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】

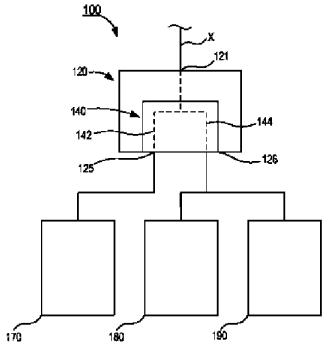


FIG. 1

【図２】

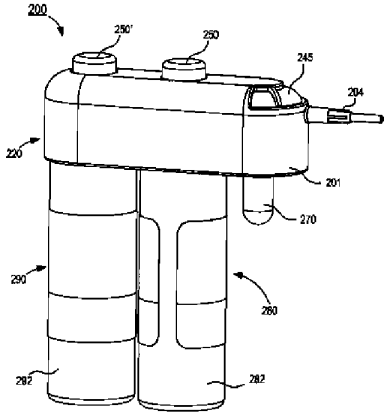


FIG. 2

【図３】

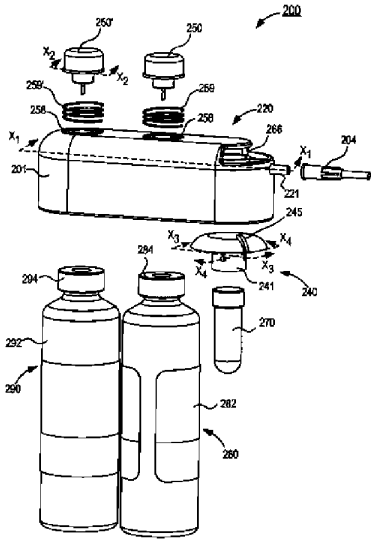


FIG. 3

【図４】

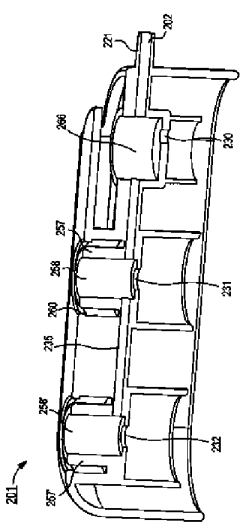


FIG. 4

【図５】

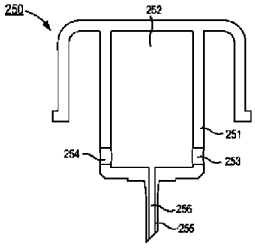


FIG. 5

【図６】

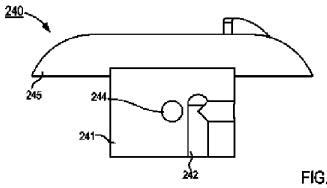


FIG. 6

【図７】

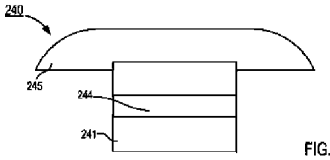


FIG. 7

【図８】

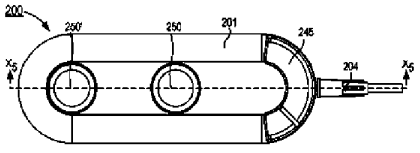


FIG. 8

【図９】

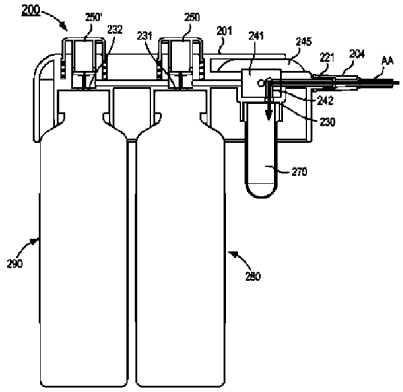


FIG. 9

【図１０】

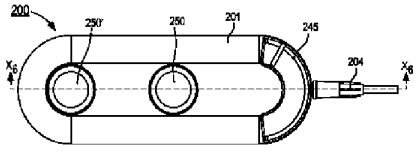


FIG. 10

【図１１】

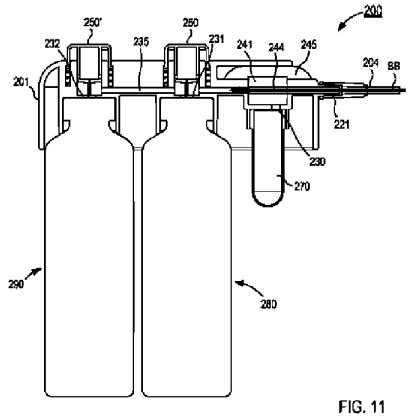


FIG. 11

【図１２】

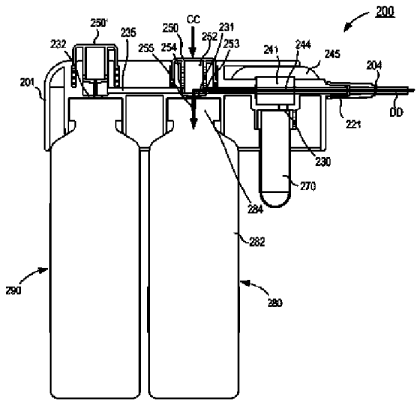


FIG. 12

【図１３】

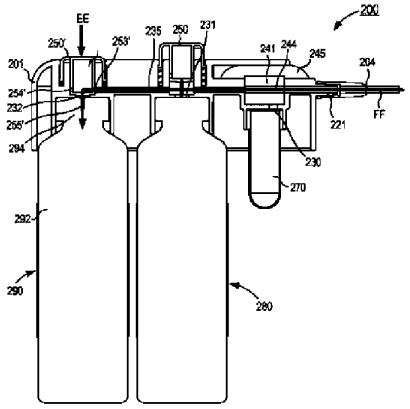


FIG. 13

【図１４】

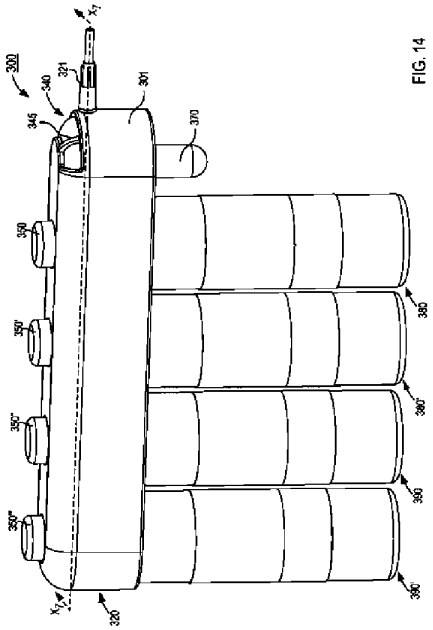


FIG. 14

【図１５】

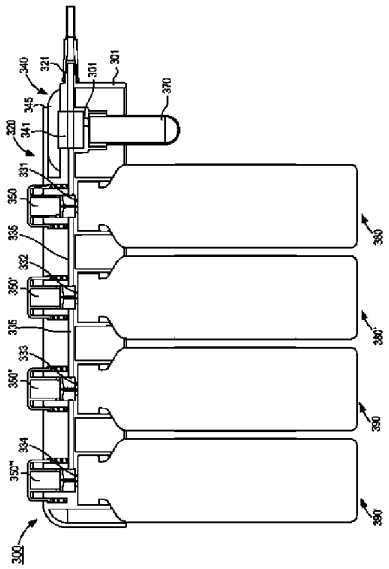


FIG. 15

【図１６】

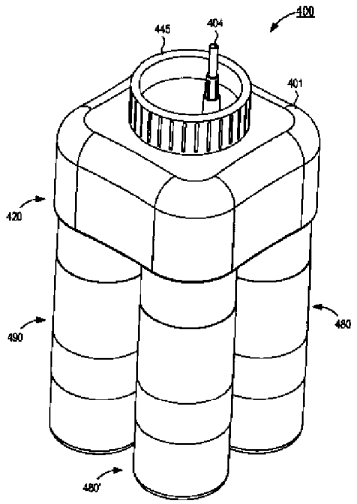


FIG. 16

【図１７】

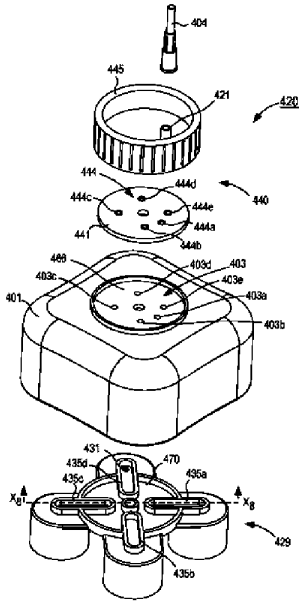


FIG. 17

【図１８】

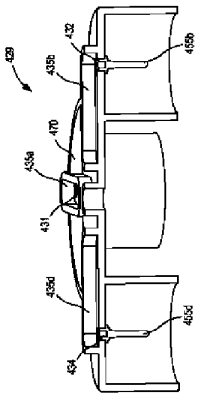


FIG. 18

【図１９】

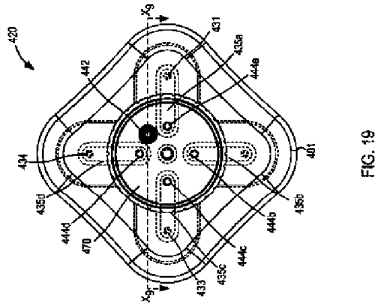


FIG. 19

【図２０】

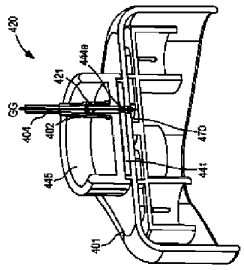


FIG. 20

【図２１】

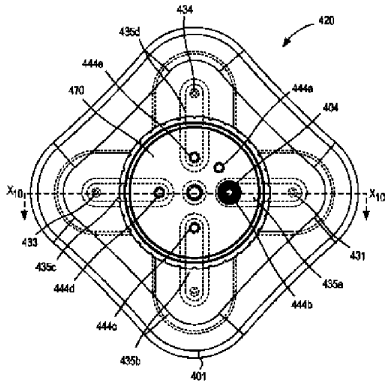


FIG. 21

【図２２】

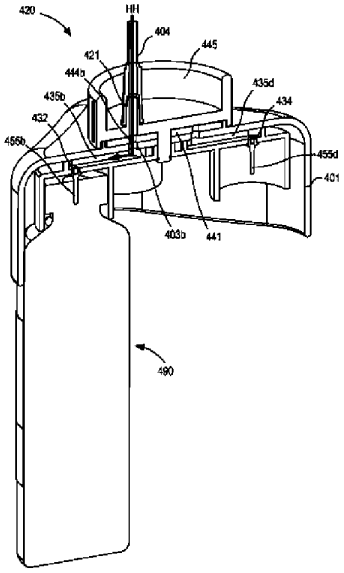


FIG. 22

【図２３】

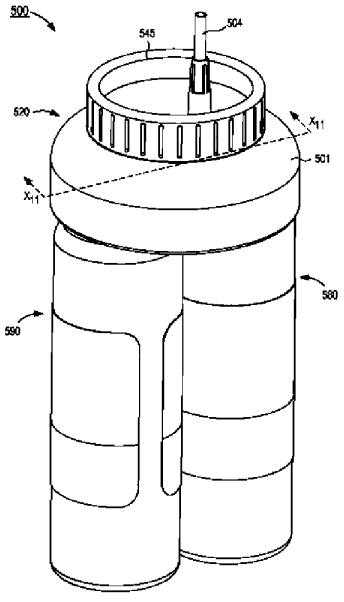


FIG. 23

【図２４】

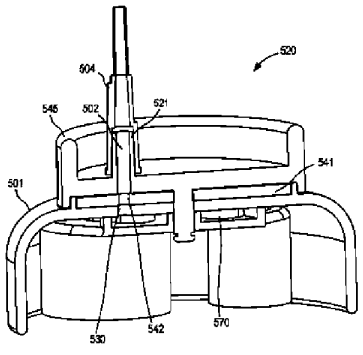


FIG. 24

【図２５】

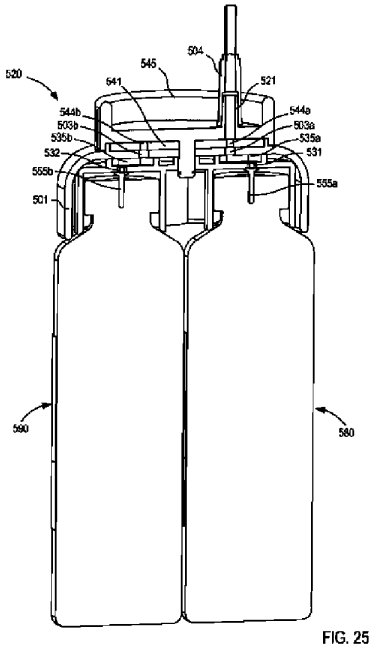


FIG. 25

【図２６】

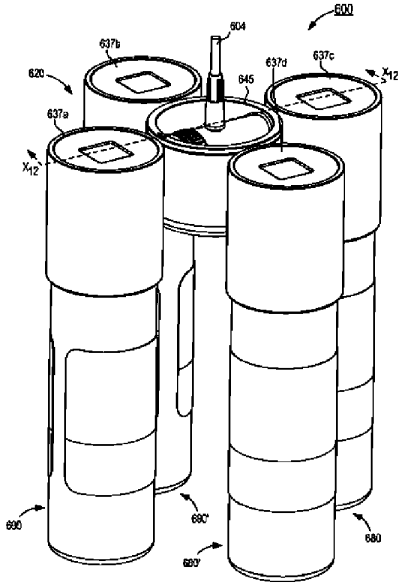


FIG. 26

【図２７】

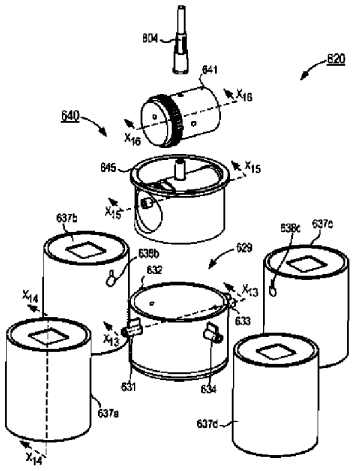


FIG. 27

【図２８】

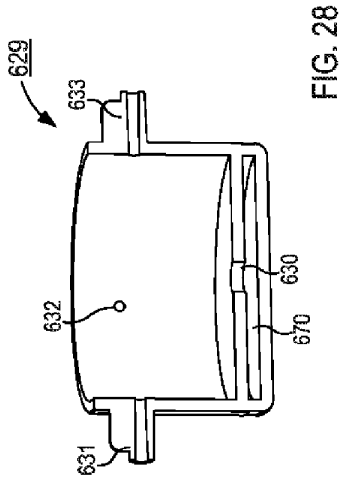


FIG. 28

【図２９】

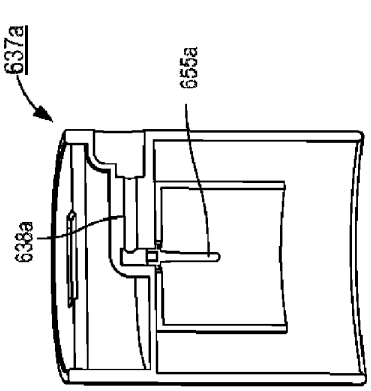


FIG. 29

【図３０】

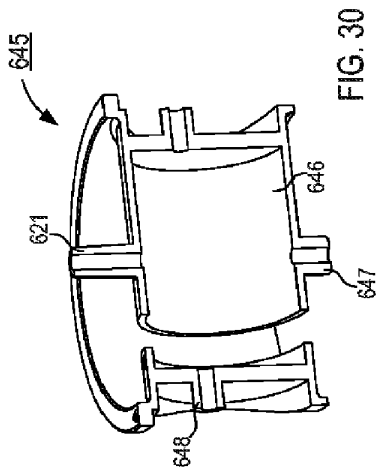


FIG. 30

【図３１】

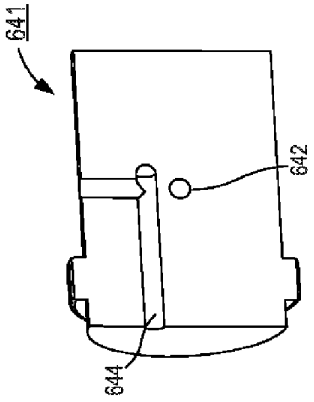


FIG. 31

【図３２】

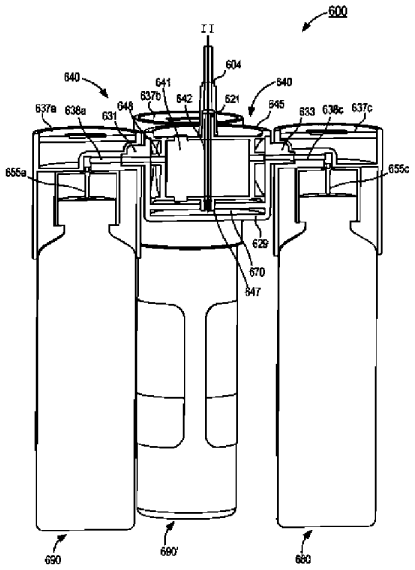


FIG. 32

【図３３】

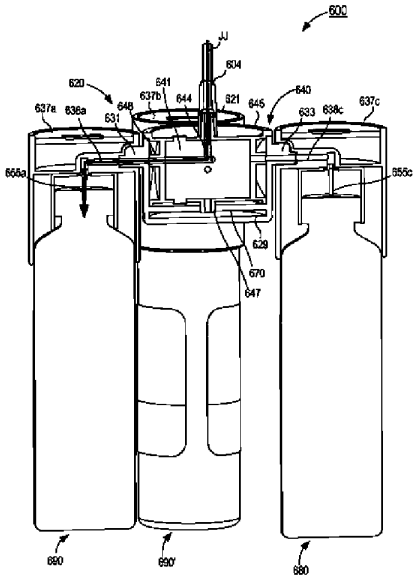
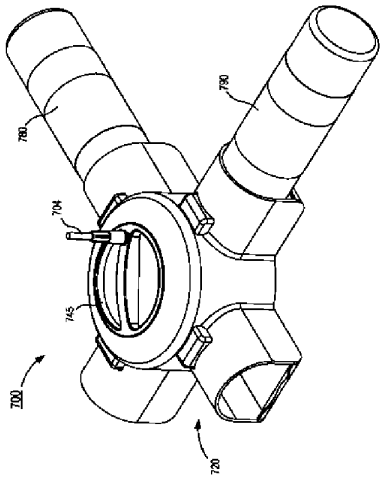


FIG. 33

【図３４】

FIG. 34



【図３５】

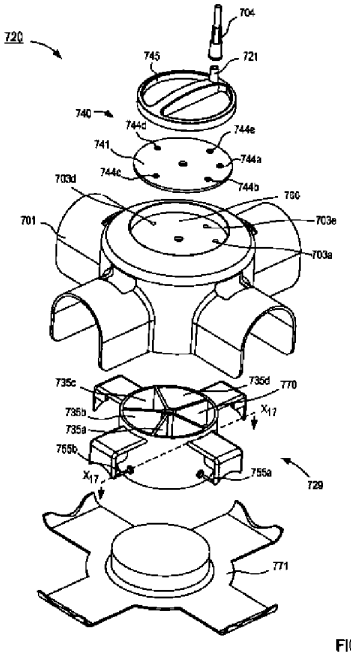


FIG. 35

【図３６】

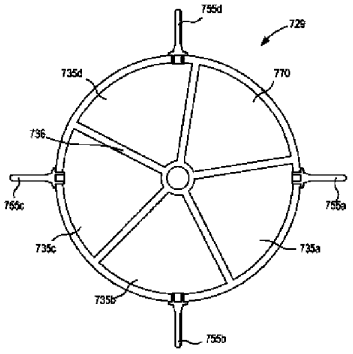


FIG. 36

【図３７】

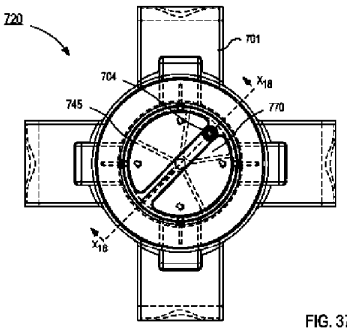


FIG. 37

【図３８】

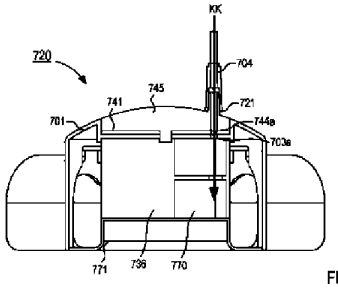


FIG. 38

【図３９】

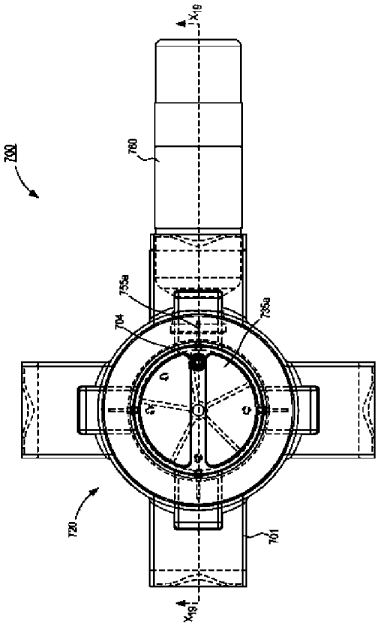


FIG. 39

【図４０】

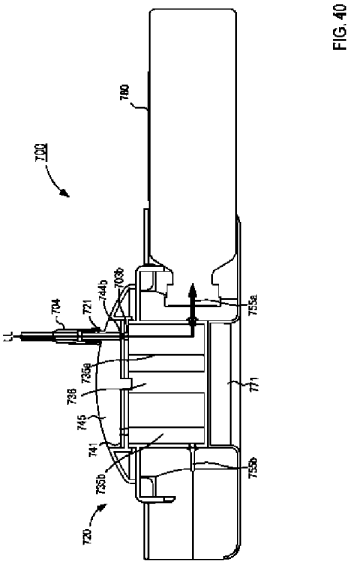


FIG. 40

【図４１】

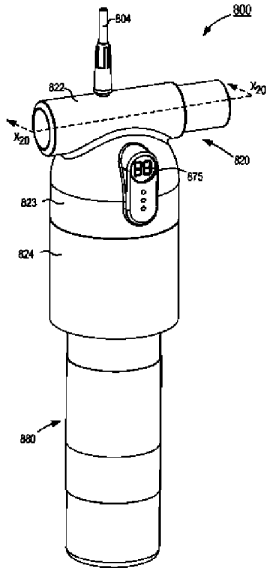


FIG. 41

【図４２】

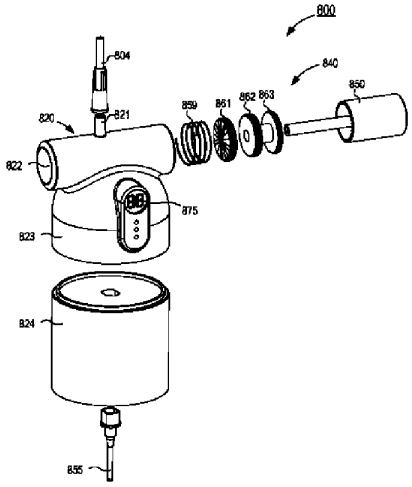


FIG. 42

【図４３】

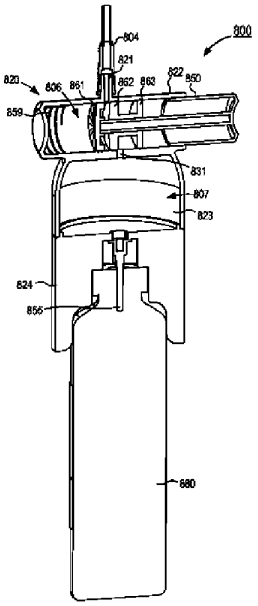


FIG. 43

【図４４】

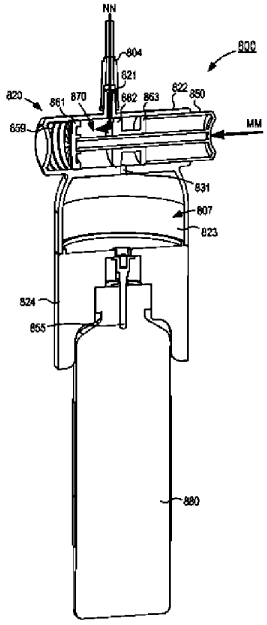


FIG. 44

【図４５】

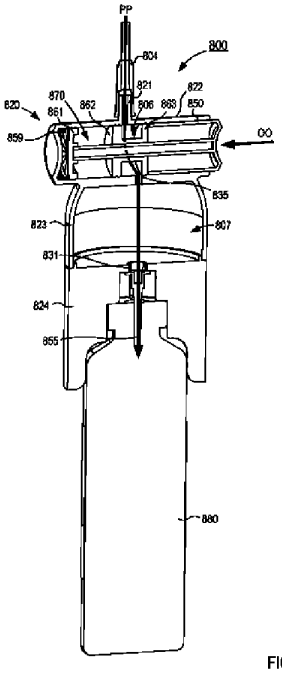


FIG. 45

【図４６】

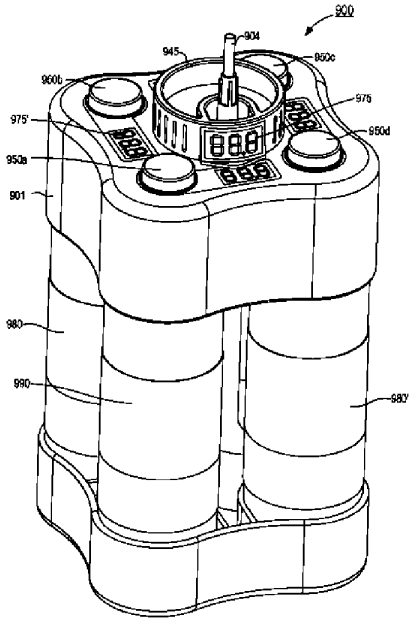


FIG. 46

【図４７】

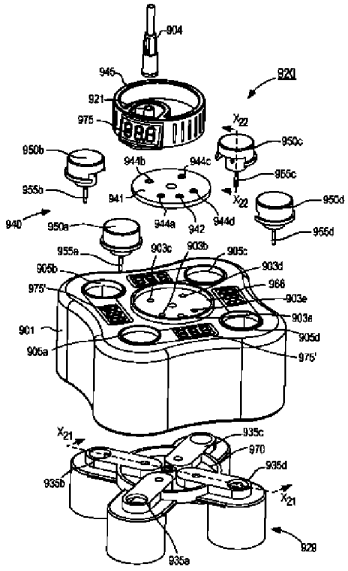


FIG. 47

【図４８】

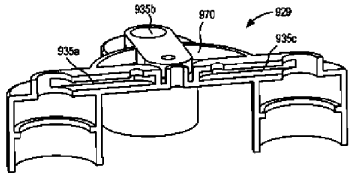


FIG. 48

【図４９】

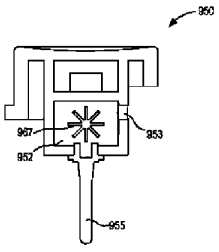


FIG. 49

【図５０】

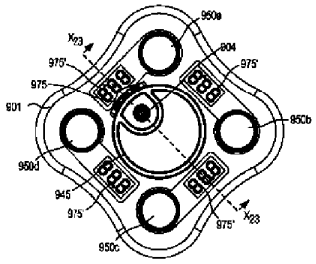


FIG. 50

【図５１】

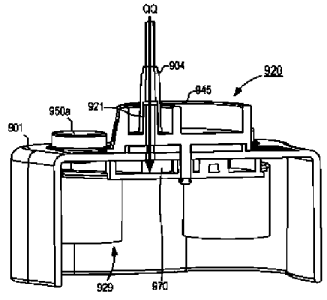


FIG. 51

【図５２】

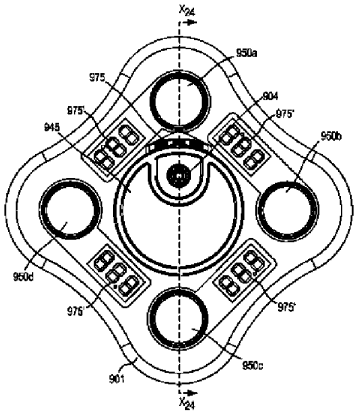


FIG. 52

【図５３】

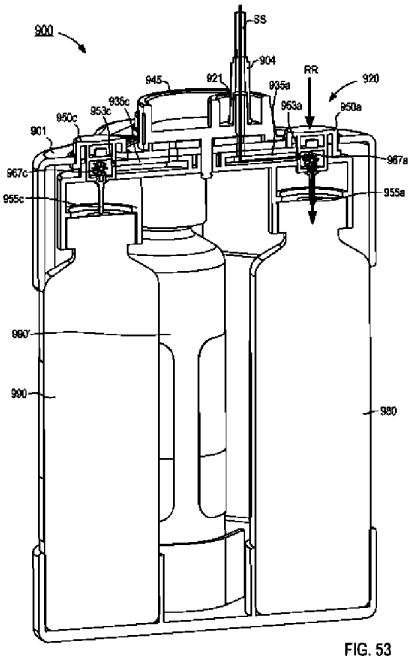
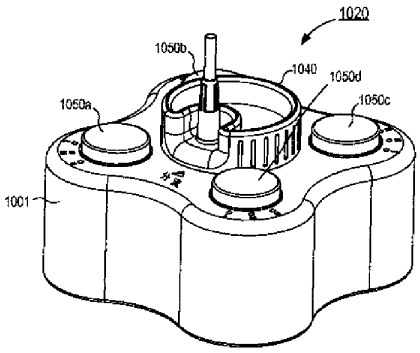
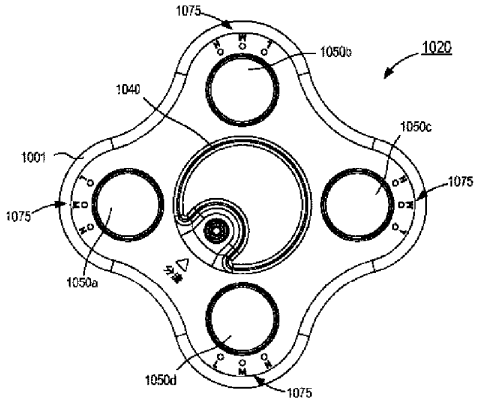


FIG. 53

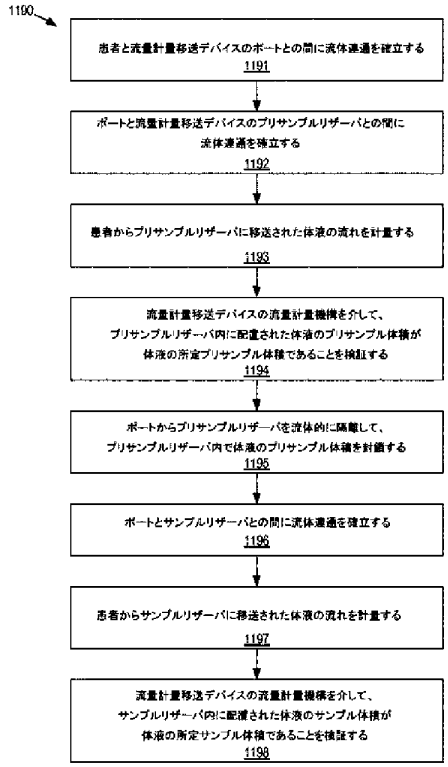
【図５４】



【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
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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" 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

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Ｆターム(参考) 4C038 TA01 UA10 UB07

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.

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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

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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.

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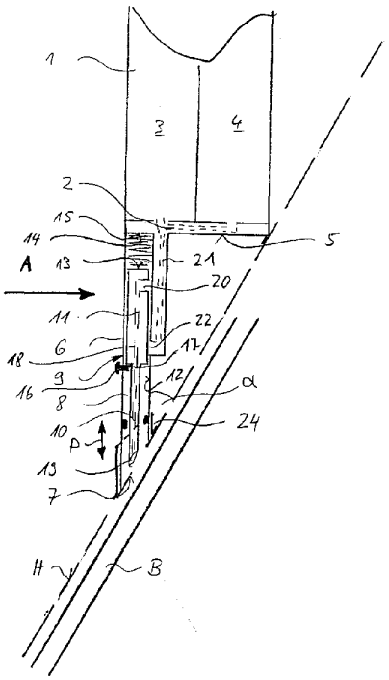
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Die folgenden Angaben sind den vom Anmelder eingereichten Unterlagen entnommen

(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.

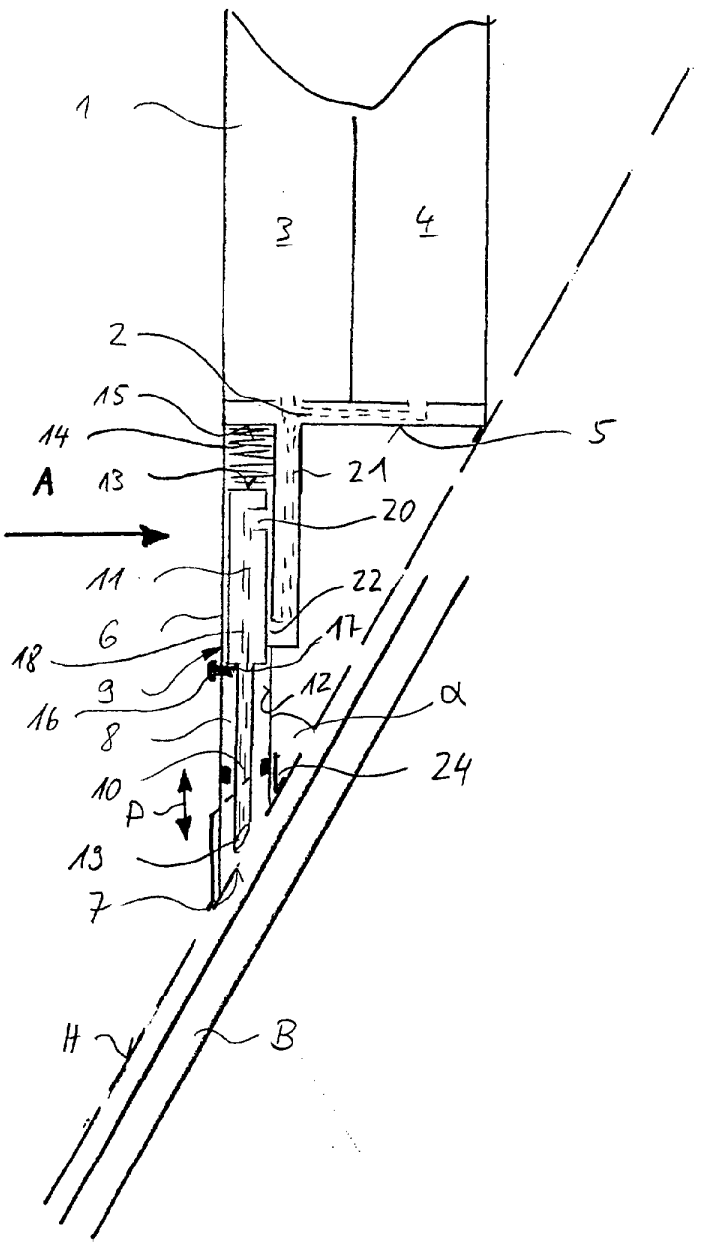
17. Vorrichtung nach Anspruch 15, dadurch gekennzeichnet, daß die Innenvolumina (**31**, **32**, **33**) oder die Behälter parallel miteinander kommunizieren.

Hierzu 6 Seite(n) Zeichnungen

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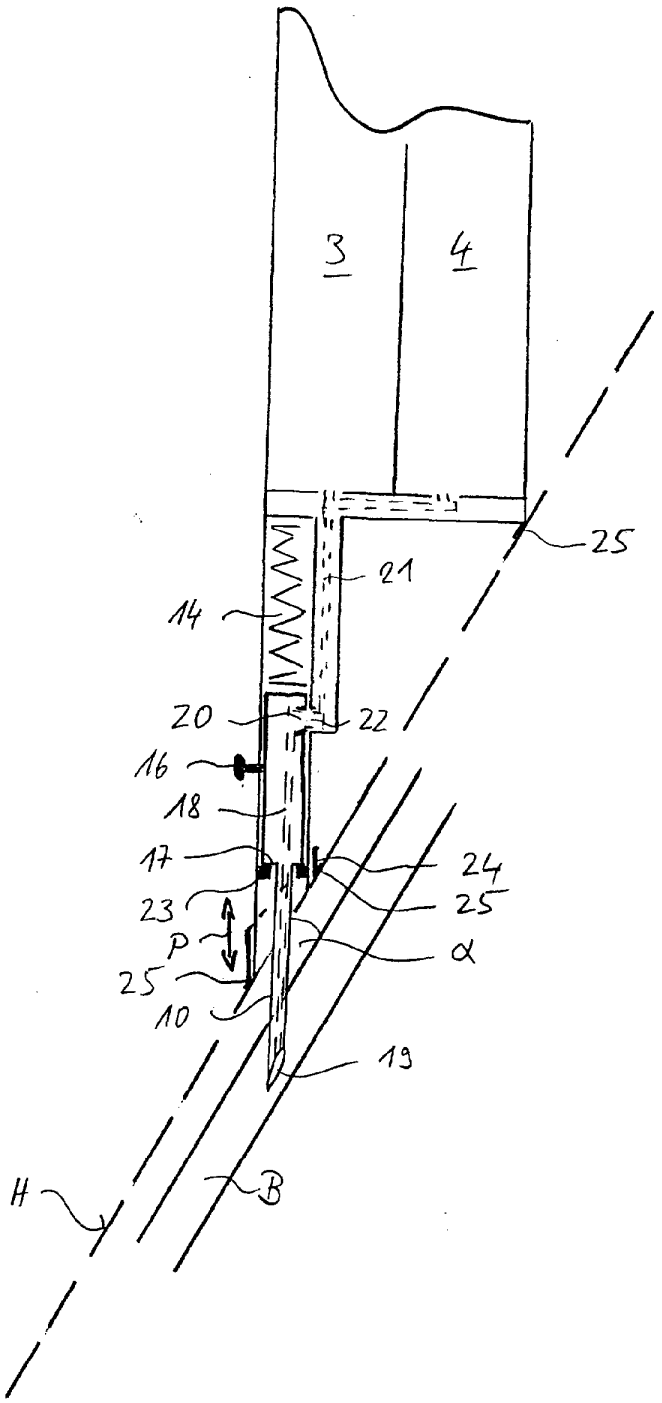
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Fig. 1



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Fig. 2



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Fig. 3

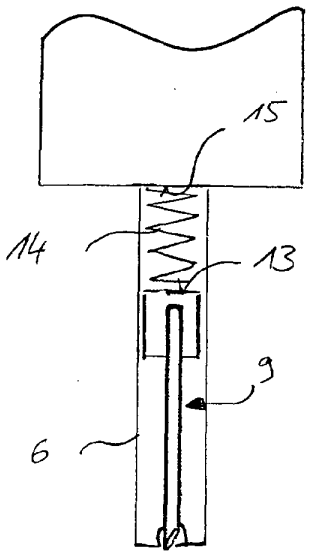
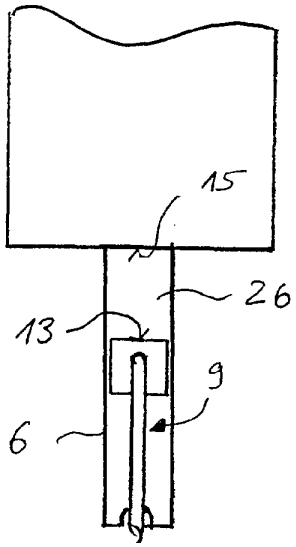


Fig. 4



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Fig. 5

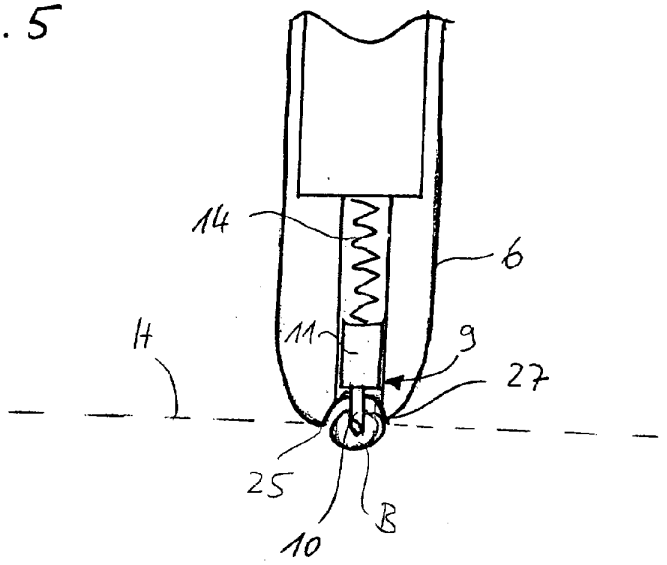
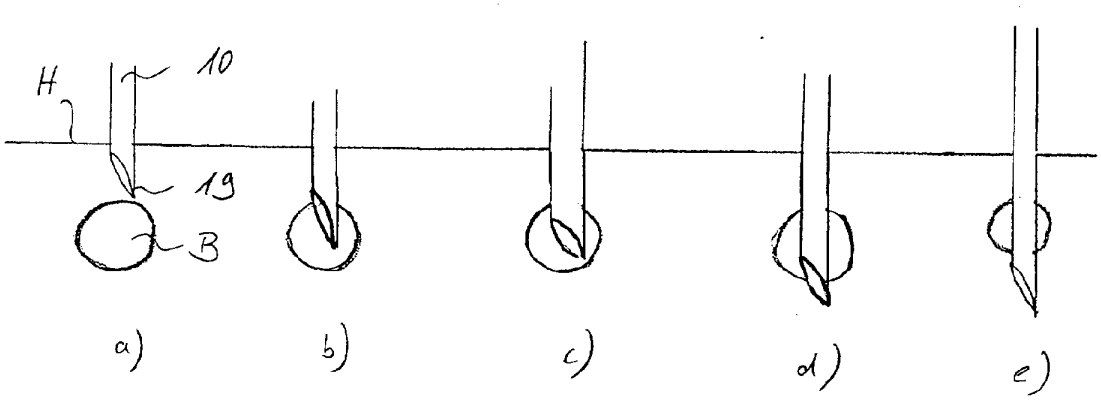


Fig. 6



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Fig. 7

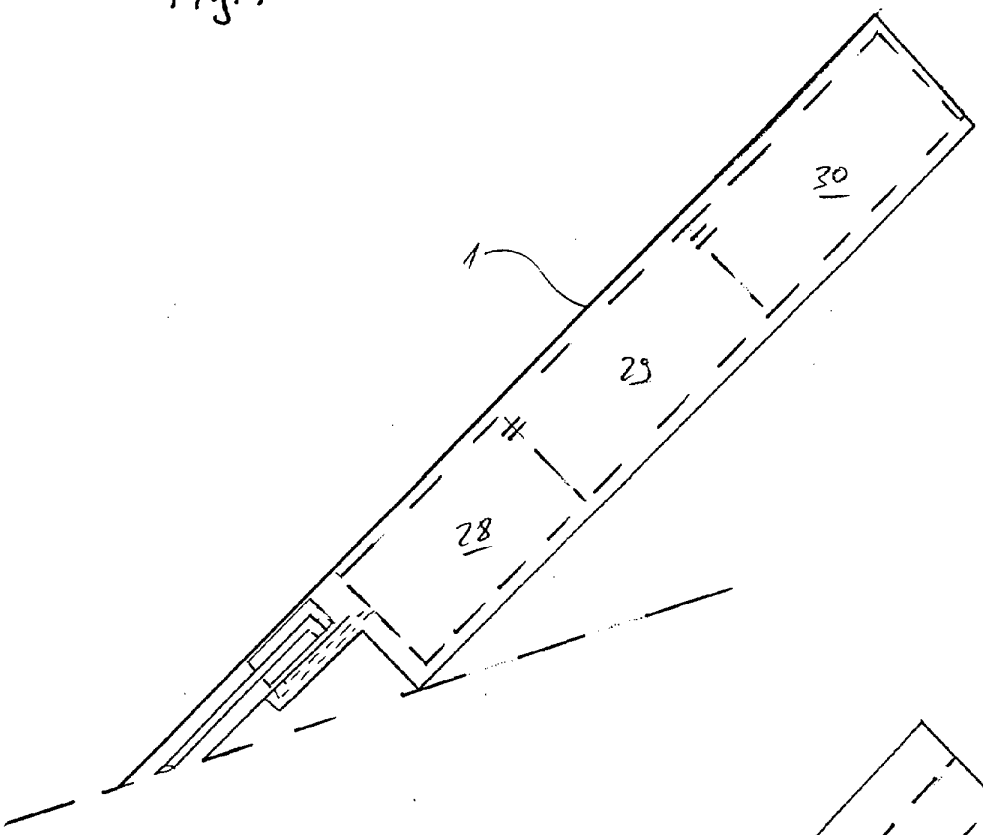
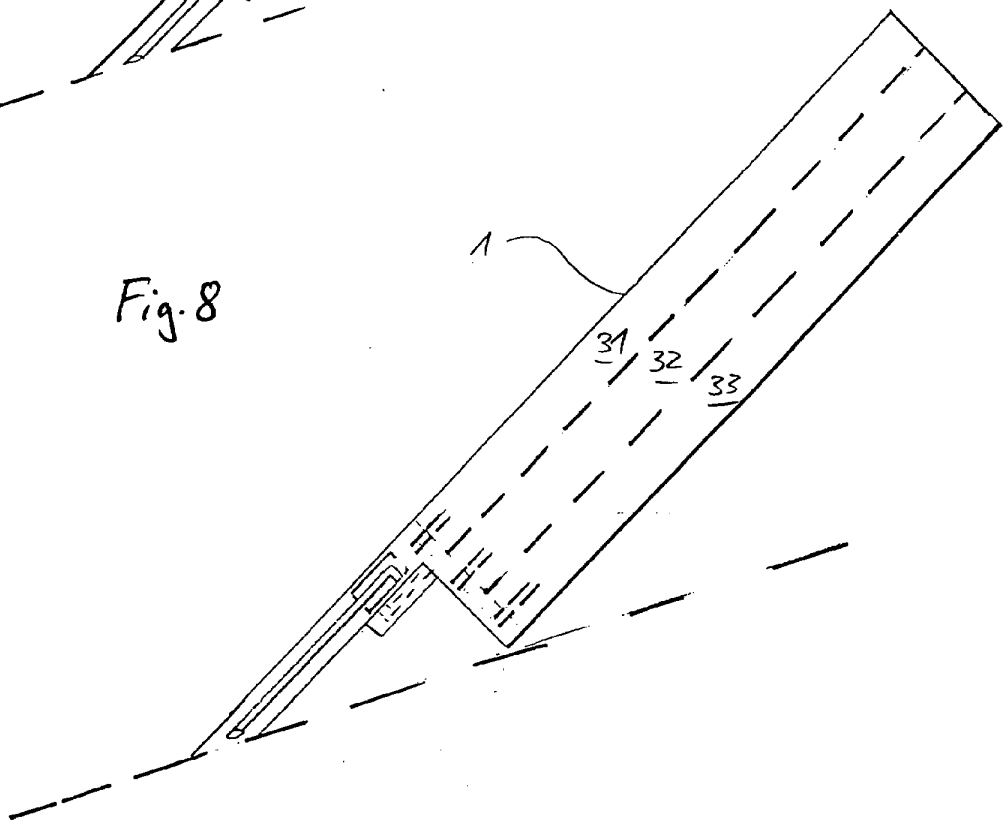
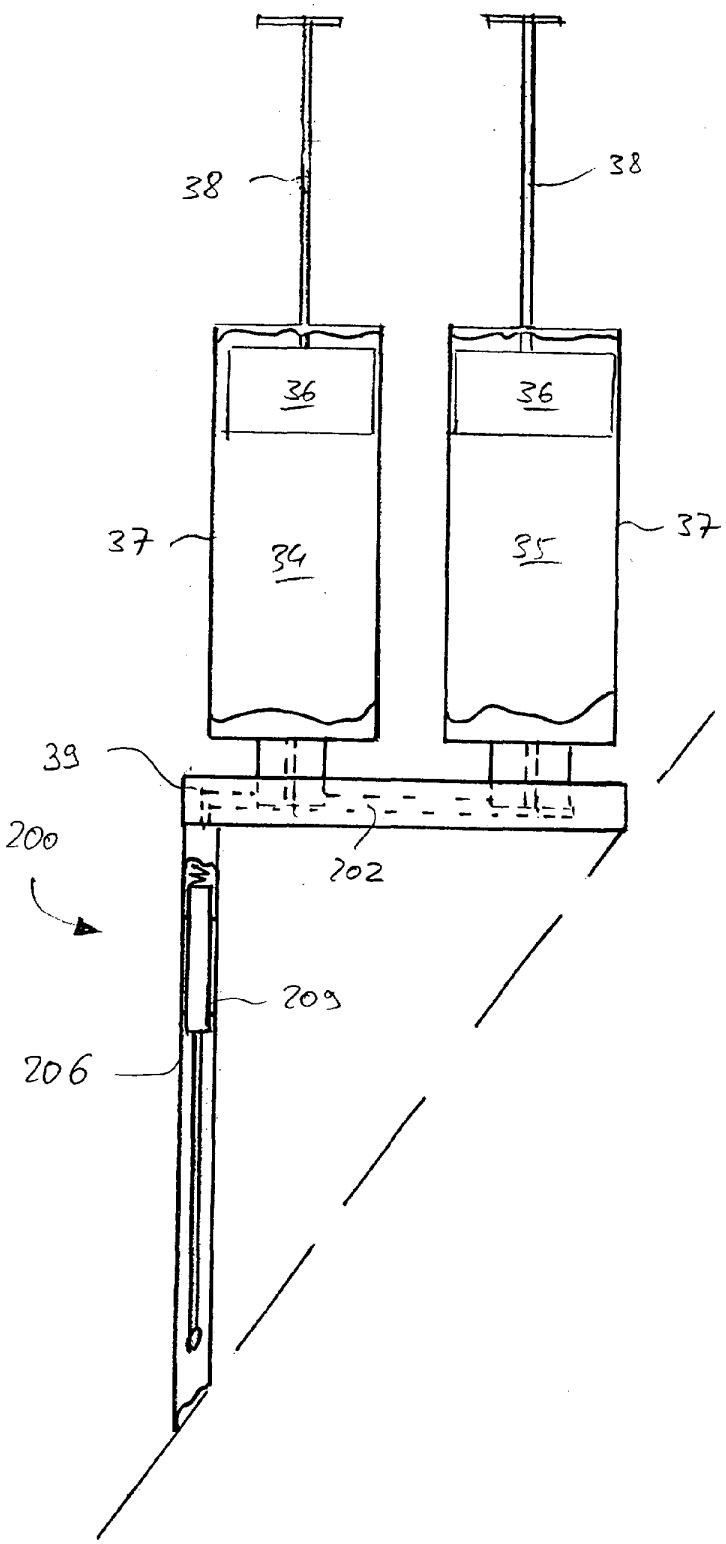


Fig. 8



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Fig. 9



Check for updates



Bacterial Contamination of Blood Components: Risks, Strategies, and Regulation

Joint ASH and AABB Educational Session in Transfusion Medicine

*Christopher D. Hillyer, Cassandra D. Josephson, Morris A. Blajchman, Jaroslav G. Vostal, Jay S. Epstein, and Jesse L. Goodman**

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Bacterial contamination of transfusion products, especially platelets, is a longstanding problem that has been partially controlled through modern phlebotomy practices, refrigeration of red cells, freezing of plasma and improved materials for transfusion product collection and storage. Bacterial contamination of platelet products has been acknowledged as the most frequent infectious risk from transfusion occurring in approximately 1 of 2,000-3,000 whole-blood derived, random donor platelets, and apheresis-derived, single donor platelets. In the US, bacterial contamination is considered the second most common cause of death overall from transfusion (after clerical errors) with mortality rates ranging from 1:20,000 to 1:85,000 donor exposures. Estimates of severe morbidity and mortality range from 100 to 150 transfused individuals each year.

Concern over the magnitude and clinical relevance of this issue culminated in an open letter calling for the "blood collection community to immediately initiate a program for detecting the presence of bacteria in units of platelets." Thereafter, the American Association of Blood Banks (AABB) proposed new standards to help mitigate transfusion of units that were contaminated with bacteria. Adopted with a final implementation date of March 1, 2004, the AABB Standard reads "*The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components.*"

This Joint ASH and AABB Educational Session reviews the risks, testing strategies, and regulatory approaches regarding bacterial contamination of blood components to aid in preparing practitioners of hematology and transfusion medicine in understanding the background and clinical relevance of this clinically important issue and in considering the approaches currently available for its mitigation, as well as their implementation.

In this chapter, Drs. Hillyer and Josephson review the background and significance of bacterial contamination, as well as address the definitions, conceptions and limitations of the terms *risk, safe* and *safety*. They then describe current transfusion risks including non-infectious serious hazards of transfusion, and current and emerging viral risks. In the body of the text, Dr. Blajchman reviews the prevalence of bacterial contamination in cellular blood components in detail with current references to a variety of important studies. He then describes the signs and symptoms of transfusion-associated sepsis and the sources of the bacterial contamination for cellular blood products including donor bacteremia, and contamination during whole blood collection and of the collection pack. This is followed by strategies to decrease the transfusion-associated morbidity/mortality risk of contaminated cellular blood products

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including improving donor skin disinfection, removal of first aliquot of donor blood, pre-transfusion detection of bacteria, reducing recipient exposure, and pathogen reduction/inactivation. In the final sections, Drs. Vostal, Epstein and Goodman describe the regulations and regulatory approaches critical to the appropriate implementation of a bacterial contamination screening and limitation program including their and/or the FDA's input on prevention of bacterial contamination, bacterial proliferation, and detection of bacteria in transfusion products. This is followed by a discussion of sampling strategy for detection of bacteria in a transfusion product, as well as the current approval process for bacterial detection devices, trials recommended under "actual clinical use" conditions, pathogen reduction technologies, and bacterial detection and the extension of platelet storage.

Bacterial contamination of transfusion products, especially platelets, is a longstanding problem that has been partially controlled through modern phlebotomy practices, refrigeration of red cells, freezing of plasma, and improved materials for transfusion product collection and storage. Indeed, bacterial contamination of platelet products has been acknowledged as the most frequent *infectious risk* from transfusion occurring in approximately 1 of 2,000–3,000 whole-blood derived, random donor platelets (hereafter RDP), and apheresis-derived, single donor platelets (hereafter SDP)[1-4] (see below). In the US, bacterial contamination is considered the second most common cause of death overall from transfusion (after clerical errors) with mortality rates for platelet-related sepsis ranging from 1:20,000 to 1:85,000 donor exposures.[5] Estimates of severe morbidity and mortality range from 100 to 150 transfused individuals each year.[6,7]

To address this problem, the US Food and Drug Administration (FDA) has sponsored scientific workshops to highlight and clarify relevant issues and to promote the development of technologic interventions.[8-10] Additionally, the Centers for Disease Control and Prevention (CDC) conducted a nationwide surveillance study on bacterial contamination in blood products.[11] Many publications (detailed later in this chapter) have added important data attempting to determine and define the true clinical effect of bacterial contamination of blood components, and a similar number of publications have offered data as to the ability of a variety of methods to detect and limit this contamination.

Concern over the magnitude and clinical relevance of this issue culminated in an open letter calling for the "blood collection community to immediately initiate a program for detecting the presence of bacteria in units of platelets" (see http://www.cbbsweb.org/bacterial risk.pdf). Thereafter, the American Association of Blood Banks (AABB), after publication of a number of Association Bulletins (see AB 96-06[3] at www.AABB.org), proposed new standards (December 2002) to help mitigate transfusion of units that were contaminated with bacteria. Adopted with a final implementation date of March 1, 2004, AABB Standard 5.1.5.1. now reads:

> **5.1.5.1** *The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components. Standard 5.6.2 applies. [Arm Prep]*

Thus, this Joint ASH and AABB Educational Session was conceived to review the risks, testing strategies, and regulatory approaches regarding bacterial contamination of blood components; to aid in preparing practitioners of hematology and transfusion medicine in understanding the background and clinical relevance of this important issue; and to consider the approaches currently available for its mitigation as well as their implementation.

Background and Significance

Whereas the risk of transfusion related transmission of viral diseases such as human immunodeficiency virus (HIV) and hepatitis has steadily decreased over the last 40 years, the risk of transmission of bacteria has remained about the same. Thus, due to our success with viral pathogens, bacterial contamination now has the dubious distinction of being the most common infectious risk from transfusion and has become a matter of increasing concern and attention.[12,13] Recent studies of platelets have suggested a bacterial contamination rate of about 1 per 1–3,000 units, clinical sepsis in about 1 per 20,000 transfusions and related fatality in about 1 per 60,000 transfusions[5,14,15] (reviewed in detail below). The fatality risk from bacterially contaminated red blood cells (RBCs) is much lower, about 1 per 500,000.[15]

Despite this longstanding, persistent infectious risk of transfusion, it has been tolerated by some as an "acceptable risk." However, with the significant risk reduction of transfusion-transmitted diseases attributable to viruses such as HIV, hepatitis C virus (HCV), and hepatitis B virus (HBV), the magnitude and relative importance of platelet-induced sepsis has moved to the forefront of blood supply safety.[16] In order to appreci-

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ate the significance of the relative importance of bacterial contamination of platelets, a perspective on the safety of the nation's blood supply is necessary.

Risk

There are approximately 30 million units of blood and blood products transfused each year in the US, and perhaps an equal number internationally. The American public, the medical profession, and the government hold the transfusion of these units to the highest standards of safety.[17] Indeed, the blood supply in the US has been described as "safer than ever relative to known risks," however, "the usual notions of safety do not necessarily apply where transfusion is concerned."[17] The CDC, the AABB, and the American Red Cross[18] have echoed these statements.

In the early 1980s, the incidence of transfusion transmitted (TT) HIV was greater than 1 case per 1,000 units in some locales, whereas the current incidence of TT-HIV is less than 1 case per 2 million screened and tested units;[19] some authorities have posited that this risk may actually be closer to 1 in 5 million screened and tested units especially if there is widespread implementation of "single unit" nucleic acid testing (NAT). Similar improvements have been made for HBV and HCV, two TT-viruses carrying significant morbidity and mortality (**Figure 1**).[20] Despite these improvements, many experts argue that the potential US blood recipient demands a "zero-risk" blood supply. Unfortunately, even for HIV in 2002, this goal has not been achieved as there were two reported cases of persons allegedly contracting HIV through transfusion and subsequently suing the blood supplier. In one case, a $100 million dollar negligence lawsuit has been filed. Additionally, a number of "emerging pathogens" still exist, as does the transfusion transmission of pathogens for which testing is not required. Thus, how safe the blood supply is becomes difficult to quantitate and by some criteria the risks to the blood recipient would be considered "very low" to "negligible" (see **Table 1**).[21]

Safe and safety

The word "safe" has been defined as free from "harm or risk" or "secure from danger, harm, or evil." However, safety is a more subjective term emanating from one's understanding and perspective, as well as the amount of control one has in determining the chance of the adverse outcome occurring. Thus, while the risk of dying in a car accident significantly exceeds the risk of dying from TT-infectious disease, the latter has elements of increased dread and less control and therefore has an increasingly fear-filled association. The Paling Perspective Scale[22] provides several examples of risks with which the public is "comfortable" (see **Figure 2**) and allows comparison to the risk of TT-HIV (< 1:2M) and bacterial contamination (see discussion of risk estimates below). Indeed, research has shown that patients, and the majority of the population, have a very poor understanding of risk. It is worthwhile to compare the risk of death from influenza, cigarette smoking, motorcycle riding, or lightning with the risk of dying or acquiring variant Creutzfeldt-Jakob disease (vCJD) though there

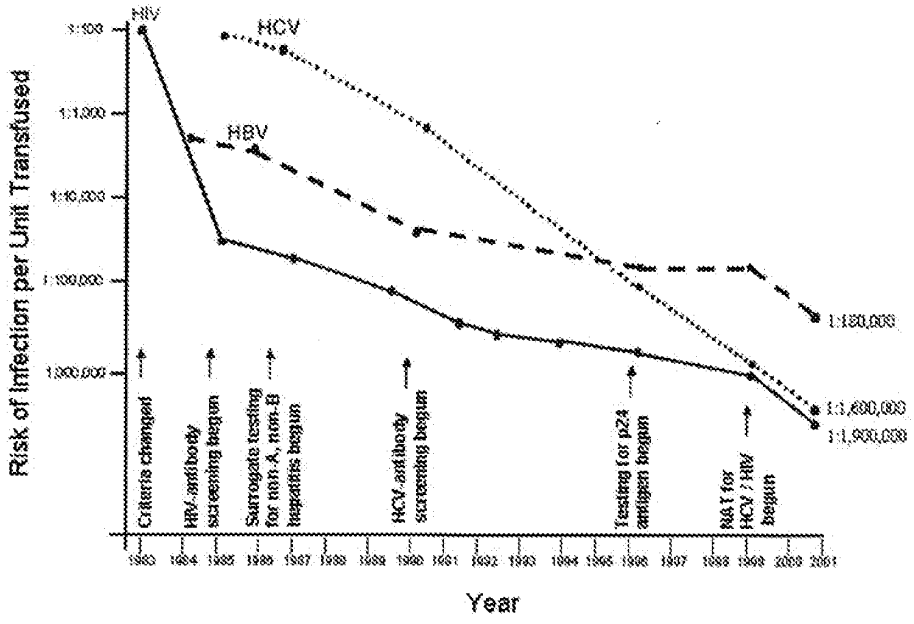


Figure 1. New test implementation and declining risk of viral infections from transfusion.[20]

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; NAT, nucleic acid testing.

Modified by M.P. Busch from table in AuBuchon JP, Birkmeyer JD, Busch MP. Safety of the Blood Supply in the United States: Opportunities and Controversies. Ann Intern Med. 1997;127:904-909 and used with permission.

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Table 1. Risk of an individual dying (D) in 1 year or developing an adverse response (A).[21]

Term Used	Risk Range	Example	Risk Estimate
High	> 1:100	(A) Transmission to susceptible household contacts of measles and chickenpox	1:1–1:2
		(A) Transmission of HIV from mother to child (Europe)	1:6
Moderate	1:100–1:1,000	(D) Smoking 10 cigarettes per day	1:200
		(D) All natural causes, age 40	1:850
Low	1:1,000–1:10,000	(D) All kinds of violence	1:3,300
		(D) Influenza	1:5,000
		(D) Accident on road	1:8,000
Very low	1:10,000–1:100,000	(D) Leukemia	1:12,000
		(D) Playing soccer	1:25,000
		(D) Accident at work	1:43,000
Minimal	1:100,000–1:1,000,000	(D) Accident on railway	1:500,000
Negligible	< 1:1,000,000	(D) Hit by lightning	1:1,000,000
		(D) Release of radiation by nuclear power station	1:10,000,000

have been no known TT-cases of vCJD, although animal models support the possibility that vCJD may be transfusion-transmitted.[23]

Transfusion risks

It is vital to consider the other risks of transfusion such as those termed non-infectious serious hazards of transfusion (often termed NiSHOTs; see **Table 2**) which dramatically outweigh the residual risk of TT-infectious diseases.[24] However, the agents that are known to be transfusion transmitted, and those that "might be" are described in **Table 3**, for it is only upon this backdrop that a decision can be made on the relative value of new technologies and their ability to abrogate the agents,

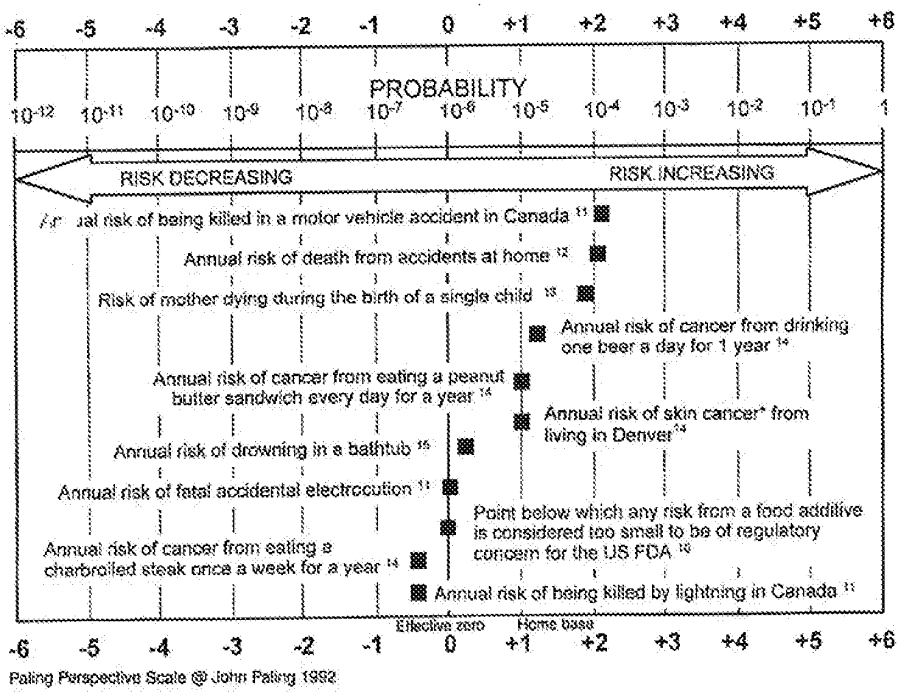


Figure 2. Risks with which the public is comfortable.

The numbers denoting references in this figure are those from the primary article and are not notations of the references found at the conclusion of this chapter.

Abbreviations: FDA, Food and Drug Administration.[22]

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Table 2. Noninfectious serious hazards of transfusion (NiSHOTs).[24]

- Mistransfusion and ABO/Rh incompatible transfusion
- Cardiopulmonary toxicity
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated graft-versus-host disease (TA-GVHD)
- Metabolic derangements in pediatric and massive transfusion
- Undertransfusion

Table 4. Criteria for transfusion transmission of viruses and other infectious agents.[25]

1. There must be an asymptomatic, viremic phase in the blood donor.
2. Virus viability must be maintained during storage.
3. There must be a seronegative recipient population.
4. The agent must be capable of inducing disease.

including bacterial contamination of platelet products.

Typically, four elements are required for an infectious disease–causing agent to be transmitted by transfusion and the criteria are listed in **Table 4**.[25] However, despite many possible agents that can be transmitted by transfusion, units are regularly tested only for HIV, HCV, HBV, HTLV, and *Treponema pallidum*. Donor demographics may bring changes in risk level of transfusion-transmitted agents and affect future choices for routine screening. For example, the incidence of malaria and Chagas disease seems to be rising due to increasing travel to endemic areas, climate changes, and immigration.

Clinical relevance

The unique aspect of most bacterial species when compared to viral pathogens is that they can readily proliferate in the nutrient-rich blood product environment during storage. This is particularly true in platelet products that are stored at room temperature, rather than in the cold. It is estimated that the level of contamination at the time of collection is generally relatively low, probably on the order of 1–10 colony forming units/mL or less.[26] Once the product is contaminated, the inoculated bacterial seed can proliferate within hours to reach levels of 10^6/mL or greater. Such quantities of bacteria infused with the transfusion product over a short period of time can cause bacteremia that may progress to sepsis and death. The outcome of a contaminated transfusion is highly dependent on the amount of bacteria transfused, the type of bacteria and its pathogenicity for humans, the rate of transfusion, and the clinical status of the recipient. Immunosuppressed patients and older individuals with poor nutritional status will be the most susceptible population. However, even healthy individuals can have a rapidly fatal outcome when transfused with a large load of endotoxin-producing Gram-negative bacteria.

Thus, there is significant concern about, and demand for, a "safe" or "safer" blood supply in order to provide the best and safest patient care. This, in turn, has the public, government, and blood suppliers' attention keenly focused on preventing bacterial contamination of platelets and subsequent sepsis due to platelet transfusions. This risk has become "unacceptable" in a climate where the blood supply remains "the safest that it has ever been."

Table 3. Agents and their likelihood of transfusion transmission in qualitative terms.

Agent	Transfusion Transmission
Parasites	
Malaria	Rare cases
Babesia	Occasional cases, endemic
T. cruzii	Occasional cases, US
T. gondii	Rare cases
Leishmania	Rare cases (< 5 worldwide)
Bacteria	
Contaminants	Approximately 1:3,000 platelet units
Specific Agents	
T. pallidum	Rare cases
B. burgdorferi	No known cases
E. chaffeensis	No known cases
E. cytophagophilia	One possible case
R. rickettsii	One reported case
Viruses	
HIV	Rare cases
HCV	Rare cases
HBV	Occasional cases
HTLV	Rare cases
CMV	Occurs, threat to specific pts
EBV	Occurs, threat to specific pts
B19	Occurs, threat to specific pts
HAV	Rare cases
HGV	Occurs, not a threat to pts
TTV	Occurs, not a threat to pts
Sen-V	Occurs, not a threat to pts
HHV-8	No known cases
WNV	Several cases reported
Enterovirus	Known donor viremia
Prions	
CJD	No known cases
vCJD	No known cases*

* Animal models support the possibility that this agent may be able to be transmitted by transfusion

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; HBV, hepatitis B virus; HTLV, human T-cell lymphotrophic virus; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HAV, hepatitis A virus; HGV, hepatitis G virus; TTV, transfusion-transmitted virus; HHV-8, human herpes virus–8; WNV, West Nile virus; CJD, Creutzfeld-Jakob disease; vCJD, variant CJD.

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Table 5. Summary of the available prospective studies evaluating the prevalence of bacterial contamination in whole blood–derived platelets, apheresis platelets, and red blood cell units.

Blood Produce Type	Reference	Positives per Number of Units Tested	Contamination Prevalence per 100,000 Units
WB-plts	Morrow et al[32]	6 per 74,598	8
WB-plts	Barrett et al[33]	1 per 4,272	23
WB-plts	Yomtovian et al[34]	6 per 15,705	38
WB-plts	Chiu et al[35]	10 per 21,503	46
WB-plts	Blajchman et al[36]	16 per 31,610	51
WB-plts	Leiby et al[37]	4 per 4,995	80
WB-plts	Blajchman et al[38]	7 per 10,065	70
A-plts	Morrow et al[32]	1 per 9,519	5
A-plts	Blajchman et al[31]	14 per 6,055	230
A-plts	Barrett et al[33]	5 per 17,928	28
A-plts	Yomtovian et al[34]	0 per 2,476	0
A-plts	Dzieczkowski et al[39]	1 per 5,197	19
A-plts	Aubuchon et al[40]	1 per 2,678	37
RBCs	Barrett et al[33]	1 per 31,385	3
RBCs	Dzieczkowski et al[39]	1 per 7,080	0
Overall	*n* = 15	89 per 274,379	32.4*

* 95% confidence intervals 25.6 to 39.1

Abbreviations: A-plts, apheresis platelets; WB-plts, whole blood–derived platelets; RBCs, red blood cells; *n*, number of studies.

Prevalence of Bacterial Contamination in Cellular Blood Components

The contamination of RBCs and platelets with bacteria occurs relatively frequently.[12,15,27-31] However, the available prevalence data vary considerably from one study to the next. The data from the available prospective studies evaluating frequency of bacterial contamination of blood components are summarized in **Table 5**. The mean prevalence of bacterial contamination in whole blood–derived, RDP platelets is 33.9 per 100,000 units and for apheresis-derived, SDP platelet units is 51.0 per 100,000 units. For RBCs it is 2.6 per 100,000 units. The overall cellular blood product contamination prevalence from all of the data shown in **Table 5** is 32.4 per 100,000 units. This translates into an approximate rate of 1 bacterially contaminated cellular blood product unit per 3,000 cellular blood product units released.

In contradistinction to the available data on the bacterial contamination of cellular blood products (RBCs and platelets), the frequency of clinically apparent septic transfusion events or reactions due to such contaminated products is considerably lower. The available data on the prevalence of transfusion-associated septic events is summarized in **Table 6**. It should be noted that these summaries report only the more severe or potentially life threatening septic reactions. It is likely, therefore, that these reports represent only one end of the clinical spectrum of transfusion-associated septic transfusion reactions. Moreover, it is very likely that even severe and even fatal septic transfusion reactions go unrecognized as being transfusion-associated. Thus, the actual prevalence of septic transfusion reactions may be considerably higher than reported, due to the observational bias that occurs. For all of these reasons, it has been very difficult to determine the true morbidity and mortality risk of transfusing bacterially contaminated cellular blood products.

The variation in the reported prevalence of clinical events is shown clearly in **Table 6**. This table enumerates the risk of septic clinical events per million units transfused from 3 published studies: (1) the BaCon Study from the US, (2) the Hémovigilance system in France, and (3) the Johns Hopkins Hospital, which reports a 10-year follow-up of platelet transfusion episodes detected in that institution.[11,41,5] From the data in **Table 6**, it is impossible to define a specific prevalence of clinical transfusion-associated septic events, except to say that they probably occur with a frequency of 1 per approximately 25,000 platelet units transfused, and 1 per approximately 250,000 RBC units transfused. This latter estimate excludes the data from the BaCon study (1:5 million), as this study was likely limited by an underestimation bias.[11]

It is important to note that transfusion-associated septic reactions due to bacterially contaminated cellular blood products often go unrecognized as such, because of the high frequency of febrile non-hemolytic transfusion reactions

Table 6. Prevalence of transfusion-associated septic reactions per million (10^6) apheresis platelets, whole blood–derived platelets, and red blood cell units transfused.[17-19]

Study	Country	A-Plts	WB-Plts	Case Fatality Rate - Plts	RBCs	Case Fatality Rate - RBCs
Perez et al[41]	France	31.8	71.8	31.3%	5.8	24.0%
Kuehnert et al[11]	US	9.9	10.6	20.7%	0.2	60.0%
Ness et al[5]	US	74.5	67.0	17.4%	ND	ND

Abbreviations: A-plts; apheresis platelets; WB-plts, whole blood–derived platelets; RBCs, red blood cells; ND, not determined.

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(FNHTR) that occur following the transfusion of cellular blood products, particularly following platelet transfusions. For platelets, the FNHTR rate may be as high as 15% per unit transfused, whereas for RBCs the FNHTR rate is less than 1% per RBC unit transfused. As the symptoms of septic transfusion reactions often mimic those occurring with FNHTRs, many apparently mild septic transfusion reactions may not be recognized as such. Moreover, most of the organisms isolated from contaminated platelet and RBC units tend to be skin-associated organisms (i.e., Gram-positive cocci), which are not usually implicated in RBC-associated septic transfusion reactions, and are often considered contaminants related to procedure of taking the sample for culture (i.e., a false positive).

Signs and Symptoms of Transfusion-Associated Sepsis

The transfusion of a contaminated cellular blood product unit may be associated with variable signs and symptoms. As indicated above, not all contaminated blood products cause symptoms in the recipient; in fact, it appears that many do not.[28] The initial signs and symptoms, when they occur, include fever and chills, which usually begin shortly after (within 2 hours) the start of the transfusion. Subsequent signs may include: hypotension, nausea, vomiting, diarrhea, oliguria, and shock. Other potential presenting symptoms include: respiratory symptoms (dyspnea, wheezing, and/or cough) and bleeding due to the consequence of endotoxin-induced disseminated intravascular coagulation. It is important to note that a majority of septic transfusion reactions associated with contaminated RBCs usually occur with units that have been stored for more than 21 days, whereas septic reactions associated with contaminated platelets usually occur with units that have been stored for 3 days or more.[28]

The clinical severity of a transfusion-associated septic reaction can vary considerably, depending on: (1) the species of bacteria present in the blood product unit, with Gram-negative organisms tending to cause more severe reactions, due to the presence of endotoxin often elaborated by such organisms; (2) the total number of bacteria infused or present in the cellular blood product unit infused to a recipient; (3) the rate of propagation of the bacteria present; and (4) recipient characteristics, such as underlying disease, leukocyte count, the status of the immune system, and whether the recipient is receiving concomitant antibiotic therapy.

Sources of the Bacterial Contamination for Cellular Blood Products

Possible mechanisms of the bacterial contamination of blood components include: donor bacteremia, contamination during the whole blood collection procedure, contamination of the collection pack, and contamination during the blood processing procedure.

Donor bacteremia

Blood donors with an asymptomatic bacteremia or who are in the recovery phase of a bacterial infection, may have transient bacteremic episodes and still qualify as a blood donor. Approximately 30 cases of *Yersinia enterocolitica* sepsis associated with RBC transfusion have been reported in the literature. This Gram-negative bacillus may cause enterocolitis, characterized by diarrhea, low-grade fever, and abdominal pain in the donor. Symptoms may be very mild and asymptomatic cases have been documented. In cases of transfusion-associated *Yersinia enterocolitica* septicemia reported to the CDC, approximately 75% of the implicated blood donors recalled having had diarrhea in the days preceding or following their blood donation, on retrospective questioning.[42] Transfusion-associated *Yersinia enterocolitica* sepsis varies markedly from country to country, with an estimated incidence of 1 per 65,000 transfusions in New Zealand to 1 per 500,000 transfusions in the US.[43,44] It is important to note that *Yersinia*-related sepsis is very episodic. Thus, over longer time intervals, the rates in these two countries might be different.

Bacteremia of short duration may also occur following dental manipulation such as tooth extraction, the use of gum irrigation devices, and even tooth brushing. A case of transfusion-associated *Staphylococcus aureus* platelet contamination has been documented, likely the result of a bacteremia in a blood donor who had undergone the repair of a tooth 3 hours before the donation.[45]

Contamination during whole blood collection

Contamination at the time of blood collection is the major cause of bacterial contamination of platelet units. The majority of organisms present in both culture studies and case reports of platelet-associated sepsis is usually normal skin flora as it may be virtually impossible to totally decontaminate human skin. Blood culture results show an incidence of positive cultures, ranging from 2% to 6% after the cleansing of the skin.[46] In addition, it has been postulated that a small core of skin may enter the phlebotomy needle at the time of donation and that viable bacteria remain associated with the deep layers of skin, in spite of adequate skin disinfection.[47] In the presence of a scarred phlebotomy site, surface cultures may be negative, while blood cultures are positive.[48] Organisms not part of the normal skin flora may colonize on the skin and be associated with a septic transfusion reaction. A recent report of a fatal reaction due to *Clostridium perfringens* was linked to a

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donor who frequently changed his infant children's diapers. This organism, as well as other species, normally part of fecal flora, grew in arm swab cultures from the implicated donor.[49] Although not linked to episodes of bacterial contamination of blood products, skin disinfection materials including swab sticks containing iodine or alcohol have been reported to be contaminated by various bacterial species.[28]

Contamination of the collection pack

Leaky seals, damaged tubing, or micro-punctures in collection bags have been linked to episodes of bacterial sepsis.[50] Regularly, blood packs used to collect donor blood have been found to have micro-punctures, possibly leading to the bacterial contamination of a cellular blood product.[28] Moreover, it has been reported that blood packs in the absence of any defects may be heavily contaminated. A report published in 1999 reported 6 patients who developed septicemia with *Serratia marcescens*, following transfusions with red cells or platelets.[51] This outbreak was traced to the heavy contamination of the exterior of blood packs. Upon investigation, 0.73% of blood bags from the same lot of packs grew the same ribotype of *Serratia marcescens*. It was postulated that the bacteria probably entered the blood bag at the time of blood donation, either by suction into the needle or due to contamination of the phlebotomist's hands and subsequently the donor's skin.[51]

Strategies to Decrease the Transfusion-Associated Morbidity/Mortality Risk of Contaminated Cellular Blood Products

A variety of strategies have evolved in recent years in an attempt to decrease the morbidity and mortality risk associated with transfusion-associated bacteremic and septic episodes. These measures are aimed at reducing the risk of the transfusion of cellular blood product units that are contaminated with bacteria by: (1) reducing recipient exposure; (2) avoiding contamination (i.e., improved donor screening or better skin disinfection); (3) optimizing blood component processing and storage; and (4) implementing tests and procedures that can be used to detect the presence of bacteria in blood product units.[28] These approaches are summarized in **Table 7**.

Improving donor skin disinfection

Because most of the bacteria isolated from contaminated blood products are normal skin flora, optimal disinfection of donor venesection sites may significantly reduce the bacterial contamination of blood products.[52,53] Recent studies exploring blood culture contamination rates of blood products have demonstrated that both the quality of the antiseptic used and/or the mode of application of the antiseptic can influence the efficacy of skin disinfection. Thus, one possibility of reducing the prevalence of blood product bacterial contamination might be to improve donor skin disinfection.

Removal of first aliquot of donor blood

Even if skin disinfection is optimal, bacteria may be introduced into the blood container by means of a skin core, which is often taken inadvertently when the blood collection needle enters the skin.[31] This has been reported to occur in approximately 65% of all venepunctures.[47] Recently, studies have suggested that when a needle tip is contaminated, the majority of the contaminating bacteria can be detected in the first few millimeters of blood passing through the venepuncture needle. Several recent studies suggest that the diversion of the initial 15 to 30 mL of whole blood from the main container might be associated with reduced risk of bacterial contamination.[54-56] Several blood bag manufacturers have developed plastic software to accommodate such an option. Several countries, including Canada, have recently introduced this intervention to try to reduce the rate of transfusion-associated sepsis.

Pretransfusion detection of bacteria

The pretransfusion detection of bacteria is an important potential method to reduce the risk of transfusion-associated bacteremia and septic reactions. However, no single

Table 7. Proposed strategies to reduce transfusion-associated septic risk.

A. Reducing risk of blood product contamination:
   1. Improved donor screening.
   2. Improved venepuncture site disinfection.
   3. Removal of first aliquot of donor blood.

B. Optimizing blood component processing and storage:
   1. Optimize storage temperature.
   2. Limit storage time.
   3. Universal leukocyte reduction.

C. Reduce recipient exposure to blood donors:
   1. Optimize transfusion indications.
   2. Reduce transfusion triggers for RBCs and platelets.
   3. Increase use of apheresis-derived products.

D. Pretransfusion bacterial detection:
   1. Visual inspection of components before issue.
   2. Direct staining for bacteria.
   3. Bacterial ribosomal assays.
   4. Assays for bacterial endotoxin.
   5. NAT for bacterial DNA.
   6. Measure CO_2 production by bacteria.
   7. Measure O_2 consumption by bacteria.
   8. Direct bacterial culture (manual or automated).

E. Implement pathogen reduction methodology when available.

Abbreviations: NAT, nucleic acid test; RBCs, red blood cell units.

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currently available laboratory technique is ideal.[15] Pretransfusion detection of bacteria is much more complex than traditional transmissible disease testing, because the amount of bacteria present in a particular cellular blood component usually changes over time. Moreover, because the initial inoculum is usually very small (less than 10 organisms per mL) even a very sensitive technique will miss some contaminated units, if the testing is performed very soon after blood collection.[15]

Automated blood culture methods are being used currently in some European and US centers to test buffy-coat platelets or apheresis platelet concentrates for the presence of bacterial contamination. Because of the larger volume of these products, a 10-mL sample can be used for bacterial culture, substantially improving the sensitivity of detection. Various protocols are in use to culture platelet units: this can be done either shortly after component production, or only for platelet units that have not been transfused by day 3 of storage. A quarantine period of 24–48 hours after inoculation into a culture tube is used in some European centers, prior to issuing such platelet units. In several European countries, the regulatory authorities have accepted the extension of the platelet shelf life to 7 days, for platelet units on which bacterial cultures have been performed. Reduced platelet outdating appears to offset the cost of such bacterial testing.[40]

Because the number of bacteria present in a contaminated blood unit increases over time of storage, less sensitive methods potentially can be used in the hospital blood bank to perform bacterial screening prior to transfusion. Relatively rapid methods of bacterial detection, such as Gram-staining or the detection of metabolic changes, are being used. However, screening with such low sensitivity methods may be inadequate to prevent some transfusion-associated septic reactions.[7]

Reducing recipient exposure

One approach that has not been extensively utilized in an attempt to prevent transfusion-associated bacterial contamination is to reduce recipient exposure. In this regard, it would be possible to reduce transfusion-associated septic events by reducing transfusion triggers. Recent studies for both the use of allogeneic RBCs as well as prophylactic platelet transfusions have suggested that reduced transfusion triggers do not endanger recipients. One suggested approach to reducing the risk of transfusion-associated sepsis due to contaminated platelets is to use apheresis platelets in preference to pools of whole blood-derived platelets.[5] The universal use of apheresis platelets would significantly reduce recipient exposure to contaminated blood products by a factor of 5. Five is the number of whole blood-derived platelet units usually used per platelet transfusion episode to an adult recipient. Finally, attention should be paid to optimizing transfusion indications. Audits of cellular blood transfusion use have regularly indicated that cellular blood products are often prescribed inappropriately. The reduction of such inappropriate use of cellular blood products should significantly reduce the incidence of transfusion-associated septic reactions.

Pathogen inactivation

Over the past 10 years, a number of photodynamic or photochemical methods have been reported that could lead to the reduction of viruses, bacteria, and protozoa that are present in cellular blood products.[15] These pathogen reduction devices include: the use of a combination of a psoralen and ultraviolet A (UVA) light; riboflavin and visible light; ultraviolet B irradiation; and the addition of methylene blue or phthalocyanines with visible light.[57-60] With regard to the bacterial inactivation of contaminated platelet concentrates, Lin et al reported that the novel psoralen amotosalen (S-59), combined with UVA light exposure has effective bacterial inactivation capability.[61] Thus, a combination of 150 μmol/L of the psoralen S-59 and 3 joules/cm UVA light result in significant bacterial reduction of contaminated apheresis platelets, as well as whole blood–derived platelets. Such methodologies are undergoing regulatory review in both North America and Western Europe.

Regulation and Regulatory Approaches

Prevention of bacterial contamination

Several approaches have been instituted by the transfusion community and the FDA to help minimize the chances of bacterial contamination of transfusion products at the time of collection. However, the improvement of collection techniques cannot prevent product contamination when the source is occult bacteremia in the donor; this risk may potentially be reduced by more careful and specific questioning of donors to identify recent medical procedures or symptoms that could indicate the onset of an infectious process. For sources of contamination associated with the collection method, steps can be taken that are more likely to decrease the risk.

An obvious first step is more effective sterilization of the phlebotomy site. The FDA has publicly discussed education about proper application of disinfectants and the problems with scar tissue.[62] More effective disinfectants have been recommended to sterilize the collection sites and the use of ineffective disinfectants, such as green soap, have been discouraged.[62] However, a careful review of the literature by FDA revealed that certain skin disinfection procedures using isopropyl

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alcohol followed by tincture of iodine that have been thought to be superior to those using povodone iodine actually are comparably effective in studies using hospitalized patients.[62] Sterilization of the skin surface also has limits when the phlebotomy needle cores out a skin plug as it passes through the skin. This inherently nonsterile skin plug can be carried into and seed the collected blood.

Recently, two studies have suggested that diversion of the initially collected blood to a separate container (referred to as a diversion pouch) away from the rest of the collected product that is to be used in transfusion could reduce the contamination rate. In a European study of actual transfusion products, diverting the first 15 mL of whole blood appeared to reduce the contamination rate of the final container.[63] Similar findings were also shown in an artificial model of blood collection.[56] The diversion pouch approach, using two recently FDA approved collection systems, is now being adopted by many blood centers as a way to lower the contamination risk. However, the ability of initial aliquot diversion to prevent clinical cases of transfusion-associated sepsis has not, as yet, been reported. It is important to note that this approach will only reduce the level of skin contaminants in blood products.

Prevention of bacterial proliferation—Refrigeration of platelets?

For red cells that are stored at 4°C, bacterial growth is slow and limited to a few psychrophilic bacteria such as *Yersinia enterocolitica*, *Pseudomonas* species and *Serratia liquefaciens*.[64] In comparison, platelets are stored at room temperature and provide a good medium for growth of both Gram-negative and Gram-positive bacteria. For most bacterial species, growth in platelet units can occur, rapidly reaching log phase within 24-48 hours.[12,26] An exception is the common skin contaminant, *Staphylococcus epidermidis* which is a slower growing organism and usually reaches the log phase in 48–72 hours. Since this and similar organisms account for a large proportion of the bacterial species found to contaminate blood units, such slower growth characteristics need to be considered when optimizing sampling strategies for bacterial detection.[65]

Rapid proliferation of bacteria during storage of transfusion products could be decreased if cold temperatures were used. For red cells, this is generally a standard practice and reduces the growth of most bacterial species and the risk of transfusion related sepsis. On the other hand, platelets do not maintain adequate function when stored at cold temperatures. Even relatively short exposures to cold are associated with irreversible changes in platelets that significantly decrease their ability to remain in circulation.[66] Attempts to understand the basis of the temperature sensitivity of platelets have only recently been productive.

A new study has suggested that platelets may respond to cold by clustering of GpIb on their surface which is then recognized by macrophages as a signal for clearance.[67] Better understanding of the molecular changes in platelet physiology after cold exposure could lead to alternate storage conditions that would allow cold temperature storage and a reduction of bacterial proliferation while preserving platelet function and viability. Evaluation of novel storage conditions would involve in vitro experiments to demonstrate that the platelets have not been extensively activated or damaged by the conditions. Since in vitro tests have a poor predictive value for clinical performance of platelets, the gold standard for platelet evaluation remains the recovery and survival of radiolabeled transfused platelets.[68] Platelets, collected from a single donor by apheresis, are divided into two products and stored under either conventional or novel conditions. At the end of storage a small portion of the cells is labeled with either ^{51}Cr or ^{111}In and the radiolabeled cells are reinfused into the original donor. Serial blood samples are then taken to monitor clearance of the cells from circulation. The double label allows for a direct comparison of the same platelets stored under different conditions in the same recipient.

Detection of bacteria in transfusion products

Ultimately, the reduction of bacterial contamination of transfusion products will require routine testing of the products for the presence of bacteria. Attempts to detect bacteria in transfusion products have spanned the range of simple to highly sophisticated state-of-the-art methodologies. On the low tech side, changes in the appearance of the product, such as platelet swirling or the color of the red cell units, have been utilized but with low specificity and sensitivity.[69] Other tests such as determining pH or glucose levels, or direct bacterial staining with Gram's stain or acridine orange have similarly not been very useful due to relatively low sensitivity when compared with bacterial concentrations that can cause sepsis. Tests with bacteria-specific nucleic acid probes or fluorescent dyes or antibodies are currently being developed.[70,71] However, the most useful detection systems currently available appear to be automated, culture-based methods similar to what has been used for clinical detection of bacteremia in blood cultures obtained from patients.[65]

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Sampling strategy for detection of bacteria in a transfusion product

Currently utilized platelet products are either random donor or apheresis units. Both types of units may be stored individually for up to 5 days at room temperature. Approximately 4–6 random donor units are pooled prior to transfusion to achieve a transfusion product with sufficient platelet content. The major factor in sampling either a random donor unit or an apheresis unit is the difference in volume. A typical apheresis unit contains approximately 200–250 mL while the random donor unit contains only 45–55 mL. Thus, the volume of the sample taken for bacterial detection can have a significant impact on the amount of product left for transfusion, particularly for random donor units. On the other hand, a larger sample volume increases sensitivity and thus a balance has to be reached to optimize sensitivity and minimize the impact on the product.

The timing of sampling is highly dependent on the method of detection. For culture-based methods, the product sample is inoculated into a container (bottle or bag) that allows for bacterial growth. Usually this occurs at 37°C and in the presence of sodium polysulfone (SPS), a bacteria growth-potentiating substance, that allows the bacteria to grow faster in the device than in the transfusion product. As the bacteria proliferate in the device, there is a fixed amount of time before a positive signal can be detected. The time to detection, dependent on the initial inoculum and the growth characteristic of the bacteria, is usually 24-48 hours when employing currently available detection methods. Because of this time required, the ideal sampling time for culture-based devices is as early as possible in the storage period so that a test-based decision about the clinical usefulness of the product can be made prior to its use. However, since the level of contamination at the time of collection is low and bacteria could be missed by a sampling error (especially with a low sample volume) at the beginning of storage, a certain amount of presampling storage time is usually allowed for the bacteria to begin to proliferate in the product. For platelets this is usually 24–48 hours.

The length of this presampling incubation period also depends on the sensitivity of the detection device. A more sensitive device can utilize a sample collected earlier in the product storage period while a less sensitive device would require a sample that contains more bacteria as occurs later in storage. The sampling strategy can be altered for a detection method that detects bacteria in real time. These approaches utilize probes, antibodies or nucleic acid–based detection system and can produce an answer within hours of sampling. The sensitivity of culture-based assays should be in the range of 10–100 CFU/mL and the sensitivity of methods that could be used at the point of transfusion would most likely be in the range of 100–1000 CFU/mL.[26]

Current approval process for bacterial detection devices

The FDA has encouraged manufacturers to submit applications for devices that will detect bacteria in transfusion products. The most urgent need is for bacterial screening of platelet products. Two devices have recently been cleared by the FDA for use in quality control monitoring of the platelet collection process that, in the past, was performed by manual culture (BioMeriuex, Inc. BK 000042; Pall Corp. BK 020014). The current devices allow sampling of the platelet product and automation of the quality control culture process. One device detects bacteria based on elaboration of CO_2 in the sample culture, while the other detects a decrease in pO_2. *However, these devices have not yet been specifically approved for use in release of platelets for transfusion because the effectiveness of the devices to detect bacterial contamination in the clinical setting has not been established.*

For the quality control indication, the validation was based on in vitro "spiking" experiments. A unit of platelets, either whole blood–derived, random donor, or apheresis-derived, single donor, was deliberately contaminated with a known amount of a single bacterial species. The unit was then repeatedly sampled 10 times and each time the sample was inoculated into the device. Thus, 10 separate readings were performed by the device for each bacterial species. The manufacturers were encouraged to validate their devices for as many bacterial species as possible and a list of the most common relevant bacteria was agreed on based on literature search, FDA advisory committee input and public workshops input.[10,65]

Trials recommended under "actual clinical use" conditions

The FDA has proposed that validation of bacterial detection devices for release of platelets for transfusion would require a field trial of the device under actual clinical use conditions.[62] The design of such a trial would be to obtain a sample for bacterial detection by a culture-based device early in the storage period. A second sample would then be taken at the end of the storage period or at the time of release of platelets. The results of both cultures would be compared to determine if the first culture was predictive of the result of the second culture. If the unit is contaminated at collection, then the bacteria will have time to grow between the first and second sampling. The bacterial load

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should be higher and detection of bacteria should be easier at the second sampling.

The needed studies should demonstrate that a sample taken early in the storage period and screened by the automatic culture device is predictive of the culture results up to the time of outdate of the product. Although some aspects of the study could be modeled in vitro it is not clear what is the expected level of bacterial contamination under actual clinical conditions, whether the devices will have sufficient sensitivity or whether sampling errors may occur when low levels of bacteria are present early in the storage period. In addition, such studies will also demonstrate the false positive rate and rate of contamination, if any, from bacteria introduced by sampling and inoculation procedures.[72] An excessive false positive rate would lead to an unnecessarily high discard rate for transfusion products.

Such issues raise the level of safety and efficacy concerns for devices intended for release of blood products for transfusion and are the basis for the current FDA practice of requesting clinical or field study data prior to approval of the devices. The field trials of the bacterial detection devices could be combined, under an IND or IDE application, with an extension of storage to day 7 or with pre storage pooling, allowing some costs to potentially be offset by savings from decreasing platelet product loss due to expiration and/or from pre storage leukoreduction of a pool instead of individual units.

Pathogen reduction technologies

As an additional measure of safety, transfusion products could potentially be treated with a pathogen reduction process to decrease or eliminate pathogens, including bacteria, which were not detected by testing. Methods are being developed that allow selective targeting of pathogens in blood products. The selectivity is based on absence of nucleic acids in platelets and red cells. A chemical compound is added to the transfusion product that interacts with the nucleic acids of pathogens and, upon spontaneous or light energy–induced activation, cross links nucleic acids and prevents their transcription and replication. Efficacy of these methods is usually established by in vitro studies where various pathogens are "spiked" into a platelet or red cell unit and then treated using the pathogen reduction methodology. The efficacy of these treatments should be in the range of 6–10 log reduction of common bacterial pathogens.[10]

However, from an FDA perspective, evaluation of the safety aspects of these methods is more complex and challenging. It includes assessment of possible damage caused by the treatment to the transfusion product (including functionality and survival of transfused cells) and evaluation of the potential toxicities of any residual chemicals to the recipients of the product. In fact, concerns about the safety of these products may arise because of mutagenicity of some of the chemical agents employed and thus their potential to be carcinogenic and genotoxic. In addition, the reactions of the chemical agent(s) with plasma and cellular proteins and lipids can create novel chemical entities that may have unexpected toxicities and increased immunogenicity when administered to certain patient populations. Because of the uncertainties that surround the treated products, even after extensive preclinical and clinical evaluation, it is likely that postmarketing studies will be needed to identify any low frequency adverse events associated with their use in a broader patient population. Another issue is whether the therapeutic efficacy of the treated transfusion products has been fully preserved after treatment with the pathogen reduction process. This is again being evaluated both in vitro and in Phase 2 and 3 clinical trials designed to follow efficacy endpoints, such as hemostasis in the case of platelet transfusions.

The final analysis of the documented and theoretical risks of the pathogen reduction process to the recipient of treated transfusion products will need to be weighed against the risk of the transfusion-transmitted diseases they could prevent, a risk which currently is relatively low. Thus, the clinical use of these products will ultimately depend on the appropriate risk benefit analysis for proposed uses and upon the data submitted for evaluation.

Transfusion product substitutes

The risk of transmitting pathogens by transfusion has been a major driving force for the development of manufactured substitutes for transfusion products. Such products would ideally be free of pathogens, have a long shelf life and may also not present the requirement of having to be serologically typed for each recipient. However, initial results of efforts to engineer red cells or platelets have so far fallen short of matching the natural cells. For example, initial efforts using the hemoglobin molecule to carry oxygen has been associated with a variety of toxicity issues.[73] Additional research and clinical testing will need to be done to fully evaluate and, hopefully, realize the potential of these types of products.

Bacterial detection and the extension of platelet storage

Increased risk of bacterial contamination has been the major concern regarding prestorage pooling of platelets and extension of platelet storage beyond the currently allowed 5 days. For pooled platelets it has been demonstrated that a platelet pool created by combining

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1 contaminated unit with 3–4 other units permits greater levels of bacteria at stationary phase.[74] Until 1986, platelets could be stored for up to 7 days at room temperature. However, due to concerns over a rise in clinically significant transfusion-associated infections from an increased bacterial load at the end of an extended storage period, this was shortened to 5 days on the advice of an FDA scientific advisory committee.

Returning to platelet storage beyond 5 days and allowing prestorage pooling of platelets would require an appropriately validated effective bacterial detection system. Such validation would involve in vitro testing with pooled products and a field trial in a clinical setting. In addition to bacterial detection the storage conditions for pooled platelets and platelets stored beyond 5 days will need to be validated to demonstrate that platelet quality is preserved under these conditions.[75] Use of FDA-approved sterile connection devices otherwise allows pooling and sampling of platelets without introducing bacterial contamination through the pooling process itself.[62]

Regulatory summary

Bacterial contamination of transfusion products, especially platelets, is a significant clinical problem with multiple causes. Based on recognition of this issue, the FDA and the blood industry have taken steps to improve control of bacterial contamination at multiple steps during blood collection and processing. Dealing effectively with this problem will involve continued and enhanced education of phlebotomy, technical, nursing, and medical staff with regard to sources of contamination and the importance of the problem. Using approved products and procedures, blood collection centers can implement practices that may decrease bacterial contamination, including better skin disinfection, collection of blood with a diversion pouch set, testing for bacteria, and, potentially, the use of safe and effective pathogen reduction technologies if and when available. Promising technologies for bacterial detection appear to be close at hand and offer significant potential to screen out contaminated units. The FDA and the blood community share a common goal that increased efforts focused on the problem of bacterial contamination will be translated into successes comparable to those we have already achieved in decreasing risks from most transfusion transmitted viral diseases.

Concluding Comments

Septic transfusion reactions associated with the use of contaminated blood products remain a very significant adverse event. Nonetheless, clear-cut approaches to reduce the frequency of such events are appearing. A wide variety of measures have been proposed in order to reduce the frequency of transfusion-associated septic reactions and many of these measures are being actively investigated, and in some countries being instituted.[15,76] Thus, the potential reduction in the risk of transfusion-associated septic reactions is a realistic possibility in the foreseeable future.

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Updated Review of Blood Culture Contamination

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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

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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

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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).

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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

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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

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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

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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.

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Differential Quantitative Blood Cultures in the Diagnosis of Catheter-Related Sepsis in Intensive Care Units

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The aim of this prospective study was to compare differential blood cultures and quantitative catheter tip cultures for the diagnosis of catheter-related sepsis. Over a period of 2 years, 283 central venous catheters were inserted in 190 adult patients. Catheters were removed when they were no longer needed or when infection was suspected. Immediately before removal of the central venous catheters, blood cultures were performed, with blood drawn simultaneously from the catheter and the peripheral vein. After removal, quantitative catheter culture was performed according to the Brun-Buisson modified Cleri technique. Fifty-five quantitative catheter cultures were positive. They were classified as contaminated (n = 18), colonized (n = 23), or infected (n = 14). Differential blood cultures correctly identified 13 infections. With a catheter/peripheral cfu ratio of 8, differential blood cultures had a sensitivity of 92.8% and a specificity of 98.8%. When the catheters were removed because of suspected infection, differential blood cultures had a sensitivity of 92.8% and a specificity of 100%. Differential blood culture, a technique that does not necessitate catheter removal, seems effective in the diagnosis of catheter-related sepsis in patients in the intensive care unit.

Infection is the main complication related to the use of central venous catheters (CVCs). Catheter-related infection (CRI) is a major cause of nosocomial infection and may be life-threatening [1]. The diagnosis of CRI remains difficult. Clinical signs lack sensitivity and specificity. It is widely accepted that when a patient in the intensive care unit (ICU) becomes febrile, infection of the CVC is suspected and it is removed [2]. However, 70%–85% of CVCs are removed unnecessarily [2–4]. Moreover, the insertion of a new CVC is not without complications, especially mechanical [5]. Therefore, a technique allowing the diagnosis of CRI without removal of the catheter would be of great interest.

Differential quantitative blood cultures (DBCs) of blood withdrawn from the CVC and from a peripheral vein have been evaluated in hematology and oncology patients and in patients receiving long-term parenteral nutrition [6–10]. The few studies comparing this technique to a "gold standard" have given conflicting results [11–14]. Moreover, few data are available concerning ICU patients. The aim of our study was to compare DBC with a reference technique for the diagnosis of CRI in patients treated in ICUs.

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Informed consent was obtained from all patients or their next of kin.
This study followed the guidelines of the Institutional Review Board.
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Patients and Methods

The study was approved by the hospital's Institutional Review Board. Informed consent was obtained from all patients or their next of kin. Patients hospitalized in a surgery-trauma ICU and in a medical ICU were included during the 25-month period of November 1992 through November 1994. Patients were eligible if a CVC (either single or multiple lumen) inserted while the patient was in the ICU was scheduled to be removed. Several CVCs inserted in the same patient could be included in the study. Many patients in the study units were not eligible because they entered the units with a CVC inserted elsewhere or were discharged with their CVC still in place. People who died in the units with their CVC in place were not included. Arterial and pulmonary catheters were excluded, but introducer sheaths were included. All inserted CVCs were polyurethane. The insertion site was the jugular, subclavian, or femoral vein. None of the CVCs were tunneled.

Physicians of both ICUs inserted the CVCs after surgical hand-washing and the donning of masks, sterile gowns, and gloves. The puncture site was prepared first with a solution of quaternary ammonium, then ether, and then iodine/alcohol. The surrounding areas were covered with sterile drapes. After insertion of the CVC, an occlusive gauze dressing was placed following application of povidone-iodine. The dressings were changed every 48 hours.

When it was decided to remove the CVC, the connection of the CVC and the venous line were externally disinfected with iodine/alcohol. Then the line was disconnected and a sterile syringe was inserted in order to withdraw 5 mL of blood. For multiple-lumen CVCs, blood was withdrawn from each port.

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Immediately after, 5 mL of blood was obtained from a peripheral vein by standard venipuncture and placed in a heparinized tube. Then each intravascular device was removed aseptically after sterilization of the skin-puncture site. The distal segment of the catheter tip (5 cm) was cut off with sterile scissors, dropped into a tube, and sent to the laboratory.

The catheter tip was cultured according to the technique described by Brun-Buisson et al. [15], adapted from Cleri et al. [16]. In brief, 1 mL of sterile water was added into the tube containing the catheter tip. The contents were mixed for 1 minute, and 0.1 mL was sampled and plated on the surface of 5% horse blood agar. The agar plates were incubated at 37°C for 5 days. If colonies were observed, the number was recorded. The culture was considered positive when bacterial growth was observed. Identification and antimicrobial susceptibility assessment were conducted according to standard laboratory methods.

Blood withdrawn from the CVC and the peripheral vein was treated with use of the pour-plate technique [6–12]: 1 mL of nondiluted blood and 1 mL of serial blood dilutions (10^{-1}, 10^{-2}, 10^{-3}) were added to 19 mL of melted brain-heart infusion agar cooled to 45°C and poured into petri dishes. All plates were incubated for 5 days, and cfu were counted. When no growth was observed, the count was taken as 1 for the calculation of catheter/peripheral ratio. The DBC was considered positive when the catheter/peripheral cfu ratio was greater than 1.

Catheter findings were divided into three categories [4–15]. Catheter contamination was defined as the presence of $<10^3$ cfu/mL by the quantitative catheter-tip technique, without any local or general sign of infection. Catheter colonization was defined as the presence of $>10^3$ cfu/mL by the quantitative technique, without any local sign of infection. In this category, general signs of infection might be present and related to a remote septic focus, and clinical sepsis did not resolve within 48 hours after catheter removal. CRI was defined as a positive tip culture with a bacterial count of $>10^3$ cfu/mL, in association with general signs of infection (which disappeared after catheter removal), without any focus of infection with the same microorganism. The CRI could be accompanied by bacteremia.

Statistical Analysis

Published studies were analyzed to estimate the sample size for catheters. Assuming a prevalence of CRI in ICU patients of 5%–10%, and using data from a preliminary study indicating sensitivity of 90% and specificity of 94%, we decided 250–300 catheters would be required to obtain a positive predictive value between 60% and 80% with a precision of 5% α level. Thus, 300 catheters were included.

Using the quantitative catheter-tip culture as a reference, the sensitivity, specificity, and positive and negative predictive values were calculated at different catheter/peripheral cfu ratios. Sensitivity was plotted against specificity with use of a receiver operating characteristic (ROC) curve [17]. Quantitative results were expressed as mean ± standard deviation. Categorical results were given with their 95% confidence interval.

Results

During the 2 years, 283 CVCs were inserted in 190 adult patients.

Quantitative cultures of the catheter tip. One hundred and fifteen patients were hospitalized in the surgical unit and 75 in the medical unit. They were comparable with respect to age (45.9 ± 19.2 vs. 56.6 ± 19.6 years), sex, simplified acute physiologic score (SAPS) (11 ± 5 vs. 14 ± 4) [18], length of ICU stay (24 ± 16 vs. 21 ± 22 days), and antibiotic treatment (112/115 vs. 73/75).

Of the 283 studied catheters, 55 (19%) were positive in quantitative catheter-tip cultures. Of these positive results, 18 were considered contaminations; 23, colonizations; and 14, infections (table 1). The organism distribution pattern was similar among contaminated, colonized, and infected catheters, with a large predominance of staphylococci (76% of all isolates).

Fourteen catheters from different patients were considered infected. These catheters were inserted in 14 patients (age, 56.9 ± 18.4 years; SAPS, 13 ± 5; ICU stay, 36 ± 18 days), of whom 12 were treated with antibiotics for a remote septic focus. Bacteremia was associated with nine of these catheters. None of the bacteria were susceptible to the antibiotics previously prescribed. For the patients with infected catheters, the quantitative cultures, indicative of infection, were positive within 18–36 hours.

Differential blood cultures. Among the 283 catheters, 19 (from 19 patients) were DBC-positive (table 2). Among the catheters, 8 were inserted in the jugular vein, 7 in the femoral vein, and 4 in the subclavian vein. Of the 14 CRIs according to the quantitative catheter-tip cultures, 13 were associated with a positive DBC.

ROC curve analysis was carried out by varying the catheter/peripheral cfu ratio (figure 1). The combined sensitivity and specificity were most satisfactory at a ratio of 8. With use of this threshold, the DBCs were positive for 16 catheters as well as for the 13 catheters previously considered infected. Sensitivity, specificity, and predictive values are reported in table 3.

Discussion

When CRI is suspected in ICU patients, the removal of the catheter is generally proposed. However, as many as 80% of the catheters removed will be sterile [4]. Furthermore, the insertion of a new catheter carries its own risk of complications, especially mechanical. In a study of 160 ICU patients, insertion of CVCs at new sites has been shown to lead to complications such as pneumothorax or arrhythmias in 9% of patients [5].

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Table 1. Characteristics of the catheters removed from ICU patients and analyzed in the study.

	Positive in catheter tip culture			Negative in culture (n = 228)	All catheters (n = 283)
	Contaminated (n = 18)	Colonized (n = 23)	Infected (n = 14)		
Insertion site					
Jugular	13	15	6	143	177
Subclavian	4	3	2	46	55
Femoral	1	5	6	39	51
Mean (±SD) duration of stay (d)	10 ± 5	10 ± 3	13 ± 5	10 ± 6	10 ± 5
Reason for catheter removal					
Infection suspected	7	11	14	86	118
No longer useful	11	12	0	142	165
Organism(s) identified					
Staphylococcus aureus	5	8	7		
Coagulase-negative staphylococci	8	10	4		
Other gram-positives	3	1	1		
Enteric gram-negatives	2	4	2		

Therefore, a technique allowing for the diagnosis of CRI without catheter removal would be useful in clinical practice. The ideal technique should have good specificity to prevent the removal of sterile catheters, but, more important, it should have good sensitivity. Indeed, this technique needs to be safe, presenting minimal risk of leaving an infected catheter in place. False-negative results should be minimized.

In 1979 Wing et al. first had the idea of performing cultures of blood withdrawn from the CVC and from a peripheral vein [6]. They compared both results and could establish the diagnosis of CRI in a patient. This observation led to the development of differential blood cultures for the diagnosis of CRI.

The aim of our study was to evaluate DBCs for ICU patients. As the ''gold standard'' for the microbiological diagnosis technique, we chose that proposed by Brun-Buisson et al. [15], adapted from Cleri et al. [16]. This technique allows for the detection of colonization of the external surface of the catheter tip and of its internal lumen. To identify false-negatives in the

Table 2. Data concerning the 19 positive differential blood cultures.

Catheter classification	Insertion site	Isolate	Differential blood cultures: cfu/mL in indicated specimen		
			CVC	P	CVC/P ratio
Sterile	Jugular	*Klebsiella oxytoca*	10^2	<1	10^2
Sterile	Subclavian	*Klebsiella oxytoca*	16	<1	16
Sterile	Femoral	*Enterobacter cloacae*	10^2	<1	10^2
Sterile	Subclavian	*Staphylococcus epidermidis*	2	<1	2
Colonized	Jugular	*Staphylococcus aureus*	2	<1	2
Colonized	Jugular	*Escherichia coli*	4.4×10^3	<1	4.4×10^3
Infected	Jugular	*Staphylococcus aureus*	10^4	20	5×10^2
Infected	Jugular	*Staphylococcus aureus*	5×10^3	10	5×10^2
Infected	Femoral	*Staphylococcus aureus*	10^4	3	3.3×10^3
Infected	Jugular	*Staphylococcus aureus*	4.6×10^3	<1	4.6×10^3
Infected	Subclavian	*Staphylococcus aureus*	7×10^2	90	8
Infected	Femoral	*Staphylococcus aureus*	3×10^5	2×10^3	1.5×10^2
Infected	Femoral	*Staphylococcus epidermidis*	8×10^2	<1	8×10^2
Infected	Femoral	*Staphylococcus epidermidis*	4×10^6	10^3	4×10^3
Infected	Femoral	*Staphylococcus epidermidis*	1.5×10^6	<1	1.5×10^6
Infected	Jugular	*Staphylococcus epidermidis*	5×10^2	<1	5×10^2
Infected	Subclavian	*Escherichia coli*	4×10^3	<1	4×10^3
Infected	Jugular	*Escherichia coli*	3.5×10^3	<1	3.5×10^3
Infected	Femoral	*Corynebacterium* species	6×10^4	<1	6×10^4

NOTE. CVC = central venous catheter; P = peripheral vein. When the number of cfu in the peripheral vein was <1, it was considered as 1 for the calculation of the CVC/P ratio.

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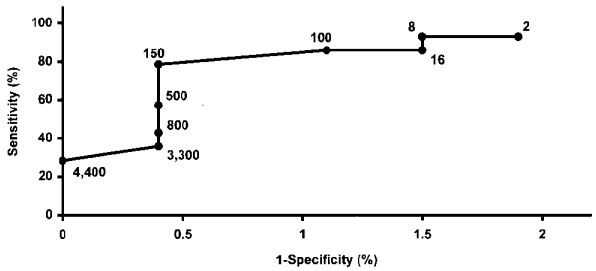


Figure 1. Receiver operating characteristic curve for ratio of bacterial counts in culture of the blood withdrawn from the catheter and culture of blood from a peripheral vein. The numbers on the curve are respective cutoffs in the differential blood cultures.

microbiological techniques, local and general signs of infection were noted at the time of the sepsis suspicion and after catheter removal. The reason for removal could be either that infection was suspected because of local signs (local inflammation or infection) or general signs (fever, chills, etc.), or else that the catheter was no longer needed.

We found a rate of 4.9% of infected catheters and 7.3% of patients with CRI. Bacteremia followed catheter infection in 3.1% of catheterized patients. *Staphylococcus aureus* was the predominant organism associated with bacteremia. This is in accordance with findings in other studies of ICU patients [11, 12, 15]. Although yeast may be responsible for CRI in the ICU, especially in immunocompromised patients, no fungal infection was identified.

DBCs have been evaluated in several studies, including a comparison with another microbiological technique. In a group of 24 patients receiving parenteral nutrition, Fan et al. found that DBC correctly identified seven of nine infected catheters [12]. They used an arbitrary threshold of seven for the catheter/peripheral cfu ratio. Sensitivity was 77.8% and specificity was 100%, with no false-positive results.

These interesting findings were brought into question by the results from Paya et al. [13]. In a study including 44 patients in a surgical ICU with suspected CRI, 15 catheters were considered infected according to a semiquantitative technique; DBC identified only 7 of these catheters. In that study, with regard to six catheters classified as DBC-false-negative, high organism concentrations (>100 cfu/mL) were observed in the blood withdrawn from the catheter and from the vein. In fact, a dilution of these samples might have yielded a positive DBC. In addition, the investigators did not include any clinical information in the definition of CRI. Thus, it was impossible to separate colonizations and infections of the catheters.

Finally, bacteria responsible for CRI were different from those found in other studies, including ours. *Pseudomonas aeruginosa* was found in more than half of the CRIs, and *S. aureus* accounted for only 6% of the isolated organisms. This difference may be explained by variations in the pathogenesis of the infections and may reflect differences in the efficiency of DBC.

In another study of patients hospitalized in internal medicine and surgical wards and the ICU, 107 catheters were evaluated, and DBCs identified 16 of 17 CRIs. DBC was found to be reliable, with a sensitivity of 94% and a specificity of 100% [11]. Recently, in patients with cancer (n = 31) and in the ICU (n = 27), DBC identified correctly 30 of 36 CRIs; the 6 remaining cases were false-negatives because removal of these catheters led to resolution of clinical signs of infection [14]. It is interesting that 16 patients with CRI had a negative tip culture, and CRIs were found to be related to hub infection. If this finding is confirmed, the efficacy of DBC as compared with that of tip cultures would be reinforced.

In all of these studies the catheter/peripheral cfu ratio was chosen arbitrarily. The range of this ratio was wide, between 2 and 30. In our study, the ROC curve technique was used to determine the ratio of the DBC that gives the best performance in diagnosis of CRI. With a threshold of 8, sensitivity was maximal, decreasing the number of false-negatives with the technique. This value is close to those chosen arbitrarily in other studies [11–14]. With this cutoff, sensitivity and specificity of DBC were very high. The few false-positive results led to the removal of sterile catheters, but these cases are few in contrast to the large number of catheters that can be safely left in place.

The DBC technique may have some potential drawbacks. First, the one false-negative result of the study raises an important issue because an infected catheter may remain inserted. All the studies of DBC have found false-negative results, but sensitivity remained up to 80%. These results may be explained by strictly external contamination of the catheter, missed by the DBC. However, to our knowledge, a method of diagnosis of CRI with 100% sensitivity and 100% specificity does not

Table 3. Sensitivity, specificity, and predictive values of differential blood cultures for all catheters and for catheters removed for a suspected infection. (Percentages and 95% confidence limits are given.)

Catheters removed	Sensitivity	Specificity	PPV	NPV	Accuracy
All (n = 283)	92.8 ± 3.0	98.8 ± 1.2	81.2 ± 4.5	99.6 ± 0.7	98.5 ± 1.4
For suspected infection (n = 118)	92.8 ± 3.0	100	100	99.0 ± 0.9	99.1 ± 1.7

NOTE. NPV = negative predictive value; PPV = positive predictive value.

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exist. In all circumstances, the results of the technique must be interpreted cautiously and clinical evaluation must remain the first criterion of CRI diagnosis, leading to the removal of the catheter if there is any doubt.

The second problem is related to the time necessary to obtain results from quantitative cultures, generally between 24 and 48 hours. In some circumstances, this delay will be too long for a patient with signs of severe infection. In this case, the catheter has to be removed. In our study, the catheters were cultured over 5 days to be certain not to miss late bacterial growth. However, no culture was positive after 48 hours.

Finally, the technique of DBC has a cost. However, this is balanced by the savings due to the limitation in wasting sterile catheters. In our study, 14 of 118 patients with a suspected CRI had a positive DBC, so 104 catheters were removed unnecessarily. Their replacement could have been avoided. A cost-benefit evaluation of the DBC technique must be done.

In conclusion, for ICU patients, DBC may be considered a useful tool for diagnosis of CRI without removal of the catheter. The possibility of false-negative results, although uncommon, must be kept in mind, and the persistence of sepsis syndrome without any evidence of other sources of infection must lead to the removal of the catheter. The technique cannot be used for all ICU patients, especially because of the time lag in obtaining culture results. However, this technique seems to decrease the waste of sterile catheters removed when ICU patients become febrile.

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Direct labeling and visualization of blood vessels with lipophilic carbocyanine dye DiI

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Abstract

We describe a protocol to rapidly and reliably visualize blood vessels in experimental animals. Blood vessels are directly labeled by cardiac perfusion using a specially formulated aqueous solution containing 1,1′-dioctadecyl-3,3,3′,3′-tetramethylindocarbocyanine perchlorate (DiI), a lipophilic carbocyanine dye, which incorporates into endothelial cell membranes upon contact. By lateral diffusion, DiI also stains membrane structures, including angiogenic sprouts and pseudopodial processes that are not in direct contact. Tissues can be immediately examined by conventional and confocal fluorescence microscopy. High-quality serial optical sections using confocal microscopy are obtainable from thick tissue sections, especially at low magnification, for three-dimensional reconstruction. It takes less than 1 h to stain the vasculature in a whole animal. Compared with alternative techniques to visualize blood vessels, including space-occupying materials such as India ink or fluorescent dye-conjugated dextran, the corrosion casting technique, endothelial cell-specific markers and lectins, the present method simplifies the visualization of blood vessels and data analysis.

INTRODUCTION

We describe here a direct labeling protocol[1,2] to visualize blood vessels in small experimental animals rapidly and reliably using a lipophilic carbocyanine dye, DiI ($DiIC_{18}(3)$). Lipophilic carbocyanine dyes, including DiI, have been widely used to label cell membranes[3–8] and to trace neuronal connections in live and fixed tissues[7–14]. In the cell membrane, a DiI molecule has its two hydrocarbon chains buried in the lipid bilayer parallel to the phospholipid acyl chains, and the chromophores are on the surface of the bilayer[15].

The direct labeling technique takes advantage of the lipophilic property of DiI. A special aqueous DiI solution is formulated to have the maximum sodium chloride concentration without causing precipitation of DiI. Glucose is added to maintain the physiological osmolarity. Labeling is achieved by bringing DiI solution in direct contact with endothelial cells through cardiac perfusion. A simple perfusion device is assembled with two three-way stopcocks, a butterfly needle and three 10-ml disposable syringes for phosphate-buffered saline (PBS), DiI solution and fixative, respectively (Fig. 1).

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During perfusion, DiI partitions quickly into the cell membrane (lipid) phase, the endothelial cell membrane lining the blood vessels, resulting in instantaneous labeling of blood vessels (Fig. 2). Once in the membrane, DiI molecules diffuse laterally within the lipid bilayer[3]. The lateral diffusion helps to stain membrane structures that are not in direct contact with the DiI solution, including angiogenic sprouts and psuedopodial processes of angiogenic endothelial cells (Fig. 3c,d).

As DiI is directly delivered to the endothelial cell membrane, it is possible to achieve high concentration in cell membrane and thus high signal intensities, which dramatically increases the signal-to-noise ratio. In addition, the dye itself is intensely fluorescent with slow fading when exposed to the excitation light[7,8]. The strong intensity and slow fading feature are ideal for serial optical sections using laser scanning confocal microscopy, especially at low magnification. Images can be obtained throughout the entire thickness of a tissue sample of 100 μm without noticeable deterioration of image quality. The vasculature in the inner surface of a hollow organ like the eye can be scanned as a single stack of confocal images at very low magnification (×5 objective lens). Digitized data of thick tissue sections can be used to reconstruct 3-dimemsional (3-D) images of vascular network in the samples of interest and/or to perform other analyses with suitable software. The 3-D images have the advantage of viewing the vascular network in its entirety (Fig. 3; Supplementary Movies 1–3 online). In addition, the use of thick tissue sections would save time and effort, as fewer tissue sections need to be prepared to cover the entire tissue sample. This is especially important when many samples are to be examined.

Many alternative techniques are available to visualize blood vessels. Space-occupying high-contrast materials, including India ink[16] and fluorescent dye-conjugated dextran (e.g., fluorescein isothiocyanate or FITC)[17], are used to fill blood vessels to render them visible. However, the dye molecules are not bound to blood vessels but move freely in the filling solution. When a tissue sample is compressed, especially during sample preparation, the filling solution can be squeezed out of blood vessels, resulting in interrupted or 'broken' vascular patterns. This method, however, directly stains the endothelial cell membranes.

The corrosion casting technique using low-viscosity plastics, another type of space-occupying material, to make casts of blood vessel network has been employed to study the three dimensionality of vasculature[18,19] in combination with scanning electron microscopy (SEM) [20,21]. The casts are viewed with SEM to obtain 3-D images of the vasculature. It is technically demanding to make casts and requires access to SEM[20,21]. It is also difficult to visualize angiogenic sprouts and pseudopodial processes. In comparison, the method described here is technically much simpler in sample preparation and data collection.

Blood vessels can also be visualized by endothelial cell-specific markers, including factor VIII (see ref. [22]) or CD34 (see ref. [23]). Lectins have been used as surrogate markers for endothelial cells. For example, *Ulex europaeus* I lectin recognizes human endothelial cells[24], and *Griffonia simplicifolia* isolectin B_4 specifically labels endothelial cells in mouse, rat and other laboratory animals[25,26]. Use of these markers usually requires multistep procedures. In addition, it is difficult for these techniques to achieve the high signal intensities that can be achieved by direct labeling methods described here.

The direct labeling technique with DiI provides an efficient, reliable and low-cost (the amount of DiI used per rat is less than 1 mg that costs less than USD $2) alternative to obtain high intensity, high signal-to-noise ratio labeling of blood vessels in the entire body for both low- and high-power microscopic observation. It can also be used to study angiogenic sprouts and pseudopodial processes. Although described here for use in rodents, this procedure can be adapted easily to the study of vasculature in other vertebrate animals including rabbits, either

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for the vasculature of the entire body or for *ex vivo* perfusion of a particular organ, such as rabbit kidneys.

In this method, DiI molecules are directly incorporated into the membrane of endothelial cells. As it is a lipophilic dye, the molecules in the membrane could be washed away by lipophilic solvents. It is therefore not easy to combine DiI staining with other techniques, such as immunohistochemical analysis, if the subsequent procedures involve those lipophilic solvents. This issue could be overcome by using a fixable DiI derivative, CM-DiI (C-7001, Invitrogen/Molecular Probes). CM-DiI is particularly useful in experiments that combine membrane labeling with subsequent immunohistochemical analysis, fluorescence *in situ* hybridization or electron microscopy. DiI staining is, however, compatible with the nuclear dye DAPI (4′-6-diamidino-2-phenylindole).

MATERIALS

REAGENTS

- DiI (D-282, Invitrogen/Molecular Probes; 42364, Sigma-Aldrich)
- Ethanol (100% vol/vol)
- NaCl (S7653, Sigma-Aldrich)
- KCl (P9333, Sigma-Aldrich)
- Na_2HPO_4 (S8282, Sigma-Aldrich)
- NaH_2PO_4 (S7907, Sigma-Aldrich)
- Glucose (G7568, Sigma-Aldrich)
- HCl (1 M) (13-1700, Sigma-Aldrich)
- NaOH (5 M) (S8263, Sigma-Aldrich)
- Glycerol (G6279, Sigma-Aldrich)
- Paraformaldehyde (158127, Sigma-Aldrich)
- Agarose (A5939, Sigma-Aldrich)
- Superglue (can be obtained from regular hardware stores)
- Experimental animals (rats and mice, Charles River)

▲ CRITICAL All animal experiments must comply with national laws and institutional regulations.

EQUIPMENT

- 25 gauge butterfly needles
- Microscope slides
- Standard BK7 glass coverslip (no. 1.5, 170 μm thickness)
- Three-way stopcocks
- 10-ml disposable syringes
- Aluminum boats
- Vibratome (VT1000S, Leica Microsystems)

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REAGENT SETUP

DiI stock solution—Dissolve 100 mg of DiI crystal in 16.7 ml of 100% ethanol on a rocker overnight (covered with aluminum foil when rocking) and store in the dark at room temperature (RT, 20–25 °C) for up to 1 year. ⁑ CAUTION DiI solution stains easily on skin and other surfaces. If accidental staining occurs, it can be wiped off easily by 70% ethanol.

PBS (pH 7.4)—Dissolve 8 g of NaCl, 0.2 g of KCl, 1.44 g of Na_2HPO_4 and 0.23 g of NaH_2PO_4 in 800 ml of distilled water. Adjust pH to 7.4 with HCl. Add water to 1,000 ml, filter through a 0.22-μm bottle-top filter. Store at RT for up to 1 year.

5% (wt/vol) glucose—Dissolve 50 g of glucose in 1,000 ml of distilled water. Filter through a 0.22-μm bottle-top filter. Store at RT for up to 1 year.

Diluent—Mix PBS and 5% glucose at a ratio of 1:4. Store at RT for up to 1 year.

DiI work solution—Immediately before use, add 200 μl of DiI stock solution into 10 ml of diluent, mix by quick shaking. DiI work solution should be freshly made under room lighting.

Phosphate buffer (pH 7.4)—Prepare separately a solution of 0.2 M NaH_2PO_4 and another one of 0.2 M Na_2HPO_4. Mix the two solutions at a ratio of 19:81. Check the pH with a pH meter. Adjust pH with either HCl or NaOH. Store at RT for up to 1 year.

8% (wt/vol) paraformaldehyde—Under a chemical hood, add 8 g of paraformaldehyde to 90 ml of distilled water in a beaker with a magnetic stirrer. Heat to 65 °C and adjust the pH to 7.4 (using pH paper) with 5 M NaOH. Add distilled water to adjust the final volume to 100 ml. Cool the solution and filter. Store at 4 °C for up to 1 month.

4% (wt/vol) paraformaldehyde solution—Mix 8% paraformaldehyde with 0.2 M phosphate buffer at a ratio of 1:1 before use. Store at 4 °C for up to 1 month.

80% (vol/vol) glycerol—Add 1 ml of distilled water into 4 ml of glycerol and mix well. Store at RT for up to 1 year.

5% (wt/vol) agarose—Add 20 ml of distilled water to a beaker, and add 1 g of agarose. Heat on a heat place until agarose melts. Keep 5% agarose to 60 °C. Agarose (5%) can be stored at 4 °C for up to 1 month. To use the agarose again, heat until it melts and keep it at 60 °C.

EQUIPMENT SETUP

Perfusion device—The perfusion device is assembled with two three-way stopcocks, a 25 gauge butterfly needle and three 10-ml syringes (Fig. 1). First, connect the two three-way stopcocks in series (Fig. 1, inset) and then the 25-gauge butterfly needle to the outflow port of the stopcocks (Fig. 1). Load the three syringes with 2 ml of PBS, DiI solution (5 ml for a mouse, 10 ml for a rat) and 10 ml of fixative (4% paraformaldehyde), respectively. Connect the syringe with fixative to the first inflow port and inject solution until there is no air in the line; turn the stopcock to block the port. Then, connect the DiI syringe to the second inflow port, inject solution until there is no air in the line, and turn the stopcock to block the port. Finally, connect the PBS syringe to the last inflow port and inject solution until there is no air in the line. Assembly is under room lighting. ⁂ CRITICAL Make sure that no air is trapped in the line or the syringes before proceeding to perfusion. Once in the circulation system, air will block blood vessels, resulting in poor perfusion.

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Aluminum boats—Cut a piece of Styrofoam into the shape and size of the samples of interest. Wrap the Styrofoam with a piece of aluminum foil, leaving one side open. Remove the Styrofoam and store the aluminum boats appropriately at RT.

PROCEDURE

Perfusion ● TIMING **~45 min**

▲ CRITICAL All steps are carried out under ambient lighting unless specified.

1¦ Assemble the perfusion device as described in EQUIPMENT SETUP.

? TROUBLESHOOTING

2¦ Kill a mouse or rat by CO_2 overdose in a CO_2 chamber, or by sodium phenobarbital overdose (120 mg kg^{-1}, i.p).

▲ CRITICAL STEP All animal experiments must comply with national laws and institutional regulations.

3¦ In a glass tray with an absorbing blue pat or several paper towels, position the animal on its back. Make a transverse incision to open the abdominal cavity. Expose and cut the diaphragm. Cut the chest wall on both sides up to the first or the second rib.

4¦ Take a small hemostat to hold the lower tip of the sternum and the turn the anterior chest wall toward the head of the animal to expose the chest cavity.

5¦ (Optional) If the tissues of interest are in the upper body, such as the brain or the eye, there is no need to perfuse the lower body. If this is the case, load half amount of the regular perfusion solutions in Step 1 and clamp the descending aorta to block the flow to the lower body before perfusion. This is not necessary for mice.

6¦ Insert the butterfly needle of the perfusion device into the left ventricle and then puncture the right atrium with a 16-gauge needle.

▲ CRITICAL STEP Make sure that the needle is in the left ventricle, which appears lighter than the right ventricle. Do not penetrate the opposite side of the ventricular wall. Such penetration will result in a leak in the left ventricle, making perfusion difficult.

? TROUBLESHOOTING

7¦ Inject 2 ml of PBS from the perfusion device at the rate of 1–2 ml min^{-1} (total 1–2 min). A sign of good perfusion is bleeding from the right atrium. After injection, turn the switch to block the port of PBS syringe and open the port to the DiI syringe.

? TROUBLESHOOTING

8¦ Inject 5–10 ml of the DiI solution at the rate of 1–2 ml min^{-1} (total 5–10 min). Monitor color change in the ears, nose and palms. DiI appears purple in visible light. During perfusion with DiI solution, the ears, nose and palms will turn slightly purple. After injection, turn the switch to block the port of DiI syringe and open the port to the fixative syringe.

9¦ Inject 5–10 ml of the fixative at the rate of 1–2 ml min^{-1} (total 5–10 min).

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10| Harvest tissues of interest. To make eyecup preparation, eyes are enucleated and the anterior segments are removed. The retinas are further dissected from eyecups[1]. Other tissues of interest can be harvested by directly removing them from the body.

PAUSE POINT Samples can be left in the fixative or PBS in the dark for up to 1 month at 4 °C.

CRITICAL STEP Be sure to place the used needles into a sharp container and to dispose of the animal and waste appropriately.

TROUBLESHOOTING

Tissue sectioning TIMING ~1–2 h, depending on the size of the tissue to be sectioned

11| Rinse samples in PBS 2× 15 min.

12| Embed tissue sample in 5% agarose: heat agarose in a 100-ml beaker to 60 °C and pour it (about one-third of the volume required to submerge the sample) into an aluminum boat that fits the sample. Submerge the tissue sample into the agarose and adjust the orientation. Add more agarose into the boat to keep the sample totally submerged. Samples can be kept at 4 °C in the dark up to 1 month when wrapped in plastic wrap to prevent dehydration. Remove the sample block from the aluminum boat before sectioning. Embedding is not necessary for solid tissue such as the brain and the liver.

TROUBLESHOOTING

13| Trim off excess agarose. Glue the sample to the section stage of the Vibratome using Superglue. Secure the section stage in the section chamber and adjust the sample to the appropriate orientation. Fill the sectioning chamber with PBS to submerge the sample.

TROUBLESHOOTING

14| Set the start and the end point of sectioning (for additional information regarding operating the Leica VT1000S Vibratome, please read the manufacturer's manual).

TROUBLESHOOTING

15| Set the thickness of the section to 100 μm (for additional information regarding operating the Leica VT1000S Vibratome, please read the manufacturer's manual).

TROUBLESHOOTING

16| Section the tissue and collect a section with a small (no. 6 or 8) round watercolor brush; put it on a glass slide. One slide may hold several sections.

TROUBLESHOOTING

17| Use a larger watercolor brush to remove excess PBS, add a small amount of 80% glycerol to the sections and cover with no. 1.5 cover slip. Seal it with nail polish.

PAUSE POINT Sections are better viewed as soon as possible but can be kept for several days at 4 °C in the dark.

TROUBLESHOOTING

View sections TIMING Depending largely on the number of the sections and the area of interest to be examined, ~1 h to 1 d

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18| View tissue sections under a fluorescence microscope or a confocal microscope using the filter set for rhodamine.

19| Collect a stack of confocal images. Reconstruction of 3-D images can be achieved using any image analysis software that has such a function. We used AutoVisualize 3-D (version 5.5, AutoQuant Image Inc.) and Leica Application Suite Advanced Fluorescence (LAS AF, TCS-SP5) (Leica).

● TIMING

Steps 1–10: ~45 min

Steps 11–17: ~1–2 h, depending on the size of the tissue to be sectioned

Steps 18 and 19: depending largely on the number of the sections and the area of interest to be examined, ~1 h to 1 d

? TROUBLESHOOTING

Troubleshooting advice can be found in Table 1.

ANTICIPATED RESULTS

Perfusion with DiI solution delivers dye molecules to endothelial cells lining blood vessels in the entire circulation system, thus blood vessels in the whole body are stained. DiI appears purple in color under visible light, so tissues that are well stained should appear slightly purple. Large blood vessels on the surface should be visible. Blood vessels appear intensely red under a fluorescence microscope using a rhodamine filter set (Fig. 2). Stacks of confocal images could be obtained and used to reconstruct 3-D images in hollow organs like the eye (Fig. 3a) and thick tissue samples (Fig. 3b). Because of lateral diffusion, DiI also stains membrane structures that are not in direct contact with the dye solution, including angiogenic sprouts and pseudopodial processes. Images of angiogenic sprouts with their extruding processes (3-D reconstruction) are shown in Figure 3c,d. Thick tissue sections allow efficient screening of the entire tissue of interest at low magnifications for relatively rare events, which can then be studied in detail at high magnifications and/or using an electronic zoom. For example, to study choroidal neovascularization, it is important to find the site where new blood vessels from the choriocapillaris penetrate the Bruch's membrane. In our study on choroidal neovascularization in a subretinal Matrigel model of choroidal neovascularization in the rat[1], we routinely screen the entire Matrigel-injected area (20–25 sections of 100 μm thick) to identify the penetration sites and then to carefully study them. One such site is shown in Figure 4. The combined DiI staining and DIC (differential interference contrast) image shows the site at which a new blood vessel originated in the choriocapillaris penetrated the Bruch's membrane and entered the space between the retinal pigment epithelium and the Bruch's membrane.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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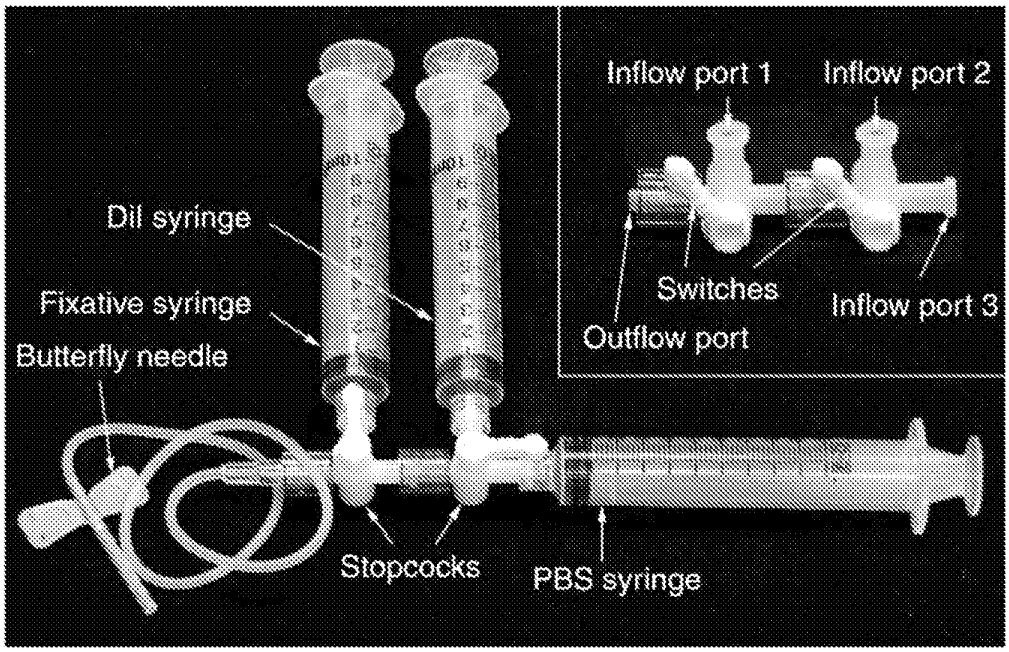


Figure 1.
Perfusion device. The main body of the perfusion device is two three-way stopcocks connected in series (inset). The output port of the stopcocks is connected to a butterfly needle. The inflow ports are connected to three 10-ml disposable syringes for PBS, DiI solution and fixative, respectively. The positions of the three syringes depend on the specific stopcock used, as stopcocks of different brands may have different configurations. It is also possible to use a single stopcock for the device. In that case, it will require change of syringes after perfusion with DiI solution. During syringe change, it is important to avoid air from entering the perfusion line.

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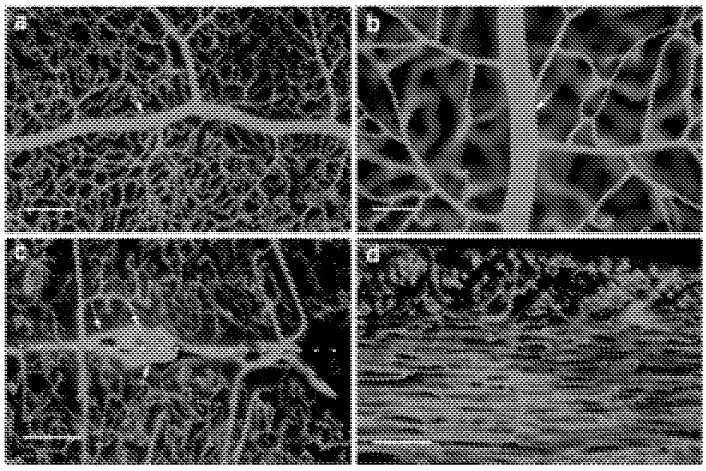


Figure 2.

Vasculature visualized by DiI labeling. (**a**) Retinal whole-mount showing an artery (arrow) on the retinal inner surface along with its branches connecting to the deep capillaries, which are also visible, although out of focus (10 objective lens). (**b**) Retinal whole-mount-showing another artery (arrow) at a higher magnification (×20 objective lens). The nuclei of endothelial cells are identifiable as oval spots in both **a** and **b**. (**c**) A brain section (100 μm thick, ×10 objective lens) showing three large blood vessels (arrows) located in the midline (dashed line) between the two hemispheres and the vascular network in the tissue. (**d**) A heart section (left ventricle, 100 μm thick, ×10 objective lens) showing capillaries in the left ventricle wall. In the outer layer (upper part), they are perpendicular to the section plane and appear as bright dots, whereas in the inner layer (lower part), they are parallel to the section plane. Tissues were viewed by fluorescence microscopy (Nikon Eclipse E800 fluorescence microscope with plan fluo ×10/0.3 numerical aperture (**NA**) or plan fluo ×20/0.5 NA objective lens and Chroma 34,000 rhodamine filter set, with the excitation wavelength of 570 nm and the emission of 590). Scale bars, 200 μm for **a**, **c** and **d**, and 100 μm for **b**.

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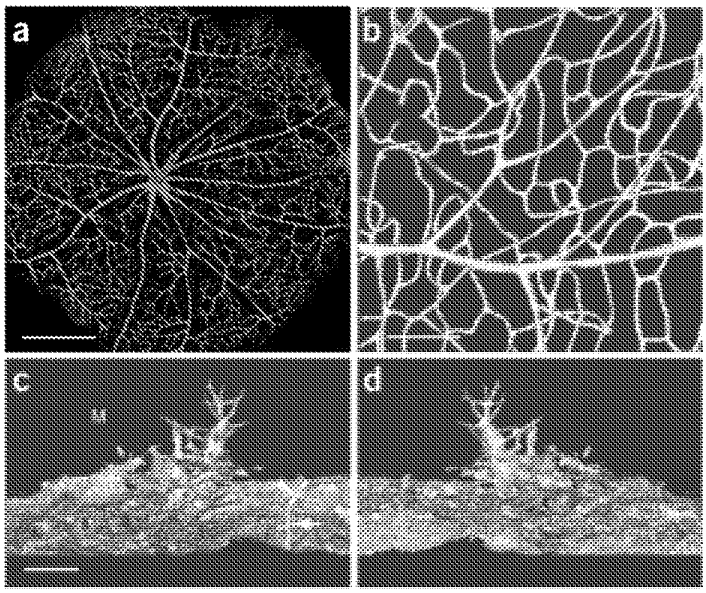


Figure 3.

Three-dimensional reconstructed images of retinal vasculature and angiogenic sprouts and pseudopodial processes. (**a**) A 3-D reconstructed image of the eyecup as a 'bird's eye' view of the vasculature of the posterior retina. The eyecup was placed in a holder and submerged in PBS for direct imaging. A ×5/0.15 NA objective lens was used to take a stack of confocal images, which were used for the reconstruction. DiI signal was detected using Leica DM6000B microscope with the ×5 objective (HC PL Fluotar/0.15) (Leica). Images were acquired by a Leica Application Suite Advanced Fluorescence (LAS AF), 1.7.0, Build 1240 software TCS-SP5 (Leica). The same software was used to create 3-D reconstruction of images and a movie clip, which shows the retinal vasculature rotated around the *x* axis (Supplementary Movie 1). (**b**) A 3-D image showing an artery on the retinal surface connected to the deep capillaries. A movie clip shows the artery and its network rotated around the *y* axis (Supplementary Movie 2). (**c**) A 3-D image of angiogenic sprouts and pseudopodial processes in a subretinal Matrigel of choroidal neovascularization[1] at a viewing angle of 0° (from the coverslip side downward). The vertical line (arrow) indicates the cross section of the choroid. Another line (arrowhead) indicates the surface of the choroicapillaris. Several sprouts from the choriocapillaris invaded the Matrigel layer (M) in the subretinal space. Their pseudopodial processes protruded into the Matrigel deposit (M) in different directions. (**d**) 3-D image of angiogenic sprouts and pseudopodial processes at a viewing angle of 180°. A movie clip shows the sprouts rotated around the *y* axis (Supplementary Movie 3). Scale bar, 400 μm for **a**, 100 μm for **b** and 20 μm for **c** and **d**.

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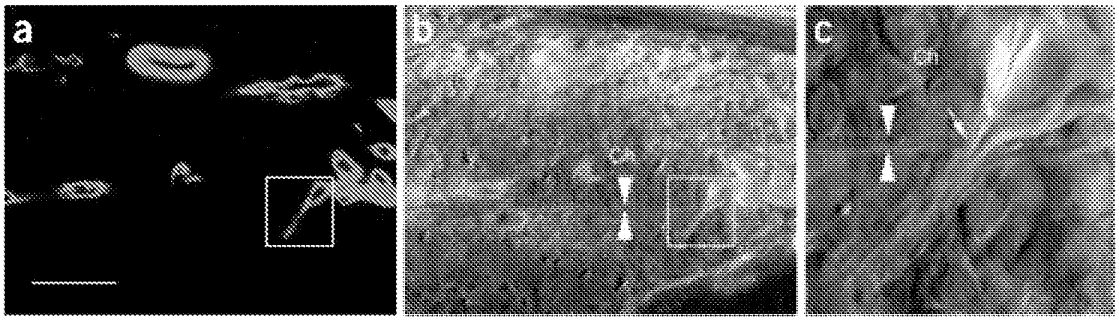


Figure 4.

Penetration of Bruch's membrane by choroidal neovascularization. Choroidal neovascularization was induced by subretinal injection of Matrigel[1]. To locate the penetration sites of choroidal neovascularization, serial tissue sections (100 μm thick each) were cut through the entire Matrigel injected area (about 2 mm in diameter). Tissue sections were screened at low power (×10 objective) under a fluorescence microscope. Potential penetration sites were further examined by confocal microscopy. (**a**) A confocal image of a new blood vessel that had penetrated the Bruch's membrane (square). (**b**) A superimposed image of DIC (differential interference contrast) and fluorescence (red) shows the penetrating blood vessel (square) relative to Bruch's membrane (between two arrowheads). (**c**) The penetration site (arrow) at higher magnification to show Bruch's membrane (between two arrowheads). Ch, choroid. Scale bar, 50 μm for **a** and **b**; 7 μm for **c** .

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TABLE 1

Troubleshooting table

Problem	Possible reason	Possible solution
Weak signal	Poor perfusion due to air trapped in the system (Steps 1 and 6)	Make sure no air is trapped in the perfusion line before perfusion. When inserting the needle into the left ventricle, slightly press the PBS syringe to allow a fluid drop to appear at the needle tip
	Poor perfusion because of a leak in the left ventricle (Step 6)	Do not penetrate the opposite side of the ventricle when inserting the butterfly needle. Using a small hemostat to clamp the leaking point sometimes works
	Poor staining because of too much PBS perfusion (Step 7)	Make sure not more than 2 ml of PBS is used before DiI perfusion
'Leak' staining	The inner lining of blood vessels are broken because of rough handling of tissue preparation and sectioning (Steps 10, 12–17)	DiI will not 'leak' to the surrounding tissues if blood vessels are intact. Be gentle during tissue harvesting. View tissue sections as soon as possible

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

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

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

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

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

MATERIALS AND METHODS

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

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

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

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

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

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

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

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

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

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

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

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

RESULTS

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

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

DISCUSSION

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

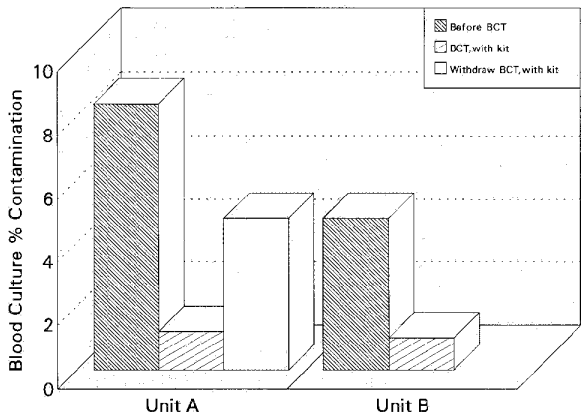


FIG. 1. Effect of BCT and commercial prep kits on rate of blood culture contamination.

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

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

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

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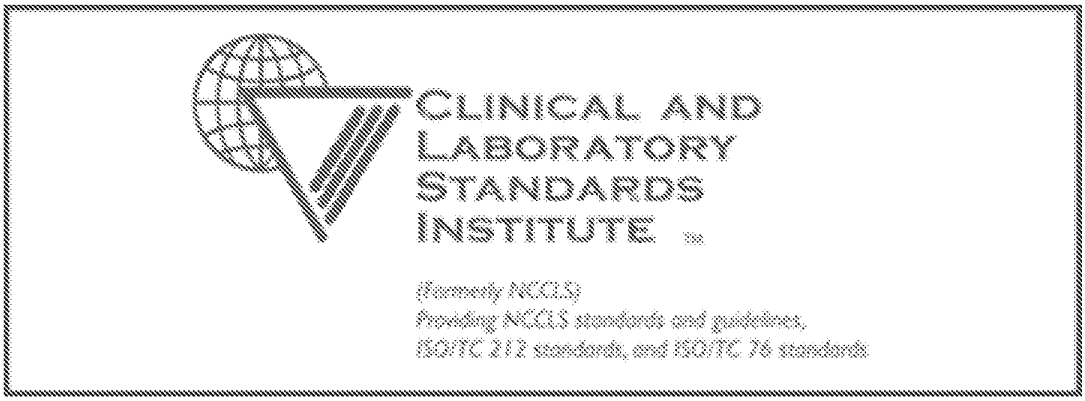
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Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition



This document provides procedures for the collection of diagnostic specimens by venipuncture, including line draws, blood culture collection, and venipuncture in children.

A standard for global application developed through the NCCLS consensus process.



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Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition

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Abstract

H3-A5—*Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition* provides a descriptive, stepwise procedure for the collection of diagnostic blood specimens by venipuncture. Special considerations for venipuncture in children, line draws, blood culture collection, and venipuncture in isolation situations are included.

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Foreword

The errors that can occur during the collection and handling of blood specimens are potentially numerous (e.g., inaccurate identification of specimens, specimen hemolysis, the improper handling of anticoagulants, the formation of hematomas, hemoconcentration). Standards for venipuncture can reduce or alleviate many of these errors in much the same way that quality control standards have reduced errors within the laboratory.

Reducing errors during blood collecting will result in biologically representative specimens that are comparable from one institution to another. A well-planned, attractive environment in which to perform venipunctures will reduce patient anxiety and increase the efficiency and accuracy of the phlebotomist. Phlebotomists need a complete assortment of equipment at their fingertips so they can judiciously select the most appropriate materials for each patient. Standards governing the processing of paperwork will reduce errors and save time. Without question, a comprehensive training program is needed to produce efficient, well-trained phlebotomists. Finally, standards for the actual venipuncture procedure are needed to help eliminate the many errors that can occur during blood collection. Biologically representative specimens for laboratory testing will be obtained if national venipuncture standards are used.

Various comments received on the previous edition of this standard have been reviewed and incorporated where appropriate. All comments and the subcommittee's responses are summarized at the end of the document.

This document replaces the fourth edition approved standard, H3-A4, which was published in 1998. Several changes have been made in this edition; chief among them is the revised order of draw (Section 8.10.2), which reflects the increased use of plastic blood collection tubes. This standard also contains revised recommendations regarding collection of blood specimens in relation to intravenous sites (Section 11.6). The recommendations regarding the collection of coagulation specimens (Section 8.10.3) have been revised for consistency with NCCLS document H21—*Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays.*

Key Words

Accession, blood specimen, phlebotomist, sample, venipuncture

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Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition

1 Scope[a]

This document establishes criteria for the correct collection of blood specimens by venipuncture. These procedures are intended to be a suitable model for adoption by all healthcare providers responsible for the collection and handling of blood specimens in both outpatient and inpatient settings.

2 Introduction

Since 1977, NCCLS has progressively recognized the quality requirement that significant attention be directed towards the preanalytical components of laboratory testing, specifically, the correct collection and handling of blood specimens. Highly sophisticated testing technology cannot produce a good result from a poor specimen. Proper specimen collection and handling are of the utmost importance because significant errors occur in the preanalytical phase of laboratory testing.[1]

Preanalytical errors have the potential to be numerous: incorrect patient ID, incorrect order-of-draw, incorrect use of additive tubes, labeling errors, incorrect timing of collection, clerical errors, etc. Standard procedures and protocols are intended to prevent these problems and protect patient results quality.

3 Standard Precautions

Because it is often impossible to know what might be infectious, all human blood specimens are to be treated as infectious and handled according to "standard precautions." Standard precautions are guidelines that combine the major features of "universal precautions and body substance isolation" practices. Standard precautions cover the transmission of any pathogen and thus are more comprehensive than universal precautions which are intended to apply only to transmission of blood-borne pathogens. Standard precaution and universal precaution guidelines are available from the U.S. Centers for Disease Control and Prevention (*Guideline for Isolation Precautions in Hospitals*. Infection Control and Hospital Epidemiology. CDC. 1996;Vol 17;1:53-80), (MMWR 1987;36[suppl 2S]2S-18S), and (MMWR 1988;37:377-382, 387-388). For specific precautions for preventing the laboratory transmission of blood-borne infection from laboratory instruments and materials and for recommendations for the management of blood-borne exposure, refer to the most current edition of NCCLS document M29—*Protection of Laboratory Workers from Occupationally Acquired Infections.*

4 Definitions

In the context of this publication, the terms listed below are defined as follows:

Accession – The steps required to ensure that a specific patient specimen and the accompanying documentation are unmistakably identified as referring to a specific person.

Angle of insertion – The angle formed by the surface of the arm and the needle entering the arm.

[a] This standard reflects recent revisions to OSHA's Blood Borne Pathogens Standard (29 CFR 1910.1030). Therefore, all references to needles/winged blood collection sets indicate sharps with engineered safety features. This also encompasses safety accessories used in combination with conventional needles.

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(Patient) sample – A sample taken from the patient specimen and used to obtain information by means of a specific laboratory test.

(Patient) specimen – The discrete portion of a body fluid or tissue taken for examination, study, or analysis of one or more quantities or characteristics to determine the character of the whole.

Pre-evacuation – The creation of a vacuum (in a collection tube), induced by either the manufacturer or by the user immediately before a liquid specimen is taken.

Vascular access device (VAD) – A device inserted into a vein or artery to allow access to the circulatory system for the administration of intravenous fluids and/or medications.

Venipuncture – The puncture of a vein for surgical, or therapeutic, purposes, or for collecting blood specimens for analysis.

5 Factors That Affect Laboratory Values

Interpretation of laboratory data has assumed new importance and attracted increased attention with both more frequent testing and multiple testing. The increased use of laboratories predictably yields abnormal unsolicited data that requires interpretation and may lead to costly, unproductive, and unnecessary sequential testing. Even when an analytical procedure has been performed correctly and precisely, variables can affect the test result. Knowledge of these variables and standardization of laboratory testing procedures are essential for correct interpretation and optimal use of the data.

Major causes of "laboratory error" can be related to nonanalytical factors such as specimen collection, handling, and transport. Nonbiological factors—such as patient misidentification, and biological factors—such as patient posture and the time a specimen is drawn, all contribute to the total "laboratory error."

Physiological factors that influence results include age, activity, bed rest, food ingestion, alcohol ingestion, menstrual cycle, obesity, oral contraceptives, posture, pregnancy, race, gender, smoking, and time of day. All biological phenomena exhibit rhythms, with the circadian rhythm (the change in a 24-hour period) being the most important to laboratory testing. Many factors with documented effects on laboratory values have been published.[2-6]

6 Facilities

The venipuncture should be performed in a clean, quiet, and private environment. Reasonably soundproof rooms for pediatric patients should be considered.

The room should have facilities to allow the phlebotomist to wash his/her hands between patients. Washing with soap and running water is recommended; however, any standard detergent product acceptable to personnel may be used. In settings where water is not available, alcohol-based gels or liquids, hand-wipe towelettes, and cleansing foams can be used.[b]

6.1 Venipuncture Chairs

Venipuncture chairs should be designed for the maximum comfort and safety of the patient. Consideration should be given to the ergonomic comfort plus easy accessibility to the patient for the phlebotomist. Both armrests of the chairs should be adjustable so that the best venipuncture position for

[b] In the U.S., employees must wash their hands with soap and running water as soon as feasible thereafter.

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each patient can be achieved. The chair should have a safety device to prevent patients from falling if feeling faint.

6.2 Hospital Area

A central venipuncture area should be designed to include the following features.

6.2.1 Central Desk

The central desk is a location for a telephone system used to handle emergency request calls, facilities for processing daily and future requests, and a paging system for contacting the phlebotomist who is collecting specimens outside of the central area.

6.2.2 Cart Area

The cart area is constructed to allow easy access to the supplies.

6.2.3 Storage Area

The storage area should be large enough to accommodate the necessary supplies.

6.2.4 Counter Space

Counter space should be adequate for efficient sorting and dispatching of specimens.

6.2.5 Sampling Time Recorder

The sampling time recorder (i.e., time stampers, bar codes, or information system) should be located for convenient time recording of venipuncture paperwork.

7 Supplies

The following supplies should be available at any location where venipunctures are performed routinely.

7.1 Utility Carts

Utility carts, designed to roll smoothly and silently over all types of surfaces, may be useful. The phlebotomist may also find it very useful to have a specially designed rack on the top shelf for storing supplies.

7.2 Blood Collecting Trays

Blood collecting trays or carts may be used. The trays should be lightweight and easy to handle with enough space and compartments for the various supplies that are needed.

7.3 Gloves

Latex, vinyl, or nitrile gloves provide barrier protection. Disposable latex, vinyl, or nitrile gloves are available from hospital suppliers.

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Some workers may develop dermatitis from wearing latex gloves for long periods of time. These workers should experiment with nitrile, polyethylene or other gloves of various composition or gloves without powdered lubricant or they may wear cotton gloves under latex or plastic gloves.

Severe hypersensitivity has been reported and cases of anaphylactic shock have occurred. In such hypersensitive individuals, latex gloves must be avoided.

7.4 Needles and Holders

Needles/holders should be compatible with the tubes selected for use. For more information on venous blood collection tubes and additives, refer to the most current edition of NCCLS document H1—*Evacuated Tubes and Additives for Blood Specimen Collection.*

Needles and winged blood collection sets are individually color-coded according to their respective gauge sizes. The gauge number indicates the size of the needle. A large gauge number indicates a small needle, while a small gauge number indicates a large needle. The sizes for venipuncture range from 19 through 23. Needles must always be sterile.

In order to prevent potential worker exposure, the needle safety feature should be activated immediately after specimen collection and discarded without disassembly into a sharps container.[c]

7.5 Sterile Syringes

In general, venipuncture using a needle and syringe should be avoided for safety reasons; however, it may be suitable under some circumstances to have sterile syringes of the appropriate size available.

7.6 Venous Blood Collection Tubes

Venous blood collection tubes are manufactured to withdraw a predetermined volume of blood. At present, venous blood collection tubes used in venipuncture are designated sterile. It is recommended that information regarding the venous blood collection tubes selected for general use be clearly displayed in venipuncture areas for easy reference. Similar information should also be made available to all personnel who collect blood. Instructions furnished in the package insert by the manufacturer of venous blood collection tubes and needles should be available. (See also the most current version of NCCLS document H1—*Evacuated Tubes and Additives for Blood Specimen Collection* for information on venous blood collection tubes.)

7.7 Tourniquets

Tourniquets or products for use as tourniquets should be available. Examples include:

- Single-use disposable tourniquet, preferably latex-free.
- Blood pressure cuff inflated to 40 mmHg.
- Rubber/fabric-type tourniquets with closure tape, plastic clip, buckle, or similar type of fastening.

Tourniquets must be discarded immediately when contaminated with blood or body fluids or must be discarded if contamination is suspected.

[c] In the U.S., refer to OSHA's Bloodborne Pathogens Standard (29 CFR 1910.1030), the safe practice of phlebotomy and blood tube holder use (CPL2-2.9 at XIII.D.5).

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7.8 Antiseptics

Antiseptics for skin preparation are necessary. The following are some examples:

- Isopropyl or ethyl alcohol: 70%
- 1 to 10% povidone-iodine as swab sticks or chlorhexidine gluconate for blood cultures[7] (see Section 8.8.2).
- Nonalcohol-based cleanser for blood alcohol specimens (e.g., chlorhexidine).

7.9 Gauze Pads

Small prepackaged gauze pads, (i.e., 2 x 2 in or 3 x 3 in [5.0 x 5.0 cm or 7.5 x 7.5 cm]) should be available. Cotton balls are not recommended because of the possibility of dislodging the platelet plug at the venipuncture site.

7.10 Puncture-Resistant Disposal Container

An approved puncture-resistant disposal container that is compliant with OSHA regulations must be available.

7.11 Ice

Ice or refrigerant should be available.

7.12 Adhesive Bandages

Adhesive bandages and/or gauze pads should be available. Hypoallergenic adhesives should also be available.

7.13 Warming Devices

Warming devices may be used to increase blood flow.

7.14 Test Reference Manual

A test manual which explains which tube is to be used, that also indicates minimum volume requirements, special handling, and precautions to be taken should be consulted.

8 Venipuncture Procedure

The venipuncture procedure is complex and requires both knowledge and skill (refer to Sections 8.1 to 8.17 for detailed information on the procedure). When drawing a blood specimen, the trained phlebotomist must:

Step 1. Prepare accession order.
Step 2. Approach and identify the patient.
Step 3. Verify patient's diet restrictions, as appropriate, and inquire if patient has a latex sensitivity. Select appropriate gloves and tourniquet.
Step 4. Assemble necessary supplies and select appropriate tubes according to test requests.
Step 5. Position the patient.
Step 6. Apply the tourniquet, ensure the patient's hand is closed, and select the vein site.
Step 7. Put on gloves.

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Step 8. Cleanse the venipuncture site.
Step 9. Perform venipuncture; once blood flow begins, request patient to open hand.
Step 10. Use the correct order of draw.
Step 11. Release and remove the tourniquet.
Step 12. Place the gauze pad over the puncture site.
Step 13. Remove the needle, activating any safety feature according to manufacturers' instructions.
Step 14. Apply pressure to the site, making sure bleeding has stopped, and then bandage the arm.
Step 15. Label the tubes and record the time of collection.
Step 16. Chill the specimen (if required).
Step 17. Send properly labeled blood collection tubes to the appropriate laboratories.

8.1 Step 1: Prepare Accession Order

Each request for a blood specimen must be accessioned to identify all paperwork and supplies associated with each patient. An organized system will ensure prompt and accurate processing of the various forms required when performing a venipuncture and analyzing the results. Record all information on the test request form.

8.1.1 Information for Test Request Form

The following information should be included:

- The patient's name and age from identification plate
- An identification number
- The date and time the specimen is to be obtained
- An accessioning number
- The doctor's name
- The department or location for which the work is being done
- Other information as needed (e.g., special comments: intravenous site, sampling site if other than arm).

8.2 Step 2: Approach and Identify the Patient

The phlebotomist should identify himself or herself, establish a rapport, and gain the patient's confidence. Information given to the patient regarding the testing to be performed and specimen to be drawn must be in accordance with institutional policy. The phlebotomist must **NOT** perform blood collection against the patient's or guardian's consent. Instead, report the patient's objections to the physician's/nurse's station.

8.2.1 Identify Patient

Identification of the patient is crucial. The phlebotomist must ensure that the blood specimen is being drawn from the individual designated on the request form. The phlebotomist must not rely on a bed tag, or on charts or records placed on the bed, nearby tables, or equipment. The following steps are a suggested sequence for ensuring patient identification, regardless of the clinical setting.

8.2.2 Patient Who Is Conscious

The suggested sequence of steps for a patient who is conscious:

(1) Ask outpatients to give full name, address, identification number, and/or birth date.

(2) Compare this information with the information on the request form.

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(3) Ask inpatients for the same information and compare this information with the information on the request form and the patient's identification bracelet, which must be attached to the patient.

(4) Report any discrepancy, however minor, to the responsible person in the area (as determined by institutional policy) and have the patient identified by name and identification number before drawing any specimen.

8.2.3 Patient Who Is Semiconscious, Comatose, or Sleeping

The phlebotomist must take special care when drawing blood from semiconscious, comatose, or sleeping patients to anticipate any unexpected movements or jerks either while introducing the needle, or while it is in place in the arm. Sleeping patients should be awakened before drawing blood. A gauze pad should be readily available and the tourniquet quickly released in the event the needle is violently removed or repositioned. If the needle accidentally goes much deeper into the arm, the phlebotomist must inform the doctor's/nurse's station. If unable to identify the patient, then contact the nurse or physician.

8.2.4 Patient Who Is Unconscious, Too Young, Mentally Incompetent, or Does Not Speak the Language of the Phlebotomist

In any of these circumstances, the phlebotomist should follow this suggested sequence of steps:

(1) Ask the nurse, a relative, or a friend to identify the patient by name, address, identification number, and/or birth date. If unable to identify the patient, then contact the nurse or physician.

(2) Compare these data with the information on the request form and the patient's identification bracelet, which must be attached to the patient.

(3) Report any discrepancy, however minor, to the responsible person in the area (as determined by institutional policy) and have the patient identified by name and identification number before drawing any specimen.

8.2.5 Procedure for Identifying Unidentified Emergency Patients

Identification standards established by the American Association of Blood Banks (AABB) provide clear guidelines for unidentified emergency patients.[8]

The patient must be positively identified when the blood specimen is collected. The unidentified emergency patient should be given some temporary but clear designation until positive identification can be made. For a person who cannot be identified immediately, it is necessary to:

- Assign a master identification number (temporary) to the patient in accord with institutional policy.
- Select the appropriate test request forms and record with master identification number.
- Complete the necessary labels either by hand or by computer and apply the labels to the test request forms and specimens.
- When a permanent identification number is assigned to the patient, make sure the temporary identification number is cross-referenced to the permanent number to ensure correct identification and correlation of patient and test result information.

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In all cases, the name and permanent or temporary identification designation must be attached to the patient's body either by wristband or some similar device. Except in the case of isolation patients, bed labels must not be used in place of wristbands.

8.2.6 Physician Relationship

The physician has priority with the patient. The phlebotomist should not enter the room without permission while the physician or nurse is consulting with the patient. If the order is stat or the specimen is a "timed" specimen, the phlebotomist should request permission to draw the blood specimen.

8.3 Step 3: Verify Patient Diet Restrictions and Latex Sensitivity

Some tests require the patient to fast and/or eliminate certain foods from the diet before the blood is drawn. Time and diet restrictions vary according to the test. Such restrictions are necessary to ensure accurate test results.

The procedure for holding meals and notifying appropriate personnel that the patient has been drawn should be according to institutional policy.

Please refer to Section 7.3 for information regarding latex sensitivity to gloves and to Section 7.7 for tourniquets.

8.4 Step 4: Assemble Supplies

8.4.1 Supplies[d]

It is important that phlebotomy devices used reflect the most current local and regional safety regulations.[9]

Inspect all supplies for possible defects and applicable expiration dates. The following supplies should be available at any location where venipunctures are performed routinely:

- Blood collection tubes/blood culture bottles
- Needle
- Single-use tube/needle holder
- Syringe
- Syringe transfer device
- A tourniquet
- Alcohol prep pads
- 1 to 10% povidone-iodine pads, tincture iodine, or chlorhexidine compounds if blood culture is to be drawn
- Nonalcohol-based cleanser if blood alcohol is to be drawn
- Gauze pads, adhesive bandages, or tape (including hypoallergenic adhesives)
- Gloves
- Sharps container, consistent with OSHA regulations

8.4.2 Needles

The phlebotomist must select the appropriate needle gauge based on the physical characteristics of the vein, location of the vein, and the volume of blood to be drawn.

[d] In the U.S., OSHA mandates the use of engineering and work practice controls that eliminate occupational exposure or reduce it to the lowest feasible extent (e.g., safety needles, shielded needle devices, etc.).

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8.4.3 Syringes

The plunger must be moved within the barrel of the syringe to show syringe and needle patency and freedom of plunger movement.

8.4.4 System

The phlebotomist must select the appropriate blood collection system according to the patient's physical characteristics.

8.4.4.1 Venous Blood Collection Systems

When venous blood collection tubes are used, the phlebotomist must:

- Select the correct types and sizes of venous blood collection tubes. (Color-coded closures and labels make it easy to perform this step.)
- Apply a label to each of the necessary tubes and all test forms immediately after blood specimen has been drawn
- Refer to institutional policy.

All tubes should be labeled immediately *after* the blood specimen has been drawn. The completed label must be attached to the tube before leaving the side of the patient, and there must be a mechanism to identify the person who drew the blood.[8] If preprinted labels are not available, complete patient information can be handwritten on the tube label. This procedure eliminates the possibility of mixing up the blood specimens.

It is recommended that blood specimens be collected by venipuncture using a blood collection system that collects the blood directly into tubes. (For greater detail on venous blood collection tubes and additives, refer to the most current edition of NCCLS document H1—*Evacuated Tubes and Additives for Blood Specimen Collection.)* If the components are from different manufacturers, they should be checked to ensure compatibility.

8.4.4.2 Plastic Syringe

In general, the use of a syringe and needle should be avoided for safety reasons. If a syringe is used, a safety syringe shielded transfer device should be used to transfer blood to the appropriate venous blood collection tube.

8.4.4.3 Blood Collection Set

The blood collection set (i.e., winged blood collection set) is described in Section 9.2.

8.5 Step 5: Position Patient

8.5.1 Procedure for Seating Patient

(1) Ask the patient to be seated comfortably in a chair suitable for venipuncture. The chair should have arms to provide support and prevent falls if the patient loses consciousness. Chairs without arms do not provide adequate support for the arm or protect fainting patients from falls.

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(2) Have the patient position his/her arm on the slanting armrest and extend the arm to form a straight line from the shoulder to the wrist. The arm should be supported firmly by the armrest and should not be significantly bent at the elbow. A slight bend may be important in avoiding hyperextension of the arm.

8.5.2 Procedure for Having Patient Lie Down

(1) Ask the patient to lie on his/her back in a comfortable position.

(2) If additional support is needed, place a pillow under the arm from which the specimen is being drawn.

(3) Have the patient extend his/her arm to form a straight line from the shoulder to the wrist.

8.5.3 Foreign Objects in Mouth

No food or liquid, chewing gum, or thermometer should be in the patient's mouth at the time the specimen is drawn.

8.6 Step 6: Apply Tourniquet

A tourniquet is used to increase venous filling. This makes the veins more prominent and easier to enter. (See Section 7.7).

8.6.1 Precautions When Using a Tourniquet

Tourniquet application for preliminary vein selection should not exceed one minute as localized stasis with hemoconcentration and infiltration of blood into tissue can occur. This may result in erroneously high values for all protein-based analytes, packed cell volume, and other cellular elements. If the patient has a skin problem, the tourniquet should be applied over the patient's gown or a piece of gauze pad or paper tissue should be used so that the skin is not pinched.

8.6.2 Tourniquet Location

Wrap the tourniquet around the arm 3 to 4 inches (7.5 to 10.0 cm) above the venipuncture site.

8.6.3 Blood Pressure Cuff

If a blood pressure cuff is used as a tourniquet, inflate it to 40 mm Hg.

8.6.4 Ensure Patient's Hand Is Closed

The veins become more prominent and easier to enter when the patient forms a fist. There must not be vigorous hand exercise ("pumping"). Vigorous hand pumping can cause changes in the concentration of certain analytes in the blood.

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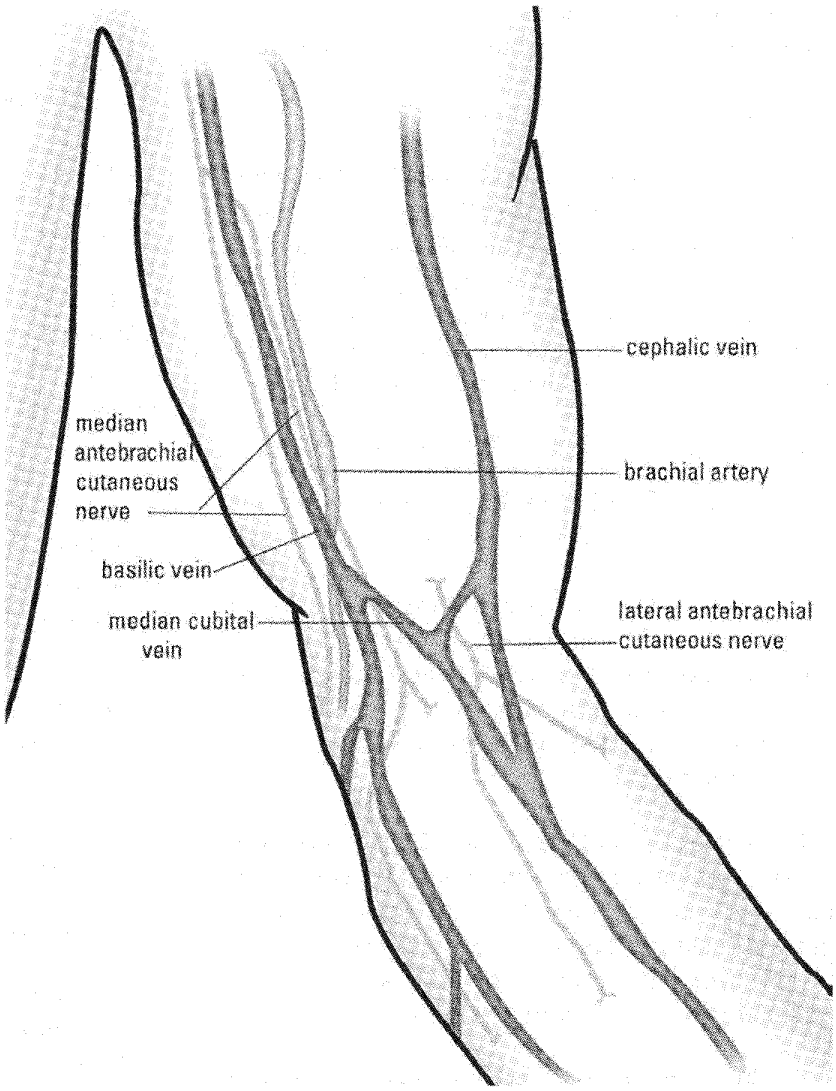


Figure 1. Superficial Veins of the Anterior Surface of the Upper Extremity (From Ernst DJ, Ernst C. Phlebotomy tools of the trade: Part 2—Surveying the antecubital area. *Home Healthcare Nurse.* 2002;20:402-403. Reprinted with permission from Lippincott Williams & Wilkins.)

8.6.5 Select Vein

Refer to Figure 1 for a description of the superficial veins of the anterior surface of the upper extremity.

8.6.5.1 Caution

It is important to select the vein carefully for blood collection because the veins also provide an avenue of entry for transfusion, infusion, and therapeutic agents. Because the brachial artery passes through the antecubital area, caution must be exercised to avoid the artery. If, during the procedure, arterial puncture is suspected, direct forceful pressure must be applied to the puncture site for a minimum of five minutes upon removal of the needle or until active bleeding has ceased. The nursing staff and physician are to be notified immediately thereafter.

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8.6.6 Preferred Veins

Arterial punctures should not be considered as an alternative to venipuncture for difficult draws. If this appears to be the only alternative, consult with the physician.

Although the larger and fuller median cubital and cephalic veins (see Figure 1) are used most frequently, veins on the back of the hand are also acceptable for venipuncture. Veins on the underside of the wrist must not be used.

Draws to the median cubital veins are preferred because they are typically closer to the surface of the skin, more stationary, less painful upon needle insertion, and less likely to injure nerves if needle placement is not accurate. Attempt to locate the median cubital vein on either arm before considering alternative veins. Due to the proximity of the basilic vein to the brachial artery and the median nerve, this vein should only be considered if no other vein is more prominent. Above all, phlebotomists should be aware of the potential for injury associated with each vein and select the vein that brings the greatest degree of confidence of being accessed successfully without risking nerve or arterial involvement. (See Figure 1.)

Alternative sites such as ankles or lower extremities must not be used without the permission of the physician because of the potential for significant medical complications (e.g., phlebitis, thrombosis, tissue necrosis, etc.)[10-12]

8.6.7 Factors in Site Selection

8.6.7.1 Extensive Scarring

Healed burn areas are to be avoided.

8.6.7.2 Mastectomy

A physician must be consulted before drawing blood from the side on which a mastectomy was performed because of the potential for complications due to lymphostasis.

8.6.7.3 Hematoma

Specimens collected through a hematoma area may cause erroneous test results. Phlebotomy must not be performed on any size hematoma. If another vein site is not available, the specimen is collected distal to the hematoma.

8.6.7.4 Intravenous Therapy

Preferably, specimens should not be collected from an arm with an intravenous site. (See Section 11.6).[13]

8.6.7.5 Cannula, Fistula, Vascular Graft

A cannulated arm is used only after consulting the attending physician.

8.6.8 Procedure for Vein Selection

8.6.8.1 Locating Veins

To locate veins, it is necessary to palpate and trace the path of veins several times with the index finger. Unlike veins, arteries pulsate, are more elastic, and have a thick wall. Thrombosed veins lack resilience,

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feel cord-like, roll easily, and should not be used. A tourniquet must be used to aid in the selection of a vein site unless specific tests require tourniquets not be used (e.g., lactate). If a tourniquet must be applied for the preliminary vein selection, it should be released and reapplied after two minutes.

8.7 Step 7: Put on Gloves

The phlebotomist must put gloves on before the venipuncture is performed, for each patient, with consideration for latex sensitivity as discussed in Section 7.3.

8.8 Step 8: Cleanse Venipuncture Site

The puncture site must be cleansed to prevent microbiological contamination of either the patient or the specimen.

8.8.1 Cleansing Method for Venipuncture

(1) Use a gauze pad with 70% isopropyl alcohol solution, or a commercially prepared alcohol pad.

(2) Cleanse the site with a circular motion from the center to the periphery.

(3) *Allow the area to air dry* to prevent hemolysis of the specimen and to prevent the patient from experiencing a burning sensation when the venipuncture is performed.

8.8.2 For Blood Culture Collection

For blood cultures, it is necessary to carefully disinfect the venipuncture site. Chlorhexidine gluconate is recommended for infants two months and older and patients with iodine sensitivity. Cleanse the site with 70% alcohol, then swab concentrically, starting at the middle of the site with a 1 to 10% povidone-iodine solution (0.1 to 1% available iodine) or chlorhexidine gluconate. Allow the site to air dry, then remove the iodine or chlorhexidine from the skin with alcohol.[8]

When specimens are obtained for blood cultures, disinfect the culture bottle stopper according to the manufacturer's instructions.

8.8.3 Touching the Site After Cleansing

If the venipuncture proves difficult and the vein must be touched again to draw blood, the site should be cleansed again.

8.9 Step 9: Perform Venipuncture

8.9.1 Venipuncture Procedure When Venous Blood Collection Tubes Are Used

There are several different blood collection systems available that collect blood samples using different principles. For example, there are evacuated tube systems and systems that have a flexible/dual collection technique that employ either a vacuum—user evacuates the tube immediately prior to use referred to as pre-evacuation—or aspiration principle of collection. For the proper venipuncture technique using the blood collection system selected refer to the manufacturers' instructions for use.

(1) If pre-evacuation is required, and the blood collection tubes are not evacuated by the manufacturer, evacuate the tubes immediately prior to use according to the manufacturer's instructions.

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(2) If not preassembled by the manufacturer, thread the appropriate needle into the holder until it is secure.

(3) When drawing blood for cultures, wipe the stopper with a suitable antiseptic solution. Make certain the stopper is dry before performing the venipuncture.

(4) Make sure the patient's arm or other venipuncture site is in a downward position to prevent reflux or "backflow."

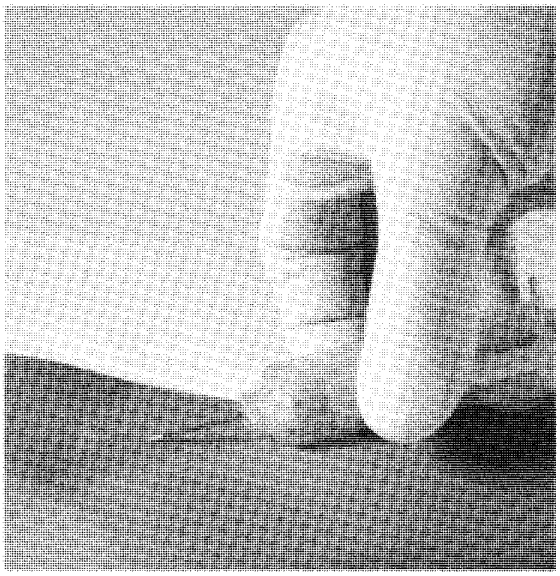


Figure 2. Proper Angle of Insertion (Figure contributed by the Center for Phlebotomy Education, Inc.)

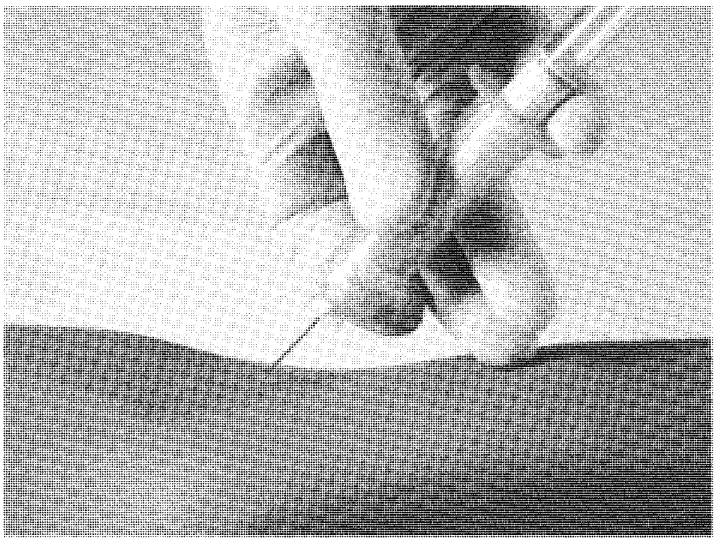


Figure 3. Improper Angle of Insertion (Figure contributed by the Center for Phlebotomy Education, Inc.)

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(5) Prior to venipuncture, if required, assemble the tube to the needle/holder according to the manufacturer's instructions.

(6) Hold the patient's arm firmly distal to the intended puncture site. The phlebotomist's thumb should be used to draw the skin taut. This anchors the vein. The thumb should be 1 to 2 inches (2.5 to 5.0 cm) below the venipuncture site.

(7) To prepare the patient, inform him or her that the venipuncture is about to occur. **NOTE:** From this point on, be prepared to react to a sudden and unexpected loss of consciousness.

(8) With the bevel up, puncture the vein with the needle at an angle of insertion of 30 degrees or less (See Figure 2). Keeping the needle as stable as possible in the vein, push/connect the first tube onto the needle. Maintain the tube below the site when the needle is in the vein.

(9) Release the tourniquet as soon as possible after the blood begins to flow. Do not change the position of the tube until it is removed from the needle. During the collection, do not allow the contents of the tube to contact the closure. Movement of the blood back and forth in the tube can cause reflux into the venous system and possible adverse patient reaction.

(10) Allow the tube to fill until the vacuum is exhausted and blood flow ceases. For tubes that contain additives, this will ensure there is a correct ratio of blood to additive.

NOTE: For systems that collect blood using an aspiration principle of collection rather than a vacuum, gently pull back on the piston rod until the piston reaches the base of the tube. This will ensure there is a correct ratio of blood to additive.

(11) When the blood ceases to flow, remove/disconnect the tube from the needle/holder. The sleeve re-covers the needlepoint that pierces the tube closure, stopping blood flow until the next tube is inserted/connected to the needle/holder. To obtain additional specimens, insert/connect the next tube to the needle/holder and repeat the collection procedure. Always remove the last tube collected from the needle/holder prior to withdrawing the needle from the vein. If only one tube is collected this must be removed prior to withdrawing the needle from the vein.

(12) Immediately after drawing each tube that contains an additive mix the blood gently and thoroughly by inverting the tube five to ten times. To avoid hemolysis, do not mix vigorously. For tubes that have been drawn using an aspiration principle, lock the piston into the base of the tube and snap off the piston rod after mixing.

8.9.2 Venipuncture Procedure Using Needle and Syringe

In general, venipuncture using a needle and syringe should be avoided for safety reasons. If conditions require a syringe draw, the following procedure is recommended:

(1) Assemble the needle and syringe.

(2) Hold the patient's arm firmly distal to the intended puncture site. The phlebotomist's thumb should be used to draw the skin taut. This anchors the vein. The phlebotomist's thumb should be 1 or 2 inches (2.5 cm or 5.0 cm) below the venipuncture site.

(3) Prepare the patient by informing him or her that the venipuncture is about to occur.

(4) With the bevel up, puncture the vein with the needle at an angle of insertion of 30 degrees or less (see Figure 2).

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(5) Keeping the needle as stable as possible in the vein, slowly withdraw the desired amount of blood.

(6) Release the tourniquet as soon as possible, after the blood begins to flow.

8.9.3 Fill the Tubes If Syringe and Needle Are Used

Syringe method of drawing venous blood is not recommended since it is much safer and easier to use a closed, venous blood collection tube system. If it is necessary to use a syringe, proceed with the following recommendations to transfer the blood from a syringe to a blood collection tube:

- Use the same "order of draw" as for a venous blood collection tube system (see Section 8.10.2).
- Rubber stoppers should not be removed from venous blood collection tubes to transfer blood to multiple tubes.
- To transfer the blood from the syringe to a venous blood collection tube, activate the safety feature of the needle or winged blood collection set used to withdraw the specimen, remove and discard the needle or winged collection set, and apply a safety transfer device.
- The stopper is pierced with the needle and the tube is allowed to fill (without applying any pressure to the plunger) until flow ceases. This technique helps to maintain the correct ratio of blood to additive if an additive tube is being used.
- Mix additive tubes by inversion.

8.9.4 Blood Specimen That Cannot Be Obtained

When a blood specimen cannot be obtained, it may be necessary to:

- Change the position of the needle. If the needle has penetrated too far into the vein, pull it back a bit. If it has not penetrated far enough, advance it farther into the vein. Rotate the needle half a turn. Lateral needle relocation should never be attempted in an effort to access the basilic vein, since nerves and the brachial artery are in close proximity.
- Try another tube to ensure the tube selected is not defective.
- Manipulation other than that recommended above is considered probing. Probing is not recommended. Probing is painful to the patient. In most cases another puncture in a site below the first site, or use of another vein on the other arm, is advisable.
- It is not advisable to attempt a venipuncture more than twice. If possible, have another person attempt to draw the specimen or notify the physician.

8.9.5 Ensure Patient's Hand Is Open

Opening the patient's hand reduces the amount of venous pressure as muscles relax. The patient must not be allowed to pump the hand.

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8.10 Step 10: Order of Draw

8.10.1 Additive Tubes

Gel separator tubes with clotting activators or anticoagulants are classified as additive tubes.[14] (For further information, refer to the most current edition of NCCLS document H18— *Procedures for the Handling and Processing of Blood Specimens*). These tubes should be drawn after the coagulation tube (blue stopper) and before other additive tubes (green, lavender, gray). All additive tubes should have a complete draw (see Section 8.9.1[10]).

8.10.2 Glass and Plastic Venous Blood Collection Tubes

The following order-of-draw is recommended when drawing multiple specimens for clinical laboratory testing during a single venipuncture. Its purpose is to avoid possible test result error due to cross contamination from tube additives.[15] This procedure should be followed for both glass and plastic venous blood collection tubes.

(1) Blood culture tube
(2) Coagulation tube (e.g., blue closure)
(3) Serum tube with or without clot activator, with or without gel (e.g., red closure)
(4) Heparin tube with or without gel plasma separator (e.g., green closure)
(5) EDTA (e.g., lavender closure)
(6) Glycolytic inhibitor (e.g., gray closure)

NOTE: The order of draw has been revised to reflect the increased use of plastic blood collection tubes. Plastic serum tubes containing a clot activator may cause interference in coagulation testing. Glass non-additive serum tubes may be drawn before the coagulation tube.

NOTE: When using a winged blood collection set for venipuncture and a coagulation tube is the first tube to be drawn, a discard tube should be drawn first. The discard tube must be used to fill the blood collection tubing dead space and to assure maintenance of the proper anticoagulant/blood ratio and need not be completely filled. The discard tube should be a nonadditive or a coagulation tube.

8.10.3 Coagulation Testing

Studies have shown that the PT (INR) and APTT results are not affected if tested on the first tube drawn.[16-18] Since it is not known whether other coagulation testing is affected, it may be advisable to draw a second tube for other coagulation assays. When a syringe system is used and a large specimen is taken, part of the blood from the second syringe should be used for the coagulation specimen. In the case of any unexplained abnormal coagulation test result, a new specimen should be obtained and the test repeated. If heparin contamination is suspected, the test should be repeated after the specimen is treated with a method that removes or neutralizes heparin. For more detailed descriptions of collection for coagulation testing, see the most current edition of NCCLS document H21—*Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays*.

8.11 Step 11: Release the Tourniquet

Release the tourniquet as soon as possible after the blood begins to flow.

8.12 Step 12: Place the Gauze Pad

A clean gauze pad should be placed lightly over the venipuncture site. Cotton balls are not recommended because of the possibility of dislodging the platelet plug at the venipuncture site.

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8.13 Step 13: Remove and Dispose of the Needle

Remove the needle and activate the safety mechanism according to the device manufacturer's instructions. Safely dispose of the unit into an easily accessible sharps container, consistent with OSHA regulations. Needles should not be resheathed, bent, broken, or cut, nor should they be removed from disposable syringes unless attaching a safety transfer device prior to disposal. Phlebotomists should anticipate a loss of consciousness and be prepared to react according to institutional policy. The use of ammonia inhalants may be associated with untoward effects and is not recommended. (See Section 11.8.1).

8.14 Step 14: Bandage the Arm

8.14.1 Normal Conditions

Under normal conditions, the phlebotomist should:

(1) Place the gauze pad over the site, continuing mild pressure.

(2) Check that bleeding has ceased, observe for hematoma, and apply an adhesive or gauze bandage over the venipuncture site. It is recommended that hypoallergenic adhesives be available.

(3) Tell patient to leave the bandage on for at least 15 minutes.

8.14.2 Continued Bleeding

The phlebotomist should watch for excessive bleeding. If a hematoma develops or bleeding persists longer than five minutes, a nurse should be alerted so that the attending physician can be notified. Pressure, applied with a gauze pad, must continue at the site as long as necessary to stop the bleeding. Wrap a gauze bandage tightly around the arm to keep the pad in place and tell the patient to leave the bandage on the site for at least 15 minutes.

8.15 Step 15: Label Blood Collection Tubes and Record Time of Collection

The patient and the patient's blood specimen must be positively identified at the time of collection. Blood specimens must be obtained in tubes identified with a firmly attached label bearing at least the following:

- The patient's first and last names
- An identification number
- The date
- The time (as required, e.g., therapeutic drug monitoring)
- The identification of the person collecting specimen.

The completed label must be attached to the tube before leaving the side of the patient, and there must be a mechanism to identify the person who drew the blood.[8] Alternatively, the manufacturer's tube label can be inscribed with the patient's complete information. Blood bank specimens must be labeled according to the standards set by the American Association of Blood Banks (AABB).

If an encoded (bar code) label is used, attach the label according to established institutional policy.

A permanent record is needed by the physician who must know exactly when each specimen was drawn to correlate the results with any change in the patient's condition. The laboratory also must document the

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time when the specimen was collected. If unable to obtain specimens, a record of the reasons and initials of the venipuncturist are necessary.

8.16 Step 16: Chill the Specimen (This is done only for certain specimens.)

Some tests require that blood specimens be cooled immediately following the venipuncture to slow down metabolic processes which may alter some test results. For more information on blood specimen handling and processing, see the most current edition of NCCLS document H18—*Procedures for the Handling and Processing of Blood Specimens*.

Examples of tests requiring chilling the specimen are:[19]

- Gastrin
- Ammonia
- Lactic acid
- Catecholamines
- pH/blood gas
- Parathyroid hormone (PTH).

8.17 Step 17: Send Blood Collection Tubes to the Proper Laboratories

Appropriately labeled blood collection tubes should be sent to appropriate laboratories designated to perform the required testing procedures. (See Section 8.15 for recommendations for labeling of tubes.)

9 Venipuncture in Children and Difficult Collections

If a venipuncture is requested on a child younger than one year of age, the phlebotomist should consult with the physician or follow institutional policy. For information on skin puncture blood collection, refer to the most current edition of NCCLS document H4—*Procedures and Devices for the Collection of Diagnostic Blood Specimens by Skin Puncture.*

9.1 Procedure

Except where indicated below, the procedure for venipuncture of adults as described in Section 8 should be followed for pediatric venipuncture.

9.2 Equipment

Venipunctures should be performed using equipment that can help to reduce the stress exerted on a vein to prevent vascular collapse. Examples include a venous blood collection system with a 22- to 23-gauge needle, or a 22- to 23-gauge (winged) blood collection set with attached tubing and venous blood collection tube holder. For pediatric patients, through the age of 16, larger gauge needles may be appropriate.

10 Additional Considerations

10.1 Monitoring Blood Volume Collected

It is recommended that a mechanism be in place to monitor the amount of blood drawn for pediatric and critically ill patients to avoid phlebotomy-induced anemia.

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10.2 Hematoma

To prevent a hematoma when performing a venipuncture, the phlebotomist should:

- Make sure the needle fully penetrates the uppermost wall of the vein (partial penetration may allow blood to leak into the soft tissue surrounding the vein by way of the needle bevel).
- Remove the tourniquet before removing the needle.
- Use the major superficial veins.
- Hold the venous blood collection assembly still while collecting the specimen.
- Before bandaging, ensure that the puncture to the vein has sealed by observing for hematoma formation after pressure is released.
- Apply a small amount of pressure to the area with the gauze pad when bandaging the arm.

10.3 Hemolysis

To prevent hemolysis when performing a venipuncture, the phlebotomist should:

- After cleansing, allow the venipuncture site to air dry.
- Never draw blood through a hematoma.
- If using a syringe, make sure the needle is fitted securely on a syringe to avoid frothing.
- When using a syringe and needle, avoid drawing the plunger back too forcibly.
- Gently invert the blood collection tube to mix additive specimens as recommended by the manufacturer.

11 Special Situations

11.1 Timed Intervals

Some specimens must be drawn at timed intervals because of medications, fasting requirements, and/or biological variations (circadian rhythm). It is important that collection of specimens for timed tests be obtained at the precisely specified interval. Directions should be given to the venipuncture team to obtain these specimens accurately.

11.1.1 Examples of Tests Requiring Timed Specimens

- Tolerance tests (e.g., two-hour postprandial glucose and three-hour glucose tolerance test), cortisol
- Therapy monitoring (e.g., prothrombin time, APTT, digoxin, and other drugs)

11.1.2 Documentation

For therapeutic drug monitoring, the dose of the medication and the time of the last dose given, as well as the time of the specimen collection, should be recorded accurately on the request slip.

11.2 Specific Collection Techniques

11.2.1 Blood Alcohol

When drawing a blood specimen for alcohol testing, a nonalcohol-based cleanser should be used to cleanse the venipuncture site (e.g., soap). (See the most current edition of NCCLS document T/DM6—*Blood Alcohol Testing in the Clinical Laboratory* for further information.)

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11.2.2 Legal Specimens

Appropriate chain-of-custody procedure should be followed. (See NCCLS document T/DM6—*Blood Alcohol Testing in the Clinical Laboratory*.)

11.2.3 Blood Culture Specimens

There are time and temperature requirements to be followed in collection, transport and storage of specimens for blood culture. In addition, there are variations in the volume of blood needed for culture. In general, adult blood cultures require 10 to 20 mL/set and infant blood cultures are done on 1 to 2 mL/set.[7] Please refer to the manufacturer's instructions for specific blood volume requirements. These requirements may vary considerably depending on the device.

11.2.4 Trace Elements

For collection of blood for trace elements testing (e.g., zinc) special, metal-free collection containers should be used. (See the most current edition of NCCLS document C38—*Control of Preanalytical Variation in Trace Element Determinations*, for more information.)

11.2.5 Immunohematology Specimens

Gel separator tubes must not be used for immunohematology specimens.[8] It is important to refer to manufacturer's package inserts for collection tubes and for test methods for other possible gel tube application limitations.

11.3 Indwelling Lines or VADs

A line is a piece of tubing inserted into a patient's vein or artery for administering fluids and medications, monitoring pressures, and obtaining blood samples for diagnostic tests. Without complete, thorough and documented training, it is not recommended that phlebotomists draw blood from indwelling cardiovascular (arterial, central venous) or umbilical lines. Institutional policy should be followed.

NOTE: Under certain circumstances, blood specimens for clinical laboratory testing may be drawn from a vascular access device (VAD) using a blood collection system or a syringe. When obtaining a blood specimen from a VAD, the components of the blood collection system (VAD, connecting device, syringe, needle, and collection device) should be checked to ensure compatibility to avoid air leaks, which may cause hemolysis and incorrect draw volumes. Collection of the blood through lines that have been previously flushed with heparin should be avoided, if possible. If the blood must be drawn through a VAD, possible heparin contamination and specimen dilution should be considered. The line should be flushed with 5 mL of saline, and the first 5 mL of blood or six dead space volumes of the VAD discarded.

11.3.1 Potential Error

Obtaining blood specimens from indwelling lines or VADs may be a problem and a potential source of test error because of incomplete flushing of collection site resulting in contamination and/or dilution of the specimen contributing to inaccurate results.[20-22]

11.3.2 Flushing Lines

Because it is normal practice to flush lines with a solution to reduce the risk of thrombosis, lines must be cleared of this fluid before blood specimens can be drawn for diagnostic testing. An adequate amount of blood must be withdrawn from the line and discarded before drawing a specimen to ensure that the actual specimen is not diluted or contaminated with the flush solution. Discard volume is dependent on the dead

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space volume of the particular line. Discarding two times the dead-space volume is recommended for noncoagulation testing, and 5 mL or six times the dead-space volume for coagulation tests.[20,23-25] (For additional information, please refer to the most current edition of NCCLS document H21—*Collection, Transport, and Processing of Blood Specimens for Coagulation Testing and General Performance of Coagulation Assays.*) See the "NOTE" in Section 11.3 for specific recommendations for coagulation testing specimens with line draws.

11.4 Heparin or Saline Locks

An indwelling winged infusion set can be successfully left in a vein from 36 to 48 hours for intravenous administration of medication or as a vein source to obtain a blood specimen. This procedure, known as a "heparin or saline lock," has become more common in hospitals to "save" veins for therapeutic use and also to cause less trauma to the patient. With this system, it is not necessary to keep the vein open with a continuous intravenous infusion, thus allowing the patient more comfort and mobility.

11.5 Fistula

A fistula is an artificial shunt connection done by a surgical procedure to fuse the vein and artery together. It is used for dialysis only.

An arm with a fistula should not be used routinely for blood drawing. When possible, specimens should be drawn from the opposite arm. Care must be taken of the fistula, as it is permanent.

11.6 Intravenous Fluids

Skin puncture is recommended when venous access is not readily available. (See the most current edition of NCCLS document H4—*Procedures and Devices for the Collection of Diagnostic Blood Specimens by Skin Puncture* for more information.)

When an intravenous fluid (including transfused blood products) is being administered in a patient's arm, blood should not be drawn from that arm if at all possible. Test results from this blood may be erroneous and thus misleading to the physician.

Satisfactory specimens may be drawn distal to the intravenous infusion site. If this is not possible, a specimen may be obtained from a proximal site.[13,26] However, it has been shown that blood drawn proximal to the intravenous site can be contaminated with the fluid being administered. Facilities should establish their own policy. The collection procedure is as follows:

(1) Ask the responsible caregiver for the intravenous infusion to be turned off for at least two minutes before venipuncture. Care should be taken to ensure that the flow has been completely discontinued.

(2) Apply the tourniquet. When drawing distal to the intravenous infusion site, apply the tourniquet between the intravenous and the intended venipuncture site.

(3) Perform the venipuncture.

It must be documented that the venipuncture was performed proximal or distal to an infusion site and from which arm.

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11.7 Isolation

Patients are isolated to prevent disease from spreading to other patients, visitors, or employees.[27] Some hospitals may also provide a different, protective isolation for patients who could be placed at increased risk from outside contamination.

11.7.1 Isolation Systems

Each hospital determines the system which best provides for their particular mix of patients, visitors, and employees. In most cases, a color-coded card placed just outside the patient's room describes the type of isolation and the precautions to be taken by those entering the room. It is important to understand and use the appropriate precautions.

11.7.1.1 Types of Isolation

Recent guidance emphasizes two tiers of infection control precautions[27]:

- standard, to be used for all patients, and
- transmission-based.

There are three types of transmission based isolation precautions[23]:

- airborne,
- droplet, and
- contact.

Hospitals have protocols for isolation procedures available through their infection control practitioner, infection control committee, or hospital epidemiologist. The example given in Sections 11.7.1.2 through 11.7.2 is an example of such a protocol. Some hospitals may provide for disinfection, dedication or disposal of equipment used in isolation rooms.

11.7.1.2 Clean Area

Gowns, gloves, masks, etc., are kept in a clean area. In some hospitals, a stand containing these supplies is kept outside the room. The new modern hospital often has an anteroom which serves as the "clean area." Here, the person entering the room can gown and apply other protective barriers as necessary before entering the patient's room. Doctors' suit coats, jackets, and other apparel are left here.

11.7.2 Isolation Room

11.7.2.1 Procedures to Follow Before Entering the Isolation Room

(1) Read the isolation sign on the door. It will explain the type of isolation, protective clothing to be worn, and the procedure to follow. Follow these instructions carefully.

(2) Check the orders and assemble an adequate amount of necessary equipment for the patient.

NOTE: Any supplies taken into the room must be left there, or discarded.

(3) Never take trays into the isolation room.

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11.7.2.2 Procedures to Follow in an Isolation Room

(1) Place paper towels on the table and place the equipment on one or two towels that have been spread open.

(2) Wash hands.

(3) Put on gloves.

(4) Obtain blood specimens in the usual manner, avoiding any unnecessary contact with the patient and bed.

(5) After mixing, place the filled tubes on a clean paper towel.

(6) Dispose of blood collection assembly into an easily accessible, approved puncture resistant disposal container, consistent with OSHA regulations, according to institutional policy.

NOTE: Recapping of needle is not recommended. (See the most current edition of NCCLS publication M29—*Protection of Laboratory Workers from Occupationally Acquired Infections*.)

(7) Dispose of the tourniquet in the proper container.

(8) Remove gown and gloves and dispose of them in the proper container.

(9) Wash hands.

(10) Turn off the faucet with a clean paper towel so that hands are not contaminated.

(11) Pick up the tubes from the paper towel and clean the outside of the tube with 1:10 dilution of bleach. Place tubes in a secondary container, which will contain the specimen if the primary container breaks or leaks in transit to the laboratory. A plastic bag with a sealable, leakproof closure can be used.

(12) If blood smears were made, place the smears on two clean paper towels. When ready to leave, wrap the smears and tubes in the top paper towel and discard the bottom paper towel and place in a secondary container.

11.7.3 Exposure

The phlebotomist must immediately report an accidental needlestick or contamination of a break in the skin by blood or excreta to a supervisor, and follow institutional guidelines. (See also NCCLS document M29—*Protection of Laboratory Workers from Occupationally Acquired Infections*.)

11.8 Emergency Situations

At least one member of available on-site healthcare personnel should have extensive first aid training, including special training in cardiopulmonary resuscitation, so that medical attention can be given to a needy patient while the physician on call is en route. This individual should be identified to phlebotomists. Emergency numbers should be posted in phlebotomy drawing areas.

11.8.1 Syncope (Fainting) or Unexpected Nonresponsiveness

The procedure for dealing with a patient who has fainted or is unexpectedly nonresponsive is to:

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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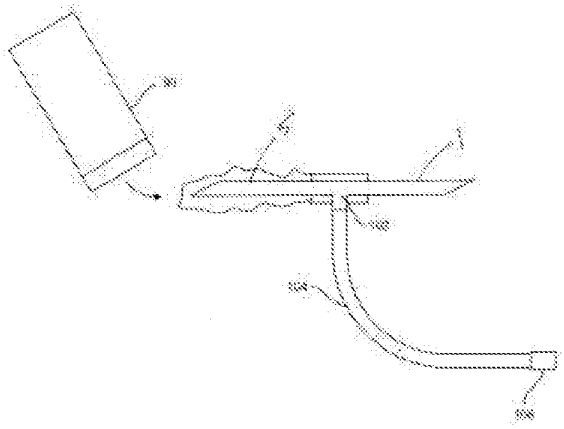
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Abstract of CA2993646 (A1)

Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.



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

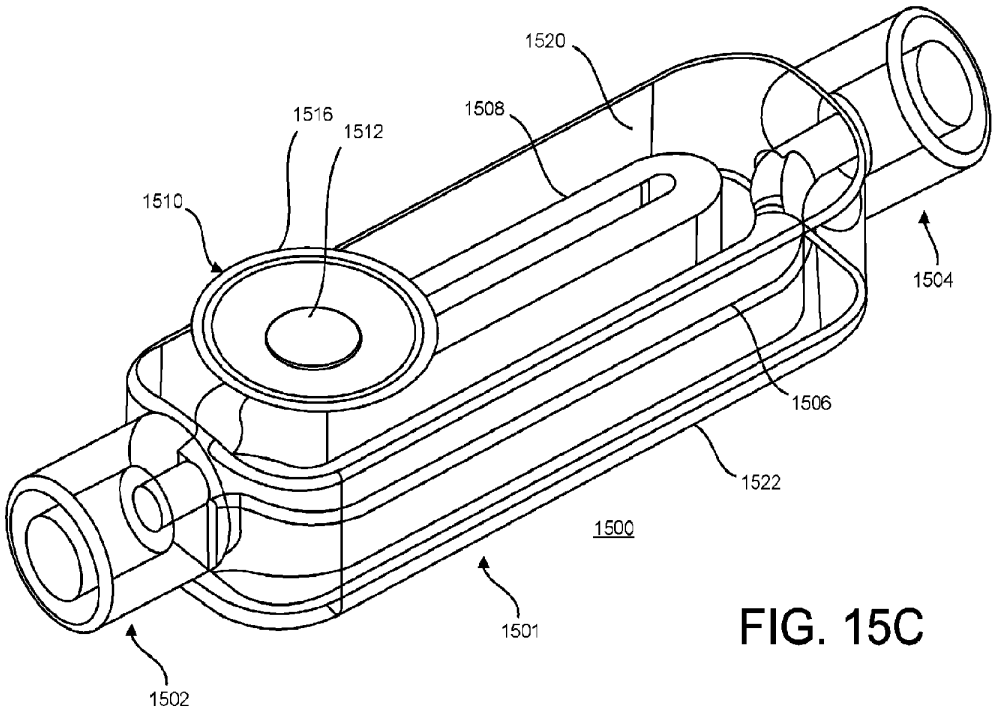


FIG. 15C

(57) Abrégé/Abstract:
Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

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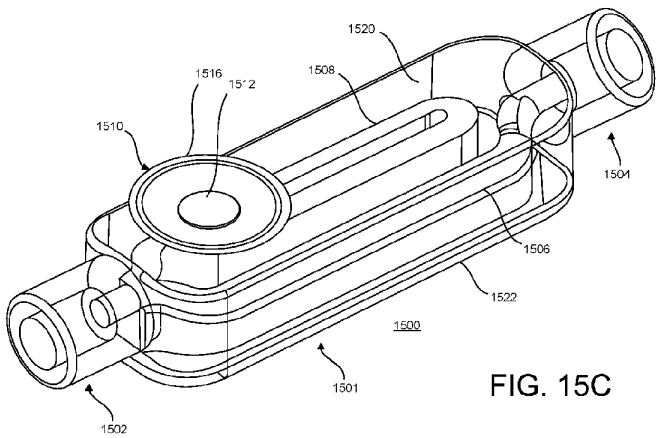


FIG. 15C

(57) Abstract: Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of U.S. Non-Provisional Application Serial No. 15/140,443, filed on April 27, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD" and U.S. Non-Provisional Application Serial No. 15/140,448, filed on April 27, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD", both of which claim priority to U.S. Provisional Application Serial No. 62/196,797, filed on July 24, 2015 and titled "BLOOD CULTURE IMPROVEMENT SYSTEM AND METHOD"; U.S. Provisional Application Serial No. 62/238,636, filed on October 7, 2015 and titled "BLOOD SEQUESTRATION SYSTEM FOR NON-CONTAMINATED BLOOD SAMPLING"; and U.S. Provisional Application Serial No. 62/318,194, filed on April 4, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD," the disclosures of which are incorporated by reference in their entirety.

BACKGROUND

[0002] Bacteraemia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteraemia in the presence of clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteraemia and sepsis are associated with a high mortality and an increased incidence and duration of hospital stay and associated costs. Many bacteraemias, sepsis, fungaemias and other pathogens actually occur within a hospital or other healthcare settings with catheters and venipunctures being a source of contamination as potential carriers of these pathogens.

[0003] Blood cultures are the standard test used to detect microbial pathogens related to bacteraemia and sepsis in a patient's blood. The term blood culture refers to a single venipuncture, either from a peripheral site or central or arterial line, with the blood inoculated into one or more blood culture bottles or containers. One bottle is considered a blood culture where two or more are considered a set. Multiple sets may be obtained from multiple venipunctures and are associated with different sites on the patient.

[0004] These methods allow for microbial identification and susceptibility testing to be performed, which is a critical component to managing sepsis, however the lack of rapid results and decreased sensitivity for fastidious pathogens has led to the development of improved systems and adjunctive molecular or proteomic testing.

[0005] Collection of blood samples for conducting blood cultures is a critical component of modern patient care and can either positively affect the patient outcome by providing an accurate diagnosis, or can adversely affect the outcome by prolonging unnecessary antimicrobial therapy, the length of hospital stays, and increasing costs.

[0006] One outcome of collection of blood cultures is contamination. Blood culture contamination can lead to a false positive culture result and/or significant increase in healthcare related costs. Sources of blood culture contamination include improper skin antisepsis, improper collection tube disinfection, and contamination of the initial blood draw which may then skew results.

[0007] Blood culture collection kits generally consist of a "butterfly" set, infusion set, or other type of venipuncture device as offered by companies like BD, Smiths, B. Braun and others, and aerobic and anaerobic blood culture bottles. Various different bottles are also available depending on the test requirements. These bottles are specifically designed to optimize recovery of both aerobic and anaerobic organisms. In conventional kits, a bottle used is known generally as a "Vacutainer," which is a blood collection tube formed of a sterile glass or plastic tube with a closure that is evacuated to create a vacuum inside the tube to facilitate the draw of a predetermined volume of liquid such as blood.

[0008] False positive blood cultures are typically a result of poor sampling techniques. They cause the use of antibiotics when not needed, increasing hospital costs and patient anxiety. Blood cultures are drawn from a needlestick into the skin, and then a Vacutainer is attached to capture a sample of blood. Contamination may occur from improper or incomplete disinfection of the skin area in and around the puncture site. It may also occur from the coring of the skin by the needle during insertion, with the cored skin cells and any associated contamination being pulled into the sample.

[0009] Blood flow through a hypodermic needle is laminar, and as such, a velocity gradient can be developed over the flow tube as a pressure drop is applied to the hypodermic needle. Either forceful aspiration of blood, or using a very small hypodermic needle, can cause lysis and a release of potassium from the red blood cells, thereby rendering the blood samples abnormal.

[0010] In other instances, some patients have delicate veins that can collapse under a pressure drop or vacuum, particularly as applied by a syringe's plunger that is drawn too quickly for the patient's condition. Since such condition is impossible to know beforehand, such vein collapses are a risk and very difficult to control.

[0011] Various strategies have been implemented to decrease blood culture contamination rates, e.g. training staff with regard to aseptic collection technique, feedback with regard to contamination rates and implementation of blood culture collection kits. Although skin antisepsis can reduce the burden of contamination, 20% or more of skin organisms are located deep within the dermis and are unaffected by antisepsis. Changing needles before bottle inoculation is not advisable as it increases the risk to acquire needle stick injuries without decreasing contamination rates.

[0012] Some conventional systems and techniques for reducing blood culture contamination include discarding the initial aliquot of blood taken from central venous catheters, venipunctures, and other vascular access systems. However, these systems require the user to mechanically manipulate an intravascular device, or require a complex series of steps that are difficult to ensure being followed.

SUMMARY

[0013] This document presents systems and methods for reducing blood culture contamination, lysing of cells, and vein collapse. In some implementations, a system and method can eliminate user variability in disinfection, and also eliminate the risk of skin cells getting into the blood culture sample. The systems and methods disclosed herein do not require a change in existing clinical processes, other than to potentially indicate when a vacutainer or other blood collection device (i.e., syringe) should be attached for drawing contaminant-free blood samples.

[0014] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

[0015] In one aspect, a blood sequestration device is presented. The blood sequestration device includes an inlet port and an outlet port. The blood sequestration device further includes a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

[0016] In another aspect, a blood sequestration device connected with a blood sampling pathway is described. The blood sampling pathway has a patient needle and a sample collection device. The blood sequestration device includes an inlet port connected with the patient needle, and a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, and an outlet port connected with a distal end of the sampling channel and with the sample collection device.

[0017] In yet another aspect, a blood sequestration device connected with a blood sampling system is described. The blood sampling system includes a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed and adapted for receiving an evacuated blood collection tube. The blood sequestration device includes an inlet port connected with the patient needle to receive the blood sample from the patient. The blood sequestration device further includes a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed by the evacuated blood collection tube. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a subsequent portion of the blood sample once the sample needle is unsealed by the evacuated blood collection tube. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel for conveying the subsequent portion of the blood sample to the sample needle.

[0018] In yet another aspect, a blood sample optimization system is disclosed and described. The blood sample optimization system includes a blood sampling system for accessing and acquiring one or more samples of a patient's blood, and a blood sequestration device for receiving and sequestering a first portion of the one or more samples of the patient's blood which might be contaminated by a venipuncture process and which could result in a false positive identification of a pathogen in the patient's blood.

[0019] The blood sampling system includes a patient needle configured for a venipuncture of a patient to access a sample of blood of a patient, a blood sampling pathway connected with the patient needle for conveying the sample of blood, and a sample needle configured for receiving an evacuated blood collection container to collect and contain a subsequent portion of the sample of blood.

[0020] In yet another aspect, a blood sequestration device is disclosed and described. In some implementations, the blood sequestration device can include an inlet port, an outlet port connected with the inlet port, and a sequestration chamber connected with the inlet port. The sequestration chamber can have a vent comprising an air permeable blood barrier.

[0021] The blood sequestration device is connected along the blood sampling pathway between the patient needle and the sample needle, and includes an inlet port for receiving the sample of blood. The blood sequestration device further includes a sequestration chamber connected with the inlet port for receiving a first amount of the sample of blood, the sequestration chamber having a vent comprising an air permeable blood barrier for sequestering at least a first portion of the first amount of the sample of blood. The blood sequestration device may further include a sampling channel having a proximal end connected with the inlet port, the sampling channel conveying a subsequent amount of the sample of blood to the evacuated blood collection container upon the sequestration chamber sequestering at least the first portion of the first amount of the sample of blood. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel, the outlet port for outputting the subsequent amount of the sample of blood.

[0022] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] These and other aspects will now be described in detail with reference to the following drawings.

[0024] FIG. 1 illustrates a blood sample optimization system.

[0025] FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0026] FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0027] FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0028] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0029] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0030] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.

[0031] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.

[0032] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.

[0033] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.

[0034] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.

[0035] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.

[0036] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

[0037] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.

[0038] FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.

[0039] FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

[0040] FIGS. 17A – 17E illustrate a bottom member of a housing for a blood sequestration device.

[0041] FIGS. 18A – 18F illustrate a top member of a housing for a blood sequestration device.

[0042] FIGS. 19A and 19B illustrate a blood sequestration device having a top member mated with a bottom member.

[0043] FIG. 20 shows a blood sample optimization system including a blood sequestration device.

[0044] FIG. 21 illustrates a non-vented blood sequestration device using a wicking material chamber.

[0045] FIGS. 22A and 22B illustrate a material makeup of a filter for sequestering blood in a sequestration chamber of a blood sequestration device.

[0046] FIGS. 23A and 23B illustrate another implementation of a blood sequestration device that uses a vacuum force from a blood collection device.

[0047] Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

[0048] This document describes blood sample optimization systems and methods for reducing or eliminating contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated

aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[0049] FIG. 1 illustrates a blood sample optimization system in accordance with some implementations. The system includes a patient needle 1 to puncture the skin of a patient to access the patient's vein and blood therein. The system further includes a sample needle (i.e., a resealably closed needle for use with Vacutainers™ or the like) 5, which may be contained within and initially sealed by a resealable boot 10, a Luer activated valve, or another collection interface or device. The resealable boot 10 can be pushed aside or around the sample needle 5 by application of a Vacutainer™ bottle (not shown) for drawing the patient's blood. The system can further include a low volume chamber 30 that leads to the sample needle 5, but also includes an orifice or one or more channels 45 that lead to a sequestration chamber 55 formed by a housing 50.

[0050] The sequestration chamber 55 is a chamber, channel, pathway, lock, or other structure for receiving and holding a first aliquot of the patient's blood, which may be in a predetermined or measured amount, depending on a volume of the sequestration chamber 55. The first draw of blood typically contains or is more susceptible to containing organisms that cause bacteraemia and sepsis or other pathogens than subsequent blood draws. The sequestration chamber 55 can be a vessel encased in a solid housing, formed in or defined by the housing itself, or can be implemented as tubing or a lumen. The sequestration chamber 55, regardless how formed and implemented, may have a predetermined volume. In some implementations, the predetermined volume may be based on a volume of the patient needle, i.e. ranging from less than the volume of the patient needle to any volume up to or greater than 20 times or more of the volume of the patient needle. The predetermined volume of the sequestration chamber 55 may also be established to economize or minimize an amount of blood to be sequestered and disposed of.

[0051] The sequestration chamber 55 can be formed, contained or housed in a chamber housing 50, and can be made of plastic, rubber, steel, aluminum or other suitable material. For example, the sequestration chamber 55 could be formed of flexible tubing or

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

[0052] The orifice or channel 45 can be any desired length, cross-sectional shape or size, and/or can be formed to depart from the low volume chamber 30 at any desired angle or orientation. The orifice or channel 45 may also include a one-way flap or valve 60 that maintains an initial aliquot of blood sample within the sequestration chamber 55. In some specific implementations, the orifice or channel 45 can include a "duck bill" or flapper valve 60, or the like, for one-way flow of blood from low volume chamber 30 to the sequestration chamber 55. The air permeable blood barrier 20 can also be constructed of a material that allows air to exit but then seals upon contact with blood, thereby not allowing external air to enter sequestration chamber 55. This sealing would eliminate the need for a valve.

[0053] Valve 60 can be any type of valve or closing mechanism. Chamber 30 is designed to hold virtually no residual blood, and can be designed to be adapted to hold or allow pass-through of a particular volume or rate of blood into sequestration chamber 55. Likewise, sequestration chamber 55 may also include any type of coating, such as an anti-microbial coating, or a coating that aids identification and/or diagnosis of components of the first, sequestered blood draw.

[0054] Housing 50 and 40 can be formed of any suitable material, including plastic, such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric material, rubber, steel, or aluminum. The air permeable blood barrier 20 can include a color-providing substance, or other signaling mechanism, that is activated upon contact with blood from the initial blood draw, or when air displacement is stopped, or any combination of events with blood in the sequestration chamber 55. The air permeable barrier may also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents the inadvertent or premature sealing of the filter by an external fluid source, splash etc. Sequestration chamber 55 can also be translucent or clear to enable a user to visually confirm the chamber is filled.

[0055] FIG. 2 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown in FIG. 2, a sequestration chamber 55, or waste chamber, surrounds the patient needle 1, with an open-ended cuff or housing connected with the waste chamber and encircling the sample needle housing base and housing. The patient needle 1 and sample needle 5 are connected together by a boot 56, which forms a continuous blood draw channel therethrough. The boot 56 includes a single orifice or channel leading from the blood draw channel into sequestration chamber 55. The device can include more than one single orifice or channel, in other implementations. Each orifice or channel can include a one-way valve, and can be sized and adapted for predetermined amount of blood flow.

[0056] The sequestration chamber 55 includes an air permeable blood barrier. The filter can further include a sensor or indicator to sense and/or indicate, respectively, when a predetermined volume of blood has been collected in the sequestration chamber 55. That indication will alert a user to attach an evacuated blood collection tube or bottle, such as a Vacutainer™ to the sample needle 5. The housing for the sequestration chamber 55 can be any size or shape, and can include any type of material to define an interior space or volume therein. The interior space is initially filled only with air, but can also be coated with an agent or substance, such as a decontaminate, solidifying agent, or the like. Once evacuated blood collection tube is attached to the sample needle 5, blood will flow automatically into the patient needle 1, through the blood draw channel and sample needle 5, and into the bottle.

The sample needle 5 is covered by a resealable boot, coating or membrane that seals the sample needle when a blood collection bottle is not attached thereon or thereto.

[0057] FIG. 3 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is surrounded by a resealable boot or membrane, and is further connected with a patient needle 1. A blood flow channel is formed through the sample needle and the patient needle. The connection between the sample needle and patient needle includes a "T" or "Y" connector 102, which includes a channel, port or aperture leading out from the main blood flow channel to a sequestration chamber 104.

[0058] The T or Y connector 102 may include a flap or one-way valve, and have an opening that is sized and adapted for a predetermined rate of flow of blood. The sequestration chamber 104 can be formed from tubing, or be formed by a solid housing, and is initially filled with air. The sequestration chamber 104 will receive blood that flows out of a patient automatically, i.e. under pressure from the patient's own blood pressure. The sequestration chamber 104 includes an air permeable blood barrier 106, preferably at the distal end of tubing that forms the sequestration chamber 104, and which is connected at the proximal end to the T or Y connector 102. The T or Y connector 102 can branch off at any desired angle for most efficient blood flow, and can be formed so as to minimize an interface between the aperture and channel and the main blood flow channel, so as to minimize or eliminate mixing of the initial aliquot of blood with main blood draw samples.

[0059] In some alternative implementations, the sample needle may be affixed to a tubing of any length, as shown in FIG. 4, connecting at its opposite end to the T or Y connector 102. The sequestration chamber 104 can be any shape or volume so long as it will contain a predetermined amount of blood sample in the initial aliquot. The T or Y connector 102 may also include an opening or channel that is parallel to the main blood flow channel. The air permeable blood barrier may further include an indicator 107 or other mechanism to indicate when a predetermined amount of blood has been collected in the sequestration chamber, or when air being expelled reaches a certain threshold, i.e. to zero. The tubing can also include a clip 109 that can be used to pinch off and prevent fluid flow therethrough.

[0060] Once the air permeable blood barrier and primary chamber are sealed the initial aliquot of blood is trapped in the sequestration chamber 104, an evacuated blood collection tube, such as a Vacutainer™ bottle may be attached to the sample needle 5 to obtain the sample. The blood collection tube can be removed, and the sample needle 5 will be resealed. Any number of follow-on blood collection tubes can then be attached for further blood draws or samples. Upon completion of all blood draws, the system can be discarded, with the initial aliquot of blood remaining trapped in the sequestration chamber 104.

[0061] FIG. 5 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is connected with a patient needle by tubing. A "T" or "Y" connector 120 is added along the tubing at any desired location, and includes an aperture, port or channel leading to a sequestration chamber 204, substantially as described above.

[0062] FIG. 6 illustrates a blood sample optimization system in accordance with some alternative implementations, in which a sequestration chamber 304, formed as a primary collection channel, receives an initial aliquot of blood, and is provided adjacent to the blood sampling channel. The sequestration chamber 304 can encircle the blood sampling channel, the patient needle 1, and/or the sample needle 5. The primary collection channel can include a T or Y connector 120, or other type of aperture or channel. The sequestration chamber 304 includes an air permeable blood barrier, which can also include an indicator of being contacted by a fluid such as blood, as described above.

[0063] In some implementations, either the patient needle 1 or the sample needle 5, or both, can be replaced by a Luer lock male or female connector. However, in various implementations, the connector at a sample needle end of the blood sample optimization system is initially sealed to permit the diversion of the initial aliquot of blood to the sequestration chamber, which is pressured at ambient air pressure and includes the air outlet of the air permeable blood barrier. In this way, the system passively and automatically uses a patient's own blood pressure to overcome the ambient air pressure of the sequestration chamber to push out air through the air permeable blood barrier and displace air in the sequestration chamber with blood.

[0064] FIG. 7 is a flowchart of an exemplary method for optimizing the quality of a blood culture. At 702, a clinician places a needle into a patient's vein. At 704, blood then flows into a sequestration chamber, pushing the air in the sequestration chamber out of the sequestration chamber through an air permeable blood barrier. In some implementations, the volume of the sequestration chamber is less than 0.1 to more than 5 cubic centimeters (cc's), or more. The sequestration chamber is sized and adapted to collect a first portion of a blood sample, which is more prone to contamination than secondary and other subsequent portion of the blood sample or subsequent draws. Since the sequestration chamber has an air-permeable blood barrier through which air can be displaced by blood pushed from the patient's vein, such blood will naturally and automatically flow into the sequestration chamber before it is drawn into or otherwise enters into a Vacutainer or other bottle for receiving and storing a blood sample.

[0065] When the sequestration chamber fills, the blood will gather at or otherwise make contact with the air permeable blood barrier, which will inhibit or prevent blood from passing therethrough. At 706, when the blood comes into contact with the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is then closed and air no longer flows out or in. At 708, the clinician may be provided an indictor or can see the full chamber, to indicate the evacuated blood collection tube, such as a Vacutainer™ can be attached. The indicator can include visibility into the primary chamber to see whether it is full, the blood barrier changing color, for example, or other indicator. The fill time of the sequestration chamber may be substantially instantaneous, so such indicator, if present, may be only that the sequestration chamber is filled.

[0066] Prior to an evacuated blood collection tube being attached, communication between the needle, sampling channel, and the sequestration chamber is restricted by the sealing of the sequestration chamber blood barrier thereby not permitting air to reenter the system through the sequestration. Sealing the communication path could also be accomplished with a mechanical twist or other movement, a small orifice or tortuous pathway, eliminating the need for a separate valve or mechanical movement or operation by the clinician. At 710, once the evacuated blood collection tube is removed, the self-sealing membrane closes the sample needle, and at 712, additional subsequent evacuated blood

collection tubes may be attached. Once samples have been taken, at 714 the device is removed from the patient and discarded.

[0067] FIGS. 8A – 8E illustrate an exemplary blood sample optimization system 800 for non-contaminated blood sampling, in accordance with some implementations. The blood sample optimization system 800 includes an inlet port 802 that can be connected to tubing, a patient needle (or both), or other vascular or venous access device, and a pathway splitter 804 having a first outlet to a sequestration chamber tubing 806 and a second outlet to sample collection tubing 808. One or both of the sequestration chamber tubing 806 and the sample collection tubing 808 can be formed of tubing. In some implementations, the sequestration chamber tubing 806 is sized so as to contain a particular volume of initial blood sample. The sample collection tubing 808 will receive a blood sample once the sequestration chamber tubing 806 is filled. The sample collection tubing 808 can be connected to a Vacutainer™ base or housing 810, or other blood sample collection device.

[0068] The blood sequestration system 800 further includes a blood sequestration device 812 which, as shown in more detail in FIGS. 8B – 8D, includes a housing 818 that includes a sampling channel 820 defining a pathway for the non-contaminated sample collection tubing 808 or connected at either end to the non-contaminated sample collection tubing 808. The sampling channel 820 can be curved through the housing 818 so as to better affix and stabilize the housing 818 at a location along the non-contaminated sample collection tubing 808.

[0069] The blood sequestration device 812 further includes a sequestration chamber 822 connected with the sequestration chamber tubing 806 or other chamber. The sequestration chamber 822 terminates at an air permeable blood barrier 824. The air permeable blood barrier 824 can also include a coloring agent that turns a different color upon full contact with blood, as an indicator that the regular collection of blood samples (i.e. the non-contaminated blood samples) can be initiated. Other indicators may be used, such as a small light, a sound generation mechanism, or the like. In some implementations, the air permeable blood barrier is positioned at a right angle from the direction of sequestration chamber 822, but can be positioned at any distance or orientation in order to conserve space

and materials used for the housing 818. The housing 818 and its contents can be formed of any rigid or semi-rigid material or set of materials.

[0070] FIG. 9 illustrates a pathway splitter 900 for use in a blood sequestrations system, such as those shown in FIGS. 8A – 8E, for example. The pathway splitter 900 includes an inlet port 902, a main line outlet port 904, and a sequestration channel outlet port 906. The inlet port 902 can be connected to main tubing that is in turn connected to a patient needle system, or directly to a patient needle. The main line outlet port 904 can be connected to main line tubing to a blood sampling system, such as a vacutainer base or housing, or directly to such blood sampling system. The sequestration channel outlet port 906 can be connected to sequestration tubing for receiving and sequestering a first sample of blood, up to a measured amount or predetermined threshold. Alternatively, the sequestration channel outlet port 906 can be connected to a sequestration chamber. The sequestration channel outlet port 906 is preferably 20-70 degrees angled from the main line outlet port 904, which in turn is preferably in-line with the inlet port 902. Once the predetermined amount of initial blood sample is sequestered in the sequestration tubing or chamber, in accordance with mechanisms and techniques described herein, follow-on blood samples will flow into the inlet port 902 and directly out the main line outlet port 904, without impedance.

[0071] FIGS. 10A – 10D illustrate a blood sequestration device 1000 in accordance with alternative implementations. The blood sequestration device 1000 includes an inlet port 1002, a main outlet port 1004, and a sequestration channel port 1006. The inlet port 1002 can be connected to a patient needle or related tubing. The main outlet port 1004 can be connected to a blood sample collection device such as a Vacutainer, associated tubing, or a Luer activated valve, or the like. The sequestration channel port 1006 splits off from the main outlet port 1004 to a sequestration chamber 1008. In some implementations, the sequestration chamber 1008 is formed as a helical channel within a housing or other container 1001.

[0072] The sequestration chamber 1008 is connected at the distal end to an air permeable blood barrier 1010, substantially as described above. Air in the sequestration chamber 1008 is displaced through the air permeable blood barrier 1010 by an initial aliquot

of blood that is guided into the sequestration channel port 1006. Once the sequestration chamber 1008 is filled, further blood draws through the main outlet port 1004 can be accomplished, where these samples will be non-contaminated.

[0073] FIGS. 11A – 11E illustrate a blood sequestration device 1100 in accordance with other alternative implementations. The blood sequestration device 1100 includes an inlet port 1102, similar to the inlet ports described above, a main outlet port 1104, and a sequestration channel port 1106 that splits off from the main outlet port 1104 and inlet port 1102. The sequestration channel port is connected to a sequestration chamber 1108. In the implementation shown in FIGS. 11A – 11E, the blood sequestration device includes a base member 1101 having a channel therein, which functions as the sequestration chamber 1108. The channel can be formed as a tortuous path through the base member 1101, which is in turn shaped and formed to rest on a limb of a patient.

[0074] A portion of the sequestration chamber 1108 can protrude from the base member or near a top surface of the base member, just before exiting to an air permeable blood barrier 1110, to serve as a blood sequestration indicator 1109. The indicator 1109 can be formed of a clear material, or a material that changes color when in contact with blood.

[0075] In some implementations, the blood sequestration device 1100 can include a blood sampling device 1120 such as a normally closed needle, Vacutainer™ shield or other collection device. The blood sampling device 1120 can be manufactured and sold with the blood sequestration device 1100 for efficiency and convenience, so that a first aliquot of blood that may be contaminated by a patient needle insertion process can be sequestered. Thereafter, the blood sampling device 1120 can draw non-contaminated blood samples to reduce the risk of false positive testing and ensure a non-contaminated sample.

[0076] FIGS. 12A-12D illustrate a blood sample optimization system 1200 in accordance with yet other alternative implementations. The system 1200 includes a blood sequestration device 1202 for attaching to a blood sampling device 1204, such as a Vacutainer™ or other collection and sampling device. The blood sequestration device 1202 is configured and arranged to receive, prior to a Vacutainer™ container or vial being attached to a collection needle of the blood sampling device 1204, a first aliquot or amount of blood,

and sequester that first aliquot or amount in a sequestration channel of the blood sequestration device 1202.

[0077] In some implementations, the blood sequestration device 1202 can include an inlet port 1212, a main outlet port, and a sequestration channel port. The inlet port 1212 can be connected to a patient needle or related tubing. The main outlet port 1214 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port splits off from the main outlet port to a sequestration chamber 1218.

[0078] In some implementations, the sequestration chamber 1218 is formed as a channel within the body of a sequestration device 1202. The sequestration chamber 1218 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel. The sequestration device 1202 can include a housing or other containing body, and one or more channels formed therein. As shown in FIGS. 12A and 12B, the sequestration device 1202 includes a main body 1206 and a cap 1208. The main body 1206 is formed with one or more cavities or channels, which are further formed with one or more arms 1210 that extend from the cap 1208, and which abut the cavities or channels in the main body 1206 to form the primary collection port and main outlet port.

[0079] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet other alternative implementations. The system 1300 includes a blood sequestration device 1302 for attaching to a blood sampling device 1304, such as a Vacutainer or other bodily fluid collection and sampling device. The blood sequestration device 1302 is configured and arranged to receive, prior to a Vacutainer container or vial being attached to a collection needle of the blood sampling device 1304, a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood or other bodily fluid in a sequestration channel of the blood sequestration device 1302.

[0080] The blood sequestration device 1302 includes a housing 1301 having an inlet port 1314, a main outlet port 1312, and a sequestration channel port 1316. The inlet port 1314 can be connected to a patient needle or associated tubing. The main outlet port 1312

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

[0081] In the implementation shown in FIGS. 13A-D, the sequestration chamber 1318 is formed as a cavity or chamber within housing 1301 or formed by walls that define housing 1301. The sequestration chamber 1318 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel, that is defined by the cooperation and connection of housing 1301 with cap 1307 which cap 1307 can include a protrusion 1305 that provides one or more walls or directors for the winding channel in the sequestration chamber 1318. The protrusion 1305 from the cap 1307 can be straight or curved, and may have various channels, apertures or grooves embedded therein, and can extend from the cap 1307 any angle or orientation. When the cap 1307 is connected with the housing 1301 to complete the formation of the sequestration chamber 1318, the protrusion 1305 forms at least part of the winding channel to sequester a first aliquot or amount of blood or other bodily fluid in a sequestration channel formed in the sequestration chamber 1318 and by the winding channel.

[0082] The sequestration chamber 1318 includes an air permeable blood barrier 1310, substantially as described above. Air in the sequestration chamber 1318 is displaced through the air permeable blood barrier 1310 by an initial aliquot of blood that is provided into the sequestration chamber 1318 by the blood pressure of the patient. Once the sequestration chamber 1318 is filled and the air in the sequestration chamber 1318 displaced, the blood pressure of the patient will be insufficient to drive or provide further blood into the blood sequestration device 1302, and in particular the outlet port 1312, until a force such as a vacuum or other pressure, such as provided by the blood sample collection device like Vacutainer is provided to draw out a next aliquot or amount of blood or bodily fluid. Further blood draws through the main outlet port 1312 can be accomplished, where these samples will be non-contaminated since any contaminants would be sequestered in the sequestration chamber 1318 with the first aliquot of blood.

[0083] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system 1400 to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[0084] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more. The blood sequestration device 1401 further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a non threaded interference or glue joint fitting for attachment of various devices including but not limited to tubing, or the like.

[0085] The blood sequestration device 1401 further includes a sampling channel 1406 between the inlet port 1402 and the outlet port 1404, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1406 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1406 has a substantially similar cross sectional area as the opening of the inlet port 1402. In other implementations, the sampling channel 1406 can gradually widen from the inlet port 1402 to the outlet port 1404.

[0086] The blood sequestration device 1401 further includes a sequestration chamber 1408 that is connected to and split off or diverted from the sampling channel 1406 at any point between the inlet port 1402 and the outlet port 1404, but preferably from a proximal end of the sampling channel 1406 near the inlet port 1402. The sequestration chamber 1408 is at first maintained at atmospheric pressure, and includes an air outlet 1412 at or near a distal end of the sequestration chamber 1408 opposite the diversion point from the sampling channel 1406. The air outlet 1412 includes an air permeable blood barrier 1412. As shown in FIG. 14B, the air permeable blood barrier 1412 can be overlaid with a protective cover 1416. The protective cover 1416 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1412 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1412 as the air is displaced from the sequestration chamber 1408 by blood being forced into the sequestration chamber 1408 by a patient's own blood pressure. In addition the protective cover 1416 can be constructed to inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0087] As shown in FIGS. 14C and 14D, the sampling channel 1406 can be cylindrical or frusto-conical in shape, going from a smaller diameter to a larger diameter, to minimize a potential to lyse red blood cells. Likewise, the sampling channel 1406 is formed with a minimal amount of or no sharp turns or edges, which can also lyse red blood cells. The sampling channel 1406 splits off to the sequestration chamber 1408 near the inlet port 1402 via a diversion pathway 1409. The diversion pathway 1409 can have any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least part of the inlet port 1402.

[0088] In some implementations, the sampling channel 1406 and the sequestration chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414. The housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a bottom member that sealably mates with a top member. One or both of the bottom member and the top member can include the sampling channel 1406 and the sequestration chamber 1408, as well as the diversion pathway 1409, the inlet port 1402,

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

[0089] FIGS. 15A-15G illustrate a blood sequestration device 1500. The blood sequestration device 1500 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like.

[0090] The blood sequestration device 1500 includes an inlet port 1502 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1502 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1502 defines an opening into the blood sequestration device 1500, which opening may be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[0091] The inlet port 1502 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1502, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner,

the blood sequestration device 1500 can be fabricated and sold with the patient needle as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1500 at the time of blood draw or sampling.

[0092] The blood sequestration device 1500 further includes an outlet port 1504, which defines an opening out of the blood sequestration device 1500 and to the blood sample collection device. The outlet port 1504 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1500 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1500 at the time of blood draw or sampling.

[0093] The blood sequestration device 1500 further includes a sampling channel 1506 between the inlet port 1502 and the outlet port 1504, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1506 can be any sized, shaped or configured channel or conduit. In some implementations, the sampling channel 1506 has a substantially similar cross sectional area as the opening of the inlet port 1502. In other implementations, the sampling channel 1506 can gradually widen from the inlet port 1502 to the outlet port 1504.

[0094] The blood sequestration device 1500 further includes a sequestration chamber 1508 that is connected to and split off or diverted from the sampling channel 1506 at any point between the inlet port 1502 and the outlet port 1504, but preferably from a proximal end of the sampling channel 1506 near the inlet port 1502. In some implementations, the diversion includes a Y-shaped junction. The sequestration chamber 1508 is preferably maintained at atmospheric pressure, and includes a vent 1510 at or near a distal end of the sequestration chamber 1508. The vent 1510 includes an air permeable blood barrier 1512. FIG. 15C illustrates the blood sequestration device 1500 with the sequestration chamber 1508 filled with a first aliquot or sample of blood from the patient.

[0095] The air permeable blood barrier 1512 can be covered with a protective cover 1516. The protective cover 1516 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1512 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1512 as the air is displaced from the sequestration chamber 1508 by blood being forced into the sequestration chamber 1508 by a patient's own blood pressure. The protective cover 1516 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0096] FIG. 15B is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating an initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before a sample collection device is activated. FIG. 15G is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and bottom side of the housing 1501 of the blood sequestration device 1500, and illustrating the initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before the sample collection device is activated. FIG. 15C is another perspective view of the blood sequestration device 1500 from the inlet port 1502 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating blood now being drawn through sampling channel 1506 while the sequestered blood remains substantially in the sequestration chamber 1508.

[0097] FIG. 15D is a cross section of the blood sequestration device 1500 in accordance with some implementations, showing the housing 1501 that defines the sampling channel 1506 and the sequestration chamber 1508. FIGS. 15E and 15F illustrate various form factors of a housing for a blood sequestration device, in accordance with one or more implementations described herein.

[0098] The sequestration chamber 1508 can have a larger cross-sectional area than the sampling channel 1506, and the cross-sectional area and length can be configured for a predetermined or specific volume of blood to be sequestered or locked. The sampling

channel 1506 can be sized to be compatible with tubing for either or both of the patient needle tubing or the blood collection device tubing.

[0099] The housing 1501 can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIG. 15D, the housing 1501 includes a top member 1520 and a bottom member 1522 that are mated together, one or both of which having grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc. The top member 1520 can be connected with the bottom member 1522 by any mating or connection mechanism, such as by laser welding, thermal bonding, ultrasonic welding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like.

[00100] In some implementations, such as shown in FIG. 15D, the top member 1520 can include the grooves, channels, locks, conduits or other pathways, while the bottom member 1522 can include a protrusion 1524 that is sized and adapted to fit into at least one of the grooves, channels, locks or other pathways of the top member 1520. The protrusion 1524 can provide a surface feature, such as a partial groove or channel, for instance, to complete the formation of either the sampling channel 1506 and/or the sequestration chamber 1508. In some implementations, the protrusion 1524 can be formed with one or more angled sides or surfaces for a tighter fit within the corresponding groove, channel, lock or other pathway. In yet other implementations, both the top member 1520 and the bottom member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524.

[00101] In some implementations, the sampling channel 1506 and the sequestration chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501. The housing 1501 can be made of any suitable material, including rubber, plastic, metal or other material. The housing 1501 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1501 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1506 and/or the sequestration chamber 1508 is clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1508 is first filled to the

extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1506. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1512 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00102] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will make its way into the input port 1502 blood sequestration device 1500 and flow into the sequestration chamber 1508 by following the path of least resistance, as the patient's own blood pressure overcomes the atmospheric pressure in the sequestration chamber 1508 to displace air therein through the air permeable blood barrier 1512. The patient's blood pressure will not be sufficient to overcome the air pressure that builds up in the sealed sampling channel 1506. Eventually, the sequestration chamber 1508, which has a predetermined volume, is filled with blood that displaces air through the air permeable blood barrier 1512. Once the blood hits the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1512 material to completely or partially seal the vent 1510. A signal or indication may be provided that the practitioner can now utilize the Vacutainer capsule or other blood sample collection device to acquire a next amount of the patient's blood for sampling. The blood in the sequestration chamber 1508 is now effectively sequestered in the sequestration chamber.

[00103] Upon filling the blood sequestration pathway 1508 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1506, possibly resulting in a small amount of blood moving past the diversion point to the sequestration chamber 1508 and into the sampling channel 1506, queuing up the uncontaminated blood to be drawn through the sampling channel 1506.

[00104] FIGS. 16-19 illustrate yet another implementation of a blood sequestration device. FIGS. 16A-16D illustrate a blood sequestration device 1600 that can be connected

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

[00105] Referring to FIGS. 16A – D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00106] The inlet port 1602 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1602, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1600 at the time of blood draw or sampling.

[00107] The blood sequestration device 1600 further includes an outlet port 1604, which defines an opening out of the blood sequestration device 1600 and to the blood sample collection device. The outlet port 1604 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing

or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

[00108] The blood sequestration device 1600 further includes a sampling channel 1606 between the inlet port 1602 and the outlet port 1604, and a sequestration chamber 1608 that is connected to and split off or diverted from the sampling channel 1606 at any point between the inlet port 1602 and the outlet port 1604. The sampling channel 1606 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 1608. The sampling channel 1606 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1606 has a substantially similar cross sectional area as the opening of the inlet port 1602. In other implementations, the sampling channel 1606 can gradually widen from the inlet port 1602 to the outlet port 1604. The sequestration chamber 1608 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 1606, as is shown more fully in FIGS. 17 and 19.

[00109] In some exemplary implementations, the diversion between the sampling channel 1606 and the sequestration chamber 1608 is by diverter junction 1607. Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 1607 is configured such that the flow out of the inlet port 1602 is preferentially directed toward the sequestration chamber 1608. The sequestration chamber 1608 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 1608.

[00110] The sequestration chamber 1608 is preferably maintained at atmospheric pressure, and includes a vent 1610 at or near a distal end of the sequestration chamber 1608. The vent 1610 may include an air permeable blood barrier 1612 as described above.

[00111] The blood sequestration device 1600 can include a housing 1601 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIGS. 17A – 17D and FIGS. 18A – 18F, the housing 1601 includes a top member 1620 and a bottom member 1622 that are mated together. The blood sequestration device 1600 can also include a gasket or other sealing member (not shown) so that when the top member 1620 is mechanically attached with the bottom member 1622, the interface between the two is sealed by the gasket or sealing member. The FIGS. 17A – 17D illustrate a bottom member 1622 of a housing for a blood sequestration device 1600. The bottom member 1622 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 1606, the sequestration chamber 1608, and diverter junction 1607.

[00112] The sequestration chamber 1608 may have a larger cross section than the sampling channel 1606 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 1606.

[00113] FIGS. 18A – 18F illustrate the top member 1620, which can be connected with the bottom member 1622 by any mating or connection mechanism, such as by laser welding, thermal bonding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like. The top member 1620 can include some or all of the grooves, channels, locks, conduits or other pathways to form the sampling channel 1606, the sequestration chamber 1608, and the diverter junction 1607. In yet other implementations, both the top member 1620 and the bottom member 1622 can include the grooves, channels, locks or other pathways.

[00114] In some implementations, the sampling channel 1606 and the sequestration chamber 1608 are formed by grooves, channels, locks or other pathways formed in housing 1601. The housing 1601 can be made of rubber, plastic, metal or any other suitable material. The housing 1601 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1601 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1606 and/or the sequestration chamber 1608 may be clear or translucent, giving a practitioner a

visual cue or sign that the sequestration chamber 1608 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1606. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1612 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00115] As shown in FIGS. 18A – 18F, the air permeable blood barrier 1612 can be covered with, or surrounded by, a protective member 1616. The protective member 1616 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1612 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1612 as the air is displaced from the sequestration chamber 1608. In some implementations, the protective member 1616 includes a protrusion that extends up from a top surface of the top member 1620 and around the air permeable blood barrier 1612. The protective cover 1616 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00116] In use, the blood sequestration device 1600 includes a sampling channel 1606 and a sequestration chamber 1608. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 1606 is directed to an output port 1604 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 1608 terminates at a vent 1610 to atmosphere that includes an air permeable blood barrier 1612.

[00117] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through input port 1602 of blood sequestration device 1600. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 1608 by finding the path of least resistance. The patient's own blood

pressure overcomes the atmospheric pressure in the vented sequestration chamber 1608 to displace air therein through the air permeable blood barrier 1612, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 1606. In various exemplary embodiments, the sequestration chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00118] Eventually, the sequestration chamber 1608 fills with blood that displaces air through the air permeable blood barrier 1612. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1612 material to completely or partially seal the vent 1610. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00119] Upon filling the blood sequestration pathway 1608 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1606, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 1606, queuing up the uncontaminated blood to be drawn through the sampling channel 1606.

[00120] FIG. 19A is a side view, and FIG. 19B is a cross-sectional view, of the blood sequestration device 1600, illustrating the top member 1620 mated with the bottom member 1622.

[00121] FIG. 20 shows a blood sample optimization system 2000 that includes a patient needle 2002 for vascular access to a patient's bloodstream, a blood sample collection device 2004 to facilitate the collecting of one or more blood samples, and a conduit 2006 providing a fluid connection between the patient needle 2002 and the blood sample collection device 2004. In some implementations, the blood sample collection device 2004 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2002.

[00122] The blood sample optimization system 2000 further includes a blood sequestration device 2008, located at any point on the conduit 2006 between the patient needle 2002 and the blood sample collection device 2004 as described herein.

[00123] FIG. 21 illustrates a non-vented blood sequestration device 2100 using a wicking material chamber. The blood sequestration device 2100 includes a housing 2101 that has a sampling channel 2104 that is at least partially surrounded or abutted by a sequestration chamber 2102 that is filled with a wicking material. An initial aliquot of blood is drawn in from the patient needle into the sampling channel 2104 where it is immediately wicked into the wicking material of the sequestration chamber 2102. The wicking material and/or sequestration chamber 2102 is sized and adapted to receive and hold a predetermined amount of blood, such that follow-on or later blood draws pass by the wicking material and flow straight through the sampling channel 2104 to a sampling device such as a Vacutainer. The wicking material can include a substance such as a solidifier, a decontaminate, or other additive.

[00124] As described herein, an air permeable blood barrier may be created using a wide variety of different structures and materials. As shown in FIGS. 22A and B, an air permeable blood barrier 2202 of a blood sequestration device 2200 can include a polymer bead matrix 2204, in which at least some beads are treated to make them hydrophilic. The air permeable blood barrier 2202 further includes a self-sealing material 2206, such as carboxymethyl cellulose (CMC) or cellulose gum, or other sealing material. The air permeable blood barrier 2202 can further include voids 2208 that permit air flow before contact or during partial contact with a fluid such as blood. As shown in FIG. 22B, contact with a fluid causes the self-sealing material 2206 to swell and close off the voids 2208, occluding air flow through the voids 2208 and creating a complete or partial seal.

[00125] FIGS. 23A and B illustrate yet another implementation of a blood sequestration device 2300, having an inlet port 2302 to connect with a patient needle, an outlet port 2304 to connect with a blood sample collection device, a sequestration chamber 2306, and a sampling channel 2308 that bypasses the sequestration chamber 2306 once the sequestration chamber is filled to an initial aliquot of potentially contaminated blood to be

sequestered. The sequestration chamber 2306 includes a hydrophobic plug 2312 at a distal end of the sequestration chamber 2306 that is farthest from the inlet port 2302. A vacuum or other drawing force applied from the outlet port 2304, such as from a Vacutainer or the like, draws in blood into the inlet port 2302 and directly into the sequestration chamber 2306, where the initial aliquot of blood will contact the hydrophobic plug 2312 and cause the initial aliquot of blood to back up into the sequestration chamber 2306 and be sequestered there. A small amount of blood may make its way into the sampling channel 2308, which is initially closed off by valve 2308. Upon release of the valve 2308, and under further force of the vacuum or other force, follow-on amounts of blood will flow into inlet port 2302, bypass the sequestration chamber 2306, and flow into and through sampling channel 2308 toward the outlet port 2304 and to the collection device.

[00126] The sampling channel 2308 can have any suitable geometry and can be formed of plastic tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pinch, shunt, bend or otherwise close off the sampling channel before the initial aliquot of blood is sequestered in the sequestration chamber 2306.

[00127] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

CLAIMS

1. A blood sequestration device comprising;

an inlet port;

an outlet port;

a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier;

a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port; and

a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

2. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes an air permeable material that seals at least partially upon contact with blood.

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

4. The blood sequestration device in accordance with claim 3, further comprising a blood sampling pathway connected with the inlet port, and wherein the inlet port defined by the housing has a cross-sectional geometry consistent with the blood sampling pathway.

5. The blood sequestration device in accordance with claim 3, wherein the sampling channel defined by the housing has a cross-sectional geometry consistent with the inlet port.

6. The blood sequestration device in accordance with claim 1, wherein the sequestration chamber and the sampling channel are connected with the inlet port by a junction that is configured to direct a first portion of blood to the sequestration chamber.

7. The blood sequestration device in accordance with claim 3, wherein the housing comprises a bottom member mated with a top member, each of the bottom member and the top member defining a part of each of the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

8. A blood sequestration device connected with a blood sampling pathway having a patient needle and a sample collection device, the blood sequestration device comprising;

an inlet port connected with the patient needle;

a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier;

a sampling channel having a proximal end connected with the inlet port; and

an outlet port connected with a distal end of the sampling channel and with the sample collection device; and

a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

9. The blood sequestration device in accordance with claim 8, wherein the inlet port is connected with the patient needle via a first portion of the blood sampling pathway.

10. The blood sequestration device in accordance with claim 8, wherein the outlet port is connected with the sample collection device via a second portion of the blood sampling pathway.

11. The blood sequestration device in accordance with claim 8, wherein the air permeable blood barrier includes an air permeable material that seals at least partially upon contact with blood.

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

13. The blood sequestration device in accordance with claim 12, wherein the sequestration channel has a proximal end connected with the inlet port, and a distal end having the vent comprising an air permeable blood barrier.

14. The blood sequestration device in accordance with claim 8, wherein the sequestration chamber and the sampling channel are connected with the inlet port by a junction that is configured to direct a first portion of blood to the sequestration chamber.

15. The blood sequestration device in accordance with claim 8, wherein the sampling channel has a substantially uniform cross-sectional geometry that is consistent with the blood sampling pathway.

16. The blood sequestration device in accordance with claim 15, wherein the sequestration chamber includes a sequestration chamber that has a cross-sectional area that is larger than the cross-sectional geometry of the sampling channel.

17. A blood sequestration device connected with a blood sampling system comprising a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed, the blood sequestration device comprising;

an inlet port connected with the patient needle to receive the blood sample from the patient;

a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed; and

a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a second portion of the blood sample once the sample needle is unsealed;

an outlet port connected with a distal end of the sampling channel for conveying the second portion of the blood sample to the sample needle; and

a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

18. The blood sequestration device in accordance with claim 17, wherein the sequestration chamber is at ambient air pressure, and wherein the sequestration chamber receives the first portion of the blood sample by blood pressure of the patient overcoming the ambient air pressure in the sequestration chamber.

19. The blood sequestration device in accordance with claim 17, wherein the sampling channel causes the second portion of the blood sample to bypass the sequestered first portion of blood, and exit the outlet port for conveyance to a blood collection device.

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

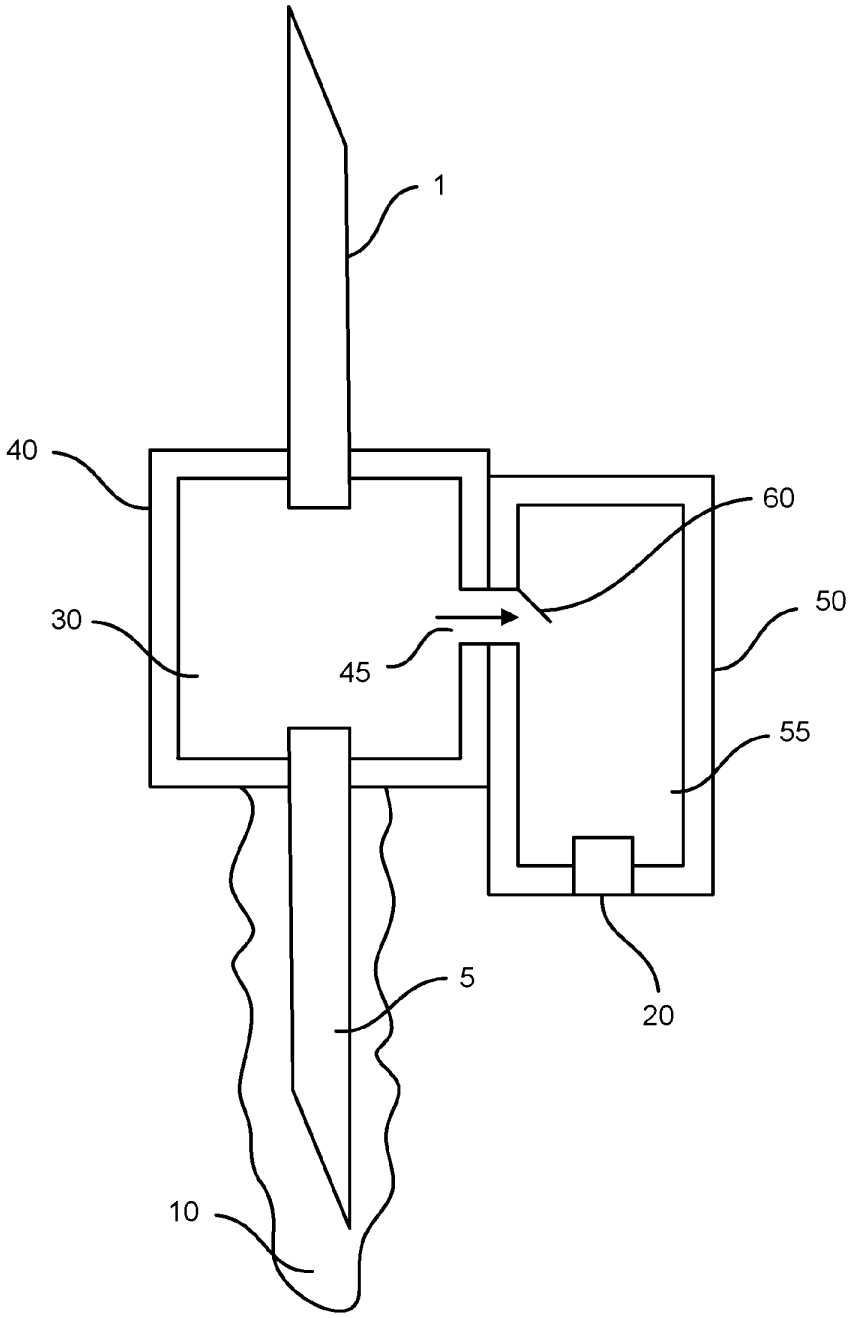


FIG. 1

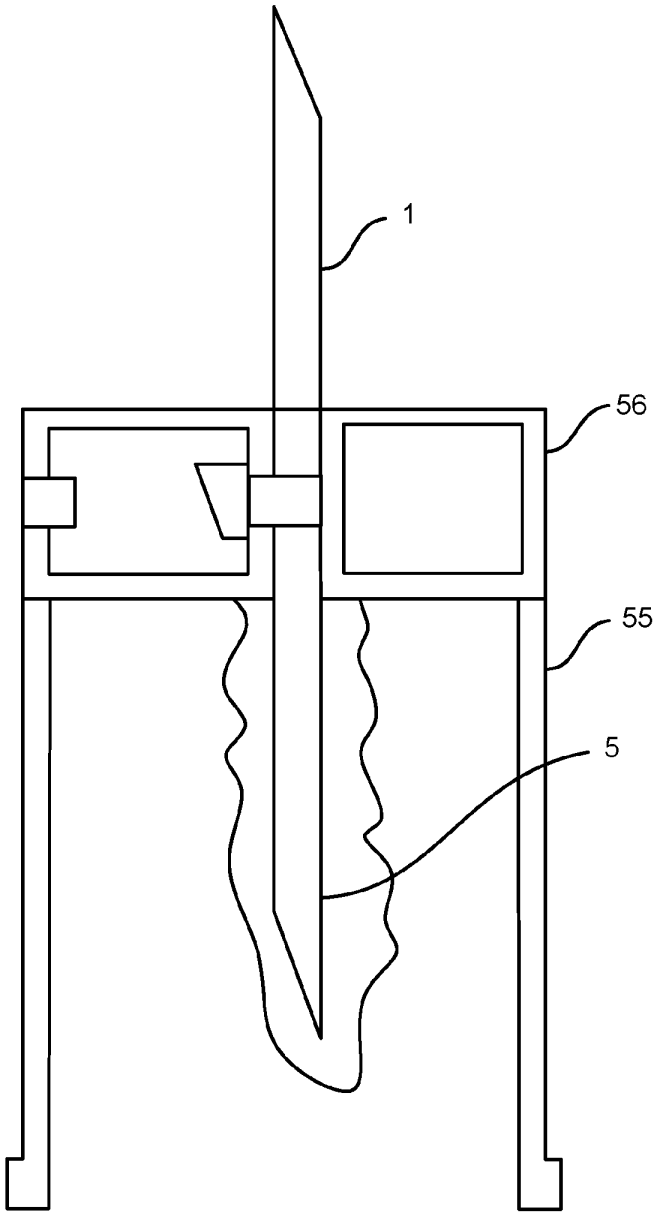


FIG. 2

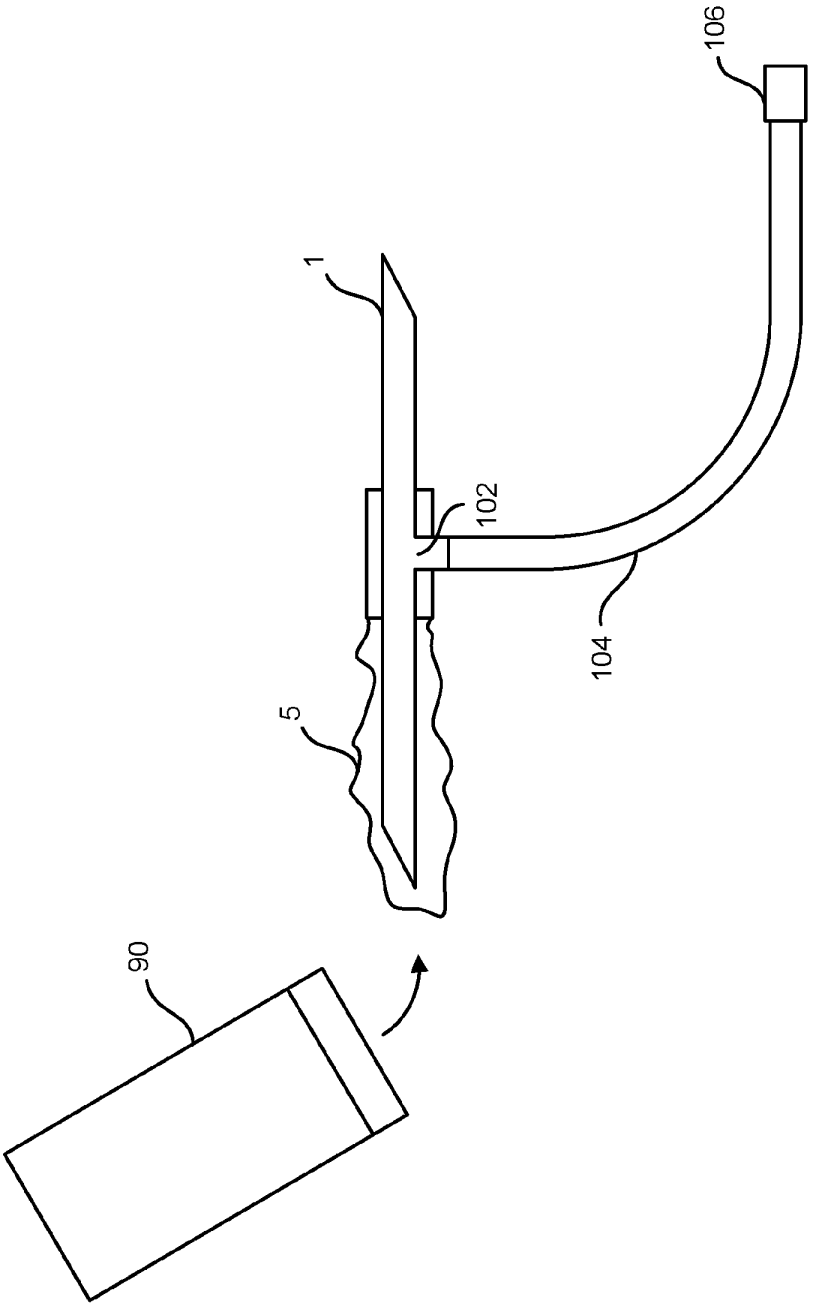


FIG. 3

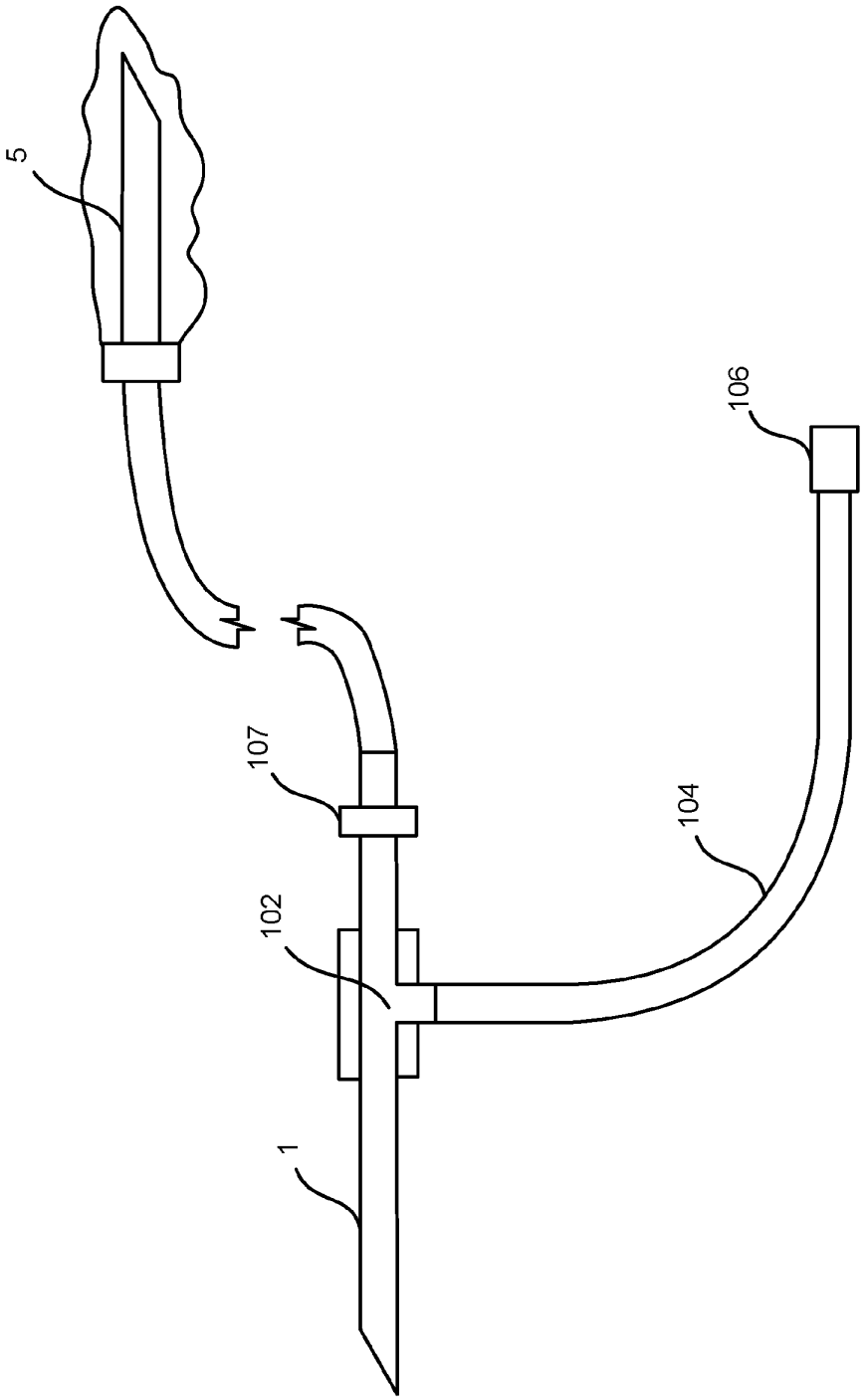


FIG. 4

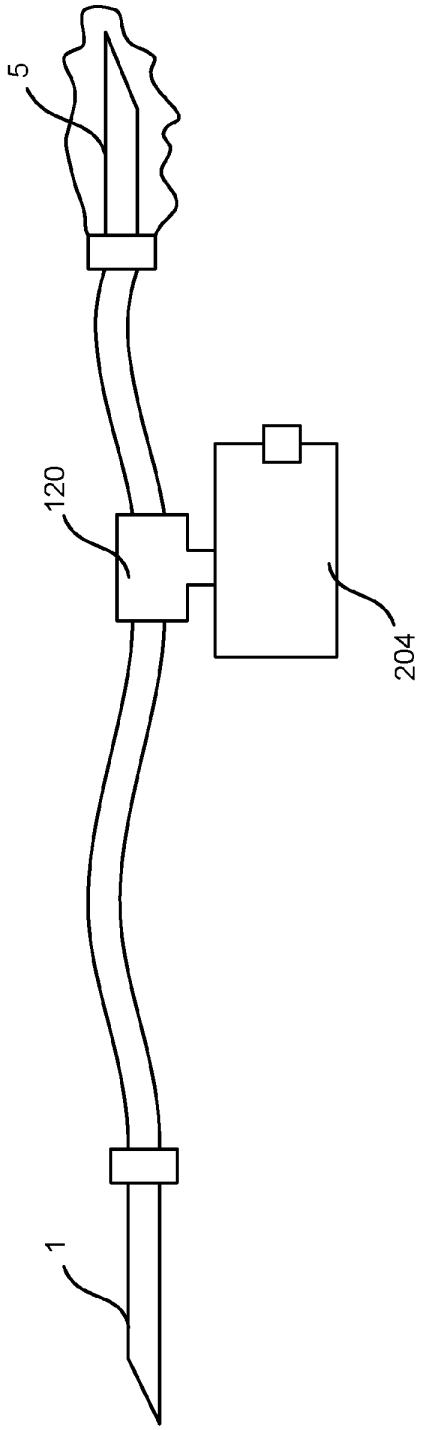


FIG. 5

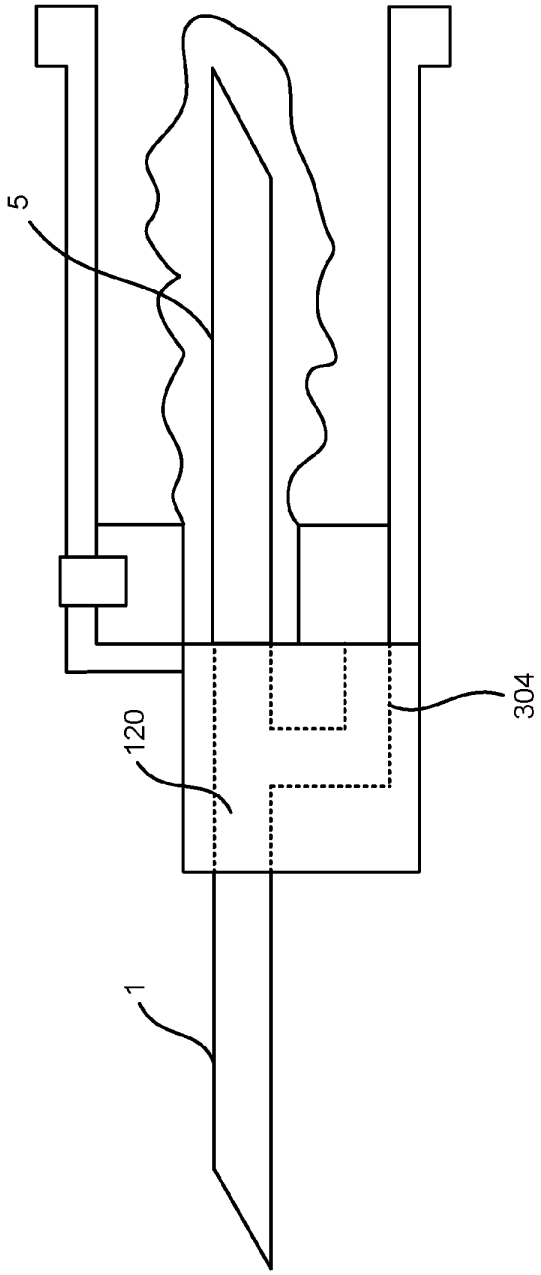


FIG. 6

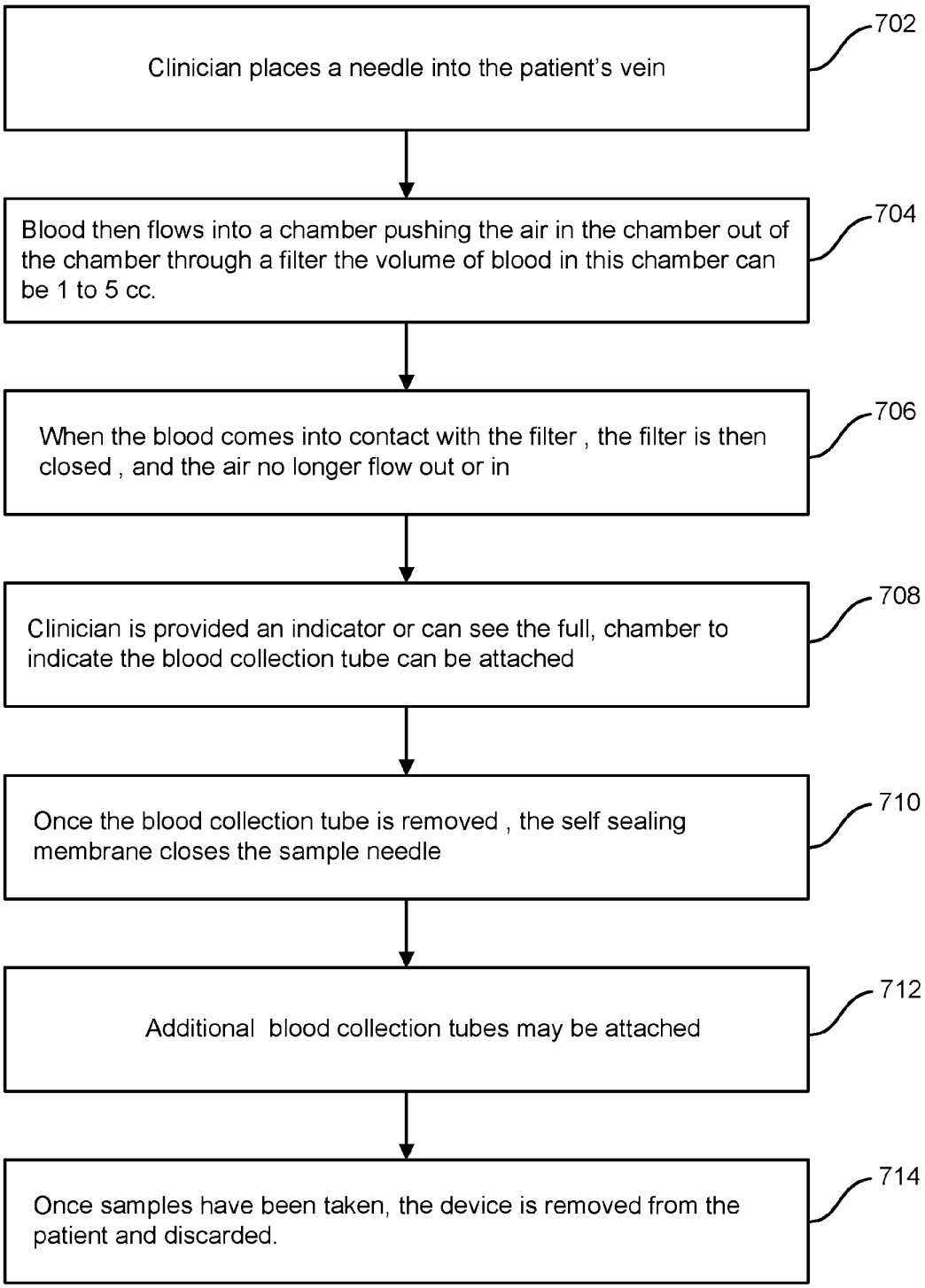

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air no longer flow out or in
706
Clinician is provided an indicator or can see the full, chamber to indicate the blood collection tube can be attached
708
Once the blood collection tube is removed , the self sealing membrane closes the sample needle
710
Additional blood collection tubes may be attached
712
Once samples have been taken, the device is removed from the patient and discarded.
714

