infection control activities that depend heavily on the accurate differentiation of contamination from true bacteremia. Reliably making this determination continues to be very challenging for clinicians, epidemiologists, and microbiologists. In recent decades, multiple approaches have been studied, advocated, and utilized for this purpose. Clues that may help to differentiate contamination from bacteremia include identity of the organism, number of positive culture sets, number of positive bottles within a set, time to growth, quantity of growth, clinical and laboratory data, source of culture, and automated classification using information technology.

Identity of Organism

Often, the identity of the microbe that grows from a blood culture is a very helpful clue that the results may or may not represent contamination. The CAP Q-Probes study described above found that the most important indicator when interpreting blood culture results was the identity of the organism, which was cited as very important to 79% of laboratories (113). Bates et al. found that the identity of the organism was the most important predictor in a predictive model for differenti-

TABLE 2. False-positive rates for organisms that frequently represent contamination

Organism(s)	Source			
	1,585 blood culture-positive episodes from 3 U.S. hospitals[a]		497,134 blood cultures from 640 U.S. institutions[b]	
	% of all positive cultures (n = 1,585)	Contamination rate (%)	% of all positive cultures	Contamination rate (%)
Coagulase-negative staphylococci	44.3	82	Not reported	62–63
Corynebacterium spp. (other than *C. jeikieum*)	33.4	96	Not reported	68–78
Bacillus spp.	0.8	91.7	Not reported	68–70 (other than *B. anthracis*)
Propionibacterium acnes	3.0	100	Not reported	84–85
Viridans group streptococci	4.5	49.3	Not reported	32–33
Clostridium perfringens	0.8	76.9	Not reported	Not reported

[a] Data are from reference 155.
[b] Data are from reference 113.

ating contaminated blood culture results from results indicating bacteremia (14).

Weinstein et al.'s study of 843 episodes of positive blood cultures in adult inpatients from three hospitals around the country suggested that certain organisms should almost always be thought to represent true bacteremia or fungemia when isolated from a blood culture (155). These organisms included *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli* and other *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Candida albicans*. Furthermore, Weinstein's personal observation is that the following organisms almost always represent a true infection when isolated from a blood culture: *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, members of the *Bacteroides fragilis* group, all *Candida* species, and *Cryptococcus neoformans* (151).

Along the same vein, certain organisms have been found to represent contamination in a significant proportion of cases. These organisms include coagulase-negative staphylococci, *Corynebacterium* species, *Bacillus* species other than *Bacillus anthracis*, *Propionibacterium acnes*, *Micrococcus* species, viridans group streptococci, enterococci, and *Clostridium perfringens* (151, 155). However, it is crucial to recognize that each of these organisms can also represent true bacteremias with devastating consequences, particularly if untreated due to misinterpretation as contaminants. Of these organisms, the ones that are thought to represent true bacteremia only rarely are *Corynebacterium* species, *Bacillus* species other than *B. anthracis*, and *Propionibacterium acnes* (151, 155). In addition to the work of Weinstein et al., the CAP Q-Probes study provided valuable information on contamination rates for organisms that frequently represent contamination (Table 2).

Despite the high likelihood that certain organisms usually represent contaminants when isolated from blood cultures, determining the likelihood of true bacteremia can be challenging for clinicians. Coagulase-negative staphylococci represent an important, all-too-frequent case in point. In the past, coagulase-negative staphylococci were usually believed to represent contamination when isolated from blood cultures. In fact, coagulase-negative staphylococci are the most common blood culture contaminants, typically representing 70% to 80% of all contaminated blood cultures (25, 92, 105, 113, 125).

Recently, however, studies have shown that these organisms are an increasing source of true bacteremia in patients with prosthetic devices and central venous catheters (30, 53, 105, 139, 155), although the majority of isolates of coagulase-negative staphylococci from blood cultures continue to be contaminants. Weinstein et al. found that even though only 12.4% of coagulase-negative staphylococcal isolates were clinically significant, they ranked as the third most common cause of bacteremia because of their high prevalence (155). In another study, among 81 episodes of coagulase-negative staphylococcal blood culture results, the incidence of clinically significant bacteremia was 20 (24.7%) episodes, that of indeterminate bacteremia was 10 (12.3%) episodes, and that of contamination was 59 (72.8%) episodes (125). Other studies found rates of true bacteremias ranging from 10% to 26.4% when coagulase-negative staphylococci are isolated from blood cultures (51, 125).

Similarly, other organisms can be difficult to interpret when isolated from blood cultures. One study found that enterococci were pathogens 70% of the time, whereas viridans group streptococci were pathogens 38% of the time (155). Furthermore, that same study found that *Clostridium perfringens* was a contaminant 77% of the time, whereas other *Clostridium* species were true pathogens 80% of the time. Given these data, clinicians attempting to differentiate true infections from simply contaminated blood cultures cannot rely solely on the identity of the organism.

Often, bloodstream infections involve only a single organism, prompting clinicians to sometimes conclude that a blood culture bottle that grows multiple organisms is contaminated. However, studies have found that 6% to 21% of all true bacteremias are polymicrobial, usually in patients in high-risk groups (121). Furthermore, multiple coagulase-negative species have been found to cause polyclonal coagulase-negative staphylococcal infections (42, 142, 143). Therefore, one cannot conclude that the mere presence of multiple organisms in a blood culture bottle always indicates contamination.

Number of Positive Blood Culture Sets

One proven methodology that can help differentiate blood culture contamination from true infection is the number of blood culture sets that grow organisms. The proportion of positive sets as a function of the total number of sets obtained can be a particularly useful tool (16, 69, 154, 155). If only one

KUR-MAG-DE003922

set of at least two sets grows an organism known to often cause contamination, this often represents a contaminant. For true bacteremias, multiple blood culture sets will usually grow the same organism (53, 139, 155). In fact, this indicator is one of the most frequently used tools to help differentiate contamination from bacteremia as indicated in the CAP Q-Probes study, which revealed that 77% of laboratories cited the proportion of positive blood cultures in a series of cultures as very important for interpreting blood culture results (113). In their examination of 11,167 episodes in which coagulase-negative staphylococci were isolated from blood cultures, 27.8% were interpreted as contaminants if at least two sets were positive compared to 75.2% if only one of at least two sets were positive. In 2,440 cases, only a single blood culture was available; in these cases, 66.9% of the isolates were determined to be contaminants.

When multiple cultures are obtained and return positive, the positive predictive value for true bacteremia has been shown to improve (51). In one modeling study of patients with a central vascular line and a positive culture for coagulase-negative staphylococci, the positive predictive value was 55% when one of one culture was positive, 20% when one of two cultures was positive, and only 5% when one of three cultures was positive (139). In the face of such data, it has become increasingly clear that maximizing the diagnostic utility of blood cultures requires at least two sets be performed.

Because coagulase-negative staphylococci represent contaminants more often than true infections when isolated from blood culture bottles, even when two sets are positive for this organism, it can be difficult to determine whether both sets are contaminated as opposed to representing a true infection. Souvenir et al. found that only a single set of blood cultures was positive for 35% of samples from patients with coagulase-negative staphylococcal bacteremia, whereas two or more sets were positive for 12% of the patients in the contamination category (125).

Evidence based on molecular studies also highlights the fact that multiple positive culture results may be helpful but imperfect in discerning contamination. An approach using pulsed-field gel electrophoresis (PFGE) was explored in 14 febrile neutropenic patients who had matched peripheral and catheter-drawn cultures that both grew *Staphylococcus epidermidis* (86). Of these 14 patients, 10 had identical or closely related strains, and the remaining 4 were thought to represent either mixed infection or contamination. Another study of 42 patients with at least two positive cultures for coagulase-negative staphylococci drawn within a 14-day interval found that PFGE plus arbitrary primed PCR detected the same strain in 19 (45%) cultures, suggesting that the 23 (55%) cultures that grew different strains were either contamination events or infections involving multiple strains of coagulase-negative staphylococci (117). In that study, patients with three or more positive blood cultures were significantly more likely to have same-strain bacteremia than those with only two positive cultures (11 [73%] of 15 versus 8 [30%] of 27; $P = 0.006$). A similar study that used clinical criteria to differentiate true bacteremia from contamination in 22 patients who had at least two positive cultures for coagulase-negative staphylococci found that only 1 of 41 blood cultures in bacteremic patients had an unrelated strain by PFGE, compared to 6 of 16 in contaminated samples (121). Their statistically significant findings provide further evidence that genotypic variation is more common in contaminated samples, and recurring identical strains of coagulase-negative staphylococcal are more likely to represent bacteremia.

Because molecular testing of culture isolates is not realistic in clinical practice, many clinicians use the antimicrobial susceptibility patterns to indicate whether the isolates represent identical strains (51, 58). In the aforementioned study, of the 14 patients who grew *S. epidermidis* from matching sets, 13 had identical susceptibility patterns, whereas 10 had identical or closely related PFGE patterns (as defined by $\leq$3 band differences), thereby indicating that three of the four patients who did not match on the basis of PFGE would have been misclassified as identical isolates if only antimicrobial susceptibility patterns had been used (86). Another study of paired blood culture isolates of identical species with identical MICs found that 9 to 18% of the isolates were actually distinctly different strains (121). Khatib et al. found that the antibiograms of all 21 episodes of true bacteremia (as indicated by molecularly identical coagulase-negative staphylococcal strains in multiple sets) were identical and that 7 (15.9%) of 44 unrelated pairs of coagulase-negative staphylococci had identical antibiograms (57). In that study, identical antibiograms, determined by using the individual MICs of 10 antibiotics, were highly predictive of strain relatedness, with a sensitivity of 100% and a specificity of 83.7%, and a fourfold difference in a single MIC was always predictive of strain variation even if the difference did not change the susceptibility category for the strain. Moreover, the specificity of the antibiogram was lower when nonquantitative methods were used, and the level of specificity correlated with the number of antibiotics compared.

Clearly, speciating any coagulase-negative staphylococci that grow from multiple blood cultures can help determine the likelihood of contamination, because if the species from one set differs from the species from the other set, the culture results indicate either mixed infection or contamination (153). However, speciation of coagulase-negative staphylococci is not always automatically performed by clinical microbiology laboratories. Indeed, one study found that only 20 (59%) of 34 hospitals surveyed routinely identified coagulase-negative staphylococci to the species level (105).

For these reasons, it has been recommended that multiple sets of blood cultures be obtained to work up potential bloodstream infections. The presence of only one positive set among at least two sets drawn at the same time may be indicative of culture contamination. Additionally, the presence of one positive set over several cultures drawn over a period of time may also indicate contamination, although it may conversely indicate transient bacteremia. In order to differentiate transient bacteremia from contamination, it has been recommended that at least two sets of cultures be obtained at the same time (6, 30, 53, 71, 102, 107, 118, 152).

However, obtaining at least two sets is not always done (93, 105, 111). In a study of 333 small public and private hospitals (median occupancy of 57), the median rate of obtaining only a solitary blood culture was 12.7%, and the rates for the 10th and 90th percentiles were 42.5% and 3.4%, respectively (93). The same study found that solitary blood culture rates were lower for institutions with phlebotomists, with institutional policies

that required at least two sets, with notification of ordering clinicians when only one set was ordered, and with quality control programs aimed at monitoring solitary blood cultures. In two broader Q-Probes studies described by Schifman et al., significant variation in the utilization of solitary blood cultures was also found. In 289,572 blood culture sets from 909 hospitals, those authors found median proportions of solitary blood cultures of 10.1% and 12.1% among adult inpatients, 25.4% and 33.3% among adult outpatients, and 89.0% and 100% among pediatric/infant patients in the two studies, respectively (111).

Number of Positive Blood Culture Bottles within a Blood Culture Set

Another method that has been used by health care workers to differentiate contaminated blood cultures from cultures that represent bacteremia is the number of blood culture bottles that exhibit growth within a given blood culture set. Theoretically, if only one bottle exhibits growth within a given set, the likelihood of contamination is greater. However, there is at least one study that suggested that these criteria should not be used for this purpose (84). In their study, Mirrett et al. found that the number of bottles positive for coagulase-negative staphylococci within blood culture sets comprising two, three, or four bottles was not correlated with the likelihood of infection using clinical parameters (84). Among 486 sets that were comprised of two bottles, the positive predictive value for sepsis was 18% when one bottle was positive versus 37% when both bottles were positive. Among 235 sets comprised of three bottles, the positive predictive value for sepsis was 28, 52, and 30% when one, two, and three bottles, respectively, were positive. For 303 sets comprised of four bottles, the positive predictive value was 27, 28, 19, and 27% when one, two, three, and four bottles, respectively, were positive. Those authors concluded that the number of positive bottles in a given set did not reliably predict clinically significant infection. Another study found that increasing numbers of positive bottles did predict the likelihood of true bacteremia as defined by clinical parameters: of 129 patients with coagulase-negative staphylococci isolated from a single venipuncture using sets comprised of four bottles, the positive predictive value for true infection was 2% when one bottle was positive, 9% when two bottles were positive, 13% when three bottles were positive, and 27% when all four bottles were positive (94).

Usually, a set of blood cultures involves one aerobic bottle and one anaerobic bottle in an attempt to optimize the isolation of both aerobic and anaerobic organisms. It makes sense intuitively that if growth of a given organism is more likely in aerobic conditions than anaerobic conditions, the number of positive culture bottles within a set that consists of one aerobic and one anaerobic bottle should not be used to differentiate contaminated from clinically significant cultures. Not surprisingly, recent studies have found that the presence of growth for a given organism varies between the aerobic and anaerobic bottles. One study of 644 positive blood culture sets found that 413 (59.8%) were recovered from both bottles, 206 (29.8%) were recovered only from the aerobic bottle, and 72 (10.4%) were recovered only from the anaerobic bottle (108). In that study, the aerobic bottle was significantly superior to the anaerobic bottle for both recovery and detection time for overall organisms, and there was no significant difference in detection time for facultative anaerobic bacteria between the two bottles. Another study of coagulase-negative staphylococcal isolates found that the majority (59.7%) of isolates grew in the aerobic bottle only, whereas 27.7% grew in both bottles and 12.6% grew only in the anaerobic bottle (57). Other studies have shown the same lower yields for anaerobic blood cultures (87).

Time to Growth (Time to Positivity)

Another factor in determining contamination that has been explored by several investigators is the amount of time required for the organism to grow in the culture medium. Conceptually, it is thought that perhaps the blood from a bacteremic patient will have a much higher inoculum of bacteria than a contaminated culture. Theoretically, it follows that a larger inoculum will grow faster than a smaller inoculum, a theory that seems to have been verified in prior studies of catheter-related bloodstream infections (28, 41, 48, 53, 104). In support of this theory, several studies have shown that cultures that become positive more than 3 to 5 days after incubation have been more likely to represent contaminants (37, 49, 50, 53, 62, 75, 103, 108). Because it can be difficult to obtain more than one set of cultures in the pediatric population, Haimi-Cohen et al. used clinical parameters to differentiate true coagulase-negative infections from contaminants and found that a time to positivity of $\leq$15 h had a positive predictive value of 84% for true infection in children (48).

Bates et al. found that the time to growth was a useful variable in a multivariate algorithm for predicting true bacteremia from a positive culture result, although it did not perform as well as either the identification of the organism or the presence of multiple positive cultures (14). Other studies have not found time to growth to be a useful parameter. Souvenir et al.'s study, which differentiated coagulase-negative staphylococcus-contaminated cultures from bacteremias using clinical parameters, found no significant difference between the contaminant group and the true bacteremia in the time to detection of a positive culture (125). Khatib et al.'s molecular study of 47 episodes of multiple positive cultures for coagulase-negative staphylococci found that time to growth did not help differentiate cultures that grew identical strains (2.1 $\pm$ 1.4 days) from culture sets that differed by strain (1.9 $\pm$ 0.9 days) (57).

In the CAP Q-Probes study, the difference in time to detection for contaminant versus true-positive coagulase-negative staphylococci was statistically significant but, as those authors pointed out, probably not clinically significant due in part to a substantial overlap in growth time (113). Furthermore, as the technology of continuous monitoring of blood cultures to detect growth advances, the time to growth and sensitivity for detecting growth can be expected to change, making the use of this technology in this regard questionable (77, 83). Thus far, some experts recommend that this technological variable should not be relied upon to distinguish contaminants from pathogens in blood cultures (151).

KUR-MAG-DE003924

Quantity of Growth per Culture Bottle

Another method that has been used to determine the clinical significance of culture results is the quantity of growth in a given culture sample. This method has been used to differentiate sputum colonization from pneumonia, urine colonization from urinary tract infection, and catheter-related bloodstream infection from non-catheter-related bloodstream infection (2, 53, 106, 127, 128). However, limited data exist to support use of this methodology for differentiating contaminated blood cultures from truly positive blood cultures in adults. St. Geme III et al. found that quantitative cultures in conjunction with specific clinical information may distinguish sepsis from contamination with coagulase-negative staphylococci in young infants but cautioned that low colony counts should not be dismissed as contamination in this high-risk population (129).

Clinical and Laboratory Clues

Others have recommended that the addition of clinical information is essential to appropriately classify positive blood culture results (14, 43, 48, 51, 69). Studies have found that clinicians often diagnose infection when rigid laboratory-based algorithms for differentiating contamination from bacteremia would not have diagnosed infection. The CAP Q-Probes study noted that the median contamination rate differed depending upon whether a clinical assessment was used to make the determination (2.1%) versus laboratory assessment (2.5%) (113). In that study, when coagulase-negative staphylococci were isolated from only one of at least two sets, 84.3% of the cases were interpreted as contaminants by using laboratory methods compared to 73.9% by using laboratory and clinical evaluation.

Many clinicians use fever and other signs of sepsis syndrome to help with the interpretation of positive blood cultures. Weinstein et al. found that hypothermia (temperature of <36°C) or marked fever (temperature of >40°C), leukocyte counts of <4,000 leukocytes/μl or >20,000 leukocytes/μl, and hypotension predicted true infection as opposed to contamination (155). However, another study found that fever at the onset of a blood culture positive for *Staphylococcus epidermidis* did not help differentiate true bacteremia from contamination in leukemic patients (68). Other studies have found similar results in which sepsis-like syndromes, including fever, did not help differentiate episodes thought to be contaminants from true bacteremias (118).

Clinical criteria combined with laboratory data have been used in several studies to differentiate contaminated cultures from clinically significant cultures (14, 30, 43, 51, 59, 125, 129, 155). Bates et al. developed a multivariate algorithm utilizing many predictors, one of which was a "clinical risk score," which consisted of fever, rigors, outcome, intravenous drug abuse, acute abdomen, and comorbidities as variables (14). This clinical risk score was found to be predictive of contamination, as was the organism type, days to culture positivity, and the presence of multiple positive cultures. Khatib et al.'s molecular analysis of 47 episodes of coagulase-negative staphylococcus-positive cultures found that strain relatedness was more frequent in patients who had a fever (15 [71.4%] of 21), an identifiable source (7 [77.8%] of 9), or a bacteremia that met the definition of nosocomial acquisition (18 [50%] of 36) (57). The presence of an identifiable source, specifically, a central venous catheter, was found to be predictive of true bacteremia in another study as well (68).

National Nosocomial Infection Surveillance (NNIS) parameters and surveillance criteria often utilize the treating clinician's diagnosis of bloodstream infection to differentiate true bacteremia from contamination for common contaminants (43). However, one study that correlated cultures that grew the same strain of coagulase-negative staphylococci with the clinician's suspicion/treatment found that the classification of coagulase-negative staphylococcal bacteremias as the same strain correlated poorly with the clinical assessment utilizing the clinician's diagnosis (117). Furthermore, in another study, even though treating clinicians and reviewers who performed retrospective analyses agreed on 100% of coagulase-negative staphylococcal bacteremias and 95% of contaminations, one-half of patients with contaminated blood cultures were still treated with antibiotics, leading to vancomycin misuse in 34% of patients (125). Of course, this may be related to a lower threshold for interpreting an uncertain result as an infection until proven otherwise in the presence of a gravely ill patient rather than true disagreements about what represents contamination.

Other surrogate markers for infection have been studied as well, including the use of C-reactive protein measurements. In neonates, a single C-reactive protein obtained at least 12 h after the onset of symptoms has been found to be helpful to diagnose clinical sepsis (18, 98, 110). In another study of leukemic patients, the level of a single C-reactive protein did not help differentiate between contamination and bacteremia, but the median increase in C-reactive protein over 24 h from the first positive blood culture did help (68). Given these data, some neonatal intensive care unit (NICU) clinicians are beginning to utilize C-reactive protein for this purpose: a survey of 35 NICUs found that C-reactive proteins were routinely obtained at 23% of NICUs and by 30% of NICU clinicians (105).

Source of Cultures (Catheter Drawn versus Percutaneous)

When blood cultures drawn from a vascular catheter are positive, the results could indicate one of three possibilities: true bacteremia, catheter colonization, or culture contamination. Catheter colonization is not contamination, nor is it infection—it occurs when microorganisms grow on the surface of a catheter such that the colonizing organisms would be expected to grow in blood samples obtained from the catheter (in contrast to culture contamination). Catheter colonization may or may not progress to cause symptoms of infection or true bacteremia. Studies have shown that 15 to 25% of short-term central venous catheters are colonized, usually by coagulase-negative staphylococci, and most patients have no evidence of infection (46, 133). Therefore, cultures drawn from central lines could be expected to be positive due to colonization in a substantial number of patients.

Because of the uncertainties surrounding blood cultures obtained from vascular catheters, the clinical utility of these cultures has been evaluated. In one study that used blinded assessments by infectious disease experts to determine the presence of true bacteremia, catheter-drawn cultures had a

sensitivity of 89%, compared to 78% for peripheral cultures, with a positive predictive value of 63% for catheter-drawn cultures versus 73% for percutaneous cultures (34). The results of that study were similar to those of other studies, leading many to suggest that if cultures are obtained from a catheter, at least one set should be drawn percutaneously (13, 20, 38, 74, 76, 92). The advantage of drawing a percutaneous culture to aid the interpretation of catheter-drawn cultures was mathematically evaluated by Tokars in a modeling study of coagulase-negative staphylococcal bacteremia (139). Tokars found that when two of two cultures were positive, the positive predictive value would be 98% if both samples were obtained through the vein, 96% if one sample was obtained through a catheter and the other was obtained through a vein, and only 50% if both samples were obtained through a catheter (139). Other studies, however, have not found a significant difference between results of catheter-drawn and peripheral cultures (39, 125, 158). If it is in fact true that blood cultures obtained from vascular catheters are more likely to be contaminated than percutaneously obtained cultures, the reason may be that sterilizing catheters prior to accessing them is more difficult than sterilizing skin or that catheter colonization is confounding catheter-drawn culture results (151).

One instance in which multiple sets of cultures are often not obtained is in NICU infants for whom the removal of too much blood is of concern and difficulty obtaining peripheral cultures is a reality. Indeed, in a survey of 35 NICUs, 83% of clinicians drew only one blood culture when a catheter-drawn sample was unavailable (105). In that same study, if blood was able to be obtained from a catheter, 224 (80%) of 279 clinicians said that they would obtain at least two blood cultures, including at least one from a peripheral vein; 37 (13%) would obtain a single culture through the central venous catheter; and 18 (6%) would obtain a single blood culture from a peripheral vein. Because of these concerns in the NICU population, antimicrobials that are active against coagulase-negative staphylococci (usually vancomycin) are often overutilized in the NICU. When practice habits from 35 NICUs were evaluated, 47 to 85% of clinicians completed a full course of antimicrobials when a single blood culture was obtained and grew coagulase-negative staphylococci, whereas a significantly lower percentage (22 to 47%) completed a full course when one of two blood culture sets grew coagulase-negative staphylococci (105).

Role of Information Technology: Automated Classification of Positive Blood Cultures

In recent decades, health information technology has played an increasingly important role in the field of infectious disease. Infection control activities are extremely data intensive, and health care information technology offers tremendous potential for improvements in the efficiency of surveillance and reporting systems. Health care institutions are increasingly turning to data-warehousing technologies to support these activities (23, 47, 109, 157). With respect to the challenge of blood culture contamination, investigators have explored automated, computer-based approaches for the classification of culture results as likely contaminants or pathogens. Such an approach offers at least two potential benefits: assisting clinical interpretation and decision-making in the face of ambiguous culture results and providing objective, reproducible, cost-efficient approaches to surveillance of nosocomial infections and bloodstream infection rates. In addition, such methods are almost always significantly faster, as they do not rely on manual identification of positive blood cultures or subsequent labor-intensive review of potentially incomplete or unavailable clinical data.

From the standpoint of surveillance, differentiating contamination from true bacteremia is essential for the accurate measurement of nosocomial bloodstream infection rates. Automated approaches to this task have been shown to perform very well compared with infection control practitioners (ICP) applying the traditional NNIS criteria (56, 141, 161). Yokoe et al. demonstrated that an automated approach for detecting nosocomial infections that relied solely upon microbiology data agreed with an NNIS-based retrospective assessment by ICP 91% of the time for cultures of adult patients (161). Disagreements were due primarily to situations in which only a single positive culture had been identified. In this scenario, CDC definitions rely on additional clinical data such as patient findings or treatment information, while the automated approach relied on a subsequent positive culture within a 5-day period. As a result of this difference in approach, 5/65 cultures were labeled as contaminated by the automated approach and as true bacteremia by the NNIS definition. In pediatric patients, agreement was found only 50% of the time, suggesting that its utility in this population may be limited. Graham et al. specifically studied the ability of a similar system in the neonatal population (47). They examined the performance of an automated system for detecting nosocomial bloodstream infections in two neonatal intensive care units in support of infection control activities. They found that their sensitivity and specificity for detecting such infections were 79% and 96%, respectively, although when coagulase-negative staphylococci were excluded, those numbers rose to 84% and 99%.

Trick et al. focused on the evaluation of a computer-based approach for detecting hospital-acquired, CVC-associated bloodstream infections (141). A comprehensive comparison of prospective ICP review, retrospective investigator assessment, and various computer algorithms was conducted on positive blood cultures from adult patients. Making this determination required several specific steps, including (i) the appropriate classification of hospital-acquired infection versus infection present upon admission, (ii) the correct ascertainment of true bacteremia versus contamination, (iii) distinguishing primary versus secondary infections, and (iv) detection of CVC use. The automated rules varied with respect to the inclusion of medication data and the time period over which data were used by a given rule. Those authors found that their computer-based algorithms performed at least as well as the ICP assessment and in fact outperformed them when combined with a manual determination of CVC use. When they looked specifically at the classification of pathogens versus contaminant organisms, a computer-based algorithm that included both microbiology data as well as pharmacy data had a sensitivity and specificity of 77% and 73%, respectively. The use of microbiology data only resulted in a drop of sensitivity to 55%.

Other investigators focused on the automated classification of blood culture results in order to provide clinical decision

support by estimating probabilities of contamination and displaying this information to clinicians at the point of care. Wang et al. utilized a previously validated prediction model (14) and revised it to include only readily available electronic data (146). By eliminating clinical data such as blood pressure, temperature, etc., they found only a slight degradation in the performance of the model. They then implemented a clinical rule into the laboratory information system to display the probability information along with blood culture results. In a subsequent house staff survey, they found that half of the respondents indicated that the results had influenced their assessment of the probability of true bacteremia, and 98% indicated a desire to continue to receive the reports. These findings suggest that computer-based approaches offer not only benefits for surveillance activities but also an opportunity to change physician behavior for individual patients. Other investigators have also shown that models that use only readily available electronic data perform well in correctly predicting contamination (100).

PREVENTING CONTAMINATION

By definition, the specificity of the blood culture is directly related to the rate of false-positive results, which are caused primarily by contamination. Reducing contamination rates would lead to improved specificity and better performance of this important test. Unfortunately, there has been a dearth of blinded, randomized, controlled trials that might provide clear and compelling guidance on the best methods for the prevention of contamination. While few would claim that the complete elimination of contamination is possible, a number of efforts to reduce contamination rates have been explored, advocated, and utilized. Factors that have been explored for reducing contamination include skin preparation, culture bottle preparation, single versus double needle for bottle inoculation, source of culture (catheter versus percutaneous), the use of dedicated phlebotomy teams, and the use of commercial blood culture collection kits.

Skin Preparation

The most common source of contaminated percutaneous blood cultures is often thought to be the skin of the patient at the site where the cultures are obtained. One study attempted to find the source of coagulase-negative staphylococcal contaminants by performing molecular analysis to compare each blood isolate to isolates obtained from swabs of the patient and from the individual who obtained the cultures (144). Of 19 patients with contaminated cultures, six of the isolates were able to be matched to swabs, and all six matching swabs came from the patient, implying that the most common source of contamination is the patient's own skin flora. However, it is important that no matching sources were found for 13 of the 19 isolates.

Skin antisepsis cannot entirely prevent the contamination of blood cultures from skin flora because as many as 20% of skin-associated bacteria have been found to survive disinfection, as found by culturing skin samples harvested with a sterile surgical technique (21, 116). These skin bacteria can be located in deep layers of the skin or in other structures that antiseptics cannot penetrate. Nonetheless, inadequate skin preparation is thought to be the most common cause of blood culture contamination (30, 89, 147).

Many studies have been performed to determine the best skin antiseptic product to use for blood culturing. Perhaps the most commonly studied and traditionally used skin antiseptic for blood culturing is povidone-iodine, an iodophor. Three studies have found significantly lower contamination rates using iodine tincture compared with povidone-iodine (67, 113, 131), although two of those studies did not have standardized phlebotomy protocols and drying times for the antiseptics. The CAP Q-Probes study investigators found that the median contamination rate was significantly lower in settings where tincture of iodine was used (2.1%) versus an iodophor (2.6%) ($P = 0.036$), but these differences were not found in organizations that relied on a dedicated phlebotomy service, suggesting that contamination may be more related to technique than the actual antiseptic used (113). One study of chlorine peroxide versus povidone-iodine found contamination in 22 (1.3%) of 1,639 cultures in the chlorine peroxide group compared to 37 (2.3%) of 1,637 in the povidone-iodine group ($P = 0.065$) (125). Another study found that 0.5% chlorhexidine plus alcohol had significantly lower contamination rates than standard povidone-iodine (82). In contrast, two studies that compared chlorhexidine to tincture of iodine did not find a statistically significant difference in contamination rates between the two products (11, 140).

Alcohol-based products are also frequently utilized for skin preparation for blood cultures. Calfee and Farr performed a randomized comparative trial of four skin antiseptics for 12,692 percutaneous blood cultures—10% povidone iodine, 70% isopropyl alcohol, tincture of iodine, or povidone-iodine plus 70% ethyl alcohol (25). The overall contamination rate was 2.62% during the study period. The contamination rates were 2.93% with povidone-iodine, 2.58% with tincture of iodine, 2.50% with isopropyl alcohol, and 2.46% with povidone-iodine plus 70% ethyl alcohol ($P = 0.62$). Although there were no significant differences between the groups, those authors concluded that the antiseptics that contained alcohol may have had greater efficacy. Other studies that examined the difference between alcohol solutions and iodine were unable to detect a statistically significant difference in contamination rates (64, 119).

Several barriers can prevent the skin antisepsis technique from being effective for preventing contamination. The time required for the antiseptic to have maximal effect is an important consideration, since the agent with the most efficacy will not be effective if the time required to become effective is longer than clinically feasible. Individuals who draw blood cultures may not have knowledge of the minimum contact time for their chosen skin antiseptic, or circumstances may not allow a sufficient drying time. For example, povidone-iodine preparations require 1.5 to 2 min of contact time to have a maximal antiseptic effect, whereas tincture of iodine requires 30 s (151). This difference in time to effect may account for differences seen in many of the aforementioned studies as opposed to a clear difference in efficacy. Although controversial, some experts recommend that the culture site be prepped with 70% isopropyl or ethyl alcohol and allowed to air dry and that a

second prep should be performed using 1 to 2% tincture of iodine or 10% povidone-iodine (30, 71).

Culture Bottle Preparation

Although data are limited, it is standard practice to disinfect the tops of the culture bottles before inoculating them with blood (30). The rubber stopper on each bottle is not sterile despite being covered with a lid that requires removal prior to inoculation. In the CAP Q-Probes study of 640 institutions, investigators found that 95.5% of organizations routinely applied an antiseptic to the top of the culture bottle before inoculating the bottle (113). Those institutions that prepped the bottle tops had significantly lower contamination rates (2.3%) than those that did not prep the bottle tops (3.4%) ($P = 0.018$).

It has been recommended that individuals should not use iodine alone because it may cause erosion of the rubber stopper during incubation, thereby introducing contaminants. Some institutions use alcohol, whereas others use an iodine solution that is allowed to dry and is then wiped off with fresh alcohol prep prior to inoculating the bottle (36).

Single Needle versus Double Needle

Until the late 1980s, discarding the needle used to draw blood cultures and using a new, different needle to inoculate the bottles (double-needle technique) was standard practice. This was based on the theory that the needle used for phlebotomy may be contaminated, thereby leading to blood culture contamination. However, with the emergence of human immunodeficiency virus, this practice became questionable, as the process of changing needles was felt to increase the risk of needlestick injuries to phlebotomists. Confirmation of the risk associated with this procedure was shown in studies revealing that most (42%) needlestick injuries occurred after use and before disposal of the naked needle, and transferring specimens from one container to another with a hollow-bore needle has been responsible for 5% of needlestick injuries (134). Subsequently, since 1990, the double-needle technique has been discouraged in favor of using the same needle to draw blood and to inoculate the culture bottles (single-needle technique).

The effect of the double-needle technique versus the single-needle technique on blood culture contamination rates has been evaluated by several controlled studies (7, 31, 54, 60, 66, 114, 124, 136). For each of these studies, the authors admitted to inadequate power to detect the level of difference that was actually observed between the two techniques. In order to improve power, a meta-analysis of these studies was performed, and it was concluded that the double-needle technique did in fact decrease contamination rates from 3.7% to 2.0% ($P < 0.001$) (126). Furthermore, the 1997 CAP survey of 640 institutions found that the median contamination rate was 2.2% in settings where the double-needle technique was used (42% of institutions), compared to 2.7% in settings where a single needle was used, but this difference was not statistically significant (112).

At the time of publication, each study's authors reasonably concluded that any benefit from the double-needle technique did not outweigh the risk of needlestick injuries. However, since the publication of those studies, the risk of needlestick injury during phlebotomy has decreased, partially due to modern safety needles (134). Additionally, vacuum-activated transfer devices have been developed to prevent the necessity of using a hollow-bore needle to inoculate blood culture bottles, which allows phlebotomists to engage the safety mechanisms on safety needles immediately after withdrawal from the patient. It remains to be seen whether these newer, safer technologies will reinvigorate the controversy about any potential relative benefits of the double-needle technique.

Obtaining Cultures Percutaneously instead of via Vascular Catheters

As stated above, cultures obtained from vascular catheters can be quite difficult to interpret. However, this technique remains a very common practice for many reasons. Many clinicians seek to prevent inflicting pain on patients by drawing cultures from a catheter instead of percutaneously. Others may wish to decrease the likelihood of inducing transient bacteremia by phlebotomy, especially for highly immunosuppressed patients. For the neonatal population, the difficulty of venous access is a real problem. Finally, practitioners may fear causing nosocomial volume depletion or anemia by drawing too many blood cultures, a potential issue with neonates or profoundly anemic patients.

Despite these good intentions, there are many undesirable consequences of this practice. The consequences could include the requirement for more cultures for clarification, more diagnostic studies, or the unnecessary use of antibiotics with the associated potential for allergic reactions, unanticipated drug interactions, or adverse drug events. Additionally, if falsely positive culture results from vascular catheters are misinterpreted, unnecessary and prolonged vascular access for intravenous antibiotics may be a consequence.

Phlebotomy Team

Trained phlebotomy or blood culture teams have been found to decrease blood culture contamination rates (132, 150, 151). In one study at a community teaching hospital, blood cultures drawn by a dedicated blood culture team using a commercially available kit had a contamination rate of 1%, as opposed to cultures drawn by resident physicians, which had a contamination rate of 4.8% using the same kit. They compared the costs of this team to the cost savings associated with a reduction in contamination rates and reported a net savings of $40,000 over a 6-month period (150). Investigators in the CAP Q-Probes study found that contamination rates were 3.9% at institutions where more than half of all blood cultures were collected by resident physicians, versus 2.2% at institutions where less than half of all blood cultures were obtained by resident physicians (112). In the more recent Q-Tracks study, there was a statistically significant difference in contamination rates between institutions that utilized a dedicated phlebotomy team versus other staff for culture collection. Institutions in which the large majority of cultures were drawn by nursing staff had a contamination rate of 4.21%, while those institutions in which those same individuals did not collect any culture specimens had a contamination rate of 2.17% (17). Dedicated

KUR-MAG-DE003928

phlebotomy teams are increasingly common in the inpatient setting; in a study of 640 institutions, Schifman et al. noted that, on average, 70% of cultures were collected by phlebotomy teams at teaching institutions, while 85% of cultures were collected by such teams at nonteaching hospitals (113).

For those facilities that have not invested in the establishment of a dedicated phlebotomy team, another method that could be used is monitoring and feedback of contamination rates to the collectors. Weinstein performed a pilot study that monitored phlebotomists' contamination rates on a monthly basis. Those results revealed a contamination rate of 3% for phlebotomists compared with nearly 11% for blood cultures obtained by resident physicians, nondegree nursing assistants, and nurses (151). Monitoring and feeding back contamination rates to individuals who obtain blood cultures were used successfully in at least one other institution that achieved a 50% reduction in contamination rates using this methodology (45). Many institutions are using this technique, as indicated in the CAP Q-Probes survey, which found that 47% of laboratories stratified contamination rates on the basis of individual phlebotomists (112).

Commercial Blood Culture Collection Kits

Whether commercially marketed blood culture collection kits reduce infection rates has been debated. In one teaching hospital, cultures drawn by resident physicians who used a commercial kit had a contamination rate of 4.8%, compared to 8.4% for residents who did not use the kit (150). Kits have been found to be beneficial in other studies as well (112). Another study compared povidone-iodine pledgets and alcohol pledgets to a collection kit containing breakable ampules of alcohol and 2% iodine tincture and found no difference in contamination rates when commercial kits were used (156).

SUPPORTING OPTIMAL USE OF BLOOD CULTURES

Blood cultures are frequently ordered tests. Unpublished data from our own academic health center, which includes a 565-bed tertiary hospital with approximately 30,000 admissions per year, suggest that over 20% of our hospitalizations involve at least one blood culture. The high utilization of blood culture testing can be partially attributed to two important reasons: the difficulty that most clinicians have in predicting the risk of bacteremia (72, 80, 97) and their low threshold for ordering the test, given the significant risk of morbidity and mortality associated with this condition (15, 147, 155). Additionally, for some specific clinical conditions, such as patients admitted to the hospital with community-acquired pneumonia, professional or governmental organizations have recommended universal blood culture testing (73). As discussed above, the pretest probability for bacteremia greatly influences the positive predictive value of a blood culture result. Accordingly, several investigators have developed and evaluated clinical prediction rules for bacteremia in a wide variety of patient populations in an effort to assist decision-making regarding diagnostic workup and management. The scientific community has also assessed the rates of bacteremia in a wide variety of patient populations to better understand disease prevalence, potentially allowing the development and refinement of consensus guidelines for specific clinical scenarios.

Clinical Prediction Models

Accurate clinical bacteremia prediction models have the potential to improve the use of blood culture testing and to aid in the interpretation of indeterminate culture results by providing pre- and posttest probabilities (12). Prediction models are generally developed using two consecutive analyses: an initial derivation step that is used to determine the independent predictors of the outcome of interest, which is followed by a validation set that is used to test the model in another population. For a prediction model to be maximally useful, it should be applicable to other settings (148). Researchers have developed or studied models for predicting bacteremia in hospitalized adults (12, 65, 72, 80, 85, 88, 160) and adult patients seen in emergency departments (40, 120, 159). Similar efforts have been explored in pediatric populations, although the motivation for many of these models is targeted primarily at decision-making regarding hospital admission versus outpatient management and initiation of empirical therapy and not whether or not to obtain blood cultures (3, 4, 8, 61, 70, 99). In recent years, greater attention has been paid to the impact of contamination rates on the utility and effectiveness of the blood culture test and the implications for its use in pediatric patients (9, 63, 115, 130, 138).

In hospitalized adults, clinical prediction rules for bacteremia have been found to have mixed results, at least from the perspective of the potential for reducing unnecessary blood cultures. Bates et al. developed a model that grouped patients into four different levels of bacteremia risk based on a combination of clinical and laboratory findings (12). In this prospective cohort study, they found that patients in the lowest risk category had a 1% chance of having bacteremia in the derivation set and a 2% chance in the validation set. In this low-risk group, the positive predictive value of a positive culture was 18%. Leibovici et al. developed a similar model that focused on evaluation of newly admitted febrile adults and found the prevalence of bacteremia in the low-risk groups to be 5% in the derivation set and 1% in the validation set (65). In an attempt to test these models outside their originating institutions, Yehezkelli et al. studied the accuracy of both the Bates and Leibovici prediction models in two hospitals (academic and community) in Israel. They found that the accuracy of both models "deteriorated significantly," with misclassification rates in the low-risk groups of 13 to 15% using the Bates model and 7 to 8% using the Leibovici model (160). Mylotte et al. attempted to validate Bates' model in a different institution with similar patients and found a slight degradation in performance, with a 3% misclassification rate for low-risk patients (88). Misclassification rates for low-risk groups in models developed by other investigators ranged from 4.6 to 5.1% (80, 85, 148). As several of the authors of those studies acknowledged, such results may be insufficient for reducing blood culture testing. Indeed, based on one survey of 149 physicians that included house staff and infectious disease specialists, investigators concluded that the sensitivity of a clinical prediction rule for bacteremia would have to be extremely high (99 to 100%) to be widely accepted.

Bacteremia prediction modeling in the emergency department setting has been studied as well (40, 120, 159). Shapiro et al. described a general clinical prediction rule for bacteremia in the emergency department setting that identified low-risk groups that were associated with a 0.8% and 1.8% risk of bacteremia (derivation and validation populations, respectively) (120). The sensitivity of the model was 98% in the derivation model and 96% in the validation model. While such prediction rules may well prove clinically useful for decision-making regarding hospitalization or the initiation of empirical antibiotic therapy, it remains unclear whether or not such tools will reduce unnecessary blood culture use.

Population Studies of Bacteremia Prevalence

Efforts to ascertain bacteremia prevalence in specific subpopulations have the potential benefit to inform the appropriate use of diagnostic tests such as blood cultures. In the pediatric population, investigators have studied the risk of occult bacteremia, given the widespread adoption of vaccinations to prevent infection caused by *Haemophilus influenzae* type b and *Streptococcus pneumoniae* (1, 9, 130). In a study of well-appearing, highly febrile children aged 2 to 36 months, Stoll and Rubin found that the incidence of occult bacteremia was 0.91% (95% confidence interval, 0 to 1.9%) and concluded that universal blood culture testing in this population may be unnecessary (130). In a recent similar study, Herz et al. conducted a retrospective review of blood cultures obtained from children aged 3 to 36 months during a 5-year period from 1998 to 2003 at Kaiser Permanente Northern California ambulatory facilities (52). Bacteremia rates dropped from 1.62% to 0.71% from the first year to the last year of the study period, while the contaminant-to-pathogen ratio increased from 1.2:1 to 2.3:1, leading the authors to agree with Stoll and Rubin about the decreased role for blood culture testing in highly febrile children in this age group, who are otherwise well-appearing and were previously healthy. The necessity of blood cultures remains controversial, however. Other investigators who studied occult bacteremia rates in similar age groups (although using somewhat different inclusion/exclusion criteria) found slightly higher rates of 1.9 to 3%, prompting them to suggest obtaining blood cultures and deferring treatment pending culture results (9).

The emergency department is another setting that has received significant attention in terms of blood culture utilization, bacteremia prevalence, and the impact of blood cultures on patient management. Innes et al. (53a) found that during a 6-month period at a hospital in British Columbia, blood culture results for patients seen in the emergency department were rarely helpful, with only 2.1% of 767 culture episodes yielding "potentially helpful" information. Similarly, in a retrospective study of 1,350 patients who had blood cultures taken in the emergency department (and who were subsequently discharged) of a large U.S. urban teaching hospital, only 0.52% had results that potentially affected their management. The prevalence of bacteremia in that population was 1.8%, leading those authors to conclude that specific criteria were needed to help guide the decision regarding blood culture testing (131a).

Finally, the question of whether or not all patients hospitalized for community-acquired pneumonia require pretreatment blood cultures, as recommended by consensus guidelines (73, 91), has become intensely debated in recent years (20a, 52a). Fueling the controversy are increasing reports suggesting that due in part to a combination of high contamination rates and low bacteremia risk, the PPV for blood cultures is low and test results are often clinically unhelpful (26, 27, 29, 33, 137). Consequently, investigators have attempted to develop specific bacteremia prediction rules for community-acquired pneumonia patients to help guide decision-making surrounding the use of blood cultures (81, 149). Metersky et al. developed a model that stratified patients into three different groups on the basis of their bacteremia risk and concluded that their tool would lead to a 38% reduction in blood culture utilization while missing 11% of individuals with true bacteremia (81). It remains to be seen whether such a model can be incorporated into routine practice.

While controversy remains in each of these areas about the proper criteria for blood culture testing and initiation of antibiotic therapy, many agree that the combination of low pretest probability (i.e., disease prevalence) with high contamination rates often leads to unhelpful culture results.

BLOOD CULTURE CONTAMINATION IN THE PEDIATRIC POPULATION

Contaminated blood cultures are a particular challenge for infants and children for several reasons. While an in-depth discussion of the topic is beyond the scope of this review, evidence suggests that contamination occurs more frequently in this population, particularly in young infants (78, 92, 101, 135). In addition, concerns about the risk of occult bacteremia have led to guidelines recommending the use of blood cultures and empirical therapy, particularly in children less than 3 years of age (10). As described above, however, the tides may be starting to turn, as the past decade has seen multiple studies suggesting that in the current era of influenza and pneumococcal vaccination, the risk of occult bacteremia has significantly lowered. As a result, the use of blood culture testing in this patient population is associated with a lower positive predictive value. Moreover, analysis of current practice patterns reveals that in most cases, only single blood cultures are collected (93, 105, 111). In an effort to reduce unnecessary discomfort, pediatricians often use existing intravenous catheters for obtaining cultures instead of peripheral venipuncture (105). The data on the impact of this practice on contamination rates are mixed. In a 2-year observational study comparing contamination rates for culture specimens drawn via venipuncture to those for culture specimens drawn via intravenous catheters in children, Norberg et al. found a large, statistically significant decrease in the rate of false-positive blood cultures (9.1% to 2.8%) after their institution adopted a policy eliminating the use of intravenous catheters for this purpose (92). While compelling, conclusions based on that study are limited by its design, which lacked a control group to account for any potential confounders such as temporal trends. Ramsook et al. found similar results in a 6-month study of 2,431 pediatric blood cultures, with contamination rates of 3.4% for specimens collected via intravenous catheters versus 2.0% for those obtained by separate venipuncture ($P = 0.043$) (101). While

that study used a large sample size, details of the study design and methods are somewhat unclear, making it difficult to ascertain both internal and external validity. Other studies have shown no difference in contamination rates according to specimen collection routes (55, 124). Given pediatricians' disinclination to subject children and infants to unnecessary painful procedures, and the lack of clear evidence on which approach best prevents specimen contamination, the use of existing catheters for blood culture collection continues in this patient population (79). As described above, single blood cultures are particularly common in pediatric patients; this fact, combined with the increased utilization of catheter-based culture specimens, makes discrimination between true bacteremia and contamination challenging, particularly when coagulase-negative staphylococci are grown in culture (24). To combat this challenge, investigators have explored multiple avenues, including the use of C-reactive protein, time to positivity, quantity of growth, and clinical status (3, 18, 19, 32, 44, 98, 110, 129). While none of these factors have performed well enough individually to warrant widespread adoption, they continue to be under investigation.

CONCLUSION

Clearly, progress has been made on several fronts in the battle against blood culture contamination. Better strategies for preventing contamination in the first place are being established, and we are improving our ability to distinguish contamination from true bacteremia. New research on measures to estimate the pretest likelihood of bacteremia offers promise in reducing unnecessary blood culture utilization. Despite the progress that has been made, however, significant barriers remain. Without a gold standard for truly distinguishing contaminant organisms from true pathogens, studies that seek to measure the success of prevention strategies are inherently limited. Similarly, efforts to help establish the posttest probability of bacteremia given a positive result are restricted. Genomic and proteomic approaches for identifying bacteremia are being explored but remain in the early stages (96, 122, 123). There is evidence, however, to suggest that even these methods can be hampered by problems with contamination (95). Furthermore, additional research on the value of time to positivity and quantity of growth for differentiating culture contamination from bacteremia is necessary. Of the various prevention strategies, additional investigation would help to determine the relative effect of each strategy on overall contamination rates. In the meantime, information technology may have a role in facilitating the detection of contamination, assisting clinical decision-making, and enabling better systems for tracking contamination rates both within and between institutions. Additional research on how to make these tools more useful and more acceptable in the clinical work environment is needed. Similarly, while clinical prediction rules for bacteremia have received much scrutiny in the past 15 years, it remains unclear whether they perform at a level that is accurate enough to influence physician behavior and affect blood culture utilization. More research is needed to refine these models and test them in other settings. In the pediatric arena, additional studies are clearly needed to help physicians interpret the results of single blood cultures that grow coagulase-negative staphylococci, a persistent challenge. Ultimately, blood culture contamination is a complex, challenging problem that requires a multidisciplinary approach. Well-conceived and effectively implemented strategies are important for reconciling the sometimes contradictory requirements of individual patient care, population health, and effective resource allocation.

REFERENCES

1. **Alpern, E. R., E. A. Alessandrini, L. M. Bell, K. N. Shaw, and K. L. McGowan.** 2000. Occult bacteremia from a pediatric emergency department: current prevalence, time to detection, and outcome. Pediatrics **106:** 505–511.
2. **American Thoracic Society and the Infectious Disease Society of America.** 2005. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am. J. Respir. Crit. Care Med. **171:**388–416.
3. **Ammann, R. A., A. Hirt, A. R. Luthy, and C. Aebi.** 2003. Identification of children presenting with fever in chemotherapy-induced neutropenia at low risk for severe bacterial infection. Med. Pediatr. Oncol. **41:**436–443.
4. **Ammann, R. A., A. Hirt, A. R. Luthy, and C. Aebi.** 2004. Predicting bacteremia in children with fever and chemotherapy-induced neutropenia. Pediatr. Infect. Dis. J. **23:**61–67.
5. **Anonymous.** 1996. National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986-April 1996, issued May 1996. A report from the National Nosocomial Infections Surveillance (NNIS) System. Am. J. Infect. Control **24:**380–388.
6. **Aronson, M. D., and D. H. Bor.** 1987. Blood cultures. Ann. Intern. Med. **106:**246–253.
7. **Ashdown, L. R.** 1988. Blood culture collection techniques and bacterial contamination. Pathology **20:**397–398.
8. **Bachur, R. G., and M. B. Harper.** 2001. Predictive model for serious bacterial infections among infants younger than 3 months of age. Pediatrics **108:**311–316.
9. **Bandyopadhyay, S., J. Bergholte, C. D. Blackwell, J. R. Friedlander, and H. Hennes.** 2002. Risk of serious bacterial infection in children with fever without a source in the post-Haemophilus influenzae era when antibiotics are reserved for culture-proven bacteremia. Arch. Pediatr. Adolesc. Med. **156:**512–517. (Erratum, **156:**749.)
10. **Baraff, L. J., J. W. Bass, G. R. Fleisher, J. O. Klein, G. H. McCracken, Jr., K. R. Powell, D. L. Schriger, et al.** 1993. Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. Ann. Emerg. Med. **22:**1198–1210. (Erratum, **22:**1490.)
11. **Barenfanger, J., C. Drake, J. Lawhorn, and S. J. Verhulst.** 2004. Comparison of chlorhexidine and tincture of iodine for skin antisepsis in preparation for blood sample collection. J. Clin. Microbiol. **42:**2216–2217.
12. **Bates, D. W., E. F. Cook, L. Goldman, and T. H. Lee.** 1990. Predicting bacteremia in hospitalized patients. A prospectively validated model. Ann. Intern. Med. **113:**495–500.
13. **Bates, D. W., L. Goldman, and T. H. Lee.** 1991. Contaminant blood cultures and resource utilization. The true consequences of false-positive results. JAMA **265:**365–369.
14. **Bates, D. W., and T. H. Lee.** 1992. Rapid classification of positive blood cultures. Prospective validation of a multivariate algorithm. JAMA **267:** 1962–1966.
15. **Bates, D. W., K. E. Pruess, and T. H. Lee.** 1995. How bad are bacteremia and sepsis? Outcomes in a cohort with suspected bacteremia. Arch. Intern. Med. **155:**593–598.
16. **Beekmann, S. E., D. J. Diekema, and G. V. Doern.** 2005. Determining the clinical significance of coagulase-negative staphylococci isolated from blood cultures. Infect. Control Hosp. Epidemiol. **26:**559–566.
17. **Bekeris, L. G., J. A. Tworek, M. K. Walsh, and P. N. Valenstein.** 2005. Trends in blood culture contamination: a College of American Pathologists Q-Tracks study of 356 institutions. Arch. Pathol. Lab. Med. **129:**1222–1225.
18. **Berger, C., J. Uehlinger, D. Ghelfi, N. Blau, and S. Fanconi.** 1995. Comparison of C-reactive protein and white blood cell count with differential in neonates at risk for septicaemia. Eur. J. Pediatr. **154:**138–144.
19. **Berger, R. M., M. Y. Berger, H. A. van Steensel-Moll, G. Dzoljic-Danilovic, and G. Derksen-Lubsen.** 1996. A predictive model to estimate the risk of serious bacterial infections in febrile infants. Eur. J. Pediatr. **155:**468–473.
20. **Beutz, M., G. Sherman, J. Mayfield, V. J. Fraser, and M. H. Kollef.** 2003. Clinical utility of blood cultures drawn from central vein catheters and peripheral venipuncture in critically ill medical patients. Chest **123:**854–861.

20a. **Birnbaumer, D. M.** 24 November 2004, posting date. Blood cultures aren't useful for managing immunocompetent CAP inpatients. J. Watch Emerg. Med. [Online.] http://emergency-medicine.jwatch.org/cgi/content/full/2004/1124/1.

21. **Brown, E., R. P. Wenzel, and J. O. Hendley.** 1989. Exploration of the microbial anatomy of normal human skin by using plasmid profiles of

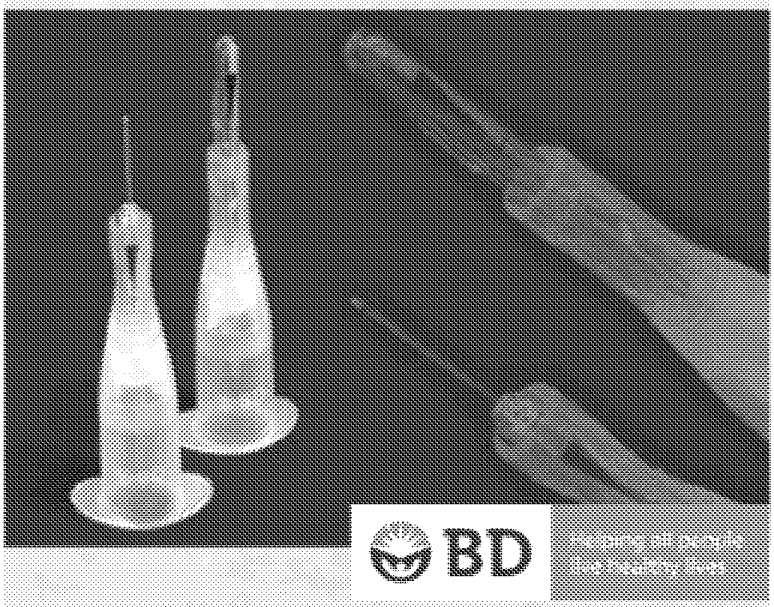
coagulase-negative staphylococci: search for the reservoir of resident skin flora. J. Infect. Dis. **160:**644–650.
22. **Bryan, C. S.** 1989. Clinical implications of positive blood cultures. Clin. Microbiol. Rev. **2:**329–353.
23. **Burke, J. P., D. C. Classen, S. L. Pestotnik, R. S. Evans, and L. E. Stevens.** 1991. The HELP system and its application to infection control. J. Hosp. Infect. **18**(Suppl. A)**:**424–431.
24. **Buttery, J. P.** 2002. Blood cultures in newborns and children: optimising an everyday test. Arch. Dis. Child. Fetal Neonatal Ed. **87:**F25–F28.
25. **Calfee, D. P., and B. M. Farr.** 2002. Comparison of four antiseptic preparations for skin in the prevention of contamination of percutaneously drawn blood cultures: a randomized trial. J. Clin. Microbiol. **40:**1660–1665.
26. **Campbell, S. G., T. J. Marrie, R. Anstey, S. Ackroyd-Stolarz, and G. Dickinson.** 2003. Utility of blood cultures in the management of adults with community acquired pneumonia discharged from the emergency department. Emerg. Med. J. **20:**521–523.
27. **Campbell, S. G., T. J. Marrie, R. Anstey, G. Dickinson, and S. Ackroyd-Stolarz.** 2003. The contribution of blood cultures to the clinical management of adult patients admitted to the hospital with community-acquired pneumonia: a prospective observational study. Chest **123:**1142–1150.
28. **Catton, J. A., B. M. Dobbins, P. Kite, J. M. Wood, K. Eastwood, S. Sugden, J. A. Sandoe, D. Burke, M. J. McMahon, and M. H. Wilcox.** 2005. In situ diagnosis of intravascular catheter-related bloodstream infection: a comparison of quantitative culture, differential time to positivity, and endoluminal brushing. Crit. Care Med. **33:**787–791.
29. **Chalasani, N. P., M. A. Valdecanas, A. K. Gopal, J. E. McGowan, Jr., and R. L. Jurado.** 1995. Clinical utility of blood cultures in adult patients with community-acquired pneumonia without defined underlying risks. Chest **108:**932–936.
30. **Chandrasekar, P. H., and W. J. Brown.** 1994. Clinical issues of blood cultures. Arch. Intern. Med. **154:**841–849.
31. **Chapnick, E. K., B. C. Schaffer, J. D. Gradon, L. I. Lutwick, S. A. Krigsman, and M. Levi.** 1991. Technique for drawing blood for cultures: is changing needles truly necessary? Southern Med. J. **84:**1197–1198.
32. **Chiu, Y. H., T. J. Chen, C. T. Chen, and C. C. Lu.** 2005. Positive blood cultures in pediatric emergency department patients: epidemiological and clinical characteristics. Acta Paediatr. Taiwan. **46:**11–16.
33. **Corbo, J., B. Friedman, P. Bijur, and E. J. Gallagher.** 2004. Limited usefulness of initial blood cultures in community acquired pneumonia. Emerg. Med. J. **21:**446–448.
34. **DesJardin, J. A., M. E. Falagas, R. Ruthazer, J. Griffith, D. Wawrose, D. Schenkein, K. Miller, and D. R. Snydman.** 1999. Clinical utility of blood cultures drawn from indwelling central venous catheters in hospitalized patients with cancer. Ann. Intern. Med. **131:**641–647.
35. **Dunagan, W. C., R. S. Woodward, G. Medoff, J. L. Gray III, E. Casabar, M. D. Smith, C. A. Lawrenz, and E. Spitznagel.** 1989. Antimicrobial misuse in patients with positive blood cultures. Am. J. Med, **87:**253–259.
36. **Ernst, D. J.** 2004. Controlling blood-culture contamination rates. Med. Lab. Obs. **36:**14–18; quiz, 20–21.
37. **Evans, M. R., A. L. Truant, J. Kostman, and L. Locke.** 1991. The detection of positive blood cultures by the BACTEC NR660. The clinical importance of four-day versus seven-day testing. Diagn. Microbiol. Infect. Dis. **14:**107–110.
38. **Everts, R. J., E. N. Vinson, P. O. Adholla, and L. B. Reller.** 2001. Contamination of catheter-drawn blood cultures. J. Clin. Microbiol. **39:**3393–3394.
39. **Felices, F. J., J. L. Hernandez, J. Ruiz, J. Meseguer, J. A. Gomez, and E. Molina.** 1979. Use of the central venous pressure catheter to obtain blood cultures. Crit. Care Med. **7:**78–79.
40. **Fontanarosa, P. B., F. J. Kaeberlein, L. W. Gerson, and R. B. Thomson.** 1992. Difficulty in predicting bacteremia in elderly emergency patients. Ann. Emerg. Med. **21:**842–848.
41. **Franklin, J. A., A. H. Gaur, J. L. Shenep, X. J. Hu, and P. M. Flynn.** 2004. In situ diagnosis of central venous catheter-related bloodstream infection without peripheral blood culture. Pediatr. Infect. Dis. J. **23:**614–618.
42. **Galdbart, J. O., A. Morvan, N. Desplaces, and N. el Solh.** 1999. Phenotypic and genomic variation among *Staphylococcus epidermidis* strains infecting joint prostheses. J. Clin. Microbiol. **37:**1306–1312.
43. **Garner, J. S., W. R. Jarvis, T. G. Emori, T. C. Horan, and J. M. Hughes.** 1988. CDC definitions for nosocomial infections, 1988. Am. J. Infect. Control **16:**128–140. (Erratum, **16:**177.)
44. **Gaur, A. H., P. M. Flynn, D. J. Heine, M. A. Giannini, J. L. Shenep, and R. T. Hayden.** 2005. Diagnosis of catheter-related bloodstream infections among pediatric oncology patients lacking a peripheral culture, using differential time to detection. Pediatr. Infect. Dis. J. **24:**445–449.
45. **Gibb, A. P., B. Hill, B. Chorel, and R. Brant.** 1997. Reduction in blood culture contamination rate by feedback to phlebotomists. Arch. Pathol. Lab. Med. **121:**503–507.
46. **Gowardman, J. R., C. Montgomery, S. Thirlwell, J. Shewan, A. Idema, P. D. Larsen, and J. H. Havill.** 1998. Central venous catheter-related bloodstream infections: an analysis of incidence and risk factors in a cohort of 400 patients. Intensive Care Med. **24:**1034–1039.
47. **Graham, P. L., III, P. San Gabriel, S. Lutwick, J. Haas, and L. Saiman.** 2004. Validation of a multicenter computer-based surveillance system for hospital-acquired bloodstream infections in neonatal intensive care departments. Am. J. Infect. Control **32:**232–234.
48. **Haimi-Cohen, Y., S. Shafinoori, V. Tucci, and L. G. Rubin.** 2003. Use of incubation time to detection in BACTEC 9240 to distinguish coagulase-negative staphylococcal contamination from infection in pediatric blood cultures. Pediatr. Infect. Dis. J. **22:**968–974.
49. **Han, X. Y., and A. L. Truant.** 1999. The detection of positive blood cultures by the AccuMed ESP-384 system: the clinical significance of three-day testing. Diagn. Microbiol. Infect. Dis. **33:**1–6.
50. **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.
51. **Herwaldt, L. A., M. Geiss, C. Kao, and M. A. Pfaller.** 1996. The positive predictive value of isolating coagulase-negative staphylococci from blood cultures. Clin. Infect. Dis. **22:**14–20.
52. **Herz, A. M., T. L. Greenhow, J. Alcantara, J. Hansen, R. P. Baxter, S. B. Black, and H. R. Shinefield.** 2006. Changing epidemiology of outpatient bacteremia in 3- to 36-month-old children after the introduction of the heptavalent-conjugated pneumococcal vaccine. Pediatr. Infect. Dis. J. **25:**293–300.
52a. **Houck, P. M., D. W. Bratzler, J. G. Bartlett, L. Mandell, M. S. Niederman.** 27 April 2005, posting date. The CMS Blood Cultures for CAP Program: the architects speak out. J. Watch Emerg. Med. [Online.] http://emergencymedicine.jwatch.org/cgi/content/full/2005/427/1.
53. **Huang, A. H., J. J. Yan, and J. J. Wu.** 1998. Comparison of five days versus seven days of incubation for detection of positive blood cultures by the Bactec 9240 system. Eur. J. Clin. Microbiol. Infect. Dis. **17:**637–641.
53a. **Innes, G., K. Roland, E. Grafstein, and J. M. Christenson.** 2000. Utility of blood cultures in the emergency department. Acad. Emerg. Med. **7:**579.
54. **Isaacman, D. J., and R. B. Karasic.** 1990. Lack of effect of changing needles on contamination of blood cultures. Pediatr. Infect. Dis. J. **9:**274–278.
55. **Isaacman, D. J., and R. B. Karasic.** 1990. Utility of collecting blood cultures through newly inserted intravenous catheters. Pediatr. Infect. Dis. J. **9:**815–818.
56. **Kahn, M. G., S. A. Steib, V. J. Fraser, and W. C. Dunagan.** 1993. An expert system for culture-based infection control surveillance, p. 171–175. *In* Proceedings of the Annual Symposium on Computer Applications in Medical Care. Hanley & Belfus, Inc., Philadelphia, Pa.
57. **Khatib, R., K. M. Riederer, J. A. Clark, S. Khatib, L. E. Briski, and F. M. Wilson.** 1995. Coagulase-negative staphylococci in multiple blood cultures: strain relatedness and determinants of same-strain bacteremia. J. Clin. Microbiol. **33:**816–820.
58. **Kim, S. D., L. C. McDonald, W. R. Jarvis, S. K. McAllister, R. Jerris, L. A. Carson, and J. M. Miller.** 2000. Determining the significance of coagulase-negative staphylococci isolated from blood cultures at a community hospital: a role for species and strain identification. Infect. Control Hosp. Epidemiol. **21:**213–217.
59. **Krause, R., R. Haberl, A. Wolfler, F. Daxbock, H. W. Auner, G. J. Krejs, C. Wenisch, and E. C. Reisinger.** 2003. Molecular typing of coagulase-negative staphylococcal blood and skin culture isolates to differentiate between bacteremia and contamination. Eur. J. Clin. Microbiol. Infect. Dis. **22:**760–763.
60. **Krumholz, H. M., S. Cummings, and M. York.** 1990. Blood culture phlebotomy: switching needles does not prevent contamination. Ann. Intern. Med. **113:**290–292. (Erratum, **113:**723.)
61. **Kuppermann, N., G. R. Fleisher, and D. M. Jaffe.** 1998. Predictors of occult pneumococcal bacteremia in young febrile children. Ann. Emerg. Med. **31:**679–687.
62. **Kurlat, I., B. J. Stoll, and J. E. McGowan, Jr.** 1989. Time to positivity for detection of bacteremia in neonates. J. Clin. Microbiol. **27:**1068–1071.
63. **Lee, G. M., G. R. Fleisher, and M. B. Harper.** 2001. Management of febrile children in the age of the conjugate pneumococcal vaccine: a cost-effectiveness analysis. Pediatrics **108:**835–844.
64. **Lee, S., I. Schoen, and A. Malkin.** 1967. Comparison of use of alcohol with that of iodine for skin antisepsis in obtaining blood cultures. Am. J. Clin. Pathol. **47:**646–648.
65. **Leibovici, L., S. Greenshtain, O. Cohen, F. Mor, and A. J. Wysenbeek.** 1991. Bacteremia in febrile patients. A clinical model for diagnosis. Arch. Intern. Med. **151:**1801–1806.
66. **Leisure, M. K., D. M. Moore, J. D. Schwartzman, G. F. Hayden, and L. G. Donowitz.** 1990. Changing the needle when inoculating blood cultures. A no-benefit and high-risk procedure. JAMA **264:**2111–2112.
67. **Little, J. R., P. R. Murray, P. S. Traynor, and E. Spitznagel.** 1999. A randomized trial of povidone-iodine compared with iodine tincture for venipuncture site disinfection: effects on rates of blood culture contamination. Am. J. Med. **107:**119–125.
68. **Lyytikainen, O., V. Valtonen, V. J. Anttila, and P. Ruutu.** 1998. Evaluation of clinical and laboratory findings in leukaemic patients with blood cultures positive for Staphylococcus epidermidis. J. Hosp. Infect. **38:**27.
69. **MacGregor, R. R., and H. N. Beaty.** 1972. Evaluation of positive blood cultures. Guidelines for early differentiation of contaminated from valid positive cultures. Arch. Intern. Med. **130:**84–87.

70. **Madsen, K., M. Rosenman, S. Hui, and P. P. Breitfeld.** 2002. Value of electronic data for model validation and refinement: bacteremia risk in children with fever and neutropenia. J. Pediatr. Hematol. Oncol. **24:**256–262.
71. **Magadia, R. R., and M. P. Weinstein.** 2001. Laboratory diagnosis of bacteremia and fungemia. Infect. Dis. Clin. N. Am. **15:**1009–1024.
72. **Makadon, H. J., D. Bor, G. Friedland, P. Dasse, A. L. Komaroff, and M. D. Aronson.** 1987. Febrile inpatients: house officers' use of blood cultures. J. Gen. Intern. Med. **2:**293–297.
73. **Mandell, L. A., J. G. Bartlett, S. F. Dowell, T. M. File, Jr., D. M. Musher, C. Whitney, et al.** 2003. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. Clin. Infect. Dis. **37:**1405–1433.
74. **Martinez, J. A., J. A. DesJardin, M. Aronoff, S. Supran, S. A. Nasraway, and D. R. Snydman.** 2002. Clinical utility of blood cultures drawn from central venous or arterial catheters in critically ill surgical patients. Crit. Care Med. **30:**7–13.
75. **Masterson, K. C., and J. E. McGowan, Jr.** 1988. Detection of positive blood cultures by the Bactec NR660. The clinical importance of five versus seven days of testing. Am. J. Clin. Pathol. **90:**91–94.
76. **McBryde, E. S., M. Tilse, and J. McCormack.** 2005. Comparison of contamination rates of catheter-drawn and peripheral blood cultures. J. Hosp. Infect. **60:**118–121.
77. **McDonald, L. C., J. Fune, L. B. Gaido, M. P. Weinstein, L. G. Reimer, T. M. Flynn, M. L. Wilson, S. Mirrett, and L. B. Reller.** 1996. Clinical importance of increased sensitivity of BacT/Alert FAN aerobic and anaerobic blood culture bottles. J. Clin. Microbiol. **34:**2180–2184.
78. **McGowan, J. E., Jr., L. Bratton, J. O. Klein, and M. Finland.** 1973. Bacteremia in febrile children seen in a "walk-in" pediatric clinic. N. Engl. J. Med. **288:**1309–1312.
79. **McQuillen, K. K., K. A. Santucci, M. A. Conrad, D. G. Nelson, W. Lewander, S. J. Duffy, and A. C. Anderson.** 1999. Intravenous catheter blood cultures: utility and contamination. Pediatrics **103:**e52.
80. **Mellors, J. W., R. I. Horwitz, M. R. Harvey, and S. M. Horwitz.** 1987. A simple index to identify occult bacterial infection in adults with acute unexplained fever. Arch. Intern. Med. **147:**666–671.
81. **Metersky, M. L., A. Ma, D. W. Bratzler, and P. M. Houck.** 2004. Predicting bacteremia in patients with community-acquired pneumonia. Am. J. Respir. Crit. Care Med. **169:**342–347.
82. **Mimoz, O., A. Karim, A. Mercat, M. Cosseron, B. Falissard, F. Parker, C. Richard, K. Samii, and P. Nordmann.** 1999. Chlorhexidine compared with povidone-iodine as skin preparation before blood culture. A randomized, controlled trial. Ann. Intern. Med. **131:**834–837.
83. **Mirrett, S., L. B. Reller, C. A. Petti, C. W. Woods, B. Vazirani, R. Sivadas, and M. P. Weinstein.** 2003. Controlled clinical comparison of BacT/ALERT standard aerobic medium with BACTEC standard aerobic medium for culturing blood. J. Clin. Microbiol. **41:**2391–2394.
84. **Mirrett, S., M. P. Weinstein, L. G. Reimer, M. L. Wilson, and L. B. Reller.** 2001. Relevance of the number of positive bottles in determining clinical significance of coagulase-negative staphylococci in blood cultures. J. Clin. Microbiol. **39:**3279–3281.
85. **Mozes, B., D. Milatiner, C. Block, Z. Blumstein, and H. Halkin.** 1993. Inconsistency of a model aimed at predicting bacteremia in hospitalized patients. J. Clin. Epidemiol. **46:**1035–1040.
86. **Muller-Premru, M., and P. Cernelc.** 2004. Molecular epidemiology of catheter-related bloodstream infections caused by coagulase-negative staphylococci in haematological patients with neutropenia. Epidemiol. Infect. **132:**921–925.
87. **Murray, P. R., P. Traynor, and D. Hopson.** 1992. Critical assessment of blood culture techniques: analysis of recovery of obligate and facultative anaerobes, strict aerobic bacteria, and fungi in aerobic and anaerobic blood culture bottles. J. Clin. Microbiol. **30:**1462–1468.
88. **Mylotte, J. M., M. A. Pisano, S. Ram, S. Nakasato, and D. Rotella.** 1995. Validation of a bacteremia prediction model. Infect. Control Hosp. Epidemiol. **16:**203–209.
89. **Mylotte, J. M., and A. Tayara.** 2000. Blood cultures: clinical aspects and controversies. Eur. J. Clin. Microbiol. Infect. Dis. **19:**157–163.
90. **National Nosocomial Infections Surveillance System.** 2004. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. Am. J. Infect. Control **32:**470–485.
91. **Niederman, M. S., L. A. Mandell, A. Anzueto, J. B. Bass, W. A. Broughton, G. D. Campbell, N. Dean, T. File, M. J. Fine, P. A. Gross, F. Martinez, T. J. Marrie, J. F. Plouffe, J. Ramirez, G. A. Sarosi, A. Torres, R. Wilson, V. L. Yu, et al.** 2001. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. Am. J. Respir. Crit. Care Med. **163:**1730–1754.
92. **Norberg, A., N. C. Christopher, M. L. Ramundo, J. R. Bower, and S. A. Berman.** 2003. Contamination rates of blood cultures obtained by dedicated phlebotomy vs intravenous catheter. JAMA **289:**726–729.
93. **Novis, D. A., J. C. Dale, R. B. Schifman, S. G. Ruby, and M. K. Walsh.** 2001. Solitary blood cultures: a College of American Pathologists Q-Probes study of 132,778 blood culture sets in 333 small hospitals. Arch. Pathol. Lab. Med. **125:**1290–1294.
94. **Peacock, S. J., I. C. Bowler, and D. W. Crook.** 1995. Positive predictive value of blood cultures growing coagulase-negative staphylococci. Lancet **346:**191–192.
95. **Peters, R. P., T. Mohammadi, C. M. Vandenbroucke-Grauls, S. A. Danner, M. A. van Agtmael, and P. H. Savelkoul.** 2004. Detection of bacterial DNA in blood samples from febrile patients: underestimated infection or emerging contamination? FEMS Immunol. Med. Microbiol. **42:**249–253.
96. **Peters, R. P., M. A. van Agtmael, S. A. Danner, P. H. Savelkoul, and C. M. Vandenbroucke-Grauls.** 2004. New developments in the diagnosis of bloodstream infections. Lancet Infect. Dis. **4:**751–760.
97. **Poses, R. M., and M. Anthony.** 1991. Availability, wishful thinking, and physicians' diagnostic judgments for patients with suspected bacteremia. Med. Decis. Making **11:**159–168.
98. **Pourcyrous, M., H. S. Bada, S. B. Korones, V. Baselski, and S. P. Wong.** 1993. Significance of serial C-reactive protein responses in neonatal infection and other disorders. Pediatrics **92:**431–435.
99. **Rackoff, W. R., R. Gonin, C. Robinson, S. G. Kreissman, and P. B. Breitfeld.** 1996. Predicting the risk of bacteremia in children with fever and neutropenia. J. Clin. Oncol. **14:**919–924.
100. **Ram, S., J. M. Mylotte, and M. Pisano.** 1995. Rapid classification of positive blood cultures: validation and modification of a prediction model. J. Gen. Intern. Med. **10:**82–88.
101. **Ramsook, C., K. Childers, S. G. Cron, and M. Nirken.** 2000. Comparison of blood-culture contamination rates in a pediatric emergency room: newly inserted intravenous catheters versus venipuncture. Infect. Control Hosp. Epidemiol. **21:**649–651.
102. **Reimer, L. G., M. L. Wilson, and M. P. Weinstein.** 1997. Update on detection of bacteremia and fungemia. Clin. Microbiol. Rev. **10:**444–465.
103. **Reisner, B. S., and G. L. Woods.** 1999. Times to detection of bacteria and yeasts in BACTEC 9240 blood culture bottles. J. Clin. Microbiol. **37:**2024–2026.
104. **Rogers, M. S., and B. A. Oppenheim.** 1998. The use of continuous monitoring blood culture systems in the diagnosis of catheter related sepsis. J. Clin. Pathol. **51:**635–637.
105. **Rubin, L. G., P. J. Sanchez, J. Siegel, G. Levine, L. Saiman, W. R. Jarvis, et al.** 2002. Evaluation and treatment of neonates with suspected late-onset sepsis: a survey of neonatologists' practices. Pediatrics **110:**e42.
106. **Rubin, R. H., E. D. Shapiro, V. T. Andriole, R. J. Davis, W. E. Stamm, et al.** 1992. Evaluation of new anti-infective drugs for the treatment of urinary tract infection. Clin. Infect. Dis. **15**(Suppl. 1)**:**S216–S227.
107. **Safdar, N., and D. G. Maki.** 2004. The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. Intensive Care Med. **30:**62–67.
108. **Saito, T., K. Senda, S. Takakura, N. Fujihara, T. Kudo, Y. Iinuma, M. Tanimoto, and S. Ichiyama.** 2003. Detection of bacteria and fungi in BacT/Alert standard blood-culture bottles. J. Infect. Chemother. **9:**227–232.
109. **Samore, M., D. Lichtenberg, L. Saubermann, C. Kawachi, and Y. Carmeli.** 1997. A clinical data repository enhances hospital infection control, p. 56–60. *In* Proceedings of the AMIA Annual Fall Symposium. Hanley & Belfus, Inc., Philadelphia, Pa.
110. **Santolaya, M. E., J. Cofre, and V. Beresi.** 1994. C-reactive protein: a valuable aid for the management of febrile children with cancer and neutropenia. Clin. Infect. Dis. **18:**589–595.
111. **Schifman, R. B., P. Bachner, and P. J. Howanitz.** 1996. Blood culture quality improvement: a College of American Pathologists Q-Probes study involving 909 institutions and 289 572 blood culture sets. Arch. Pathol. Lab. Med. **120:**999–1002.
112. **Schifman, R. B., and A. Pindur.** 1993. The effect of skin disinfection materials on reducing blood culture contamination. Am. J. Clin. Pathol. **99:**536–538.
113. **Schifman, R. B., C. L. Strand, F. A. Meier, and P. J. Howanitz.** 1998. Blood culture contamination: a College of American Pathologists Q-Probes study involving 640 institutions and 497134 specimens from adult patients. Arch. Pathol. Lab. Med. **122:**216–221.
114. **Scott, A. C.** 1979. Blood-culture technique: two needles or one. Lancet **i:**1414.
115. **Segal, G. S., and J. M. Chamberlain.** 2000. Resource utilization and contaminated blood cultures in children at risk for occult bacteremia. Arch. Pediatr. Adolesc. Med. **154:**469–473.
116. **Selwyn, S., and H. Ellis.** 1972. Skin bacteria and skin disinfection reconsidered. Br. Med. J. **i:**136–140.
117. **Seo, S. K., L. Venkataraman, P. C. DeGirolami, and M. H. Samore.** 2000. Molecular typing of coagulase-negative staphylococci from blood cultures does not correlate with clinical criteria for true bacteremia. Am. J. Med. **109:**697–704.
118. **Shafazand, S., and A. B. Weinacker.** 2002. Blood cultures in the critical care unit: improving utilization and yield. Chest **122:**1727–1736.
119. **Shahar, E., B. S. Wohl-Gottesman, and L. Shenkman.** 1990. Contamination of blood cultures during venepuncture: fact or myth? Postgrad. Med. J. **66:**1053.

120. **Shapiro, N. I., R. E. Wolfe, S. Wright, J. Spears, and D. W. Bates.** 2003. Who needs a blood culture? A prospectively derived and validated clinical prediction rule. Acad. Emerg. Med. **10:**435–436.
121. **Sharma, M., K. Riederer, L. B. Johnson, and R. Khatib.** 2001. Molecular analysis of coagulase-negative Staphylococcus isolates from blood cultures: prevalence of genotypic variation and polyclonal bacteremia. Clin. Infect. Dis. **33:**1317–1323.
122. **Siondalski, P., J. Siebert, A. Samet, M. Bronk, B. Krawczyk, and J. Kur.** 2004. Usefulness of the PCR technique for bacterial DNA detection in blood of the patients after "opened heart" operations. Pol. J. Microbiol. **53:**145–149.
123. **Sleigh, J., R. Cursons, and M. La Pine.** 2001. Detection of bacteraemia in critically ill patients using 16S rDNA polymerase chain reaction and DNA sequencing. Intensive Care Med. **27:**1269–1273.
124. **Smart, D., C. Baggoley, J. Head, D. Noble, B. Wetherall, and D. L. Gordon.** 1993. Effect of needle changing and intravenous cannula collection on blood culture contamination rates. Ann. Emerg. Med. **22:**1164–1168.
125. **Souvenir, D., D. E. Anderson, Jr., S. Palpant, H. Mroch, S. Askin, J. Anderson, J. Claridge, J. Eiland, C. Malone, M. W. Garrison, P. Watson, and D. M. Campbell.** 1998. Blood cultures positive for coagulase-negative staphylococci: antisepsis, pseudobacteremia, and therapy of patients. J. Clin. Microbiol. **36:**1923–1926.
126. **Spitalnic, S. J., R. H. Woolard, and L. A. Mermel.** 1995. The significance of changing needles when inoculating blood cultures: a meta-analysis. Clin. Infect. Dis. **21:**1103–1106.
127. **Stamm, W. E.** 1984. Quantitative urine cultures revisited. Eur. J. Clin. Microbiol. **3:**279–281.
128. **Stamm, W. E., G. W. Counts, K. R. Running, S. Fihn, M. Turck, and K. K. Holmes.** 1982. Diagnosis of coliform infection in acutely dysuric women. N. Engl. J. Med. **307:**463–468.
129. **St. Geme, J. W., III, L. M. Bell, S. Baumgart, C. T. D'Angio, and M. C. Harris.** 1990. Distinguishing sepsis from blood culture contamination in young infants with blood cultures growing coagulase-negative staphylococci. Pediatrics **86:**157–162.
130. **Stoll, M. L., and L. G. Rubin.** 2004. Incidence of occult bacteremia among highly febrile young children in the era of the pneumococcal conjugate vaccine: a study from a children's hospital emergency department and urgent care center. Arch. Pediatr. Adolesc. Med. **158:**671–675.
131. **Strand, C. L., R. R. Wajsbort, and K. Sturmann.** 1993. Effect of iodophor vs iodine tincture skin preparation on blood culture contamination rate. JAMA **269:**1004–1006.
131a. **Sturmann, K. M., J. Bopp, D. Molinari, S. Akhtar, and J. Murphy.** 1996. Blood cultures in adult patients released from an urban emergency department: a 15-month experience. Acad. Emerg. Med. **3:**768–775.
132. **Surdulescu, S., D. Utamsingh, and R. Shekar.** 1998. Phlebotomy teams reduce blood-culture contamination rate and save money. Clin. Perform. Qual. Health Care **6:**60–62.
133. **Tacconelli, E., M. Tumbarello, M. Pittiruti, F. Leone, M. B. Lucia, R. Cauda, and L. Ortona.** 1997. Central venous catheter-related sepsis in a cohort of 366 hospitalised patients. Eur. J. Clin. Microbiol. Infect. Dis. **16:**203–209.
134. **Tan, L., J. C. Hawk III, and M. L. Sterling.** 2001. Report of the Council on Scientific Affairs: preventing needlestick injuries in health care settings. Arch. Intern. Med. **161:**929–936.
135. **Teele, D. W., S. I. Pelton, M. J. Grant, J. Herskowitz, D. J. Rosen, C. E. Allen, R. S. Wimmer, and J. O. Klein.** 1975. Bacteremia in febrile children under 2 years of age: results of cultures of blood of 600 consecutive febrile children seen in a "walk-in" clinic. J. Pediatr. **87:**227–230.
136. **Thamlikitkul, V., S. Chokloikaew, T. Tangtrakul, P. Siripoonkiat, N. Wongpreedee, and S. Danchaivijitr.** 1992. Blood culture: comparison of outcomes between switch-needle and no-switch techniques. Am. J. Infect. Control **20:**122–125.
137. **Theerthakarai, R., W. El-Halees, M. Ismail, R. A. Solis, and M. A. Khan.** 2001. Nonvalue of the initial microbiological studies in the management of nonsevere community-acquired pneumonia. Chest **119:**181–184.
138. **Thuler, L. C., M. Jenicek, J. P. Turgeon, M. Rivard, P. Lebel, and M. H. Lebel.** 1997. Impact of a false positive blood culture result on the management of febrile children. Pediatr. Infect. Dis. J. **16:**846–851.
139. **Tokars, J. I.** 2004. Predictive value of blood cultures positive for coagulase-negative staphylococci: implications for patient care and health care quality assurance. Clin. Infect. Dis. **39:**333–341.
140. **Trautner, B. W., J. E. Clarridge, and R. O. Darouiche.** 2002. Skin antisepsis kits containing alcohol and chlorhexidine gluconate or tincture of iodine are associated with low rates of blood culture contamination. Infect. Control Hosp. Epidemiol. **23:**397–401.
141. **Trick, W. E., B. M. Zagorski, J. I. Tokars, M. O. Vernon, S. F. Welbel, M. F. Wisniewski, C. Richards, and R. A. Weinstein.** 2004. Computer algorithms to detect bloodstream infections. Emerg. Infect. Dis. **10:**1612–1620.
142. **Van Eldere, J., W. E. Peetermans, M. Struelens, A. Deplano, and H. Bobbaers.** 2000. Polyclonal Staphylococcal endocarditis caused by genetic variability. Clin. Infect. Dis. **31:**24–30.
143. **Van Wijngaerden, E., W. E. Peetermans, S. Van Lierde, and J. Van Eldere.** 1997. Polyclonal staphylococcus endocarditis. Clin. Infect. Dis. **25:**69–71.
144. **Viagappan, M., and M. C. Kelsey.** 1995. The origin of coagulase-negative staphylococci isolated from blood cultures. J. Hosp. Infect. **30:**217–223.
145. **Waltzman, M. L., and M. Harper.** 2001. Financial and clinical impact of false-positive blood culture results. Clin. Infect. Dis. **33:**296–299.
146. **Wang, S. J., G. J. Kuperman, L. Ohno-Machado, A. Onderdonk, H. Sandige, and D. W. Bates.** 2000. Using electronic data to predict the probability of true bacteremia from positive blood cultures. p. 893–897. *In* Proceedings of the AMIA Annual Symposium. Hanley & Belfus, Inc., Philadelphia, Pa.
147. **Washington, J. A., II, and D. M. Ilstrup.** 1986. Blood cultures: issues and controversies. Rev. Infect. Dis. **8:**792–802.
148. **Wasson, J. H., H. C. Sox, R. K. Neff, and L. Goldman.** 1985. Clinical prediction rules. Applications and methodological standards. N. Engl. J. Med. **313:**793–799.
149. **Waterer, G. W., and R. G. Wunderink.** 2001. The influence of the severity of community-acquired pneumonia on the usefulness of blood cultures. Respir. Med. **95:**78–82.
150. **Weinbaum, F. I., S. Lavie, M. Danek, D. Sixsmith, G. F. Heinrich, and S. S. Mills.** 1997. Doing it right the first time: quality improvement and the contaminant blood culture. J. Clin. Microbiol. **35:**563–565.
151. **Weinstein, M. P.** 2003. Blood culture contamination: persisting problems and partial progress. J. Clin. Microbiol. **41:**2275–2278.
152. **Weinstein, M. P.** 1996. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. Clin. Infect. Dis. **23:**40–46.
153. **Weinstein, M. P., S. Mirrett, L. Van Pelt, M. McKinnon, B. L. Zimmer, W. Kloos, and L. B. Reller.** 1998. Clinical importance of identifying coagulase-negative staphylococci isolated from blood cultures: evaluation of MicroScan Rapid and Dried Overnight Gram-Positive panels versus a conventional reference method. J. Clin. Microbiol. **36:**2089–2092.
154. **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.
155. **Weinstein, M. P., M. L. Towns, S. M. Quartey, S. Mirrett, L. G. Reimer, G. Parmigiani, and L. B. Reller.** 1997. 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. Clin. Infect. Dis. **24:**584–602.
156. **Wilson, M. L., M. P. Weinstein, S. Mirrett, L. G. Reimer, C. Fernando, F. T. Meredith, and L. B. Reller.** 2000. Comparison of iodophor and alcohol pledgets with the Medi-Flex Blood Culture Prep Kit II for preventing contamination of blood cultures. J. Clin. Microbiol. **38:**4665–4667.
157. **Wisniewski, M. F., P. Kieszkowski, B. M. Zagorski, W. E. Trick, M. Sommers, and R. A. Weinstein.** 2003. Development of a clinical data warehouse for hospital infection control. J. Am. Med. Inform. Assoc. **10:**454–462.
158. **Wormser, G. P., I. M. Onorato, T. J. Preminger, D. Culver, and W. J. Martone.** 1990. Sensitivity and specificity of blood cultures obtained through intravascular catheters. Crit. Care Med. **18:**152–156.
159. **Wyllie, D. H., I. C. Bowler, and T. E. Peto.** 2005. Bacteraemia prediction in emergency medical admissions: role of C reactive protein. J. Clin. Pathol. **58:**352–356.
160. **Yehezkelli, Y., S. Subah, G. Elhanan, R. Raz, A. Porter, A. Regev, and L. Leibovici.** 1996. Two rules for early prediction of bacteremia: testing in a university and a community hospital. J. Gen. Intern. Med. **11:**98–103.
161. **Yokoe, D. S., J. Anderson, R. Chambers, M. Connor, R. Finberg, C. Hopkins, D. Lichtenberg, S. Marino, D. McLaughlin, E. O'Rourke, M. Samore, K. Sands, J. Strymish, E. Tamplin, N. Vallonde, and R. Platt.** 1998. Simplified surveillance for nosocomial bloodstream infections. Infect. Control Hosp. Epidemiol. **19:**657–660.

Venous Blood Collection

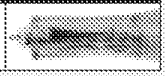
BD Vacutainer® Passive Shielding Blood Collection Needle

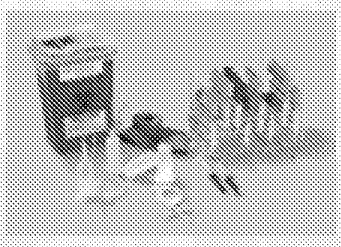


A New Generation of Safety from BD, the leader in safety-engineered technology

The BD Vacutainer® Passive Shielding Blood Collection Needle is designed to provide the highest amount of protection against needlesticks during a blood draw. The needle's safety shield releases automatically upon insertion of the first tube, providing protection from the time the first tube is inserted through product disposal.

BD Vacutainer® Passive Shielding Blood Collection Needle

Ordering Information				
[illegible]	Passive Shielding Blood Collection Needle	21g x 1" needle	25/Box 200/Case	
[illegible]	Passive Shielding Blood Collection Needle	22g x 1" needle	25/Box 200/Case	



A part of the BD Vacutainer® Family of Venous Blood Collection Products

CAUTION: Handle all biologic samples and blood collection "sharps" (lancets, needles, luer adapters, and blood collection sets) in accordance with the policies and procedures of your facility. Obtain appropriate medical attention in the event of any exposure to biologic samples (e.g., through a puncture injury) since samples may transmit viral hepatitis, HIV (AIDS), or other infectious diseases. Utilize any safety-engineered feature if the blood collection device provides one. Discard all blood collection "sharps" in biohazard containers approved for their disposal.

BD Global Technical Services
1.800.631.0174

BD Customer Service
1.888.237.2762

www.bd.com/vacutainer

BD

BD Diagnostics
Preanalytical Systems
1 Becton Drive
Franklin Lakes, NJ 07417

BD, BD Logo and all other trademarks are property of Becton, Dickinson and Company.
©2005 BD. Printed in USA 01/05 VS7355

6. Morley C, Miller N, Bangham AD, Davis JA: Dry artificial surfactant and its effect on very premature babies. Lancet **1**:64, 1981.
7. Johnson JWC, Permutt S, Sipple JH, Salem ES: Effect of intra-alveolar fluid on pulmonary surface tension properties. J Appl Physiol **19**:769, 1964.
8. Krauss AN, Auld P: Measurement of functional residual capacity in distressed neonates by helium rebreathing. J PEDIATR **77**:228, 1970.
9. Ivey HH, Kattwinkel J, Roth S: Nebulization of sonicated phospholipids for treatment of respiratory distress syndrome of infancy. *In* Tom B, Six H, editors: Liposomes and immunobiology. New York, 1980, Elsevier North-Holland, pp 301-314.

Fibronectin (cold insoluble globulin) in the neonate

Dorothy Ruth Barnard, M.D., and Mary Maureen Arthur *Halifax, N.S., Canada*

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

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

MATERIALS AND METHODS

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

Cord blood samples were collected from 18 healthy full-term infants (gestational age mean 40 weeks, range 37 to 41 weeks) and 15 healthy preterm infants (gestational age mean 35 weeks, range 32 to 36 weeks). Infants met the following criteria: (1) definite maternal dates that agreed within two weeks with the Dubowitz score; (2) Apgar scores at 1 minute of ≥ 7 and at 5 minutes of ≥ 8 in preterm infants (32 to 36 weeks gestational age), and Apgar scores of ≥ 8 at 1 minute and ≥ 9 at 5 minutes in full-term infants; (3) appropriate weight for gestational age; (4) no hypoxia, acidosis, hypotension, or hypothermia by gestational and postnatal age-appropriate definitions; (5) healthy during the first 48 hours of life; (6) inborn; (7) no family history of bleeding disorders; (8) the mothers had not received medications during pregnancy except vitamins, iron, inhibitors of uterine activity, steroids for maturation of fetal lung, and local, general, or epidural anesthesia; (9) the mothers had uncomplicated pregnancies; (10) the mothers of full-term infants delivered by cesarian section did not have labor.

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

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

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

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

From the Department of Pediatrics, School of Medicine, Dalhousie University.

Supported by Grant Ma-6645 from the Medical Research Council of Canada.

Reprint requests: D. R. Barnard, M.D., Department of Pediatrics, School of Medicine, Dalhousie University, Halifax, N.S., Canada B3J 3G9.

KUR-MAG-DE005307

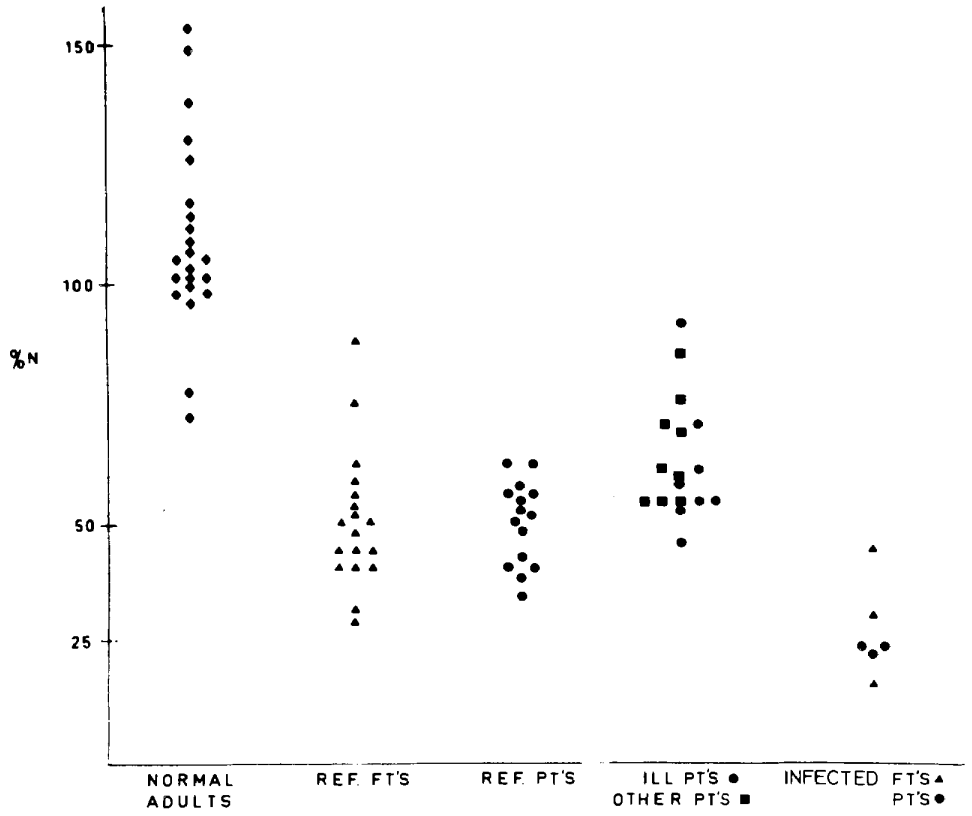


Figure. Fibronectin values in adults, in infected infants, and in healthy infants. *FT*, Full-term; *PT*, preterm.

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

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

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

KUR-MAG-DE005308

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

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

RESULTS

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

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

DISCUSSION

Several thorough reviews have been published recently stressing potential physiologic roles for fibronectin.[1, 2, 7, 8]

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

The six full-term and preterm neonates with early-onset sepsis (mean age 14 hours, range 4 to 20 hours at testing) had depressed fibronectin concentrations in plasma from venous blood collected into anticoagulant B. The two infants who died had the lowest plasma fibronectin values measured. Decreased survival[9] has been reported in adults with sepsis and persistently low plasma fibronectin values. In an uncontrolled study, adult patients with sepsis and pulmonary dysfunction (ventilation-perfusion imbalance and presumed increase of lung water) improved after infusion of cryoprecipitate containing approximately 1 gm fibronectin.[10] Decreased levels of fibronectin in neonates may increase their susceptibility to and morbidity from septicemia.

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

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

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

REFERENCES

1. Mosher DF: Fibronectin. Prog Hemost Thromb **5**:111, 1980.
2. Ruoslahti E, Engvall E, Hayman E: Fibronectin: Current concepts of its structure and functions. Coll Res **1**:95, 1980.
3. MacDonald JA, Baum BJ, Rosenburg DM, et al: Destruction of a major extracellular adhesive glycoprotein (fibronectin) of human fibroblasts by neutral proteases from polymorphonuclear leucocyte granules. Lab Invest **40**:350, 1979.
4. Ganrot PO: Variation of the concentrations of some plasma proteins in normal adults, in pregnant women and in newborns. Scand J Clin Lab Invest **29**(suppl 124):83, 1972.
5. Saba TM, Blumenstock FA, Weberg PB, et al: Physiologic role of cold insoluble globulin in systemic host defence: Implications of its characterization as the opsonic alpha-2-surface binding protein. Ann NY Acad Sci **312**:43, 1978.
6. Laurell CB: Electroimmunoassay. Scand J Clin Invest **29**(suppl 124):21, 1972.
7. Mosesson MW, Amrani DL: The structure and biologic activities of plasma fibronectin. Br J Haematol **56**:145, 1980.
8. Pearlstein E, Gold LI, Garcia-Pardo A: Fibronectin: A review of its structure and biological activity. Mol Cell Biochem **29**:103, 1980.
9. Saba TM, Jaffa E: Plasma fibronectin (opsonic glycoprotein): Its synthesis by vascular endothelial cells and role in cardiopulmonary integrity after trauma as related to reticuloendothelial function. Am J Med **68**:577, 1980.
10. Scovill WA, Annest SJ, Saba TM, et al: Cardiovascular hemodynamics after opsonic alpha-2-surface binding glycoprotein therapy in injured patients. Surgery **86**:284, 1979.

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Japanese Patent Laid-Open No. 58-067238

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-58-67238
(43) [Published date] 1983 (1983) April 21
(54) [Title of Invention] Apparatus for collecting a plurality of liquid samples
(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 57-156500
(22) [Filing date] September 8, 1982
(31) [Priority claim number] 311494
(32))[Priority date] October 15, 1981 (33) [Country claiming
priority] United States of America (
US) 72) [Inventor] [Name] Edward El Nagyant (72) [Inventor] [Name] Josef Kaufmann (74

[Attorney] [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 housing having a forward end and a rearward end; a sample collection chamber within s aid housing; and a first open passageway at said forward end and in fluid communication with said sample collection chamber. a first puncture needle extending outwardly from said first op en passageway for insertion into a collection source; and a second puncture needle at said rea rward end in fluid communication with said sample collection chamber. a sample collection de vice for collecting one or more liquid samples from a collection source and discharging into a n egative pressure vessel for collection, comprising: an open passageway in said second open p assageway; a second piercing needle extending into the sample collection chamber to a point spaced from the first open passageway, the second piercing needles mutually extending into t he sample collection chamber; having spaced apart first and second openings, the first and se cond openings providing fluid communication between the sample collection chamber and the lumen of the second puncture needle; from a first position that closes the opening of and ope ns the second opening to a second position that opens the first opening along the second pun cture needle so as to be able to reciprocate the sample collection a gas permeable, liquid imp ermeable, annular porous plug positioned within the chamber, wherein liquid is introduced int o the sample collection chamber when the first puncture needle is engaged with the collection source; all of the gas is pushed out and flows into the second puncture needle through the firs t and second openings, and when the second puncture needle receives the negative pressure

container, the annular porous plug is closed on both sides thereof. The action of the differentia l pressure moves toward the second opening passage to open the first opening and into the s ample collection chamber to the second opening located on the negative pressure side of the annular porous plug. A sample collection device, wherein residual gas is expelled so that the li quid in the sample collection chamber can be collected into the negative pressure container th rough the second puncture needle.

(2) The sample collection device according to claim 1, wherein the annular porous plug is mad e of sintered polyethylene, open-cell foamed polyethylene, or porous polyethylene.A sample c ollection device which is a member made from any of the group consisting of ethylene, porous polyfluorocarbon, and mixtures thereof.

(3) In the sample collection device according to claim 1, a third opening provided in a portion of the second puncture needle extending outward from the housing and the second puncture needle a resilient sleeve extending over the distal end of the sample collection chamber oppos ite the sample collection chamber, wherein the sleeve extends into the third opening when the negative pressure container is penetrated by the second puncture needle; A sample collection device, characterized in that it closes the

(4) The sample collection device of claim 1, having a resilient sleeve slidably engaging said se cond puncture needle at an end opposite said sample collection chamber. and said needle-eng aging surface on the inside of said sleeve has a plurality of longitudinally extending grooves, s aid needle-engaging grooves being gas permeable and liquid impermeable. A sample collectio n device characterized by:

(5) A sample collection device as claimed in claim 1, wherein said housing includes means for connecting a support for a vacuum vessel.

(6) A sample-collecting device according to claim 5, wherein a support for a negative pressure vessel is connected to said housing.

(7) The sample collection device of claim 3, wherein said housing includes means for connecti ng a support for a vacuum vessel.

(8) The sample collection device of claim 1, wherein said housing includes a device for observi ng the contents of said sample collection chamber.

(9) A sample collection device according to claim 8, wherein the device for observing the cont ents is a transparent housing wall adjacent to the sample collection chamber.

(10) The collection device of claim 1, comprising a resilient sleeve slidingly engaging the punc ture needle at the end of the puncture needle opposite the sample collection chamber, The ne edle-engaging surface on the inside of the sleeve forms a stepped inner surface, and a portion of the longitudinal region of the surface sealingly engages the outer surface of the associated second needle. forming an internal bore of small diameter for mating, and another portion of t he lengthwise region of the stepped inner surface forms an air passageway with the mating o uter surface of the second puncture needle. A sample collection device characterized by formi ng a large diameter internal aperture.

detailed description open —

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a device for collecting a liquid sample such as blood from a p atient. More particularly, the invention relates to needle assemblies for collecting one or more liquid samples from such patients. The device of the present invention employs an introductio n chamber with transparent or translucent walls to allow observation of whether the needle in question is in close proximity to the proper position. The introduction chamber has therein a r eciprocating plug formed of a material which provides an obstruction wall for the liquid receive d and an exhaust passageway for the gas pushed out by the liquid sample received in the intr oduction chamber. incorporated.

When the stopper initially receives the sample liquid, it reciprocates to prevent the liquid sam ple from being expelled while at the same time causing gas to be expelled by the liquid sampl e. Then, as the liquid sample is discharged into one or more of the vacuum collection vessels, the plug is assembled to continuously discharge the collected sample through the one or more vacuum collection vessels. It reciprocates in cooperation with vent holes in the discharge are a. In the case where multiple samples are continuously collected and discharged into multiple vacuum vessels, the assembly may be used with the discharge opening of the device during t he exchange period of the vacuum collection vessel in preparation for the next sample dischar ge. It includes a cooperating flexible sleeve.

As noted above, it is desirable to provide a mechanism for informing the user of such a needle assembly that the venous needle has penetrated the patient's vein from which a blood sample is to be collected. Venous placement is often difficult when collecting blood from a patient and there may be inadequate blood flow to the collection container for other reasons. thisIn such c ases, it is beneficial to be able to quickly perceive the entry of the needle into the vein and th e flow of blood into the needle assembly. Upon such sensing of needle entry, a negative press ure collection container is inserted into the collection assembly in accordance with well-known blood sampling techniques during a single sample collection procedure.

One of the problems encountered during the venipuncture step is air pockets found in various needle assemblies for one or more blood samplings. When a venipuncture is performed and a negative pressure collection container is not yet attached to the opposite end of the needle as sembly, under normal atmospheric conditions blood will always flow through the needle due to the pool of air remaining inside the needle assembly. It does not necessarily flow into the asse mbly. Thus, once the venipuncture is accomplished, blood flow is not initiated simply by the o bstruction of an air pocket within the needle assembly.

In accordance with the present invention, by contrast, the use of a porous plug within the coll ection chamber forces air out of the collection chamber so that the collection chamber receive s the collected blood sample. In addition, the plug initially evacuates expelled air during the a cceptance period of the procedure for receiving the sample, and the needle assembly to disch arge the sample to the vacuum collection container when the vacuum container is attached to the needle assembly. is positioned within the collection chamber to cooperate with an outlet in the negative pressure puncture needle. For example, in one embodiment for a single sample c ollection procedure of the present invention, the assembly of the present invention vents expe lled air as the sample is introduced, and a negative pressure vessel is attached to the assembl y for evacuation of the negative pressure puncture. A porous plug that moves to open a passa geway in the assembly in response to the differential pressure to expel the introduced sample into the vacuum collection vessel when the needle penetrates into the vacuum collection vess el. have.