FIG. 7

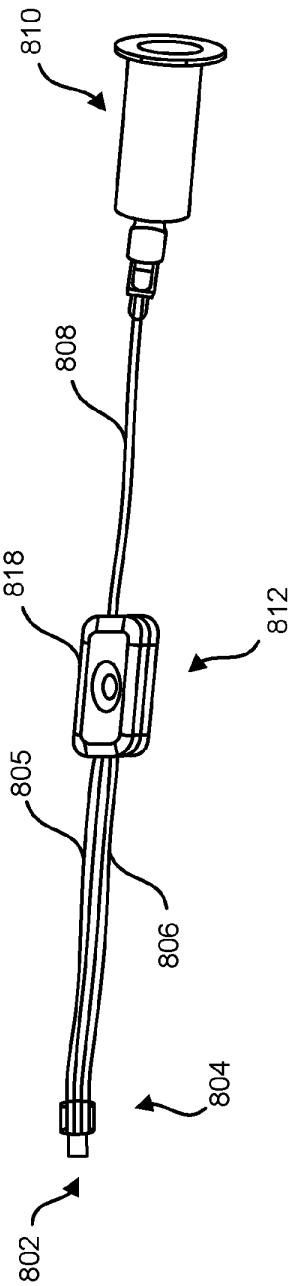


FIG. 8A

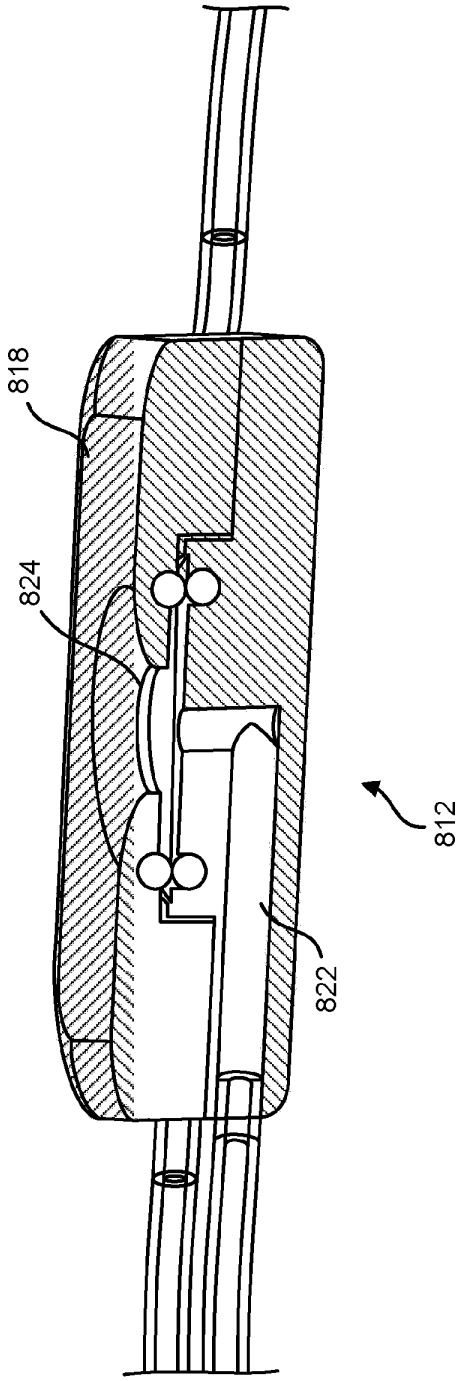


FIG. 8B

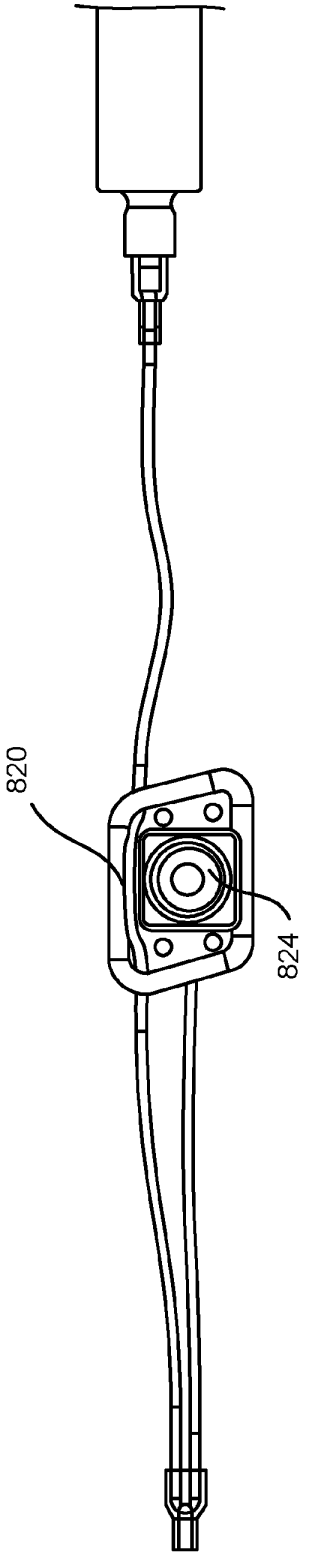


FIG. 8C

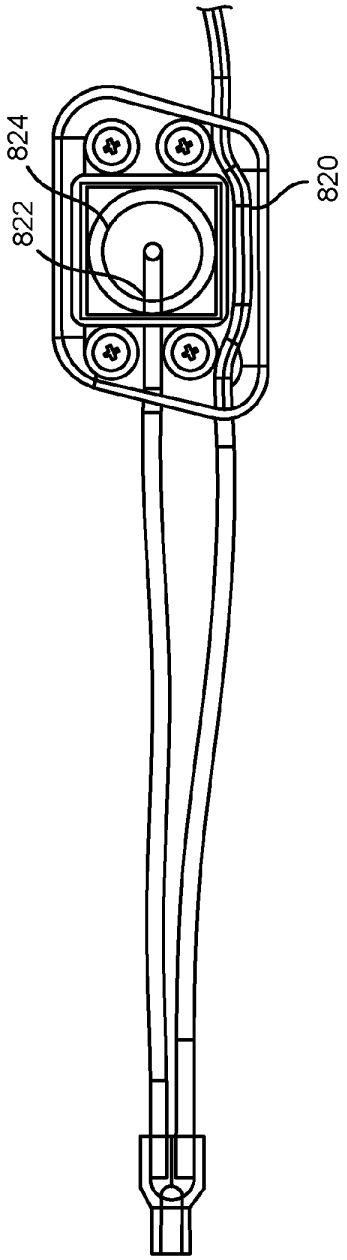


FIG. 8D

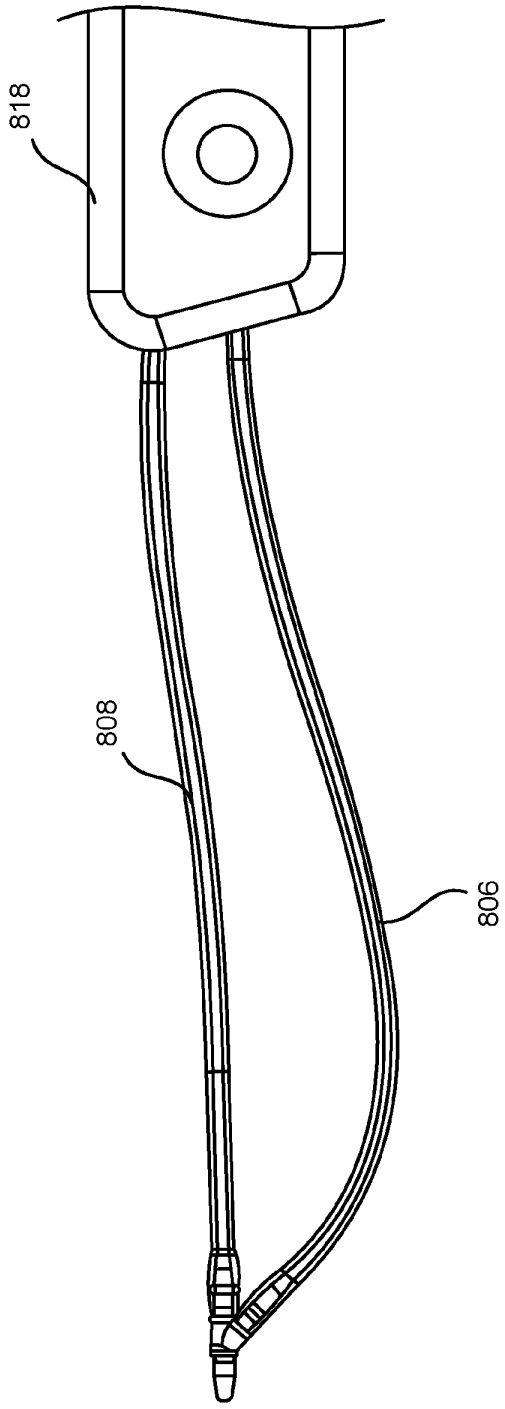


FIG. 8E

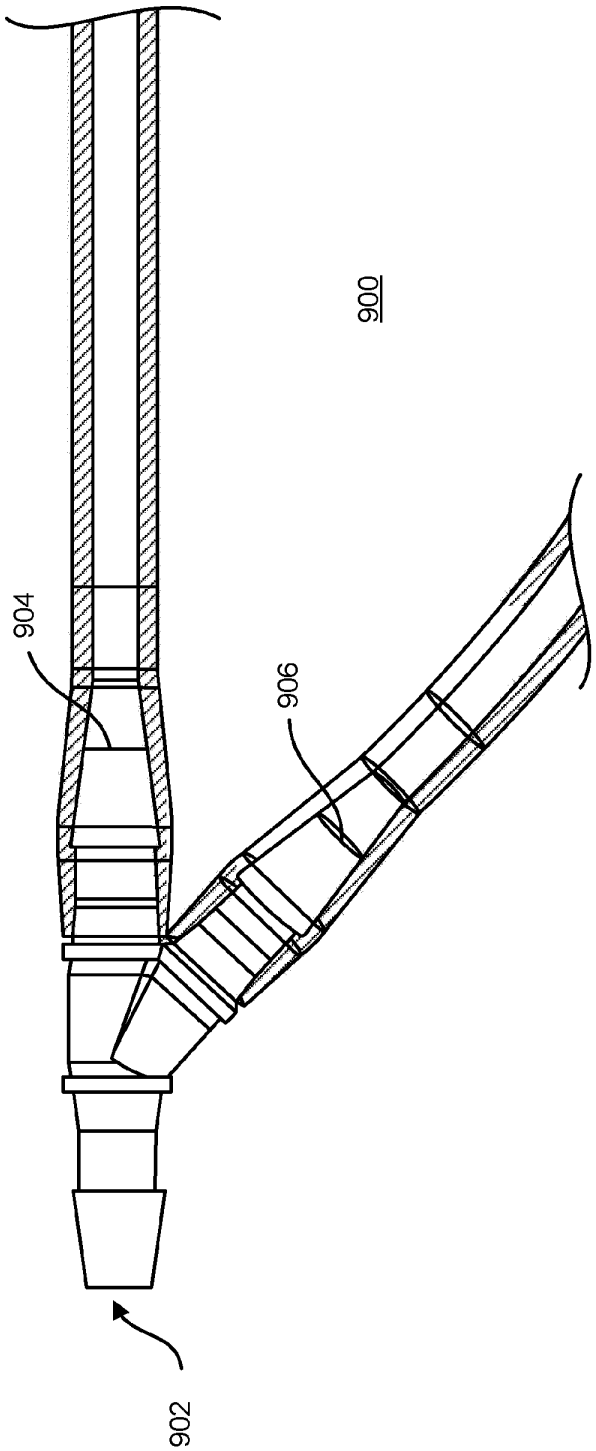


FIG. 9

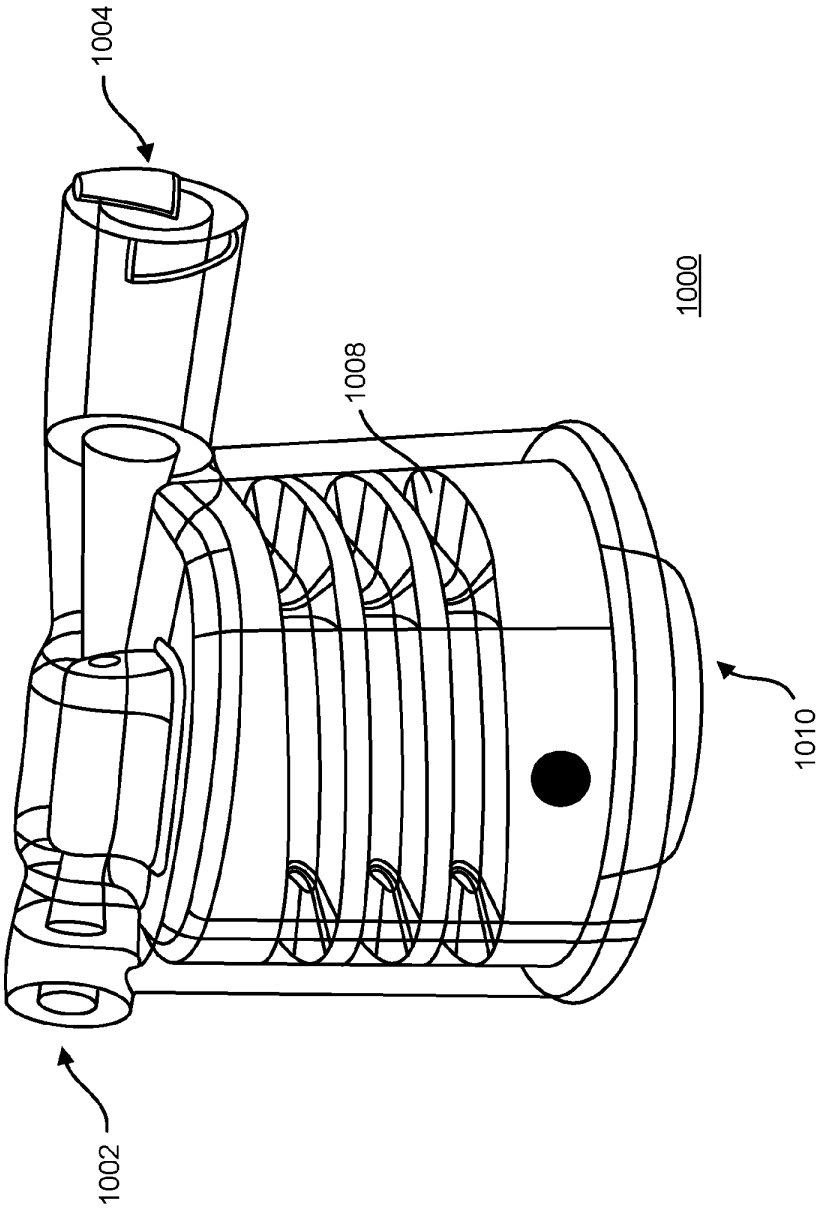


FIG. 10A

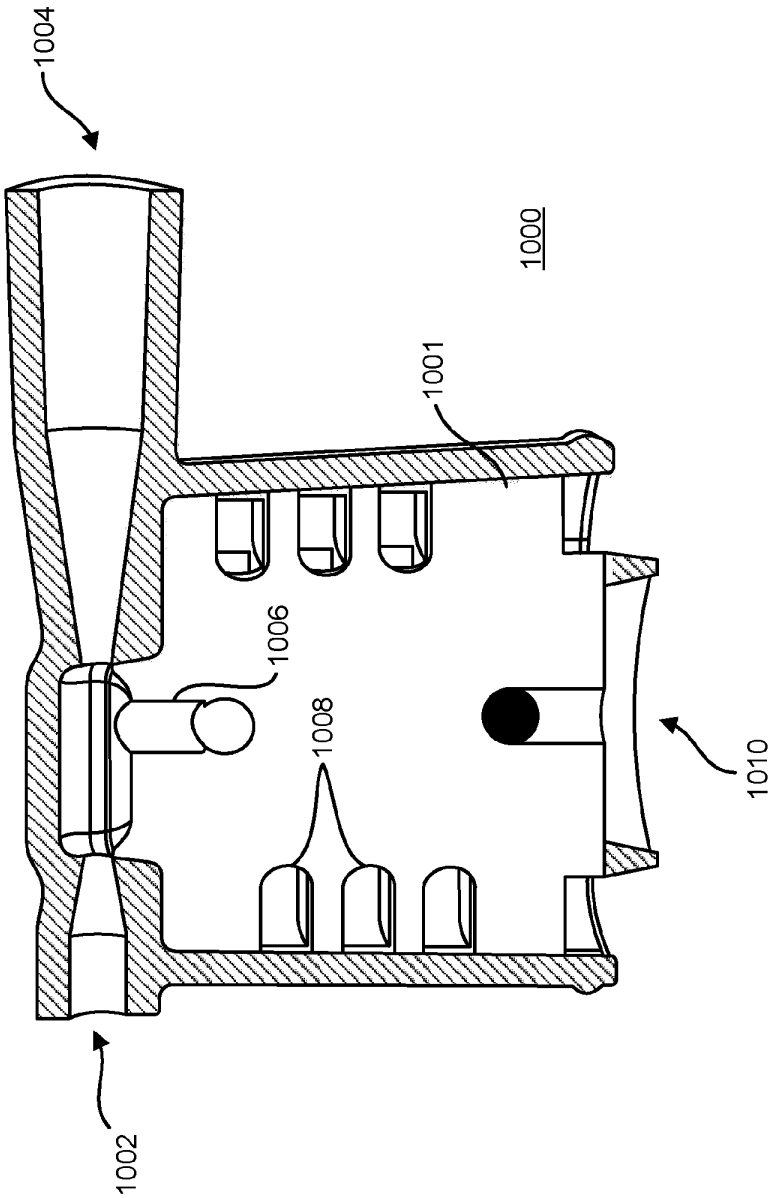


FIG. 10B

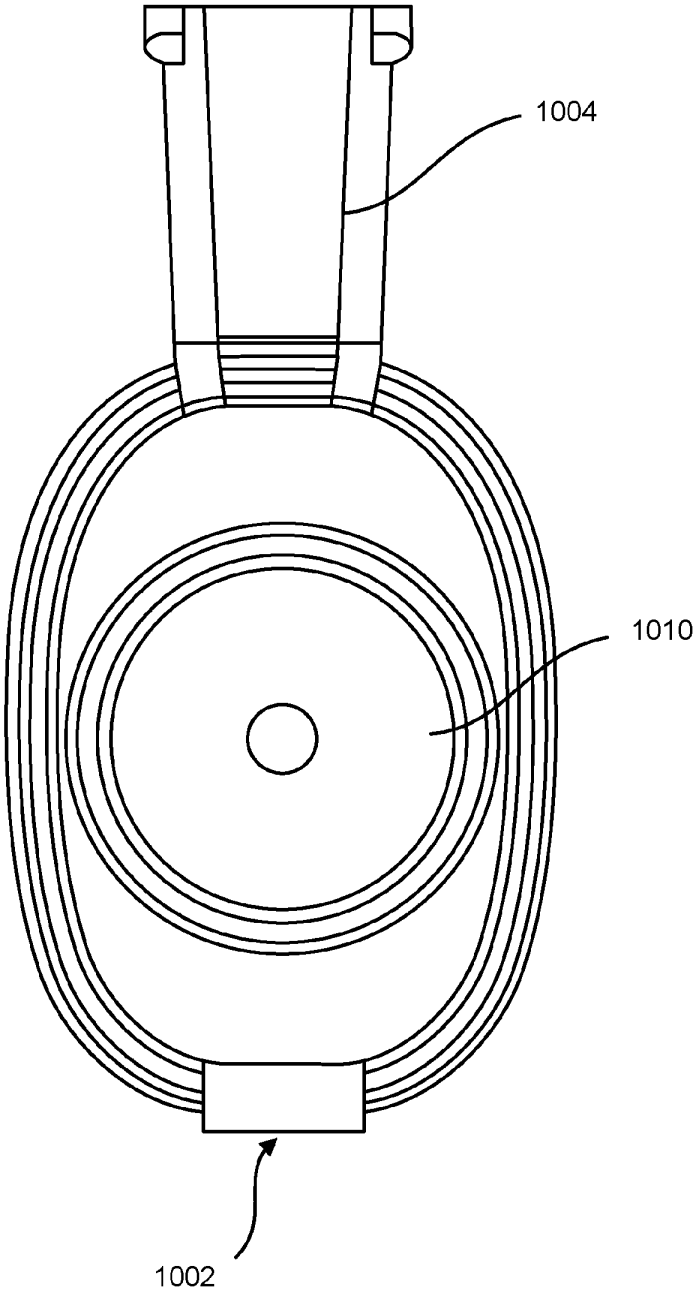


FIG. 10C

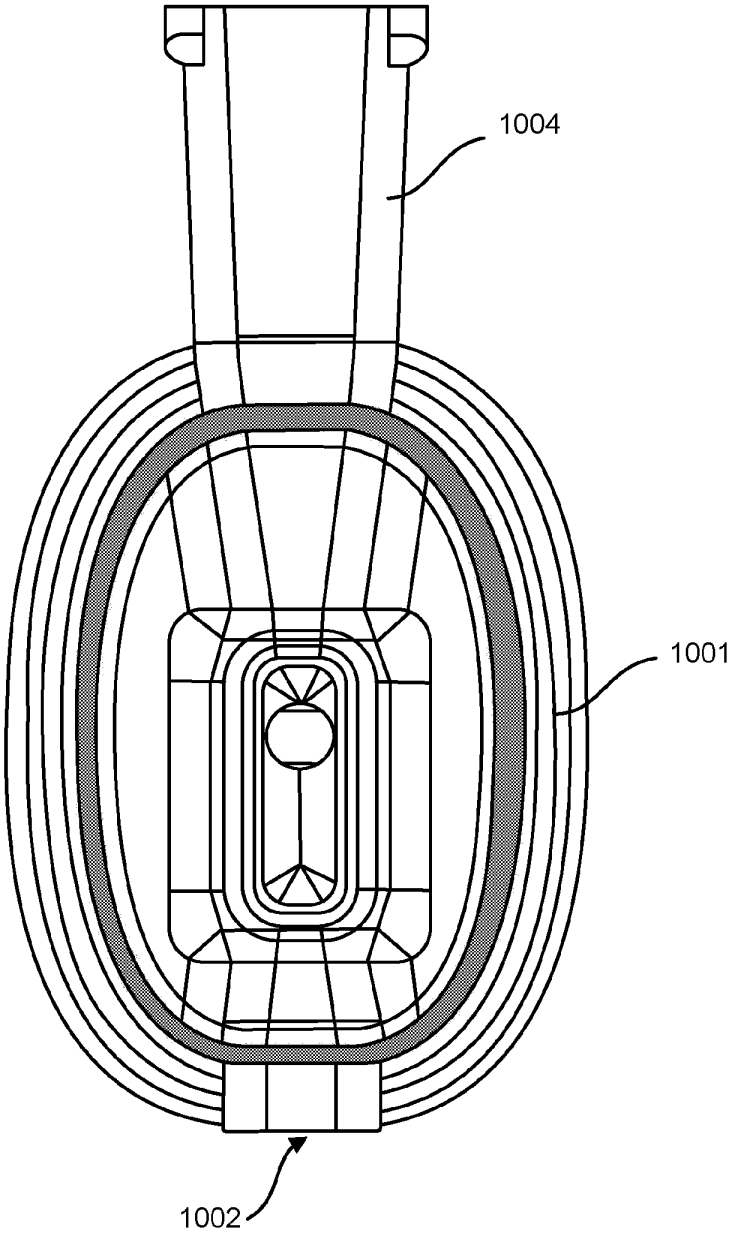


FIG. 10D

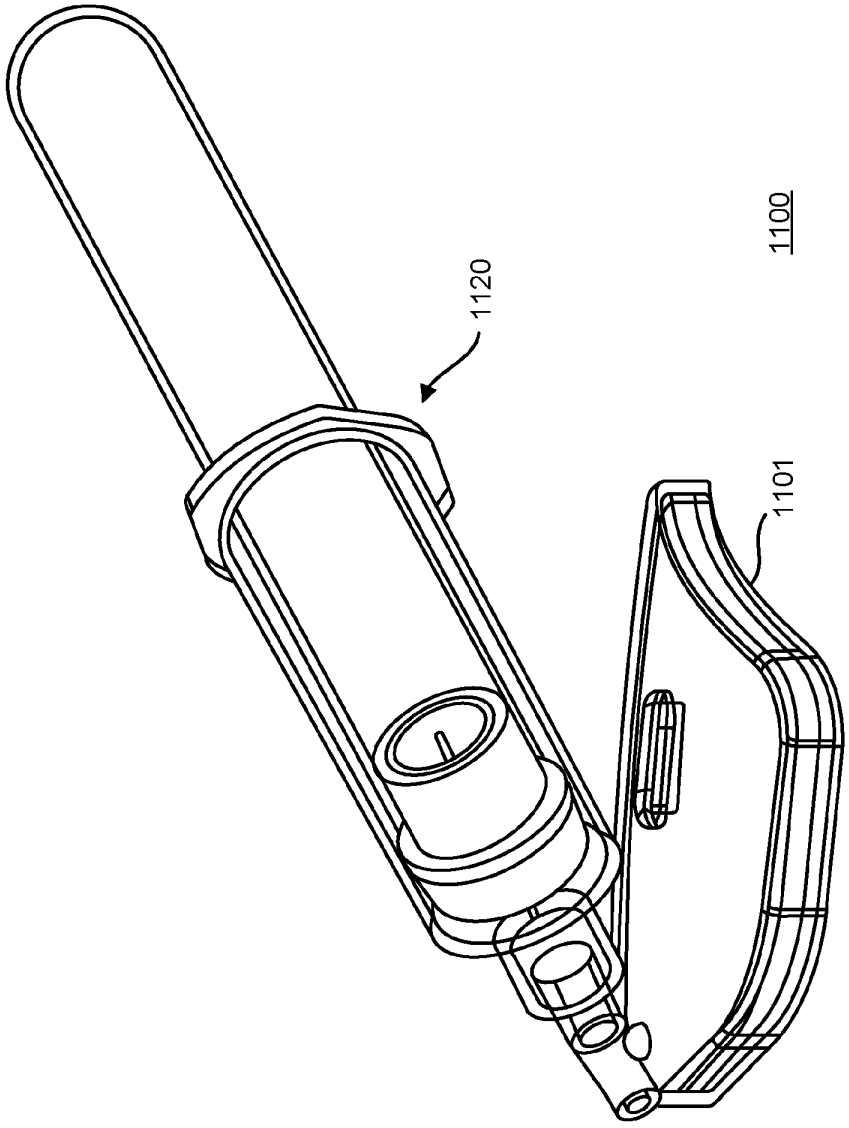


FIG. 11A

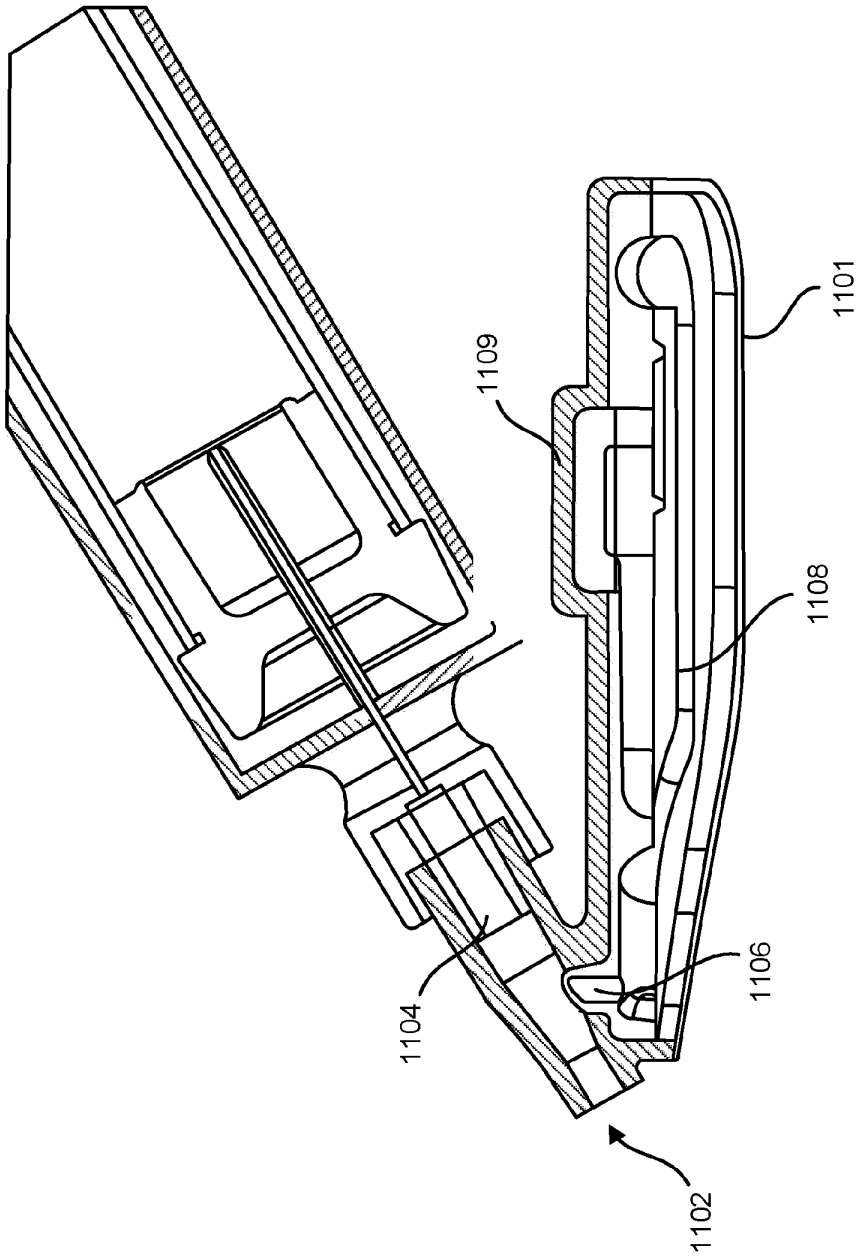


FIG. 11B

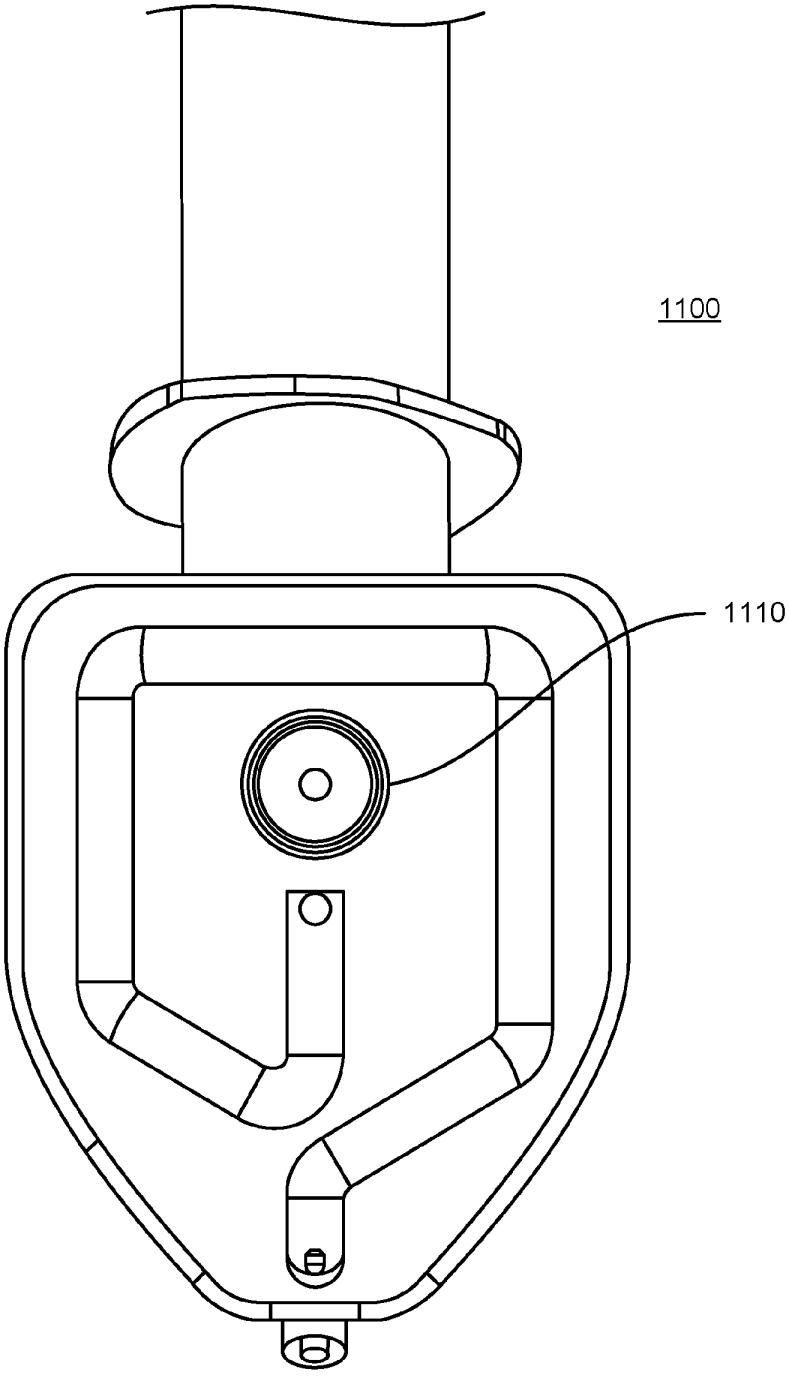


FIG. 11C

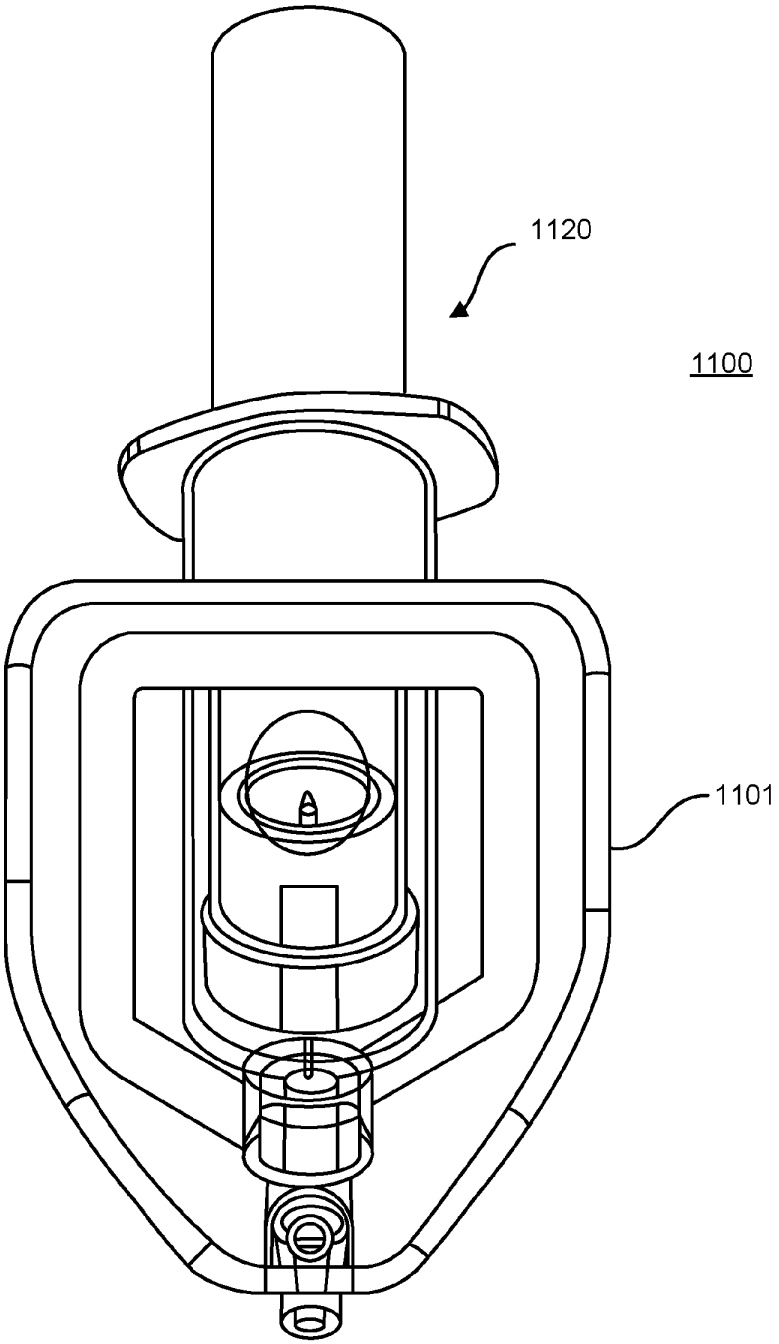


FIG. 11D

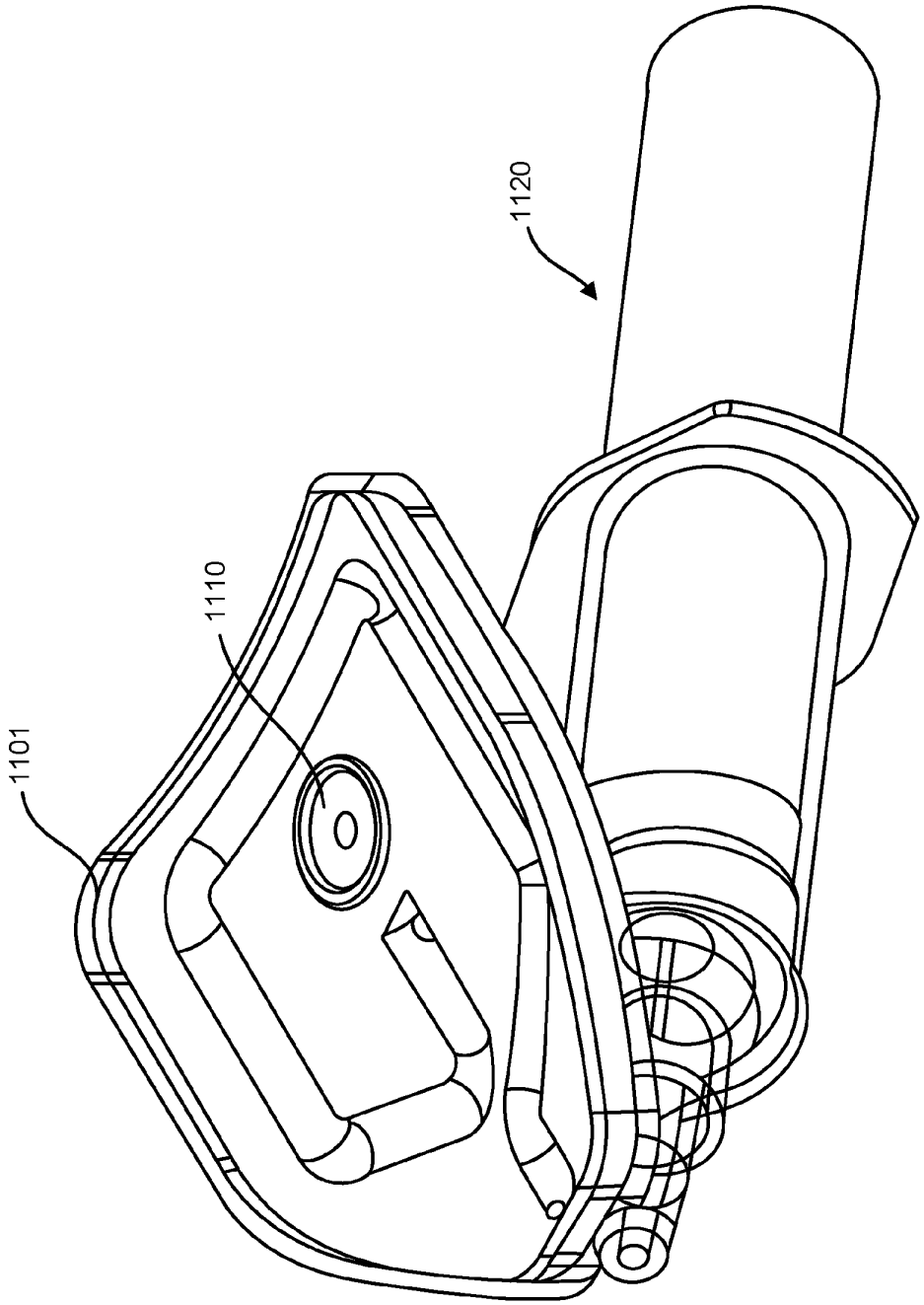


FIG. 11E

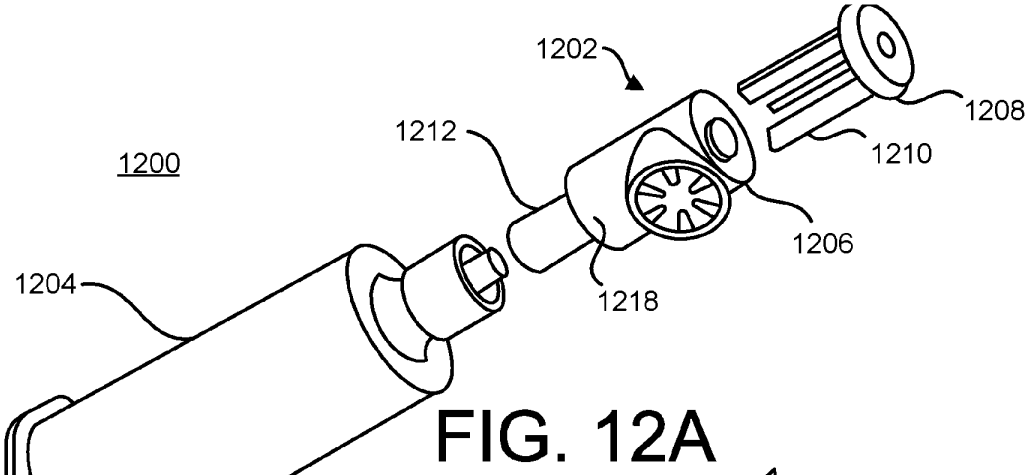


FIG. 12A

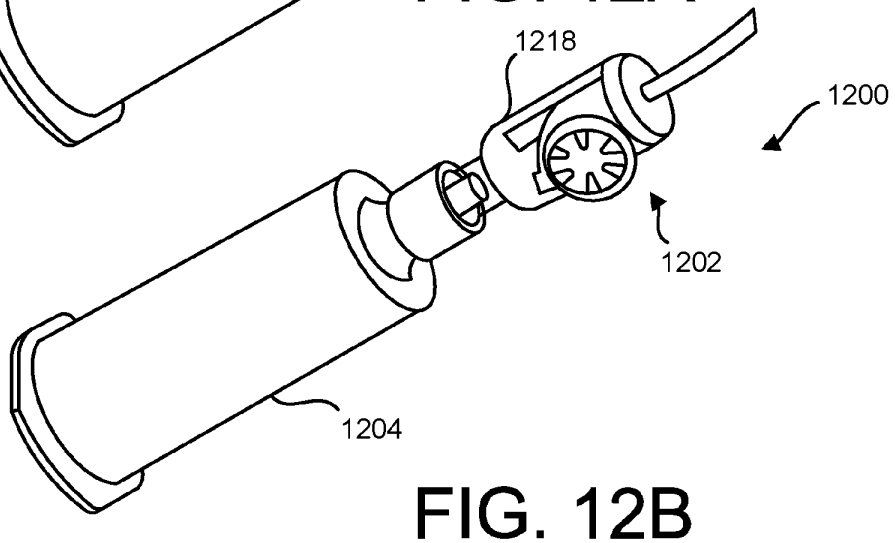


FIG. 12B

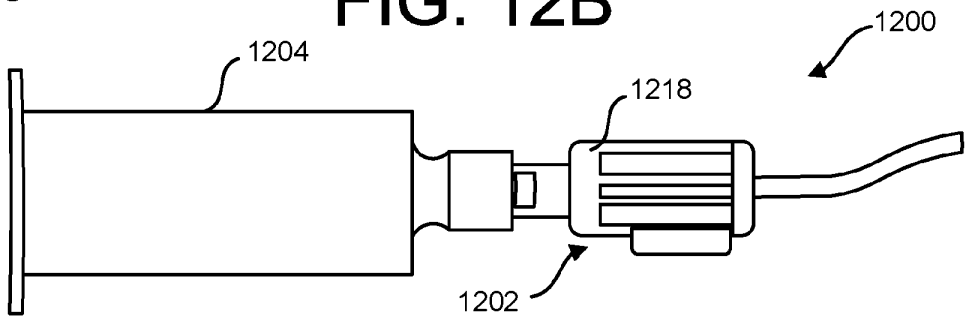


FIG. 12C

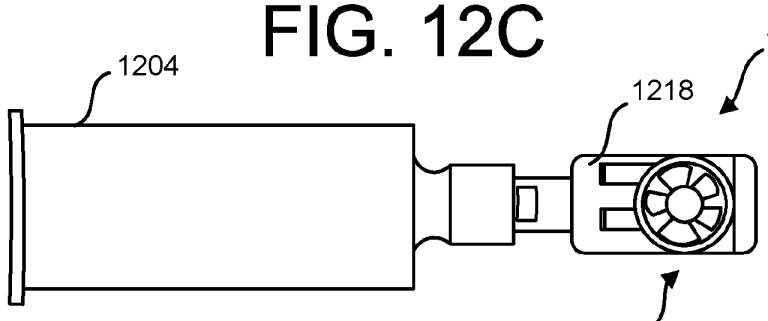


FIG. 12D

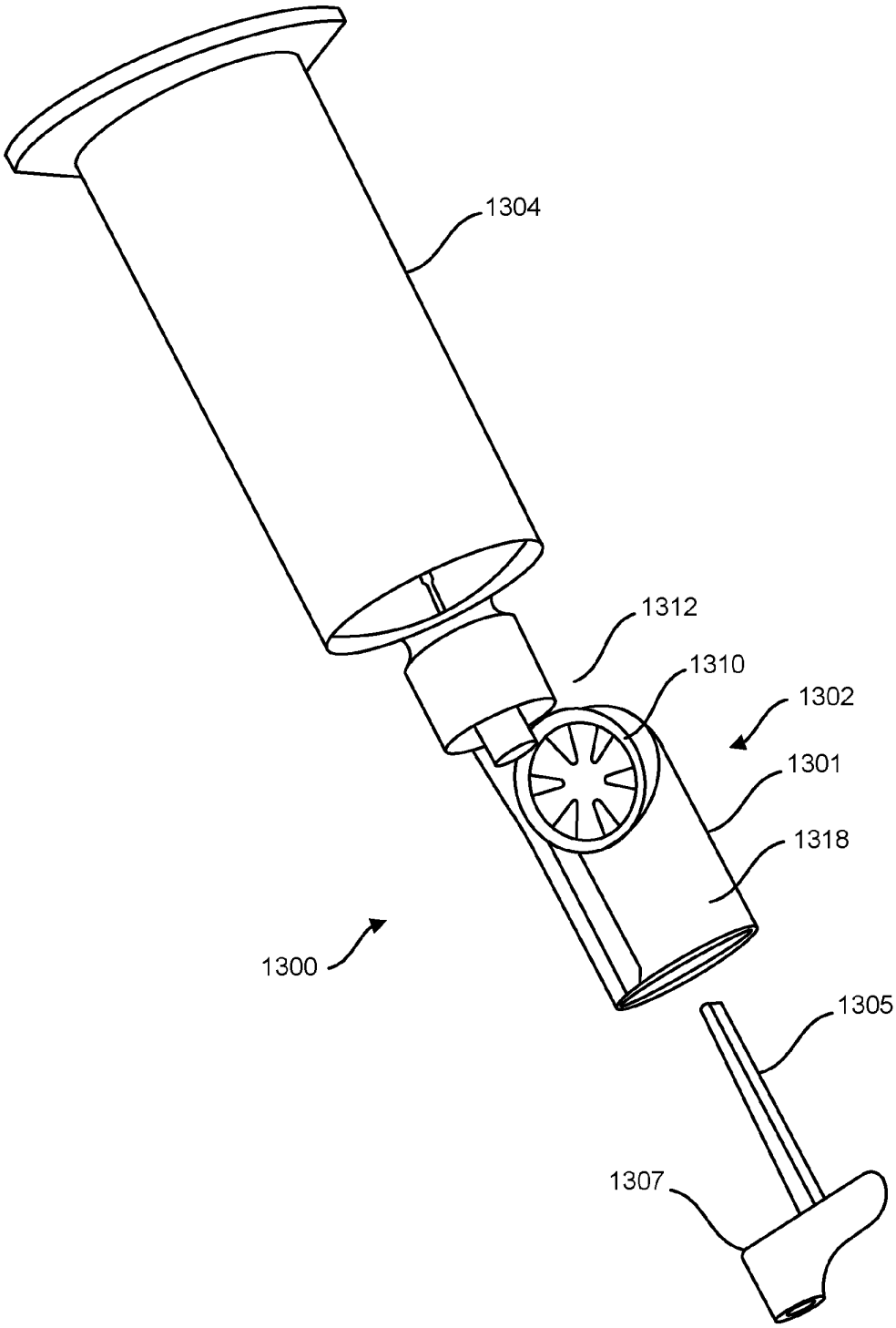


FIG. 13A

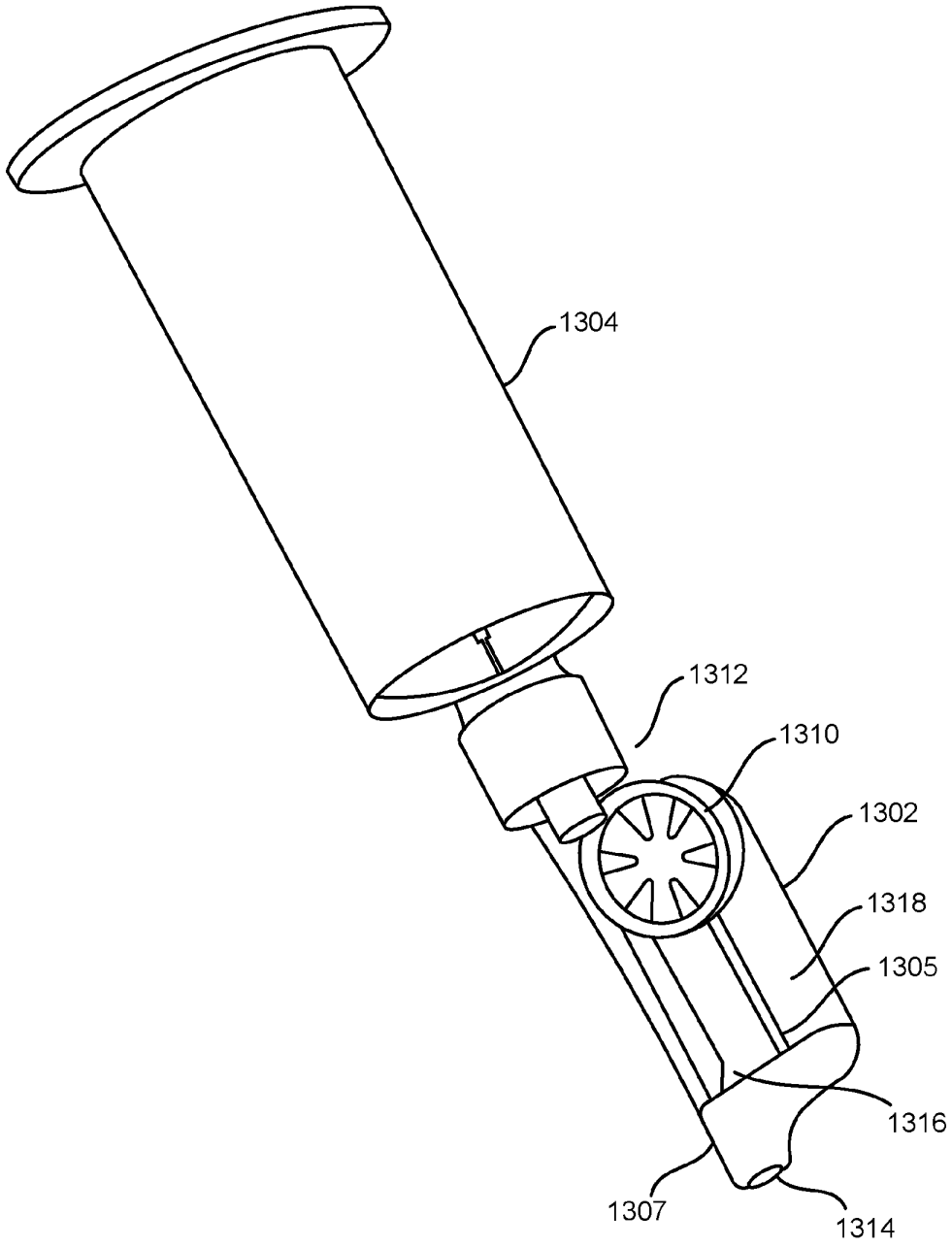


FIG. 13B

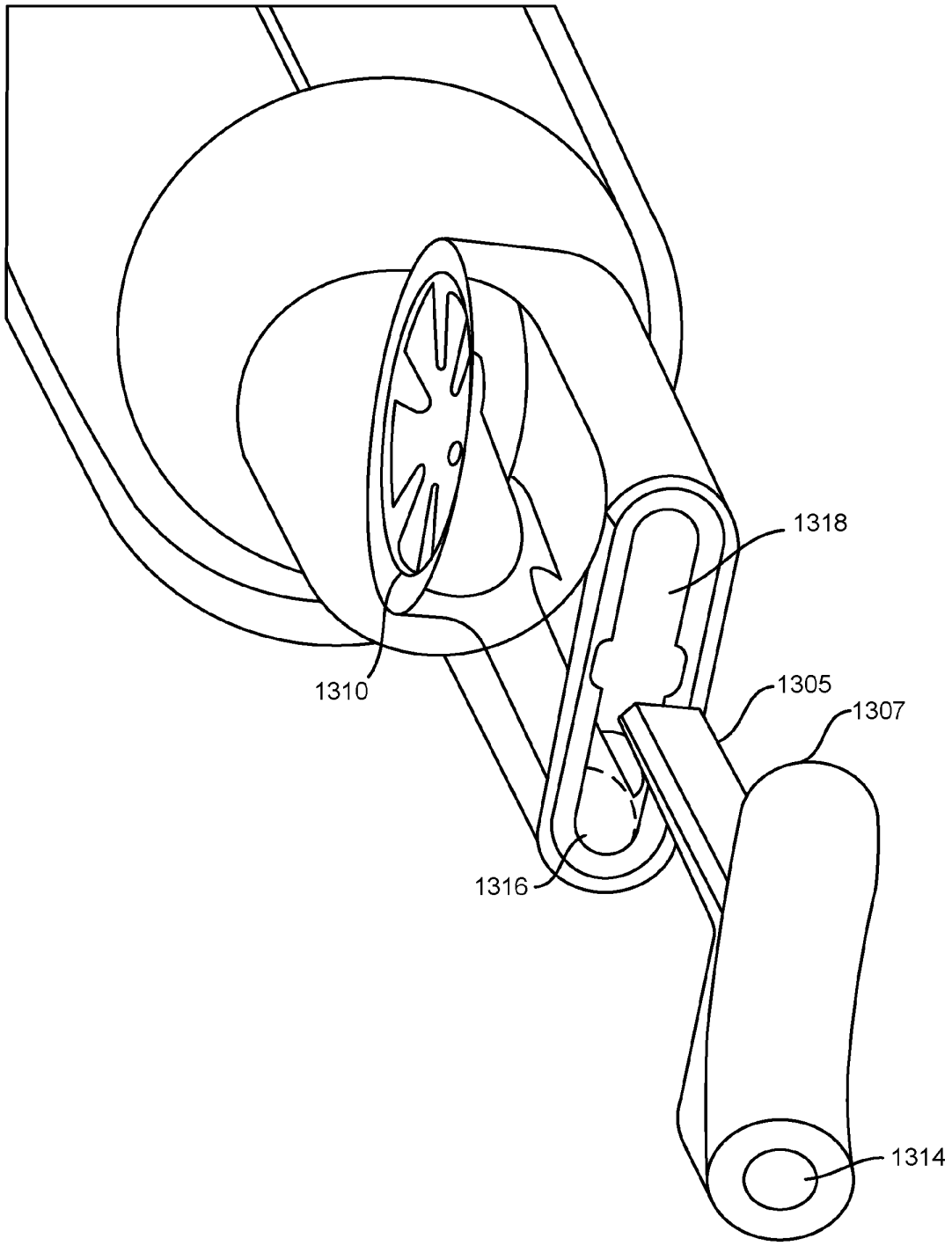


FIG. 13C

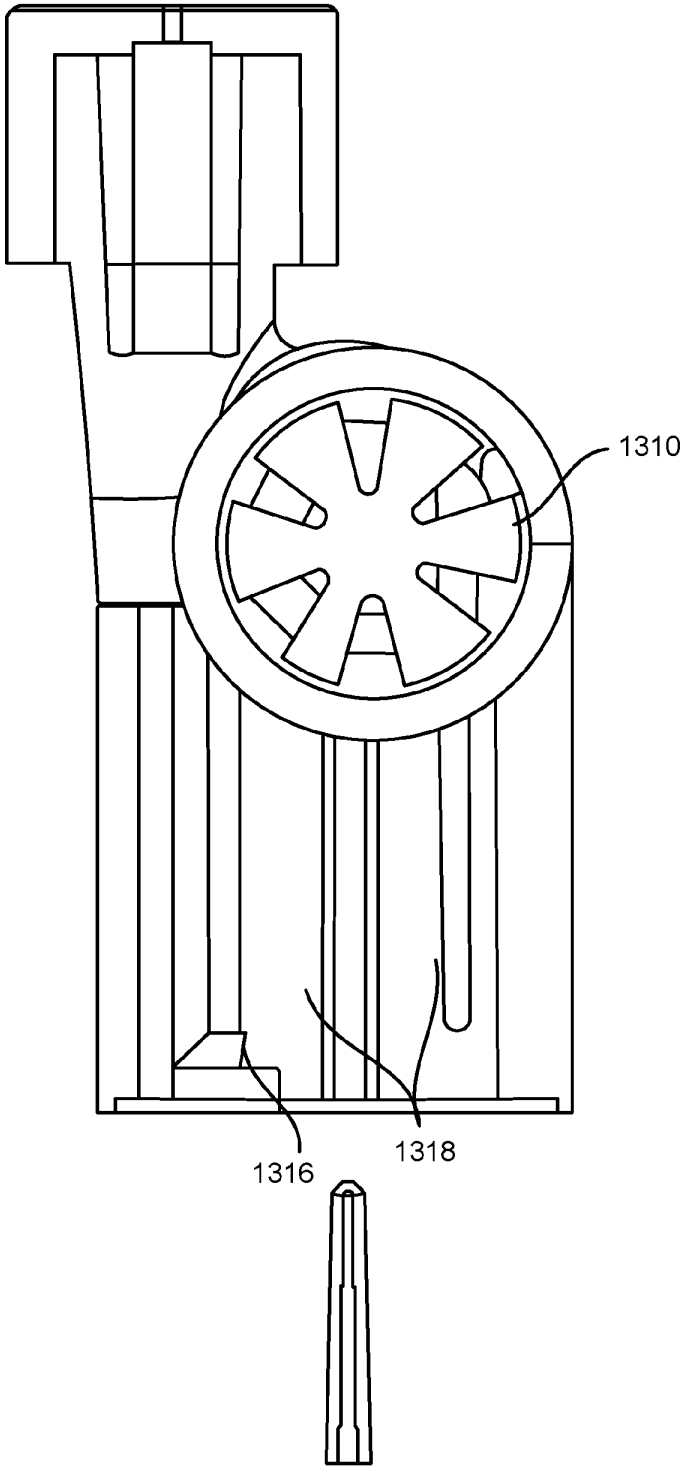


FIG. 13D

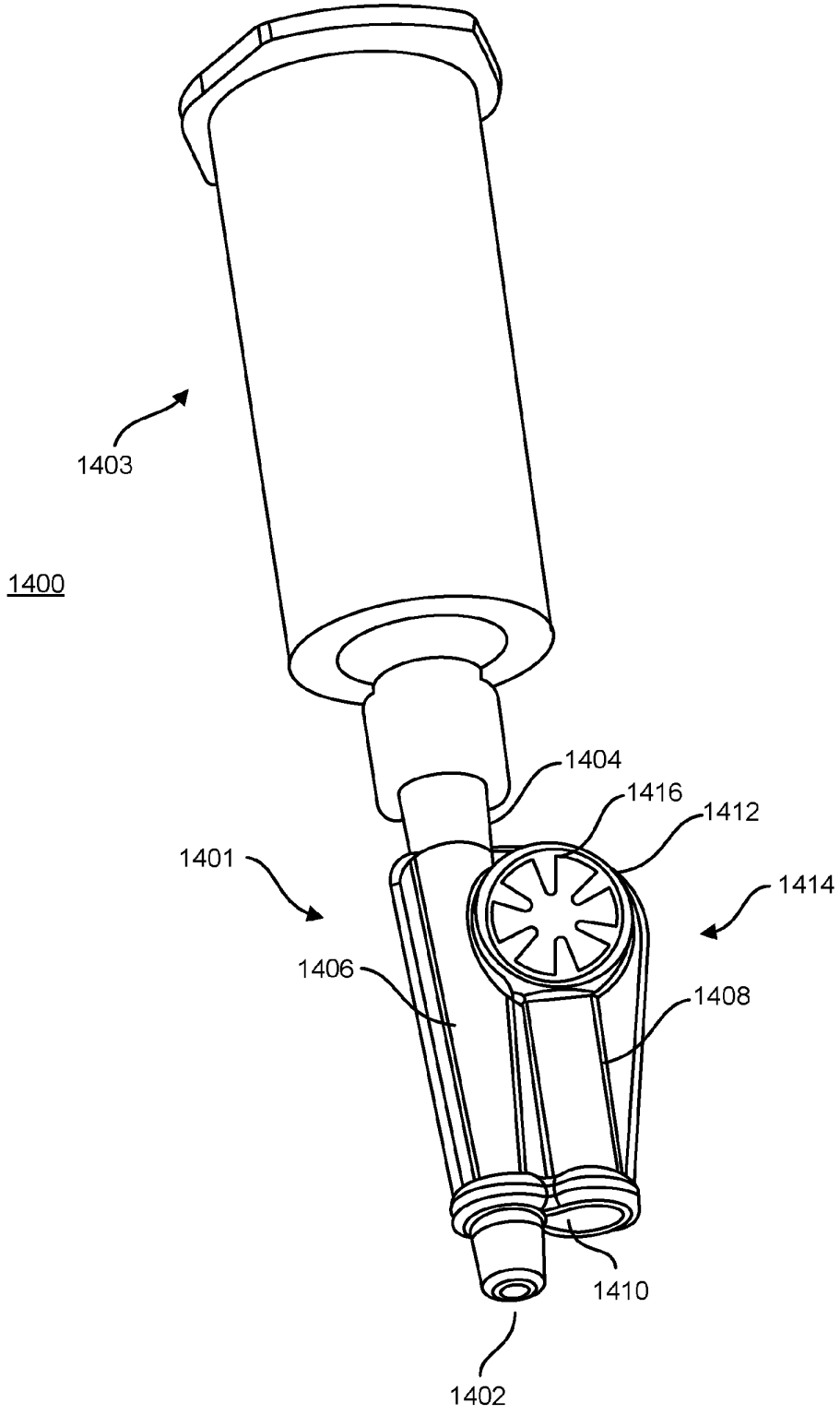


FIG. 14A

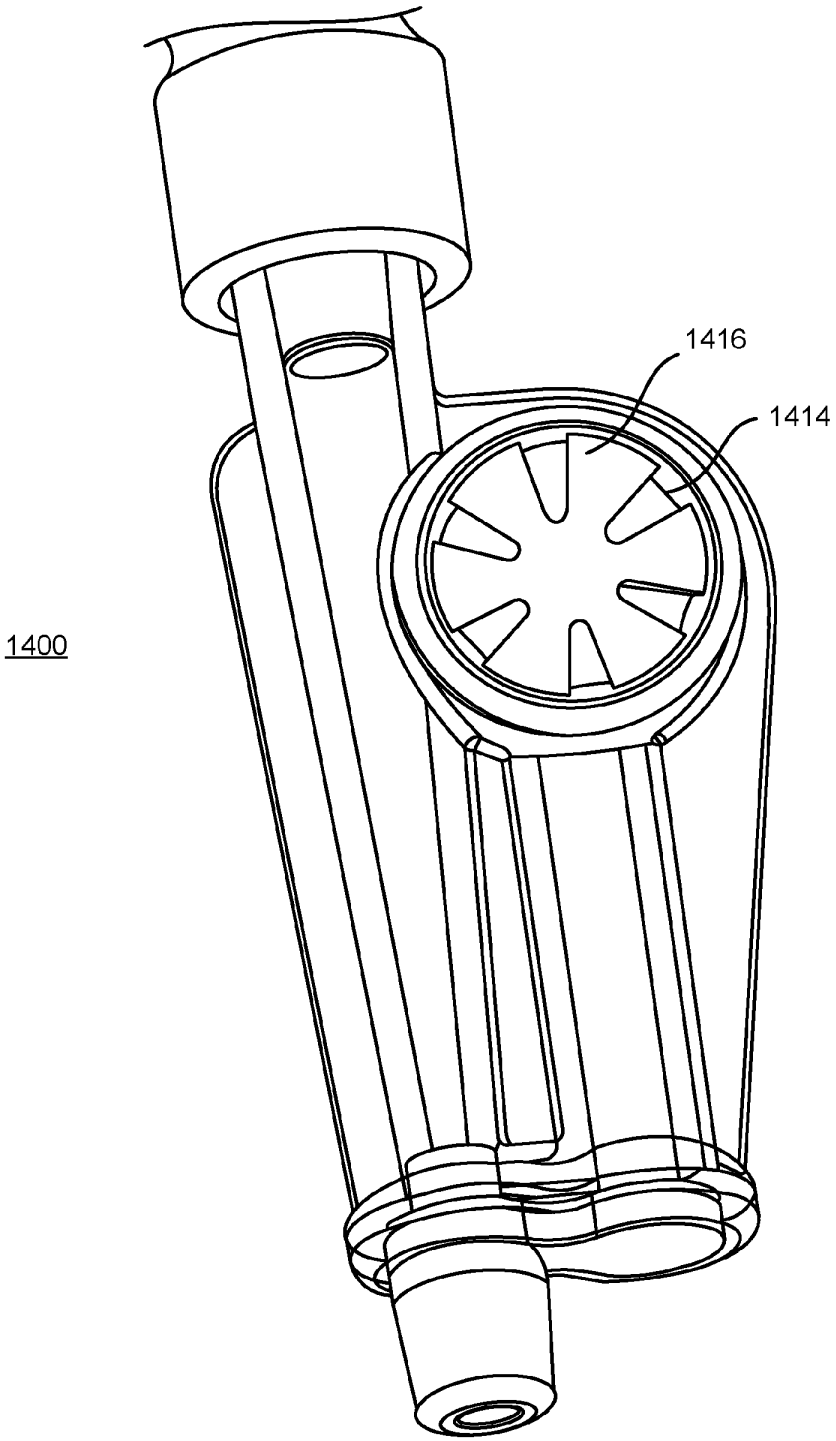


FIG. 14B

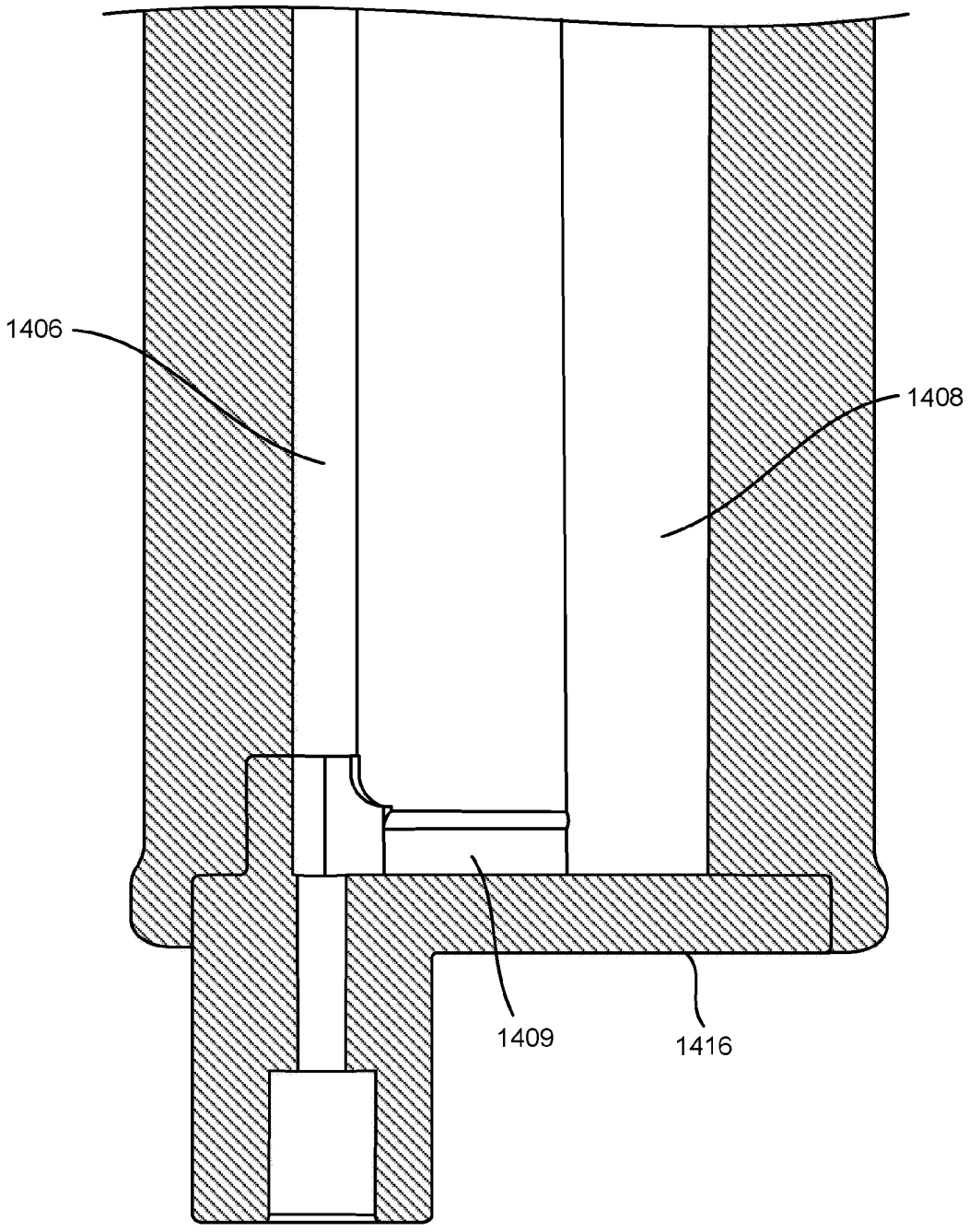


FIG. 14C

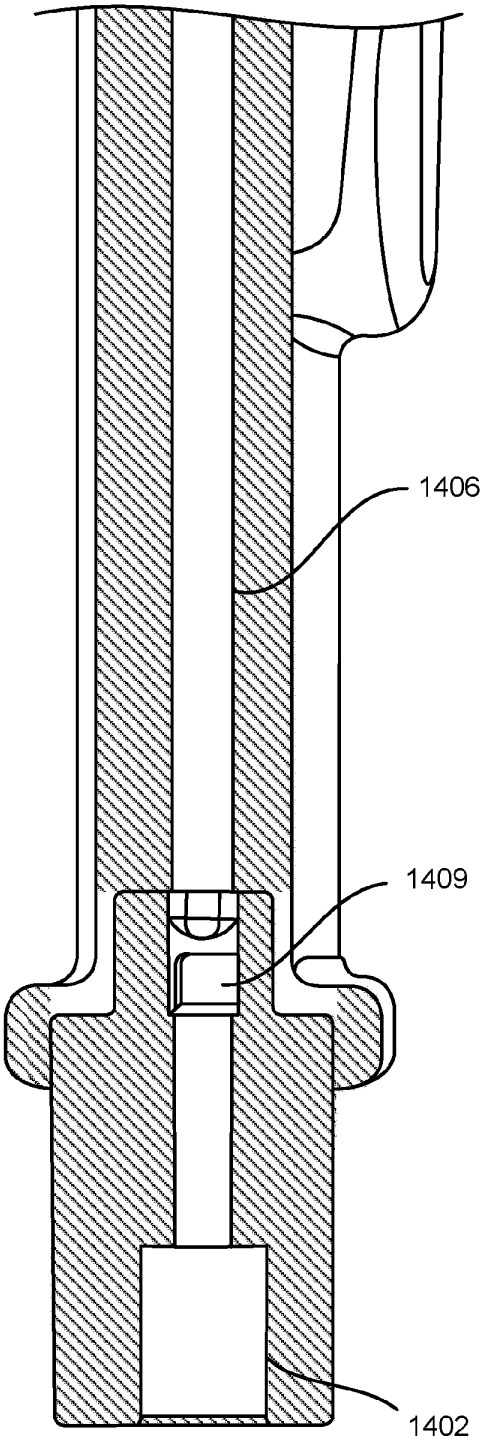


FIG. 14D

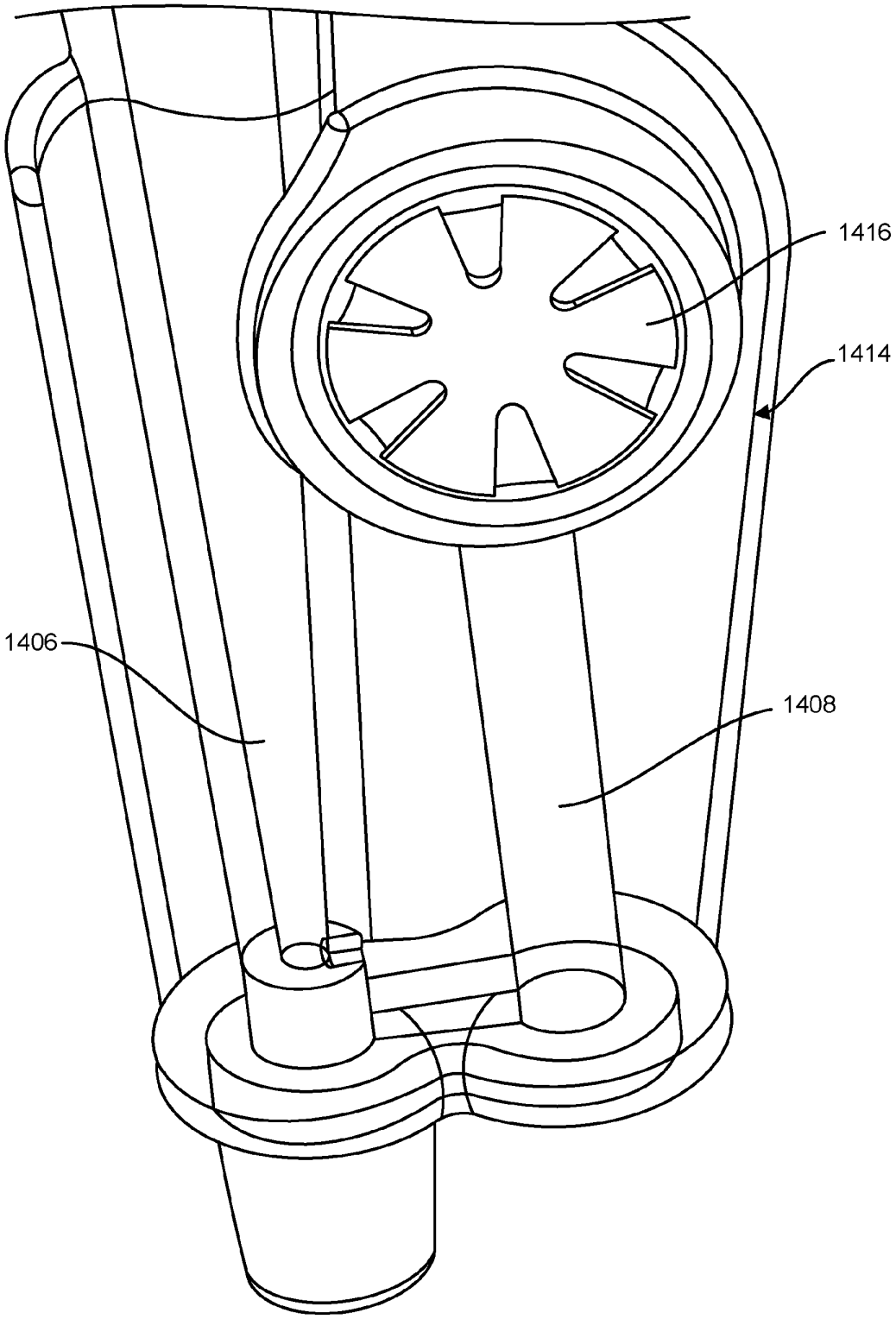


FIG. 14E

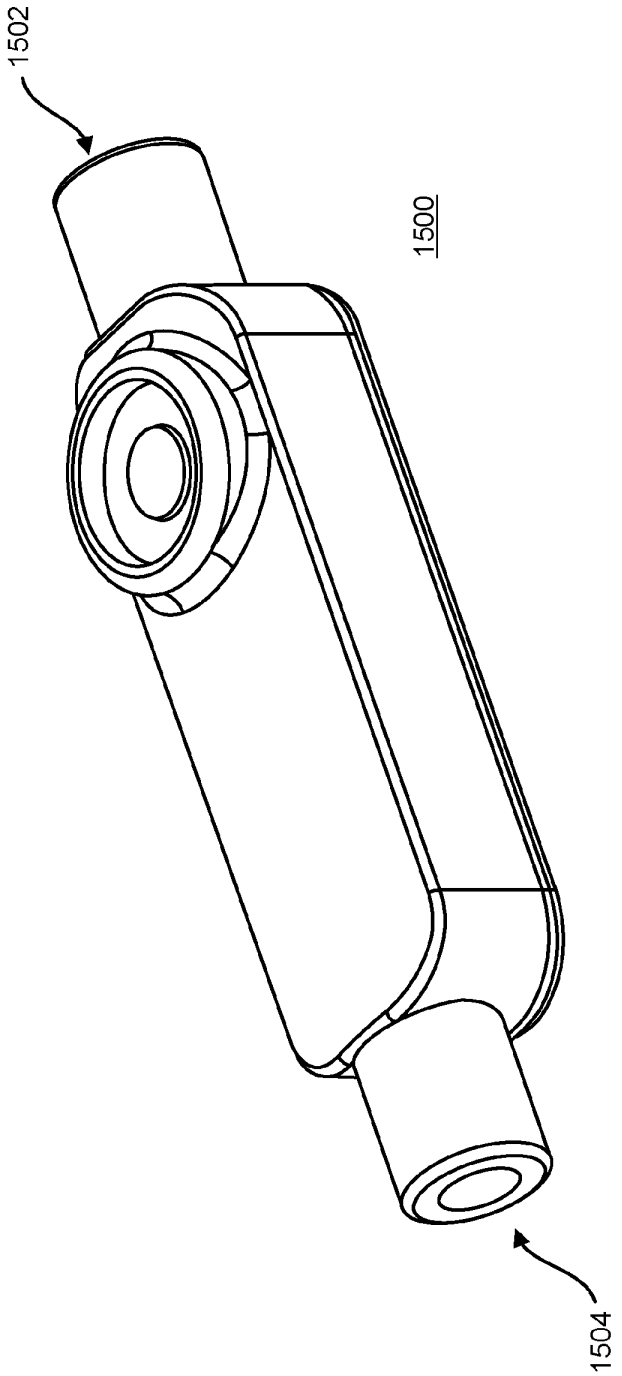


FIG. 15A

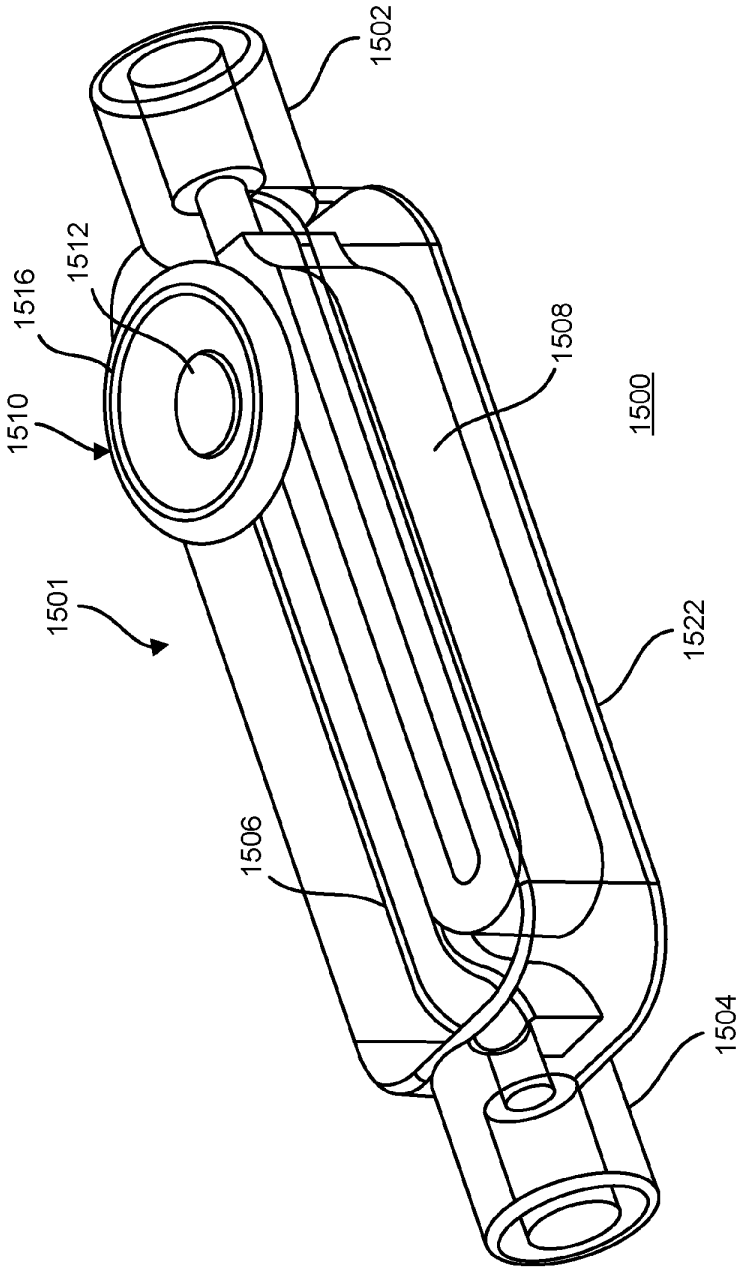


FIG. 15B

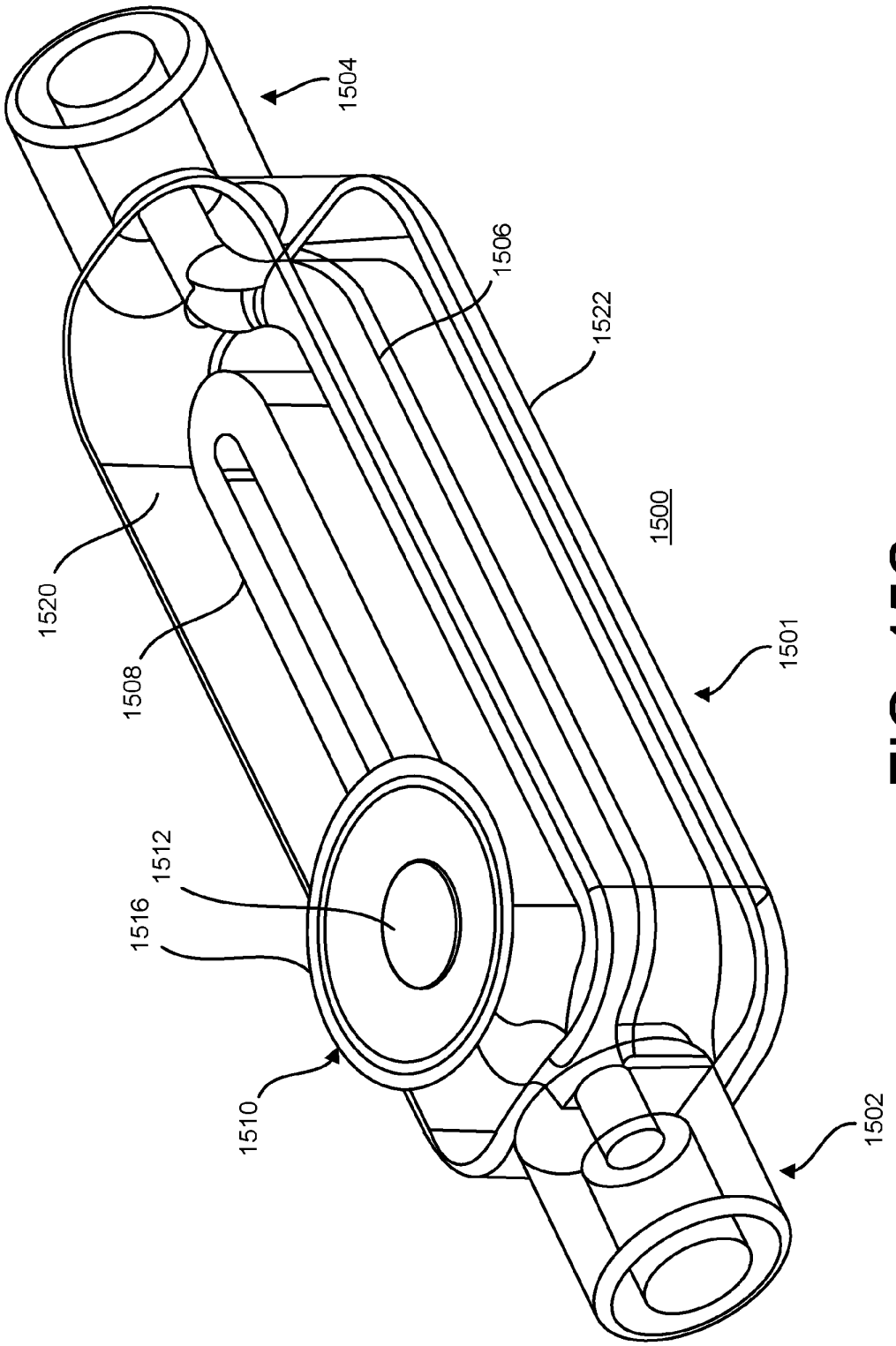


FIG. 15C

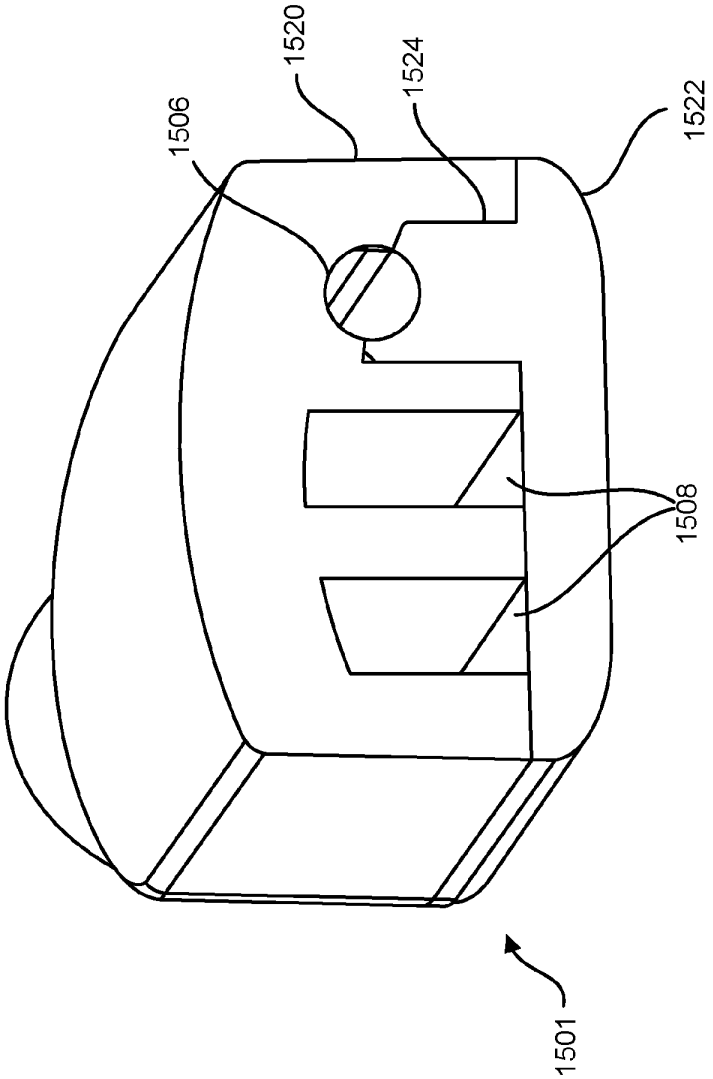


FIG. 15D

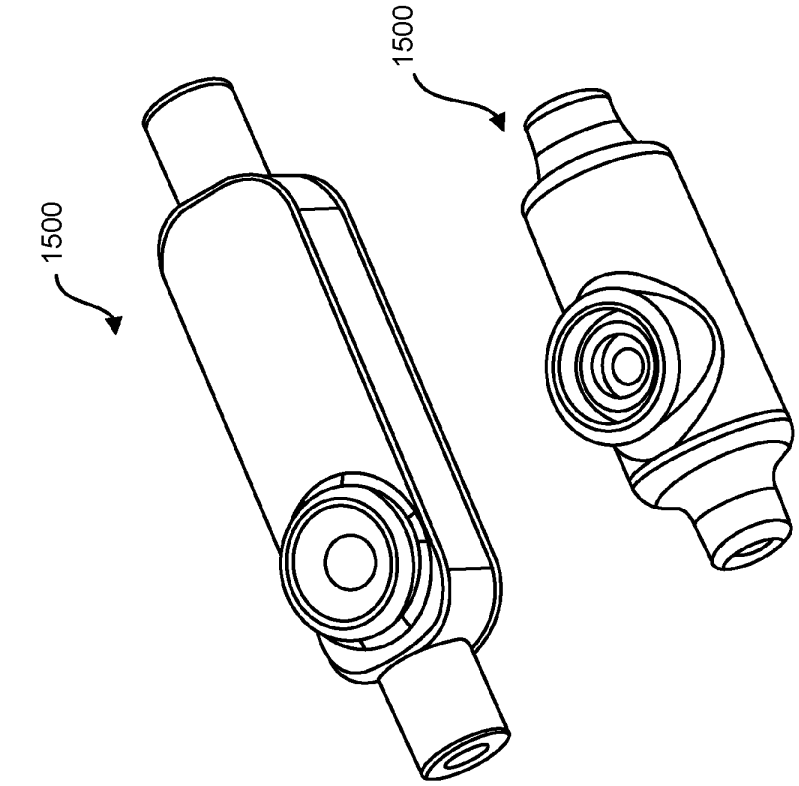


FIG. 15F

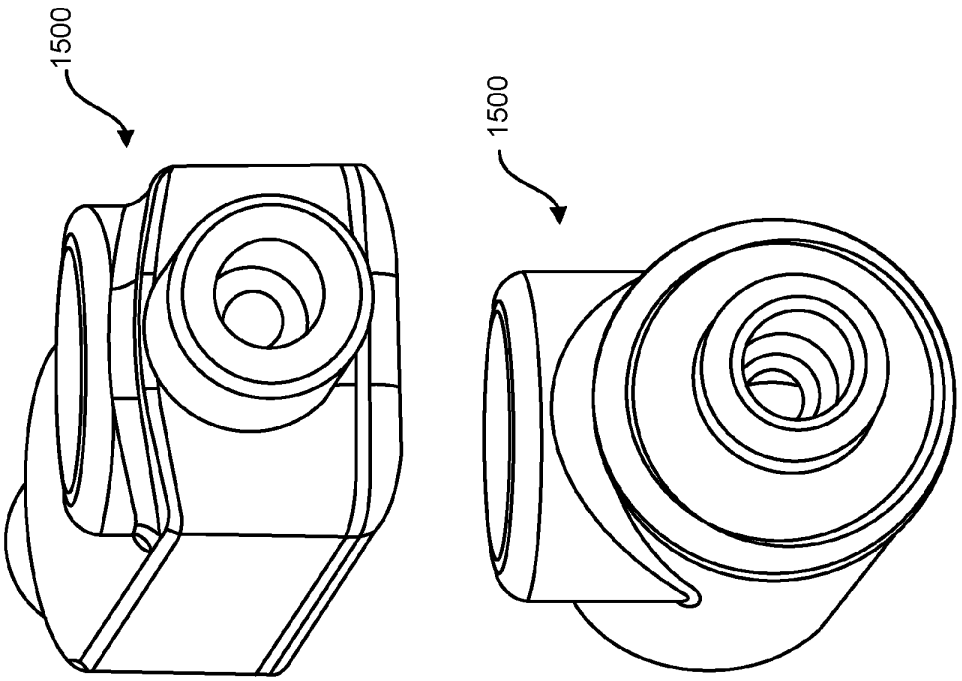


FIG. 15E

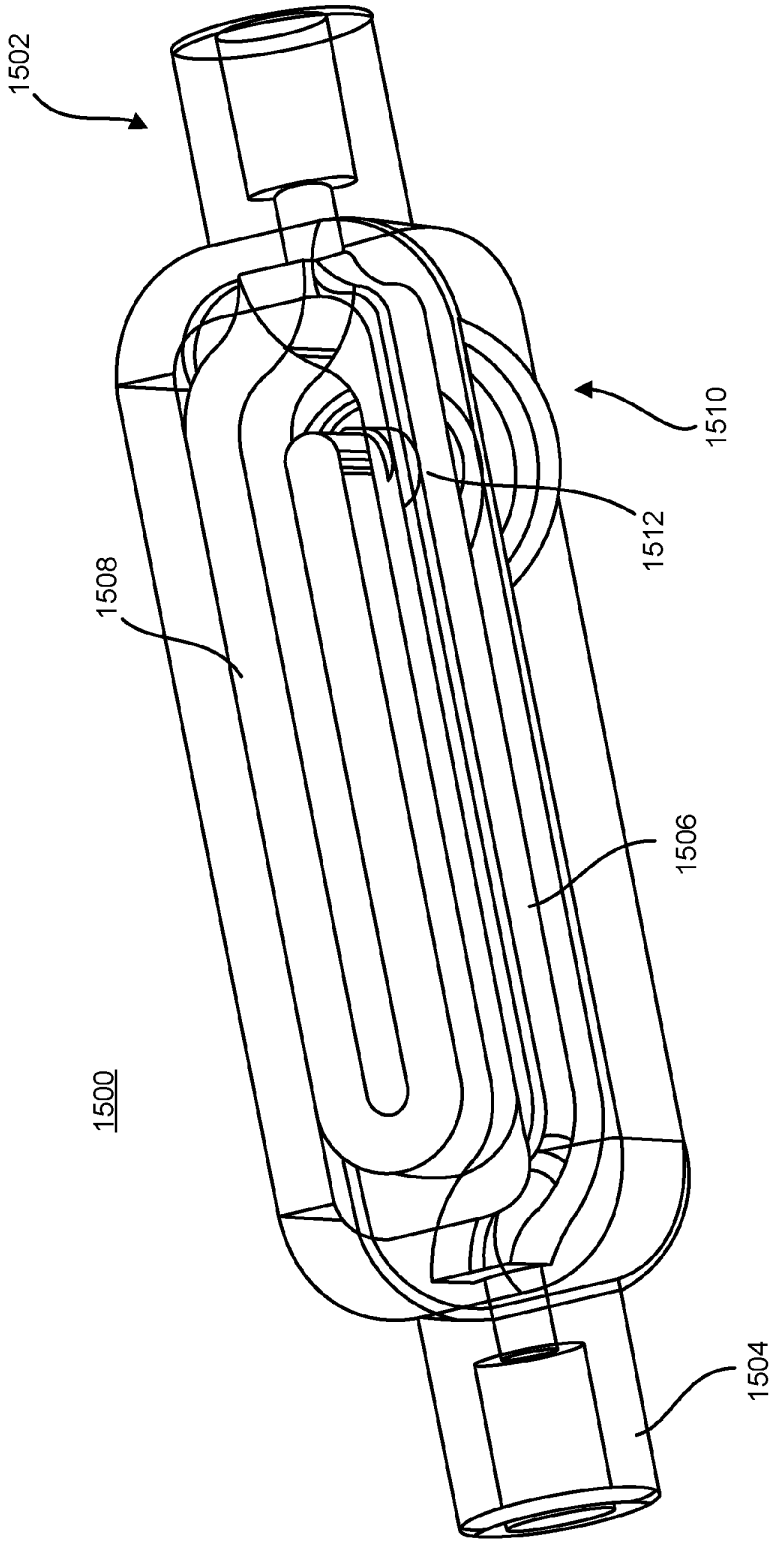


FIG. 15G

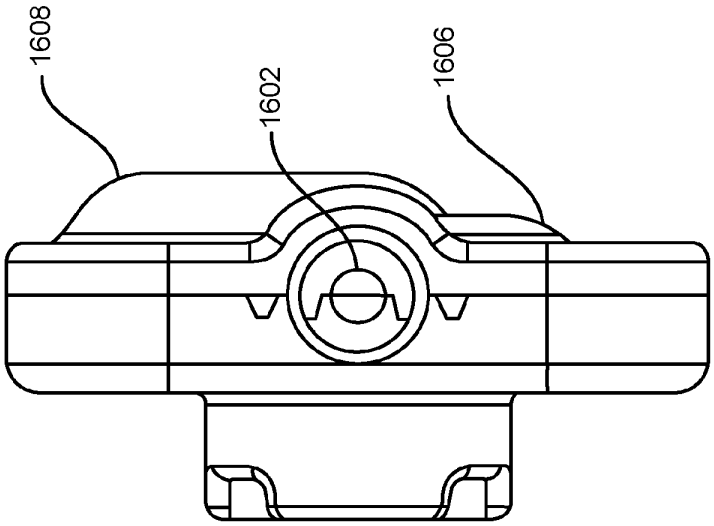


FIG. 16C

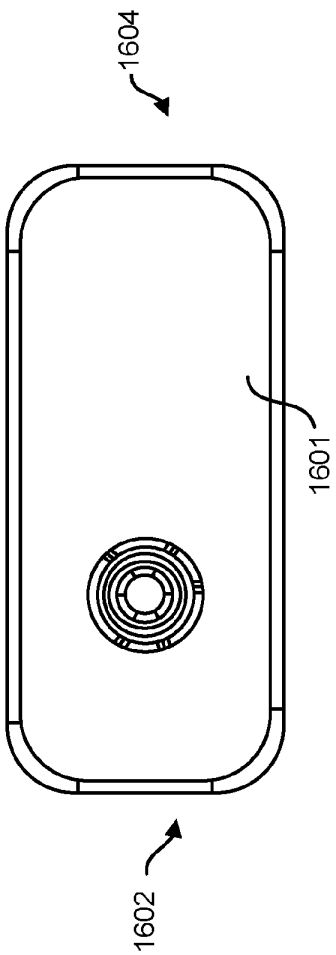


FIG. 16A

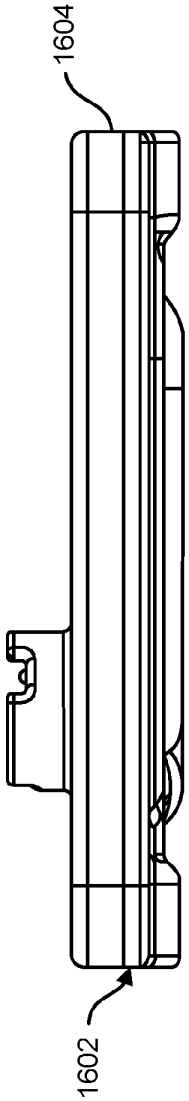


FIG. 16B

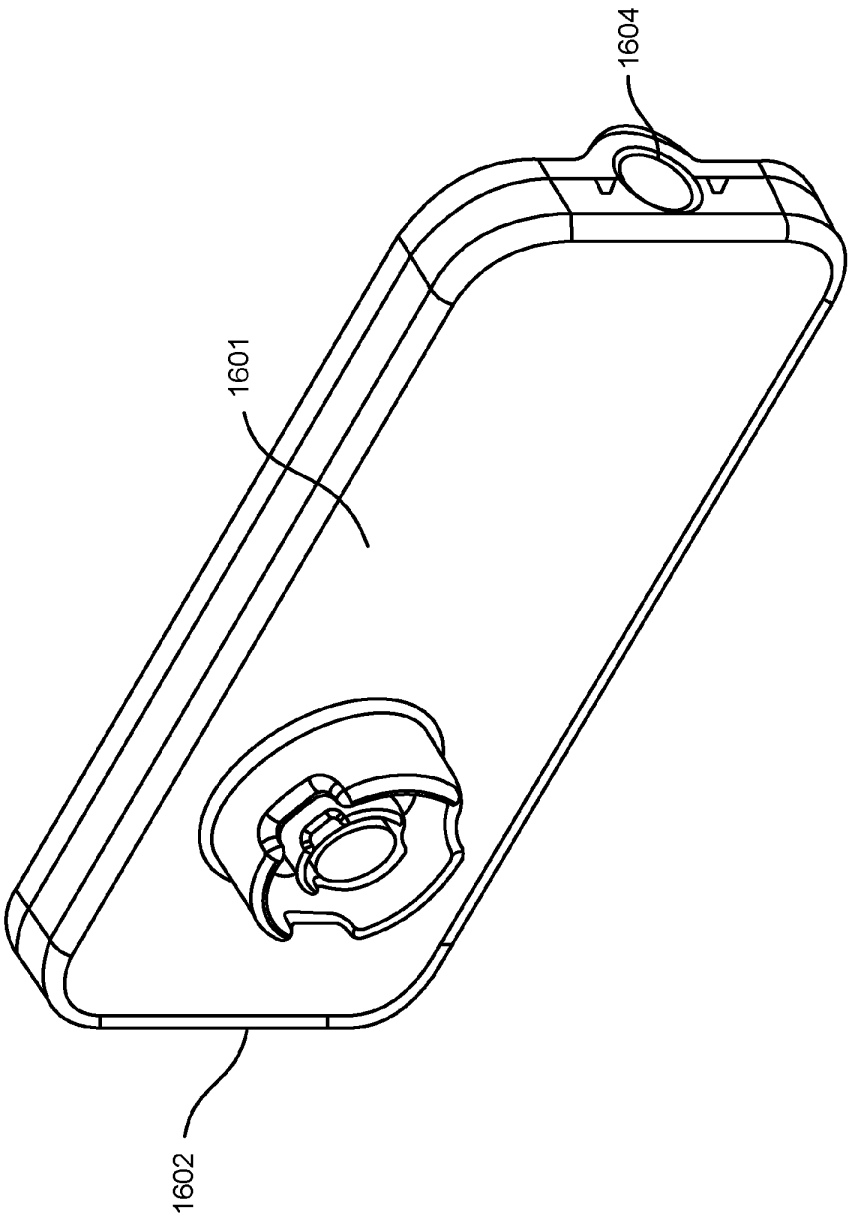


FIG. 16D

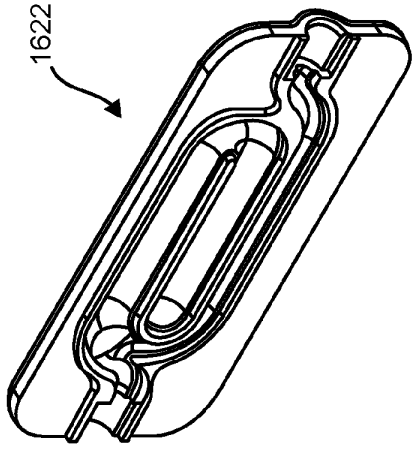


FIG. 17B



FIG. 17E

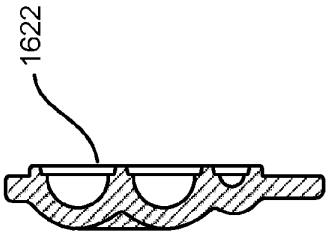


FIG. 17D

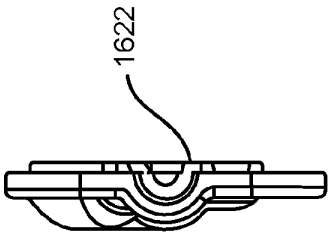


FIG. 17C

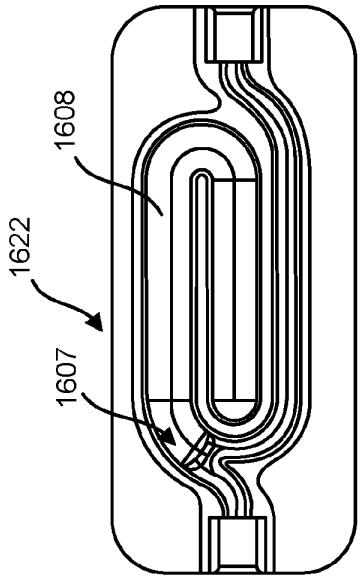


FIG. 17A

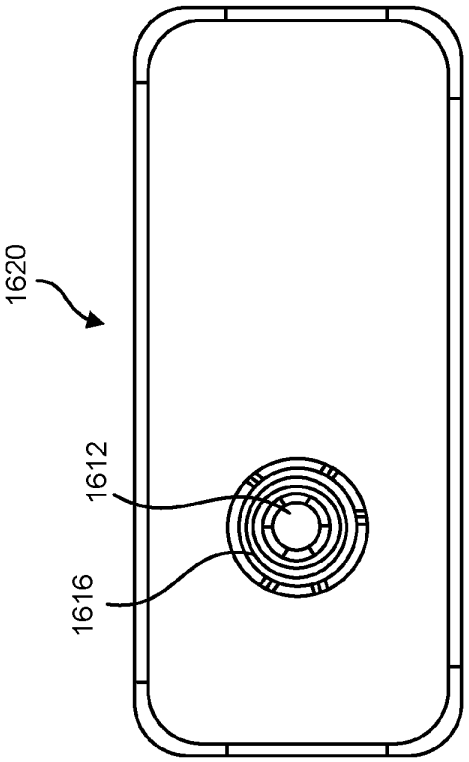


FIG. 18A

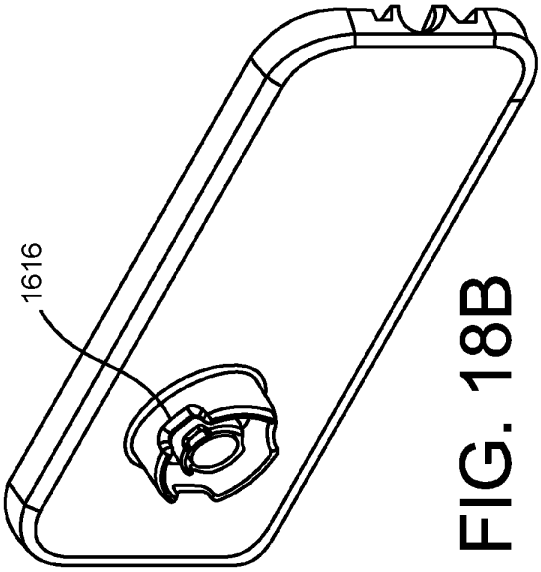


FIG. 18B

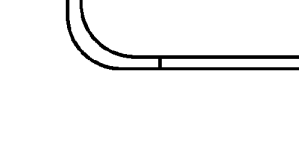


FIG. 18C

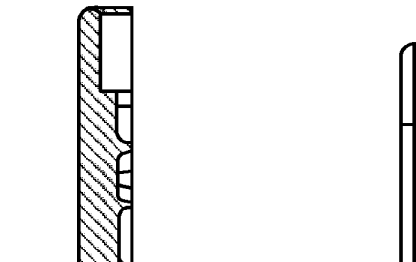


FIG. 18F

FIG. 18D

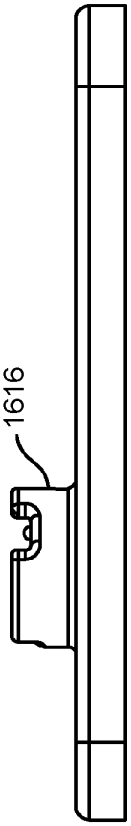


FIG. 18E

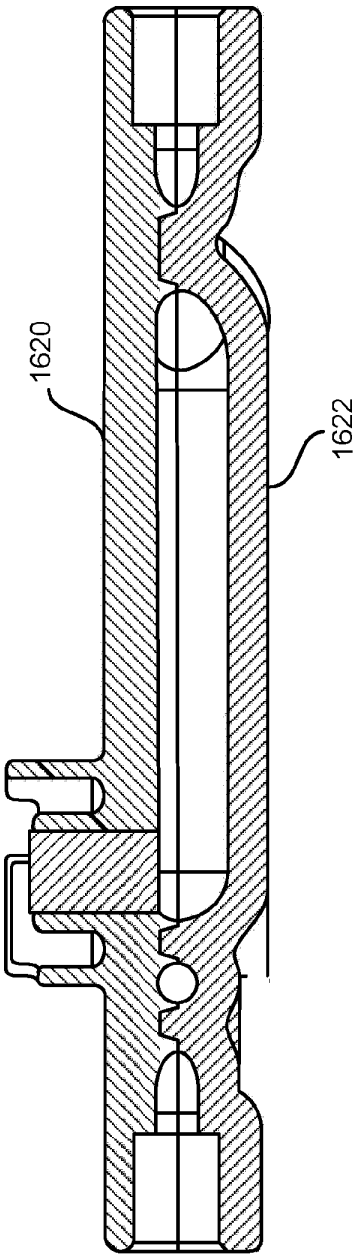


FIG. 19A

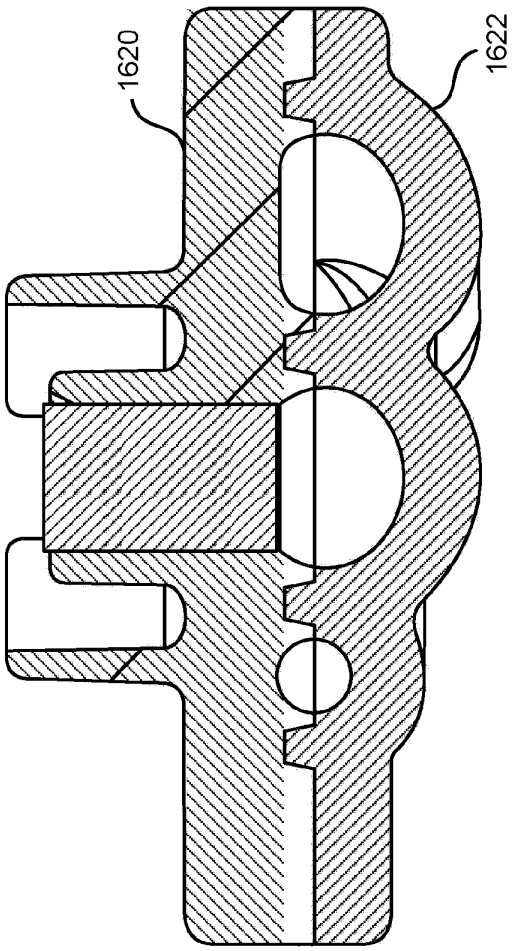


FIG. 19B

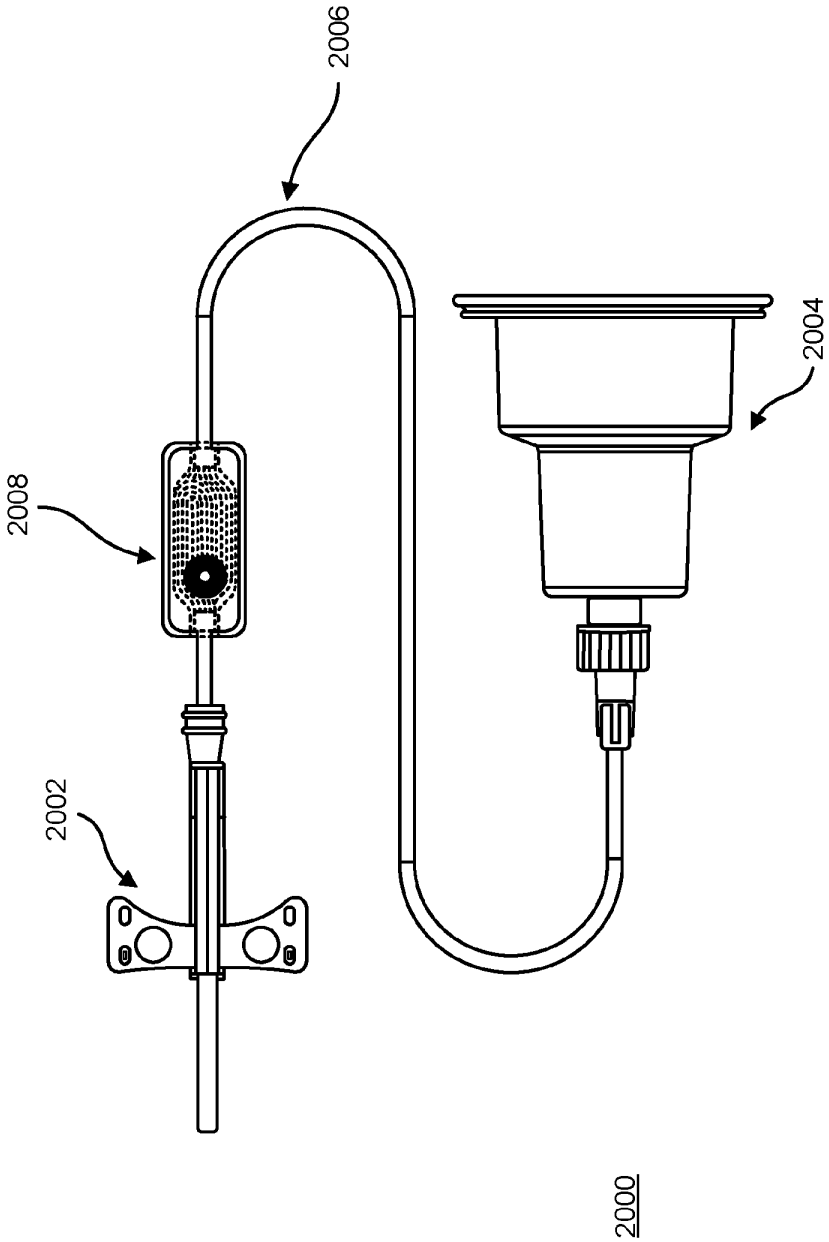


FIG. 20

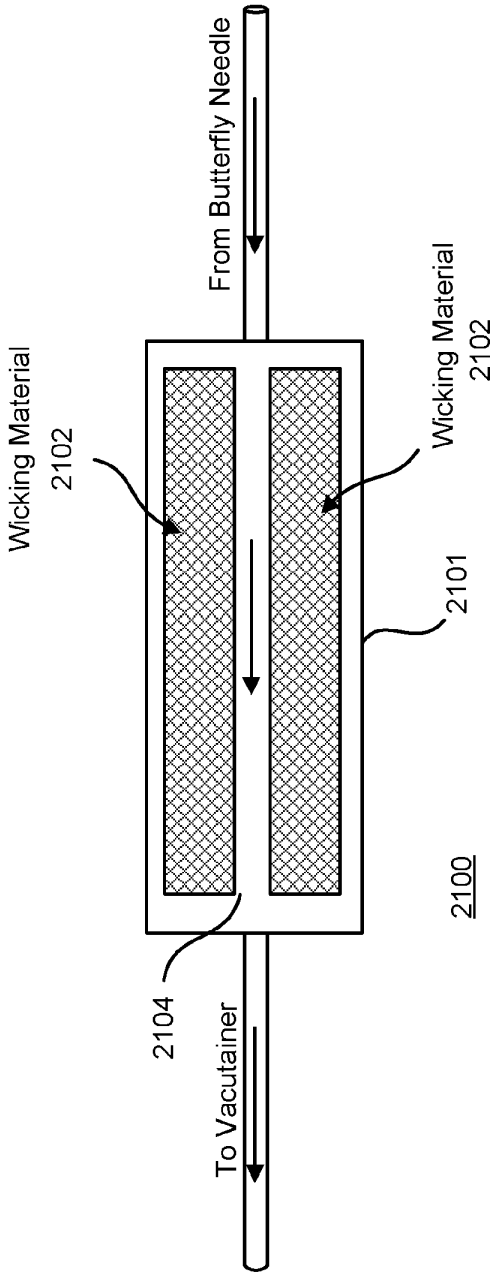

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

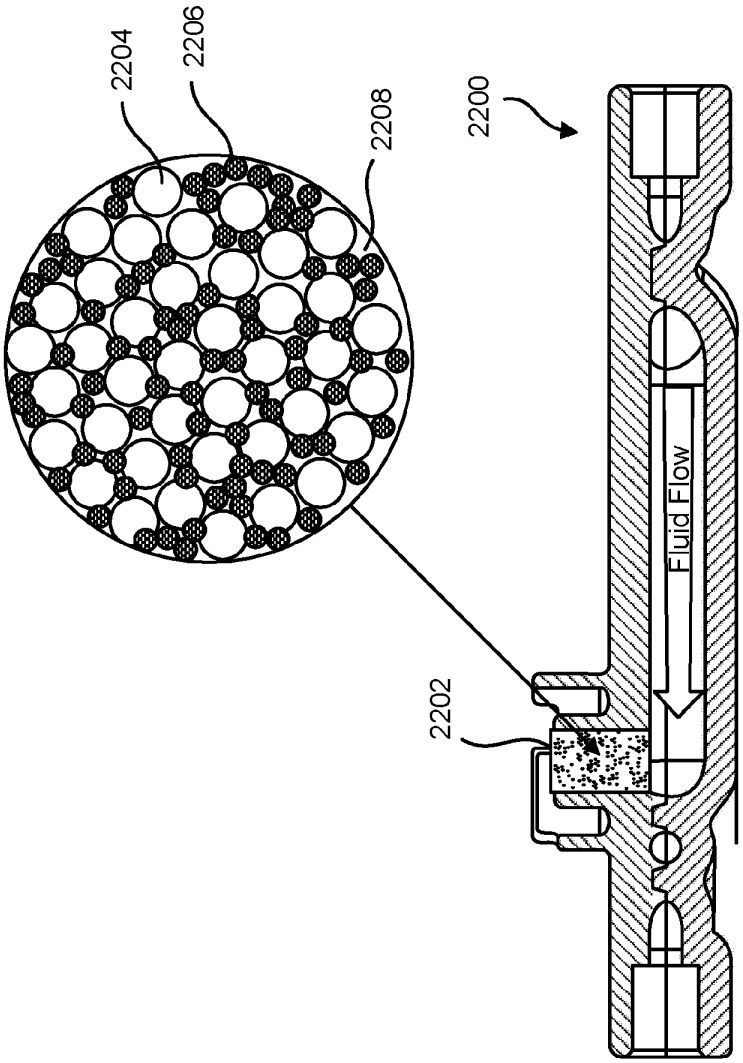


FIG. 22A

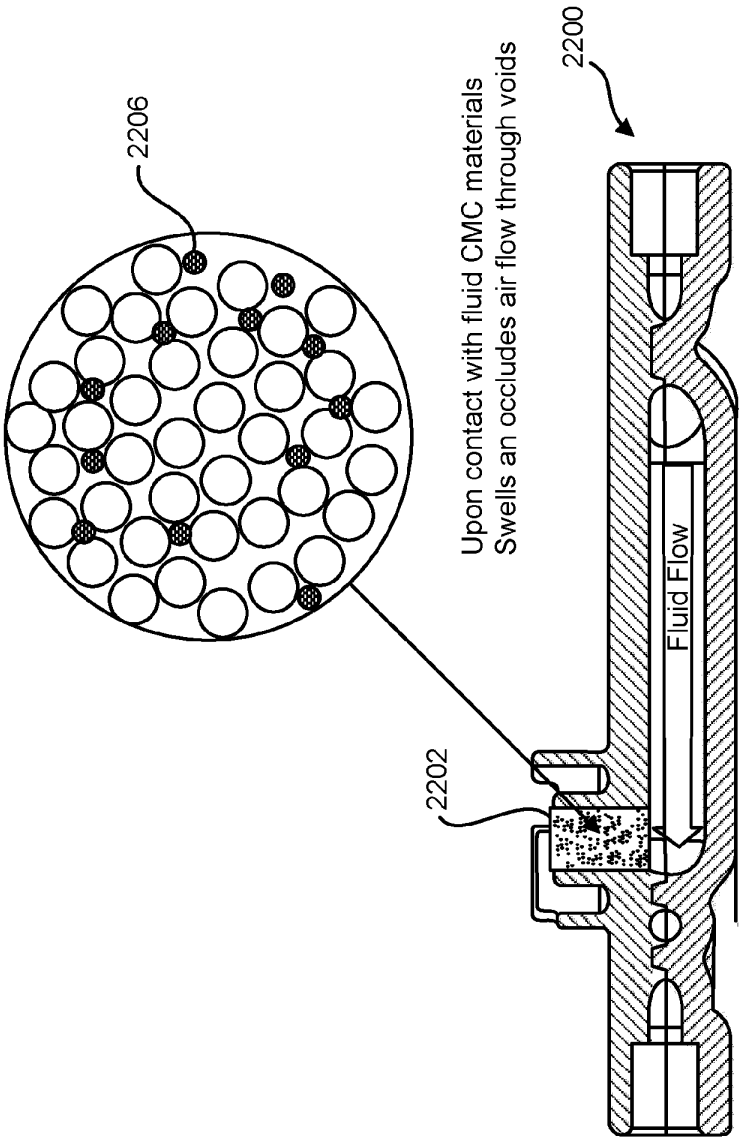

2206
2200
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

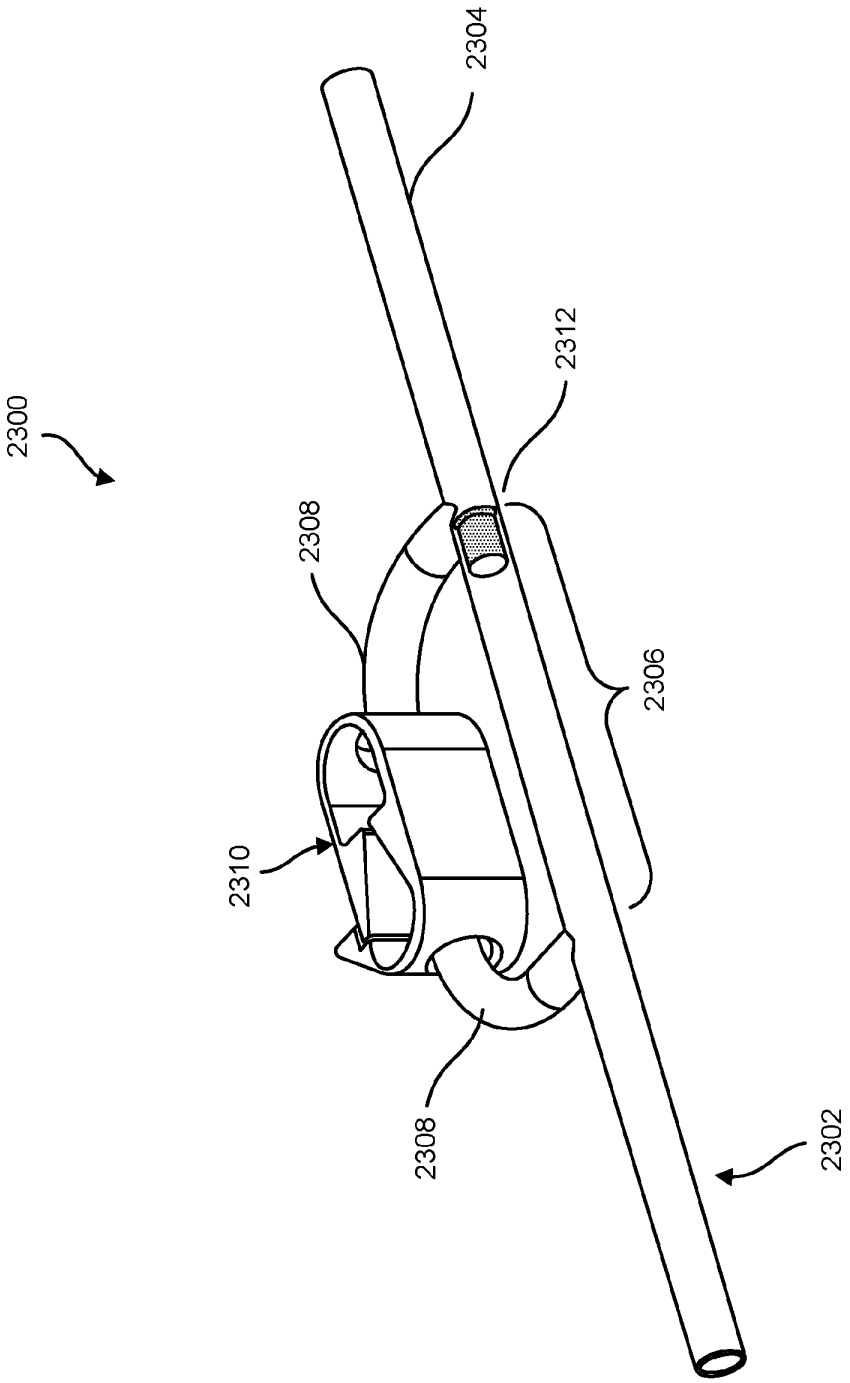


FIG. 23A

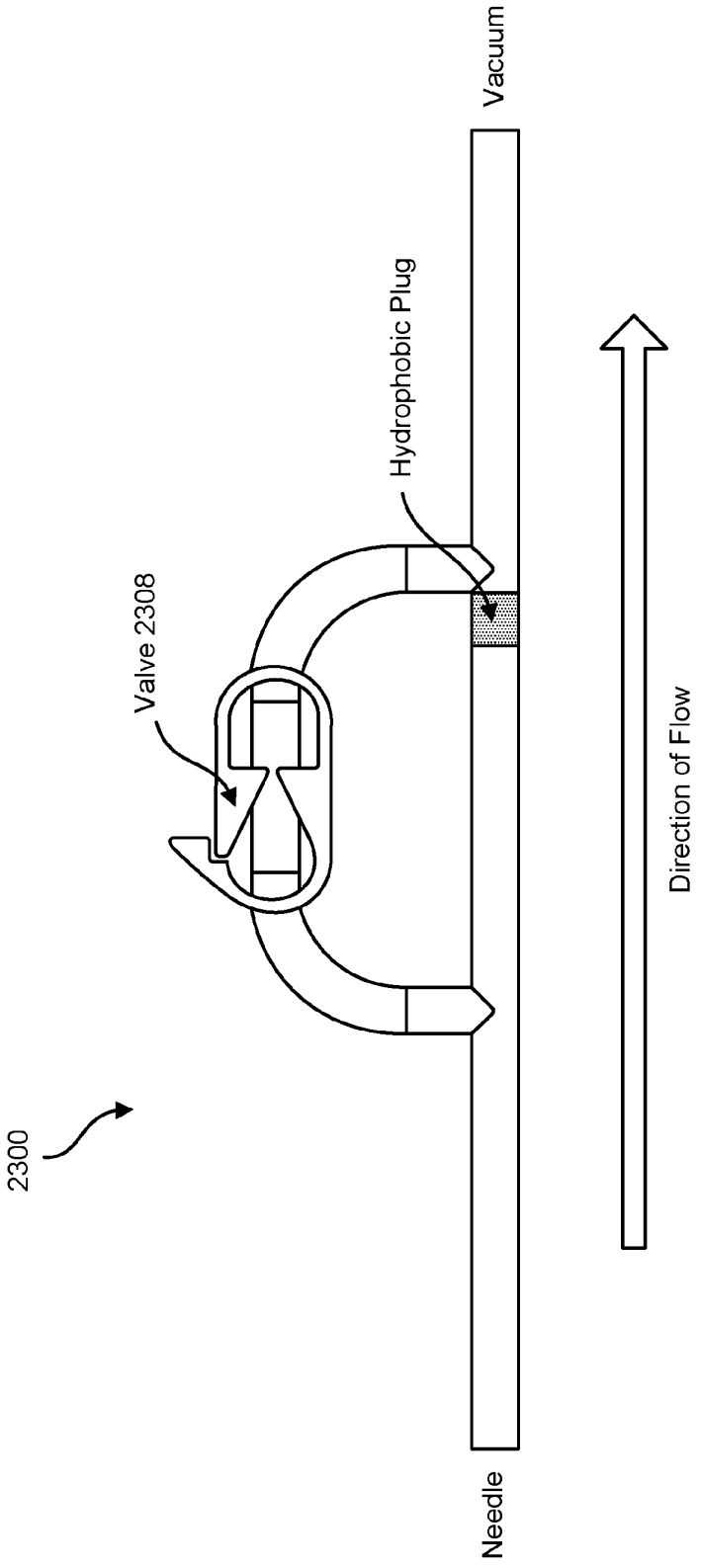

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

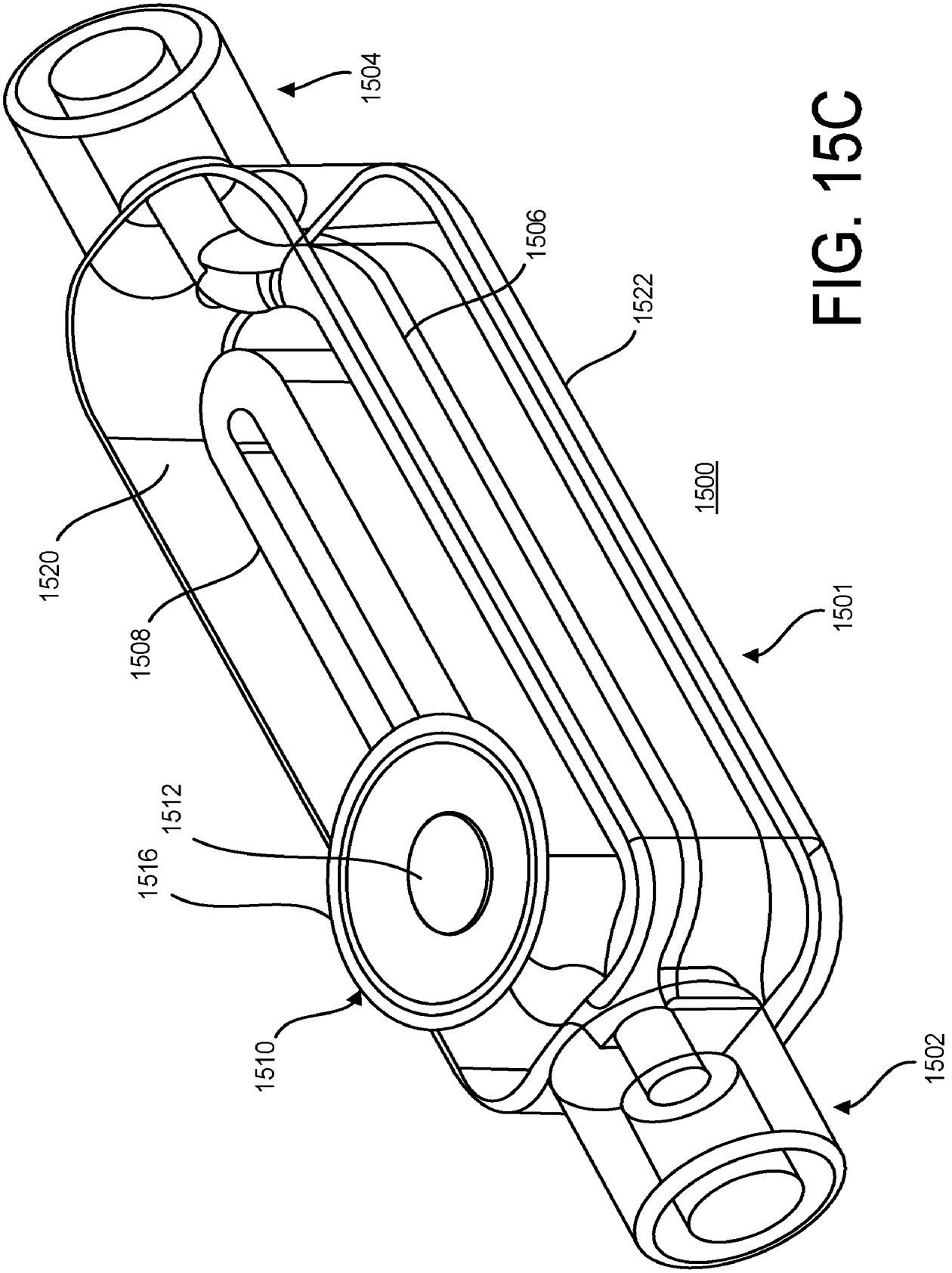


FIG. 15C

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B01L 3/14 (2006.01) *G01N 33/49* (2006.01)

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Filed on 29 May 2013 (29.05.2013)

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

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[Continued on next page]

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

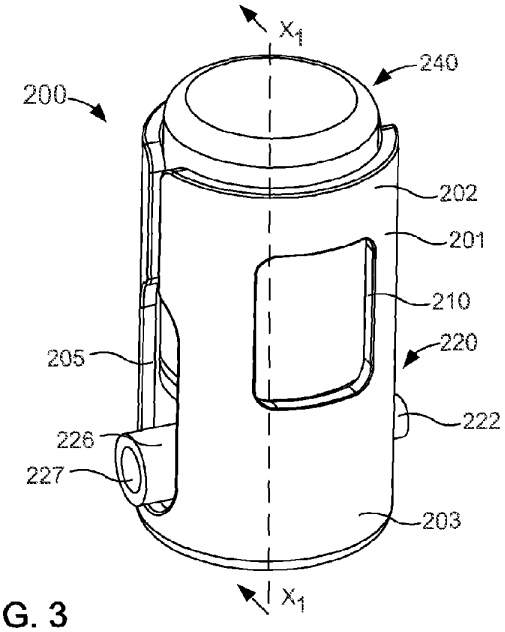


FIG. 3

(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.

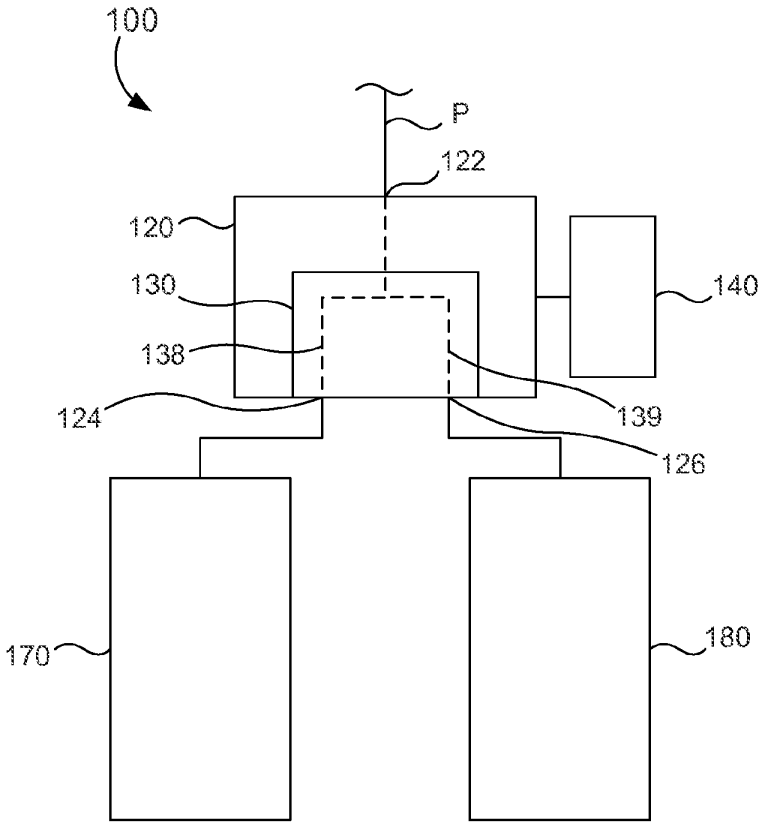


FIG. 1

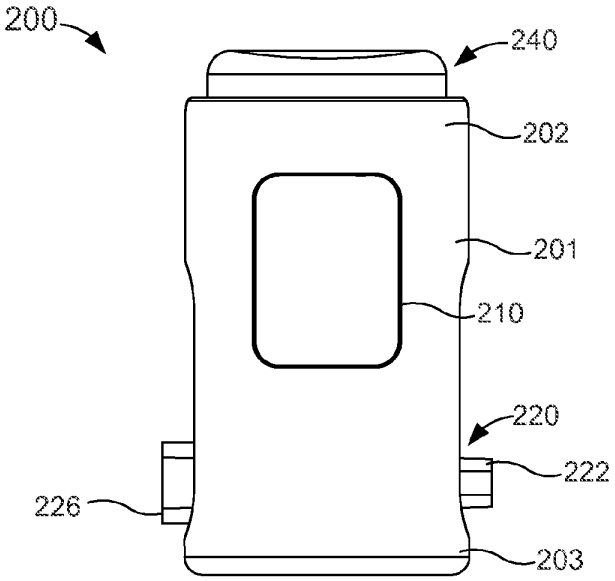

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FIG. 2

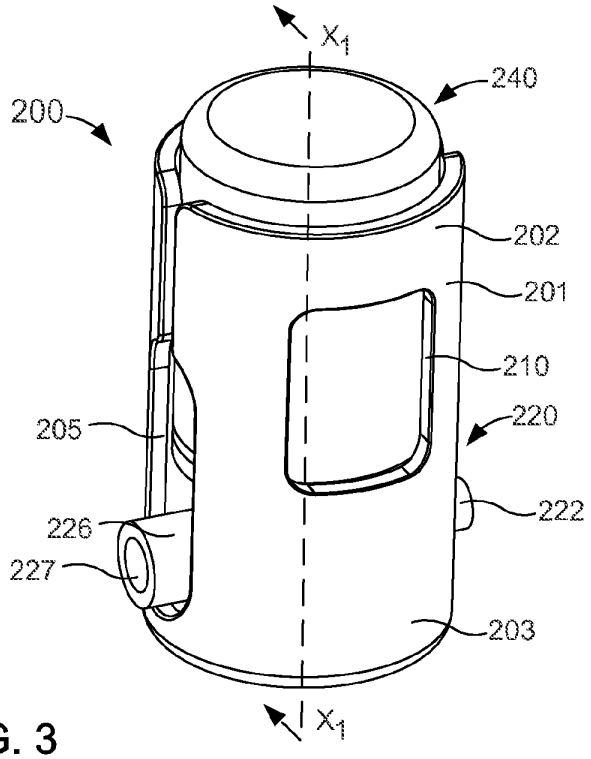

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FIG. 3

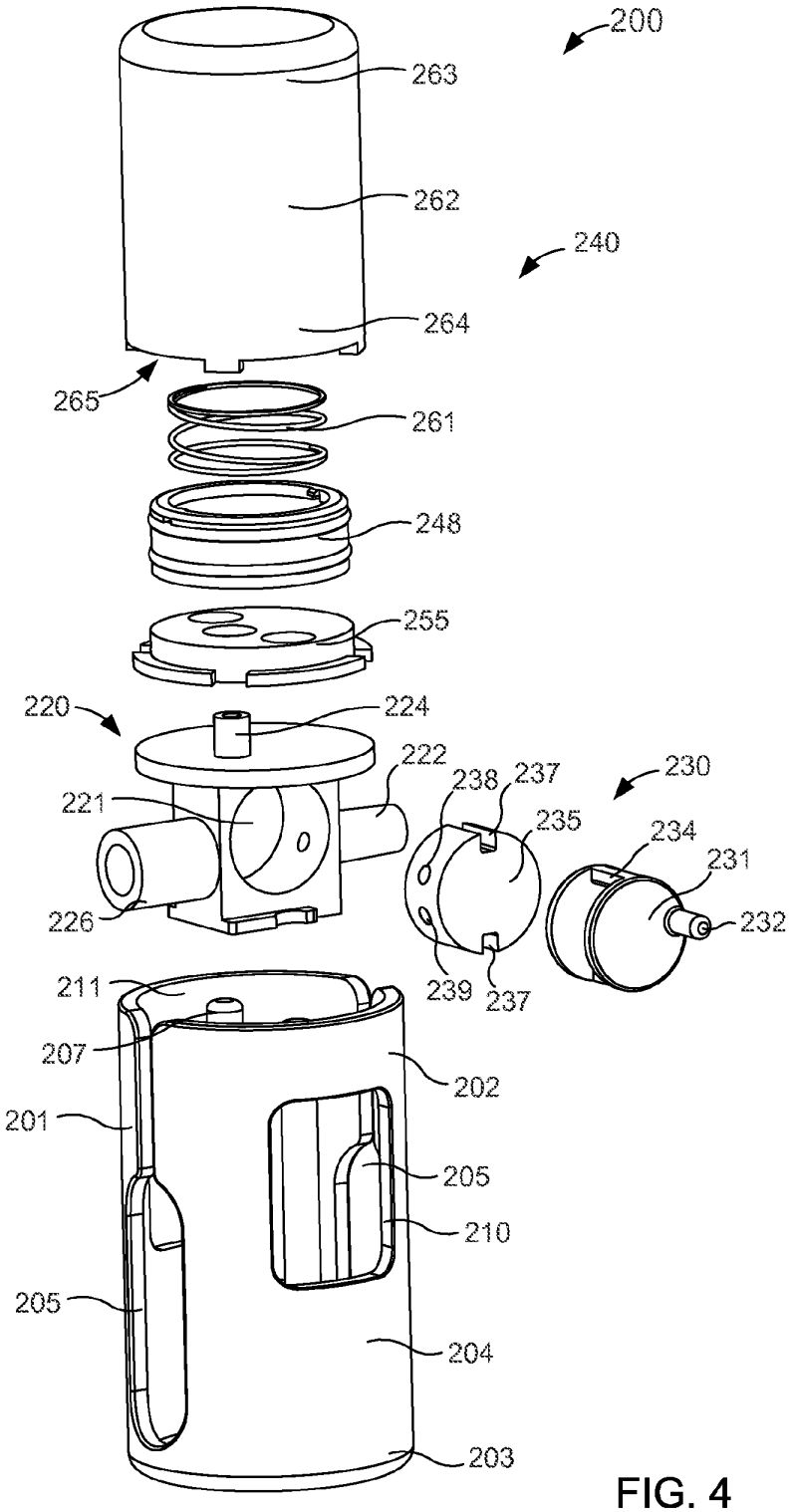

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FIG. 4

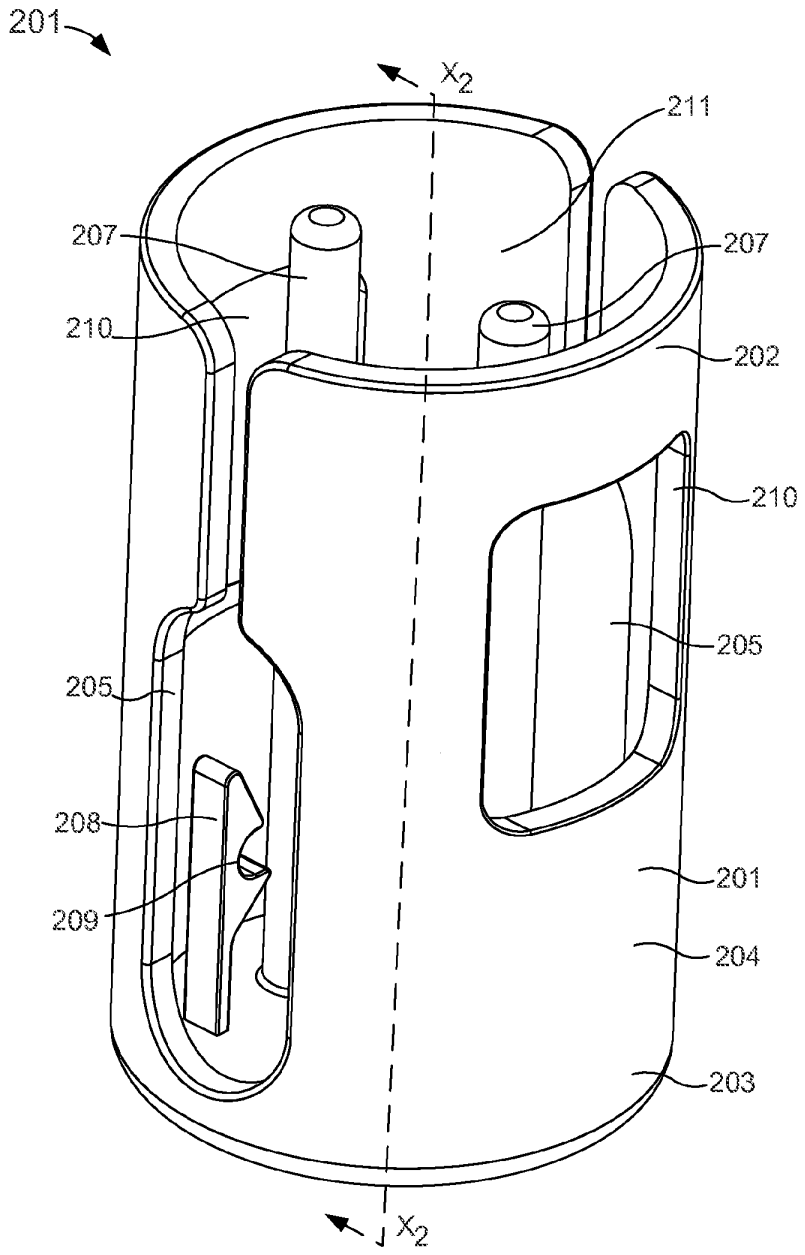


FIG. 5

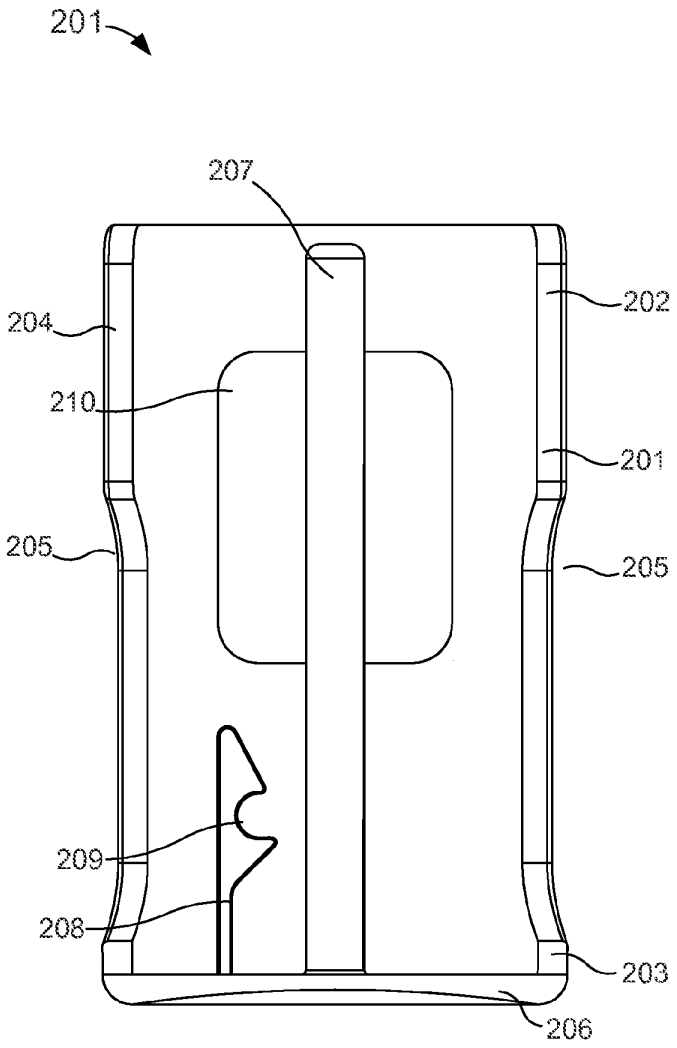


FIG. 6

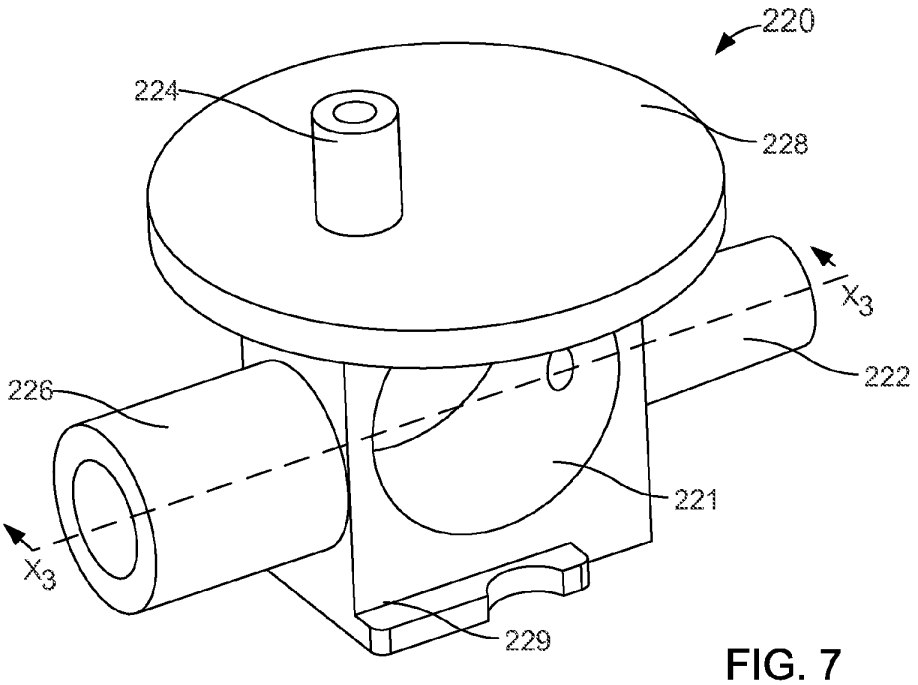

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FIG. 7

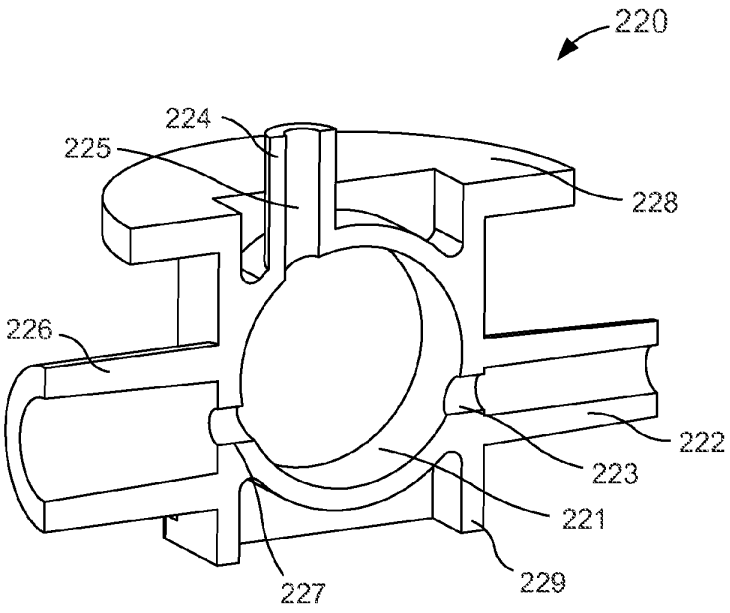

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FIG. 8

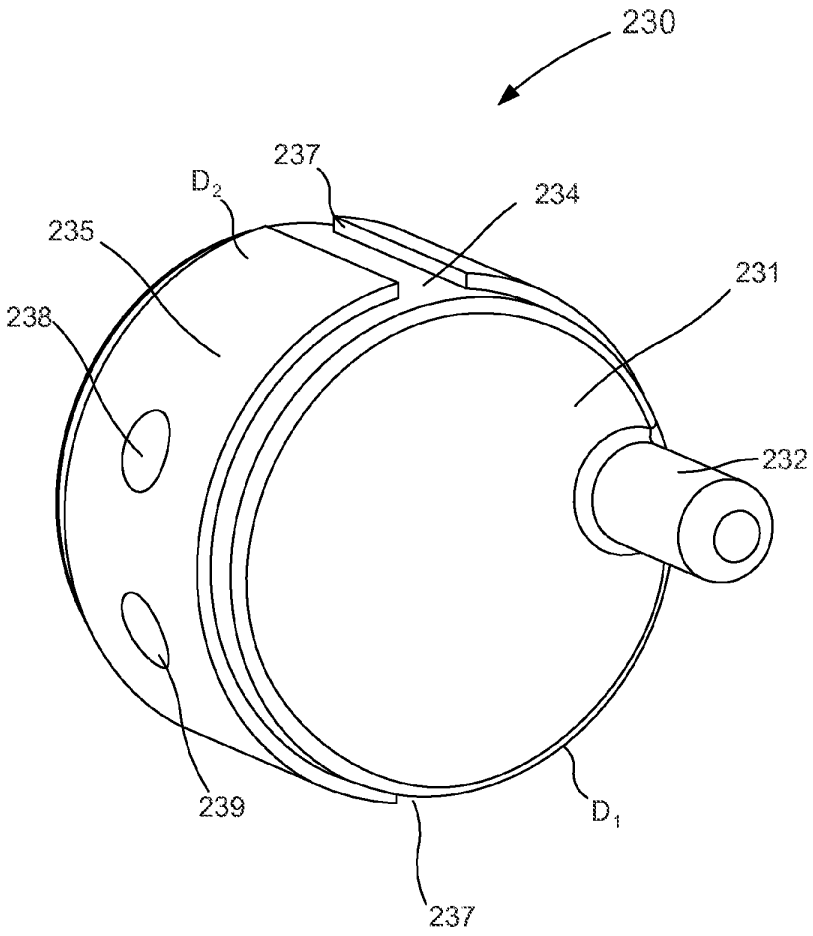


FIG. 9

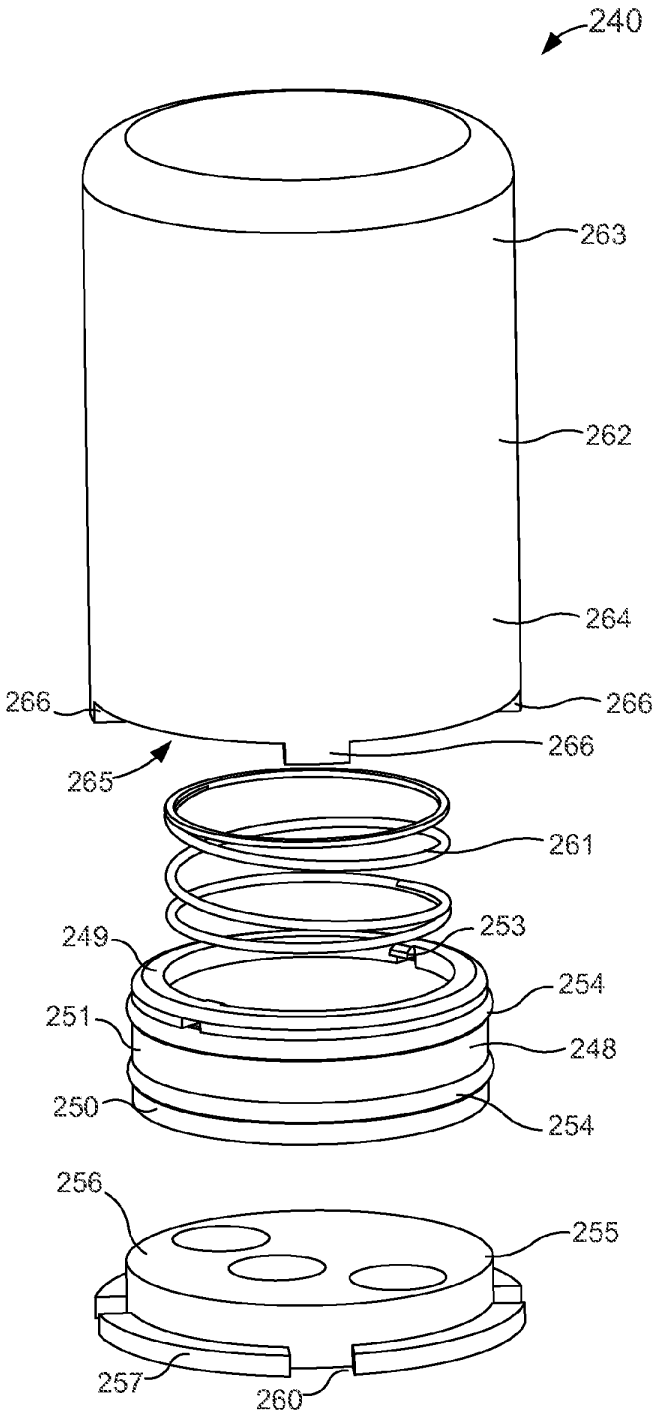

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FIG. 10

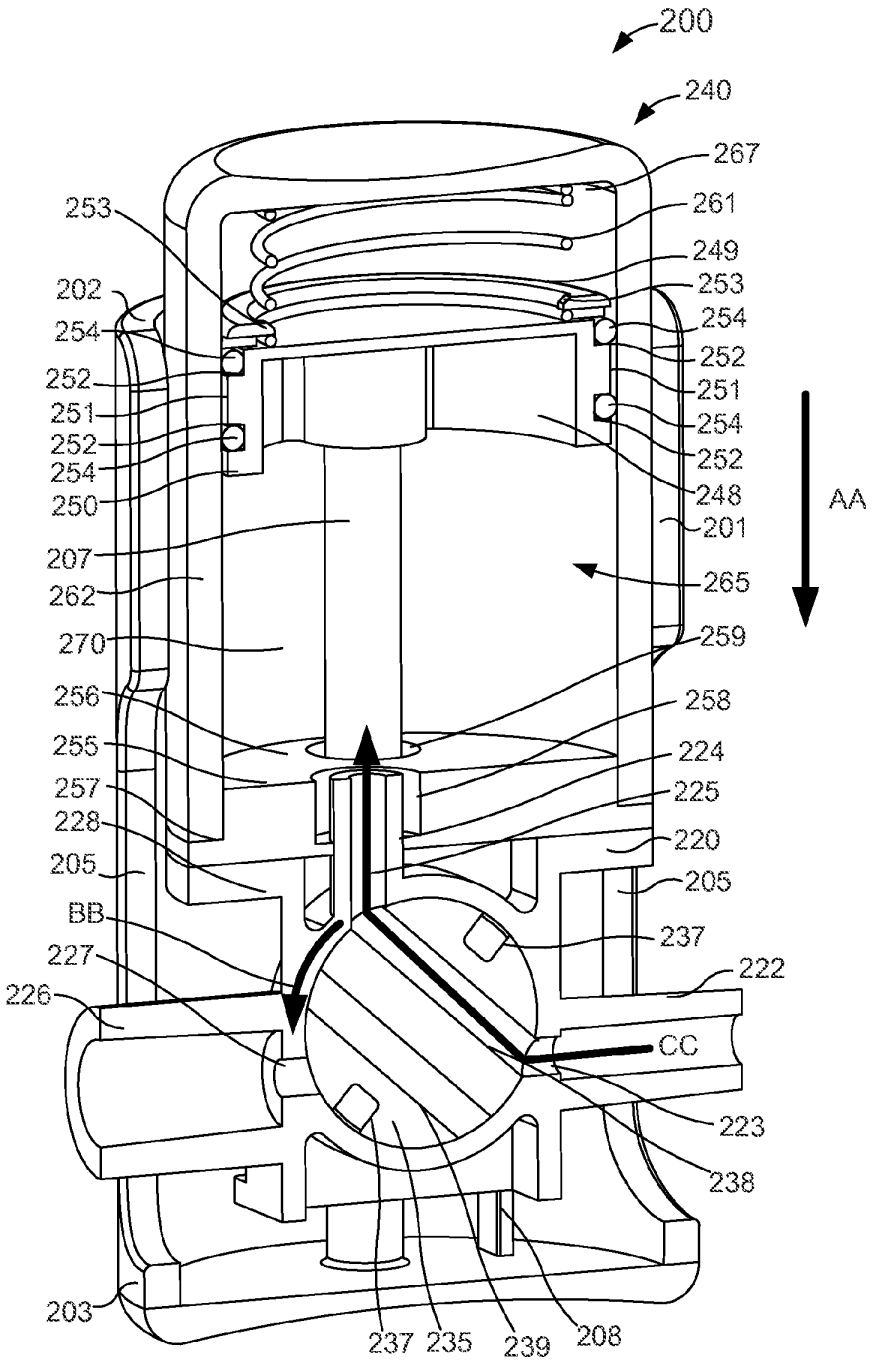

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FIG. 11

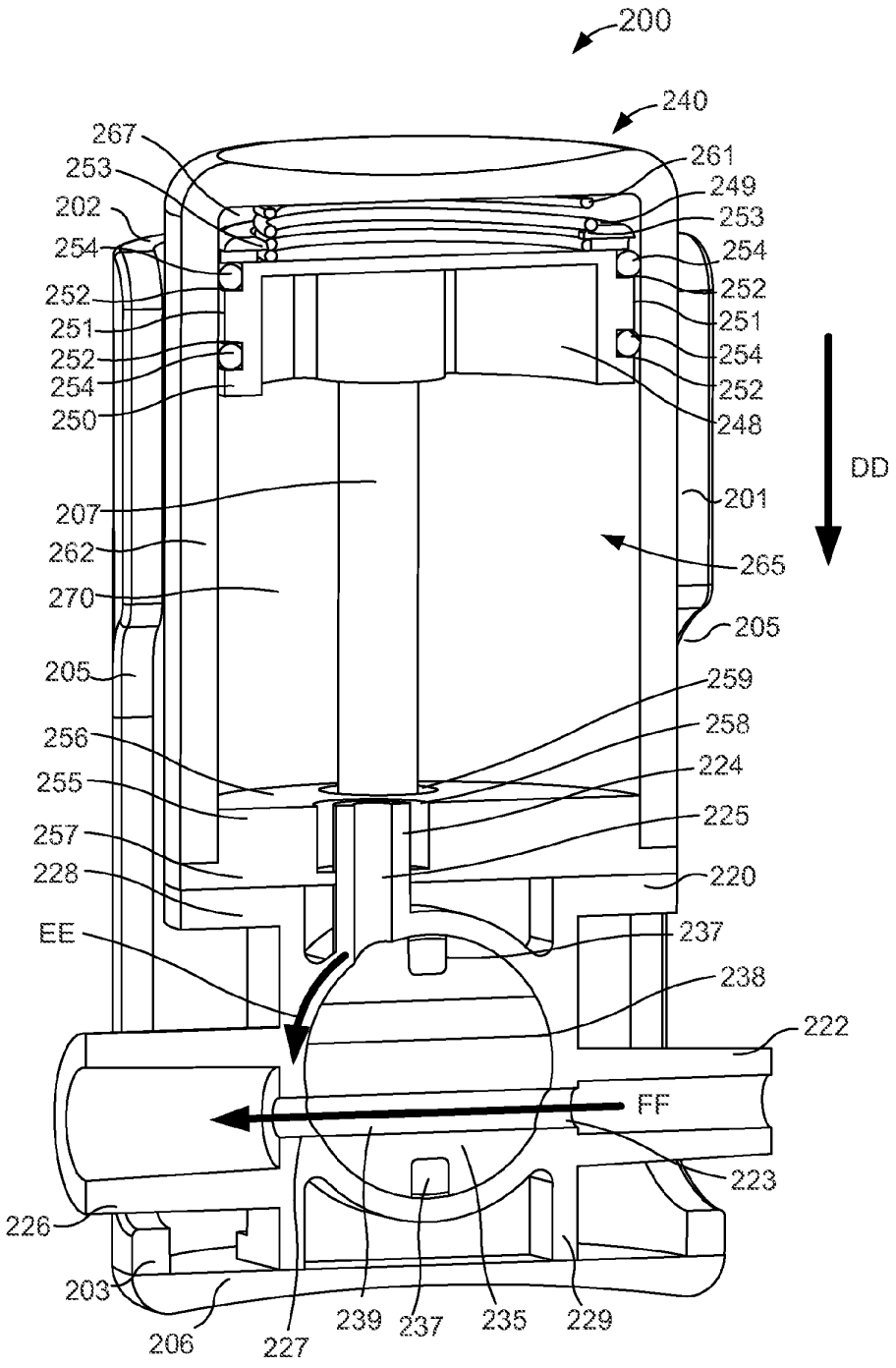

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FIG. 12

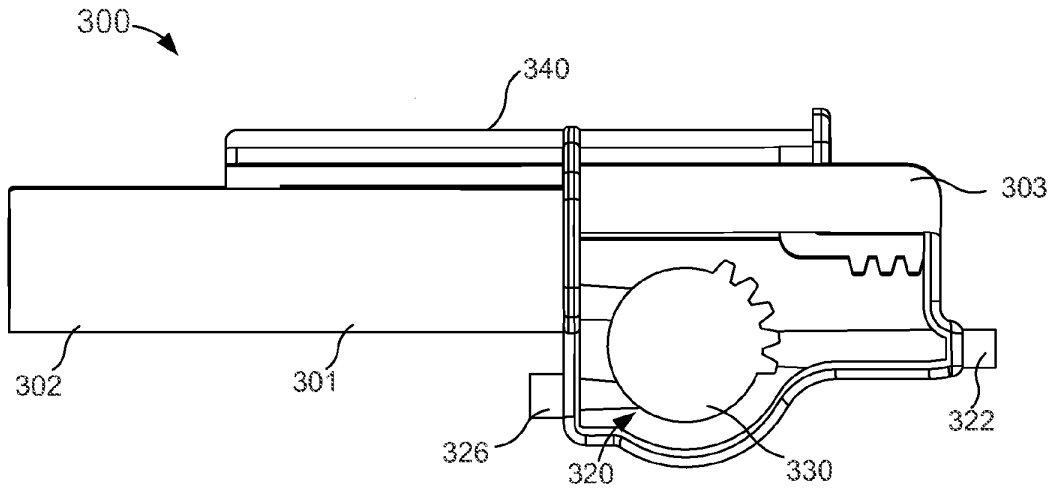

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FIG. 13

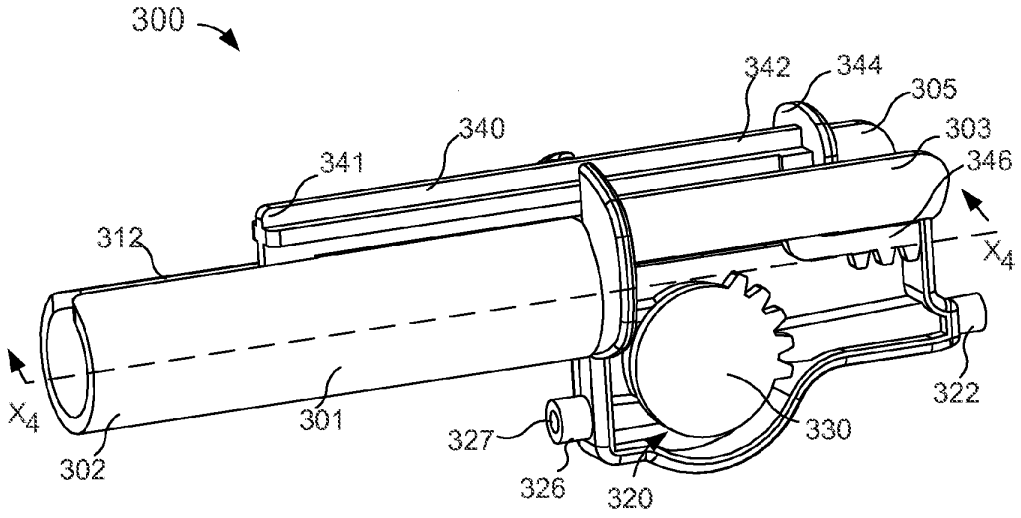

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FIG. 14

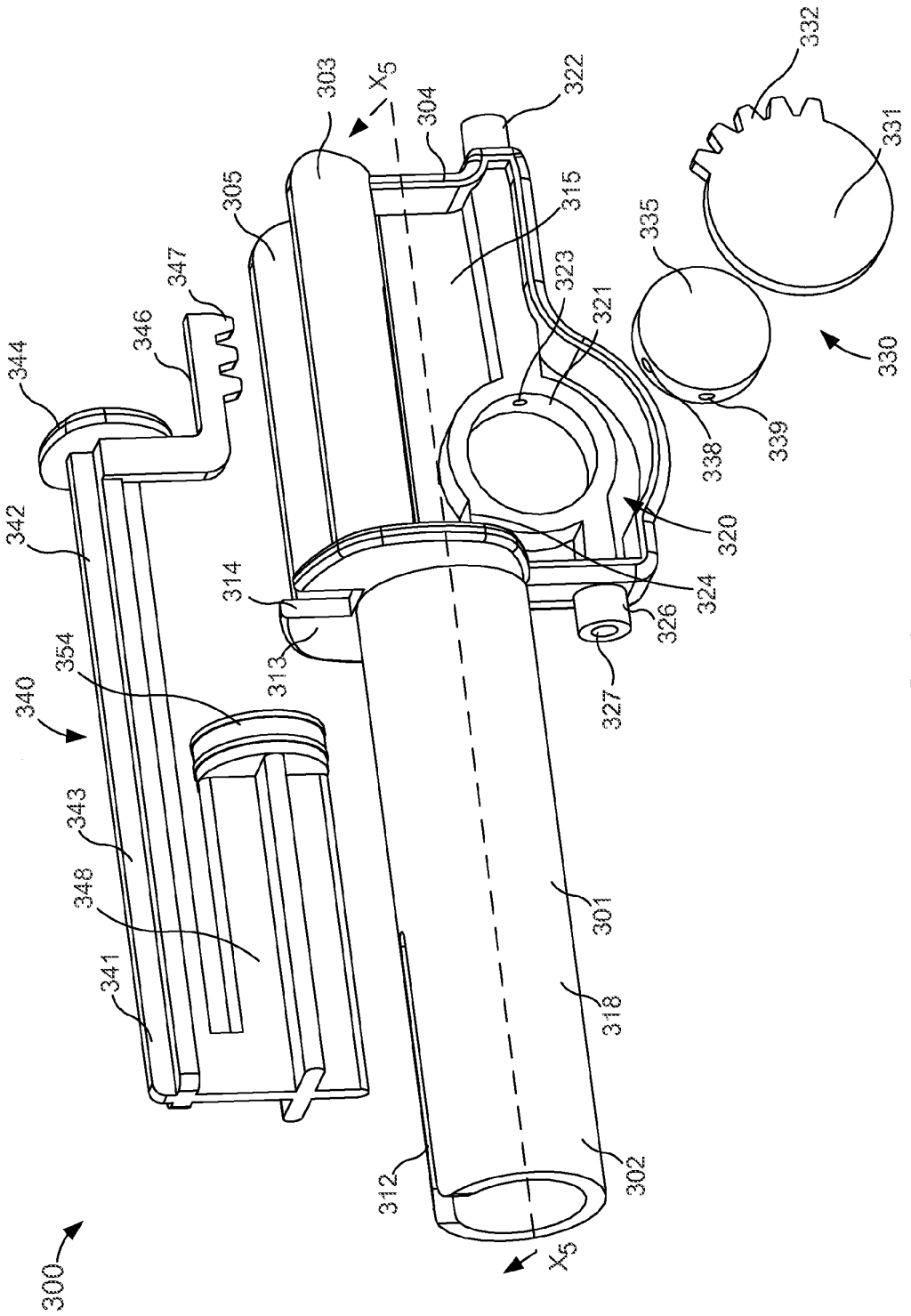

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FIG. 15

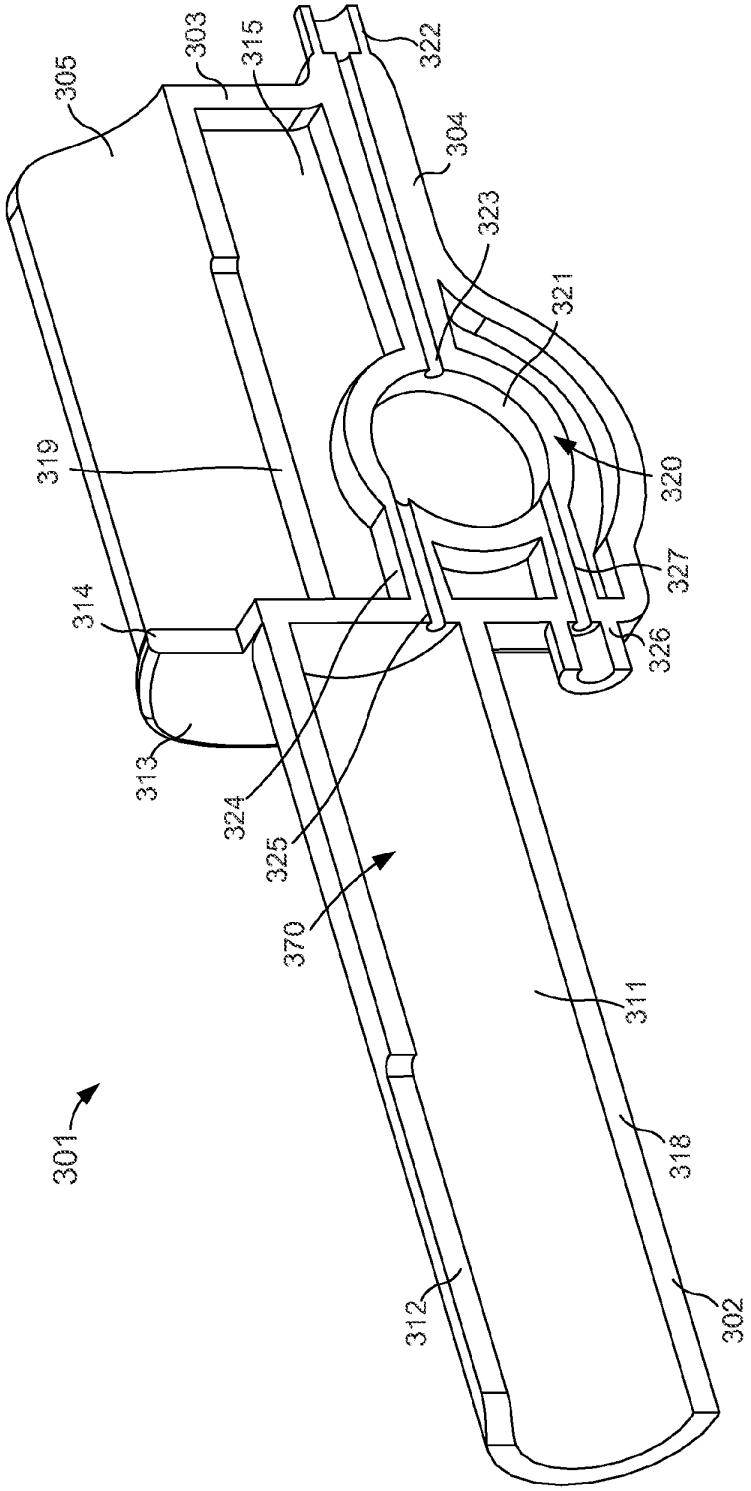

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FIG. 16

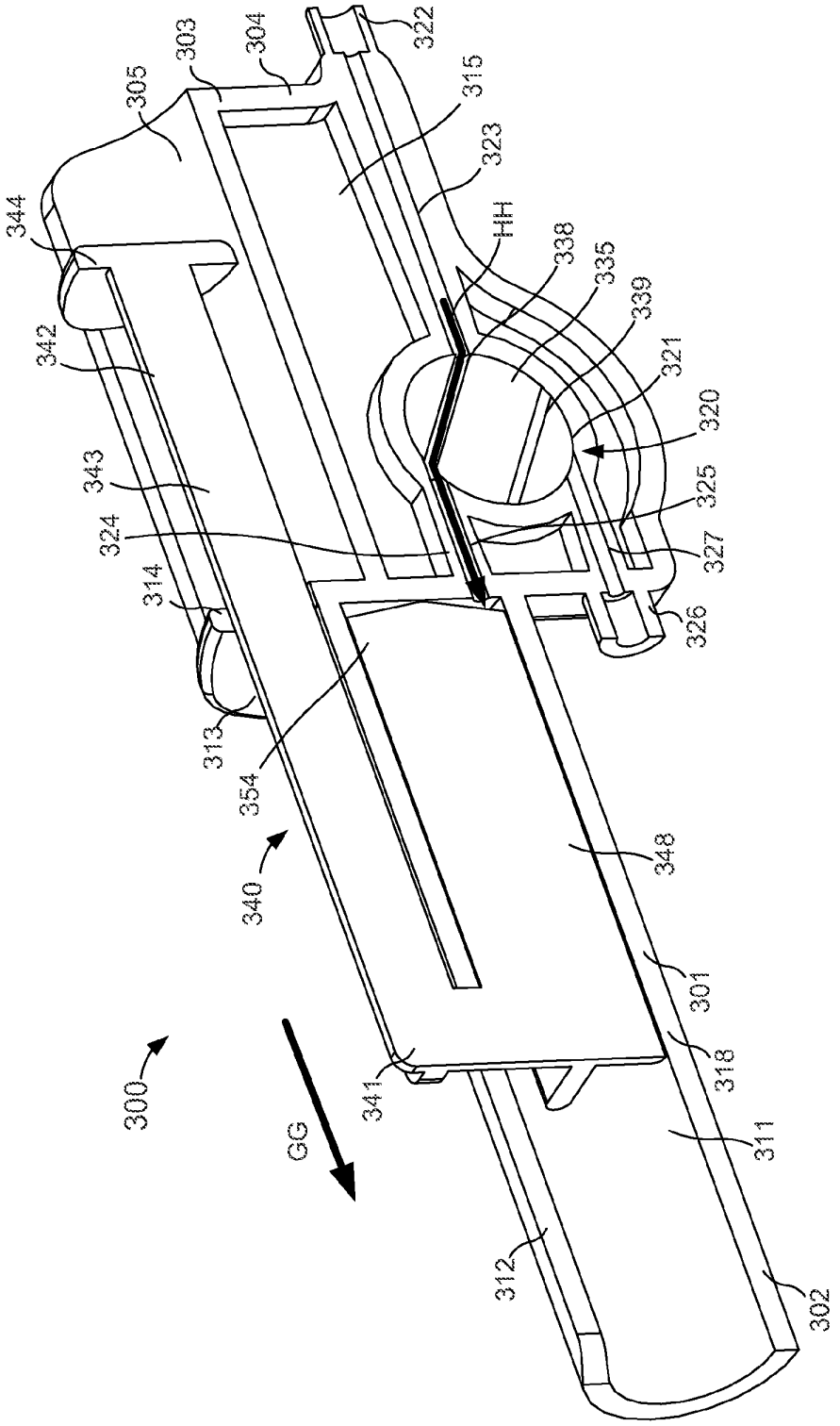

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GG
HH

FIG. 17

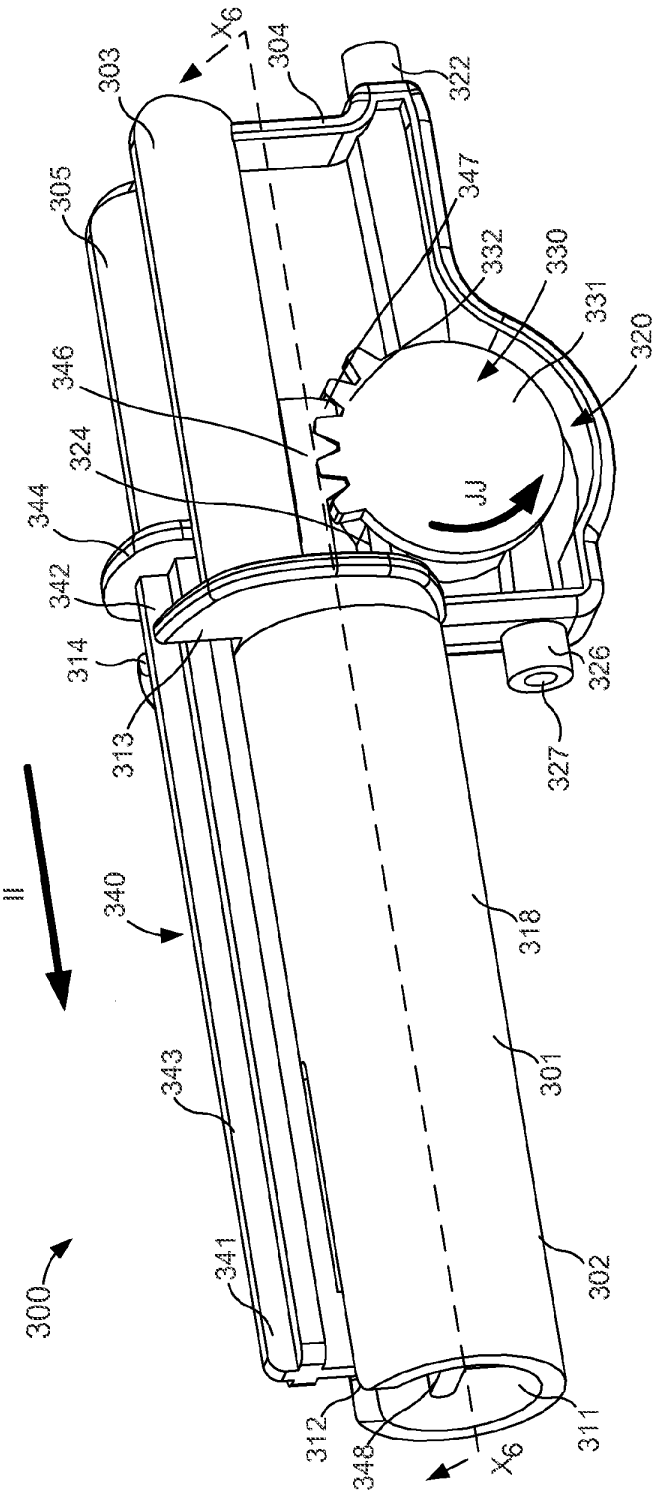

X6
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332
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JJ
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II
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318
343
301
341
302
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312
348
311
X6

FIG. 18

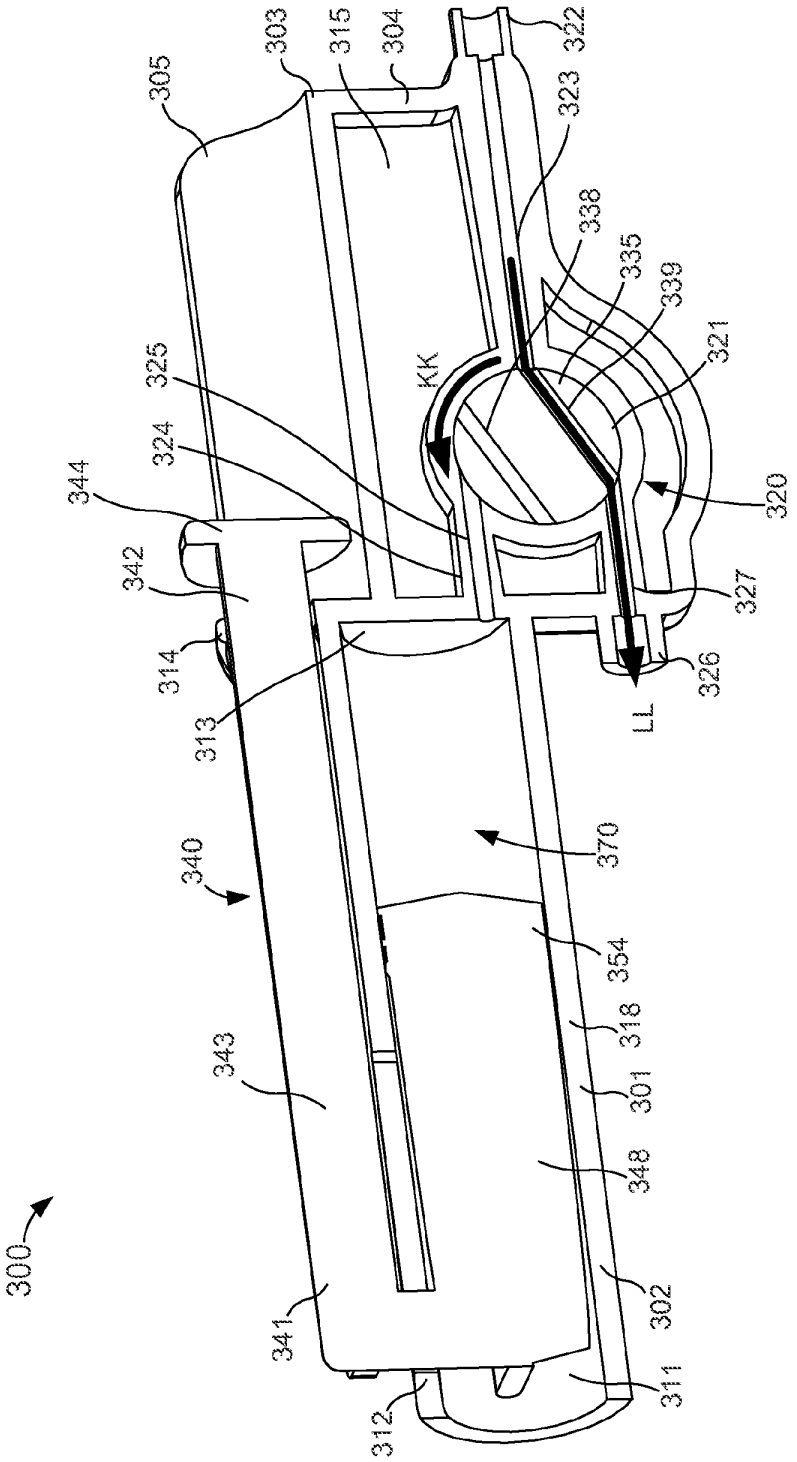

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KK
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LL
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FIG. 19

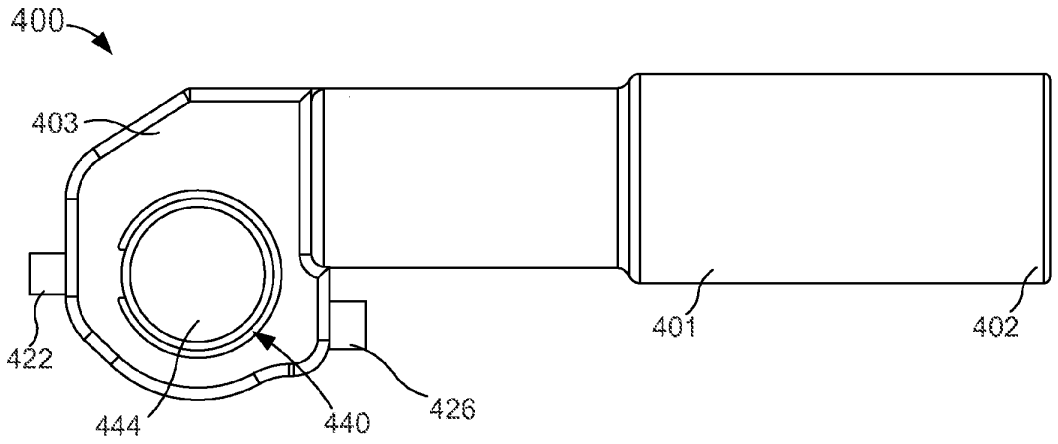

400
403
422
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402

FIG. 20

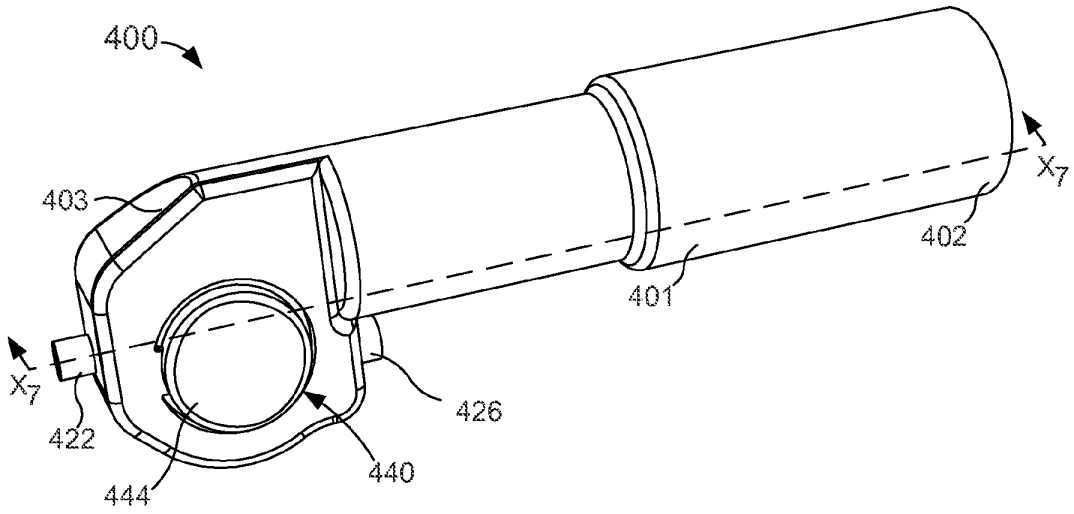

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X7
X7

FIG. 21

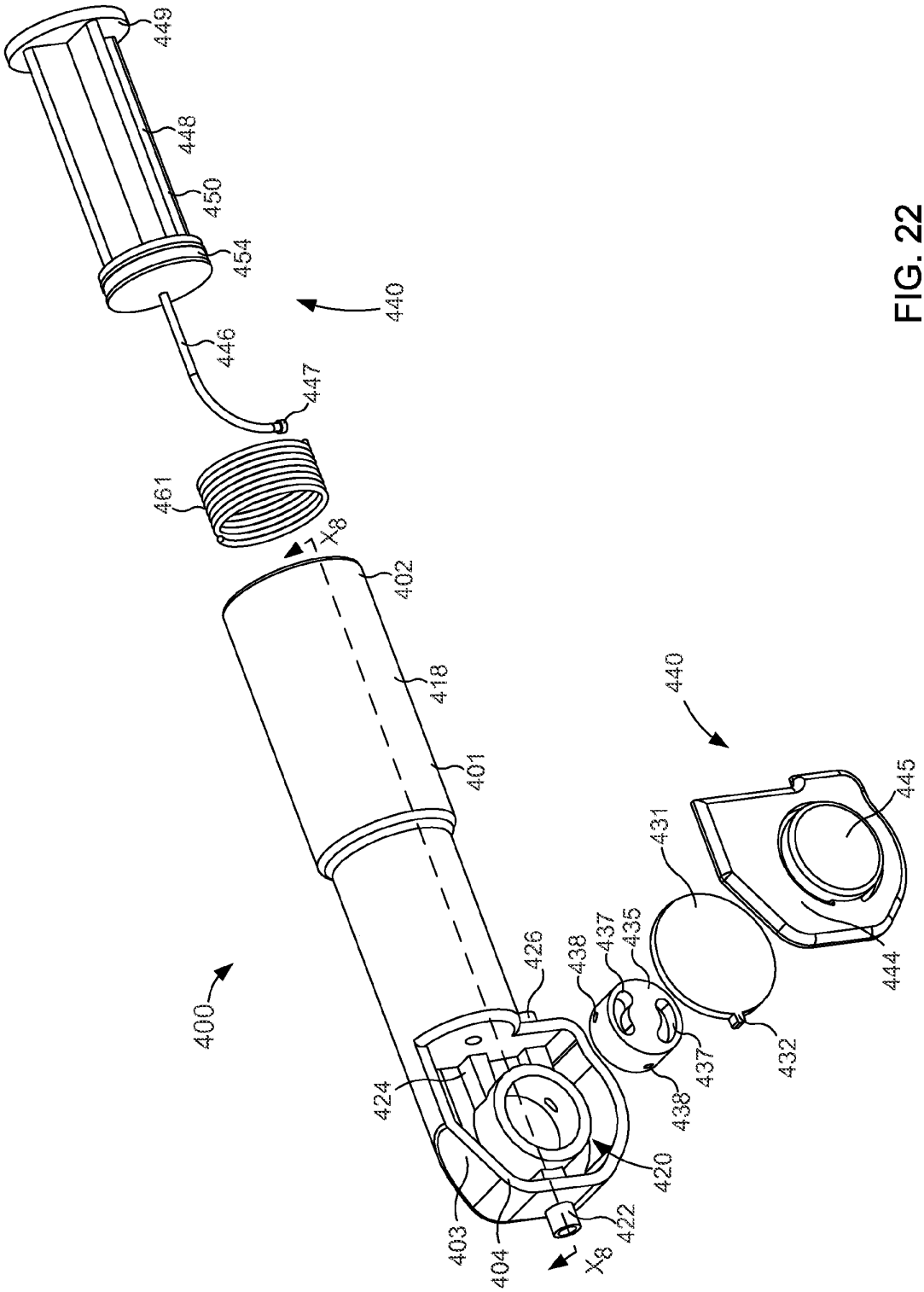

449
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461
X8
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422
403
404
X8

FIG. 22

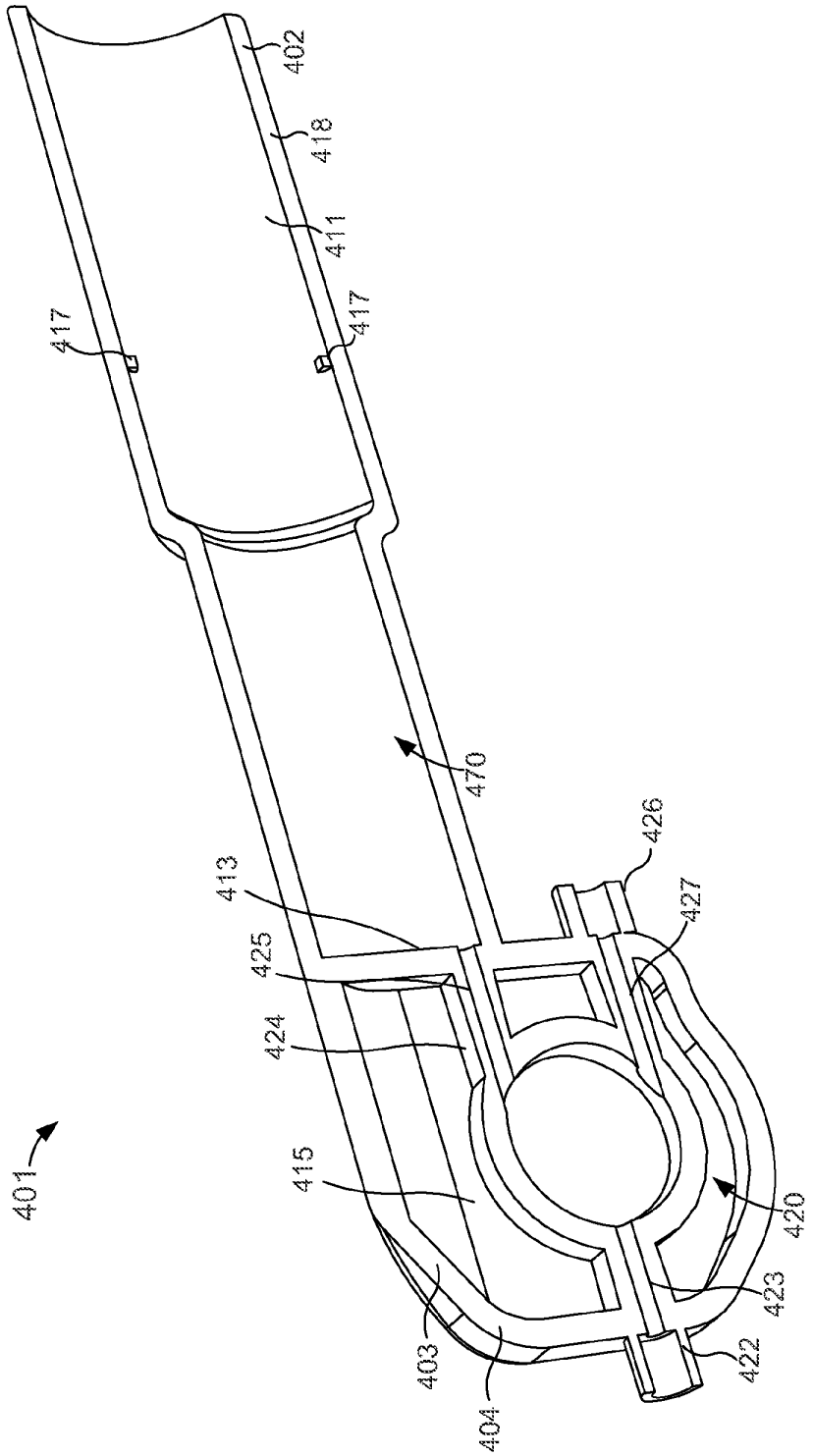

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FIG. 23

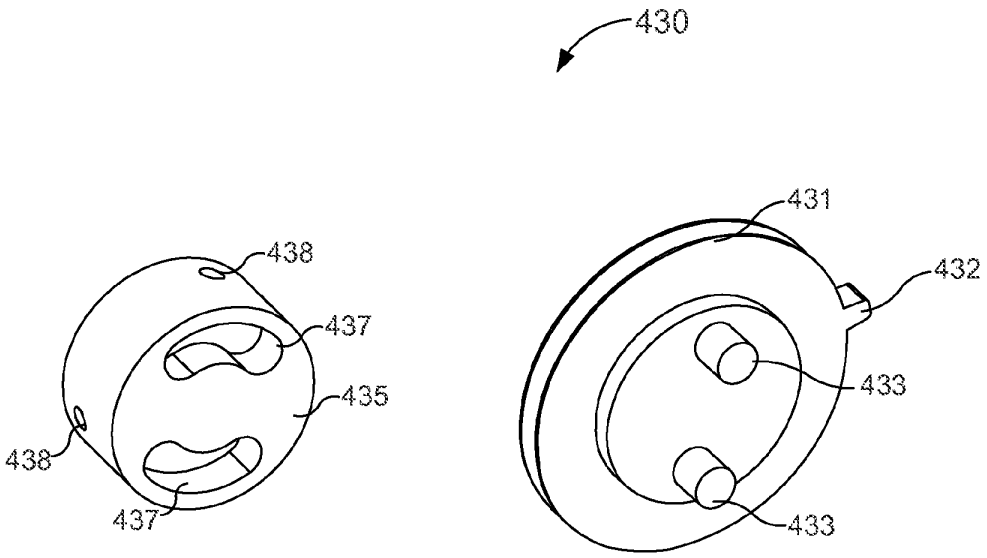


FIG. 24

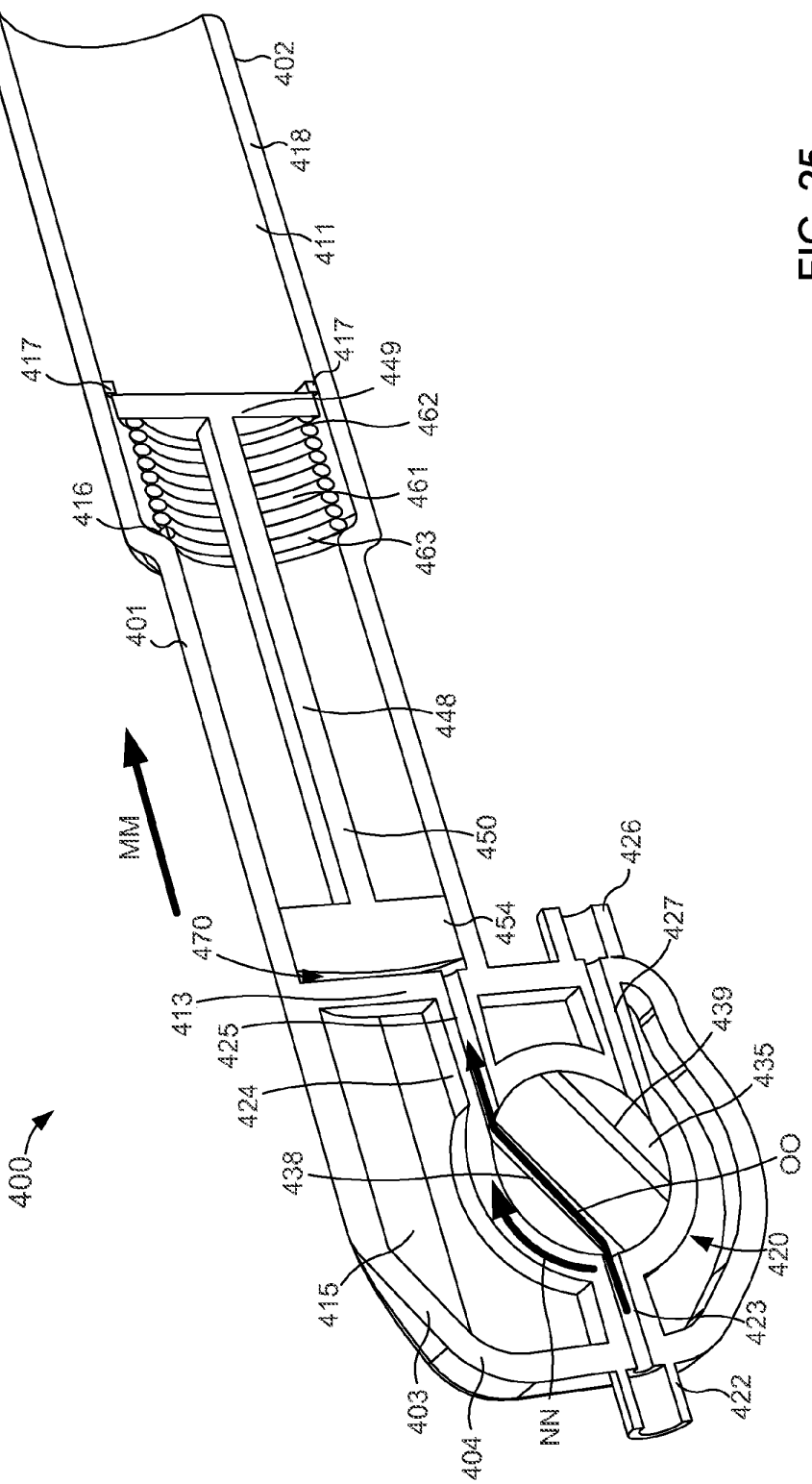

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NN
MM

FIG. 25

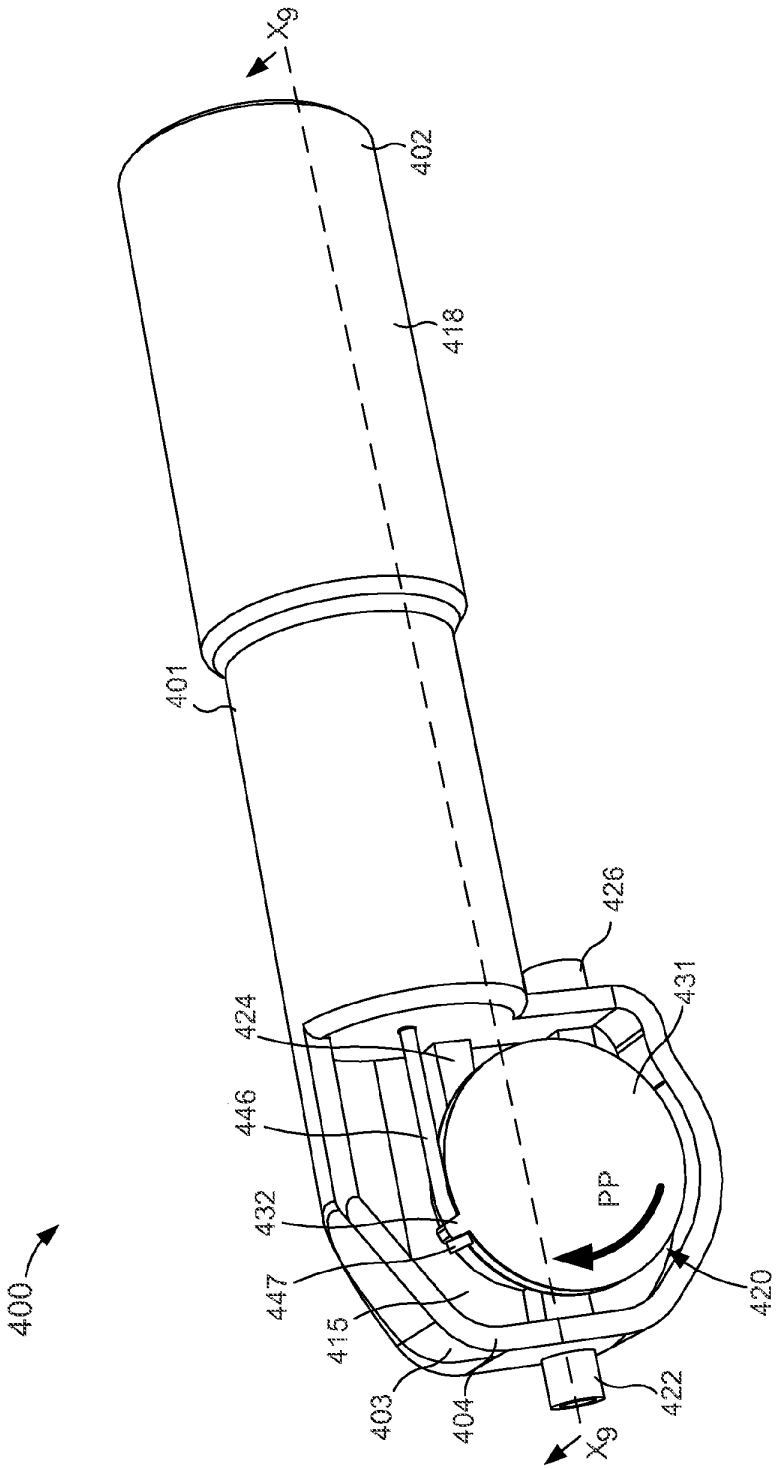

X9
402
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422
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PP
400
X9

FIG. 26

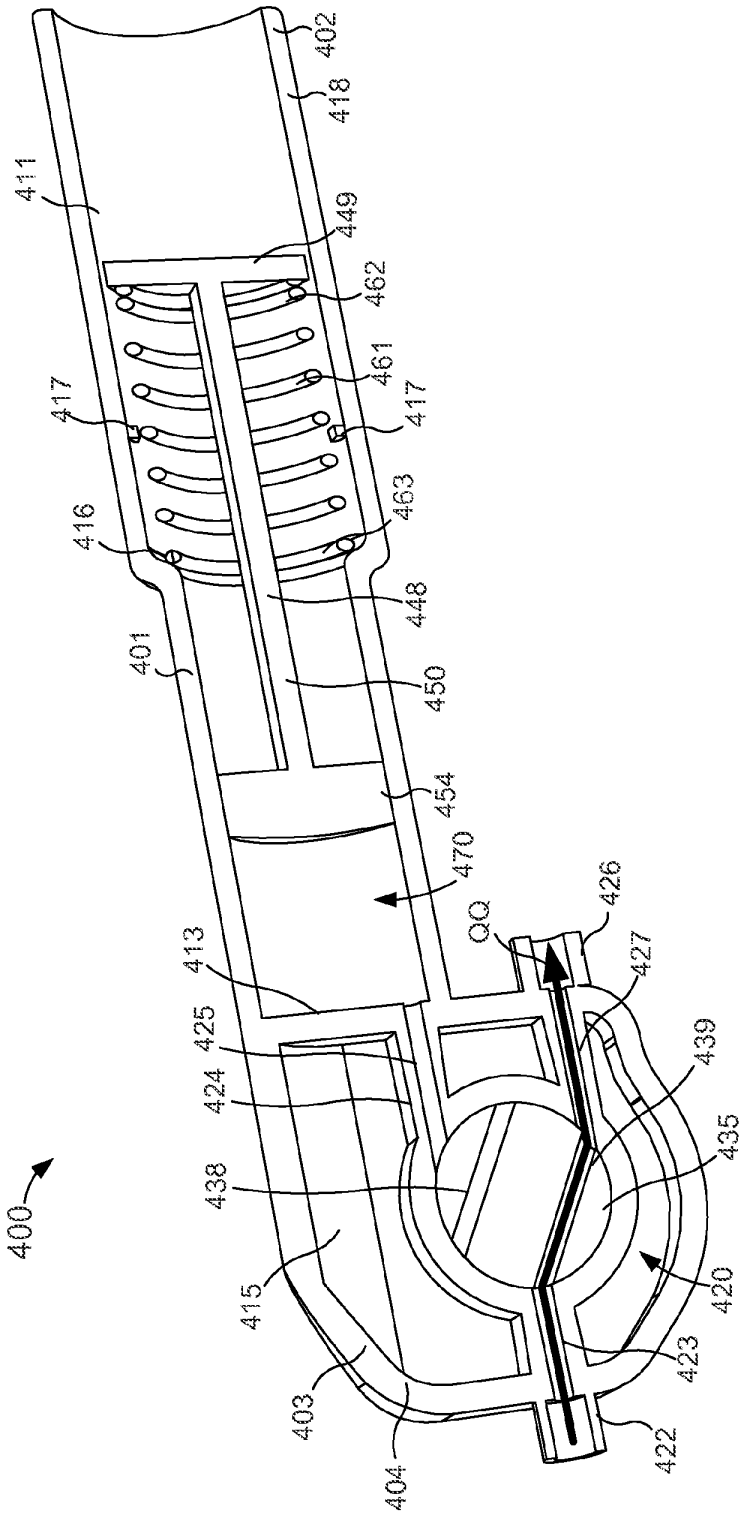

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QQ

FIG. 27

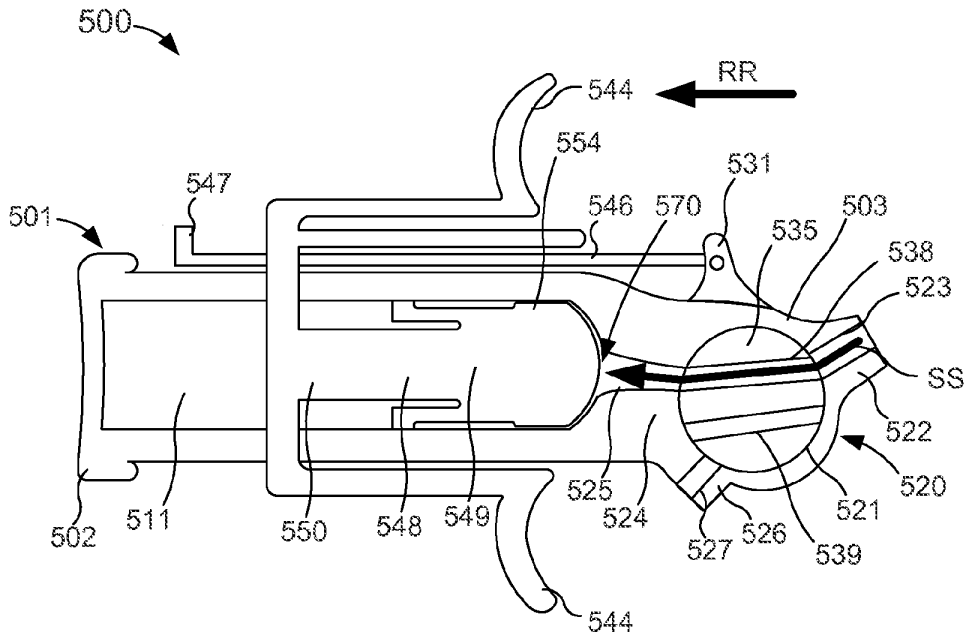

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RR
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SS
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FIG. 28

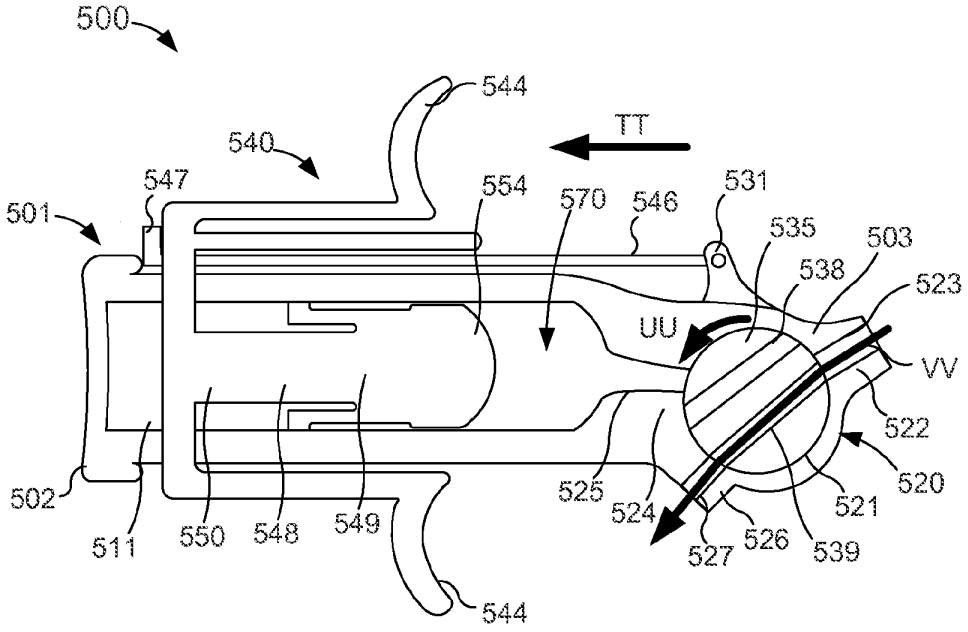

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VV
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FIG. 29

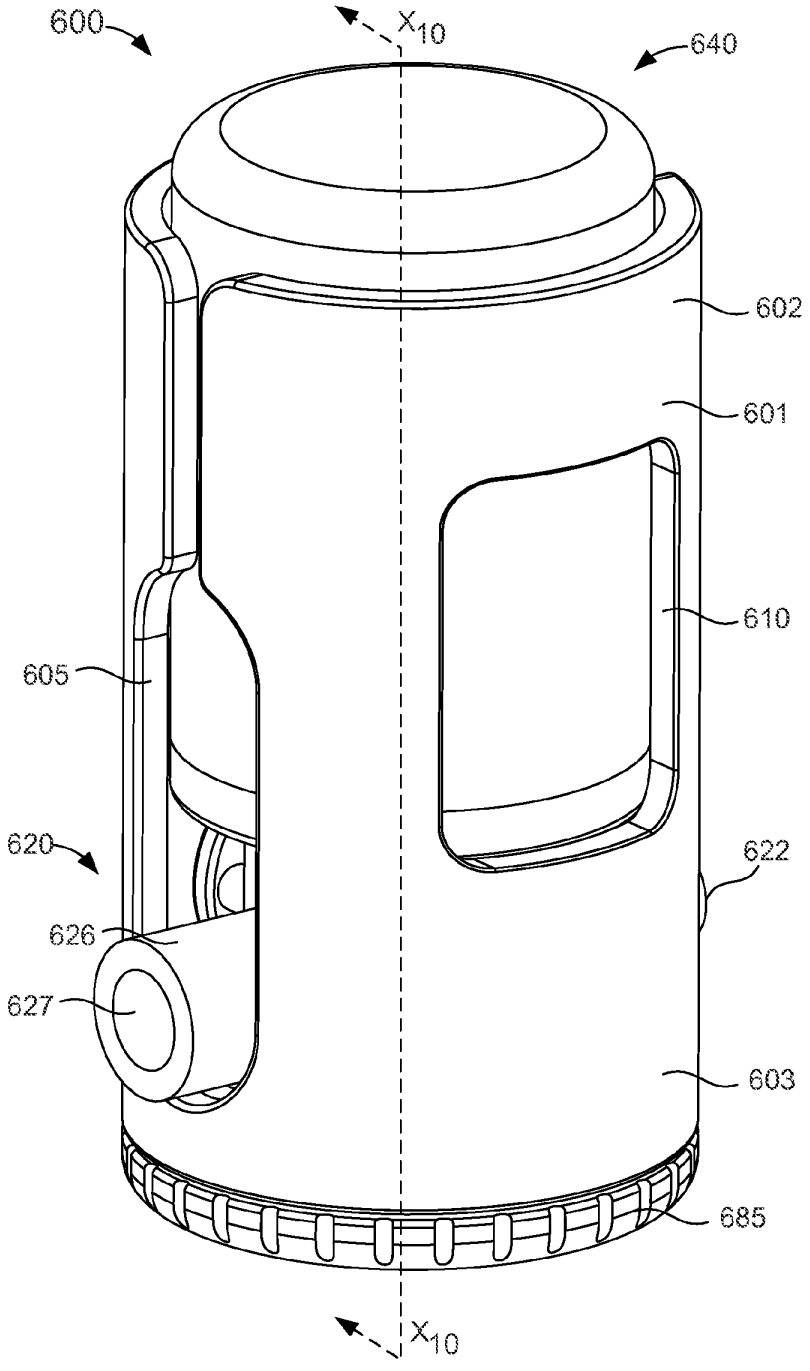


FIG. 30

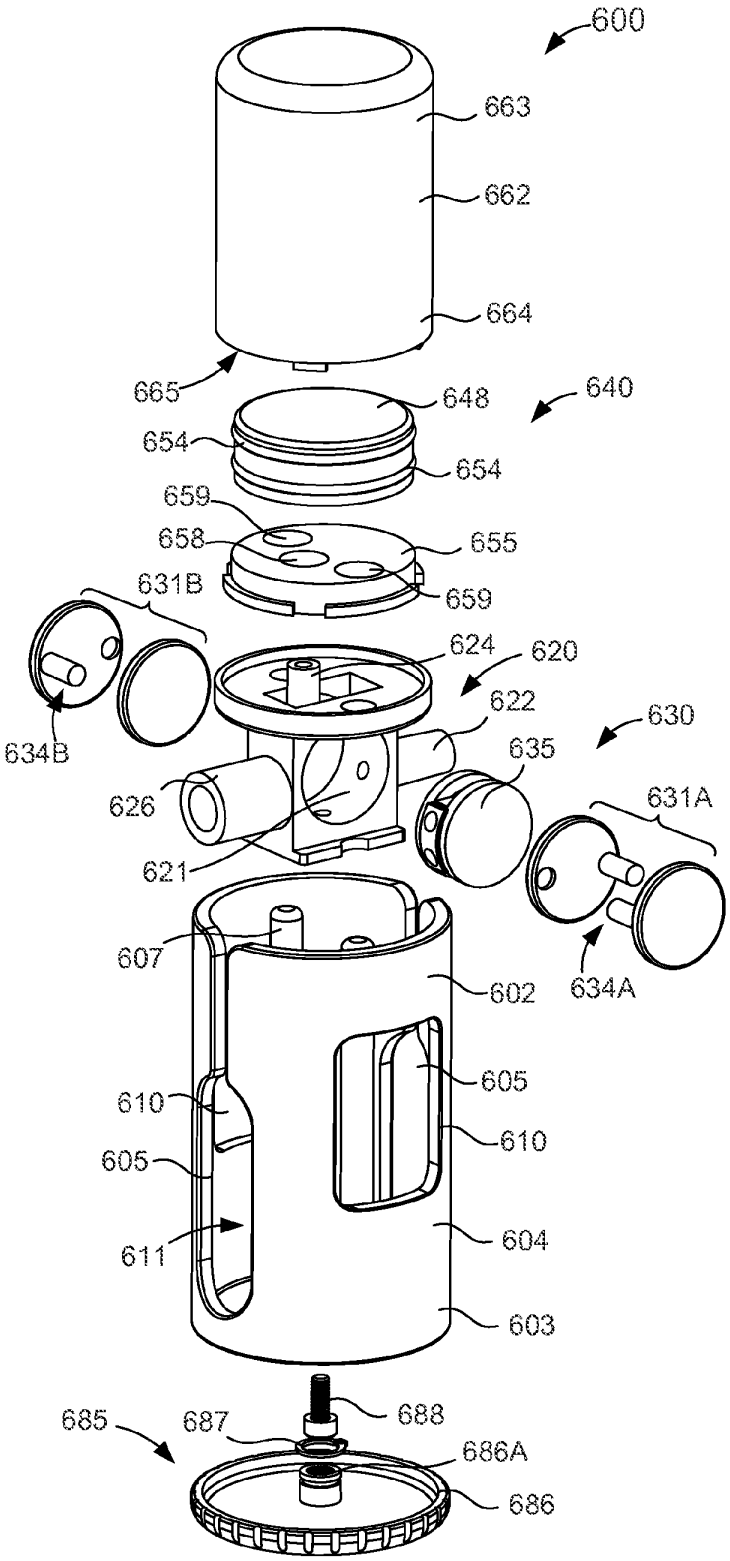

600
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659
631B
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634B
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626
631A
621
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602
634A
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604
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603
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686A
686

FIG. 31

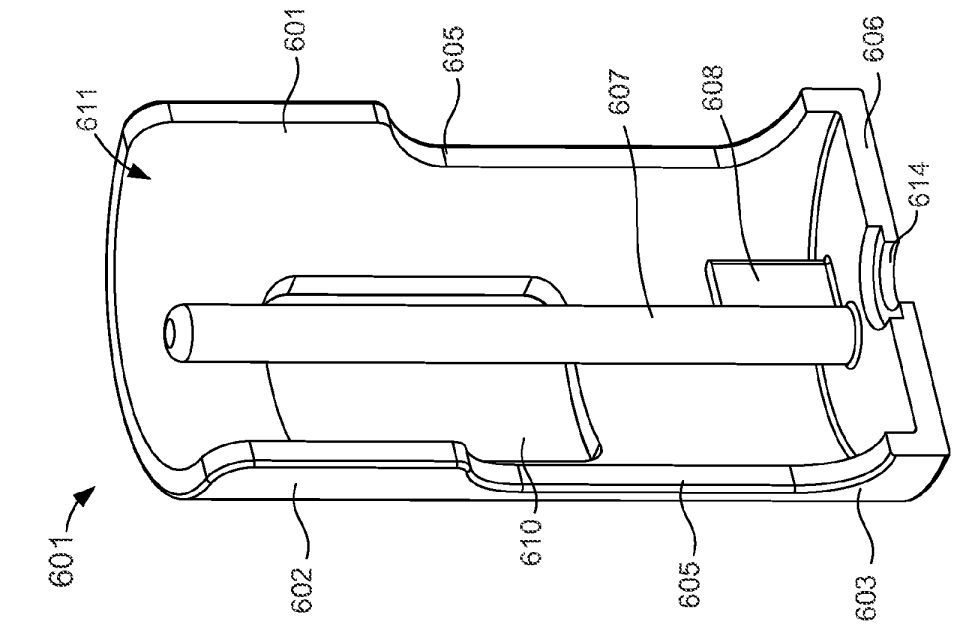

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FIG. 33

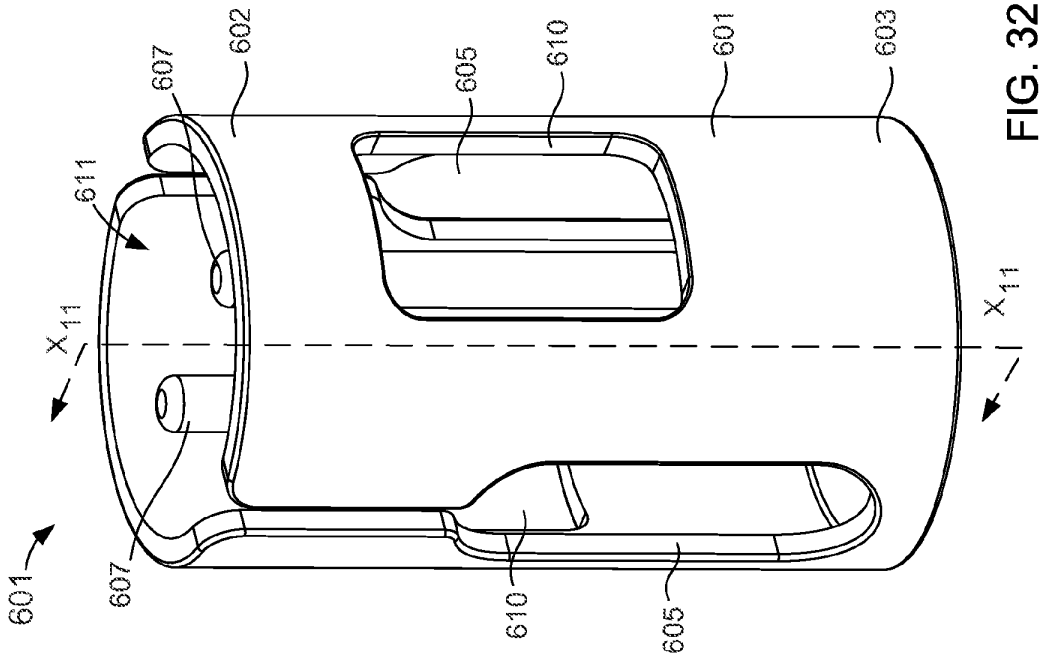

607
602
605
610
601
603
611
X11
X11
601
607
610
605

FIG. 32

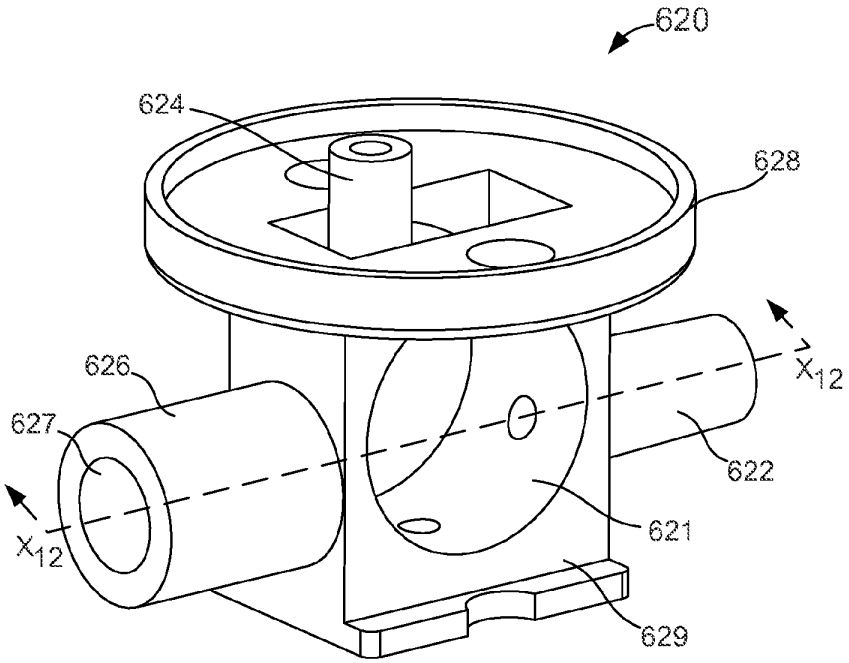

620
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628
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627
X_{12}
622
621
X_{12}
629

FIG. 34

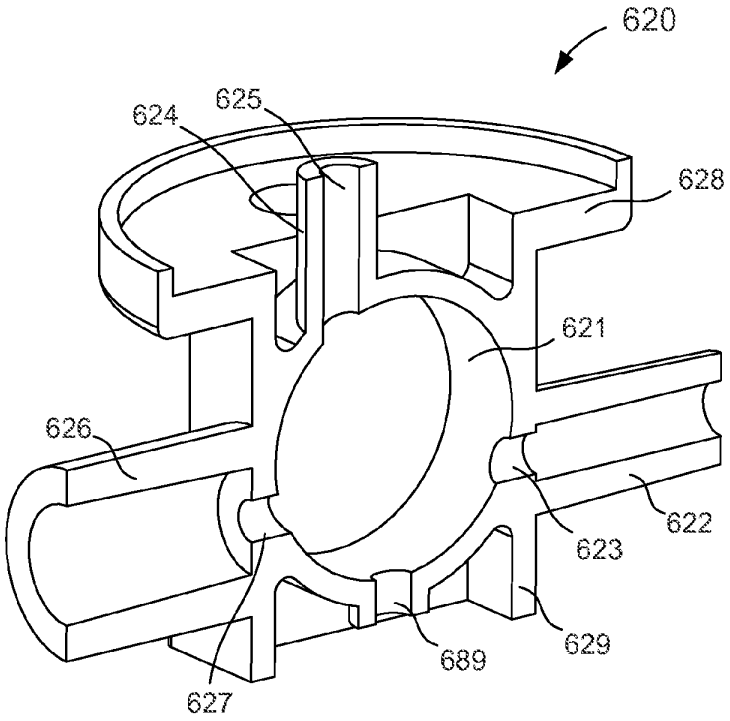

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689
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FIG. 35

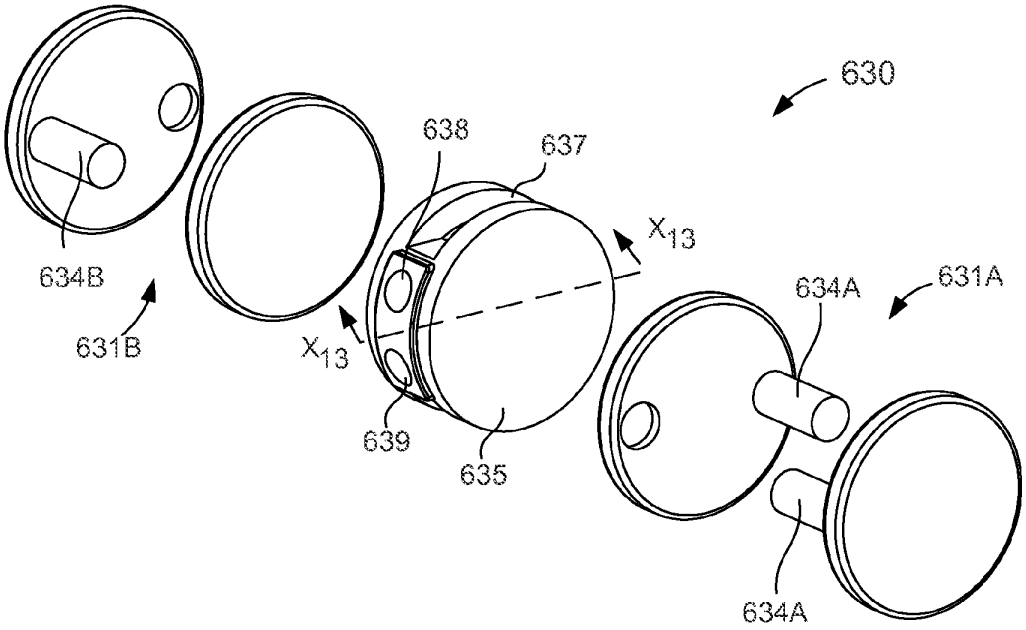

630
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637
X_{13}
634B
631B
X_{13}
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634A
631A
634A

FIG. 36

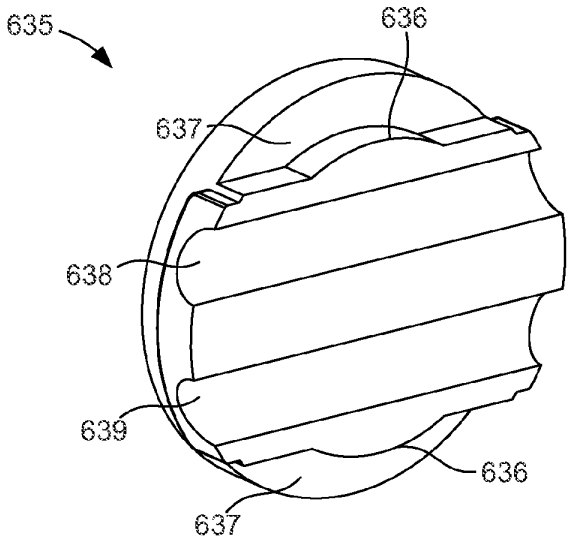

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FIG. 37

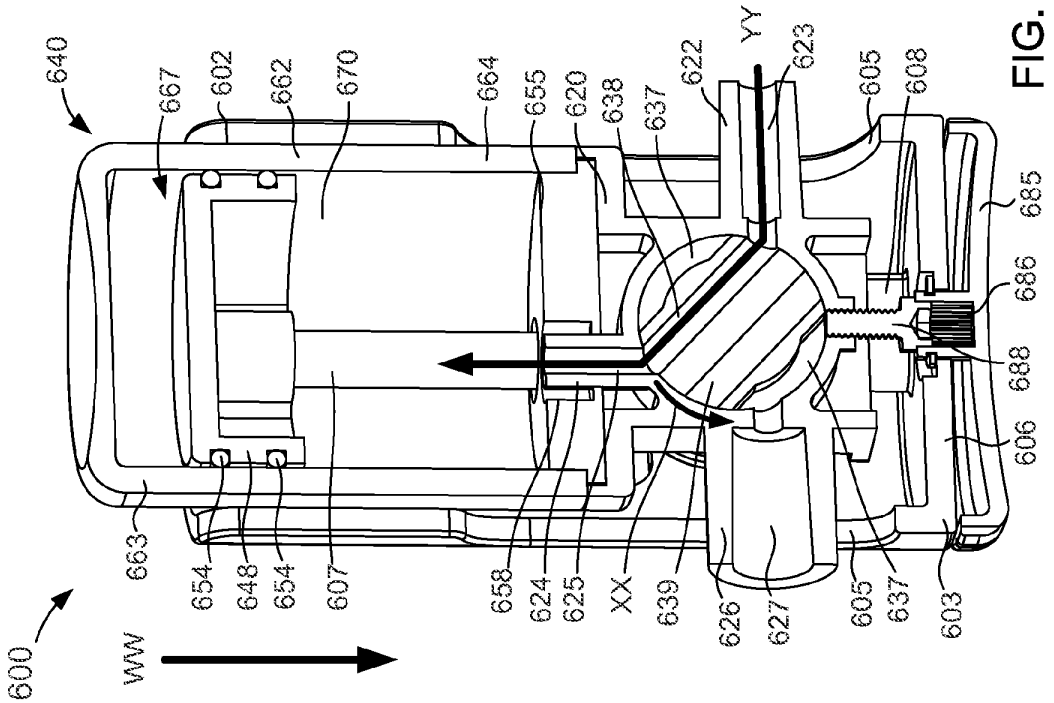

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624
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XX
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626
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605
637

FIG. 39

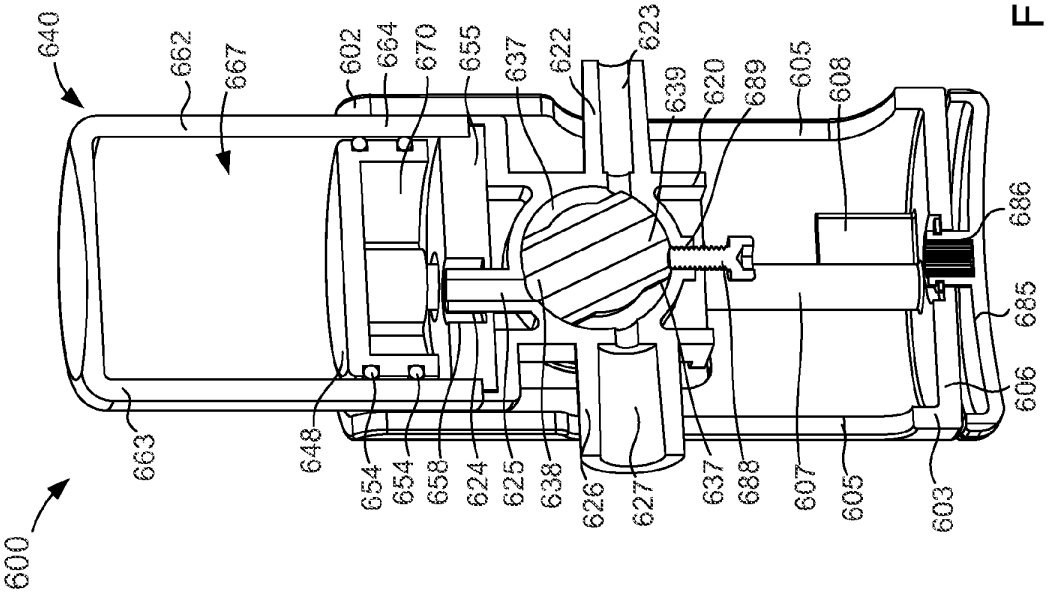

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689
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607
605

FIG. 38

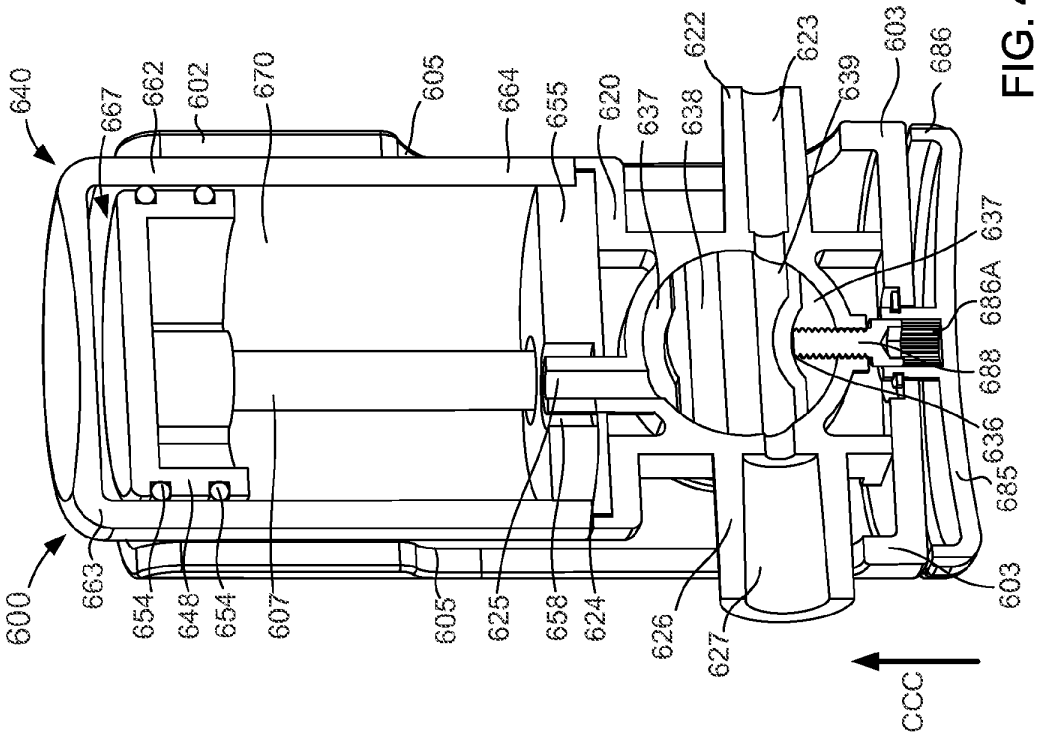

640
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637
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622
623
639
603
686
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686A
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636
685
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600
663
654
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654
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605
625
658
624
626
627
CCC

FIG. 41

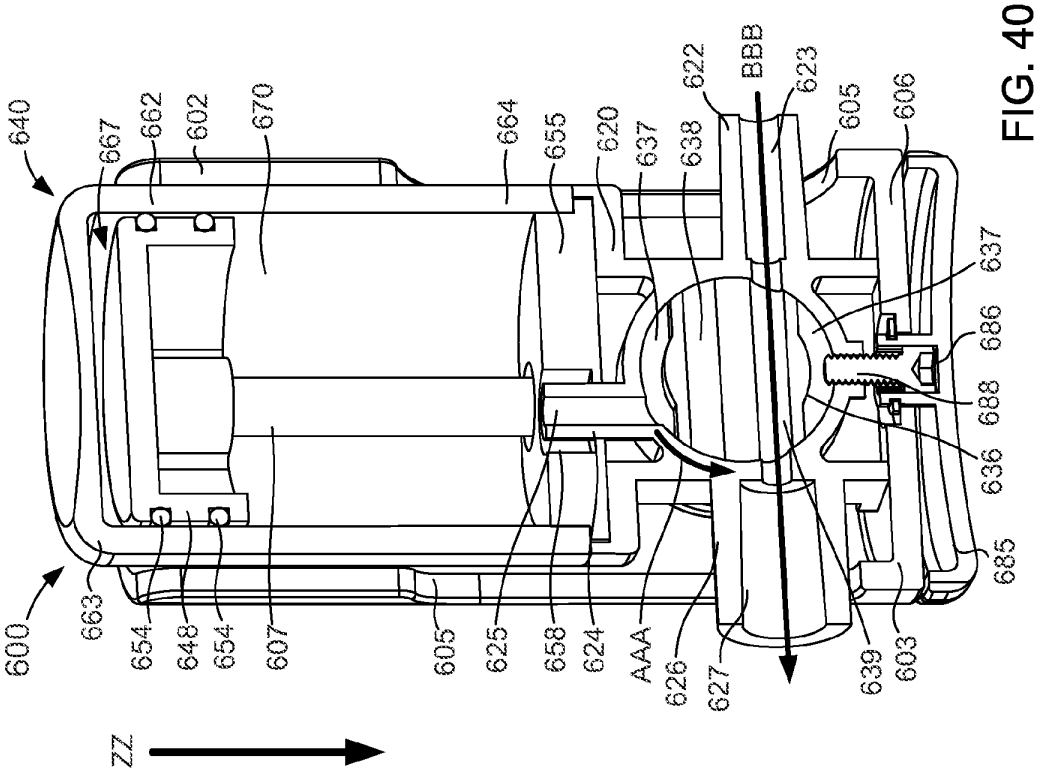

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662
602
670
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622
BBB
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605
606
637
686
688
636
685
600
663
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605
625
658
624
AAA
626
627
639
603
ZZ

FIG. 40

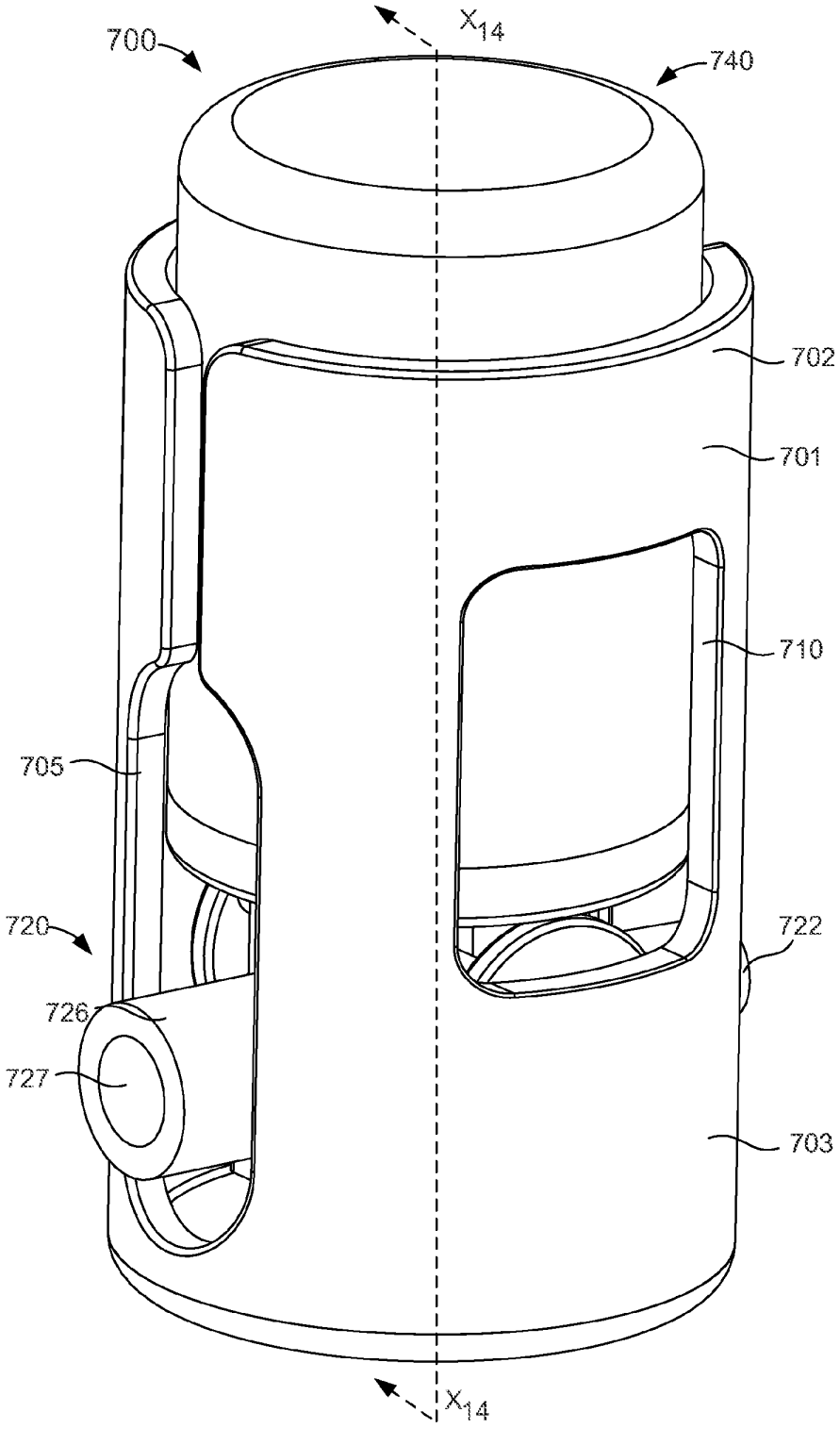


FIG. 42

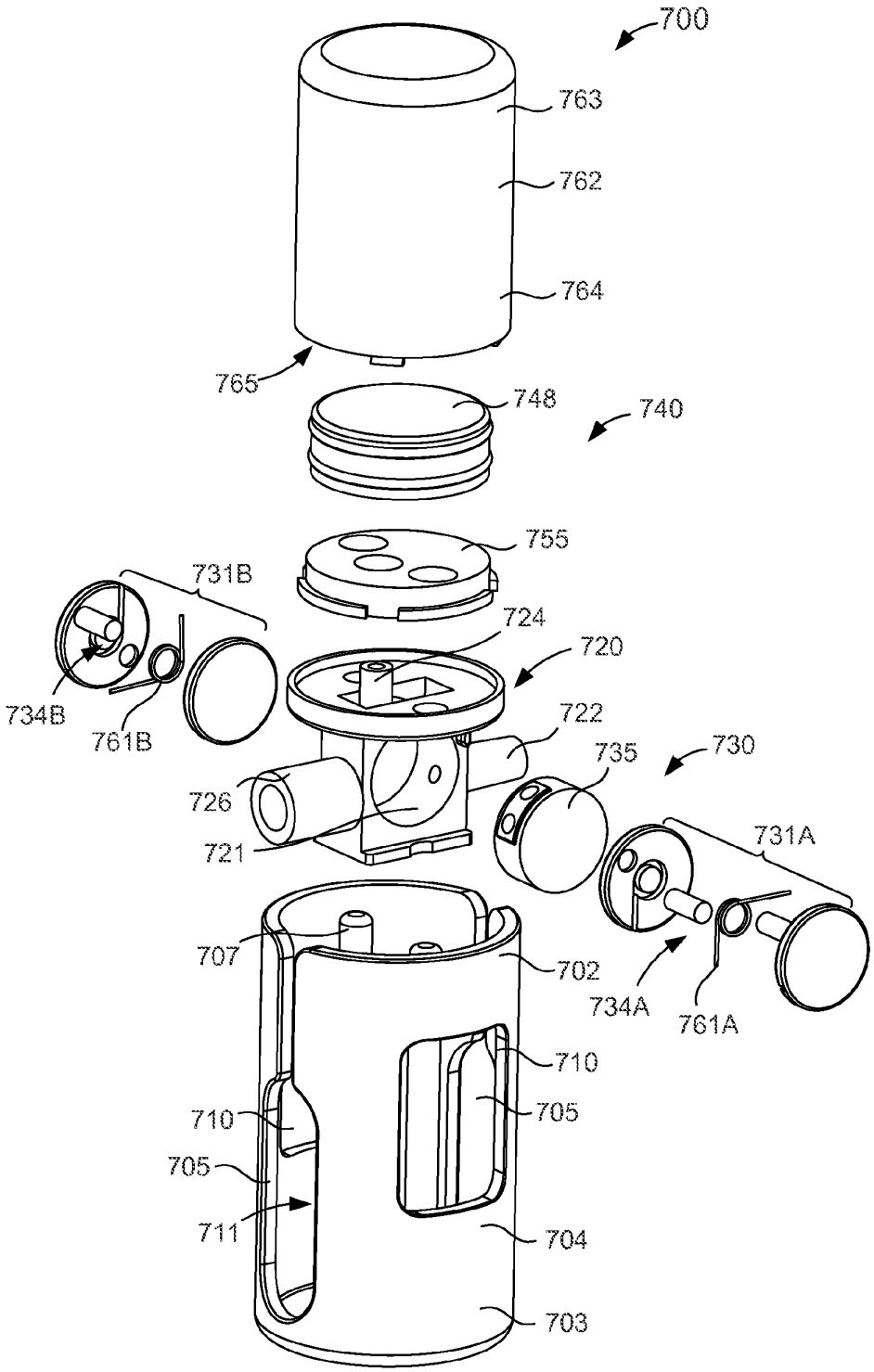

700
763
762
764
765
748
740
755
731B
724
720
734B
761B
722
735
730
726
721
731A
707
702
734A
761A
710
705
710
705
711
704
703

FIG. 43

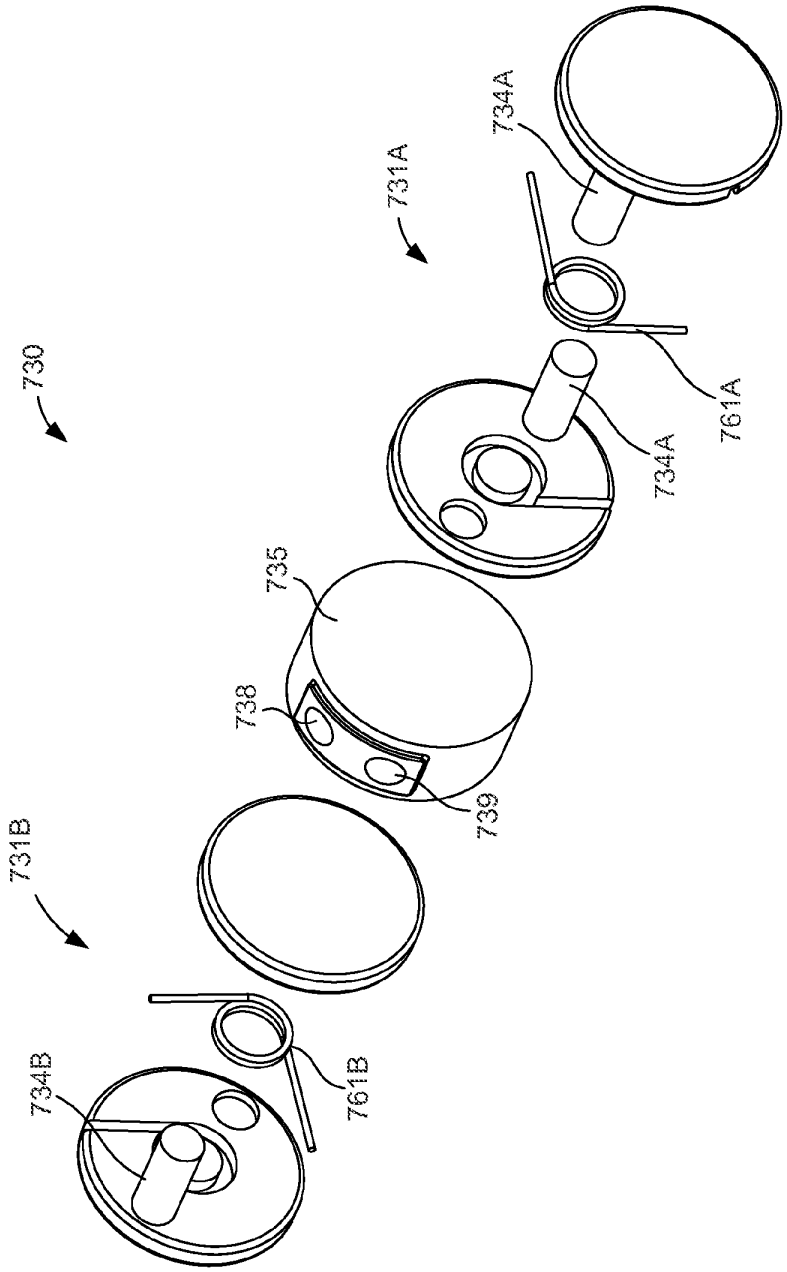


FIG. 44

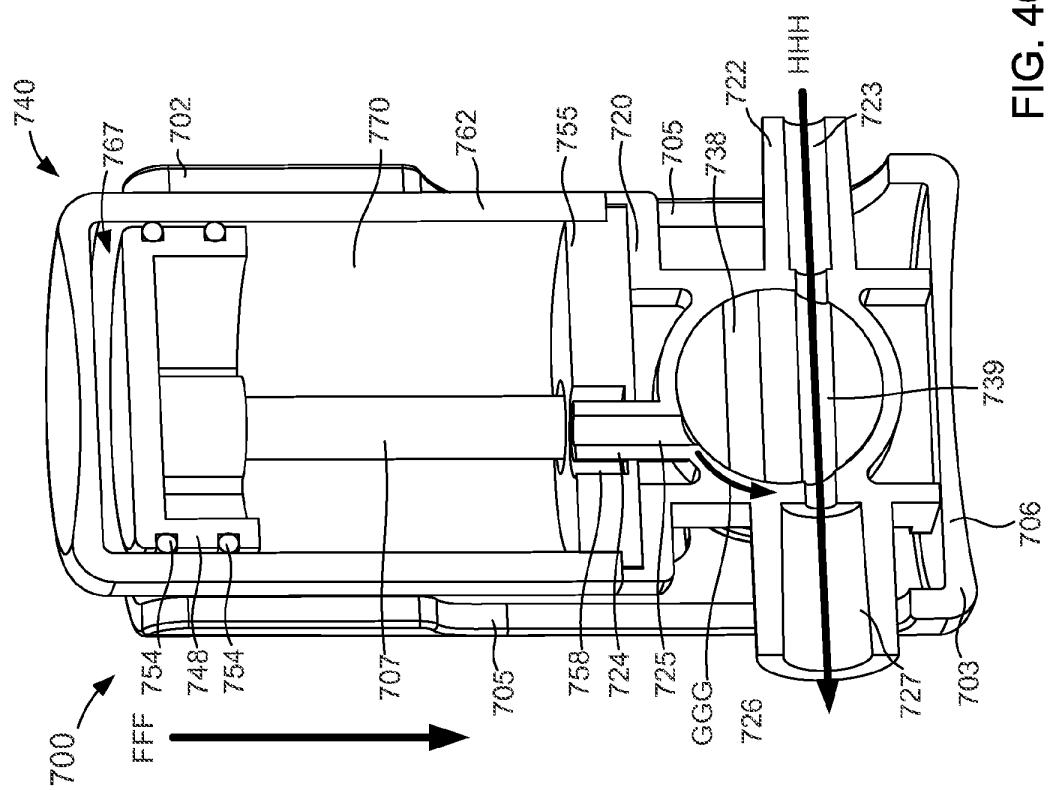

740
767
702
770
762
755
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705
738
722
HHH
723
739
706
754
748
754
707
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758
724
725
GGG
726
727
703
FFF
700

FIG. 46

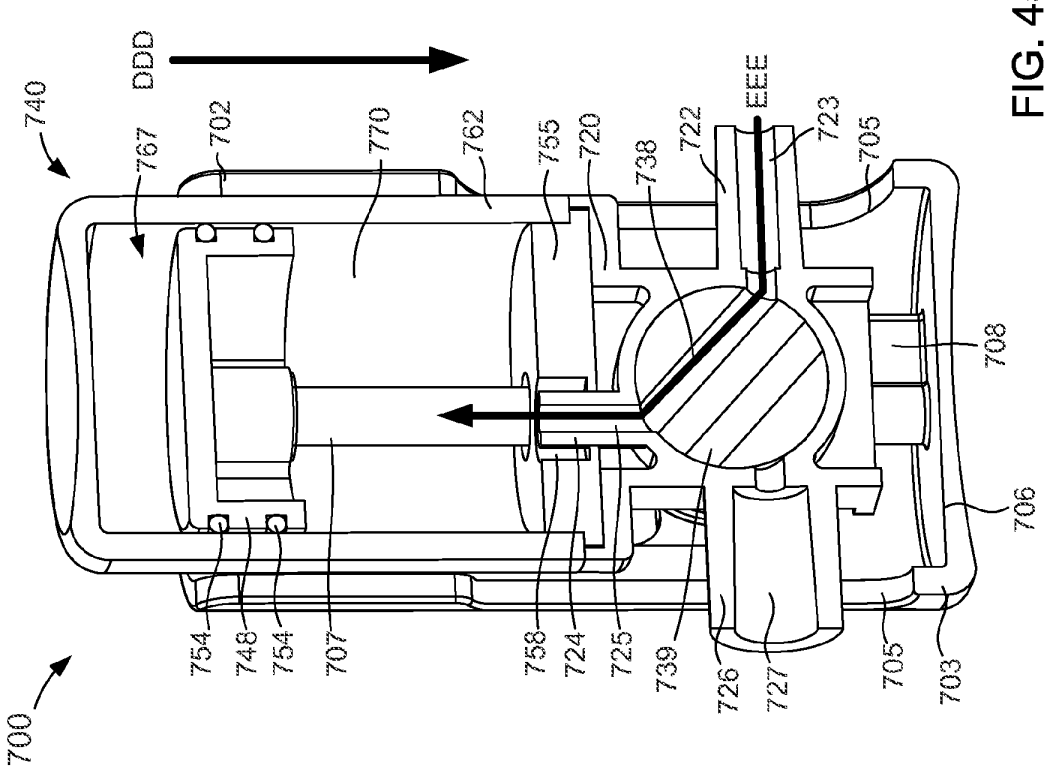

740
DDD
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702
770
762
755
720
738
722
EEE
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705
708
706
754
748
754
707
758
724
725
739
726
727
705
703
700

FIG. 45

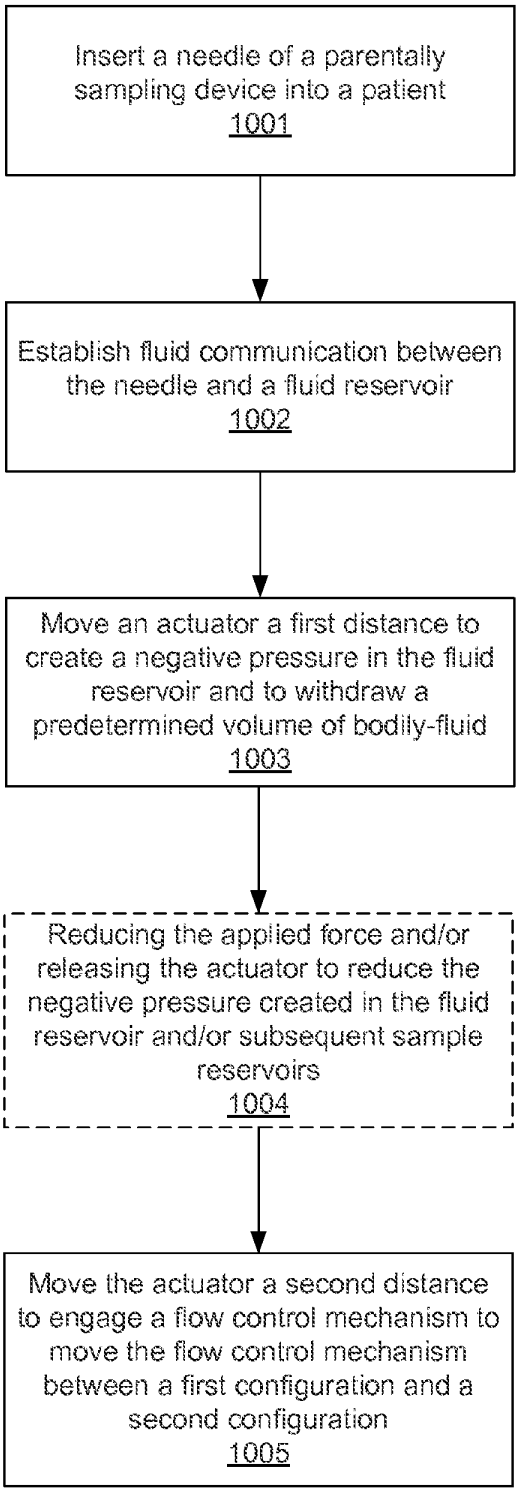

Insert a needle of a parentally sampling device into a patient
1001
Establish fluid communication between the needle and a fluid reservoir
1002
Move an actuator a first distance to create a negative pressure in the fluid reservoir and to withdraw a predetermined volume of bodily-fluid
1003
Reducing the 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.

Espacenet

Bibliographic data: EP0448795 (A2) — 1991-10-02

Compartmental body fluid collection tube.

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Abstract of EP0448795 (A2)

A compartmented body fluid specimen collection tube (10) is provided which allows the user to select a size compartment (14,16) depending upon the quantity of specimen required. Thus, the tube of the invention may be of the standard size which is much easier for the user to handle than very small tubes when taking a blood sample, but a selected size compartment (14,16) is available. The manufacturer of the tube itself may use a single moid for making tubes accommodating differing required specimen quantities, and, thereafter the vendor may select either size compartment (14,16) for imparting a vacuum and the other processing required into a final product. The invention allows the use of a single standard size laboratory equipment array for processing collected specimens of varying quantities, as well as a single standard stopper (28). Finally, reduced vacuum application or "partial draw" tubes are avoided, thus eliminating the problem of unpredictable specimen draw response because of varying atmospheric pressures at different locations of use.

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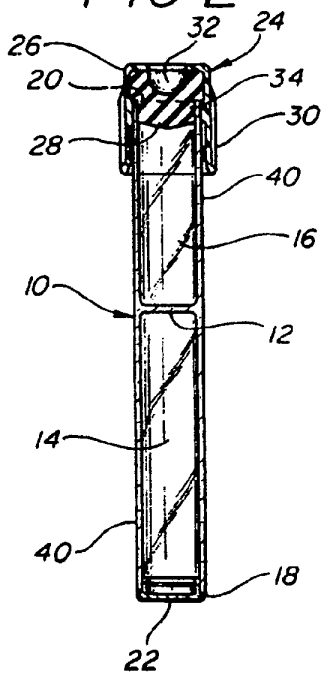
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(54) **Compartmental body fluid collection tube.**

(57) A compartmented body fluid specimen collection tube is provided which allows the user to select a size compartment depending upon the quantity of specimen required. Thus, the tube of the invention may be of the standard size which is much easier for the user to handle than very small tubes when taking a blood sample, but a selected size compartment is available. The manufacturer of the tube itself may use a single mold for making tubes accommodating differing required specimen quantities, and, thereafter the vendor may select either size compartment for imparting a vacuum and the other processing required into a final product. The invention allows the use of a single standard size laboratory equipment array for processing collected specimens of varying quantities, as well as a single standard stopper. Finally, reduced vacuum application or "partial draw" tubes are avoided, thus eliminating the problem of unpredictable specimen draw response because of varying atmospheric pressures at different locations of use.

FIG-2



EP 0 448 795 A2

BACKGROUND AND STATEMENT OF THE INVENTION

This invention relates to body fluid collection tubes for collecting a body fluid specimen from a patient for subsequent examination in a laboratory. More particularly, this invention relates to a blood collection tube for taking such specimens in which the tube has imparted thereto an internal vacuum with the vacuum being utilized for drawing the blood specimen from the vein of a patient.

Attempts have been made to overcome the problem of proliferation of a number of tubes for taking a plurality of specimens from a single venous entry into a patient. For example, Japanese Patent Application No. 62-51238, filed March 6, 1987 teaches a device in which a tube is divided axially into two chambers for taking two blood specimens simultaneously. However, there is no recognition for arranging different size compartments for taking different separate specimens of different size to accommodate subsequent laboratory testing of those specimens.

Other prior art arrangements, such as that taught in U.S. Patent 3,894,951, for example, provide for compartmentalized blood collection tubes in which the compartments have fluid connections for subsequent separation of a single blood sample into separate components.

In taking such specimens, differing quantities or volumes of specimens are required for certain applications. For this reason, larger and smaller tubes are manufactured for this purpose. As an alternative to making larger and smaller tubes, so-called "partial draw" tubes are provided in which the vacuum imparted to the tube is varied in order to accommodate differing quantities of specimen as required. All of these variations increase the cost of collecting blood specimens, and when it is understood that literally billions of such tubes are used and discarded after a single use each year the costs become substantial for medical applications.

This invention overcomes this problem by using a conventionally sized tube of, for example, 6cc in volume and incorporates an integral divider substantially centrally of the length of the tube to provide two compartments of differing size. Such compartments may be, for example, 2cc and 3cc. Thus, the manufacturer, rather than having to use two separate molds and two separate production lines, may manufacture a single tube having a selection of a 2cc and a 3cc compartment or chamber. Thereafter, the user or vendor may utilize or select one of the sizes of compartment and impart a vacuum thereto and place a stopper in the open end of the compartment size selected. The remaining compartment or chamber not being utilized for this particular series of tubes has a plug for closing the open end of the non-utilized chamber or compartment.

Conventional blood collection tubes have only one chamber, and volume in those conventional tubes is varied by using either larger or smaller diameter tubes, taller or shorter length tubes or varying the degree of vacuum imparted. As will be understood by practitioners-in-the-art, larger and smaller diameter tubes require specific dimensioned stoppers for accommodating those various sizes. Moreover, taller and shorter tubes require different packaging to accommodate tube length. If an accommodation is made to utilizing only a single size tube and imparting a partial vacuum for subsequent use in which only a small quantity of specimen is required in relatively large tubes, there is inconsistent draw over different areas of use because of differing atmospheric pressure gradients.

Finally, the users of tubes of different length and diameter must have varying size equipment, such as centrifuges, tube racks and like supporting arrangements to accommodate the varying sizes of tubes being utilized for collecting differing quantities of body fluid specimens for different applications.

With this invention, by contrast, a single size tube, as noted above is utilized. For this reason, the user, in the sometimes tense environment of taking a blood specimen from an individual, has a relatively large tube for handling during the collection activity Nevertheless the tube has a smaller compartment; for accommodating the actual size specimen required. Moreover, because only a single size tube relative to diameter is being utilized with the invention here, a single stopper size is required rather than a plurality of stopper sizes of differing diameters to accommodate differing diametered tubes. This reduces manufacturing requirements as well as storage requirements for such a variety of stopper sizes.

Moreover, because of the large size tubes having small compartmentalized areas, no "partial draw" vacuum applications are required. This eliminates the problem of inconsistency depending upon the atmospheric pressure gradients over many areas of use of such tubes. Finally, because of the uniformity of size of the tube, the hospital or clinical laboratory only needs to have one size equipment necessary for handling the tubes of a standard size.

A further feature of the invention may be the use of both compartments of a single tube by the phlebotomist. That is, the vendor or manufacturer of the tubes may, for example, impart vacuum to both a 3cc and a 2cc compartment or chamber in a single tube and place stoppers for sealing and

maintaining the vacuum. Thereafter, the phlebotomist, in requiring two separate blood sample volumes for different tests subsequently can first draw blood into one chamber followed by inversion of the tube and collection of blood into the second chamber. Two blood samples would then be contained in a single tube for subsequent examination in the clinical laboratory, and with only one venous entry.

Other objects and advantages of this invention will be apparent from the following description, the accompanying drawings and the appended claims.

DESCRIPTION OF THE DRAWINGS

Fig. 1 is longitudinal sectional view of the compartmentalized blood collection tube of the invention;

Fig. 2 is a longitudinal sectional view of one embodiment of the invention wherein a vacuum has been imparted to the smaller chamber or compartment of the tube of the invention and showing the sealing stopper arrangement for such a tube, together with a plug for the unused chamber;

Fig. 3 is a longitudinal sectional view of the tube of the invention reversed in its application from that shown in Fig. 2;

Fig. 4 is an enlarged partial cross-sectional view of one open end of the tube of the invention showing the mating configuration of a sealing plug applied to the open end for closing off the non-utilized chamber or compartment of the tube of the invention;

Fig. 5 is a longitudinal sectional view of a blood sample tube holder for taking a blood sample from a vein of a patient with the tube of the invention inserted therein; and

Fig. 6 is a longitudinal sectional view of a tube similar to that shown in Fig. 1, but both chambers being closed with a stopper closure for use in evacuating two chambers for collecting two specimens sequentially.

DETAILED DESCRIPTION OF THE INVENTION

Referring to the drawings in which like reference characters refer to like parts throughout the several views thereof, Fig. 1 illustrates the invention in the form of a conventionally sized blood collection tube compartmentalized in its formation to provide two chambers or compartments of differing size to accommodate differing blood sample requirements.

In Fig. 1, the device 10 is an elongated tube with walls 40 and having open ends 18, 20 at each end thereof. As can be seen in Fig. 1, tube 10 is divided by a wall 12 into compartments or chambers 14 and 16. Also, as will be seen in Fig. 1, chamber 14 is larger than chamber 16. For example, in a 6cc tube, chamber 14 may be, for example, 3cc in volume while chamber 16 may be 2cc in volume.

It will be understood that the volume amounts may be varied as use requirements dictate. Tube 10 may be comprised of a thermoplastic resin material, for example, formed in a mold to provide wall 12 integrally joined to wall 40 of tube 10.

Referring now to Fig. 2, tube 10 is shown in a prepared form for use by a vendor. In this case, the smaller dimensioned chamber 16 has had, for example, a vacuum applied thereto with a subsequent insertion of a stopper assembly 24 for maintaining the vacuum in chamber 16. The assembly 24 includes a rubber stopper for closing the open end, 20 of the tube, assembly 10. That is, the outer surface of lower portion of stopper 28 seals against the internal surface of walls 40 of the upper end of tube 10. The assembly 24 includes a plastic cap 26 connected to and surrounding elastomer stopper 28. This serves to accommodate removal of stopper 28 in a simple fashion, when required, to obtain access to the collected sample in chamber 16.

Stopper 28 includes a well 32 formed in the top surface thereof which has the purpose of reducing the vertical extent of stopper 28 in the center portion thereof to provide a diaphragm 34 of vertically smaller dimension through stopper 28 for receiving a needle such as needle 52 and the point 54 thereof, as shown in Fig. 5. The plastic portion 26 of stopper 24 assembly includes outer ridges 34 to provide an easier grip of the assembly 24 for removal thereof from the evacuated chamber 16, when required.

Referring to Fig. 4, the open end 18 of chamber 14, which in this case is not being utilized for fluid collection includes a plug 22 for stabilizing the open end 18 of the tube assembly 10 for subsequent use of the tube or for storing the tube prior to use.

In Fig. 4, an enlarged view of the open end 18 or 20 is shown to accommodate the snap-fit arrangement of plug 22 in the open end 18 or 20 of chamber 14 or 16, as the case may be, when they are not being utilized in a particular tube 10 assembly. That is, the lower end of wall 40 may include an annular indentation 36 for receiving in snap-fit engagement an annular abutment, 38 on plug 22.

Referring now to Fig. 3, a tube 10 is shown reversed from the Fig. 2 showing for accommodating use of the 3cc and/or larger compartment 14 as desired by the user. In this case, stopper assembly 24 closes the open end 18 rather than 20, while the open end 20 is closed with a plug 22. It will be understood by practitioners-in-the-art that both compartments or chambers 14, 16 may be utilized in a single tube 10 by imparting a vacuum to both chambers and using a stopper closure assembly

24 for closing both open ends 18 and 20. In such cases, a plug 22 is not utilized.

Such an arrangement is shown in Fig. 6 wherein a tube 60 similar to tube 10 is shown with chambers 64, 66 divided by wall 62. Tube 60 includes two open ends 68 and 70. In this case, a stopper assembly 24 is applied to both open ends after application of vacuum to chambers 64, 68, respectively. As discussed above, in such an application, the user collects two different volumes of specimen from a patient as required for subsequent testing purposes.

In use, the assembly 10 of the invention is inserted into a blood collection needle holder such as 42 shown in Fig. 5. Holders 42, for example, include at the closed end thereof a hub 46 with internal screw threads 48 for accommodating the screw threads of a needle holder hub 50. Thus, a plurality of needle holder hubs 50 may be, sequentially, screwed into hub 46 of needle holder 42 for repeated use. The needle 52 includes a sharpened end 56 which is inserted into the vein of a patient for collecting a blood Specimen.

Subsequent to insertion of the needle 56 into the vein of a patient, the laboratory technician, doctor or nurse inserts the tube assembly 10 into the blood collection holder 42 at the open end 43 thereof. In doing so, the technician holds onto the holder 42 utilizing the flange 44. Subsequently, the tube 10 is moved forward toward the closed end of the holder 42 until such time as the negative pressure needle point 54 passes through stopper 28. When this happens, access to the vacuum in chamber 16 takes place and the vacuum draws blood from the patient's vein through the needle 52 into chamber 16.

As will be understood by practitioners-in-the-art, the smaller chamber 16 may be, for example, of a volume of 2ccs which is all that is required for certain subsequent examinations of the specimen in the lab. A tube such as tube 60 shown in Fig. 6 may be used in holder 42 instead of tube 10. With such an arrangement, the double-ended needle assembly would include a sealing valve sleeve well known in the art so that the tube 60 may be pulled off needle point 54, and reversed for inserting the needle point 54 into the subsequent stopper 28 without blood loss, for collecting a second blood sample in chamber 66, for example.

Alternatively, the technician may use a standard size blood collection container and collect a subsequent larger blood sample, as required from the single insertion of point 56 of needle 52 in the patient's vein all as will be understood by the practitioner-in-the-art.

The blood collection tube of the invention may be comprised, preferably, from a clear molded thermoplastic material such as polyethylene, for example, or glass. Other materials which may be used, as will be appreciated by practitioners-in-the-art include various other thermoplastics such as polypropylene, polyethylene terephthalate, and polyvinyl chloride.

The evacuated chambers utilized for collection in the device of the invention here may have incorporated therein materials for reaction with the specimen being collected for providing a proper response to the collected specimen for subsequent examination in the clinical laboratory. The stopper may be comprised of an elastomer appropriate for providing the sealing required to maintain the imparted vacuum in the chamber selected for subsequent use by the laboratory technician. The plastic cover portion 26 of stopper assembly 24 may be comprised of polyethylene or other thermoplastic which may be molded into the proper shape for the assembly of the invention.

Whereas, as discussed above, specific embodiments of associated stoppers and caps have been shown, it should be understood that it is within the purview of this invention to provide other forms of closures for blood collection tubes of the kind discussed herein.

It will be understood that the invention here is most appropriate for medical applications because of the substantial reduced cost in accommodating a variety of different requirements for a body fluid specimen collection, and for reducing the number of molds required for providing an assembly which is nevertheless, much easier to handle than the miniaturized collection tubes presently being utilized for small volume specimen collection. Moreover, the arrangement herein eliminates the need for the application of "partial draw" tubes and the inconsistency apparent with the use of such partial draw tubes.

While the forms of apparatus herein described constitute preferred embodiments of the invention, it is to be understood that the invention is not limited to these precise forms of apparatus and that changes may be made therein without departing from the scope of the invention which is defined in the appended claims.

Claims

1. A blood collection tube; comprising
   (a) a tube body;
   (b) said tube body comprised of walls formed as a cylinder to define a tube body chamber;
   (c) said tube body chamber having a first open end at one end of said tube body chamber and a second open end at the end of said tube body chamber opposite said first open end;

(d) a divider wall positioned between said first and second open ends;
(e) said divider wall dividing said tube body chamber into a first and a second compartment; and
(f) said divider wall being formed integrally as one piece with said cylindrical tube body walls.

2. The blood collection tube of Claim 1, further comprising
(a) said first and second compartments being of different volume capacity.

3. The blood collection tube of Claim 1 further comprising
(a) a stopper closing one of said first and second open ends; and
(b) a plug closing the other of said open ends not closed by said stopper.

4. The blood collection tube of Claim 3, further comprising
(a) said compartment with the open end closed by said stopper being evacuated.

5. The blood collection tube of Claim 3, further comprising said stopper being comprised of
(a) a first elastomeric portion inserted into said open end in sealing engagement therewith;
(b) a plastic portion fitted over and surrounding said elastomeric portion;
(c) said plastic portion encompassing said tubular walls adjacent said open end into which said stopper is inserted;
(d) the top of said plastic portion having an opening adjacent the axis thereof for providing needle access to said elastomeric portion; and
(e) cooperating abutment means on said elastomeric portion and said plastic portion for holding said elastomeric portion and said plastic portion together.

6. The blood collection tube of Claim 3, further comprising
(a) said tube walls and said divider wall are comprised of a material selected from the group consisting of polyethylene, polypropylene, polyethylene terephthalate, polyvinyl chloride and glass.

7. A blood collection tube; comprising
(a) a tube body;
(b) said tube body comprised of walls formed as a cylinder to define a tube body chamber;
(c) said tube body chamber having a first open end at one end of said tube body chamber and a second open end at the end of said tube body chamber opposite said first open end;
(d) a divider wall positioned between said first and second open ends;
(e) said divider wall dividing said tube body chamber into a first and a second compartment;
(f) said divider wall being formed integrally as one piece with said cylindrical tube body walls;
(g) said first and second compartments being of different volume capacity;
(h) a first stopper closing said first open end; and
(i) a second stopper closing said second open end.

8. The blood collection tube of Claim 7, further comprising
(a) both said first and said second compartments being evacuated.

9. The blood collection tube of Claim 7, further comprising each of said first and second stoppers comprised of
(a) a first elastomeric portion inserted into said open end in sealing engagement therewith;
(b) a plastic portion fitted over and surrounding said elastomeric portion;
(c) said plastic portion encompassing said tubular walls adjacent said open end into which said stopper is inserted;
(d) the top of said plastic portion having an opening adjacent the axis thereof for providing needle access to said elastomeric portion; and
(e) cooperating abutment means on said elastomeric portion and said plastic portion for holding said elastomeric portion and said plastic portion together.

10. The blood collection tube of Claim 7, further comprising
(a) said tube walls and said divider wall are comprised of a material selected from the group consisting of polyethylene, polypropylene, polyethylene terephthalate, polyvinyl chloride and glass..

FIG-1

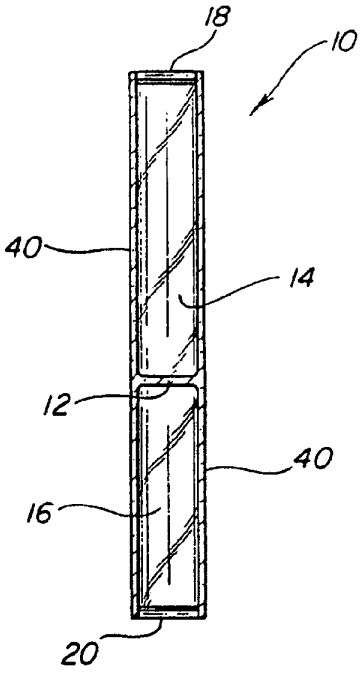


FIG-2

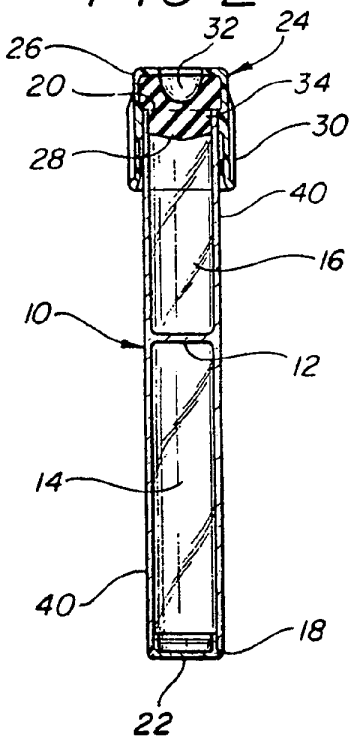


FIG-3

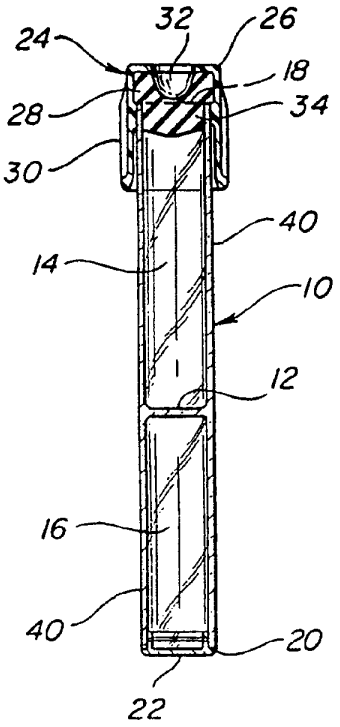


FIG-4

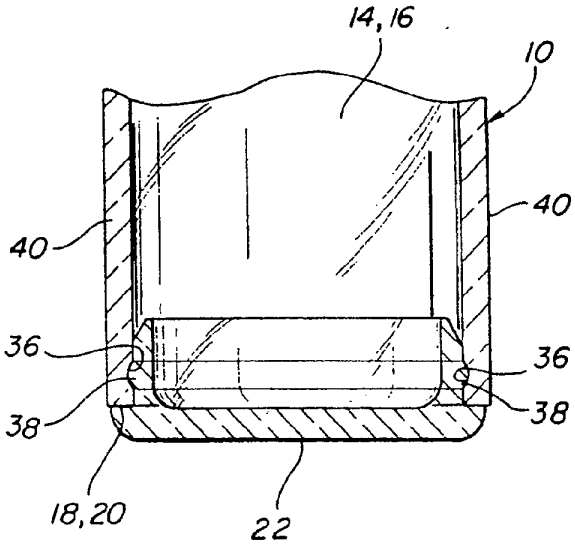


FIG-5

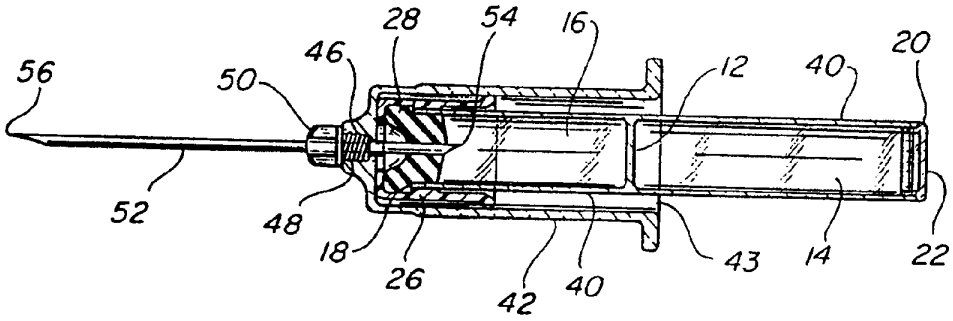
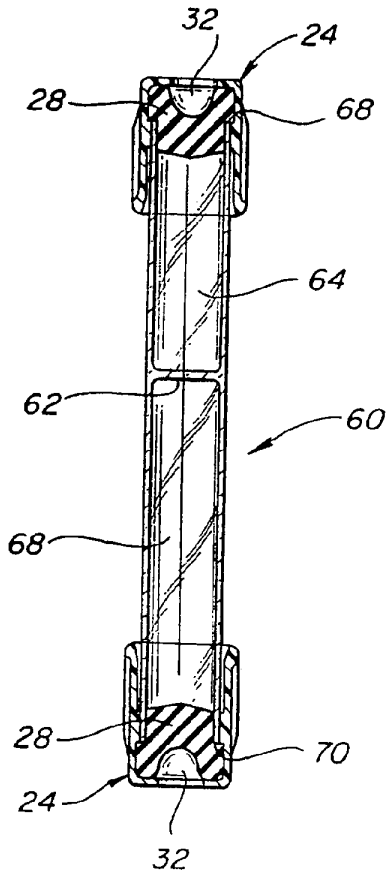

28
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FIG-6


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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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

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

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

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

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

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

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

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

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

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

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

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

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

FOR FURTHER ACTION
See paragraph 2 below

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

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

Applicant
KURIN, INC

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

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

2. **FURTHER ACTION**

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

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

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

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

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

Box No. I Basis of the opinion

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

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

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

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

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

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

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

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

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

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

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

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

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

5. Additional comments:

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

1. Statement

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

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

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

see separate sheet

Re Item V

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

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

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

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

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

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

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

Re Item VII

Certain defects in the international application

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

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

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

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

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

Application Number
PCT/US2017/068569

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

APPLICANT: KURIN, INC

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

EXAMINER: Nielsen, Michael

CONSULTED DATABASES: WPI

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

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

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:

EPO FORM P04A42

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/068569

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/039348 A1 (BULLINGTON GREGORY J [US] ET AL) 6 February 2014 (2014-02-06) the whole document	1-20
A	US 2014/107564 A1 (BULLINGTON GREGORY J [US] ET AL) 17 April 2014 (2014-04-17) the whole document	1-20
A	US 4 813 433 A (DOWNEY JOHN M [US]) 21 March 1989 (1989-03-21) the whole document	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) abstract paragraph [0048] - paragraph [0075]; figures 2-12	1-20

-/--

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"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

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

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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

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

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

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

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

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

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

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

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

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

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

Blood sample optimization systems and methods are described that reduce or eliminate contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61B5/153 A61B5/154
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHEL LLOYD [US]; BR) 29 December 2011 (2011-12-29)	1-5, 7-13, 15-20
A	paragraph [0070] figure 15 abstract	6,14
A	US 2009/227953 A1 (TAN CHEE LEONG [SG] ET AL) 10 September 2009 (2009-09-10) the whole document	1-20
A	JP H08 257018 A (NISSHO KK) 8 October 1996 (1996-10-08) abstract; figures	1-20

-/--

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Schultz, Ottmar

2

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

International application No
PCT/US2016/043709

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18	1-20

2

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011162772 A1	29-12-2011	NONE	
US 2009227953 A1	10-09-2009	US 2009227953 A1	10-09-2009
		US 2010262038 A1	14-10-2010
		US 2012330187 A1	27-12-2012
JP H08257018 A	08-10-1996	NONE	
US 4416290 A	22-11-1983	NONE	
US 3648684 A	14-03-1972	NONE	
EP 1665986 A1	07-06-2006	BR PI0505336 A	11-07-2006
		EP 1665986 A1	07-06-2006
		JP 4914601 B2	11-04-2012
		JP 2006150083 A	15-06-2006
		US 2006129064 A1	15-06-2006
US 4056101 A	01-11-1977	NONE	
US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015

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

Application Number
PCT/US2016/043709

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

APPLICANT: CALLIOPE SOLUTIONS, INC.

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

EXAMINER: Schultz, Ottmar

CONSULTED DATABASES: EPODOC, WPI, COMBI, TXT+

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

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

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:
See claims.

EPO FORM P04A42

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

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

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

FOR FURTHER ACTION
See paragraph 2 below

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

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

Applicant
CALLIOPE SOLUTIONS, INC.

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

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

2. **FURTHER ACTION**

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

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

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

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

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

Box No. I Basis of the opinion

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

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

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

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

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

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

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

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

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

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

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

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

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

5. Additional comments:

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

1. Statement

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

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

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

see separate sheet

Box No. VIII Certain observations on the international application

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

see separate sheet

+++++

Reference is made to the following document:

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

+++++

Re Item V

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

+++++

1 INDEPENDENT CLAIMS 1, 8, 17

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

+++++

Re Item VII

Certain defects in the international application

+++++

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

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

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

+++++

Re Item VIII

Certain observations on the international application

+++++

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

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

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

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

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

+++++

J-PlatPat 特許情報プラットフォーム English close

Literature display help

1 / 1 display

Special table 09-504726

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

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

primary literature

bibliography close

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[Examination] Claim: Unclaimed
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E), AU, CA, JP (71
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[Patent Attorney]
[Name] Michio Akaoka (1 other person))

wrap up close

(57) [Summary]
The present invention is a bifurcated capillary tube (10) including closed system blood sampli
ng devices. A second branch (32) of the bifurcated capillary tube is connected to and in fluid c
ommunication with the blood collection area. It terminates in an opening adapted to receive a
blood withdrawal device.

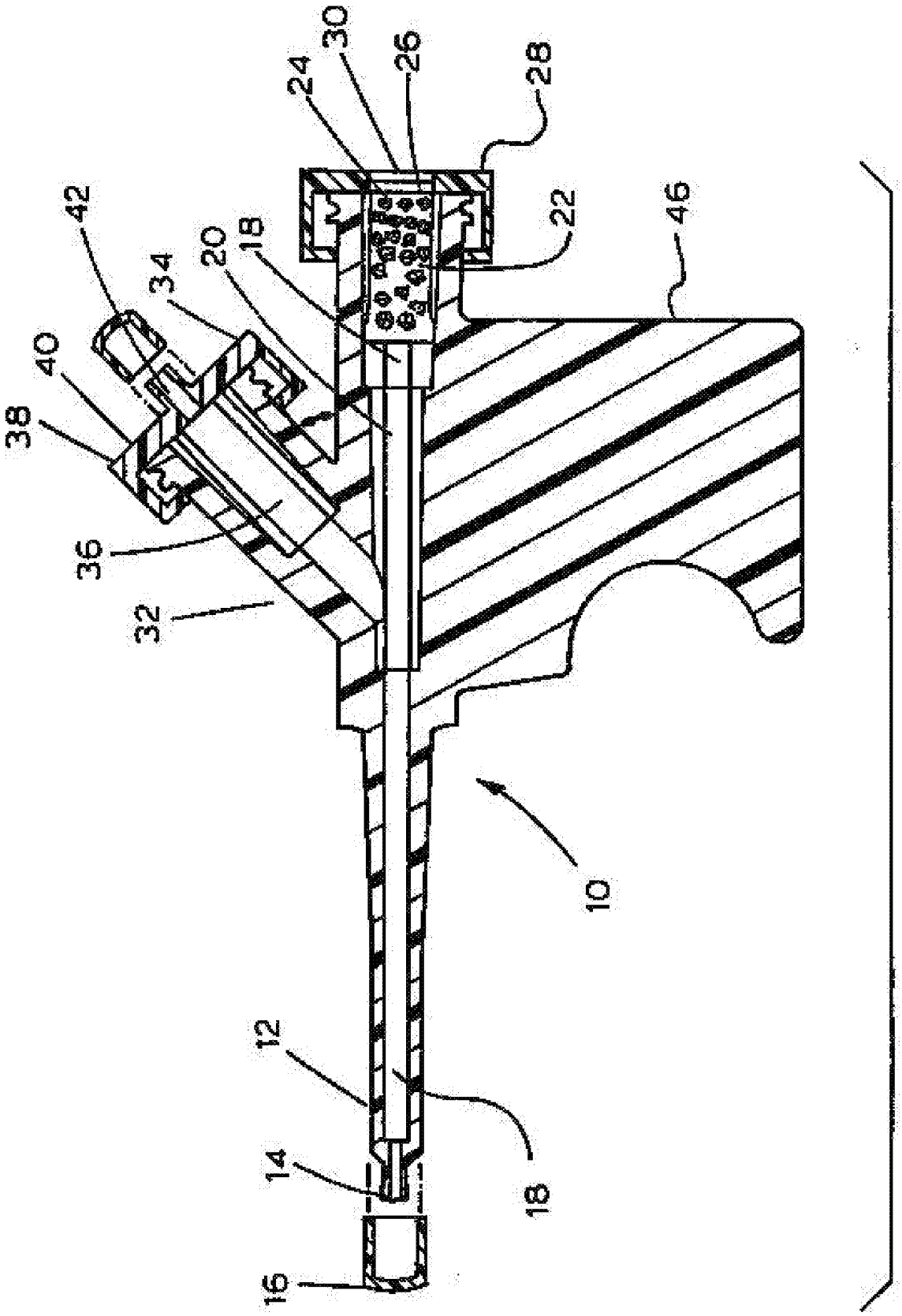


FIG. 1

The scope of the claims open ----

[Claims]

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

a. a first branch having a cannulated

end ;

b. a blood collection area for storing an amount of withdrawn blood and supplying a first to the communicating channel;

c. a blood disposal chamber having an air permeable liquid closed end; and

d.

a second device connected to and in fluid communication with said blood collection area terminating in an opening adapted to

receive a blood extraction device.

2. 4. The cannula-shaped end is blunt, the blood waste chamber has a cap containing an air permeable hydrophobic membrane

on the end, and the blood waste chamber contains a porous blood

adsorbent 1 closed system blood sampling device.

3.

2. The closed system blood sampling device of claim 1, wherein the second branch has an internal angle of no greater than 90 degrees .

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

.

5. 3. The closed system blood

sampling .

6. 3. The closed system blood sampling device of Claim 2 , wherein said blunt cannulated distal end is

adapted to be received by an injection site including a resilient resealing means. 7. 7. The closed . 8. 3. The closed system blood sampling device of claim 2, wherein said blood collection area has a volume greater than the volume of said blood waste chamber . 9. A method of sampling blood from a patient having an artery connected to a venipuncture device attached to an injection site comprising the closed system blood sampling device of claim 1.

A law comprising:

a.

drawing blood through the cannulated end of the closed system blood sampling device , there by subsequently

filling the blood waste chamber and then the blood collection area;

b. withdrawing the blood contained within the blood collection area

through the opening in the second branch for subsequent processing; and then

c. and discarding the closed system blood sampling device

.

10. 10. The method of claim 9, wherein said cannula is blunt, said blood disposal chamber is c apped at its end with an air permeable hydrophobic

membrane and comprises a porous blood adsorbent. 11. 10. The method of claim 9, wherein t he second branch has an internal angle of no greater than 90 degrees . 12. Claim 1, wherein t he second branch has an angle of about 60 degrees.

1 method.

13. 11. The method of claim 10, wherein the cannulated end is tapered.

14.

11. The method of claim 10, wherein the blunt cannula-shaped distal end is adapted to be rec eived by an injection site including a resilient resealing means

.

15. 15. The method of claim 14, wherein the injection site is a pre-slit injection site

.

16.

11. The method of Claim 10, wherein the blood collection area has a volume greater than the volume of the blood waste chamber .

detailed description open —

Description:

CLOSED SYSTEM BLOOD SAMPLING APPARATUS

FIELD OF THE INVENTION The

present invention relates to closed system blood sampling apparatus.

BACKGROUND OF THE INVENTION

Arterial blood gas sampling is a standard procedure often used to . In some cases, samples . For a typical neonatal patient weighing 1000 grams and having a total blood volume , blood sample volume becomes a critical factor. A technique called the "three drops method" is gaining substantial clinical acceptance in neonatal units throughout the country . This method requires inserting a blunt hypodermic needle as far as possible into a standard sleeved T-connector . Three drops of blood, estimated at about 0.06 cc , are drawn onto the gauge pad, thereby removing heparinized or non-circulating blood from the cannula while providing a fresh arterial blood sample on its surface. Three more drops are then collected in the microcontainer after which the cannula is withdrawn. The blood cannula contents within the cannula lumen and the immediately prior collected microcontainer sample are then blood tested for testing.

Aspirated into a tuberculin-type syringe for transport to the chamber. A wash of the T-connector is then subsequently performed to remove residual blood. This procedure uses a controlled blood volume (0.06 cc as required to discard, and actual It provides the ability to draw 0.12 cc to possibly 0.20 cc) for blood gas testing on-the-fly.

There are several opportunities for procedure refinement. One problem is that the collection method is an open environment, which could facilitate the spread of blood contamination and/or communicable diseases . Second, the acquisition process is difficult to control with respect to volumetric accuracy and is highly sensitive to variations in physician technique, catheter placement and arterial pressure. In the treatment of neonatal patients where blood volume levels are critical, if a device could be designed for closed system collection that would also ensure sample volume consistency every time.

, improved accuracy could be of great clinical benefit.

BRIEF

DESCRIPTION OF THE DRAWING FIG. 1 is a horizontal cut away side .

FIG. 2 is an upright, partial schematic showing a closed system blood sampling device conne

cted to an injection site, which is then connected
into a venipuncture device used to draw arterial blood.
is a diagram.

In the drawings, similar parts have similar numbers.

The Invention The present invention is a closed system blood sampling device that includes a bifurcated capillary tube having a first branch

with a
cannulated .
A blood collection area is
for .
It also supplies the first fraction of blood withdrawn to a communicating blood waste chamber having an air permeable liquid closed end.

A second branch of the bifurcated capillary is connected to and communicates with the blood collection area.
liquid communication. It
terminates .

In a preferred embodiment, the cannulated
end blunt, the blood waste chamber
is capped at its end with an air permeable hydrophobic membrane, and the blood waste chamber is porous. of blood adsorbents. The second branch
has an interior angle no greater than 90 degrees, and preferably the interior angle is 60 degrees.
It is also desirable that the cannulated end be tapered
so that fully below .

Preferably, the closed system blood sampling device
is
withdrawn from the injection site before the blood sample is withdrawn therefrom by means such as by direct aspiration into a tuberculin syringe or blood gas analyzer.

Although closed system blood sampling devices are particularly well suited for obtaining neonatal blood samples
, the devices are readily adaptable for obtaining samples from a variety of patient types.
be done.

Detailed Description of the Invention

In FIG
.
It is preferably formed of a transparent, chemically inert, non-toxic plastic such as polycarbonate or the like . It includes a blood withdrawal
cannula shaped end 12 . The cannula tip 14 is blunt and
narrowed to prevent backflow of blood at the injection site during arterial blood sampling.

A blood sampling device is used at the cannula tip to maintain sterility
It is fitted with a removable cap 16, which is removed just before.

FIG. 1 shows a cannulated distal end 12 that is tapered.
This particular configuration was chosen so that the cannula could engage and
generally later . The internal bore 18 at the cannulated distal end is sized
by capillary action driven by normal positive arterial blood pressure . The internal capillary 1 8 connects with and leads into a larger diameter lumen 20 . The continuous bore 18 and lume n 20 of the cannula 12 constitute the blood collection area. Hole 18 where it exits lumen 20 tr ansitions into blood waste chamber 22 . In a preferred embodiment of the invention , blood di sposal chamber 22 includes blood retention means such as absorbent material 24, which may be rayon or cellulose wadding or the like. The open end 26 of the blood waste chamber 22 has a cap 28 fitted on top of it with a liquid impervious, air permeable hydrophobic membrane 30 that allows air to escape from the blood sampling device 10 of the present invention. is closed by A suitable thin film material is sheet polytetrafluoroethylene . Connected to the lumen 20 and in fluid communication therewith is a second branch or port 32 . It is arranged to have an internal angle 34 not exceeding 90 degrees. The interior angle is

Preferably it is about 60 degrees. Hole 36 connects with hole 18 and matches it in dimensions . The port 32 is terminated at its distal end with an adapter cap 38 (at its top 40 a capillary lu er
Joint 42 is connected
is sealed by The capillary luer is protected from contamination
by a protective cap 44 that is removed just before blood is drawn from the closed blood sampl ing device.
Port 32 and its hole 36 form
part . For convenience of use, the closed blood sampling device is connected with
a pistol grip handle 46.

The blood collection area has a liquid volume greater than the liquid volume of the blood dis posal chamber. If
the closed blood sampling device described is to be used
in , the fluid volume of the blood collection area
may be 0.12 cc, and the fluid volume of the blood waste chamber 22 may be It would be abo ut 0.06cc.

The use of the closed blood
sampling is illustrated in FIG
. A communicating artery 48 is shown. Neck 54 of venipuncture device 50
is adapted to receive injection site 56 . Although a conventional injection site may
be used as such or adapted for use in the practice of the present invention, the injection site i s preferably pre-slit with a resilient reseal. It is desirable to be of a type having a possible par tition. This type of injection site is available from Baxter Healthcare Corporation and is availab le from Baxter Healthca.

Neonatal Tee Connector Luer Fitting sold under the trademark InterLink, a registered tradema rk of re Corporation .

Such pre-slit, resilient, resealable injection
sites and methods of their manufacture are described in US Pat. No. 5,188,620.
, the disclosure of which is incorporated herein by reference.
The pre-slit, resilient, resealable injection site described in this patent
is designed to accept a blunt cannula.
Another injection site related to the injection site detailed in US Pat. No. 5,188,620
is described in US Pat. No. 5,300,034. This patent is also a preferred embodiment used in the practice of this invention.
The plethora of publications and references describing various injection sites are elaborated
. This patent and publications cited therein are also
incorporated .

Injection site 56 is connected to a T-connector 58 which in turn is connected to
microbore tubing which is connected through female luer fitting 62 to intravenous line 64
. The distal end of injection site 56 is connected to neck 54 of venipuncture device 50 . A prox imal end 66 of injection site 56 is a pre-slit, resilient member adapted to receive blood withdr awal cannula 12 sized to fit snugly into
the injection site. , is connected with the resealing septum 68 . Inserted into the second branc h or port 32 is a conventional syringe 70 such as a tuberculin blood aspiration syringe or an ar terial blood gas loss resistant syringe. The cannula 12 of the device is inserted through the s

eptum 68 of the injection site 56 and positioned so that the tip 14 of the cannula 12 is fully in serted into the injection site adjacent the venipuncture device. be. Doing so would remove the residual from the blood draw volume as a measurable factor. Arterial pressure causes blood to enter and flow up the device through capillary action.

will let As blood rises to the hydrophobic membrane 30 of the device, air
will escape through the upstream hydrophobic membrane 30 . Original blood originally presen t in the catheter will be forced up past
the luer fitting branch for retention and eventual disposal in the device . The device will be wit hdrawn from the T-connector as soon as visual confirmation
of a blood-filled lumen is formed.
The vent
removal cap 44 will be removed from the bifurcated luer fitting 42 and replaced by a syringe 7 0 that will be aspirated to remove the arterial blood
sample
. Residual blood volume upstream of the bifurcation will remain in the device for subsequent d isposal
.

drawing open —

[Fig. 1]

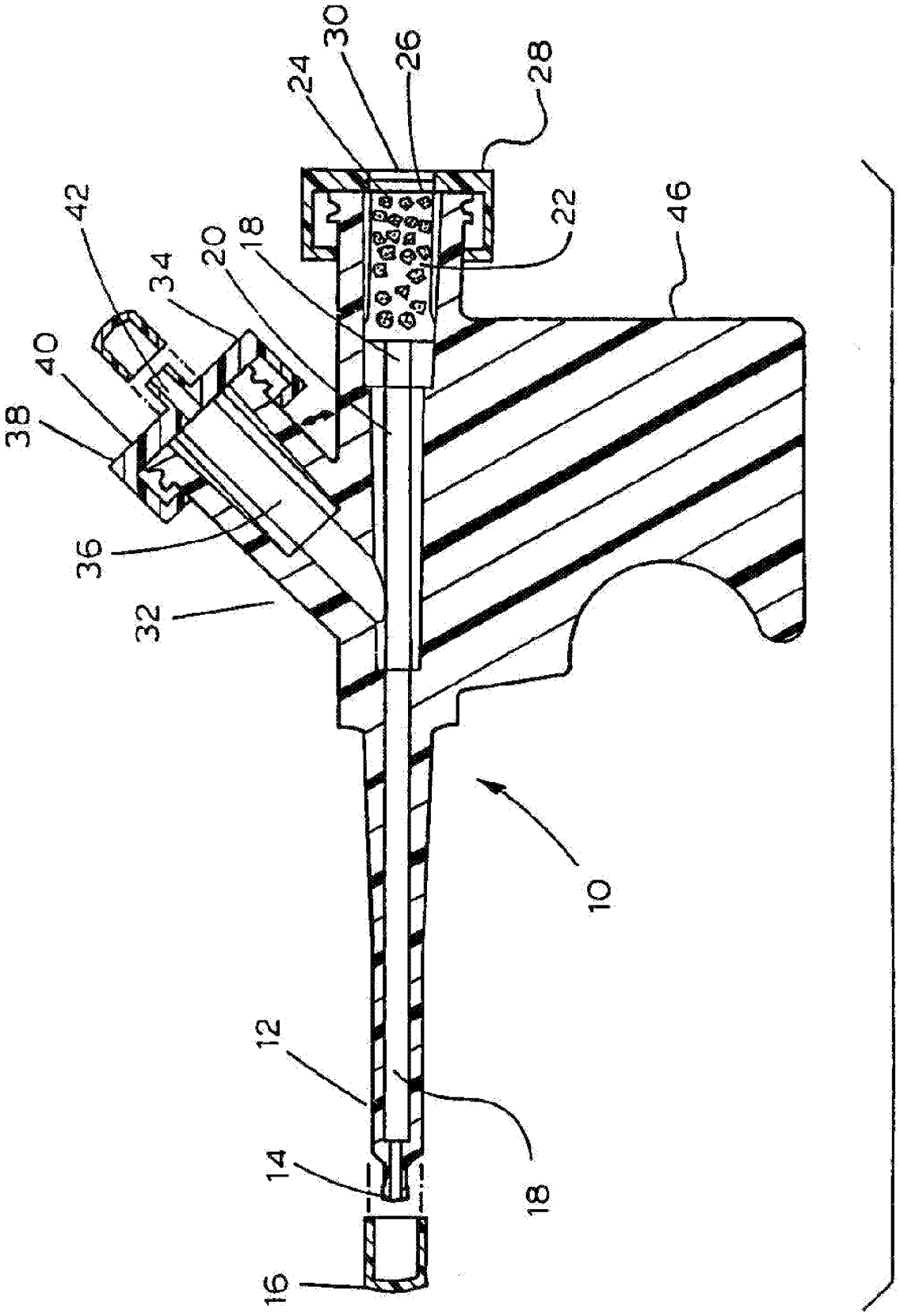


FIG. 1

[Figure 2]

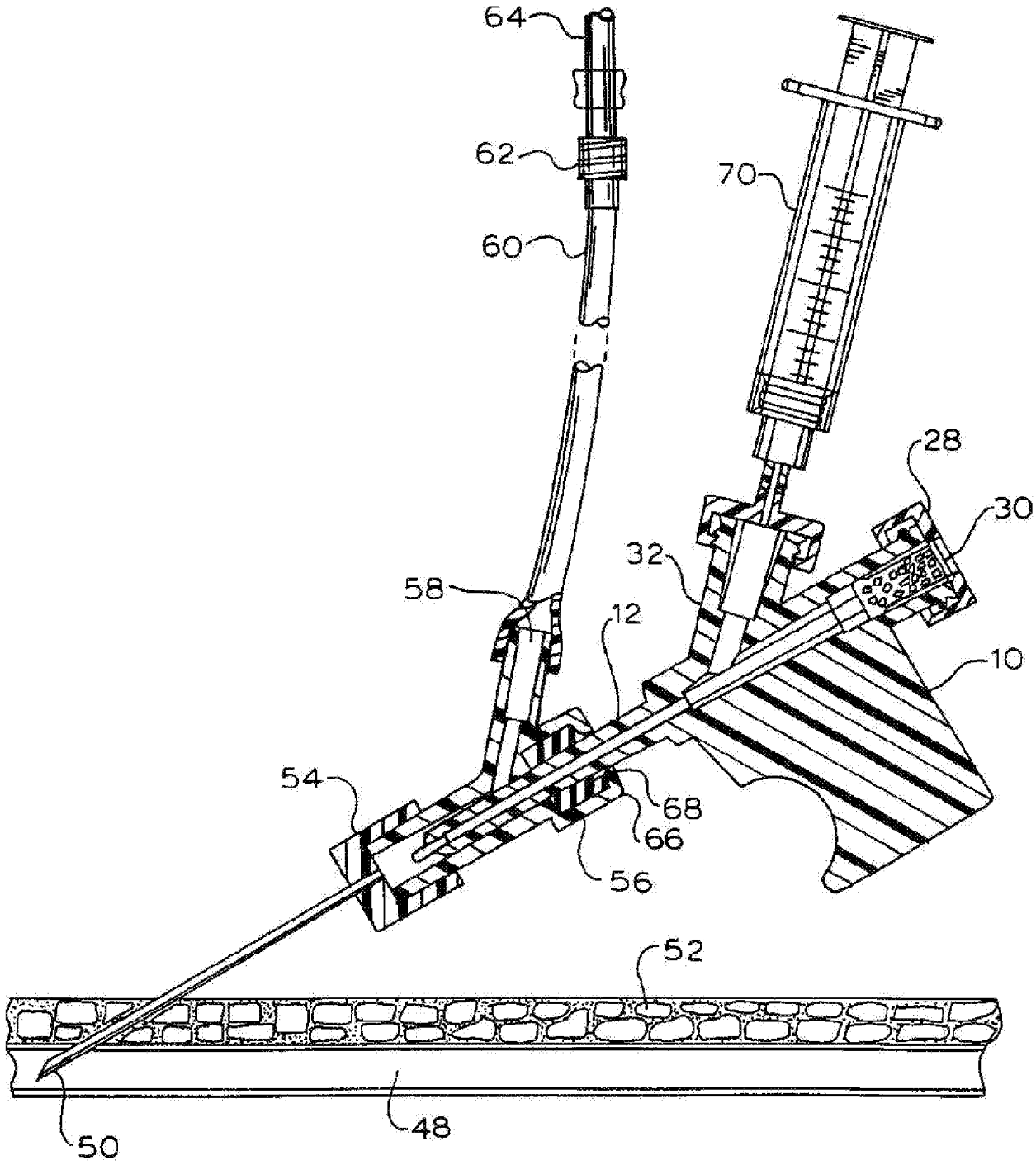


FIG. 2

search report open —

[International search report]

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/10702

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A 61M 5/00
US CL : 604/122
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

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

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

Date of the actual completion of the international search 08 DECEMBER 1995	Date of mailing of the international search report 04 JAN 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT	Authorized officer ANDRE ROBERT

Washington, D.C. 20231
Facsimile No.
SAM KIMELL
Telephone No. (703) 308-0858

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

drawing open

Representative drawing 1 2

Magnify and Rotate

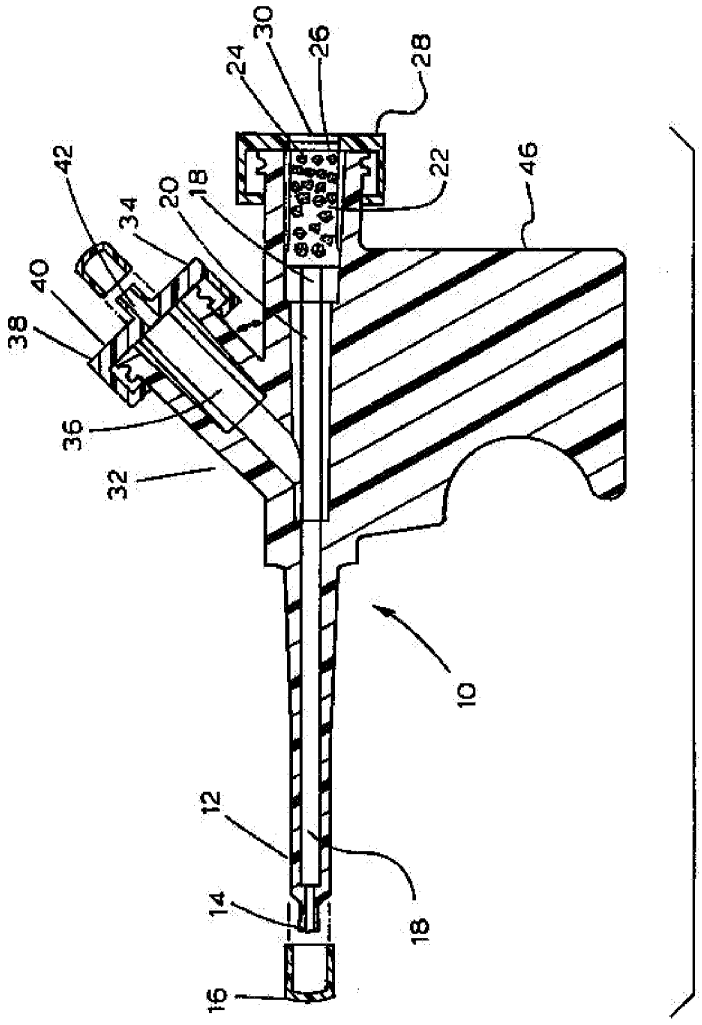


FIG. 1

Representative drawing

1 / 1 display

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Espacenet

Bibliographic data: JPH09504726 (A) — 1997-05-13

CLOSED SYSTEM BLOOD SAMPLING DEVICE

Inventor(s):

Applicant(s):

Classification: - **international:** *A61B5/15;* (IPC1-7): A61B5/14
- **cooperative:** A61B5/15003 (EP); A61B5/150213 (EP); A61B5/150259 (EP); A61B5/150992 (EP); A61B5/155 (EP)

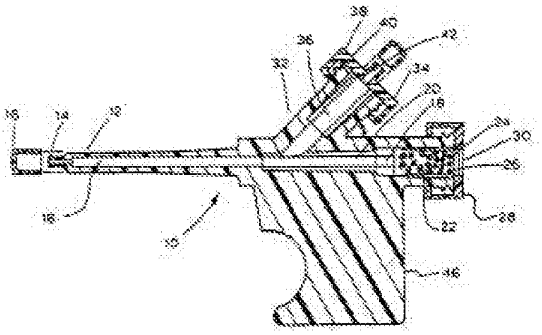
Application number: JP19950508283 19950822

Priority number(s): WO1995US10702 19950822 ; US19940296207 19940825

Also published as: AT208640 (T) AU3412795 (A) AU686450 (B2) CA2173331 (A1) DE69523887 (T2) more

Abstract not available for JPH09504726 (A)
Abstract of corresponding document: WO9605875 (A1)

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



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(43)公表日　平成９年(1997)５月13日

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審査請求　未請求　　予備審査請求　未請求(全 11 頁)

(21)出願番号　特願平8－508283
(86)(22)出願日　平成７年(1995)８月22日
(85)翻訳文提出日　平成８年(1996)４月10日
(86)国際出願番号　ＰＣＴ／ＵＳ９５／１０７０２
(87)国際公開番号　ＷＯ９６／０５８７５
(87)国際公開日　平成８年(1996)２月29日
(31)優先権主張番号　０８／２９６，２０７
(32)優先日　1994年８月25日
(33)優先権主張国　米国（ＵＳ）
(81)指定国　ＥＰ(ＡＴ，ＢＥ，ＣＨ，ＤＥ，ＤＫ，ＥＳ，ＦＲ，ＧＢ，ＧＲ，ＩＥ，ＩＴ，ＬＵ，ＭＣ，ＮＬ，ＰＴ，ＳＥ)，ＡＵ，ＣＡ，ＪＰ

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(54)【発明の名称】　閉鎖系血液サンプリング装置

(57)【要約】
本発明は、血液を抜き取りそして連通した血液収集区域へ血液を移送するための、カニューレ形の末端(14)を有する第一の枝(12)を有する、分岐した毛細管(10)を含む閉鎖系血液サンプリング装置を含む。該分岐した毛細管の第二の枝(32)は、該血液収集区域へと連結され、そしてそれと液体連通している。それは、血液抜き取り装置を受け入れるのに適合させた開口に終わっている。

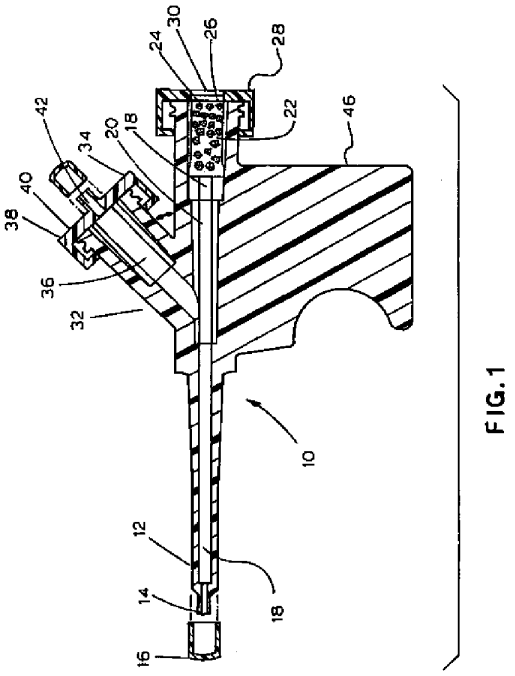


FIG. 1

【特許請求の範囲】

１．　分岐した毛細管を含む閉鎖系血液サンプリング装置であって、

ａ．血液を抜取って連通路へと血液を移送するためのカニューレ形の末端を有する第一の枝と、

ｂ．ある量の抜き取られた血液を貯蔵し、そして抜き取られた血液の最初の画分を連通路へと供給するための血液収集区域と、

ｃ．空気透過性の液体閉鎖性の末端を有する血液廃棄室と、そして、

ｄ．血液抜き取り装置を受け入れるのに適合させた開口に終わる該血液収集区域に連結されそしてこれと液体連通している第二の技と、

を含む閉鎖系血液サンプリング装置。

２．　該カニューレ形の末端が鈍く、該血液廃棄室が空気透過性の疎水性薄膜を含むキャップをその末端に嵌めてあり、そして該血液廃棄室が多孔性の血液吸着剤を含むものである、請求項１の閉鎖系血液サンプリング装置。

３．　第二の枝が９０度よりも大きくない内角を有するものである、請求項１の閉鎖系血液サンプリング装置。

４．　第二の枝が約６０度の角度を有するものである、請求項３の閉鎖系血液サンプリング装置。

５．　該カニューレ形の末端が先細っている、請求項２の閉鎖系血液サンプリング装置。

６．　該鈍いカニューレ形の末端が、弾力のある再シールする手段を含む注射部位によって受け入れられるのに適合させてあるものである、請求項２の閉鎖系血液サンプリング装置。

７．　該注射部位が予めスリットを入れてある注射部位である、請求項６の閉鎖系血液サンプリング装置。

８．　該血液収集区域が、該血液廃棄室の体積よりも大きな体積を有するものである、請求項２の閉鎖系血液サンプリング装置。

９．　請求項１の該閉鎖系血液サンプリング装置を含む注射部位に取付けられた静脈穿刺装置と連結された動脈を有する患者から、血液をサンプリングする方

法であって、

ａ．該閉鎖系血液サンプリング装置の該カニューレ形の末端を通して血液を抜き取り、それによってその後該血液廃棄室そして次いで該血液収集区域を満たすステップと、

ｂ．その後の処理のために、該血液収集区域内に含まれた該血液を該第二の枝にある該開口を通して抜き取るステップと、そして、次いで、

ｃ．該閉鎖系血液サンプリング装置を捨てるステップと、

を含む方法。

１０．　該カニューレが鈍く、該血液廃棄室がその末端に空気透過性の疎水性薄膜を含むキャップを嵌めてあり、そして多孔性の血液吸着剤を含むものである、請求項９の方法。

１１．　第二の枝が９０度よりも大きくない内角を有するものである、請求項９の方法。

１２．　第二の枝が約６０度の角度を有するものである、請求項１

１の方法。

１３．　該カニューレ形の末端が先細っている、請求項１０の方法。

１４．　該鈍いカニューレ形の末端が、弾力のある再シールする手段を含む注射部位によって受け入れられるのに適合させてあるものである、請求項１０の方法。

１５．　該注射部位が予めスリットを入れてある注射部位である、請求項１４の方法。

１６．　該血液収集区域が、該血液廃棄室の体積よりも大きな体積を有するものである、請求項１０の方法。

【発明の詳細な説明】

閉鎖系血液サンプリング装置

本発明の分野

本発明は、閉鎖系血液サンプリング装置に関する。

本発明の背景

動脈血のガスサンプリングは、重態の疾病において呼吸機能の評価を助けるためにしばしば使用される標準的な手順である。場合により、一日に20回ものサンプルが抜き取られることができる。1000グラムの体重でそして約85ccの全血液体積を有する典型的な新生児患者にとって、血液サンプルの体積は重大な要素になる。

「３滴法」と呼ばれる技術が、国中の新生児ユニットにおいて実質的に臨床上受入れられつつある。この方法は標準のスリーブで止められたＴ字形コネクターの中へとできる限り遠く、鈍い皮下針を挿入することを要求する。約０06ccと推定される三滴の血液が、ゲージパッド上へとたらされ、それによってその表面に新鮮な動脈血サンプルを提供する間にヘパリン加血液又は非循環血をカニューレから取り除く。次いで、更なる三滴がマイクロコンテナー中に集められ、その後にカニューレが引き抜かれる。カニューレ管腔内の血液カニューレ内容物へ及び直前に収集されたマイクロコンテナーサンプルは、次いで検査のために血液試験室へと輸送するためにツベルクリンタイプの注射器中へと吸引される。次いで残りの血液を除去するためにＴコネクターの洗浄がその後行われる。この手順は制御された血液体積（捨てるのに必要なものとして０06cc、及び実

際の血液ガス検査のために０12cc乃至多分０20cc）を抜き取る能力を提供する。

手順の改良のための幾つかの機会が存在する。一つの問題は、血液汚染及び／又は伝染病の拡散を促進し得るであろうその収集方法が開放した環境であることである。第二には、体積の正確さに関しては収集過程が制御しにくく、そして医者の技術、カテーテル配置及び動脈圧の変化に対して非常に影響されやすい。もし、毎回サンプル体積の一貫性も保証することができるであろう閉鎖系の収集のための装置が設計できれば、血液体積レベルが重大である新生児患者の治療では

、正確さの改善は大きな臨床上の利益になりうる。

図面

図１は、本発明の閉鎖系血液サンプリング装置を示す水平方向の切り取った側面図である。

図２は、注射部位に連結され、次いで、該注射部位が動脈血を抜き取るために使用される静脈穿刺装置中へと連結されている閉鎖系血液サンプリング装置を示す直立の部分的に概要的な図である。

該図面中では、類似の部品は類似の番号を有する。

本発明

本発明は、血液を抜き取って連通した血液収集区域へ移送するためのカニューレ形の末端を有する第一の枝を有する分岐した毛細管を含む閉鎖系血液サンプリング装置である。血液収集区域はある量の抜き取られた血液を貯蔵するためのものである。それは、抜き取られた血液の最初の画分を空気透過性の液体閉鎖性の末端を有する連通した血液廃棄室へ供給をもする。

分岐した毛細管の第二の分岐は血液収集区域に連結されてこれと

液体連通している。それは血液抜取り装置を受け入れるのに適合させた開口に終わっている。

好ましい具体例においては、閉鎖系血液サンプリング装置のカニューレ形の末端は鈍く、血液廃棄室はその末端に空気透過性の疎水性薄膜を含むキャップがはめてあり、そして血液廃棄室は多孔性の血液吸着剤を含む。第二の枝は90度より大きくない内角を有し、そして好ましくは該内角は60度である。後に一層完全に記述される好ましい注射部位中へと、カニューレ形の末端がぴったり嵌合するように、カニューレ形の末端が先細りであることも同様に望ましい。

好ましくは、閉鎖系血液サンプリング装置は、血液サンプルがツベルクリン注射器又は血液ガス分析器中へと直接的に吸引される等のような手段によってそこから抜き取られる前に、注射部位から抜き取られる。

閉鎖系血液サンプリング装置は、新生児の血液サンプルを得るのに特に適しているが、該装置はさまざまな患者のタイプからサンプルを得るために直ちに適合

される。

本発明の詳細な記述

図１において、閉鎖系血液サンプリング装置は全体として数字１０によって指示されている。それは、ポリカーボネート等のような透明で化学的に不活性な毒性のないプラスチックによって好ましくは形成される。それは血液抜取りカニューレ形の末端１２を含む。カニューレ先端１４は鈍く、そして動脈血サンプリングの間注射部位の血液逆流を防止するようにくびれて細まっている。無菌性を維持するために、カニューレ先端には、血液サンプリング装置が使用される

直前に取り外される、取外し可能なキャップ１６が嵌められている。

図１は、先細りにされるカニューレ形の末端１２を示している。その詳細は後に一層完全に記述されるであろうが、カニューレが特有の注射部位と係合そして一般的に嵌合することができるように、この特有の構成が選ばれた。カニューレ形の末端の内部穴１８は、正常な正の動脈血圧によって駆動される毛管作用によって、抜き取られた血液が該穴に沿って移動することを許容するように寸法が与えられている。

内部毛細穴１８は、一層大きな直径の管腔２０と連結しその中へと続いている。該カニューレ１２の連続した穴１８及び管腔２０は血液収集区域を構成する。それが管腔２０を出るところの穴１８は、血液廃棄室２２内へと移行している。本発明の好ましい具体例では、血液廃棄室２２は、レーヨン又はセルロース詰め綿等であってよい吸着材料２４のような血液保持手段を含む。血液廃棄室２２の開口末端２６は、本発明の血液サンプリング装置１０から空気が排出されることを許容する、液体を通さない、空気透過性の疎水性薄膜３０をその頂部に嵌めてあるキャップ２８によって閉じられている。適した薄膜材料は、約０８ミクロンの厚さを有するシート状のポリテトラフルオロエチレンである。

該管腔２０に連結されてそれと液体連通しているのは第二の分岐又はポート３２である。それは、９０度を越えない内角３４を有するように配置されている。該内角は好ましくは約６０度である。穴３６は穴１８と連結し、そして寸法においてそれと一致する。ポート３２は末端においてアダプターキャップ３８（その頂部４０に毛管ルアー

継手 42が連結

されている）によってシールされている。毛管ルアーは、血液が閉鎖された血液サンプリング装置から抜き取られる直前に取り外される保護キャップ 44によって、汚染から保護される。ポート 32とその穴 36は前に記述された血液収集区域の一部を形成する。使用の便宜のために、閉鎖された血液サンプリング装置はピストル握り把手 46と連結される。

血液収集区域は、血液廃棄室の液体容積よりも大きな液体容積を有する。もし、記述された閉鎖された血液サンプリング装置が新生児の血液サンプリングにおいて用いられるためであれば、血液収集区域の液体容積は 0 12ccであるかもしれず、そして血液廃棄室 22の液体容積は約 0 06ccであろう。

血液を抜き取ってサンプリングするための本発明の閉鎖された血液サンプリング装置の使用が図 2 中に図解されており、該図には皮下組織 52を突き通して挿入された静脈穿刺装置 50と連通した動脈 48を示している。静脈穿刺装置 50の首 54は注射部位 56を受け入れるよう適合させてある。慣用の注射部位がそのようなものとして使用されてよく、又は本発明の実施において用いられるのに適合させてよいが、該注射部位は好ましくは予めスリットを入れてある弾力性のある再シール可能な隔壁を有するタイプであることが望ましい。このタイプの注射部位は Baxter Hea1thcare Corporationから入手可能であり、そしてこれは Baxter Healthcare Corporationの登録商標である InterLinkという商標の下に販売される新生児 T 字形コネクタールアー継手である。

そのような予めスリットを入れてある、弾力性のある、再シール可能な注射部位及びそれらの製造の方法が米国特許 5 188 620中に

記述されており、その開示が参照によってここに導入される。この特許中に記述されている予めスリットを入れてある、弾力性のある、再シール可能な注射部位は鈍いカニューレを受け入れるように設計されている。米国特許 5 188 620中に詳しく述べられた注射部位に関係した他の一つの注射部位が米国特許 5 300 034中に記述されている。この特許も同じく、この発明の実施中で使用される好まし

い注射部位を記述するおびただしい数の刊行物及び参照文献を詳しく述べている。この特許及びその中に挙げられた刊行物も同じく参照によってここに導入される。

注射部位 56はＴ字形コネクター 58と連結され、Ｔ字形コネクター 58が今度は、雌のルアー継手 62を通じて静脈内ライン 64へと連結される微細穴チューブと連結される。注射部位 56の先端側末端は静脈穿刺装置 50の首 54へと連結されている。注射部位 56の根元側末端 66は、該注射部位中へぴったり嵌合するように寸法が与えられた、血液抜取りカニューレ 12を受け入れるよう適合させた、予めスリットを入れてある、弾力性のある、再シールする隔壁 68と連結されている。第二の枝又はポート 32中へと挿入されているのは、ツベルクリン血液吸引注射器のような慣用の注射器 70又は動脈血ガス損失抵抗性注射器である。

装置のカニューレ 12は、注射部位 56の隔壁 68を貫通して挿入され、そしてカニューレ 12の先端 14が静脈穿刺装置に隣接した注射部位中へと完全に挿入されるように配置されるであろう。そのように実施すると、実際のＴ字形ハウジングの残余の体積が血液吸引体積中から、測定可能な要素としては除かれるであろう。動脈圧が、血液をして毛細管作用を通じて該装置へと入りそして該装置を流れ登らせるであろう。血液が該装置の疎水性薄膜 30へと上昇するにつれて、空気が上流の疎水性の薄膜 30を通して散逸するであろう。該カテーテル中に最初に存在した元々の血液は、該装置中における保持及び最終的な廃棄のためにルアー継手分岐を通り越して押し上げられるであろう。該装置は、血液が満たされた管腔の視覚的確認が形成されるとすぐにＴ字形コネクターから引き抜かれるであろう。ガス抜き除去キャップ 44が分岐したルアー継手 42から除去され、そして動脈血サンプルを取り除くために吸引されるであろう注射器 70によって置き換えられるであろう。分岐の上流の残余血液体積が、その後の廃棄のために該装置中に残るであろう。

【図１】

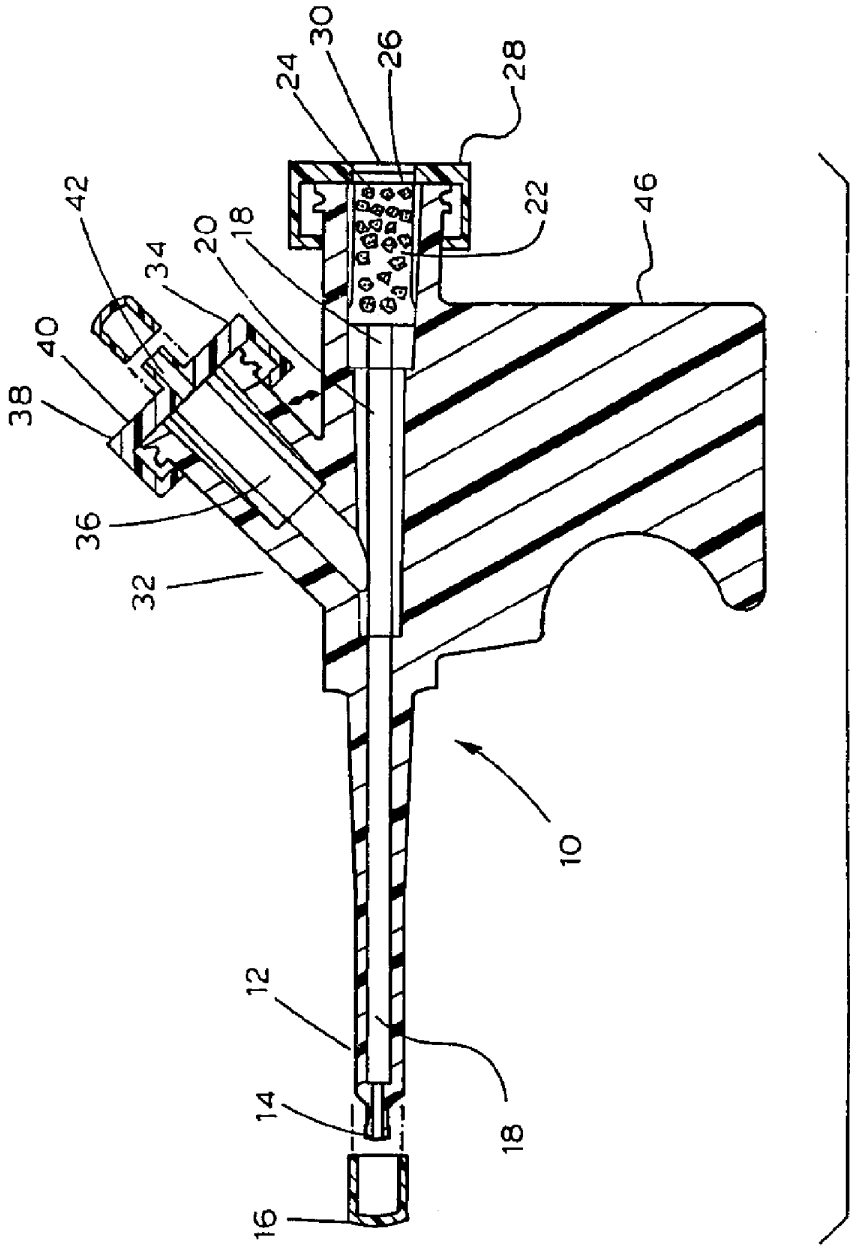


FIG. 1

【図２】

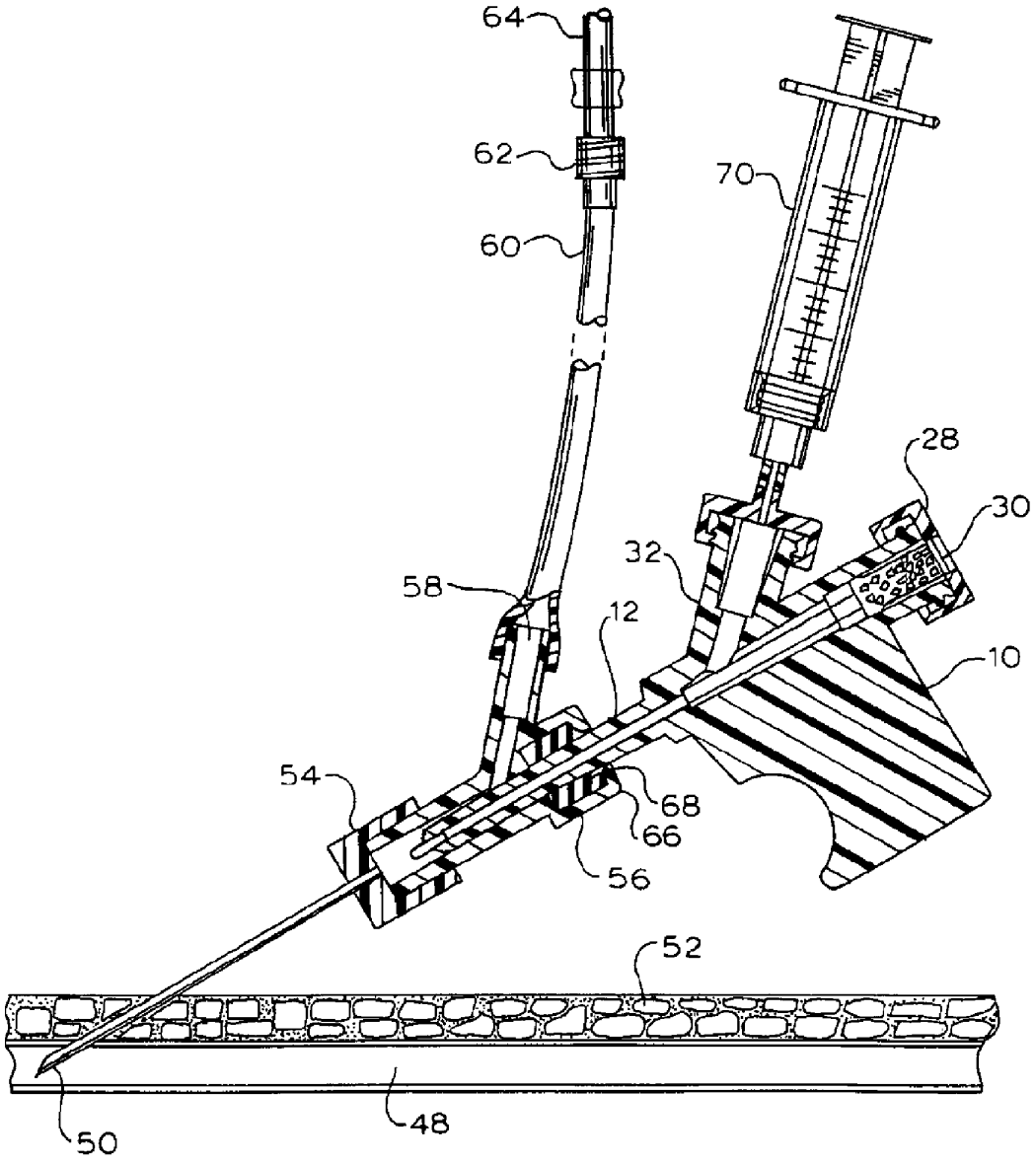


FIG. 2

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/10702

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A 61M 5/00
US CL. : 604/122
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

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

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
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"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

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

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

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Literature display help

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Patent 6734490

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(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
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(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)
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(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]
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(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]

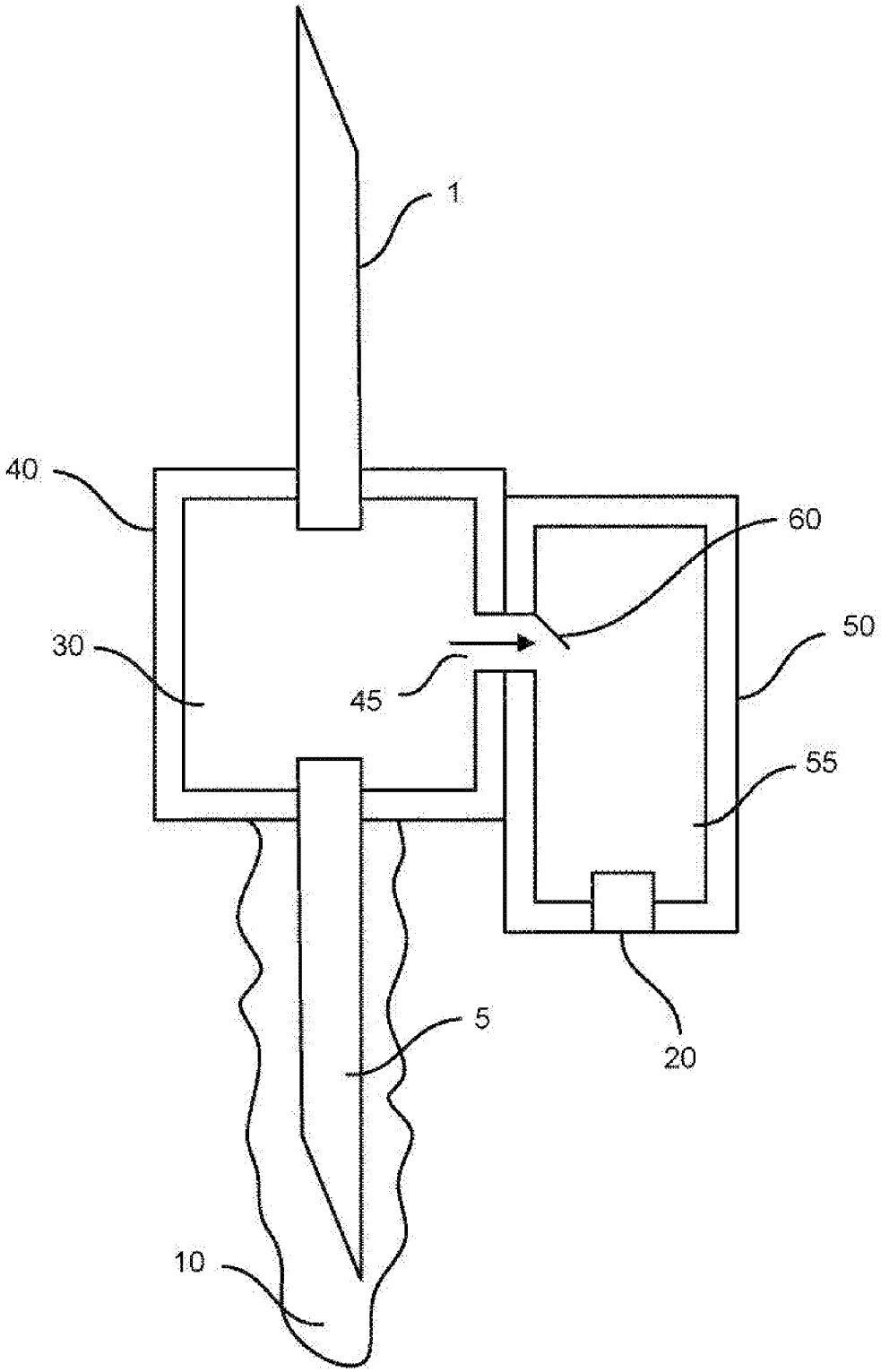


FIG. 1

[Figure 2]



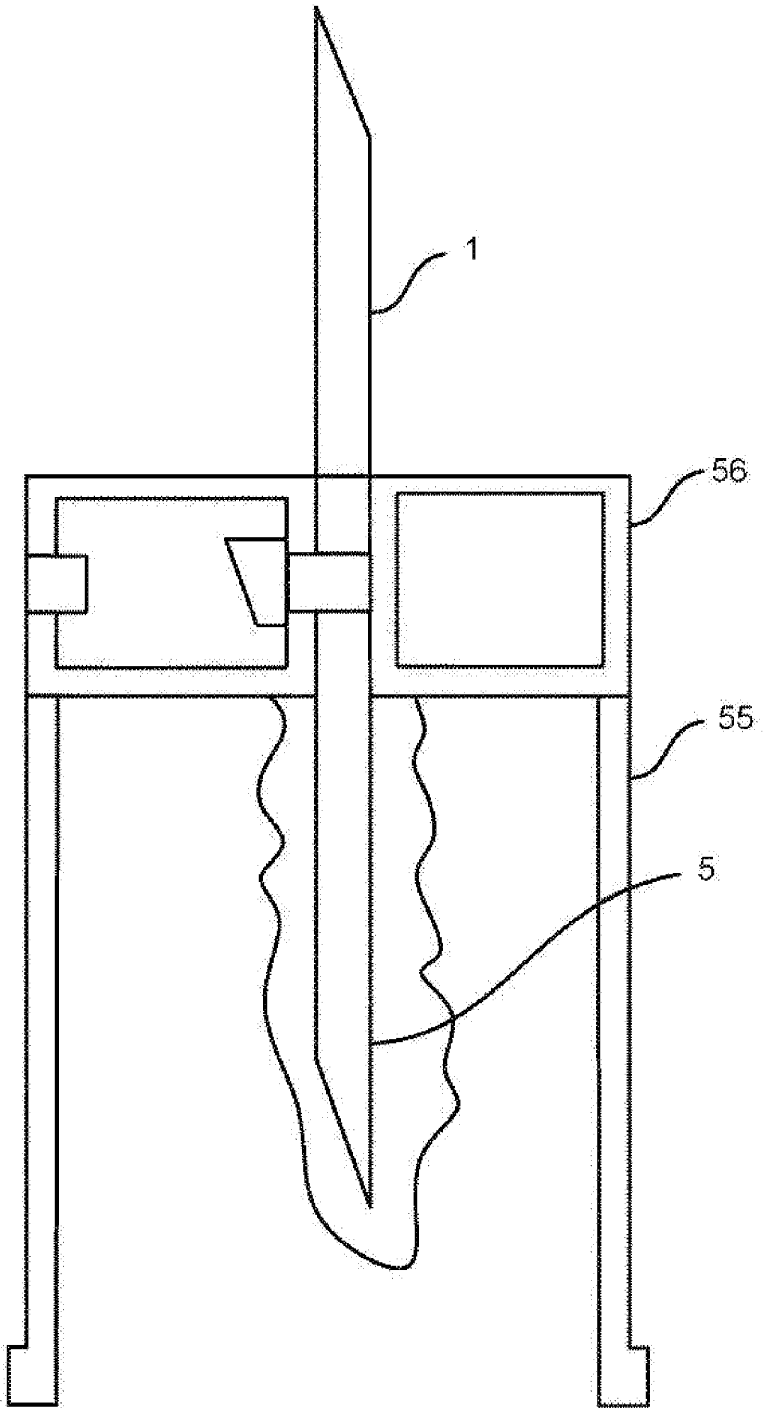


FIG. 2

[Figure 3]

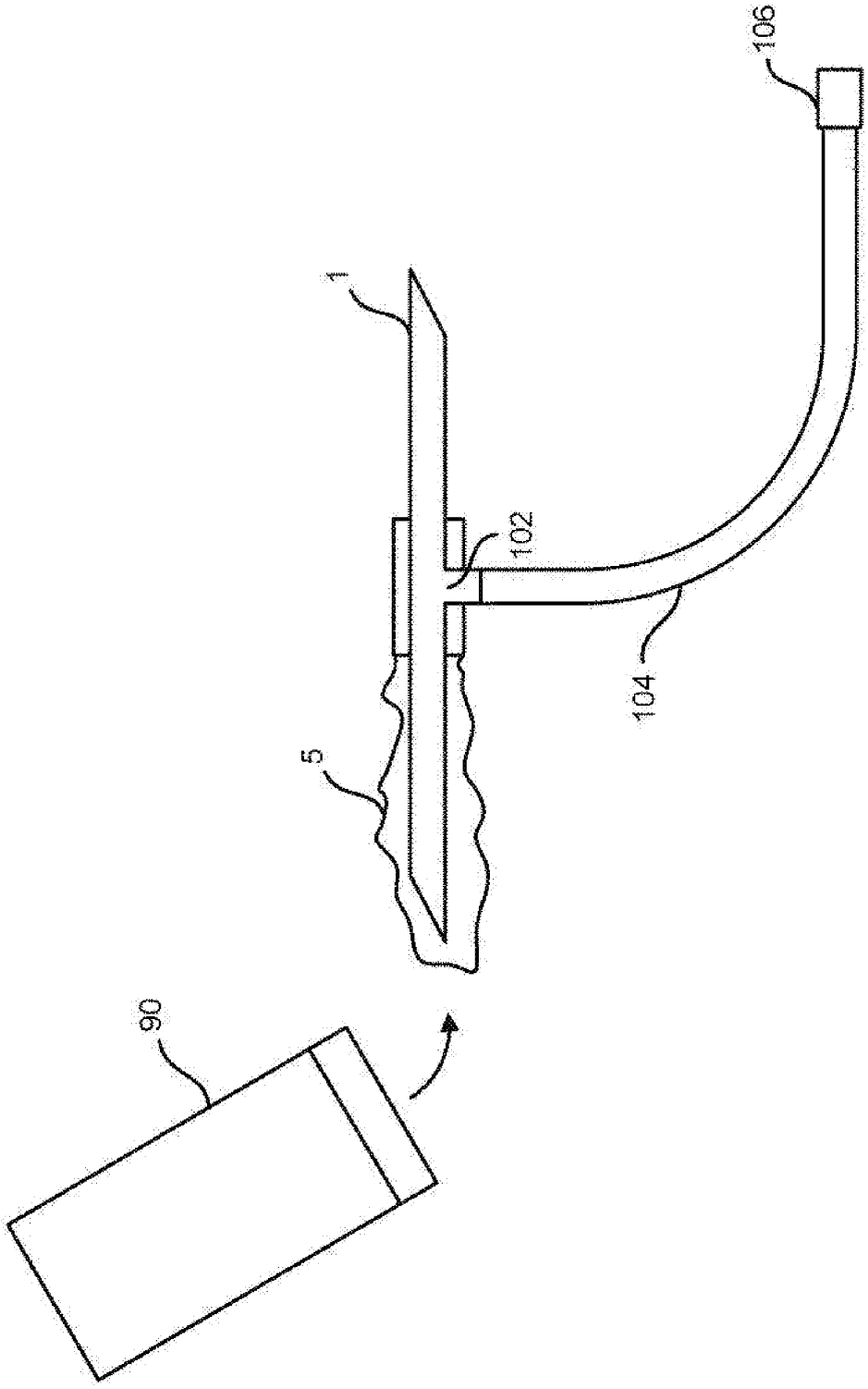


FIG. 3

[Figure 4]

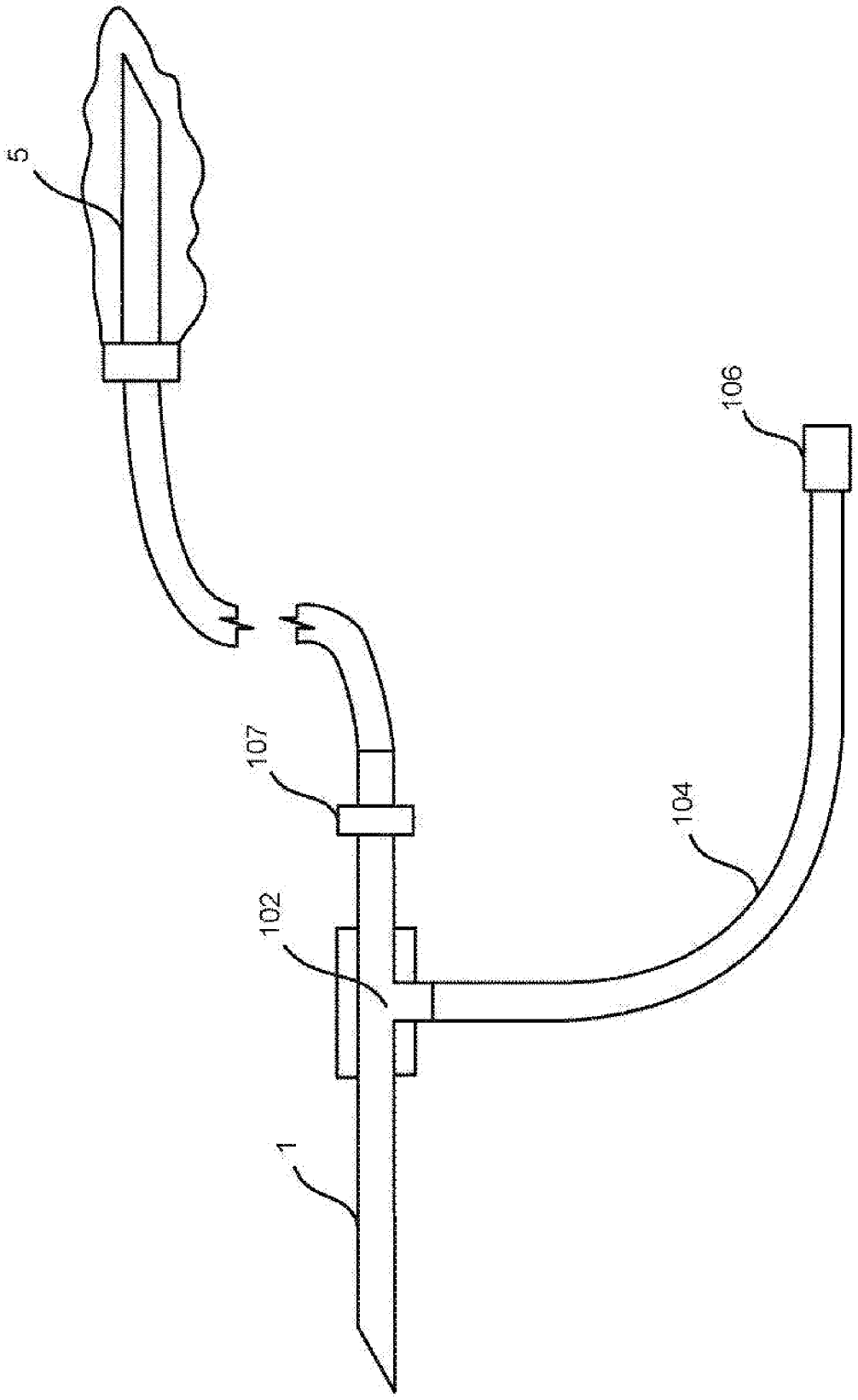


FIG. 4

[Figure 5]

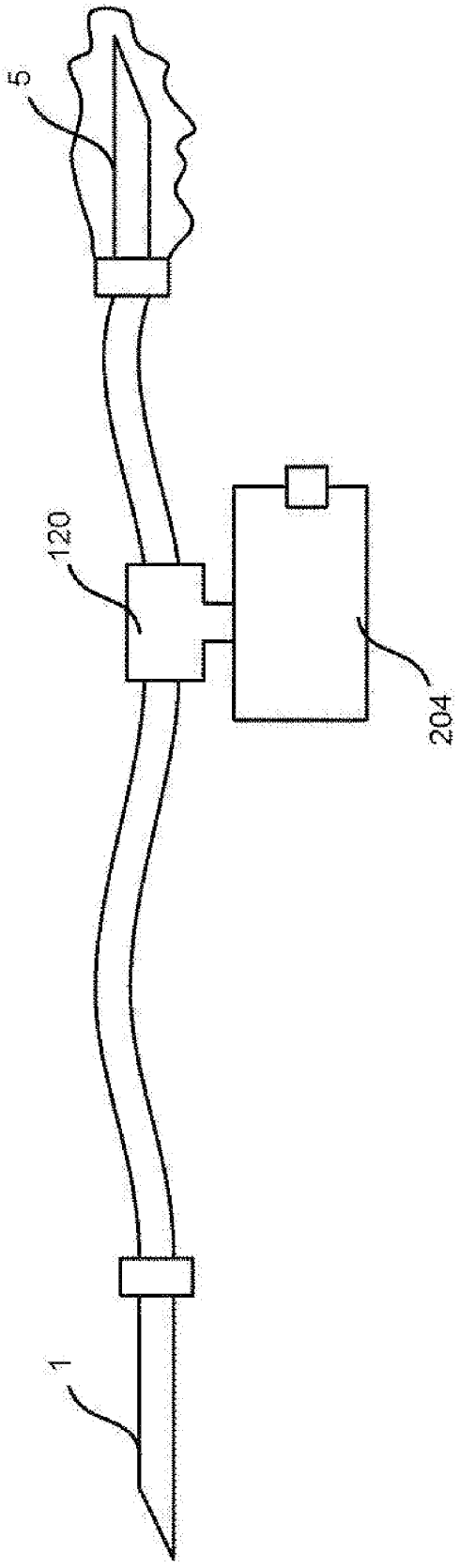


FIG. 5

[Fig. 6]

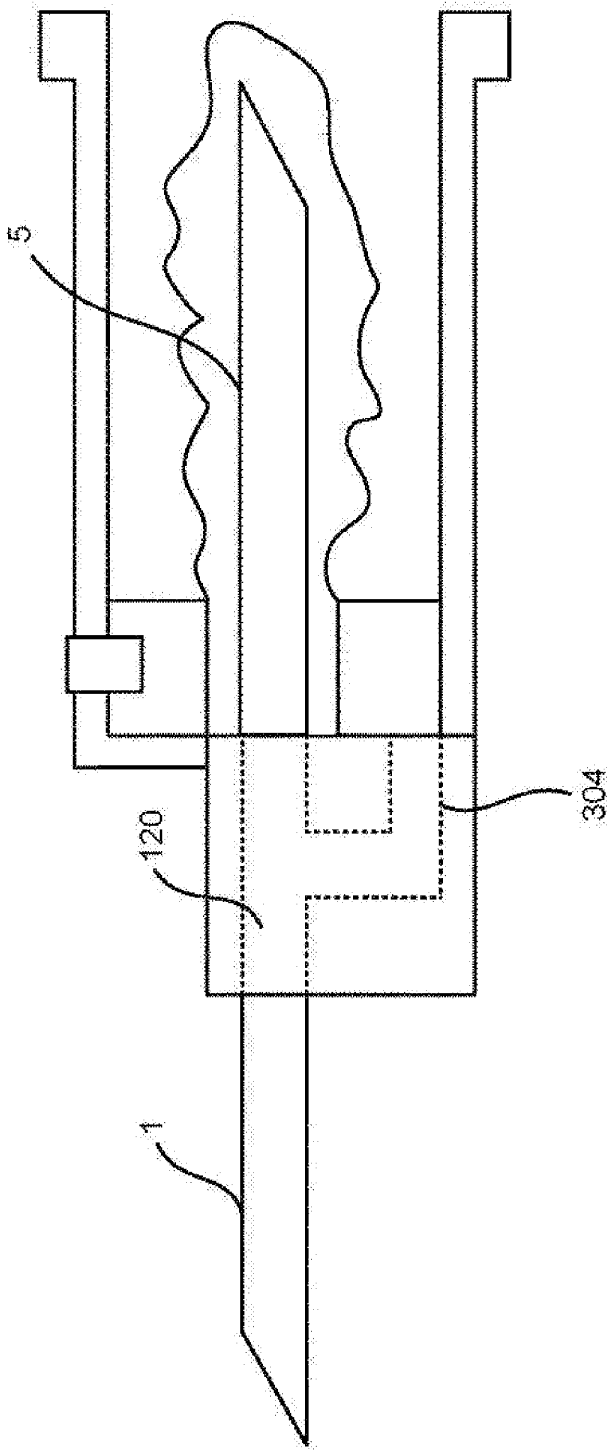


FIG. 6

[Fig. 7]

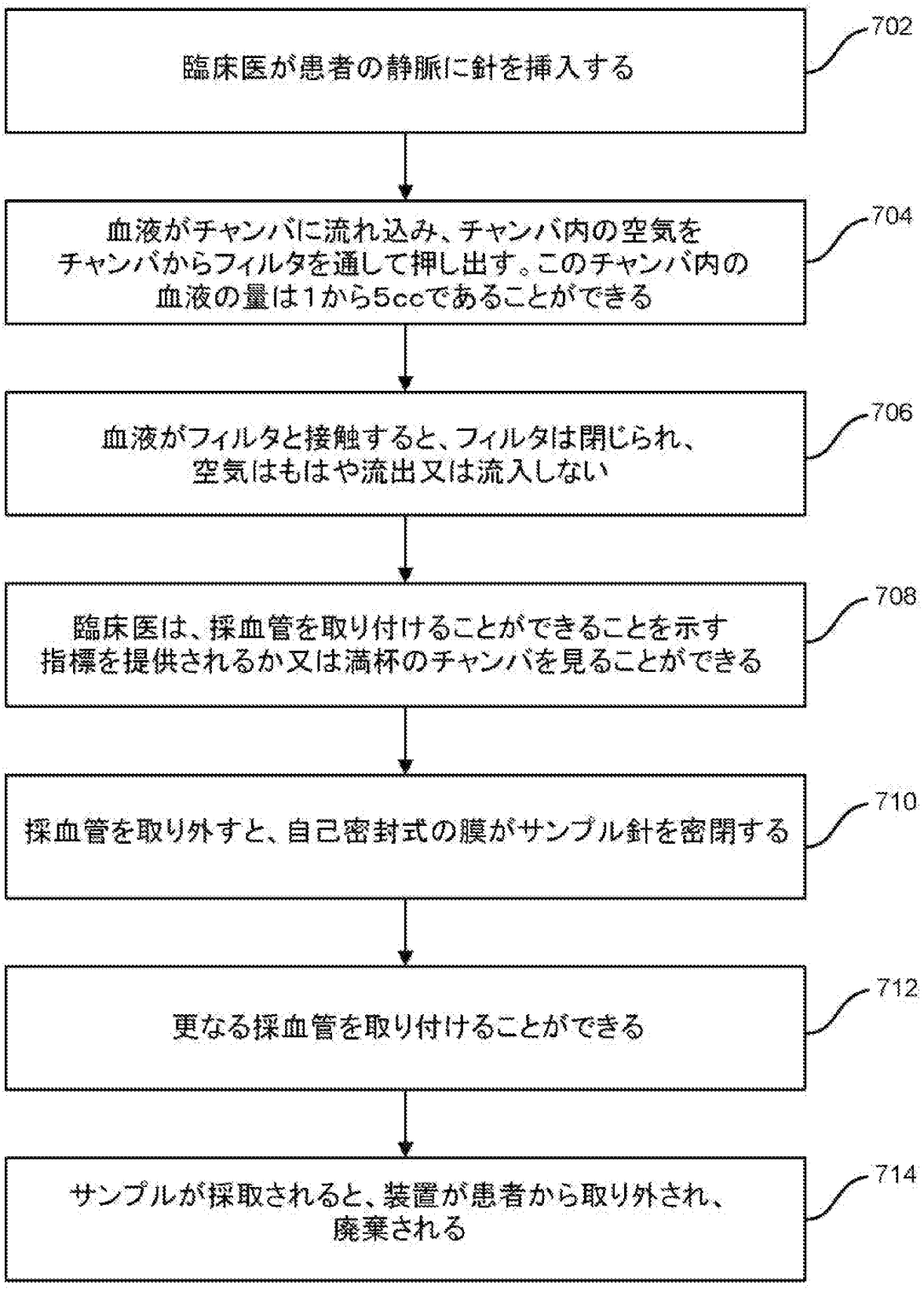

臨床医が患者の静脈に針を挿入する
702
血液がチャンバに流れ込み、チャンバ内の空気を
チャンバからフィルタを通して押し出す。このチャンバ内の
血液の量は1から5ccであることができる
704
血液がフィルタと接触すると、フィルタは閉じられ、
空気はもはや流出又は流入しない
706
臨床医は、採血管を取り付けることができることを示す
指標を提供されるか又は満杯のチャンバを見ることができる
708
採血管を取り外すと、自己密封式の膜がサンプル針を密閉する
710
更なる採血管を取り付けることができる
712
サンプルが採取されると、装置が患者から取り外され、
廃棄される
714

FIG. 7

[Fig. 8A]

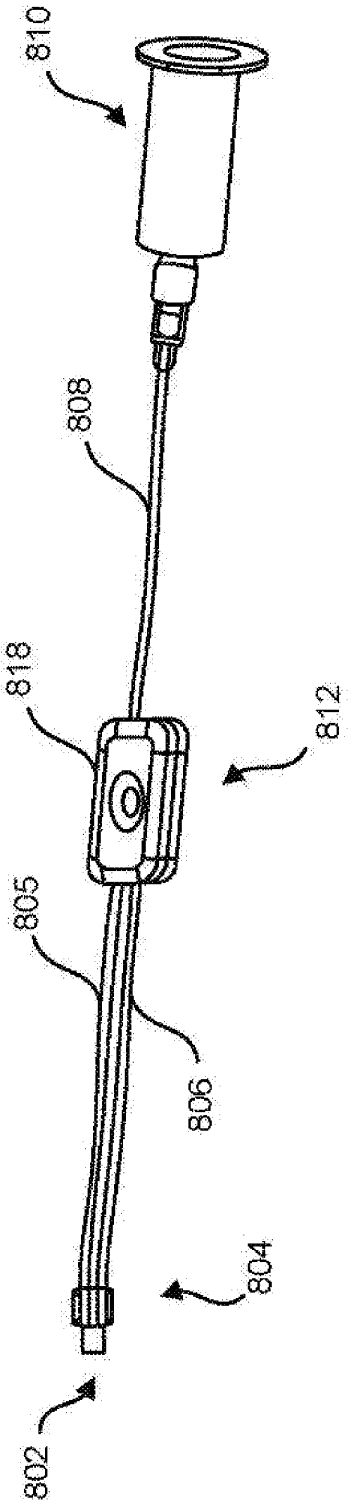


FIG. 8A

[Fig. 8B]

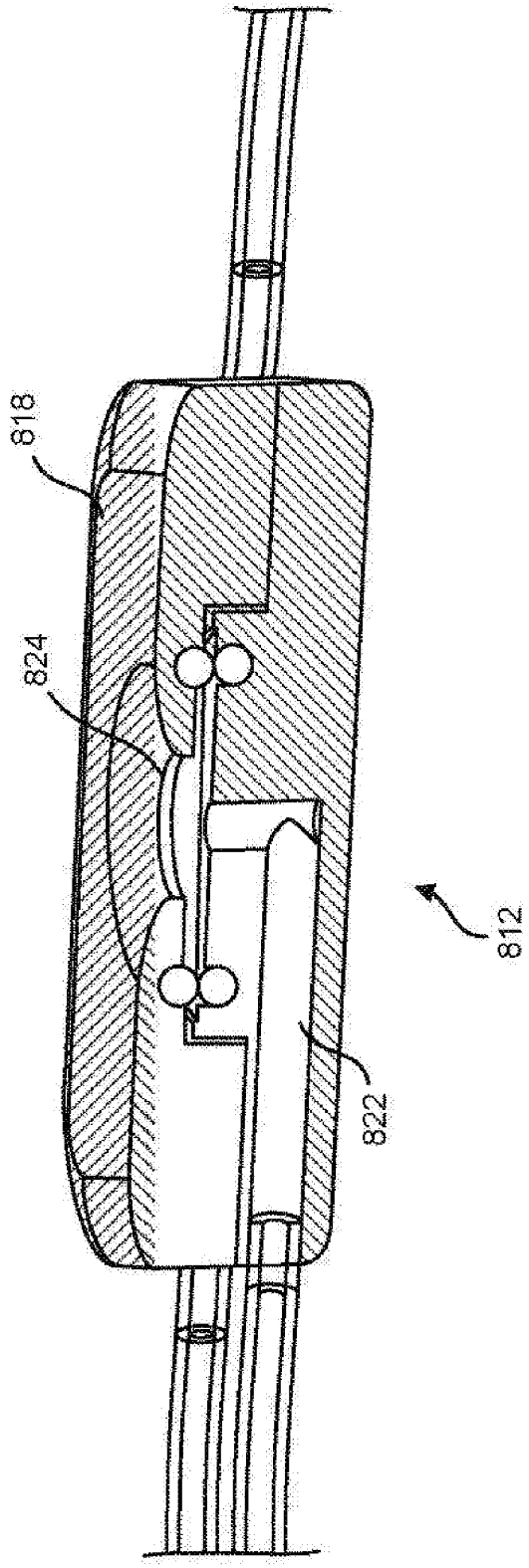


FIG. 8B

[Fig. 8C]

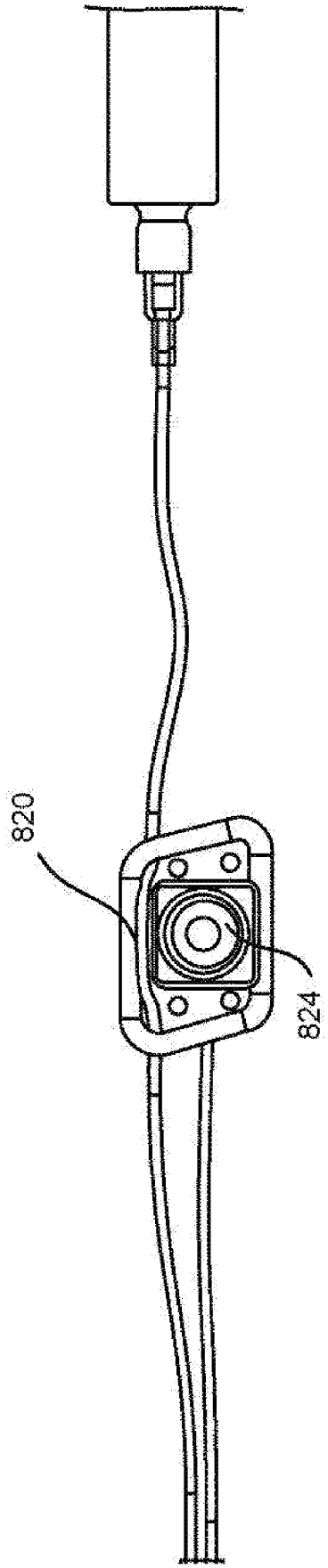


FIG. 8C

[Fig. 8D]



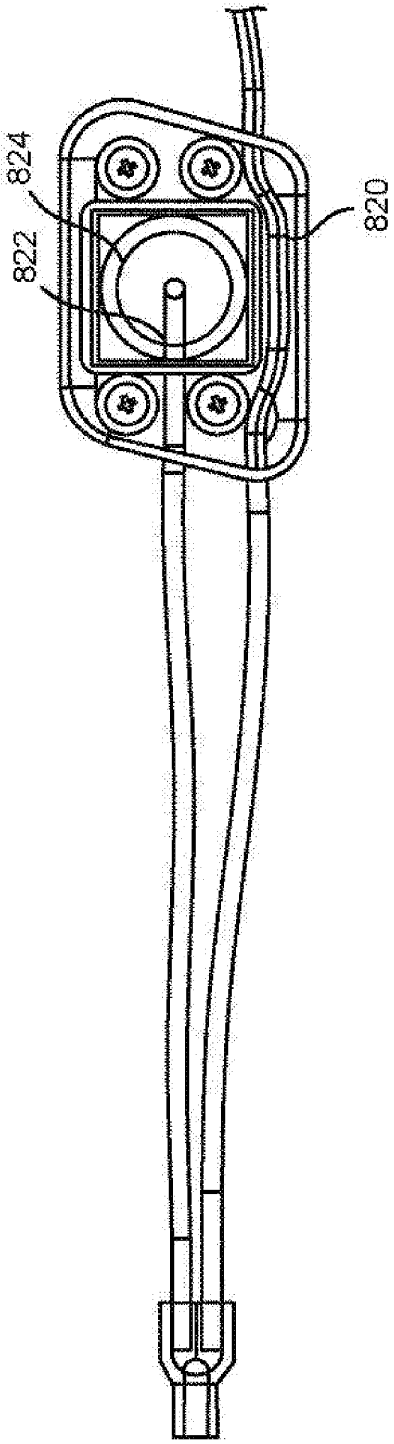


FIG. 8D

[Fig. 8E]

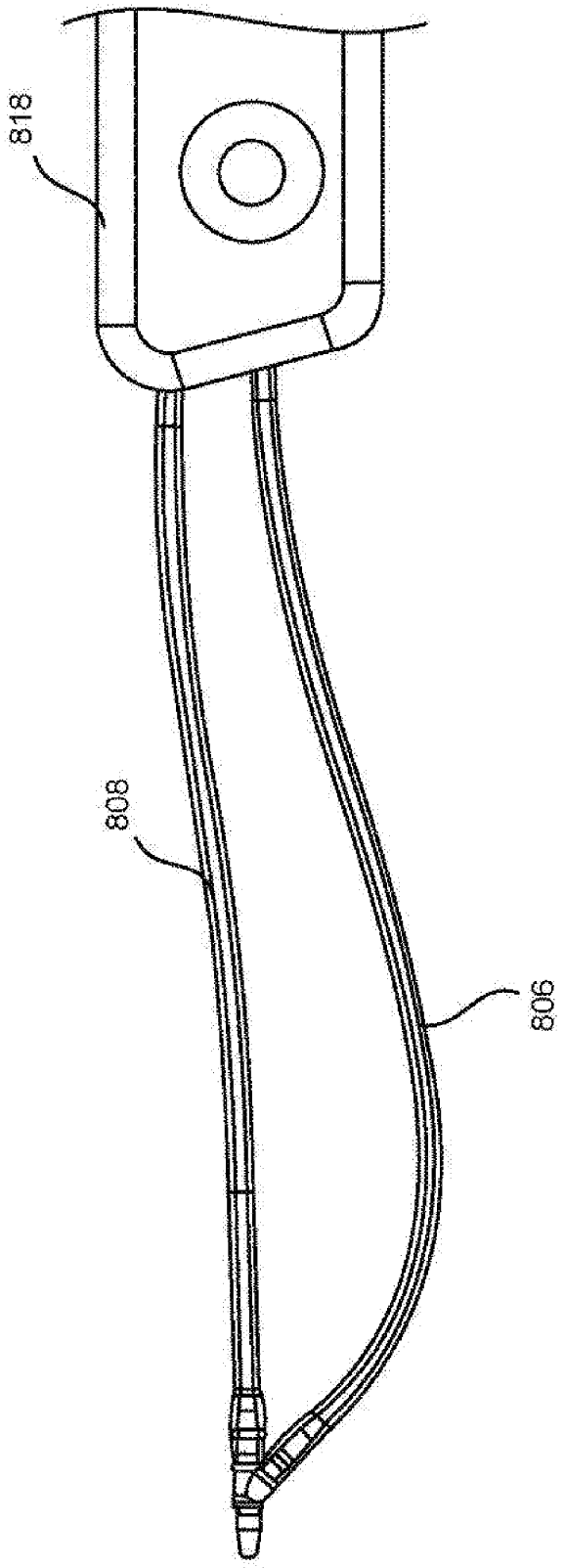


FIG. 8E

[Fig. 9]

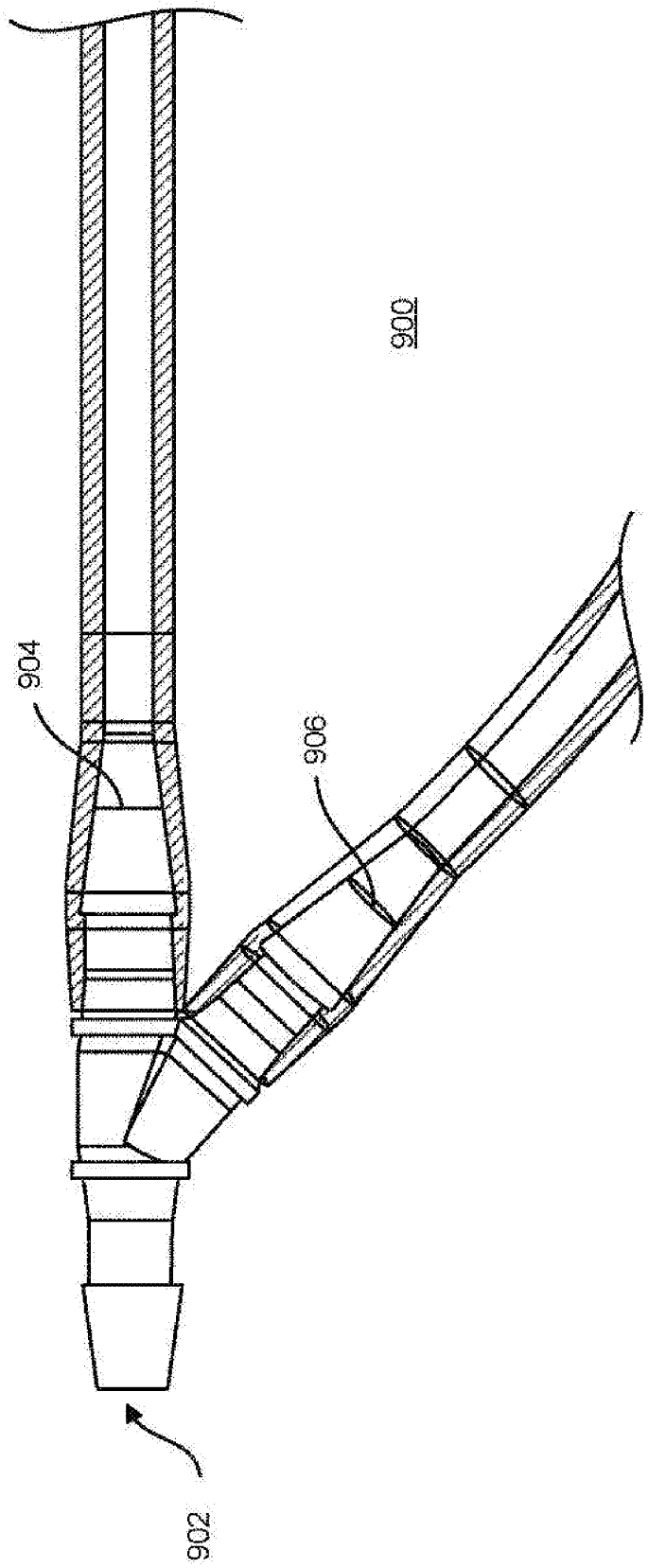


FIG. 9

[Fig. 10A]

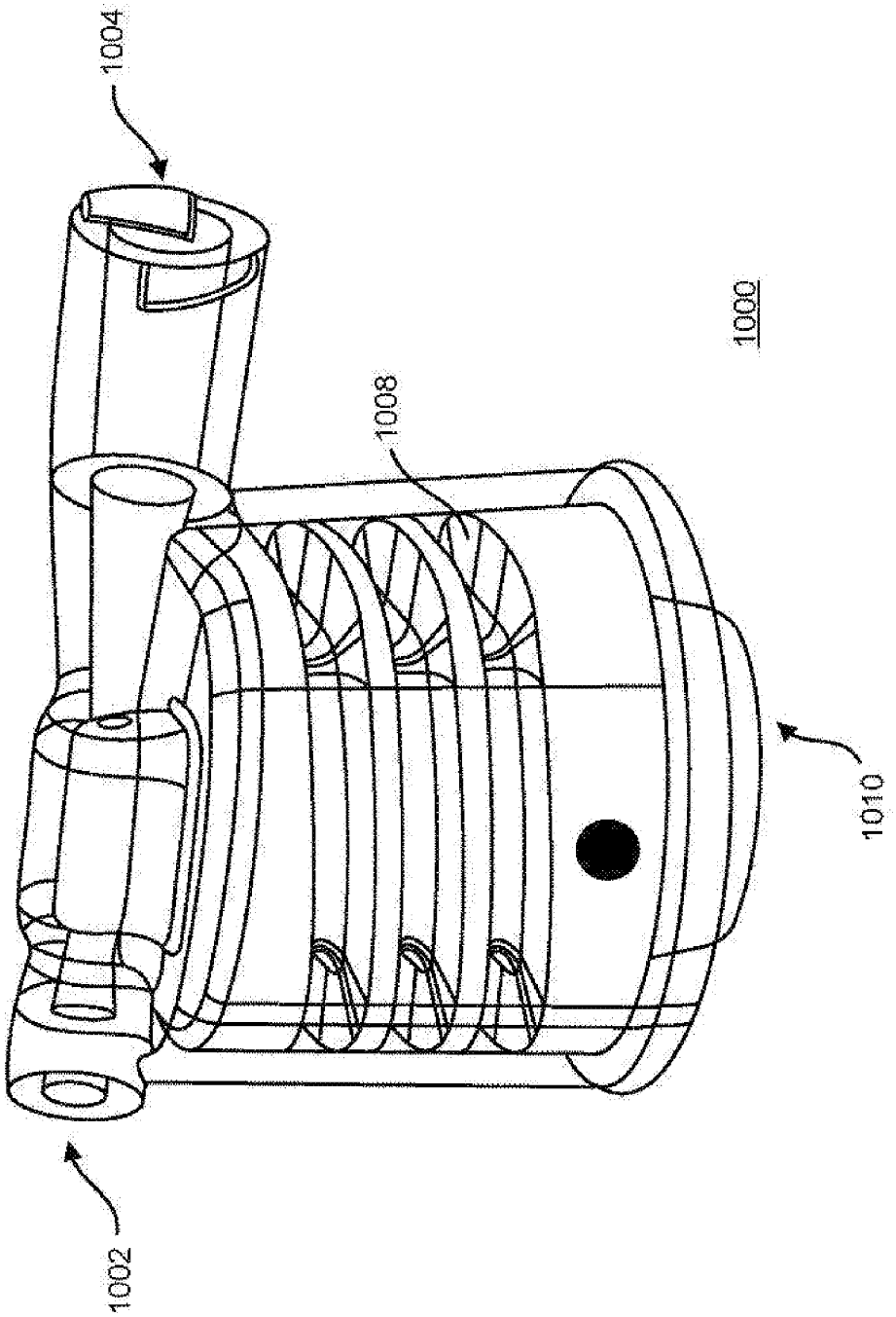


FIG. 10A

[Fig. 10B]

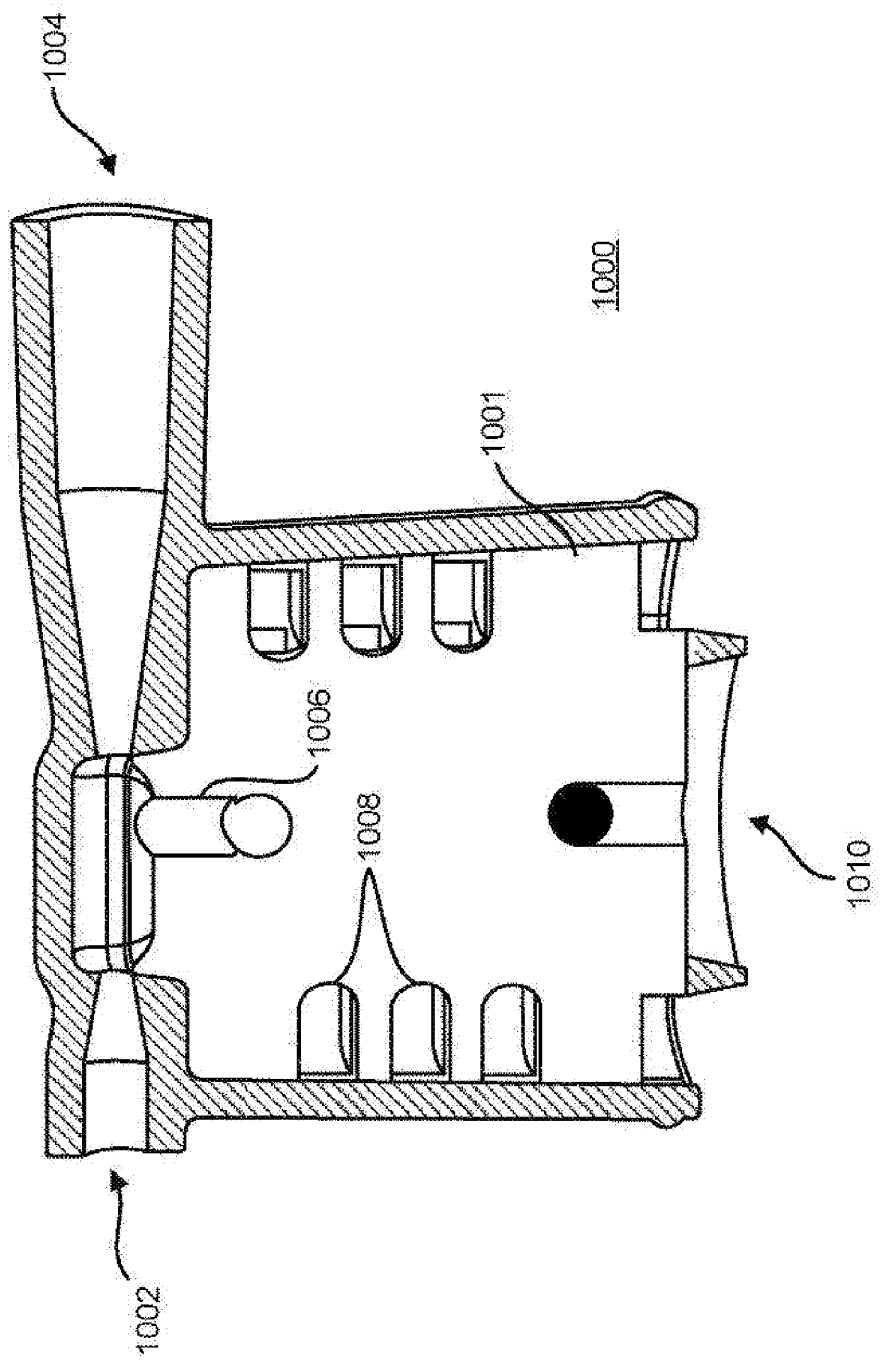


FIG. 10B

[Fig. 10C]

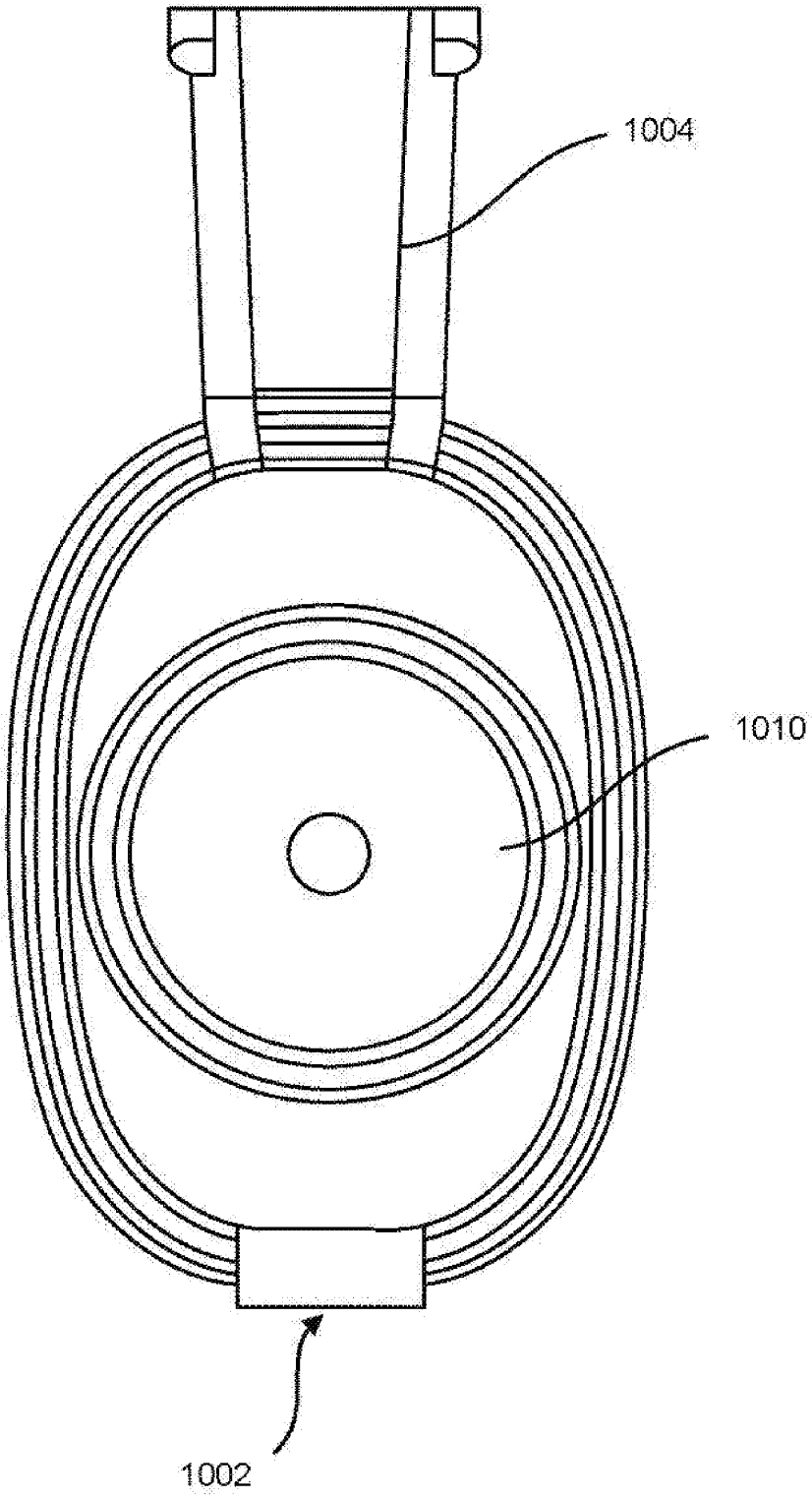
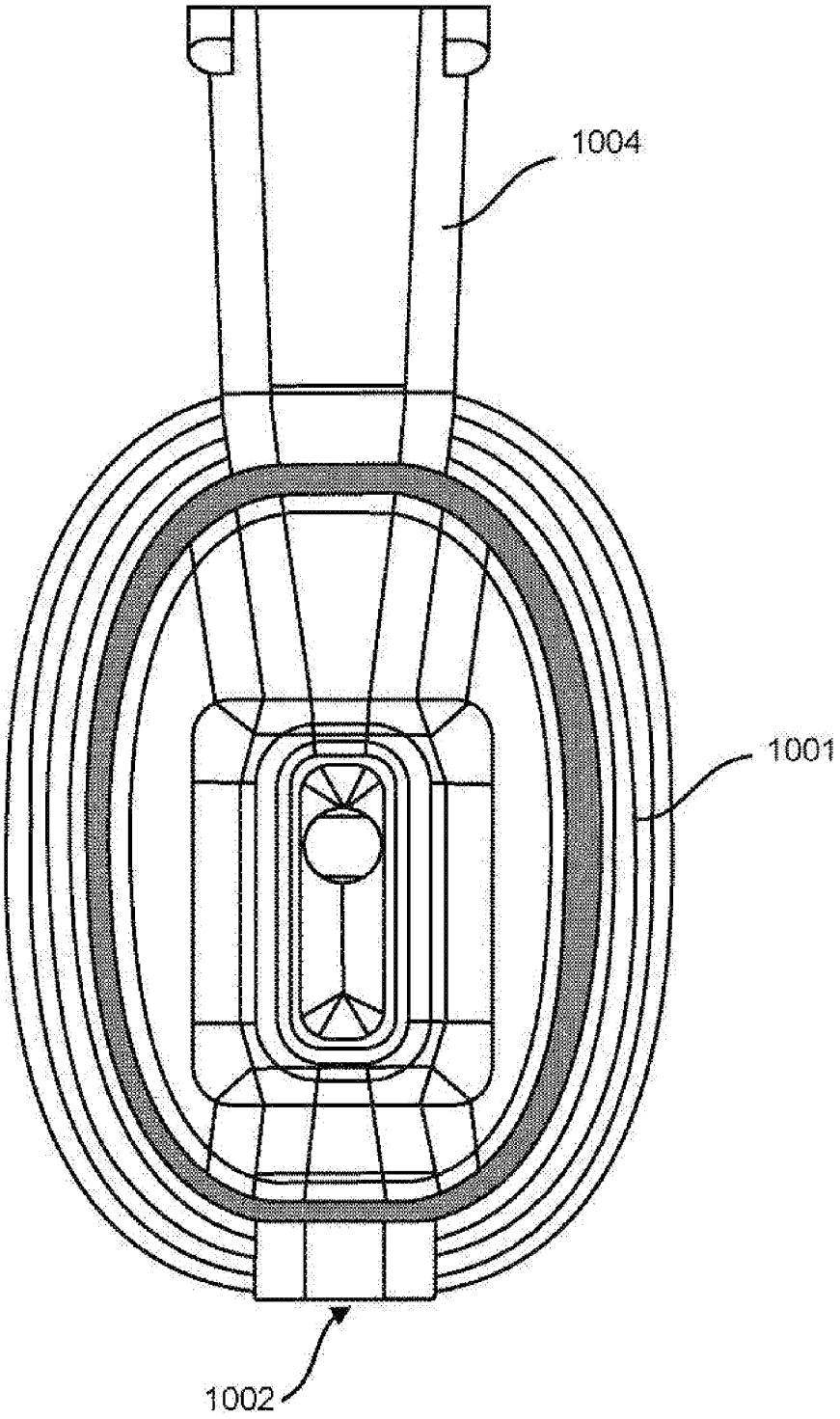


FIG. 10C

[Fig. 10D]




1004
1001
1002

[Fig. 11A]

FIG. 10D

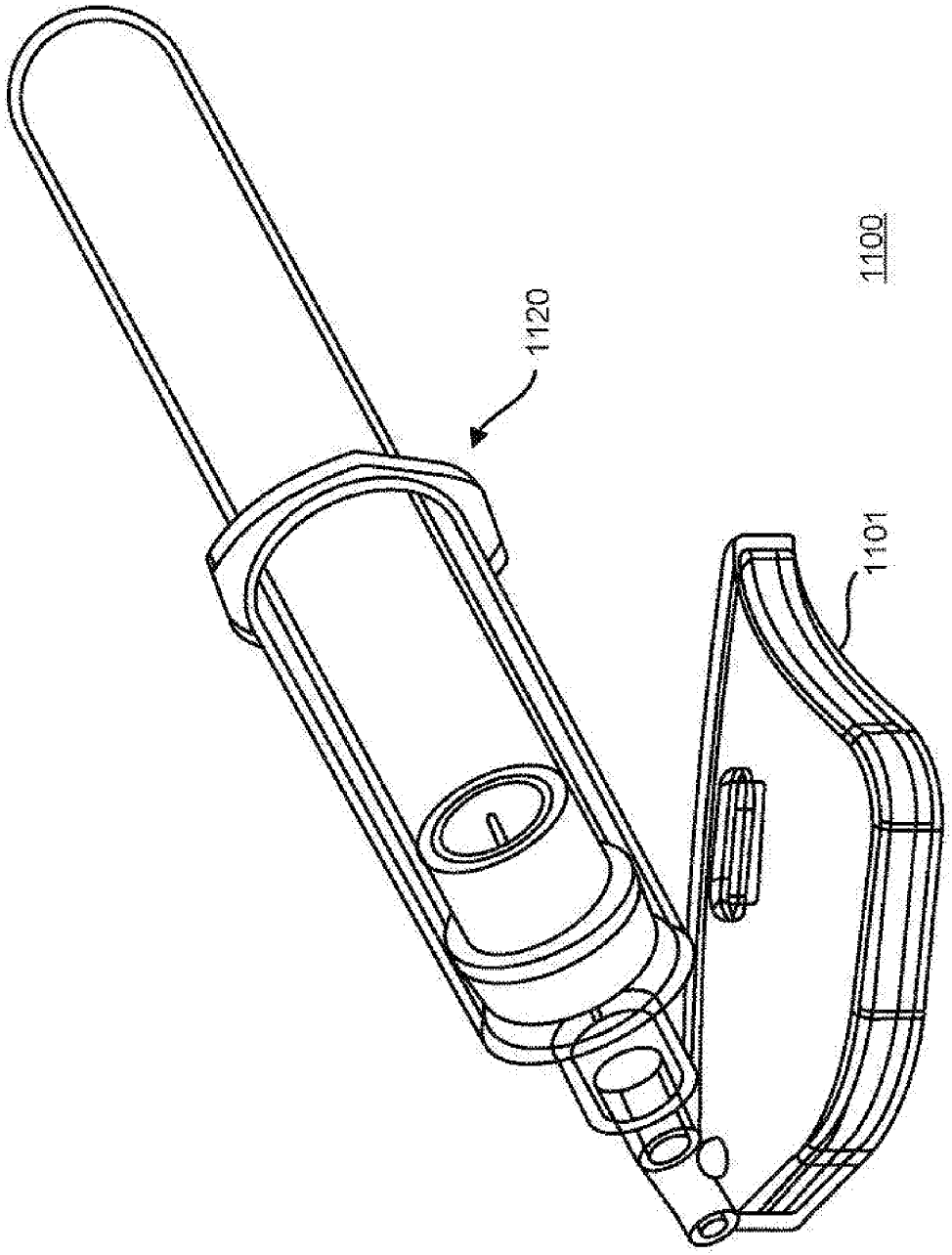


FIG. 11A

[Fig. 11B]

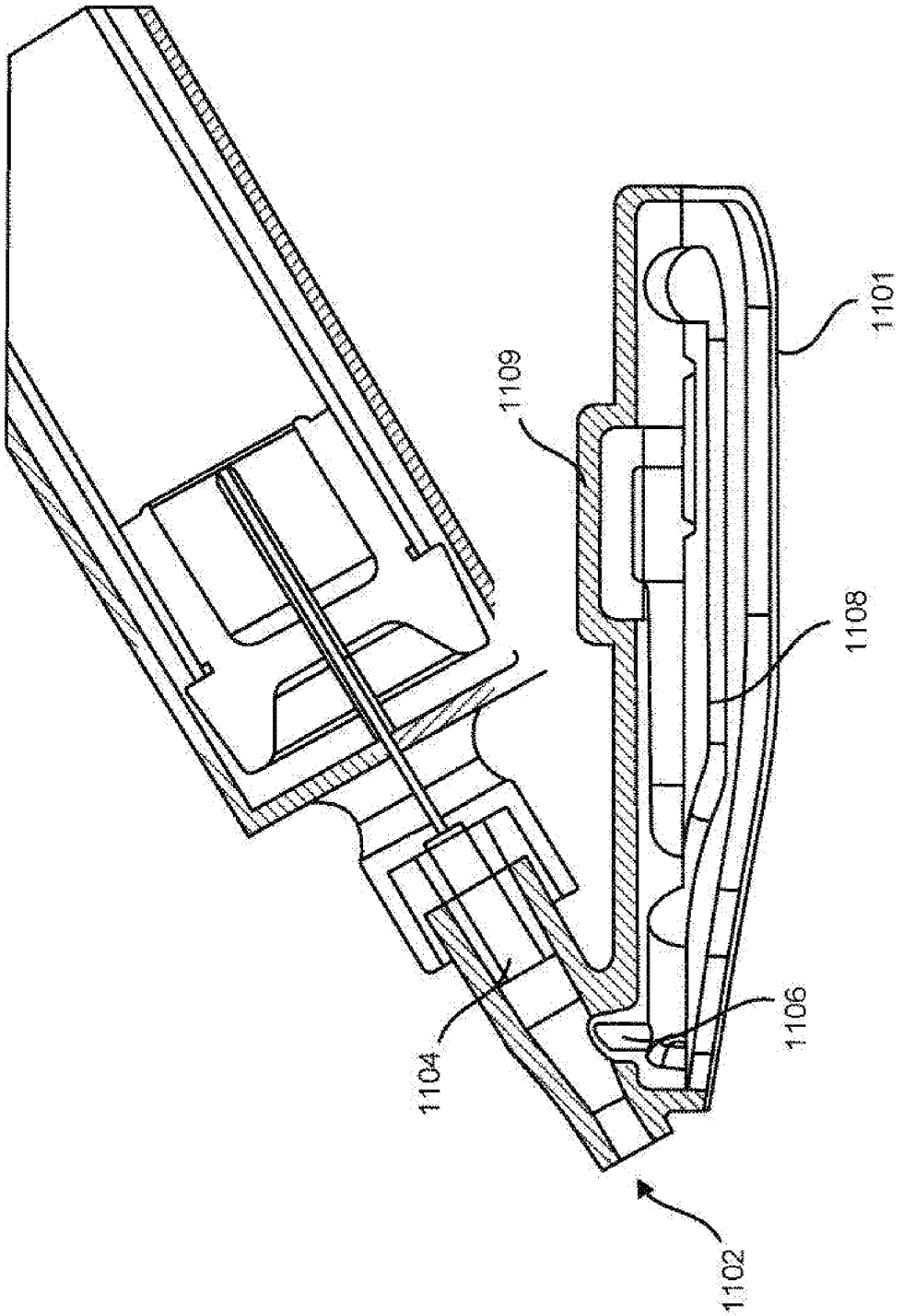
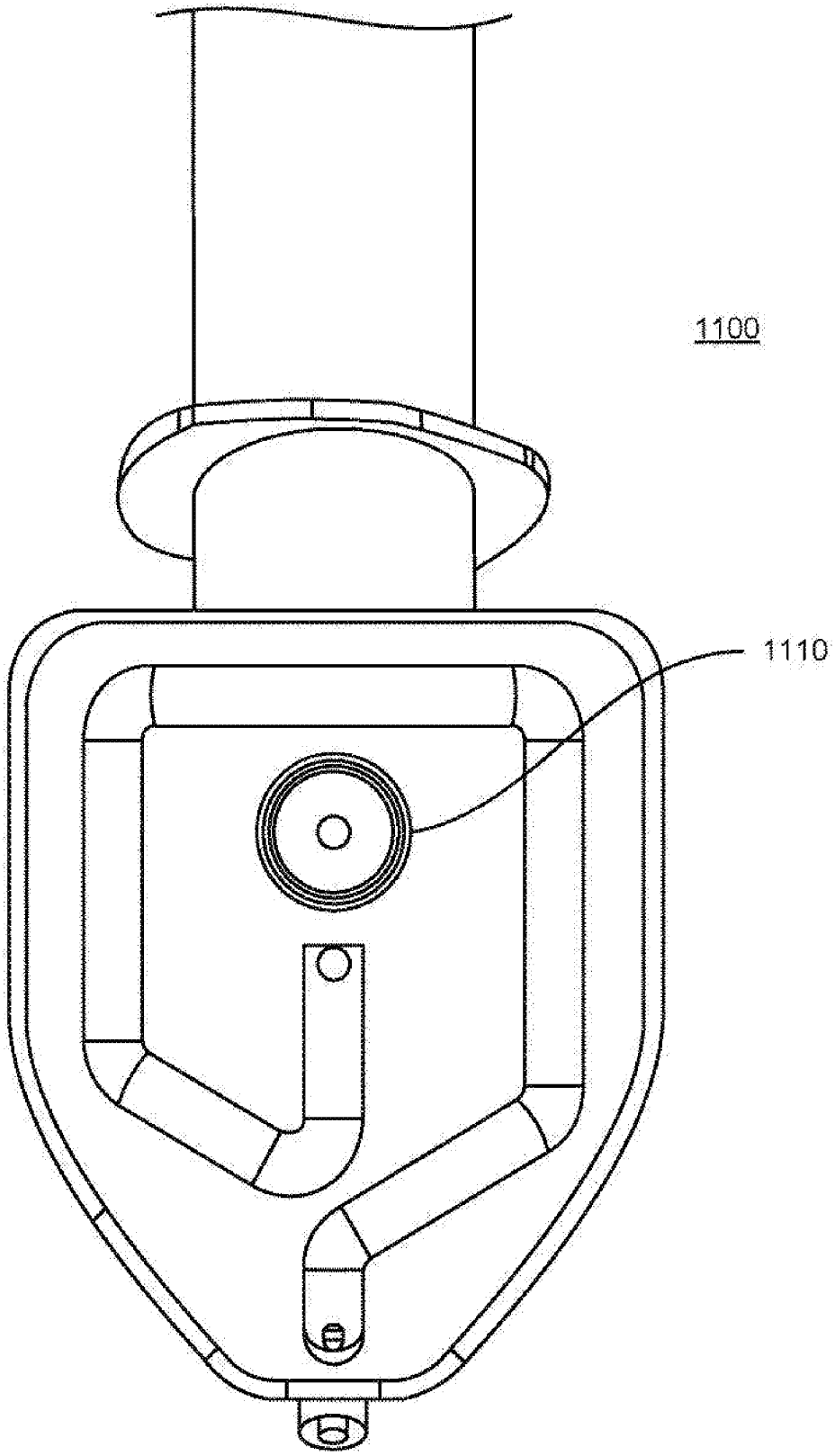


FIG. 11B

[Fig. 11C]


1100
1110

[Fig. 11D]

FIG. 11C

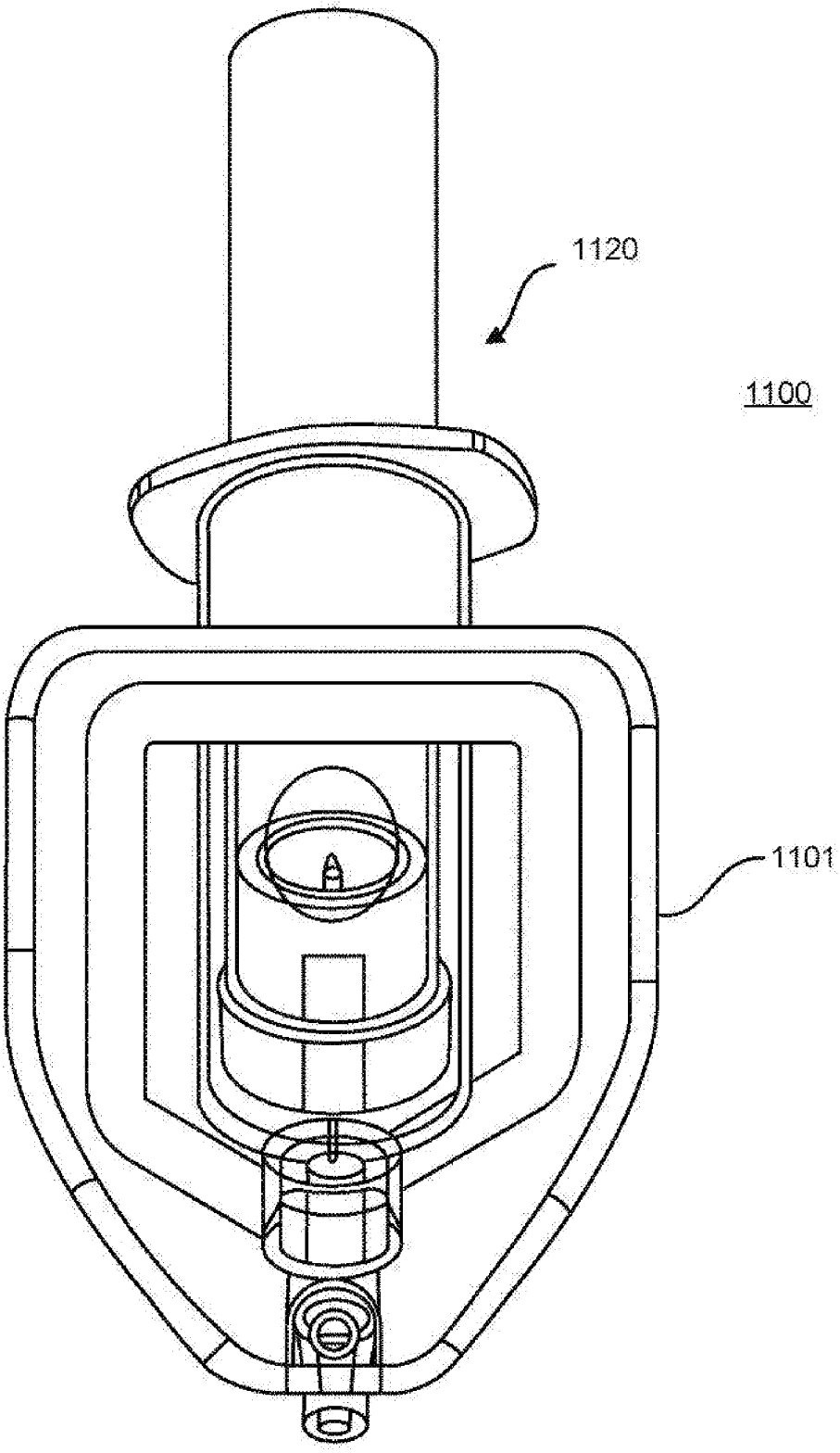


FIG. 11D

[Fig. 11E]

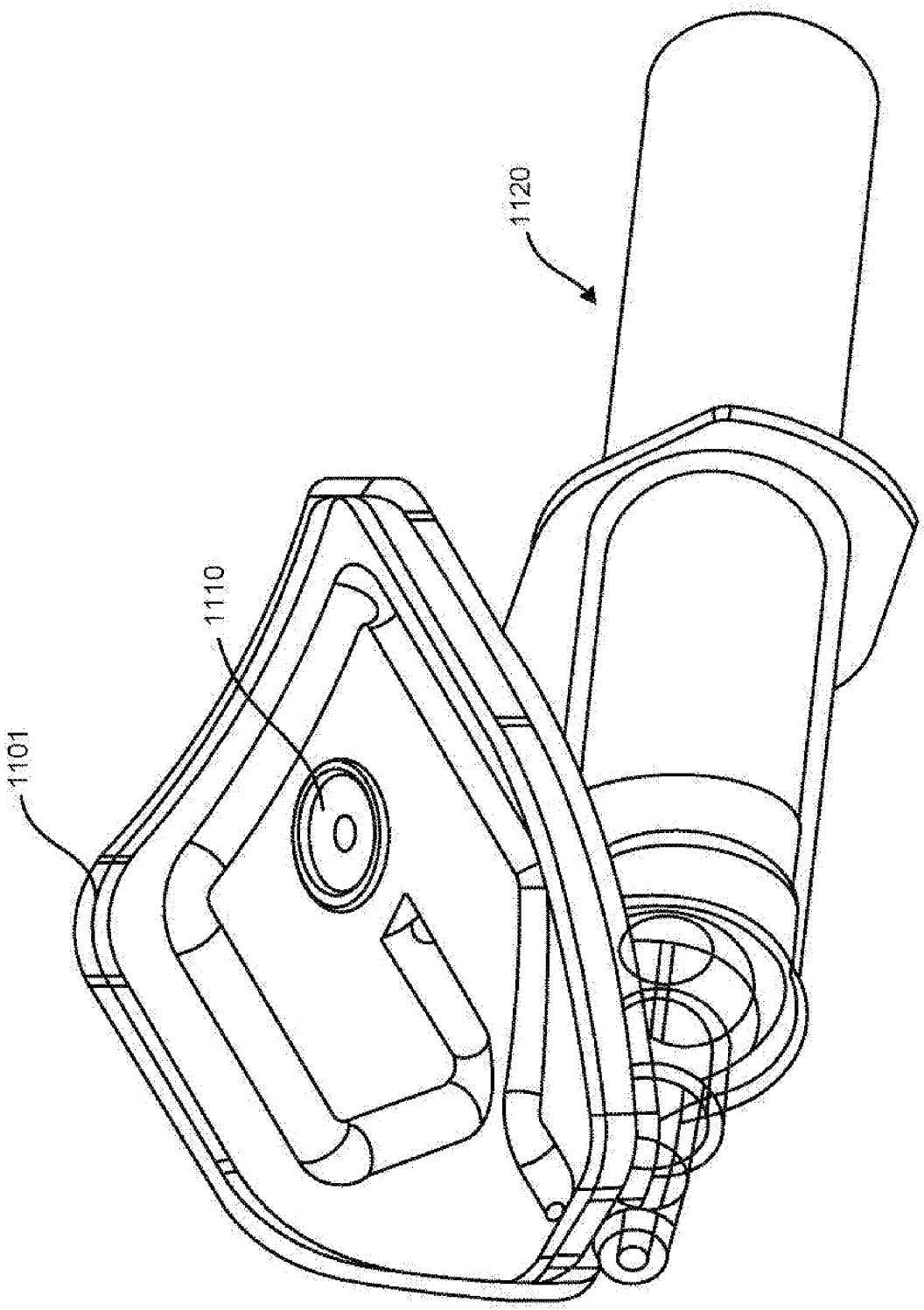


FIG. 11E

[Fig. 12A]

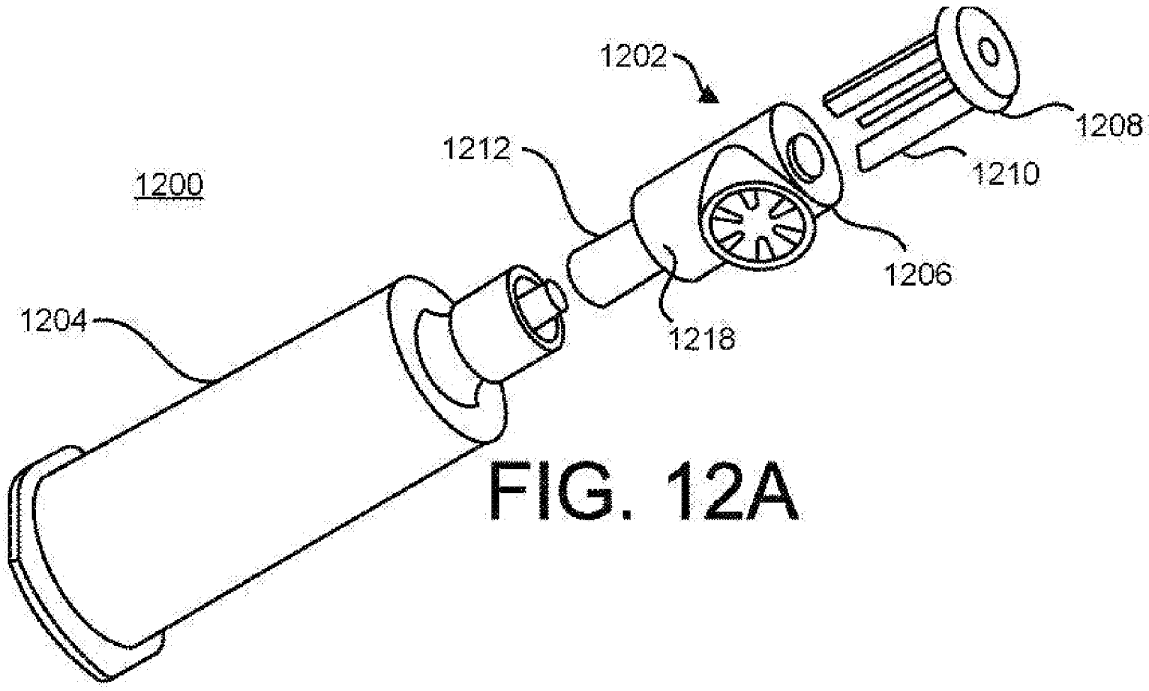


FIG. 12A

[Fig. 12B]

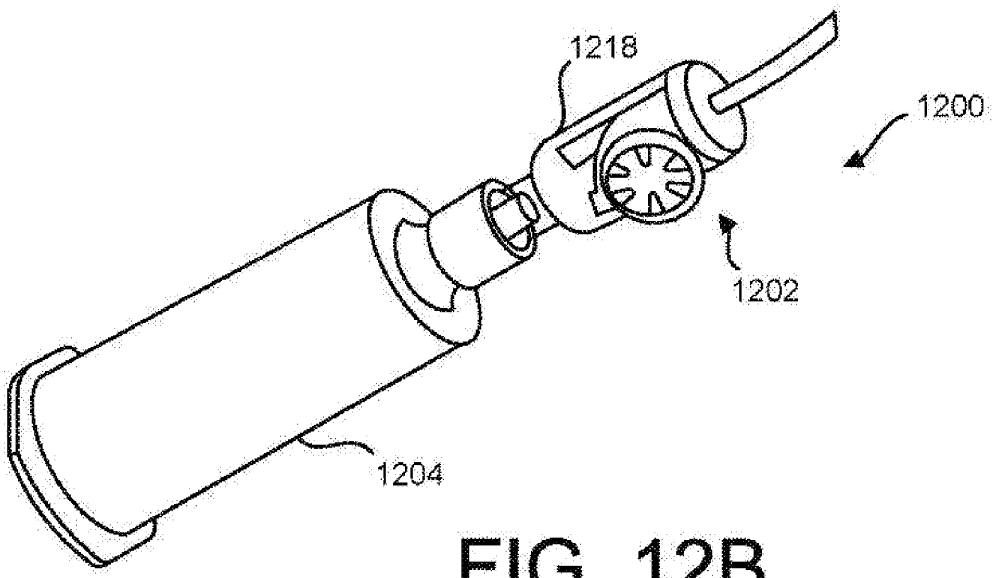


FIG. 12B

[Fig. 12C]

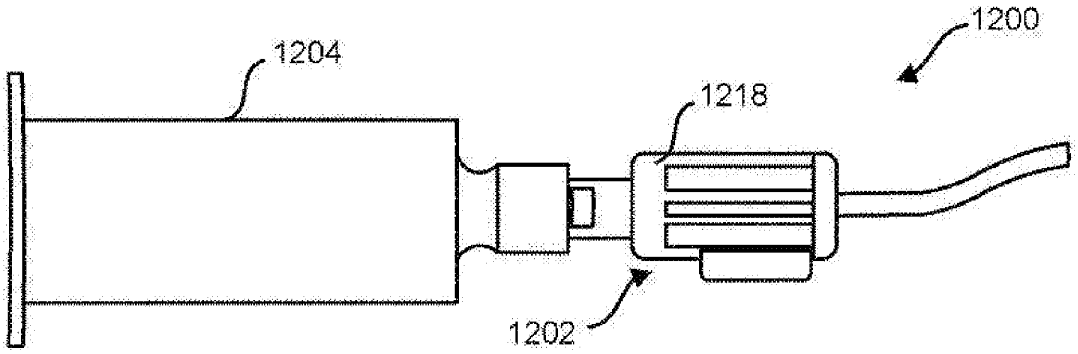


FIG. 12C

[Fig. 12D]

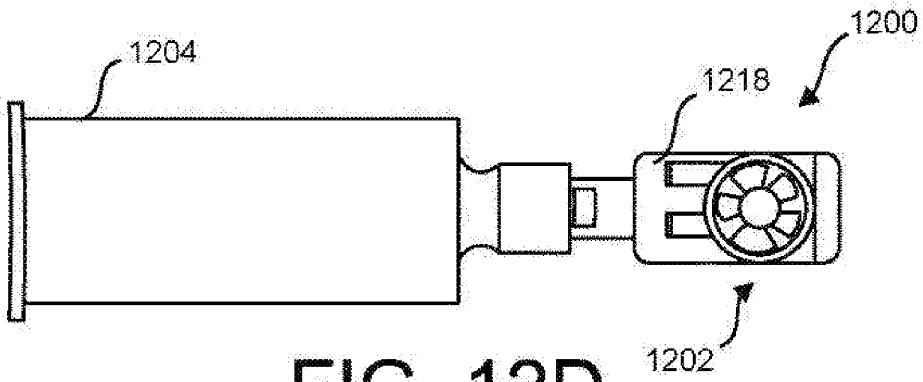


FIG. 12D

[Fig. 13A]

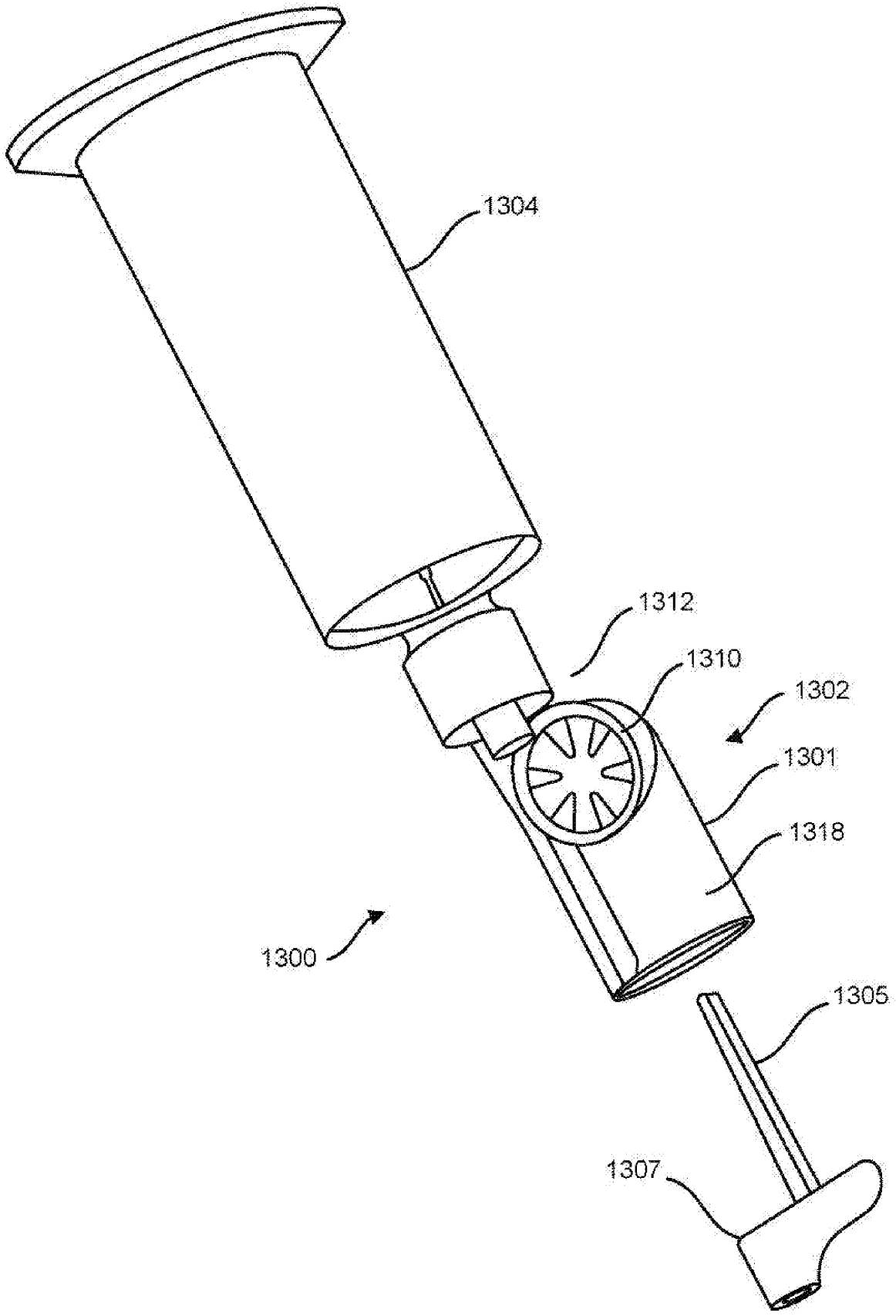


FIG. 13A

[Fig. 13B]

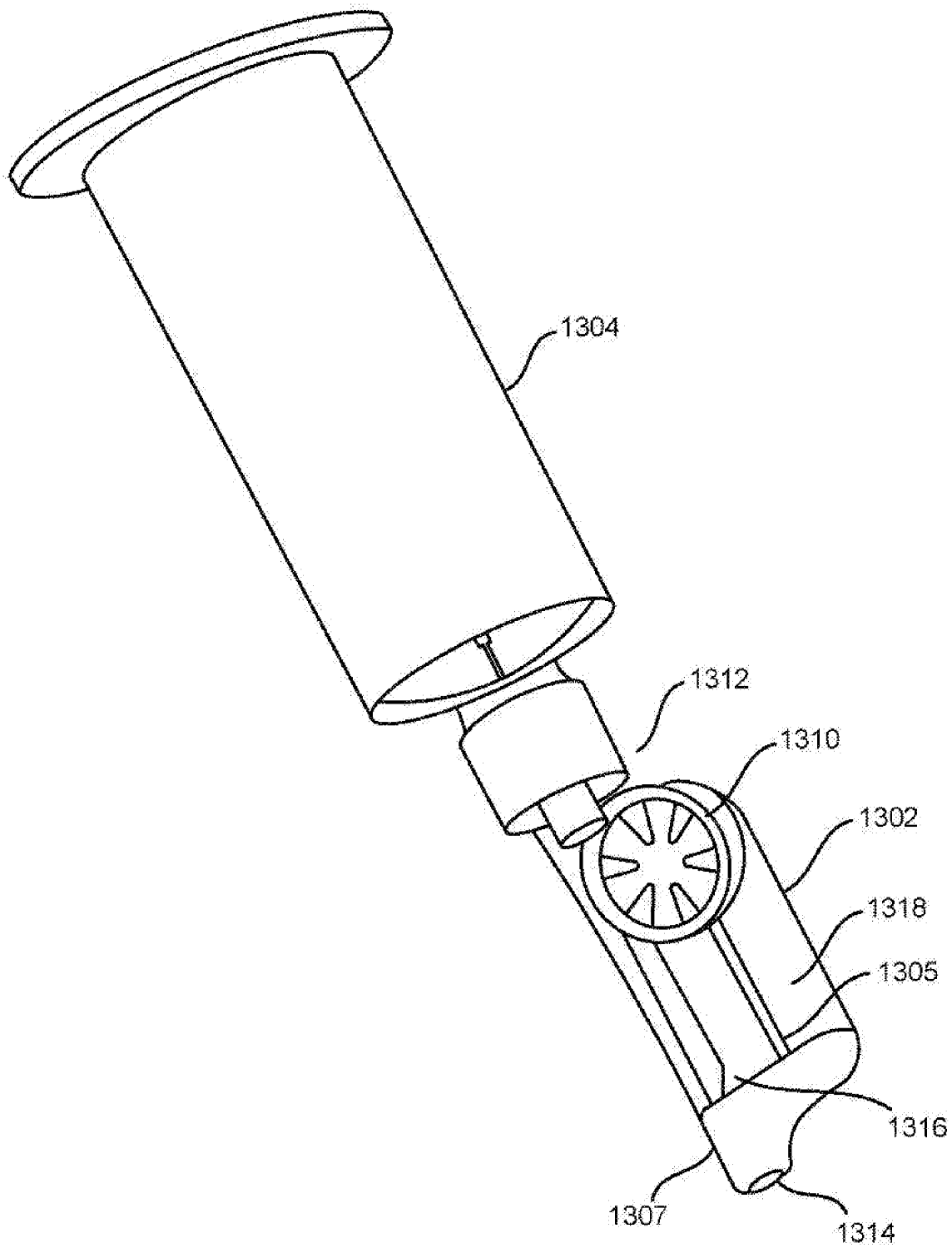


FIG. 13B

[Fig. 13C]

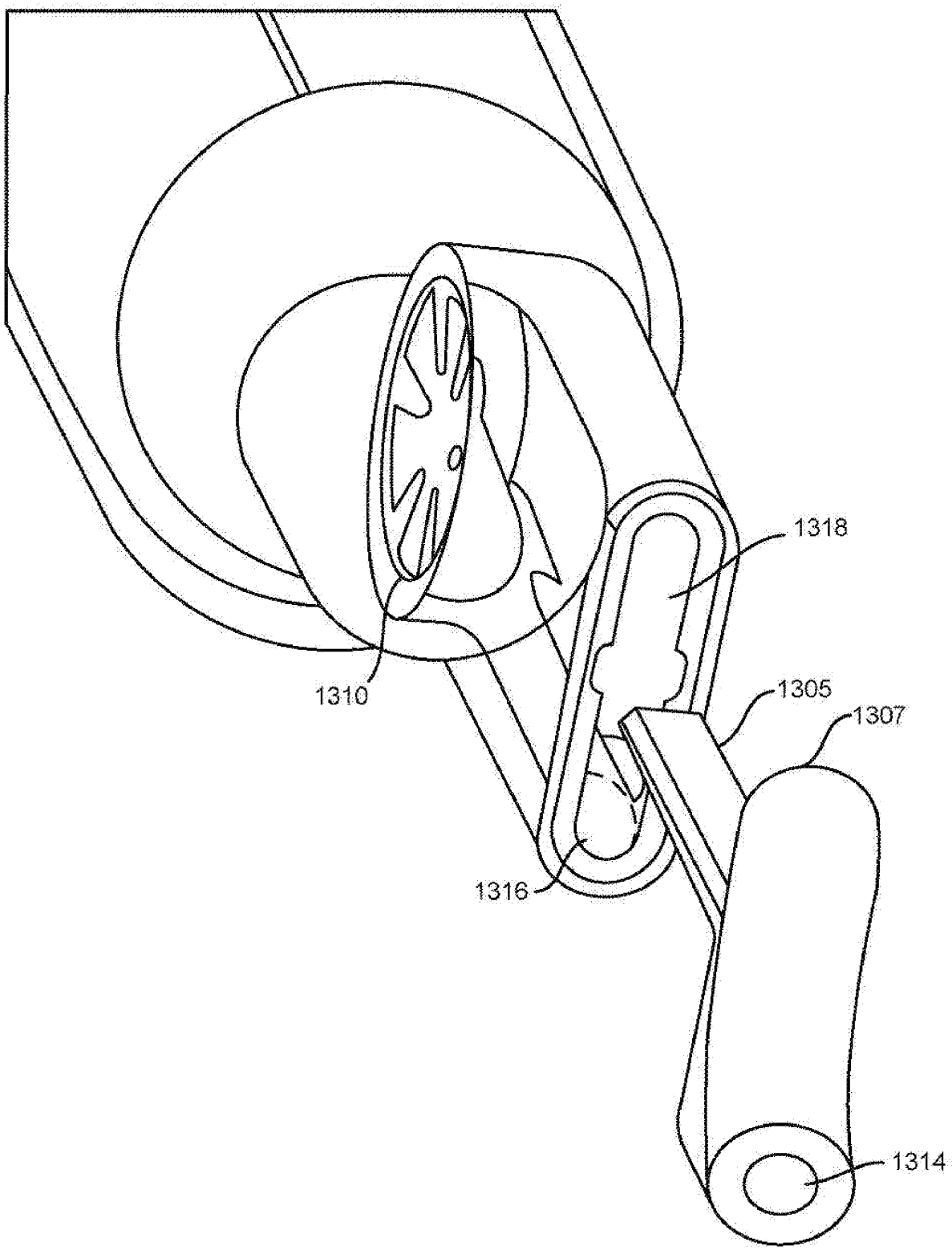
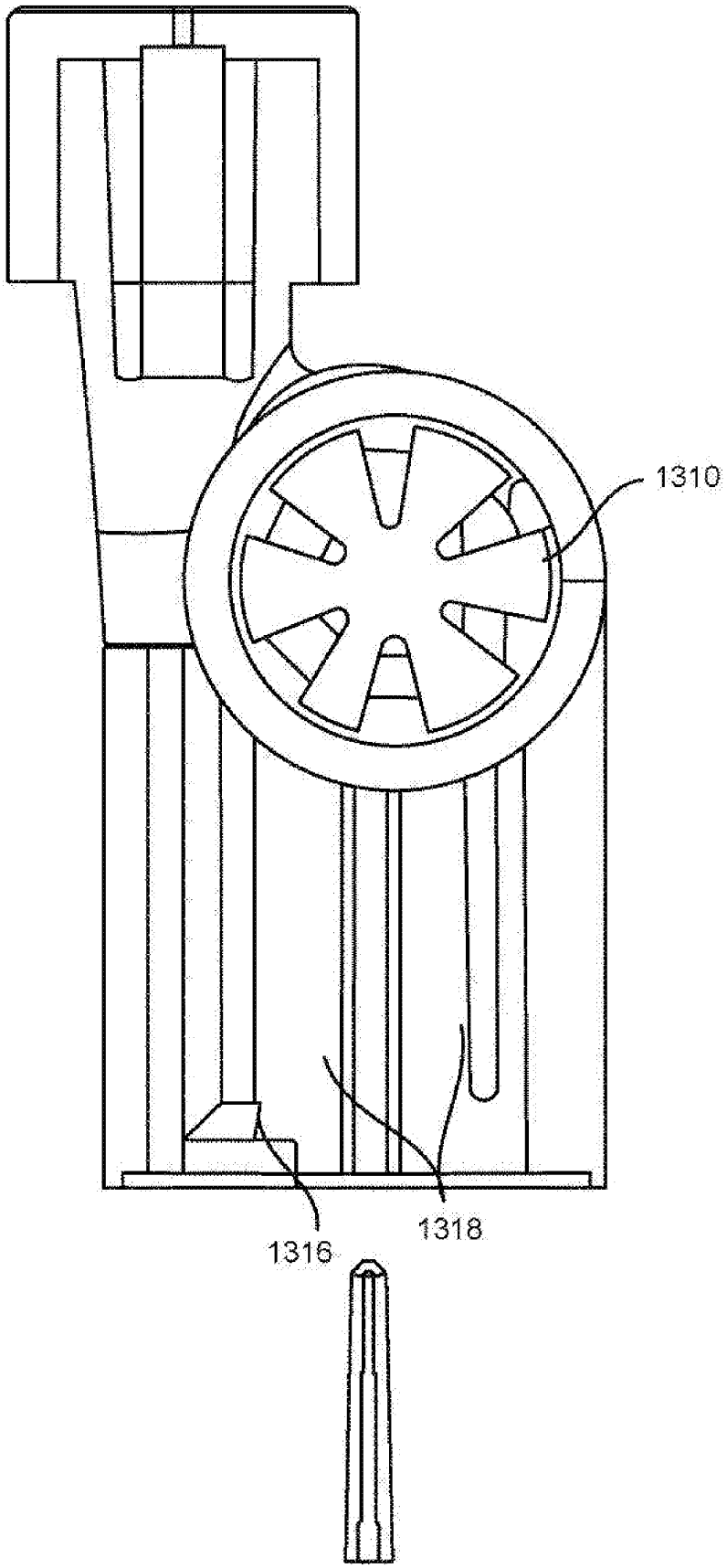


FIG. 13C

[Fig. 13D]


1310
1316
1318

[Fig. 14A]

FIG. 13D

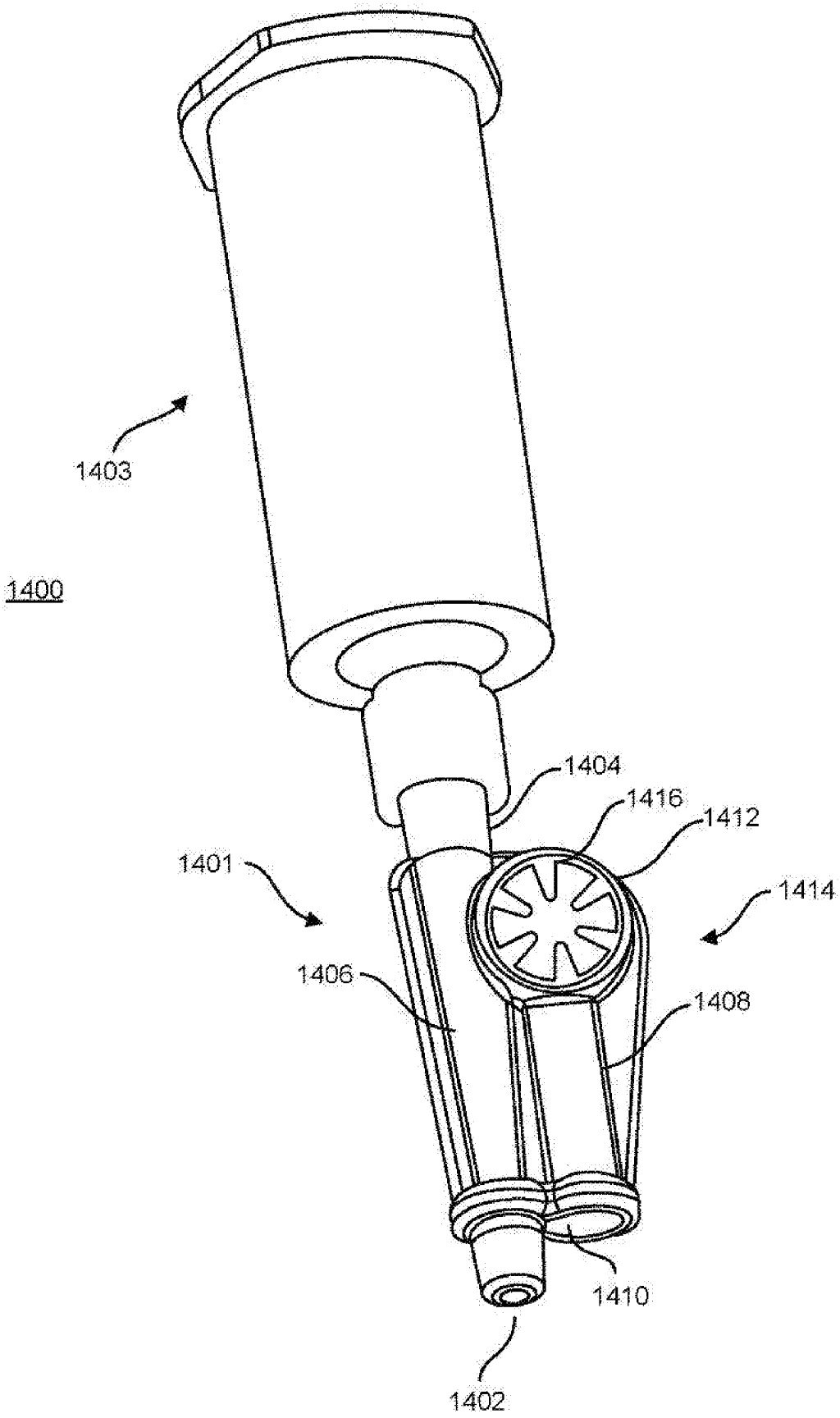
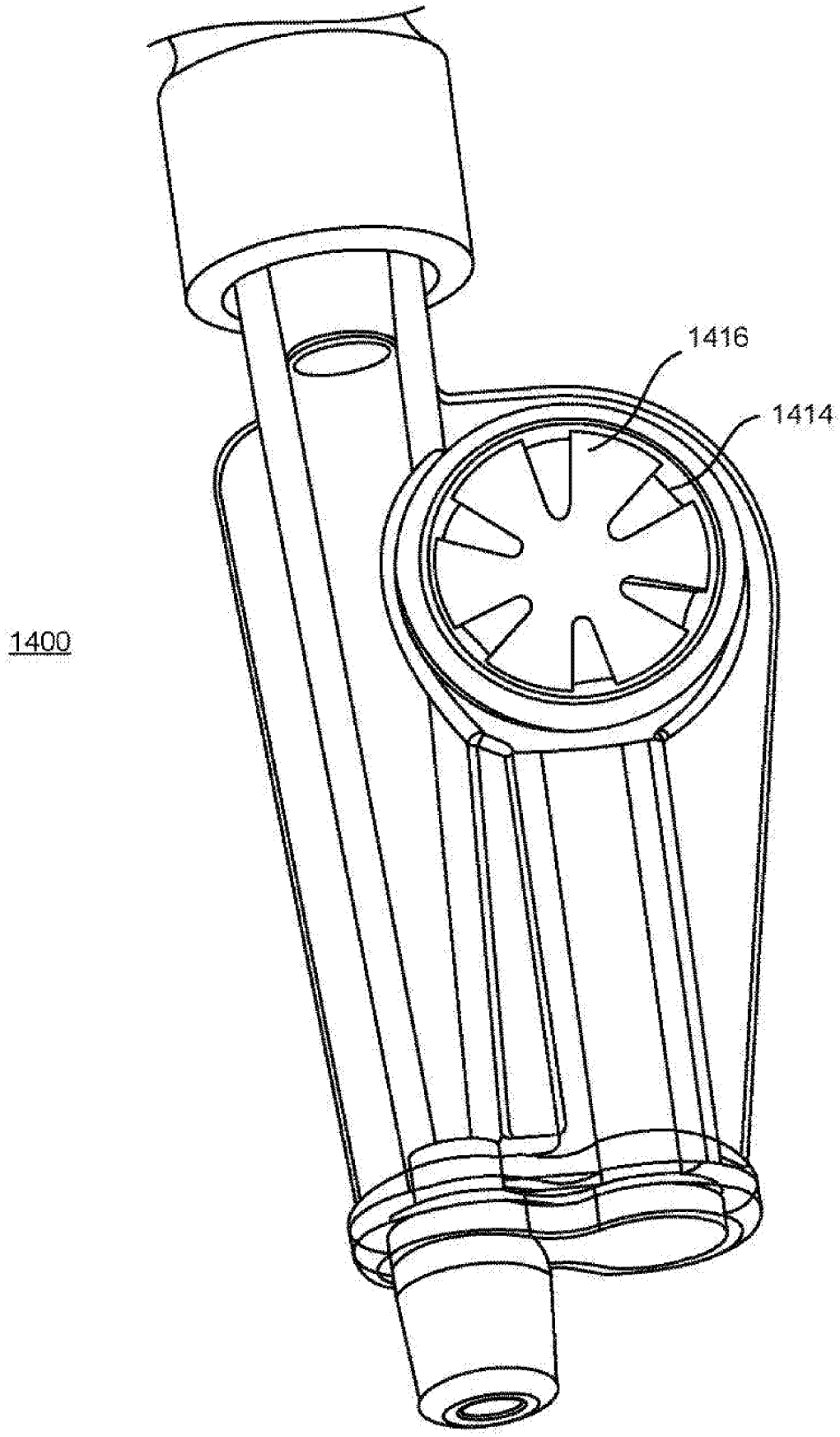


FIG. 14A

[Fig. 14B]


1400
1416
1414

[Fig. 14C]

FIG. 14B

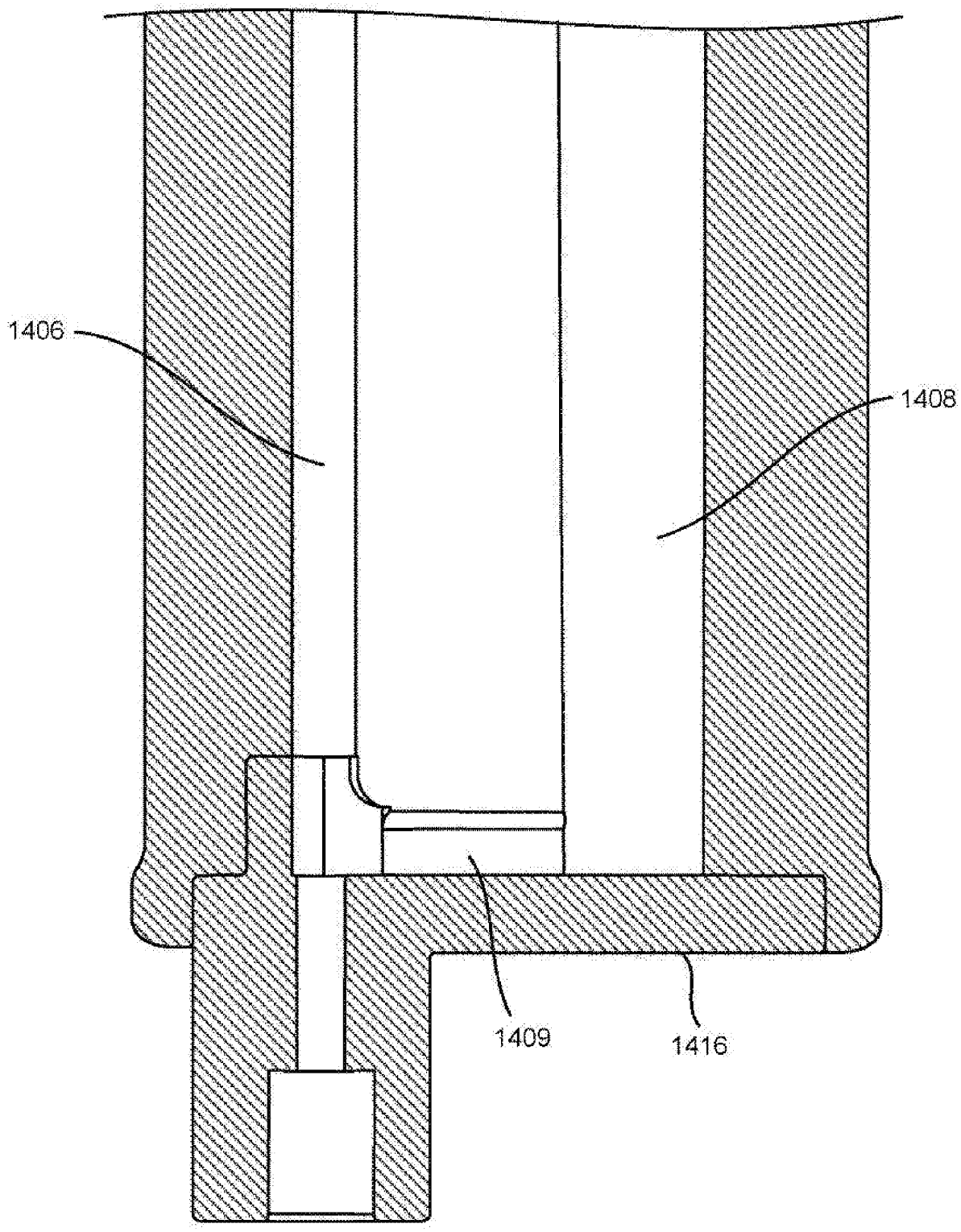
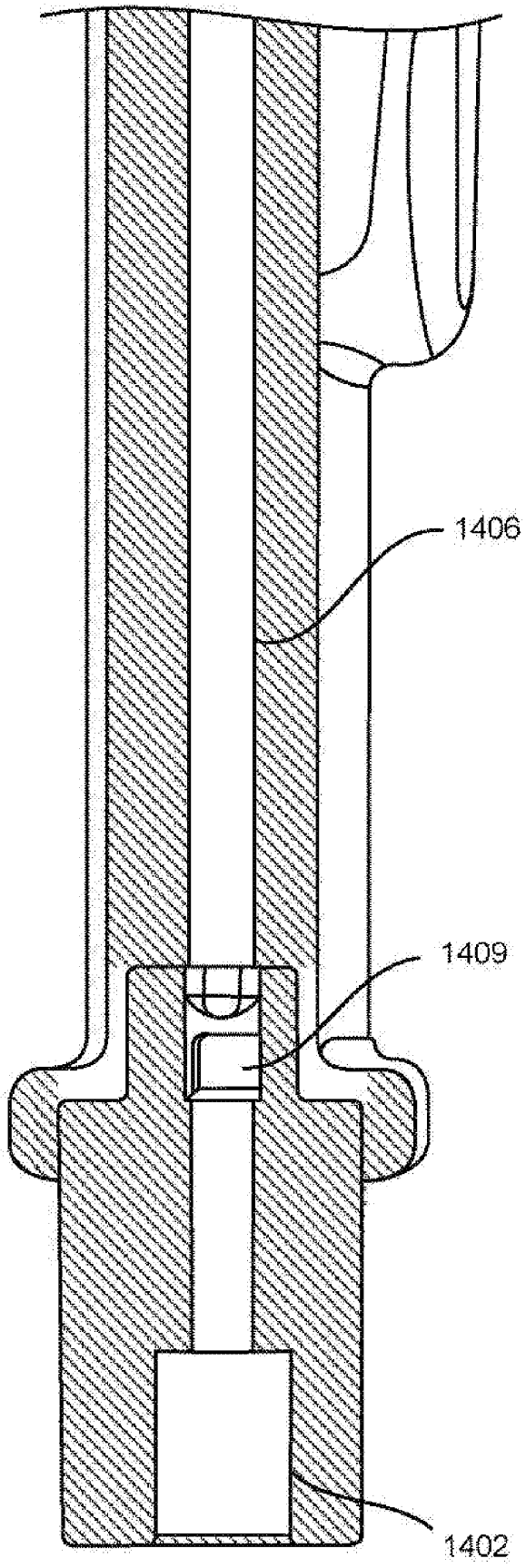


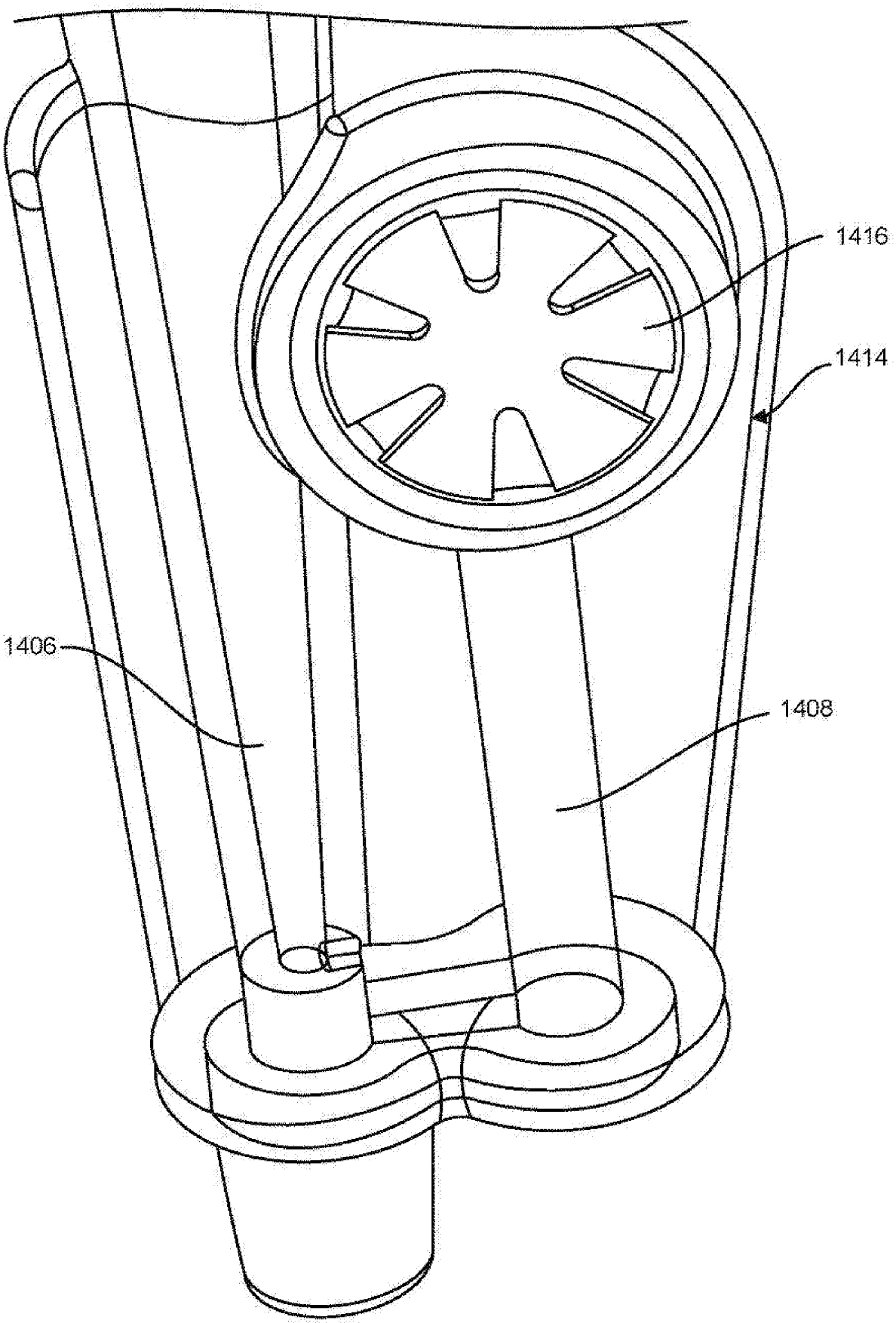
FIG. 14C

[Fig. 14D]


1406
1409
1402

[Fig. 14E]

FIG. 14D


1416
1414
1406
1408

[Fig. 15A]

FIG. 14E

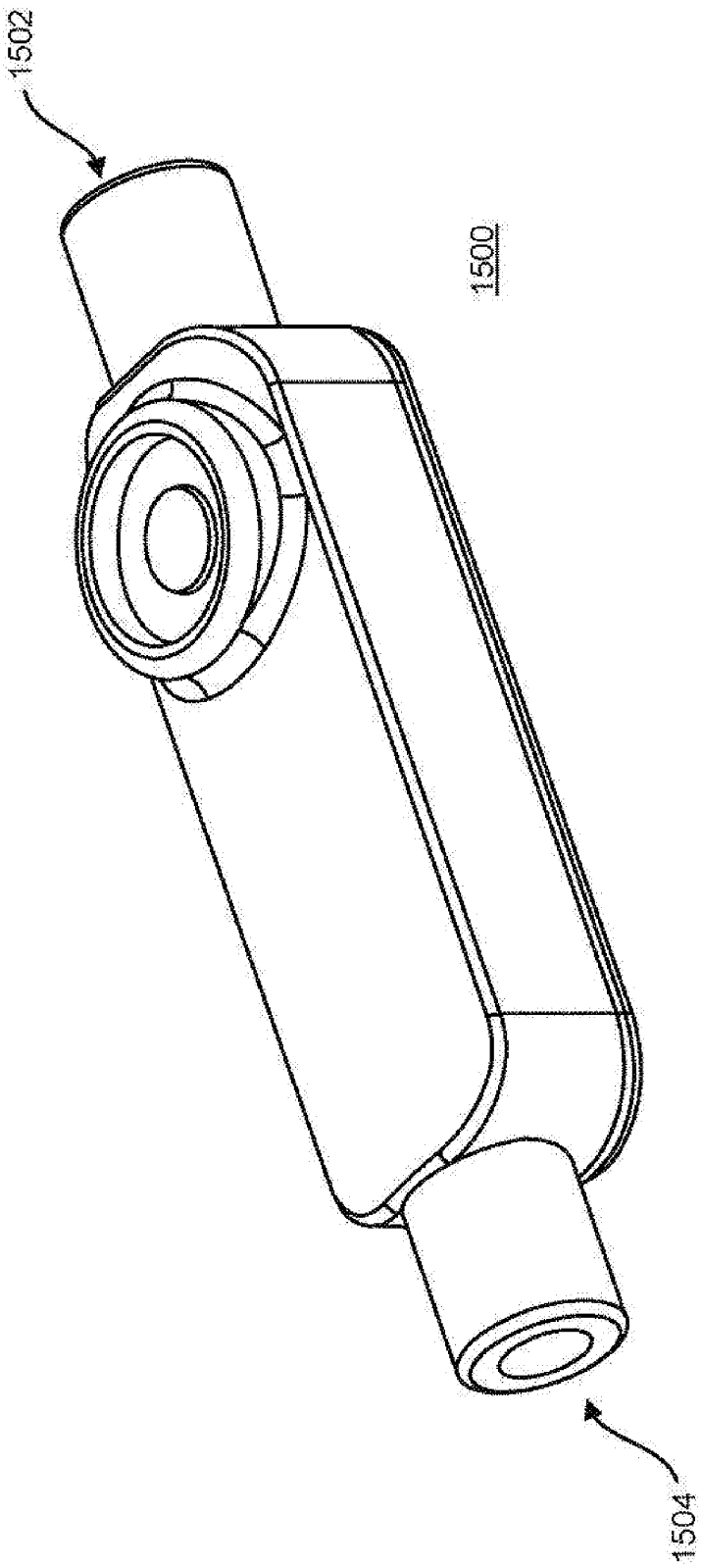


FIG. 15A

[Fig. 15B]

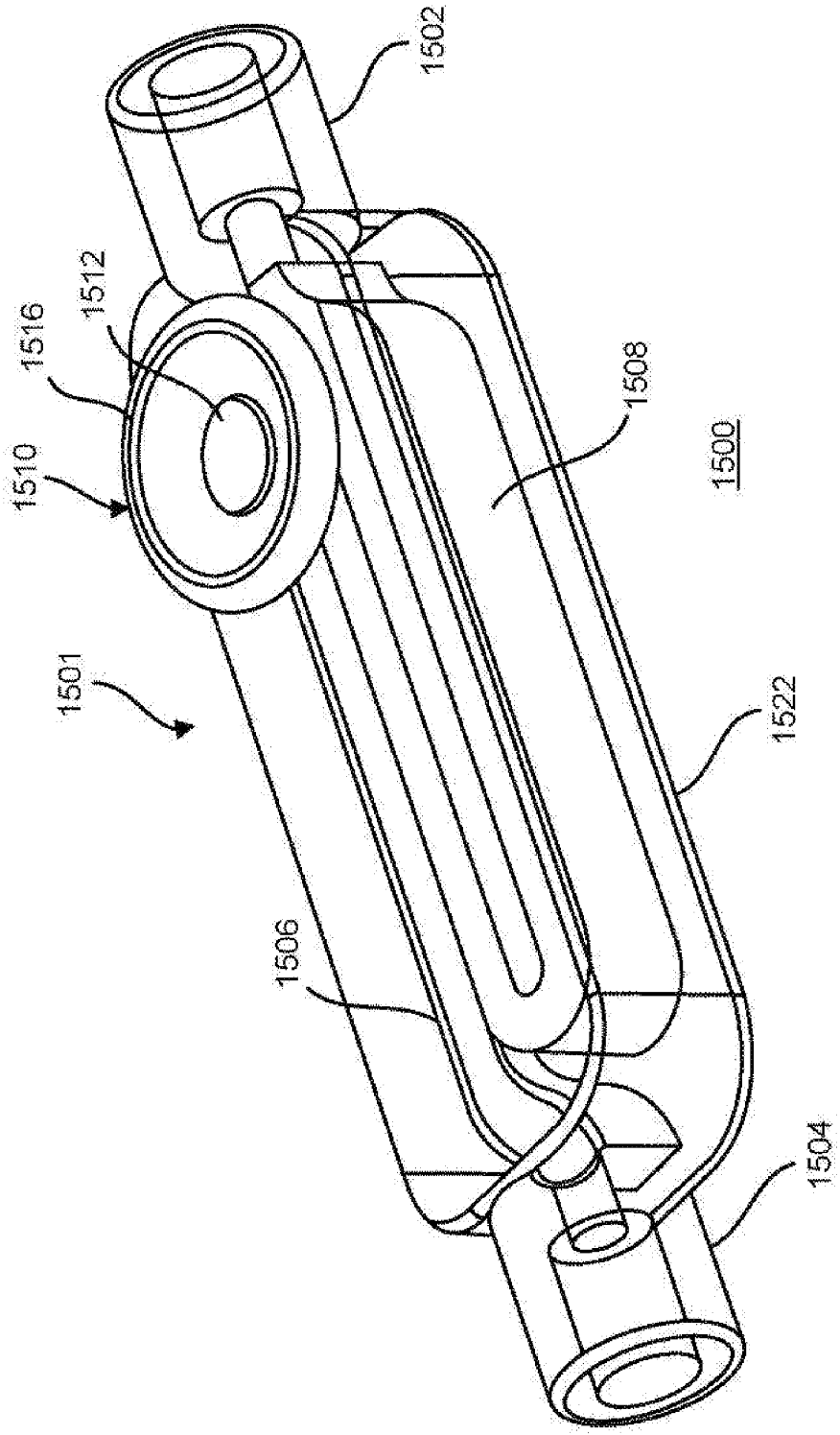


FIG. 15B

[Fig. 15C]

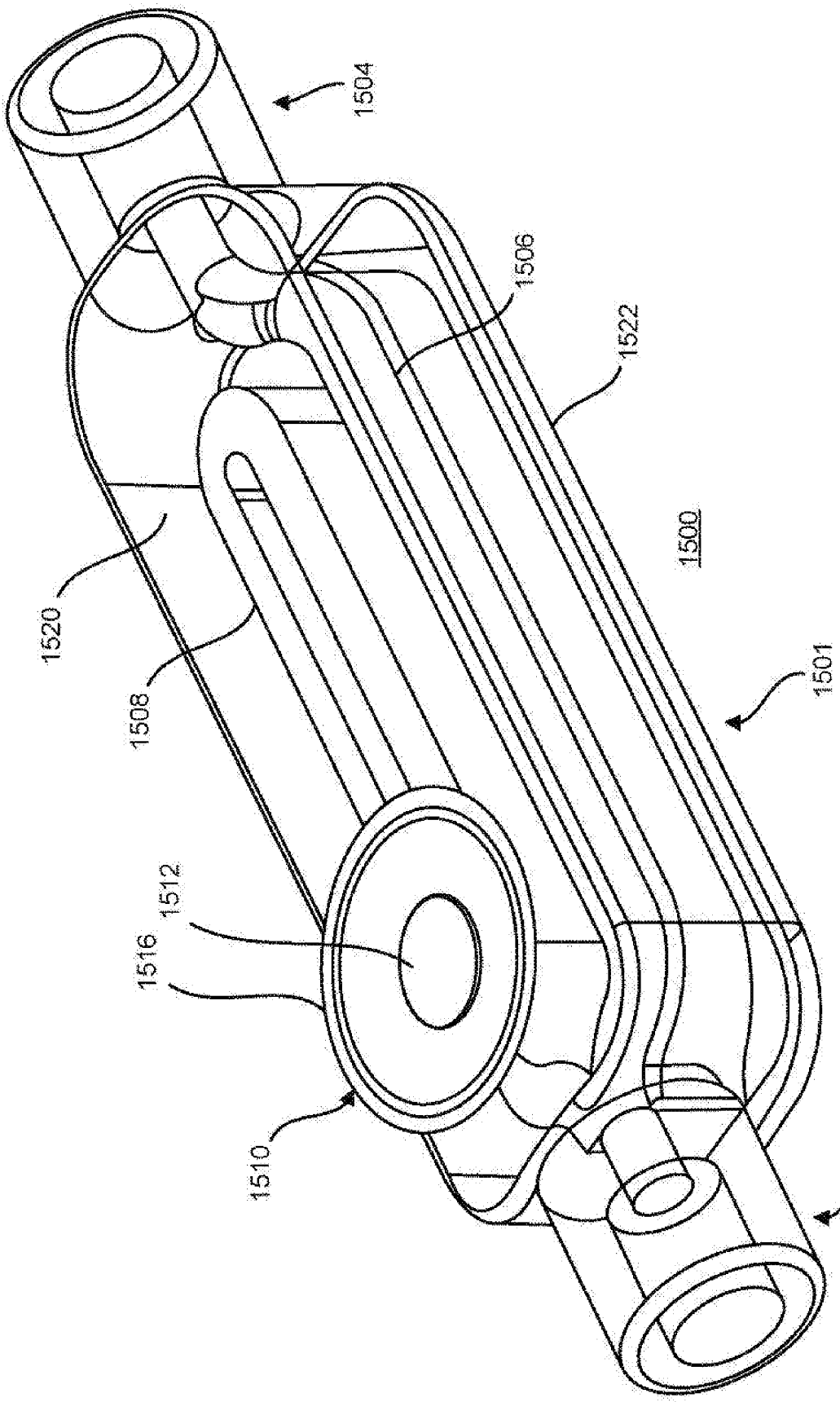


FIG. 15C

[Fig. 15D]

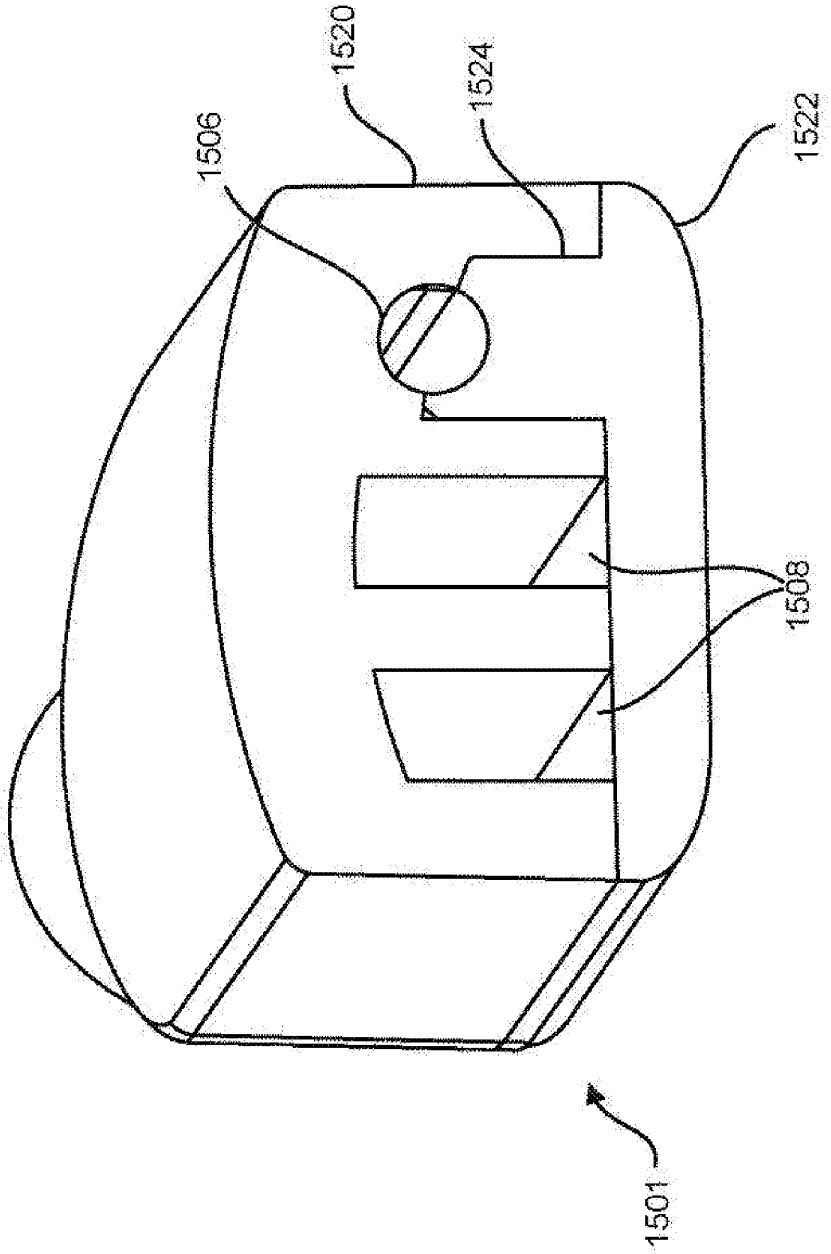


FIG. 15D

[Fig. 15E]

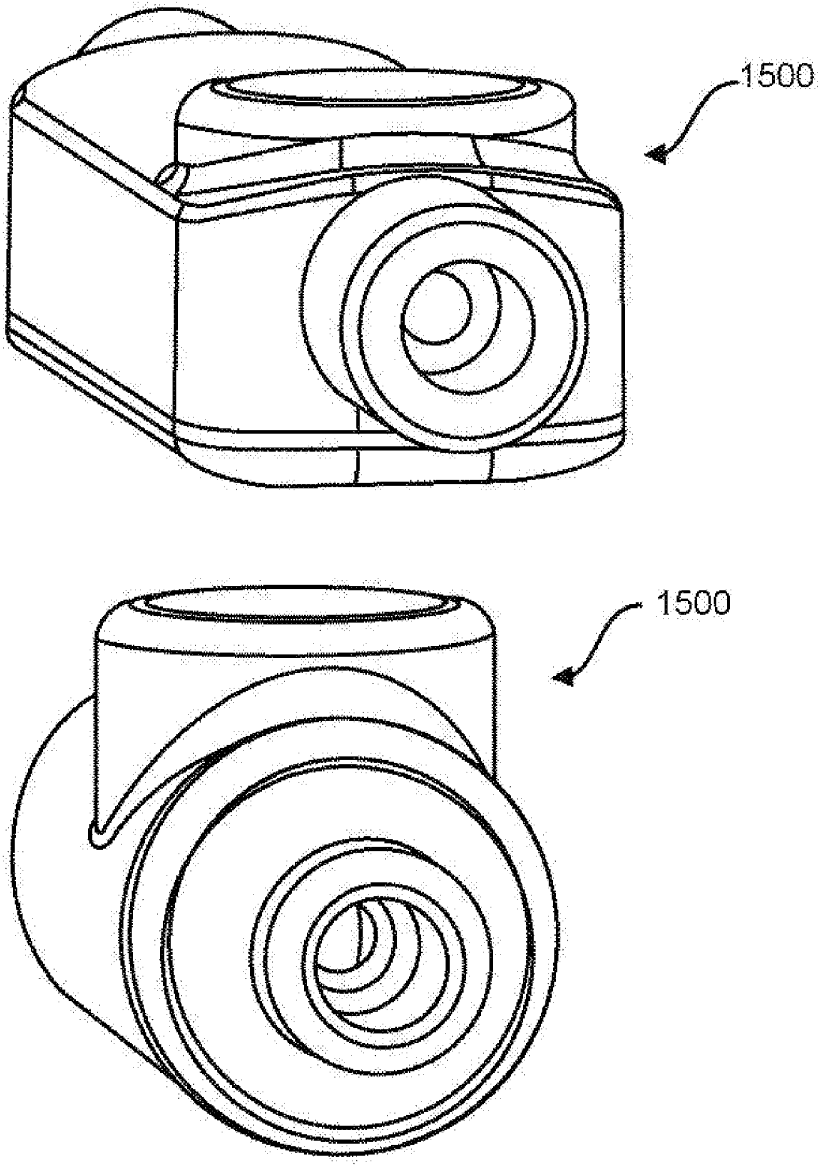


FIG. 15E

[Fig. 15F]

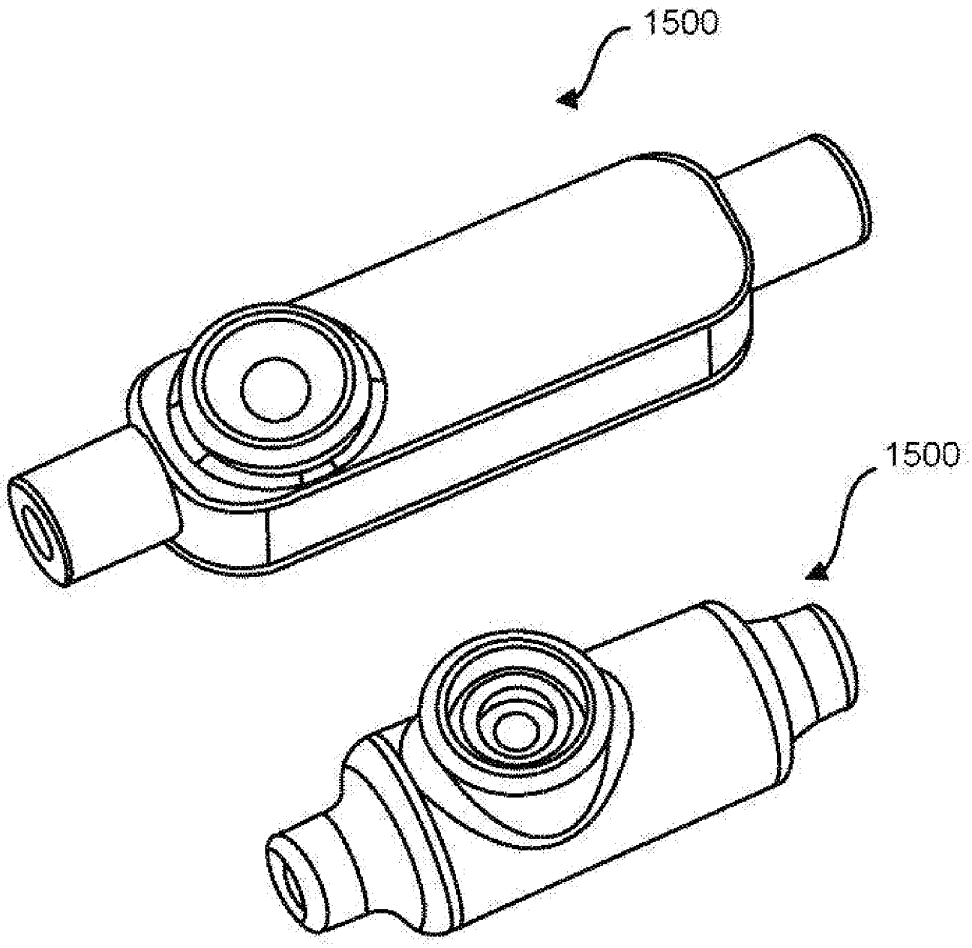


FIG. 15F

[Fig. 15G]

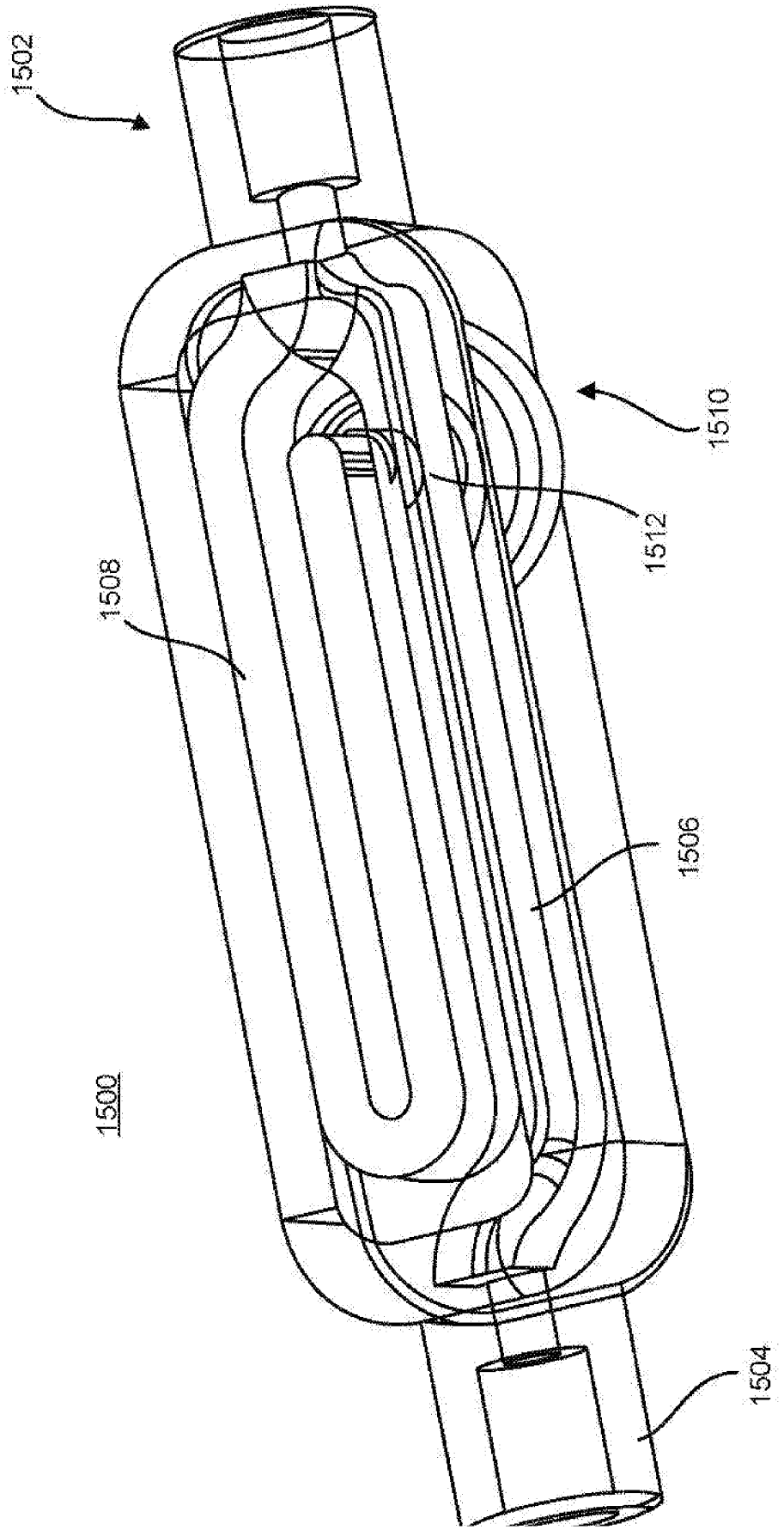


FIG. 15G

[Fig. 16A]

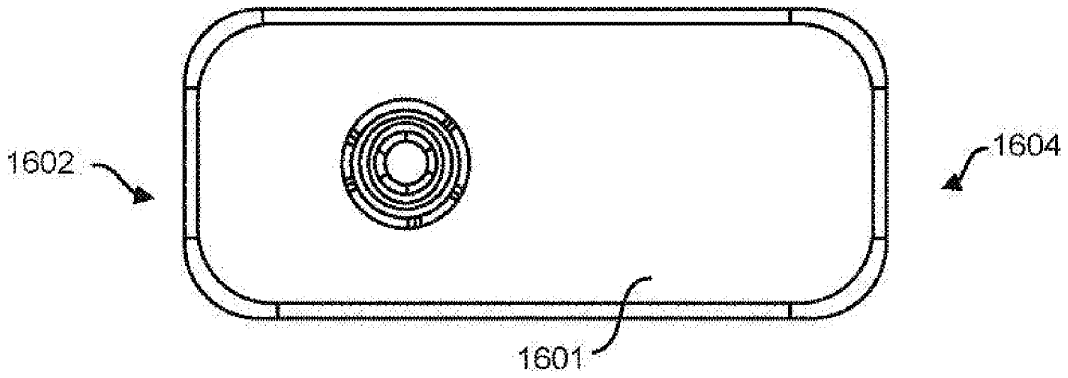


FIG. 16A

[Fig. 16B]

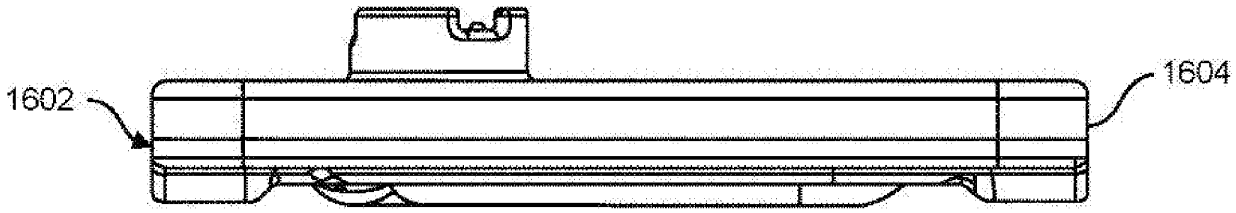


FIG. 16B

[Fig. 16C]

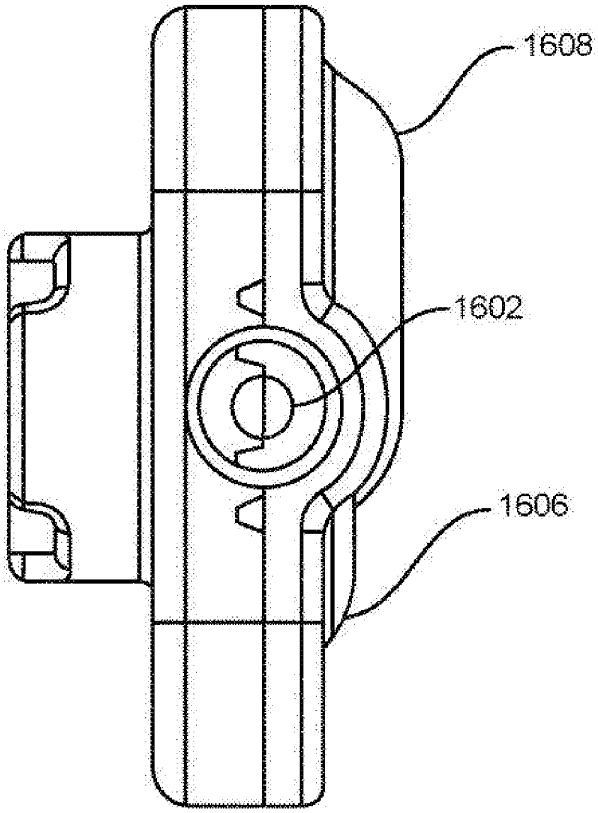


FIG. 16C

[Fig. 16D]

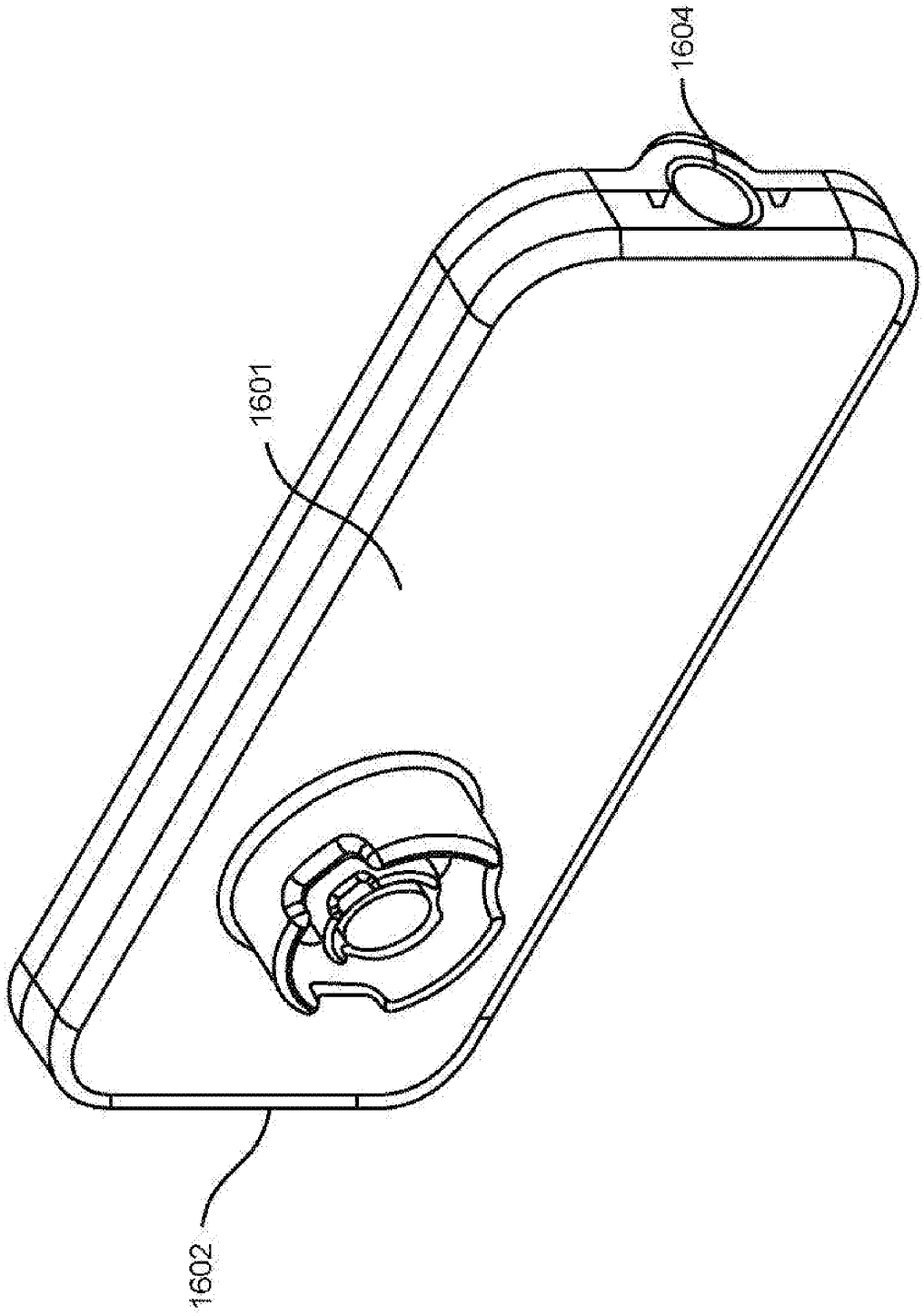


FIG. 16D

[Fig. 17A]

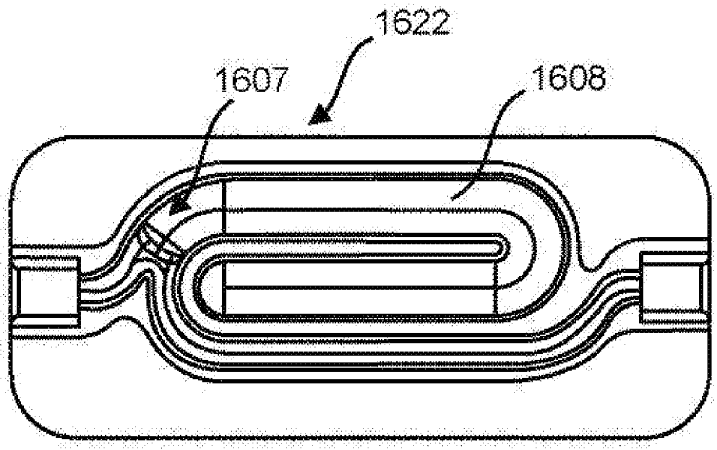


FIG. 17A

[Fig. 17B]

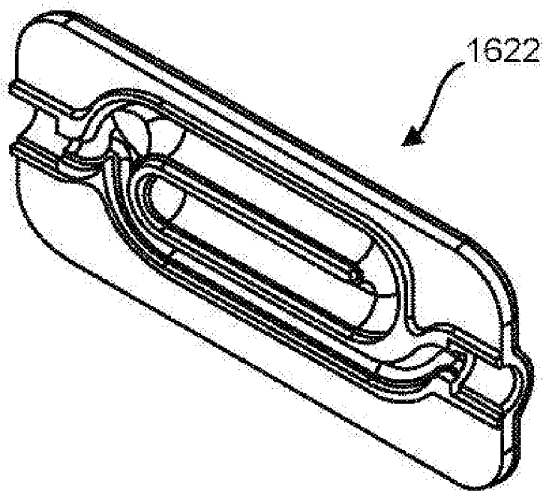


FIG. 17B

[Fig. 17C]

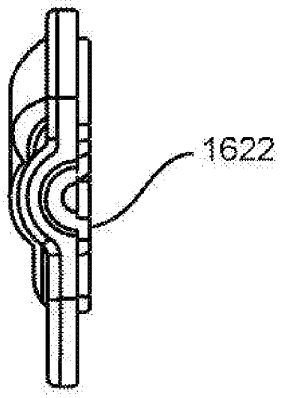


FIG. 17C

[Fig. 17D]

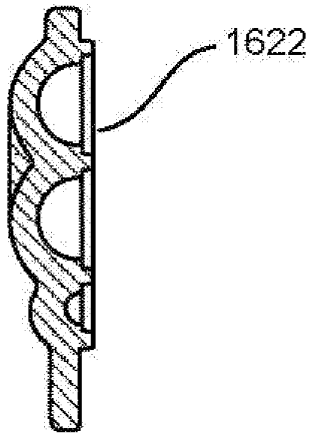


FIG. 17D

[Fig. 17E]

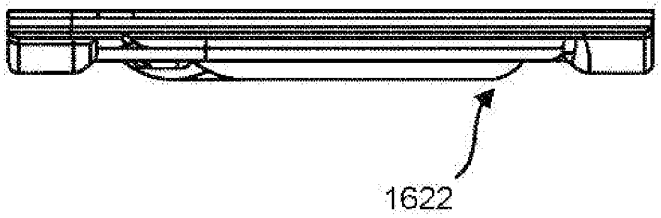


FIG. 17E

[Fig. 18A]

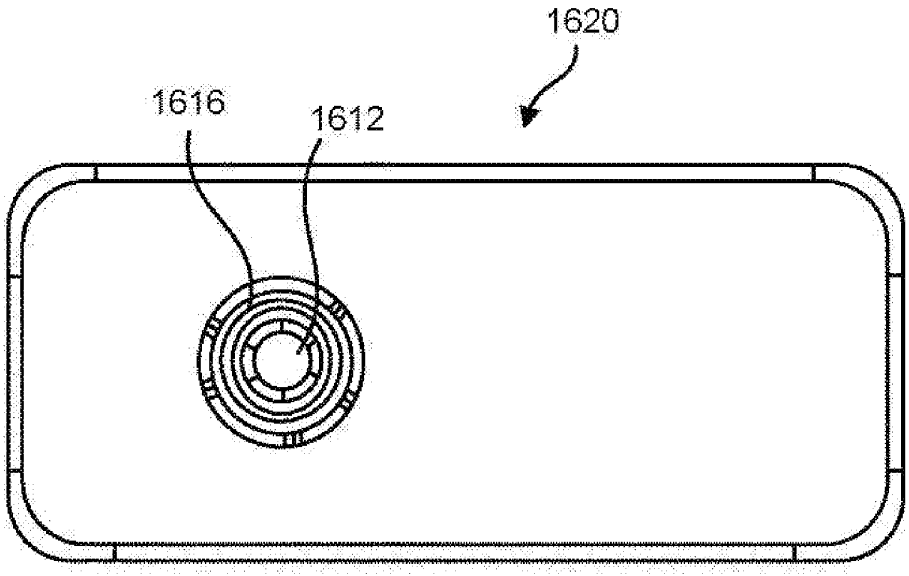


FIG. 18A

[Fig. 18B]

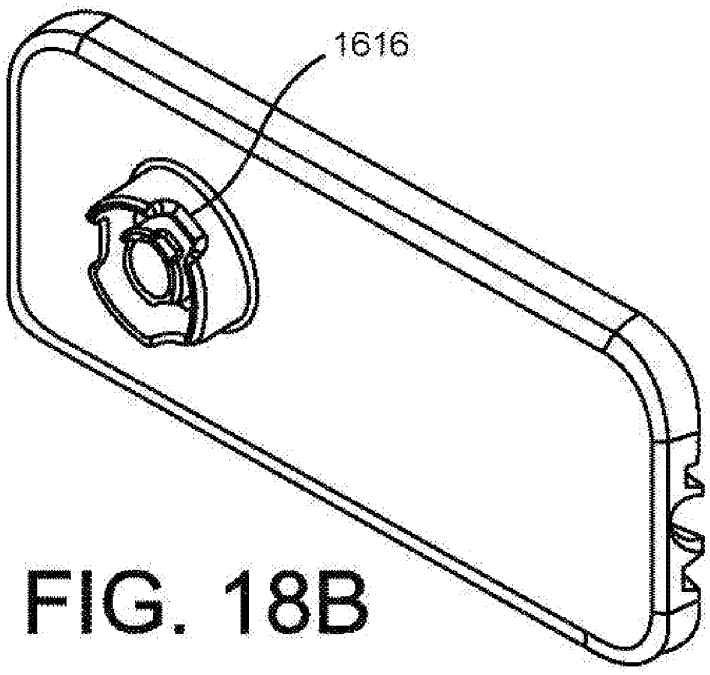


FIG. 18B

[Fig. 18C]

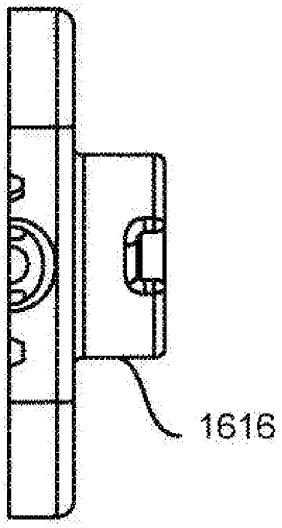


FIG. 18C

[Fig. 18D]

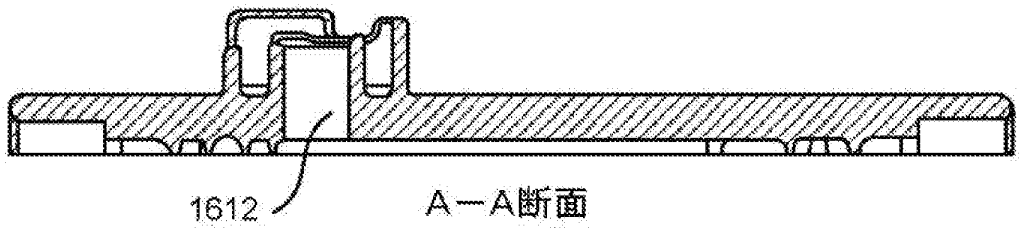


FIG. 18D

[Fig. 18E]

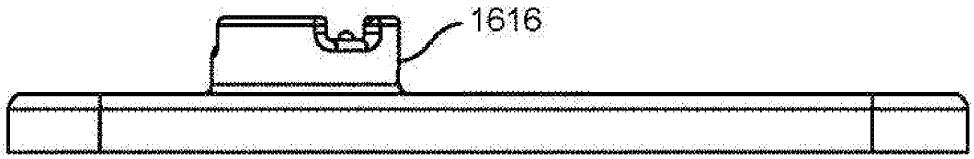


FIG. 18E

[Fig. 18F]

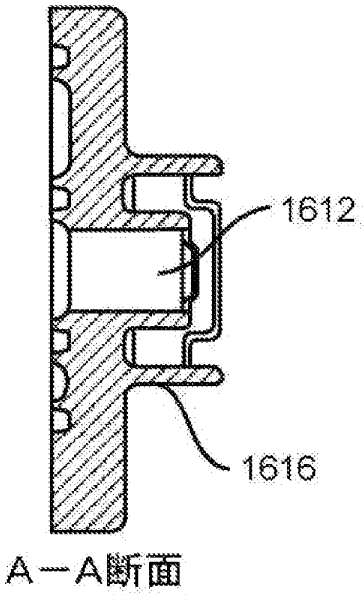


FIG. 18F

[Fig. 19A]

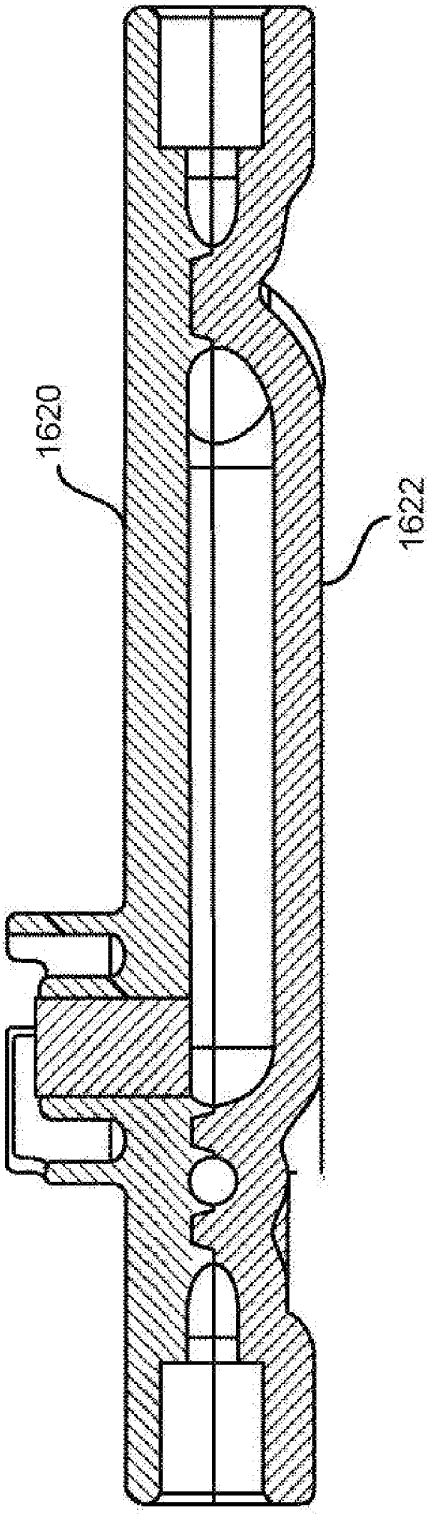


FIG. 19A

[Fig. 19B]

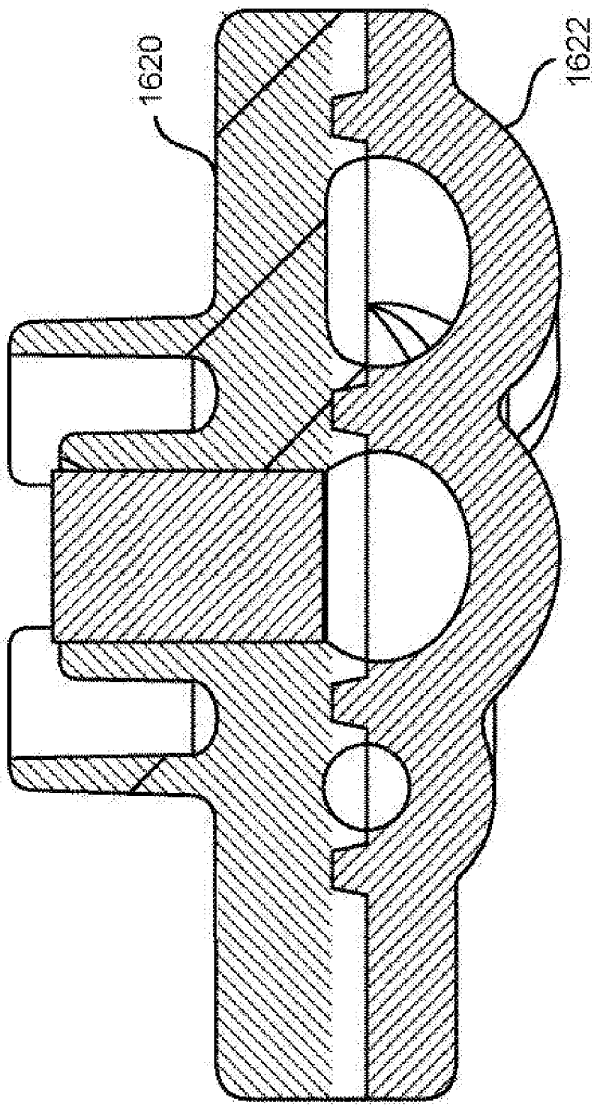


FIG. 19B

[Fig. 20]

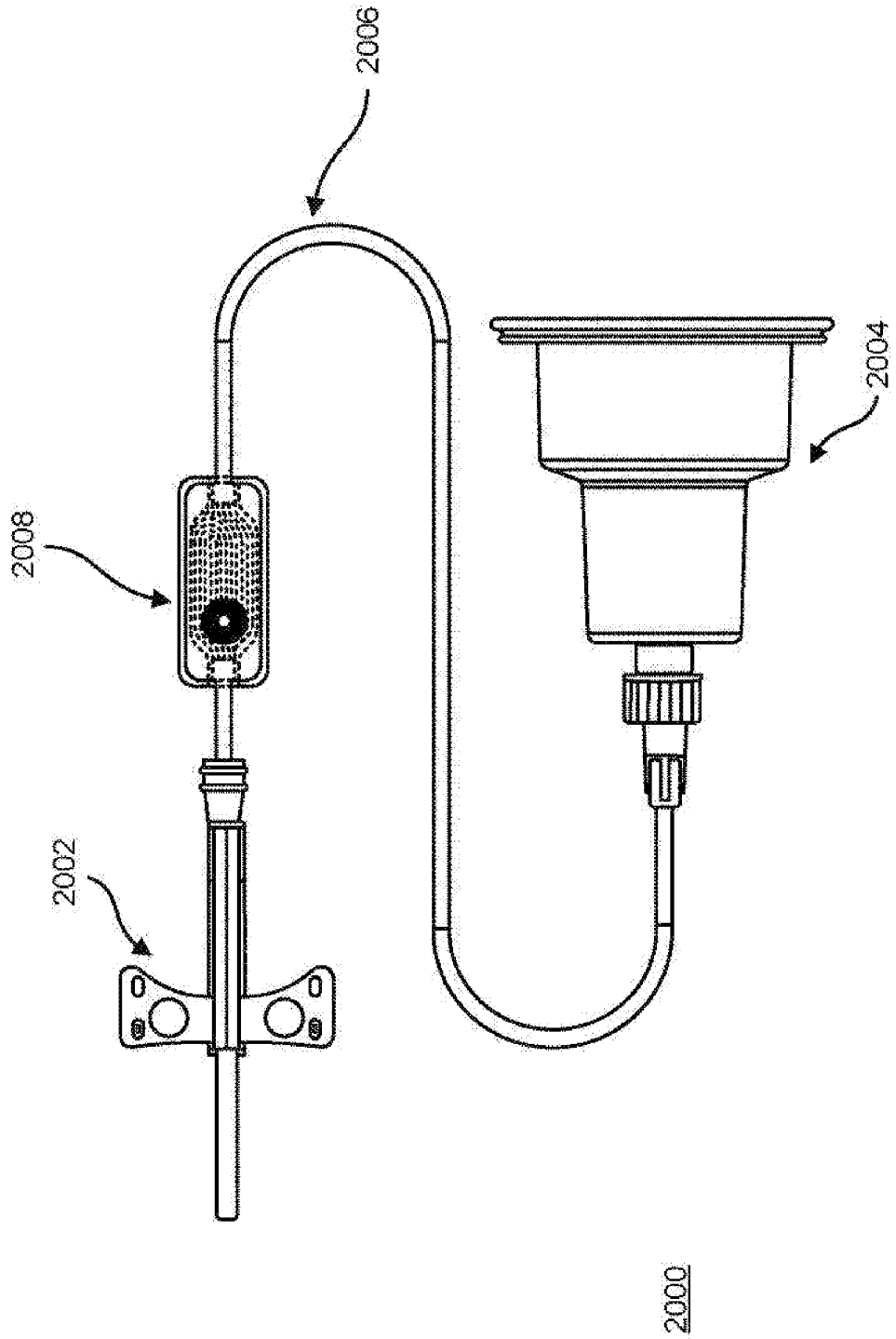


FIG. 20

[Fig. 21]

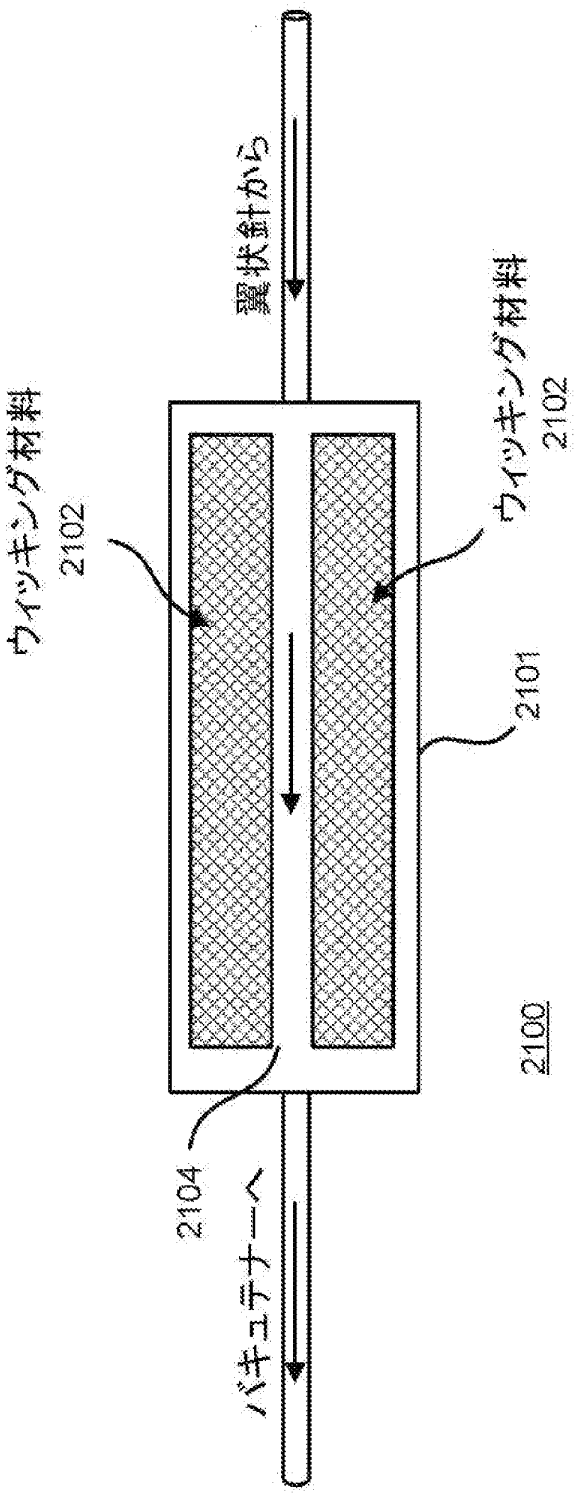


FIG. 21

[Fig. 22A]

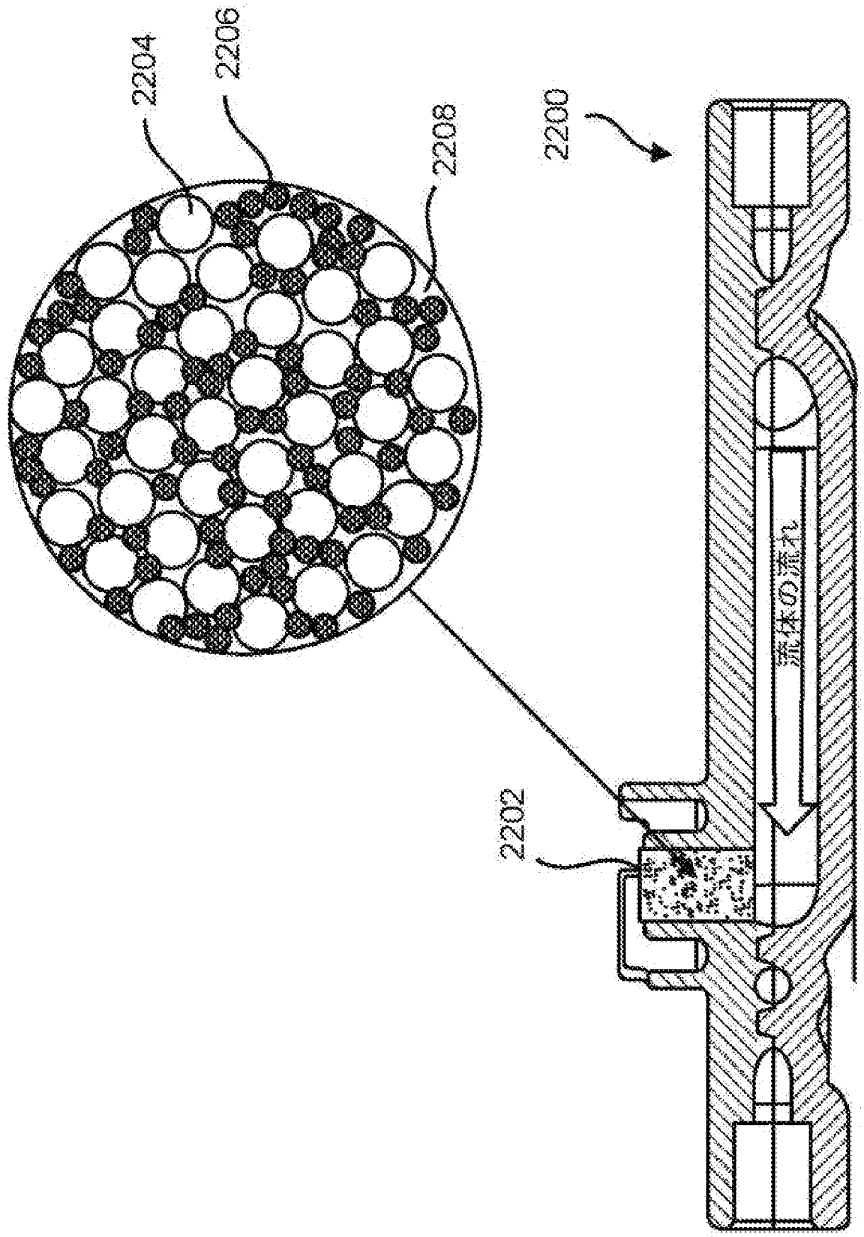


FIG. 22A

[Fig. 22B]

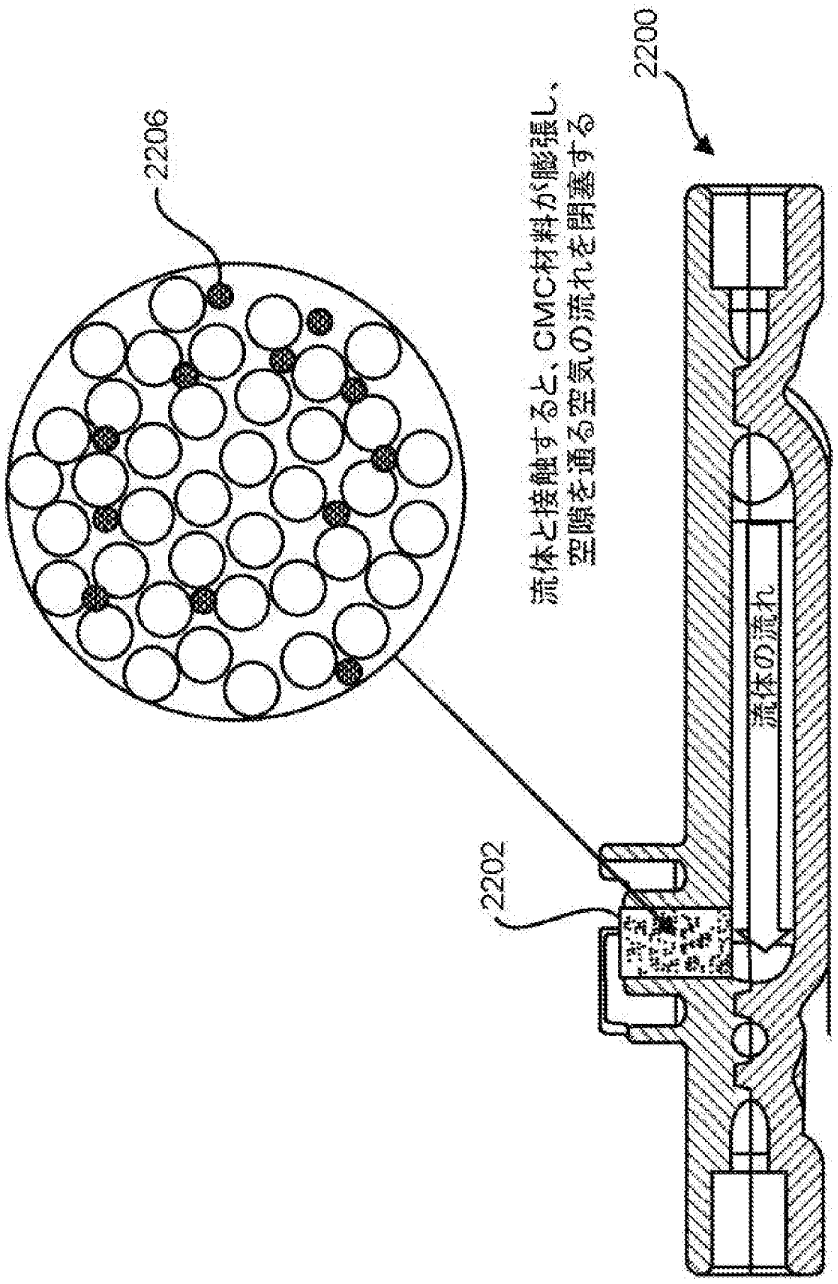


FIG. 22B

[Fig. 23A]

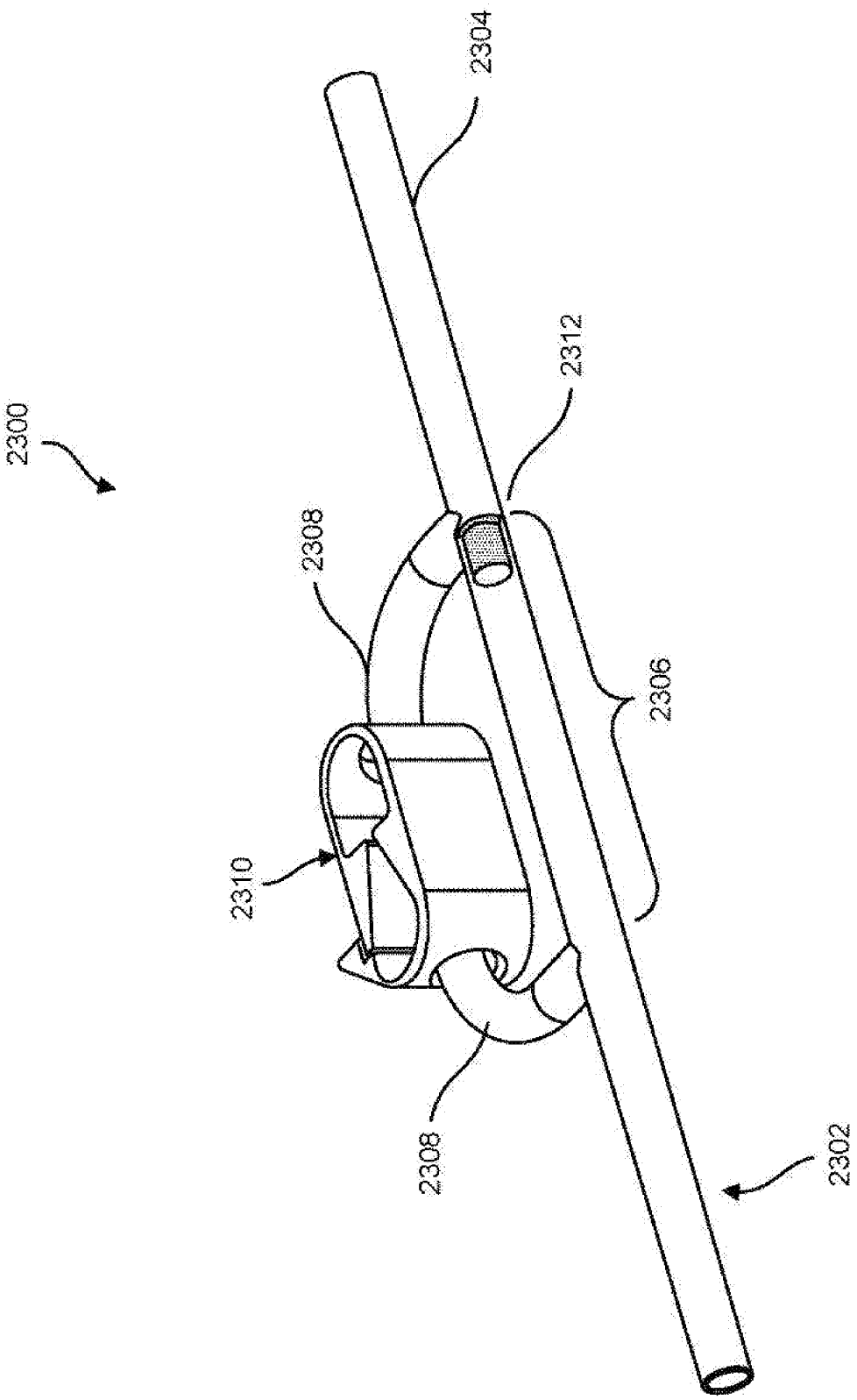


FIG. 23A

[Fig. 23B]

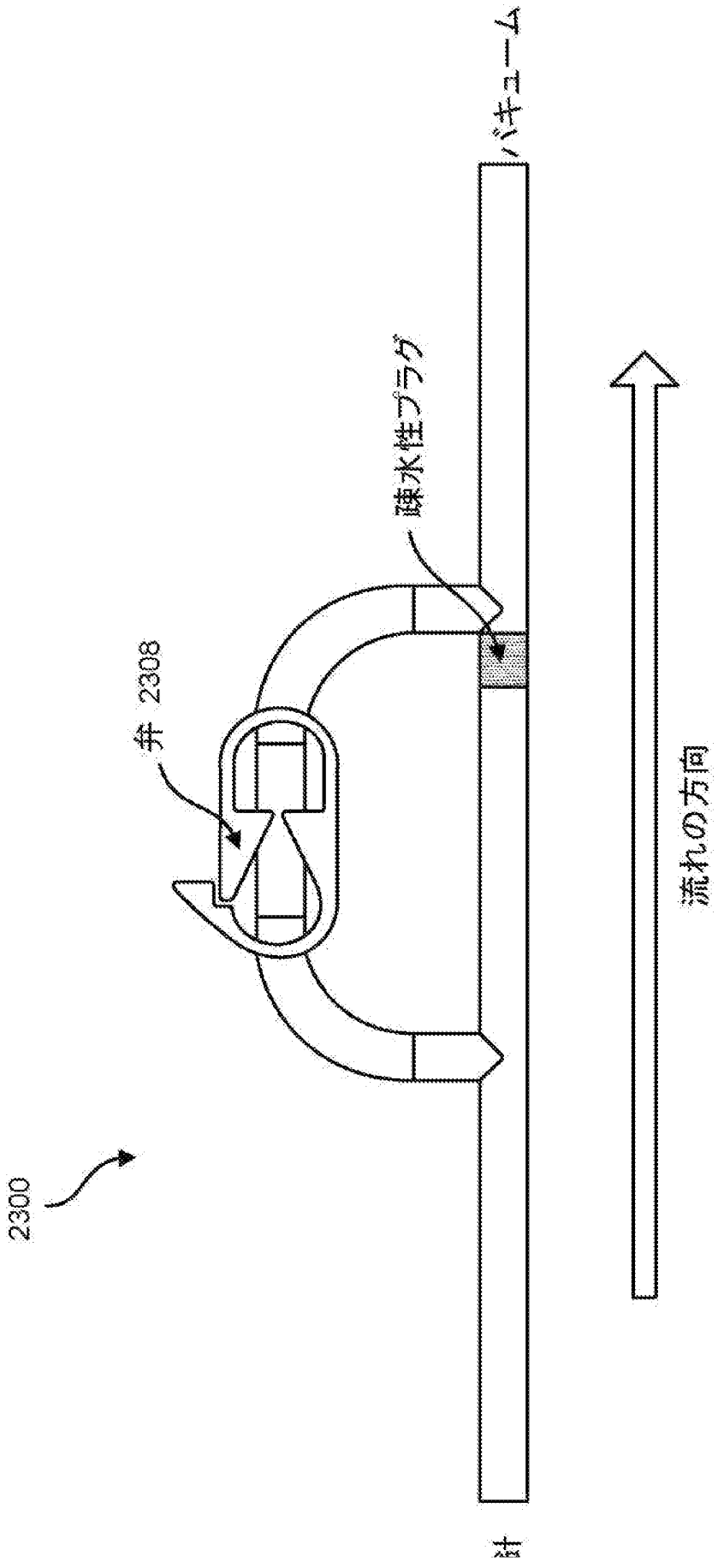


FIG. 23B

drawing open

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

Magnify and Rotate

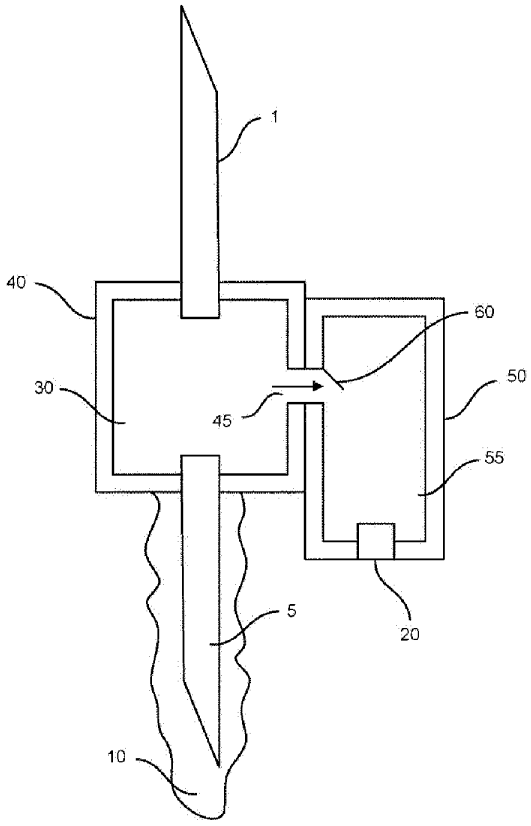


FIG. 1

Figure 1

1 / 1 display

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

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

【００２２】

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

【図面の簡単な説明】

【００２３】

以下、これら及び他の態様について、以下の図面を参照して詳細に説明する。

【図１】血液サンプル最適化システムを示す。

【図２】代替的な実施に従う血液サンプル最適化システムを示す。

【図３】別の代替的な実施に従う血液サンプル最適化システムを示す。

【図４】別の代替的な実施に従う血液サンプル最適化システムを示す。

【図５】別の代替的な実施に従う血液サンプル最適化システムを示す。

【図６】代替的な実施に従う血液サンプル最適化システムを示す。

【図７】血液培養の質を最適化するための方法のフローチャートである。

【図８Ａ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｂ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｃ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｄ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図８Ｅ】一部の実施に従う非汚染採血用の血液隔離システムを示す。

【図９】血液隔離システムに用いる経路スプリッタを示す。

【図１０Ａ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１０Ｂ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１０Ｃ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１０Ｄ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ａ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｂ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｃ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｄ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

【図１１Ｅ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。

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

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

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

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

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

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

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

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

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

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

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

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

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

【００２５】

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

【００２６】

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

【００２７】

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

【００２８】

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

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

【００２９】

弁６０は、任意のタイプの弁又は開閉機構であることができる。チャンバ３０は、実質的に残留血液を保持しないように設計されており、特定の容積又は割合の血液を隔離チャンバ５５に保持し又は通過させるように構成することができる。同様に、隔離チャンバ５５は、抗凝固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

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【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】

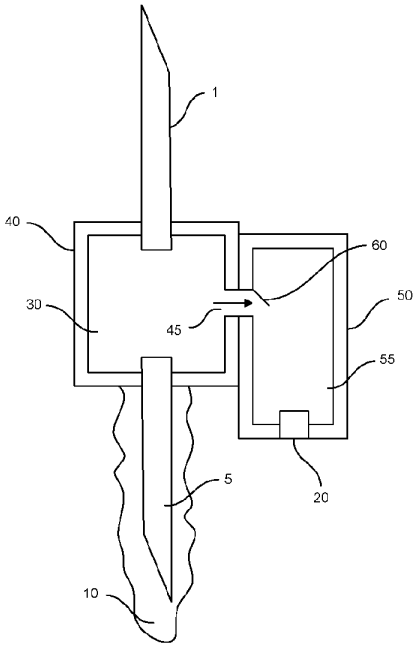


FIG. 1

【図２】

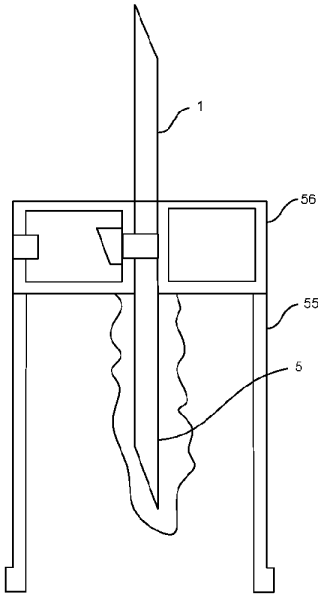


FIG. 2

【図３】

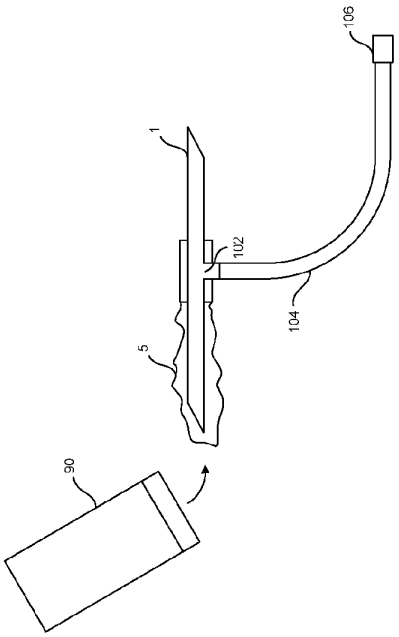


FIG. 3

【図４】

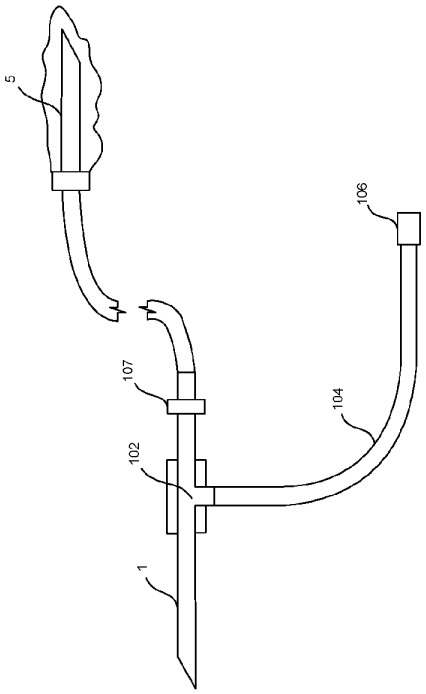


FIG. 4

【図５】

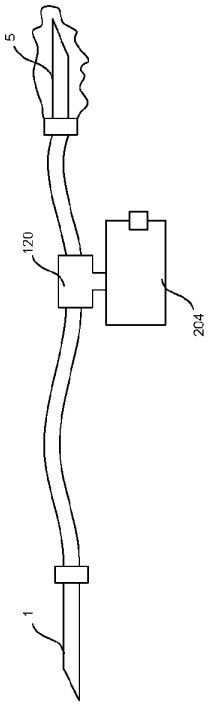


FIG. 5

【図６】

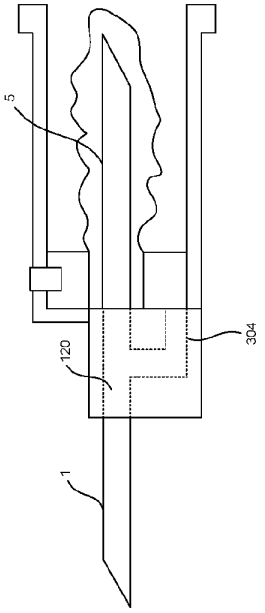


FIG. 6

【図７】

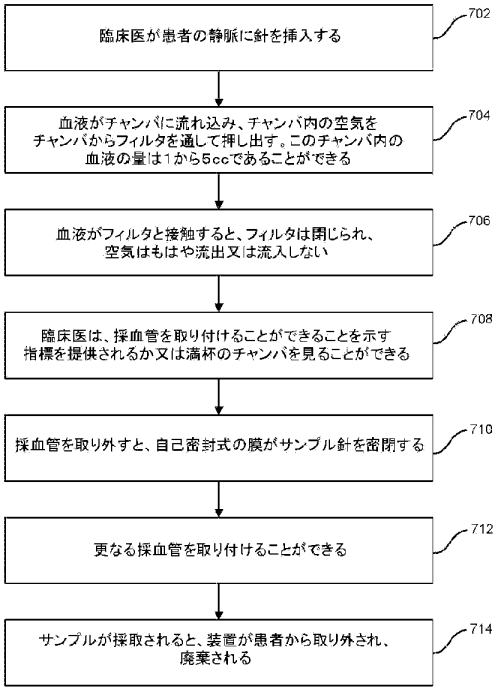


FIG. 7

【図８Ａ】

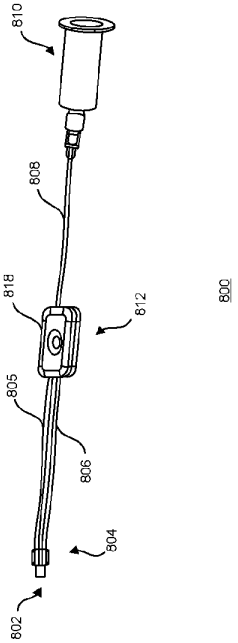


FIG. 8A

【図８Ｂ】

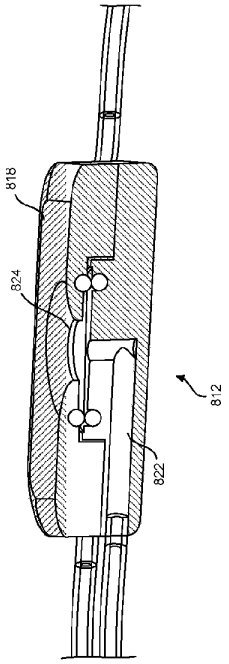


FIG. 8B

【図８Ｃ】

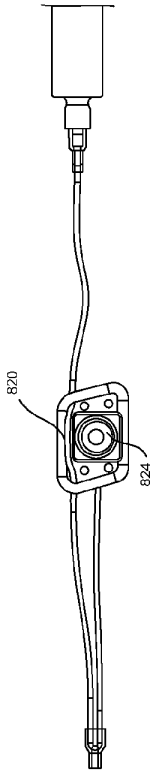


FIG. 8C

【図８Ｄ】

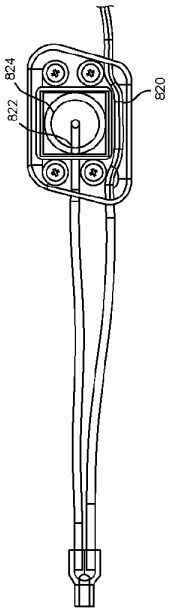


FIG. 8D

【図８Ｅ】

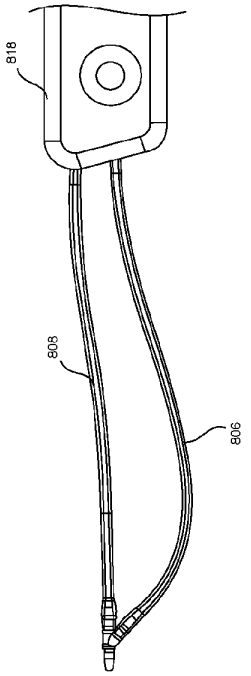


FIG. 8E

【図９】

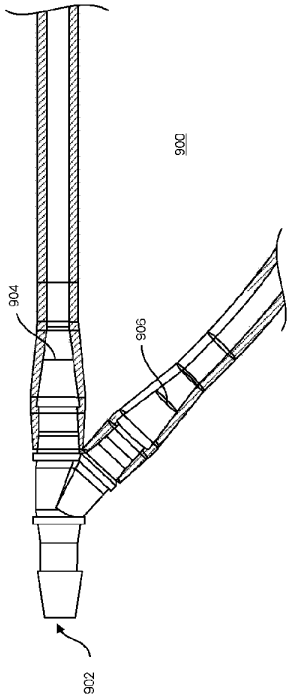


FIG. 9

【図１０Ａ】

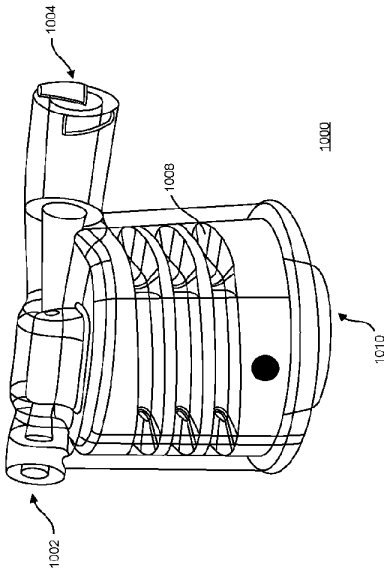


FIG. 10A

【図１０Ｂ】

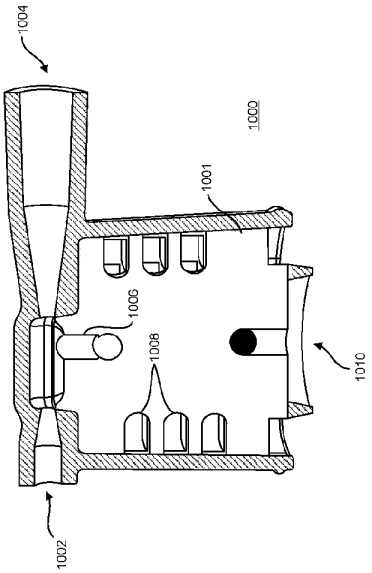


FIG. 10B

【図１０Ｃ】

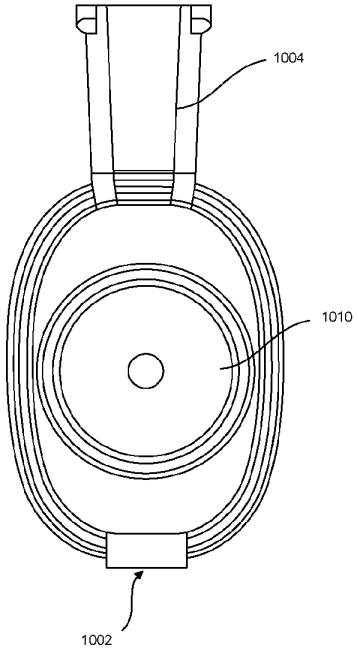


FIG. 10C

【図１０Ｄ】

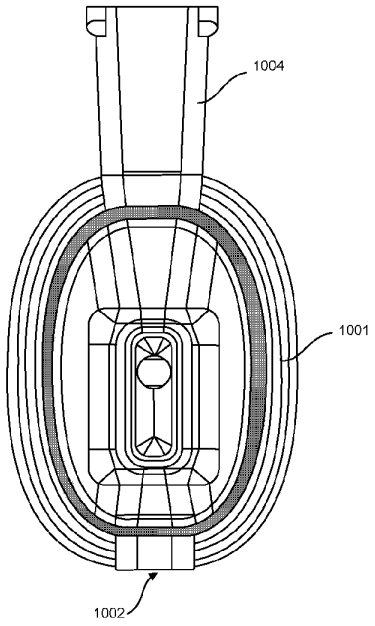


FIG. 10D

【図１１Ａ】

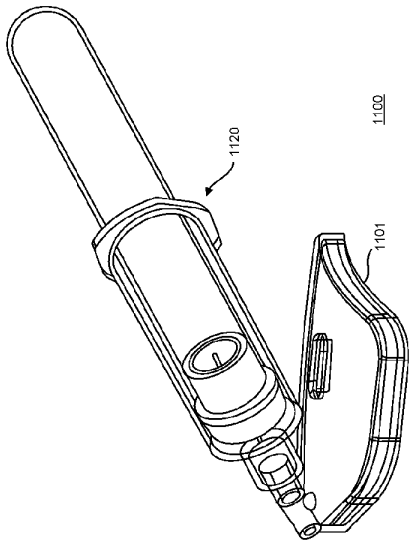


FIG. 11A

【図１１Ｂ】

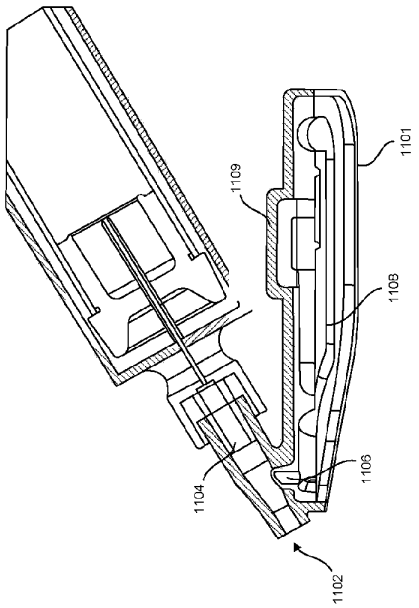


FIG. 11B

【図１１Ｃ】

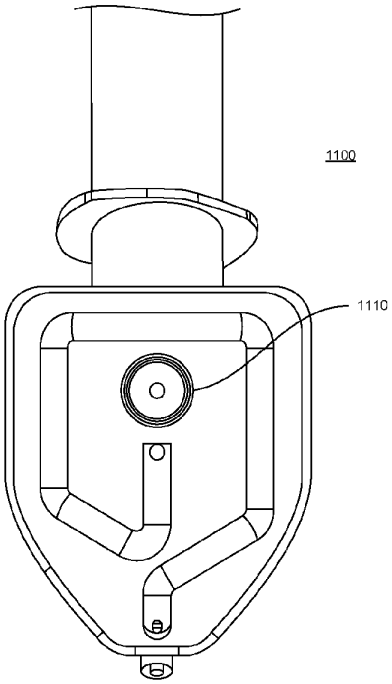


FIG. 11C

【図１１Ｄ】

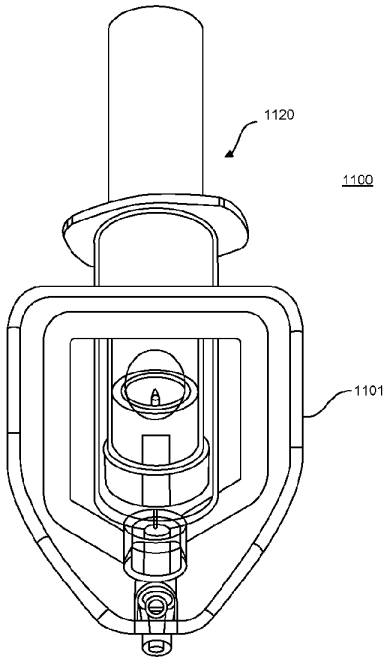


FIG. 11D

【図１１Ｅ】

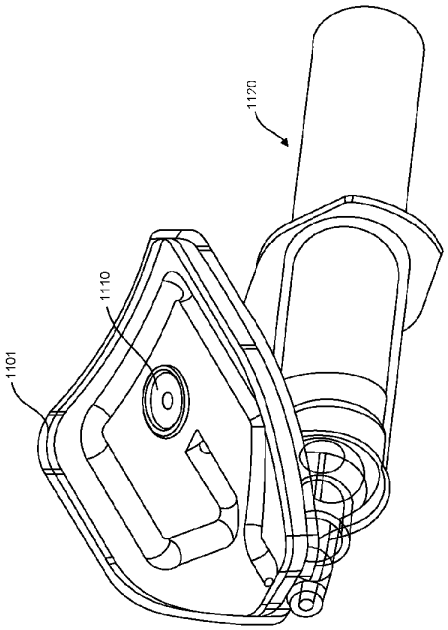


FIG. 11E

【図１２Ａ】

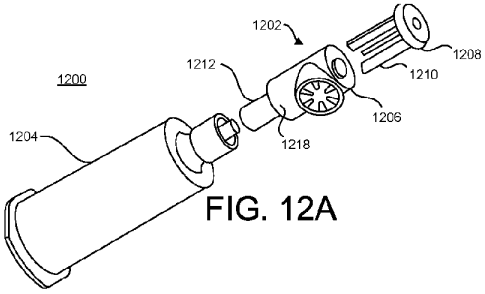


FIG. 12A

【図１２Ｂ】

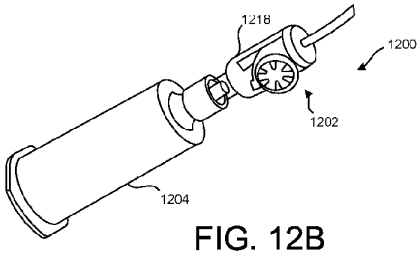


FIG. 12B

【図１２Ｃ】

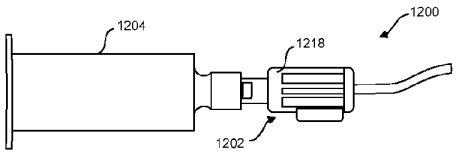


FIG. 12C

【図１２Ｄ】

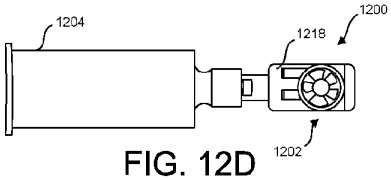


FIG. 12D

【図１３Ａ】

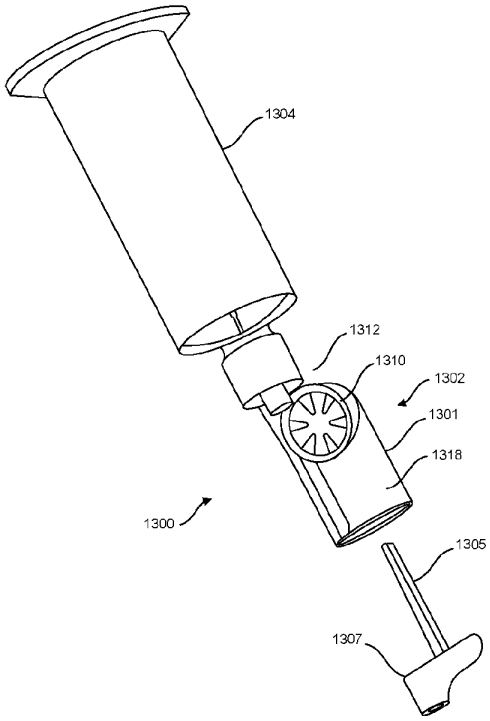


FIG. 13A

【図１３Ｂ】

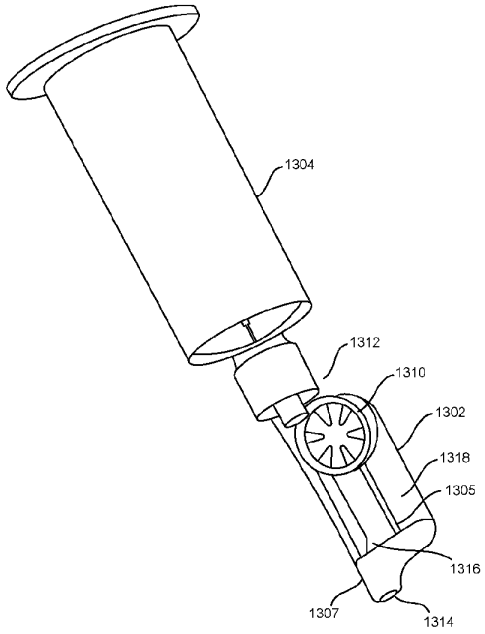


FIG. 13B

【図１３Ｃ】

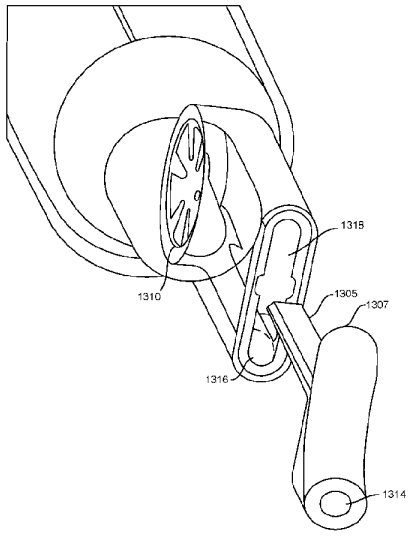


FIG. 13C

【図１３Ｄ】

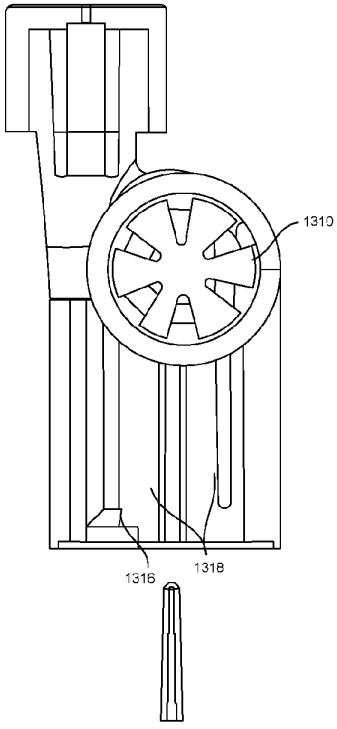


FIG. 13D

【図１４Ａ】

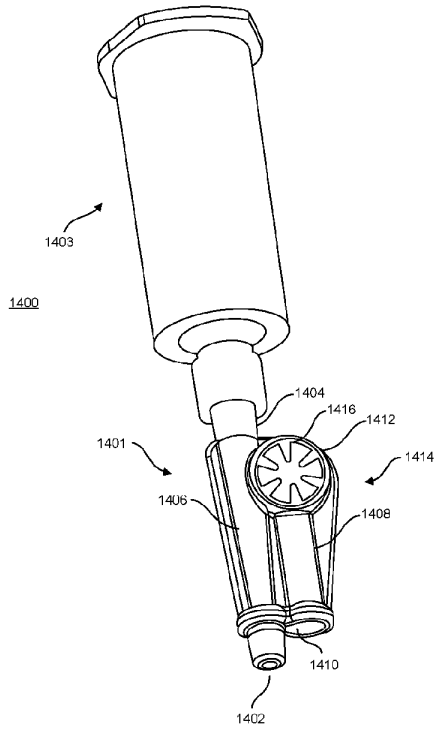


FIG. 14A

【図１４Ｂ】

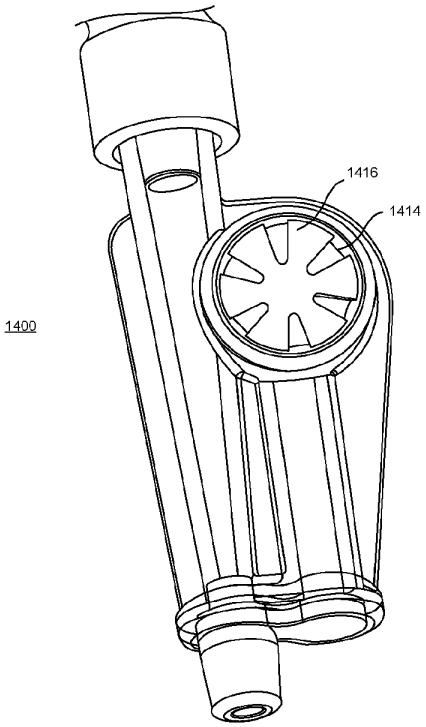


FIG. 14B

【図１４Ｃ】

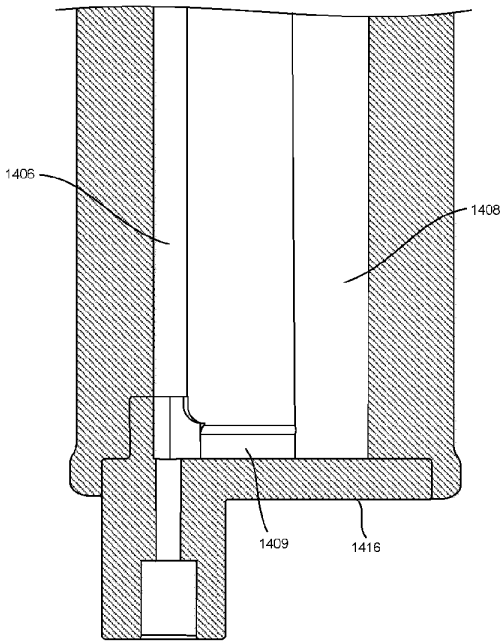


FIG. 14C

【図１４Ｄ】

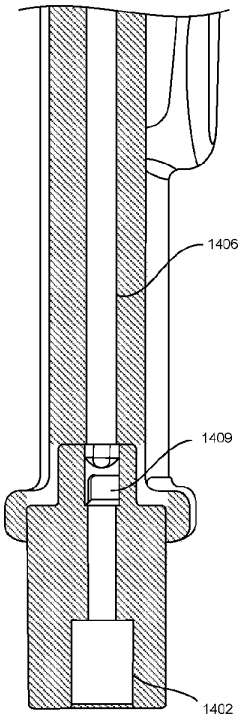


FIG. 14D

【図１４Ｅ】

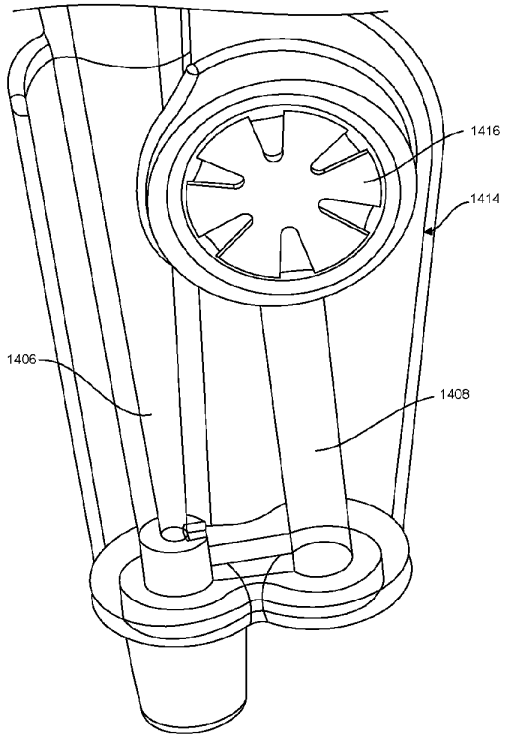


FIG. 14E

【図１５Ａ】

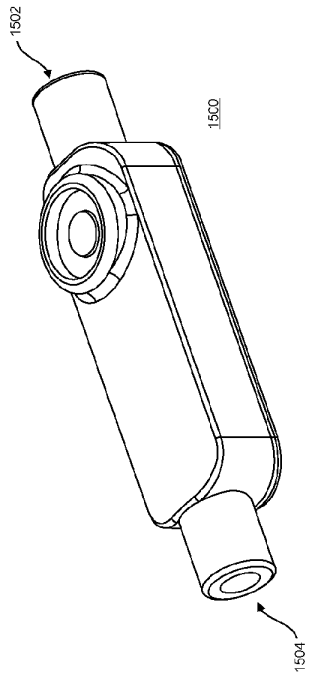


FIG. 15A

【図１５Ｂ】

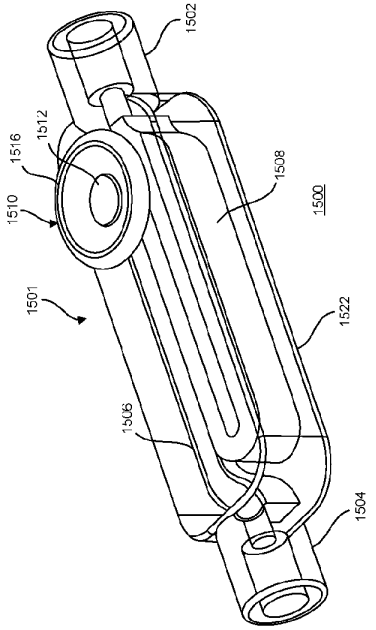


FIG. 15B

【図１５Ｃ】

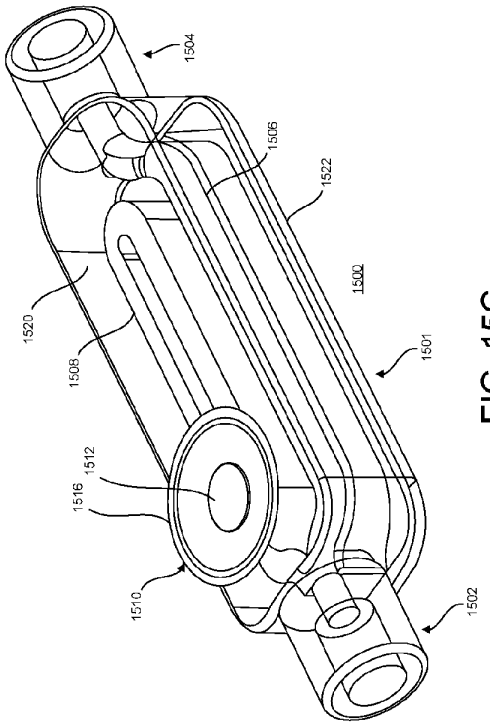


FIG. 15C

【図１５Ｄ】

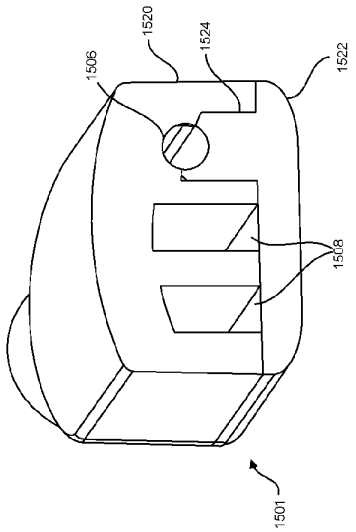


FIG. 15D

【図１５Ｅ】

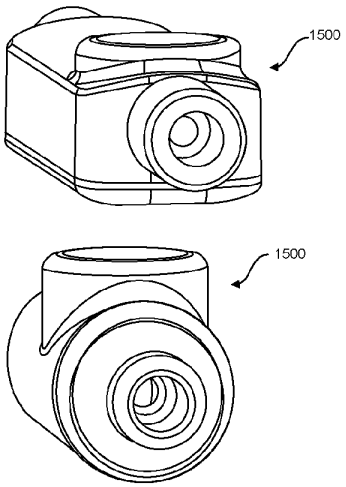


FIG. 15E

【図１５Ｆ】

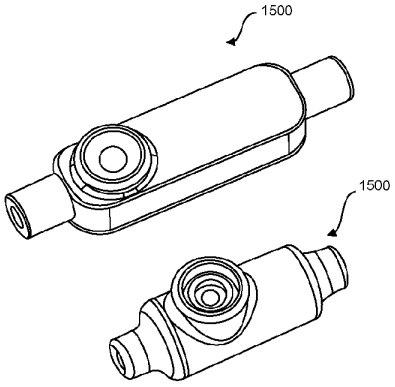


FIG. 15F

【図１５Ｇ】

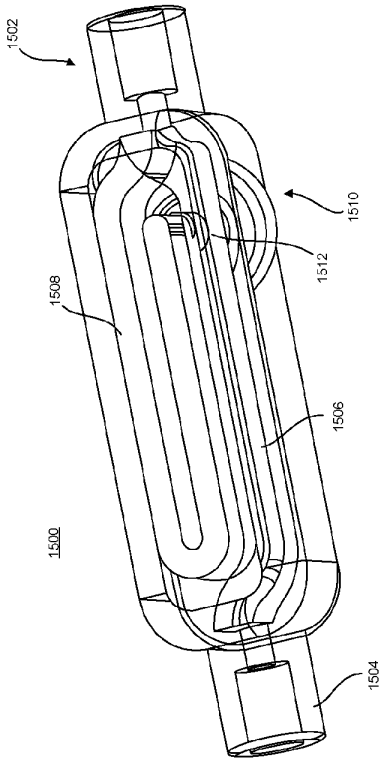


FIG. 15G

【図１６Ａ】

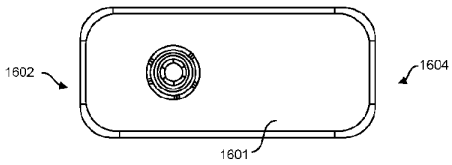


FIG. 16A

【図１６Ｂ】

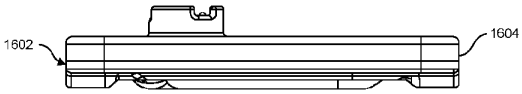


FIG. 16B

【図１６Ｃ】

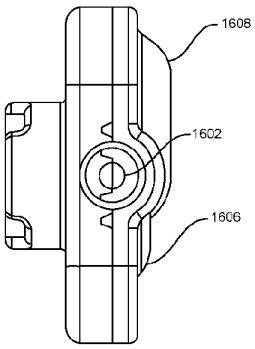


FIG. 16C

【図１６Ｄ】

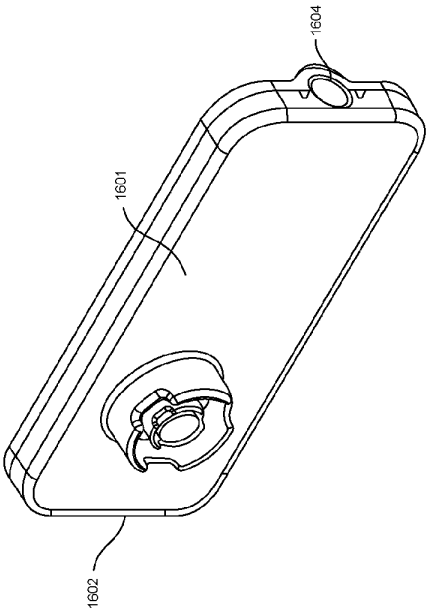


FIG. 16D

【図１７Ａ】

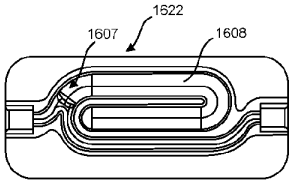


FIG. 17A

【図１７Ｂ】

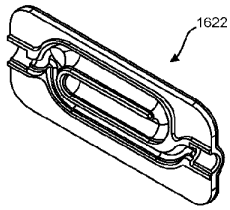


FIG. 17B

【図１７Ｃ】

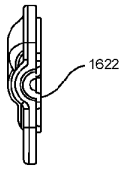


FIG. 17C

【図１７Ｄ】

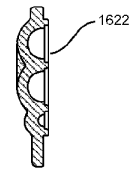


FIG. 17D

【図１７Ｅ】

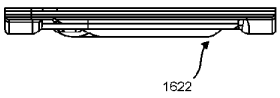


FIG. 17E

【図１８Ａ】

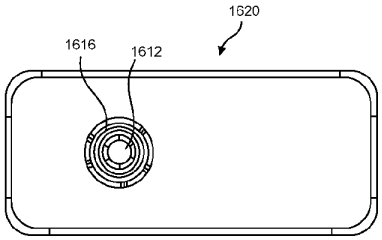


FIG. 18A

【図１８Ｂ】

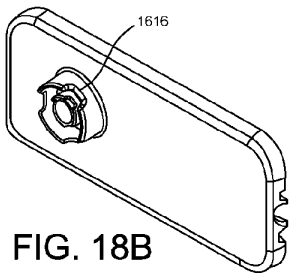


FIG. 18B

【図１８Ｃ】

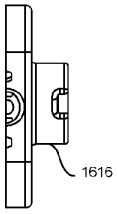


FIG. 18C

【図１８Ｄ】

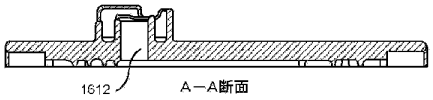


FIG. 18D

【図１８Ｅ】

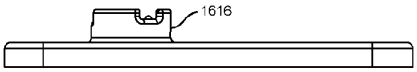


FIG. 18E

【図１８Ｆ】

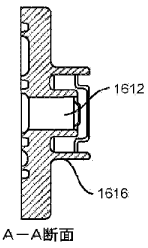


FIG. 18F

【図１９Ａ】

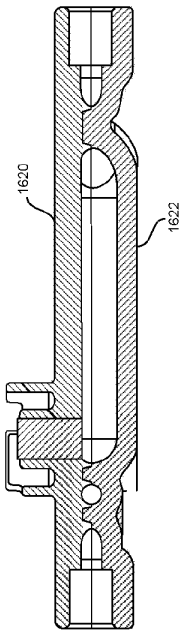


FIG. 19A

【図１９Ｂ】

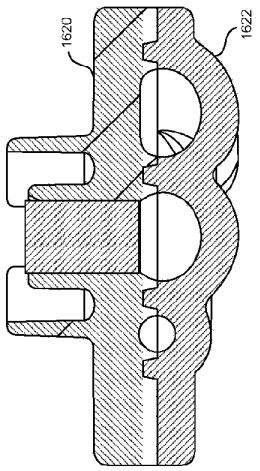


FIG. 19B

【図２０】

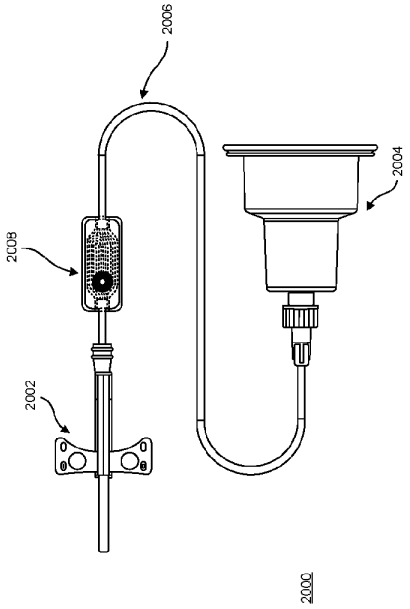


FIG. 20

【図２１】

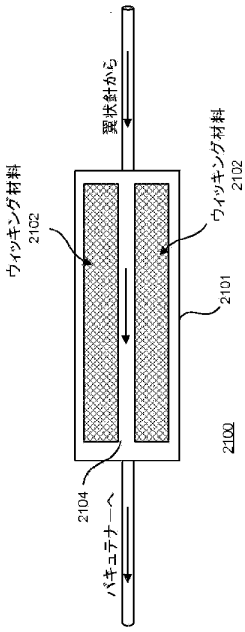


FIG. 21

【図２２Ａ】

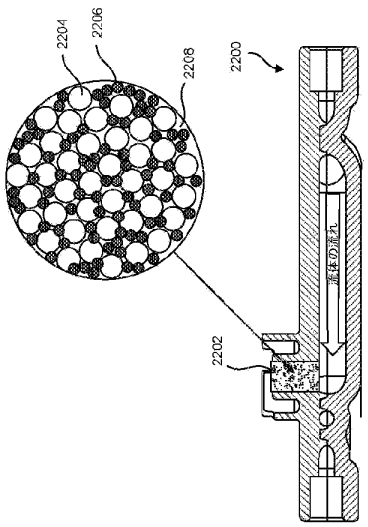


FIG. 22A

【図２２Ｂ】

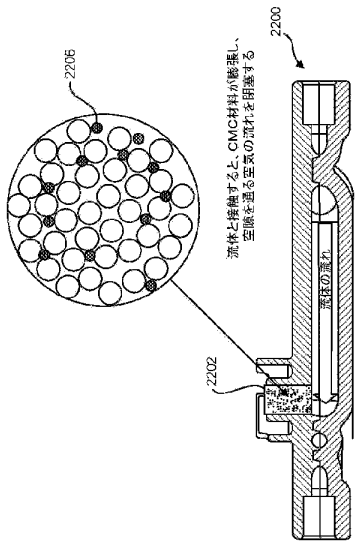


FIG. 22B

【図２３Ａ】

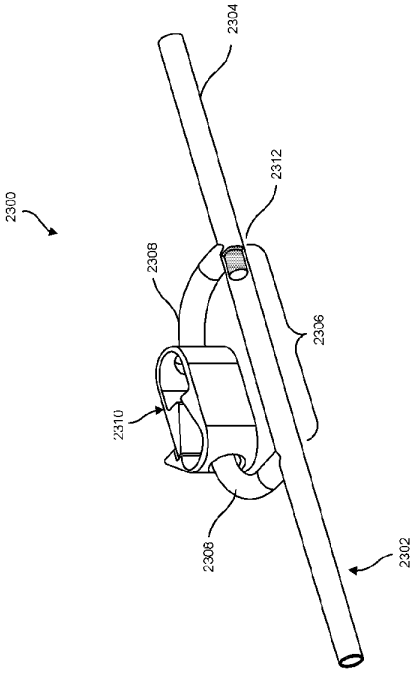


FIG. 23A

【図２３Ｂ】

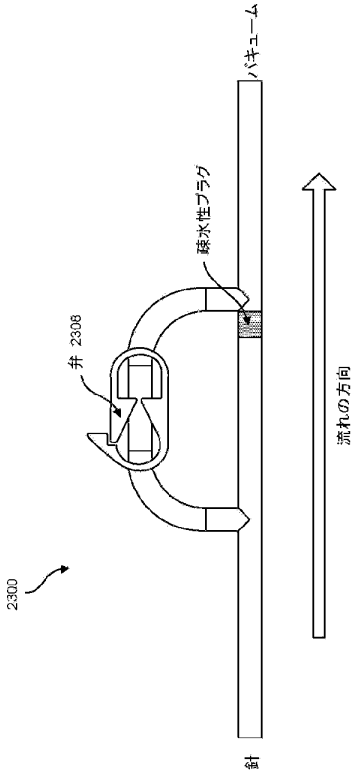


FIG. 23B

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
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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

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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

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.

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[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

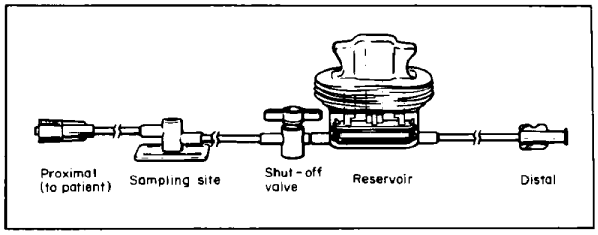


Fig. 1. Baxter venous/arterial blood management protection system (VAMPTM).

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.

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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

Current Blood Culture Methods and Systems: Clinical Concepts, Technology, and Interpretation of Results

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Since the mid-1970s there has been a number of advances in blood culture practices and technology; these advances have been based largely on well-designed controlled clinical evaluations of blood culture systems and media. Thus, a sound scientific basis for the fundamental principles of blood culturing now exists. In this article, I will address issues of clinical and technical importance with regard to blood culturing; these issues include skin antisepsis, the number and timing of blood cultures, the appropriate volume of blood for culture, culture media and additives, length and atmosphere of incubation, and interpretation of positive blood culture results. Finally, I will discuss the currently available blood culture systems, with an emphasis on the newer continuous-monitoring blood culture systems.

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Detection of bacteremia and fungemia traditionally has been one of the most important functions of clinical microbiology laboratories. When blood cultures yield clinically important microorganisms, it is a sign that host defenses have failed to contain an infection at its primary site or that the clinician has failed to adequately eradicate the infectious process. During the past two decades, there has been a number of changes in blood culture practices; these changes have been based on clinical investigations that have established a stronger scientific basis for this diagnostic test. Moreover, manufacturers of blood culture systems and media have improved their products, and there has been a marked trend toward the use of automated systems—most recently, continuous-monitoring blood culture devices. In this review, I will focus on important clinical and technical issues related to blood culturing, as well as on the interpretation of positive blood cultures.

Clinical Issues

Skin antisepsis. The likelihood that a positive culture represents infection rather than contamination is, at least in part, a function of skin antisepsis at the time of culture. The recommended antiseptic preparations are 70% isopropyl alcohol, followed by an iodophor or iodine tincture [1]. Iodophors require 1.5–2 minutes of contact time for maximum antiseptic effect. Iodine tincture exerts its antiseptic effect more rapidly than do iodophors [2] and may lower contamination rates in institutions where these rates are high [3], including centers where house officers and medical students, who may not wait for the iodophor to exert its effect, obtain the blood samples for culture. In one study, a commercially available skin-preparation kit for blood cultures has been shown to reduce contamination [4].

Method of obtaining blood for culture. Venipuncture remains the method of choice for obtaining blood for culture; arterial blood cultures are not associated with higher diagnostic yields than are venous blood cultures [1]. Studies comparing contamination rates for blood cultures obtained from intravascular devices vs. those obtained by venipuncture have reported conflicting results [5–8]. My observations support those of Bryant and Strand [8], who noted significantly increased rates of contamination when blood for culture was obtained from intravenous catheters ($P < .001$).

Furthermore, the American College of Physicians guidelines also recommend that blood for culture not be obtained from intravascular devices [9]. Although blood may occasionally be obtained from intravenous lines, a culture of blood obtained from such a device should be paired with another culture of blood obtained by peripheral venipuncture. Finally, I am unaware of published data from systematic studies that support obtaining separate blood samples from different ports of triple-lumen catheters.

Several recent studies have documented that the two-needle technique, formerly recommended for blood cultures, is not associated with significantly lower contamination rates than is the single-needle technique [10–12]. Because the handling of any needle is associated with a small but finite risk of needlestick injury, the authors of these studies have recommended that the single-needle method become the standard. However, the results of a recently published meta-analysis have suggested that the two-needle method may reduce contamination rates slightly [13]. Nevertheless, pending further data, the single-needle method probably should continue to be the standard.

Number of blood cultures. Several studies have addressed the issue of the number of blood cultures needed to detect

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bacteremia and fungemia in adults. Washington [14] reported the cumulative yield from three 20-mL blood samples obtained in sequence and cultured with use of conventional manual methods; 64 (80%) of 80 bacteremic epidoses were detected with the first culture, 70 (88%) of 80 were detected with the first two cultures, and 79 (99%) of 80 were detected with three blood cultures. My colleagues and I also used conventional manual methods and found that the first blood culture detected 257 (91%) of 282 bacteremic episodes and that the first two blood cultures detected 281 (>99%) of 282 episodes [15].

More recently my colleagues and I used the BacT/Alert continuous-monitoring blood culture system (Organon Teknika, Durham, NC) and evaluated the yield of clinically important microorganisms from three consecutive 20-mL blood samples obtained and cultured during a 24-hour period [16]. During a 15-month period, three blood cultures were performed for 218 patients; the third blood culture was the only one positive on only six occasions, and only one of these positive cultures represented true sepsis. The conclusion that we drew from this small quality assurance study was that for the great majority of patients, two blood cultures should be sufficient to detect septicemia.

On the other hand, single blood cultures should be discouraged, if not forbidden altogether [9]. Not only will single blood cultures be insufficiently sensitive for detecting some bacteremias and fungemias, but they also may be difficult to interpret. For example, a single blood culture that yields a coagulase-negative staphylococcus may represent contamination or clinically important infection. However, if two samples obtained in sequence by separate venipunctures yield the same coagulase-negative staphylococcal species with the same antibiogram, the probability is high that the isolates represent true bacteremia.

On the basis of the concepts reviewed above, laboratories should recommend two blood cultures under routine circumstances. In institutions where phlebotomists or nurses obtain the blood for culture, two blood cultures should be performed automatically, even when the physician orders a single culture. On the other hand, ordering more than two blood cultures during any 24-hour period probably is unnecessary, except when the physician wishes to document the continuous bacteremia associated with an endovascular infection such as endocarditis. Therefore, it may be appropriate to require the approval of the laboratory director when more than two (or perhaps three) blood cultures are ordered during any 24-hour period.

Timing of blood cultures. Few studies have systematically evaluated the timing of blood cultures and the optimum interval between successive blood cultures. Strand [17] has arbitrarily recommended a 30- to 60-minute interval except for critically ill, septic patients, from whom specimens should be obtained minutes before initiating therapy. Li et al. [18] recently showed no difference in yield whether blood samples for cultures performed within a 24-hour period were drawn simultaneously or at spaced intervals [18]. However, drawing blood at intervals may be helpful if the clinician wishes to document continuous bacteremia in patients with suspected endovascular infections.

Technical Factors

Many technical factors affect the sensitivity of blood culture systems. Of these factors, the most important are probably the volume of blood cultured and the broth medium used for culture. Other important factors include the ratio of blood to broth, agitation during incubation, length of incubation, atmosphere of incubation, and additives to the media (e.g., those that neutralize the effect of antimicrobial agents present in the blood at the time the sample is drawn). These and other technical issues have been reviewed in detail elsewhere [1, 19, 20], and the reader is referred to those publications for additional discussion of these matters.

Volume of blood required for culture. During bloodstream infections, especially those in adults, there may be relatively few microorganisms present in a given volume of blood—often in the range of $<1-10$ cfu/mL. Moreover, in numerous studies of adult patients, a direct relationship between the diagnostic yield of blood cultures and the volume of blood cultured has been documented [21–24]. On the basis of this information, the recommended volume of blood per culture set for an adult is 10–30 mL [1], and the preferred volume is 20–30 mL. Blood volumes of >30 mL do not enhance the diagnostic yield and contribute to nosocomial anemia; as a practical matter, blood at these volumes may clot in the syringe, thereby making it impossible to inoculate the blood culture bottles.

The optimal volume of blood that should be obtained from children has not been defined with certainty [25]. However, for infants and small children, Szymczak et al. [26] concluded that the chance of failing to detect bacteremia was greater with blood volumes of <1 mL per culture than with blood volumes of ≥ 1 mL. On the basis of the available data, Paisley and Lauer [25] have recommended 1–2 mL of blood per culture for neonates, 2–3 mL for infants aged 1 month to 2 years, 3–5 mL for older children, and 10–20 mL for adolescents.

Culture media. All but one of the commercially available blood culture systems marketed in the United States are based on the inoculation of blood into broth culture media. No one medium or system is capable of detecting all microorganisms. Thus the results of innumerable clinical studies that evaluated different blood culture media and additives have been published. In general, most commercially marketed blood culture media perform well. However, many manufacturers supplement their base media with proprietary additives designed to enhance microbial growth, and it cannot be assumed that common generic media (e.g., supplemented soybean casein digest broth) from different manufacturers will perform in an equivalent manner. Decisions as to the choice of media formulations should be based on data from well-controlled field trials in which large numbers of cultures were assessed. The U.S. Food and Drug Administration has recently issued guidelines for

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manufacturers that sponsor such clinical field trials; these guidelines have been summarized by Wilson [27].

Blood-to-broth ratio. Human blood contains a number of substances (e.g., complement, lysozyme, and phagocytic WBCs) capable of inhibiting microbial growth. Moreover, nearly one-third of patients are receiving antimicrobial agents at the time blood for cultures is obtained (author's unpublished observations). Thus, to optimize the diagnostic yield, blood should be diluted adequately in the culture broth to minimize the effect of these substances. The results of studies that have addressed this issue have led to the recommendation that blood be diluted fivefold to tenfold [28–30]. Dilutions of <1:5 may result in a reduced yield; thus, filling blood culture bottles with more than the recommended amount of blood should be avoided. Dilutions of >1:10 may also be associated with a reduced yield that is not based on blood-to-broth ratio but rather on inadequate blood volume for culture.

Although commercially available blood culture bottles have a partial vacuum in the headspace, direct-draw techniques may result in overfilling and reduced blood-to-broth ratios. Collection of specimens with a needle and syringe provides greater control for inoculating blood culture bottles with the correct amount of blood and thus is preferred.

Neutralization and inactivation of antimicrobials. Given the frequency with which blood for cultures is obtained from patients already receiving antimicrobial agents, several manufacturers have marketed products designed to counteract the potential inhibitory effect on growth. These include the antimicrobial removal device (ARD; Becton Dickinson Microbiology Systems, Cockeysville, MD), BACTEC resin-containing media (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD), and BacT/Alert FAN media (Organon Teknika).

The ARD, which was first introduced in 1980, has been the subject of many studies that have not defined a clear mandate for its use. By contrast, the results of studies of BACTEC resin media used with the semiautomated radiometric (BACTEC 460) and nonradiometric (BACTEC 660 and 730) systems generally were favorable [20]. In one study in which aerobic nonradiometric resin medium was used, the authors speculated that the improved yield of microorganisms might be due, at least in part, to factors other than the binding of antibiotics [31].

The resin medium is available for use in BACTEC continuous-monitoring blood culture devices (9240 and 9120). The manufacturer of the BacT/Alert continuous-monitoring blood culture instrument has recently marketed an aerobic medium, FAN, that uses activated charcoal in a proprietary substance (Ecosorb) to counter the potential inhibitory effects of antibiotics. Use of both the aerobic and the as yet unmarketed anaerobic formulations of the FAN media was associated with improved yields when they were compared with the standard BacT/Alert media [32–33]. The results of a comparative study of the FAN and BACTEC resin media suggest that the performance of these media is equivalent in the respective continuous-monitoring blood culture instruments [34].

Atmosphere of incubation. Traditional two-bottle blood culture systems have included one aerobic bottle and one anaerobic bottle, with the blood distributed equally between the two bottles. However, during the past two decades, the proportion of bacteremias due to obligate anaerobes has decreased substantially [35–37], leading some authorities to question the need for routine use of the anaerobic bottle. In fact, several recent studies of adults [35, 38, 39] and children [40] have concluded that the routine use of anaerobic blood culture bottles is not necessary and have recommended that these bottles be used only selectively for patients who are at high risk for bacteremia due to anaerobes.

Whether the data from these studies can be generalized to all institutions remains a subject of controversy for several reasons. Only a limited number of culture media and systems have been evaluated in these studies; for example, reports that assess the relative value of the BACTEC anaerobic resin or lytic media, the BacT/Alert anaerobic FAN medium, or the ESP anaerobic (80N) medium (Difco, Detroit) have not been published. Moreover, selective use of anaerobic bottles requires that certain logistic issues be addressed within each institution.

These issues include notifying physicians and staff of the change in procedure and the reasons the change was implemented; determining which, if any, nursing units (e.g., the gynecologic unit and the colon and rectal surgery unit) should be stocked routinely with anaerobic bottles; and, possibly, developing algorithms for the physicians ordering blood cultures or for the individuals obtaining the blood for culture (i.e., the phlebotomists, nurses, clinical care technicians, house officers, and medical students).

Indeed, an orderly and stepwise plan that includes both in-service education and postimplementation quality assurance evaluations to confirm that the recommended blood culture protocols are being followed should be developed at institutions where these changes are implemented.

Length of incubation of blood cultures. In routine circumstances, blood cultures need not be incubated for >7 days. Indeed, several recent studies in which instrumented blood culture systems were used have shown that 5-day incubation periods are sufficient for detecting the majority of pathogens [41–44]. Moreover, after 5 days most newly positive cultures represent contamination [44]. Incubation periods longer than 7 days may be useful when fungemia or bacteremia due to fastidious organisms such as the HACEK group of bacteria or species of *Legionella* or *Brucella* are suspected. Longer incubation periods may also be useful for patients with suspected endocarditis who have been treated with antimicrobial agents before blood cultures are performed. However, Washington [45] has noted that such extended incubation periods rarely increase yield. Mycobacterial blood cultures should be incubated for ≥4 weeks.

Microorganisms that Deserve Special Consideration

Yeasts and filamentous fungi. The incidence of fungemia has increased in recent decades because of the AIDS epidemic and

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because patients with malignancies survive longer, the number of patients with organ transplants has increased, and long-term indwelling intravascular devices are being used more frequently. The Isolator (Wampole Laboratories, Cranbury, NJ) lysis-centrifugation system continues to be the best system for detecting filamentous fungi. The Septi-Chek biphasic blood culture system (Becton Dickinson) also has performed well. Instrumented blood culture systems in which the newer media (e.g., the BACTEC aerobic resin, nonradiometric fungal media, and the BacT/Alert aerobic FAN medium) are used have performed well for the detection of yeasts other than *Cryptococcus neoformans* [32, 34, 46, 47].

Mycobacteria. Before the AIDS epidemic, blood cultures for detecting mycobacteria were rarely, if ever, performed. However, mycobacterial blood cultures are now commonly performed in many laboratories. The Isolator system and the BACTEC radiometric system with 13A media have excellent sensitivity and perform comparably [48, 49]. Manufacturers of continuous-monitoring blood culture systems are in various stages of evaluating these devices in terms of their utility for mycobacterial blood cultures, but no published data are yet available.

Blood Culture Systems that Are Currently Available

Manual blood culture systems. Conventional manual systems and media are available from many commercial sources. Aerobic blood culture bottles and (usually) anaerobic blood culture bottles are inoculated with blood and usually incubated for 7 days. Each bottle is examined daily for macroscopic evidence of microbial growth (e.g., hemolysis, turbidity of the media, gas production, or formation of discrete colonies). An aliquot of the contents of the aerobic bottle is gram stained and subcultured after the first overnight incubation. A terminal subculture is usually done at the end of the incubation period. Conventional manual systems are flexible and require no purchase of expensive instruments, but they are labor intensive.

The biphasic Septi-Chek system and the Opticult blood culture systems (Becton Dickinson) and the Oxoid Signal broth displacement blood culture system (Oxoid Unipath, Basingstoke, England) are labor-saving variations of the conventional manual method.

The Septi-Chek and Opticult systems utilize agar-coated paddles or slants attached to the broth-containing culture bottle and allow subcultures to be done daily or more frequently by inverting the blood-broth mixture so that it covers the agar. Microbial growth is often identified on the agar rather than in the broth, allowing for prompt preliminary identification and susceptibility testing. As mentioned earlier, comparative studies have shown that the Septi-Chek biphasic system performs well in detecting yeasts and other microorganisms [31, 50–52].

The Oxoid Signal system is a one-bottle system. After blood is inoculated into the bottle, a clear-plastic cylindrical signal device is attached to the top of the bottle; a long needle from the lower end of the device extends below the surface of the blood-broth mixture, creating a closed system. Gases produced as a by-product of microbial growth increase the pressure in the headspace and force some of the blood-broth mixture through the needle into the cylinder, thereby "signaling" a positive culture. Comparasons of this system with other manual systems and with the BACTEC radiometric system have yielded mixed results [53–56].

The Isolator is a unique manual blood culture system that is based on lysis of blood cells, centrifugation, and direct inoculation of the centrifugate into solid media. For children, from whom only small volumes of blood may be collected, the centrifugation step is deleted. Many studies that have compared the Isolator system with other systems have been reported (as reviewed by Doern [57]). Overall, the Isolator system performs well in the detection of most microorganisms—especially yeasts, filamentous fungi, mycobacteria, and opportunists such as *Bartonella (Rochalimaea) henselae.* Certain microorganisms, including *Streptococcus pneumoniae,* other streptococci, *Pseudomonas aeruginosa,* and anaerobic bacteria, may not be recovered optimally with this system. A potential advantage of the system is that it allows quantitation of the level of bacteremia or fungemia.

Disadvantages of the Isolator system include the following: the lysing solution is toxic for some microorganisms; specimens must be processed within 8 hours of blood collection (most microbiology laboratories are staffed for only one daily shift); substantial labor is required for the initial processing of Isolator cultures; and the contamination rates for this system are higher than those for conventional broth and automated systems.

Instrumented blood culture systems. Commercially available intsrumented blood culture methods were introduced in the 1970s. Until recently, the BACTEC instrumented systems were the only products commercially available in the United States; these systems were initially equipped with radiometric instruments and media, followed in the mid-1980s by the nonradiometric instruments and media. Both systems (as well as in the newer BACTEC and BacT/Alert continuous-monitoring devices) are based on the utilization of carbohydrate substrates in the culture media and subsequent production of CO_2 by growing microorganisms.

For the radiometric system, the instrument detects $^{14}CO_2$ in the bottle headspace, and for the nonradiometric system, CO_2 is detected by infrared spectrophotometry. For both systems, bottles are loaded onto the detection portion of the instrument, where needles perforate the bottle diaphragm and sample the gas contents of the headspace once or twice daily; a bottle is flagged as positive if the amount of CO_2 in the bottle exceeds a threshold value. The flagged bottle is then removed from the instrument, and an aliquot of its contents is gram-stained and subcultured for further testing. Numerous controlled clinical evaluations of the BACTEC radiometric and nonradiometric

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systems and media have been published; the advantages and disadvantages of these systems have been summarized recently by Wilson et al. [58].

Continuous-monitoring blood culture systems. With changes in health care financing, including the recognition that labor costs need to be better controlled, manufacturers are increasingly looking to the use of automation in clinical microbiology. The early-generation BACTEC instruments had the following disadvantages: culture bottles had to be manually manipulated, gas canisters were needed for every instrument; detection needles had to be changed periodically; sterilization of the needle devices occasionally failed, resulting in a false diagnosis of bacteremia (pseudobacteremia); cultures were sometimes instrument false-positive; and bottle throughput was relatively slow (35–60 seconds per bottle). Continuous-monitoring blood culture systems were developed in an effort to address these problems.

Three of these systems are currently available in the United States: the BACTEC 9000 series (Becton Dickinson), Difco ESP, and the BacT/Alert, which was the first to be marketed in 1991. All systems have several features in common including self-contained modular incubation; agitation; detection units, of which up to five or six can be controlled by a single computer; lack of the need for manual manipulation of culture bottles once they have been loaded into the instrument; instrument monitoring of microbial growth at 10- to 24-minute intervals; and culture bottles that each accept 10 mL of blood.

The BacT/Alert and BACTEC systems detect the production of CO_2 as change in pH; this is accomplished by means of colorimetry in the BacT/Alert system and by means of a fluorescent sensor in the BACTEC system. The ESP system detects changes in pressure, either as gases are used during early microbial growth or as they are produced later during growth. The BacT/Alert and BACTEC systems monitor every bottle at 10-minute intervals and gently rock all bottles 34 and 30 times a minute, respectively. The ESP system monitors aerobic bottles every 12 minutes and agitates them at 160 cycles per minute; anaerobic bottles are monitored every 24 minutes without agitation.

All comparative studies to date have shown that the three continuous-monitoring blood culture systems have detected growth sooner than earlier-generation BACTEC instruments and manual systems [46, 59–66]; these systems have been found to be comparable in terms of performance [66, 67]. All three systems have performed reliably in my laboratory.

Interpretation of Positive Blood Cultures

Since the presence of a bloodstream infection is important in terms of both diagnosis and prognosis, correct interpretation of the positive test result is crucial. Misinterpretation of positive results can be costly both to the institution and to the patient. Bates and colleagues [68] recently calculated that the excess cost associated with each blood culture contaminant was ~$4,500 [68]. Parameters that may be useful in interpreting results include the identity of the microorganism, the presence of more than one blood culture positive for the same microorganism, and the presence of the same microorganism as that found in the blood from another normally sterile site.

Microorganisms that almost always (>90% of isolates) represent true infection when isolated from the blood include *Staphylococcus aureus, Escherichia coli* and other Enterobacteriaceae, *P. aeruginosa, S. pneumoniae,* and *Candida albicans.* Isolates from blood that rarely (<5% of isolates) represent true infection include *Corynebacterium* species, *Bacillus* species, and *Propionibacterium acnes.*

Coagulase-negative staphylococci are particularly problematic, not only because they are so ubiquitous, but also because 12%–15% of the blood isolates are pathogens rather than contaminants [69]. Some authorities have suggested that the number of bottles positive in a culture set is a predictor of the clinical significance of an isolate. However, Mirrett and colleagues [70] and Peacock et al. [71] have found that this criterion is unreliable, at least for coagulase-negative staphylococci.

A useful interpretive concept is the number of culture sets found to be positive vs. the number obtained. If most or all cultures in a series are positive, regardless of the microorganism recovered, the probability that the organism is clinically important is high [15]. Of course, it is the physician who must ultimately make the final judgment, taking into account not only the laboratory findings but also the clinical presentation of the patient.

Limitations of Blood Cultures

Blood cultures, as described herein, currently represent the "gold standard" for diagnosis of septicemia. Nonetheless, they have limitations. Positive results require hours to days of incubation. No one culture medium or system in use has been shown to be best suited to the detection of all potential bloodstream pathogens. Some microorganisms grow poorly, or not at all, in conventional blood culture media and systems. Whether culture-based systems will remain the diagnostic methods of choice into the next century or be replaced by molecular techniques or other methods remains to be determined.

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

(57) Abstract: A fluid control device (200) includes an inlet (212) configured to be placed in fluid communication with a bodily fluid source and an outlet (216) configured to be placed in fluid communication with a fluid collection device, which can produce a negative pressure differential between the outlet and the inlet. A sequestration portion (214) is in fluid communication with the inlet and includes a first flow controller (222) configured to transition from a first state to a second state to place the sequestration portion in fluid communication with the outlet when the negative pressure differential has a first magnitude. A sampling portion (224) is in fluid communication with an outlet and includes a second flow controller (221) configured to transition from a first state to a second state to place the sampling portion in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

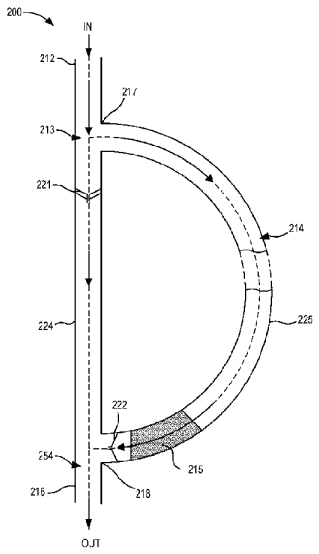


FIG. 2

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[Continued on next page]

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FLUID CONTROL DEVICES AND METHODS OF USING THE SAME

Cross-Reference to Related Applications

[0001] This application claims priority to and the benefit of U.S. Provisional Patent Application Serial No. 62/678,637 entitled, "Fluid Control Devices and Methods of Using the Same," filed May 31, 2018, the disclosure of which is incorporated herein by reference in its entirety.

Background

[0002] Embodiments described herein relate generally to the procurement of bodily fluid samples, and more particularly to fluid diversion, sequestration, and/or isolation devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source.

[0003] Health care practitioners routinely perform various types of microbial as well as other broad diagnostic tests on patients using parenterally obtained bodily fluids. As advanced diagnostic technologies evolve and improve, the speed, accuracy (both sensitivity and specificity), and value of information that can be provided to clinicians continues to improve. Maintaining the integrity of the bodily fluid sample during and/or after collection also ensures that analytical diagnostic results are representative of the in vivo conditions of a patient. Examples of diagnostic technologies that are reliant on high quality, non-contaminated, and/or unadulterated bodily fluid samples include but are not limited to microbial detection, molecular diagnostics, genetic sequencing (e.g., deoxyribonucleic acid (DNA), ribonucleic acid (RNA), next-generation sequencing (NGS), etc.), biomarker identification, and/or the like.

[0004] Inaccurate results from such testing can be due to the presence biological matter including cells external to the intended sample source and/or other external contaminants that inadvertently are included in the bodily fluid sample being analyzed. In short, when the purity of the bodily fluid sample is compromised during the specimen procurement process, resultant analytical test results may be inaccurate, distorted, adulterated, falsely positive, falsely negative, and/or otherwise not representative of the actual condition of the patient. In turn, these results can lead to faulty, inaccurate, confused, unsure, low-confidence, and/or otherwise undesired clinical decision making.

[0005] In some instances, devices and/or systems can be used to reduce the likelihood of contamination, adulteration, and/or the like of bodily fluid samples for testing. For example, some known devices can be configured to collect, divert, separate, and/or sequester (e.g., isolate) an initial volume of bodily fluid that may be more likely to contain contaminants such as dermally residing microbes or the like. Some such devices, however, can be cumbersome, non-intuitive, perceived as difficult to use, inappropriate or unusable for a target patient population, etc. In addition, some such devices can require training, user observation, intervention by more than one user, and/or can otherwise present challenges that can lead to limited efficacy. In some instances, these and/or other challenges can complicate the collection of consistently high quality samples that are non-contaminated, sterile, unadulterated, etc., which in turn, can influence the validity of test result outcomes.

[0006] As such, a need exists for fluid control and/or diversion devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source that result in consistent bodily fluid collection (e.g., from a general patient population and/or a challenging patient population). In addition, a need exists for devices and methods that can include, for example, bodily fluid collection with the assistance of various sources of external energy and/or negative pressure.

Summary

[0007] Devices and methods for procuring bodily fluid samples with reduced contaminants such as dermally residing microbes and/or other contaminants exterior to the bodily fluid source are described herein. In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source and the outlet is configured to be placed in fluid communication with a fluid collection device. The coupling of the outlet to the fluid collection device can produce a negative pressure differential within the fluid control device between the outlet and the inlet. The fluid control device has a sequestration portion in fluid communication with the inlet and a sampling portion in fluid communication with the outlet. The sequestration portion includes a first flow controller configured to transition from a first state in which the sequestration portion is sequestered from the outlet to a second state in which the sequestration portion is in fluid communication with the outlet when the negative pressure differential has a first magnitude. The sampling portion includes a second flow controller configured to transition from a first

state in which the sampling portion is sequestered from the inlet to a second state in which the sampling portion is in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

Brief Description of the Drawings

[0008] FIG. 1 is a schematic illustration of a fluid control device according to an embodiment.

[0009] FIG. 2 is a schematic illustration of a fluid control device according to an embodiment.

[0010] FIG. 3 is a schematic illustration of a fluid control device according to an embodiment.

[0011] FIG. 4 is a schematic illustration of a fluid control device according to an embodiment.

[0012] FIGS. 5-7 are each a schematic illustration of a flow controller included in a fluid control device according to various embodiments.

[0013] FIG. 8 is a schematic illustration of a fluid control device according to an embodiment.

[0014] FIGS. 9 and 10 are schematic cross-sectional illustrations of the fluid control device illustrated in FIG. 8, taken along the line A-A, and shown in a first state and a second state, respectively.

[0015] FIGS. 11 and 12 are schematic cross-sectional illustrations of a fluid control device in a first state and a second state, respectively, according to an embodiment.

[0016] FIGS. 13 and 14 are schematic cross-sectional illustrations of a fluid control device in a first state and a second state, respectively, according to an embodiment.

[0017] FIGS. 15 and 16 are flowcharts, each of which illustrates a method of using a fluid control device to divert an initial volume of bodily fluid to procure bodily fluid samples with reduced contamination, according to different embodiments.

Detailed Description

[0018] Devices and methods for collecting, diverting, sequestering, isolating, etc. an initial volume of bodily fluid to reduce contamination in subsequently procured bodily fluid samples

are described herein. Any of the fluid control devices described herein can be configured to receive, procure, and/or transfer a flow, bolus, volume, etc., of bodily fluid. A first reservoir, channel, flow path, chamber, and/or portion of the device can receive an initial amount of the bodily fluid flow, which then can be substantially or fully sequestered therein (e.g., contained or retained, circumvented, isolated, segregated, vapor-locked, separated, and/or the like). In some instances, contaminants such as dermally residing microbes or the like can be included and/or entrained in the initial amount of the bodily fluid and likewise are sequestered in or by the first reservoir, flow path, or portion of the device. Once the initial amount is sequestered, any subsequent amount of the bodily fluid flow can be diverted, channeled, directed, and/or otherwise allowed to flow to or through a second portion of the device and/or any additional flow path(s) thereof. Based at least in part on the initial amount being sequestered, subsequent amount(s) of bodily fluid can be substantially free from contaminants that may otherwise produce inaccurate, distorted, adulterated, and/or false results in some diagnostics and/or testing. In some instances, the initial amount of bodily fluid also can be used, for example, in other testing such as those less affected by the presence of contaminants, can be discarded as a waste volume, can be infused back into the patient, and/or can be used for any other suitable clinical application.

[0019] In some embodiments, a feature of the fluid control devices and/or methods described herein is the use of an external negative pressure source (e.g., provided by a fluid collection device or any other suitable means) that can (1) overcome physical patient challenges which can limit and/or prevent a sufficient pressure differential to fully engage the sequestration chamber or sequestration portion of the control device and/or to transition fluid flow to the fluid collection device; (2) result in proper filling of the sequestration chamber with a clinically validated and/or desirable volume of bodily fluid; (3) result in efficient, timely, and/or user-accepted consistency with bodily fluid collection process; and/or (4) provide a means of transitioning fluid flow (e.g., automatically or by manipulation to move any number of physical components of the system or by changing, switching, engaging, and/or otherwise providing desired fluid flow dynamics) to enable sequestration and/or isolation of the initial amount (e.g., pre-sample) and collection of a subsequent sample.

[0020] In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source and the outlet is configured to be placed in fluid communication with a fluid collection device. The coupling of the outlet to the fluid collection device can produce a negative pressure differential within

the fluid control device between the outlet and the inlet. The fluid control device has a sequestration portion in fluid communication with the inlet and a sampling portion in fluid communication with the outlet. The sequestration portion includes a first flow controller configured to transition from a first state in which the sequestration portion is sequestered from the outlet to a second state in which the sequestration portion is in fluid communication with the outlet when the negative pressure differential has a first magnitude. The sampling portion includes a second flow controller configured to transition from a first state in which the sampling portion is sequestered from the inlet to a second state in which the sampling portion is in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

[0021] In some embodiments, a fluid control device includes a housing, a first flow controller, and a second flow controller. The housing has an inlet configured to establish fluid communication with a bodily fluid source and an outlet configured to be coupled to a fluid collection device. The housing defines a sequestration flow path that is in fluid communication with the inlet and a sampling flow path that is in fluid communication with the outlet. The first flow controller has a flow state in which the sequestration flow path is in fluid communication with the outlet and a non-flow state in which the sequestration flow path is sequestered from the outlet. The second flow controller has a flow state in which sampling flow path is in fluid communication with the inlet and a non-flow state in which the sampling flow path is sequestered from the inlet. The first flow controller configured to be in the flow state when a negative pressure differential generated by coupling the outlet to the fluid collection device has a first magnitude such that an initial volume of bodily fluid flows through the sequestration flow path toward the first flow controller. The first flow controller is configured to transition to the non-flow state when the initial volume of bodily fluid is received in the sequestration flow path such that (1) the sequestration flow path is sequestered from the outlet and (2) the negative pressure differential is increased to a second magnitude operable to transition the second flow controller from the non-flow state to the flow state.

[0022] In some embodiments, a method of using a fluid control device to obtain a bodily fluid sample with reduced contamination includes coupling a fluid collection device to an outlet of the fluid control device. The coupling of the fluid collection device to the outlet is configured to produce a negative pressure differential within at least a portion of the fluid control device. A first flow controller is transitioned from a first state to a second state when the negative pressure differential has a first magnitude. The first flow controller is configured

to sequester a sequestration portion of the fluid control device from the outlet when in the first state and to establish fluid communication between the sequestration portion and the outlet when in the second state. An initial volume of bodily fluid is received from an inlet of the fluid control device into the sequestration portion in response to the negative pressure differential when the first flow controller is in the second state. The first flow controller is configured to transition from the second state to a third state in response to the sequestration portion receiving the initial volume of bodily fluid. When the first flow controller is in the third state, the first flow controller sequesters the sequestration portion from the outlet the negative pressure differential increases from the first magnitude to a second magnitude. A second flow controller is transitioned from a first state to a second state when the negative pressure differential has the second magnitude. The second flow controller is configured to sequester a sampling portion of the fluid control device from the inlet when in the first state and to establish fluid communication between the sampling portion and the inlet when in the second state. A subsequent volume of bodily fluid is transferred from the inlet to the fluid collection device via the sampling portion and the outlet.

[0023] In some embodiments, a fluid control device includes an inlet and an outlet. The inlet is configured to be placed in fluid communication with a bodily fluid source or an intermediary bodily fluid transfer device. The outlet is configured to be placed in fluid communication with a fluid collection device such as, for example, a sample reservoir (bottle, container, dish, vial, etc.), a culture bottle, and evacuated container, a syringe, a lumen-containing device, and/or any other suitable bodily fluid collection and/or transfer device. The fluid control device has a first state in which a negative pressure differential produced from an external source (e.g., the fluid collection device such as a sample reservoir, a syringe, a vessel, and/or any suitable intermediary fluid reservoir) is applied to the fluid control device to draw an initial volume of bodily fluid from the bodily fluid source, through the inlet, and into a sequestration and/or diversion portion of the fluid control device (which can be formed by or in the fluid control device or coupled thereto). The fluid control device has a second state in which (1) the sequestration and/or diversion portion sequesters the initial volume, and (2) the negative pressure differential draws a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source, through the fluid control device, and into the fluid collection device.

[0024] Any of the embodiments and/or methods described herein can be used in the procurement of clean or substantially unadulterated bodily fluid samples such as, for example,

blood samples. In some instances, bodily fluid samples (e.g., blood samples) can be tested for the presence of one or more potentially undesirable microbes, such as bacteria (e.g., Gram-Positive bacteria and/or Gram-Negative bacteria), fungi, yeast (e.g., Candida), and/or other undesirable microbes. Various technologies can be employed to assist in the detection of the presence of microbes as well as other types of biological matter, specific types of cells, biomarkers, proteins, antigens, enzymes, blood components, and/or the like during diagnostic testing. Examples include but are not limited to molecular polymerase chain reaction (PCR), magnetic resonance and other magnetic analytical platforms, automated microscopy, spatial clone isolation, flow cytometry, whole blood ("culture free") specimen analysis (e.g., NGS) and associated technologies, morphokinetic cellular analysis, and/or other common or evolving and advanced technologies to characterize patient specimens and/or to detect, identify, type, categorize, and/or characterize specific organisms, antibiotic susceptibilities, and/or the like.

[0025] For example, in some instances, microbial testing and/or detection can include incubating blood samples in one or more vessels that may contain culture media (e.g., a nutrient rich and/or environmentally controlled medium to promote growth and/or any number of other mediums), common additives, and/or other types of solutions conducive to microbial growth. Any of the microbes and/or organisms present in the blood sample flourish and/or grow over time in the culture medium (e.g., a variable amount of time from less than an hour to more than several days – which can be longer or shorter depending on the diagnostic technology employed). The presence of the microbes and/or organisms can be detected by automated, continuous monitoring, and/or other methods specific to the analytical platform and/or technology used for detection, identification, and/or the like (e.g., by observing carbon dioxide levels and/or any other suitable methods of detection).

[0026] The presence of microbes and/or organisms in the culture medium suggests the presence of the same microbes and/or organisms in the blood sample, which in turn, suggests the presence of the same microbes and/or organisms in the bodily fluid of the patient from whom the sample was obtained. In other instances, a bodily fluid sample may be analyzed directed (i.e., not incubated) for the presence of the microbes and/or organisms. Accordingly, when the microbes and/or organisms are determined to be present in the blood sample, the patient may be diagnosed and prescribed one or more antibiotics or other treatments specifically designed to treat or otherwise remove the undesired microbes and/or organisms from the patient.

[0027] Patient samples, however, can become contaminated during procurement and/or otherwise can be susceptible to false results. For example, microbes from a bodily surface (e.g., dermally residing microbes) that are dislodged during the specimen procurement process (e.g., either directly or indirectly via tissue fragments, hair follicles, sweat glands, and other skin adnexal structures) can be subsequently transferred to a culture medium, test vial, or other suitable specimen collection or transfer vessel with the patient sample and/or otherwise included in the specimen that is to be analyzed. Another possible source of contamination is from the person drawing the patient sample (e.g., a doctor, phlebotomist, nurse, technician, etc.) and/or the equipment used for drawing the patient sample. For example, equipment, supplies, and/or devices used during a patient sample procurement process often include multiple fluidic interfaces (e.g., patient to needle, needle to transfer adapter, transfer adapter to sample vessel, catheter hub to syringe, syringe to transfer adapter, needle/tubing to sample vessels, and/or any other fluidic interface or any combination(s) thereof) that can each introduce points of potential contamination. In some instances, such contaminants may thrive in a culture medium and/or may be otherwise identified, thereby increasing a risk or likelihood of false, compromised, and/or erroneous microbial test results, which may inaccurately reflect the presence or lack of such microbes within the patient (i.e., in vivo).

[0028] Such inaccurate results because of contamination and/or any other sources of adulteration are a concern when attempting to diagnose or treat a wide range of suspected illnesses, diseases, infections, patient conditions, and/or other maladies. For example, false results from microbial tests may result in a misdiagnosis and/or delayed treatment of a patient illness (which could result in the harm to and/or death of the patient or, on the other hand, may result in the patient being unnecessarily subjected to one or more anti-microbial therapies, which may cause serious side effects to and/or consequences for the patient including, for example, death. As such, false results produce an unnecessary burden and expense on the health care system due to extended length of patient stay and/or other complications associated with erroneous treatments. The use of diagnostic imaging equipment to arrive at these false results is also a concern from both a cost perspective and a patient safety perspective as unnecessary exposure to concentrated radiation associated with a variety of imaging procedures (e.g., CT scans) has many known adverse effects on long-term patient health.

[0029] As used in this specification and/or any of the claims included herein, 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.

[0030] As used herein, the terms "about," "approximately," and/or "substantially" when used in connection with a stated value(s) and/or a geometric structure(s) or relationship(s) is intended to convey that the value or characteristic so defined is nominally the value stated and/or characteristic described. In some instances, the terms "about," "approximately," and/or "substantially" can generally mean and/or can generally contemplate a value or characteristic stated within a desirable tolerance (e.g., plus or minus 10% of the value or characteristic stated). For example, a value of about 0.01 would include 0.009 and 0.011, a value of about 0.5 would include 0.45 and 0.55, a value of about 10 would include 9 to 11, and a value of about 1000 would include 900 to 1100. While a value, structure, and/or relationship stated may be desirable, it should be understood that some variance may occur as a result of, for example, manufacturing tolerances or other practical considerations (such as, for example, the pressure or force applied through a portion of a device, conduit, lumen, etc.). Accordingly, the terms "about," "approximately," and/or "substantially" can be used herein to account for such tolerances and/or considerations.

[0031] As used herein, "bodily fluid" can include any fluid obtained directly or indirectly from a body of a patient. For example, "bodily fluid" includes, but is not limited to, blood, cerebrospinal fluid, urine, bile, lymph, saliva, synovial fluid, serous fluid, pleural fluid, amniotic fluid, mucus, sputum, vitreous, air, and the like, or any combination thereof.

[0032] 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.

[0033] As used herein, the terms "pre-sample," "first," and/or "initial," can be used interchangeably to describe an amount, portion, or volume of bodily fluid that is collected and/or sequestered prior to procuring the "sample" volume. A "pre-sample," "first," and/or "initial" volume can refer to a predetermined, defined, desired, and/or given volume of bodily fluid. For example, a predetermined and/or desired pre-sample volume of bodily fluid can be a drop of bodily fluid, a few drops of bodily fluid, and/or a volume of bodily fluid equal to about 0.1 milliliter (mL), about 0.2 mL, about 0.3 mL, about 0.4 mL, about 0.5 mL, about 1.0

mL, about 2.0 mL, about 3.0 mL, about 4.0 mL, about 5.0 mL, about 10.0 mL, about 20.0 mL, about 50.0 mL, and/or any volume or fraction of a volume therebetween. Alternatively, a pre-sample volume can be greater than 50.0 mL or less than 0.1 mL. In some specific embodiments, a predetermined and/or desired pre-sample volume can be between about 0.1 mL and about 5.0 mL. In other embodiments, a pre-sample volume can be, for example, a combined volume of any number of lumen (e.g., lumen that form at least a portion of a flow path from the bodily fluid source to an initial collection chamber, portion, reservoir, etc...

[0034] As used herein, the terms "sample," "second," and/or "subsequent" can be used interchangeably to describe a volume, portion, or amount of bodily fluid that is used, for example, in one or more sample or diagnostic tests. A "sample" volume can be either a random volume or a predetermined or desired volume of bodily fluid collected after collecting, sequestering, and/or isolating a pre-sample volume of bodily fluid. A desired sample volume of bodily fluid can be, for example, between about 10.0 mL to about 60.0 mL. Alternatively, a desired sample volume of bodily fluid can be less than 10.0 mL or greater than 60.0 mL. In some embodiments, for example, a sample volume can be at least partially based on one or more tests, assays, analyses, and/or processes to be performed on the sample volume.

[0035] The embodiments described herein can be configured to transfer bodily fluid with reduced contamination and/or substantially free from contamination to one or more fluid collection device(s). In some embodiments, a fluid collection device can include, but is not limited to, any suitable vessel, container, reservoir, bottle, adapter, dish, vial, syringe, device, diagnostic and/or testing machine, and/or the like. In some embodiments, a fluid collection device can be substantially similar to or the same as known sample containers such as, for example, a Vacutainer ® (manufactured by Becton Dickinson and Company (BD)), a BacT/ALERT ® SN or BacT/ALERT ® FA (manufactured by Biomerieux, Inc.), and/or any suitable reservoir, vial, microvial, microliter vial, nanoliter vial, container, microcontainer, nanocontainer, and/or the like. In some embodiments, a fluid collection device can be similar to and/or substantially the same as any of those described in U.S. Patent No. 8,197,420 entitled, "Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination," filed December 13, 2007 ("the '420 Patent"), the disclosure of which is incorporated herein by reference in its entirety.

[0036] In some embodiments, a fluid collection device can be devoid of contents prior to receiving a sample volume of bodily fluid. For example, in some embodiments, a fluid collection device or reservoir can define and/or can be configured to define or produce a

vacuum or suction such as, for example, a vacuum-based collection tube (e.g., a Vacutainer ®), a syringe, and/or the like. In some embodiments, a sample reservoir can include, for example, any suitable additives, substances, enzymes, oils, fluids, compounds, chemicals, etc. (e.g., heparin, citrate, acid citrate dextrose (ACD), ethylenediaminetetraacetic acid (EDTA), oxalate, sodium polyanethol sulfonate (SPS), and/or the like). In other embodiments, a sample reservoir can contain, for example, an aerobic culture medium or an anaerobic culture medium. The sample reservoir (e.g., culture bottle) can receive a bodily fluid sample, which can then be tested (e.g., after incubation via in vitro diagnostic (IVD) tests and/or any other suitable test) for the presence of, for example, Gram-Positive bacteria, Gram-Negative bacteria, yeast, fungi, and/or any other organism. If testing of the culture medium yields a positive result, the culture medium can be subsequently tested using, for example, a PCR-based system to identify a specific organism.

[0037] While the term "culture medium" can be used to describe a substance configured to react with organisms in a bodily fluid (e.g., microorganisms such as bacteria) and the term "additive" can be used to describe a substance configured to react with portions of the bodily fluid (e.g., constituent cells of blood, serum, synovial fluid, etc.), it should be understood that a sample reservoir can include any suitable substance, liquid, solid, powder, lyophilized compound, gas, etc. Moreover, when referring to an "additive" within a sample reservoir, it should be understood that the additive could be a culture medium, an additive, and/or any other suitable substance, and/or any combination(s) thereof. That is to say, the embodiments described herein can be used with any suitable fluid collection device, reservoir, and/or the like containing any suitable substance.

[0038] While some of the embodiments are described herein as being used for procuring bodily fluid for one or more culture sample testing, it should be understood that the embodiments are not limited to such a use. Any of the embodiments and/or methods described herein can be used to transfer a flow of bodily fluid to any suitable device that is placed in fluid communication therewith. Thus, while specific examples are described herein, the devices, methods, and/or concepts are not intended to be limited to such specific examples.

[0039] The embodiments described herein and/or portions thereof can be formed or constructed of one or more biocompatible materials. In some embodiments, the biocompatible materials can be selected based on one or more properties of the constituent material such as, for example, stiffness, toughness, durometer, bioreactivity, etc. Examples of suitable biocompatible materials include metals, glasses, ceramics, or polymers. Examples of suitable

metals include pharmaceutical grade stainless steel, gold, titanium, nickel, iron, platinum, tin, chromium, copper, and/or alloys thereof. A polymer material may be biodegradable or non-biodegradable. Examples of suitable biodegradable polymers include polylactides, polyglycolides, polylactide-co-glycolides (PLGA), polyanhydrides, polyorthoesters, polyetheresters, polycaprolactones, polyesteramides, poly(butyric acid), poly(valeric acid), polyurethanes, and/or blends and copolymers thereof. Examples of non-biodegradable polymers include nylons, polyesters, polycarbonates, polyacrylates, polysiloxanes (silicones), 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.

[0040] The embodiments described herein and/or portions thereof can include components formed of one or more parts, features, structures, etc. When referring to such components it should be understood that the components can be formed by a singular part having any number of sections, regions, portions, and/or characteristics, or can be formed by multiple parts or features. For example, when referring to a structure such as a wall or chamber, the structure can be considered as a single structure with multiple portions, or multiple, distinct substructures or the like coupled to form the structure. Thus, a monolithically constructed structure can include, for example, a set of substructures. Such a set of substructures may include multiple portions that are either continuous or discontinuous from each other. A set of substructures can also be fabricated from multiple items or components that are produced separately and are later joined together (e.g., via a weld, an adhesive, and/or any other suitable method).

[0041] Referring now to the drawings, FIG. 1 is a schematic illustration of a fluid control device 100 according to an embodiment. Generally, the fluid control device 100 (also referred to herein as "control device" or "device") is configured to withdrawal bodily fluid from a patient. A first portion or amount (e.g., an initial amount) of the withdrawn bodily fluid is sequestered from a second portion or amount (e.g., a subsequent amount) of the withdrawn bodily fluid which can be subsequently used for additional testing, discarded, and/or reinfused into the patient. In this manner, contaminants or the like can be sequestered within the first portion or amount, leaving the second portion or amount substantially free of contaminants. The second portion or amount of bodily fluid can then be used as a biological sample in one or more tests for the purpose of medical diagnosis and/or treatment (e.g., a blood culture test or the like), as described in more detail herein. The first portion or amount of bodily fluid can be

discarded as waste or can be used in any suitable test that is less likely to produce false, inaccurate, distorted, inconsistent, and unreliable results as a result of potential contaminants contained therein. In some circumstances, for example in patients with limited supply of the bodily fluid such as blood, the first portion or amount of bodily fluid can be reinfused back into the patient via any suitable method.

[0042] The control device 100 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the control device 100 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in a sequestration, diversion, isolation, and/or storage portion of the control device 100. As described in further detail herein, the control device 100 can be configured to transition between operating modes such that (1) the first portion or amount of bodily fluid selectively flows through at least a first portion of the fluid control device and is subsequently sequestered therein, and (2) the second portion or amount of bodily fluid selectively flows through at least a second portion of the fluid control device and into a fluid collection device or the like. In some embodiments, the control device 100 can be configured to transition between operating modes automatically (e.g., based on pressure differential, time, electronic signal or instruction, saturation of a membrane or member, an absorbent and/or barrier material, etc.) or via and/or in response to intervention (e.g., user intervention, mechanical intervention, or the like).

[0043] The control device 100 includes an inlet 112, at least one outlet 116, and a sequestration chamber 114. In addition, the control device 100 defines one or more fluid flow paths 113 between the inlet 112 and at least the sequestration chamber 114 and/or one or more fluid flow paths 154 between the inlet 112 and the outlet(s) 116.

[0044] The inlet 112 of the control device 100 is configured to be placed in fluid communication with a bodily fluid source such as, for example, the vasculature of a patient. In some embodiments, the inlet 112 can be coupled to and/or can include an inlet device such as, for example, an intravenous (IV) catheter, a needle, a peripherally inserted central catheter (PICC), a syringe, one or more pieces of sterile tubing, and/or any other suitable lumen-containing device and/or intermediary transfer device. In some embodiments, the inlet 112 can be a port, a valve, and/or the like such as, for example, a Luer Lok ® or any other suitable coupler. In such embodiments, the inlet 112 (e.g., port or coupler) can be configured to couple to an access or inlet device in fluid communication with a patient (e.g., a placed or indwelling IV catheter or needle). In some embodiments, the inlet 112 can be physically and fluidically coupled to the access or inlet device via a lock, coupler, port, etc. In other embodiments, the

inlet 112 can be in fluid communication with the access or inlet device via an intermediate lumen-containing device such as, for example, sterile tubing or the like. In still other embodiments, the inlet 112 of the control device 100 can form and/or can be integrally or monolithically formed with the access or inlet device.

[0045] The sequestration chamber 114 is at least temporarily placed in fluid communication with the inlet 112 via the fluid flow path(s) 113. As described in further detail herein, the sequestration chamber 114 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 112 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein.

[0046] Although not shown in FIG.1, in some embodiments, the fluid control device 100 can have one or more flow path(s) 113 that include one or more flow modulating features (e.g., flow restrictors, fluid flow retardants, etc.) that selectively modulate the flow of bodily fluid drawn therethrough. In some embodiments, the flow modulating features can be structural and built into the fluid control device 100. In other embodiments, the flow modulating features can be separately formed or can be a material that can be introduced within the fluid control device 100, for example within the sequestration chamber 114, as described in further detail herein.

[0047] The sequestration chamber 114 can be any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 114 can be at least partially formed by a body portion of the control device 100 (not shown in FIG. 1). In other embodiments, the sequestration chamber 114 can be a reservoir placed and/or disposed within a portion of the control device 100. In other embodiments, the sequestration chamber 114 can be formed and/or defined by a portion of the fluid flow path 113. That is to say, the control device 100 can define one or more lumen and/or can include one or more lumen-defining device(s) configured to receive a flow of bodily fluid from the inlet 112, thereby defining the fluid flow path 113. In such embodiments, at least a portion of the lumen and/or a portion of the lumen-defining device(s) can form and/or can define the sequestration chamber 114.

[0048] The sequestration chamber 114 can have any suitable volume and/or fluid capacity. For example, in some embodiments, the sequestration chamber 114 can have a volume and/or fluid capacity between about 0.25 milliliters (mL) and about 5.0 mL. In some embodiments, the sequestration chamber 114 can have a volume measured in volumes as small as a microliter or less of bodily fluid (e.g., a volume as small as 20 drops of bodily fluid, 10 drops of bodily

fluid, 5 drops of bodily fluid, a single drop of bodily fluid, or any suitable volume therebetween). In other embodiments, the sequestration chamber 114 can have a volume up to, for example, about 5.0 mL, 10.0 mL, 15.0 mL, 20.0 mL, 30.0 mL, 40.0 mL, 50.0 mL, or more. In some embodiments, the sequestration chamber 114 can have a volume that is equal to and/or that is based at least in part on the volumes of a lumen of the inlet device coupled to and/or included in the control device 100, the lumen of the inlet 112, and a portion of the fluid flow path 113 defined between the inlet 112 and the sequestration chamber 114 and/or any combination thereof. In other embodiments, the sequestration chamber 114 can have a volume that is equal to and/or that is based at least in part on the individual and/or combined volumes of a portion of the inlet device, the inlet 112 of the control device 100, and the portion of the fluid flow path 113 defined between the inlet 112 and the sequestration chamber 114.

[0049] Although not shown in FIG. 1, in some embodiments, the fluid control device 100 and/or the sequestration chamber 114 can include and/or can be formed of one or more features or materials configured to interact with a portion of the bodily fluid transferred into the sequestration chamber 114. For example, in some embodiments, the fluid control device 100 and/or the sequestration chamber 114 can include and/or define a valve, a membrane, a diaphragm, a restrictor, a vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that at least selectively allows the passage of air or gas therethrough), a port, a junction, an actuator, and/or the like, or any suitable combination thereof (collectively referred to herein as a "flow controller"). Such flow controllers can be configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 114 and/or any other suitable portion of the fluid control device 100. In this context, the flow of fluids, for example, can be a liquid such as water, oil, dampening fluid, bodily fluid, and/or any other suitable liquid, and/or can be a gas such as air, oxygen, carbon dioxide, helium, nitrogen, ethylene oxide, and/or any other suitable gas.

[0050] In some embodiments, one or more openings and/or one or more flow controllers can be configured to facilitate air displacement into or out of the sequestration chamber 114. In some embodiments, the air displacement from the sequestration chamber 114 as an initial portion of the bodily fluid is transferred into the sequestration chamber 114 can allow for a redistribution of pressure in the sequestration chamber 114 and/or between the sequestration chamber 114 and, for example, the fluid source and/or a portion of the fluid flow path outside of the sequestration chamber 114, or a pressure of an ambient environment into which the sequestration chamber 114 is vented. In some embodiments, the redistribution of pressure can

be a factor in determining and/or defining how bodily fluid flows through the control device 100 and/or the amount or volume of bodily fluid to be transferred into the sequestration chamber 114.

[0051] In other embodiments, the sequestration chamber 114 and/or control device 100 can include a flow controller operable to selectively control a flow of bodily fluid through the fluid flow paths 113 in any suitable manner. For example, in some embodiments, the control device 100 can be configured to selectively transfer a volume of bodily fluid to the sequestration chamber 114 or to the outlet 116 based at least in part on a pressure differential between two or more portions of the control device 100. In some embodiments, the pressure differential can result from fluidically coupling the outlet 116 to an evacuated fluid collection device 160 (e.g., a sample reservoir, a syringe, a pressure charged canister, and/or other source or potential energy to create a vacuum or pressure differential). In other embodiments, the pressure differential can result from a change in volume and/or temperature. In still other embodiments, the pressure differential can result from at least a portion of the control device 100, and/or other portions of the flow paths 113 and/or 154 being evacuated and/or charged (e.g., the sequestration chamber 114 and/or any other suitable portion). In some embodiments, the pressure differential can be established automatically or via direct or indirect intervention and/or manipulation (e.g., by the user). Moreover, a flow of a fluid (e.g., gas and/or liquid) resulting from a pressure differential can be selectively controlled via one or more flow controllers that can, for example, transition between one or more operating conditions to control the fluid flow. It should be understood that the flow controllers included in the embodiments described herein are presented by way of example and not limitation. Thus, while specific flow controllers are described herein, it should be understood that fluid flow can be controlled through the control device 100 by any suitable means.

[0052] In some embodiments, a wall or structure of the fluid control device 100 can define an opening, aperture, port, orifice, and/or the like that is in fluid communication with the sequestration chamber 114. In some embodiments, the control device 100 can include a semi-permeable member, film, membrane, or material such as a hydrophobic or hydrophilic membrane disposed in or about the opening or elsewhere in the flow paths 113 to selectively allow a flow of air or gas through the opening while limiting or substantially preventing a flow of fluid (e.g., bodily fluid such as blood) through the opening.

[0053] In some embodiments, for example, the control device 100 can include an absorbent and/or hydrophilic material disposed within the sequestration chamber 114. Accordingly,

when bodily fluid is transferred into the sequestration chamber 114, the absorbent and/or hydrophilic material can absorb, attract, retain, expand, and/or otherwise interact with at least a portion of the bodily fluid, which in turn, can sequester and/or retain at least an initial portion of the bodily fluid within the sequestration chamber 114, as described in further detail herein.

[0054] In some embodiments, the fluid control device 100 can include one or more self-sealing vent materials that permit the flow of air or air pressure (e.g., vacuum) but not the flow of fluid (i.e., liquid). For example, the self-sealing material when wetted or when in contact with a fluid may absorb or otherwise become saturated and transition to a sealed configuration such that the self-sealing material does not permit air or liquid therethrough. The transitioning of the self-sealing material (e.g., vent) may be associated with the fluid control device 100 moving from a first state (e.g., wherein an initial portion of the bodily fluid is being transferred into the sequestration chamber 114) to a second state (e.g., after the initial portion of the bodily fluid is transferred into the sequestration chamber 114).

[0055] In some embodiments, the sequestration chamber 114 or any other portion of the fluid control device 100 can include and/or can be formed of an expandable or collapsible material configured to transition between a first state (e.g., while an initial portion of the bodily fluid is being transferred into the sequestration chamber 114) to a second state (e.g., after the initial portion of the bodily fluid is transferred into the sequestration chamber 114). For example, the collapsible material can be in the form of a dissolvable substance that initially blocks the flow path 113 within which it is present and does not permit the flow of fluid (e.g., gas or liquid) therethrough. Upon coming into contact with a predetermined amount of fluid, however, the material can be dissolved or otherwise transitioned to a dissolved configuration to release the obstruction of the fluid flow path 113 in which the material is disposed. In some embodiments, the change in configuration resulting from such a material expanding, collapsing, dissolving, etc. can be operable to transition the control device 100 and/or any suitable portion of the control device 100 from a first state, mode, position, configuration, etc., to a second state, mode, position, configuration, etc., as described in further detail herein.

[0056] In some embodiments, the control device 100 and/or the sequestration chamber 114 can include a valve such as, for example, a duckbill valve, a butterfly valve, a one-way check valve, etc. and can be made from any suitable material with any suitable cracking pressure (e.g., an amount of pressure or force sufficient to open the valve) to be used to direct fluid flow as desired. For example, the fluid control device 100 can include two or more valves with varying cracking pressure such that they open sequentially with increasing pressure. Such a

configuration can be used, for example, in conjunction with a suitable source of negative pressure and suitable flow controllers to direct fluid flow.

[0057] The outlet(s) 116 is/are in fluid communication with and/or is/are configured to be placed in fluid communication with the fluid flow paths 113 and/or 154. The outlet 116 can be any suitable outlet, opening, port, stopcock, lock, seal, coupler, valve (e.g., a one-way check valve, duckbill valve, umbrella valve, and/or the like), etc. and is configured to be fluidically coupled to the fluid collection device 160. In some embodiments, the outlet 116 can be monolithically formed with the collection device 160, a syringe, and/or other intermediary bodily-fluid transfer device. In other embodiments, the outlet 116 can be at least temporarily coupled to the collection device 160 via an adhesive, a resistance fit, a mechanical fastener, a threaded coupling, a piercing or puncturing arrangement, any number of mating recesses, and/or any other suitable coupling or combination thereof. Similarly stated, the outlet 116 can be physically (e.g., mechanically) and/or fluidically coupled to the collection device 160 such that an interior volume defined by the collection device 160 is in fluid communication with the outlet 116. In still other embodiments, the outlet 116 can be operably coupled to the collection device 160 via an intervening structure (not shown in FIG. 1), such as a flexible sterile tubing. In still other embodiments, the outlet 116 can be fluidically coupled to a downstream source of negative pressure that suitably directs the flow of fluid into the collection device 160.

[0058] In some embodiments, the arrangement of the outlet 116 can be such that the outlet 116 is physically and/or fluidically sealed prior to coupling to the collection device 160. In some embodiments, the outlet 116 can be transitioned from a sealed configuration to an unsealed configuration in response to being coupled to the collection device 160 and/or in response to a negative pressure differential between an environment within the outlet 116 and/or control device 100 and an environment within the collection device 160.

[0059] The fluid collection device 160 can be any suitable device for at least temporarily containing a bodily fluid, such as, for example, those described above. For example, in some embodiments, the fluid collection device 160 can be a single-use disposable collection tube(s), a syringe, a vacuum-based collection tube(s), an intermediary bodily-fluid transfer device, and/or the like. In some embodiments, the fluid collection device 160 can be substantially similar to or the same as known sample containers such as, for example, a Vacutainer ®, a BacT/ALERT ® SN or BacT/ALERT ® FA, and/or any other suitable reservoir, vial, microvial, microliter vial, nanoliter vial, container, microcontainer, nanocontainer, and/or the like. In some embodiments, the collection device 160 can be a sample reservoir that includes

a vacuum seal that maintains negative pressure conditions (vacuum conditions) inside the sample reservoir, which in turn, can facilitate withdrawal of bodily fluid from the patient, through the fluid control device 100, and into the sample reservoir, via a vacuum or suction force, as described in further detail herein. In embodiments in which the fluid collection device 160 is an evacuated container or the like, the user can couple the collection device 160 to the outlet 116 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the bodily fluid is transferred into and sequestered by the sequestration chamber 114 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 114 and flows into the fluid collection device 160.

[0060] Although the outlet 116 of the control device 100 is described above as being fluidically coupled to and/or otherwise placed in fluid communication with the fluid collection device 160 (e.g., a sample reservoir, syringe, etc.), in other embodiments, the control device 100 can be used in conjunction with any suitable bodily fluid collection device, system, and/or the like. For example, in some embodiments, the fluid control device 100 can be used in any suitable fluid transfer device such as those described in U.S. Patent Publication No. 2015/0342510 entitled, "Sterile Bodily-Fluid Collection Device and Methods," filed June 2, 2015 (referred to herein as the "'510 publication"), the disclosure of which is incorporated herein by reference in its entirety. More particularly, the control device 100 can be used in an "all-in-one" or pre-assembled device (e.g., such as those described in the '510 publication) to receive and sequester an initial volume of bodily fluid such that contaminants in subsequent volumes of bodily fluid are reduced and/or eliminated. In other embodiments, the outlet 116 can include and/or can be coupled to an adapter, outlet needle, and/or the like. For example, in some embodiments, the outlet 116 can be coupled to and/or can include a transfer adapter and/or the like such as, for example, the transfer adapters described in U.S. Patent Publication No. 2015/0246352 entitled, "Apparatus and Methods for Disinfection of a Specimen Container," filed March 3, 2015 (referred to henceforth as the "'352 publication"), the disclosure of which is incorporated herein by reference in its entirety.

[0061] As described above, the device 100 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 100 to establish fluid communication between the inlet 112 and the bodily fluid source (e.g., a vein of a patient, cerebral spinal fluid (CSF) from the spinal cavity, urine collection, and/or the like). As a specific example, in some

instances, the inlet 112 can be coupled to and/or can include a needle or the like that can be manipulated to puncture the skin of the patient and to insert at least a portion of the needle in the vein of the patient, thereby placing the inlet 112 in fluid communication with the bodily fluid source (e.g., the vein, an IV catheter, a PICC, etc.).

[0062] In some embodiments, once the inlet 112 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 116 can be fluidically coupled to the collection device 160. As described above, the collection device 160 can be any suitable reservoir, container, and/or collection system configured to receive a volume of bodily fluid. More particularly, the collection device 160 can be, for example, an evacuated reservoir or container that defines a negative pressure and/or can be a syringe that can be manipulated to produce a negative pressure. In some instances, coupling the outlet 116 to the collection device 160 selectively exposes at least a portion of the fluid flow paths 113 and/or 154 to the negative pressure, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 112, and into the fluid control device 100.

[0063] In some embodiments, the arrangement of the control device 100 is such that when a volume of bodily fluid is transferred to and/or through the inlet 112, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 112, through at least a portion of the fluid flow path 113, and into the sequestration chamber 114. That is to say, in some embodiments, the control device 100 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 113 and into the sequestration chamber 114. For example, in some embodiments, the initial state of the control device 100 can be one in which one or more flow controllers (e.g., valves, membranes, diaphragms, restrictors, vents, air permeable and fluid impermeable barriers, ports, and/or the like) are in a first state in which the fluid flow path 113 is exposed to the negative pressure differential via the sequestration chamber 114. In other words, the negative pressure within the sample reservoir 160 (or created by a syringe or other source of negative pressure) can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 114 that is operable in drawing an initial flow of bodily fluid into the sequestration chamber 114 when one or more flow controllers is in a first or initial state.

[0064] For example, in some embodiments, the control device 100 can include one or more flow controller(s) such as those described above that is at least temporarily fluidically coupled

to a flow path between the fluid collection device 160 and the sequestration chamber 114. In some embodiments, the flow controller(s) can be at least temporarily fluidically coupled to a flow path between the fluid collection device 160 and the inlet 112. While in some embodiments the flow controller examples noted above can be, for example, known off-the-shelf components that are used in medical devices to control the flow of fluids and air, in other embodiments, the flow controller can be a custom, proprietary, and/or specifically tailored component integrated into the device 100. When the flow controller is in the first or initial state, the flow controller can allow a flow of fluid therethrough in response to the negative pressure of the collection device 160. In some embodiments, the flow controller is configured to allow only a flow of air or gas through the flow controller and is configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) through the flow controller. As such, the collection device 160 can produce a negative pressure differential that is operable to draw an initial portion and/or amount of bodily fluid into the sequestration chamber 114 when the flow controller is in a first or initial state without allowing the initial portion of bodily fluid to flow into the fluid flow path 154 and/or otherwise out of the sequestration chamber 114.

[0065] Although not shown in FIG. 1, in some embodiments, the control device 100 can include a member, device, mechanism, etc. configured to modulate a magnitude of the negative pressure to which the sequestration chamber 114 is exposed. For example, in some embodiments, the control device 100 can include a valve, a membrane, a porous material, a restrictor, and/or any other suitable member and/or device configured to modulate pressure. In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 114 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein (e.g., which is particularly important in fragile patients needing microbial and/or other diagnostic testing associated with use of the control device 100). In addition, the modulation of the negative pressure can, for example, at least partially control a rate at which the fluid control device 100 transitions between a first configuration or state and a second configuration or state. In some embodiments, modulating the negative pressure can act like a timer. For example, a time between the introduction of the negative pressure differential and the transitioning of the diverter from the first state to the second state can be known, predetermined, calculated, and/or controlled. As such, in some instances, modulating the negative pressure can at least partially control an amount or volume of bodily fluid transferred

into the sequestration chamber 114 (e.g., can control a volume of the initial amount of bodily fluid).

[0066] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described above. For example, in some instances, the control device 100 can remain in the first state until a predetermined and/or desired volume (e.g., the initial volume) of bodily fluid is transferred to the sequestration chamber 134. In some embodiments, the initial volume can be associated with and/or at least partially based on a volume of the sequestration chamber 114. In other embodiments, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that can be transferred into the device prior to one or more portions of the control device 100 transitioning from a first operating state or mode to a second operating state or more (e.g., an amount of bodily fluid that can be absorbed by an absorbent, expandable, hydrophilic, and/or a wicking material, an amount of bodily fluid sufficient to fully wet or saturate a vent material or semi-permeable member or membrane, an amount sufficient to equalize one or more pressure differentials within the control device 100, an amount sufficient to transition a valve or actuator, and/or the like).

[0067] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 114, the initial volume is sequestered, segregated, retained, contained, isolated, etc. in the sequestration chamber 114. For example, in some embodiments, the transitioning of the one or more flow controllers from a first state to a second state can be operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 114. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, other external sources of contamination, colonization of catheters and PICC lines that are used to collect samples, and/or the like can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 114 when the initial volume is sequestered therein.