Another embodiment of the invention has a flexible sleeve that covers the exit opening of the negative pressure needle. The flexible sleeve is arranged to evacuate air from the third evacu ation outlet in the evacuation needle during sample introduction. The flexible sleeve then flexe s and moves to cover the third discharge outlet when the negative pressure blood collection c ontainer is inserted into the assembly as it is penetrated by the negative pressure puncture n eedle. Once one sample is obtained in the negative pressure blood collection device and the n egative pressure container is removed from the assembly, the flexible sleeve is then held neg ative until the negative pressure container is attached for a second sample collection. It cover s the exit opening of the pressure puncture needle. As is well known to those skilled in the ar t, this procedure is repeated to collect the required number of samples into separate negative pressure blood collection containers.

Considering the use of porous plugs in blood collection devices of the type described herein, p rior U.S. Ser. William N. Eldvidge, inventor (assigned to the same person) in "Blood Sampling Assembly Having Vein Entry Indicator" states that an air pool can be perceived by the user thr ough a venous needle. He knew he was preventing the desired flow of blood to the point. The Eldridge invention includes a porous plug that mates with a one-way valve that allows air insid e the needle assembly to pass out of this vent during the initial stages of the blood collection procedure. The vent prevents the passage of blood until the user adheres the blood collection device to the needle assembly. Upon contact with the negative pressure of the negative press ure blood collection container, a separate one-way valve opens to carry blood from the patien t's vein through the needle assembly and into the collection container.

Although the Eldridge invention recognized the use of a porous material to vent the displaced air while receiving blood, there remains room for improvement of such devices, particularly th e present invention. Related. That is, the plug of the present invention does not reciprocate a nd act merely as a vent, but acts as a valve mechanism itself without a separate and complex structure to provide valve action. That is, the plug of the present invention cooperates with a

d reciprocally engages the blood introduction chamber to vent air from the introduction cham ber, but not to expel the blood sample, but not the blood introduced when the assembly is ad hered to the negative pressure blood collection container. move to expel the

Next, description will be made with reference to the drawings. In the drawings, the same part s are denoted by the same reference numerals. Fig. 1 shows the housing12 shows the basic e xternal components of the needle assembly 10 including a first needle 14 for insertion into a p atient and a second needle 15 subjected to negative pressure at the opposite end of the housi ng 12; ing. A second puncture needle 15 is adapted to be inserted into a negative pressure co ntainer 16 for collecting a blood sample. Housing 12 includes a threaded portion 25 having thr eads 18 adjacent a second puncture needle 15 into which a container support 19 is threaded by an inner combination thread 20 provided at its forward end. The vacuum container 16 is in serted into the container support 19 so that the second puncture needle 15 penetrates the sto pper 21 at the front end of the vacuum container 16 . Such general aspects of sample collecti on vessels are well known to those skilled in the art.

Description will be made with reference to FIG. Housing 12 preferably has a forward end 24 a nd a rearward end 25 which are separable for insertion of a porous plug 27 therein. Forward e nd 24 is preferably cylindrical and has a large mouth opening 28 for reciprocatingly receiving a porous plug 27 therein. The opposite end of this portion is provided with a small port 29 for receiving the first puncture needle 14 therein. In this embodiment the small port 29 extends t o a smaller small diameter conduit 30 which communicates the ports 29 and 28 with each oth er. A stepped portion 33 for receiving the first puncture needle 14 in a contacting state is form ed at the junction of the mouth hole 29 and the conduit 30 . The first puncture needle 14 may be secured within the aperture 29 by a suitable adhesive. Those skilled in the art will recogniz e that the conduit 30 is not an essential element for this construction, but merely a preferred form. Further, the diameter of conduit 30 can be varied to regulate the flow rate of fluid passi ng therethrough.

The forward end 24 of the housing also includes a number of longitudinal ribs 31 surrounding the outwardly extending first needle. A sheath (not shown) having internal ribs that mate with ribs 31 substantially covers the outwardly extending first puncture needle. Interlocking ribs be tween the puncture needle armor and the needle assembly facilitate insertion and removal of the armor from the needle assembly by the user. Forward end 24 also includes an annular flan ge 32 which serves as a mating surface when the two portions of the housing are joined into an assembly. Again, an adhesive or similar suitable fastening material can be used to secure t he two parts of the housing and assembly.

Rear end 25 includes a slightly protruding cylindrical portion 40 sized to fit inside port 28 of th e forward end. Opposite this rearward end, external threads 18 are provided at 26 on rearwar d end 25, as previously described in connection with the tube support. An aperture 70 similar to aperture 29 at the forward end of the housing extends through the rearward end of the hou sing. The aperture 70 is sized to match the diameter of the second puncture needle 15 and a

ain the second puncture needle is secured to the aperture 70 by a suitable material such as a n adhesive. An annular flange 46 is provided corresponding to the annular flange 32 to join th e two ends 24 and 25 of the housing together. It will be appreciated that the flanges 32 and 4 6 may be secured by a suitable securing material such as adhesive when the two portions of t he housing are assembled with the plug 27 positioned therein. A mouth opening 28 in forward end 24 defines a tubular chamber 50 for receiving the liquid sample to be collected.

Annular wall 88 at the forward end of tubular chamber 50 is made of a translucent or transpar ent material to allow viewing of the contents of tubular chamber 50 and to inform the user of the device that the puncture needle has reached the vein. It is preferably formed of Those skil led in the art will appreciate that from a manufacturing standpoint, the entire front end of the needle assembly is preferably made of a transparent material such as a hard thermoplastic. H owever, a sealed window, port or other device for observing the contents of tubular chamber 50 by the user of the device is within the scope of the invention.

The porous plug 27 is reciprocally mounted in the orifice 28 and has an inner orifice 72 for rec iprocating engagement with the forward end of the puncture needle 15 which is subjected to negative pressure. As is well known, the porous plug 27 is an opening.The bore 28 is cylindric al in shape, the diameter of which engages the wall of the tubular chamber 50 in a fluid-tight manner, and the action of the differential pressure on the opposite surface thereof causes the plug 27 to reciprocate within the bore 28. It is defined so that it can be done.

The porous plug 27 is made of a so-called gas-permeable, liquid-impermeable material which allows the passage of gas, eg air, but not the passage of liquid, eg blood. Examples of materia ls that may be used to form the porous plug 27 include sintered polyethylene, open cell foame d polyethylene, and other similar moldable polymeric materials such as porous polypropylene and porous polyfluorocarbon.

As shown in FIG. 2, negative pressure needle 15 includes a notch 74 adjacent end 84 thereof. In this regard, depending on the positioning of the porous plug 27, the notch 74 communicate s between the tubular chamber 50 and the lumen of the second piercing needle 15 so that the end 84 of the porous plug 27 is not blocked by the plug. or deformed or otherwise closed. An additional notch or opening 76 is provided to provide communication between the rearward en d 51 of tubular chamber 50 and second puncture needle 15 . Further, as shown in FIG. 2, a thi rd notch or opening 78 is provided which provides communication between the atmosphere, t he peripheral region of the assembly of the present invention, and the lumen of the second pu ncture needle 15 .

Next, description will be made with reference to FIG. A needle assembly connected to support 19 is shown. A first puncture needle 14 is shown being inserted into a patient P during venipu ncture. When first puncture needle 14 enters patient P's vein, blood flows from the vein throu gh first puncture needle 14 and small bore conduit 30 into tubular chamber 50 . When blood e nters tubular chamber 50 , the air in tubular chamber 50 is forced out of tubular chamber 50 t hrough porous plug 27 , but blood does not pass through porous plug 27 due to the characte

stics of porous plug 27 . Air that has passed through plug 27 passes from tubular chamber 50 through notches 74 and 76 and further through the lumen of second puncture needle 15 and external notch 78 to the flexible tube covering the outer end of negative pressure puncture ne edle 15 . 2, into the area 82 (FIG. 2) between the flange 92 of the armor 80 and the end face 106 of the end 25 of the housing. The plug 27 now remains in the position shown in FIG. 2 ov er the orifice or notch 74. FIG. Further here a blood sample taken from patient P is located in tubular chamber 50 .

Referring now to FIG. 3, the assembly is shown having support 19 attached to hub portion 26 of rear housing 25. As shown in FIG. Negative pressure blood collection container 16 is shown fitted into support 19 with a resilient plug pierced by the end or point 100 of negative pressur e puncture needle 15 . Penetration of puncture needle 15 into plug 21 creates a vacuum that draws any air remaining in tubular chamber 50 away from the inner region of vacuum contain er 16 and notch 74 and Withdraw through porous plug 27 by communicating 76 through the l umen of puncture needle 15 . As plug 27 becomes occluded by blood, a differential pressure i s created between upper tubular chamber 50 and lower tubular chamber 51, causing plug 27 to move downward toward the plane of extension 40 as shown in FIG.

This movement causes plug 27 to uncover opening or notch 74 . Any residual air trapped in th e lower tubular chamber 51 during this movement passes through the notch 76 and aids the movement of the plug 27 . When the notch 74 is uncovered, communication is provided betwe en the tubular chamber 50 and the negative pressure container 16 through the lumen of the n egative pressure puncture needle 15 . On the other hand, the insertion of the vacuum vessel 16 into the support 19 and the penetration of the puncture needle 15 through the plug 21 by t he point 100 causes the armor 80 to be pulled upwards, as shown in FIG. 26 to a position wh ere it engages the bottom surface 106 . Thus, the blood sample that has been drawn from the patient P's vein and contained in the tubular chamber 50 moves into the negative pressure col lection container 16 . Once the sample has been withdrawn into container 16 , container 16 is removed from support 19 thereby returning armor 80 to a position covering notch 78 and ove r end 100 of negative pressure puncture needle 15 . In this manner, the first puncture needle 14 remains in the vein without leaking blood, allowing a plurality of needles to be inserted int o the vein.Allows for continuous mounting of container 16 into support 19 for receiving a bloo d sample.

Referring now to FIG. 4, there is shown another embodiment in which notch 78 is not used in negative pressure puncture needle 15a. Identical parts in this device are designated by the sa me reference numerals with the suffix a. In this embodiment, puncture needle 15a has flange 108 instead of air passage or opening 78 which is always positioned adjacent surface 106a of extension 26a and in gas-tight closed engagement. A sleeve 90 is formed. As shown in FIG. 6, the sleeve 90 is positioned in sliding engagement over the puncture needle 15a. However, sle eve 90 has a plurality of internal grooves 94 where points 95 inside the grooves actually enga ge the outer surface of puncture needle 15a. The groove thus provides gas communication b

tween the puncture needle end 100a and the upper end of the sleeve 90 where air leaks betw een the adjacent surface of the flange 108 of the sleeve 90 and the surface 106a of the exten sion 26a. The grooves 94 are sized to allow passage of gas but not liquid. It will be appreciate d that the upper surface of flange 108 may similarly include grooves to provide ventilation bet ween end 100a and the atmosphere.

Yet another example of the invention which provides a single blood sample collection assembl y is shown in FIG. As shown in this assembly, no special sleeve 80 is used and puncture needl e 15b does not have a third notch or opening such as notch 78 in the embodiment shown in F IG. . Thus, when puncture needle 14 is inserted into a patient's vein, fluid communication is p rovided between the vein and tubular chamber 50 and a sample is collected in tubular chamb er 50 . The device does not allow the blood sample to flow through the porous plug 27 as in t he embodiment shown in FIG. However, the air forced out by the blood sample entering tubul ar chamber 50 passes through air permeable plug 27, notches 74, 76, the lumen of puncture needle 15, and exits end 100b of negative pressure puncture needle 15b. be done. When a su pport is mounted on extension 26b and point 100b of puncture needle 15b is inserted through the plug into negative pressure blood collection container 16, tubular chamber 50 above and t ubular chamber 51 below plug 27 are closed. A differential pressure is created between them which causes the plug 27 to move downward and open the notch 74 . This provides fluid com munication between the tubular chamber 50 and the vacuum vessel 16 for single sample colle ction into the vacuum vessel 16 . Since no further samples are collected by this assembly in t his embodiment, the puncture needle 14 is removed from the patient P's vein and the assemb ly is discarded as the required single sample has been collected into the vacuum container.

Another multiple sampling embodiment similar to that shown in FIG. 4 is shown in FIGS. 8a a nd 8b, in which air is communicated between point 100c of negative pressure puncture needle 15c and the atmosphere. In this embodiment, the inner diameter of sleeve 110 is stepped, an d the surface of sleeve 110 and puncture needle 15 combined with the small inner diameter 1 14 of sleeve 110 in close contact with the outer surface of puncture needle 15c. provides a lar ge inner diameter 116 that forms a vent passageway 118 for the . Thus, in the position shown in Figure 8a, ventilation occurs between the end 100c of the puncture needle 15c and the atm osphere through the passageway 118, and in the position shown in Figure 8b, the passagewa y 118 is closed preventing all ventilation.

As will be appreciated from the foregoing, in accordance with the present invention, a blood c ollection needle assembly is provided for collecting single or multiple samples incorporating a device that indicates venous penetration to its user. be. In addition, the device of the present i nvention with a porous plug having a simple form which is permeable to gas but impermeable to liquid and has the function of a valve is very simple and inexpensive to manufacture. It is p articularly suitable for mass production as will be appreciated by those skilled in the art.

Brief description of the drawing open —

BRIEF DESCRIPTION OF THE DRAWINGS FIG.
1 is a perspective view of a sample collection needle assembly, a support for a negative press ure container and a negative pressure blood collection container used to obtain a blood sampl e from a patient.
2 is an enlarged cross-sectional view taken along line 2--2 of FIG. 1 showing one embodiment of the present invention; FIG.
3 is an enlarged cross-sectional view along line 3--3 of FIG. 1; FIG.
FIG. 4 is a partial sectional view similar to FIG. 2 showing the present invention.Fig. 3 shows another embodiment of the light;
FIG. 5 is a perspective view of a needle assembly inserted into a patient and connected to a s upport to allow the user to visualize venous entry;
6 is a cross-sectional view along line 6--6 of FIG. 4; FIG.
FIG. 7 is a view similar to FIG. 2 but an enlarged cross-sectional view of a single sampling ne edle assembly illustrating another embodiment of the present invention;
Figure 8a is an enlarged partial cross-sectional view of a single sampling needle assembly sho wing another embodiment of the present invention;
Figure 8b is the embodiment of Figure 8a in the closed, non-vented position.
DESCRIPTION OF SYMBOLS 10... Needle assembly 12... Housing
14... First puncture needle 15... Second puncture needle 16
... Negative pressure container 19... Support member 24
... Front end 25... Rear end
27... Annular shape Porous plug 29 First opening
50 Sample collection chamber 70 Second opening
74 First opening 76 Second opening
78 Third opening 80 Flexible sleeve
94 Groove 114 Small inner diameter
116 Large inner diameter

Copyright JPO and INPIT

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—67238

⑤1Int. Cl.³	識別記号	庁内整理番号	⑬公開　昭和58年(1983) 4 月21日
A 61 B　5/14		6530—4C	

発明の数　1
審査請求　未請求

（全 9 頁）

⑤4試料採集装置

⑳特　　願　昭57—156500
㉒出　　願　昭57(1982) 9 月 8 日
優先権主張　㉜1981年10月15日㉝米国（US）
㉛311494

⑦2発 明 者　エドワード・エル・ナジヤント
アメリカ合衆国ニユージヤージー州ノース・カルドウエル・シエフイールド・ロード10
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4名

明　　細　　書

1.〔発明の名称〕

試料採集装置

2.〔特許請求の範囲〕

(1)　前方端および後方端を有するハウジングと；該ハウジングの中にある試料採集室と；前記前方端にあり前記試料採集室と液体的に連通する第1の開口通路と；採集源の中に挿入するために前記第1の開口通路から外方へ向つて伸長する第1の穿刺針と；前記後方端にあり前記試料採集室と流体的に連通する第2の開口通路と；から構成され採集源から1つ又はそれ以上の液体試料を採集し負圧容器の中へ排出して採集するための試料採集装置において、前記第2の開口通路の中にあり前記試料採集室の中へ前記第1の開口通路から間隔を置いた点まで伸長する第2の穿刺針を有し、該第2の穿刺針は前記試料採集室の中へ伸長する部分に互に離間する第1および第2の開口部を有し、該第1および第2の開口部は前記試料採集室と前記第2の穿刺針の管腔の間を流体的に連通し、前記第1の開口部を閉鎖し前記第2の開口部を開口する第1の位置から前記第1の開口部を開口する第2の位置まで前記第2の穿刺針に沿つて往復動可能に前記試料採集室の中に置かれた気体透過性で液体不透可性の環状多孔質栓を有し、前記第1の穿刺針が前記採集源と係合すると液体が前記試料採集室の中へその中の気体を全て押し出して流入し前記第1および第2の開口部を通じて前記第2の穿刺針へ出てまた前記第2の穿刺針が負圧容器を受け入れると前記環状多孔質栓はその両側の差圧の作用によつて前記第2の開口通路に向つて移動して前記第1の開口部を閉口し、前記環状多孔質栓の負圧側に位置する前記第2の開口部へ前記試料採集室に残留する気体を押し出して前記試料採集室の中の液体を前記第2の穿刺針を通じて前記負圧容器の中へ採集できるようになつていることを特徴とする試料採集装置。

(2)　特許請求の範囲第1項に記載の試料採集装置において、前記環状多孔質栓が、焼結ポリエチレン、開放セル型発泡ポリエチレン、多孔性ポリ

エチレン、多孔性ポリフルオロカーボン、及びこれらの混合物、より成る群のいづれかにより作られた部材である試料採集装置。

(3) 特許請求の範囲第1項に記載の試料採集装置において、前記第2の穿刺針の前記ハウジングから外方へ伸長する部分に設けられた第3の開口部と前記第2の穿刺針の前記試料採集室とは反対側の端末部の上に伸長する弾力のあるスリーブとを有し、負圧容器が前記第2の穿刺針によつて貫入されると前記スリーブが前記第3の開口部を閉鎖することを特徴とする試料採集装置。

(4) 特許請求の範囲第1項に記載の試料採集装置において、前記試料採集室とは反対側の端末部において前記第2の穿刺針と滑動的に係合する弾力のあるスリーブを有し、該スリーブの内側の前記穿刺針に係合する面は複数個の縦方向に伸長する溝部を有し、前記穿刺針と係合した前記溝部が気体透過性で液体不透過性であることを特徴とする試料採集装置。

(5) 特許請求の範囲第1項に記載の試料採集装

置において、前記ハウジングが負圧容器用支持具を接続するための装置を有することを特徴とする試料採集装置。

(6) 特許請求の範囲第5項に記載の試料採集装置において、負圧容器用支持具が前記ハウジングに接続されることを特徴とする試料採集装置。

(7) 特許請求の範囲第3項に記載の試料採集装置において、前記ハウジングが負圧容器用支持具を接続するための装置を含むことを特徴とする試料採集装置。

(8) 特許請求の範囲第1項に記載の試料採集装置において、前記ハウジングが前記試料採集室の内容物を観察するための装置を有することを特徴とする試料採集装置。

(9) 特許請求の範囲第8項に記載の試料採集装置において前記内容物を観察するための装置が前記試料採集室に隣接した透明なハウジング壁であることを特徴とする試料採集装置。

(10) 特許請求の範囲第1項に記載の採集装置において前記穿刺針の前記試料採集室とは反対側の

端部で前記穿刺針と滑動的に係合する弾力のあるスリーブを有し、該スリーブの内側の前記穿刺針に係合する面は段付きの内側表面を形成し、該面の長さ方向領域の一部は組み合わされる前記第2の穿刺針の外側表面と密閉的に係合するために小さな径の内部口孔を形成しており、前記段付きの内側表面の長さ方向領域の他の一部は組み合わされる前記第2の穿刺針の外側表面と共に空気通路を形成する大口径の内部口孔を形成することを特徴とする試料採集装置。

3.〔発明の詳細な説明〕

本発明は患者から血液の如き液体試料を採集するための装置に関する。特に本発明はそのような患者から1つあるいは複数の液体試料を採集するための針組み立て体に関する。本発明の装置は問題となる針が適正な位置に近接したか否かを観察できるような透明あるいは半透明の壁を有する導入室を用いている。再に導入室は、受け入れた液体に対しては障害壁となりその導入室に受け入れられた液体試料によつて押し出される気体に対し

ては排気通路となる材料で形成される往復動する栓をその中に組み込んでいる。

その栓は試料液体を最初に受け入れるとその液体試料が排出されるのを防ぎながら同時にその液体試料によつて気体が排気するように往復動する。次いで液体試料が1つあるいは複数の負圧採集容器に排出される時にその栓は採集された試料を1つあるいはそれ以上の負圧採集容器へ連続的に排出して通過させるように組み立て体の排出領域にある通気孔との協働作用で往復動する。複数の試料を採集し続けて複数個の負圧容器へ排出する場合において、その組立体は次の試料の排出に備えての負圧採集容器の交換期間の間にその装置の排出開口部と協働する可撓性スリーブを包含する。

上述の如くそのような針組立体の使用者に静脈針が血液試料を採集する患者の静脈に貫入した事を知らせる機構を備えることが望ましい。患者から血液を採集する際に往々にして静脈に定置することは困難でありまた他の理由によつて採集容器への血液の流れが適正でないことがある。このよ

うな場合に静脈の中へ針が入り血液が針組み立て体の中へ流入することを迅速に知覚できることは有益である。針が入つたことをこのように知覚すると単一試料採集の手順中の周知の血液試料採集手法に従つて負圧採集容器が採集組み立て体の中へ挿入される。

静脈穿刺段階で起こる問題の1つは1つあるいは複数の血液試料採取のための種々の針組み立て体において見い出される空気の溜りである。静脈穿刺がなされ負圧採集容器がまだ針組み立て体の反対側端部に取り付けられていない時には、通常の大気圧条件下では針組み立て体の内側に残留する空気の溜りのために血液は常に針組み立て体の中へ流入するとは限らない。したがつて静脈穿刺が完遂されても、単に針組み立て体の中の空気溜りの妨害によつて血液の流れは開始されない。

本発明によれば、対照的に採集室内の多孔質栓の使用によつてその栓が採集された血液試料を採集室が受け入れるように採集室から空気を押し出す。更にこの栓は試料を受け入れるための手順の

受け入れ期間において最初は押し出された空気を排気し、負圧容器が針組み立て体に取り付けられるとその試料を負圧採集容器へ排出するように針組み立て体の負圧穿刺針における出口と協働するように採集室の中に配置されている。例えば本発明の単一試料採集手順用の1つの実施態様において本発明の組み立て体は試料が導入されると押し出された空気を通気し、負圧容器が組み立て体に取り付けられ排出用負圧穿刺針が負圧採集容器の中へ貫入するとその導入された試料を負圧採集容器の中へ排出するために差圧に応答して組み立て体の通路を開口するために移動する多孔質の栓を有する。

本発明の他の実施態様は負圧穿刺針の排出開口部を覆う可撓性スリーブを有する。可撓性スリーブは試料導入中に排出穿刺針における第3の排出出口から空気を排出するように配置される。続いてこの可撓性袖部は負圧血液採集容器が負圧穿刺針によつて貫入されるように組み立て体の中へ挿入されるとたわみかつ移動しこの第3の排出出口

を塞う。一旦1つの試料を負圧血液採集装置の中に得て組み立て体から負圧容器が取り外されると、可撓性スリーブは次に第2の試料採集のために負圧容器が取り付けられるまでは負圧穿刺針の排出開口部を被つている。当業者には周知であるがこの手順は必要とされる数の試料を別々の負圧血液採集容器の中へ採集するために繰り返される。

ここに記載する種類の血液採集装置における多孔質栓の使用について考えてみると、先願である1978年6月15日に出願された米国出願番号915,670の「静脈穿刺表示付血液採集組み立て体」(Blood Sampling Assembly Having Vein Entry Indicator)において発明者(譲受人は本願と同一人)ウイリアム・エヌ・エルドリッジ(William N. Eldvidge)は空気の溜りが静脈針を通つて使用者が知覚し得る点まで流れる望ましい血液の流れを防げていることを認識していた。エルドリッジの発明においては1方向性弁と結合する多孔質栓を備えておりその1方向性弁は針組み立て体の内側の空気を血液採集手順の

最初の段階でこの通気装置の外へ通過させる。この通気装置は使用者が血液採集装置を針組み立て体に接着させるまで血液の通過を防止する。負圧血液採集容器の負圧と接すると分離された1方向性弁が開き患者の静脈から血液を運び針組み立て体を通して採集容器へ血液を入れる。

エルドリッジの発明は血液を受け入れている間に押しのけられた空気を通気させる多孔質材料の使用を認識していたがそのような装置の改良する余地は残されており、特にその余地は本発明に関連する。すなわち本発明の栓は往復動し単に通気口として作用するのではなく弁作用を提供するような分離されたまた複雑な構造を持たずにそれ自身が弁機構として作用する。すなわち本発明の栓は血液導入室と協働して往復動的に係合し導入室から空気は通気するが血液試料は排出せず組み立て体が負圧血液採集容器と接着した時に導入した血液を排出するように移動する。

次に図面を参照し説明する。なお図面において同一部分は同一符号で示す。第1図はハウジング

１２、患者の中へ挿入するための第１の穿刺針１４およびハウジング１２の反対端にある負圧を受ける第２の穿刺針１５を包含する針組み立て体１０の基本的な外部構成要素を示している。第２の穿刺針１５は血液試料を採集するための負圧容器１６の中へ挿入されるようになつている。ハウジング１２は容器支持具１９がその前方端に設けられている内側の組み合わせねじ２０によつてねじ込まれる第２の穿刺針１５に隣接するねじ１８を有するねじ部２５を包含する。負圧容器１６は第２の穿刺針１５が負圧容器１６の前方端にあるストツパ２１を貫通するように容器支持具１９の中へ挿入される。試料採集容器のこのような一般的な態様は当業者には周知である。

第２図を参照し説明する。ハウジング１２は前方端２４および後方端２５を有しこれら両端は多孔質の栓２７を挿入するために分離できることが好ましい。前方端２４は円筒状であるのが好ましくその中に多孔質の栓２７を往復運動可能に受け入れるように大きな口孔２８を有する。この部分

(11)

入あるいは針状組み立て体からの脱着を容易にする。前方端２４はまたハウジングの２つの部分を接合して組立体にするとき接合面としての役割を果す環状のフランジ３２を包含する。ここでもハウジングおよび組み立て体の２つの部分を固定するために接着剤あるいは類似の適当な固定材料を用いることができる。

後方端２５は前方端の口孔２８の内側に適合するように寸法を定められた少し突き出た円筒部４０を包含している。この後方端の反対側には管支持体の連結機構で前述したように外ねじ１８が後方端２５の符号２６の部分に設けられている。ハウジングの前方端における口孔２９と同様の口孔７０がハウジングの後方端を通つて伸長している。口孔７０は第２の穿刺針１５の直径と適合するように寸法を定められておりここにおいても例えば接着剤の如き適当な材料によつて第２の穿刺針が口孔７０に固定される。ハウジングの２つの端部２４および２５を組合わせるにあたり環状フランジ３２に対応し環状フランジ４６が設けられ

(13)

の反対端にはその中に第１の穿刺針１４を受け入れるための小さな口孔２９が設けられている。本実施例においては小さな口孔２９は口孔２９と口孔２８を互いに連通させるさらに小さな小口径導管３０まで伸長している。口孔２９と導管３０の接合点には第１の穿刺針１４を接する状態で受け入れるための段付部３３が形成されている。第１の穿刺針１４は適宜な接着剤によつて口孔２９の中に固定されても良い。この構造に対しては導管３０は必須の要素ではなく単に好ましい形態に過ぎないことは当業者には周知であろう。更に導管３０の直径はその中を通過する流体の流量を調節するために変えることができる。

ハウジングの前方端２４はまた外側に向つて伸長する第１の穿刺針を包囲する多数の縦方向のリブ３１を包含している。リブ３１と組み合わされるリブを内部に有する鎧装（図示せず）が外側に向つて伸長する第１の穿刺針をほぼ被つている。穿刺針の鎧装と針状組み立て体の間の組み合わされるリブは使用者の鎧装の針状組み立て体への挿

(12)

ている。ハウジングの２つの部分をその中に位置定めされた栓２７とともに組み立てる際にフランジ３２および４６が例えば接着剤の如き適当な固定材料によつて固定できることは理解されるであろう。前方端２４の口孔２８は採集する液体試料を受け入れるための管状室５０を形成する。

管状室５０の内容物を観察するためにまた本装置の使用者に穿刺針が静脈に到達したことを知らせるために、管状室５０を形成する前方端の環状壁８８は半透明あるいは透明な材料で形成されるのが好ましい。製造面から考えれば針状組み立て体の前方端全体が熱可塑性硬質樹脂の如き透明な材料で作られるのが好ましいことは当業者に理解されるであろう。しかしながら本装置の使用者が管状室５０の内容物を観察するための密閉された窓、口孔あるいは他の装置も本発明の範囲にある。

多孔質栓２７は口孔２８の中に往復運動可能に取り付けられまた負圧を受ける穿刺針１５の前方端と往復運動可能に嵌入させるための内側の口孔７２を有している。多孔質栓２７は周知の如く口

(14)

孔２８に従つて円筒形の形状をしておりその径は管状室５０の壁と液体密封的に係合するがまたその反対面との差圧の作用によつて口孔２８の中で栓２７が往復動することができるように定められている。

多孔質栓２７は例えば空気の如き気体の通過は許すが例えば血液の如き液体の通過は許さないいわゆる気体透過性・液体不透過性材料でできている。多孔質栓２７を形成するために用いられる材料の例として焼結ポリエチレンや開放セル型の発泡ポリエチレンや他の同様な型成形可能な重合体物質例えば多孔のポリプロピレンや多孔のポリフルオロカーボン等がある。

第２図に示すように負圧穿刺針１５はその端部８４に隣接した切り欠き７４を包含する。この点において多孔質栓２７の位置定めに依存するが切り欠き７４が管状室５０と第２の穿刺針１５の管腔の間を連通するので多孔質栓２７の端部８４は栓で塞がれるかあるいは変形させるか又は他の方法により閉じられる。付加的な切り欠きすなわち

開口７６が管状室５０の後方端５１と第２の穿刺針１５の間を連通するために設けられている。更に第２図に示されるように大気すなわち本発明の組み立て体の外周領域と第２の穿刺針１５の管腔の間を連通させる第３の切り欠きすなわち開口７８が設けられている。

つぎに第５図を参照し説明する。支持具１９に連結されている針状組み立て体が図示されている。静脈穿刺中の患者Ｐの中に挿入されている第１の穿刺針１４が示されている。第１の穿刺針１４が患者Ｐの静脈に入ると血液は静脈から第１の穿刺針１４および小口径導管３０を経て管状室５０の中へ流入する。血液が管状室５０に流入すると管状室５０の中の空気は多孔質栓２７を通じて管状室５０から押し出されるが血液は多孔質栓２７の特性によつて多孔質栓２７を通過しない。栓２７を通過した空気は管状室５０から切り欠き７４および７６を経てさらに第２の穿刺針１５の管腔および外部切り欠き７８を通つて負圧穿刺針１５の外側端部を被つている柔軟な鎧装８０のフランジ

９２とハウジングの端部２５の端面１０６の間の領域８２（第２図）の中へ押し出される。ここにおいて栓２７はオリフイスすなわち切り欠き７４を覆つて第２図に示す位置に留つている。更にここにおいて患者Ｐから採集された血液試料は管状室５０の中に位置している。

次に第３図を参照すると、組み立て体が後方ハウジング２５のハブ部２６に取り付けられた支持具１９を有するのが示されている。負圧穿刺針１５の端部すなわち点１００によつて貫通された弾力性の栓を有し支持具１９の中に嵌入されている負圧の血液採集容器１６が示されている。穿刺針１５が栓２１に貫入することによつて真空状態が作り出されるがこの真空すなわち負圧は管状室５０の中に残留しているすべての空気を、負圧容器１６の内部領域と切り欠き７４および７６を穿刺針１５の管腔を通じて連通することによつて、多孔質栓２７を通して引き抜く。栓２７が血液によつて閉塞されるため上部管状室５０と下部管状室５１の間に差圧が生じ栓２７は第３図に示すよ

うに延長部４０の面に向つて下方へ移動する。

この移動によつて栓２７は開口すなわち切り欠き７４の覆いを取り除く。この移動の間に下部管状室５１の中に閉じ込められていた残留空気は全て切り欠き７６を通りプラグ２７の運動を助長する。切り欠き７４の被覆が取り除かれると負圧穿刺針１５の管腔を通じて管状室５０と負圧容器１６の間の流通がもたらされる。一方、負圧容器１６の支持具１９の中への挿入および穿刺針１５の点１００による栓２１への貫通によつて第３図に示すように鎧装８０は鎧装８０の上側フランジ９２が軸頭２６の底面１０６と係合する位置まで上方へ移動する。このように患者Ｐの静脈から抜かれ管状室５０に収納されていた血液試料は負圧採集容器１６の中へ移動する。試料が容器１６の中へ引き抜かれたならば容器１６は支持具１９から取り外されこれによつて鎧装８０は切り欠き７８を塞ぎかつ負圧穿刺針１５の端部１００を覆う位置まで戻る。このように第１の穿刺針１４は血液を漏洩することなく静脈の中に留つて複数の

血液試料を受け入れるために容器１６を支持具１９の中へ連続して取り付けることを可能にする。

次に第４図を参照すると、負圧穿刺針１５ａに切り欠き７８が用いられていない別の実施態様が示されている。この装置では同一の部分は添字ａを付した同一符号で示してある。本実施態様においては、穿刺針１５ａには空気通路すなわち開口７８に代つてそのフランジ１０８が常に延長部２６ａの表面１０６ａと隣接して気体は密閉しないように閉じて係合して位置するようなスリーブ９０が形成されている。第６図に示されるようにスリーブ９０は穿刺針１５ａの上に摺動式に係合するように配置されている。しかしながらスリーブ９０は溝の内側の点９５が穿刺針１５ａの外側面と実際に係合する複数の内部溝９４を有する。したがつて溝は穿刺針端部１００ａとスリーブ９０の上側端部の間の気体連通を提供しそこにおいて空気はスリーブ９０のフランジ１０８の隣接面と延長部２６ａの表面１０６ａの間を漏洩する。溝９４は気体は通過させ液体は通過させないよう

な寸法に定められる。フランジ１０８の上方面も同様に端部１００ａと大気の間の通気作用を提供する溝を包含可能なことは理解されるであろう。

単一血液試料採集組み立て体を提供する本発明の更に他の例を第７図に示す。この組み立て体に示されるように特殊なスリーブ８０は使用されておらずかつ穿刺針１５ｂは第２図に示される実施態様における切り欠き７８のような第３の切り欠きすなわち開口を有していない。したがつて穿刺針１４が患者の静脈に挿入されると静脈と管状室５０の間に液体的連通がもたらされ管状室５０の中に試料が採集される。本装置は第２図に示される実施態様のように血液試料は多孔質栓２７を通つて流れない。しかしながら血液試料が管状室５０に入ることによつて押し出された空気は空気透過性栓２７を通り更に切り欠き７４，７６、穿刺針１５の管腔を通つて負圧穿刺針１５ｂの端部１００ｂから排出される。支持具が延長部２６ｂの上に取り付けられ穿刺針１５ｂの点１００ｂが栓を通つて負圧血液採集容器１６の中へ挿入され

ると栓２７の上方の管状室５０と下方の管状室５１の間に差圧が生じそれによつて栓２７は下方へ移動して切り欠き部７４を開口する。これによつて負圧容器１６の中への単一試料採集のための管状室５０と負圧容器１６の間の液体の連通が提供される。この実施態様においてはこの組み立て体によつて更に試料を採集しないので穿刺針１４は患者Ｐの静脈から取り外され組み立て体は必要とする１個の試料が負圧容器の中に採集されたので捨てられる。

負圧穿刺針１５ｃの点１００ｃと大気の間で空気を流通させる第４図に示す態様と類似の他の複数試料採集の実施態様を第８ａおよび８ｂ図に示す。本実施態様においては袖部１１０の内径は段付きになつており、穿刺針１５ｃの外側表面と密着する袖部１１０の小さな内側の径１１４と組み合わされる袖部１１０の表面と穿刺針１５の間の通気通路１１８を形成する大きな内側の径１１６を提供する。したがつて第８ａ図に示す位置においては穿刺針１５ｃの端部１００ｃと大気の間で

通路１１８を通じて通気が起こり、第８ｂ図に示す位置においては通路１１８は閉じられてすべての通気を妨げる。

上述のことから理解されるように本発明においては血液採集針組み立て体はその使用者に静脈への針入を示す装置を組み込んだ単一あるいは複数の試料を採集するために提供されるものである。更に気体を通過させ液体を通過させず弁の機能を有する単純な形態を有する多孔質栓をした本発明の装置は非常に簡素化され製造するに廉価である。当業者に理解されるように特に大量生産に適している。

4.〔図面の簡単な説明〕

第１図は試料採集針組み立て体、負圧容器用支持体および患者からの血液試料を得るために用いる負圧血液採集容器の斜視図。

第２図は本発明の１つの実施態様を示す第１図の線２－２に沿つた拡大断面図。

第３図は第１図の線３－３に沿つた拡大断面図。

第４図は第２図に類似の部分断面図にして本発

明の他の実施態様を示す。

第５図は患者に挿入され使用者が静脈への針入を視覚できるように支持体に連結された針組み立て体の斜視図。

第６図は第４図の線６－６に沿つた断面図。

第７図は第２図に類似の図面であるが本発明の他の実施態様を示す単一試料採集針組み立て体の拡大断面図。

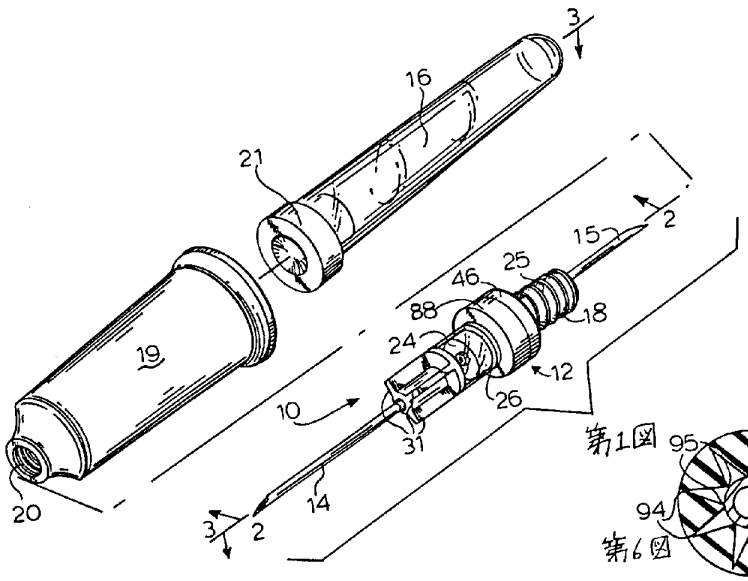
第８ａ図は本発明の他の実施態様を示す単一試料採集針組み立て体の部分拡大断面図。

第８ｂ図は閉鎖されて非通気位置にある第８ａ図の実施態様。

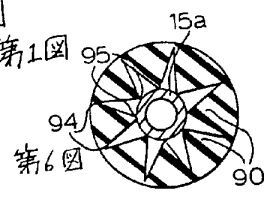
１０……針組み立て体、１２……ハウジング、
１４……第１の穿刺針、１５……第２の穿刺針、
１６……負圧容器、　１９……支持具、
２４……前方端、　２５……後方端、
２７……環状多孔質栓、２９……第１の口孔、
５０……試料採集室、　７０……第２の口孔、
７４……第１の開口部、７６……第２の開口部、
７８……第３の開口部、８０……可撓性スリーブ、
９４……溝、　１１４……小さな内側口径、
１１６……大きな内側口径

特許出願人　ベクトン・ディッキンソン・アンド・カンパニー

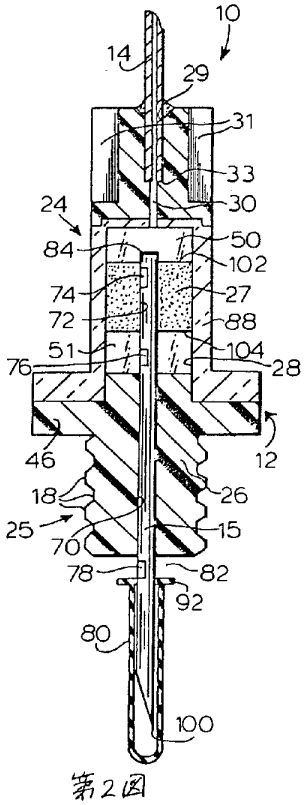
代理人　弁理士　湯浅恭三（外４名）



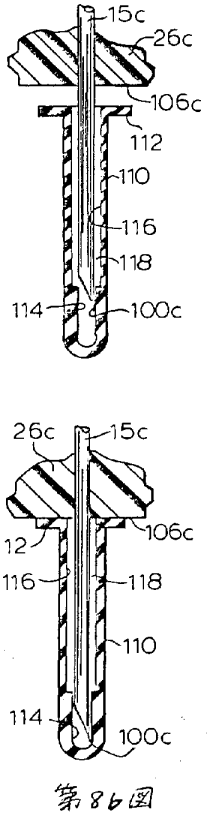
第1図



第6図

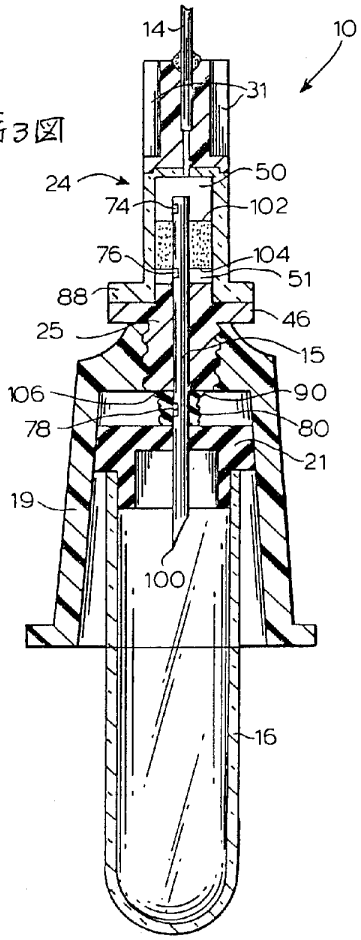


第2図



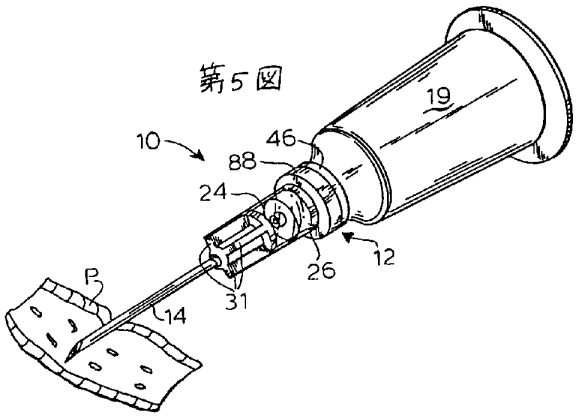
第8a図

第8b図

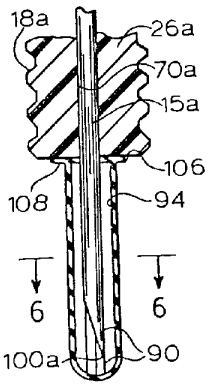


第3図

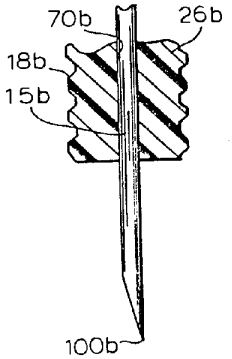
第5図


19
10
46
88
24
26
12
P
14
31

第4図


18a
26a
70a
15a
106
108
94
6
6
100a
90

第7図


70b
26b
18b
15b
100b

Espacenet

Bibliographic data: WO2007033319 (A1) — 2007-03-22

CLOSED BLOOD SAMPLING SYSTEM WITH ISOLATED PRESSURE MONITORING

Inventor(s): GORDON MARK C [US]; LIU JUN [US]; COUCHMAN W SCOTT [US]; DRORI HAGAY [IL] ± (GORDON, MARK, C, ; LIU, JUN, ; COUCHMAN, W., SCOTT, ; DRORI, HAGAY)

Applicant(s): EDWARDS LIFESCIENCES CORP [US]; GORDON MARK C [US]; LIU JUN [US]; COUCHMAN W SCOTT [US]; DRORI HAGAY [IL] ± (EDWARDS LIFESCIENCES CORPORATION, ; GORDON, MARK, C, ; LIU, JUN, ; COUCHMAN, W., SCOTT, ; DRORI, HAGAY)

Classification: **- international:** ***A61B5/15***
- cooperative: **A61B5/0215 (EP, US); A61B5/15003 (EP, US); A61B5/150221 (EP, US); A61B5/150816 (EP, US); A61B5/150824 (EP, US); A61B5/150992 (EP, US); A61B5/1535 (EP, US);** A61B5/150236 (EP, US); A61B5/150244 (EP, US)

Application number: WO2006US35832 20060913 Global Dossier

Priority number(s): US20050717119P 20050913 ; US20050720263P 20050921

Also published as: AT440541 (T) CA2623420 (A1) CA2623420 (C) CN101262818 (A) CN101262818 (B) more

Abstract of WO2007033319 (A1)

A closed blood sampling system within a pressure monitoring line having a control valve that enables a clearance reservoir to be isolated from the pressure column when no samples are being taken. The valve is a stopcock-like device that includes a rotating valve member and attached control handle with clear visible and tactile indicators for the mode of operation. The rotating valve member has a number of internal and circumferential channels for connecting or disconnecting select ports in the core of the valve. By isolating the clearance reservoir, the quality of the pressure signal is improved such that the sampling line can be lengthened for greater convenience in the intensive care or operating room. The valve may also incorporate a blunt cannula sampling site therewithin.

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 March 2007 (22.03.2007)

PCT

(10) International Publication Number
WO 2007/033319 A1

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

(21) International Application Number:
PCT/US2006/035832

(22) International Filing Date:
13 September 2006 (13.09.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/717,119	13 September 2005 (13.09.2005)	US
60/720,263	21 September 2005 (21.09.2005)	US

(71) Applicant *(for all designated States except US)*: **EDWARDS LIFESCIENCES CORPORATION** [US/US]; One Edwards Way, Irvine, CA 92614 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **GORDON, Mark, C.** [US/US]; 615 Orchid Ave., Corona Del Mar, CA 92625 (US). **LIU, Jun** [CN/US]; 2311 Marsant Avenue, Corona, CA 92882 (US). **COUCHMAN, W., Scott** [US/US]; 4 Trenton, Irvine, CA 92620 (US). **DRORI, Hagay** [IL/IL]; 36 Pney Golan St., 12000 Rosh-pina XX (IL).

(74) Agents: **YADAV, Rajiv** et al.; EDWARDS LIFESCIENCES LLC, One Edwards Way, Irvine, CA 92614 (US).

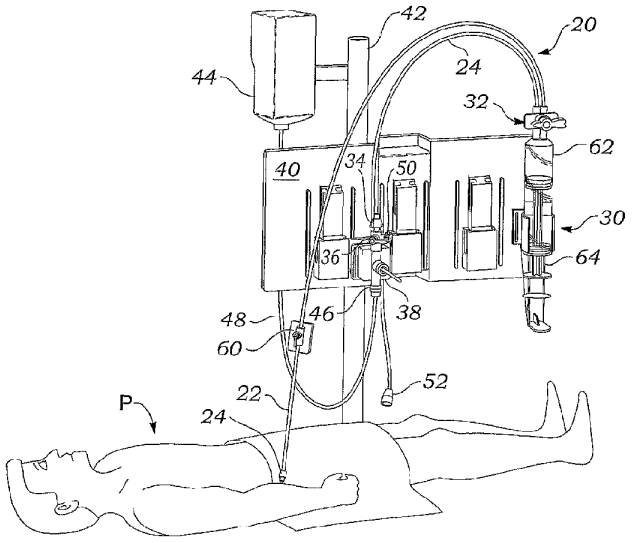
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, 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, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

[Continued on next page]

(54) Title: CLOSED BLOOD SAMPLING SYSTEM WITH ISOLATED PRESSURE MONITORING



(57) Abstract: A closed blood sampling system within a pressure monitoring line having a control valve that enables a clearance reservoir to be isolated from the pressure column when no samples are being taken. The valve is a stopcock-like device that includes a rotating valve member and attached control handle with clear visible and tactile indicators for the mode of operation. The rotating valve member has a number of internal and circumferential channels for connecting or disconnecting select ports in the core of the valve. By isolating the clearance reservoir, the quality of the pressure signal is improved such that the sampling line can be lengthened for greater convenience in the intensive care or operating room. The valve may also incorporate a blunt cannula sampling site therewithin.

WO 2007/033319 A1

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

CLOSED BLOOD SAMPLING SYSTEM WITH ISOLATED PRESSURE MONITORING

Field of the Invention

[0001] The present invention relates to blood sampling systems and, in particular, to closed blood sampling systems with a clearing reservoir and pressure monitoring.

Background of the Invention

[0002] In a hospital setting there is always the need to monitor patient health through the evaluation of blood chemistry profile. The simplest method employed in the hospital is to use a syringe carrying a sharpened cannula at one end and insert that cannula into a vein or artery to extract a blood sample from the patient. Patients that are in the critical care units or the operating room sometimes require as many as twelve samples a day. Such frequent sampling injections potentially expose the patient to airborne bacteria and viruses which can enter the bloodstream through the opening made by the sharpened cannula.

[0003] One way to obtain a blood sample is to draw the blood from a catheter that is already inserted in the patient, either in a central venous line, such as one placed in the right atrium, or in an arterial line. Typically, existing injection sites for arterial or venous drug infusion or pressure monitoring lines are used to take periodic blood samples from the patient. Conventional mechanisms for drawing blood from the lines used for infusion or pressure monitoring utilize a plurality of stopcock mechanisms that preclude flow from the infusion fluid supply or from the pressure column drip supply, while allowing blood to flow from the patient into a collecting syringe connected to a proximal port formed in one of the stopcocks. Typically, a blunt cannula through a slit septum is used to remove the danger of sticking the nurse or clinician, in a so-called "needle-less" system.

[0004] Most early systems required a two-step operation where a first sample of fluid, generally about 5ml in volume for intensive care environments was withdrawn into the sampling syringe and discarded. This first sample potentially included some of the infusion fluid and thus would be an unreliable blood chemistry measurement sample. After the initial sample had been discharged, the second sample was pure blood from the artery or vein and was typically re-infused to the patient.

[0005] In response to the drawbacks associated with earlier two-step sampling systems, closed systems were developed as described in U.S. Patent No. 4,673,386 to Gordon, and more recently in U.S. Patent No. 5,961,472 to Swendson, which are expressly incorporated by reference herein. Commercial closed systems such as the Edwards VAMP® and VAMP Plus® Venous Arterial blood Management Protection systems of Edwards Lifesciences in Irvine, CA feature a reservoir in the tubing line from the patient that can draw fluid past a sampling port. The clearing volume is held in the in-line reservoir, and not set-aside in a syringe for re-infusion later. The sampling systems are often used in conjunction with a pressure monitor having a transducer continually or periodically sensing pressure within the sampling line except during the draw of a blood sample.

[0006] The VAMP Plus® system conveniently utilizes a reservoir with one-handed operability, and includes a line from the patient into and out of the reservoir and to a proximal source of flushing fluid and a pressure transducer. (The standard directional nomenclature is that proximal is toward the clinician, or away from the patient, and distal is toward the patient). A stopcock valve at the reservoir controls the mode of operation. Prior to drawing a blood sample, the reservoir plunger is latched closed, though a reservoir gap allows a continuous drip of IV flushing fluid through an inlet port to an outlet port. A pressure transducer in the line proximal to the reservoir senses fluid pressure within the line and conveys the signal to a monitor. One exemplary pressure transducer used with both the VAMP® and

VAMP Plus® systems is the Edwards TruWave® Disposable Pressure Transducer.

[0007] When a blood sample is to be taken, the flow of flushing or infusion fluid is halted by turning the handle of the reservoir stopcock valve. The nurse or clinician then withdraws an amount of fluid into the reservoir chamber and distal line sufficient to pull pure blood past one or more fluid sampling sites. After full retraction of the plunger, the stopcock valve closes off the reservoir from the patient and a sample of blood is taken at one or the other sampling sites. Subsequently, the clinician manipulates the stopcock valve so that the volume within the reservoir can be reinfused back into the patient by depressing the plunger, and the flushing drip and pressure monitoring resumes.

[0008] In the closed blood sampling/pressure monitoring systems described above, the pressure transducer typically includes a diaphragm exposed to the in-line fluid on one side and has a device for measuring deflection of the diaphragm on the other. Such pressure lines typically make use of relatively stiff tubing primed with a suitable physiological fluid such as saline or 5% dextrose solution as a pressure column. For adults, a bag pressurized with air surrounds the fluid supply bag to maintain a constant pressure differential in the line urging fluid toward the patient through a restrictor orifice. The slow drip of physiological fluid flushes the line to prevent clotting. Some transducers such as the TruWave® Disposable Pressure Transducer include a flush device that also can be used for sending transient pressure waves through the line. A Snap-Tab™ device of the TruWave® is a rubber tab which when pulled and then released sends a square wave through the pressure column to check the inherent frequency response of the entire system, which includes the tubing and any components attached thereto, such as the sampling ports and reservoir. Proper system frequency response is necessary for reliable blood pressure measurements. In general, a more accurate signal may be obtained with a shorter sampling line and fewer

components so that the transducer is closer to the patient and there is less delay between the generation and receipt of the blood pressure signal, and less interference. However the limited amount of space available or the location of the anesthesiologist during a surgical procedure often necessitates a relatively long tubing line which degrades the signal. Furthermore, minimum functionality of the system requires various components such as sampling sites be included.

[0009] In view of the foregoing, there is a need for a blood sampling system used in conjunction with a pressure transducer that produces more accurate pressure readings.

Summary of the Invention

[0010] The present invention provides a fluid sampling system within a pressure monitoring line having a control valve that enables a clearance reservoir to be isolated from the pressure column when no samples are being taken. The control valve further permits complete flushing of the system with no dead spaces. Additionally, control valve desirably incorporates a sampling port therein capable of isolating the sampling port from the clearance reservoir. By isolating the clearance reservoir, the quality of the pressure signal is improved such that the sampling line can be lengthened for greater convenience in the intensive care or operating room.

[0011] In accordance with a first embodiment of the invention, a medical system for fluid sampling and pressure monitoring of a fluid system of a patient is provided. The system includes a conduit line with a proximal segment adapted to be supplied with a physiological fluid (e.g., saline) and a distal segment adapted to be in communication with a fluid system of a patient. A control valve has a manifold defining an interior chamber. The manifold has a proximal port fluidly connected to the proximal segment, a distal port fluidly connected to the distal segment, and a reservoir port,

wherein each of the manifold ports opens to the interior chamber. A system further includes a fluid sampling port and pressure transducer connected to the conduit line for sensing the pressure of the fluid therein. A reservoir fluidly communicates with the reservoir port of the control valve manifold. The control valve further includes a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports. The valve member is movable into at least two positions:

a first position that provides open fluid communication from the proximal segment to the patient through the control valve so as to eliminate any dead spaces therein, wherein reduced pressure within the reservoir pulls fluid from the distal segment through the control valve and into the reservoir sufficient to draw fluid from the fluid system of the patient past the sampling port, and

a second position that provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member to the distal segment while bypassing the reservoir, such that the pressure of fluid within the conduit line exclusive of the reservoir can be sensed by the pressure transducer.

[0012] Desirably, the valve member also has a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

[0013] In a preferred embodiment the valve member comprises a core rotatable within the interior chamber of the manifold and a control handle external to the manifold, wherein mating features on the valve member core and manifold provide tactile feedback and positive positioning of the core in both first and second positions. Alternatively, or in addition, coordinated visible features on the control handle and manifold provide symbolic indicators of both first and second positions of the valve member.

[0014] The sampling port may be formed within the control valve or along the distal segment of the conduit line. If within the control valve, the sampling port may be formed within the valve member and communicates with a sampling cavity formed internally within the valve member open to at least one of the channels. Alternatively, the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the interior chamber of the manifold. Furthermore, the system may include a second sampling port having a sampling cavity positioned along the distal segment of the conduit line.

[0015] In accordance with one embodiment, the valve member comprises a core movable within the interior chamber of the manifold and a control handle external to the manifold, the core having an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core. The internal channel desirably opens to the exterior surface of the core at two separated locations spaced from the external channel.

[0016] System further may include means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position. Desirably, the reservoir has an inlet open to an outlet port of the control valve manifold and an outlet open to an inlet port of the control valve manifold. In this embodiment, the first position of the valve member provides open fluid communication between the control valve flow passages through the inlet and outlet of the reservoir to flush a chamber of the reservoir.

[0017] A second embodiment of the present invention comprises a medical system for fluid sampling of a fluid system of a patient. The system encompasses a conduit line with a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with a fluid system of a patient. A control valve connects between the proximal segment and the distal segment of the conduit line. A

fluid sampling port defines a flow path therethrough whose opposite ends open to internal channels in the control valve. A reservoir fluidly communicates with a reservoir port of the control valve manifold. The control valve further includes a valve member movable into at least three positions:

a first position that provides open fluid communication from the proximal segment through the control valve to the distal segment,

a second position that provides open fluid communication from the proximal segment to the distal segment while bypassing the reservoir and sampling port, and

a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

[0018] Desirably, the control valve further includes a manifold defining an interior chamber. The manifold has a proximal port fluidly connected to the proximal segment of the conduit line, a distal port fluidly connected to the distal segment, an outlet port, and an inlet port, wherein each of the manifold ports opens to the interior chamber. The valve member also comprises a core movable within the interior chamber of the manifold and having channels therein that selectively communicate with the manifold ports. The reservoir has an inlet open to the manifold outlet port and an outlet open to the manifold inlet port. In this embodiment:

the first position provides open fluid communication from the proximal segment to the proximal port and the outlet port of the control valve, through the inlet and outlet of the reservoir, to the inlet port and the distal port of the control valve to the distal segment,

the second position provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member core to the distal segment while bypassing the reservoir and sampling port, and

the third position provides open fluid communication from the distal segment to distal port and one of the channels of the valve member core, and to the sampling port.

[0019] The valve member core may have an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core. Desirably, the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.

[0020] Another aspect of the invention is a method of taking samples and measuring the pressure of a fluid system of a patient. The method provides a fluid sampling system with a conduit line and a reservoir connected thereto between a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with a fluid system of a patient. A control valve interposed between the reservoir and the conduit line has a movable valve member with a control handle, the valve member movable into at least a first position and a second position. A pressure transducer connects to the conduit line for sensing the pressure of the fluid therein, and a fluid sampling port is provided in the sampling system.

[0021] The method includes selecting the first position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve and the reservoir, and creating a reduced pressure within the reservoir such that fluid flows from the distal segment through the control valve into the reservoir sufficient to draw fluid from the fluid system of the patient past the sampling port. The method further includes selecting the second position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve while bypassing the reservoir, and monitoring the pressure sensed by the pressure transducer. Desirably, the valve member has a third position, and the method includes selecting the third position of the valve

member to provide open fluid communication from the distal segment to the sampling port but prevent communication between the sampling port and both the reservoir and the proximal segment, and sampling fluid from the conduit line through the sampling port.

[0022] In a preferred embodiment, the fluid system of the patient is the blood system, and the method further including means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position. In this instance, the method including the steps of:

selecting the first position of the valve member such that the physiological fluid flows through the conduit line to the patient; then

creating a reduced pressure within reservoir and collecting sufficient fluid therein such that blood flows past the sampling port; then

selecting the third position of the valve member; then

sampling blood from the conduit line through the sampling port; then

creating an elevated pressure within the reservoir to expel blood therefrom into the distal segment of the conduit line; then

selecting the first position of the valve member such that the physiological fluid flows through the conduit line to the patient and flushes the reservoir of blood; and then

selecting the second position of the valve member and monitoring the pressure sensed by the pressure transducer.

[0023] Preferably, the control valve has a manifold defining an interior chamber within which the valve member rotates, and further including mating features on the valve member and manifold that provide tactile feedback and positive positioning of the core in both first and second positions, the method of selecting the first and second positions further including rotating the valve member until the tactile feedback is sensed. Or, the control valve includes

visible features that provide symbolic indicators of the first and second positions of the control handle, the method of selecting the first and second positions further includes interpreting the symbolic indicators to determine the placement of the control handle corresponding to the first and second positions.

[0024] Another useful aspect of the present invention is a medical system for fluid sampling of a fluid system of a patient. The sampling system includes a conduit line with a proximal end adapted to be supplied with a physiological fluid and a distal end adapted to be in communication with a fluid system of a patient. A pressure transducer connects to the conduit line for sensing the pressure of the fluid therein, and a fluid sampling port is provided having a sampling cavity. A control valve interposes between the conduit line and the sampling port and has a manifold defining an interior chamber. The manifold further includes a proximal port fluidly connected to the conduit line, a distal port fluidly connected to the conduit line, an outlet port, and an inlet port, wherein each of the manifold ports opens to the interior chamber. The control valve also has a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports, the valve member being movable into at least three positions:

a first position that provides open fluid communication from the conduit line to the proximal port and the outlet port of the control valve to the sampling cavity, and to the inlet port and the distal port of the control valve to the conduit line,

a second position that provides open fluid communication from the conduit line to the proximal port and through at least one channel in the valve member and back to the conduit line while bypassing the sampling port, such that the pressure of fluid within the conduit line exclusive of the sampling port can be sensed by the pressure transducer, and

a third position that provides open fluid communication from the distal end of the conduit line through the control valve to the sampling port but prevents communication between the sampling port and the proximal end of the conduit line.

[0025] A further understanding of the nature and advantages of the present invention are set forth in the following description and claims, particularly when considered in conjunction with the accompanying drawings in which like parts bear like reference numerals.

Brief Description of the Drawings

[0026] Features and advantages of the present invention will become appreciated as the same become better understood with reference to the specification, claims, and appended drawings wherein:

[0027] Fig. 1 illustrates a typical hospital room setup of a fluid sampling system of the present invention incorporating a reservoir, the sampling port, and a pressure transducer within a conduit line to a patient;

[0028] Figure 2 is a perspective view of a reservoir of the fluid sampling system in Figure 1 having an attached control valve of the present invention;

[0029] Figures 3A-3C are several orthogonal views of one end of the reservoir showing the control valve;

[0030] Figure 4 is a close-up perspective view of the control valve on the end of the reservoir having a central sampling port in a rotatable valve member;

[0031] Figure 5 is an exploded perspective view of the control valve;

[0032] Figures 6-11 are various external and sectional views of the rotatable valve member used in the control valve shown in Figures 4 and 5;

[0033] Figures 12-15 are various external and sectional views of a manifold of the control valve of Figures 4 and 5;

[0034] Figures 16 and 17 are axial sectional views of the control valve of the present invention taken along lines 16-16 and 17-17, respectively, of Figure 4;

[0035] Figures 18A-18C are axial sectional views of the control valve taken along line 18-18 of Figure 4 showing the positions of interior fluid flow channels for different positions of the valve member;

[0036] Figures 19A-19C are views similar to Figures 18A-18C of the interior fluid flow channels for the three different positions of the control valve showing selective interconnections between the various manifold ports;

[0037] Figures 20A-20E are various external and sectional views of an alternative control valve of the present invention with a different arrangement of internal flow paths and a central sampling port;

[0038] Figures 21A-21E are various external and sectional views of an alternative control valve with a different arrangement of internal flow paths and a luer-style central sampling port;

[0039] Figures 22A-22E are various external and sectional views of an alternative control valve with a sampling port extending from the side of a manifold;

[0040] Figures 23A-23E are various external views of a luer-style valved sampling port;

[0041] Figure 24 is an axial sectional view of the valved sampling port of Figures 23A-23E; and

[0042] Figures 25A-25E are various external and sectional views of a further alternative valved sampling port with the sampling port extending from the side of a manifold.

Detailed Description of the Preferred Embodiments

[0043] The present invention provides an improved closed blood sampling system in conjunction with pressure monitor. As mentioned above, continuous or periodic blood pressure monitoring is a common and extremely

useful tool in the intensive care or operating room. However, it should be mentioned that the apparatuses and methods described herein could be utilized in conjunction with any fluid system of a patient which would benefit from pressure monitoring. For instance, intracranial pressures could be monitored and cerebrospinal fluid samples taken by placing the system described herein in fluid communication with an intraventricular catheter. Therefore, the appended claims cover the sampling and monitoring of any fluid system within a patient unless otherwise specified.

[0044] The present invention comprises an improved, closed, one-handed fluid sampling system especially useful for sampling blood in the operating room or critical care unit (CCU). The overall functioning of the system is similar to those in the prior art, in particular the VAMP Plus® Venous Arterial blood Management Protection system available from Edwards Lifesciences of Irvine, CA. Furthermore, the blood sampling function is desirably combined with a pressure transducer and monitoring hardware. The term "closed fluid sampling system" should be understood to include both systems that have a dedicated reservoir (i.e., one that remains connected) and that utilize a removable reservoir (or syringe) that gains access to the fluid column through a port. As explained above, dedicated reservoirs are preferred because of their enhanced sterility, but the feature of the present invention that isolates the reservoir from the fluid pressure column may also be useful with removable reservoirs.

[0045] Figure 1 illustrates an exemplary blood sampling system 20 of the present invention in the environment of a typical set up in a hospital room and connected to a patient P. The blood sampling system 20 comprises a conduit line having a distal segment 22 toward the patient and a proximal segment 24. The conduit line is primarily medical grade pressure tubing. The distal segment 22 may terminate in a male luer connector 26 for attaching to a female luer connector (not shown) of an injection site, or other conduit leading to the patient. A reservoir 30 connects to the conduit line via a control valve

32 interposed between the distal segment 22 proximal segment 24. The control valve 32 externally resembles a stopcock and controls fluid flow between the conduit line and the reservoir 30.

[0046] The proximal segment 24 extends from the control valve 32 and terminates in a female luer connector 34 attached to a stopcock 36 of a pressure transducer 38. The reservoir 30 and pressure transducer 38 removably mount to a bracket 40 which, in turn, may be secured to a conventional pole support 42 with the reservoir in a vertical orientation.

[0047] As mentioned above, the blood sampling system 20 forms a portion of a pressure monitoring system, and the fluid pressure transducer 36 may be a TruWave™ Disposable Pressure Transducer available from Edwards Lifesciences of Irvine, CA. A supply of flush solution 44 connects to a flush port 46 of the transducer 38 via tubing 48. Typically for adults, the flush solution 44 comprises a bag of physiological fluid such as saline surrounded by a pressurized sleeve that squeezes the fluid and forces it through the tubing 48. In addition, an infusion fluid supply (not shown) may be provided in communication with an infusion port 50 of the stopcock 36. The pressure transducer 38 is thus placed in fluid communication with the arterial or venous system of the patient through the conduit line, and preferably includes a cable and plug 52 to connect to a suitable display monitor (not shown). Though the pressure transducer 38 is shown positioned within the proximal segment 24, it could also be located in the distal segment 22.

[0048] The sampling system 20 further comprises a fluid sampling site 60 that desirably defines a Z-shaped flow passage adjacent a pre-slit septum (not numbered). With this configuration, a minimal amount of flush volume is needed to clear the line after sampling. The septum preferably comprises an elastomeric disc which accepts a blunt cannula and reseals after each sample is drawn, reducing the potential for contamination and eliminating the danger of needle sticks. Such sampling site is described in U.S. Patent No. 5,135,489 to Jepson, et al., which is hereby expressly incorporated by reference.

[0049] Figure 2 better illustrates one embodiment of a blood sampling reservoir 30 of the present invention removed from the bracket 40. The reservoir 30 desirably includes a syringe-type variable volume chamber 62, though other reservoirs that have constant volume chambers or other receptacles for receiving fluid may be used. Preferably, the reservoir 30 is of a type that includes a constantly open flow channel through the variable volume chamber 62 for passage of flushing fluid therethrough. A particularly useful such reservoir 30 is the Edwards VAMP Plus® system mentioned above.

[0050] In one mode of operation of the system 20, a reduced pressure is created within the variable volume chamber 62 by withdrawing the plunger 64 such that a fluid sample from the distal segment 22 is drawn into the chamber. The chamber 62 has a sufficient volume, typically 12 ml, to draw blood from the patient P passed the sampling site 60. The clinician can then take a sample of undiluted blood from the site 60. Subsequently, the blood and other fluids drawn into the reservoir 30 during the sampling operation are re-infused by depressing the plunger 64. It should be noted that the pressure transducer 38 may include a flow restrictor or flow control means to prevent flushed solution from going proximally through the sensor rather than back to the patient. For instance, the stopcock 36 may be used to close off the fluid path through the pressure transducer 38 prior to re-infusing the reservoir clearance volume.

[0051] The entire sampling system 20 is thus closed as the "priming" volume that ensures a pure sample of blood reaches the sampling site 60 remains within the system 20 and is reinfused into the patient. It will be understood by those skilled in the art that the syringe-type reservoir 30 shown in Figures 1-2 is only exemplary and other configurations may be designed to adequately provide the variable volume chamber.

[0052] With reference now to Figures 3A-3C and 4-5, the proximate relationship between the reservoir 30 and the control valve 32 will be described. Desirably, the reservoir 30 and control valve 32 are molded plastic

pieces that are rigidly mounted together such as with adhesive or ultrasonic welding. However, the reservoir 30 simply needs to be in proximity with the control valve 32 such that they are connected by two fluid flow paths. For convention, the ordinary flow path of the whole system as seen in Figure 1 is from proximal to distal, or from the fluid bag 44 to the patient P. With reference back to Figure 2, the saline or other physiological fluid flows into the reservoir 30 and control valve 32 combination through the proximal segment 24 of the conduit line and flows out of the distal segment 22. In this regard, therefore, the reservoir 30 has an inlet that receives saline from an outlet port of the control valve 32, and also an outlet through which saline flows to an inlet port of the control valve. These internal flow paths and channels will become clearer below, and as mentioned are desirably molded into the mating sections of the reservoir 30 and control valve 32. It is entirely feasible, however, to separate these two components with short lengths of tubing.

[0053] The control valve 32 as best seen in Figures 4-5 comprises a manifold 70 that receives a movable valve member 72. In the exemplary embodiment, the manifold 70 defines a cylindrical interior chamber 74 sized to rotatably receive a generally cylindrical core 76 of the valve member 72. A control handle 78 extends externally from the chamber 74 and provides leverage for rotating the core 76 within the chamber. The interior chamber 74 is shown oriented 90° from the axis of the reservoir 30, although other arrangements are possible.

[0054] Figures 4 and 5 further illustrate an exemplary fluid sampling port 84 provided in an outer portion of the control handle 78. The fluid sampling 44 may take a variety of forms, but as illustrated includes an elastomeric slit septum 86 captured by a cap 88 over a sampling cavity 90 within the valve member 72. The assembly seen in Figure 4 provides access for a blunt cannula through the slit septum 86 to withdraw fluid from within the sampling cavity 90. The sampling site 84 is located along the center line

of the rotating valve member 72, although as will be explained below, other locations for a sampling site within the control valve are contemplated.

[0055] Figures 4 and 5 also illustrate exemplary indicators for the various rotational positions of the valve member 72 within the manifold 70. More specifically, the preferred form of the invention includes both tactile and visual indicators to help reduce clinician errors, speed up and clarify the process. The visual indicators include an arrow-shaped control handle 78 with a pointed end 92 that registers with one of three symbols 94a, 94b, 94c raised and/or printed on a faceplate 96 of the control valve 32. The valve member 72 may be rotated to one of the three positions with the pointed end 92 registering with one of the three symbols 94a, 94b, 94c. The indicator plate 96 shows the three position indicators 94 at the 0°, 90°, and 180° locations relative to a 0° horizontal reference line to the right (3:00). The 90° angular separation between the positions of the valve member 72 facilitates selection of one of three modes. An arc-shaped lip 98 projecting from an outer end of the interior chamber body desirably interferes with a small tooth 99 (see Fig. 6A) on the valve member 72 to prevent its rotation into the fourth, unmarked quadrant. The meaning of the symbols 94a, 94b, 94c will become apparent below. 91 psuedo inlet/outlet port, good flushing

[0056] In addition to visual indicators, the control valve 32 also desirably provides tactile feedback to the operator when the valve member 72 is in one of the three discrete positions. There are a number of ways to indicate tactilely the proper positioning of a rotating body within another, but the means used in the present context also preferably provide positive positioning of the valve member 72 within the interior chamber 74. For example, a small rib or bump 100 extending inward from the chamber 74 or lip 78 may be sized in position to register with small grooves or depressions 102 formed in the valve member core 76. These mating features are preferably sized large enough for the male portion to fit within the female portion and nominally restrain motion of the valve member 72, but small

enough to allow the user to relatively easily overcome their engagement and further rotate the valve member. As the engaging pieces are molded plastic, and the assembly is designed to be used once and disposed of, small rounded bumps engaging equal sized depressions are an effective short-term tactile indicator. It should be understood that the bumps and depressions could be provided on the parts as shown, or on the opposite elements in a reverse configuration. Moreover, these physical mating features desirably emit a small click when engaging, which provides a third, aural indicator.

[0057] Figures 6A-6E and 7-11 provide details of the exemplary valve member 72 having the central sampling port 84 therein. With reference to Figure 6A, the core 76 has a generally cylindrical exterior that slightly narrows away from the control handle 78 and is interrupted at a lower end by a trough 110 bordered by two shoulders 112. A pair of channels 114, 116 through the interior of the core 76 open to the core exterior at two locations separated circumferentially by almost 90° but in a common radial plane (as used herein, "radial" is relative to the rotational axis of the valve member 72). Looking at the reverse orientation of Figure 6E, the core 76 further features an arc-shaped groove or channel 120 that extends around the circumference of the core in a radial plane, preferably the same plane as that of the openings of the channels 114, 116. Figure 9 is a radial sectional view through that common plane and illustrates the relative positions and orientations of the channels 114, 116, 120.

[0058] The generally cylindrical portion of the core 76 is sized to closely fit within the interior chamber 74 of the manifold 70 (see Figure 5) such that the valve member 72 can rotate within the manifold but there is no unintended fluid leakage between the various ports and channels. The openings of the channels 14, 16 and the circumferential channel 120 lying in a common radial plane provide the only avenue for fluid passage around or through the valve member 72 when it is closely fit within the interior chamber 74. It should be understood that alternative configurations are possible with,

for example, the openings to the channels 114, 116 and circumferential channel 120 being spaced apart axially with respect to one or the others.

[0059] Figure 7 is an axial cross-sectional view through the valve member 72 that illustrates the inner components of the sampling port 84. Namely, the cap 88 restrains the elastomeric slit septum 86 over the sampling cavity 90. Figure 8 illustrates the sampling cavity 90 along a different axial plane that passes directly between a pair of axially-oriented channels 130, 132 seen in Figure 7 that communicate, respectively, with the radial channels 114, 116. Figure 8 further illustrates the generally semi-circular cross-section of the circumferential channel 120. With reference again to Figure 9, it should therefore be apparent that the radial channels 114, 116 are in constant fluid communication with each other via the respective connecting channels 130, 132 opening into the common sampling cavity 90. As will be explained below, these bifurcated channels through the valve member 72 function to permit blood or other body fluid into the sampling cavity 90, and also effectively flush the sampling cavity 90 in between samples. An axial extension 134 of the wall separating the connecting channels 130, 132 continues into close proximity with the slit septum 86. The extension 134 creates a pseudo inlet/outlet to the sampling cavity 90 such that a flow of flushing fluid therethrough is directed all the way to the slit septum 86 before turning the corner and continuing through the valve member 72. The extension 134 therefore enhances the efficacy of the flushing step and helps eliminate dead zones within the simply cavity 90 that might otherwise be a source of blood coagulation and contamination.

[0060] Structural details of the manifold 70 are seen in Figures 12-15. Specifically, the manifold 70 features a plurality of ports that opened into the interior chamber 74. A distal port 140 and a proximal port 142 extend upward from the chamber 74 in the orientation where the reservoir 30 plunger points downward. These ports 140, 142 are shown respectively connected to the distal segment 22 and proximal segment 24 of the conduit line in Figures 1

and 2. Therefore these ports 140, 142 represent the two diverging segments of the conduit line, the former extending toward the patient and the latter to the pressure transducer 38 and saline drip.

[0061] On the opposite side of the chamber 74, a manifold outlet port 144 leads to an inlet 146 to the reservoir variable volume chamber 62. An outlet 148 of the reservoir 30 leads directly into a manifold inlet port 150. The distal and proximal ports 140, 142 and outlet and inlet ports 144, 150 all open directly to the interior chamber 74 of the manifold 70. Note that one possible configuration is a reservoir connected through the control valve 32 using only a single reservoir port as opposed to inlet and outlet ports. For example, a syringe-type removable reservoir may be connected to a single port of the control valve 32. In such a system, the benefit of isolating the reservoir remains although the flush mode of operation will not pass through the reservoir. The term "reservoir port" therefore includes one or both of the outlet and inlet ports 144, 150.

[0062] Figures 13-14 show the manifold 70 having relatively long outlet and inlet ports 144, 150 leading to and from the reservoir 30 to provide some clearance for rotation of the valve member 72. Desirably, the manifold 70 is a single molded piece that is rigidly secured to the end of the reservoir 30. However, the manifold 70 could be a combination of more than one piece, and could be connected to the reservoir 30 through short tubes.

[0063] Figures 15A and 15B show the gradual taper of the interior chamber 74 at the narrow end of the chamber 74, a circular rib 160 projects inward for engaging and retaining the valve member 72, as will be explained next.

[0064] Figures 16 and 17 illustrate in cross-section the coupling of the valve member 72 within the manifold 70. Specifically, the gradual tapers of both closely match and provide an effective fluid seal at the point that the inward rib 160 of the manifold passes over the first shoulder 112 of the valve member 72 and resides within the trough 110. A cavity 162 in the narrow end

of the valve member 72 permits inward flexing of the shoulder 112 such that it can be forced passed the rib 160. Interference between the outwardly-sprung shoulder 112 and rib 160 effectively locks the valve member 72 within the manifold 70 and ensures good fluid sealing around the various ports and openings. Figure 16 shows the alignment of the proximal port 142 with the circumferential groove 120 two valve member 72. Likewise, the radial channel 114 also lies in the same plane. It is worth mentioning again at this stage that the coplanar nature of all of the ports and openings is an efficient and relatively straightforward design, but more complex fluid pathways between the rotating valve member 72 and manifold 70 could be designed to perform the same function. For example, one or more of the internal channels could be curvilinear, or there could be more than one circumferential surface channel.

[0065] Now with reference to Figures 18A-18C and 19A-1C, the fluid flow paths for the three positions of the valve member 72 will be explained.

[0066] The reader will recall from the description of the system of Figure 1 that there is a physiological fluid flush drip, preferably pressurized. When such flush is needed, the clinician rotates the valve member 72 to the downward position, as indicated by the arrow F/C in Figure 18A. This corresponds to a "Flush/Clear" mode of operation, and is symbolically indicated by the symbol 94a of three divergent flow paths in Figure 5, meaning all fluid communications are open. When pressure monitoring is desirable, the clinician rotates the valve member 72 to the left position, as indicated by the arrow M in Figure 18B. This corresponds to a "Monitoring" mode of operation, and is symbolically indicated by the symbol 94b of a pressure wave in Figure 5. Finally, when the clinician requires a fluid sample, he/she rotates the valve member 72 to the right position, as indicated by the arrow S in Figure 18C. This corresponds to a "Sampling" mode of operation, and is symbolically indicated by the symbol 94C of a drop of fluid in Figure 5. As mentioned above, the symbolic indicators 94a, 94b, and 94c are desirably

supplemented by the clear directional nature of the arrow-shaped control handle 78, and by tactile and audible feedback measures, to help avoid error.

[0067] Figures 18A-18C further illustrate the change in rotational orientation of the valve member 72 within the internal chamber of the manifold 70, in particular through the radial plane passing through the flow channels that open to the exterior of the valve member core 76. The same illustrations of the flow channels in the three positions are shown more clearly in Figures 19A-19C with relevant labels and fluid flows indicated. The two sets of diagrams further indicate the four manifold ports 140, 142, 144, and 150.

[0068] In the F/C position of the valve member 72 of Figures 18A and 19A, a slow drip of flushing fluid travels from the supply of flush solution 44 (Figure 1) through the proximal segment 24 (Figure 2) to the manifold proximal port 142, through the circumferential channel 120 and the outlet port 144. As indicated by the flow arrows in Figure 19A, the drip continues through the inlet 146 and outlet 148 of the reservoir 30 passing through the variable volume chamber 62. The fluid then passes through the inlet port 150 into the radial channel 114, and along the axial channel 130 into the sampling reservoir 90 (see Figure 7), and back through the parallel axial channel 132 into the other radial channel 132. Finally, the fluid exits the valve member 72 into the manifold distal port 140 and from there continues through the distal segment 22 of the conduit line to the patient.

[0069] In the F/C position of the valve member 72, all of the internal flow paths within the reservoir 30 and control valve 32 are open to form a single continuous flushing pathway. This desirably permits any blood or other bodily fluid to be completely flushed from within the system 20, leaving no dead spots for bubbles to form or blood to coagulate. This "pocket-less" fluid pathway through the system in conjunction with the ability to isolate components that degrade the pressure signal is extremely useful. Furthermore, the control valve 32 is desirably made of transparent or frosted plastic that

permits the user to visualize blood flow therethrough, thus insuring blood as been completely flushed out of the system after a sample is taken.

[0070] The F/C position also enables a clearing volume to be pulled into the reservoir 30. Specifically, a reduced pressure within the variable volume chamber 62 pulls fluid from the distal segment 22 into the reservoir 30 in a reverse flow from that shown in Fig. 19A. The volume of the chamber 62 is sufficient to draw blood from the patient past the sampling port 84 (sampling cavity 90), that is, through the internal channels of the valve member 72. A flow restrictor or control valve at the pressure transducer 38 toward the proximal segment 24 ensures that the reservoir 30 fills with fluid from the distal segment 22. That is, there is greater resistance to flow into the reservoir from the proximal segment 24 as compared to the distal segment 22.

[0071] Before a sample is taken, however, the control handle 78 must be rotated into the third S position shown in Figures 18C and 19C. In this position, the channels of the valve member 72 provide open fluid communication only from the distal port 140 to the radial channel 114 as shown, and from there to the sampling cavity 90 (Figure 7). A fluid sample is taken from the port 84 using a blunt cannula or other sampling device.

[0072] Pressure monitoring occurs with the valve member 72 in the second M position shown in Figures 18B and 19B. In that position, the pressure transducer 38 (or DPT, Disposable Pressure Transducer), is in fluid communication with the patient directly though the circumferential channel 120, bypassing the reservoir 30 and sampling port 84. This feature of the control valve 32 isolates the elastomeric elements of the reservoir 30 and sampling port 84, as well as the associated channels leading thereto, from the fluid pressure column. The fluid pressure column therefore extends directly from the patient through the distal segment 22, making a U-turn in the circumferential channel 120 to the proximal segment 24. Bypassing the reservoir 30, and in particular the elastomeric seal of the plunger 64, and the sampling port 84 (elastomeric septum 86), greatly improves the signals

received by the pressure transducer 38. A distal sampling port 60 in the distal segment 22 may be of a conventional type which includes an elastomeric septum that would affect the pressure signal, or that sampling port may also be isolated from the pressure column as will be described below. One benefit of improving the pressure response of the system by isolating the various functional elements is that the entire conduit line can be lengthened to move the reservoir 30 farther away from the patient. In conventional blood sampling systems, where the elastomeric components remain in contact with the pressure column, the maximum length of the conduit line from the reservoir to the patient is about __ cm. By isolating just the reservoir 30 as indicated above, the conduit line can be lengthened to about __cm. [Mark, please fill in these distances]

[0073] It is important to understand that the principles of the control valve 32 described above are applicable to other configurations of fluid sampling systems. In the exemplary system described above, a sampling port 84 is incorporated centrally in the rotating valve member 72 of the control valve 32, which is connected or adjacent to the reservoir 30. The control valve 32 isolates both the reservoir and the sampling port in the sampling mode. However, the sampling port in the control valve may connect through the manifold 70 instead of the valve member 72. Also, the exemplary valve member has three positions 90° apart from each other, but the arrangement of the channels within the valve member and manifold may be altered to change the amount of the valve member rotates in each position. Furthermore, the principles of isolating the elastomeric elements of the reservoir and sampling port can be transferred to a stand-along sampling port in the conduit line. Examples of each of these alternatives will be described below, and it should be clear that these are representative of numerous other alternatives.

[0074] Figures 20A-20E illustrate an alternative control valve 170 of the present invention adjacent a reservoir 30 with a modified arrangement of internal flow paths than the exemplary embodiment described above. The

control valve 170 is similar to the first embodiment in that a housing or manifold 172 connects to the reservoir 30 and rotatably receives therein a valve member 174. Furthermore, the valve member 174 carries a central sampling port 176, which is illustrated as a slit septum-type but could be any number of kinds of sampling ports. Figure 20B shows a control handle 178 of the valve member 174 oriented with its pointed and 180 down into the right at about a 45° angle. The indicator plate 182 shows the three position indicators at the 45°, 90°, and 180° locations relative to a horizontal reference line to the right at 0°. This is a departure from the 90° separation between the valve member positions in the first embodiment.

[0075] The control handle 178 in Figure 20B is in the "S" or sampling position. The internal flow channels defined within the valve member 174 in the radial plane of the ports of the manifold 172 are illustrated in Figure 20E. Comparing this view with a similar view shown in Figure 18C, the reader will discern the slightly different orientations of the internal channels within the valve member 174. By rotating the valve member 174 clockwise another 45°, the control valve 170 will be placed in the F/C mode wherein all of the internal flow paths are in series so that the system can be flushed. Rotating the valve member 174 a further 90° into the M position isolates both the reservoir 30 and the sampling port 176 from the attached conduit line for undegraded pressure monitoring. Although the relative spacing between the S position and the F/C position is only 45°, in contrast with 90° in the first embodiment, the flow channels are modified to prevent cross-talk or pressure perturbations transmitted to the proximal segment and pressure transducer when switching positions. Furthermore, the channels are arranged so that there is greater separation between the internal channels in the sampling mode.

[0076] Figures 21A-21E show another alternative control valve 190 similar to the valve 170 of Figure 20A-20E, but with a luer-style central sampling port. Specifically, the control valve 190 includes the modified internal flow paths such that the three operating positions of a control handle

192 seen in Figure 21B are other than 90° apart. More particularly, the cross-section of Figure 21E is the same as that of Figure 20E. Also, the control valve 190 includes a sampling port 194 provided in the center of a rotatable valve member 196. In contrast to the embodiments of Figures 20A-20E, however, the sampling port 194 includes a luer-style connector 198, best seen in Figure 21C. The male luer-style connector 198 mates with a female luer connector on a sampling syringe (not shown). Because of the typically larger sizes of the blunt cannulas in such sampling syringes, the septum 200 of the sampling port 194 is highly compliant, or at least more compliant than the slit septum 86 used in the sampling port 84 described above. The ability to isolate the luer-style sampling port 194 using the control valve 190 is therefore highly desirable as it greatly improves the quality of the pressure signal received by the pressure transducer by removing the compliance of the septum 200 from the pressure column.

[0077] Figures 22A-22E illustrates a control valve 210 that, as before, may be associated with or connected to a reservoir 30, but includes an alternative fluid sampling port 212. Specifically, the fluid sampling port 212 comprises a side port from a control valve manifold 214 rather than being formed centrally in a rotatable valve member 216. The sampling port 212 is shown in cross-section in Figure 22E which reveals an elastomeric septum 220 captured by a cap 222 over a sampling cavity 224. A pair of flow channels 226, 228 open into the sampling cavity 224. The opposite ends of the flow channels 226, 228 opened to an interior chamber of the control valve manifold 214. In this sense, the sampling port 212 communicates with internal channels in the control valve 210 via a through flow path defined by the channels 226, 228.

[0078] Figure 22E also shows six openings to the internal channel of the manifold 214, two of which lead to the sampling port channels 226, 228. Another two openings lead to proximal and distal ports 230, 232 that connect to the proximal and distal conduit line segments. Finally, two more openings

lead respectively to the inlet and outlet of the reservoir 30. The valve member 216 includes circumferential channels that selectively communicate with these 6 ports depending on the rotational position of a handle 234. As with the earlier embodiments, there are 3 positions of flush, monitor, and sample. In the monitor position, the control valve 210 isolates both the reservoir 30 and sampling port 212 from the conduit line for a more accurate pressure signal. Also, the valve 210 prevents flow from the proximal conduit line segment in the sampling mode. This embodiment illustrates the alternative of having the sampling port connected with the control valve manifold as opposed to the rotating valve member. ;

Figures 23A-23E are various views of a luer-style valved sampling station 250 which can be incorporated into a pressure monitoring line in conjunction with a reservoir or independently. The valved sampling station 250 includes a housing or manifold 252 that defines therewithin an internal chamber 254 as seen in Figure 24 with which a pair of ports 256, 258 communicate. The downstream port 256 may be connected to the patient, while an upstream port 258 is connected to a pressure transducer (not shown), in like manner as the manifold ports 140, 142 seen in Figure 12. Additionally, a loop-shaped channel 260 formed in the manifold 252 has opposite ends that open to the internal chamber 254. A valve member 262 rotates within the internal chamber 254. The valve member 262 has the same configuration has the valve member 196 shown in Figures 21A-21E. That is, the internal flow channels are the same and the valve member 262 carries a central luer-type sampling port 264.

[0079] With reference to Figure 23B, the manifold 252 includes an indicator plate 266 on which are provided the familiar three operational mode symbols of sampling, flush, and pressure monitoring. A control handle 268 is used to rotate the valve member 262 into the three operational positions. The reader will recognize that the three positions have the same spacing as the positions for the control valve 190 in Figures 21A-21E. Indeed, the valved

sampling station 250 functions analogously to the control valve 190 in that in the pressure monitoring position of the control handle 268, the central sampling port 264 is isolated from the ports 256, 258, and thus the attached conduit line and pressure column. The sole difference between the valved sampling station 250 and the control valve 190 is the substitution of the loop-shaped channel 260 for the clearance reservoir. The channel 260 is important in that a flow of fluid passes through it and through all of the internal channels of the valved sampling station 250 when the control handle 268 is in the flush position, seen in Figure 23B. Again, the valved sampling station 250 can be used in a conduit line of a pressure monitoring system where a clearance volume of fluid is pulled past the sampling port using a reservoir as described above, or other such clearing device.

[0080] Finally, Figures 25A-25E illustrate a further alternative valved sampling station 280 with a sampling port 282 extending from one side of a manifold 284. The manifold 284 is configured in a T-shape with a pair of ports 286, 288 that open to an internal chamber projecting outward at 90° with respect to one another, and with respect to the sampling port 282. The valve member 290 rotates within the internal chamber. As seen in Figure 25E, the valve member 290 includes two circumferential channels 292, 294 that selectively communicate with the ports 286, 288, and with two ports 296, 298 leading to and from the sampling port 282. As in the valved sampling station 250 of Figures 23-24, the valve member 290 rotates into three positions corresponding to flush, sampling, and pressure monitoring. The ports 286, 288 attach to proximal and distal segments of a conduit line in a manner described above. In the pressure monitoring mode, the sampling station 280 excludes the sampling port 282 from the conduit line. This embodiment is similar to the immediately preceding sampling station 250, but illustrates a sampling port 282 that connects directly to the manifold 284 rather than to the rotating valve member 290. Furthermore, the sampling port 282 has a slit

septum 299 for receiving a blunt cannula (not shown), but a luer-type sampling port could also be used.

[0081] While the invention has been described in its preferred embodiments, it is to be understood that the words which have been used are words of description and not of limitation. Therefore, changes may be made within the appended claims without departing from the true scope of the invention.

WHAT IS CLAIMED IS:

1. A medical system for fluid sampling and pressure monitoring of a fluid system of a patient, comprising:

a conduit line with a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with a fluid system of a patient;

a control valve with a manifold defining an interior chamber, the manifold having a proximal port fluidly connected to the proximal segment, a distal port fluidly connected to the distal segment, and a reservoir port, wherein each of the manifold ports opens to the interior chamber,

a pressure transducer connected to the conduit line for sensing the pressure of the fluid therein;

a fluid sampling port in the medical system;

a reservoir in fluid communication with the reservoir port of the control valve manifold;

the control valve further including a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports, the valve member being movable into at least two positions:

a first position that provides open fluid communication from the proximal segment to the patient through the control valve so as to eliminate any dead spaces therein, wherein reduced pressure within the reservoir pulls fluid from the distal segment through the control valve and into the reservoir sufficient to draw fluid from the fluid system of the patient past the sampling port, and

a second position that provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member to the

distal segment while bypassing the reservoir, such that the pressure of fluid within the conduit line exclusive of the reservoir can be sensed by the pressure transducer.

2. The system of claim 1, wherein the valve member has a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

3. The system of claim 1, wherein the valve member comprises a core rotatable within the interior chamber of the manifold and a control handle external to the manifold, and further including mating features on the valve member core and manifold that provide tactile feedback and positive positioning of the core in both first and second positions.

4. The system of claim 1, wherein the valve member comprises a core rotatable within the interior chamber of the manifold and a control handle external to the manifold, further including coordinated visible features on the control handle and manifold that provide symbolic indicators of both first and second positions of the valve member.

5. The system of claim 1, wherein the sampling port is formed within the control valve.

6. The system of claim 5, wherein the sampling port is formed within the valve member and communicates with a sampling cavity formed internally within the valve member open to at least one of the channels.

7. The system of claim 5, wherein the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the interior chamber of the manifold.

8. The system of claim 5, further including a second sampling port having a sampling cavity positioned along the distal segment of the conduit line.

9. The system of claim 8, further including a second control valve interposed between the second sampling port and the distal segment and having a valve member movable into at least three positions:

a first position that provides open fluid communication from the conduit line through the control valve to the sampling cavity and back to the conduit line,

a second position that provides open fluid communication from the conduit line through the valve member and back to the conduit line while bypassing the second sampling port, such that the pressure of fluid within the conduit line exclusive of the second sampling port can be sensed by the pressure transducer, and

a third position that provides open fluid communication from the distal segment through the control valve to the second sampling port but prevents communication between the second sampling port and the conduit line proximal from the second sampling port.

10. The system of claim 1, wherein the sampling port is positioned along the distal segment of the conduit line.

11. The system of claim 10, further including a second control valve interposed between the sampling port and the distal segment and having a valve member movable into at least three positions:

a first position that provides open fluid communication from the conduit line through the control valve to the sampling cavity and back to the conduit line,

a second position that provides open fluid communication from the conduit line through the valve member and back to the conduit line while bypassing the sampling port, such that the pressure of fluid within the conduit line exclusive of the sampling port can be sensed by the pressure transducer, and

a third position that provides open fluid communication from the distal segment through the control valve to the sampling port but prevents communication between the sampling port and the conduit line proximal from the sampling port.

12. The system of claim 1, wherein the valve member comprises a core movable within the interior chamber of the manifold and a control handle external to the manifold, the core having an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core.

13. The system of claim 12, wherein the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.

14. The system of claim 1, further including means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position.

15. The system of claim 1, wherein the reservoir has an inlet open to an outlet port of the control valve manifold and an outlet open to an inlet port of the control valve manifold, and wherein the first position of the valve member provides open fluid communication between the control valve flow passages through the inlet and outlet of the reservoir to flush a chamber of the reservoir.

16. A medical system for fluid sampling of a fluid system of a patient, comprising:

a conduit line with a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with a fluid system of a patient;

a control valve connected between the proximal segment and the distal segment of the conduit line;

a fluid sampling port having a flow path therethrough whose opposite ends open to internal channels in the control valve;

a reservoir in fluid communication with a reservoir port of the control valve manifold;

the control valve further including a valve member movable into at least three positions:

a first position that provides open fluid communication from the proximal segment through the control valve to the distal segment,

a second position that provides open fluid communication from the proximal segment to the distal segment while bypassing the reservoir and sampling port, and

a third position that provides open fluid communication from the distal segment to the sampling port but prevents communication between the sampling port and both the reservoir and the proximal segment.

17. The system of claim 16, wherein:

the control valve further includes a manifold defining an interior chamber, the manifold having a proximal port fluidly connected to the proximal segment of the conduit line, a distal port fluidly connected to the distal segment, an outlet port, and an inlet port, wherein each of the manifold ports opens to the interior chamber, and wherein the valve member comprises a core movable within the interior chamber of the manifold and having channels therein that selectively communicate with the manifold ports, and the reservoir has an inlet open to the manifold outlet port and an outlet open to the manifold inlet port, and wherein:

the first position provides open fluid communication from the proximal segment to the proximal port and the outlet port of the control valve, through the inlet and outlet of the reservoir, to the inlet port and the distal port of the control valve to the distal segment,

the second position provides open fluid communication from the proximal segment to the proximal port and through at least one channel in the valve member core to the distal segment while bypassing the reservoir and sampling port, and

the third position provides open fluid communication from the distal segment to distal port and one of the channels of the valve member core, and to the sampling port.

18. The system of claim 17, wherein the valve member core has an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core.

19. The system of claim 18, wherein the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.

20. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber in which the valve member moves, and wherein the sampling port is formed within the valve member and includes a sampling cavity open to channels within the valve member that communicate with the manifold interior chamber.

21. The system of claim 20, wherein the valve member comprises a cylindrical core rotatable within the manifold interior chamber, and wherein the fluid sampling port opens in a control handle of the valve member and is centered along the axis of rotation of the valve member core.

22. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber in which the valve member moves, and wherein the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the manifold interior chamber.

23. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber and the valve member comprises a core movable within the interior chamber of the manifold, and further including mating features on the valve member core and manifold that

provide tactile feedback and positive positioning of the core in all three positions of the valve member.

24. The system of claim 16, wherein the control valve further includes a manifold defining an interior chamber and the valve member comprises a movable within the interior chamber of the manifold and a control handle external to the manifold, and further including coordinated visible features on the control handle and manifold that provide symbolic indicators of all three positions of the valve member.

25. A method of taking samples and measuring the pressure of a fluid system of a patient, comprising:

providing a fluid sampling system with a conduit line and a reservoir connected thereto between a proximal segment adapted to be supplied with a physiological fluid and a distal segment adapted to be in communication with a fluid system of a patient;

interposing a control valve between the reservoir and the conduit line having a movable valve member with a control handle, the valve member movable into at least a first position and a second position;

providing a pressure transducer connected to the conduit line for sensing the pressure of the fluid therein;

providing a fluid sampling port in the sampling system;

selecting the first position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve and the reservoir, and creating a reduced pressure within the reservoir such that fluid flows from the distal segment through the control valve into the reservoir sufficient to draw fluid from the fluid system of the patient past the sampling port; and

selecting the second position of the valve member to provide open fluid communication from the proximal segment to the distal segment via the control valve while bypassing the reservoir, and monitoring the pressure sensed by the pressure transducer.

26. The method of claim 25, wherein the valve member has a third position, and the method includes selecting the third position of the valve member to provide open fluid communication from the distal segment to the sampling port but prevent communication between the sampling port and both the reservoir and the proximal segment, and sampling fluid from the conduit line through the sampling port.

27. The method of claim 26, wherein the fluid system of the patient is the blood system, and further including means for pressurizing the physiological fluid such that at least some fluid continues to flow through the conduit line to the patient when the valve member is in the first position, the method including the steps of:

selecting the first position of the valve member such that the physiological fluid flows through the conduit line to the patient; then

creating a reduced pressure within reservoir and collecting sufficient fluid therein such that blood flows past the sampling port; then

selecting the third position of the valve member; then

sampling blood from the conduit line through the sampling port; then

creating an elevated pressure within the reservoir to expel blood therefrom into the distal segment of the conduit line; then

selecting the first position of the valve member such that the physiological fluid flows through the conduit line to the patient and flushes the reservoir of blood; and then

selecting the second position of the valve member and monitoring the pressure sensed by the pressure transducer.

28. The method of claim 25, wherein the control valve has a manifold defining an interior chamber within which the valve member rotates, and further including mating features on the valve member and manifold that provide tactile feedback and positive positioning of the core in both first and second positions, the method of selecting the first and second positions further including rotating the valve member until the tactile feedback is sensed.

29. The method of claim 25, wherein the control valve includes visible features that provide symbolic indicators of the first and second positions of the control handle, the method of selecting the first and second positions further includes interpreting the symbolic indicators to determine the placement of the control handle corresponding to the first and second positions.

30. A medical system for fluid sampling of a fluid system of a patient, comprising:

a conduit line with a proximal end adapted to be supplied with a physiological fluid and a distal end adapted to be in communication with a fluid system of a patient;

a pressure transducer connected to the conduit line for sensing the pressure of the fluid therein;

a fluid sampling port having a sampling cavity;

a control valve interposed between the conduit line and the sampling port and having a manifold defining an interior chamber, the manifold having a proximal port fluidly connected to the conduit line, a distal port fluidly connected to the conduit line, an outlet port, and an

inlet port, wherein each of the manifold ports opens to the interior chamber,

the control valve further including a valve member movable within the interior chamber and having channels therein that selectively communicate with the manifold ports, the valve member being movable into at least three positions:

a first position that provides open fluid communication from the conduit line to the proximal port and the outlet port of the control valve to the sampling cavity, and to the inlet port and the distal port of the control valve to the conduit line,

a second position that provides open fluid communication from the conduit line to the proximal port and through at least one channel in the valve member and back to the conduit line while bypassing the sampling port, such that the pressure of fluid within the conduit line exclusive of the sampling port can be sensed by the pressure transducer, and

a third position that provides open fluid communication from the distal end of the conduit line through the control valve to the sampling port but prevents communication between the sampling port and the proximal end of the conduit line.

31. The system of claim 30, wherein the valve member comprises a core movable within the interior chamber of the manifold and having an external channel formed along an exterior surface of the core and an internal channel formed along an interior bore of the core.

32. The system of claim 31, wherein the internal channel opens to the exterior surface of the core at two separated locations spaced from the external channel.

33. The system of claim 30, wherein the sampling port is formed within the valve member and includes a sampling cavity open to the valve member channels.

34. The system of claim 33, wherein the valve member comprises a cylindrical core rotatable within the manifold interior chamber, and wherein the fluid sampling port opens in a control handle of the valve member and is centered along the axis of rotation of the valve member core.

35. The system of claim 30, wherein the sampling port connects to the control valve manifold and defines a flow path therethrough whose opposite ends open to the manifold interior chamber.

36. The system of claim 30, wherein the valve member comprises a core movable within the interior chamber of the manifold and a control handle external to the manifold.

37. The system of claim 36, further including mating features on the valve member core and manifold that provide tactile feedback and positive positioning of the core in all three positions of the valve member.

38. The system of claim 36, further including coordinated visible features on the control handle and manifold that provide symbolic indicators of all three positions of the valve member.

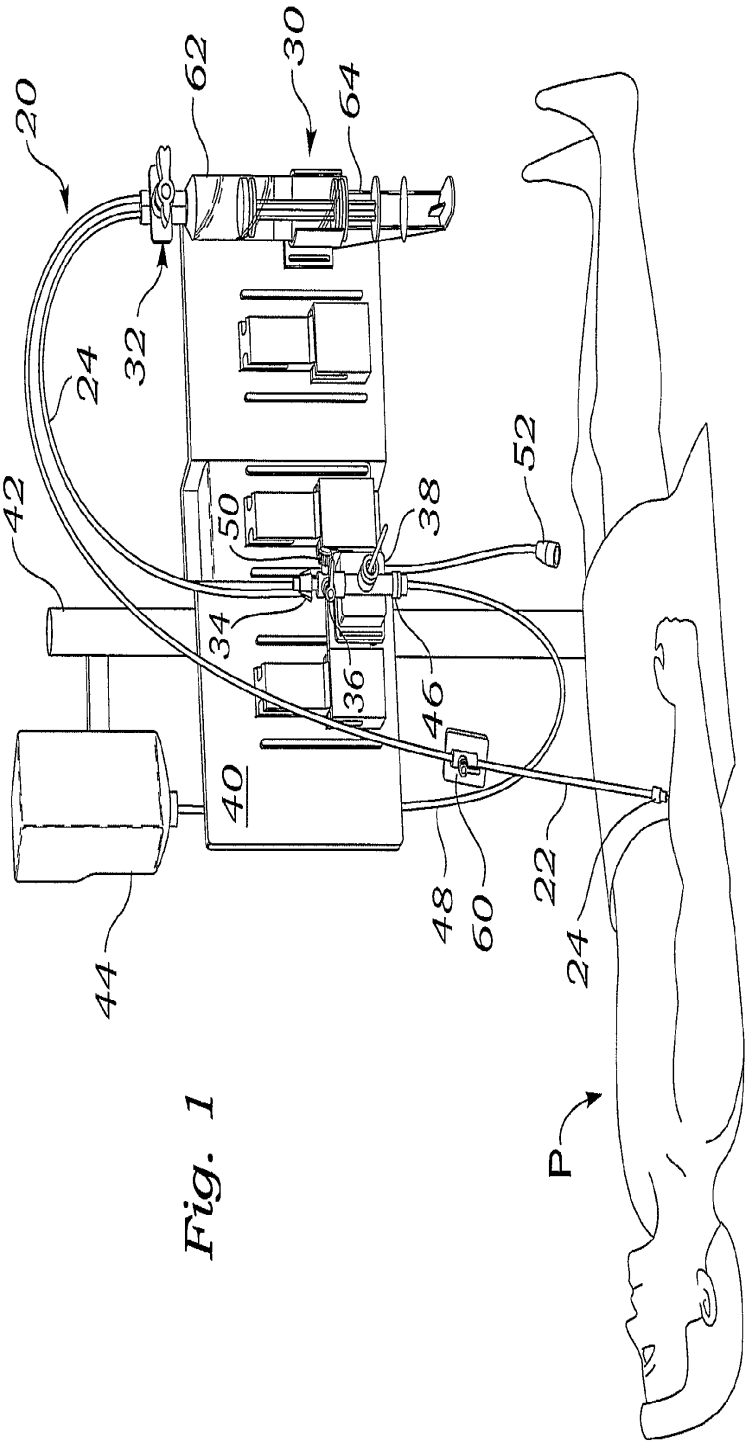


Fig. 1

Fig. 2

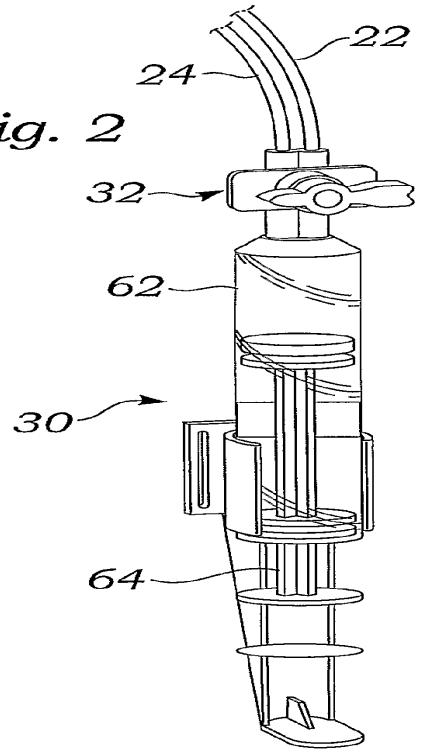


Fig. 3

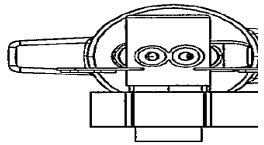


Fig. 3B

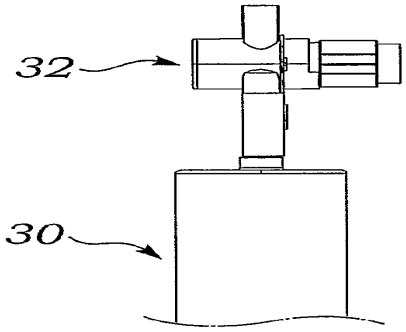


Fig. 3A

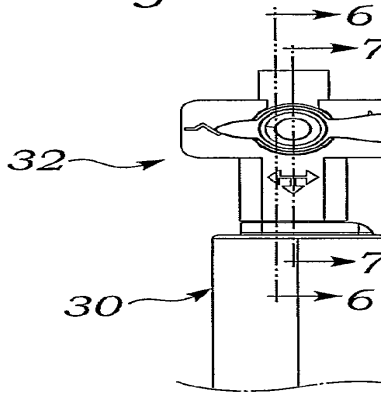


Fig. 4

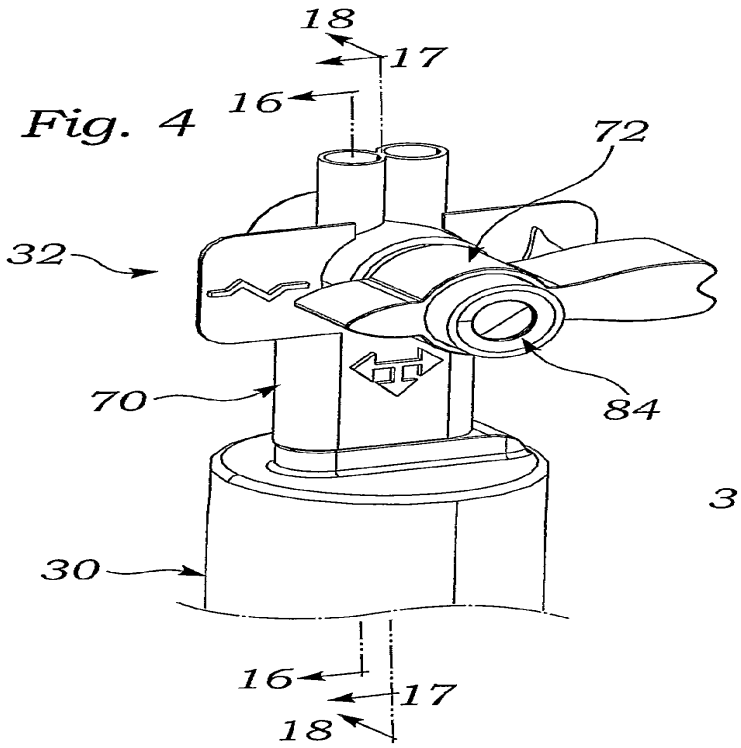

18
17
16
72
32
70
84
30
16
17
18

Fig. 5

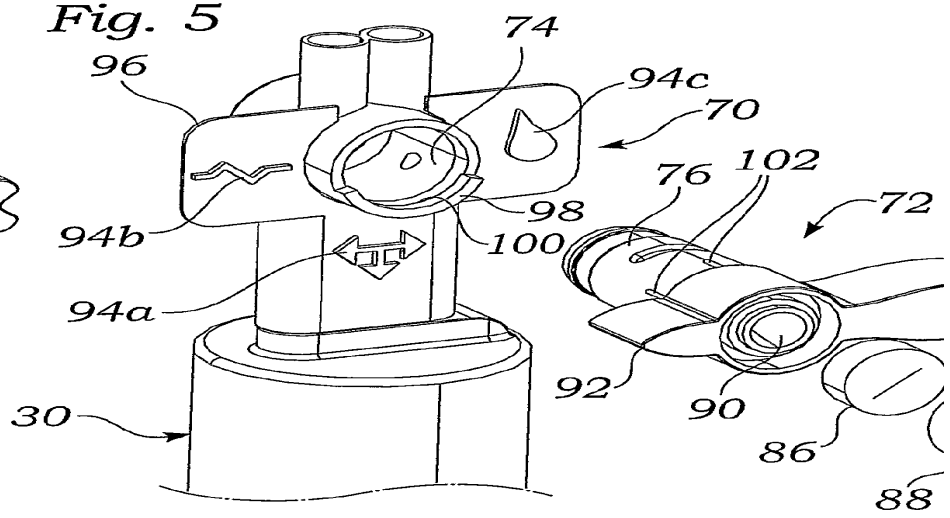

74
96
94c
70
76
102
72
98
94b
100
94a
92
90
86
88
30

Fig.6B

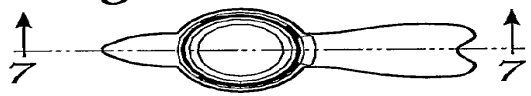


Fig.6D

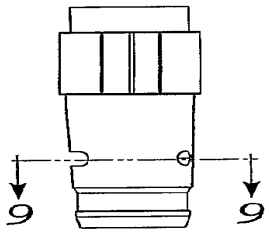


Fig.6A

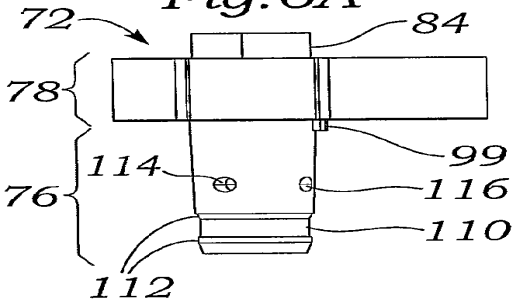


Fig.7

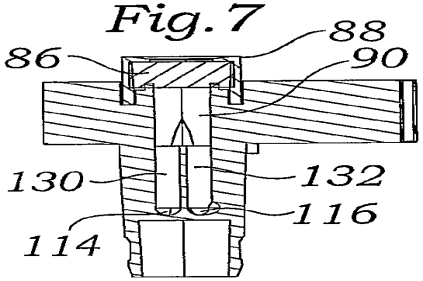


Fig.6

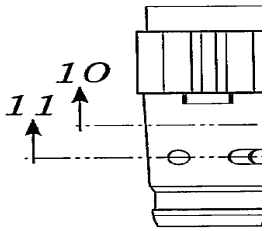


Fig.9



Fig.6E

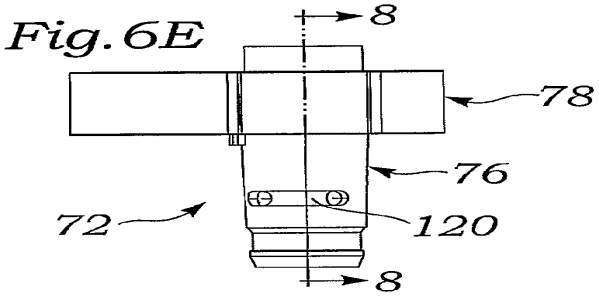


Fig.8

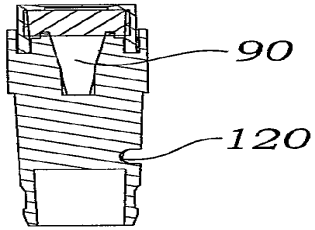


Fig.10

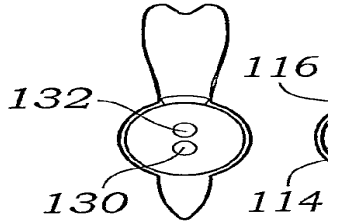


Fig. 12

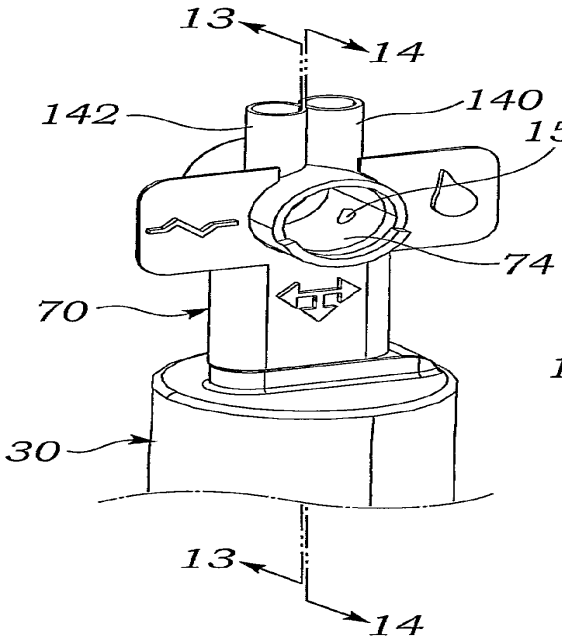


Fig. 13

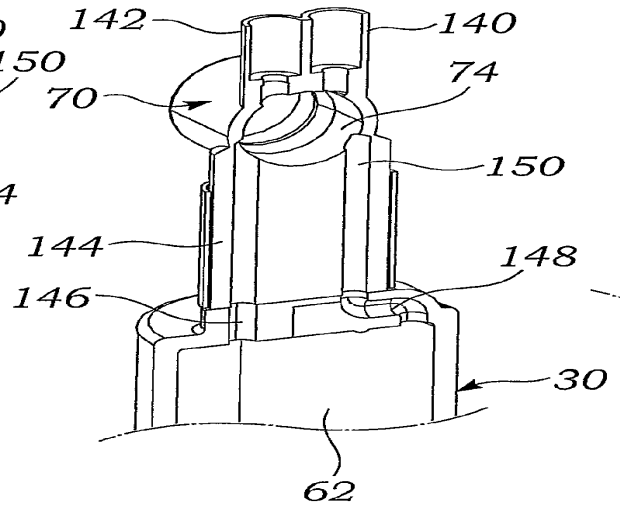


Fig. 14

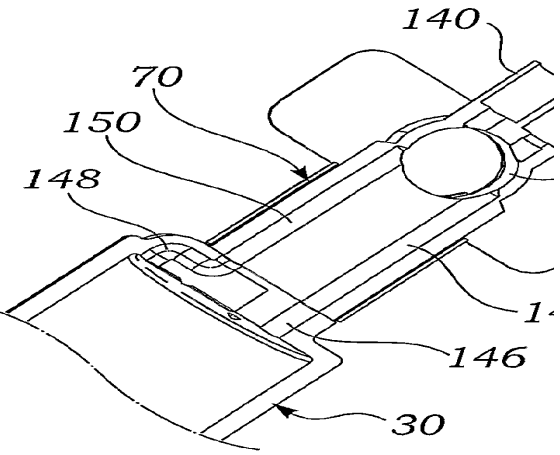


Fig. 15B

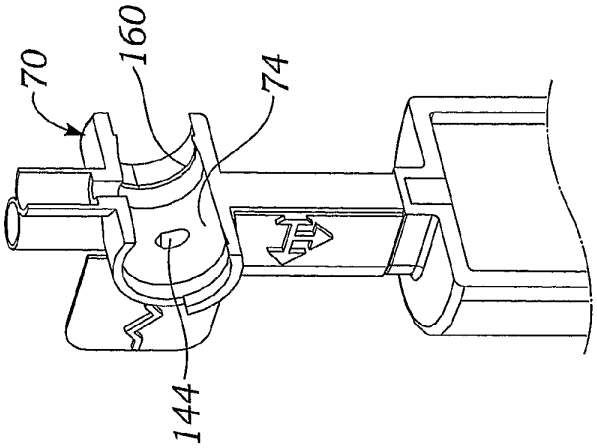


Fig. 15A

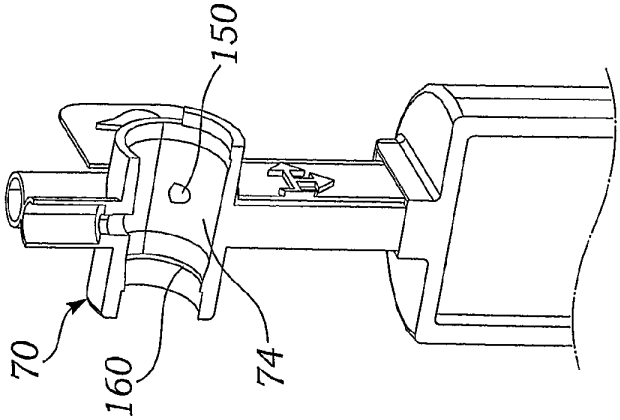


Fig. 17

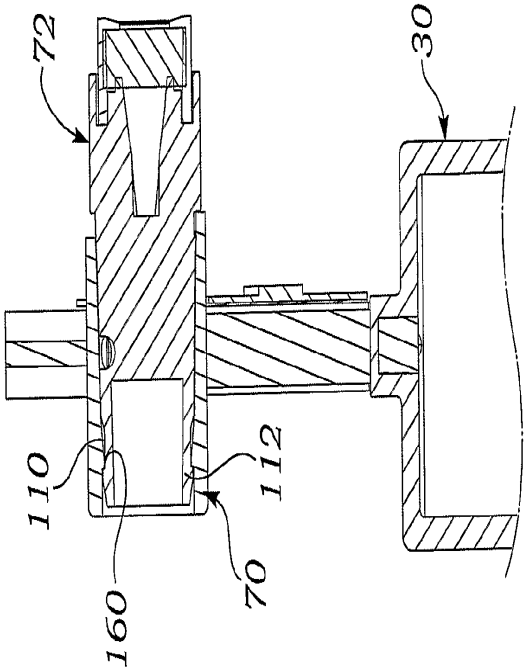


Fig. 16

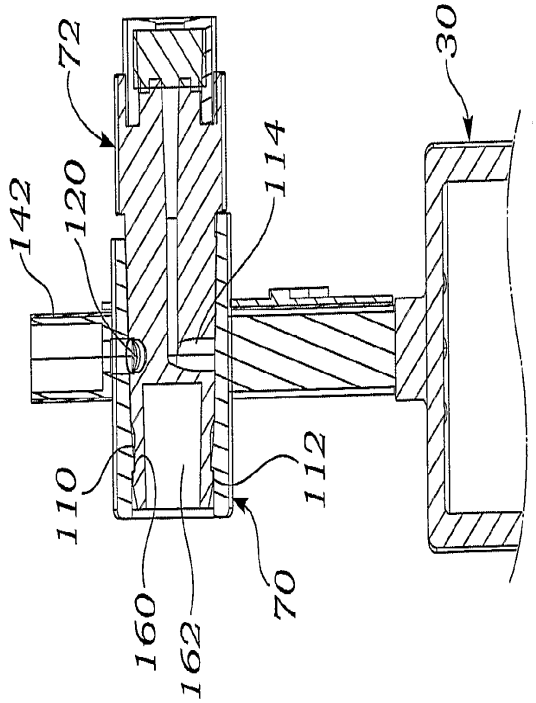


Fig. 18A

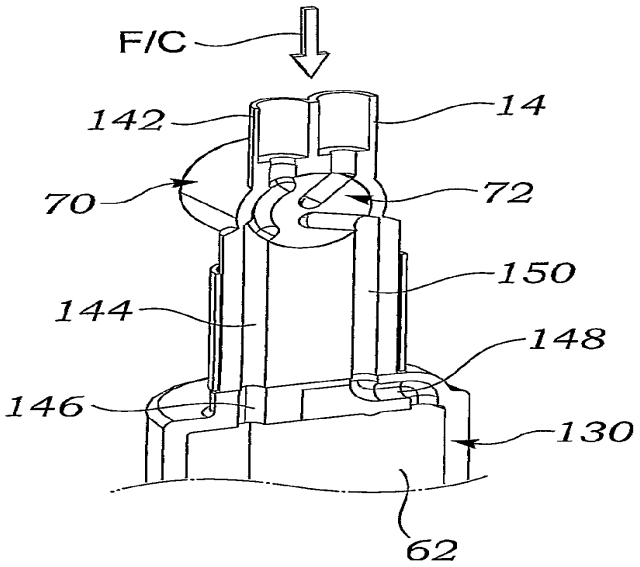


Fig. 18B

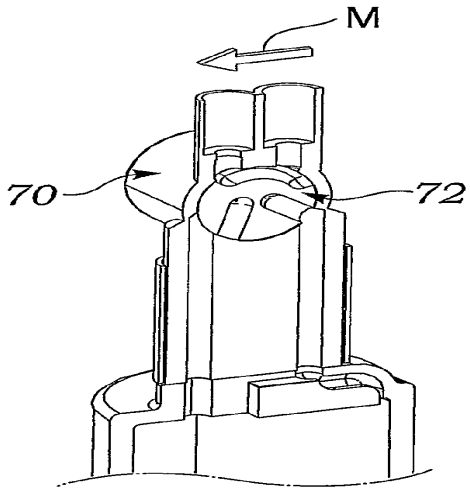


Fig. 18

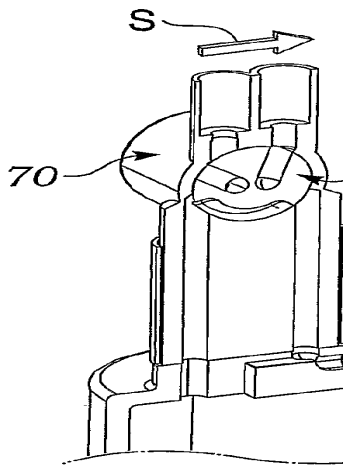


Fig. 19A

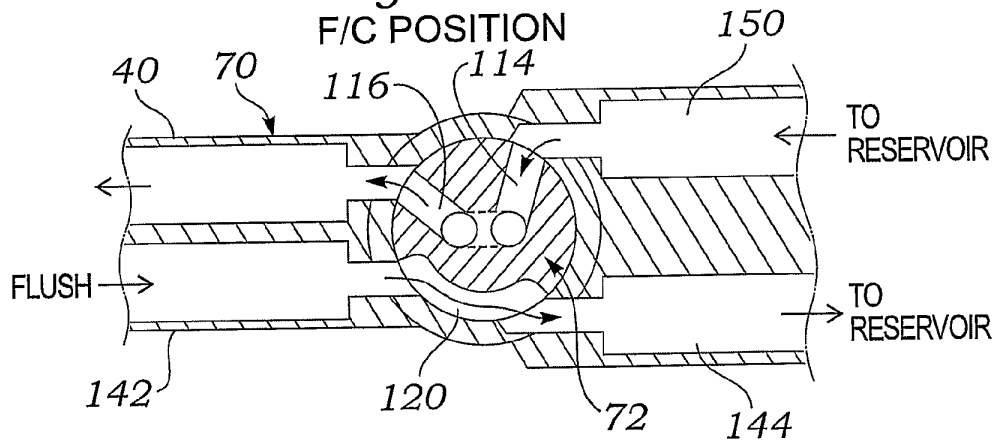


Fig. 19B

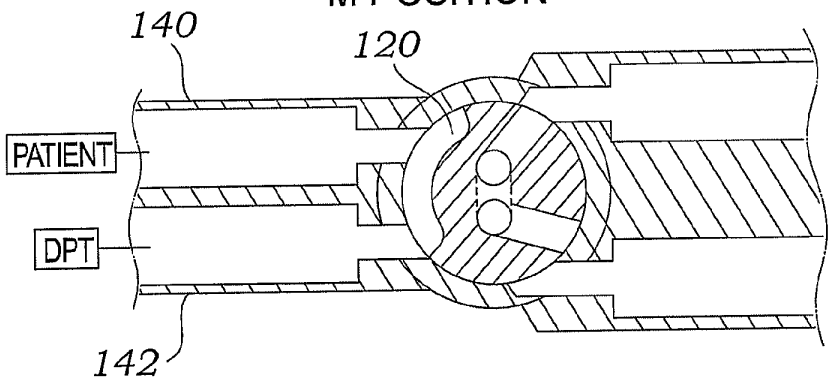


Fig. 19C

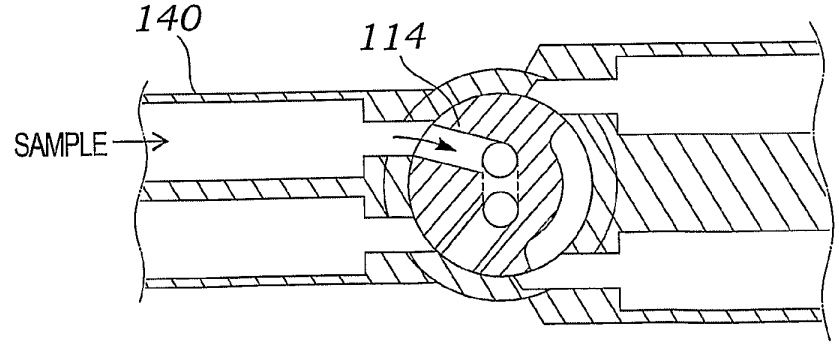


Fig.20A

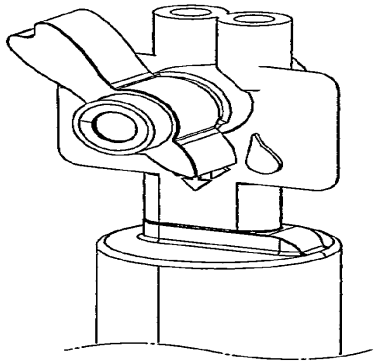


Fig.20D

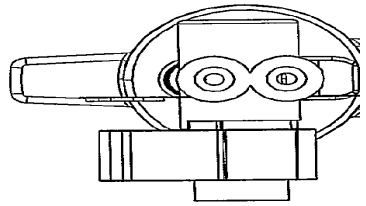


Fig.20C

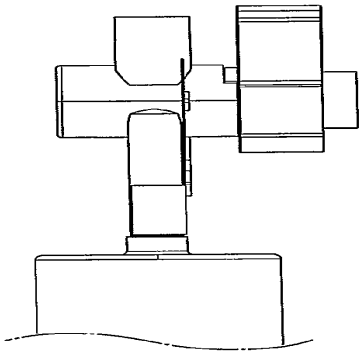


Fig.20B

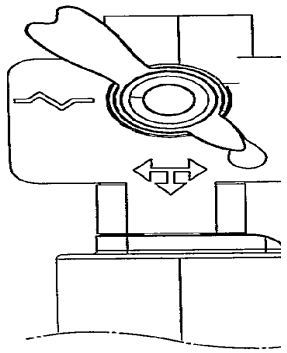


Fig.21A

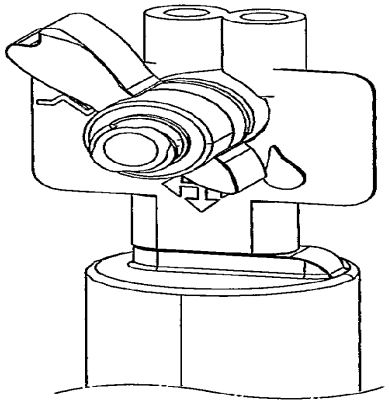


Fig.21L

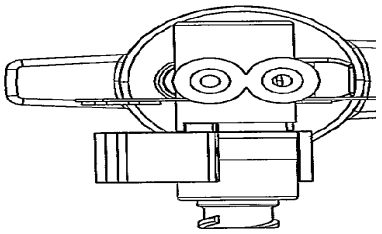


Fig.21C

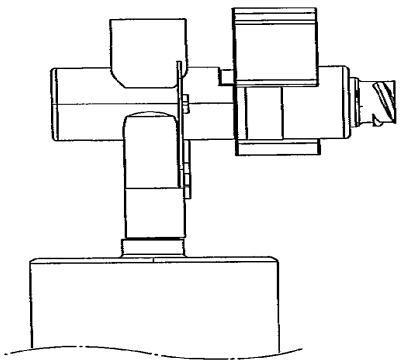


Fig.21B

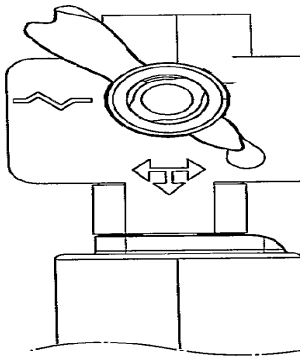


Fig.22A

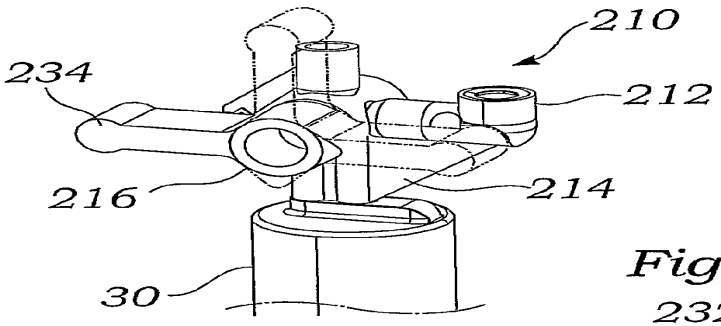


Fig.22

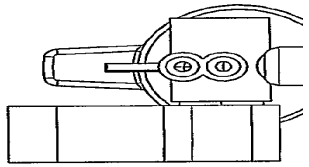


Fig.22E

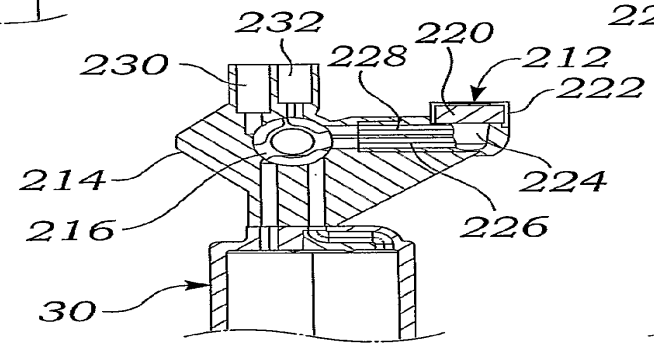


Fig.22C

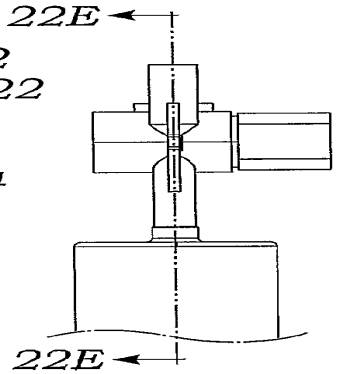


Fig.22

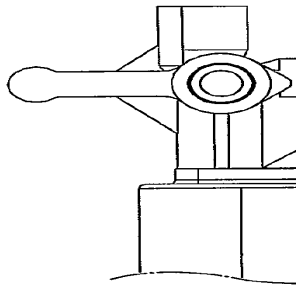


Fig.24D

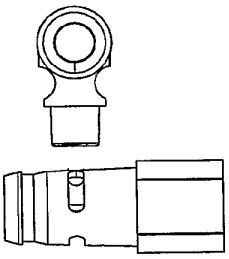


Fig.24B

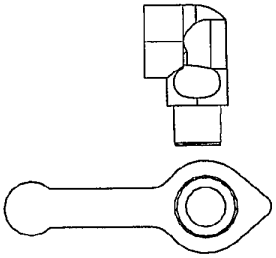


Fig.24A

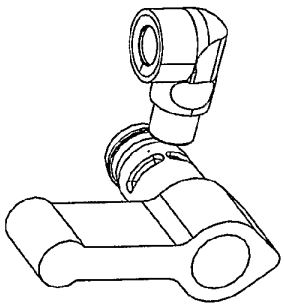


Fig.24C

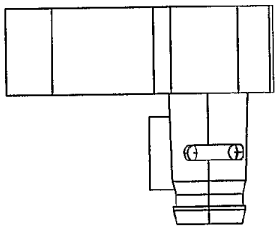


Fig.25D

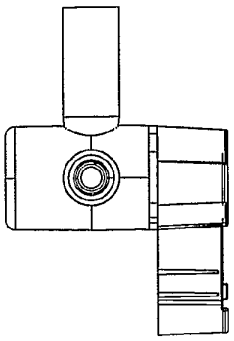


Fig.25B

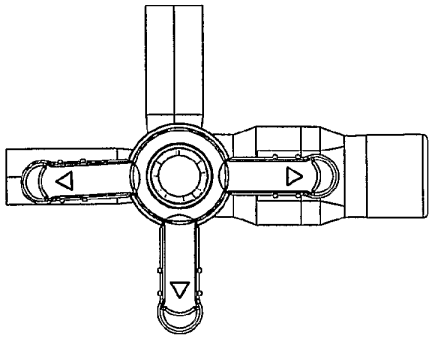


Fig.25C

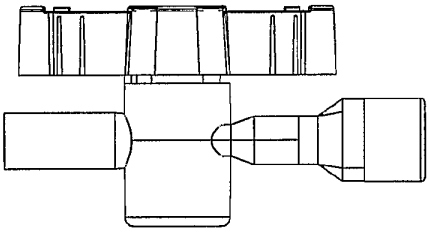
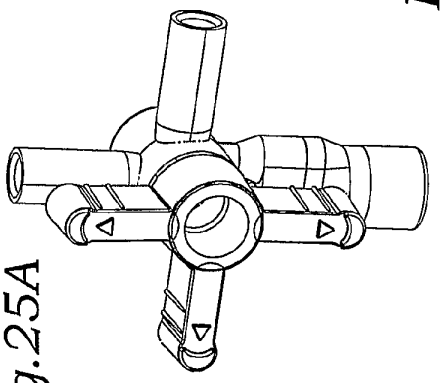


Fig.25A



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/035832

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 643 218 A (LYNN LAWRENCE A [US] ET AL) 1 July 1997 (1997-07-01) column 13, line 42 - column 14, line 57	1-24, 30-38
A	US 5 961 472 A (SWENDSON DAVID L [US] ET AL) 5 October 1999 (1999-10-05) cited in the application column 12, line 31 - column 14, line 64	1-24, 30-38
A	EP 0 376 603 A (MEDEX INC [US]) 4 July 1990 (1990-07-04) column 3, line 53 - column 4, line 58	1-24, 30-38

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

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 December 2006	27/12/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Manschot, Jan

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/035832

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 25-29
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

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

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2006/035832

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5643218 A	01-07-1997	US 5743886 A	28-04-1998
US 5961472 A	05-10-1999	AT 309743 T	15-12-2005
		AU 732501 B2	26-04-2001
		AU 9508798 A	23-04-1999
		BR 9812532 A	25-07-2000
		CA 2304146 A1	08-04-1999
		CN 1278710 A	03-01-2001
		DE 69832399 D1	22-12-2005
		DE 69832399 T2	14-06-2006
		EP 1017317 A1	12-07-2000
		ES 2256960 T3	16-07-2006
		JP 3421320 B2	30-06-2003
		JP 2001517522 T	09-10-2001
		WO 9916354 A1	08-04-1999
		US 6224561 B1	01-05-2001
EP 0376603 A	04-07-1990	CA 2005042 A1	22-06-1990
		DK 653189 A	23-06-1990
		US 5002066 A	26-03-1991

Notice of Reasons for Refusal

Application number: Japanese Patent Application No. 2019-534792
Date of Drafting: Reiwa 3(2021) June 8
Patent examiner: SETOI, Ayana 1569 2Q00
Representative/Applicant: MIYOSHI, Hidekazu (and 3 others)
Applied Provisions: Article 36

This application should be refused for the reason mentioned below. If the applicant has any opinion(s) against the reason, a written opinion should be submitted within 3 months from the date on which this notification was dispatched. Reason

1. (Clarity) This patent application does not fulfill the requirement of the provision of Patent Act Article 36(6)(ii) in terms of the item(s) listed below regarding the statement of the scope of claims.

Note

- Reason 1 (Clarity)

- Claim 1-20
It describes in Claim 1 as "the aforementioned wall." Claim 1 has the description an "outer wall" as a related description. In these descriptions, "the aforementioned wall" has pointed out the same composition as an "outer wall" -- or it is not clear whether different composition is pointed out. Since there is no description which specifies a "wall" before the description "the aforementioned wall" in the case of the latter, it is unknown which description the "above" has pointed out. The same point is pointed out also in invention concerning Claims 8 and 15. Therefore, The invention in the Claims 2-7 and 9-14 which cite either invention concerning Claims 1, 8 and 15, and the claim concerned, and 16-20 is not clear.

- Claims 4-5, 11-12, and 18-19
Although it describes in Claim 4 as "the aforementioned wall", since there is no description which specifies a "wall" in Claim 1 which Claim 4 cites, it is unknown which description the "above" has pointed out. The same point is pointed out also in invention concerning Claims 11 and 18. Therefore, The invention in the Claims 5, 12 and 19 which cite either invention concerning Claims 4, 11 and 18, and the claim concerned is not clear.

- Claim 8-14
It describes in Claim 8 as "the aforementioned blood extraction course." Claim 8 has the description a "blood collecting course" as a related description. In these descriptions, "the aforementioned blood extraction course" has pointed out the same composition as a "blood collecting course" -- or it is not clear whether different composition is pointed out. Since there is no description which specifies a "blood extraction course" before the description "the aforementioned blood extraction course" in the case of the latter, it is unknown which description the "above" has pointed out. Therefore, The invention in the Claims 9-14 which cite an invention according to claim 8 and the claim concerned is not clear.

Record of the result of prior art search

- Technical fields searched:

IPC
A61B 5/15-5/157

- Prior art documents: JP 2016 - 504075A
International Publication No. WO2014/058945

This record of the result of prior art search does not constitute the reasons for refusal.

<Suggestions in amending>
(1) When making amendment to the description or the scope of claims, the amended parts should be underlined so as to be clearly identified (please refer to Note 6 and 7 of Form 13, Regulations under the Patent Act).
(2)The amendment shall be made within the scope of the matters stated in the translation of the description or drawings (limited to descriptions in the drawings) of the international patent application at the international filing date, the translation of the scope of claims of the international patent application at the international filing date (in the case where a translation of the amended scope of claims under the provisions of Article 19 (1) of the Patent Cooperation Treaty is submitted, the relevant translation), or the drawing of the international patent application at the international filing date (except the descriptions in the drawings) (hereinafter referred to as a translation, etc.) (in the case of having amended the description, scope of claims or the drawings by submitting a mistranslation correction document, the translation, etc. or the amended description, amended claims or amended drawings). In addition, for the evidence of the legality of each amendment, allege the legality of each amendment in a written opinion with clear indication of the corresponding parts in the translation, etc. (in the case of amending the description or drawings by submitting a Correction of Mistranslation, the translation, etc., or the amended description, or the scope of claims, or the drawings).

(3) One should make sure not to perform any corrections that invoke a violation against Patent Act Article 17-2(4) when amending the scope of claims.

If you have any question or are willing to make an interview with the examiner to discuss issues on this notification of reasons for refusal, please contact us at:When sending of a draft amendment etc. is wished by E-mail etc., please inform me of that by telephone.

The first partial analysis diagnosis (medicine diagnosis) of an examination a current -- Toi ** (it is with * and there is Aya)
TEL.03-3581-1101 Extension 3291

A Director General(p.p.), a Director(p.p.), an examiner, an assistant examiner, OKUMA, Yasuo, SETOI, and 9710 1569

拒絶理由通知書

特許出願の番号	特願２０１９-５３４７９２
起案日	令和　３年　６月　８日
特許庁審査官	▲瀬▼戸井　綾菜　　１５６９　２Ｑ００
特許出願人代理人	三好　秀和（外　３名）　様
適用条文	第３６条

この出願は、次の理由によって拒絶をすべきものです。これについて意見がありましたら、この通知書の発送の日から３か月以内に意見書を提出してください。

理由

１．（明確性）この出願は、特許請求の範囲の記載が下記の点で、特許法第３６条第６項第２号に規定する要件を満たしていない。

記

●理由１（明確性）について

・請求項　１-２０
請求項１に「前記壁」と記載されている。また、関連する記載として、請求項１に「外壁」という記載がある。
これらの記載において、「前記壁」は「外壁」と同じ構成を指しているのか、もしくは、異なる構成を指しているかが明確でない。
また、後者の場合、「前記壁」という記載よりも前に「壁」を特定する記載がないため、「前記」がどの記載を指しているかが不明である。
請求項８、１５に係る発明においても、同様の点が指摘される。
よって、請求項１、８、１５に係る発明及び当該請求項のいずれかを引用する請求項２-７、９-１４、１６-２０に係る発明は明確でない。

・請求項　４-５、１１-１２、１８-１９
請求項４に「前記内壁」と記載されているが、請求項４が引用する請求項１には「内壁」を特定する記載がないため、「前記」がどの記載を指しているかが不明である。
請求項１１、１８に係る発明においても、同様の点が指摘される。

よって、請求項４、１１、１８に係る発明及び当該請求項のいずれかを引用する請求項５、１２、１９に係る発明は明確でない。

・請求項　８－１４
請求項８に「前記血液採取経路」と記載されている。また、関連する記載として、請求項８に「採血経路」という記載がある。
これらの記載において、「前記血液採取経路」は「採血経路」と同じ構成を指しているのか、もしくは、異なる構成を指しているかが明確でない。
また、後者の場合、「前記血液採取経路」という記載よりも前に「血液採取経路」を特定する記載がないため、「前記」がどの記載を指しているかが不明である。
よって、請求項８に係る発明及び当該請求項を引用する請求項９－１４に係る発明は明確でない。

＜先行技術文献調査結果の記録＞

・調査した分野　　ＩＰＣ　　Ａ６１Ｂ　５／１５－５／１５７

・先行技術文献　　特表２０１６－５０４０７５号公報
国際公開第２０１４／０５８９４５号

この先行技術文献調査結果の記録は、拒絶理由を構成するものではありません。

＜補正をする際の注意＞
（１）明細書、特許請求の範囲について補正をする場合は、補正により記載を変更した個所に下線を引いてください（特許法施行規則様式第１３備考６、７）。
（２）補正は、この出願の国際出願日における国際特許出願の明細書若しくは図面（図面の中の説明に限る。）の翻訳文、国際出願日における国際特許出願の請求の範囲の翻訳文（特許協力条約第１９条（１）の規定に基づく補正後の請求の範囲の翻訳文が提出された場合にあっては、当該翻訳文）又は国際出願日における国際特許出願の図面（図面の中の説明を除く。）（以下、翻訳文等という。）（誤訳訂正書を提出して明細書、特許請求の範囲又は図面について補正をした場合にあっては、翻訳文等又は当該補正後の明細書、特許請求の範囲若しくは図面）に記載した事項の範囲内で行わなければなりません。また、意見書で、各補正事項について補正が適法なものである理由を、根拠となる翻訳文等（誤訳訂正書を提出して明細書、特許請求の範囲又は図面について補正をした場合にあっては、翻訳文等又は当該補正後の明細書、特許請求の範囲若しくは図面）の記載箇所

を明確に示したうえで主張してください。
（３）特許請求の範囲について補正をする際には、特許法第１７条の２第４項に違反する補正とならないよう、注意してください。

この拒絶理由通知の内容に関するお問合せ又は面接のご希望がありましたら次の連絡先までご連絡ください。電子メール等で補正案等の送付を希望される場合は、その旨を電話でお知らせください。

審査第一部　分析診断（医学診断）　瀬戸井綾菜（せといあやな）
ＴＥＬ．０３-３５８１-１１０１　内線３２９１

部長／代理	審査長／代理	審査官	審査官補
	大熊　靖夫	▲瀬▼戸井	
	９７１０	１５６９	

EXHIBIT H

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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

Secrecy Order 37 CFR 5.2:

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

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Gregory	J.	Bullington	

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

City	State/Province	Country of Residence
Bellevue	WA	US

Mailing Address of Inventor:

Address 1	5825 134th Place SE
Address 2	
City	Bellevue
State/Province	WA
Postal Code	98006
Country i	US

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Richard	G.	Patton	

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

City	State/Province	Country of Residence
Seattle	WA	US

Mailing Address of Inventor:

Address 1	2561 Magnolia Blvd. W
Address 2	
City	Seattle
State/Province	WA
Postal Code	98199
Country i	US

Inventor 3 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Shan	E.	Gaw	

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

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

City	Seattle	State/Province	WA	Country of Residence	US

Mailing Address of Inventor:

Address 1	4027 Sunnyside Ave. N		
Address 2			
City	Seattle	State/Province	WA
Postal Code	98103	Country	US

Inventor 4 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Jay	M.	Miazga	

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

City	Seattle	State/Province	WA	Country of Residence	US

Mailing Address of Inventor:

Address 1	4025 McKinley Pl. N		
Address 2			
City	Seattle	State/Province	WA
Postal Code	98103	Country	US

Inventor 5 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Jed		McCann	

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

City	Seattle	State/Province	WA	Country of Residence	US

Mailing Address of Inventor:

Address 1	7321 22nd Ave. NW		
Address 2			
City	Seattle	State/Province	WA
Postal Code	98117	Country	US

Inventor 6 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Paul		Goldenbaum	

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

City	San Antonio	State/Province	TX	Country of Residence	US

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

Mailing Address of Inventor:

Address 1	4218 Black Rock		
Address 2			
City	San Antonio	**State/Province**	TX
Postal Code	78253	**Country**	US

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

Correspondence Information:

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

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

Customer Number	58249		
Email Address	zpatdcdocketing@cooley.com	Add Email	Remove Email

Application Information:

Title of the Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS		
Attorney Docket Number	MGMD-012/01US 316052-MGMD	**Small Entity Status Claimed**	☒
Application Type	Provisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	36	**Suggested Figure for Publication (if any)**	

Filing By Reference:

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

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

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

Publication Information:

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

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

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

Representative Information:

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

Please Select One:	● Customer Number	US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	68249		

Domestic Benefit/National Stage Information:

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

Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button. Add

Foreign Priority Information:

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

Remove

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

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

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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

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

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

Authorization or Opt-Out of Authorization to Permit Access:

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

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

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

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

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

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

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

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

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

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

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

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

Applicant Information:

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

Applicant 1 — Remove

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

Clear

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

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

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Magnolia Medical Technologies, Inc.		
Mailing Address Information For Applicant:			
Address 1	2001 Sixth Avenue		
Address 2	Suite 1630		
City	Seattle	**State/Province**	WA
Country	US	Postal Code	98121
Phone Number		Fax Number	
Email Address			

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

Assignee Information including Non-Applicant Assignee Information:

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

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

Assignee 1

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

Remove

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

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1			
Address 2			
City		**State/Province**	
Country i		Postal Code	
Phone Number		Fax Number	
Email Address			

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

Signature:

Remove

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

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

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

Signature	/Michael D. Wintemitz/			Date (YYYY-MM-DD)	2016-11-18
First Name	Michael	Last Name	Wintemitz	Registration Number	73102

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

PTO/AIA/14 (11-15)
Approved for use through 04/30/2017. 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 contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	MGMD-012/01US 316052-MGMD
	Application Number	
Title of Invention	SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS	

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

Privacy Act Statement

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

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

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

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

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

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

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

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

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

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

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

SYSTEMS AND METHODS FOR SAMPLE COLLECTION WITH REDUCED HEMOLYSIS

Background

[1001] Embodiments described herein relate generally to the parenteral procurement of bodily-fluid samples, and more particularly to systems and methods for parenterally procuring bodily-fluid samples, such as blood, with reduced hemolysis.

[1002] Health care practitioners routinely draw bodily-fluids from a patient for various testing and/or donation purposes. In some instances, the process of obtaining the bodily-fluids, and in particular, blood, can result in a degradation and/or breakdown of portions and/or constituents contained in the bodily-fluid. Specifically, hemolysis of red blood cells (i.e., a rupturing of the red blood cells and the release of cytoplasm) during blood draw is a known problem in the field of phlebotomy and/or medical testing. Hemolysis of blood is the most common pre-analytical source of error in clinical testing, accounting for nearly 60% of all rejected samples (Bonini P, Plebani M, Ceriotti F, Rubboli F (2002). Errors in laboratory medicine. *Clinical Chemistry*, 48, 691-698; and Plebani M, Carraro P (1997). Mistakes in a stat laboratory: types and frequency. *Clinical Chemistry*, 43, 1348-1351). Moreover, hemolyzed sample rates from hospital emergency rooms can be as high as 30% (Grant M (2003). The effect of blood drawing techniques and equipment on the hemolysis of ED laboratory blood samples. *Journal of Emergency Nursing*, 29 (2), 116-121, and Soderberg J, Jonsson PA, Wallin O, Grankvist K, Hultdin J (2009). Hemolysis index—an estimate of pre-analytical quality in primary health care. *Clinical Chemistry and Laboratory Medicine*, 47, 940-944). In some know blood draw systems, the arrangement and/or coupling of multiple devices to form a fluid flow path from a patient to, for example, a sample reservoir or container, shear stress exerted on or within the red blood cells, exposure time, and/or the like can lead to an increased likelihood of hemolysis within a sample volume.

[1003] Thus, a need exists for systems and methods for sample collection with reduced hemolysis.

Summary

[1004] Systems and methods for parenterally procuring bodily-fluid samples, such as blood, with reduced hemolysis are described herein. In some embodiments, a collection system has a proximal end portion, a distal end portion, and an inner surface defining a fluid flow path therethrough. The distal end portion is configured to be placed in fluid communication with a patient. The proximal end portion is configured to be placed in fluid communication with a fluid reservoir. The fluid flow path defined by the inner surface is associated with at least one flow characteristic configured to limit a stress within the flow of the bodily-fluid between the distal end portion and the proximal end portion.

Brief Description of the Drawings

[1005] FIG. 1 is a schematic illustration of a bodily-fluid collection device according to an embodiment.

[1006] FIG. 2 is a perspective view of a needle included in a bodily-fluid collection device according to an embodiment.

[1007] FIG. 3 is an enlarged view of a portion of the needle of FIG. 2, identified by the region A_1.

[1008] FIGS. 4-6 are illustrations of a needle used to deliver a cannula to a portion of the body according to an embodiment.

[1009] FIG. 7 is a perspective view of a portion of a needle included in a bodily-fluid collection device according to another embodiment.

[1010] FIG. 8 is a perspective view of a portion of a bodily-fluid collection device according to an embodiment.

[1011] FIG. 9 is a cross-sectional view of the bodily-fluid collection device of FIG. 8, taken along the line 9-9.

[1012] FIG. 10 is an enlarged view of a portion of the bodily-fluid collection device of FIG. 9, identified by the region A_2.

[1013] FIG. 11 is a front view of a portion of a bodily-fluid collection device according to an embodiment.

[1014] FIG. 12 is a cross-sectional view of the portion of the bodily-fluid collection device of FIG. 11, taken along the line 12-12.

[1015] FIG. 13 is an enlarged view of a portion of the bodily-fluid collection device of FIG. 12, identified by the region A_3.

[1016] FIG. 14 is a cross-sectional view of a portion of a bodily-fluid collection device according to another embodiment.

[1017] FIG. 15 is an enlarged view of a portion of the bodily-fluid collection device of FIG. 14, identified by the region A_4.

[1018] FIG. 16 is a cross-sectional view of a portion of a bodily-fluid collection device according to another embodiment.

[1019] FIG. 17 is a cross-sectional view of a portion of a bodily-fluid collection device according to another embodiment.

[1020] FIG. 18 is a perspective view of a portion of a bodily-fluid collection device according to an embodiment.

[1021] FIG. 19 is an exploded view of the portion of the bodily-fluid collection device of FIG. 18.

[1022] FIG. 20 is a cross-sectional view of the portion of the bodily-fluid collection device of FIG. 18, taken along the line 20-20.

[1023] FIG. 21 is a perspective view of a restrictor included in a bodily-fluid collection device according to an embodiment.

[1024] FIG. 22 is a cross-sectional view of the restrictor of FIG. 21, taken along the line 22-22.

[1025] FIG. 23 is a top view of a baffle included in the restrictor of FIG. 21.

[1026] FIG. 24 is a cross-sectional view of the baffle of FIG. 23, taken along the line 24-24.

[1027] FIG. 25 is a perspective view of a restrictor included in a bodily-fluid collection device according to an embodiment.

[1028] FIG. 26 is a cross-sectional view of the restrictor of FIG. 25, taken along the line 26-26.

[1029] FIG. 27 is a perspective view of an adapter included in a bodily-fluid collection device according to an embodiment.

[1030] FIG. 28 is a cross-sectional view of the adapter of FIG. 27, taken along the line 28-28.

[1031] FIG. 29 is a front view of a portion of the adapter of FIG. 27.

[1032] FIG. 30 is a cross-sectional view of the portion of the adapter illustrated in FIG. 29, taken along the line 30-30.

[1033] FIG. 31 is a perspective view of the portion of the adapter illustrated in FIG. 29 coupled to a fluid reservoir according to an embodiment.

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

[1035] FIG. 33 is a cross-sectional view of the portion of the adapter and the fluid reservoir illustrated in FIG. 31, taken along the line 33-33.

[1036] FIG. 34 is a cross-sectional view of an adapter coupled to a fluid reservoir according to another embodiment.

[1037] FIG. 35 is a cross-sectional view of an adapter coupled to a fluid reservoir according to another embodiment.

[1038] FIG. 36 is a cross-sectional view of an adapter coupled to a fluid reservoir according to another embodiment.

[1039] FIG. 37 is a perspective view of an adapter coupled to a fluid reservoir according to another embodiment.

[1040] FIG. 38 is a cross-sectional view of the adapter and the fluid reservoir of FIG. 37, taken along the line 38-38.

[1041] FIG. 39 is a perspective view of an adapter coupled to a fluid reservoir according to another embodiment.

[1042] FIG. 40 is a perspective view of an adapter coupled to a fluid reservoir according to another embodiment.

[1043] FIGS. 41 and 42 are cross-sectional views of the adapter and the fluid reservoir of FIG. 40, taken along the line 41-41, in a first configuration and a second configuration, respectively.

[1044] FIG. 43 is a perspective view of an adapter and a fluid reservoir according to another embodiment.

[1045] FIG. 44 is a cross-sectional view of the adapter and the fluid reservoir of FIG. 43, taken along the line 44-44.

[1046] FIGS. 45-47 are cross-sectional views of an adapter and a fluid reservoir each according to a different embodiment.

[1047] FIG. 48 is a perspective of an adapter included in a bodily-fluid collection device according to another embodiment.

[1048] FIG. 49 is a cross-sectional view of the adapter of FIG. 48, taken along the line 49-49.

[1049] FIG. 50 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to an embodiment.

[1050] FIG. 51 is a cross-sectional view of the adapter illustrated in FIG. 49 coupled to the fluid reservoir illustrated in FIG. 50, taken along the line 51-51 in FIG. 50.

[1051] FIG. 52 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1052] FIG. 53 is a cross-sectional view of the fluid reservoir of FIG. 52, taken along the line 53-53.

[1053] FIG. 54 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1054] FIG. 55 is an exploded view of a plunger included in the fluid reservoir of FIG. 54.

[1055] FIG. 56 is a cross-sectional view of the fluid reservoir of FIG. 54, taken along the line 56-56.

[1056] FIG. 57 is a perspective view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1057] FIG. 58 is a cross-sectional view of the fluid reservoir of FIG. 57, taken along the line 58-58.

[1058] FIG. 59 is a front view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1059] FIG. 60 is a cross-sectional view of a fluid reservoir included in a bodily-fluid collection device according to another embodiment.

[1060] FIG. 61 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1061] FIG. 62 is an exploded view of the adapter of FIG. 61.

[1062] FIG. 63 is a cross-sectional view of the adapter of FIG. 61, taken along the line 63-63.

[1063] FIG. 64 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1064] FIG. 65 is an exploded view of the adapter of FIG. 64.

[1065] FIG. 66 is a cross-sectional view of the adapter of FIG. 65, taken along the line 66-66.

[1066] FIG. 67 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1067] FIG. 68 is a cross-sectional view of the adapter of FIG. 67, taken along the line 68-68.

[1068] FIG. 69 is a perspective view of an adapter included in a bodily-fluid collection device according to another embodiment.

[1069] FIG. 70 is an exploded view of the adapter of FIG. 69.

[1070] FIG. 71 is a cross-sectional view of the adapter of FIG. 69, taken along the line 71-71.

Detailed Description

[1071] Systems and methods for parenterally procuring bodily-fluid samples, such as blood, with reduced hemolysis are described herein. In some embodiments, a collection system has a proximal end portion, a distal end portion, and an inner surface defining a fluid flow path therethrough. The distal end portion is configured to be placed in fluid communication with a patient. The proximal end portion is configured to be placed in fluid communication with a fluid reservoir. The fluid flow path defined by the inner surface is associated with at least one flow characteristic configured to limit a stress within the flow of the bodily-fluid between the distal end portion and the proximal end portion.

[1072] As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, the term "a member" is intended to mean a single member or a combination of members, "a material" is intended to mean one or more materials, or a combination thereof.

[1073] As used herein, "bodily-fluid" can include any fluid obtained from a body of a patient, including, but not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, and the like, or any combination thereof. Moreover, while the embodiments and/or devices herein are specifically described as reducing, limiting, inhibiting, and/or substantially preventing hemolysis of blood withdrawn therethrough, any of the embodiments and/or devices can be used for controlling a flow of any suitable bodily-fluid (e.g., such as those listed above) when withdrawn from the body of a patient through that device.

[1074] As used herein, the term "set" can refer to multiple features or a singular feature with multiple parts. For example, when referring to set of walls, the set of walls can be considered as one wall with distinct portions, or the set of walls can be considered as multiple walls. Similarly stated, a monolithically constructed item can include a set of walls. Such a set of walls can include, for example, multiple portions that are discontinuous from each other. A set of walls can also be fabricated from multiple items that are produced separately and are later joined together (e.g., via a weld, an adhesive, or any suitable method).

[1075] As used herein, the terms "proximal" and "distal" refer to the direction closer to and away from, respectively, a user who would place the device into contact with a patient. Thus, for example, the end of a device first touching the body of the patient would be the distal end, while the opposite end of the device (e.g., the end of the device being manipulated by the user) would be the proximal end of the device.

[1076] As used herein, the terms "about," "approximately," and "substantially" when used in connection with a numerical value is intended to convey that the value so defined is nominally the value stated. Said another way, the terms about, approximately, and substantially when used in connection with a numerical value generally include the value stated plus or minus a given tolerance. For example, in some instances, a suitable tolerance can be plus or minus 10% of the value stated; thus, about 0.5 would include 0.45 and 0.55, about 10 would include 9 to 11, about 1000 would include 900 to 1100. In other instances, a suitable tolerance can be plus or minus an acceptable percentage of the last significant figure in the value stated. For example, a suitable tolerance can be plus or minus 10% of the last significant figure; thus, about 10.1 would include 10.09 and 10.11, approximately 25 would include 24.5 and 25.5. Such variance can result from manufacturing tolerances or other practical considerations (such as, for example, tolerances associated with a measuring instrument, acceptable human error, or the like).

[1077] As used herein, the term "laminar" refers to an organized and/or orderly fluid flow in parallel layers without lateral mixing, crosscurrents, eddy currents, and/or the like. More generally, the term "laminar" is intended to convey a flow of fluid that is smooth and/or free of turbulence. Moreover, the term "substantially" when used in connection with "laminar" is intended to convey that a fluid flow so defined is nominally a laminar fluid flow. As one example, a portion of a fluid transfer device defining a lumen that is described as facilitating and/or otherwise causing a "substantially laminar" fluid flow therethrough is intended to

convey that, although laminar fluid flow is desirable, some non-laminar flow can occur. Such variances (e.g., turbulence or the like) can result from manufacturing tolerances, or other practical considerations. Thus, a fluid having a "substantially laminar" flow includes such non-laminar flow characteristics within an industry-accepted tolerance. For example, while it may be desirable that a bodily-fluid transfer device transfer a laminar flow of blood therethrough a "substantially laminar flow" of blood can be 99% laminar, 95% laminar, 90% laminar, or any other acceptable tolerance thereof.

[1078] The embodiments described herein can be formed or constructed of one or more biocompatible materials. Examples of suitable biocompatible materials include metals, glasses, ceramics, or polymers. Examples of suitable metals include pharmaceutical grade stainless steel, gold, titanium, nickel, iron, platinum, tin, chromium, copper, and/or alloys thereof. A polymer material may be biodegradable or non-biodegradable. Examples of suitable biodegradable polymers include polylactides, polyglycolides, polylactide-co-glycolides (PLGA), polyanhydrides, polyorthoesters, polyetheresters, polycaprolactones, polyesteramides, poly(butyric acid), poly(valeric acid), polyurethanes, and/or blends and copolymers thereof. Examples of non-biodegradable polymers include nylons, polyesters, polycarbonates, polyacrylates, polymers of ethylene-vinyl acetates and other acyl substituted cellulose acetates, non-degradable polyurethanes, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonate polyolefins, polyethylene oxide, and/or blends and copolymers thereof.

[1079] In some current phlebotomy procedures, blood is drawn from a patient using multiple components that are physically and fluidically coupled to define a fluid flow path between the patient and a collection device and/or fluid reservoir used to capture the bodily-fluid sample. In some such systems, however, the physical and/or fluidic interfaces formed between the components can result in turbulent regions and/or eddy currents within the flow of the blood, which in turn, can result in a stress within the flow that is sufficient to sheer, rupture, and/or otherwise damage the red blood cells. In addition, the process of drawing blood from a patient often involves exposing the blood to a negative pressure differential produced, for example, by placing an evacuated container (e.g., a Vacutainer ™) in fluid communication with a portion of the body. In some instances, the pressure differential can increase an internal stress within a flow of blood to an extent that results in hemolysis of the red blood cells. In other instances, the pressure differential can be attributed to the physical

exertion associated with a clinician actuating, for example, a syringe with a force sufficient to rupture the red blood cells during the collection process. A number of factors (for example, small veins, dehydration, veins with scar tissue, presence of sclerosis, and/or the like) can make vascular access a challenge. In such cases, excess negative pressure exerted during the collection process can result in hemolysis.

[1080] While such a negative pressure differential often facilitates withdraw of the blood, it also can produce a relatively high shear stresses within the red blood cells and/or a relatively high flow velocity of the blood through a flow path defined between the patient and the fluid reservoir (e.g., evacuated container). As a result, the red blood cells contained within the flow of blood can be damaged as the cells pass through the physical and/or fluidic interfaces formed between different components of a transfer device. In some instances, the relatively high velocity of the blood flow as the blood enters the containers can result in the blood impacting an inner surface of the container with a force sufficient to damage the red blood cells and/or other components of the blood. In addition, exposure time of a needle and/or catheter within the vein can result in hemolysis of the red blood cells.

[1081] Thus, to mitigate the risk of hemolysis of a sample volume of blood, various portions of a fluid flow path between the patient and the sample reservoir can be optimized. Such optimization can be done holistically (i.e., a system wide optimization) or done piecemeal (i.e., optimization of at least one potential source of hemolysis). By way of example, in some instances, any of the embodiments described herein, can be used independently to mitigate the risk of hemolysis at a specific point along a fluid flow path between a patient and a sample reservoir. That is to say, the embodiments described herein can be characterized by the potential source of hemolysis that the embodiments, so characterized, mitigate. For example, the embodiments described herein generally address six potential categories, portions, and/or sources of hemolysis along a fluid flow path between a patient and a fluid reservoir. Namely, the embodiments described herein can be used to mitigate the risk of hemolysis otherwise associated with (1) blood flow from, for example, a vein into a puncture member, needle, cannula, and/or the like, (2) blood flow through changing geometries and/or physical and fluidic interfaces; (3) blood flow rates and/or velocity within the fluid flow path; (4) blood flow from an adapter, puncture member, needle, cannula, and/or the like into a fluid reservoir; (5) blood flow exposure to a negative

pressure differential within a fluid reservoir, and (6) blood flow through a multi-lumen adapter and/or the like.

[1082] FIG. 1 is a schematic illustration of a portion of a bodily-fluid collection device 100, according to an embodiment. Generally, the bodily-fluid collection device 100 (also referred to herein as "fluid collection device," "collection device," or "device") can be used to percutaneously withdraw bodily-fluid from a patient. In some instances, the device 100 can be used to withdraw a volume of blood from a patient that is to be used as a biological sample for testing and/or assays associated with medical diagnosis and/or treatment. In other instances, the device 100 can be used to withdraw a volume of blood for collection purposes such as, for example, blood donation or the like. More particularly, the device 100 is configured to limit, inhibit, and/or substantially prevent hemolysis of at least a portion of the blood drawn therethrough, as described in further detail herein.

[1083] The device 100 has a proximal end portion 101 and a distal end portion 102 and defines a lumen 104 therethrough. More specifically, the device 100 includes an inner surface 103 that defines the lumen 104. The device 100 can be any suitable device or group of devices (e.g., a system including multiple devices). In some embodiments, for example, the device 100 can be a needle, a cannula, a trocar, a catheter, and/or the like. In such embodiments, the distal end portion 102 of the device 100 can include a sharpened, angled, or beveled edge configured to puncture the cutaneous layer of the body to place the lumen 104 in fluid communication with, for example, a vascular structure and/or the like. The proximal end portion 101 of the device 100 can be physically and/or fluidically coupled to any other suitable device such as, for example, a collection reservoir (not shown in FIG. 1). As such, the lumen 104 defined by the device 100 defines fluid pathway through which blood can flow from the patient to an intermediary collection device and/or directly to the collection reservoir.

[1084] As described above, in some embodiments, the device 100 is configured to reduce, limit, inhibit, and/or substantially prevent hemolysis of blood withdrawn from the body and through the device. For example, in embodiments in which the device 100 is a needle, cannula, catheter, and/or the like, the distal end portion 102 of the device 100 can include rounded edges and/or a substantially smooth contour. As such, the constituents of the blood (e.g., the red blood cells or "erythrocytes") can flow relatively smoothly into the lumen

104 (e.g., in response to a negative pressure differential produced, for example, by a syringe and/or an evacuated container coupled thereto) substantially without being damaged.

[1085] Moreover, in some embodiments, the shape, size, and/or contour of the inner surface 103 can selectively control the flow of blood through the device 100. By way of example, in some embodiments, the inner surface 103 can form a substantially smooth contour, which can facilitate a laminar flow of the blood therethrough. In addition, the inner surface 103 can have a contour that can selectively control an amount of negative pressure within a region of the lumen 104. For example, in some embodiments, the inner surface 103 can have a diameter that is varied along the length of the device 100. That is to say, a first portion of the inner surface 103 can have a diameter that is different from a diameter of a second portion of the inner surface 103 and thus, can reduce, constrict, limit, and/or otherwise control a flow of blood therethrough. In some such embodiments, the first portion of the inner surface 103 can be disposed between the second portion of the inner surface 103 and a third portion of the inner surface 103 having a diameter greater than or equal to the diameter of the second portion of the inner surface 103. In such embodiments, a region of the lumen 104 having a relatively larger diameter can be associated with a larger pressure than a region of the lumen 104 having a relatively smaller diameter, while conversely, a velocity associated with the region of the lumen 104 having the relatively larger diameter is less than a velocity associated with the region of the lumen having the relatively smaller diameter based on the simplified Bernoulli's Equation mathematically represented by equation 1 below:

$$P_1 + {}^1/_2\,\rho V_1^2 = P_2 + {}^1/_2\,\rho V_2^2 \qquad \text{Equation 1}$$

wherein P is pressure within the lumen, ρ is density of the fluid, and V is velocity of the fluid.

[1086] While described above as being a needle, catheter, cannula, trocar, and/or the like, in other embodiments, the device 100 can be any suitable component included in a fluid transfer system. For example, the device 100 can be an adapter, a locking mechanism, a cannula, a coupling mechanism, a port, an inlet, and outlet, and/or the like. By way of example, in some embodiments, the device 100 can be an adapter configured to be physically and fluidically coupled to at least one other device such as, for example, a needle. Thus, the adapter (i.e., the device 100) can have an inner surface with a contour that can control a flow of bodily-fluid therethrough. Moreover, an interface between the device 100 and the needle

(and/or any other suitable device) can be arranged to reduce turbulence of a flow of bodily-fluid therebetween, as described in further detail herein.

[1087] In some embodiments, the device 100 can be coupled to a fluid reservoir or container (e.g., at the proximal end portion 101). As such, the contour of the inner surface 103 of the device 100 can control a flow of bodily-fluid therethrough (as described above), while the orientation of the device 100 relative to the fluid reservoir or container can control and/or direct the flow of bodily-fluid through the proximal end portion 101 toward an inner surface of the fluid reservoir to, for example, reduce a force associated with a portion of the flow of bodily-fluid impacting the inner surface. In some embodiments, the device 100 can be an insert or the like at least partially disposed within the fluid reservoir or container.

[1088] Although not shown in FIG. 1, in some embodiments, the device 100 can be used with (e.g., physically and fluidically coupled to) a device or mechanism configured to modulate a negative pressure within a fluid reservoir or container. For example, in some embodiments, the device 100 can be coupled to a syringe or the like configured to transition between a first configuration and a second configuration to produce a negative pressure within an inner volume. As such, a rate at which the syringe can be transitioned from the first configuration (e.g., associated with a plunger in a distal position) to the second configuration (e.g., associated with the plunger in a proximal position) can be constrained (e.g., limited, inhibited, slowed, governed, controlled, etc.), thereby reducing a negative pressure exerted through the lumen 104 of the device, as described in further detail herein.

[1089] While the device 100 is described above as including a surface, mechanism, portion, etc. configured to reduce hemolysis of a volume of blood in a mechanical manner (e.g., reducing pressure and/or turbulence within a flow path via a contour, restrictor, or the like; reducing forces associated with a portion of the volume of blood impacting a surface of a fluid reservoir via a coupling mechanism, interface, etc.; reducing damage to constituents in the volume of blood by limiting or eliminating sharp edges, corners, etc.; and/or the like), in other embodiments, the device can be configured to chemically modify one or more characteristics associated with the volume of blood. For example, in some embodiments, the inner surface 103 of the device 100 can be coated with a chemical configured to limit lysis of erythrocytes (red blood cells) by strengthening or weakening a cell wall of the erythrocytes. More specifically, in some embodiments, the device 100 can be configured to introduce a chemical into a flow of blood that can, for example, increase a rigidity of the cell wall of

erythrocytes (e.g., decrease flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes (e.g., hemolysis of the blood) as the blood flows through the device 100. In other embodiments, the device 100 can be configured to introduce a chemical into a flow of blood that can, for example, decrease a rigidity of the cell wall of erythrocytes (e.g., increase flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes as the blood flows through the device 100.

[1090] While described above as coating the inner surface 103 with the chemical configured to modify a characteristic of the cell wall of the erythrocytes, in other embodiments, the device 100 can include any suitable device, mechanism, and/or method for introducing such a chemical to the volume of blood flowing therethrough. For example, the device 100 can include a chamber containing such a chemical, a baffle impregnated with such a chemical, a dispensing or dispersing device (e.g., sprayer or the like) configured to dispense a volume of such a chemical, impregnation of the chemical directly into the material used to produce the device 100 and/or any other suitable means for introducing such a chemical.

[1091] FIGS. 2-7 illustrate embodiments configured to mitigate the risk of hemolysis as a volume of blood flows from the patient (e.g., a vein of a patient) and into a lumen-defining device such as a needle or the like. Specifically, FIGS. 2 and 3 illustrate a puncture member 210 coupled to an adapter 220 according to an embodiment. The puncture member 210 has a proximal end portion 211 and a distal end portion 212 and defines a lumen 213 therebetween. The proximal end portion 211 of the puncture member 210 is physically and fluidically coupled to a distal end portion 222 of the adapter 220, as described above with reference to FIG. 1. More specifically, the proximal end portion 211 of the puncture member 210 is coupled to the adapter 220 such that an interface therebetween forms a substantially smooth and/or continuous surface. Said another way, the interface between the puncture member 210 and the adapter 220 can be such that a transition between the lumen 213 of the puncture member 210 and a lumen (not shown in FIGS. 2-6) defined by the adapter is substantially smooth and/or continuous (i.e., does not introduce a discontinuity such as a change in alignment and/or diameter), as described in further detail herein.

[1092] The distal end portion 212 of the puncture member 210 is configured to be inserted through the cutaneous layer of the patient to transfer fluid to and/or from the patient. For example, the distal end portion 212 can be inserted into a vein of a patient and the adapter 220 can be coupled to a fluid reservoir and/or intermediary collection device configured to

receive a volume of blood from the patient via the lumen 213. More specifically, as shown in FIGS. 2 and 3, the distal end portion 212 of the puncture member 210 is sharpened, angled, and/or beveled, which facilitates the insertion of the puncture member 210 into the body. The lumen 213 of the puncture member 210 extends through the distal end portion 212, thereby defining an opening 214 that places the lumen 213 in fluid communication with, for example, a vascular structure (e.g., a vein) within which the distal end portion 212 is disposed. Furthermore, as shown in FIG. 3, a distal edge 215 of the puncture member 210 defining the opening 214 is substantially rounded, smoothed, contoured, blunted, and/or the like. In other words, the distal edge 215 defining the opening 214 forms a substantially round corner. Thus, blood drawn through the opening 214 and into the lumen 213 can flow past the distal edge 214 with reduced damage to, for example, the constituents of the blood (e.g., the erythrocytes) that would otherwise result from contact with a sharper, more abrupt, substantially orthogonal, and/or otherwise non-rounded distal edge 215.

[1093] In some instances, a puncture member can be used to deliver and/or place a portion of a catheter in a desired lumen within the body of a patient. For example, as shown in FIGS. 4-6, a puncture member 310 can be used to place a stented catheter and/or the like within a vein V. The puncture member 310 can be substantially similar to the puncture members 210 and/or 310 described above and thus, the puncture member is not described in further detail herein. As shown in FIG. 4, a user (e.g., a phlebotomist, nurse, technician, physician, doctor, etc.) can manipulate a portion of the puncture member 310 (e.g., either directly or indirectly) to place at least a distal end portion 312 of the puncture member 310 within a lumen defined by the vein V. Once disposed in the vein V, a guidewire 316 can be advanced through the lumen defined by the puncture member 310, as shown in FIG. 4. With the guidewire 316 positioned within the vein V, the user can advance an introducer catheter 317 and, for example, a stented catheter 318 along the guide wire 316 to dispose a distal end portion of at least the introducer catheter 317 within the lumen of the vein V, as indicated by the arrow AA in FIG. 5. In some instances, the stented catheter 318 can be inserted into the vein V concurrently with the introducer catheter 317. In other instances, the stented catheter 318 can be advanced within the introducer catheter 317 after the distal end portion of the introducer catheter 317 is disposed in the vein 317.

[1094] With the distal end portion of the stented catheter 318 disposed in the vein V, the guidewire 316 and the introducer catheter 317 can be moved in the proximal direction (i.e.,

withdrawn from the vein V), as indicated by the arrow BB in FIG. 6. In some embodiments, as the introducer catheter 317 is withdrawn from the vein V, the distal end portion of the stented catheter 318 can transition from a first configuration to a second configuration. For example, the stented catheter 318 can be in a collapsed configuration (e.g., the first configuration) when disposed in the introducer catheter 317 (FIG. 5) such that a diameter of the stented catheter 318 is substantially uniform. When the introducer catheter 318 is withdrawn from the vein (FIG. 6), the distal end portion of the stented catheter 318 can expand and/or otherwise reconfigure such that a diameter of the distal end portion of the stented catheter 318 is greater than a diameter of a portion of the stented catheter 318 still disposed in the introducer catheter 317.

[1095] In some embodiments, the distal end portion of the stented catheter 318 can expand to an extent that places an outer surface of the stented catheter 318 in close proximity to or directly in temporary contact with an inner surface of the vein V defining the lumen. As such, blood can be withdrawn from the vein V into a fluid reservoir (not shown in FIGS. 4-6) via a lumen defined by the stented catheter 318. Moreover, with the distal end portion of the stented catheter 318 in close proximity to or directly in contact with the inner surface of the vein, the stented catheter 318 can inhibit, limit, and/or substantially prevent a collapse of at least a portion of the vein V (e.g., in response to a negative pressure differential between the vein V and the fluid reservoir (not shown). In some embodiments, the arrangement of at least the distal end portion of the stented catheter 318, when in the second configuration, can allow a flow of blood to enter the stented catheter 318 substantially without damaging the constituents of the blood, as described above with reference to FIGS. 2 and 3. While the puncture member 310 is described above as being retracted once the stented catheter 318 is placed in a desired position with the vein, in other embodiments, the puncture member 310 need not be retracted. As such, the stented catheter 318 can be, for example, a sleeve or the like disposed about the distal end portion 312 of the puncture member 310 to control a flow of blood entering the lumen of the puncture member 310. Moreover, as described above with reference to the puncture member 210, a surface of the puncture member 310 and/or the stented catheter 318 defining a distal opening can be substantially rounded, smoothed, contoured, blunted, and/or the like. In other words, a distal edge of the puncture member 310 and/or stented catheter 318 defining the distal opening forms a substantially round corner. Thus, blood drawn through the opening can flow past the distal edge with reduced damage to

the erythrocytes that would otherwise result from contact with a sharper, more abrupt, substantially orthogonal, and/or otherwise non-rounded distal edge 215.

[1096] While described above as placing a stented catheter, in other embodiments, a puncture member can be used to place any suitable catheter and/or cannula. For example, FIG. 7 illustrates a puncture member 410 and a catheter 418 according to another embodiment. The puncture member 410 can be used, for example, to place at least a portion of the catheter 418 within a lumen defined by the body (e.g., a vein). As shown in FIG. 7, a distal end portion 412 of the puncture member 410 can include a substantially rounded distal edge 415, as described above with reference to the puncture member 210. In this manner, a flow of blood can flow past the distal edge 415 to enter a lumen 413 defined by the puncture member 410. Similarly, the catheter 418 can include a distal edge 418A that is substantially rounded. As shown in FIG. 7, the distal end portion 412 of the puncture member 410 extends beyond the distal edge 418A of the catheter 418. In some embodiments, the distal end portion 412 of the puncture member 410 can form and/or can define a recessed portion 419 or the like that corresponds with a position at or near the distal edge 418A of the catheter 418. In this manner, when the puncture member 410 is inserted into, for example, a vein of a patient, an opening in the vein defined by the puncturing can be a diameter that is substantially the same as an outer diameter of the catheter 418. As such, the catheter 418 can be positioned within the vein without rupturing and/or otherwise dilating the opening in the vein. In some instances, once the catheter 418 is disposed in the lumen defined by the vein, the puncture member 410 can be retracted through the catheter 418 while at least a distal end portion of the catheter 418 remains within the vein. In such instances, the substantially rounded distal edge 418A can reduce and/or can substantially prevent hemolysis of a volume of blood flowing to the catheter 418, as described above with reference to the puncture member 310 in FIGS. 2 and 3.

[1097] While the puncture members 210, 310, and 410 are particularly shown and described above, in other embodiments, any suitable puncture member can be coupled to any compatible adapter, which in turn, can place the puncture member in fluid communication with a fluid collection device. For example, FIGS. 8-17 illustrate embodiments configured to mitigate the risk of hemolysis as a volume of blood flows through changing geometries and/or physical and fluidic interfaces of one or more adapters. Specifically, FIGS. 8-10 illustrate a puncture member 510 coupled to an adapter 520, according to another

embodiment. In some embodiments, the puncture member 510 and the adapter 520 can be and/or can form, for example, a butterfly needle or the like. More specifically, the puncture member 510 has a proximal end portion 511 and a distal end portion 512 and defines a lumen 513 therethrough. The proximal end portion 511 is coupled to the adapter 520, as described in further detail herein. The distal end portion 512 of the puncture member 510 can be any suitable configuration. For example, the distal end portion 512 of the catheter 510 can be substantially similar to or the same as the distal end portion 212 of the catheter 210 described above with reference to FIGS. 2 and 3. That is to say, the arrangement of the distal end portion 512 of the catheter 510 can limit and/or substantially prevent damage (e.g., hemolysis) to blood as blood flow past the distal end portion 512 and into the lumen 513.

[1098] The adapter 520 has a proximal end portion 521, a distal end portion 522, and an inner surface 523. As described above, the adapter 520 can have an overall shape substantially similar to known butterfly needles. While shown in FIG. 8 as being substantially cylindrical with varying diameters, the adapter 520 can be any suitable shape, size, or configuration such as square, rectangular, polygonal, and/or any other non-cylindrical shape. In this manner, the overall shape of the adapter 520 can facilitate the handling of the transfer device 520 by including similar geometric features as known butterfly needles. The distal end portion 522 of the adapter 520 is physically and fluidically coupled to the proximal end portion 511 of the puncture member 510, as described in further detail herein. The proximal end portion 521 of the adapter 520 can be any suitable configuration. In some embodiments, the proximal end portion 521 can be a port and/or a portion of a locking mechanism. For example, in this embodiment, the proximal end portion 521 of the adapter 520 is a locking mechanism configured as a male portion of a Luer Lok ®. Moreover, in this embodiment, such a locking mechanism is disposed at a proximal end portion of a cannula configured to extend between the proximal end portion 521 and the distal end portion 522 of the adapter 520. In other embodiments, the adapter 520 is monolithically formed without a cannula between the proximal end portion 521 and the distal end portion 522. Although the proximal end portion 521 is described as including a locking mechanism, in other embodiments, the proximal end portion 521 can be any suitable configuration configured to interface with any suitable device such that blood flows in a substantially laminar, smooth, and/or non-turbulent flow between the adapter 520 and the device.

[1099] As shown in FIGS. 9 and 10, the inner surface 523 of the adapter 520 defines a lumen 524 extending through the proximal end portion 521 and the distal end portion 522. In some embodiments, the arrangement of the inner surface 523 can reduce, inhibit, and/or substantially prevent, for example, hemolysis of a volume of blood flowing within the lumen 524. More specifically, as shown in FIG. 10, the distal end portion 522 of the adapter 520 is coupled to the proximal end portion 511 of the puncture member 510 such that the lumen 513 of the puncture member 510 is substantially aligned with and substantially the same diameter as the lumen 524 of the adapter 520. That is to say, the proximal end portion 511 of the puncture member 510 is coupled to the distal end portion 522 of the adapter 520 such that a substantially smooth and/or continuous transition is defined between the lumen 513 of the puncture member 510 and the lumen 524 of the adapter 520. Similarly, in embodiments including the cannula extending between the end portions, a distal end portion of the cannula can be coupled to the distal end portion 522 of the adapter 520 in such a manner as to define a substantially smooth transition therebetween.

[1100] In addition, the inner surface 523 of the adapter 520 defines a tapered portion that extends between the puncture member 510 and the cannula. Expanding further, a first portion of the inner surface 523 (e.g., a more proximal portion) defines a first diameter that is substantially the same as an inner diameter defined by the cannula, while a second portion of the inner surface (e.g., a more distal portion) defines a second diameter, smaller than the first diameter, that is substantially the same as an inner diameter defined by the lumen 513 of the puncture member 510. As shown in FIG. 10, the tapered portion can form a substantially smooth transition between, for example, the first diameter and the second diameter. In some instances, such a smooth transition, for example, from the first diameter to the second diameter can facilitate, produce, encourage, and/or force a substantially laminar flow (e.g., consistent, uniform, non-turbulent, uninterrupted, smooth, etc.) of a volume of bodily-fluid (e.g., blood) through the lumen 524. Moreover, the smooth or substantially uniform transitions between the puncture member 510 and the adapter 520 and/or the smooth or substantially uniform transitions between the various components of the adapter 520 can reduce eddy currents (i.e., circulating currents often resulting from a discontinuity) or the like within the flow of blood. Thus, when the distal end portion 512 of the puncture member 510 is disposed in a vein or the like and the proximal end portion 521 (e.g., a locking mechanism) is physically and fluidically coupled to a fluid reservoir, a volume of blood can flow within the lumens 513 and 524 from the patient to the fluid reservoir with reduced damage to the

constituents of the blood (e.g., hemolysis of the erythrocytes) that might otherwise occur as a result of misaligned interfaces and/or discontinuities; abrupt changes in diameter; turbulence and/or eddy currents within a flow of blood therethrough; and/or the like.

[1101] While the adapter 520 is particularly shown and described above with reference to FIGS. 8-10, in other embodiments, an adapter can be any suitable configuration and can be arranged within a system of components to form a physical and/or fluidic interface therebetween. For example, FIGS. 11-13 illustrate a first adapter 620 coupled to a second adapter 630 according to an embodiment. The first adapter 620 has a proximal end portion 621, a distal end portion 622 and an inner surface 623. The inner surface 623 of the first adapter 620 defines a lumen 624 extending through its proximal end portion 621 and its distal end portion 622.

[1102] As shown in FIGS. 12 and 13, the inner surface 623 of the first adapter 620 includes and/or otherwise forms a shoulder 625. More specifically, the shoulder 625 formed by the inner surface 623 is associated with a change in diameter of the inner surface 623. As shown in FIG. 13, the shoulder 625 forms a substantially annular discontinuity that has substantially rounded corners or edges. In this manner, the transition from a diameter of the inner surface 623 proximal to the shoulder 625 to a diameter of the inner surface distal to the shoulder 625 can be relatively smooth rather than forming a relatively sharp, abrupt, and/or orthogonal corner (e.g., shoulder). As such, the arrangement of the shoulder 625 can limit, inhibit, and/or substantially prevent hemolysis of blood as the blood flows within the lumen 624 past the shoulder 625.

[1103] The second adapter 630 has a proximal end portion 631, a distal end portion 632, and an inner surface 633. The inner surface 633 of the second adapter 630 defines a lumen 624 extending through its proximal end portion 631 and its distal end portion 632. As shown in FIGS. 11-13, a portion of the second adapter 630 can be inserted into a portion of the lumen 624 defined by the first adapter 620 to couple the second adapter 630 to the first adapter 620. In some embodiments, the first adapter 620 and the second adapter 630 can form a friction fit and/or the like, which in turn, can define a substantially fluid tight seal therebetween. Thus, the second adapter 630 can be inserted into the first adapter 620 to couple the second adapter 630 thereto.

[1104] Similarly, the distal end portion 632 of the second adapter 630 is configured to reduce, limit, and/or substantially prevent hemolysis of blood as the blood flow therethrough. Specifically, as shown in FIG. 13, a distal most surface of the second adapter 630 and the inner surface 633 of the second adapter 630 form a rounded corner 635 and/or smooth transition therebetween. The rounded corner 635 formed by the second adapter 630 defines a relatively smooth transition from an outer diameter of the second adapter 630 (e.g., at the distal end) to an inner diameter of the second adapter 630 (e.g., at the distal end) rather than forming a relatively sharp, abrupt, and/or orthogonal corner. In some embodiments, a radius of curvature associated with the rounded corner 635 of the second adapter 630 can be substantially similar to a radius of curvature associated with the shoulder 625 of the first adapter 620. Thus, when the second adapter 630 is disposed within the first adapter 620, a volume of bodily-fluid (e.g., blood) can flow through the lumen 624 of the first adapter 620 and the lumen 634 of the second adapter 630 to be disposed within a fluid reservoir or the like. Moreover, the arrangement of the shoulder 625 of the first adapter 620 and the rounded corner 635 of the second adapter 630 can, for example, reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough that might otherwise result from contact substantially abrupt, sharp, and/or orthogonal corners or the like. In addition, the arrangement of the shoulder 625 of the first adapter 620 and the rounded corner 635 of the second adapter 630 can facilitate, produce, encourage, and/or otherwise result in a substantially laminar flow through the lumens 624 and 634, respectively (e.g., with little turbulence, eddy currents, etc.).

[1105] Although the first adapter 620 and the second adapter 630 are shown in FIGS. 11-13 as each forming substantially rounded corners and/or shoulders, in other embodiments, a first adapter and a second adapter can be coupled together to form an interface therebetween having any suitable arrangement and/or configuration. For example, FIGS. 14 and 15 illustrate a first adapter 720 coupled to a second adapter 730 according to another embodiment. The first adapter 720 has a proximal end portion 721, a distal end portion 722 and an inner surface 723. The inner surface 723 of the first adapter 720 defines a lumen 724 extending through its proximal end portion 721 and its distal end portion 722. Furthermore, the inner surface 723 includes and/or otherwise forms a shoulder 725. In this embodiment, the shoulder 725 is associated with a change in diameter of the inner surface 723. As shown in FIG. 15, the shoulder 725 forms a substantially annular discontinuity with a substantially orthogonal corner. Said another way, the shoulder 725 has a substantially non-rounded

corner (e.g., has no radius of curvature of a nominal radius of curvature) that defines an edge or the like.

[1106] The second adapter 730 has a proximal end portion 731, a distal end portion 732, and an inner surface 733. The inner surface 733 of the second adapter 730 defines a lumen 724 extending through its proximal end portion 731 and its distal end portion 732. As shown in FIGS. 14 and 15, a portion of the second adapter 730 can be inserted into a portion of the lumen 724 defined by the first adapter 720 to couple the second adapter 730 to the first adapter 720. As shown in FIG. 14, the distal most surface of the second adapter 730 and the inner surface 733 of the second adapter 730 form a substantially orthogonal corner 735 (e.g., a substantially non-rounded corner, as described above). In some embodiments, the first adapter 720 and the second adapter 730 can be substantially similar to known adapters (e.g., each adapter forms relatively abrupt and/or substantially orthogonal corners and/or edges).

[1107] While such corners, discontinuities, and/or edges are described above as a potential source of blood hemolyzation, in this embodiment, a gasket 726 is disposed between and in contact with the shoulder 725 of the first adapter 720 and the distal surface of the second adapter 730, as shown in FIG. 15. The gasket 726 can be, for example, an elastomeric gasket and/or the like that is in contact with the distal surface of the second adapter 730 and the shoulder 725 of the first adapter 720 to define a substantially fluid tight seal therebetween. Moreover, the gasket 726 defines an opening and/or lumen therethrough that can have a size and/or diameter substantially similar to the size and/or diameter of the lumens 724 and 734. Thus, the arrangement of the gasket 726 can reduce a magnitude of the discontinuities formed by the shoulder 725 of the first adapter 720 and the distal end of the second adapter 730. As a result, the gasket 726 disposed between the shoulder 725 of the first adapter 720 and the distal surface of the second adapter 730 can, for example, reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough that might otherwise result from relatively large changes and/or discontinuities in the diameters of the inner surfaces 723 and 733, respectively. In addition, the gasket 726 can facilitate, produce, encourage, and/or otherwise result in a substantially laminar flow of fluid through the lumens 724 and 734, respectively (i.e., with little to no turbulence, eddy currents, etc.).

[1108] In some embodiments, the gasket 726 can be configured to restrict, limit, reduce, and/or otherwise control a flow of blood and/or a pressure exerted therethrough. For example, while the gasket 726 is described above as having substantially the same size and/or

diameter as the lumens 724 and 734, in other embodiments, the gasket 726 can have a size and/or diameter that is greater than or less than the diameter of the lumens 724 and 734. Specifically, in some embodiments, the size and/or diameter of the gasket 726 can be less than the diameter of the lumens 724 and 734 and, as such, the gasket 726 can restrict, constrict, reduce, limit, and/or otherwise control a flow of blood therethrough. In some embodiments, such a reduction and/or restriction of the blood flowing through the gasket 726 can reduce a likelihood of hemolysis of the blood resulting from, for example, a flow rate and/or a large pressure differential between a volume having a relatively high pressure disposed on a first side of the gasket 726 and a volume having a relatively low pressure disposed on a second side of the gasket 726.

[1109] FIG. 16 illustrates a portion of a first adapter 820 coupled to a portion of a second adapter 830 according to another embodiment. The first adapter 820 has a proximal end portion 821 configured to be coupled to a distal end portion 832 of the second adapter 830, as described in further detail herein. Although only the proximal end portion 821 of the first adapter 820 is shown in FIG. 16, the first adapter 820 can be similar in size and/or shape as the first adapters 620 and/or 720, unless otherwise expressed. The first adapter 820 includes an inner surface 823 that defines a lumen 824 extending through at least its proximal end portion 821. As shown in FIG. 16, the inner surface 823 of the first adapter 820 includes and/or otherwise forms a shoulder 825. The shoulder 825 formed by the inner surface 823 is associated with a change in diameter of the inner surface 823. More specifically, the shoulder 825 is associated with and/or forms a tapered or chamfered portion of the inner surface 823, as described in further detail herein.

[1110] Although only the distal end portion 832 of the second adapter 830 is shown in FIG. 16, the second adapter 830 can be any suitable shape, size, or configuration. For example, the distal end portion 832 of the second adapter 830 can form and/or can include a locking mechanism or the like while a proximal end portion (not shown in FIG. 16) can be coupled to and/or can form any suitable portion of a fluid collection device such as, for example, a fluid reservoir, a conduit, a flow control mechanism, and/or the like. In this embodiment, the distal end portion 832 of the second adapter 830 includes and/or forms a locking mechanism configured to form a threaded coupling with, for example, the proximal end portion 821 of the first adapter 820. In other embodiments, the distal end portion 832 of the second adapter 830 can be any suitable configuration.

[1111] As shown in FIG. 16, the second adapter 830 includes an inner surface 833 that defines a lumen 834 extending through at least its distal end portion 832. Moreover, the distal end portion 832 of the second adapter 830 includes and/or forms a distal surface 835 that is substantially tapered or chamfered. In some embodiments, the distal surface 835 of the second adapter 830 can have a size, shape, angle, etc. that substantially corresponds with the shoulder 825 defined by the first adapter 820. Thus, when the first adapter 820 is coupled to the second adapter 830 (e.g., via a threaded coupling or the like), the distal surface 835 of the second adapter 830 can be brought into contact with the shoulder 825 of the first adapter 820. Moreover, the arrangement of the first adapter 820 and the second adapter 830 is such that when the distal surface 835 of the second adapter 830 is placed in contact with the shoulder 825 of the first adapter 820, the inner surfaces 833 and 823, respectively, are brought into alignment, as shown in FIG. 16. In this manner, the inner surfaces 823 and 833 can form a substantially continuous surface having, for example, a substantially constant diameter. Thus, by reducing and/or substantially eliminating a discontinuity otherwise associated with the physical and fluidic coupling of the first adapter 820 and the second adapter 830, blood can flow within the lumens 824 and 834 of the adapters 820 and 830, respectively, with little or substantially no hemolysis of the blood flowing therethrough.

[1112] Although the inner surfaces 823 and 833 of the first adapter 820 and the second adapter 830, respectively, are described above as having a substantially constant diameter, in other embodiments, a diameter of each inner surface 823 and 833 can be varied. Such arrangement, however, is such that the inner surfaces 823 and 833 form a substantially smooth transition between, for example, a smaller diameter and a larger diameter. Thus, the substantially smooth transition in the diameters of the inner surfaces 823 and 833 can still facilitate a substantially laminar flow therethrough, which in some instances, can limit and/or substantially prevent hemolysis of blood flowing from the first adapter 820 and through the second adapter 830.

[1113] While the flow of bodily-fluid (i.e., blood) is described above as first flowing through the first adapter 820 and then flowing through the second adapter 930, in other embodiments, the flow through a set of adapters can be reversed. For example, FIG. 17 illustrates a first adapter 920 and a second adapter 930 according to another embodiment. The first adapter 920 has a distal end portion 922 configured to be coupled to a proximal end portion 931 of the second adapter 930, as described in further detail herein. Although only

the distal end portion 922 of the first adapter 920 is shown in FIG. 17, the first adapter 920 can be similar in size and/or shape as the first adapters 620 and/or 720, unless otherwise expressed. The first adapter 920 includes an inner surface 923 that defines a lumen 924 extending through at least its distal end portion 922. As shown in FIG. 17, a portion of the second adapter 930 is inserted into the lumen 924, as described in further detail herein.

[1114] Although only the proximal end portion 931 of the second adapter 930 is shown in FIG. 17, the second adapter 930 can be any suitable shape, size, or configuration. For example, the proximal end portion 931 of the second adapter 930 can form and/or can include a locking mechanism or the like while a proximal end portion (not shown in FIG. 17) can be coupled to and/or can form any suitable portion of a fluid collection device such as, for example, a puncture member, a needle, a conduit, a flow control mechanism, and/or the like. In this embodiment, the proximal end portion 931 of the second adapter 930 includes and/or forms a locking mechanism configured to form a threaded coupling with, for example, the distal end portion 922 of the first adapter 920. In other embodiments, the proximal end portion 931 of the second adapter 930 can be any suitable configuration.

[1115] As shown in FIG. 17, the second adapter 930 includes an inner surface 933 that defines a lumen 934 extending through at least its proximal end portion 931. Moreover, a region of the proximal end portion 931 of the second adapter 930 is disposed within the lumen 924 of the first adapter 920. For example, the inner surface 923 of the first adapter 920 has a diameter that corresponds to an outer diameter associated with the region of the proximal end portion 931 of the second adapter 930. Thus, as shown in FIG. 17, the diameter defined by the inner surface 923 of the first adapter 920 is greater than a diameter defined by the inner surface 933 of the second adapter 930, as described in further detail herein.

[1116] The proximal end portion 931 of the second adapter 930 includes and/or forms a proximal surface 935 with a substantially rounded corner and/or smooth transition. For example, the proximal surface 935 formed by the second adapter 930 defines a relatively smooth transition from an inner diameter of the second adapter 930 (e.g., defined by the inner surface 933) to an outer diameter of the second adapter 930 (e.g., at the distal end) rather than forming a relatively sharp, abrupt, and/or orthogonal corner. When a portion of the second adapter 930 is disposed within the lumen 923 of the first adapter 920, a volume of bodily-fluid (e.g., blood) can flow through the lumen 934 of the second adapter 930 and into the lumen 924 of the first adapter 920. Thus, the arrangement of the proximal surface 935 of the

second adapter 930 can, for example, facilitate, produce, encourage, and/or otherwise result in a substantially laminar flow of a volume of bodily-fluid (i.e., blood) as the volume flows from the lumen 934 of the second adapter 930 into the lumen 924 of the first adapter 920. Specifically, the proximal surface 935 of the second adapter 930 allows for a gradual transition from the diameter associated with the lumen 934 of the second adapter 930 (i.e., the smaller diameter) to the diameter associated with the lumen 924 of the first adapter 920 (i.e., the larger diameter). Such a smooth transition can, for example, reduce eddy currents and/or other forms of turbulence that can otherwise result from a substantially abrupt change in diameter or the like. Thus, the arrangement of the first adapter 920 and the second adapter 930 can allow a volume of blood to expand as the flow of blood exits the lumen 934 of the second adapter 930, which in some instances, can reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough.

[1117] While the first adapters 620, 720, 820, and 920 are shown and described above as receiving and/or otherwise being directly coupled to the second adapters 630, 730, 830, and 930, respectively, in other embodiments, a first adapter can be indirectly coupled to a second adapter via an intervening structure. In such embodiments, the intervening structure can define a lumen that can place the first adapter in fluid communication with the second adapter. Moreover, the intervening structure can limit, modulate, and/or control a flow rate of a volume of fluid (i.e., blood) therethrough. For example, FIGS. 18-26 illustrate embodiments configured to mitigate the risk of hemolysis otherwise associated with a relatively high flow rate and/or velocity along a fluid flow path that exceeds known shear force and exposure time limits that can rupture red blood cells. Specifically, FIGS. 18-20 illustrate a first adapter 1020 indirectly coupled to a second adapter 1030 via a restrictor 1050, according to an embodiment. The first adapter 1020 includes a proximal end portion 1021, a distal end portion 1022, and an inner surface 1023. The inner surface 1023 defines a lumen 1024 extending through the proximal end portion 1021 and the distal end portion 1022 (see e.g., FIG. 20). In some embodiments, the first adapter 1020 can be substantially similar to and/or the same as the first adapter 720 described above with reference to FIGS. 14 and 15. Thus, aspects of the first adapter 1020 are not described in further detail herein.

[1118] The second adapter 1030 has a proximal end portion 1031, a distal end portion 1032, and an inner surface 1033. The inner surface 1033 of the second adapter 1030 defines a lumen 1024 extending through its proximal end portion 1031 and its distal end portion 1032

(see e.g., FIG. 20). In some embodiments, the second adapter 1030 can be substantially similar to and/or the same as the second adapter 730 described above with reference to FIGS. 14 and 15. Thus, aspects of the second adapter 1030 are not described in further detail herein.

[1119] The restrictor 1050 has a proximal end portion 1051, a distal end portion 1052, and an inner surface 1053. The inner surface 1053 of the restrictor 1050 defines a lumen 1054 extending through its proximal end portion 1051 and its distal end portion 1052 (see e.g., FIG. 20). In this embodiment, the restrictor 1050 is coupled between the first adapter 1020 and the second adapter 1030 to define a fluid pathway therebetween (e.g., via the lumen 1054). More specifically, the restrictor 1050 can include any suitable interface, locking mechanism, surface, etc. at or near the proximal end portion 1051 and the distal end portion 1052 configured to couple the restrictor 1050 to the first adapter 1020 or the second adapter 1030. As shown in FIGS. 18-20, the restrictor 1050 includes a locking mechanism or the like at its distal end portion 1052 that is configured to couple the distal end portion 1052 of the restrictor 1050 to the proximal end portion 1021 of the first adapter 1020. For example, in some embodiments, the distal end portion 1052 of the restrictor 1050 can include a threaded female Luer Lok ® configured to form a threaded coupling with a corresponding threaded male Luer Lok ® of the first adapter 1020, as shown in FIG. 20.

[1120] As shown in FIGS. 19 and 20, the proximal end portion 1051 of the restrictor 1050 receives the second adapter 1030. For example, as described above with reference to the first adapter 620 and the second adapter 630 in FIGS. 11-13, a portion of the second adapter 1030 is inserted through the proximal end portion 1051 of the restrictor 1050 to be disposed in the lumen 1054. In some embodiments, the restrictor 1050 and the second adapter 1030 can form a friction fit and/or the like, which in turn, can define a substantially fluid tight seal therebetween. In other embodiments, the proximal end portion 1051 of the restrictor 1050 and the distal end portion 1032 of the second adapter 1030 can include any suitable coupling and/or locking mechanism configured to couple the second adapter 1030 to the restrictor 1050 (e.g., as described above with reference to the coupling between the first adapter 1020 and the restrictor 1050).

[1121] As shown in FIGS. 19 and 20, the restrictor 1050 or the first adapter 1020 includes a gasket 1026 configured to minimize a discontinuity between the lumen 1024 of the first adapter 1020 and the lumen 1054 of the restrictor 1050 when coupled. Similarly, the

second adapter 1030 or the restrictor 1050 includes a gasket 1036. The gaskets 1026 and 1036 can be substantially similar in form and function to the gasket 726 shown and described above with reference to FIGS. 14 and 15. Thus, the gaskets 1026 and 1036 are disposed within the lumen 1024 of the first adapter 1020 and the lumen 1054 of the restrictor 1050, respectively. The arrangement of the gaskets 1026 and 1036 can reduce a magnitude of the discontinuities formed between the inner surfaces 1023, 1033, and 1053 of the first adapter 1020, the second adapter 1030, and the restrictor 1050, respectively, which in turn, can reduce, limit, and/or substantially prevent hemolysis of blood flowing therethrough, as described in detail above. In some embodiments, the gaskets 1026 and 1036 can be configured to restrict and/or reduce a pressure and/or a flow rate associated with the first adapter 1020, the second adapter 1030, and/or the restrictor 1050, as described above with reference to the gasket 726. In some instances, restricting and/or reducing the pressure and/or flow rate associated with the first adapter 1020, the second adapter 1030, and/or the restrictor 1050 (e.g., via the gaskets 1026 and 1036) can, for example, limit shear forces and/or exposure time experienced by red blood cells as the red blood cells flow through the first adapter 1020, the second adapter 1030, and the restrictor 1050, and/or the interfaces therebetween.

[1122] The inner surface 1053 of the restrictor 1050 is configured to control a flow of fluid through the lumen 1053. For example, as shown in FIG. 20, the inner surface 1053 of the restrictor 1050 includes a choke portion 1055 or the like. In some embodiments, the choke portion 1055 corresponds to a portion of the inner surface 1053 having a reduced diameter relative to the other portions of the inner surface 1053. More specifically, the choke portion 1055 forms a relatively smooth transition (e.g., a gradual change) from a region of the inner diameter 1053 associated with a first diameter to a region (i.e., the choke portion 1055) associated with a second diameter, smaller than the first diameter. Thus, the choke portion 1055 restricts, controls, and/or reduces a flow of fluid therethrough.

[1123] Expanding further, the reduction in the diameter of the inner surface 1053 at or along the choke portion 1055 selectively controls a pressure within the lumen 1054. For example, in some embodiments, the second adapter 1030 can be fluidically coupled (e.g., either directly or indirectly) to an evacuated container or the like, resulting in a negative pressure within the lumens 1034, 1054, and 1024. Thus, the reduced diameter associated with the choke portion 1055 results in a reduced pressure differential between the lumen 1024

of the first adapter 1020 (i.e., at a time directly before the exposure to the negative pressure) and a portion of the lumen 1054 of the restrictor 1050 that is distal to the choke portion 1055. As such, when the first adapter 1020 is in fluid communication with, for example, a vascular structure (e.g., via a needle, catheter, cannula, etc.), a magnitude of the negative pressure exerted on or in the vascular structure is reduced, thereby limiting, reducing, and/or substantially preventing hemolysis of blood as it flows into the lumen 1024 defined by the first adapter 1020. Moreover, the smooth transition in the diameter of the inner surface 1053 from the first diameter to the second diameter (associated with the choke portion 1055), facilitates, encourages, and/or otherwise results in a substantially laminar flow through the lumen 1054 of the restrictor 1050.

[1124] While the restrictor 1050 is particularly shown and described above with reference to FIGS. 18-20, in other embodiments, a restrictor, configured to control a flow of fluid therethrough, can be any suitable configuration. For example, FIGS. 21-24 illustrate a restrictor 1150 according to another embodiment. The restrictor 1150 has a proximal end portion 1151, a distal end portion 1152, and an inner surface 1153. The inner surface 1153 of the restrictor 1150 defines a inner volume 1154 extending through its proximal end portion 1151 and its distal end portion 1152 (see e.g., FIG. 22). Although not shown in FIGS. 21-24, the restrictor 1150 can be disposed between two components of a fluid transfer device to define a fluid flow path therethrough. For example, in some embodiments, the proximal end portion 1151 can be coupled to an adapter such as, for example, the second adapter 1030, described above with reference to FIGS. 18-20. Similarly, the distal end portion 1152 can be coupled to an adapter such as, for example, the first adapter 1020, described above. As such, the proximal end portion 1151 and the distal end portion 1152 can be substantially similar to or the same as the proximal end portion 1051 and the distal end portion 1052, respectively, of the restrictor 1050 and thus, are not described in further detail herein.

[1125] As shown in FIGS. 22-24, the restrictor 1150 includes a baffle 1156 disposed in the inner volume 1154. The baffle 1156 can be any suitable shape, size, or configuration. For example, in this embodiment, the baffle 1156 is substantially rectangular (see e.g., FIG. 20) with a size that substantially corresponds to the inner volume 1154 of the restrictor 1150, as described in further detail herein. The baffle 1156 includes an inner surface 1157 that defines an inner volume 1158. As shown in FIG. 24, the inner surface 1157 of the baffle 1156 defines a gradual bow toward the center of the baffle 1156. More specifically, the

arrangement of the inner surface 1157 is such that a distance between opposite sides of the baffle 1156 gradually varies as the inner surface 1157 extends outward from a longitudinal centerline CL (shown in FIG. 22) of the baffle 1156. For example, in this embodiment, a distance between opposite portions of the inner surface 1157 gradually increases from a first distance, at a first position associated with a perimeter of the inner surface 1157, to second distance, at a second position disposed between the perimeter of the inner surface 1157 and the longitudinal centerline CL, and then gradually decreases from the second distance to a third distance, at a position associated with and/or near the longitudinal center CL. In this manner, the baffle 1156 can selectively control a flow of fluid through the inner volume 1158, as described in further detail herein.

[1126] Referring back to FIG. 22, in this embodiment, an outer surface of the baffle 1156 is in contact with the inner surface 1153 of the restrictor 1150 when disposed in the inner volume 1154. In some embodiments, the outer surface of the baffle 1156 and the inner surface 1153 of the restrictor 1150 define a friction fit or the like that forms a substantially fluid tight seal. As such, the arrangement of the baffle 1156 and the inner surface 1153 of the restrictor 1150 can limit, inhibit, and/or substantially prevent a flow of fluid between the outer surface of the baffle 1156 and the inner surface 1153 of the restrictor 1150. More specifically, the inner volume 1158 of the baffle 1156 defines a fluid flow path that places a first portion of the inner volume 1154, which is distal to the baffle 1156, in fluid communication with a second portion of the inner volume 1154, which is proximal to the baffle 1156. In this manner, the arrangement of the inner surface 1157 of the baffle 1156 can restrict, inhibit, guide, limit, choke, and/or otherwise control a flow of fluid through the restrictor 1150. Moreover, the smooth or gradual change in distance between opposite portions of the inner surface 1157 of the baffle (as described above) facilitates, encourages, and/or otherwise results in a substantially laminar flow through the inner volume 1154 of the restrictor 1150.

[1127] Although not shown in FIGS. 21-24, in some embodiments, the inner volume 1158 of the baffle 1156 can include a medium disposed therein. For example, in some embodiment, the baffle 1156 can include a substantially porous material or the like that can slow and/or filter a flow of fluid (e.g., blood) therethrough. In other embodiments, the user can manipulate the restrictor 1150 to modify and/or control a flow of fluid through the restrictor 1150. For example, in some instances, the user can exert a force on a portion of the

restrictor 1150 sufficient to deform that portion. As such, a portion of the force can correspondingly deform the baffle 1156, which in turn, can change a contour of the inner surface 1157. Thus, the user can exert a force on the restrictor 1150 to, for example, increase, decrease, or otherwise control a flow of fluid through the baffle 1156. By way of example, a user can exert a force of the restrictor 1150 to reduce a distance between opposite portions of the inner surface 1157, which in turn, can reduce a negative pressure differential produced by an evacuated container being placed in fluid communication with the restrictor 1150.