[0068] With the initial volume transferred and/or diverted into the sequestration chamber 114, the device 100 can transition to the second state in which a subsequent volume(s) of bodily fluid can flow through at least a portion the fluid flow paths 113 and/or 154 from the inlet 112 to the outlet 116. In some embodiments, the control device 100 can passively and/or automatically transition (e.g., without user intervention) from the first state to the second state once the initial volume of bodily fluid is sequestered in the sequestration chamber 114. For

example, in some embodiments, filling the sequestration chamber 114 to capacity and/or fully saturating, wetting, and/or impregnating an absorbent or similar material disposed between the sequestration chamber 114 and the sample reservoir 160 can be such that further transfer of bodily fluid into the sequestration chamber 114 is limited and/or substantially prevented due to a removal or diversion of the negative pressure. In other embodiments, the control device 100 can be manually transitioned or transitioned in response to at least an indirect interaction by a user. For example, in some embodiments, a user can at least partially obstruct the opening and/or vent. In other embodiments, the user can actuate an actuator or the like (not shown in FIG. 1) to transition the control device 100 from the first state to the second state. In still other embodiments, at least a portion of the initial volume of bodily fluid can transition the control device 100 from the first state to the second state. For example, the control device 100 can include a bodily fluid activated switch, valve, port, and/or the like. In other embodiments, a volume of bodily fluid can move and/or displace one or more actuators or the like that can, for example, open a port, flow path, and/or outlet. In still other embodiments, a user can manipulate such a switch, valve, port, actuator, etc. to transition the control device 100 from the first state to the second state.

[0069] With the collection device 160 fluidically coupled to the outlet 116 and with the control device 100 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 134), any subsequent volume(s) of the bodily fluid can flow from the inlet 112, through at least one of the fluid flow paths 113 and/or 154, through the outlet 116, and into the collection device 160. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 114 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates and amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 100 can be such that the control device 100 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 114.

[0070] FIG. 2 illustrates a cross-sectional side-view of a fluid control device 200 according to an embodiment. The fluid control device 200 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1. Accordingly, portions of the fluid control device 200 that can be similar to portions of the fluid control device 100 are not described in further detail herein.

[0071] As shown in FIG. 2, the fluid control device 200 (also referred to herein as "control device" or "device") includes an inlet 212, an outlet 216, and a sequestration chamber 214. As described above with reference to the control device 100, the inlet 212 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 216 is configured to be fluidically coupled to a fluid collection device, a syringe, and/or other intermediary bodily fluid transfer device or vessel (not shown in FIG. 2) such as, for example, a transfer device similar to those described in the '510 publication.

[0072] As described above with reference to the fluid control device 100, the control device 200 includes one or more fluid flow paths 213 between the inlet 212 and a sequestration chamber 214 and/or one or more fluid flow paths 254 between the inlet 212 and the outlet 216. The device 200 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the device 200 can be substantially similar in at least form and/or function to the device 100 described above with reference to FIG. 1. In some embodiments, the device 200 can include a first portion 224 and a second portion 225. As shown in FIG. 2, in some embodiments, the second portion 225 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 224. Moreover, the device 200 includes and/or forms a first junction 217 at a position where a first end (e.g., an inlet end) of the second portion 225 is coupled to the first portion 224 and includes and/or forms a second junction 218 at a position where a second end (e.g., an outlet end) of the second portion 225 is coupled to the first portion 224. That is to say, the device 200 can be configured to have and/or form a bifurcation (e.g., the second portion 225) at the first junction 217 which is rejoined at, for example, the second junction 218. In some embodiments, the second portion 225 can form and/or can have a D-shaped configuration and/or arrangement. In other embodiments, the first portion 224 and/or the second portion 225 can form and/or can have any suitable configuration and/or arrangement (e.g., a serpentine configuration, a looping configuration, a spiraled configuration, any suitable geometric configuration, and/or the like). In some embodiments, the first portion 224 and/or the second portion 225 of the device 200 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0073] In some embodiments, the sequestration chamber 214 of the device 200 can be formed by and/or included in the second portion 225 of the device 200. The coupling of the

second portion 225 to the first portion 224 (e.g., at the first junction 217) is such that the sequestration chamber 214 can be selectively placed in fluid communication with the inlet 212 via the fluid flow path 213 and the first junction 217. Similarly, the coupling of the second portion 225 to the first portion 224 (e.g., at the second junction 218) is such that the sequestration chamber 214 can be selectively placed in fluid communication with the outlet 216 and/or a fluid collection device coupled to the outlet 216 via the fluid flow path 254 and the second junction 218,.

[0074] As described in further detail herein, the sequestration chamber 214 is configured to (1) selectively receive a flow and/or volume of bodily fluid from the inlet 212 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 214 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 214 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114. In some embodiments, at least a portion of the fluid flow path 213 can extend through a portion of the device 200 and/or the first junction 217 to form and/or define at least a portion of the sequestration chamber 214. In other embodiments, the first junction 217 and/or the sequestration chamber 214 can include a flow control mechanism and/or the like that can at least temporarily separate the fluid flow path 213 from the sequestration chamber 214. In some embodiments, the device 200 can include, form, and/or define one or more flow controllers such as flow controllers 221, 222, and/or 215. The flow controllers 221, 222, and/or 215 can be, for example, a valve, membrane, diaphragm, restrictor, vent, a selectively permeable member (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air such as, for example, a blood barrier like Porex ®, and/or the like), port, etc. (collectively referred to herein as a "flow controller") placed in one or more desired positions and configured to selectively control (at least in part) a flow of fluids into and/or out of the sequestration chamber 214 and/or any other suitable portion of the device 200.

[0075] More particularly, in the embodiment shown in FIG. 2, the flow controllers 221 and 222 each can be a valve configured to have a specific, desired, and/or predetermined cracking pressure or the like. The valves 221 and/or 222 can be, for example, inline or Lined Pipe Insert (LP) valves that can configured to be suitably placed in any position along pipe or tubing systems. In some embodiments, the valves 221 and/or 222 can be configured to stay in a closed state, limiting or substantially preventing the flow of air or liquid, until a specific amount of

pressure greater than the cracking pressure is applied on the valves 221 and/or 222 to transition the valve 221 and/or 222, respectively, from a closed state to an open state.

[0076] In some embodiments, the valves 221 and/or 222 and other additional valves (not shown) each can be configured to have a variable cracking pressure and to be placed in any suitable position in and/or along the device 200. For example, in some embodiments, as shown in FIG.2, the valve 221 can be disposed in the first portion 224 of the device 200 and downstream of the first junction 217 and the valve 222 can be disposed in the second portion 225 of the device 200 upstream and/or before the second junction 218. In some embodiments, the device 200 can be configured such that the valve 221 has a greater cracking pressure than the valve 222 such that an applied vacuum source may be used to result in a sequential opening of the valves 221 and 222. For example, the cracking pressure of each of the valves 221 and 222 and the pressure exerted by the source of negative pressure can be collectively configured to achieve a sequential and/or otherwise desired first flow of bodily fluid towards and/or into the sequestration chamber 214 and then a desired second flow of bodily fluid towards the outlet 216 and the fluid collection device.

[0077] By way of specific example, in some embodiments, a source of negative pressure (e.g., a fluid collection device and/or the like) can define a vacuum having a magnitude of approximately 8 pounds per square inch (psi). Thus, when the source of negative pressure is coupled to the outlet 216, the pressure is communicated to both valves 221 and 222. In some embodiments, the valve 221 may have, for example, a cracking pressure of 3.4 psi and the valve 222 may have, for example, a cracking pressure of 0.017 psi. As such, the negative pressure differential produced as a result of coupling the negative pressure source to the outlet 216, in turn, can transition the valve 222 (having the lower cracking pressure) from a substantially closed configuration or state to a substantially open configuration or state prior to transitioning the valve 221 (having the higher cracking pressure) from a substantially closed configuration or state to a substantially open configuration or state. In some instances, this sequential opening of the valves (i.e., valve 222 before valve 221), can be operable to direct a flow of fluid (e.g., a first flow) towards the sequestration chamber 214 and then direct the flow of fluid (e.g., a second flow) towards the fluid collection device and/or negative pressure source coupled to the outlet 216, as described further below.

[0078] The device 200, can in some embodiments, include one or more flow controllers in the form of materials that are selectively permeable to air but impermeable or at least selectively permeable to fluid (e.g., liquid). For example, the device 200 can include one or

more membranes made of material that permit the flow of air or convey a vacuum from a source of negative pressure but do not permit or convey a flow of bodily fluid (e.g., hydrophobic). In some embodiment, the device 200 can include flow controllers that can be in a first or initial state or configuration before interaction with a bodily fluid or any other suitable form of actuation, and then transition and/or be transitioned to a second state or configuration upon interaction with the bodily fluid or a suitable form of actuation. For example, in some embodiments, such flow controllers can be in an initial or first state that selectively permits a flow of air therethrough while substantially limiting and/or preventing a flow of bodily fluid therethrough. Upon interaction with a bodily fluid (or any other suitable fluid), the flow controller can transition to a second state, in which the flow controller can be substantially impermeable to the flow of air and the flow of bodily fluid therethrough.

[0079] As shown in the embodiment illustrated in FIG.2, the device 200 can include a flow controller 215 in the form of a membrane, porous material, absorbent material, etc. The flow controller 215 can be any suitable shape, size, and/or configuration. In some embodiments, the flow controller 215 can be formed of a porous material having any suitable pore size to, for example, permit a flow of air therethrough while limiting and/or substantially preventing a flow of liquid therethrough. For example, in some embodiments, the flow controller 215 can be a membrane or the like having a diameter of about 17 mm and having a pore size of about 0.45 micrometers (μm). In other embodiments, the flow controller 215 can be a membrane and/or the like having any suitable diameter (e.g., 1 mm, 2 mm, 3 mm ,4 mm, 5 mm, 10 mm, 15 mm, 20 mm, 30 mm, or more, and/or any diameter therebetween). Likewise, in other embodiments, the flow controller 215 can be a membrane and/or the like having any suitable pore size. In some embodiments, a pore size for a flow controller, membrane, and/or the like can be based on, for example, the type of fluid (e.g., bodily fluid) to be withdrawn, collected, and/or sequestered, the amount or type of particulate matter expected in the fluid flow (e.g., in the flow of the bodily fluid and/or the flow of air), the vacuum source to be used and/or a magnitude of an expected negative pressure differential, and/or any other suitable factor or consideration.

[0080] As shown, the flow controller 215 is positioned within the device 200 to selectively establish fluid communication between the second portion 225 and/or the sequestration chamber 214 and the outlet 216 via the junction 218. Thus, with the flow controller 215 being configured as a semi-permeable member, the flow controller 215 can be configured to at least temporarily allow a gas or air to transfer from the second portion 225 of the device 200 and/or the sequestration chamber 214, through the flow controller 215 and the junction 218, and into

the fluid flow path 254 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 225 and/or the sequestration chamber and the fluid flow path 254 (e.g., via the junction 218), as described in further detail herein. Although not shown, in some embodiments, the device 200 can include one or more actuators or the like configured to control and/or transition the state of the flow controller 215. The outlet 216 of the device 200 is in fluid communication with and/or is configured to be placed in fluid communication with the fluid flow paths 213 and/or 254. The outlet 216 can be any suitable outlet, opening, port, lock, seal, coupler, etc. and is configured to be fluidically coupled to a fluid collection device, such as a sample reservoir, a syringe, container, and/or other sample vessel. In some embodiments, the outlet 216 can be monolithically formed with the fluid collection device or can be at least temporarily coupled to the fluid collection device, as described above with reference to the outlet 116 of the device 100. The fluid collection device can be any suitable collection system for containing a bodily fluid, such as, for example, any of those described in detail above with reference to the collection device 160. More particularly, in some embodiments, the outlet 216 can be configured to couple to an evacuated sample reservoir. In some other embodiments, the outlet 216 can be configured to couple to a source of negative pressure downstream of the outlet 216, while also coupled to the fluid collection device. As such, the user can couple the fluid collection device to the outlet 216 to initiate a flow of bodily fluid from the patient such that a first or initial portion of the bodily fluid is transferred into and sequestered by the sequestration chamber 214 and such that any subsequent portion or volume of bodily fluid bypasses and/or is otherwise diverted away from the sequestration chamber 214 and flows into the fluid collection device.

[0081] In operation, the device 200 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 200 to establish fluid communication between the inlet 212 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 212 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 216 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIG. 2, the fluid collection device can be a negative pressure source and/or can be configured to produce a negative pressure differential. For example, the fluid collection device can be an evacuated reservoir or container that defines a negative pressure, a syringe, a pump, and/or any other negative pressure source. In other embodiments, the fluid

collection device can be a container, reservoir, or device configured to be coupled to a separate negative pressure source.

[0082] Coupling the outlet 216 to the fluid collection device and/or the source of negative pressure selectively exposes at least a portion of the fluid flow path 254 to the negative pressure within or passing through the fluid collection device. As described above, the flow controller 215 and/or the valves 221 and 222 can be configured to selectively control the flow of fluid through the device 200. More particularly, coupling the outlet 216 to the fluid collection device and/or source of negative pressure results in a negative pressure differential within the fluid flow path 254, which in turn, exposes the valves 221 and 222 to the negative pressure. As described above, in some embodiments, the valve 221 can have a greater cracking pressure (e.g., 3.4 psi) compared to that of the valve 222 (e.g., 0.017 psi). Furthermore, the flow controller 215 upstream of the valve 222 can be a membrane in an initial or first state, in which the flow controller 215 is permeable to a flow of air or gas. In some instances, such an arrangement results in the valve 222 being transitioned from a closed state to an open state such that the negative pressure is communicated through the valve 222 and the flow controller 215 and into the sequestration chamber 214.

[0083] Accordingly, a negative pressure differential is produced that is operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 212, and into the fluid flow path 213. Moreover, with the valve 222 in the open state and the valve 221 in the closed state, the bodily fluid can flow through the fluid flow path 213 and into the sequestration chamber 214 (e.g., via the junction 217). As described above with reference to the control device 100, the arrangement of the device 200 is such that when a volume of bodily fluid is transferred to and/or through the inlet 212, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 212, through at least a portion of the fluid flow path 213 and/or the junction 217, and into the sequestration chamber 214. That is to say, in some embodiments, the control device 200 can be in first or initial state in which the initial portion or volume of bodily fluid can flow in or through at least a portion the fluid flow path 213 and/or junction 217 and into the sequestration chamber 214. When the device 200 is in the first or initial state, the valve 221 is in a closed state and as such, the bodily fluid does not pass through the valve 221 nor substantially enter the fluid flow path 254.

[0084] As described above, the control device 200 can be in the initial state when the flow controller 222 (valve) is in an open state, which in turn, allows the negative pressure differential

to draw the initial amount of bodily fluid into the sequestration chamber 214. In some instances, the bodily fluid can flow through the second portion 225 (e.g., the sequestration chamber 214) until the flow reaches the flow controller 215 (e.g., a selectively permeable membrane or member, as described above). The membrane 215 can be in its initial or first state and therefore can be permeable to air but impermeable to liquids. As such, the membrane 215 isolates, separates, segregates, sequesters and/or otherwise prevents direct liquid communication between the fluid flow paths 213 and the sequestration chamber 214. In addition, the inlet 212 is exposed to the negative pressure differential via the sequestration chamber 214. In other words, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least the second portion 225 of the device 200 (e.g., the sequestration chamber 214) that is operable in drawing an initial flow of bodily fluid from the inlet 212, through at least a portion of the fluid flow path 213 and/or the junction 217, and into the sequestration chamber 214 when the control device 200 is in the first or initial state.

[0085] When the flow controller 215 is in the first or initial state, the flow controller 215 can allow a flow of fluid (e.g., a gas or air) therethrough in response to the negative pressure of the sample reservoir (or a syringe or other source of potential energy used to create negative pressure), as described above with reference to the device 100. The flow controller 215 (e.g., selectively permeable membrane or member) can be configured to transition from the first state of being permeable to air and impermeable to liquid, to a second state of being impermeable to air and liquid in response to the flow of the initial amount of bodily fluid into the sequestration chamber 214. For example, the filling of the sequestration chamber 214 to capacity can correspond to and/or otherwise result in the bodily fluid saturating, wetting, and/or impregnating the flow controller 215 (e.g., membrane material), which can transition the flow controller 215 from the first state to the second state. In the second state the flow controller 215 is impermeable to air and liquid, thereby limiting and/or substantially preventing fluid communication between the sequestration chamber 214 and the source of negative pressure (e.g., the fluid collection device). In other words, the sequestration chamber 214 can be sequestered from the negative pressure source in response to initial volume of bodily fluid filling the sequestration chamber 214.

[0086] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control device 100. For example, in some instances, the initial volume can be associated with and/or at least partially based on

an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 215 (e.g., selectively permeable membrane or member). In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 215 to a second state (e.g., a saturated or fully wetted state). In some embodiments, the flow controller 215 is placed in a sealed configuration when transitioned to the second state. That is to say, saturating and/or fully wetting the flow controller 215 (e.g., the semi-permeable material) places the flow controller 215 in a sealed configuration in which the flow controller 215 substantially prevents a flow of a liquid and a gas therethrough.

[0087] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 214, the control device 200 can be transitioned to its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 214. For example, as described above, the flow controller 215 is placed in the sealed configuration, which fluidically isolates the sequestration chamber 214 from the fluid flow path 254. In addition, the transitioning of the flow controller 215 can be in response to the initial amount of bodily fluid filling the sequestration chamber 214. Accordingly, the initial amount of bodily fluid in the sequestration chamber 214 can limit and/or substantially prevent further amounts of bodily fluid from being transferred into the sequestration chamber 214. Thus, the initial amount and/or portion of bodily fluid is sequestered and/or retained within the sequestration chamber 214. As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 214 when the initial volume of bodily fluid is sequestered therein.

[0088] With the flow controller 215 in the second state (e.g., an impermeable or sealed state), the negative pressure otherwise exerted on or through the sequestration chamber 214 is now exerted on or through the fluid flow path 254 and thus, on the flow controller 221. In some instances, a magnitude of the negative pressure can build and/or increase within the fluid flow path 254 until the negative pressure becomes sufficient to transition the flow controller 221 from its first state to its second state. More specifically, when the flow controller 221 is a valve, the negative pressure can increase until it becomes sufficient to overcome the cracking pressure of the valve 221. As such, when the valve is placed in its open state (and/or when the flow controller 221 is otherwise in its second state), the inlet 212 is exposed to the negative pressure differential via the fluid flow path 213. With the fluid collection device fluidically

coupled to the outlet 216 and with the control device 200 being in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 214), any subsequent volume(s) of the bodily fluid can flow from the inlet 212, through the fluid flow paths 213 and 254, through the flow controller 221 (e.g., valve), through the outlet 216, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 214 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates and amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the control device 200 can be such that the control device 200 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 214.

[0089] Although not shown in FIG. 2, in some embodiments, the control device 200 can include an actuator and/or the like configured to be moved (e.g., via a force applied by a user) between a first state and a second state. In other embodiments, a control device can include any suitable member, device, mechanism, etc. configured to selectively establish fluid communication between two or more fluid flow paths (e.g., the fluid flow paths 213 and 254).

[0090] In some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential to which the sequestration chamber 214 is exposed. Although not shown in FIG. 2, the device 200 can include one or more means for reducing and/or controlling a magnitude of the negative pressure differential. For example, in some embodiments, the device 200 can include a restricted flow path path(s) or portions of flow path(s) having a smaller diameter than the fluid flow paths 213 and/or 254. For example, in some embodiments, the one or more restricted flow paths can have a diameter of about 1.0 micrometers (μm), about 10.0 μm, about 100.0 μm, about 1000.0 μm, about 10,000.0 μm, about 100,000.0 μm, and/or any suitable diameter therebetween. In other embodiments, the restricted flow path(s) can have a diameter smaller than 1.0 μm or larger than 100,000.0 μm. In such embodiments, a restricted flow path having a smaller diameter may result in a lower magnitude of negative pressure being applied through the sequestration chamber 214 than a magnitude of negative pressure when the restricted flow path has a larger diameter. Moreover, in some such embodiments, the one or more restricted flow paths can be, for example, gas flow path(s) configured to receive a flow of gas or air but not a flow of a liquid (e.g., bodily fluid). In some embodiments, the diameter of the restricted flow path can be sufficiently small to limit and/or prevent a flow of a liquid therethrough.

[0091] In some embodiments, the restricted flow path can be, for example, disposed between the junction 218 and the flow controller 215, such that a flow of bodily fluid and/or any other liquid is substantially prevented by the flow controller 215 (e.g., a selectively permeable barrier or seal). More specifically, in some embodiments, the restricted flow path can be disposed between, for example, the flow controller 222 (e.g., valve) and the flow controller 215 (e.g., selectively permeable membrane or member). Accordingly, the flow controller 222 can be exposed to a greater magnitude of negative pressure than the magnitude of negative pressure to which the flow controller 215 is exposed. In such embodiments, the greater magnitude of negative pressure can facilitate the transition of the flow controller 222 from its first state to its second state. For example, in some embodiments, when the flow controller 222 is a valve, this arrangement can allow for the valve to be exposed to a negative pressure differential that is sufficient to overcome the cracking pressure of the valve.

[0092] Although the pressure modulation is described above as being based on a diameter of a restricted flow path, it should be understood that this is presented by way of example only and not limitation. For example, in some embodiments, a control device can include any suitable number of restricted flow paths, each of which can have substantially the same diameter or can have varied diameters. For example, in some embodiments, a control device can include up to 100 restricted flow paths or more. In such embodiments, each of the restricted flow paths can have a diameter of between about 1.0 μm and about 100.0 μm, between about 1.0 μm and about 10.0 μm, or between about 1.0 μm and about 5.0 μm. In some embodiments, multiple restricted flow paths can be configured to (1) selectively provide a flow path between the outlet 216 and the sequestration chamber 214 that exposes the sequestration chamber 214 to the negative pressure differential, and (2) act as a flow controller configured to selectively allow the passage of a gas and/or air while substantially preventing the passage of a liquid (e.g., bodily fluid). Other means of modulating the magnitude of negative pressure to which the sequestration chamber is exposed can include, for example, a porous material, a valve, a membrane, a diaphragm, a specific restriction, a vent, a deformable member or flow path, and/or any other suitable means. In some embodiments, the flow controller 215 can be a selectively permeable membrane or member having a predetermined and/or desired porosity to provide the desired amount of negative pressure modulation.

[0093] In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 214 is exposed can, in turn, modulate a magnitude of pressure exerted on the bodily fluid and/or within a vein of a patient. In some instances, such

pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein. In some instances, the ability to modulate and/or control an amount or magnitude of negative pressure can allow the control device 200 to be used across a large spectrum of patients that may have physiological challenges whereby negative pressure is often needed to facilitate collection of bodily fluid such as, for example, blood (e.g., a pressure differential between atmospheric pressure and a patient's vascular pressure may not be sufficient to facilitate consistent and sufficiently forceful flow) but not so much pressure that a rapid force flattens, collapses, caves-in, and/or otherwise inhibits patency and ability to collect blood.

[0094] FIG. 3 illustrates a fluid control device 300 according to another embodiment. The fluid control device 300 (also referred to herein as "control device" or "device") can be of any suitable shape, size, and/or configuration. For example, in some embodiments, the fluid control device 300 can be similar in at least form and/or function to the fluid control device 100 described above with reference to FIG. 1 and/or the fluid control device 200 described above with reference to FIG. 2. Accordingly, portions of the fluid control device 300 that can be similar to portions of the fluid control devices 100 and/or 200 are not described in further detail herein.

[0095] As described above with reference to the fluid control device 200 shown in FIG. 2, the fluid control device 300 shown in FIG. 3 includes an inlet 312, an outlet 316, and a sequestration chamber 314. The inlet 312 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC line, or the like). The outlet 316 is configured to be fluidically coupled to a fluid collection device, a syringe, an evacuated container, and/or other intermediary bodily fluid transfer device or vessel (not shown in FIG. 3) such as, for example, a transfer device similar to those described in the '510 publication. Furthermore, the control device 300 includes and/or defines one or more fluid flow paths 313 between the inlet 312 and the sequestration chamber 314 and/or one or more fluid flow paths 354 between the inlet 312 and the outlet 316.

[0096] In some embodiments, the device 300 can include a first portion 324 and a second portion 325. As shown in FIG. 3, in some embodiments, the second portion 325 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 324. Moreover, the device 300 includes and/or forms a first junction 317 at a position where a first end (e.g., an inlet end) of the second portion 325 is

coupled to the first portion 324 and includes and/or forms a second junction 318 at a position where a second end (e.g., an outlet end) of the second portion 325 is coupled to the first portion 324. That is to say, the device 300 can be configured to have and/or form a bifurcation (e.g., the second portion 325) at the first junction 317 which is rejoined at, for example, the second junction 318. In some embodiments, the first portion 324 and/or the second portion 325 of the device 300 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0097] As described in further detail herein, the sequestration chamber 314 is configured to (1) receive a flow and/or volume of bodily fluid from the inlet 312 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein. The sequestration chamber 314 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 314 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114 and/or 214. In some embodiments, at least a portion of the fluid flow path 313 can extend through a portion of the device 300 to form and/or define at least a portion of the sequestration chamber 314. In some embodiments, the sequestration chamber 314 of the device 300 can be substantially similar in form and/or function to one or more of the sequestration chambers 114 and/or 214. Accordingly, portions of the sequestration chamber 314 may not be described in further detail herein.

[0098] As shown in FIG. 3, the sequestration chamber 314 can be formed by and/or included in the second portion 325 of the device 300 and can be selectively placed in fluid communication with (1) the inlet 312 via the fluid flow path 313 and the first junction 317, and (2) the outlet 316 via the fluid flow path 354 and the second junction 318. As such, the sequestration chamber 314 can be configured to (1) selectively receive a flow and/or volume of bodily fluid from the inlet 312 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein.

[0099] In some embodiment, the fluid control device 300 can include and/or define one or more flow controllers. Flow controllers can include for example, valves, membranes, diaphragms, restrictors, vents, selectively permeable members (e.g., a fluid impermeable barrier or seal that allows at least selective passage of gas or air such as, for example, a blood barrier like Porex ®, and/or the like), ports, etc. (collectively referred to herein as a "flow controller") placed suitably and configured to selectively control (at least in part) a flow of

fluids into and/or out of the sequestration chamber 314 and/or any other suitable portion of the device 300. Some embodiments of the device 300, as shown in FIG. 3, can include flow controllers such as a selectively permeable member 315, a check valve 322, and a dissolvable member 323 that are arranged to, under certain states of function and/or under certain conditions, permit, direct, control, and/or obstruct the flow of fluid in one or more specific directions.

[0100] As shown in FIG. 3, the second portion 325 of the device 300 can include the check valve 322 and the selectively permeable member 315. For example, in some embodiments, the check valve 322 and/or the selectively permeable member 315 can be disposed on, at, or near a proximal or second end of the sequestration chamber 314. In other words, the check valve 322 and the selectively permeable member 315 can be positioned at, on, or near an outlet or outlet portion of the sequestration chamber 314. Said another way, the check valve 322 and/or the selectively permeable member can be positioned at, on, or near an end portion of the sequestration chamber 314 that is closer to the second junction 318 than it is to the first junction 317. In some embodiments, the check valve 322 and/or the selectively permeable member 315 can be integrated into at least a portion of the second junction 318. In some embodiments, the check valve 322 can be substantially similar to the valve 222 described above with reference to the device 200. For example, in some embodiments, the check valve 322 can be configured to have a desired cracking pressure such as those described above with reference to the valve 222. Accordingly, the check valve 322 can be configured to selectively control a flow of fluid between, for example, the fluid flow path 354 and the sequestration chamber 314, as described above with reference to the device 200. As such, the check valve 322 is not described in further detail herein. Moreover, in some embodiments, the device 300 need not include a check valve and/or any other suitable valve.

[0101] The selectively permeable member can be any suitable shape, size, and/or configuration. For example, in some embodiments, the selectively permeable member 315 can be, for example, a membrane, a porous material, an absorbent material, a hydrophilic or hydrophobic material, a selectively permeable barrier, etc. In some embodiments, the selectively permeable member 315 can be substantially similar to the flow controller 215 (e.g., selectively permeable member and/or membrane) and thus, aspects of the selectively permeable member 315 are not described in further detail herein. The selectively permeable member 315 can be configured to at least temporarily allow a gas or air to transfer from the second portion 325 of the device 300 and/or the sequestration chamber 314, through the

selectively permeable member 315 and the junction 318, and into the fluid flow path 354 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 325 and/or the sequestration chamber and the fluid flow path 354 (e.g., via the junction 318). In some embodiments, the selectively permeable member 315 can be in a first or initial state, in which the selectively permeable member 315 allows a flow of air or gas to transfer therethrough, when the device 300 is in its first state and/or configuration. As described in further detail herein, the selectively permeable member 315 can be transitioned to and/or otherwise can be in a second state or configuration, in which the selectively permeable member 315 is substantially impermeable to all fluids (gasses and/or liquids), when the device 300 is in its second state and/or configuration.

[0102] In some embodiments, the dissolvable member 323 can be situated at a suitable position within the first portion of the device 300. For example, in some embodiments, the dissolvable member 323 can be positioned at and/or near the first junction 317, as shown in FIG. 3. In some embodiments, the dissolvable member 323 can be integrated into the junction 317 and/or at least a portion of the junction 317. As such, the dissolvable member 323 can be, for example, upstream of the selectively permeable member 315.

[0103] As described in further detail herein, the dissolvable member 323 can be configured to transition from a first or initial state to a second state in response to contact with a fluid such as, for example, bodily fluid. In some embodiments, for example, the dissolvable member 323 can be disposed within and/or near the first junction 317 to isolate the inlet 312 from the fluid flow path 354 when the device 300 is in the first or initial state. In response to and/or after transferring an initial volume of bodily fluid to the sequestration chamber 314, the device 300 can be transitioned from the first or initial state to the second state. In some embodiments, when the device 300 is in the second state, the dissolvable member 323 can be substantially dissolved, which in turn, can allow fluid communication to be established between the inlet 312 and the fluid flow path 354. In some instances, for example, a portion of the bodily fluid can contact the dissolvable member 323 as the initial volume of bodily fluid flows into the sequestration chamber 314. The contact with the bodily fluid can, in turn, begin to dissolve the dissolvable member 323 such that when the device 300 is transitioned to its second state and/or configuration, the dissolvable member 323 is at least substantially dissolved, thereby placing the inlet 312 in fluid communication with the fluid flow path 354, as described in further detail herein.

[0104] As described above, the device 300 can be used to procure a bodily fluid sample having reduced contamination from microbes such as, for example, dermally residing microbes and/or the like. For example, in some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 300 to establish fluid communication between the inlet 312 and the bodily fluid source (e.g., a vein of a patient). Once the inlet 312 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 316 can be fluidically coupled to the fluid collection device. As described above, in the embodiment shown in FIG. 3, the fluid collection device can be, for example, an evacuated reservoir, a syringe, and/or any container that defines a negative pressure, or is coupled to a downstream source of negative pressure.

[0105] Coupling the outlet 316 to the fluid collection device selectively exposes at least a portion of the fluid flow path 354 to the negative pressure within the fluid collection device. The arrangement of the device 300 when in its first or initial state includes one or more flow controllers in their first state or configuration. For example, the selectively permeable member 315, the check valve 322, and the dissolvable member 323 can each be in their first states and/or configurations when the outlet 316 is coupled to the fluid collection device. In response to the negative pressure, the check valve 322 can be configured to transition from a substantially closed state (e.g., its first configuration or state) to a substantially open state (e.g., its second configuration and/or state). For example, in some instances, establishing fluid communication between the outlet 316 and the fluid collection device can expose the check valve 322 to a negative pressure differential that exceeds, for example, a cracking pressure of the check valve 322. Thus, the check valve 322 can be placed in its second state and/or configuration. In other embodiments, the device 300 need not include a check valve and/or other suitable valve. In such embodiments, the negative pressure differential otherwise operable to transition the check valve 322 would instead be exerted on the selectively permeable member 315, which is substantially similar to when the check valve 322 is in the second or opened state.

[0106] As described above, the selectively permeable member 315 and the dissolvable member 323 are each in their first state or configuration when the outlet 316 is coupled to the fluid collection device. As such, the selectively permeable member 315 can be configured to permit a flow of air, gas, and/or negative pressure therethrough while blocking and/or preventing a flow of liquid therethrough, as described above with reference to the flow controller 215. Furthermore, with the dissolvable member 323 in its first state or configuration, the dissolvable member 323 can be configured to block, isolate, and/or obstruct fluid

communication between, for example, the inlet 312 and the fluid flow path 354 such that it does not permit any flow of fluid (air or liquid or negative pressure) therethrough. Thus, coupling the outlet 316 to the fluid collection device exposes the sequestration chamber 314 to the negative pressure of the fluid collection device, thereby resulting in a negative pressure differential operable in drawing bodily fluid from the bodily fluid source (e.g., the patient), through the inlet 312, and into the sequestration chamber 314.

[0107] As described above with reference to the control devices 100 and 200, the arrangement of the device 300 is such that when a volume of bodily fluid is transferred to and/or through the inlet 312, an initial portion of the volume of bodily fluid (also referred to herein as an "initial volume" or a "first volume") flows from the inlet 312 and into the sequestration chamber 314. That is to say, in some embodiments, the device 300 is in its first or initial state in which the initial portion or volume of bodily fluid can flow from the inlet 312 and into the sequestration chamber 314 in response to the negative pressure differential associated with the fluid collection device. In other words, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 314 that is operable in drawing an initial flow of bodily fluid from the inlet 312 into the sequestration chamber 314 when the control device 300 is in the first or initial state. As described in detail above, in some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential by any suitable means such as those described herein.

[0108] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100 and/or 200. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the membrane 315. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the selectively permeable member 315 to a second state (e.g., a saturated or fully wetted state). As described above with reference to the flow controller 215, the selectively permeable member 315 is placed in a sealed configuration when transitioned to the second state. Thus, transitioning the selectively permeable member 315 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents flow through the selectively permeable member 315.

[0109] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 314, the control device 300 can be transitioned to its second state or

operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 314. As described above, the selectively permeable member 315 is placed in the sealed configuration and thus, substantially prevents a flow of fluid therethrough. In this embodiment, the arrangement of the control device 300 is such that when the selectively permeable member 315 is placed in the sealed configuration, at least a portion of the negative pressure otherwise being exerted through the selectively permeable member 315 is instead exerted on and/or in the fluid flow path 354. The negative pressure, however, can be isolated within the fluid flow path 354 until the dissolvable member 323 is transitioned from its first state and/or configuration to its second state and/or configuration (e.g., until it is at least partially dissolved).

[0110] With the selectively permeable member 315 sealed in its second state and the filling of the sequestration chamber 314 to capacity by the initial volume of bodily fluid drawn, the amount of bodily fluid held at least temporarily at and/or near the junction 317 can place a sufficient amount of bodily fluid in contact with the dissolvable member 323 to transition the dissolvable member 323 from its first state to its second state. In other words, filing the sequestration chamber 314 can place a sufficient volume or amount of bodily fluid into contact with the dissolvable member 323 to substantially dissolve the dissolvable member 323, thereby transitioning it to its second state or configuration. The transition of the dissolvable member 323, in turn, is sufficient to transition the fluid control device 300 from its first state to its second state.

[0111] With the dissolvable member 323 in its second state and/or configuration (e.g., at least partially dissolved), the negative pressure within the fluid flow path 354 can be exerted on the fluid flow path 313 and/or the inlet 312. In some embodiments, the arrangement of the dissolvable member 323 can be such that as the dissolvable member 323 is dissolved, the inlet 312 is exposed to a greater amount and/or magnitude of negative pressure. In other words, the dissolvable member 323 can be configured to dissolve of a predetermined and/or desired period of time, which in turn, can modulate and/or control an amount of negative pressure to which the inlet 312 is exposed. In some embodiments, the dissolvable member 323 can include one or more characteristics that can be tuned, adjusted, and/or the like configured to adjust (e.g., increase or decrease) a rate at which the dissolvable member 323 transitions to its second state (e.g., dissolves). As the dissolvable member 323 is transitioned to its second state and/or configuration, the negative pressure within the fluid flow path 354, urges, draws, and/or induces a flow of bodily fluid from the inlet 312 and the first junction 317, through the fluid

flow path 354 and the outlet 316, and into the fluid collection device. Moreover, the sealed state of the selectively permeable member 315 and the presence of check valves 322 (or other suitable flow controller) can limit and/or substantially prevent flow of bodily fluid from the fluid flow path 354, through the second junction 318, and toward the sequestration chamber 314. In some embodiments, the transitioning of the selectively permeable member 315 and the dissolvable member 323 from their respective first states to their respective second states is operable to sequester and/or retain the initial portion of the bodily fluid in the sequestration chamber 314. As described in further detail herein, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 314 when the initial volume is sequestered therein.

[0112] With the fluid collection device fluidically coupled to the outlet 316 and with the control device 300 in the second state (e.g., the initial volume of bodily fluid is sequestered in or by the sequestration chamber 314), any subsequent volume(s) of the bodily fluid can flow from the inlet 312, through the fluid flow paths 313 and 354, through the outlet 316, and into the fluid collection device. Thus, as described above, sequestering the initial volume of bodily fluid in the sequestration chamber 314 prior to collecting or procuring one or more sample volumes of bodily fluid reduces and/or substantially eliminates and amount of contaminants in the one or more sample volumes. Moreover, in some embodiments, the arrangement of the fluid control device 300 can be such that the device 300 cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 314.

[0113] FIG. 4 illustrates a fluid control device 400 according to an embodiment. The fluid control device 400 can be of any suitable shape, size, and/or configuration. For example, in some embodiments, the fluid control device 400 can be similar in at least form and/or function to one or more of the devices 100, 200, and/or 300 described above with reference to FIG. 1, FIG. 2, and FIG. 3, respectively. Accordingly, portions of the fluid control device 400 that can be similar to portions of the fluid control devices 100, 200, and/or 300 are not described in further detail herein.

[0114] As shown in FIG. 4, the fluid control device 400 (also referred to herein as "control device" or "device") includes an inlet 412, an outlet 416, and a sequestration chamber 414. As described above with reference to the control devices 100, 200, and/or 300, the inlet 412 is configured to be placed in fluid communication with a bodily fluid source to receive a flow of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle, IV catheter, PICC

line, and/or the like). The outlet 416 is configured to be fluidically coupled to fluid collection device, a syringe, a transfer adapter, and/or the like (not shown in FIG. 4). Furthermore, the control device 400 includes and/or defines one or more fluid flow paths 413 between the inlet 412 and at least the sequestration chamber 414 and/or one or more fluid flow paths 454 between the inlet 412 and the outlet 416.

[0115] In some embodiments, the device 400 can include a first portion 424 and a second portion 425. As shown in FIG. 4, in some embodiments, the second portion 425 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 424. Moreover, the device 400 includes and/or forms a first junction 417 at a position where a first end (e.g., an inlet end) of the second portion 425 is coupled to the first portion 424 and includes and/or forms a second junction 418 at a position where a second end (e.g., an outlet end) of the second portion 425 is coupled to the first portion 424. That is to say, the device 400 can be configured to have and/or form a bifurcation (e.g., the second portion 425) at the first junction 417 which is rejoined at, for example, the second junction 418. In some embodiments, the first portion 424 and/or the second portion 425 of the device 400 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0116] The sequestration chamber 414 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 414 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114. In some embodiments, the sequestration chamber 414 of the device 400 can be substantially similar in form and/or function to one or more of the sequestration chambers 114, 214, and/or 314. Accordingly, portions of the sequestration chamber 414 may not be described in further detail herein.

[0117] As shown in FIG. 4, the sequestration chamber 414 can be formed by and/or included in the second portion 425 of the device 400 and can be selectively placed in fluid communication with (1) the inlet 412 via the fluid flow path 413 and the first junction 417, and (2) the outlet 416 via the fluid flow path 454 and the second junction 418. As such, the sequestration chamber 414 can be configured to (1) selectively receive a flow and/or volume of bodily fluid from the inlet 412 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid therein.

[0118] The second portion 425 of the device 400 and/or the sequestration chamber 414 specifically, can include, form, and/or define a flow controller 415 disposed on, at, or near a proximal or second end of the sequestration chamber 414. In other words, the flow controller 415 can be positioned at, on, or near an outlet or outlet portion of the sequestration chamber 414. Said another way, the flow controller can be positioned at, on, or near an end portion of the sequestration chamber 414 that is closer to the second junction 418 than it is to the first junction 417. In some embodiments, the flow controller 415 can be, for example, a membrane, a porous material, an absorbent material, a hydrophilic or hydrophobic material, a selectively permeable barrier, etc. The flow controller 415 can be any suitable shape, size, and/or configuration. In some embodiments, the flow controller 415 can be substantially similar to the flow controller 215 and/or the flow controller 315 and thus, is not described in further detail herein.

[0119] As described in detail above, the flow controller 415 is positioned within the second portion 425 of the device to selectively establish fluid communication between the second portion 425 and/or the sequestration chamber 414 and the outlet 416 via the junction 418. Thus, with the flow controller 415 configured to selectively control fluid flow therethrough (e.g., configured as a semi-permeable member), the flow controller 415 can be configured to at least temporarily allow a gas or air to transfer from the second portion 425 of the device 400 and/or the sequestration chamber 414, through the flow controller 415 and the junction 418, and into the fluid flow path 454 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 425 and/or the sequestration chamber and the fluid flow path 454 (e.g., via the junction 418), as described in further detail herein.

[0120] As described above with reference to the devices 100, 200, and/or 300, the device 400 can include one or more flow controllers that is/are configured to selectively control a flow of gas or liquid (e.g., air or bodily fluid, respectively) through the device 400. For example, in the embodiment illustrated in FIG. 4, the device 400 includes a first flow restrictor 431 and a second flow restrictor 432. The flow restrictors 431 and 432 (and/or any other suitable flow controllers that may be included but not illustrated in FIG. 4) can be included at predetermined and/or desired positions along the first portion 424 and/or the second portion 425 of the device 400 to control, manipulate, divert, and/or direct the flow of air, liquid (e.g., bodily fluid), and/or negative pressure. The flow restrictors 431 and 432 can be configured with varying flow permitting or flow obstructing properties. For example, in some embodiments, the flow restrictor 431 and/or the flow restrictor 432 can have and/or can define any suitable inner cross-

sectional shape, size, and/or configuration to selectively allow fluid flow therethrough, as described in further detail herein.

[0121] In the embodiment shown in FIG. 4, the flow restrictors 431 and 432 each can be a flow restrictor configured to define a flow path therethrough having one or more specific, desired, and/or predetermined characteristics. Moreover, in some embodiments, the second flow restrictor 432 (e.g., the flow restrictor positioned between the second junction 418 and the sequestration chamber 414) can have a flow path that is less restrictive than the flow path of the first flow restrictor 431 (e.g., the flow restrictor positioned between the outlet 416 and the first junction 417). In other words, a pressure differential sufficient to allow fluid (e.g., a gas or liquid) to pass through the second flow restrictor 432 can be less than a pressure differential sufficient to allow fluid (e.g., gas or liquid) to pass through the first flow restrictor 431. Accordingly, the first flow restrictor 431 and the second flow restrictor 431 can be similar to the first valve 221 and second valve 222 described above with reference to FIG. 2.

[0122] As described in further detail herein, the arrangement of the flow restrictors 431 and 432 can be such that when a source of negative pressure (e.g., a fluid collection device and/or the like) is coupled to the outlet 416, the negative pressure differential can result in a flow through the second flow restrictor 432 prior to a flow through the first flow restrictor 431. In some instances, this sequential opening of the flow restrictors (e.g., the flow restrictor 432 before the flow restrictor 431), can be operable to direct a flow of fluid (e.g., a first flow) towards the sequestration chamber 414 and then direct the flow of fluid (e.g., a second flow) towards the fluid collection device and/or negative pressure source coupled to the outlet 416. Said another way, in some embodiments, the device 400 can be configured to transition between a first state in which (1) the inlet 412 is placed in fluid communication with the second portion 425 of the device 400 (e.g., the sequestration chamber 414) and (2) the second flow restrictor 432 establishes selective fluid communication between the sequestration chamber 414 and the outlet 416, and a second state in which (1) the second flow restrictor 432 isolates the sequestration chamber 414 from the outlet 416 and (2) the first flow restrictor 431 establishes selective fluid communication between the inlet 412 and the first portion 424 of the device 400 and/or the outlet 416.

[0123] As described above, with respect to devices 100, 200, and 300, the device 400 can be used to procure a bodily fluid sample having reduced contamination. In some instances, a user such as a doctor, physician, nurse, phlebotomist, technician, etc. can manipulate the device 400 to establish fluid communication between the inlet 412 and the bodily fluid source (e.g., a

vein of a patient). For example, in some embodiments, the user can couple the inlet 412 to an inlet device, a needle, an indwelling catheter or IV, and/or any other suitable lumen-containing device. Once the inlet 412 is placed in fluid communication with the bodily fluid source (e.g., the portion of the patient), the outlet 416 can be fluidically coupled to the fluid collection device. As described herein, the fluid collection device can be any suitable reservoir, syringe, pump, and/or device configured to define and/or produce a negative pressure. In other embodiments, the outlet 416 can be coupled to the fluid collection device, which in turn, is coupled to a downstream source of negative pressure.

[0124] The control device 400 can be in a first or initial state prior to coupling the outlet 416 to the fluid collection device. Coupling the outlet 416 to the fluid collection device selectively exposes at least a portion of the fluid flow path 454 to the negative pressure within the fluid collection device. For example, with the device 400 in its initial or first state, the flow controller 415 can be in its first state or configuration such that the flow controller 415 is permeable to a flow of air or gas but impermeable to a flow of liquid (e.g., bodily fluid). Moreover, the arrangement of the flow restrictors 431 and 432 is such that the first flow restrictor 431 is more restrictive toward a flow of liquid or air therethrough than is the second flow restrictor 432.

[0125] The negative pressure differential defined and/or produced by the fluid collection device results in a suction or drawing of fluid (e.g., air or gas) from the fluid flow path 454. In other words, the negative pressure within and/or produced by the fluid collection device results in a negative pressure differential within the fluid flow path 454. The arrangement of the flow restrictors 431 and 432, and the flow controller 415 can be such that the negative pressure differential within the fluid flow path 454, results in a negative pressure differential through and/or across the outlet 416, the second junction 418, the second flow restrictor 432, the flow controller 415, and the sequestration chamber 414. Moreover, with the first flow restrictor 431 configured to be more restrictive than the second flow restrictor 432, the flow through the second flow restrictor 432 can at least partially maintain a magnitude of the negative pressure within the fluid flow path 454 below a threshold magnitude of negative pressure otherwise operable to induce a flow of fluid through the first flow restrictor 431. That is to say, when the device 400 is in the first state, the negative pressure within the fluid flow path 454 is sufficient to result in a flow through the second flow restrictor 432 but is insufficient to result in a flow through the first flow restrictor 431. Accordingly, the negative pressure within and/or produced by the fluid collection device (coupled to the outlet 416) can draw air and/or gas through the

flow controller 415 and the second flow restrictor 432 and into the fluid flow path 454. Although not shown in FIG. 4, in some embodiments, the device 400 can include a vent or one-way valve configured to allow the air or gas withdrawn from the sequestration chamber 414 to be vented to the atmosphere. In other embodiments, the air and/or gas can be transferred to the fluid collection device, which in turn, can directly or indirectly allow the air or gas to be vented. Thus, the negative pressure within and/or produced by the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the sequestration chamber 414.

[0126] The negative pressure within the sequestration chamber 414 can be operable in drawing an initial flow of bodily fluid from the inlet 412, through the fluid flow path 413 and the first junction 417, and into the sequestration chamber 414 when the control device 400 is in the first or initial state. In some instances, it may be desirable to modulate and/or control a magnitude of the negative pressure differential by any suitable means such as those described herein, including manipulating the permissibility and/or permeability of flow restrictors 431 and/or 432 and/or the flow controller 415. In some embodiments, the flow restrictors 431 and/or 432 can be configured to have one or more external actuators, controllers, and/or adjusters configured to control the amount of flow through the flow restrictors 431 and/or 432 (e.g., by altering or adjusting an inner diameter of the flow restrictors 431 and/or 432). In some other embodiments, the flow restrictors 431 and/or 432 can be configured to adjust and/or alter their properties of permitting fluid flow therethrough based on time, interaction with one or more fluids, and/or any other suitable parameter. In some embodiments, the structure of the flow restrictors 431 and/or 432 can be manipulated (e.g., squeezed, squished, pinched, compressed, etc.) to modulate the degree of negative pressure.

[0127] In some embodiments, modulating and/or controlling a magnitude of the pressure to which the sequestration chamber 414 is exposed can, in turn, modulate a magnitude of pressure (i.e., negative pressure) exerted on the bodily fluid and/or within a vein of a patient. In some instances, such pressure modulation can reduce, for example, hemolysis of a blood sample and/or a likelihood of collapsing a vein. In some instances, the ability to modulate and/or control an amount or magnitude of negative pressure can allow the control device 400 to be used across a large spectrum of patients that may have physiological challenges whereby negative pressure is often needed to facilitate collection of bodily fluid such as, for example, blood but not so much pressure that a rapid force flattens, collapses, caves-in, and/or otherwise inhibits patency and ability to collect blood, as described above.

[0128] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100, 200, and/or 300. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 415. In other words, in some embodiments, the initial volume of bodily fluid can be a volume sufficient to transition the flow controller 415 to a second state (e.g., a saturated or fully wetted state or a sealed state), in which the flow controller 415 is placed in a sealed state and/or configuration. In some embodiments, transitioning the flow controller 415 to the second state sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents a flow of air, gas, and/or liquid (e.g., bodily fluid) through the flow controller 415.

[0129] After the initial volume of bodily fluid is transferred and/or diverted into the sequestration chamber 414, the control device 400 can be in and/or can be placed in its second state or operating mode to sequester, segregate, retain, contain, isolate, etc. the initial volume in the sequestration chamber 414. As described above, the flow controller 415 in its second state or sealed state substantially prevents a flow of fluid including air and liquid therethrough (e.g., and into the second flow restrictor 432 and/or fluid flow path 454). Therefore, the sequestration chamber 414 is fluidically isolated from the fluid collection device and/or source of negative pressure, which in turn, can allow a pressure differential between the sequestration chamber 414 and, for example, the inlet 412 to equalize such that the flow of bodily fluid to the sequestration chamber 414 is limited and/or substantially stops.

[0130] As described previously, an amount of negative pressure sufficient to induce and/or allow a flow of fluid through the first flow restrictor 431 can be greater than an amount of negative pressure sufficient to induce and/or allow a flow of fluid through the second flow restrictor 432. In this embodiment, the arrangement of the control device 400 is such that when the flow controller 415 is placed in the second or sealed configuration, at least a portion of the negative pressure otherwise being exerted through the flow controller 415 builds and/or increases within the fluid flow path 454 to an extent sufficient to induce and/or allow a flow of fluid through the first flow restrictor 431. Thus, with the device 400 in its second state, the negative pressure exerted by the fluid collection device and/or negative pressure source can result in negative pressure within the fluid flow path 454 sufficient to allow bodily fluid to flow from the inlet 412, through the first flow restrictor 431, the fluid flow path 454, and the outlet 416, and into the fluid collection device. As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture

event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 414. Moreover, as described for devices 100, 200, 300, in some embodiments, the arrangement of the fluid control device 400 can be such that the device cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 414.

[0131] While the flow restrictors 431 and 432 are particularly described above with reference to FIG. 4, in other embodiments, a fluid control device can include other forms of flow controllers and/or restrictors in addition to and/or instead of those described in association with device 400. In some embodiments, a fluid control device can include any other suitable means or combination of means for controlling fluid flow therethrough. For example, FIGS. 5-7 illustrate three different embodiments of flow controllers and/or flow restrictors, each according to a different embodiment. FIG. 5 shows a flow restrictor 433 defining an orifice or channel for the passage of air and/or fluid. In this embodiment, the fluid restrictor 433 can have a relatively large inner diameter and a relatively long length. FIG. 6, on the other hand, shows a flow restrictor 434 defining an orifice or channel having a relatively small inner diameter (e.g., smaller than the inner diameter of the flow restrictor 433) and a relatively short length (e.g., shorter than the length of the flow restrictor 433).

[0132] As will be understood, adjusting a length and/or diameter of an orifice or channel of a flow restrictor can allow for an adjusting of a magnitude of a pressure differential sufficient to induce and/or result in a flow of fluid (e.g., bodily fluid) through the orifice or channel. For example, in some embodiments, a flow restriction and/or a restricted flow path can have a diameter of about 1.0 micrometers (μm), about 10.0 μm, about 100.0 μm, about 1000.0 μm, about 10,000.0 μm, about 100,000.0 μm, and/or any suitable diameter therebetween. In other embodiments, the restricted flow path can have a diameter smaller than 1.0 μm or larger than 100,000.0 μm. In such embodiments, a restricted flow path having a smaller diameter may be designed such that a magnitude of a pressure (e.g., negative pressure) sufficient to induce or draw a flow of fluid through the restricted flow path is greater than a magnitude of a pressure sufficient to induce or draw a flow of fluid through a restricted flow path having a larger diameter. Similarly, a longer restricted flow path may be designed such that a magnitude of a pressure (e.g., negative pressure) sufficient to induce or draw a flow of fluid through the restricted flow path is greater than a magnitude of a pressure sufficient to induce or draw a flow of fluid through a restricted flow path having a shorter length.

[0133] FIG. 7 shows a flow controller 435 including a porous material 436 disposed within the flow controller 435. In such embodiments, a porosity and/or permeability of the porous material 436 can be adjusted to adjust a magnitude of a pressure differential sufficient to induce and/or result in a flow of fluid (e.g., bodily fluid) through the orifice or channel. Other examples of flow restrictors and/or flow controllers can include but are not limited to, flow controllers where the restricted or restrictive regions include regions with varying diameter of the cross-section permitting fluid flow or include structures (e.g., porous material) designed to selectively allow or deter fluid flow or air flow as desired. Other embodiments can include, for example, valves, actuators, selectively permeable membranes and/or materials, and/or the like.

[0134] FIGS. 8-10 illustrate a fluid control device 500 according to an embodiment. FIG. 8 shows, for example, a top view of the device 500 and FIGS. 9 and 10 each show a cross-sectional view of the device 500, in a first state and a second state, respectively. The fluid control device 500 can be similar in at least form and/or function to any of the fluid control devices 100, 200, 300, and/or 400. Accordingly, portions of the fluid control device 500 that can be similar to portions of the fluid control devices 100, 200, 300, and/or 400 are not described in further detail herein.

[0135] As shown in FIGS. 8-10, the fluid control device 500 (also referred to herein as "control device" or "device") includes an inlet 512 and an outlet 516, and a sequestration chamber 514. As described above with reference to the control devices 100, 200, 300, and/or 400, the inlet 512 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom (e.g., via a lumen-containing device such as a needle or the like). The outlet 516 is configured to be fluidically coupled to a fluid collection device (not illustrated). The inlet 512, the outlet 516, and the fluid collection device can be substantially similar to those described above and thus, are not described in further detail herein.

[0136] As described above, the control device 500 is configured to (1) receive an initial flow and/or volume of bodily fluid via the inlet 512 and (2) sequester (e.g., separate, segregate, contain, retain, isolate, etc.) the flow and/or volume of bodily fluid within the sequestration chamber 514. The device 500 can be any suitable shape, size, and/or configuration. In some embodiments, the device 500 can have a size that is at least partially based on a volume of bodily fluid at least temporarily stored, for example, in the sequestration chamber 514. For example, in the embodiment shown in FIGS. 8-10, the device 500 can be arranged in and/or

can have a substantially "inline" configuration in which portions of the device 500 are at least partially aligned.

[0137] The device 500 includes and/or defines one or more fluid flow paths 513 between the inlet 512 and at least the sequestration chamber 514 and/or one or more fluid flow paths 554 between the inlet 512 and the outlet 516. In some embodiments, the device 500 can include a first portion 524 and a second portion 525. As shown in FIGS. 9 and 10, in some embodiments, the second portion 525 can be, for example, a bypass and/or diversion portion that is physically coupled to and selectively in fluid communication with the first portion 524. Moreover, the device 500 includes and/or forms a junction 517 at a position where each of a first end (e.g., an inlet end) of the first portion 524 and a first end (e.g., an inlet end) of the second portion 525 couple to the inlet 512. In some embodiments, the first portion 524 and the second portion 525 can be collectively disposed in a housing or otherwise at least partially enclosed by a common structure. In other embodiments, the first portion 524 and/or the second portion 525 of the device 500 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0138] The sequestration chamber 514 can have any suitable shape, size, and/or configuration. For example, in some embodiments, the sequestration chamber 514 can have any suitable size, volume, and/or fluid capacity such as, for example, those described above with reference to the sequestration chamber 114. The sequestration chamber 514 can be formed by and/or included in the second portion 525 of the device 500 and can be selectively placed in fluid communication with (1) the inlet 512 via the fluid flow path 513 and the first junction 517, and (2) the outlet 516 via the fluid flow path 554 and a flow controller 515 (described in further detail herein). In some embodiments, the sequestration chamber 514 of the device 500 can be substantially similar in form and/or function to one or more of the sequestration chambers 114, 214, 314, and/or 414. Accordingly, portions of the sequestration chamber 514 may not be described in further detail herein.

[0139] As shown in FIGS. 9 and 10, the second portion 525 of the device 500 and/or the sequestration chamber 514 specifically, can include, form, and/or define the flow controller 515 disposed on, at, or near a proximal or second end of the sequestration chamber 514. In other words, the flow controller 515 can be positioned at, on, or near an outlet or outlet portion of the sequestration chamber 514 to establish selective fluid communication between the sequestration chamber 514 and the fluid flow path 554. The flow controller 515 can be any

suitable shape, size, and/or configuration. In some embodiments, the flow controller 515 can be, for example, a membrane, a porous material, an absorbent material, a hydrophilic or hydrophobic material, a selectively permeable barrier, etc. In some embodiments, the flow controller 515 can be configured to at least temporarily allow a gas or air to transfer from the second portion 525 of the device 500 and/or the sequestration chamber 514, through the flow controller 515, and into the fluid flow path 554 and can be configured to limit and/or substantially prevent a flow of liquid (e.g., bodily fluid) between the second portion 525 and/or the sequestration chamber 514 and the fluid flow path 554. In some embodiments, the flow controller 515 can be substantially similar in at least form and/or function to the flow controllers 215, 315, and/or 415 and thus, aspects of the flow controller 515 are not described in further detail herein.

[0140] In some embodiments, the device 500 can include one or more flow controllers in addition to the flow controller 515 configured to selectively control, direct, divert, and/or manipulate fluid flow through at least a portion of the flow paths 513 and/or 554. In some embodiments, such flow controllers can be configured to selectively control a flow of fluid through the device 500 in response to, for example, an external force or actuation (e.g., manual intervention by the user), or automatically (e.g., after a period of time and/or in response to a predetermined force, pressure, flow rate, volume of fluid, saturation level, etc. For example, in this embodiment, the device 500 includes a diaphragm 576 movably disposed within the body of the device 500 and configured to at least partially define the sequestration chamber 514. In some embodiments, the diaphragm 576 can be configured to transition, flip, move, switch, deform, etc., from a first configuration or state (FIG. 9) to a second configuration or state (FIG. 10) in response to a negative pressure differential within and/or across at least a portion of the device 500 (e.g., a negative pressure differential associated with and/or resulting from the coupling of the fluid collection device to the outlet 516).

[0141] In some embodiments, the diaphragm 576 can be coupled to a piercing member 578 and configured to move through at least a portion of the device 500 in response to movement of the diaphragm 576. As shown in FIGS. 9 and 10, the device 500 includes a film, barrier, and/or frangible member 574 (referred to herein as "barrier") configured to at least temporarily isolate, separate, and/or sequester the fluid flow path 513 (e.g., an inlet fluid flow path) from the fluid flow path 554 (e.g., an outlet fluid flow path). In some embodiments, the arrangement of the diaphragm 576 and/or the piercing member 578 can be such that as the diaphragm 576 is transitioned from its first state, configuration, and/or position to its second state,

configuration, and/or position, the piercing member 578 is transitioned and/or moved through a portion of the device 500 to pierce, puncture, rupture, break, and/or otherwise reconfigure the barrier 574.

[0142] More specifically, as shown in FIG. 9, the diaphragm 576 can have, for example, a concave shape relative to the barrier 574 when in its first or initial state and the piercing member 578 coupled to the diaphragm 576 is disengaged with and/or separated from the barrier 574. As such, the barrier 574 can be in a first or initial state in which the barrier 574 is sealed, unbroken, not punctured, and/or otherwise acting to fluidically isolate the fluid flow path 513 from the fluid flow path 554. As shown in FIG. 10, the diaphragm 576 can have, for example, a convex shape relative to the barrier 574 when in its second or subsequent state and the piercing member 578 coupled to the diaphragm 576 is engaged with, in contact with, and/or otherwise reconfiguring the barrier 574, thereby piercing through and/or defining an opening through the barrier 574. In other words, as illustrated in FIGS. 9 and 10 respectively, the device 500 and/or the diaphragm 576 is configured to move between a first or initial state in which the fluid flow path 513 is fluidically isolated and/or sequestered from the fluid flow path 554 such that a flow of fluid (e.g., bodily fluid) can flow from the inlet 512, through at least a portion of the fluid flow path 513, and into the sequestration chamber 514, and a second or subsequent state in which the fluid flow path 513 is in fluid communication with the fluid flow path 554 such that a flow of fluid (e.g., bodily fluid) can flow from the inlet 512, through the barrier 574 and the fluid flow path 554, and to the outlet 516. In some embodiments, the transitioning of the device 500 and/or diaphragm 576 from the first state to the second state can be such that a volume of the device 500 defined between the diaphragm 576, the flow controller 515, and the one or more walls of the sequestration chamber 514 is increased (i.e., a volume of the sequestration chamber 514 is increased), which in turn, results in a negative pressure therein that can be operable in drawing at least a portion of the initial volume of bodily fluid through the inlet 512 and into the sequestration chamber 514, as described further below.

[0143] As described above, with respect to devices 100, 200, 300, and/or 400, the device 500 can be used to procure a bodily fluid sample having reduced contamination. For example, in some instances, the control device 500 can be in the first or initial state and a user can manipulate the device 500 to establish fluid communication between the inlet 512 and the bodily fluid source (e.g., a vein of a patient) and to establish fluid communication between the outlet 516 and the fluid collection device (e.g., a sample vessel, syringe, reservoir, etc.). With the device 500 in its initial or first state, coupling the outlet 516 to the fluid collection device

selectively exposes at least a portion of the fluid flow path 554 to the negative pressure within the fluid collection device. Moreover, when the device 500 is in its initial or first state, the flow controller 515 can be in its first state or configuration such that the flow controller 515 is permeable to a flow of air or gas but impermeable to a flow of liquid (e.g., bodily fluid). The barrier 574 is also in its first or initial state such that the barrier 574 fluidically isolates the fluid flow path 513 from the fluid flow path 554. As such, the negative pressure differential defined and/or produced by the fluid collection device results in a suction force within the fluid flow path 554, which in turn, is exerted on or through the flow controller 515. Thus, coupling the outlet 516 to the fluid collection device exposes the sequestration chamber 514 to the negative pressure defined and/or produced by the fluid collection device, thereby resulting in a negative pressure differential operable in drawing the initial volume and/or amount of bodily fluid from the bodily fluid source (e.g., the patient's vasculature), through the inlet 512, at least a portion of the fluid flow path 513, and the junction 517, and into the sequestration chamber 514. Although not shown in FIGS. 8-10, in some embodiments, the device 500 can include any suitable device and/or mechanism configured to modulate the negative pressure to which the sequestration chamber 514 is exposed, as described in detail above.

[0144] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100, 200, 300, and/or 400. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 515 (e.g., transition the flow controller 515 from its first or selectively open state to its second or sealed state). With the flow controller 515 in its second state or sealed state, the flow controller 515 substantially prevents a flow of fluid including air and liquid therethrough, thereby sequestering and/or fluidically isolating the sequestration chamber 514 from the fluid flow path 554. As a result, in some instances, a pressure differential between, for example, the sequestration chamber 514 and the inlet 512 can equalize such that the flow of bodily fluid to the sequestration chamber 514 is limited and/or substantially stops.

[0145] In this embodiment, the arrangement of the control device 500 is such that when the flow controller 515 is placed in the second or sealed configuration, at least a portion of the negative pressure otherwise being exerted through the flow controller 515 builds and/or increases within the fluid flow path 554 to an extent sufficient to transition the diaphragm 576 from its first state or configuration (FIG. 9) to its second state or configuration (FIG. 10). In some embodiments, for example, the diaphragm 576 can flip and/or can be moved from a

concave configuration relative to the barrier 574 to a convex configuration relative to the barrier 574. Moreover, as described above, the transitioning of the diaphragm 576, in turn, moves the piercing member 578 such that the piercing member 578 engages, pierces, punctures, opens, breaks, and/or otherwise reconfigures the barrier 574, thereby placing the fluid flow path 513 in fluid communication with the fluid flow path 554. Thus, with the device 500 in its second state, the negative pressure exerted by the fluid collection device and/or negative pressure source can result in negative pressure within the fluid flow path 554 sufficient to allow bodily fluid to flow from the inlet 512, through the fluid flow path 513, barrier 574, fluid flow path 554, and outlet 516, and into the fluid collection device.

[0146] As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 514. Moreover, as described for devices 100, 200, 300, and/or 400, in some embodiments, the arrangement of the fluid control device 500 can be such that the device cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 514.

[0147] While the flow controller 515 is shown in FIGS. 8-10 as being in fluid communication with the fluid flow path 554 without a feature, device, mechanism, and/or means to modulate an amount of negative pressure disposed therebetween, in other embodiments, a fluid control device can include any suitable feature, device, mechanism, and/or means configured to modulate an amount or magnitude of negative pressure to which a flow controller is exposed. For example, FIGS. 11 and 12 are schematic illustrations of a fluid control device 600 in a first state and a second state, respectively, according to another embodiment. The fluid control device 600 (also referred to herein as "control device" or "device") can be any suitable shape, size, and/or configuration. For example, in some embodiments, the device 600 can be substantially similar in at least form and/or function to any of the devices 100, 200, 300, 400, and/or 500 described herein. More particularly, the device 600 can be substantially similar in at least form and/or function to the device 500 described above with reference to FIGS. 8-10. Accordingly, portions and/or aspects of the fluid control device 600 are not described in further detail herein.

[0148] As shown in FIGS. 11 and 12, the device 600 includes an inlet 612, an outlet 616, and a sequestration chamber 614. In addition, the device 600 includes and/or defines one or more fluid flow paths 613 between the inlet 612 and at least the sequestration chamber 614

and/or one or more fluid flow paths 654 between the inlet 612 and the outlet 616. The inlet 612 is configured to be placed in fluid communication with a bodily fluid source to receive a fluid of bodily fluid therefrom. The outlet 616 is configured to be fluidically coupled to a fluid collection device substantially similar to those described above. The sequestration chamber 614 can be included in and/or formed by a portion of the device 600 and can be selectively placed in fluid communication with (1) the inlet 612 via the fluid flow path 613, and (2) the outlet 616 via the fluid flow path 654 and a flow controller 615. The flow controller 615 can be any suitable shape, size, and/or configuration and can be configured to selectively control, permit, allow, and/or transfer a flow of fluid therethrough. For example, as described above, the flow controller 615 can be a selectively permeable member configured to be selectively permeable to a gas (e.g., air) and substantially impermeable to a liquid (e.g., bodily fluid). In some embodiments, the inlet 612, the outlet 616, the sequestration chamber 614, and the flow controller 615 can be substantially similar to the inlet 512, the outlet 516, the sequestration chamber 514, and the flow controller 515, respectively, described above with reference to the device 500 shown in FIGS. 8-10. Accordingly, portions and/or aspects of the inlet 612, the outlet 616, the sequestration chamber 614, and/or the flow controller 615 are not described in further detail herein.

[0149] In some embodiments, the device 600 can include a first portion 624 and a second portion 625. As shown in FIGS. 11 and 12, in some embodiments, the second portion 625 can be, for example, a bypass and/or diversion portion that (1) is physically coupled to and selectively in fluid communication with the first portion 624 and (2) includes and/or forms the sequestration chamber 614. Moreover, the device 600 includes and/or forms a junction 617 at a position where each of a first end (e.g., an inlet end) of the first portion 624 and a first end (e.g., an inlet end) of the second portion 625 couple to the inlet 612. In some embodiments, the first portion 624 and the second portion 625 can be collectively disposed in a housing or otherwise at least partially enclosed by a common structure. In other embodiments, the first portion 624 and/or the second portion 625 of the device 600 can include and/or can be formed by flexible tubing or the like having any suitable shape and/or size and being reconfigurable or movable to be placed in any suitable configuration and/or arrangement.

[0150] As described above with reference to the device 500, the device 600 includes a diaphragm 676 movably disposed within at least a portion of the device 600 and a piercing member 678 coupled to the diaphragm 676. In some embodiments, the diaphragm 676 can define at least a portion of the sequestration chamber 614. In some embodiments, the

diaphragm 676 and the piercing member 678 can be substantially similar in at least form and/or function to the diaphragm 576 and piercing member 578, respectively, of the device 500. For example, as described above with reference to the diaphragm 576 of the device 500, the diaphragm 676 is configured to transition between a first state, in which the fluid flow path 613 is fluidically isolated from the fluid flow path 654, and a second state, in which the fluid flow path 613 is in fluid communication with the fluid flow path 654, as described in further detail herein.

[0151] While the device 500 is shown and described above as including a single barrier 574 configured to selectively isolate and/or otherwise selectively prevent fluid communication between the fluid flow paths 513 and 554, in the embodiment shown in FIGS. 11 and 12, the device 600 includes a set of barriers configured to selectively prevent or selectively allow fluid flow through the device 600. For example, in some embodiments, the device 600 can include two barriers 674 and 675. Each of the barriers 674 and 675 can be substantially similar in at least form and/or function to the barrier 574 of the device 500 described above with reference to FIGS. 9 and 10. Accordingly, the arrangement of the device 600 can be such that when the diaphragm 676 is in its first state, the piercing member 678 can be disengaged and/or separated from the barriers 674 and 675, which in turn, remain in a sealed, closed, and/or substantially undeformed state (FIG. 11). As the diaphragm 676 is transitioned to its state, however, the piercing member 678 can be moved within the device 600 such that the piercing member 678 engages, contacts, pierces, punctures, and/or otherwise reconfigures each of the barriers 674 and 675, thereby transitioning the barriers 674 and 675 to an unsealed, opened, pierced, and/or deformed state (FIG. 12), as described in further detail herein.

[0152] As described above, the device 600 can include one or more features, mechanisms, devices, and/or means of modulating a negative pressure exerted through one or more portions of the device 600. For example, as shown in FIGS. 11 and 12, the device 600 includes and/or defines a restricted flow path 631 (also referred to herein as a "flow restrictor") configured to establish fluid communication between, for example, the flow controller 615 and the fluid flow path 654. As described above with reference to the flow restrictors 431 and 432 of the device 400 shown in FIG. 4, the flow restrictor 631 can be configured to define a restricted and/or limited flow path therethrough having one or more specific, desired, and/or predetermined characteristics. As described in further detail herein, the arrangement of the flow restrictor 631 can be such that when a source of negative pressure (e.g., a fluid collection device and/or the like) is coupled to the outlet 616, a negative pressure differential can result in a restricted and/or

modulated flow or suction force through the flow restrictor 631, which in turn, results in a restricted and/or modulated negative pressure being exerted on the flow controller 615. Accordingly, the flow restrictor 631 can be substantially similar in at least form and/or function to the flow restrictor 432 described above with reference to FIG. 4.

[0153] As described above with respect to devices 100, 200, 300, 400, and/or 500, the device 600 can be used to procure a bodily fluid sample having reduced contamination. For example, in some instances, the control device 600 can be in the first or initial state (see e.g., FIG. 11) and a user can manipulate the device 600 to establish fluid communication between the inlet 612 and the bodily fluid source (e.g., a vein of a patient) and to establish fluid communication between the outlet 616 and the fluid collection device (e.g., a sample vessel, syringe, reservoir, etc.). With the control device 600 in its first or initial state, coupling the outlet 616 to the fluid collection device selectively exposes at least a portion of the fluid flow path 654 to the negative pressure within the fluid collection device. When the control device 600 is in the first state, the diaphragm 676, the flow controller 615, and the barriers 674 and 675 each can be in their respective first states. Accordingly, the diaphragm 676 can be disposed in a position and/or state such that the piercing member 678 is separated and/or disengaged from the barriers 674 and 675. As such, the barriers 674 and 675 are in their first or sealed state such that the barrier 674 (e.g., a first barrier) fluidically isolates and/or sequesters the fluid flow path 613 from the flow restrictor 631 (e.g., restricted flow path) and such that the barrier 675 (e.g., a second barrier) fluidically isolates and/or sequesters the fluid flow path 613 (e.g., an inlet flow path) from the fluid flow path 654 (e.g., an outlet flow path), as shown in FIG. 11.

[0154] With the fluid collection device coupled to the outlet 616, the negative pressure within the fluid collection device can result in a negative pressure (or negative pressure differential) within at least a portion of the fluid flow path 654. As shown in FIG. 11, however, the barrier 675 fluidically isolates at least a portion of the fluid flow path 654 from other portions of the device 600 and thus, the negative pressure within the fluid flow path 654 is transferred and/or exerted through the flow restrictor 631. Accordingly, a modulated and/or desired portion of the negative pressure within and/or produced by the fluid collection device (coupled to the outlet 616) is transferred through the flow restrictor 631 and in turn, exerted on the flow controller 615. Moreover, with the flow controller 615 in its first state (e.g., a selectively permeable state), the modulated and/or desired portion of the negative pressure within and/or produced by the fluid collection device can result in a negative pressure (or

negative pressure differential) within at least a portion of the sequestration chamber 614 that is operable in drawing an initial flow of bodily fluid from the inlet 612, through at least a portion of the fluid flow path 613, and into the sequestration chamber 614, as described above with reference to, for example, the devices 100, 200, 300, 400, and/or 500.

[0155] The initial portion and/or amount of bodily fluid can be any suitable volume of bodily fluid, as described in detail above with reference to the control devices 100, 200, 300, 400, and/or 500. For example, in some instances, the initial volume can be associated with and/or at least partially based on an amount or volume of bodily fluid that is sufficient to fully wet or saturate the flow controller 615 (e.g., transition the flow controller 615 from its first or selectively open state to its second or sealed state). With the flow controller 615 in its second or sealed state, the flow controller 615 substantially sequesters, blocks, isolates, separates, segregates, and/or otherwise prevents a flow of fluid (e.g., gas and liquid) through the flow controller 615, thereby sequestering and/or fluidically isolating the sequestration chamber 614 from the fluid flow path 654. As a result, in some instances, a pressure differential between, for example, the sequestration chamber 614 and the inlet 612 can equalize such that the flow of bodily fluid to the sequestration chamber 614 is limited and/or substantially stops.

[0156] As described above with reference to the device 500, the arrangement of the control device 600 is such that when the flow controller 615 is placed in its second or sealed state, at least a portion of the negative pressure otherwise being exerted through the flow controller 615 is instead exerted on a concave side or surface of the diaphragm 676. The increased negative pressure on the concave side and/or surface of the diaphragm 676 can be operable to flip, switch, and/or transition the diaphragm 676 from its first state (e.g., a concave state relative to the barrier 674) to its second state (e.g., a convex state relative to the barrier 674). In some embodiments, the flow restrictor 631 can be configured to modulate and/or regulate a magnitude or change in magnitude of the negative pressure being exerted on the diaphragm 676 in substantially the same manner as the modulation and/or regulation of the negative pressure being exerted on or through the flow controller 615. In some instances, modulating the negative pressure exerted on the diaphragm 676 can in turn, modulate, reduce, and/or control a rate at which the diaphragm 676 is transitioned from its first state to its second state.

[0157] As described above, the transitioning of the diaphragm 676, in turn, moves the piercing member 678 coupled thereto such that the piercing member 678 engages, pierces, punctures, opens, breaks, and/or otherwise reconfigures each of the barriers 674 and 675 such that each barrier 674 and 675 is placed in an open state and/or otherwise defines an opening

through which fluid can flow. In other embodiments, the barrier 674 can be configured to form a substantially fluid tight seal with an outer surface of the piercing member 678 as the piercing member 678 extends therethrough. Moreover, as described above with reference to the device 500, the opening of the barrier 675 places the fluid flow path 613 in fluid communication with the fluid flow path 654. As such, the device 600 can be in and/or can be placed in its second state, and the negative pressure exerted by the fluid collection device and/or negative pressure source can result in negative pressure within the fluid flow path 654 sufficient to allow bodily fluid to flow from the inlet 612, through the fluid flow path 613, barrier 675, fluid flow path 654, and outlet 616, and into the fluid collection device (not shown). As described above, in some instances, contaminants such as, for example, dermally residing microbes or the like dislodged during the venipuncture event, can be entrained and/or included in the initial volume of the bodily fluid and thus, are sequestered in the sequestration chamber 614. Moreover, as described for devices 100, 200, 300, 400, and/or 500, in some embodiments, the arrangement of the fluid control device 600 can be such that the device cannot transition to the second state prior to collecting and sequestering the initial volume in the sequestration chamber 614.

[0158] While the device 600 is described above as including the piercing member 678 that pierces the barrier 675 to place the device 600 in the second state, in other embodiments, a device can include any suitable member configured to transition any suitable barrier. For example, FIGS. 13 and 14 illustrate a device 700 according to an embodiment. The device 700 can be substantially similar to the device 600 and thus, similar portions are not described in further detail herein. The device 700 (FIGS. 13 and 14) can differ from the device 600 (FIGS. 11 and 12), however, by including a diaphragm 776 that includes and/or that is coupled to a rod, a pusher, a plunger, an actuator, and/or the like (referred to herein for simplicity as an "actuator"). Moreover, rather than including the barriers 674 and 675 that are configured to be pierced, as described above with reference to the device 600), the device 700 includes barriers 774 and 775 that can have any suitable shape, size, and/or configuration and that can be transitioned, in some instances, in any suitable manner. For example, the barrier 774 can be configured and/or otherwise disposed to form a substantially fluid tight seal with one or more inner surfaces of the device 700 and with one or more outer surfaces of the actuator 778. In this manner, the barrier 774 can limit and/or substantially prevent bodily fluid from undesirably flowing out of a fluid flow path 754 and into other portions of the device 700 (e.g., in a manner similar to that described above with reference to the barrier 674).

[0159] As shown in FIG. 13, when the device 700 is in a first state, the diaphragm 776 can be in a first state (e.g., a non-flipped, unactuated, and/or initial state). Similarly, the actuator 778 coupled to the diaphragm 776 and the barrier 775 can be in a first or initial state. As described in detail above with reference to the device 600, when the barrier 775 is in the first state, a flow path 713 of the device 700 (e.g., an inlet flow path or the like) can be sequestered from the flow path 754 (e.g., an outlet flow path or the like). In other words, the barrier 775 (e.g., a flow controller) can be configured to sequester the flow path 713 from the flow path 754. Thus, when a negative pressure is generated within a portion of the device 700 (e.g., in response to coupling a fluid collection device to an outlet of the device 700), an initial volume of bodily fluid can flow into a sequestration chamber of the device 700 (e.g., a sequestration portion of the device 700, a sequestration flow path, a sequestration reservoir or container, etc.), as described in detail above with reference to the device 600.

[0160] After the initial volume of bodily fluid is received in the sequestration chamber, the arrangement of the device 700 can be such that the diaphragm 776 flips, actuates, moves, and/or otherwise transitions from the first state (FIG. 13) to a second state (FIG. 14). As described in detail above, the movement of the diaphragm can result in a similar movement of the actuator 778 such that the actuator 778 is placed in contact with and moves and/or otherwise transitions the barrier 775 within the device 700. For example, as shown in FIG. 14, the actuator 778 can move the barrier 775 in a substantially linear motion from a first position to a second position, which in turn, can be a position in which the barrier 775 no longer sequesters the flow path 713 from the flow path 754. Thus, a subsequent volume of bodily fluid that is substantially free of contaminants can flow through the device 700 and into the fluid collection device coupled thereto. In this manner, the device 700 can be substantially similar in at least form and/or function to the device 600 and thus, is not described in further detail herein.

[0161] Referring now to FIG. 15, a flowchart is shown illustrating a method 10 of using a fluid control device, such as those described herein, to divert an initial volume of bodily fluid to procure bodily fluid samples with reduced contamination, according to an embodiment. The fluid control device (also referred to herein as "control device") can be similar to and/or substantially the same as any of the control devices 100, 200, 300, 400, 500, 600, and/or 700 described herein.

[0162] The method 10 includes establishing fluid communication between a bodily fluid source and an inlet of the control device, at 11. In some instances, for example, the bodily fluid source can be a fluid source within a patient's body. More specifically, in some instances, the

bodily fluid source can be a vein and/or vascular structure in the patient's body. As described above, the control device can be configured to couple to and/or include an inlet device such as, for example, an intravenous catheter, a butterfly needle, and/or the like. In other embodiments, the inlet device can be any suitable coupler, port, etc. configured to fluidically couple to the bodily fluid source. As such, the inlet device can be manipulated to establish fluid communication between the bodily fluid source and the fluid control device, as described in detail above.

[0163] Having established fluid communication with the bodily fluid source, an initial volume of bodily fluid is transferred from the bodily fluid source to a sequestration chamber included in and/or defined by the control device when the control device is in a first state, at 12. In some embodiments, the control device or a portion thereof (e.g., the sequestration chamber, a junction, an actuator, a flow controller, etc.) is in a first state and/or configuration prior to use. As such, establishing fluid communication with the bodily fluid source automatically establishes fluid communication with the sequestration chamber. More particularly, in some embodiments, a flow controller such as, for example, a valve, a flow restrictor, a selectively permeable member, and/or the like can be in a first state and/or configuration such a flow of at least a gas can pass and/or can be conveyed therethrough.

[0164] As described in detail herein, the initial volume can be any suitable volume of bodily fluid. For example, in some instances, the initial volume can be as small as one drop of bodily fluid (or a relatively few drops of bodily fluid). In other instances, the initial volume can be, for example, up to about 30 mL, 40 mL, 50 mL, or more. Moreover, as described in detail above with reference to specific embodiments, the initial volume can be at least partially based on and/or can be associated with an amount of bodily fluid that can be contained and/or sequestered in the sequestration chamber. In some instances, the initial volume can be at least partially based on and/or associated with a desired amount of fluid sufficient to transition the control device from an initial or first state to a subsequent or second state, using a negative pressure differential defined and/or produced by a negative pressure source coupled to the outlet of the fluid control device. In some instances, the initial volume can be at least partially based on and/or associated with a desired amount of fluid sufficient to transition one or more flow controllers included in the fluid control device from its/their first state to its/their second state. For example, in some instances one or more flow controllers can be driven and/or transitioned by a pressure differential, a predetermined and/or desired fluid volume, a fluid contact, the passage of predetermined and/or desired time, and/or the like, as described herein.

In some instances, the initial volume can be a volume that is sufficient to entrain and/or contain substantially all the undesired microbes that may have been dislodged and/or the like as the fluid communication was being established between the bodily fluid source and the inlet device.

[0165] In response to the initial volume of bodily fluid being disposed in the sequestration chamber, the control device is transitioned (e.g., automatically, passively, or in response to an actuation) from the first state to the second state to sequester the initial volume of bodily fluid in the sequestration chamber, at 13. In some embodiments, for example, the initial volume of bodily fluid can fill the sequestration chamber such that any additional volume of bodily fluid is substantially prevented from entering and/or being contained in the sequestration chamber. In such embodiments, the filled sequestration chamber can form, for example, a fluid lock or the like that substantially prevents additional amounts of bodily fluid from entering the sequestration chamber and/or that substantially prevents bodily fluid from exiting the sequestration chamber. In some embodiments, the sequestration chamber can include a membrane or material interacting with the bodily fluid (e.g., a semi-permeable membrane or the like such as described above with reference to the control devices 100, 200, 300, 400, 500, 600, and/or 700). In some embodiments, the sequestration chamber and/or device can include one or more flow controllers that can be activated (e.g., diaphragms as described with reference to control device 500, 600, and/or 700, and/or any other suitable flow controller) that are activated using any suitable mechanism to draw, divert, and/or sequester bodily fluid. For example, such flow controllers can use a change in a pressure differential (e.g., a pressure differential that can occur when portions of the flow path are sealed and/or closed off from interacting with bodily fluid), as described with reference to control device 500, 600, and/or 700, or can be user activated or activated on the basis of other variables like time, gravity, or the like.

[0166] In some instances, two or more of these mechanisms can be used in combination. For example, in some embodiments, the diversion and/or sequestration of bodily fluid can be carried out using passive mechanisms (e.g., based on one or more pressure differentials and/or filling of the sequestration chamber). In other embodiments, the diversion and sequestration or fluid can also result from one or more active methods such as, for example, one or more actuators operated with or without user intervention. In some embodiments, one or more user mediated mechanisms, actuators, controllers, etc. can be included to provide additional control functions such as, for example, a supervisory or safety override function that may be used in

certain settings such as, for example, during training of personnel on the use of the control devices. In other embodiments, the sequestration chamber can retain and/or sequester the initial volume of bodily fluid in any suitable manner such as those described herein and/or any suitable combination(s) thereof.

[0167] With the control device being transitioned to the second state (e.g., passively or through user intervention), a subsequent volume of bodily fluid is transferred from the bodily fluid source to a fluid collection device (e.g., any of those described herein) in fluid communication with the control device, at 14. As described in detail above, the sequestering of the initial volume of bodily fluid in the sequestration chamber can be operable to sequester any contaminants contained in the initial volume of bodily fluid in the sequestration chamber. Accordingly, the subsequent volume of bodily fluid transferred to the fluid collection device is substantially free of contaminants.

[0168] Referring now to FIG. 16, a flowchart is shown illustrating a method 20 of using a fluid control device, such as those described herein, to divert an initial volume of bodily fluid to procure bodily fluid samples with reduced contamination, according to an embodiment. The fluid control device (also referred to herein as "control device") can be similar to and/or substantially the same as any of the control devices 100, 200, 300, 400, 500, 600, and/or 700 described herein. In some embodiments, for example, the fluid control device can include an inlet configured to be placed in fluid communication with a bodily fluid source and an outlet configured to be coupled to a fluid collection device. Moreover, the fluid control device can include a sequestration portion that is in fluid communication with the inlet and a sampling portion that is in fluid communication with the outlet.

[0169] The method 20 includes coupling a fluid collection device to the outlet of the fluid control device, at 21. The fluid collection device can be any of those described herein. For example, in some embodiments, the fluid collection device can be an evacuated container, sample bottle, syringe, and/or the like. Moreover, the coupling of the fluid collection device to the outlet can be such that a negative pressure differential is produced and/or generated within at least a portion of the fluid control device, as described in detail above.

[0170] A first flow controller of the fluid control device is transitioned from a first state to a second state when the negative pressure differential within the fluid control device has a first magnitude, at 22. As described above, the first flow controller can be a valve, selectively permeable material, restricted flow path, and/or the like configured to sequester the

sequestration portion of the fluid control device from the outlet when in the first state and to establish fluid communication between the sequestration portion and the outlet when in the second state, as described in detail above.

[0171] An initial volume of bodily fluid is received from the inlet of the fluid control device and into the sequestration portion of the fluid control device in response to the negative pressure differential when the first flow controller is in the second state, at 23. In some instances, for example, the inlet can be in fluid communication with a bodily fluid source such as a bodily fluid source within a patient's body (e.g., a vein and/or vascular structure in the patient's body). In some embodiments, for example, the inlet can be coupled to an inlet device such as, for example, an intravenous catheter, a butterfly needle, and/or the like, which in turn, is inserted into a portion of the patient. Thus, bodily fluid can flow from the bodily fluid source, through the inlet of the fluid control device, and into the sequestration portion.

[0172] The first flow controller is transitioned from the second state to a third state in response to the sequestration portion receiving the initial volume of bodily fluid, at 24. As described in detail herein, the initial volume can be any suitable volume such as, for example, a volume as small as one drop of bodily fluid (or a relatively few drops of bodily fluid) up to, for example, 50.0 mL or more. In some instances, the initial volume can be at least partially based on and/or associated with a desired amount of fluid sufficient to transition the first flow controller from the second state to the third state. In some instances, the initial volume can be a volume of bodily fluid that is transferred into the sequestration portion until a negative pressure differential (e.g., between the first flow controller and the inlet) is in substantial equilibrium or the like. In such instances, the first flow controller can automatically transitioned from the second state to the third state when the negative pressure differential operable to draw the initial volume of bodily fluid is in substantial equilibrium. In some embodiments, the first flow controller can include, for example, a selectively permeable material that can be saturated by at least a portion of the initial volume of bodily fluid to transition the first flow controller from the second state to the third state, as described in detail above. As such, the first flow controller can sequester the sequestration portion from the outlet when in the third state.

[0173] With the first flow controller in the third state, the negative pressure differential within a portion of the fluid control device can increase from the first magnitude to a second magnitude. When the negative pressure differential has the second magnitude, a second flow controller is transitioned from a first state to a second state, at 25. The second flow controller

can be configured to, for example, sequester the sampling portion of the fluid control device from the inlet when in the first state and is configured to establish fluid communication between the sampling portion and the inlet when in the second state. As described above with reference to specific embodiments, the second flow controller can be any suitable control device or mechanism such as, for example, a valve, a selectively permeable material, a restricted flow path, a dissolvable material, a frangible barrier, a movable barrier, and/or the like.

[0174] As described above, a pressure differential sufficient to transition the second flow controller from the first state (e.g., a non-flow state) to the second state (e.g., a flow state) is greater than a pressure differential sufficient to transition the first flow controller from the first state (e.g., a non-flow state) to the second state (e.g., a flow state). As such, the second flow controller can be configured to transition to the second state after the first flow controller has transitioned between its first, second, and third states. Thus, a subsequent volume of bodily fluid is transferred from the inlet to the fluid collection device via the sampling portion and the outlet, at 26. As described in detail above, receiving the initial volume of bodily fluid in the sequestration portion and sequestering the sequestration portion from the outlet can be operable to sequester any contaminants contained in the initial volume of bodily fluid in the sequestration portion of the fluid control device. Accordingly, the subsequent volume of bodily fluid transferred to the fluid collection device can have reduced contamination and/or can be substantially free of contaminants.

[0175] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation. Where schematics and/or embodiments described above indicate certain components arranged in certain orientations or positions, the arrangement of components may be modified. While the embodiments have been particularly shown and described, it will be understood that various changes in form and details may be made. For example, while the control devices 100, 200, 300, 400, 500, 600, and/or 700, are described as transferring a bodily fluid into the device as a result of a negative pressure within a fluid collection device, in other embodiments, the devices described herein can be used with any suitable device configured to establish a pressure differential (e.g., a negative pressure differential). For example, in some embodiments, an outlet of a control device can be coupled to a syringe or pump. In other embodiments, a control device can include a pre-charged sequestration chamber, a vented sequestration chamber, a manually activated device configured to produce a negative pressure, an energy source, and/or

any other suitable means of defining and/or forming a pressure differential within a portion of the control device.

[0176] In some other embodiments, the source of negative pressure can be associated with but independent of the fluid collection device. For example, a source of negative pressure such as a syringe, a pump, a passive source like a gravity aided or structurally aided container, etc., can be placed downstream of the outlet of the fluid control device such that the negative pressure imparted is communicated to the fluid collection device and the outlet. For example the source of negative pressure may be in fluid communication with the outlet via the fluid collection device. In other embodiments, under some circumstances, the source of negative pressure may be placed in fluid communication with the outlet to impart the pressure differential and the outlet may then be placed in fluid communication with the collection device to collect the fluid drawn by the pressure differential imparted, as described in further detail herein.

[0177] In some embodiments, any of the fluid control devices described herein can be formed from any suitable components that can be manufactured, sterilized, and packaged as individual parts or components. In such embodiments, a user can, for example, open one or more packages containing one or more components, can assemble the components to form the fluid control device, and can use the fluid control device as described above. In other embodiments, any of the fluid control devices described herein can be formed from any suitable components that can be manufactured, sterilized, assembled, and packaged as an assembly or integrated device. In such embodiments, a user can, for example, open a packaging containing such an assembly or integrated device and can use the device as described above without further assembly of components. In some embodiments, any of the control devices can be monolithically formed in whole or at least in part.

[0178] In some embodiments, any of the control devices can be physically and/or fluidically coupled to a collection device (e.g., a sample reservoir, a syringe, a blood culture bottle, a collection vial, a fluid transfer container, and/or any other suitable reservoir, collection device, and/or transfer device) by a user prior to or during use, as described in detail above. In other embodiments, any of the control devices can be physically coupled, attached, formed, and/or otherwise mated to a fluid collection device during a manufacturing process. This can be done prior to sterilization so the collection pathway(s) and connection interface(s) (e.g., where the control device couples to the fluid collection device) maintain a closed-system,

mechanical diversion device within a sterile environment that is not subject to touch-point contamination from external sources.

[0179] In some embodiments, the pre-assembly of the control device and the collection device can be such that the user is forced first to sequester, segregate, and/or isolate at least a portion of the initial bodily fluid volume or flow prior to transferring a sample volume to the pre-assembled fluid collection device. For example, the control device can include an actuator that is configured to isolate an outlet from other portions of the control device, thereby isolating the collection device from such portions of the control device. Moreover, after transferring the initial volume of bodily fluid, the actuation of the actuator can result in sequestration of the initial volume of bodily fluid and the fluidic coupling of the outlet to additional portions of the control device (e.g., an inlet). In some embodiments, pre-assembling the control device and the collection device (e.g., during manufacturing) can, for example, force compliance with a sample procurement protocol that calls for the sequestration of an initial amount of bodily fluid prior to collecting a sample volume of bodily fluid.

[0180] In some embodiments, the coupling, mating, and/or attachment of the fluid control device to the fluid collection device (e.g., during manufacturing) can be executed such that the control device can be removed (physically decoupled, removed with a specific "key," and/or any other approach used to separate the control device from the fluid collection device) after use to allow access to the fluid collection device. After decoupling, the collection device can be placed in an incubator and/or any other type of analytical machine, and accessed for analysis and/or otherwise further processed. In some embodiments, such decoupling may be blocked, limited, and/or substantially prevented prior to use and unblocked or allowed after use. In other embodiments, the fluid control device and the fluid collection device can be permanently coupled and/or monolithically formed (at least in part) to prevent such decoupling.

[0181] Any of the embodiments described herein can be used in conjunction with any suitable fluid transfer, fluid collection, and/or fluid storage device such as, for example, the fluid reservoirs described in the '420 patent, the transfer devices described in the '510 publication, and/or the transfer adapters described in the '352 publication. In some embodiments, any of the embodiments described herein can be used in conjunction with fluid transfer, fluid collection, and/or fluid storage devices such as, for example, the 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; U.S. Patent Publication No. 2016/0361006 entitled, "Devices and Methods for Syringe Based Fluid Transfer for Bodily-Fluid Sampling," filed June 13, 2016; U.S. Patent Publication No. 2018/0140240 entitled, "Systems and Methods for Sample Collection with Reduced Hemolysis," filed November 20, 2017; and/or U.S. Patent Publication No. 2017/0065733 entitled, "Apparatus and Methods for Maintaining Sterility of a Specimen Container," filed September 6, 2016, the disclosures of each of which are incorporated herein by reference in their entireties.

[0182] While some of the embodiments described above include a flow controller that selectively establishes fluid communication between a sequestration chamber and a fluid collection device (or other source of negative pressure) in other embodiments, a control device can be arranged to transfer a flow of bodily fluid in response to negative pressure differentials resulting from any suitable portion(s) of the device. For example, while the control device 200 is described above as including the flow controllers (e.g., the membrane 215, and/or the like) that place the sequestration chamber 214 in selective fluid communication with the fluid collection device (e.g., a sample reservoir or syringe) until the membrane 215 is transitioned to a sealed or closed state (e.g., until the membrane 215 is sufficiently wetted), in other embodiments, a control device can include a sequestration chamber that is a pre-sealed, evacuated, and/or pre-charged chamber such that establishing fluid communication between an inlet and the sequestration chamber results in a negative pressure differential that is sufficient to draw an initial volume of bodily fluid into the sequestration chamber. In such embodiments, the control device can be configured to transfer bodily fluid to the sequestration chamber until the pressure differential is sufficiently reduced and/or until pressures otherwise substantially equalize. Moreover, in some such embodiments, the sequestration chamber and/or the inlet can include a coupler, an actuator, a needle, a septum, a port, and/or any other suitable member that can establish fluid communication therebetween (e.g., that can transition the sequestration chamber from a sealed to an unsealed configuration).

[0183] While the embodiments have been described above as including particular means for modulating and/or controlling a magnitude of negative pressure applied on or through at least a portion of the device(s), in other embodiments, a control device can include any suitable feature, mechanism, and/or device configured to modulate, create, and/or otherwise control one or more pressure differentials through at least a portion of the control device. For example, in some embodiments, a user can transition and/or move an actuator to change (e.g., reduce or

increase) the size of one or more portions of a fluid flow path or fluid flow interface within a portion of the control device to manually modulate and/or otherwise control an amount or magnitude of negative pressure within one or more portions of a control device.

[0184] By way of another example, any of the embodiments described herein can include any suitable actuator and/or flow controller configured to selectively control fluid flow through at least a portion of the device. Specifically, a flow controller or the like can be one or more of a selectively permeable material or membrane, a valve, a diaphragm, and/or any other suitable flow controller. While some of the embodiments have been described as including an actuator rod configured to be transitioned from a first configuration or position to a second configuration or position, in other embodiments, any actuator described herein can include an actuator rod configured to transition from between a first position and second position to at least temporarily isolate an outlet from of the device from one or more other portions of the device. In some embodiments, such an actuator can be configured for use with a given and/or predetermined collection device such as, for example, a syringe. In other embodiments, such an actuator can be used with any suitable collection device.

[0185] While the embodiments have been described above as including or coupling to an inlet device such as a needle or the like that is configured to puncture the skin of a patient to place the lumen of the needle in fluid communication with a vein in the patient, in other embodiments, a fluid control device can include and/or can couple to any suitable inlet device. For example, in some embodiments, an inlet device can include a trocar or the like and a catheter. The trocar is configured to puncture the skin of a patient and then configured to be withdrawn from the patient, leaving the catheter of the inlet device placed within the patient. In other embodiments, the inlet device need not puncture the skin of a patient. For example, in some embodiments, the inlet device can include a needle or catheter that can be placed in a dish, well, sample volume, container, reservoir, etc. In still other embodiments, the inlet device can be and/or can include a coupler or port configured to couple to an indwelling needle or intravenous catheter. In other embodiments, such a coupler or port can be configured to couple to any suitable bodily fluid source (or port thereof) such as, for example, a syringe, a reservoir, a container, etc.

[0186] Accordingly, while the embodiments are described above as withdrawing and sequestering an initial volume of bodily fluid to sequester contaminants such as, for example, dermally-residing microbes, in other embodiments, the inlet device can be coupled to any suitable bodily fluid source and the control device can be configured to sequester an initial

volume of bodily fluid withdrawn from that bodily fluid source to sequester contaminants that may be present within the source and/or any an interface of the container or reservoir containing the bodily fluid. For example, in some embodiments, a needle of an inlet device can be configured to puncture a port or surface of a reservoir to place the needle in fluid communication with an interior volume of the container or device. In such embodiments, the devices described herein can be used to sequester an initial volume of bodily fluid from the bodily fluid source, which in turn, can sequester contaminants or the like that may have been present on the interface, port, or surface that was punctured. Thus, the devices and methods described herein can be used to procure bodily fluid samples having reduced contamination from any suitable bodily fluid source. Moreover, while some such contaminants are described herein as being dermally residing microbes, it should be understood that the contaminants can be any contaminant that is, for example, exterior to the bodily fluid source and/or otherwise that is or that includes any constituent component (e.g., microbe, virus, molecule, particle, element, etc.) that is otherwise foreign to the bodily fluid.

[0187] Although various embodiments have been described as having particular features, concepts, and/or combinations of components, other embodiments are possible having any combination or sub-combination of any features, concepts, and/or components from any of the embodiments described herein. For example, as described above, the device 700 includes concepts, features, and/or elements of the device 600, the device 600 includes concepts, features, and/or elements of the device 500, and the device 400 includes concepts, features, and/or elements of the devices 200 and 300. 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 and/or volume of bodily fluid flow into a fluid reservoir. Likewise, the size and/or shape of the various components can be specifically selected for a desired or intended usage. Thus, it should be understood that the size, shape, and/or arrangement of the embodiments and/or components thereof can be adapter for a given use unless the context explicitly states otherwise.

[0188] In some embodiments, the specific configurations of the various components can also be varied. For example, the size and specific shape of the various components can be different from the embodiments shown, while still providing the functions as described herein. More specifically, the size and shape of the various components can be specifically selected

for a desired rate and/or volume of bodily fluid flow into a fluid reservoir. Likewise, the size and/or shape of the various components can be specifically selected for a desired or intended usage. For example, in some embodiments, a device such as those described herein can be configured for use with or on seemingly healthy adult patients. In such embodiments, the device can include a sequestration chamber that has a first volume (e.g., about 0.5 ml to about 5.0 ml). In other embodiments, a device such as those described herein can be configured for use with or on, for example, very sick patients and/or pediatric patients. In such embodiments, the device can include a sequestration chamber that has a second volume that is less than the first volume (e.g., less than about 0.5 ml). Thus, it should be understood that the size, shape, and/or arrangement of the embodiments and/or components thereof can be adapted for a given use unless the context explicitly states otherwise.

[0189] Although not shown, any of the devices described herein can include an opening, port, coupler, septum, Luer-Lok, gasket, valve, threaded connecter, standard fluidic interface, etc. (referred to for simplicity as a "port") in fluid communication with the sequestration chamber. In some such embodiments, the port can be configured to couple to any suitable device, reservoir, pressure source, etc. For example, in some embodiments, the port can be configured to couple to a reservoir, which in turn, can allow a greater volume of bodily fluid to be diverted and/or transferred into the sequestration chamber. In other embodiments, the port can be coupled to a negative pressure source such as an evacuated container, a pump, a syringe, and/or the like to collect a portion of or the full volume of bodily fluid in the sequestration chamber, channel, reservoir, etc. and use that volume of bodily fluid (e.g., the pre-sample volume) for additional clinical and/or in vitro diagnostic testing purposes. In other embodiments, the port can be coupled to any suitable pressure source or infusion device configured to infuse the initial volume of bodily fluid sequestered in the sequestration chamber back into the patient and/or bodily fluid source (e.g., in the case of pediatric patients, very sick patients, patients having a low blood volume, and/or the like).

[0190] In some embodiments, the port can be configured to receive a probe, sampling tool, testing device, and/or the like that can be used to perform one or more tests (e.g., tests not sensitive to potential contamination) on the initial volume while the initial volume is disposed or sequestered in the sequestration chamber. In other embodiments, the sequestration channel, chamber, and/or reservoir can be configured with the addition of other diagnostic testing components integrated into the chamber (e.g., a paper test) such that the initial bodily fluid is used for that test. In still other embodiments, the sequestration chamber, channel, and/or

reservoir can be designed, sized and configured to be removable and compatible with testing equipment and/or specifically accessible for other types of bodily fluid tests commonly performed on patients with suspected conditions. By way of example, a patient with suspected sepsis commonly has blood samples collected for lactate testing, procalcitonin testing, and blood culture testing. All of the fluid control devices described herein can be configured such that the sequestration chamber, channel, reservoir, etc. can be removed (e.g., after receiving the initial volume of bodily fluid) and the bodily fluid contained therein can be used for these additional testing purposes before or after the subsequent sample is collected for microbial testing.

[0191] Although not shown, in some embodiments, a fluid control device can include one or more lumen, channels, flow paths, etc. configured to selectively allow for a "bypass" flow of bodily fluid, where an initial amount or volume of bodily fluid can flow from the inlet, through the lumen, cannel, flow path, etc. to bypass the sequestration chamber, and into the collection device. In some embodiments, the fluid control device can include an actuator having, for example, at least three states – a first in which bodily fluid can flow from the inlet to the sequestration chamber, a second in which bodily fluid can flow from the inlet to the outlet after the initial volume is sequestered in the sequestration chamber, and a third in which bodily fluid can flow from the inlet, through the bypass flow path, and to the outlet. In other embodiments, the control device can include a first actuator configured to transition the device between a first and second state, as described in detail above with reference to specific embodiments, and can include a second actuator configured to transition the device to a bypass configuration or the like. In still other embodiments, the control device can include any suitable device, feature, component, mechanism, actuator, controller, etc. configured to selectively place the fluid control device in a bypass configuration or state.

[0192] In some embodiments, a method of using a fluid control device employing an external negative pressure source can include the ordered steps of establishing fluid communication between a bodily fluid source (e.g., a vein of a patient or the like) and an inlet of the fluid control device. An outlet of the fluid control device is then placed in fluid communication with and/or otherwise engages a negative pressure source. Such a negative pressure source can be a sample reservoir, a syringe, an evacuated container, an intermediate transfer device, and/or the like. The fluid control device can be in a first state or operating mode when the outlet is coupled to the negative pressure source and, as such, a negative pressure differential is applied through at least a portion of the fluid control device that can be

operable to draw an initial volume of bodily fluid into a sequestration chamber of the fluid control device. Once the initial volume of bodily fluid is disposed in the sequestration chamber, the fluid control device is transitioned, either automatically or via user intervention, from the first state or operating mode to a second state or operating mode such that (1) the initial volume is sequestered in the sequestration chamber and (2) fluid communication is established between the inlet and the outlet. The sequestration of the initial volume can be such that contaminants entrained in the flow of the initial volume are likewise sequestered within the sequestration chamber. With the initial volume of bodily fluid sequestered in the sequestration chamber and with fluid communication established between the inlet and the outlet, subsequent volumes of bodily fluid that are substantially free of contamination can be collected in one or more sample reservoirs.

[0193] While the method of using the fluid control device is explicitly described as including the recited ordered steps, in other embodiments, the ordering of certain events and/or procedures in any of the methods or processes described herein may be modified and such modifications are in accordance with the variations of the invention. Additionally, certain events and/or procedures may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above. Certain steps may be partially completed or may be omitted before proceeding to subsequent steps.

[0194] For example, while the devices are described herein as transitioning from a first state to a second state in a discrete operation or the like, it should be understood that the devices described herein can be configured to automatically and/or passively transition from the first state to the second state and that such a transitioning may occur over a period of time. In other words, the transitioning from the first state to the second state may, in some instances, be relatively gradual such that as a last portion of the initial volume of bodily fluid is being transferred into the sequestration chamber, the housing begins to transition from the first state to the second state. In some instances, the rate of change when transitioning from the first state to the second state can be selectively controlled to achieve one or more desired characteristics associated with the transition. Moreover, in some such instances, the inflow of the last portion of the initial volume can limit and/or substantially prevent bodily fluid already disposed in the sequestration chamber from escaping therefrom. Accordingly, while the transitioning from the first state to the second state may occur over a given amount of time, the sequestration chamber can nonetheless sequester the volume of bodily fluid disposed therein.

What is claimed:

1. A fluid control device, comprising:

an inlet configured to be placed in fluid communication with a bodily fluid source;

an outlet configured to be placed in fluid communication with a fluid collection device, a negative pressure differential being produced between the outlet and the inlet when the outlet is placed in fluid communication with the fluid collection device;

a sequestration portion in fluid communication with the inlet, the sequestration portion including a first flow controller configured to transition from a first state in which the sequestration portion is sequestered from the outlet to a second state in which the sequestration portion is in fluid communication with the outlet when the negative pressure differential has a first magnitude; and

a sampling portion in fluid communication with the outlet, the sampling portion including a second flow controller configured to transition from a first state in which the sampling portion is sequestered from the inlet to a second state in which the sampling portion is in fluid communication with the inlet when the negative pressure differential has a second magnitude greater than the first magnitude.

2. The system of claim 1, wherein the fluid collection device is a sample bottle, the sample bottle being at least partially evacuated such that coupling the outlet to the sample bottle generates the negative pressure differential.

3. The system of claim 1, wherein the fluid collection device is a syringe that is configured to be manipulated after the outlet is coupled to the syringe to generate the negative pressure differential.

4. The system of claim 1, wherein the first flow controller is configured to transition from the first state to the second state automatically.

5. The system of claim 1, wherein the second flow controller is configured to transition from the first state to the second state automatically.

6. The system of claim 1, wherein the sequestration portion is configured to receive an initial volume of bodily fluid withdrawn from the bodily fluid source in response to the first flow controller transitioning to the second state.

7. The system of claim 6, wherein the first flow controller has a third state in which the sequestration portion is sequestered from the outlet, the first flow controller configured to transition from the second state to the third state as a result of the sequestration portion receiving the initial volume of bodily fluid.

8. The system of claim 7, wherein the first flow controller being placed in the third state results in an increase in a magnitude of the negative pressure differential within the sampling portion from the first magnitude to the second magnitude.

9. The system of claim 7, wherein the first flow controller includes a selectively permeable material, the selectively permeable material configured to (1) allow a flow of a gas and prevent a flow of bodily fluid through the selectively permeable material when in a first state and (2) prevent a flow of gas and bodily fluid through the selectively permeable material when in a second state.

10. The system of claim 9, wherein the selectively permeable material is configured to transition from the first state to the second state as a result the initial volume of bodily fluid being received in the sequestration portion, thereby placing the first flow controller in the third state.

11. A fluid control device, comprising:

a housing having an inlet configured to establish fluid communication with a bodily fluid source and an outlet configured to be coupled to a fluid collection device, the coupling of the outlet to the fluid collection device resulting in a negative pressure differential within at least a portion of the housing, the housing defining a sequestration flow path in fluid communication with the inlet and a sampling flow path in fluid communication with the outlet;

a first flow controller having a flow state in which fluid communication is established between the sequestration flow path and the outlet and a non-flow state in which the sequestration flow path is sequestered from the outlet; and

a second flow controller having a flow state in which fluid communication is established between the sampling flow path and the inlet and a non-flow state in which the sampling flow path is sequestered from the inlet,

the first flow controller configured to be in the flow state when the negative pressure differential generated by coupling the outlet to the fluid collection device has a first magnitude

such that an initial volume of bodily fluid flows through the sequestration flow path toward the first flow controller, and

the first flow controller configured to transition to the non-flow state when the initial volume of bodily fluid is received in the sequestration flow path such that (1) the sequestration flow path is sequestered from the outlet and (2) the negative pressure differential is increased to a second magnitude operable to transition the second flow controller from the non-flow state to the flow state.

12. The system of claim 11, wherein the fluid collection device is a sample bottle, the sample bottle being at least partially evacuated such that coupling the outlet to the sample bottle generates the negative pressure differential.

13. The system of claim 11, wherein the fluid collection device is a syringe that is configured to be manipulated after the outlet is coupled to the syringe to generate the negative pressure differential.

14. The system of claim 11, wherein the first flow controller is configured to transition from the first state to the second state automatically.

15. The system of claim 11, wherein the second flow controller is configured to transition from the first state to the second state automatically.

16. The system of claim 11, wherein the first flow controller is at least one of a valve, a selectively permeable material, or a restricted flow path.

17. The system of claim 16, wherein the second flow controller is at least one of a valve, a selectively permeable material, a dissolvable material, a frangible barrier, a movable barrier, or a restricted flow path.

18. The system of claim 11, wherein the first flow controller includes a selectively permeable material configured to (1) allow a flow of a gas and prevent a flow of bodily fluid through the selectively permeable material when in a first state and (2) prevent a flow of gas and bodily fluid through the selectively permeable material when in a second state.

19. The system of claim 18, wherein the selectively permeable material is configured to transition from the first state to the second state as a result of the sequestration flow path receiving the initial volume of bodily fluid, the transitioning of the selectively permeable material from the first state to the second state places the first flow controller in the non-flow state.

20. The system of claim 19, wherein the first state of the selectively permeable material is an unsaturated state and the second state of the selectively permeable material is a saturated state.

21. A method of using a fluid control device to obtain a bodily fluid sample with reduced contamination, the method comprising:

coupling a fluid collection device to an outlet of the fluid control device, the coupling of the fluid collection device to the outlet configured to produce a negative pressure differential within at least a portion of the fluid control device;

transitioning a first flow controller from a first state to a second state when the negative pressure differential has a first magnitude, the first flow controller sequestering a sequestration portion of the fluid control device from the outlet when in the first state and establishing fluid communication between the sequestration portion and the outlet when in the second state;

receiving an initial volume of bodily fluid from an inlet of the fluid control device and into the sequestration portion in response to the negative pressure differential when the first flow controller is in the second state;

transitioning the first flow controller from the second state to a third state in response to the receiving, the first flow controller sequestering the sequestration portion from the outlet when in the third state, the negative pressure differential being increased from the first magnitude to a second magnitude when the first flow controller is in the third state;

transitioning a second flow controller from a first state to a second state when the negative pressure differential has the second magnitude, the second flow controller sequestering a sampling portion of the fluid control device from the inlet when in the first state and establishing fluid communication between the sampling portion and the inlet when in the second state; and

transferring a subsequent volume of bodily fluid from the inlet to the fluid collection device via the sampling portion and the outlet.

22. The method of claim 21, wherein the transitioning of the first flow controller from the first state to the second state includes automatically transitioning the first flow controller from the first state to the second state without manual intervention.

23. The method of claim 22, wherein the transitioning of the first flow controller from the second state to the third state includes automatically transitioning the first flow controller from the first state to the second state without manual intervention.

24. The method of claim 21, wherein the transitioning of the second flow controller from the first state to the second state includes automatically transitioning the second flow controller from the first state to the second state without manual intervention.

25. The method of claim 21, wherein the first flow controller includes a selectively permeable material configured to (1) allow a flow of a gas and prevent a flow of bodily fluid through the selectively permeable material when in a first state and (2) prevent a flow of gas and bodily fluid through the selectively permeable material when in a second state,

the transitioning of the first flow controller from the second state to the third state includes the selectively permeable material being placed in its second state.

26. The method of claim 21, further comprising:

establishing fluid communication between the inlet and a bodily fluid source, wherein the initial volume of bodily fluid contains contaminants associated with the establishing of fluid communication between the inlet and the bodily fluid source.

27. The method of claim 26, wherein the initial volume of bodily fluid and the contaminants are sequestered within the sequestration portion when the first flow controller is in the third state such that the subsequent volume of bodily fluid is substantially free of contaminants.

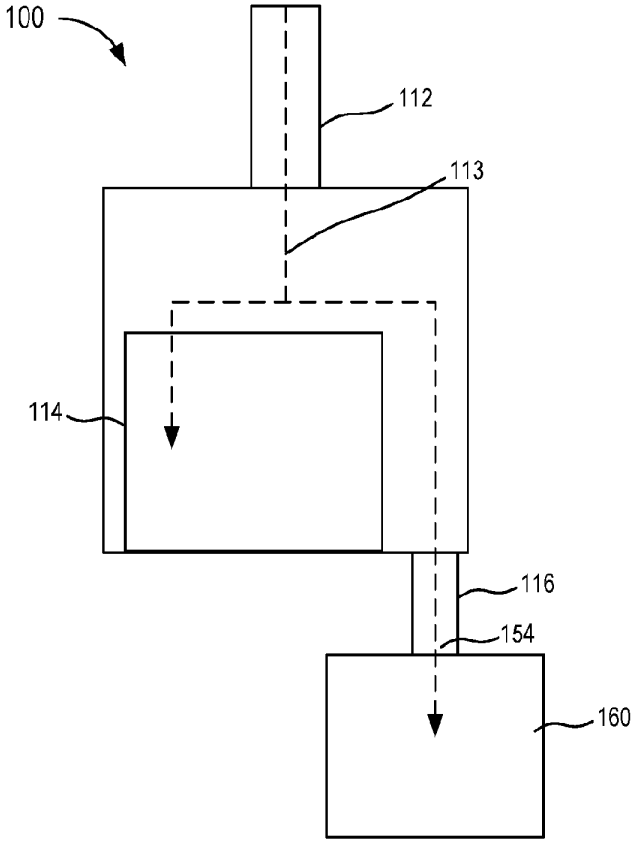


FIG. 1

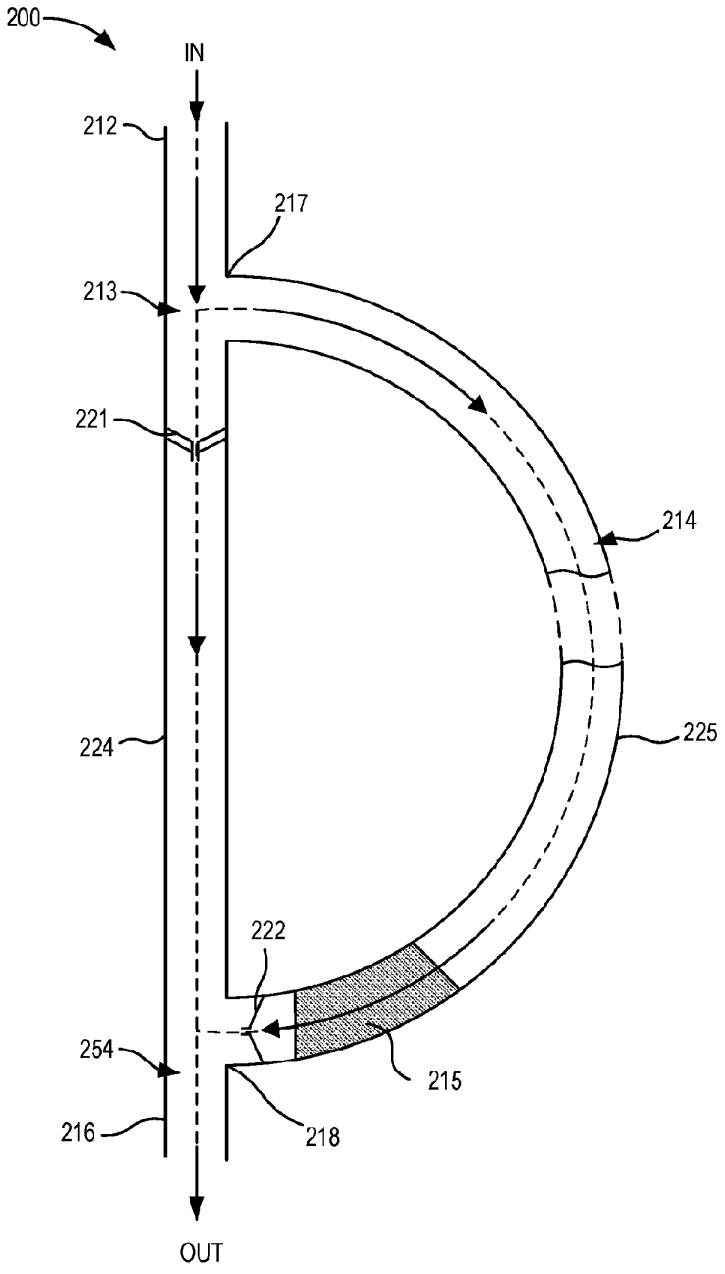


FIG. 2

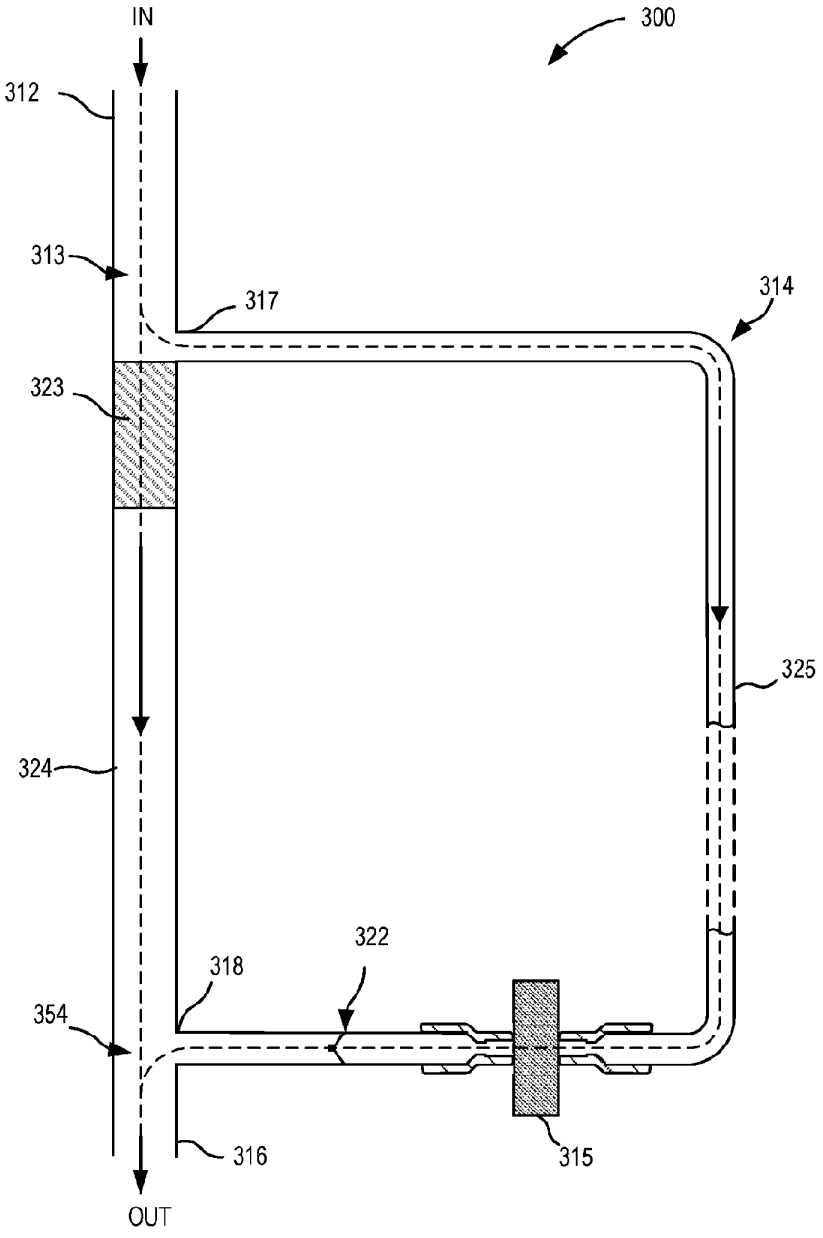


FIG. 3

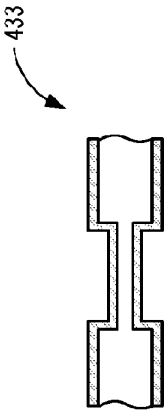


FIG. 5

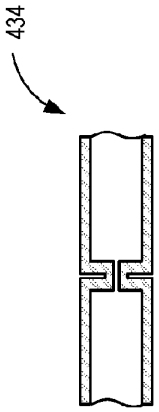


FIG. 6

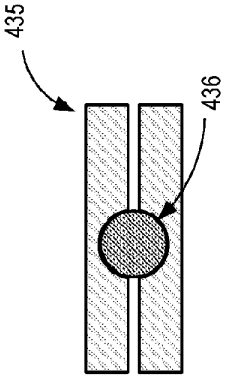


FIG. 7

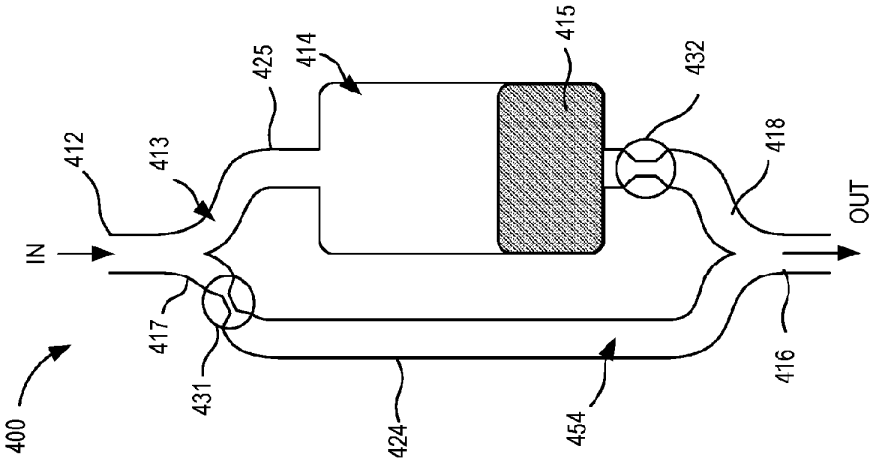


FIG. 4

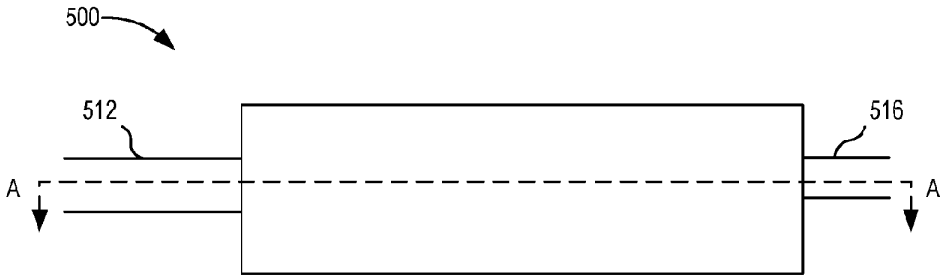


FIG. 8

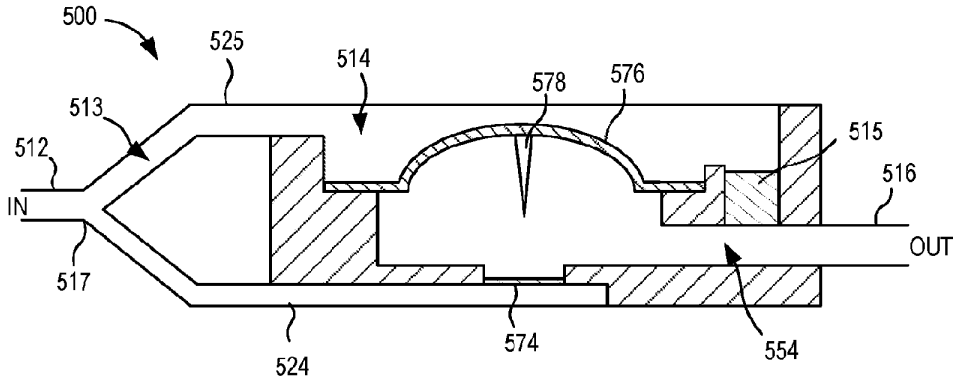


FIG. 9

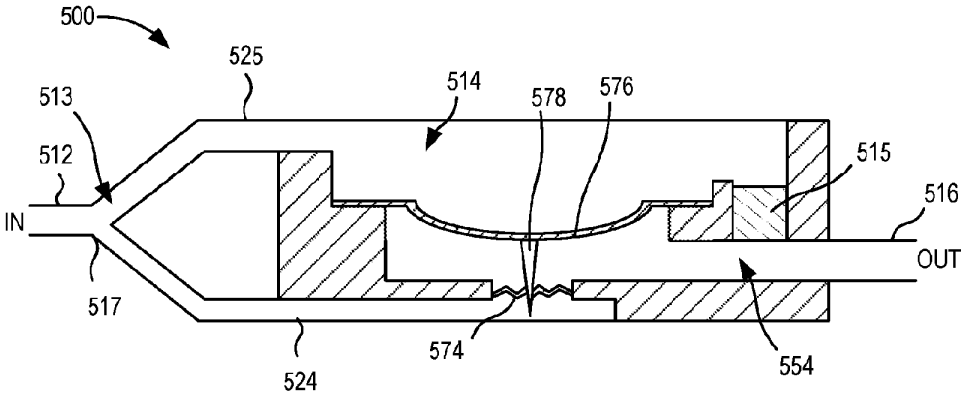


FIG. 10

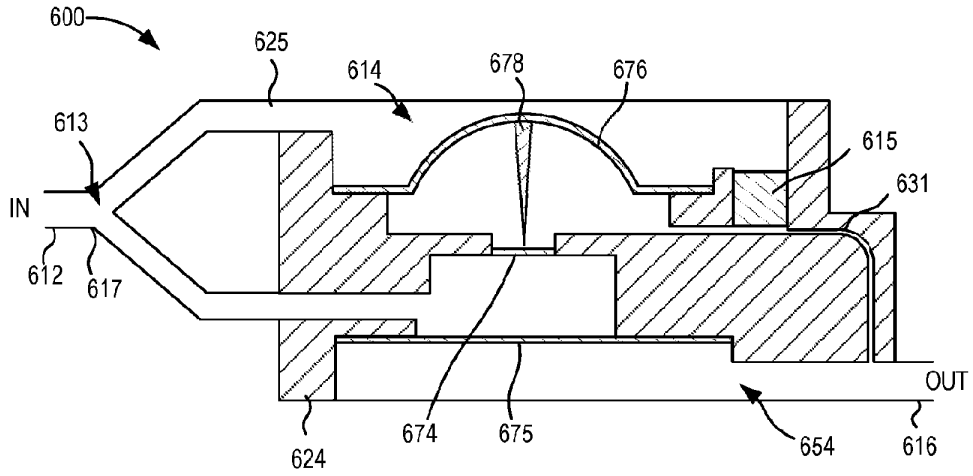

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FIG. 11

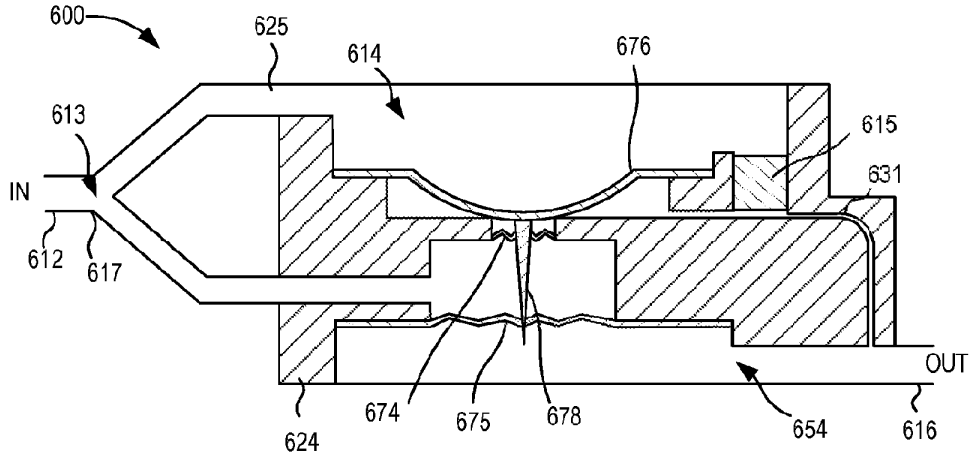

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FIG. 12

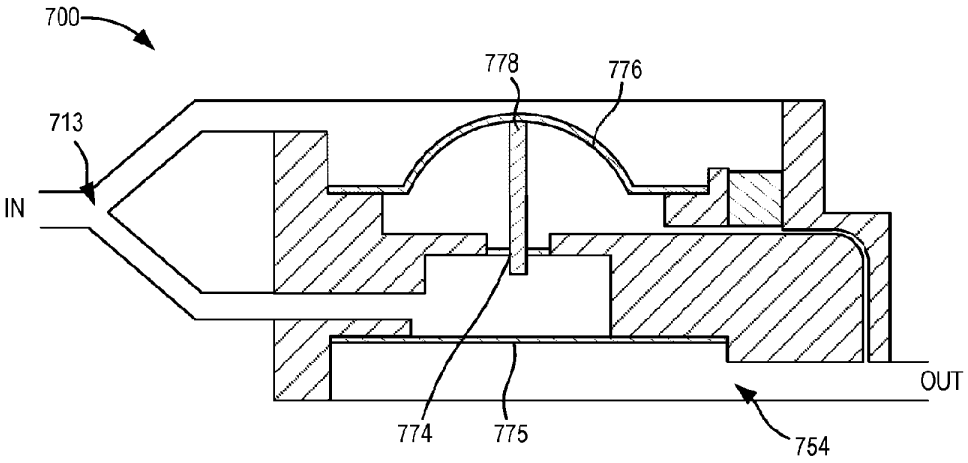

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FIG. 13

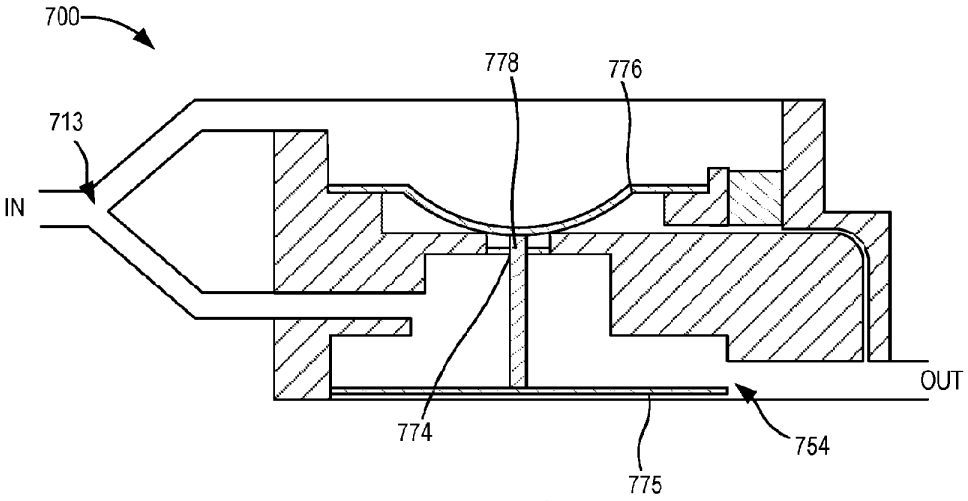

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FIG. 14

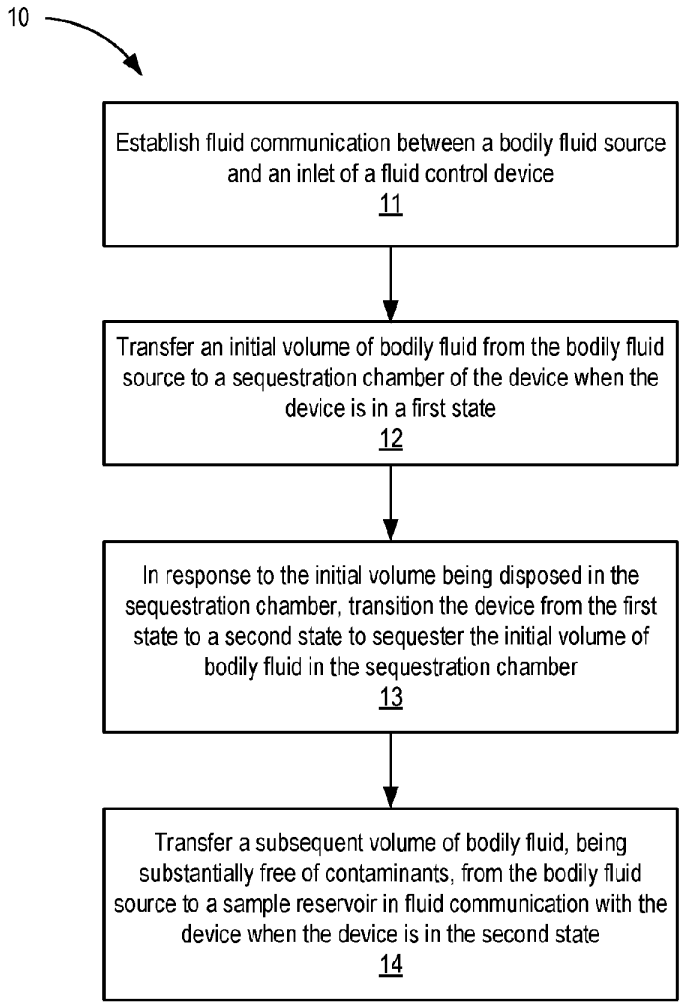

10
Establish fluid communication between a bodily fluid source and an inlet of a fluid control device
11
Transfer an initial volume of bodily fluid from the bodily fluid source to a sequestration chamber of the device when the device is in a first state
12
In response to the initial volume being disposed in the sequestration chamber, transition the device from the first state to a second state to sequester the initial volume of bodily fluid in the sequestration chamber
13
Transfer a subsequent volume of bodily fluid, being substantially free of contaminants, from the bodily fluid source to a sample reservoir in fluid communication with the device when the device is in the second state
14

FIG. 15

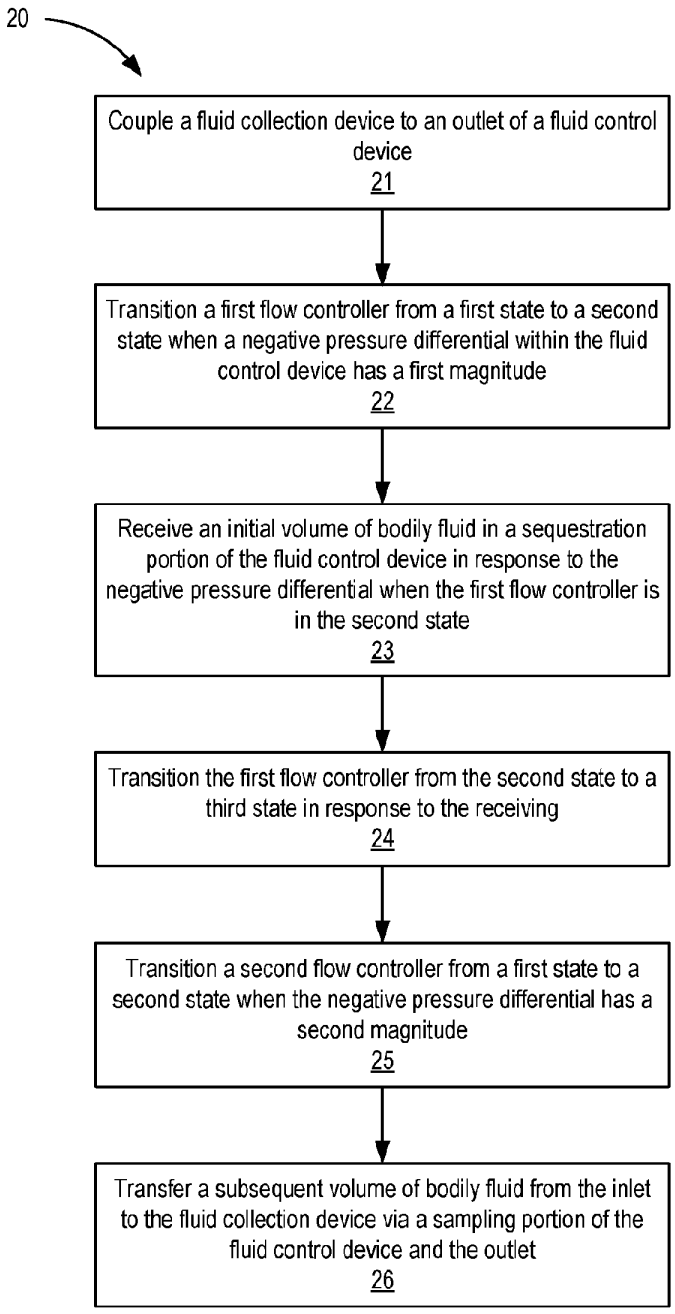

20
Couple a fluid collection device to an outlet of a fluid control device
21
Transition a first flow controller from a first state to a second state when a negative pressure differential within the fluid control device has a first magnitude
22
Receive an initial volume of bodily fluid in a sequestration portion of the fluid control device in response to the negative pressure differential when the first flow controller is in the second state
23
Transition the first flow controller from the second state to a third state in response to the receiving
24
Transition a second flow controller from a first state to a second state when the negative pressure differential has a second magnitude
25
Transfer a subsequent volume of bodily fluid from the inlet to the fluid collection device via a sampling portion of the fluid control device and the outlet
26

FIG. 16

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/034626

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/15 A61B5/153 A61B5/154
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2017/020427 A1 (ROGERS BOBBY E [US] ET AL) 26 January 2017 (2017-01-26) paragraphs [0125], [0126] figures 23A, 23B	1-27
A	US 2016/361006 A1 (BULLINGTON GREGORY J [US] ET AL) 15 December 2016 (2016-12-15) cited in the application paragraphs [0040] - [0073] figures 1-7	1-27
A	US 2015/011910 A1 (BULLINGTON GREGORY [US] ET AL) 8 January 2015 (2015-01-08) paragraphs [0078] - [0104] figures 2-12	1-27

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

[X] See patent family annex.

* Special categories of cited documents :

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

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 August 2019	22/08/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Schultz, Ottmar

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/034626

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 2014/163419 A1 (BULLINGTON GREGORY J [US] ET AL) 12 June 2014 (2014-06-12) the whole document	1-27
A	US 8 535 241 B2 (BULLINGTON GREGORY [US]; PATTON RICHARD G [US] ET AL.) 17 September 2013 (2013-09-17) cited in the application the whole document	1-27

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

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European Patent Office
Office européen des brevets

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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
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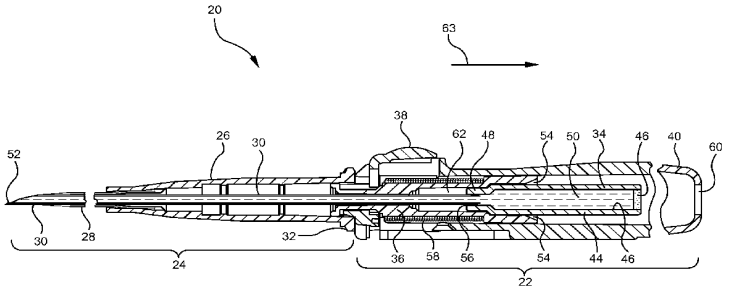
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(54) **Title**: A REMOVABLE FLASH CHAMBER

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.

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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.

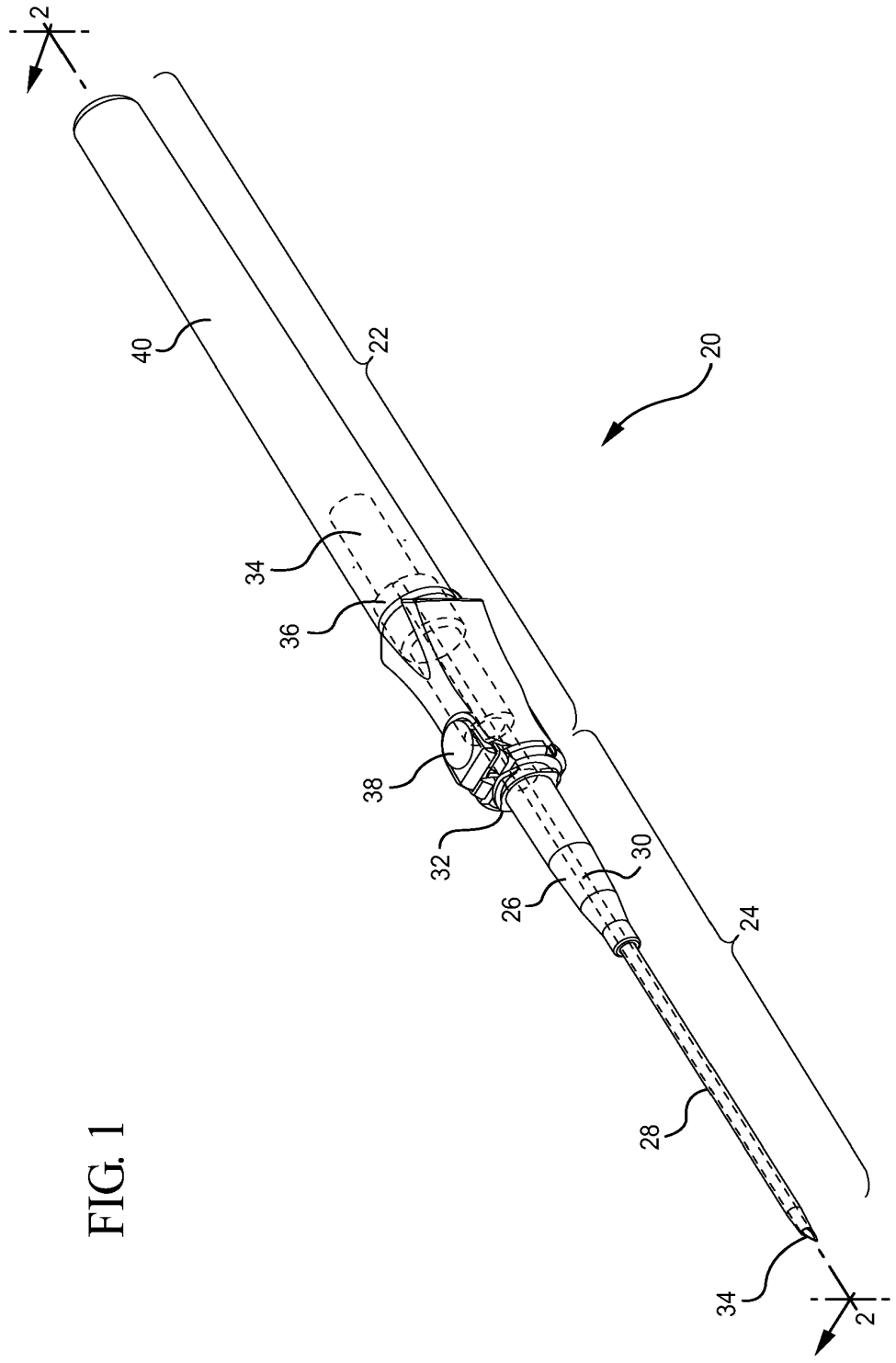


FIG. 1

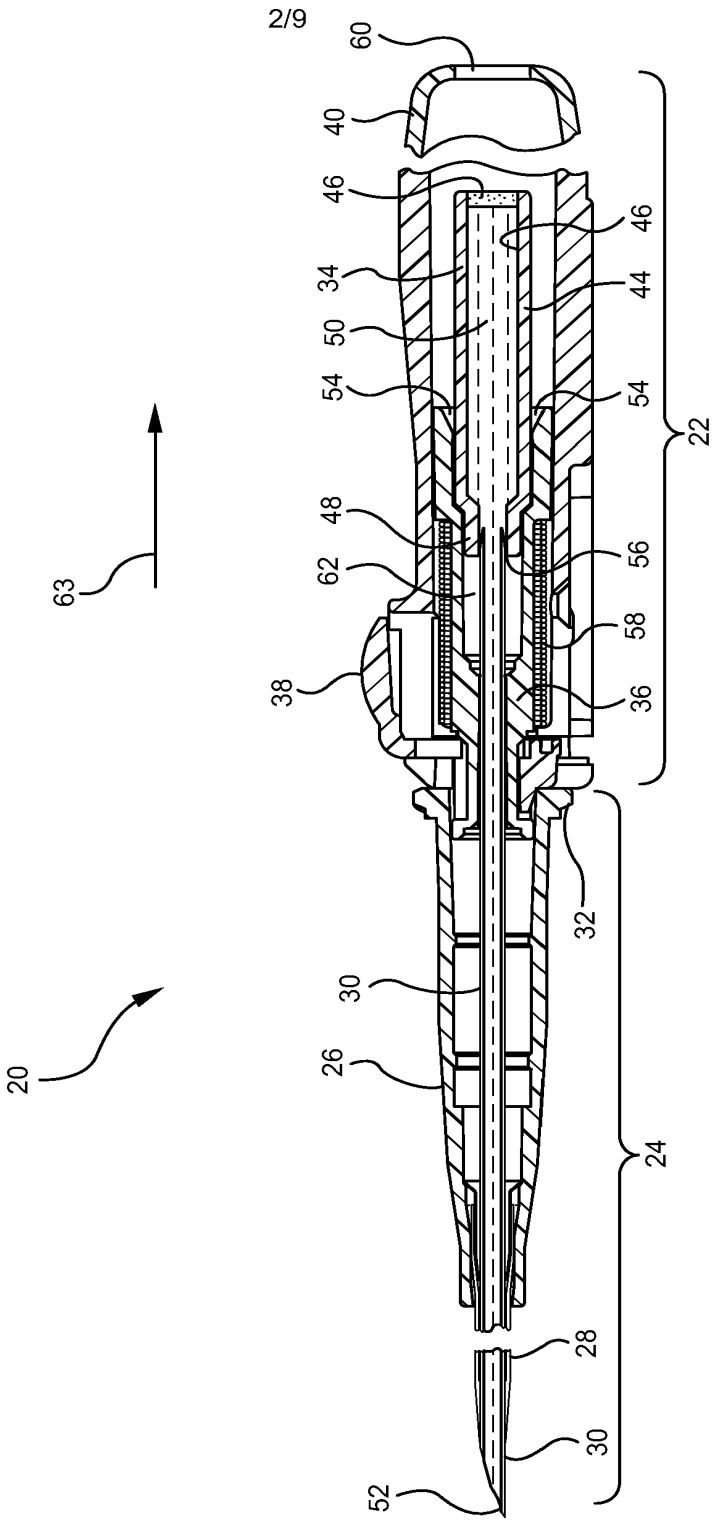

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FIG. 2

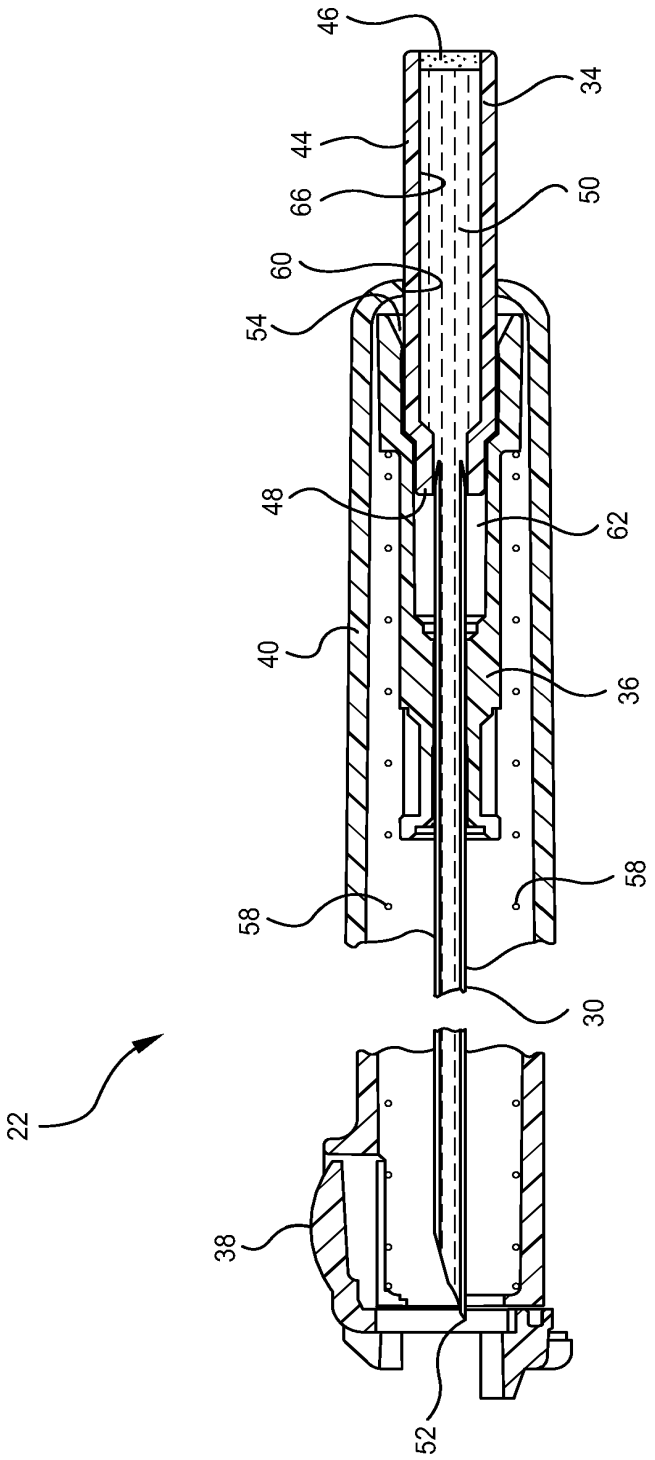


FIG. 3

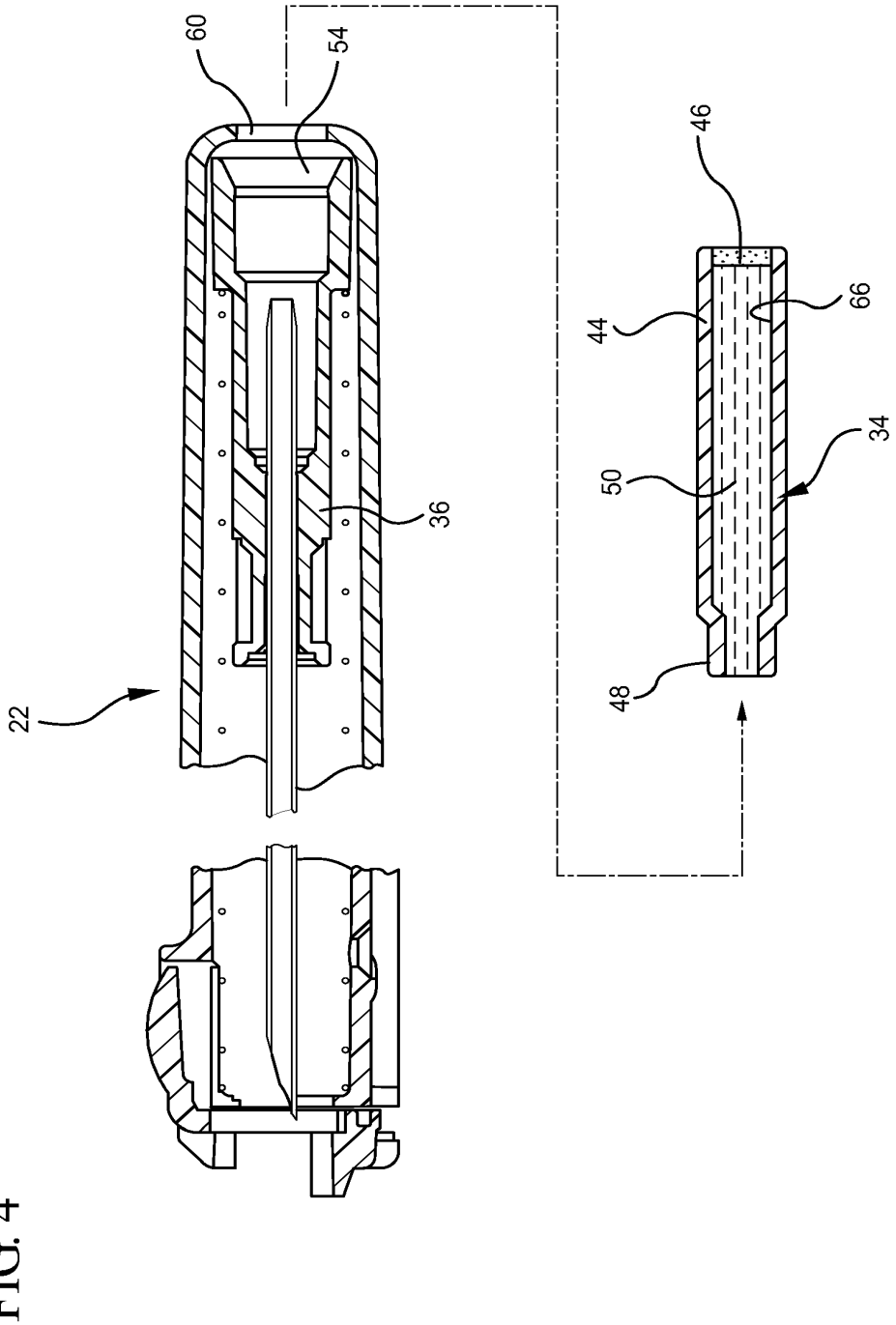


FIG. 4

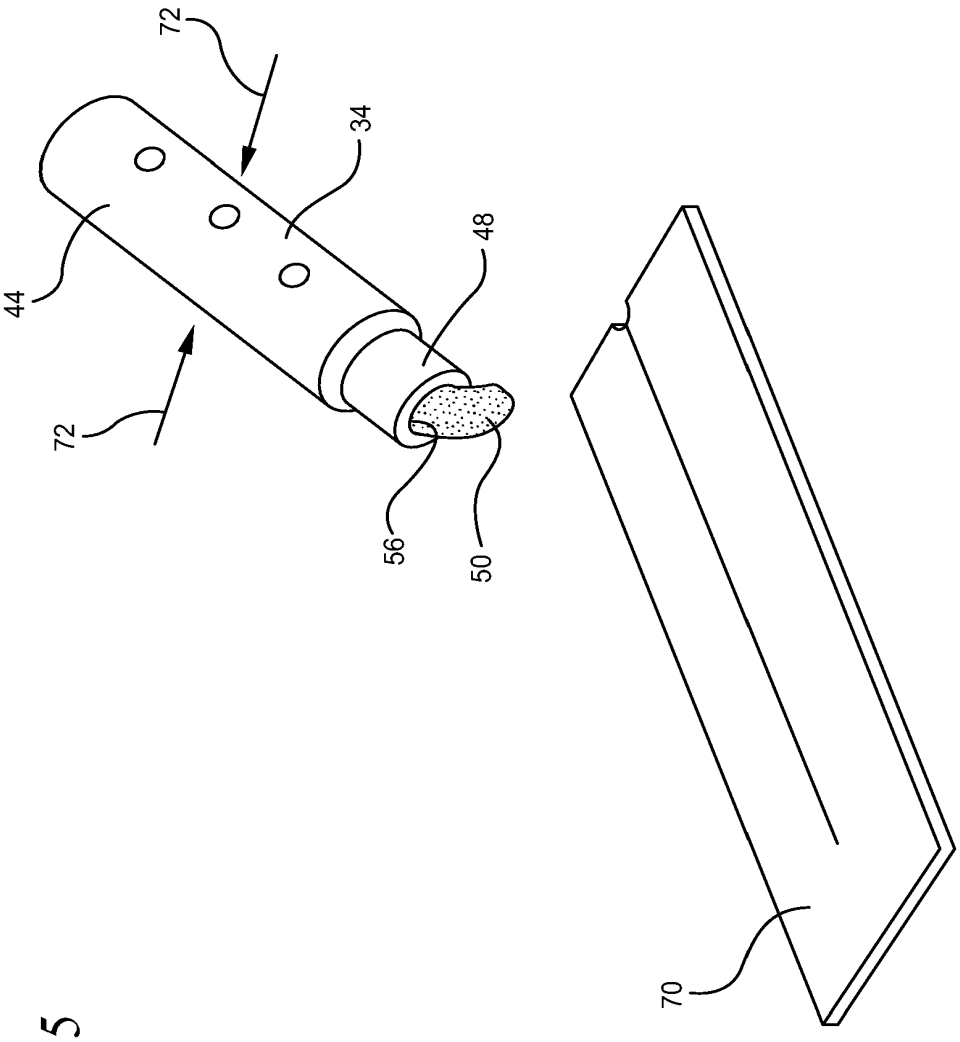


FIG. 5

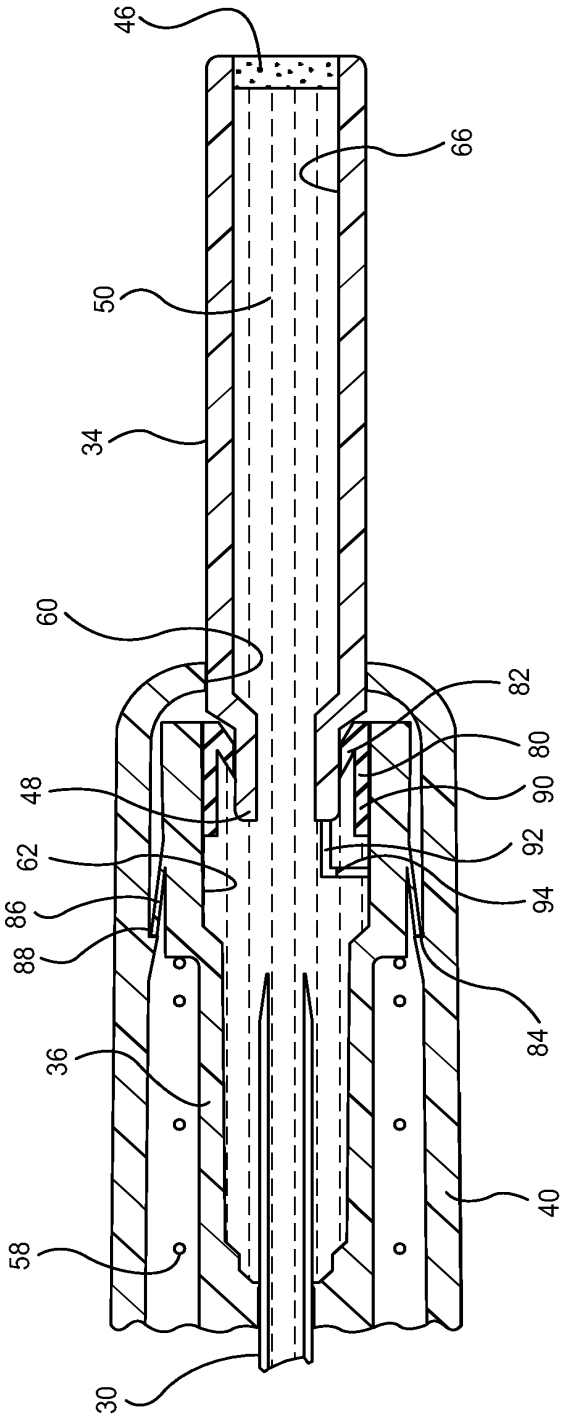


FIG. 6

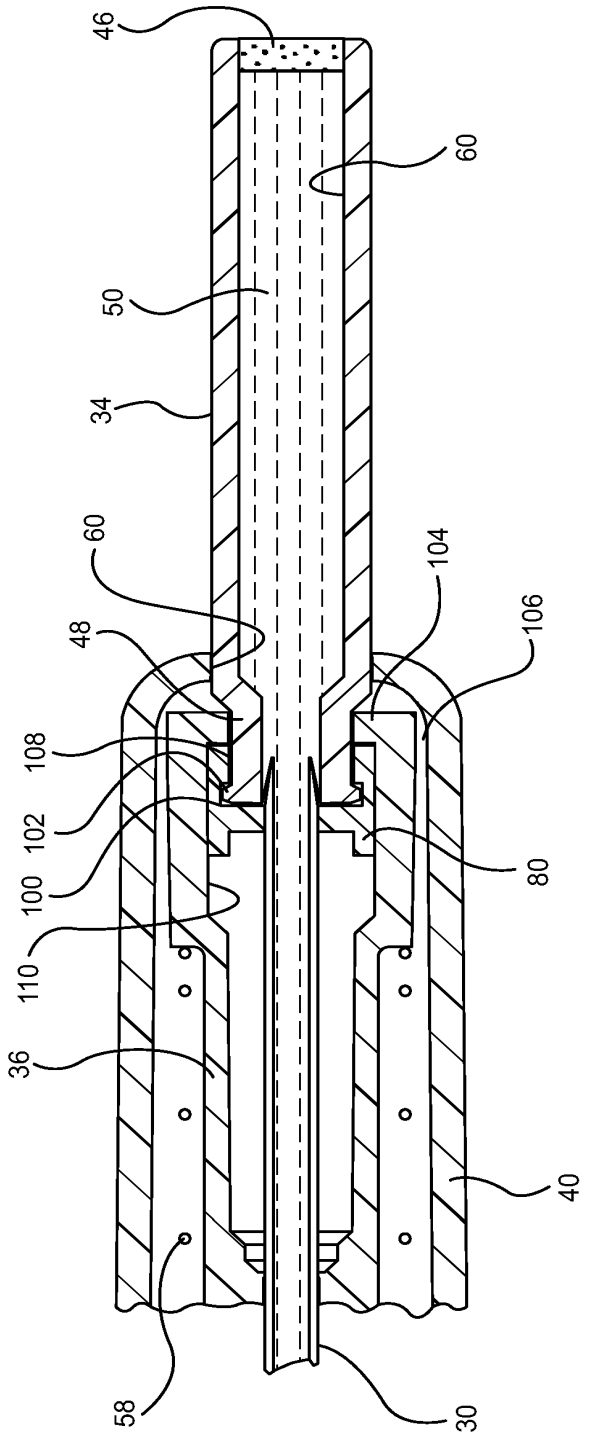


FIG. 7

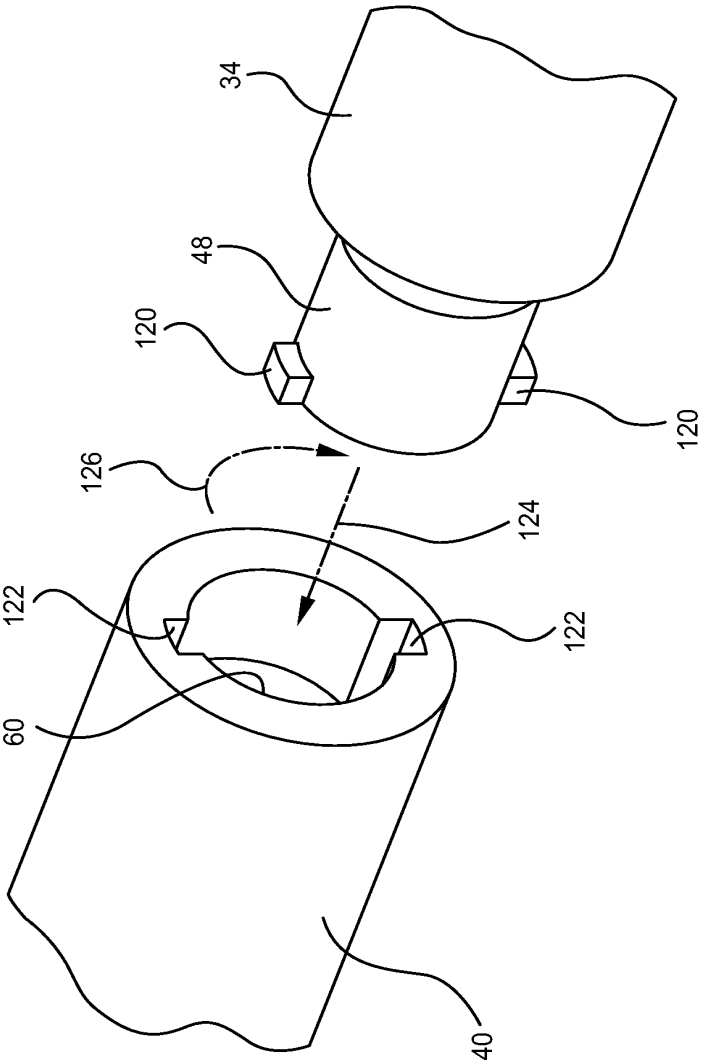


FIG. 8

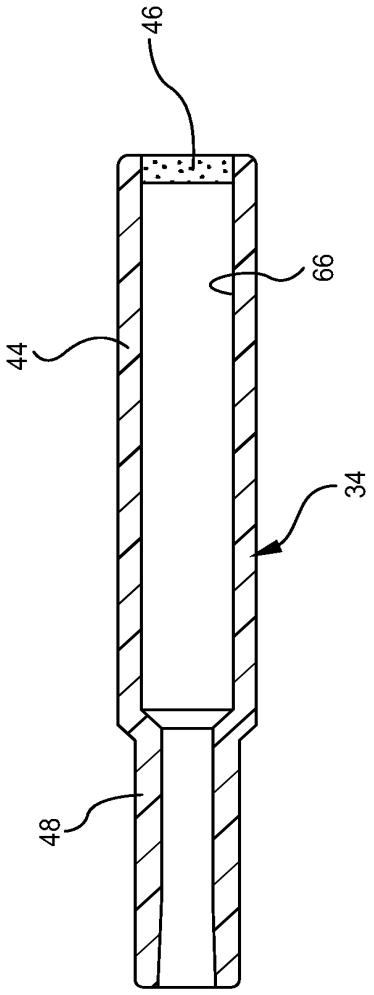


FIG. 9

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

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Literature display help

1 / 1 display

Japanese Patent Application Laid-Open No. 08-257018

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

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

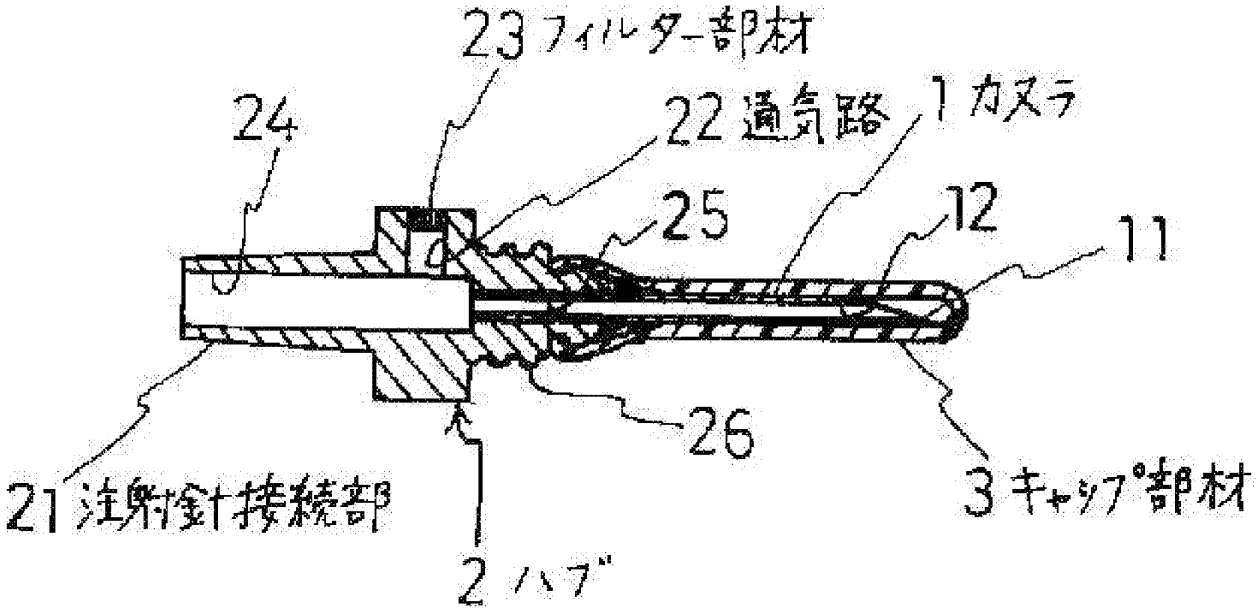
bibliography close

(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Published patent publication (A)
(11) [Publication number] JP-A-8-257018
(43) [Published date] 1996 (1996) October 8
(54) [Title of Invention] Blood collection adapter
(51) [International Patent Classification 6th Edition]
A61B 5/14 300
A61M 5/32
[FI]
A61B 5/14 300 E 7638-2J
A61M 5/32
[Request for examination] Unclaimed
[Number of claims] 4
[Application form] OL
[Total number of pages] 4
(21) [Application number] Japanese Patent Application 7-62943
(22) [Filing date] 1995 (1995) March 22
(71) [Applicant]

[Identification number] 000135036
[Name] Nissho Co., Ltd.
(72) [Inventor]
[Name] Yoshio Higaki
(72) [Inventor]
[Name] Ikegami filial piety

wrap up close

(57) [Summary]
[Purpose] When the cutting edge of an injection needle connected to this needle is inserted in to a blood vessel, blood flows into the intermediate portion of the transparent hub, which caus es the cutting edge to be inserted into the blood vessel. To provide a blood collection adapter capable of confirming that
The blood collection adapter comprises a hollow cannula 1 having a cutting edge 11 at its tip, a transparent hollow hub 2 supporting and fixing the rear end of the cannula 1 at its tip, and a cannula 1 crowned. It consists of a cap member 3 made of a rubber elastic body. An injectio n needle connecting portion 21 is provided at the rear end portion of the hub 2, and an air pa ssage 22 is provided at the intermediate portion of the hub 2. The outlet of the air passage 22 is gas-permeable and liquid-impermeable. is closed with a filter member 23 of .



The scope of the claims open

[Scope of Claims]

[Claim 1] A hollow cannula having a cutting edge at its tip, a tip supporting and fixing a rear end of the cannula, and a liquid-tight hub of an injection needle at the rear end of the cannula. It consists of a transparent hollow hub equipped with an insertable injection needle connector, and a cap member made of a rubber elastic body covering the cannula, and a hollow between the tip of the hub and the injection needle connector. A blood collection adapter in which an air passage is provided in a portion to communicate the hollow portion with the outside air, and an outlet of the air passage is closed with a gas-permeable and liquid-impermeable filter member.

2. The blood collection adapter according to claim 1, wherein the injection needle connecting portion is formed on a luer tip that can be fitted to the hub of the injection needle.

3. The blood collection adapter according to claim 2, wherein the luer tip is concentrically and externally provided with female coupling means that can be coupled with the hub of the injection needle.

4. A blood collection needle comprising an injection needle connected to the blood collection adapter of claim 1.

detailed description open —

Description: BACKGROUND OF THE INVENTION

1.

Field of the Invention The present invention relates to blood collection adapters. More specifically, it is a blood-collecting adapter used for a vacuum blood-collecting tube for collecting blood from a blood vessel, which can be used as a blood-collecting needle by connecting an ordinary injection needle, and has a cutting edge inserted into the blood vessel. The present invention relates to a blood collection adapter capable of confirming that

2.

Description of the Related Art Conventionally, when collecting blood using a blood collection tube, a blood collection needle as shown in FIG. 4 is used to collect blood. . However, in such blood sampling, which relies on intuition and experience, it is not possible to check whether the cutting edge has been inserted into the blood vessel for beginners with little intuition or experience, or for patients with narrow blood vessels that are difficult to see or cannot be seen. As a result, it places a heavy burden on both the person collecting blood and the person receiving blood. Blood collection had to be repeated, which was uneconomical. Therefore, there has been proposed a blood collection needle that can confirm that the cutting edge has been inserted into a blood vessel (Japanese Unexamined Patent Publication No. 4-132541, etc.).

[0003] In the blood collection needle disclosed in JP-A-4-132541, the hub is provided with a v entilation hole for communication between the inner cavity of the elastic tip and the outside at mosphere, and an air-permeable filter is attached to the outer opening of the ventilation hole. By confirming the blood (so-called flashback) flowing into the blood collection needle, it is con firmed that the cutting edge has been inserted into the blood vessel. However, since the blood collection needle described above tries to guide the blood that has flowed into the elastic tip t o the ventilation hole of the transparent hub, it is necessary to confirm flashback.It takes a lo ng time, and there is a problem that the blood collected inside the elastic tip may leak. SUMM ARY OF THE INVENTION The present invention has been made in view of the above-mentione d circumstances

.

To provide a blood collecting adapter which enables confirmation of the insertion of a cutting e dge into a blood vessel by blood flowing into an intermediate part of the blood vessel. Another object of the present invention is to provide a blood collection needle comprising a combinatio n of this blood collection adapter and an injection needle.

[0005]

To solve the above problems, the present invention provides a hollow cannula having a cutting edge at its distal end, and a distal end of the hollow cannula supporting and fixing the rear en d of the cannula. and a transparent hollow hub equipped with an injection needle connecting portion to which the injection needle hub can be inserted in a liquid-tight manner at its rear e nd, and a cap member made of a rubber elastic body covering the cannula, An air passage is provided in the hollow portion between the distal end portion of the hub and the injection nee dle connection portion to communicate the hollow portion with the outside air, and the outlet of the air passage is closed with a gas-permeable and liquid-impermeable filter member. A re movable blood collection adapter is used. In addition, a configuration in which an injection ne edle is connected to this blood collection adapter is adopted. Here, the injection needle conne ction part may be formed in a luer tip that can be fitted with the hub of the injection needle c onnected thereto, and the luer tip is concentrically threaded with the hub of the injection need le. A female coupling means may be provided which may be mated or luer coupled.

[0006]

[Operation] According to the above configuration, when the blood collection adapter is attache d to the blood collection needle holder, the injection needle is connected to the injection needl e connecting portion, and the injection needle is inserted into the blood vessel, the hollow por tion of the injection needle and the blood collection are removed. Air existing in the hollow por tion of the adapter passes through the gas-permeable filter member through the gas-permea ble filter member by the inflowing blood, and is expelled to the outside. It flows into the hollo w portion of the adapter and then through the air passage to reach the filter member. Therefo re, by observing the air passage formed in the transparent hub, insertion of the injection need le into the blood vessel can be easily confirmed. Also, at this time, since the filter member is i

mpermeable to liquid, blood does not leak through the filter member to the outside.

[0007]

Next, an embodiment of the present invention will be described with reference to the drawing s. FIG. 1 is a vertical cross-sectional view of a blood sampling adapter according to one embo diment of the present invention, FIG. 2 is a diagram showing another embodiment, and FIG. 3 shows a state in which an injection needle is attached to the blood sampling adapter shown in FIG. FIG. 10 shows. As shown in FIG. 1, the blood collection adapter of the present invention comprises a hollow cannula 1 having a cutting edge 11 at its distal end, and a transparent holl ow hub 2 supporting and fixing the rear end of this cannula 1 at its distal end. , the rubber ela stic body crowned on the cannula 1It consists of a cap member 3 made of An injection needle connecting portion 21 is provided at the rear end portion of the hub 2, and an air passage 22 i s provided at the intermediate portion of the hub 2. The outlet of the air passage 22 is gas-pe rmeable and liquid-impermeable. is closed with a filter member 23 of .

The hub 2 is a hollow member made of transparent synthetic resin such as polyethylene, poly propylene, polyester, or polystyrene, and consists of a front end, an intermediate portion, and a rear end. The rear end of the cannula 1 generally made of stainless steel is inserted into the hollow portion 25 at the tip of the hub 2 and fixed with an adhesive. It is covered with a cap member 3 made of isoprene rubber, butadiene rubber, nitrile rubber or the like. A male coupli ng means such as a male screw 26 is formed on the outer wall of the tip of the hub 2 so that i t can be screwed into a blood collection needle holder (not shown).

[0009] The rear end of the hub 2 is an injection needle connecting portion 21 having a hollow portion 24 communicating with a hollow portion 25 at the distal end of the hub 2, and is gene rally external so that a hub 41 of the injection needle 4 can be fitted. It is formed into a so-cal led luer tip whose diameter is reduced in a tapered shape. For example, as shown in FIG. A h ood-shaped female coupling means 27 extending concentrically from the intermediate portion of the hub 2 toward the injection needle connection portion 21 is provided, and a male couplin g means (not shown) is provided on the outer wall of the end portion of the hub 41 of the inje ction needle 4 . (not connected) may be threaded or luer connected. As the injection needle c onnecting portion 21, a male coupling member that is inserted into the hub 41 of the injection needle 4 is usually employed. coupling members can also be employed.

The intermediate portion of the hub 2 is a wide brim-like projecting portion, and is provided w ith an air passage 22 that communicates a hollow portion 24 with the outside air. ing. This filt er member 23 is a gas-permeable and liquid-impermeable filter (hydrophobic filter), and as su ch a filter, a layered filter made of a polymer sintered body such as polypropylene or polyethyl ene is usually preferably employed. However, a film-like so-called membrane filter made of a hydrophobic resin such as polypropylene or polyethylene may also be used.

Next, use of the blood collection adapter of the present inventionwill be described with referen ce to FIG. First, the blood collection adapter A is attached to a blood collection needle holder (not shown), and the injection needle 4 is connected to the injection needle connecting portio

n 21 of the blood collection adapter A. As shown in FIG. Next, when the cutting edge 43 of th e injection needle 4 is pierced into the blood vessel, the air existing in the hollow portion 44 of the injection needle 4 and the hollow portions 24 and 25 of the blood collection adapter A is p ushed into the air passage of the blood collection adapter A by the inflowing blood. 22, it per meates the gas-permeable filter member 23 and is expelled to the outside. Then, the blood p asses through the hollow portion 44 of the injection needle 4 and flows into the hollow portion 24 of the blood collection adapter A, passes through the air passage 22 and reaches the filter member 23 . Therefore, by observing the injection needle connecting portion 21 and the air p assage 22 provided on the transparent hub 2, it is possible to easily confirm that the cutting e dge 43 of the injection needle 4 has been inserted into the blood vessel. At this time, since th e filter member 23 is impermeable to liquid, the blood will not pass through the filter member 23 and leak to the outside.

INDUSTRIAL APPLICABILITY

As is clear from the above description, the following effects can be obtained by adopting the b lood sampling adapter of the present invention.

①It is economical because it can be used as a blood collection needle by connecting a normal injection needle.

②Since it can be easily confirmed that the cutting edge of the injection needle connected to t his has been pierced into the blood vessel, it is possible to eliminate the burden on the subjec t of blood collection due to re-insertion of the injection needle.

③No need to redo blood collection.

Brief description of the drawing

open —

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a vertical cross-sectional view of a blood sampling adapter according to one embodi ment of the present invention;

FIG. 2 is a diagram showing another embodiment of the present invention;

3 is a view showing a state where an injection needle is attached to the blood collection adapt er shown in FIG. 1; FIG.

FIG. 4 is a diagram showing a conventional blood collection needle;

[Description of Reference Symbols]

1 Cannula

2 Hub

21 Injection needle connecting portion

22 Air passage

23 Filter member

27 Female coupling means

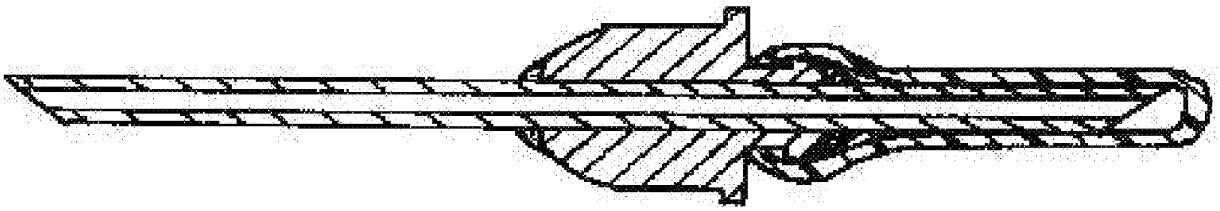
3 Cap member

4 Injection needle

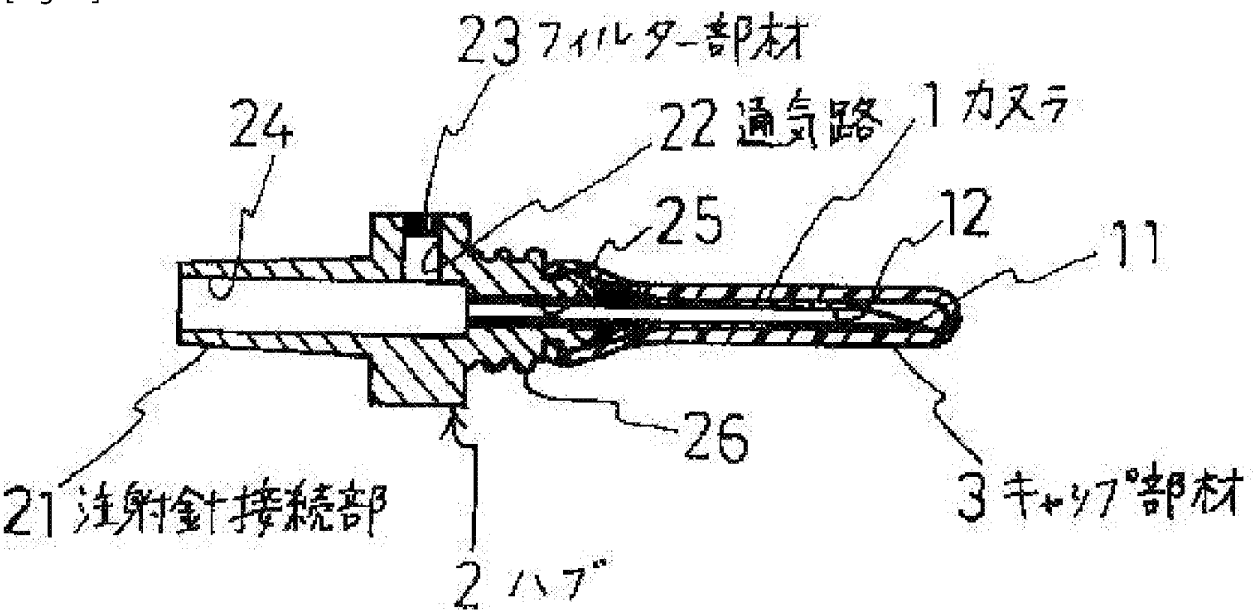
A Blood sampling adapter

drawing open —

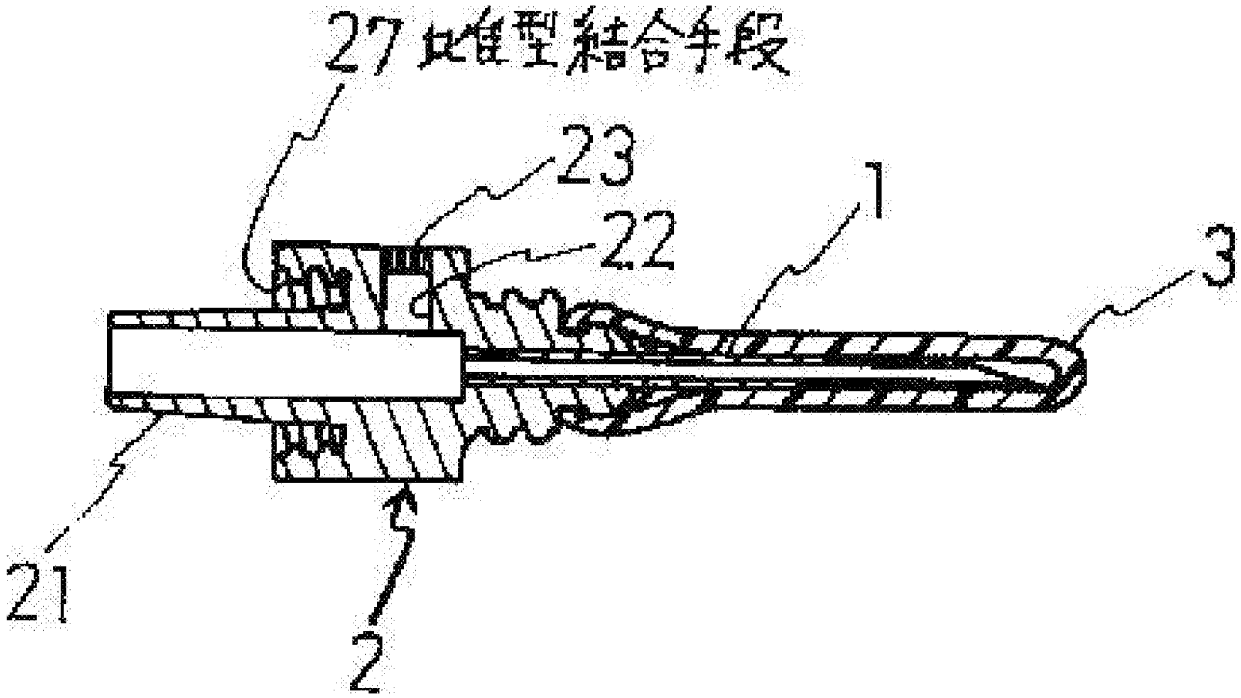
[Figure 4]



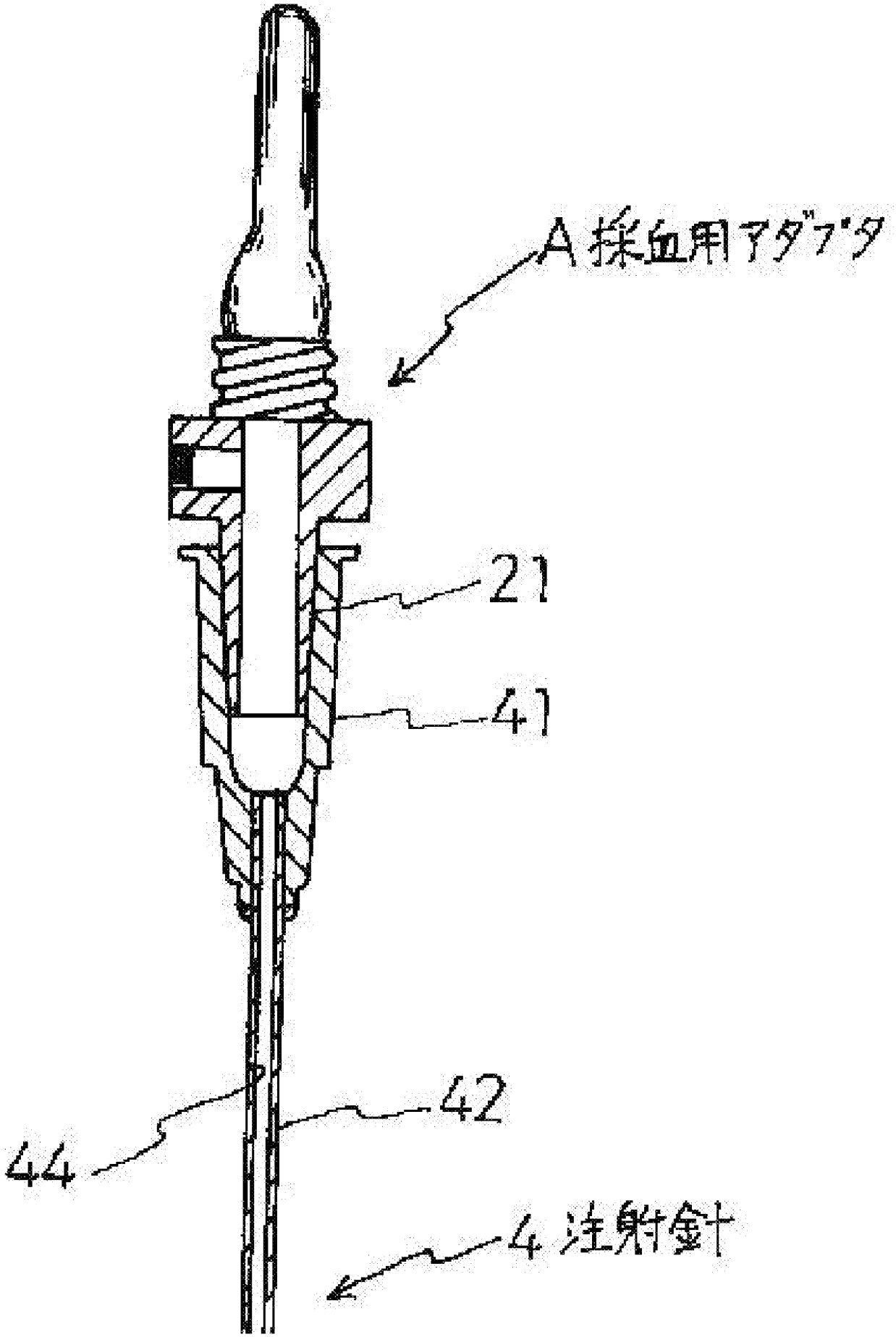
[Fig. 1]



[Figure 2]



[Figure 3]


A 採血用アダプタ
21
41
42
44
4 注射針

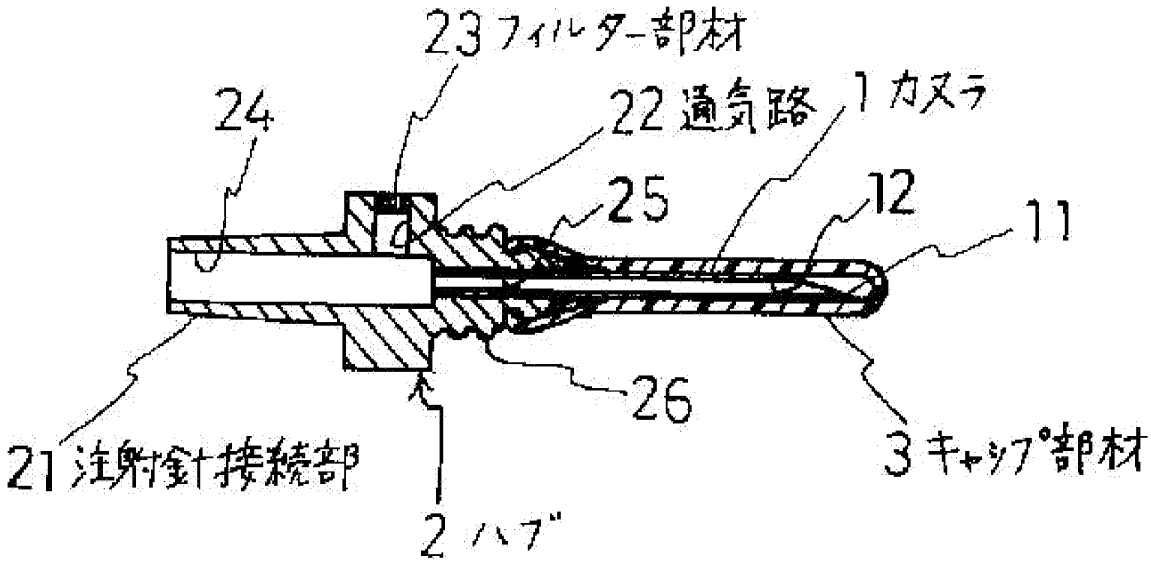


d

open

Representative drawing | 1 | 2 | 3 | Four

Magnify and Rotate



Representative drawing

1 / 1 display

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Bibliographic data: JPH08257018 (A) — 1996-10-08

BLOOD-GATHERING ADAPTER

Inventor(s): HIGAKI YOSHIO; IKEGAMI TAKASHI ± (HIGAKI YOSHIO, ; IKEGAMI TAKASHI)

Applicant(s): NISSHO KK ± (NISSHO CORP)

Classification: **- international:** ***A61B5/15; A61B5/154; A61M5/32;*** (IPC1-7): A61B5/14; A61M5/32

- cooperative: **A61B5/15003 (EP)**; **A61B5/150213 (EP)**; **A61B5/150389 (EP)**; **A61B5/150473 (EP)**; **A61B5/150503 (EP)**; **A61B5/150732 (EP)**; **A61B5/1535 (EP)**; A61B5/150572 (EP); A61B5/1545 (EP)

Application number: JP19950062943 19950322

Priority number(s): JP19950062943 19950322

Abstract of JPH08257018 (A)

PURPOSE: To provide a blood-gathering adapter by which the fact that the edge tip is stuck into a blood vessel can be confirmed since blood flows in an intermediate part of its transparent hub when the edge tip of an injection needle connected to this is stuck into a blood vessel. CONSTITUTION: A blood gathering adapter is composed of a hollow cannula 1 having the edge tip 11 on the tip, a transparent hollow hub 2 to support and fix a rear end part of this cannula 1 by its tip part and a cap member 3 which is put on the cannula 1 and is made of a rubber elastic body. An injection needle connecting part 21 is arranged in a rear end part of the hub 2, and a ventilating passage 22 is arranged in an intermediate part of the hub 2, and an outlet of this ventilating passage 22 is blocked up by a gas permeable and liquid impermeable filter member 23.

(19)日本国特許庁（ＪＰ）　(12) **公開特許公報**（Ａ）　(11)特許出願公開番号

特開平8－257018

(43)公開日　平成８年(1996)10月８日

(51)Int.Cl.[6]		識別記号	庁内整理番号	ＦＩ		技術表示箇所
Ａ６１Ｂ	5/14	３００	7638－2Ｊ	Ａ６１Ｂ	5/14	３００Ｅ
Ａ６１Ｍ	5/32			Ａ６１Ｍ	5/32	

審査請求　未請求　請求項の数４　ＯＬ　（全　４　頁）

(21)出願番号　特願平7－62943

(22)出願日　平成７年(1995)３月22日

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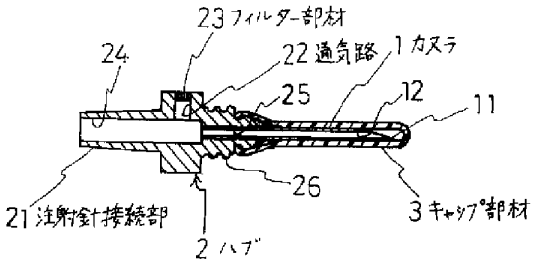
(72)発明者　池上　孝
大阪市北区豊崎３丁目３番13号　株式会社ニプロ内

(54)【発明の名称】　採血用アダプタ

(57)【要約】

【目的】　これに接続される注射針の刃先が血管に刺入されたときに、その透明なハブの中間部分に血液が流れ込み、これによって刃先が血管内に刺入されたことを確認できる採血用アダプタを提供する。

【構成】　採血用アダプタは、先端に刃先１１を有する中空のカヌラ１と、その先端部でこのカヌラ１の後端部を支持し固定する透明な中空のハブ２と、カヌラ１に被冠されたゴム弾性体製のキャップ部材３からなっている。そして、ハブ２の後端部には注射針接続部２１が設けられており、ハブ２の中間部には通気路２２が設けられ、この通気路２２の出口はガス透過性かつ液体不透過性のフィルター部材２３で塞がれている。



【特許請求の範囲】
【請求項１】　先端に刃先を有する中空のカヌラと、その先端部で該カヌラの後端部を支持し固定するとともに、その後端部に注射針のハブを液密に挿着可能な注射針接続部を備えた透明な中空のハブと、前記カヌラに被冠されたゴム弾性体製のキャップ部材とからなり、前記ハブの先端部と注射針接続部の間の中空部分に、該中空部分を外気と連通する通気路が設けられ、該通気路の出口がガス透過性かつ液体不透過性のフィルター部材で塞がれてなる採血用アダプタ。
【請求項２】　注射針接続部が注射針のハブと嵌合可能なルアーチップに形成されている請求項１に記載の採血用アダプタ。
【請求項３】　ルアーチップと同心状かつその外側に注射針のハブと結合可能な雌型結合手段を設けた請求項２に記載の採血用アダプタ。
【請求項４】　請求項１の採血用アダプタに注射針を接続してなる採血針。
【発明の詳細な説明】
【０００１】
【産業上の利用分野】本発明は採血用アダプタに関する。より詳しくは、血管より血液を採取するための真空採血管に用いる採血用アダプタであって、これに通常の注射針を接続することにより採血針として使用できるとともに、刃先が血管に刺入されたことを確認することができる採血用アダプタに関する。
【０００２】
【従来の技術】従来より、採血管による採血に際して、図４に示すような採血針を用いて採血しており、勘と経験によって刃先が血管内に入ったことを確認していた。しかしながら、このような勘と経験に頼る採血では、勘や経験の乏しい初心者や、血管が細くて見にくいまたは見えない患者の場合、血管内への刃先の刺入を確認できないため、何回も刺し直したりすることがあり、そのため、採血者にとっても被採血者にとっても大きな負担を強いられることになり、また、場合によっては、新たに真空採血管、採血針、その他の採血器具を用意して採血のし直しをしなければならず、不経済であった。そこで、刃先が血管に刺入されたことを確認することができる採血針が提案されている（特開平４－１３２５４１号公報など）。
【０００３】上記特開平４－１３２５４１号公報の採血針は、ハブに弾性チップの内腔部と外部雰囲気とを連通させる通気孔を設け、この通気孔の外部口部に通気性フィルタを取り付けたことを特徴とするもので、採血針に流入する血液（いわゆるフラッシュバック）を確認することにより、刃先が血管に刺入されたことを確認するようにしたものである。しかしながら、上記の採血針は弾性チップ内に流入した血液を透明なハブの通気孔に導こうとするものなので、フラッシュバックの確認に要する時間が長く、また、弾性チップの内部に溜まった血液が漏れる虞があり問題である。
【０００４】
【発明が解決しようとする課題】本発明は、上記の事情に鑑みてなされたもので、これに接続される注射針の刃先が血管に刺入されたときに、その透明なハブの中間部分に血液が流れ込み、これによって刃先が血管内に刺入されたことを確認できる採血用アダプタを提供することを目的とする。また、この採血用アダプタと注射針の組合せからなる採血針を提供することを目的とする。
【０００５】
【課題を解決するための手段】本発明は、上記の課題を解決するために、先端に刃先を有する中空のカヌラと、その先端部で該カヌラの後端部を支持し固定するとともに、その後端部に注射針のハブを液密に挿着可能な注射針接続部を備えた透明な中空のハブと、前記カヌラに被冠されたゴム弾性体製のキャップ部材とからなり、前記ハブの先端部と注射針接続部の間の中空部分に、該中空部分を外気と連通する通気路が設けられ、該通気路の出口がガス透過性かつ液体不透過性のフィルター部材で塞がれてなる採血用アダプタを採用している。また、この採血用アダプタに注射針を接続した構成を採用している。ここで、注射針接続部はこれに接続される注射針のハブと嵌合可能なルアーチップに形成してもよく、また、ルアーチップの外側にはこれと同心状に注射針のハブと螺合あるいはルアー結合可能な雌型結合手段を設けてもよい。
【０００６】
【作用】上記構成によれば、採血用アダプタを採血針ホルダーに取り付け、その注射針接続部に注射針を接続して、この注射針を血管に刺入すると、注射針の中空部分および採血用アダプタの中空部分に存在する空気が、流入する血液により採血用アダプタの通気路を通りガス透過性のフィルター部材を透過して外部に追い出されるので、血液は注射針の中空部分を通って採血用アダプタの中空部分に流入し、さらに通気路を通ってフィルター部材に達する。従って、透明なハブに形成された通気路を観察すれば、容易に注射針の血管内への刺入を確認することができる。また、この時、フィルター部材が液体不透過性なので、血液がフィルター部材を透過して外部に漏れることはない。
【０００７】
【実施例】次に本発明の実施例について図面に基づいて説明する。図１は本発明の一実施例に係る採血用アダプタの縦断面図であり、図２は他の実施例を示す図、図３は図１に示す採血用アダプタに注射針を取り付けた状態を示す図である。図１に示すように、本発明の採血用アダプタは、先端に刃先１１を有する中空のカヌラ１と、その先端部でこのカヌラ１の後端部を支持し固定する透明な中空のハブ２と、カヌラ１に被冠されたゴム弾性体

製のキャップ部材３からなっている。そして、ハブ２の後端部には注射針接続部２１が設けられており、ハブ２の中間部には通気路２２が設けられ、この通気路２２の出口はガス透過性かつ液体不透過性のフィルター部材２３で塞がれている。

【０００８】ハブ２は例えばポリエチレンやポリプロピレン、ポリエステル、ポリスチレンなどの透明な合成樹脂で中空に形成された部材であり、先端部と中間部および後端部からなる。ハブ２の先端部の中空部分２５には一般にステンレス鋼で形成されたカヌラ１の後端部が挿入され、接着剤で固定されており、このカヌラ１にはゴム弾性体の例えば天然ゴムや、イソプレンゴム、ブタジエンゴム、ニトリルゴムなどで形成されたキャップ部材３が被せられている。また、ハブ２の先端部の外壁には雄型結合手段の例えば雄ネジ２６が形成されており、採血針ホルダー（図示していない）に螺合できるようになっている。

【０００９】ハブ２の後端部はハブ２の先端部の中空部分２５と連通する中空部分２４を有する注射針接続部２１になっており、注射針４のハブ４１を嵌合できるよう一般に外径がテーパ状に縮径された所謂ルアーチップに形成されている。ルアーチップに形成された注射針接続部２１の外側には、採血操作の途中で注射針４のハブ４１が注射針接続部２１から脱落することがないように、例えば図２に示すように、ハブ２の中間部から注射針接続部２１方向にこれと同心状に延びるフード状の雌型結合手段２７を設け、注射針４のハブ４１の端部外壁に設けた雄型結合手段（図示していない）と螺合またはルアー結合するようにしてもよい。尚、注射針接続部２１としては通常、注射針４のハブ４１に挿着される雄型の結合部材が採用されるが、注射針のハブを雄型の結合端に形成することにより雌型の結合部材を採用することもできる。

【００１０】ハブ２の中間部は幅広の鍔状に突出した部分であり、中空部分２４を外気と連通する通気路２２が設けられており、通気路２２の出口はフィルター部材２３で塞がれている。このフィルター部材２３はガス透過性かつ液体不透過性のフィルター（疎水性フィルター）であり、このようなフィルターとしては、通常ポリプロピレンやポリエチレンなどのポリマー焼結体からなる層状のフィルターが好適に採用されるが、ポリプロピレンやポリエチレンなどの疎水性樹脂からなる膜状のいわゆるメンブレンフィルターであっても構わない。

【００１１】次に、本発明の採血用アダプタの使用について図３を用いて説明する。先ず、採血用アダプタＡを採血針ホルダー（図示していない）に取り付け、採血用アダプタＡの注射針接続部２１に注射針４を接続する。次に注射針４の刃先４３を血管に刺入すると、注射針４の中空部分４４および採血用アダプタＡの中空部分２４、２５に存在する空気が、流入する血液により採血用アダプタＡの通気路２２を通りガス透過性のフィルター部材２３を透過して外部に追い出される。すると、血液は注射針４の中空部分４４を通って採血用アダプタＡの中空部分２４に流入し、さらに通気路２２を通ってフィルター部材２３に達する。従って、透明なハブ２に設けられた注射針接続部２１や通気路２２を観察すれば、容易に注射針４の刃先４３の血管内への刺入を確認することができる。また、この時、フィルター部材２３が液体不透過性なので、血液がフィルター部材２３を透過して外部に漏れることはない。

【００１２】

【発明の効果】以上説明してきたことから明らかなように、本発明の採血用アダプタを採用することにより、次のような効果を奏することができる。

通常の注射針を接続することにより採血針として使用することができるので、経済的である。

これに接続された注射針の刃先が血管に刺入されたことを容易に確認できるので、注射針の刺し直しによる被採血者の負担を無くすることができる。

採血のし直しをしなくて済む。

【図面の簡単な説明】

【図１】本発明の一実施例に係る採血用アダプタの縦断面図である。

【図２】本発明の他の実施例を示す図である。

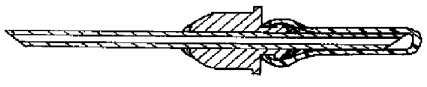
【図３】図１に示す採血用アダプタに注射針を取り付けた状態を示す図である。

【図４】従来の採血針を示す図である。

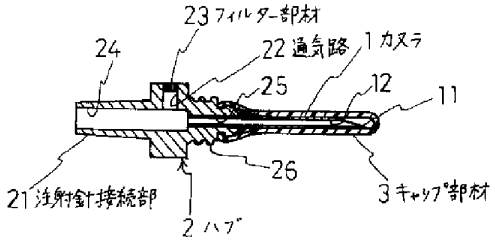
【符号の説明】

１　カヌラ
２　ハブ
２１　注射針接続部
２２　通気路
２３　フィルター部材
２７　雌型結合手段
３　キャップ部材
４　注射針
Ａ　採血用アダプタ

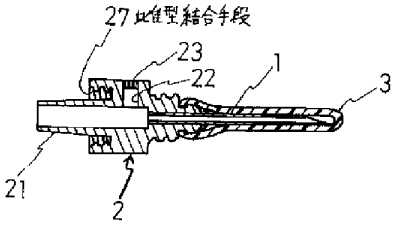
【図４】



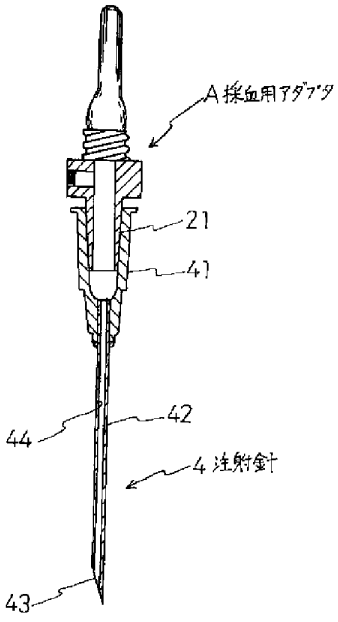
【図１】


23 フィルター部材
24
22 通気路
1 カヌラ
25
12
11
21 注射針接続部
26
3 キャップ部材
2 ハブ

【図２】


27 血液型結合手段
23
22
1
3
21
2

【図３】


A 採血用アダプタ
21
41
42
44
4 注射針
43

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THE STANDARD CLOTTING TIME

A METHOD BASED ON THE USE OF WHOLE VENOUS BLOOD IN CAPILLARY TUBES

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In 1955, Mayer[1] described a method for testing the coagulation time of whole blood that was later referred to as the *standard clotting time*.[2] The method was reported to be reliable and to reveal a rather narrow range of normal values, as compared with the more widely used Lee-White technic for clotting time, and with the now almost abandoned capillary method for clotting time. In the course of investigating possible clotting abnormalities in patients with prostatic cancer,[5] we re-evaluated the method, particularly because its claimed normal range of 11.9 ± 0.9 min. was based merely on values obtained from 40 healthy, fasting men, in the age group of 25 to 35 years.

MATERIALS AND METHODS

Because Mayer's procedure as outlined in 1957 was followed in detail,[2] it will not be described fully. It is necessary to note, however, that the No. 19 gage stainless steel needle was replaced by the Becton, Dickinson and Company No. 20 sterile disposable needle. With this method, venous blood is drawn and diverted by a special adapter to 3 capillary tubes, which are maintained at a temperature of 21 C. in a water bath. The end point is obtained by means of breaking off each capillary tube in succession and observing a fibrin clot. The average value determined from the 3 tubes represents the standard clotting time. It differs considerably from the ordinarily performed capillary clotting time because of the use of venous blood, with minimal admixture of tissue thromboplastin, and because the temperature is controlled. The test is readily performed by 1 technologist, and it is possible to examine 2 patients at the same time. Although it is of necessity performed at the bedside and requires minutes rather than seconds, the total time of performance is comparable to that of other coagulation tests if preparation of blood samples and reagents is considered. The following groups of persons, who were generally in a postprandial state, were examined:

1. Fifty-three women in the age group of 17 to 60 years.
2. Fifteen healthy men, 25 to 50 years of age.
3. Thirty healthy employees in the age group of 60 to 80 years, to serve as controls for patients with prostatic cancer.
4. Twenty-two men with cancer of the prostate gland, in the age group of 60 to 80 years.
5. Twelve persons on 2 different occasions, 1 to 12 months apart, in order to determine the standard deviation of the test.
6. Thirty-six outpatients maintained on anticoagulants (Coumadin) over a period of 1 year, for comparison of the standard clotting time with Quick's 1-stage prothrombin time.[4]
7. Twenty-five persons with miscellaneous cases who were investigated because of a history of a suspected bleeding tendency, for comparison with the clotting time (Lee-White) for whole blood, and a battery of other screening tests for blood coagulation.[4]

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RESULTS

1. Fifty-three healthy women (17 to 60 years) manifested a normal value of 11.2, with a standard deviation from the mean of ±1.1 min.

2. Fifteen healthy men (25 to 50 years) manifested normal values of 11.1 ± 1.1 min.

3. Thirty healthy male employees (60 to 80 years of age), with 42 determinations manifested normal values of 10.1 ± 1.3 min.

4. Twenty-two men (44 determinations) with cancer of the prostate gland manifested an average value of 10.5 ± 1.5 min. These men were also in the age group of 60 to 80 years.

5. Twelve controls taken on 2 different occasions (1 to 12 months apart) revealed a standard deviation from the mean of ±1.0 min.

6. One hundred thirty-nine determinations of the standard clotting time and also the prothrombin time on 36 patients being treated with anticoagulants revealed a poor correlation between these 2 tests. For the prothrombin activity in the so-called therapeutic range of from 20 to 30 per cent, the values in the standard clotting time ranged from 10.2 to 21.0 min. (Fig. 1). Prothrombin activity of less than 20 per cent revealed a range in the standard clotting time of 11.5 to 23.5 min.; values of prothrombin activity of more than 30 per cent manifested in the standard clotting time a range of 10.5 to 18.4 min. If, conversely, the therapeutic range of the standard clotting time is considered, which, according to Mayer and Connell[3] is between 15 and 20 min., the corresponding prothrombin activities revealed a range of 16 to 49 per cent (Fig. 1); taking values of the standard clotting time of less than 15 min., the range of the corresponding prothrombin activity varied from 15 to 70 per cent, and similarly, in values above 20 min., the variation of prothrombin activity was between 15 and 24 per cent.

7. Comparison of the standard clotting time with the clotting time for whole blood, and other screening tests, revealed that the standard clotting time was within the normal range whenever the clotting time for whole blood (Lee-White) was less than 20 min., with the following exceptions: 3 instances of patients treated with salicylates in whom the clotting time for whole blood was normal and the standard clotting time moderately prolonged (less than 20 min.); 3 other persons with a history of minor bleeding dif-

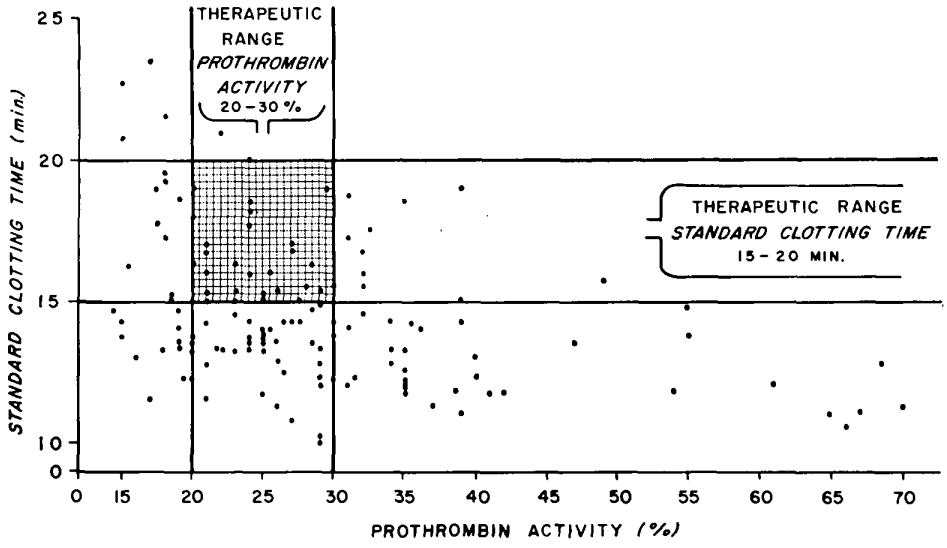


FIG. 1. A scattergram of the standard clotting time (min.) and prothrombin activity (per cent) of 139 determinations on 36 patients being treated with anticoagulants. Except for the *cross-hatched area*, there is no consistent correlation between the 2 tests.

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ficulty in whom the standard clotting time revealed a slight prolongation, in the range of from 15 to 20 min., whereas tests for other phases in blood coagulation, including the thromboplastin generation test, were normal. In addition, a patient with hemophilia A manifested a great prolongation of the standard clotting time, as well as the clotting time of the whole blood. There were 2 patients in whom, for unexplained reasons, the clotting time was less than normal, 9:00 and 7:33 min. One of these, a 34-year-old woman, had pulmonary coccidioidomycosis with multiple segmental pulmonary resections; her only other abnormality was a slightly positive tourniquet and petechiometer test. The other person, a 68-year-old man, is a patient with probable cirrhosis of the liver.

COMMENTS

We have found the standard clotting time a reliable and reproducible test for coagulation of whole blood. The normal range of values corresponds well with the figures reported by Mayer and Connell, except in the older age group, for whom the values are slightly less (approximately 1 min.).

The observation made by Mayer and Connell that there is poor correlation between the standard clotting time and the 1-stage prothrombin time is confirmed. The controversy[7] concerning which of the 2 tests more adequately represents a response to anticoagulation therapy is not resolved by our study; its resolution would require a very close clinical follow-up over a long period of time, which is not feasible for a study based on outpatients. According to Rapaport and Ames,[6] a Factor IX deficiency that is not measured by the prothrombin time does not seem to be the explanation. The standard clotting time may prove valuable whenever a discrepancy is encountered between 1 type of test, such as the 1-stage prothrombin time, and the clinical manifestations in anticoagulated patients. We also found that it may be a helpful procedure in evaluating a "borderline" prolonged clotting time, although it is by no means a substitute for detailed investigation of the patient with a history of definite bleeding. We have not determined whether or not values lower than normal (excluding faulty venipuncture) indicate a state of hypercoagulability. The greatest value of the test results from the fact that the normal range is rather narrow, as stated by Mayer and Connell.

SUMMARY

A re-evaluation of the standard clotting time, using several control groups, demonstrates that it is a reproducible test for coagulation of whole blood. It may be regarded as an additional useful test in the evaluation of an abnormal clotting time for whole blood, of patients with bleeding problems, and of patients being treated with anticoagulants.

SUMMARIO IN INTERLINGUA

Un re-evaluation del tempore standard de coagulation, utilisante plure gruppos de controlo, demonstra que illo es un reproducibile test pro le coagulation de sanguine total. Illo pote esser reguardate como un test additional de utilitate in le evalutation de anormal tempores de coagulation in sanguines total ab patientes con problemas hemorrhagic e ab patientes sub tractamento con anticoagulantes.

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The Clinical Significance of Positive Blood Cultures in the 1990s: A Prospective Comprehensive Evaluation of the Microbiology, Epidemiology, and Outcome of Bacteremia and Fungemia in Adults

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To assess changes since the mid-1970s, we reviewed 843 episodes of positive blood cultures in 707 patients with septicemia. The five most common pathogens were *Staphylococcus aureus, Escherichia coli,* coagulase-negative staphylococci (CNS), *Klebsiella pneumoniae,* and *Enterococcus* species. Although CNS were isolated most often, only 12.4% were clinically significant. Half of all episodes were nosocomial, and a quarter had no recognized source. Leading identifiable sources included intravenous catheters, the respiratory and genitourinary tracts, and intraabdominal foci. Septicemia-associated mortality was 17.5%. Patients who received appropriate antimicrobial therapy throughout the course of infection had the lowest mortality (13.3%). Multivariate analysis showed that age (relative risk [RR], 1.80), microorganism (RR, 2.27), source of infection (RR, 2.86), predisposing factors (RR, 1.98), blood pressure (RR, 2.29), body temperature (RR, 2.04), and therapy (RR, 2.72) independently influenced outcome. Bloodstream infections in the 1990s are notable for the increased importance of CNS as both contaminants and pathogens, the proportionate increase in fungi and decrease in anaerobes as pathogens, the emergence of *Mycobacterium avium* complex as an important cause of bacteremia in patients with advanced human immunodeficiency virus infection, and the reduction in mortality associated with infection.

The presence of living microorganisms in blood has substantial clinical importance. From the diagnostic standpoint, a positive blood culture yielding a clinically important microorganism represents either failure of host defenses to contain an infection at its primary focus or failure of the physician to effectively eradicate, drain, excise, or otherwise remove that focus of infection. The presence of bacteremia or fungemia also is an indicator of disseminated infection and, as such, generally indicates a poorer prognosis than that associated with localized disease. A positive blood culture, however, is not always clinically significant, since contamination may occur or the positive result might represent the transient and self-limited presence of microorganisms in the blood [1].

Our current understanding of the clinical significance of positive blood cultures has been enhanced by studies reported over several decades [2–21]. In recent years there have been many changes in medical practice, influenced in part by technologic advances and in part by the increased incidence of diseases not recognized previously. Just a few examples include the more frequent use of invasive or prosthetic devices; the increase in solid-organ and bone marrow transplantation as well as improvements in posttransplantation medical management; the introduction of HIV infection and AIDS as a scourge on late 20th century society; and therapeutic advances in the form of improved imaging techniques, less invasive methods of draining pus from closed spaces, and availability of broader spectrum antiinfective therapy.

We therefore undertook a comprehensive analysis of positive blood cultures in the 1990s. As a template for this project, we used an earlier review of bacteremia and fungemia [10, 11] authored by two of the current investigators (M.P.W. and L.B.R.). Although the earlier work has been widely recognized, the aforementioned changes in medicine and its practice argued for the need to reevaluate the clinical and prognostic importance of positive blood cultures. The primary goal of this study, therefore, was to determine the current microbiology, epidemiology, and prognostic importance of positive blood cultures, with special reference to similarities with and differences from the earlier reports from our group [10, 11, 22, 23].

Materials and Methods

For a 12-month period, February 1992 through January 1993, all inpatients ≥18 years of age with culture-positive blood

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were evaluated at Duke University Medical Center (DUMC), in Durham, NC; Robert Wood Johnson University Hospital (RWJUH), in New Brunswick, NJ; and the Salt Lake City Veterans Administration Medical Center (SLCVAMC), in Salt Lake City. Each patient was observed prospectively from the time the blood culture became positive, unless the patient had been discharged or had died before review of the hospital records by one of the investigators, in which case the review of the medical record was retrospective. Charts were evaluated according to the method of Feinstein et al. [24, 25], such that if the presence or absence of a particular finding was not clearly indicated, that case was excluded from analysis for that finding.

During the study period, 20 mL or more of blood was obtained for each culture and inoculated into media for processing on the BACTEC NR660 (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) or BacT/Alert (Organon Teknika, Durham, NC) blood culture system or both systems at all three centers. Blood was obtained at the bedside by house officers, medical students, or other trained health care personnel (nurses, phlebotomists, etc.) using 70% isopropyl alcohol and then 10% povidone-iodine. Although most of the blood culture specimens were obtained by peripheral venipuncture, it was not possible to determine specifically which ones were obtained in this manner and which were obtained through access devices.

Bottles were transported to the laboratory and incubated until flagged as positive or for 7 days in either BACTEC nonradiometric instruments (NR6 and NR7 bottles) or BacT/Alert continuous-monitoring instruments (BacT/Alert aerobic and anaerobic bottles). Broth from positive bottles was gram-stained and subcultured with use of standard techniques [26]. Susceptibility testing of isolates was done according to guidelines established by the National Committee on Clinical Laboratory Standards [27, 28].

All information obtained from patients' records was recorded on data worksheets and then transferred to a database software program for analysis.

Definitions

Definitions for this study for the most part were identical to those of Weinstein et al. [10, 11]. Only a few will be detailed here. New or modified definitions also will be detailed.

True septicemia vs. contamination. Each positive blood culture was assessed critically by one of the investigators, each an infectious disease physician. All isolates were categorized as true-positives, contaminants, or of unknown clinical significance. The categorical decision was made after the following factors were taken into account: the patient's clinical history, physical findings, body temperature at the time of the blood culture, leukocyte count and differential cell counts, number of positive blood cultures out of the total number performed, results of cultures of specimens from other sites, imaging results, histopathologic findings, and clinical course and response to therapy. If the clinical significance of the positive culture was not clear on the basis of the available information, the isolate was categorized as being of unknown significance.

Episode. An episode of bacteremia, fungemia, or mycobacteremia was defined by the first positive blood culture in a series or by any new positive blood culture result that occurred >48 hours after the previous positive result, unless it was clear to the investigator that the new positive culture was part of the same episode. For example, a positive blood culture for *Staphylococcus aureus* on the fifth day of antibiotic therapy for *S. aureus* endocarditis was considered part of the original bacteremic episode.

Community- vs. hospital-acquired septicemia. Each episode was classified as either community- or hospital-acquired septicemia, according to guidelines of the Centers for Disease Control and Prevention [29]. Septicemia in nursing home patients with positive blood cultures was always classified as hospital-acquired, whereas that in patients transferred from other outside facilities was classified according to their total period of hospitalization at both institutions.

Antimicrobial Therapy

Data on antimicrobial therapy were obtained at four chronologic points for each episode. These points were as follows: (1) at the time the first positive blood culture specimen was obtained, (2) after the blood culture was performed but before positive culture results were reported (i.e., empirical therapy), (3) after the blood culture was reported to be positive and gram-stained smear results were made known to the primary physician(s) but before organism identification and susceptibility test results were available, and (4) after organism identification and susceptibility test results were reported to the physicians.

Therapy was assessed critically at each time point on the basis of the clinical information available (time points 1–3) or the identification of the isolate and susceptibility test results (time point 4).

Treatment was judged to be the first choice if it was in accordance with the recommendations of a standard reference for antimicrobial therapy [30] and an alternative choice if the etiologic microorganism(s) was (were) susceptible to the agent administered but that agent was not considered the first choice. For purposes of judging the adequacy of therapy, both first-choice and alternative-choice agents were considered appropriate. Therapy was designated as the wrong choice if the causative microorganism was resistant to the antibiotic given. Superfluous therapy was defined as either the administration of unnecessary antibiotics in addition to a first- or alternative-choice agent or the administration of antibiotics for contaminant isolates. Ineffective or superfluous agents given for infections elsewhere in the body were recorded separately.

If a patient died before susceptibility results became available, that fact was recorded. When no therapy was given after the report of a positive blood culture to the physician, one of

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three assessments was made: (1) appropriate, if the isolate was a contaminant; (2) appropriate, if the episode was judged to represent true but transient bacteremia or fungemia that resolved spontaneously without adversely affecting the patient; or (3) inappropriate, if the culture represented true sepsis and the patient's status deteriorated because of the infection.

Outcome

The outcome of each episode was categorized as follows. The patient was (1) discharged alive, (2) alive but still hospitalized 30 days or longer after the onset of bacteremia or fungemia, (3) dead from causes attributable to the septicemic episode, or (4) dead from causes unrelated to septicemia. For the purposes of this study, mortality is termed associated or nonassociated in the subsequent text and tables.

Statistical Methods

For univariate analyses, statistical significance was calculated with the χ^2 test as described by O'Brien and Shampo [31]. The multivariate analysis and the resulting significance calculations were based on the logistic regression model [32], as implemented by the function "glm" in the statistical package S+ [33].

Results

During the study period, 1,585 blood culture–positive episodes occurred in 1,267 patients and yielded 1,844 microorganisms. Nine hundred forty-four microorganisms were isolated from 707 patients who had 843 episodes of true bacteremia or fungemia. There were 658 contaminant episodes and 84 episodes of unknown clinical significance.

Microbiological Features

The microorganisms isolated from positive blood cultures and the frequency with which they caused true bacteremia or fungemia are shown in table 1. The most common isolates from blood were coagulase-negative staphylococci. *S. aureus* was the microorganism most frequently causing true bacteremia; 87.2% of isolates were judged clinically significant. In contrast, only 12.4% of the coagulase-negative staphylococci were clinically significant, but they ranked as the third most frequent cause of bacteremia by virtue of their high prevalence.

Given the frequency with which coagulase-negative staphylococci were isolated from blood and the difficulty in determining their clinical significance, we analyzed *Staphylococcus epidermidis* isolates on the basis of the number of culture sets positive vs. the number of sets performed for each episode. The results are shown in table 2. When only a single culture set yielded *S. epidermidis,* the culture result almost always was judged to be of indeterminate significance or to represent contamination. When all of two or three culture sets yielded *S. epidermidis,* the isolates usually were judged clinically significant, but a substantial minority were of unknown (i.e., indeterminate) significance.

Whereas pneumococci always represented real infection, enterococcal isolates did so only 70% of the time, and viridans streptococci more often were contaminants (49%) than clinically significant isolates (38%) (table 1). Among the gram-negative aerobic and facultative bacteria, *Escherichia coli* was the most common isolate, and this microorganism was second only to *S. aureus* as a cause of septicemia. Overall, the Enterobacteriaceae and *Pseudomonas aeruginosa* represented true bacteremia >95% of the time when isolated.

Anaerobic bacteria were not common blood pathogens, accounting for only 3.9% of clinically important isolates. The isolation of a member of the *Bacteroides fragilis* group, however, almost always indicated true bacteremia (89%). *Clostridium perfringens* usually represented contamination when isolated from the blood, whereas the isolation of other *Clostridium* species usually represented true bacteremia.

Yeasts were relatively common isolates from blood cultures and almost always represented true fungemia when detected (91.7%). These organisms were present as clinically important pathogens almost twice as often as anaerobic bacteria, and *Candida albicans* ranked among the top 10 microorganisms causing septicemia. All mycobacteria and all but one *Cryptococcus neoformans* isolate were isolated from HIV-infected patients.

Of the 843 episodes of bacteremia and fungemia, 764 (90.6%) were unimicrobial and 79 (9.4%) were polymicrobial. Two microorganisms were isolated in 57 (72.2%) of the polymicrobial episodes, and ⩾3 microorganisms were isolated in 22 episodes (27.8%).

Epidemiological Features

Age and sex. Patients ranged in age from 17 to 103 years (mean, 56.2 years). Patients with HIV infection were younger (mean age, 36.9 years). Four hundred ninety of the episodes (58.1%) occurred in men. Ninety-nine percent of the episodes at the SLCVAMC, vs. 54% at both DUMC and RWJUH, were in men.

Community- vs. hospital-acquired infection. Of the 843 episodes, 404 (47.9%) were of community-acquired infection and 439 (52.1%) were of nosocomial infection. The microorganisms isolated in these episodes, categorized according to place of acquisition, are shown in table 3. Microorganisms more often associated with nosocomial acquisition were coagulase-negative staphylococci, enterococci, Enterobacteriaceae other than *E. coli, P. aeruginosa, Clostridium* species, *Bacteroides* species, and yeasts other than *C. neoformans.* A somewhat surprising finding was that nearly 40% of *P. aeruginosa* bacteremias were community-acquired.

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Table 1. Microorganisms isolated from blood of patients at Duke University Medical Center, Robert Wood Johnson University Hospital, and the Salt Lake City VA Medical Center, February 1992 through January 1993.

Microorganism (no. of isolates)	No. (%) of isolates per indicated category		
	True pathogen	Contaminant	Unknown
Aerobic and facultative bacteria			
Gram-positive			
Staphylococcus aureus (204)	178 (87.2)	13 (6.4)	13 (6.4)
Coagulase-negative staphylococci (703)	87 (12.4)	575 (81.9)	41 (5.8)
Enterococcus species (93)	65 (69.9)	15 (16.1)	13 (14.0)
Viridans streptococci (71)	27 (38.0)	35 (49.3)	9 (12.7)
Streptococcus pneumoniae (34)	34 (100)	0	0
Group A streptococci (3)	3 (100)	0	0
Group B streptococci (15)	10 (66.7)	3 (20.0)	2 (13.3)
Other streptococci (13)	8 (61.5)	3 (23.1)	2 (15.4)
Bacillus species (12)	1 (8.3)	11 (91.7)	0
Corynebacterium species (53)	1 (1.9)	51 (96.2)	1 (1.9)
Listeria monocytogenes (2)	1 (50.0)	0	1 (50.0)
Lactobacillus species (15)	6 (54.5)	2 (18.2)	3 (27.3)
Other gram-positive bacteria (15)	2 (13.3)	12 (80)	1 (6.7)
Gram-negative			
Escherichia coli (143)	142 (99.3)	0	1 (0.7)
Klebsiella pneumoniae (65)	65 (100)	0	0
Enterobacter cloacae (25)	25 (100)	0	0
Serratia marcescens (22)	22 (100)	0	0
Proteus mirabilis (16)	16 (100)	0	0
Other Enterobacteriaceae (45)	41 (91)	1 (2.2)	3 (6.7)
Pseudomonas aeruginosa (55)	53 (96.4)	1 (1.8)	1 (1.8)
Pseudomonas species (8)	6 (75)	0	2 (25)
Stenotrophomonas maltophilia (7)	5 (71.4)	0	2 (28.6)
Acinetobacter baumanii (16)	13 (81.2)	1 (6.2)	2 (12.5)
Haemophilus influenzae (3)	3 (100)	0	0
Other gram-negative bacteria (16)	10 (62.5)	3 (18.8)	3 (18.8)
Anaerobic bacteria			
Clostridium perfringens (13)	3 (23.1)	10 (76.9)	0
Clostridium species (15)	12 (80)	3 (20)	0
Propionibacterium species (48)	0	48 (100)	0
Other gram-positive anaerobic bacteria (7)	4 (57.1)	2 (28.6)	1 (14.3)
Bacteroides fragilis group (18)	16 (88.9)	0	2 (11.1)
Other gram-negative anaerobic bacteria (5)	2 (40)	2 (40)	1 (20)
Yeasts and fungi			
Candida albicans (30)	27 (90)	0	3 (10)
Other *Candida* species (15)	15 (100)	0	0
Cryptococcus neoformans (8)	8 (100)	0	0
Torulopsis glabrata (15)	14 (93.3)	0	1 (6.7)
Other yeasts and fungi (4)	2 (50)	1 (25)	1 (25)
Mycobacteria			
Mycobacterium avium complex (16)	16 (100)	0	0
M. tuberculosis (1)	1 (100)	0	0
All microorganisms (1,844)	944 (51.2)	791 (42.9)	109 (5.9)

Hospital service. Six hundred twenty of the 843 bacteremic and fungemic episodes (73.5%) occurred in patients hospitalized on the medical services of our institutions. Patients hospitalized on the nontransplantation surgical services accounted for 21.3% of total episodes, with the remaining 5.2% of episodes distributed among the transplantation surgery, obstetric and gynecologic services, and emergency and outpatient departments. Pneumococcal bacteremia, not surprisingly, was seen almost exclusively in patients on the medical service.

Proportionately, enterococcal and pseudomonas bacteremias were twofold more common on the general and transplantation surgical services than on the medical service. Indeed, *P. aeruginosa* accounted for only 4.4% of septicemias on the medical service. Fungemia was proportionately most common on the

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Table 2. Clinical significance of *Staphylococcus epidermidis* isolates (unimicrobial episodes only).

No. of culture sets		Clinical significance: no. (%) of isolates		
Positive	Performed	Significant	Contaminant	Indeterminate
1	1	0	33 (97.1)	1 (2.9)
1	2	3 (2.2)	129 (94.8)	4 (3.0)
2	2	18 (60.0)	1 (3.3)	11 (36.7)
1	3	0	2 (100)	0
2	3	3 (75.0)	0	1 (25)
3	3	4 (100)	0	0

transplantation surgical service, accounting for nearly 25% of septicemic episodes. Anaerobic bacteremia, which was uncommon in general, was seen most frequently in patients on the general surgery service (6.6% of episodes) and obstetric and gynecologic service (11.1% of episodes).

Sources of infection. The sources of bacteremia and fungemia were identifiable in 627 (74.4%) of episodes and are listed in table 4. Intravenous catheters were the most common primary foci for septicemia. Despite the availability of increasingly sophisticated imaging techniques, the sources for nearly one-fourth of episodes could not be determined.

The relationship between microorganism and sources of unimicrobial bacteremia and fungemia are presented in table 5, which also delineates those episodes confirmed by cultures of specimens other than blood or by clinical evidence. The majority of *S. aureus* and coagulase-negative staphylococcal bacteremias were associated with intravascular devices. Not surprisingly, pneumococcal bacteremia was most often associated with pneumonia, but in 7 of 34 episodes (20.6%) a primary source could not be determined. Among the Enterobacteriaceae, primary foci of infection below the diaphragm predominated (table 5), as would be expected given the normal habitat of these bacteria. In contrast, the most common focus for bacteremia due to *P. aeruginosa* was the respiratory tract, which was the focus more than twice as frequently as the next most common focus, the genitourinary tract.

Several microorganisms or microorganism groups were associated at a particularly high frequency with bacteremia or fungemia in which a primary focus for infection could not be determined. These included the viridans streptococci (44.4%), *Enterobacter cloacae* (58.3%), *Klebsiella pneumoniae* (33.3%), *Candida* species (37.5%), *Torulopsis glabrata* (41.7%), and *Mycobacterium avium* complex (100%). All of the *E. cloacae* bacteremias and many of the fungemias and *K. pneumoniae* bacteremias with unknown sources occurred in patients with underlying malignancies.

Table 3. Community-acquired and hospital-acquired microorganisms and major microorganism groups involved in episodes of bacteremia and fungemia.

	No. (%) of isolates per place of acquisition of infection	
Microorganisms	Community	Hospital
Staphylococcus aureus	90 (50.6)	88 (49.4)
Coagulase-negative staphylococci	27 (31.0)	60 (69.0)
Streptococcus pneumoniae	31 (91.2)	3 (8.8)
Other streptococci	32 (68.1)	15 (31.9)
Enterococcus species	15 (23.1)	50 (76.9)
Escherichia coli	87 (61.3)	55 (38.7)
Other Enterobacteriaceae	61 (36.1)	108 (63.9)
Pseudomonas aeruginosa	21 (39.6)	32 (60.4)
Other nonfermentative gram-negative rods	16 (51.6)	15 (49.4)
Clostridium species	5 (33.3)	10 (66.7)
Bacteroides species	7 (38.9)	11 (61.1)
Candida species	7 (16.7)	35 (83.8)
Cryptococcus neoformans	8 (100)	0
Torulopsis glabrata	2 (14.3)	12 (85.7)
Mycobacterium avium complex	16 (100)	0

Clinical Observations

In order to determine whether certain indicators might assist in assessing the clinical significance of positive blood cultures, we examined the relationship between positive cultures and the peripheral leukocyte count, absolute neutrophil count, blood pressure, and body temperature at the time the first positive blood culture specimen was obtained for a given episode. We also examined the relationship between each of these variables and the microorganisms isolated from true positive cultures. In addition, we critically assessed the antimicrobial therapy as described in the Materials and Methods section.

Leukocyte count and absolute neutrophil count. Patients with culture-positive blood and a peripheral leukocyte count of $<4{,}000/\mu L$ or $\geq 20{,}000/\mu L$ were significantly more likely

Table 4. Sources of bacteremia and fungemia.

	No. of episodes confirmed by		
Source	Culture	Clinical evidence	Total no. (%) of episodes
Intravascular catheter	29	97	161 (19.1)
Genitourinary tract	115	28	147 (17.4)
Respiratory tract	56	46	104 (12.3)
Bowel and peritoneum	22	21	45 (5.3)
Biliary tract	9	21	33 (3.9)
Intraabdominal abscess	9	15	24 (2.8)
Skin	11	29	42 (5.0)
Bone and joint	11	5	16 (2.0)
Surgical wound	7	2	11 (1.3)
Other	25	18	44 (5.2)
Unknown	0	0	216 (25.6)

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Table 5. Sources and confirmatory evidence for episodes of unimicrobial bacteremia and fungemia, according to microorganism.

Microorganism(s) (no. of episodes)	No. of sources confirmed by		Common source(s) (no. of episodes)*
	Culture	Clinical evidence	
Staphylococcus aureus (159)	56	74	IV (56), skin (19), respiratory (18), bone/joint (10)
Coagulase-negative staphylococci (73)	16	45	IV (59), skin (5)
Streptococcus pneumoniae (34)	5	22	Respiratory (26)
Group B streptococci (8)	4	3	Skin (3), GU (3)
Viridans group streptococci (24)	3	10	Respiratory (3), skin (2)
Enterococcus species (38)	13	9	GU (15), IV (3)
Escherichia coli (116)	70	30	GU (67), biliary (11), peritoneal (10)
Klebsiella pneumoniae (48)	15	15	Biliary (10), GU (8), peritoneal (5)
Enterobacter cloacae (12)	3	2	Biliary (2), respiratory (2)
Serratia marcescens (20)	11	6	GU (4), respiratory (4), IV (3)
Proteus mirabilis (13)	10	2	GU (9)
Pseudomonas aeruginosa (48)	25	12	Respiratory (19), GU (9)
Acinetobacter baumanii (12)	4	0	Respiratory (3)
Bacteroides fragilis group (9)	3	4	Abscess (6)
Candida albicans (21)	7	2	IV (5), peritoneal (2)
Candida tropicalis (7)	1	4	IV (1), GU (1), peritoneal (1)
Torulopsis glabrata (12)	1	4	GU (4)
Mycobacterium avium (15)	0	0	No sources identified

NOTE. The list of microorganisms includes all those isolated ≥5 times as causes of unimicrobial bacteremia or fungemia.

* Abscess = intraabdominal abscess; GU = genitourinary tract; IV = intravascular device; respiratory = respiratory tract.

($P < .001$) to have true bacteremia or fungemia episodes (62.5% and 60.3%, respectively) than contaminant episodes when compared with patients who had peripheral leukocyte counts between 4,000 and 19,999/μL (proportion of true bacteremias, 49.2%). Similarly, patients with absolute neutropenia were significantly more likely ($P < .001$) than nonneutropenic patients to have a positive blood culture represent true bacteremia or fungemia (70.2% vs. 51.4% of positive cultures, respectively).

The distribution of microorganisms causing septicemia in neutropenic and nonneutropenic patients is shown in table 6. Neutropenic patients were significantly less likely to have bacteremia due to *S. aureus* ($P < .0001$; RR, 0.33) but were significantly more likely to have fungemia ($P < .01$; RR, 1.81) and polymicrobial bacteremia ($P < .0001$; RR, 2.63) than were nonneutropenic individuals.

Blood pressure. Approximately 14% of patients were hypotensive at the time the first positive blood culture specimen was obtained. The positive blood cultures of these patients were more likely to represent true bacteremia than were positive blood cultures of patients with normal blood pressure at the time cultures were performed (72.7% vs. 51.1% of positive cultures, respectively; $P < .0001$). The distribution of microorganisms causing bacteremia and fungemia in these patients is shown in table 7. There were no statistically significant differences in microorganisms or microorganism groups in hypotensive vs. normotensive patients. However, polymicrobial episodes occurred significantly more often in hypotensive patients than in patients whose blood pressure was normal at the time of blood culture ($P < .05$; RR, 1.58).

Temperature. Cultures of patients who were hypothermic (temperature, <36°C) or who had marked fever (temperature, ≥40°C) were more likely to be true-positives (67.7% and 69.6% of positive cultures, respectively) than were those of patients whose temperatures were normal (39.2% of positive cultures) or moderately elevated (55.9% of positive cultures) at the time the positive blood culture specimen was obtained.

Endocarditis. Of 31 episodes (in 31 patients) of endocarditis, 11 were due to *S. aureus,* 10 to viridans streptococci, and 3 to enterococci. All episodes were unimicrobial; 30 of the 31 were due to gram-positive bacteria, and one was caused by *K. pneumoniae.* Twenty-one patients presented following <1 week of symptoms, 8 following 1–3 weeks of symptoms, and 2 following >3 weeks of symptoms. Seven of 11 patients with endocarditis due to *S. aureus* and 7 of 10 patients with endocarditis caused by viridans streptococci presented following <1 week of symptoms.

Antibiotic therapy. Of the 1,585 episodes of positive blood cultures, 454 (28.6%) involved patients receiving antimicrobial agents at the time the first positive blood culture specimen was obtained. The proportion of patients who were receiving antibiotics was the same regardless of whether growth repre-

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Table 6. Microorganisms recovered from and types of episodes in patients with bacteremia and fungemia, according to absolute neutrophil count.

Variable	No. (%) of isolates from patients with indicated neutrophil count	
	<1,000/μL	≥1,000/μL
Microorganisms		
Staphylococcus aureus	9 (6.0)*	169 (21.1)*
Coagulase-negative staphylococci	12 (8.1)	75 (9.4)
Streptococci	9 (6.0)	78 (9.7)
Enterococcus species	13 (8.7)	52 (6.5)
Enterobacteriaceae	58 (38.9)	253 (31.6)
Pseudomonas aeruginosa	11 (7.4)	42 (5.2)
Other nonfermentative gram-negative rods	2 (1.3)	29 (3.6)
Anaerobic bacteria	9 (6.1)	29 (3.6)
Yeasts and fungi	17 (12.1)†	48 (6.0)†
Type of episode: total no. (%)		
Unimicrobial	96 (69.6)	668 (87.4)
Polymicrobial	24 (30.4)*	55 (12.6)*

* $P < .0001$.
† $P < .01$.

sented true bacteremia or contamination. Of the 843 episodes of true bacteremia or fungemia, 71 (8.4%) occurred in patients who were receiving therapy that was effective against the microorganism(s) that grew in the blood culture. This proportion was the same at all three hospitals (range, 8.0%–9.1%).

Appropriate antimicrobial therapy was administered to a substantial majority of patients at all of the time points assessed. Excluding the 48 patients who died prior to the availability of susceptibility test results, 620 of 795 patients (78%) received appropriate therapy at all time points. In addition, 111 patients (14%) were given appropriate therapy after susceptibility test results were available, regardless of whether they had received inappropriate empirical therapy at an earlier time point.

Patients with unimicrobial septicemia were more likely than those with polymicrobial septicemia to be treated with appropriate therapy, especially after susceptibility test results were available (92.7% vs. 83.6%, respectively). At all time points assessed, medical patients were somewhat more likely than surgical patients to receive appropriate therapy. Among medical patients, the proportion who received appropriate therapy at the different time points ranged from 89.4% to 91.0%, versus a range of 83.0% to 87.1% among surgical patients.

After susceptibility test results were available, approximately one-quarter of all patients were receiving antimicrobial agents judged to be superfluous for the infecting microorganism(s) and clinical setting. Twenty-six patients (3.3%) were receiving agents to which their infecting organisms were resistant in vitro, and nine patients (1.1%) received no antimicrobials despite a clinical setting that should have mandated therapeutic intervention.

Outcome and Factors Influencing Prognosis

One hundred forty-eight patients (17.5%) died of causes directly or indirectly attributable to an episode of septicemia (associated mortality). Five hundred thirty-five patients (63.5%) were discharged alive, 118 (14.0%) were alive but remained hospitalized 30 days after onset of the septicemic episode, and 42 (5.0%) died from causes that were judged by the investigators not to be associated with the bacteremia or fungemia. There were no significant differences in mortality at the three collaborating hospitals.

Univariate Analyses

Age and sex. The effect of age on outcome of bacteremia and fungemia was assessed according to the decade of life of the infected patients. As shown in figure 1, septicemia-associated mortality gradually increased with age and was especially notable after the age of 70 years. The infection-associated mortality for septicemic patients over 70 years of age was 24.2% compared with 15.2% for patients 70 years of age or less. In comparison with other patients, the relative risks of death from bacteremia and fungemia for patients between 71 and 80 years of age and >80 years of age were 2.58 and 3.4, respectively. There were no significant differences in infection-associated mortality between septicemic men and women.

Hospital service. The septicemia-associated mortality rates ranged from zero among obstetric and gynecologic patients to 19% and 23% among medical and cardiovascular surgery patients, respectively. However, none of the differences in mortality, when sorted according to hospital service, were statistically significant.

Table 7. Microorganisms recovered from and types of episodes in hypotensive and normotensive patients with bacteremia and fungemia.

Variable	No. (%) of isolates from patients with indicated blood pressure status	
	Hypotensive	Normotensive
Microorganism		
Staphylococcus aureus	21 (16.0)	157 (19.3)
Coagulase-negative staphylococci	6 (4.6)	81 (10.0)
Streptococcus pneumoniae	8 (6.1)	26 (3.2)
Other streptococci	6 (4.6)	41 (5.0)
Enterococcus species	13 (10.0)	52 (6.4)
Enterobacteriaceae	46 (35.1)	265 (32.6)
Pseudomonas aeruginosa	7 (5.3)	46 (5.7)
Other nonfermentative gram-negative rods	1 (0.8)	30 (3.7)
Anaerobic bacteria	5 (3.8)	33 (4.1)
Yeasts and fungi	12 (9.2)	54 (6.6)
Type of episode: total no. (%)		
Unimicrobial	96 (85.7)	668 (91.4)
Polymicrobial	16 (14.3)*	63 (8.6)*

* $P < .05$.

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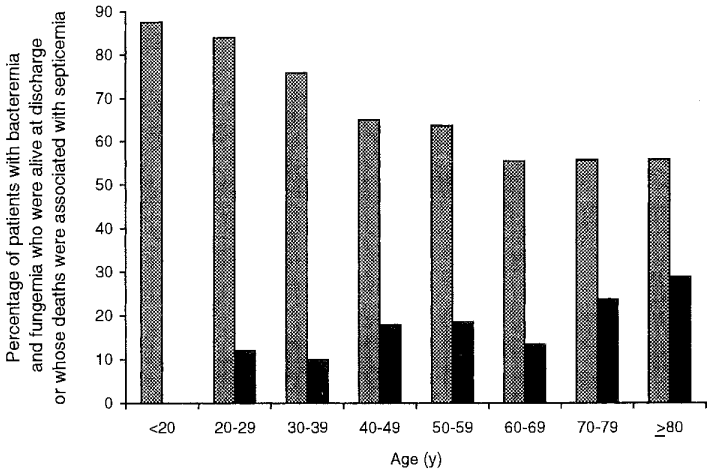


Figure 1. Outcome of bacteremia or fungemia, according to age group of patients (▩ = alive at discharge; ■ = death, associated with septicemia).

Place of acquisition of bacteremia and fungemia. Patients who developed bacteremia or fungemia during the course of hospitalization had an infection-associated mortality rate of 20.3%, vs. 14.6% for patients with community-acquired disease. The relative risk of death associated with nosocomial septicemia was 1.39 ($P < .05$).

Table 8. Associated mortality in episodes of bacteremia and fungemia and relative risk of death, as related to etiologic microorganisms in unimicrobial episodes and to the type of episode.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Microorganisms		
Staphylococcus aureus	19/159 (11.9)	2.18
Coagulase-negative staphylococci	4/73 (5.5)*	1.0
Streptococcus pneumoniae	6/34 (17.6)	3.22
Other streptococci	5/38 (13.1)	2.40
Enterococcus species	5/38 (13.1)	2.40
Other gram-positive aerobic bacteria	1/9 (11.1)	2.03
Escherichia coli	14/116 (12.1)	2.20
Other Enterobacteriaceae	31/125 (24.8)†	4.53
Pseudomonas aeruginosa	8/48 (16.7)	3.04
Other nonfermentative gram-negative rods	3/25 (12.0)	2.19
Other gram-negative aerobic bacteria	0/6	0.04
Gram-negative anaerobic bacteria	2/14 (14.3)	2.61
Gram-positive anaerobic bacteria	2/8 (25.0)	3.65
Yeasts and fungi	19/53 (35.8)‡	6.54
Mycobacteria	2/16 (12.5)	2.28
Type of episode		
Unimicrobial	120/764 (15.7)	1.0
Polymicrobial	27/79 (34.2)‡	2.16

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Microorganism. The microorganism isolated and type of bacteremia or fungemia (i.e., unimicrobial or polymicrobial) influenced outcome (table 8). Among the common etiologic agents of bacteremia and fungemia, the lowest associated mortality occurred with coagulase-negative staphylococci (5.5%) and the highest with yeasts and fungi (35.8%). Infection-associated mortality was lower with gram-positive unimicrobial bacteremia (11.1%) than with gram-negative bacteremia (17.6%), anaerobic bacteremia (18.2%), or fungemia (35.8%).

The mortality associated with pneumococcal bacteremia was greater than that associated with enterococcal or *S. aureus* bacteremia (table 8). Also noteworthy was the mortality rate with *P. aeruginosa* bacteremia, which was less than that with bacteremia due to enteric gram-negative rods other than *E. coli* (table 8). The mortality associated with polymicrobial bacteremia was more than twice that associated with unimicrobial episodes.

Table 9. Associated mortality in episodes of bacteremia and fungemia, according to source of infection.

Source of infection	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Intravascular catheter	12/161 (7.4)*	1.0
Genitourinary tract	16/147 (10.8)†	1.46
Respiratory tract	26/104 (25.0)†	3.35
Bowel and peritoneum	23/45 (51.1)‡	6.86
Biliary tract	4/33 (12.1)	1.63
Intraabdominal abscess	3/24 (12.5)	1.68
Skin	6/42 (14.3)	1.92
Bone and joint	1/16 (6.25)	0.84
Surgical wound	0/11	0.01
Other	3/44 (6.8)	0.91
Unknown	54/216 (25.0)*	3.35

* $P < .01$.
† $P < .05$.
‡ $P < .001$.

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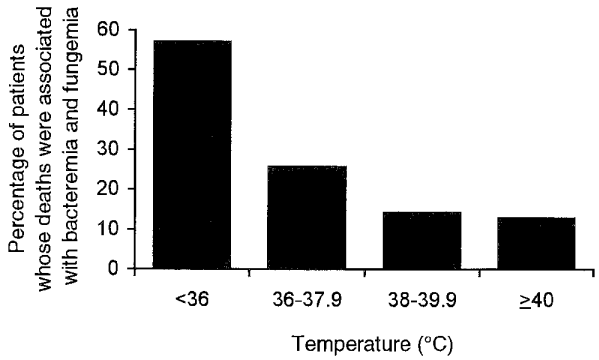


Figure 2. Septicemia-associated mortality as related to temperature of patients at the time the first positive blood culture specimen was obtained.

Source of infection. The outcome of bacteremia and fungemia was affected by the primary source of infection (table 9). For risk factor analysis, we assigned a risk of 1.0 to septicemia associated with iv catheters in order to maintain consistency with our earlier work [11]. Significantly increased septicemia-associated mortality and relative risk of death occurred with respiratory tract sources ($P < .05$), with bowel and peritoneal sources ($P < .01$), and when a primary focus of infection could not be found ($P < .05$).

Body temperature. The mortality associated with bacteremia and fungemia was inversely related to the body temperature of patients at the time the first positive blood culture specimen was obtained (figure 2). Risk factor analysis showed significantly increased mortality ($P < .05$) among the patients who were hypothermic at the onset of septicemia.

Blood pressure. Septic shock, as evidenced by the presence of hypotension at the time the first positive blood culture specimen was obtained, was associated with increased mortality. Table 10 reveals that this relationship was a virtually uniform finding, regardless of the etiologic microorganism or the type of septic episode.

Leukocyte count and absolute neutrophil count. The relationship between septicemia-associated mortality and total leukocyte count or absolute neutrophil count is shown in table 11. Patients who had leukocyte counts of $<4{,}000/\mu L$ or $\geq 20{,}000/\mu L$ had a twofold increase in relative risk of death from septicemia. Patients with absolute neutropenia had a significantly increased relative risk of death in comparison with that for nonneutropenic patients.

Predisposing factors. The influence of predisposing factors on the outcome of septicemia was analyzed both when individual factors were present alone and when multiple factors were present (table 12). Nearly one-quarter of the patients had no predisposing factors, and these patients had the lowest septicemia-associated mortality (8.2%; RR, 1.0). The greatest mortality was associated with moderate renal failure (61.5%; RR, 7.54).

Table 10. Associated mortality in episodes of bacteremia and fungemia, as related to etiologic microorganism in unimicrobial episodes, type of episode, and blood pressure status at the time of onset of septicemia.

Variable	Associated mortality: no. (%) of deaths per no. of episodes in indicated group	
	Hypotensive	Normotensive
Microorganisms		
Staphylococcus aureus	5/18 (27.8)*	14/141 (9.9)*
Coagulase-negative staphylococci	1/4 (25)	3/69 (4.3)
Streptococcus pneumoniae	1/8 (12.5)	5/26 (19.2)
Other streptococci	1/3 (33.3)	3/35 (8.6)
Enterococcus species	1/5 (20)	4/33 (12.1)
Escherichia coli	4/13 (30.8)*	10/103 (9.7)*
Other Enterobacteriaceae	12/23 (52.2)†	19/104 (18.3)†
Pseudomonas aeruginosa	3/6 (50)*	5/42 (11.9)*
Other nonfermentative gram-negative rods	0/1	3/28 (10.7)
Anaerobic bacteria	1/2 (50)	3/24 (12.5)
Yeasts and fungi	5/7 (71.4)*	14/46 (30.4)*
Type of episode		
Unimicrobial	35/96 (36.4)‡	85/668 (12.7)
Polymicrobial	10/16 (62.5)†	17/63 (27.0)

* $P < .05$.
† $P < .01$.
‡ $P < .001$.

Although the relative risk of death was high in the presence of severe renal failure and biopsy-proven cirrhosis, statistical significance was not achieved because of the relative infrequency of each of these predisposing factors as the sole underlying problem. Not surprisingly, there was a direct relationship between septicemia-associated mortality and the number of predisposing factors present. Thus, mortality was greater among the patients with multiple predisposing factors than among patients with only a single factor.

Table 11. Associated mortality in episodes of bacteremia and fungemia, as related to leukocyte count and absolute neutrophil count.

Variable	Associated mortality: no. (%) of deaths per no. of episodes	Relative risk of death
Total leukocyte count (per μL)		
$<4{,}000$	42/177 (23.7)	2.11*
4,000–10,999	28/249 (11.2)	1.0
11,000–19,999	48/293 (16.4)	1.46
20,000–49,999	27/115 (23.5)	2.09*
$\geq 50{,}000$	2/8 (25)	2.22
Absolute neutrophil count (per μL)		
$<1{,}000$	31/120 (25.8)	1.58*
$\geq 1{,}000$	115/702 (16.4)	1.0

* $P < .05$.

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Table 12. Influence of predisposing factors on associated mortality in episodes of bacteremia and fungemia.

Factor(s)	Associated mortality: no. (%) of deaths* per no. of episodes	Relative risk of death
None	16/196 (8.2)	1.0
Hematologic malignancy	14/70 (20.0)	2.45†
Other neoplasm	27/150 (18.0)	2.20†
Corticosteroids	3/28 (10.7)	1.31
AIDS	11/51 (21.6)	2.64†
Trauma	1/11 (9.1)	1.11
Recent surgery	7/49 (14.3)	1.75
Diabetes mellitus	6/59 (10.2)	1.25
Creatinine level, 2–5 mg/dL	16/26 (61.5)	7.54‡
Creatinine level, >5 mg/dL	4/16 (25)	3.06
Cirrhosis	2/6 (33.3)	4.08
One factor	91/477 (19.1)	2.34†
Two or more factors	41/168 (24.4)	2.99†

* No. of deaths among patients in whom listed predisposing factor was the only one present.
† $P < .05$.
‡ $P < .01$.

Antibiotic and other therapy. The mortality associated with bacteremia and fungemia clearly was affected by the type of antimicrobial therapy administered (table 13). The great majority (78%) of patients received appropriate therapy at all three time points at which assessments were made, and this group of patients had the lowest septicemia-associated mortality. Patients who received inappropriate empirical therapy but whose physicians administered appropriate therapy once the blood culture was reported to be positive also had low mortality. By contrast, among the small group of patients who received inappropriate therapy at all three time points, three of nine (33%) died of causes attributable to sepsis.

Indeed, the data shown in table 13 clearly indicate that septicemia-associated mortality increased in proportion to the duration of inappropriate antimicrobial therapy. Since our definition of appropriate empirical therapy allowed for the possibility that the organism(s) grown in blood culture might not be susceptible to the agents given, we also assessed outcome in terms of whether the infecting organisms were susceptible to therapy being administered at each time point. The results of this analysis were very similar; that is, associated mortality was lowest (9.8%) when the organism was susceptible at all three time points and also was low (12.6%) when patients received effective antimicrobial therapy after blood cultures were reported to be positive.

When mortality following the availability of susceptibility test results was analyzed alone, the mortality rates when first-choice or alternative-choice agents were given were identical (8.3%), but the rate was 24% when superfluous therapy was given. Since superfluous therapy included at least one agent with in vitro activity against the infecting microorganism, other factors that may have influenced outcome were assessed. Patients receiving superfluous therapy were twofold to threefold more likely to have absolute granulocytopenia, fungemia, or polymicrobial episodes than were patients who received first-choice or alternative-choice agents.

The removal, excision, or drainage of a primary focus of infection, if feasible, often has a salutary effect on the outcome of septicemia. Therefore, we assessed outcome when such therapeutic maneuvers were undertaken. The results confirmed the beneficial effect of these interventions. Among patients who survived until susceptibility test results were available, associated mortality was 6.2% (14 of 224) when an infected focus was excised, drained, or removed, vs. 15.6% (87 of 557) when no additional interventions were (or could be) undertaken ($P < .001$). Among patients with catheter-associated bacteremia or fungemia, removal of the catheter was associated with death due to septicemia in only 3.9%.

Table 13. Associated mortality in episodes of bacteremia and fungemia, as related to appropriateness of antimicrobial therapy at different time points during septicemia.

Assessment of therapy at indicated time point*				
Initial empirical therapy	After culture reported positive	After susceptibility results available	Associated mortality: no. (%) of deaths per no. of patients	RR
A	A	A	65/620 (10.5)	1.0
I	A	A	6/45 (13.3)	1.27
A	I	A	7/35 (20.0)	1.91
A	A	I	7/35 (20.0)	1.91
I	I	A	8/31 (25.8)	2.46
A	I	I	4/14 (28.6)	2.73
I	A	I	0/2	0.05
I	I	I	3/9 (33.3)	3.18

* A = appropriate; I = inappropriate. Therapy was considered appropriate after susceptibility test results became available if the microorganism(s) were susceptible (on the basis of in vitro testing) to at least one agent administered, whereas therapy was considered appropriate at the earlier time points it if was appropriate for the clinical situation.

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Multivariate Analysis

Based on the results of univariate analysis, high- and low-risk categories were established for each variable assessed. When there was more than one high-risk component for a variable (e.g., microorganism, source, or predisposing factor), these components were grouped and assigned a univariate relative risk for the purpose of multivariate analysis. Then, with use of logistic regression, the relative risk of death was determined for each variable in the presence of all others.

The results of this analysis are shown in table 14. Those variables associated with a significantly increased risk of death in multivariate analysis were advanced age (>70 years); isolation of fungi or Enterobacteriaceae other than *E. coli;* a primary source of infection in the respiratory tract, bowel, or peritoneum or that was unknown; underlying malignancy, AIDS, or renal failure; shock, as manifested by hypotension; inability to mount a febrile response to sepsis; and inappropriate antibiotic therapy at two or more of the time points assessed.

Discussion

It was our hypothesis that the many changes in medicine since the mid-1970s, when two of us and other investigators [10, 11] comprehensively reviewed a large series of patients with bacteremia and fungemia, would lead to substantive changes in the microbiology, epidemiology, and clinical and prognostic significance of positive blood cultures in the 1990s. Indeed, the more aggressive and widespread use of prosthetic materials and intravascular devices, the occurrence of syndromes such as AIDS not known 2 decades ago, and therapeutic advances in imaging, interventional radiology, and antimicrobial therapy virtually ensured the presence of important differences and underscored the need for this update.

In order to best compare the differences and similarities of bacteremia and fungemia in the 1990s versus the mid-1970s, we used definitions, including clinical and diagnostic criteria, that were similar to those in our earlier work [10, 11]. However, we performed this study prospectively, gathering data concurrently on patients with culture-positive blood, to better assess the ways in which physicians used laboratory results for therapeutic decisions.

Laboratory Observations

True septicemia vs. contamination. The observations from this study suggest that contaminants in blood cultures are more frequent in the 1990s than they were 2 decades ago. Of 1,582 positive blood culture episodes in the current study, 656 (41.5%) were judged to represent contamination and another 84 (5.3%) were of indeterminate significance. Thus, only about half of all positive blood cultures represented true bloodstream infection. These findings contrast markedly with the observations in our earlier study, in which approximately one-third of all positive blood cultures represented contamination [10].

There are several possible explanations for these findings. One is the increasing use of central, long-term intravascular catheters (e.g., Hickman and Broviac) and the utilization of these access devices for the purpose of obtaining blood for culture. Access ports from intravascular devices may be more difficult to sterilize than skin at venipuncture sites, thereby resulting in increased contamination rates; at least one study has documented increased contamination rates when blood culture specimens are obtained from central lines [34].

Although physicians may believe they are benefiting their patients by obtaining blood culture specimens from catheters (i.e., saving patients from needlesticks), they actually may be doing a disservice, since culture contaminants (false-positives)

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Table 14. Comparison of univariate and multivariate analysis of factors affecting risk of death in patients with bacteremia and fungemia.

Variable	Univariate high risk	Univariate RR	Multivariate RR
Age	>70 y	1.88	1.80*
Place of acquisition	Hospital	1.39	1.12
Microorganisms	Fungi and Enterobacteriaceae other than *E. coli*	5.13	2.27†
Type of episode	Polymicrobial	2.16	1.55
Source of infection	Respiratory tract, bowel, peritoneum, or unknown	2.56	2.86†
Predisposing factor	Malignancy, AIDS, or renal failure	1.92	1.98†
Blood pressure	Hypotension	2.85	2.29†
Leukocyte count	<4,000/μL or >20,000/μL	1.67	1.24
Absolute neutrophil count	<1,000/μL	1.58	0.65
Body temperature	Absence of fever (<37.9°C)	2.06	2.04†
Antibiotic therapy	Inappropriate at ≥2 time points	2.32	2.72†

* $P < .05$.
† $P < .01$.

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cultures) have been shown to result in longer hospitalizations and increased costs to patients and institutions [35].

A second possible reason for the increased incidence of contaminants is blood culture technique. Although several recent studies have indicated that the current single-needle technique for obtaining blood and inoculating cultures is not associated with increased rates of contamination [14, 36, 37], Spitalnic et al. [38], in a meta-analysis, have suggested otherwise. Alternatively, it may be that in institutions such as ours, in which house officers and medical students obtain the majority of blood culture specimens, failure to apply antiseptic solutions (usually iodophors and alcohol) properly and to let them exert their antimicrobial effect over 1–2 minutes as recommended results in increased contamination.

Possible remedies include use of blood culture teams from the laboratory's phlebotomy service, which seems unlikely in the managed care era, or the development and use of potentially more effective antiseptic skin preparation materials (e.g., 2% iodine tincture) before blood sampling. A final possible explanation for increased rates of contamination of blood cultures could be that newer blood culture systems and media are more sensitive and capable of detecting the few viable skin bacteria that might remain after appropriate antiseptic preparation.

Of the 843 septicemias, a source was confirmed by culture in 294 (34.9%) and by clinical evidence in 282 (33.4%). Of the remaining 267 episodes, at least two blood cultures were positive for the same microorganism in 181 (67.8%; 21.5% of total septicemias). Thus, there was objective evidence of true infection in 757 of the 843 episodes (89.8%), an observation that is remarkably similar to that in our earlier study [10]. This finding is important clinically, since it suggests that, despite increased rates of contamination of blood cultures, in the great majority of instances physicians should be able to determine with some confidence whether a positive blood culture represents significant infection.

Nevertheless, positive blood cultures yielding coagulase-negative staphylococci may present great interpretative difficulties, even when more than one culture set is positive. For example, Zaidi et al. [39] have found that coagulase-negative staphylococci with identical species designations, serotypes, and antibiograms recovered from the blood of infants sometimes represented different strains when the isolates were analyzed by molecular typing techniques. Similarly, even when both of two blood cultures yielded *S. epidermidis* of the same biotype in the current study, we were frequently not certain of the isolates' clinical significance (table 2).

Patterns of positive blood cultures. In our earlier study [10], we noted different patterns of blood culture positivity in patients with endocarditis, those with true septicemia that was not due to endocarditis, and those with contaminant isolates. Similar observations were made in this study. Thus, in patients with endocarditis, a disease characterized by continuous seeding of blood from the infected heart valve, all blood cultures obtained in a series were positive.

By contrast, for patients with septicemia not due to endocarditis, most but not all blood cultures obtained in a series were positive, a finding consistent with the understanding that bloodstream infection in such patients may be short-lived or intermittent (abscesses). For patients whose blood cultures were contaminated, an initial positive culture in a series virtually always was followed by negative cultures. When a subsequent culture was positive, it usually was positive with a different microorganism (e.g., *S. epidermidis* followed by a diphtheroid).

The proportion of patients with polymicrobial septicemia in this study (79 of 843; 9.4%) is consistent with findings in earlier studies, in which frequencies of polymicrobial bacteremia ranged from 6% to 18% [10, 17, 40–43].

Epidemiological Observations

Place of acquisition of septicemia. At our institutions the proportions of episodes that were of community-acquired septicemia and hospital-acquired septicemia were nearly equal (48% vs. 52%). This observation contrasts with the results of our earlier study at the University of Colorado hospitals, in which nearly two-thirds of episodes were nosocomial [10]. The difference may relate not only to patient-population variability [44, 45] but also to changes in health care, particularly shorter lengths of stay in the 1990s than those of 2 decades ago, as well as outpatient surgery and chemotherapy.

In contrast to the relative equivalence of community- and hospital-acquired septicemic episodes overall, there were important differences with regard to individual microorganisms. For example, 91% of pneumococcal bacteremias and all mycobacteremias and cryptococcemias were community-acquired. These observations are consistent with prior reports (on pneumococci) and with our understanding of the epidemiology of infections due to these microorganisms [10, 44, 46]. However, nosocomial pneumococcal bacteremia can occur and may be relatively common in institutions with longer patient stays [47, 48].

Fungemia, enterococcal bacteremia, and coagulase-negative staphylococcal bacteremia disproportionately were nosocomial in origin (table 3). The observations for fungi and enterococci were virtually identical to those in our earlier studies of bacteremia [10] and probably relate to the fact that infection with these microorganisms tend to occur in more debilitated patients. The predominance of hospital-acquired coagulase-negative staphylococcal bacteremia is explained by the current use of long-term indwelling central and peripheral catheters as well as other prosthetic devices, the ubiquity of these bacteria as normal skin flora, and the ability of these relatively avirulent microorganisms to adhere to the surfaces of biomaterials.

P. aeruginosa bacteremia usually occurs as a nosocomial infection. In the current study, *P. aeruginosa* bacteremia was community-acquired in 39.6% of episodes, compared with 17% in our earlier study. The explanation for this difference in the epidemiology of *P. aeruginosa* bacteremia may be related in

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part to the prevalence of HIV infection. In bacteremic patients known to be infected with HIV, *P. aeruginosa* was the third most frequently isolated pathogen, and in seven of 11 episodes in these patients, bacteremia was community-acquired. Several recent reports have documented similar findings in patients with HIV infections [49–51].

Hospital service. The overwhelming majority of bloodstream infections in this series occurred in patients hospitalized on either the medical services (73.6%) or nontransplantation surgical services (21.3%), an observation similar to that in our previous report [10] in which 54.6% of episodes occurred in medical patients and 27.2% of episodes occurred in surgical patients.

The current study also confirmed the rarity of *P. aeruginosa* bacteremia in medical patients (4.4% of episodes), the absence of enterococcal bacteremias in obstetrical and gynecologic patients, the high proportion of fungemias in transplantation patients (23.1% of episodes), and the proportionately increased frequency of anaerobic bacteremia in patients hospitalized on the surgical and gynecologic services (6.6% and 11.1% of episodes, respectively).

Sources of septicemia. Onc of the striking findings in the currcnt scries in comparison with our earlier work [10] was the ascendancy of intravascular catheters as an important source of bloodstream infections. Whereas only 3% of episodes were catheter-related in the previous study, iv catheters were the source of 19% of the episodes in the current series. The increasing importance of intravascular catheters also was noted by Mylotte et al. [47], who examined nosocomial bacteremia between 1979 and 1987; in that study, the proportion of episodes associated with intravascular devices increased from 6% (1979) to 19% (1987). During a similar time period, the proportion of bloodstream infections due to intravascular devices at a university hospital in Berlin was consistently ~16% [19].

The inability to determine the focus of bacteremia and fungemia remains a vexing problem. Despite substantial advances in diagnostic imaging over the past 2 decades, 26% of the septicemic episodes in this series, compared with 31% in our earlier study [10], had no discernible focus. Leibovici and colleagues [20] noted similar results; 23% of episodes during 1988 and 1989 at their university hospital in Israel were of unknown origin.

Since episodes with unknown foci are associated with increased mortality ([11, 20] and present study), improved methods for determining the primary site of infection in septicemic patients clearly are needed. Microorganisms from unknown foci commonly are assumed to have a gut mucosal source. The organisms associated highly with an unknown source in this study (e.g., *E. cloacae, K. pneumoniae, Candida* species, *T. glabrata,* viridans streptococci, and *M. avium* complex) support this hypothesis.

When we examined the sources of septicemia according to each microorganism or microorganism group (table 5), there were several noteworthy observations. For example, in the years since our previous study, the proportion of *S. aureus* bacteremias associated with intravascular catheters has nearly doubled, from 20% to 35%. Respiratory and skin sources remained important primary foci for staphylococcal bacteremia. The recent report by Roberts and colleagues [18] confirmed the importance of intravascular and pulmonary foci for staphylococcal bacteremia. In addition, in the current study and in the report by Roberts et al. [18], respiratory foci for klebsiella bacteremia were considerably less prominent than we observed previously [10]; intraabdominal and genitourinary sources now predominate. In contrast to the findings of Roberts et al., who found enterococcal bacteremia most commonly to have wound sources [18], our patients most often had genitourinary tract foci.

Epidemiology of septicemia in neutropenic patients. The differences in the microbiology of bacteremia and fungemia in neutropenic patients compared with nonneutropenic patients (table 6) stand in contrast with the observations in our earlier report [10]. In the present series bacteremia due to *S. aureus* was significantly less common and fungemia significantly more common in neutropenic than nonneutropenic patients, whereas there were no such differences noted in the previous study. However, in both series, polymicrobial episodes were more frequent in granulocytopenic patients.

A study of bacteremia and fungemia in granulocytopenic patients during 1985 and 1986 at the University of Colorado Health Sciences Center [52], which was the site of our earlier study, showed both similarities to and differences from the distributions of microorganisms in the 1975–1977 review [10] and the current one. For example, in the study by Ehni et al. [52], fungemias were proportionately less common (2%, vs. 11% [10] and 12% [current study]) and *P. aeruginosa* bacteremias were more common (27%, vs. 9% [10] and 7% [current study]). However, the proportionate frequency of bacteremias due to Enterobacteriaceae was similar in all three studies.

In the study by Ehni and colleagues [52] and the present report, bacteremia due to *S. aureus* accounted for ~5% of episodes in neutropenic patients, whereas in the 1975–1977 review [10], 13% of episodes in neutropenic patients were caused by *S. aureus.* Finally, the increasing importance of bacteremia due to coagulase-negative staphylococci in neutropenic patients was evident in the study of Ehni et al. [52] and in the current one (14% and 8% of episodes in neutropenic patients, respectively). In our earlier review, coagulase-negative staphylococcal bacteremia was sufficiently uncommon in granulocytopenic patients that it did not merit mention [10].

A possible explanation for the higher rates of fungemia currently includes the extensive use of more effective antipseudomonal β-lactam drugs such as piperacillin, ceftazidime, and imipenem. Although their early and empirical use may decrease mortality owing to *P. aeruginosa* infection, their prolonged pressure on normal gut flora is associated with overgrowth of yeasts and increased risk of subsequent fungemia [53]. The relative importance of coagulase-negative staphylococci presently probably relates to the common and prolonged use of

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central iv catheters and the resistance of this group of organisms to commonly used antimicrobial agents.

Epidemiology of septicemia in hypotensive patients. Septic shock most frequently has been associated with gram-negative bacteremia. Indeed, in our earlier review [10], aerobic or facultative gram-negative rods accounted for 53% of the isolates from hypotensive patients. In the current series, however, whereas we observed that aerobic or facultative gram-negative rods continued to be common etiologic agents of septic shock, they were isolated less frequently than in the past (43% of isolates). *S. aureus* was detected twice as frequently in hypotensive patients in the current series (16%, vs. 7% in the earlier series), and anaerobic bacteria were detected substantially less often in hypotensive patients (4%, vs. 11% in the earlier series). In both series, hypotensive patients were twice as likely as normotensive patients to have polymicrobial bacteremia ([10] and table 7).

Clinical and Prognostic Observations

Our observations suggest that the mortality associated with bacteremia and fungemia appears to have decreased during the past 2 decades. However, this conclusion may not be applicable widely and should be interpreted with caution. Indeed, the differences in patient population as well as the prospective nature of the current study vs. our retrospective earlier review [11] limited the ability to make direct comparisons with the previous work. Nonetheless, mortality attributable to septicemia in this study was markedly less than in the 1975–1977 study (17.5% vs. 31%, respectively). Moreover, Geerdes et al. [19] recently reported that between 1979 and 1989, mortality from septicemia at a university hospital in Berlin decreased from 34% to 21%.

Crude mortality has varied substantially in recent reports of bacteremic patients, ranging from 16% at a Swedish university hospital from 1973 to 1980 [54] to >40% among patients with nosocomial bacteremia from 1981 to 1983 at a university hospital in the United States [55] and with gram-negative bacteremia at a Turkish university hospital from 1983–1989 [21]. By comparison, crude mortality among septicemic patients at the University of Colorado during 1975–1977 was 42% [11], vs. 22.5% in this study (patients were followed for a maximum of 30 days after detection of bacteremia). Most comparable to our data are the observations of Roberts and colleagues, who recently reported a 30-day mortality of 27% among bacteremic patients studied during 1984–1987 in western Canada [18].

Age and sex. Numerous reports have emphasized the importance of advanced age as an unfavorable prognostic factor in septicemic patients [11, 15, 18, 21, 54, 55]. In contrast to our earlier data, which showed a statistically significant increase in mortality due to septicemia after age 40 years [11], in this series significantly increased mortality occurred after age 70 years. No differences in mortality according to sex were evident in this study or in a recent report from a Swedish university hospital [54].

Place of acquisition of bacteremia and fungemia. Nosocomial septicemias historically have been associated with substantially higher mortality than community-acquired septicemias [9, 11, 44]. In the current series and in another recent report [21], however, the evidence suggests that the increase in mortality associated with hospital-acquired bacteremia and fungemia may be less dramatic than reported in the past. Uzun et al. [21] noted crude mortality of 46% in episodes of nosocomial bacteremia vs. 37% in those of community-acquired bacteremia. In this series, associated mortality due to nosocomial septicemia was 20.3%, vs. 14.6% due to community-acquired septicemia.

Microorganisms. Many studies have looked at the mortality rates with bloodstream infections due to individual microorganisms; some have focused only on certain patient populations. Unfortunately, definitions of mortality in the various reports have not been uniform: some have evaluated total (or crude) mortality, others have evaluated only septic deaths (those judged to be directly related to septicemia), and still others have addressed mortality judged directly or indirectly attributable to septicemia. Furthermore, not all studies have indicated clearly whether mortality rates have been calculated on the basis of unimicrobial episodes, thereby excluding the confounding variable of concomitant bacteremia with other microorganisms. These differences make direct comparisons of mortality in other reports problematic, and the comments that follow should be interpreted accordingly.

The lower mortality overall from bacteremia in this series compared with that noted in our earlier work [11] was reflected in the mortality rates associated with individual microorganisms or groups thereof (table 8). Several comparisons and contrasts with regard to etiologic microorganisms deserve emphasis.

Fungemia, which was associated with more than a sixfold increased risk of death in the earlier series [11], also carried a sixfold increased relative risk of death in the present study (table 8). Overall mortality associated with fungemia, however, was lower in the current series than in our earlier report [11], and the associated mortality in this series was somewhat less (36%) than that due to candida and torulopsis fungemias (44%) in Detroit in the mid-1980s [56].

Among episodes of polymicrobial septicemia, for which the directly related mortality was 35% in the earlier series [11], the associated mortality in this series was 34% and the risk of death was significantly increased compared with that in unimicrobial episodes. The mortality associated with polymicrobial bacteremia in the recent report by Cooper et al. [17] was remarkably similar to the observations in our earlier and current series.

In our earlier review, the mortality directly related to pneumococcal bacteremia was 15% (crude mortality, 22%), vs. 17.6% associated mortality in this series. Data from other recent reports are consistent with these findings [57, 58]. These data

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provide impressive evidence that there has been little change in the outcome of *Streptococcus pneumoniae* bacteremia since the classic studies of Austrian and Gold >3 decades ago [59].

By contrast, the dramatically increased risk of death from bacteremia due to *P. aeruginosa* in our earlier report (RR, 6.84) was moderated in this study (RR, 3.04). The mortality associated with pseudomonas bacteremia was 16.7%, compared with 36% for deaths directly due to bacteremia in the earlier review [11]. Two studies examining pseudomonas bacteremia during the early 1980s revealed case fatality rates attributable to sepsis of 41% and 48% [60, 61]. Thus, our data suggest the possibility that the outcome of bacteremia due to *P. aeruginosa* may have improved over the past decade.

Mortality from bacteremia due to gram-positive organisms also was lower in the current study than in the prior review [11]. In the case of *S. aureus,* septicemia-associated mortality in the current series was 11.9%, compared with crude mortality of 33% and directly related mortality of 9% in the earlier series. By comparison, in the recent report from Lautenschlager et al. [62] encompassing the years 1980–1986 in Basel, Switzerland, total mortality was 34% and directly related mortality was 20%.

Coagulase-negative staphylococcal bacteremia had the lowest attributable mortality of all microorganism groups in the current study (5.5%); case-fatality rates were somewhat higher during the mid-1980s: 13.6% at the University of Iowa Hospital [63] and 18% at a large hospital in Spain [64]. The mortality associated with enterococcal bacteremia was 13% in this series, considerably lower than the crude or directly related mortality (45% and 27%, respectively) in our earlier series [11], despite the presence of vancomycin-resistant enterococci at both RWJUH and DUMC during the current study period. By comparison, reports based on data from the 1980s have described case fatality rates associated with enterococcal bacteremia varying from 12% to 51% [65–67].

Several studies have recently provided data on the outcome of bacteremia due to members of the family Enterobacteriaceae. Mortality due to *E. coli* bacteremia appears to be lower now than 2 decades ago. In our earlier report [11], 41% of patients died of causes directly related to bacteremia, compared with an associated mortality of 10.3% in this study.

Grandsen et al. [68] prospectively evaluated *E. coli* bacteremia in London from 1969 through 1987 and noted a case-fatality rate of 20.7%; approximately half the deaths were judged to be directly related to sepsis. Similarly, the recent review by Roberts and colleagues [18] noted that the 30-day mortality due to *E. coli* bacteremia was 21.5%. Mortality associated with *K. pneumoniae* bacteremia has ranged from 14.6% in the current study to 37% (crude mortality) in another recent report [69]. Korvick et al. [70] reported 19% mortality at 14 days in a recent multicenter study of 230 patients with klebsiella bacteremia.

Mortality associated with serratia bacteremia was 30% among our patients; by contrast, Saito and colleagues [71] reported a mortality rate of 23% in cancer patients between 1982 and 1987. In the present series, associated mortality among 12 patients with *E. cloacae* bacteremia was 8.3%, compared with crude mortality of 24% in a recent multicenter study of 129 patients with enterobacter (all species) bacteremia [72]. The attributable mortality between 1980 and 1992 among patients with *Proteus mirabilis* bacteremia was 25.6% in a recent report [73], remarkably similar to the bacteremia-associated mortality of 23.1% in this series.

Source of infection. As in our earlier study [11], the mortality associated with bacteremia was increased when the primary focus of infection was either unknown or at a site that was difficult to treat, such as the respiratory tract or the bowel and peritoneum. Similarly, when the primary focus of infection could be removed or drained easily (e.g., the genitourinary tract), the mortality was reduced (table 9). The higher mortality in septicemia with an unknown primary focus of infection also has been noted by others [19–21].

Body temperature. The current study confirmed the observations made in our earlier report [11], namely, that the inability of a patient to mount a febrile response to septicemia is a poor prognostic sign (figure 2). This relationship has been noted by others [9, 74, 75] but could not be confirmed in a study designed to examine independent predictors of mortality associated with bloodstream infections [55]. Kluger [76] and Roberts [77] have each recently presented information to support the premise that the presence of physiologically elevated body temperature is beneficial.

Blood pressure. The well-known association between hypotension as a marker for septic shock and poor outcome was again confirmed during this study. This association was noted not only in prior studies [9, 11, 74] but also in more recent reports [18–21]. Compared with data in our earlier review [11], the incremental risk of death when hypotension was present was greater in the current series than was noted previously (RR, 2.8 vs. 2.0).

Total leukocyte count and absolute neutrophil count. Infection-associated mortality and relative risk of death from bacteremia were increased among patients with leukopenia and absolute granulocytopenia, as in our earlier study [11]. In addition, in this study mortality was increased also among patients with total leukocyte counts $\geq 20{,}000/\mu L$. Recent studies in varied patient groups have provided similar observations [17, 60].

Predisposing factors. For consistency and to enable accurate comparisons of risk associated with various underlying conditions that may affect mortality among patients with bacteremia and fungemia, we used the same criteria and definitions as in our earlier review [11] and included HIV infection and AIDS, neither of which were known at the time the earlier study was undertaken. Moreover, the risk associated with each factor was judged when that condition was the only one present (table 12).

As in the earlier study [11], increased risk of death in bacteremia was associated with the presence of malignancies and

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biopsy-proven hepatic cirrhosis. In contrast with our earlier observations, the presence of moderate renal failure (serum creatinine level, 2.0–5.0 mg/dL) but not severe renal failure (serum creatinine level, >5 mg/dL) was associated with increased mortality among bacteremic patients.

Although this observation may seem paradoxical, we interpret the results to suggest that patients with chronic renal failure probably were undergoing dialysis and therefore had stable albeit poor renal function, whereas those with moderate renal failure were more likely to have acute deterioration of function and greater metabolic instability which, in turn, was associated with a greater likelihood of a poor outcome. Finally, the presence of AIDS was associated with an increased risk of death associated with bacteremia or fungemia.

Antibiotic and other therapy. Intuitively, one would expect that administration of antimicrobial agents active in vitro against the infecting microorganism(s) would be associated with improved prognosis. Our prior study and others [11, 78, 79] have supported this assumption, and the current study again confirmed the principle (table 13). By assessing therapy at several different time points, we hoped to determine that degree to which appropriate treatment affected outcome at each stage.

One might have expected, for example, that appropriate therapy given early (empirical therapy time point) would be associated with lower attributable mortality than would appropriate therapy delayed until after susceptibility test results were available to the physician. Indeed, this was the case. As is evident in table 13, the lowest attributable mortality occurred among those patients who received appropriate therapy throughout the course of their septicemic episodes (10.4%). Prompt initiation of appropriate therapy by physicians after notification of a positive blood culture also was associated with low mortality (13.3%). If appropriate therapy was not initiated until after susceptibility test results were available, mortality was 25.8%.

Why 60 (7.6%) of 791 septicemic patients received inappropriate therapy even after the identification and antibiotic susceptibilities of infecting microorganisms were reported is uncertain (table 13). Antibiotic misuse has been studied by others. In one report [80], the most common form of misuse in bacteremic patients was the administration of superfluous agents, a finding that corroborates our observations. In another study [81], multivariate analysis showed that four clinical variables (i.e., nosocomial bacteremia, recent prior antibiotic therapy, nursing home residence, and central iv catheters) and four microorganisms (i.e., *Candida, Acinetobacter, Enterococcus,* and *Pseudomonas* species) were independently associated with inappropriate antimicrobial therapy. Our data also showed that the use of inappropriate therapy was more likely to occur on the surgical services.

A fundamental principle in the management of bloodstream infections has always been that eradication of the primary source of infection is a necessary component of the therapeutic regimen. Thus, removal, drainage, or excision of an infected focus, when possible, should result in an improved prognosis. Both the current study and our prior report [11] provide support for this principle. Indeed, in the current study, infection-associated mortality among patients who had a primary focus that was excised, drained, or removed was less than one-third that among patients who did not have these interventions (6.2% vs. 22.0%, respectively).

Multivariate Analysis of Factors Influencing Prognosis

As in the earlier review by our group [11], we subjected each of the variables that were associated with an increased risk of death in univariate analyses to multivariate analysis (table 14). In the earlier report, seven variables were independently associated with an increased risk of death; all but one were confirmed in the current study. These included advanced age, microorganism, source of infection, predisposing factors, hypotension, and absence of fever. Nosocomial acquisition of bacteremia was not an independent predictor of death in the current study, in contrast to the observations in the earlier report.

In our earlier report we were unable to include antimicrobial therapy in the multivariate analysis. Inclusion of therapy was possible in this study and confirmed the importance of administering appropriate antimicrobial agents.

Although advanced age again was an independent predictor of poor prognosis, the increased risk statistically was greatest after age 70 years in the current study, compared with age >40 years in the earlier series. Septicemia caused by a high-risk microorganism also was again an independent risk factor in multivariate analysis, but there were some changes in the individual microorganisms associated with a high risk of death. In the earlier report there was increased risk with gram-negative rods generally, whereas in the current study increased risk was observed only with Enterobacteriaceae other than *E. coli.*

The reasons for this difference are not readily apparent. Speculation might focus on greater resistance to antimicrobial agents among these strains than among *E. coli.* In contrast to the results of the earlier series, enterococcal bacteremia was not associated with increased risk in the current study. However, fungemia was confirmed to be associated with poor prognosis, in concordance with our earlier observations.

Primary foci of infection in the respiratory tract, bowel, or peritoneum and septicemia from an unknown source again were shown to be independent predictors of poor prognosis. However, primary foci in abscesses, skin, and surgical wounds, each of which was associated with an increased risk of death in the earlier series, were not associated independently with increased risk in the present study.

As in the earlier study, the presence of underlying diseases associated with high risk in univariate analysis was an independent predictor of increased mortality in the multivariate analysis. The underlying diseases associated with high risk were somewhat different from those in the earlier report and included AIDS, a syndrome that was unknown at the time of the earlier

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review; renal failure, which was not a high-risk factor in the prior study; and malignancies, which were high-risk factors in the earlier study.

Comparative Features of Bacteremia and Fungemia in the 1970s and 1990s

During the past 20 years, numerous changes have occurred in medicine and health care. Nevertheless, several fundamental aspects of bloodstream infections have remained constant. Major examples include the continued frequency with which *S. aureus* and *E. coli* are causative agents of bacteremia; the importance of the respiratory tract, genitourinary tract, and bowel as primary foci; the association between gram-negative or polymicrobial bacteremia and septic shock; and the importance of advanced age, difficult-to-eradicate or unknown sources, malignancies and renal failure, hypotension, and absence of fever as independent predictors of a poor outcome (table 15).

The differences noted in the 1990s provide cause for concern but perhaps also for optimism (table 15). The increased proportion of blood isolates representing contamination is of concern, especially in an environment that mandates cost-effective care. The frequency of coagulase-negative staphylococcal isolation particularly is problematic, since it often is difficult for clinicians to determine the clinical significance of these bacteria. The decrease in anaerobic bacteremia and proportionate increase in fungemia have prompted some authorities to recommend changes in routine blood culture techniques [82].

Table 15. Major similarities and differences in positive blood cultures, 1975–1977 [10, 11] and 1992–1993.

Similarities	• *Staphylococcus aureus* and *Escherichia coli* most frequent etiologic agents
	• Importance of respiratory tract, genitourinary tract, and bowel as primary foci
	• Association of gram-negative and polymicrobial bacteremia with septic shock
	• Importance of age, source of infection, predisposing factors, hypotension, and absence of fever as independent predictors of poor outcome
Differences	• Increased importance of iv catheters as source of septicemia
	• Increased proportion of isolates representing contamination
	• Increased isolation of coagulase-negative staphylococci, both as contaminants and as pathogens
	• Increased frequency of *Pseudomonas aeruginosa* as a community-acquired pathogen
	• Emergence of *M. avium* complex as cause of bloodstream infection in HIV-infected patients
	• Proportionate increase in fungemia and decrease in anaerobic bacteremia
	• Decreased mortality

The most frequent source of bloodstream infections has become the intravenous catheter, and it may be expected that prosthetic materials and devices will continue to be important sources of infection. HIV infection and AIDS have allowed *M. avium* complex to become a bloodstream pathogen, and the increased frequency of community-acquired *P. aeruginosa* bacteremia also seems to be associated with HIV-infected patients [49–51].

The most optimistic finding with regard to bacteremia and fungemia in the 1990s is that mortality associated with these serious infections has decreased. The reasons for this improved outcome are not fully explained but could be related to earlier detection with use of modern blood culture systems; more sophisticated imaging methods that better elucidate primary foci of infection; the frequency of infections emanating from easily removed (iv catheters) or drained (genitourinary tract) foci; and improved antimicrobial agents and use thereof by clinicians.

Although we have shown that mortality is lower than it was 2 decades ago, bacteremia and fungemia remain serious syndromes with substantial risk. Moreover, the combination of an aging population, improved survival among immunocompromised patients and those with organ transplants, and the emergence of β-lactam-drug-resistant gram-positive and gram-negative bacteria as well as vancomycin-resistant enterococci (and possibly staphylococci in the future) [83], will continue to challenge all who care for patients with bloodstream infections.

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The scope of the claims open ----

(57) [Claims]
[Claim 1]
A blood sample optimization system, a blood
collection system,
a patient configured for venipuncture of a patient to allow withdrawal of a patient blood sample. a needle,
a blood collection path connected to said patient needle and configured to carry said blood sample, and a
sample configured to receive an evacuated blood collection tube for collecting and contain

g a subsequent portion of said blood sample. a blood isolation
device
connected along the blood collection path between the patient needle and the sample needl e, the inlet port
configured to receive the blood sample
; An isolation chamber connected to the inlet port and having a vent including an air perme able blood barrier for receiving said initial volume of blood sample and isolating at least a first portion of said initial volume of blood sample. a configured isolation chamber and a samplin g flow path having a proximal end connected to the inlet port and configured to receive a s ubsequent portion of the blood sample; the passageway and the inlet port are connected to th e blood sample

bypassing the isolation chamber and a first portion of the blood sample isolated in the isolatio n chamber and connecting the subsequent portion of the blood sample to the distal end of the sampling channel. an outlet port configured to direct a subsequent portion of the blood sampl e into the evacuated blood collection tube, the inlet port, the outlet port, the isolation chambe r and
the
blood sample optimization system, further comprising a housing containing and defining a sa mpling flow path; and a blood isolation device .
2.
The isolation chamber of the blood isolation device is at ambient air pressure, and wherein t he isolation chamber receives a first portion of the blood sample by patient blood pressure ov ercoming the ambient air pressure within the isolation chamber. 2. The blood sample optimiza tion system of claim 1. 3. The blood of claim 2, wherein said sample needle includes a seal p ierced by said evacuated blood collection tube to open access to said patient needle via said bl ood collection path and said sampling flow path
.
Sample optimization system.
4. The
blood isolation device of claim 3, wherein said sampling channel of said blood isolation devic e permits a subsequent portion of said blood sample to enter said inlet port under vacuum pre ssure by said evacuated blood collection tube opening said sample needle. blood sample opti mization system.
5.
The blood sample optimization system of claim 1, wherein said air permeable blood barrier o f said blood isolation device comprises an air permeable material that seals upon contact wit

blood.

[Claim 6]

3. The blood sample optimization system of Claim 1, wherein the blood collection path of the blood collection system comprises a tube.

7. A

patient needle configured to enable removal of a blood sample from a patient and a sealed s ample needle, wherein the sample needle is unsealed and the blood sample adapted to be re moved from the patient. a blood isolation device connected to a blood collection system comp rising a sample needle adapted to receive an evacuated blood collection tube

for receiving a blood sample from a patient connected to said patient needle; an isolation ch amber having a configured inlet port,

an outlet port connected to the inlet port, and

a vent connected to the inlet port and including an air permeable blood barrier, wherein the sample needle is connected to the vacuum an isolation chamber configured to receive and isol ate a first portion of the blood sample before it is opened by a blood vessel; and a proximal e nd connected to the inlet port for receiving subsequent portions of the blood sample

. a sampling channel configured to receive said isolation chamber

,

said sampling channel and said inlet port are adapted to receive said blood sample with subs equent portions of said blood sample isolated within said isolation chamber and said isolation chamber. and to direct subsequent portions of the blood sample to the outlet port connected t o the distal end of the sampling channel, said inlet port, said outlet

port , a blood isolation device, further comprising a housing containing and defining said isol ation chamber and said sampling channel.

[Claim 8]

8. The blood isolation device of claim 7, wherein the isolation chamber is at ambient air pres sure and the isolation chamber receives an initial portion of the blood sample by patient blood pressure overcoming the ambient air pressure within the isolation chamber.

[Claim 9]

8. The blood isolation device of Claim 7, wherein the air permeable blood barrier comprises a n air permeable material that seals upon contact with blood.

10.

The blood isolation device of claim 7, wherein said isolation chamber includes an isolation ch annel defined within said housing.

11.

A blood sample optimization system, a blood

collection system, comprising:

a patient needle configured for venipuncture of a patient to enable withdrawal of a patient blood sample; and a patient

needle connected to the patient needle. a blood collection system comprising: a blood colle ction path configured to carry said blood sample; and a sample needle

configured to receive an evacuated blood collection tube for withdrawing and containing a s ubsequent portion of said blood sample; A blood isolation device connected along the blood co llection path between a patient needle and the sample needle, the inlet port configured to rec eive the blood sample, and a sample needle of the inlet port and the blood collection syste m . and an isolation chamber having a vent connected to the inlet port and including an air permeable blood barrier for receiving the initial volume of the blood sample and for removi ng the initial volume of the blood sample. an isolation chamber configured to isolate at least a first portion ;

a sampling channel having a proximal end connected to said inlet port and configured to re ceive a subsequent portion of said blood sample, said isolation chamber, said sampling channe l and said inlet port being connected to said blood
sample

; allowing a subsequent portion of the blood sample to bypass the isolation chamber and a first portion of the blood sample isolated within the isolation chamber and directing the subse quent portion of the blood sample to a distal end of the sampling channel; and a blood isolatio n device configured to direct the outlet port connected to a

blood vessel and further comprising a housing containing and defining the inlet port, the ou tlet port, the isolation chamber and the sampling flow path.
Sample optimization system.
12.
The isolation chamber of the blood isolation device is at ambient air pressure, and wherein t he isolation chamber receives a first portion of the blood sample by patient blood pressure ov ercoming the ambient air pressure within the isolation chamber. 12. The blood sample optimiz ation system according to 11.
13.
The blood sample optimization system of claim 11, wherein said sample needle includes a se al pierced by said evacuated blood collection tube to open access to said patient needle via sai d blood collection pathway.
14.
The blood sample optimization system of claim 11, wherein said air permeable blood barrier of said blood isolation device comprises an air permeable material that seals upon contact wit h blood.

15.

The blood sample optimization system of claim 11, wherein said isolation chamber includes a n isolation flow path defined within said housing.

[Claim 16]

12. The blood sample optimization system of Claim 11, wherein the blood collection path of t he blood collection system includes a tube.

detailed description open —

[Detailed description of the invention]

[Background art]

CROSS

-REFERENCE TO RELATED APPLICATIONS

This application is based on US Nonprovisional Application Serial No. 15/140,443, entitled "B lood Sample Optimization System and Blood Contaminant Isolation Apparatus and Method," fil ed April 27, 2016. and U.S. nonprovisional application Ser. and both of these U.S. nonprovisio nal applications are U.S. Provisional Patent Application Serial No. 62/196,797, entitled "Blood Culture Improvement Systems and Methods," filed on Jul. 24, 2015, dated Oct. 7, 2015; U.S. Provisional Application No. 62/238,636, entitled "Blood Isolation System for Clean Blood Colle ction," filed on April 4, 2016, and "Blood Sample Optimization System and Blood Contaminant Isolation Device and No. 62/318,194 entitled "Methods", the disclosure of which is hereby inc orporated by reference in its entirety.

Bacteremia

is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteremia wit h clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bactere mia and sepsis are associated with high mortality, hospitalization incidence and length of stay and associated costs. Many bacteremia, sepsis, fungemia, and other pathogens do occur withi n hospitals or other medical facilities, and catheters and venipunctures are sources of contami nation as potential carriers of these pathogens.

[0003]

Blood cultures are the standard test used to detect microbial pathogens associated with bact eremia and sepsis in the blood of patients. The term blood culture refers to a single venipunct ure from a peripheral site or central or arterial line in which blood is inoculated into one or mo re blood culture bottles or vessels. One bottle is considered one blood culture and two or mor e are considered a set. Multiple sets are obtained from multiple venipunctures and are associa ted with different sites in the patient.

[0004]

Although these methods enable microbial identification and susceptibility testing, which are important factors in the management of sepsis, their lack of rapid results and low sensitivity to nasty pathogens pose challenges for improvement. This has led to the development of refined systems and adjunctive molecular or proteomics tests.

[0005]

The collection of blood samples for blood culture is an important component of modern patient care, both positively impacting patient outcome by providing an accurate diagnosis and eliminating unnecessary antimicrobial therapy. It can also adversely affect outcomes by prolonging morbidity, lengthening hospital stays, and increasing costs.

One

consequence of blood culture collection is contamination. Contamination of blood cultures can lead to false positive culture results and/or significantly increased healthcare-related costs. Sources of blood culture contamination include inadequate skin disinfection, inadequate collection tube disinfection, and contamination of the initial blood draw, which can skew results.

[0007]

Blood culture collection kits generally include "butterfly" sets, infusion sets, or other types of venipuncture devices provided by companies such as BD, Smith, and B.Brown, as well as aerobic and anaerobic blood culture bottles. Consists of a bottle and A variety of different bottles are also available depending on inspection requirements. These bottles are specially designed to optimize the collection of both aerobic and anaerobic organisms. In conventional kits, the bottle used is commonly known as a "vacutainer", which is used to create a vacuum inside the tube to facilitate the collection of a predetermined amount of liquid, such as blood. A blood collection tube formed from a sterile glass or plastic tube with a lid that is evacuated to a vacuum.

[0008]

False positive blood cultures are generally the result of poor sampling techniques. They cause antibiotics to be used when they are not needed, increasing hospital costs and patient anxiety. Blood cultures are taken from a needle prick into the skin, after which a Vacutainer® is attached to take a sample of blood. Contamination can result from improper or incomplete disinfection of the puncture site and the surrounding skin area. It can also result from the piercing of the skin by the needle during insertion, which draws pierced skin cells and associated contaminants into the sample.

[0009]

Blood flow through a hypodermic needle is laminar, which causes a flow velocity gradient across the flow tube when a pressure drop is applied across the hypodermic needle. Strong aspiration of blood or use of a very small hypodermic needle can cause lysis and release of potassium from red blood cells, thereby making the blood sample abnormal.

[0010]

In another example, some patients have delicate veins that are subject to pressure drops or vacuums, such as those exerted by the plunger of a syringe that is withdrawn too rapidly, esp ecially for the patient's condition. can collapse under Such venous collapse is dangerous and v ery difficult to control because such a condition cannot be known in advance. Various strateg ies have been implemented to reduce the contamination rate of blood cultures, such as staff t raining in sterile collection techniques, feedback on contamination rates, and the introduction of blood culture collection kits

.