[1128] FIGS. 25 and 26 illustrate a restrictor 1250 according to another embodiment. The restrictor 1250 has a proximal end portion 1251, a distal end portion 1252, and an inner surface 1253. The inner surface 1253 of the restrictor 1250 defines a inner volume 1254 extending through its proximal end portion 1251 and its distal end portion 1252 (see e.g., FIG. 26). As described above, the restrictor 1250 can be physically and fluidically coupled between, for example, a pair of components of a fluid transfer device to restrict and/or otherwise control a flow of fluid therebetween. For example, although not shown in FIGS. 25-26, the proximal end portion 1251 can be coupled to an adapter such as, for example, the second adapter 1030, described above with reference to FIGS. 18-20. Similarly, the distal end portion 1252 can be coupled to an adapter such as, for example, the first adapter 1020, as described above. In this manner, the proximal end portion 1251 and the distal end portion 1252 can be substantially similar to or the same as the proximal end portion 1051 and the distal end portion 1052, respectively, of the restrictor 1050 and thus, are not described in further detail herein.

[1129] The restrictor 1250 includes and/or defines a set of chambers 1259, as shown in FIG. 26. More specifically, the restrictor 1250 includes a set of walls that can form, for example, a set of semi-spherical portions, which in turn, result in the inner surface 1253 defining the set of chambers 1259. Thus, the chambers 1259 are, for example, a set of semi-spherical portions of the inner volume 1254. As shown in FIG. 26, the chambers 1259 are serially arranged along a longitudinal centerline CL of the restrictor 1250. In some embodiments, the size and/or shape of each chamber 1259 can vary. For example, as shown in FIG. 26, the chamber 1259 disposed at or near the proximal end portion 1251 of the restrictor 1250 is smaller than the adjacent chamber 1259. In other embodiments, the size and/or shape of each chamber 1259 can be substantially uniform. With the inner surface 1253 defining the semi-spherical chambers 1259, a diameter of the inner volume 1254 (e.g.,

associated with a cross-sectional shape of the inner surface 1253) is varied along a length of the longitudinal centerline CL. For example, a diameter of the inner volume 1254 gradually increases or decreases in an alternating manner between a relatively smaller diameter, associated with a position along the longitudinal centerline substantially between adjacent chambers 1259 and a relatively larger diameter, associated with a position along the longitudinal centerline substantially in the center of a given chamber 1259.

[1130] In some embodiments, the arrangement of the chambers 1259 selectively controls a pressure within the inner volume 1254. For example, in some embodiments, the proximal end portion 1251 of the restrictor 1250 can be fluidically coupled (e.g., either directly or indirectly) to an evacuated container or the like, resulting in a negative pressure within the inner volume 1254. Thus, the alternating increase and decrease corresponding to each chamber 1259 results in a changing pressure differential along the longitudinal centerline CL. In some embodiments, such an alternating arrangement can, for example, act as a peristaltic pump or the like. Thus, the restrictor 1250 can draw a fluid through the inner volume 1254 via a pressure differential that is at least partially controlled by the arrangement of the inner surface 1253. That is to say, while an evacuated container is the source of a negative pressure, the arrangement of the chambers 1259 at least partially controls a pressure differential between the proximal end portion 1251 and the distal end portion 1252. In this manner, hemolysis of blood can be reduced and/or substantially prevented, which might otherwise occur in response to a shear force produced by a relatively rapid and/or relatively large pressure drop associated with placing an evacuated container in fluid communication with a vascular structure. Moreover, the smooth and/or gradual transitions in the diameter of the inner surface 1253 associated with the chambers 1259, facilitates, encourages, and/or otherwise results in a substantially laminar flow through the inner volume 1254 of the restrictor 1250.

[1131] Although not shown, any of the restrictors 1050, 1150, and/or 1250 can be fluidically coupled (either directly or indirectly) to and/or monolithically formed with an adapter configured to engage a fluid reservoir such as an evacuated container. In some embodiments, such adapters can include an inner surface configured to reduce discontinuities or the like within a portion of a fluid flow path and/or otherwise configured to facilitate a substantially laminar fluid flow therethrough, as described in detail above. Moreover, the adapters can engage any suitable fluid reservoir or container. For example, FIGS. 27-44

illustrate embodiments (i.e., adapters and fluid reservoirs) configured to mitigate the risk of hemolysis as blood flow from an adapter, a puncture member, a needle, a cannula, and/or the like into a fluid reservoir. Specifically, FIGS. 27-33 illustrate an adapter 1330 configured to engage a fluid reservoir 1360 (FIGS. 29-33) according to an embodiment. The adapter 1330 has a proximal end portion 1331, a distal end portion 1332, and an inner surface 1333. The inner surface 1333 defines a lumen 1334 extending through the proximal end portion 1331 and the distal end portion 1332 (see e.g., FIG. 27). As shown in FIGS. 27 and 28, in some embodiments, the adapter 1330 can include and/or can be coupled to a shroud 1343. In such embodiments, the shroud 1343 can define an inner volume 1344 within which a portion of a fluid reservoir can be disposed. In other embodiments, the adapter 1330 need not include and/or need not be coupled to the shroud 1343.

[1132] The adapter 1330 can be any suitable shape, size, or configuration. For example, as shown in FIGS. 29 and 30, the distal end portion 1332 of the adapter 1330 includes and/or is coupled to a lock mechanism or the like. In this embodiment, the distal end portion 1332 includes and/or forms a female portion of a Luer Lok ® or the like. Thus, the distal end portion 1332 of the adapter 1330 can be coupled to a corresponding male portion of a Luer Lok ® or the like, as described above with reference to the distal end portion 1052 of the restrictor 1050 shown in FIG. 20. The proximal end portion of the adapter 1330 includes and/or is coupled to a puncture member 1338 defining a lumen 1339 in fluid communication with the lumen 1334 of the adapter 1330. The puncture member 1338 can be any suitable configuration. For example, in some embodiments, the puncture member 1338 is a needle. As shown in FIG. 30, the puncture member 1325 is disposed within a sheath 1341. More specifically, the sheath 1341 is at least temporarily disposed about the puncture member 1338 and is configured to limit and/or substantially prevent an accidental contact with the puncture member 1338. Furthermore, the sheath 1341 can maintain the puncture member 1338 in a substantially sterile environment prior to use and can selectively control a flow of bodily-fluid through the puncture member 1338, as described in further detail herein.

[1133] As shown in FIG. 30, a diameter of the inner surface 1333 at or near the distal end portion 1332 is larger than a diameter of the puncture member 1338. In this manner, the inner surface 1333 forms and/or defines a smooth transition from a larger diameter at or near the distal end portion 1332 to a smaller diameter at or near the puncture member 1338. In some instances, such a smooth transition from the larger diameter to the smaller diameter can

facilitate, produce, encourage, and/or force a substantially laminar flow of a volume of bodily-fluid (e.g., blood) through the lumen 1334. Moreover, the smooth transition can reduce eddy currents or the like within the flow of blood that can otherwise result from a relatively abrupt change in diameter or the like. Thus, a volume of blood can flow within the lumens 1334 and 1339 with reduced damage to the constituents of the blood (e.g., hemolysis of the erythrocytes) that might otherwise occur as a result of misaligned interfaces and/or discontinuities; abrupt changes in diameter; turbulence and/or eddy currents within a flow of blood therethrough; and/or the like.

[1134] As described above, the adapter 1330 is configured to couple to and/or otherwise engage a fluid reservoir 1360. The fluid reservoir 1360 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1360 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any other type of container, vial, bottle, reservoir, etc. As shown in FIGS. 31-33, the fluid reservoir 1360 includes a proximal end portion 1361 and a distal end portion 1362, and defines an inner volume 1364. The distal end portion 1362 includes a port 1363 through which the puncture member 1338 can be inserted to place the inner volume 1364 of the fluid reservoir 1360 in fluid communication with the lumen 1334 of the adapter 1330. For example, in some embodiments, the port 1363 can be a self-healing septum or the like. Thus, the port 1363 can be substantially in a sealed configuration prior to insertion of, for example, the puncture member 1338 and subsequently, can transition from an open configuration to the sealed configuration when, for example, the puncture member 1338 is removed from the port 1363.

[1135] In some embodiments, a fluid reservoir can include a flow control member or the like disposed in its inner volume. For example, as shown in FIGS. 32 and 33, the fluid reservoir 1360 includes a flow control member 1367 disposed within the inner volume 1364. In this embodiment, the flow control member 1367 can be, for example, an insert or funnel that defines a channel 1368 configured to receive a flow of fluid from the lumen 1339 of the puncture member 1338. More specifically, as shown in FIG. 33, a first end of the flow control member 1367 can be disposed adjacent to and/or can be coupled to the port 1363 and a second end, opposite the first end, can extend toward an inner surface of the fluid reservoir 1360. In this manner, the second end of the flow control member 1367 can be adjacent to the inner surface of the fluid reservoir 1360 such that an axis associated with a portion of the

channel 1368 at or near the second end is substantially parallel to and/or otherwise directed toward the inner surface of the fluid reservoir 1360.

[1136] In use, the adapter 1330 and/or the fluid reservoir 1360 can be manipulated to insert the puncture member 1338 through the port 1363 of the fluid reservoir 1360. As such, the sheath 1341 disposed about the puncture member 1338 can deform to allow the puncture member 1338 to be inserted through the port 1363. With the fluid reservoir 1360 being an evacuated container, the insertion of the puncture member 1338 is such that a negative pressure within the fluid reservoir 1360 is exerted through the lumen 1334 of the adapter 1330 (e.g., via the lumen 1339 of the puncture member 1338). Thus, when the distal end portion 1332 is fluidically coupled (either directly or indirectly) to a device or member in fluid communication with the body of a patient, the negative pressure draws a volume of bodily-fluid (e.g., blood) from the patient and into the fluid reservoir 1360. More specifically, the distal end portion 1332 of the adapter 1330 can be coupled (either directly or indirectly) to any suitable adapter, restrictor, and/or needle described herein to receive a flow of, for example, blood from the patient with reduced or substantially no hemolyzation of the blood. Furthermore, by disposing the flow control member 1367 in the inner volume 1364, a flow of blood can be directed within the channel 1338 toward the inner surface, which in turn, can decrease a force otherwise associated with an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1137] While the adapter 1330 is shown in FIGS. 31-33 as not including and/or not be coupled to the shroud 1343, in other embodiments, the adapter 1330 can be coupled to the shroud 1343 when engaging the fluid reservoir 1360. Furthermore, while the flow control member 1367 is particularly shown in FIG. 33, in some embodiments, a second end of a flow control member can extend within the inner volume 1364 to a position adjacent to and/or substantially abutting a bottom or proximal surface (i.e., a surface opposite the port 1363). In other embodiments, a flow control member can extend in a spiral or helical manner from the port 1363. As such, a second end of the flow control member can be substantially tangential to the inner surface of the fluid reservoir and thus, fluid exiting a channel defined by the flow control member can flow along a circumference of the inner surface (e.g., tangent to the inner surface).

[1138] In other embodiments, a fluid reservoir can include any suitable flow control member. For example, FIG. 34 illustrates a fluid reservoir 1460 according to another embodiment. The fluid reservoir 1460 includes a proximal end portion 1461 and a distal end portion 1462, and defines an inner volume 1464. The distal end portion 1462 includes a port 1463 configured to receive, for example, a puncture member 1438 of an adapter 1430, as described in detail above with reference to FIGS. 31-33. The inner volume 1464 of the fluid reservoir 1460 includes and/or houses a flow control member 1467 operable to control a flow of fluid from, for example, the adapter 1430 into the inner volume 1464, as described in further detail herein. The fluid reservoir 1460 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1460 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any other type of container, vial, bottle, reservoir, etc. In some embodiments, the fluid reservoir 1460 can be substantially similar to or the same as the fluid reservoir 1360 described above with reference to FIGS. 31-33. Thus, such similar aspects of the fluid reservoir 1460 are not described in further detail herein.

[1139] The fluid reservoir 1460 can differ from the fluid reservoir 1360, however, in the arrangement of the flow control member 1467. More specifically, while the flow control member 1367 is shown in FIG. 33 as tapering to a substantially uniform diameter as the flow control member 1367 extends away from the port 1363, in this embodiment, the flow control member 1467 has a varying diameter as the flow control member 1467 extends away from the port 1463. In this manner, a channel 1468 defined by the flow control member 1467 has a cross-sectional area and/or diameter that is dependent on, for example, a position along a longitudinal centerline CL defined by the flow control member 1467. For example, the channel 1468 can have a first diameter at a first end portion nearest to the port 1463, a second diameter at an end portion opposite the first end portion, and a third diameter at a portion disposed therebetween. As shown in FIG. 34, the end portions of the flow control member 1467 can be flared or the like such that the first diameter and the second diameter are each greater than the third diameter. Said another way, the diameter of the channel 1468 can taper along the longitudinal centerline CL from a larger diameter associated with the end portions of the flow control member 1467 to a smaller diameter at or near a center portion of the flow control member 1467.

[1140] With the fluid reservoir 1460 being an evacuated container or the like, a pressure (i.e., a negative pressure) within the channel 1468 is dependent on a position along the longitudinal centerline CL. That is to say, the pressure within the channel 1468 is dependent on the diameter of the channel 1468, in which a larger diameter is associated with a larger pressure. In a similar manner, the velocity of a flow of bodily-fluid (e.g., blood) within the channel 1468 is also dependent on the diameter of the channel 1468, however, such dependency is inverse to that associated with the pressure (i.e., a larger diameter is associated with less velocity). Thus, as blood (or other bodily-fluid) flows through the channel 1468, the increase in diameter at the end portion of the flow control member 1467 opposite the port 1463 results in a decrease in velocity associated with the flow of bodily-fluid therethrough. As such, a force otherwise associated with a volume of blood contacting an inner surface of the fluid reservoir 1460 is reduced, which in turn, can reduce and/or substantially prevent hemolysis of the volume of blood. Moreover, the diameter of the channel 1468 can be such that a pressure within the channel 1468 is maintained below a threshold that can otherwise result in hemolysis of blood flowing therethrough.

[1141] While the flow control members 1367 and 1467 are shown and described above as controlling a flow of, for example, blood through the channels 1368 and 1468, respectively, in other embodiments, a fluid reservoir can include a flow control member having any suitable configuration. For example, FIG. 35 illustrates a fluid reservoir 1560 according to another embodiment. The fluid reservoir 1560 includes a proximal end portion 1561 and a distal end portion 1562, and defines an inner volume 1564. The distal end portion 1562 includes a port 1563 configured to receive, for example, a puncture member 1538 of an adapter 1530, as described in detail above with reference to FIGS. 31-33. The inner volume 1564 of the fluid reservoir 1560 includes and/or houses a flow control member 1565 operable to control a flow of fluid from, for example, the adapter 1530 into the inner volume 1564, as described in further detail herein. The fluid reservoir 1560 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1560 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any other type of container, vial, bottle, reservoir, etc. In some embodiments, the fluid reservoir 1560 can be substantially similar to or the same as the fluid reservoir 1360 described above with reference to FIGS. 31-33. Thus, such similar aspects of the fluid reservoir 1560 are not described in further detail herein.

[1142] As shown in FIG. 35, the flow control member 1565 is disposed within the inner volume 1564 at or near the port 1563. In this embodiment, the flow control member 1565 is a baffle insert or the like. Specifically, the flow control member 1565 forms and/or includes an angled baffle having a set of substantially parallel angled surfaces configured to direct a flow of blood or other bodily-fluid. For example, the puncture member 1538 of the adapter 1530 can be inserted through the port 1563 to place a distal end portion of the puncture member 1538 within the flow control member 1565. As such, when a flow of blood is expelled and/or drawn through a lumen defined by the puncture member 1538 (e.g., via a negative pressure differential produced by the evacuated container), the flow of blood contacts at least one angled surface of the flow control member 1565. Thus, the blood can flow along the angled surface toward an inner surface of the fluid reservoir 1560. By diverting, guiding, and/or otherwise directing the flow of blood to the inner surface, a force is reduced, which can otherwise result from an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1143] While the flow control member 1565 is shown and described as forming and/or including a set of parallel angled surfaces configured to direct a flow of bodily-fluid toward the inner surface of the fluid reservoir 1560, in other embodiments, a flow control member can be any suitable baffle or the like. For example, in some embodiments, a flow control member can be an angled baffle or the like having a set of angled surfaces with an alternating orientation or the like. By way of example, a flow control member can include a first set of angled surfaces with a cross-sectional orientation (as shown in FIG. 35) that forms a 30° with a given plane and a second set of angled surfaces with a cross-sectional orientation that forms a 150° orientation with the given plane (i.e., a mirrored orientation), with each angled surface of the first set being disposed between two angled surfaces of the second set (or vice versa). In some embodiments, a baffle can include a set of surfaces that are each substantially V-shaped or U-shaped.

[1144] In other embodiments, a flow control member can be an absorbent or porous baffle or the like that can fill at least a portion of an inner volume of a fluid reservoir. In this manner, a flow of blood can be expelled or drawn from a lumen of an adapter (e.g., a lumen of a puncture member or the like) and absorbed by the absorbent baffle. In such embodiments, a volume of blood can be subsequently released or expelled from the absorbent

baffle via a centripetal or centrifugal action and/or the like. In some embodiments, a flow control member can be a baffle including a set of angled surfaces with an absorbent material disposed therebetween.

[1145] While the flow control members 1367, 1467, and 1565 are shown as independent components disposed within the fluid reservoirs 1360, 1460, and 1560, respectively, in other embodiment, a fluid reservoir can include a flow control member that is integral with another portion of the fluid reservoir such as, for example, a port. For example, FIG. 36 illustrates a fluid reservoir 1660 according to another embodiment. The fluid reservoir 1660 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 1660 is an evacuated container such as a Vacutainer™, a BacT/ALERT® SN, a BacT/ALERT® FA, and/or any of type of container, vial, bottle, reservoir, etc. In some embodiments, the fluid reservoir 1660 can be substantially similar to or the same as the fluid reservoir 1360 described above with reference to FIGS. 31-33. Thus, such similar aspects of the fluid reservoir 1660 are not described in further detail herein.

[1146] The fluid reservoir 1660 includes a proximal end portion 1661 and a distal end portion 1662, and defines an inner volume 1664. The distal end portion 1662 includes a port 1663 configured to receive, for example, a puncture member 1638 of an adapter 1630, as described in detail above with reference to FIGS. 31-33. The port 1663 in this embodiment, however, includes an inner surface 1665 configured to control a flow of fluid into the inner volume 1664 of the fluid reservoir 1660. As shown in FIG. 36, the inner surface 1665 of the port 1663 has a varied diameter that forms a constriction disposed between a proximal end portion and a distal end portion of the port 1663. For example, in some embodiments, the inner surface 1665 can form a constriction or otherwise can have a reduced diameter at or near a center of the port 1663 (i.e., at or near a midpoint between the proximal end portion and the distal end portion of the port).

[1147] In some embodiments, the inner surface 1665 can have a reduced diameter at a position that is proximal to the puncture member 1638 when the adapter 1630 is engaged with the fluid reservoir 1660. Similarly stated, the arrangement of the fluid reservoir 1660 and the adapter 1630 is such that when the adapter 1630 engages the fluid reservoir 1660, the puncture member 1638 is disposed in a distal position relative to a portion of the inner surface 1665 associated with the smallest diameter. Thus, the arrangement of the inner surface 1665 of the port 1663 can, for example, result in a venturi effect within a volume of

bodily-fluid as the volume of bodily-fluid flows from the puncture member 1638 into the port 1663. In other words, with the inner surface 1665 forming a constriction and/or reduction in diameter, a pressure associated with a volume on opposite sides of the constriction and/or reduction in diameter can be controlled. For example, the fluid reservoir 1660, being an evacuated container, defines a negative pressure within a portion of the inner volume 1664 proximal to the portion of the inner surface 1665 having the reduced diameter. In some embodiments, the constriction and/or reduced diameter formed by the inner surface 1665 results in a corresponding decrease in pressure associated with the reduced diameter. Thus, by selectively controlling a portion of the inner surface 1665 that is distal to the reduced diameter (i.e., selectively increasing the diameter of the inner surface 1665) a pressure within a volume distal to the reduced diameter can be less than, for example, the pressure within the volume proximal to the reduced diameter. Thus, hemolysis within a flow of blood is reduced or substantially prevented that might otherwise result from a rapid exposure to the negative pressure differential produced by the fluid reservoir 1660.

[1148] While the flow control members 1367, 1467, 1565, and the port 1663 are shown and described above as receiving and/or otherwise guiding a flow of bodily-fluid (e.g., blood) into the inner volumes 1364, 1464, 1564, 1664, respectively, in some embodiments, an adapter can be arranged to selectively direct a flow of bodily-fluid into a fluid reservoir. For example, FIGS. 37 and 38 illustrate an adapter 1760, according to another embodiment. The adapter 1760 is configured for selective engagement with a fluid reservoir 1760 to deliver a flow of bodily-fluid into an inner volume 1764. The adapter 1760 includes at least a shroud 1743 and a puncture member 1768. Although not shown in FIGS. 37 and 38, an inner surface of the adapter 1760 can be substantially similar to or the same as the inner surface 1363 of the adapter 1360 described above with reference to FIG. 30. That is to say, the adapter 1760 can include an inner surface that defines a substantially smooth transition between, for example, a lumen associated with an inlet of the adapter 1760 (e.g., a catheter, cannula, and/or locking mechanism) and a lumen of the puncture member 1768, thereby reducing and/or substantially preventing hemolysis of blood flowing therethrough.

[1149] As shown in FIG. 38, the arrangement of the adapter 1760 is such that the puncture member 1768 is disposed at non-orthogonal orientation relative to the shroud 1743. More specifically, at least a portion of the puncture member 1768 extends within an inner volume 1744 of the shroud 1743 and toward an inner surface. Thus, when the fluid reservoir

1760 is inserted into the inner volume 1744 of the shroud 1743, the puncture member 1768 punctures a port 1763 of the fluid reservoir 1760 (e.g., substantially similar to the port 1363 of the fluid reservoir 1360 described above with reference to FIGS. 31-33) at a substantially non-orthogonal angle. For example, the fluid reservoir 1760 can be inserted into the inner volume 1743 of the shroud 1744 with a substantially parallel or orthogonal orientation relative thereto. As the fluid reservoir 1760 is moved in the distal direction, the port 1763 is brought into contact with the puncture member 1768 and with the fluid reservoir 1760 parallel or orthogonal to the shroud 1743, the puncture member 1768 punctures the port 1763 at an angle associated with the orientation of the puncture member 1768 relative to the shroud (e.g., non-orthogonal). Therefore, as shown in FIG. 38, an end portion of the puncture member 1768 can be adjacent to, in contact with, and/or otherwise near an inner surface of the reservoir 1760 defining the inner volume 1764. In this manner, directing the flow of blood to the inner surface reduces a force, which can otherwise result from an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1150] In some embodiments, the adapter 1730 can be configured to engage, for example, a standard fluid reservoir such as, for example, a Vacutainer ™ or the like. That is to say, in some embodiments, the adapter 1730 is configured to be compatible with existing fluid reservoirs without modifications being made thereto. In other embodiments, a fluid reservoir can have any suitable configuration. For example, FIG. 39 illustrates an adapter 1830 physically and fluidically coupled to a fluid reservoir 1860 according to another embodiment. The adapter 1830 can be any suitable adapter such as, for example, the adapter 1330 described above with reference to FIGS. 29 and 30. In this manner, the adapter 1830 includes a puncture member 1838 configured to puncture a port or the like of the fluid reservoir 1860, as described in further detail herein.

[1151] The fluid reservoir 1860 includes a proximal end portion 1861 and a distal end portion 1862, and defines an inner volume (not shown in FIG. 39). The distal end portion 1862 includes a port 1863 configured to receive, for example, the puncture member 1838 of the adapter 1830, as described in detail above with reference to FIGS. 31-33. The port 1863 in this embodiment, however, is disposed in a substantially horizontal position. More specifically, in some embodiments, the port 1863 can be disposed in a substantially tangential arrangement relative to, for example, an inner surface of the fluid reservoir 1860. Thus,

when the puncture member 1838 is inserted through the port 1863, an end portion of the puncture member 1838 can be placed adjacent to, at, or substantially near a portion of the inner surface of the fluid reservoir 1860, as described above with reference to the adapter 1730 and fluid reservoir 1760. Similarly stated, the arrangement of the port 1863 can be such that when the puncture member 1838 is inserted therethrough, at least the end portion of the puncture member 1838 (not shown in FIG. 39) is in a tangential orientation relative to the inner surface of the fluid reservoir 1860. In this manner, directing a flow of blood to the inner surface reduces a force, which can otherwise result from an impact of the volume of blood contacting the inner surface. Thus, hemolysis of the blood associated with such a contact is reduced or substantially prevented.

[1152] While a flow of bodily-fluid (e.g., blood) into the fluid reservoirs 1360, 1460, 1560, 1660, 1760, and 1860 is described above as being passively controlled by, for example, the flow control members 1367, 1467, 1565, the port 1663, the adapter 1730, and/or the port 1863, respectively, in other embodiments, a flow of bodily-fluid into a fluid reservoir can be actively controlled. That is to say, while the flow of bodily-fluid into the fluid reservoirs 1360, 1460, 1560, 1660, 1760, 1860 is controlled without user intervention (i.e., beyond the intervention of coupling the adapters 1330, 1430, 1530, 1660, 1760, and 1860 to the fluid reservoirs 1360, 1460, 1560, 1660, 1760, and 1860 respectively), in other embodiments, a user can manipulate an adapter and/or fluid reservoir to actively control a flow of fluid into the fluid reservoir. For example, FIGS. 40-42 illustrate an adapter 1930 and a fluid reservoir 1960, according to another embodiment. The fluid reservoir 1960 can be any suitable reservoir that defines an inner volume 1964 configured to receive a flow of bodily-fluid such as, for example, an evacuated container or the like. More specifically, as described above with reference to the fluid reservoir 1360 in FIGS. 31-33, the fluid reservoir 1960 includes a port 1963 through which a portion of the adapter 1930 can be inserted to gain access to the inner volume 1964, as described in further detail herein.

[1153] As shown in FIGS. 40-42, the adapter 1930 includes a proximal end portion 1931 and a distal end portion 1932, and defines an inner volume 1934. Although not shown, the distal end portion 1932 of the adapter 1930 can be coupled to any suitable lumen-defining device such as a needle, cannula, catheter, and/or sterile flexible tubing. In some embodiments, the distal end portion 1932 can include a locking mechanism or the like that can physically and fluidically couple the adapter 1930 to any suitable corresponding device

and/or component. The proximal end portion 1931 of the adapter 1930 receives a portion of the fluid reservoir 1960. For example, as shown in FIGS. 41 and 42, at least a portion of the port 1963 is inserted through the proximal end portion 1931 of the adapter 1930 to be disposed within a portion of the inner volume 1934.

[1154] As shown in FIGS. 41 and 42, the adapter 1930 further includes a cannula 1935 and an actuator 1945. Specifically, the cannula 1935 extends through the proximal end portion 1931 and the distal end portion 1932 of the adapter 1930, thereby defining a fluid pathway through the adapter 1930. The cannula 1935 can be any suitable shape, size, or configuration. For example, in some embodiments, the cannula 1935 is a substantially flexible tube formed of a biocompatible plastic or the like. In this manner, at least a portion of the cannula 1935 can be manipulated (e.g., by the actuator 1945) to bend, flex, kink, and/or otherwise reconfigure the cannula 1935, as described in further detail herein. The arrangement of the cannula 1935 can be such that when the fluid reservoir 1960 is inserted into the inner volume 1934 of the adapter 1930, an end portion of the cannula 1935 punctures the port 1963 of the fluid reservoir 1960 and thus, places the inner volume 1964 of the fluid reservoir 1960 in fluid communication with a lumen defined by the cannula 1935. Thus, a negative pressure within the fluid reservoir 1960 (e.g., the fluid reservoir 1960 is an evacuated container) exerts or draws suction through the lumen defined by the cannula 1935, as described in further detail herein.

[1155] The actuator 1945 of the adapter 1930 can be any suitable configuration. For example, as shown in FIGS. 41 and 42, the actuator 1945 can be a trigger or the like coupled to the adapter 1930 via a pivot point, pin, axle, etc. More specifically, a first portion of the actuator 1945 extends from and/or beyond an outer surface of the adapter 1930 and a second portion is disposed within the inner volume 1934 defined by the actuator 1930. Thus, a user (e.g., a phlebotomist, doctor, technician, nurse, etc.) can actuate the actuator 1945 by pivoting the actuator 1945 relative to the adapter 1930. In this manner, a portion of the actuator 1945 disposed in the inner volume 1934 of the adapter 1930 can be increased or decreased, for example, by exerting a force or removing a force, respectively, on the actuator 1945 (i.e., pivoting the actuator 1945 relative to the adapter 1930).

[1156] As shown, the portion of the actuator 1945 disposed within the inner volume 1934 of the adapter 1930 defines an opening 1946 through which the cannula 1935 can extend. Therefore, actuating the actuator 1945 (e.g., pivoting the actuator 1945 relative to the adapter

1930) results in a corresponding manipulation of a portion of the cannula 1935. For example, in some instances, while the actuator 1945 is in a first configuration, the position of the opening 1946 relative to the adapter 1930 can be such that the cannula 1935 (disposed therein) is pulled, bent, bowed, deformed, kinked, etc. Such deformation of the cannula 1935 can result in, for example, a constriction and/or pinching of the cannula 1935, which in turn, can constrict and/or at least partially obstruct the lumen defined by the cannula 1935, as shown in FIG. 41.

[1157] Conversely, a force can be exerted to actuate the actuator 1945, thereby pivoting the actuator 1945 relative to the adapter 1930. As described above, such pivoting motion can, for example, increase a portion of the actuator 1945 disposed in the inner volume 1934, which in turn, can change the position and/or orientation of the opening 1946 relative to the adapter 1930. Thus, the repositioning and/or reorienting of the opening 1946 actively (e.g., by exerting a force) or passively (e.g., by removing or reducing an existing force) reconfigures at least the portion of the cannula 1935 disposed therein. For example, as shown in FIG. 42, when the actuator 1945 is placed in the second configuration, the cannula 1935 can be substantially straight or substantially undeformed. Thus, the lumen defined by the cannula 1935 is substantially unobstructed and/or otherwise not constricted by the actuator 1945.

[1158] In use, when the fluid reservoir 1960 is placed in fluid communication with the lumen defined by the cannula 1935 (see e.g., FIGS. 41 and 42), the negative pressure and/or suction (described above) within the lumen of the catheter 1935 can be modulated by actuating the actuator 1945 between its first configuration, associated with a smaller amount of suction, and its second configuration, associated with a larger amount of suction. Moreover, when the distal end portion 1932 of the adapter 1930 is placed in fluid communication with the body of a patient (e.g., either directly or indirectly via a lumen-defining device, a needle, etc.), the negative pressure within the fluid reservoir 1960 draws blood, or other bodily-fluids, through the lumen defined by the cannula 1935 and into the inner volume 1964. In this manner, actuating the actuator 1945 to control or modulate the amount of suction or negative pressure within the lumen of the cannula 1935 can reduce a magnitude of negative pressure that would otherwise be exerted on the flow of blood. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the fluid reservoir 1960.

[1159] Although the lumen of the cannula 1935 is shown in FIG. 41 as being partially constricted when the actuator 1945 is in its first configuration, in other embodiments, the actuator 1945 can deform the cannula 1935 a sufficient amount to result in a substantially complete constriction of the lumen. Moreover, while not shown in FIGS. 40-42, in some embodiments, the actuator 1945 can include and/or can be operably coupled to a bias member such as a spring or the like. As such, the bias member can exert a force that at least temporarily maintains the actuator 1945 in, for example, the first configuration until an actuating force is exerted on the actuator 1945, which is sufficient to overcome the force of the bias member.

[1160] While the adapter 1930 is shown and described above as controlling a flow of bodily-fluid into the fluid reservoir 1960 by manipulating the cannula 1935, in other embodiments, an adapter can control a flow of bodily-fluid into a fluid reservoir in any suitable manner. For example, FIGS. 43 and 44 illustrate an adapter 2030 and a fluid reservoir 2060, according to another embodiment. The fluid reservoir 2060 can be any suitable reservoir that defines an inner volume 2064 configured to receive a flow of bodily-fluid such as, for example, an evacuated container or the like. More specifically, as described above with reference to the fluid reservoir 1360 in FIGS. 31-33, the fluid reservoir 2060 includes a port 2063 through which a portion of the adapter 2030 can be inserted to gain access to the inner volume 2064, as described in further detail herein.

[1161] As shown in FIGS. 43 and 44, the adapter 2030 includes a proximal end portion 2031 and a distal end portion 2032. The proximal end portion 2031 of the adapter 2030 is open and/or defines an opening configured to receive at least a portion of the port 2063 of the fluid reservoir 2060. The distal end portion 2032 of the adapter 2030 includes a port 2033 or the like that can be coupled to any suitable lumen-defining device such as a cannula, catheter, and/or sterile flexible tubing (not shown in FIGS. 43 and 44). In some embodiments, the distal end portion 2032 can include a locking mechanism or the like fluidically coupled to the port 2033 and configured to physically and fluidically couple the adapter 2030 to any suitable corresponding device and/or component.

[1162] As shown in FIG. 44, the adapter 2030 includes a puncture member 2038 that extends from a surface of the adapter 2030 to, for example, puncture the port 2063 of the fluid reservoir 2060. Furthermore, the adapter 2030 defines a lumen 2036 that extends through a portion of the adapter 2030 to fluidically couple the port 2033 to the puncture

member 2038. Thus, the puncture member 2038 can puncture the port 2063 of the fluid reservoir 2060 to place the inner volume 2064 of the fluid reservoir 2060 in fluid communication with, for example, the port 2033 of the adapter 2030, which in turn, can be in fluid communication (e.g., either directly or indirectly via an intervening structure) a portion of the body of a patient. Moreover, a negative pressure within the fluid reservoir 2060 (e.g., the fluid reservoir 2060 is an evacuated container) exerts or draws suction through the lumen 2036 and the port 2033 of the adapter 2030 to, for example, draw a flow of bodily-fluid from the patient through the adapter 2030 and into the inner volume 2064 of the fluid reservoir 2060.

[1163] As shown in FIGS. 43 and 44, the arrangement of the adapter 2030 is such that the fluid reservoir 2060 is in a substantially vertical orientation when coupled to the adapter 2030. Thus, when a volume of bodily-fluid (e.g., blood) is expelled from the puncture member 2038, in response to the negative pressure within the fluid reservoir 2060, the bodily-fluid flows in a substantially vertical direction from a lower position to an upper position. While the fluid reservoir 2060 defines a negative pressure that produces a suction force operable in drawing a flow of bodily-fluid from the puncture member 2038, the bodily-fluid expelled therefrom is also exposed to a substantially opposing force associated with gravitational acceleration (i.e., approximately 9.81 meters-per-second-squared ($^{m}/_{s^2}$)). Thus, when a volume of blood is drawn through the adapter 2030 and into the inner volume 2064 of the fluid reservoir 2060, the force associated with gravity acts to slow a velocity of the flow of blood within the inner volume 2064. As such, hemolysis of blood is reduced and/or substantially prevented that can otherwise result from a force associated with a volume of blood impacting an inner surface of the fluid reservoir 2060 defining the inner volume 2064.

[1164] While the adapters and fluid reservoirs described above with reference to FIGS. 27-44 control and/or direct a flow of fluid (i.e., blood) into a fluid reservoir to, for example, reduce hemolysis, in some embodiments, the arrangement of a fluid reservoir and/or an adapter can be such that a negative pressure operable in drawing a volume of blood into the fluid reservoir can be configured modulated and/or controlled. For example, FIGS. 45-60 illustrate embodiments configured to mitigate the risk of hemolysis associated with blood flow to a negative pressure differential within a fluid reservoir. Specifically, FIG. 45 illustrates an adapter 2130 and a fluid reservoir 2160 according to another embodiment. The adapter 2130 can be any suitable adapter such as, for example, the adapter 1330 described

above with reference to FIGS. 29 and 30. In this manner, the adapter 2130 includes a puncture member 2138 configured to puncture a port or the like of the fluid reservoir 2160, as described in further detail herein. The fluid reservoir 2160 includes a proximal end portion 2161 and a distal end portion 2162, and defines an inner volume 2164. The proximal end portion 2161 includes a port 2163A configured to receive, for example, an output member (e.g., a needle, puncture member, cannula, etc.) from, for example, a vacuum source or the like, as described in further detail herein. Similarly, the distal end portion 2162 includes a port 2163 configured to receive, for example, the puncture member 2138 of the adapter 2130, as described in detail above with reference to FIGS. 31-33. In some embodiments, the ports 2163A and 2163 can be substantially similar in form and/or function. In some embodiments, the port 2163A disposed at or near the proximal end portion 2161, for example, can include a frangible seal, a self-healing port, a one-way valve, and/or the like.

[1165] As shown in FIG. 45, the fluid reservoir 2160 includes an elastomeric member 2178 (and/or any other suitable member or material) disposed within the inner volume 2164. The elastomeric member 2178 is in contact with an inner surface of the fluid reservoir 2160 (defining at least a portion of the inner volume 2164) to form a substantially fluid tight seal therebetween. Thus, a portion of the inner volume 2164 that is proximal to the elastomeric member 2178 is substantially fluidically isolated from a portion of the inner volume 2164 that is distal to the elastomeric member 2178. In some embodiments, the portion of the inner volume 2164 disposed between the elastomeric member 2178 and the port 2163 (i.e., disposed at the distal end portion 2162 of the fluid reservoir 2160) can define, for example, a negative pressure, prior to the insertion of the puncture member 2138 through the port 2163. In other embodiments, both portions of the inner volume 2164 (e.g., on either side of the elastomeric member 2178) define a negative pressure, prior to the insertion of the puncture member 2138 through the port 2163. In still other embodiments, the inner volume 2164, in its entirety, need not define a negative pressure, prior to the insertion of the puncture member 2138 through the port 2163.

[1166] As shown in FIG. 45, the plunger 2145 can "float" and/or otherwise be disposed in a substantially fixed position within the inner volume 2164 prior to the port 2163A being fluidically coupled to a vacuum source (not shown in FIG. 45). Moreover, the arrangement of the fluid reservoir 2160 is such that when the actuator 2130 engages the fluid reservoir 2160, the puncture member 2138 is in a distal position relative to the elastomeric member

2178 and thus, substantially fluidically isolated from the portion of the inner volume 2164 that is proximal to the elastomeric member 2178. In a similar manner, the fluid reservoir 2160 can be manipulated such that an outlet of a vacuum source (not shown in FIG. 45) punctures and/or is otherwise inserted through the port 2163A to be placed in fluid communication with the portion of the inner volume 2164 proximal to the elastomeric member 2178. Thus, a user can actuate the vacuum source (e.g., via an electric switch, a pre-charged negative pressure created in a manufacturing process, mechanical actuation, and/or the like), such that the vacuum source draws a vacuum (e.g., a suction force) through its output and into the portion of the inner volume 2164 proximal to the elastomeric member 2178.

[1167] In some instances, the suction force and/or negative pressure can be sufficient to overcome a friction force between the elastomeric member 2178 and the inner surface, thereby resulting in a movement of the elastomeric member 2178 within the inner volume 2164 towards the port 2163A. The movement of the elastomeric member 2178 results in a change in volume associated with the portions of the inner volume 2164 disposed on either side of the elastomeric member 2178. In some instances, the increase in volume of the portion of the inner volume 2164 distal to the elastomeric member 2178 results in a negative pressure that is sufficient to draw a flow of bodily-fluid through the puncture member 2138 and into the inner volume 2164. As such, in some instances, a rate and/or magnitude of the vacuum drawn by the vacuum source can be controlled to, for example, change a characteristic associated with a pressure difference within the inner volume 2164 of the fluid reservoir 2160 and, for example, the adapter 2130. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the fluid reservoir 2160.

[1168] While the elastomeric member 2178 is shown and described above as "floating" within the inner volume 2164, in other embodiments, a fluid reservoir can include an elastomeric member and/or the like that is coupled to a plunger. For example, FIG. 46 illustrates an adapter 2230 and a fluid reservoir 2260 according to another embodiment. The adapter 2230 can be any suitable adapter such as, for example, the adapter 1330 described above with reference to FIGS. 29 and 30. In this manner, the adapter 2230 includes a puncture member 2238 configured to puncture a port or the like of the fluid reservoir 2260, as described in further detail herein.

[1169] The fluid reservoir 2260 includes a proximal end portion 2261 and a distal end portion 2262, and defines an inner volume 2264. The proximal end portion 2261 includes a port 2263A configured to be coupled to, for example, a vacuum source or the like, as described in further detail herein. Similarly, the distal end portion 2262 includes a port 2263 configured to receive the puncture member 2238 of the adapter 2230, as described in detail above with reference to FIGS. 31-33. In some embodiments, the ports 2263A and 2263 can be substantially similar in form and/or function. In some embodiments, the port 2263A disposed at or near the proximal end portion 2261, for example, can include a frangible seal, a self-healing port, a one-way valve, a locking mechanism, and/or the like. Thus, the port 2263A can physically and fluidically couple to a corresponding outlet port of a vacuum source (not shown in FIG. 46). For example, in some embodiments, an outlet port of a vacuum source and the port 2263A can form a threaded coupling or the like. In such embodiments, when the vacuum source is actuated, the port 2263A can be transitioned from a first, substantially sealed configuration to a second, substantially open configuration.

[1170] As shown in FIG. 46, the fluid reservoir 2260 includes a plunger 2275 disposed within the inner volume 2264. The plunger 2275 includes and/or is coupled to an elastomeric member 2278 disposed within the inner volume 2264. The elastomeric member 2278 is in contact with an inner surface of the fluid reservoir 2260 (defining at least a portion of the inner volume 2264) to form a substantially fluid tight seal therebetween. Thus, a portion of the inner volume 2264 that is proximal to the elastomeric member 2278 is substantially fluidically isolated from a portion of the inner volume 2264 that is distal to the elastomeric member 2278, as described above with reference to the elastomeric member 2178 in FIG. 46. In this embodiment, at least a portion of the plunger 2275 is movably disposed within a support member 2264A extending from a surface of the fluid reservoir 2260. As shown, the support member 2264A can, for example, divide the inner volume into a first portion and a second portion. Moreover, the support member 2264A can include a seal or the like that is in contact with an outer surface of the plunger to form a substantially fluid tight seal therebetween. Thus, the first portion of the inner volume 2264 can be substantially isolated from the second portion of the inner volume 2264.

[1171] The arrangement of the fluid reservoir 2260 is such that when the actuator 2230 engages the fluid reservoir 2260, the puncture member 2238 is in a distal position relative to the elastomeric member 2278 and thus, substantially fluidically isolated from the portion of

the inner volume 2264 that is proximal to the elastomeric member 2278. A user can similarly manipulate the fluid reservoir to couple the port 2263A to an outlet of a vacuum source (not shown in FIG. 46). In this manner, the portion of the inner volume 2264 that is proximal to the support member 2264A is placed in fluid communication with the vacuum source. Thus, a user can actuate the vacuum source (e.g., via an electric switch, a pre-charged negative pressure created in a manufacturing process, mechanical actuation, and/or the like) such that the vacuum source draws a vacuum (e.g., a suction force) through its output and into the portion of the inner volume 2264 proximal to the support member 2264A.

[1172] In some instances, the suction force and/or negative pressure can be sufficient to move the plunger 2275 within the inner volume 2264 towards the port 2263A. The movement of the plunger 2275 results in a corresponding movement of the elastomeric member 2278 and thus, changes a volume associated with the portions of the inner volume 2264 disposed on either side of the elastomeric member 2278. In some instances, the increase in volume of the portion of the inner volume 2264 distal to the elastomeric member 2278 results in a negative pressure that is sufficient to draw a flow of bodily-fluid through the puncture member 2238 an into the inner volume 2264. As such, in some instances, a rate and/or magnitude of the vacuum drawn by the vacuum source can be controlled to, for example, change a characteristic associated with a pressure difference within the inner volume 2264 of the fluid reservoir 2260 and, for example, the adapter 2230. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the movement of the plunger 2375 within the fluid reservoir 2260.

[1173] In some embodiments, the arrangement of the plunger 2275 and the support member 2264A can, for example, maintain a sterility of a portion of the inner volume 2264 distal to the support member 2264A. Specifically, as described above, the support member 2264A can include the seal that engages the outer surface of the plunger 2275 to fluidically isolate a portion of the inner volume 2264 proximal to the support member 2264A from a different portion of the inner volume 2264 distal to the support member 2264A. As such, when the port 2263A is placed in fluid communication with the vacuum source (not shown in FIG. 46), the portion of the inner volume 2264 proximal to the support member 2264A can be exposed, for example, to a non-sterile environment (e.g., associated with the vacuum source), while the sterility of the portion of the inner volume 2264 is maintained.

[1174] FIG. 47 illustrates an adapter 2330 and a fluid reservoir 2360 according to another embodiment. The adapter 2330 can be any suitable adapter such as, for example, the adapter 1330 described above with reference to FIGS. 29 and 30. In this manner, the adapter 2330 includes a puncture member 2338 configured to puncture a port or the like of the fluid reservoir 2360, as described in further detail herein.

[1175] The fluid reservoir 2360 includes a proximal end portion 2361 and a distal end portion 2362, and defines an inner volume 2364. The proximal end portion 2361 includes a port 2363A configured to be coupled to, for example, a vacuum source or the like, as described in further detail herein. Similarly, the distal end portion 2362 includes a port 2363 configured to receive the puncture member 2338 of the adapter 2330, as described in detail above with reference to FIGS. 31-33. As shown in FIG. 47, the fluid reservoir 2360 includes a plunger 2375 disposed within the inner volume 2364. The plunger 2375 includes and/or is coupled to an elastomeric member 2378 disposed within the inner volume 2364. The elastomeric member 2378 is in contact with an inner surface of the fluid reservoir 2360 (defining at least a portion of the inner volume 2364) to form a substantially fluid tight seal therebetween. As such, the fluid reservoir 2360 can be substantially similar to the fluid reservoir 2260 described above with reference to FIG. 46.

[1176] The fluid reservoir 2360 can differ from the fluid reservoir 2260, however, by including a bias member 2377 (e.g., a linear spring, a torsion spring, a leaf spring, a compression member, and/or the like) disposed about and in contact with a portion of the plunger 2375. In this manner, when the port 2363A is physically and fluidically coupled to an outlet of a vacuum source (not shown in FIG. 47) and the vacuum source is actuated, the vacuum source draws a vacuum (e.g., a suction force) through its output and into the portion of the inner volume 2364. Thus, the vacuum source can exert a suction force within a portion of the inner volume 2364 that results in a proximal movement of the plunger 2375. The arrangement of the bias member 2377, however, is such that the bias member 2377 exerts a reaction force in response to the movement of the plunger 2375. As such, the bias member 2377 can at least partially control a movement of the plunger 2375 within the inner volume 2364, for example, to reduce speed at which the plunger 2375 is moved. Thus, hemolysis of the blood is reduced or substantially prevented that might otherwise result from a rapid exposure to a negative pressure differential produced by the movement of the plunger 2375 within the fluid reservoir 2360.

[1177] While the adapters in the embodiments above have been shown and described as being physically and/or fluidically coupled to a corresponding fluid reservoir configured as an evacuated container, in other embodiments, an adapter can be configured to physically and/or fluidically couple to any suitable fluid reservoir and/or any suitable intervening structure. For example, FIGS. 49 and 50 illustrate an adapter 2430 according to another embodiment. The adapter 2430 can be any suitable shape or size and can be configured to be placed in fluid communication with any suitable fluid reservoir. For example, as described in further detail herein with reference to FIGS. 51 and 52, in some instances, the adapter 2430 can be physically and fluidically coupled to a fluid reservoir 2460 configured as, for example, a syringe or the like.

[1178] As shown in FIGS. 49 and 50, the adapter 2430 has a proximal end portion 2431 and a distal end portion 2432. In this embodiment, the distal end portion 2432 of the adapter 2430 includes, for example, a locking mechanism (e.g., a Luer Lok® or the like) that can physically and fluidically couple the adapter 2430 to a corresponding locking mechanism of any other suitable device such as, for example, an extension set or the like. In other embodiments, the distal end portion 2432 can be any suitable configuration such as, for example, a port, a septum, and/or the like. In a similar manner, the proximal end portion 2431 of the adapter 2430 includes, for example, a locking mechanism (e.g., a Luer Lok® or the like) that can physically and/to fluidically couple the adapter 2430 to, for example, the fluid reservoir 2460, as described in further detail herein.

[1179] The adapter 2430 includes a delivery member 2438 that extends from a portion of adapter 2430 toward the proximal end portion 2431. The delivery member 2438 defines a lumen 2439 extending at least partially through the delivery member 2438. More specifically, in this embodiment, the lumen 2439 extends through the distal end portion 2432 of the adapter 2430 but does not extend through the proximal end portion 2431. Similarly stated, the lumen 2439 does not extend through a proximal surface of the delivery member 2438. For example, as shown in FIGS. 49 and 50, the delivery member 2438 can have a substantially rounded or hemispherical proximal surface that is substantially closed and/or continuous. Alternatively, the delivery member 2438 defines at least one opening 2440 disposed along a circumference of the delivery member 2438 at a position distal to, for example, the proximal surface. Thus, while the delivery member 2438 does not define an

opening though a proximal most surface, opening(s) 2440 place a proximal end portion of the lumen 2439 in fluid communication with a volume outside of the delivery member 2438.

[1180] As described above, the adapter 2430 can be physically and fluidically coupled to the fluid reservoir 2460 (see e.g., FIG. 52). The fluid reservoir 2460 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2460 is a syringe or the like, as shown in FIG. 51. The fluid reservoir 2460 has a proximal end portion 2461 and a distal end portion 2462 and defines an inner volume 2464. The distal end portion 2462 is configured to be physically and fluidically coupled to an adapter such as, for example, the adapter 2430. For example, the distal end portion 2462 can include a locking mechanism (e.g., a Luer Lok® or the like) configured to be physically and fluidically coupled to the proximal end portion 2431 (e.g., the corresponding locking member included therein) of the adapter 2430. Moreover, when the adapter 2430 is coupled to the fluid reservoir 2460, the delivery member 2438 is at least partially disposed in the inner volume 2464 of the fluid reservoir 2460 and as such, the opening(s) 2440 defined by the delivery member 2438 place the lumen 2439 of the adapter 2430 in fluid communication with the inner volume 2464 of the fluid reservoir 2460, as described in further detail herein.

[1181] As shown in FIGS. 51 and 52, the proximal end portion 2461 movably receives a plunger 2475 that is at least partially disposed in the inner volume 2464, as described in further detail herein. As shown in FIG. 52, the fluid reservoir 2460 includes a seal member 2479 disposed within the inner volume 2464. More specifically, the seal member 2479 is disposed within a proximal portion of the inner volume 2464 and about a portion of the plunger 2475. As such, the seal member 2479 forms a substantially fluid tight seal between an inner surface of the fluid reservoir 2460 and an outer surface of the seal member 2479 and an outer surface of the plunger 2475 and an inner surface of the seal member 2479. Furthermore, the seal member 2479 defines an opening 2479A extending therethrough that can place a portion of the inner volume 2464 proximal to the seal member 2479 in fluid communication with a portion of the inner volume 2464 distal to the seal member 2479. The arrangement of the fluid reservoir 2460 is such that the seal member 2479 is maintained in a substantially fixed position when the plunger 2475 is moved within the inner volume 2464, as described in further detail herein.

[1182] As shown in FIG. 52, the plunger 2475 has a proximal end portion 2476 and a distal end portion 2477. The distal end portion 2477 of the plunger 2475 includes and/or is

coupled to an elastomeric member 2478 or the like. For example, in some embodiments, the elastomeric member 2478 can form a substantially fluid tight seal with an inner surface of the fluid reservoir 2460. As described above, the plunger 2475 is movably disposed within the inner volume 2464 of the fluid reservoir 2460. More specifically, the plunger 2475 can be moved within the inner volume 2464 in an axial direction between a first position (e.g., a distal position) and a second position (e.g., a proximal position) relative to the fluid reservoir 2460. For example, in some embodiments, the plunger 2475 can be disposed in a distal position relative to the fluid reservoir 2460 prior to use. A user can then manipulate the fluid reservoir 2460 and/or the plunger 2475 to move the plunger 2474 in a proximal direction within the inner volume 2464. With the elastomeric member 2478 in contact with the inner surface of the fluid reservoir 2460, the proximal movement of the plunger 2475 relative to the fluid reservoir 2460 produces a negative pressure within a portion of the inner volume 2464 that is distal to the elastomeric member 2478.

[1183] When the adapter 2430 is coupled to the fluid reservoir 2460 (as shown in FIG. 52), the negative pressure within the portion of the inner volume 2464 results in a suction through the lumen 2439 of the delivery member 2438. Thus, when the distal end portion 2431 of the adapter 2430 is coupled to a device or other intervening structure, which in turn, is in fluid communication with a portion of the body and/or intervening device (e.g. catheter, fluid reservoir, etc.), the suction force within the lumen 2439 can draw a bodily-fluid (e.g., blood) through the lumen 2439 and into the inner volume 2464 of the fluid reservoir 2460. Moreover, the arrangement of the seal member 2479 within the inner volume 2464 can reduce, limit, modulate, and/or otherwise at least partially control a rate at which the plunger 2479 can be moved within the inner volume 2464. For example, with the elastomeric member 2478 forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2460, the proximal movement of the plunger 2464 reduces and/or compresses a volume defined between the elastomeric member 2478 and the seal member 2479, which in turn, increases a pressure within that volume. Therefore, with the seal member 2479 similarly forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2460 and with an outer surface of the plunger 2475, air within the volume between the seal member 2479 and the elastomeric member 2478 is forced through the opening 2479A defined by the seal member 2479, thereby limiting the rate at which the plunger 2479 is moved within the inner volume 2464. As such, a negative pressure and/or a suction force drawn through the lumen 2439 of the adapter 2430 is correspondingly controlled and/or modulated.

[1184] As described above, in some embodiments, the arrangement of the delivery member 2438 can also limit and/or otherwise modulate a pressure and/or a suction force within the lumen 2439. In this manner, when withdrawing a volume of blood, hemolysis of the blood flowing through the lumen 2439 and into the inner volume 2464 of the fluid reservoir 2460 is reduced or substantially prevented. Specifically, the arrangement opening(s) 2440 and the lumen 2439 of the delivery member 2438 can, for example, reduce a negative pressure within the lumen 2439 and/or can slow a flow of blood delivered to the inner volume 2464 of the fluid reservoir 2460 to an extent that can reduce and/or substantially prevent hemolysis of the blood that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like. In addition, the arrangement of an inner surface defining the lumen 2439 can, for example, reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like.

[1185] While the fluid reservoir 2460 is particularly shown and described above with reference to FIGS. 51 and 52, in other embodiments, any suitable fluid reservoir can be coupled to, for example, the adapter 2430 to receive a volume of blood with reduced hemolysis of its constituents. For example, FIGS. 53 and 54 illustrate a fluid reservoir 2560 according to another embodiment. In this embodiment, the fluid reservoir 2560 is, for example, a syringe or the like having a proximal end portion 2561 and a distal end portion 2562 and defining an inner volume 2564. The distal end portion 2562 is configured to be physically and fluidically coupled to an adapter such as, for example, the adapter 1530, as described in detail above.

[1186] The proximal end portion 2561 of the fluid reservoir 2560 is substantially open and receives at least a portion of a plunger 2575. Moreover, the proximal end portion 2561 of the fluid reservoir 2560 includes an actuator 2570 that is operable in moving the plunger 2575 within the inner volume 2564. For example, as shown in FIGS. 53 and 54, the fluid reservoir 2560 includes a protrusion 2569 to which the actuator 2570 is pivotally coupled. More specifically, the actuator 2570 includes a first end portion 2571, a second end portion 2572, and a pivot portion 2573 disposed therebetween. The second end portion 2572 of the actuator 2570 is coupled to a portion of the plunger 2575, as described in further detail herein. The pivot portion 2573 is coupled to the protrusion 2569 via, for example, a pin, an axle, a rod, and/or the like configured to allow the actuator 2570 to pivot about the protrusion

2569 (e.g., about an axis defined by the protrusion 2569) in response to a force exerted on the first end portion 2571. In this manner, the actuator 2570 can be arranged, for example, as a trigger or the like which when actuated, is operable in moving the plunger 2575 relative to the fluid reservoir 2560, as described in further detail herein.

[1187] As shown in FIG. 54, the plunger 2575 has a proximal end portion 2576 and a distal end portion 2577. The distal end portion 2577 of the plunger 2575 includes and/or is coupled to an elastomeric member 2578 or the like. For example, in some embodiments, the elastomeric member 2578 can form a substantially fluid tight seal with an inner surface of the fluid reservoir 2560. As described above, the plunger 2575 is movably disposed within the inner volume 2564 of the fluid reservoir 2560. More specifically, the proximal end portion 2576 of the plunger 2575 is coupled to the second end portion 2572 of the actuator 2570 such that an actuation of the actuator 2570 results in a movement of the plunger 2570 within the inner volume 2564.

[1188] For example, a user can exert a force on the first end portion 2571 (e.g., with his or her thumb or finger) of the actuator 2570, which in turn, results in a pivoting motion about the protrusion 2569 that places the first end portion 2571 in a position closer to an outer surface of the fluid reservoir 2560 and places the second end portion 2572 in a corresponding position farther away from the fluid reservoir 2560. In other words, the pivoting of the actuator 2570 about the protrusion 2569 moves the second end portion 2572 in a proximal direction. Moreover, the trigger arrangement of the actuator 2570 (as described above) defines a range of motion through which the actuator 2570 can pivot and thus, defines a range of motion through which the plunger 2575 is moved in the proximal direction (i.e., a stroke length). As such, the user can serially actuate the actuator 2570 to move the plunger 2575 a desired distance in the proximal direction.

[1189] With the elastomeric member 2578 of the plunger 2575 forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2560, the proximal movement of the plunger 2575 relative to the fluid reservoir 2560 produces a negative pressure within a portion of the inner volume 2564 that is distal to the elastomeric member 2578. Thus, when the fluid reservoir is coupled to an adapter and/or any other suitable lumen-defining device in fluid communication with the body of a patient, the negative pressure results in a suction force within that lumen that can draw a bodily-fluid (e.g., blood) through the lumen and into the inner volume 2564 of the fluid reservoir 2560. Moreover, by limiting the stroke length

(as described above) of the plunger 2575, a rate at which the plunger 2575 can be moved within the inner volume 2564 is reduced, limited, modulated, and/or otherwise at least partially controlled. As a result, a negative pressure and/or a suction force drawn through, for example, the lumen of the lumen-defining device is correspondingly controlled and/or modulated. Therefore, by limiting the stroke of the plunger 2575, a negative pressure within the inner volume 2564 of the fluid reservoir 2560 and/or a rate at which blood (or other bodily-fluid) flows into the inner volume 2564 can be controlled to an extent that can reduce and/or substantially prevent hemolysis of the blood that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1190] While the actuator 2570 is particularly shown in FIGS. 52 and 53, in other embodiments, the actuator 2570 can be any suitable device, mechanism, and/or member that is operative in moving the plunger 2575 within the fluid reservoir 2560. For example, while actuator 2570 is described above as being actuated by a user's thumb or finger, in other embodiments, and actuator can include a first end portion that extends a given length of the fluid reservoir as to be engaged by a user's palm or more than one finger (e.g., each finger excluding the thumb of the user). In other embodiments, a fluid reservoir can include an actuator that is a switch, a push button, a toggle, and/or the like configured to close an electric circuit or the like when actuated. Thus, when the electric circuit is closed, a current can flow through the electric circuit, for example, to a mechanism (e.g., including an electric motor) configured to move a plunger within the fluid reservoir.

[1191] FIGS. 54-56 illustrate a fluid reservoir 2660 according to another embodiment. The fluid reservoir 2660 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2660 is a syringe or the like, as shown in FIG. 54. The fluid reservoir 2660 has a proximal end portion 2661 and a distal end portion 2662 and defines an inner volume 2664 (see e.g., 56). The distal end portion 2662 is configured to be physically and fluidically coupled to an adapter (not shown in FIGS. 54-56) such as, for example, the adapter 2430 described above with reference to FIGS. 48-51.

[1192] The proximal end portion 2661 of the fluid reservoir 2660 movably receives a plunger 2675 that is at least partially disposed in the inner volume 2664. As shown in FIGS. 55 and 56, the plunger 2675 has a proximal end portion 2676 and a distal end portion 2677. The distal end portion 2677 of the plunger 2675 includes and/or is coupled to an elastomeric member 2678 or the like. For example, in some embodiments, the elastomeric member 2678

can form a substantially fluid tight seal with an inner surface of the fluid reservoir 2660, as described in detail above. The proximal end portion 2676 of the plunger 2675 is coupled to an actuator 2670. For example, in some embodiments, at least a portion of the actuator 2670 can be hollow and configured to be movably disposed (e.g., in an axial direction) about the proximal end portion 2676 of the plunger 2675. Expanding further, the proximal end portion 2676 of the plunger 2675 includes a set of protrusions 2676A or the like (e.g., tabs, pins, bumps, etc.) configured to engage and/or otherwise disposed in a corresponding set of openings 2670A when the actuator 2670 is disposed about the proximal end portion 2676. In some embodiments, each protrusion 2676A can include an indicator or the like that can be viewable when disposed in a corresponding opening 2670A of the actuator 2670, as described in further detail herein.

[1193] As shown in FIGS. 55 and 56, the plunger 2675 includes a bias member 2674 (e.g., a linear spring, a torsion spring, and/or the like) disposed between the proximal end portion 2676 and the actuator 2670. In this manner, the bias member 2674 can, for example, maintain the actuator 2670 is a substantially fixed position relative to the proximal end portion 2676 until a force is exerted on the actuator 2670 or the plunger 2675 that is sufficient to overcome a force exerted by the bias member 2674. For example, in some embodiments, a user can manipulate the fluid reservoir 2660 to fluidically couple the distal end portion 2662, for example, to an adapter (e.g., the adapter 2430), which in turn can be directly or indirectly coupled to a device in fluid communication with a portion of the body. Thus, the inner volume 2664 of the fluid reservoir 2660 is placed in fluid communication with the portion of the body. With the fluid reservoir 2660 in fluid communication with the portion of the body, the user can manipulate the actuator 2670, for example, to move the plunger 2675 within the inner volume 2664. For example, a user can exert a force on the actuator 2670 to move the actuator 2670 and the plunger 2675 in the proximal direction relative to the fluid reservoir 2660. The arrangement of the bias member 2674 can be such that at least a portion of the force exerted by the user on the actuator 2670 transitions the bias member 2674 from a first configuration (e.g., a compressed configuration) to a second configuration (e.g., an extended configuration). Thus, the bias member 2674 can absorb at least a portion of the force (e.g., an excess portion of force above a predetermined threshold), exerted by the user, that would otherwise be exerted on the plunger 2675. In this manner, a rate at which the plunger 2675 is moved within the inner volume 2664 can be at least partially controlled and/or otherwise limited, which in turn, can reduce and/or substantially prevent hemolysis of the blood drawn

into the inner volume 2664 that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1194] In some embodiments, the arrangement of the protrusions 2676A of the proximal end portion 2676 within the openings 2670A of the actuator 2670, for example, can define a range of motion of the actuator 2670 relative to the plunger 2675 (e.g., can prevent a movement of the actuator 2675 beyond a predetermined threshold relative to the plunger 2675. In some embodiments, the protrusions 2676A can each include an indicator or the like that are viewable through the openings 2670A and therefore, can provide an indication to the user associated with the movement of the actuator 2670 relative to the plunger 2675. For example, in some embodiments, when a force is exerted on the actuator 2670 that is greater than a predetermined threshold, the actuator 2670 can be moved relative to the plunger 2675 and at least a portion of the force can transition the bias member 2674 from its first configuration to its second configuration. Thus, when the bias member 2674 is in its second configuration (e.g., an extended configuration), the actuator 2670 can be in a position relative to the plunger 2675 that is associated with at least a portion of the indicator of the protrusions 2676A being viewable through the openings 2670A. As such, the indicators can provide a visual indication of when a force exerted by the user exceeds a predetermined threshold. In some embodiments, the arrangement of the protrusions 2676A and the openings 2670A can be such that when a force exerted on the actuator 2670 exceeds the predetermined threshold, the plunger 2675 and/or the actuator 2670 also provide an auditory (e.g., a clicking sound) or a haptic indication.

[1195] While the actuators 2570 and 2670 are particularly shown and described above, in other embodiments, a fluid reservoir can include any suitable actuator operable in moving a plunger within an inner volume of the fluid reservoir. For example, FIGS. 57 and 58 illustrate a fluid reservoir 2760 according to another embodiment. The fluid reservoir 2760 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2760 is a syringe or the like, as shown in FIG. 57. The fluid reservoir 2760 has a proximal end portion 2761 and a distal end portion 2762 and defines an inner volume 2764 (see e.g., 56). The distal end portion 2762 is configured to be physically and fluidically coupled to an adapter (not shown in FIGS. 57 and 58) such as, for example, the adapter 2430 described above with reference to FIGS. 48-51. The proximal end portion 2761 of the fluid reservoir 2760 movably receives a plunger 2775 that is at least partially disposed in the inner

volume 2764. As shown in FIG. 58, the plunger 2775 has a proximal end portion 2776 and a distal end portion 2777. The distal end portion 2777 of the plunger 2775 includes and/or is coupled to an elastomeric member 2778 or the like, as described in detail herein. The proximal end portion 2776 of the plunger 2775 is coupled to an actuator 2770 operable in moving the plunger 2775 relative to the fluid reservoir 2760.

[1196] The actuator 2770 can be any suitable shape, size, or configuration. For example, as shown in FIGS. 57 and 58, the actuator 2770, in this embodiment, is a dial rotatably coupled to the fluid reservoir 2760 and the plunger 2775. More specifically, the actuator 2770 can be disposed about the proximal end portion 2761 of the fluid reservoir 2760 such that the actuator 2770 can rotate relative thereto without, for example, unthreading or removing the actuator 2770 from the fluid reservoir 2760. In other words, the actuator 2770 can be coupled to the proximal end portion 2761 of the fluid reservoir 2760 for rotational motion while substantially preventing a linear motion of the actuator 2770 relative to the fluid reservoir 2760. As shown in FIG. 58, an outer surface of the plunger 2775 includes and/or otherwise forms a set of continuous threads 2775A arranged in a helical manner along a length of the plunger 2775 (e.g., substantially the entire length). Moreover, a portion of the plunger 2775 is configured to extend through, for example, a threaded opening defined by the actuator 2770. Thus, the set of threads 2775A engage a surface of the actuator 2770 to define a threaded coupling therebetween, which can allow the plunger 2775 to be moved in an axial direction within the inner volume 2764 of the fluid reservoir 2760.

[1197] Specifically, in use, the fluid reservoir 2760 can be manipulated to couple the distal end portion 2762 to an adapter or other device in fluid communication with a portion of the body, thereby placing the inner volume 2764 of the fluid reservoir 2760 in fluid communication with the portion of the body and/or intervening device (e.g. catheter, etc.). With the inner volume 2764 in fluid communication with the portion of the body, the actuator 2770 can be rotated relative to the fluid reservoir 2760, which in turn, results in the threads 2775A being advanced along a surface of the actuator 2770. Thus, the plunger 2775 is moved in an axial direction (e.g., a proximal direction) within the inner volume 2764, which in turn, increases a portion of the inner volume 2764 that is distal to the elastomeric member 2778. Such an increase results in, for example, a negative pressure within the portion of the inner volume 2764 distal to the elastomeric member 2778 and therefore, a suction force is exerted that is operable in drawing a bodily-fluid (i.e., blood) into the inner volume 2764 of

the fluid reservoir 2760. In some embodiments, the arrangement of the actuator 2770 and the plunger 2775 (i.e., the threaded coupling) limits a rate at which the plunger 2775 is moved within the inner volume 2764. In this manner, limiting the rate at which the plunger 2775 is moved within the inner volume 2764 can reduce and/or substantially prevent hemolysis of the blood drawn into the inner volume 2764 that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1198] While the actuator 2770 is shown and described above as forming a threading coupling with the plunger 2775, in other embodiments, a fluid reservoir can include an actuator that is monolithically formed with a plunger. For example, FIG. 59 illustrates a fluid reservoir according to another embodiment. The fluid reservoir 2860 has a proximal end portion 2861 and a distal end portion 2862 and defines an inner volume 2864. The distal end portion 2862 is configured to be physically and fluidically coupled to an adapter (not shown in FIG. 59) such as, for example, the adapter 2430 described above with reference to FIGS. 48-51. In this embodiment, the fluid reservoir 2860 includes an outer surface that defines a set of continuous threads arranged in a helical manner along a length of the fluid reservoir 2860, as described above with reference to the plunger 2775 in FIG. 58.

[1199] The fluid reservoir 2860 is rotatably coupled to an actuator 2870. The actuator 2870 includes a proximal end portion 2871, a distal end portion 2872, and a plunger 2875. The actuator 2870 further includes an inner surface that defines a set of continuous threads 2899 (e.g., female threads or grooves) arranged in a helical manner along a length of the inner surface. In this manner, the actuator 2870 can be disposed about the fluid reservoir 2860 such that the set of threads 2860A of the fluid reservoir 2860 are disposed within the corresponding set of threads 2899 of the actuator 2870, while the plunger 2875 extends from the proximal end portion 2871 of the actuator 2870 within the inner volume 2864 of the fluid reservoir 2860. Moreover, as shown in FIG. 59, a distal end portion 2877 of the plunger 2875 includes and/or is coupled to an elastomeric member 2878 configured to form a substantially fluid tight seal with an inner surface of the fluid reservoir 2860, as described in detail herein.

[1200] Thus, in use, the fluid reservoir 2860 can be manipulated to couple the distal end portion 2862 to an adapter or other device in fluid communication with a portion of the body, thereby placing the inner volume 2864 of the fluid reservoir 2860 in fluid communication with the portion of the body. With the inner volume 2864 in fluid communication with the

portion of the body, the actuator 2870 can be rotated relative to the fluid reservoir 2860, which in turn, results in the threads 2899 of the actuator 2870 being advanced along the corresponding threads 2860A of the fluid reservoir 2860. Thus, the actuator 2870 can be moved in the proximal direction relative to the fluid reservoir 2860, which results in the plunger 2875 being moved in an axial direction (e.g., a proximal direction) within the inner volume 2864. As such, a portion of the inner volume 2864 that is distal to the elastomeric member 2878 is increased. Such an increase results in, for example, a negative pressure within the portion of the inner volume 2864 distal to the elastomeric member 2878 and therefore, a suction force is exerted that is operable in drawing a bodily-fluid (i.e., blood) into the inner volume 2864 of the fluid reservoir 2860. In some embodiments, the arrangement of the actuator 2870 and the fluid reservoir 2860 (i.e., the threaded coupling) limits a rate at which the plunger 2875 is moved within the inner volume 2864. In this manner, limiting the rate at which the plunger 2875 is moved within the inner volume 2864 can reduce and/or substantially prevent hemolysis of the blood drawn into the inner volume 2864 that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1201] FIG. 60 illustrates a fluid reservoir 2960 according to another embodiment. The fluid reservoir 2960 can be any suitable shape, size, or configuration. For example, in this embodiment, the fluid reservoir 2960 can be configured to receive a portion of an actuator 2970 (e.g., arranged as a syringe or the like), as described in further detail herein. The fluid reservoir 2960 has a first chamber 2990 and a second chamber 2991, which are formed unitarily (e.g., joined at a proximal end portion of the fluid reservoir 2960. The first chamber 2990 includes a proximal end portion 2961 and a distal end portion 2962 and defines an inner volume 2964. The distal end portion 2962 is configured to be physically and fluidically coupled to an adapter such as, for example, the adapter 2430 described above with reference to FIGS. 48-51. The proximal end portion 2961 movably receives a first plunger 2975 of the actuator 2970, which is at least partially disposed in the inner volume 2964, as described in further detail herein. In this manner, the first chamber 2990 is configured to receive and at least temporarily store a volume of bodily-fluid, as described in further detail herein.

[1202] Similarly, the second chamber 2991 includes a proximal end portion 2992 and a distal end portion 2993 and defines an inner volume 2994. The distal end portion 2993 of the second chamber 2991 is closed (i.e., does not define a port or other opening). The proximal

end portion 2992 movably receives a second plunger 2995 of the actuator 2970, which is at least partially disposed in the inner volume 2994, as described in further detail herein. As shown in FIG. 60, the second chamber 2991 has a size and/or shape that are/is smaller than the first chamber 2990. Thus, in some embodiments, the second chamber 2991 can be an auxiliary chamber or the like. For example, with the distal end portion 2993 of the second chamber 2991 being closed and/or sealed, in this embodiment, the second chamber 2991 can act as a dampener or the like configured to dampen a movement of the actuator 2970 relative to the fluid reservoir 2960.

[1203] As described above, the actuator 2970 includes the first plunger 2975 movably disposed in the inner volume 2964 of the first chamber 2990 and the second plunger 2995 movably disposed in the inner volume 294 of the second chamber 2991. As shown in FIG. 60, the first plunger 2975 has a proximal end portion 2976 and a distal end portion 2977. The proximal end portion 2976 of the first plunger 2975 is coupled to and/or otherwise unitarily formed a proximal end portion 2996 of the second plunger 2995. The distal end portion 2977 of the first plunger 2975 includes and/or is coupled to an elastomeric member 2978 or the like. In some embodiments, the elastomeric member 2978 can form a substantially fluid tight seal with an inner surface of the first chamber 2990, as described in detail above. Similarly, the second plunger 2995 has the proximal end portion 2996 and a distal end portion 2997. The proximal end portion 2996 of the second plunger 2995 is coupled to and/or otherwise unitarily formed with the proximal end portion 2976 of the first plunger 2975. The distal end portion 2997 of the second plunger 2995 includes and/or is coupled to an elastomeric member 2998. As described above with reference to the elastomeric member 2978, the elastomeric member 2998 of the second plunger 2995 can form a substantially fluid tight seal with an inner surface of the second chamber 2991. In this manner, the actuator 2970 can be moved relative to the fluid reservoir 2960 to move the first plunger 2975 within the inner volume 2964 of the first chamber 2990 and the second plunger 2995 within the inner volume 2994 of the second chamber 2991 in a substantially concurrent movement, as described in further detail herein.

[1204] In use, for example, the fluid reservoir 2960 can be manipulated to couple the distal end portion 2962 to an adapter or other device in fluid communication with a portion of the body, thereby placing the inner volume 2964 of the fluid reservoir 2960 in fluid communication with the portion of the body and/or intervening device (e.g. catheter, etc.).

Once the inner volume 2964 is placed in fluid communication with the portion of the body, the actuator 2970 can be moved in the proximal direction relative to the fluid reservoir 2960, which in turn, moves the first plunger 2975 within the inner volume 2964. More specifically, with the elastomeric member 2978 of the plunger 2975 forming a substantially fluid tight seal with the inner surface of the fluid reservoir 2960, the proximal movement of the first plunger 2975 relative to the fluid reservoir 2960 produces a negative pressure within a portion of the inner volume 2964 that is distal to the elastomeric member 2978. Thus, when the fluid reservoir is coupled to an adapter and/or any other suitable lumen-defining device in fluid communication with the body of a patient, the negative pressure results in a suction force within that lumen that can draw a bodily-fluid (e.g., blood) through the lumen and into the inner volume 2964 of the fluid reservoir 2960.

[1205] In a similar manner, the proximal movement of the actuator 2970 moves the second plunger 2995 within the inner volume 2994 of the second chamber 2991 substantially concurrently with the first plunger 2975, thereby increasing a portion of the inner volume 2994 that is distal to the elastomeric member 2998. With the elastomeric member 2998 of the second plunger 2995 forming a substantially fluid tight seal with the inner surface of the second chamber 2991, such an increase in the portion of the inner volume 2994 that is distal to the elastomeric results in a negative pressure within that portion of the inner volume 2994. Moreover, with the distal end portion 2993 of the second chamber 2991 being closed and/or sealed, the movement of the second plunger 2995 within the second chamber 2991, for example, can act to dampen the movement of the actuator 2970 relative to the fluid reservoir 2960. Specifically, the increase of the portion of the inner volume 2994 distal to the elastomeric member 2998 produces, for example, a suction force therein that resists the proximal movement of the second plunger 2995. Thus, an effective force exerted on the actuator 2970 to move the first plunger 2975 within the first chamber 2990 and the second plunger 2995 within the second chamber 2991 can be modulated, reduced, limited, and/or otherwise controlled, which in turn, can limit a rate at which the actuator 2970 is moved relative to the fluid reservoir 2960. In other words, the arrangement of the second chamber 2991 and the second plunger 2995 dampen the force exerted on the actuator 2970 and thus, the movement of the actuator 2970 relative to the fluid reservoir 2960. Therefore, by limiting the rate at which the actuator 2970 is moved relative to the fluid reservoir 2960, a negative pressure within the inner volume 2964 of the first chamber 2991 and/or a rate at which blood (or other bodily-fluid) flows into the inner volume 2964 can be controlled to an extent that

can reduce and/or substantially prevent hemolysis of the blood that can otherwise result from, inter alia, a volume of blood being exposed to a rapid pressure drop or the like.

[1206] While the embodiments are shown and described above as defining a single flow path from the patient to a fluid reservoir, in some embodiments, a fluid transfer device and/or system can include, for example, any suitable extension set, Y-adapter, T-adapter, junction, split, and/or the like configured to define more than one fluid flow path. Moreover, in such embodiments, a fluid transfer device and/or system can include any suitable coupling mechanism, lock mechanism, hub, and/or the like configured to couple, for example, a first lumen-defining device to a second lumen-defining device such that hemolysis of a flow of blood therethrough is limited and/or substantially prevented. For example, FIGS. 61-71 illustrate embodiments configured to mitigate the risk of hemolysis as blood flows through a multi-lumen adapter and/or the like. Specifically, FIGS. 61-63 illustrate a hub 3020 configured to receive a lumen-defining device 3080 according to an embodiment.

[1207] The hub 3020 has a proximal end portion 3021, a distal end portion 3022 and an inner surface 3023 defining a lumen 3024 therethrough (see e.g., FIG. 63). The distal end portion 3022 of the hub 3020 includes and/or is coupled to a cannula 3022A and/or other suitable lumen-defining device. Although not shown in FIGS. 61-63, in some embodiments, the cannula 3022A can be coupled to an adapter, a restrictor, locking mechanism, and/or the like. In some embodiments, the cannula 3022A can be, for example, an indwelling cannula with a distal end portion disposed within the body of a patient. In other embodiments, the distal end portion 3022 of the hub 3020 can include and/or can form a locking mechanism configured to physically and fluidically couple the hub 3020 to any suitable device. The proximal end portion 3021 of the hub 3020 includes and/or is coupled to a proximal cap 3027 and an actuator 3045. For example, in some embodiments, the proximal cap 3027 can be coupled to the proximal end portion 3021 via a press fit, a snap fit, a friction fit, a threaded coupling, an adhesive, ultrasonic welding and/or the like. Moreover, the proximal cap 3027 defines an opening 3028 that is, for example, substantially aligned with the lumen 3024 defined by the inner surface 3023. In this manner, a portion of the lumen-defining device 3080 can be inserted through the opening 3028 of the proximal cap 3027 to be disposed within the hub 3020, as described in further detail herein.

[1208] As shown in FIGS. 62 and 63, the actuator 3045 is disposed between the proximal end portion 3021 and the proximal cap 3027. More specifically, the actuator 3045 forms a

substantially annular ring or the like that is movably disposed within a space defined between a proximal surface of the hub 3020 and a distal surface of the proximal cap 3027. In this manner, the actuator 3045 defines an opening 3046 that can be selectively aligned with the opening 3028 of the proximal cap 3027 and the inner surface 3023 of the hub 3020. Moreover, the actuator 3045 includes and/or is coupled to a bias member 3047 (see e.g., FIG. 62), which can exert a force to temporarily maintain the actuator 3045 in a predetermined position relative to the hub 3020, for example, until a force is exerted on the actuator 3045 sufficient to overcome the force exerted by the bias member 3047, as described in further detail herein.

[1209] As shown in FIG. 63, the inner surface 3023 of the hub 3020 defines the lumen 3024 extending through its proximal end portion 3021 and its distal end portion 3022, which is configured to receive a portion of the lumen-defining device 3080. Furthermore, the inner surface 3023 includes and/or otherwise forms a shoulder 3025. In this embodiment, the shoulder 3025 is associated with a change in diameter of the inner surface 3023. For example, a first portion of the inner surface 3023 (e.g., a proximal portion) can have a first diameter that is larger than a diameter of a second portion of the inner surface (e.g., a distal portion). In this manner, the shoulder 3025 can be placed in contact with a surface of the lumen-defining device 3080 when inserted therein, as described in further detail herein.

[1210] The hub 3020 further includes a valve 3026 disposed within the lumen 3024. The valve 3026 can be, for example, a one-valve, a port, and/or the like, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. Thus, when in the first configuration, the valve 3026 can fluidically isolate a portion of the lumen 3024 that is proximal to the valve 3026 from a portion of the lumen 3024 that is distal to the valve 3026. Conversely, when the valve 3026 is in the second configuration, the lumen 3024 can define a fluid flow path substantially through the hub 3020. In some embodiments, the insertion of the portion of the lumen-defining device 3080 can be operable in transitioning the valve 3026 from the first configuration to the second configuration, as described in further detail herein.

[1211] The lumen-defining device 3080 has a proximal end portion 3031, a distal end portion 3032, and a flange 3086. The lumen-defining device 3080 also defines a notch 3085 and a lumen 3083 extending through the proximal end portion 3081 and the distal end portion 3082, as described in further detail herein. As shown in FIGS. 62 and 63, the distal end

portion 3082 of the lumen-defining device 3080 is configured to be inserted through the proximal cap 3027 and the actuator 3045 to be disposed within the hub 3020, as described in further detail herein. Moreover, the lumen-defining device 3080 includes a seal member 3087 disposed about an outer surface of the distal end portion 3082, which is placed in contact with the inner surface 3023 of the hub 3020 which the lumen-defining device 3080 is disposed therein.

[1212] As shown, for example, in FIGS. 61 and 63, the proximal end portion 3081 of the lumen-defining device 3080 is physically and fluidically coupled to a cannula 3088. The cannula 3088 can be any suitable configuration. For example, in this embodiment, the cannula 3088 is a bifurcated cannula having a first portion 3088A and a second portion 3088B (also referred to herein as a "first cannula" and a "second cannula," respectively). The first portion 3088A and second portion 3088B can be physically and fluidically coupled to any suitable device (e.g., at a proximal end). For example, as shown in FIG. 61, the second portion 3088B includes a port or locking mechanism that can physically and fluidically couple the second portion 3088B to, for example, a fluid source and/or the like. Although not shown, the first portion 3088A can include a port or the like substantially similar to that of the second portion 3088B that can physically and fluidically couple the first portion 3088A to, for example, a fluid reservoir and/or the like. In other embodiments, the first portion 3088A and the second portion 3088B can be arranged in any suitable manner and can each be physically and fluidically coupled to any suitable device, mechanism, and/or member included in a fluid transfer system.

[1213] In use, a portion of the lumen-defining device 3080 can be inserted into the hub 3020 to define a fluid flow path between the cannula 3022A, coupled to the distal end portion 3022 of the hub 3020, and the cannula 3088 coupled to the proximal end portion 3081 of the lumen-defining device 3080. More specifically, in some instances, a user can manipulate the hub 3020 by exerting a force on the actuator 3045, thereby moving the actuator 3045 from a first position, in which the opening 3046 of the actuator 3045 is substantially unaligned with the opening 3028 of the proximal cap 3027, to a second position, in which the opening 3046 is aligned with the opening 3028. Thus, with the actuator 3045 in the second position, the opening 3028 of the proximal cap 3027, the opening 3046 of the actuator 3046, and the lumen 3024 of the hub 3020 are sufficiently aligned to allow the distal end portion 3082 of the lumen-defining device 3080 to be inserted through the proximal cap 3027, the actuator

3045, and into the lumen 3024. As shown in FIG. 63, the lumen-defining device 3080 can be inserted into the hub 3020 by a predetermined amount that places the distal end portion 3082 extends through the valve 3026, thereby transitioning the valve 3026 from its first, substantially closed configuration to its second, substantially open configuration. Moreover, a distal surface of the lumen-defining device 3080 in contact with the shoulder 3025, as shown in FIG. 63.

[1214] With the distal surface of the lumen-defining device 3080 in contact with the shoulder 3025, the flange 3086 of the lumen-defining device 3080 is disposed within a recessed surface defined by the proximal cap 3027. In some embodiments, the shape and/or size of the recessed surface and the flange 3086 can be such that the lumen-defining device 3080 is placed into a predetermined radial position such that the lumen 3024 of the hub 3020 and the lumen 3083 of the lumen-defining device 3080 are substantially aligned, as shown in FIG. 63. Moreover, the seal member 3087 disposed about the outer surface at or near the distal end portion 3082 of the lumen-defining device 3080 is placed in contact with the inner surface 3023 of the hub 3020. In this manner, the arrangement of the flange 3086 disposed within the recessed surface of the proximal cap 3027 and the seal member 3087 in contact with the inner surface 3023 of the hub 3020, the lumen-defining device 3080 is placed in a predetermined radial position relative to the hub 3020. For example, in this embodiment, the lumen 3083 of the lumen-defining device 3080 and the lumen 3024 of the hub 3020 form a substantially continuous transition therebetween. That is to say, the lumens 3083 and 3024 are substantially aligned and/or a discontinuity defined therebetween is sufficiently minimized or obviated so as to not produce turbulence within a flow of bodily-fluid therethrough.

[1215] In addition, once the lumen-defining device 3080 is disposed in the desired and/or predetermined position within the hub 3020, the user can remove the force exerted on the actuator 3045. As such, the bias member 3047 can exert a force to move the actuator 3045 from its second position to its first position (e.g., a biased position). Thus, as shown in FIG. 63, the actuator 3045 is moved out of alignment with the hub 3020, resulting in a portion of the actuator 3045 being disposed in the notch 3085 defined by the lumen-defining device 3080, which in turn, can maintain the lumen-defining device 3080 in a substantially fixed position within the hub 3020. In this manner, a user can couple the first portion 3088A or the second portion 3088B of the cannula 3088 to, for example, a fluid reservoir such as those

described herein, which in turn, can exert a suction force (e.g., in response to a negative pressure differential) through the lumen-defining device 3080 and the hub 3020. Therefore, when the cannula 3022A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis. Specifically, the alignment of the lumen 3024 defined by the hub 3020 and the lumen 3083 of the lumen-defining device 3080, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1216] Although the valve 3026 is particularly shown and described above with reference to FIGS. 62 and 63, in other embodiments, a hub can include any suitable valve. For example, FIGS. 64-66 illustrate a hub 3120 configured to receive a lumen-defining device 3180 according to another embodiment. The hub 3120 and the lumen-defining device 3080 can be substantially similar in form and/or function as the hub 3020 and the lumen-defining device 3080 described above with reference to FIGS. 61-63. Thus, such similar aspects are not described in further detail herein.

[1217] As shown in FIGS. 64-66, the hub 3120 has a proximal end portion 3121, a distal end portion 3122, and an inner surface 3123 defining a lumen 3124 therethrough (see e.g., FIG. 66). The distal end portion 3122 of the hub 3120 includes and/or is coupled to a cannula 3122A and/or other suitable lumen-defining device. While the hub 3020 is shown and described as being coupled to a single cannula and/or a cannula defining a single lumen, in this embodiment, the hub 3120 is coupled to a bifurcated cannula having a first portion (also referred to herein as "first cannula" or "cannula 3122A") and a second portion 3122B. In other embodiments, the hub 3120 can be coupled to a single cannula and/or a cannula defining a single lumen. The proximal end portion 3121 of the hub 3120 includes and/or is coupled to a proximal cap 3127 and an actuator 3145, as described in detail above. The proximal cap 3127 defines an opening 3128 that is, for example, substantially aligned with the lumen 3124 defined by the inner surface 3123. In this manner, a portion of the lumen-defining device 3180 can be inserted through the opening 3128 of the proximal cap 3127 to be disposed within the hub 3120, as described in further detail herein.

[1218] As shown in FIGS. 65 and 66, the actuator 3145 is disposed between the proximal end portion 3121 and the proximal cap 3128. The actuator 3145 forms a substantially annular

ring or the like that is movably disposed within a space defined between a proximal surface of the hub 3120 and a distal surface of the proximal cap 3127. In addition, the actuator 3145 includes and/or is coupled to a bias member 3147, which can exert a force to temporarily maintain the actuator 3145 in a predetermined position relative to the hub 3120, for example, until a force is exerted on the actuator 3145 sufficient to overcome the force exerted by the bias member 3147. In this manner, the arrangement of the proximal end portion 3121 of the hub 3120, the proximal cap 3127, and the actuator 3145 can be substantially similar to the proximal end portion 3021 of the hub 3020, the proximal cap 3027, and the actuator 3045 described above with reference to FIGS. 62 and 63.

[1219] As shown in FIG. 66, the inner surface 3123 of the hub 3120 defines the lumen 3124 extending through its proximal end portion 3121 and its distal end portion 3122, which is configured to receive a portion of the lumen-defining device 3180. Furthermore, the inner surface 3123 includes a valve and a sealing surface 3125. As shown in FIG. 66, in this embodiment, the valve is a ball valve 3126, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. More specifically, the hub 3120 includes a bias member 3148 in contact with the ball valve 3126. In this manner, the bias member 3148 can exert a force on the ball valve 3126 that places the ball valve 3126 in contact with the sealing surface 3125. Thus, a contact sufficient to maintain a substantially fluid tight seal can be maintained when the ball valve 3126 is in contact with the sealing surface 3125 (e.g., in the first configuration) via a force exerted by the bias member 3148. Conversely, when a force exerted on the ball valve 3126, opposite the force exerted by the bias member 3148, is sufficient to overcome the force exerted by the bias member 3148, the ball valve 3126 can be removed from contact with the sealing surface 3125 and thus, a fluid flow path can be defined therethrough. In some embodiments, the insertion of the portion of the lumen-defining device 3180 can be operable in transitioning the ball valve 3126 from the first configuration to the second configuration, as described in further detail herein.

[1220] The lumen-defining device 3180 has a proximal end portion 3181, a distal end portion 3182, and a flange 3186. The lumen-defining device 3180 also defines a notch 3185 and a lumen 3183 extending through the proximal end portion 3181 and the distal end portion 3182, as described in further detail herein. As shown, for example, in FIGS. 64-66, the proximal end portion 3181 of the lumen-defining device 3180 is physically and fluidically

coupled to a cannula 3188. The cannula 3188 can be any suitable configuration. For example, in this embodiment, the cannula 3188 is a single cannula and/or a cannula that defines a single lumen. In other embodiments, the cannula 3188 can be a bifurcated cannula, as described in detail above with reference to the cannula 3088 in FIG. 61. Moreover, although not shown in FIGS. 64-66, the cannula 3188 can include any suitable port, locking mechanism, and/or the like, as described above.

[1221] As shown in FIGS. 65 and 66, the distal end portion 3182 of the lumen-defining device 3180 is configured to be inserted through the proximal cap 3127 and the actuator 3145 to be disposed within the hub 3120, as described in further detail herein. Moreover, the lumen-defining device 3180 includes a seal member 3187 disposed about an outer surface of the distal end portion 3182, which is placed in contact with the inner surface 3123 of the hub 3120 which the lumen-defining device 3180 is disposed therein. As shown in FIG. 66, the lumen 3183 of defined by the lumen-defining device 3080 at or near the distal end portion 3182 is diverted, for example, into one or more channels and defining a substantially smooth transition therebetween. In some embodiments, the one or more channels, for example, can be offset from the lumen 3183 (e.g., non-coaxial). In other words, each channel is radially offset from a longitudinal centerline CL, as shown in FIG. 66. Thus, when a distal surface of the lumen-defining device 3180 is placed in contact with, for example, the ball valve 3126, the channels and/or the lumen 3183 are/is substantially unobstructed, as described in further detail herein.

[1222] In use, a portion of the lumen-defining device 3180 can be inserted into the hub 3120 to define a fluid flow path between the cannula 3122A, coupled to the distal end portion 3122 of the hub 3120, and the cannula 3188 coupled to the proximal end portion 3181 of the lumen-defining device 3180. More specifically, in some instances, a user can manipulate the hub 3120 by exerting a force on the actuator 3145, thereby moving the actuator 3145 from a first position, in which the opening 3146 of the actuator 3145 is substantially unaligned with the opening 3128 of the proximal cap 3127, to a second position, in which the opening 3146 is aligned with the opening 3128, as described in detail above. As shown in FIG. 66, the lumen-defining device 3180 can be inserted into the hub 3120 by a predetermined amount that places a distal surface of the lumen-defining device 3180 in contact with the ball valve 3126. In this manner, the lumen-defining device 3180 can be inserted into the hub 3180 until the flange 3186 of the lumen-defining device 3180 is disposed within a recessed surface

defined by the proximal cap 3127, thereby aligning the lumen-defining device 3180, as described in detail above. Moreover, the seal member 3187 disposed about the outer surface at or near the distal end portion 3182 of the lumen-defining device 3180 is placed in contact with the inner surface 3123 of the hub 3120. In this manner, the lumen-defining device 3180 can be inserted into a position that removes the ball valve 3126 from the sealing surface 3125, thereby defining a fluid flow path between the lumen 3124 of the hub 3120 and the lumen 3183 (and/or channels) of the lumen-defining device 3180.

[1223] Once the lumen-defining device 3180 is disposed in the desired and/or predetermined position within the hub 3120, the user can remove the force exerted on the actuator 3145. As such, the bias member 3147 can exert a force to move the actuator 3145 from its second position to its first position (e.g., a biased position), resulting in a portion of the actuator 3145 being disposed in the notch 3185 defined by the lumen-defining device 3180. Thus, the actuator 3145 can maintain the lumen-defining device 3180 in a substantially fixed position within the hub 3120, as described in detail above. In this manner, a user can couple the cannula 3188, for example, to a fluid reservoir such as those described herein. Therefore, when the cannula 3122A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis, as described in detail above. Specifically, the alignment of the lumen 3124 defined by the hub 3120 and the channels and/or lumen 3183 of the lumen-defining device 3180, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1224] Although the hubs 3020 and 3120 have a proximal end portion including an actuator, in other embodiments, a hub can have any suitable configuration and need not include an actuator. For example, FIGS. 67 and 68 illustrate a hub 3320 configured to receive a lumen-defining device 3280 according to another embodiment. The hub 3220 and the lumen-defining device 3280 can be substantially similar in form and/or function as the hub 3020 and the lumen-defining device 3080 and/or the hub 3120 and the lumen-defining device 3180, described in detail above. Thus, such similar aspects are not described in further detail herein. As shown in FIGS. 67 and 68, the hub 3220 has a proximal end portion 3221, a distal end portion 3222, a secondary port 3289, and an inner surface 3223 defining a

lumen 3224 therethrough (see e.g., FIG. 68). The hub 3220 further includes a valve 3226 disposed within the lumen 3224, as described in further detail herein.

[1225] The distal end portion 3222 of the hub 3220 includes and/or is coupled to a cannula 3222A and/or other suitable lumen-defining device, as described above with reference to the hub 3020 in FIGS. 61-63. The proximal end portion 3221 of the hub 3220 includes and/or is coupled to a proximal cap 3227. As shown in FIGS. 67 and 68, in this embodiment, the proximal cap 3237 can be, for example, a locking mechanism or the like configured to form a treaded coupling with a portion of the lumen-defining device 3280, as described in further detail herein.

[1226] As shown in FIG. 68, the inner surface 3223 of the hub 3220 defines the lumen 3224 extending through its proximal end portion 3221 and its distal end portion 3222, which is configured to receive a portion of the lumen-defining device 3280. Furthermore, the inner surface 3223 includes and/or otherwise forms a shoulder 3225. In this embodiment, the shoulder 3225 is associated with a change in diameter of the inner surface 3223. For example, a first portion of the inner surface 3223 (e.g., a proximal portion) can have a first diameter that is larger than a diameter of a second portion of the inner surface (e.g., a distal portion). In this manner, the shoulder 3225 can be placed in contact with a surface of the lumen-defining device 3280 when inserted therein, as described in detail above with reference to the hub 3020. In some embodiments, the shoulder 3225 can form, for example, a seat or a recessed portion configured to receive a portion of the lumen-defining device 3280.

[1227] The valve 3226 of the hub 3220 can be, for example, a one-valve, a port, and/or the like, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. Thus, when in the first configuration, the valve 3226 can fluidically isolate a portion of the lumen 3224 that is proximal to the valve 3226 from a portion of the lumen 3224 that is distal to the valve 3226. Conversely, when the valve 3226 is in the second configuration, the lumen 3224 can define a fluid flow path substantially through the hub 3220. In some embodiments, the insertion of the distal end portion 3282 of the lumen-defining device 3280 can be operable in transitioning the valve 3226 from the first configuration to the second configuration, as described in further detail herein.

[1228] The secondary port 3289 of the hub 3280 can be any suitable port or the like. For example, in some embodiments, the hub 3220 can be arranged as a T-adapter or the like, in

which the proximal end portion 3221 defines a first port and the secondary port 3289 extends in a substantially perpendicular direction from the first port. In this manner, the secondary port 3289 is in fluid communication with the lumen 3224 defined by the hub 3220 and can be configured to receive and/or deliver a fluid from and/or to the lumen 3224 of the hub 3220. Moreover, the arrangement of the secondary port 3289 is such that when the valve 3226 is in its closed configuration, the secondary port 3289 is fluidically isolated from a portion of the lumen 3224 proximal to the valve 3226.

[1229] The lumen-defining device 3080 has a proximal end portion 3031, a distal end portion 3032, and a flange 3086. The lumen-defining device 3080 also defines a notch 3085 and a lumen 3083 extending through the proximal end portion 3081 and the distal end portion 3082, as described in further detail herein. As shown in FIGS. 62 and 63, the distal end portion 3082 of the lumen-defining device 3080 is configured to be inserted through the proximal cap 3027 and the actuator 3045 to be disposed within the hub 3020, as described in further detail herein. Moreover, the lumen-defining device 3080 includes a seal member 3087 disposed about an outer surface of the distal end portion 3082, which is placed in contact with the inner surface 3023 of the hub 3020 which the lumen-defining device 3080 is disposed therein.

[1230] The lumen-defining device 3280 has a proximal end portion 3281 and a distal end portion 3282, and defines a lumen 3283 therethrough. As shown, for example, in FIG. 68, the proximal end portion 3281 of the lumen-defining device 3280 is physically and fluidically coupled to a cannula 3288. The cannula 3288 can be any suitable configuration. For example, in this embodiment, the cannula 3288 is a single cannula and/or a cannula that defines a single lumen. In some embodiments, the cannula 3288 can be substantially similar to the cannula 3188 described above wither reference to FIGS. 64-66.

[1231] As shown in FIG. 68, the distal end portion 3282 of the lumen-defining device 3280 is configured to be inserted through the proximal cap 3227 to be disposed within the hub 3220. More specifically, a portion of the lumen-defining device 3280 can be inserted into the proximal cap 3227 and configured to form, for example, a threaded coupling or the like. For example, in some embodiments, a portion of an outer surface of the lumen-defining device 3280 can include a set of treads or the like configured to engage a corresponding set of threads included in and/or defined by the proximal cap 3227. Thus, in use, as the lumen-defining device 3280 is inserted through the proximal cap 3227, the proximal cap 3227

and/or the lumen-defining device 3280 can be rotated to form the threaded coupling therebetween. Moreover, the arrangement of the lumen-defining device 3280 can be such that when coupled to the proximal cap 3227, the distal end portion 3282 of the lumen-defining device 3280 extends through the valve 3226. Thus, the valve 3226 is transitioned from its first, substantially closed configuration to its second, substantially open configuration. In some embodiments, the valve 3226 can be configured to form a substantially fluid tight seal about a portion of the lumen-defining device 3280, which in turn, can maintain the secondary port 3289 in fluid isolation from, for example, the lumen 3283 of the lumen-defining device 3280. Moreover, the lumen-defining device 3280 is advanced such that a distal surface of the lumen-defining device 3280 is in contact with the shoulder 3225, as shown in FIG. 68.

[1232] In this embodiment, the arrangement of the lumen-defining device 3280 and the proximal cap 3227 (i.e., the coupling therebetween) is such that the lumen 3283 of the lumen-defining device 3280 and the lumen 3224 of the hub 3220 form a substantially continuous transition therebetween. That is to say, the lumens 3283 and 3224 are substantially aligned and/or a discontinuity defined therebetween is sufficiently minimized or obviated so as to not produce turbulence within a flow of bodily-fluid therethrough. Therefore, when the cannula 3222A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis. Specifically, the alignment of the lumen 3224 defined by the hub 3220 and the lumen 3283 of the lumen-defining device 3280, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1233] While the hubs 3020, 3120, and 3220 are shown and described above as receiving the lumen-defining devices 3080, 3180, and 3280 (e.g., a connector), respectively, in other embodiments, a hub can be configured to receive a terminated end of a cannula or the like (e.g., without a connector or other lumen-defining device). For example, FIGS. 69-71 illustrate a hub 3320 configured to receive a cannula 3388 according to another embodiment. The hub 3320 and the lumen-defining device 3080 can be substantially similar in form and/or function as the hub 3020 and the lumen-defining device 3080 and/or the hub 3120 and the

lumen-defining device 3180, described in detail above. Thus, such similar aspects are not described in further detail herein.

[1234] As shown in FIGS. 69-71, the hub 3320 has a proximal end portion 3321, a distal end portion 3322, and an inner surface 3323 defining a lumen 3324 therethrough (see e.g., FIG. 71). The distal end portion 3322 of the hub 3320 includes and/or is coupled to a cannula 3322A and/or other suitable lumen-defining device. In some embodiments, the distal end portion 3322 of the hub 3320 can be substantially similar to the distal end portion 3322 of the hub 3020 described above with reference to FIGS. 61-63. The proximal end portion 3321 of the hub 3320 includes and/or is coupled to a proximal cap 3327, as described in detail above. The proximal cap 3327 defines an opening 3328 that is, for example, substantially aligned with the lumen 3324 defined by the inner surface 3323. In this manner, a portion of the cannula 3388 can be inserted through the opening 3328 of the proximal cap 3327 to be disposed within the hub 3320, as described in further detail herein.

[1235] As shown in FIGS. 70 and 71, the proximal end portion 3321 of the hub 3320 further includes and or is coupled to a first coupling member 3345 and a second coupling member 3349. As described above with reference to the actuator 3145, the first coupling member 3345 is disposed between the proximal end portion 3321 and the proximal cap 3327. The first coupling member 3345 is configured to selective receive a portion of the second coupling member 3349. The second coupling member 3349 is configured to be disposed about a portion of the cannula 3388. Thus, the second coupling member 3349 can be inserted substantially concurrently with the cannula 3388. Moreover, the second coupling member 3349 is configured to engage the first coupling member 3345 disposed within the hub 3320, for example, to at least temporarily maintain the cannula 3388 in a fixed position. For example, in some embodiments, the second coupling portion 3349 can form a snap fit, a press fit, a friction fit, and/or the like when placed in contact with the first coupling member 3345, as described in further detail herein.

[1236] As shown in FIG. 71, the inner surface 3323 of the hub 3320 defines the lumen 3324 extending through its proximal end portion 3321 and its distal end portion 3322, which is configured to receive a portion of the cannula 3388. Furthermore, the inner surface 3323 includes and/or otherwise forms a shoulder 3325. In this embodiment, the shoulder 3325 is associated with a change in diameter of the inner surface 3323. For example, a first portion of the inner surface 3323 (e.g., a proximal portion) can have a first diameter that is larger than

a diameter of a second portion of the inner surface (e.g., a distal portion). In this manner, the shoulder 3325 can be placed in contact with a surface of the cannula 3388 when inserted therein, as described in detail above with reference to the hub 3020.

[1237] The hub 3320 further includes a valve 3326 disposed within the lumen 3324. The valve 3326 can be, for example, a one-valve, a port, and/or the like, which can be transitioned between a first, substantially closed configuration and a second, substantially opened configuration. Thus, when in the first configuration, the valve 3326 can fluidically isolate a portion of the lumen 3324 that is proximal to the valve 3326 from a portion of the lumen 3324 that is distal to the valve 3326. Conversely, when the valve 3326 is in the second configuration, the lumen 3324 can define a fluid flow path substantially through the hub 3320. In some embodiments, the insertion of the portion of the cannula 3388 can be operable in transitioning the valve 3326 from the first configuration to the second configuration, as described in further detail herein.

[1238] In use, a portion of the cannula 3388 can be inserted into the hub 3320 to define a fluid flow path between the cannula 3322A, coupled to the distal end portion 3322 of the hub 3320, and the cannula 3388 coupled to the proximal end portion 3381 of the cannula 3388. More specifically, in some instances, a user can insert an end portion of the cannula 3388 through the second coupling member 3349. Once the second coupling member 3349 is disposed about the cannula 3380, the cannula 3388 can be inserted into the hub 3320 by a predetermined amount that extends, for example, a distal end portion of the cannula 3388 through the valve 3326, thereby transitioning the valve 3326 from its first, substantially closed configuration to its second, substantially open configuration. Moreover, a distal surface of the cannula 3388 in contact with the shoulder 3325, as shown in FIG. 71. As the cannula 3388 is moved into its desired position within the hub 3320, the second coupling member 3349 is inserted through the opening 3328 defined by the proximal cap 3327 and into contact with the first coupling member 3345. Thus, the second coupling member 3349 can engage the first coupling member 3345 to define, for example, a snap fit or the like. In some embodiments, the arrangement of the second coupling member 3349 can be such that when it engages the first coupling member 3349, a space through which the cannula 3388 extends is reduced. As such, the second coupling member 3349 can clamp the cannula 3388 and with the second coupling member 3349 being coupled to the first coupling member 3345, the first coupling member 3345 and the second coupling member 3349 can act to at least

temporarily maintain the cannula 3388 in a substantially fixed position relative to the hub 3320. Although described above as being moved substantially concurrently with the cannula 3388, in other embodiments, the second coupling member 3349 can be moved after the distal surface of the cannula 3388 is placed in contact with the shoulder 3325.