Skin antisepsis can reduce contamination concerns, but more than 20% of skin microbes are l ocated deep in the dermis and are not affected by antisepsis. Changing needles prior to bottle inoculation is not recommended as it increases the risk of needlestick injuries without reducin g contamination rates.

[0012]

Some conventional systems and techniques for reducing contamination of blood cultures inv olve discarding the initial aliquot of blood drawn from central venous catheters, venous punctu res and other vascular access systems. However, these systems either require the user to me chanically manipulate the intravascular device or require a complex series of steps that are dif ficult to ensure.

SUMMARY OF THE INVENTION

[

0013]

The present specification presents systems and methods for reducing blood culture contamin ation, cell lysis, and venous collapse. In some implementations, the systems and methods can eliminate variability in user disinfection and also eliminate the risk of skin cells entering blood culture samples. The systems and methods disclosed herein potentially indicate when to attac h a Vacutainer® or other blood collection device (i.e., a syringe) to obtain a contaminant-free blood sample. , does not require changes to existing clinical processes. In some implementat ions of the systems and methods disclosed herein, blood sampling is accomplished passively t hrough the use of the patient's own blood pressure, thereby reducing the risk of venous collap se and reducing current practice

.

eliminates further user steps beyond The system and method can be adapted to suit short-pat h direct puncture or butterfly venipuncture systems. It can also be used with samples taken t hrough a catheter. Means

for Solving the Problems

In one aspect, a blood isolation device is presented. A blood isolation device includes an inlet port and an outlet port. The blood isolation device further includes an isolation chamber conne cted to the inlet port, the isolation chamber having a vent including an air permeable blood b

rrier. The blood isolation device has a proximal end connected with the inlet port and a distal e nd connected with the outlet port, a sampling channel
further includes

[0016]

In another aspect, a blood isolation device is described that is connected to a blood collectio n path. The blood collection path has a patient needle and a sample collection device. The blo od isolation device includes an entry port connected to the patient needle and an isolation cha mber connected to the entry port, the isolation chamber having a vent including an air perme able blood barrier. The blood isolation device further includes a sampling channel having a pro ximal end connected to the inlet port, and an outlet port connected to the distal end of the sa mpling channel and the sample collection device.

[0017]

In yet another aspect, a blood isolation device is described that interfaces with a blood collec tion system. The blood collection system includes a patient needle for allowing a blood sample to be drawn from a patient and a sample needle that is sealed and adapted to receive an evac uated blood collection tube. A blood isolation device includes an inlet port connected to a patie nt needle for receiving a blood sample from a patient. A blood isolation device is an isolation c hamber connected to an inlet port and having a vent containing an air permeable blood barrie r for receiving and receiving an initial portion of a blood sample before the sample needle is o pened by an evacuated blood collection tube. Further includes an isolating isolation chamber. The blood isolation device further includes a sampling channel having a proximal end connect ed to the inlet port for carrying a subsequent portion of the blood sample when the sample ne edle is opened by the evacuated blood collection tube. The blood isolation device further inclu des an exit port connected with the distal end of the sampling channel for carrying subsequen t portions of the blood sample to the sample needle.

[0018]

In yet another aspect, a blood sample optimization system is disclosed and described. The bl ood sample optimization system includes a blood collection system for enabling and obtaining one or more samples of a patient's blood and false positive identification of pathogens in the p atient's blood that may have been contaminated by the venipuncture process. a blood isolatio n device for receiving and isolating an initial portion of one or more samples of the patient's bl ood that may result in

A

blood collection system includes a patient needle configured for venipuncture of a patient to enable withdrawal of a sample of the patient's blood, a blood collection channel connected to t he patient needle for carrying the blood sample, and a blood sample. and a sample needle co nfigured to receive an evacuated blood collection container for collecting and containing a sub sequent portion of the blood sample.

[0020]

In yet another aspect, a blood isolation device is disclosed and described. In some implementations, a blood isolation device can include an inlet port, an outlet port connected to the inlet port, and an isolation chamber connected to the inlet port. The isolation chamber can have a vent containing an air permeable blood barrier.

[0021]

A blood isolation device is connected along the blood collection path between the patient needle and the sample needle and includes an entry port for receiving the blood sample. A blood isolation device is an isolation chamber connected with an inlet port for receiving an initial volume of blood sample and includes an air permeable blood barrier to isolate at least a first portion of the initial volume of blood sample. Further includes an isolation chamber having a vent. The blood isolation device is a sampling channel having a proximal end connected with the inlet port, the isolation chamber isolating at least a first portion of a first volume of blood sample and a subsequent volume of blood sample into the evacuated blood collection container. It further includes a sampling channel that carries to. The blood isolation device further includes an outlet port connected to the distal end of the sampling channel for outputting a subsequent volume of the blood sample. The details of one or more embodiments are set forth in the accompanying drawings and the description below

.

Other features and advantages will be apparent from the specification and drawings, and from the claims.

[Brief description of the drawing]

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

1 shows a blood sample optimization system; FIG.

FIG. 2 shows a blood sample optimization system according to an alternative implementation;

FIG. 3 shows a blood sample optimization system according to another alternative implementation;

FIG. 4 shows a blood sample optimization system according to another alternative implementation;

FIG. 5 shows a blood sample optimization system according to another alternative implementation;

FIG. 6 shows a blood sample optimization system according to an alternative implementation;

FIG. 7 is a flowchart of a method for optimizing blood culture quality;

FIG. 8A illustrates a blood isolation system for non-contaminated blood collection, according to some implementations;

FIG. 8B illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 8C illustrates a blood isolation system for clean blood collection, according to some imp

mentations;

FIG. 8D illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 8E illustrates a blood isolation system for clean blood collection, according to some implementations.

FIG. 9 shows a path splitter for use in a blood sequestration system;

FIG. 10A shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10B shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10C shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 10D shows a blood isolation system for non-contaminated blood collection according to an alternative implementation;

FIG. 11A shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11B shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11C shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11D shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

FIG. 11E shows a blood isolation system for non-contaminated blood collection according to another alternative implementation;

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

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

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

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

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

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

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

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

mplementation.

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

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

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

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

FIG. 14E further illustrates a blood collection system that isolates contaminants of an initial ali quot or sample to reduce false positives in blood cultures or tests performed on patient blood samples.

Show another implementation.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Figure 17E shows a lower member of a housing for a blood isolation device;
Figure 18A shows a top member of a housing for a blood isolation device;
Figure 18B shows a top member of a housing for a blood isolation device;
Figure 18C shows a top member of a housing for a blood isolation device;
Figure 18D shows a top member of a housing for a blood isolation device;
Figure 18E shows a top member of a housing for a blood isolation device;
Figure 18F shows a top member of a housing for a blood isolation device;
Figure 19A shows a blood isolation device having an upper member that mates with a lower member.
Figure 19B shows a blood isolation device having an upper member that mates with a lower member.
FIG. 20 shows a blood sample optimization system including a blood sequestration device;
Figure 21 shows a non-vented blood isolation device using a wicking material chamber.
Figure 22A shows the material composition of a filter for isolating blood in an isolation chamb er of a blood isolation device;
Figure 22B shows the material composition of a filter for isolating blood in an isolation chamb er of a blood isolation device;
FIG. 23A shows another implementation of a blood isolation device using vacuum force from a blood collection device;
Figure 23B shows another implementation of a blood isolation device using vacuum force from a blood collection device. Like numbers in the various drawings indicate like elements.

DETAILED DESCRIPTION OF THE INVENTION

[0024]

The present specification provides a blood sample optimization system that reduces or elimin ates contaminants in a blood sample taken, thereby reducing or eliminating false positive read ings in blood cultures or other tests of the blood sample taken. and methods. In some implem entations, the blood sample optimization system includes a patient needle for vascular access to the patient's bloodstream and a blood collection container such as a vacutainer or evacuate d blood collection tube or other and a blood isolation device positioned between the patient ne edle and the sample needle. The blood isolation device includes an isolation chamber for isolat ing a first aliquot of blood that may be contaminated, and after the first aliquot of blood is isol ated in the isolation chamber, the blood is isolated between the patient needle and the sample needle. A sampling flow path bypassing the isolation chamber for carrying potentially unconta minated blood may also be included.

FIG .

1 shows a blood sample optimization system according to some implementations. The syste m includes a patient needle 1 for puncturing the patient's skin to access the patient's vein and intravenous blood therein. The system may include a resealable boot 10, a luer actuated valv e, or another sampling interface.

or with a sample needle (i.e., a Vacutainer®, etc.) that can be housed within the device and i nitially sealed by a resealable boot 10, a luer-actuated valve, or another collection interface or device. It further includes a resealably sealed needle) 5 for. The resealable boot 10 can be pus hed by or around the sample needle 5 by using a Vacutainer® bottle (not shown) for collectin g the patient's blood. The system can further include a low volume chamber 30 leading to the sample needle 5, but also includes a hole or one or more channels 45 leading to the isolation chamber 55 formed by the housing 50. FIG. Isolation chamber 55 includes chambers, chann els, passages for receiving and holding an initial aliquot of patient blood, which can be of a pr edetermined or measured volume, depending on the volume of isolation chamber 55

.

, locks, or other structures. Initial blood draws generally contain or are more susceptible to co ntain microorganisms or other pathogens that cause bacteremia and sepsis than subsequent blood draws. The isolation chamber 55 can be contained within a rigid housing, can be a conta iner formed in or defined by the housing itself, or can be realized as a tube or lumen. Isolation chamber 55 can have a predetermined volume, regardless of how it is formed and implement ed. In some implementations, the predetermined volume is based on the volume of the patien t needle, i.e., ranges from a volume less than the volume of the patient needle to any volume to a volume greater than 20 times the volume of the patient needle. can be done. The predet ermined volume of isolation chamber 55 can also be set to conserve or minimize the amount of blood that is isolated and disposed of.

[0027]

Isolation chamber 55 may be formed, contained, or housed within chamber housing 50 and may be made of plastic, rubber, steel, aluminum, or other suitable material. For example, isol ation chamber 55 can be formed from flexible tubing or other elastomeric material. The isolati on chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the is olation chamber 55 . As used herein, the term "air permeable blood barrier" means an air per meable but substantially blood impermeable substance, material or structure. Representative examples are hydrophobic membranes and hydrophobic coatings, hydrophilic membranes or h ydrophilic coatings in combination with hydrophobic membranes or coatings, meshes, filters, mechanical valves, antimicrobial materials, or isolation chamber 55 is blood. Any other means capable of expelling air from the isolation chamber 55 when filled with air may be included. In various exemplary embodiments, the air permeable blood barrier can be formed by one or mo re materials that allow air to pass through until it contacts liquid, such materials being air per meable. and/or completely or partially sealed to prevent or block the passage of liquids. In ot her words, the material forms an air permeable barrier prior to contact with the liquid. After c ontact with liquid, the material substantially or completely prevents further passage of air an d/or liquid.

[0028]

Holes or channels 45 can be of any desired length, cross-sectional shape or size and/or can

be formed away from low volume chamber 30 at any desired angle or orientation. The hole or channel 45 may also include a one-way flap or valve 60 that retains the first aliquot of blood sample within the isolation chamber 55 . In some particular implementations, hole or channel 45 may include a "duckbill" valve or flapper valve 60 or the like for unidirectional blood flow from low volume chamber 30 to isolation chamber 55 . Air permeable blood barrier 20 may also be constructed of a material that allows air to escape but seals upon contact with blood, thereby not allowing outside air to enter isolation chamber 55 . This seal eliminates the need for valves.

Valve 60

can be any type of valve or opening/closing mechanism. The chamber 30 is designed to retain substantially no residual blood and retains a specific volume or percentage of blood in the isolation chamber.

It can be configured to hold or pass through the member 55 . Similarly, the isolation chamber 55 may also include any type of coating, such as an antimicrobial coating, or a coating that assists in identifying and/or diagnosing components of the isolated primary blood draw. Housings 50 and 40 may be formed from any suitable material, including plastics such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric materials, rubber, steel, or aluminum

.

The air permeable blood barrier 20 is activated upon contact with blood from the first draw or when the expulsion of air is stopped, or upon any combination of events and blood in the isolation chamber 55, color A donator or other signaling mechanism may be included. The air permeable barrier can also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents inadvertent or premature sealing of the filter by external fluid sources, splashes, and the like. The isolation chamber 55 can also be translucent or transparent to allow the user to visually confirm that the chamber has been filled.

[0031]

FIG. 2 shows a blood sample optimization system according to some alternative implementations. In the implementation shown in FIG. 2, an isolation chamber 55 or waste chamber surrounds the patient needle 1 and an open-ended cuff or housing is connected to the waste chamber and surrounds the sample needle housing base and housing. The patient needle 1 and the sample needle 5 are connected to each other by a boot 56 which forms a continuous blood collection flow path therethrough. Boot 56 includes a single hole or channel leading from the blood collection channel to isolation chamber 55 . The device can include multiple holes or channels in other implementations. Each hole or channel can include a one-way valve and can be sized and adapted for a predetermined amount of blood flow.

Isolation

chamber 55 contains an air permeable blood barrier. The filter may further include sensors or indicators, respectively, for sensing and/or indicating when a predetermined volume of bloo

has been collected in the isolation chamber 55 . The instructions alert the user to attach an ev acuated blood collection tube or bottle, such as a Vacutainer®, to the sample needle 5 . The h ousing for isolation chamber 55 can be of any size or shape and can include any type of mater ial to define an interior space or volume within the housing. The interior space is initially filled with air only, but can also be coated with agents or substances such as decontamination agen ts, coagulants, and the like. When the evacuated blood collection tube is attached to the samp le needle 5, blood automatically flows into the patient needle 1, through the blood collection c hannel and the sample needle 5 into the bottle. The sample needle 5 is covered by a resealabl e boot, coating or membrane that seals the sample needle when no blood collection bottle is a ttached to the sample needle.

[0033]

FIG. 3 shows a blood sample optimization system according to some alternative implementa tions. In the illustrated implementation, sample needle 5 is surrounded by a resealable boot o r membrane and is also connected to patient needle 1 . A blood flow path is formed through t he sample needle and the patient needle. The connection between the sample needle and the patient needle includes a 'T' or 'Y' connector 102 that includes a flow path, port or opening lea ding from the main blood flow path to the isolation chamber 104 .

The T or Y connector 102 includes a

flap or one-way valve and has holes sized and adapted for a predetermined flow rate of bloo d. The isolation chamber 104 can be formed from a tube or formed by a rigid housing and is i nitially filled with air. The isolation chamber 104 receives blood flowing out of the patient auto matically, ie, under pressure due to the patient's own blood pressure. The isolation chamber 1 04 preferably includes an air permeable blood barrier 106 at the distal end of the tube formin g the isolation chamber 104 and connected at the proximal end to the T or Y connector 102 . The T or Y connector 102 can branch at any desired angle for most efficient blood flow and to minimize or eliminate mixing of the initial aliquot of blood with the main blood sample. Minimi ze the interface between the openings and channels and the main blood channel

can be configured to In some alternative implementations, the sample needle can be attache d to any length of tubing whose opposite end is connected to a T or Y connector 102, as show n in FIG

.

can be done. The isolation chamber 104 can be of any shape or volume so long as the initial a liquot contains a predetermined amount of blood sample. The T or Y connector 102 can also in clude openings or channels parallel to the main blood flow channel. The air permeable blood b arrier may further include an indicator 107 or other mechanism to indicate when a predetermi ned amount of blood has been collected in the isolation chamber or when the released air has reached a certain threshold, i.e. zero. . The tube can also include a clip 109 that can be used t o pinch and prevent fluid flow through the tube. Once the air permeable blood barrier and pr imary chamber are sealed, the first aliquot of blood is confined to the isolation chamber 104

nd a vacuum blood collection tube, such as a Vacutainer® bottle, is attached to the sample ne edle to obtain a sample

.

5 is attached. The blood collection tube can be removed and the sample needle 5 resealed. An y number of subsequent blood collection tubes can be attached for additional blood draws or s amples. When all blood draws are completed, the system is discarded, leaving the first aliquot of blood trapped in isolation chamber 104 .

FIG.

5 shows a blood sample optimization system according to some alternative implementations. In the illustrated implementation, the sample needle 5 is connected by tubing to the patient n eedle. A "T" or "Y" connector 120 is added at any desired location along the tube to include an opening, port or flow path leading to isolation chamber 204, substantially as described above.

[0038]

FIG. 6 illustrates a blood sample optimization system according to some alternative impleme ntations in which an isolation chamber 304 configured as the primary collection flow path rece ives the first aliquot of blood and is provided adjacent to the blood collection flow path. show. The isolation chamber 304 can surround the blood collection channel, patient needle 1 and/or sample needle 5 . The primary collection channel may include T or Y connectors 120, or other types of openings or channels. The isolation chamber 304 includes an air permeable blood bar rier and, as described above, may also include an indicator of contact with fluid such as blood.

In some implementations, either or both of the patient needle 1 or the sample needle 5 can be replaced with luer lock male or luer lock female connectors

.

However, in various implementations, the connector at the sample needle end of the blood sa mple optimization system is first sealed and the first aliquot is transferred to an isolation cha mber pressurized with ambient air pressure and containing the air outlet of the air permeable blood barrier. Allows blood to be diverted. In this way, the system passively and automatically uses the patient's own blood pressure to overcome the ambient air pressure in the isolation c hamber, force air through the air permeable blood barrier, and replace the air in the isolation c hamber with blood.

[0040]

FIG. 7 is a flowchart of an exemplary method for optimizing blood culture quality. At 702, a c linician inserts a needle into a patient's vein. At 704, blood flows into the isolation chamber, fo rcing air within the isolation chamber out of the isolation chamber through the air permeable blood barrier. In some implementations, the volume of the isolation chamber is from less than 0.1 cubic centimeters (cc) to 5 cubic centimeters (cc) or more. The isolation chamber is sized and adapted to collect a second portion of the blood sample and other subsequent portions or a first portion of the blood sample that is more susceptible to contamination than subsequent collections. The isolation chamber has an air permeable blood barrier through which air can

e expelled by the blood expelled from the patient's veins so that such blood can be placed in a vacutainer for receiving and storing blood samples. ® or other bottle, it necessarily and auto matically flows into the isolation chamber before being drawn into or otherwise entering the b ottle.

As the isolation chamber fills, blood collects or otherwise contacts an air permeable blood ba rrier that blocks or prevents blood from passing through . At 706, once the blood contacts the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is closed and air no longer flows out or in. At 708, the clinician is provided an indication or can view the full chamber indicating that an evacuated blood collection tube, such as a Vacutainer ®, can be attached. The indicator may include visibility of the primary chamber to see if the p rimary chamber is full, eg, a blood barrier that changes color, or other indicator. Since the fill t ime of the isolation chamber may be substantially instantaneous, such an indication, if presen t, may simply be that the isolation chamber is filled. Before the evacuated blood collection tu be is attached, communication between the needle, the sampling channel, and the isolation c hamber is restricted by the sealing of the isolation chamber's blood barrier, thus allowing air t o re-enter the system through isolation

.

do not. Sealing of the communication path is accomplished by mechanical twisting or other ac tion, small hole or tortuous path, obviating the need for a separate valve or mechanical action or manipulation by the clinician. At 710, the evacuated blood collection tube is removed, a self -sealing membrane seals the sample needle, and at 712, a further subsequent evacuated bloo d collection tube can be attached. At 714, once the sample has been taken, the device is rem oved from the patient and discarded.

[0043]

Figures 8A-8E show an exemplary blood sample optimization system 800 for non-contaminat ed blood collection, according to some implementations. Blood sample optimization system 80 0 includes an entry port 802 that can be connected to tubing, a patient needle (or both), or ot her vascular or venous access device, and a first exit to isolation chamber tubing 806 and sa mple collection tubing. a path splitter 804 with a second exit to 808; One or both of isolation c hamber tube 806 and sample collection tube 808 can be formed from tubing. In some implem entations, isolation chamber tube 806 is sized to accommodate a specific amount of initial blo od sample. A sample collection tube 808 receives a blood sample once the isolation chamber t ube 806 is filled. The sample collection tube 808 can be connected to a Vacutainer® base or h ousing 810, or other blood sample collection device. Blood isolation system 800 further inclu des blood isolation device 812, which includes housing 818, shown in more detail in FIGS

.

or connected at either end to a non-contaminated sample collection tube 808 . The sampling f low path 820 can be curved through the housing 818 to better secure and stabilize the hous

g 818 in position along the clean sample collection tube 808 .

[0045]

Blood isolation device 812 further includes an isolation chamber 822 or other chamber conne cted with isolation chamber tube 806 . Isolation chamber 822 terminates in air permeable blo od barrier 824 . The air permeable blood barrier 824 can also include a coloring agent that ch anges to a different color upon full contact with blood as an indicator that a blood sample (i. e., non-contaminated blood sample) can be properly taken. . Other indicators such as small li ghts, sound generating mechanisms, etc. can be used. In some implementations, the air per meable blood barrier is positioned perpendicular to the orientation of isolation chamber 822, b ut may be positioned at any distance or orientation to conserve space and materials used for housing 818. be able to. Housing 818 and its contents can be formed from any rigid or semi-ri gid material or range of materials.

FIG.

9 illustrates a path splitter for use in, for example, blood sequestration systems such as thos e shown in FIGS. 8A-8E.

900 is shown. Path splitter 900 includes inlet port 902 , main conduit outlet port 904 and isola tion channel outlet port 906 . The entry port 902 can be connected to a main tube that is also connected to the patient needle system or directly to the patient needle. The main line outlet port 904 can be connected to a main line tube to a blood collection system, such as a Vacutai ner® base or housing, or directly to such a blood collection system. The isolation channel outl et port 906 can be connected to an isolation tube for receiving and isolating the first sample o f blood up to a measured volume or predetermined threshold. Alternatively, the isolation flow path outlet port 906 can connect to the isolation chamber. The isolation channel outlet port 90 6 is preferably angled from 20 to 70 degrees from the main conduit outlet port 904 while the main conduit outlet port 904 is preferably in line with the inlet port 902 . Once an initial blood sample of predetermined volume has been isolated in an isolation tube or isolation chamber a ccording to the mechanisms and techniques described herein, subsequent blood samples can f low into inlet port 902 and pass unobstructed. It flows out directly from the main conduit outl et port 904 . 10A-10D show blood isolation device 1000 according to another implementatio n

.

Blood isolation device 1000 includes inlet port 1002 , main outlet port 1004 , and isolation flo w port 1006 . Entry port 1002 can be connected with a patient needle or associated tubing. T he main exit port 1004 can be connected to a blood sampling device such as a Vacutainer®, a ssociated tubing, or a luer-actuated valve. An isolation flow port 1006 separates from the mai n exit port 1004 into an isolation chamber 1008 . In some implementations, isolation chamber 1008 is formed as a spiral channel within housing or other container 1001 .

[0048]

Isolation chamber 1008 is connected at its distal end to air permeable blood barrier 1010, s

bstantially as described above. Air within the isolation chamber 1008 is expelled by the first al iquot of blood directed into the isolation flow path port 1006 through the air permeable blood barrier 1010 . Once the isolation chamber 1008 is filled, further blood draws through the main exit port 1004 are accomplished and these samples are clean.

11A -

11E show blood isolation device 1100 according to another alternative implementation. Bloo d isolation device 1100 includes an inlet port 1102 similar to the inlet ports described above, a main outlet port 1104 and an isolation flow port 1106 separate from main outlet port 1104 and inlet port 1102 . The isolation flow port is connected to isolation chamber 1108 . In the i mplementation shown in FIGS. 11A-11E, the blood isolation device includes a base member 1 101 having a flow path therein that functions as an isolation chamber 1108 . The flow path ca n be formed as a tortuous path through the base member 1101 while the base member 1101 is shaped and shaped to rest on the patient's limb. A portion of isolation chamber 1108 may protrude from or near the top surface of the base member just prior to exiting air permeable blood barrier 1110 to serve as blood isolation indicator 1109

.

Indicator 1109 can be made of a transparent material or a material that changes color when i n contact with blood.

[0051]

In some implementations, the blood isolation device 1100 can include a blood collection devi ce 1120, such as a normally closed needle, Vacutainer® shield, or other collection device. Blo od collection device 1120 may be manufactured and sold with blood isolation device 1100 for efficiency and convenience so that the initial aliquot of blood that may be contaminated by the patient needle insertion process can be isolated. can. Accordingly, the blood collection device 1120 can collect and ensure a clean blood sample so as to reduce the risk of false positive tes ts.

[0052]

Figures 12A-12D show a blood sample optimization system 1200 according to yet another al ternative implementation. System 1200 includes a blood isolation device 1202 for attachment to a blood collection device 1204, such as a Vacutainer® or other collection and sampling devi ce. Blood isolation device 1202 receives an initial aliquot or volume of blood before a Vacutain er® container or vial is attached to the collection needle of blood collection device 1204 and t ransfers that initial aliquot or volume to blood isolation device 1202 . Constructed and arrange d to isolate within the isolation channel.

[0053]

In some implementations, the blood isolation device 1202 can include an inlet port 1212, a main outlet port, and an isolation flow path port. Entry port 1212 can be connected to a patie nt needle or associated tubing. The main exit port 1214 is a normally closed needle or needle to allow connection with other collection devices such as evacuated blood collection containe

or vacutainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be co nnected to a device. The isolation flow port separates the isolation chamber 1218 from the ma in exit port.

[0054]

In some implementations, isolation chamber 1218 is formed as a channel within the body of isolation device 1202 . The isolation chamber 1218 can be a tortuous channel, such as a U-sh aped channel, an S-shaped channel, a spiral channel, or any other tortuous channel. Isolation device 1202 can include a housing or other enclosure and one or more channels formed therei n. As shown in FIGS. 12A and 12B, isolation device 1202 includes body 1206 and cap 1208 . One or more cavities or channels are formed in the body 1206, and the cavities or channels ar e further formed with one or more arms 1210 extending from the cap 1208, the one or more arms 1210 extending from the cavities or channels of the body 1206. A primary collection por t and a main outlet port are formed against the flow path.

[0055]

Figures 13A-13D illustrate a blood sample optimization system 1300 according to yet anothe r alternative implementation. System 1300 includes a blood isolation device 1302 for attachm ent to a blood collection device 1304, such as a Vacutainer® or other body fluid collection and sampling device. Blood isolation device 1302 receives an initial aliquot or volume of blood and receives that initial aliquot or volume of blood or other bodily fluid before a Vacutainer® conta iner or vial is attached to the collection needle of blood collection device 1304 . within the isol ation channel of the blood isolation device 1302 .

[0056]

Blood isolation device 1302 includes housing 1301 having inlet port 1314 , main outlet port 1312 , and isolation flow path port 1316 . Entry port 1314 can be connected to a patient need le or associated tubing. The main exit port 1312 is a normally closed needle or needle to allow connection with other collection devices such as evacuated blood collection containers or vacu tainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be connecte d to a device. An isolation flow port 1316 separates from the main inlet port 1314 into an isol ation chamber 1318 . In the embodiment shown in FIGS. 13A-13D, isolation chamber 1318 i s formed as a cavity or chamber within housing 1301 or is formed by walls defining housing 1 301

.

The isolation chamber 1318 is a tortuous flow path such as a U-shaped flow path, an S-shape d flow path, a spiral flow path, or any other tortuous flow path defined by the cooperation and connection of the housing 1301 and the cap 1307. There can be and the cap 1307 can include protrusions 1305 that provide one or more walls or directors for the tortuous flow path within the isolation chamber 1318 . Projections 1305 from cap 1307 can be straight or curved, can b e embedded with various channels, openings or grooves, and can extend from cap 1307 at an y angle or orientation. can be done. isolation chamber 13

When the cap 1307 is connected with the housing 1301 to complete the formation of 18 , the protrusions 1305 form at least a portion of the tortuous flow path and the isolation flow forme d by the tortuous flow path within the isolation chamber 1318 . Isolate the first aliquot or volu me of blood or other bodily fluid in the tract.

Isolation chamber 1318

includes air permeable blood barrier 1310 substantially as described above. Air within the iso lation chamber 1318 is expelled through the air permeable blood barrier 1310 by the first aliq uot of blood supplied into the isolation chamber 1318 by the patient's blood pressure. Once th e isolation chamber 1318 has been filled and the air within the isolation chamber 1318 has be en expelled, a force such as a vacuum or other pressure such as provided by a blood sampling device such as a Vacutainer® is applied to the next aliquot or Until a volume of blood or fluid has been provided to withdraw, the patient's blood pressure is insufficient to drive or provide additional blood to blood isolation device 1302 , particularly outlet port 1312 . Further blood d raws can be taken through the main exit port 1312 and these samples are not contaminated a s any contaminants are sequestered in the isolation chamber 1318 along with the first aliquot of blood.

[0059]

Figures 14A-14E illustrate yet another implementation of a blood collection system 1400 that sequesters contaminants in an initial aliquot or sample to reduce false positives in blood cultur es or tests performed on patient blood samples. Blood collection system 1400 includes a bloo d isolation device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutain er® or the like. Blood isolation device 1401 includes an entry port 1402 that can be connecte d to a patient needle that is inserted into the patient's vasculature for access to and collection of a blood sample. Inlet port 1402 may also be connected to a tube or other conduit that is al so connected to a patient needle.

Inlet port 1402

defines an opening to blood isolation device 1401, which opening can be of the same cross-s ectional dimensions as a tube or other conduit connected to the patient needle or the patient needle itself. For example, the opening can be circular with a diameter of about 0.045 inch (1. 143 mm), but may be from 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm) or more. can have a diameter of Blood isolation device 1401 further includes an exit port 1404 that defines an ope ning from blood isolation device 1401 and to blood sampling device 1403 . Exit port 1404 can also be connected to a tube or other conduit that is also connected to blood isolation device 1 403 . The exit port 1404 has a connector device such as an unthreaded interference or glue jo int for attachment to a variety of devices including, but not limited to, threaded caps, luer con nectors (male or female), tubing, and the like. can further include

[0061]

Blood isolation device 1401 further includes a sampling channel 1406 between inlet port 14

2 and outlet port 1404, which functions as a blood sample path once the first aliquot of blood has been isolated. Sampling channel 1406 can be a channel or conduit of any size, shape or c onfiguration. In some implementations, sampling channel 1406 has a cross-sectional area sub stantially similar to the opening of inlet port 1402 . In other implementations, sampling chann el 1406 can gradually widen from inlet port 1402 to outlet port 1404 .

Blood isolation device 1401 further includes isolation chamber 1408 , which

is connected to and separated from sampling channel 1406 at any location between inlet por t 1402 and outlet port 1404 . redirected, but preferably connected to the proximal end of sam pling channel 1406 near inlet port 1402 and from the proximal end.

separated or diverted from the The isolation chamber 1408 is initially maintained at atmosphe ric pressure and includes an air outlet 1412 at or near the distal end of the isolation chamber 1408 opposite the turning point from the sampling channel 1406 . Air outlet 1412 includes air permeable blood barrier 1412 . The air permeable blood barrier 1412 can be covered with a p rotective cover 1416, as shown in FIG. 14B. The protective cover 1416 can be sized and confi gured to prevent a user from touching the air permeable blood barrier 1412 with their fingers or other external instruments while still allowing the patient's own blood pressure to pressure the isolation chamber 1408. Allowing air to exit the air permeable blood barrier 1412 as the ai r is forced out of the isolation chamber by forcing blood into it. Protective cover 1416 can also be configured to block or prevent accidental exposure of the air permeable blood barrier to su rrounding fluids or droplets. This can be done in a variety of mechanical ways including, but n ot limited to, adding a hydrophobic membrane to the protective cover. As shown in FIGS. 14 C and 14D, the sampling channel 1406 may be cylindrical or frusto-conical in shape from a sm aller diameter to a larger diameter to minimize the possibility of lysing red blood cells

.

can. Similarly, the sampling channel 1406 is formed with a minimal amount or no sharp bends or sharp angles that could lyse red blood cells. Sampling channel 1406 splits near inlet port 1 402 through diverting path 1409 into isolation chamber 1408 . Diversion pathway 1409 can h ave any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least a portion of inlet port 1402 .

[0064]

In some implementations, sampling channel 1406 and isolation chamber 1408 are formed b y grooves, channels, locks or other pathways formed in housing 1414 . Housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a lowe r member that sealably mates with the upper member. One or both of the lower and upper m embers can include a sampling channel 1406 and an isolation chamber 1408 as well as a dive rting passageway 1409 , an inlet port 1402 and an outlet port 1404 . In some other implemen tations, one or more of diverting path 1409 , inlet port 1402 , and/or outlet port 1404 are at l east partially closed by a cap member connected to either end of housing 1414 . can be forme d in In some implementations, the upper and lower members and the cap member can be co

nected together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the lik e. In other implementations, some or all of the interior surfaces of the diversion pathway 140 9 and/or the isolation chamber 1408 can be coated or filled with agents or substances such as decontamination agents, coagulants, and the like. For example, when the sequestration cham ber 1408 fills and the first aliquot of blood returns to the diverting path 1409, the final volume of sequestered blood clots, creating a barrier between the sequestration chamber 1408 and th e sampling channel 1406. As such, turning path 1409 may be provided with a coagulant. 15 A-15G show a blood isolation device 1500. FIG

.

The blood isolation device 1500 includes a needle or needle that is normally closed to allow co nnection with other collection devices such as evacuated blood collection containers or vacutai ners, associated tubing, luer connectors, syringes, luer actuated valves, and the like. It can b e connected to a device.

[0066]

Blood isolation device 1500 includes an entry port 1502 that can be connected to a patient n eedle that is inserted into the patient's vasculature for access to and collection of a blood sam ple. Entry port 1502 can also be connected to a tube or other conduit that is also connected t o a patient needle. Entry port 1502 defines an opening to blood isolation device 1500, which o pening can be of the same cross-sectional dimensions as a tube or other conduit connected to the patient needle or the patient needle itself. For example, the opening has a diameter of ap proximately 0.045 inches (1.143 mm).

It can be circular, but can have a diameter of 0.01 inch (0.254 mm) to 0.2 inch (5.08 mm) or more. Inlet port 1502 may also include a sealed or fluid tight connector or connection such a s a threaded or luer fitting or the like

.

In some implementations, a tube or other conduit that is coupled to the patient needle can be integrated with the entry port 1502, such as by co-molding, gluing, laser welding, or heat bon ding the parts together. This allows the blood isolation device 1500 to be manufactured and s old as a single unit with the patient needle, eliminating the need to connect the patient needle to the blood isolation device 1500 during blood draw or sampling.

Blood isolation device 1500 further includes an exit port 1504 that

defines an opening from blood isolation device 1500 and to the blood sampling device. Exit p ort 1504 may also be connected to a tube or other conduit that is also connected to a blood is olation device and may include a sealed or fluid tight connector or connection such as a threa ded or luer fitting. Thus, as noted above, the blood isolation device 1500 is manufactured and sold as a single unit with the patient needle and/or tubing and blood sample collection device such that the patient needle and blood sample collection device are connected to blood isolati on during blood collection or sampling. The need to connect to device 1500 can be eliminated.

[0069]

Blood isolation device 1500 further includes a sampling channel 1506 between inlet port 150 2 and outlet port 1504, which functions as a blood sample path once the first aliquot of blood has been isolated. Sampling channel 1506 can be a channel or conduit of any size, shape, or c onfiguration. In some implementations, sampling channel 1506 has a cross-sectional area sub stantially similar to the opening of inlet port 1502 . In other implementations, sampling chann el 1506 can gradually diverge from inlet port 1502 to outlet port 1504 .

Blood isolation device 1500 further includes isolation chamber 1508 , which

is connected to and separated from sampling channel 1506 at any location between inlet por t 1502 and outlet port 1504 . Although diverted, it is preferably connected to and disconnecte d or diverted from the proximal end of sampling channel 1506 near inlet port 1502 . In some i mplementations, the diversion channel includes a Y-junction. The isolation chamber 1508 is pr eferably maintained at atmospheric pressure and includes a vent 1510 at or near the distal en d of the isolation chamber 1508 . Vent 1510 includes air permeable blood barrier 1512 . FIG. 15C shows blood isolation device 1500 with isolation chamber 1508 filled with an initial aliquo t or sample of blood from a patient.

[0071]

Air permeable blood barrier 1512 can be covered with protective cover 1516 . The protective cover 1516 can be sized and configured to prevent a user from touching the air permeable blo od barrier 1512 with their fingers or other external instruments while still allowing the patien t's own blood pressure to pressure the isolation chamber 1508. Allowing air to exit the air per meable blood barrier 1512 as the air is forced out of the isolation chamber by forcing blood int o it. The protective cover 1516 can be configured to block or prevent accidental exposure of t he filter to ambient fluids or splashes. This can be done in a variety of mechanical ways, inclu ding but not limited to adding a hydrophobic membrane to the protective cover.

FIG.

15B is a perspective view of blood isolation device 1500 from the top of housing 1501 includi ng outlet port 1504 and vent 1510 of blood isolation device 1500 and sampling channel 1506 before the sample collection device is activated. The first aliquot of blood is separated while th e is empty.

Filling the separation chamber 1508 is shown. Figure 15G is a perspective view of the blood is olation device 1500 from the bottom of the housing 1501 and the exit port 1504 of the blood i solation device 1500, showing the initial flow while the sampling channel 1506 is empty befor e the sample collection device is activated. An aliquot of blood is shown filling the isolation ch amber 1508 . FIG. 15C is another perspective view of blood isolation device 1500 from the to p of housing 1501, including inlet port 1502 and vent 1510 of blood isolation device 1500, wit h the isolated blood substantially remaining within isolation chamber 1508. FIG. Blood is draw n through sampling channel 1506 during the period of time.

FIG .

15D is a cross-sectional view of blood isolation device 1500 according to some implementat

ons, showing housing 1501 defining sampling channel 1506 and isolation chamber 1508 . 15E and 15F illustrate various form factors of housings for blood isolation devices according to one or more implementations described herein. Isolation chamber 1508 can have a larger cross-sectional area than sampling channel 1506, and the cross-sectional area or length can be conf igured such that a predetermined or specific blood volume is isolated or locked

.

can. The sampling channel 1506 can be sized to fit tubing for either or both the patient needle tubing or the blood collection device tubing.

[0075]

Housing 1501 can be formed from multiple pieces or a single unitary piece. In some implem entations, as shown in FIG. 15D, housing 1501 includes an upper member 1520 and a lower member 1522 that mate with each other, one or both of which may be formed by, for exampl e, an injection molding process or by etching, cutting, cutting, or molding. It has grooves, cha nnels, locks, conduits or other pathways pre-formed by perforations or the like. The upper me mber 1520 may be attached by any mating or connecting mechanism, such as using laser wel ding, thermal bonding, ultrasonic welding, adhesives, screws, rivets, bolts, etc., or latches, gr ooves, tongues, pins, flanges. Other mating mechanisms, such as, can connect with lower me mber 1522 . In some implementations, the upper member 1520 can include grooves, chann els, locks, conduits or other pathways, while the lower member 1522 is the upper member 15 20, as shown in FIG. 15D

.

A protrusion 1524 sized and adapted to fit into at least one of a groove, channel, lock or other pathway may be included. Protrusions 1524 can provide surface features such as partial groov es or partial channels, for example, to complete the formation of either sampling channel 150 6 and/or isolation chamber 1508 . In some implementations, the protrusions 1524 can be for med with one or more slanted sides or faces to fit more snugly within corresponding grooves, channels, locks or other pathways. In still other implementations, both the upper member 15 20 and the lower member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524 .

[0077]

In some implementations, sampling channel 1506 and isolation chamber 1508 are formed b y grooves, channels, locks or other pathways formed in housing 1501 . Housing 1501 can be made of any suitable material including rubber, plastic, metal or other material. Housing 1501 can be formed from a transparent or translucent material, or from an opaque or non-transluce nt material. In other implementations, the housing 1501 can be largely opaque or non-transp arent, but the housing surfaces immediately adjacent the sampling channel 1506 and/or the i solation chamber 1508 are transparent or translucent and initially A visual cue or sign that the sequestration chamber 1508 is filled to the required or desired degree and/or the sequestered blood is then released while a clean blood sample is drawn through the sampling channel 15

6. Provide visual cues or signs to remain isolated.

give to the artist. Other visual cues or signs of isolation include, but are not limited to, contact, penetration, or partial penetration of blood, the air permeable blood barrier 1512 turning a different color; Color-coded tabs or indicators at any location along or adjacent to the isolation chamber, audible, vibratory, or other signals may be included. After venipuncture with a patient needle (not shown), which can collect many pathogens from the patient's skin, the patient's own blood pressure overcomes the atmospheric pressure in isolation chamber 1508 to form air permeable blood barrier 1512

.

As the air in the isolation chamber 1508 is expelled through, the initial volume of the patient's blood with these pathogens enters the blood isolation device 1500 inlet port 1502 and flows into the isolation chamber 1508 by following the path of least resistance. . The patient's blood pressure is not sufficient to overcome the rising air pressure within the sealed sampling channel 1506 . Ultimately, an isolation chamber 1508 of predetermined volume is filled with blood that drives air out through an air permeable blood barrier 1512 . When blood impinges on the air permeable blood barrier, the blood interacts with the material of air permeable blood barrier 1512 to completely or partially seal vent 1510 . A signal or indication can be provided that the practitioner can now utilize the VACUTAINER® capsule or other blood sampling device to obtain the next volume of the patient's blood for sampling. The blood in the isolation chamber 1508 is now effectively isolated within the isolation chamber.

[0079]

Upon filling the blood isolation channel 1508, and prior to use of a Vacutainer® or other blood sampling device, the patient's blood pressure causes compression of the air in the sampling channel 1506 and possibly a small amount of blood. It moves past the turning point into the isolation chamber 1508 into the sampling channel 1506 and queues clean blood to be drawn through the sampling channel 1506 .

Figures 16-19

show yet another implementation of a blood isolation device. 16A-16D are connected between a blood sample collection device such as an evacuated blood collection container such as a Vacutainer® (not shown) and a patient needle (not shown) and/or associated tubing. 16 shows a blood isolation device 1600 that can be used. Figure 17 shows the lower member of the blood isolation device and Figure 18 shows the upper member of the blood isolation device, the upper and lower members interfitting to provide an inlet port as described in more detail below. Ports, exit ports, isolation chambers and sampling channels can be formed. Figures 19A and 19B show the upper and lower members mating together. It should be appreciated that FIGS. 16-19 show one exemplary method of constructing the blood isolation devices described herein and that other forms of construction are possible.

[0081]

16A-16D, blood isolation device 1600 includes an entry port 1602 that can be connected to

patient needle that is inserted into a patient's vasculature for access and collection of a blood sample. Inlet port 1602 can also be connected to a tube or other conduit that is also connecte d to a patient needle. Entry port 1602 defines an opening to blood isolation device 1600, whic h opening can be of the same cross-sectional dimensions as a tube or other conduit connecte d to the patient needle or the patient needle itself. For example, the opening can be circular w ith a diameter of about 0.045 inch (1.143 mm), but may be from 0.01 inch (0.254 mm) to 0. 2 inch (5.08 mm) or more. can have a diameter of

Inlet port 1602

may also include a sealed or fluid tight connector or connection such as a threaded or luer fit ting or the like. In some implementations, a tube or other conduit coupled to the patient need le can be integrated with the entry port 1602, such as by co-molding, gluing, laser welding, or heat bonding the parts together. Blood isolation device 1600 is thereby manufactured and sol d as a single unit along with the patient needle and/or tubing,

The need to connect the patient needle to the blood isolation device 1600 during blood draw o r sampling can be eliminated.

Blood isolation device 1600 further includes an exit port 1604 that

defines an opening from blood isolation device 1600 and to the blood sampling device. Exit p ort 1604 may also be connected to a tube or other conduit that is also connected to a blood is olation device and may include a sealed or fluid tight connector or connection such as a threa ded or luer fitting. Thus, as noted above, the blood isolation device 1600 is manufactured and sold as a single unit along with the patient needle and/or tubing and blood sample collection d evice such that the patient needle and blood sample collection device are connected to blood i solation during blood collection or sampling. The need to connect to device 1600 can be elimin ated.

[0084]

Blood isolation device 1600 is connected to sampling channel 1606 between inlet port 1602 and outlet port 1604, and at any location between inlet port 1602 and outlet port 1604, and s ampling channel 1606. and an isolation chamber 1608 that is isolated or diverted from. Sampl ing channel 1606 functions as a blood collection path once the first aliquot of blood is sequest ered in sequestration chamber 1608 . Sampling channel 1606 can be a channel or conduit of a ny size, shape or configuration. In some implementations, sampling channel 1606 has a cross -sectional area substantially similar to the opening of inlet port 1602 . In other implementatio ns, sampling channel 1606 can gradually widen from inlet port 1602 to outlet port 1604 . The isolation chamber 1608 widens toward the path of the isolation channel so that blood first atte mpts to enter the reservoir as opposed to entering the smaller diameter of the sampling chan nel 1606, as shown in more detail in FIGS. It can have a larger cross-section to form a reserv oir. In some exemplary implementations, the diversion between sampling channel 1606 and i solation chamber 1608 is accomplished by diversion junction 1607

.

Turning junction 1607 can be substantially Y-shaped, T-shaped, or U-shaped. In some preferr ed exemplary implementations, redirection junction 1607 is configured such that flow from inl et port 1602 is preferentially directed into isolation chamber 1608, as shown in FIGS. 17A-17 B. The isolation chamber 1608 can also include or form a bend or ramp to move the initial blo od flow toward and into the isolation chamber 1608 .

[0086]

The isolation chamber 1608 is preferably maintained at atmospheric pressure and includes a vent 1610 at or near the distal end of the isolation chamber 1608 . Vent 1610 can include an air permeable blood barrier 1612 as described above. Blood isolation device 1600 can includ e a housing 1601 that can be formed from multiple pieces or a single unitary piece

.

In some implementations, as shown in FIGS. 17A-17D and 18A-18F, housing 1601 includes an upper member 1620 and a lower member 1622 that fit together. Blood isolation device 1600 i ncludes a gasket or other sealing member (not shown) such that when upper member 1620 is mechanically attached to lower member 1622, the junction therebetween is sealed by the gas ket or sealing member. can also include 17A-17D show the lower member 1622 of the housing for the blood isolation device 1600. FIG. The lower member 1622 includes pre-formed groove s, channels, locks, conduits, such as by an injection molding process or by etching, cutting, dr illing, etc., to form the sampling channels 1606, the isolation chambers 1608, and the turning junctions 1607. or other routes.

Isolation chamber 1608

prevents blood from entering the smaller diameter of sampling channel 1606 .

, can have a larger cross-section than the sampling channel 1606 so as to preferentially move into the isolation chamber first.

FIGS.

18A-18F may be attached by any mating or connecting mechanism such as using laser weldi ng, thermal bonding, gluing, screws, rivets, bolts, etc., or latches, grooves, tongues, pins, flan ges. Upper member 1620 is shown connectable with lower member 1622 by other mating me chanisms such as. Top member 1620 can include some or all of grooves, channels, locks, con duits or other pathways to form sampling channels 1606 , isolation chambers 1608 and turnin g junctions 1607 . In still other implementations, both upper member 1620 and lower membe r 1622 can include grooves, channels, locks or other pathways.

[0090]

In some implementations, sampling channel 1606 and isolation chamber 1608 are formed b y grooves, channels, locks or other pathways formed in housing 1601 . Housing 1601 can be made of rubber, plastic, metal or any other suitable material. Housing 1601 can be formed fro m a transparent or translucent material, or from an opaque or non-translucent material. In ot her implementations, housing 1601 can be largely opaque or non-translucent, but housing sur faces directly adjacent sampling channel 1606 and/or isolation chamber 1608 can be transpa

ent or translucent. There may be first a visual cue or sign that the isolation chamber 1608 is fi lled to the required or desired degree, and/or a subsequent isolation while a clean blood samp le is taken through the sampling channel 1606. Gives the practitioner a visual cue or sign that the sequestered blood remains sequestered. Other visual cues or signs of isolation include, bu t are not limited to, contact, penetration, or partial penetration of blood, causing the air perm eable blood barrier 1612 to turn a different color; Color-coded tabs or indicators at any locatio n along or adjacent to the isolation chamber, audible, vibratory, or other signals may be includ ed.

[0091]

The air permeable blood barrier 1612 can be covered or surrounded by a protective member 1616, as shown in FIGS. 18A-18F. Protective member 1616 can be sized and configured to pre vent a user from touching air permeable blood barrier 1612 with their fingers or other externa l instruments, while still allowing air to be expelled from isolation chamber 1608. Occasionally allow air to exit the air permeable blood barrier 1612 . In some implementations, protective member 1616 includes protrusions that extend from the top surface of top member 1620 up a nd around air permeable blood barrier 1612 . The protective cover 1616 can be configured to block or prevent accidental exposure of the filter to ambient fluids or splashes. This can be do ne in a variety of mechanical ways, including but not limited to adding a hydrophobic membra ne to the protective cover. In use, blood isolation device 1600 includes sampling channel 160 6 and isolation chamber 1608

.

Both pathways are initially filled with air at atmospheric pressure, but the sampling channel 1 606 is initially sealed by a Vacutainer® or other such sealed blood collection device at the outl et port 1604. , the isolation chamber 1608 terminates in a vent 1610 to the atmosphere that i ncludes an air permeable blood barrier 1612 .

[0093]

After venipuncture with a patient needle (not shown), which can collect many pathogens fro m the patient's skin, an initial volume of the patient's blood with these pathogens passes thro ugh inlet port 1602 of blood isolation device 1600 . do. This initial volume of potentially conta minated blood preferentially enters isolation chamber 1608 by finding the path of least resista nce. The patient's own blood pressure overcomes the atmospheric pressure in the vented isol ation chamber 1608 and expels the air in the isolation chamber 1608 through the air permeab le blood barrier 1612, while the air pressure builds up in the sealed sampling channel 1606. is insufficient to overcome the various exemplary

In some embodiments, isolation chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome the eff ects of gravity regardless of the orientation of the blood isolation device. can.

Ultimately

, the isolation chamber 1608 fills with blood that drives air out through the air permeable b

od barrier 1612 . When blood contacts the air permeable blood barrier, the blood interacts wit h the material of air permeable blood barrier 1612 to completely or partially seal vent 1610 . A signal or indication can be provided that the practitioner can now utilize the Vacutainer® or other blood collection device. Upon filling blood isolation channel 1608 and prior to use of a Vacutainer® or other blood sampling device, the patient's blood pressure causes compression of air within sampling channel 1606, possibly a small amount

.

of blood moves past the turning point into sampling channel 1606 , queuing clean blood to be drawn through sampling channel 1506 .

FIG .

19A is a side view of blood isolation device 1600 and FIG. 19B is a cross-sectional view of bl ood isolation device 1600 showing upper member 1620 mating with lower member 1622 .

[0097]

FIG. 20 illustrates a patient needle 2002 for vascular access to a patient's bloodstream, a blo od sample collection device 2004 that facilitates the collection of one or more blood samples, and the patient needle 2002 and blood sample collection device 2004. A blood sample optimiz ation system 2000 is shown including a conduit 2006 providing a fluid connection between. In some implementations, the blood sample collection device 2004 includes a protective shield th at includes a sealed collection needle such that once a sealed vacuum container is placed on t he collection needle and the container is pierced once by the collection needle, the patient nee dle is exposed to the patient needle. A blood sample is drawn from 2002 through conduit 200 6 with vacuum pressure or force.

Blood sample optimization system 2000

further includes a blood isolation device 2008 located at any point on conduit 2006 between patient needle 2002 and blood sampling device 2004, as described herein. .

FIG.

21 shows a non-vented blood isolation device 2100 that uses wicking material chambers. Blo od isolation device 2100 includes a housing 2101 having a sampling channel 2104 at least par tially surrounded or abutted by an isolation chamber 2102 filled with wicking material. A first aliquot of blood is drawn from the patient needle into the sampling channel 2104 where it im mediately escapes into the wicking material of the isolation chamber 2102 . The wicking mate rial and/or isolation chamber 2102 is filled with a predetermined volume such that subsequent or subsequent blood draws flow past the wicking material and through the sampling channel 2 104 directly to a sampling device such as a vacutainer. Dimensioned and adapted to receive a nd retain blood. The wicking material can include substances such as solidifying agents, decon taminating agents, or other additives.

[0100]

As described herein, air permeable blood barriers can be made using a wide variety of differ ent structures and materials. As shown in Figures 22A and 22B, an air permeable blood barr

r 2202 of a blood isolation device 2200 can include a polymeric bead matrix 2204 that has be en treated to render at least some of the beads hydrophilic. Air permeable blood barrier 2202 further comprises a self-sealing material 2206 such as carboxymethylcellulose (CMC) or cellul ose gum, or other sealing material. Air permeable blood barrier 2202 may further include void s 2208 that allow air flow prior to or during partial contact with a fluid such as blood. Self-seal ing material 2206 expands upon contact with fluid, as shown in FIG. 22B.

Tightens to close void 2208, occluding air flow through void 2208, and completely or partially sealing. Figures 23A and 23B show an entry port 2302 for connection with a patient needle, an exit port 2304 for connection with a blood sampling device, an isolation chamber 2306, an isolation chamber 2306, and a contaminant to be isolated

.

23 shows yet another implementation of the blood isolation device 2300 having a sampling ch annel 2308 that bypasses the isolation chamber 2306 once the isolation chamber is filled to th e first aliquot of blood that may be present. Isolation chamber 2306 includes a hydrophobic pl ug 2312 at the distal end of isolation chamber 2306 furthest from inlet port 2302 . A vacuum or other suction force applied from outlet port 2304, such as from a Vacutainer®, draws blood into inlet port 2302 and directly into isolation chamber 2306, where the first aliquot of blood i s removed. Contacting the hydrophobic plug 2312, the first aliquot of blood is returned to the sequestration chamber 2306 where it is sequestered. A small amount of blood can enter samp ling channel 2308 which is initially closed by valve 2308 . When valve 2308 is released, a subs equent volume of blood, under additional vacuum or other force, flows into inlet port 2302, by passes isolation chamber 2306, and through sampling channel 2308 to outlet port 2304. flow towards and sent to the collection device. Sampling channel 2308 can have any suitable geo metry and can be formed from plastic tubing or any other suitable material

.

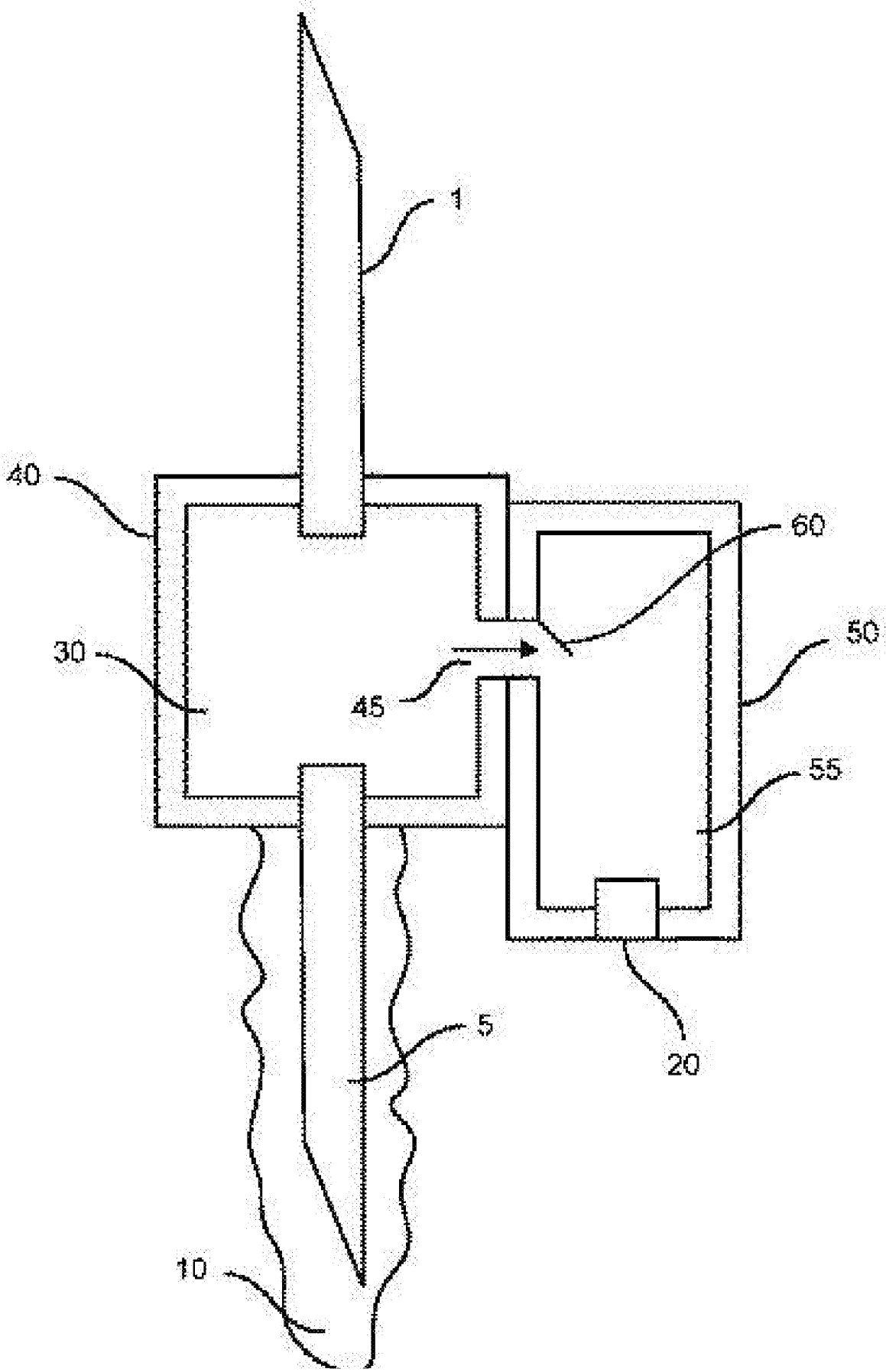
Valve 2308 can be a clip or other enclosing device to pinch, deflect, bend, or otherwise close t he sampling channel before the first aliquot of blood is sequestered in sequestration chamber 2306 . can.

[0103]

While various embodiments have been described in detail above, other modifications are pos sible. Other embodiments may be within the scope of the following claims.

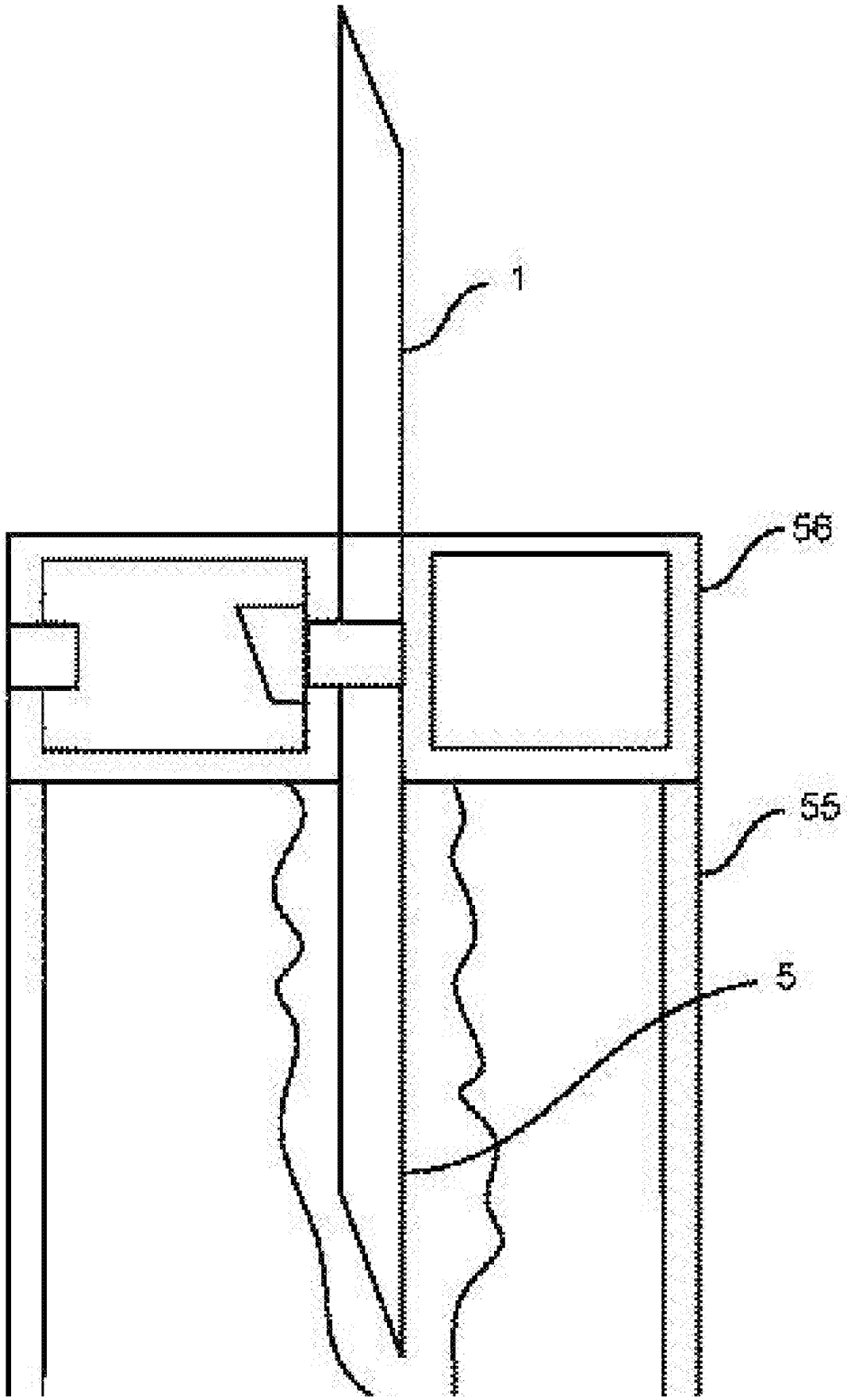
drawing open —

[Fig. 1]


1
40
60
30
50
45
55
5
20
10

[Figure 2]

FIG. 1


1
56
55
5

[Figure 3]

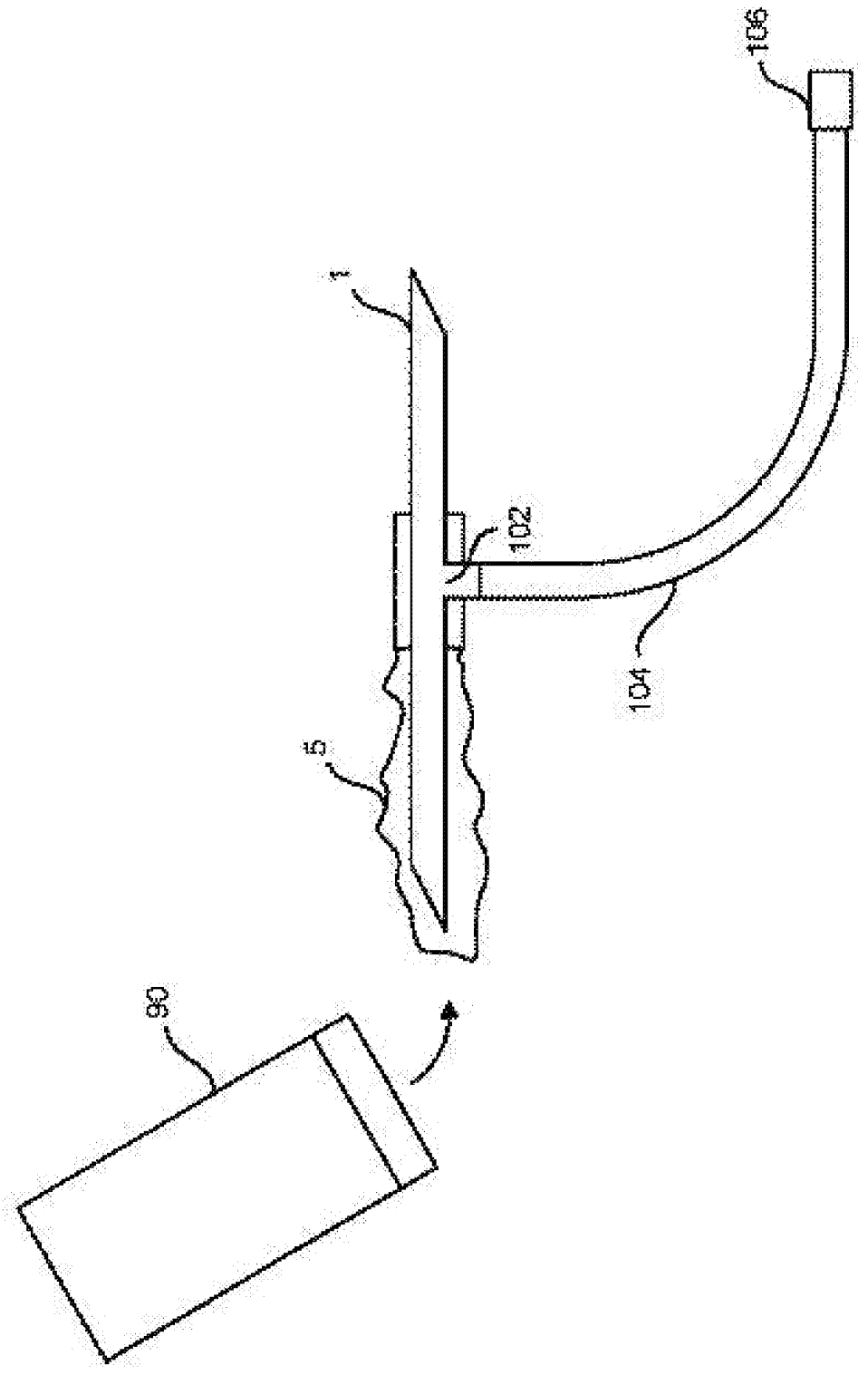


FIG. 3

[Figure 4]

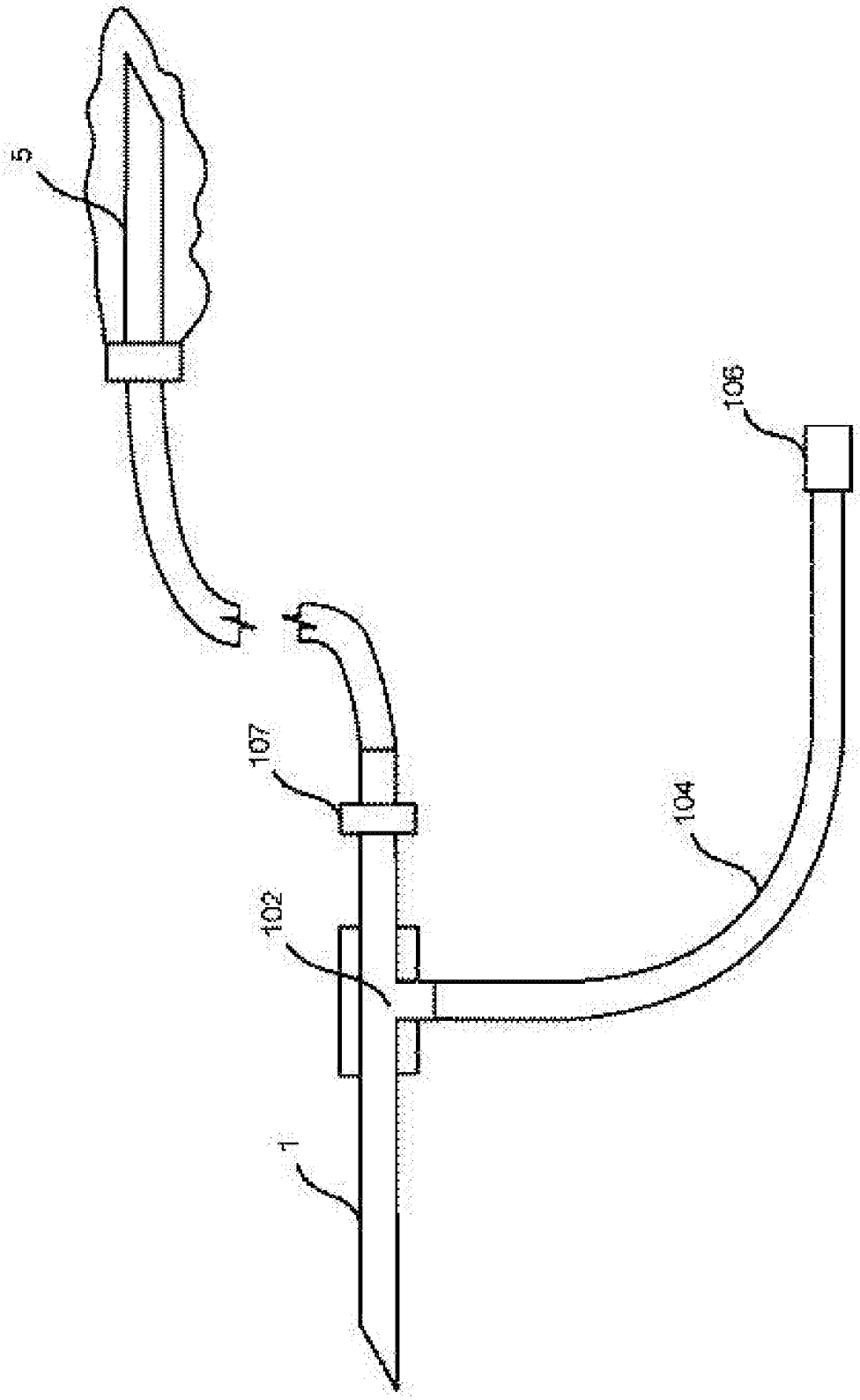


FIG. 4

[Figure 5]

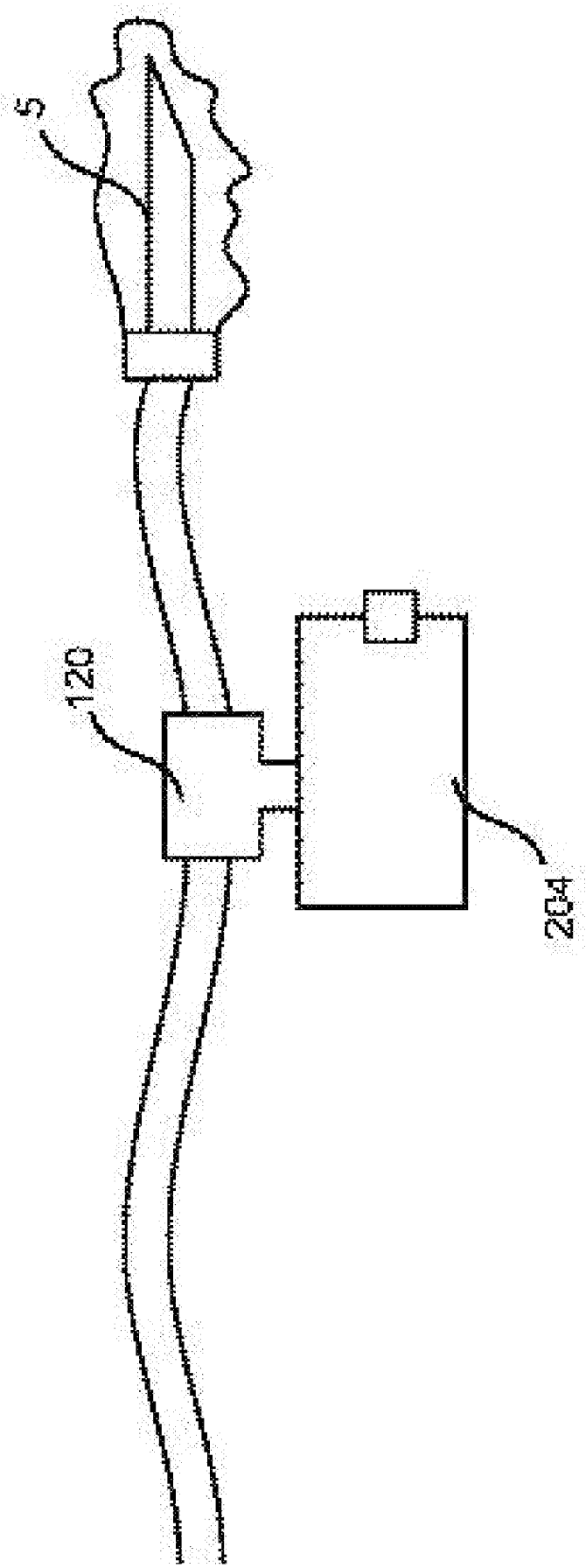
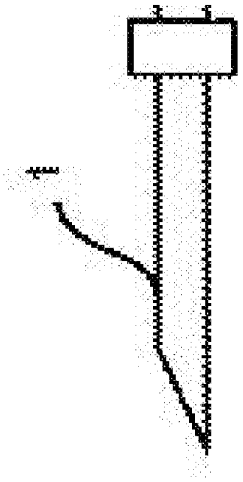


FIG. 5

[Fig. 6]



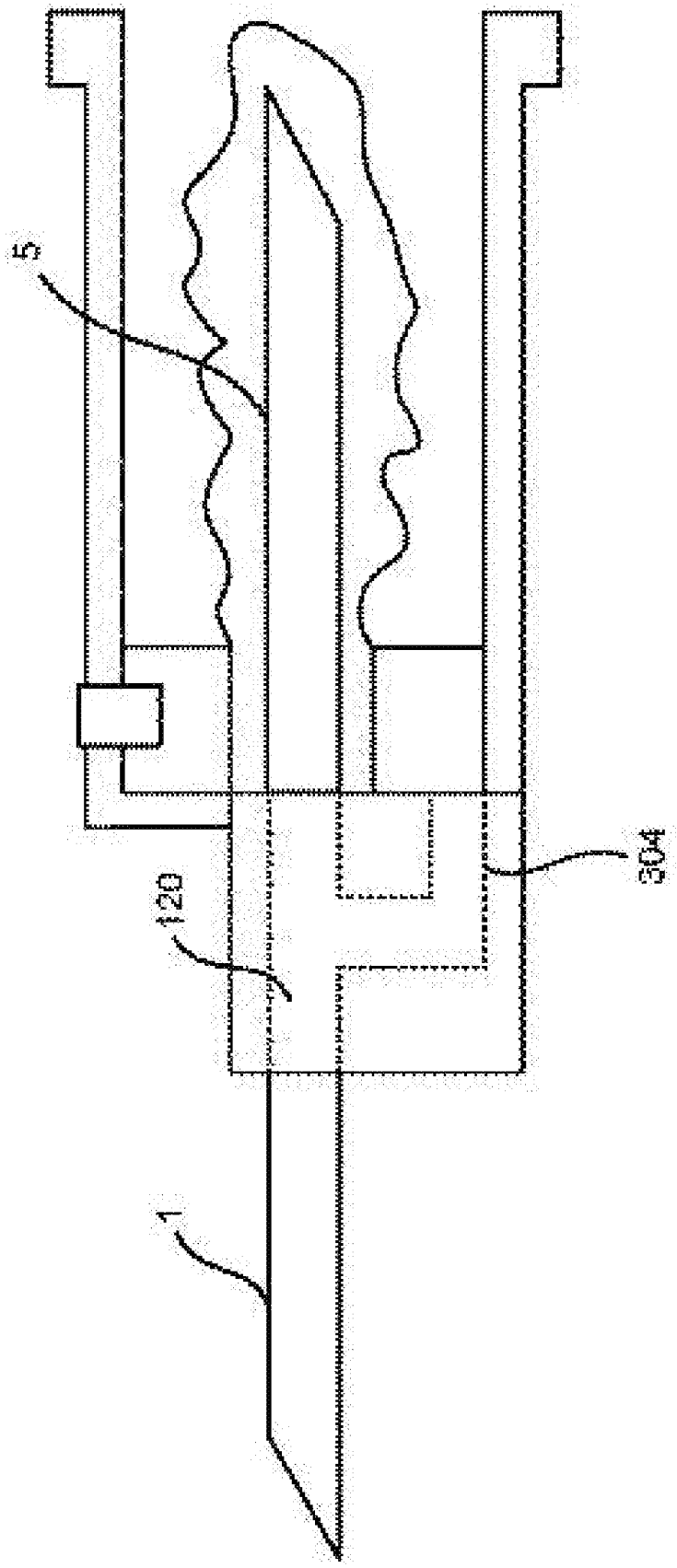


FIG. 6

[Fig. 7]

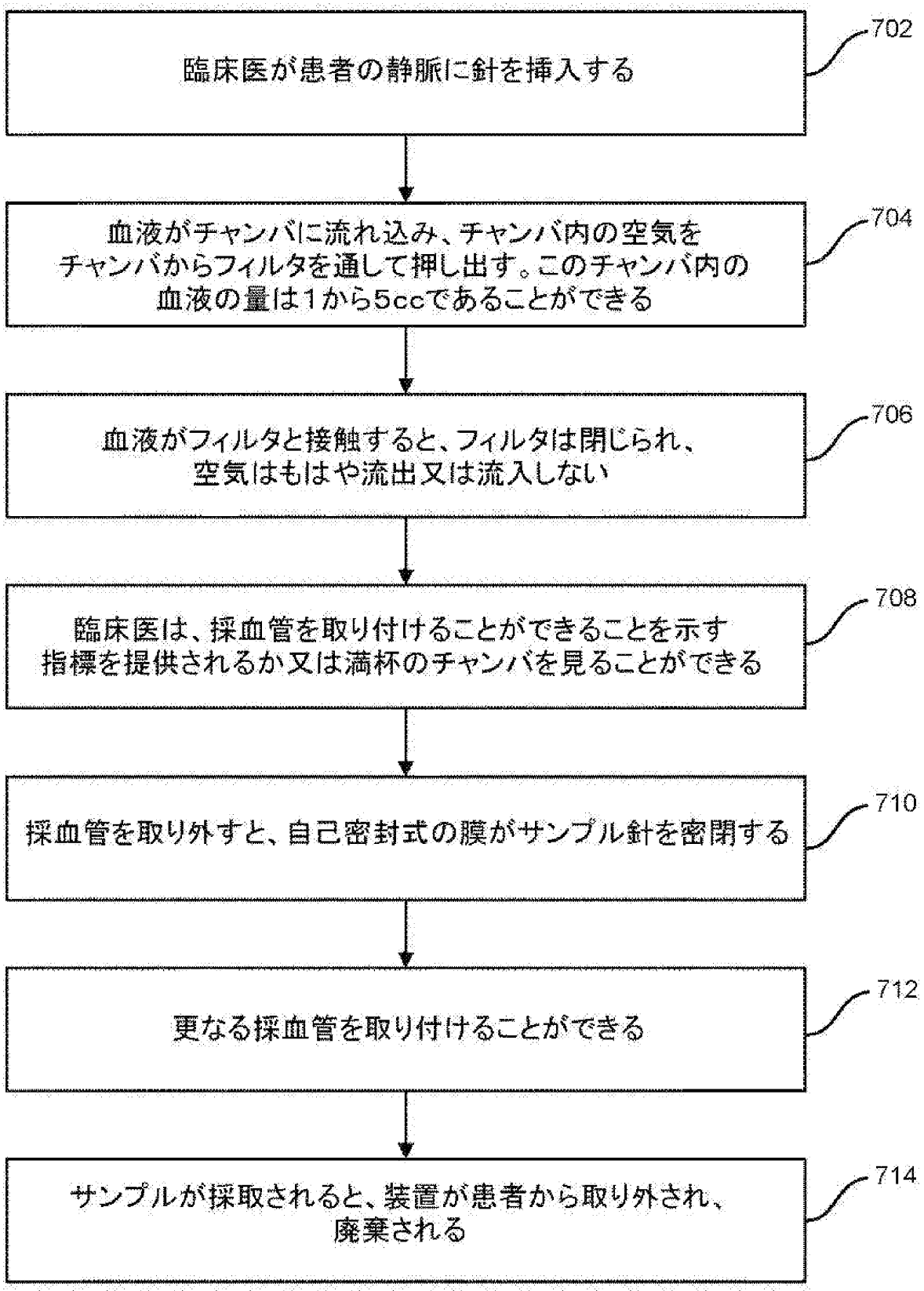
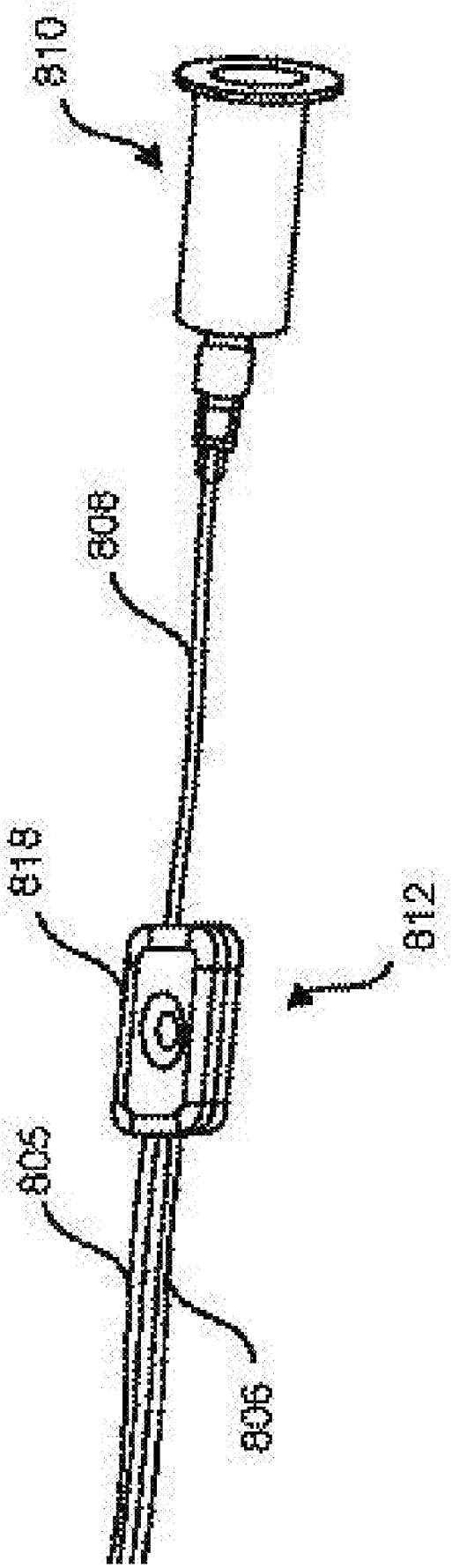

臨床医が患者の静脈に針を挿入する
702
血液がチャンバに流れ込み、チャンバ内の空気を
チャンバからフィルタを通して押し出す。このチャンバ内の
血液の量は1から5ccであることができる
704
血液がフィルタと接触すると、フィルタは閉じられ、
空気はもはや流出又は流入しない
706
臨床医は、採血管を取り付けることができることを示す
指標を提供されるか又は満杯のチャンバを見ることができる
708
採血管を取り外すと、自己密封式の膜がサンプル針を密閉する
710
更なる採血管を取り付けることができる
712
サンプルが採取されると、装置が患者から取り外され、
廃棄される
714

FIG. 7

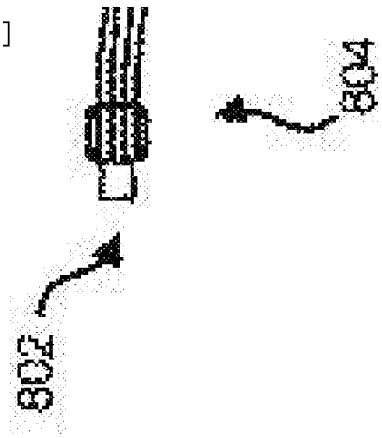
[Fig. 8A]



803

FIG. 8A

[Fig. 8B]



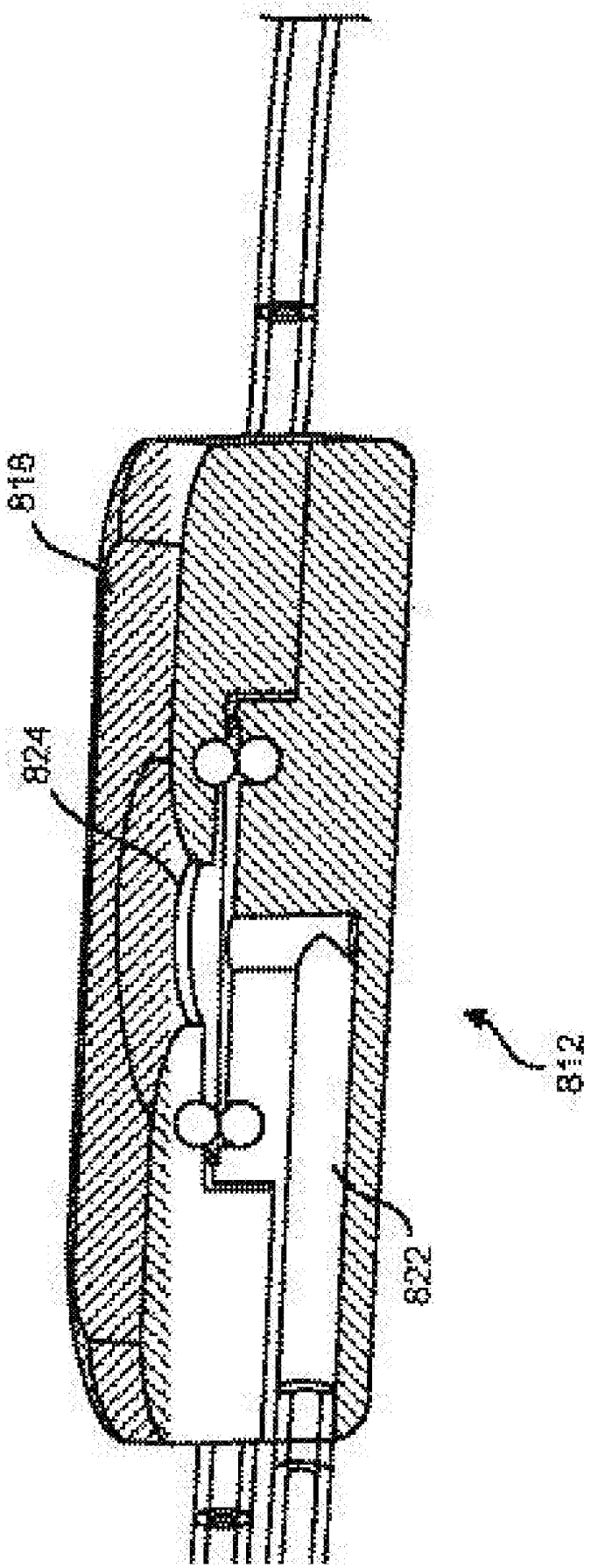
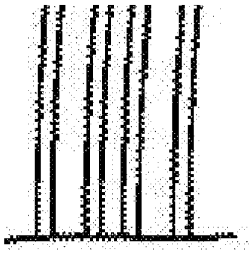


FIG. 8B

[Fig. 8C]



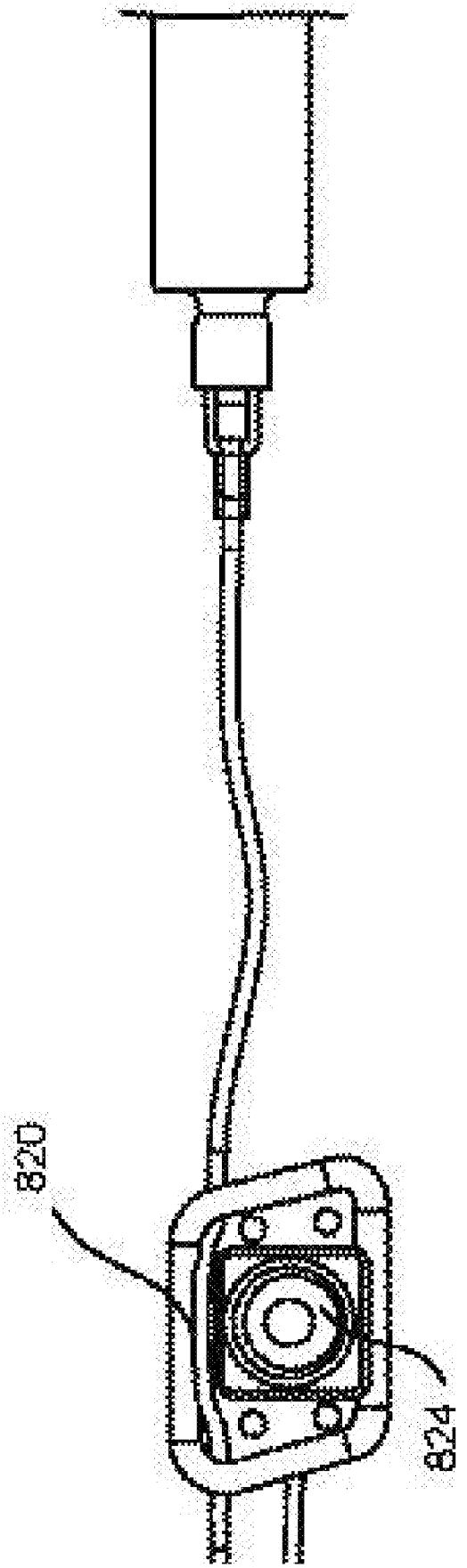
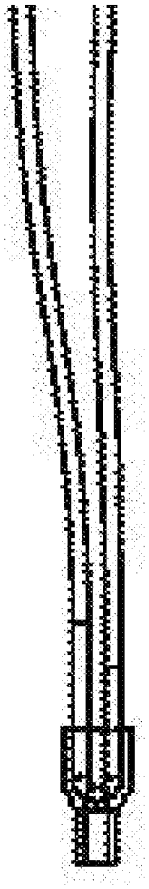


FIG. 8C

[Fig. 8D]



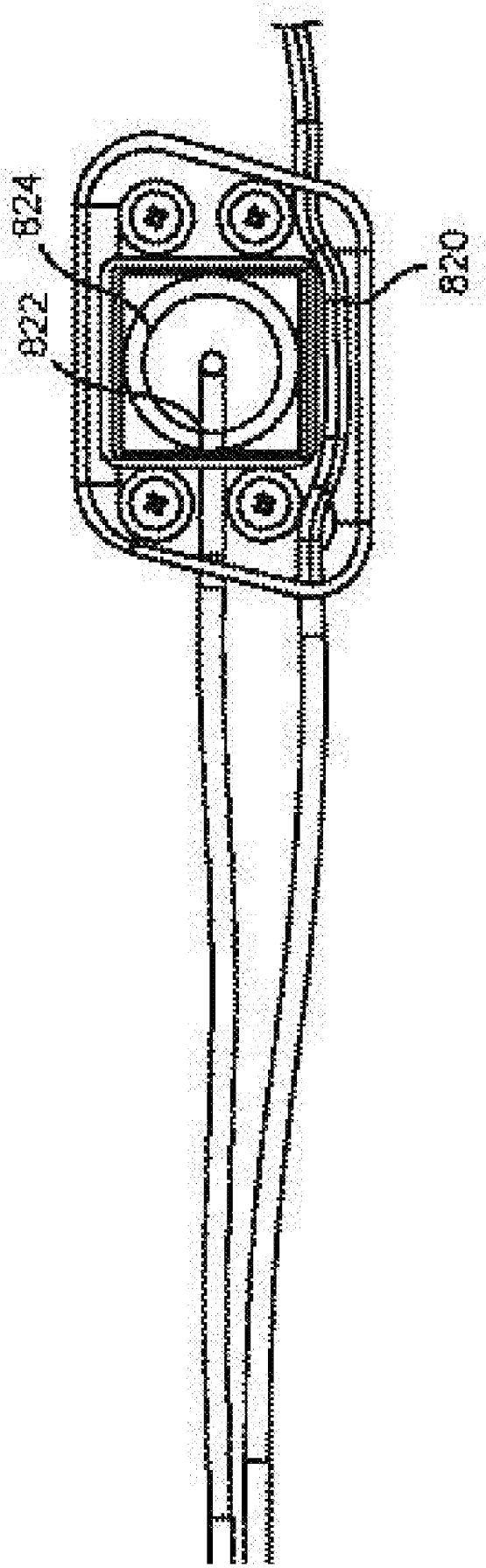
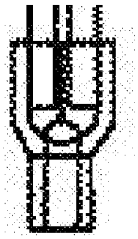


FIG. 8D

[Fig. 8E]



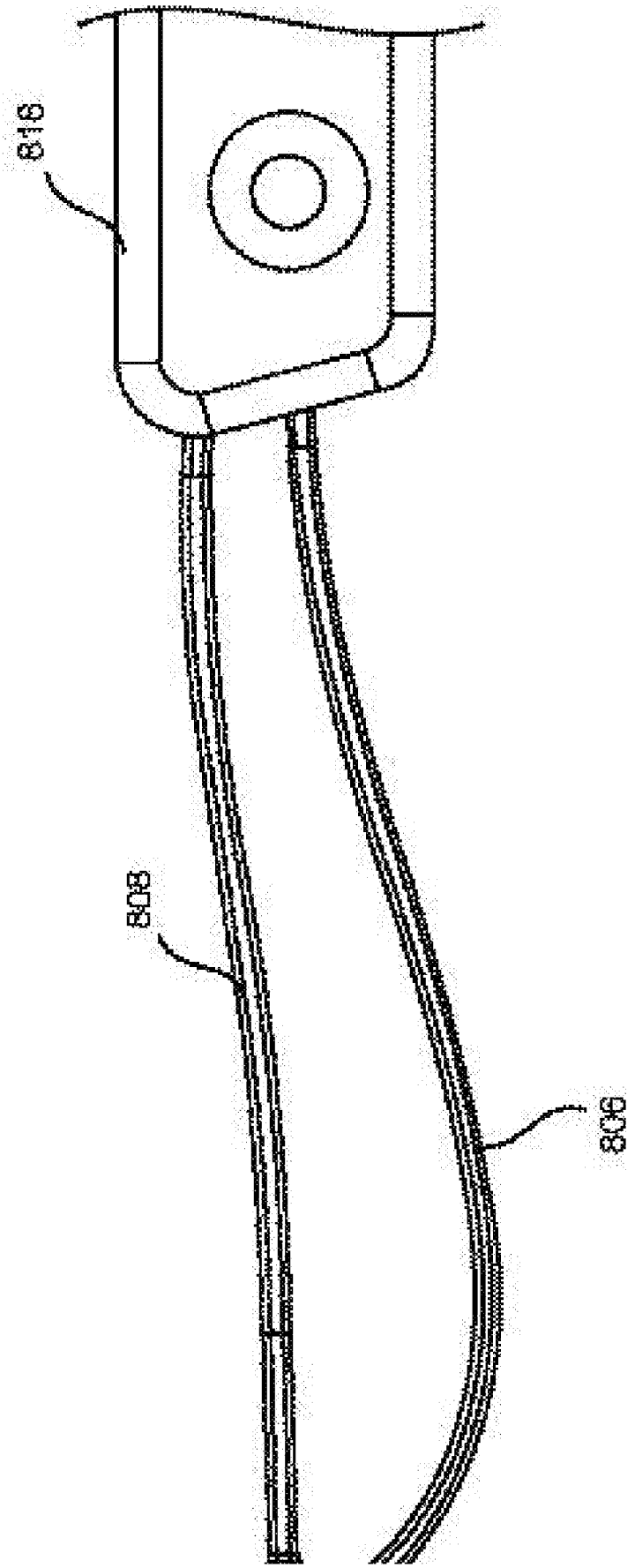
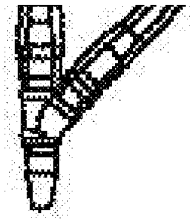


FIG. 8E

[Fig. 9]



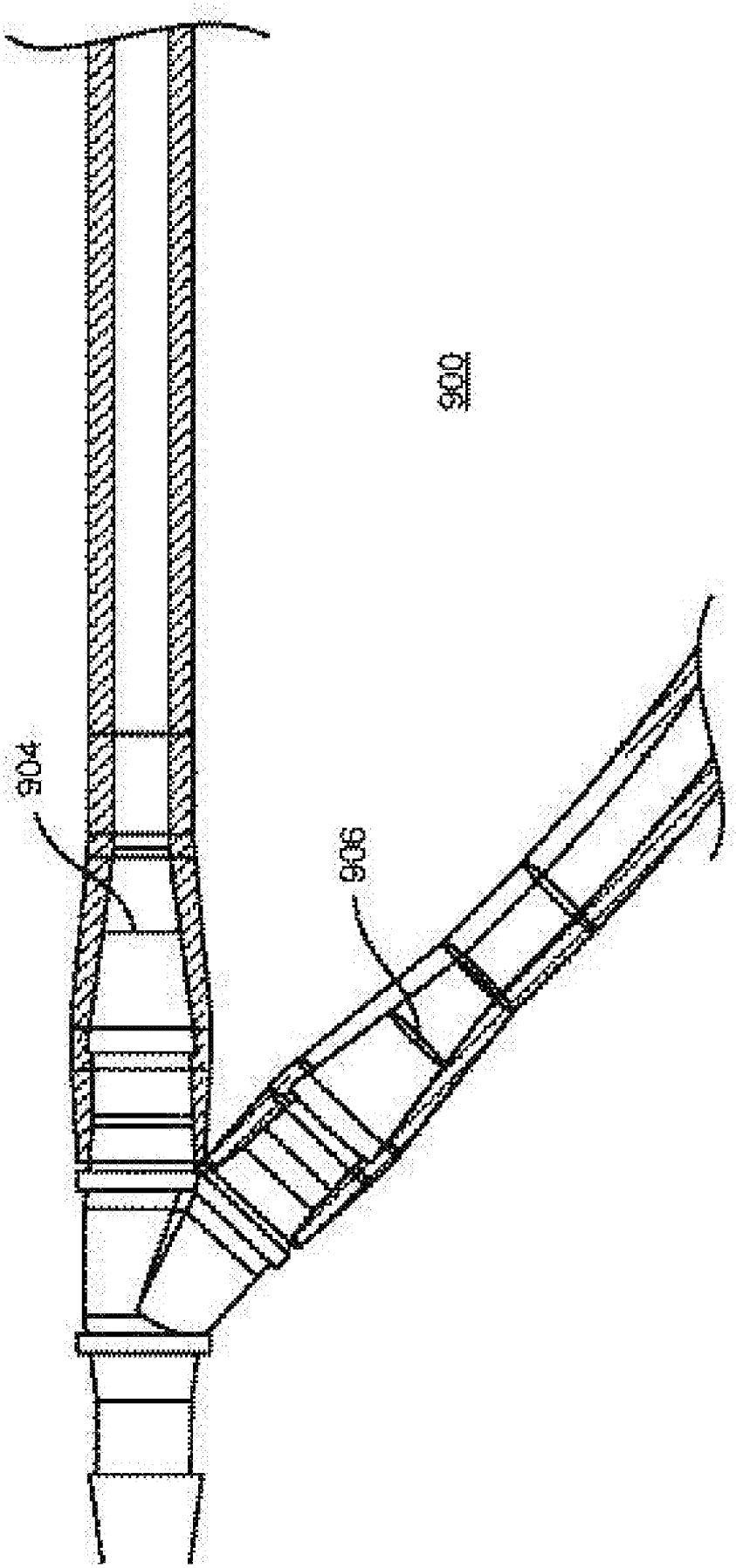


FIG. 9

[Fig. 10A]

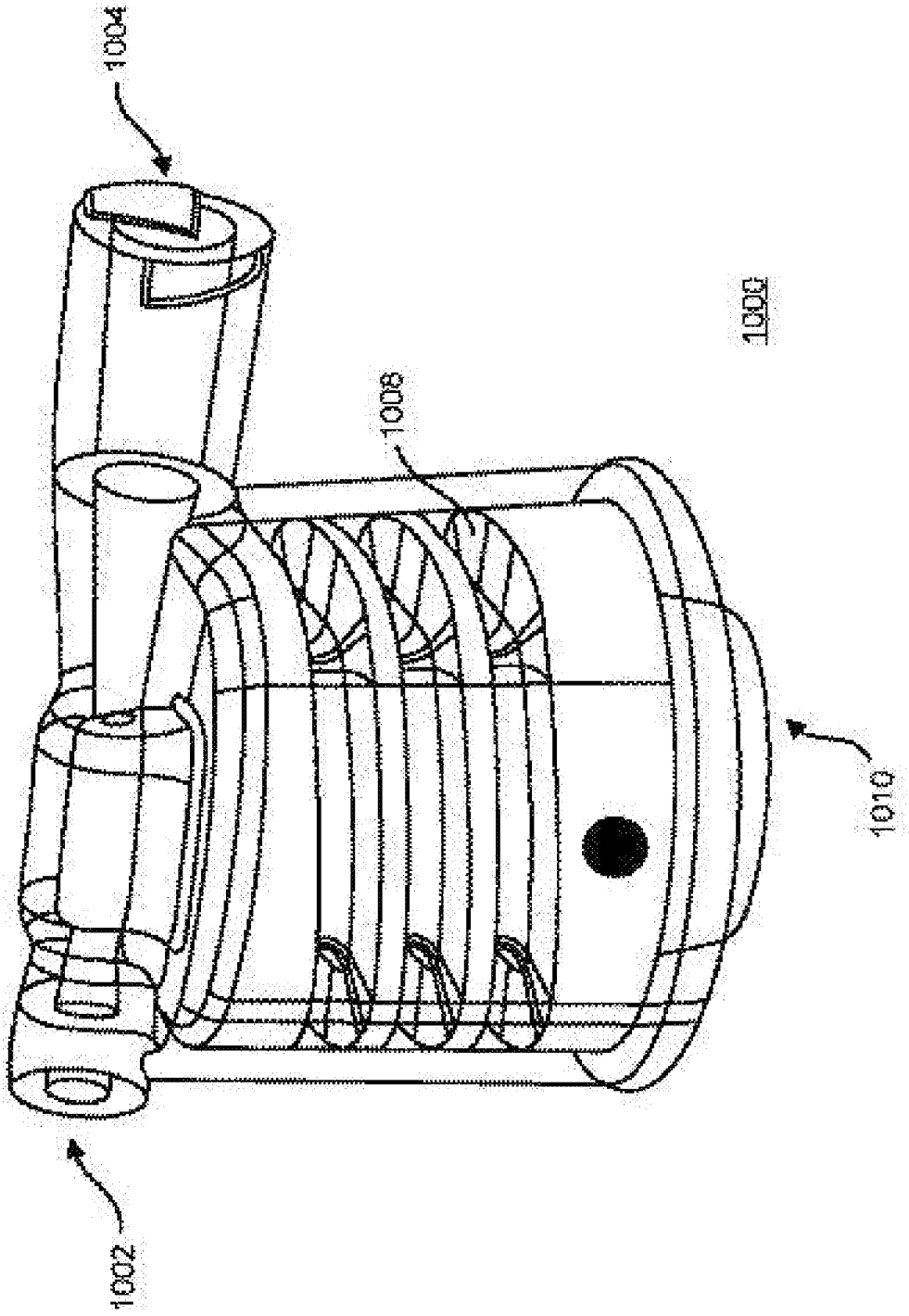


FIG. 10A

[Fig. 10B]

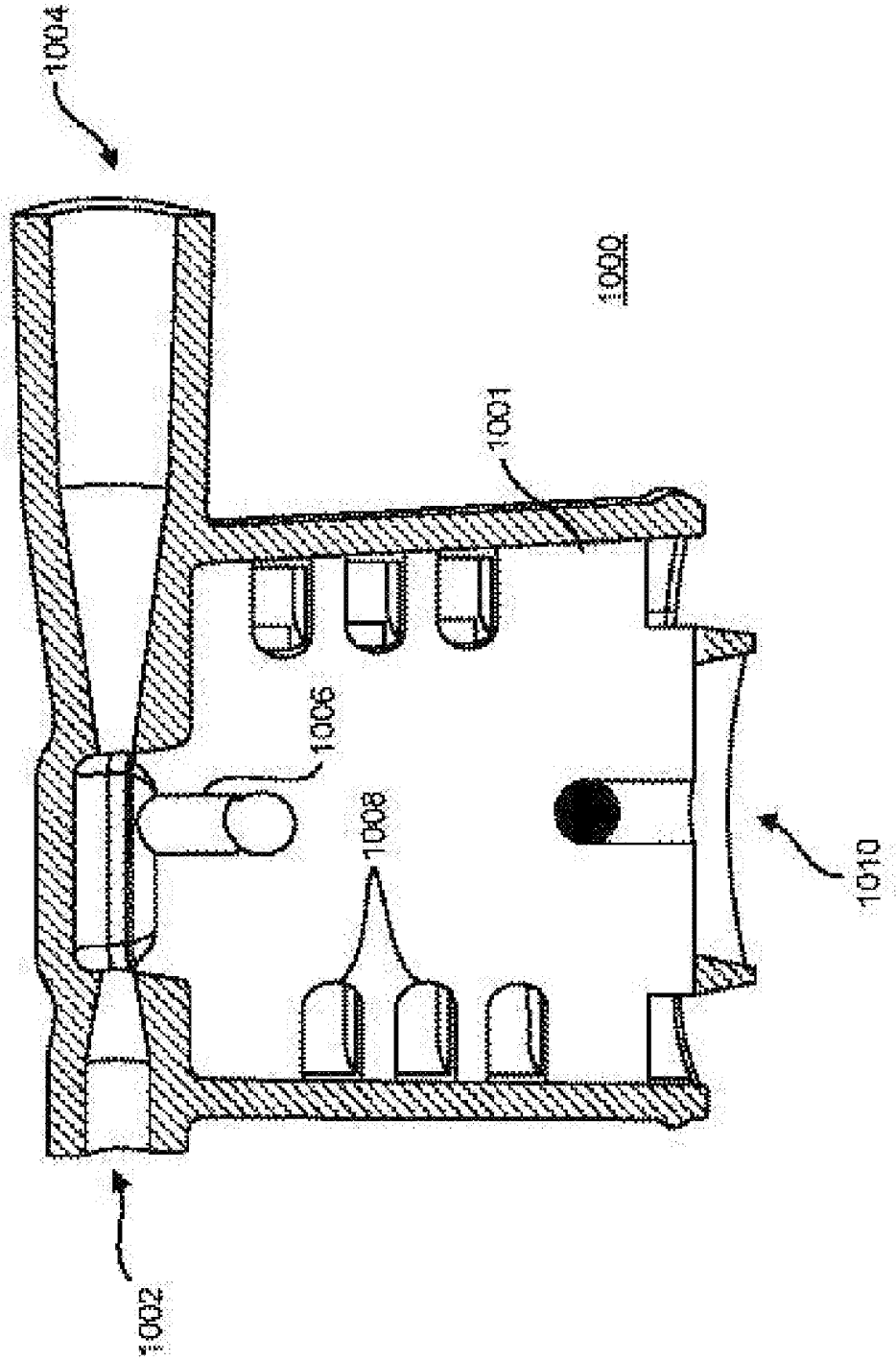
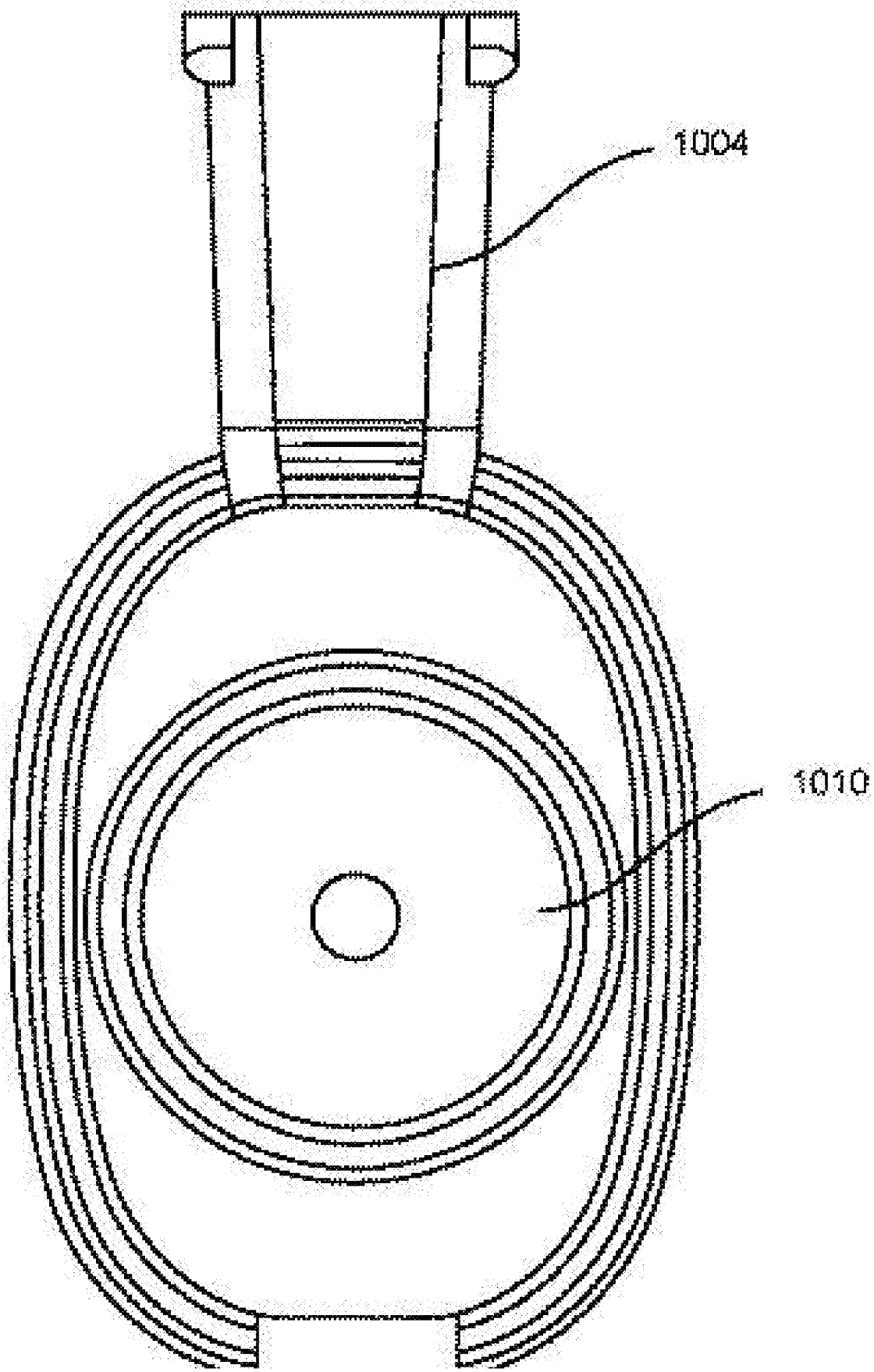


FIG. 10B

[Fig. 10C]


1004
1010

[Fig. 10D]

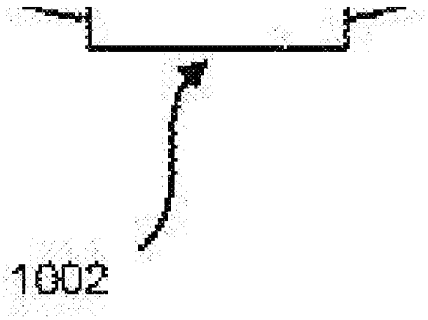
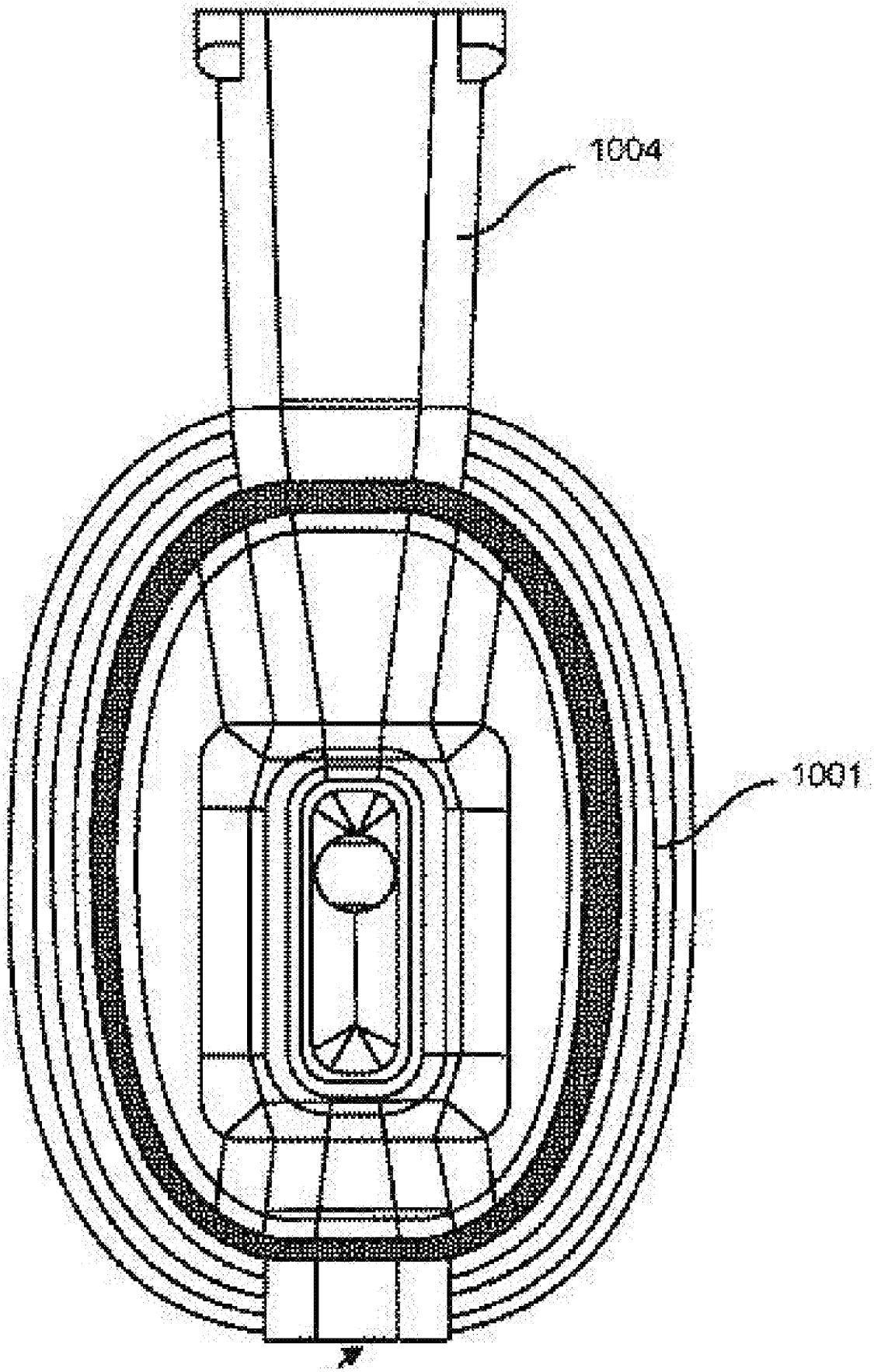


FIG. 10C


1004
1001

[Fig. 11A]

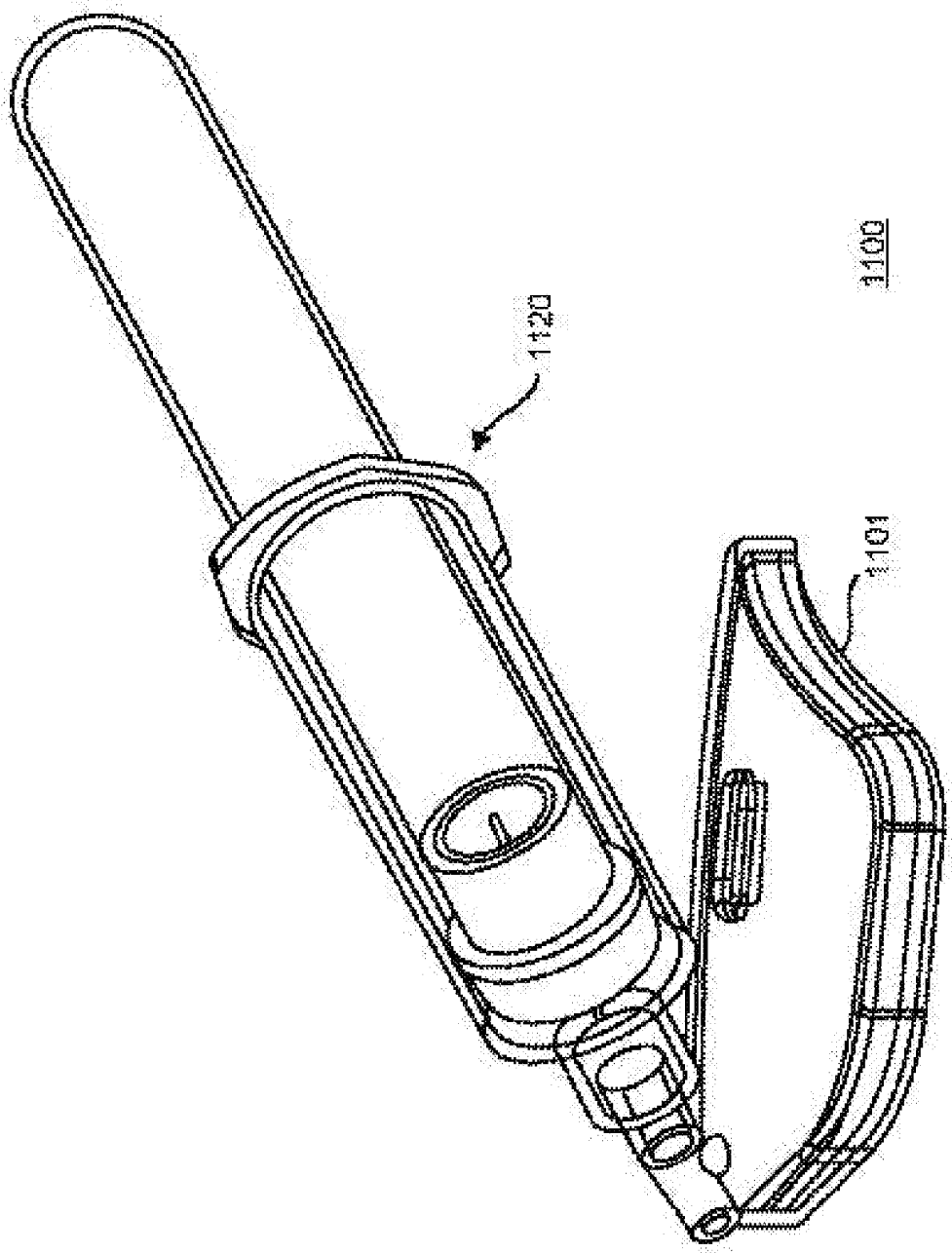


FIG. 11A

[Fig. 11B]

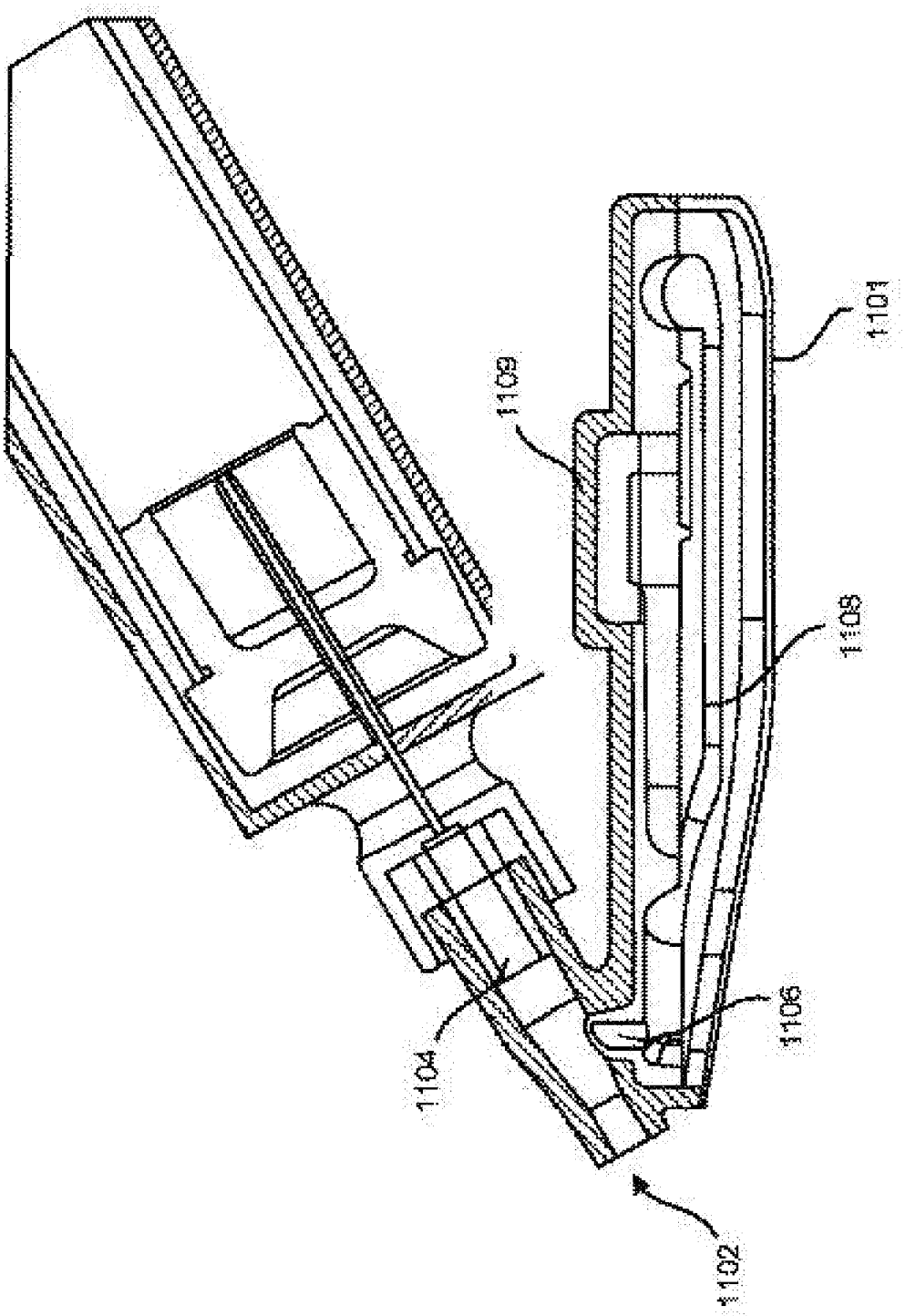
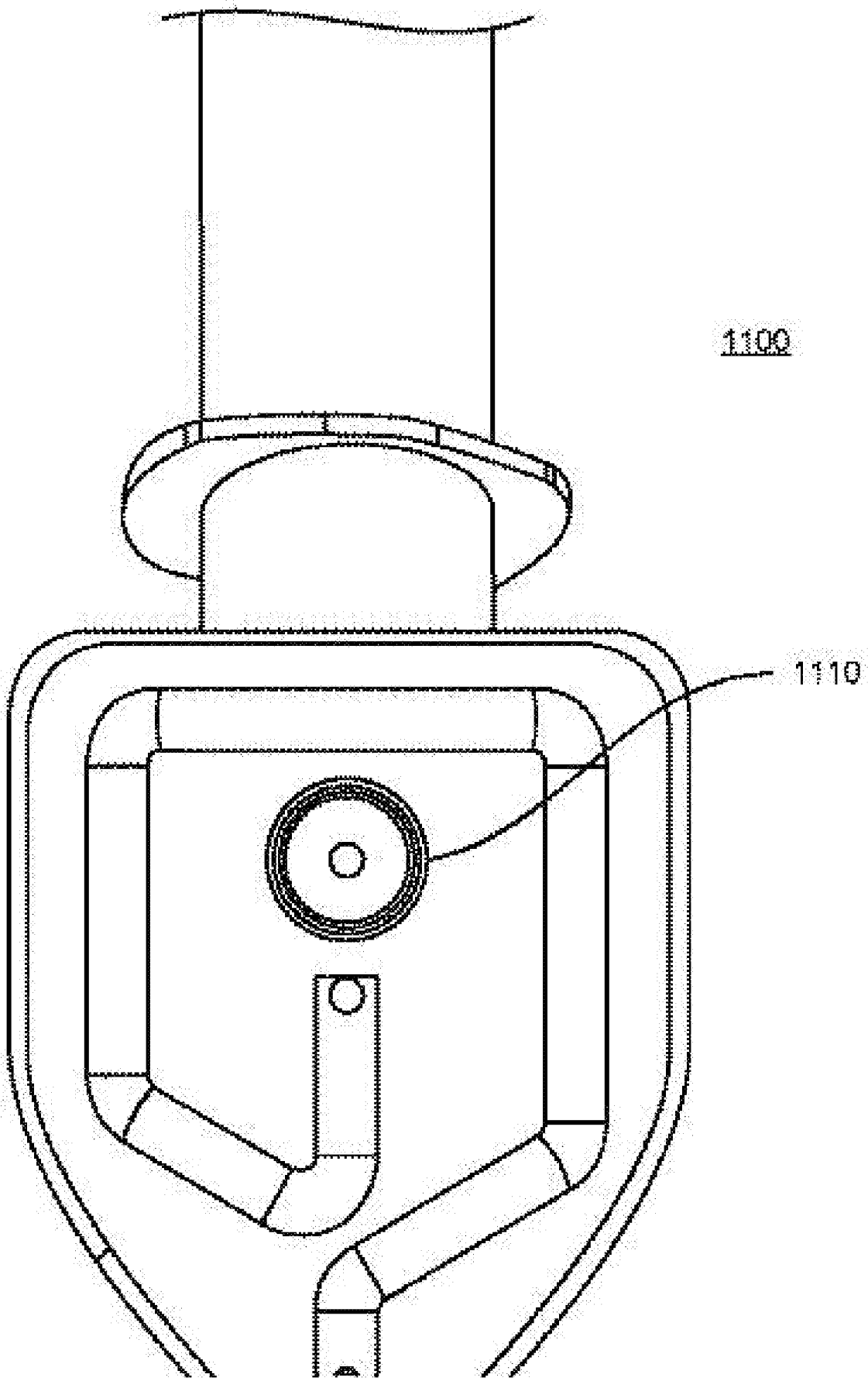


FIG. 11B

[Fig. 11C]


1100
1110

[Fig. 11D]

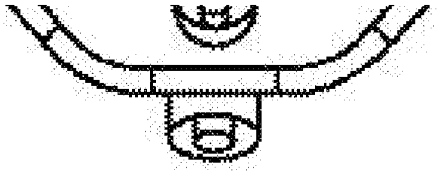
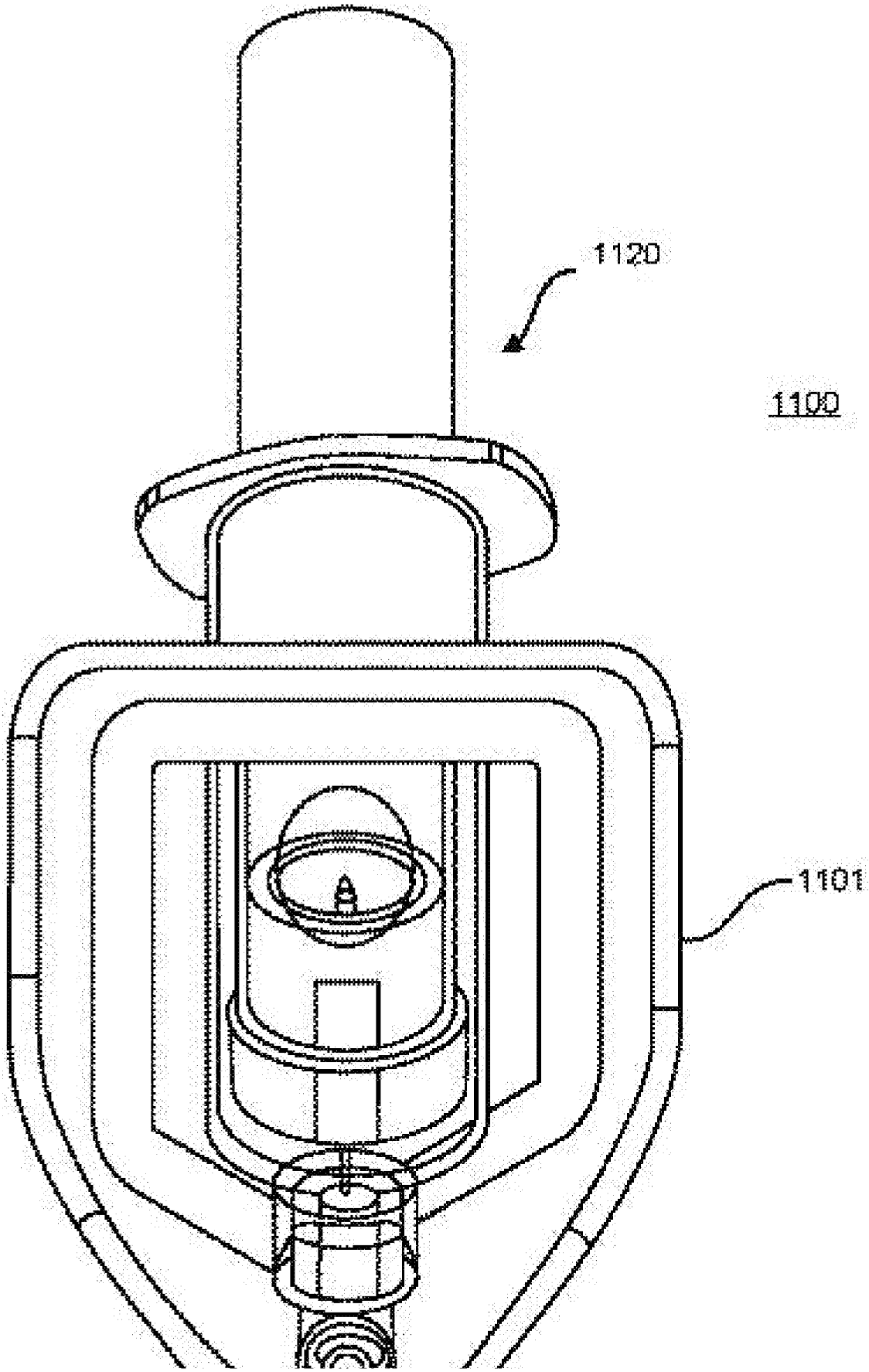


FIG. 11C


1120
1100
1101

[Fig. 11E]

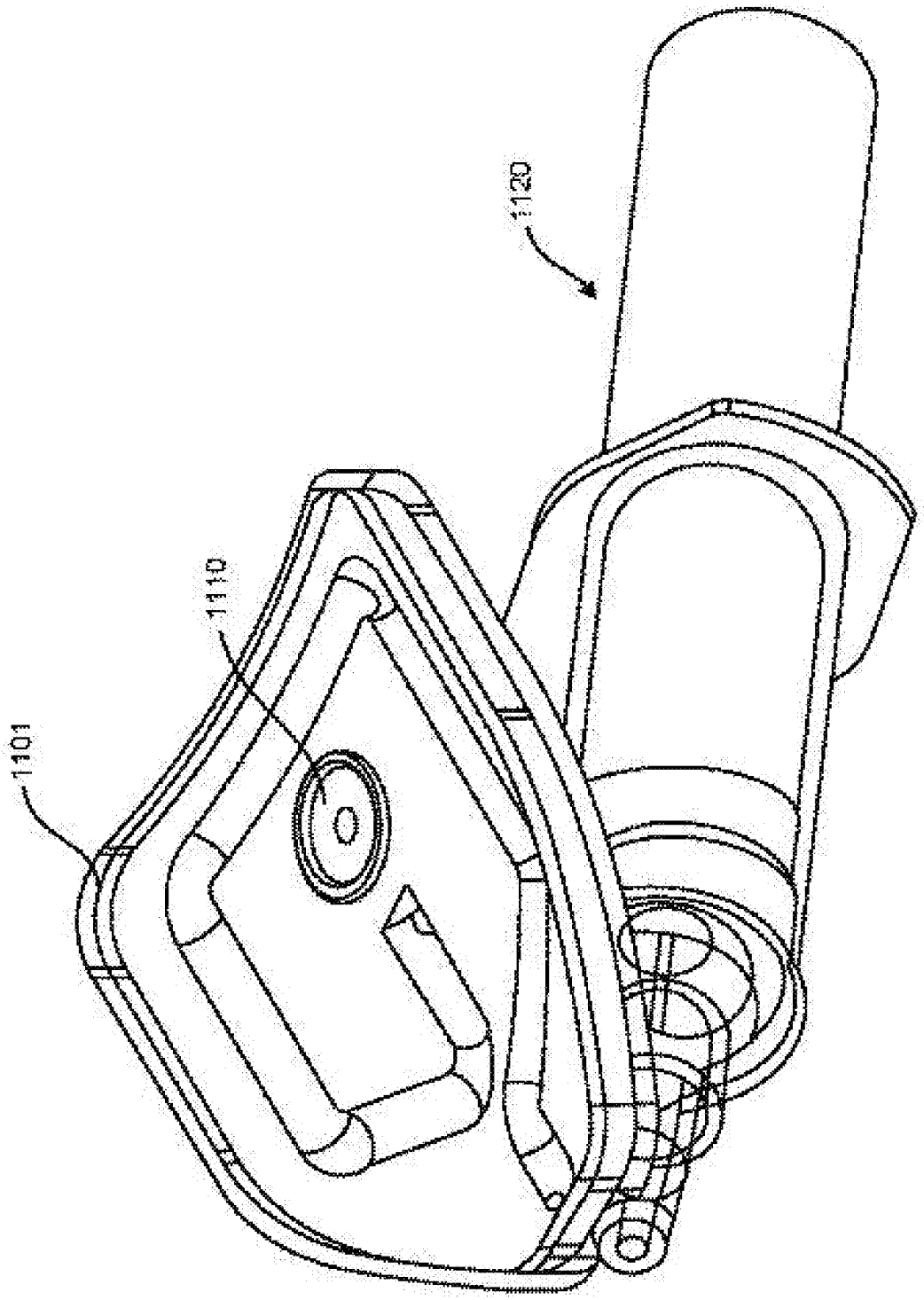


FIG. 11E

[Fig. 12A]

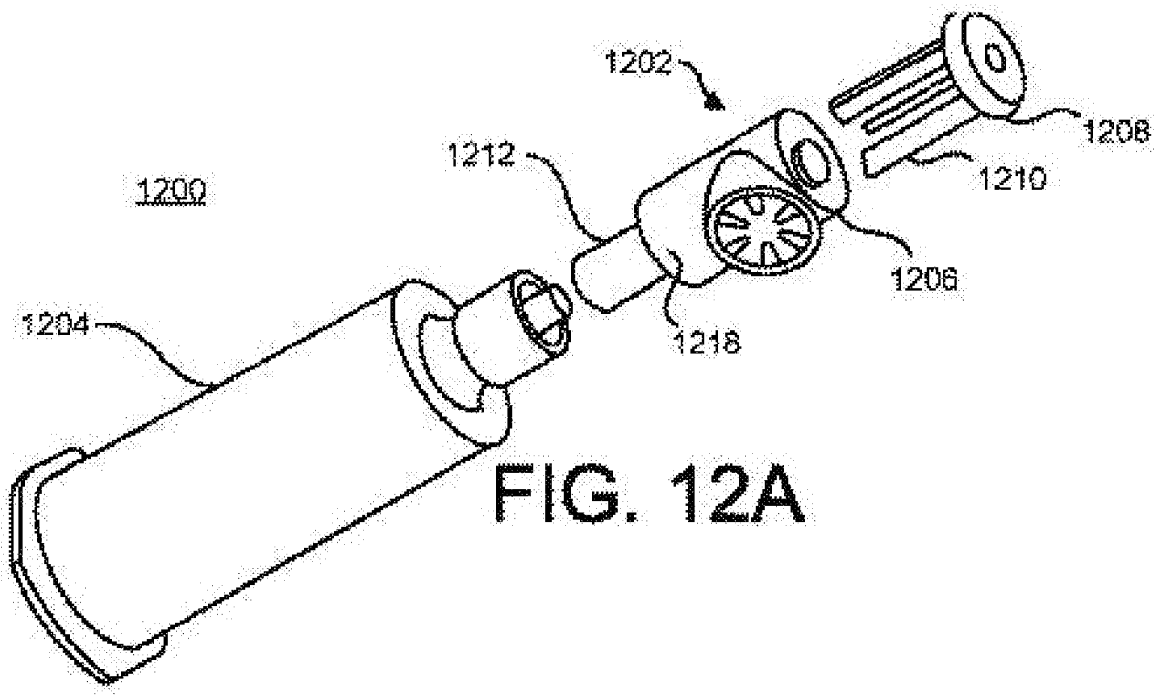


FIG. 12A

[Fig. 12B]

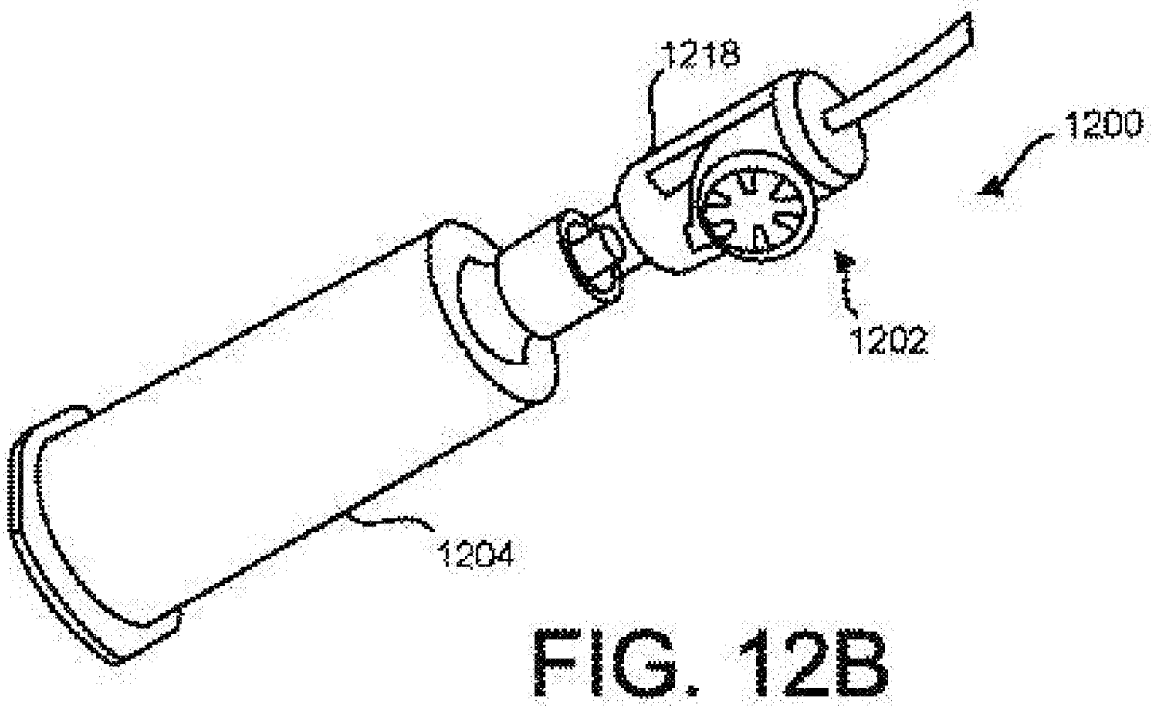


FIG. 12B

[Fig. 12C]

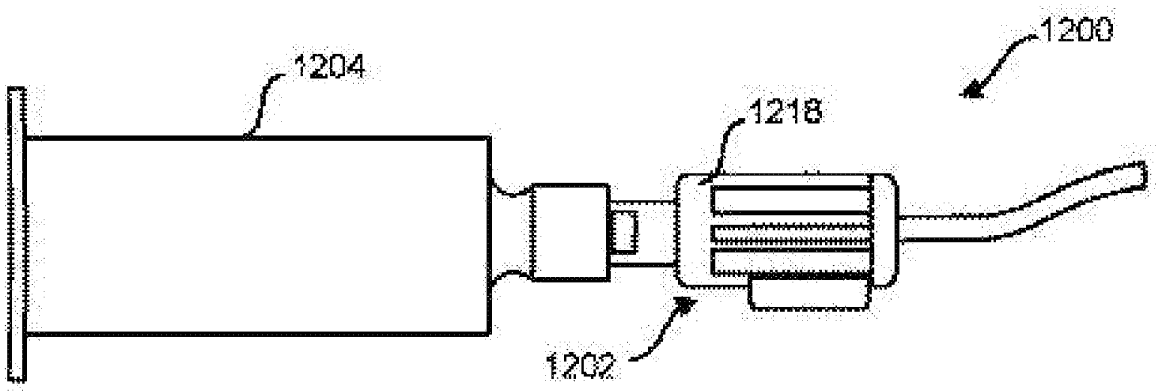


FIG. 12C

[Fig. 12D]

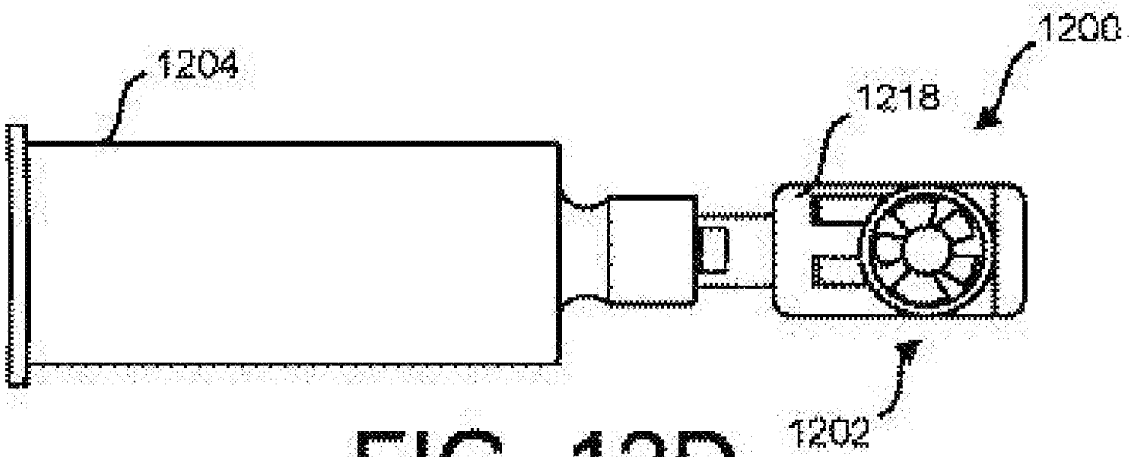


FIG. 12D

[Fig. 13A]

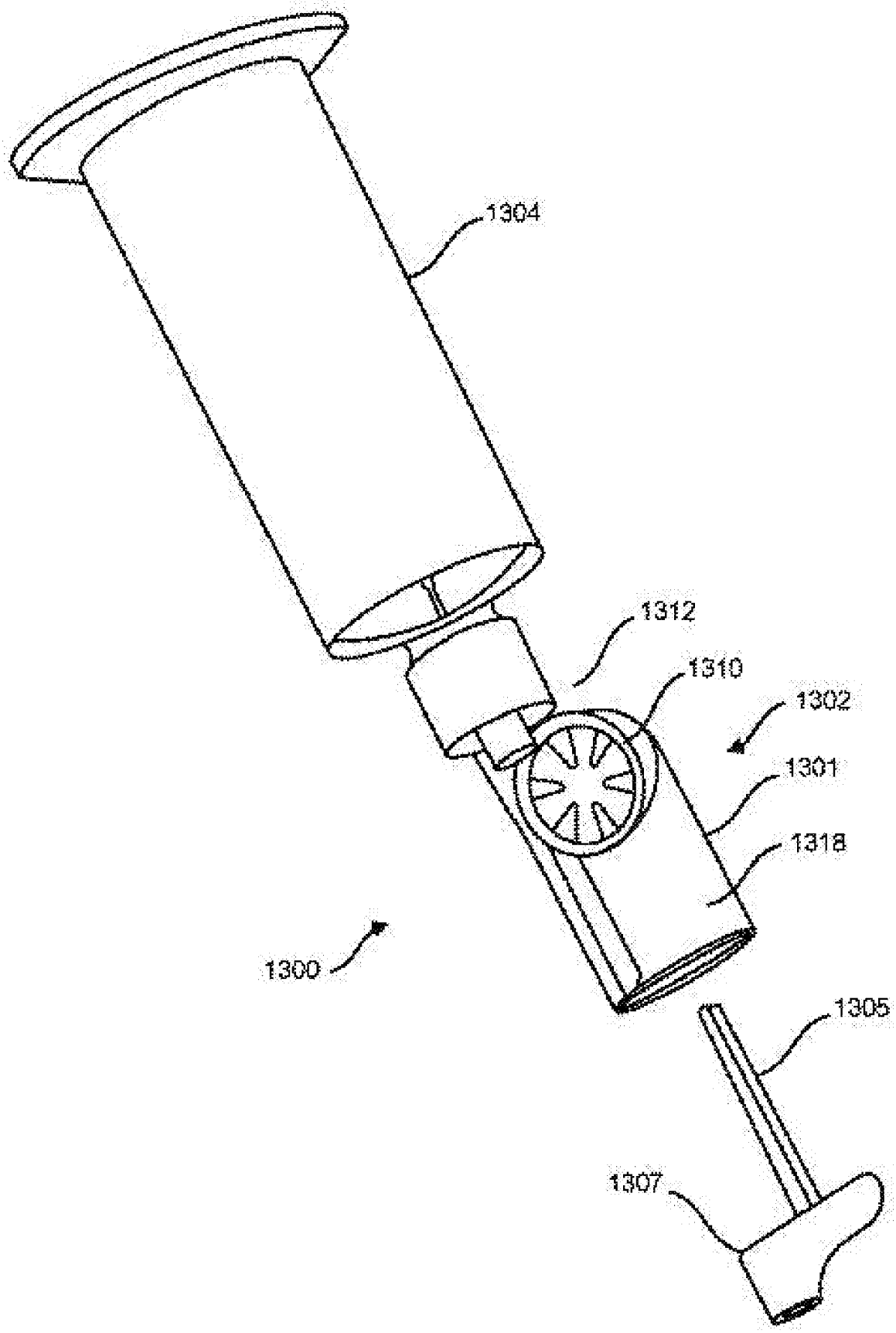


FIG. 13A

[Fig. 13B]

FIG. 13A

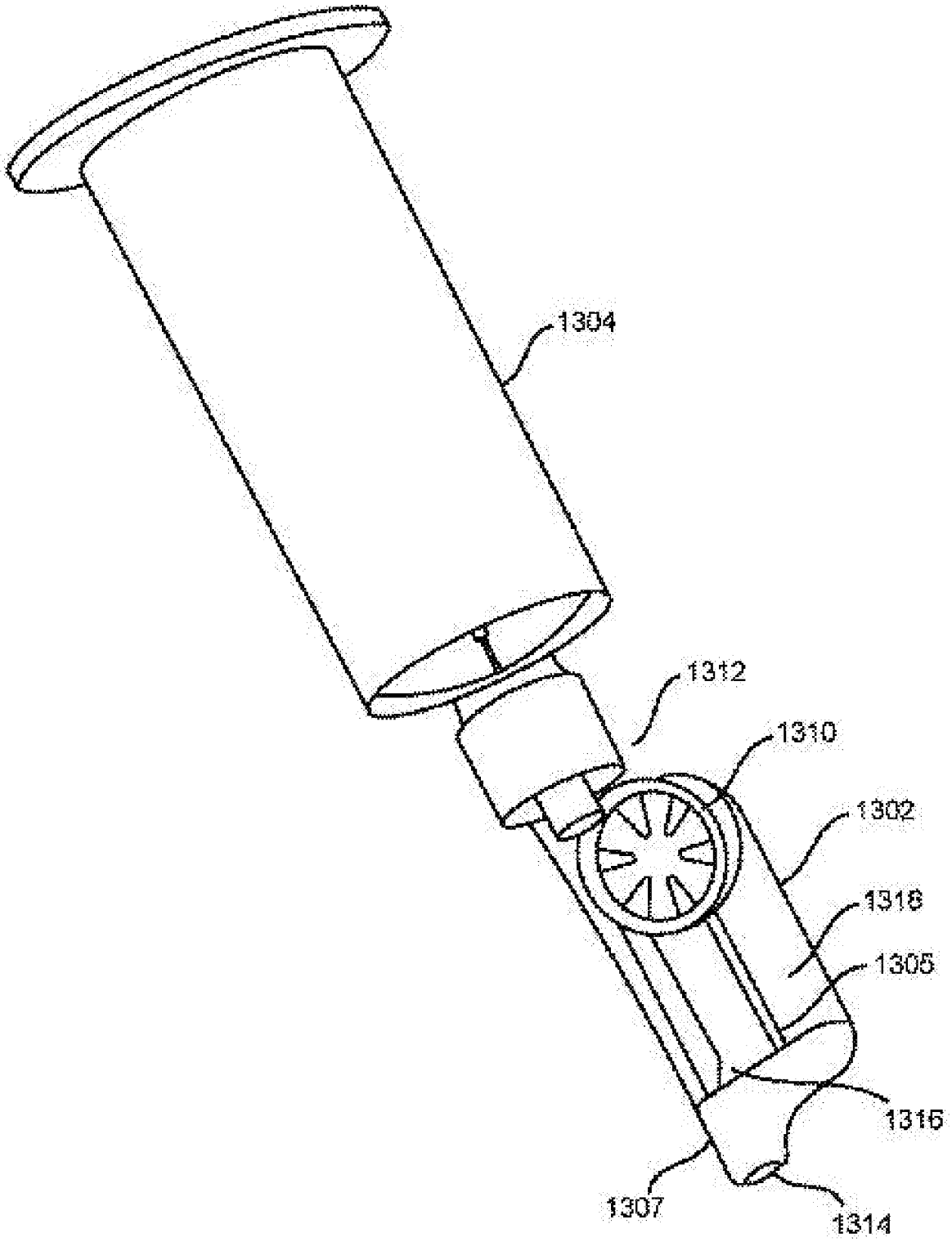


FIG. 13B

[Fig. 13C]

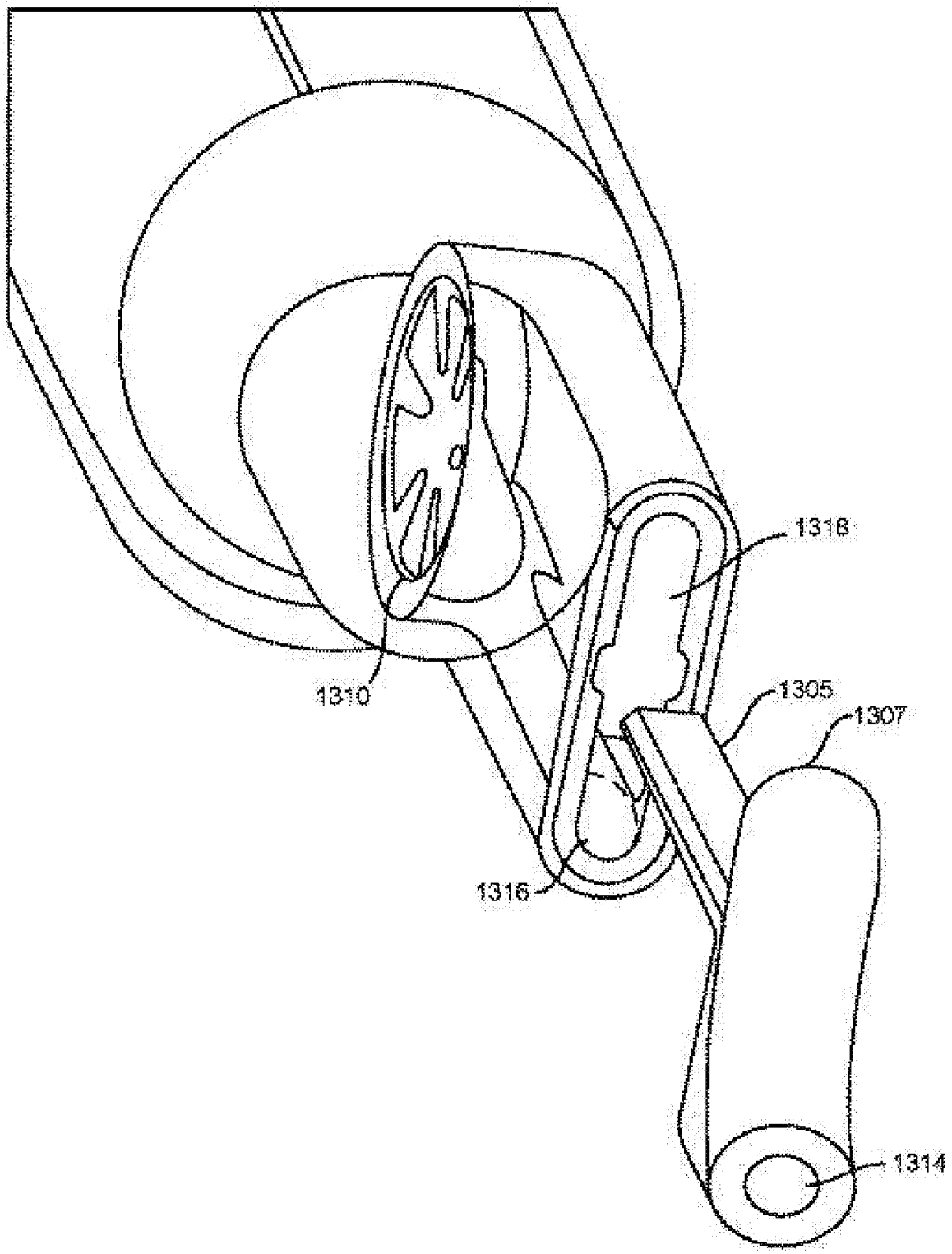
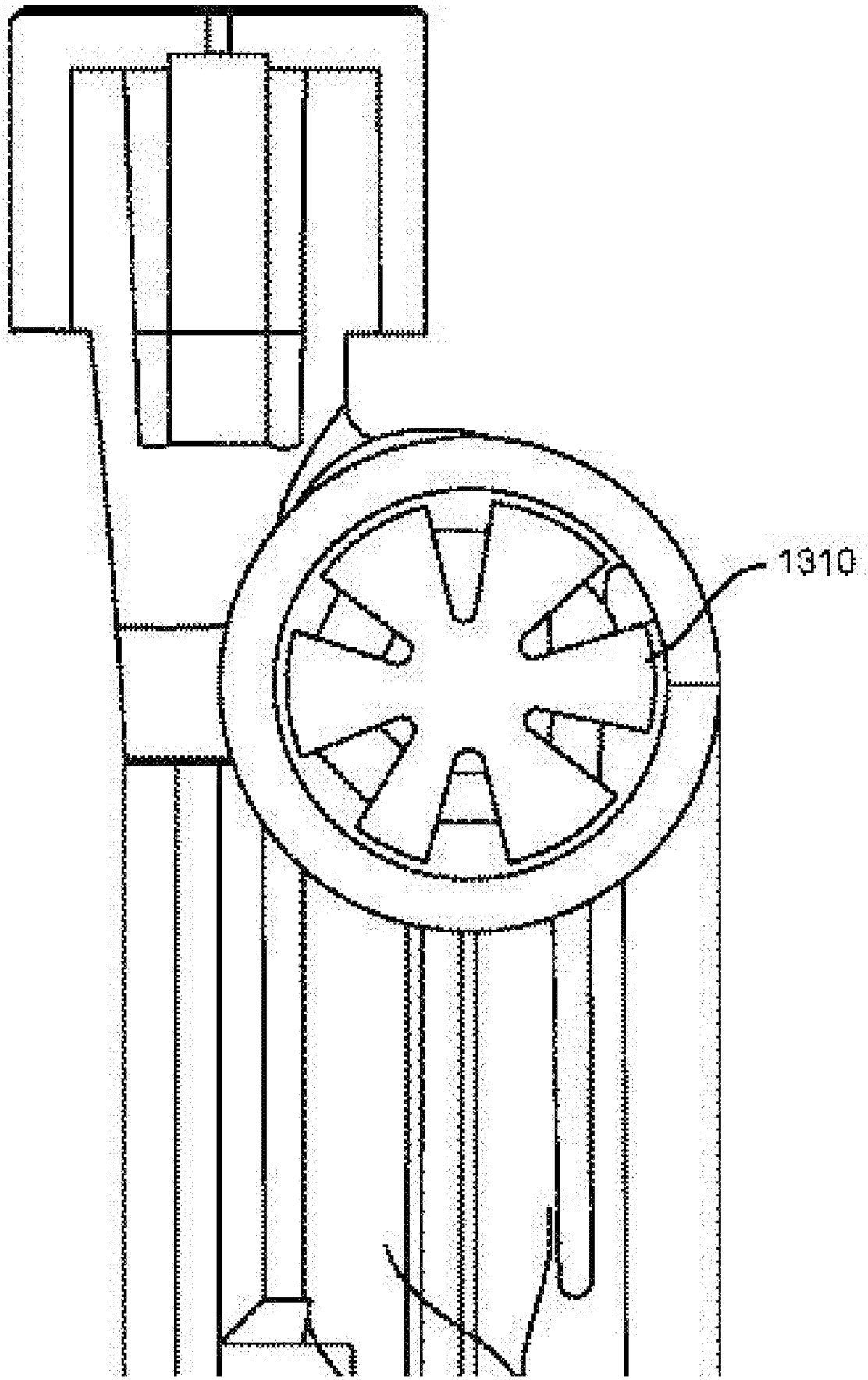


FIG. 13C

[Fig. 13D]


1310

[Fig. 14A]

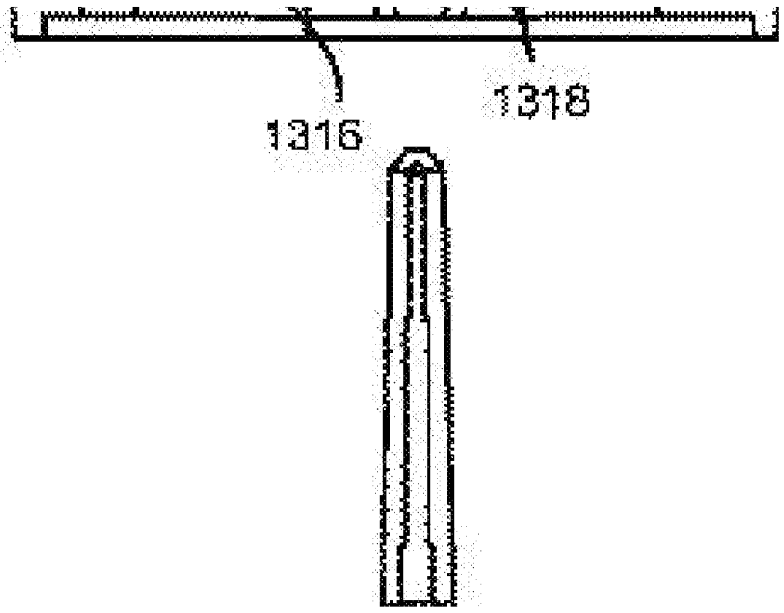
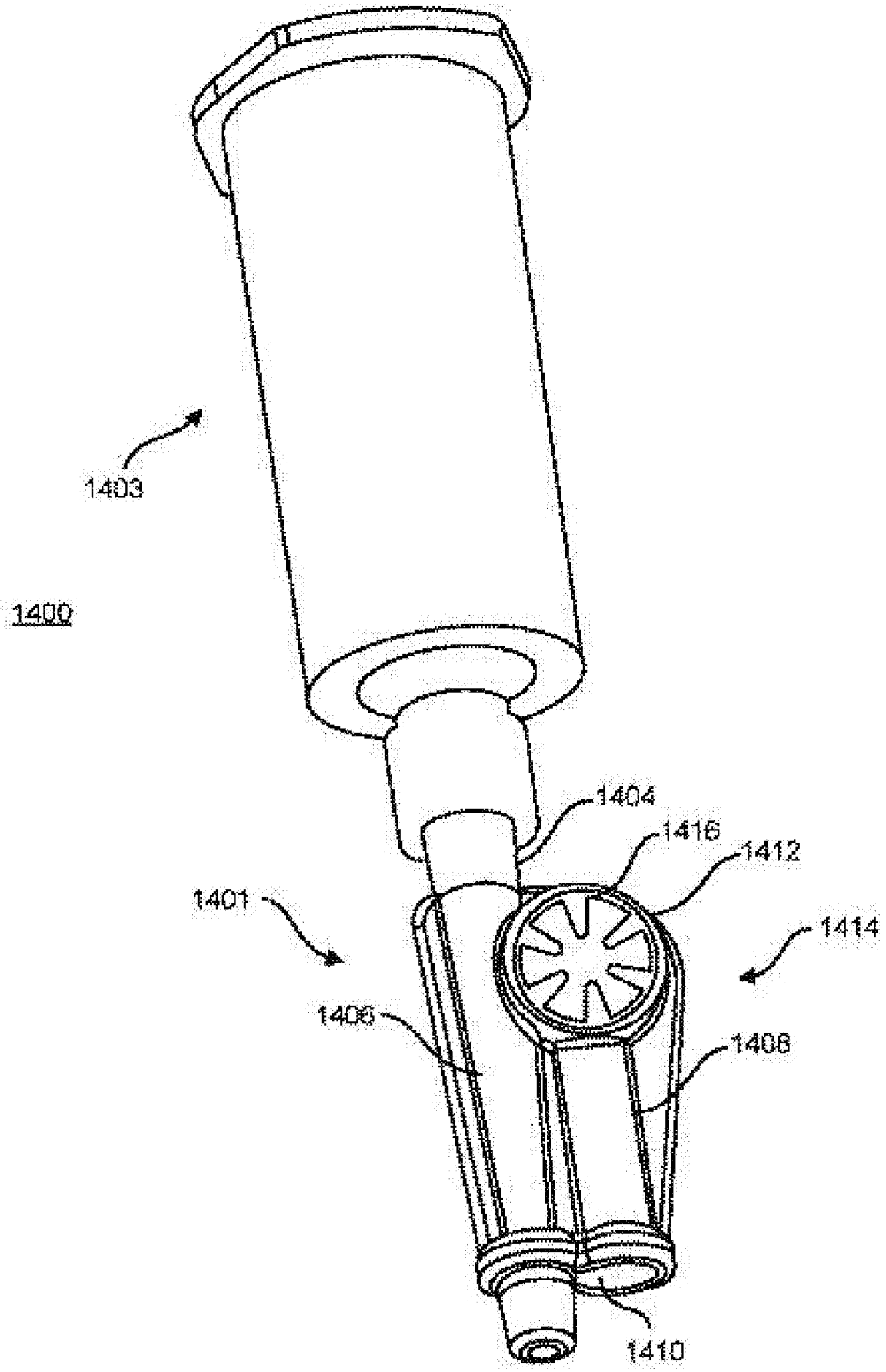


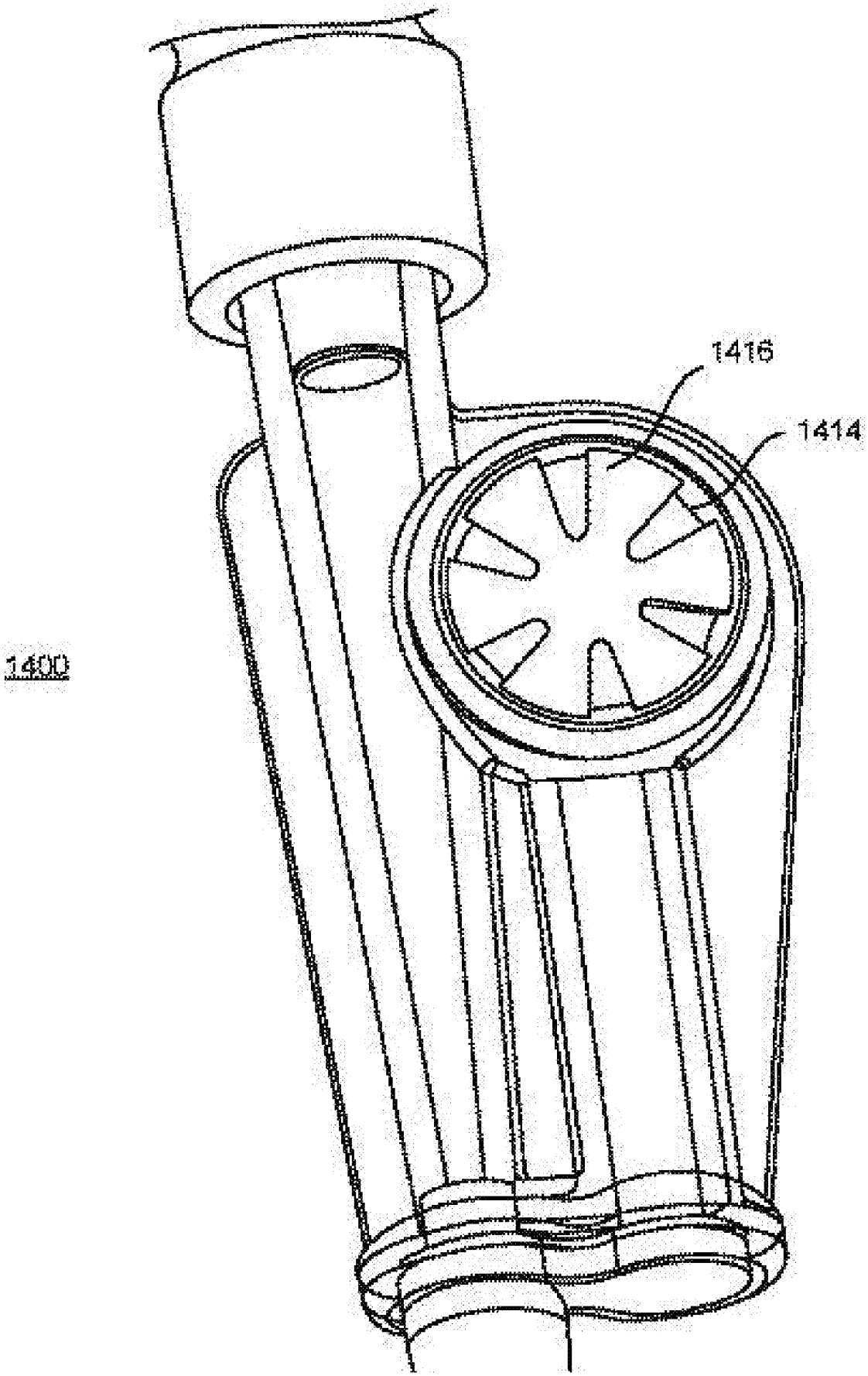
FIG. 13D


1403
1400
1404
1416
1412
1401
1414
1406
1408
1410

[Fig. 14B]



FIG. 14A


1416
1414
1400

[Fig. 14C]



FIG. 14B

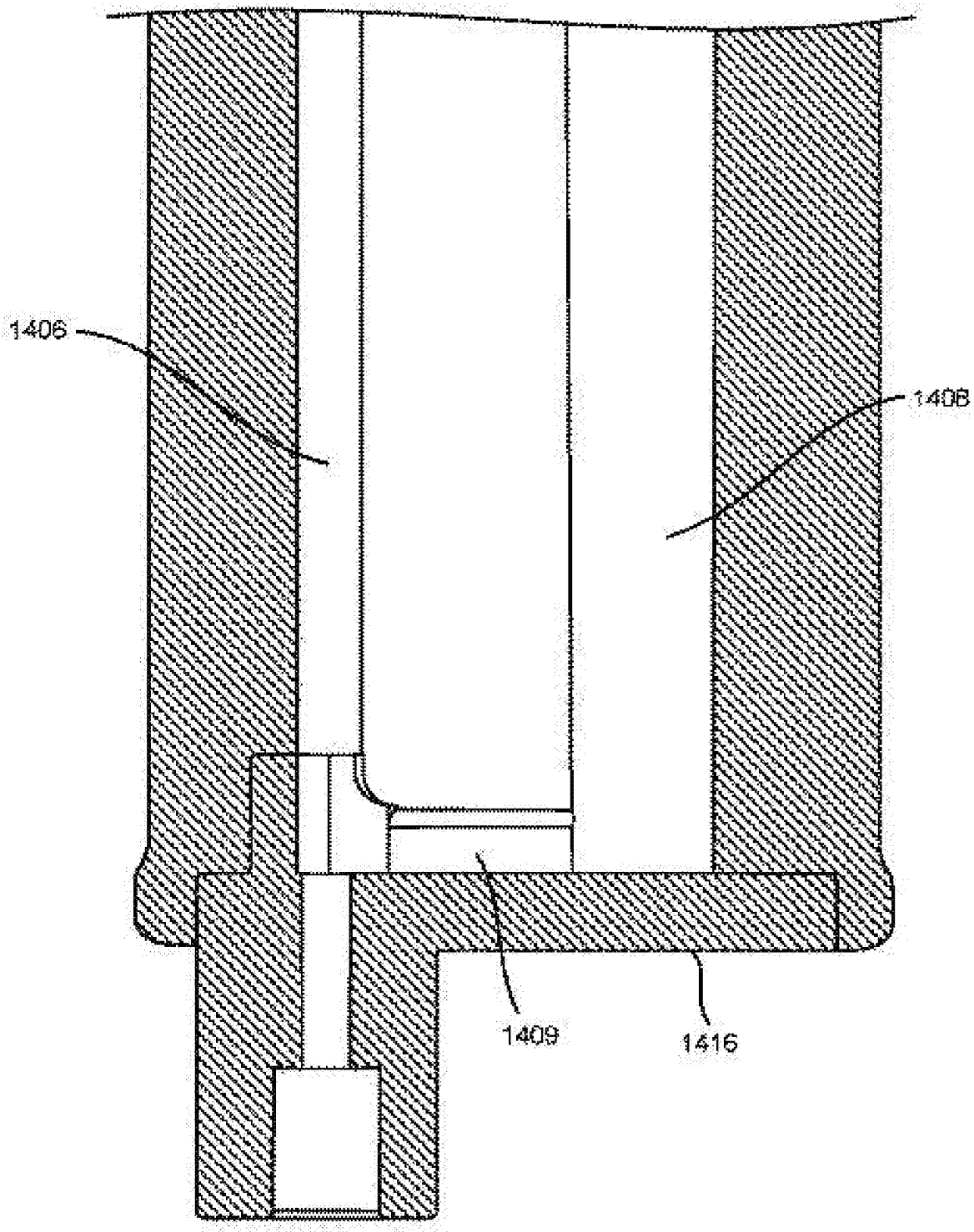
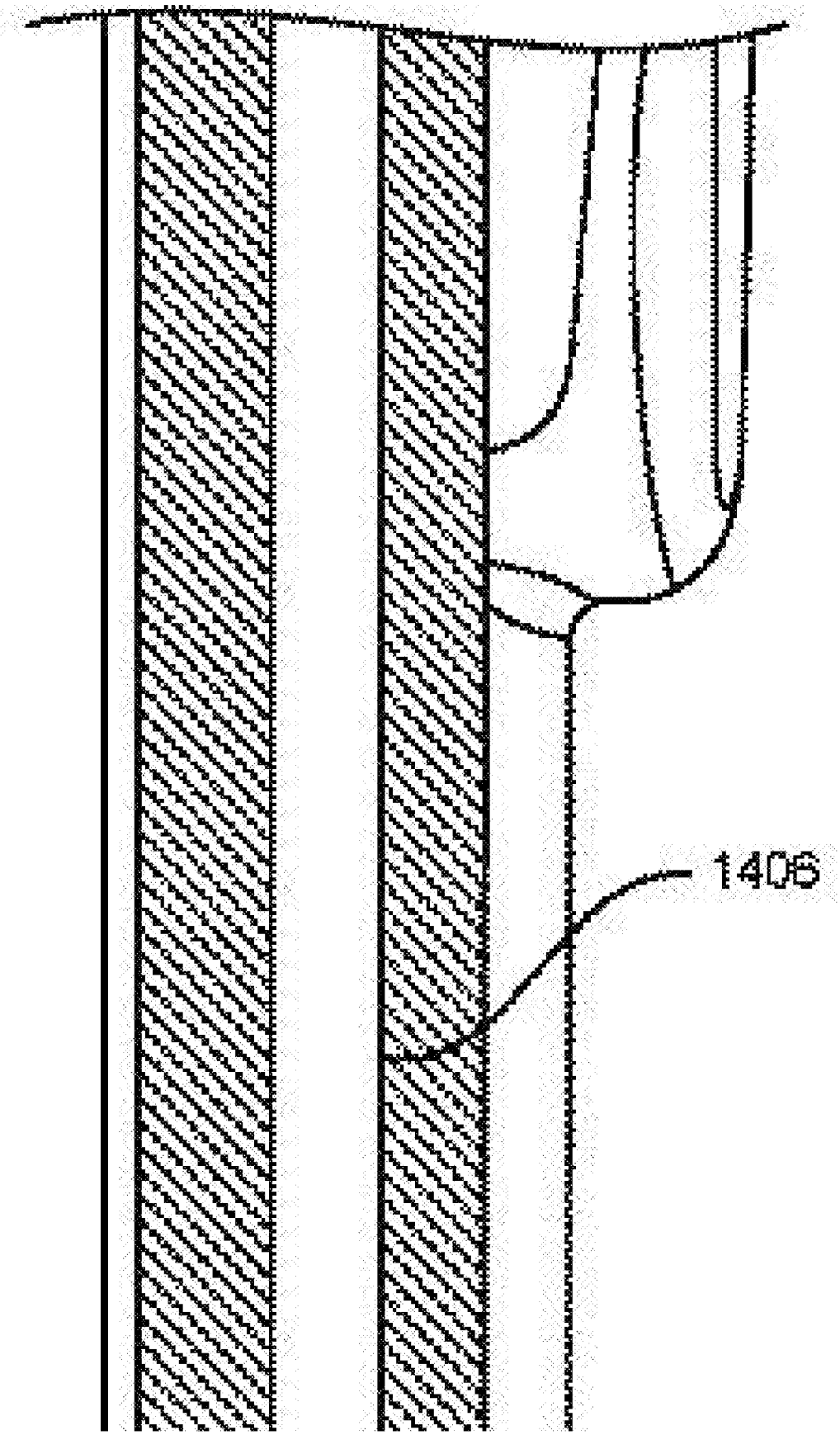


FIG. 14C

[Fig. 14D]


1406

[Fig. 14E]

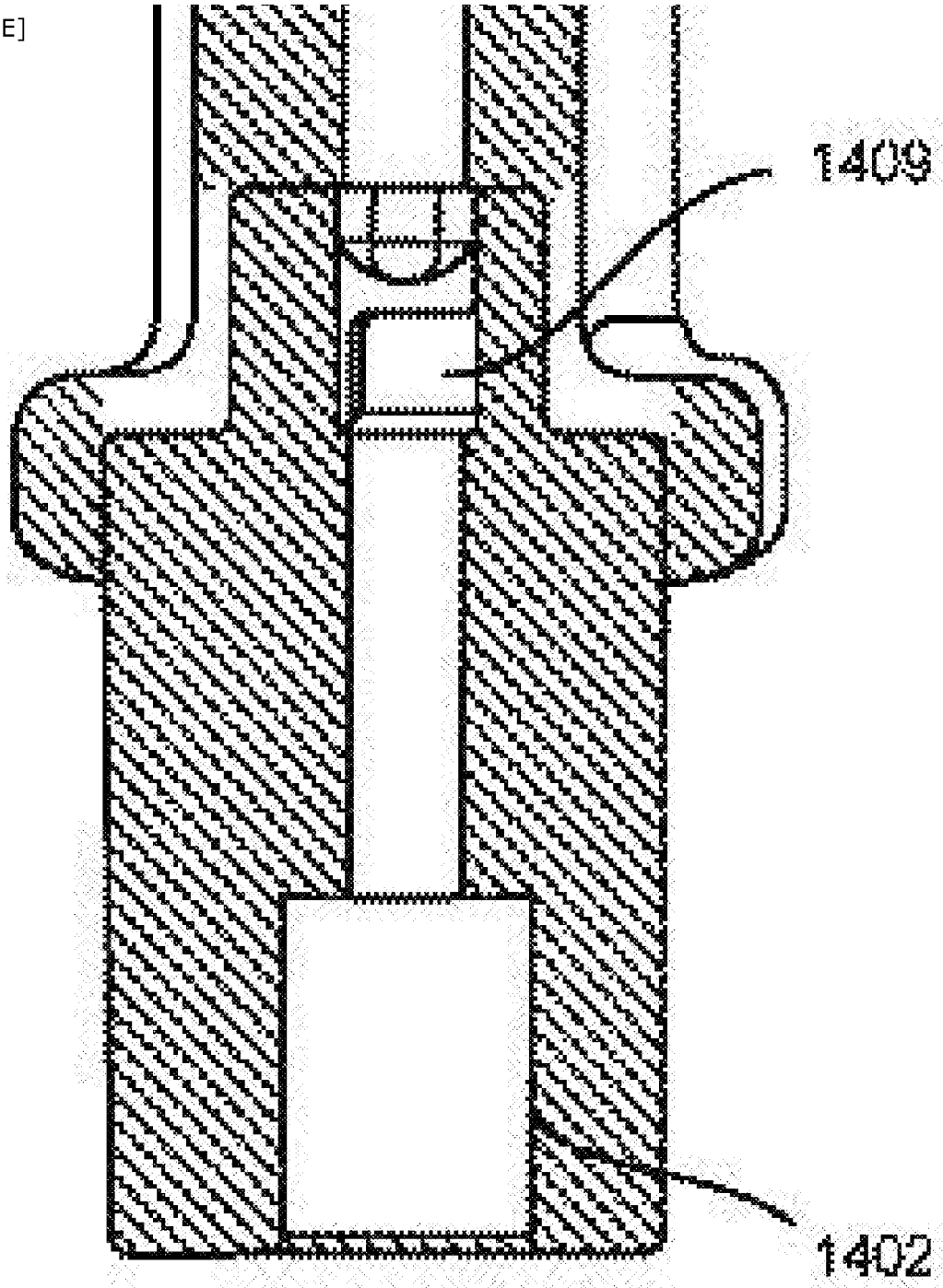


FIG. 14D

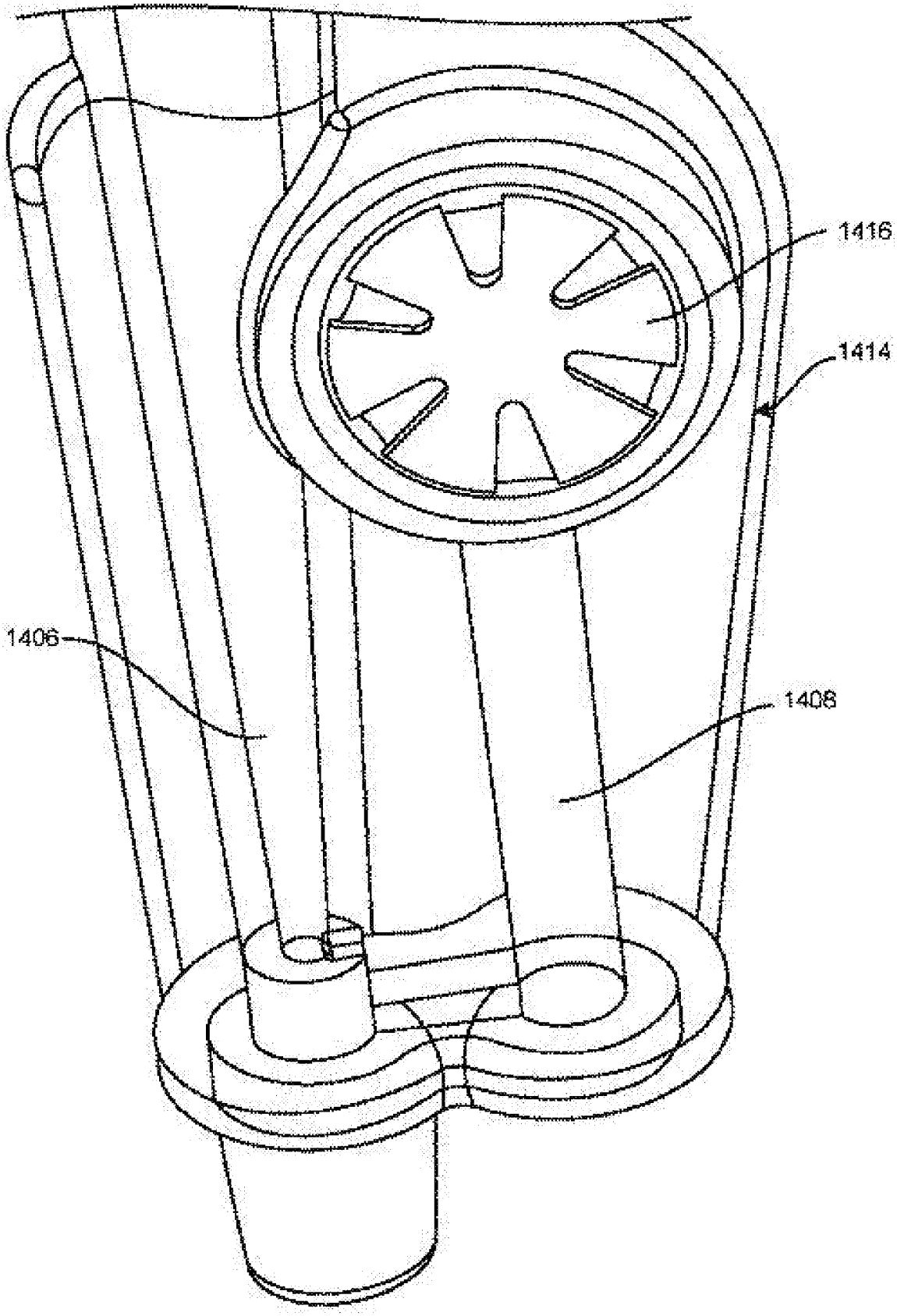


FIG. 14E

[Fig. 15A]

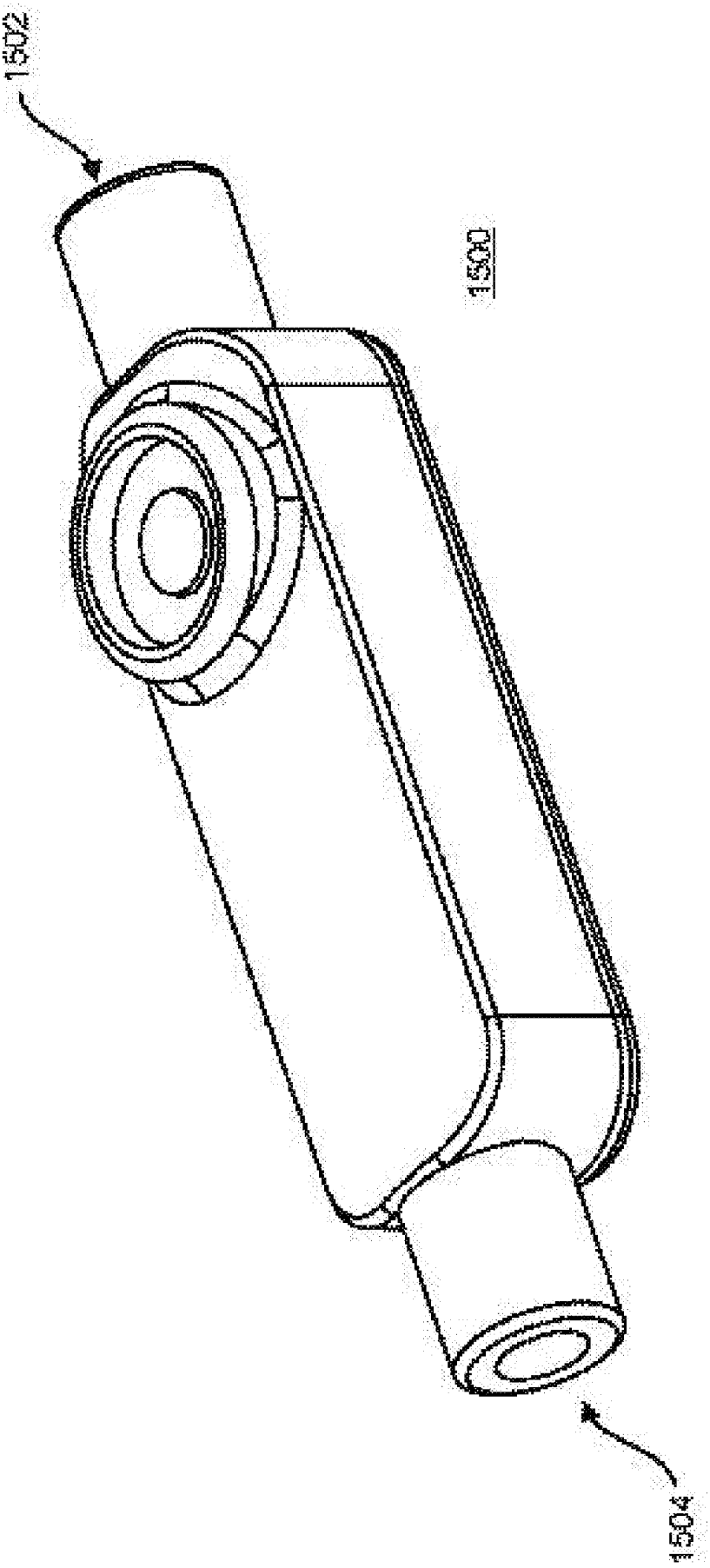


FIG. 15A

[Fig. 15B]

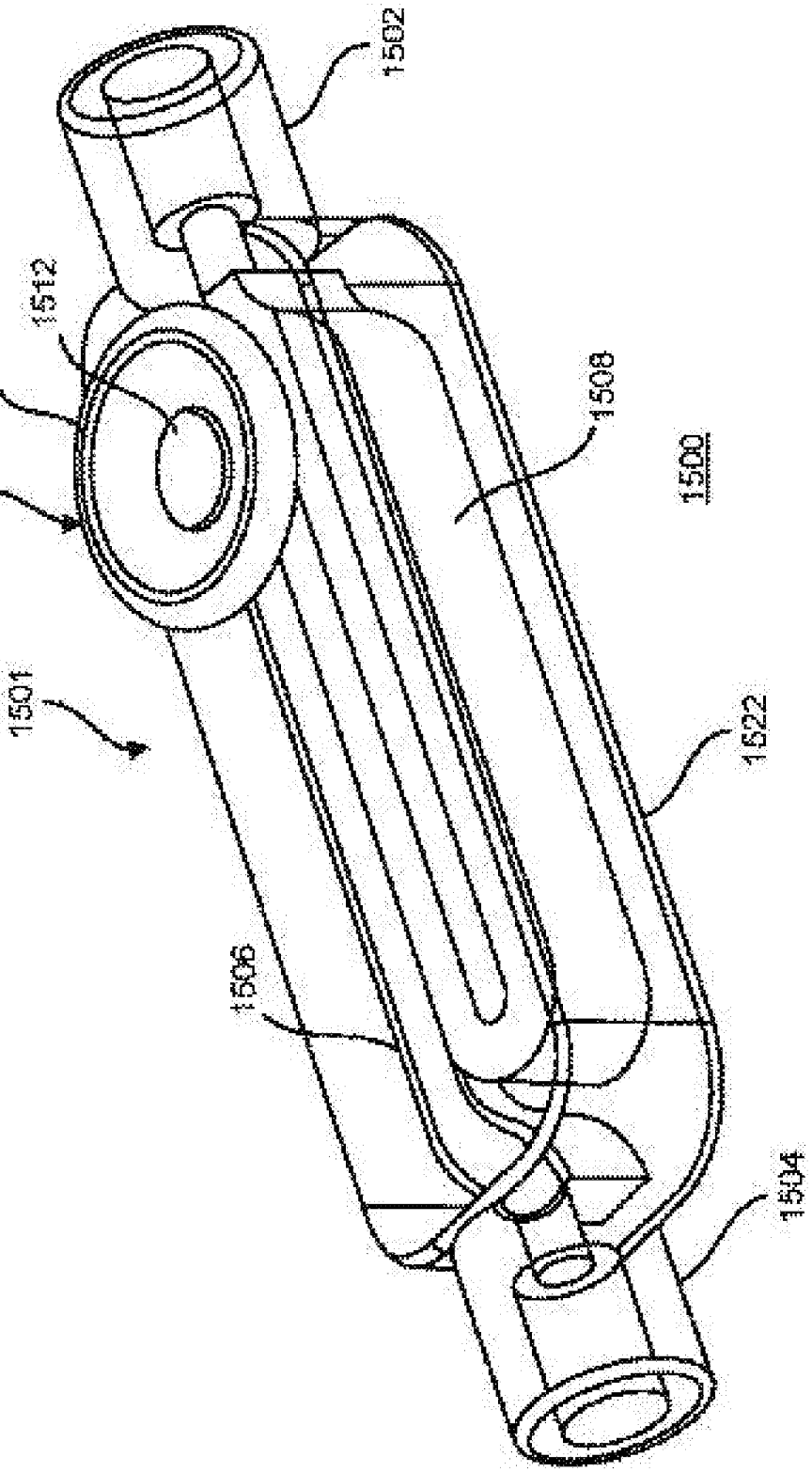


FIG. 15B

[Fig. 15C]

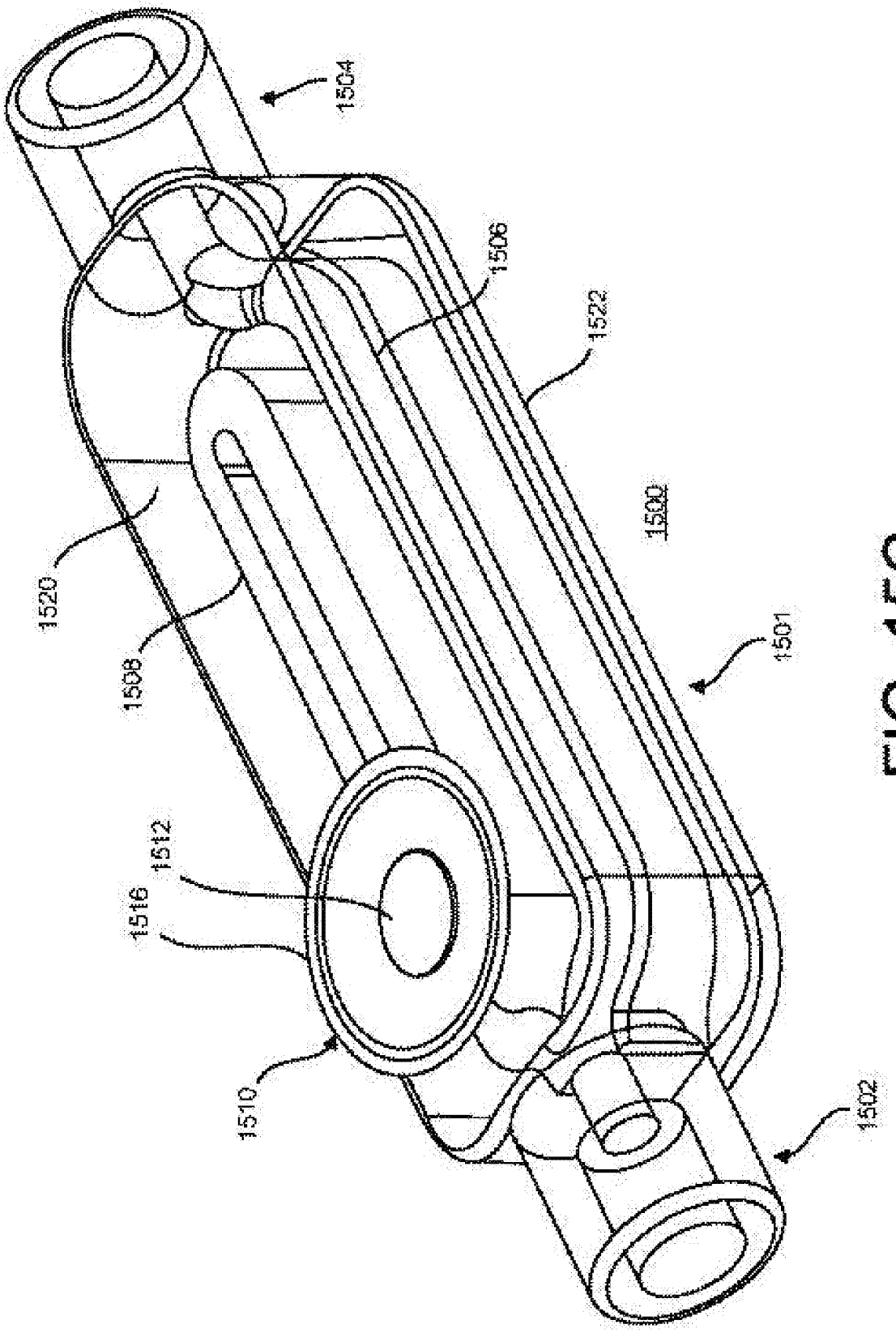


FIG. 15C

[Fig. 15D]

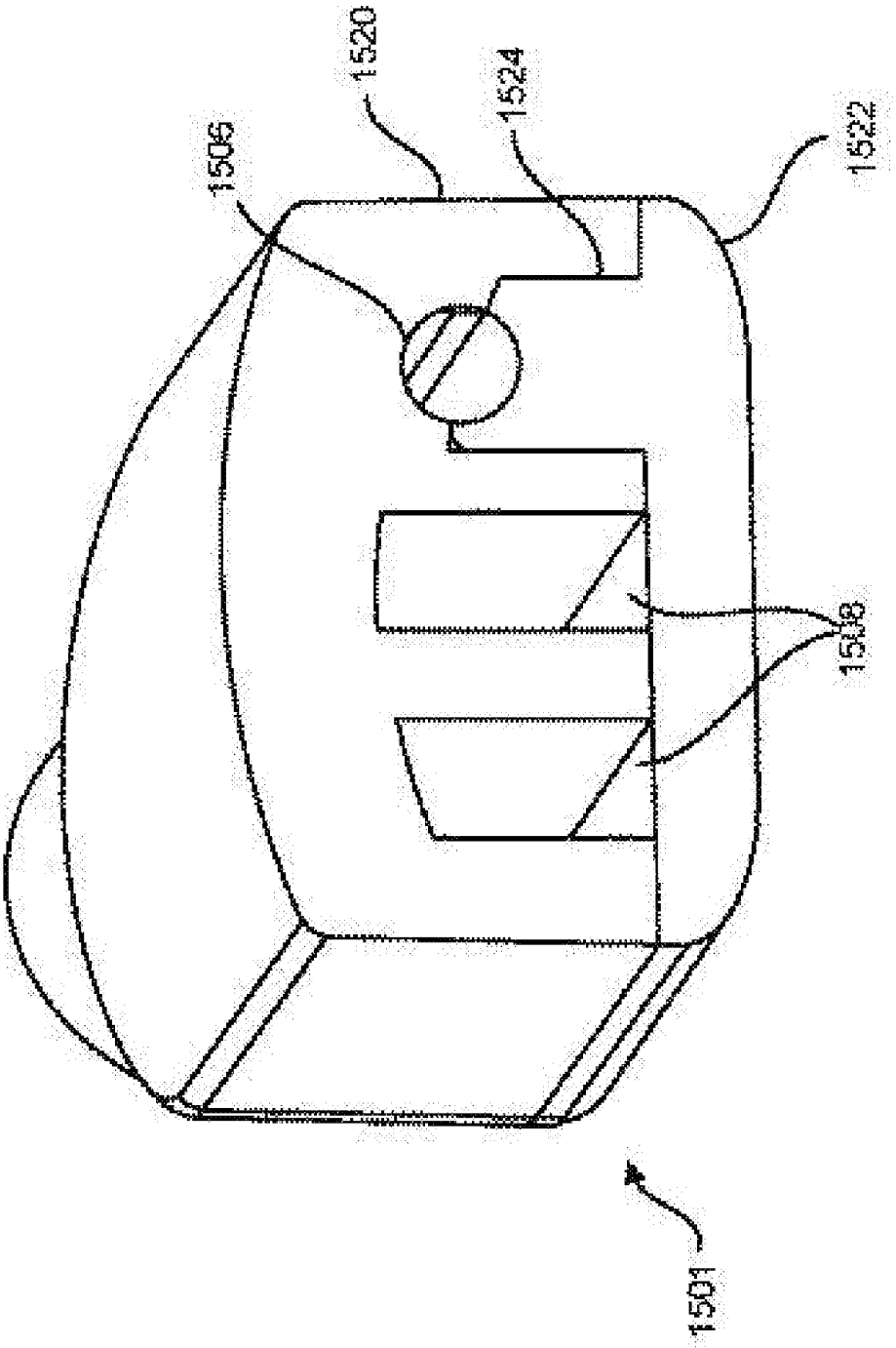


FIG. 15D

[Fig. 15E]

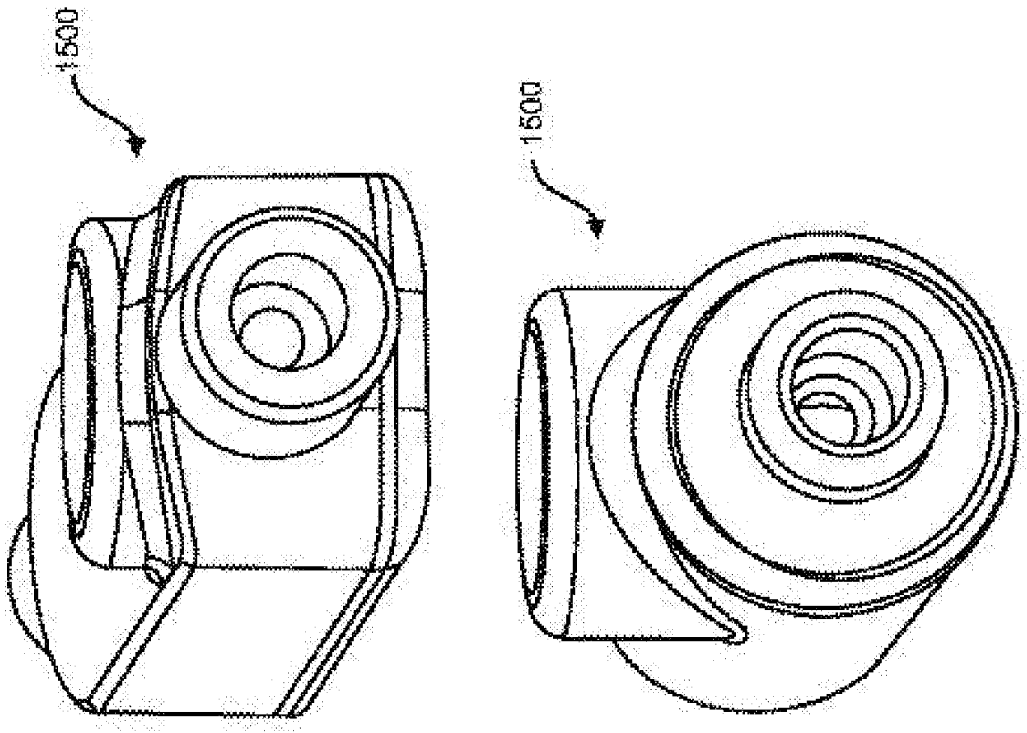


FIG. 15E

[Fig. 15F]

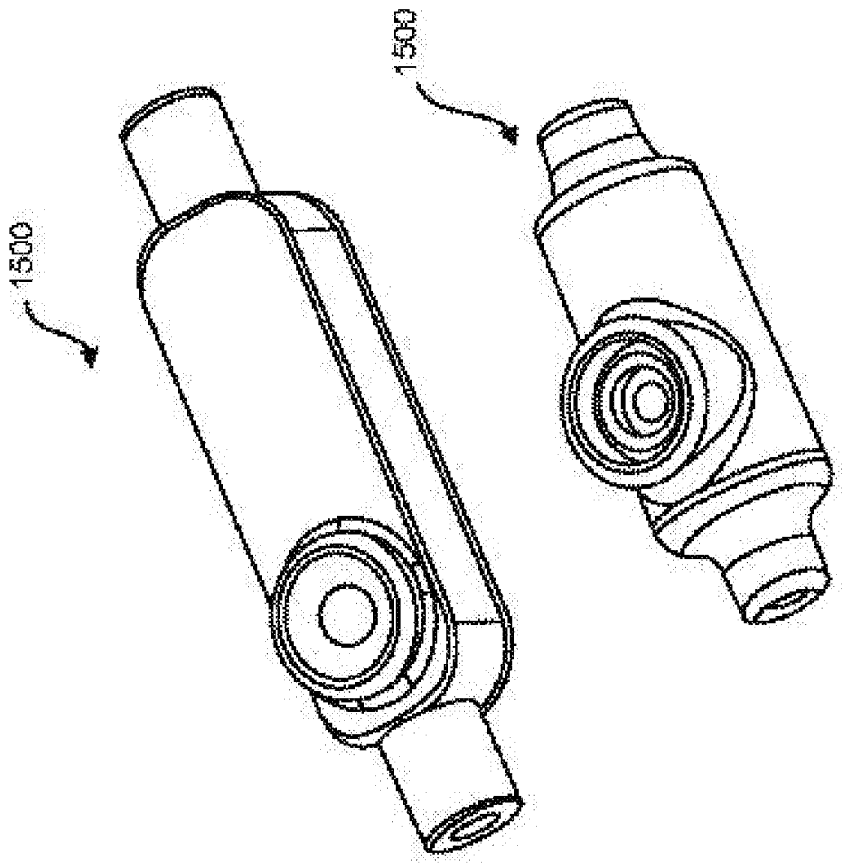


FIG. 15F

[Fig. 15G]

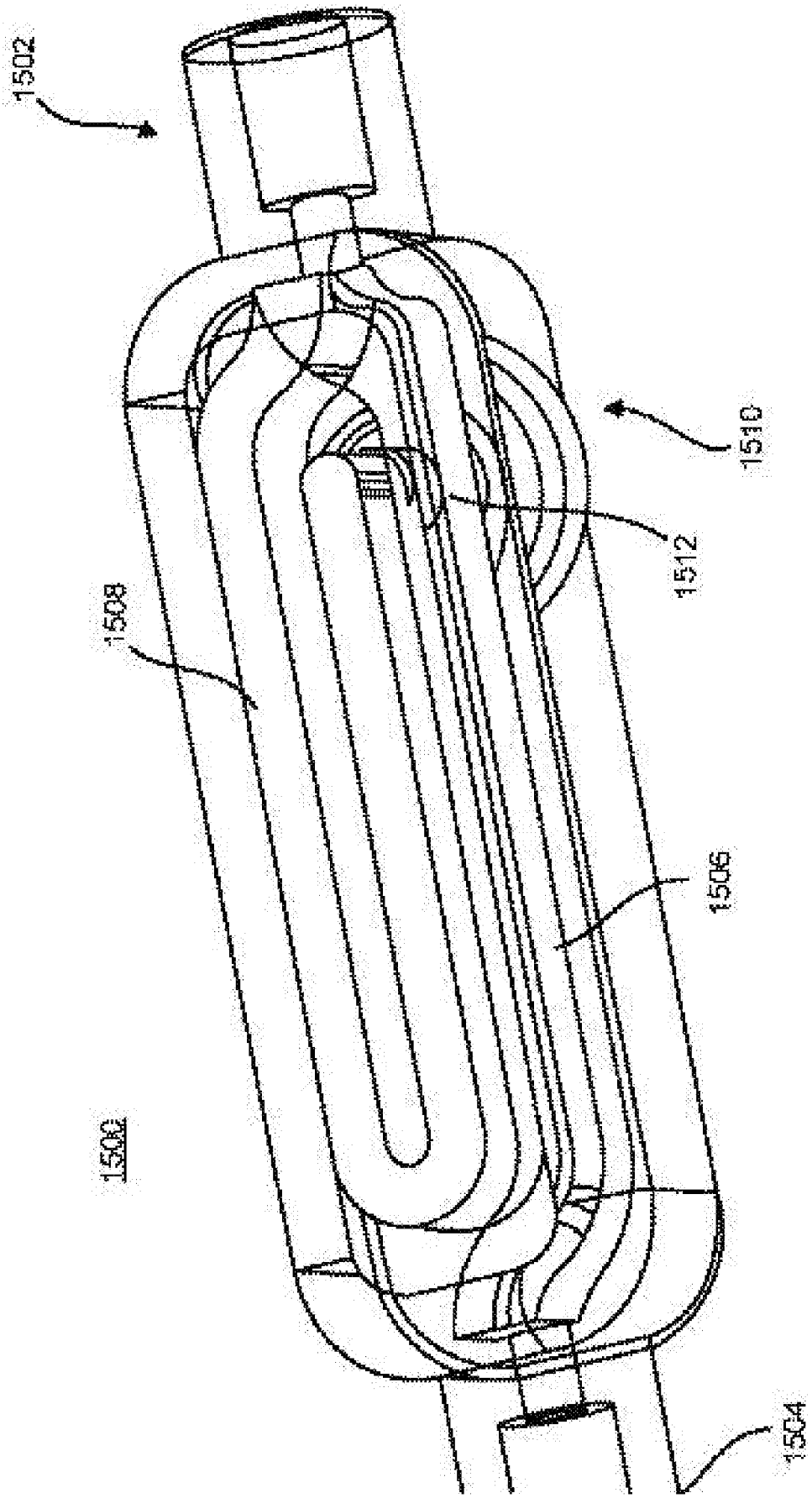


FIG. 15G

[Fig. 16A]



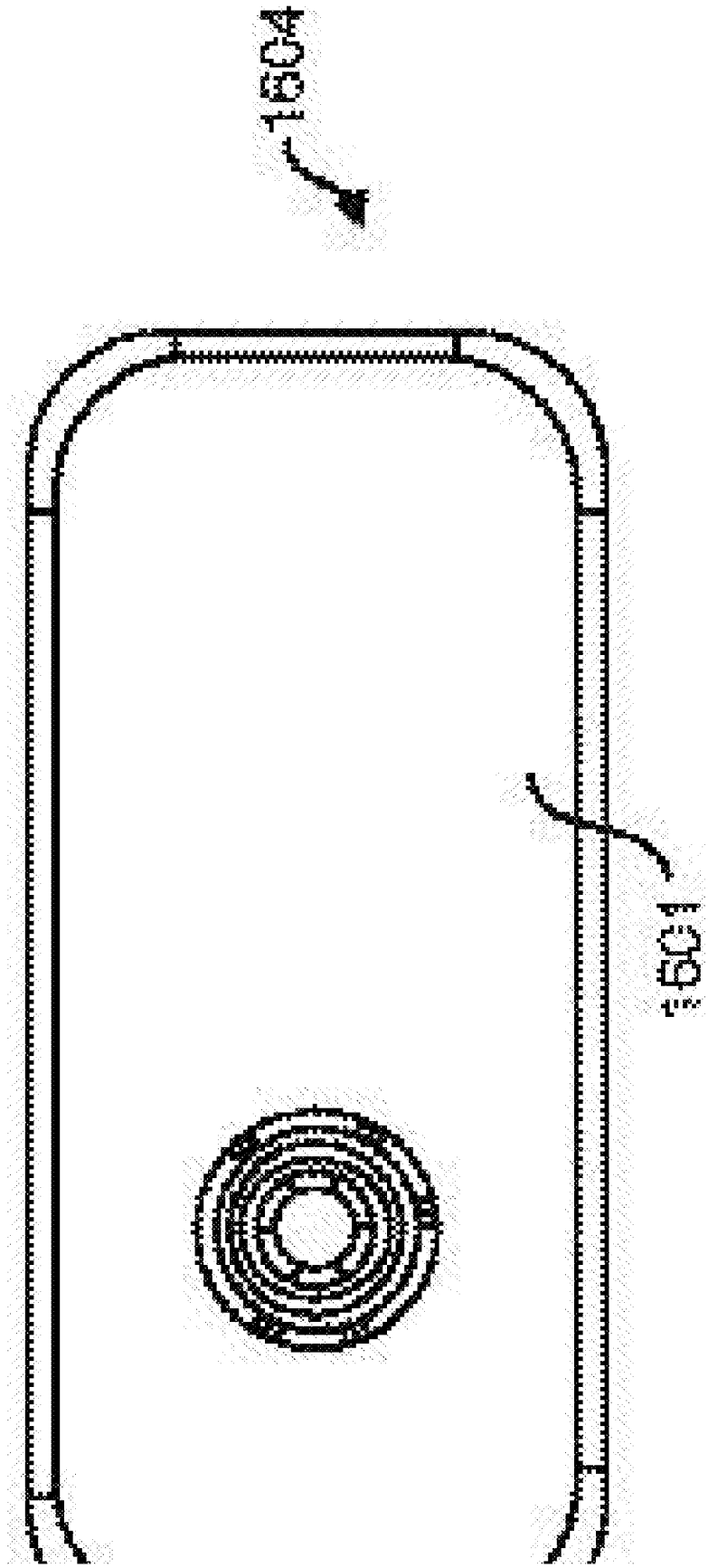
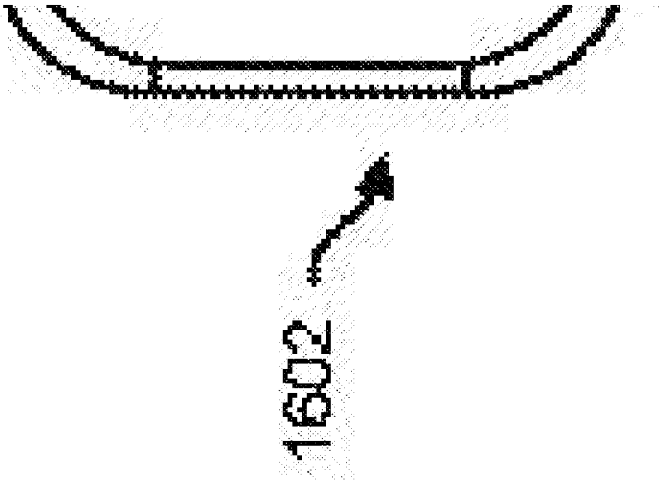


FIG. 16A

[Fig. 16B]



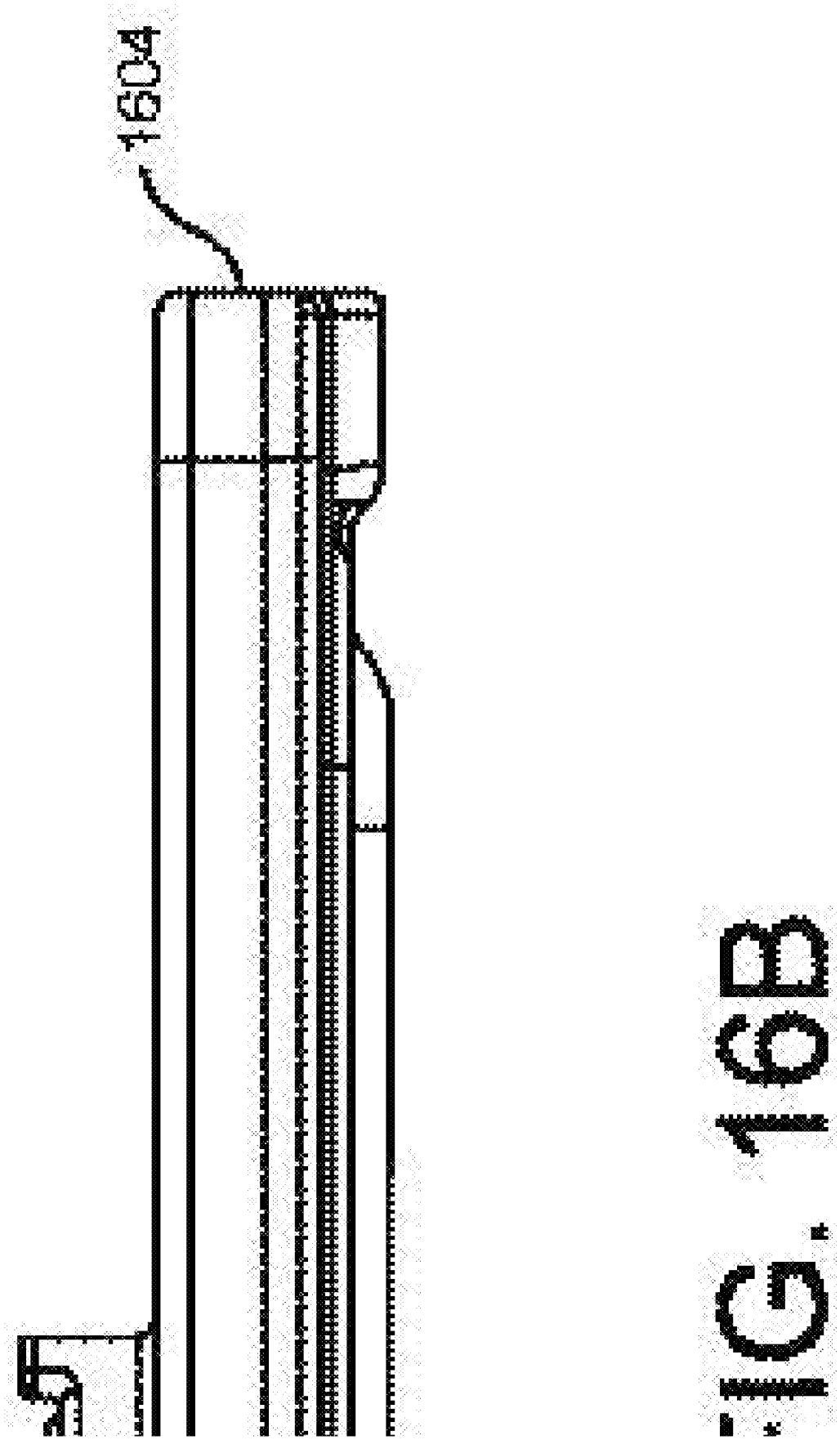


図3B

[Fig. 16C]

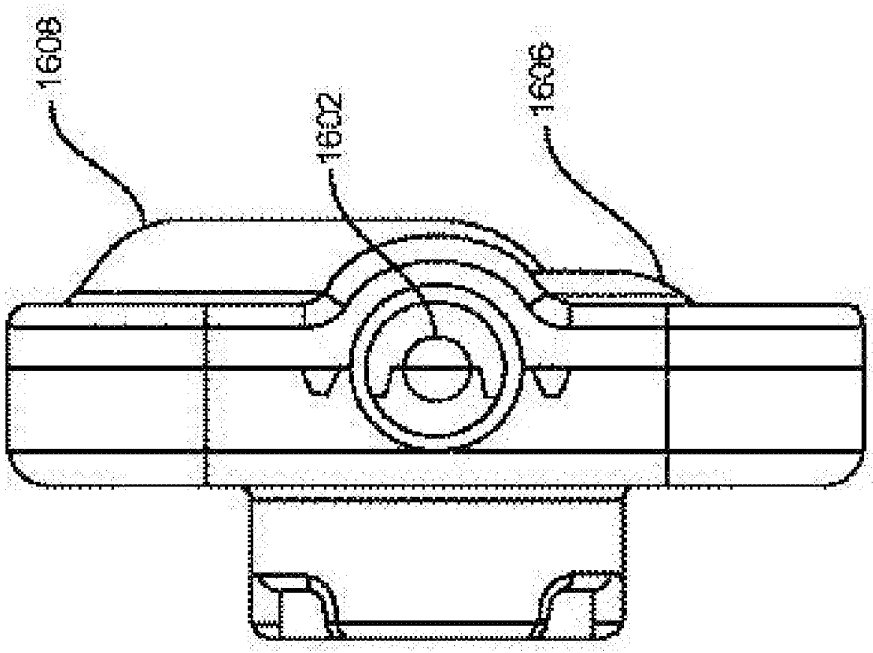
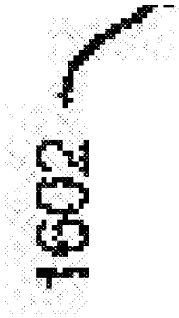


FIG. 16C

[Fig. 16D]



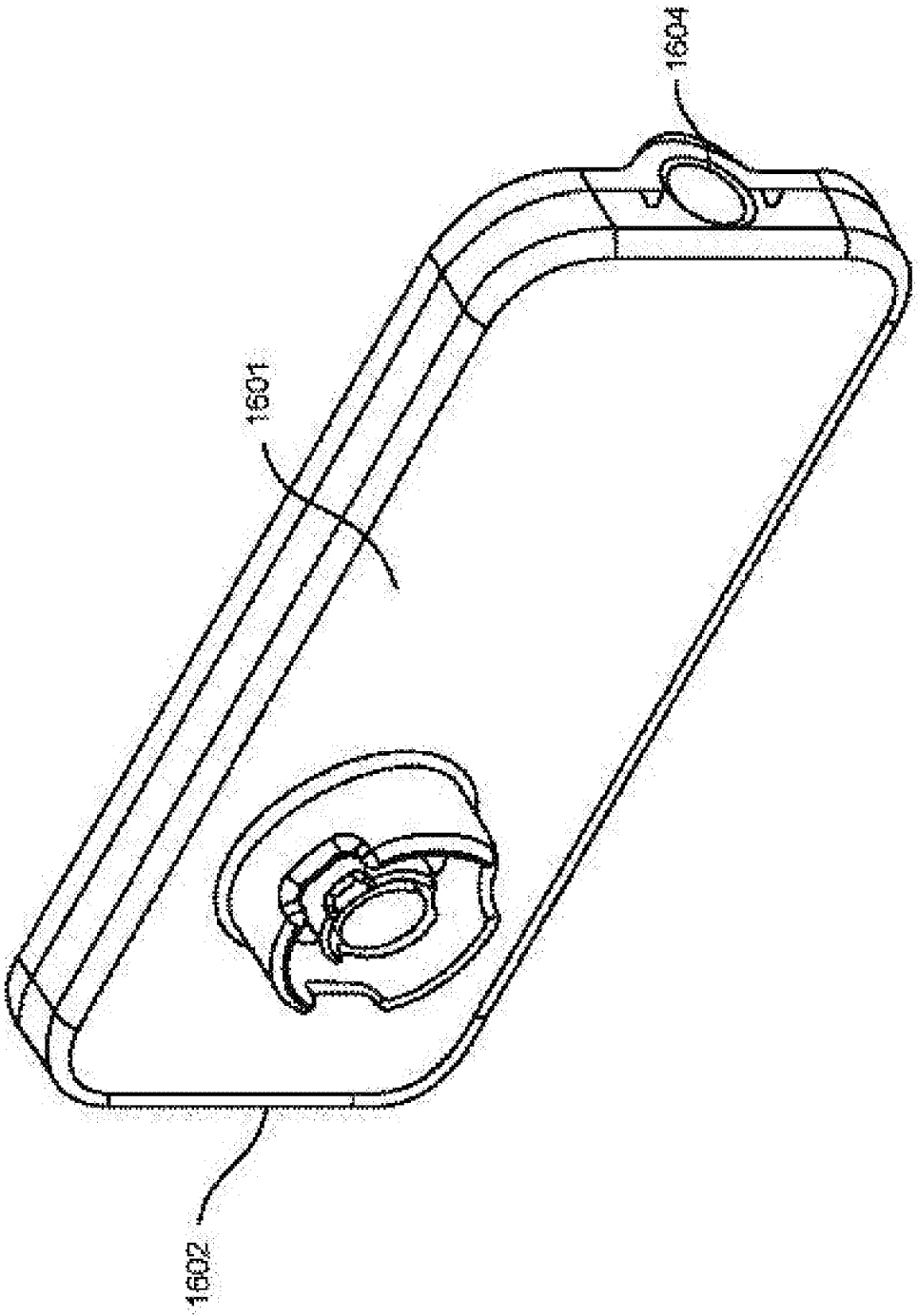


FIG. 16D

[Fig. 17A]

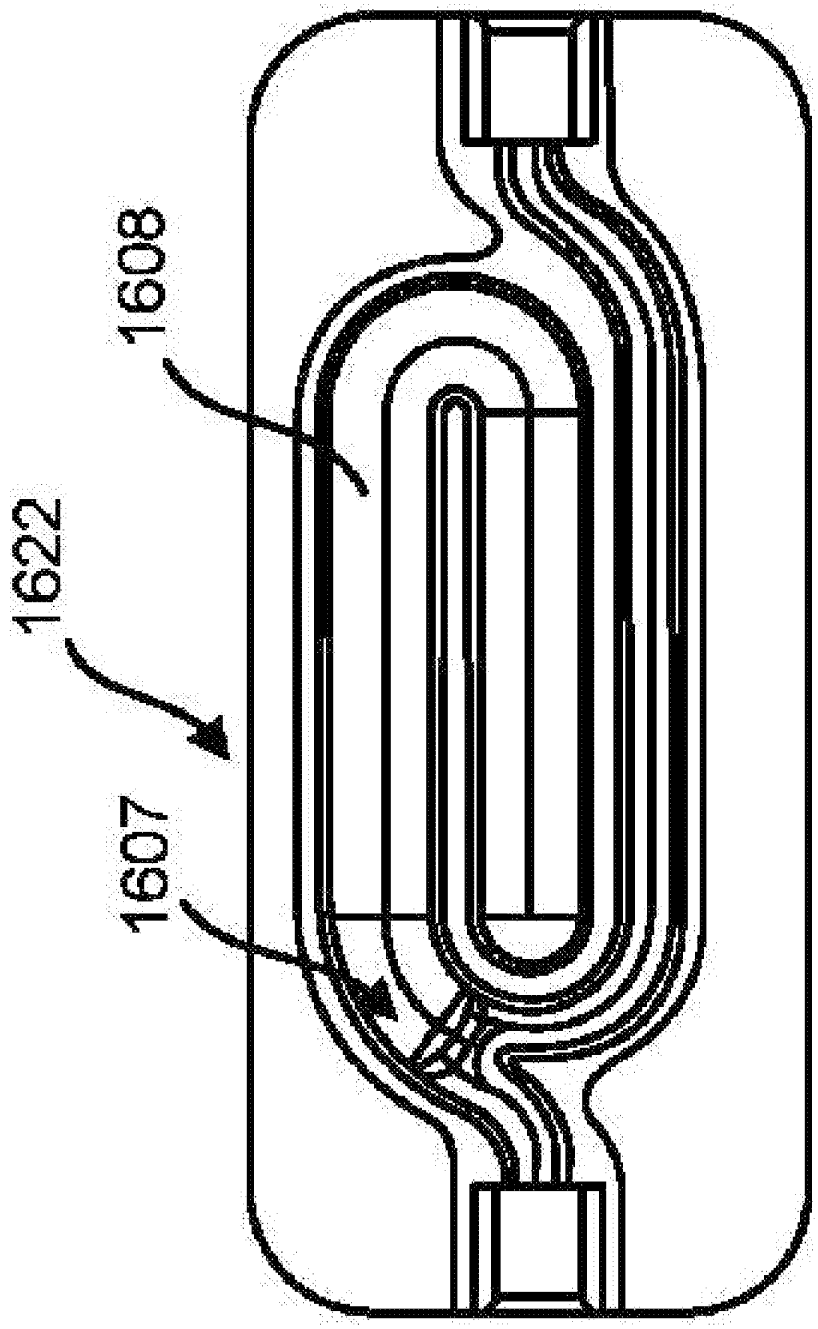


FIG. 17A

[Fig. 17B]

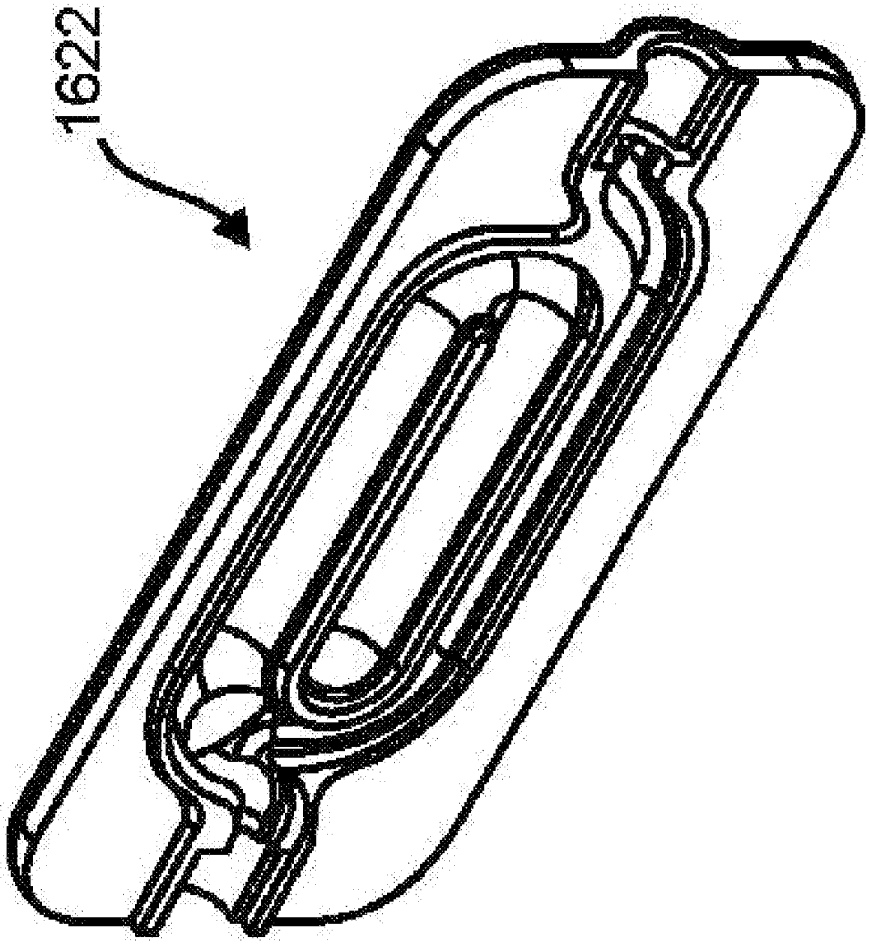


FIG. 17B

[Fig. 17C]

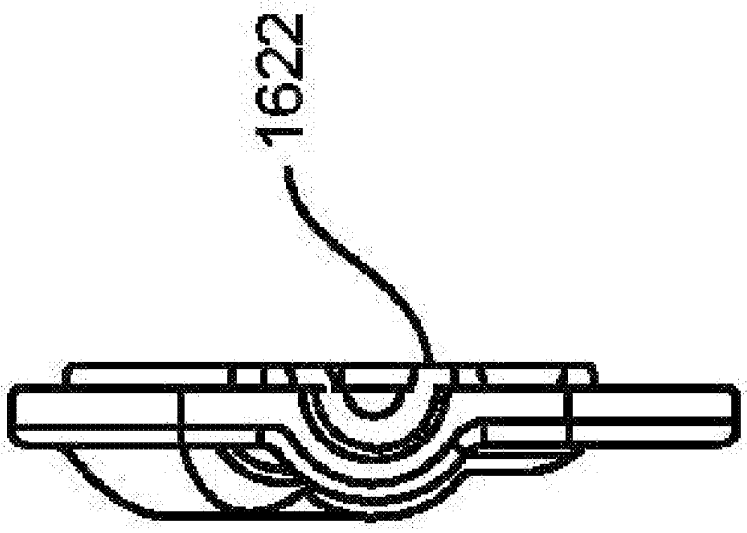


FIG. 17C

[Fig. 17D]

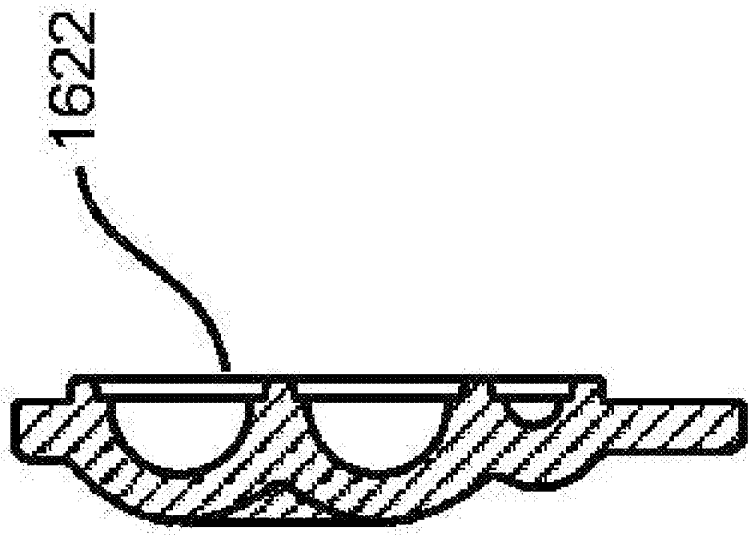


FIG. 17D

[Fig. 17E]



FIG. 17E

[Fig. 18A]

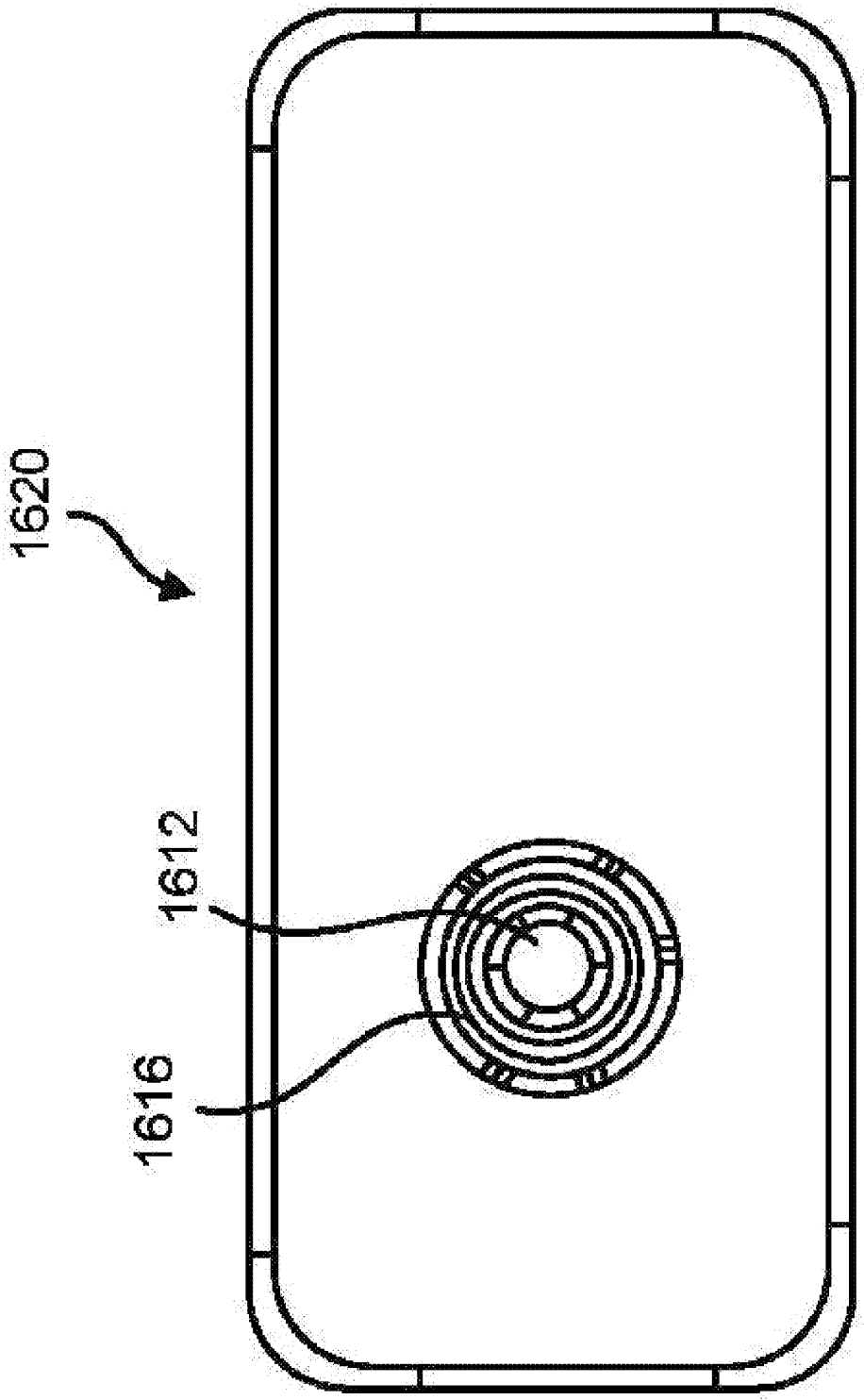


FIG. 18A

[Fig. 18B]

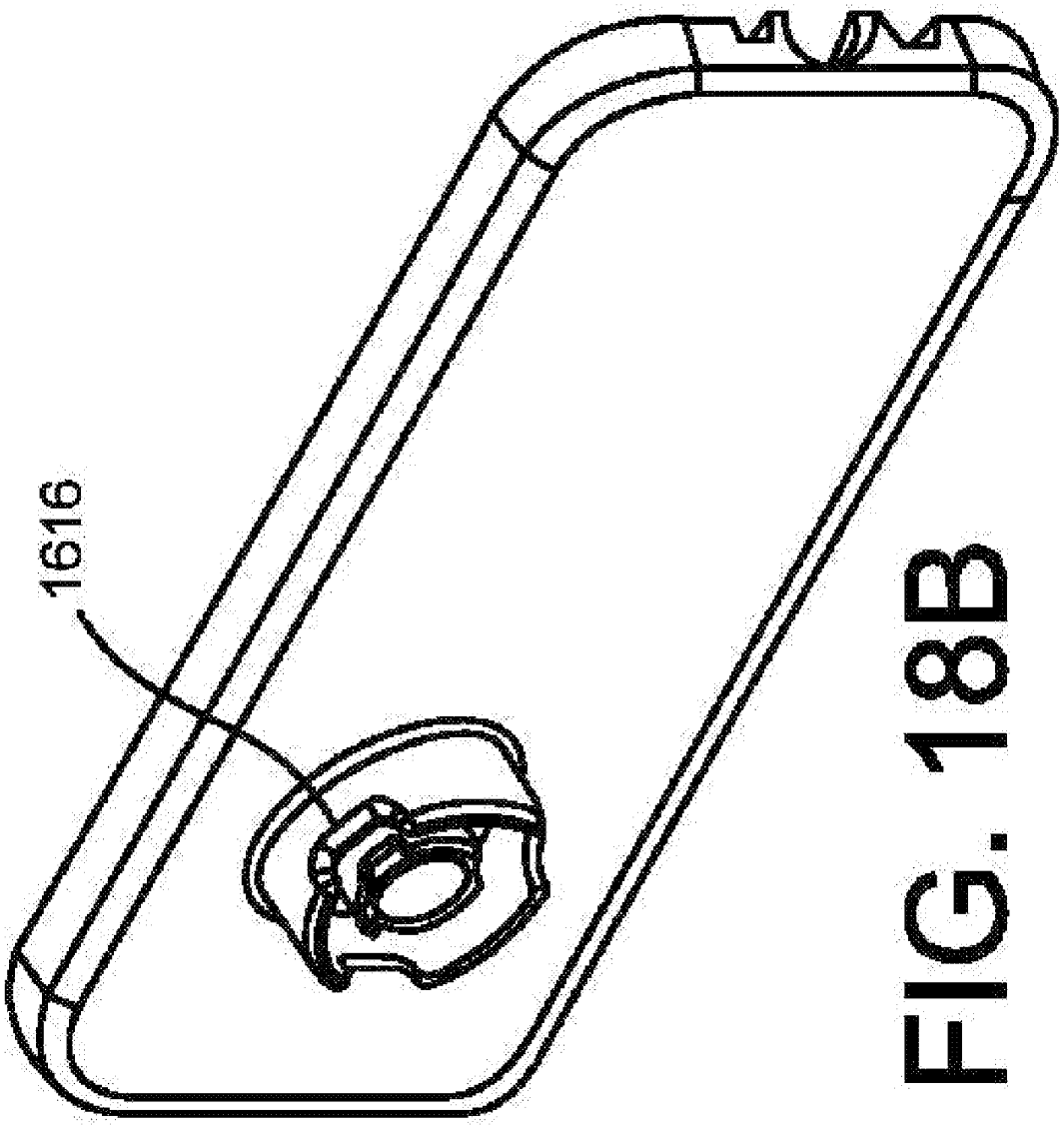


FIG. 18B

[Fig. 18C]

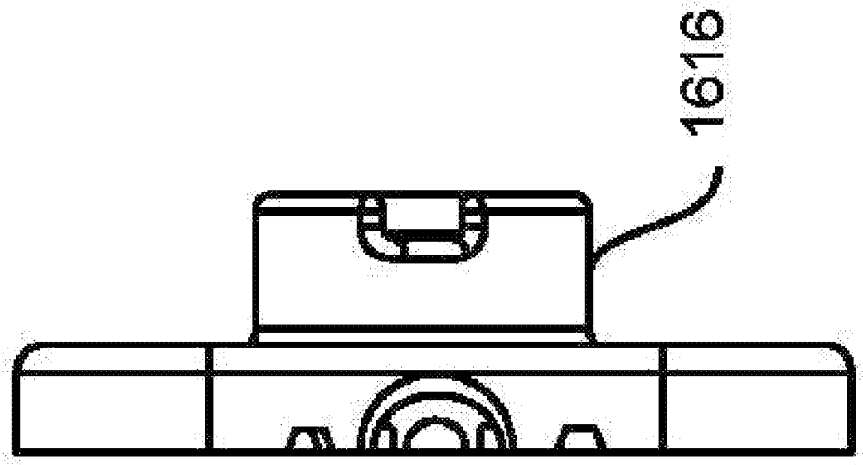


FIG. 18C

[Fig. 18D]

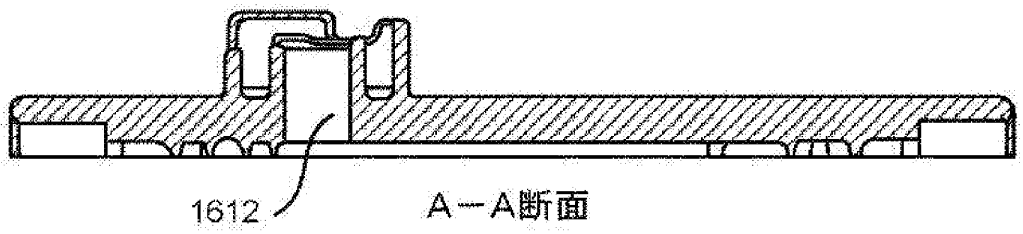


FIG. 18D

[Fig. 18E]

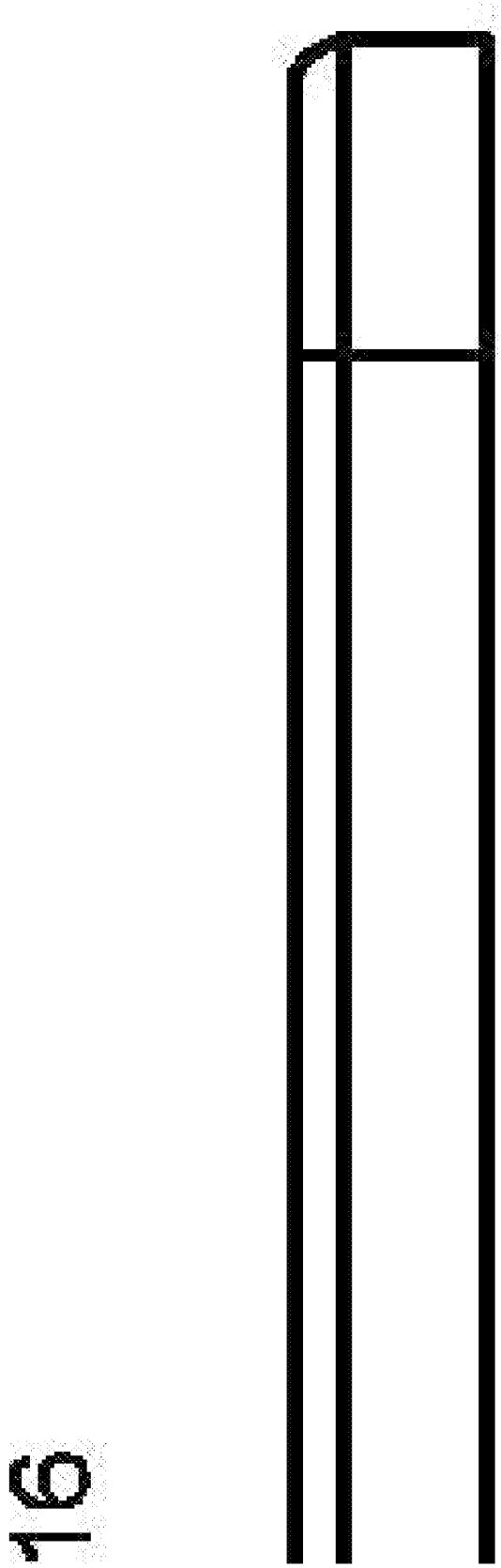
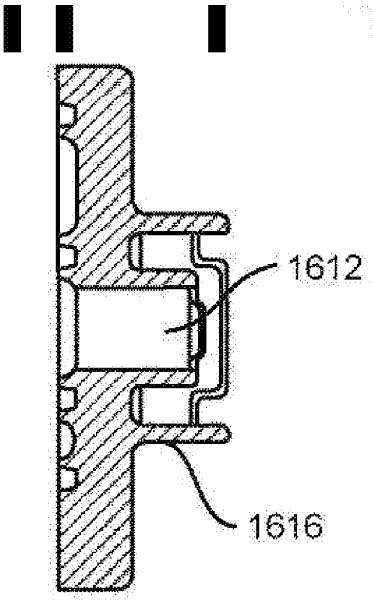


図18

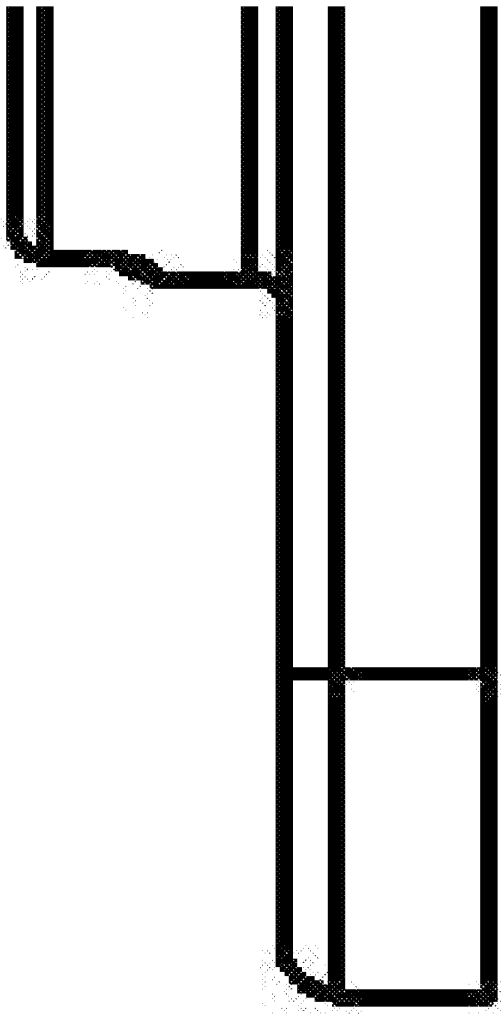
[Fig. 18F]



A－A断面

FIG. 18F

[Fig. 19A]



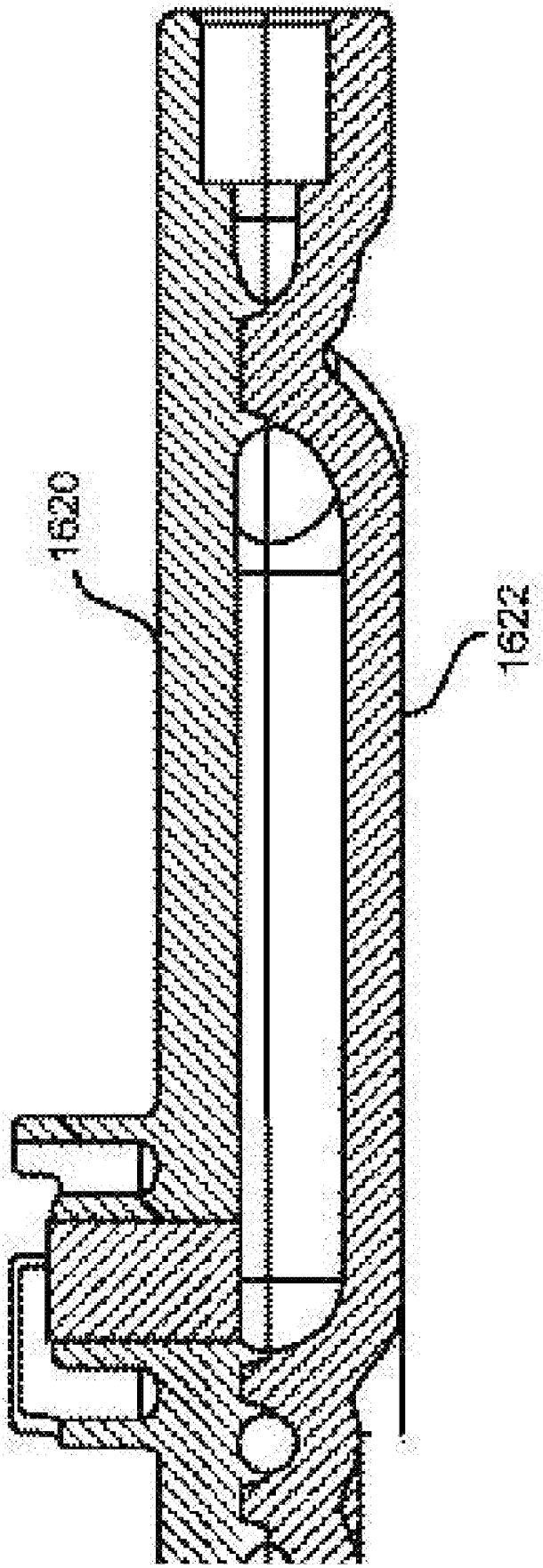


FIG. 19A

[Fig. 19B]

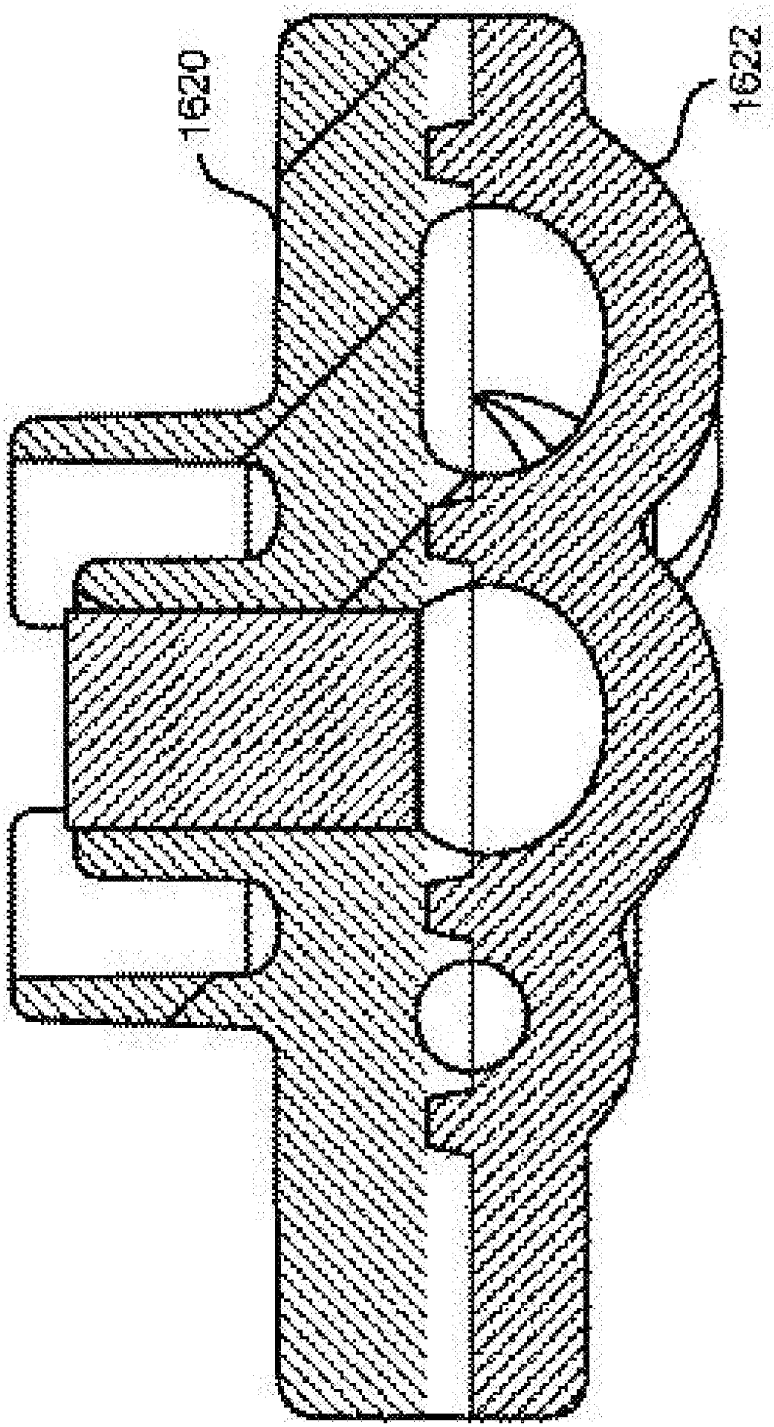


FIG. 19B

[Fig. 20]

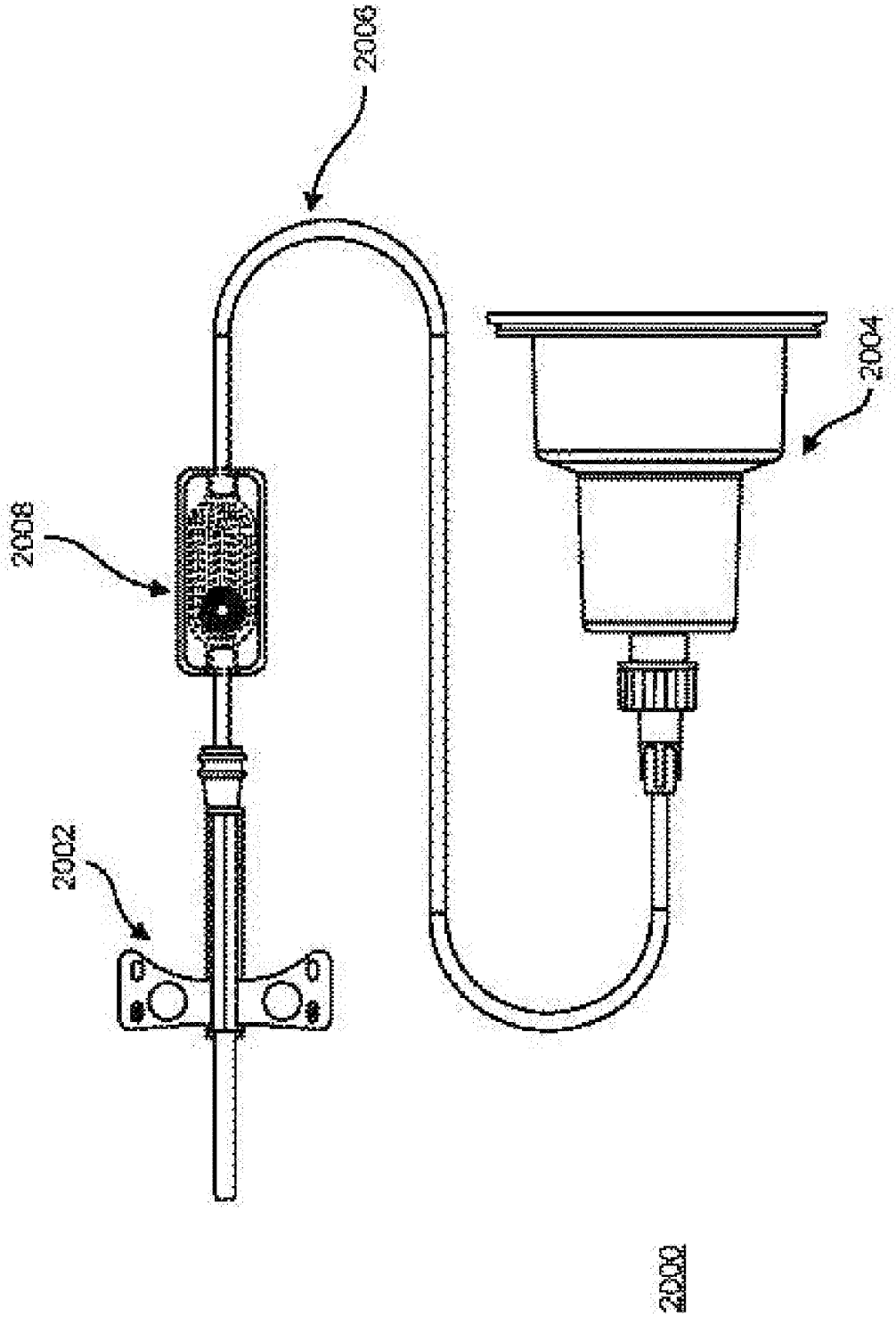


FIG. 20

[Fig. 21]

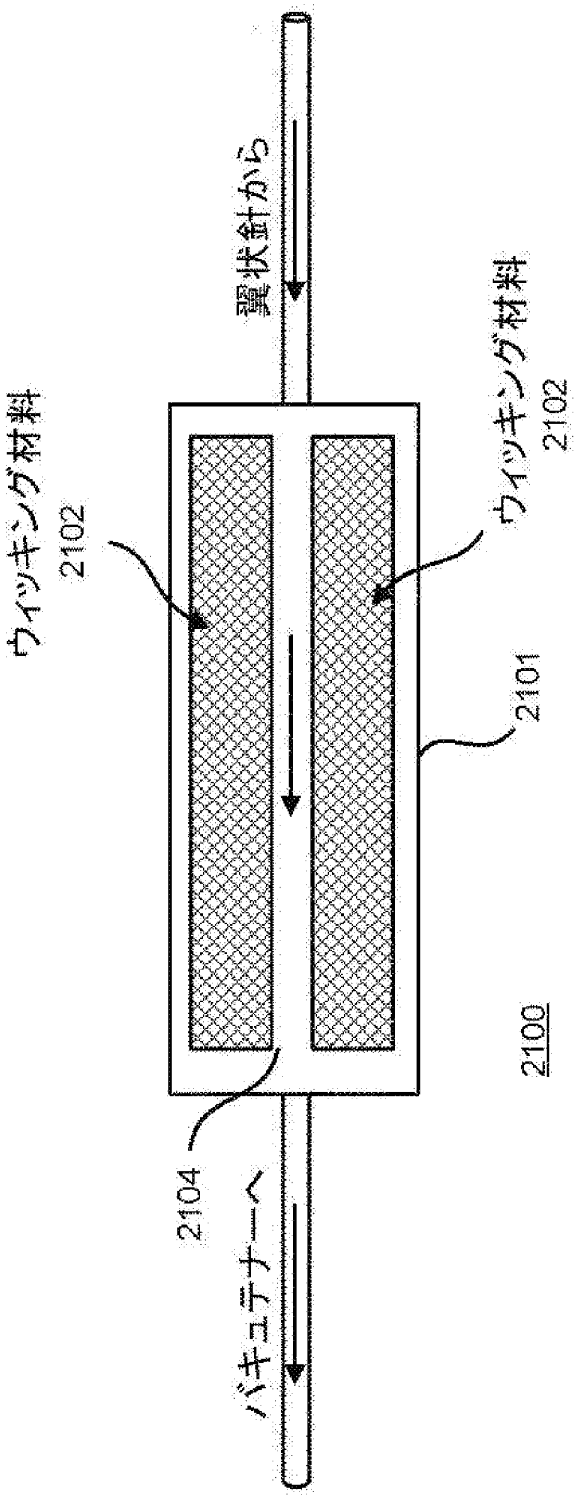


FIG. 21

[Fig. 22A]

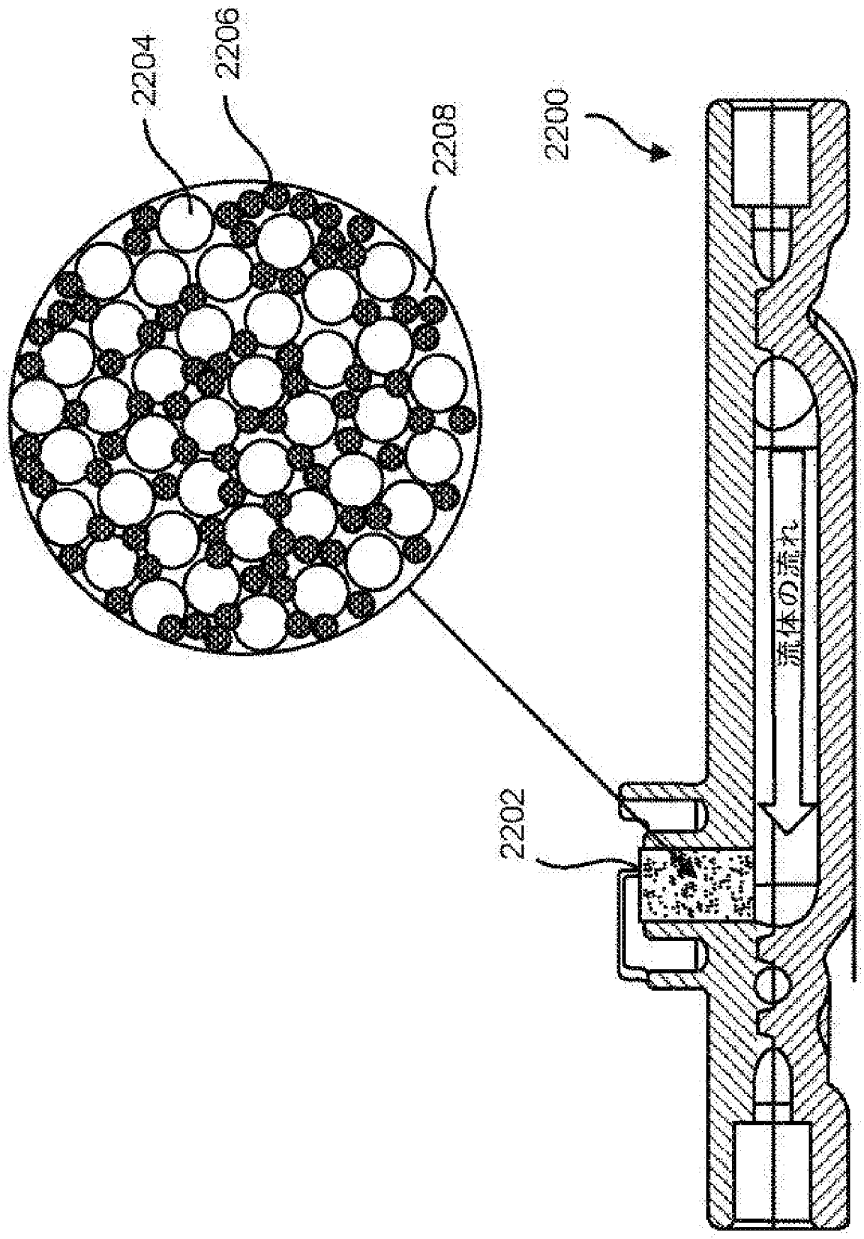


FIG. 22A

[Fig. 22B]

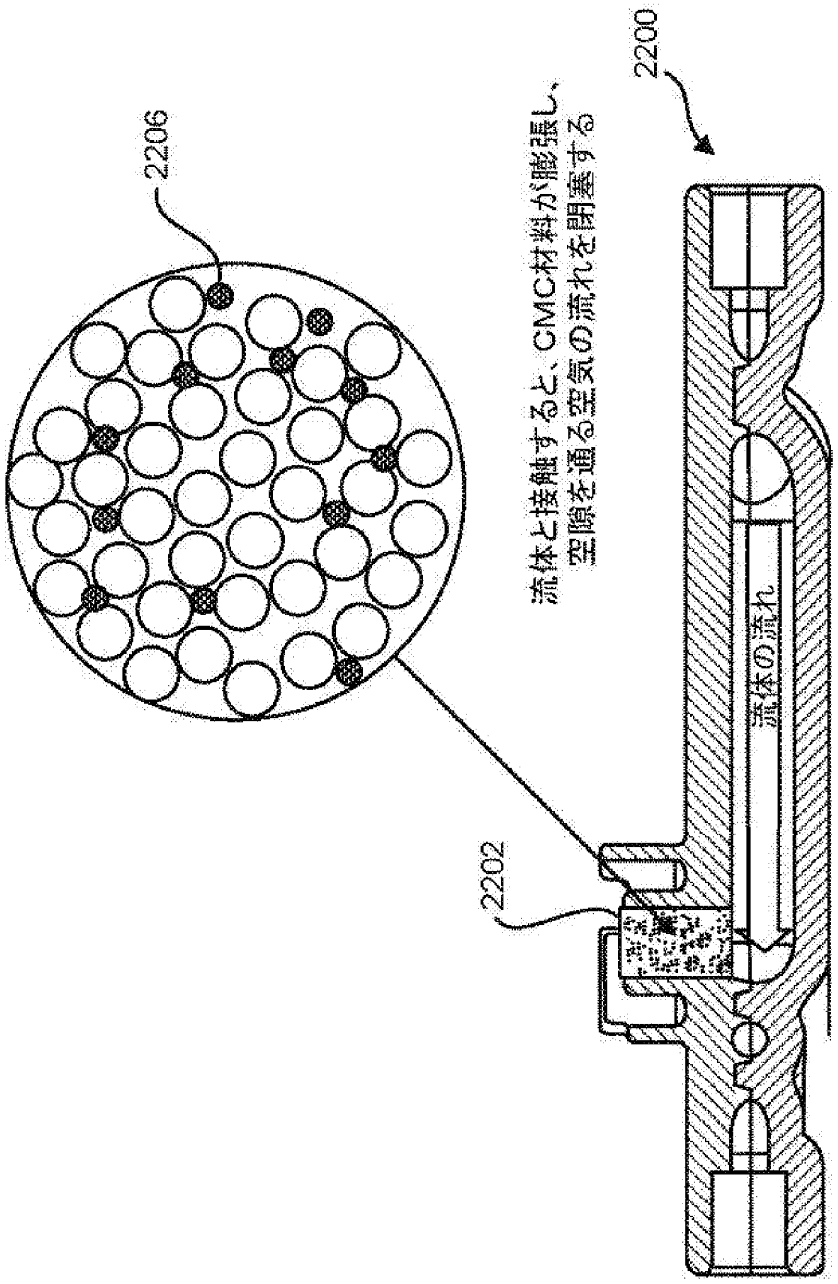


FIG. 22B

[Fig. 23A]

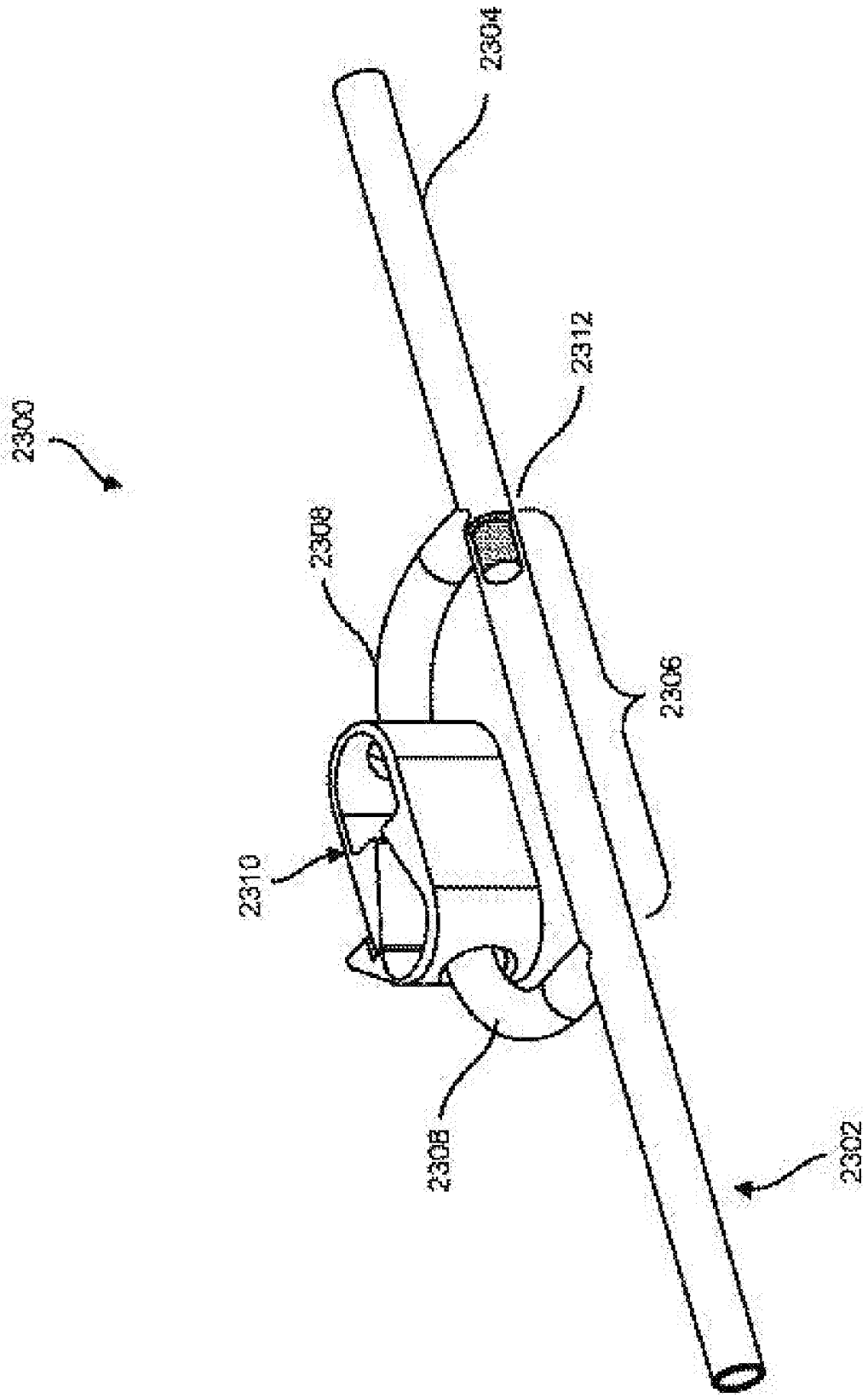


FIG. 23A

[Fig. 23B]

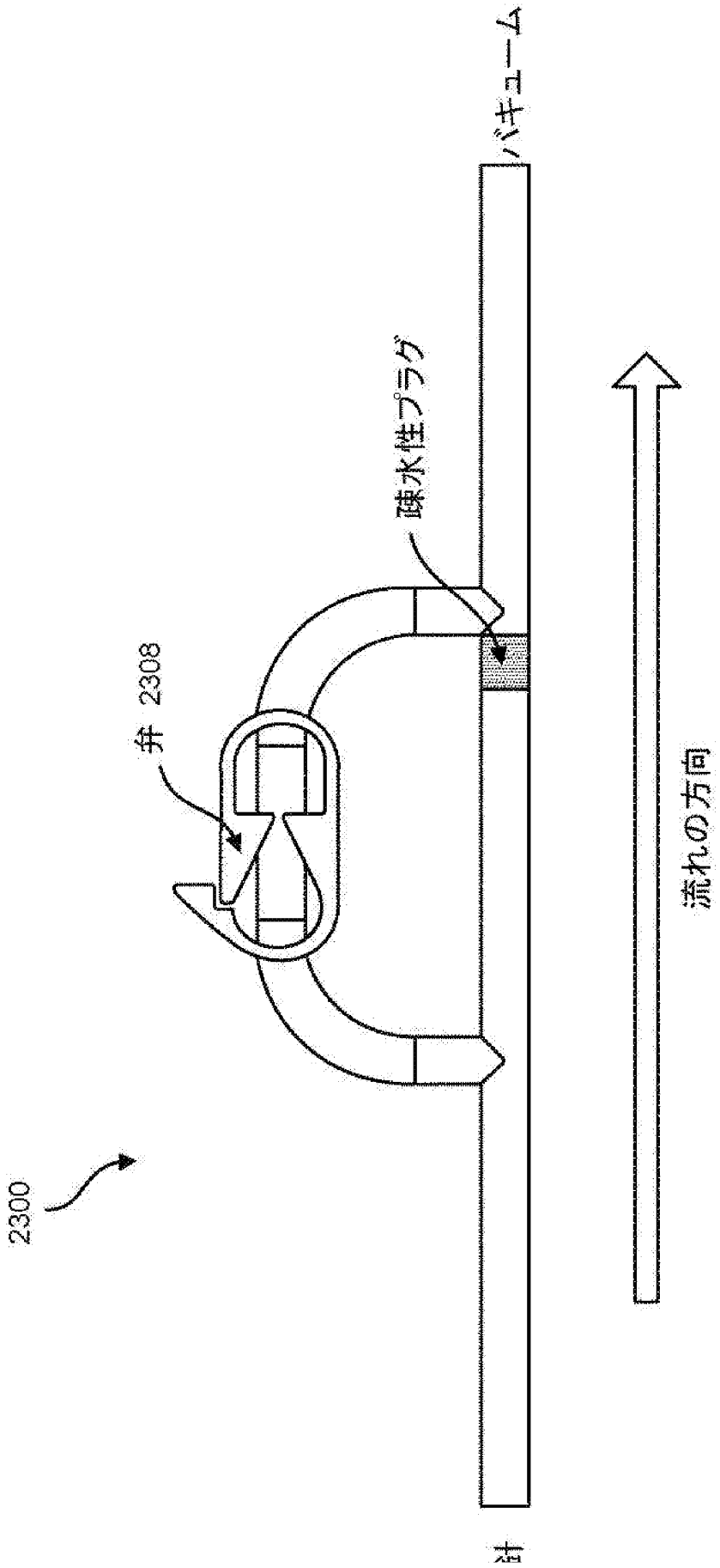


FIG. 23B

drawing open

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

Magnify and Rotate

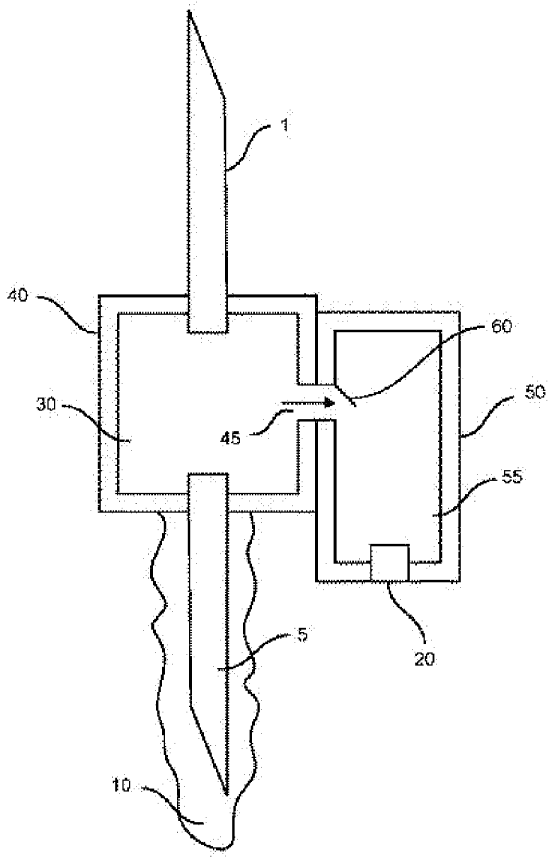


FIG. 1

Figure 1

1 / 1 display

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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Applicant(s): クリン インコーポレイテッド

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

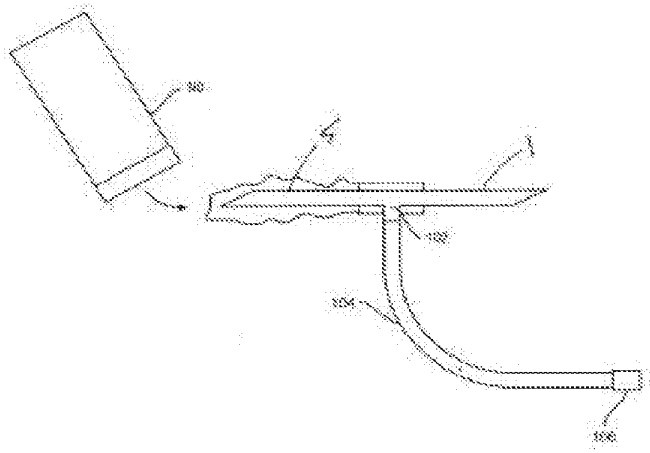
Application number: JP20180523384 20160722 Global Dossier

Priority number(s): US201562238636P 20151007 ; US201662318194P 20160404 ; US201562196797P 20150724 ; US201615140448 20160427 ; US201615140443 20160427 ; WO2016US43709 20160722

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Abstract of corresponding document: US2017020427 (A1)

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



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最終頁に続く

(54)【発明の名称】血液サンプル最適化システム及び血液隔離装置

(57)【特許請求の範囲】
【請求項１】
血液サンプル最適化システムであって、
採血システムであって、
患者の血液サンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、
前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と、
前記血液サンプルの後続の部分を採取しかつ収容するために真空採血管を受け入れるように構成されたサンプル針と
を含む採血システムと、
前記患者針と前記サンプル針との間に前記採血経路に沿って接続された血液隔離装置であって、
前記血液サンプルを受け入れるように構成された入口ポートと、
前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記血液サンプルの最初の量を受け入れかつ前記血液サンプルの最初の量の少なくとも最初の部分を隔離するように構成された隔離チャンバと、
前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と
を含み、
前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプル

の後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された出口ポートに向かわせるように構成され、前記出口ポートは、前記血液サンプルの後続の部分を前記真空採血管に排出するように構成され、

前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置と

を含む、血液サンプル最適化システム。

【請求項２】

前記血液隔離装置の前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項１に記載の血液サンプル最適化システム。

【請求項３】

前記サンプル針は、前記採血経路及び前記サンプリング流路を介した前記患者針へのアクセスを開くために前記真空採血管によって穿孔されるシールを含む、請求項２に記載の血液サンプル最適化システム。

【請求項４】

前記血液隔離装置の前記サンプリング流路は、前記サンプル針を開封する前記真空採血管によって真空圧力下で前記血液サンプルの後続部分を前記入口ポートに進入させる、請求項３に記載の血液サンプル最適化システム。

【請求項５】

前記血液隔離装置の前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項１に記載の血液サンプル最適化システム。

【請求項６】

前記採血システムの前記採血経路はチューブを含む、請求項１に記載の血液サンプル最適化システム。

【請求項７】

患者から血液サンプルを取り出せるようにするように構成された患者針と、密封されたサンプル針であって、前記サンプル針を開封しかつ取り出せるようにされた血液サンプルを患者から採取するために真空採血管を受け入れるように適合されたサンプル針とを含む血液採取システムに接続された血液隔離装置であって、

前記患者針に接続され、患者からの血液サンプルを受け入れるように構成されたた入口ポートと、

前記入口ポートに接続された出口ポートと、

前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記サンプル針が前記真空採血管によって開封される前に前記血液サンプルの最初の部分を受け入れかつ隔離するように構成された隔離チャンバと、

前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と

を含み、

前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された前記出口ポートに向かわせるように構成され、

前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置。

【請求項８】

前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項７に記載の血液隔離装置。

【請求項９】

前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項７に記載の血液隔離装置。
【請求項１０】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項７に記載の血液隔離装置。
【請求項１１】
血液サンプル最適化システムであって、
採血システムであって、
患者の血液サンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、
前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と、
前記血液サンプルの後続の部分を採取しかつ収容するために真空採血管を受け入れるように構成されたサンプル針と
を含む採血システムと、
前記患者針と前記サンプル針との間に前記採血経路に沿って接続された血液隔離装置であって、
前記血液サンプルを受け入れるように構成された入口ポートと、
前記入口ポート及び前記採血システムのサンプル針に接続された出口ポートと、
前記入口ポートに接続されかつ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、前記血液サンプルの最初の量を受け入れかつ前記血液サンプルの最初の量の少なくとも最初の部分を隔離するように構成された隔離チャンバと、
前記入口ポートに接続された近位端を有し、前記血液サンプルの後続の部分を受け入れるように構成されたサンプリング流路と
を含み、
前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの後続の部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液サンプルの最初の部分を迂回することを可能にしかつ前記血液サンプルの後続の部分を前記サンプリング流路の遠位端に接続された前記出口ポートに向かわせるように構成され、
前記入口ポート、前記出口ポート、前記隔離チャンバ及び前記サンプリング流路を収容しかつ画定するハウジングをさらに含む、血液隔離装置と
を含む、血液サンプル最適化システム。
【請求項１２】
前記血液隔離装置の前記隔離チャンバは周囲空気圧であり、前記隔離チャンバは患者の血圧が前記隔離チャンバ内の周囲空気圧に打ち勝つことによって前記血液サンプルの最初の部分を受け入れる、請求項１１に記載の血液サンプル最適化システム。
【請求項１３】
前記サンプル針は、前記採血経路を介した前記患者針へのアクセスを開くために前記真空採血管によって穿孔されるシールを含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１４】
前記血液隔離装置の前記空気透過性血液バリアは、血液と接触すると密封する空気透過性材料を含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１５】
前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項１１に記載の血液サンプル最適化システム。
【請求項１６】
前記採血システムの前記採血経路はチューブを含む、請求項１１に記載の血液サンプル最適化システム。
【発明の詳細な説明】
【背景技術】

【０００１】
関連出願との相互参照
本出願は、２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４３号及び２０１６年４月２７日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国非仮出願第１５／１４０，４４８号の優先権の利益を主張するものであり、これらの米国非仮出願の両方が２０１５年７月２４日に出願された「血液培養改良システム及び方法」と題する米国仮特許出願第６２／１９６，７９７号、２０１５年１０月７日に出願された「非汚染採血用の血液隔離システム」と題する米国仮出願第６２／２３８，６３６号、及び２０１６年４月４日に出願された「血液サンプル最適化システム及び血液汚染物質隔離装置及び方法」と題する米国仮特許出願第６２／３１８，１９４号の優先権を主張しており、これらの開示はその全体が参照により本明細書に含まれるものとする。

【０００２】
菌血症は、血液中に微生物が存在することである。一方、敗血症は、発熱、頻脈、頻呼吸及び低血圧などの臨床症状及び臨床兆候がある場合の菌血症である。菌血症及び敗血症は、高い死亡率、入院発生率及び入院期間と関連する費用の増加とを伴う。多くの菌血症、敗血症、真菌血症及び他の病原体が実際に病院又は他の医療施設内で発生し、カテーテル及び静脈穿刺がこれらの病原体の潜在的なキャリアとしての汚染源である。

【０００３】
血液培養は、患者の血液中の菌血症及び敗血症に関連する微生物病原体を検出するのに使用される標準検査である。血液培養という用語は、血液が１つ以上の血液培養ボトル又は容器に接種される、末梢部位又は中心ライン又は動脈ラインからの１回の静脈穿刺を指す。１つのボトルが１つの血液培養と見なされ、２つ以上がセットと見なされる。複数のセットは複数の静脈穿刺から得られ、患者の異なる部位に関連する。

【０００４】
これらの方法は、敗血症を管理する上で重要な要素である微生物同定及び感受性検査を可能にするが、迅速な結果が得られないことと厄介な病原体に対する感度が低いことが、改良されたシステムの開発及び補助的な分子検査又はプロテオミクス検査につながっている。

【０００５】
血液培養を行うための血液サンプルの採取は、現代の患者ケアの重要な要素であり、正確な診断を提供することによって患者の結果に良い影響を与えることも、不必要な抗菌療法を長引かせ、入院期間を長くし、コストを増加させることによって結果に悪影響を与えることもある。

【０００６】
血液培養の採取の１つの結果は、汚染である。血液培養の汚染は、偽陽性の培養結果及び／又は医療関連コストの著しい増加につながる可能性がある。血液培養の汚染の原因は、不適切な皮膚消毒、不適切な採取管の消毒、最初の採血の汚染を含み、これらは結果を歪める可能性がある。

【０００７】
血液培養採取キットは、一般に、ＢＤ、スミス、ビー・ブラウンなどの会社によって提供される「バタフライ」セット、輸液セット、又は他のタイプの静脈穿刺装置と、好気性血液培養ボトル及び嫌気性血液培養ボトルとで構成される。様々な異なるボトルも検査要件に応じて利用可能である。これらのボトルは、好気性生物と嫌気性生物の両方の回収を最適化するように特別に設計されている。従来のキットでは、使用されるボトルは一般に「バキュテナー（登録商標）」として知られており、これは、所定の量の血液などの液体の採取を容易にするべく管の内部に真空を作り出すために排気される蓋を備える滅菌ガラス管又は滅菌プラスチック管から形成される採血管である。

【０００８】

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

【０００９】

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

【００１０】

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

【００１１】

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

【００１２】

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

【発明の概要】

【発明が解決しようとする課題】

【００１３】

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

【００１４】

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

【課題を解決するための手段】

【００１５】

一態様では、血液隔離装置が提示されている。血液隔離装置は、入口ポートと出口ポートとを含む。血液隔離装置は、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端と、出口ポートと接続される遠位端とを有する、サンプリング流路

を更に含む。

【００１６】

別の態様では、採血経路と接続される血液隔離装置が記載されている。採血経路は、患者針とサンプル採取装置とを有する。血液隔離装置は、患者針と接続される入口ポートと、入口ポートと接続される隔離チャンバであって、空気透過性血液バリアを含む通気口を有する隔離チャンバとを含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路と、サンプリング流路の遠位端及びサンプル採取装置と接続される出口ポートとを更に含む。

【００１７】

更に別の態様では、採血システムと接続される血液隔離装置が記載されている。採血システムは、患者から血液サンプルを取り出せるようにするための患者針と、密封され且つ真空採血管を受け入れるように適合されたサンプル針とを含む。血液隔離装置は、患者からの血液サンプルを受け入れるために患者針と接続される入口ポートを含む。血液隔離装置は、入口ポートと接続され且つ空気透過性血液バリアを含む通気口を有する隔離チャンバであって、サンプル針が真空採血管によって開封されるより前に血液サンプルの最初の部分を受け入れ且つ隔離する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、真空採血管によってサンプル針が開封されると血液サンプルの後続の部分を運ぶサンプリング流路を更に含む。血液隔離装置は、血液サンプルの後続の部分をサンプル針に運ぶためにサンプリング流路の遠位端と接続される出口ポートを更に含む。

【００１８】

更に別の態様では、血液サンプル最適化システムが開示され、記載されている。血液サンプル最適化システムは、患者の血液の１つ以上のサンプルを取り出せるようにし且つ得るための採血システムと、静脈穿刺プロセスによって汚染されている恐れがあり且つ患者の血液中の病原体の偽陽性同定をもたらす可能性がある患者の血液の１つ以上のサンプルの最初の部分を受け入れ且つ隔離するための血液隔離装置とを含む。

【００１９】

採血システムは、患者の血液のサンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、血液サンプルを運ぶために患者針と接続される採血経路と、血液サンプルの後続の部分を採取し且つ収容するために真空採血容器を受け入れるように構成されたサンプル針とを含む。

【００２０】

更に別の態様では、血液隔離装置が開示され、記載されている。一部の実施では、血液隔離装置は、入口ポートと、入口ポートと接続される出口ポートと、入口ポートと接続される隔離チャンバとを含むことができる。隔離チャンバは、空気透過性血液バリアを含む通気口を有することができる。

【００２１】

血液隔離装置は、患者針とサンプル針との間で採血経路に沿って接続され、血液サンプルを受け入れるための入口ポートを含む。血液隔離装置は、血液サンプルの最初の量を受け入れるために入口ポートと接続される隔離チャンバであって、血液サンプルの最初の量の少なくとも最初の部分を隔離するために空気透過性血液バリアを含む通気口を有する隔離チャンバを更に含む。血液隔離装置は、入口ポートと接続される近位端を有するサンプリング流路であって、隔離チャンバが血液サンプルの最初の量の少なくとも最初の部分を隔離すると血液サンプルの後続の量を真空採血容器に運ぶサンプリング流路を更に含む。血液隔離装置は、サンプリング流路の遠位端と接続される出口ポートであって、血液サンプルの後続の量を出力する出口ポートを更に含む。

【００２２】

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

【図面の簡単な説明】

【００２３】
以下、これら及び他の態様について、以下の図面を参照して詳細に説明する。
【図１】血液サンプル最適化システムを示す。
【図２】代替的な実施に従う血液サンプル最適化システムを示す。
【図３】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図４】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図５】別の代替的な実施に従う血液サンプル最適化システムを示す。
【図６】代替的な実施に従う血液サンプル最適化システムを示す。
【図７】血液培養の質を最適化するための方法のフローチャートである。
【図８Ａ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｂ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｃ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｄ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図８Ｅ】一部の実施に従う非汚染採血用の血液隔離システムを示す。
【図９】血液隔離システムに用いる経路スプリッタを示す。
【図１０Ａ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｂ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｃ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１０Ｄ】代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ａ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｂ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｃ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｄ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１１Ｅ】他の代替的な実施に従う非汚染採血用の血液隔離システムを示す。
【図１２Ａ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｂ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｃ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１２Ｄ】更に他の代替的な実施に従う血液隔離装置を含む血液サンプル最適化システムを示す。
【図１３Ａ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｂ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｃ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１３Ｄ】更に別の代替的な実施に従う血液サンプル最適化システム１３００を示す。
【図１４Ａ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｂ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｃ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｄ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に別の実施を示す。
【図１４Ｅ】患者の血液サンプルに対して実施される血液培養又は検査における偽陽性を低減するために最初のアリコート又はサンプルの汚染物質を隔離する採血システムの更に

別の実施を示す。
【図１５Ａ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｂ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｃ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｄ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｅ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｆ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１５Ｇ】更に別の実施に従う血液隔離装置及びそれを使用する方法を示す。
【図１６Ａ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｂ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｃ】更に別の実施に従う血液隔離装置を示す。
【図１６Ｄ】更に別の実施に従う血液隔離装置を示す。
【図１７Ａ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｂ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｃ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｄ】血液隔離装置用のハウジングの下部部材を示す。
【図１７Ｅ】血液隔離装置用のハウジングの下部部材を示す。
【図１８Ａ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｂ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｃ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｄ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｅ】血液隔離装置用のハウジングの上部部材を示す。
【図１８Ｆ】血液隔離装置用のハウジングの上部部材を示す。
【図１９Ａ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図１９Ｂ】下部部材と嵌合する上部部材を有する血液隔離装置を示す。
【図２０】血液隔離装置を含む血液サンプル最適化システムを示す。
【図２１】ウィッキング材料チャンバを使用する通気口付きでない血液隔離装置を示す。
【図２２Ａ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２２Ｂ】血液隔離装置の隔離チャンバ内の血液を隔離するためのフィルタの材料構成を示す。
【図２３Ａ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。
【図２３Ｂ】採血装置による真空力を使用する血液隔離装置の別の実施を示す。　様々な図面における同様の符号は同様の要素を示す。
【発明を実施するための形態】
【００２４】
本明細書は、採取される血液サンプル中の汚染物質を低減又は排除し、その結果、採取される血液サンプルの血液培養又は他の検査における偽陽性の判断を減少又は排除する血液サンプル最適化システム及び方法を記載している。一部の実施では、血液サンプル最適化システムは、患者の血流への血管アクセスのための患者針と、バキュテナー（登録商標）のような真空採血容器又は真空採血管などの採血容器か又は他のサンプリング装置に血液サンプルを供給するためのサンプル針と、患者針とサンプル針との間に位置する血液隔離装置とを含む。血液隔離装置は、汚染されている可能性のある最初のアリコートの血液を隔離するための隔離チャンバを含み、最初のアリコートの血液が隔離チャンバ内に隔離された後に患者針とサンプル針との間の汚染されていない可能性のある血液を運ぶために隔離チャンバを迂回するサンプリング流路を更に含むことができる。
【００２５】
図１は、一部の実施に従う血液サンプル最適化システムを示す。システムは、患者の皮膚を穿刺してその中の患者の静脈及び静脈内の血液にアクセスするための患者針１を含む。システムは、再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース

又は装置内に収容され且つ再密封可能なブーツ１０、ルアー作動弁、又は別の採取インターフェース又は装置によって当初は密封されていることができる、サンプル針（すなわち、バキュテナー（登録商標）などと共に使用するための再密封可能に密封された針）５を更に含む。再密封可能なブーツ１０は、患者の血液を採取するためのバキュテナー（登録商標）ボトル（図示せず）を用いることによって、サンプル針５のそばに又はサンプル針５の周りに押し付けることができる。システムは、サンプル針５に通じる低容量チャンバ３０を更に含むことができるが、ハウジング５０によって形成される隔離チャンバ５５に通じる穴又は１つ以上の流路４５も含む。

【００２６】

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

【００２７】

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

【００２８】

穴又は流路４５は、任意の所望の長さ、断面形状又はサイズであることができ、且つ／又は任意の所望の角度又は向きで低容量チャンバ３０から離れるように形成されることができる。穴又は流路４５はまた、最初のアリコートの血液サンプルを隔離チャンバ５５内に保持する一方向フラップ又は一方向弁６０を含むことができる。一部の特定の実施では、穴又は流路４５は、低容量チャンバ３０から隔離チャンバ５５への一方向の血液の流れのための「ダックビル」弁又はフラッパ弁６０などを含むことができる。空気透過性血液バリア２０は、空気が出ることを可能にするが血液と接触すると密封する材料で構成することもでき、それによって外気が隔離チャンバ５５に入ることを許容しない。この密封は弁を不要にする。

【００２９】

弁６０は、任意のタイプの弁又は開閉機構であることができる。チャンバ３０は、実質的に残留血液を保持しないように設計されており、特定の容積又は割合の血液を隔離チャ

ンバ５５に保持し又は通過させるように構成することができる。同様に、隔離チャンバ５５は、抗菌コーティングのような任意のタイプのコーティング、又は隔離された最初の採血の成分の同定及び／又は診断を支援するコーティングも含むことができる。

【００３０】

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

【００３１】

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

【００３２】

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

【００３３】

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

【００３４】

Ｔ又はＹコネクタ１０２は、フラップ又は一方向弁を含み、所定の流量の血液のために寸法設定され且つ適合された穴を有する。隔離チャンバ１０４は、チューブから形成され又は硬いハウジングによって形成されることができ、最初は空気で満たされている。隔離チャンバ１０４は、自動的に、すなわち、患者自身の血圧による圧力下で患者から流出する血液を受け入れる。隔離チャンバ１０４は、好ましくは隔離チャンバ１０４を形成し且つ近位端がＴ又はＹコネクタ１０２に接続されたチューブの遠位端に、空気透過性血液バリア１０６を含む。Ｔ又はＹコネクタ１０２は、最も効率的な血流のために任意の所望の角度で分岐することができ、最初のアリコートの血液と主要な採血サンプルとの混合を最小限に抑え又は排除するために、開口部及び流路と主血液流路との間の接合部分を最小化

するように形成されることができる。

【００３５】

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

【００３６】

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

【００３７】

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

【００３８】

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

【００３９】

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

【００４０】

図７は、血液培養の質を最適化するための例示的な方法のフローチャートである。７０２において、臨床医が患者の静脈に針を挿入する。７０４において、血液が隔離チャンバに流れ込み、隔離チャンバ内の空気を隔離チャンバから空気透過性血液バリアを通して押し出す。一部の実施では、隔離チャンバの容積は、０．１立方センチメートル（ｃｃ）未満から５立方センチメートル（ｃｃ）以上である。隔離チャンバは、血液サンプルの第２部分及び他の後続の部分又は後続の採取よりも汚染しやすい血液サンプルの第１部分を採取するように寸法設定され且つ適合されている。隔離チャンバは空気透過性血液バリアを有し、この血液バリアを通して空気を患者の静脈から押し出された血液で追い出すことができるので、このような血液は、血液サンプルを受け入れ且つ保管するためのバキュテナー（登録商標）又は他のボトルに引き込まれるか又は他の方法で入る前に、必然的に且つ自動的に隔離チャンバに流入する。

【００４１】
隔離チャンバがいっぱいになると、血液は、血液が通過するのを阻止又は防止する空気透過性血液バリアに集まるか、さもなければ接触する。７０６において、血液が空気透過性血液バリアの全内部表面積と接触すると、空気透過性血液バリアは閉じられ、空気はもはや流出又は流入しない。７０８において、臨床医は、バキュテナー（登録商標）などの真空採血管を取り付けることができることを示す指標を提供されるか又は満杯のチャンバを見ることができる。指標は、一次チャンバがいっぱいであるか否かを確認するための一次チャンバの可視性、例えば、色を変える血液バリア、又は他の指標を含むことができる。隔離チャンバの充填時間は、実質的に瞬間的であり得るので、このような指標は、存在する場合、隔離チャンバが満たされているというだけである可能性がある。

【００４２】
真空採血管が取り付けられる前、針、サンプリング流路、及び隔離チャンバの間の連通は、隔離チャンバの血液バリアの密封によって制限され、従って隔離によって空気がシステムに再び入ることを可能にしない。連通経路の密封は、機械的にねじること又は他の動作、小さな穴又は曲がりくねった経路によって達成され、臨床医による別個の弁又は機械的な動作又は操作の必要性をなくす。７１０において、真空採血管を取り外すと、自己密封式の膜がサンプル針を密封し、７１２で、更なる後続の真空採血管を取り付けることができる。７１４において、サンプルが採取されると、装置が患者から取り外され、廃棄される。

【００４３】
図８Ａ～８Ｅは、一部の実施に従う、非汚染採血用の例示的な血液サンプル最適化システム８００を示す。血液サンプル最適化システム８００は、チューブ、患者針（又は両方）、又は他の血管又は静脈アクセス装置に接続されることができる入口ポート８０２と、隔離チャンバチューブ８０６への第１出口とサンプル採取チューブ８０８への第２出口とを有する経路スプリッタ８０４とを含む。隔離チャンバチューブ８０６及びサンプル採取チューブ８０８の一方又は両方は、チューブから形成されることができる。一部の実施では、隔離チャンバチューブ８０６は、特定の量の当初血液サンプルを収容するように寸法設定される。サンプル採取チューブ８０８は、ひとたび隔離チャンバチューブ８０６が満たされると、血液サンプルを受け入れる。サンプル採取チューブ８０８は、バキュテナー（登録商標）ベース又はハウジング８１０、又は他の血液サンプル採取装置に接続されることができる。

【００４４】
血液隔離システム８００は血液隔離装置８１２を更に含み、血液隔離装置８１２は、図８Ｂ～８Ｄにより詳細に示すようにハウジング８１８を含み、ハウジング８１８は、非汚染サンプル採取チューブ８０８用の経路を画定するか又はいずれかの端部が非汚染サンプル採取チューブ８０８と接続されるサンプリング流路８２０を含む。サンプリング流路８２０は、非汚染サンプル採取チューブ８０８に沿った位置でハウジング８１８をより良好に固定し且つ安定させるように、ハウジング８１８を通って曲線状であることができる。

【００４５】
血液隔離装置８１２は、隔離チャンバチューブ８０６と接続される隔離チャンバ８２２又は他のチャンバを更に含む。隔離チャンバ８２２は、空気透過性血液バリア８２４で終端している。空気透過性血液バリア８２４はまた、血液サンプル（すなわち、非汚染血液サンプル）の正式な採取を開始することができる指標として、血液との完全な接触時に異なる色に変わる着色剤を含むことができる。小さい光、音発生機構などの他の指標を使用することができる。一部の実施では、空気透過性血液バリアは、隔離チャンバ８２２の方向から直角に配置されているが、ハウジング８１８に使用される空間及び材料を節約するために任意の距離又は向きに配置されることができる。ハウジング８１８及びその内容物は、任意の剛性材料又は半剛性材料又は一連の材料から形成されることができる。

【００４６】
図９は、例えば、図８Ａ～８Ｅに示すような血液隔離システムに用いる経路スプリッタ

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

【００４７】

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

【００４８】

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

【００４９】

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

【００５０】

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

【００５１】

一部の実施では、血液隔離装置１１００は、常時閉じている針、バキュテナー（登録商標）シールド又は他の採取装置などの採血装置１１２０を含むことができる。採血装置１１２０は、患者針の挿入プロセスによって汚染される恐れがある最初のアリコートの血液を隔離することができるように、効率及び利便性のために血液隔離装置１１００と共に製造及び販売されることができる。従って、採血装置１１２０は、偽陽性の検査のリスクを低減するように非汚染血液サンプルを採取し且つ非汚染サンプルを確実にすることができる。

【００５２】

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

【００５３】

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

【００５４】

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

【００５５】

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

【００５６】

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

【００５７】

図１３Ａ～１３Ｄに示す実施例では、隔離チャンバ１３１８は、ハウジング１３０１内の空洞又はチャンバとして形成され、又はハウジング１３０１を画定する壁によって形成される。隔離チャンバ１３１８は、Ｕ字形流路、Ｓ字形流路、螺旋流路などの曲がりくねった流路、又はハウジング１３０１とキャップ１３０７との協働及び接続によって画定される任意の他の曲がりくねった流路であることができ、キャップ１３０７は、隔離チャンバ１３１８内の曲がりくねった流路のための１つ以上の壁又はディレクタを提供する突出部１３０５を含むことができる。キャップ１３０７からの突出部１３０５は、真っ直ぐであるか湾曲していることができ、様々な流路、開口部又は溝が埋め込まれていることができ、キャップ１３０７から任意の角度又は向きで延びることができる。隔離チャンバ１３

１８の形成を完了するためにキャップ１３０７がハウジング１３０１と接続されると、突出部１３０５は曲がりくねった流路の少なくとも一部を形成し、隔離チャンバ１３１８内に曲がりくねった流路によって形成される隔離流路に最初のアリコート又は量の血液又は他の体液を隔離する。

【００５８】

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

【００５９】

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

【００６０】

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

【００６１】

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

【００６２】

血液隔離装置１４０１は隔離チャンバ１４０８を更に含み、隔離チャンバ１４０８は、入口ポート１４０２と出口ポート１４０４との間の任意の位置でサンプリング流路１４０６に接続され且つサンプリング流路１４０６から分離又は方向転換されるが、好ましくは入口ポート１４０２の近くのサンプリング流路１４０６の近位端に接続され且つ近位端か

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

【００６３】

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

【００６４】

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

【００６５】

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

【００６６】

血液隔離装置１５００は、血液サンプルへのアクセス及び血液サンプルの採取のために患者の血管系に挿入される患者針と接続されることができる入口ポート１５０２を含む。入口ポート１５０２は、同様に患者針と接続されるチューブ又は他の導管と接続されることもできる。入口ポート１５０２は、血液隔離装置１５００への開口部を画定し、この開口部は、患者針と接続されるチューブ又は他の導管又は患者針自体と同じ断面寸法であることができる。例えば、開口部は、約０．０４５インチ（１．１４３ｍｍ）の直径を有す

る円形であることができるが、０．０１インチ（０．２５４ｍｍ）から０．２インチ（５．０８ｍｍ）又はそれ以上の直径を有することができる。

【００６７】

入口ポート１５０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封のコネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザ溶接、又は熱接合などによって、入口ポート１５０２と一体化されることができる。これによって、血液隔離装置１５００は、患者針と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針を血液隔離装置１５００に接続する必要性をなくすことができる。

【００６８】

血液隔離装置１５００は、血液隔離装置１５００から及び血液サンプル採取装置への開口部を画定する出口ポート１５０４を更に含む。出口ポート１５０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１５００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１５００に接続する必要性をなくすことができる。

【００６９】

血液隔離装置１５００は、入口ポート１５０２と出口ポート１５０４との間にサンプリング流路１５０６を更に含み、サンプリング流路１５０６は、最初のアリコートの血液が隔離されると血液サンプル経路として機能する。サンプリング流路１５０６は、任意のサイズ、形状、又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１５０６は、入口ポート１５０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１５０６は、入口ポート１５０２から出口ポート１５０４まで徐々に広がることができる。

【００７０】

血液隔離装置１５００は隔離チャンバ１５０８を更に含み、隔離チャンバ１５０８は、入口ポート１５０２と出口ポート１５０４との間の任意の位置でサンプリング流路１５０６に接続され且つサンプリング流路１５０６から分離又は方向転換されるが、好ましくは入口ポート１５０２の近くのサンプリング流路１５０６の近位端に接続され且つ近位端から分離又は方向転換される。一部の実施では、分水路はＹ字路を含む。隔離チャンバ１５０８は、好ましくは大気圧に維持され、隔離チャンバ１５０８の遠位端又はその近傍に通気口１５１０を含む。通気口１５１０は、空気透過性血液バリア１５１２を含む。図１５Ｃは、隔離チャンバ１５０８が患者からの血液の最初のアリコート又はサンプルで満たされた血液隔離装置１５００を示す。

【００７１】

空気透過性血液バリア１５１２は、保護カバー１５１６で覆されていることができる。保護カバー１５１６は、ユーザーが彼らの指又は他の外部器具で空気透過性血液バリア１５１２に触れるのを妨げるように寸法設定され且つ構成されることができ、一方それでも患者自身の血圧によって隔離チャンバ１５０８内に強制的に血液が供給されることによって空気が隔離チャンバから追い出されるときに空気が空気透過性血液バリア１５１２から出ることを可能にする。保護カバー１５１６は、フィルタが周囲の流体又は飛沫に偶発的に曝されるのを阻止又は防止するように構成されることができる。これは、保護カバーに疎水性膜を追加することを含むがそれに限定されない、様々な機械的方法で行うことができる。

【００７２】

図１５Ｂは、血液隔離装置１５００の出口ポート１５０４及び通気口１５１０を含むハウジング１５０１の上面からの血液隔離装置１５００の斜視図であり、サンプル採取装置が起動される前、サンプリング流路１５０６が空である間に最初のアリコートの血液が隔

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

【００７３】

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

【００７４】

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

【００７５】

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

【００７６】

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

【００７７】

一部の実施では、サンプリング流路１５０６及び隔離チャンバ１５０８は、ハウジング１５０１に形成された溝、流路、ロック又は他の経路によって形成される。ハウジング１５０１は、ゴム、プラスチック、金属又は他の材料を含む任意の適切な材料で作られることができる。ハウジング１５０１は、透明又は半透明の材料から、又は不透明又は非半透明の材料から形成されることができる。他の実施では、ハウジング１５０１は、大部分が不透明又は非透明であることができるが、サンプリング流路１５０６及び／又は隔離チャンバ１５０８に直接隣接するハウジング表面は、透明又は半透明であり、最初に隔離チャンバ１５０８が必要又は所望の程度まで満たされているという視覚的な合図又はサイン、及び／又は、次に汚染されていない血液サンプルがサンプリング流路１５０６を通して採取される間、隔離された血液が隔離されたままであるという視覚的な合図又はサインを施

術者に与える。隔離の他の視覚的な合図又はサインは、以下に限定されるものではないが、血液の接触、浸透、又は部分的な浸透で空気透過性血液バリア１５１２が異なる色に変わること、隔離チャンバに沿った又は隔離チャンバに隣接する任意の位置にある色分けされたタブ又は指標、可聴信号、振動信号、又は他の信号を含むことができる。

【００７８】

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

【００７９】

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

【００８０】

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

【００８１】

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

【００８２】

入口ポート１６０２はまた、ねじ切り又はルアーフィッティングなどのような密封又は流体密封コネクタ又は接続部を含むことができる。一部の実施では、患者針に結合されているチューブ又は他の導管は、部品同士の共成形、接着、レーザー溶接、又は熱接合などによって、入口ポート１６０２と一体化されることができる。これによって、血液隔離装置１６００は、患者針及び／又はチューブと共に単一ユニットとして製造及び販売され、

採血又はサンプリングの際に患者針を血液隔離装置１６００に接続する必要性をなくすことができる。

【００８３】

血液隔離装置１６００は、血液隔離装置１６００から及び血液サンプル採取装置への開口部を画定する出口ポート１６０４を更に含む。出口ポート１６０４は、同様に血液隔離装置と接続されるチューブ又は他の導管と接続されることもでき、ねじ切り又はルアーフィッティングなどの密封又は流体密封コネクタ又は接続部を含むことができる。したがって、上記のように、血液隔離装置１６００は、患者針及び／又はチューブ及び血液サンプル採取装置と共に単一ユニットとして製造及び販売され、採血又はサンプリングの際に患者針及び血液サンプル採取装置を血液隔離装置１６００に接続する必要性をなくすことができる。

【００８４】

血液隔離装置１６００は、入口ポート１６０２と出口ポート１６０４との間のサンプリング流路１６０６と、入口ポート１６０２と出口ポート１６０４との間の任意の位置でサンプリング流路１６０６に接続され且つサンプリング流路１６０６から分離又は方向転換される隔離チャンバ１６０８とを更に含む。サンプリング流路１６０６は、最初のアリコートの血液が隔離チャンバ１６０８内に隔離されると、採血経路として機能する。サンプリング流路１６０６は、任意のサイズ、形状又は構成の流路又は導管であることができる。一部の実施では、サンプリング流路１６０６は、入口ポート１６０２の開口部と実質的に同様の断面積を有する。他の実施では、サンプリング流路１６０６は、入口ポート１６０２から出口ポート１６０４まで徐々に広がることができる。隔離チャンバ１６０８は、図１７及び１９により詳しく示すように、血液がサンプリング流路１６０６のより小さい直径に入るのに対して、まずリザーバに入ろうとするように、隔離流路の経路に向かって大きいリザーバを形成するべくより大きい断面を有することができる。

【００８５】

一部の例示的な実施では、サンプリング流路１６０６と隔離チャンバ１６０８との間の方向転換は、方向転換分岐点１６０７によって行われる。方向転換分岐点１６０７は、実質的にＹ字形、Ｔ字形、又はＵ字形であることができる。一部の好ましい例示的な実施では、図１７Ａ～１７Ｂに示すように、方向転換分岐点１６０７は、入口ポート１６０２からの流れが優先的に隔離チャンバ１６０８に向けられるように構成される。隔離チャンバ１６０８はまた、最初の血液流を隔離チャンバ１６０８に向かって且つ隔離チャンバ１６０８内に移動させるための湾曲部又は傾斜路を含むか又は形成することができる。

【００８６】

隔離チャンバ１６０８は、好ましくは大気圧に維持され、隔離チャンバ１６０８の遠位端又はその近傍に通気口１６１０を含む。通気口１６１０は、上記のように空気透過性血液バリア１６１２を含むことができる。

【００８７】

血液隔離装置１６００は、複数の部品又は単一の一体部品から形成されることができるハウジング１６０１を含むことができる。一部の実施では、図１７Ａ～１７Ｄ及び図１８Ａ～１８Ｆに示すように、ハウジング１６０１は、互いに嵌合する上部部材１６２０と下部部材１６２２とを含む。血液隔離装置１６００は、上部部材１６２０が下部部材１６２２に機械的に取り付けられたときに、両者の間の接合部分がガスケット又は密封部材によって密封されるように、ガスケット又は他の密封部材（図示せず）を含むこともできる。図１７Ａ～１７Ｄは、血液隔離装置１６００用のハウジングの下部部材１６２２を示す。下部部材１６２２は、サンプリング流路１６０６、隔離チャンバ１６０８、及び方向転換分岐点１６０７を形成するために、射出成形プロセスによって又はエッチング、切削、穿孔などによって予め形成された溝、流路、ロック、導管又は他の経路を含むことができる。

【００８８】

隔離チャンバ１６０８は、血液がサンプリング流路１６０６のより小さい直径に入るの

に対して、まず隔離チャンバ内に優先的に移動するように、サンプリング流路１６０６よりも大きい断面を有することができる。

【００８９】

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

【００９０】

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

【００９１】

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

【００９２】

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

【００９３】

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

な実施形態では、隔離チャンバ１６０８及びサンプリング流路１６０６は、患者の血圧によって生じた力が、血液隔離装置の向きに関わらず、重力の影響に打ち勝つのに十分であるように構成されることができる。

【００９４】

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

【００９５】

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

【００９６】

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

【００９７】

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

【００９８】

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

【００９９】

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

【０１００】

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

張して空隙２２０８を閉鎖し、空隙２２０８を通る空気の流れを閉塞し、完全に又は部分的に密封する。

【０１０１】

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

【０１０２】

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

【０１０３】

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

【図１】

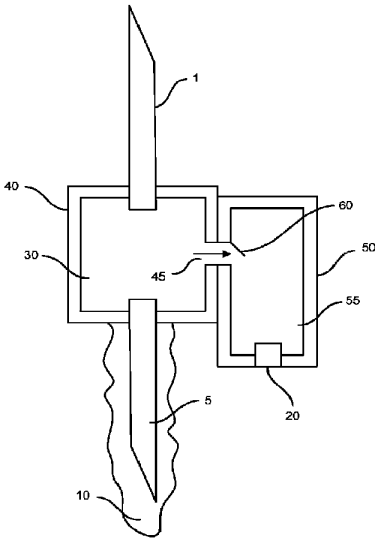


FIG. 1

【図２】

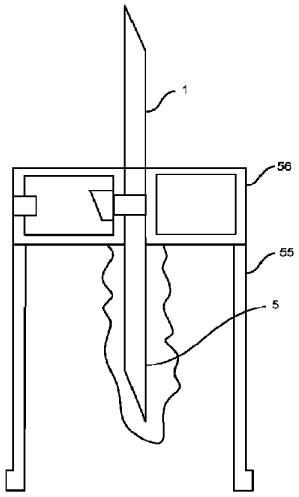


FIG. 2

【図３】

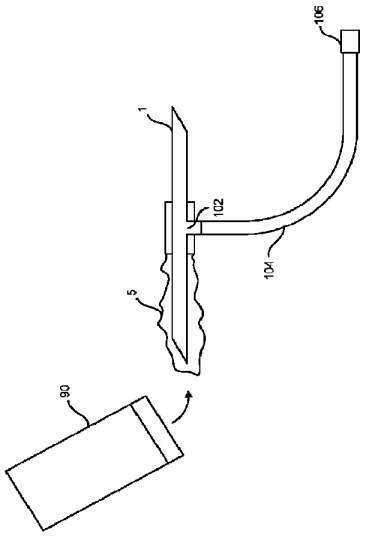


FIG. 3

【図４】

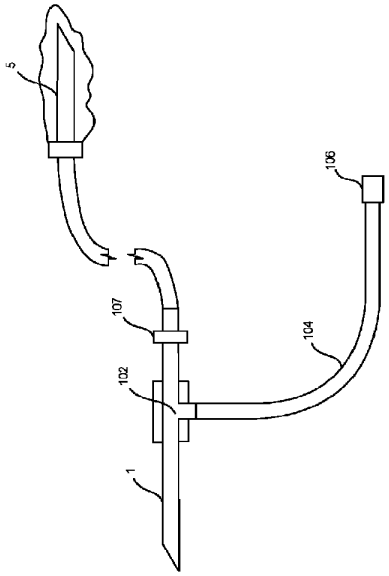


FIG. 4

【図５】

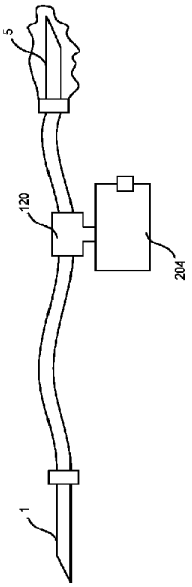


FIG. 5

【図６】

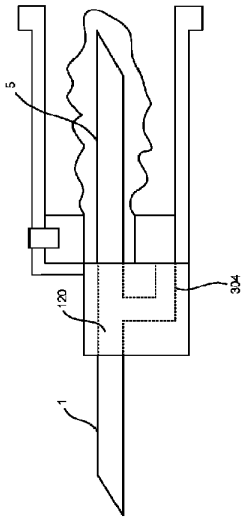


FIG. 6

【図７】

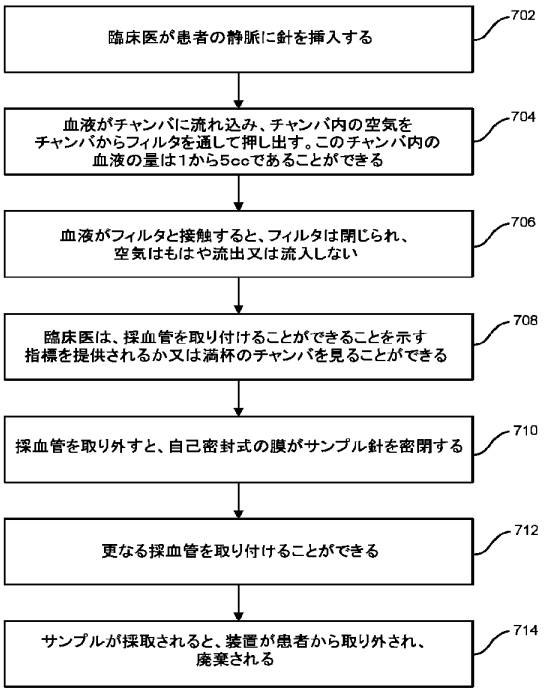


FIG. 7

【図８Ａ】

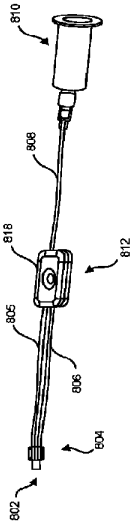


FIG. 8A

【図８Ｂ】

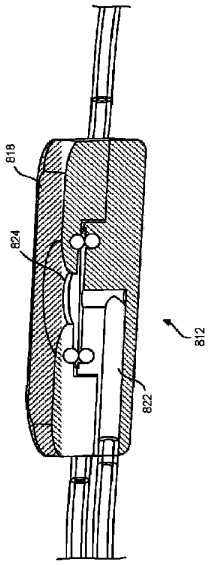


FIG. 8B

【図８Ｃ】

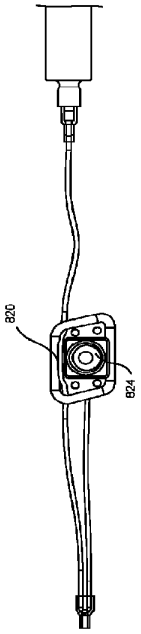


FIG. 8C

【図８Ｄ】

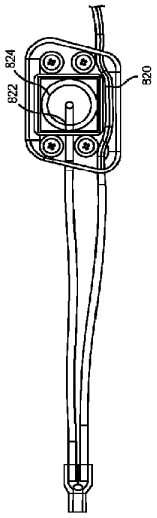


FIG. 8D

【図８Ｅ】

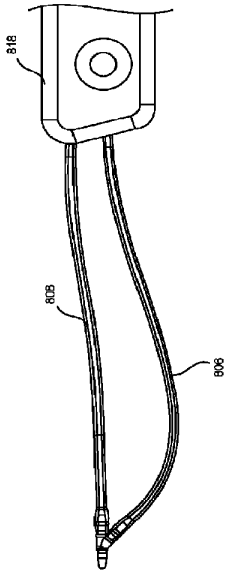


FIG. 8E

【図９】

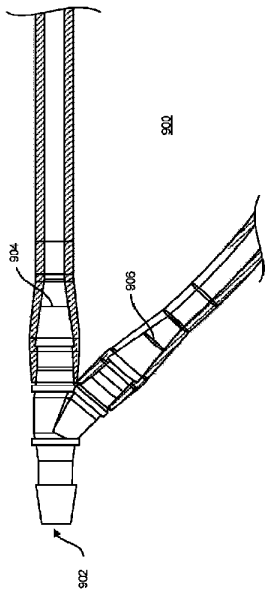


FIG. 9

【図１０Ａ】

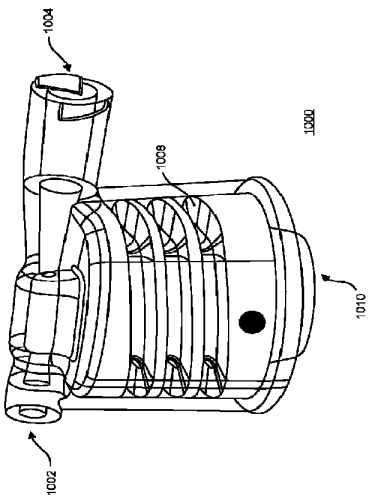


FIG. 10A

【図１０Ｂ】

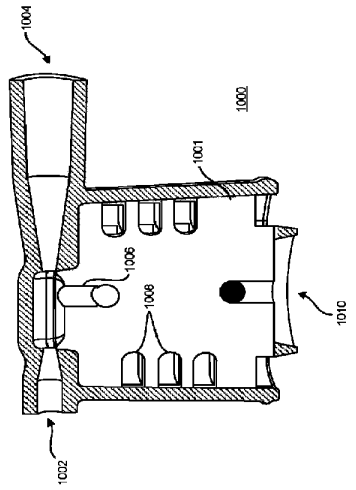


FIG. 10B

【図１０Ｃ】

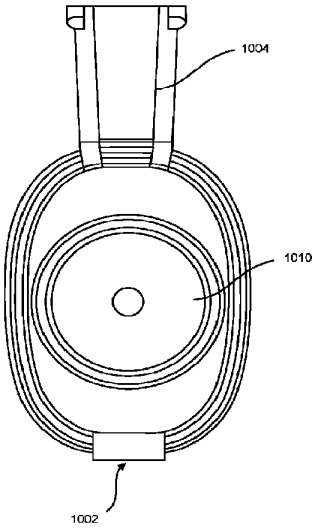


FIG. 10C

【図１０Ｄ】

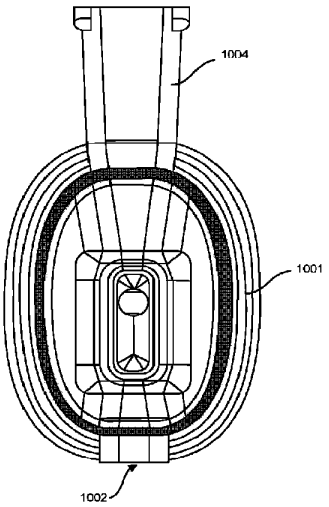


FIG. 10D

【図１１Ａ】

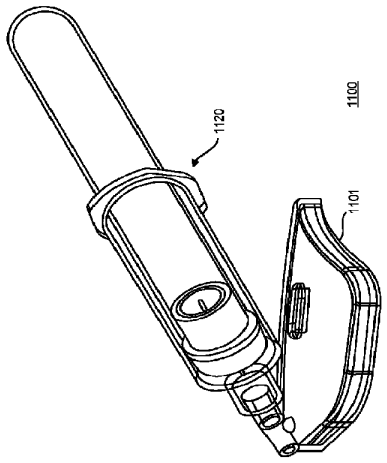


FIG. 11A

【図１１Ｂ】

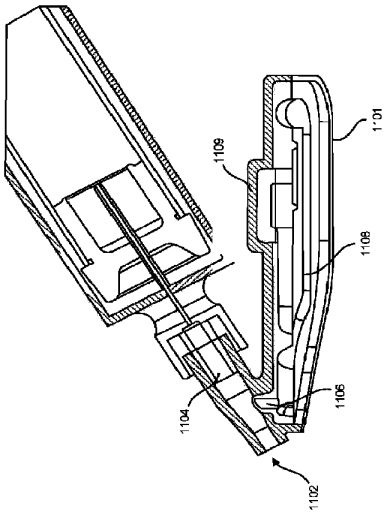


FIG. 11B

【図１１Ｃ】

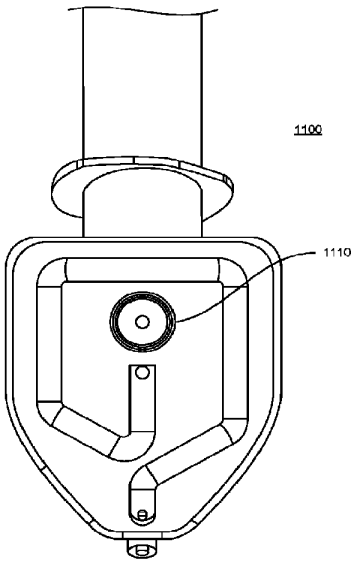


FIG. 11C

【図１１Ｄ】

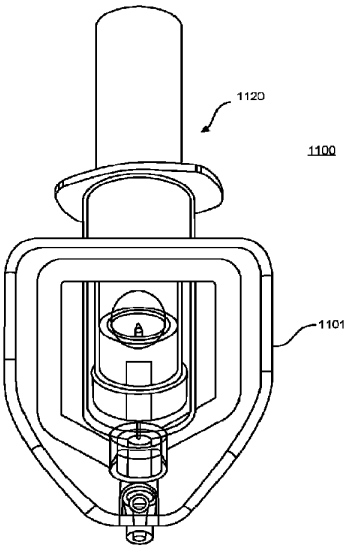


FIG. 11D

【図１１Ｅ】

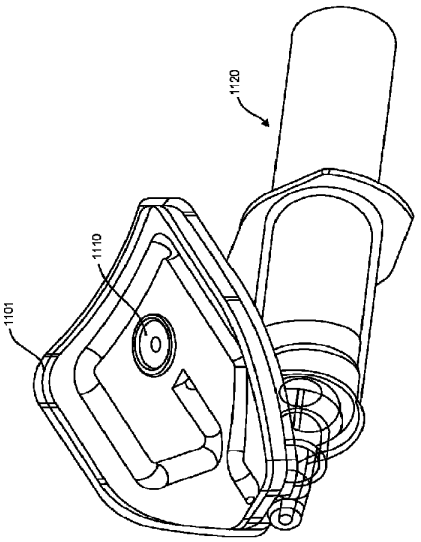


FIG. 11E

【図１２Ａ】

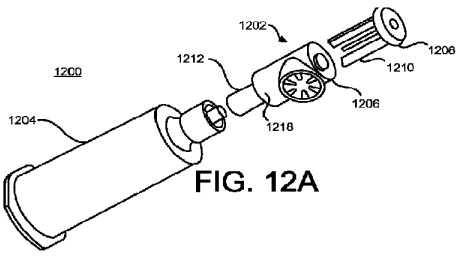


FIG. 12A

【図１２Ｂ】

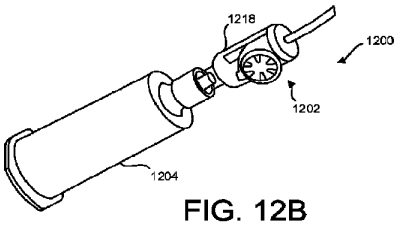


FIG. 12B

【図１２Ｃ】

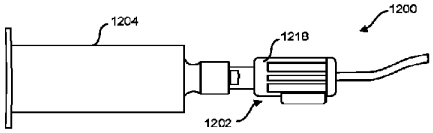


FIG. 12C

【図１２Ｄ】

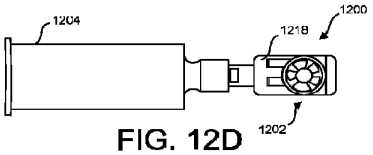


FIG. 12D

【図１３Ａ】

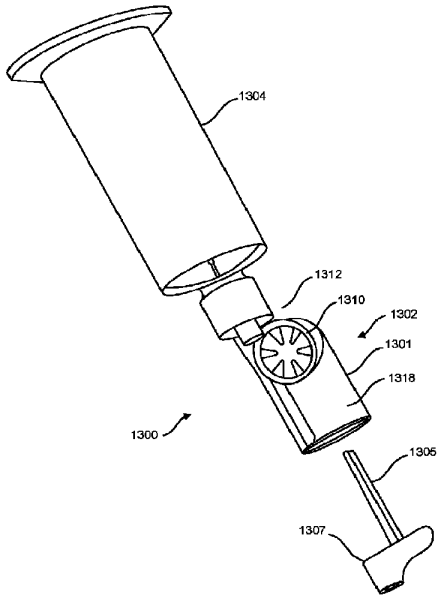


FIG. 13A

【図１３Ｂ】

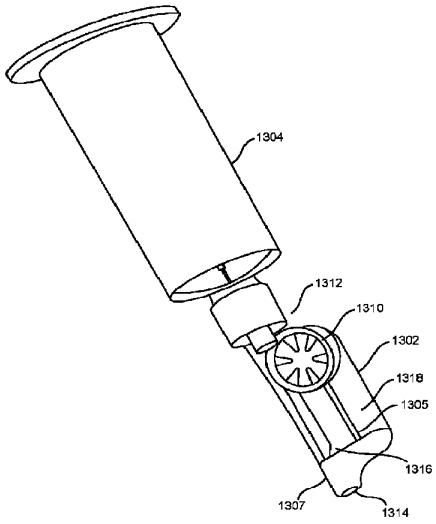


FIG. 13B

【図１３Ｃ】

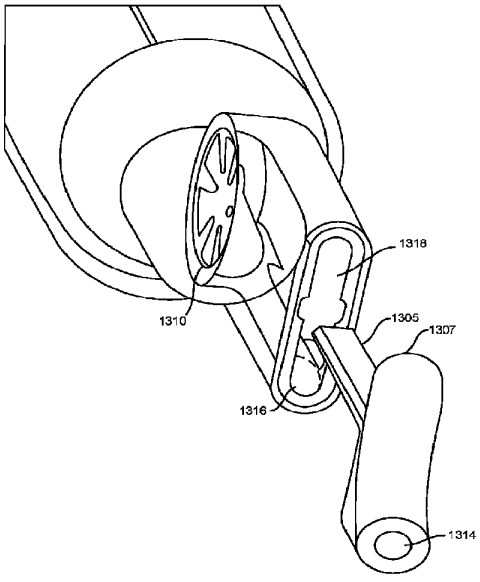


FIG. 13C

【図１３Ｄ】

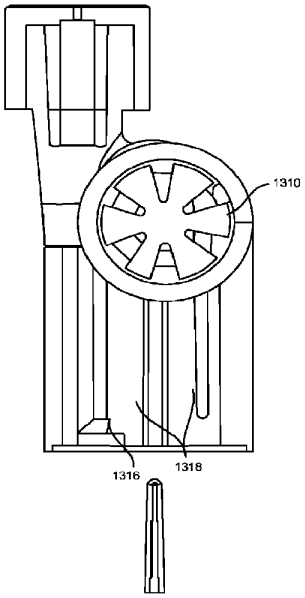


FIG. 13D

【図１４Ａ】

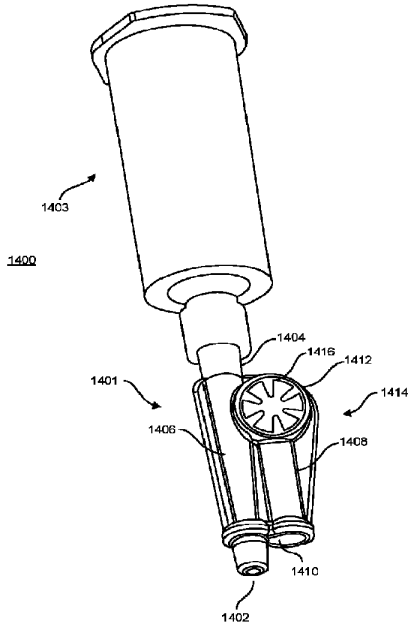


FIG. 14A

【図１４Ｂ】

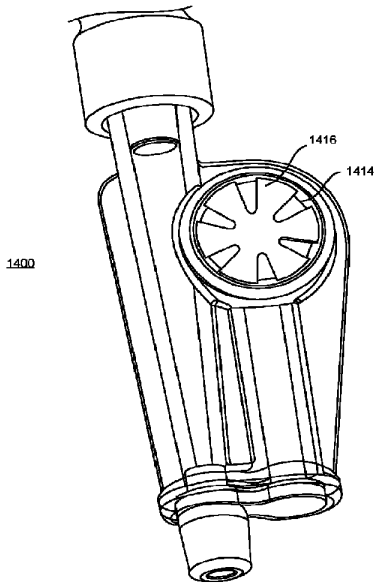


FIG. 14B

【図１４Ｃ】

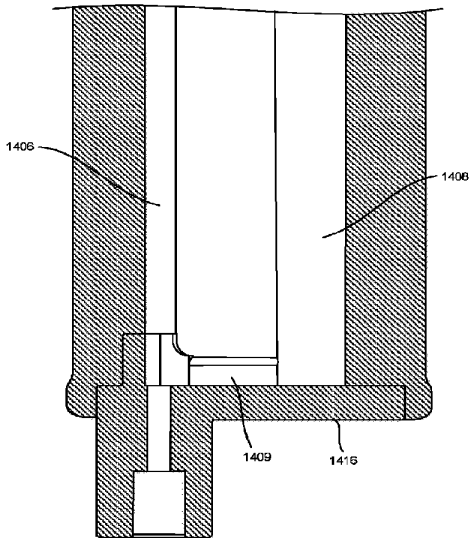


FIG. 14C

【図１４Ｄ】

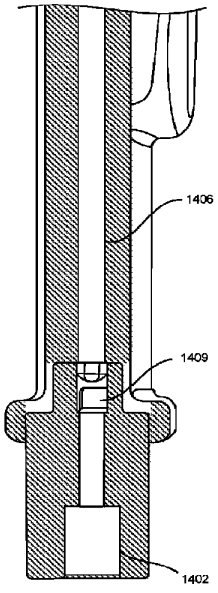


FIG. 14D

【図１４Ｅ】

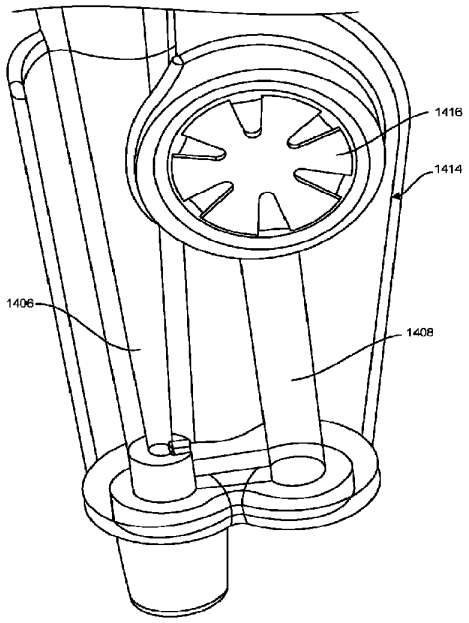


FIG. 14E

【図１５Ａ】

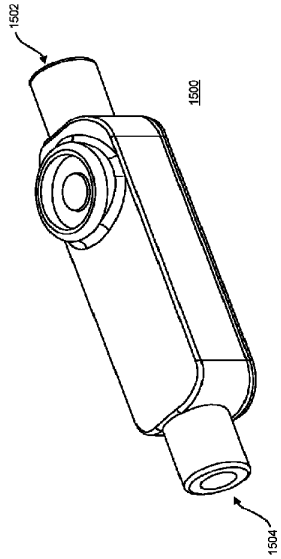


FIG. 15A

【図１５Ｂ】

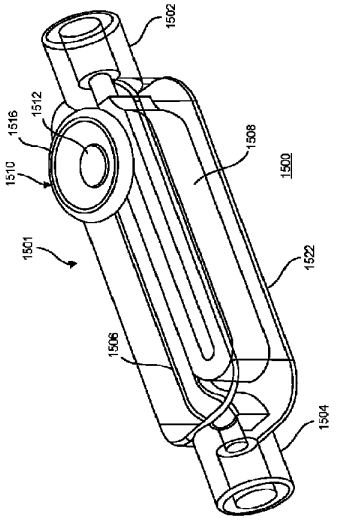


FIG. 15B

【図１５Ｃ】

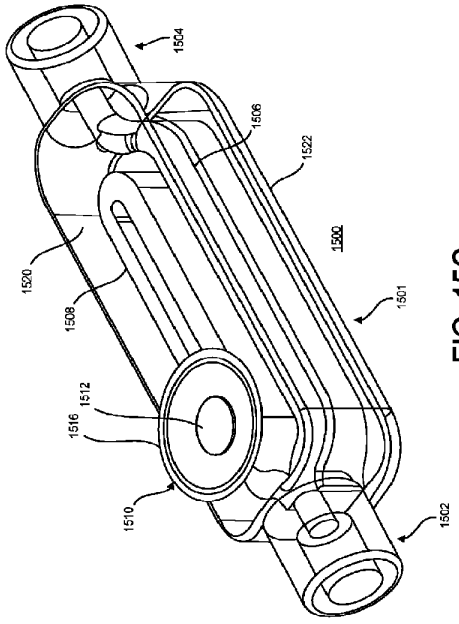


FIG. 15C

【図１５Ｄ】

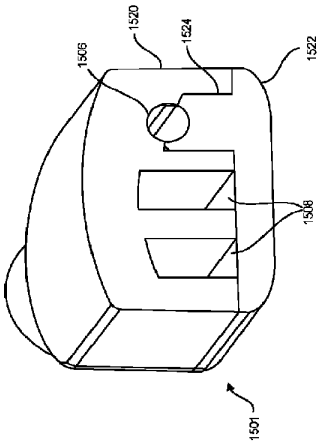


FIG. 15D

【図１５Ｅ】

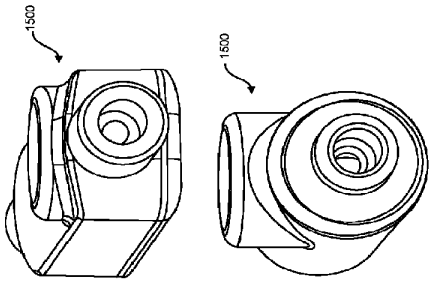


FIG. 15E

【図１５Ｆ】

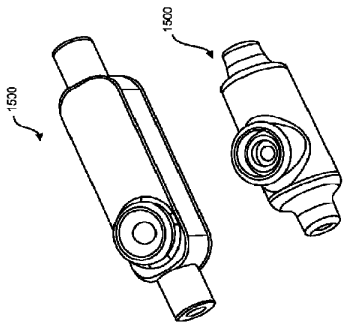


FIG. 15F

【図１５Ｇ】

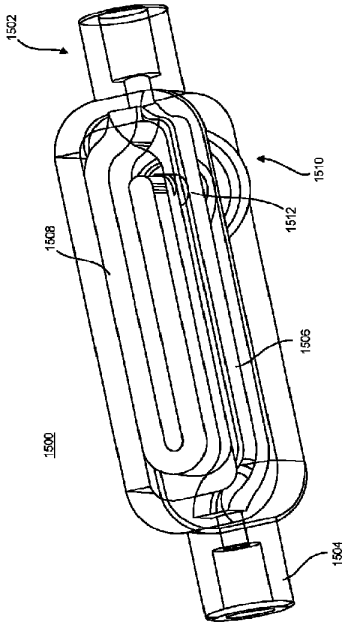


FIG. 15G

【図１６Ａ】

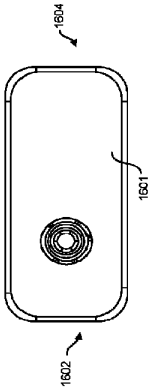


FIG. 16A

【図１６Ｂ】

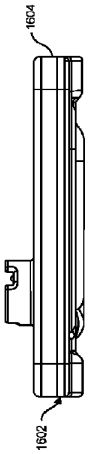


FIG. 16B

【図１６Ｃ】

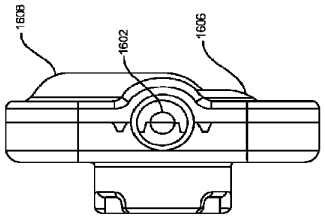


FIG. 16C

【図１６Ｄ】

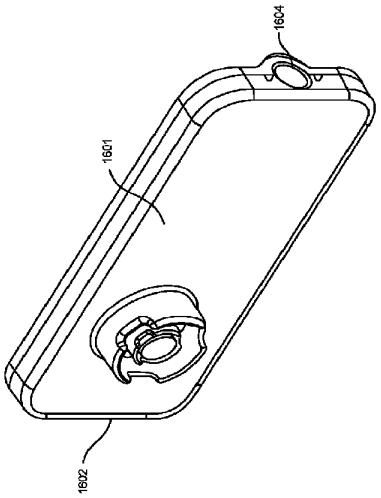


FIG. 16D

【図１７Ａ】

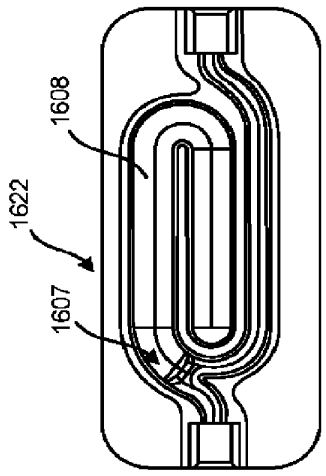


FIG. 17A

【図１７Ｂ】

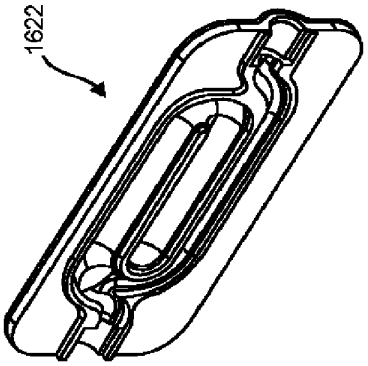


FIG. 17B

【図１７Ｃ】

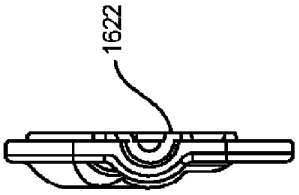


FIG. 17C

【図１７Ｄ】

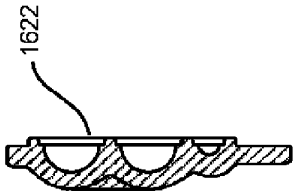


FIG. 17D

【図１７Ｅ】

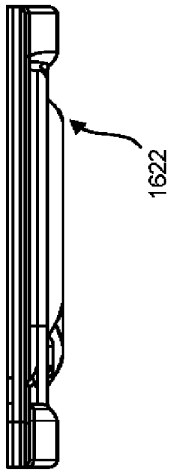


FIG. 17E

【図１８Ａ】

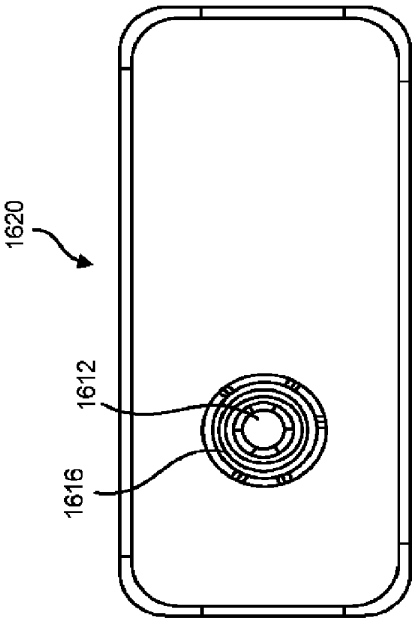


FIG. 18A

【図１８Ｂ】

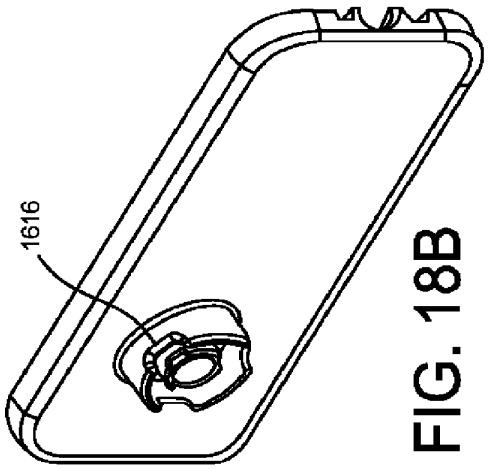


FIG. 18B

【図１８Ｃ】

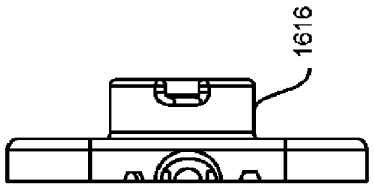


FIG. 18C

【図１８Ｄ】

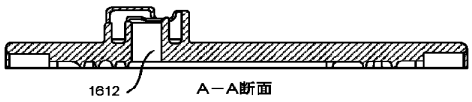


FIG. 18D

【図１８Ｅ】

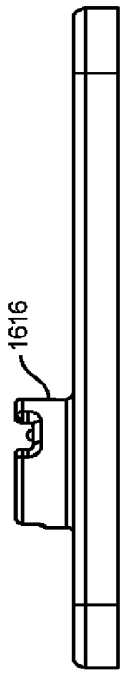


FIG. 18E

【図１８Ｆ】

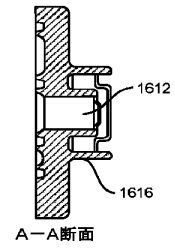


FIG. 18F

【図１９Ａ】

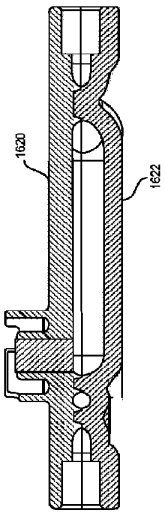


FIG. 19A

【図１９Ｂ】

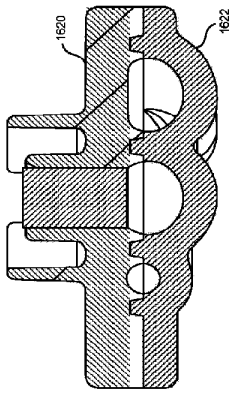


FIG. 19B

【図２０】

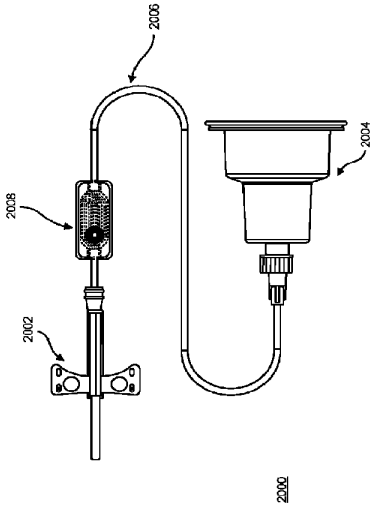


FIG. 20

【図２１】

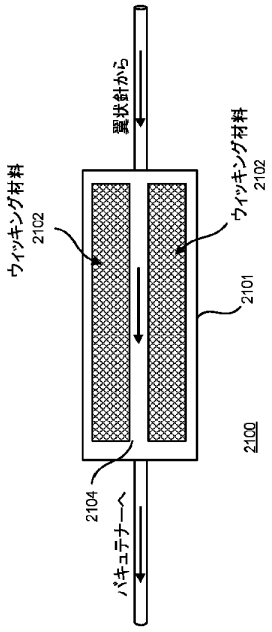


FIG. 21

【図２２Ａ】

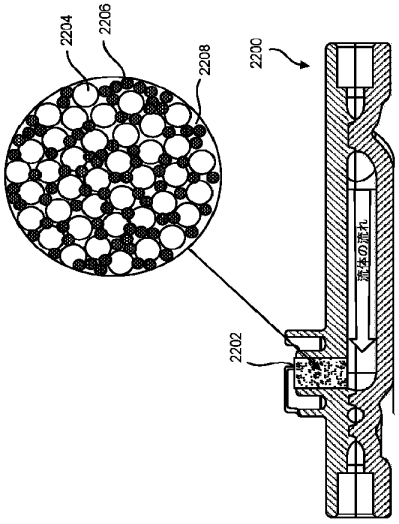


FIG. 22A

【図２２Ｂ】

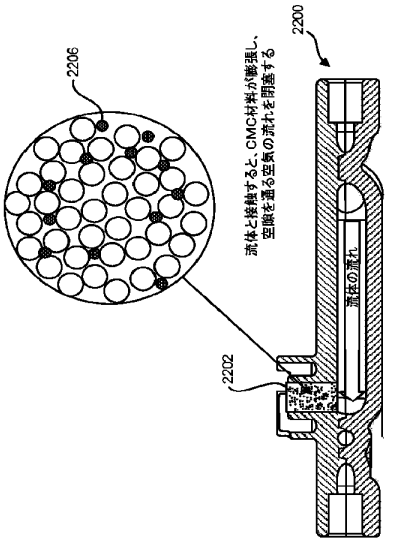


FIG. 22B

【図２３Ａ】

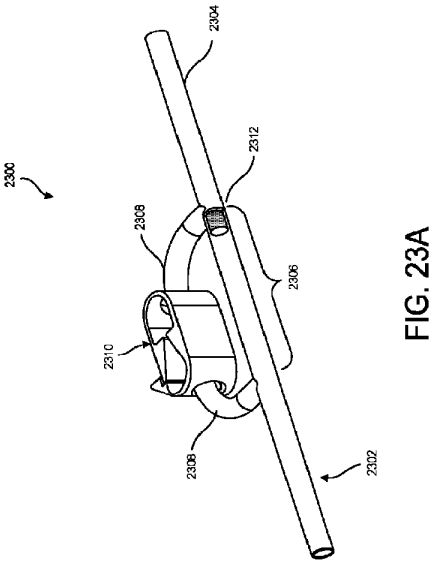


FIG. 23A

【図２３Ｂ】

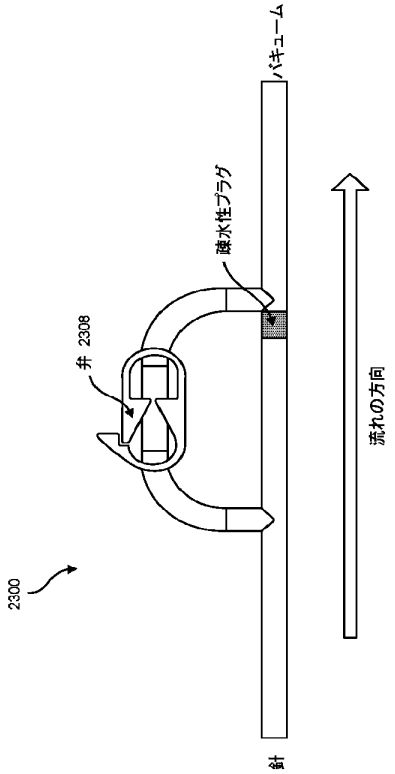


FIG. 23B

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審査官 清水 裕勝

(56)参考文献 特開昭５８－０２５１４６（ＪＰ，Ａ）
特開昭５８－０６７２３８（ＪＰ，Ａ）
特開２０１２－０１６４９６（ＪＰ，Ａ）
特開昭５７－０８９８６９（ＪＰ，Ａ）
特表平０９－５０４７２６（ＪＰ，Ａ）
特開平０２－２２４７４２（ＪＰ，Ａ）
米国特許第０４２０７８７０（ＵＳ，Ａ）

(58)調査した分野(Int.Cl.，ＤＢ名)
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(71) [Applicant]
[Identification number] 999999999
[Name] Spacelabs Inc.
(72) [Inventor]
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(74) [Agent]
[Name] Minoru Nakamura (7 others)

wrap up close —

(57) [Abstract] Since this gazette is application data before electronic filing, abstract data is n ot recorded.

The scope of the claims open —

Claims:
(1) In a coupling used by medical personnel in drawing and storing blood from a patient to ins ert the needle of the needle assembly into the patient to draw the blood sample, the coupling comprises first
and an elongated hollow shaft having a second end; and a
first portion of the shaft fixedly connecting the needle assembly to the shaft so that blood dra wn by the needle can be delivered to the shaft. and an adapter sleeve attached to a second e nd of said shaft for
connecting said shaft to a blood storage means,
for communicating blood received by said shaft; an opening connected to said shaft between an adapter sleeve and said connecting member and communicating with said connecting mem ber.
(2) The coupling of claim 1, further comprising means for blocking blood flow and exhausting air trapped within said shaft.
(3) intermediate the opening and the adapter sleeve, wherein the means for evacuating air re stricts blood flow from the shaft to the adapter sleeve while permitting air flow from the shaft to the adapter sleeve; 3. A coupling according to claim 2, comprising flow control means locat ed within said shaft of.
(4) The coupling of Claim 3, wherein said flow control means comprises a microporous hydrop hobic plug.
(5) The coupling of claim (4) further comprising needle guide means for guiding a needle coup

led to blood reservoir means through said plug and for coaxially fitting said needle with said s haft.

(6) The cup according to (2), further comprising blood storage means for temporarily storing a portion of blood drawn from a patient, said blood storage means being sealably connectable to said opening. ring.

(7) The coupling of claim (6), wherein said blood storage means comprises a syringe.

(8) Further comprising valve means fixedly positioned intermediate said opening and said shaf t for enabling selective communication between said shaft and said opening. coupling.

(9) The coupling of claim 2, further comprising means for sealing said opening.

(10) In a blood collection device used by medical personnel to withdraw and store a blood sa mple from a patient, needle means adapted to be inserted into the patient to withdraw the blo od

sample

; coupling means for connecting the means to the blood storage means,

said coupling means having first and second openings;and adapted to direct blood from said n eedle means to said first and second openings.

(11) The coupling of claim 10, further comprising means for blocking blood flow to exhaust air trapped within said coupling means.

(12) the means for evacuating air restricts blood flow from the needle means to the first openi ng while permitting air flow from the needle means to the first opening; 12. The blood collecti on device of claim 11, comprising flow control means positioned within said coupling means b etween said first and second openings.

(13) The blood collection device of Claim 12, wherein said flow control means comprises a mic roporous hydrophobic plug.

(14) The blood collection device of (13) further comprising needle guide means for guiding a n eedle coupled to blood reservoir means through said plug and coaxial with said coupling mean s.

(15) The method according to (14), further comprising blood storage means for temporarily st oring a portion of the blood drawn from the patient, said blood storage means being sealingly connectable to said second opening. A blood collection device as described.

(16) The blood collection device of (12), wherein said blood storage means comprises a syring e.

(17) The blood collection device of (12) further comprising means for sealing said second ope ning.

(18) further comprising valve means disposed intermediate said needle means and said secon d opening for enabling selective communication between said needle means and said second opening. The blood sampling device according to (12).

(19) said needle means is an elongate needle for insertion into a patient and leading from sai d needle to said coupling means;

13. The blood collection device of claim 12, comprising: a tube, said tube being generally tran sparent so that medical personnel can see blood being directed therethrough.

(20) A blood collection device for use by medical personnel in drawing and collecting blood sa mples from a patient, comprising needle means for drawing blood from a patient and coupling means for selectively connecting blood reservoir means to

said

needle means. wherein

said coupling means is secured to said needle means, said coupling means being positioned b etween said first opening and said needle means and a first opening for receiving blood storag e means; a hollow shaft, said coupling means further comprising a second opening for receivi ng blood storage means, said second opening being connected to said first opening and said n eedle; Mounted on the shaft between means,

the blood sampling device restricts the flow of blood from the shaft to the first opening, but re stricts the flow of blood from the shaft to the first opening.The blood collection device further comprising a flow control device located within the shaft intermediate the first and second ope nings to allow gas flow to the first opening.

(21) further comprising blood storage means for temporarily storing a portion of blood, said bl ood storage means being sealed to said second opening for receiving blood delivered from sai d needle means to said shaft; 21. A blood collection device according to claim 20, adapted for coupling.

(22) said blood storage means comprises a syringe having a blood storage chamber and a plu nger located within said blood storage chamber, said syringe sealing said blood storage chamb er to said second opening; 22. A blood collection device according to claim 21, further compri sing means for connecting with.

(23) The blood collection device of Claim 20, wherein said flow control means comprises a mic roporous hydrophobic plug.

(24) further comprising blood storage means for storing a blood sample, said blood storage m eans being sealingly attachable to said first opening for insertion through said plug, thereby 2 4. A blood collection device according to claim 23, comprising a needle adapted to lead blood f rom the shaft to said blood storage means.

(25) guiding means located within said shaft between said plug and said first opening for guidi ng said needle of said blood storage means through said plug and making said needle coaxial with said shaft; 25. The blood collection device of claim 24, further comprising:

(26) within said shaft between said flow control means and said first opening for guiding a ne edle coupled to said blood storage means through said flow control means and coaxial with sai d shaft; 21. A blood collection device according to claim 20, further comprising guide means l ocated at the .

(27) The blood collection device of Claim 20, further comprising valve means for selectively all owing communication between said shaft and said second opening.

(28) said needle means comprises a needle for insertion into a patient to withdraw a blood sa mple and an elongated tube for guiding blood withdrawn from a patient to said coupling mean s, said tube being flexible

; 21. A blood collection device according to claim 20, and wherein the blood being conducted by said tube is generally transparent so as to be visible to medical personnel.

(29) further comprising a syringe having a blood storage chamber and a plunger positioned wi thin the blood storage chamber, the syringe having means for sealingly connecting the blood s torage chamber to the second opening; 29. A blood collection device according to claim 28, fu rther comprising.

(30) The blood collection device of (11) further comprising cap means for sealing said second opening.

(31) in drawing and collecting a blood sample from a patientA blood collection device for use by medical personnel comprising a

first elongated needle member having an insertion end and an attachment end, said insertion end adapted for insertion into a patient, said first needle member comprising: has a coaxial p assageway for carrying blood drawn from a patient from the insertion end to the attachment e nd and includes a

needle receiving end, a mating end, and from the needle receiving end to the mating end. an d said mounting of said first needle member

such that blood drawn from a patient is conveyed by said first needle member to said first fe male connector. means for fixedly and sealingly connecting an end to a receiving end of said fi rst female connector; a

mating end; a mounting end; and a coaxial extending from said mating end to said mounting end. further comprising a first male connector having a passageway, wherein the mating end of the first male connector is adapted to receive blood conveyed to the first female connector by the first male connector;

first and second ends and a passage extending from the first end to the second end sealingly mated to the mating end of the first female connector; and wherein the first end of the tube i s connected to the attachment end of the first male connector such that blood received by the first male connector is carried by the tube. sealingly attached to the portion, the tube being fl exible and generally transparent so that blood received by the tube is visible to medical perso nnel;

Further comprising a coupling having an elongated hollow shaft and a connecting member att ached to a first end of said shaft, said coupling securing a second end of said tube to said cou pling. to sealably connect to a second end of the shaft, thereby conveying blood received by t he tube to the coupling, the coupling being attached to a second end of the shaft connecting t he shaft to blood storage means. and the coupling is fixedly attached to the shaft between the adapter sleeve and the connecting member such that blood received by the coupling flows int o and out of the second female connector. a plug communicatively further comprising a secon

d female connector in communication with said connecting member and positioned within said shaft of said coupling between said second female connector and said adapter sleeve; wherein said plug is adapted to allow gas to escape from said shaft to effectively block blood flow from said shaft to said adapter sleeve.

(32) a second needle member having an insertion end, a connecting end, a coaxial passageway extending from said insertion end to said connecting end, and a vacutainer means for storing blood drawn from a patient

; The vacutainer means is fixedly attached to the second needle member, the adapter sleeve is positioned such that the vacutainer means is press fit into the adapter sleeve, and the second 32. A blood collection device according to claim 31, wherein a needle member is configured to be inserted through said plug, thereby conveying blood received by said shaft of said coupling to said vacutainer means.

(33) located within said coupling between said plug and said adapter sleeve for guiding said second needle member to insert said second needle member into said plug coaxial with said coupling; 33. A blood collection device according to claim 32, further comprising a needle guide means for receiving the blood.

(34) needle guide means located within said coupling between said plug and said adapter sleeve for guiding a needle coupled to blood storage means for coaxial insertion of said needle into said coupling; 32. The blood collection device of claim 31, further comprising:

(35) further comprising cap means adapted to engage said second female connector and thereby seal said second female connector to prevent blood from flowing out of said second female connector; A blood sampling device according to claim (31).

(36) Further comprising a syringe for temporarily storing blood, said syringe having a blood storage chamber and a plunger located within said blood storage chamber, said syringe being in communication with said blood storage means. (31) adapted to mate with said second female connector such that blood received by said coupling is stored within said syringe.

(37) located within said coupling between said plug and said adapter sleeve for guiding said second needle member to insert said second needle member into said plug coaxial with said coupling; 37. A blood collection device according to claim 36, further comprising a needle guide means for receiving the blood.

(38) a second needle member having an insertion end, a connecting end, a coaxial passageway extending from said insertion end to said connecting end, and a vacutainer means for storing blood drawn from a patient

; The vacutainer means is fixedly attached to the second needle member, the adapter sleeve is positioned such that the vacutainer means is press fit into the adapter sleeve, and the second A needle member is configured to be inserted through said plug, thereby carrying blood received by said shaft of said coupling to said vacutainer means.38. The blood collection device of claim 37.

(39) The blood collection of claim (37) further comprising first, second and third cap means re

spectively sealing said first needle means, said second female connector and said adapter slee ve. Device.

(40) The blood collection device of claim (31) further comprising valve means coupled to said second female connector for selectively communicating between said second female connector and said shaft.

(41) needle means for withdrawing blood from a patient

and

temporarily storing a first blood portion withdrawn from the patient in a blood collection devic e used by medical personnel to withdraw and store a blood sample from a patient; syringe me ans and

coupling means sealingly connecting said needle means to said syringe means, said coupling means including flow control means for venting air trapped within said needle means and said coupling means. said coupling means further comprising adapter means adapted to receive bl ood storage means and direct blood to said coupling means for storage; A blood collection dev ice wherein the means are further configured to return said first blood portion to the patient.

(42) said coupling means comprises a coupling having an elongated hollow shaft, said couplin g means attached to a first end of said shaft fixedly connecting said needle means to said cou pling; further comprising a connecting member, said adapter means being attached to a secon d end of said shaft, said coupling receiving said syringe means, said shaft between said adapt er means and said connecting member; 42. A blood collection device according to claim 41, fu rther comprising a connecting member fixedly attached to.

(43) The blood collection device of Claim 42, wherein said flow control means comprises a plu g positioned within said shaft of said coupling between said connecting member and said adap ter means.

(44) The blood collection device of Claim 43, wherein said plug comprises a microporous hydr ophobic plug.

(45) said needle means comprises a needle for insertion into a patient to withdraw a blood sa mple and an elongated tube for conducting blood withdrawn from the patient to said coupling, said tube being flexible; 44. A blood collection device according to claim 43, and wherein bloo d being conducted by said tube is generally transparent so as to be visible to medical personn el.

(46) drawing a first blood portion from the patient to fill the blood collection device while evac uating the air trapped in the blood collection device so that the anaerobic sample is not conta minated with air trapped in the blood collection means; An anaerobic sample is taken from th e patient after generally evacuating the trapped air from the blood collection device.A method of drawing

an anaerobic blood sample from a patient comprising the step of drawing a sample of blood fr om a patient.

(47) temporarily storing the first blood portion after drawing the first blood portion and

returning the first blood portion to the patient after drawing the anaerobic blood sample
; The method of claim (46), further comprising:
(48) withdrawing the first blood portion
further comprises coupling a coupling to a syringe, the coupling sealably coupled to a needle assembly; inserting
the
needle assembly into a patient and coupling the inserted needle assembly and the coupling so that blood is directed through the needle assembly and into the coupling with the syringe atta ched
; evacuating trapped air,
connecting a vacutainer needle of a vacutainer to said vented coupling, said vacutainer needle being in communication with said inserted needle assembly, and a cup with said vacutainer at tached
.
48. The method of claim (47), comprising withdrawing said first blood portion from a ring into said syringe .
(49) wherein withdrawing the anaerobic blood sample comprises establishing blood flow betw een the needle assembly and the vacutainer after the first blood portion has been withdrawn; The method described in .
(50) The method of claim (48), wherein withdrawing the first blood portion into the syringe co mprises allowing blood to flow freely under the pressure of the patient's heart.

detailed description open —

Description:
INDUSTRIAL APPLICABILITY
The present invention is directed to apparatus for taking a blood sample from a patient, and i n particular to apparatus for obtaining a blood sample from a patient in which the partial pres sure of gas within the sample is such that the blood pressure in the patient's body is An impro ved blood collection device is directed to receiving a blood sample so as to approximately equ al the gas partial pressure therein.
(PRIOR ART)
In the medical field, it is necessary to determine the in vivo gaseous equilibrium in the blood of a patient.
A medical worker will typically be concerned with the partial pressures of oxygen and carbon d ioxide. They may also be concerned with ionic species whose activity is related to the gas bala

nce in the blood, such as hydrogen ions and calcium ions.

In order for a blood sample to be valid for gas-in-blood analysis, the sample must be under a naerobic conditions, i.e., to prevent fluctuations in the partial pressure of the gas to be tested (when the blood is outside the patient's body). Must be collected to avoid exposure to gas.The major commercially available blood collection devices that must be present are largely unsatis factory in ensuring the integrity of anaerobic blood collection. An example of a conventional d evice uses a syringe and a vented plunger, where the syringe is removed from the patient unti l the correct blood volume is obtained from the patient by pulling on the vented plunger from no void in the barrel. Slowly withdraw the blood into the barrel of the However, these devices allow some exposure of the blood sample to the atmosphere. Some amount of ambient air will be contained within the barrel before the plunger moves. Thus, the initial portion of blood is e xposed to these gases, thereby changing the partial pressure of the gases contained in this ini tial sample. No means are provided for discarding the first portion of the drawn blood, so the entire sample would be contaminated.

Further, no means are provided to protect the medical personnel of the device against acciden tal bursting or exposure to contaminated blood during the course of the procedure when using the aforementioned device.

Other devices, such as the Becton and Dickenson Vacutainer and vacutainer attachments, hav e shown improved properties to protect medical personnel from exposure to drawn blood. Ho wever, these devices also. It allows some exposure of the first part of the blood sample to the atmosphere.

In addition to the shortcomings of the prior art described above, blood collection devices that provide means for flushing, i.e., injecting, for example, nutrients, medications, etc., into the b lood stream while permitting the collection of an anaerobic blood sample are currently lackin g. not known where.

Accordingly, it is desirable to provide a device for drawing an anaerobic blood sample from a p atient, and it is further desirable to provide a device for drawing a blood sample that can also inject a liquid into the patient's blood stream, i.e., a puncture. It is further desirable to provid e such a device that allows repeated blood sampling without the need for additional needle pl acement, and during scheduled interval sampling, i.e., between other subsequent blood sampl ings. It would be desirable to provide a device for drawing blood samples that can be left in th e patient.

OBJECTS OF THE INVENTION

It is therefore an object of the present invention to provide a blood collection device for drawi ng an anaerobic blood sample from a patient.

It is also an object of the present invention to provide a blood collection device that can withd raw an initial contaminated blood sample portion and maintain complete anaerobicity in the re maining sample.

It is a further object of the present invention to provide a blood collection device that can inje

ct an external liquid into the patient's blood stream.

It is a further object of the present invention to provide a blood sampling device that allows re peated blood sampling without the need for additional puncture or needle placement.

Yet another object of the present invention is to provide a blood collection device that can be l eft on the patient between scheduled intervals of collection, ie, other subsequent blood collect ions.

These and other objects of the present invention are met by providing a coupling for use by m edical personnel when drawing blood from a patient and storing it, which coupling draws the b lood sample. The coupling is particularly adapted for use with a needle assembly for injecting a needle into a patient. A coupling fixedly

connects the elongated hollow shaft and the needle assembly to the shaft for withdrawal by th e needle. a connecting member attached to the first end of the shaft that delivers blood to the shaft, and a coupling attached to the second end of the shaft that connects the shaft to variou s blood storage means. The adapter sleeve further comprises an opening coupled to the shaft intermediate the adapter sleeve and the connecting member, the opening being in communica tion with the opening such that blood received in the shaft communicates with the opening. In another embodiment

of the present invention, a device is provided for blocking blood flow and venting air trapped i n the shaft, particularly flow control means, such as microporous A hydrophobic plug is locate d in the shaft intermediate the opening and the adapter sleeve to restrict blood flow from the shaft to the adapter sleeve while allowing air flow from the shaft to the adapter sleeve. 6 In a nother embodiment of the invention, a valve is provided intermediate the shaft and the openi ng to allow selective communication between the shaft and the opening.

Other embodiments of the invention are particularly pointed out and distinctly claimed in the c laims. The invention, however, as to organization and method of implementation, will best be understood from the following detailed description when read with the accompanying drawing s in which: FIG.

DETAILED DESCRIPTION OF THE INVENTION

A cross-sectional view showing the improved blood collection device of the present invention i s provided in FIG. The blood sampling device comprises an elongated needle 100 having an in sertion end 102 adapted for insertion into a patient's blood stream (artery or vein). Needle 10 0 further has an attachment end 104 attached to first connecting member 106 via cylindrical seal 108 . As is well known in the art, meter 100- has a coaxial passageway extending from in sertion end 102 to attachment end 104 that conducts blood withdrawn from the patient to firs t connecting member 106. As shown in FIG.

Cylindrical seal 10B has a central opening 110 in which mounting end 104 of needle 100 is fix edly mounted. Additionally, the cylindrical seal 108 isIt is fixedly attached to needle receiving end 112 of member 106 . The second connecting member 114 has a mating end 116 adapted to mate with the mating end 118 of the first connecting member 106 so that it is received by

the first connecting member. rice field. Blood from leaflet 100 is directed to second connecting member 114 via mating joints 116,118.

First end 120 of tube 122 is sealingly attached to attachment end 124 of second connecting m ember 114 . A tube 122 is provided for carrying blood withdrawn from the patient through tub e 100 to coupling 126 . Tubing 122 allows the needle to be easily inserted into the patient's bl oodstream and, after insertion, the coupling 126 can be disengaged by medical personnel wit hout undue movement of the total 100 and causing discomfort to the patient. Preferably, the t ube 122 is flexible so as to be operable, and preferably transparent so that the medical perso nnel can visually observe the blood drawn from the patient.

The combination of needle 100, first connecting member 106, second connecting member 11 4, and tube 122 constitutes a needle assembly, readily available from needles, connecting me mbers, and tubes well known in the art. Can be assembled. - By way of example, the first and second connecting members 106 and 114 consist of male and female Luer connectors, as is w ell known in the art.

A coupling 126 is provided for connecting the second end 128 of the tube with each of the firs t and second blood storage means 130 and 132 . To this end, coupling 126 has a connecting member 134 with a central opening that receives second end 128 of tube 122 . Connecting m ember 134 is integrally connected to elongated hollow shaft 136 such that blood delivered to coupling 126 by tube 122 is received within shaft 136 . Adapter sleeve 138 is integrally conne cted to shaft 136 at the end opposite to the end to which connecting member 134 is connecte d. Adapter sleeve 138 is in communication with shaft 136 and is provided for receiving second blood storage means 132, as will be described more fully below.

Coupling 126 further includes an opening 140 integrally connected to shaft 136 intermediate a dapter sleeve 138 and connecting member 134 .

An opening 140 is provided for connecting first blood storage means 130 to shaft 136 of coupl ing 126 . A passageway 162 is provided in shaft 136 proximate opening 140 such that openin g 140 communicates with connecting member 134 . Accordingly, blood delivered to coupling 1 26 by tube 122 is conveyed via adapter sleeve 138 and opening 140 to first and second blood storage means 130 and 132 for storage.

Coupling 126 also has a plug 142 disposed within the shaft between adapter sleeve 138 and o pening 140 . Plug 142 is a fluid flow, e.g., porous plug, venting air trapped within connecting members 106, 114, tube 122, shaft 136, and opening 140 during the early stages of a blood c ollection procedure. It consists of control means. The plug 142 is thus adapted to restrict bloo d flow from the shaft 136 to the adapter sleeve 138 and allow air flow from the shaft to the a dapter sleeve. 142 consists of a microporous, hydrophobic plug, well known in the art. Howev er, those skilled in the art will appreciate that other liquid flow control means may be used in place of the preferred microporous hydrophobic plug 142 .

As previously mentioned, opening 140 is adapted to receive first blood storage means 130 .

A cap 144 is engageable with opening 140 to seal the opening from inadvertent blood loss, w

hich often occurs when first blood storage means 130 is not connected to coupling 126 . Howe ver, in normal operation, cap 144 is removed from opening 140 and connects first blood stora ge means 130 thereto.

In a preferred embodiment of the present invention, the first blood storage means 130 compri ses a syringe of the type having a blood storage chamber 146 and a plunger 148 positioned w ithin the blood storage chamber 146 .

As is well known, in operation, plunger 148 is slowly withdrawn from blood storage chamber 1 46 so that blood enters the chamber. Blood storage means 130 further comprises connection means 150 for connecting blood storage means 130 to opening 140 . In a preferred embodim ent of the invention, opening 140 and connecting member 150 each comprise male and femal e luer connectors. However, it will be apparent to those skilled in the art that other connector members may be provided to sealingly connect first blood storage means 130 to coupling 126 .

In operation, the cap 144 is removed from the opening 140 and the blood reservoir means 13 0 is connected thereto.The blood is then withdrawn, or preferably allowed to flow freely under the pressure of the patient's heart. Meter 100 is inserted into the patient's blood stream so as to be able and delivered to shaft 136 via connecting members 106 , 114 and tubing 122 . Air trapped within connecting members 106, 114, tube 122, shaft 136 and opening 140 is displac ed by the patient's blood entering the flow passageway and vented through porous plug 142, as previously described. .

A first portion of the blood that is withdrawn or flows under cardiac pressure from the patient is exposed to trapped air before being ventilated.As it is exposed, it is generally contaminated and therefore not suitable for anaerobic blood sampling.

This first blood portion is thus withdrawn from the coupling 126 into the blood storage means 130 for temporary storage, while the anaerobic blood sample passes through the second bloo d storage means 132. to be received. After the anaerobic blood sample is received, the blood temporarily stored in blood storage means 130 is discarded or returned to the patient via tube 122 and meter 100 .

A second blood storage means 132 is connected to the coupling 126 via an adapter sleeve 13 8 for withdrawing an anaerobic blood sample. The second blood storage means 132 may com prise a Becton Dickenson vacutainer well known in the art. Blood storage means 132 has a blo od storage chamber 152 for receiving an anaerobic blood sample drawn from the patient. are doing. Needle 154 is sealingly connected to needle hub 156 and their assembly is connected t o blood storage chamber 152 via a compatible coupling 158 (commonly referred to as a vacut ainer adapter). Hermetically connected. Needle 154 has a seal to prevent communication with blood storage chamber 152, as is well known in the art. Additionally, as is well known in the a rt, blood storage chamber 152 is evacuated so as not to contain air that contaminates blood d rawn from the patient.

A compatible coupling 158 provides means for removing the seal from needle 154 in order to

place needle 154 in communication with blood storage chamber 152 .

Adapter sleeve 138 has an internal adapter chamber 160 sized to snugly receive needle hub 1 56 . The length of adapter sleeve 138 and the position of plug 142 within shaft 136 is such th at blood reservoir 132 is fully inserted into adapter sleeve 138 and needle 154 passes through passageway 162 and second end 128 of tube 122 through plug 142 . is selected to lie betwee n A needle guide 164 is positioned within coupling 126 between adapter sleeve 138 and plug 142 to allow a needle to be inserted into coupling 126 coaxially with shaft 136 . Needle guide 164 receives needle 154 during insertion of blood reservoir 132 into coupling 126 and guides t he needle prior to needle insertion into plug 142 so that the needle is coaxial with shaft 136 . provided for positioning.

In operation, blood reservoir means 130 is connected to coupling 126 via opening 140 as prev iously described for collecting an anaerobic blood sample. The meter 100 is inserted into the p atient's bloodstream and air trapped inside the meter 100, connectors 106, 114, tubing 122 a nd coupling 126 is evacuated through plug 142 as previously described.Total 154 of blood stor age means 132 is then inserted through plug 142 and into coupling 126 so that it lies beyond passageway 162 near tube 122 . The contaminated air of the blood sample is removed so that any fraction of contaminated air that accumulates within needle 154 is exhausted through plu g 142, i.e., removed from coupling 126 prior to receiving the anaerobic blood sample. It is des irable to insert gauge 154 into coupling 126 prior to storing the portion in storage means 130 .

After the soot 154 is properly inserted into the coupling 126, the first portion of contaminated blood is drawn from the coupling 126 into the blood storage means 130 for temporary storag e. At this time, the seal on needle 154 is removed by compatible coupling 158, as is well kno wn in the art, so that the anaerobic blood sample is directed to blood reservoir 152. FIG.

To ensure that substantially all of the blood directed to blood storage chamber 152 is blood re ceived from tube 122 and not blood received from blood storage chamber 146 of blood storag e means 130, total 154 is connected to passageway 162. and tube 122 and near second end 128 of tube 122 in coupling 126 in shaft 136 .

In an alternative embodiment of the present invention, when receiving an anaerobic blood sa mple, a valve capable of substantially isolating a contaminated blood sample stored in blood s torage means 130 from shaft 136 during operation; Alternatively, it may be desirable to provi de other selective coupling means.

In addition to the cap 144, a plurality of caps or other sealing means may be provided for posi tioning the total 100 to seal the chamber 160 of the adapter sleeve 138, as is common in the medical industry.

Although only some of the preferred embodiments of the novel blood collection device have b een described in detail herein, many modifications and variations will become readily apparent to those skilled in the art without the true scope and spirit of the invention. It is the intent of t he appended claims to cover all such improvements and modifications that fall within the scop

e of the claims.

Brief description of the drawing open —

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a cross-sectional view of one of the improved blood collection devices of the pre sent invention.

100 Needle

106 First connecting member

114 Second connecting member

122 Tube

126 Coupling

130.132 Blood reservoir Means

134 ... Connection member

136 ... Shaft

138 ·

140 ·

142,

144,

146.

148

154

Adapter sleeve

opening

plug

cam

blood storage chamber plunger

needle



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IMPROVED BLOOD SAMPLER

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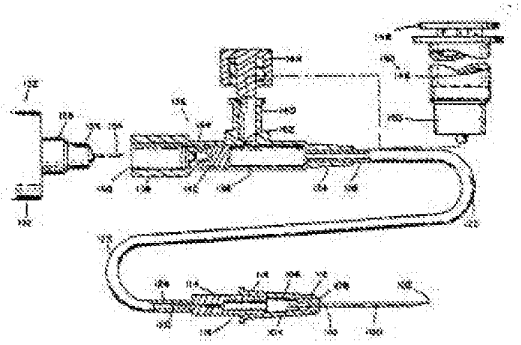
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Abstract of JPH02224742 (A)



PURPOSE: To keep completely anaerobic of the residual a blood sample, with the first sampled portion of contaminated blood removed, by fixedly coupling a slender hollow shaft and a needle assembly together, with a joint member mounted to the first end of a shaft and an adapter sleeve to the second end.

CONSTITUTION: Coupling 126 has joint member 134 which receives the second end 128 of tube 122. Adapter sleeve 138 is connected integrally to shaft 136 at an opposite end of the end to which the joint member 134 is connected. The adapter sleeve 138 communicates with the shaft 136 and receives second blood storage means 132. The coupling 126 has further opening 140 which is joined integrally to the shaft 136 between the adapter sleeve 138 and joint member 134. The blood delivered to the coupling 126 through tube 122 is transferred to the first and second blood storage means 130, 132 respectively for storage therein via the adapter sleeve 138 and opening 140.

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⑤④発明の名称　改良された血液採取装置

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明　細　書

1.発明の名称　改良された血液採取装置

2.特許請求の範囲

(1) 患者から血液を抜き取って貯蔵する際に医療作業員によって使用され、血液サンプルを抜き取るために針組立体の針を患者に挿入する、カップリングにおいて、

第1及び第2の端部を有する細長い中空シャフトと、

前記針組立体を前記シャフトに固定して連結し、それによって、前記針によって引き抜かれた血液を前記シャフトに送ることができる、前記シャフトの第1の端部に取り付けられた接続部材と、

前記シャフトを血液貯蔵手段に接続する、前記シャフトの第2の端部に取り付けられたアダプタースリーブと、

前記シャフトによって受け入れられた血液を連通させるため、前記アダプタースリーブと前記接続部材との間の前記シャフトに連結されて前記接続部材に連通している開口部と、から成るカップリング。

(2) 血液の流れを遮断して、前記シャフト内にたまった空気を排気する手段をさらに備える請求項(1)に記載のカップリング。

(3) 前記空気を排気する手段が、前記シャフトから前記アダプタースリーブへの空気の流れを可能にしつつ、シャフトからアダプタースリーブへの血液の流れを制限する、前記開口部と前記アダプタースリーブとの中間の前記シャフト内に位置している流れ制御手段から成る請求項(2)に記載のカップリング。

(4) 前記流れ制御手段が、微孔質疎水性プラグから成る請求項(3)に記載のカップリング。

(5) 血液貯蔵手段に結合している針を前記プラグを通して案内し、前記針を前記シャフトと同軸にする針案内手段をさらに備える請求項(4)に記載のカップリング。

(6) 患者から抜き取った血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記開口部に密封して連結可能である請求項(2)に記載のカップリング。

(7) 前記血液貯蔵手段が、注射器から成る請求項(6)に記載のカップリング。

(8) 前記シャフトと前記開口部との間の選択的な連通を可能にする、前記開口部と前記シャフトの中間に固定して配置されているバルブ手段をさらに備える請求項(2)に記載のカップリング。

(9) 前記開口部を密封する手段をさらに備える請求項(2)に記載のカップリング。

(10)患者から血液サンプルを抜き取って貯蔵するために医療作業員によって使用される血液採取装置において、

血液サンプルを抜き取るために、患者に挿入されるように適合している針手段と、

前記針手段を血液貯蔵手段に連結させるカップリング手段とを備え、

前記カップリング手段は、第1及び第2の開口部を有しており、前記針手段からの血液を前記第1及び第2の開口部に導くようになっている血液採取装置。

(11)血液の流れを遮断して、前記カップリング手段内にたまった空気を排気する手段をさらに備える請求項(10)に記載のカップリング。

(12)前記空気を排気する手段が、前記針手段から前記第1の開口部への空気の流れを可能にしつつ、前記針手段から前記第1の開口部への血液の流れを制限する、前記第1及び第2の開口部の間の前記カップリング手段内に位置している流れ制御手段から成る請求項(11)に記載の血液採取装置。

(13)前記流れ制御手段が、微孔質疎水性プラグから成る請求項(12)に記載の血液採取装置。

(14)血液貯蔵手段に結合している針を前記プラグを通して案内し、前記カップリング手段と同軸になる針案内手段をさらに備える請求項(13)に記載の血液採取装置。

(15)患者から抜き取った血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記第2の開口部に密封して連結可能である請求項(14)に記載の血液採取装置。

(16)前記血液貯蔵手段が、注射器から成る請求項(12)に記載の血液採取装置。

(17)前記第2の開口部を密封する手段をさらに備える請求項(12)に記載の血液採取装置。

(18)前記針手段と前記第2の開口部との間の選択的な連通を可能にする、前記針手段と前記第2の開口部の中間に配置されているバルブ手段をさらに備える請求項(12)に記載の血液採取装置。

(19)前記針手段が、患者に挿入する針と、前記針から前記カップリング手段へ導く、細長いチューブと、から成り、前記チューブは、医療作業員が導かれている血液を前記チューブを通して見ることができるように、概ね透明である請求項(12)に記載の血液採取装置。

(20)患者から血液サンプルを抜き取って集める際に医療作業員が使用する血液採取装置において、

患者から血液を抜き取る針手段と、

前記針手段に血液貯蔵手段を選択的に連結するカップリング手段と、を備え、

前記カップリング手段は前記針手段に固定されており、前記カップリング手段は、血液貯蔵手段を受け入れる第1の開口部と、前記第1の開口部と前記針手段との間にある中空のシャフトとを有しており、前記カップリング手段は、血液貯蔵手段を受け入れる第2の開口部をさらに備えており、前記第2の開口部は、前記第1の開口部と前記針手段の間の前記シャフトに取り付けられており、

前記血液採取装置は、前記シャフトから前記第1の開口部への血液の流れを制限するが、前記シャフトから前記第1の開口部への気体の流れを可能にする、前記第1及び第2の開口部の中間の前記シャフト内部に位置している流れ制御装置をさらに備える血液採取装置。

(21)血液の一部を一時的に貯蔵する血液貯蔵手段をさらに備え、前記血液貯蔵手段は、前記針手段から前記シャフトへ送られた血液を受け入れる、前記第2の開口部へ密封して連結されるようになっている請求項(20)に記載の血液採取装置。

(22)前記血液貯蔵手段が、血液貯蔵チャンバーと前記血液貯蔵チャンバー内に位置しているプラ

ンジャーとを有する注射器から成り、前記注射器は、前記血液貯蔵チャンバーを前記第２の開口部へ密封して連結する手段をさらに有している請求項(21)に記載の血液採取装置。

(23)前記流れ制御手段が、微孔質疎水性プラグから成る請求項(20)に記載の血液採取装置。

(24)血液サンプルを貯蔵する血液貯蔵手段をさらに有しており、前記血液貯蔵手段は、前記第１の開口部に密封して取り付け自在であって、前記プラグを通して挿入し、それによって、前記シャフトから前記血液貯蔵手段へ血液を導くようになっている針を有している請求項(23)に記載の血液採取装置。

(25)前記プラグを通して前記血液貯蔵手段の前記針を案内し、前記針を前記シャフトと同軸にする、前記プラグと前記第１の開口部との間の前記シャフト内に位置している案内手段をさらに備えている請求項(24)に記載の血液採取装置。

(26)前記流れ制御手段を通して前記血液貯蔵手段に結合している針を案内し、前記針を前記シャフトと同軸にする、前記流れ制御手段と前記第１の開口部との間の前記シャフト内に位置している案内手段をさらに備えている請求項(20)に記載の血液採取装置。

(27)前記シャフトと前記第２の開口部との間を選択的に連通できるように、バルブ手段をさらに備える請求項(20)に記載の血液採取装置。

(28)前記針手段が、血液サンプルを抜き取るために患者に挿入する針と、患者から抜き取られた血液を前記カップリング手段へ導く細長いチューブとを有し、前記チューブは可撓性を有し、かつ、前記チューブによって導かれている血液が医療作業員に見えるように概ね透明である請求項(20)に記載の血液採取装置。

(29)血液貯蔵チャンバーと該血液貯蔵チャンバー内に位置しているプランジャーとを有する注射器をさらに備え、前記注射器は、前記血液貯蔵チャンバーを前記第２の開口部へ密封して連結する手段をさらに備えている請求項(28)に記載の血液採取装置。

(30)前記第２の開口部を密封するキャップ手段をさらに備える請求項(11)に記載の血液採取装置。

(31)患者から血液サンプルを抜き取って集める際に医療作業員が使用する血液採取装置において、

挿入端部と取り付け端部を有する第１の細長い針部材を備え、前記挿入端部が患者に挿入するようになっており、前記第１の針部材が患者から抜き取られた血液を前記挿入端部から前記取付端部へ運ぶ同軸通路を有しており、

針受け入れ端部と、嵌合端部と、前記針受け入れ端部から前記嵌合端部へ延びる同軸通路と、を有する第１の雌コネクターと、

患者から抜き取られた血液が前記第１の針部材によって前記第１の雌コネクターに運ばれるように、前記第１の針部材の前記取り付け端部を前記第１の雌コネクターの受け入れ端部に固定してかつ密封自在に連結する手段と、

嵌合端部と、取り付け端部と、前記嵌合端部から前記取り付け端部へ延びる同軸通路を有する第１の雄コネクターをさらに備え、前記第１の雄コネクターの前記嵌合端部は、前記第１の雌コネクターへ運ばれた血液が前記第１の雄コネクターによって受け入れられるように、前記第１の雄コネクターの前記嵌合端部に密封自在に嵌合されており、

第１及び第２の端部と、前記第１の端部から前記第２の端部へ延びている通路とを有する細長いチューブをさらに備え、前記チューブの前記第１の端部は、前記第１の雄コネクターによって受け入れられた血液が前記チューブによって送られるように、前記第１の雄コネクターの前記取り付け端部に密封自在に取り付けられており、前記チューブは、可撓性を有し、かつ、前記チューブによって受け入れられた血液が医療作業員に見えるように概ね透明であり、

細長い中空のシャフトと、前記シャフトの第１の端部に取り付けられている接続部材とを有するカップリングをさらに備え、前記カップリングは、前記チューブの第２の端部を前記カップリングに固定して密封自在に連結し、それによって、前記チューブによって受け入れられた

血液を前記カップリングに送り、前記カップリングは、前記シャフトを血液貯蔵手段に接続する、前記シャフトの第２の端部に取り付けられたアダプタースリーブをさらに有し、前記カップリングは、前記アダプタースリーブと前記接続部材との間の前記シャフトに固定して取り付けられて、前記カップリングによって受け入れられた血液が前記第２の雌コネクターと連通するように、前記接続部材と連通している第２の雌コネクターをさらに有し、

前記第２の雌コネクターと前記アダプタースリーブとの間の前記カップリングの前記シャフト内に位置しているプラグをさらに備え、前記プラグは、気体を前記シャフトから逃がして前記シャフトから前記アダプタースリーブへ血液流れを有効に遮断するようになっている血液採取装置。

(32)挿入端部と、連結端部と、前記挿入端部から前記連結端部へ延びる同軸通路とを有する第２の針部材と、

患者から抜き取られた血液を貯蔵するバキュティナー手段とをさらに備え、前記バキュティナー手段は、前記第２の針部材に固定して取り付けられ、前記アダプタースリーブは、前記バキュティナー手段が前記アダプタースリーブの中へ圧入されるように、かつ、前記第２の針部材が前記プラグを通して挿入され、それによって前記カップリングの前記シャフトによって受け入れられた血液を前記バキュティナー手段へ運ぶように、形成されている請求項(31)に記載の血液採取装置。

(33)前記第２の針部材を案内して前記第２の針部材を前記カップリングと同軸の前記プラグへ挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(32)に記載の血液採取装置。

(34)血液貯蔵手段に結合している針を案内して前記針を前記カップリングへ同軸に挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(31)に記載の血液採取装置。

(35)前記第２の雌コネクターに係合しそれによって前記第２の雌コネクターから血液が流出するのを防止すべく前記第２の雌コネクターを密封するようになっているキャップ手段をさらに備える請求項(31)に記載の血液採取装置。

(36)一時的に血液を貯蔵する注射器をさらに備え、前記注射器は、血液貯蔵チャンバーと該血液貯蔵チャンバー内に位置するプランジャーとを有し、前記注射器は、前記血液貯蔵手段と連通していて、前記カップリングによって受け入れられた血液が前記注射器内に貯蔵されるように、前記第２の雌コネクターと嵌合するようになっている請求項(31)に記載の血液採取装置。

(37)前記第２の針部材を案内して前記第２の針部材を前記カップリングと同軸の前記プラグへ挿入する、前記プラグと前記アダプタースリーブとの間の前記カップリング内に位置している針案内手段をさらに備えている請求項(36)に記載の血液採取装置。

(38)挿入端部と、連結端部と、前記挿入端部から前記連結端部へ延びる同軸通路とを有する第２の針部材と、

患者から抜き取られた血液を貯蔵するバキュティナー手段とをさらに備え、前記バキュティナー手段は、前記第２の針部材に固定して取り付けられ、前記アダプタースリーブは、前記バキュティナー手段が前記アダプタースリーブの中へ圧入されるように、かつ、前記第２の針部材が前記プラグを通して挿入され、それによって前記カップリングの前記シャフトによって受け入れられた血液を前記バキュティナー手段へ運ぶように、形成されている請求項(37)に記載の血液採取装置。

(39)前記第１の針手段、前記第２の雌コネクター、及び前記アダプタースリーブを各々密封する、第１、第２及び第３のキャップ手段をさらに備える請求項(37)に記載の血液採取装置。

(40)前記第２の雌コネクターと前記シャフトとの間を選択的に連通する、前記第２の雌コネクターに連結されたバルブ手段をさらに備える請求項(31)に記載の血液採取装置。

(41)患者から血液サンプルを抜き取って貯蔵するために、医療作業員が使用する血液採取装置において、

患者から血液を抜き取る針手段と、

患者から抜き取った第1の血液部分を一時的に貯蔵する注射器手段と、

前記針手段を前記注射器手段へ密封自在に連結するカップリング手段とを備え、前記カップリング手段は、前記針手段と前記カップリング手段内にたまった空気を排気する流れ制御手段を有しており、前記カップリング手段は、血液貯蔵手段を受け入れて前記カップリング手段へ貯蔵のために血液を導くようになっているアダプター手段をさらに有しており、前記注射器手段と前記カップリング手段は、前記第1の血液部分を患者に戻すようにさらになっている血液採取装置。

(42)前記カップリング手段が、細長い中空シャフトを有するカップリングを備え、前記カップリング手段が、前記カップリングへ前記針手段を固定して連結する、前記シャフトの第1の端部に取り付けた接続部材をさらに有し、前記アダプター手段は、前記シャフトの第2の端部に取り付けられており、前記カップリングは、前記注射器手段を受け入れる、前記アダプター手段と前記接続部材との間の前記シャフトに固定して取り付けた接続部材をさらに有している請求項(41)に記載の血液採取装置。

(43)前記流れ制御手段が、前記接続部材と前記アダプター手段との間の前記カップリングの前記シャフト内に位置しているプラグから成る請求項(42)に記載の血液採取装置。

(44)前記プラグが微孔質疎水性プラグから成る請求項(43)に記載の血液採取装置。

(45)前記針手段が、血液サンプルを抜き取るために患者に挿入する針と、患者から抜き取られた血液を前記カップリングへ導く、細長いチューブとを有し、前記チューブは可撓性を有し、かつ、前記チューブによって導かれている血液が医療作業員に見えるように概ね透明である請求項(43)に記載の血液採取装置。

(46)前記血液採取装置にたまった空気を排気しながら患者から第1の血液部分を抜き取って前記血液採取装置を満たし、嫌気性サンプルが前記血液採取手段にたまった空気に汚染されないように、前記血液採取装置にたまった空気を概ね排気した後、患者から嫌気性サンプルを抜き取る、

ステップから成る患者から嫌気性血液サンプルを抜き取る方法。

(47)前記第1の血液部分を抜き取った後に、前記第1の血液部分を一時的に貯蔵し、

前記嫌気性血液サンプルを抜き取った後に、前記第1の血液部分を患者に戻す、

ステップをさらに含む請求項(46)に記載の方法。

(48)前記第1の血液部分を抜き取るステップが、

注射器にカップリングを連結するステップをさらに含み、前記カップリングは針組立体に密封自在に連結されており、

さらに、前記第1の血液部分を抜き取るステップが、

血液が前記針組立体を介して前記注射器を取り付けたカップリングの中に導かれるように、患者に前記針組立体を挿入し、

前記挿入された針組立体とカップリング内にたまった空気を排気し、

バキュティナーのバキュティナー針を前記通気されたカップリングに接続して、前記バキュティナー針を前記挿入された針組立体と連通させ、

前記バキュティナーを取り付けたカップリングから前記第1の血液部分を前記注射器の中に抜き取る、

ステップを含んでいる請求項(47)に記載の方法。

(49)前記嫌気性血液サンプルを抜き取るステップが、前記第1の血液部分が抜き取られた後で前記針組立体と前記バキュティナーとの間に血液の流れをつくるステップから成る請求項(48)に記載の方法。

(50)前記第1の血液部分を前記注射器へ抜き取るステップが、患者の心臓の圧力下で自由に血液

を流すステップから成る請求項(48)に記載の方法。

3.発明の詳細な説明

(産業上の利用分野)

本発明は、患者から血液サンプルを採取する装置に向けられたものであり、特に、サンプル内の気体分圧が、患者の生体内における血液内の気体分圧とほぼ等しくなるように、血液サンプルを受け取ることができる、改良された血液採取装置に向けられたものである。

(従来技術)

医療分野では、患者の血液内の、生体内における気体の平衡状態を決定することが必要である。医療作業員は、代表的には、酸素と二酸化炭素の分圧を気にかけるであろう。彼らは、また、例えば水素イオンやカルシウムイオンのような、活性が血液中の気体平衡に関連してくるイオンの種を気にかけるであろう。

血液サンプルを血液中の気体分析のために有効なものにするには、サンプルは、嫌気条件で、すなわち、検査すべき気体の分圧に変動が生ずるのを防止すべく血液が患者の体外の気体にさらされないように、採取されなければならない。現在市販されて利用できる主要な血液採取装置は、嫌気血液採取の完全性を保証しているという点では、概ね妥当であるとはいえない。従来装置の例としては、注射器及びベント式プランジャーが使用されており、バレル内の空隙がない状態からベント式プランジャーを引っ張ることによって、患者から正確な血液体積が得られるまで、患者から注射器のバレルの中に血液をゆっくりと抜き取る。しかしながら、これらの装置は、血液サンプルが外気にさらされるのをある程度許している。プランジャーが移動する前に、ある程度の外気量はバレル内に含有されるであろう。従って、血液の最初の部分はこれらの気体にさらされ、それによって、この最初のサンプルに含有している気体の分圧が変化する。抜き取られた血液のうち最初の部分を捨てる手段は提供されておらず、そのため、全サンプルが汚染されるであろう。

さらに、前述した装置を用いる際に、装置の医療作業員を、作業の途中で汚染された血液の偶発的な破裂や暴露に対して保護する手段も提供されていない。

ベクトンディケンソン(Becton and Dickenson)のバキュテイナー(Vacutainer)及びバキュテイナー付属装置のような他の装置は、抜き取られた血液に対する暴露から医療作業員を保護する、改良された特性を示している。しかしながら、これらの装置もまた、外気に対する血液サンプルの最初の部分の暴露を、ある程度許容してしまう。

前述した従来技術の欠点に加えて、嫌気性血液サンプルの採取を可能にしつつ、流し込み、すなわち血液の流れの中へ、例えば栄養剤や薬等を注入する手段を備える血液採取装置は、現在のところ知られていない。

従って、患者から嫌気性血液サンプルを抜き取る装置を提供することが望ましい。さらに、液体を患者の血液の流れに注入することもできる、血液サンプルを抜き取る装置を提供することがさらに望ましい。穿刺、すなわち針の配置を追加して行う必要のない、繰り返して血液を採取できる、前記装置を提供することがさらに望ましい。また、予定された区間の採取、すなわち他の引き続いて行なわれる血液の採取の間、患者に残してお

くことができる、血液サンプルを抜き取る装置を提供することが望ましい。

(発明の目的)

それゆえ、本発明の目的は、患者から嫌気性血液サンプルを抜き取る血液採取装置を提供することである。

また、本発明の目的は、最初の汚染された血液のサンプル部分を抜き取って、残りのサンプルにおける完全な嫌気性を維持できる、血液採取装置を提供することである。

さらに、本発明の目的は、外部の液体を患者の血液の流れの中に注入できる血液採取装置を提供することである。

さらに、本発明の目的は、穿刺、すなわち針の配置を追加して行なう必要のない、繰り返して血液を採取できる血液採取装置を提供することである。

さらに、本発明の別の目的は、予定された区間の採取、すなわち他の引き続いて行なわれる血液採取の間、患者に残しておくことができる血液採取装置を提供することである。

本発明の、これら及び他の目的は、患者から血液を抜き取ってこれを貯蔵するときに、医療作業員が使用するカップリングを提供することによって、かなえられる。このカップリングは、血液サンプルを引き出すべく、患者に針を注入する針組立体とともに使用するために、特に利用される。カップリングは、細長い中空シャフトと、針組立体を該シャフトに固定的に連結し、針によって引き出された血液をシャフトに送る、シャフトの第1の端部に取り付けられる接続部材と、から成る。カップリングは、シャフトを様々な血液貯蔵手段に接続する、シャフトの第2の端部に取りつけられたアダプタースリーブをさらに備えている。開口部が、アダプタースリーブと接続部材との中間のシャフトに連結されており、シャフトに受け入れられた血液がその開口部と連通するように、その開口部は、接続部材と連通している。

本発明の別の実施例では、血液の流れを遮断してシャフトにたまった空気を通気する装置が提提される。特に、流れ制御手段、例えば、微孔質の疎水性プラグが、シャフトからアダプタースリーブへの空気の流れを可能にしつつ、シャフトからアダプタースリーブへの血液の流れを制限するため、開口部とアダプタースリーブとの中間のシャフト内に位置している。本発明の他の実施例では、シャフトと開口部との選択的な連通を可能にするバルブが、シャフトと開口部との中間に設けられる。

本発明の他の実施例は、特許請求の範囲で特に示され、明瞭に請求される。しかしながら、本発明は、実施の構成や方法に関する限り、添付図面を参照して次の詳細な説明を読むことから最も良く理解できるであろう。

(実施例)

本発明の改良された血液採取装置を示す断面図が第1図に提供されている。血液採取装置は、患者の血液流れ(動脈あるいは静脈)内に挿入するようになった挿入端部102を有する細長い針100を備えている。針100は、さらに、円筒シール108を介して第1の接続部材106に取り付けられている取り付け端部104を有している。当業界で周知のように、針100は、患者から引き出された血液を第1の接続部材106へ導く、挿入端部102から取り付け端部104へ延びる同軸通路を有している。

円筒シール108は、内部に針100の取り付け端部104が固定して取り付けられている中央開口部110を有している。さらに、円筒シール108は、第1の接続部材106の針受け入れ端部112へ固定して取り付けられている。第2の接続部材114は、第1の接続部材106の嵌合端部118と嵌合するようになった嵌合端部116を有しており、その結果、第1の接続部材によって受け入れられた、針100からの血液は、嵌合接合116、118を介して第2の接続部材114に導かれる。

チューブ122の第1の端部120が、第2の接続部材114の取り付け端部124に密封して取り付けられている。チューブ122は、患者から引き出された血液を針100を介してカップリング126へ運ぶために設けられている。チューブ122は、針を患者の血液流れに容易に挿入可能であり、さらに、挿入後、針100に無用な動

きを与えて患者に不快感を生ぜしめることなく、医療作業員がカップリング１２６を操作可能となるように、可撓性であるのが好ましい。さらに、チューブ１２２は、医療作業員が患者から引き出された血液を視覚で観察できるように、透明であるのが好ましい。

針１００と、第１の接続部材１０６と、第２の接続部材１１４と、チューブ１２２との組合わせは、針組立体を構成し、当業界で周知の針、接続部材、及びチューブから容易に組立て可能である。一例として、第１及び第２の接続部材１０６及び１１４は、当業界で周知のように、雄及び雌のルエル(Luer)コネクターから成る。

カップリング１２６は、チューブの第２の端部１２８を、第１及び第２の血液貯蔵手段１３０及び１３２の各々と接続するために設けられている。この目的のために、カップリング１２６は、チューブ１２２の第２の端部１２８を受け入れる中央開口部を有する接続部材１３４を有している。接続部材１３４は、チューブ１２２によってカップリング１２６に送られる血液がシャフト１３６の内部に受け入れられるように、細長い中空シャフト１３６に一体に接続される。アダプタースリーブ１３８は、接続部材１３４が接続されている端部と反対側の端部でシャフト１３６に一体に接続されている。アダプタースリーブ１３８は、シャフト１３６と連通しており、後で完全に説明するように、第２の血液貯蔵手段１３２を受け入れるために設けられる。

カップリング１２６は、さらに、アダプタースリーブ１３８と接続部材１３４との中間のシャフト１３６に一体に接続されている開口部１４０を、さらに有している。開口部１４０は、第１の血液貯蔵手段１３０をカップリング１２６のシャフト１３６へ接続するために設けられる。通路１６２は、開口部１４０が接続部材１３４と連通するように、開口部１４０に近接してシャフト１３６に設けられている。従って、チューブ１２２によってカップリング１２６に送られてきた血液は、貯蔵のため、アダプタースリーブ１３８及び開口部１４０を経由して第１及び第２の血液貯蔵手段１３０及び１３２へ運ばれる。

カップリング１２６は、また、アダプタースリーブ１３８と開口部１４０との間のシャフト内に配置されたプラグ１４２を有している。プラグ１４２は、血液採取作業の初期の段階の間に、接続部材１０６、１１４、チューブ１２２、シャフト１３６、及び開口部１４０内にたまった空気を排気する、例えば、多孔質プラグのような液体流れ制御手段から成る。従って、プラグ１４２は、シャフト１３６からアダプタースリーブ１３８への血液の流れを制限して、シャフトからアダプタースリーブへの空気の流れを可能にするようになっている。本発明の好ましい実施例では、プラグ１４２は、当業界で周知の、微孔質の疎水性プラグから成る。しかしながら、他の液体流れ制御手段が、好ましい微孔質疎水性プラグ１４２の代わりに、用いることができることは、当業者には明らかであろう。

前述したように、開口部１４０は、第１の血液貯蔵手段１３０を受け入れるようになっている。キャップ１４４は、第１の血液貯蔵手段１３０がカップリング１２６に接続されていないときに、しばしばおこる不注意な血液損失から開口部を密封するため、開口部１４０と係合可能である。しかしながら、通常作業では、キャップ１４４は、開口部１４０から取り除かれ、そこに第１の血液貯蔵手段１３０を接続している。

本発明の好ましい実施例では、第１の血液貯蔵手段１３０は、血液貯蔵チャンバー１４６と、その血液貯蔵チャンバー１４６内に配置されたプランジャー１４８を有する形式の注射器から成る。周知のように、操作の際には、プランジャー１４８は、血液がチャンバー内に入るように、血液貯蔵チャンバー１４６からゆっくりと引き出される。血液貯蔵手段１３０は、さらに、血液貯蔵手段１３０を開口部１４０に接続するため、接続手段１５０を備えている。本発明の好ましい実施例では、開口部１４０と接続部材１５０は、各々、雄雌のルエルコネクターから成る。しかしながら、他のコネクター部材が第１の血液貯蔵手段１３０をカップリング１２６に密封して接続するために提供されることは、当業者には明らかであろう。

操作の際は、キャップ１４４は、開口部１４０から取り除かれて、そこに血液貯蔵手段１３０が接続される。次いで、血液が引き出され、あるいは好ましくは患者の心臓の圧力下で自由に流れることができるように、かつ、接続部材１０６、１１４及びチューブ１２２を介して、シャフト１３６に送られるように、患者の血液流れの中に針１００が挿入される。接続部材１０６、１１４、チューブ１２２、シャフト１３６及び開口部１４０内にたまった空気は、前述したように、流れ通路に入った患者の血液によって、置換され、多孔質プラグ１４２を介して通気される。引き出され、あるいは患者からの心臓の圧力下で流れる血液の第１の部分は、通気される前に、たまった空気にさらされるので、概ね汚染されており、それゆえ、嫌気性血液採取に適していない。従って、この第１の血液の部分は、一時的に貯蔵するために、血液貯蔵手段１３０の中へカップリング１２６から引き出され、一方、嫌気性血液サンプルは、第２の血液貯蔵手段１３２を介して受取られる。嫌気性血液サンプルが受取られた後、血液貯蔵手段１３０内に一時的に貯蔵された血液は、捨てられ、あるいは、チューブ１２２及び針１００を介して患者に戻される。

嫌気性血液サンプルを引き出すため、第２の血液貯蔵手段１３２がアダプタースリーブ１３８を介してカップリング１２６に接続されている。第２の血液貯蔵手段１３２は、当業界で周知のベクトン・ディケンソン・バキュティナーから成っていてもよい。血液貯蔵手段１３２は、患者から抜き取られた嫌気性血液サンプルを受け入れる血液貯蔵チャンバー１５２を有している。針１５４は、針ハブ１５６に密封して接続されており、それらの組立体は、適合性を有するカップリング１５８（普通は、バキュテイナーアダプターとして言及されている）を介して血液貯蔵チャンバー１５２に密封して接続されている。当業界で周知のように、針１５４は、血液貯蔵チャンバー１５２と連通することを防止するため、シールを有している。さらに、当業界で周知のように、血液貯蔵チャンバー１５２は、患者から抜き取られた血液を汚染する空気を含まないようにするため、排気されている。適合性を有するカップリング１５８は、針１５４を血液貯蔵チャンバー１５２と連通させて配置するため、針１５４からシールを取り除く手段を備えている。

アダプタースリーブ１３８は、針ハブ１５６をきちんと受け入れるような径でできた内部アダプターチャンバー１６０を有している。アダプタースリーブ１３８の長さとシャフト１３６内のプラグ１４２の位置は、血液貯蔵手段１３２がアダプタースリーブ１３８に完全に挿入され、針１５４がプラグ１４２を通って通路１６２とチューブ１２２の第２の端部１２８との間に位置するように、選択される。針がシャフト１３６と同軸になるようにカップリング１２６内に挿入されることを可能とするため、針ガイド１６４がアダプタースリーブ１３８とプラグ１４２との間のカップリング１２６内に配置されている。針ガイド１６４は、カップリング１２６内への血液貯蔵手段１３２の挿入の間、針１５４を受け入れて、かつ、針がシャフト１３６と同軸となるように、プラグ１４２への針の挿入前に針を位置決めするために、設けられている。

操作の際は、嫌気性血液サンプルを集めるために、血液貯蔵手段１３０が、前述した開口部１４０を介してカップリング１２６に連結される。針１００が患者の血液流れの中に挿入され、針１００、コネクター１０６、１１４、チューブ１２２及びカップリング１２６の内部にたまった空気が前述したようにプラグ１４２を介して排気される。次いで、血液貯蔵手段１３２の針１５４が、チューブ１２２の近傍の通路１６２を越えて位置するように、プラグ１４２を通してカップリング１２６内に挿入される。針１５４内にたまった汚染空気のどんなにわずかの部分でもプラグ１４２を介して排気されるように、すなわち、嫌気性血液サンプルを受け入れる前にカップリング１２６から取り除かれるように、血液サンプルの汚染された部分を貯蔵手段１３０内に貯蔵する前に、針１５４をカップリング１２６へ挿入することが望ましい。

針１５４がカップリング１２６内に適当に挿入された後、汚染された血液の第１の部分はカップ

リング１２６から一時貯蔵のため血液貯蔵手段１３０へ引き出される。このとき、針１５４のシールは、嫌気性血液サンプルが血液貯蔵１５２へ導かれるように、当業界で周知のように、適合性カップリング１５８によって除去される。血液貯蔵チャンバー１５２へ導かれた血液のほぼ全部がチューブ１２２から受け取った血液であって、血液貯蔵手段１３０の血液貯蔵チャンバー１４６から受け取った血液ではないようにするために、針１５４は、通路１６２とチューブ１２２との中間でかつ、チューブ１２２の第２の端部１２８の近傍の、シャフト１３６内のカップリング１２６内に位置していることが好ましい。

本発明の代わりの実施例では、嫌気性血液サンプルを受け取っているとき、血液貯蔵手段１３０内に貯蔵された汚染された血液サンプルを、操作中に、シャフト１３６からほぼ隔離することができるバルブ、あるいは他の選択性カップリング手段を備えることが望ましい。

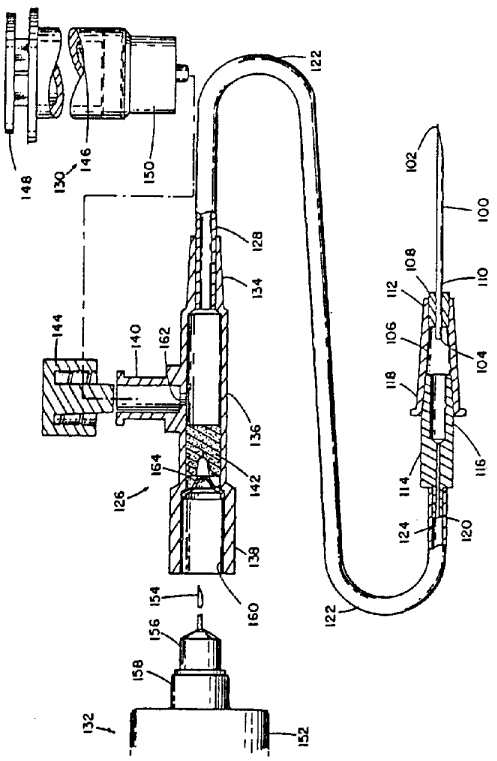
医療業界では普通となっているように、キャップ１４４に加えて、複数のキャップあるいは他のシール手段が、針１００に配置してアダプタースリーブ１３８のチャンバー１６０を密封するために設けられてもよい。

新規な血液採取装置の好ましい実施例のいくつかのみをここで詳細に説明したが、当業者には、多くの改良や変更が容易に明らかとなるであろう。本発明の真の範囲及び精神に入るこのようなすべての改良や変更を包含することが、特許請求の範囲の趣旨である。

4.図面の簡単な説明

第１図は、本発明の改良された血液採取装置の断面図を示す。

１００・・・・・針
１０６・・・・・第１の接続部材
１１４・・・・・第２の接続部材
１２２・・・・・チューブ
１２６・・・・・カップリング
１３０、１３２・血液貯蔵手段
１３４・・・・・接続部材
１３６・・・・・シャフト
１３８・・・・・アダプタースリーブ
１４０・・・・・開口部
１４２・・・・・プラグ
１４４・・・・・キャップ
１４６、１５２・血液貯蔵チャンバー
１４８・・・・・プランジャー
１５４・・・・・針



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

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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

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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,

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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

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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.

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

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Abstract

Background Arterial catheters are potential sources of nosocomial infection.

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

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

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

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

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

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

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

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

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

Materials and Methods

Setting and Sample

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

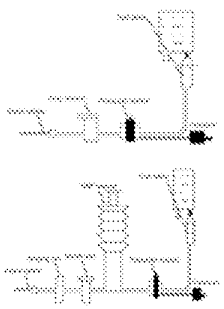
Samples and Randomization

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

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

Figure

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



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

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

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

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

Microbiological Analysis

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

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

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

Data Collection

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

Statistical Analysis

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

Results

Characteristics of the Patients and the Arterial Catheters

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

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Table 1

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

Microbiological Analysis

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

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Table 2

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

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Table 3

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

Microorganisms Identified

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

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Table 4

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

Discussion

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

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

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

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

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

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

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

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

Limitations

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

Conclusion

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

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Footnotes

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Financial Disclosures

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Interventions Implemented to Reduce the Risk of Transmission of Bacteria by Transfusion in the English National Blood Service

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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 Oltbius 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% [28, 29].

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 [27]. 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.

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wrap up close

(57) [Abstract] Since this gazette is application data before electronic filing, abstract data is n ot recorded.

The scope of the claims open

[Claims]
1. 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

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⑤4血管穿刺表示器付き多サンプル針組立体

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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ビテイー４６は両横孔48，50上となり、何れの孔も液を通さないブロックとならない。この結果、第２の穿刺針１５内の血液は血液不透過性プラグ５２によつてブロックされていたが、この障害物を廻つて供給される。即ち、第７図に示す通り、血液は横孔48，キヤビテイー46を通つて流れ、プラグ５２をバイパスする。血液はキヤビテイーから横孔５０を経て第２の穿刺針の内腔５１に戻つて連続流となる。第２の穿刺針の開放端を流出した血液は血液収集容器内に収集される。

血液が血液収集容器内に充満すれば、充満した容器はホルダー１９から取外し、この間穿刺針14は患者の血管内に穿刺された状態を保つ。血液収集容器を取外せば同時に滑動可能スリーブ４１に対する圧縮力もなくなり、スリーブは外方に滑動して第４図の位置に戻る。この位置は弁閉鎖位置であり、第２の穿刺針１５からの血液流出を防ぐ。このスリーブ弁の動きは自動的に血液が第２の穿刺針から流出するのを防ぐ。特に真空血液収集容器の交換間は血液の漏洩が生ずることはない。それ故、血液は患者の血管から室２８に流れ、次の血液収集容器がホルダーに挿入され、滑動可能の弁の内方圧縮運動が上述の通りに繰返される。多サンプル血液の収集が終れば、穿刺針１４を患者から取外し、全部の針組立体を廃棄する。

本発明は各種の変型が可能である。第８，９図に示す実施例は弁閉鎖の間は穿刺針からの血液の流出を防ぎ、空気は通過して排気目的を達する。第８図の実施例では多サンプル針組立体７０は大部分前の実施例と同様であるが、穿刺針７１は血液収集容器の貫通可能ストツパ７２を穿刺し、１個のみの横孔７４を設ける。この横孔の穿刺針71での位置は針組立体の後端部７５から著しく離れ、穿刺針の開放端７６に近い。ガス透過性液不透過性の多孔性プラグ７８を内腔７９内の横孔７４と開放端７６との間とする。スリーブ弁８０は前述のスリーブ弁４１とほゞ同様であるがいくらか長くして横孔７４を液不通過に接触する。更にスリーブ弁８０には前述のスリーブ弁４１に記したキヤビテイーを必要としない。更に、スリーブ弁80は図示の例では厚壁部８１と薄壁部８２とを設けたが、好適な例示であり、スリーブの厚さは全体を均等とすることもできる。

スリーブ８０が第８図の位置即ち閉位置にある時は針組立体内のエアは空気透過性プラグ７８を通つて流れ、血液はプラグを通らない。更に、スリーブ８０が有効に横孔７４を閉鎖するため、血液は流出しない。第９図はスリーブ弁８０の圧縮位置を示し、第７図と同様である。針７１は貫通

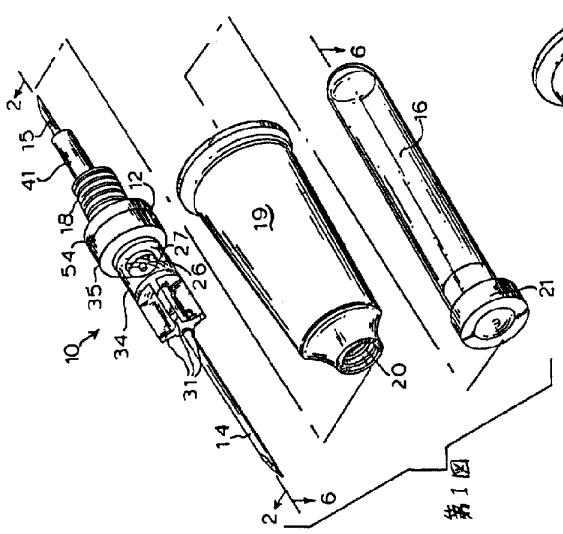
可能ストツパ７２内に穿刺し、横孔７４は血液収集容器内にある。スリーブ弁８０は滑動して針組立体の後端部７５に向けて圧縮される。横孔７４が露出したため、内腔７９内の血液は横孔７４を通つて直接血液収集容器内に流出する。第９図に示す通り、血液はプラグ７８を通らずに分流して横孔７４に流れ、穿刺針の開放端からは流れない。血液収集容器が充満すれば容器はホルダーから取外し、スリーブ弁８０は滑動して第８図に示す位置に戻る。これによつて血液収集容器の交換間に血液が穿刺針から流出するのを防ぐ。

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。

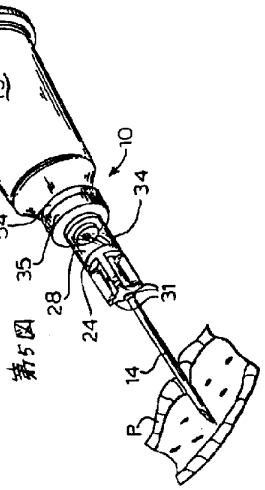
4.〔図面の簡単な説明〕

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。

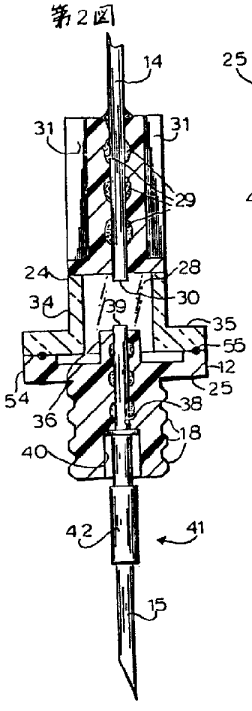
１０ … 多サンプル針組立体
１２ … ハウジング
１４，１５ … 穿刺針
１６ … 真空血液収集容器
１９ … 容器ホルダー
２４ … 前端部
２５ … 後端部
２８ … 室
４１ … スリーブ弁
４２ … 厚壁部
４４ … 薄壁部
４６ … キヤビテイー
４８，５０ … 横孔
５２ … 多孔性プラグ



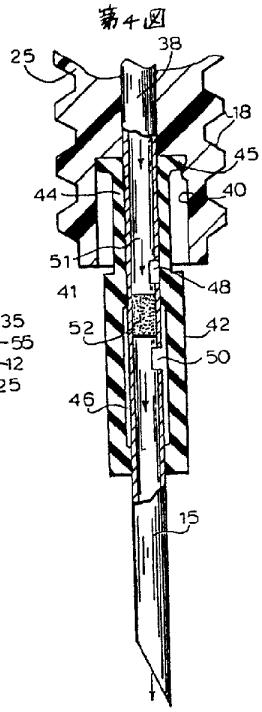
第1図



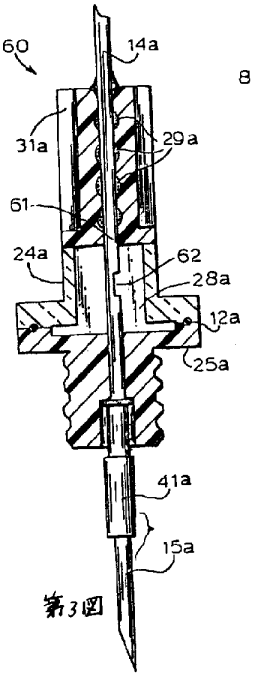
第5図



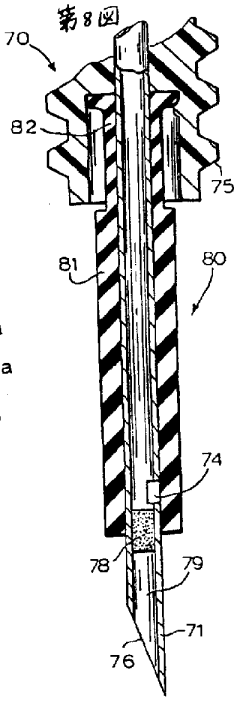
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第4図

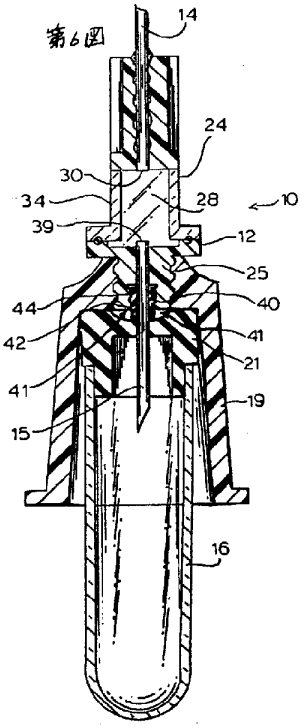


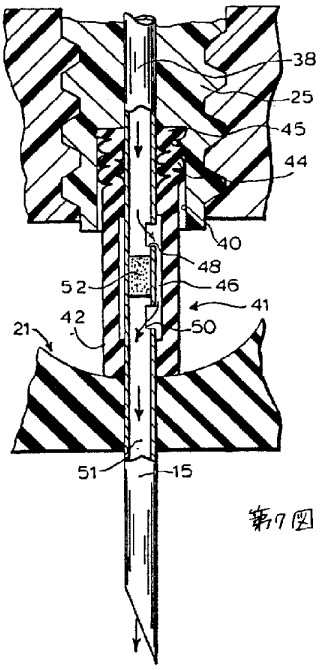
第3図



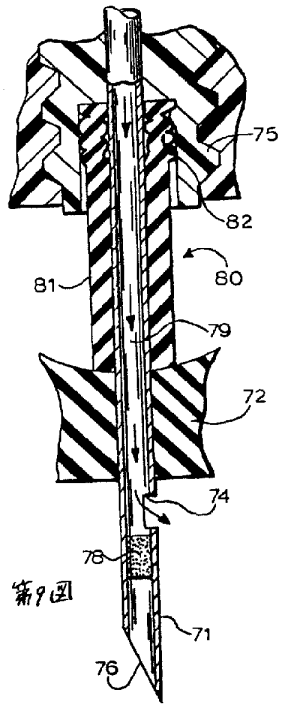
第8図

第6図


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第7図


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第9図

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Literature display help

1 / 1 display

Japanese Patent Laid-Open No. 58-067238

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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

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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

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発明の数　1
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⑤4試料採集装置

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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の開口部を開口し、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瞬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

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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

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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

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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

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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

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

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

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。

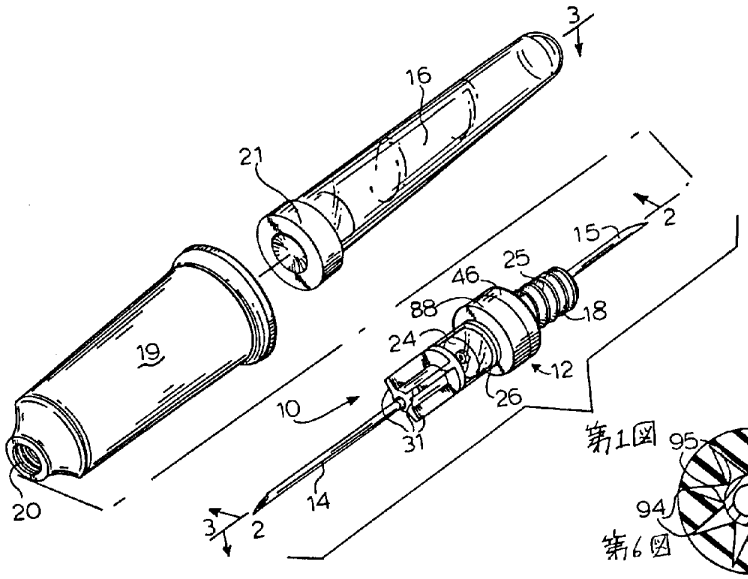
第８ａ図は本発明の他の実施態様を示す単一試料採集針組み立て体の部分拡大断面図。

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。

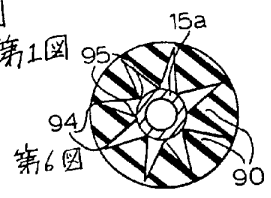
１０……針組み立て体、１２……ハウジング、
１４……第１の穿刺針、１５……第２の穿刺針、
１６……負圧容器、　１９……支持具、
２４……前方端、　２５……後方端、
２７……環状多孔質栓、２９……第１の口孔、
５０……試料採集室、　７０……第２の口孔、
７４……第１の開口部、７６……第２の開口部、
７８……第３の開口部、８０……可撓性スリーブ、
９４……溝、　１１４……小さな内側口径、
１１６……大きな内側口径

特許出願人　ベクトン・ディッキンソン・アンド・カンパニー

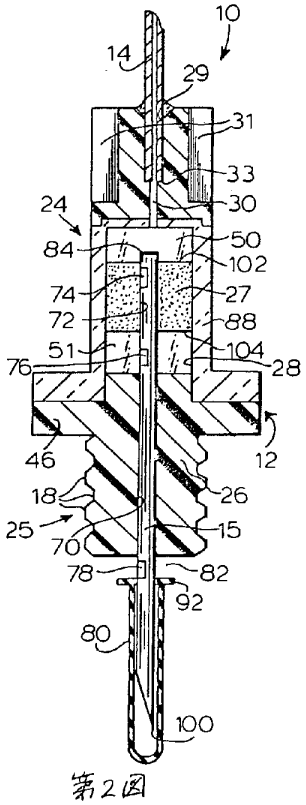
代理人　弁理士　湯浅恭三（外４名）



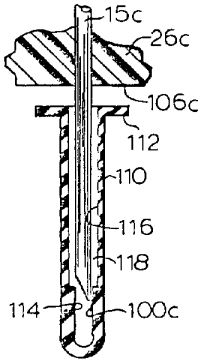
第1図



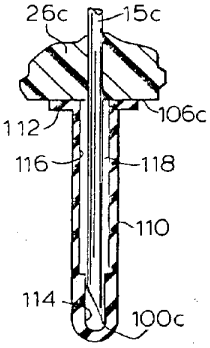
第6図



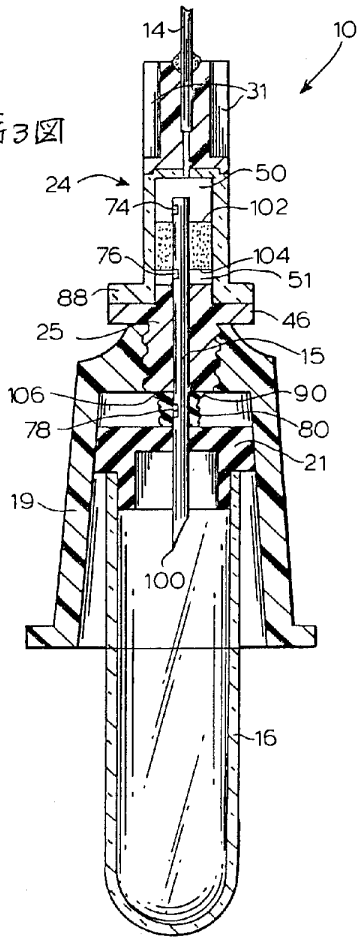
第2図



第8a図

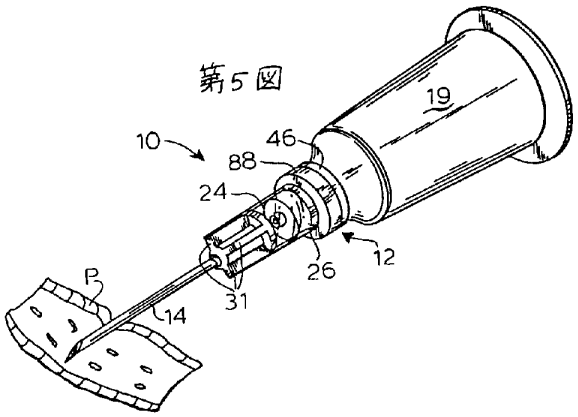


第8b図

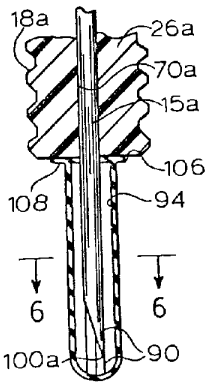


第3図

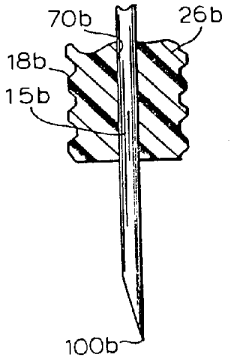
第5図


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

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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

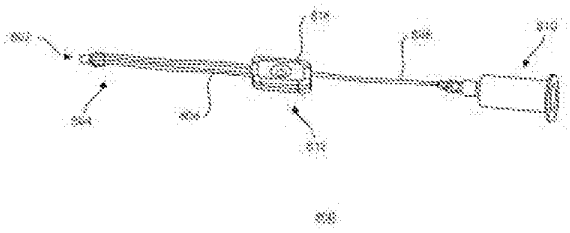
Classification: **- international:** ***A61B5/15; A61B5/153; A61B5/154; A61B5/157***
- cooperative: **A61B5/15003 (EP, US); A61B5/150213 (EP, US); A61B5/150221 (US); A61B5/150251 (EP, US); A61B5/150274 (EP, US); A61B5/150351 (US); A61B5/150755 (US); A61B5/150786 (US); A61B5/150946 (US); A61B5/150992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

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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.

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

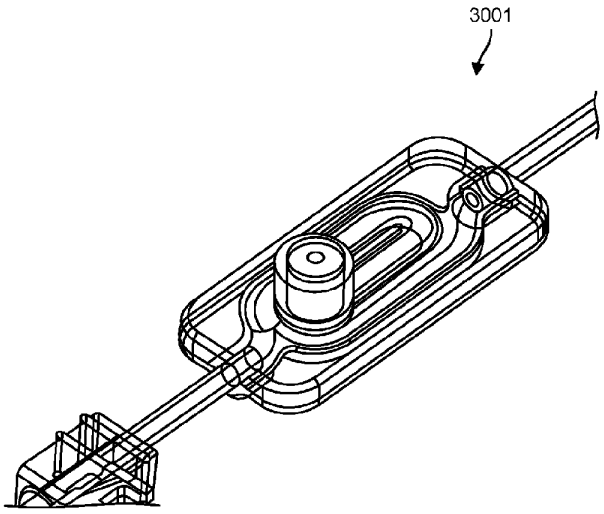


FIG. 30B

(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.

[Continued on next page]

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BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

BACKGROUND

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

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

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

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

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

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

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

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

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

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

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

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

SUMMARY

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

BRIEF DESCRIPTION OF THE DRAWINGS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

DETAILED DESCRIPTION

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

[00144] FIGS. 25A – D show a blood optimization system 2500 and blood sequestration device 2502, formed substantially as described in FIGS. 15, 16, 17, 18 and 19, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2520. Air initially in the blood sequestration chamber 2520 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2520. The air venting mechanism includes an air permeable blood barrier 2506, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2520.

[00145] The air venting mechanism includes an inner wall 2516 that at least partially circumscribes or surrounds the air permeable blood barrier 2506, and an outer wall 2504 spaced apart from the inner wall 2516. The outer wall 2504 can have one or more air vents 2514 formed therein. The outer wall 2504 extends higher upward than the inner wall 2516, such that a lid 2510, such as a cap, plug, cover, etc., can be attached to the outer wall 2504 and be displaced by a small distance from the top of the inner wall 2516. A seal 2508 in the form of a silicone wafer, or other elastomeric material, fits within the outer wall 2504 to cover the air permeable blood barrier 2506 and abut the top of the inner wall 2516. The seal 2508 covers and seals the air permeable blood barrier 2506 and inhibits air from entering the blood sequestration chamber 2520 through the air permeable blood barrier 2506. A fulcrum 2512 on an underside of the lid 2510 allows the seal 2508 to flexibly disconnect from the top of the inner wall 2516 when pushed by air displaced from the blood sequestration chamber 2520, to allow air to vent from the air permeable blood barrier 2506 and through the one or more air vents 2514 in the outer wall 2504.

[00146] FIG. 26A – E illustrate a blood sample optimization system 2600 that includes a patient needle 2602 for vascular access to a patient's bloodstream, a blood sample collection device 2604 to facilitate the collecting of one or more blood samples for blood testing or blood cultures, and a conduit 2606 providing a fluid connection between the patient needle 2602 and the blood sample collection device 2604. The conduit 2606 can include flexible tubing. In preferred implementations, the blood sample collection device 2604 includes a protective shield 2605 that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the

collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2602.

[00147] The blood sample optimization system 2600 further includes a blood sequestration device 2608, located at any point on the conduit 2606 between the patient needle 2602 and the blood sample collection device 2604. The location of the blood sequestration device 2608 can be based on a length of the conduit between the blood sequestration device 2608 and the patient needle 2602, and the associated volume that length provides.

[00148] The blood sequestration device 2608 includes an inlet port 2612 for being connected to the conduit 2606 toward the patient needle 2602, and an outlet port 2614 for being connected to the conduit 2606 toward the blood sample collection device 2604. The blood sequestration device 2608 includes an outer housing 2616 and an inner housing 2617, both having a cylindrical form, and being connected concentrically. The outer housing 2616 includes an outer wall 2618 and an inner conduit 2620 that defines a blood sampling channel 2622 to convey blood through the conduit 2606 to the blood sampling device 2604. The inner housing 2617 fits snugly between the inner conduit 2620 and the outer wall 2618 of the outer housing, and is rotatable in relation to the outer housing 2616. The fit between the outer housing 2616 and the inner housing 2617 can be a friction fit that maintains the housings in a particular position. The inner housing 2617 defines a blood sequestration chamber 2624, preferably a helical or corkscrew channel around the outer surface of inner conduit 2620 of the outer housing 2616, and which terminates at an air vent 2628 having an air permeable blood barrier, as shown in FIG. 26E.

[00149] The blood sequestration chamber 2624 is connected with the blood sampling channel 2622 via diversion junction 2624 formed in the inner conduit 2620, when the blood sequestration device in a first state, illustrated in FIG. 26C. The protective shield 2606 on the collection needle 2604 provides a block for air or blood, enabling a diversion of an initial aliquot of blood into the blood sequestration chamber 2624 as the patient's blood pressure overcomes the ambient air pressure in the blood sequestration channel 2624 to displace air therefrom through air vent 2628.

[00150] When the inner housing 2617 is rotated relative to the outer housing 2616, or vice versa, to a second state, as illustrated in FIG. 26D, the blood sequestration chamber 2624 is shut off from diversion junction 2624, enabling a direct path from the patient needle through the conduit 2606 to the collection needle 2604, via blood sampling channel 2622. The outer housing 2616 and/or inner housing 2617 can include ridges or grooves formed within a portion of their surfaces, to facilitate relative rotation from the first state to the second state.

[00151] FIGS. 27A – D illustrate a blood optimization system 2700 and blood sequestration device 2702, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, and 25, but being formed to inhibit a user or other object from touching or blocking an air venting mechanism from a blood sequestration chamber 2720. Air initially in the blood sequestration chamber 2720 is displaced by an initial aliquot of blood upon venipuncture, where a patient's blood pressure overcomes the ambient air pressure in the blood sequestration chamber 2720. The air venting mechanism includes an air permeable blood barrier 2706, such as a porous material or set of materials that allows air to escape but blocks blood from leaving the blood sequestration chamber 2720.

[00152] The air venting mechanism includes an inner wall 2716 that at least partially circumscribes or surrounds the air permeable blood barrier 2706, and an outer wall 2704 spaced apart from the inner wall 2716. A cap 2722 is positioned on the air venting mechanism, preferably by having a lower cap wall 2728 that fits between the inner wall 2716 and the outer wall 2704 of the air venting mechanism, and frictionally abutting either the the inner wall 2716 or the outer wall 2704 or both. The cap 2722 further includes one or more vent holes 2724 or slits, apertures, openings, or the like, which extend through an upper surface of the cap 2722 around a downwardly extending plug 2726. The plug 2726 is sized and adapted to fit snugly within the space defined by inner wall 2716.

[00153] In a first position, as illustrated in FIG. 27C, the cap 2722 is extended from the air venting mechanism to allow air from the blood sequestration chamber 2720 to exit through the air permeable blood barrier 2706 and through the one or more vent holes 2724. Once the air from the blood sequestration chamber 2720 has been displaced, i.e., when the blood sequestration chamber 2720 is filled with the first aliquot of potentially tainted blood from the patient, then the cap 2722 can be pushed down on the air venting

mechanism in a second position as shown in FIG. 27D, so that the plug 2726 fits within the inner wall 2716 over the air permeable blood barrier 2706 to seal the air venting mechanism. In either the first position or the second position, the cap 2722 protects the air permeable blood barrier 2706 from outside air or from being touched by a user.

[00154] FIGS. 28A – F illustrate a blood optimization system 2800 and blood sequestration device 2802, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but utilizing a multi-layered filter, and in some implementations, a filter with trapped reactive material, for an air permeable blood barrier. As shown in FIGS. 28C and D, an air permeable blood barrier 2803 includes a first layer 2804 of an air permeable but blood impermeable material, and a second layer 2806 that includes a reactive material, such as a hydrophobic material, for repelling blood while still allowing air to pass through both layers. As shown in FIGS. 28E and F, the air permeable blood barrier 2803 can include any number of layers, such as a third layer 2808 formed of the same air permeable but blood impermeable material as first layer 2804, while a second layer 2806 includes trapped or embedded blood reactive material.

[00155] FIGS. 29A – C illustrate a blood optimization system 2900 and blood sequestration device 2902, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26, but in which a blood sequestration chamber 2904 is at least partially filled with a blood-absorptive material 2906. The blood-absorptive material 2906 can act as a wicking material to further draw in blood to be sequestered upon venipuncture of the patient, and prior to use of a blood drawing device such as a Vacutainer™ or a syringe, or the like.

[00156] FIGS. 30A – G illustrate a blood optimization system 3000 and blood sequestration device 3002, formed substantially as described with reference to at least FIGS. 15, 16, 17, 18, 19, 25 and 26. The blood sequestration device 3000 includes an inlet port 3002 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 3002 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 3002 defines an opening into the blood sequestration device 3000, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the

opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00157] The inlet port 3002 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 3002, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 3000 at the time of blood draw or sampling.

[00158] The blood sequestration device 3000 further includes an outlet port 3004, which defines an opening out of the blood sequestration device 3000 and to the blood sample collection device. The outlet port 3004 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 3000 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 3000 at the time of blood draw or sampling.

[00159] The blood sequestration device 3000 further includes a sampling channel 3006 between the inlet port 3002 and the outlet port 3004, and a sequestration chamber 3008 that is connected to and split off or diverted from the sampling channel 3006 at any point between the inlet port 3002 and the outlet port 3004. The sampling channel 3006 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 3008. The sampling channel 3006 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 3006 has a substantially similar cross sectional area as the opening of the inlet port 3002. In other implementations, the sampling channel 3006 can gradually widen from the inlet port 3002 to the outlet port 3004. The sequestration chamber 3008 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the

blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 3006.

[00160] In some exemplary implementations, the diversion between the sampling channel 3006 and the sequestration chamber 3008 is by diverter junction 3007. Diverter junction 3007 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008. The sequestration chamber 3008 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 3008.

[00161] The sequestration chamber 3008 is preferably maintained at atmospheric pressure, and includes a vent 3010 at or near a distal end of the sequestration chamber 3008. The vent 3010 may include an air permeable blood barrier 3012 as described above.

[00162] The blood sequestration device 3000 can include a housing 3001 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated FIG. 30F, the housing 3001 includes a top member 3020 and a bottom member 3022 that are mated together. The blood sequestration device 3000 can also include a gasket or other sealing member (not shown) so that when the top member 3020 is mechanically attached with the bottom member 3022, the interface between the two is sealed by the gasket or sealing member. The bottom member 3022 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 3006, the sequestration chamber 3008, and diverter junction 3007.

[00163] The sequestration chamber 3008 may have a larger cross section than the sampling channel 3006 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 3006.

[00164] In some implementations, the sampling channel 3006 and the sequestration chamber 3008 are formed by grooves, channels, locks or other pathways formed in housing 3001. The housing 3001 can be made of rubber, plastic, metal or any other suitable material. The housing 3001 can be formed of a clear or translucent material, or

of an opaque or non-translucent material. In other implementations, the housing 3001 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 3006 and/or the sequestration chamber 3008 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 3008 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 3006. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 3012 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00165] The air permeable blood barrier 3012 can be covered with, or surrounded by, a cap 3032. The cap 3032 can be sized and configured to inhibit a user from touching the air permeable blood barrier 3012 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 3012 as the air is displaced from the sequestration chamber 3008. The cap 3032 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00166] The air venting mechanism includes a wall 3030 that at least partially circumscribes or surrounds the air permeable blood barrier 3012. The wall 3030 can have one or more air vents formed therein. The cap 3032 covers wall 3030 and can be snapped, glued, or otherwise attached in place. A seal 3017 in the form of a silicone wafer, or other elastomeric material, fits within the wall 3030 to cover the air permeable blood barrier 3012 and abut the top of the wall 3030. The seal 3017 covers and seals the air permeable blood barrier 3012 and inhibits air from entering the blood sequestration chamber 3008 through the air permeable blood barrier 3012. A fulcrum 3012 on an underside of the cap 3032 allows the seal 3008 to flexibly disconnect from the top of the inner wall 3016 when pushed by air displaced from the blood sequestration chamber 3008, to allow air to vent from the air permeable blood barrier 3012 and through the one or more air vents in the wall 3030 and/or cap 3032.

[00167] In use, the blood sequestration device 3000 includes a sampling channel 3006 and a sequestration chamber 3008. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 3006 is directed to an outlet port 3004 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 3008 terminates at a vent 3010 to atmosphere that includes an air permeable blood barrier 3012.

[00168] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through inlet port 3002 of blood sequestration device 3000. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 3008 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 3008 to displace air therein through the air permeable blood barrier 3012, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 3006. In various exemplary embodiments, the sequestration chamber 3008 and sampling channel 3006 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00169] Eventually, the sequestration chamber 3008 fills with blood that displaces air through the air permeable blood barrier 3012. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 3012 material to completely or partially seal the vent 3010. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00170] Upon filling the blood sequestration pathway 3008 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 3006, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 3006, queuing up the uncontaminated blood to be drawn through the sampling channel 3006.

[00171] In yet another aspect, the blood sequestration chamber and/or blood sampling channel, or other component, of any of the implementations described herein,

can provide a visually discernable warning or result in a component adapted for operative fluid communication with the flash chamber of an introducer for an intravenous catheter into a blood vessel of a patient. The device and method provides a visually discernable alert when blood from the patient communicates with a test component reactive to communicated blood plasma, to visually change. The reaction with the blood or the plasma occurs depending on one or a plurality of reagents positioned therein configured to test for blood contents, substances or threshold high or low levels thereof, to visually change in appearance upon a result.

[00172] In yet other aspects, the blood sequestration chamber and/or blood sampling channel can be sized and adapted to provide a particular volumetric flow of blood, either during the sequestration process and/or the sampling process.

[00173] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

CLAIMS

1. A blood sequestration device comprising;

an inlet port;

an outlet port;

a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

the sequestration chamber, the sampling channel and the junction being sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

2. The blood sequestration device in accordance with claim 1, further comprising a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

3. The blood sequestration device in accordance with claim 1, wherein the vent further includes an inner wall within the outer wall and that contains the air permeable blood barrier.

4. The blood sequestration device in accordance with claim 1, wherein the one-way seal is positioned over the inner wall and within the outer wall of the vent.

5. The blood sequestration device in accordance with claim 4, wherein the cap includes an inner surface that faces the air permeable blood barrier, the

inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

6. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a sealing material that seals the vent upon contact with blood.

7. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

8. A blood sequestration and sampling system comprising;

a blood sampling pathway having a patient needle on a proximal end and a sample collection device on a distal end; and

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

an inlet port coupled with the blood sampling pathway toward the patient needle;

an outlet port coupled with the blood sampling pathway toward the sample collection device;

a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

the sequestration chamber, the sampling channel and the junction being sized and configured such that a first portion of blood flows into the sequestration chamber toward the air permeable blood barrier for sequestration therein, and a second portion of blood bypasses the sequestration chamber and the

first portion of blood sequestered therein and is directed into the sampling channel toward the outlet port.

9. The blood sequestration system in accordance with claim 8, wherein the blood sequestration device further comprises a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

10. The blood sequestration system in accordance with claim 8, wherein the vent of the blood sequestration device further includes an inner wall within the outer wall and that contains the air permeable blood barrier.

11. The blood sequestration system in accordance with claim 8, wherein the one-way seal of the vent is positioned over the inner wall and within the outer wall of the vent.

12. The blood sequestration system in accordance with claim 11, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

13. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a sealing material that seals the vent upon contact with blood.

14. The blood sequestration system in accordance with claim 8, wherein the air permeable blood barrier of the blood sequestration device includes a filter having a first layer and a second layer, the second layer of the filter having a hydrophobic material to repel blood.

15. A blood sequestration device comprising;

an inlet port;

an outlet port;

a sequestration chamber connected with the inlet port via a junction, the sequestration chamber having a vent that includes an air permeable blood barrier, the vent being defined by an outer wall that at least partially circumscribes the air permeable blood barrier and includes one or more air vents, the vent further including a cap that at least partially covers the wall and a one-way seal abutting the air permeable blood barrier that inhibits air from entering the sequestration chamber; and

a sampling channel having a proximal end connected with the inlet port via the junction, and a distal end connected with the outlet port;

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

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

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

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

19. The blood sequestration device in accordance with claim 18, wherein the cap includes an inner surface that faces the air permeable blood barrier, the inner surface of the cap including a fulcrum against which the seal can flexibly unseal from the air permeable blood barrier to allow air to escape the sequestration chamber.

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

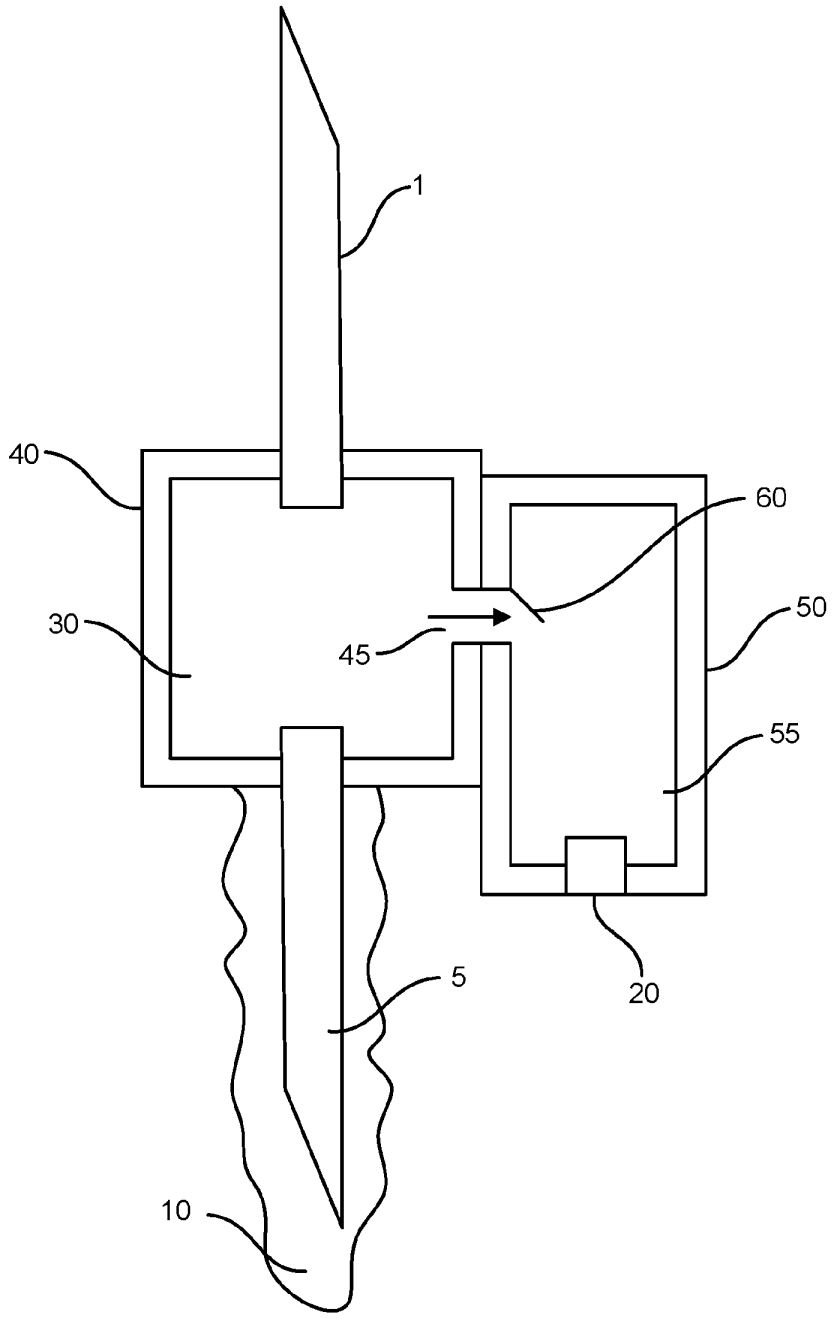


FIG. 1

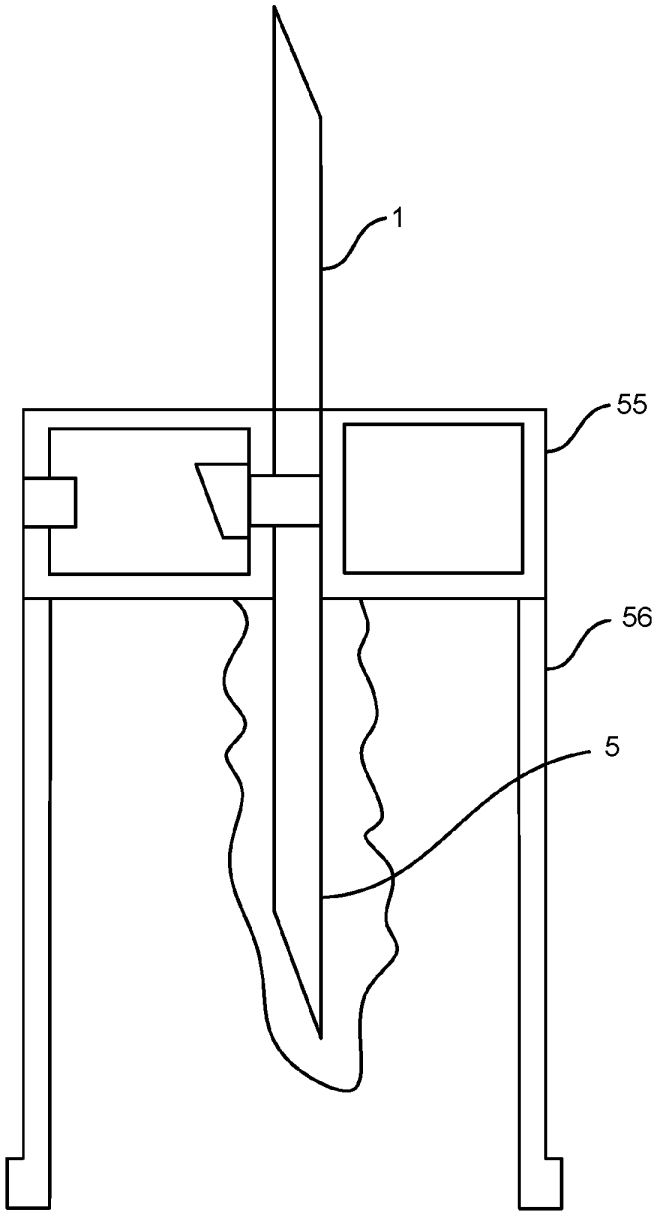


FIG. 2

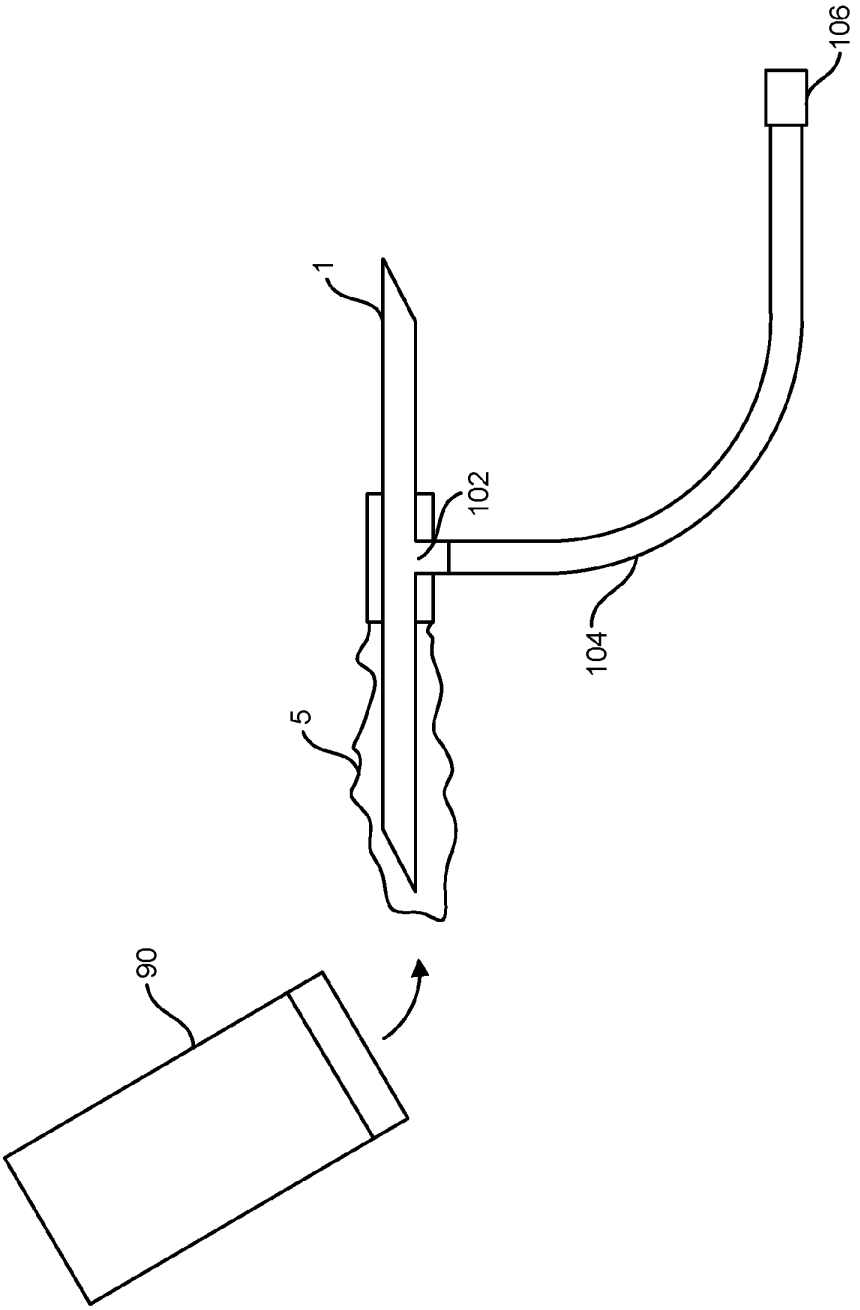


FIG. 3

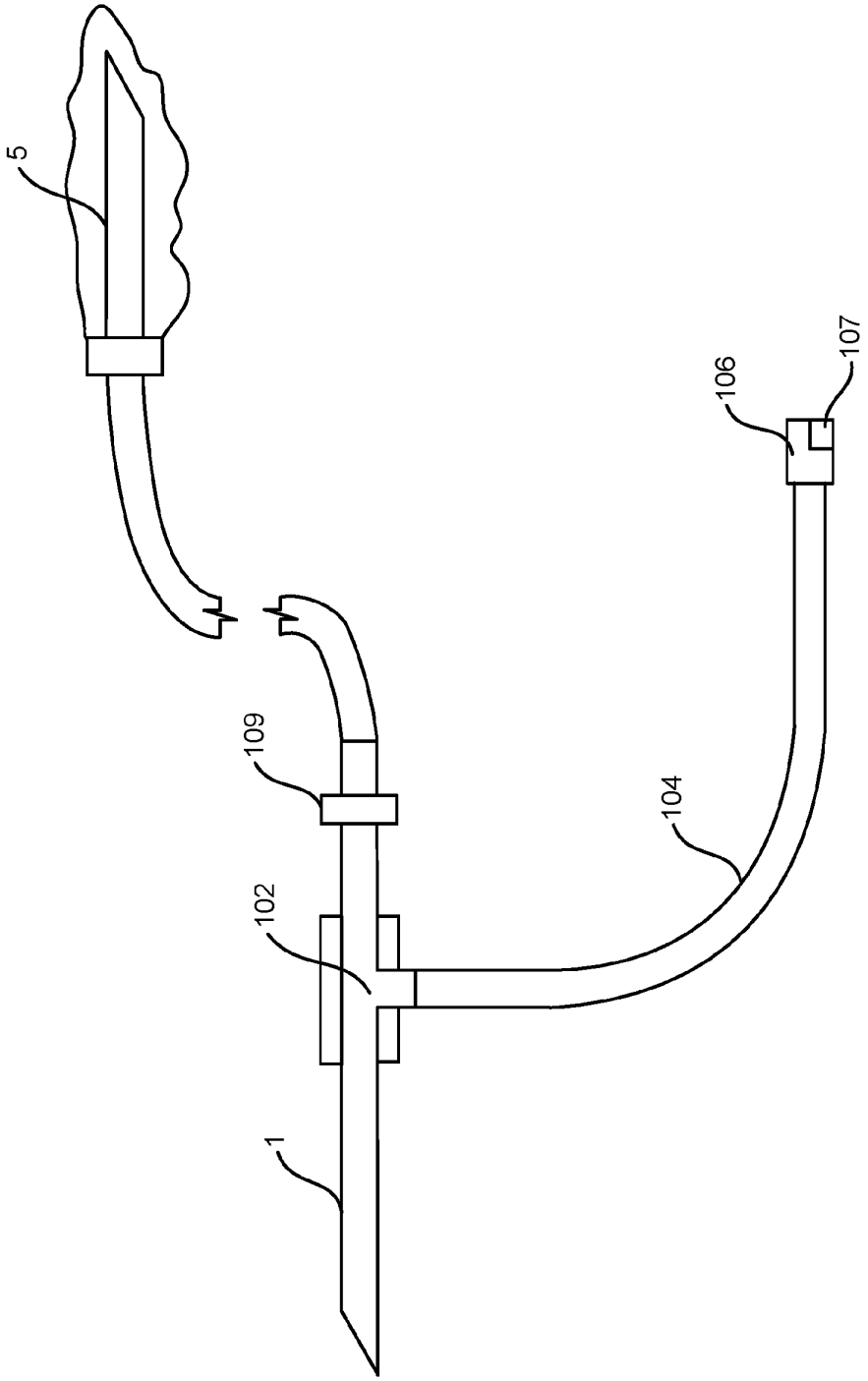


FIG. 4

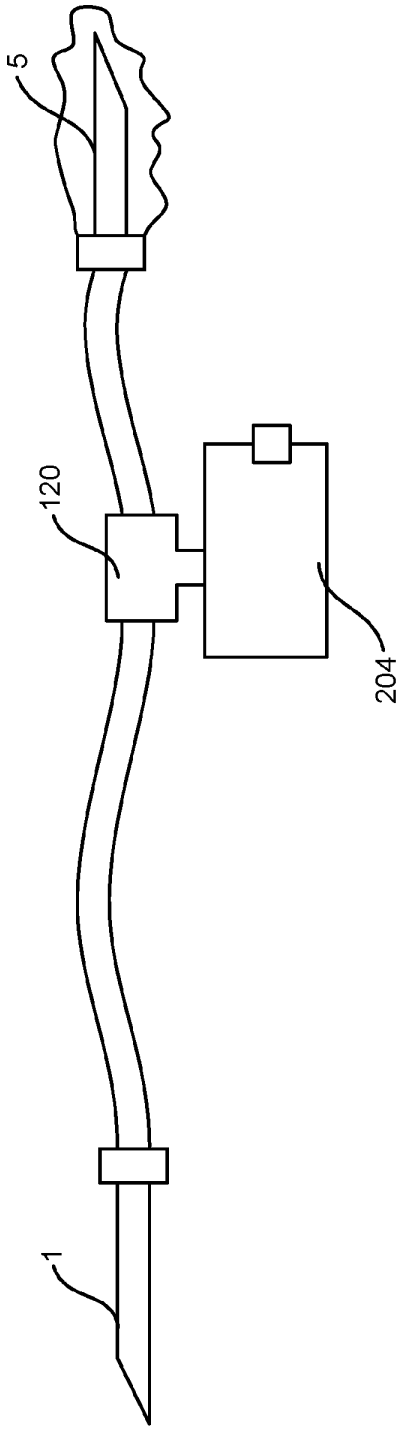


FIG. 5

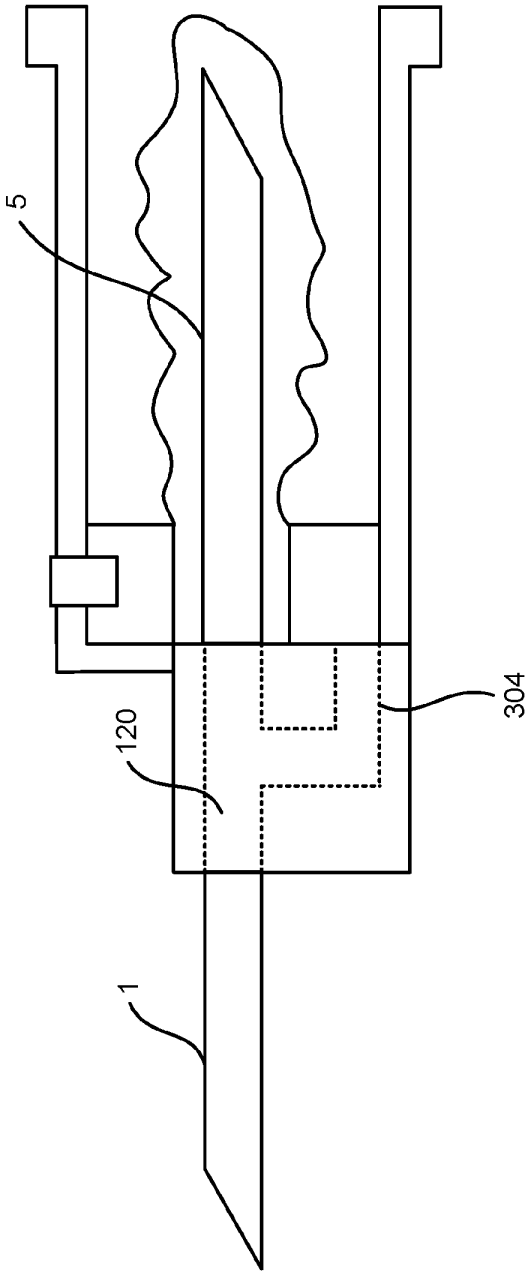


FIG. 6

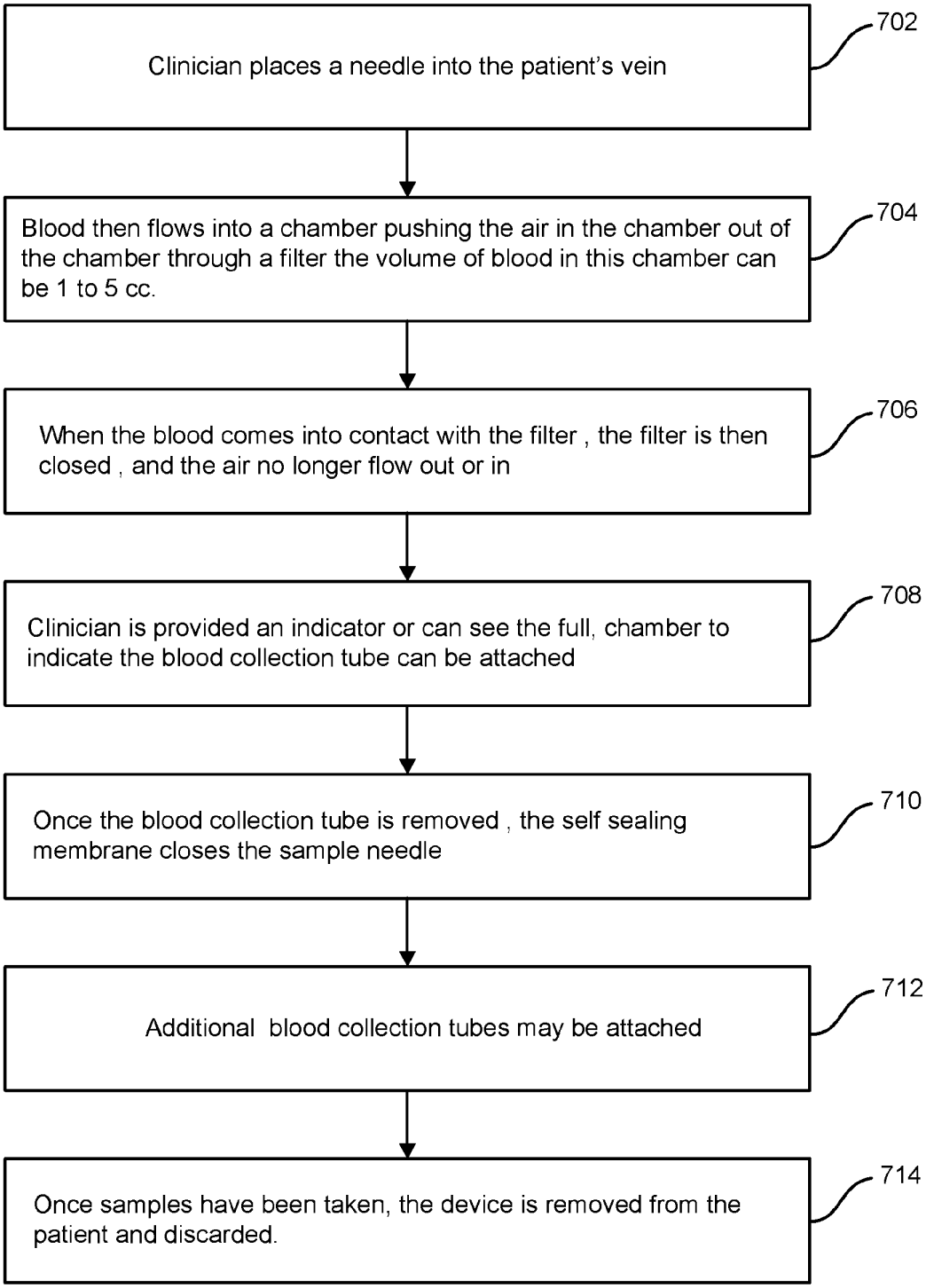

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter , the filter is then closed , and the air no longer flow out or in
706
Clinician is provided an indicator or can see the full, chamber to indicate the blood collection tube can be attached
708
Once the blood collection tube is removed , the self sealing membrane closes the sample needle
710
Additional blood collection tubes may be attached
712
Once samples have been taken, the device is removed from the patient and discarded.
714

FIG. 7

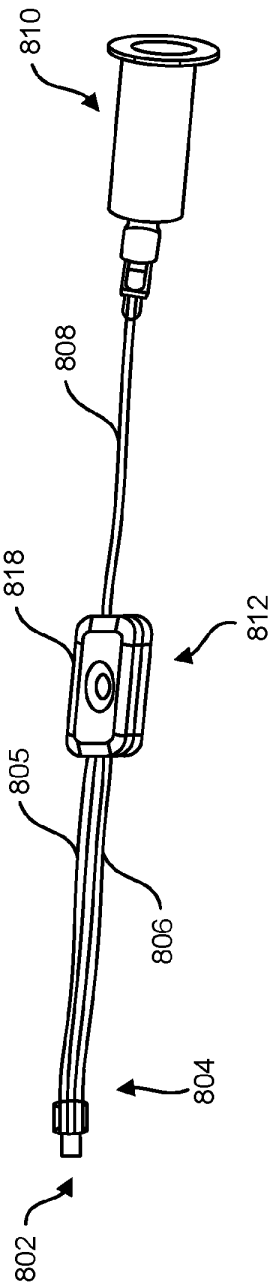


FIG. 8A

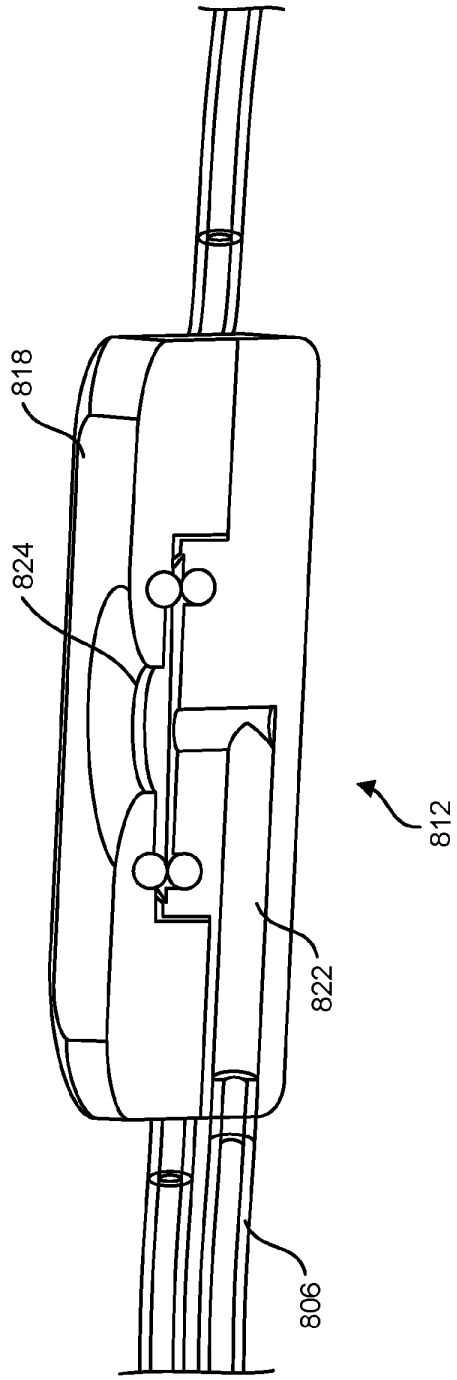


FIG. 8B

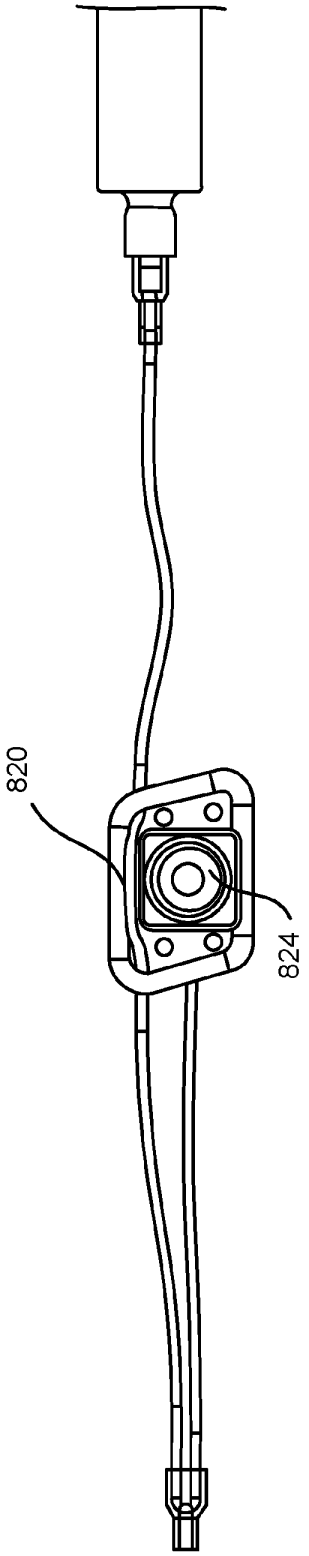


FIG. 8C

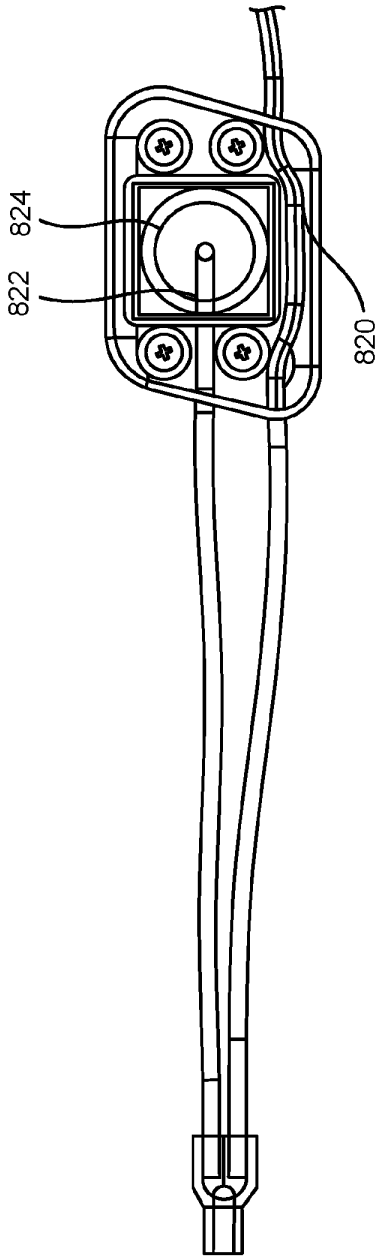


FIG. 8D

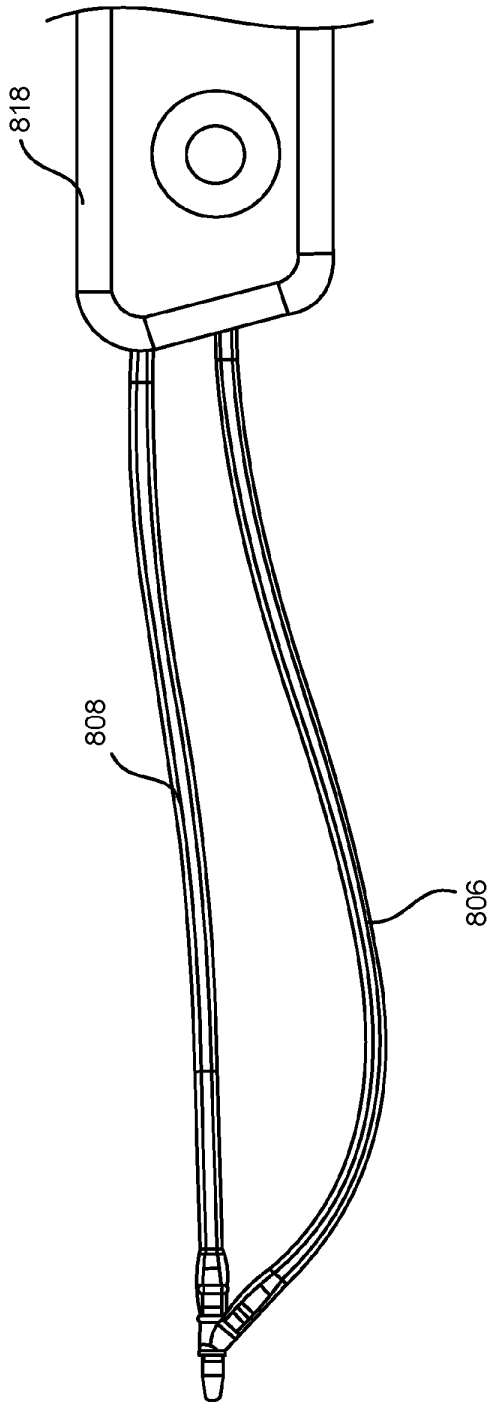


FIG. 8E

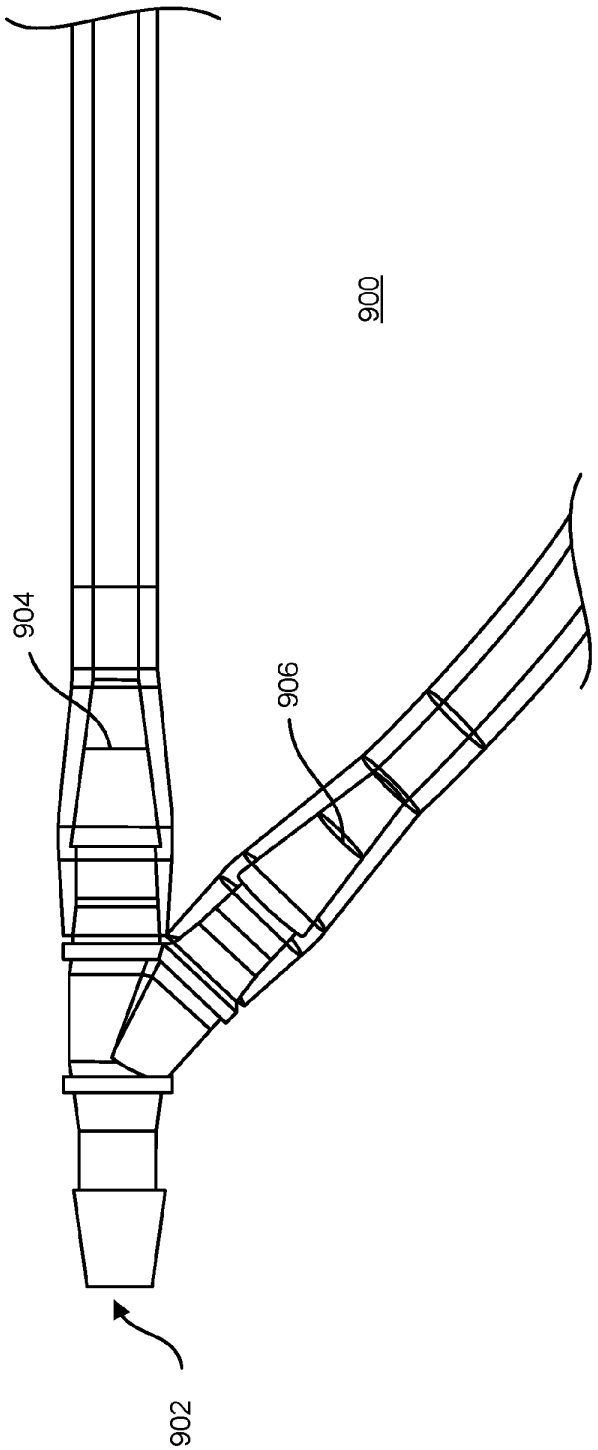


FIG. 9

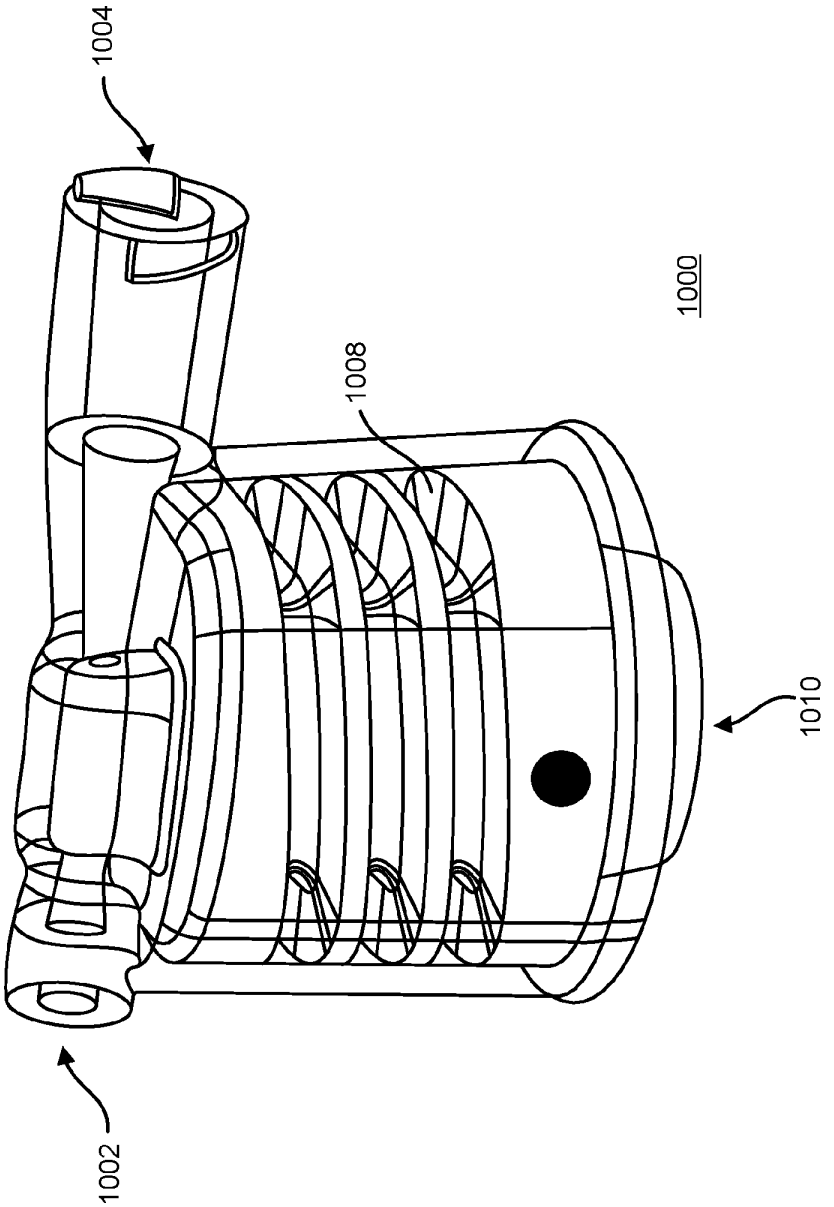


FIG. 10A

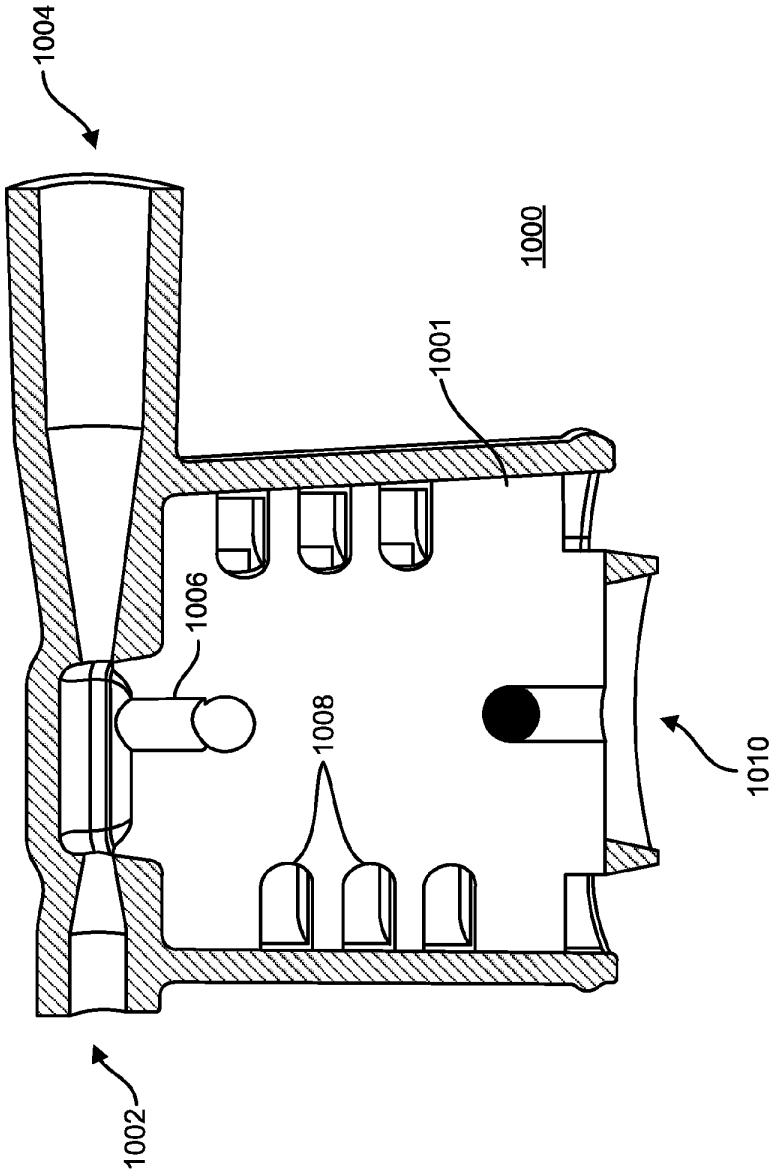


FIG. 10B

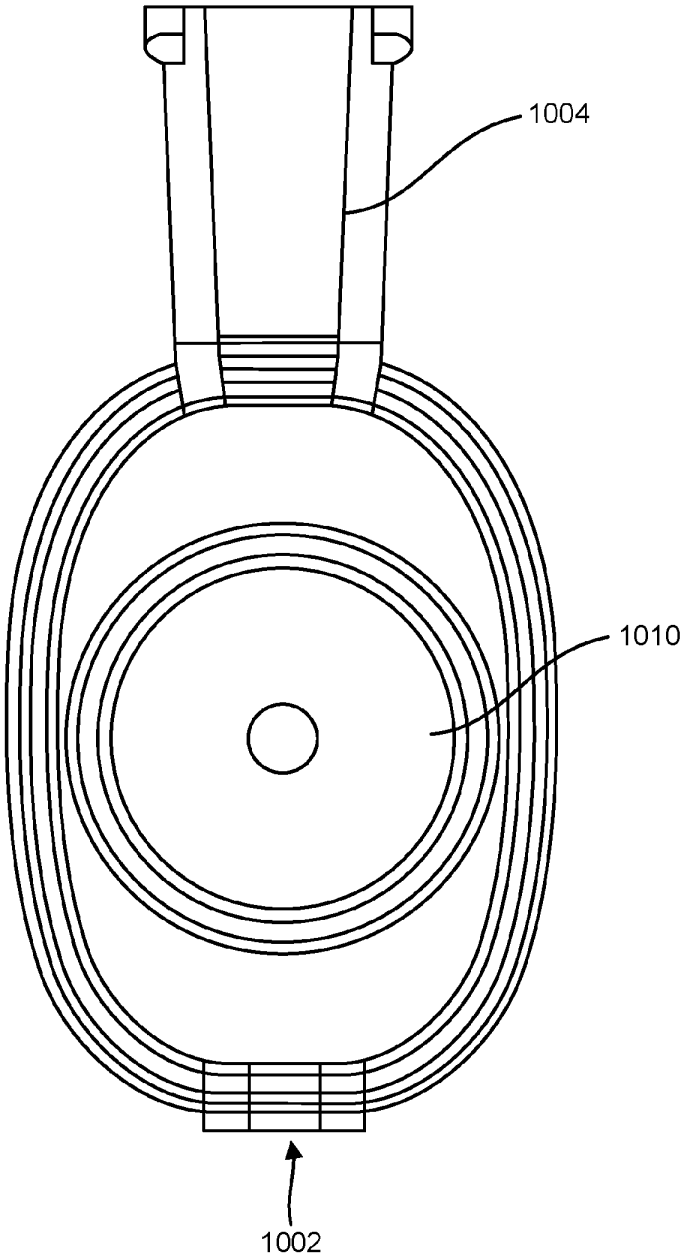


FIG. 10C

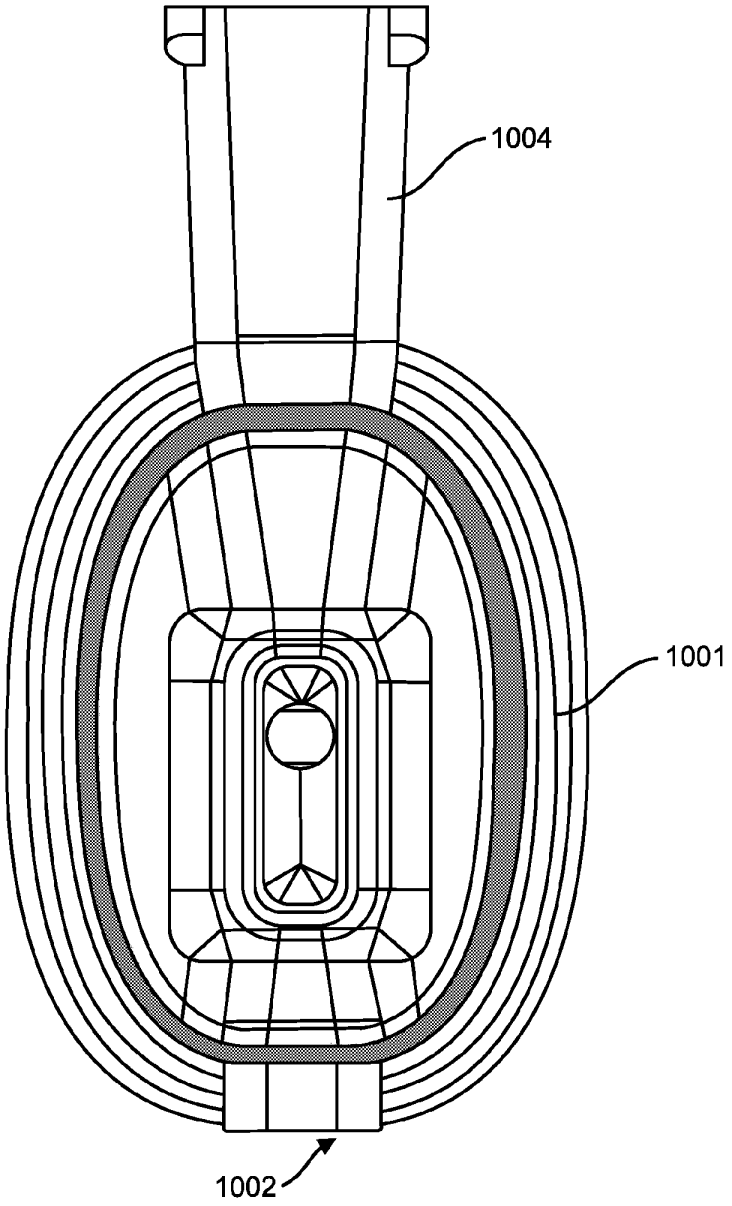


FIG. 10D

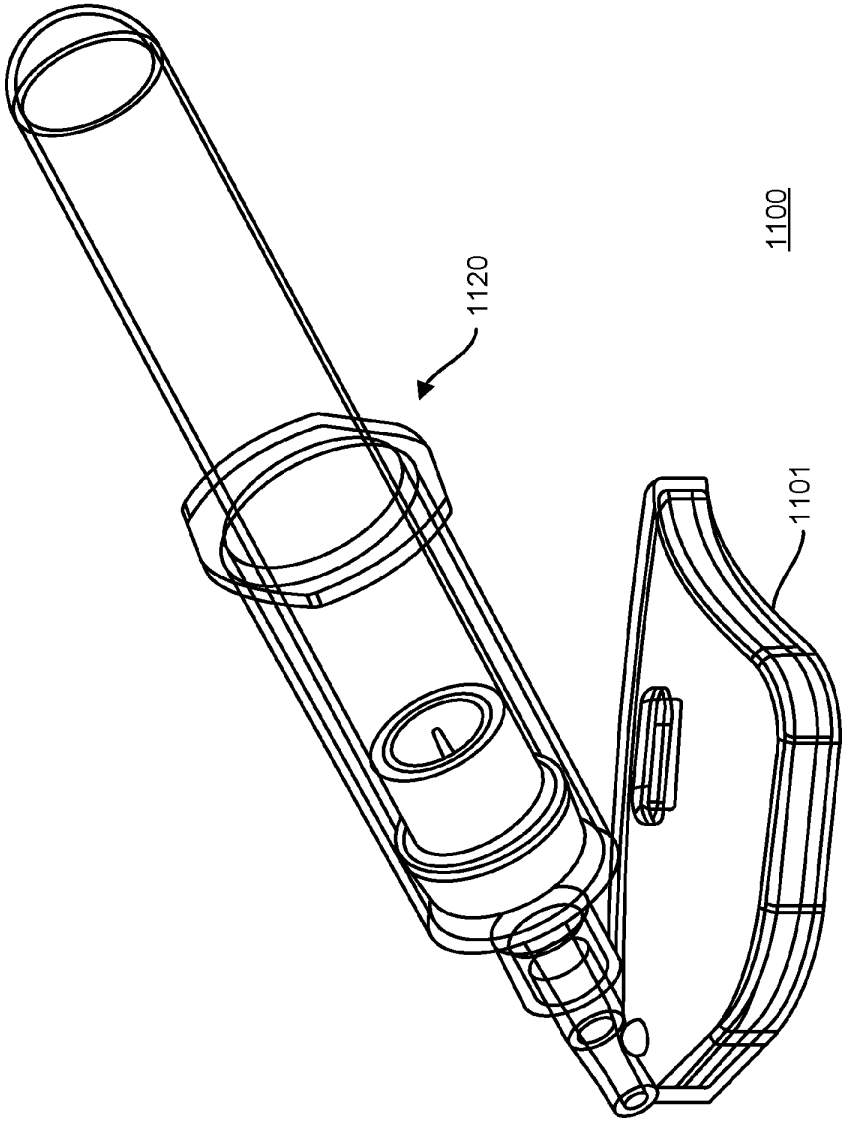


FIG. 11A

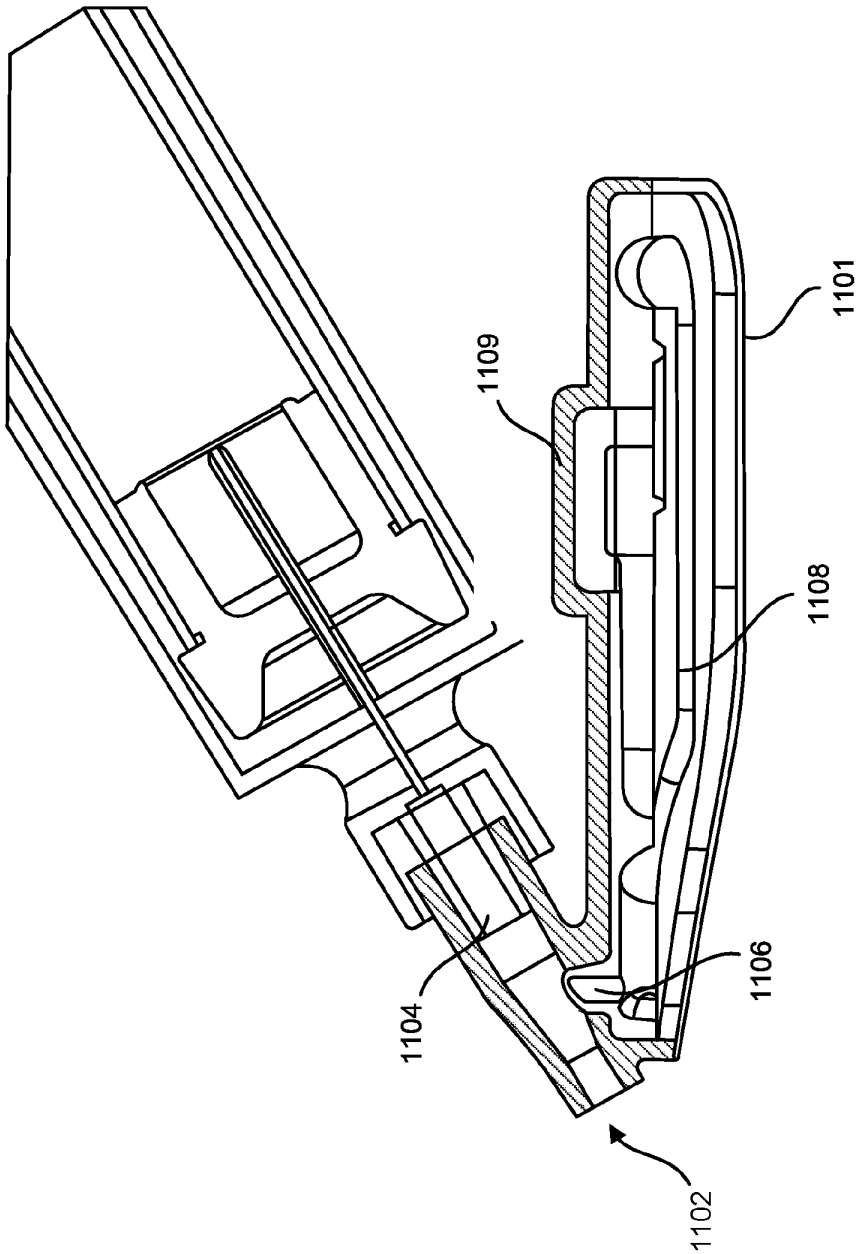


FIG. 11B

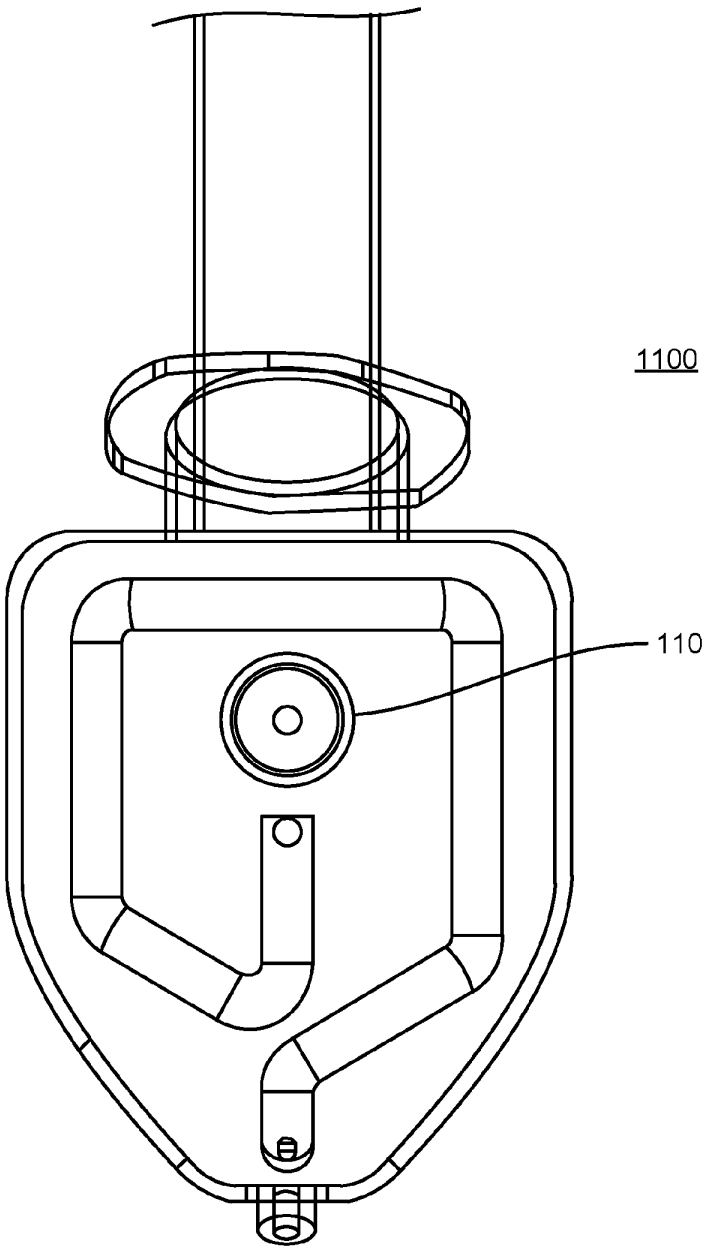


FIG. 11C

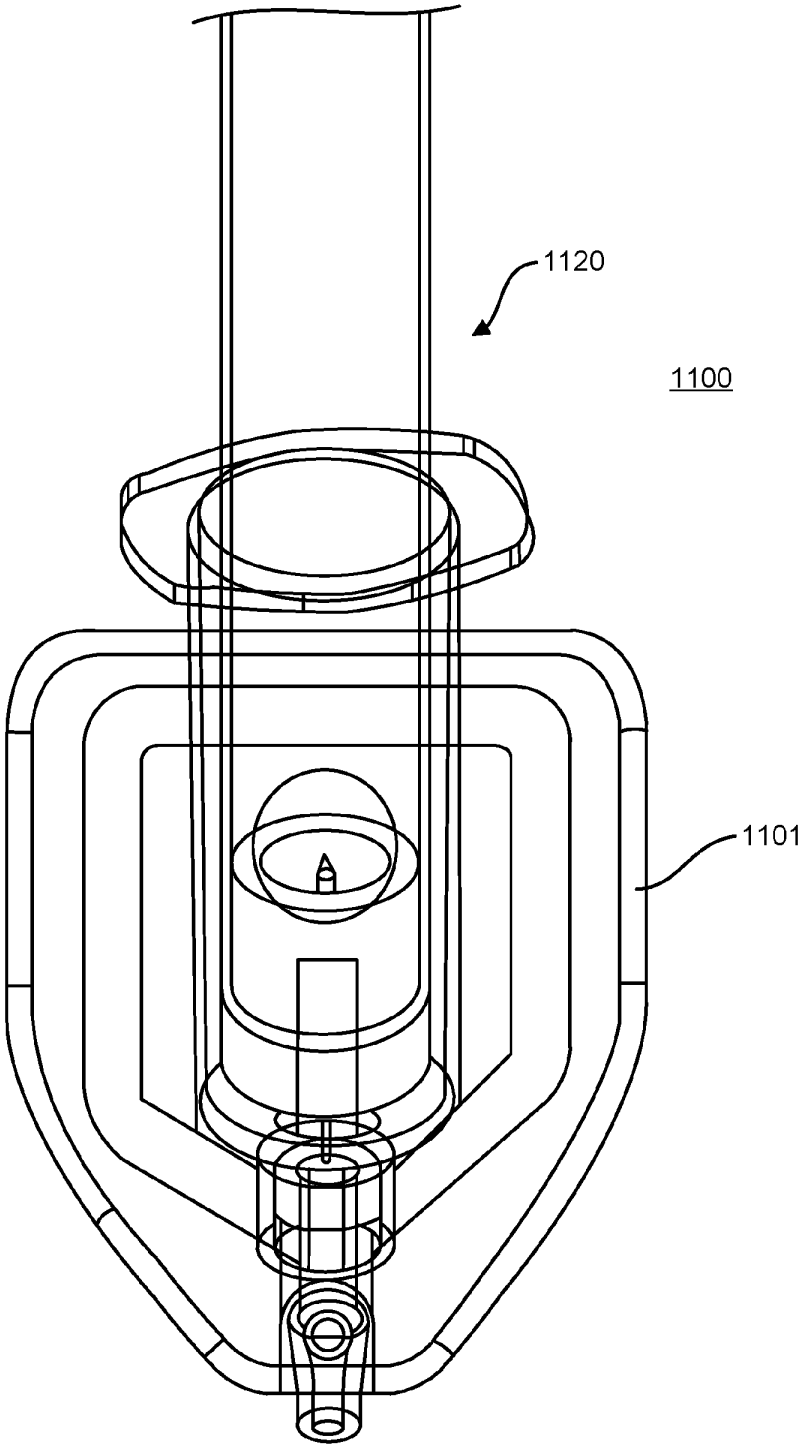


FIG. 11D

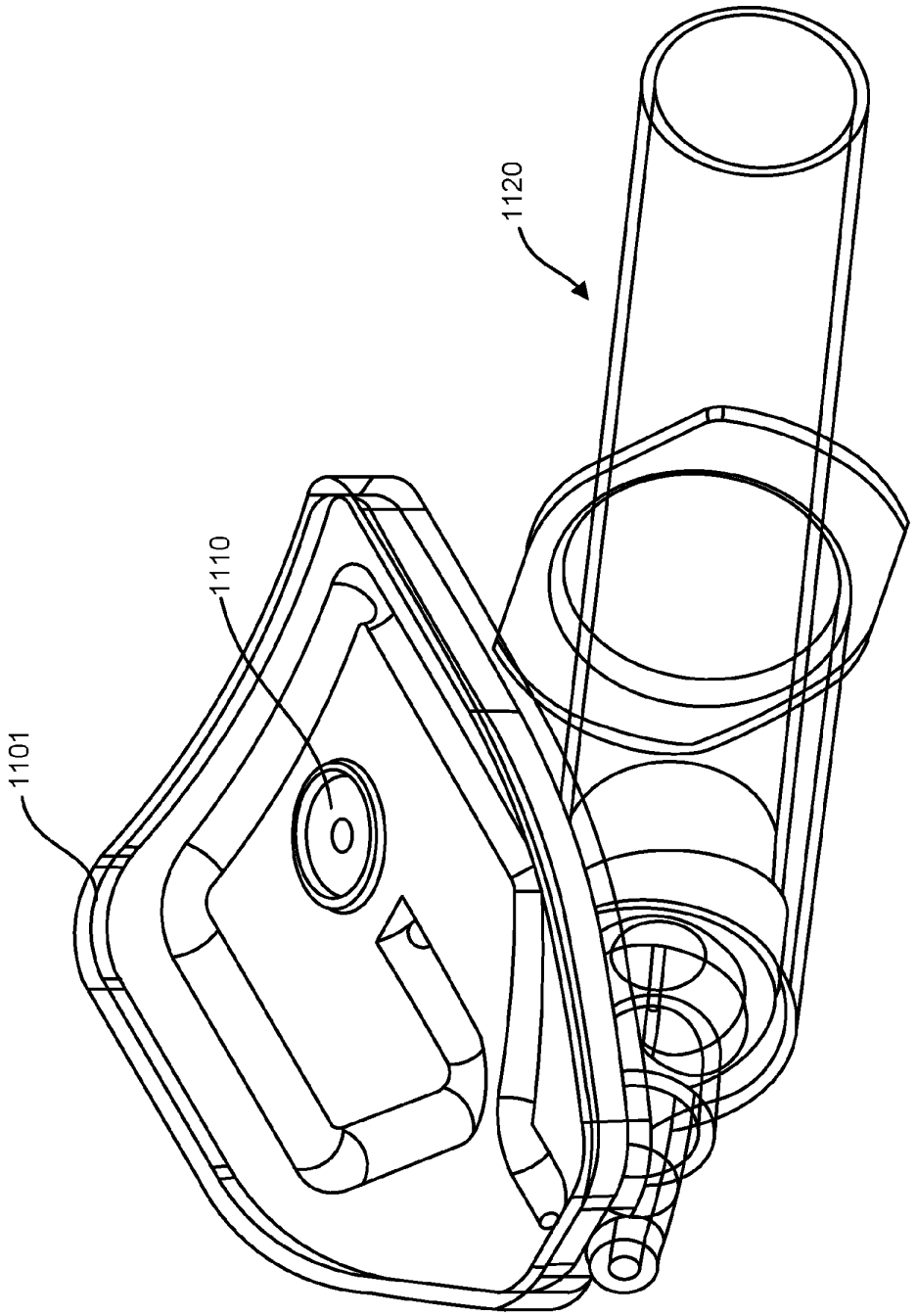


FIG. 11E

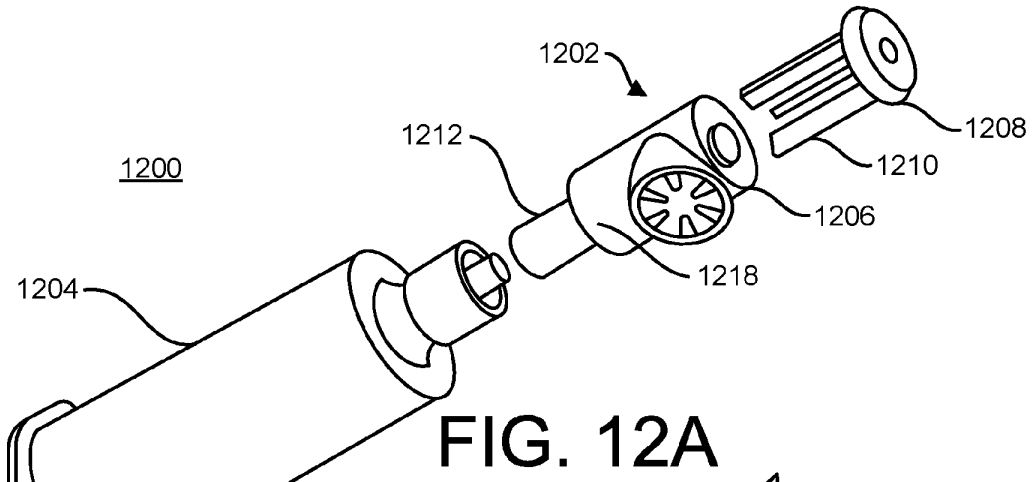


FIG. 12A

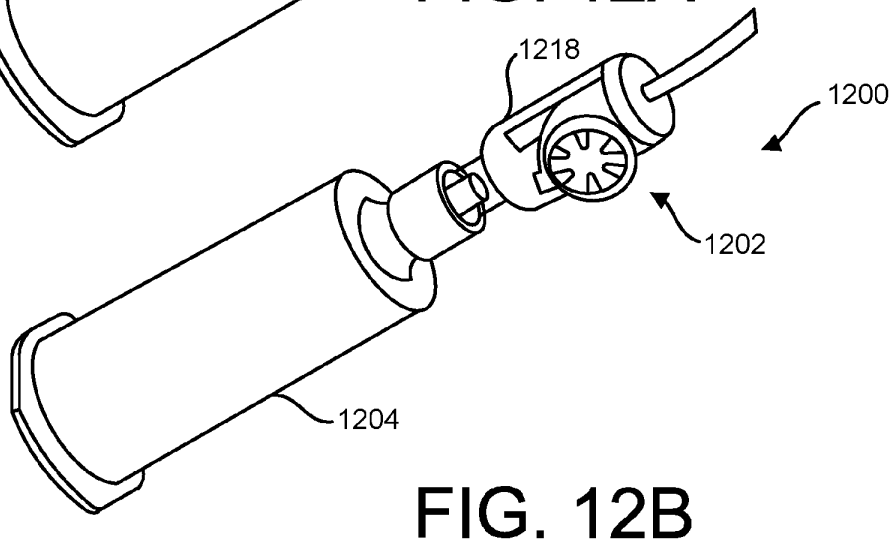


FIG. 12B

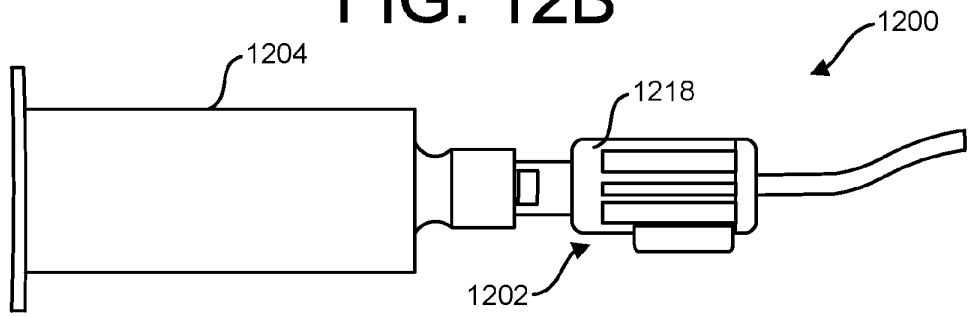


FIG. 12C

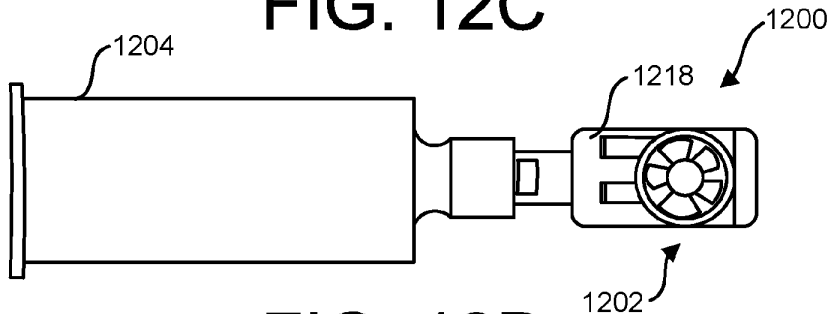


FIG. 12D

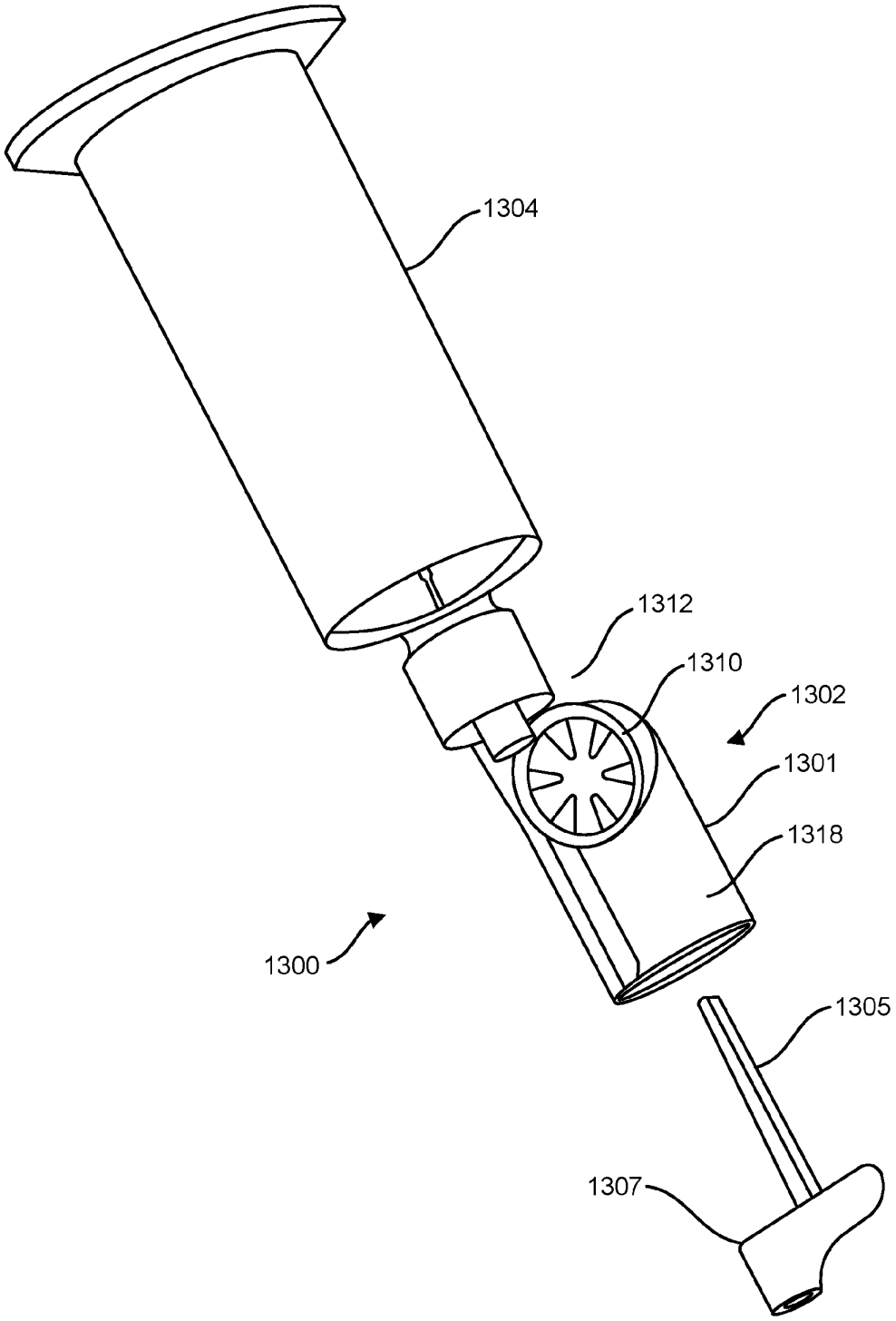


FIG. 13A

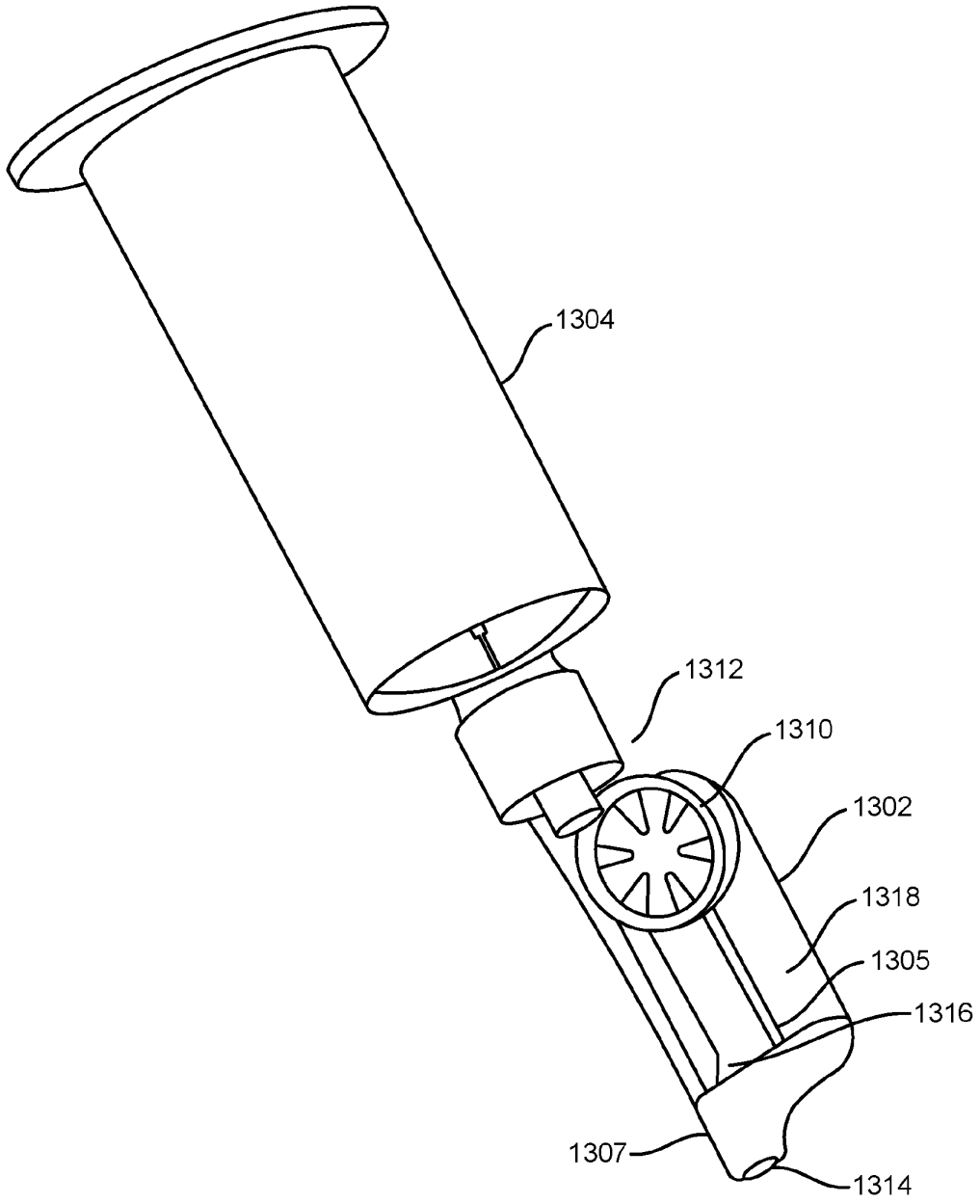


FIG. 13B

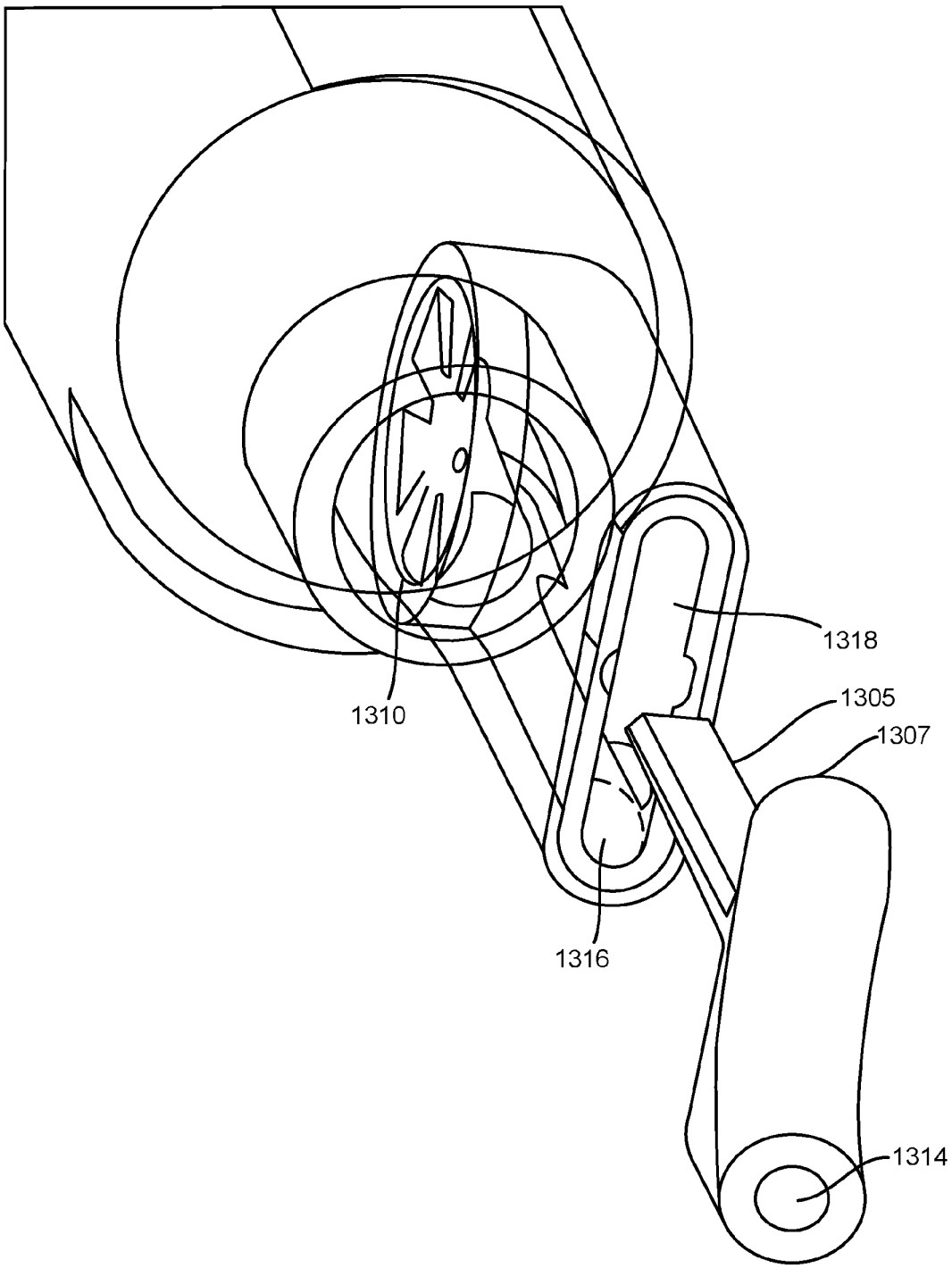


FIG. 13C

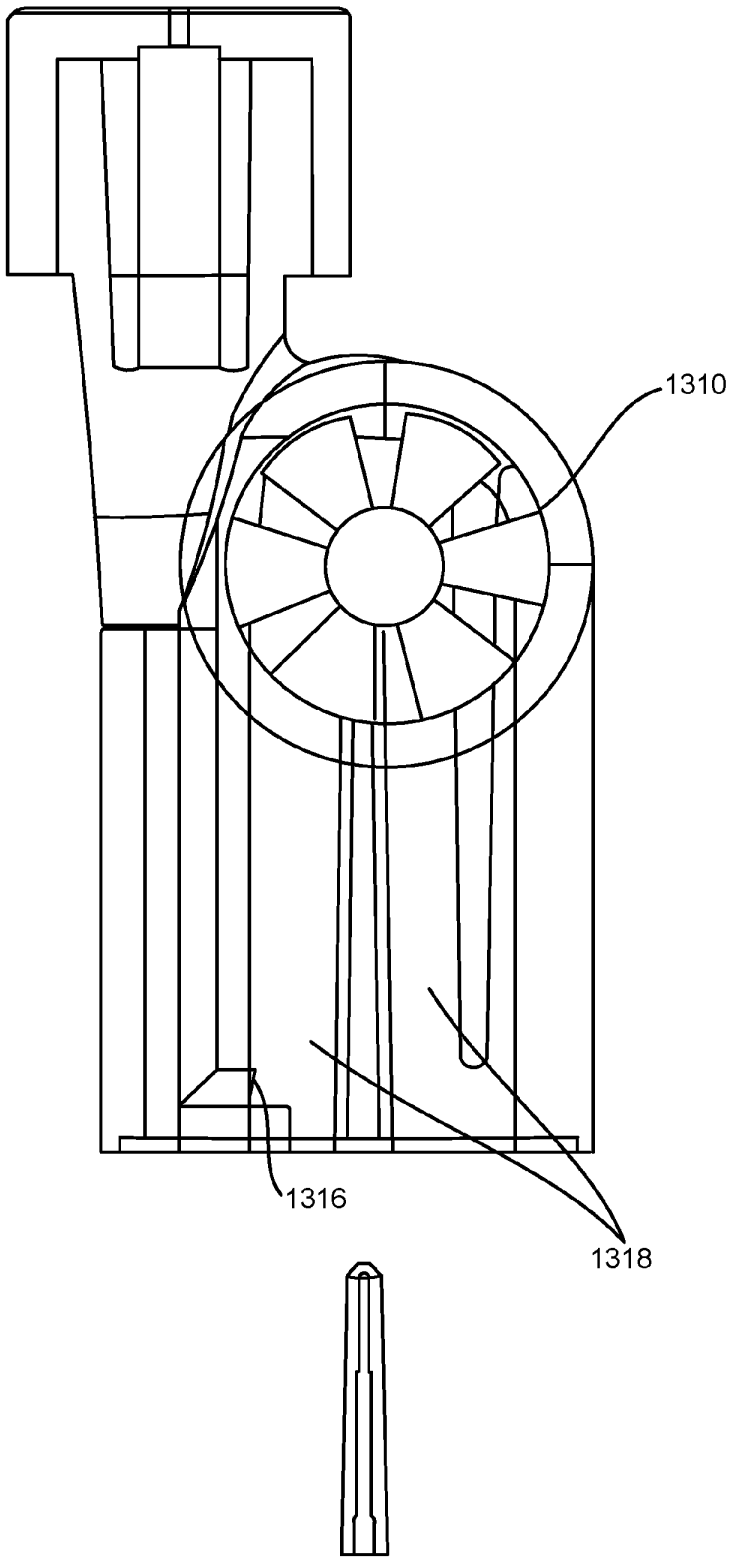


FIG. 13D

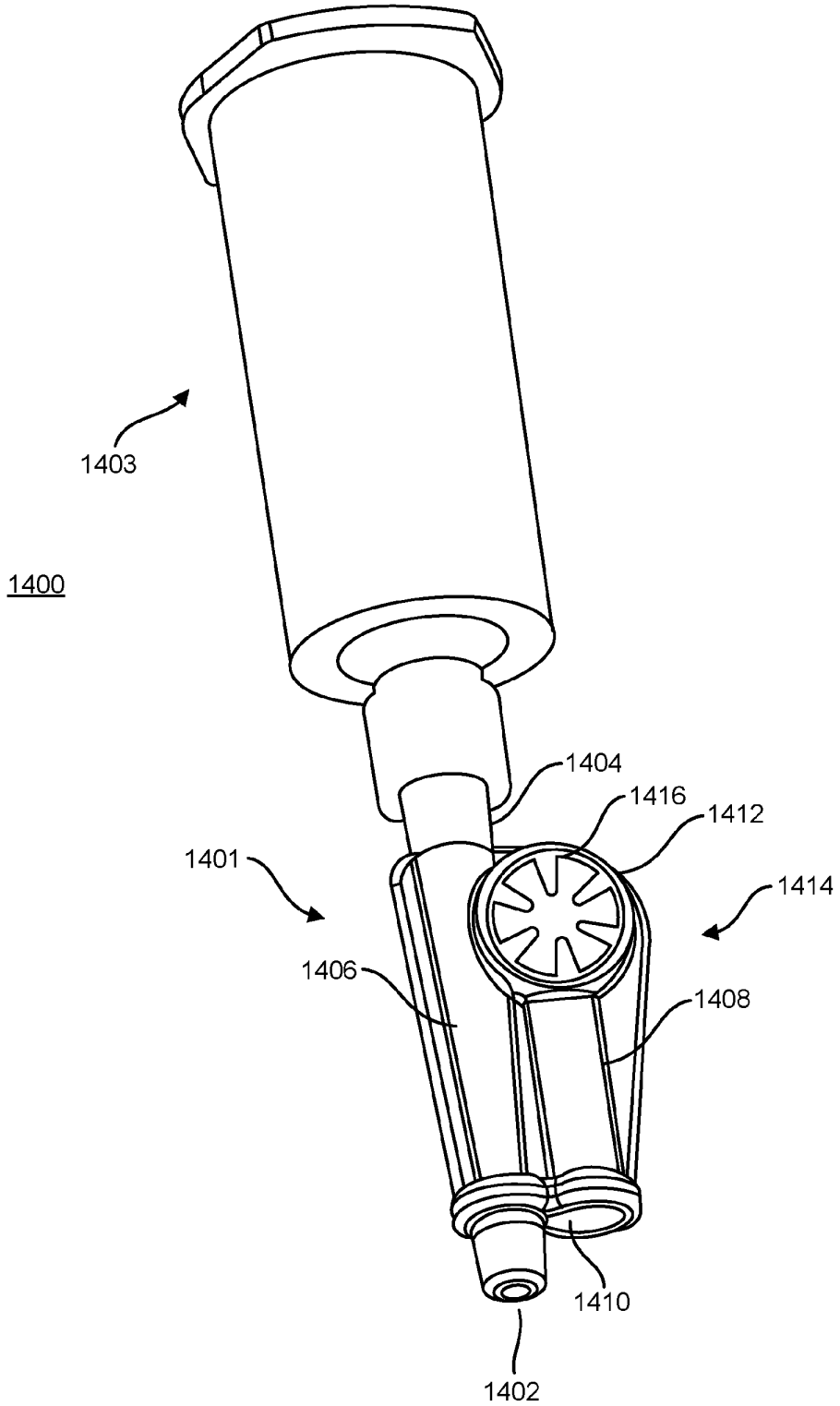


FIG. 14A

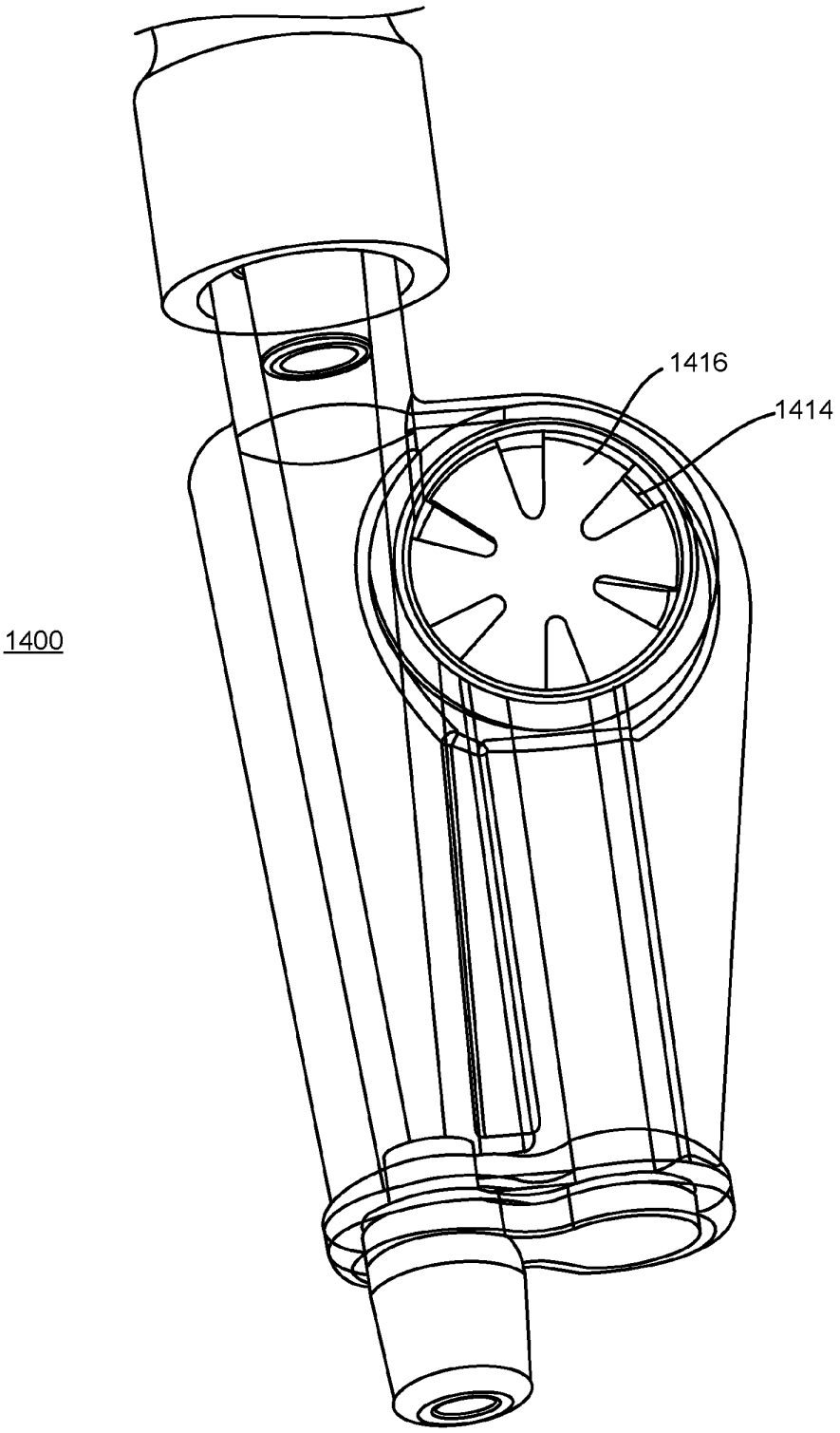


FIG. 14B

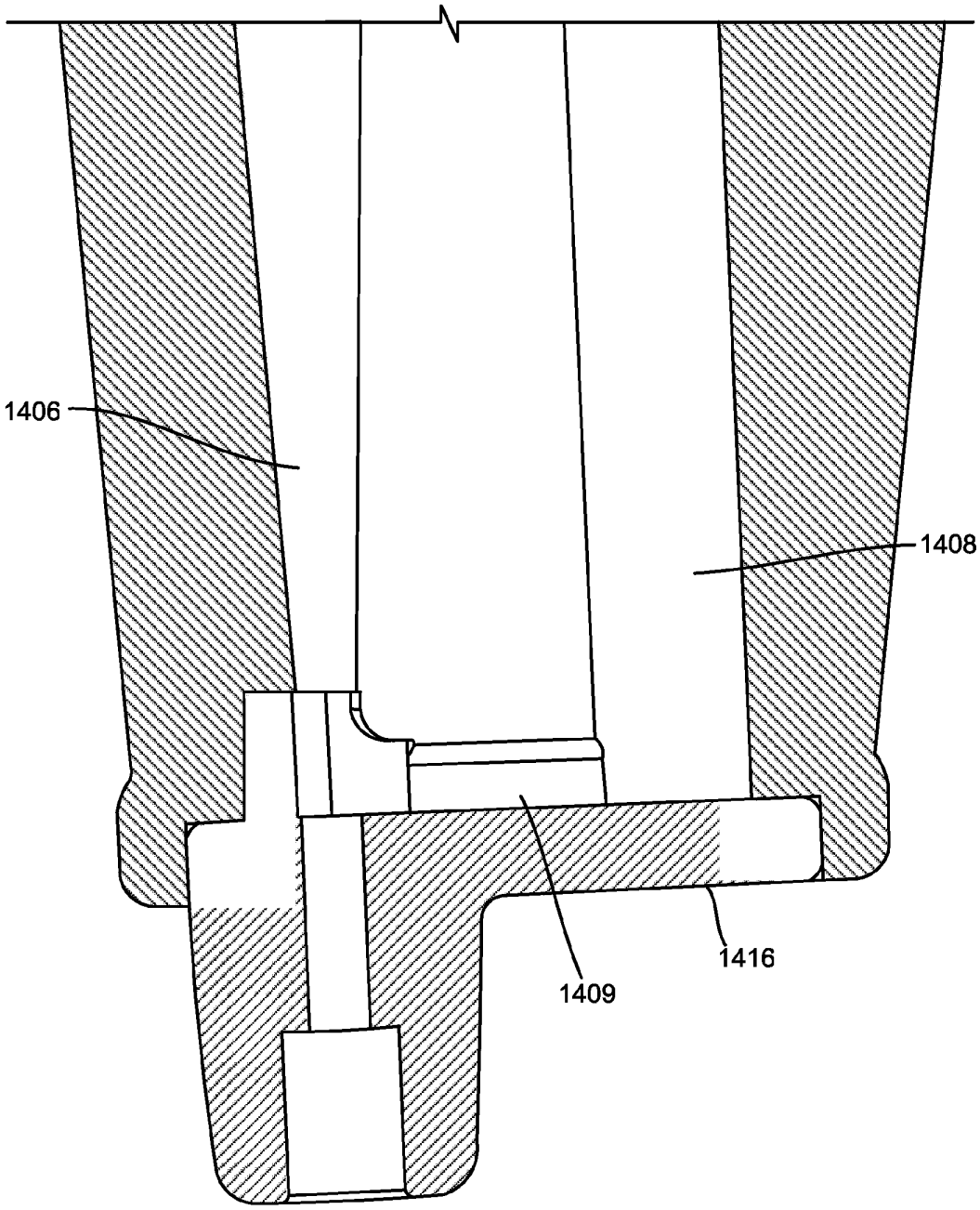


FIG. 14C

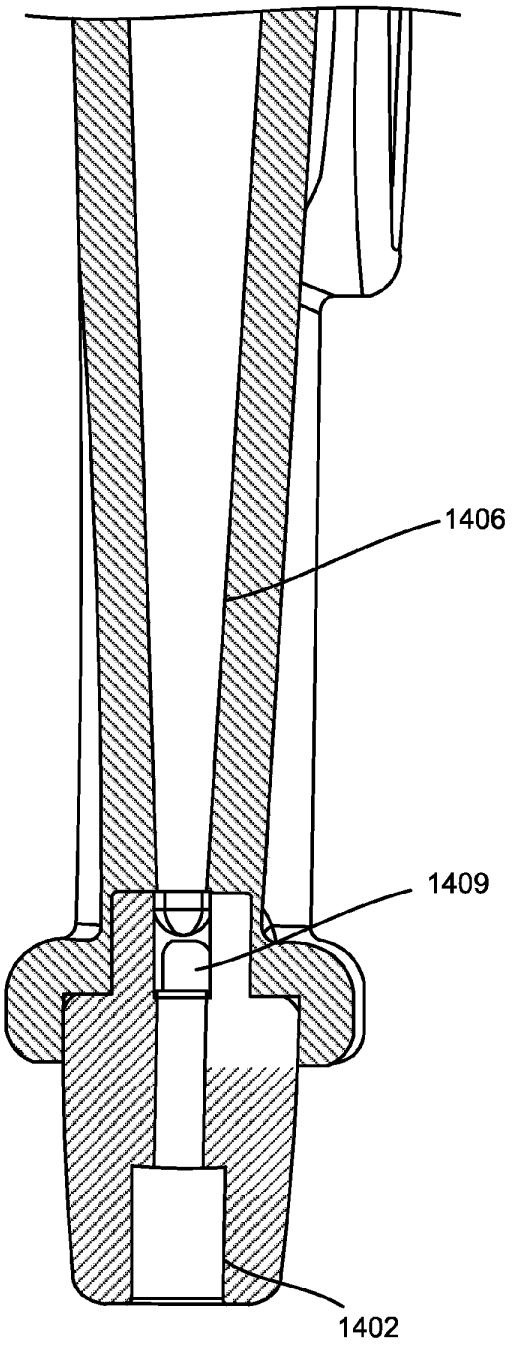


FIG. 14D

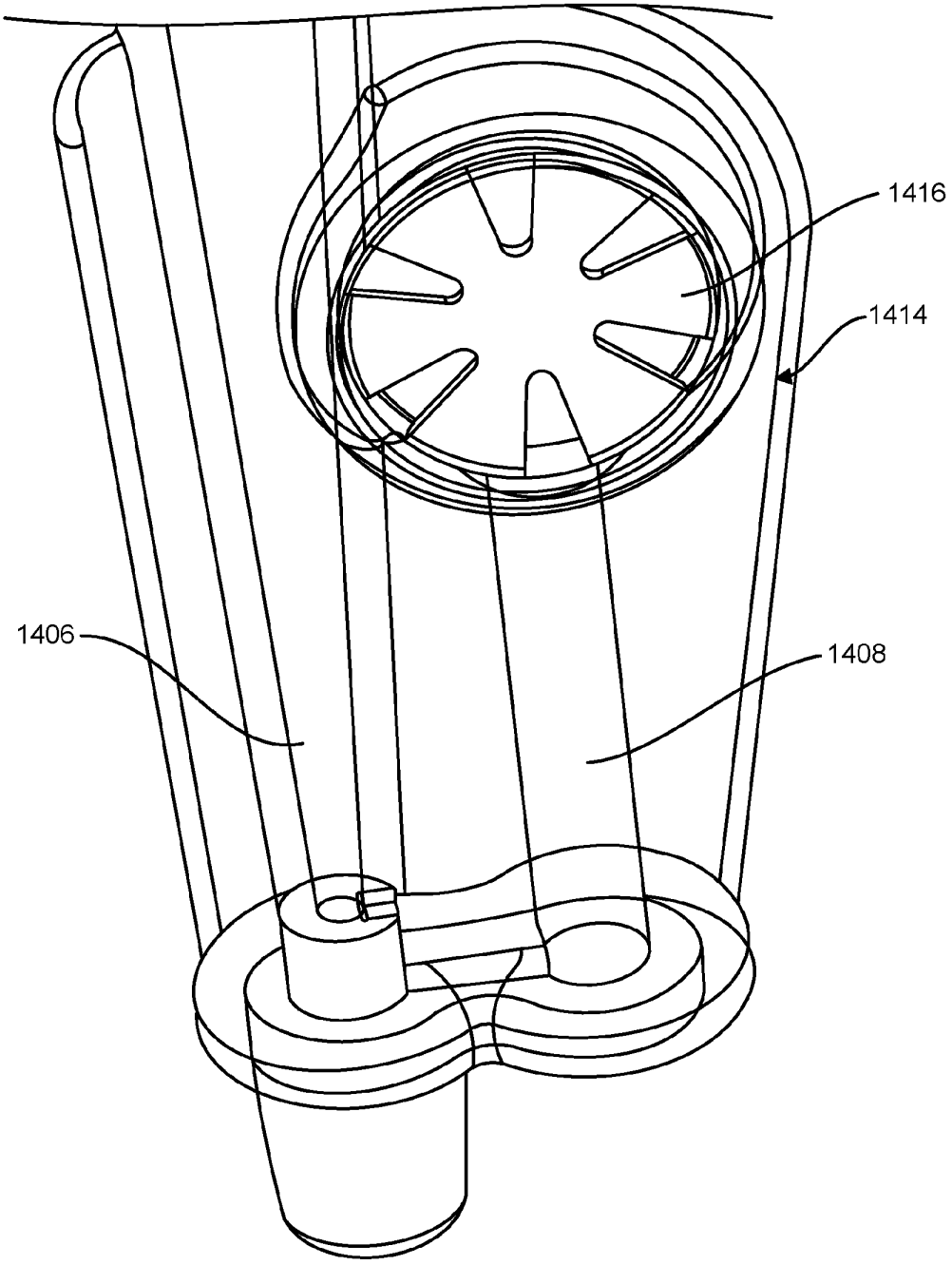


FIG. 14E

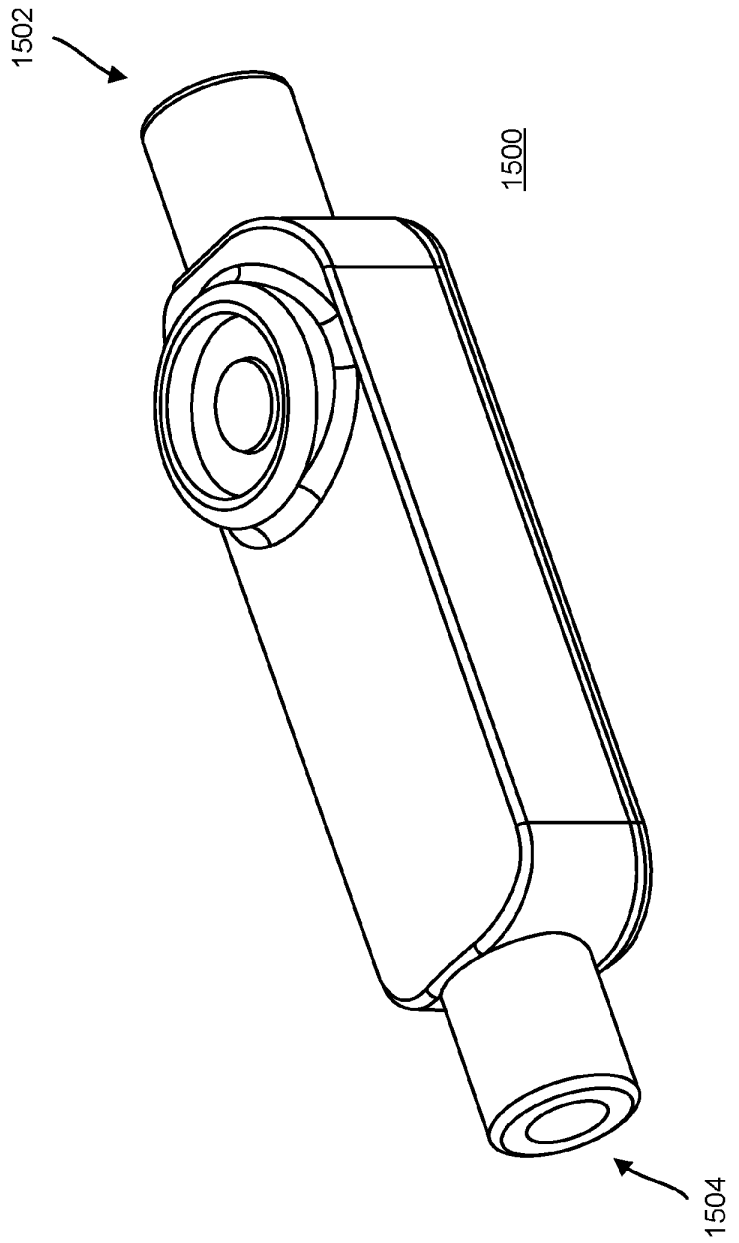


FIG. 15A

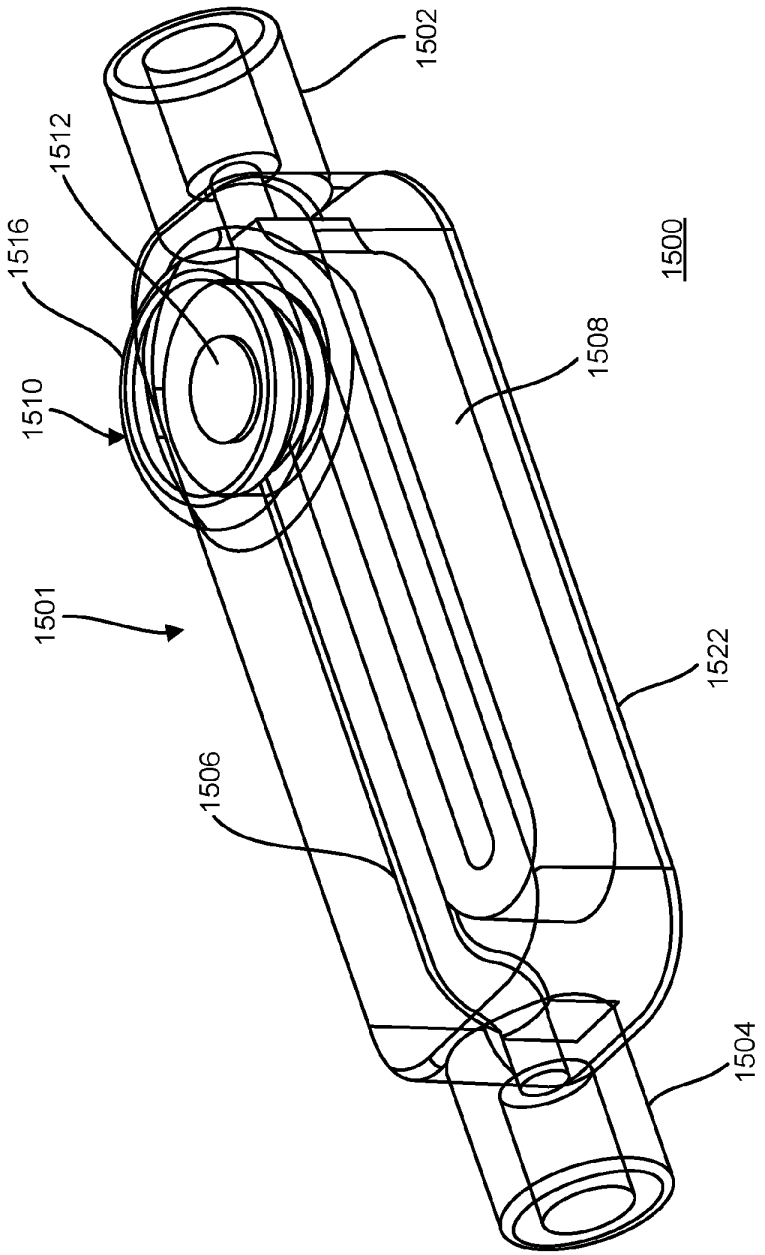


FIG. 15B

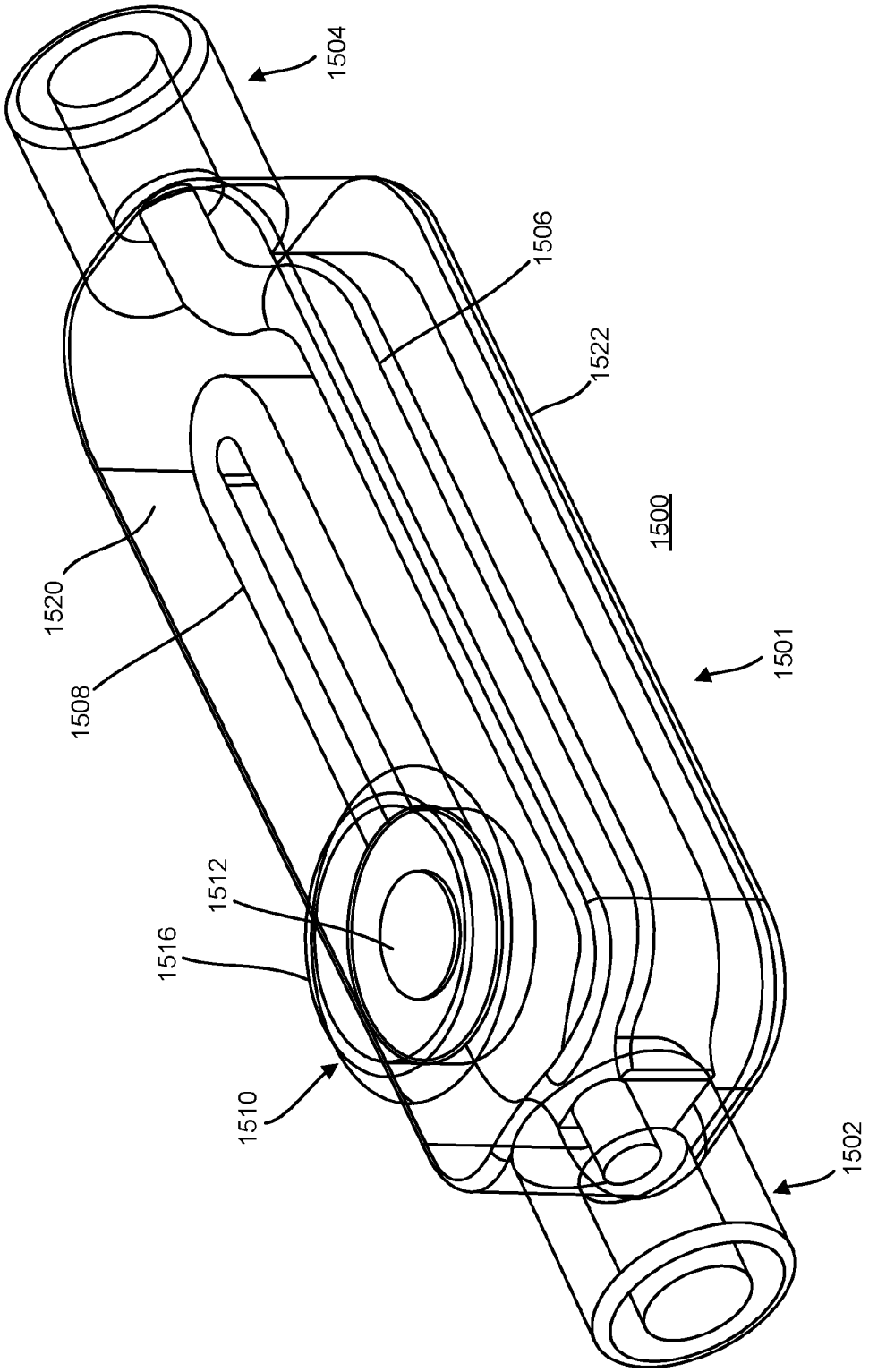


FIG. 15C

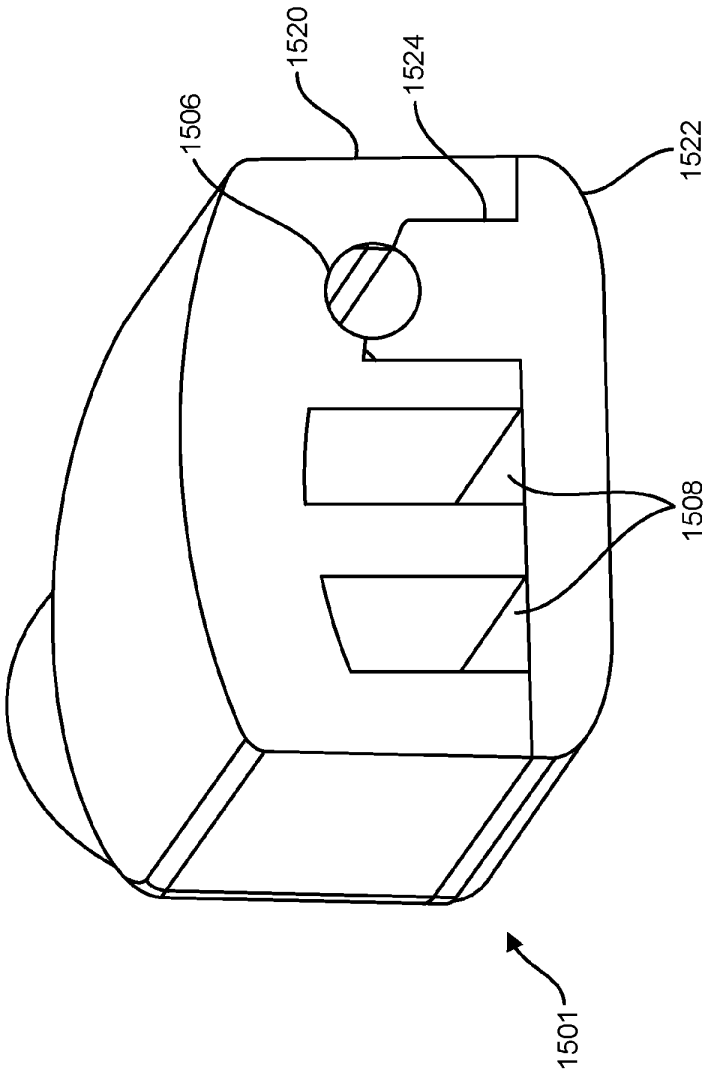


FIG. 15D

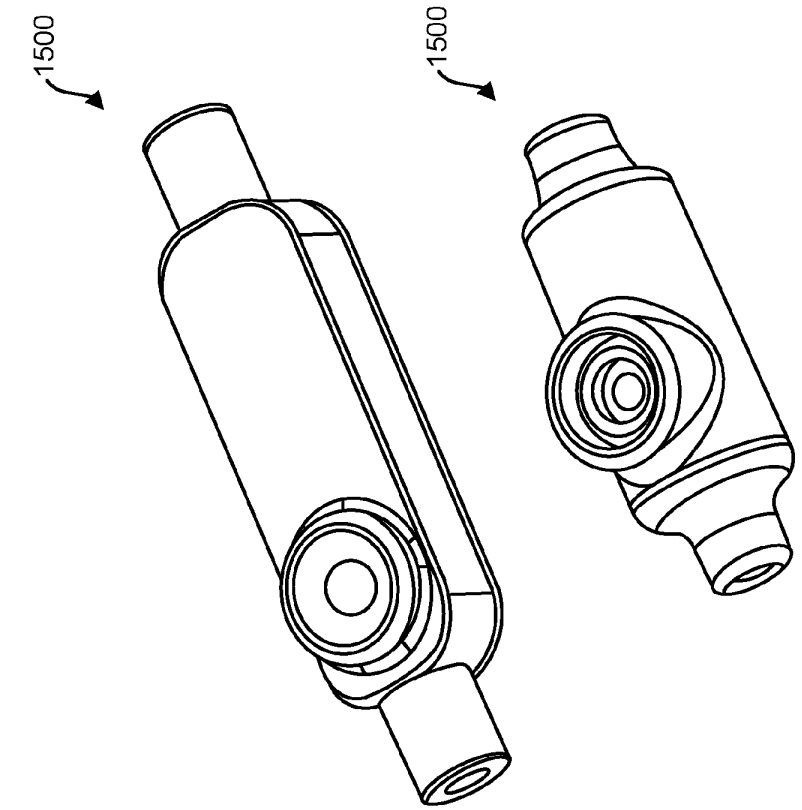


FIG. 15F

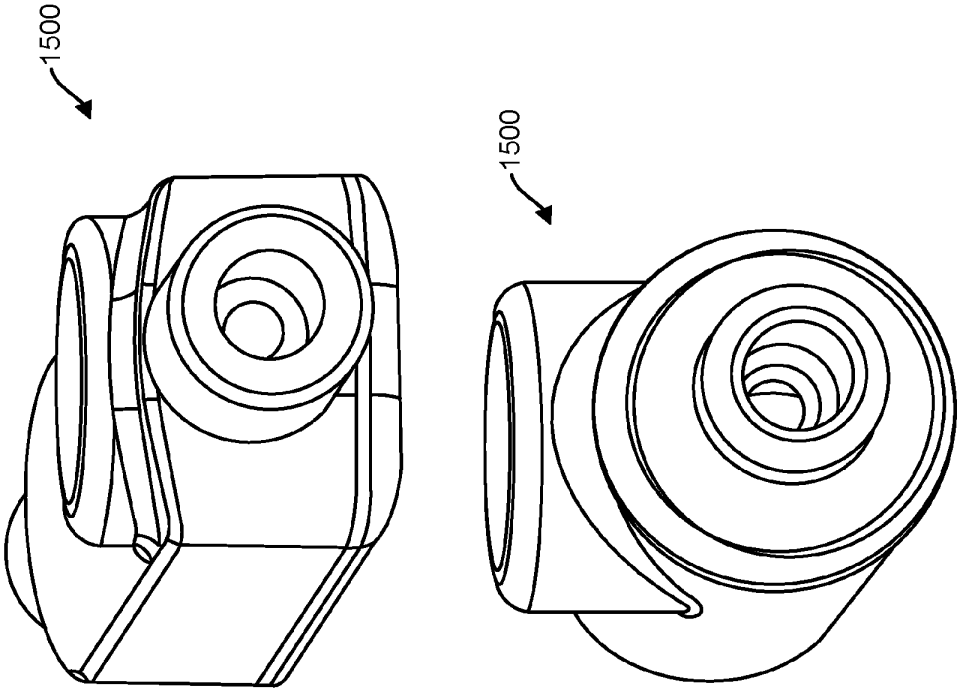


FIG. 15E

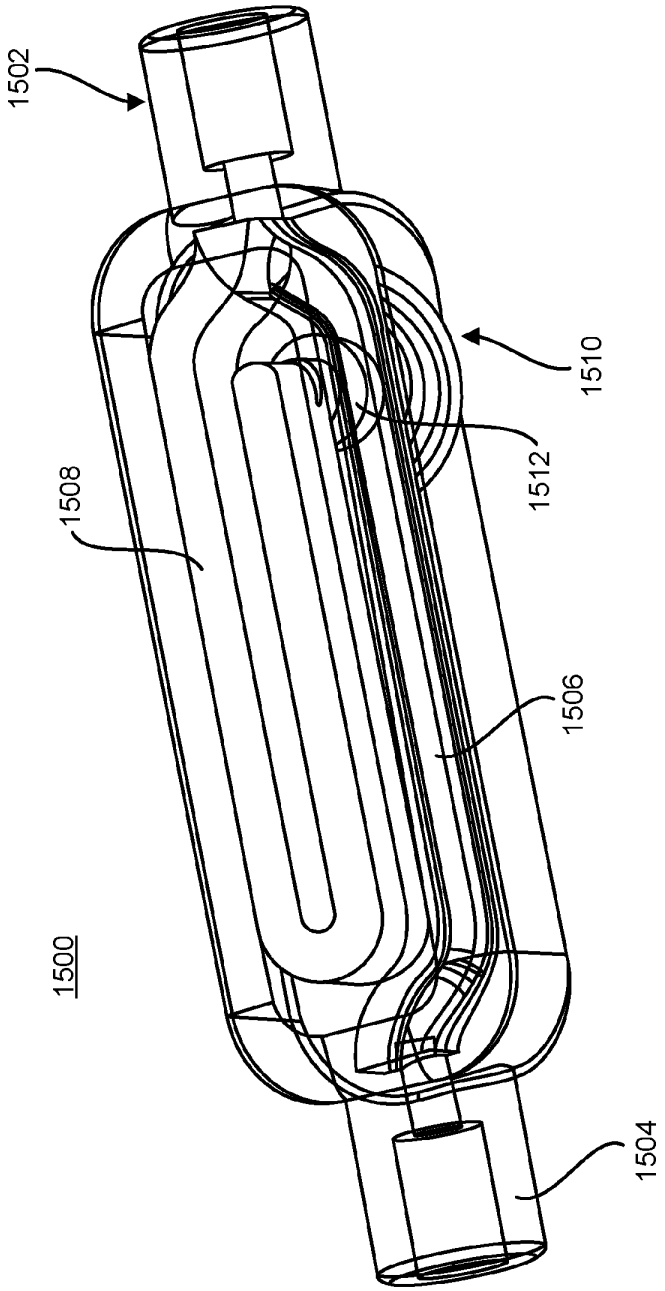


FIG. 15G

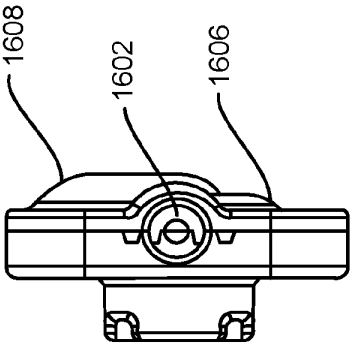


FIG. 16C

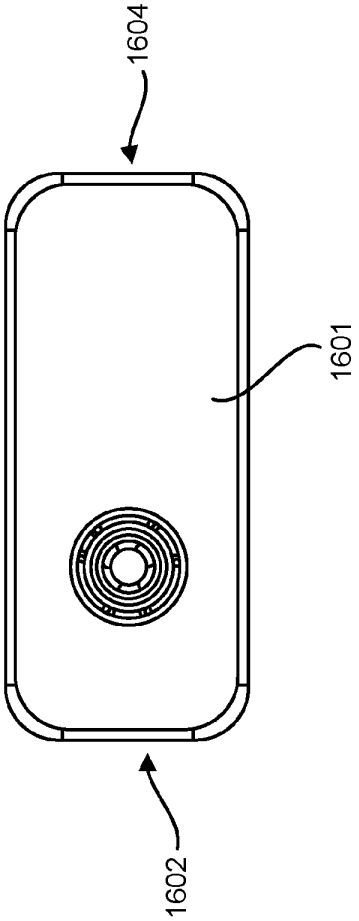


FIG. 16A

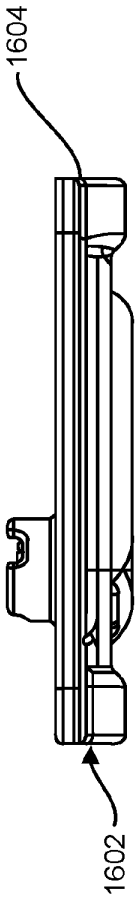


FIG. 16B

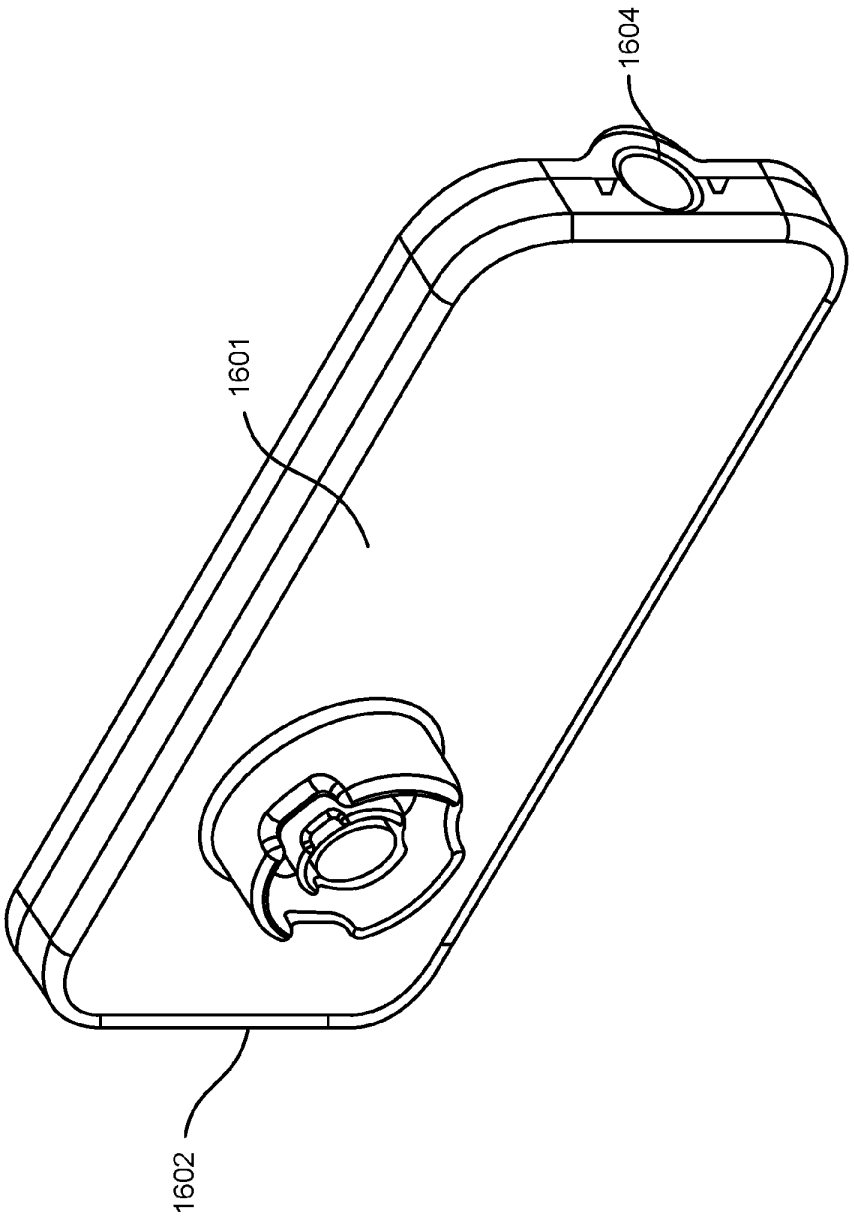


FIG. 16D

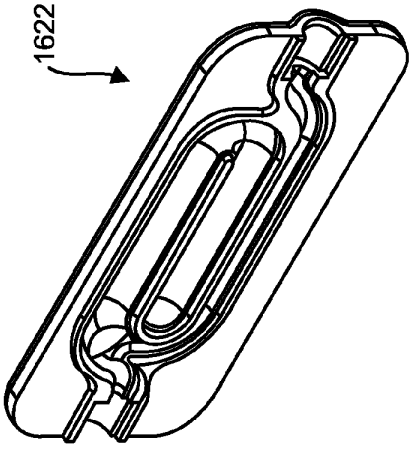


FIG. 17B



FIG. 17E

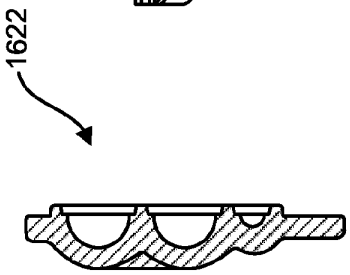


FIG. 17D

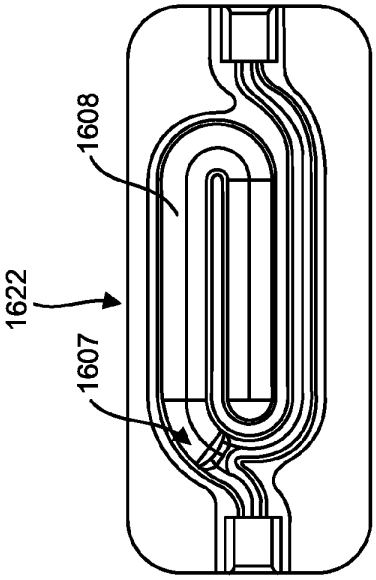


FIG. 17A

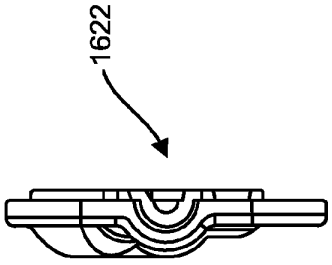


FIG. 17C

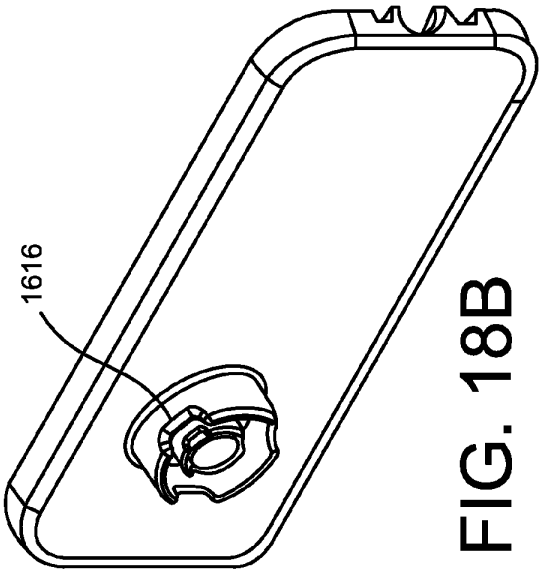


FIG. 18B

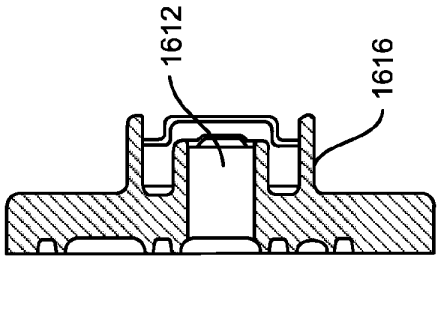


FIG. 18F

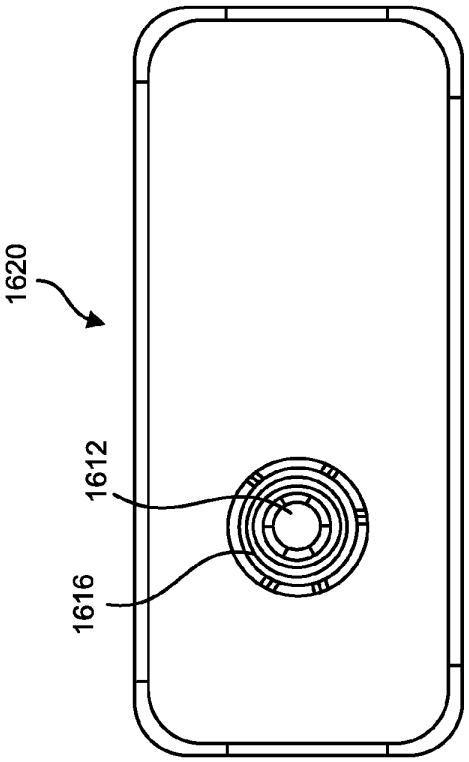


FIG. 18A

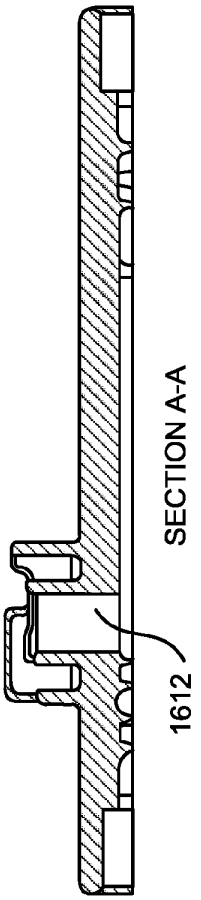


FIG. 18D

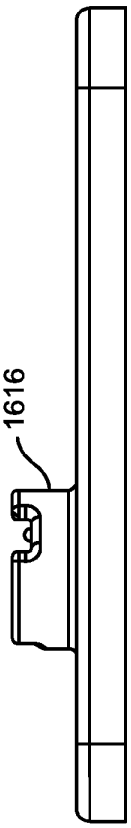


FIG. 18E

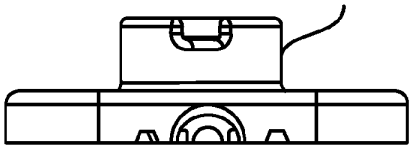


FIG. 18C

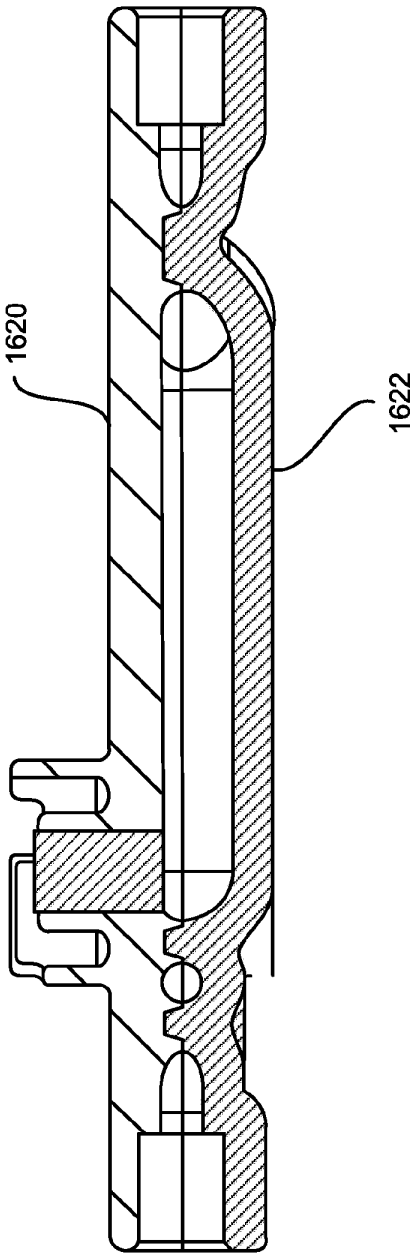


FIG. 19A

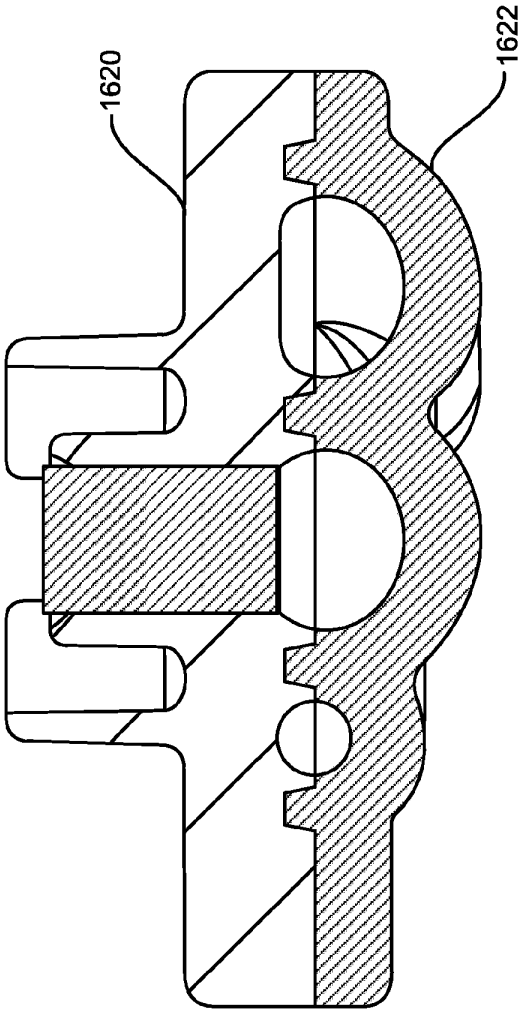


FIG. 19B

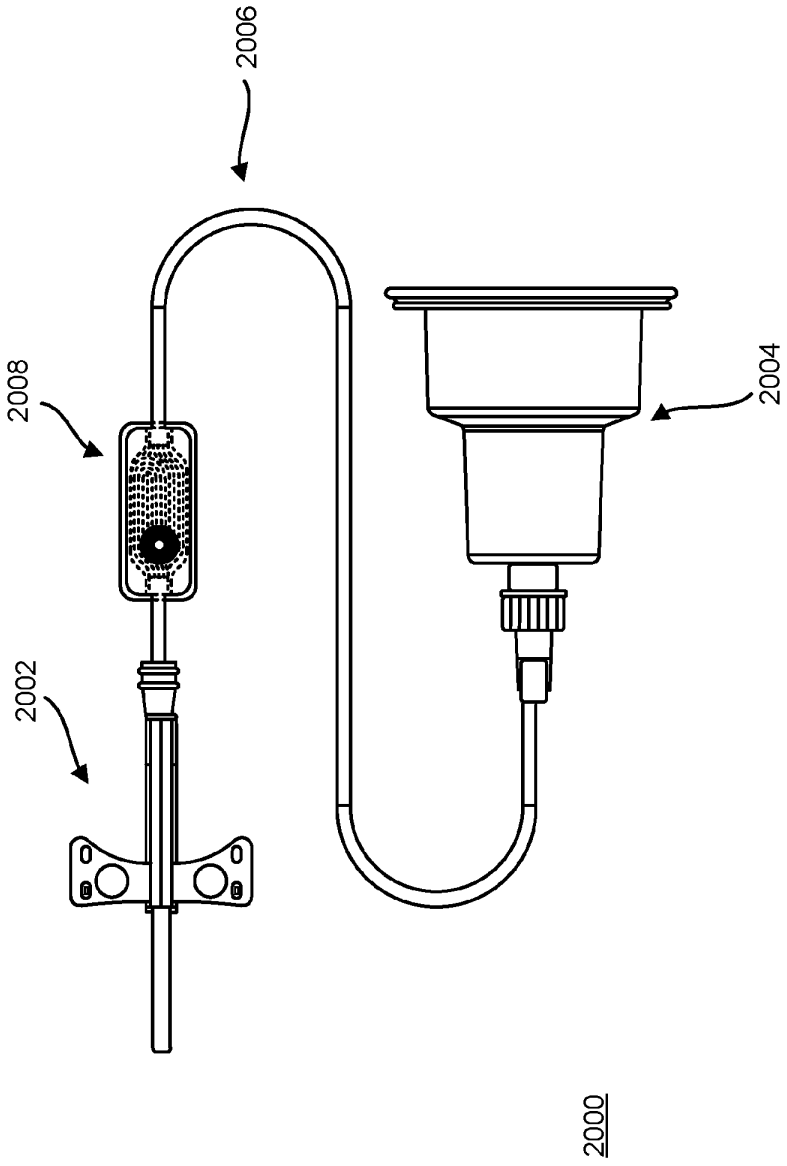


FIG. 20

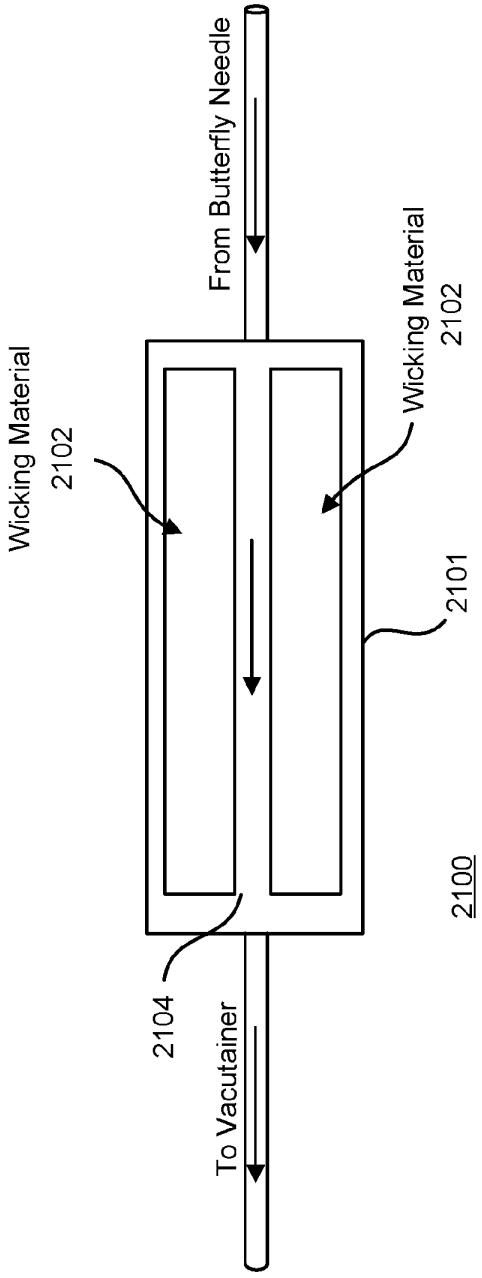

From Butterfly Needle
Wicking Material
2102
Wicking Material
2102
2101
2100
2104
To Vacutainer