[1239] In some embodiments, the arrangement of the hub 3320 and the cannula 3388 is such that when the cannula 3388 is maintained in the substantially fixed position, the lumen 3324 of the hub 3320 is substantially aligned with a lumen defined by the cannula 3388. For example, in this embodiment, the lumen of the cannula 3388 and the lumen 3324 of the hub 3320 form a substantially continuous transition therebetween. That is to say, the lumens are substantially aligned and/or a discontinuity defined therebetween is sufficiently minimized or obviated so as to not produce turbulence within a flow of bodily-fluid therethrough. In this manner, a user can couple the cannula 3388 to, for example, a fluid reservoir such as those described herein, which in turn, can exert a suction force (e.g., in response to a negative pressure differential) through the cannula 3388 and the hub 3320. Therefore, when the cannula 3322A is in fluid communication with the body of a patient (e.g., either directly or indirectly via an intervening structure), a volume of, for example, blood can be withdrawn with a reduced amount of hemolysis. Specifically, the alignment of the lumen 3324 defined by the hub 3320 and the lumen of the cannula 3388, for example, can reduce turbulence, eddy currents, and/or any other disturbance that can otherwise result from a discontinuity or the like. Thus, the flow of blood therethrough can be substantially laminar and substantially free of hemolysis.

[1240] Although the embodiments are shown and described above as mitigating the risk of hemolysis of a volume of blood at a given point along a fluid flow path between a patient and a fluid reservoir, any embodiment configured to mitigate the risk of hemolysis at a given point along the fluid flow path can be used in conjunction with any suitable embodiment(s) configured to mitigate the risk of hemolysis at a different point along the fluid flow path. In some instances, a fluid transfer device can include any combination of the embodiments described herein, for example, to mitigate the risk of hemolysis otherwise associated with (1) blood flow from, for example, a vein into a puncture member, needle, cannula, and/or the like; (2) blood flow through changing geometries and/or physical and fluidic interfaces; (3) blood flow rates, pressures, and/or velocities within the fluid flow path; (4) blood flow from an adapter, puncture member, needle, cannula, and/or the like into a fluid reservoir; (5) blood

flow exposure to a negative pressure differential within a fluid reservoir; and/or (6) blood flow through a multi-lumen adapter and/or the like.

[1241] While the embodiments are shown and described above as mitigating the risk of hemolysis of a volume of blood during, for example, aspiration, blood draw, and/or any other procedure in which blood is withdrawn from the body, in other instances, any embodiment configured to mitigate the risk of hemolysis described herein, and/or any combination thereof, can be used in any suitable medical device and/or procedure in which it is desirable to reduce hemolysis. For example, any of the embodiments or combinations of the embodiments described herein such as the adapters, puncture members, restrictors, fluid reservoirs, gaskets, etc., and/or characteristics, geometries, and/or features thereof can be used to mitigate the risk of hemolysis in any suitable device and/or during any suitable medical procedure. Such devices and/or procedures can include but are not limited to, mechanical hearts and/or other organs, perfusion machines used, for example, during open-heart surgery, dialysis machines, and/or the like. In some instances, the embodiments and/or combination of embodiments described herein can be used to modulate pressure within such devices, produce a laminar flow through at least a portion of such devices, reduce and/or limit shear stress and/or exposure time experienced by red blood cells, and/or the like.

[1242] Although not shown or described herein, any of the embodiments can be used in a fluid transfer device configured to, for example, divert a predetermined pre-sample volume of bodily-fluid that can contain, for example, externally residing microbes prior to collection of a sample volume of bodily. For example, in some embodiments, the predetermined pre-sample volume can be about a drop or a few drops of blood, about 0.1 mL, about 0.3 mL, about 0.5 mL, about 1.0 mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, about 5.0 mL, about 11.0 mL, about 20 mL, about 50 mL, and/or any volume or fraction of a volume therebetween. In other embodiments, the pre-sample volume can be greater than 50 mL or less than 0.1 mL. In other embodiments, the predetermined pre-sample volume can be between about 2 mL and about 5 mL. In one embodiment, the predetermined pre-sample volume can be about 3 mL. In some instances, a venipuncture event can result in trauma to the blood flowing within the punctured vein that can at least temporarily hemolyze a portion of the blood. Thus, in some embodiments, the diverted pre-sample volume of blood can include, for example, the hemolyzed portion of the blood. Furthermore, by collecting the

predetermined pre-sample volume, the predetermined sample volume disposed in one or more sample reservoirs can be substantially free-from externally residing microbes.

[1243] Fluid transfer devices configured to divert a predetermined pre-sample volume of bodily-fluid can be any suitable configuration. For example, in some embodiments, such a fluid transfer device can be substantially similar to or the same as the fluid transfer devices described in U.S. Patent No. 8,535,241 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed October 12, 2012; U.S. Patent No. 9,060,724 entitled, "Fluid Diversion Mechanism for Bodily-Fluid Sampling," filed May 29, 2013; U.S. Patent No. 9,155,495 entitled, "Syringe-Based Fluid Diversion Mechanism for Bodily-fluid Sampling," filed December 2, 2013; and/or U.S. Patent Publication No. 2014/0155782 entitled, "Sterile Bodily-Fluid Collection Device and Methods," filed December 4, 2012, the disclosures of which are incorporated herein by reference in their entireties and attached hereto as Exhibit A, Exhibit B, Exhibit C, and Exhibit D, respectively. Moreover, in some embodiments, such transfer devices can be configured to selectively obstruct a needle to prevent hemolyzed blood from entering a lumen defined by the needle during a venipuncture event. Such devices can be substantially similar to and/or the same as those described in U.S. Patent Publication No. 2014/0276578, entitled, "Methods and Apparatus for Selectively Occluding the Lumen of a Needle," filed September 18, 2014, the disclosure of which is incorporated herein by reference in its entirety and attached hereto as Exhibit E.

[1244] In some embodiments, the bodily-fluid transfer devices described herein can include and/or can be partially formed from antisepsis-saturated materials. For example, any of the valves, gaskets, seals, ports, and/or the like can be saturated with, for example, isopropyl alcohol. As such, when various components of a fluid transfer device are coupled and/or otherwise collectively form an interface, the components can be contemporaneously sterilized. In some embodiments, such a device can be substantially similar to or the same as those described in U.S. Patent Publication No. 2015/0246352 entitled, "Apparatus and Methods for Disinfection of a Specimen Container," filed March 3, 2015, the disclosure of which is incorporated herein by reference in its entirety and attached as Exhibit F.

[1245] While the device 100 is described above as including a surface, mechanism, portion, etc. configured to reduce hemolysis of a volume of blood in a mechanical manner (e.g., by mechanically changing one or more characteristics of a flow of blood within a fluid flow path), in other embodiments, any of the devices can be configured to chemically modify

one or more characteristics associated with the volume of blood. For example, in some embodiments, an inner surface of any of the embodiments described herein can be coated with a chemical configured to limit lysis of erythrocytes (red blood cells) by strengthening or weakening a cell wall of the erythrocytes. More specifically, in some embodiments, a can be configured to introduce a chemical into a flow of blood that can, for example, increase a rigidity of the cell wall of erythrocytes (e.g., decrease flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes (e.g., hemolysis of the blood) as the blood flows through the device. In other embodiments, a device can be configured to introduce a chemical into a flow of blood that can, for example, decrease a rigidity of the cell wall of erythrocytes (e.g., increase flexibility), which in turn, can reduce a likelihood of lysis of the erythrocytes as the blood flows through the device.

[1246] While described above as coating an inner surface of a device with the chemical configured to modify a characteristic of the cell wall of the erythrocytes, in other embodiments, any of the embodiments described herein can include any suitable device, mechanism, and/or method for introducing such a chemical to the volume of blood flowing therethrough. For example, a device can include a chamber containing such a chemical (e.g., a chamber within a Luer lock or the like), a baffle, wipe, valve, porous material (e.g., sintered glass or plastic), etc. impregnated with such a chemical, a dispensing or dispersing device (e.g., sprayer or the like) configured to dispense a volume of such a chemical, and/or any other suitable means for introducing such a chemical. Moreover, a device can include any suitable combination of devices, interfaces, members, mechanisms, etc. included in the embodiments described herein as well as any suitable means for introducing a chemical into a volume of blood flowing through such a device.

[1247] As described above, in some instances, introducing a chemical into a volume of blood (e.g., whole blood) can result in a strengthening of an erythrocyte membrane or outer structure, or in other words, can modify a magnitude of stability associated with the erythrocyte membrane. In some instances, such stabilization can result in an increased resistance to hemolysis caused by mechanical stress, osmotic stress, peroxyl radicals attack, heat, and/or the like. Examples of chemicals that can modify a characteristic associated with an erythrocyte membrane include phloridzin, cremophore (glycerol polyethylene glycol ricinoleate, lidocaine, antioxidants such as reduced glutathione (GSH), N-acetylcysteine, ebselen (2-phenyl-1, 2-benzoselenazol-3-one) and/or albumin, papaya leaf and/or other plant

extracts, tranquilizers and/or antihistamines such as phenothiazine, reserpine, and/or haloperidol, saponins and/or sapogenins, polyamines, anti-inflammatory drugs such as phenylbutazone, methylsergide, and/or indomethacin, and/or any other suitable chemical.

[1248] While various embodiments have been particularly shown and described, various changes in form and details may be made. While embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Although various embodiments have been described as having particular features and/or combinations of components, other embodiments are possible having any combination or sub-combination of any features and/or components from any of the embodiments described herein. For example, in some embodiments, a restrictor such as, for example, the restrictor 650 can be used when collecting a bodily-fluid using any of the fluid reservoirs described herein. Similarly, the hub 3020 and lumen-defining device 3080 described above with reference to FIGS. 61-63 can be used with any of the adapters described herein. Moreover, any suitable combination of components described herein can be physically and/or fluidically coupled together to form a bodily-fluid collection device configured, for example, to reduce hemolysis in a withdrawn volume of blood.

[1249] The specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different from the embodiments shown, while still providing the functions as described herein. More specifically, the size and shape of the various components can be specifically selected for a desired rate of bodily-fluid flow into a fluid reservoir. While various components have been described above a being physically and fluidically coupled, in other embodiments, any of the devices and/or embodiments can be, for example, monolithically formed with and/or otherwise joined to any other suitable device and/or embodiment. For example, while the first adapter 1020, the second adapter 1030, and the restrictor 1050 are described above with reference to FIGS. 18-20 as being formed separately and subsequently coupled, in other embodiments, the first adapter 1020 and/or the second adapter 1030 can be monolithically formed with the restrictor 1050. In some instances, such a monolithically formed component can be included in, for example, a pre-assembled and sterile blood collection device and/or the like.

[1250] Where methods and/or events described above indicate certain events and/or procedures occurring in certain order, the ordering of certain events and/or procedures may

be modified. Additionally, certain events and/or procedures may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above.

Abstract

A collection system has a proximal end portion, a distal end portion, and an inner surface defining a fluid flow path therethrough. The distal end portion is configured to be placed in fluid communication with a patient. The proximal end portion is configured to be placed in fluid communication with a fluid reservoir. The fluid flow path defined by the inner surface is associated with at least one flow characteristic configured to limit a stress within the flow of the bodily-fluid between the distal end portion and the proximal end portion.

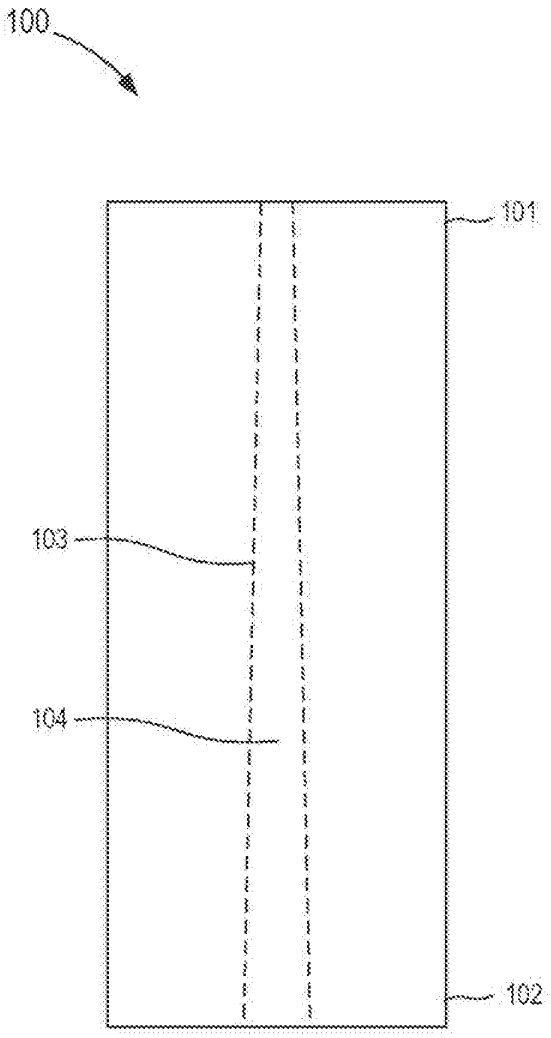


FIG. 1

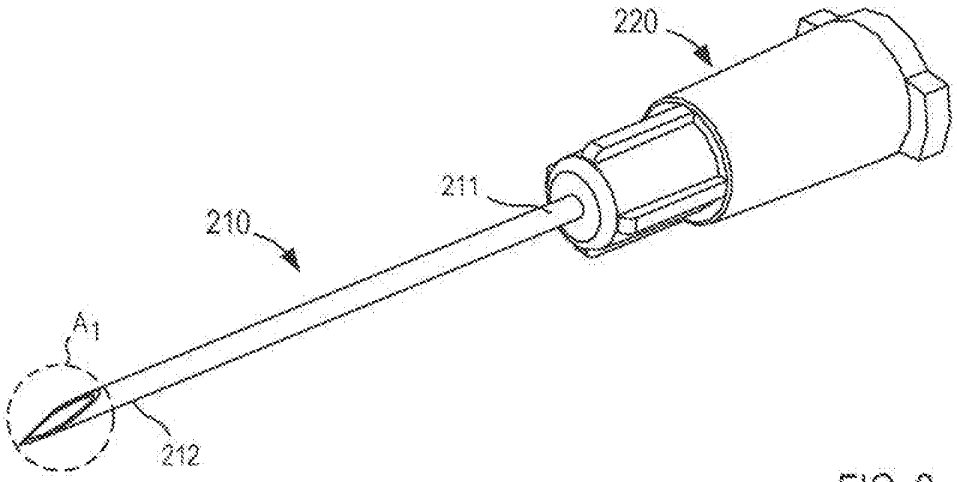


FIG. 2

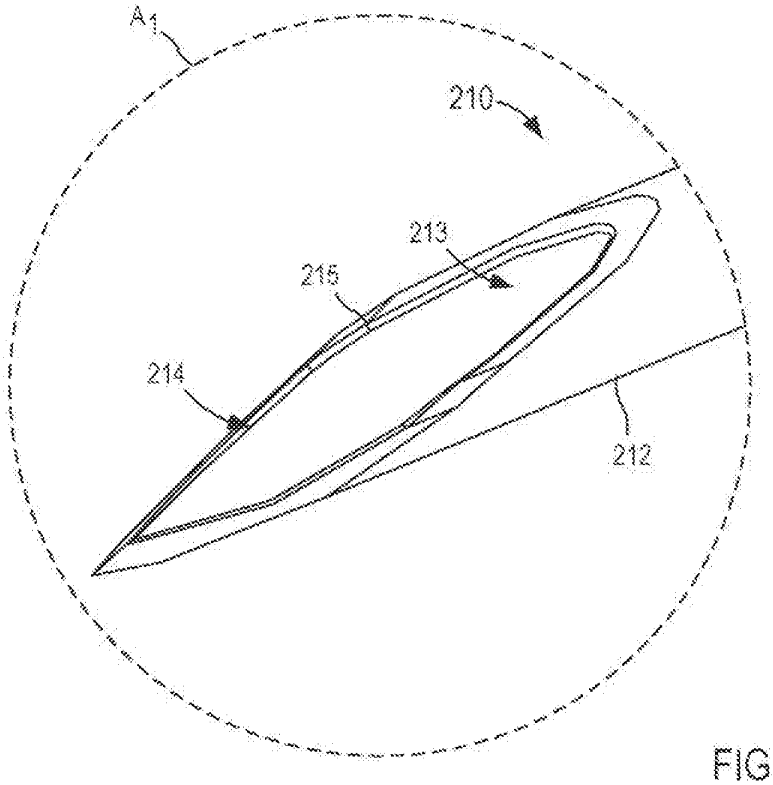


FIG. 3

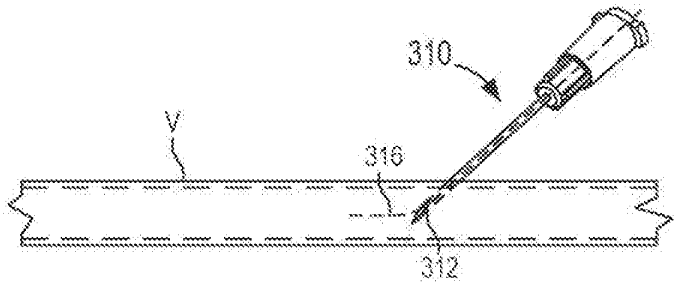


FIG. 4

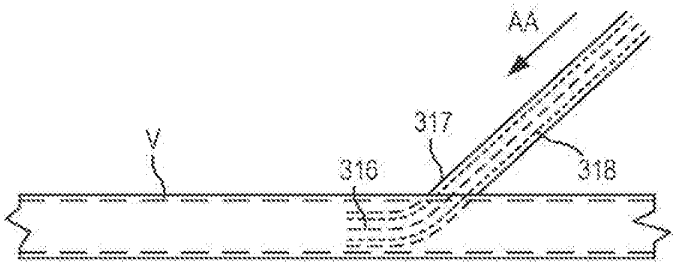


FIG. 5

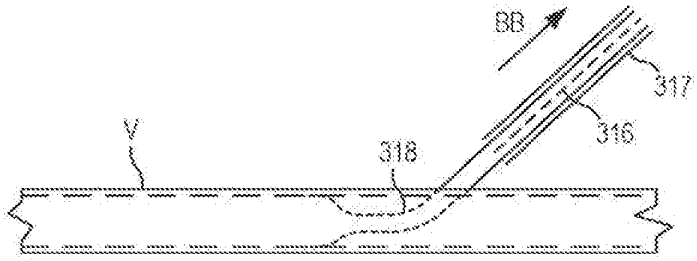


FIG. 6

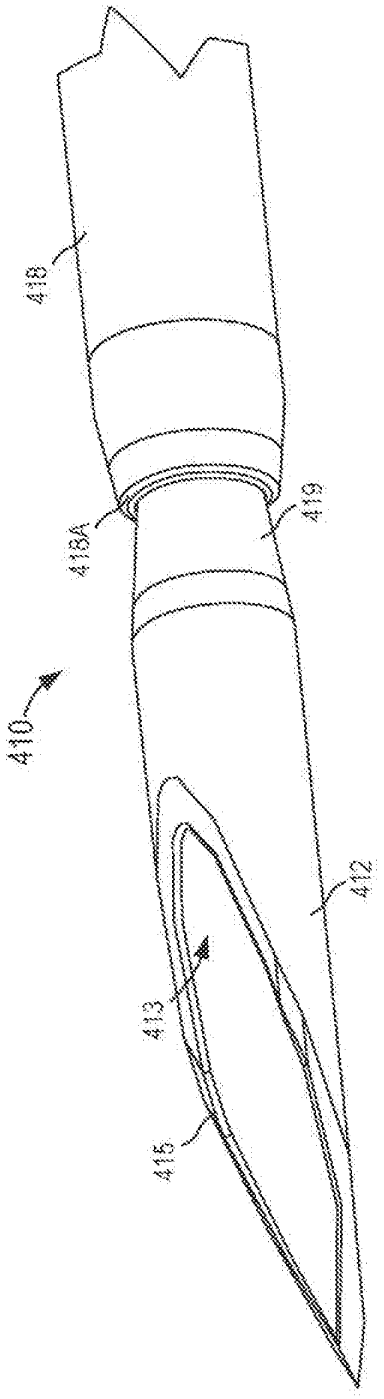


FIG. 7

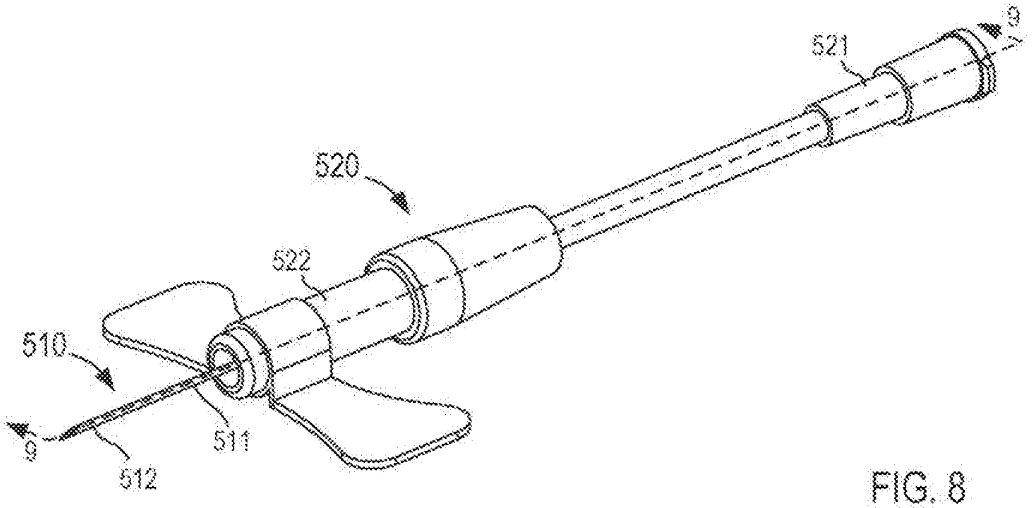


FIG. 8

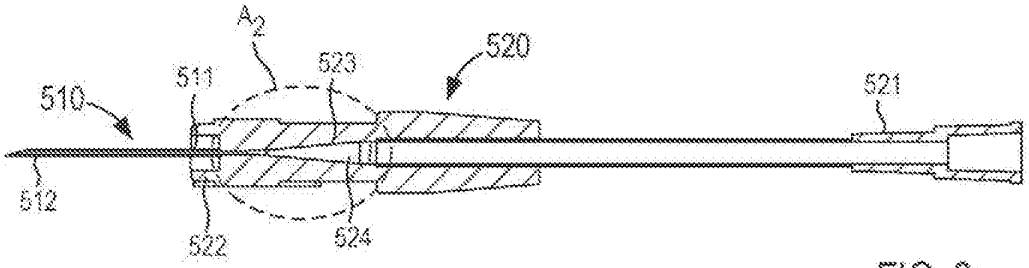


FIG. 9

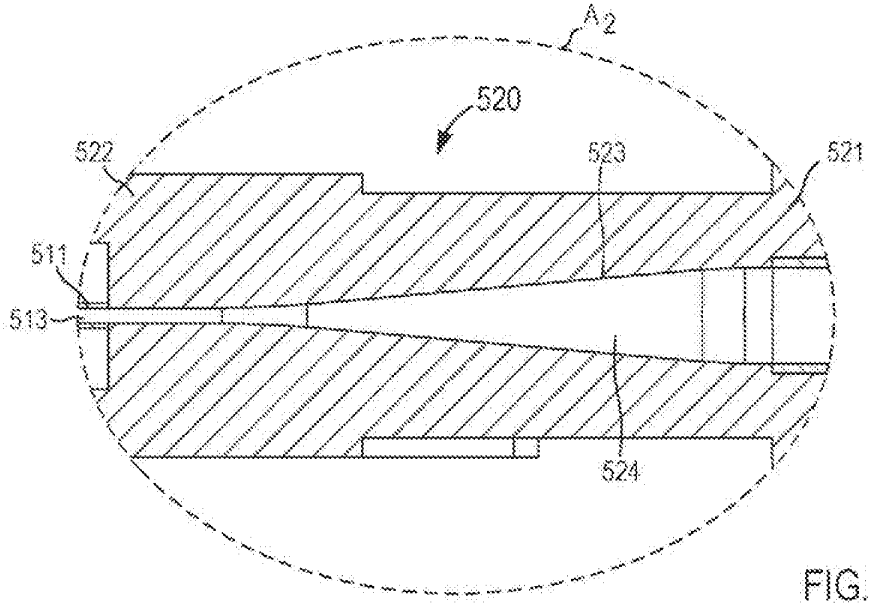


FIG. 10

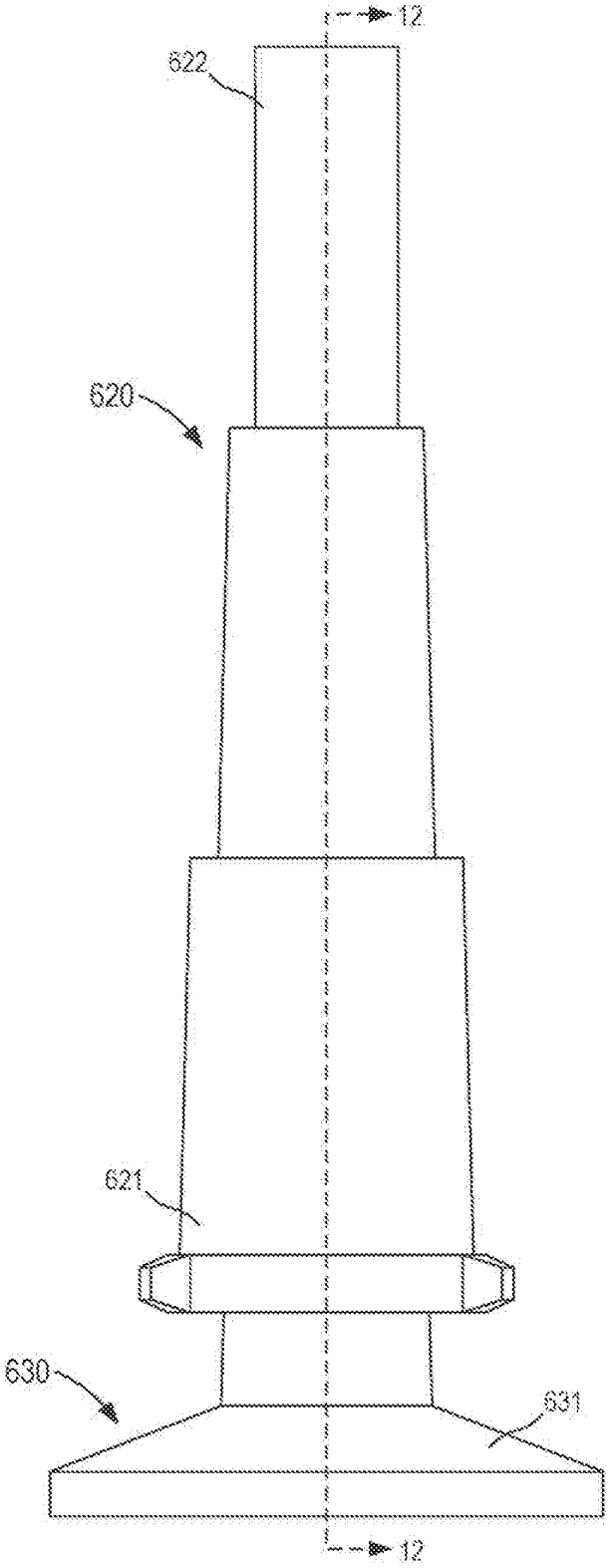


FIG. 11

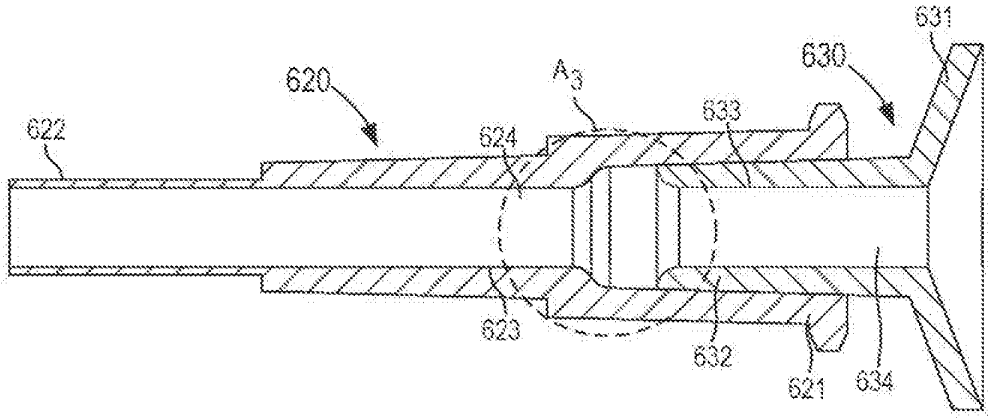

631
630
620
A_3
633
622
624
623
632
621
634

FIG. 12

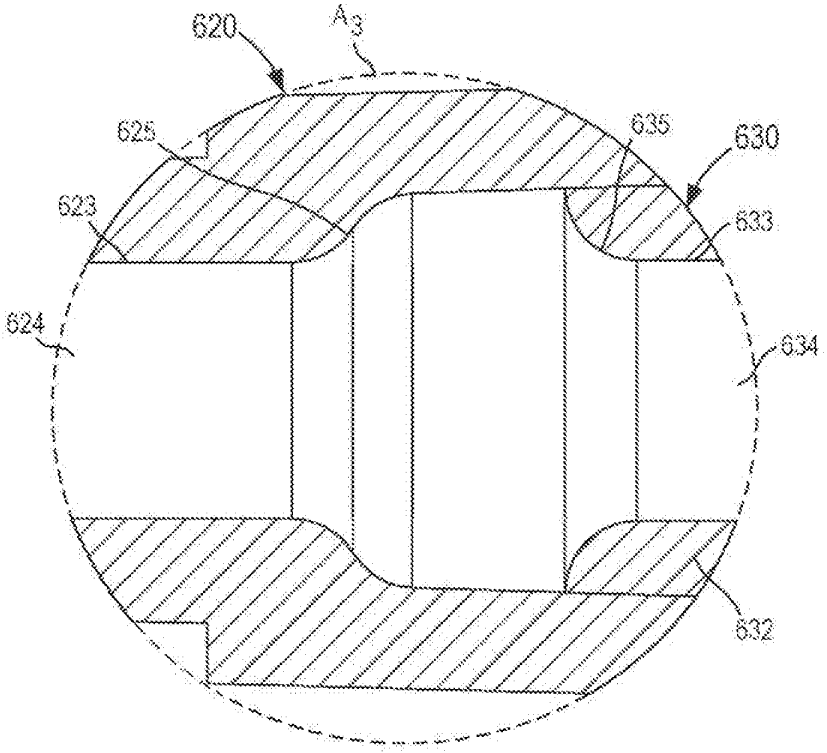

620
A_3
625
635
630
623
633
624
634
632

FIG. 13

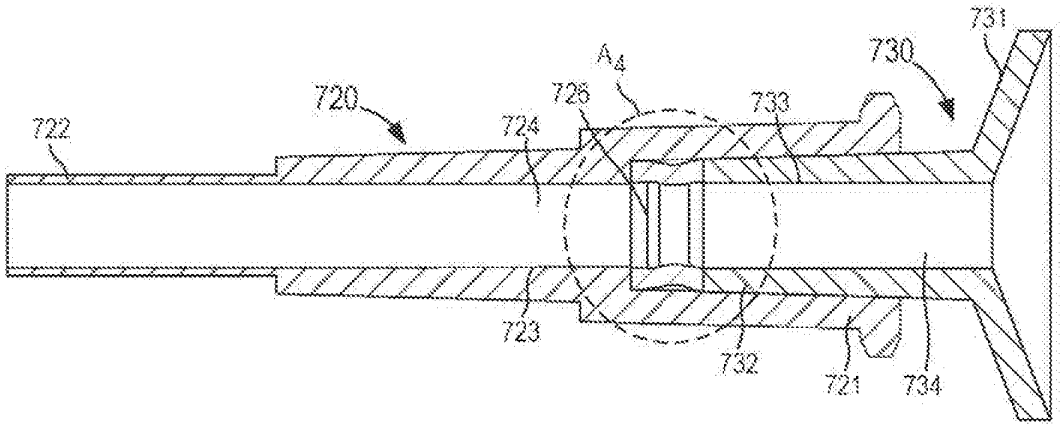

731
730
A_4
720
726
733
722
724
723
732
721
734

FIG. 14

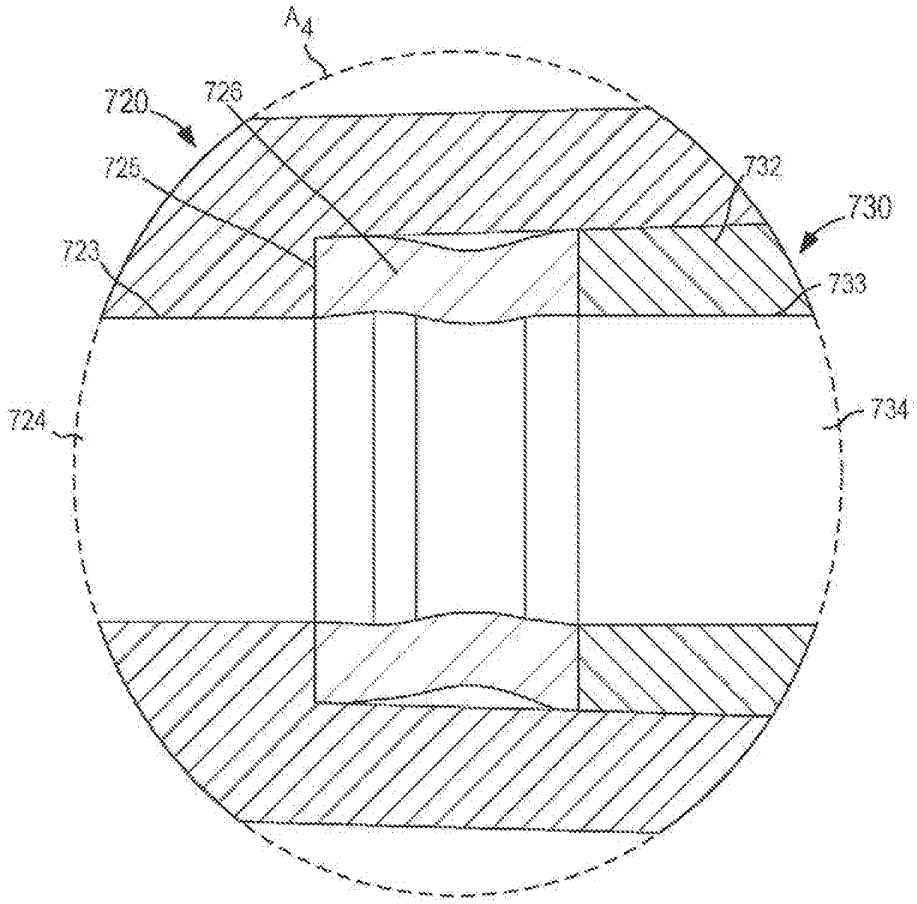

A_4
720
726
725
732
730
723
733
724
734

FIG. 15

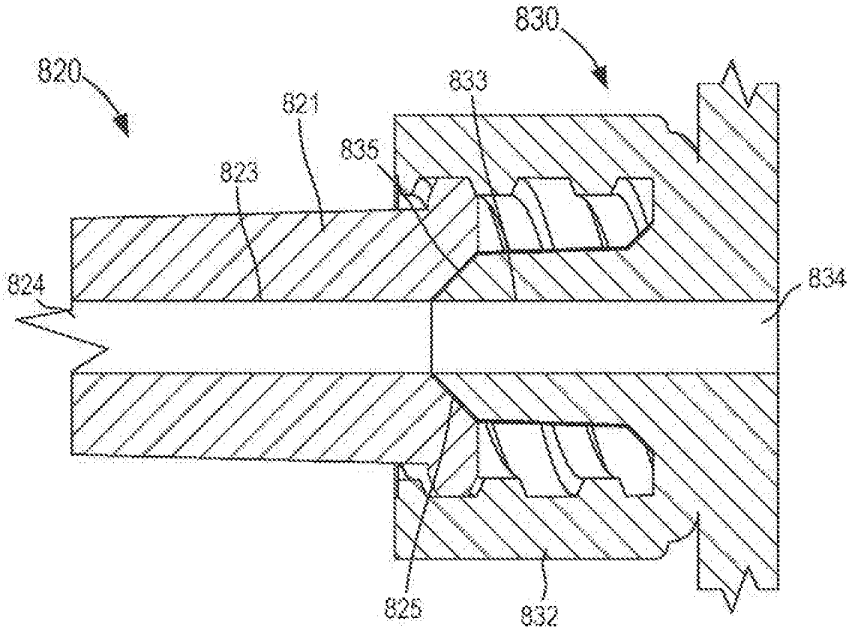

830
820
833
821
835
823
824
834
825
832

FIG. 16

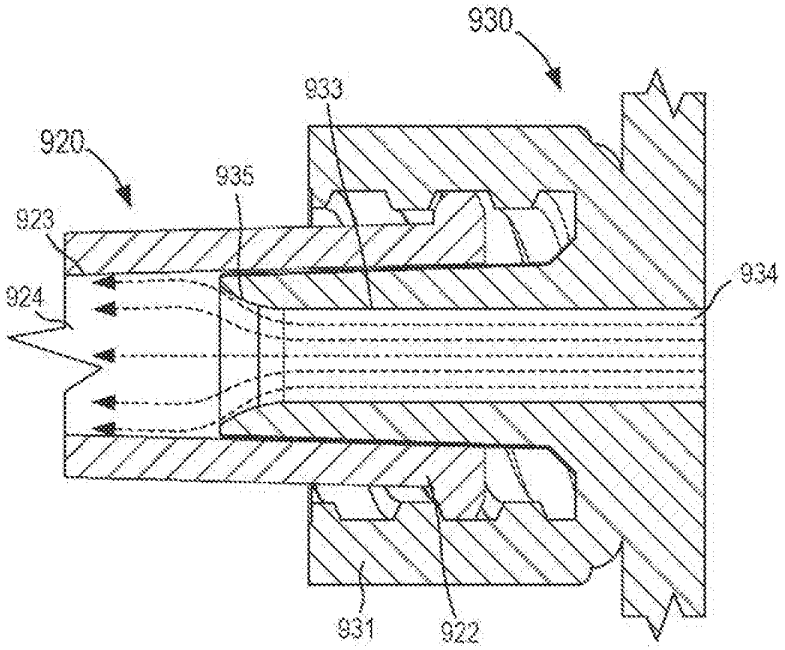

930
933
920
935
923
934
924
931
922

FIG. 17

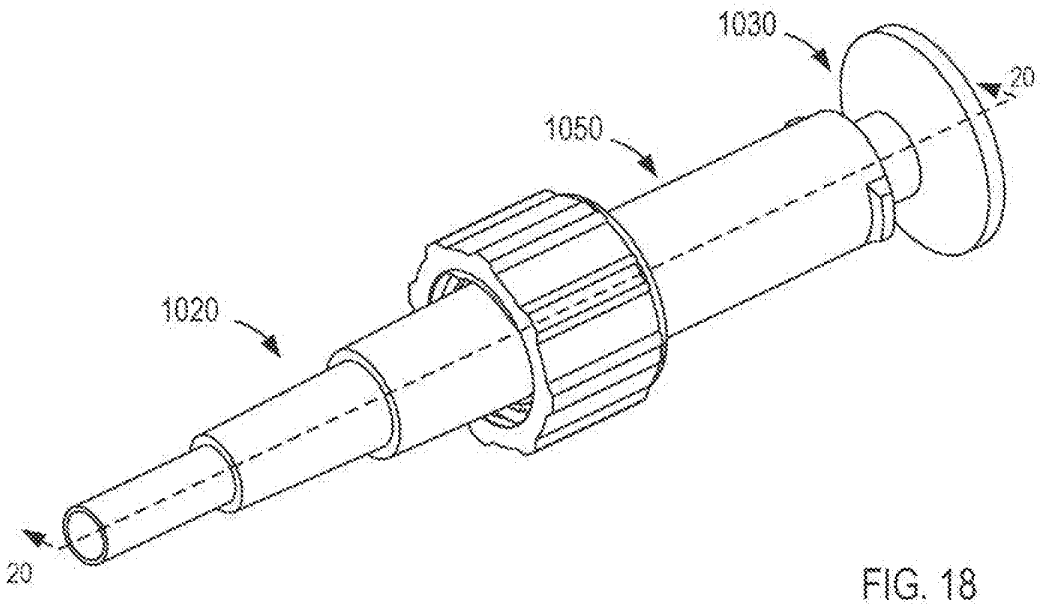

1030
20
1050
1020
20

FIG. 18

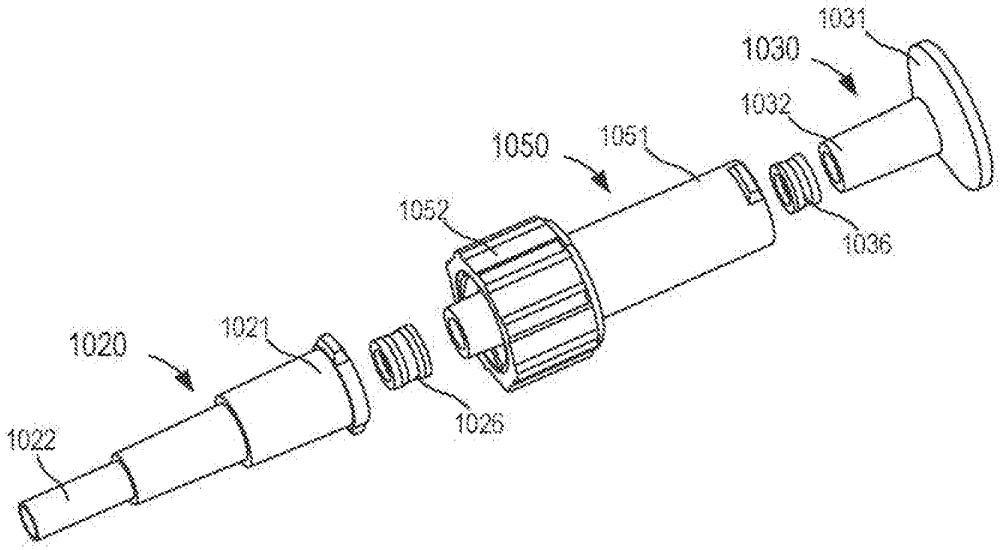

1031
1030
1032
1050
1051
1052
1036
1020
1021
1026
1022

FIG. 19

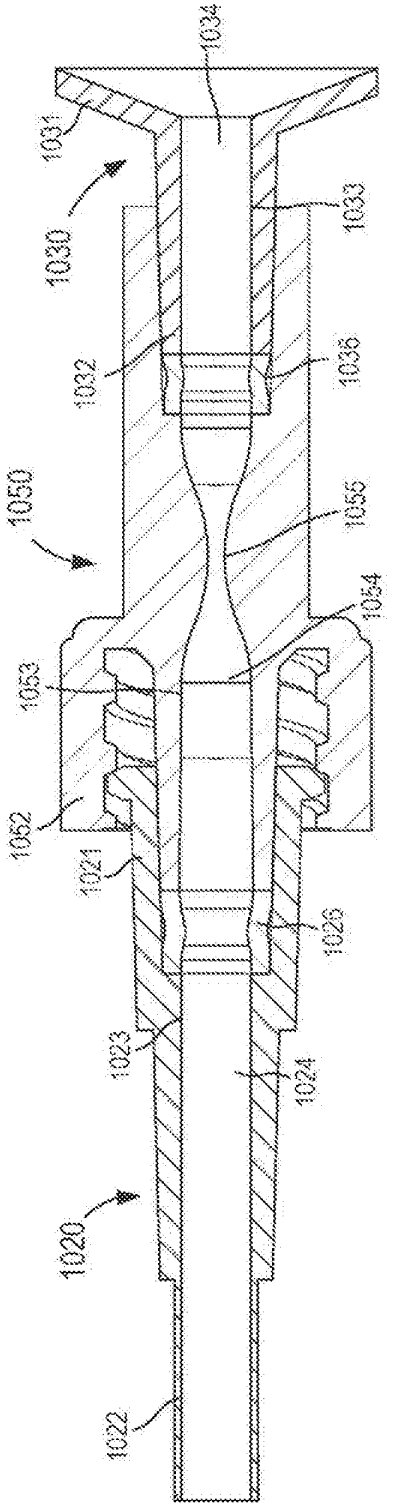

1034
1031
1030
1033
1032
1036
1050
1055
1054
1053
1052
1021
1026
1023
1024
1020
1022

FIG. 20

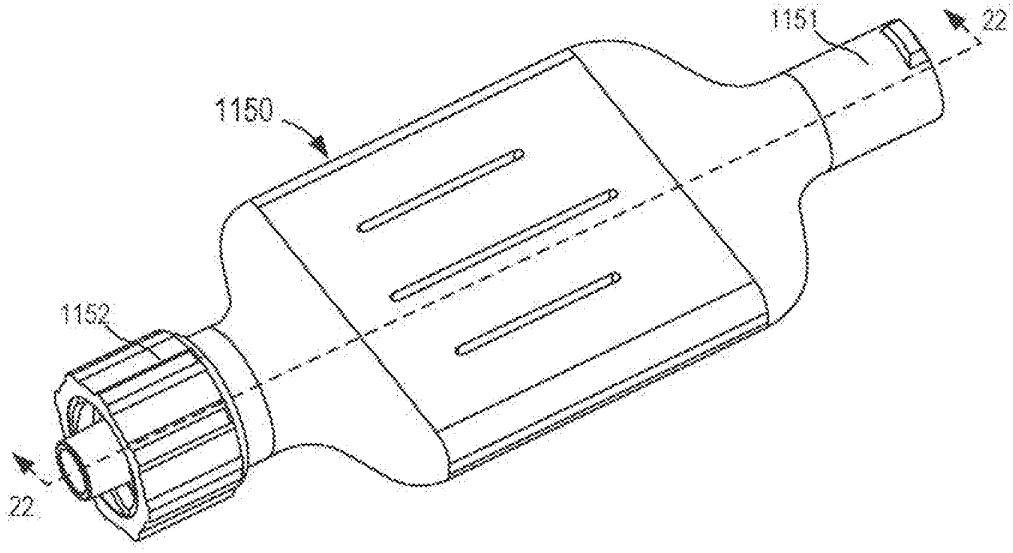


FIG. 21

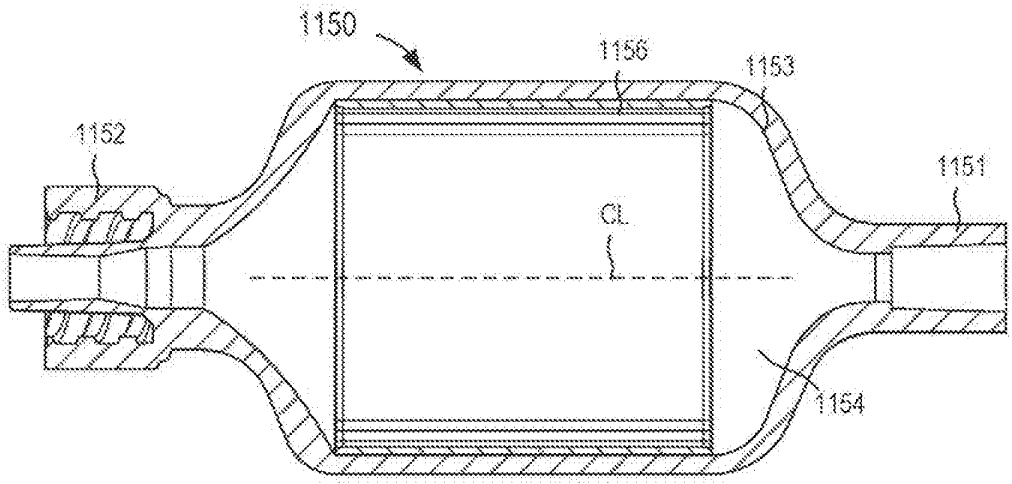


FIG. 22

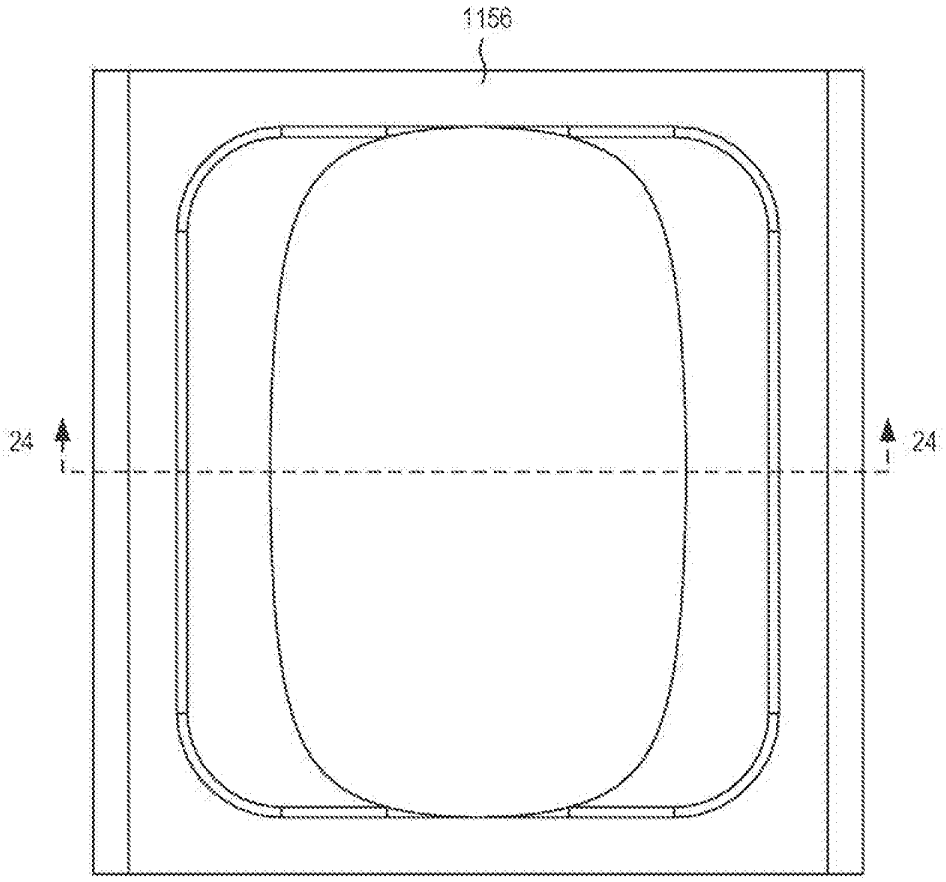


FIG. 23

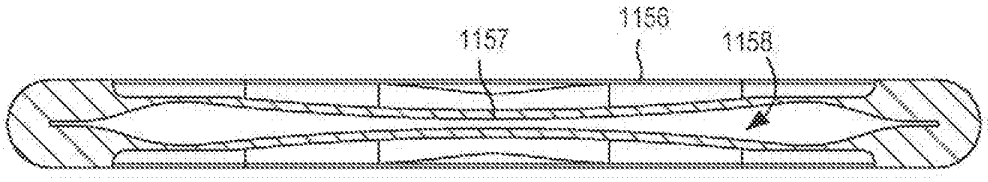


FIG. 24

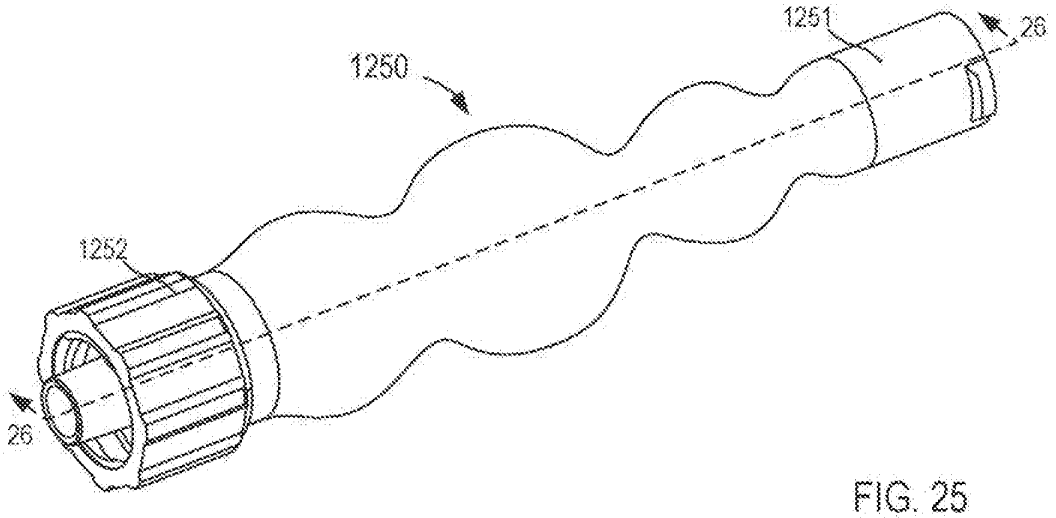

1251
26
1250
1252
26

FIG. 25

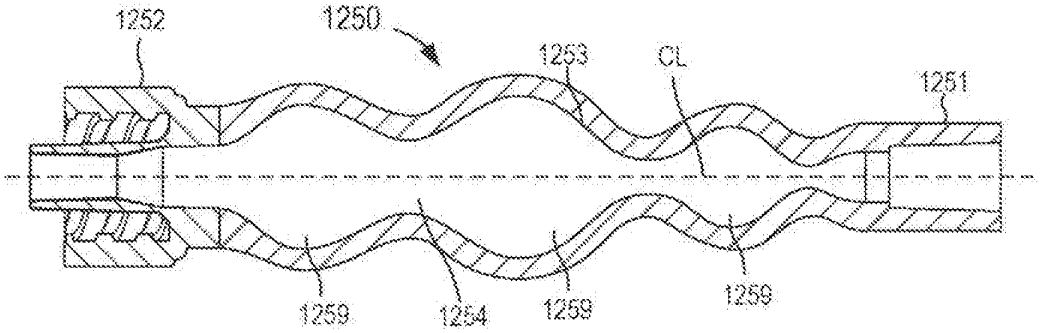

1252
1250
1253
CL
1251
1259
1254
1259
1259

FIG. 26

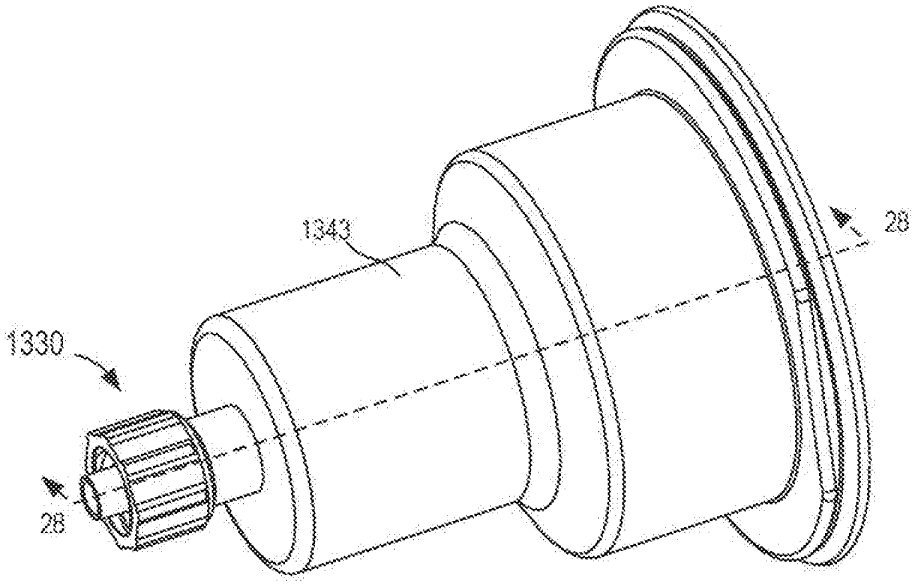


FIG. 27

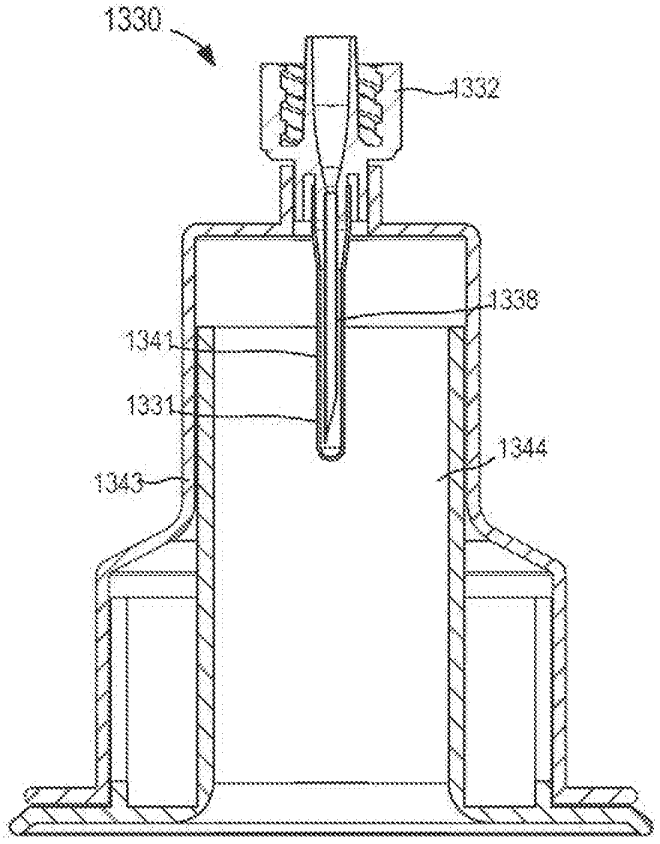


FIG. 28

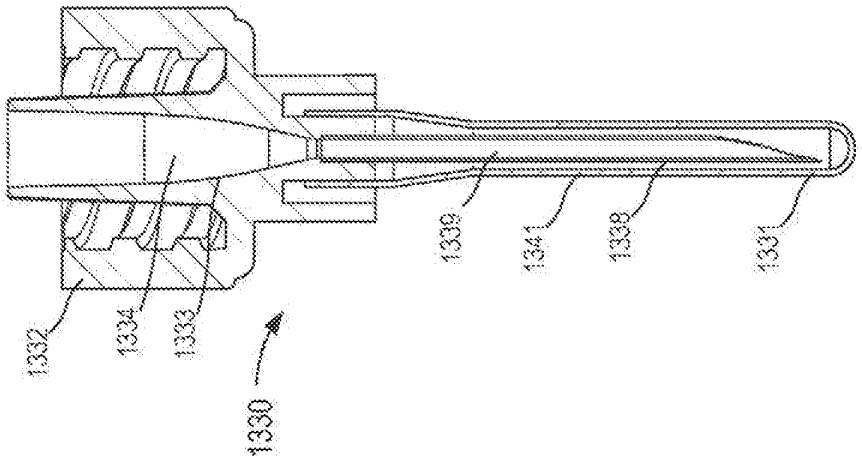


FIG. 30

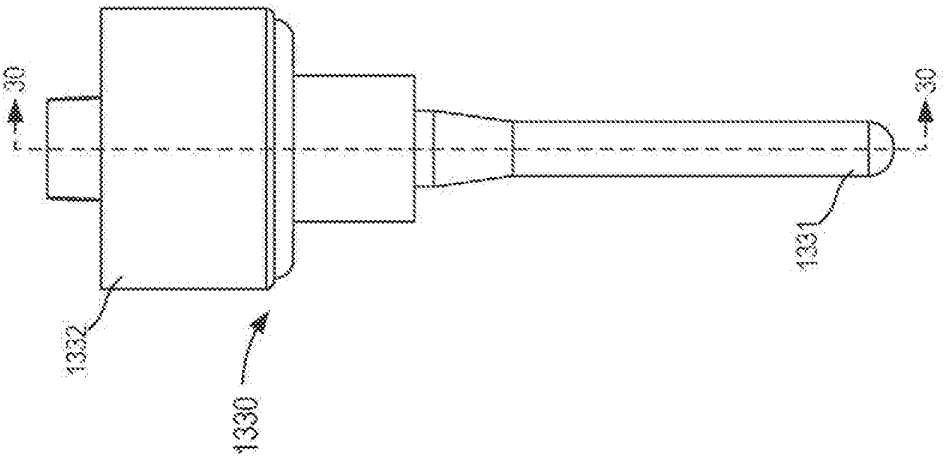


FIG. 29

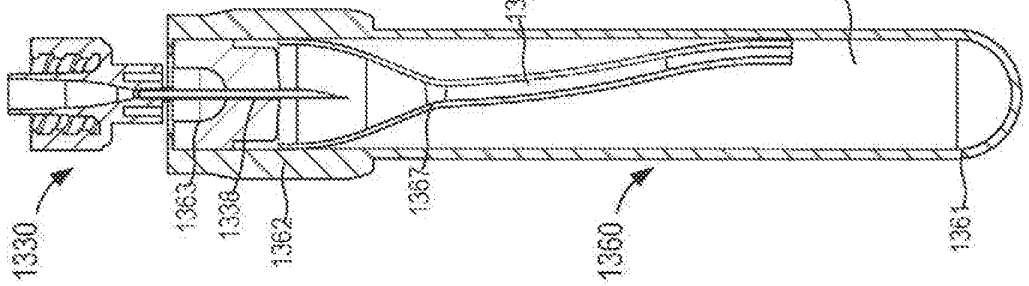


FIG. 33

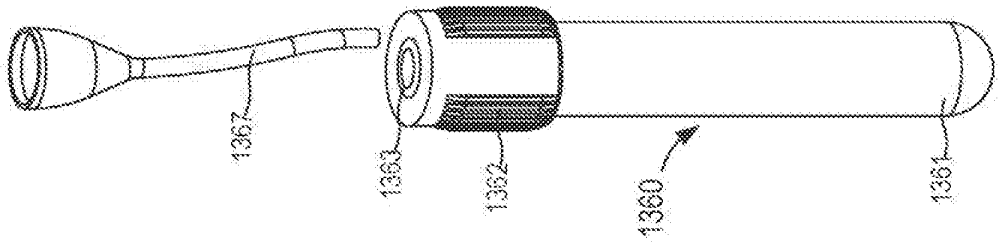


FIG. 32

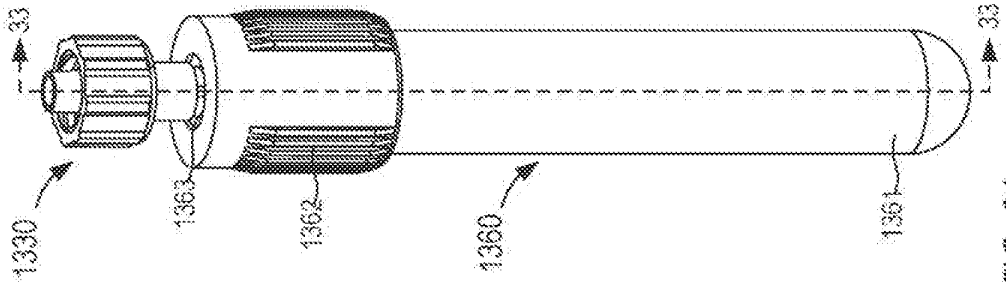


FIG. 31

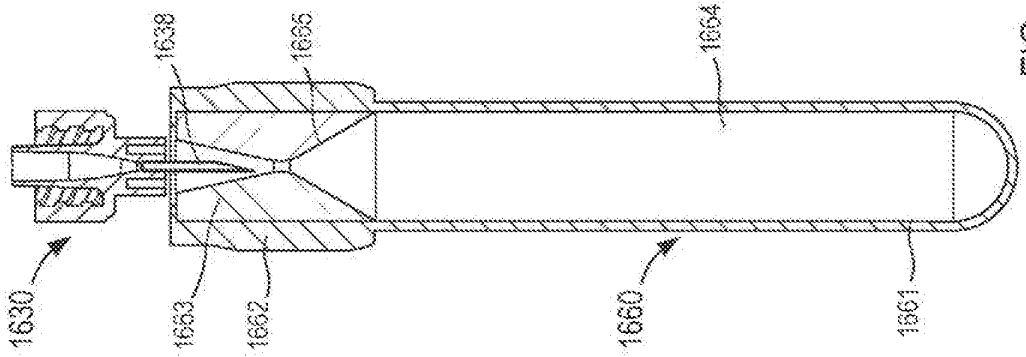


FIG. 36

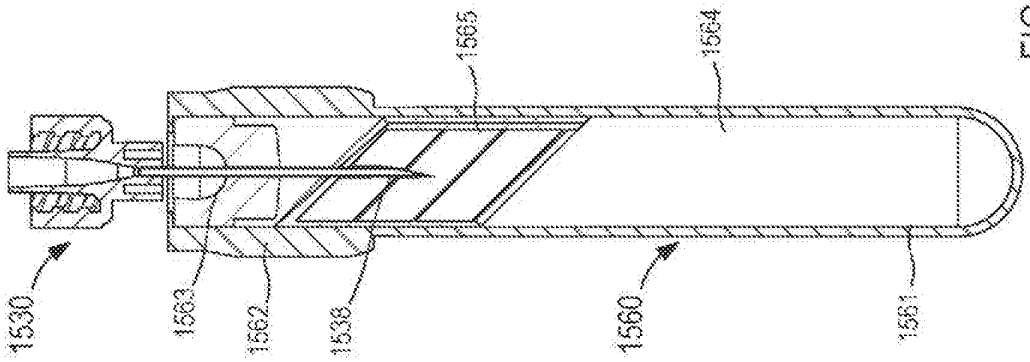


FIG. 35

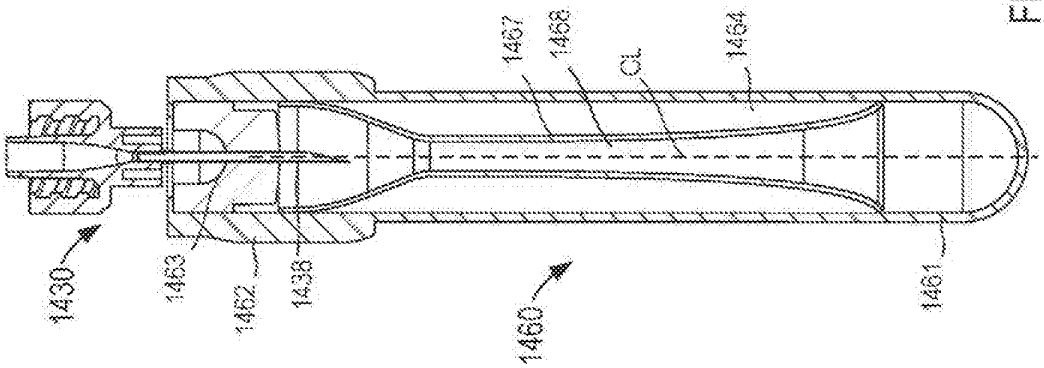


FIG. 34

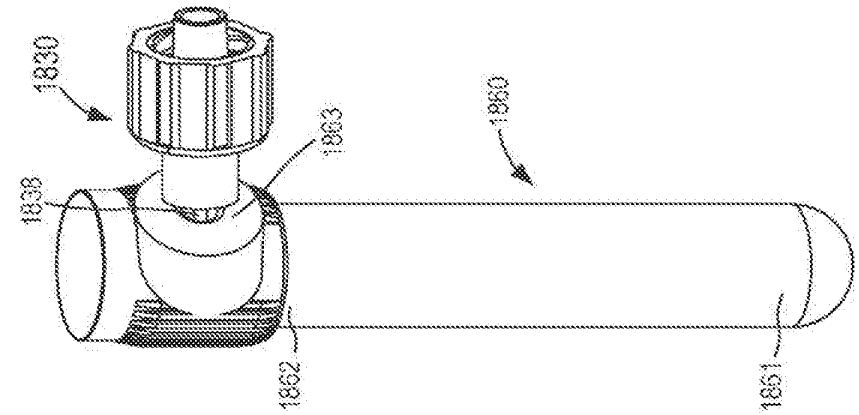


FIG. 39

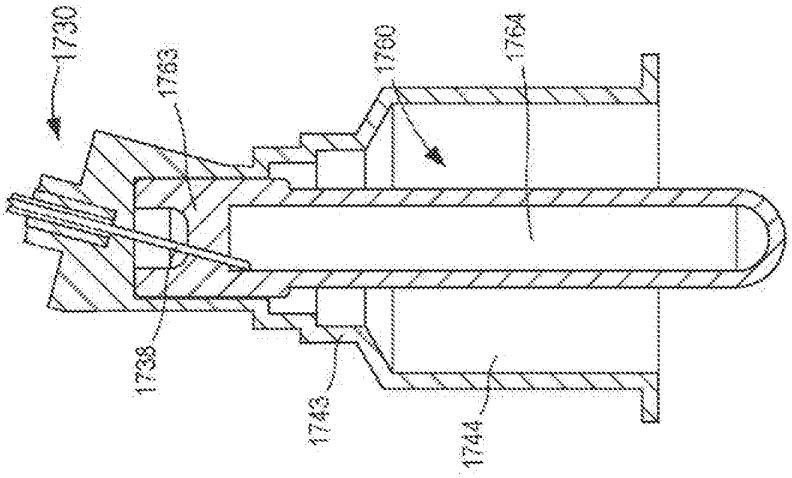


FIG. 38

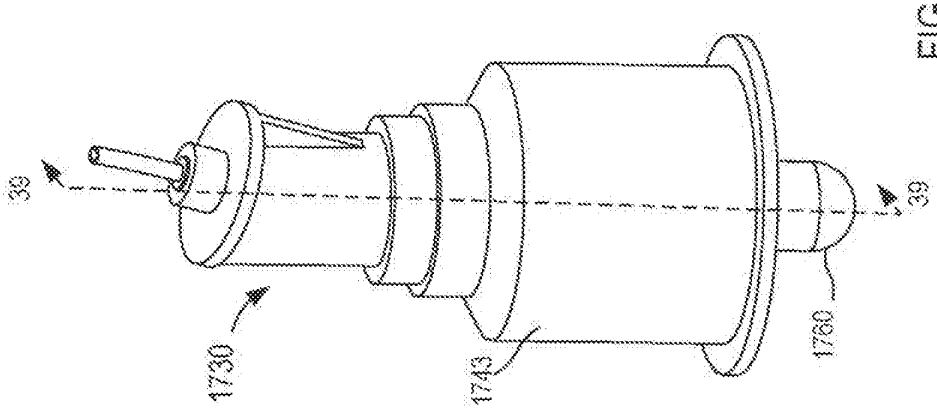


FIG. 37

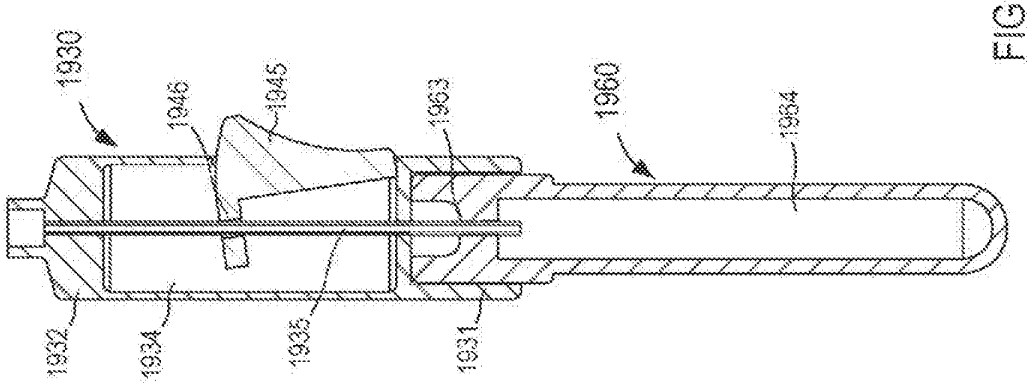


FIG. 42

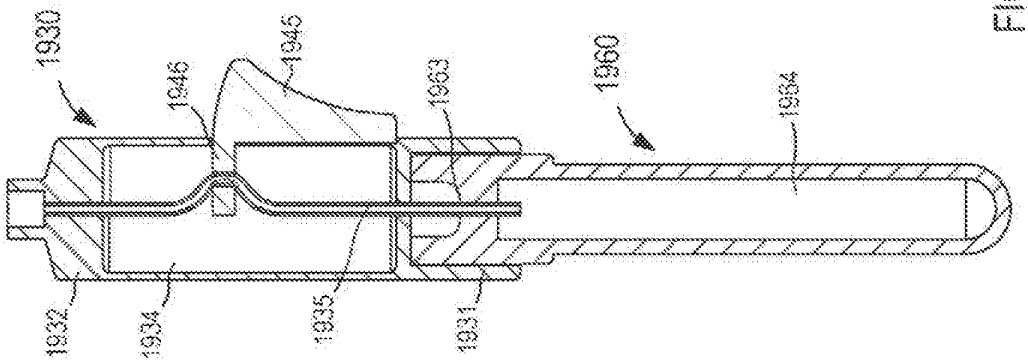


FIG. 41

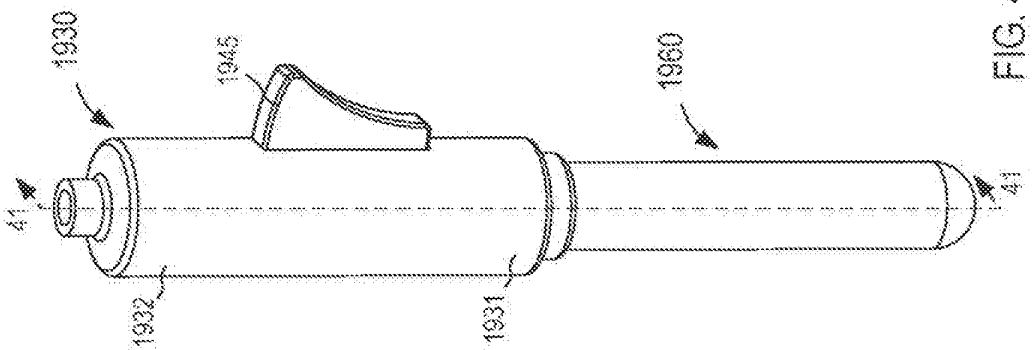


FIG. 40

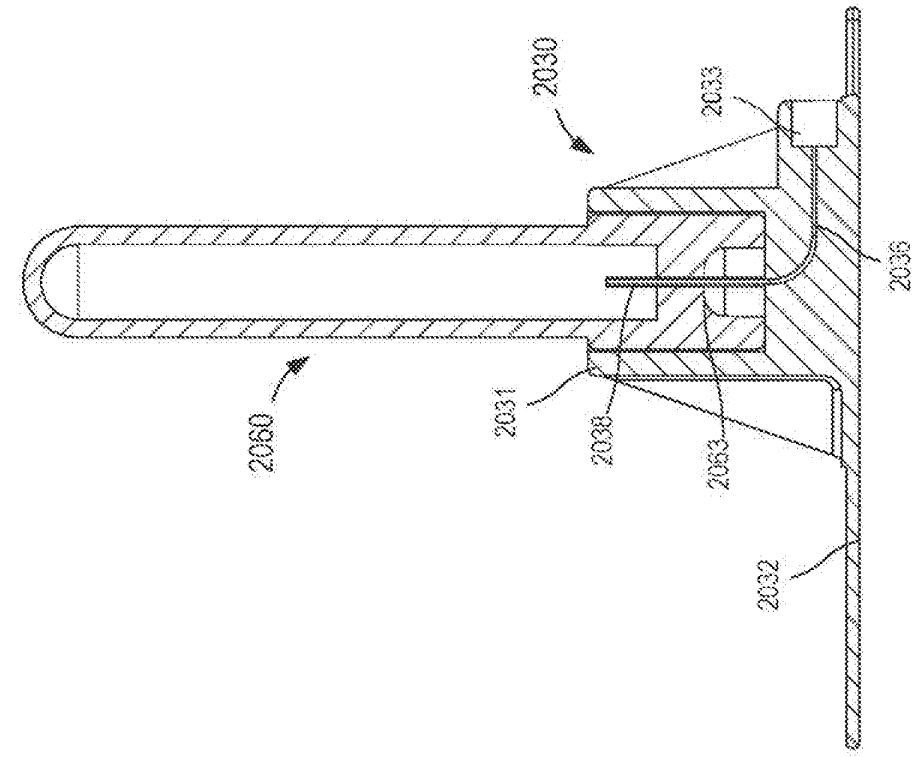

2030
2033
2036
2060
2031
2038
2063
2032

FIG. 44

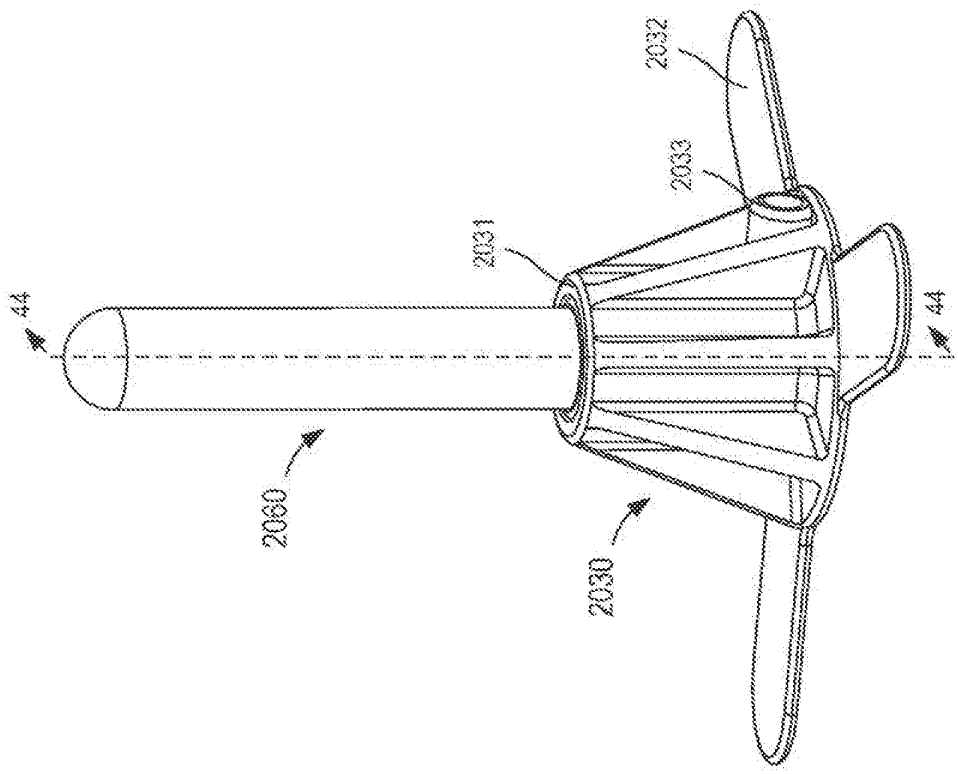

2032
2033
2031
44
44
2060
2030

FIG. 43

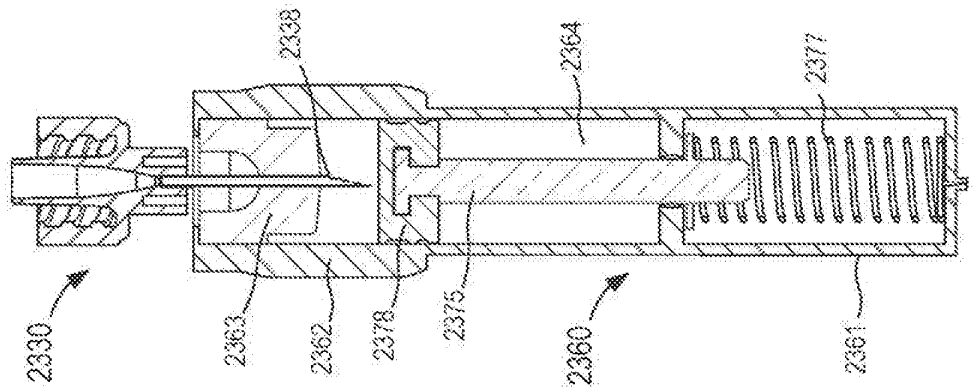


FIG. 47

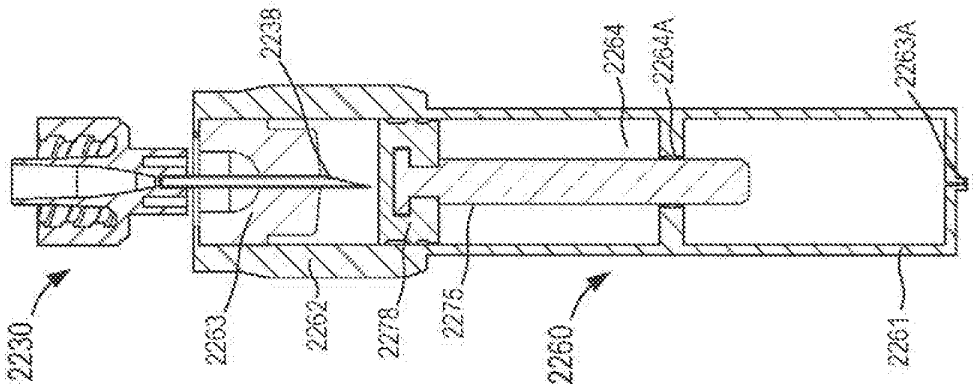


FIG. 46

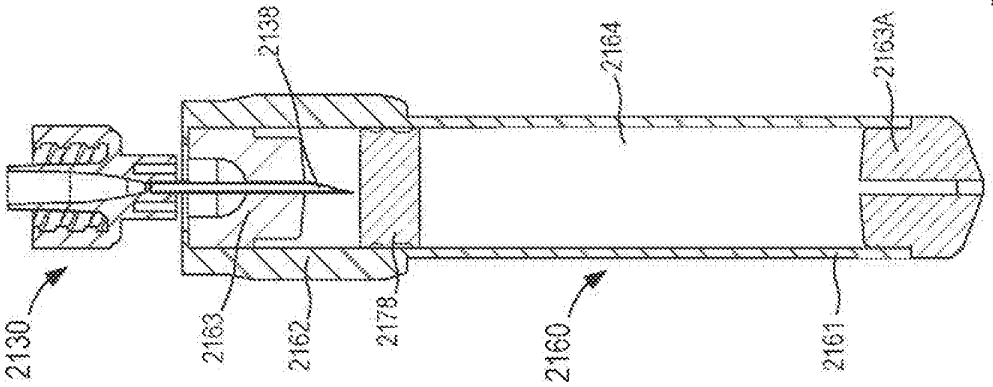


FIG. 45

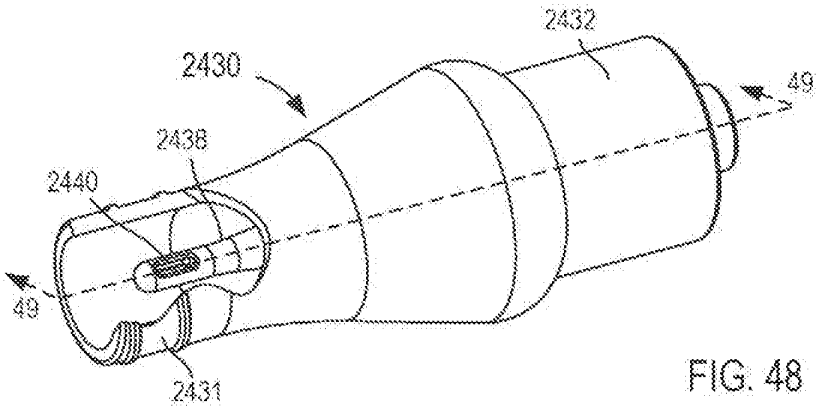


FIG. 48

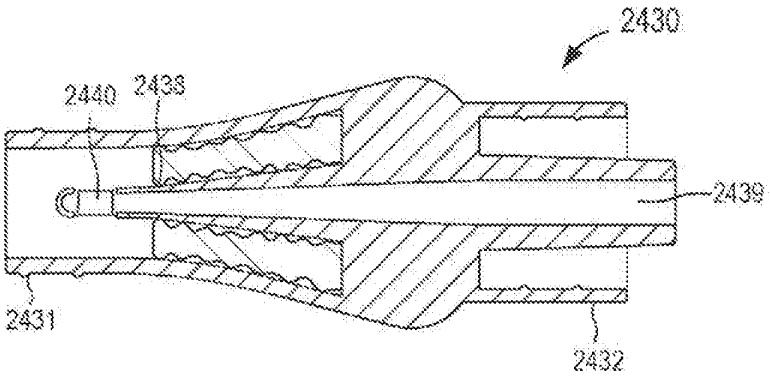


FIG. 49

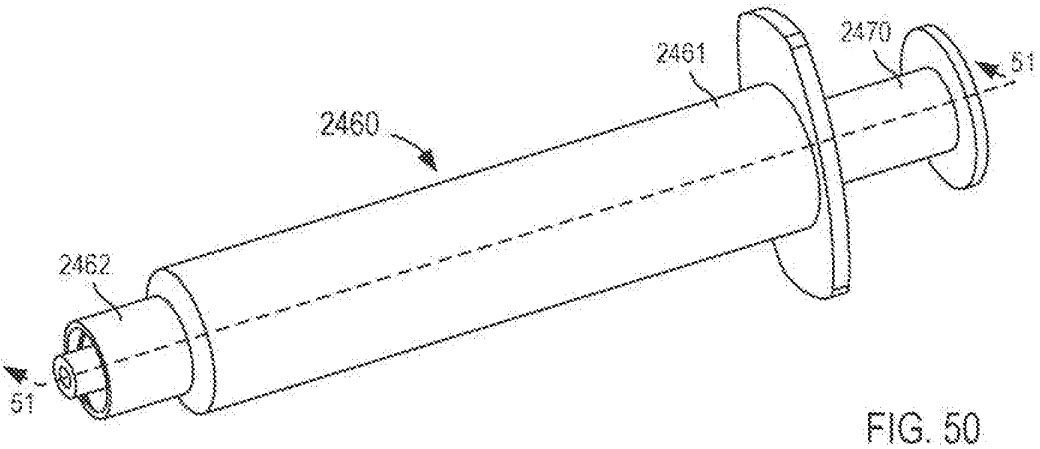


FIG. 50

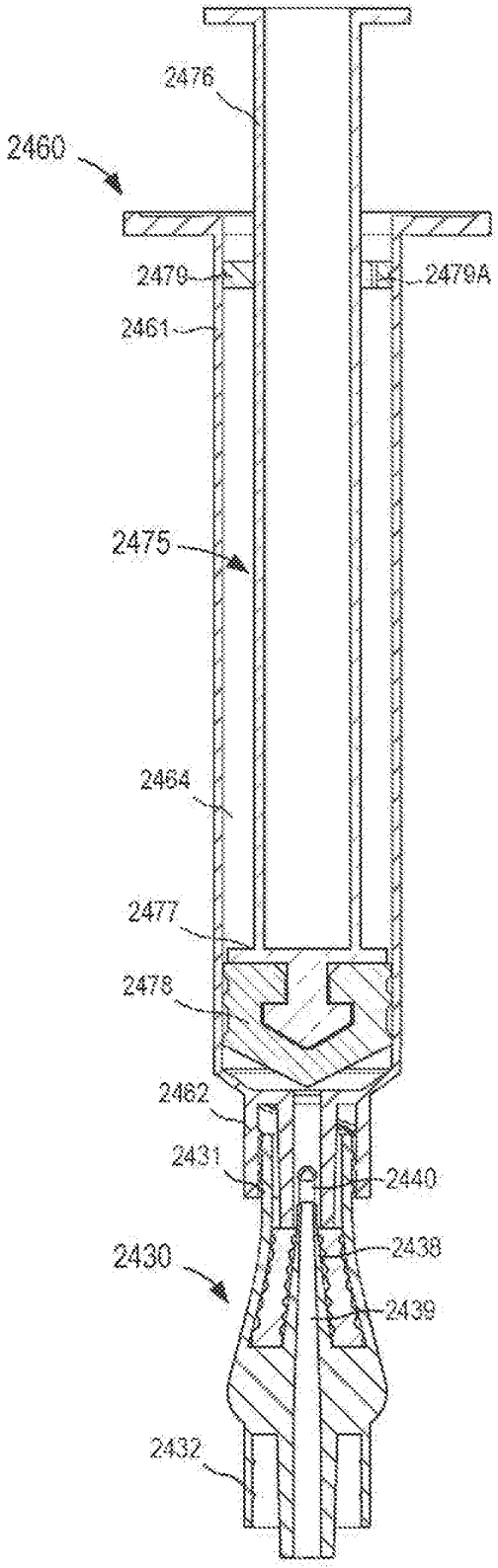

2476
2460
2470
2479A
2461
2475
2464
2477
2478
2462
2431
2440
2438
2430
2439
2432

FIG. 51

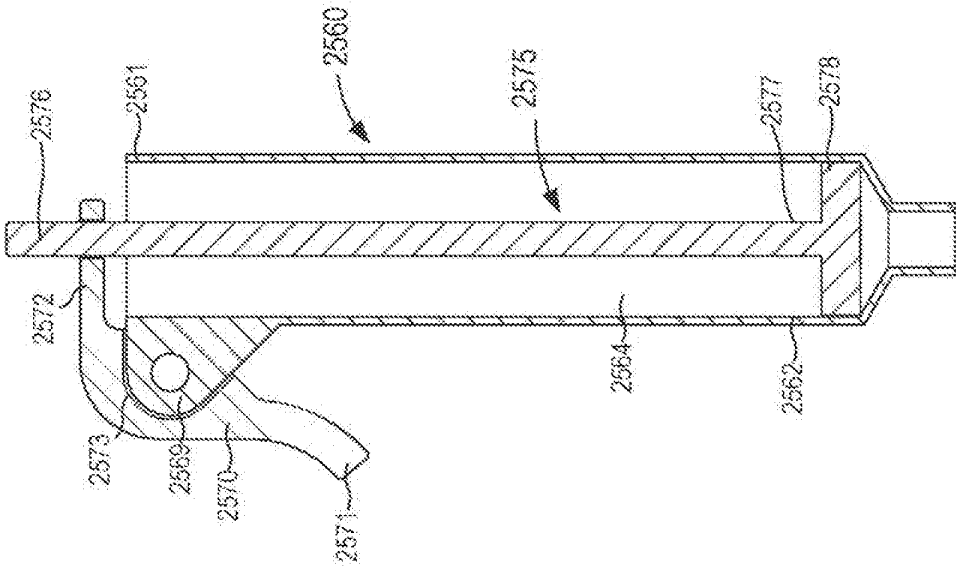

2560
2561
2575
2576
2577
2578
2572
2573
2569
2570
2571
2564
2562

FIG. 53

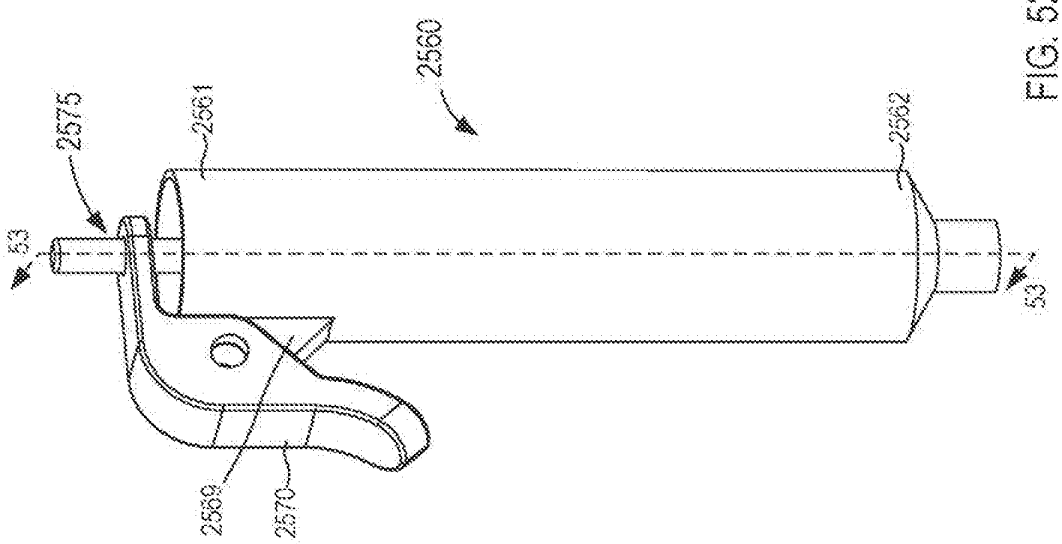

2560
2575
2561
2562
53
53
2569
2570

FIG. 52

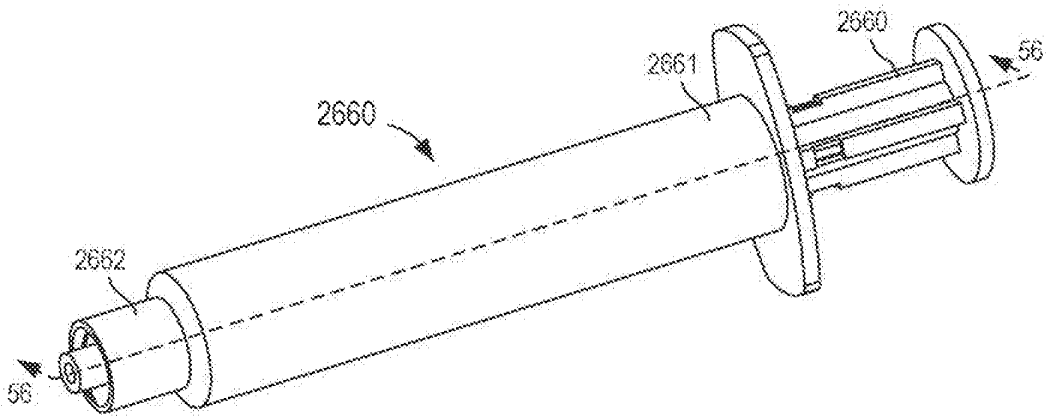

2660
2661
2660
56
2662
56

FIG. 54

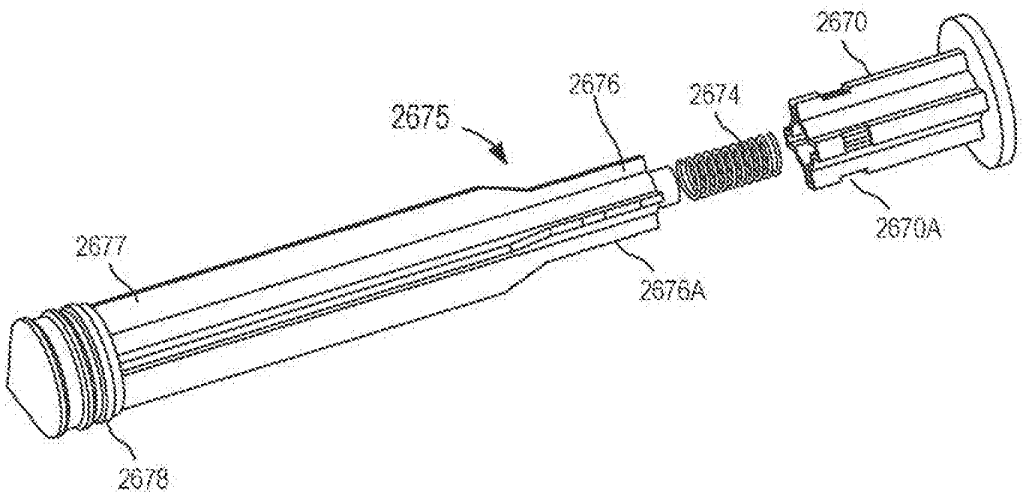

2670
2676
2674
2675
2670A
2677
2676A
2678

FIG. 55

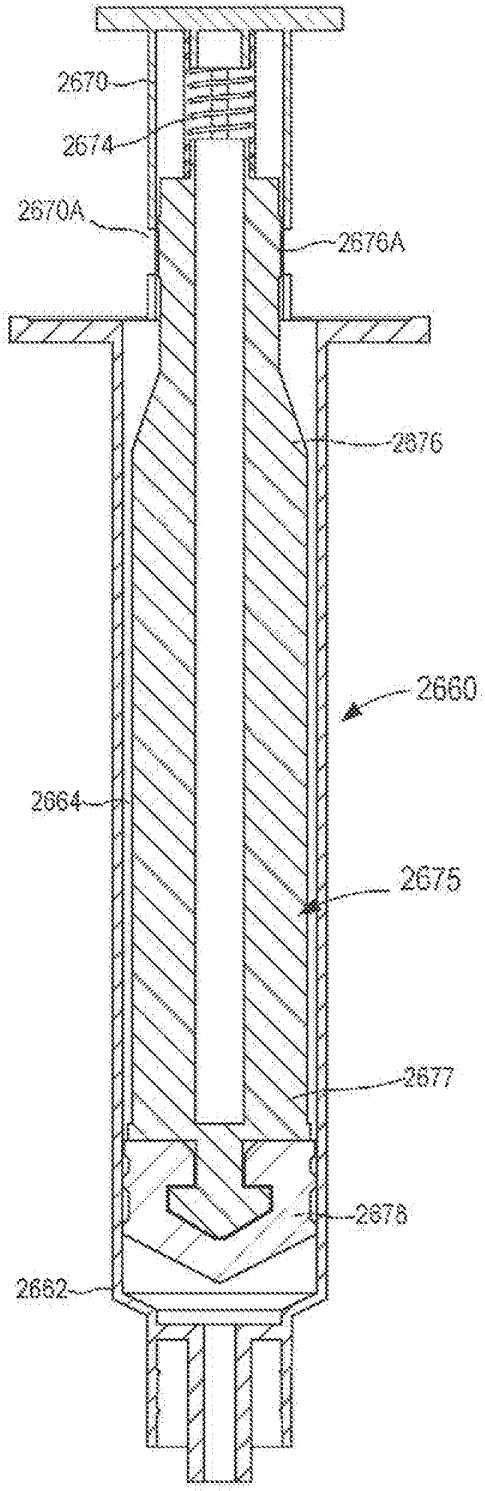


FIG. 56

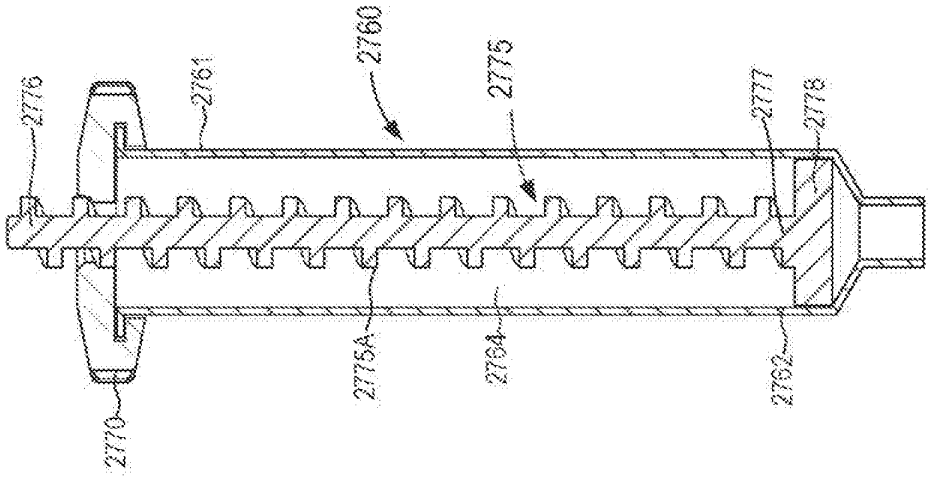

2776
2761
2760
2775
2777
2778
2775A
2764
2762
2770

FIG. 58

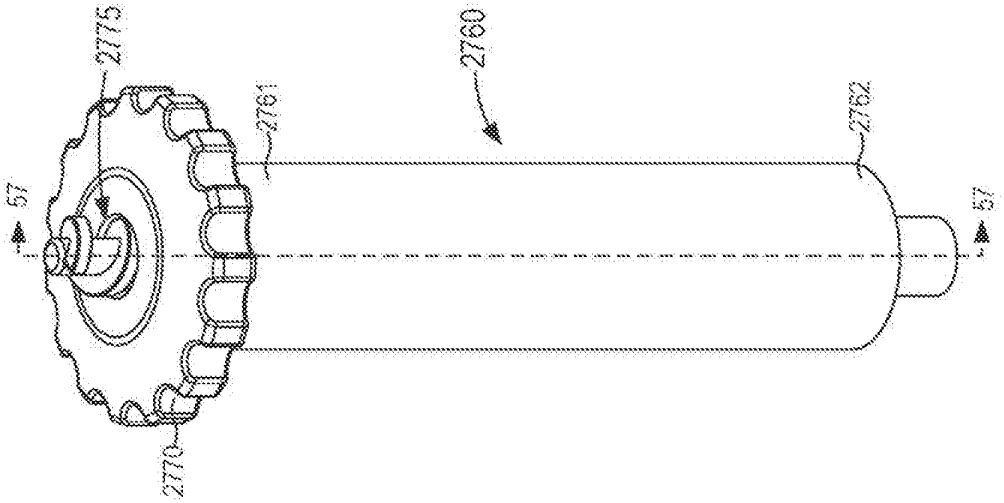

2775
2761
2760
2762
57
57
2770

FIG. 57

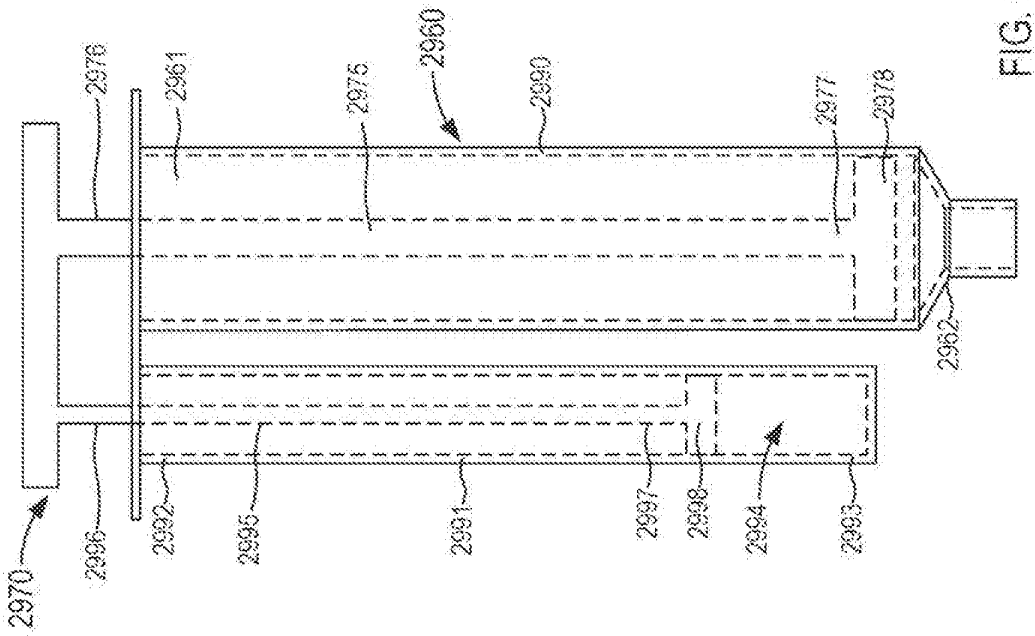

2976
2961
2975
2960
2990
2977
2978
2962
2970
2996
2992
2995
2991
2997
2998
2994
2993