FIG. 21

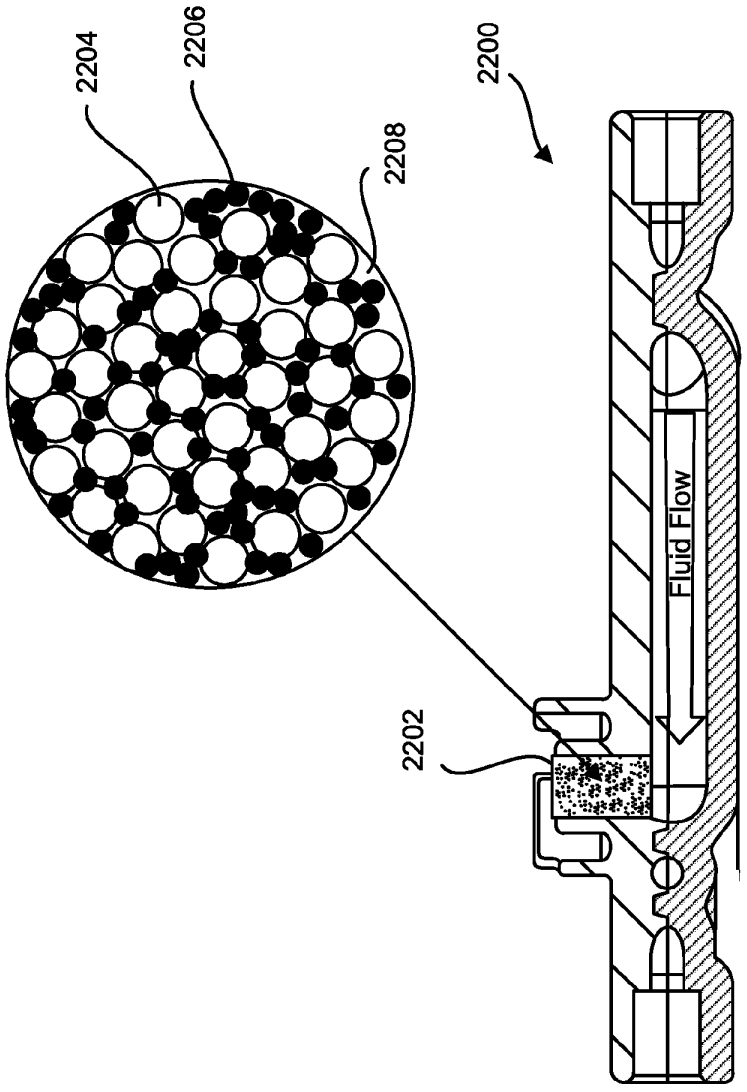


FIG. 22A

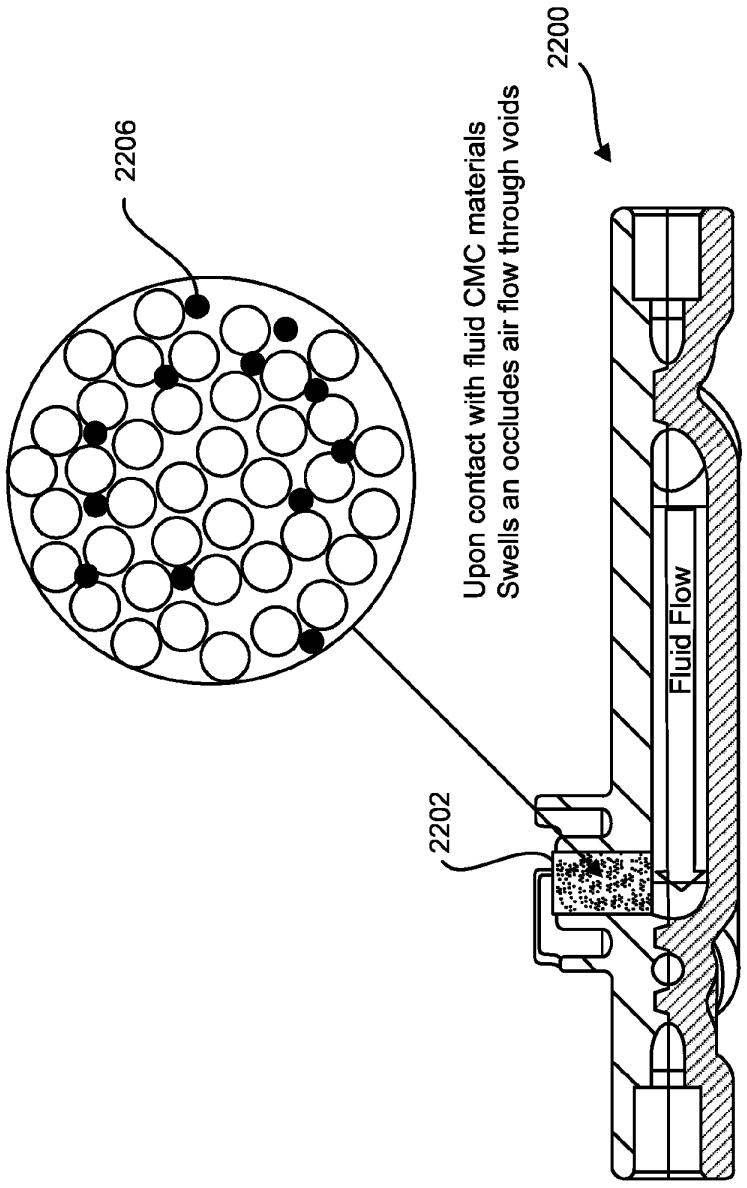

2200
2206
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
Fluid Flow
2202

FIG. 22B

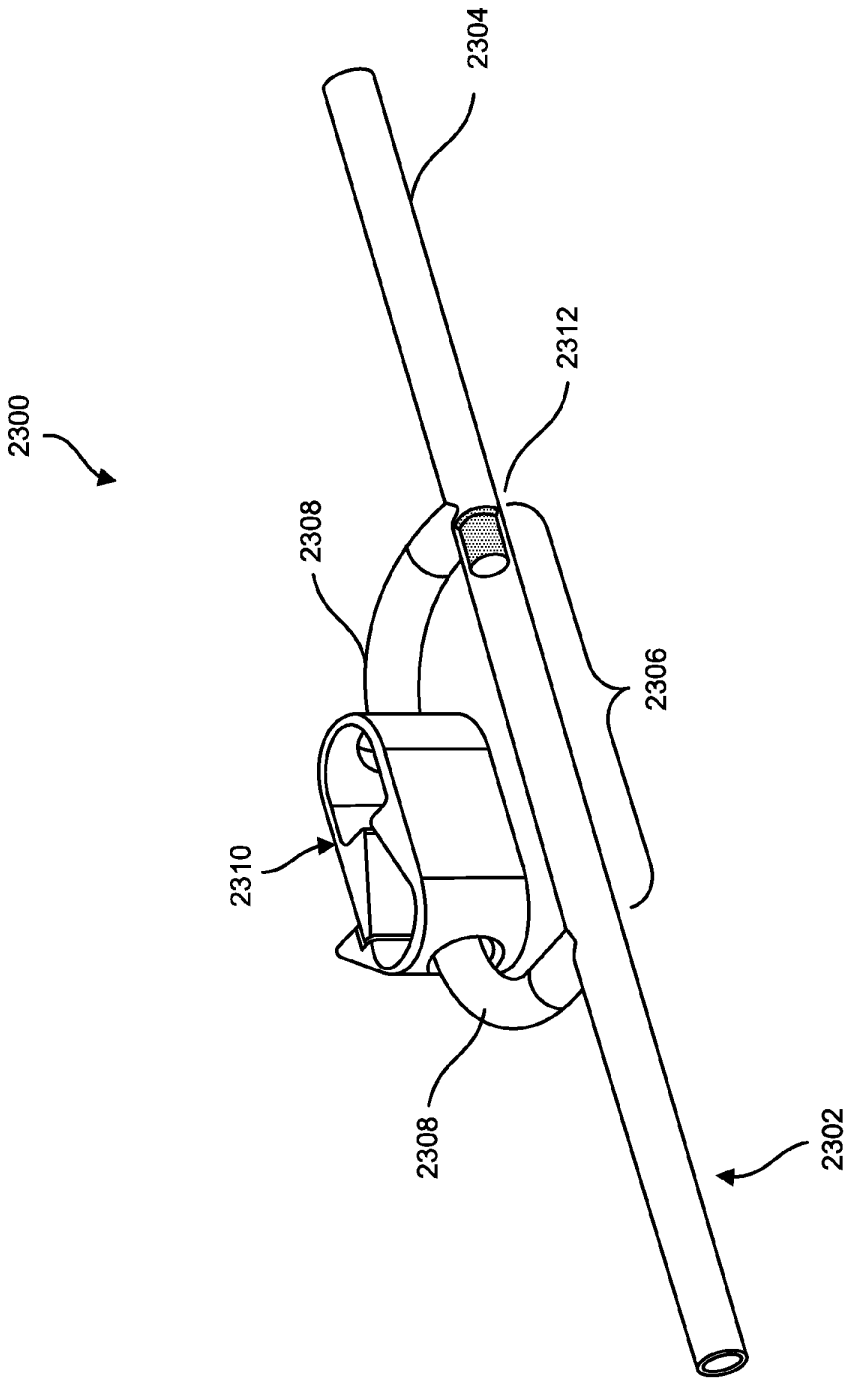


FIG. 23A

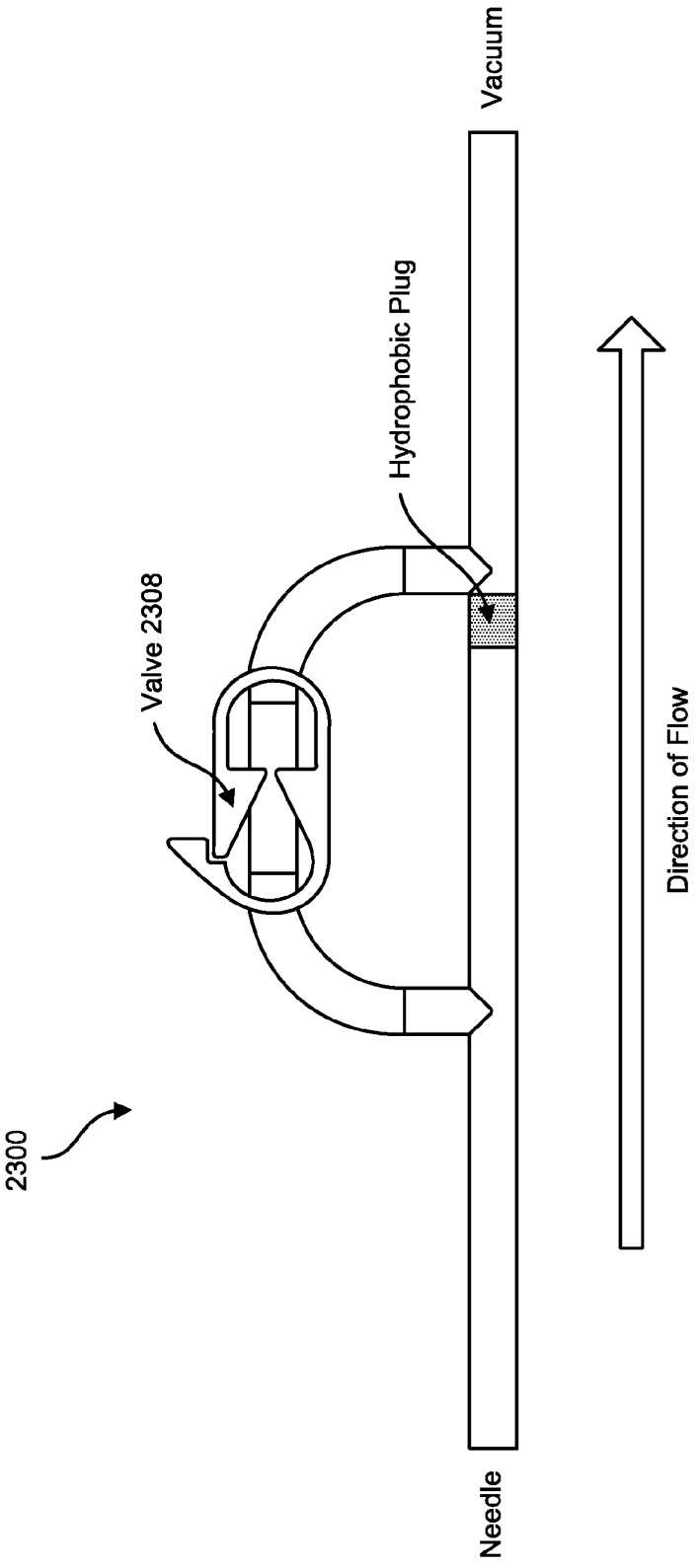

Vacuum
Hydrophobic Plug
Valve 2308
Direction of Flow
2300
Needle

FIG. 23B

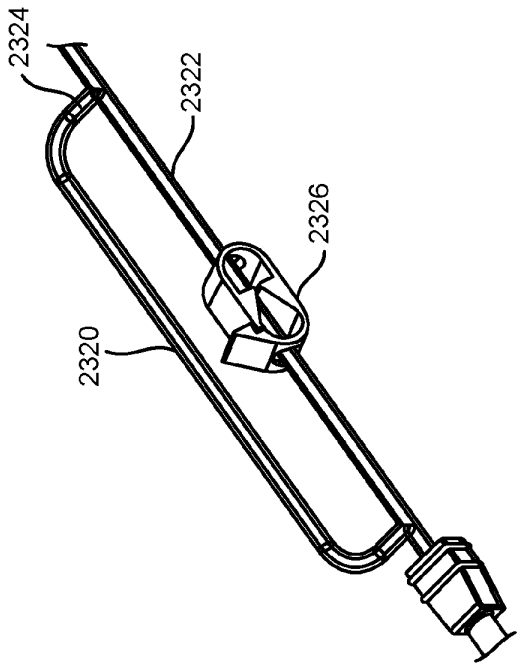


FIG. 23D

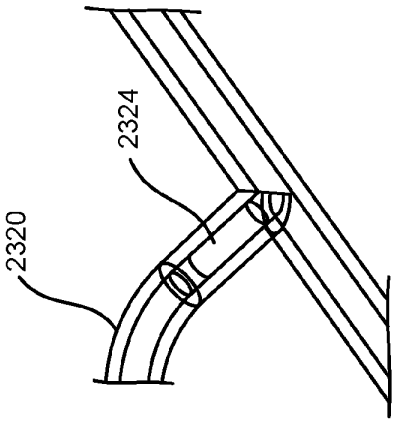


FIG. 23E

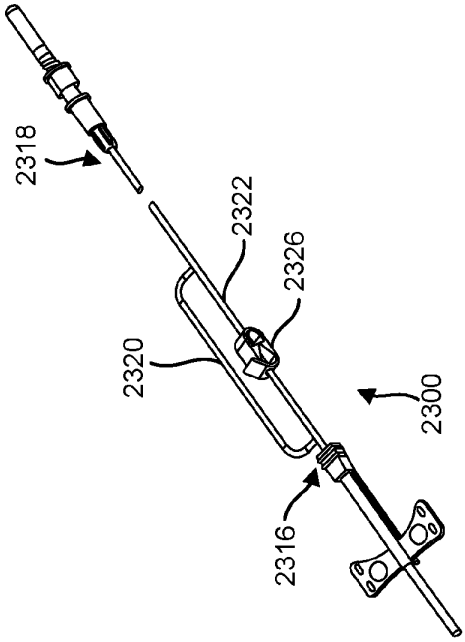


FIG. 23C

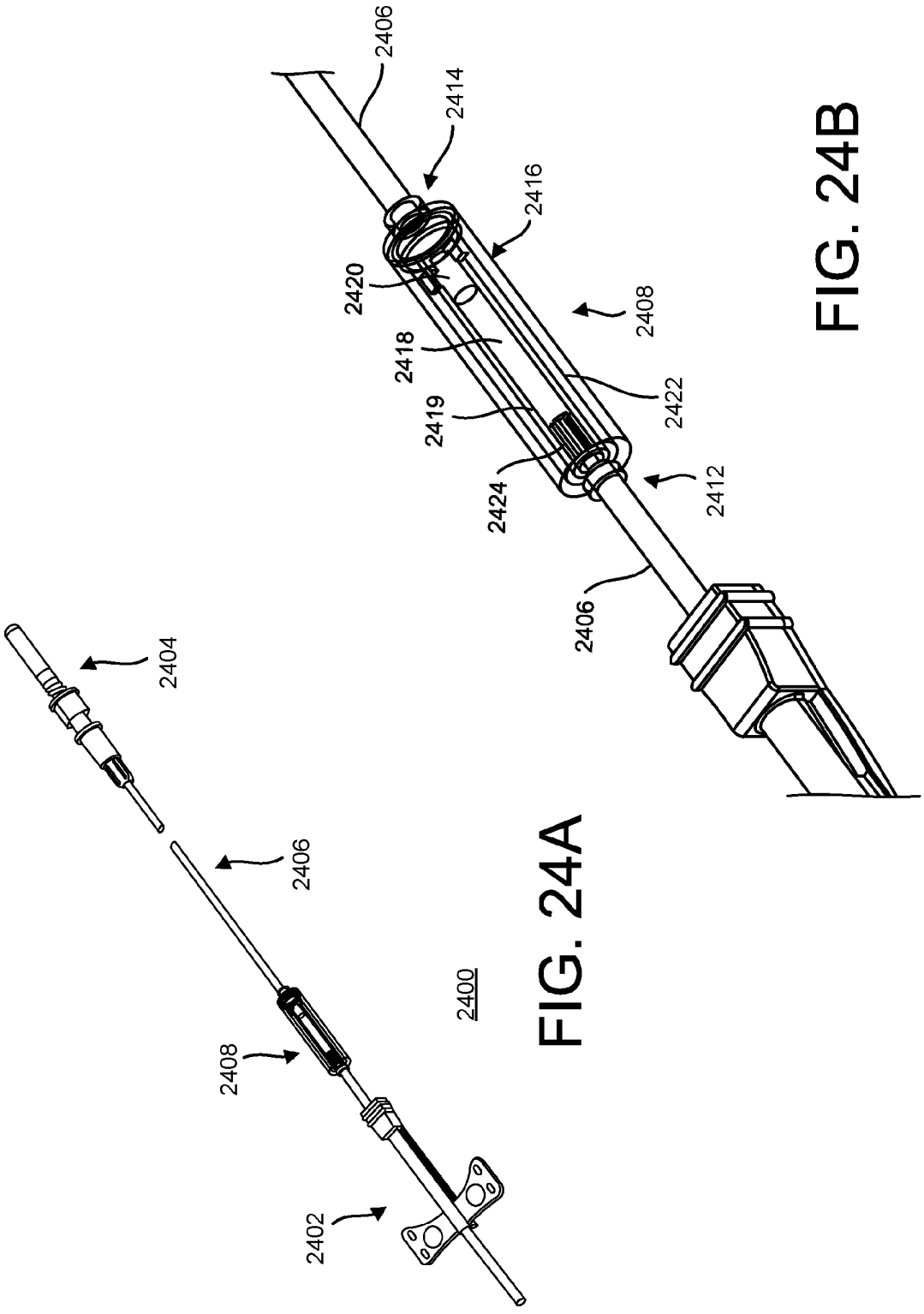


FIG. 24B

FIG. 24A

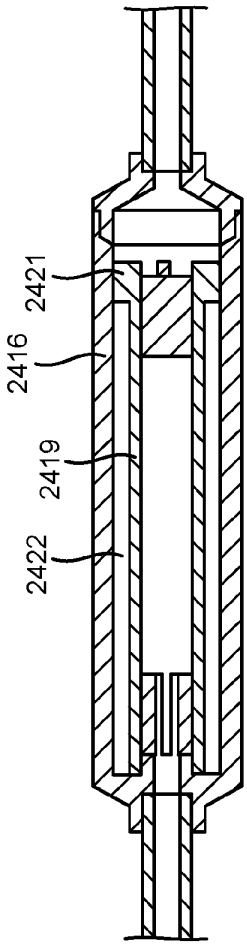


FIG. 24C

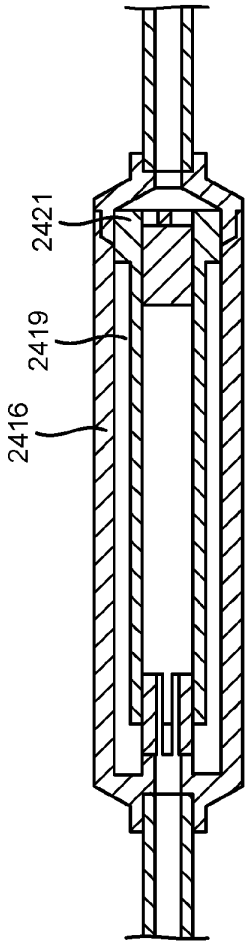


FIG. 24D

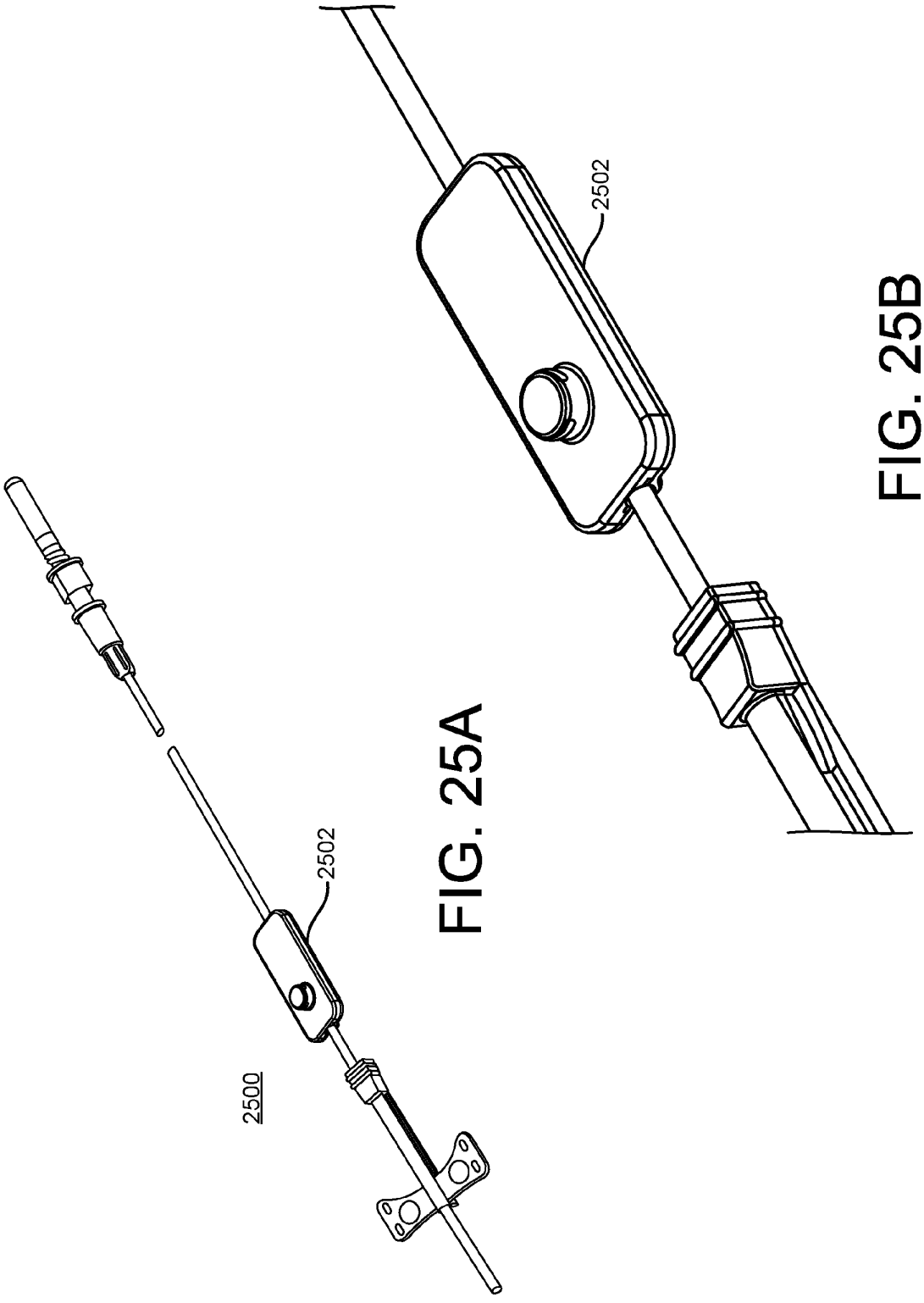


FIG. 25A

FIG. 25B

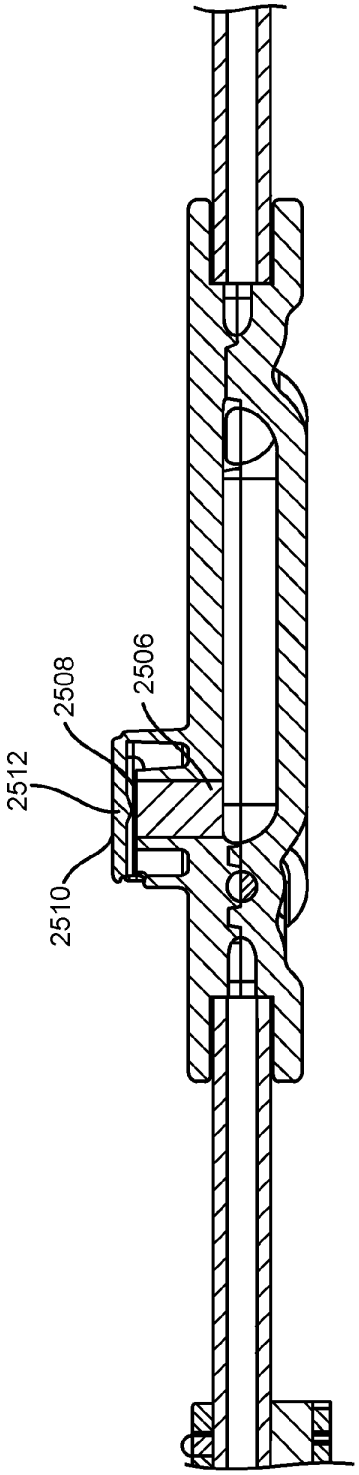


FIG. 25C

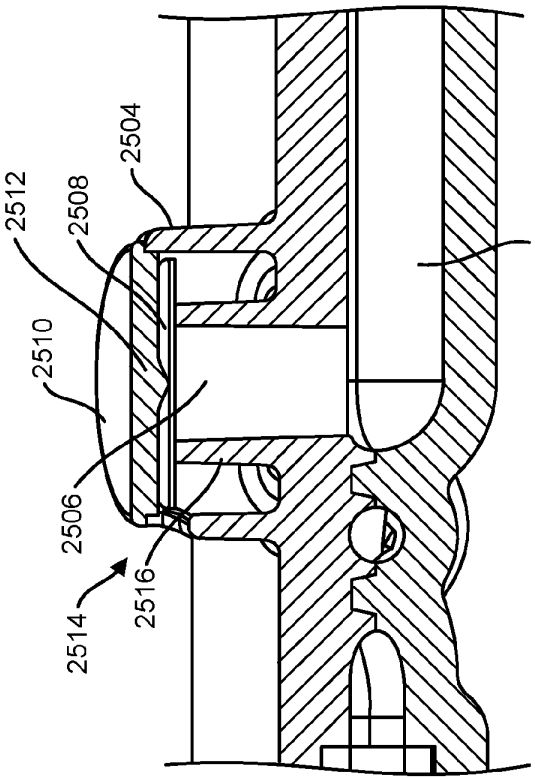


FIG. 25D

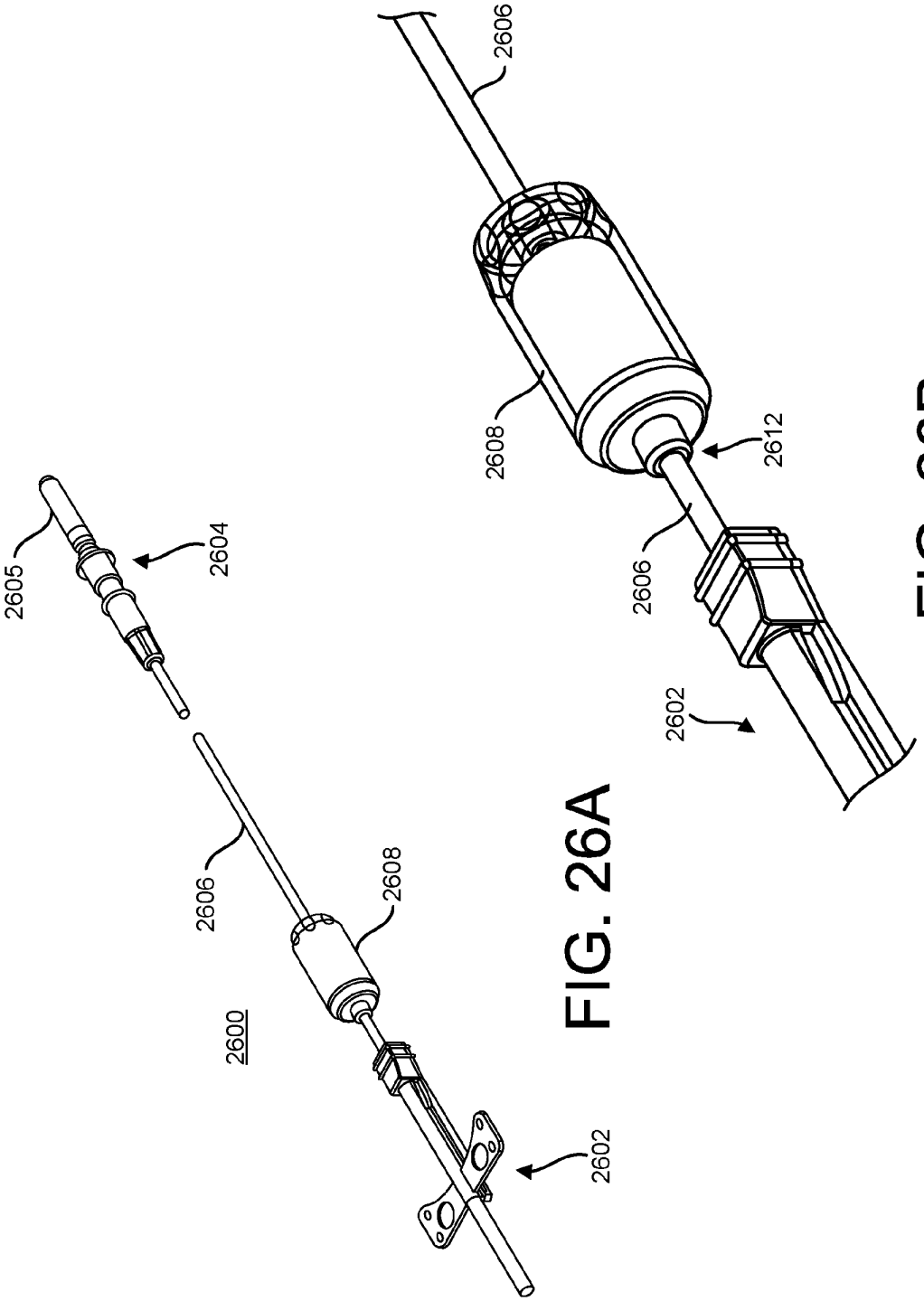


FIG. 26A

FIG. 26B

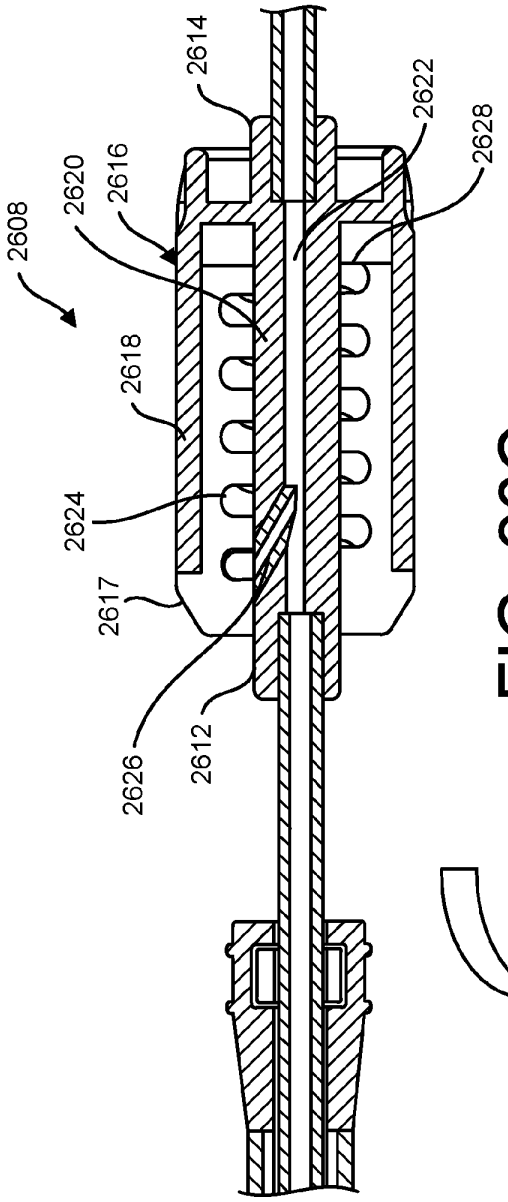


FIG. 26C

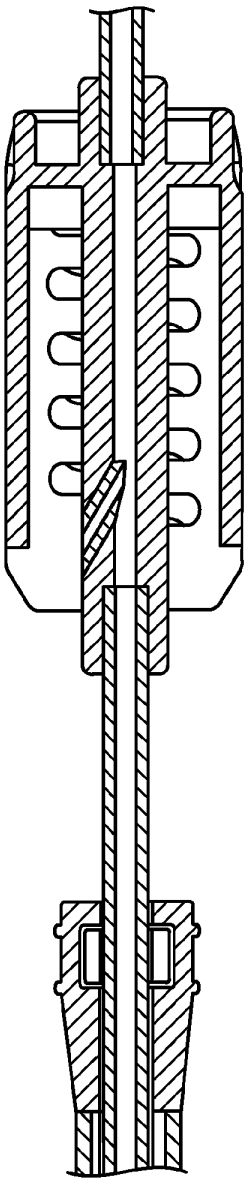


FIG. 26D

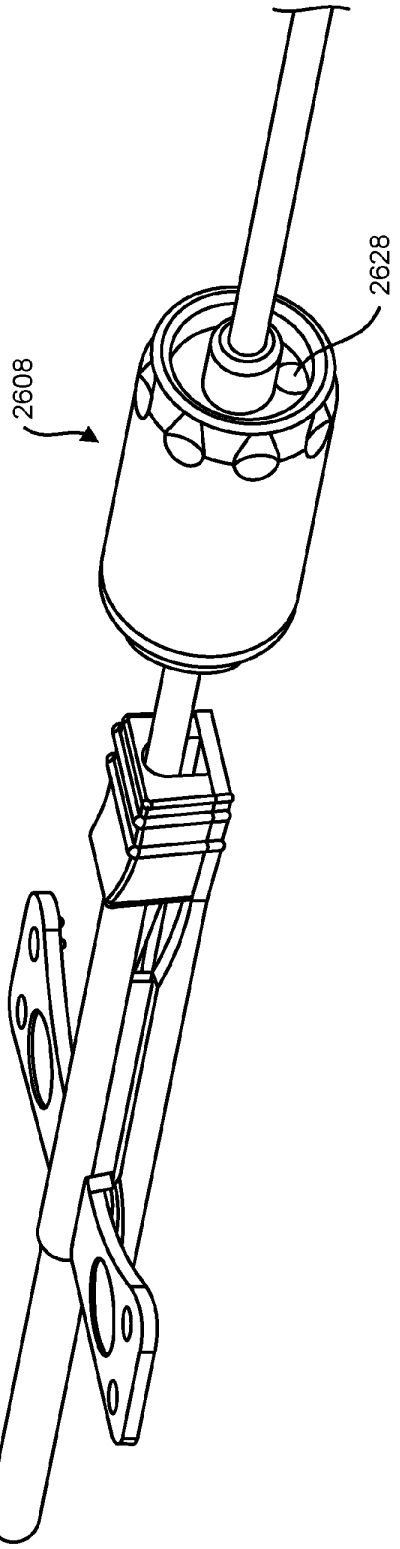


FIG. 26E

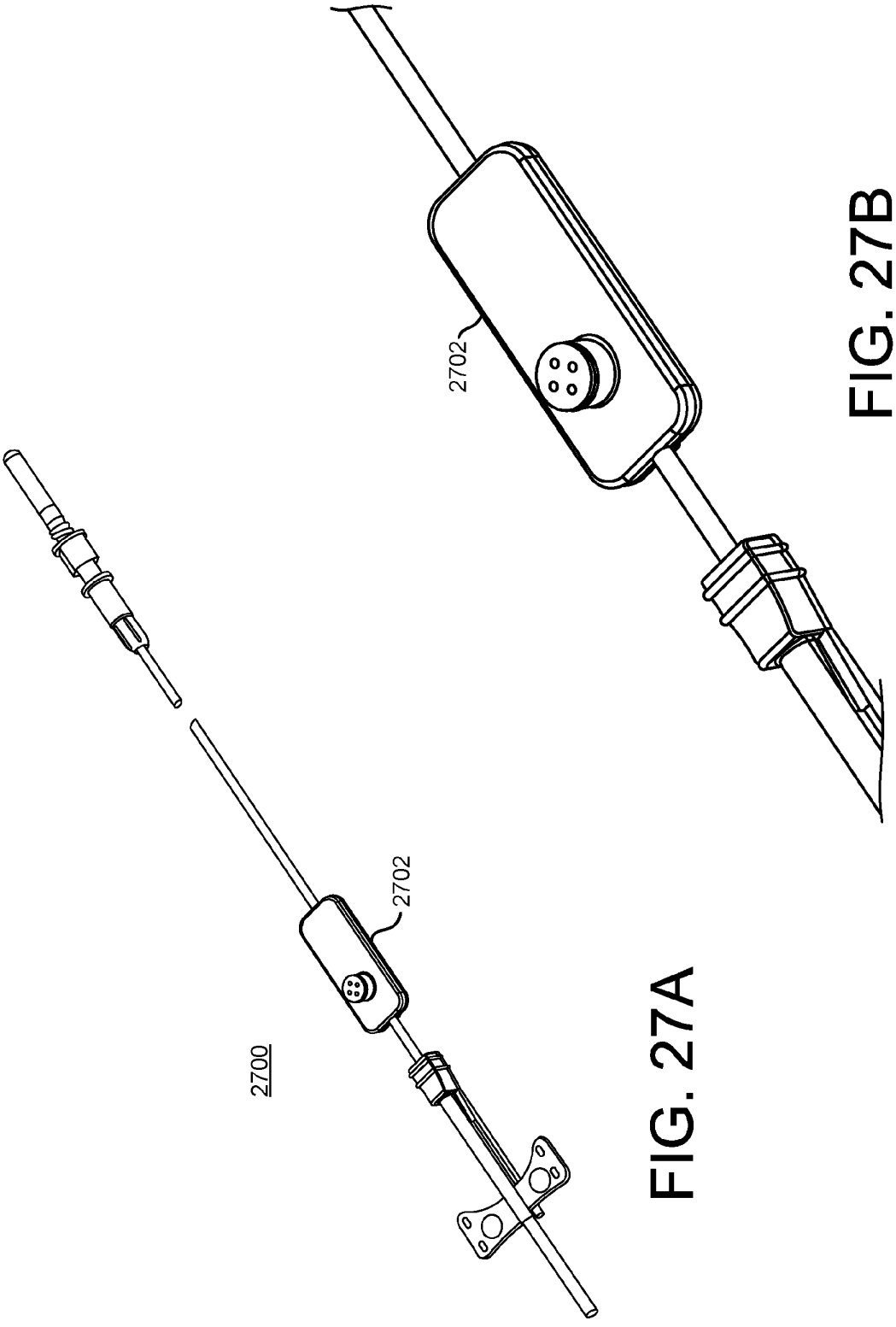


FIG. 27B

FIG. 27A

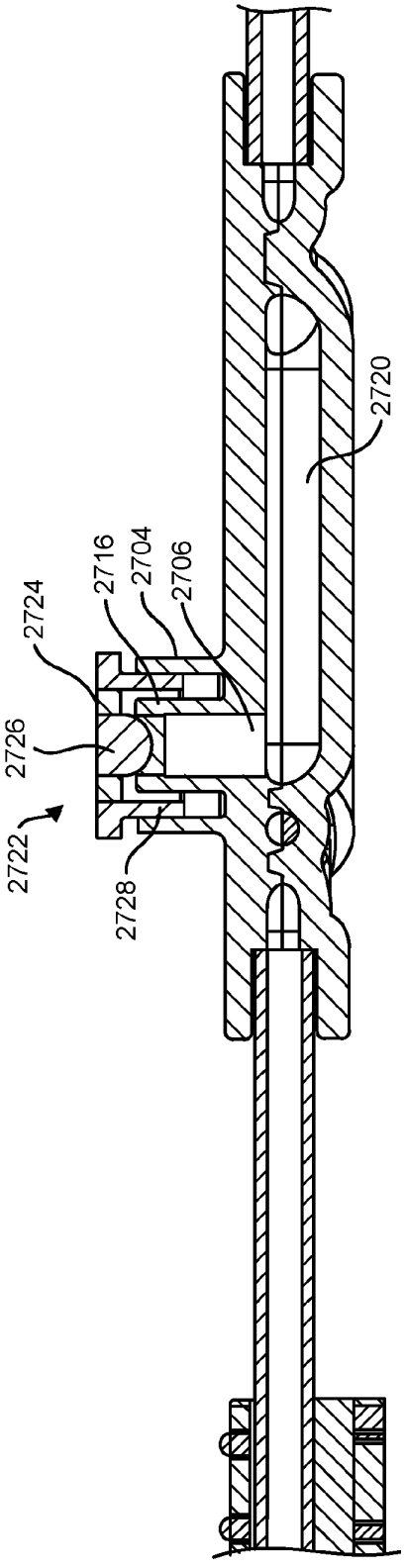


FIG. 27C

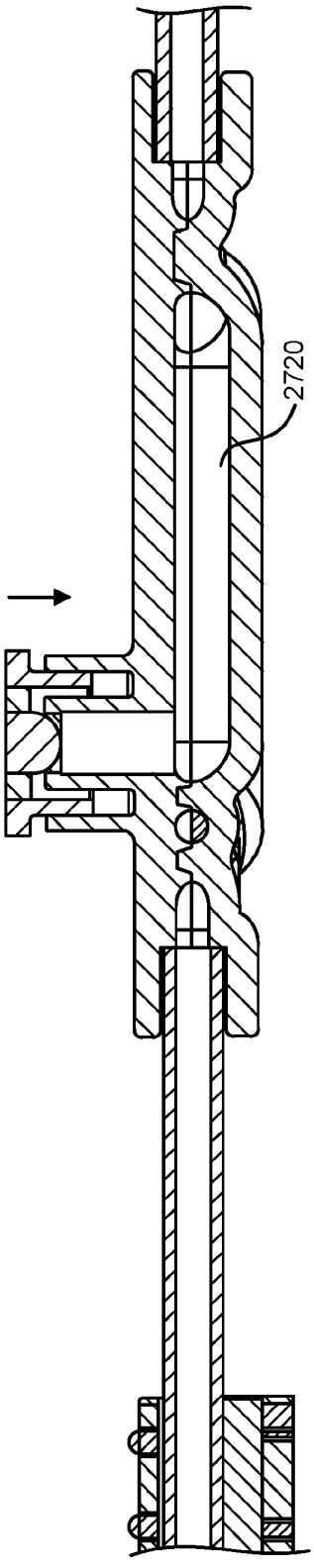


FIG. 27D

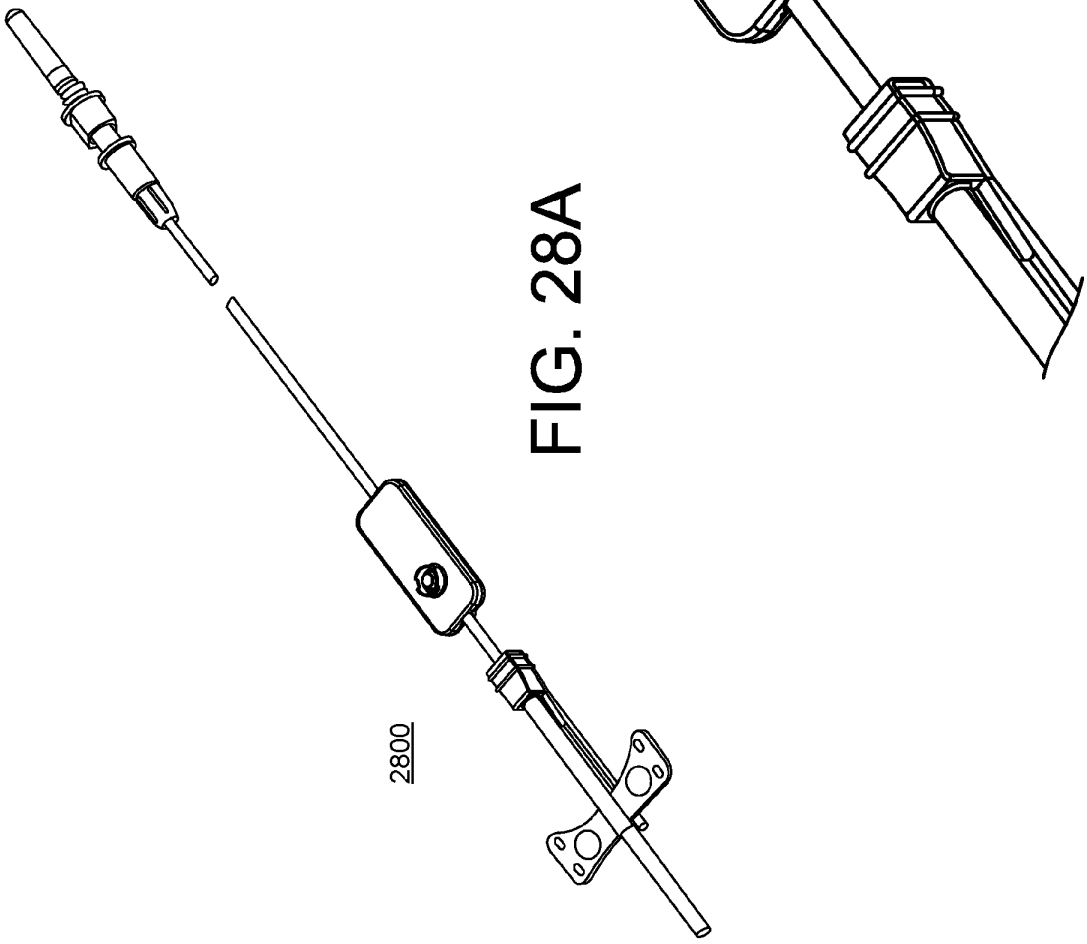


FIG. 28B

FIG. 28A

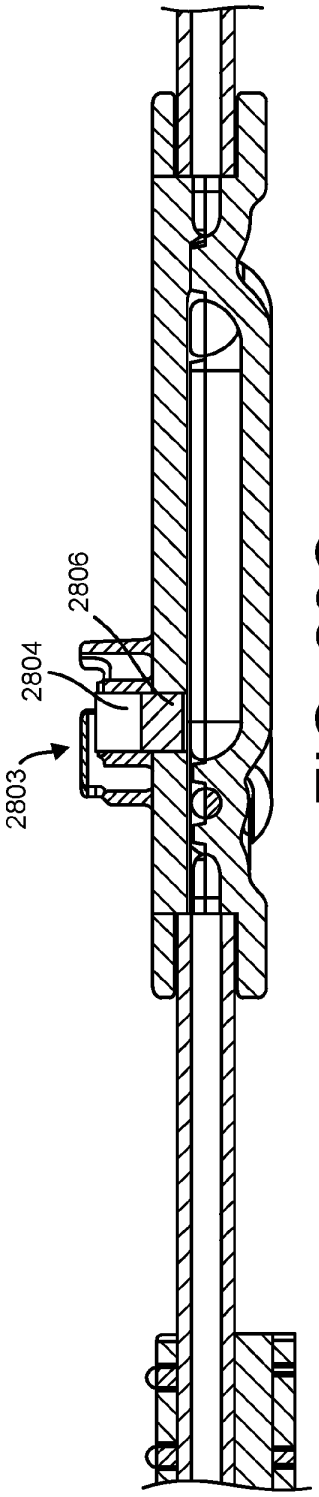


FIG. 28C

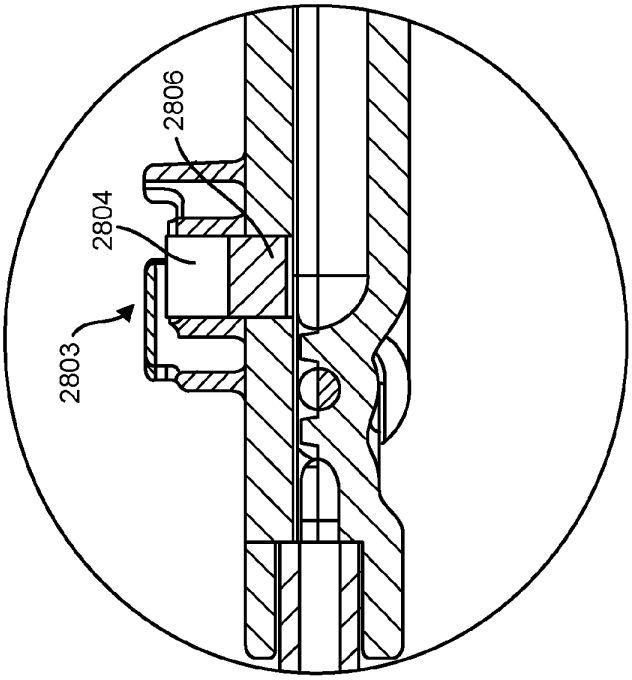


FIG. 28D

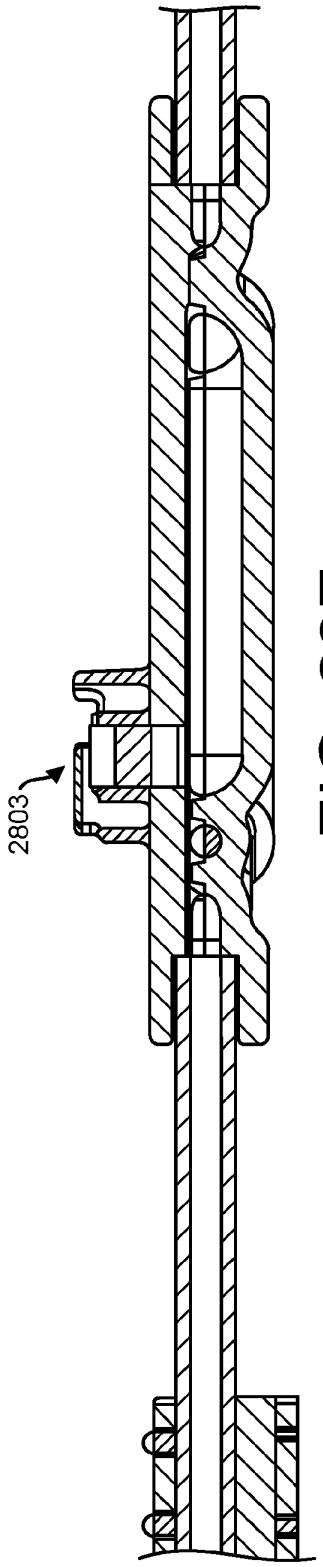


FIG. 28E

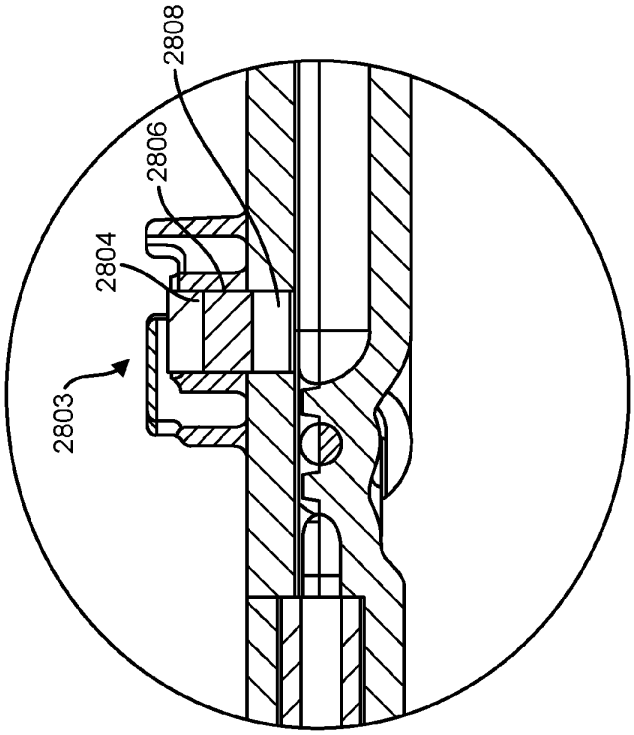


FIG. 28F

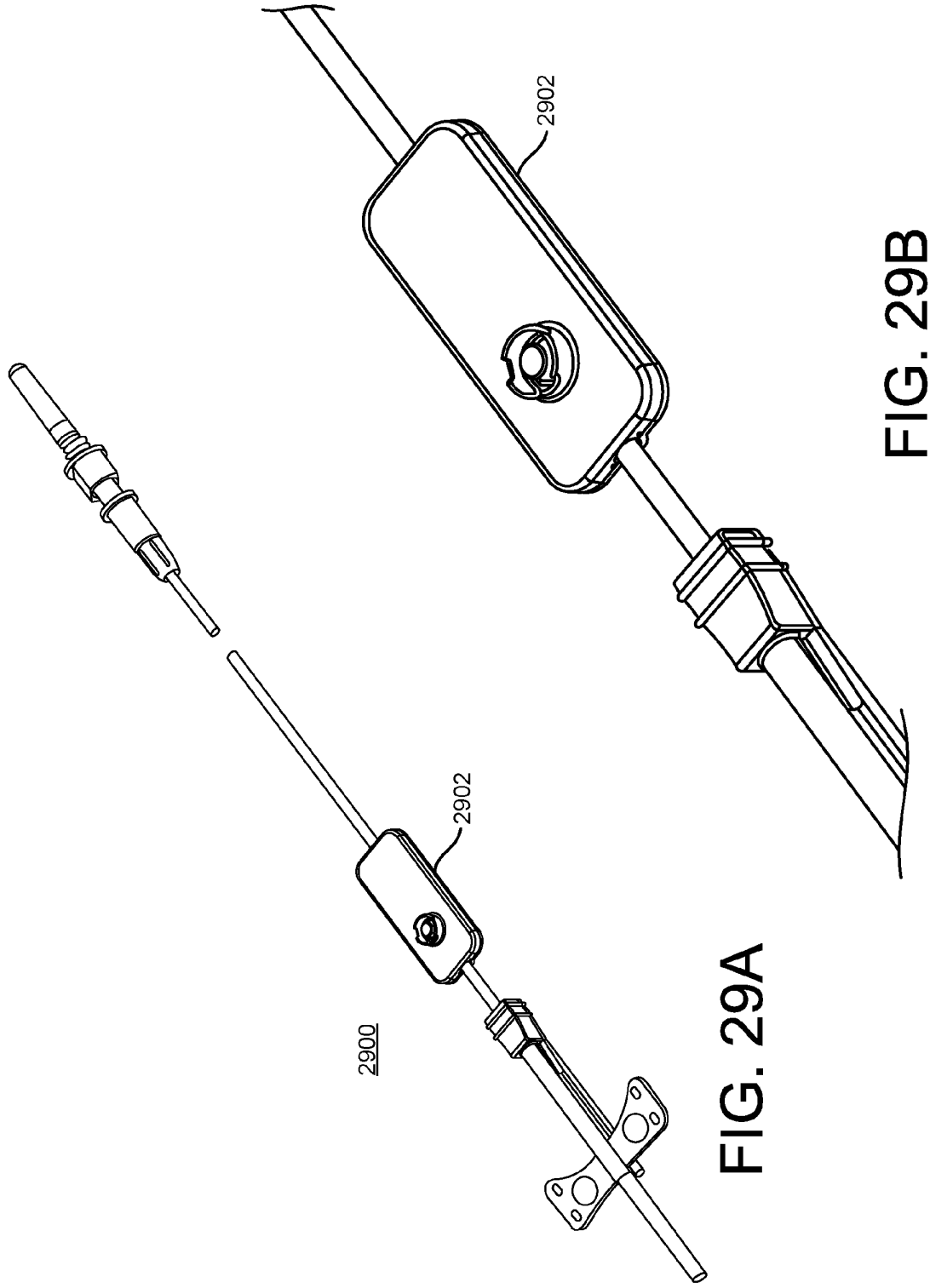


FIG. 29B

FIG. 29A

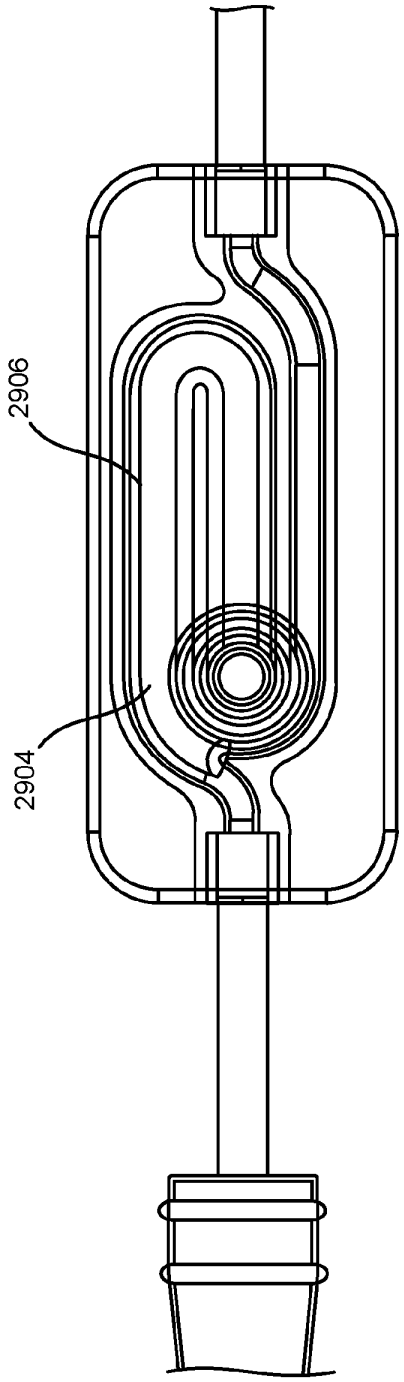


FIG. 29C

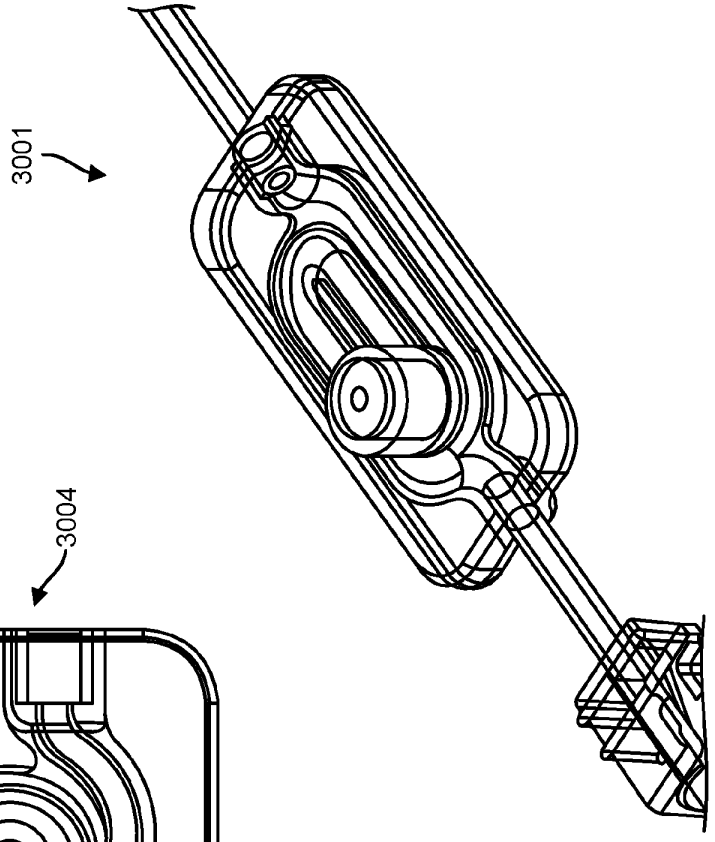


FIG. 30B

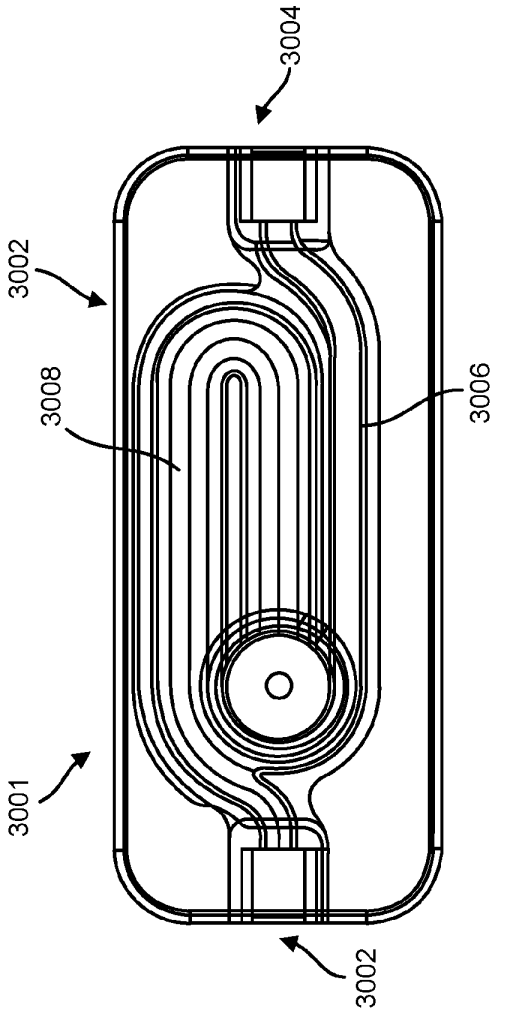


FIG. 30A

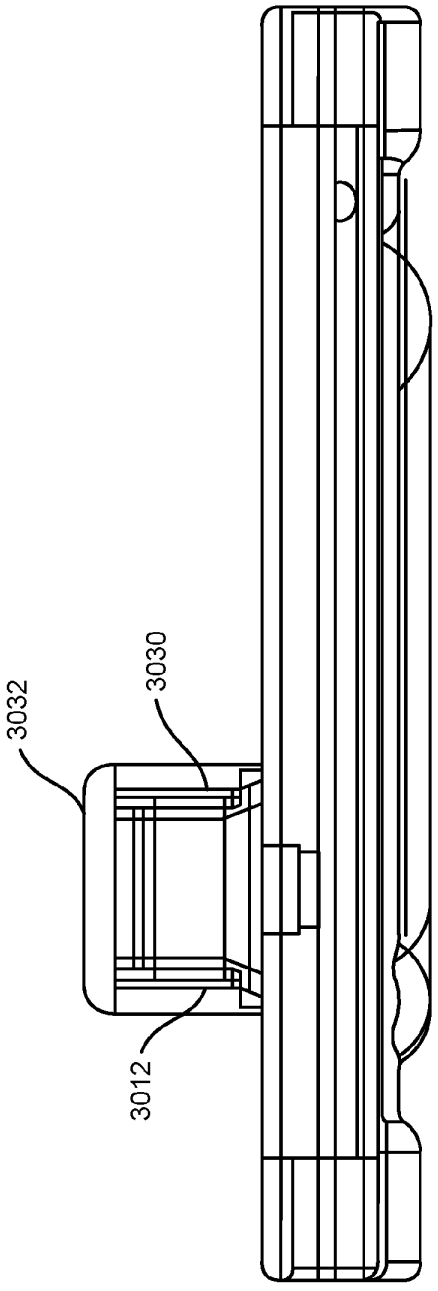


FIG. 30C

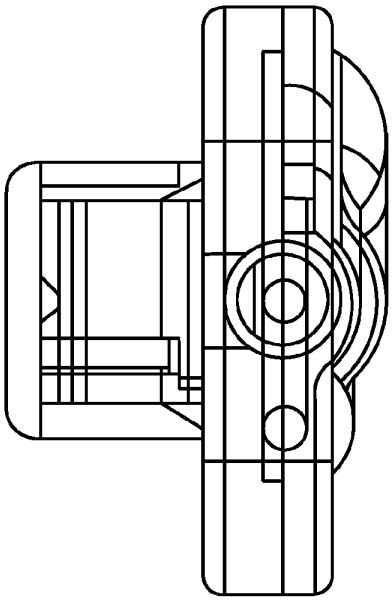


FIG. 30D

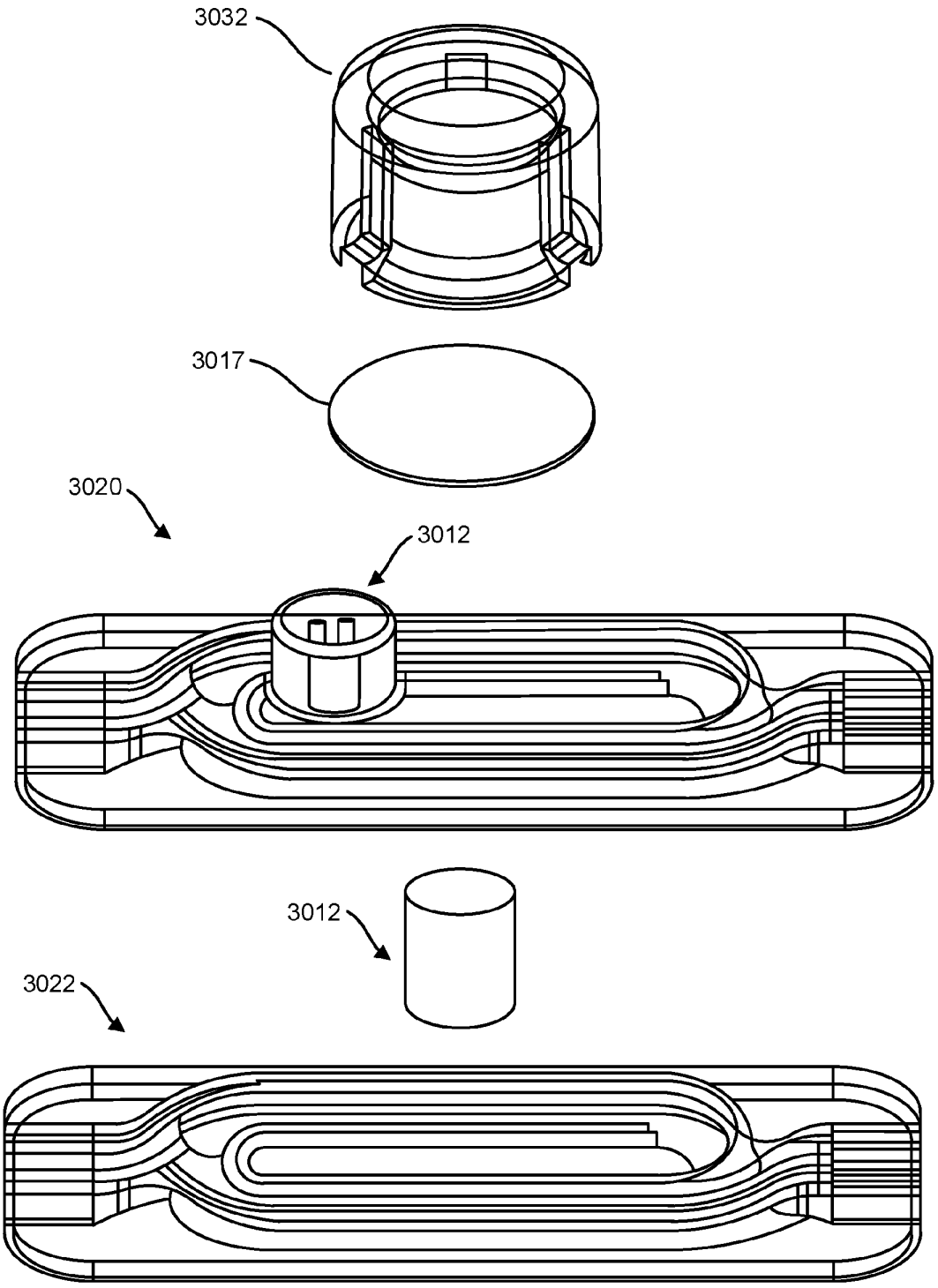


FIG. 30E

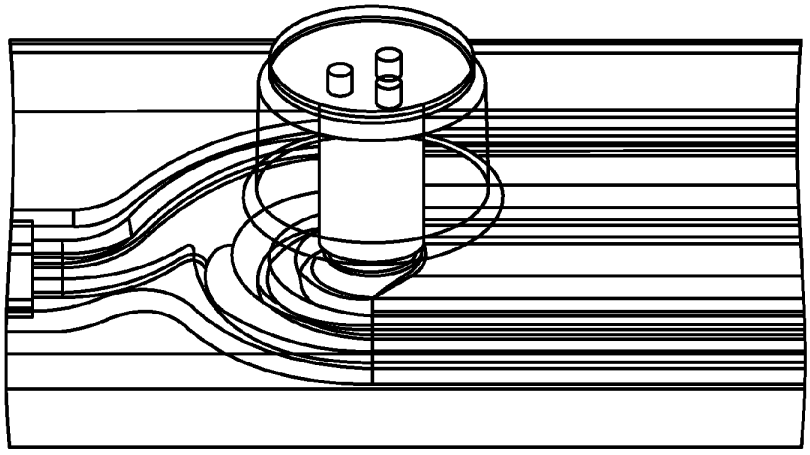


FIG. 30F

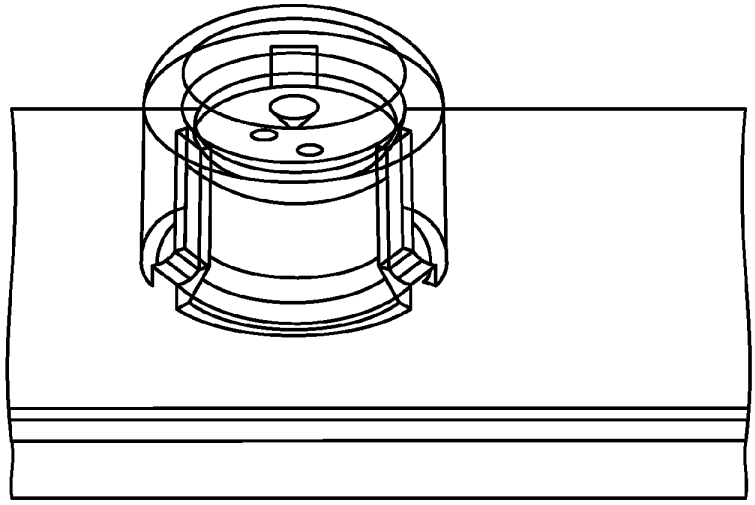


FIG. 30G

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

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.

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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.

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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

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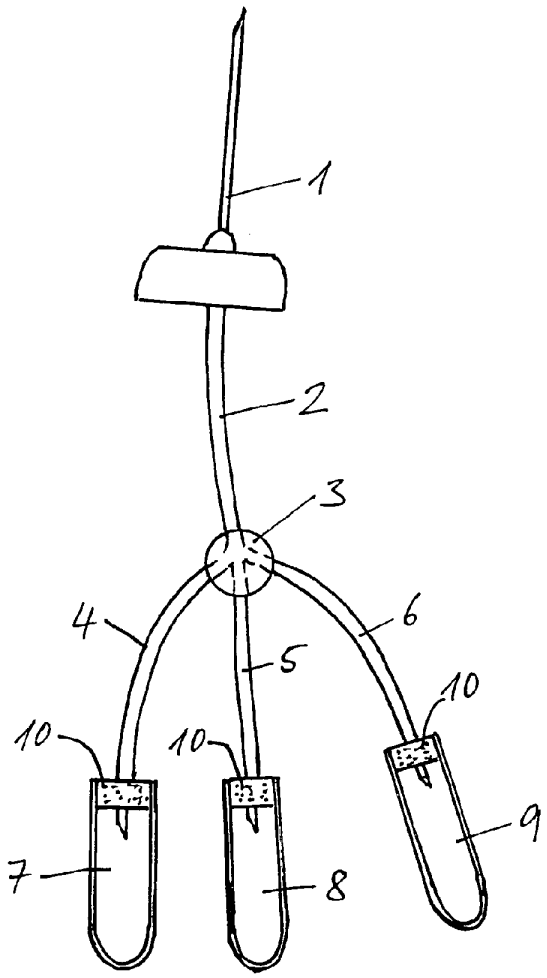
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Rechercheantrag gemäß § 43 Abs. 1 Satz 1 PatG ist gestellt.

(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

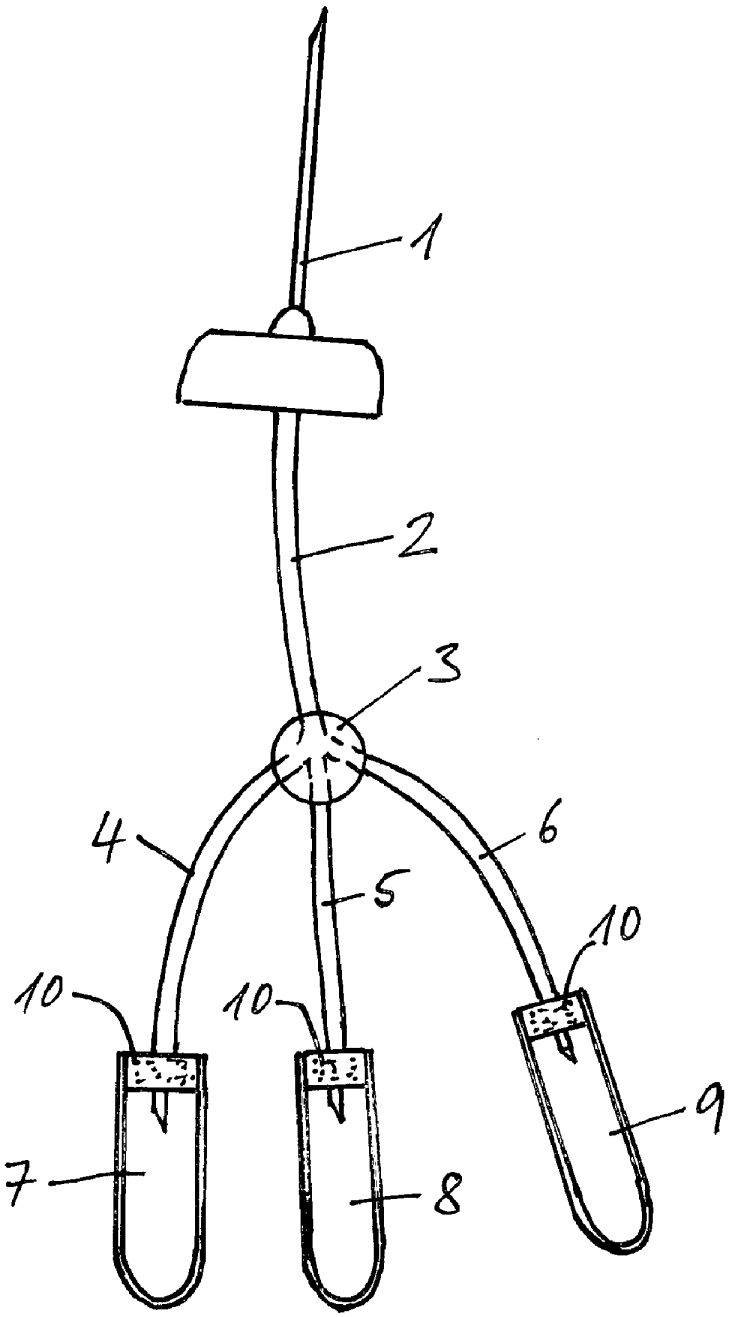
4. Blutentnahmegerät nach Anspruch 2 oder 3, wobei jeder Zweig der Schlauchverbindung eine den Stopfen (**10**) durchdringende Hohlnadel aufweist, und wobei der Stopfen nach Herausziehen der Hohlnadel selbstschließend ist.

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



Anaesth Intens Care 1993, 21, 20-23

Hazards of Bacterial Contamination of Blood Products

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SUMMARY

Post-transfusion bacterial sepsis is infrequent. It is, however, associated with a high mortality due to septic shock. This reflects the release of endotoxin from gram negative bacteria. Lesser transfusion reactions are usually under-reported. These are frequently caused by gram positive bacteria. Gram positive species such as staphylococci and other skin surface organisms may be cultured from platelets stored at room temperature. Typically, gram negative "psychrophyllic" species which survive storage at 4°C are cultured from stored refrigerated blood implicated in transfusion reactions. These include Yersinia enterocolitica, Pseudomonas fluorescens *etc. Bacterial contamination of the blood supply can occur via an endogenous or an exogenous source. Endogenous donor bacteraemia due to* Y.enterocolitica *may be asymptomatic or may follow an episode of gastroenteritis. Exogenous infections occur through some defect in the usual collection practice. Transfusion-acquired syphilis is now extremely uncommon. In the third world, beside the need for effective screening for viral pathogens, infections with protozoa, in particular plasmodia, trypanosoma and leishmania remain a major obstacle to ensuring safe blood supplies. Prevention of transfusion reactions demands rigorous attention to details of collection, storage, reissuing and infusion of blood products, as well as prompt treatment, testing and reporting of suspected reactions.*

Key Words: TRANSFUSION: reaction, post-transfusion bacterial sepsis, bacterial contamination, Yersinia enterocolitica, Pseudomonas fluorescens, Pseudomonas, Trypanosomiasis

In recent years attention has focused on the likelihood of transmission of viral pathogens such as HIV, HTLV-I, hepatitis B and C via blood transfusion. By contrast, reactions following transfusion of bacterial pathogens are less well recognised. These may however be acutely life-threatening with a mortality of up to 25%. From 1975 to 1989, 14 fatal transfusion-related events were reported to the United States Food and Drug Authority (FDA).[1] When all blood products were considered (red blood cells, platelets and plasma) 24 fatal events were reported in a similar time period (1976-85).[2] Although non-fatal events are more frequent, these often are under-reported, estimates of 1-7/1000 having been quoted.[1]

Transfusion of contaminated blood may cause septic shock. This may in part be due to massive release of endotoxin from gram-negative bacteria. Nausea and vomiting, fevers, chills, tachycardia and hypotension can occur during or following transfusion.

Numerous bacteria have been incriminated in post-transfusion sepsis. Of 36 bacteria causing clinical sepsis after red cell transfusion,[3] the most frequently isolated bacteria were *Yersinia enterocolitica* (17) and *Pseudomonas fluorescens* (10). Other bacteria included other pseudomonads (3), enterobacter, flavobacteria (2), *Treponema pallidum* (2) and *Campylobacter jejuni*. A similar group of organisms were seen following platelet and plasma transfusions, i.e. pseudomonas, serratia and enterobacter species. However gram-positive bacteria, such as *Streptococcus pyogenes*, *Staphylococcus aureus* and *Staphylococcus epidermidis*, have also been not infrequently cultured in episodes of clinical sepsis after platelet transfusions,[2,3] (vide infra).

It is possible to divide transfusion reactions into those originating from an endogenous source (donor bacteraemia or parasitaemia) or an exogenous source (surface colonisation or contamination).

ENDOGENOUS BACTERIA (AND PROTOZOA)

Donor bacteraemia may occur in several settings.

Bacteraemia may occur during chronic or low-grade infections, usually unrecognised by the patient. Examples include osteomyelitis, endocarditis and specific diseases such as syphilis and brucellosis. A case report documents a donor with salmonella osteomyelitis who transmitted salmonella to seven

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platelet recipients.[4] Subacute parasitic infections with plasmodia (malaria) and with trypanosoma (Chagas' disease) are frequent causes of blood transfusion transmission in the tropics and in South America.

Bacteraemia may follow recovery from an episode of bacterial gastroenteritis, particularly after infection with *Yersinia enterocolitica* and salmonella sp.[5,6] In a review of seven cases of yersinia transfusion reactions, four patients had preceding diarrhoea within four weeks of transfusion and one had concomitant diarrhoea. However, two patients gave no history of diarrhoeal symptoms. Asymptomatic bacteraemia was usual at the time of donation.

Transient bacteraemia may follow procedures such as dental work. The bacteraemia is usually of a very short duration, not exceeding 30 minutes, unless endocarditis ensues. In such instances the micro-organisms comprise oral streptococci and anaerobes. These are generally of lesser virulence and are unlikely to survive refrigeration compared with gram-negative bacteria.

EXOGENOUS BACTERIA

In this instance bacteria enter blood through some defect in the usual collection practice. Most commonly contamination occurs through inadequate skin preparation.[1,3,7] Less frequently bacteria may colonise collection tubing as occurred in an outbreak of serratia infection.[8] Contamination may occur during storage. An episode of sepsis due to *Pseudomonas cepacia* followed port contamination after the thawing of platelets in a water bath.[9]

A review of UK reports of exogenous post-transfusion sepsis documented 14 episodes between 1980-89.[10] Of these, ten were due to "environmental" pseudomonads (eight were *Pseudomonas fluorescens*) and eight of the ten patients died. Of the many organisms that may colonise skin surfaces, pseudomonas species, serratia, flavobacteria etc, are notable in that they can survive paltry disinfection or may actually be present in the disinfectant solution. These gram-negative isolates are associated with more severe transfusion reactions compared with gram-positive species such as coagulase-negative staphylococci and viridans streptococci.

The increase in notification of bacterial infections is paralleled by the increase in demand for platelet transfusion. Storage at room temperature enhances bacterial proliferation. In many cases bacteria are grown on culture without clinical disease: in these the bacteria are usually skin saprophytes such as pro-*Pionibacterium acnes* or corynebacterium species, often referred to as "diphtheroids". However any of a large number of both gram-positive and negative organisms have been isolated in episodes of sepsis.

Following refrigeration most gram-positive bacteria will not survive. Moreover these are often present in low number and are usually destroyed by host defences—complement, lysosyme and other opsonins. By contrast, gram-negative, psychrophilic (cold-loving) bacteria will survive refrigeration.

PSYCHROPHILIC BACTERIA

Bacteria can be divided into thermophiles growing at $>50°C$, mesophiles, and psychrophiles capable of growth at $<5°C$. The latter organisms prefer growth at room temperature but will survive refrigeration. At 5°C metabolism is significantly reduced and growth occurs at a slow linear rate. After prolonged storage, between one and three weeks, there is sufficient build-up of bacteria or endotoxin to cause a severe transfusion reaction. Alternately once blood is rewarmed these organisms will re-establish their usual logarithmic growth within two to four hours.[1] Metabolic enzymes with optimal activity at room temperature will be switched on. This highlights the need for proper storage and transportation of blood.

The psychrophile most commonly associated with transfusion reactions is *Yersinia enterocolitica*. Other species encountered include enterobacter, klebsiella species, pseudomonas species especially *P. fluorescens* and *P. putida*, and *E. coli*.

Yersinia enterocolitica

Yersinia belongs to the enterobacteriaceae and is a facultative anaerobe. It is usually a zoonotic organism and is transmitted to humans via the food chain, especially from contaminated pork as well as from water and milk. Yersinia lacks siderophores necessary to scavenge iron when bound to transferrin. As they require exogenous free iron, their growth and virulence is enhanced in the presence of iron overload states such as haemachromatosis, cirrhosis and following the use of desferrioxamine.

Gastroenteritis is the usual presentation of yersinia infection. When bacteraemia occurs, symptoms may range from endotoxic shock to an asymptomatic carrier state. Numerous examples of yersinia blood transfusion infection have been reported including several from Australia.[1-3,5,10-16] Diarrhoea may precede blood donation by 8-30 days, however yersinia is rarely cultured from the donor's stool. A rise in yersinia antibodies can however be detected in the donor. In most reports transfused blood had been stored for more than three weeks prior to transfusion.

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OTHER BACTERIA

Treponema pallidum

Transfusion-acquired syphilis is now uncommon both due to donor screening and due to reduced disease prevalence. One should note a rise in syphilis in the United States more recently. Storage at 4°C will inactivate *T. pallidum.*[3] However transmission may occur following transfusion of fresh blood products.

PARASITES (PROTOZOA)

Plasmodia which parasitise red blood cells, and trypanosoma and leishmania which parasitise reticulo-endothelial cells can all be transmitted by blood transfusion. These are important in tropical and subtropical areas of the world, and in perspective the scale of the problem of transmission of protozoa overshadows our concern with bacterial infection. Over three thousand cases of transfusional malaria occur yearly. However the true incidence is considerably higher.

Trypanosoma cruzi (Chagas' disease) is endemic in Central and South America. Twenty million people are believed to be infected, and at least twenty thousand cases of Chagas' disease are acquired through blood transfusion yearly. There is a 15-20% infection rate following transfusion of blood from an infected but asymptomatic donor. Such donors are potentially infective for life. In Brazil, 0.4% crystal violet, which is trypanosomocidal, is added to stored blood for transfusion. Several reports of transfusion-associated acute trypanosomiasis have now been reported from non-endemic areas (USA, Canada).[17-19] One in a thousand residents of Los Angeles are seropositive. Serology is available in special circumstances.

Leishmania donovani is a protozoan organism transmitted by sandflies. Leishmania species have been detected in blood from more than twenty US army personnel who served in the Middle East during Operation Desert Storm.[20] In response to this donations of blood have been recently deferred from this group until 1993.

PREVENTION OF TRANSFUSION REACTIONS

Blood donors should be questioned rather than asked to tick boxes. Specific details of recent medical procedures, dental work, febrile illnesses, tattooing etc. should be sought. Whether patients with recent abdominal pain and/or diarrhoea should be excluded from blood donation remains a vexed question. Patient description of recent symptoms is very likely to be influenced by the manner of questioning. A detailed patient assessment of recent gastrointestinal symptoms could lead to considerable wastage of blood products.

Collection of blood requires detailed attention to antisepsis. Patients with scarred phlebotomy sites may require exclusion.

Blood should be visually inspected prior to transfusion. The presence of haemolysis and the presence of any particulate matter may indicate contamination. Bacteriological screening of blood has been recommended by some.[3] However considering the low frequency of bacterial transfusion reactions this is likely to have a low yield, be expensive and lead to discarding of blood falsely culture-positive.

Blood that has been stored at room temperature for more than 30 minutes is recommended for rejection for re-use. This has recently been questioned.[1] It has been suggested that two hours may be more practicable and less wasteful, in view of the lag period before bacterial growth is re-established after warming to room temperatures. However the safety margin for error may be reduced by such eased restrictions which may lead to even longer periods during which blood is held at room temperature in operating theatres.[16] If these blood units are then returned and re-used they be more likely to be associated with transfusion reactions by virtue of storage for more than 21 days and prolonged periods of time at room temperature.

Storage of blood in ward refrigerators should not occur. These may have poor temperature regulation, may be used for other purposes and consequently be frequently opened and closed.

Prolonged infusions of blood for greater than four hours should be avoided.

Platelets are held at room temperature for up to seven days. Recently this period was reduced from seven to five days in the United States.

MANAGEMENT OF BACTERIAL TRANSFUSION REACTIONS

In the case of a suspected bacterial transfusion reaction, the specimen being transfused should be gram stained. Both donor and recipient bloods should be cultured, as should any related blood products. Any residual blood should be refrigerated promptly. Syphilis serology can be subsequently tested on donor blood.

Broad spectrum antibiotics should be started quickly. The choice of antibiotic may be determined by gram stain result. In its absence, broad spectrum gram-negative antibiotic cover should be provided. Antibiotics of choice would include anti-pseudomonal penicillins, timentin, piperacillin, or the third generation cephalosporins such as cefotaxime or ceftriaxone. Initially these should be combined with an aminoglycoside such as gentamicin, at least until the presence of a pseudomonas species infection is excluded.

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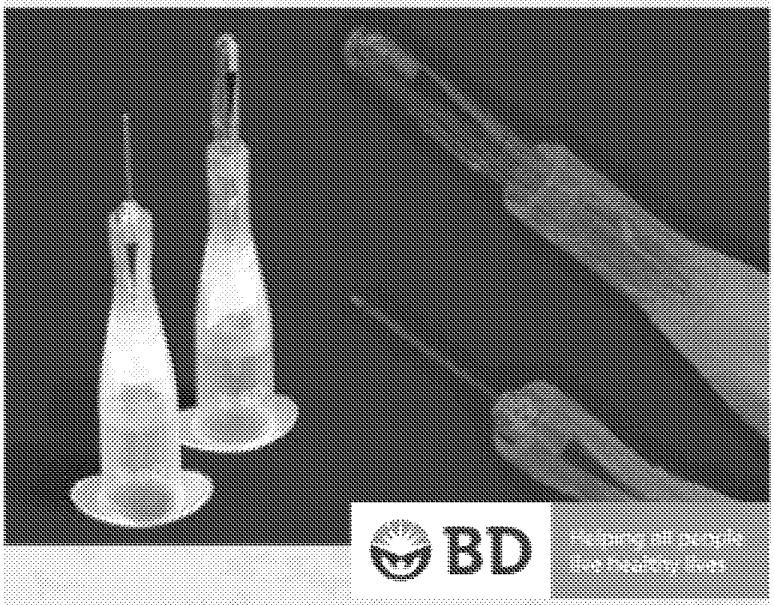
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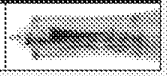
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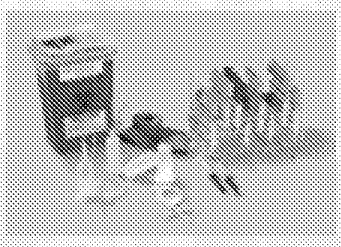


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The scope of the claims open —

(57) [Claims]
[Claim 1] In a system that distributes and executes
requested processing to a plurality of virtualized
computer nodes, a computer node that manages tasks executed in the system comprises: When a processing request with a specified delivery date is received, the management information stored in the storage unit for managing the tasks executed by the computer nodes of the system is referred to, and the task of the processing request is assigned to the computer node.

A simulation is performed, and

the simulation of the assignment shows that there is no computer node that can complete th e processing of the task of the processing request within the delivery date, and even if anothe r computer node moves the task that can complete the processing within the delivery date, th e processing will be performed. An auto-scaling method characterized by executing a proces s of increasing the number of computer nodes in the system when it is determined that a com puter node capable of completing the processing of the requested task within the deadline can not be prepared. 2. The computer node that manages the task further refers to the manag ement information and executes a simulation of moving a task running on one computer node to another computer node, and simulating the movement of the task . If it is determined tha t a computer node that does not have a task to be executed can be prepared by moving tasks that can be completed within the deadline on other computer nodes, the other computer node s can also complete the processing within the deadline. move the task,

2. The autoscaling method of claim 1, further comprising removing from the system compu ter nodes that have no tasks to execute .

3.

The computer node that manages the tasks further

moves tasks that can be completed by other computer nodes within the delivery date by sim ulating the movement so that the number of tasks to be executed is equal to or less than a pr edetermined number. If it is determined that a computer node can be prepared to meet the pr ocessing request, tasks that can be completed within the deadline are moved to other comput er nodes, and computer

nodes with a predetermined number or less of tasks to be executed are assigned to the proc essing request task.

3. The auto-scaling method according to claim 2, further comprising executing a process of s etting the object to be excluded from allocation .

4.

In the process of adding a computer node to the system, the task of the processing request can be completed within the deadline even if the setting of the computer node set to be exclu ded from the assignment of the task of the processing request is cancelled.

4. The autoscaling method according to claim 3, further comprising adding a computer node to said system when it is determined that a computer node capable of completing processing cannot be prepared.

5. In a system that distributes and executes

requested processing to a plurality of virtualized computer nodes, a computer node that manages tasks executed in the system includes:

When a processing request with a specified delivery date is received, the management information stored in the storage unit for managing the tasks executed by the computer nodes of the system is referred to, and the task of the processing request is assigned to the computer node. A simulation is performed, and

the simulation of the assignment shows that there is no computer node that can complete the processing of the task of the processing request within the delivery date, and even if another computer node moves the task that can complete the processing within the delivery date, the processing will be performed. An auto-scaling program for increasing the number of computer nodes in the system when it is determined that a computer node capable of completing the processing of the requested task within the deadline cannot be prepared. 6. In a system comprising a plurality of virtualized computer nodes, a computer node that manages tasks executed in the system, and management information that manages the tasks executed by the computer nodes in the system a storage unit, a schedule processing unit that, when receiving a processing request with a specified delivery date, refers to the management information and executes a simulation that allocates the task of the processing request to a computer node ; , Even if there is no computer node that can complete the processing of the task of the processing request within the delivery date, and even if another computer node moves the task that can complete the processing of the task within the delivery date, the processing of the task of the processing request can be completed within the delivery date. If it is determined that a sufficient computer node cannot be prepared, the system

A computer node, comprising: a scale-out processing unit that executes processing for increasing the number of computer nodes.

detailed description open —

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to an autoscaling method, an autoscaling

program, and computer nodes for controlling the number of computer nodes provided in a system. [Background technology]

[0002]

In a conventional on-premise system, the resource amount of the system was fixed, and therefore it was not possible to accept processing requests from clients exceeding the resource amount of the system.

[0003]

On the other hand, in a system using cloud computing, which has been developed in recent years, the amount of resources possessed by the system can be changed dynamically. Therefore, even if the amount of system resource consumption exceeds the available resources of the system by executing the processing requested by the client, requests from the client can be accepted by dynamically increasing the system resources. It becomes possible.

As a technique for increasing or decreasing such system resources, there is a technique called scale-up/scale-down for increasing or

decreasing the amount of resources of virtualized computer nodes in the system. However, increasing the resources of virtualized computer nodes is limited by the amount of physical machine resources.

Another

technique for increasing or decreasing system resources is called scale-out/scale-shrink, which increases or decreases the number of computer nodes in the system. With this technology, there is no limit to the amount of physical machine resources when increasing the amount of system resources. There is also a technology called autoscaling that automatically scales out and scales down according to the resource consumption rate of the system.

[0006]

In a distributed batch system, when a new batch process is requested, the batch process being executed by a certain processing server is transferred to another server, and the new batch process is executed by the server that is ready for processing. There is known a technique for managing deadlines for batch processing by doing so.

[Patent Document] [Patent

Document 1] Japanese Unexamined Patent Application Publication No. 2002-342098 [Summary of the Invention] [Problems to be Solved by the Invention] When auto-scaling is performed according to the resource consumption rate, unnecessary computer nodes may be added due to scale-out, and processing being executed by the system may be forcibly interrupted due to incorrect scale-shrink. In cloud computing, when pay-as-you-go billing is performed according to the number of computer nodes, useless scale-out may result in unnecessary billing. [0009] In one aspect, the object of the present invention is to provide a technique that enables

the operation of a system with good billing efficiency. [0010] In one aspect, an autoscaling method distributes requested processing to a plurality of virtualized

In a system in which execution is distributed to computer nodes, when a computer node that manages tasks to be executed in the system receives a processing request with a specified de livery date, the computer node that is stored in the storage unit is referring to management in formation for managing tasks to be executed, executing a simulation of allocating the task of t he processing request to a computer node; Furthermore, even if a task that can be completed within the deadline is moved to another computer node, a computer node that can complete t he processing of the requested task within the deadline is used.
If it is determined that the number of computer nodes in the system cannot be increased, pro cessing is executed to increase the number of computer nodes in the syste
m. EFFECTS OF THE INVENTION [0011] According to one a spect, it is possible to operate a system with good billing efficiency. BRIEF DESCRIPTION OF T HE DRAWINGS [0012] FIG. 1 is a diagram explaining a problem of a system realized on-premi ses; FIG. 2 is a diagram explaining a problem of a system realized by cloud computing; FIG. 3 is a diagram showing a configuration example of a system according to this embodiment; FIG. 4 is a diagram showing an example of functional configuration of each node according to the e mbodiment; FIG. 5 is a diagram showing an example of a virtual machine system that implem ents a node according to this embodiment; FIG. 6 is a diagram illustrating an example of a si mulation of assignment of processing-requested tasks by a scheduler in a master node accord ing to the present embodiment; FIG. 7 is a diagram illustrating an example of a simulation of assignment of processing request tasks by a schedule processing unit in a master node accord ing to the present embodiment; FIG. 8 is a diagram illustrating an example of a simulation of assignment of processing request tasks by a schedule processing unit in a master node accord ing to the present embodiment; FIG. 9 is a diagram illustrating an example of a simulation of assignment of processing request tasks by a schedule processing unit in a master node accord ing to the present embodiment;

FIG. 10 is a diagram illustrating an example of a task migration simulation by a rescheduling processor in a master node according to the embodiment;
FIG. 11 is a diagram illustrating an example of a task movement simulation by a rescheduling processor in a master node according to the embodiment;
12A and 12B are diagrams for explaining an example of lock setting for a slave node by a resc heduling processor in a master node according to the present embodiment; FIG.
13A and 13B are diagrams for explaining an example of lock setting for a slave node by a resc heduling processor in a master node according to the present embodiment; FIG.
14A and 14B are diagrams illustrating an example of unlocking of a slave node by a schedule processing unit in the master node according to the present embodiment; FIG.
FIG. 15 is a processing flowchart when a processing request is accepted by the master node a ccording to the embodiment;
16 is a processing flowchart when a processing request is received by the master node accord ing to the embodiment; FIG.
FIG. 17 is a flowchart of rescheduling by the master node according to the embodiment; BEST MODE FOR CARRYING OUT THE INVENTION The present embodiment will be described belo w with reference to the drawings. [0014] FIG. 1 is a diagram for explaining problems of a sy stem implemented on-premise. In the example shown in FIG. 1, the vertical length of a grap hic representing a task indicates the resource consumption of the task, and the horizontal len gth indicates the processing time of the task. In the example shown in FIG. 1, the vertical axi s of the graph indicates the resource consumption of the system, and the horizontal axis indic ates the passage of time. t0 _

~ t 3 indicates the times at equal intervals.

[0016]

In an on-premise system, the amount of resources that the system has is fixed. That is, it is not possible to process resource consumption that exceeds the amount of resources that the system has in advance. In the example shown in Figure 1, the System Resources line represents the amount of resources the system has.

indicate. For example, in FIG. 1A, it is assumed that the processing requests for tasks #1 to #4 are issued to the system at approximately the same

time t0 . At this time, the system starts processing in the order in which the processing requests are accepted, here in the order of task #1, task #2, task #3, and task #4. However, as shown in FIG. 1A, when the processing of task #3 is started, the resource consumption of the system reaches the amount of resources that the system has, and the processing of task #4 cannot be started. will not be able to accept processing requests for The example shown in FIG . 1B is an example of a scheduling system. In a scheduling system, the task processing time is estimated at the time a processing request is received, and even if there are no available resources at the time the processing request is generated, the task of the processing request that is received after the completion of other tasks in progress. Schedule tasks to execute For example, it is assumed that the deadline for processing task #4, which is finally accepted, is time t3 . As shown in FIG. 1B, the processing end time of task #3, which has the earliest processing end time, is t1, so if task #4 is scheduled after task #3, the processing end time of task #4 is is t3 , and the deadline is met. In this case, the processing request for task #4 can be accepted by the system. [0020]

However, in the example shown in FIG. 1(C), if task #4 is scheduled after task #2, which has the earliest processing end time, the processing end time of task #4 will exceed t3, and the deadline will not be met . In this case, the processing request for task #4 is not accepted by the system. On-premises systems may not be able to accept processing requests even after scheduling. Cloud computing technology exists at the opposite end of such on-premise technology

.

The amount of system resources realized by cloud computing is variable. In cloud computing, each computer node provided in the system is realized by, for example, a virtual machine (VM)

.

In the following description, the computer nodes included in the system are simply referred to as nodes. In cloud computing, there is, for example, a scale-up/scale-down technique as a t echnique for changing the amount of system resources

.

Scaling up is a technique for increasing the resource amount of a node. Also, scaling down is a technique to reduce the resource amount of a node. By using scale-up technology, for exam ple, even if a task with a new processing request cannot be executed in time with the current resources, by increasing the amount of node resources, the new processing request can be ful filled. Be able to complete tasks on time.

[0024]

However, since the resources that can be scaled up are limited to the resources of the physic al machines that implement the nodes, which are virtual machines, there is a limit to how mu ch nodes can be scaled up. In addition, usually multiple virtual machine nodes are arranged o n one physical machine, and if there is no surplus after allocating the resources of the physica l machine to each node, it can be specified without reducing the performance of other nodes. It becomes impossible to increase the performance of the nodes of For example, in a multi-te nant environment, multiple tenants' virtual machines are running on a single physical machin e, and in order to increase the resource amount of one tenant's virtual machine, it is possible to reduce the resource amount of other tenants. cannot be done easily. Therefore, even if scal e-up techniques are used, the required processing

Not all tasks can be executed with a guaranteed delivery date. In cloud computing, there is a scale-out/scale-shrink technique in addition to the scale-up/scale-down technique as a tech nique for changing the amount of system resources

.

Scale-out is a technique for adding nodes to a system. Scale shrink is a technique for removin g nodes from a system. By using scale-out technology, it is almost certain that all requested p rocessing tasks can be executed with a guaranteed delivery date.

[0026]

However, in the world of cloud computing, the service usage fee is normally based on a pay-as-you-go system, and as the number of nodes provided in the system increases due to scale-out, the service usage fee increases.

FIG.

2 is a diagram for explaining problems of a system realized by cloud computing.

In the example shown in FIG. 2, the

vertical length of a graphic representing a task indicates the resource consumption of the tas k, and the horizontal length indicates the processing time of the task. In the example shown i n FIG. 2, the vertical axis of the graph indicates the total amount of resource consumption of the nodes that make up the system, and the horizontal axis indicates the passage of time. t_0 to t_3 indicate times at equal intervals. In the example shown in FIG. 2, the system resource li

ne indicates the total amount of resources possessed by the nodes that make up the system.

[0029]

In FIG. 2A, it is assumed that the system initially has three nodes VM#1 to VM#3. Here, it is assumed that the processing requests of task #1 to task #4 are issued to the system at approximately the same time t0 . At this time, in the system, tasks are assigned to the nodes in the order in which the processing requests are accepted, here in the order of task #1, task #2, task #3, and task #4, and processing is started. However, as shown in FIG. 2A, when task #3 is assigned to node VM#3, the resource consumption of all nodes in the system becomes the upper limit, and task #4 can be assigned. node disappears. At this time, as shown in FIG. 2A, for example, the system is scaled out and a VM#4 node is added to the system

.

As shown in FIG. 2A, by adding a VM#4 node to the system by scale-out, the processing of the requested task #4 can be executed. For example, in cloud computing, as a service of an IaaS (Infrastructure as a Service) vendor that provides infrastructure such as virtual machines and networks as a service, it automatically scales out when the resource consumption rate of the system exceeds a predetermined level. There is service. In cloud computing, the technology for automatically expanding/reducing the system is also called autoscaling. Here, it is assumed that the deadline for processing task #4 is

time t3 . As shown in FIG. 2A, the processing end time of task #3, which has the earliest processing end time, is t 1

Therefore, if task #4 is scheduled after task #3, the processing end time of task #4 will be t 3, and the deadline will be met . If task scheduling can be performed in this way, it is possible to execute the processing of task #4 in time for the delivery date without increasing the number of nodes for VM #4 due to scale-out

.

. However, such a judgment cannot be made just by looking at resource consumption as in the case of the IaaS service described above. As mentioned above, in cloud computing, the usage fee increases as the number of nodes increases. I have a request.

[0033]

Further, in order to suppress useless node usage charges, a scale shrink is performed on a node that is determined not to be in operation in the system, and the node is removed from the system. For example, in cloud computing, as a service of an IaaS vendor, when the CPU (Central Processing Unit) usage rate of a node falls below a predetermined level, task processing is not performed at the node and only middleware such as the OS operates. There is a service that automatically scales and shrinks if it judges that it is not.

[0034]

However, even if the resource consumption of a node is low, it does not necessarily mean that the requested task is not being processed. For example, in the example shown in FIG. 2B, in the node of VM#3, the amount of resource consumption is drastically reduced after the proc

essing of task #3 is completed. However, in the example shown in FIG. 2B, in the node of VM #3, task #4, which consumes less resources, is being executed in parallel with task #3. If the node of VM#3 is scale-shrinked at the same time as the processing of task #3 ends, the proce ssing of task #4 will be forcibly terminated. In this way, if scale shrinkage is determined just b y looking at resource consumption as in the above-mentioned IaaS vendor service, for exampl e, task #4 shown in FIG. It is possible to accidentally remove a running node.

[0035]

The auto-scaling technique according to the present embodiment for solving such problems will be described below.

FIG.

3 is a diagram showing a configuration example of a system according to this embodiment.

[0037]

In this embodiment, the system 100 shown in FIG. 3 is assumed to be a computer system c omposed of virtual machine nodes provided from the IaaS side in cloud computing. The syste m 100 distributes and executes the processing requested by the client 200 over a plurality of nodes. The system 100 and the client 200 are connected by a network 300 such as a LAN (Lo cal Area Network) or the Internet. The system 100 comprises a master node 110 and slave no des 120 .

The master node 110 receives processing requests from the client 200 , assigns

tasks to each slave node 120 , and manages tasks to be executed in the system 100 . Note t hat the master node 110 according to this embodiment performs auto-scaling processing such as scale-out and scale-shrink of the slave node 120 . Note that the master node 110 may be o ne of the slave nodes 120 at the same time.

The slave node 120 is a computer node that

executes tasks requested by the master node 110 . The slave node 120 is capable of parallel processing of multiple tasks. The slave node 120 is added to the system 100 or deleted from t he system 100 by autoscaling processing. For example, in FIG. 3, when the slave node 120a #a and the slave node 120b #b are executing task processing, if there is a processing request that cannot be executed by those slave nodes 120, #c A slave node 120 c is added to system 100 . Also, for example, when there are no more tasks to be executed by the #c slave node 1 20c, the #c slave node 120c is deleted from the system 100 .

[0040]

The client 200 is a computer having a high-level application that requests the system 100 to execute processing provided by the system 100 . In the example shown in FIG. 1, the client 2 00 is an external device of the system 100.

Node 200 may be a node within system 100 .

FIG.

4 is a diagram showing an example of the functional configuration of each node according to this embodiment.

The master

node 110 comprises a client communication section 111 , a schedule processing section 112 , a schedule information storage section 113 , a scale-out processing section 114 , a slave co mmunication section 115 , a rescheduling processing section 116 and a scale shrink processin g section 117 .

[0043]

The client communication unit 111 receives a processing request from the client 200 . If the processing of the received request is executable within the system 100, the client communicat ion unit 111 passes it to the schedule processing unit 112. FIG. If the processing of the receiv ed request cannot be processed within the system 100, the client communication unit 111 res ponds to that effect to the client 200. FIG. Processes that cannot be executed within the syste m 100 include, for example, application processes that are not present in the slave node 120 and large-scale processes that cannot be completed by the slave node 120 of one virtual mac hine by the due date. The technique of distributing and executing large-scale processing on a plurality of nodes is outside the scope of the technique according to the present embodiment, and will not be described here. The client communication unit 111 notifies the client 200 of th e processing result received from the slave node 120 . When the client communication unit 1 11 receives a processing request with a specified delivery date, the schedule processing unit 1 12 refers to the management information stored in the schedule information storage unit 113 and slaves the task of the processing request

.

Run the simulation assigned to node 120 .

[0045]

The schedule information storage unit 113 is a management information storage unit for ma naging tasks executed by the slave nodes 120 provided in the system 100 . The management information stored in the schedule information storage unit 113 records schedules of tasks to be executed by all the slave nodes 120 .

More

specifically, the schedule processing unit 112 first detects the slave node 120 that can compl ete the processing of the received processing request within the specified delivery date in the current state. Here, the schedule processing unit 112 not only selects the slave nodes 120 tha t can immediately execute the processing, but also the slave nodes 120 that can complete the processing within the deadline even if the processing request task is executed after the proces sing of other tasks is completed. To detect. The schedule processing unit 112 selects the slave node 120 to which the task of the processing request is to be assigned from among the slave nodes 120 detected here. Note that the locked slave node 120 is excluded from detection her e. In the present embodiment, locking refers to setting the slave node 120 as a non-allocation target for the task of the processing request.

[0047]

In the current state, if there is no slave node 120 that can complete the processing of the requested task within the deadline, the schedule processing unit 112 detects a task that can complete the processing within the deadline even if the task is moved to another slave node 120. . By moving the detected task, the schedule processing unit 112 determines whether or not the slave node 120 capable of completing the processing of the requested task within the delivery date can be prepared. If it is determined that by moving the task, the slave node 120 capable of completing the processing of the task requested by the deadline can be prepared, the schedule processing unit 112 performs the process of moving the task to another slave node 120 as follows: It is executed via the slave communication unit 115 . The task may be moved by, for example, stopping the processing of the task at the source slave node 120 and restarting it at the destination slave node 120. A method of transferring data to the destination slave node 120 may also be used. In this embodiment, the task is moved by a method of restarting the processing of the task in the destination slave node 120 . Schedule processing unit 11
In step 2, the slave node 120 that has become free due to the movement of the task is determined as the target slave node 120 to which the task of the processing request is to be assigned. If the schedule processing unit 112 cannot prepare a slave node 120 capable of completing the processing of the requested task within the delivery date even if the task is moved, the schedule processing unit 112 unlocks the locked slave node 120 if any

.

For example, it is determined whether the processing of the requested task can be completed within the deadline. When it is determined that the processing of the requested task can be completed within the due date by unlocking, the schedule processing unit 112 unlocks the locked slave node 120 . The schedule processing unit 112 determines the unlocked slave node 120 as the target slave node 120 to which the task of the processing request is to be assigned.

[0049]

If the slave node 120 to which the task of the processing request is to be assigned is not found in the processing up to this point, the schedule processing unit 112 determines that the slave node 120 should be added to the system 100 by scale-out.

The scale-out processing unit 114 performs processing for

adding computer nodes to the system 100 by scale-out. More specifically, the scale-out processing unit 114 accesses the management computer on the IaaS side using an interface prepared by the IaaS side and requests scale-out to the own system 100 .

[0051]

The slave communication unit 115 communicates with the slave node 120 . For example, the slave communication unit 115 requests the slave node 120 to which the task of the received processing request is to be assigned to process the task. The slave communication unit 115 also receives the processing result of the requested task from the slave node 120 as a response. When a task is moved, the slave communication unit 115 notifies the source slave node 120 of the stop of the task, and notifies the destination slave node 120 of the execution of the task.

. The rescheduling processing unit 116, for example, periodically refers to the management i nformation stored in the schedule information storage unit 113, and targets slave nodes 120 t hat do not have tasks to be executed

. The rescheduling processing unit 116 also refers to the management information stored in the schedule information storage unit 113 and executes a simulation of migrating a task runni ng on a certain slave node 120 to another slave node 120 . . The rescheduling processing unit 116 detects tasks that can be completed within the deadline even if they are moved to anothe r slave node 120 . [0054]

The rescheduling processing unit 116 determines whether or not the slave node 120 having no task to be executed can be prepared by moving the detected task. If it is determined that a slave node 120 that does not have a task to be executed can be prepared by moving the tas k, the rescheduling processing unit 116 transfers the task to another slave node 120 via the sl ave communication unit 115. to run. The movement of tasks is the same as in the case of the schedule processing unit 112 described above. The rescheduling unit 116 targets the slave no de 120, which no longer has tasks to be executed due to the movement of tasks, for scale shr ink.

The rescheduling processing unit 116 also determines whether or not it

is possible to prepare a slave node 120 in which the number of tasks to be executed is equal to or less than a predetermined number by moving the detected tasks. If it is determined that a slave node 120 can be prepared in which the number of tasks to be executed by task move ment is equal to or less than a predetermined number, the rescheduling processing unit 116 p erforms the process of moving the corresponding task to another slave node 120 via slave co mmunication. 115. Reschedule processing part

116 sets a lock on the slave node 120 for which the number of tasks to be executed due to ta sk movement is equal to or less than a predetermined number. As a general rule, the locked sl ave node 120 is not assigned a task with a new processing request, so it becomes the target of scale shrink after the processing of the remaining tasks is completed. The scale shrink pro cessing unit 117 performs processing for deleting the target slave node 120 from the system 100 by scale shrink

.

More specifically, the scale shrink processing unit 117 uses an interface prepared by the IaaS side to access the management computer on the IaaS side and request scale shrinking of the target slave node 120 . The slave node 120 has a master communication section 121 and an application 122

.

As shown in FIG. 4, the slave node 120 can run multiple types of applications 122a, b, . When the task of the processing request is assigned, the task processing is executed by the applicati on 122 corresponding to the processing request.

[0058]

The master communication unit 121 communicates with the master node 110 . For example, the master communication unit 121 receives a task execution request or a stop request from t he master node 110, and performs processing for starting or stopping task execution. Further, when task processing is completed, the master communication unit 121 returns a processing r esult response to the master node 110 .

FIG.

5 is a diagram showing an example of a virtual machine system that implements a node acc ording to this embodiment.

[0060]

The virtual machine system shown in FIG. 5 is, for example, a system in which one or more virtual machines operate on one physical machine. In the example of the virtual machine syst em shown in FIG. 5, a plurality of virtual machines 30 including a master node 110 and slave nodes 120 are operating using the resources of the computer 10, which is a physical machine, such as the CPU 11 and memory 12. . In the virtual machine system shown in FIG. 5, the ma ster node 110 and slave nodes 120 are realized by the same physical machine, but in a cloud computing environment, the master node 110 and each slave node 120 are different. It is ofte n implemented on a physical machine.

In the virtual machine system shown in FIG .

5, the hypervisor 20 is software that implements a virtual environment using the computer 1 0 . A virtual machine 30 including the master node 110 and slave node 120 can be constructe d on the hypervisor 20 . The computer 10, which implements the master node 110 and slave node 120 shown in FIG

.

, an input device 16, an output device 17, and other hardware. The storage device 13 is, for e xample, an external storage device such as a HDD (Hard Disk Drive) or an auxiliary storage d evice. The medium reading/writing device 15 is, for example, a CD-R (Compact Disc Recordab le) drive or a DVD-R (Digital Versatile Disc Recordable) drive. The input device 16 is, for exam ple, a keyboard/mouse. The output device 17 is, for example, a display device such as a displ ay. Note that the hardware configuration of the computer 10 can be arbitrarily designed as re quired.

The master node 110, slave node 120, and functional units provided in each node shown in F IG. 4 can be realized by hardware such as the CPU 11 and memory 12 provided in the comput er 10, and software programs . A program executable by the computer 10

The gram is stored in the storage device 13, for example, read out to the memory 12 when ex

ecuted, and executed by the CPU 11. FIG.

The computer 10

can also read a program directly from a portable recording medium and execute processing according to the program. The computer 10 can also execute processing according to the received program every time the program is transferred from the server computer. Furthermore, this program can be recorded in a computer-readable recording medium.

Processing by the master node 110 according to this embodiment will now be described using a

more specific example.

FIGS.

6 to 9 are diagrams for explaining an example of a simulation of assignment of processing request tasks by the schedule processor in the master node of this embodiment.

FIG .

6A shows an example of notation of tasks. In FIG. 6A, solid figures represent task processing. The vertical length of the figure indicating task processing indicates the resource consumption of the task, and the horizontal length indicates the processing time of the task. Also, in FIG. 6A, the right end of the outline figure indicates the due date of the task. The due date is the deadline for completing the processing of the task designated by the client 200 . In the following description, all tasks are represented as shown in FIG. 6(A).

FIG . 6B shows the time t_0

from the client 200. shows the schedule of tasks executed by the slave nodes 120a and 120b included in the system 100 when a processing request is received. As shown in FIG. 6(B), the system 100 has two slave nodes 120 at this time: #a slave node 120a and #b slave node 120b. Note that the schedule information storage unit 113 stores management information in which the schedule of tasks executed by the slave nodes 120 included in the system 100 is converted into data, for example, as shown in the graph of FIG. 6B. In FIG. 6B, the vertical axis of the graph indicates the amount of resources consumed by the slave node, and the horizontal axis indicates the passage of time. t_{-1} to t_3 indicate times at equal intervals.

FIG. 6C

is a diagram showing the task X of the processing request received from the client 200 at time t_0 . As shown in FIG. 6(C), the processing of the processing request task X is indicated by hatching so as to be distinguished from other tasks. As shown in FIG. 6C, the due date of time t3 is specified for task X of the processing request .

[0070]

Note that there are many well-known techniques for estimating the task processing time and resource consumption, such as methods based on past results and theoretical methods, so a detailed description is omitted here. Estimation of the processing time of a task differs depending on the target processing of the task. For example, the image processing time is affected by the image file size. Processing using a database is affected by the number of accesses to th

e database. As for the resource consumption of a task, for example, if a value is determined f or each application 122 that processes the task, that value can be used. The resource consum ption amount may be inquired of the slave node 120 . In addition, various well-known techniq ues can be used.

In the master node 110 , when the schedule processing unit 112 receives a processing reques t, it

first verifies whether the task of the processing request can be assigned to the slave node 1 20 under the current circumstances.

FIG .

7(A) shows the execution of the process request task X at #a so that the process execution i s started at time t0 .

An example of verification assigned to a slave node 120a is shown. Also, FIG. 7B shows an ex ample of verification in which the task X of the processing request is assigned to the #b slave node 120b so as to start processing execution at time t0 . In either case, the resource consum ption of the node exceeds the resource limit of the node, so the verification result is NG.

FIG. 7C

shows an example of verification in which task X requesting processing is scheduled after tas k A#1 executed by slave node 120a of #a, which finishes processing the earliest, is complete d. In this case, the verification result is NG because the processing end time of the processing request task X exceeds the due date t3 . Next, the schedule processing unit 112 performs ver ification to move a task whose processing can be completed by the due date even if the task i s restarted with another task

.

As shown in FIG. 8A, task B#3 executed by the #b slave node 120b can be moved to the #a s lave node 120a in terms of resource consumption. Processing can be completed by the due da te even if the system is restarted. FIG. 8(B) shows an example of verification in which the pro cessing request task X is assigned to the #b slave node 120b whose resource consumption ha s decreased due to the movement of the tasks shown in FIG. 8(A). Even if the task is moved, the resource consumption of the node exceeds the resource limit of the node, so the verificati on result is NG.

[0075]

Since there is no other locked slave node 120 , the schedule processing unit 112 determines that the slave node 120 will be added by the scale-out processing by the scale-out processing unit 114 . FIG. 9 shows a state in which the task X requesting processing is assigned to the # c slave node 120 c added by the scale-out processing unit 114 . As described above, the ma ster node 110 according to the present embodiment performs verification including scheduling in the current state of the slave node 120, and furthermore, even if verification including task migration is performed, the task can be completed within the deadline

.

Scale out only if the task of the processing request cannot be assigned so that the processing is finished. As a result, useless scale-out can be suppressed, so that the system 100 can be o perated efficiently without unnecessary billing.

10 and 11 are diagrams for explaining an

example of task movement simulation by the rescheduling processor in the master node of t his embodiment.

FIG .

10 shows the schedule of tasks executed by the slave nodes 120a, 120b, and 120c of the sy stem 100 at time t0 . As shown in FIG. 10, at this point, the system 100 has three slave node s 120: #a slave node 120a, #b slave node 120b, and #c slave node 120c.

[0079]

First, in the master node 110, the rescheduling processing unit 116 periodically refers to the schedule information storage unit 113 to check whether there is a slave node 120 that has no task to be executed. As shown in FIG. 10, all the slave nodes 120 are executing processing at this point, so there is no slave node 120 that has no task to execute. At this time, the resched uling processing unit 116 determines that there is no slave node 120 that can be scaled down as it is.

Next, the rescheduling processing unit 116 performs verification to move the task that can be completed by the due date even if it

is restarted by another task.

FIG. 11A

shows an example of verification in which task B#1 executed by slave node 120b of #b is re started by slave node 120a of #a. As shown in Figure 11(A), the task

If B#1 is restarted by another slave node 120, the processing end time will exceed the deliver y date t2 , so the verification result will be NG. The rescheduling unit 116 determines that it is not possi ble to move the task and perform scale shrinking on the #b slave node 120b.

FIG. 11B

shows an example of verification in which task C#1 executed by slave node 120c of #c is res tarted by slave node 120a of #a. As shown in FIG. 11B, task C#1 can be completed by the de adline t3 even if the slave node 120a of #a is restarted. Furthermore, when task C#1 is move d to the slave node 120a of #a, there is no task to be executed by the slave node 120c of #C, so scale shrinking can be performed on the slave node 120c of #C. The rescheduling unit 11 6 instructs the #C slave node 120c to stop task C#1 and the #A slave node 120a to execute t ask C#1 via the slave communication unit 115

.

do. Since there are no more tasks to be executed by the #C slave node 120c, the reschedulin g unit 116 targets the #C slave node 120c for scale shrink. The scale shrink processing unit 1 17 executes scale shrink processing for the #C slave node 120c.

[0084]

In this way, the master node 110 according to the present embodiment actively creates slav e nodes 120 that do not have tasks to be executed by moving tasks to other slave nodes 120, and executes scale shrink. As a result, it is possible to positively delete useless slave nodes 12 0, so that it is possible to operate the system 100 efficiently without unnecessary billing. 12 and 13 are diagrams for explaining an example of setting a lock on a slave node by the resche duling processor in the master node of this embodiment
. FIG . 12 shows the schedule of tasks executed by the slave nodes 120a and 120b of the sy stem 100 at time t0 . As shown in FIG. 12, the system 100 has two slave nodes 120 at this ti me: #a slave node 120a and #b slave node 120b. In the master node 110, when the slave no de 120 that has no tasks to be executed cannot be prepared even if the tasks are moved, th e rescheduling processing unit 116 reduces the number of tasks to be executed by moving the tasks to a predetermined number or less. Verifies whether the slave node 120 can be prepare d. For example, the predetermined number is 1 here. FIG. 13A shows an example of verifica tion in which task B#2 executed by the #b slave node 120b is restarted by the #a slave node 120a. As shown in FIG. 13(A), task B#2 has a deadline of t 3 even if the slave node 120a of #a is restarte d.

Processing can be completed by Even if task B#1 executed by slave node 120b of #b is to be restarted by slave node 120a of #a, task B#1 will be moved because the processing end time will exceed the due date t2 . Can not.
Assuming that task B#2 is
moved to #a slave node 120a, as shown in FIG. . At this time, the rescheduling processing u nit 116 instructs the #B slave node 120b to stop the task B#2 and instructs the #A slave nod e 120a to execute the task B#2 via the slave communication unit 115. do.

Also, as shown in FIG. 13(B), a lock is set for the slave node 120b of #b, for which the only task to be executed is B#1 . Information on the slave node 120 that has set the lock is record ed in a storage unit such as the schedule information storage unit 113 that can be accessed b y the schedule processing unit 112 . As a general rule, the #b slave node 120b is not assigne d a new processing request task. can be deleted. As described above, the master node 110 according to the present embodiment moves tasks to other slave nodes 120, actively creates slave nodes 120 with fewer tasks to be executed, and creates new slave nodes 120 for those slave nodes 120
.

Suppress task allocation for processing requests. As a result, the environment of the system 1 00 becomes an environment where it is easy to create slave nodes 120 that do not have tasks to be executed, and it is possible to positively delete useless slave nodes 120, so it is efficient to avoid unnecessary billing. Operation of the system 100 becomes possible.

FIG.

14 is a diagram for explaining an example of unlocking a slave node by the schedule process ing unit in the master node of this embodiment.

[0093]

Here, it is assumed that the system 100 receives a processing request for task X shown in FI G. 6(C) from the client 200 in the state shown in FIG. 13(B). At this time, the schedule proces sing unit 112 attempts to allocate the processing request task X to the unlocked #a slave nod e 120a as shown in FIG. Cannot be allocated because it would exceed the resource limit. Furt hermore, there is no other slave node 120 to which the task can be transferred. At this time, the schedule processing unit 112 verifies whether or not task X requested by the slave node 1 20b of #b can be completed by the due date by unlocking the locked slave node 120b of #b

.

do. As shown in FIG. 14B, the slave node 120b of #b can complete the processing of the task X of the processing request by the due date. is released, and the task X of the processing req uest is assigned to the #b slave node 120b.

As described above, the slave node 120 that is locked is assigned

a task requesting processing only when the task requesting processing cannot be assigned t o another slave node 120 . As a result, it is possible to suppress the occurrence of scale-out w hile maintaining an environment that facilitates scale-shrinking to the very limit, so that the s ystem 100 can be operated efficiently without unnecessary billing.

The master node 110 according to this embodiment gives the highest priority to completing ta sk processing within the deadline, so the system 100

always maintains the minimum processing performance.

[0097]

15 and 16 are processing flowcharts when the master node of this embodiment accepts a pr ocessing request. In the master node 110, the client communication section 111 receives a processing request from a client (step S10)

.

A delivery date is specified in the processing request received here. The client communication unit 111 determines whether the processing request can be accepted (step S11). If the proce ssing request is not acceptable (NO in step S11), the client

The communication unit 111 responds to the client that the processing request cannot be acc epted (step S12), and terminates the processing. If the processing request can be accepted (YES in step S11), the schedule processing unit 112 refers to the management information in the schedule information storage unit 113 and performs a simulation of allocating the task of t

he processing request to the current slave node 120

.

(step S13). Here, for example, verification including scheduling is performed as shown in FIG. The

schedule processing unit 112 determines whether or not it is possible to allocate the task of the processing request to the current slave node 120 (step S14). If the task of the processing request can be assigned (YES in step S14), the schedule processing unit 112 determines the s lave node 120 to which the task of the processing request is assigned (step S15). The slave c ommunication unit 115 requests the determined slave node 120 to process the task of the pro cessing request (step S22).

If it is not possible to assign the task of the processing request (NO in step S14), the schedule processing unit

112 refers to the management information in the schedule information storage unit 113, mo ves the existing task, and A simulation of assigning tasks is performed (step S16). Here, for e xample, as shown in FIG. 8, if there is an existing task that can be completed within the deliv ery date even if it is moved to another slave node 120 and re-executed, the existing task is m oved and resource It is verified whether the task of the processing request can be assigned to the slave node 120 that has become free.

[0102]

The schedule processing unit 112 determines whether it is possible to allocate the task of th e processing request by moving the existing task (step S17). If the task of the processing req uest can be assigned (YES in step S17), the schedule processing unit 112 moves the correspo nding existing task (step S18). More specifically, the schedule processing unit 112 requests, vi a the slave communication unit 115, the slave node 120 from which the existing task is move d to stop the task. Also, the schedule processing unit 112 requests the slave node 120 to whic h the existing task is moved to execute the task via the slave communication unit 115 . The sl ave communication unit 115 requests the slave node 120, whose resource becomes available due to the migration of the existing task, to process the requested task (step S22).

If it is not possible to allocate the task of the processing request (NO in step S17), the schedu le processing unit 112 determines that there is a locked slave node 120 ,

and if the slave node 120 is unlocked, It is determined whether or not the task of the proces sing request can be assigned (step S19). If the lock is released and it becomes possible to all ocate the task of the processing request (YES in step S19), the schedule processing unit 112 unlocks the locked slave node 120 (step S20). The slave communication unit 115 requests the unlocked slave node 120 to process the requested task (step S22). This case is the case show n in the example of FIG.

[0104]

If there is no locked slave node 120 or if it is not possible to allocate the processing request task even if the lock is released (NO in step S19), the scale-out processing unit 114 executes

scale-out processing (step S21). A slave node 120 is added to the system 100 by scale-out. T he slave communication unit 115 requests the added slave node 120 to process the requested task (step S22). This case is the case shown in the example of FIG. The slave communicatio n unit 115 receives a processing result response to the processing request from the slave nod e 120

.

is received (step S23), the client communication unit 111 transmits the response to the client (step S24).

FIG.

17 is a flow chart of rescheduling by the master node of this embodiment. In the master no de 110, the rescheduling processing section 116 starts this processing at a predetermined tim ing

. The rescheduling processing unit 116 refers to the management information in the schedul e information storage unit 113 and determines whether there is a slave node 120 that current ly has no task to be executed (step S30). If there is a slave node 120 that does not have a ta sk to be executed (YES in step S30), the scale shrink processing unit 117 executes scale shrin k processing for that slave node 120 (step S31). The scale shrink removes the slave node 120 from the system 100 . The rescheduling processing unit 116 refers to the management infor mation in the schedule information storage unit 113 and performs a task migration simulation (step S32). Here, for example, as shown in FIG. 11, if there is a task that can be completed w ithin the deadline even if it is moved to another slave node 120 and re-executed, there is no t ask to move and execute the task. It is verified whether the slave node 120 can be created. F or example, as shown in FIG. 13, if there is a task that can be completed within the deadline even if it is moved to another slave node 120 and re-executed, a predetermined number of ta sks are moved and executed. It is verified whether the following slave nodes 120 can be gene rated. [0110]

The rescheduling unit 116 determines whether it is possible to generate a slave node 120 th at does not have a task to be executed by moving the task, that is, whether it is possible to m ove the task and perform scale shrinking (step S33). If scale shrinking becomes possible by m oving the task (YES in step S33), the rescheduling processor 116 moves the task (step S34). More specifically, the rescheduling processing unit 116 requests the slave node 120 from whic h the task is moved to stop the task via the slave communication unit 115 . Also, the resched

uling processing unit 116 requests the slave node 120 to which the task is moved to execute t he task via the slave communication unit 115 . The scale shrink processing unit 117 executes scale shrink processing for the slave node 120 that has no tasks to be executed due to the mo vement of the tasks (step S35). The scale shrink removes the slave node 120 from the syste m 100 . If scale shrinking is not possible even after the task is moved (NO in step S33), the rescheduling processing unit 116 determines that there is a slave node 120 where the number of tasks to be executed by moving the task is less than the predetermined number

.

It is determined whether or not (step S36). If there is no slave node 120 whose number of tas ks to be executed is equal to or less than the predetermined number even after the task is mo ved (NO in step S36), the rescheduling processing unit 116 ends the process.

[0112]

If there is a slave node 120 in which the number of tasks to be executed by migrating tasks i s equal to or less than the predetermined number (YES in step S36), the rescheduling process ing unit 116 migrates the tasks (step S37). More specifically, the rescheduling processing unit 116 requests the slave node 120 from which the task is moved to stop the task via the slave c ommunication unit 115 . Also, the rescheduling processing unit 116 requests the slave node 1 20 to which the task is moved to execute the task via the slave communication unit 115 . The rescheduling processing unit 116 locks the slave node 120 for which the number of tasks to b e executed by moving tasks is less than a predetermined number.

is set (step S38). If all tasks remaining without being unlocked are processed, the slave node 120 to which the lock is set becomes the target of scale shrink in subsequent steps S30 and S 31.

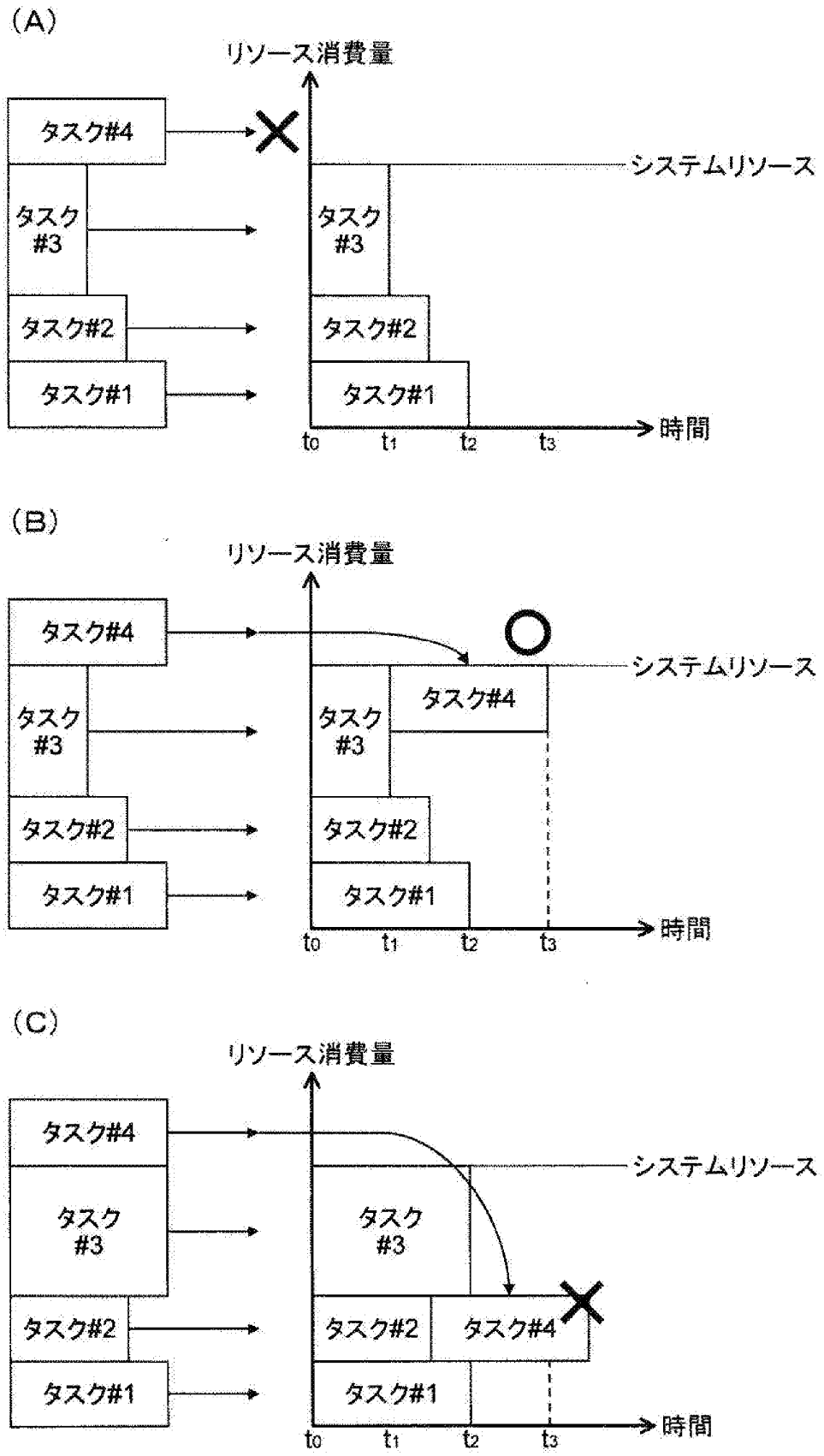
Although the present embodiment has been described above

, it is a matter of course that the present invention can be modified in various ways within th e spirit and scope of the invention. 100

System 110 Master node 111 Client communication unit 112 Schedule processing unit 113 Schedule information storage unit 114 Scale-out processing unit 115 Slave communic ation unit 116 Reschedule processing unit 117 Scale shrink processing unit 120 Slave nod e 121 Master Communication unit 122 Application 200 Client 300 Network

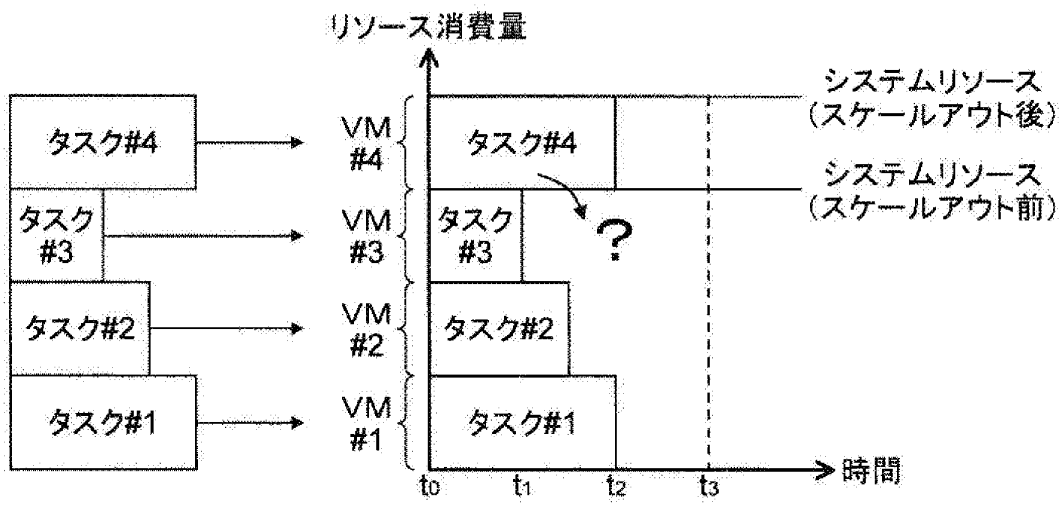
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[Fig. 1]

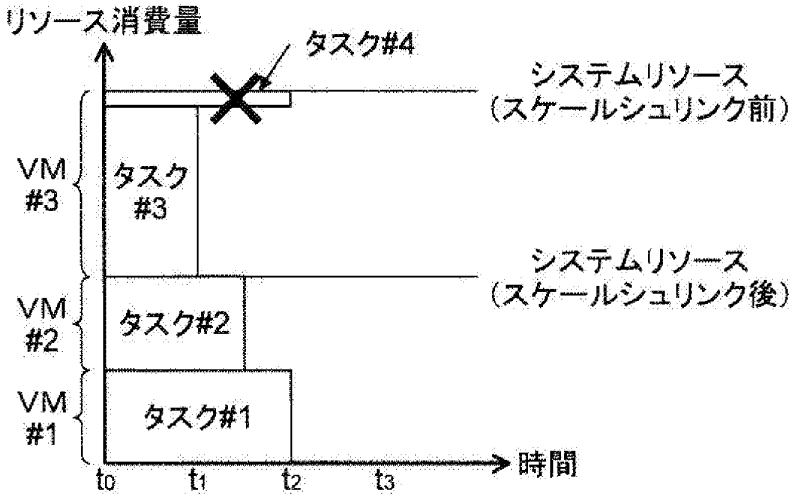

(A)
リソース消費量
タスク#4
タスク#3
タスク#2
タスク#1
システムリソース
タスク#3
タスク#2
タスク#1
時間
t0
t1
t2
t3
(B)
リソース消費量
タスク#4
タスク#3
タスク#2
タスク#1
システムリソース
タスク#4
タスク#3
タスク#2
タスク#1
時間
t0
t1
t2
t3
(C)
リソース消費量
タスク#4
タスク#3
タスク#2
タスク#1
システムリソース
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タスク#1
時間
t0
t1
t2
t3

[Figure 2]

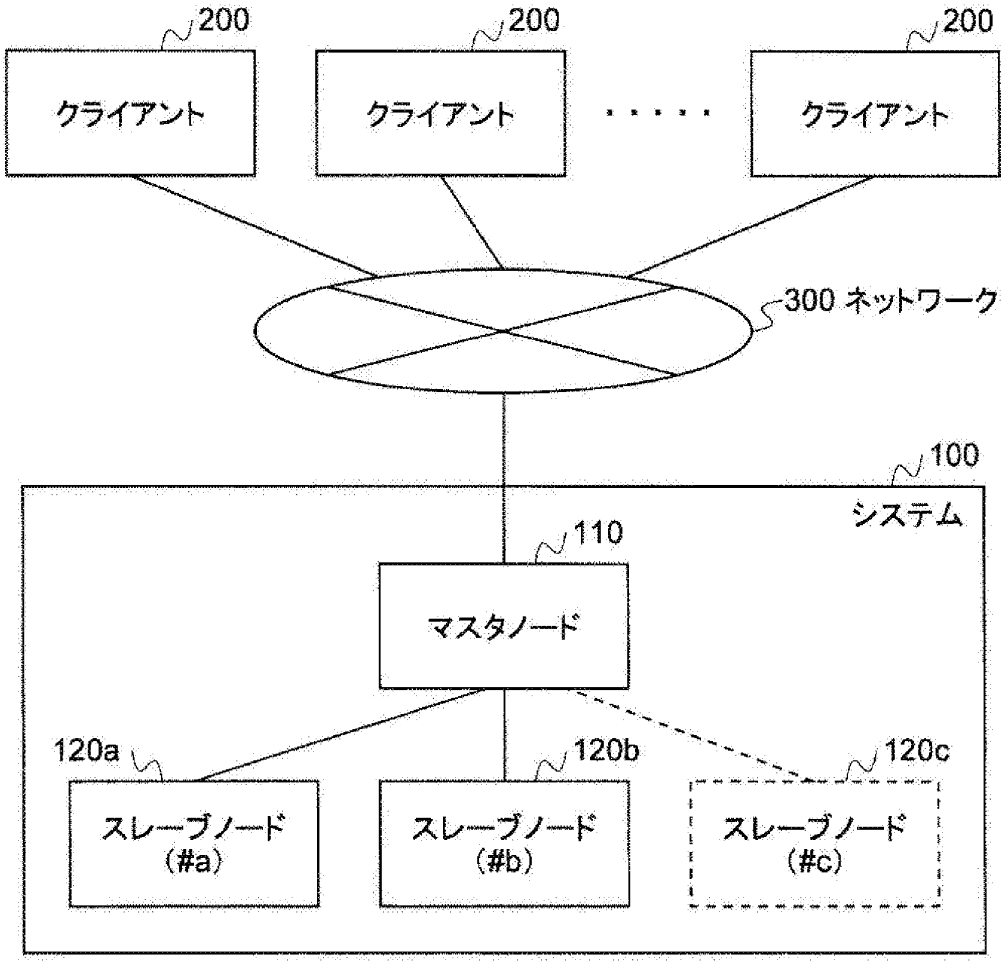
（A）


リソース消費量
タスク#4
タスク
#3
タスク#2
タスク#1
VM
#4
VM
#3
VM
#2
VM
#1
タスク#4
タスク
#3
?
タスク#2
タスク#1
システムリソース
（スケールアウト後）
システムリソース
（スケールアウト前）
時間
t0
t1
t2
t3

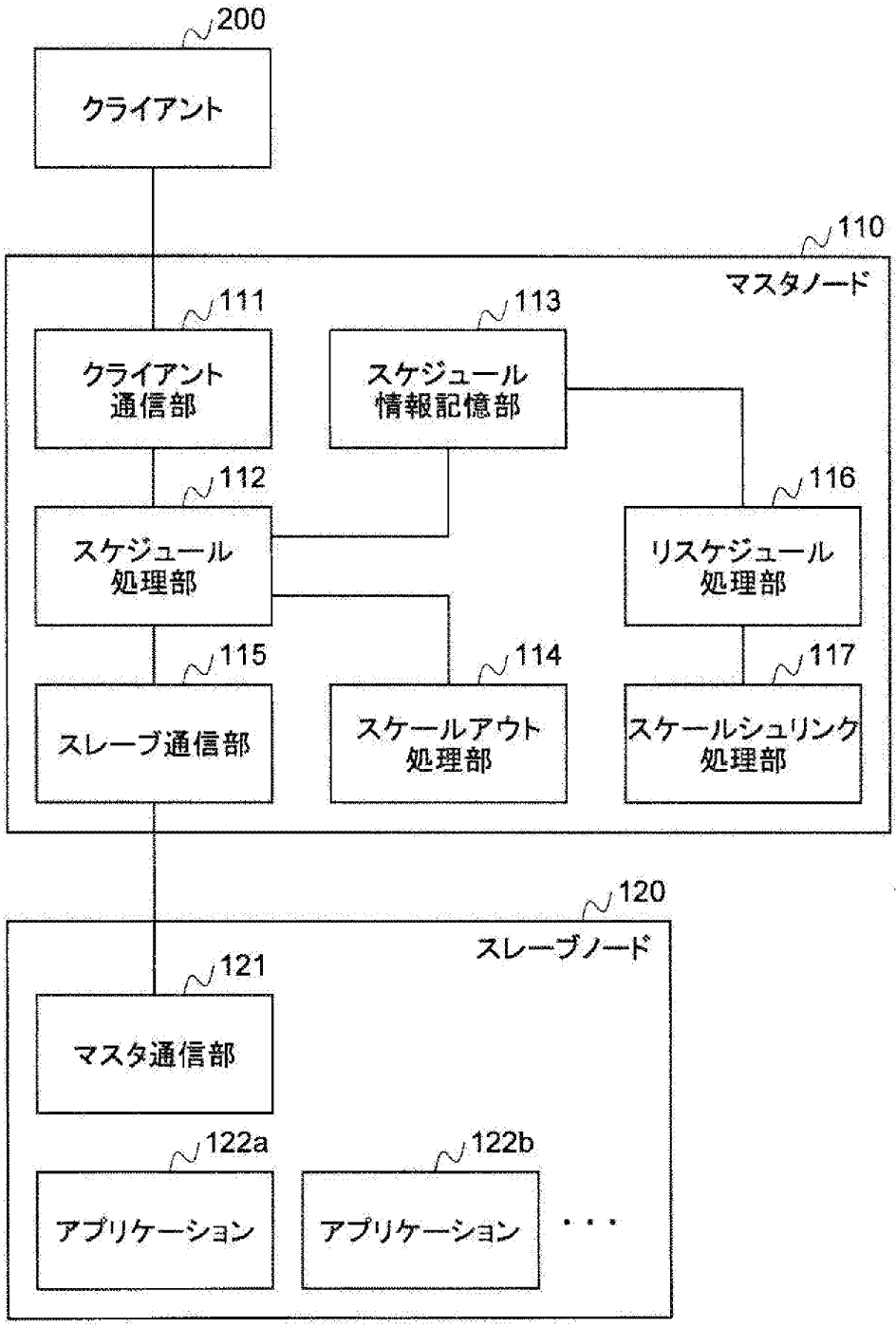
（B）


リソース消費量
タスク#4
システムリソース
（スケールシュリンク前）
VM
#3
タスク
#3
システムリソース
（スケールシュリンク後）
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時間
t0
t1
t2
t3

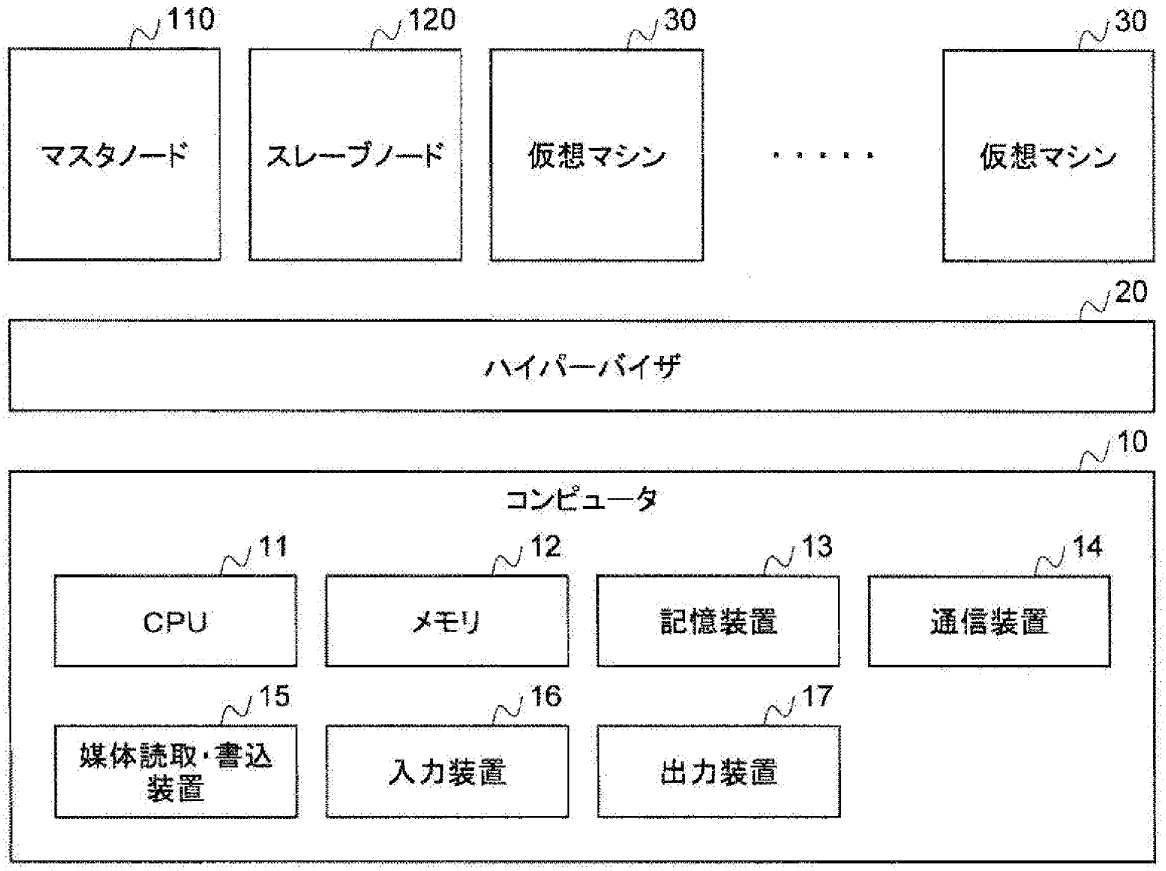
[Figure 3]


200
クライアント
200
クライアント
・・・・・
200
クライアント
300 ネットワーク
100
システム
110
マスタノード
120a
スレーブノード
(#a)
120b
スレーブノード
(#b)
120c
スレーブノード
(#c)

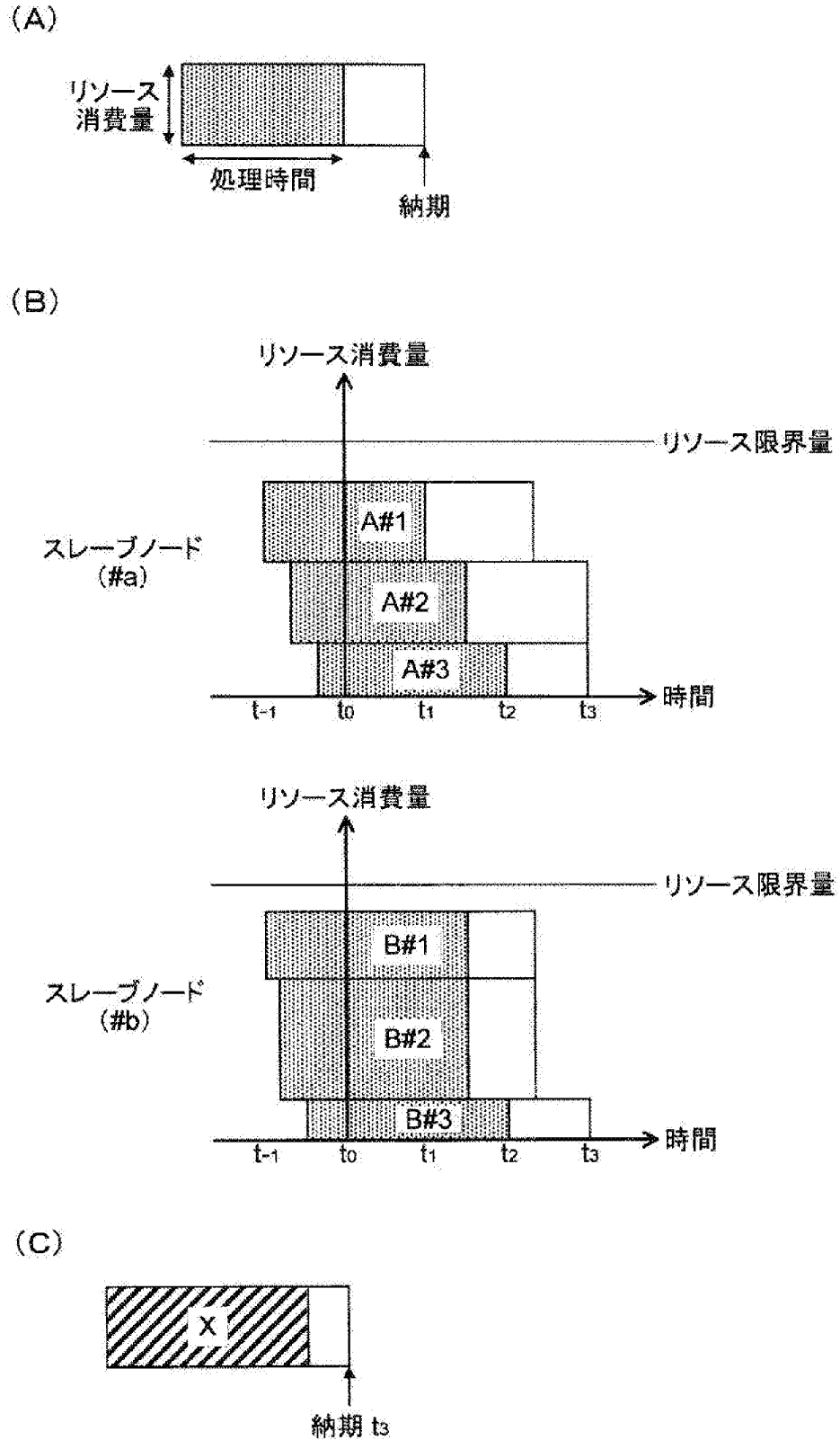
[Figure 4]


200
クライアント
110
マスタノード
111
クライアント
通信部
113
スケジュール
情報記憶部
112
スケジュール
処理部
116
リスケジュール
処理部
115
スレーブ通信部
114
スケールアウト
処理部
117
スケールシュリンク
処理部
120
スレーブノード
121
マスタ通信部
122a
アプリケーション
122b
アプリケーション
・・・

[Figure 5]

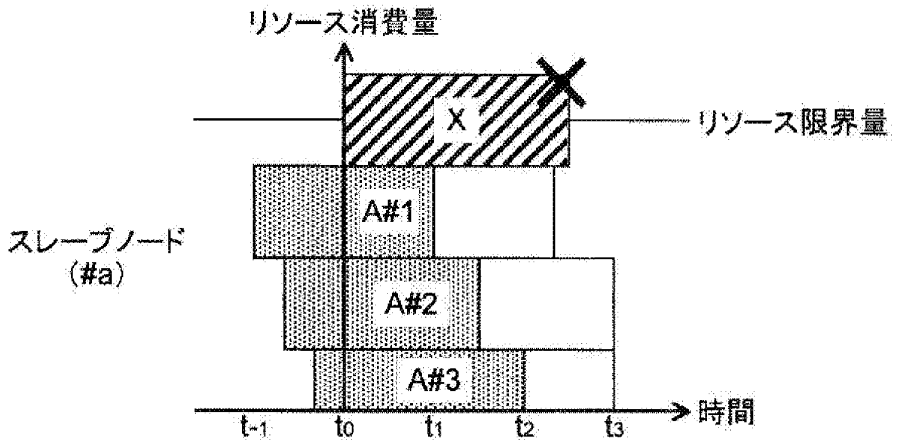

110
120
30
30
マスタノード
スレーブノード
仮想マシン
・・・・・
仮想マシン
20
ハイパーバイザ
10
コンピュータ
11
12
13
14
CPU
メモリ
記憶装置
通信装置
15
16
17
媒体読取・書込装置
入力装置
出力装置

[Fig. 6]

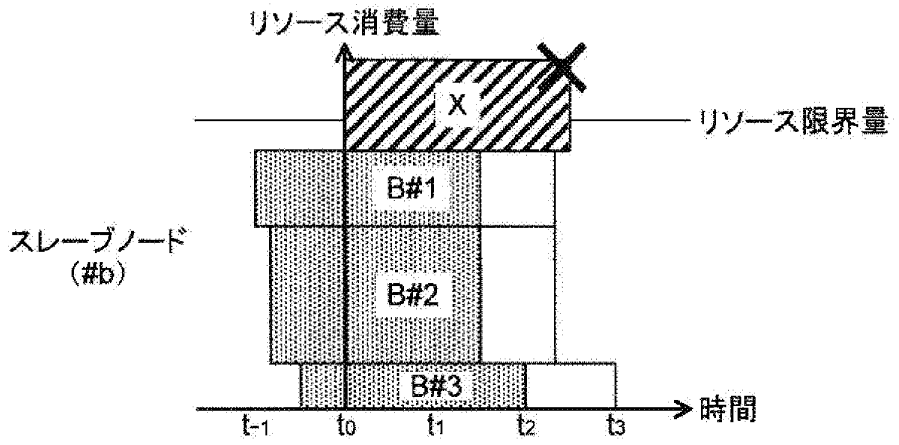

(A)
リソース
消費量
処理時間
納期
(B)
リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
t-1
t0
t1
t2
t3
(C)
X
納期 t3

[Fig. 7]

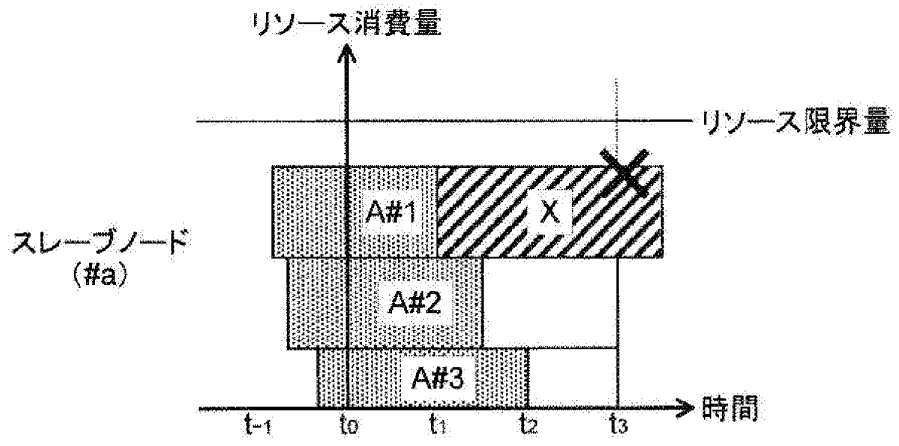
(A)


リソース消費量
X
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
t-1
t0
t1
t2
t3

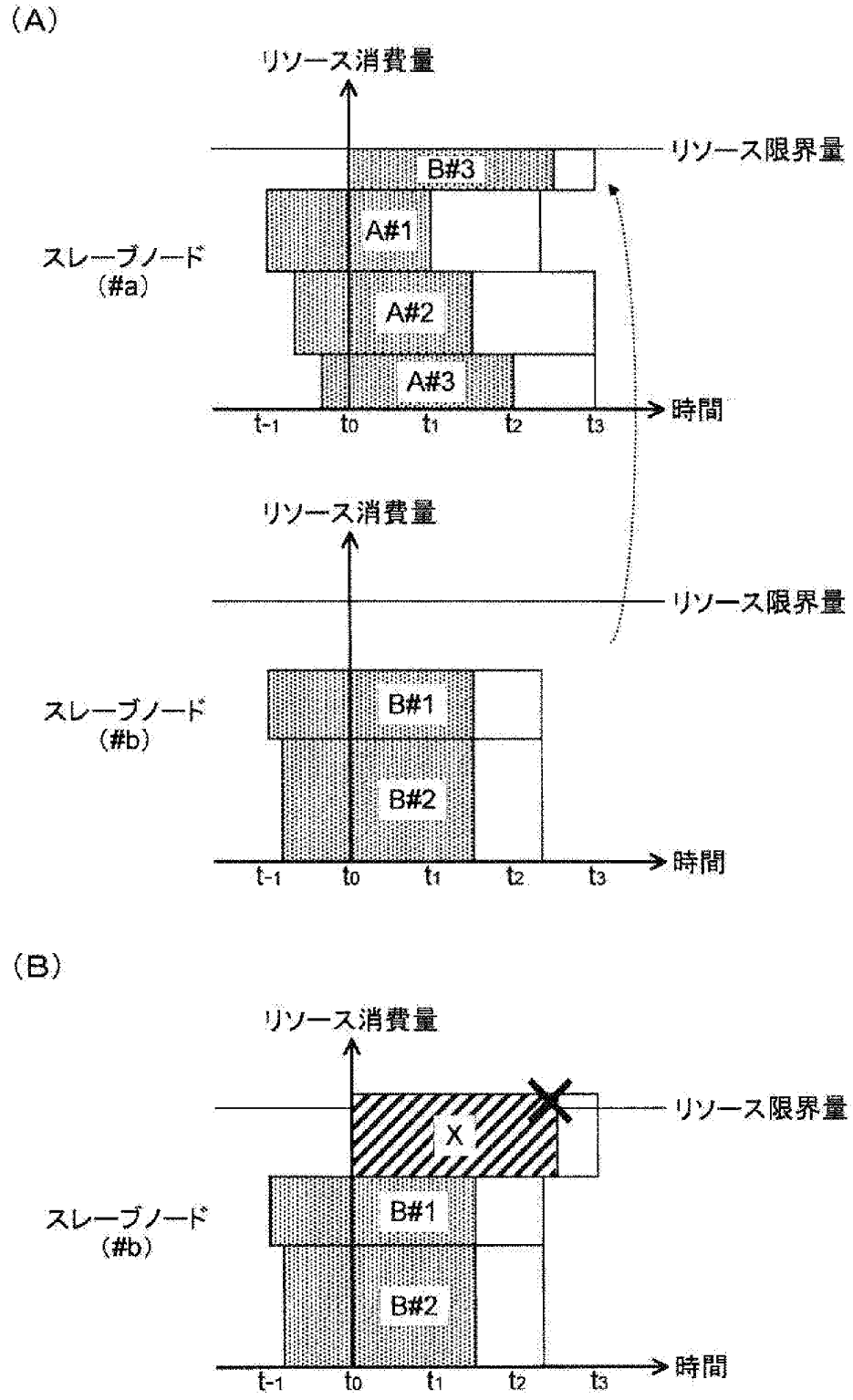
(B)


リソース消費量
X
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
t-1
t0
t1
t2
t3

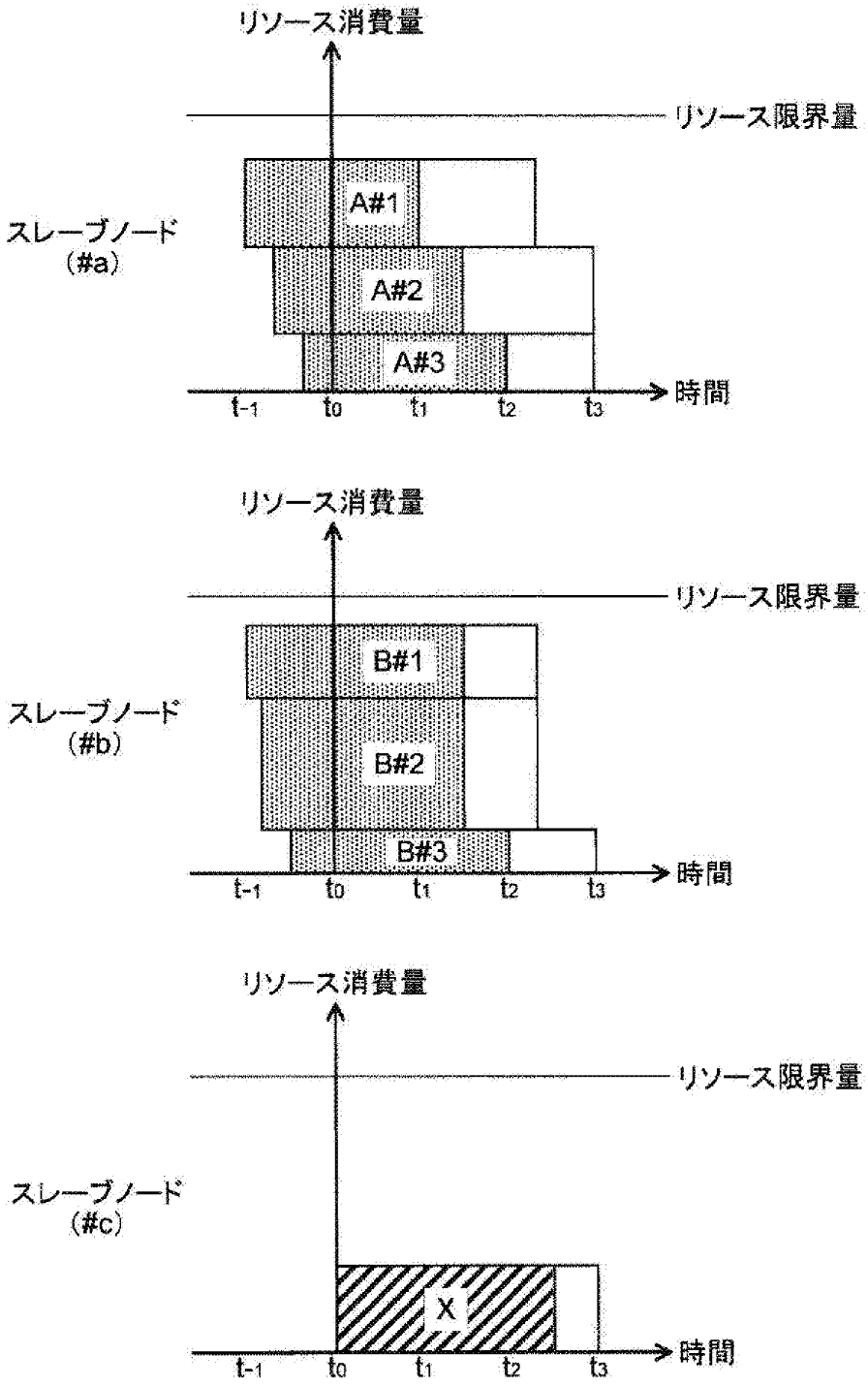
(C)


リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
X
A#2
A#3
時間
t-1
t0
t1
t2
t3

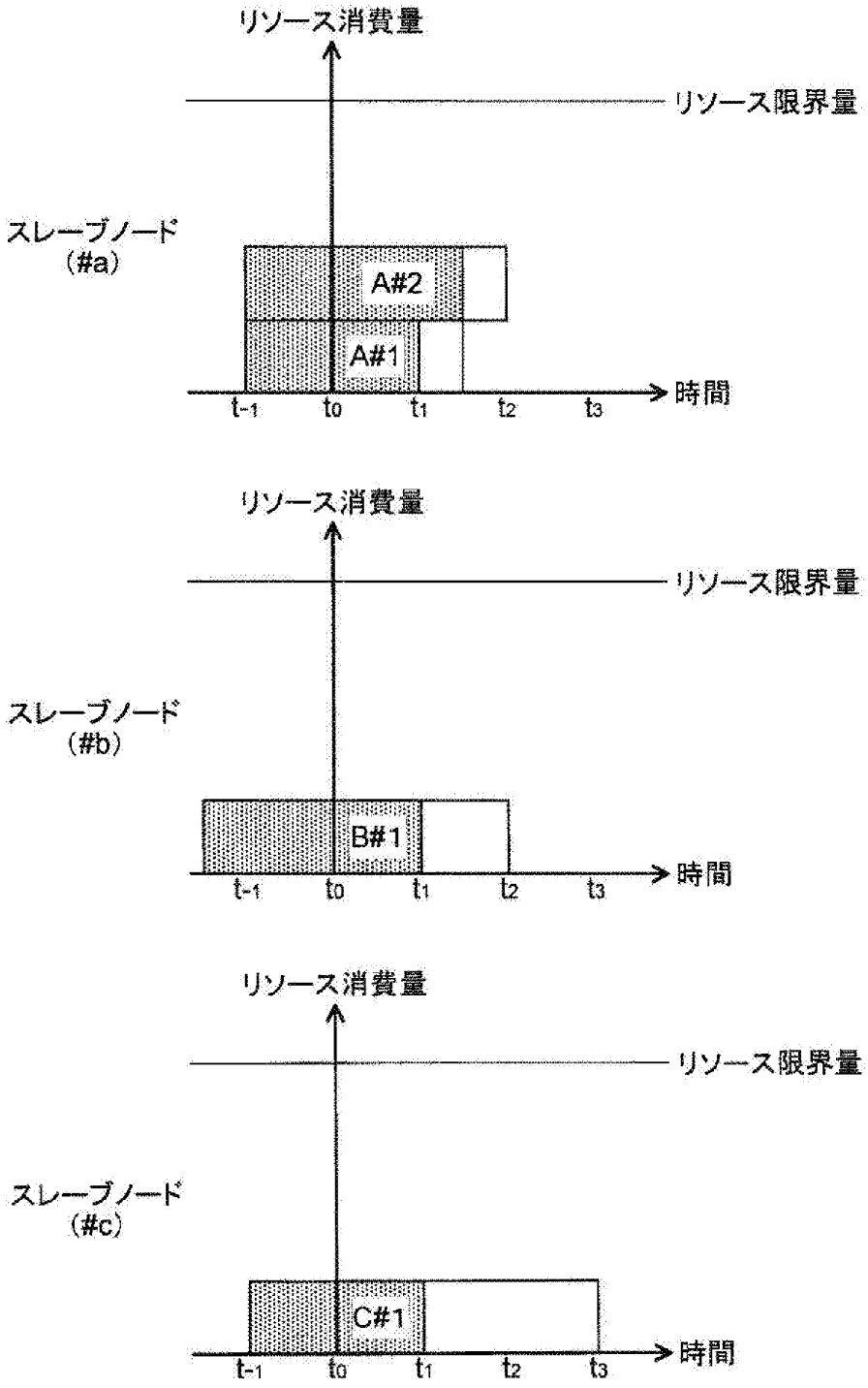
[Fig. 8]


(A)
リソース消費量
リソース限界量
B#3
A#1
スレーブノード
(#a)
A#2
A#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
時間
t-1
t0
t1
t2
t3
(B)
リソース消費量
リソース限界量
X
スレーブノード
(#b)
B#1
B#2
時間
t-1
t0
t1
t2
t3

[Fig. 9]

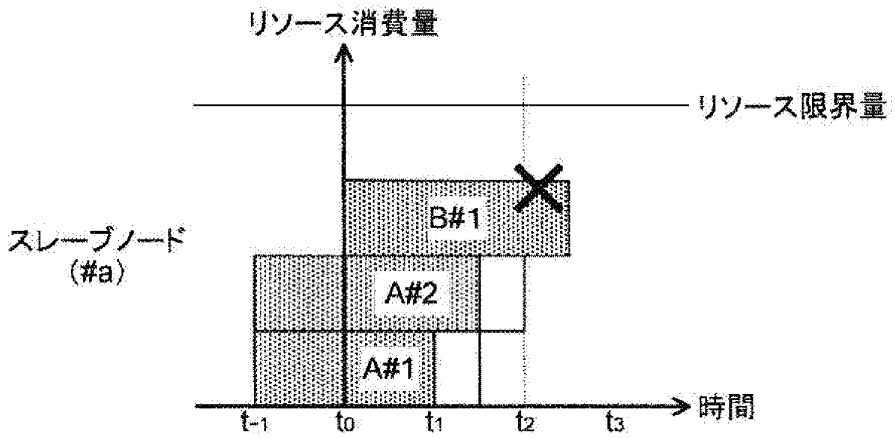

リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#c)
X
時間
t-1
t0
t1
t2
t3

[Fig. 10]

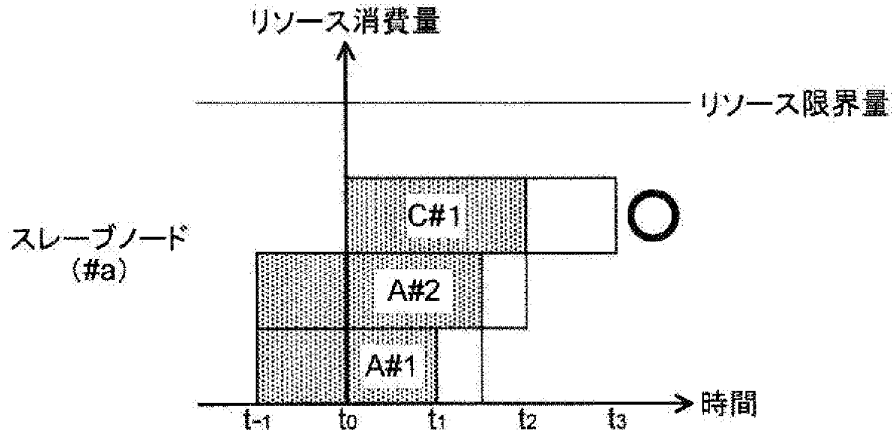

リソース消費量
リソース限界量
スレーブノード
(#a)
A#2
A#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#c)
C#1
時間
t-1
t0
t1
t2
t3

[Fig. 11]

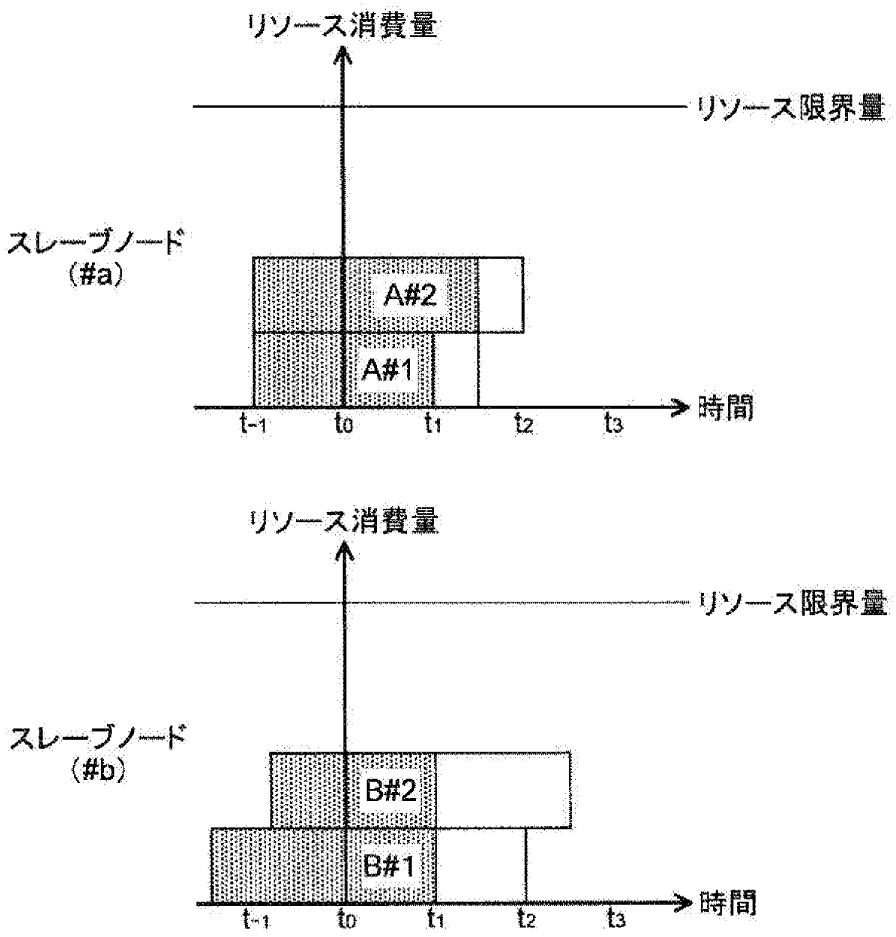
（A）


リソース消費量
リソース限界量
スレーブノード
（#a）
B#1
A#2
A#1
時間
t-1
t0
t1
t2
t3

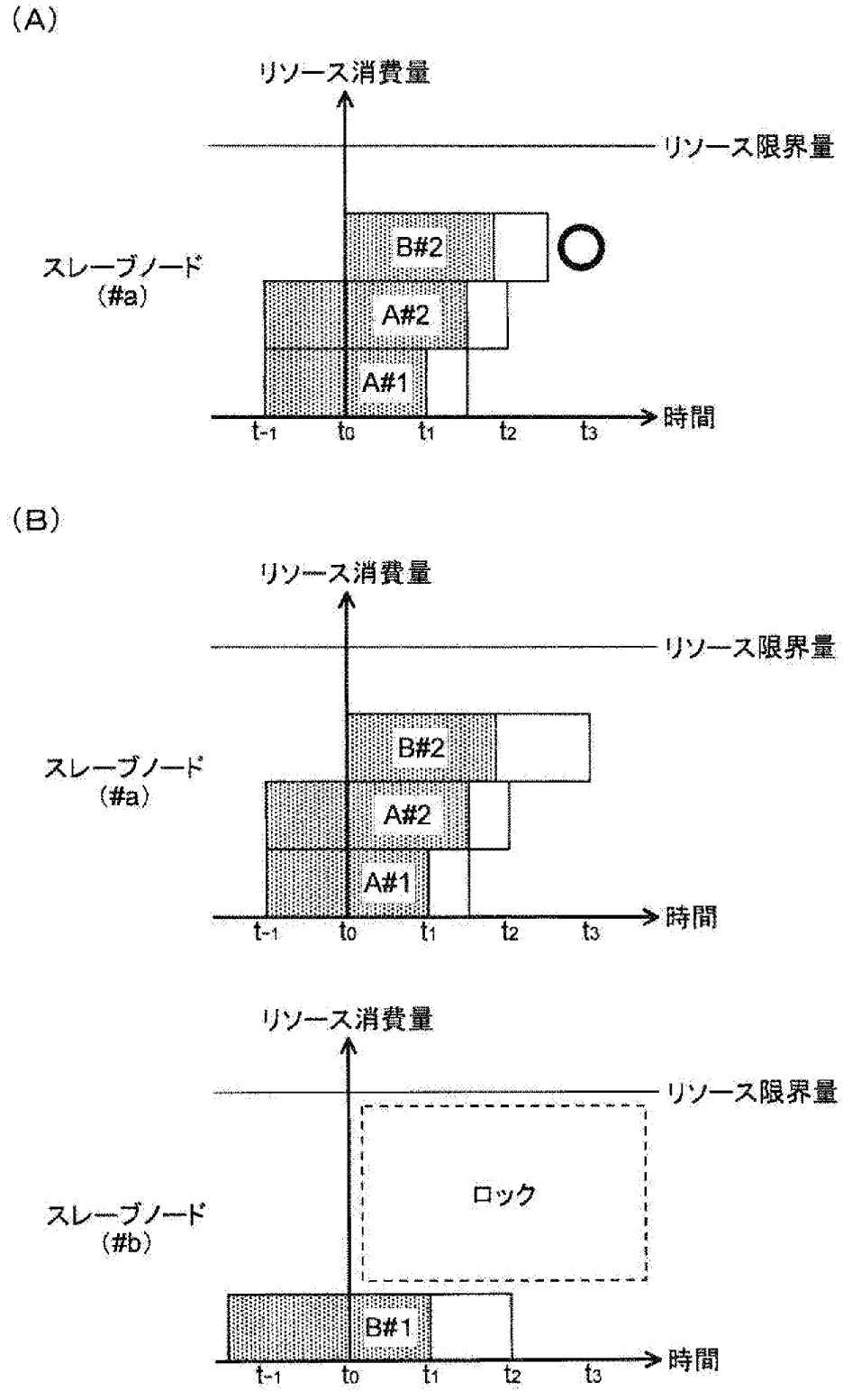
（B）


リソース消費量
リソース限界量
スレーブノード
（#a）
C#1
A#2
A#1
時間
t-1
t0
t1
t2
t3

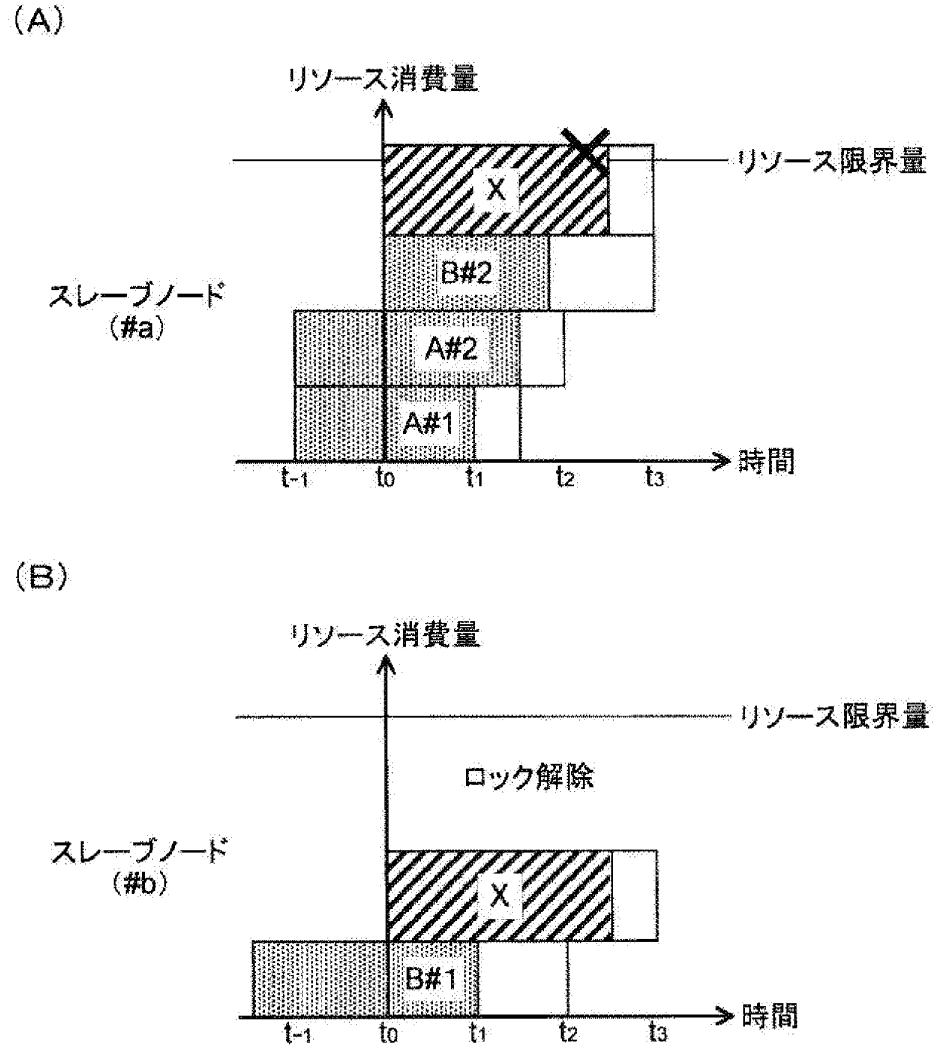
[Fig. 12]


リソース消費量
リソース限界量
スレーブノード
(#a)
A#2
A#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
B#2
B#1
時間
t-1
t0
t1
t2
t3

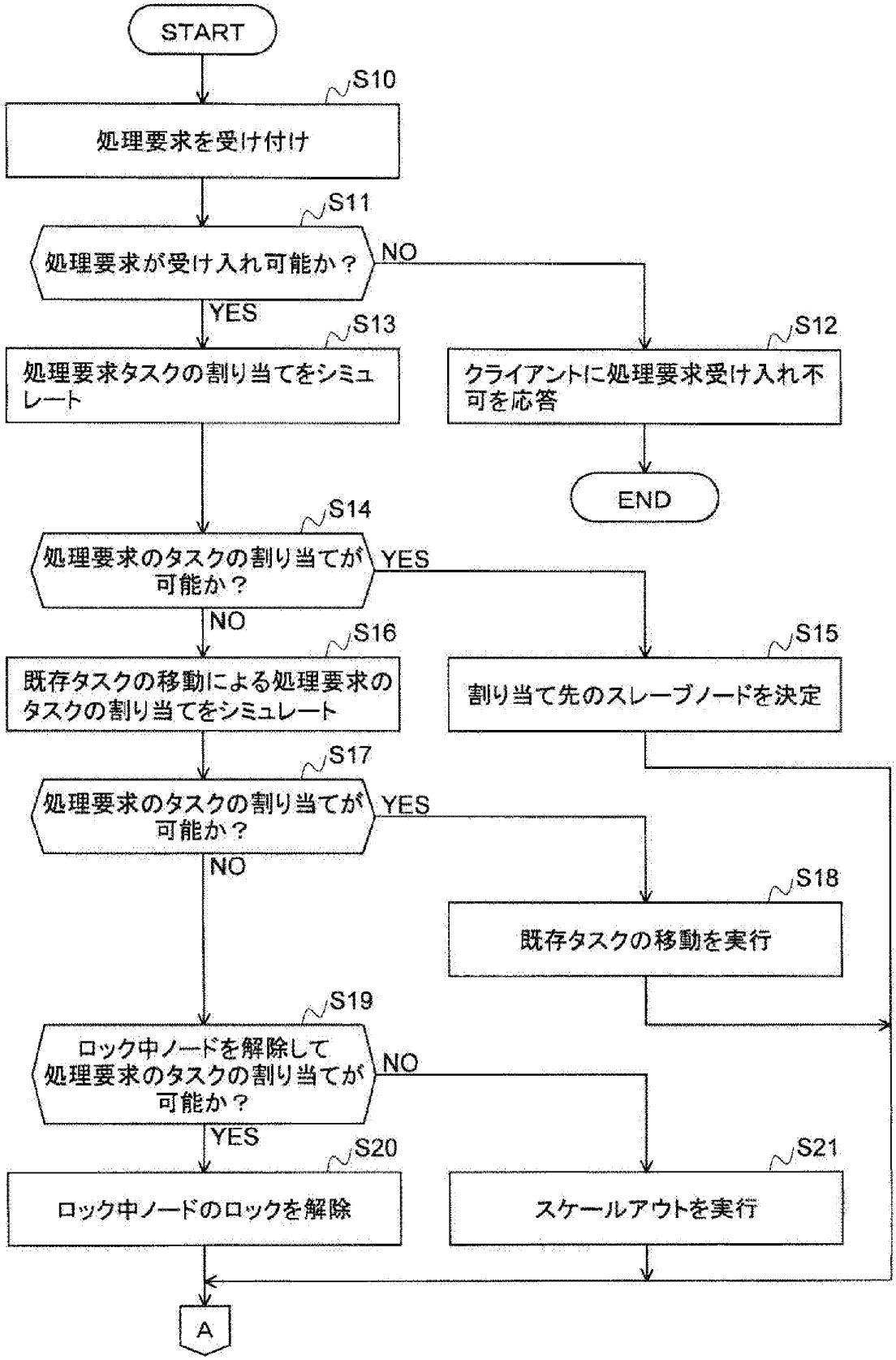
[Fig. 13]


(A)
リソース消費量
リソース限界量
スレーブノード
(#a)
B#2
A#2
A#1
時間
t-1
t0
t1
t2
t3
(B)
リソース消費量
リソース限界量
スレーブノード
(#a)
B#2
A#2
A#1
時間
t-1
t0
t1
t2
t3
リソース消費量
リソース限界量
スレーブノード
(#b)
ロック
B#1
時間
t-1
t0
t1
t2
t3

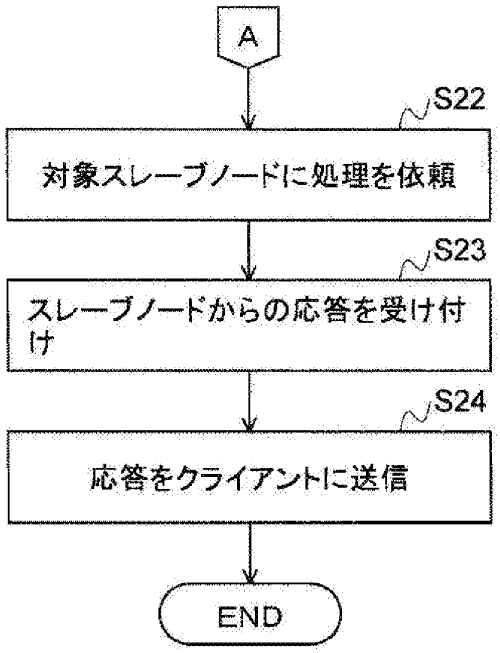
[Fig. 14]


(A)
リソース消費量
リソース限界量
X
B#2
スレーブノード
(#a)
A#2
A#1
時間
t-1
t0
t1
t2
t3
(B)
リソース消費量
リソース限界量
ロック解除
スレーブノード
(#b)
X
B#1
時間
t-1
t0
t1
t2
t3

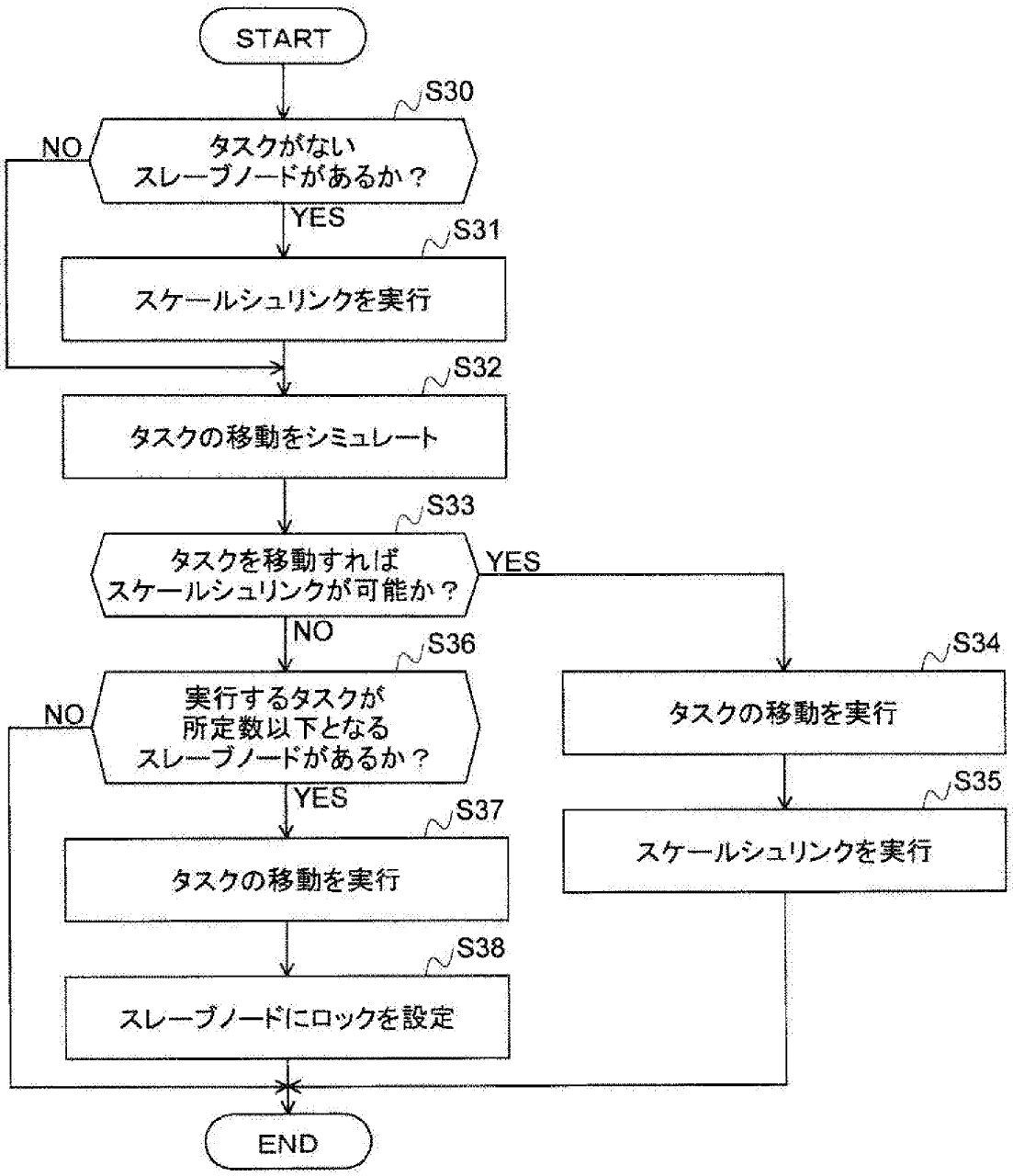
[Fig. 15]


START
S10
処理要求を受け付け
S11
処理要求が受け入れ可能か？
NO
YES
S13
処理要求タスクの割り当てをシミュレート
S12
クライアントに処理要求受け入れ不可を応答
END
S14
処理要求のタスクの割り当てが可能か？
YES
NO
S16
既存タスクの移動による処理要求のタスクの割り当てをシミュレート
S15
割り当て先のスレーブノードを決定
S17
処理要求のタスクの割り当てが可能か？
YES
NO
S18
既存タスクの移動を実行
S19
ロック中ノードを解除して処理要求のタスクの割り当てが可能か？
NO
YES
S20
ロック中ノードのロックを解除
S21
スケールアウトを実行
A

[Fig. 16]


A
S22
対象スレーブノードに処理を依頼
S23
スレーブノードからの応答を受け付け
S24
応答をクライアントに送信
END

[Fig. 17]


START
S30
タスクがない
スレーブノードがあるか？
NO
YES
S31
スケールシュリンクを実行
S32
タスクの移動をシミュレート
S33
タスクを移動すれば
スケールシュリンクが可能か？
YES
NO
S34
タスクの移動を実行
S35
スケールシュリンクを実行
S36
実行するタスクが
所定数以下となる
スレーブノードがあるか？
NO
YES
S37
タスクの移動を実行
S38
スレーブノードにロックを設定
END

drawing open

1 2 3 Four Five 6 7 8 9 Ten ...

Magnify and Rotate

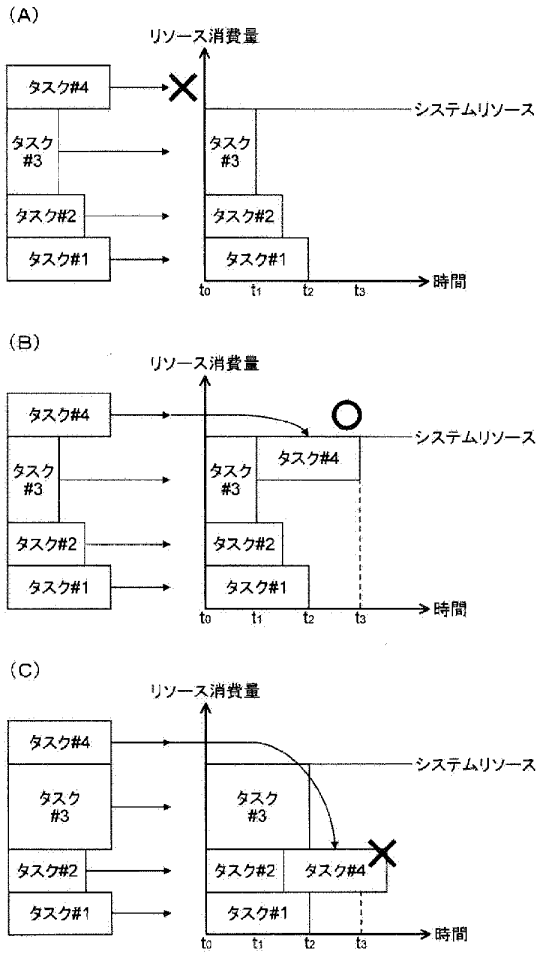


Figure 1

1 / 1 display

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Bibliographic data: JP5867238 (B2) — 2016-02-24

AUTOSCALING METHOD, AUTOSCALING PROGRAM AND COMPUTER NODE

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Applicant(s): FUJITSU LTD, ; 富士通株式会社

Classification: **- international:** ***G06F9/50***
- cooperative:

Application number: JP20120078501 20120330 Global Dossier

Priority number(s): JP20120078501 20120330

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Abstract of JP2013210683 (A)

PROBLEM TO BE SOLVED: To provide a technology for allowing application of a system with excellent efficiency of charging.SOLUTION: A master node 110 manages tasks to be executed by the respective slave nodes 120. A schedule information storage part 113 stores management information for managing the tasks to be executed by the respective slave nodes 120. A schedule processing part 112 verifies whether or not there is a slave node 120 capable of terminating processing of a task of a processing request in a delivery. In addition, the schedule processing part 112 verifies whether or not a computer node capable of terminating processing of the task of the processing request can be prepared in the delivery when a task whose processing can be terminated even by other computer nodes is moved. As results of verification, when both are negative, a scale out processing part 114 increases the slave nodes 120 by scale out.

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最終頁に続く

(54)【発明の名称】オートスケーリング方法，オートスケーリングプログラムおよびコンピュータノード

(57)【特許請求の範囲】
【請求項１】
要求された処理を複数の仮想化されたコンピュータノードに分散して実行するシステムにおいて，該システムで実行するタスクの管理を行うコンピュータノードが，
納期が指定された処理要求を受け付けた際に，記憶部に記憶された，前記システムが備えるコンピュータノードが実行するタスクを管理する管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行し，
前記割り当てのシミュレーションにより，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムのコンピュータノードの数を増加する処理を実行する
ことを特徴とするオートスケーリング方法。
【請求項２】
前記タスクの管理を行うコンピュータノードが，さらに，
前記管理情報を参照して，あるコンピュータノードで動作するタスクを，他のコンピュータノードに移動するシミュレーションを実行し，
前記移動のシミュレーションにより，他のコンピュータノードでも納期内に処理終了可能なタスクを移動して，実行するタスクがないコンピュータノードを用意できると判定された場合に，該他のコンピュータノードでも納期内に処理終了可能なタスクを移動し，

実行するタスクがないコンピュータノードを前記システムから削除する処理とを実行する
ことを特徴とする請求項１に記載のオートスケーリング方法。
【請求項３】
前記タスクの管理を行うコンピュータノードが，さらに，
前記移動のシミュレーションにより，他のコンピュータノードでも納期内に処理終了可能なタスクを移動して，実行するタスクの数が所定数以下となるコンピュータノードを用意できると判定された場合に，該他のコンピュータノードでも納期内に処理終了可能なタスクを移動し，
実行するタスクの数が所定数以下のコンピュータノードを処理要求のタスクの割り当て対象外に設定する処理を実行する
ことを特徴する請求項２に記載のオートスケーリング方法。
【請求項４】
前記システムにコンピュータノードを増設する処理では，さらに，前記処理要求のタスクの割り当て対象外に設定されたコンピュータノードの設定を解除しても，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムにコンピュータノードを増設する
ことを特徴とする請求項３に記載のオートスケーリング方法。
【請求項５】
要求された処理を複数の仮想化されたコンピュータノードに分散して実行するシステムにおいて，該システムで実行するタスクの管理を行うコンピュータノードに，
納期が指定された処理要求を受け付けた際に，記憶部に記憶された，前記システムが備えるコンピュータノードが実行するタスクを管理する管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行し，
前記割り当てのシミュレーションにより，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムのコンピュータノードの数を増加する
処理を実行させるためのオートスケーリングプログラム。
【請求項６】
複数の仮想化されたコンピュータノードを備えるシステムにおいて，該システムで実行されるタスクの管理を行うコンピュータノードであって，
前記システムが備えるコンピュータノードが実行するタスクを管理する管理情報の記憶部と，
納期が指定された処理要求を受け付けた際に，前記管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行するスケジュール処理部と，
前記スケジュール処理部により，前記処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に，前記システムのコンピュータノードの数を増加する処理を実行するスケールアウト処理部とを備える
ことを特徴とするコンピュータノード。
【発明の詳細な説明】
【技術分野】
【０００１】
本発明は，システムが備えるコンピュータノード数を制御するオートスケーリング方法，オートスケーリングプログラムおよびコンピュータノードに関するものである。
【背景技術】

【０００２】
従来のオンプレミスのシステムでは，システムが持つリソース量が固定であったので，そのシステムが持つリソース量を超えて，クライアントからの処理要求を受け付けることができなかった。
【０００３】
これに対して，近年発展しているクラウドコンピューティングを利用したシステムでは，システムが持つリソース量を動的に変更可能である。そのため，クライアントから要求される処理を実行することによってシステムのリソース消費量がシステムが持つリソース量を超えてしまうような場合でも，システムのリソースを動的に増やすことで，クライアントからの要求を受け付け可能となる。
【０００４】
このようなシステムのリソースを増減する技術として，システムにおける仮想化されたコンピュータノードのリソース量を増減するスケールアップ・スケールダウンと呼ばれる技術がある。しかし，仮想化されたコンピュータノードのリソースの増加には，物理マシンのリソース量の限界がある。
【０００５】
システムのリソースを増減する別の技術として，システムにおけるコンピュータノードの数を増減するスケールアウト・スケールシュリンクと呼ばれる技術がある。この技術では，システムのリソース量の増加に，物理マシンのリソース量の限界がない。システムのリソース消費率に応じて自動でスケールアウト・スケールシュリンクを行う，オートスケーリングと呼ばれる技術もある。
【０００６】
なお，分散バッチシステムにおいて，新たなバッチ処理が要求された際に，ある処理サーバで実行中のバッチ処理を他のサーバに移行し，処理可能となったサーバで新しいバッチ処理を実行することで，バッチ処理のデッドラインを管理する技術が知られている。
【先行技術文献】
【特許文献】
【０００７】
【特許文献１】特開２００２－３４２０９８号公報
【発明の概要】
【発明が解決しようとする課題】
【０００８】
しかし，上述のように，システムのリソース消費率に応じてオートスケーリングを行うと，スケールアウトによって無駄なコンピュータノードが増設されたり，誤ったスケールシュリンクによってシステムが実行中の処理が強制的に中断される場合がある。クラウドコンピューティングにおいて，コンピュータノードの数に応じた従量課金が行われる場合には，無駄なスケールアウトによって無駄な課金が発生してしまう場合がある。
【０００９】
一側面では，本発明は，課金の効率がよいシステムの運用が可能となる技術を提供することを目的とする。
【課題を解決するための手段】
【００１０】
１態様では，オートスケーリング方法では，要求された処理を複数の仮想化されたコンピュータノードに分散して実行するシステムにおいて，該システムで実行するタスクの管理を行うコンピュータノードが，納期が指定された処理要求を受け付けた際に，記憶部に記憶されたシステムが備えるコンピュータノードが実行するタスクを管理する管理情報を参照して，該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行し，割り当てのシミュレーションにより，処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく，さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても処理要求のタスクを納期内に処理終了可能なコンピュータノードを用

意できないと判定された場合に，システムのコンピュータノードの数を増加する処理を実行する。

【発明の効果】

【００１１】

１態様では，課金の効率がよいシステムの運用が可能となる。

【図面の簡単な説明】

【００１２】

【図１】オンプレミスで実現されるシステムの課題を説明する図である。

【図２】クラウドコンピューティングで実現されるシステムの課題を説明する図である。

【図３】本実施の形態によるシステムの構成例を示す図である。

【図４】本実施の形態による各ノードの機能構成例を示す図である。

【図５】本実施の形態によるノードを実現する仮想マシンシステムの例を示す図である。

【図６】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図７】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図８】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図９】本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【図１０】本実施の形態のマスタノードにおけるリスケジュール処理部によるタスクの移動シミュレーションの例を説明する図である。

【図１１】本実施の形態のマスタノードにおけるリスケジュール処理部によるタスクの移動シミュレーションの例を説明する図である。

【図１２】本実施の形態のマスタノードにおけるリスケジュール処理部によるスレーブノードにロック設定を行う例を説明する図である。

【図１３】本実施の形態のマスタノードにおけるリスケジュール処理部によるスレーブノードにロック設定を行う例を説明する図である。

【図１４】本実施の形態のマスタノードにおけるスケジュール処理部によるスレーブノードのロック解除を行う例を説明する図である。

【図１５】本実施の形態のマスタノードによる処理要求受け付け時の処理フローチャートである。

【図１６】本実施の形態のマスタノードによる処理要求受け付け時の処理フローチャートである。

【図１７】本実施の形態のマスタノードによるリスケジュールの処理フローチャートである。

【発明を実施するための形態】

【００１３】

以下，本実施の形態について，図を用いて説明する。

【００１４】

図１は，オンプレミスで実現されるシステムの課題を説明する図である。

【００１５】

図１に示す例において，タスクを示す図形の縦の長さは該タスクのリソース消費量を示し，横の長さは該タスクの処理時間を示す。また，図１に示す例において，グラフの縦軸はシステムのリソース消費量を示し，横軸は時間の経過を示す。t_0 ～ t_3 は，等間隔の時刻を示す。

【００１６】

オンプレミスのシステムでは，システムが持つリソースの量は固定となる。すなわち，あらかじめシステムが持つリソース量を超えたリソース消費量の処理を行うことはできない。図１に示す例において，システムリソースのラインは，システムが持つリソースの量

を示す。

【００１７】

例えば，図１（Ａ）において，システムに対して，タスク＃１～タスク＃４の処理要求が，ほぼ同時刻t_0にあったものとする。このとき，システムは，処理要求を受け付けた順，ここではタスク＃１，タスク＃２，タスク＃３，タスク＃４の順に処理を開始する。しかし，図１（Ａ）に示すように，タスク＃３の処理を開始したところで，システムのリソース消費量がシステムが持つリソース量に達してタスク＃４の処理を開始できない状態となり，タスク＃４の処理要求を受け付けられなくなる。

【００１８】

図１（Ｂ）に示す例は，スケジューリングを行うシステムの例である。スケジューリングを行うシステムでは，処理要求を受け付けた時点でタスクの処理時間を見積もり，処理要求が発生した時点でリソースに空きがなくても，実行中の他のタスクの終了後に受け付けた処理要求のタスクを実行するように，タスクのスケジューリングを行う。

【００１９】

例えば，最後に受け付けるタスク＃４の処理の納期が，時刻t_3であるものとする。図１（Ｂ）に示すように，最も処理終了時刻が早いタスク＃３の処理終了時刻がt_1であるので，タスク＃４をタスク＃３の後にスケジュールすれば，タスク＃４の処理終了時刻はt_3となり，納期に間に合う。この場合，タスク＃４の処理要求は，システムで受け付け可能となる。

【００２０】

ところが，図１（Ｃ）に示す例では，最も処理終了時刻が早いタスク＃２の後にタスク＃４をスケジュールすると，タスク＃４の処理終了時刻はt_3を超えてしまい，納期に間に合わない。この場合，タスク＃４の処理要求は，システムで受け付けられない。オンプレミスのシステムでは，スケジューリングを行っても，処理要求を受け付けできない場合がある。

【００２１】

このようなオンプレミスの技術の対極に存在するのが，クラウドコンピューティングの技術である。クラウドコンピューティングによって実現されるシステムのリソース量は，可変となる。

【００２２】

クラウドコンピューティングでは，システムが備える各コンピュータノードが，例えば仮想マシン（ＶＭ：Virtual Machine ）で実現される。なお，以下では，システムが備えるコンピュータノードを，単にノードとも呼ぶ。

【００２３】

クラウドコンピューティングにおいて，システムのリソース量を変更する技術として，例えば，スケールアップ・スケールダウンの技術がある。スケールアップは，ノードのリソース量を増加させる技術である。また，スケールダウンは，ノードのリソース量を減少させる技術である。スケールアップの技術を利用すれば，例えば，現状のリソースでは新たな処理要求のタスクを実行しても納期に間に合わないような場合でも，ノードのリソース量を増加させることで，新たな処理要求のタスクを納期に間に合うように実行できるようになる。

【００２４】

しかし，スケールアップ可能なリソースは，仮想マシンであるノードを実現する物理マシンのリソースが上限となるため，ノードのスケールアップには限界がある。また，通常は１つの物理マシン上に複数の仮想マシンのノードが配置されており，物理マシンのリソースを各ノードに配分しきって余剰がない場合には，他のノードの性能を下げることなく特定のノードの性能を上げることは不可能となる。例えば，マルチテナントの環境では，１つの物理マシン上で複数のテナントの仮想マシンを動作することになり，あるテナントの仮想マシンのリソース量を増やすために，他のテナントのリソース量を減らすといったことは，簡単にはできない。よって，スケールアップの技術を用いても，要求された処理

のタスクをすべて納期を保証して実行できるわけではない。

【００２５】

クラウドコンピューティングにおいて，システムのリソース量を変更する技術として，スケールアップ・スケールダウンの技術以外に，スケールアウト・スケールシュリンクの技術がある。スケールアウトは，システムにノードを増設する技術である。スケールシュリンクは，システムからノードを撤去する技術である。スケールアウトの技術を用いれば，ほぼ確実に要求された処理のタスクをすべて納期を保証して実行できるようになる。

【００２６】

ただし，クラウドコンピューティングの世界では，通常はサービス使用料金が従量制となっており，スケールアウトによってシステムが備えるノードの数が増加するにつれて，サービスの使用料金が増えてしまう。

【００２７】

図２は，クラウドコンピューティングで実現されるシステムの課題を説明する図である。

【００２８】

図２に示す例において，タスクを示す図形の縦の長さは該タスクのリソース消費量を示し，横の長さは該タスクの処理時間を示す。また，図２に示す例において，グラフの縦軸はシステムを構成するノードのリソース消費量の合計を示し，横軸は時間の経過を示す。t_0 ～ t_3 は，等間隔の時刻を示す。図２に示す例において，システムリソースのラインは，システムを構成するノードが持つリソースの量の合計を示す。

【００２９】

図２（Ａ）において，システムは，当初，ＶＭ＃１～ＶＭ＃３の３つのノードを備えているものとする。ここで，システムに対して，タスク＃１～タスク＃４の処理要求が，ほぼ同時刻 t_0 にあったものとする。このとき，システムでは，処理要求を受け付けた順，ここではタスク＃１，タスク＃２，タスク＃３，タスク＃４の順に，ノードにタスクが割り当てられ，処理が開始される。しかし，図２（Ａ）に示すように，ＶＭ＃３のノードにタスク＃３の処理を割り当てたところで，システムのすべてのノードのリソース消費量が上限となり，タスク＃４の処理を割り当て可能なノードがなくなる。

【００３０】

このとき，例えば図２（Ａ）に示すように，システムではスケールアウトが行われ，ＶＭ＃４のノードがシステムに増設される。図２（Ａ）に示すように，スケールアウトによってＶＭ＃４のノードがシステムに増設されることで，要求されたタスク＃４の処理が実行可能となる。例えば，クラウドコンピューティングにおいて，仮想マシンやネットワークなどのインフラをサービスとして提供するＩａａＳ（Infrastructure as a Service）ベンダのサービスとして，システムのリソース消費率が所定以上となったときに自動でスケールアウトを行うサービスがある。クラウドコンピューティングにおいて，自動でシステムの拡張／縮小を行う技術は，オートスケーリングとも呼ばれる。

【００３１】

ここで，タスク＃４の処理の納期が時刻 t_3 であるものとする。図２（Ａ）に示すように，最も処理終了時刻が早いタスク＃３の処理終了時刻が t_1 であるので，タスク＃４をタスク＃３の後にスケジュールすれば，タスク＃４の処理終了時刻は t_3 となり，納期に間に合う。

【００３２】

このように，タスクのスケジューリングを行うことができれば，スケールアウトによりＶＭ＃４のノードを増設しなくても，納期に間に合うようにタスク＃４の処理を実行することが可能であった。しかし，このような判断は，上述のＩａａＳのサービスのようにリソース消費を見ただけではできない。上述したように，クラウドコンピューティングでは，ノードが増えるごとに使用料金が増えるため，ノードを増設しなくても納期に間に合うようにタスクの処理を実行できるのであれば，ノードを増設したくないという要望がある。

【００３３】
また，無駄なノードの使用料金を抑えるために，システムで運用されていないと判断されるノードに対するスケールシュリンクが行われ，該ノードがシステムから撤去される。例えば，クラウドコンピューティングにおいて，ＩａａＳベンダのサービスとして，ノードのＣＰＵ（Central Processing Unit ）使用率が所定以下となったときに，該ノードではタスクの処理が行われておらずＯＳなどのミドルウェアしか動作していないと判断し，自動でスケールシュリンクを行うサービスがある。
【００３４】
だだし，ノードのリソース消費量が少ないからといって，必ずしも要求されたタスクの処理が行われていないとは限らない。たとえば，図２（Ｂ）に示す例において，ＶＭ＃３のノードでは，タスク＃３の処理が終了すると，リソース消費量が極端に減ってしまう。しかし，図２（Ｂ）に示す例において，ＶＭ＃３のノードでは，タスク＃３と並列にリソース消費量が少ないタスク＃４が実行されている。タスク＃３の処理の終了と同時にＶＭ＃３のノードに対するスケールシュリンクが行われると，タスク＃４の処理が強制終了されてしまう。このように，上述のＩａａＳベンダのサービスのようにリソース消費を見ただけでスケールシュリンクを判断すると，例えば，図２（Ｂ）に示すタスク＃４のようにリソース消費量が少ないタスクの処理を実行中であるノードを，誤って撤去してしまう可能性がある。
【００３５】
以下では，このような問題の解決を図った本実施の形態によるオートスケーリングの技術を説明する。
【００３６】
図３は，本実施の形態によるシステムの構成例を示す図である。
【００３７】
本実施の形態において，図３に示すシステム１００は，クラウドコンピューティングにおいて，ＩａａＳ側から提供される仮想マシンのノードから構成されるコンピュータシステムであるものとする。システム１００は，クライアント２００から要求された処理を，複数のノードで分散して実行する。システム１００とクライアント２００とは，ＬＡＮ（Local Area Network）やインターネットなどのネットワーク３００で接続されている。システム１００は，マスタノード１１０，スレーブノード１２０を備える。
【００３８】
マスタノード１１０は，クライアント２００からの処理要求を受け付け，各スレーブノード１２０に対するタスクの割り当てや，システム１００で実行するタスクの管理を行う。なお，本実施の形態によるマスタノード１１０は，スレーブノード１２０のスケールアウトやスケールシュリンクなどのオートスケーリングの処理を行う。なお，マスタノード１１０が，同時にスレーブノード１２０の１つであってもよい。
【００３９】
スレーブノード１２０は，マスタノード１１０から割り当てられた処理要求のタスクを実行するコンピュータノードである。スレーブノード１２０は，複数のタスクの並列処理が可能である。スレーブノード１２０は，オートスケーリングの処理によって，システム１００に増設，またはシステム１００から削除される。例えば，図３において，＃ａのスレーブノード１２０ａと＃ｂのスレーブノード１２０ｂがタスクの処理を実行している場合に，それらのスレーブノード１２０で実行しきれない処理要求があれば，＃ｃのスレーブノード１２０ｃがシステム１００に増設される。また，たとえば，＃ｃのスレーブノード１２０ｃが実行するタスクがなくなれば，＃ｃのスレーブノード１２０ｃがシステム１００から削除される。
【００４０】
クライアント２００は，システム１００に対して，システム１００が提供する処理の実行要求を行う上位アプリケーションを有するコンピュータである。なお，図１に示す例では，クライアント２００がシステム１００外部の装置となっているが，例えばクライアン

ト２００がシステム１００内部のノードであってもよい。

【００４１】

図４は，本実施の形態による各ノードの機能構成例を示す図である。

【００４２】

マスタノード１１０は，クライアント通信部１１１，スケジュール処理部１１２，スケジュール情報記憶部１１３，スケールアウト処理部１１４，スレーブ通信部１１５，リスケジュール処理部１１６，スケールシュリンク処理部１１７を備える。

【００４３】

クライアント通信部１１１は，クライアント２００からの処理要求を受け付ける。クライアント通信部１１１は，受け付けた要求の処理がシステム１００内で実行可能なものであれば，スケジュール処理部１１２に渡す。クライアント通信部１１１は，受け付けた要求の処理がシステム１００内で処理実行不可能なものであれば，その旨をクライアント２００に応答する。システム１００内で処理実行不可能な処理は，例えばスレーブノード１２０にないアプリケーションの処理や，１仮想マシンのスレーブノード１２０では納期までに終了できない大規模な処理などである。大規模な処理を，複数のノードで分散して実行する技術については，本実施の形態による技術の範囲外であるので，ここでは説明を行わない。クライアント通信部１１１は，スレーブノード１２０から受け取った処理結果をクライアント２００に通知する。

【００４４】

スケジュール処理部１１２は，クライアント通信部１１１が納期が指定された処理要求を受け付けた際に，スケジュール情報記憶部１１３に記憶された管理情報を参照して，該処理要求のタスクをスレーブノード１２０に割り当てるシミュレーションを実行する。

【００４５】

スケジュール情報記憶部１１３は，システム１００が備えるスレーブノード１２０が実行するタスクを管理する管理情報の記憶部である。スケジュール情報記憶部１１３に記憶された管理情報には，すべてのスレーブノード１２０で実行するタスクのスケジュールが記録されている。

【００４６】

より具体的には，スケジュール処理部１１２は，まず，現行の状態で，受け付けた処理要求のタスクを，指定された納期内に処理終了可能なスレーブノード１２０の検出を行う。ここでは，スケジュール処理部１１２は，即時に処理実行可能なスレーブノード１２０だけではなく，他のタスクの処理終了後に処理要求のタスクを実行しても，納期内に処理終了可能なスレーブノード１２０も検出する。スケジュール処理部１１２は，ここで検出されたスレーブノード１２０から，処理要求のタスクを割り当てるスレーブノード１２０を選択する。なお，ここでは，ロック中のスレーブノード１２０については，検出の対象外とする。本実施の形態において，ロックは，スレーブノード１２０を，処理要求のタスクの割り当て対象外に設定することをいう。

【００４７】

スケジュール処理部１１２は，現行の状態で処理要求のタスクを納期内に処理終了可能なスレーブノード１２０がなければ，他のスレーブノード１２０に移動しても納期内に処理終了可能なタスクを検出する。スケジュール処理部１１２は，検出されたタスクを移動することで，処理要求のタスクを納期内に処理終了可能なスレーブノード１２０を用意できるかを判定する。タスクを移動することで処理要求のタスクを納期内に処理終了可能なスレーブノード１２０を用意できると判定される場合，スケジュール処理部１１２は，該当タスクを他のスレーブノード１２０に移動する処理を，スレーブ通信部１１５を介して実行する。タスクの移動は，例えば該タスクの処理を移動元のスレーブノード１２０で停止し，移動先のスレーブノード１２０で再起動させる方法でもよいし，移動元のスレーブノード１２０における該タスクの実行中のイメージデータを移動先のスレーブノード１２０に転送する方法でもよい。本実施の形態では，該タスクの処理を移動先のスレーブノード１２０で再起動させる方法でタスクの移動を行うものとする。スケジュール処理部１１

２は，タスクの移動により空きができたスレーブノード１２０を，処理要求のタスクを割り当てる対象のスレーブノード１２０に決定する。

【００４８】

スケジュール処理部１１２は，タスクを移動しても処理要求のタスクを納期内に処理終了可能なスレーブノード１２０を用意できない場合，ロック中のスレーブノード１２０があれば，そのロックを解除すれば，処理要求のタスクを納期内に処理終了可能であるかを判定する。ロック解除により，処理要求のタスクを納期内に処理終了可能となると判定される場合には，スケジュール処理部１１２は，ロック中のスレーブノード１２０のロックを解除する。スケジュール処理部１１２は，ロックを解除したスレーブノード１２０を，処理要求のタスクを割り当てる対象のスレーブノード１２０に決定する。

【００４９】

スケジュール処理部１１２は，ここまでの処理で，処理要求のタスクを割り当てる対象のスレーブノード１２０が見つけられなかった場合，スケールアウトにより，システム１００にスレーブノード１２０を増設すると判断する。

【００５０】

スケールアウト処理部１１４は，スケールアウトによって，システム１００にコンピュータノードを増設する処理を行う。より具体的には，スケールアウト処理部１１４は，ＩａａＳ側で用意しているインタフェースを用いて，ＩａａＳ側の管理コンピュータにアクセスし，自システム１００へのスケールアウトを要求する。

【００５１】

スレーブ通信部１１５は，スレーブノード１２０との通信を行う。例えば，スレーブ通信部１１５は，受け付けた処理要求のタスクを割り当てる対象のスレーブノード１２０に対して，該タスクの処理を依頼する。また，スレーブ通信部１１５は，スレーブノード１２０から，依頼したタスクの処理結果を応答として受け付ける。また，スレーブ通信部１１５は，タスクの移動が行われる際に，移動元のスレーブノード１２０に対して該当タスクの停止を通知し，移動先のスレーブノード１２０に対して該当タスクの実行を通知する。

【００５２】

リスケジュール処理部１１６は，例えば定期的に，スケジュール情報記憶部１１３に記憶された管理情報を参照し，実行するタスクがないスレーブノード１２０を，スケールシュリンクの対象とする。

【００５３】

また，リスケジュール処理部１１６は，スケジュール情報記憶部１１３に記憶された管理情報を参照して，あるスレーブノード１２０で動作するタスクを，他のスレーブノード１２０に移動するシミュレーションを実行する。リスケジュール処理部１１６は，他のスレーブノード１２０に移動しても納期内に処理終了可能なタスクを検出する。

【００５４】

リスケジュール処理部１１６は，検出されたタスクを移動することで，実行するタスクがないスレーブノード１２０を用意できるかを判定する。タスクを移動することで実行するタスクがないスレーブノード１２０を用意できると判定される場合，リスケジュール処理部１１６は，該当タスクを他のスレーブノード１２０に移動する処理を，スレーブ通信部１１５を介して実行する。タスクの移動については，上述のスケジュール処理部１１２の場合と同様である。リスケジュール処理部１１６は，タスクの移動により実行するタスクがなくなったスレーブノード１２０を，スケールシュリンクの対象とする。

【００５５】

また，リスケジュール処理部１１６は，検出されたタスクを移動することで，実行するタスクの数が所定数以下となるスレーブノード１２０を用意できるかを判定する。タスクの移動により実行するタスクの数が所定数以下となるスレーブノード１２０を用意できると判定される場合，リスケジュール処理部１１６は，該当タスクを他のスレーブノード１２０に移動する処理を，スレーブ通信部１１５を介して実行する。リスケジュール処理部

１１６は，タスクの移動により実行するタスクの数が所定数以下となるスレーブノード１２０にロックを設定する。ロック中のスレーブノード１２０には，原則として新たな処理要求のタスクが割り当てられないので，残ったタスクの処理が終了した後で，スケールシュリンクの対象となる。

【００５６】

スケールシュリンク処理部１１７は，スケールシュリンクによって，対象のスレーブノード１２０をシステム１００から削除する処理を行う。より具体的には，スケールシュリンク処理部１１７は，ＩａａＳ側で用意しているインタフェースを用いて，ＩａａＳ側の管理コンピュータにアクセスし，対象スレーブノード１２０のスケールシュリンクを要求する。

【００５７】

スレーブノード１２０は，マスタ通信部１２１，アプリケーション１２２を備える。図４に示すように，スレーブノード１２０では，複数種類のアプリケーション１２２ａ，ｂ，... を稼働することが可能である。処理要求のタスクが割り当てられた際には，該処理要求に対応するアプリケーション１２２によって，タスクの処理が実行される。

【００５８】

マスタ通信部１２１は，マスタノード１１０との通信を行う。例えば，マスタ通信部１２１は，マスタノード１１０からタスクの実行要求や停止要求を受け付け，タスクの実行開始または実行停止の処理を行う。また，タスクの処理が終了した場合には，マスタ通信部１２１は，マスタノード１１０に処理結果の応答を返す。

【００５９】

図５は，本実施の形態によるノードを実現する仮想マシンシステムの例を示す図である。

【００６０】

図５に示す仮想マシンシステムは，例えば，１台の物理マシン上で１または複数台の仮想マシンが動作するシステムである。図５に示す仮想マシンシステムの例では，ＣＰＵ１１やメモリ１２などの，物理マシンであるコンピュータ１０の資源を利用して，マスタノード１１０やスレーブノード１２０を含む複数の仮想マシン３０が動作している。なお，図５に示す仮想マシンシステムでは，マスタノード１１０とスレーブノード１２０とが同じ物理マシンで実現されているが，クラウドコンピューティングの環境では，マスタノード１１０や，各スレーブノード１２０が，それぞれ異なる物理マシンで実現されることも多い。

【００６１】

図５に示す仮想マシンシステムにおいて，ハイパーバイザ２０は，コンピュータ１０を利用した仮想化環境を実現するソフトウェアである。マスタノード１１０やスレーブノード１２０を含む仮想マシン３０は，ハイパーバイザ２０上に構築可能である。

【００６２】

図４に示すマスタノード１１０，スレーブノード１２０を仮想マシンで実現するコンピュータ１０は，例えば，ＣＰＵ１１，主記憶となるメモリ１２，記憶装置１３，通信装置１４，媒体読取・書込装置１５，入力装置１６，出力装置１７等のハードウェアを備える。記憶装置１３は，例えばＨＤＤ（Hard Disk Drive ）等の外部記憶装置や，補助記憶装置などである。媒体読取・書込装置１５は，例えばＣＤ－Ｒ（Compact Disc Recordable ）ドライブやＤＶＤ－Ｒ（Digital Versatile Disc Recordable ）ドライブなどである。入力装置１６は，例えばキーボード・マウスなどである。出力装置１７は，例えばディスプレイ等の表示装置などである。なお，コンピュータ１０のハードウェア構成は，必要に応じて任意の設計が可能である。

【００６３】

図４に示すマスタノード１１０，スレーブノード１２０および各ノードが備える機能部は，コンピュータ１０が備えるＣＰＵ１１，メモリ１２等のハードウェアと，ソフトウェアプログラムとによって実現することが可能である。コンピュータ１０が実行可能なプロ

グラムは，例えば，記憶装置１３に記憶され，その実行時にメモリ１２に読み出され，ＣＰＵ１１により実行される。

【００６４】

コンピュータ１０は，可搬型記録媒体から直接プログラムを読み取り，そのプログラムに従った処理を実行することもできる。また，コンピュータ１０は，サーバコンピュータからプログラムが転送されるごとに，逐次，受け取ったプログラムに従った処理を実行することもできる。さらに，このプログラムは，コンピュータで読み取り可能な記録媒体に記録しておくことができる。

【００６５】

以下，本実施の形態によるマスタノード１１０による処理について，より具体的な例を用いて説明する。

【００６６】

図６～図９は，本実施の形態のマスタノードにおけるスケジュール処理部による処理要求のタスクの割り当てシミュレーションの例を説明する図である。

【００６７】

図６（Ａ）は，タスクの表記の例を示す。図６（Ａ）において，塗り潰しされた図形が，タスクの処理を表す。タスクの処理を示す図形の縦の長さは該タスクのリソース消費量を示し，横の長さは該タスクの処理時間を示す。また，図６（Ａ）において，白抜き図形の右端は，該タスクの納期を示す。納期は，クライアント２００に指定されたタスクの処理を終了する期限である。以下の説明において，タスクについてはすべて図６（Ａ）に示す通りの表記が行われる。

【００６８】

図６（Ｂ）は，クライアント２００から時刻t_0に処理要求を受け付けた時点における，システム１００が備える各スレーブノード１２０ａ，ｂが実行するタスクのスケジュールを示す。図６（Ｂ）に示すように，この時点でシステム１００が備えるスレーブノード１２０は，＃ａのスレーブノード１２０ａと＃ｂのスレーブノード１２０ｂの２つである。なお，スケジュール情報記憶部１１３には，例えば図６（Ｂ）のグラフに示すようなシステム１００が備えるスレーブノード１２０が実行するタスクのスケジュールをデータ化した管理情報が記憶されている。図６（Ｂ）において，グラフの縦軸はスレーブノードのリソース消費量を示し，横軸は時間の経過を示す。t_{-1}～t_3は，等間隔の時刻を示す。

【００６９】

図６（Ｃ）は，時刻t_0の時点でクライアント２００から受け付けた処理要求のタスクＸを示す図形である。図６（Ｃ）に示すように，処理要求のタスクＸの処理については，他のタスクと区別がつくように，ハッチングで表されている。図６（Ｃ）に示すように，処理要求のタスクＸについては，時刻t_3の納期が指定されている。

【００７０】

なお，タスクの処理時間やリソース消費量の推定については，過去の実績から求める方法や理論的に求める方法などで多数の周知技術が存在するので，ここでは詳細な説明を省略する。タスクの処理時間の推定は，タスクが対象とする処理によって異なる。例えば画像の処理の処理時間については，画像ファイルサイズの影響を受ける。データベースを用いた処理では，データベースへのアクセス回数の影響を受ける。また，タスクのリソース消費量については，例えば，タスクの処理を行うアプリケーション１２２ごとに値が決まっている場合にはその値を用いることができる。スレーブノード１２０にリソース消費量を問い合わせるようにしてもよい。その他，様々な周知技術の利用が可能である。

【００７１】

マスタノード１１０において，スケジュール処理部１１２は，処理要求を受け付けると，まず，現状で，処理要求のタスクをスレーブノード１２０に割り当て可能であるかを検証する。

【００７２】

図７（Ａ）は，処理要求のタスクＸを，時刻t_0に処理実行を開始するように，＃ａの

スレーブノード１２０ａに対して割り当てした検証の例を示す。また，図７（Ｂ）は，処理要求のタスクＸを，時刻t_0に処理実行を開始するように，＃ｂのスレーブノード１２０ｂに対して割り当てした検証の例を示す。いずれも，ノードのリソース消費量が，ノードのリソース限界量を超えてしまうため，検証結果はＮＧとなる。

【００７３】

図７（Ｃ）は，最も早く処理が終了する，＃ａのスレーブノード１２０ａが実行するタスクＡ＃１の処理終了後に，処理要求のタスクＸをスケジュールした検証の例を示す。この場合，処理要求のタスクＸの処理終了時刻が納期t_3を超えてしまうため，検証結果はＮＧとなる。

【００７４】

次に，スケジュール処理部１１２は，他のタスクで再起動しても納期までに処理終了可能なタスクを移動する検証を行う。図８（Ａ）に示すように，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃３は，リソース消費量の面でも＃ａのスレーブノード１２０ａに移動可能であり，＃ａのスレーブノード１２０ａで再起動しても納期までに処理終了可能である。図８（Ｂ）は，図８（Ａ）に示すタスクの移動によってリソース消費量が減った＃ｂのスレーブノード１２０ｂに対して，処理要求のタスクＸを割り当てした検証の例を示す。タスクの移動を行っても，ノードのリソース消費量が，ノードのリソース限界量を超えてしまうため，検証結果はＮＧとなる。

【００７５】

他にロック中のスレーブノード１２０が存在しないので，スケジュール処理部１１２は，スケールアウト処理部１１４によるスケールアウトの処理でスレーブノード１２０を増設すると判断する。図９は，スケールアウト処理部１１４によって増設された＃ｃのスレーブノード１２０ｃに，処理要求のタスクＸが割り当てられた状態を示す。

【００７６】

このように，本実施の形態によるマスタノード１１０は，現状のスレーブノード１２０の状態でスケジューリングを含めた検証を行っても，さらにタスクの移動を行う検証を行っても，納期内に処理が終了するように処理要求のタスクを割り当てできない場合にのみ，スケールアウトを実行する。これにより，無駄なスケールアウトを抑制できるので，無駄な課金が発生しない，効率がよいシステム１００の運用が可能となる。

【００７７】

図１０，図１１は，本実施の形態のマスタノードにおけるリスケジュール処理部によるタスクの移動シミュレーションの例を説明する図である。

【００７８】

図１０は，時刻t_0の時点での，システム１００が備える各スレーブノード１２０ａ，ｂ，ｃが実行するタスクのスケジュールを示す。図１０に示すように，この時点でシステム１００が備えるスレーブノード１２０は，＃ａのスレーブノード１２０ａと，＃ｂのスレーブノード１２０ｂと，＃ｃのスレーブノード１２０ｃの３つである。

【００７９】

まず，マスタノード１１０において，リスケジュール処理部１１６は，定期的にスケジュール情報記憶部１１３を参照して，実行するタスクがないスレーブノード１２０があるかをチェックする。図１０に示すように，この時点では，すべてのスレーブノード１２０が処理を実行しているので，実行するタスクがないスレーブノード１２０はない。このとき，リスケジュール処理部１１６は，現状のままでスケールシュリンクできるスレーブノード１２０はないと判断する。

【００８０】

次に，リスケジュール処理部１１６は，他のタスクで再起動しても納期までに処理終了可能なタスクを移動する検証を行う。

【００８１】

図１１（Ａ）は，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃１を，＃ａのスレーブノード１２０ａで再起動する検証の例を示す。図１１（Ａ）に示すように，タスク

Ｂ＃１を他のスレーブノード１２０で再起動すると，処理の終了時刻が納期t_2を超えてしまうため，検証結果はＮＧとなる。リスケジュール処理部１１６は，タスクを移動して＃ｂのスレーブノード１２０ｂに対してスケールシュリンクを行うことはできないと判断する。

【００８２】

図１１（Ｂ）は，＃ｃのスレーブノード１２０ｃが実行するタスクＣ＃１を，＃ａのスレーブノード１２０ａで再起動する検証の例を示す。図１１（Ｂ）に示すように，タスクＣ＃１は，＃ａのスレーブノード１２０ａで再起動しても納期t_3までに処理終了可能である。さらに，タスクＣ＃１を＃ａのスレーブノード１２０ａに移動すると，＃Ｃのスレーブノード１２０ｃが実行するタスクがなくなるため，＃Ｃのスレーブノード１２０ｃに対してスケールシュリンクを行うことが可能である。

【００８３】

リスケジュール処理部１１６は，スレーブ通信部１１５を介して，＃Ｃのスレーブノード１２０ｃにタスクＣ＃１の停止を指示し，＃Ａのスレーブノード１２０ａにタスクＣ＃１の実行を指示する。＃Ｃのスレーブノード１２０ｃが実行するタスクがなくなるので，リスケジュール処理部１１６は，＃Ｃのスレーブノード１２０ｃをスケールシュリンクの対象とする。スケールシュリンク処理部１１７は，＃Ｃのスレーブノード１２０ｃに対するスケールシュリンクの処理を実行する。

【００８４】

このように，本実施の形態によるマスタノード１１０は，他のスレーブノード１２０にタスクを移動することで，実行するタスクがないスレーブノード１２０を積極的に作り，スケールシュリンクを実行する。これにより，無駄なスレーブノード１２０を積極的に削除することが可能となるので，無駄な課金が発生しない効率がよいシステム１００の運用が可能となる。

【００８５】

図１２，図１３は，本実施の形態のマスタノードにおけるリスケジュール処理部によるスレーブノードにロック設定を行う例を説明する図である。

【００８６】

図１２は，時刻t_0の時点での，システム１００が備える各スレーブノード１２０ａ，ｂが実行するタスクのスケジュールを示す。図１２に示すように，この時点でシステム１００が備えるスレーブノード１２０は，＃ａのスレーブノード１２０ａと＃ｂのスレーブノード１２０ｂの２つである。

【００８７】

マスタノード１１０において，リスケジュール処理部１１６は，タスクを移動しても実行するタスクがないスレーブノード１２０が用意できない場合に，タスクを移動することで実行するタスクの数が所定数以下となるスレーブノード１２０を用意できるかを検証する。例えば，ここでは，所定数を１とする。

【００８８】

図１３（Ａ）は，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃２を，＃ａのスレーブノード１２０ａで再起動する検証の例を示す。図１３（Ａ）に示すように，タスクＢ＃２は，＃ａのスレーブノード１２０ａで再起動しても納期t_3までに処理終了可能である。なお，＃ｂのスレーブノード１２０ｂが実行するタスクＢ＃１を，＃ａのスレーブノード１２０ａで再起動しようとしても，処理の終了時刻が納期t_2を超えてしまうため，タスクＢ＃１は移動できない。

【００８９】

タスクＢ＃２を＃ａのスレーブノード１２０ａに移動したとすると，図１３（Ｂ）に示すように，＃ｂのスレーブノード１２０ｂは，実行するタスクの数が所定数１以下となる。このとき，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，＃Ｂのスレーブノード１２０ｂにタスクＢ＃２の停止を指示し，＃Ａのスレーブノード１２０ａにタスクＢ＃２の実行を指示する。

【００９０】
また，図１３（Ｂ）に示すように，実行するタスクがＢ＃１のみとなった＃ｂのスレーブノード１２０ｂに，ロックを設定する。なお，ロックを設定したスレーブノード１２０の情報は，スケジュール情報記憶部１１３など，スケジュール処理部１１２がアクセス可能な記憶部に記録しておく。これで，＃ｂのスレーブノード１２０ｂには，原則として，新規の処理要求のタスクが割り当てされないので，残っている＃Ｂ１のタスクの終了後に，スケールシュリンク処理部１１７によって，＃ｂのスレーブノード１２０ｂを削除することができる。
【００９１】
このように，本実施の形態によるマスタノード１１０は，他のスレーブノード１２０にタスクを移動して，実行するタスクが少ないスレーブノード１２０を積極的に作り，そのスレーブノード１２０に対する新規の処理要求のタスクの割り当てを抑制する。これにより，システム１００の環境が，実行するタスクがないスレーブノード１２０ができやすい環境となり，無駄なスレーブノード１２０を積極的に削除することが可能となるので，無駄な課金が発生しない効率がよいシステム１００の運用が可能となる。
【００９２】
図１４は，本実施の形態のマスタノードにおけるスケジュール処理部によるスレーブノードのロック解除を行う例を説明する図である。
【００９３】
ここで，システム１００が，図１３（Ｂ）に示す状態で，クライアント２００から，図６（Ｃ）に示すタスクＸの処理要求を受けたものとする。このとき，スケジュール処理部１１２は，処理要求のタスクＸを，図１４（Ａ）に示すようにロックされていない＃ａのスレーブノード１２０ａに割り当てしようとするが，ノードのリソース消費量がノードのリソース限界量を超えてしまうため，割り当てできない。さらに，他にタスクを移動できる相手先のスレーブノード１２０もない。
【００９４】
このとき，スケジュール処理部１１２は，ロック中の＃ｂのスレーブノード１２０ｂのロックを解除すれば，＃ｂのスレーブノード１２０ｂで処理要求のタスクＸが納期までに処理終了可能かを検証する。図１４（Ｂ）に示すように，＃ｂのスレーブノード１２０ｂで処理要求のタスクＸが納期までに処理終了可能であるので，スケジュール処理部１１２は，ロック中の＃ｂのスレーブノード１２０ｂのロックを解除し，＃ｂのスレーブノード１２０ｂに処理要求のタスクＸを割り当てる。
【００９５】
このように，ロック中のスレーブノード１２０には，他のスレーブノード１２０に処理要求のタスクを割り当てできない場合にのみ，処理要求のタスクの割り当てが行われる。これにより，スケールシュリンクを実行しやすい環境をギリギリまで維持しながら，スケールアウトの発生を抑制できるので，無駄な課金が発生しない効率がよいシステム１００の運用が可能となる。
【００９６】
なお，本実施の形態によるマスタノード１１０は，納期内にタスクの処理が終了することを最優先としているので，システム１００では常に最低限の処理性能が維持されている。
【００９７】
図１５，図１６は，本実施の形態のマスタノードによる処理要求受け付け時の処理フローチャートである。
【００９８】
マスタノード１１０において，クライアント通信部１１１は，クライアントから処理要求を受け付ける（ステップＳ１０）。ここで受け付ける処理要求には，納期が指定されている。クライアント通信部１１１は，処理要求が受け入れ可能かを判定する（ステップＳ１１）。処理要求が受け入れ可能でなければ（ステップＳ１１のＮＯ），クライアント通

信部１１１は，クライアントに処理要求の受け入れが不可能である旨を応答し（ステップＳ１２），処理を終了する。

【００９９】

処理要求が受け入れ可能であれば（ステップＳ１１のＹＥＳ），スケジュール処理部１１２は，スケジュール情報記憶部１１３の管理情報を参照し，現状のスレーブノード１２０に処理要求のタスクを割り当てるシミュレーションを行う（ステップＳ１３）。ここでは，例えば，図７に示すようにスケジューリングを含めた検証が行われる。

【０１００】

スケジュール処理部１１２は，現状のスレーブノード１２０に対する処理要求のタスクの割り当てが可能かを判定する（ステップＳ１４）。処理要求のタスクの割り当てが可能であれば（ステップＳ１４のＹＥＳ），スケジュール処理部１１２は，処理要求のタスクを割り当てる先のスレーブノード１２０を決定する（ステップＳ１５）。スレーブ通信部１１５は，決定されたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。

【０１０１】

処理要求のタスクの割り当てが可能でなければ（ステップＳ１４のＮＯ），スケジュール処理部１１２は，スケジュール情報記憶部１１３の管理情報を参照し，既存のタスクを移動して，処理要求のタスクを割り当てるシミュレーションを行う（ステップＳ１６）。ここでは，例えば，図８に示すように，他のスレーブノード１２０に移動して再実行しても納期内に処理を終了可能な既存のタスクがある場合に，その既存タスクを移動してリソースに空きができたスレーブノード１２０に処理要求のタスクを割り当てることができるかが検証される。

【０１０２】

スケジュール処理部１１２は，既存タスクを移動して処理要求のタスクの割り当てが可能となるかを判定する（ステップＳ１７）。処理要求のタスクの割り当てが可能となれば（ステップＳ１７のＹＥＳ），スケジュール処理部１１２は，該当既存タスクの移動を実行する（ステップＳ１８）。より具体的には，スケジュール処理部１１２は，スレーブ通信部１１５を介して，既存タスクの移動元のスレーブノード１２０に該タスクの停止を依頼する。また，スケジュール処理部１１２は，スレーブ通信部１１５を介して，既存タスクの移動先のスレーブノード１２０に該タスクの実行を依頼する。スレーブ通信部１１５は，既存タスクの移動によりリソースに空きができたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。

【０１０３】

処理要求のタスクの割り当てが可能とならなければ（ステップＳ１７のＮＯ），スケジュール処理部１１２は，ロック中のスレーブノード１２０が存在して，該スレーブノード１２０のロックを解除すれば，処理要求のタスクの割り当てが可能となるかを判定する（ステップＳ１９）。ロックを解除して処理要求のタスクの割り当てが可能となれば（ステップＳ１９のＹＥＳ），スケジュール処理部１１２は，ロック中のスレーブノード１２０のロックを解除する（ステップＳ２０）。スレーブ通信部１１５は，ロックが解除されたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。このケースは，図１４の例に示されるケースである。

【０１０４】

ロック中のスレーブノード１２０がないか，ロックを解除しても処理要求のタスクの割り当てが可能とならなければ（ステップＳ１９のＮＯ），スケールアウト処理部１１４は，スケールアウトの処理を実行する（ステップＳ２１）。スケールアウトにより，システム１００にスレーブノード１２０が増設される。スレーブ通信部１１５は，増設されたスレーブノード１２０に処理要求のタスクの処理を依頼する（ステップＳ２２）。このケースは，図９の例に示されるケースである。

【０１０５】

スレーブ通信部１１５が，スレーブノード１２０から処理要求に対する処理結果の応答

を受け付けると（ステップＳ２３），クライアント通信部１１１は，その応答をクライアントに送信する（ステップＳ２４）。

【０１０６】

図１７は，本実施の形態のマスタノードによるリスケジュールの処理フローチャートである。

【０１０７】

マスタノード１１０において，リスケジュール処理部１１６は，所定のタイミングで本処理を開始する。

【０１０８】

リスケジュール処理部１１６は，スケジュール情報記憶部１１３の管理情報を参照し，現状で実行するタスクがないスレーブノード１２０があるかを判定する（ステップＳ３０）。実行するタスクがないスレーブノード１２０があれば（ステップＳ３０のＹＥＳ），スケールシュリンク処理部１１７は，該当スレーブノード１２０に対するスケールシュリンクの処理を実行する（ステップＳ３１）。スケールシュリンクにより，システム１００からスレーブノード１２０が削除される。

【０１０９】

リスケジュール処理部１１６は，スケジュール情報記憶部１１３の管理情報を参照し，タスクを移動するシミュレーションを行う（ステップＳ３２）。ここでは，例えば図１１に示すように，他のスレーブノード１２０に移動して再実行しても納期内に処理を終了可能なタスクがある場合に，そのタスクを移動して実行するタスクがないスレーブノード１２０を生成できるかが検証される。また，例えば図１３に示すように，他のスレーブノード１２０に移動して再実行しても納期内に処理を終了可能なタスクがある場合に，そのタスクを移動して実行するタスクが所定数以下となるスレーブノード１２０を生成できるかが検証される。

【０１１０】

リスケジュール処理部１１６は，タスクを移動して実行するタスクがないスレーブノード１２０を生成できるか，すなわちタスクを移動してスケールシュリンクが可能となるかを判定する（ステップＳ３３）。タスクを移動してスケールシュリンクが可能となれば（ステップＳ３３のＹＥＳ），リスケジュール処理部１１６は，該当タスクの移動を実行する（ステップＳ３４）。より具体的には，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動元のスレーブノード１２０に該タスクの停止を依頼する。また，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動先のスレーブノード１２０に該タスクの実行を依頼する。スケールシュリンク処理部１１７は，タスクの移動により実行するタスクがなくなったスレーブノード１２０に対するスケールシュリンクの処理を実行する（ステップＳ３５）。スケールシュリンクにより，システム１００からスレーブノード１２０が削除される。

【０１１１】

タスクを移動してもスケールシュリンクが可能とならなければ（ステップＳ３３のＮＯ），リスケジュール処理部１１６は，タスクを移動して実行するタスクが所定数以下となるスレーブノード１２０があるかを判定する（ステップＳ３６）。タスクを移動しても実行するタスクが所定数以下となるスレーブノード１２０がなければ（ステップＳ３６のＮＯ），リスケジュール処理部１１６は，処理を終了する。

【０１１２】

タスクを移動して実行するタスクが所定数以下となるスレーブノード１２０があれば（ステップＳ３６のＹＥＳ），リスケジュール処理部１１６は，該当タスクの移動を実行する（ステップＳ３７）。より具体的には，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動元のスレーブノード１２０に該タスクの停止を依頼する。また，リスケジュール処理部１１６は，スレーブ通信部１１５を介して，タスクの移動先のスレーブノード１２０に該タスクの実行を依頼する。リスケジュール処理部１１６は，タスクを移動して実行するタスクが所定数以下となったスレーブノード１２０にロック

を設定する（ステップＳ３８）。このまま，ロックが解除されずに残ったタスクの処理がすべて終了すれば，ロックが設定されたスレーブノード１２０は，その後のステップＳ３０，Ｓ３１の処理でスケールシュリンクの対象となる。

【０１１３】

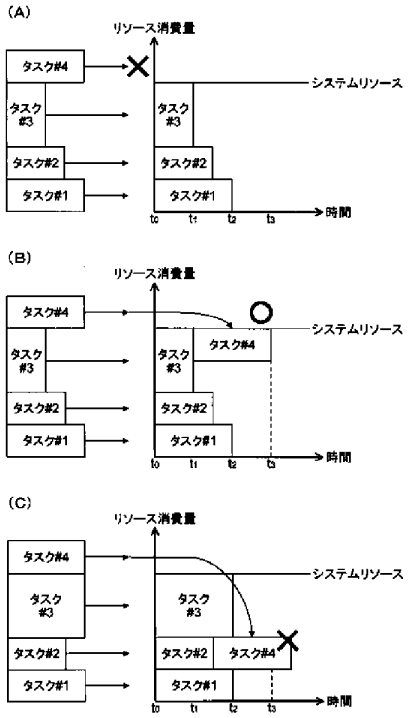
以上，本実施の形態について説明したが，本発明はその主旨の範囲において種々の変形が可能であることは当然である。

【符号の説明】

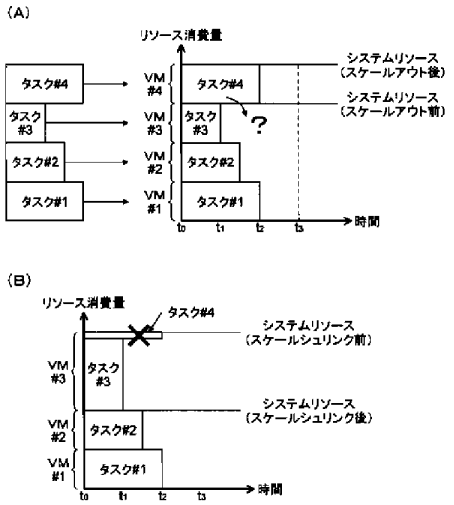
【０１１４】

１００　システム
１１０　マスタノード
１１１　クライアント通信部
１１２　スケジュール処理部
１１３　スケジュール情報記憶部
１１４　スケールアウト処理部
１１５　スレーブ通信部
１１６　リスケジュール処理部
１１７　スケールシュリンク処理部
１２０　スレーブノード
１２１　マスタ通信部
１２２　アプリケーション
２００　クライアント
３００　ネットワーク

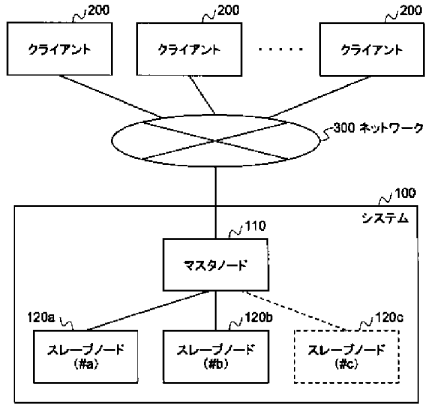
【図１】



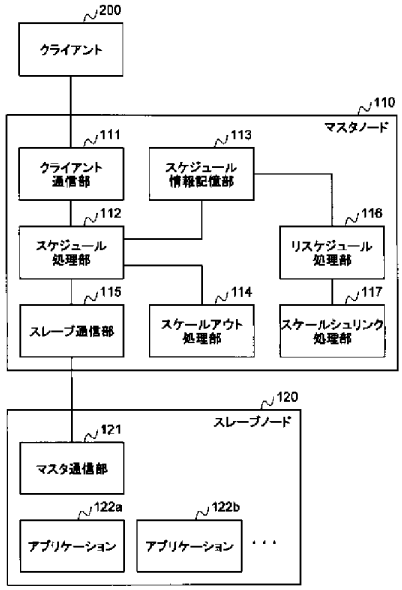
【図２】



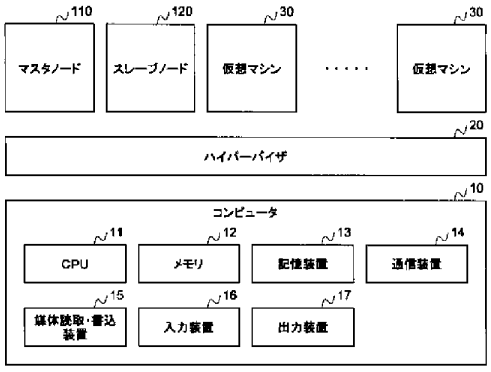
【図３】


200
クライアント
200
クライアント
200
クライアント
300 ネットワーク
100
システム
110
マスタノード
120a
スレーブノード
(#a)
120b
スレーブノード
(#b)
120c
スレーブノード
(#c)

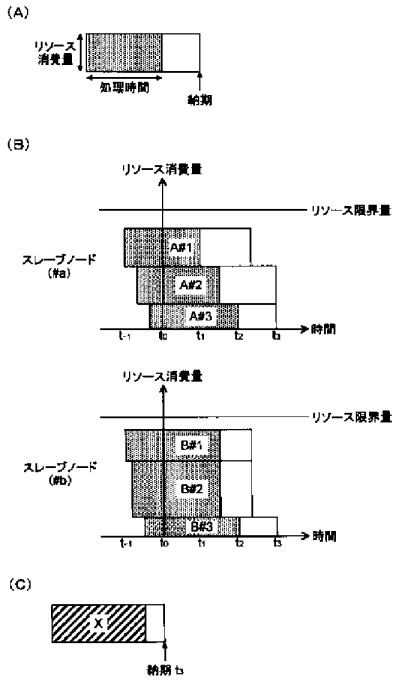
【図４】


200
クライアント
110
マスタノード
111
クライアント
通信部
113
スケジュール
情報記憶部
112
スケジュール
処理部
116
リスケジュール
処理部
115
スレーブ通信部
114
スケールアウト
処理部
117
スケールシュリンク
処理部
120
スレーブノード
121
マスタ通信部
122a
アプリケーション
122b
アプリケーション

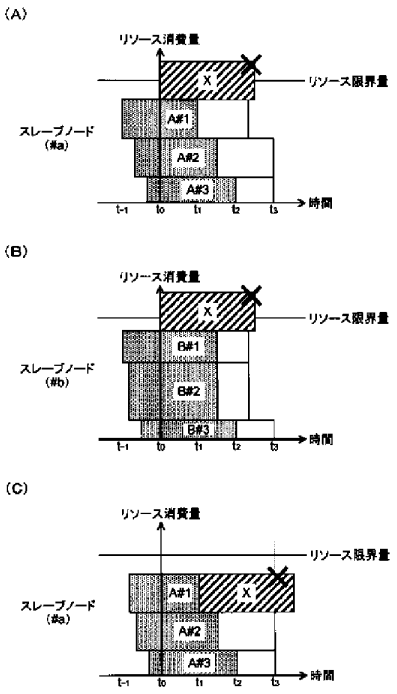
【図５】


110
マスタノード
120
スレーブノード
30
仮想マシン
30
仮想マシン
20
ハイパーバイザ
10
コンピュータ
11
CPU
12
メモリ
13
記憶装置
14
通信装置
15
媒体読取・書込
装置
16
入力装置
17
出力装置

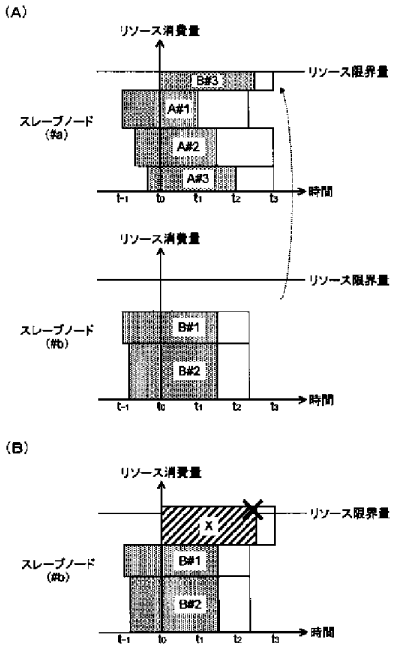
【図６】


(A)
リソース
消費量
処理時間
納期
(B)
リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
(C)
納期 b

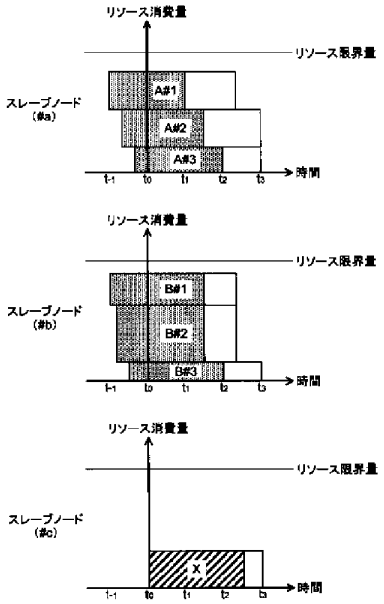
【図７】


(A)
リソース消費量
リソース限界量
X
スレーブノード
(#a)
A#1
A#2
A#3
時間
(B)
リソース消費量
リソース限界量
X
スレーブノード
(#b)
B#1
B#2
B#3
時間
(C)
リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
X
A#2
A#3
時間

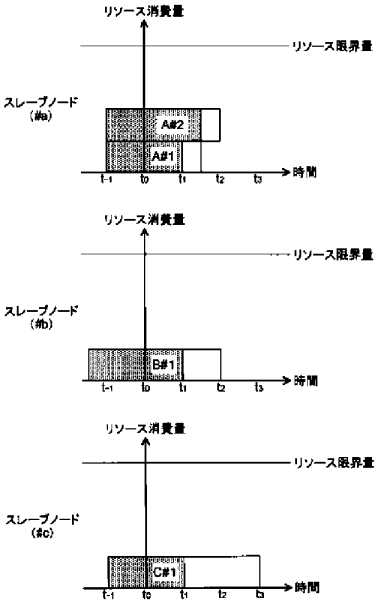
【図８】


(A)
リソース消費量
リソース限界量
B#3
スレーブノード
(#a)
A#1
A#2
A#3
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
時間
(B)
リソース消費量
リソース限界量
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スレーブノード
(#b)
B#1
B#2
時間

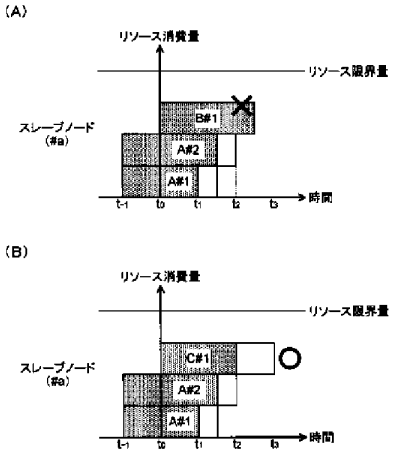
【図９】


リソース消費量
リソース限界量
スレーブノード
(#a)
A#1
A#2
A#3
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
B#2
B#3
時間
リソース消費量
リソース限界量
スレーブノード
(#c)
X
時間

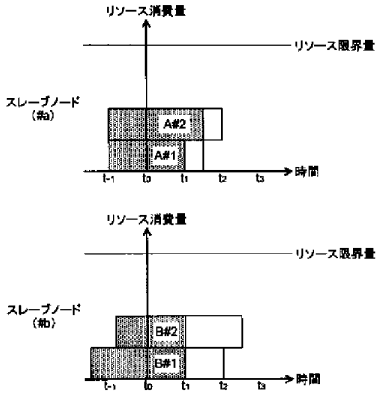
【図１０】


リソース消費量
リソース限界量
スレーブノード
(#a)
A#2
A#1
時間
リソース消費量
リソース限界量
スレーブノード
(#b)
B#1
時間
リソース消費量
リソース限界量
スレーブノード
(#c)
C#1
時間

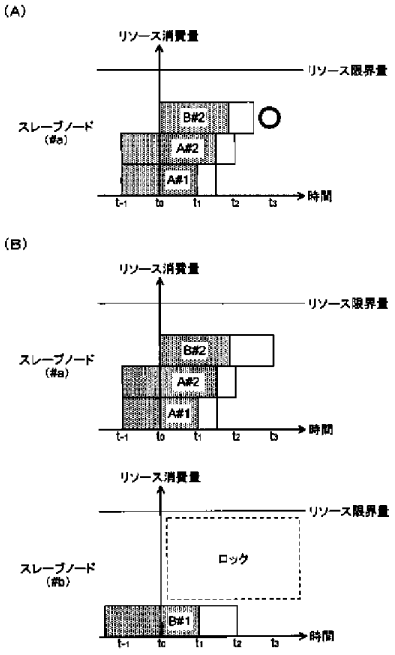
【図１１】



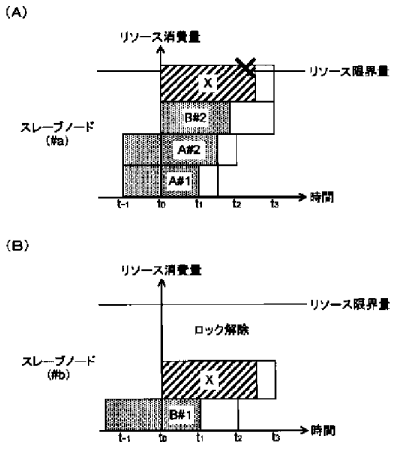
【図１２】



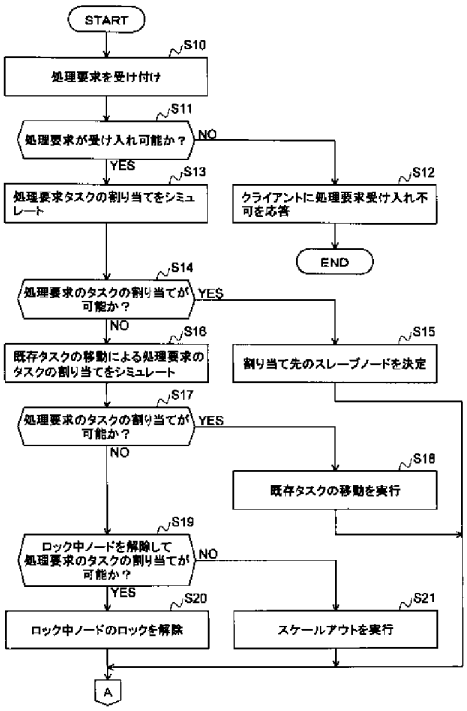
【図１３】



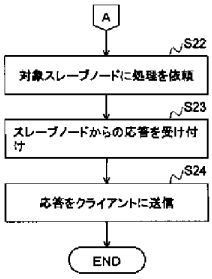
【図１４】



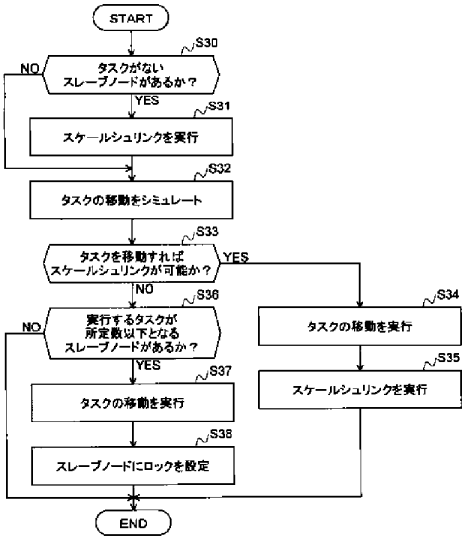
【図１５】


START
S10
処理要求を受け付け
S11
処理要求が受け入れ可能か？
NO
YES
S12
クライアントに処理要求受け入れ不可を応答
END
S13
処理要求タスクの割り当てをシミュレート
S14
処理要求のタスクの割り当てが可能か？
YES
NO
S15
割り当て先のスレーブノードを決定
S16
既存タスクの移動による処理要求のタスクの割り当てをシミュレート
S17
処理要求のタスクの割り当てが可能か？
YES
NO
S18
既存タスクの移動を実行
S19
ロック中ノードを解除して処理要求のタスクの割り当てが可能か？
NO
YES
S20
ロック中ノードのロックを解除
S21
スケールアウトを実行
A

【図１６】


A
S22
対象スレーブノードに処理を依頼
S23
スレーブノードからの応答を受け付け
S24
応答をクライアントに送信
END

【図１７】


START
S30
タスクがないスレーブノードがあるか？
NO
YES
S31
スケールシュリンクを実行
S32
タスクの移動をシミュレート
S33
タスクを移動すればスケールシュリンクが可能か？
YES
NO
S34
タスクの移動を実行
S35
スケールシュリンクを実行
S36
実行するタスクが所定数以下となるスレーブノードがあるか？
NO
YES
S37
タスクの移動を実行
S38
スレーブノードにロックを設定
END

フロントページの続き

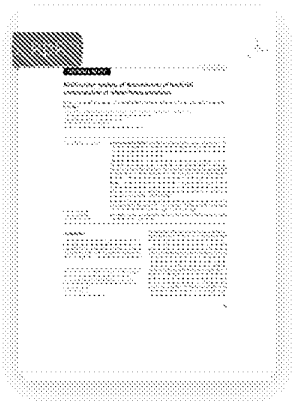
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審査官 田中 幸雄

(56)参考文献 特開２００９－２６５７７８（ＪＰ，Ａ）
特開２００８－０１５９５８（ＪＰ，Ａ）

(58)調査した分野(Int.Cl.，ＤＢ名)
Ｇ０６Ｆ ９／５０

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations



Multivariate analysis of determinants of bacterial contamination of whole-blood donations

Vox Sanguinis, 2002

Luc Noel P. Perez Paul Pérez

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ORIGINAL PAPER

Multivariate analysis of determinants of bacterial contamination of whole-blood donations

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Vox Sanguinis

Background and Objectives Introduction of bacteria into blood components at the collection stage seems to be a frequent occurrence. We therefore assessed determinants of bacterial contamination of whole-blood donations to gain insight into contamination mechanisms and direct prevention.

Materials and Methods A cross-sectional study was carried out on donors accepted for whole-blood donation in four French blood banks. Each blood bank used its own two-stage procedure for phlebotomy site preparation. Contamination was identified by culturing two 15-ml samples (collected aseptically at the outset of donation) in a BacT/Alert 240® system. Determinants were assessed by logistic regression analysis.

Results Bacterial contamination, mainly by skin flora, occurred in 76 (2·2%) out of 3385 donations. Significant determinants were as follows: the blood bank (odds ratio (OR) range = 3·0–5·6, $P < 0·001$); lack of repetition of scrub (OR = 2·7, $P = 0·032$); and donor age > 35 years (OR = 1·8, $P = 0·036$).

Conclusion Systematic scrub repetition should be implemented to reduce bacterial contamination by skin flora at the collection stage. Further research is required to clarify the role of different antiseptic agents and of donor age.

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Key words: adverse effects, bacterial infections, blood donors, blood transfusion, logistic models, prevention, risk factors.

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Introduction

Transfusion-associated bacterial contamination (TABC) is a potentially serious transfusion adverse event, reported to be responsible for 10% of transfusion-related fatalities reported in the USA from 1976 to 1999 [1], and for 22% in France from 1994 to 1999 [2]. TABC was considered by the United States National Institute of Health to be a real priority for improving transfusion safety [3] and has been recently acknowledged as the most frequent transfusion-transmitted infection [4].

The most effective measures for preventing TABC would be systematic culture of every blood component or the application of bacterial inactivation steps during manufacture. However, bacterial inactivation methods are still under development [5], and techniques currently available for aseptic sampling and culture of cellular blood components may need further validation [6]. Other possible interventions may be aimed at avoiding or reducing the introduction of bacteria from all possible sources [7]. Contamination sources are rarely found, but that most frequently reported is the blood donor [7,8]. Bacteria may come from the bloodstream of infected but asymptomatic donors, or from the donor skin [8]. Despite well-conducted antisepsis, high concentrations of bacteria

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may remain on the skin surface [9,10]. Moreover, a core of deeper skin layers, which might not be adequately disinfected, may enter the needle during collection and introduce bacteria into the donation [7]. Pilot studies have reported that 0·3–0·6% of whole-blood donations are contaminated by bacteria, probably of skin origin [11,12].

Research on factors contributing to bacterial contamination at the collection stage may help to identify contamination mechanisms and consequently lead to the development of new interventions to improve the safety of blood transfusion. Possible factors favouring bacterial multiplication might include a high ambient temperature (leading to sweating) and poor skin hygiene. In addition, factors leading to a higher possibility of unintentional inclusion of bacteria from the phlebotomy site might be important; these factors include: skin lesions (because of their possible infectious origin); hairs (because hair follicles, rich in bacteria, may be touched by the needle); and scars (already reported to contain higher concentrations of bacteria than healthy skin) [13].

The objective of our study was to assess determinants associated with bacterial contamination of whole-blood donations.

Subjects and methods

Data collection

This cross-sectional study was nested in a study implemented to assess the efficacy of diverting the first 15 ml of blood collection to reduce bacterial contamination of whole-blood donations [14]. The study was carried out from March to December 1997 in four French volunteer blood banks: Etablissement Français du Sang (EFS) Centre-Atlantique (Tours); Centre de Transfusion Sanguine des Armées Jean Julliard (Clamart); EFS Alpes-Méditerranée (Marseille); and EFS Île-de-France (Versailles). To culture blood samples on the day of donation, collection sites were selected if they collected whole-blood donations in the morning. Donors were included if they had been accepted for donation after a medical selection complying with French regulations [15] and had given their informed consent to participate.

The phlebotomy site was prepared according to a two-stage procedure complying with the French Blood Agency recommendations [16]. This involved preparation of an area of skin of ≈ 3·5 cm in all directions around the intended phlebotomy site. The site was then scrubbed with a gauze pad soaked with an antiseptic or detergent agent (the regulations recommend that this stage is to be repeated 'if needed'). The second stage involved application of an antiseptic agent compatible with the one used in the first stage. The skin was then allowed to dry for the time recommended by the manufacturer of the antiseptic agent. Different antiseptic agents were used by each of the participating blood banks. However, all of the blood banks used the same agent for both stages of skin preparation. The scrub duration was 5–10 seconds. Application times were 5–10 seconds in all blood banks except in blood bank 4 where the second gauze pad soaked with antiseptic was left on the intended phlebotomy site for 30 seconds before being used to wipe the site. Drying times after application varied according to the antiseptic agent used: more than 15–20 seconds for iodine tincture in blood bank 1; more than 30 s for Hibisprint® (chlorhexidine) in blood bank 2; and 1 min for non-alcoholic Betadine® (povidone-iodine) in blood bank 3. Blood bank 4 used Bisseptine® (chlorhexidine, benzalkonium chloride, benzylic alcohol) and did not recommend any drying time. An additional drying time of 30 seconds between stages 1 and 2 was applied in blood bank 2.

The age and gender of the donor, the time since the last meal (as stated by the donor), and the site, date and hour of collection, were recorded by the physician. The skin at the phlebotomy site was carefully inspected by the nurse who recorded the presence of hairs, scars from previous phlebotomies, or skin lesions less than 10 cm away from the phlebotomy site. The requirement to repeat the scrub stage when the first gauze pad was dirty, and the ease of phlebotomy, were also recorded.

Blood was collected into standard Maco Pharma packs (Maco Pharma, Tourcoing, France), specially equipped with two small sample bags into which the first (S1) and second (S2) 15 ml of donation were aseptically collected, before blood was allowed to enter the unit bag. At the end of donation, the two sample bags were separated from the rest of the pack by double welding, placed into an isothermal box and brought to the bacteriology laboratory within 6 h.

Bacteriological methods

Samples were cultured in a BacT/Alert® 240 automated system (Organon Teknika, Durham, NC). Each sample bag was equipped with a needle allowing direct inoculation through the rubber cap of an anaerobic then an aerobic FAN culture bottle. Bottles were incubated in the BacT/Alert® for 7 days at 35 °C, according to the manufacturer's instructions.

A sample from each bottle detected as positive was subcultured onto trypticase–soy 5% blood agar (for aerobic culture) and onto Columbia blood agar (for anaerobic culture), both at 37 °C. When a subculture was positive, bacteria were identified according to standard microbiological methods and stored. A donation was defined as contaminated with bacteria if at least one aerobic or anaerobic bottle inoculated with S1 or S2 was culture positive.

The correct functioning of the automated culture systems was verified by inoculation and incubation of positive controls in the same conditions as study samples. One out of four strains was cultured each week in each centre, alternately: *Staphyloccocus aureus* CIP 53·156 (American Type Culture Collection [ATCC] 6538P; ATCC, Rockville, MD), *Clostridium sporogenes* CIP 79·03 (ATCC 19404), *Propionibacterium*

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acnes CIP 53·117T (ATCC 6919) and *Pseudomonas aeruginosa* CIP 76·110 (ATCC 27853). Bottles were expected to be culture positive within 10–24 h, depending on the strain of bacteria used. The rate of secondary contamination related to handling or inoculation was estimated by culturing the anticoagulant from 189 S1 and 189 S2 sample bags which were not used for donation, but which were transported, inoculated and incubated under the same experimental conditions as the study samples.

Data management and analysis

For each donation, information regarding blood collection was recorded on a report form. Culture results were recorded on a separate form at the laboratory and transferred to the corresponding donation form. Data were entered in each centre on the EPI INFO software (6·04b French version, January 1997, ENSP – Epiconcept) and files were transmitted to the Institut de Santé Publique, d'Epidémiologie et de Développement (Université Victor Segalen Bordeaux 2). Donations were excluded from analysis if clots or welding problems were reported during collection or inoculation, or if the blood volumes collected in S1 or S2 or inoculated in FAN bottles, were less than 5 ml.

The bacterial contamination rates of donations were estimated by the proportion of donations for which S1 or S2 was culture positive and its exact binomial 95% confidence intervals (95% CI). Comparisons were based upon standard tests [17]. The association between a variable and donation contamination was estimated by the odds ratio (OR) [18]. To analyse the simultaneous effect of several variables on the risk of contamination, a logistic regression model was used [19]. All variables were included in the multivariate model, regardless of their association with bacterial contamination in univariate analysis. A stepwise backward procedure was used to remove variables that were less significantly associated with donation contamination, according to Wald or the likelihood ratio test [19]. Statistical analysis was conducted using the STATA software (Stata 5·0; Stata Corporation, College Station, TX).

Results

Study population

Among 3441 whole-blood donations, collected from March through December 1997, 56 (1·6%) were excluded because of clots, welding problems or insufficient collection or culture volumes. Most donations were collected during mobile sessions (premises, 50%; vehicle, 37%), and before 14·00 h (99·4%); the time since the last meal was less than 3 h in 60·4% of the donors. A high percentage of the donors were male (73·3%) and their median age was 39 years (first quartile: 27 years; third quartile: 48 years). The presence of hairs at the phlebotomy site was reported in 29·5% of men and 2·0% of women; skin lesions close to the phlebotomy site were present in 2·3% of donors; and scars were present in 14·3% (minor signs, 10·6%; multiple scars, 2·9%; dimpled skin, 0·7%). The scrub stage of antisepsis was repeated in 8·5% of donations, and phlebotomy was reported as easy in 43·3%.

Bacteriological results

All positive controls were detected by the automated culture system. One negative control out of 378 (0·26%) was culture positive for coagulase negative staphylococci (CNS).

Seventy-nine bacteria were cultured from samples originating from 76 donations. The most common bacterial species were Gram-positive cocci, which accounted for 81% of the bacterial species and were mostly CNS (66%). Gram-positive bacilli, mostly Bacillus species and *P. acnes*, accounted for 14%, and Gram-negative bacilli for 5%, of species.

The overall prevalence rate of bacterial contamination was 2·2% (95% CI: 1·8–2·8%).

Determinants of bacterial contamination

In the univariate analysis, characteristics significantly associated with bacterial contamination were the blood bank, period of collection, time since last meal, donor age and the presence of hairs at the phlebotomy site (Table 1). As the rate of contamination was more than twofold higher when donors were > 35 years, this characteristic was used as a binary variable.

Characteristics significantly associated with bacterial contamination in the final multivariate model were the blood bank, a donor age > 35 years and the lack of repetition of the antisepsis scrub stage (Table 1).

Discussion

Our study confirmed the high frequency of bacterial contamination of whole-blood donations and revealed a strong protective role of repeating the antisepsis scrub stage. Other main determinants were the collecting blood bank and donor age. Contaminating bacteria, isolated after culture, were most likely to have a skin origin.

Our estimation of bacterial contamination rates of blood donations is higher than those previously reported in whole-blood units, but consistent with those of the first few ml collected [20] and with blood-culture contamination rates reported in clinical settings, where the same mechanisms may be implicated [21,22].

The major influence of the collecting blood bank may be related to the agent used for antisepsis. The risk of bacterial contamination was the highest in the blood bank using non-alcoholic povidone-iodine. This is consistent with studies

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Table 1 Univariate (3385 donations) and multivariate (3227 donations) analysis of associations between whole-blood donation characteristics and bacterial contamination in four French blood banks, March–December 1997

	Univariate analysis	Multivariate analysis (final model)

https://www.academia.edu/10154576/Multivariate_analysis_of_determinants_of_bacterial_contamination_of_whole-blood_donations 3/6

KUR-MAG-DE005598

Page 3718 of 5923

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

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1	1·59	2·71		2·05 (0·66–6·37)	
2	0·59	Ref.[d]		Ref.[d] (Ref.[d])	
3	3·92	6·87	< 0·001	5·63 (1·92–16·48)	0·0002
4	2·42	4·18		3·56 (1·16–10·91)	
Collection site					
Mobile session (premises)	2·74	1·58			
Mobile session (truck)	1·75	Ref.[d]	0·15		
Blood bank premises	1·77	1·01			
Period of collection					
March to May	1·59	Ref.[d]		Ref.[d] (Ref.[d])	
June to September	1·89	1·19	0·03	0·87 (0·41–1·86)	0·091
October to December	3·32	2·13		1·53 (0·70–3·36)	
Time since last meal (19 missing data)					
0 to 59 min	1·74	Ref.[d]		Ref.[d] (Ref.[d])	
1 h to 1 h 59 min	3·16	1·96		1·95 (0·87–4·36)	
2 h to 2 h 59 min	1·52	0·87	0·02	1·01 (0·43–2·37)	0·052
3 h to 3 h 59 min	1·57	0·90		1·01 (0·42–2·43)	
4 h or more	3·53	2·06		2·22 (0·98–5·02)	
Donor gender					
Male	2·14	Ref.[d]			
Female	2·55	1·20	0·47		
Donor age > 35 years					
No	1·43	Ref.[d]		Ref.[d] (Ref.[d])	
Yes	2·82	2.00	0·008	1·77 (1·02–3·07)	0·036
Phlebotomy site features					
Hairs (14 missing data)					
None	1·98	Ref.[d]		Ref.[d] (Ref.[d])	
Yes	3·21	1·64	0·05	1·51 (0·90–2·54)	0·125
Skin lesions (98 missing data)					
None	2·31	Ref.[d]			
Yes	2·60	1·13	0·87		
Scars					
None	2·31	Ref.[d]			
Minor signs	1·39	0·60			
Multiple scars	3·03	1·32	0·60		
Dimpled skin	4·00	1·76			
Scrub stage repeated (30 missing data)					
Yes	1·40	Ref.[d]		Ref.[d] (Ref.[d])	
No	2·35	1·68	0·32	2·72 (0·96–7·73)	0·032
Easiness of phlebotomy (29 missing data)					
Yes	1·72	Ref.[d]			
No	2·68	1·57	0·07		

[a]χ^2 or Fisher's exact test.
[b]CI: confidence interval of odds ratio (OR).
[c]Likelihood ratio test.
[d]Reference category for OR estimation.

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A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

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A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT		
	Application Number	18/494,622
	Filing Date	10/25/2023
	First Named Inventor	Bobby E. ROGERS
	Art Unit	
	Client Number	069366
Page 1 of 1	**Matter Number**	0577657_KUR2C05US

GENERAL

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

Although the information submitted herewith may be "material" to the Examiner's consideration of the subject application, this submission is not intended to constitute an admission that such information is "prior art" as to the claimed invention, nor is it intended to constitute an admission that such information is "analogous prior art".

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

TIMING

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

CERTIFICATION STATEMENT

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

FEE

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

ADDITIONAL COMMENTS

SIGNATURE

Signature	/Benjamin F. Hudson/	**Date**	2024-04-23
Name	Benjamin F. Hudson	**Registration Number**	71,474

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
18/494,622	10/25/2023		728	069366-0577657_KUR2C05US	1	1

CONFIRMATION NO. 9839

UPDATED FILING RECEIPT

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

OC000000071580545

Date Mailed: 04/25/2024

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

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Inventor(s)

Bobby E. ROGERS, Park City, UT;
Gino KANG, Irvine, CA;
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Applicant(s)

Kurin, Inc., San Diego, CA;

Assignment For Published Patent Application

Kurin, Inc., San Diego, CA

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 18/113,710 02/24/2023 PAT 11,832,944
which is a CON of 17/538,990 11/30/2021 PAT 11,963,769
which is a CON of 16/208,559 12/04/2018 PAT 11,185,266
which is a CON of 15/994,559 05/31/2018 PAT 10,143,412
which is a CON of 15/140,448 04/27/2016 PAT 10,010,282
which claims benefit of 62/318,194 04/04/2016
and claims benefit of 62/238,636 10/07/2015
and claims benefit of 62/196,797 07/24/2015

Foreign Applications for which priority is claimed (You may be eligible to benefit from the Patent Prosecution Highway program at the USPTO. Please see http://www.uspto.gov for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 11/07/2023

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

Projected Publication Date: 08/01/2024

Non-Publication Request: No

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

BLOOD SAMPLE OPTIMIZATION DEVICE

Preliminary Class

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

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Title 37, Code of Federal Regulations, 5.11 & 5.15

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 18/494,622

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	64		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	280		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	320		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	1 minus 20 =	* 0	x =	0	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*	x =	0			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	664		TOTAL	

APPLICATION AS AMENDED - PART II

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

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

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

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

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

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

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FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Thu Apr 25 05:05:07 EDT 2024

Dear Patent Center Customer:

Correspondence Address:

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UNITED STATES

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Application	Document	Mailroom Date	Attorney Docket No.
18494622	APP.FILE.REC	04/25/2024	069366-0577657_KUR2C05US

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR/ PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
18/494,622	10/25/2023	ROGERS et al.	069366-0577657_ KUR2C05US

		EXAMINER	
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV) ATTENTION: DOCKETING DEPARTMENT P.O BOX 10500 McLean, VA 22102		--	
		ART UNIT	PAPER
		--	20240427-QzSh4M

DATE MAILED: 27 April 2024

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

PTO-90C (Rev.04-03)

Notice of Potential Erroneous Release of Patent Application Titles

On February 5, 2024, the United States Patent and Trademark Office (USPTO), replaced the Electronic Patent Assignment System (EPAS) and Electronic Trademark Assignment System (ETAS) with Assignment Center.

Between February 5, 2024 and March 29, 2024, the USPTO, unintentionally, through a computer programming error, permitted bibliographic information to be viewed by unauthorized individuals with access to registered Assignment Center accounts. This bibliographic information was limited to the application number (the two-digit series code plus the six-digit serial number) and title of the invention.

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We're committed to data security and are taking enhanced steps to prevent incidents such as this from happening in the future. The USPTO sincerely regrets this error and is instituting more testing controls, both manual and automated testing, to prevent similar processing errors in the future.

Inquiries regarding this matter may be directed to Mark Polutta, Senior Legal Advisor, at (571) 272-7709 or Andrew Stclair, Legal Advisor, at (571) 270-0238, both of the Office of Patent Legal Administration or via email addressed to Patent.Practice@uspto.gov.



Henry "Jamie" Holcombe
Chief Information Officer
US Patent and Trademark Office
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Dated: April 27th, 2024

China National Intellectual Property Administration

1110-11, A, Floor 11, Chengjian Plaza, 18 Beitaipingzhuang Road, Haidian District, Beijing 100088, PR China Beijing Pat SF Intellectual Property Agency Co Ltd	Issue Date: August 3, 2023

Application No. or patent No.: 202010300942.7 Issue serial No.: 2023080301552950

Applicant（s）: KURIN, INC.

Title of invention-creation: BLOOD OPTIMIZATION DEVICE

First Office Action

1 ☒ Upon the request of the applicant for substantive examination, the China National Intellectual Property Administration has performed the examination for the above-identified application for a patent for invention according to the provisions of Article 35.1 of the Patent Law.

☐ The China National Intellectual Property Administration itself has decided to perform the substantive examination for the above-identified application for a patent for invention according to the provisions of Article 35.2 of the Patent Law.

2 ☒ The applicant requested to designate the filing date of

March 13, 2020 in the Patent Office of US as the priority date;

March 19, 2020 in the Patent Office of US as the priority date.

3 ☐ After examination, the amendment submitted on_____is not in conformity with the provisions of Rule 51.1 of the Implementing Regulations of the Patent Law, so it has not been accepted.

4 ☐ Examination is made based on the Chinese text or translation of the international application as originally filed.

☒ Examination is made based on the following documents:

Drawings and abstract as filed on the filing date;

items 1-23 of claims and paragraphs 1-251 of description as filed on June 29, 2023.

5 ☒ This notification cited reference documents as follows:（its code will continue to be used in the future when examined.）

code	File No. or title	Publication date (or filing date of conflicting application)
1	US2018177445A1	20180628
2	US4349035A	19820914
3	US5401262A	19950328

6 The conclusion of the examination:

In regard to the Description:

☐ The subject matter of the application belongs to the objects mentioned in Article 5 of the Patent Law, for which no patent right shall be granted.

☐ The description is not in conformity with the provisions of Article 26.3 of the Patent Law.

☐ The description is not in conformity with the provisions of Article 33 of the Patent Law.

☐ The description is not in conformity with the provisions of Rule 17 of Implementing Regulations of the Patent Law.

☐

In regard to the Claims:

☐ Claims_____are not in conformity with the provisions of Article 2.2 of the Patent Law.
☐ Claims_____are not in conformity with the provisions of Article 9.1 of the Patent Law.
☒ Claims__1-4, 12, 18_____do not possess the novelty under Article 22.2 of the Patent Law.
☒ Claims__5-11, 13-17, 19-23_____do not possess the inventiveness under Article 22.3 of the Patent Law.
☐ Claims_____do not possess the practical applicability under Article 22.4 of the Patent Law
☐ Claims_____belong to the objects mentioned in Article 25 of the Patent Law, for which no patent right shall be granted.
☒ Claims__1, 12_____are not in conformity with the provisions of Article 26.4 of the Patent Law.
☐ Claims_____are not in conformity with the provisions of Article 31.1 of the Patent Law.
☒ Claim____19___is not in conformity with the provisions of Article 33 of the Patent Law.
☐ Claims_____are not in conformity with the provisions of Article 19 of the Patent Law.
☐ Claims_____are not in conformity with the provisions of Article 20 of the Patent Law.
☐ Claims_____are not in conformity with the provisions of Article 21 of the Patent Law.
☐ Claims_____are not in conformity with the provisions of Rule 22 of Implementing Regulations of the Patent Law.
☐ _____
☐ The application is not in conformity with the provisions of Article 26.5 of the Patent Law or with the provisions of Rule 26 of Implementing Regulations of the Patent Law.
☐ The application is not in conformity with the provisions of Article 20.1 of the Patent Law.
☐ The division application is not in conformity with the provisions of Rule 43.1 of Implementing Regulations of the Patent Law.

7. According to the above conclusion, the examiner deems that:
☐ The applicant shall amend the application documents as required by the text of Office Action.
☐ The applicant shall state the reason why the application can be accepted and amend the part that is indicated not to be in conformity with the provisions, otherwise the application will be rejected.
☒ No subject matter in the application is patentable, the application will be rejected if the applicant does not make a statement or the statement is not convincing.
☐ ___

8. The applicant shall pay attention to the following items:
(1) In accordance with the provisions of Article 37 of the Patent Law, the applicant shall submit the observations within __**4**___months from the date of receiving this notification. If the applicant, without any justified reason, fails to reply within the time limit, the application shall be deemed to have been withdrawn.
(2) The amendments to the application made by the applicant shall be in conformity with the provisions of Article 33 of the Patent Law. The amended text shall not go beyond the disclosure scope of the initial description and claims. The amendment should be in conformity with the provisions of Rule 51.3 of the Implementing Regulations of the Patent Law. The applicant shall make the amendment according to the request of this notification.
(3) Any observation and/or amended text shall be mailed or sent by hand to the Receiving Division of the Patent Office. Any document that is not mailed or sent by hand to the Receiving Division does not have legal effect.
(4) The applicant and/or his agent shall not go to the Patent Office to hold an interview with the examiner if no interview is arranged in advance.
(5) For an invention patent application that entered the substantive examination stage, if the applicant withdraws the application on his own initiative before the due date for responding to the first Office Action (except for the case that a response has already been filed), the applicant can request a refund of 50% of the substantive examination fee.

9. The text of the notification embraces __4__ pages, along with the enclosures herein:
☐ _____Copy(ies) of the cited references is enclosed in pages of _____.
☐ _____

Examiner: Examining Department:
Tel:

Text of the First Office Action

Application number: 202010300942.7

The present application relates to blood optimization device. The following examination opinions are now set forth.

Claim 19 does not comply with the provision under Article 33[1] of the Patent Law.

Claim 19 defines "the vent further comprises a cover that inhibits air from reentering the chamber after air has been displaced". It can be known from the disclosure contained in the original description that: "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" (see paragraph [0070] of the description <*Translator's note: corresponding to paragraph [0067] of the English description provided by the former Chinese agency*>), "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" (see the description, paragraph [0105] <*Translator's note:*

[1] Article 33 An applicant may amend his or its patent application documents, however, the amendment to the patent application documents for an invention or utility model may not go beyond the scope of disclosure contained in the original description and claims, and the amendment to the patent application documents for a design may not go beyond the scope of the disclosure as shown in the original drawings or photographs.

corresponding to paragraph [00102] of the English description provided by the former Chinese agency>). Accordingly, it is the air permeable blood barrier rather than the structure e.g., protective cover or cover, etc., that inhibits air from reentering the chamber after the air is displaced, and the protective cover or cover is to inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes (see paragraphs [0105], [0115], [0136] of the description <*Translator's note: corresponding to paragraphs [00102], [00112], [00133] of the English description provided by the former Chinese agency*>). The limitation in claim 19 is not disclosed in the original application documents, nor can be directly and unambiguously determined from the original application documents. Therefore, claim 19 goes beyond the scope of disclosure contained in the original description and claims, and does not comply with the provision under Article 33 of the Patent Law.

Claims 1-4, 12, and 18 do not possess novelty prescribed under Article 22.2[2] of the Patent Law, and claims 5-11, 13-17, and 19-23 do not possess inventiveness prescribed under Article 22.3[3] of the Patent Law.

1. Claims 1 and 12 seek to protect a device. Reference 1 (US2018177445A1) discloses (see the description, paragraphs [0058]-[0170], and Figs. 1-30G): a blood sequestration device comprises an inlet port (see the description, paragraphs [0156], [0161]) and an outlet port (see the description, paragraphs [0159], [0161]), and a housing 3001 (see the description, paragraph [0161]), the housing 3001 comprising:

an inlet path 3002 (see the description, paragraph [0156], Fig. 30A)

[2] Article 22.2 Novelty means that, the invention or utility model does not form part of the prior art; nor has any entity or individual filed a patent application for the identical invention or utility model with the patent administrative department under the State Council before the filing date, and the content of the application is disclosed in patent application documents published or patent documents announced after the filing date.

[3] Article 22.3 Inventiveness means that, as compared with the prior art, the invention possesses prominent substantive features and represents a notable progress and that the utility model possesses substantive features and represents a progress.

(namely comprising an inlet port, an inlet path connected with the inlet port);

an outlet path 3004 (see the description, paragraph [0158], Fig. 30A) (namely comprising an outlet port, an outlet path connected with the outlet port);

a chamber 3008 (see the description, paragraph [0160], Fig. 30A) connected with the inlet path 3002 by a junction 3007 and being configured to receive a first portion of blood through the inlet path 3002 (see the description, paragraphs [0160], [0163]-[0164]), the junction 3007 being configured to inhibit a return to the inlet path 3002 of any of the first portion of blood received by the chamber 3008 (see the description, paragraphs [0061], [0067], [0156], [0160]-[0161]); and

a sampling channel 3006 connected between the inlet path 3002 and the outlet path 3004 (see the description, paragraphs [0159]-[0160]), the sampling channel 3006 being configured to convey subsequent amounts of blood between the inlet path 3002 and the outlet path 3004 after the first amount of blood is received by the chamber 3008 (see the description, paragraphs [0160]-[0170]).

As can be seen, Reference 1 has disclosed all the technical features of claim 1. Moreover, the technical solution disclosed by Reference 1 and the technical solution sought for protection in claim 1 belong to the same technical field, are used for solving the same technical problem, and can produce the same technical effect. Therefore, the technical solution sought for protection in claim 1 does not possess novelty.

2. Claim 20 seeks to protect a blood sample optimization system. Reference 1 (US2018177445A1) discloses (see the description, paragraphs [0058]-[0170], and Figs. 1-30G): a blood sample optimization system (see the description, paragraph [0156]) comprises a blood sampling system comprising:

the blood sequestration device 3000 includes an inlet path 3002 that can

be connected with a patient needle (namely the venipuncture apparatus) that is inserted into a patient's vascular system for access to and withdrawing of a blood sample (namely configuring the same for venipuncture of a patient to access a sample of blood of the patient);

the blood sequestration device 3000 includes a sampling channel 3006 (namely the blood sampling pathway connected with the venipuncture apparatus for conveying the sample of blood) between the inlet port 3002 and the outlet port 3004;

an outlet path 3004 (comprising a reservoir) for collecting a subsequent portion of the sample of blood; and

a device connected along the blood sampling pathway 3006 between the patient needle and the outlet path 3004 (comprising a reservoir), the device comprising:

an inlet path 3002 connected with the patient needle (see the description, paragraph [0156], Fig. 30A) (namely comprising an inlet port, an inlet path connected with the inlet port);

an outlet path 3004 (see the description, paragraph [0158], Fig. 30A) (namely comprising an outlet port, an outlet path connected with the outlet port);

a chamber 3008 (see the description, paragraph [0160], Fig. 30A) connected with the inlet path 3002 by a junction 3007 and being configured to receive a first portion of blood through the inlet path 3002 (see the description, paragraphs [0160], [0163]-[0164]), the junction 3007 being configured to inhibit a return to the inlet path 3002 of any of the first portion of blood received by the chamber 3008 (see the description, paragraphs [0061], [0067], [0156], [0160]-[0161]); and

a sampling channel 3006 connected between the inlet path 3002 and the outlet path 3004 (see the description, paragraphs [0159]-[0160]), the sampling channel 3006 being configured to convey subsequent amounts of blood between the inlet path 3002 and the outlet path 3004 after the first

amount of blood is received by the chamber 3008 (see the description, paragraphs [0160]-[0170]).

The differences of the technical solution sought for protection in claim 20 as compare with the contents disclosed by Reference 1 lie in: a reservoir configured for receiving an evacuated blood collection tube to collect a subsequent portion of the sample of blood; an outlet path connected with the sample needle. Based on the differences, it is determined that the technical problem to be practically solved by the present application is how to collect a sample. However, Reference 1 discloses in another embodiment: a reservoir configured for receiving an evacuated blood collection tube to collect a subsequent portion of the sample of blood; an outlet path connected with the sample needle 5 (see the description, paragraph [0065], Figs. 1, 7). The above differences are disclosed by another embodiment of Reference 1.

Thus, it is obvious for a person skilled in the art to obtain the technical solution sought for protection in claim 20 on the basis of Reference 1 in combination with routine technical means in the art. Therefore, the technical solution sought for protection in claim 20 does not possess prominent substantive features or represent notable progress, and does not possess inventiveness prescribed under Article 22.3 of the Patent Law.

3. Claims 2-4 refer to claim 1, claim 10 refers to claim 1, and claim 11 refers to claim 10. It is disclosed: the junction is angled from the inlet path toward the chamber (see the description, paragraph [0160], Figs. 17A, 30A); the junction has a cross-sectional area that is smaller than a cross-sectional area of the inlet path (see the description, paragraph [0160], Figs. 17A, 30A); the junction has a cross-sectional area that is larger than a cross-sectional area of the inlet path (see the description, paragraphs [0160], [0163], Figs. 17A, 30A); the chamber 3008 has a vent 3010 that allows air to be displaced by the first

portion of blood (see the description, paragraphs [0161], [0163]-[0165], Figs. 30A-D); the vent 3010 includes two or more vent apertures 3012 (see the description, paragraphs [0160]-[0161]). Therefore, where the claims referred to do not possess novelty, claims 2-4 and 10-11 do not possess novelty prescribed under Article 22.2 of the Patent Law, either.

4. Claim 5 refers to claim 1, claim 13 refers to claim 12, and claim 21 refers to claim 20. Reference 2 (US4349035A) discloses (see the description, line 20 in column 4 to line 7 in column 8, and Figs. 1-10): a blood collection assembly comprises a cannular 19 (comprising an inlet path) (see the description, lines 23-28 in column 4, Fig. 5), a valve 22 connected to a receptacle 21 (comprising a chamber) (see the description, lines 23-28 in column 4, Figs. 4-5); the purpose of valve 22 (namely one or more passive structures) is to operably open to allow blood to only flow into receptacle 21, but to operably close to prevent blood from backflowing out of the receptacle 21 toward the patient (namely passive structures configured to inhibit the return to the inlet path of any of the first portion of blood received by the chamber); valve 22 is an elastomeric material, such as rubber, which is substantially tubular in cross-section and which projects from stopper 25 a short distance into receptacle 21; at the far or distal end of valve 22, it tapers to a point; at the point of the tubular valve is a slit 28 which communicates with space 26; this slit serves as an operable passageway to open up to allow blood to flow into receptacle 21; when slit 28 is closed, it forms a liquid tight seal so as to prevent blood from flowing therethrough in that closed position; other configurations in this type valve may be employed, for example, a dome-shaped valve with an operable hole therein. Accordingly, partial of the additional technical features of claim 5 is disclosed by Reference 2. Moreover, the disclosed feature performs the same function in Reference 2 as in the present application, namely inhibiting backflow of the blood. Reference 2 provides a technical inspiration, based on which the person skilled in the art would easily envisage disposing

the junction of Reference 1 to have said structure, thereby inhibiting backflow of the blood. Therefore, where the claims referred to do not possess novelty, claims 5, 13, and 21 do not possess inventiveness prescribed under Article 22.3 of the Patent Law, either.

5. Claim 6 refers to claim 5, and claim 14 refers to claim 13. The additional features of claims 6 and 14 are disclosed by Reference 1: the valve 22 exhibits a conical shape (namely the feature "one or more passive structures include a conical baffle having a tapered end directed toward the chamber") (see the description, lines 13-17 in column 5, and Figs. 4-5). Therefore, where the claims referred to do not possess inventiveness, claims 6 and 14 do not possess inventiveness prescribed under Article 22.3 of the Patent Law, either.

6. Claim 7 refers to claim 5, and claim 15 refers to claim 13. Reference 3 (US5401262A) discloses (see the description, line 9 in column 8 to line 53 in column 26, Figs. 1-15): a blood drainage device; the plurality of curved baffles 112a-112c (namely two or more staggered baffles) in the upper portion of the manometer chamber return spray and condensate to the water column, resulting in further effectiveness of fluid retention in the column. The disclosed feature performs the same function in Reference 3 as in the present application, namely retaining fluid. Reference 3 provides with a technical inspiration. In view of this, the remaining additional features belong to routine technical means easily envisaged by the person skilled in the art. Therefore, where the claims referred to do not possess inventiveness, claims 7 and 15 do not possess inventiveness prescribed under Article 22.3 of the Patent Law, either.

7. Claims 8 and 9 refer to claim 5, claims 16 and 17 refer to claim 13, and claim 22 refers to claim 21. The additional features of claims 8-9, 16-17, and 22 belong to routine technical means easily envisaged by the person skilled in the

art on the basis of valve 22 disclosed by Reference 2. Therefore, where the claims referred to do not possess inventiveness, claims 8-9, 16-17, and 22 do not possess inventiveness prescribed under Article 22.3 of the Patent Law, either.

8. Claim 18 refers to claim 12. The additional feature of claim 18 is disclosed by Reference 1 (*ibid*): the chamber 3008 has a vent 3010 that allows air to be displace by the first portion of blood, and the vent 3010 is further configured to close upon the chamber 3008 being filled with the first portion of blood. Therefore, where the claim referred to does not possess novelty, claim 18 does not possess novelty prescribed under Article 22.2 of the Patent Law, either.

9. Claim 23 refers to claim 20. The additional feature of claim 23 is disclosed by Reference 1 (*ibid*): the chamber 3008 has a vent 3010 that allows air to be displaced by the first portion of blood (see the description, paragraphs [0161], [0163]-[0165], Figs. 30A-D). Therefore, where the claim referred to does not possess inventiveness, claim 23 does not possess inventiveness prescribed under Article 22.3 of the Patent Law, either.

Claims 1 and 12 do not comply with the provision under Article 26.4[4] of the Patent Law.

The subject matter of claims 1 and 12 cannot clearly reflect the technical field to which the technical solutions sought for protection relate, with the result that the protection scope of claims 1 and 12 is unclear. Therefore, claims 1 and 12 do not comply with the provision under Article 26.4 of the Patent Law.

[4] Article 26.4 The claims shall be supported by the description and shall define the scope of the patent protection sought for in a clear and concise manner.

For the above reasons, no patent right can be granted for the present application. Moreover, the description of the present application does not disclose any other patentable substantive content. Therefore, the present application does not possess a prospect of grant even if the amendments would be made to the application documents. If the Applicant cannot present convincing causes within the time limit specified in the present office action, the present application will be rejected.

Moreover, pursuant to *Announcement on Suspending the Collection and Adjustment of Some Patent Charges* (No. 272) issued by China National Intellectual Property Administration, where an invention patent application that entered into the substantive examination phase is withdrawn on the Applicant's own initiative prior to expiration of the time limit for responding to the First Office Action (except the case where a response has been filed) from 1 August 2018, it is allowed to request a refund 50% of the substantive examination fee.

Should you have any questions on the examination opinions, you may feed back your opinions via the following ways: phone of the Examiner: 010-53962499, or phone on-duty: 010-53962356, or email address: sxbjzx_yijian@cnipa.gov.cn. Please note that the contents fed back through the email address should not have legal force and formal observation and/or amendment texts should be submitted to the Receiving Department of the Patent Office within the time limit specified.

Examiner: Peijie JIANG

Code: 30082386

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100088

北京市海淀区北太平庄路 18 号 11 层 A1110-11 北京世峰知识产权代理有限公司
卓霖(010-82800919) 许向彤(010-82800919)

发文日：

2023 年 08 月 03 日

申请号：202010300942.7 **发文序号：2023080301552950**

申请人：酷睿有限公司

发明创造名称：具有被动流体控制接合部的血液污染物分离装置

第 一 次 审 查 意 见 通 知 书

1.☒应申请人提出的实质审查请求，根据专利法第 35 条第 1 款的规定，国家知识产权局对上述发明专利申请进行实质审查。

☐根据专利法第 35 条第 2 款的规定，国家知识产权局决定自行对上述发明专利申请进行审查。

2.☒申请人要求以其在：

US 专利局的申请日 2020 年 03 月 13 日为优先权日， US 专利局的申请日 2020 年 03 月 19 日为优先权日。

☒申请人已经提交了经原受理机构证明的第一次提出的在先申请文件的副本。

☐申请人尚未提交经原受理机构证明的第一次提出的在先申请文件的副本，根据专利法第 30 条的规定视为未要求优先权要求。

3.☐经审查，申请人于_____提交的修改文件，不符合专利法实施细则第 51 条第 1 款的规定，不予接受。

4.审查针对的申请文件：

☐原始申请文件。☐分案申请递交日提交的文件。☒下列申请文件：

申请日提交的说明书摘要、说明书附图； 2023 年 6 月 29 日提交的权利要求第 1-23 项、说明书第 1-251 段。

5.☐本通知书是在未进行检索的情况下作出的。

☒本通知书是在进行了检索的情况下作出的。

☒本通知书引用下列对比文件(其编号在今后的审查过程中继续沿用)：

编号	文 件 号 或 名 称	公开日期（或抵触申请的申请日）
1	US2018177445A1	2018-06-28
2	US4349035A	1982-09-14
3	US5401262A	1995-03-28

6.审查的结论性意见：

关于说明书：

☐申请的内容属于专利法第 5 条规定的不授予专利权的范围。
☐说明书不符合专利法第 26 条第 3 款的规定。
☐说明书不符合专利法第 33 条的规定。
☐说明书的撰写不符合专利法实施细则第 17 条的规定。
☐_____

关于权利要求书：

☐权利要求_____不符合专利法第 2 条第 2 款的规定。
☐权利要求_____不符合专利法第 9 条第 1 款的规定。
☒权利要求 1-4、12、18 不具备专利法第 22 条第 2 款规定的新颖性。
☒权利要求 5-11、13-17、19-23 不具备专利法第 22 条第 3 款规定的创造性。
☐权利要求_____不具备专利法第 22 条第 4 款规定的实用性。
☐权利要求_____属于专利法第 25 条规定的不授予专利权的范围。
☒权利要求 1、12 不符合专利法第 26 条第 4 款的规定。
☐权利要求_____不符合专利法第 31 条第 1 款的规定。
☒权利要求 19 不符合专利法第 33 条的规定。
☐权利要求_____不符合专利法实施细则第 19 条的规定。
☐权利要求_____不符合专利法实施细则第 20 条的规定。
☐权利要求_____不符合专利法实施细则第 21 条的规定。
☐权利要求_____不符合专利法实施细则第 22 条的规定。
☐_____

☐申请不符合专利法第 26 条第 5 款或者实施细则第 26 条的规定。
☐申请不符合专利法第 19 条第 1 款的规定。
☐分案申请不符合专利法实施细则第 43 条第 1 款的规定。

上述结论性意见的具体分析见本通知书的正文部分。

7.基于上述结论性意见，审查员认为：

☐申请人应当按照通知书正文部分提出的要求，对申请文件进行修改。
☐申请人应当在意见陈述书中论述其专利申请可以被授予专利权的理由，并对通知书正文部分中指出的不符合规定之处进行修改，否则将不能授予专利权。
☒专利申请中没有可以被授予专利权的实质性内容，如果申请人没有陈述理由或者陈述理由不充分，其申请将被驳回。
☐_____

8.申请人应注意下列事项：

(1) 根据专利法第 37 条的规定，申请人应在收到本通知书之日起的 4 个月内陈述意见，如果申请人无正当理由逾期不答复，其申请被视为撤回。

(2) 申请人对其申请的修改应当符合专利法第 33 条的规定，不得超出原说明书和权利要求书记载的范围，同时申请人对专利申请文件进行的修改应当符合专利法实施细则第 51 条第 3 款的规定，按照本通知书的要求进行修改。

(3) 申请人的意见陈述书和/或修改文本应邮寄或递交国家知识产权局专利局受理处，凡未邮寄或递交给受理处的文件不具备法律效力。

(4) 未经预约，申请人和/或代理师不得前来国家知识产权局专利局与审查员举行会晤。

(5) 对进入实质审查阶段的发明专利申请，在第一次审查意见通知书答复期限届满前（已提交答复意见的除外），主动申请撤回的，可以请求退还 50%的专利申请实质审查费。

9.本通知书正文部分共有 4 页，并附有下述附件：

☐引用的对比文件的复印件共_____份_____页。
☐_____



审查员：姜佩杰　　联系电话：010-53962499　　审查部门：专利审查协作北京中心

第 一 次 审 查 意 见 通 知 书

申请号:202010300942 7

本申请涉及血液优化装置，现提出如下的审查意见：

权利要求 19 不符合专利法第 33 条的规定

权利要求 19 中限定“通气口还包括盖，在空气被置换后，所述盖抑制空气重新进入所述腔室”，而通过原说明书中记载可知，“透气性血液屏障可以由一种或多种材料形成，该材料允许空气通过直到与液体接触，然后这种材料被完全或部分密封以防止或抑制空气和/或液体的通过”（参见说明书第 0070 段）；“透气性血液屏障 1412 可以覆盖有保护罩 1416。保护罩 1416 的尺寸和构造可以设定成禁止使用者通过其手指或其他外部器具触摸透气性血液屏障 1412，同时当由于血液借助患者自身的血压而被迫进入隔离室 1408 中而使空气从隔离室 1408 中排出时，仍允许空气离开透气性血液屏障 1412。另外，保护罩 1416 可被构造成抑制或防止透气性血液屏障对环境流体或飞溅物的意外暴露。”（参见说明书第 0105 段）；由此可知，空气被置换后，抑制空气重新进入腔室的是透气性血液屏障，而非保护罩或盖等结构，保护罩或盖是用于抑制或防止透气性血液屏障对环境流体或飞溅物的意外暴露（可参见说明书第 0105、0115、0136 段）。权利要求 9 的上述限定并未记载在原申请文件中，且不能由原申请文件直接的、毫无疑义确定得到，权利要求 9 超出了原说明书和权利要求书记载范围，不符合专利法第 33 条的规定。

权利要求 1-4、12、18 不符合专利法第 22 条第 2 款规定的新颖性；权利要求 5-11、13-17、19-23 不符合专利法第 22 条第 3 款规定的创造性

1.权利要求 1、12 请求保护一种装置，对比文件 1（US2018177445A1）公开了（说明书第 0058-0170 段，附图 1-30G）：一种血液隔离装置，包括具有入口端口（说明书第 0156、0161 段）和出口端口（说明书第 0159、0161 段）的壳体 3001（说明书第 0161 段），该壳体 3001 包含：

入口路径 3002（说明书第 0156 段，图 30A）（即包含入口端口，与入口端口连接的入口路径）；

出口路径 3004（说明书第 0158 段，图 30A）（即包含出口端口，与出口端口连接的出口路径）；

腔室 3008（说明书第 0160 段，图 30A），通过接合部 3007 与所述入口路径 3002 连接，并被构造成通过所述入口路径 3002 接收第一部分血液（说明书第 0160、0163-0164 段），所述接合部 3007 被构造为抑制由腔室 3008 接收的任何所述第一部分血液返回所述入口路径 3002（说明书第 0061、0067、0156、0160-0161 段）；以及

在入口路径 3002 和出口路径 3004 之间连接的采样通道 3006（说明书第 0159-0160 段），所述采样通道 3006 被构造为在第一量的血液被腔室 3008 接收之后在入口路径 3002 和出口路径 3004 之间输送后续量的血液（说明书第 0160-0170 段）。

由此可见，对比文件 1 已经公开了上述权利要求的全部技术特征，且对比文件 1 所公开的技术方案与该

权利要求所要求保护的技术方案属于同一技术领域，用于解决相同的技术问题，并能产生相同的技术效果，因此上述权利要求所要求保护的技术方案不具备新颖性。

2. 权利要求 20 请求保护一种血液样本优化系统，对比文件 1（US2018177445A1）公开了（说明书第 0058-0170 段，附图 1-30G）：一种血液样本优化系统（说明书第 0156 段），包括血液采样系统，包括：血液隔离装置 3000 包括入口路径 3002，该入口路径 3002 可以与患者针（即静脉穿刺设备）连接，该患者针插入患者的血管系统中以用于进入和抽出血液样品（即其构造成对患者进行静脉穿刺以获取患者的血液样本）。血液隔离装置 3000 包括从入口路径 3002 到出口路径 3004 的采样通道 3006（即与所述静脉穿刺设备连接的血液采样通路，用于输送所述血液样本）；出口路径 3004（包含储存器），以收集血液样本的后续部分；以及沿患者针和出口路径 3004（包含储存器）之间的血液采样通路 3006 连接的装置，该装置包括：

与患者针连接的入口路径 3002（说明书第 0156 段，图 30A）（即包含入口端口，与入口端口连接的入口路径）；

出口路径 3004（说明书第 0158 段，图 30A）（即包含出口端口，与出口端口连接的出口路径）；

腔室 3008（说明书第 0160 段，图 30A），通过接合部 3007 与所述入口路径 3002 连接，并被构造成通过所述入口路径 3002 接收第一部分血液（说明书第 0160、0163-0164 段），所述接合部 3007 被构造为抑制由腔室 3008 接收的任何所述第一部分血液返回所述入口路径 3002（说明书第 0061、0067、0156、0160-0161 段）；以及

在入口路径 3002 和出口路径 3004 之间连接的采样通道 3006（说明书第 0159-0160 段），所述采样通道 3006 被构造为在第一量的血液被腔室 3008 接收之后在入口路径 3002 和出口路径 3004 之间输送后续量的血液（说明书第 0160-0170 段）。

权利要求 20 所要求保护的技术方案与对比文件 1 公开的内容相比，其区别在于：储存器，其构造成用于接收抽空的采血管，以收集血液样本的后续部分；与样本针连接的出口路径，基于上述区别，本申请实际要解决的技术问题是：如何采集样本。但是对比文件 1 的另一实施例公开：储存器，其构造成用于接收抽空的采血管，以收集血液样本的后续部分；与样本针 5 连接的出口路径（说明书第 0065 段，图 1、7），上述区别被对比文件 1 的另一实施例公开。

由此可知，在对比文件 1 的基础上结合常规技术手段以获得该权利要求请求保护的技术方案对本领域技术人员来说是显而易见的，因此，该权利要求的技术方案不具备突出的实质性特点和显著的进步，不具备专利法第 22 条第 3 款规定的创造性。

3.权利要求 2-4 引用权利要求 1、权利要求 10 引用权利要求 1、权利要求 11 引用权利要求 10，接合部从入口路径朝向腔室成角度（说明书第 0160 段，图 17A、30A）；接合部的截面积小于入口路径的截面积（说明书第 0160 段，图 17A、30A）；接合部的截面积大于入口路径的截面积（说明书第 0160、0163 段，图

17A、30A）；腔室 3008 具有通气口 3010，所述通气口 3010 允许空气被所述第一部分血液置换（说明书第 0161、0163-0165 段，图 30A-D）；通气口 3010 包括两个或更多个通气孔 3012(说明书第 0160-0161 段）；因此，在其引用的权利要求不具备新颖性时，上述权利要求也不具备专利法第 22 条第 2 款规定的新颖性。

4.权利要求 5 引用权利要求 1，权利要求 13 引用权利要求 12，权利要求 21 引用权利要求 20，对比文件 2（US4349035A）公开（说明书第 4 栏第 20 行至第 8 栏第 7 行，图 1-10）：一种血液采集组件，包括管 19（包含入口路径）（参见说明书第 4 栏第 23-28 行，图 5），连接到容器 21（具有腔室）的阀 22（参见说明书第 4 栏第 23-28 行，图 4-5），阀 22（即一个或多个被动结构）的目的是可操作地打开以允许血液仅流入容器 21，但是可操作地关闭以防止血液从容器 21 向患者回流（即被动结构构造成抑制由腔室接收的任何第一部分血液返回到入口路径）。阀 22 是弹性体材料，例如橡胶，其横截面基本上是管状的并且从止动件 25 突出短距离到容器 21 中。在阀 22 的远端或远端处，它逐渐变细到一点。在管状阀的点处是与空间 26 连通的狭缝 28。该狭缝用作可操作通道以打开以允许血液流入容器 21；当狭缝 28 闭合时，其形成液密密封，以便防止血液在该闭合位置流过其中。在这种类型的阀中可以采用其他构造，例如，其中具有可操作孔的圆顶形阀。故部分附加特征 5 被对比文件 2 公开，且其在对比文件 2 中的所起的作用与其在本申请中所起的作用相同，都是用于抑制血液回流。对比文件 2 给出技术启示，在此基础上，本领域技术人员容易想到将对比文件 1 的接合部设置成具有上述结构，进而抑制血液回流。因此，在其引用的权利要求不具备新颖性时，上述权利要求也不具备专利法第 22 条第 3 款规定的创造性。

5.权利要求 6 引用权利要求 5，权利要求 14 引用权利要求 13，其附加特征被对比文件 1 公开：阀 22 程锥形（即一个或多个被动结构包括锥形挡板，所述锥形挡板具有指向所述腔室的锥形端）（参见说明书第 5 栏第 13-17 行，图 4-5），因此，在其引用的权利要求不具备创造性时，上述权利要求也不具备专利法第 22 条第 3 款规定的创造性。

6.权利要求 7 引用权利要求 5，权利要求 15 引用权利要求 13，对比文件 3（US5401262A）公开（说明书第 8 栏第 9 行至第 26 栏第 53 行，图 1-15）：一种血液引流装置，压力计腔室的上部中的多个弯曲挡板 112a-112c（即两个或更多个交错的挡板）将喷雾和冷凝物返回到水柱，从而进一步有效地保持柱中的流体。其在对比文件 3 中的作用与其在本申请中作用相同，都是用于流体潴留，对比文件 3 给出了技术启示，在此基础上，其余附加特征属于本领域技术人员容易想到的常规技术手段，因此，在其引用的权利要求不具备创造性时，上述权利要求也不具备专利法第 22 条第 3 款规定的创造性。

7.权利要求 8、9 引用权利要求 5，权利要求 16、17 引用权利要求 13，权利要求 22 引用权利要求 21，其附加特征属于本领域技术人员在对比文件 2 公开的阀 22 的基础上容易想到的常规技术手段，因此，在其引用的权利要求不具备创造性时，上述权利要求也不具备专利法第 22 条第 3 款规定的创造性。

8.权利要求 18 引用权利要求 12，其附加特征被对比文件 1 公开（参见同上）：腔室 3008 具有通气口

3010，所述通气口 3019 允许空气被所述第一部分血液置换，所述通气口 3010 进一步构造成在所述腔室 3008 中充满所述第一部分血液时关闭。因此，在其引用的权利要求不具备新颖性时，上述权利要求也不具备专利法第 22 条第 2 款规定的新颖性。

9.权利要求 23 引用权利要求 20，其附加特征被对本比文件 1 公开（参见同上）：腔室 3008 具有通气口 3010，所述通气口 3010 允许空气被所述第一部分血液置换（说明书第 0161、0163-0165 段，图 30A-D）；因此，在其引用的权利要求不具备创造性时，上述权利要求也不具备专利法第 22 条第 3 款规定的创造性。

权利要求 1,12 不符合专利法第 26 条第 4 款的规定

权利要求 1、12 主题名称未能清楚反映出请求保护的技术方案所涉及的技术领域，导致该权利要求的保护范围不清楚，不符合专利法第 26 条第 4 款的规定。

基于上述理由，本申请不能被授予专利权，而且本申请的说明书中也没有记载其它任何可获得专利权的实质性内容，因而即使对申请文件进行修改，本申请也不具备被授予专利权的前景。如果申请人不能在本通知书规定的答复期限内提出具有说服力的理由，本申请将被驳回。

另根据国家知识产权局《关于停征和调整部分专利收费的公告》（第 272 号）规定，对进入实质审查的发明专利申请，在第一次审查意见通知书答复期限前（已提交答复意见的除外）主动申请撤回的，可以请求退还 50%的专利申请实质审查费。

如您对审查意见存在疑问，可拨打审查员电话 010-53962499，或值班电话 010-53962356 ，也可通过邮箱 sxbjzx_yijian@cnipa.gov.cn 反馈意见。请注意：邮箱反馈的内容不具备法律效力，请将正式的意见陈述书和/或修改文本在规定期限内提交给专利局受理部门。

审查员姓名:姜佩杰
审查员代码:30082386

国 家 知 识 产 权 局

检 索 报 告

申请号：2020103009427	申请日：2020 年 04 月 16 日	首次检索
申请人：酷睿有限公司	最早的优先权日：2020 年 03 月 13 日	
权利要求项数：23	说明书段数：251+117	

审查员确定的 IPC 分类号：A61B 5/15,A61B 5/153

检索记录信息：US2004073171A1: 美局检索报告

US2018177445A1: 欧局检索报告

US2018271425A1: 欧局检索报告

US2018353117A1: 欧局检索报告

US4349035A: 欧局检索报告

US5401262A: 欧局检索报告

US2018177445A1: 3 VCN, /PN US2018177445 or us4349035 OR US5401246

相 关 专 利 文 献

类型	国别以及代码[11] 给出的文献号	代码[43]或[45] 给出的日期	IPC 分类号	相关的段落 和/或图号	涉及的权 利要求
X	US2018177445A1	2018-06-28	A61B5/15	说明书第 0058-0170 段，附图 1-30G	1-4、6、8-12、14、16-18、20、23
Y	US2018177445A1	2018-06-28	A61B5/15	说明书第 0058-0170 段，附图 1-30G	5、7、13、15、21、22
Y	US4349035A	1982-09-14	A61M1/00	说明书第 4 栏第 20 行至第 8 栏第 7 行，图 1-10	5、13、21、22
Y	US5401262A	1995-03-28	A61M1/00	说明书第 8 栏第 9 行至第 26 栏第 53 行，图 1-15	7、15

A	US2004073171A1	2004-04-15	A61M5/178	全文	1-18、20-23
A	US2018271425A1	2018-09-27	A61B5/15	全文	1-18、20-23
A	US2018353117A1	2018-12-13	A61B5/15	全文	1-18、20-23

相 关 非 专 利 文 献					
类型	书名（包括版本号和卷号）	出版日期	作者姓名和出版者名称	相关页数	涉及的权利要求
类型	期刊或文摘名称 （包括卷号和期号）	发行日期	作者姓名和文章标题	相关页数	涉及的权利要求
类型	网址	网络发布日 或公开日	作者姓名和网页标题	相关部分	涉及的权利要求

表格填写说明事项：

1. 审查员实际检索领域的 IPC 分类号应当填写到大组和／或小组所在的分类位置。
2. 期刊或其它定期出版物的名称可以使用符合一般公认的国际惯例的缩写名称。
3. 相关文件的类型说明：

   X：单独影响权利要求的新颖性或创造性的文件；

   Y：与本检索报告中其他 Y 类文件组合后影响权利要求的创造性的文件；

   A：背景技术文件，即反映权利要求的部分技术特征或者有关的现有技术的文件；

   R：任何单位或个人在申请日向专利局提交的、属于同样的发明创造的专利或专利申请文件。

   P：中间文件，其公开日在申请的申请日与所要求的优先权日之间的文件，或者会导致需要核实该申请优先权的文件；

E：单独影响权利要求新颖性的抵触申请文件；

T：申请日或优先权日当天或之后公布的，可以对所要求保护发明的理论或原理提供清楚解释的文件，或者可显示出所要求保护发明的推理或事实不成立的文件；

L：除 X、Y、A、R、P、E 和 T 类文件之外的文件。

审 查 员：姜佩杰　　审查部门：专利审查协作北京中心
2023 年 08 月 01 日

(Translation)

Reference No.: Letter No.: 150687 Mailing Date: April 4, 2023 1

Notice of Allowance

(Divisional)

Application Serial No.:	2020-118498
Drafting Date:	March 23, 2023
Examiner:	ISONO Koji 3411 2Q00
Title of the Invention:	BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD
Number of Claims:	15
Applicant(s):	KURIN, INC.
Agent:	MURAKOSHI, Satoshi

A decision is hereby made to grant patent right to the above identified patent application on the ground that no cause for rejecting the application has been found in the examination.

This is to certify that all the above-referenced items are identical to the JPO's official record.
Certificated: March 28, 2023
Administrative Official of Ministry of Economy, Trade and Industry, Takashi SATO

Note: Applicant must pay Issue Fee within 30 days from the mailing date indicated above.

(Translation)

- Type of Application: Divisional Application
- Cited References: Yes
- Grace Period under Patent Act Article 30: No
- Amendment to Title of the Invention: No
- Deposit of Biological Material : N/A

(Translation)

Reference No.: Letter No.: 150687 Mailing Date: April 4, 2023 /E

Reference Information

Application Serial No.: 2020-118498

- FI

  A61B 5/15 100 ,
  A61B 5/15 200

- Search Fields (IPC, DB Name):

  A61B 5/00-5/398

- References Cited :

US Patent Application Publication No.2008/0145933	(US,A1)
Japanese Patent Application Publication No.2001-000424	(JP,A)
Japanese Patent Application Publication No.H09-504726	(JP,A)
US Patent Application Publication No.2006/0009713	(US,A1)
Japanese Patent Application Publication No.S58-025146	(JP,A)
Japanese Patent Application Publication No.H02-224742	(JP,A)
US Patent Application Publication No.2011/0306899	(US,A1)

- Non-patent literatures:

特許査定

（分割）

特許出願の番号	特願２０２０－１１８４９８
起案日	令和　５年　３月２３日
特許庁審査官	磯野　光司　３４１１　２Ｑ００
発明の名称	血液サンプル最適化システム及び血液隔離装置
請求項の数	１０
特許出願人	クリン　インコーポレイテッド
代理人	村越　智史（ほか　４名）

この出願については、拒絶の理由を発見しないから、特許査定をします。

上記はファイルに記録されている事項と相違ないことを認証する。
認証日　令和 5年 3月28日　経済産業事務官　佐藤　隆

注意：この書面を受け取った日から３０日以内に特許料の納付が必要です。

・出願種別　分割
・参考文献　有
・特許法第３０条適用　無
・発明の名称の変更　無

・菌寄託

参考情報

特許出願の番号　特願２０２０－１１８４９８

・ＦＩ

Ａ６１Ｂ　５／１５　１００　，
Ａ６１Ｂ　５／１５　２００

・調査した分野（ＩＰＣ，ＤＢ名）

Ａ６１Ｂ　５／００－５／３９８

・参考特許文献

米国特許出願公開第２００８／０１４５９３３	（ＵＳ，Ａ１）
特開２００１－０００４２４	（ＪＰ，Ａ）
特表平０９－５０４７２６	（ＪＰ，Ａ）
米国特許出願公開第２００６／０００９７１３	（ＵＳ，Ａ１）
特開昭５８－０２５１４６	（ＪＰ，Ａ）
特開平０２－２２４７４２	（ＪＰ，Ａ）
米国特許出願公開第２０１１／０３０６８９９	（ＵＳ，Ａ１）

・参考図書雑誌

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NOTICE OF ALLOWANCE AND FEE(S) DUE

27500 7590 01/17/2024

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

EXAMINER	
ABOUELELA, MAY A	
ART UNIT	**PAPER NUMBER**
3791	

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

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

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	04/17/2024

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27500 7590 01/17/2024
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/538,990	11/30/2021	Bobby E. ROGERS	069366-0572201_KUR2C03US	3420

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APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	04/17/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
ABOUELELA, MAY A	3791	600-573000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via the USPTO patent electronic filing system ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

❑ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

❑ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

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27500 7590 01/17/2024

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

EXAMINER	
ABOUELELA, MAY A	

ART UNIT	PAPER NUMBER
3791	

DATE MAILED: 01/17/2024

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/ owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).
https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to:

1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;
2) a federal, state, local, or international agency, in response to its request;
3) a contractor of the USPTO having need for the information in order to perform a contract;
4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;
5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c));
9) the Office of Personnel Management (OPM) for personnel research purposes; and
10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Notice of Allowability	Application No. 17/538,990	Applicant(s) ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 12/20/2023.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 1-20 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☑ Interview Summary (PTO-413), Paper No./Mail Date. 10/08/2024.
5. ☑ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/MAY A ABOUELELA/
Primary Examiner, Art Unit 3791

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 12/20/2023. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Terminal Disclaimer

3. The terminal disclaimer filed on 12/20/2023 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S Patent Applications No. 9820682, 10143412 and 11185266 has been reviewed and is accepted. The terminal disclaimer has been recorded.