FIG. 60

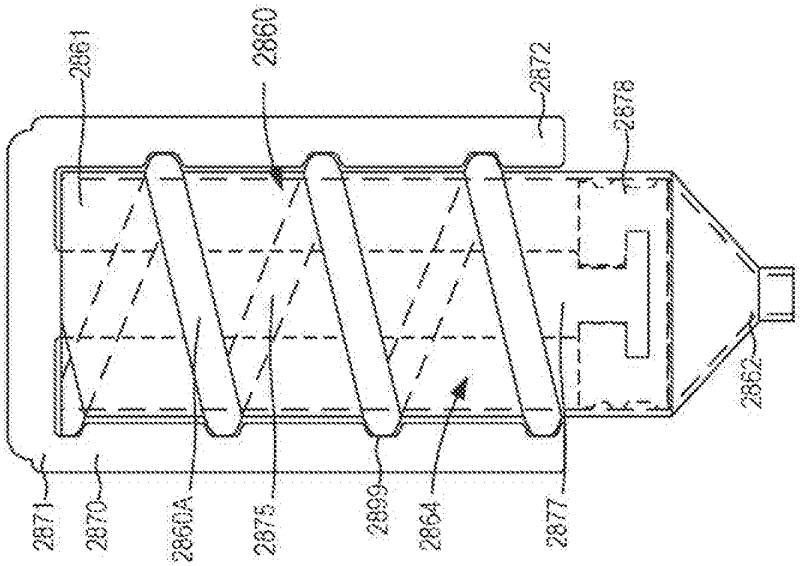

2861
2860
2872
2878
2862
2871
2870
2860A
2875
2869
2864
2877

FIG. 59

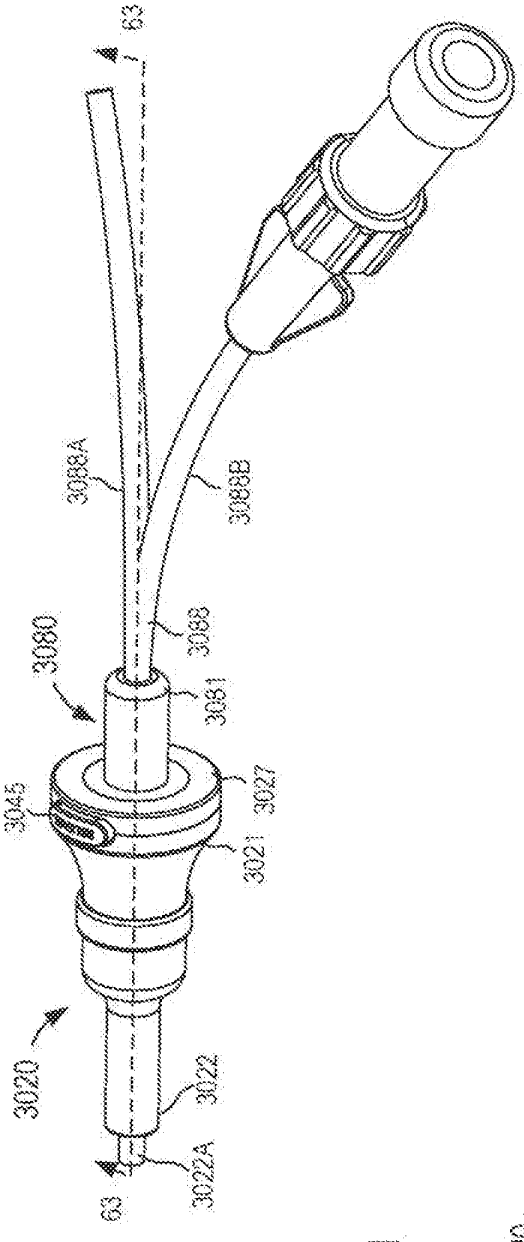

63
3088A
3088B
3080
3088
3081
3045
3027
3021
3020
3022
3022A
63

FIG. 61

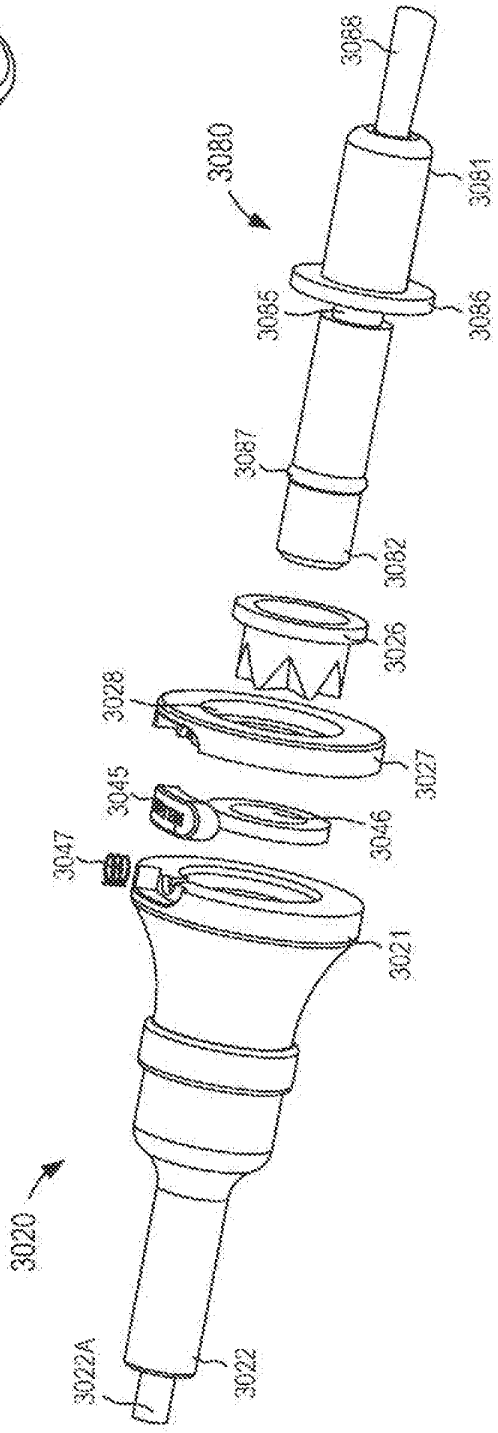

3088
3081
3080
3085
3086
3087
3082
3026
3028
3027
3045
3046
3047
3021
3020
3022A
3022

FIG. 62

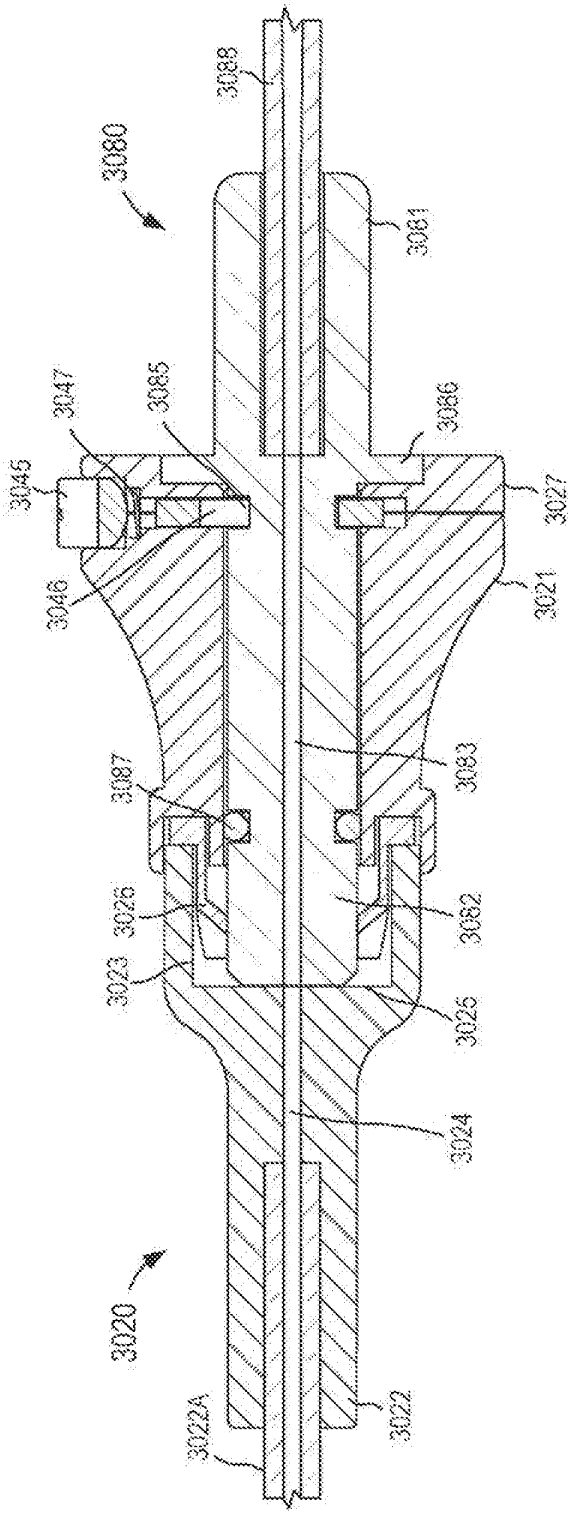

3088
3080
3081
3047
3085
3086
3045
3027
3046
3021
3087
3083
3026
3082
3023
3025
3024
3020
3022A
3022

FIG. 63

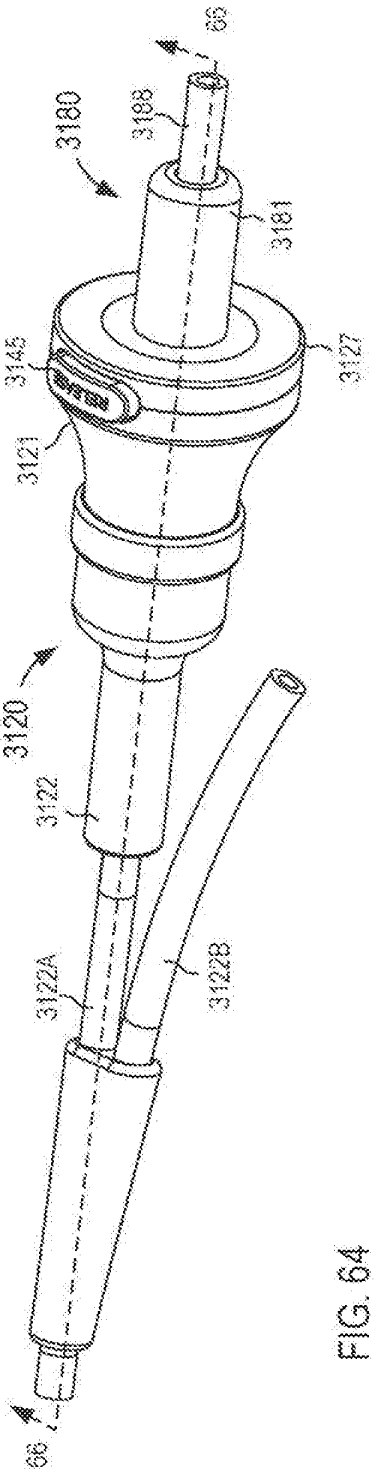

66
3188
3180
3181
3127
3145
3121
3120
3122
3122A
3122B
66

FIG. 64

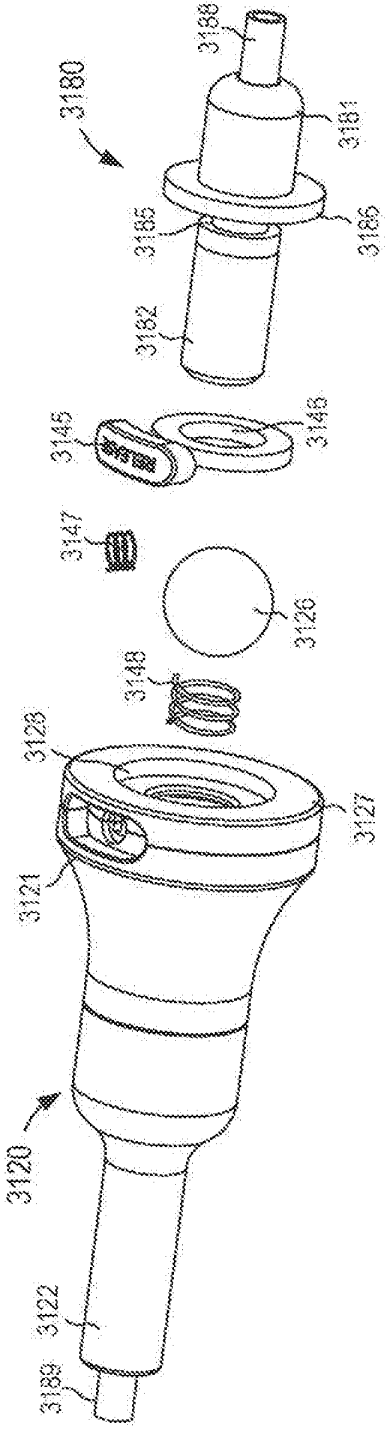

3188
3180
3181
3185
3186
3182
3145
3146
3147
3126
3148
3123
3127
3121
3120
3122
3189

FIG. 65

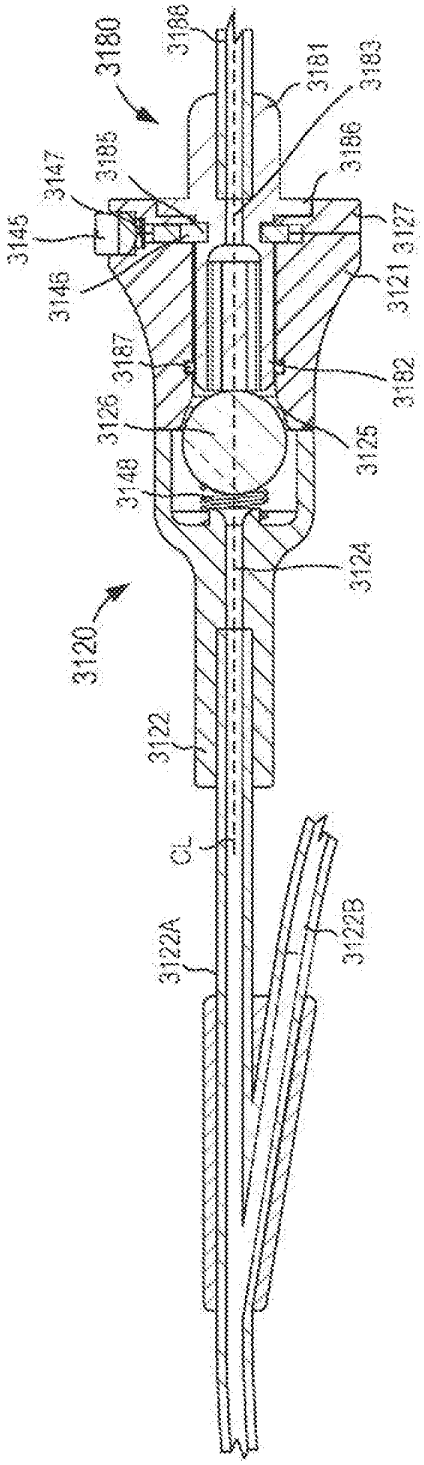

3180
3186
3181
3183
3185
3147
3186
3145
3127
3146
3121
3187
3182
3126
3125
3148
3124
3120
3122
CL
3122A
3122B

FIG. 66

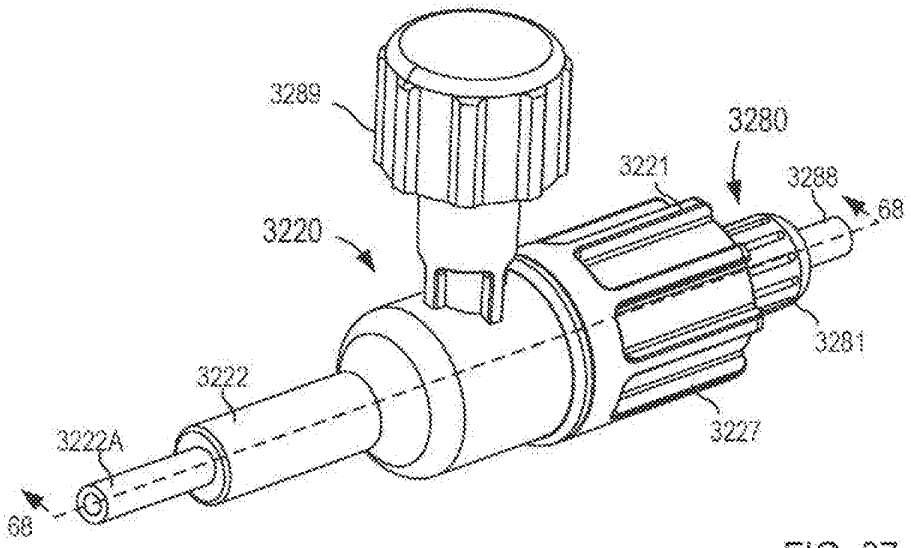

3289
3280
3221
3288
68
3220
3281
3222
3227
3222A
66

FIG. 67

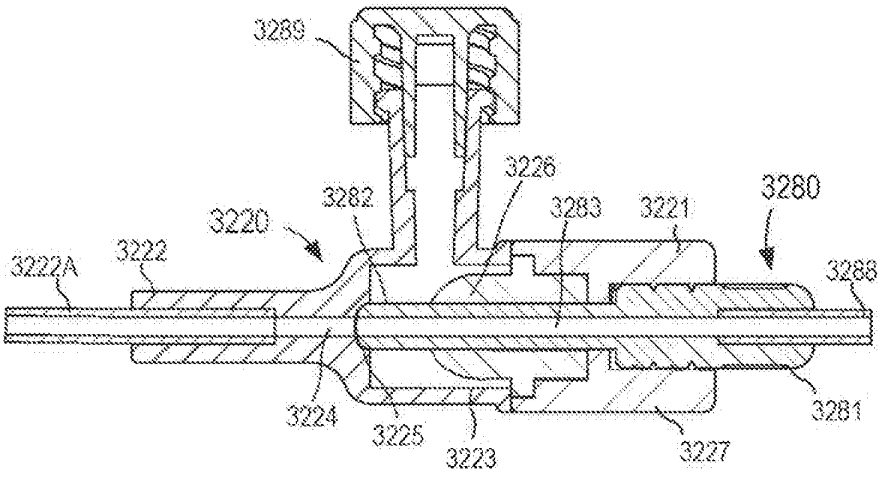

3289
3226
3282
3283
3221
3280
3220
3222
3222A
3288
3224
3225
3223
3227
3281

FIG. 68

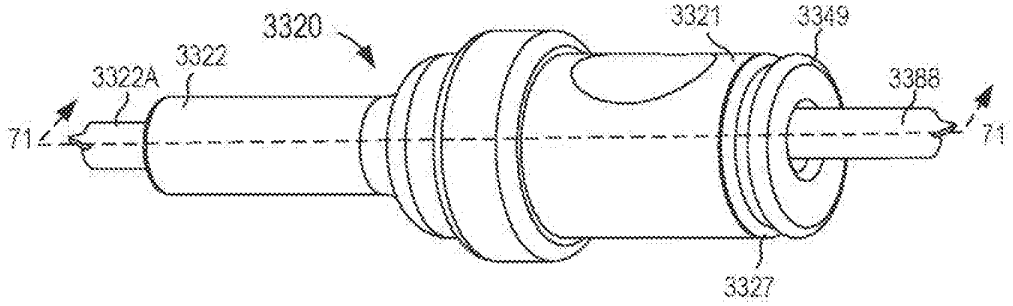

3320
3321
3349
3322
3322A
3388
71
71
3327

FIG. 69

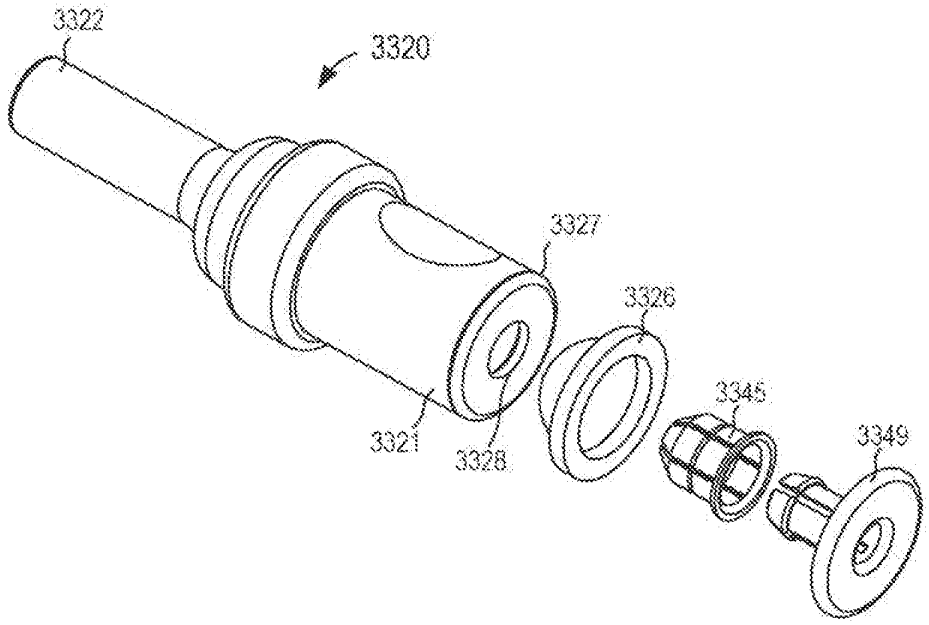

3322
3320
3327
3326
3345
3349
3321
3328

FIG. 70

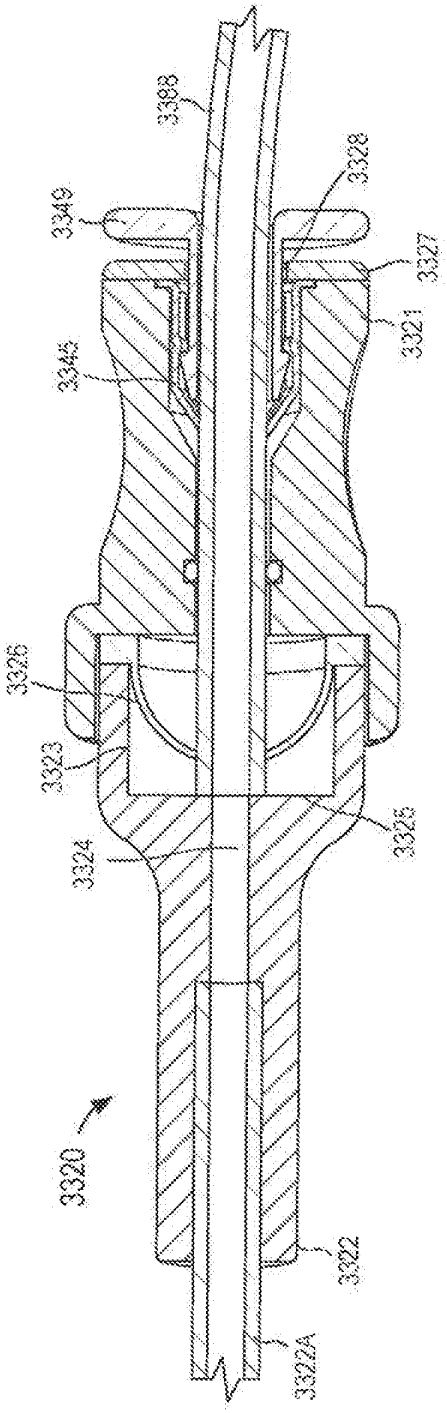

3308
3328
3349
3327
3321
3345
3326
3323
3325
3324
3320
3322
3322A

FIG. 71

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

Page 2420 of 5977

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.

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. +44 208 967 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 1999, the French haemovigilance surveillance system (a mandatory requirement under French law), attributed 18 deaths (four occurring in 1997) to blood components contaminated with bacteria [5, 6]. Between 1994 and 1999, bacterial transmissions comprised 22% of total transfusion-associated fatalities [7]. Transmission of bacteria by transfusion was reported to the haemovigilance surveillance system as the most frequently identified cause of death [5].

In the USA, from 1985 to 1989 bacterial contamination was second only to haemolytic reactions as the most frequent reported cause of mortality, accounting for over 10% (77/694) of transfusion fatalities [8]. From 2001 to 2003, the transmission of bacteria by transfusion accounted for 37 deaths, amounting to 14.1% of all transfusion fatalities [9].

A National Health Service Blood and Transplant (NHSBT) retrospective monitoring study was established in 1995 to determine the bacterial contamination rate in blood components using an automated microbial detection system [10, 11]. The study was also used to determine the effectiveness of any interventions implemented to reduce bacterial contamination.

Data from this study and SHOT surveillance data indicated that the vast majority of organisms that contaminate blood components are skin commensals derived from the skin of the donor at venepuncture. NHSBT therefore explored two interventions:

– improved donor arm disinfection,
– diversion.

Material and Methods

Improved Donor Arm Disinfection

A study was undertaken to determine the effectiveness of in-house and commercial disinfection protocols [12]. Swabbing of the venepuncture site was performed before and after disinfection. Swabs were inoculated onto agar plates, and the reduction in bioburden pre and post disinfection was determined. A second study was undertaken to derive a disinfection procedure that would only take 1 min to perform [13].

Diversion

In 1995, Olthuis et al. [14] proposed that diversion of the initial volume of blood donation from the collection bag had the potential to dramatically reduce bacterial contamination. The rationale behind this is that (as previously mentioned) the major source of bacterial contamination of blood components occurs at the collection stage, due to inadequate donor arm disinfection and/or a small core of skin entering the collection bag from coring by the phlebotomy needle. Re-direction of the initial flow of blood from the collection bag into a pouch or side arm would thus reduce the risk of bacterial contamination of the donation contents.

Special collection bags were manufactured for a study to determine the effectiveness of diversion [15]. These bags consisted of two sampling pouches attached to the standard collection bag configuration. At donation, blood was made to flow initially into pouch P1, which represented a diversion pouch. Pouch P1 was then closed causing the blood to flow into pouch P2, which acted as a representative sample of the collection bag post diversion. P2 was then closed, and blood was

diverted into the collection bag as in a routine donation. The pouches were sampled and inoculated into culture bottles and incubated on an automated microbial detection system for 7 days. Any bacteria that grew were sub-cultured and identified.

Results

Improved Donor Arm Disinfection

The Donor Prep Kit (DPK) (Ecolab (formerly Medi-Flex), Leadwood, KS, USA) was shown to be a best-practice technique, consisting of an initial application of isopropyl alcohol and tincture of iodine. The procedure took 2 min, with an application time of 30 s and drying time of 30 s for each disinfectant. A percentage reduction of 99.79% ($\log_{10}$ reduction 2.67%) was obtained compared with 78.2% ($\log_{10}$ reduction 1.31%) for the then current method, 0.5% chlorhexidine isopropyl alcohol wipe (Guardpack, Chelmsford, Essex, UK) [12].

The DPK was implemented for apheresis platelet donations in July 2001, and the reduction in the bacterial contamination rate of time-expired platelet donations was shown to be 57% [16]. Previously an experimental study predicted a 57% reduction in contamination [15]. A 67% reduction in clinically apparent cases of bacterial transmission following transfusion of NHSBT blood donations reported to SHOT was observed [17]. In the period 1997 to 2000 prior to implementation, 6 clinical cases (including 2 deaths) were reported. After the introduction of the DPK at apheresis clinics in the 4-year period from July 2001 to 2005, only 2 clinically apparent reactions from transfusion of platelet concentrates manufactured by NHSBT have been reported.

An extensive field evaluation of the use of the DPK procedure has been undertaken at mobile blood donor sessions. It was however, deemed inappropriate for routine use by NHSBT because it would increase donor waiting times. This was due to the additional 3 min that was required with the DPK compared with the routine method in use at that time. The NHSBT National Bacteriology Laboratory (NBL) was therefore tasked with identifying a disinfection procedure that was of comparable disinfection efficacy as the DPK, but was only 1 min in duration.

The ChloraPrep® disinfection method (CareFusion Ltd, Reigate, UK), consisting of a 30-second application of 70% isopropyl alcohol and 2% chlorhexidine gluconate with a 30-second drying time was shown to give equivalent disinfection efficiency as the DPK [13]. In 2006, ChloraPrep was implemented throughout NHSBT for both routine and apheresis donations.

Diversion

A 47% reduction in bacterially contaminated blood donations was observed in our study on the effectiveness of diversion [15]. On the basis of this study, diversion was implemented nationally in 2002. Monitoring data derived from testing outdated platelet concentrates showed a 66% reduction in contamination [16]. Prior to the implementation of diversion in the 3-year period 1999 to 2001, there were 11 clinically apparent cases from NHSBT-produced pooled platelet concentrates (n = 9) and red cell units (n = 2). After the implementation of diversion in the 3-year period 2003 to 2005, there were only 2 reports of clinically apparent transmission of bacteria by transfusion, a reduction of 82% [17].

The NHSBT diversion study also indicated that diversion, together with improved donor arm disinfection, would reduce bacterial contamination by approximately 77% [15].

Discussion

Donor arm disinfection is the first physical intervention applied to prevent microbial contamination of a blood donation. Many blood services have now validated and implemented best-practice procedures [18, 19]. In Canada the DPK system was shown to be a best-practice procedure, a finding confirmed by our studies [20]. Studies in the USA and Canada with the ChloraPrep disinfection device have confirmed the findings of NHSBT [21, 22]. This device has been adopted for use in these countries. Since the work of NHSBT, the evidence-based practice in Infection Control Guidelines Version 2 (epic 2) for National Health Service hospitals in England recommend "a single patient use application of alcoholic chlorhexidine gluconate solution, preferably 2% chlorhexidine in 70% isopropyl alcohol" for central venous access device decontamination [23].

The NHSBT diversion study indicated that a 47% reduction in bacterial contamination would be obtained, although a greater reduction of 66% was observed in the outdated platelet study, and clinically apparent transmissions were reduced by as much as 82%. Studies in the Netherlands by de Korte et al. [24] and by Ohlbius et al. [14] showed a 40% and 82% reduction respectively. Brunead et al. [25] in France reported a 72% and Benjamin et al. in the USA a 54% reduction in bacterial contamination [26]. Diversion has now been widely adopted by blood services.

Improved donor arm disinfection and diversion have been shown to be highly effective, relatively low-cost interventions for reducing the transmission of bacteria by transfusion. An NHSBT study indicated that improved donor arm disinfection in conjunction with diversion would reduce bacterial contamination by approximately 77% [27]. Residual contamination levels of blood units after the introduction of diversion may be in the order of 30–40% [23, 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.uk/portals/0/Publications/SHOTReport/SHOTReport09.pdf

5. Debets J, Noel L, Allen J-P, Frette 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, Slepecki 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**

Europäisches Patentamt
European Patent Office
Office européen des brevets

European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840

Thum, Bernhard
Wuesthoff & Wuesthoff
Patentanwälte PartG mbB
Schweigerstraße 2
81541 München
ALLEMAGNE

Formalities Officer
Name: Golze, Doreen
Tel: +49 30 25901 - 704
or call
+31 (0)70 340 45 00

Application No.	Ref.	Date
17 840 467.9 - 1132	EPA-147 134	22.04.2020
Applicant: Kurin, Inc.		

Communication under Rule 71(3) EPC

1. Intention to grant

You are informed that the examining division intends to grant a European patent on the basis of the above application, with the text and drawings and the related bibliographic data as indicated below.

A copy of the relevant documents is enclosed.

1.1 In the text for the Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

Description, Pages

1, 2, 4-44	as published	
3, 3a	filed in electronic form on	16-12-2019

Claims, Numbers

1-14	filed in electronic form on	16-12-2019

Drawings, Sheets

1/69-69/69	as published

With the following amendments to the above-mentioned documents proposed by the division

Description, Pages 1, 20, 23, 27, 40

Comments

Registered letter
EPO Form 2004C 12.17CXP

DESCRIPTION
Page 1: Deletion of irrelevant and/or superfluous information (Rule 48(1)(c) EPC, Guidelines F-II, 7.4)
Pages 20, 23, 27, 40: Insertion of SI/metric units (Rule 49(10) EPC)
CLAIMS
Page 1: Deletion of irrelevant and/or superfluous information (Rule 48(1)(c) EPC, Guidelines F-II, 7.4)

1.2 Bibliographic data

The title of the invention in the three official languages of the European Patent Office, the international patent classification, the designated contracting states, the registered name(s) of the applicant(s) and the other bibliographic data are shown on **EPO Form 2056** (enclosed).

2. Invitation

You are invited, **within a non-extendable period of four months** of notification of this communication,

2.1 to EITHER approve the text communicated above and verify the bibliographic data (Rule 71(5) EPC)

(1) by filing a translation of the claim(s) in the other two official languages of the EPO

		Fee code	EUR
(2a)	by paying the fee for grant including the fee for publication:	**007**	960.00
	minus any amount already paid (Rule 71a(5) EPC):		0.00
		Total amount:	960.00
(3)	by paying additional claims fees under Rule 71(4) EPC; number of claims fees payable: 0	**016**	0.00
	minus any amount already paid (Rule 71a(5) EPC):		0.00
		Total amount:	0.00

Important: If the translations of the claims and fees have already been filed and paid respectively in reply to a previous communication under Rule 71(3) EPC, e.g. in the case of resumption of examination after approval (see Guidelines C-V, 6), **agreement as to the text to be granted** (Rule 71a(1) EPC) must be expressed within the same time limit (e.g. by approving the text and verifying the bibliographic data, by confirming that grant proceedings can go ahead with the documents on file and/or by stating which translations of the claims already on file are to be used).

Note 1: See "Notes concerning fee payments" below.
Note 2: Any overpaid "minus" amounts will be refunded when the decision to grant (EPO Form 2006A) has been issued.
Note 3: For the calculation of the grant fee under Article 2(2), No. 7, RFees (old fee structure), the number of pages is determined on the basis of a clean copy of the application documents, in which text deleted as a result of any amendments by the examining division is not shown. Such clean copy is made available via on-line file inspection only.

2.2 OR, in the case of disapproval, to request reasoned amendments or corrections to the text communicated above or keep to the latest text submitted by you (Rule 71(6) EPC).

In this case the translations of the claims and fee payments mentioned under point 2.1 above are NOT due.

The terms "amendment(s)" and "correction(s)" refer only to amendments or corrections of the application documents and not of other documents (e.g. bibliographic data, the designation of the inventor, etc.).

If filing amendments, you must identify them and indicate the basis for them in the application as filed. Failure to meet either requirement may lead to a communication from the examining division requesting that you correct this deficiency (Rule 137(4) EPC).

2.3 Bibliographic data

Where you request a change or correction of bibliographic data in response to the Rule 71(3) communication, this will **not** cause the sending of a further communication under Rule 71(3) EPC. You will still have to pay the fees and file translations in reply to the Rule 71(3) communication in the case of 2.1 above, unless you also file a reasoned request for amendments or corrections in response to the Rule 71(3) communication (see case 2.2 above).

3. Loss of rights

If neither of the two possible actions above (see points 2.1 or 2.2) is performed in due time, the European patent application will be deemed to be withdrawn (Rule 71(7) EPC).

4. Further procedure

4.1 In the case of point 2.1 above

4.1.1 The decision to grant the European patent will be issued, and the **mention of the grant** of the patent will be published in the European Patent Bulletin, if the requirements concerning the translation of the claims and the payment of all fees are fulfilled and there is agreement as to the text to be granted (Rule 71a(1) EPC).

Note on payment of the renewal fee:
If a renewal fee becomes due before the next possible date for publication of the mention of the grant of the European patent, publication will be effected only after the renewal fee and any additional fee have been paid (Rule 71a(4) EPC).

Under Article 86(2) EPC, the obligation to pay renewal fees to the European Patent Office terminates with the payment of the renewal fee due in respect of the year in which the mention of the grant of the European patent is published.

Note on payment of the designation fee(s):
If the designation fee(s) become(s) due after the communication under Rule 71(3) EPC, the mention of the grant of the European patent will not be published until these fees have been paid (Rule 71a(3) EPC).

4.1.2 After publication, the **European patent specification** can be downloaded free of charge from the EPO publication server https://data.epo.org/publication-server.

4.1.3 Filing of translations in the contracting states

As regards translation requirements prescribed by the contracting states under Article 65(1) EPC, please consult the website of the European Patent Office
www.epo.org →Law & practice →Legal texts, National law relating to the EPC
www.epo.org →Law & practice →All Legal texts →London Agreement

In the case of a valid extension or validation

As regards translation requirements prescribed by the extension or validation states, please consult the website of the European Patent Office

www.epo.org →Law & practice →Legal texts, National law relating to the EPC

Failure to supply a prescribed translation in a contracting state, or in an extension or validation state may result in the patent being deemed to be void *ab initio* in the state concerned (Art. 65(3) EPC).

4.2 In the case of 2.2 above

If the present communication under Rule 71(3) EPC is based on an auxiliary request and, within the time limit, you maintain the main request or a higher ranking request which is not allowable, the application will be refused (Art. 97(2) EPC).

If the examining division gives its consent to the requested amendments or corrections, it will issue a new communication under Rule 71(3) EPC; otherwise, it shall resume the examination proceedings (Rule 71(6) EPC).

5. Filing of a divisional application

Any divisional application relating to this European patent application must be filed directly with the European Patent Office in Munich, The Hague or Berlin and will be in the language of the proceedings for the present application, or if the latter was not in an official language of the EPO, the divisional application may be filed in the language of the present application as filed (see Article 76(1) and Rule 36(2) EPC). Any such divisional application must be filed while the present application is still pending (Rule 36(1) EPC; Guidelines A-IV, 1.1.1).

6. Notes concerning fee payments

6.1 Making payments

For payments made via deposit account, please note that as from 1 December 2017 debit orders will only be carried out if filed in an electronically processable format (xml), using an accepted means of filing as laid down in the Arrangements for deposit accounts (ADA), published in the Supplementary publication in the Official Journal.

All relevant information related to the modes of payment of fees to the EPO can be retrieved from the EPO website at "**Making Payments**".

6.2 Information concerning fee amounts

Procedural fees are usually adjusted every two years, on even years, with effect from 1 April. Therefore, before making a payment, parties should verify the amounts actually due on the date of payment using the applicable version of the Schedule of fees and expenses, published as a Supplement to the Official Journal of the EPO, available on the EPO website (**www.epo.org**) at **www.epo.org/schedule-of-fees**. The "Schedule of fees" table allows the viewing, downloading and searching of individual fee amounts, both current and previous.

6.3 Note to users of the automatic debiting procedure

The fee for grant, including the fee for publication, and any additional claims fees due under Rule 71(4) EPC will be debited automatically on the date of filing of the translations of the claims, or on the last day of the period of this communication. However, if the designation fee(s) become(s) due as set out in Rule 71a(3) EPC and/or a renewal fee becomes due as set out in Rule 71a(4) EPC, these should be paid separately by another permitted way of payment in order not to delay the publication of the mention of the grant. The same applies in these circumstances to the payment of extension and validation fees. The same applies in these circumstances to the payment of extension and validation fees.

Note: If a waiver is expressed in response to a Rule 71(3) communication (see OJ EPO 2015, A52), the fee for grant, including the fee for publication/printing, and any additional claims fees will not be debited automatically. These fees must be paid separately by another means of payment allowed under the Rules relating to Fees.

Examining Division:

Chairman:	Schultz, Ottmar
2nd Examiner:	Amaro, Henrique
1st Examiner:	Nielsen, Michael

Golze, Doreen
For the Examining Division
Tel. No.: +49 30 25901 - 704 **Berlin sub-office**

Enclosures: Text intended for grant

EPO Form 2056

Registered letter
EPO Form 2004C 12.17CXP

Europäisches Patentamt
European Patent Office
Office européen des brevets

European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840

Annex to EPO Form 2004, Communication pursuant to Rule 71(3) EPC

Bibliographical data of European patent application No. 17 840 467.9

For the intended grant of the European patent, the bibliographical data are set out below, for information:

Title of invention:	- BLUTPROBENOPTIMIERUNGSSYSTEM SOWIE VORRICHTUNG ZUR SEQUESTRIERUNG VON BLUTKONTAMINANTEN - BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE - SYSTÈME D'OPTIMISATION D'ÉCHANTILLON DE SANG ET DISPOSITIF DE SÉQUESTRATION DE CONTAMINANT DU SANG
Classification:	INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157
Date of filing:	27.12.2017
Priority claimed:	US / 27.12.2016 / USP201662439426
Contracting States* for which fees have been paid:	AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR
Extension States* for which fees have been paid:	
Validation States* for which fees have been paid:	
Applicant(s):**	Kurin, Inc. 10755 Scripps Poway Parkway No. 257 San Diego, California 92131 US
Inventor(s):	ROGERS, Bobby E. c/o Kurin Inc. 10755 Scripps Poway Parkway No. 257 San Diego California 92131 US

European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840

KANG, Gino
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

STROUP, David Karl
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

COCHRAN, Jonas Dean
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

DEPTALA, Arthur
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

DETLOFF, John
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

POGUE, Lonnie
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

MACOWSKI,Brian
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

Europäisches Patentamt
European Patent Office
Office européen des brevets

European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840

GARRETT, Chad
c/o Kurin Inc.
10755 Scripps Poway Parkway
No. 257
San Diego
California 92131
US

*)	If the time limit for the payment of designation fees according to Rule 39(1) EPC has not yet expired and the applicant has not withdrawn any designation, **all Contracting States/Extension States/Validation States** are currently still deemed to be designated. See also Rule 71a(3) EPC and, if applicable, the above Note to users of the automatic debiting procedure.
**)	If two or more applicants have designated different Contracting States, this is indicated here.

~~BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD~~

BACKGROUND

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

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

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

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

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

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

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

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

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

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

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

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

US 2014/039348 A1 discloses a device including a pre-sample reservoir, an actuator mechanism and a diverter. The pre-sample reservoir can be fluidically coupled to a delivery member to receive and isolate a predetermined volume of bodily-fluid withdrawn from a patient. US 2014/107564 A1 discloses an apparatus including a cannula assembly, a housing, a fluid reservoir, a flow control mechanism and an actuator. US 4 813 433 A discloses a syringe for withdrawing fluids which consists of one-handed operated syringe. The syringe comprises a double compartmented housing, a piston disposed in one of said compartments, a piston rod connected to said piston controlling the movement of said piston in a barrel, and vent means. US 2013/317391 A1 discloses an apparatus including a housing, a flow control mechanism and an actuator. At least a portion of the flow control mechanism is movably disposed within the housing.

SUMMARY

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

[0013] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate

short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

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

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

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

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

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

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

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

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

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

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

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

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

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

BRIEF DESCRIPTION OF THE DRAWINGS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

DETAILED DESCRIPTION

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

[0093] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately ≥ 0,1143 cm (0,045 inches), ≥ ~~0.045 inches,~~ but can have a diameter of between ≥ 0,0254 cm (0,01 inches) ≥ ~~0.01 inches~~ or less to ≥ 0,508 cm (0,2 inches) ≥ ~~0.2 inches~~ or more. The blood sequestration device 1401 further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a

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

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

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

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

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

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

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

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

patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately ~~0.045 inches,~~ 0,1143 cm (0,045 inches), but can have a diameter of between ~~0.01 inches~~ 0,0254 cm (0,01 inches) or less to ~~0.2 inches~~ 0,508 cm (0,2 inches) or more.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

[00115] Referring to FIGS. 16A – D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately ≥ 0,1143 cm (0,045 inches), ≥ ~~0.045 inches,~~ but can have a diameter of between ≥ 0,0254 cm (0,01 inches) ≥ ~~0.01 inches~~ or less to ≥ 0,508 cm (0,2 inches) ≥ ~~0.2 inches~~ or more.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

[00144] FIGS. 25A – D show a blood optimization system 2500 and blood sequestration device 2502, formed substantially as described in FIGS. 15, 16, 17, 18 and 19, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2520. Air initially in the blood sequestration chamber 2520 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2520. The air venting mechanism includes an air permeable blood barrier 2506, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2520.

[00145] The air venting mechanism includes an inner wall 2516 that at least partially circumscribes or surrounds the air permeable blood barrier 2506, and an outer wall 2504 spaced apart from the inner wall 2516. The outer wall 2504 can have one or more air vents 2514 formed therein. The outer wall 2504 extends higher upward than the inner wall 2516, such that a lid 2510, such as a cap, plug, cover, etc., can be attached to the outer wall 2504 and be displaced by a small distance from the top of the inner wall 2516. A seal 2508 in the form of a silicone wafer, or other elastomeric material, fits within the outer wall 2504 to cover the air permeable blood barrier 2506 and abut the top of the inner wall 2516. The seal 2508 covers and seals the air permeable blood barrier 2506 and inhibits air from entering the blood sequestration chamber 2520 through the air permeable blood barrier 2506. A fulcrum 2512 on an underside of the lid 2510 allows the seal 2508 to flexibly disconnect from the top of the inner wall 2516 when pushed by air displaced from the blood sequestration chamber 2520, to allow air to vent from the air permeable blood barrier 2506 and through the one or more air vents 2514 in the outer wall 2504.

[00146] FIG. 26A – E illustrate a blood sample optimization system 2600 that includes a patient needle 2602 for vascular access to a patient's bloodstream, a blood sample collection device 2604 to facilitate the collecting of one or more blood samples for blood testing or blood cultures, and a conduit 2606 providing a fluid connection between the patient needle 2602 and the blood sample collection device 2604. The conduit 2606 can include flexible tubing. In preferred implementations, the blood sample collection device 2604 includes a protective shield 2605 that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the

collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2602.

[00147] The blood sample optimization system 2600 further includes a blood sequestration device 2608, located at any point on the conduit 2606 between the patient needle 2602 and the blood sample collection device 2604. The location of the blood sequestration device 2608 can be based on a length of the conduit between the blood sequestration device 2608 and the patient needle 2602, and the associated volume that length provides.

[00148] The blood sequestration device 2608 includes an inlet port 2612 for being connected to the conduit 2606 toward the patient needle 2602, and an outlet port 2614 for being connected to the conduit 2606 toward the blood sample collection device 2604. The blood sequestration device 2608 includes an outer housing 2616 and an inner housing 2617, both having a cylindrical form, and being connected concentrically. The outer housing 2616 includes an outer wall 2618 and an inner conduit 2620 that defines a blood sampling channel 2622 to convey blood through the conduit 2606 to the blood sampling device 2604. The inner housing 2617 fits snugly between the inner conduit 2620 and the outer wall 2618 of the outer housing, and is rotatable in relation to the outer housing 2616. The fit between the outer housing 2616 and the inner housing 2617 can be a friction fit that maintains the housings in a particular position. The inner housing 2617 defines a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of inner conduit 2620 of the outer housing 2616, and which terminates at an air vent 2628 having an air permeable blood barrier, as shown in FIG. 26E.

[00149] The blood sequestration chamber 2624 is connected with the blood sampling channel 2622 via diversion junction 2624 formed in the inner conduit 2620, when the blood sequestration device in a first state, illustrated in FIG. 26C. The protective shield 2606 on the collection needle 2604 provides a block for air or blood, enabling a diversion of an initial aliquot of blood into the blood sequestration chamber 2624 as the patient's blood pressure overcomes the ambient air pressure in the blood sequestration channel 2624 to displace air therefrom through air vent 2628.

[00150] When the inner housing 2617 is rotated relative to the outer housing 2616, or vice versa, to a second state, as illustrated in FIG. 26D, the blood sequestration chamber 2624 is shut off from diversion junction 2624, enabling a direct path from the patient needle through the conduit 2606 to the collection needle 2604, via blood sampling channel 2622. The outer housing 2616 and/or inner housing 2617 can include ridges or grooves formed within a portion of their surfaces, to facilitate relative rotation from the first state to the second state.

[00151] FIGS. 27A – D illustrate a blood optimization system 2700 and blood sequestration device 2702, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, and 25, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2720. Air initially in the blood sequestration chamber 2720 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2720. The air venting mechanism includes an air permeable blood barrier 2706, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2720.

[00152] The air venting mechanism includes an inner wall 2716 that at least partially circumscribes or surrounds the air permeable blood barrier 2706, and an outer wall 2704 spaced apart from the inner wall 2716. A cap 2722 is positioned on the air venting mechanism, preferably by having a lower cap wall 2728 that fits between the inner wall 2716 and the outer wall 2704 of the air venting mechanism, and frictionally abutting either the the inner wall 2716 or the outer wall 2704 or both. The cap 2722 further includes one or more vent holes 2724 or slits, apertures, openings, or the like, which extend through an upper surface of the cap 2722 around a downwardly extending plug 2726. The plug 2726 is sized and adapted to fit snugly within the space defined by inner wall 2716.

[00153] In a first position, as illustrated in FIG. 27C, the cap 2722 is extended from the air venting mechanism to allow air from the blood sequestration chamber 2720 to exit through the air permeable blood barrier 2706 and through the one or more vent holes 2724. Once the air from the blood sequestration chamber 2720 has been displaced, i.e., when the blood sequestration chamber 2720 is filled with the first aliquot of potentially tainted blood from the patient, then the cap 2722 can be pushed down on the air venting

mechanism in a second position as shown in FIG. 27D, so that the plug 2726 fits within the inner wall 2716 over the air permeable blood barrier 2706 to seal the air venting mechanism. In either the first position or the second position, the cap 2722 protects the air permeable blood barrier 2706 from outside air or from being touched by a user.

[00154] FIGS. 28A – F illustrate a blood optimization system 2800 and blood sequestration device 2802, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but utilizing a multi-layered filter, and in some implementations, a filter with trapped reactive material, for an air permeable blood barrier. As shown in FIGS. 28C and D, an air permeable blood barrier 2803 includes a first layer 2804 of an air permeable but blood impermeable material, and a second layer 2806 that includes a reactive material, such as a hydrophobic material, for repelling blood while still allowing air to pass through both layers. As shown in FIGS. 28E and F, the air permeable blood barrier 2803 can include any number of layers, such as a third layer 2808 formed of the same air permeable but blood impermeable material as first layer 2804, while a second layer 2806 includes trapped or embedded blood reactive material.

[00155] FIGS. 29A – C illustrate a blood optimization system 2900 and blood sequestration device 2902, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but in which a blood sequestration chamber 2904 is at least partially filled with a blood-absorptive material 2906. The blood-absorptive material 2906 can act as a wicking material to further draw in blood to be sequestered upon venipuncture of the patient, and prior to use of a blood drawing device such as a Vacutainer™ or a syringe, or the like.

[00156] FIGS. 30A – G illustrate a blood optimization system 3000 and blood sequestration device 3002, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26. The blood sequestration device 3000 includes an inlet port 3002 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 3002 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 3002 defines an opening into the blood sequestration device 3000, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the

opening can be circular with a diameter of approximately ≥ ≤ 0,1143 cm (0,045 inches), ≤ ≥ ~~0.045 inches,~~ but can have a diameter of between ≥ ≤ 0,0254 cm (0,01 inches) ≤ ≥ ~~0.01 inches~~ or less to ≥ ≤ 0,508 cm (0,2 inches) ≤ ≥ ~~0.2 inches~~ or more.

[00157] The inlet port 3002 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 3002, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 3000 at the time of blood draw or sampling.

[00158] The blood sequestration device 3000 further includes an outlet port 3004, which defines an opening out of the blood sequestration device 3000 and to the blood sample collection device. The outlet port 3004 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 3000 at the time of blood draw or sampling.

[00159] The blood sequestration device 3000 further includes a sampling channel 3006 between the inlet port 3002 and the outlet port 3004, and a sequestration chamber 3008 that is connected to and split off or diverted from the sampling channel 3006 at any point between the inlet port 3002 and the outlet port 3004. The sampling channel 3006 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 3008. The sampling channel 3006 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 3006 has a substantially similar cross sectional area as the opening of the inlet port 3002. In other implementations, the sampling channel 3006 can gradually widen from the inlet port 3002 to the outlet port 3004. The sequestration chamber 3008 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the

blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 3006.

[00160] In some exemplary implementations, the diversion between the sampling channel 3006 and the sequestration chamber 3008 is by diverter junction 3007. Diverter junction 3007 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008. The sequestration chamber 3008 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 3008.

[00161] The sequestration chamber 3008 is preferably maintained at atmospheric pressure, and includes a vent 3010 at or near a distal end of the sequestration chamber 3008. The vent 3010 may include an air permeable blood barrier 3012 as described above.

[00162] The blood sequestration device 3000 can include a housing 3001 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated FIG. 30F, the housing 3001 includes a top member 3020 and a bottom member 3022 that are mated together. The blood sequestration device 3000 can also include a gasket or other sealing member (not shown) so that when the top member 3020 is mechanically attached with the bottom member 3022, the interface between the two is sealed by the gasket or sealing member. The bottom member 3022 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 3006, the sequestration chamber 3008, and diverter junction 3007.

[00163] The sequestration chamber 3008 may have a larger cross section than the sampling channel 3006 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 3006.

[00164] In some implementations, the sampling channel 3006 and the sequestration chamber 3008 are formed by grooves, channels, locks or other pathways formed in housing 3001. The housing 3001 can be made of rubber, plastic, metal or any other suitable material. The housing 3001 can be formed of a clear or translucent material, or

of an opaque or non-translucent material. In other implementations, the housing 3001 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 3006 and/or the sequestration chamber 3008 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 3008 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 3006. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 3012 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00165] The air permeable blood barrier 3012 can be covered with, or surrounded by, a cap 3032. The cap 3032 can be sized and configured to inhibit a user from touching the air permeable blood barrier 3012 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 3012 as the air is displaced from the sequestration chamber 3008. The cap 3032 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00166] The air venting mechanism includes a wall 3030 that at least partially circumscribes or surrounds the air permeable blood barrier 3012. The wall 3030 can have one or more air vents formed therein. The cap 3032 covers wall 3030 and can be snapped, glued, or otherwise attached in place. A seal 3017 in the form of a silicone wafer, or other elastomeric material, fits within the wall 3030 to cover the air permeable blood barrier 3012 and abut the top of the wall 3030. The seal 3017 covers and seals the air permeable blood barrier 3012 and inhibits air from entering the blood sequestration chamber 3008 through the air permeable blood barrier 3012. A fulcrum 3012 on an underside of the cap 3032 allows the seal 3008 to flexibly disconnect from the top of the inner wall 3016 when pushed by air displaced from the blood sequestration chamber 3008, to allow air to vent from the air permeable blood barrier 3012 and through the one or more air vents in the wall 3030 and/or cap 3032.

[00167] In use, the blood sequestration device 3000 includes a sampling channel 3006 and a sequestration chamber 3008. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 3006 is directed to an outlet port 3004 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 3008 terminates at a vent 3010 to atmosphere that includes an air permeable blood barrier 3012.

[00168] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through inlet port 3002 of blood sequestration device 3000. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 3008 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 3008 to displace air therein through the air permeable blood barrier 3012, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 3006. In various exemplary embodiments, the sequestration chamber 3008 and sampling channel 3006 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00169] Eventually, the sequestration chamber 3008 fills with blood that displaces air through the air permeable blood barrier 3012. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 3012 material to completely or partially seal the vent 3010. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00170] Upon filling the blood sequestration pathway 3008 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 3006, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 3006, queuing up the uncontaminated blood to be drawn through the sampling channel 3006.

[00171] In yet another aspect, the blood sequestration chamber and/or blood sampling channel, or other component, of any of the implementations described herein,

can provide a visually discernable warning or result in a component adapted for operative fluid communication with the flash chamber of an introducer for an intravenous catheter into a blood vessel of a patient. The device and method provides a visually discernable alert when blood from the patient communicates with a test component reactive to communicated blood plasma, to visually change. The reaction with the blood or the plasma occurs depending on one or a plurality of reagents positioned therein configured to test for blood contents, substances or threshold high or low levels thereof, to visually change in appearance upon a result.

[00172] In yet other aspects, the blood sequestration chamber and/or blood sampling channel can be sized and adapted to provide a particular volumetric flow of blood, either during the sequestration process and/or the sampling process.

[00173] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

~~Amended~~ claims

1. A blood sequestration device (812, 1000, 1100, 1202, 1302, 1401, 1500, 1600, 2008, 2100, 2200, 2300, 2408, 2502, 2608, 2702, 2802, 2902, 3000) comprising;

an inlet port (802, 902, 1002, 1102, 1212, 1314, 1402, 1502, 1532, 1602, 2302, 2316, 2412, 2612, 3002);

an outlet port (904, 1004, 1104, 1214, 1312, 1404, 1504, 1534, 1604, 2304, 2318, 2414, 2614, 3004) ;

a sequestration chamber (55, 104, 204, 304, 822, 1008, 1108, 1218, 1318, 1408, 1508, 1608, 2102, 2306, 2320, 2418, 2520, 2624, 2720, 2904, 3008) connected with the inlet port via a junction, the sequestration chamber having a vent (1510, 1610, 2628, 3010) that includes an air permeable blood barrier (20, 106, 824, 1010, 1110, 1310, 1412, 1512, 1612, 2202, 2420, 2506, 2706, 2803, 3012), the vent being defined by an outer wall (2504, 2618, 2704) that at least partially circumscribes the air permeable blood barrier and includes one or more air vents (2514), the vent further including a cap (1208, 1307, 2722, 3032), that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel (820, 1406, 1508, 1606, 2104, 2308, 2422, 2622, 3006) having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

the sequestration chamber, the sampling channel and the junction being sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

2. The blood sequestration device in accordance with claim 1, further comprising a housing (40, 50, 818, 1301, 1414, 1501, 1601, 2101, 2416, 2616, 3001) that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

3. The blood sequestration device in accordance with claim 1, wherein the vent further includes an inner wall (2516, 2716, 3016) within the outer wall and that contains the air permeable blood barrier.

4. The blood sequestration device in accordance with claim 1, wherein the one-way seal is positioned over the inner wall and within the outer wall of the vent.

5. The blood sequestration device in accordance with claim 4, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum (2512, 3012) against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

6. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a sealing material that seals the vent upon contact with blood.

7. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

8. A blood sequestration and sampling system (800, 1200, 1300, 1400, 2000, 2400, 2500, 2600, 2700, 2800, 2900, 3000) comprising;

a blood sampling pathway having a patient needle on a proximal end and a sample collection device on a distal end; and

a blood sequestration device in accordance with any of claims 1 to 7 attached on the blood sampling pathway between the proximal end and distal end of the blood sampling pathway, wherein the inlet port is coupled with the blood sampling pathway toward the patient needle;

the outlet port is coupled with the blood sampling pathway toward the sample collection device.

9. The blood sequestration system in accordance with claim 8, wherein the blood sequestration device further comprises a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

10. The blood sequestration system in accordance with claim 8, wherein the vent of the blood sequestration device further includes an inner wall within the outer wall and that contains the air permeable blood barrier.

11. The blood sequestration system in accordance with claim 8, wherein the one-way seal of the vent is positioned over the inner wall and within the outer wall of the vent.

12. The blood sequestration system in accordance with claim 11, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

13. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a sealing material that seals the vent upon contact with blood.

14. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

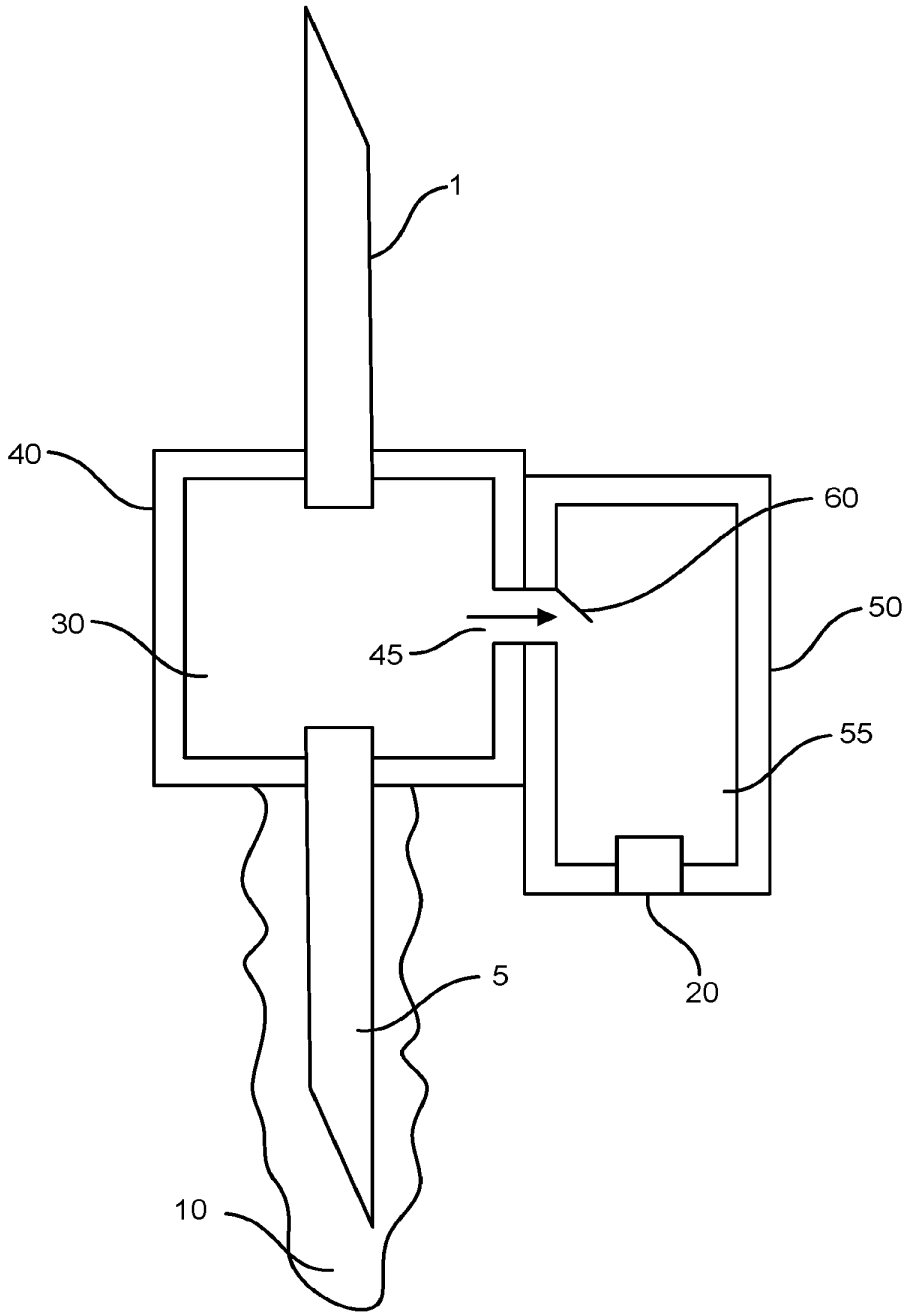


FIG. 1

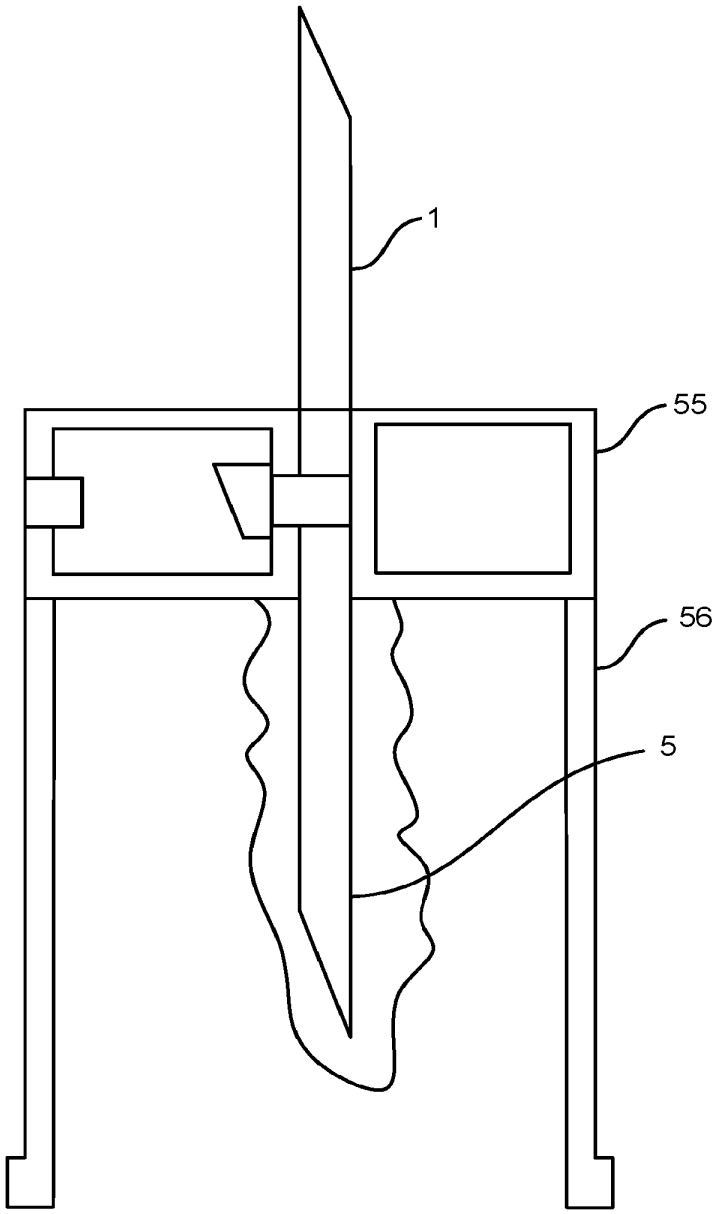


FIG. 2

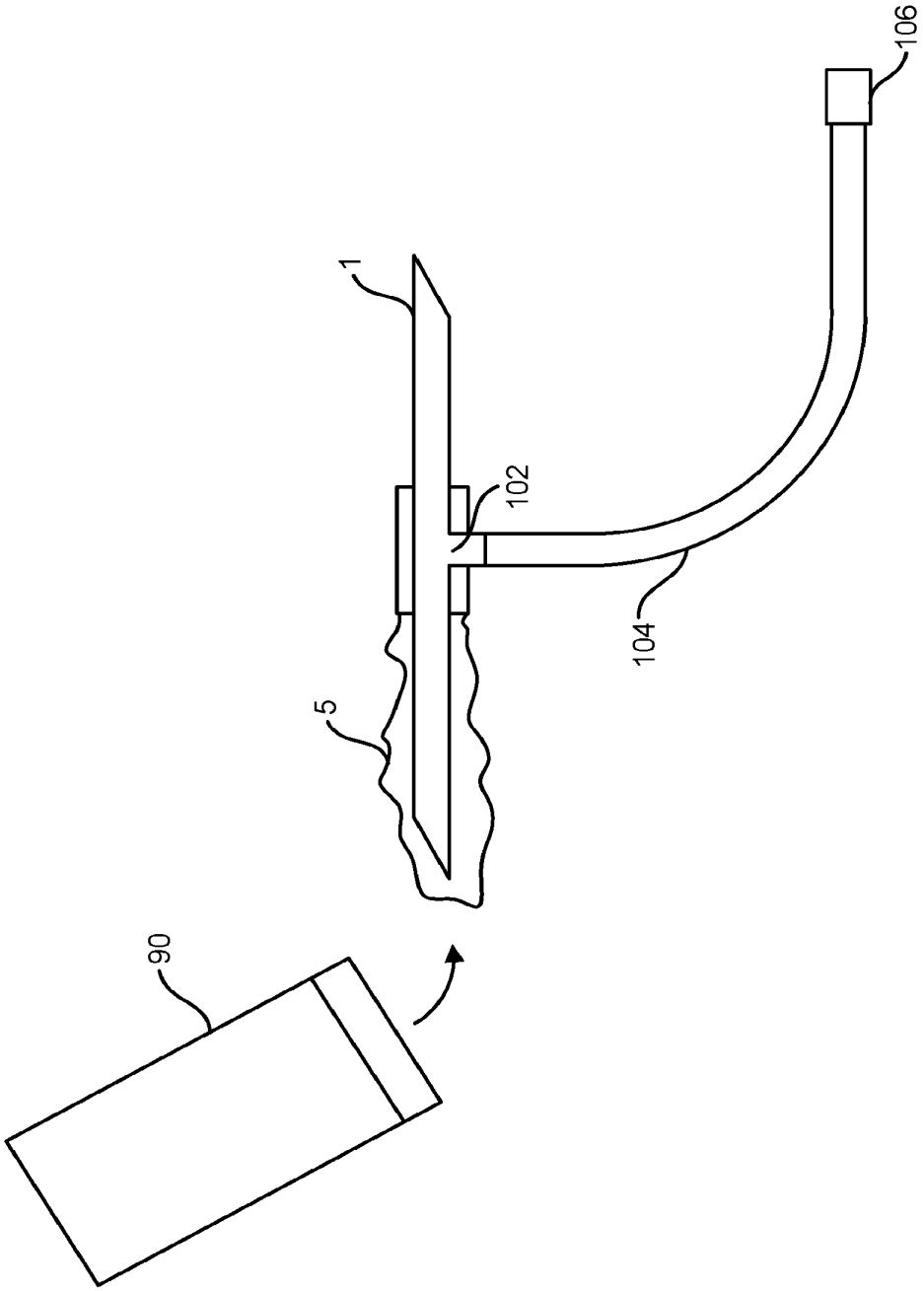


FIG. 3

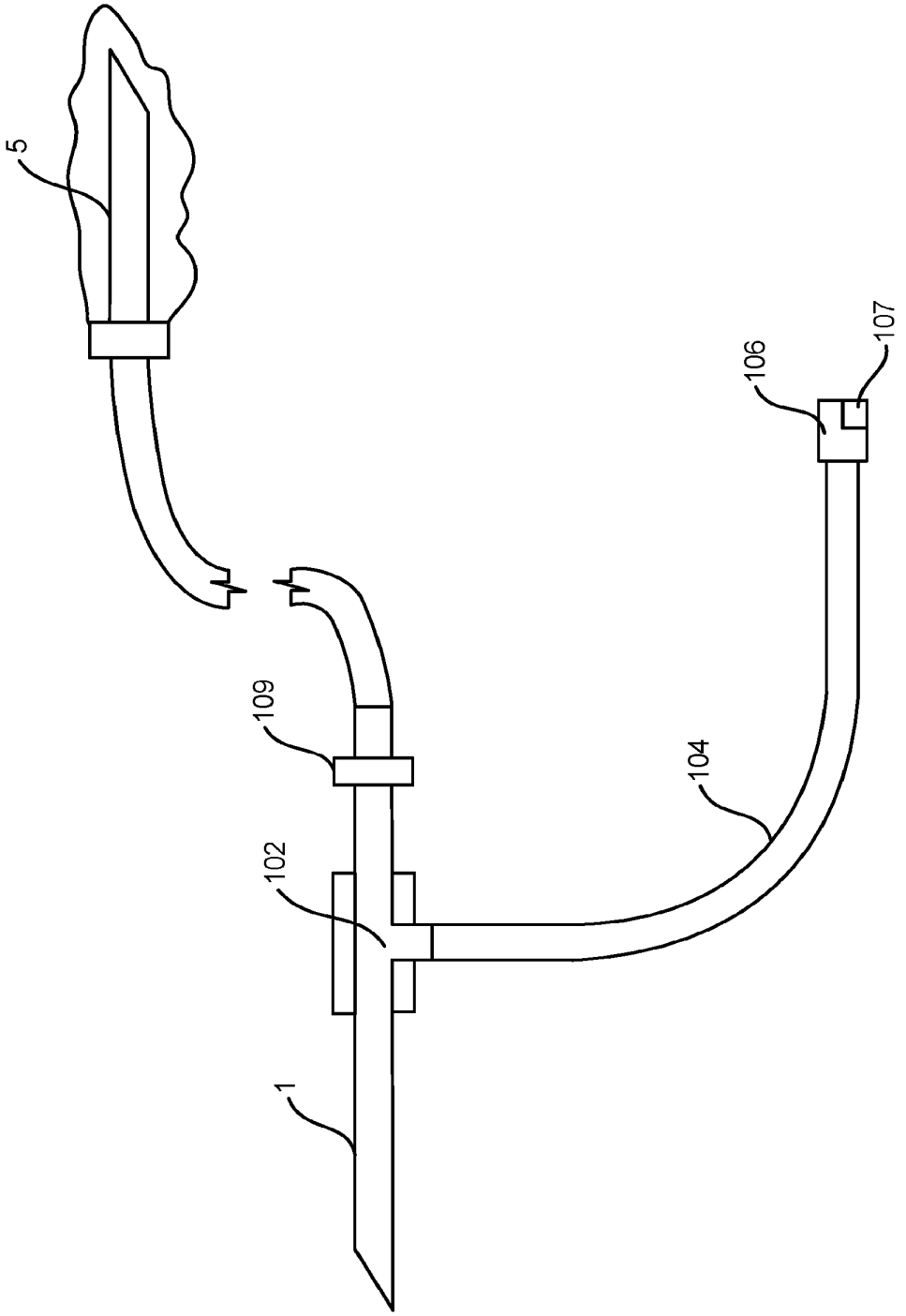


FIG. 4

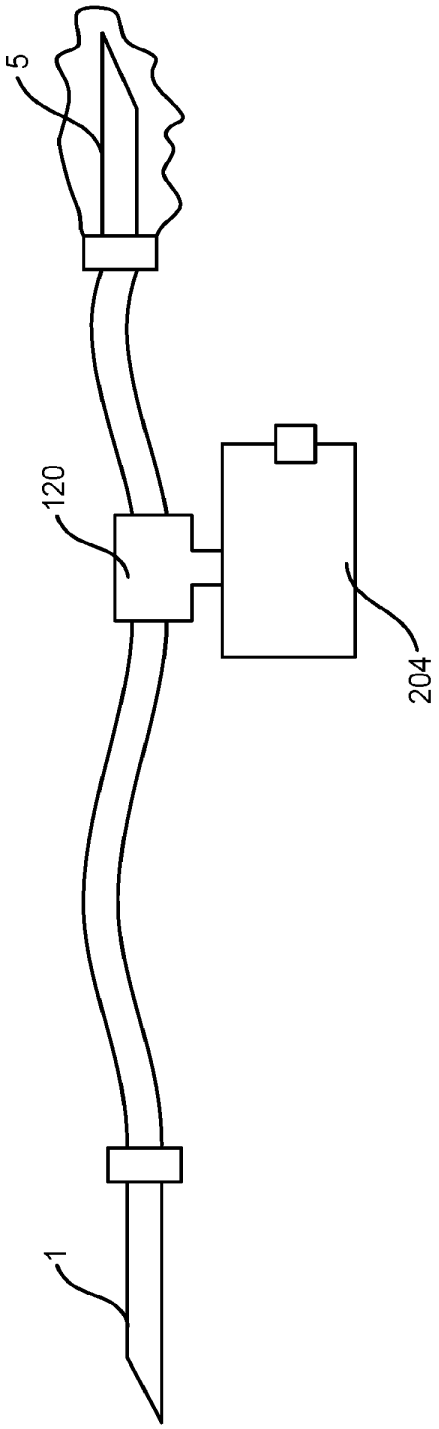


FIG. 5

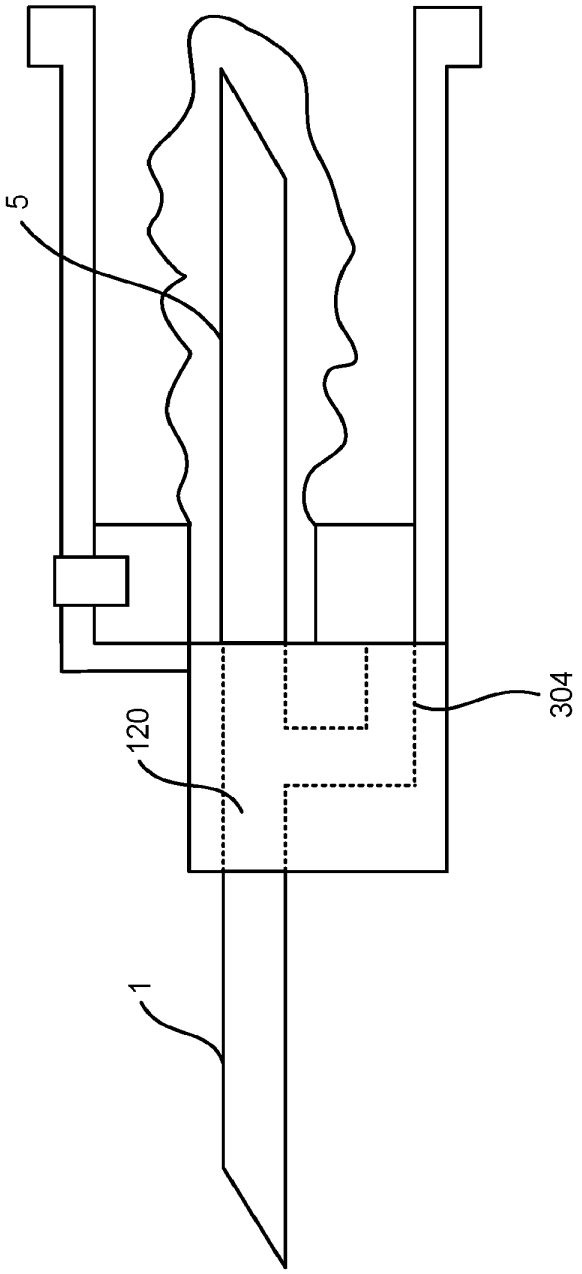


FIG. 6

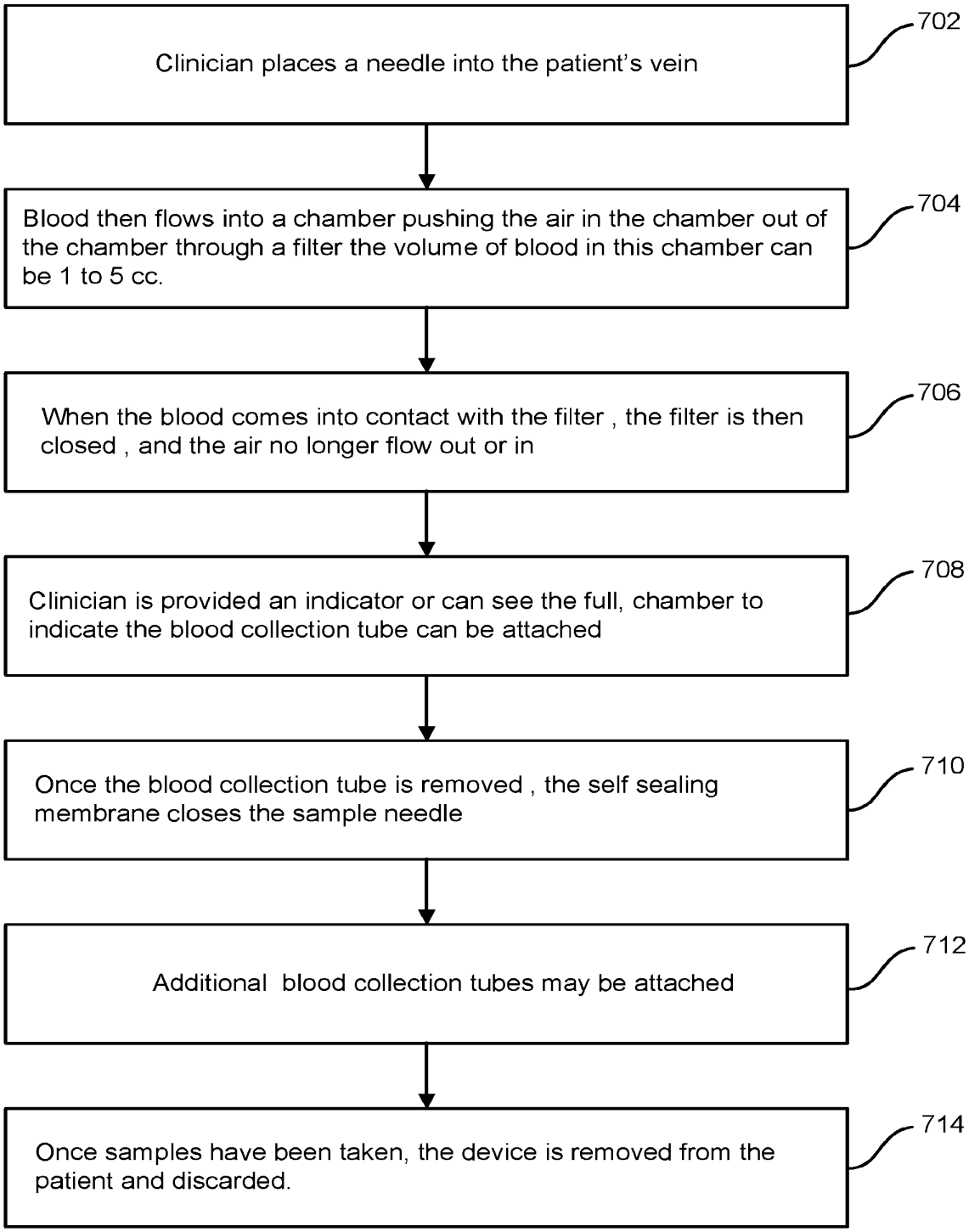
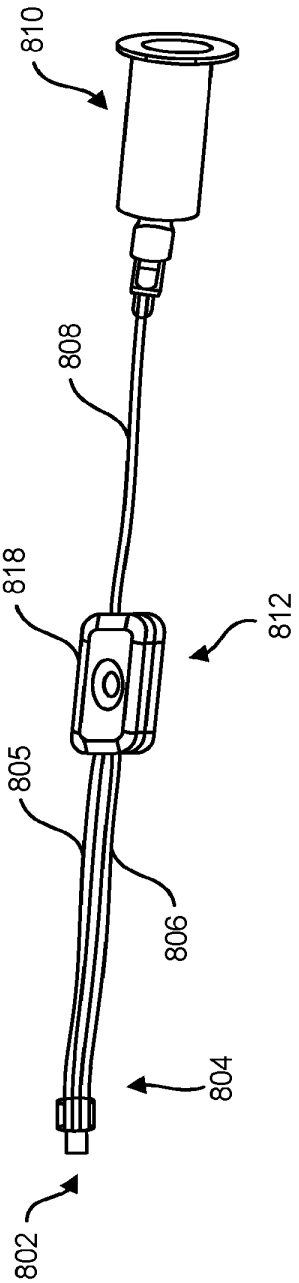

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air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

FIG. 7



800

FIG. 8A

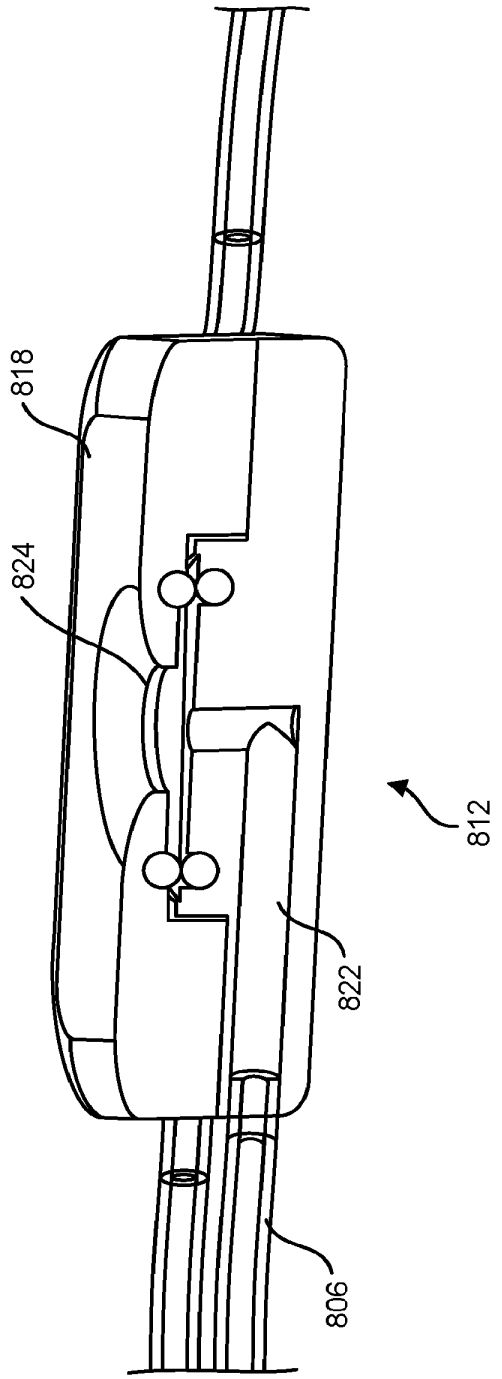


FIG. 8B

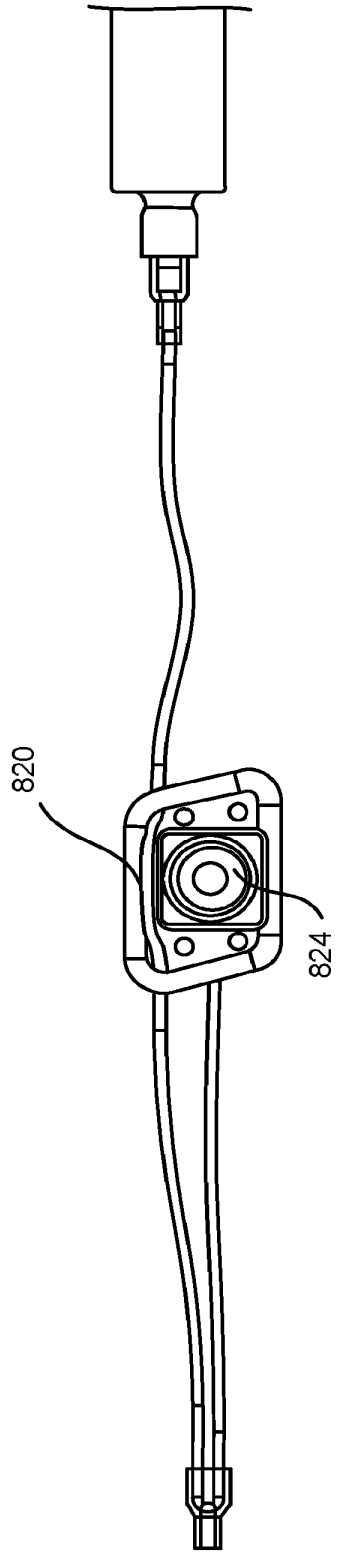


FIG. 8C

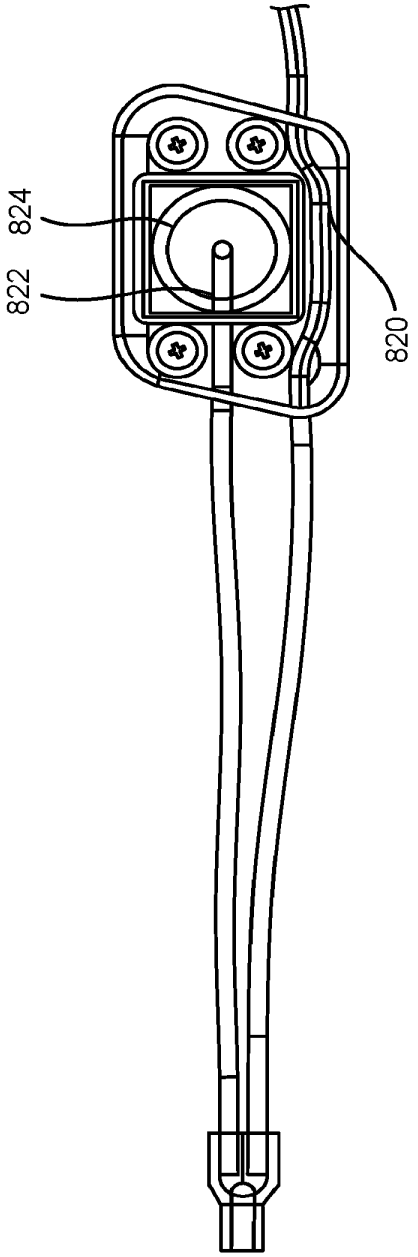


FIG. 8D

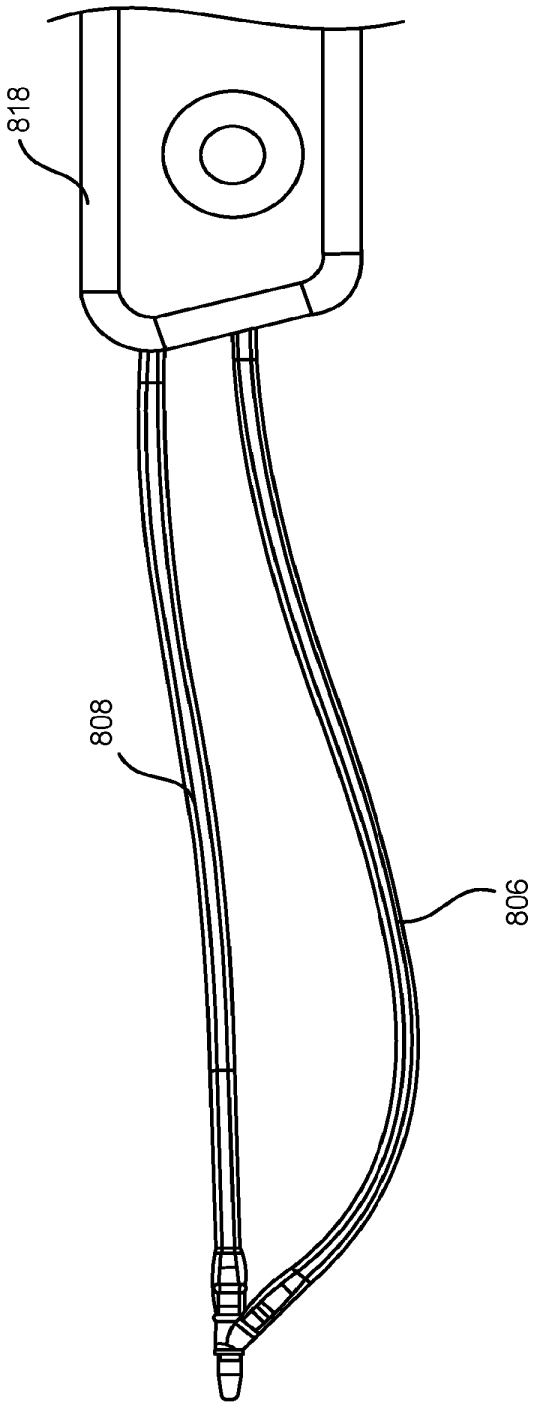


FIG. 8E

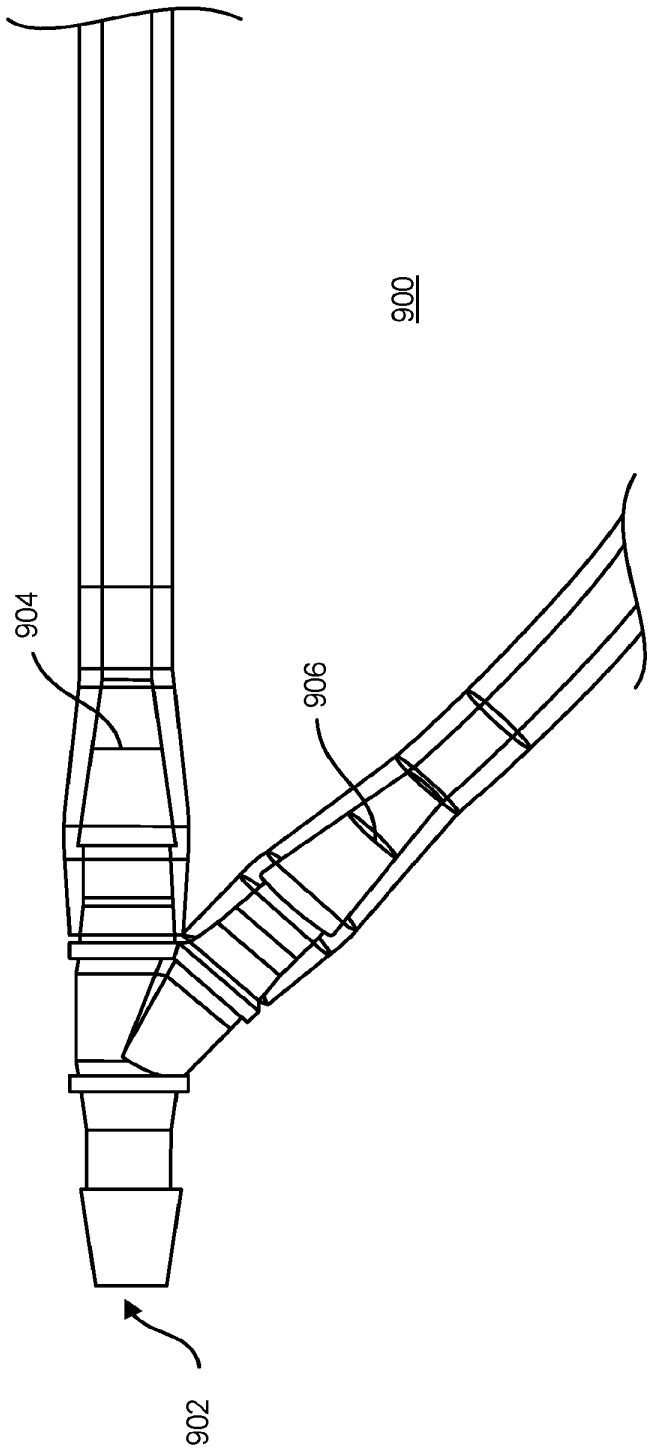


FIG. 9

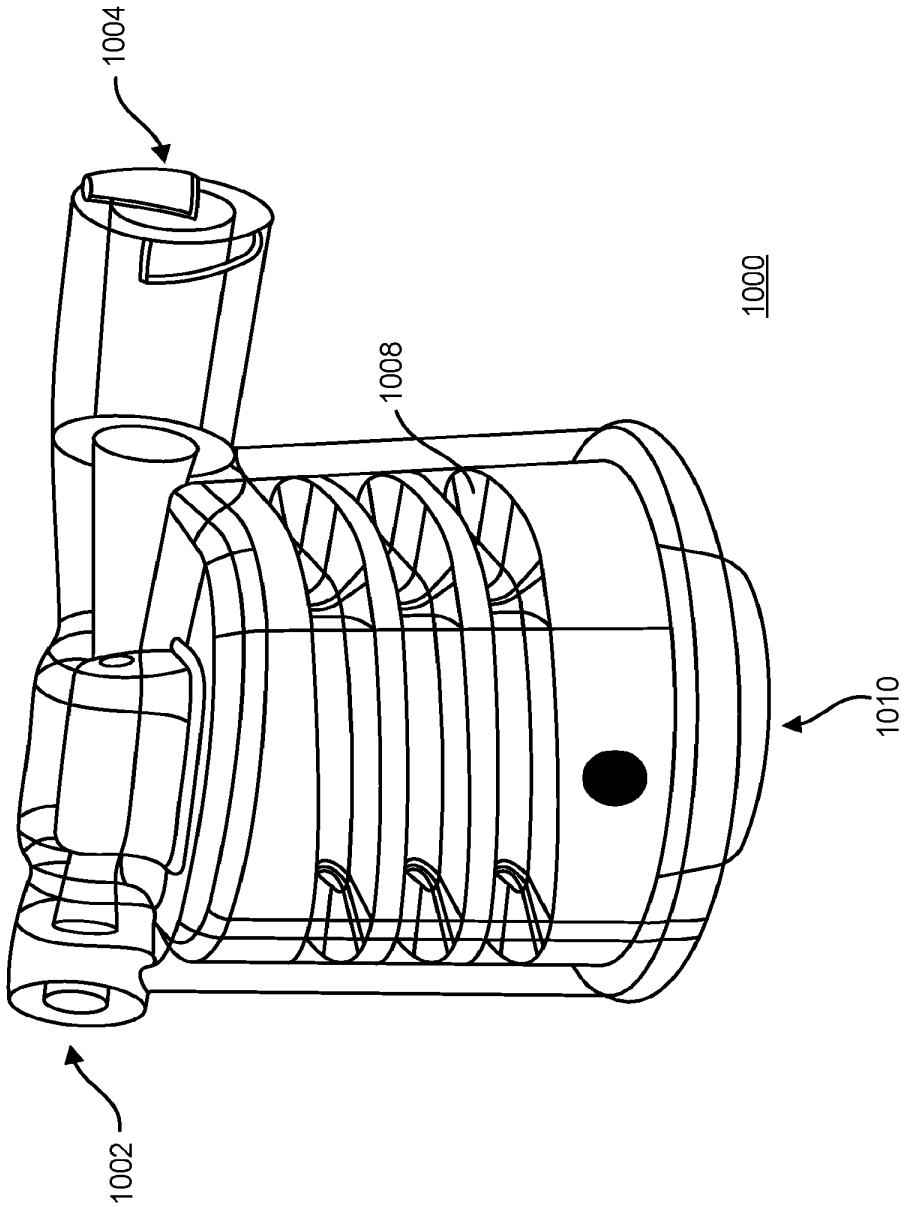


FIG. 10A

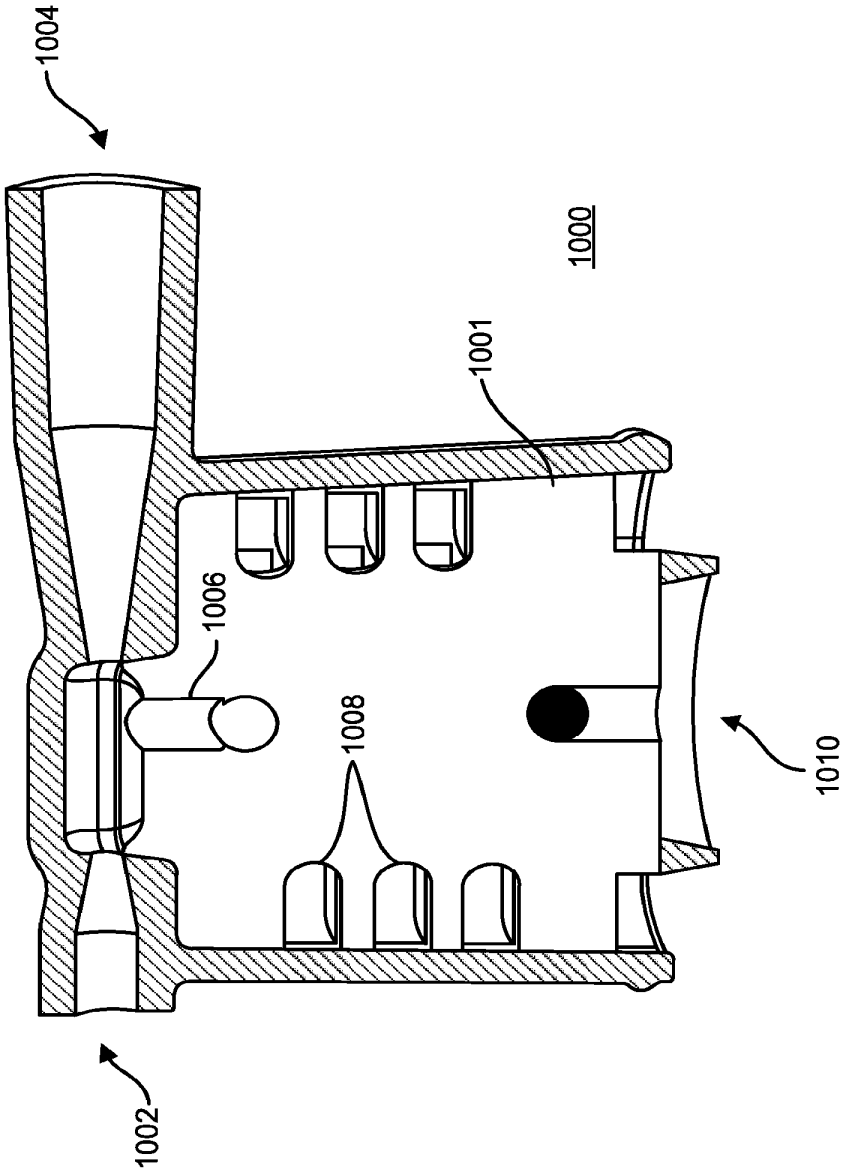


FIG. 10B

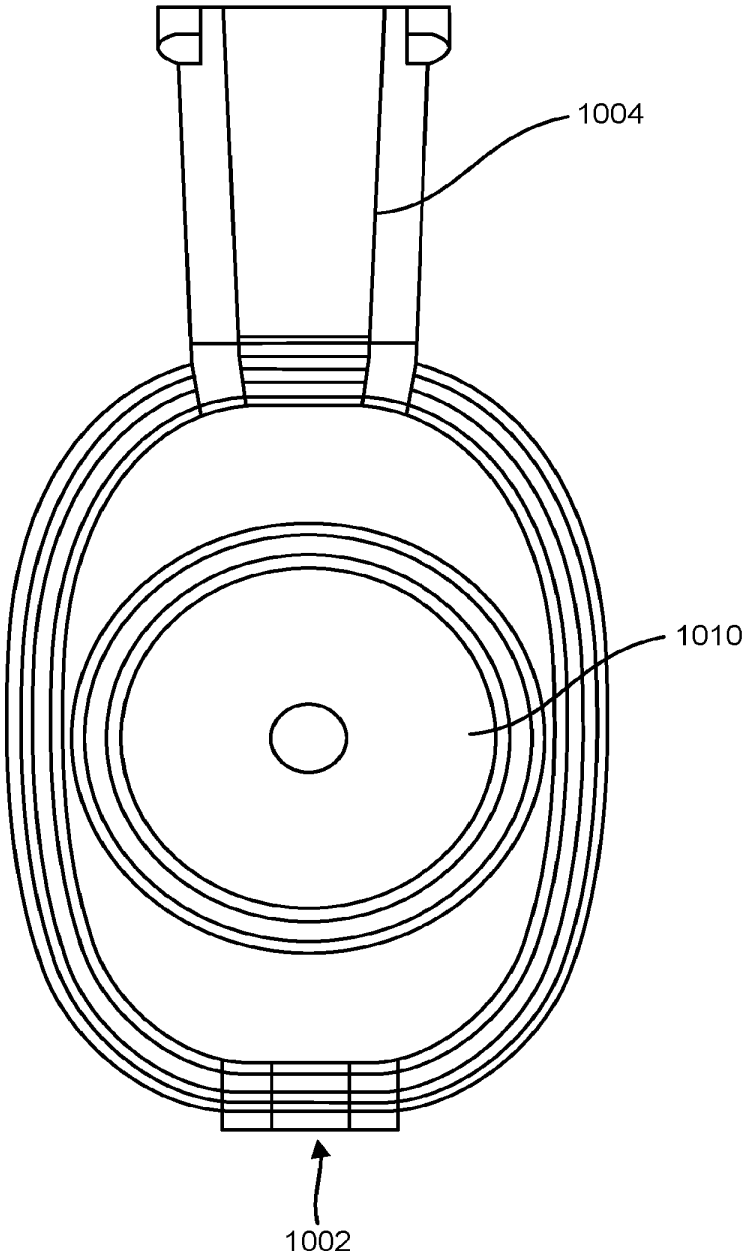


FIG. 10C

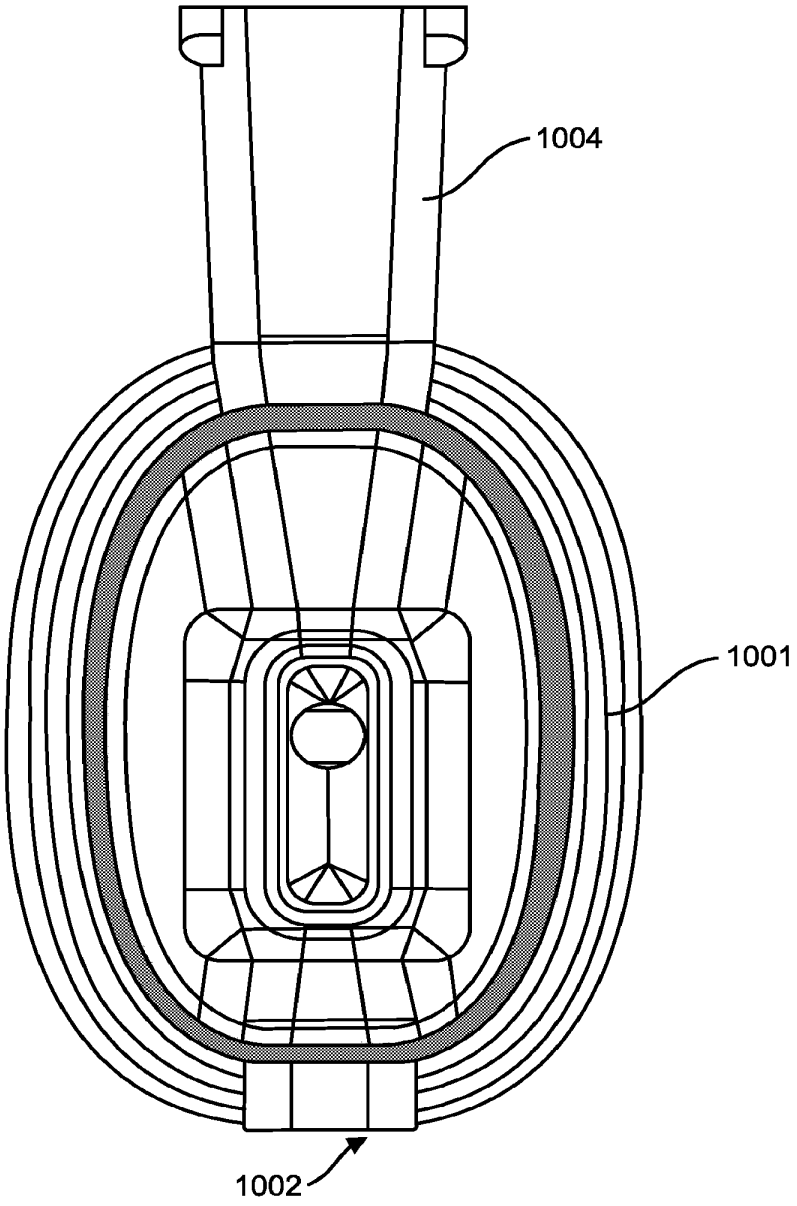


FIG. 10D

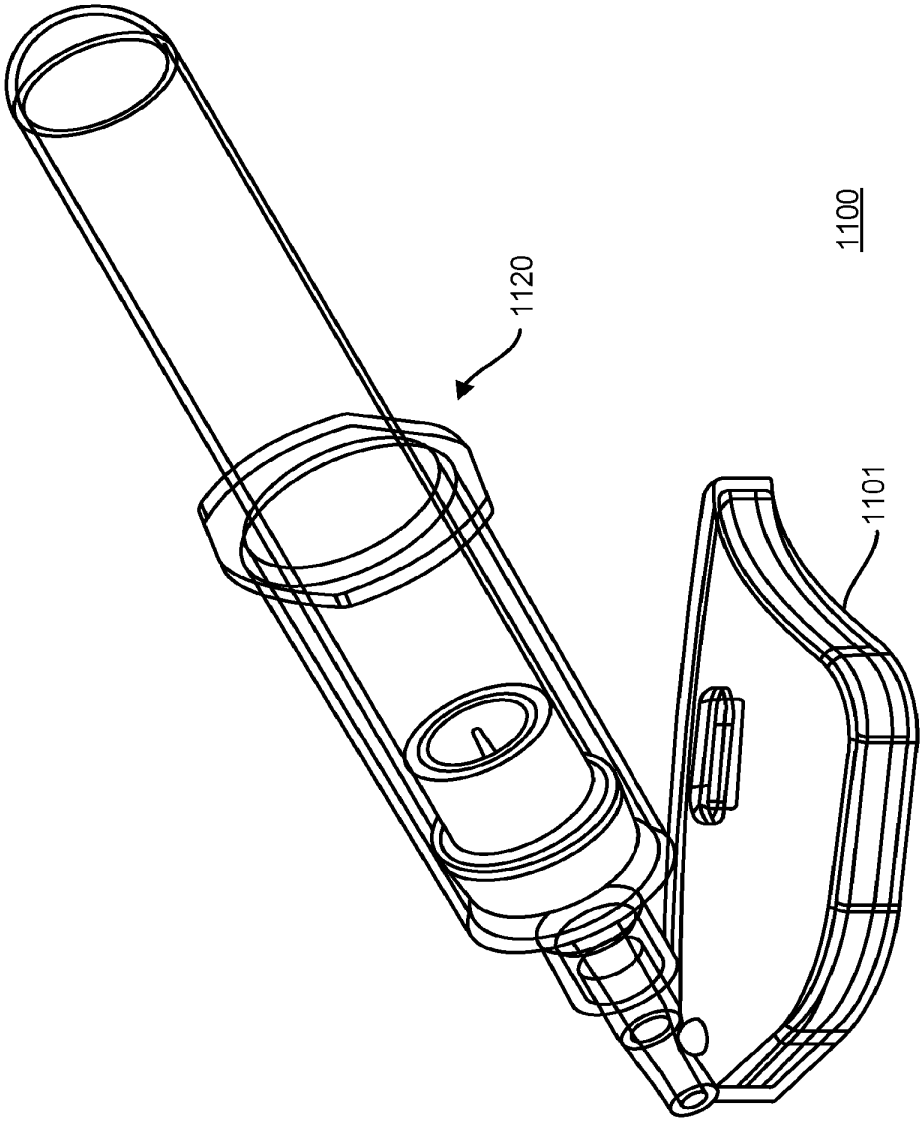


FIG. 11A

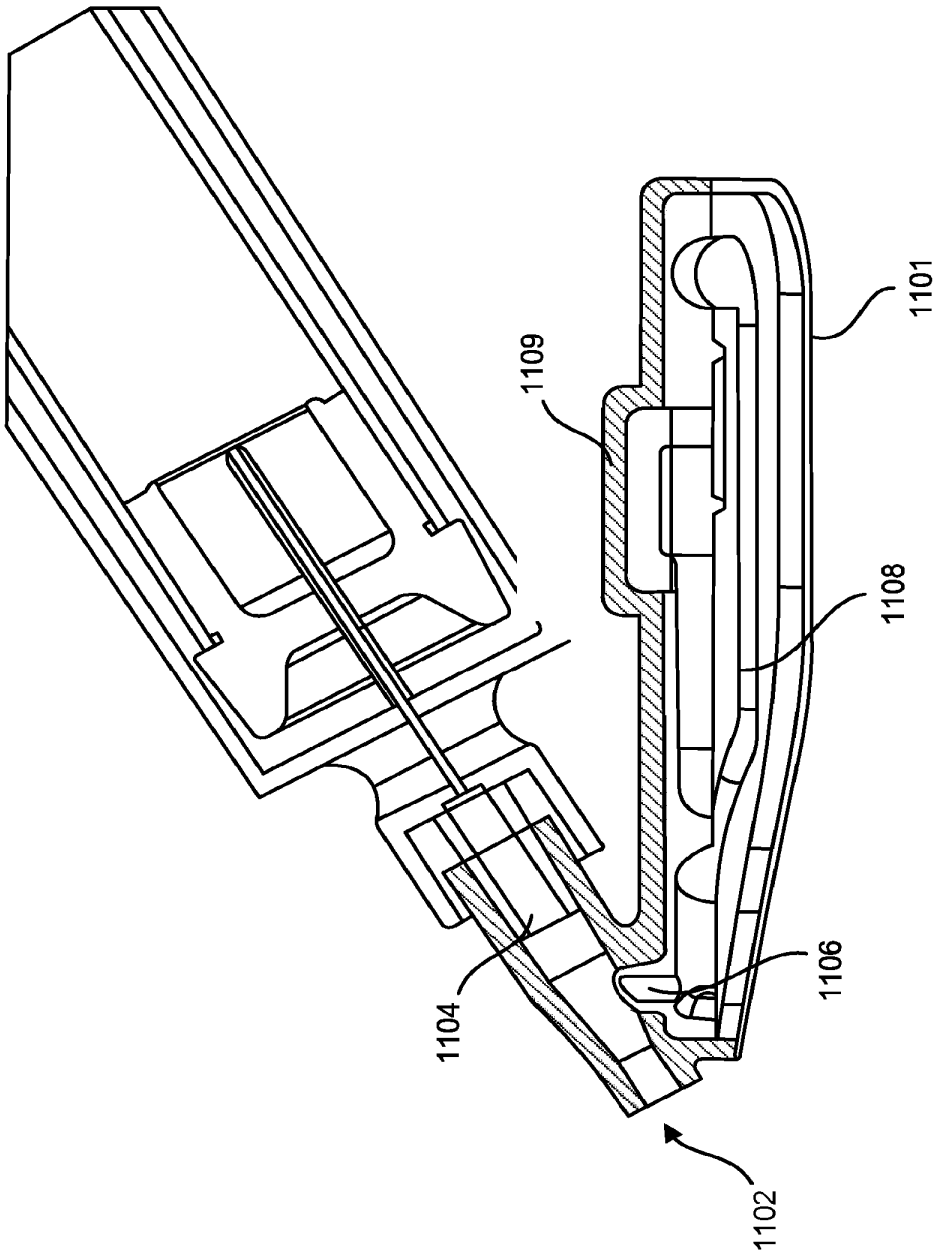


FIG. 11B

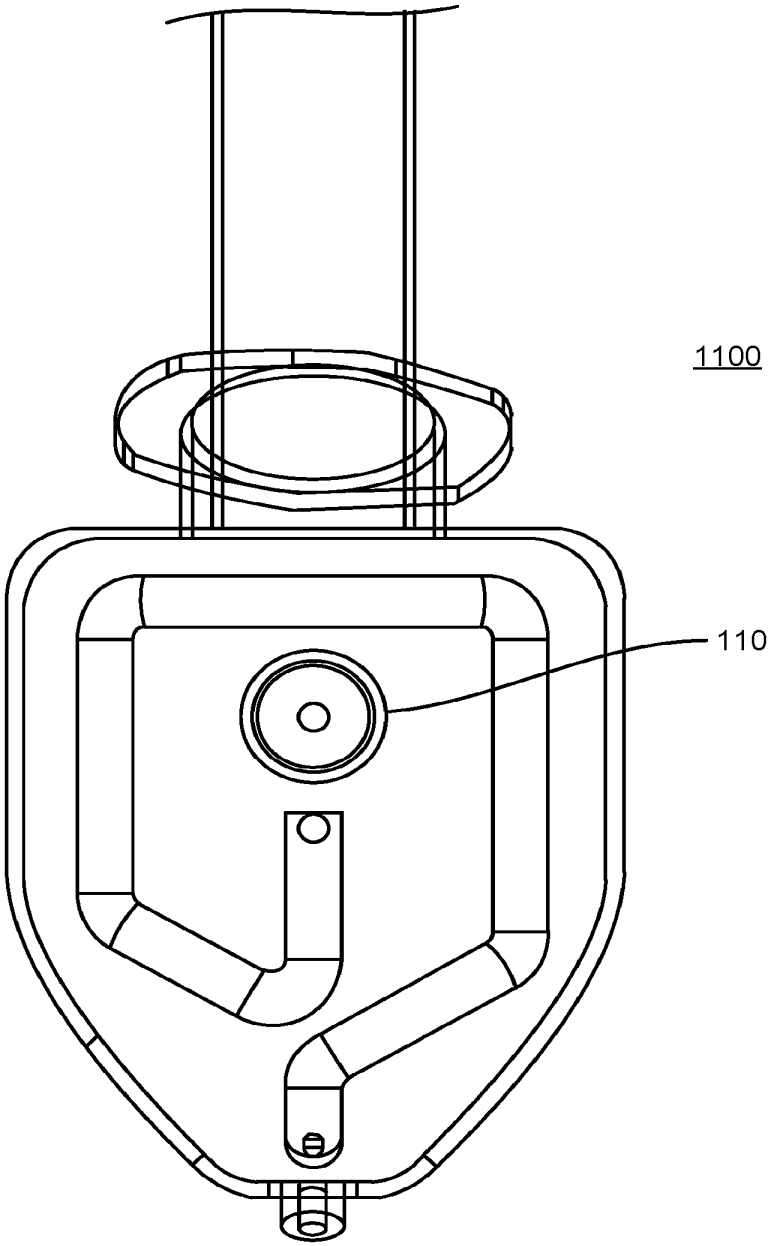


FIG. 11C

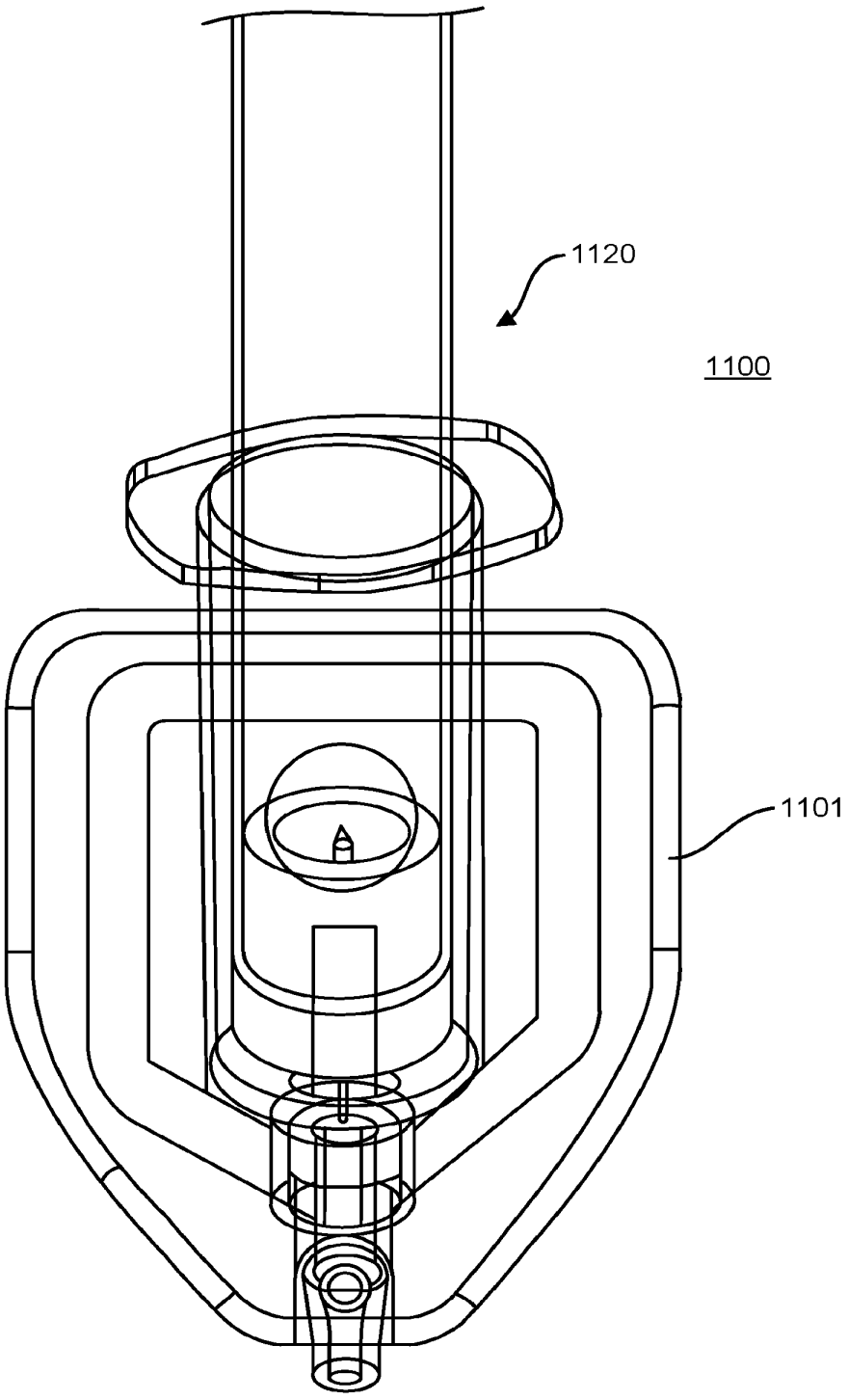


FIG. 11D

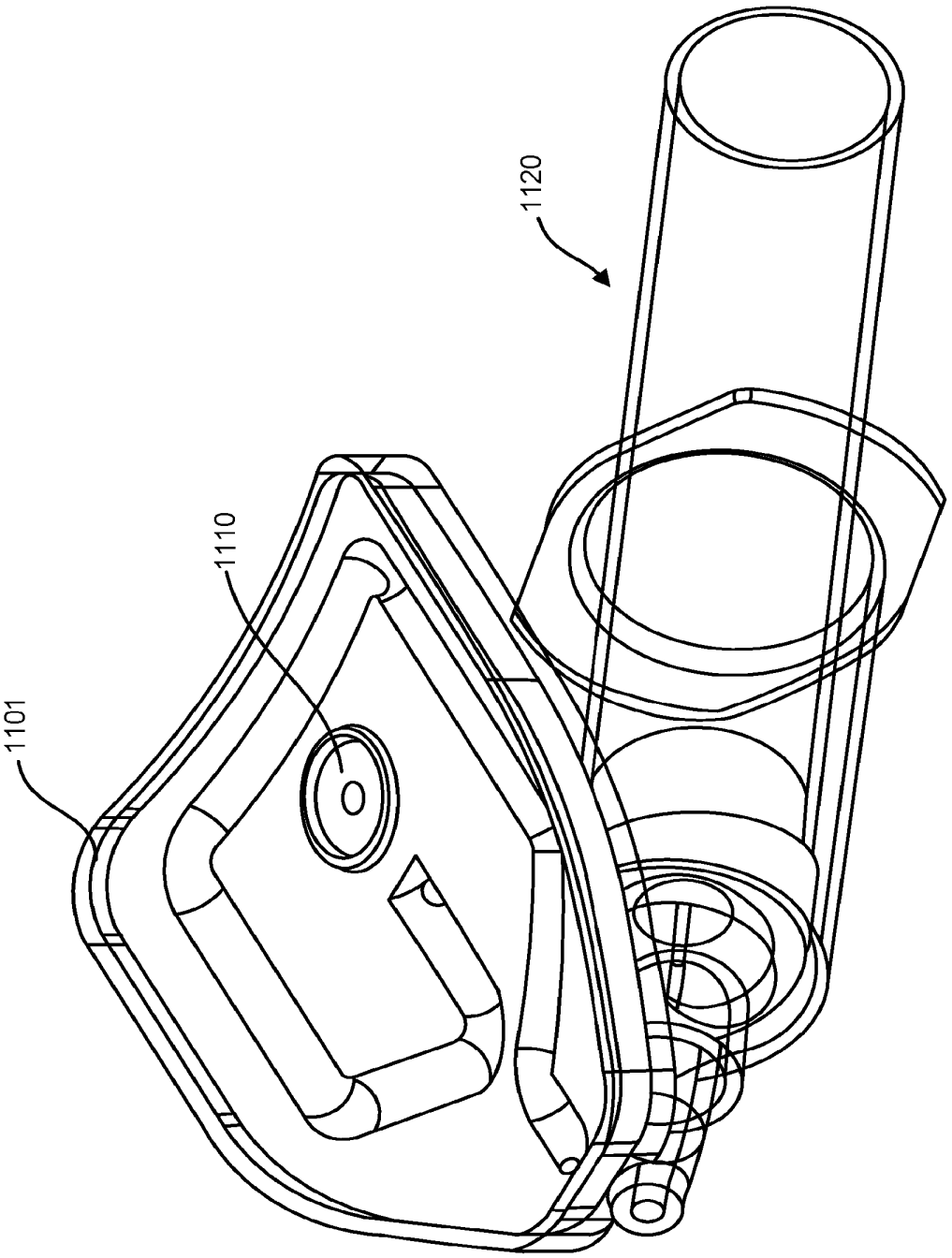


FIG. 11E

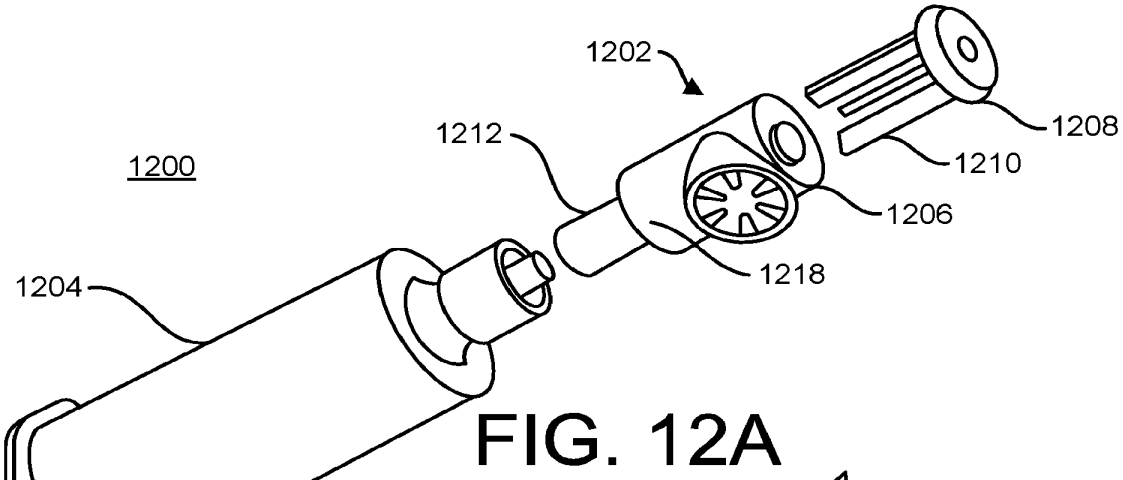


FIG. 12A

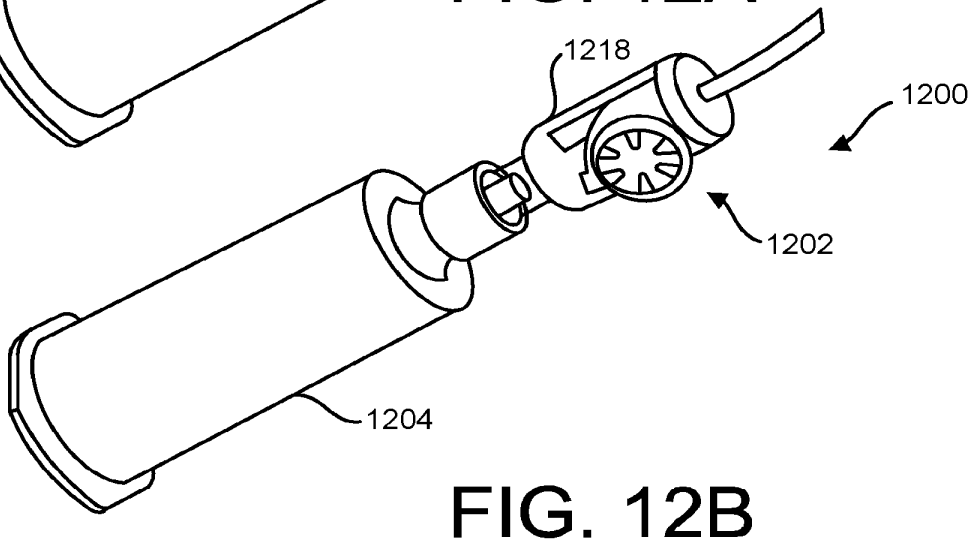


FIG. 12B

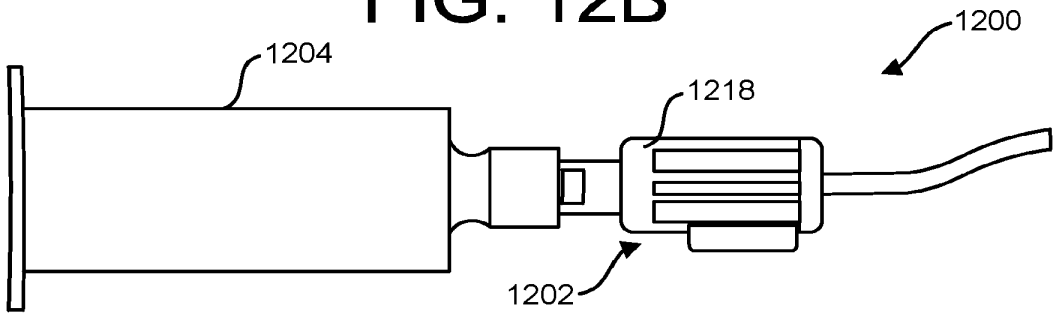


FIG. 12C

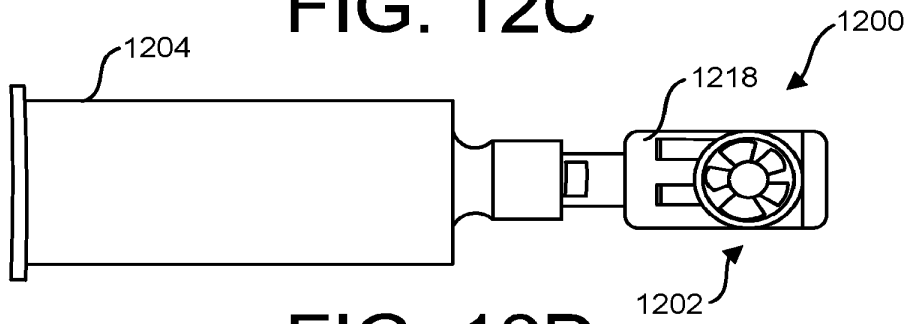


FIG. 12D

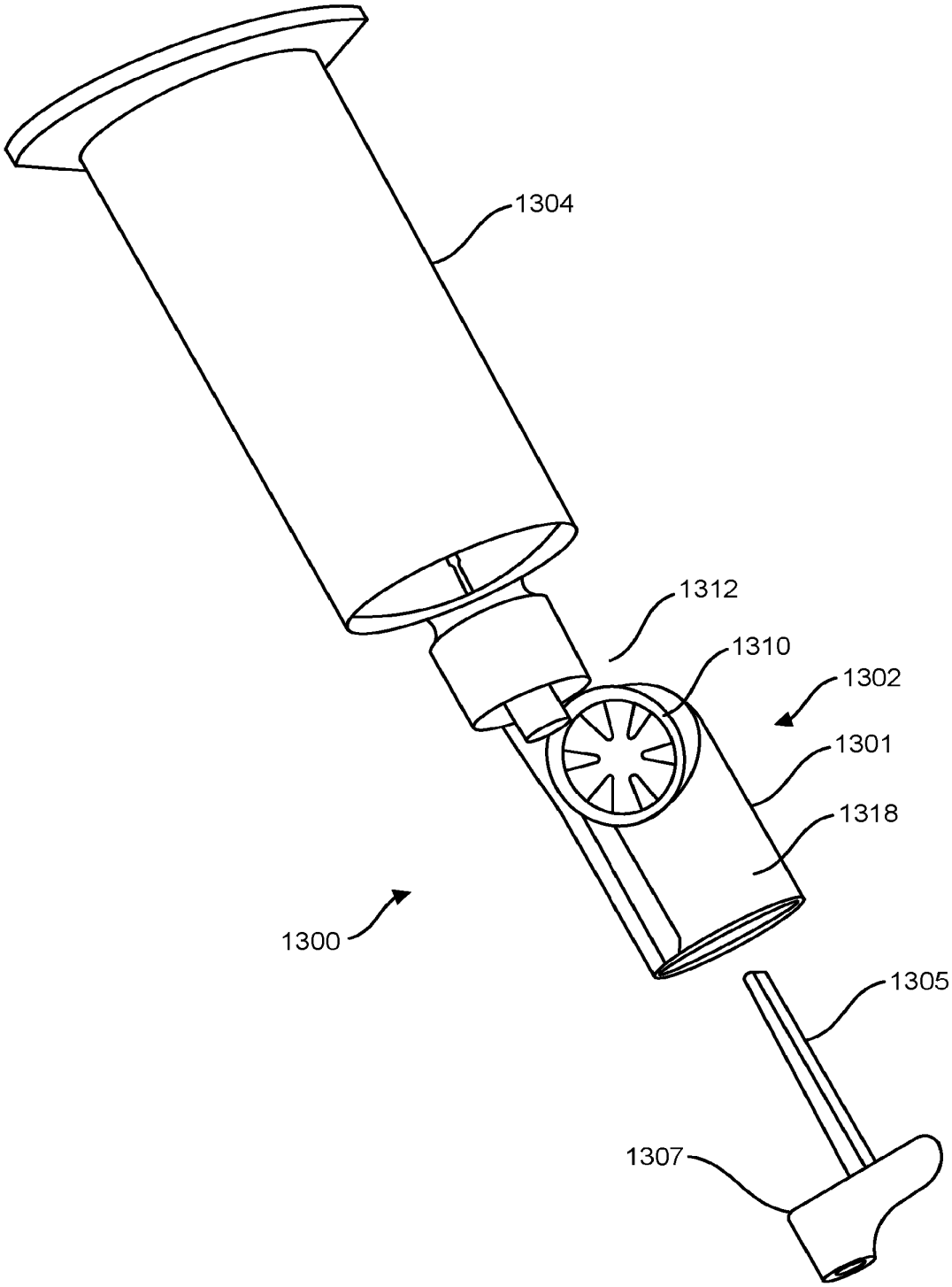


FIG. 13A

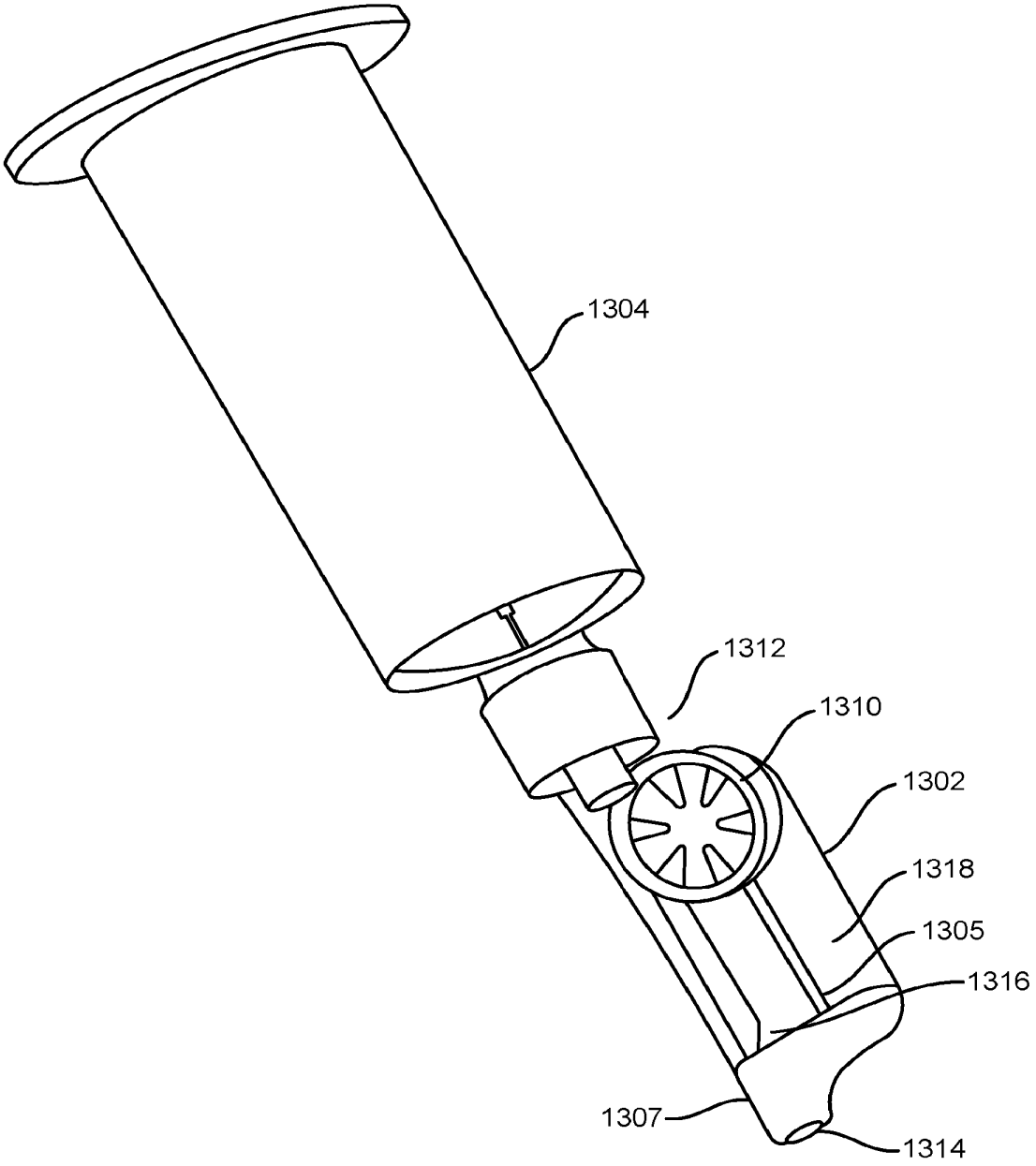


FIG. 13B

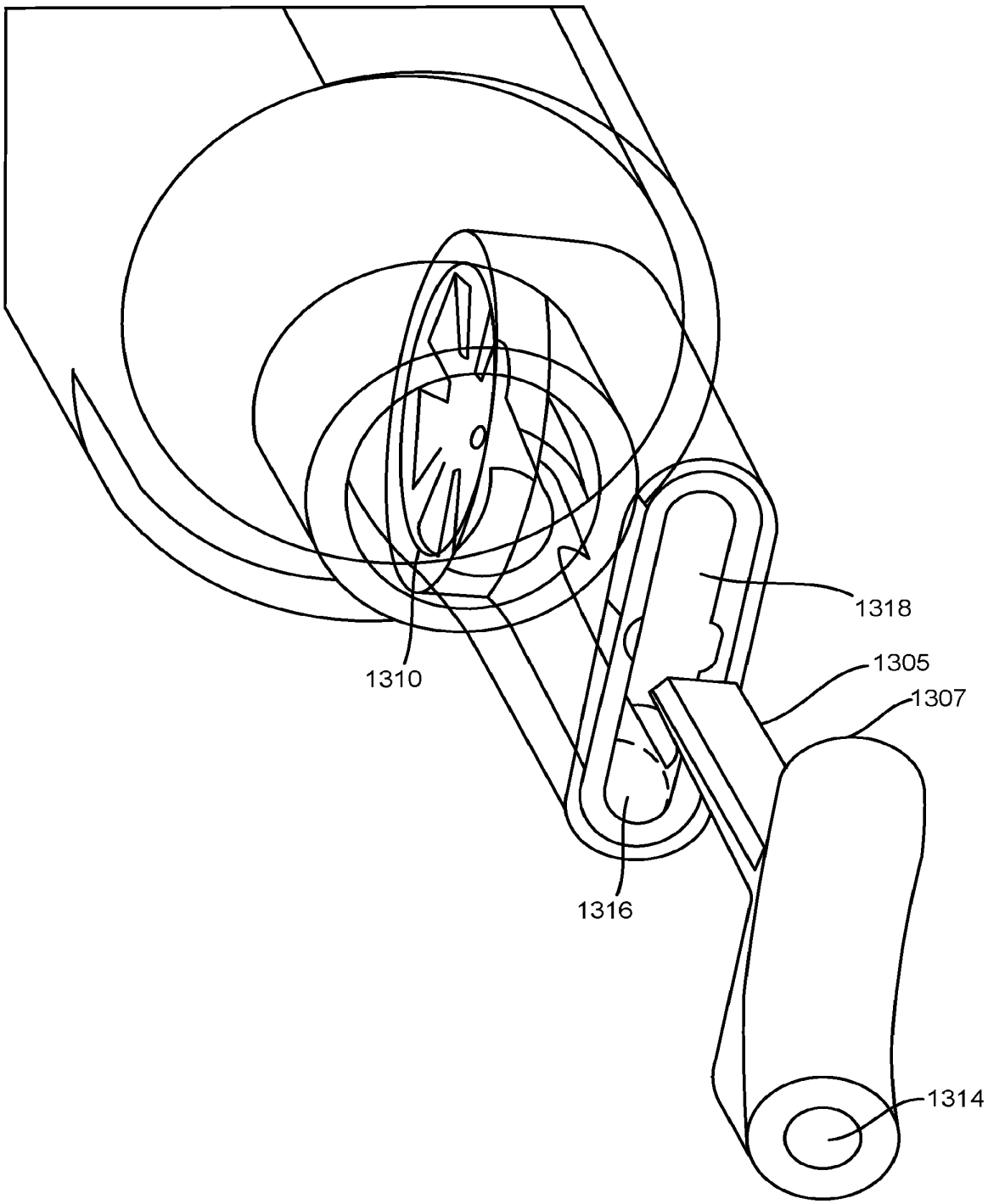


FIG. 13C

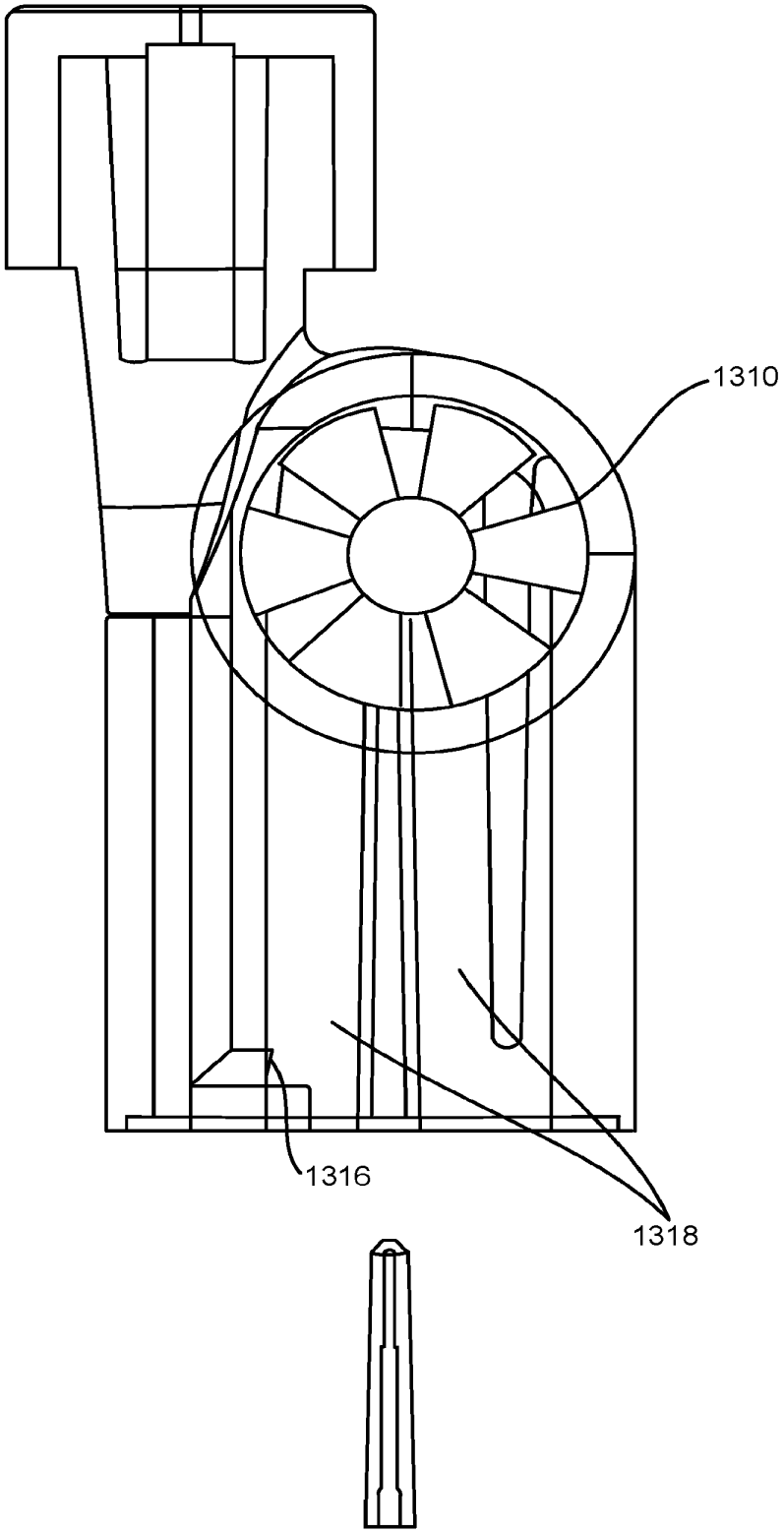


FIG. 13D

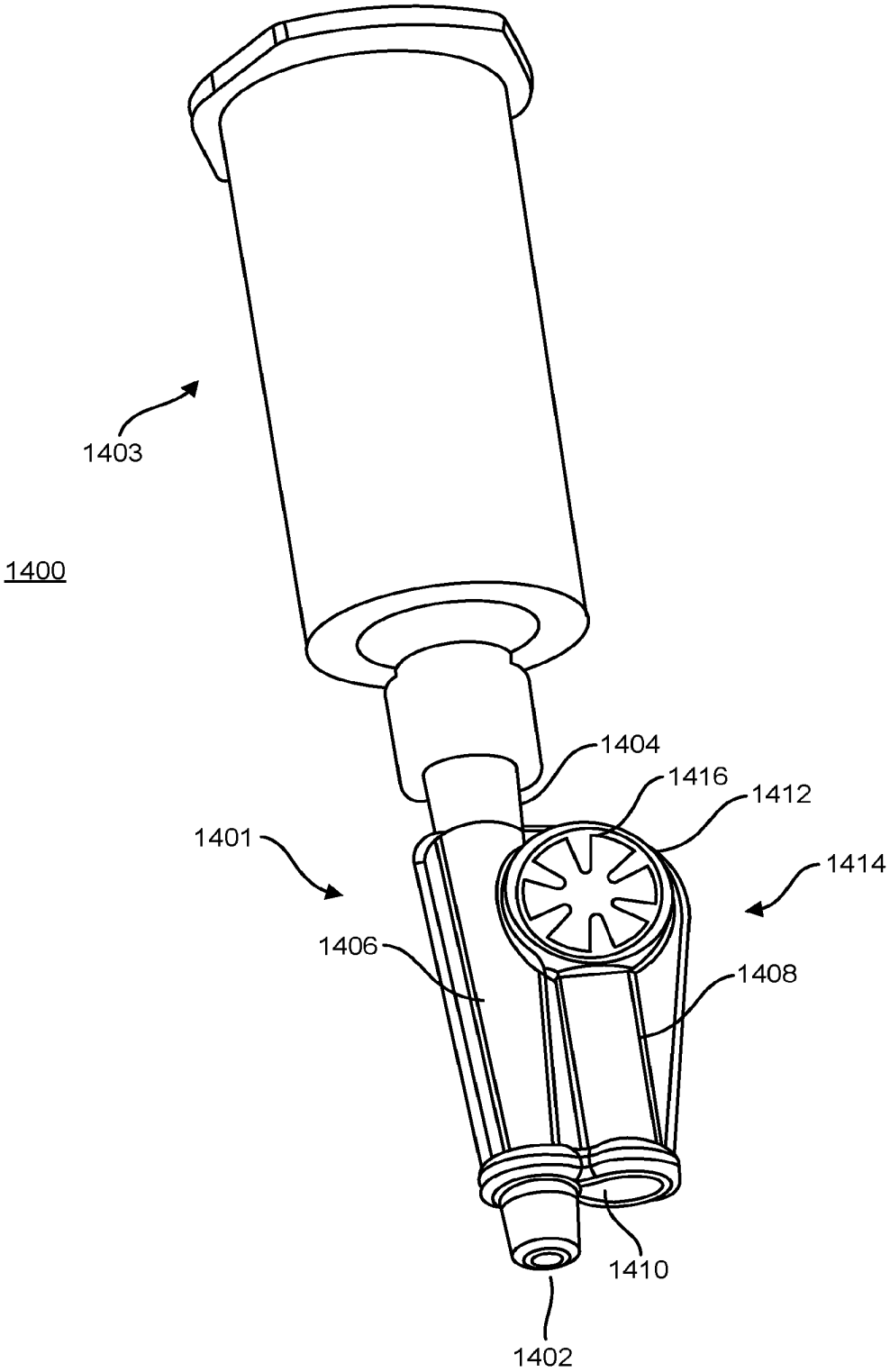


FIG. 14A

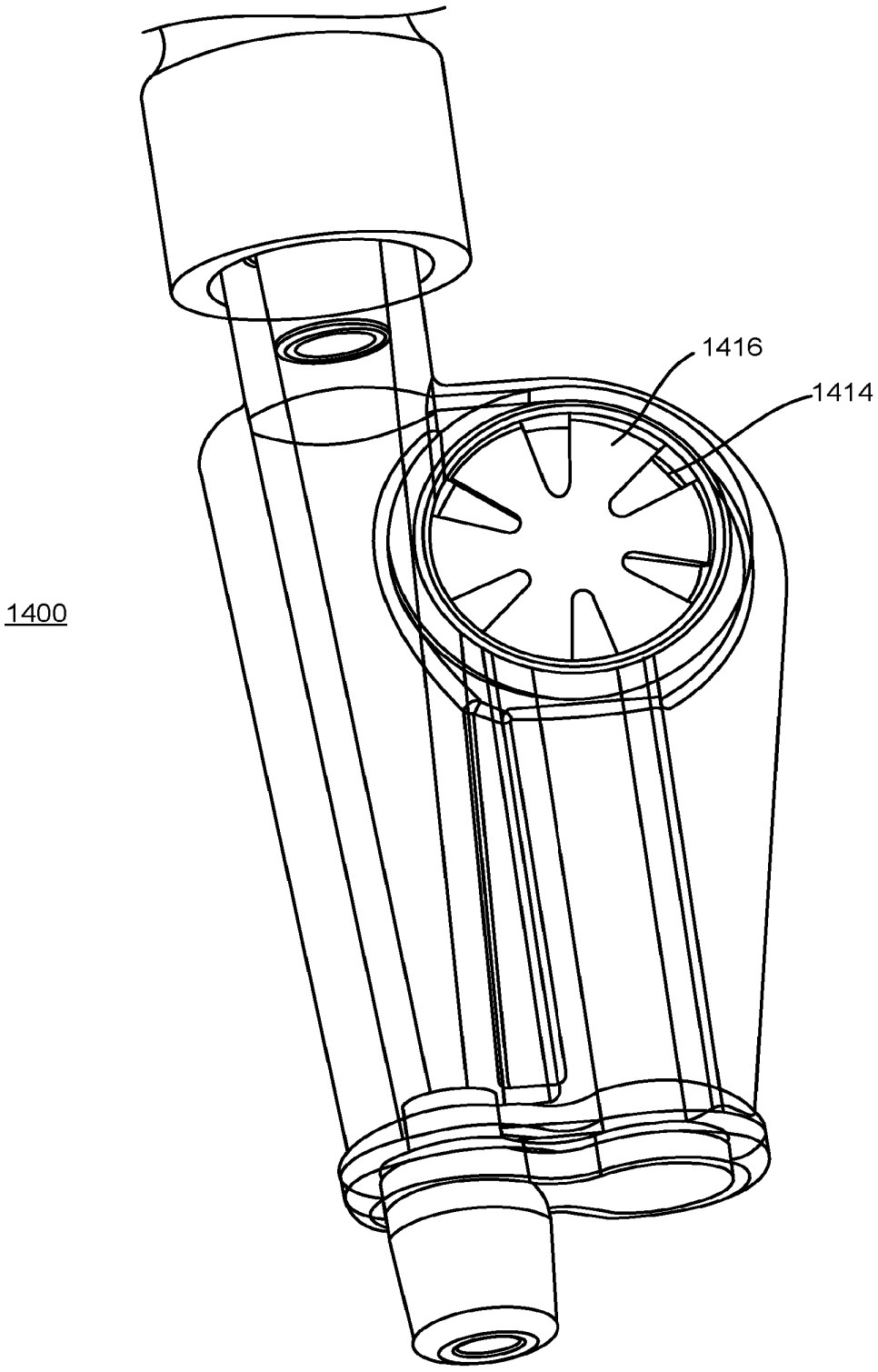


FIG. 14B

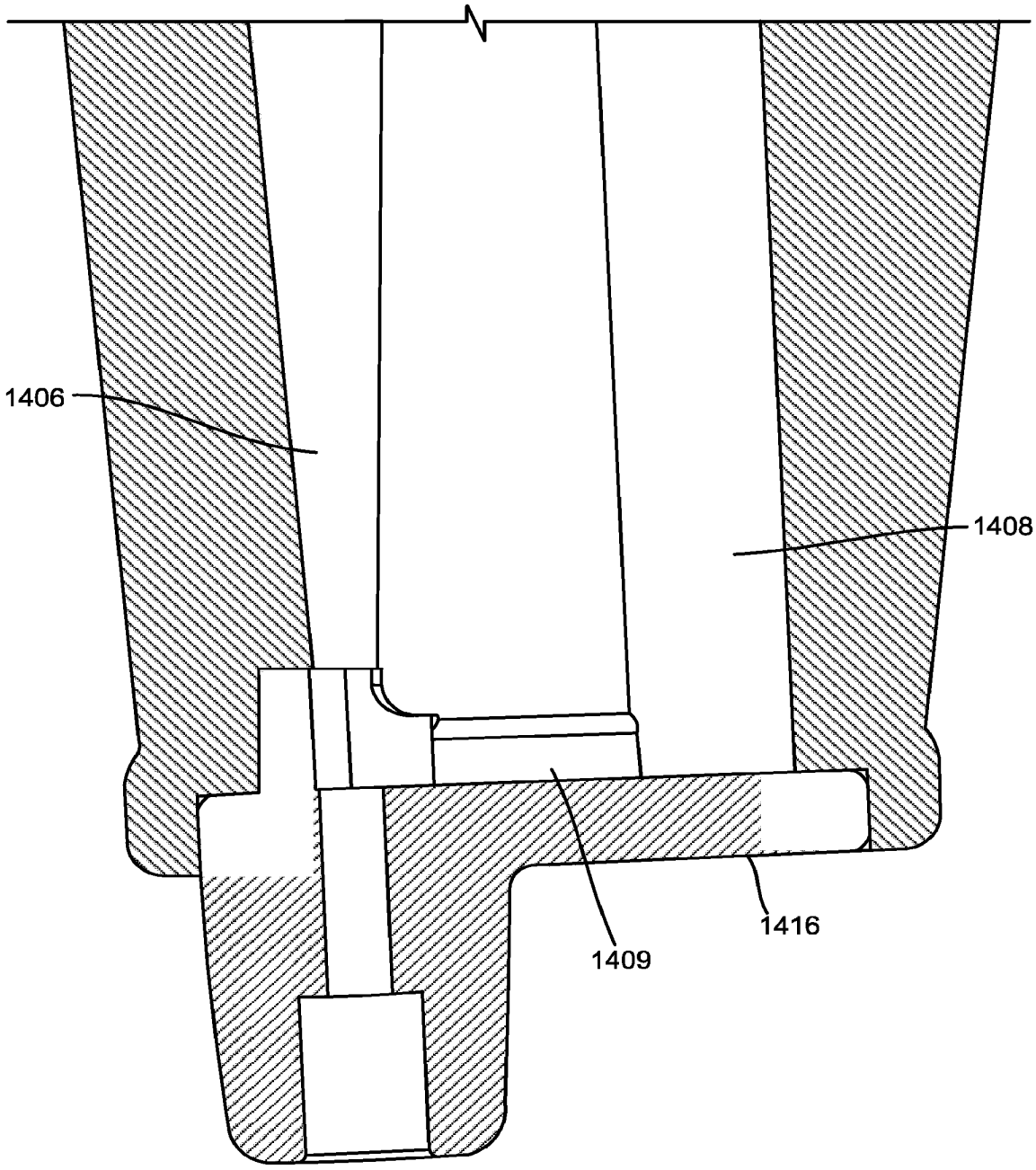


FIG. 14C

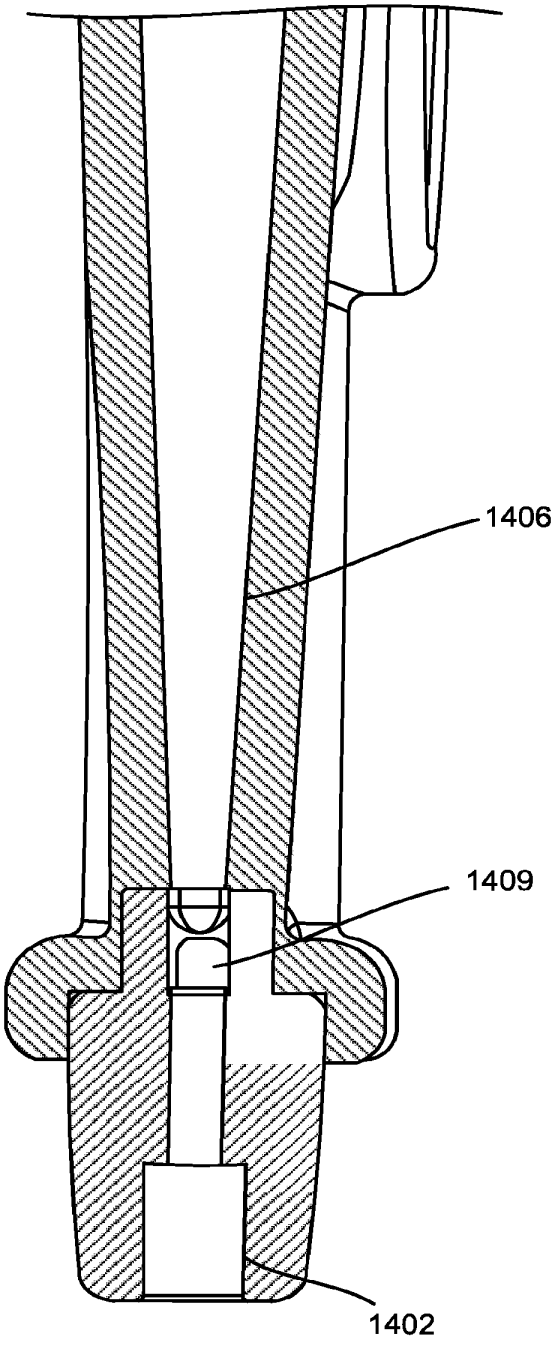


FIG. 14D

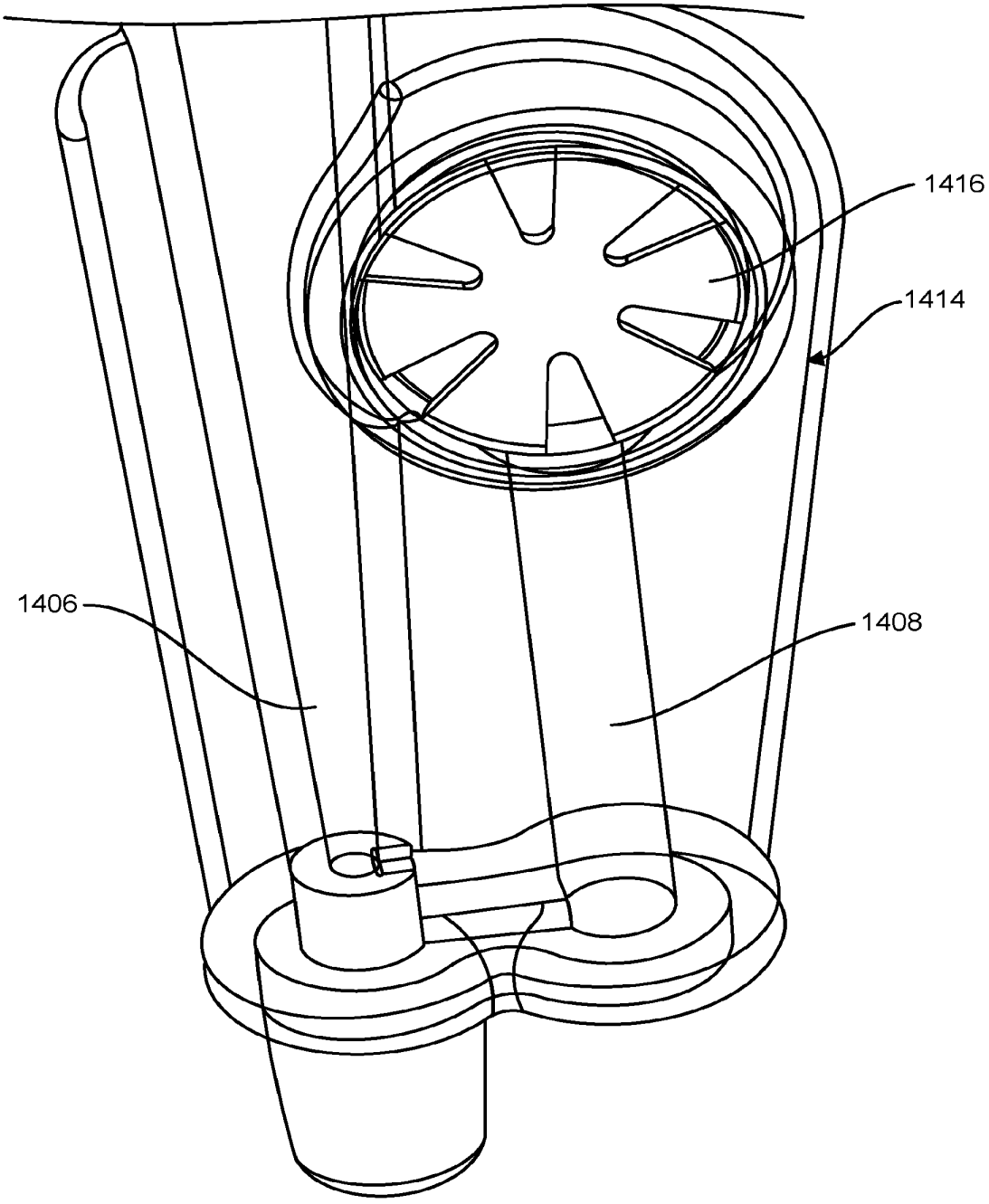


FIG. 14E

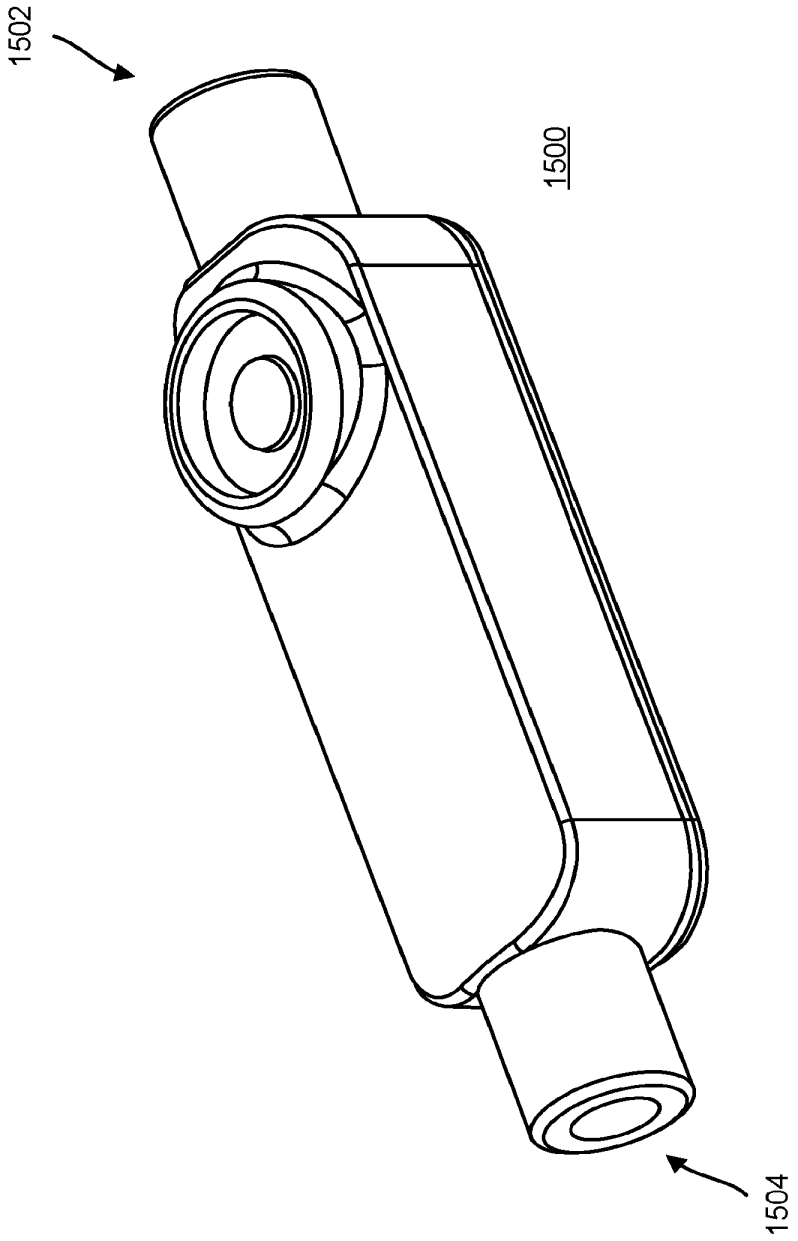


FIG. 15A

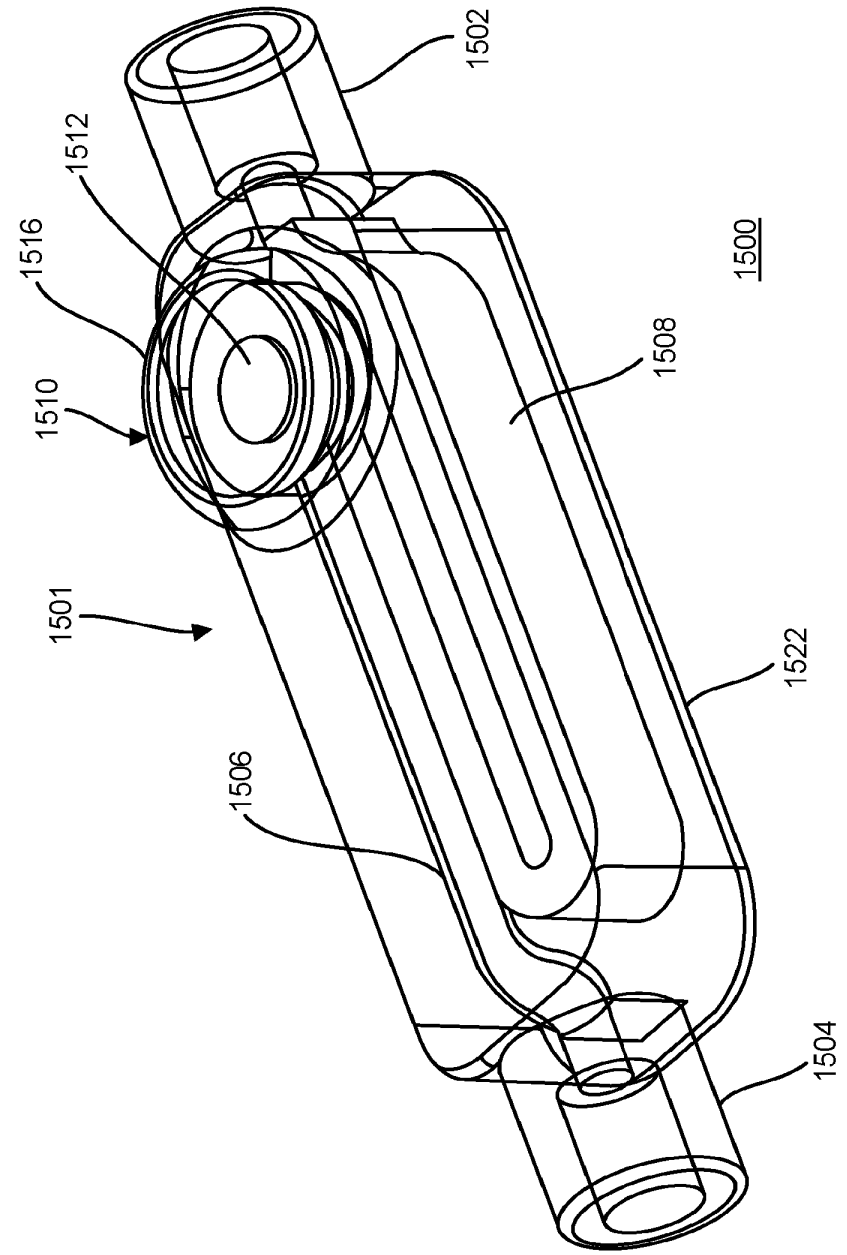


FIG. 15B

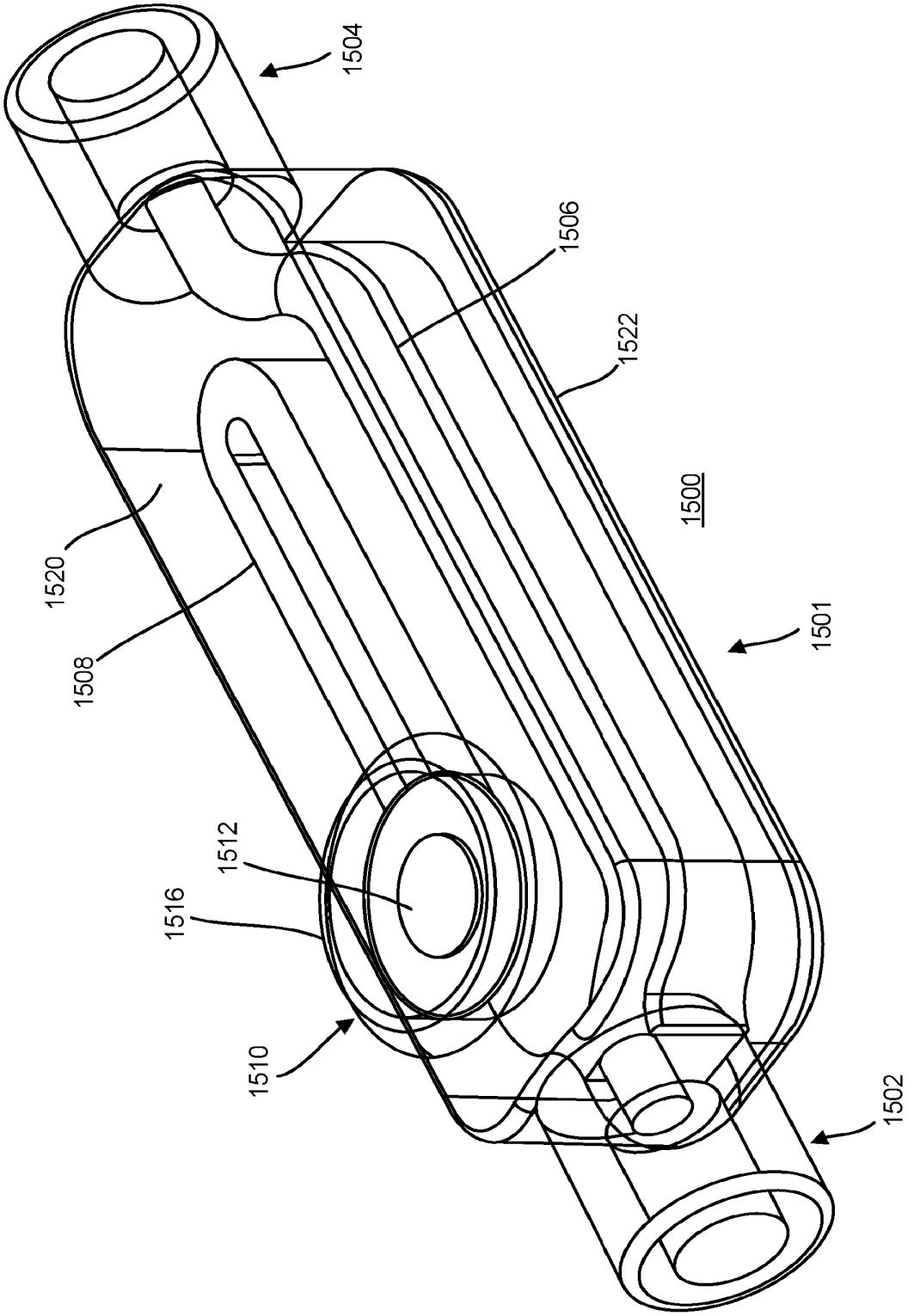


FIG. 15C

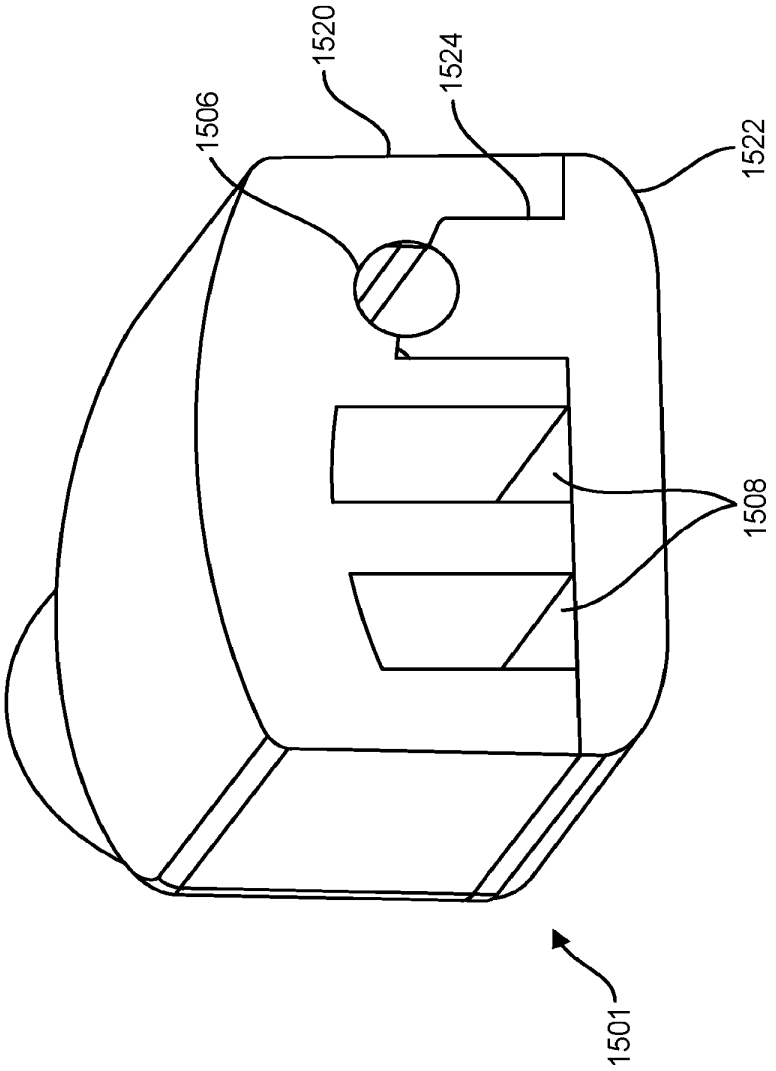


FIG. 15D

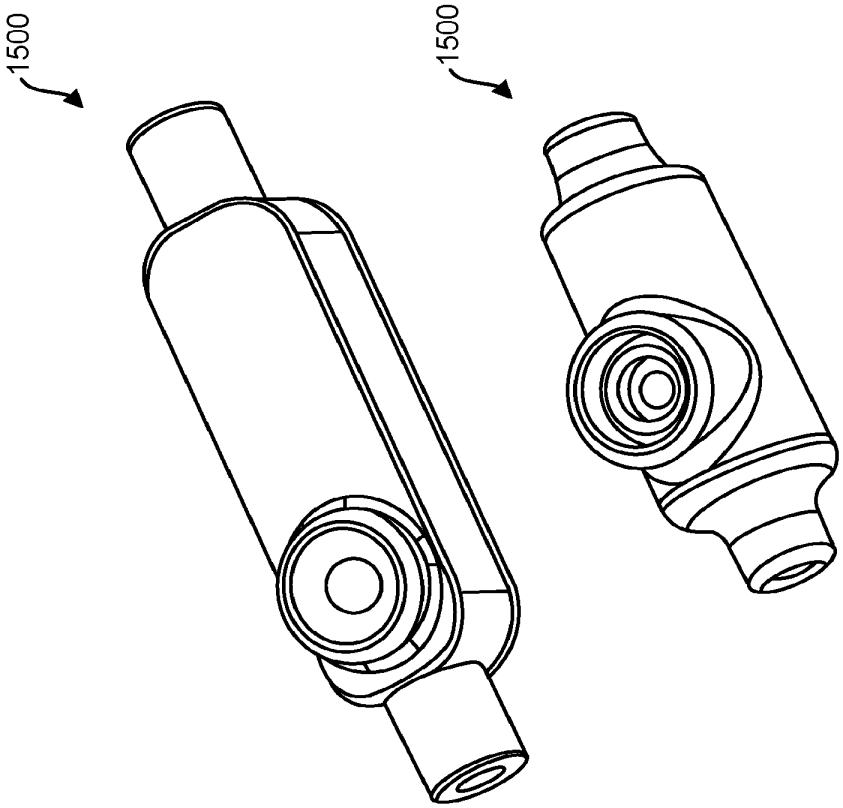


FIG. 15F

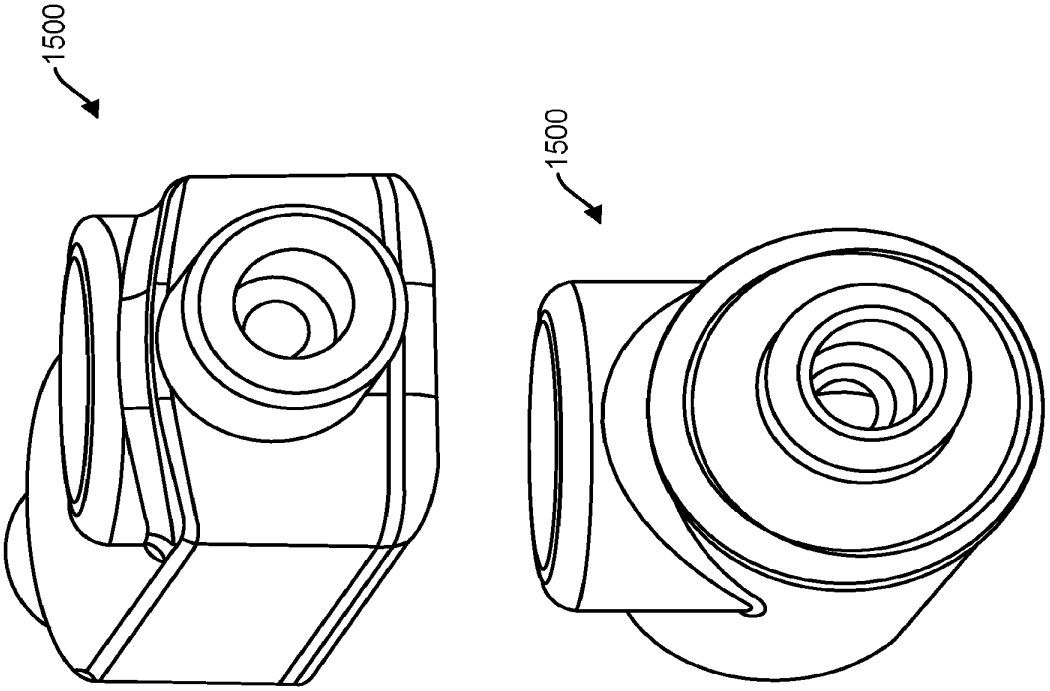


FIG. 15E

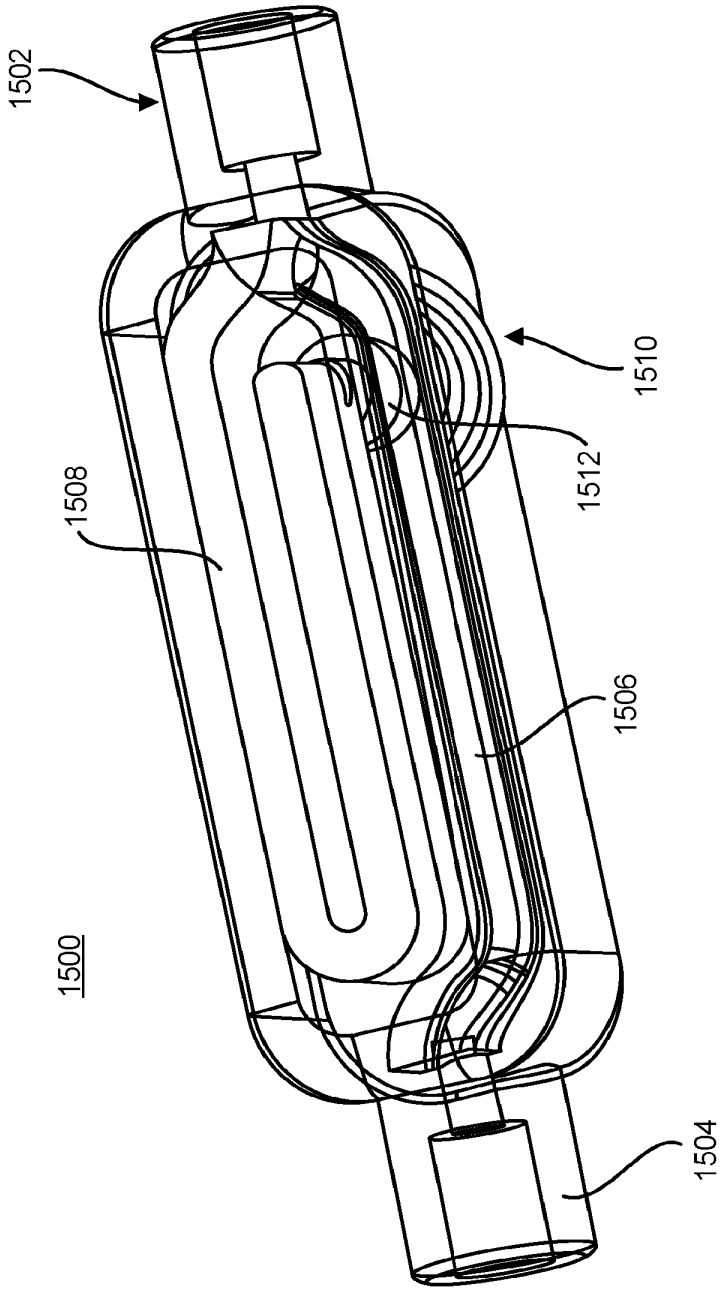


FIG. 15G

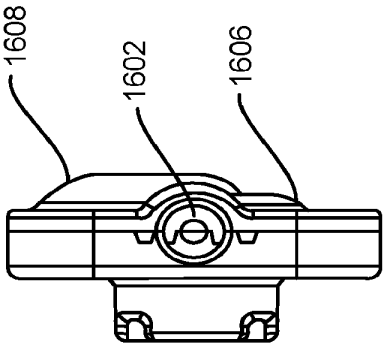


FIG. 16C

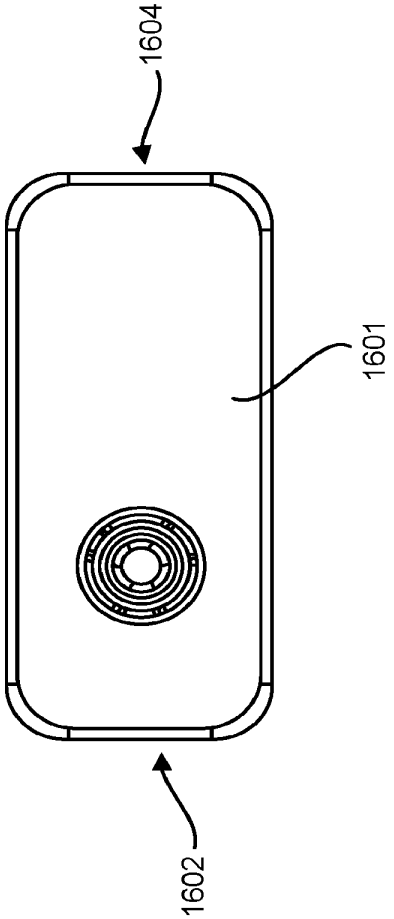


FIG. 16A

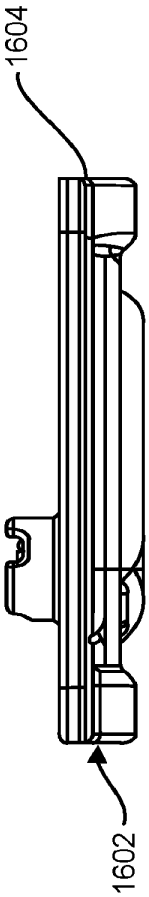


FIG. 16B

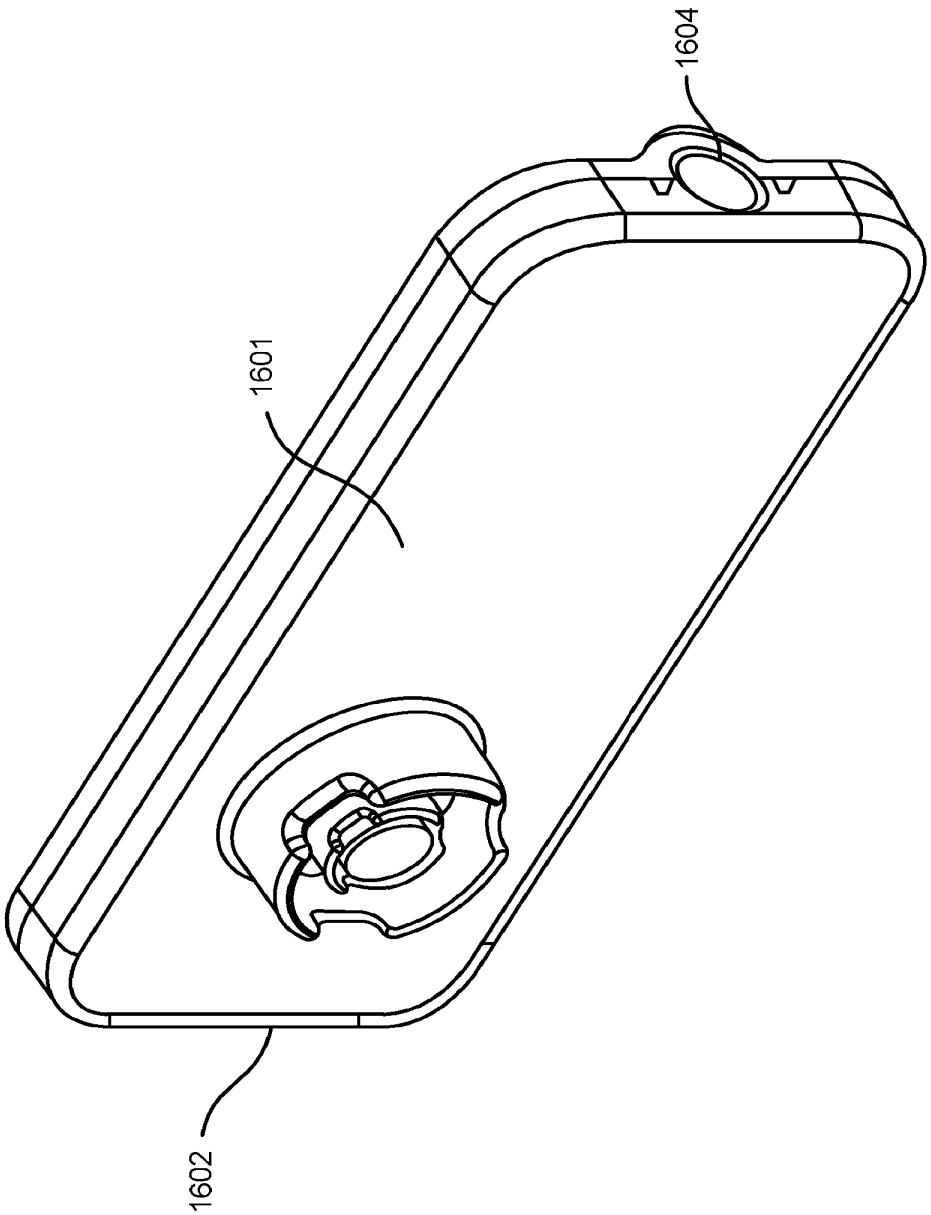


FIG. 16D

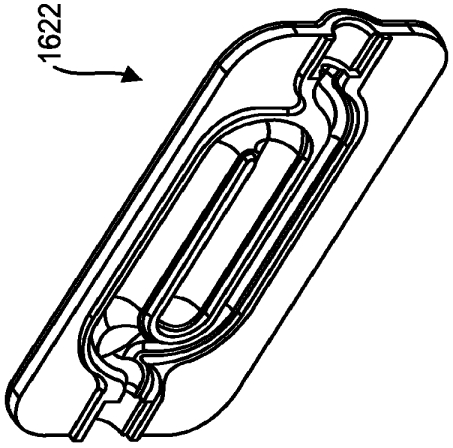


FIG. 17B



FIG. 17E

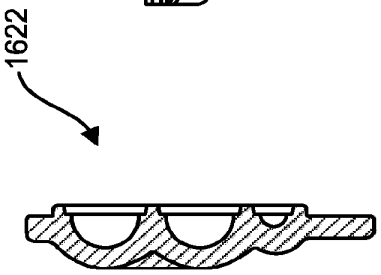


FIG. 17D

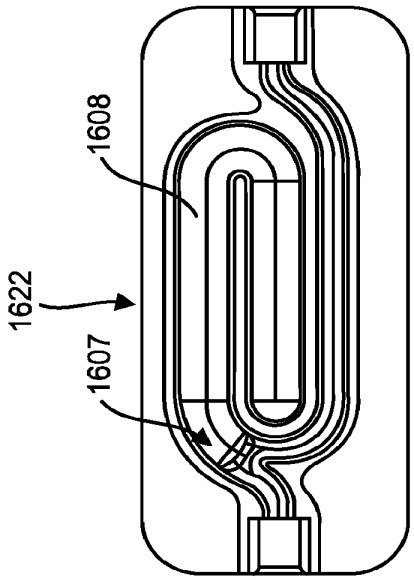


FIG. 17A

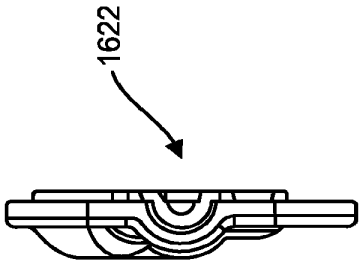


FIG. 17C

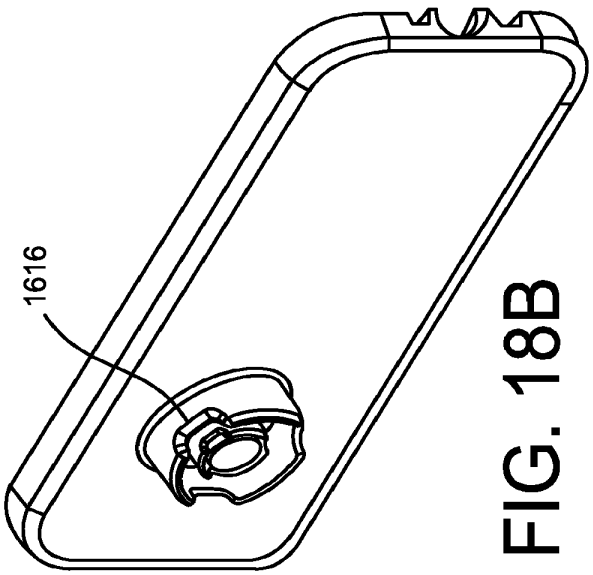


FIG. 18B

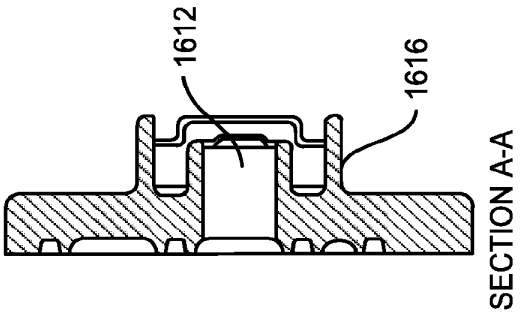


FIG. 18F

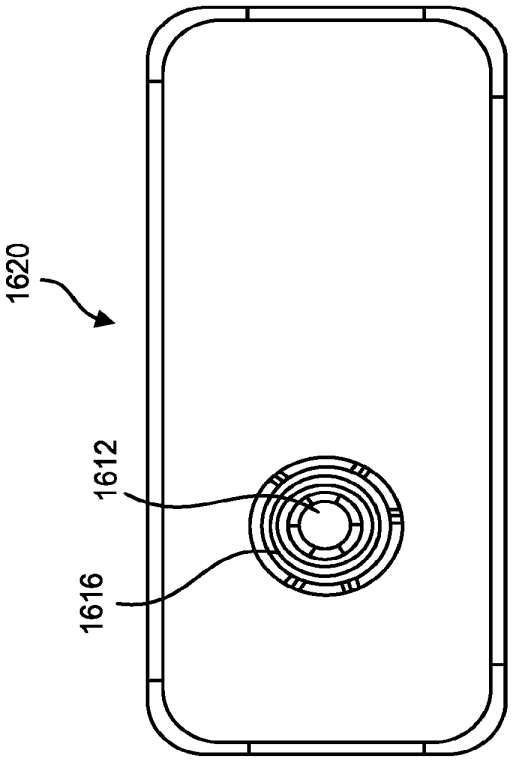


FIG. 18A

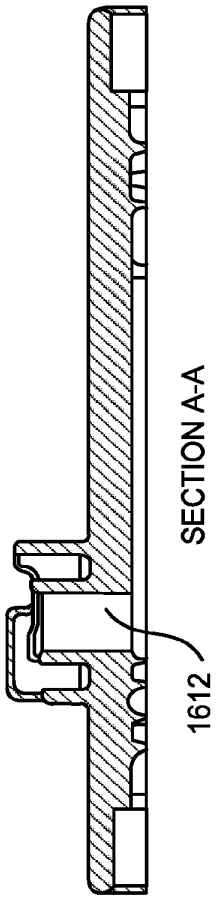


FIG. 18D

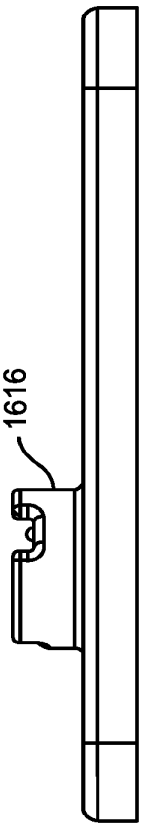


FIG. 18E

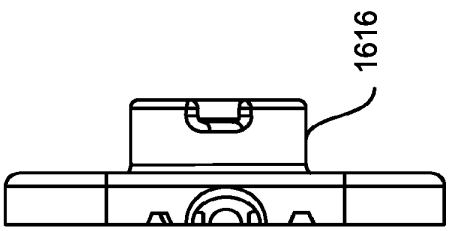


FIG. 18C

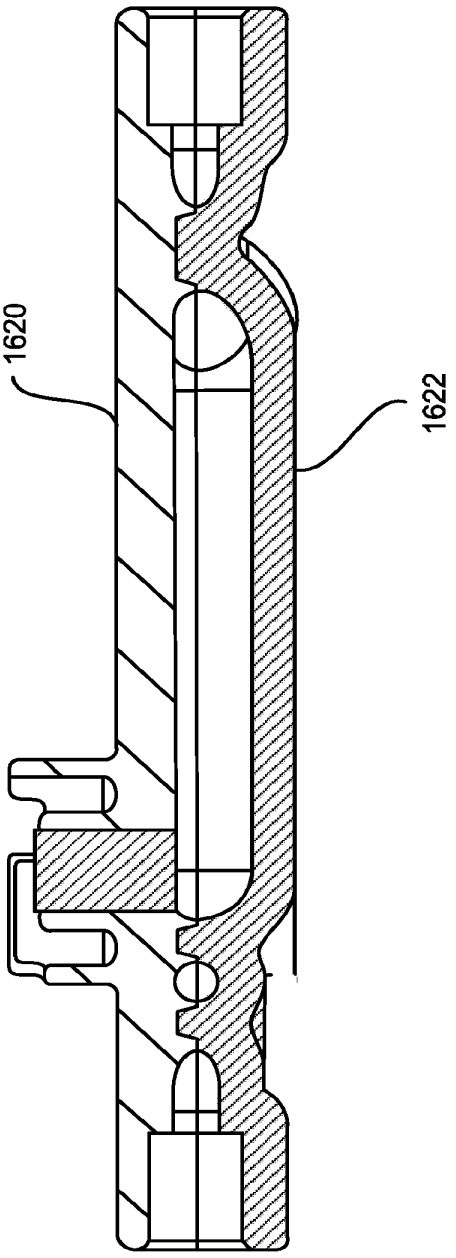


FIG. 19A

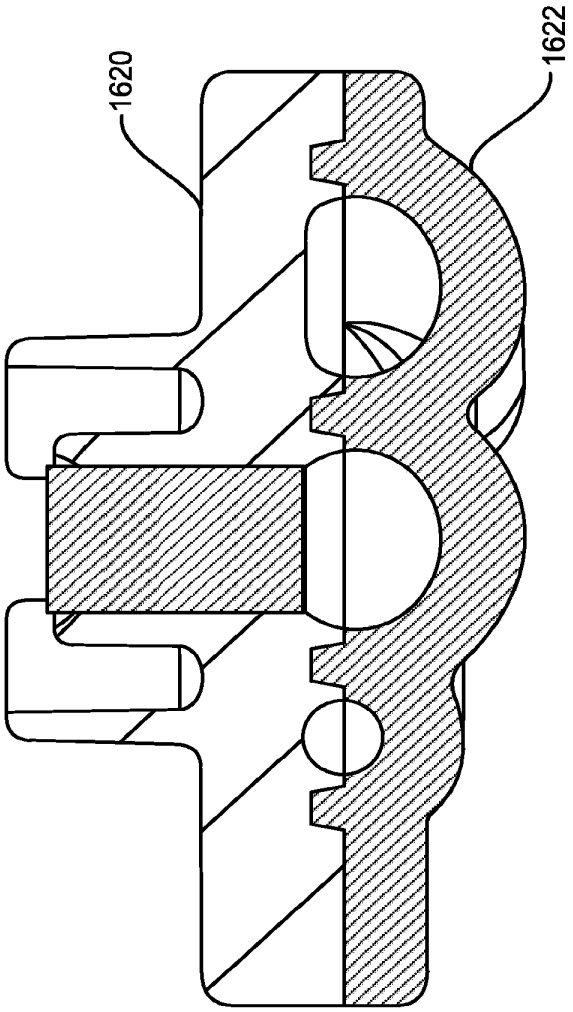


FIG. 19B

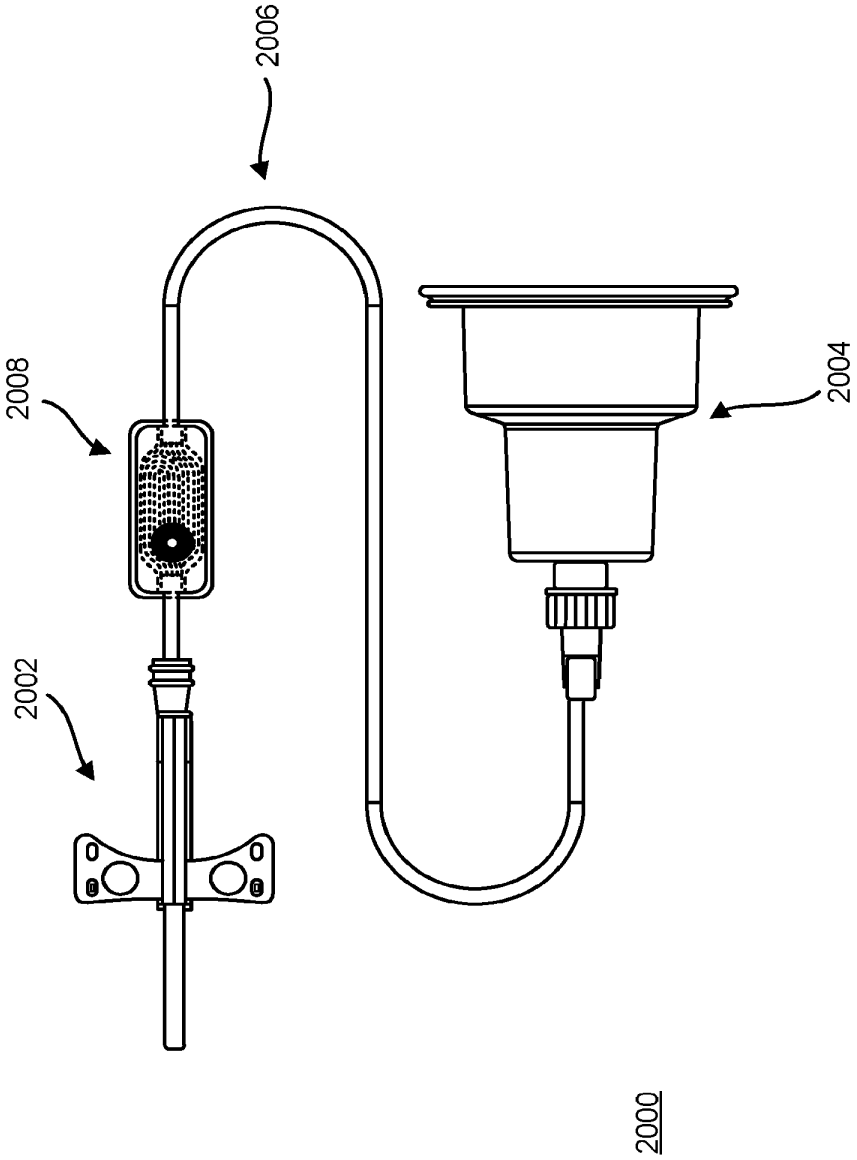


FIG. 20

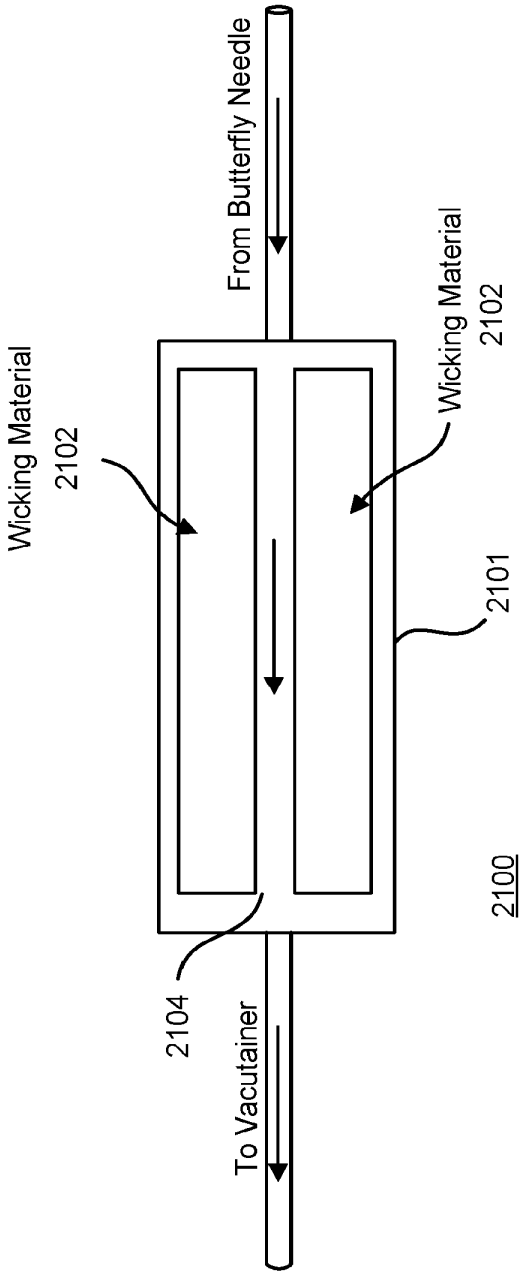

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

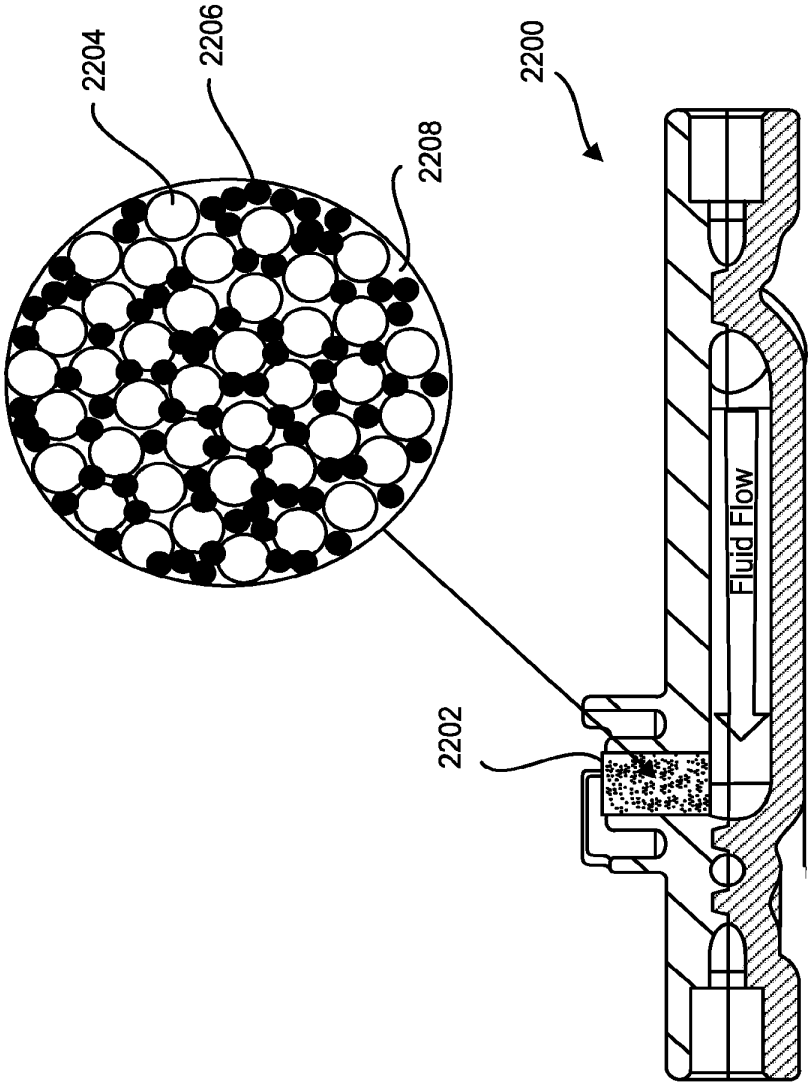


FIG. 22A

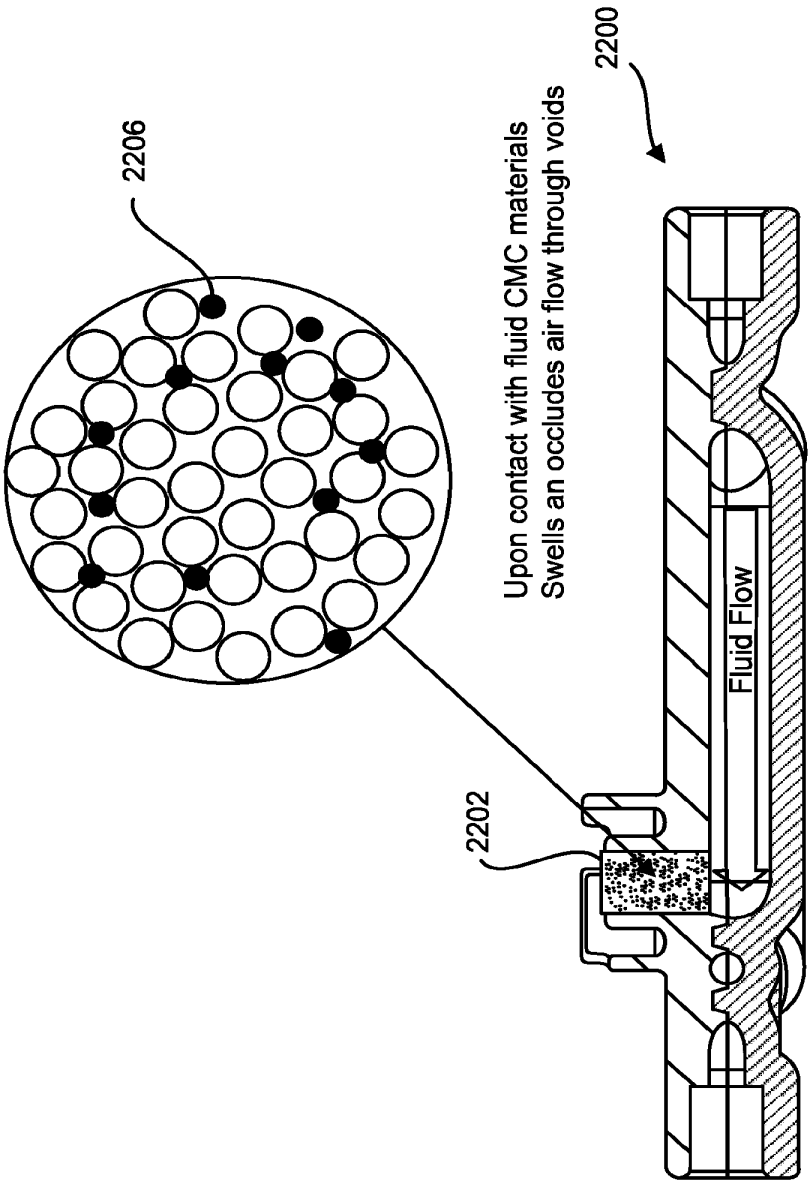

2200
2206
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

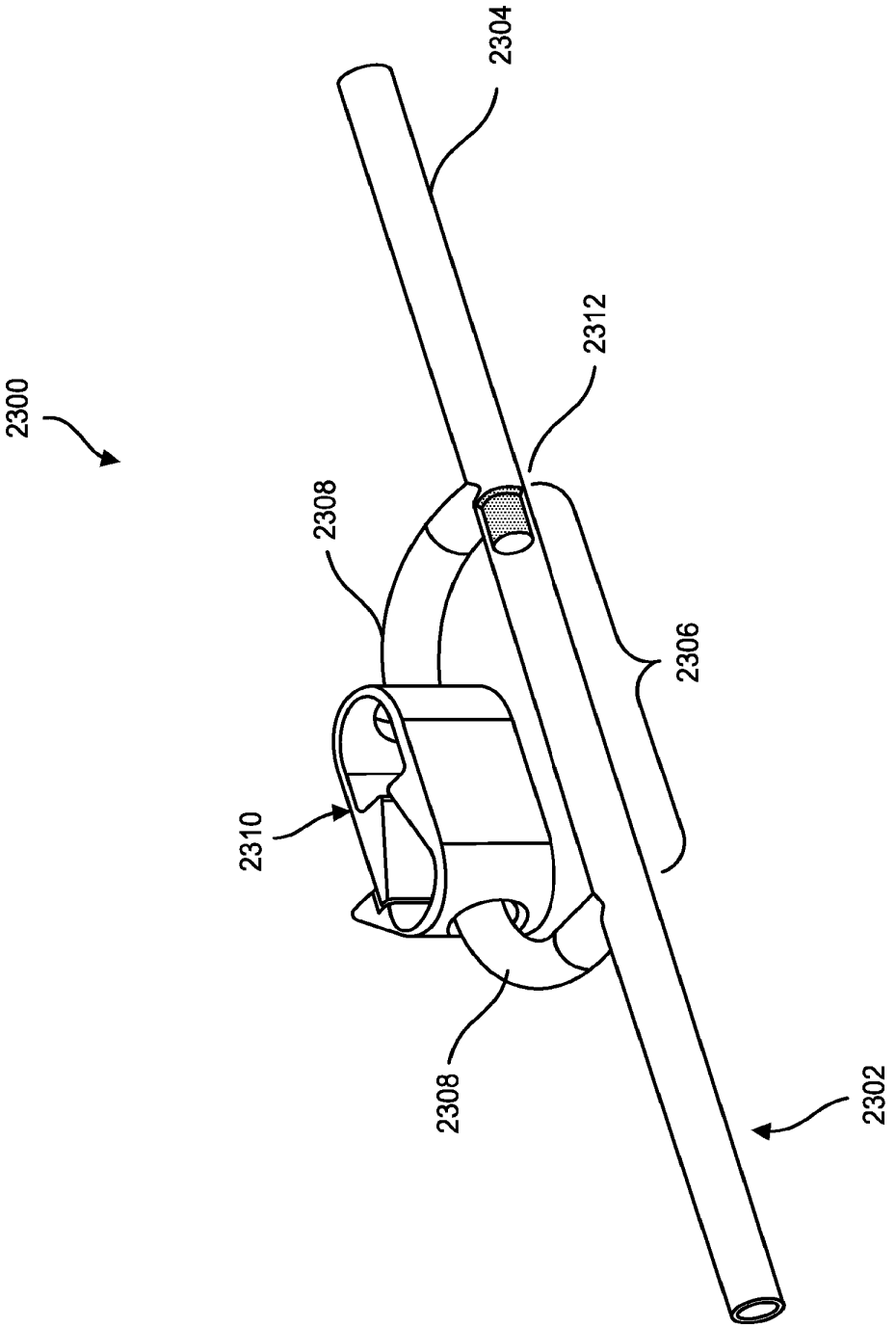


FIG. 23A

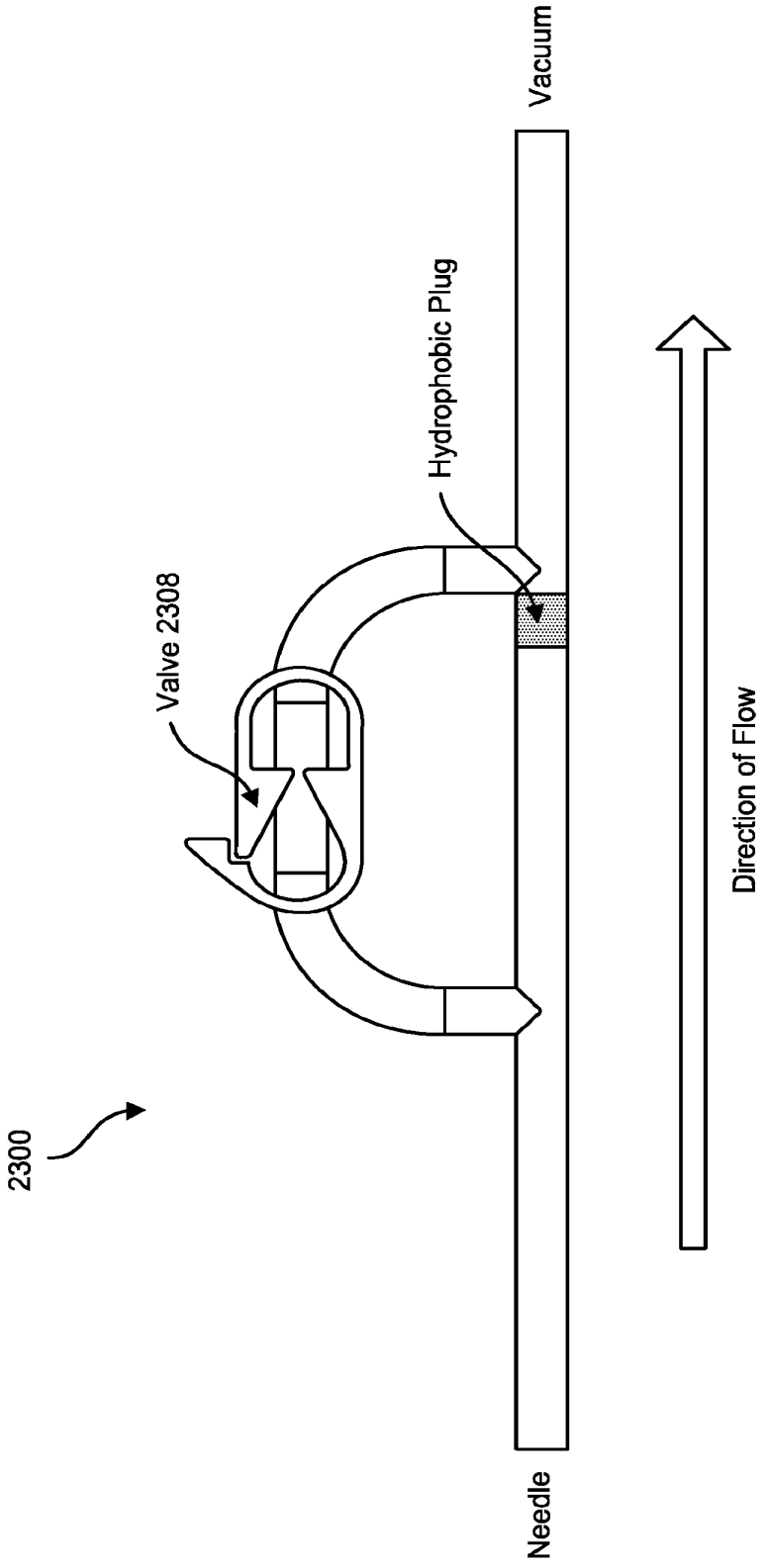

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

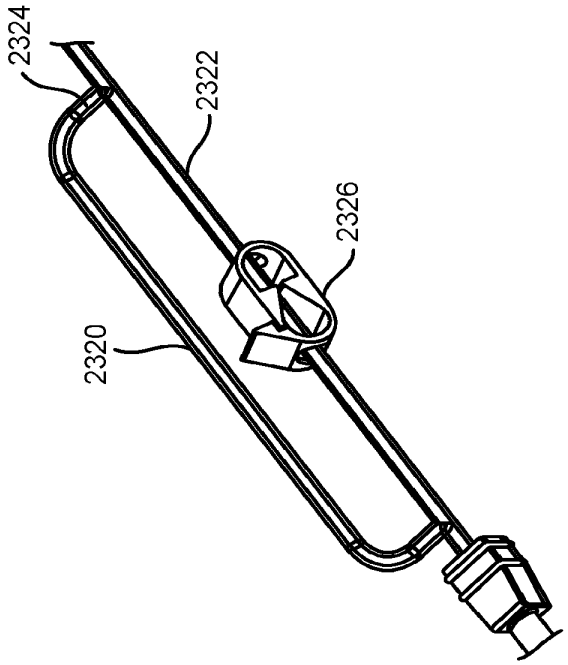


FIG. 23D

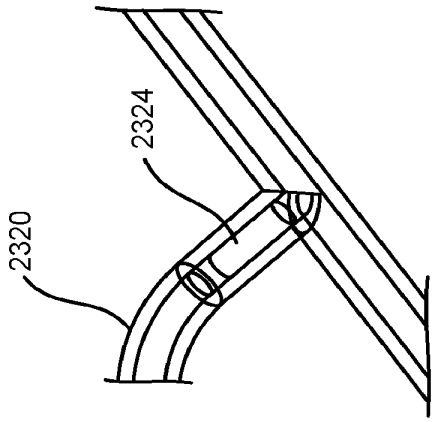


FIG. 23E

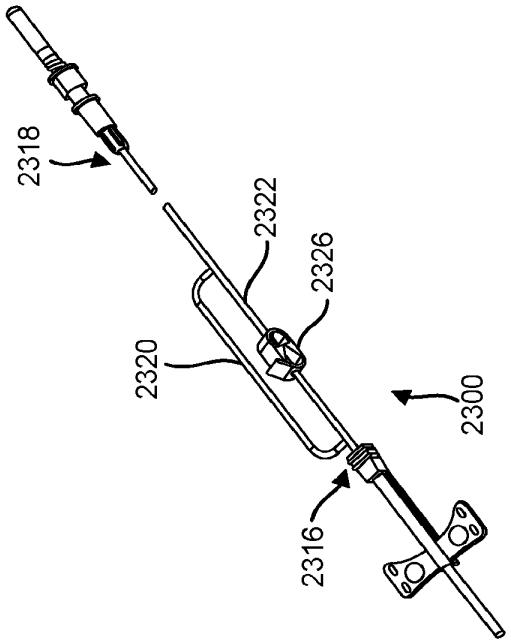


FIG. 23C

Replacement Sheet
52/69

Docket No. KURIN3PCT
PCT/US2017/068569

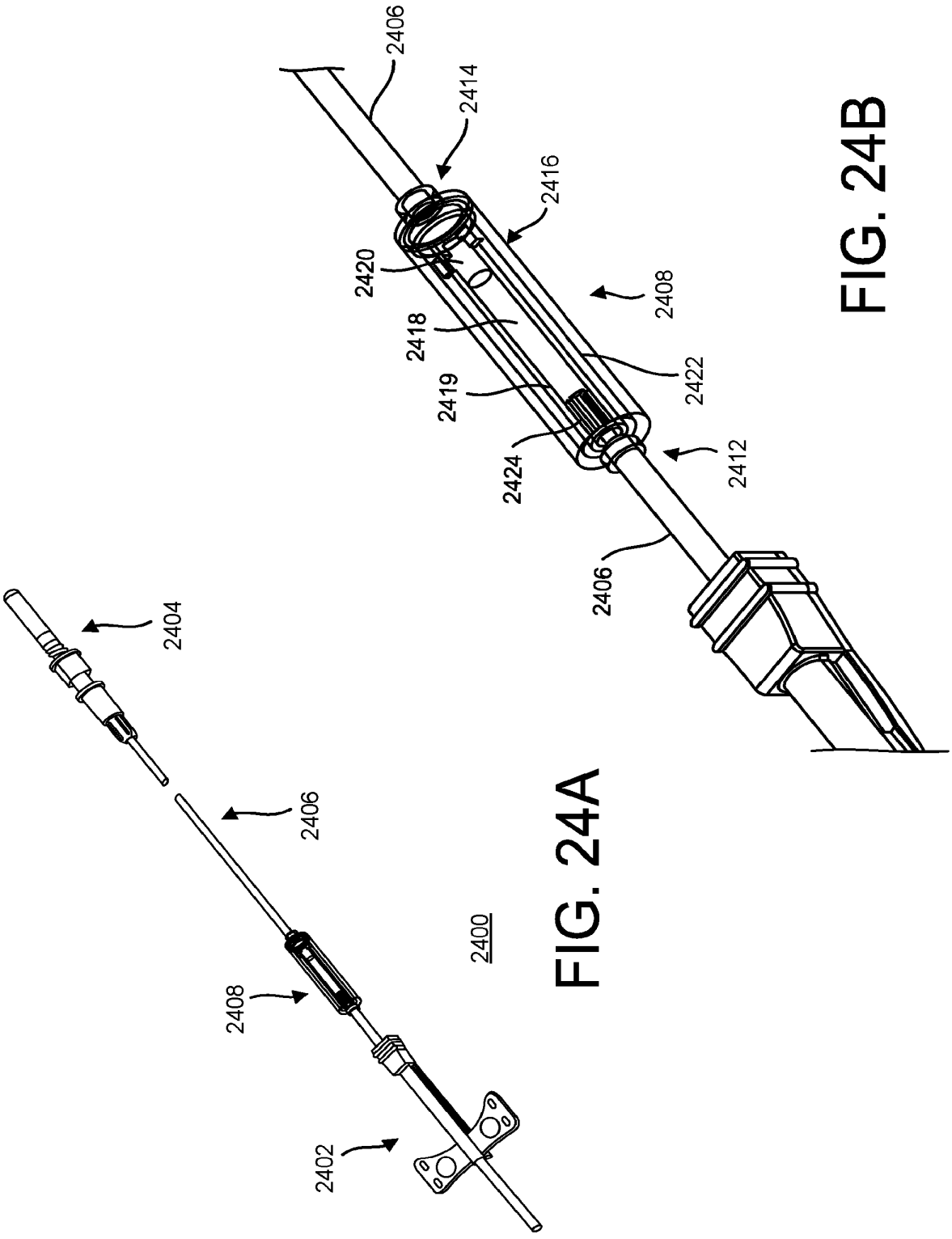


FIG. 24B

FIG. 24A

Replacement Sheet
53/69

Docket No. KURIN3PCT
PCT/US2017/068569

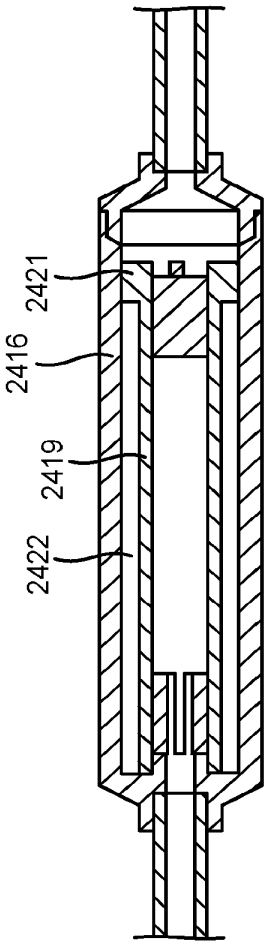


FIG. 24C

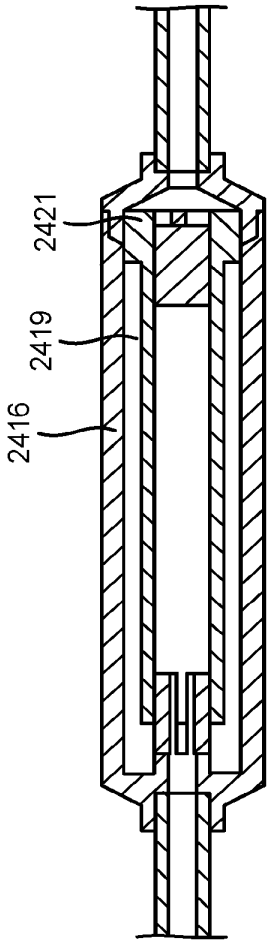


FIG. 24D

Replacement Sheet
54/69

Docket No. KURIN3PCT
PCT/US2017/068569

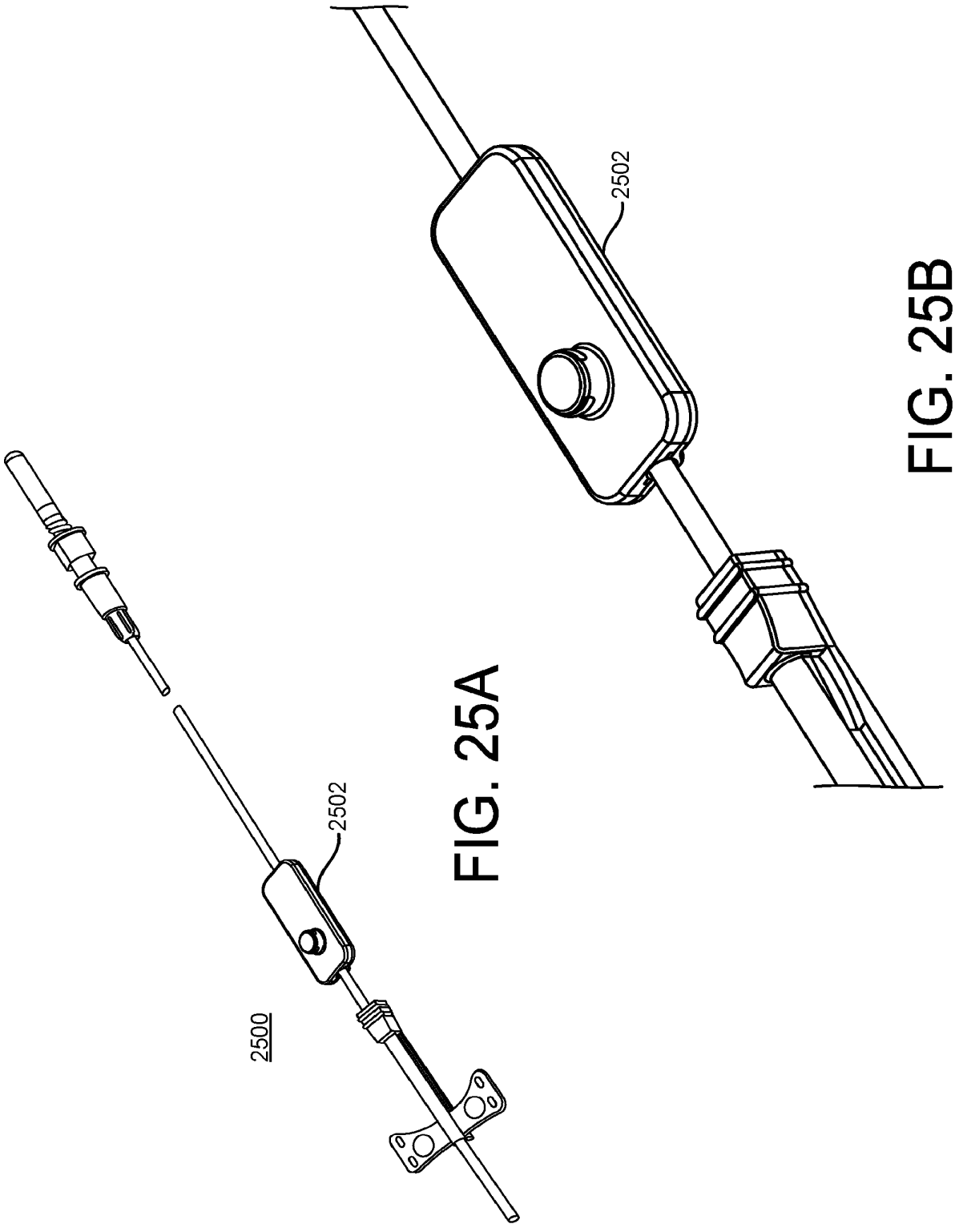


FIG. 25A

FIG. 25B

Replacement Sheet
55/69

Docket No. KURIN3PCT
PCT/US2017/068569

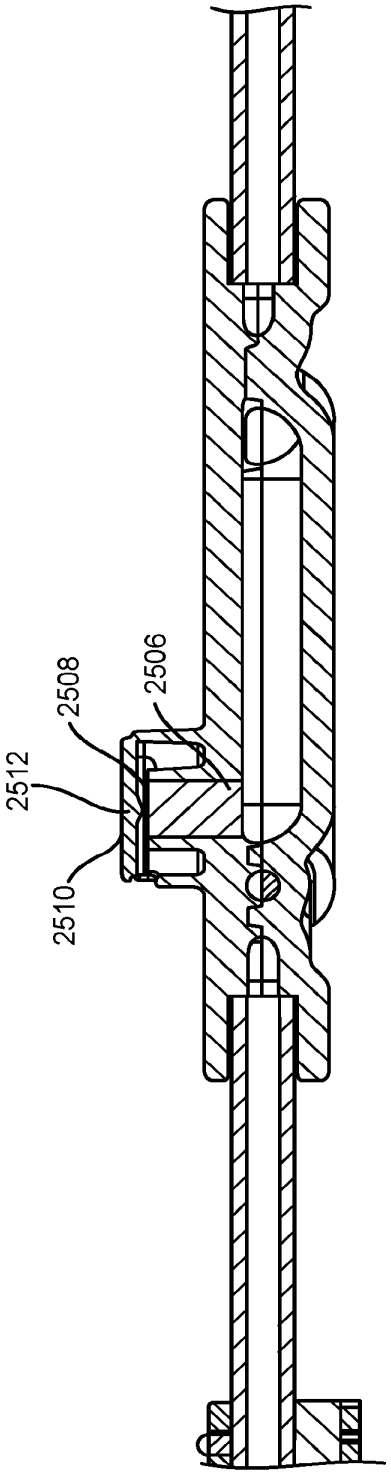


FIG. 25C

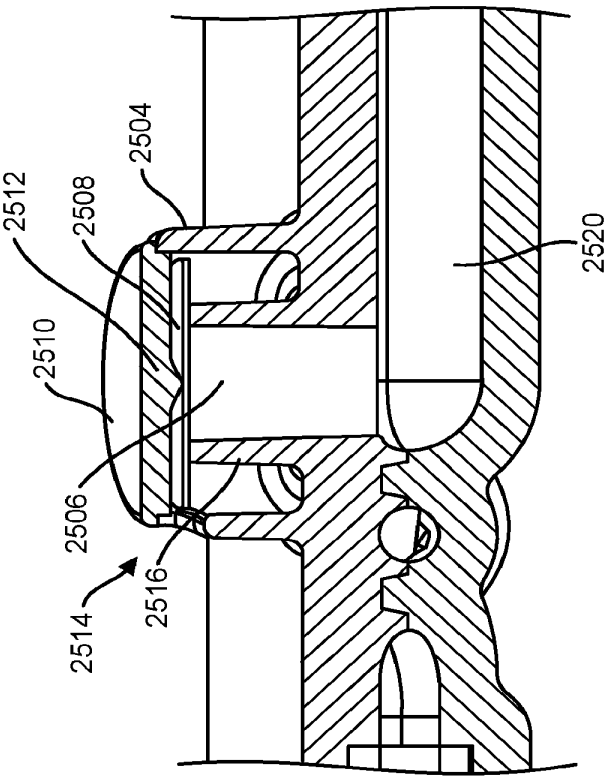


FIG. 25D

Replacement Sheet
56/69

Docket No. KURIN3PCT
PCT/US2017/068569

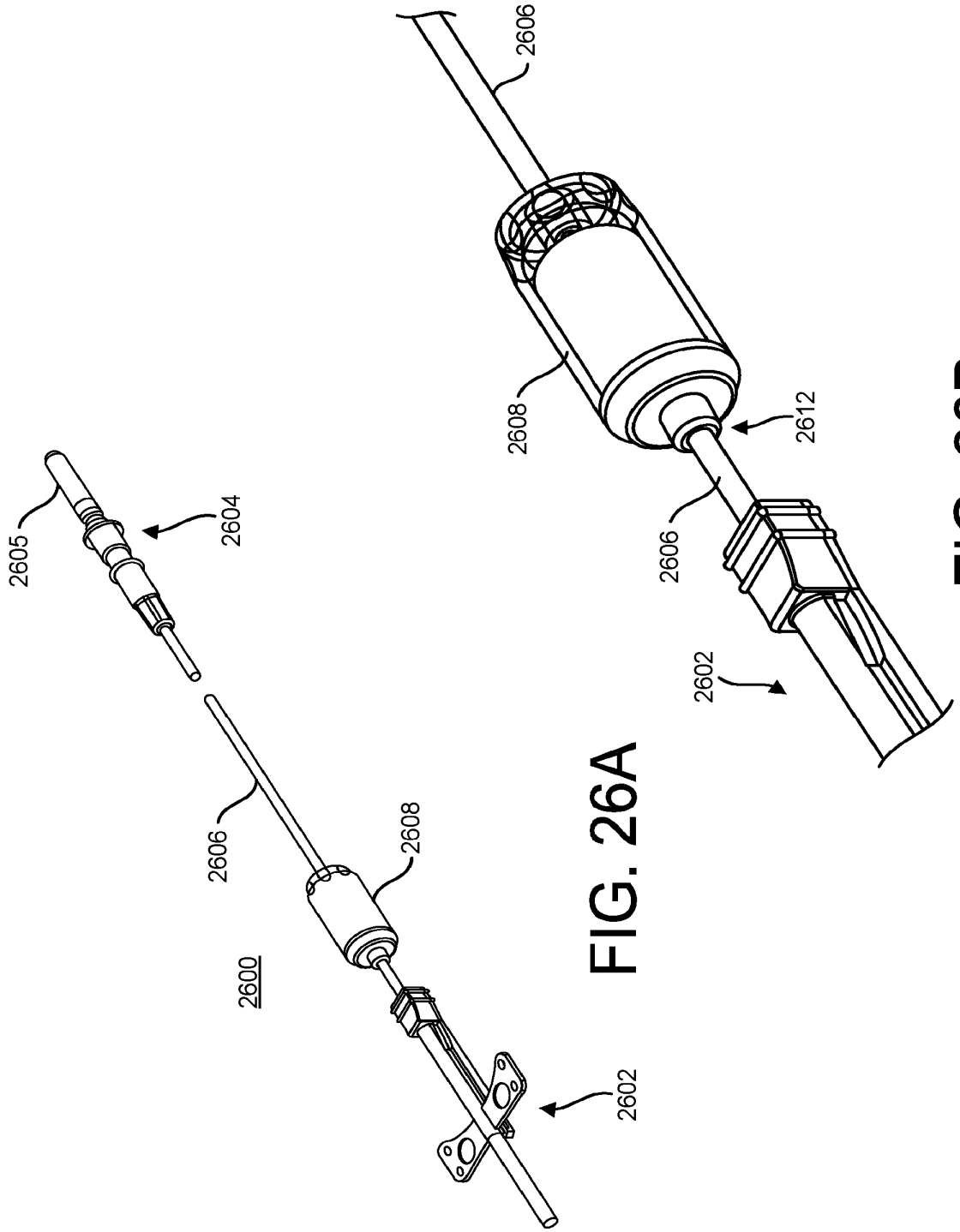


FIG. 26B

FIG. 26A

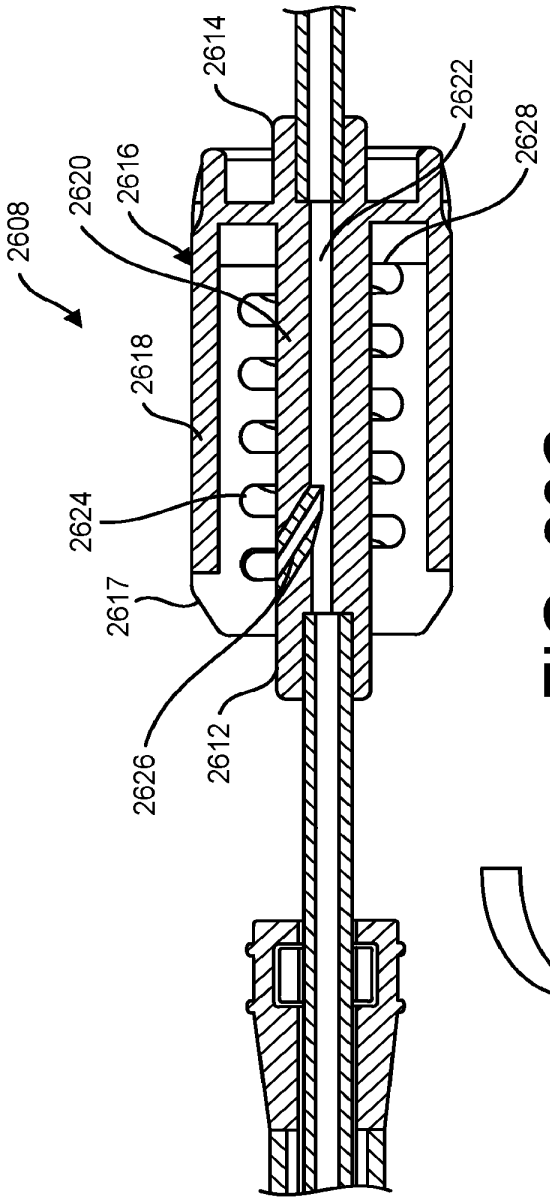


FIG. 26C

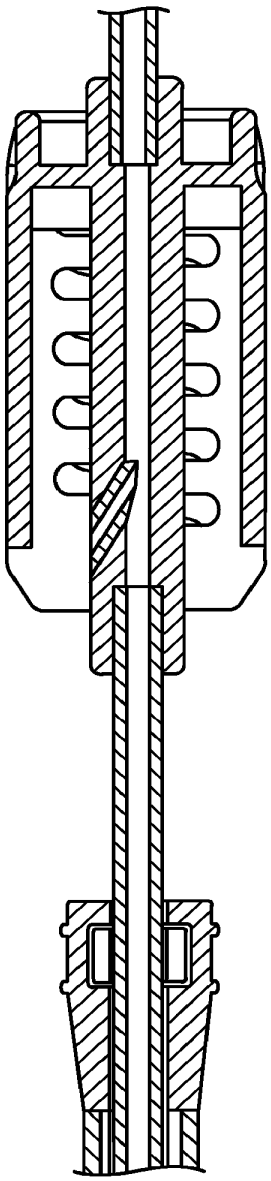


FIG. 26D

Replacement Sheet
58/69

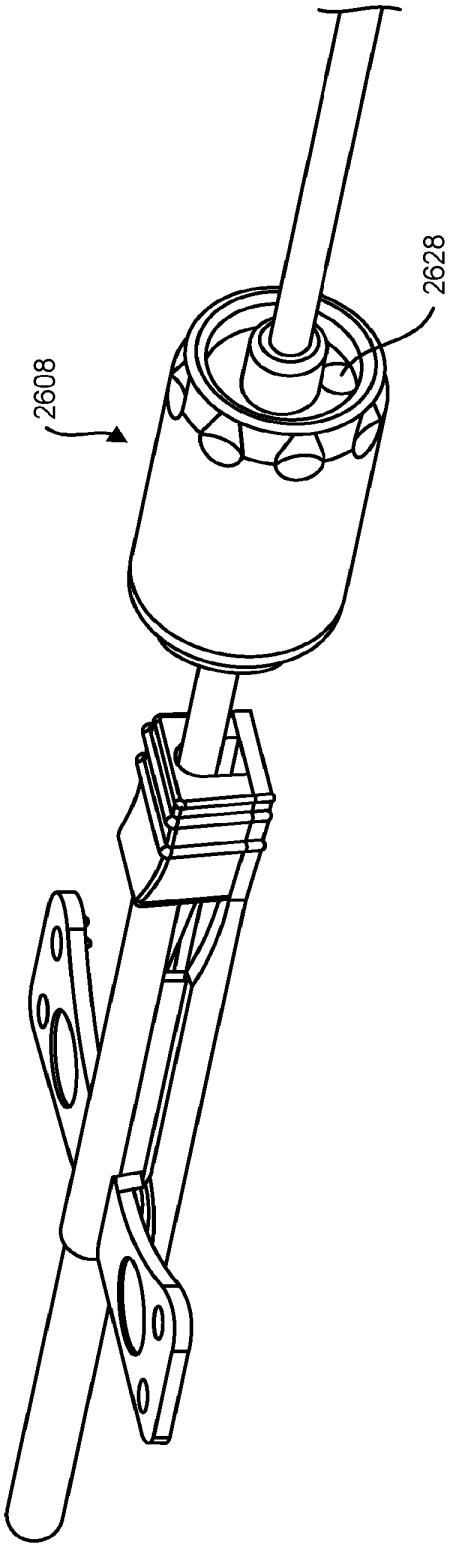


FIG. 26E

Replacement Sheet
59/69

Docket No. KURIN3PCT
PCT/US2017/068569

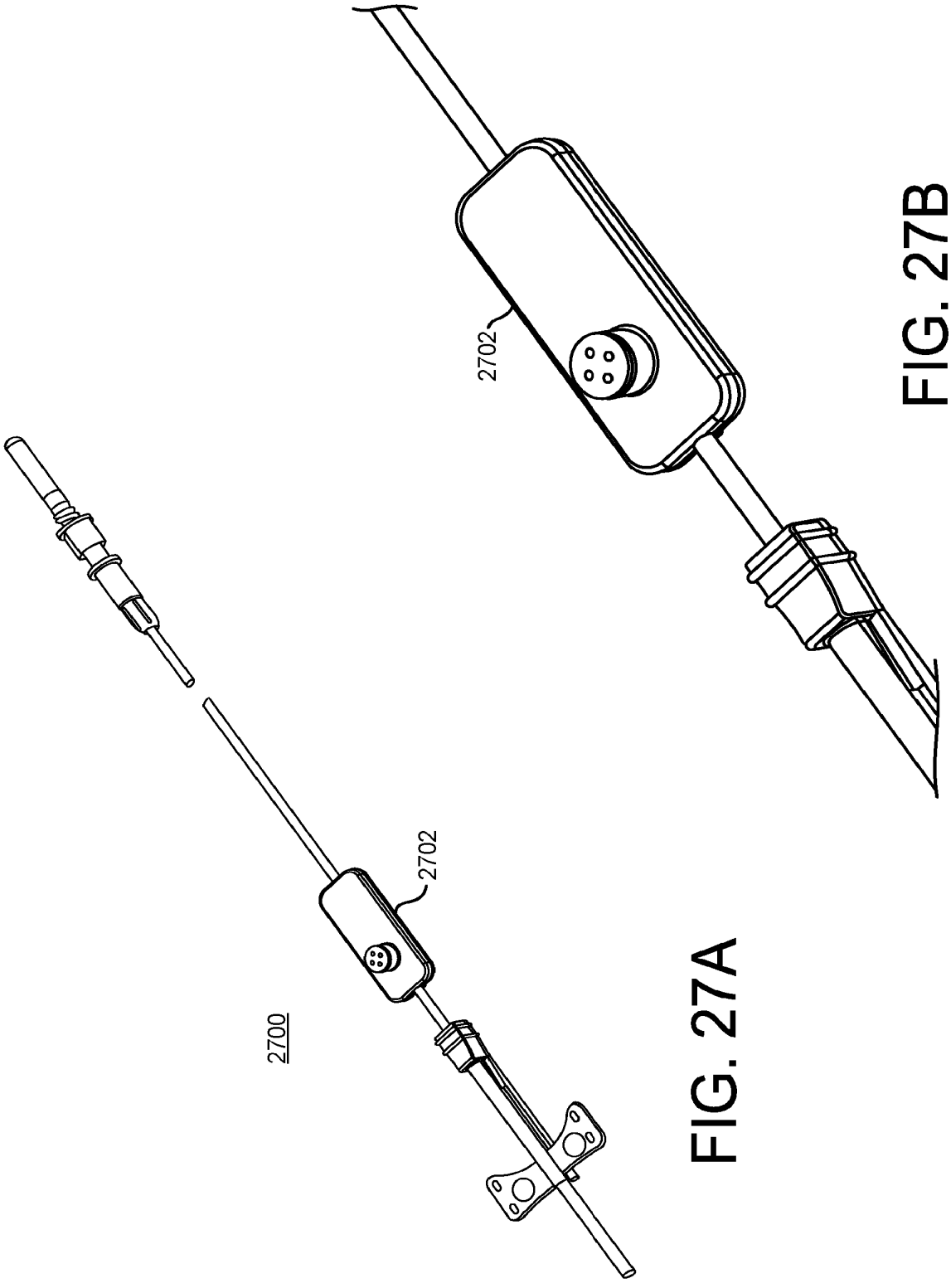


FIG. 27B

FIG. 27A

Replacement Sheet
60/69

Docket No. KURIN3PCT
PCT/US2017/068569

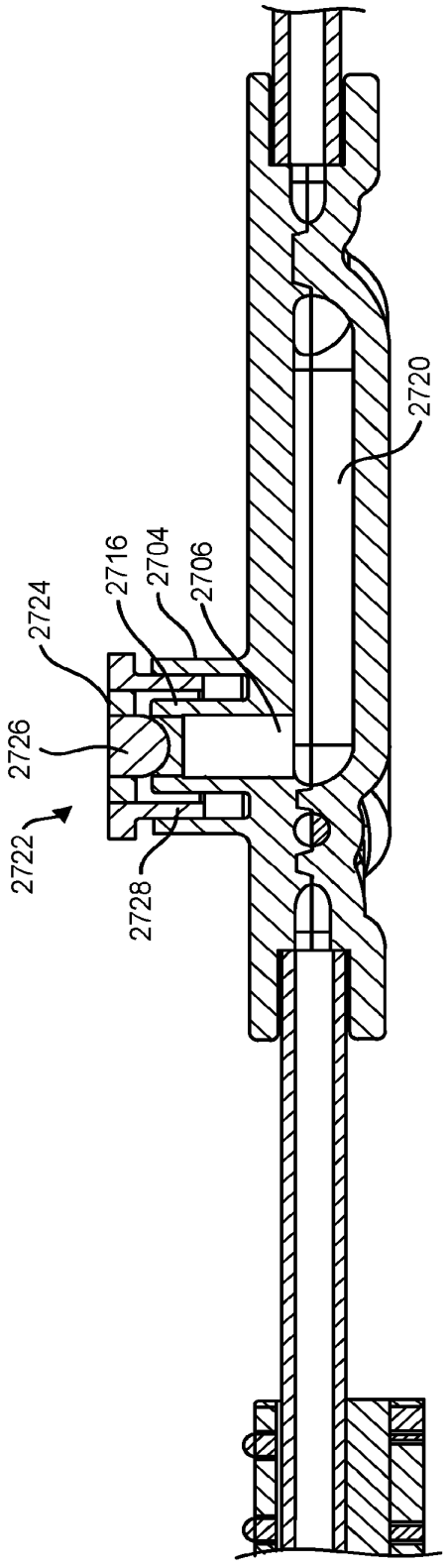


FIG. 27C

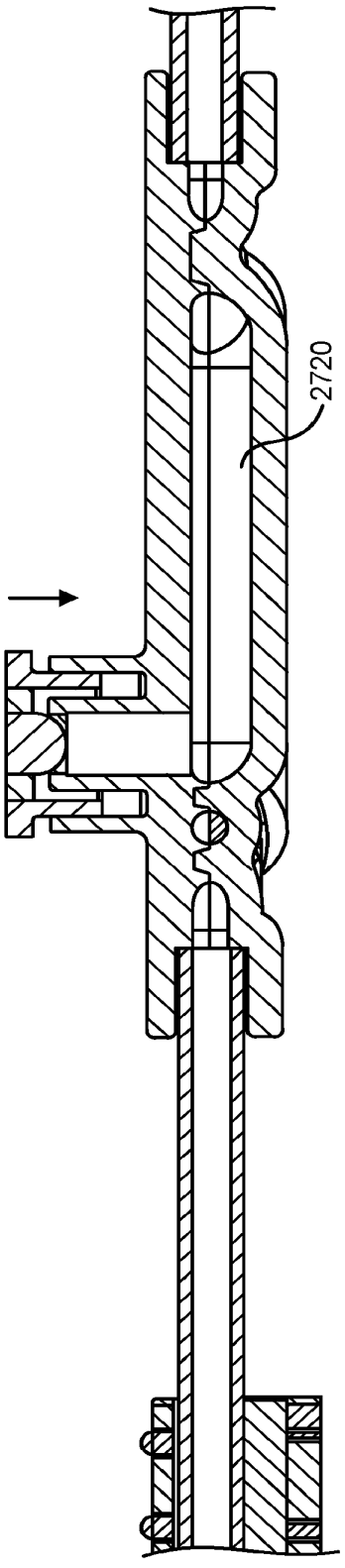


FIG. 27D

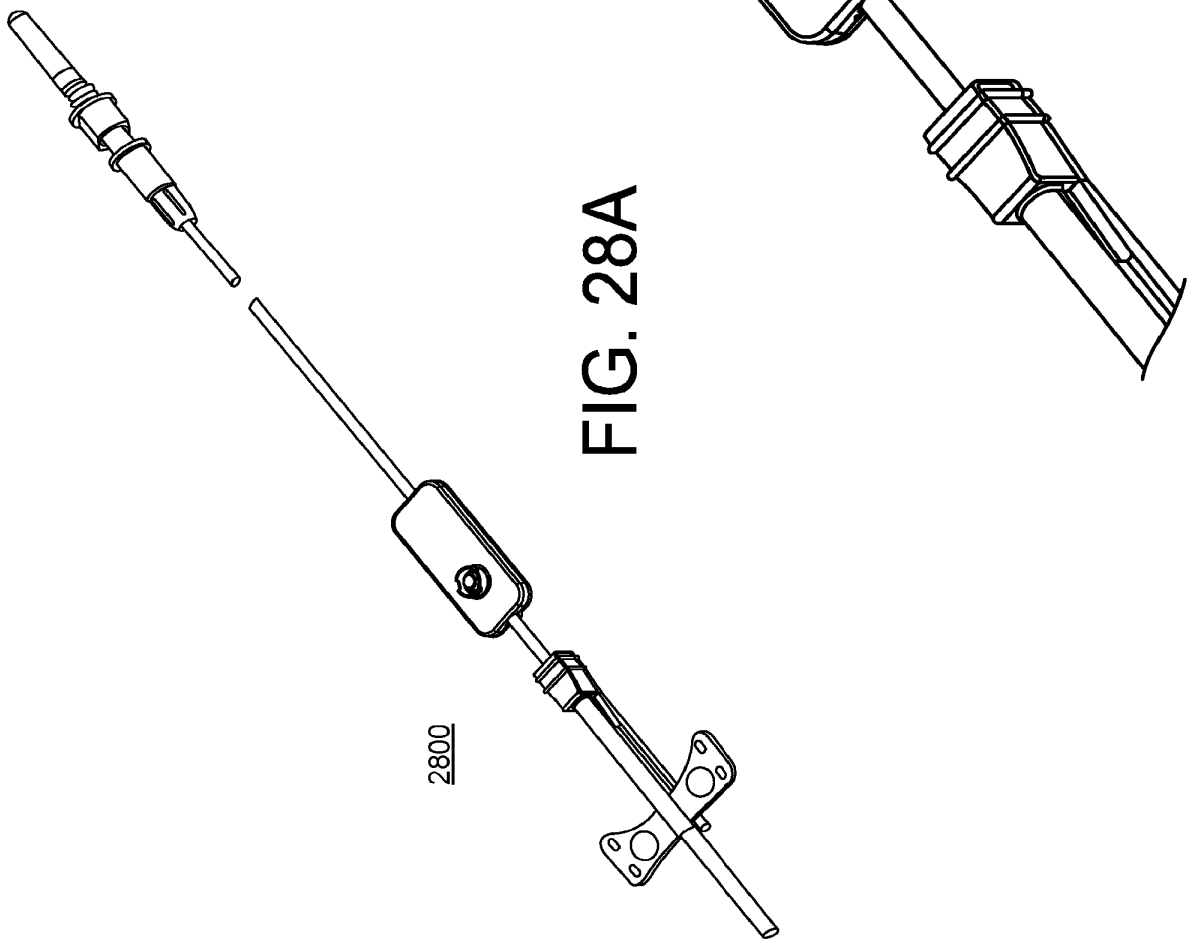


FIG. 28A

FIG. 28B

Replacement Sheet
62/69

Docket No. KURIN3PCT
PCT/US2017/068569

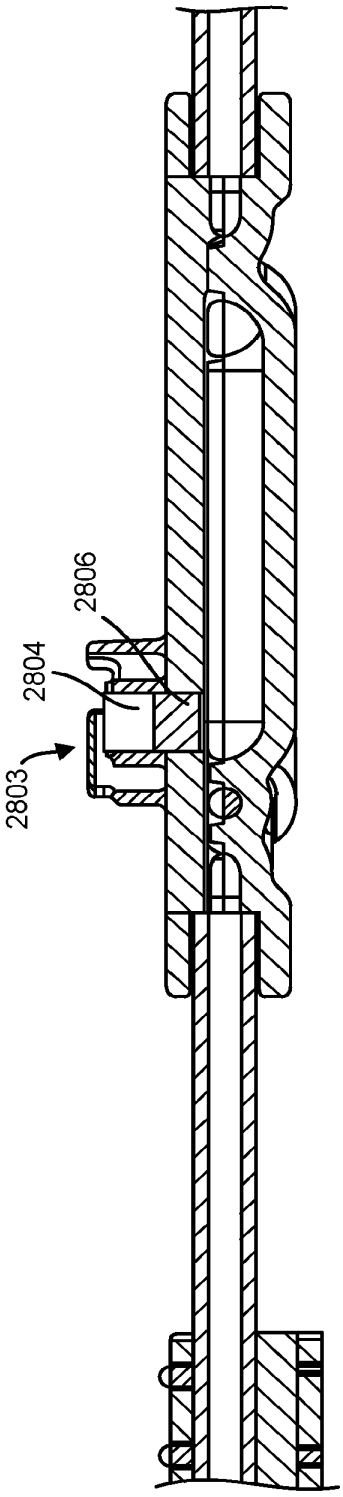


FIG. 28C

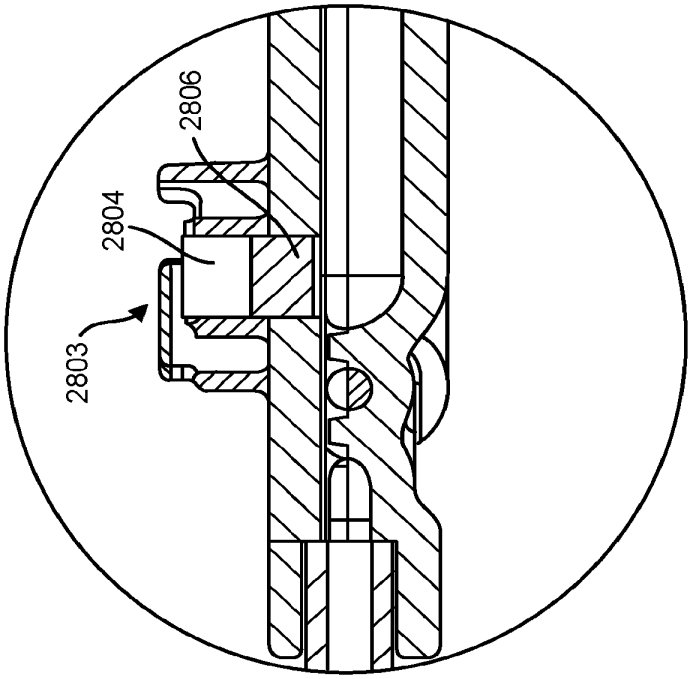


FIG. 28D

Replacement Sheet
63/69

Docket No. KURIN3PCT
PCT/US2017/068569

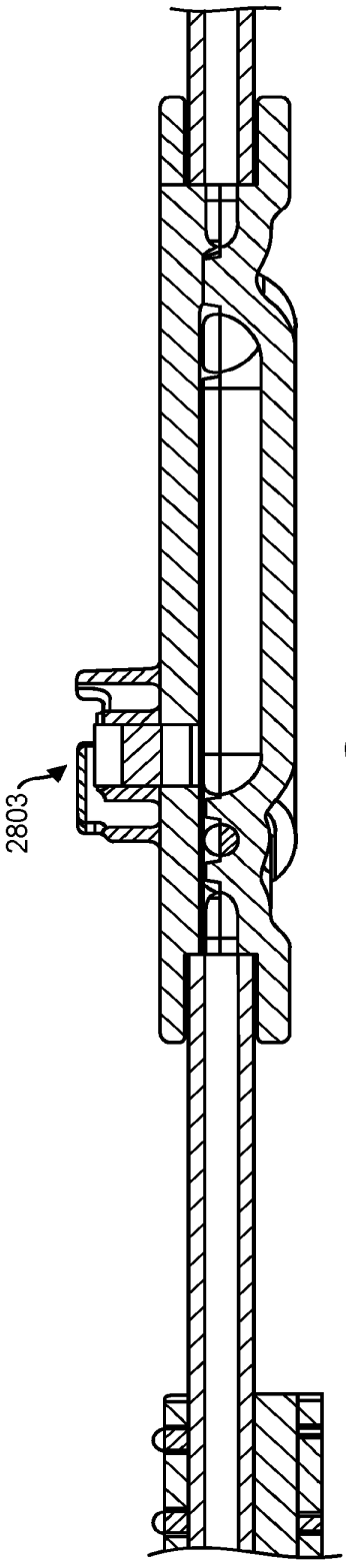


FIG. 28E

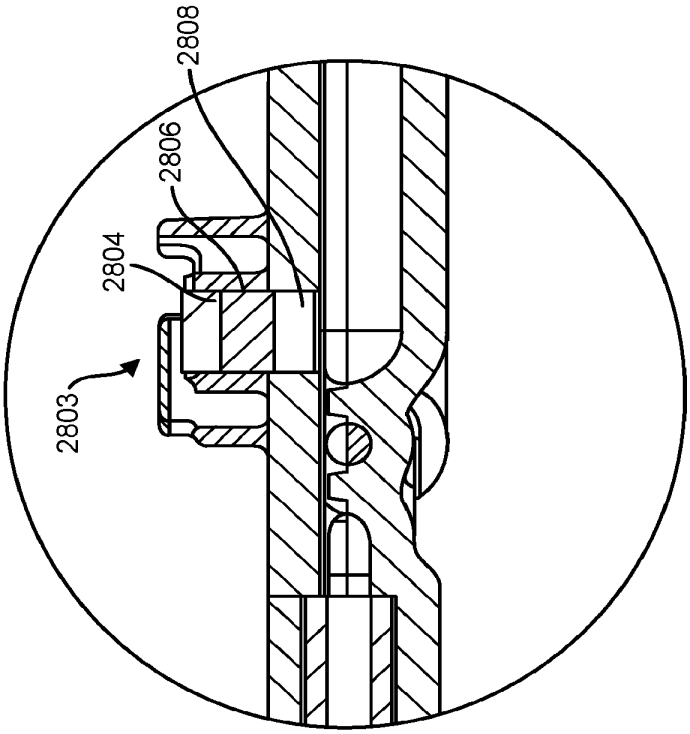


FIG. 28F

Replacement Sheet
64/69

Docket No. KURIN3PCT
PCT/US2017/068569

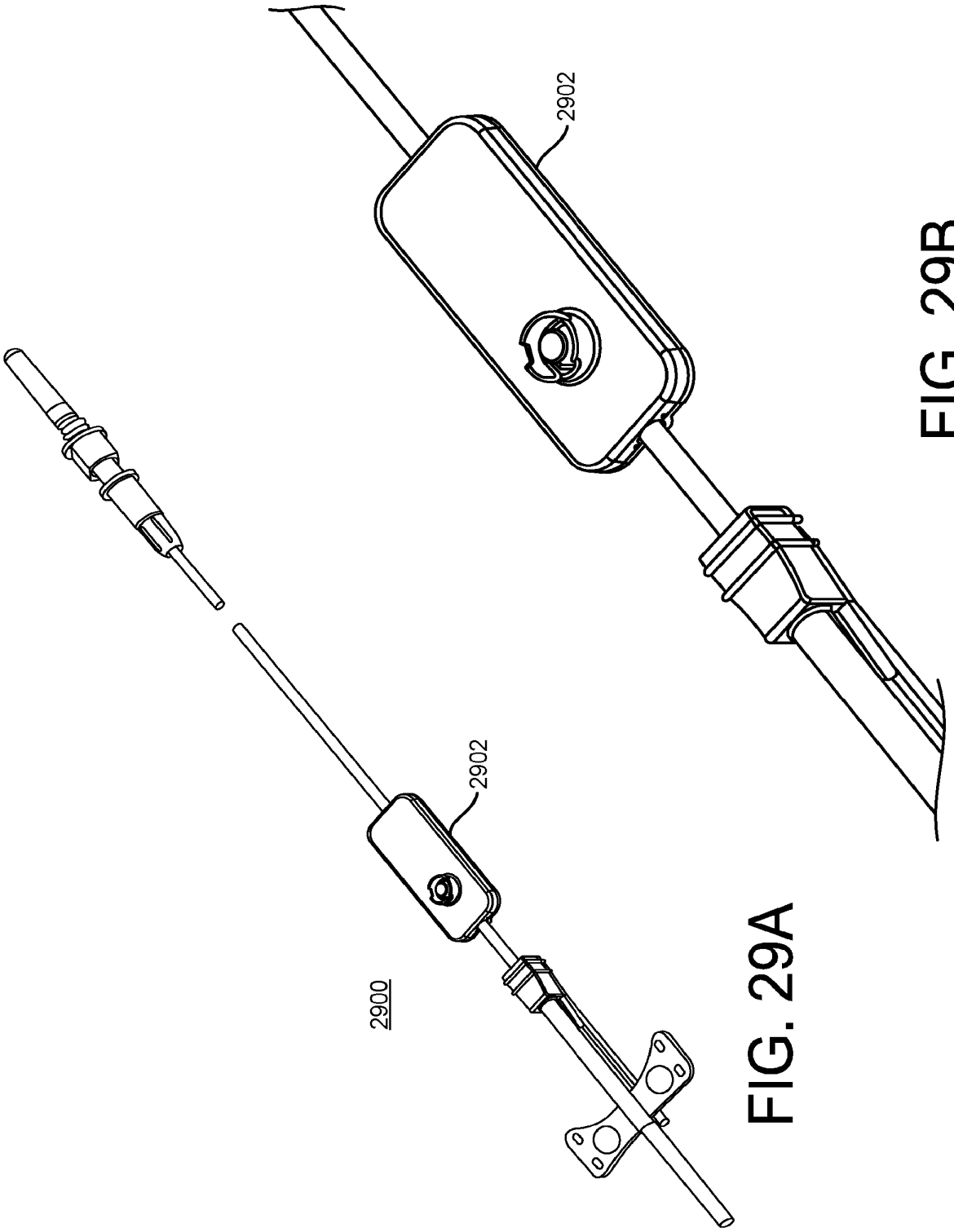


FIG. 29B

FIG. 29A

Replacement Sheet
65/69

Docket No. KURIN3PCT
PCT/US2017/068569

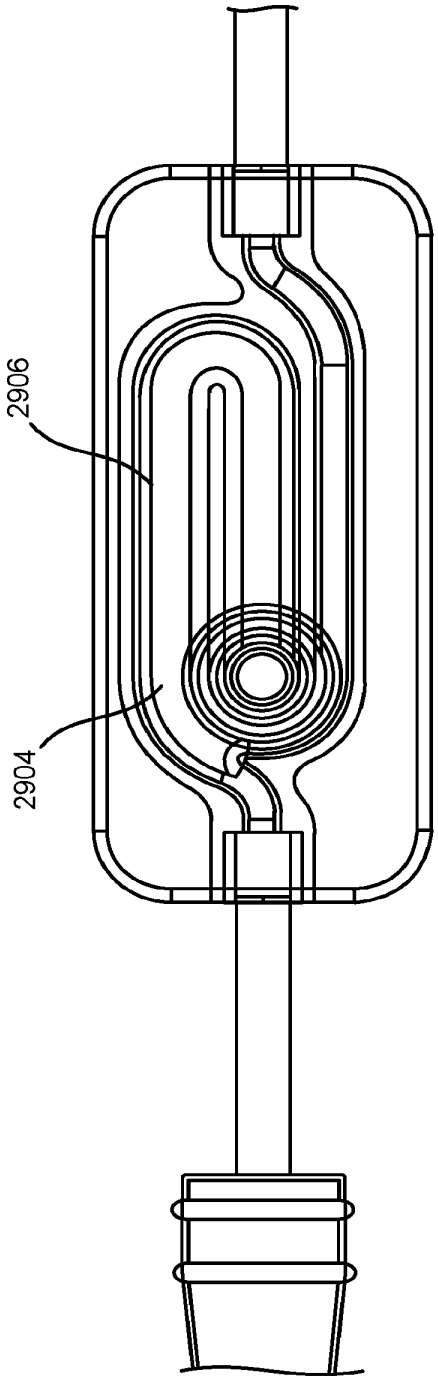


FIG. 29C

Replacement Sheet
66/69

Docket No. KURIN3PCT
PCT/US2017/068569

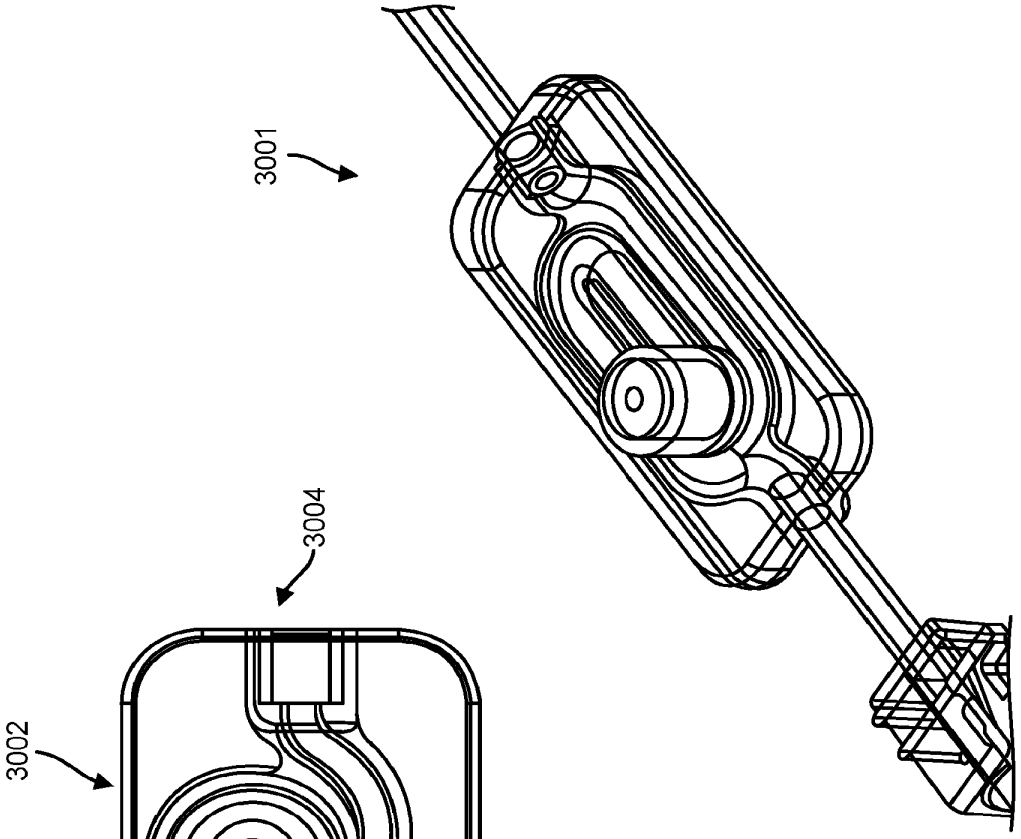


FIG. 30B

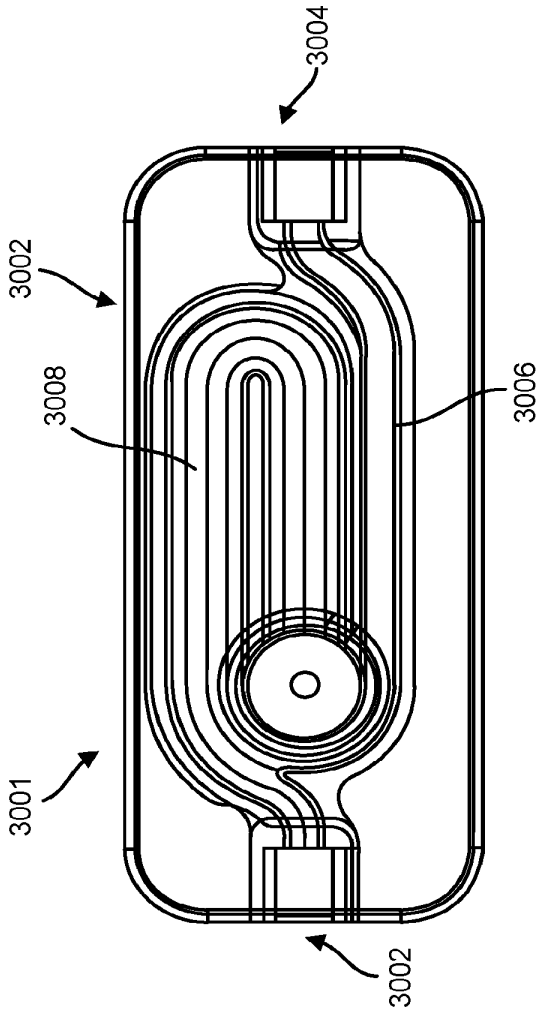


FIG. 30A

Replacement Sheet
67/69

Docket No. KURIN3PCT
PCT/US2017/068569

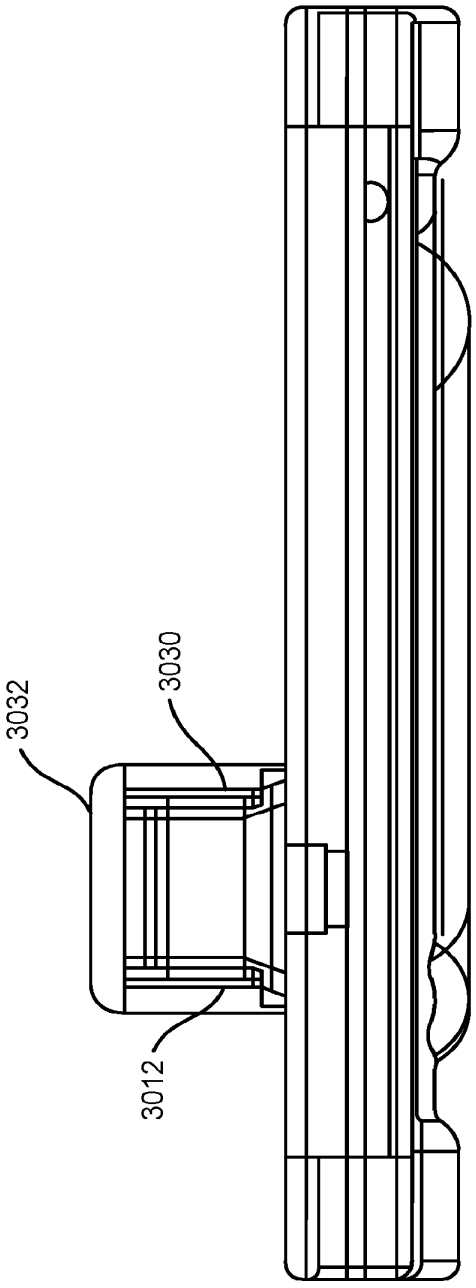


FIG. 30C

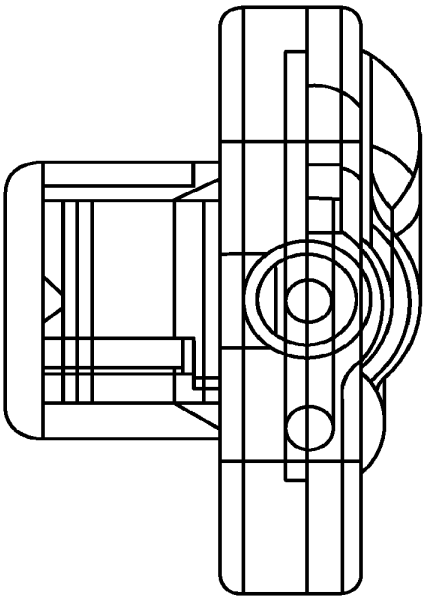


FIG. 30D

Replacement Sheet
68/69

Docket No. KURIN3PCT
PCT/US2017/068569

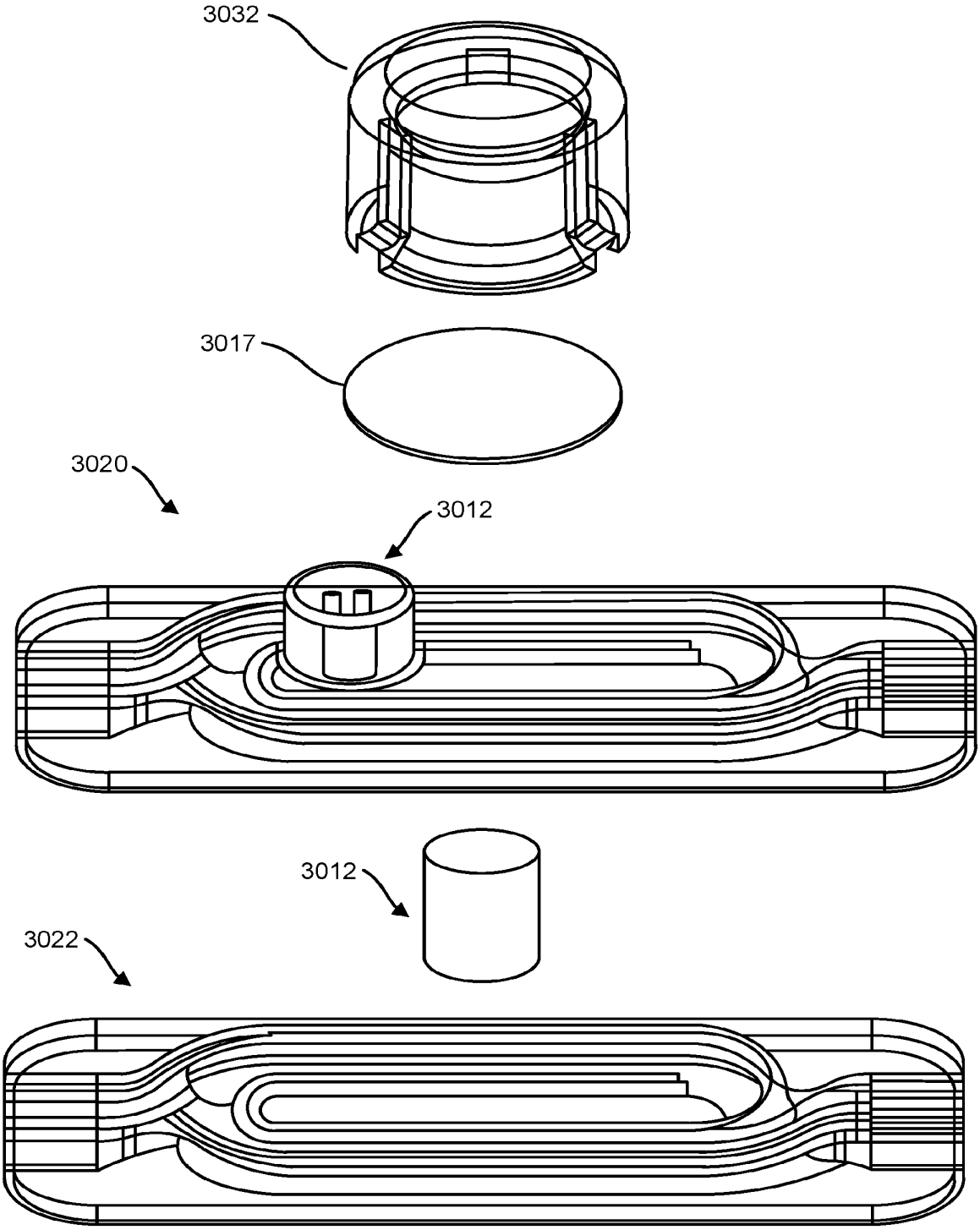


FIG. 30E

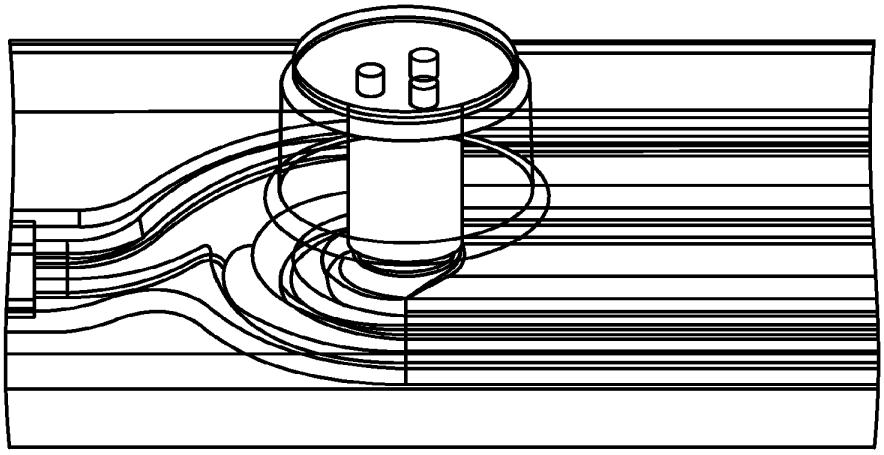


FIG. 30F

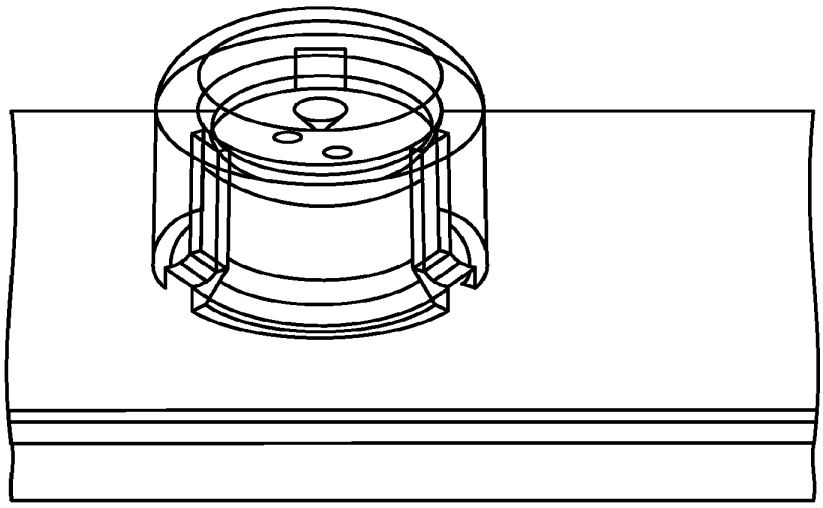


FIG. 30G

JCI The Journal of Clinical Investigation

Effect of Portal Venous Blood Flow Diversion on Portal Pressure

David S. Zimmon, Richard E. Kessler

J Clin Invest. 1980;65(6):1388-1397. https://doi.org/10.1172/JCI109803.

Research Article

To anticipate the hepatic vascular response to portacaval anastomosis, we studied portal pressure during diversion of portal blood through a temporary extracorporeal umbilical vein to saphenous vein shunt. The relationship of portal pressure to shunted flow was approximately linear. In five schistosomiasis patients (controls) portal diversion to 1,250 ml/min gave portal pressure-shunted flow curve slopes ranging from 0.13 to 0.57 cm water/100 ml per min (0.31±0.18, mean±SD). In 17 cirrhotic patients with portal hypertension a continuum of slopes was observed from within mean±2 SD of control (type A) to larger slopes (type B) indicating failure of portal pressure regulation. When portal flow was augmented by shunting from saphenous vein to portal vein, cirrhotic patients who had slopes less than mean±2 SD of controls during diversion (type A) exhibited a compliant system with small increases in portal pressure, whereas type B patients had significantly greater pressure increases. Selective investigations suggested that changes in portal pressure provoked compensatory changes in hepatic arterial blood flow that tended to maintain portal pressure at a set point. Type B patients demonstrated failure of this mechanism to varying degrees.

After end-to-side portacaval shunt, seven type A cirrhotic patients maintained residual intrahepatic venous pressure unchanged from prior portal pressure, whereas six type B patients had a significant decrease. Residual intrahepatic venous pressure was measured after portacaval shunt [...]

Find the latest version:

http://jci.me/109803-pdf

KUR-MAG-DE004215

Effect of Portal Venous Blood Flow Diversion on Portal Pressure

DAVID S. ZIMMON and RICHARD E. KESSLER, *Medical Service, Gastroenterology Section and the Surgical Service, New York Veterans Administration Medical Center, and the New York University School of Medicine, New York 10010*

ABSTRACT To anticipate the hepatic vascular response to portacaval anastomosis, we studied portal pressure during diversion of portal blood through a temporary extracorporeal umbilical vein to saphenous vein shunt. The relationship of portal pressure to shunted flow was approximately linear. In five schistosomiasis patients (controls) portal diversion to 1,250 ml/min gave portal pressure-shunted flow curve slopes ranging from 0.13 to 0.57 cm water/100 ml per min (0.31±0.18, mean±SD). In 17 cirrhotic patients with portal hypertension a continuum of slopes was observed from within mean±2 SD of control (type A) to larger slopes (type B) indicating failure of portal pressure regulation. When portal flow was augmented by shunting from saphenous vein to portal vein, cirrhotic patients who had slopes less than mean±2 SD of controls during diversion (type A) exhibited a compliant system with small increases in portal pressure, whereas type B patients had significantly greater pressure increases. Selective investigations suggested that changes in portal pressure provoked compensatory changes in hepatic arterial blood flow that tended to maintain portal pressure at a set point. Type B patients demonstrated failure of this mechanism to varying degrees.

After end-to-side portacaval shunt, seven type A cirrhotic patients maintained residual intrahepatic venous pressure unchanged from prior portal pressure, whereas six type B patients had a significant decrease. Residual intrahepatic venous pressure was measured after portacaval shunt in 40 cirrhotic patients who were followed for as long as 9 yr (median survival 4.0 yr). The 13 patients who developed chronic encephalopathy had significantly lower pressure (21.1±4.4 cm, mean±SD) and shorter survival (median 0.6 yr) than the other 27 patients (32.6±5.3 cm, 5.0 yr). The preoperative estimation of portal pressure-diverted portal flow curve slope anticipates the hepatic vascular response to portacaval anastomosis and identifies a group of patients in whom loss of portal blood flow results in a low residual intrahepatic venous pressure that is associated with early death and chronic encephalopathy.

INTRODUCTION

The increase in hepatic vascular resistance accompanying liver disease raises portal pressure and diminishes portal venous flow to the liver. Prograde portal flow may cease or even become retrograde as portal-systemic collaterals divert portal flow (1, 2). Increased hepatic arterial flow is presumed to compensate for reduced portal flow and account for normal values of total hepatic flow observed occasionally in cirrhotic patients with portal hypertension and portal systemic collateral circulation (3–6). An abrupt compensatory increase in hepatic arterial flow has been documented during acute portal flow diversion at the creation of a portacaval anastomosis (7–9). These facts imply homeostatic activity of the splanchnic vascular system to maintain portal pressure and/or hepatic blood flow when portal blood flow decreases (10–12). To evaluate the splanchnic hemodynamic response to portal blood flow diversion, we studied the response of portal pressure to acute incremental diversion of portal venous blood through a temporary extracorporeal umbilical vein to saphenous vein portal-systemic shunt (13).

METHODS

Subjects. In the schistosomiasis patients (Table I) described here, portal pressure and liver function tests including Bromsulfalein retention were normal. These patients were assumed to have normal splanchnic hemodynamics. They

This work was presented in part at the annual meetings of the American Association for the Study of Liver Disease, 4 November 1970, 1 November 1972, and 8 November 1978, Chicago Illinois; of the American Federation of Clinical Research, 12 May 1971 and 29 April 1973; and of the American College of Surgery, 14 November 1969. Abstracts were published in *Gastroenterology*. **60:** 169 (1970), **64:** 166 (1973), **75:** 996 (1978); *Clin. Res.* **19:** 406 (1971), **21:** 529 (1973); and *Surg. Forum.* **22:** 351–352 (1971), **23:** 334–336 (1972).

Address reprint requests to Dr. Zimmon.

Received for publication 11 April 1977 and in revised form 31 January 1980.

KUR-MAG-DE004216

Page 2552 of 5977

were studied after heparinization, but before the administration of tartar emetic (13). The initial 17 cirrhotic patients (Table I) with documented esophageal varices were studied after umbilical vein catheterization for measurement of portal pressure (14), for umbilical vein angiography before portal-systemic shunt surgery (15), or for the establishment of an extracorporeal portal-systemic shunt to reduce portal pressure and control life threatening variceal hemorrhage (16). Subsequent patients evaluated before and after or during portacaval shunt received internal therapeutic end-to-side portacaval anastomosis after endoscopically documented variceal hemorrhage (17). In our institution umbilical vein catheterization is the preferred method for evaluating the portal circulation because of its safety and reliability (18). Informed consent was obtained from all subjects. These studies were performed under a research protocol approved by the Research Committee of the Veterans Administration Medical Center, New York, and the New York University School of Medicine.

Except where specifically indicated all procedures were performed under local anesthesia. The umbilical vein was catheterized extraperitoneally (19) and connected to a saphenous catheter by a silicon rubber tube with an occluding roller pump (solid state varistaltic pump; Manostat Corp., New York) and cannulating square wave electromagnetic flow meter (model E-3000; Statham Instruments Inc., Oxnard, Calif.). The umbilical vein catheter has an integral molded wire to prevent collapse and a second 1-mm lumen within its wall to allow continuous recording of portal pressure (model 1956 SP-BJBI, U. S. Catheter and Instrument Co., Glen Falls, N. Y.). Pressures were recorded using Statham P37 perfused strain gauges that permitted a continuous infusion of heparin (0.1 mg/min). Electrical mean pressures were used to obviate respiratory fluctuation. Zero pressure level was taken as 12 cm above the couch.

The hepatic vein was catheterized from an antecubital vein (20, 21). The achievement of a wedged position was confirmed by the demonstration of an arterial pulse in the pressure recording, by the identity of wedged hepatic venous pressure and portal pressure, and by injection of radiopaque contrast at the completion of a study.

Flow through the extracorporeal shunt was monitored by the cannulating square wave flow meter calibrated for zero flow with the shunt occluded. In vitro calibration for flow rates to 3,000 ml/min with pumped whole blood and occluding roller pump yields an accuracy of ±5%. The pumping circuit was primed with 200 ml of normal saline.

Procedure. After catheter placement and shunt construction, portal pressure was recorded and portal to systemic shunting initiated at 100 ml/min. Stabilization of pump rate required 5–10 s. By that time, pressures were stable and were recorded. Shunting was increased in 100 ml/min increments. When maximum hepatofugal flow was achieved as evidenced by portal vein flutter, shunting was stopped and pressure recorded. Systemic to portal shunting was then begun in 100 ml/min increments until limited by saphenous vein flutter. The shunting portion of the procedure required 15–20 min.

The response of portal pressure to shunting at different

TABLE I

Effect of Portal Venous Flow Diversion or Augmentation on Portal Pressure

Case	Diagnosis etiology	Documentation	Ascites (-4+)	Direction portal flow	Basal PP	Hepatofugal pumping			Hepatopetal pumping		
						Max flow	Pressure change	Pressure-flow slope	Max flow	Pressure change	Pressure-flow slope
					cm	*ml/min*	*cm*	*cm/100 ml*	*ml/min*	*cm*	*cm/100 ml*
1	C,A	Biopsy	0	Prograde	37	1,100	0	0.00	500	+2	+0.40
2	S	—	—	Prograde	15	750	−1	−0.13			
3	S	—	—	Prograde	11	1,200	−2	−0.17			
4	C,A	Biopsy	+1	Prograde	35	1,450	−3	−0.20			
5	S	—	—	Prograde	15	1,250	−3.5	−0.28			
6	C	Biopsy	3+	Prograde	27	1,600	−6	−0.38	1,000	+3	+0.30
7	S	—	—	Prograde	14	1,100	−5	−0.43			
8	C,A	Biopsy	0	Retrograde	37	900	−4	−0.44			
9	C,A	Biopsy	0	Prograde	36	1,000	−5	−0.50	700	+1	+0.14
10	S	—	—	Prograde	8	700	−4	−0.57	1,100	0	0.0
11	C,A	Biopsy	2+	Retrograde	39	1,700	−10	−0.59	1,200	+1	+0.08
12	C,A	W,biopsy	0	Prograde	35	2,500	−15	−0.60	900	+2.5	+0.27
13	C,HEM	Biopsy	+1	Prograde	29	1,500	−9	−0.60	600	+3	+0.50
14	C,A	Biopsy	0	Prograde	39	1,500	−13	−0.87	1,000	+16	+1.6
15	C,A	W,biopsy	2+	Prograde	42	600	−6	−1.00	1,400	+6	+0.43
16	C,A	Biopsy	1+	Prograde	26	1,000	−10	−1.00	750	+9	+1.20
17	C,CR	Biopsy	1+	Prograde	29	850	−18	−2.11			
18	C,A	Autopsy	0	Prograde	37	900	−28	−3.10	700	+11	+1.57
19	C,A	Biopsy	2+	Prograde	39	900	−31	−3.44	700	+9	+1.28
20	C,A	Biopsy	4+	Prograde	35	800	−31	−3.87			
21	C,A,HEP	Biopsy	0	Prograde	55	1,100	−48	−4.36			
22	C,A	Biopsy	0	Prograde	35	500	−30	−6.00	500	+18	+3.6

Abbreviations used in this table: C, cirrhosis; S, schistosomiasis; A, alcoholism; HEM, hemachromatosis; HEP, hepatoma; CR, cryptogenic; W, wedged hepatic venous pressure; PP, portal pressure; max, maximum.

KUR-MAG-DE004217

vascular volumes was studied after phlebotomy accomplished by draining the extracorporeal circuit into a sterile infusion bottle containing 20 mg of heparin. 1 liter of blood was withdrawn in 3 min. After studying the response of portal pressure to shunting the blood was reinfused. Then, for volume expansion 5% dextran or blood was infused. Final volume was dictated by the patient's clinical status (22). Since the elapsed time for phlebotomy and volume expansion was <15 min, vascular volume shifts were considered to be negligible. Therefore, changes in blood volume were calculated from the measured quantity withdrawn or infused.

At the completion of a study the direction of portal venous flow (prograde or retrograde) was determined by observing the course of a gentle hand injection of 50% sodium diazotrate (Hypaque, Winthrop Laboratories, Sterling Drug Co., New York) through the primary lumen of the umbilical vein catheter (3). Radiopaque contrast media were not administered before pressure or flow measurements because of their effect on systemic and splanchnic hemodynamics (23). Finally, a pressure injection with serial x rays was used to visualize the portal vasculature (15).

Definition of residual intrahepatic venous pressure. Wedged hepatic venous pressure and portal pressure measured by umbilical vein catheterization are identical in patients with cirrhosis when the portal circulation is intact (24). Simultaneous measurement of wedged hepatic venous pressure and umbilical portal pressure in two cirrhotic patients during shunting of portal flow agreed within ±1 cm water (Fig. 1). After disconnection of the extrahepatic portal venous system from the liver by end-to-side portacaval shunt, residual intrahepatic venous pressure was measured by wedged hepatic venous catheterization or by umbilical vein catheterization of the intrahepatic portal vein. The extrahepatic portal venous system drains into the vena cava.

Construction of portal pressure-shunted portal flow curves. Curves constructed for controls with *Schistosoma mansoni* infections and cirrhotic patients with portal pressure-shunted portal flow curve slopes < -0.67 cm water/100 ml per min diverted flow were linear (Figs. 1 and 2) and allow a simple arithmetic expression of slope as change in pressure/100 ml per min shunted flow. Cirrhotic patients with steep slopes have a smaller range of flow and curves that are increasingly convex (Figs. 2 and 3). For the purpose of this paper, the arithmetic portal pressure-shunted portal flow curve slope is derived from the sum change in pressure divided by maximum flow before vein flutter was detected by palpation of the shunt or pumping was stopped because of increased portal pressure. As indicated, certain patients were studied at laparotomy under anesthesia or during rescuscitation from hemorrhage. These circumstances provide unique opportunities to gain physiologic insights in man but undoubtedly influence to a greater or lesser extent the data obtained. Therefore, we confined data in Table I describing the control (schistosomiasis) patients and values in cirrhotic patients with portal hypertension for portal pressure-shunted portal flow curve slope to subjects studied without anesthesia or laparotomy when hemodynamically stable.

Statistical significance was determined with the Wilcoxon two sample ranked test, unpaired t test, and log rank test (25, 26).

RESULTS

Schistosomiasis (control) subjects

During portal to systemic shunting averaging 1,000 ml/min (range, 700–1,350) in five schistosomiasis pa-

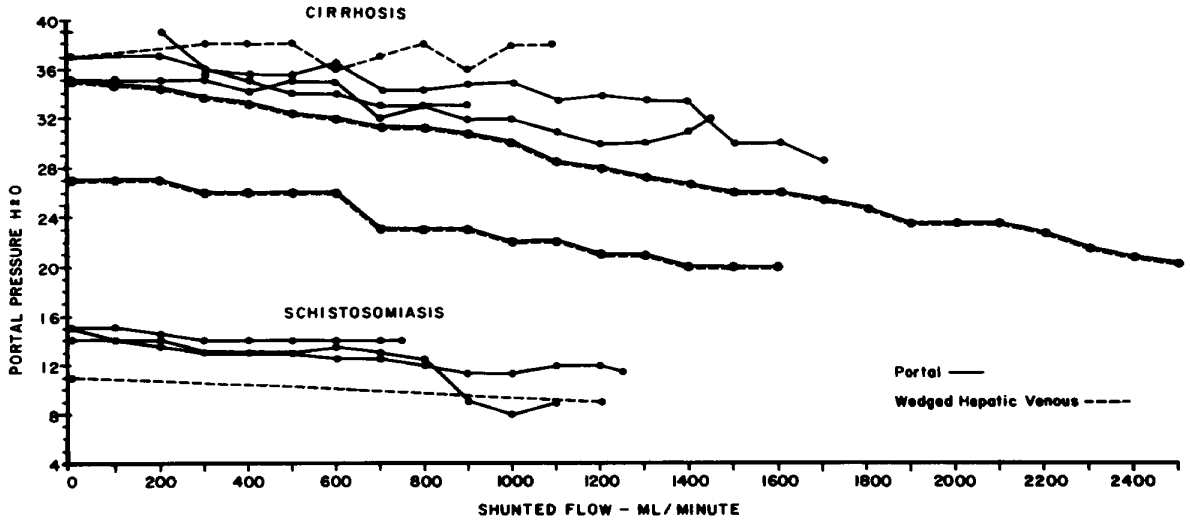


FIGURE 1 Response of portal pressure to portal venous blood flow diversion in type A cirrhotic patients and control subjects. Portal pressure (centimeters water) is plotted against volume of shunted portal venous flow (milliliters per minute) diverted through an umbilicosaphenous shunt. Six representative cirrhotic patients are shown in order of decreasing basal portal pressure (case Nos. 11, 1, 8, 4, 12, and 6, Table I). Four representative controls (2, 5, 7, and 3, Table I) are shown in order of decreasing basal portal pressure. The solid line indicates portal pressure measured through an umbilical vein catheter in the left portal vein. The interrupted line indicates portal pressure measured by wedged hepatic venous catheterization. The combined solid and interrupted lines in two cirrhotic patients (11, 1, Table I) indicate simultaneous measurement of portal and wedged hepatic venous pressures.

KUR-MAG-DE004218

Page 2554 of 5977

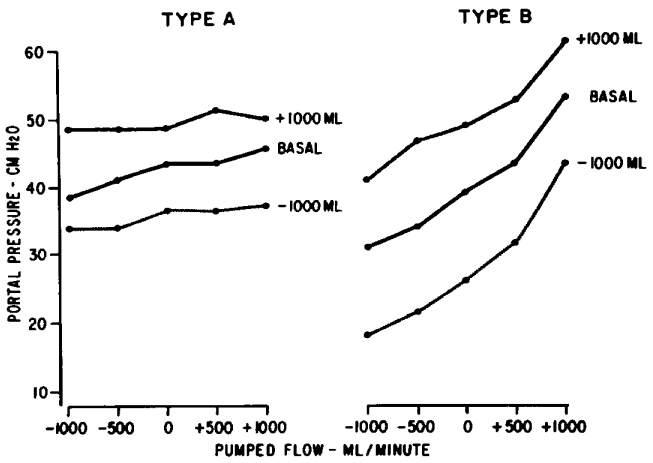


FIGURE 2 Effect of changes in blood volume on portal pressure and portal pressure-shunted flow curve slope. In a single type A patient (left) basal portal pressure of 43 cm was reduced to 36 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000 ml-volume load in addition to replacement of the 1,000-ml phlebotomy, whereas portal pressure-shunted flow slope varied from 0.35 to 0.15 to 0.10 cm/100 ml per min shunted flow, respectively. In a single type B patient, a basal portal pressure of 39 cm was reduced to 26 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000-ml volume load after replacement of the phlebotomy, whereas portal pressure-shunted flow curve slope varied from 1.15 to 1.25 to 1.05, respectively.

tients portal pressure decreased an average of 3.1 cm water (range, 1–4). Portal pressure-shunted portal flow slope averaged -0.31 ± 0.18 (mean±SD) cm water/100 ml per min diverted flow (range -0.13 to -0.57) (Table I).

Cirrhotic patients

In cirrhotic patients (n = 17) with portal hypertension, the response to portal diversion was varied and the portal pressure-shunted portal flow slope ranged from -0.0 to -6.0. In patient 1 (Table I) portal pressure was unchanged by portal diversion of 1,000 ml/min, whereas in patient 22 (Table I) portal pressure fell to central venous levels with diversion of only 500 ml/min (Table I). A histogram (Fig. 4, upper) of portal pressure-shunted portal flow slope during diversion in cirrhotic patients with portal hypertension shows a continuum from slopes similar to *S. mansoni* patients with normal portal pressure (Fig. 4, hatched bars) to extremely high values. A relationship between basal portal pressure and portal pressure-shunted portal flow slope is not apparent (Table I). The lack of correlation between portal pressure and portal pressure-shunted portal flow slope arises, in part, from the influence of blood volume on portal pressure (Fig. 2). Increasing or decreasing blood volume produces a corresponding shift in portal pressure (22) with little change in portal pressure-shunted portal flow slope.

Definition of type A and B cirrhotic patients

Type A cirrhotic patients (Figs. 1 and 2) are defined as those with portal pressure-shunted portal flow slopes < -0.67 cm/100 ml per min (control mean±2 SD). Type B cirrhotic patients have portal pressure-shunted portal flow slopes in excess of -0.67 cm/100 ml per min diverted flow (Table I, Figs. 2 and 3). In the initial 17 patients studied (Table I) the mean basal portal pressure (34.4±4.2 cm of water, mean±SD) of eight cirrhotic patients with portal pressure-shunted flow slopes for portal flow diversion within the mean±2 SD of the five control (schistosomiasis) patients was not significantly different from the mean basal portal pressure (37.4±8.3 cm) of the nine cirrhotic patients with greater slopes. Similarly, in a group of 13 patients clinically considered candidates for portacaval anastomosis (Fig. 5), the basal portal pressures of seven type A patients were not significantly different from the six type B patients. The 23 cirrhotic patients with endoscopically documented bleeding esophageal varices classified as type A or type B when hemodynamically stable under local anesthesia had basal portal pressure ranging from 55 to 26 cm. The 55-cm value (Table I, No. 21) occurred in a patient with hepatoma. Although the three highest values (55, 45, and 42 cm) and the two lowest values (26 and 28 cm) were found in type B patients, the pressures of type A patients were not significantly different (Wilcoxon rank test) from type B.

Mechanism for maintenance of portal pressure during portal venous flow diversion

Hepatic arterial response to extracroporeal portal diversion. Hepatic arterial flow was measured at laparotomy for portacaval anastomosis by noncannulating square wave electromagnetic flow meter in two type A cirrhotic patients before and during diversion of 1 liter/min. Hepatic arterial flow increased 40 and 46%.

Spontaneous total retrograde portal flow in type A portal hypertension. Two (Nos. 8 and 11) of 17 cirrhotic patients described had total retrograde portal venous flow (Table I) (3). Both had type A portal hypertension with portal pressure-shunted portal flow slopes of 0.44 and 0.59 cm/100 ml per min. The presence of total retrograde portal flow implies sufficient portal-systemic collateral vessels for egress from the splanchnic chamber of all splenic and mesenteric inflow and a portion of hepatic arterial flow. The most likely source for additional splanchnic inflow to maintain portal pressure during portal diversion in this situation is the hepatic artery.

Portal pressure response to portal flow augmentation by systemic to portal shunting. In portal hypertension an added load should increase portal pressure, since mechanisms for reducing splanchnic inflow or in-

KUR-MAG-DE004219

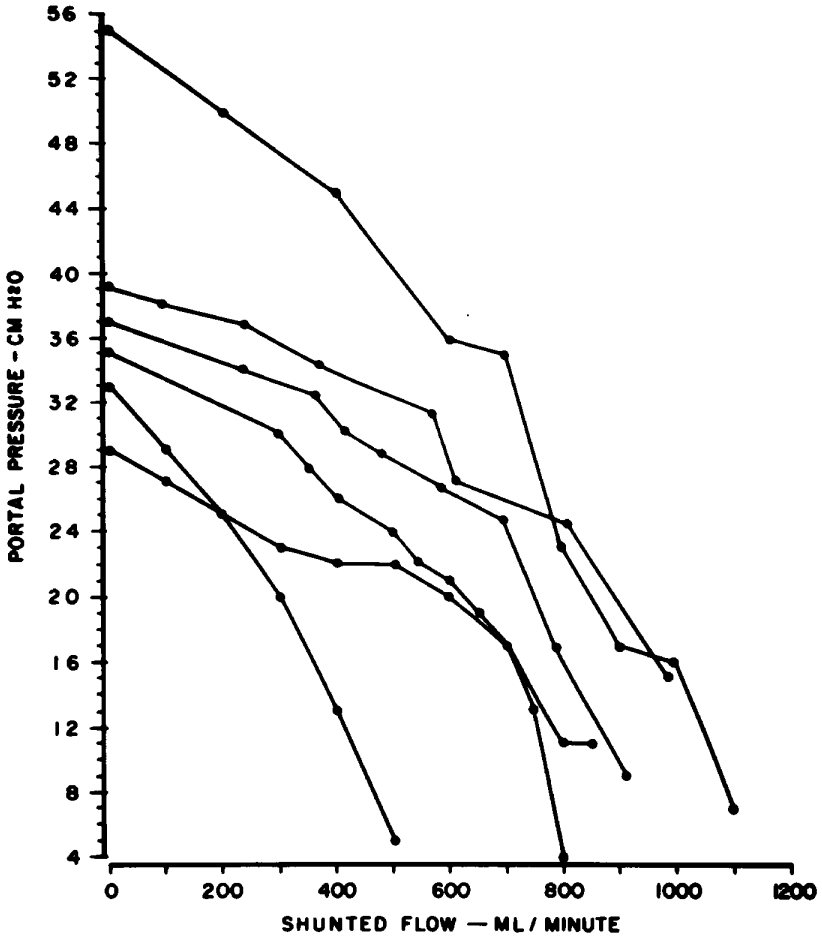


FIGURE 3 Response of portal pressure to portal diversion in type B cirrhotic patients. Portal pressure (centimeters water) is plotted against volume of portal venous flow diverted through the umbilicosaphenous shunt. Six representative type B cases in order of decreasing basal portal pressure (case Nos. 21, 19, 18, 20, 22, and 17, Table I) are shown.

creasing outflow already would be activated by existing portal hypertension. Type A patients accommodate their portal pressure as well to portal flow augmentation as diversion (Table I, Figs. 2 and 4). Portal pressure-shunted portal flow curve slopes are more varied for augmentation but are similar to slopes (Table I) for diversion in the 12 patients where both maneuvers were performed (Fig. 4).

Type A cirrhotic subjects who during portal diversion had portal pressure-shunted portal flow slopes less than the mean±2 SD of control exhibit a compliant system in that relatively small increases in portal pressure were observed (range, +0.08 to +0.50, mean±SD, 0.3±1.6 cm/100 ml per min, $n = 6$). Cirrhotic patients with steep type B slopes during portal diversion demonstrated steep slopes during augmentation (range, +0.43 to +3.60, mean±SD, 1.6±1.1 cm/100 ml per min, $n = 6$) that were increased ($P < 0.01$) when compared to the compliant group. The basal portal pressures of the eight cirrhotic patients with type A slopes (34.4±4.2 cm water, mean±SD) were not significantly different from the nine cirrhotic patients with type B slopes (37.4 ±8.3 cm water).

Induced retrograde portal flow during portal venous flow diversion. If increasing hepatic arterial flow, rather than changing portal-systemic collateral, splenic, or mesenteric inflow, accounts for the maintenance of portal pressure during portal diversion, sampling of indocyanine green from the umbilicosaphenous shunt during diversion should demonstrate extraction of indocyanine green from portal blood when increased hepatic arterial flow reverses through hepatic sinusoids to enter the extracorporeal circuit. At laparotomy for portacaval shunt with 750 ml/min portal diversion, prograde portal flow was evidenced by absence of extraction. Retrograde flow of hepatic arterial blood into the

KUR-MAG-DE004220

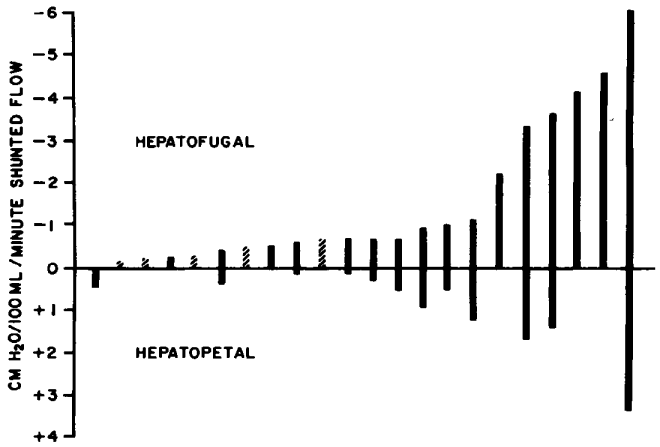


FIGURE 4 Histogram of portal pressure-shunted portal venous flow slope. Patients 1 (left) through 22 (right) are presented in order of increasing slope (Table I). The upper bars refer to the slope for portal diversion (hepatofugal shunting). The lower bars refer to the slope for portal blood flow augmentation (hepatopetal shunting) performed in 12 patients. Hatched bars indicate schistosomiasis patients (controls).

portal vein with extraction occurred at diversion rates in excess of 1,000 ml/min. This type A patient (Table IIA) accommodated to 1,000 ml/min portal diversion or augmentation (portal pressure-shunted portal flow slope −0.3, +0.0) with little change in portal pressure.

Portal pressure and intrahepatic venous pressure response to occlusion of hepatic artery or portal vein. Intraoperative occlusion of hepatic artery or portal vein before and during diversion of blood from the hepatic side of the occluded portal vein was studied in two patients to compare hepatic artery and portal venous (splenic and mesenteric) capacity to sustain intrahepatic venous pressure (Table II). Intrahepatic venous pressure was measured and blood was shunted through the umbilical catheter on the hepatic side of the occluded portal vein.

The type A patient maintained intrahepatic venous pressure with flow from either hepatic artery or portal vein (Table II experiments 5A and 6A). Portal venous flow alone maintained portal venous pressure when the hepatic artery was occluded (experiment 5A) suggesting adequate portal flow to support pressure. When portal flow is stopped, hepatic artery flow is adequate to prevent a reduction in intrahepatic venous pressure (experiment 6A). The response to 1,000 ml/min portal to systemic shunting between the site of portal vein occlusion and the liver (experiment 7A) shows the hepatic artery to have a greater capacity to support intrahepatic venous pressure than mesenteric and splenic vessels, since pressure falls less when the portal vein is occluded and the hepatic artery supplies the liver (experiment 8A) than when the hepatic artery is occluded and the portal vein supplies liver (experiment 7A). This suggests that increased hepatic artery flow is the most important mechanism in maintaining portal pressure during portal diversion in this type A patient.

In a type B patient (Table II) occlusion of the portal vein precipitated an 11-cm decrease in intrahepatic venous pressure (experiment 6B) indicating the failure of hepatic artery flow to maintain pressure. This inadequacy was exaggerated by simultaneous portal vein occlusion and portal diversion (Experiment 8B). This type B patient relies on portal flow to sustain intrahepatic venous pressure. The failure of hepatic artery occlusion to reduce portal pressure (experiment 5B) indicates a small hepatic artery contribution to maintenance of portal pressure in this patient. The steep portal pressure-shunted portal flow slope when the portal vein is patent (experiment 2B) demonstrates the failure of portal-systemic collateral flow to compensate for increasing or decreasing portal flow.

Maintenance of residual intrahepatic venous pressure after end-to-side portacaval anastomosis. If the portal pressure-shunted portal flow slope estimates he-

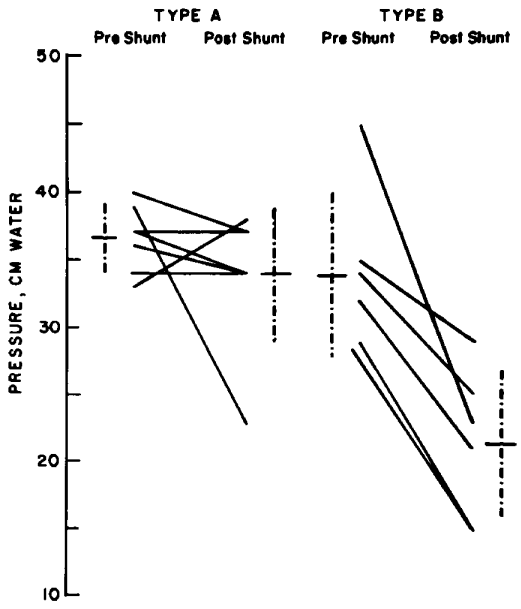


FIGURE 5 Effect of total portal venous flow diversion by end-to-side portacaval anastomosis on intrahepatic venous pressure in type A and type B patients. The horizontal solid bar indicates the mean. The vertical interrupted line indicates SD. Preoperative portal pressures for type A and type B patients were not significantly different. After portacaval shunt mean intrahepatic venous pressure in type B patients (21.3±5.6, $n = 6$) is significantly decreased ($P < 0.01$) when compared to preshunt portal pressure or postshunt intrahepatic venous pressure in type A patients (33.9±5.0, $n = 7$). Four type A and four type B patients shown here had portal pressure-shunted portal flow slope determined under anesthesia at laparotomy for portacaval anastomosis and are excluded from Table I.

KUR-MAG-DE004221

Page 2557 of 5977

TABLE II
Response of Intrahepatic Venous Pressure to Occlusion of Hepatic Artery and Portal Vein

Experiment	Hemodynamic type	A	B
1	Basal portal pressure	46	29
2	Portal pressure during diversion, 1,000 ml/min	43	16
3	Portal pressure during augmentation, 1,000 ml/min	46	37
4	Pressure-flow slope (cm water/100 ml per min)		
	diversion	−0.3	−1.3
	augmentation	+0.0	+0.8
5	Portal pressure with hepatic artery occluded	44	31
6	Intrahepatic pressure with portal vein occluded	44	18
7	Portal pressure with hepatic artery occluded plus diversion, 1,000 ml/min	35	22
8	Intrahepatic pressure portal vein occluded plus diversion, 1,000 ml/min	39	3

patic vascular capacity to sustain portal pressure during portal venous diversion, the residual intrahepatic venous pressure after end-to-side portacaval anastomosis when the hepatic artery alone supplies the liver should correlate with the preoperative portal pressure and postoperative intrahepatic venous pressure. In 13 patients undergoing end-to-side portacaval anastomosis (Fig. 5) after determination of portal pressure-shunted portal flow slope preoperative portal pressure in seven type A patients (36.6±2.5 cm, mean±SD) was not significantly different from six type B patients (33.8±6.1 cm). After end-to-side portacaval anastomosis in type A patients intrahepatic venous pressure was not significantly changed (33.9±5.0) indicating hepatic vascular compensation for loss of portal venous flow. Type B patients suffered a decrease in intrahepatic venous pressure (21.3±5.6) that was significant when compared to their preoperative portal pressure ($t = 3.38$, $P < 0.01$) or to the postoperative intrahepatic venous pressure of the type A patients ($t = 3.90$, $P < 0.01$).

Residual intrahepatic venous pressure after end-to-side portacaval shunt and prognosis. Our initial clinical observations suggested that type B patients in whom residual intrahepatic venous pressure fell after portacaval anastomosis (Fig. 5) frequently died shortly after surgery or suffered from chronic encephalopathy. Therefore, residual intrahepatic venous pressure was measured in 40 patients with cirrhosis associated with ethanol abuse shortly after interval end-to-side portacaval anastomosis when they were hemodynamically stable. The patients were followed clinically for as long as 9 yr (median, 4.0 yr). 13 patients developed chronic hepatic encephalopathy defined as diminished mental function that was improved by and required continued dietary protein restriction and antibiotic or lactulose therapy. Six of these died within 1 mo of surgery and were classified as early deaths (Fig. 6). The mean residual intrahepatic venous pressure of these 13 patients (21.1±4.4 cm) was significantly less ($P < 0.001$) than the 27 patients that did not have chronic encephalopathy (32.6±5.3 cm).

Life table analysis (25, 26) demonstrated a significantly ($P < 0.01$) shorter survival (median, 0.6 yr) for the 13 patients with lower pressures when compared to the other patients (median, 5.0 yr) (Fig. 7). None of the 27 patients with relatively favorable postoperative courses had a residual intrahepatic venous pressure <25 cm. 6 of 8 patients who died within 1 mo, 8 of 10 patients who died within 1 yr, and 6 of 7 patients who survived the postoperative period, but suffered from chronic encephalopathy, were unable to maintain residual intrahepatic venous pressure above 25 cm. These findings suggest that 25 cm is a critical lower limit of pressure, below which hepatic function is not maintained and chronic encephalopathy with early death supervenes.

DISCUSSION

A lesser fall in portal pressure than would be expected for a given quantity of portal blood flow diversion indicates a compensatory vascular mechanism. Therefore, the steepest portal pressure-shunted portal flow slope observed (Table I, patient 22) most clearly approaches the absence of this postulated mechanism. Lesser slopes result from its activity. The failure of the portal pressure-shunted portal flow slope to be altered by changing blood volume, portal pressure, and presumably cardiac output (27) points to a splanchnic rather than systemic origin of the proposed mechanism. The small portal pressure-shunted portal flow slopes recorded in control subjects may reflect both low and variable hepatic resistance to flow (28, 29). Similarly, a lesser increase in portal pressure than expected during portal blood flow augmentation by systemic to portal shunting in the presence of portal hypertension suggests a compensatory decrease in arterial inflow to the splanchnic chamber since hepatic and portal-systemic collateral outflow resistance should be limiting when cirrhosis and portal hypertension are present (30–32). Failure or absence of this mechanism in some patients with cirrhosis is indicated by the continuum of portal pressure-shunted portal flow slopes observed.

An increase of mesenteric and splenic venous flow

KUR-MAG-DE004222

Page 2558 of 5977

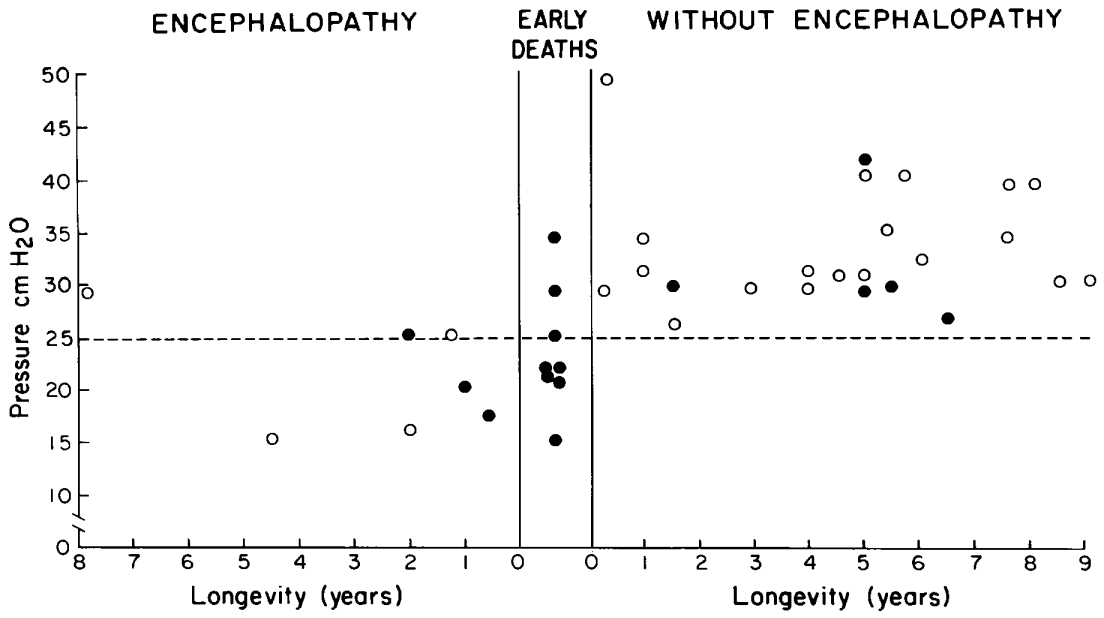


FIGURE 6 Relationship of survival and clinical status (encephalopathy) to residual intrahepatic venous pressure after end-to-side portacaval anastomosis (open circle, alive; closed circle, dead). The 13 patients with encephalopathy (left) had significantly lower pressures than those without encephalopathy (right, $n = 27$) and a significantly shorter survival (median, 0.6 vs. 5.0 yr). Early mortality is defined as death within 1 mo of surgery.

in response to reduced portal pressure is suggested by the maintenance of portal pressure despite hepatic artery occlusion (Table II) and published studies demonstrating an increase in portal and splenic flow after

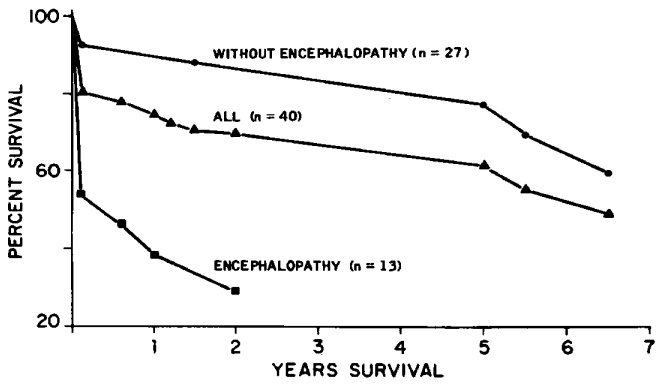


FIGURE 7 Life table analysis of 40 patients followed for up to 9 yr after end-to-side portacaval anastomosis (center curve, all patients). The 13 patients with chronic encephalopathy had a lower residual intrahepatic venous pressure and reduce median survival (0.6 yr, lower curve) when compared to the 27 patients with residual intrahepatic venous pressure > 25 cm and medial survival 5.0 yr who did not have chronic encephalopathy (highest curve). The highest and lowest curves are significantly different (log rank test, $P = 0.01$). Cumulative survival for the 13 patients in the lower curve was not carried beyond 2 yr because experience was limited to only two patients surviving beyond this point.

portacaval anastomosis (10, 33). Hepatic (9, 34–36), mesenteric, and splenic (33) arteries may all contribute to maintenance of portal pressure in type A patients when the portal circulation is intact. Conversely, the steep portal pressure-shunted portal flow slopes in type B patients indicate a limited response of all these vessels to changing portal flow and suggests a widespread defect in vascular function.

Abnormal vascular responses in the cardiac (37, 38), pulmonary (39), renal (40), integumentary (41), and splanchnic (36) systems have been demonstrated in patients with liver disease. The increased cardiac output (37) functional renal failure (42) and portal hypertension (43) of liver disease may be reversible. The portal hypertension of cirrhotic patients in this study consisting of an elevated portal pressure setpoint and a variable limitation of the response to changing portal flow also, at least in part, may be a reversible alteration in vascular responsiveness (44) rather than a consequence of the presumed fixed anatomic hepatic outflow block previously conceived as the cause of portal hypertension (45).

Alternatively, the continuum of response to changing portal flow could result from anatomic alterations in the hepatic artery associated with cirrhosis (46, 47). Herrick (48), and later Dock (49), perfused the livers of alcoholic hypertropic cirrhotic patients in vitro and demonstrated a reciprocal relationship between hepatic arterial pressure and portal pressure. They speculated on the role

KUR-MAG-DE004223

Page 2559 of 5977