EXAMINER'S AMENDMENT

4. Authorization for this examiner's amendment was given in an interview with BEN HUDSON on 01/08/2024.

Claim 5 should be amended as follow:

5. (Currently Amended) The blood sample control device in accordance with claim **3** ~~2~~, wherein the housing comprises a bottom member mated with a top member, each of the

bottom member and the top member defining a part of each of the inlet, the outlet, the chamber, and the sampling channel.

Claim 10 should be amended as follow:

10. (**Currently Amended**) The bodily fluid control device in accordance with claim 6, wherein the air permeable blood barrier includes an air permeable material that at least partially seals upon contact with **the bodily fluid** ~~blood~~.

Claim 13 should be amended as follow:

13. (Currently Amended) A bodily fluid control device comprising;

an inlet;

a junction connected with the inlet;

an outlet;

a chamber connected with the inlet via the junction, the chamber having a vent that includes an air permeable bodily fluid barrier that at least partially seals upon contact with a first portion of bodily fluid;

a housing that houses and defines the inlet, the outlet, and the chamber; and

wherein the chamber and the junction **are** ~~being~~ configured to direct the first portion of the bodily fluid from the inlet into the chamber toward the air permeable bodily fluid barrier and to displace air in the chamber, whereupon at least partially sealing of the air permeable bodily fluid barrier enables at least temporary containment of the first portion of the bodily fluid in the chamber, and enables a second portion of the bodily fluid from the inlet to bypass the chamber via the junction and be directed toward the outlet.

Allowable Subject Matter

5. Claims 1-20 are allowed.

6. The following is an examiner's statement of reasons for allowance: the most pertinent prior art Eldridge et al (U.S 4,207,870) teaches a blood sample device for sampling blood conveyed from a patient, the blood device comprising; an inlet port configured to receive the blood conveyed from the patient; an outlet port; a chamber; and a sampling channel having a distal end connected with the outlet port; a junction connected between the inlet port, the chamber and the sampling channel, the junction being sized and configured such that a first portion of blood conveyed from the patient flows into the chamber to displace air therein through the air permeable blood barrier and to be sequestered in the chamber.

The prior art does not teach, disclose and/or fairly suggest the chamber having a vent that includes an air permeable blood barrier, and wherein the junction is configured to allow a second portion of blood to bypass the chamber and the first portion of blood sequestered therein to be directed into the sampling channel toward the outlet port.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAY A ABOUELELA whose telephone number is (571)270-7917. The examiner can normally be reached 8-5.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JACQUELINE CHENG can be reached on 5712725596. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MAY A ABOUELELA/
Primary Examiner, Art Unit 3791

Examiner-Initiated Interview Summary	**Application No.** 17/538,990	**Applicant(s)** ROGERS et al.		
	Examiner MAY A ABOUELELA	**Art Unit** 3791	**AIA (First Inventor to File) Status** Yes	**Page** 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	**Title**	**Type**
MAY A ABOUELELA	Primary Examiner	Telephonic
BEN HUDSON	Attorney of Record	

Date of Interview: 08 January 2024

Issues Discussed:

35 U.S.C. 112

Applicant and Examiner discussed the claims set mailed on 12/20/2023. Applicant and Examiner discussed the claim language with respect to the applied prior art and the disclosure. Applicant and Examiner discussed proposed claim amendments represented by the Examiner to overcome 112 rejection for claims 5, 10 and 13. The Applicant has authorized the Examiner to amend the claims.

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	

Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04
Please further see:
MPEP 713.04
Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b)
37 CFR § 1.2 Business to be transacted in writing

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	17538990
Filing Date	2021-11-30
First Named Inventor	Bobby E. ROGERS
Art Unit	OPAP
Examiner Name	CENTRAL, DOCKET
Attorney Docket Number	069366-0572201_KUR2C03US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4416291		1983-11-22	KAUFMAN JOSEPH	
	2	10299713		2019-05-28	PATTON RICHARD G	
	3	10265007		2019-04-23	BULLINGTON GREGORY	
	4	11395612		2022-07-26	BULLINGTON GREGORY J	
	5	10881343		2021-01-05	BULLINGTON GREGORY J	
	6	10596315		2020-03-24	BULLINGTON GREGORY J	
	7	11660030		2023-05-30	BULLINGTON GREGORY J	
	8	11259727		2022-03-01	BULLINGTON GREGORY J	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
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	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

	9	11737693		2023-08-29	BULLINGTON GREGORY J	
	10	11439332		2022-09-13	BULLINGTON GREGORY J	
	11	11589843		2023-02-28	BULLINGTON GREGORY J	
	12	11612340		2023-03-28	BULLINGTON GREGORY J	
	13	11234626		2022-02-01	BULLINGTON GREGORY J	
	14	10624977		2020-04-21	BULLINGTON GREGORY J	
	15	11653863		2023-05-23	BULLINGTON GREGORY J	
	16	11419531		2022-08-23	BULLINGTON GREGORY J	
	17	11786155		2023-10-17	BULLINGTON GREGORY J	
	18	11789017		2023-10-17	BULLINGTON GREGORY J	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20220151525		2022-05-19	BULLINGTON GREGORY J	
	2	20220151527		2022-05-19	BULLINGTON GREGORY J	
	3	20200289039		2020-09-17	BULLINGTON GREGORY J	
	4	20210275068		2021-09-09	MIAZGA JAY M	
	5	20220304664		2022-09-29	HAMMER JEREMY	
	6	20160073937		2016-03-17	BURKHOLZ JONATHAN KARL	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.A.A/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17538990
	Filing Date	2021-11-30
	First Named Inventor	Bobby E. ROGERS
	Art Unit	OPAP
	Examiner Name	CENTRAL, DOCKET
	Attorney Docket Number	069366-0572201_KUR2C03US

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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FLUID DELIVERY

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Certain embodiments of the present invention relate to apparatus and methods for providing a target liquid at a desired location. In certain embodiments, the apparatus includes a piercing member locatable with respect to a sealing membrane of a respective blister pouch that has a tip region which is locatable in an abutting relationship with the sealing membrane in a first mode of operation and through the sealing member in a further mode of operation for providing liquid from the blister pouch at a desired location. Also included in the present invention, inter alia, is a piercing plate comprising a piercing member, together with devices, for example, bio chips and microfluidic devices, which are for use in combination with the apparatus.

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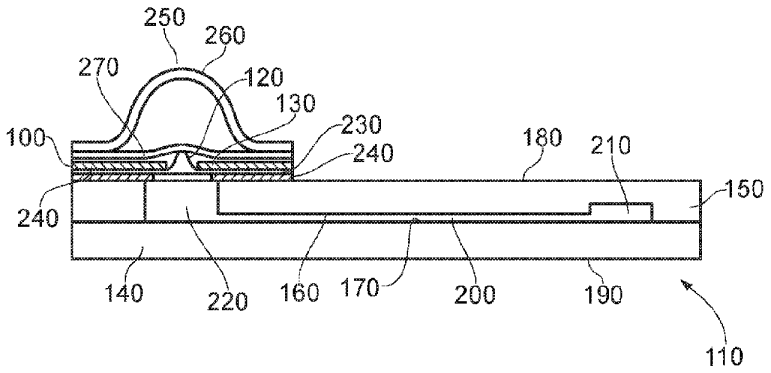


FIG. 1

(57) Abstract: Certain embodiments of the present invention relate to apparatus and methods for providing a target liquid at a desired location. In certain embodiments, the apparatus includes a piercing member locatable with respect to a sealing membrane of a respective blister pouch that has a tip region which is locatable in an abutting relationship with the sealing membrane in a first mode of operation and through the sealing member in a further mode of operation for providing liquid from the blister pouch at a desired location. Also included in the present invention, *inter alia*, is a piercing plate comprising a piercing member, together with devices, for example, bio chips and microfluidic devices, which are for use in combination with the apparatus.

WO 2015/150742 A1

FLUID DELIVERY

Field of the Invention

Certain embodiments of the present invention relate to apparatus and methods for providing a target liquid at a desired location. In certain embodiments, the apparatus includes a piercing member locatable with respect to a sealing membrane of a respective blister pouch that has a tip region which is locatable in an abutting relationship with the sealing membrane in a first mode of operation and through the sealing member in a further mode of operation for providing liquid from the blister pouch at a desired location. Also included in the present invention, *inter alia,* is a piercing plate comprising a piercing member, together with devices, for example, bio chips and microfluidic devices, which are for use in combination with the apparatus.

Background to the Invention

Microfluidic systems have recently emerged as powerful tools for bio-sensing, particularly in enriching and purifying molecules and cells in biological samples. Microfluidic technology has enabled the miniaturisation of normal sized equipment and has resulted in more readily portable devices and the sensing of increasingly small sample volumes and target analyte concentrations which have not been possible with previous technologies.

Microfluidic devices can be laboratory-based devices for use in genomics, sequencing, high-throughput screening and separations. Additionally, microfluidic devices provide the opportunity to integrate processes and measurement systems on a single technology platform leading to the concept of the “lab on a chip”. Thus, microfluidic devices are also sometimes known as "bio-chips" or lab-on-chip" systems. Microfluidic technology has found applications in chemical and system biology, point-of-care analysis, high-throughput biological screening. Advantages associated with lab-on-chip include consumption of small volumes of reagents and sample, and delivery of results in a short timescale.

Microfluidic devices often comprise a substrate together with microstructures such as micropumps, micromixers, ports, microchannels and the like.

The delivery of fluids plays an important role in fields such as chemistry, microbiology and biochemistry. These fluids may include liquids or gases and may provide reagents, buffers, solvents or reactants, to chemical and/or biological processes, including processes involving

microfluidic technology. A problem often associated with fluid delivery to microfluidic devices is the difficulty of delivering known volumes of reagents into the microfluidic flow system in a controlled manner at a steady rate.

Existing technology often relies upon pipetting of reagents and/or samples into wells or chambers of the device. As a result, whilst microfluidic technology may have resulted in portable devices being developed, there still remains the problem of how to easily transport and deliver reagents and/or samples outside a laboratory environment.

One way of storing and delivering fluids such as reagents and/or samples that has been developed is by way of a "blister pouch". Blister pouches include individually sealed units which store fluids or solids prior to delivery and have been used to store and subsequently deliver fluids to microfluidic devices. In order to deliver the fluid or solid to a target location, a user breaks the seal of the unit. The seal may be broken by a user manually applying a force to the seal or by way of an actuator applying pressure. Often, when the seal is broken, the release of the stored fluid is not always controlled and thus at least some of the stored fluid is not directed to the target location. Also there is a risk of fluid "surging" from the blister.

One way of automatically providing the right reagents in the correct volume is to package the reagents into blister packages and allow the blister to release the reagents once the sample is on the chip. However, most conventional blister popper constructs lead to the blisters rupturing in the wrong place and the reagent splashing outside of the chip. This results in a waste of reagent and can lead to a reduction in accuracy if a precise amount of the fluid is required. In addition, on occasion there is a failure of the sealed unit to burst.

Certain embodiments of the present invention aim to at least partially mitigate the problems associated with the prior art.

Summary of Certain Embodiments of the Invention

Certain embodiments of the present invention aim to provide a device and/or method which delivers a fluid, e.g. a liquid, in a controlled manner to a target location.

It is an aim of certain embodiments of the present invention to provide a mechanism that can selectively burst a blister pouch when desired and in a controlled way but which doesn't pose a risk (in terms of causing an undesired breach) at other times.

In a first aspect of the present invention, there is provided apparatus for providing a target liquid at a desired location, comprising at least one piercing member upstanding from a support surface at a height of about around 300 to 1200 microns and locatable with respect to a sealing membrane of a respective blister pouch; wherein a tip region of the piercing member is locatable in an abutting relationship with the sealing membrane in a first mode of operation and through the sealing membrane in a further mode of operation for providing liquid from the blister pouch at a desired location.

In one embodiment, the piercing member is upstanding from a support surface at a height of about around 300 to 1200 microns e.g. 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150 or 1200 microns.

In one embodiment, the piercing member has a height of from about 300 to 1200 microns.

Aptly, in the first mode of operation the piercing member is locatable to deform but not pierce the sealing membrane. In one embodiment, in the first mode of operation, the piercing member does not pierce the sealing membrane when an abutment force of up to about around 1N is applied by the piercing member to the sealing membrane. In one embodiment, in the first mode of operation, the piercing member does not pierce the sealing membrane when an abutment force of up to about around 1N, e.g. 0.80, 0.85, 0.9, 0.95 or 1.0N, is applied by the piercing member to the sealing membrane.

In one embodiment, the tip region comprises a rounded nose region having a generally arcuate shape with a radius of curvature of about around 50 to 1000 microns. Aptly, the radius of curvature is about around 100 to 500 microns. In one embodiment, the radius of curvature of the rounded nose region of the piercing member is approximately 100, 150, 200, 250, 300, 350, 400, 450 or 500 microns.

Thus, in certain embodiments of the present invention the piercing member has a comparatively blunt nose region, which is used to pierce the sealing membrane of the blister pouch when desired. As a result of the "blunt" nose region, when the sealing membrane is

pierced, substantially all of the fluid held in the blister pouch flows over and through the piercing member, rather than, as is the case with many prior art fluid delivery systems, the fluid is released in an uncontrolled manner leading to a portion of the liquid not being directed into the chamber.

In one embodiment, the piercing member further comprises a plurality of abutment wall regions extending from the support surface to the tip region at a predetermined angle so that each wall region forms a tangent with an arc of a rounded nose region at an end of the tip region. Aptly, each abutment wall region meets the nose region at an angle of about around 45 degrees. In one embodiment, each abutment wall region meets the nose region at an angle of approximately 45 degrees e.g. 40, 41, 42, 43, 44, 45, 46 or 47 degrees. Aptly, each abutment wall region meets the nose region at substantially the same angle. Alternatively, each abutment wall region meets the nose region at a different angle to each other abutment wall region.

In one embodiment, the piercing member provides a plurality of fluid communication passageways proximate to the tip region that each communicate liquid urged from a pierced blister pouch to at least one collection chamber under the support surface. In one embodiment, the piercing member comprises two or more fluid communication passageways proximate to the tip region, e.g. 2, 3, 4 or more. In one embodiment, the piercing member comprises four fluid communication passageways.

In an embodiment, the piercing member comprises a plurality of arms extending upwards and in an inclined manner from the support surface. Aptly, the fluid communication passageways are provided by openings in the support surface in notched regions between adjacent arms. In one embodiment, the piercing member comprises two or more upwardly extending arms e.g. 2, 3, 4, or more. In one embodiment, the piercing member comprises four upwardly extending arms.

Certain embodiments of the present invention provide the advantage of a piercing member which provides openings through which the fluid, e.g. a liquid, released from the blister pouch may flow. The liquid may subsequently flow into a chamber e.g. a collection chamber as described herein below. As a result, the likelihood of the reagent being spilt and not collected in the chamber is reduced. Blister pouches are often pre-filled with a required volume of liquid and thus it follows that certain embodiments of the present invention may

provide a more accurate result in a method which is based on calculations involving the known volume of the liquid in the blister pouch.

Certain embodiments of the present invention provide a piercing member which comprises a plurality of openings which allow fluid released from the blister pouch to flow into a chamber situated beneath the piercing member. The plurality of openings results in the fluid flowing downwardly in a plurality of flow streams which should enable the flow of fluid to be controlled more effectively.

Aptly, the first mode of operation comprises a transportation mode during which a blister pouch is transportable in an abutting relationship with the piercing member without risk of puncture.

Certain embodiments of the present invention provide the advantage that the piercing member is capable of piercing a sealing membrane of a blister pouch when a predetermined level of force is applied to either the piercing member or the blister pouch but does not pierce the sealing member when simply in an abutting relationship with the sealing membrane. Thus, certain embodiments of the present invention provide an apparatus which is capable of being transported in an abutting relationship with a sealed blister pouch pre-filled with a reagent for example without the blister pouch being pierced and its contents released.

In one embodiment, in the further mode of operation in which the blister pouch is urged against the piercing member, the piercing member is disposed to rupture the sealing membrane at a rupture force of about around 3 to 12N. Aptly, the piercing member is disposed to rupture the sealing membrane at a force of about 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 N.

In one embodiment, each piercing member is manufactured from a material selected from a group comprising glass, polycarbonate or polymethyl methacrylate (PMMA), cyclic olefin copolymer (COC), polystyrene (PS), polyether ether ketone (PEEK), polytetrafluoroethylene (PTFE) and polypropylene (PP).

In a further aspect of the present invention, there is provided a piercing plate, securable to at least one blister pouch, comprising an apparatus for providing a target liquid at a desired location comprising at least one piercing member upstanding from a support surface at a

height of about around 300 to 1200 microns and locatable with respect to a sealing membrane of a respective blister pouch; wherein a tip region of the piercing member is locatable in an abutting relationship with the sealing membrane in a first mode of operation and through the sealing member in a further mode of operation for providing liquid from the blister pouch at a desired location. Aptly, the apparatus is as further described herein.

In one embodiment, the piercing plate further comprises a planar upper surface, comprising the support surface, and a planar lower surface that is securable to an upper surface of a bio chip. Aptly the piercing plate further comprises an adhesive layer on the lower surface.

In one embodiment, the piercing plate further comprises at least one alignment element that locates the piercing plate at a desired position with respect to each blister pouch. Aptly, the alignment element comprises at least one edge of the piercing plate. In one embodiment, the alignment element comprises at least one locating lug or recess that mates with a complimentary alignment element of the blister pouch.

Aptly, the piercing plate further comprises one further alignment element that locates the piercing plate at a desired position with respect to a bio chip. In one embodiment, each further alignment element comprises at least one edge of the piercing plate.

Aptly, each further alignment element comprises at least one locating lug or recess that mates with a complimentary alignment element of the bio chip. In one embodiment, the piercing plate further comprises a cavity under each piercing member that is locatable in fluid communication with a collection chamber of a bio chip.

Aptly, the piercing plate has a thickness of about around 200 to 1000 microns.

In one embodiment, the piercing plate is manufactured from a material selected from glass, polycarbonate and PMMA.

In one embodiment, the plate and each piercing member are integrally formed. In one embodiment, the plate and the apparatus are integrally formed.

In one embodiment, the plate is retrofittable to an underside of a blister package comprising one or more blister pouches sealed with a sealing membrane.

In a further aspect of the present invention, there is provided a blister pack, comprising a plurality of blister pouches secured together via a web and a common sealing membrane; and at least one piercing plate as described herein secured to a lower surface of the sealing membrane. In one embodiment, the blister pack may be fabricated using vacuum thermoforming of polymer films, for example.

In one embodiment, the blister pack comprises a plurality of frangible lines or perforation lines in the web. In one embodiment, the frangible lines or perforation lines are provided between each blister pouch so as to enable a single blister pouch to be removed from the blister pack.

In a further aspect of the present invention, there is provided a bio chip comprising an apparatus according to the first aspect of the invention as described herein.

As used herein, the term "bio chip" refers to a device which can be used to analyse samples having a volume of from about 10nl and 10ml. The terms "microfluidic device", "microfluidic assembly", "microfluidic systems" and the like may also be used herein to indicate devices, assembly and systems wherein samples for the processing and/or analysis of samples having a volume of from about 10 nl to about 10 ml. In one embodiment, the bio chip is used to analyse samples having a volume of between about 100µl and 2000µl. In one embodiment, the bio-chip is a microfluidic device.

In one embodiment, the bio chip comprises an upper chip layer comprising one or more piercing member as an integral unit. In one embodiment, the bio chip comprises an upper chip layer comprising each piercing member as an integral unit.

In an embodiment, the bio chip further comprises an upper chip layer having an upper surface on which at least one piercing plate comprising said at least one piercing member is secured.

In one embodiment, the bio chip comprises a lower surface of the upper chip layer and wherein the lower surface of the upper chip layer comprises a collection chamber located

beneath each piercing member and at least one channel connecting a collection chamber to a respective sample chamber. Aptly, the channel comprises a channel region that provides a serpentine pathway. Aptly, the channel comprises an inlet end and an outlet end.

In one embodiment, the bio chip comprises a plurality of channels.

In one embodiment, the bio chip comprises a plurality of piercing members and a corresponding plurality of collection chambers. Aptly, a collection chamber is located beneath the piercing element. Aptly, the bio chip comprises a first collection chamber and at least one further collection chamber. In one embodiment, the first collection chamber and the further collection chamber are in fluid communication via a channel region. Aptly, the channel region comprises a T-junction region and/or a Y-junction region.

Certain embodiments of the present invention provide a bio-chip which incorporates at least one blister pouch which is integrally formed with the bio-chip. Certain embodiments of the present invention provide an advantage that fluids may be stored on the bio-chip and delivered using the piercing member when required. Thus, certain embodiments of the present invention may result in a reduction of gas exchange with stored solutions and reagent waste, as well as cost reduction. Certain embodiments of the present invention provide a portable bio-chip device, e.g. a microfluidic device, which incorporates a blister pouch pre-filled with one or more reagents.

Certain embodiments of the present invention provide the advantage that precise location of the piercing member relative to the sealed unit of the blister pouch is not required providing that the piercing member contacts at least a portion of the blister pouch.

In one embodiment, the bio chip is formed from a material selected from glass, polycarbonate, polymethyl methacrylate (PMMA), cyclic olefin copolymer (COC), polystyrene (PS), polyether ether ketone (PEEK), polytetrafluoroethylene (PTFE) and polypropylene (PP).

In one embodiment, the bio chip may be fabricated from a metal. Aptly, the chip may be formed from a metal which could be readily formed into the required shapes using a range of fabrication techniques. Aptly, the chip may be formed a technique selected from die casting, injection moulding and subtractive milling.

In one embodiment, the bio chip is fabricated from a ceramic material. Aptly, the bio chip is produced using an injection moulding technique. In one embodiment, the bio chip is formed from a polymer. Aptly, the polymer is an injection moulded polymer.

Aptly, the bio chip further comprises one or more further elements. In one embodiment, the bio chip comprises one or more of the following elements: one or more micropumps, one or more microvalves, a power source e.g. a battery, and/or a sensor.

In a further aspect of the present invention, there is provided a method of delivering a target fluid to a desired location, comprising locating an apparatus as described herein such that the piercing member of the apparatus abuts a sealing membrane of a respective blister pouch; wherein the fluid is located in the blister pouch; and applying a predetermined force to the sealing membrane such that the sealing membrane is pierced by the piercing member. Aptly, the method comprises applying a force of between about 3N and about 12N to the sealing membrane.

In one embodiment, the method comprises: locating a biochip comprising a collection chamber as described herein underneath the piercing member prior to the piercing of the sealing membrane; and collecting the fluid from the blister pouch in the collection chamber.

Aptly, the method further comprises locating the apparatus in an abutting relationship with the sealing membrane prior to application of a predetermined force.

Further details of certain embodiments are provided below.

Detailed Description of Embodiments of the Invention

Certain embodiments of the present invention will now be described hereinafter, by way of example only, with reference to the accompanying drawings in which:

Figure 1 illustrates a bio chip and blister pouch according to certain embodiments of the present invention;

Figure 2 illustrates a bio chip according to certain embodiments of the present invention;

Figure 3A illustrates an apparatus according to certain embodiments of the present invention which comprises a piercing member;

Figure 3B illustrates an apparatus according to certain embodiments of the present invention which comprises a piercing member;

Figure 3C illustrates an apparatus according to certain embodiments of the present invention which comprises two piercing members;

Figure 4 illustrates a cross-sectional view of a blister pouch located above a piercing member according to certain embodiments of the present invention;

Figure 5 illustrates a cross-sectional view of a blister pouch located above a piercing member according to certain embodiments of the present invention;

Figure 6 illustrates a side view of an apparatus comprising a piercing member according to certain embodiments of the present invention;

Figure 7 illustrates a cross sectional view of section A-A as shown in Figure 6 of an apparatus comprising a piercing member according to certain embodiments of the present invention;

Figure 8 illustrates a top view of an apparatus comprising a piercing member according to certain embodiments of the present invention;

Figure 9 illustrates a bottom view of an apparatus comprising a piercing member according to certain embodiments of the present invention;

Figure 10 illustrates an exploded view of a blister pack and a piercing plate comprising a piercing member according to certain embodiments of the present invention;

Figure 11 illustrates a blister pouch located above a piercing member according to certain embodiments of the present invention; and

Figure 12 illustrates a cross-sectional side view of a blister pouch located above a piercing member according to certain embodiments of the present invention;

Figure 1 illustrates an apparatus 100 for providing a target liquid at a desired location according to certain embodiments of the present invention. In certain embodiments, the desired location is situated on a device e.g. a bio-chip 110. The apparatus may be a distinct element from the bio-chip 110 or may be an integrally formed portion of the bio-chip. Further details of the bio chip which are not shown in the Figures are provided below.

The bio-chip may comprise a number of other elements e.g. one or more of sensing regions, micropumps, valves, heaters, microchannels and other elements known in the art (not shown).

In one embodiment, the bio chip comprises one or more elements for controlling fluid flow thereon e.g. electroosmotic flow, vacuum pumps, electrokinetic pumps, membrane actuated pumps, centrifugal force, gas bubbles, ferrofluidic plugs, capillary action, electrohydrodynamic pumps, and/or magnetohydrodynamic pumps. Aptly, pumps for microfluidics may be governed by electrokinetic principles or by the mechanism of differential pressure.

The bio chip can be used for automating a variety of bioassay protocols, such as absorption, fluorescence, ELISA, enzyme immunoassay (EIA), light scattering, electrochemical measurement assays and chemiluminescence for testing a variety of analytes. Such analytes include for example proteins, nucleic acids, cells, receptors, and the like. The biochip can be configured and designed for whole blood, tears, sweat, serum, plasma, urine, and other biological fluid applications. In one embodiment, the bio-chip is adapted to perform DNA hybridization assays, expression analysis of mRNA, certain forms of DNA detection and/or DNA sequencing. Aptly, the bio chip may be used in one or more of the techniques described in Sensors (Basel). 2012; 12(8): 10713–10741, incorporated herein by reference in its entirety.

Aptly, the bio chip is made of elastomers or polymers such as for example, PDMS, PMMA, polyurethane, PFPE, SIFEL and parylene. In one embodiment, the bio-chip is formed from a material selected from for example plastic, glass, silicon, polycarbonate, polycarbonate, polydimethylsiloxane, polymethyl methacrylate (PMMA), cyclic olefin copolymer (COC),

polystyrene (PS), polyether ether ketone (PEEK), polytetrafluoroethylene (PTFE) and polypropylene (PP).

The bio-chip may comprise a sample region. As used herein, the term "sample region" refers to any portion of a bio-chip that provides storage, analysis, separation or that provides, conducts or is otherwise involved in any processing step on or with the sample liquid. In one embodiment, the sample region is involved in the analysis of a sample liquid or components therein, and the sample region is considered a sensor (or sensor region), for example a sensor surface.

In one embodiment, the sample is taken from a plant, e.g. a tree, a shrub and/or a flowering plant. In one embodiment, the sample is selected from a human and/or animal sample. In one embodiment, the sample is whole blood, serum and/or plasma. Aptly the sample is urine sample, a sample taken from a swab e.g. a nasal swab, a pharyngeal swab, a vaginal swab or a rectal swab. In one embodiment, the sample is taken from tears and/ or sweat. Aptly, multiple analytes or multiple samples may be detected in a very small quantity.

In one embodiment, the bio-chip comprises a sensor (not shown). As used herein, the term "sensor" refers to a device that detects a change in at least one physical property and produces a signal, or induces a change in a signal, in response to the detectable change. The manner in which the sensor detects a change may include, for example, acousto-mechanical changes, electrochemical changes, optical changes and/or electro-optical changes. For example, acousto-mechanical sensors can utilise resonant frequency, phase-shifts, piezoelectric properties. Aptly, electrochemical sensors utilise potentiometric and amperometric measurements. Aptly, optical sensors may utilise absorbance, fluorescence, luminescence and/or evanescent waves.

In one embodiment, the sensor is a biosensor and comprises at least one detection moiety attached thereto. In one embodiment, the detection moiety is selected from one or more of: an antibody; a nucleic acid, e.g. DNA, RNA, or PNA; a protein; a peptide; an aptamer; a cell; a charged molecule; a membrane; a vesicle; a chemical and/or electrochemical receptor.

The detection moiety may be immobilised directly to a surface of the bio-chip. In certain embodiments the detection moiety may be immobilised on a solid support e.g. latex beads or magnetic beads using techniques known in the art. The detection moiety may comprise a

label for detection. Alternatively, the detection moiety may be directly detectable via a label free detection method.

The bio-chip of certain embodiments of the present invention may be used to detect for example the presence or absence of a target protein, a target DNA molecule and/or a target RNA molecule. The target molecule for detection may be for example a hormone, a cell surface molecule, a cardiac protein, a tumour marker and/or a small molecule. In one embodiment, the target molecule is a drug of abuse. In one embodiment, the target molecule may be a plurality of target molecules and the bio-chip is for the detection of the presence and/or absence of one or more target molecules.

Turning to Figure 1 again, the apparatus 100 comprises a piercing member 120 located on a support surface 130. The piercing member 120 is described in more detail below and illustrated in Figures 6 to 9. In one embodiment, the apparatus 100 may comprise a plurality of spaced apart piercing members 120.

The bio chip 110 comprises a lower chip sealing plate 140. The lower chip sealing plate 140 may be rectangular for example in shape. The chip sealing plate may have dimensions of for example a length of about 120mm and a width of about 60mm, although it will be appreciated that bio-chips of other dimensions are encompassed by certain embodiments of the present invention. The lower chip sealing plate 140 may comprise a rectangular glass plate. Other materials which may be suitable to fabricate the bio chip plates are described herein.

The bio chip also comprises a chip top layer 150. The lower surface 160 of the chip top layer 150 can be bonded to the upper surface 170 of the lower chip sealing plate 140 by a suitable known method e.g. thermal bonding. The upper surface 180 of the chip top layer 150 forms an upper external surface of the bio chip and the lower surface 190 of the lower chip sealing plate 140 forms a lower external surface of the bio chip 110. By way of example, the chip top layer 150 may have a thickness of for example about 3mm and the lower chip sealing plate may have a thickness of 1mm.

The bio chip 110 further comprises one or more channels. Figure 1 illustrates that the chip top layer comprises one or more channels 200. The chip top layer also comprises a sample chamber 210 which is in fluid communication with at least one channel. The chip top layer

150 further comprises a collection chamber 220. The collection chamber may be considered a fluid introduction chamber. In use, the collection chamber 220 is situated beneath a piercing member as described herein. The collection chamber is in fluid communication with at least one channel 200 and may provide an inlet for the channel 200.

The dimensions of the channels may differ between devices. In one embodiment, the channels may have a cross-sectional width of between about 0.1 mm and 5mm. The channels may have a depth of e.g. 20 microns and 1mm.

As shown in Figure 1, in certain embodiments the piercing member 120 is provided on a piercing plate 230. The piercing plate 230 is secured to the chip top layer 150 by a layer of adhesive 240. Prior to application of the layer of adhesive, the piercing plate is positioned such that the piercing member is located above the collection chamber 220. The piercing plate may be about around 200 to 1000 microns thick and/or manufactured from a material e.g. glass, polycarbonate or PMMA.

Figure 1 illustrates a blister pouch 250 located above the piercing member 120. The blister pouch 250 is formed from a blister forming material. The blister pouch comprises a reservoir 260 which may be filled with a predetermined volume of liquid e.g. a reagent. The reservoir is sealed by a blister sealing membrane 270. The liquid may be a reagent such as for example a buffer, a liquid comprising one or more detection molecule and/ or a liquid comprising a sample material. The nature of the liquid may depend on the reaction being carried out on the bio chip.

The blister sealing membrane 270 is formed from a blister sealing material. The blister sealing material is capable of being pierced by the piercing member 120 when brought into contact with the piercing member with a predetermined level of force. Aptly, the piercing member does not pierce the blister sealing membrane when it is located abutting the blister membrane at a level of force which is less than about 1N.

When the reagent or other liquid stored in the blister pouch is required, force may be applied manually by a user pressing the blister pouch on a surface opposing the blister sealing material. Alternatively, force may be applied by an automated actuator. The force is aptly greater than about 3N.

Figure 2 illustrates an embodiment in which two piercing members 120a, 120b are located in a bio chip 110. The illustrated bio chip may be generally square in shape as shown in Figure 2. In other embodiments, the bio chip may be alternative shapes e.g. rectangular, circular, hexagonal or pentagonal.

The piercing members 120a, 120b are each provided above a respective collection chamber 220a, 220b. During use, the collection chamber holds the liquid released from the blister pouch when the sealing membrane 270 is pierced by the corresponding piercing member. Thus, the collecting chamber helps to prevent liquid being released from the blister pouch over the surface of the bio-chip and thus away from the target location i.e. the channels of the bio-chip.

The bio chip 110 of Figure 2 includes a channel 200a which is generally linear and extends between a first piercing member 120a and a second piercing member 120b. The channel 200a includes a T-junction intersection with a further portion of the channel 200b. The further portion of the channel is serpentine and is connected to a sample chamber 210.

Figure 3 illustrates alternative embodiments of a bio chip 110. Figure 3A illustrates a bio chip 110 which comprises a linear channel 200. The linear channel is in fluid communication with the collection chamber 220 and the sample chamber 210. The linear channel 200 connects the collection chamber 220 and the sample chamber 210. The piercing member 120 located above the collection chamber 220 and is either integrally formed with the upper surface of the biochip or within a piercing plate.

Figure 3B illustrates an alternative embodiment of a bio chip according to certain embodiments of the present invention. The bio chip comprises a channel 200 which follows a serpentine path between the collection chamber 220 and the sample chamber 210. The piercing member 120 is located above the collection chamber 220 and can be either integrally formed with the bio chip 110 or within a separate piercing plate 230 as described herein.

Figure 3C illustrates a further alternative embodiment of a bio-chip 110 according to certain embodiments of the present invention. Two piercing members 120a and 120b are located above two separate collection chambers 220a and 220b. One or both piercing members

120a and 120b are either integrally formed with the upper surface of the biochip or within a piercing plate 230.

The collection chambers 220a, 220b are linked by a linear channel 200a. The channel 200a is intersected by and in fluid communication with a further portion of the channel 200b at an intersection point 300. The further portion of the channel 200b is in fluid communication with the sample chamber 210. The channel has a linear portion 310 extending from the intersection point 300, a middle serpentine section 320 and an end linear section 330 which is connected to the sample chamber 210.

Figure 4 illustrates a cut through of a piercing member 120 provided on a piercing plate 230 and located above a collection chamber 220 located in a bio chip. As described above, the collection chamber 220 is provided in an upper chip plate 150 of the bio chip 110. The piercing plate 230 is secured to the upper surface of the upper chip plate by a layer of adhesive 240.

A blister pouch 250 is located above the piercing member 120. The blister membrane 270 of the blister pouch 250 is in contact with the piercing member 120 but since the force applied to the blister sealing membrane by the piercing member does not exceed about 1N, the blister sealing material of the blister membrane is not punctured by the piercing member. As a result, the fluid is retained in the blister pouch 250 shown in Figure 4.

Figure 5 is an alternative view of the blister pouch 250, piercing plate 230 and bio chip shown in Figure 4.

The piercing member 120 is shown in more detail in Figures 6 to 9. The piercing member illustrated in Figures 6 to 9 may be comprised in a piercing plate or a bio chip as described herein.

Figure 6 illustrates a cross sectional view of a piercing member 120. The piercing member 120 is located upstanding from a support surface 130 at a height of about around 300 to 1200 microns. As noted herein, the support surface 130 may be provided as an integral surface of the bio chip. Alternatively, the support surface 130 may be provided on a piercing plate or as an integral part of the piercing plate. The piercing member 120 comprises a tip region 600 which has a rounded nose region 610. In use, the upper surface of the rounded

nose region 610 is locatable in an abutting relationship with the sealing membrane of the blister pouch and is capable of piercing the blister sealing membrane when a force is applied. Aptly, the force required to pierce the blister membrane is about 3N or more.

As illustrated in Figure 6, Figure 8 and Figure 9, the piercing member 120 also comprises a plurality of abutment wall regions or angled struts 620, 630, 640 and 650 which extend upwardly from the support surface to the tip region 600. Each strut extends from the support surface 130 to the tip region at a predetermined angle so that each wall region or strut forms a tangent with an arc of the rounded nose region 610 at an end of the tip region. In the illustrated embodiment, the piercing member comprises four angled struts, however, in alternative embodiments the piercing member may comprise a different number of angled struts e.g. two, three or five.

The abutment wall regions 620, 630, 640, 650 form a cross when viewed from above with the centre of the cross being the rounded nose region 610. The abutment wall regions extend upwardly from the support surface at an angle of approximately 90°, as shown in Figure 6. The rounded nose region of the piercing member allows the piercing member to abut a blister sealing membrane without piercing it. This embodiment has the advantage that a blister pouch may be stored and e.g. transported in an abutting relationship with a piercing member which may be an integral part of a microfluidic device e.g. a bio-chip. Thus, certain embodiments of the present invention may have utility in systems which need to be easily transported e.g. lab-on-chip portable devices.

Thus, between each abutment wall region and an adjacent abutment wall region is a passageway 660, 670, 680, 690 through which fluid stored in the blister pouch can flow once the blister sealing membrane is punctured by the piercing member. The fluid can then flow into the collection chamber 220 located beneath the passageways formed by adjacent abutment wall regions. The passageways are sized such that liquid may pass through the passageway and do not pool on top of the piercing member and therefore the bio-chip. As a result, substantially all of the liquid stored in the blister pouch passes into the biochip which means that the amount of liquid used in the process taking place on the bio-chip can be accurately determined.

Figure 7 is a cross sectional view of section A-A of Figure 6 and shows the collection chamber 220 located underneath the rounded nose region 610 of the piercing member 120.

Figure 9 is a bottom view of the apparatus 100 showing a lower surface 900 of for example a piercing plate or a bio chip.

Figure 10 is an exploded view illustrating a blister pack 710 which comprises two blister pouches 250a, 250b which protrude from and are supported by a backing web 720. It will be appreciated that a blister pack 710 may comprise a plurality of blister pouches 250. Figure 10 also illustrates a piercing plate 230 which comprises two piercing members 120a, 120b.

Each blister pouch may be filled with the same type of fluid or a different type of fluid. The backing web 720 includes one or more interconnecting regions 730 between the blister pouches. The backing web 720 may be provided with frangible lines or perforations (not shown) in the interconnecting regions between blister pouches to enable a section comprising one or more blister pouches to be "snapped-off" or removed from the blister pack.

The backing web may be formed from the same material as the blister forming material. In one embodiment, the backing web is formed from a plastic, a composite material, a film material or a combination of such materials.

The blister pack 710 may also include a sealing membrane (not shown) which extends across the backing web 720 and the otherwise open entrance of a plurality of blister pouches 250, thus sealing a plurality of blister pouches. The sealing membrane may comprise one or more perforations (not shown) which coincide with an outer perimeter surrounding an individual blister pouch. In embodiments in which the backing web comprises frangible lines or perforations, the sealing membrane may comprise corresponding frangible lines or perforations. The blister pouch may be sealed by a heat-sealing method. Alternatively, the blister pouch may be sealed by way of a cold-sealing method.

Alternatively, the blister pack may comprise a plurality of sealing membranes, each sealing membrane extending across an otherwise open blister pouch thus sealing a single blister pouch. The sealing membrane may be heat sealed to an upper surface of the backing web.

In one embodiment, the blister pouch 250 is filled with a pre-determined amount of a fluid e.g. a reagent. The blister pouch may be filled with the fluid using an automated filling

process. Alternatively, or in addition, the blister pouch may be filled with a liquid manually or using a semi-automated process.

Figure 10 also illustrates a layer of adhesive or adhesive material 740 which secures the blister pack to a piercing plate or to a biochip which comprises the piercing member. The embodiment illustrated in Figure 10 shows the piercing members being composed in a piercing plate.

The adhesive material 740 comprises one or more apertures 750a, 750b which are located to correspond to the location of the piercing members 120a, 120b respectively. The apertures 750a, 750b also provide a through passageway for fluid stored in the blister pouch to flow through the piercing member once the blister sealing membrane is pierced.

In the embodiment illustrated in Figure 10, the piercing member 120 is an integrally formed portion of a piercing plate 230. A piercing plate 230 can be used in conjunction with microfluidic devices of differing types. The piercing plate may be secured to a bio chip 110 by an adhesive element e.g. a layer of adhesive 240. Prior to being secured to the bio chip, the piercing plate will be aligned to the bio chip such that each piercing member is positioned above a collection chamber. The piercing plate can be used in combination with a variety of bio chips providing that the bio chip comprises at least one collection chamber in a position which corresponds to the positioning of at least one piercing member of the piercing plate.

Aptly, the piercing member 120 when comprised in the piercing plate 230 is upstanding from the upper surface of the piercing plate to a height of between about 300 to 1200 microns. Aptly, the piercing member 120 when comprised in the bio chip is upstanding from the upper surface of the piercing plate to a height of between about 300 to 1200 microns.

In certain embodiments, the piercing plate comprising one or more piercing members may be supplied in combination with a blister pack. The blister pack may be supplied with the piercing member abutting but not piercing the sealing membrane of a blister pouch comprised in the blister pack. The piercing member may pierce the blister sealing membrane only when a predetermined force is applied e.g. about 3N or greater.

Additionally or alternatively, the piercing plate may include at least one alignment element (not shown) which locates the piercing plate at a desired position with respect to each blister

pouch. Aptly, the alignment element comprises at least one edge of the piercing plate. Alternatively, the alignment element comprises at least one locating lug or recess which mates with a complimentary alignment element of the blister pouch.

Figure 11 illustrates an alternative view of an individual blister pouch 250. The blister pouch 250 comprises a continuous curved exterior wall 1100 which define a cavity in which fluids are introduced and stored prior to use. If individual blister pouches are used, which are not an integral part of a blister pack, the blister pouch may comprise a lip region 1110 which a user can grip to handle the blister pouch.

Figure 12 illustrates a side view of a blister pouch 250 positioned over a piercing member 120 which is in turn located above a collection chamber of a device e.g. a bio chip as described herein. The piercing member abuts the blister sealing membrane at an abutment point 1200 and deforms the membrane but since there is insufficient force applied the sealing membrane is not pierced. In certain embodiments, the apparatus comprising the piercing member may be stored and/or transported packaged such that the piercing member abuts but does not pierce the sealing membrane.

In use, a blister pouch 250 is prefilled with a predetermined volume of a liquid. As noted herein, the liquid may be any reagent for use in a process taking place on a microfluidic device e.g. a bio chip 110 as defined herein. An open mouth of the blister pouch is subsequently sealed by a sealing membrane 270. As described herein, the blister pouch may be one of a plurality of blister pouches in a blister pack. Alternatively, the blister pouch may be supplied as an individual pouch.

Aptly, the blister pouch is sealed in an air tight manner and as such may be suitable for long term storage of the liquid. Additionally, the blister pouch can be stored at low temperatures, e.g. in a refrigerator, if the liquid needs to be stored in this way. The provision of reagents in blister pouches in this way enable different liquids to be stored in their optimum conditions ready for use in a process carried out on a microfluidic device.

As discussed herein, a piercing member 120 is provided in an apparatus 100. The piercing member may be an integral element of a piercing plate 230 or an integral feature of a bio chip 110. The piercing member may be provided in an abutting relationship with the sealing membrane of the blister pouch such that it deforms but does not break the sealing

membrane in a first mode of operation. Aptly, the piercing member deforms but does not pierce the sealing membrane when a force of up to about 1N is applied.

In a second mode of operation, a predetermined amount of force is applied to the blister pouch and/or the piercing member such that the sealing membrane is punctured by the piercing member. Aptly, when the blister pouch is urged against the piercing member, the piercing member is disposed to rupture the membrane when a force of about around 3 to 12N is applied to the membrane.

The force may be applied to the blister pouch or the piercing member manually by a user or by an actuator. In one embodiment, the actuator may be adapted to apply a pressure at a predetermined rate. The actuator may further comprise a control element adapted to instruct the actuator to apply a force to a plurality of blister pouches at substantially the same time or at predetermined time intervals.

Once the blister sealing membrane has been broken by the piercing member, the liquid stored in the blister pouch is released in a controlled manner and substantially all of the liquid flows over the piercing member and through the openings formed between the abutment wall regions. The liquid then collects underneath the piercing member e.g. in a collection chamber comprised in a biochip. The liquid can then be used in a process on the bio-chip.

Throughout the description and claims of this specification, the words "comprise" and "contain" and variations of them mean "including but not limited to" and they are not intended to (and do not) exclude other moieties, additives, components, integers or steps. Throughout the description and claims of this specification, the singular encompasses the plural unless the context otherwise requires. In particular, where the indefinite article is used, the specification is to be understood as contemplating plurality as well as singularity, unless the context requires otherwise.

Features, integers, characteristics or groups described in conjunction with a particular aspect, embodiment or example of the invention are to be understood to be applicable to any other aspect, embodiment or example described herein unless incompatible therewith. All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may

be combined in any combination, except combinations where at least some of the features and/or steps are mutually exclusive. The invention is not restricted to any details of any foregoing embodiments. The invention extends to any novel one, or novel combination, of the features disclosed in this specification (including any accompanying claims, abstract and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

The reader's attention is directed to all papers and documents which are filed concurrently with or previous to this specification in connection with this application and which are open to public inspection with this specification, and the contents of all such papers and documents are incorporated herein by reference.

CLAIMS:

1. Apparatus for providing a target liquid at a desired location, comprising:

at least one piercing member upstanding from a support surface at a height of about around 300 to 1200 microns and locatable with respect to a sealing membrane of a respective blister pouch; wherein

a tip region of the piercing member is locatable in an abutting relationship with the sealing membrane in a first mode of operation and through the sealing membrane in a further mode of operation for providing liquid from the blister pouch at a desired location.

2. The apparatus as claimed in claim 1, further comprising:

in the first mode of operation the piercing member is locatable to deform but not pierce the sealing membrane.

3. The apparatus as claimed in claim 2, further comprising:

in the first mode of operation the piercing member does not pierce the sealing membrane when an abutment force of up to about around 1N is applied by the piercing member to the sealing membrane.

4. The apparatus as claimed in any preceding claim, further comprising:

said tip region comprises a rounded nose region having a generally arcuate shape with a radius of curvature of about around 50 to 1000 microns.

5. The apparatus as claimed in claim 4 wherein the radius of curvature is about around 100 to 500 microns.

6. The apparatus as claimed in any preceding claim, further comprising:

said piercing member further comprises a plurality of abutment wall regions extending from the support surface to the tip region at a predetermined angle so that each wall region forms a tangent with an arc of a rounded nose region at an end of the tip region.

7. The apparatus as claimed in claim 6, further comprising:

each abutment wall region meets the nose region at an angle of about around 45 degrees.

8. The apparatus as claimed in any preceding claim, further comprising:

the piercing member provides a plurality of fluid communication passageways proximate to the tip region that each communicate liquid urged from a pierced blister pouch to at least one collection chamber under the support surface.

9. The apparatus as claimed in claim 8 wherein the piercing member comprises a plurality of arms extending upwards and in an inclined manner from the support surface and the fluid communication passageways are provided by openings in the support surface in notched regions between adjacent arms.

10. The apparatus as claimed in any preceding claim wherein the first mode of operation comprises a transportation mode during which a blister pouch is transportable in an abutting relationship with said piercing member without risk of puncture.

11. The apparatus as claimed in any preceding claim wherein in the further mode of operation in which the blister pouch is urged against the piercing member the piercing member is disposed to rupture the membrane at a rupture force of about around 3 to 12N.

12. The apparatus as claimed in any preceding claim wherein each piercing member is manufactured from a material selected from a group comprising glass, polycarbonate, polymethyl methacrylate (PMMA), cyclic olefin copolymer (COC), polystyrene (PS), polyether ether ketone (PEEK), polytetrafluoroethylene (PTFE) and polypropylene (PP).

13. A piercing plate, securable to at least one blister pouch, comprising the apparatus as claimed in any preceding claim.

14. The piercing plate as claimed in claim 13, further comprising:

a planar upper surface, comprising said support surface, and a planar lower surface that is securable to an upper surface of a bio chip.

15. The piercing plate as claimed in claim 14 further comprising an adhesive layer on the lower surface.

16. The piercing plate as claimed in any one of claims 13 to 15, further comprising:

at least one alignment element that locates the piercing plate at a desired position with respect to each blister pouch.

17. The piercing plate as claimed in claim 16 wherein said alignment element comprises at least one edge of the piercing plate.

18. The piercing plate as claimed in claim 16 wherein said alignment element comprises at least one locating lug or recess that mates with a complimentary alignment element of the blister pouch.

19. The piercing plate as claimed in any one of claims 13 to 18 further comprising at least one further alignment element that locates the piercing plate at a desired position with respect to a bio chip.

20. The piercing plate as claimed in claim 19 wherein each further alignment element comprises at least one edge of the piercing plate.

21. The piercing plate as claimed in claim 19 wherein said further alignment element comprises at least one locating lug or recess that mates with a complimentary alignment element of the bio chip.

22. The piercing plate as claimed in any one of claims 13 to 21, further comprising:

a cavity under each piercing member that is locatable in fluid communication with a collection chamber of a bio chip.

23. The piercing plate as claimed in any one of claims 13 to 22, further comprising:

the plate is about around 200 to 1000 microns thick.

24. The piercing plate as claimed in any one of claims 13 to 23 wherein the plate is manufactured from a material selected from the list of glass, polycarbonate and PMMA.

25. The piercing plate as claimed in any one of claims 13 to 24 wherein the plate and each piercing member are integrally formed.

26. The piercing plate as claimed in any one of claims 13 to 25 wherein the plate is retrofittable to an underside of a blister package comprising one or more blister pouches sealed with a sealing membrane.

27. A blister pack, comprising:

a plurality of blister pouches secured together via a web and a common sealing membrane; and

at least one piercing plate as claimed in any one of claims 13 to 26 secured to a lower surface of the sealing membrane.

28. The blister pack as claimed in claim 27, further comprising:

a plurality of frangible lines or perforation lines in the web.

29. A bio chip, comprising the apparatus as claimed in any one of claims 1 to 9.

30. The bio chip as claimed in claim 29, further comprising:

an upper chip layer comprising each piercing member as an integral unit.

31. The bio chip as claimed in claim 29, further comprising:

an upper chip layer having an upper surface on which at least one piercing plate comprising said at least one piercing member is secured.

32. The bio chip as claimed in claim 30 or claim 31 wherein a lower surface of the upper chip layer includes a collection chamber located beneath each piercing member and at least one channel connecting a collection chamber to a respective sample chamber.

33. The bio chip as claimed in claim 32 wherein said channel comprises a channel region that provides a serpentine pathway.

34. Apparatus constructed and arranged substantially as hereinbefore described with reference to the accompanying drawings.

35. A piercing plate constructed and arranged substantially as hereinbefore described with reference to the accompanying drawings.

36. A bio chip constructed and arranged substantially as hereinbefore described with reference to the accompanying drawings.

37. A method substantially as hereinbefore described with reference to the accompanying drawings.

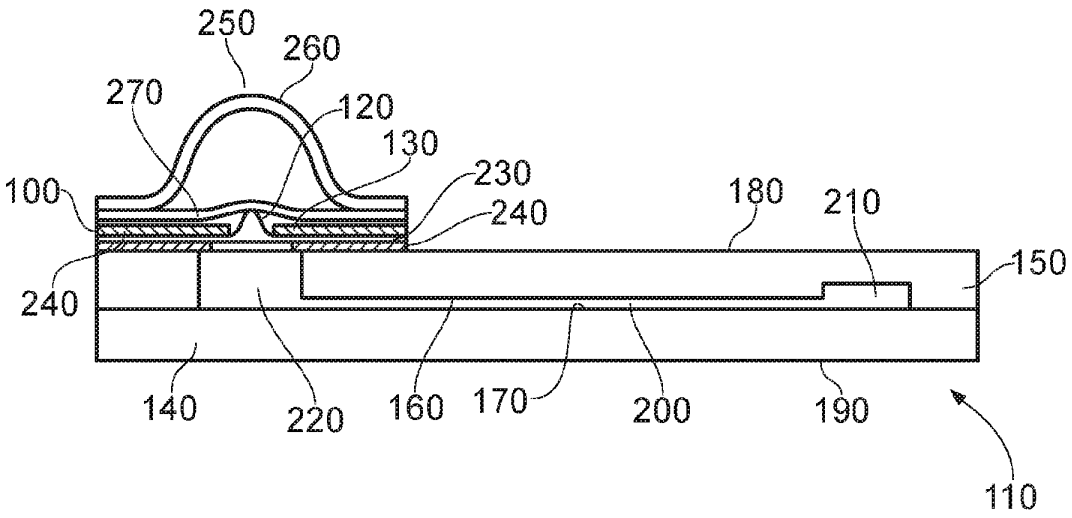

250
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110

FIG. 1

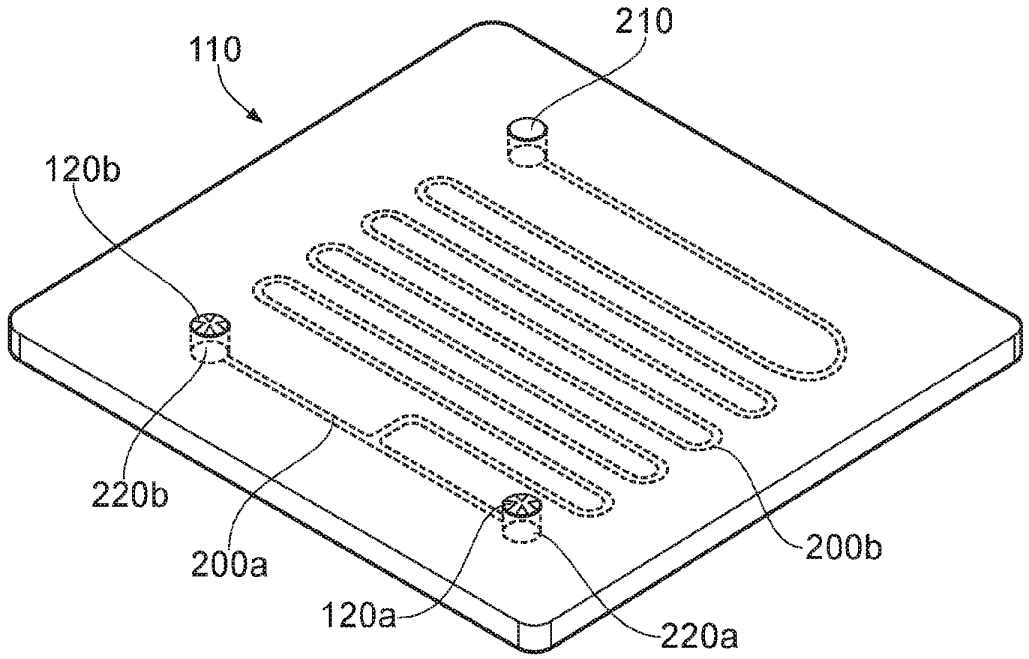


FIG. 2

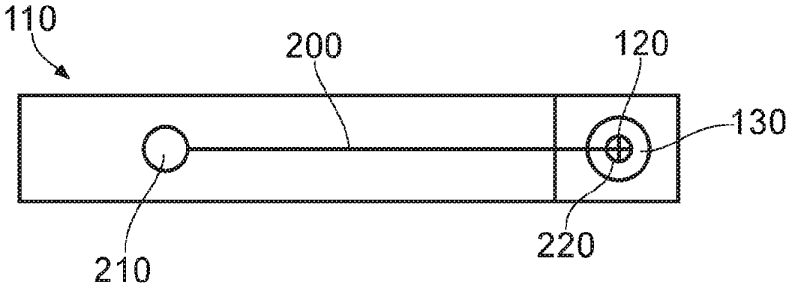


FIG. 3A

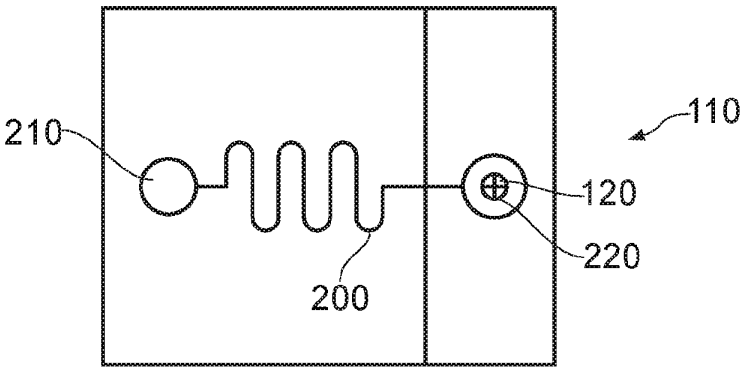


FIG. 3B

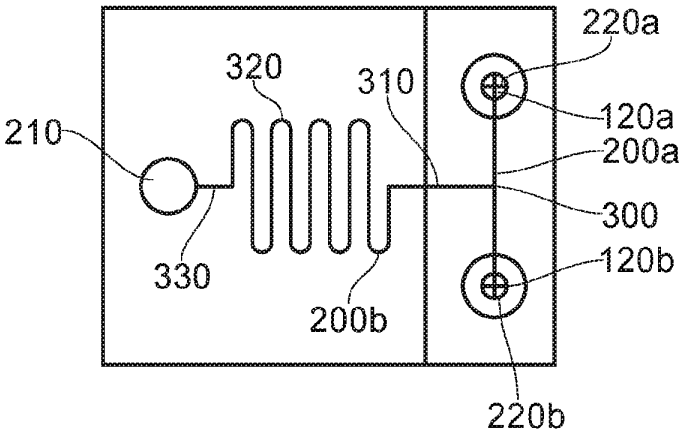


FIG. 3C

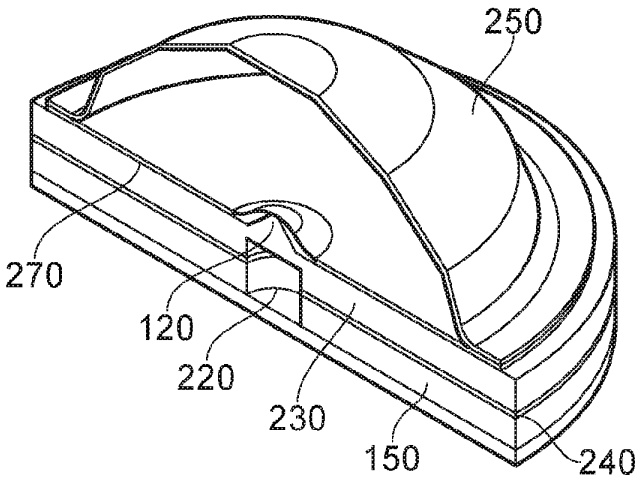


FIG. 4

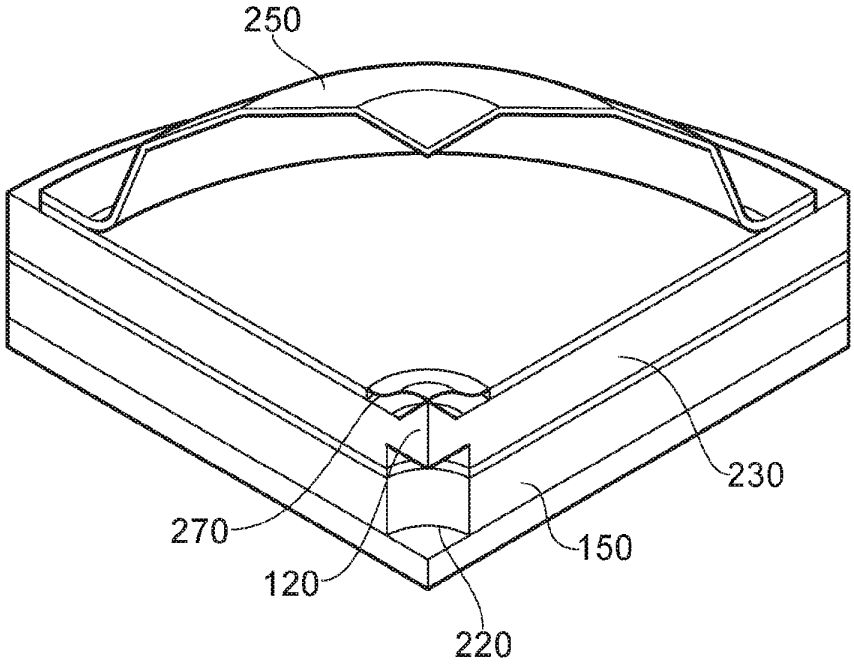


FIG. 5

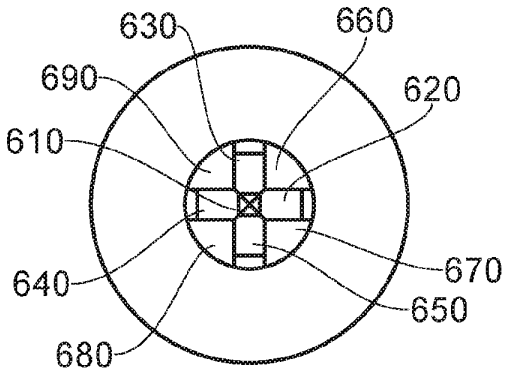


FIG. 8

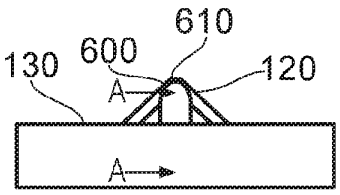
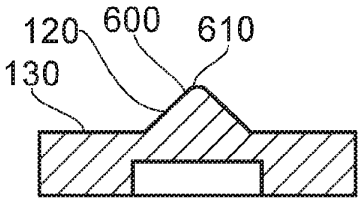


FIG. 6



SECTION A - A

FIG. 7

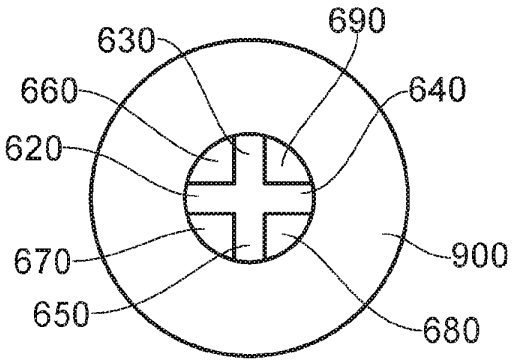


FIG. 9

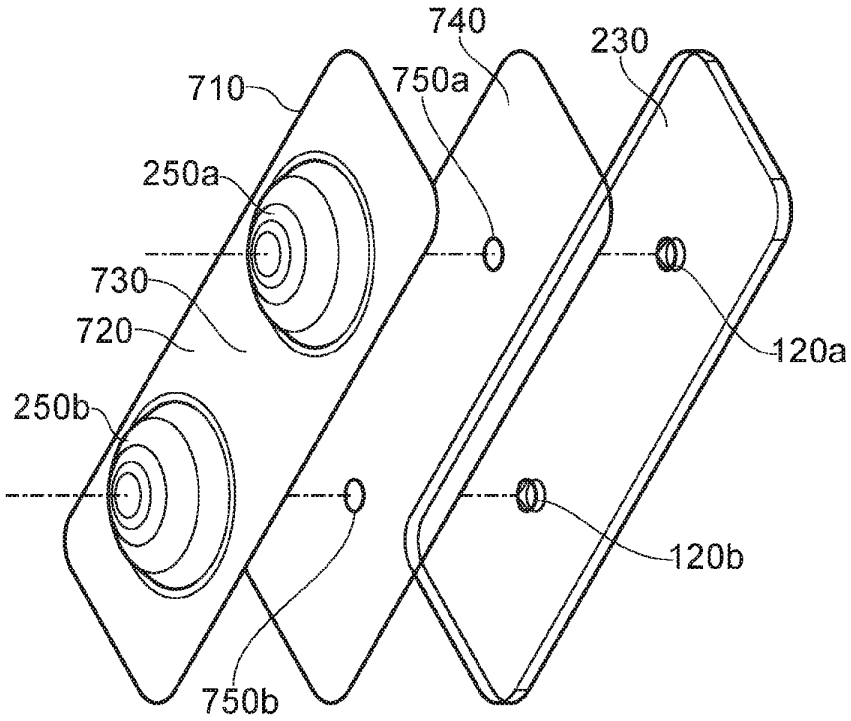


FIG. 10

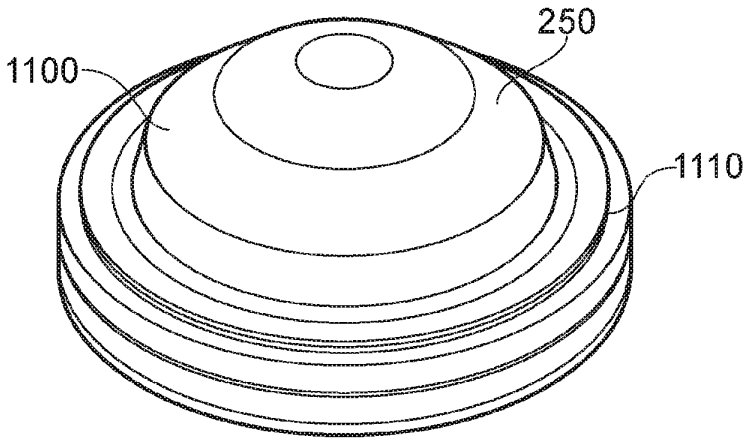


FIG. 11

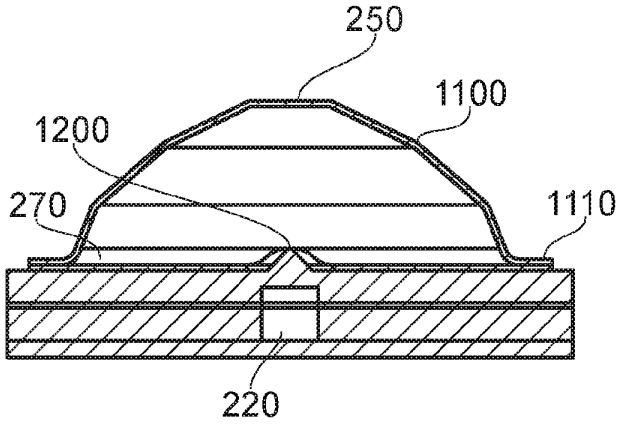


FIG. 12

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2015/050905

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L3/00
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)
B01L

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/057744 A2 (INVERNESS MEDICAL SWITZERLAND [CH]; PANESAR SATWINDER SINGH [GB]; HANN) 24 May 2007 (2007-05-24) page 10, line 5 - page 12, line 10 page 14, line 18 - line 25 figures 6A, 6B, 7A, 7B, 7C, 8	1-37
A	US 5 096 669 A (LAUKS IMANTS R [US] ET AL) 17 March 1992 (1992-03-17) the whole document	1-37
A	US 2010/291588 A1 (MCDEVITT JOHN T [US] ET AL) 18 November 2010 (2010-11-18) the whole document	1-37
A	US 2006/183216 A1 (HANDIQUE KALYAN [US] ET AL) 17 August 2006 (2006-08-17) the whole document	1-37

-/--

[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
16 June 2015	29/06/2015

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	Bischoff, Laura

1

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

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2015/050905

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 2010/304986 A1 (CHEN ZONGYUAN [US] ET AL) 2 December 2010 (2010-12-02) the whole document	1-37

1

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2015/050905

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007057744 A2	24-05-2007	NONE	
US 5096669 A	17-03-1992	AT 130092 T	15-11-1995
		CA 1330888 C	26-07-1994
		DE 68924782 D1	14-12-1995
		DE 68924782 T2	21-03-1996
		EP 0434742 A1	03-07-1991
		HK 1007797 A1	23-04-1999
		JP H0820398 B2	04-03-1996
		JP H04501768 A	26-03-1992
		US 5096669 A	17-03-1992
		WO 9002938 A1	22-03-1990
US 2010291588 A1	18-11-2010	AU 2006261953 A1	04-01-2007
		CA 2613078 A1	04-01-2007
		EP 1899450 A2	19-03-2008
		EP 2508867 A1	10-10-2012
		US 2010291588 A1	18-11-2010
		WO 2007002480 A2	04-01-2007
US 2006183216 A1	17-08-2006	NONE	
US 2010304986 A1	02-12-2010	US 2010304986 A1	02-12-2010
		WO 2008076395 A2	26-06-2008

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

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	

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18 March 2022

Examination report No. 1 for standard patent application

Griffith Hack
GPO Box 4164
Sydney NSW 2001
Australia

Your reference:	P108089.AU.1
Application number:	2021202622
Applicant name:	KURIN, INC.
Earliest priority date:	24 July 2015

Final date for acceptance:	**18 March 2023**
Date of this report:	18 March 2022
Examination request date:	6 July 2021

Dear Griffith Hack,

Your application has been examined under *section 45 of the Patents Act 1990*.

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

You will also need to pay any annual continuation fees that apply. Your next continuation fee is due on **22 July 2022**.

While the application is otherwise in order for acceptance, it cannot be accepted because there is a current postponement of acceptance in place.

You must respond to this report in order to gain acceptance. The Commissioner will only proceed to accept the application if you file a clear and unambiguous statement requesting the postponement be withdrawn with sufficient time for the request to be processed. If the application is not accepted by **18 March 2023**, your application will lapse.

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

Yours sincerely,

Kevin Sivieng
Section: MECH 4 - MEDICAL DEVICES
Phone: +61 2 6283 2609

Alternate contact: Vijay Singh
Phone: +61 2 6283 2665

Report details

Basis of the report

In examining this application I have considered:

- the specification as filed.
- allowed and/or proposed amendment/s under S104 including amendment item number 1, filed on 4 May 2021.

Summary of novelty, inventive step and patentable subject matter

	Satisfy requirements?	*Claim numbers*
Novelty/inventive step	**Yes**	1-16
	No	NONE
Patentable subject matter	**Yes**	1-16
	No	NONE

Detailed objections on issues that have been identified

Documents cited or considered relevant

D1: WO 2011162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US], et al) 29 December 2011 [1]
Category: A

D2: WO 1996005875 A1 (BAXTER INT [US]) 29 February 1996 [2]
Category: A

D3: US 20130317391 A1 (BULLINGTON GREGORY J [US], et al) 28 November 2013 [3]
Category: A

D4: US 4207870 A (ELDRIDGE WILLIAM N [US]) 17 June 1980 [3]
Category: A

D5: US 4416291 A (KAUFMAN) 22 November 1983 [4]
& JP S 5825146 A
Category: A

D6: US 20080145933 A1 (PATTON RICHARD G [US]) 19 June 2008 [5]
Category: A

D7: JP 2001000424 A (NISSHO KK) 9 January 2001, English translation retrieved from Espacenet [5]
Category: A

[1] Cited in the search/examination report of WO 2017/019552 A1

[2] Cited in the search/examination report of EP 3622890

[3] Cited in the search/examination report of US 2017/0020427 A1

[4] Cited in the search/examination report of JP 2018525191

[5] Cited in the search/examination report of JP 2020192333

Special categories of cited documents:

A: Document defining the general state of the art which is not considered to be of particular relevance.
&: Document member of the same patent family.

END OF REPORT

Japanese Patent Application No. 2020-118498
Your Ref: KURIN2JP-DIV2
Our Ref: TS/KRN-C0137JP03
March 28, 2022

Translation of "Notice of Reasons for Rejection"

Patent Application Number: JP 2020-118498
Date of Delivery: February 15, 2022
Applied Provision: Patent Law Article 29(2)

The present application should be rejected for the following reasons. The applicant may present an argument against the reasons within three months from the date of delivery of this notice.

Reasons

1. The inventions of the following claims should not be granted a patent under Patent Law Article 29(2) as lacking inventive step over the documents listed below.

Remarks (See the Document List below)

- Reason 1 (Inventive step)
- Claims 1 to 10
- Documents D1 to D4

[Claim 1]

D1 ([0019]-[0055], Figs. 5-8) discloses

a blood sample optimization system (sample-procurement system; [0038], etc.) for optimizing a blood sample ([0020], etc.) collected by a blood collector (sample vessels 506; [0038], etc.), the system comprising:

a patient needle (first needle 508; [0038], etc.) configured for a venipuncture of a patient to access a sample of blood of a patient, the sample of blood including a first portion containing contaminants ([0021], etc.) and a second portion following the first portion;

a blood sampling pathway connected with the patient needle configured for conveying the sample of blood (see Fig. 5, etc.); and

a sample needle configured for receiving the blood collector to collect a second portion of the sample of blood(see suggestions in Fig. 5, etc.); and

a blood sequestration device connected on the blood sampling pathway between the patient needle and the sample needle, the blood sequestration device comprising;

an inlet port (sterile input tubing 514; [0039], etc.) configured for receiving the sample of blood;

a sequestration chamber (pre-sample reservoirs 504; [0038], etc.) connected with the inlet port, the sequestration chamber configured for receiving the first portion of the sample of blood to contain the contaminants in the first portion of the blood sample; and

a sampling channel (second sterile output tubing 518; [0038], Fig. 5, etc.) having a proximal end connected with the inlet port, configured for receiving the second portion of the

sample of blood,

the sequestration chamber, the sampling channel and the inlet port being configured to allow the second portion of the sample of blood to bypass the sequestration chamber and direct the second portion of the sample of blood toward an outlet port that is configured to output the second portion of the sample of blood to the blood collector ([0038], etc.).

As explained in the previous Notice of Reasons for Rejection, D2 ([0012]-[0013] etc.) discloses arts in a blood sample optimization system (blood sampling needle) of configuring a sequestration chamber having a vent comprising an air permeable blood barrier (air permeable blood impermeable member 23) to displace air in the sequestration chamber through the vent, and of configuring a housing (needle tube support 2) that houses and defines ports, the sequestration chamber and a channel.

In addition, newly cited D3 (see pages 5-6, FIG. 1, etc.) discloses arts in a blood sample optimization system (closed system blood sampling device) of configuring a sequestration chamber (blood disposal chamber 22) having a vent comprising an air permeable blood barrier (air permeable hydrophobic membrane 30) to displace air in the sequestration chamber through the vent, and of configuring a housing that houses and defines ports, the sequestration chamber and a channel (see FIG. 1, etc.).

Further, D4 ([0042], etc.) also discloses art of configuring a sequestration chamber having a vent comprising an air permeable blood barrier to displace air in the sequestration chamber through the vent.

And, as supported by the disclosure of D2 to D4 described above, in a blood sample optimization system, configuring a sequestration chamber having a vent comprising an air permeable blood barrier to displace air in the sequestration chamber through the vent, and configuring a housing that houses and defines ports, the sequestration chamber and a channel are both well-known arts.

The system disclosed in D1 and the well-known arts disclosed in D2 to D4 belong to the same technical field called the blood collection field.

Configuring the system disclosed in D1 to have an air permeable blood barrier and a housing similar to the invention of claim 1 of the present application with reference to the well-known arts disclosed in D2 to D4 is easy for those skilled in the art, or a matter that those skill in the art could have made as appropriate.

[Claims 2 and 4]

See [0012]-[0013] of D2.

[Claim 3]

Placing a seal on the sample needle can be said to be a design matter.

[Claim 5]

See [0011] of D2.

[Claim 6]

See Fig. 5 of D1.

[Claims 7-10]

See the above explanations including the descriptions of D1 to D4.

Document List

D1: US 2008/0145933A

D2: JP 2001-000424A

D3: JP H09-504726A (newly cited; document disclosing well-known art)

D4: US 2006/0009713A (newly cited; document disclosing well-known art)

Record of the Result of Prior Art Search

Technical field(s) searched	IPC A61B 5/00-5/398
Prior art document(s)	JP S58-025146A
	JP H02-224742A
	US 2011/0306899A

This record is not a component of the reasons for rejection.

Japanese Patent Application No. 2020-118498
Your Ref: KURIN2JP-DIV2
Our Ref: TS/KRN-C0137JP03
September 2, 2021

Translation of "Notice of Reasons for Rejection"

Patent Application Number: JP 2020-118498
Date of Delivery: August 10, 2021
Applied Provision: Patent Law Articles 29(2), and 36

The present application should be rejected for the following reasons. The applicant may present an argument against the reasons within three months from the date of delivery of this notice.

Reasons

1. The inventions of the following claims should not be granted a patent under Patent Law Article 29(2) as lacking inventive step over the documents listed below.

2. The following claims do not comply with the requirements under Patent Law Article 36(6)(ii) as being unclear.

Remarks (See the Document List below)

- Reason 1 (Inventive step)
- Claims 1 to 10
- Documents D1 and D2

[Claim 1]

D1 ([0019]-[0055], Figs. 5-8) discloses

a blood sample optimization system (sample-procurement system; [0038], etc.) for optimizing a blood sample ([0020], etc.) collected by a blood collector (sample vessels 506; [0038], etc.), the system comprising:

a patient needle (first needle 508; [0038], etc.) configured for a venipuncture of a patient to access a sample of blood of a patient, at least a first portion of the sample of blood containing contaminants ([0021], etc.);

a blood sampling pathway connected with the patient needle configured for conveying the sample of blood (see Fig. 5, etc.); and

a sample needle configured for receiving the blood collector to collect a second portion of the sample of blood(see suggestions in Fig. 5, etc.); and

a blood sequestration device connected on the blood sampling pathway between the patient needle and the sample needle, the blood sequestration device comprising;

an inlet port (sterile input tubing 514; [0039], etc.) configured for receiving the sample of blood;

a sequestration chamber (pre-sample reservoirs 504; [0038], etc.) connected with the inlet port, the sequestration chamber configured for receiving the first portion of the sample of

blood to contain the contaminants in the first portion of the blood sample; and

a sampling channel (second sterile output tubing 518; [0038], Fig. 5, etc.) having a proximal end connected with the inlet port, configured for receiving the second portion of the sample of blood,

the sequestration chamber, the sampling channel and the inlet port being configured to allow the second portion of the sample of blood to bypass the sequestration chamber and direct the second portion of the sample of blood toward an outlet port that is configured to output the second portion of the sample of blood to the blood collector ([0038], etc.).

D2 ([0012]-[0013] etc.) discloses arts in a blood sample optimization system (blood sampling needle) of configuring a sequestration chamber having a vent comprising an air permeable blood barrier (air permeable blood impermeable member 23) to displace air in the sequestration chamber through the vent, and of configuring a housing (needle tube support 2) that houses and defines ports, the sequestration chamber and a channel.

Those disclosed in D1 and D2 belong to the same technical field called the blood collection field. It is easy for those skilled in the art to configure the one disclosed in D1 to have an air permeable blood barrier and a housing similar to the invention of claim 1 of the present application, with reference to the arts disclosed in D2.

[Claims 2 and 4]

See [0012]-[0013] of D2.

[Claim 3]

Placing a seal on the sample needle can be said to be a design matter.

[Claim 5]

See [0011] of D2.

[Claim 6]

See Fig. 5 of D1.

[Claims 7-10]

See the above explanations including the descriptions of D1 and D2.

- Reason 2 (Clarity)
- Claims 1 to 10

The recitations of claims 1-10 are unclear in the following points. Therefore, the

inventions of claims 1-10 are unclear.

(1) Claim 1

The recitation of "a sample of blood of a patient, at least a first portion of the sample of blood containing contaminants" is unclear in Japanese as to whether "at least containing contaminants" is related to the "a sample of blood" or to the "a first portion of the sample of blood". The same applies to the claims referring to claim 1.

(2) Claims 4 and 7

The recitation of "subsequent portion of the blood sample" is unclear as to what portion the "subsequent portion" follows. The same applies to the claims referring to claim 4 or 7.

Document List

D1: US 2008/0145933A

D2: JP 2001-000424A

Record of the Result of Prior Art Search

Technical field(s) searched	IPC A61B 5/00-5/398
Prior art document(s)	JP S58-025146A
	JP H09-504726A
	JP H02-224742A
	US 2011/0306899A

This record is not a component of the reasons for rejection.

拒絶理由通知書

特許出願の番号	特願２０２０－１１８４９８
起案日	令和　３年　８月　２日
特許庁審査官	岡▲さき▼　潤　　３３３０　２Ｑ００
特許出願人代理人	三好　秀和（ほか　３名）　様
適用条文	第２９条第２項（進歩性） 第３６条第６項第２号（明確性）

この出願は、次の理由によって拒絶をすべきものです。これについて意見がありましたら、この通知書の発送の日から３か月以内に意見書を提出してください。

理由

１．（進歩性）この出願の下記の請求項に係る発明は、その出願前に日本国内又は外国において、頒布された下記の刊行物に記載された発明又は電気通信回線を通じて公衆に利用可能となった発明に基いて、その出願前にその発明の属する技術の分野における通常の知識を有する者が容易に発明をすることができたものであるから、特許法第２９条第２項の規定により特許を受けることができない。

２．（明確性）この出願は、特許請求の範囲の記載が下記の点で、特許法第３６条第６項第２号に規定する要件を満たしていない。

記　　（引用文献等については引用文献等一覧参照）

●理由１（進歩性）について

・請求項　１－１０

・引用文献等　１－２

・備考

[請求項１について]

引用文献１（[0019]-[0055],図5-8）には、

採血器（sample vessels 506;[0038]等）によって集められる血液サンプル（[0020]等）を最適化するための血液サンプル最適化システム（sample-procurement system;[0038]等）であって、

患者の血液サンプル、少なくとも汚染物質を含む（[0021]等）前記血液サンプルの第１の部分を取り出せるようにするために患者の静脈穿刺用に構成された患者針（first needle 508;[0038]等）と、

前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と（図5等参照）、

前記血液サンプルの第２の部分を集めるために前記採血器を受け入れるように構成されたサンプル針（図5等の示唆参照）と、

前記患者針と前記サンプル針との間の前記採血経路に接続された血液隔離装置であって、

前記血液サンプルを受け入れるように構成された入口ポート（sterile input tubing 514;[0039]等）と、

前記入口ポートに接続され、隔離チャンバであって、前記血液サンプルの第１の部分を受け入れ、前記血液サンプルの第１の部分に汚染物質を含むように構成された隔離チャンバ（pre-sample reservoirs 504;[0038]等）と、

前記入口ポートに接続される近位端を有し、前記血液サンプルの第２の部分を受け入れるように構成されたサンプリング流路と（second sterile output tubing 518;[0038],図5等）を含み、

前記隔離チャンバ、前記サンプリング流路及び前記入口ポートは、前記血液サンプルの第２の部分が前記隔離チャンバを迂回することを可能にし、前記血液サンプルの第２の部分を前記出口ポートに向かわせるように構成され、前記出口ポートは、前記血液サンプルの第２の部分を前記採血器に排出するように構成される（[0038]等）、血液隔離装置とを含む、血液サンプル最適化システム、

が記載されている。

引用文献２（[0012]-[0013]等）には、血液サンプル最適化システム（採血針）において、空気透過性血液バリア（空気透過性血液不透過性部材２３）を含む通気口を有する隔離チャンバであって、通気口を通して隔離チャンバ内の空気を追い出す隔離チャンバを構成する技術、ポート、隔離チャンバ及び流路を収容及び画定するハウジング（針管支持体２）を構成する技術、が開示されている。

引用文献１－２に記載のものは、採血分野という同一の技術分野に属する。

引用文献１に記載のものにおいて、引用文献２に記載の技術を参考として、本願の請求項１に係る発明と同様の空気透過性血液バリアとハウジングを具備するよう構成することは、当業者にとって容易である。

[請求項２，４について]

引用文献２の[0012]-[0013]を参照。

[請求項３について]

サンプル針に密封材を配置することは、設計的な事項といえる。

[請求項５について]

引用文献２の[0011]参照。

[請求項６について]

引用文献１の図5を参照。

[請求項７－１０について]

引用文献１－２の記載を含め既述の説示を参照。

●理由２（明確性）について

・請求項　１－１０

請求項１－１０の記載は、以下の点で不明確である。よって、請求項１－１０に係る発明は、明確でない。

（１）請求項１の記載について

請求項１の「患者の血液サンプル、少なくとも汚染物質を含む前記血液サンプルの第１の部分」との記載は、「少なくとも汚染物質を含む」ことが「血液サンプル」に係っているのか、「前記血液サンプルの第１の部分」に係っているのか、日本語として不明確である。引用項においても同様。

（２）請求項４，７の記載について

請求項４，７の「前記血液サンプルの後続の部分」との記載は、いかなる部分に「後続」するものを特定しているのか不明確である。引用項においても同様。

＜引用文献等一覧＞

１．米国特許出願公開第２００８／０１４５９３３号明細書

２．特開２００１－０００４２４号公報

－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－

＜先行技術文献調査結果の記録＞

・調査した分野　　ＩＰＣ　Ａ６１Ｂ　　５／００　－　５／３９８

ＤＢ名

・先行技術文献　　特開昭５８－０２５１４６号公報

特表平０９－５０４７２６号公報

特開平０２－２２４７４２号公報

米国特許出願公開第２０１１／０３０６８９９号明細書

この先行技術文献調査結果の記録は、拒絶理由を構成するものではありません

。

＜補正をする際の注意＞
（１）明細書、特許請求の範囲について補正をする場合は、補正により記載を変更した個所に下線を引いてください（特許法施行規則様式第１３備考６、７）。
（２）補正は、この出願の外国語書面の翻訳文（又は誤訳訂正書による補正後の明細書、特許請求の範囲若しくは図面）に記載した事項の範囲内で行わなければなりません。また、意見書で、各補正事項について補正が適法なものである理由を、根拠となる翻訳文（又は誤訳訂正書による補正後の明細書、特許請求の範囲若しくは図面）の記載箇所を明確に示したうえで主張してください。
（３）特許請求の範囲について補正をする際には、特許法第１７条の２第４項に違反する補正とならないよう、注意してください。

この拒絶理由通知の内容に関するお問合せ又は面接のご希望がありましたら、次の連絡先までご連絡ください。電子メール等で補正案等の送付を希望される場合は、その旨を電話でお知らせください。

審査第一部分析診断（医学診断）　岡崎　潤
ＴＥＬ．０３－３５８１－１１０１　内線３２９１

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/838,017	04/01/2020	Bobby E. ROGERS	069366-0572158_KUR7001US	1044

27500 7590 01/29/2024

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
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EXAMINER	
PORTILLO, JAIRO H	

ART UNIT	PAPER NUMBER
3791	

NOTIFICATION DATE	DELIVERY MODE
01/29/2024	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Docket_IP@pillsburylaw.com

Office Action Summary	Application No. 16/838,017	Applicant(s) ROGERS et al.	
	Examiner JAIRO H PORTILLO	Art Unit 3791	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 7/19/2023.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☑ This action is **FINAL.** 2b) ☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 1-4,6-9,14,16-18 and 21-26 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-4,6-9,14,16-18 and 21-26 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim(s) 1-4, 6-9, 14, 16-18, and 21-23 is/are rejected under 35 U.S.C. 103 as being unpatentable over **Rogers et al (US 2017/0020428) ("Rogers")** in view of **Davis et al (US 2007/0031283) ("Davis").**

Regarding Claim 1, while Rogers teaches a device for optimizing a fluid sample collected by a fluid collection device from a fluid source (Abstract, [0124] Figs. 23A and 23B), the device comprising:

an inlet configured to connect with the fluid source ([0124] inlet port 2302);

an outlet configured to connect with the fluid collection device ([0124] outlet port 2304);

a sample path connected between the inlet and the outlet ([0124] sample path/sampling channel 2308), the sample further having a resistive plug ([0124] valve 2308); and

a chamber connected between the inlet and the outlet (Figs. 23A and 23B, [0124] sequestration chamber 2306), the chamber having an air permeable fluid resistor proximate the outlet (Figs. 23A and 23B, hydrophobic plug 2312), the chamber 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, such that upon receipt of the first portion of the fluid sample in the chamber, subsequent portions of the fluid sample can be conveyed by the sample path from the inlet to the outlet ([0124] "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.),

Rogers fails to teach

The resistive plug including a membrane that is pierceable; and

A piercing member configured to pierce the membrane.

However Davis teaches a medical sampling device (Abstract) comprising a valve composition of a film that is pierceable and a piercing element to allow fluid flow ([0278], [0280]).

It would have been obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to substitute the pinching valve of Rogers for a needle-pierceable membrane valve of Davis as a simple substitution of one form of controlling fluid flow for another to obtain predictable results of sample optimization by denying the initial aliquot of blood.

Regarding Claim 2, Rogers and Davis teach the device in accordance with claim 1, further comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the chamber (*See Claim 1 Rejection,* the tubing of the blood sequestration device 2300 acts as a housing).

Regarding Claim 3, Rogers and Davis teach the device in accordance with claim 1, wherein the air permeable fluid resistor includes a material that seals upon contact with the first portion of the fluid sample (*See Claim 1 Rejection)*.

Regarding Claim 4, Rogers and Davis teach the device in accordance with claim 1, and Rogers teaches in a separate embodiment that a chamber includes a tortuous path ([0072]).

It would have been obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to configure the contaminant containment reservoir of Rogers with a tortuous path as Rogers teaches that a tortuous path has a sealing function ([0065]) which would be useful for containing contaminants.

Regarding Claim 21, Rogers and Davis teach the device in accordance with claim 1, wherein the membrane is spaced apart from the piercing member in an initial state (*See Claim 1 Rejection*, for needle pierceable membrane to act as a valve, the membrane must be initially spaced apart from a piercing member).

Regarding Claim 6, Rogers teaches a device for optimizing a fluid sample collected by a fluid collection device from a fluid source (Abstract, [0124] Figs. 23A and 23B), the device comprising:

an inlet configured to connect with the fluid source ([0124] inlet port 2302);

an outlet configured to connect with the fluid collection device ([0124] outlet port 2304 connected to a blood sample collection device);

a sample path connected between the inlet and the outlet ([0124] sample path/sampling channel 2308), 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 from entering the sample path ([0124] valve 2310. Examiner notes that the patent publication has the valve written as 2308, but the language of paragraph [0124] and the Figures heavily imply the valve should be understood as corresponding to reference character 2310); and

a chamber connected between the inlet and the outlet (Figs. 23A and 23B, [0124] sequestration chamber 2306), the chamber further having an air permeable fluid resistor proximate the outlet (Figs. 23A and 23B, hydrophobic plug 2312), the chamber 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, such that upon receipt of the first portion of the fluid sample in the chamber, 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 ([0124] "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.),

Rogers fails to teach

The resistive plug including a membrane that is pierceable; and

A piercing member configured to pierce the membrane.

However Davis teaches a medical sampling device (Abstract) comprising a valve composition of a film that is pierceable and a piercing element to allow fluid flow ([0278], [0280]).

It would have been obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to substitute the pinching valve of Rogers for a needle-pierceable membrane valve of Davis as a simple substitution of one form of controlling fluid flow for another to obtain predictable results of sample optimization by denying the initial aliquot of blood.

Regarding Claim 7, Rogers and Davis teach the device in accordance with claim 6, further comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the chamber (*See Claim 6 Rejection*, the tubing of the blood sequestration device 2300 acts as a housing).

Regarding Claim 8, Rogers and Davis teach the device in accordance with claim 6, wherein the air permeable fluid resistor includes a material that seals upon contact with the first portion of the fluid sample (*See Claim 6 Rejection*).

Regarding Claim 9, Rogers and Davis teach the device in accordance with claim 6, and Rogers teaches in a separate embodiment that a chamber includes a tortuous path ([0072]).

It would have been obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to configure the contaminant containment reservoir of Rogers with a tortuous path as Rogers teaches that a tortuous path has a sealing function ([0065]) which would be useful for containing contaminants.

Regarding Claim 22, Rogers and Davis teach the device in accordance with claim 6, wherein the membrane is spaced apart from the piercing member in an initial state (*See Claim 6 Rejection*, for needle pierceable membrane to act as a valve, the membrane must be initially spaced apart from a piercing member).

Regarding Claim 14, Rogers teaches a device for optimizing a fluid sample (Abstract, Figs. 23A and 23B), the device comprising:

an inlet ([0124] inlet port 2302);

an outlet ([0124] outlet port 2304);

a sample path connected between the inlet and the outlet ([0124] sample path/sampling channel 2308); and

a chamber connected between the inlet and the outlet (Figs. 23A and 23B, [0124] sequestration chamber 2306), the chamber having an air permeable fluid resistor proximate the

outlet (Figs. 23A and 23B, hydrophobic plug 2312), the chamber 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, such that upon receipt of the first portion of the fluid sample in the chamber, subsequent portions of the fluid sample can be conveyed by the sample path from the inlet to the outlet ([0124] "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.),

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 from entering the sample path during receipt of the first portion of the fluid sample in the chamber ([0124] valve 2310. Examiner notes that the patent publication has the valve written as 2308, but the language of paragraph [0124] and the Figures heavily imply the valve should be understood as corresponding to reference character 2310),

Rogers fails to teach the resistive plug including a membrane that is pierceable; and

a piercing member configured to pierce the membrane,

However Davis teaches a medical sampling device (Abstract) comprising a valve composition of a film that is pierceable and a piercing element to allow fluid flow ([0278], [0280]).

It would have been obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to substitute the pinching valve of Rogers for a needle-pierceable

membrane valve of Davis as a simple substitution of one form of controlling fluid flow for another to obtain predictable results of sample optimization by denying the initial aliquot of blood.

Regarding Claim 16, Rogers and Davis teach the device in accordance with claim 14, further comprising a housing that houses and/or defines one or more of the inlet, the outlet, the sample path, and the chamber (*See Claim 14 Rejection*, the tubing of the blood sequestration device 2300 acts as a housing).

Regarding Claim 17, Rogers and Davis teach the device in accordance with claim 14, wherein the air permeable fluid resistor includes a material that seals upon contact with the first portion of the fluid sample (*See Claim 14 Rejection*).

Regarding Claim 18, Rogers and Davis teach the device in accordance with claim 14, and Rogers teaches in a separate embodiment that a chamber includes a tortuous path ([0072]).

It would have been obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to configure the contaminant containment reservoir of Rogers with a tortuous path as Rogers teaches that a tortuous path has a sealing function ([0065]) which would be useful for containing contaminants.

Regarding Claim 23, Rogers and Davis teach the device in accordance with claim 14, wherein the membrane is spaced apart from the piercing member in an initial state (*See Claim 14 Rejection*, for needle pierceable membrane to act as a valve, the membrane must be initially spaced apart from a piercing member).

Claim(s) 24-26 is/are rejected under 35 U.S.C. 103 as being unpatentable over **Rogers** in view of **Davis** as evidenced by **"Membrane Definition & Meaning."**

Regarding Claim 24, Rogers and Davis teach the device in accordance with claim 21, wherein the membrane is configured to stretch and contact the piercing member after the first portion of the fluid sample is received by the chamber (*See Claim 21 Rejection*, a membrane is

defined as “a thin soft *pliable* sheet or layer especially of animal or plant origin” by the “Membrane Definition & Meaning.” And is thus configured to stretch. Further, as a needle-pierceable membrane, it is configured contact the piercing member after the first portion of the fluid sample is received by the chamber as it is by nature configured to contact the piercing member).

Regarding Claim 25, Rogers and Davis teach the device in accordance with claim 22, wherein the membrane is configured to stretch and contact the piercing member after the first portion of the fluid sample is received by the chamber (*See Claim 22 Rejection*, a membrane is defined as “a thin soft *pliable* sheet or layer especially of animal or plant origin” by the “Membrane Definition & Meaning.” And is thus configured to stretch. Further, as a needle-pierceable membrane, it is configured contact the piercing member after the first portion of the fluid sample is received by the chamber as it is by nature configured to contact the piercing member).

Regarding Claim 26, Rogers and Davis teach the device in accordance with claim 23, wherein the membrane is configured to stretch and contact the piercing member after the first portion of the fluid sample is received by the chamber (*See Claim 23 Rejection*, a membrane is defined as “a thin soft *pliable* sheet or layer especially of animal or plant origin” by the “Membrane Definition & Meaning.” And is thus configured to stretch. Further, as a needle-pierceable membrane, it is configured contact the piercing member after the first portion of the fluid sample is received by the chamber as it is by nature configured to contact the piercing member).

Response to Arguments

Applicant's amendments and arguments filed 7/19/2023 with respect to the 35 USC 112(f) interpretation have been fully considered and are persuasive. The interpretation is obviated.

Applicant's amendments and arguments filed 7/19/2023 with respect to the 35 USC 103 rejection have been fully considered, but are not persuasive.

Applicant argues that Davis does not teach or motivate a fluid sample being forced through a membrane when a pressure differential is applied. Examiner respectfully notes that the independent claims as written do not state a pressure differential is applied to actuate the use of the membrane. Thus, even a user actuated needle piercing of the membrane would fulfill the current claim set.

Applicant's next argument is that the piercing member of Davis is an external instrument and is therefore not part of the device. Examiner respectfully disagrees. As a necessary sub-unit for the piercing of the membrane, Examiner consider the needle to be part of the device.

The rejection(s) stands.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAIRO H PORTILLO whose telephone number is (571)272-1073. The examiner can normally be reached M-F 9:00 am - 5:15 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jacqueline Cheng can be reached on (571)272-5596. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAIRO H. PORTILLO/
Examiner
Art Unit 3791

/KAYLEE R WILSON/
Primary Examiner, Art Unit 3791

Notice of References Cited	Application/Control No. 16/838,017	Applicant(s)/Patent Under Reexamination ROGERS et al.	
	Examiner JAIRO H PORTILLO	Art Unit 3791	Page 1 of 1

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membrane

Entries 1 to 10 of 15. Next 5

On Off

membrane
basement membrane
basilar membrane
cell membrane

Main Entry: **mem·brane**
Pronunciation: \'mem-ˌbrān\
Function: *noun*
Etymology: Middle English, from Latin *membrana* skin, parchment, from *membrum*
Date: 15th century

1 : a thin soft pliable sheet or layer especially of animal or plant origin
2 : a piece of parchment forming part of a roll
— mem·braned \'mem-ˌbrānd\ *adjective*

Learn more about "membrane" and related topics at Britannica.com

See a map of "membrane" in the Visual Thesaurus

Pronunciation Symbols

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	First Named Inventor	Bobby E. ROGERS
	Art Unit	3791
	Examiner Name	PORTILLO, JAIRO H
	Attorney Docket Number	069366-0572158_KUR7001US

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Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

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☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-07-19
Name/Print	Benjamin F. Hudson	Registration Number	71,474

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

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.H.P/

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	16838017
Filing Date	2020-04-01
First Named Inventor	Bobby E. ROGERS
Art Unit	3791
Examiner Name	PORTILLO, JAIRO H
Attorney Docket Number	069366-0572158_KUR7001US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.H.P/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	16838017
	Filing Date	2020-04-01
	First Named Inventor	Bobby E. ROGERS
	Art Unit	3791
	Examiner Name	PORTILLO, JAIRO H
	Attorney Docket Number	069366-0572158_KUR7001US

	1	Pall Medical, "Leukotrap Filtration Systems for Whole Blood Derived Platelets, Leukotrap RC PL and Leukotrap PL Systems" literature, (2005) 8 pages.	☐
	2	Meissner, George F. , et al., "The Standard Clotting Time, A Method Based on the Use of Whole Venous Blood in Capillary Tubes," The American Journal of Clinical Pathology, Vol. 39, No. 3., pp. 321-323, March 1963.	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/JAIRO H PORTILLO/	Date Considered	01/12/2024

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.H.P/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	16838017
	Filing Date	2020-04-01
	First Named Inventor	Bobby E. ROGERS
	Art Unit	3791
	Examiner Name	PORTILLO, JAIRO H
	Attorney Docket Number	069366-0572158_KUR7001US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-07-19
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.H.P/

Privacy Act Statement

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

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

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

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

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

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

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

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

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.H.P/

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: JAMES SCOTT NOLAN
P.O. BOX 371710
SAN DIEGO, CA 92110

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference KURIN4PCT	Date of mailing *(day month year)* 19JUN 2020 **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 20/23617	International filing date *(day month year)* 19 March 2020 (19.03.2020)
Applicant KURIN, INC.	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   How? Directly to the International Bureau preferably through ePCT, or on paper to:
   The International Bureau of WIPO, 34, chemin des Colombettes, 1211 Geneva 20, Switzerland

   For more detailed instructions, see the *PCT Applicant's Guide*, International Phase, paragraphs 9.004 – 9.011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.
   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   The applicant may **submit comments on an informal basis on the written opinion of the International Searching Authority** to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

   Shortly after the expiration of **18 months from the priority date, the international application will be published** by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for **entry into the national phase** before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

   Within **22 months from the priority date, the applicant may request that a supplementary international search be carried out** by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

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/220 (revised January 2020)

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

Publication 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
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.

Examination Processing

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)

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.
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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

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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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.
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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 Publication

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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	

פ.ק 13

תאריך: ז' שבט תשפ"ג
29/01/2023
מספרכם: 1000-016-01

לכבוד
כץ, פרזנטי ושות'
דרך אבא הלל 14,
רמת גן, מיקוד 52506

א. ג. נ.,

הנדון: **<u>הודעה לפני קיבול בקשת פטנט מספר 286030</u>**

סימוכין: מכתבכם מיום 25/08/2022

לתשומת לבכם: מקום בו הנכם מופנים ל"חוק", הכוונה היא לחוק הפטנטים, התשכ"ז – 1967. מקום בו הנכם מופנים ל"תקנות", הכוונה היא לתקנות הפטנטים (נוהלי הרשות, סדרי דין, מסמכים ואגרות), התשכ"ח – 1968. בהתאם לחוזר רשם 035/2017 – פטנטים **לא ניתן להשהות פרסום בקשות פטנט לפי סעיף 26 לחוק.**

<u>הודעה זו מבוססת על המסמכים הבאים:</u>

שרטוטים מתאריך: 01/09/2021
פרטי הבקשה מתאריך: 01/09/2021
תביעות מתאריך: 25/08/2022

<u>מענה לטיעוני המבקש</u>

מערכת התביעות המוצעת מתקבלת.

<u>הריני להודיעכם כי בחינת הבקשה הנ"ל הושלמה לפי הוראות סעיף 48ו(ג)(1) ו- (2) לחוק.</u>

<u>תשלום אגרת קיבול</u>

1. הבקשה תתקבל בהתאם לסעיף 26 לחוק לאחר תשלום אגרת הקיבול.
2. יש לשלם את האגרה תוך 3 חודשים מתאריך הודעה זו.
3. סכום האגרה נכון למועד הודעה זו הינו 764.00 ש"ח. הסכום כפוף לעדכונו על פי המדד בהתאם לתקנה 6א.

<u>הפניה בפירוט למסמך הבכורה</u>

לפי הוראות **סעיף 20 לחוזר הרשם 034/2017-פטנטים** במידה ופירוט הבקשה מכיל הפניה למסמך בכורה באמצעות הביטוי "incorporated by reference" ובמידה וחלפו 14 חודשים ממועד דין הקדימה (אם נדרש) לא ניתן עוד להוסיף דבר מתוך מסמך הבכורה והמבקש לא יכול להסתמך על האמור במסמך הבכורה, לצורך סעיפים 12 ו-13 לחוק.

רחוב אגודת ספורט הפועל מס' 1,
הגן הטכנולוגי מלחה בניין מס' 5
ירושלים, מיקוד 9695101
טל': 972-73-3927100 פקס: 972-2-6467774
https://www.gov.il/he/departments/ilpo

<u>עדכון רשימות האסמכתאות והפרסומים לפי סעיף 18א לחוק</u>

לתשומת לבכם, בהתאם להוראות פרק ג' בחוזר רשם 035/2017-פטנטים חובת המבקש לעדכן את הרשות בכל שינוי שחל ברשימת הפרסומים בהתאם לסעיף 18 לחוק נמשכת עד קיבול הבקשה.

באם ברצונכם להחזיר את הבקשה לבחינה בעקבות שינוי ברשימת הפרסומים שהתרחש לאחר תשובתכם להודעת הליקויים האחרונה, עליכם להגיש בקשה לבחינה חוזרת בה עליכם לציין מהו השינוי ברשימת הפרסומים ומתי נודע על שינוי זה.

בקשה לבחינה חוזרת יש להגיש באמצעות פניה ל-"בקשה לתיקונים לאחר פ.ק. 13".

<u>הגשת בקשות חלוקה</u>

בהתאם להוראות סעיף 24(א) לחוק זכאי המבקש כל עוד לא קובלה הבקשה לדרוש את חלוקת הבקשה לבקשות אחדות. לפיכך, באם ברצונכם להגיש בקשות חלוקה מבקשה זו עליכם לעשות זאת בטרם מועד הקיבול. לא נוכל להכיר בבקשות שיוגשו לאחר מועד הקיבול של הבקשה הנוכחית כבקשות חלוקה לעניין סעיף 24(ג) לחוק.

<u>בדיקה פורמלית</u>

להודעה הנוכחית מצורף העתק פירוט הבקשה המעודכן - אם נפלו טעויות נא להודיע עליהן לרשות לפני מועד תשלום אגרת הקיבול.

לצורך אימות פרטי הפרסום בהתאם לסעיף 26 לחוק ניתן לעיין בנסח הבקשה באתר הרשות בקישור הבא:

https://israelpatents.justice.gov.il/#/en/patent-extract/286030

ניתן לעיין בפרטי תיק הבקשה באתר הרשות בקישור:

https://israelpatents.justice.gov.il/#/en/patent-file/details/286030

בכבוד רב

אלברט אקרמן
בוחן פטנטים בכיר
טלפון: 073-3927233
דואר אלקטרוני: albertak@justice.gov.il
ראש צוות: מוריה שלמה לוי

claims

1. A blood device connected with a blood sampling system comprising:

a patient needle for accessing a blood sample from a patient and a sample needle that is sealed,

an inlet port connected with the patient needle to receive the blood sample from the patient;

a chamber connected with the inlet port and having a vent

comprising an air permeable blood barrier, wherein the chamber for receiving a first portion of the blood sample prior to the sample needle is unsealed;

a sampling channel having a proximal end connected with the inlet port, wherein the sampling channel for conveying a second portion of the blood sample once the sample needle is unsealed;

an outlet port connected with a distal end of the sampling channel for conveying the second portion of the blood sample to the sample needle; and

a housing that houses and defines the inlet port, the outlet port, the chamber, and the sampling channel.

2. The blood device in accordance with claim 1, wherein the chamber is at ambient air pressure, and wherein the chamber receives the first portion of the blood sample by blood pressure of the patient overcoming the ambient air pressure in the chamber.

3. The blood device in accordance with claim 1, wherein the sampling channel causes the second portion of the blood sample to bypass the first portion of blood in the chamber and exit the outlet port for conveyance to a blood collection device.

4. The blood device in accordance with claim 1, wherein the air permeable blood barrier includes an air permeable material that seals upon contact with blood.

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

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.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of U.S. Non-Provisional Application Serial No. 15/140,443, filed on April 27, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD" and U.S. Non-Provisional Application Serial No. 15/140,448, filed on April 27, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD", both of which claim priority to U.S. Provisional Application Serial No. 62/196,797, filed on July 24, 2015 and titled "BLOOD CULTURE IMPROVEMENT SYSTEM AND METHOD"; U.S. Provisional Application Serial No. 62/238,636, filed on October 7, 2015 and titled "BLOOD SEQUESTRATION SYSTEM FOR NON-CONTAMINATED BLOOD SAMPLING"; and U.S. Provisional Application Serial No. 62/318,194, filed on April 4, 2016 and titled "BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT

SEQUESTRATION DEVICE AND METHOD," the disclosures of which are incorporated by reference in their entirety.

BACKGROUND

[0002] Bacteraemia is the presence of microorganisms in the blood. Sepsis, on the other hand, is bacteraemia in the presence of clinical symptoms and signs such as fever, tachycardia, tachypnea and hypotension. Bacteraemia and sepsis are associated with a high mortality and an increased incidence and duration of hospital stay and associated costs. Many bacteraemias, sepsis, fungaemias and other pathogens actually occur within a hospital or other healthcare settings with catheters and venipunctures being a source of contamination as potential carriers of these pathogens.

[0003] Blood cultures are the standard test used to detect microbial pathogens related to bacteraemia and sepsis in a patient's blood. The term blood culture refers to a single venipuncture, either from a peripheral site or central or arterial line, with the blood inoculated into one or more blood culture bottles or containers. One bottle is considered a blood culture where two or more are considered a set. Multiple sets may be obtained from multiple venipunctures and are associated with different sites on the patient.

[0004] These methods allow for microbial identification and susceptibility testing to be performed, which is a critical component to managing sepsis, however the lack of rapid results and decreased sensitivity for fastidious pathogens has led to the development of improved systems and adjunctive molecular or proteomic testing.

[0005] Collection of blood samples for conducting blood cultures is a critical component of modern patient care and can either positively affect the patient outcome by providing an accurate diagnosis, or can adversely affect the outcome by prolonging unnecessary antimicrobial therapy, the length of hospital stays, and increasing costs.

[0006] One outcome of collection of blood cultures is contamination. Blood culture contamination can lead to a false positive culture result and/or significant increase in healthcare related costs. Sources of blood culture contamination include improper skin

antisepsis, improper collection tube disinfection, and contamination of the initial blood draw which may then skew results.

[0007] Blood culture collection kits generally consist of a "butterfly" set, infusion set, or other type of venipuncture device as offered by companies like BD, Smiths, B. Braun and others, and aerobic and anaerobic blood culture bottles. Various different bottles are also available depending on the test requirements. These bottles are specifically designed to optimize recovery of both aerobic and anaerobic organisms. In conventional kits, a bottle used is known generally as a "Vacutainer," which is a blood collection tube formed of a sterile glass or plastic tube with a closure that is evacuated to create a vacuum inside the tube to facilitate the draw of a predetermined volume of liquid such as blood.

[0008] False positive blood cultures are typically a result of poor sampling techniques. They cause the use of antibiotics when not needed, increasing hospital costs and patient anxiety. Blood cultures are drawn from a needlestick into the skin, and then a Vacutainer is attached to capture a sample of blood. Contamination may occur from improper or incomplete disinfection of the skin area in and around the puncture site. It may also occur from the coring of the skin by the needle during insertion, with the cored skin cells and any associated contamination being pulled into the sample.

[0009] Blood flow through a hypodermic needle is laminar, and as such, a velocity gradient can be developed over the flow tube as a pressure drop is applied to the hypodermic needle. Either forceful aspiration of blood, or using a very small hypodermic needle, can cause lysis and a release of potassium from the red blood cells, thereby rendering the blood samples abnormal.

[0010] In other instances, some patients have delicate veins that can collapse under a pressure drop or vacuum, particularly as applied by a syringe's plunger that is drawn too quickly for the patient's condition. Since such condition is impossible to know beforehand, such vein collapses are a risk and very difficult to control.

[0011] Various strategies have been implemented to decrease blood culture contamination rates, e.g. training staff with regard to aseptic collection technique, feedback

with regard to contamination rates and implementation of blood culture collection kits. Although skin antisepsis can reduce the burden of contamination, 20% or more of skin organisms are located deep within the dermis and are unaffected by antisepsis. Changing needles before bottle inoculation is not advisable as it increases the risk to acquire needle stick injuries without decreasing contamination rates.

[0012] Some conventional systems and techniques for reducing blood culture contamination include discarding the initial aliquot of blood taken from central venous catheters, venipunctures, and other vascular access systems. However, these systems require the user to mechanically manipulate an intravascular device, or require a complex series of steps that are difficult to ensure being followed.

SUMMARY

[0013] This document presents systems and methods for reducing blood culture contamination, lysing of cells, and vein collapse. In some implementations, a system and method can eliminate user variability in disinfection, and also eliminate the risk of skin cells getting into the blood culture sample. The systems and methods disclosed herein do not require a change in existing clinical processes, other than to potentially indicate when a vacutainer or other blood collection device (i.e., syringe) should be attached for drawing contaminant-free blood samples.

[0014] In some implementations of the systems and methods disclosed herein the withdrawal of blood is accomplished passively by use of the patient's own blood pressure, thereby reducing the risk of vein collapse and eliminating any additional user steps over current practice. The systems and methods can be applied to accommodate short-path direct stick or butterfly venipuncture systems. They can also be used with samples drawn through a catheter.

[0015] In one aspect, a blood sequestration device is presented. The blood sequestration device includes an inlet port and an outlet port. The blood sequestration device further includes a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration

device further includes a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

[0016] In another aspect, a blood sequestration device connected with a blood sampling pathway is described. The blood sampling pathway has a patient needle and a sample collection device. The blood sequestration device includes an inlet port connected with the patient needle, and a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, and an outlet port connected with a distal end of the sampling channel and with the sample collection device.

[0017] In yet another aspect, a blood sequestration device connected with a blood sampling system is described. The blood sampling system includes a patient needle for accessing a blood sample from a patient, and a sample needle that is sealed and adapted for receiving an evacuated blood collection tube. The blood sequestration device includes an inlet port connected with the patient needle to receive the blood sample from the patient. The blood sequestration device further includes a sequestration chamber connected with the inlet port and having a vent comprising an air permeable blood barrier, the sequestration chamber for receiving and sequestering a first portion of the blood sample prior to the sample needle being unsealed by the evacuated blood collection tube. The blood sequestration device further includes a sampling channel having a proximal end connected with the inlet port, the sampling channel for conveying a subsequent portion of the blood sample once the sample needle is unsealed by the evacuated blood collection tube. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel for conveying the subsequent portion of the blood sample to the sample needle.

[0018] In yet another aspect, a blood sample optimization system is disclosed and described. The blood sample optimization system includes a blood sampling system for accessing and acquiring one or more samples of a patient's blood, and a blood sequestration device for receiving and sequestering a first portion of the one or more samples of the

patient's blood which might be contaminated by a venipuncture process and which could result in a false positive identification of a pathogen in the patient's blood.

[0019] The blood sampling system includes a patient needle configured for a venipuncture of a patient to access a sample of blood of a patient, a blood sampling pathway connected with the patient needle for conveying the sample of blood, and a sample needle configured for receiving an evacuated blood collection container to collect and contain a subsequent portion of the sample of blood.

[0020] In yet another aspect, a blood sequestration device is disclosed and described. In some implementations, the blood sequestration device can include an inlet port, an outlet port connected with the inlet port, and a sequestration chamber connected with the inlet port. The sequestration chamber can have a vent comprising an air permeable blood barrier.

[0021] The blood sequestration device is connected along the blood sampling pathway between the patient needle and the sample needle, and includes an inlet port for receiving the sample of blood. The blood sequestration device further includes a sequestration chamber connected with the inlet port for receiving a first amount of the sample of blood, the sequestration chamber having a vent comprising an air permeable blood barrier for sequestering at least a first portion of the first amount of the sample of blood. The blood sequestration device may further include a sampling channel having a proximal end connected with the inlet port, the sampling channel conveying a subsequent amount of the sample of blood to the evacuated blood collection container upon the sequestration chamber sequestering at least the first portion of the first amount of the sample of blood. The blood sequestration device further includes an outlet port connected with a distal end of the sampling channel, the outlet port for outputting the subsequent amount of the sample of blood.

[0022] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] These and other aspects will now be described in detail with reference to the following drawings.

[0024] FIG. 1 illustrates a blood sample optimization system.

[0025] FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0026] FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0027] FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0028] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.

[0029] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.

[0030] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.

[0031] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.

[0032] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.

[0033] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.

[0034] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.

[0035] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.

[0036] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

[0037] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.

[0038] FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.

[0039] FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

[0040] FIGS. 17A – 17E illustrate a bottom member of a housing for a blood sequestration device.

[0041] FIGS. 18A – 18F illustrate a top member of a housing for a blood sequestration device.

[0042] FIGS. 19A and 19B illustrate a blood sequestration device having a top member mated with a bottom member.

[0043] FIG. 20 shows a blood sample optimization system including a blood sequestration device.

[0044] FIG. 21 illustrates a non-vented blood sequestration device using a wicking material chamber.

[0045] FIGS. 22A and 22B illustrate a material makeup of a filter for sequestering blood in a sequestration chamber of a blood sequestration device.

[0046] FIGS. 23A and 23B illustrate another implementation of a blood sequestration device that uses a vacuum force from a blood collection device.

[0047] Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

[0048] This document describes blood sample optimization systems and methods for reducing or eliminating contaminates in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[0049] FIG. 1 illustrates a blood sample optimization system in accordance with some implementations. The system includes a patient needle 1 to puncture the skin of a patient to access the patient's vein and blood therein. The system further includes a sample needle (i.e., a resealably closed needle for use with Vacutainers™ or the like) 5, which may be contained within and initially sealed by a resealable boot 10, a Luer activated valve, or another collection interface or device. The resealable boot 10 can be pushed aside or around the sample needle 5 by application of a Vacutainer™ bottle (not shown) for drawing the patient's blood. The system can further include a low volume chamber 30 that leads to the sample needle 5, but also includes an orifice or one or more channels 45 that lead to a sequestration chamber 55 formed by a housing 50.

[0050] The sequestration chamber 55 is a chamber, channel, pathway, lock, or other structure for receiving and holding a first aliquot of the patient's blood, which may be in a predetermined or measured amount, depending on a volume of the sequestration chamber 55. The first draw of blood typically contains or is more susceptible to containing organisms that cause bacteraemia and sepsis or other pathogens than subsequent blood draws. The sequestration chamber 55 can be a vessel encased in a solid housing, formed in or defined by

the housing itself, or can be implemented as tubing or a lumen. The sequestration chamber 55, regardless how formed and implemented, may have a predetermined volume. In some implementations, the predetermined volume may be based on a volume of the patient needle, i.e. ranging from less than the volume of the patient needle to any volume up to or greater than 20 times or more of the volume of the patient needle. The predetermined volume of the sequestration chamber 55 may also be established to economize or minimize an amount of blood to be sequestered and disposed of.

[0051] The sequestration chamber 55 can be formed, contained or housed in a chamber housing 50, and can be made of plastic, rubber, steel, aluminum or other suitable material. For example, the sequestration chamber 55 could be formed of flexible tubing or other elastomeric materials. The sequestration chamber 55 further includes an air permeable blood barrier 20 that allows air to exit the sequestration chamber 55. As used herein the term "air permeable blood barrier" means an air permeable but substantially blood impermeable substance, material, or structure. Examples may include hydrophobic membranes and coatings, a hydrophilic membrane or coating combined with a hydrophobic membrane or coating, mesh, a filter, a mechanical valve, antimicrobial material, or any other means of allowing air to be displaced from the sequestration chamber 55 as it is filled with blood. In various exemplary embodiments, an air permeable blood barrier may be formed by one or more materials that allow air to pass through until contacted by a liquid, such material then becomes completely or partially sealed to prevent or inhibit the passage of air and/or liquid. In other words, prior to contact with liquid, the material forms a barrier that is air permeable. After contact with a liquid, the material substantially or completely prevents the further passage of air and/or liquid.

[0052] The orifice or channel 45 can be any desired length, cross-sectional shape or size, and/or can be formed to depart from the low volume chamber 30 at any desired angle or orientation. The orifice or channel 45 may also include a one-way flap or valve 60 that maintains an initial aliquot of blood sample within the sequestration chamber 55. In some specific implementations, the orifice or channel 45 can include a "duck bill" or flapper valve 60, or the like, for one-way flow of blood from low volume chamber 30 to the sequestration chamber 55. The air permeable blood barrier 20 can also be constructed of a material that

allows air to exit but then seals upon contact with blood, thereby not allowing external air to enter sequestration chamber 55. This sealing would eliminate the need for a valve.

[0053] Valve 60 can be any type of valve or closing mechanism. Chamber 30 is designed to hold virtually no residual blood, and can be designed to be adapted to hold or allow pass-through of a particular volume or rate of blood into sequestration chamber 55. Likewise, sequestration chamber 55 may also include any type of coating, such as an anti-microbial coating, or a coating that aids identification and/or diagnosis of components of the first, sequestered blood draw.

[0054] Housing 50 and 40 can be formed of any suitable material, including plastic, such as acrylonitrile butadiene styrene (ABS) or other thermoplastic or polymeric material, rubber, steel, or aluminum. The air permeable blood barrier 20 can include a color-providing substance, or other signaling mechanism, that is activated upon contact with blood from the initial blood draw, or when air displacement is stopped, or any combination of events with blood in the sequestration chamber 55. The air permeable barrier may also include an outer layer such as a hydrophobic membrane or cover that inhibits or prevents the inadvertent or premature sealing of the filter by an external fluid source, splash etc. Sequestration chamber 55 can also be translucent or clear to enable a user to visually confirm the chamber is filled.

[0055] FIG. 2 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown in FIG. 2, a sequestration chamber 55, or waste chamber, surrounds the patient needle 1, with an open-ended cuff or housing connected with the waste chamber and encircling the sample needle housing base and housing. The patient needle 1 and sample needle 5 are connected together by a boot 56, which forms a continuous blood draw channel therethrough. The boot 56 includes a single orifice or channel leading from the blood draw channel into sequestration chamber 55. The device can include more than one single orifice or channel, in other implementations. Each orifice or channel can include a one-way valve, and can be sized and adapted for predetermined amount of blood flow.

[0056] The sequestration chamber 55 includes an air permeable blood barrier. The filter can further include a sensor or indicator to sense and/or indicate, respectively, when a

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

[0057] FIG. 3 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is surrounded by a resealable boot or membrane, and is further connected with a patient needle 1. A blood flow channel is formed through the sample needle and the patient needle. The connection between the sample needle and patient needle includes a "T" or "Y" connector 102, which includes a channel, port or aperture leading out from the main blood flow channel to a sequestration chamber 104.

[0058] The T or Y connector 102 may include a flap or one-way valve, and have an opening that is sized and adapted for a predetermined rate of flow of blood. The sequestration chamber 104 can be formed from tubing, or be formed by a solid housing, and is initially filled with air. The sequestration chamber 104 will receive blood that flows out of a patient automatically, i.e. under pressure from the patient's own blood pressure. The sequestration chamber 104 includes an air permeable blood barrier 106, preferably at the distal end of tubing that forms the sequestration chamber 104, and which is connected at the proximal end to the T or Y connector 102. The T or Y connector 102 can branch off at any desired angle for most efficient blood flow, and can be formed so as to minimize an interface between the aperture and channel and the main blood flow channel, so as to minimize or eliminate mixing of the initial aliquot of blood with main blood draw samples.

[0059] In some alternative implementations, the sample needle may be affixed to a tubing of any length, as shown in FIG. 4, connecting at its opposite end to the T or Y connector 102. The sequestration chamber 104 can be any shape or volume so long as it will contain a predetermined amount of blood sample in the initial aliquot. The T or Y connector 102 may also include an opening or channel that is parallel to the main blood flow channel. The air permeable blood barrier may further include an indicator 107 or other mechanism to indicate when a predetermined amount of blood has been collected in the sequestration chamber, or when air being expelled reaches a certain threshold, i.e. to zero. The tubing can also include a clip 109 that can be used to pinch off and prevent fluid flow therethrough.

[0060] Once the air permeable blood barrier and primary chamber are sealed the initial aliquot of blood is trapped in the sequestration chamber 104, an evacuated blood collection tube, such as a Vacutainer™ bottle may be attached to the sample needle 5 to obtain the sample. The blood collection tube can be removed, and the sample needle 5 will be resealed. Any number of follow-on blood collection tubes can then be attached for further blood draws or samples. Upon completion of all blood draws, the system can be discarded, with the initial aliquot of blood remaining trapped in the sequestration chamber 104.

[0061] FIG. 5 illustrates a blood sample optimization system in accordance with some alternative implementations. In the implementation shown, a sample needle 5 is connected with a patient needle by tubing. A "T" or "Y" connector 120 is added along the tubing at any desired location, and includes an aperture, port or channel leading to a sequestration chamber 204, substantially as described above.

[0062] FIG. 6 illustrates a blood sample optimization system in accordance with some alternative implementations, in which a sequestration chamber 304, formed as a primary collection channel, receives an initial aliquot of blood, and is provided adjacent to the blood sampling channel. The sequestration chamber 304 can encircle the blood sampling channel, the patient needle 1, and/or the sample needle 5. The primary collection channel can include a T or Y connector 120, or other type of aperture or channel. The sequestration chamber 304 includes an air permeable blood barrier, which can also include an indicator of being contacted by a fluid such as blood, as described above.

[0063] In some implementations, either the patient needle 1 or the sample needle 5, or both, can be replaced by a Luer lock male or female connector. However, in various implementations, the connector at a sample needle end of the blood sample optimization system is initially sealed to permit the diversion of the initial aliquot of blood to the sequestration chamber, which is pressured at ambient air pressure and includes the air outlet of the air permeable blood barrier. In this way, the system passively and automatically uses a patient's own blood pressure to overcome the ambient air pressure of the sequestration chamber to push out air through the air permeable blood barrier and displace air in the sequestration chamber with blood.

[0064] FIG. 7 is a flowchart of an exemplary method for optimizing the quality of a blood culture. At 702, a clinician places a needle into a patient's vein. At 704, blood then flows into a sequestration chamber, pushing the air in the sequestration chamber out of the sequestration chamber through an air permeable blood barrier. In some implementations, the volume of the sequestration chamber is less than 0.1 to more than 5 cubic centimeters (cc's), or more. The sequestration chamber is sized and adapted to collect a first portion of a blood sample, which is more prone to contamination than secondary and other subsequent portion of the blood sample or subsequent draws. Since the sequestration chamber has an air-permeable blood barrier through which air can be displaced by blood pushed from the patient's vein, such blood will naturally and automatically flow into the sequestration chamber before it is drawn into or otherwise enters into a Vacutainer or other bottle for receiving and storing a blood sample.

[0065] When the sequestration chamber fills, the blood will gather at or otherwise make contact with the air permeable blood barrier, which will inhibit or prevent blood from passing therethrough. At 706, when the blood comes into contact with the entire internal surface area of the air permeable blood barrier, the air permeable blood barrier is then closed and air no longer flows out or in. At 708, the clinician may be provided an indictor or can see the full chamber, to indicate the evacuated blood collection tube, such as a Vacutainer™ can be attached. The indicator can include visibility into the primary chamber to see whether it is full, the blood barrier changing color, for example, or other indicator. The fill time of

the sequestration chamber may be substantially instantaneous, so such indicator, if present, may be only that the sequestration chamber is filled.

[0066] Prior to an evacuated blood collection tube being attached, communication between the needle, sampling channel, and the sequestration chamber is restricted by the sealing of the sequestration chamber blood barrier thereby not permitting air to reenter the system through the sequestration. Sealing the communication path could also be accomplished with a mechanical twist or other movement, a small orifice or tortuous pathway, eliminating the need for a separate valve or mechanical movement or operation by the clinician. At 710, once the evacuated blood collection tube is removed, the self-sealing membrane closes the sample needle, and at 712, additional subsequent evacuated blood collection tubes may be attached. Once samples have been taken, at 714 the device is removed from the patient and discarded.

[0067] FIGS. 8A – 8E illustrate an exemplary blood sample optimization system 800 for non-contaminated blood sampling, in accordance with some implementations. The blood sample optimization system 800 includes an inlet port 802 that can be connected to tubing, a patient needle (or both), or other vascular or venous access device, and a pathway splitter 804 having a first outlet to a sequestration chamber tubing 806 and a second outlet to sample collection tubing 808. One or both of the sequestration chamber tubing 806 and the sample collection tubing 808 can be formed of tubing. In some implementations, the sequestration chamber tubing 806 is sized so as to contain a particular volume of initial blood sample. The sample collection tubing 808 will receive a blood sample once the sequestration chamber tubing 806 is filled. The sample collection tubing 808 can be connected to a Vacutainer™ base or housing 810, or other blood sample collection device.

[0068] The blood sequestration system 800 further includes a blood sequestration device 812 which, as shown in more detail in FIGS. 8B – 8D, includes a housing 818 that includes a sampling channel 820 defining a pathway for the non-contaminated sample collection tubing 808 or connected at either end to the non-contaminated sample collection tubing 808. The sampling channel 820 can be curved through the housing 818 so as to better

affix and stabilize the housing 818 at a location along the non-contaminated sample collection tubing 808.

[0069] The blood sequestration device 812 further includes a sequestration chamber 822 connected with the sequestration chamber tubing 806 or other chamber. The sequestration chamber 822 terminates at an air permeable blood barrier 824. The air permeable blood barrier 824 can also include a coloring agent that turns a different color upon full contact with blood, as an indicator that the regular collection of blood samples (i.e. the non-contaminated blood samples) can be initiated. Other indicators may be used, such as a small light, a sound generation mechanism, or the like. In some implementations, the air permeable blood barrier is positioned at a right angle from the direction of sequestration chamber 822, but can be positioned at any distance or orientation in order to conserve space and materials used for the housing 818. The housing 818 and its contents can be formed of any rigid or semi-rigid material or set of materials.

[0070] FIG. 9 illustrates a pathway splitter 900 for use in a blood sequestrations system, such as those shown in FIGS. 8A – 8E, for example. The pathway splitter 900 includes an inlet port 902, a main line outlet port 904, and a sequestration channel outlet port 906. The inlet port 902 can be connected to main tubing that is in turn connected to a patient needle system, or directly to a patient needle. The main line outlet port 904 can be connected to main line tubing to a blood sampling system, such as a vacutainer base or housing, or directly to such blood sampling system. The sequestration channel outlet port 906 can be connected to sequestration tubing for receiving and sequestering a first sample of blood, up to a measured amount or predetermined threshold. Alternatively, the sequestration channel outlet port 906 can be connected to a sequestration chamber. The sequestration channel outlet port 906 is preferably 20-70 degrees angled from the main line outlet port 904, which in turn is preferably in-line with the inlet port 902. Once the predetermined amount of initial blood sample is sequestered in the sequestration tubing or chamber, in accordance with mechanisms and techniques described herein, follow-on blood samples will flow into the inlet port 902 and directly out the main line outlet port 904, without impedance.

[0071] FIGS. 10A – 10D illustrate a blood sequestration device 1000 in accordance with alternative implementations. The blood sequestration device 1000 includes an inlet port 1002, a main outlet port 1004, and a sequestration channel port 1006. The inlet port 1002 can be connected to a patient needle or related tubing. The main outlet port 1004 can be connected to a blood sample collection device such as a Vacutainer, associated tubing, or a Luer activated valve, or the like. The sequestration channel port 1006 splits off from the main outlet port 1004 to a sequestration chamber 1008. In some implementations, the sequestration chamber 1008 is formed as a helical channel within a housing or other container 1001.

[0072] The sequestration chamber 1008 is connected at the distal end to an air permeable blood barrier 1010, substantially as described above. Air in the sequestration chamber 1008 is displaced through the air permeable blood barrier 1010 by an initial aliquot of blood that is guided into the sequestration channel port 1006. Once the sequestration chamber 1008 is filled, further blood draws through the main outlet port 1004 can be accomplished, where these samples will be non-contaminated.

[0073] FIGS. 11A – 11E illustrate a blood sequestration device 1100 in accordance with other alternative implementations. The blood sequestration device 1100 includes an inlet port 1102, similar to the inlet ports described above, a main outlet port 1104, and a sequestration channel port 1106 that splits off from the main outlet port 1104 and inlet port 1102. The sequestration channel port is connected to a sequestration chamber 1108. In the implementation shown in FIGS. 11A – 11E, the blood sequestration device includes a base member 1101 having a channel therein, which functions as the sequestration chamber 1108. The channel can be formed as a tortuous path through the base member 1101, which is in turn shaped and formed to rest on a limb of a patient.

[0074] A portion of the sequestration chamber 1108 can protrude from the base member or near a top surface of the base member, just before exiting to an air permeable blood barrier 1110, to serve as a blood sequestration indicator 1109. The indicator 1109 can be formed of a clear material, or a material that changes color when in contact with blood.

[0075] In some implementations, the blood sequestration device 1100 can include a blood sampling device 1120 such as a normally closed needle, Vacutainer™ shield or other collection device. The blood sampling device 1120 can be manufactured and sold with the blood sequestration device 1100 for efficiency and convenience, so that a first aliquot of blood that may be contaminated by a patient needle insertion process can be sequestered. Thereafter, the blood sampling device 1120 can draw non-contaminated blood samples to reduce the risk of false positive testing and ensure a non-contaminated sample.

[0076] FIGS. 12A-12D illustrate a blood sample optimization system 1200 in accordance with yet other alternative implementations. The system 1200 includes a blood sequestration device 1202 for attaching to a blood sampling device 1204, such as a Vacutainer™ or other collection and sampling device. The blood sequestration device 1202 is configured and arranged to receive, prior to a Vacutainer™ container or vial being attached to a collection needle of the blood sampling device 1204, a first aliquot or amount of blood, and sequester that first aliquot or amount in a sequestration channel of the blood sequestration device 1202.

[0077] In some implementations, the blood sequestration device 1202 can include an inlet port 1212, a main outlet port, and a sequestration channel port. The inlet port 1212 can be connected to a patient needle or related tubing. The main outlet port 1214 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port splits off from the main outlet port to a sequestration chamber 1218.

[0078] In some implementations, the sequestration chamber 1218 is formed as a channel within the body of a sequestration device 1202. The sequestration chamber 1218 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel. The sequestration device 1202 can include a housing or other containing body, and one or more channels formed therein. As shown in FIGS. 12A and 12B, the sequestration device 1202 includes a main body 1206 and a cap 1208. The main body 1206 is formed with one or more cavities or channels, which are further formed with

one or more arms 1210 that extend from the cap 1208, and which abut the cavities or channels in the main body 1206 to form the primary collection port and main outlet port.

[0079] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet other alternative implementations. The system 1300 includes a blood sequestration device 1302 for attaching to a blood sampling device 1304, such as a Vacutainer or other bodily fluid collection and sampling device. The blood sequestration device 1302 is configured and arranged to receive, prior to a Vacutainer container or vial being attached to a collection needle of the blood sampling device 1304, a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood or other bodily fluid in a sequestration channel of the blood sequestration device 1302.

[0080] The blood sequestration device 1302 includes a housing 1301 having an inlet port 1314, a main outlet port 1312, and a sequestration channel port 1316. The inlet port 1314 can be connected to a patient needle or associated tubing. The main outlet port 1312 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like. The sequestration channel port 1316 splits off from the main inlet port 1314 to a sequestration chamber 1318.

[0081] In the implementation shown in FIGS. 13A-D, the sequestration chamber 1318 is formed as a cavity or chamber within housing 1301 or formed by walls that define housing 1301. The sequestration chamber 1318 can be a winding channel, such as a U-shaped channel, an S-shaped channel, a helical channel, or any other winding channel, that is defined by the cooperation and connection of housing 1301 with cap 1307 which cap 1307 can include a protrusion 1305 that provides one or more walls or directors for the winding channel in the sequestration chamber 1318. The protrusion 1305 from the cap 1307 can be straight or curved, and may have various channels, apertures or grooves embedded therein, and can extend from the cap 1307 any angle or orientation. When the cap 1307 is connected with the housing 1301 to complete the formation of the sequestration chamber 1318, the protrusion 1305 forms at least part of the winding channel to sequester a first aliquot or

amount of blood or other bodily fluid in a sequestration channel formed in the sequestration chamber 1318 and by the winding channel.

[0082] The sequestration chamber 1318 includes an air permeable blood barrier 1310, substantially as described above. Air in the sequestration chamber 1318 is displaced through the air permeable blood barrier 1310 by an initial aliquot of blood that is provided into the sequestration chamber 1318 by the blood pressure of the patient. Once the sequestration chamber 1318 is filled and the air in the sequestration chamber 1318 displaced, the blood pressure of the patient will be insufficient to drive or provide further blood into the blood sequestration device 1302, and in particular the outlet port 1312, until a force such as a vacuum or other pressure, such as provided by the blood sample collection device like Vacutainer is provided to draw out a next aliquot or amount of blood or bodily fluid. Further blood draws through the main outlet port 1312 can be accomplished, where these samples will be non-contaminated since any contaminants would be sequestered in the sequestration chamber 1318 with the first aliquot of blood.

[0083] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system 1400 to sequester contaminates of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[0084] The inlet port 1402 defines an opening into the blood sequestration device 1401, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more. The blood sequestration device 1401

further includes an outlet port 1404, which defines an opening out of the blood sequestration device 1401 and to the blood sample collection device 1403. The outlet port 1404 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device 1403. The outlet port 1404 can further include a connector device such as a threaded cap, a Luer connector (male or female), a non threaded interference or glue joint fitting for attachment of various devices including but not limited to tubing, or the like.

[0085] The blood sequestration device 1401 further includes a sampling channel 1406 between the inlet port 1402 and the outlet port 1404, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1406 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1406 has a substantially similar cross sectional area as the opening of the inlet port 1402. In other implementations, the sampling channel 1406 can gradually widen from the inlet port 1402 to the outlet port 1404.

[0086] The blood sequestration device 1401 further includes a sequestration chamber 1408 that is connected to and split off or diverted from the sampling channel 1406 at any point between the inlet port 1402 and the outlet port 1404, but preferably from a proximal end of the sampling channel 1406 near the inlet port 1402. The sequestration chamber 1408 is at first maintained at atmospheric pressure, and includes an air outlet 1412 at or near a distal end of the sequestration chamber 1408 opposite the diversion point from the sampling channel 1406. The air outlet 1412 includes an air permeable blood barrier 1412. As shown in FIG. 14B, the air permeable blood barrier 1412 can be overlaid with a protective cover 1416. The protective cover 1416 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1412 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1412 as the air is displaced from the sequestration chamber 1408 by blood being forced into the sequestration chamber 1408 by a patient's own blood pressure. In addition the protective cover 1416 can be constructed to inhibit or prevent accidental exposure of the air permeable blood barrier to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0087] As shown in FIGS. 14C and 14D, the sampling channel 1406 can be cylindrical or frusto-conical in shape, going from a smaller diameter to a larger diameter, to minimize a potential to lyse red blood cells. Likewise, the sampling channel 1406 is formed with a minimal amount of or no sharp turns or edges, which can also lyse red blood cells. The sampling channel 1406 splits off to the sequestration chamber 1408 near the inlet port 1402 via a diversion pathway 1409. The diversion pathway 1409 can have any cross-sectional shape or size, but is preferably similar to the cross-sectional shape of at least part of the inlet port 1402.

[0088] In some implementations, the sampling channel 1406 and the sequestration chamber 1408 are formed by grooves, channels, locks or other pathways formed in housing 1414. The housing 1414 can be made of plastic, metal or other rigid or semi-rigid material. The housing 1414 can have a bottom member that sealably mates with a top member. One or both of the bottom member and the top member can include the sampling channel 1406 and the sequestration chamber 1408, as well as the diversion pathway 1409, the inlet port 1402, and the outlet port 1404. In some other implementations, one or more of the diversion pathway 1409, the inlet port 1402, and/or the outlet port 1404 can be at least partially formed by a cap member that is connected to either end of the housing 1414. In some implementations, the top member and the bottom member, as well as the cap member(s), can be coupled together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations, some or all of the interior surface of the diversion pathway 1409 and/or sequestration chamber 1408 can be coated or loaded with an agent or substance, such as a decontaminate, solidifying agent, or the like. For instance, a solidifying agent can be provided at the diversion pathway 1409 such that when the sequestration chamber 1408 is filled and the initial aliquot of blood backs up to the diversion pathway 1409, that last amount of sequestered blood could solidify, creating a barrier between the sequestration chamber 1408 and the sampling channel 1406.

[0089] FIGS. 15A-15G illustrate a blood sequestration device 1500. The blood sequestration device 1500 can be connected to a normally closed needle or device to enable connection with an evacuated blood collection container or other collection device such as a Vacutainer™, associated tubing, luer connectors, syringe, a Luer activated valve, or the like.

[0090] The blood sequestration device 1500 includes an inlet port 1502 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1502 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1502 defines an opening into the blood sequestration device 1500, which opening may be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[0091] The inlet port 1502 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1502, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1500 can be fabricated and sold with the patient needle as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1500 at the time of blood draw or sampling.

[0092] The blood sequestration device 1500 further includes an outlet port 1504, which defines an opening out of the blood sequestration device 1500 and to the blood sample collection device. The outlet port 1504 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1500 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1500 at the time of blood draw or sampling.

[0093] The blood sequestration device 1500 further includes a sampling channel 1506 between the inlet port 1502 and the outlet port 1504, and which functions as a blood sample pathway once a first aliquot of blood has been sequestered. The sampling channel 1506 can be any sized, shaped or configured channel or conduit. In some implementations, the

sampling channel 1506 has a substantially similar cross sectional area as the opening of the inlet port 1502. In other implementations, the sampling channel 1506 can gradually widen from the inlet port 1502 to the outlet port 1504.

[0094] The blood sequestration device 1500 further includes a sequestration chamber 1508 that is connected to and split off or diverted from the sampling channel 1506 at any point between the inlet port 1502 and the outlet port 1504, but preferably from a proximal end of the sampling channel 1506 near the inlet port 1502. In some implementations, the diversion includes a Y-shaped junction. The sequestration chamber 1508 is preferably maintained at atmospheric pressure, and includes a vent 1510 at or near a distal end of the sequestration chamber 1508. The vent 1510 includes an air permeable blood barrier 1512. FIG. 15C illustrates the blood sequestration device 1500 with the sequestration chamber 1508 filled with a first aliquot or sample of blood from the patient.

[0095] The air permeable blood barrier 1512 can be covered with a protective cover 1516. The protective cover 1516 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1512 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1512 as the air is displaced from the sequestration chamber 1508 by blood being forced into the sequestration chamber 1508 by a patient's own blood pressure. The protective cover 1516 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[0096] FIG. 15B is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating an initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before a sample collection device is activated. FIG. 15G is a perspective view of the blood sequestration device 1500 from the outlet port 1504 and bottom side of the housing 1501 of the blood sequestration device 1500, and illustrating the initial aliquot of blood filling sequestration chamber 1508 while the sampling channel 1506 is empty, before the sample collection device is activated. FIG. 15C

is another perspective view of the blood sequestration device 1500 from the inlet port 1502 and top side of a housing 1501 of the blood sequestration device 1500 that includes the vent 1510, and illustrating blood now being drawn through sampling channel 1506 while the sequestered blood remains substantially in the sequestration chamber 1508.

[0097] FIG. 15D is a cross section of the blood sequestration device 1500 in accordance with some implementations, showing the housing 1501 that defines the sampling channel 1506 and the sequestration chamber 1508. FIGS. 15E and 15F illustrate various form factors of a housing for a blood sequestration device, in accordance with one or more implementations described herein.

[0098] The sequestration chamber 1508 can have a larger cross-sectional area than the sampling channel 1506, and the cross-sectional area and length can be configured for a predetermined or specific volume of blood to be sequestered or locked. The sampling channel 1506 can be sized to be compatible with tubing for either or both of the patient needle tubing or the blood collection device tubing.

[0099] The housing 1501 can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIG. 15D, the housing 1501 includes a top member 1520 and a bottom member 1522 that are mated together, one or both of which having grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc. The top member 1520 can be connected with the bottom member 1522 by any mating or connection mechanism, such as by laser welding, thermal bonding, ultrasonic welding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like.

[00100] In some implementations, such as shown in FIG. 15D, the top member 1520 can include the grooves, channels, locks, conduits or other pathways, while the bottom member 1522 can include a protrusion 1524 that is sized and adapted to fit into at least one of the grooves, channels, locks or other pathways of the top member 1520. The protrusion 1524 can provide a surface feature, such as a partial groove or channel, for instance, to complete the formation of either the sampling channel 1506 and/or the sequestration chamber 1508. In

some implementations, the protrusion 1524 can be formed with one or more angled sides or surfaces for a tighter fit within the corresponding groove, channel, lock or other pathway. In yet other implementations, both the top member 1520 and the bottom member can include grooves, channels, locks or other pathways, as well as one or more protrusions 1524.

[00101] In some implementations, the sampling channel 1506 and the sequestration chamber 1508 are formed by grooves, channels, locks or other pathways formed in housing 1501. The housing 1501 can be made of any suitable material, including rubber, plastic, metal or other material. The housing 1501 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1501 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1506 and/or the sequestration chamber 1508 is clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1508 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1506. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1512 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00102] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will make its way into the input port 1502 blood sequestration device 1500 and flow into the sequestration chamber 1508 by following the path of least resistance, as the patient's own blood pressure overcomes the atmospheric pressure in the sequestration chamber 1508 to displace air therein through the air permeable blood barrier 1512. The patient's blood pressure will not be sufficient to overcome the air pressure that builds up in the sealed sampling channel 1506. Eventually, the sequestration chamber 1508, which has a predetermined volume, is filled with blood that displaces air through the air permeable blood barrier 1512. Once the blood hits the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1512 material to completely or partially seal the vent 1510. A signal or indication may be provided that the practitioner can now utilize the Vacutainer

capsule or other blood sample collection device to acquire a next amount of the patient's blood for sampling. The blood in the sequestration chamber 1508 is now effectively sequestered in the sequestration chamber.

[00103] Upon filling the blood sequestration pathway 1508 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1506, possibly resulting in a small amount of blood moving past the diversion point to the sequestration chamber 1508 and into the sampling channel 1506, queuing up the uncontaminated blood to be drawn through the sampling channel 1506.

[00104] FIGS. 16-19 illustrate yet another implementation of a blood sequestration device. FIGS. 16A-16D illustrate a blood sequestration device 1600 that can be connected between a blood sample collection device, such as an evacuated blood collection container like a Vacutainer™ (not shown), and a patient needle (not shown) and/or associated tubing. FIG. 17 illustrates a bottom member of the blood sequestration device, and FIG. 18 illustrates a top member of the blood sequestration device, which top member and bottom member can be mated together to form an input port, and output port, a sequestration chamber and a sampling channel, as explained more fully below. FIGS. 19A and B show the top member and bottom member mated together. It should be understood that FIGS. 16-19 illustrate one exemplary manner of constructing a blood sequestration device as described herein, and other forms of construction are possible.

[00105] Referring to FIGS. 16A – D, the blood sequestration device 1600 includes an inlet port 1602 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1602 may also be connected with tubing or other conduit that is in turn connected with the patient needle. The inlet port 1602 defines an opening into the blood sequestration device 1600, which opening can be the same cross sectional dimensions as tubing or other conduit connected with the patient needle or the patient needle itself. For instance, the opening can be circular with a diameter of approximately 0.045 inches, but can have a diameter of between 0.01 inches or less to 0.2 inches or more.

[00106] The inlet port 1602 can also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. In some implementations, tubing or other conduit associated with the patient needle can be integral with the inlet port 1602, such as by co-molding, gluing, laser weld, or thermally bonding the parts together. In this manner, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing as a single unit, eliminating the need for connecting the patient needle to the blood sequestration device 1600 at the time of blood draw or sampling.

[00107] The blood sequestration device 1600 further includes an outlet port 1604, which defines an opening out of the blood sequestration device 1600 and to the blood sample collection device. The outlet port 1604 may also be connected with tubing or other conduit that is in turn connected with the blood sequestration device, and may also include a sealing or fluid-tight connector or connection, such as threading or Luer fitting, or the like. Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

[00108] The blood sequestration device 1600 further includes a sampling channel 1606 between the inlet port 1602 and the outlet port 1604, and a sequestration chamber 1608 that is connected to and split off or diverted from the sampling channel 1606 at any point between the inlet port 1602 and the outlet port 1604. The sampling channel 1606 functions as a blood sampling pathway once a first aliquot of blood has been sequestered in the sequestration chamber 1608. The sampling channel 1606 can be any sized, shaped or configured channel, or conduit. In some implementations, the sampling channel 1606 has a substantially similar cross sectional area as the opening of the inlet port 1602. In other implementations, the sampling channel 1606 can gradually widen from the inlet port 1602 to the outlet port 1604. The sequestration chamber 1608 may have a larger cross section to form a big reservoir toward the sequestration channel path so that the blood will want to enter the reservoir first versus entering a smaller diameter on the sampling channel 1606, as is shown more fully in FIGS. 17 and 19.

[00109] In some exemplary implementations, the diversion between the sampling channel 1606 and the sequestration chamber 1608 is by diverter junction 1607. Diverter junction 1607 may be a substantially Y-shaped, T-shaped, or U-shaped. In some preferred exemplary implementations, and as shown in FIG. 17A – 17B, the diverter junction 1607 is configured such that the flow out of the inlet port 1602 is preferentially directed toward the sequestration chamber 1608. The sequestration chamber 1608 may also include or form a curve or ramp to direct the initial blood flow toward and into the sequestration chamber 1608.

[00110] The sequestration chamber 1608 is preferably maintained at atmospheric pressure, and includes a vent 1610 at or near a distal end of the sequestration chamber 1608. The vent 1610 may include an air permeable blood barrier 1612 as described above.

[00111] The blood sequestration device 1600 can include a housing 1601 that can be formed of multiple parts or a single, unitary part. In some implementations, and as illustrated in FIGS. 17A – 17D and FIGS. 18A – 18F, the housing 1601 includes a top member 1620 and a bottom member 1622 that are mated together. The blood sequestration device 1600 can also include a gasket or other sealing member (not shown) so that when the top member 1620 is mechanically attached with the bottom member 1622, the interface between the two is sealed by the gasket or sealing member. The FIGS. 17A – 17D illustrate a bottom member 1622 of a housing for a blood sequestration device 1600. The bottom member 1622 can include grooves, channels, locks, conduits or other pathways pre-formed therein, such as by an injection molding process or by etching, cutting, drilling, etc., to form the sampling channel 1606, the sequestration chamber 1608, and diverter junction 1607.

[00112] The sequestration chamber 1608 may have a larger cross section than the sampling channel 1606 so that the blood will preferentially move into the sequestration chamber first versus entering a smaller diameter on the sampling channel 1606.

[00113] FIGS. 18A – 18F illustrate the top member 1620, which can be connected with the bottom member 1622 by any mating or connection mechanism, such as by laser welding, thermal bonding, gluing, using screws, rivets, bolts, or the like, or by other mating mechanisms such as latches, grooves, tongues, pins, flanges, or the like. The top member

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

[00114] In some implementations, the sampling channel 1606 and the sequestration chamber 1608 are formed by grooves, channels, locks or other pathways formed in housing 1601. The housing 1601 can be made of rubber, plastic, metal or any other suitable material. The housing 1601 can be formed of a clear or translucent material, or of an opaque or non-translucent material. In other implementations, the housing 1601 can be mostly opaque or non-translucent, while the housing surface directly adjacent to the sampling channel 1606 and/or the sequestration chamber 1608 may be clear or translucent, giving a practitioner a visual cue or sign that the sequestration chamber 1608 is first filled to the extent necessary or desired, and/or then a visual cue or sign that the sequestered blood remains sequestered while a clean sample of blood is drawn through the sampling channel 1606. Other visual cues or signs of the sequestration can include, without limitation: the air permeable blood barrier 1612 turning a different color upon contact, saturation, or partial saturation with blood; a color-coded tab or indicator at any point along or adjacent to the sequestration chamber; an audible signal; a vibratory signal; or other signal.

[00115] As shown in FIGS. 18A – 18F, the air permeable blood barrier 1612 can be covered with, or surrounded by, a protective member 1616. The protective member 1616 can be sized and configured to inhibit a user from touching the air permeable blood barrier 1612 with their finger or other external implement, while still allowing air to exit the air permeable blood barrier 1612 as the air is displaced from the sequestration chamber 1608. In some implementations, the protective member 1616 includes a protrusion that extends up from a top surface of the top member 1620 and around the air permeable blood barrier 1612. The protective cover 1616 can be constructed to inhibit or prevent accidental exposure of the filter to environmental fluids or splashes. This can be accomplished in a variety of mechanical ways including but not limited to the addition of a hydrophobic membrane to the protective cover.

[00116] In use, the blood sequestration device 1600 includes a sampling channel 1606 and a sequestration chamber 1608. Both pathways are initially air-filled at atmospheric pressure, but the sampling channel 1606 is directed to an output port 1604 that will be initially sealed by a Vacutainer or other such sealed blood sampling device, and the sequestration chamber 1608 terminates at a vent 1610 to atmosphere that includes an air permeable blood barrier 1612.

[00117] After a venipuncture by a patient needle of a patient (not shown), which could gather a number of pathogens from the patient's skin, a first amount of the patient's blood with those pathogens will pass through input port 1602 of blood sequestration device 1600. This initial volume of potentially contaminated blood will preferentially flow into the sequestration chamber 1608 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented sequestration chamber 1608 to displace air therein through the air permeable blood barrier 1612, but is not sufficient to overcome the air pressure that builds up in the sealed sampling channel 1606. In various exemplary embodiments, the sequestration chamber 1608 and sampling channel 1606 can be configured such that the force generated by the patient's blood pressure is sufficient to overcome any effect of gravity, regardless of the blood sequestration device's orientation.

[00118] Eventually, the sequestration chamber 1608 fills with blood that displaces air through the air permeable blood barrier 1612. Once the blood contacts the air permeable blood barrier, the blood interacts with the air permeable blood barrier 1612 material to completely or partially seal the vent 1610. A signal or indication may be provided that the practitioner can now utilize the Vacutainer or other blood sampling device.

[00119] Upon filling the blood sequestration pathway 1608 but prior to use of the Vacutainer or other blood sample collection device, the patient's blood pressure may drive compression of the air in the sampling channel 1606, possibly resulting in a small amount of blood moving past the diversion point into the sampling channel 1606, queuing up the uncontaminated blood to be drawn through the sampling channel 1606.

[00120] FIG. 19A is a side view, and FIG. 19B is a cross-sectional view, of the blood sequestration device 1600, illustrating the top member 1620 mated with the bottom member 1622.

[00121] FIG. 20 shows a blood sample optimization system 2000 that includes a patient needle 2002 for vascular access to a patient's bloodstream, a blood sample collection device 2004 to facilitate the collecting of one or more blood samples, and a conduit 2006 providing a fluid connection between the patient needle 2002 and the blood sample collection device 2004. In some implementations, the blood sample collection device 2004 includes a protective shield that includes a sealed collection needle on which a sealed vacuum-loaded container is placed, which, once pierced by the collection needle, draws in a blood sample under vacuum pressure or force through the conduit 2006 from the patient needle 2002.

[00122] The blood sample optimization system 2000 further includes a blood sequestration device 2008, located at any point on the conduit 2006 between the patient needle 2002 and the blood sample collection device 2004 as described herein.

[00123] FIG. 21 illustrates a non-vented blood sequestration device 2100 using a wicking material chamber. The blood sequestration device 2100 includes a housing 2101 that has a sampling channel 2104 that is at least partially surrounded or abutted by a sequestration chamber 2102 that is filled with a wicking material. An initial aliquot of blood is drawn in from the patient needle into the sampling channel 2104 where it is immediately wicked into the wicking material of the sequestration chamber 2102. The wicking material and/or sequestration chamber 2102 is sized and adapted to receive and hold a predetermined amount of blood, such that follow-on or later blood draws pass by the wicking material and flow straight through the sampling channel 2104 to a sampling device such as a Vacutainer. The wicking material can include a substance such as a solidifier, a decontaminate, or other additive.

[00124] As described herein, an air permeable blood barrier may be created using a wide variety of different structures and materials. As shown in FIGS. 22A and B, an air permeable blood barrier 2202 of a blood sequestration device 2200 can include a polymer bead matrix 2204, in which at least some beads are treated to make them hydrophilic. The

air permeable blood barrier 2202 further includes a self-sealing material 2206, such as carboxymethyl cellulose (CMC) or cellulose gum, or other sealing material. The air permeable blood barrier 2202 can further include voids 2208 that permit air flow before contact or during partial contact with a fluid such as blood. As shown in FIG. 22B, contact with a fluid causes the self-sealing material 2206 to swell and close off the voids 2208, occluding air flow through the voids 2208 and creating a complete or partial seal.

[00125] FIGS. 23A and B illustrate yet another implementation of a blood sequestration device 2300, having an inlet port 2302 to connect with a patient needle, an outlet port 2304 to connect with a blood sample collection device, a sequestration chamber 2306, and a sampling channel 2308 that bypasses the sequestration chamber 2306 once the sequestration chamber is filled to an initial aliquot of potentially contaminated blood to be sequestered. The sequestration chamber 2306 includes a hydrophobic plug 2312 at a distal end of the sequestration chamber 2306 that is farthest from the inlet port 2302. A vacuum or other drawing force applied from the outlet port 2304, such as from a Vacutainer or the like, draws in blood into the inlet port 2302 and directly into the sequestration chamber 2306, where the initial aliquot of blood will contact the hydrophobic plug 2312 and cause the initial aliquot of blood to back up into the sequestration chamber 2306 and be sequestered there. A small amount of blood may make its way into the sampling channel 2308, which is initially closed off by valve 2308. Upon release of the valve 2308, and under further force of the vacuum or other force, follow-on amounts of blood will flow into inlet port 2302, bypass the sequestration chamber 2306, and flow into and through sampling channel 2308 toward the outlet port 2304 and to the collection device.

[00126] The sampling channel 2308 can have any suitable geometry and can be formed of plastic tubing or any other suitable material. Valve 2308 can be a clip or other enclosing device to pinch, shunt, bend or otherwise close off the sampling channel before the initial aliquot of blood is sequestered in the sequestration chamber 2306.

[00127] Although a variety of embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

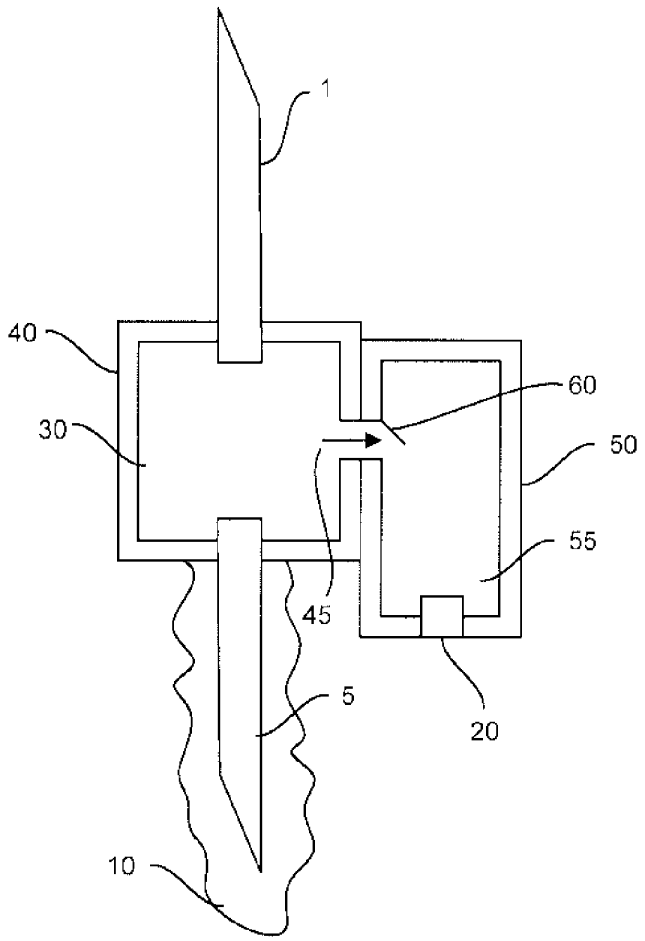


FIG. 1

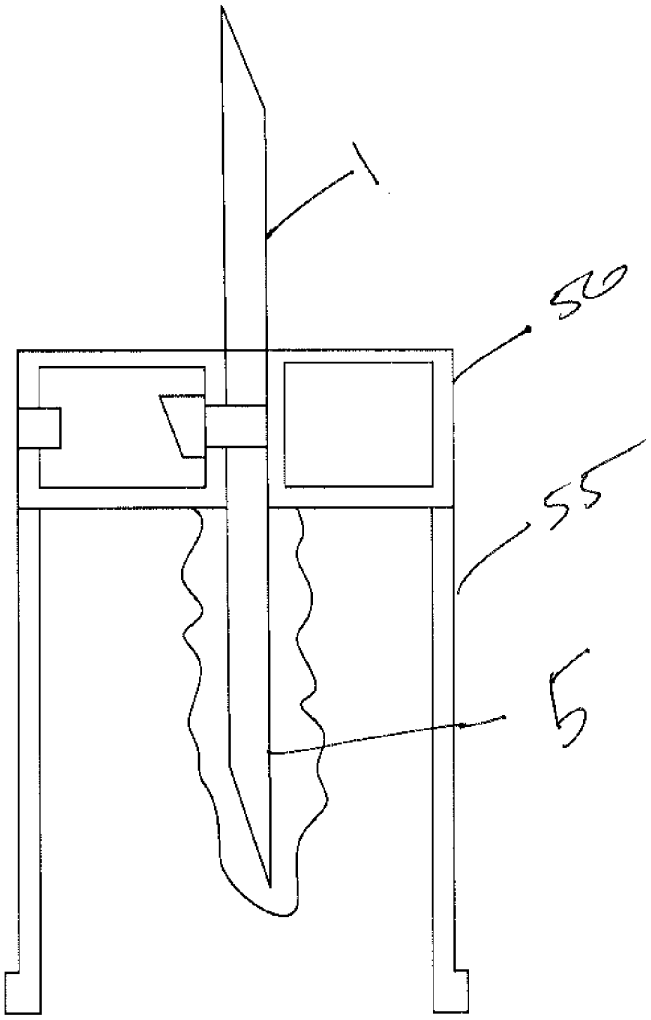


FIG. 2

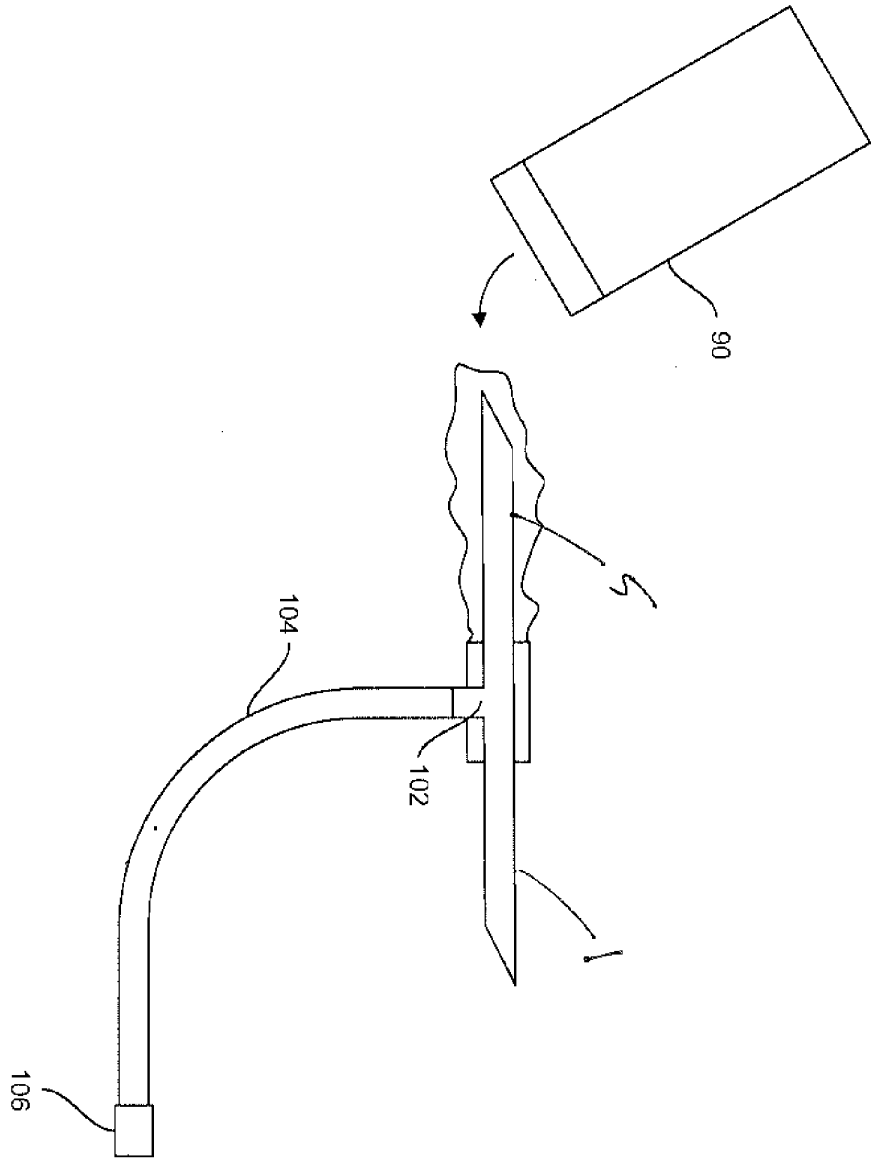


FIG. 3

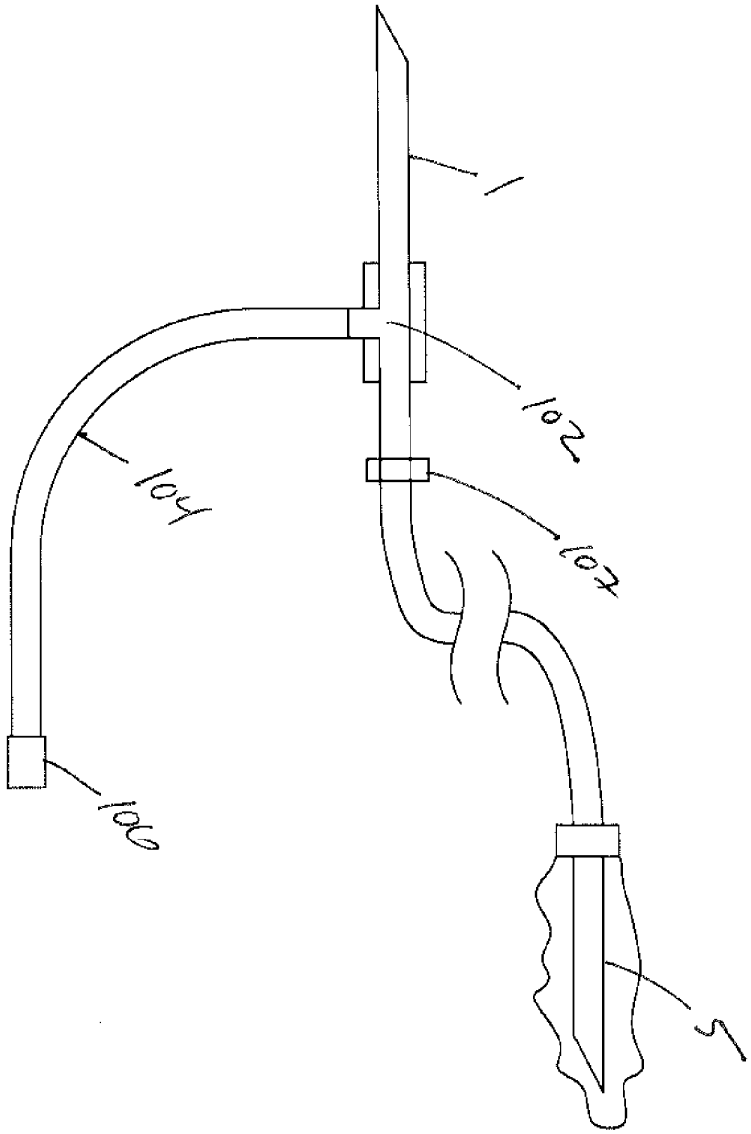


FIG. 4

FIG. 5

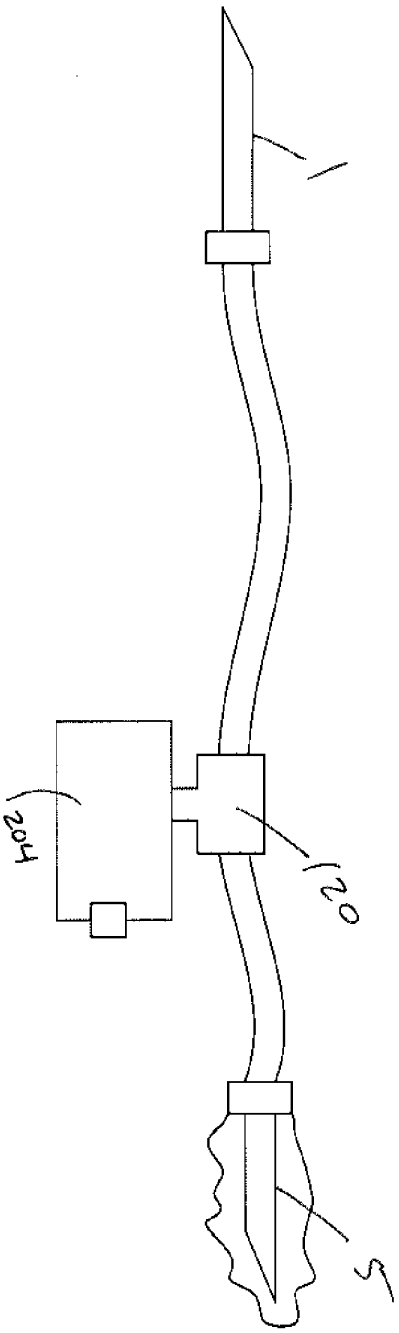
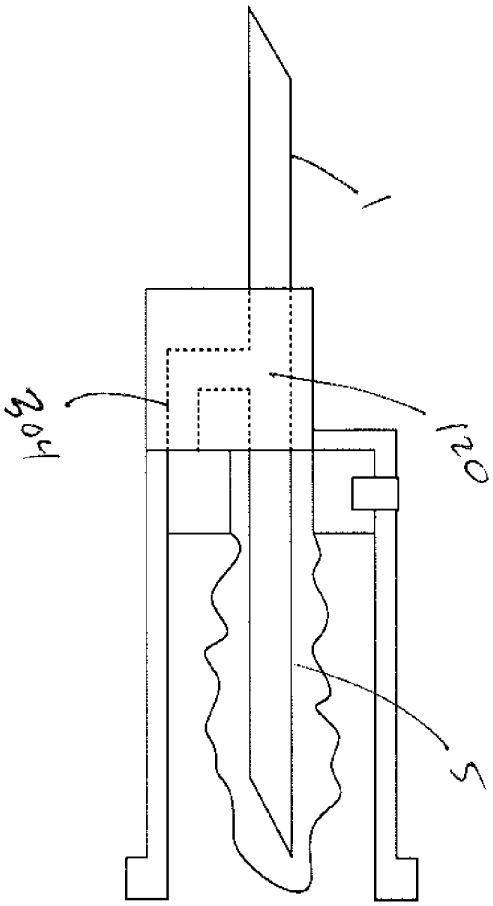


FIG. 6



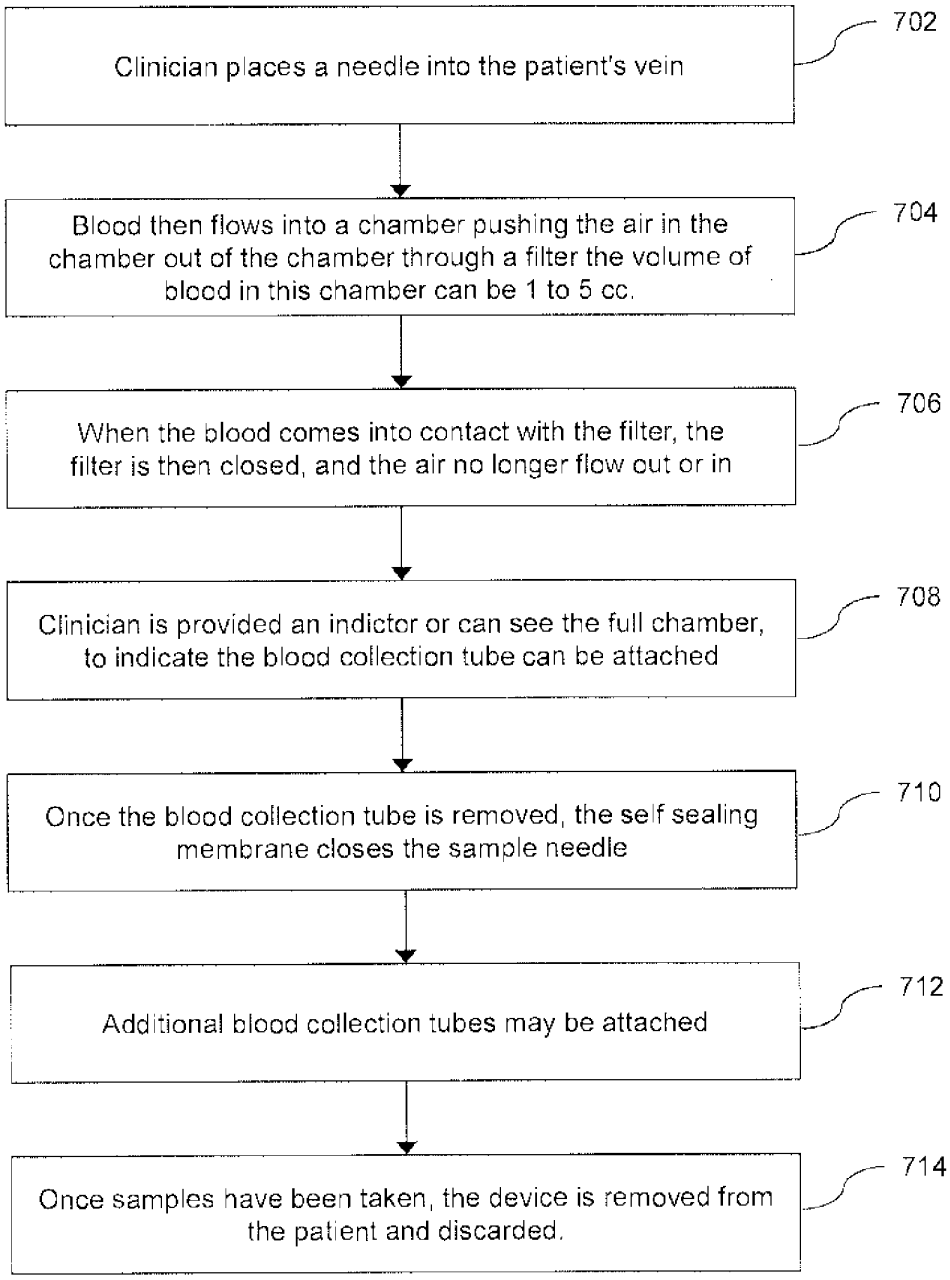

Clinician places a needle into the patient's vein
702
Blood then flows into a chamber pushing the air in the chamber out of the chamber through a filter the volume of blood in this chamber can be 1 to 5 cc.
704
When the blood comes into contact with the filter, the filter is then closed, and the air no longer flow out or in
706
Clinician is provided an indictor or can see the full chamber, to indicate the blood collection tube can be attached
708
Once the blood collection tube is removed, the self sealing membrane closes the sample needle
710
Additional blood collection tubes may be attached
712
Once samples have been taken, the device is removed from the patient and discarded.
714

FIG. 7

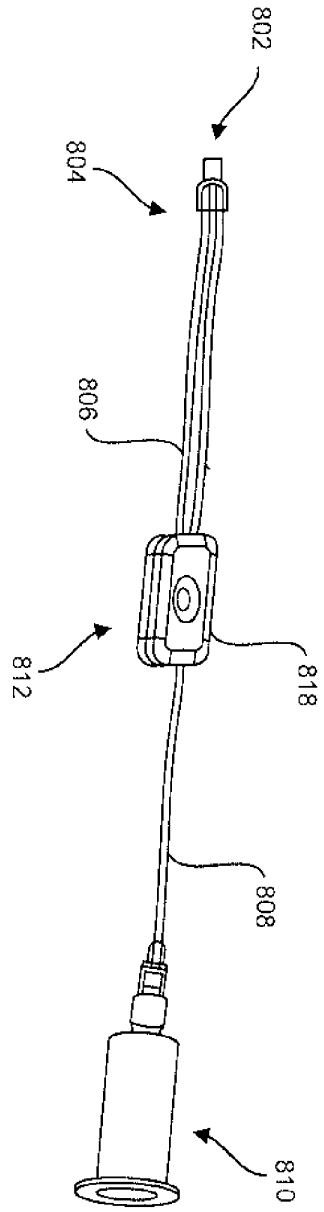


FIG. 8A

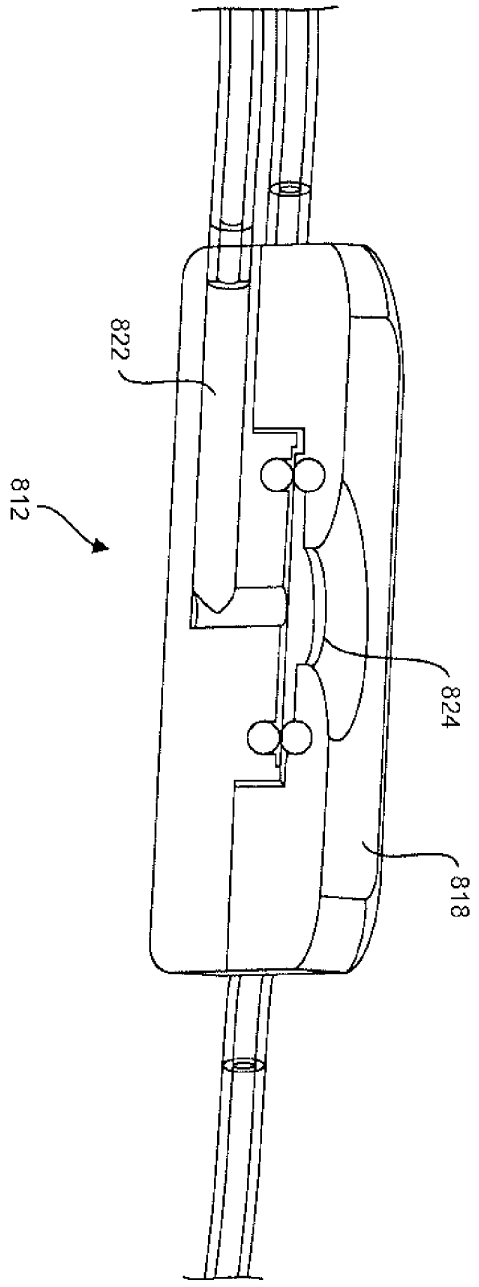


FIG. 8B

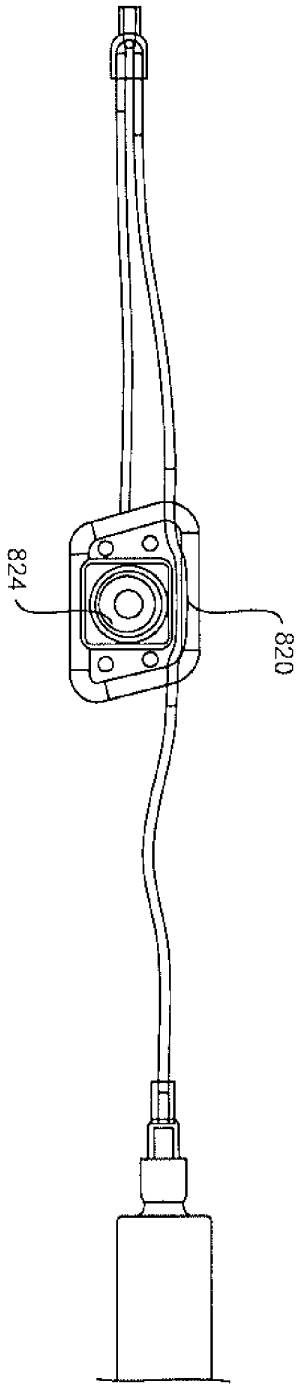


FIG. 8C

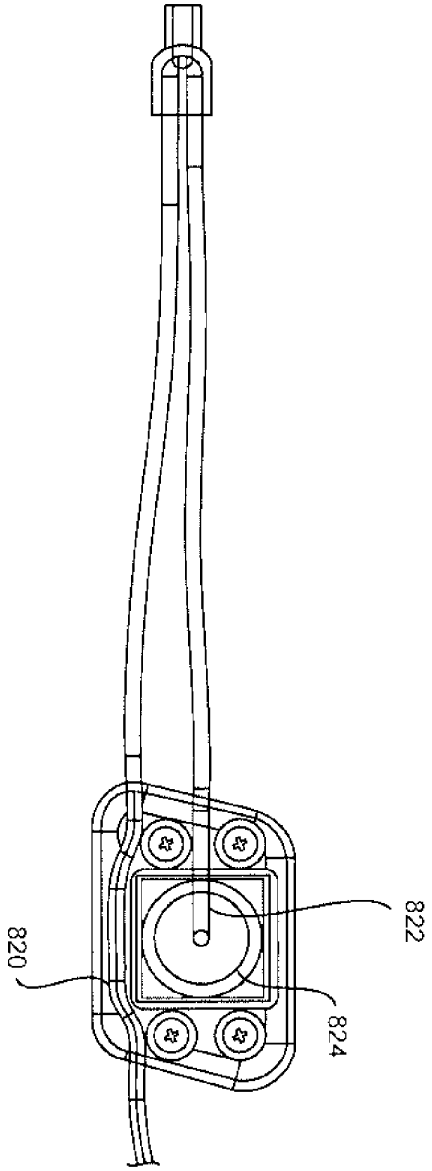


FIG. 8D

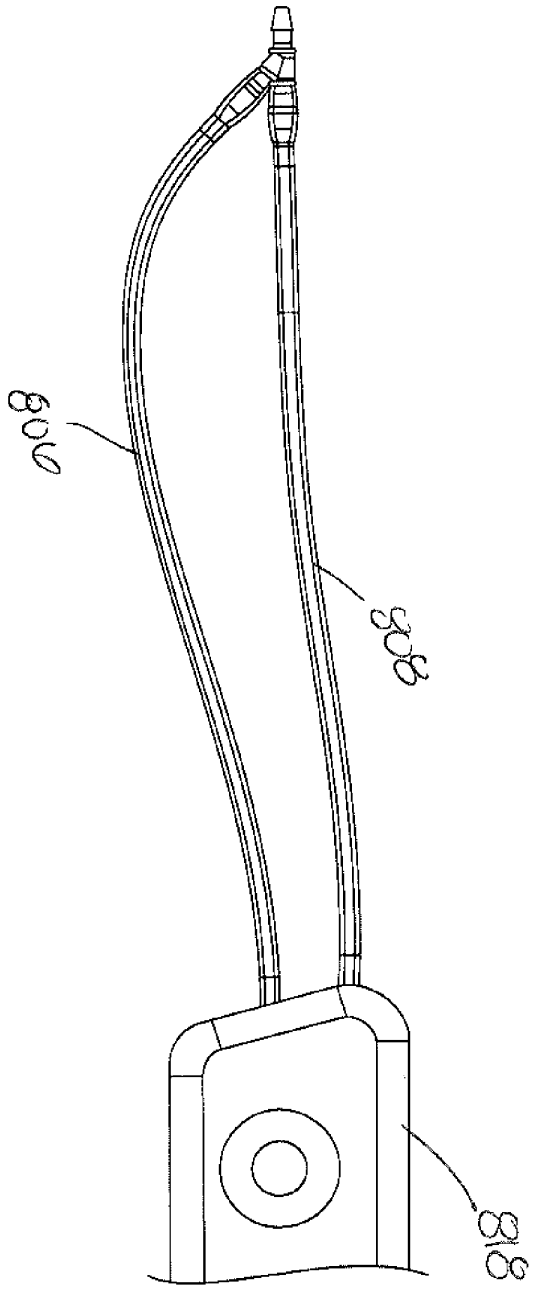


FIG. 8E

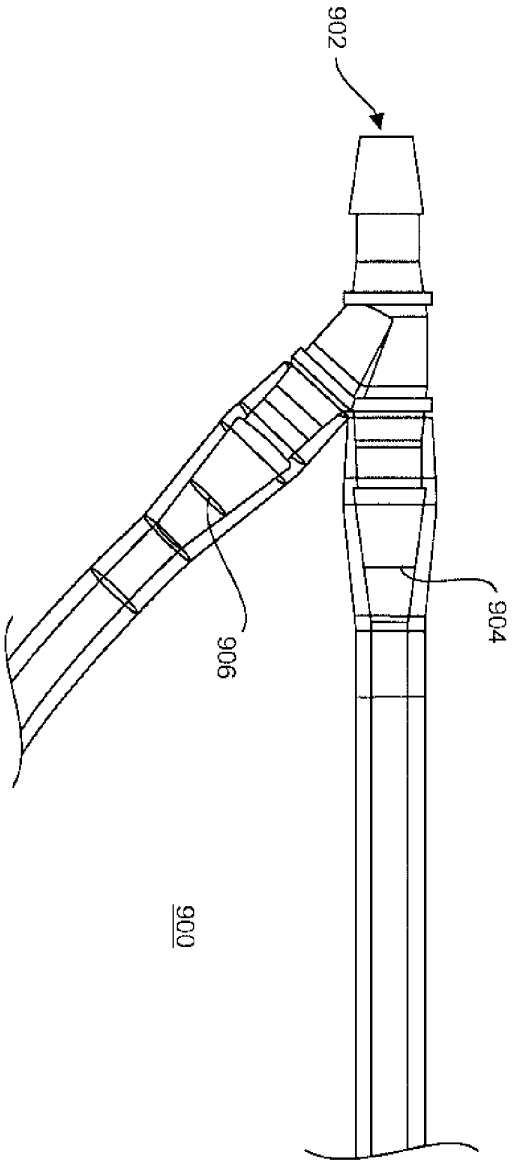


FIG. 9

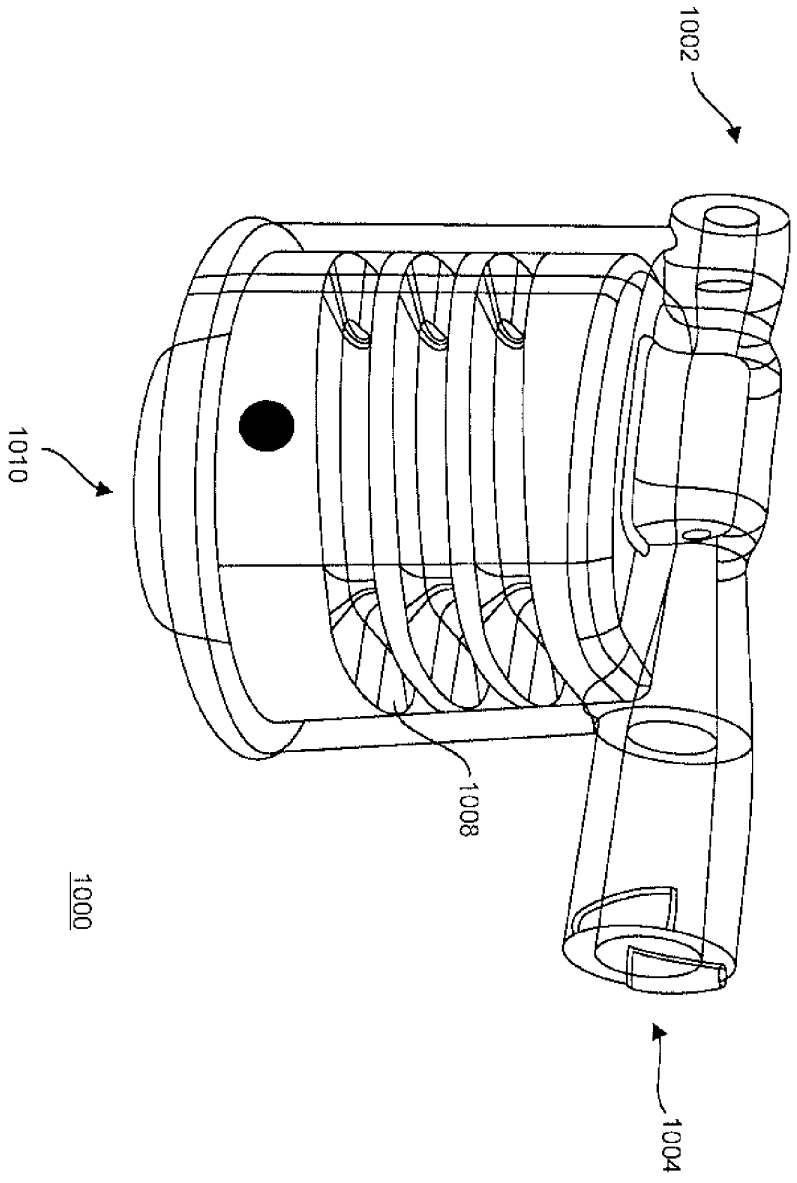


FIG. 10A

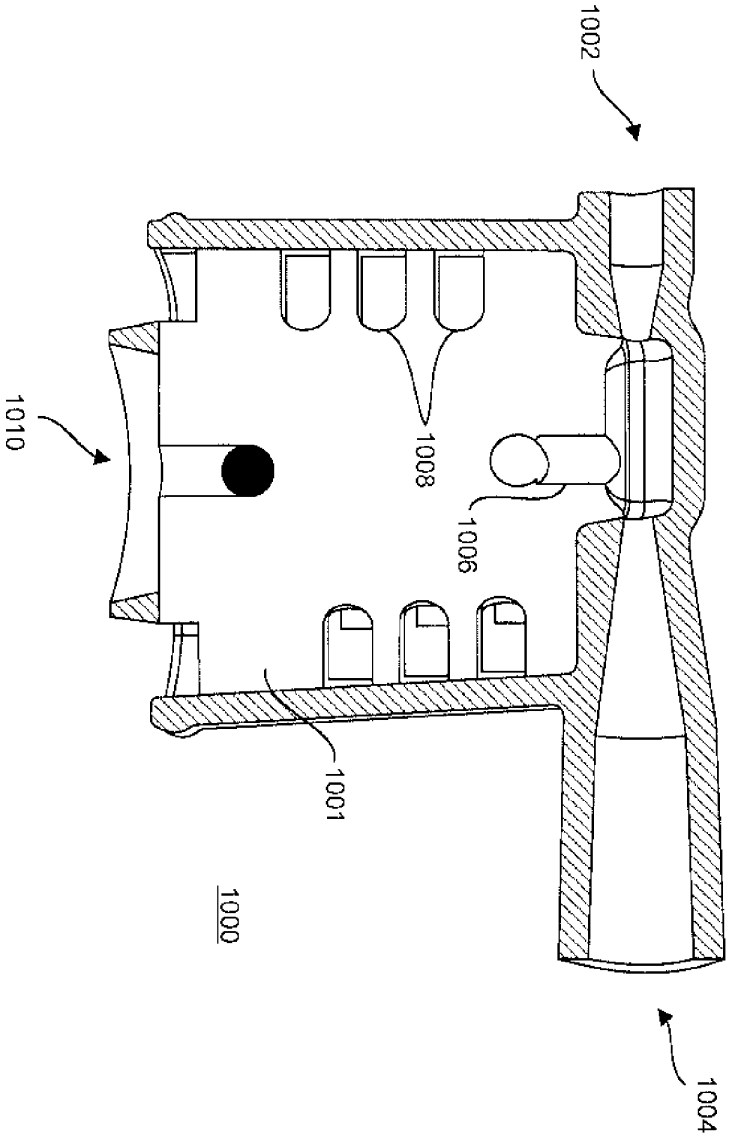


FIG. 10B

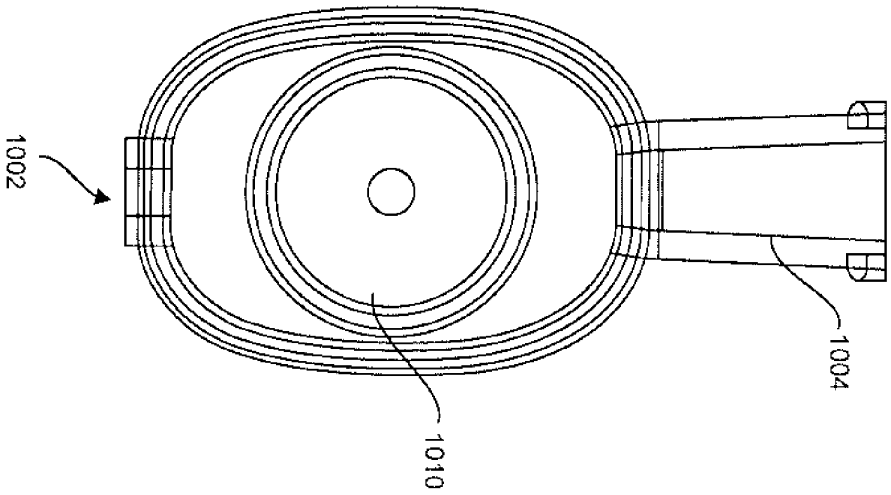


FIG. 10C

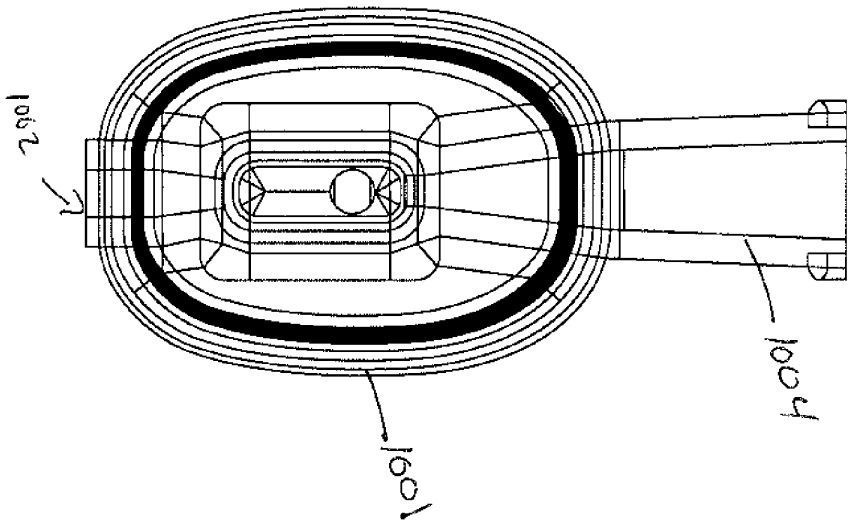


FIG. 10D

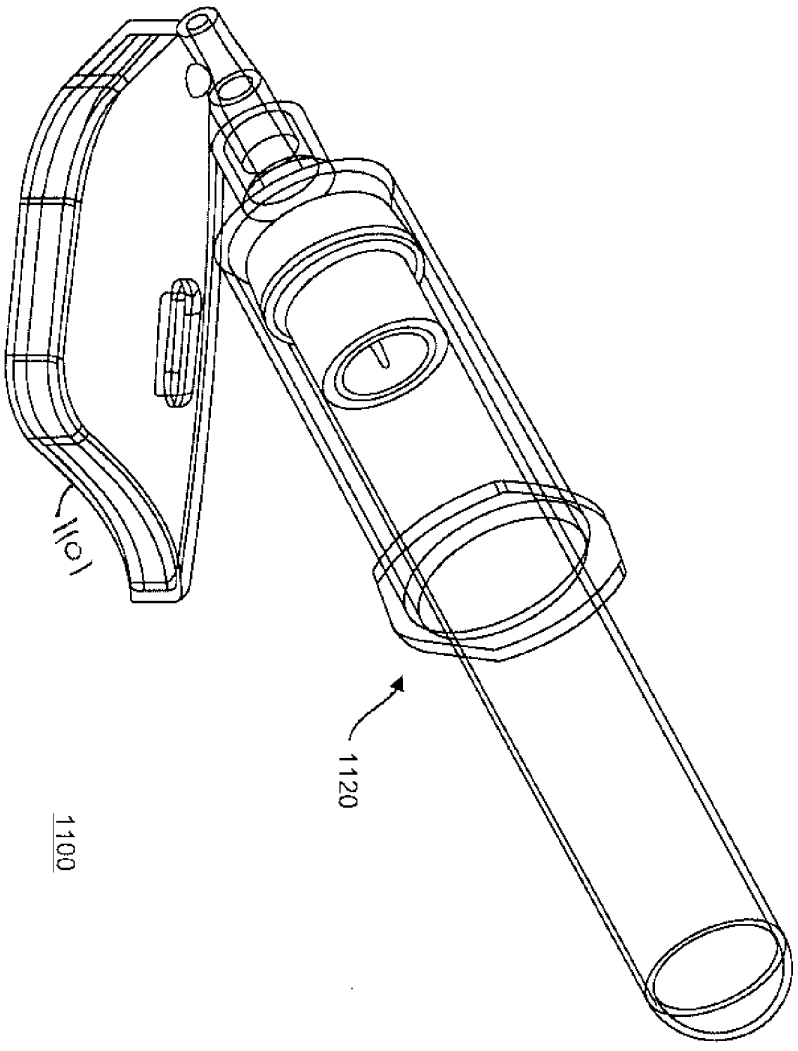


FIG. 11A

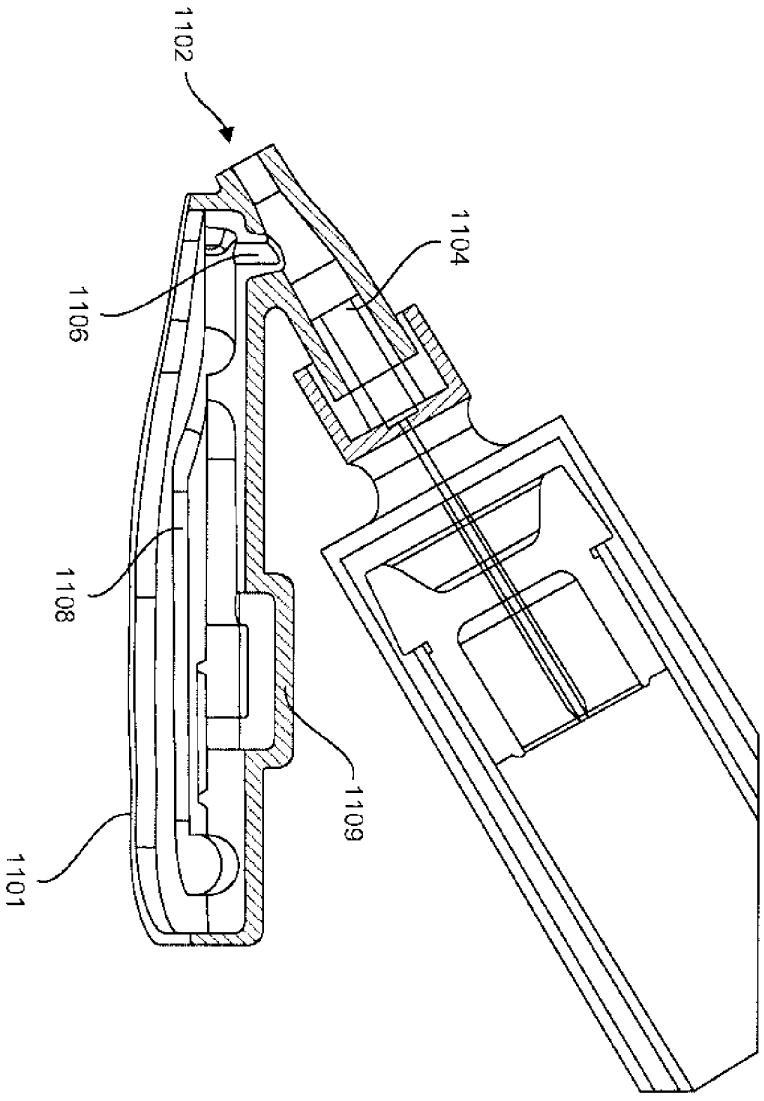


FIG. 11B

FIG. 11C

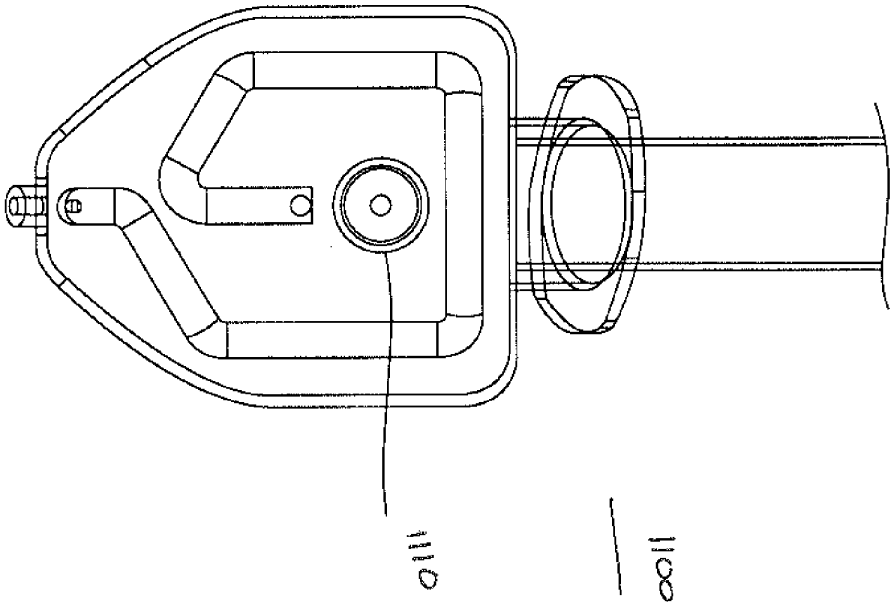
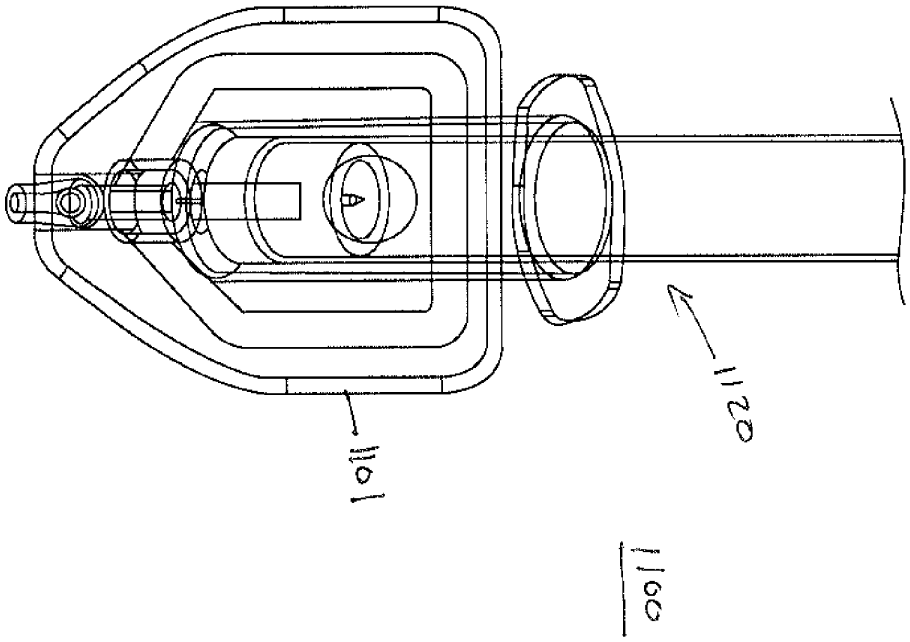


FIG. 11D



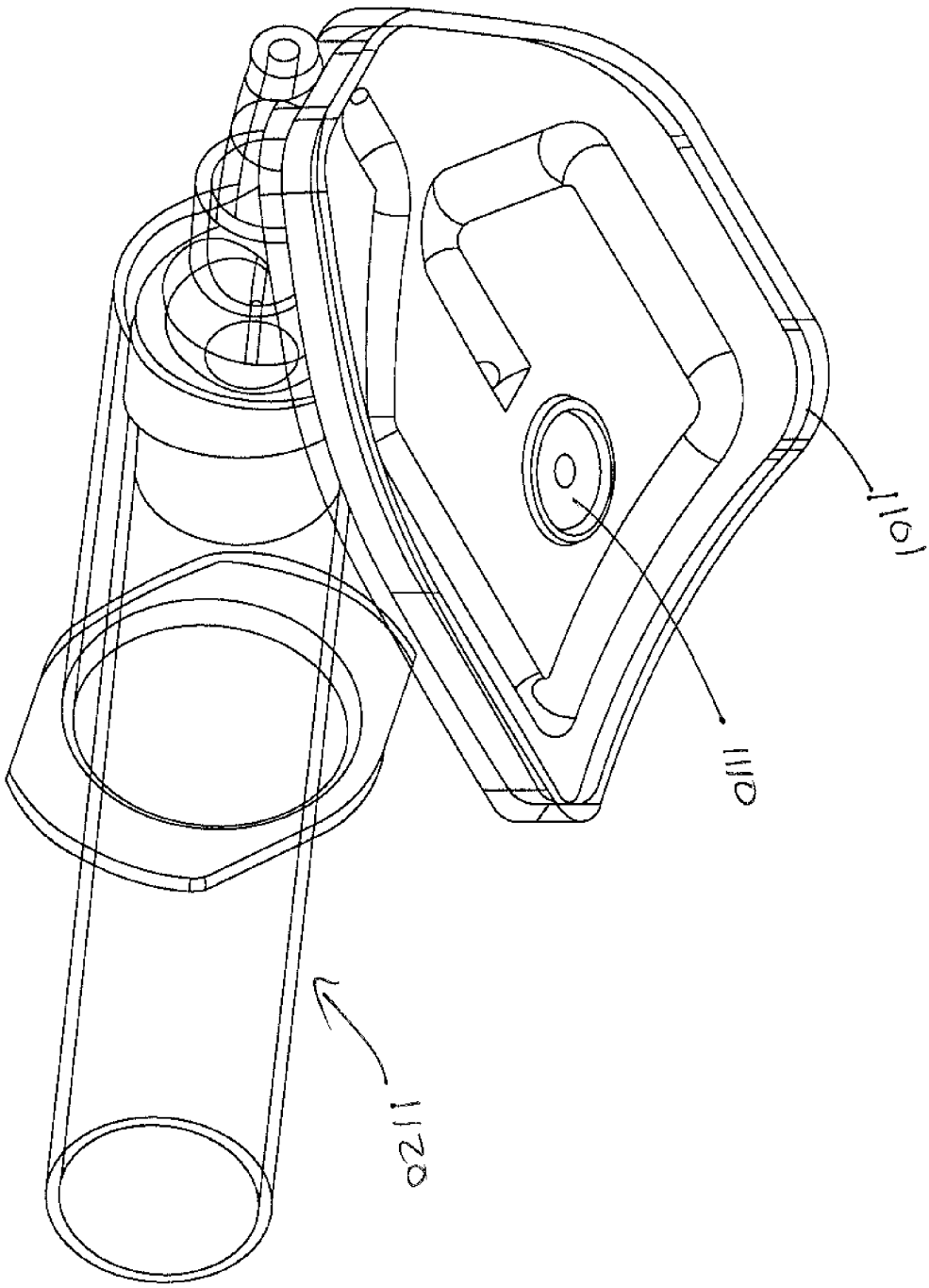


FIG. 11E

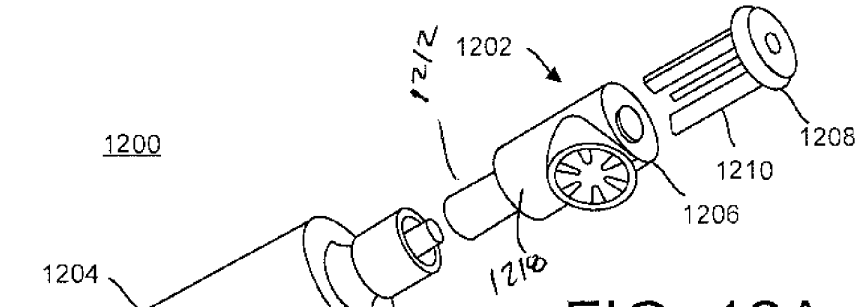


FIG. 12A

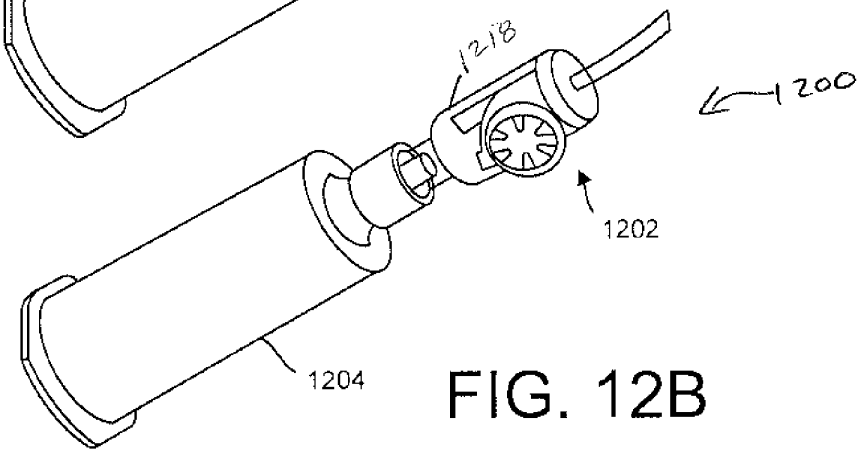


FIG. 12B

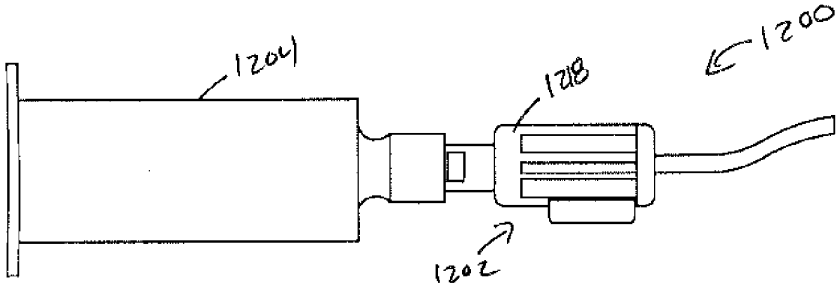


FIG. 12C

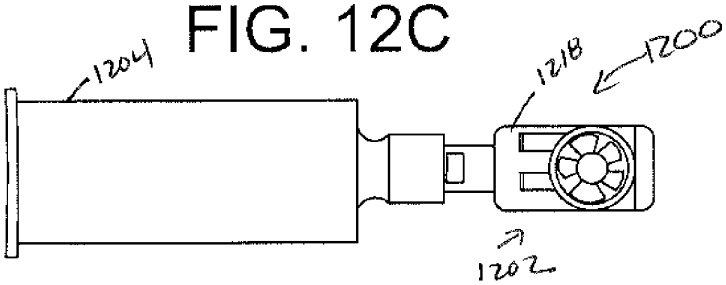


FIG. 12D

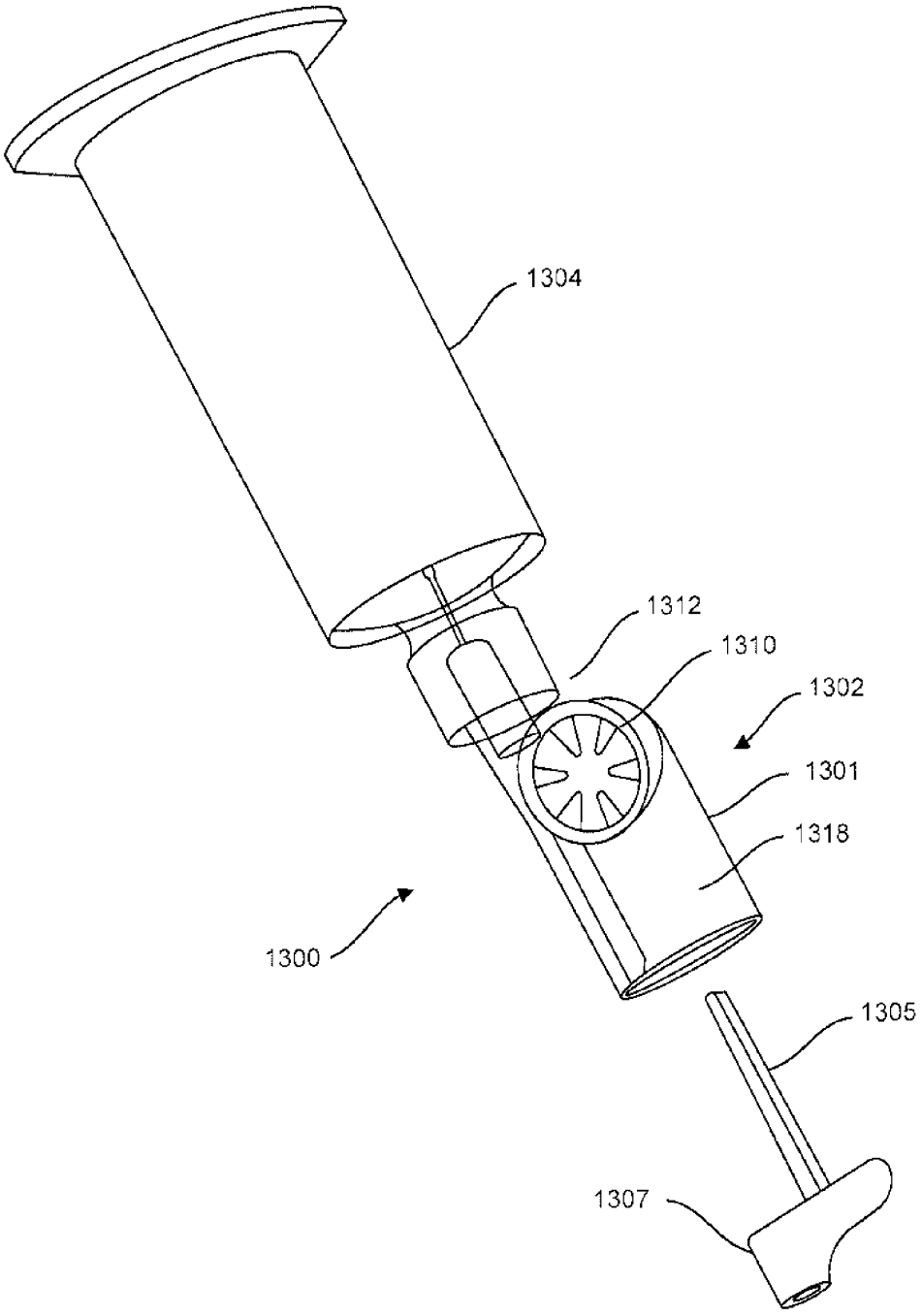


FIG. 13A

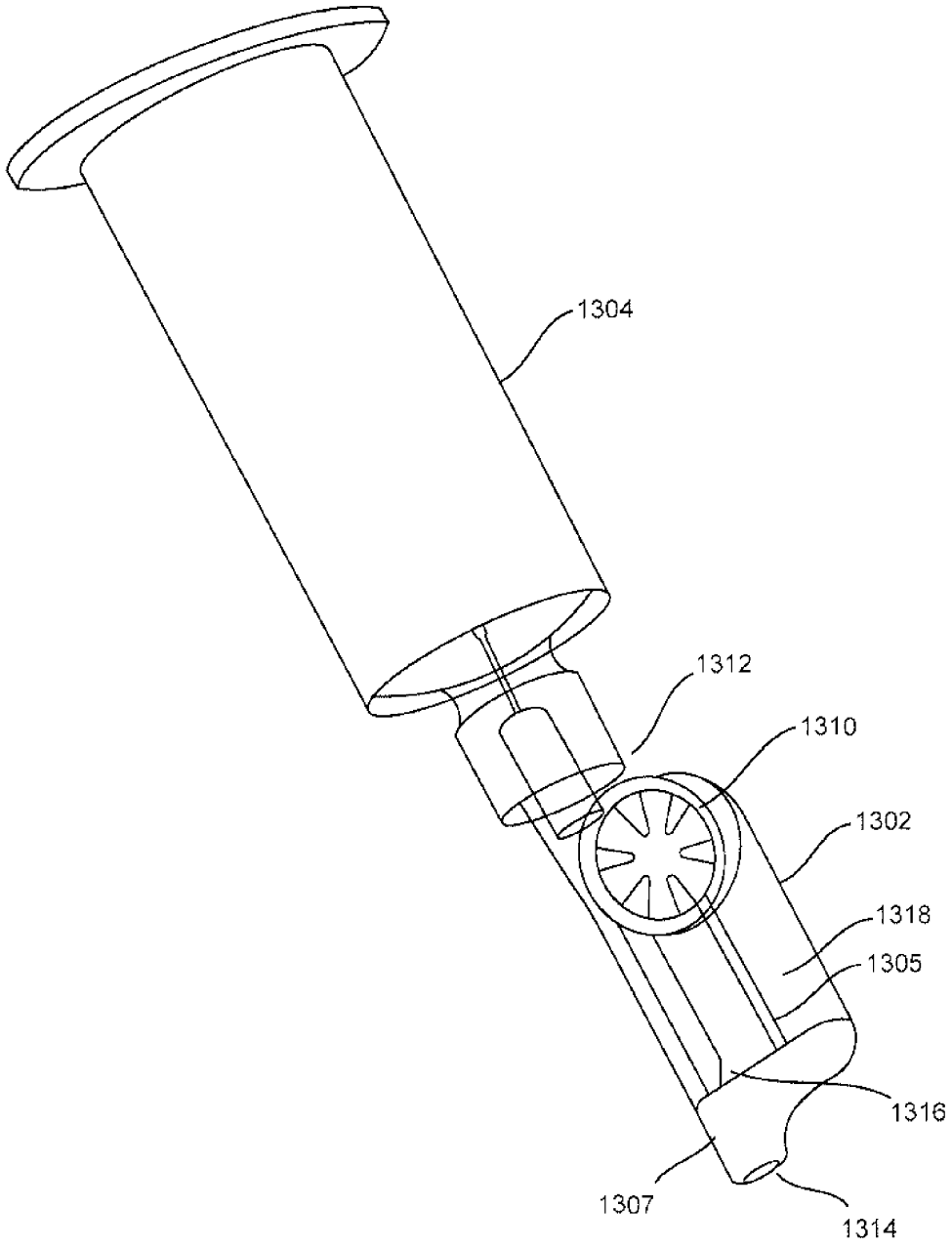


FIG. 13B

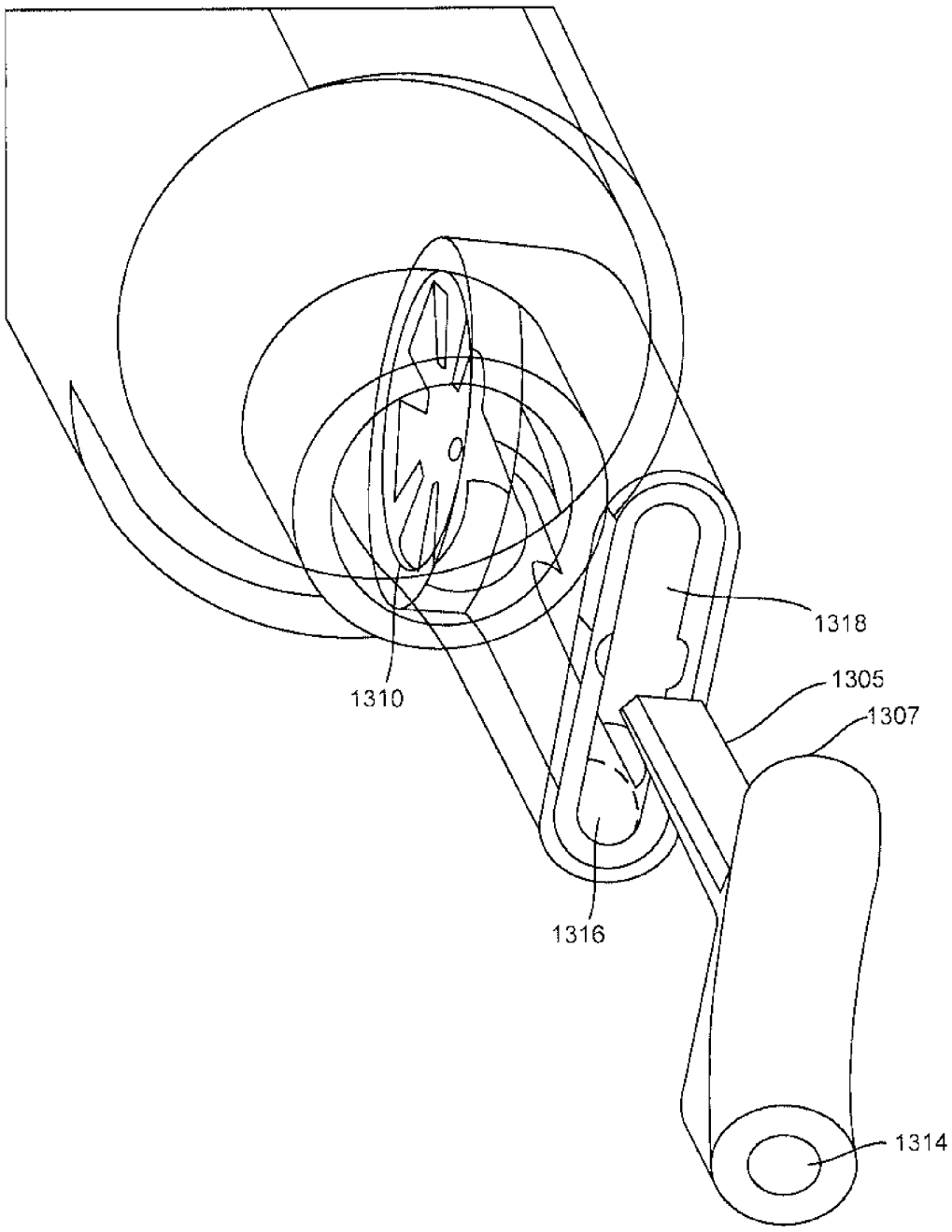


FIG. 13C

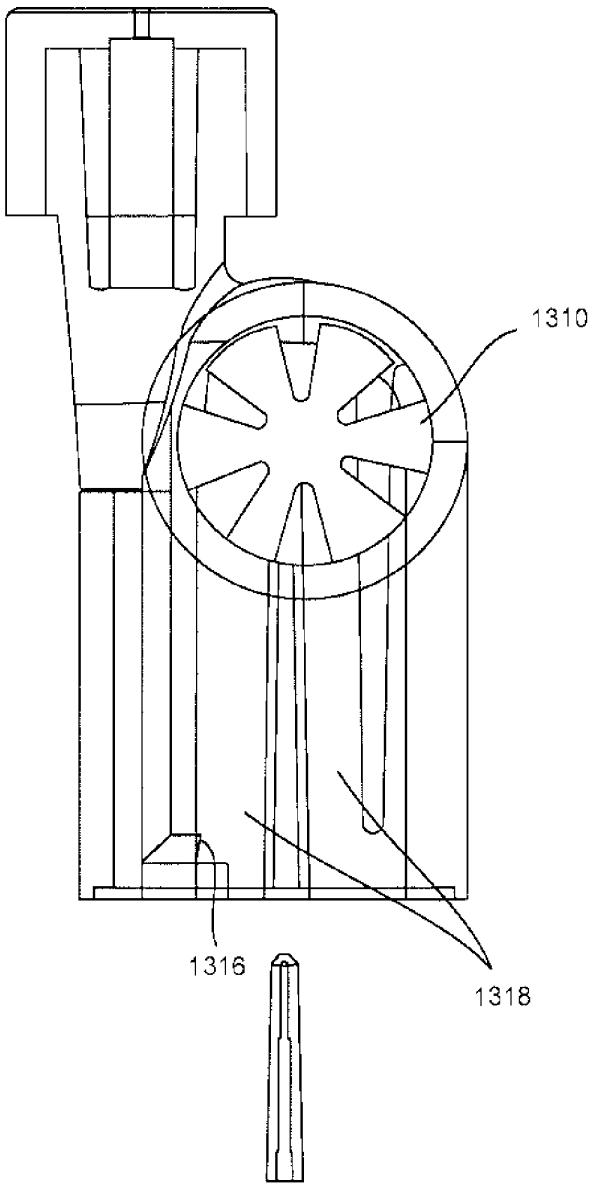


FIG. 13D

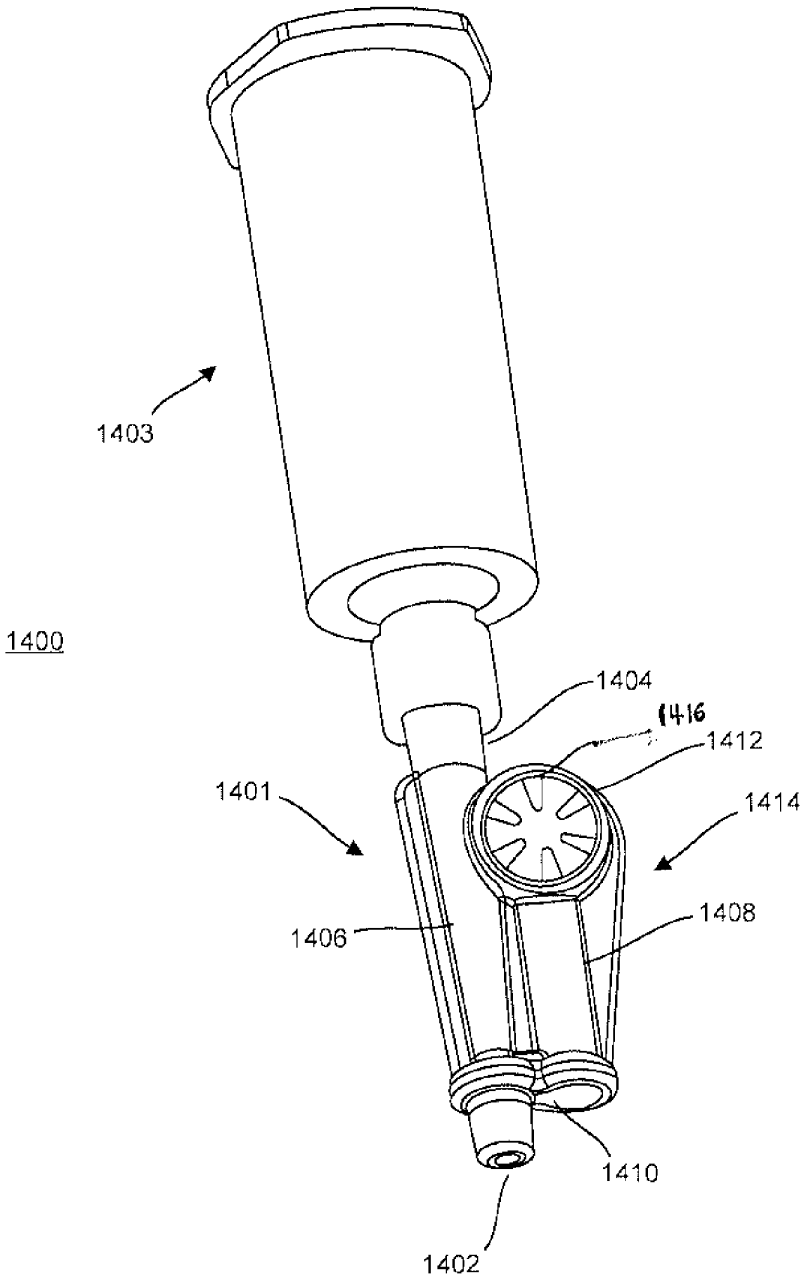


FIG. 14A

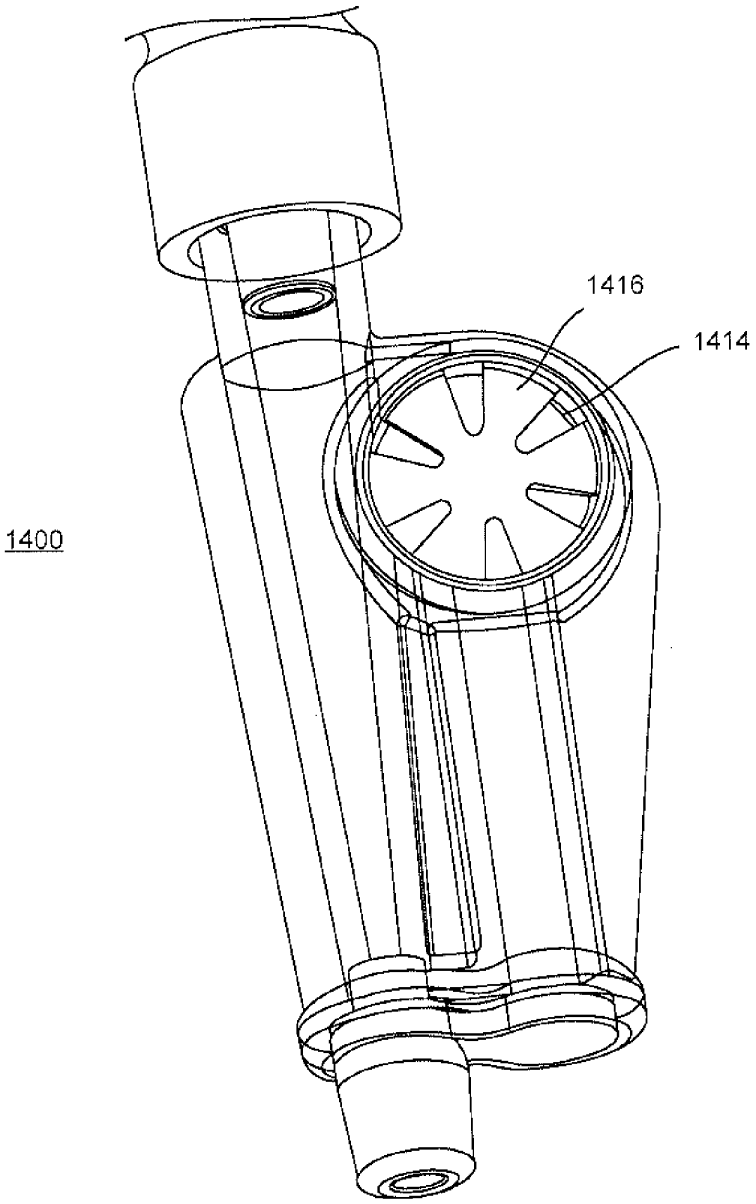


FIG. 14B

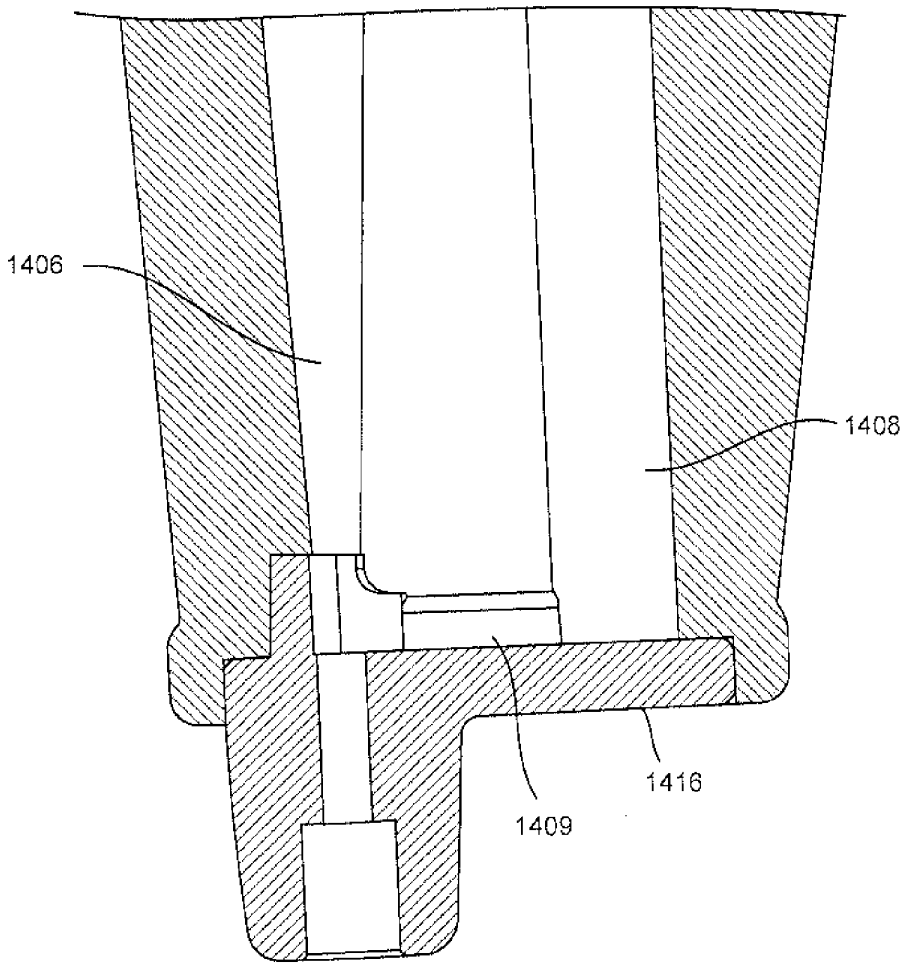


FIG. 14C

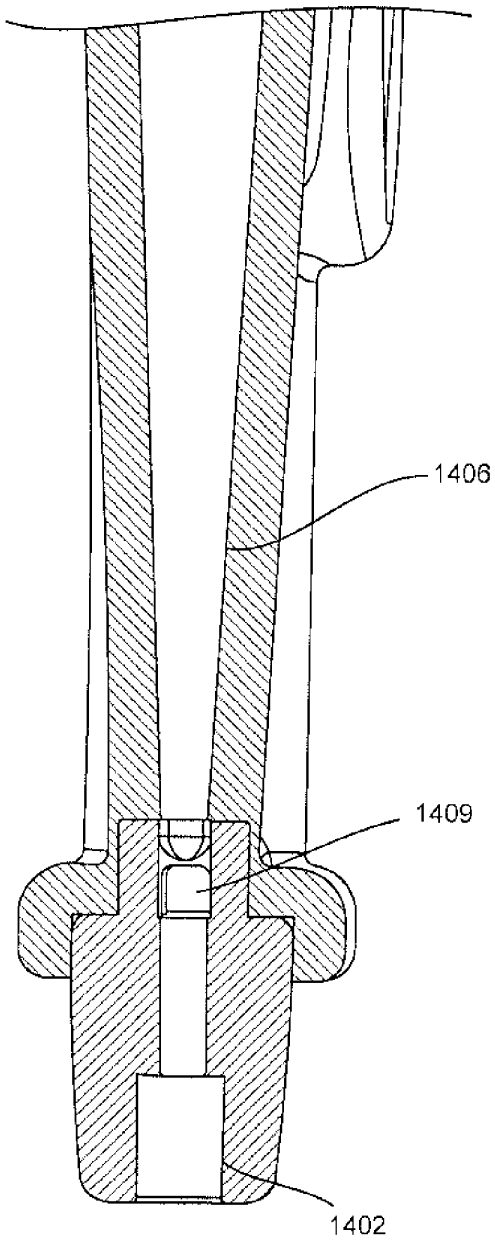


FIG. 14D

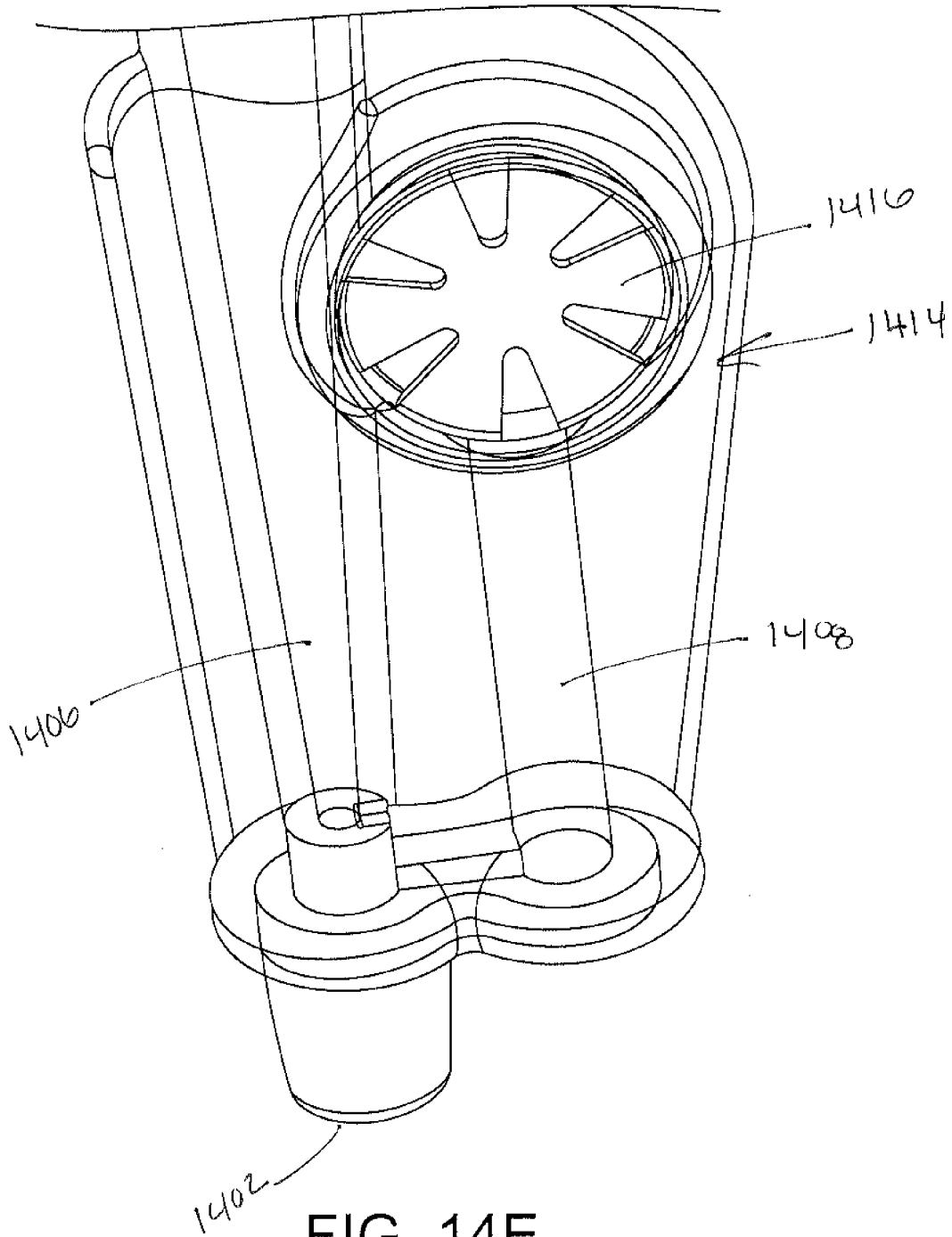


FIG. 14E

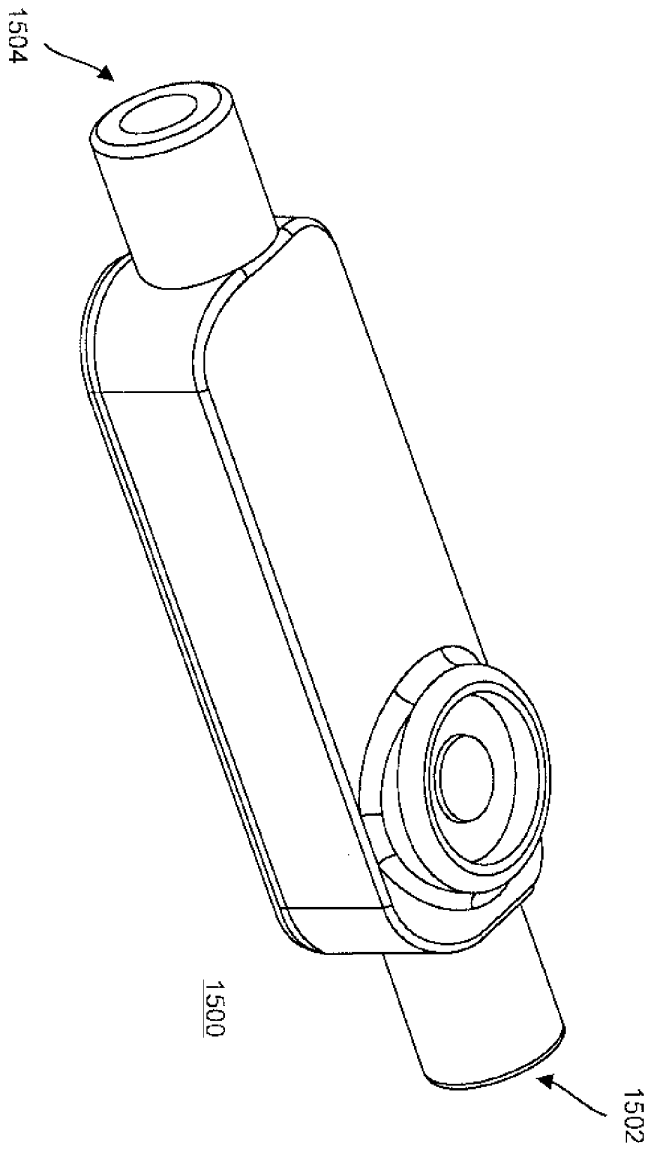


FIG. 15A

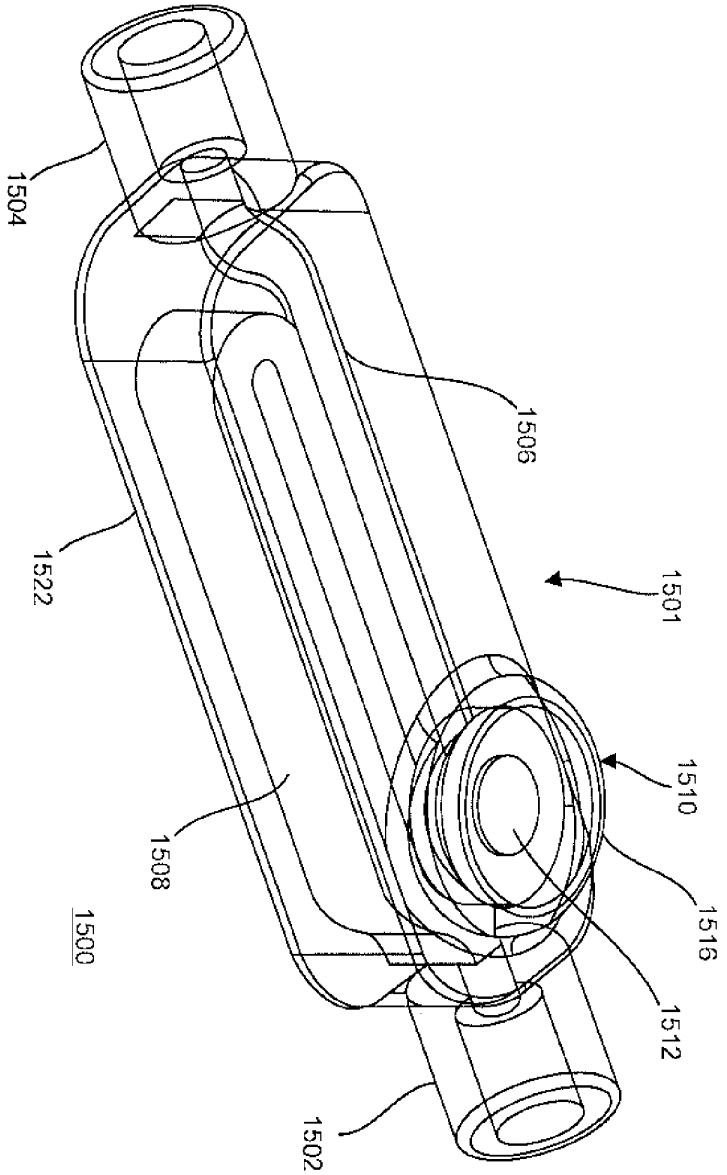


FIG. 15B

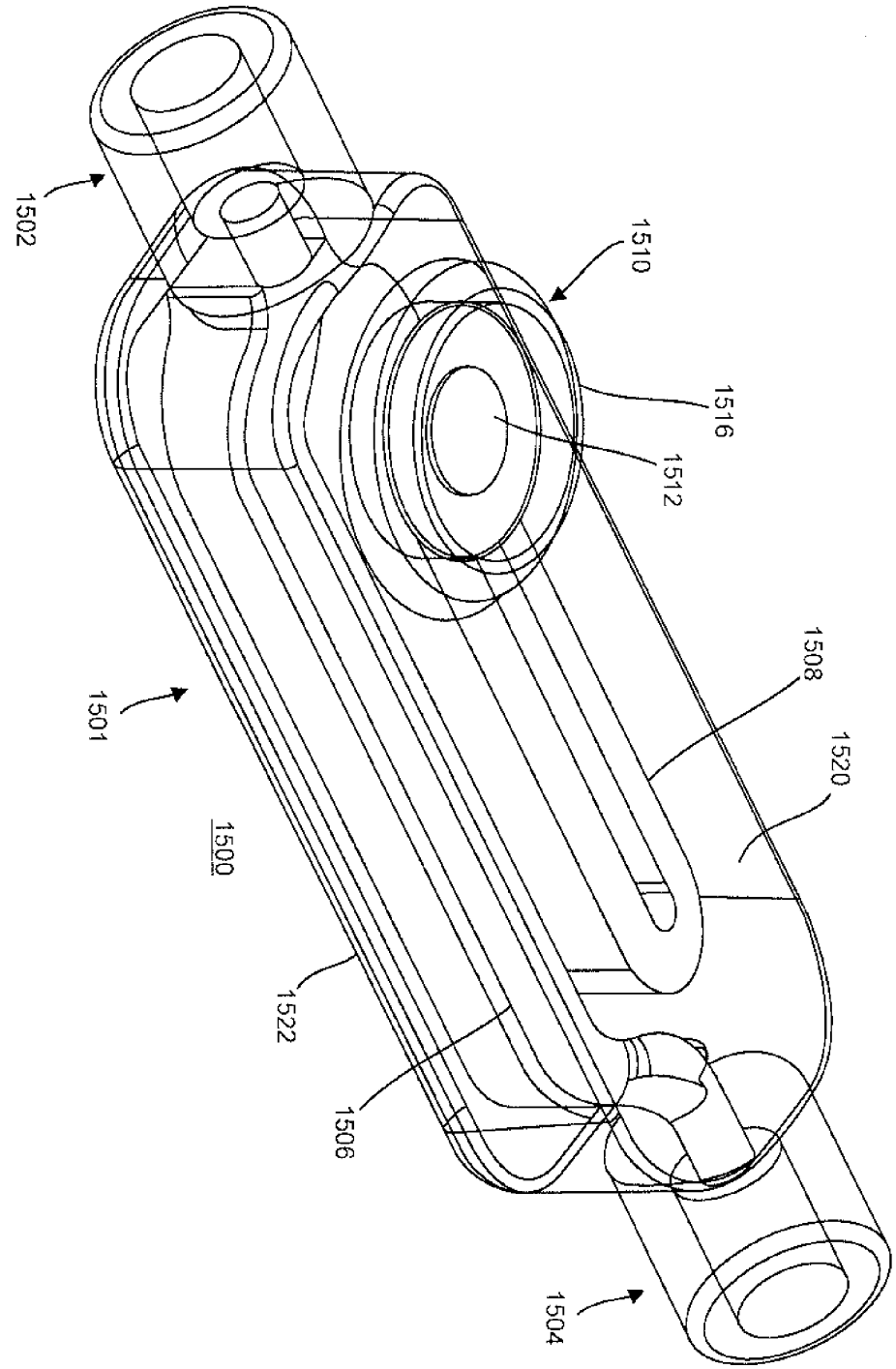


FIG. 15C

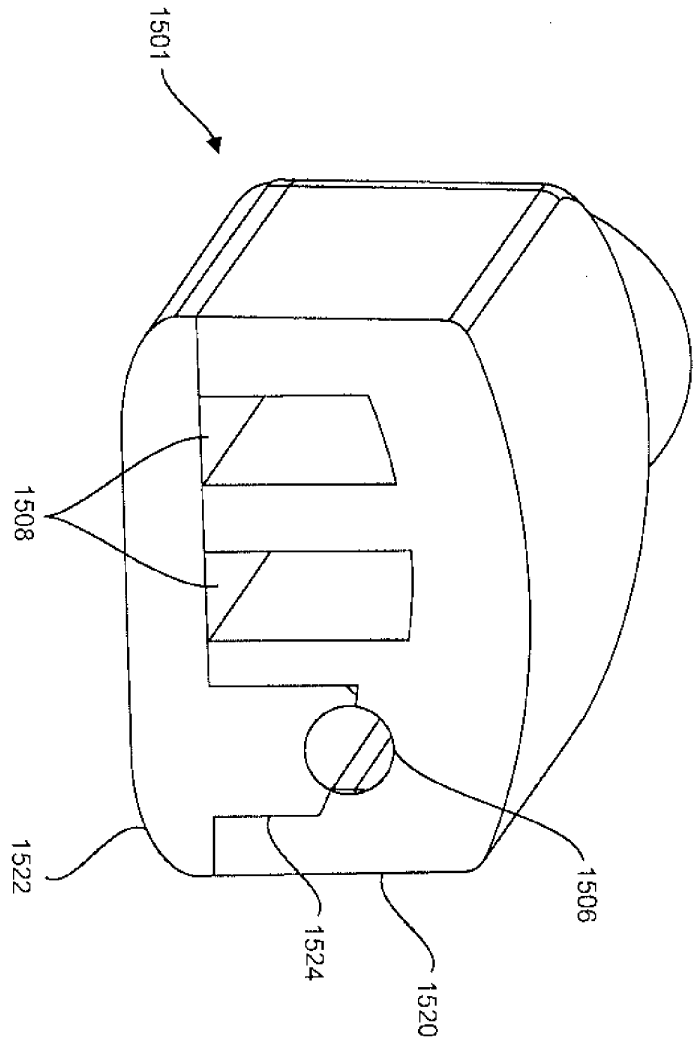


FIG. 15D

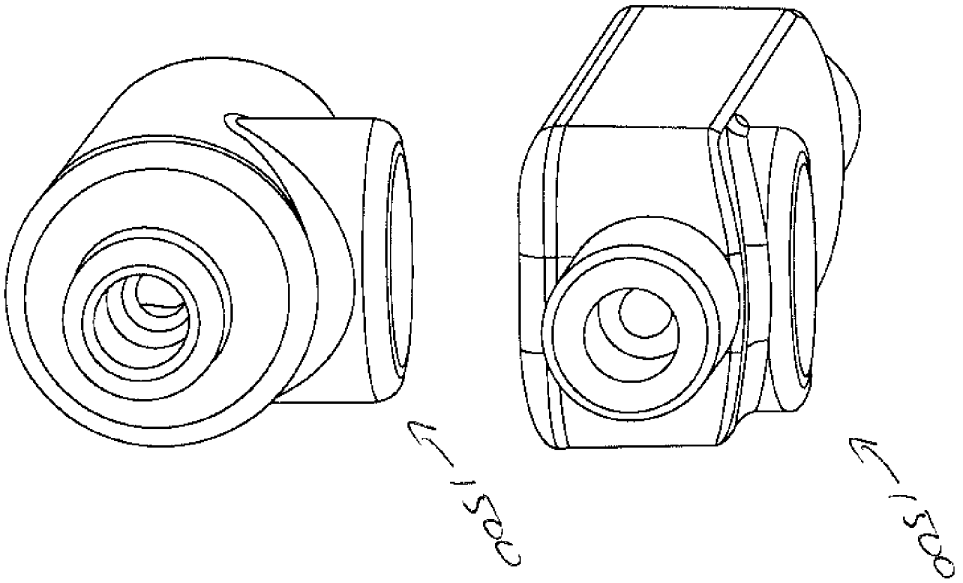


FIG. 15E

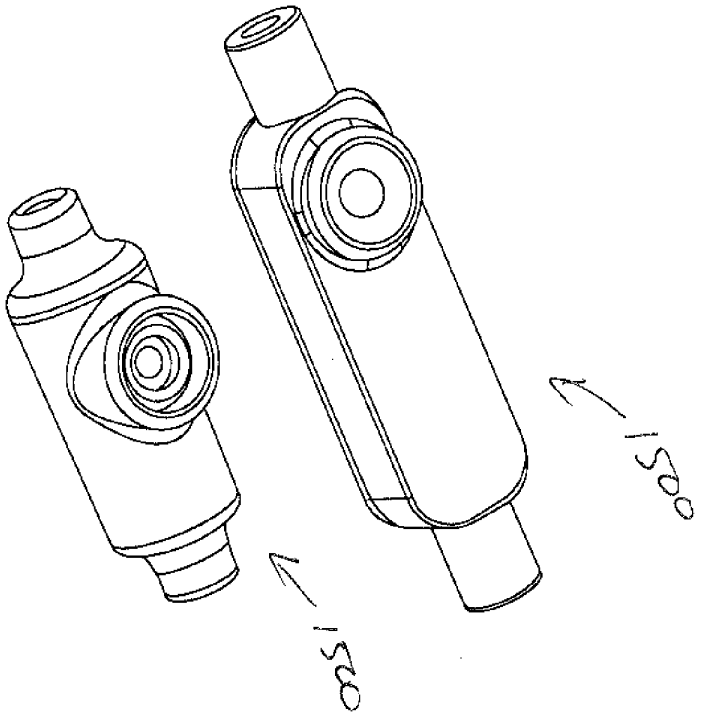


FIG. 15F

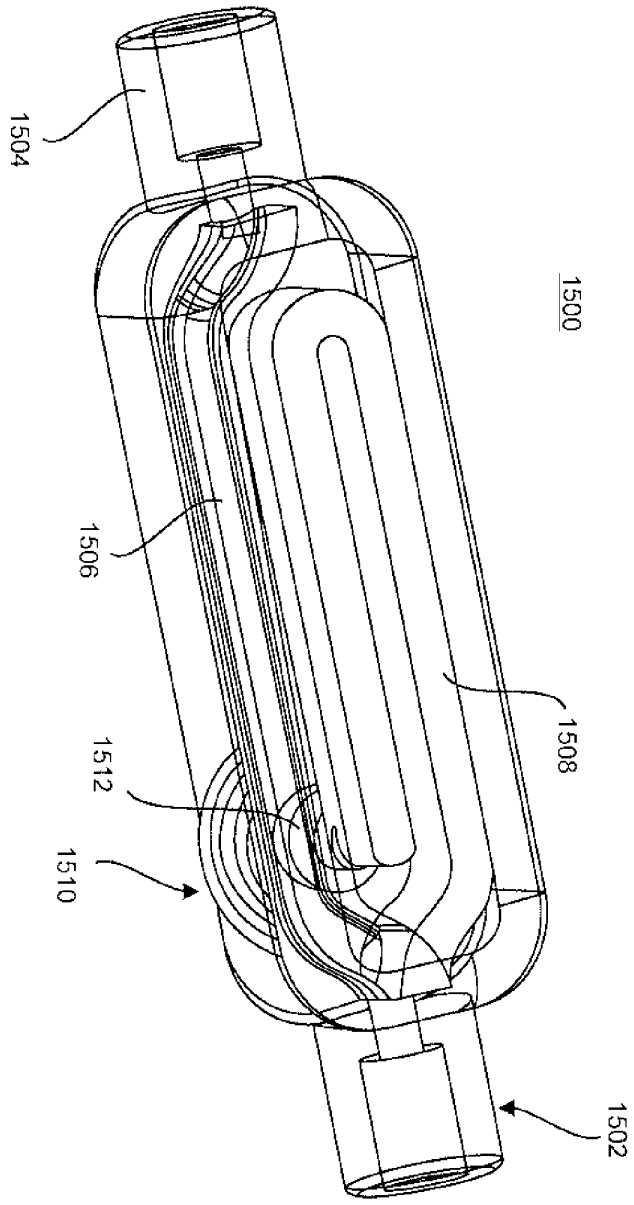


FIG. 15G



FIG. 16B

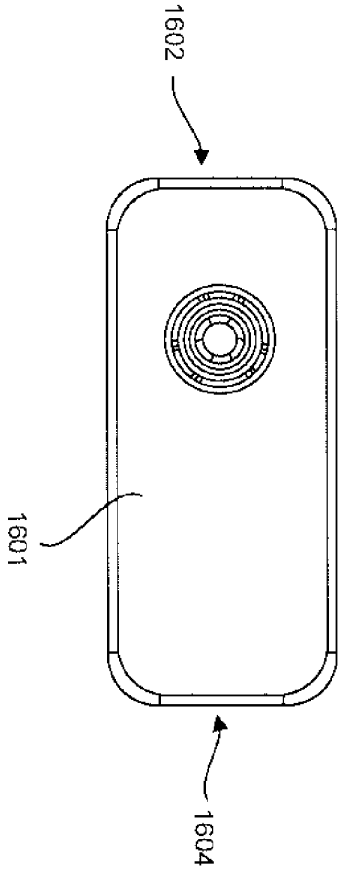


FIG. 16A

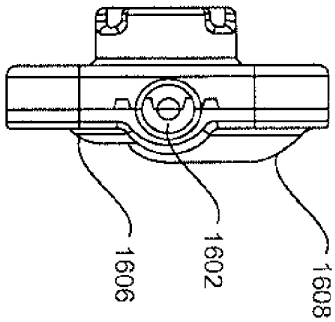


FIG. 16C

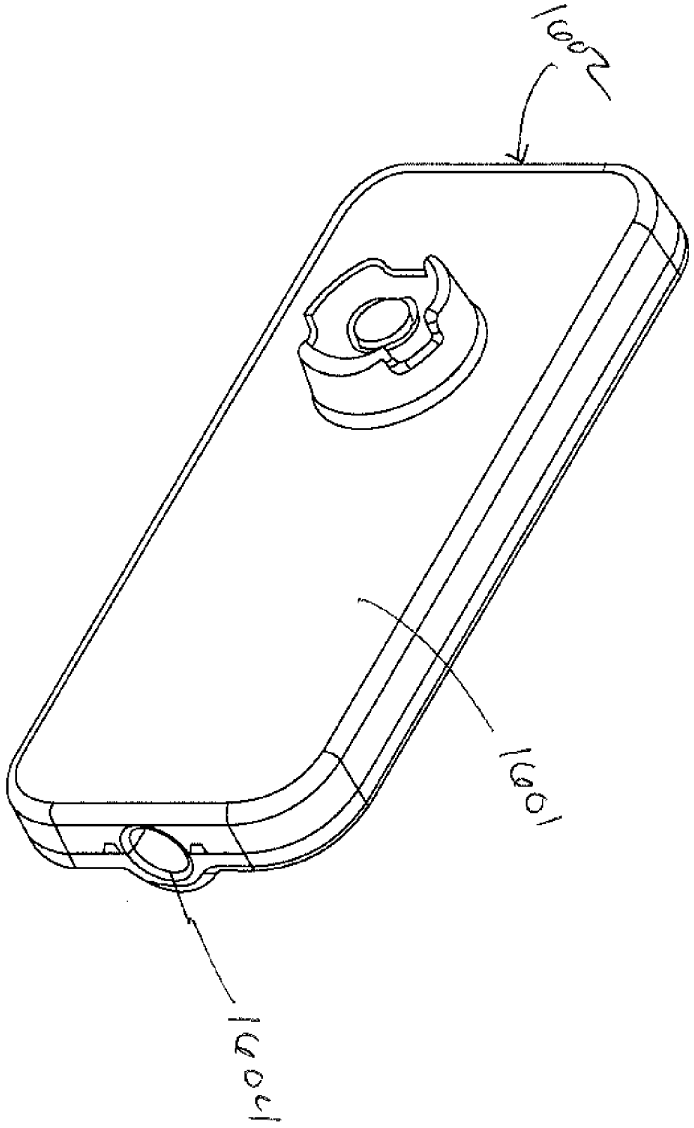


FIG. 16D

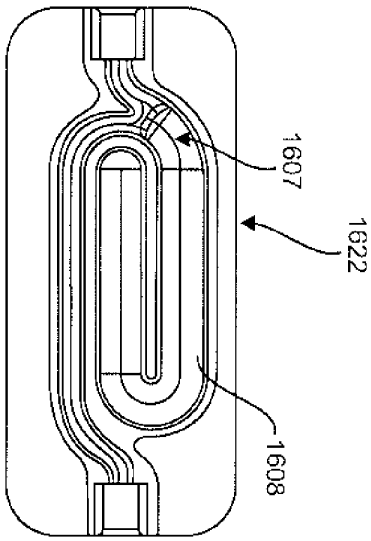


FIG. 17A

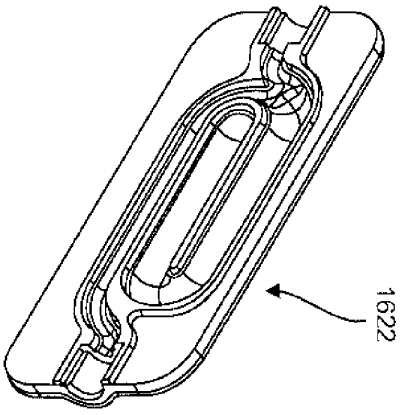


FIG. 17B

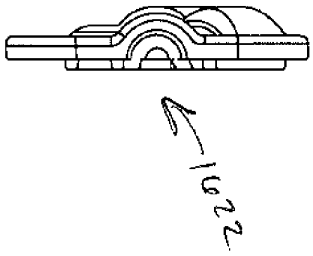


FIG. 17C

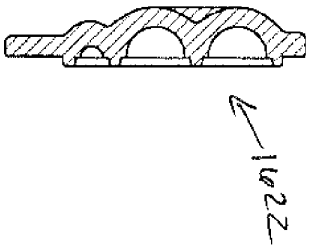


FIG. 17D

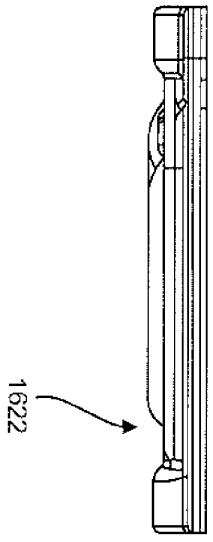


FIG. 17E

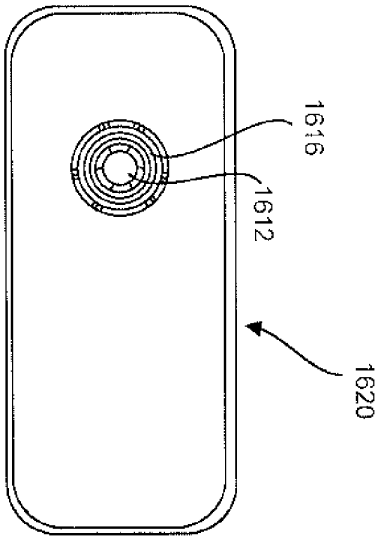


FIG. 18A

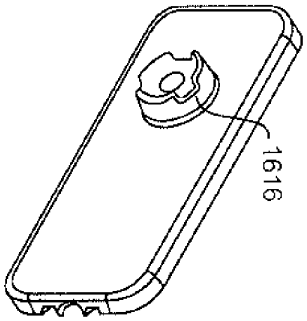


FIG. 18B

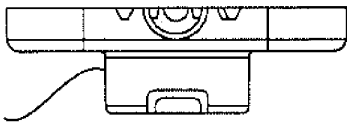


FIG. 18C

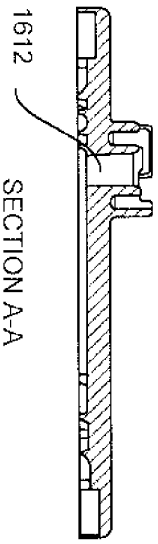


FIG. 18D

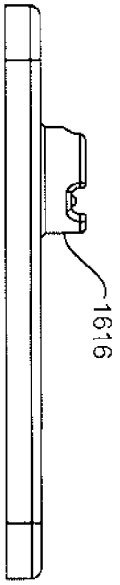


FIG. 18E

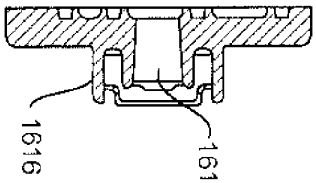


FIG. 18F

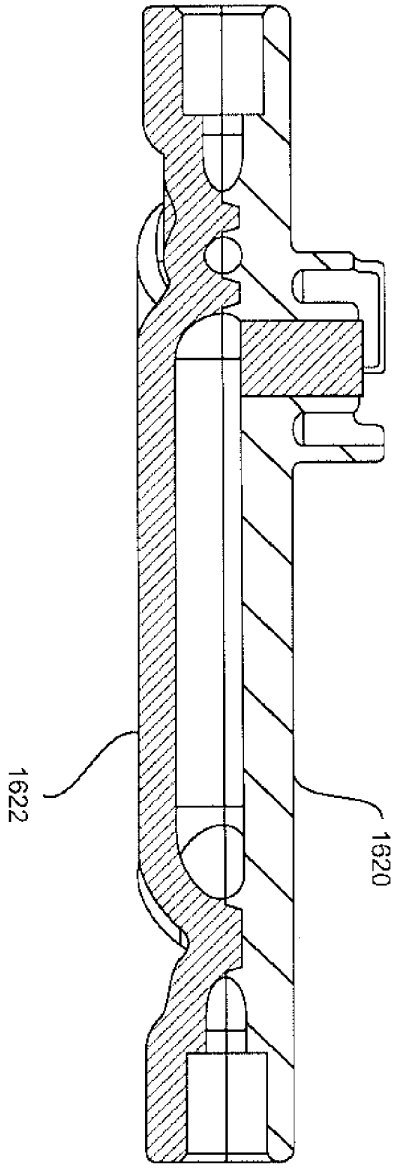


FIG. 19A

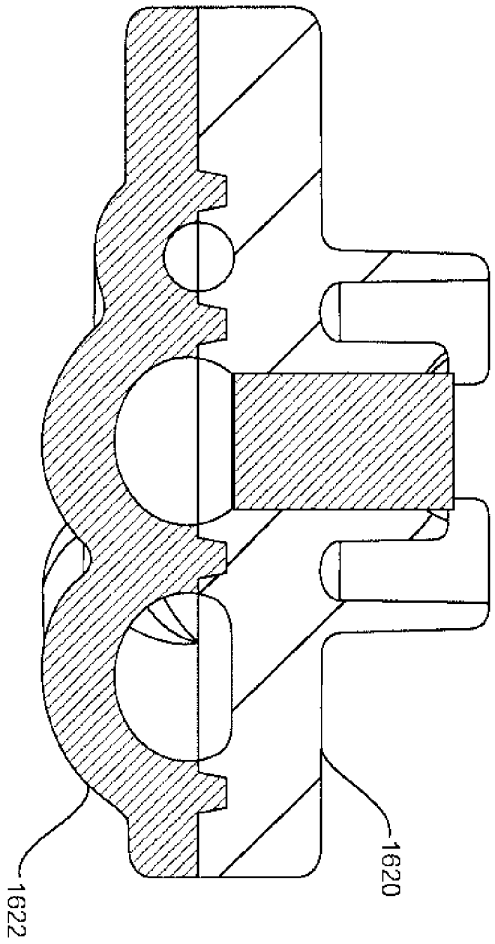


FIG. 19B

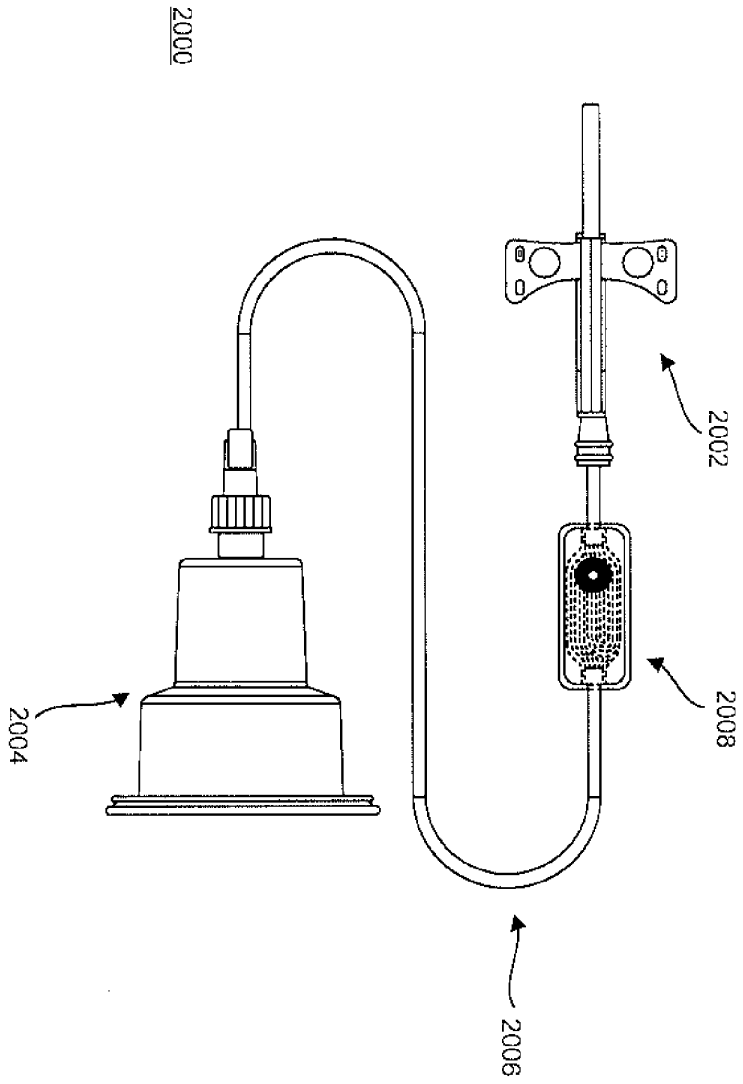


FIG. 20

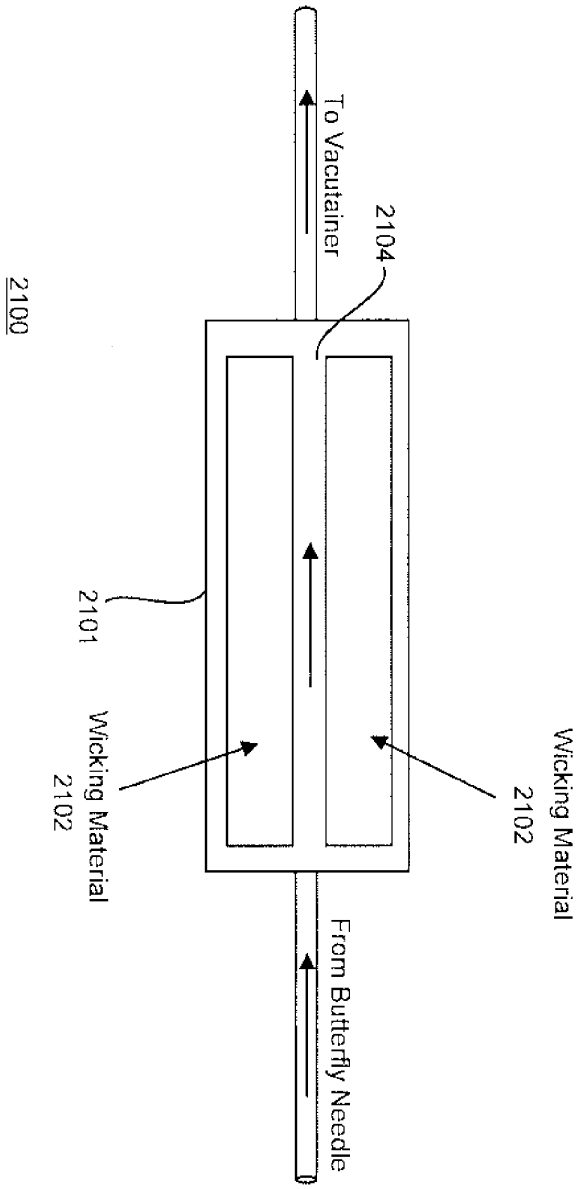

2100
To Vacutainer
2104
2101
Wicking Material
2102
Wicking Material
2102
From Butterfly Needle

FIG. 21

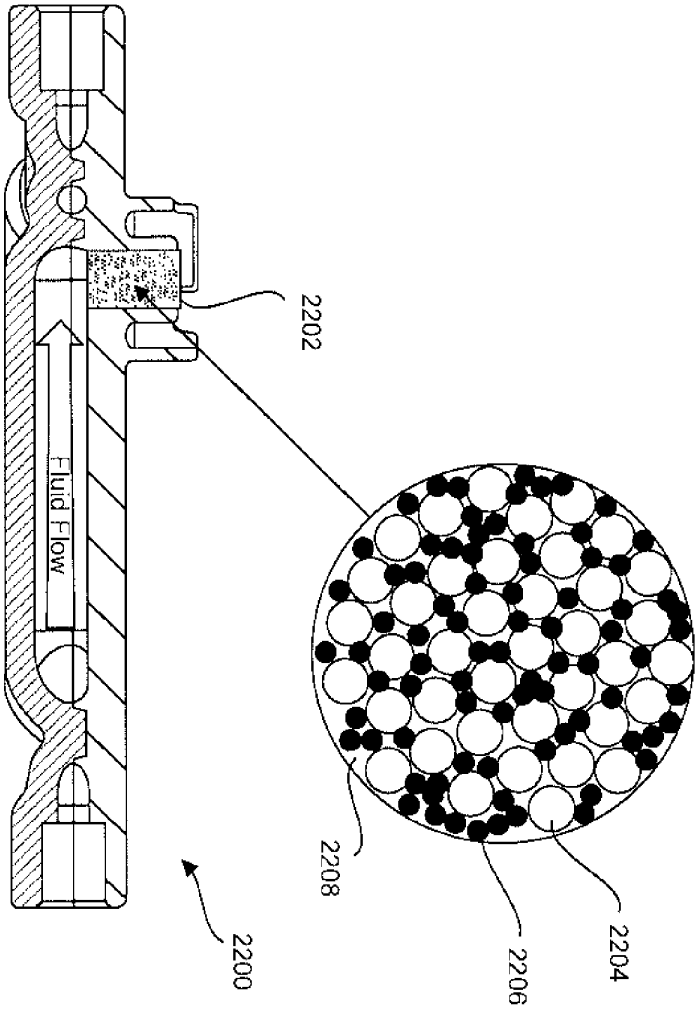


FIG. 22A

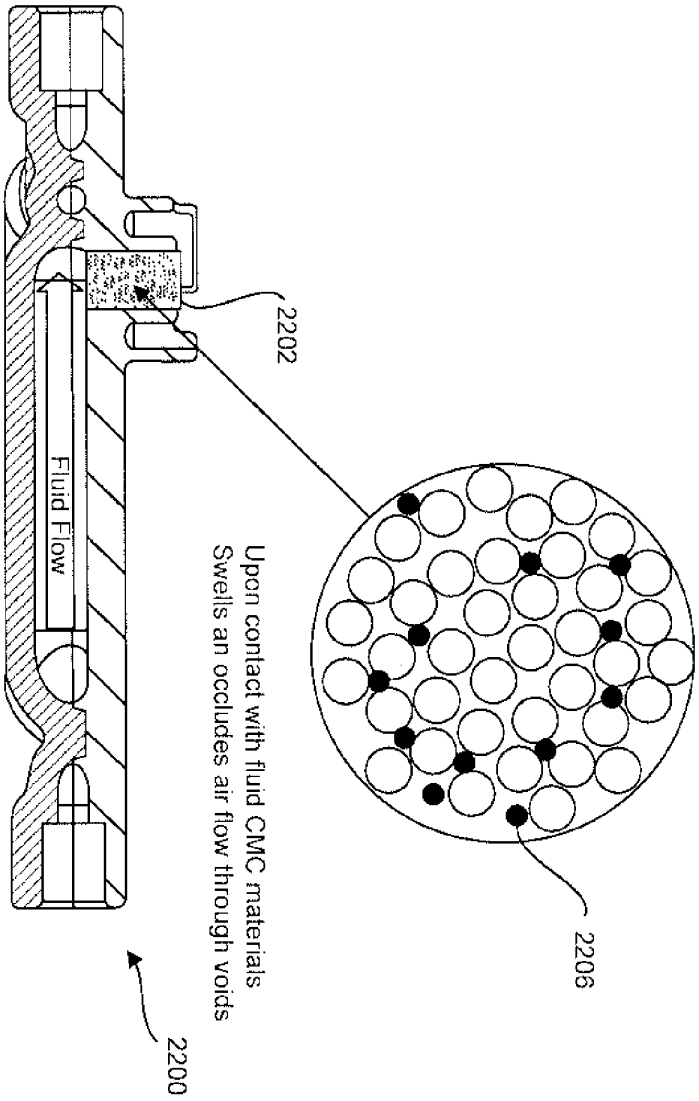

2202
Fluid Flow
Upon contact with fluid CMC materials
Swells an occludes air flow through voids
2206
2200

FIG. 22B

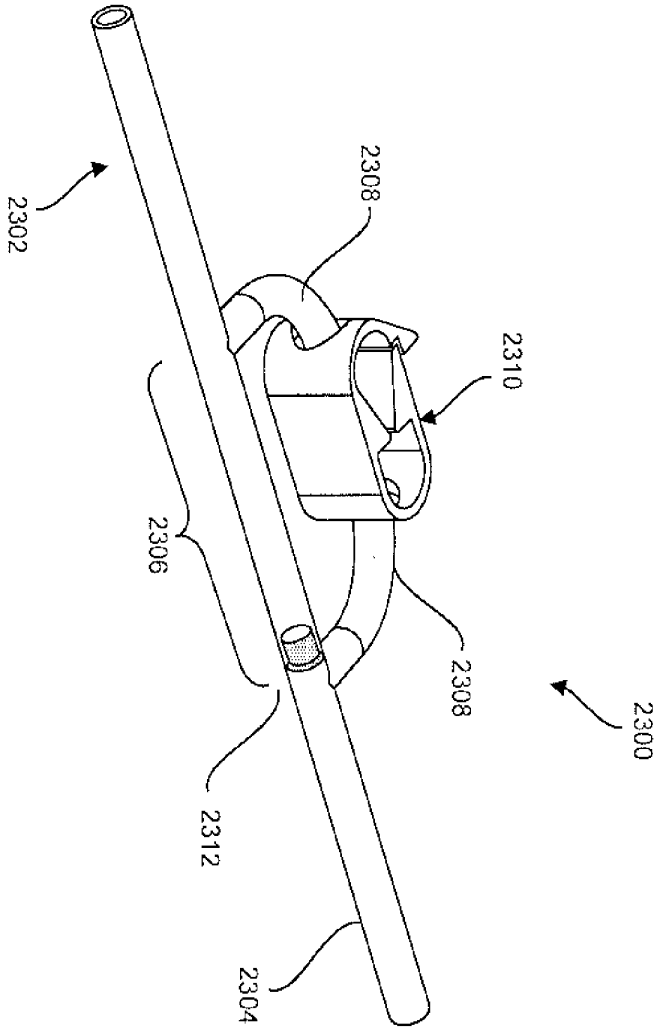


FIG. 23A

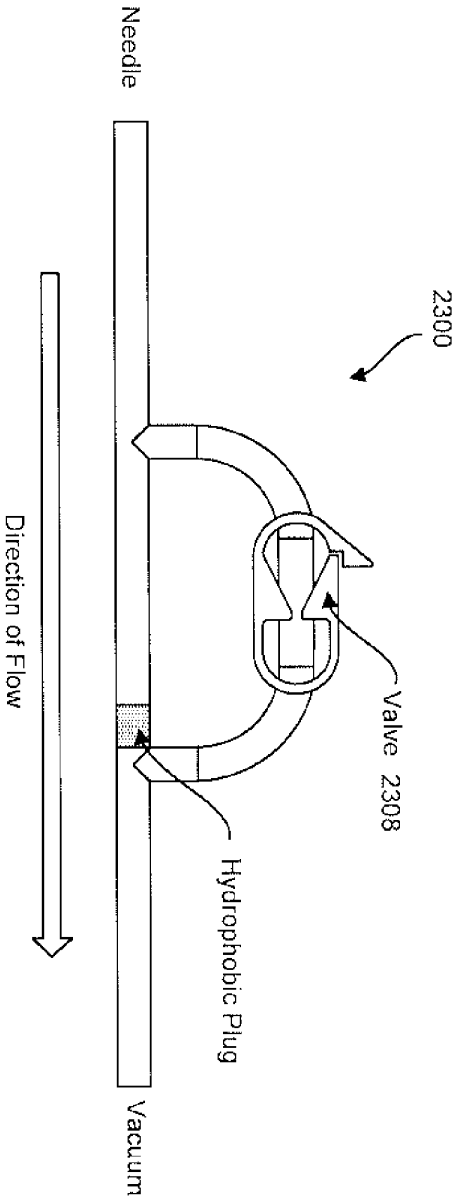

Needle
2300
Valve 2308
Hydrophobic Plug
Vacuum
Direction of Flow

FIG. 23B

Japanese Patent Application No. 2020-118498
Your Ref: KURIN2JP-DIV2
Our Ref: TS/KRN-C0137JP03
October 13, 2022

Translation of "Notice of Reasons for Rejection"

Patent Application Number:	JP 2020-118498	
Date of Delivery:	September 6, 2022	
Applied Provision:	Patent Law Article(s)	36(6)(ii) (Clarity)
		36(6)(i) (Support requirement)

The present application should be rejected for the following reasons. The applicant may present an argument against the reasons within three months from the date of delivery of this notice.

Reasons

1. (Clarity) The following claims do not comply with the requirements under Patent Law Article 36(6)(ii) as being unclear.

2. (Support requirement) The following claims do not comply with the requirements under Patent Law Article 36(6)(i) as lacking the support of the detailed description.

Remarks

- Reason 1 (Clarity)
- Claims 1 to 8

Claim 1 recites "an air permeable material that seals upon contact with blood from the first portion of the sample of blood". However, it is not clear from the above recitation whether the "air permeable material" after contact with blood seals from air.

From the recitation of "seals … from the first portion of the sample of blood", it can be understood that it is sufficient if the "air permeable material" seals from the sample of blood that is liquid. Further, the recitation of "air permeable material" can be interpreted by itself as always permeable to air. Therefore, the "air permeable material" after contact with blood can be understood as not sealing from air. On the other hand, from the recitation of "seals upon contact with blood", since the "air permeable material", which is originally permeable to air, changes in its sealing, the "air permeable material" after contact with blood can be understood as sealing from air. In addition, the applicant's argument in the Argument (especially, comparison with the invention disclosed in D2) is found to presuppose that the "air permeable material" after contact with blood seals from air.

Therefore, the property of the "air permeable material" after contact with blood, referred to by the recitation of "an air permeable material that seals upon contact with blood from the first portion of the sample of blood" in claim 1, is unclear.

Further, regarding the recitation of "an air permeable material that seals upon contact with blood" in claim 6, the recitation does not include "from the first portion of the sample of blood".

However, from the recitation of "air permeable material" the "air permeable material" after contact with blood can be understood as not sealing from air. On the other hand, from the recitation of "seals upon contact with blood", the "air permeable material" after contact with blood can be understood as sealing from air. Therefore, as in claim 1, the property of the "air permeable material" after contact with blood is unclear.

The same applies to claims 2-5 and 7-8 that refer to claims 1 and 6.

Therefore, the inventions of claims 1-8 are unclear.

- Reason 2 (Support requirement)
- Claims 1 to 8

As pointed out in Reason 1, in the inventions of claims 1 and 6, as a result of it being unclear whether the "air permeable material" after contact with blood seals from the air, a configuration may be included in which the "air permeable material" after contact with blood does not seal from air.

On the other hand, the Detailed Description of the Invention (see, in particular, paragraphs [0041], [0100], etc.) exclusively describes that the "air permeable material" after contact with blood seals from air. And it is not allowed that the invention can be extended or generalized from the Detailed Description of the Invention to a configuration in which the "air permeable material" after contact with blood does not seal from air.

The same applies to claims 2-5 and 7-8 that refer to claims 1 and 6.

Therefore, the inventions of claims 1-8 are not described in the Detailed Description of the Invention.

拒絶理由通知書

特許出願の番号	特願２０２０－１１８４９８
起案日	令和　４年　９月　１日
特許庁審査官	磯野　光司　３４１１　２Ｑ００
特許出願人代理人	三好　秀和（ほか　３名）　様
適用条文	第３６条第６項第２号（明確性） 第３６条第６項第１号（サポート要件）

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。

２．（サポート要件）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１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　１－８

請求項１において「血液と接触すると前記血液サンプルの第１の部分から密封する空気透過性材料」と記載されているが、血液と接触した後の「空気透過性材料」が空気から密封するものであるのか否かが、上記記載からは明確でない。

すなわち、「血液サンプルの第１の部分から密封する」という記載からすると、「空気透過性材料」は液体である血液サンプルから密封すれば足りるようにも解せ、また、「空気透過性材料」という記載のみからは、常に空気を透過するようにも解せるため、血液と接触した後の「空気透過性材料」は空気からは密封しないようにも解せる。その一方、「血液と接触すると・・・密封する」という記載からは、元々空気を透過する「空気透過性材料」に密封に関する変化が生じる訳であるから、血液と接触した後の「空気透過性材料」は空気から密封するようにも解せる。また、意見書における出願人の主張（特に、引用文献２に記載され

た発明との対比）は、血液と接触した後の「空気透過性材料」は空気から密封するものであることを前提としていると認められる。

そのため、請求項１における「血液と接触すると前記血液サンプルの第１の部分から密封する空気透過性材料」という記載が指す、血液と接触した後の「空気透過性材料」の性質は明確でない。

また、請求項６における「血液と接触すると密封する空気透過性材料」という記載について、当該記載には「血液サンプルの第１の部分から」という記載はないものの、「空気透過性材料」という記載のみからは、血液と接触した後の「空気透過性材料」は空気からは密封しないようにも解せ、その一方、「血液と接触すると・・・密封する」という記載からは、血液と接触した後の「空気透過性材料」は空気から密封するようにも解せるため、請求項１の記載と同様に、血液と接触した後の「空気透過性材料」の性質は明確でない。

請求項１，６を引用する、請求項２－５，７－８についても同様である。

よって、請求項１－８に係る発明は明確でない。

●理由２（サポート要件）について

・請求項　１－８

理由１において指摘したように、請求項１，６に係る発明において、血液と接触した後の「空気透過性材料」が空気から密封するものであるのか否かが明確でない結果、血液と接触した後の「空気透過性材料」が空気からは密封しない構成をも含みうるものとなっている。

一方、発明の詳細な説明（特に、段落［００４１］，［０１００］等参照）には、血液と接触した後の「空気透過性材料」が空気から密封するものであることが専ら記載されている。そして、発明の詳細な説明の記載から、血液と接触した後の「空気透過性材料」が空気からは密封しない構成にまで拡張ないし一般化することができるとは認められない。

請求項１，６を引用する、請求項２－５，７－８についても同様である。

よって、請求項１－８に係る発明は、発明の詳細な説明に記載したものでない。

－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－－

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）（PA2J）　磯野光司（いその　こうじ）
ＴＥＬ．０３－３５８１－１１０１　内線３２９１

Date: 20 December 2023

Your ref: 1000-016-04

Attn.

Katz, Presenti & Co.

14 Abba Hillel Rd.

Ramat Gan 52506

Greetings,

Re: **Notice prior to an Examination of Patent Application no. 309380 pursuant to Section 18 of the Law and Regulation 36 of the Regulations**

Please be advised: any reference to the Law, shall mean a reference to the Patents Law, 5727-1967; any reference to the Regulations, shall mean a reference to the Patents Regulations (Office Practices, Rules of Procedure, Documents and Fees), 5728-1968.

Please note: you must reply to this notice (even if all the answers are negative) within 4 months from the date hereof; however, you may request to extend the period in accordance with the rules prescribed in the Patents Registrar's Circular 035/2017-Patents. **In accordance with this circular, an extension of up to six months shall be granted for a notice prior to an examination.** Upon filing such an application prior to the end of the period, a fee at the sum of NIS 208 shall be paid for each month of delay or any part thereof.

1. List of References and Publications

Pursuant to the provisions of Section 18 of the Law and Regulation 36 of the Regulations, the following documents must be provided to the Patent Office:

a) The list of references relied on by the patent offices of the countries in which patent applications were filed with respect to the invention subject of the application contemplated herein during their examination of such applications (Section 18(a)(1) of the Law).

The applicant must enclose a copy of publications that are neither patents nor patent applications, which are specified in the list above mentioned.

b) In a separate list, publications that were published prior to the application date, which are known to the applicant and pertain directly to the invention. It is not required to include in this list any publications explicitly mentioned in the patent application (Section 18(a)(2) of the Law).

Pursuant to the provisions of Patents Registrar's Circular 035-2017-Patents, the following should also be specified as part of the said list:

- Any publications published or submitted by the applicant itself or by its predecessor in holding the right of ownership, including patent applications, patents and researches that directly pertain to the claimed invention;
- In the event of filing an application in Israel while claiming a priority right under an application of continuation or continuation in part (as the same are known in the U.S.), it will be required to submit a notice to the Patent Office regarding the publication dates of the applications in the chain of the applications of continuation or continuation in part and the numbers of such applications.

c) A list of the countries in which protection was sought for the invention subject of the application, by the applicant or by its predecessor in holding the right of ownership and the numbers of the applications filed in the said countries (**Regulation 36 of the Regulations**).

Please note: pursuant to Regulation 36(4) of the Regulations, if the applicant failed to respond to this requirement, it shall be deemed to have failed to remove deficiencies for which it was given notice under Section 20 of the Law.

2) **The Details of the Application**

a) **Please be advised:** each claim beyond the first 50 claims shall require a payment of an additional fee. If the application includes more than 50 claims, you must pay the fee; alternatively, you may reduce the number of claims. If the said fees have not been paid or if the number of claims was not reduced, this notice shall be deemed a notice of deficiencies. An applicant who fails to rectify the said deficiency upon filing its response to this notice will receive a notice prior to abandonment of the application, and if no payment was made - the application will be abandoned (the Patents Registrar notice dated December 3, 2012).

b) With respect to patent applications in the field of biotechnology, you must submit the list of sequences in a *.txt file only, and in accordance with the WIPO ST.25 standard. If the sequences file has already been submitted to the Patent Office in a *.txt file as of the application submission date, there is no need to submit it again.

c) Please be advised: in accordance with the provisions of the Patents Registrar Circular 0034/2017-Patents, if it will be determined that more than one invention was claimed under the application, the examiner will examine the first one among them according to the order of claims.

With respect to some fields, it is possible that the examination of the application shall not commence immediately after the Patent Office's requirements listed herein have been satisfied.

Please be advised: the examination of this application may be accelerated based on a parallel application, for which a positive report/patent was granted by an equivalent patent authority that has entered into a PPH arrangement vis-à-vis the Israeli Patent Office, thus free of any additional fees. For further details, please review the PPH webpage (the Patent Department) on the Israeli Patent Office website.

Respectfully,
Cohen Carmela
On behalf of the Patents Registrar

תאריך: ח' טבת תשפ"ד
20/12/2023
סימוכין: 1000-016-04

לכבוד
כץ, פרזנטי ושות'
דרך אבא הלל 14,
רמת גן, מיקוד 52506

א.ג.נ.,

<u>הודעה לפני בחינת הבקשה לפטנט מס' 309380 בהתאם לסעיף 18 לחוק ותקנה 36 לתקנות</u>

לתשומת לבכם: מקום בו הנכם מופנים לחוק, הכוונה היא לחוק הפטנטים, התשכ"ז – 1967.
מקום בו הנכם מופנים לתקנות, הכוונה היא לתקנות הפטנטים (נוהלי הרשות , סדרי דין, מסמכים ואגרות), התשכ"ח – 1968.
<u>הערה:</u> עליכם להשיב על הודעה זו (אף אם כל התשובות הן שליליות) תוך ארבעה חודשים מתאריכה, אך הנכם רשאים לבקש את הארכת התקופה בהתאם לכללים שנקבעו בחוזר הרשם 035/2017 – פטנטים. **בהתאם לחוזר זה לא יינתנו יותר משישה חודשי ארכה בגין הודעה לפני בחינה.** עם בקשה כאמור שתוגש לפני תום התקופה יש לשלם אגרה בסך 218 בעד כל חודש איחור או חלק ממנו.

1. רשימת פירסומים

בהתאם לאמור בסעיף 18 לחוק ובתקנה 36 לתקנות, יש להמציא לרשות את המסמכים הבאים:

(א) רשימת פירסומים (אסמכתאות) עליהם הסתמכו רשויות הפטנטים בארצות בהן הוגשו בקשות לפטנט על האמצאה מושא הבקשה דנן בשעת הבחינה של בקשות אלה (סעיף 18 (א)(1) לחוק).
על המבקש לצרף עותק של פרסומים שאינם פטנטים או בקשות לפטנט המצוינים ברשימה הנ"ל.

(ב) ברשימה נפרדת, פרסומים שפורסמו לפני תאריך הבקשה, הידועים למבקש והנוגעים במישרין לאמצאה. אין צורך לכלול ברשימה זו פרסומים שאוזכרו במפורש בבקשת הפטנט (סעיף 18(א)(2) לחוק).
על פי הוראות חוזר רשם 035/2017 - פטנטים במסגרת רשימה זו יש להודיע בין היתר גם על:

- פרסומים שפרסם או הגיש המבקש עצמו או מי שקדם לו בזכות בעלות, לרבות בקשות לפטנט, פטנטים, מחקרים הנוגעים במישרין לאמצאה הנתבעת;
- בקשה שהוגשה בישראל תוך תביעת דין קדימה מבקשת המשך או המשך בחלקה (Continuation, Continuation In Part כפי שאלה נעשות בארה"ב) תחייב הודעה לרשות אודות תאריכי הפרסום של הבקשות בשרשרת בקשות ההמשך או בקשות המשך בחלקן ומספרי הבקשות.

(ג) רשימת הארצות שבהן נתבקשה הגנה על האמצאה נושא הבקשה על ידי המבקש או מי שקדם לו בזכות בעלות ואת מספרי הבקשות שהוגשו באותן ארצות **(תקנה 36 לתקנות).**

לתשומת לבכם, בהתאם לתקנה 36(4) לתקנות אם לא השיב המבקש על דרישה זו, יהיה דינו כדין מי שלא סילק ליקויים שעליהם נמסרה לו הודעה לפי סעיף 20 לחוק.

2. פירוט הבקשה

(א) **תשומת לבכם** כי כל תביעה שמעבר ל-50 התביעות הראשונות מחייבת בתשלום אגרה נוספת. ככל שהבקשה כוללת מעל 50 תביעות עליכם לשלם את האגרה, לחלופין באפשרותכם לצמצם את מספר התביעות. לא שולמה האגרה כאמור או לא צומצם מספר התביעות, יראו בהודעה זו מכתב ליקויים. מבקש שלא יתקן את הליקוי האמור במועד תשובתו להודעה זו יקבל הודעה לפני סגירת הבקשה ובהעדר תשלום תיסגר הבקשה (הודעת הרשם מיום 3/12/2012).

(ב) בבקשה לפטנט בתחום הביוטכנולוגיה הכוללת רשימת רצפים:
עבור בקשה שתאריכה מאוחר מ- 1/7/2022 עליכם להגיש את רשימת הרצפים בקובץ מסוג XML ערוך בהתאם לתקן ST.26 של WIPO;
עבור בקשה שתאריכה מוקדם מתאריך זה עליכם להגיש את רשימת הרצפים בקובץ מסוג TXT ערוך בהתאם לתקן ST.25 של WIPO;
במידה וקובץ הרצפים הוגש לרשות בסוג הקובץ הנדרש במועד הגשת הבקשה, אין צורך להגישו בשנית.

(ג) **לתשומת לבכם בהתאם להוראות חוזר רשם 0034/2017 - פטנטים, באם יקבע כי נתבעו בבקשה יותר מאמצאה אחת, הבוחן יבחן את <u>הראשונה</u> מביניהן לפי סדר התביעות.**

ייתכן כי בתחומים מסויימים בחינתה של בקשה לא תחל מייד עם מילוי דרישות הרשות המפורטות בהודעה זו.

נבקש לידע שניתן לזרז את בחינת בקשה זו על סמך בקשה מקבילה אשר קיבלה דוח חיובי/פטנט ברשות מקבילה שיש לה הסדר PPH עם רשות הפטנטים הישראלית וזאת ללא צורך בתשלום אגרה נוספת. לפרטים נוספים נא לפנות לדף ה-PPH (מחלקת פטנטים) באתר רשות הפטנטים.

בכבוד רב,
רשות הפטנטים

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Sterile bodily-fluid collection device and methods

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Applicant(s): MAGNOLIA MEDICAL TECHNOLOGIES INC ± (MAGNOLIA MEDICAL TECHNOLOGIES INC, ; 木兰医药技术股份有限公司)

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Abstract of CN104981203 (A)

An apparatus includes a pre-sample reservoir, a diversion mechanism, and a flow metering mechanism. The diversion mechanism has an inlet port couplable to a lumen-defining device to receive bodily-fluids from a patient, a first outlet port fluidically couplable to the pre-sample reservoir, and a second outlet port fluidically couplable to a sample reservoir. The diversion mechanism defines a first fluid flow path and a second flow path that are configured to place the first outlet port and the second outlet port, respectively, in fluid communication with the inlet port. The flow metering mechanism is configured to meter a flow of a predetermined volume of bodily-fluid through the first fluid flow path into the pre-sample reservoir, to meter a flow of a second volume of bodily-fluid through the second fluid flow path into the sample reservoir, and to display a volumetric indicator associated with the predetermined volume and the second volume.

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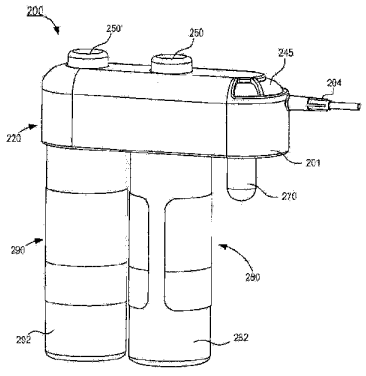
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(54)发明名称

无菌体液采集装置和方法

(57)摘要

一种设备包括前样本储存器、转移机构和流计量机构。转移机构具有可耦接到内腔限定装置以从患者接收体液的入口端口、可流体耦接到前样本储存器的第一出口端口和可流体耦接到样本储存器的第二出口端口。转移机构限定被配置为使第一出口端口和第二出口端口分别与入口端口流体连通的第一流体流路径和第二流体流路径。流计量机构被配置为计量通过第一流体流路径流入前样本储存器的预定体积的体液流，计量通过第二流体流路径流入样本储存器的第二体积的体液流，并且显示与预定体积和第二体积相关的体积指示。



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1. 一种用于从患者获取体液样本的设备，所述设备包括：

前样本储存器，其被配置为接收从患者抽取的第一体积的体液；

转移机构，其包括入口端口、第一出口端口和第二出口端口，所述入口端口被配置为耦接到用于从患者接收体液的内腔限定装置，所述第一出口端口被配置为将所述前样本储存器流体耦接到所述转移机构，并且所述第二出口端口被配置为将样本储存器流体耦接到所述转移机构，所述转移机构限定被配置为使所述第一出口端口与所述入口端口流体连通的第一流体流路径和被配置为使所述第二出口端口与所述入口端口流体连通的第二流体流路径；以及

流计量机构，其与所述第一流体流路径和所述第二流体流路径流体连通，所述流计量机构被配置为计量通过所述第一流体流路径流入所述前样本储存器的第一体积的体液流并计量通过所述第二流体流路径流入所述样本储存器的第二体积的体液流，所述流计量机构被配置为显示与第一体积和第二体积相关的体积指示。

2. 如权利要求 1 所述的设备，其中，在第一时间段内所述第一体积的体液在所述第一流体流路径内流动，并且在第一时间段之后的第二时间段内所述第二体积的体液在所述第二流体流路径内流动。

3. 如权利要求 1 所述的设备，其中，所述第一体积的体液包括皮肤驻留的污染物，并且所述第二体积的体液基本不存在皮肤驻留的污染物。

4. 如权利要求 1 所述的设备，其中，所述前样本储存器至少部分地由所述转移机构的一部分限定。

5. 如权利要求 1 所述的设备，其中，所述体积指示是视觉指示。

6. 如权利要求 1 所述的设备，其中，所述转移机构包括被配置为移动通过所述第二出口端口以使所述样本储存器与所述第二流体流路径流体连通的可移动构件。

7. 如权利要求 6 所述的设备，其中，所述流计量机构至少部分地位于所述可移动构件的一部分内。

8. 如权利要求 1 所述的设备，其中，所述转移机构被配置为一旦第一体积的血液位于所述前样本储存器中就流体隔离所述前样本储存器和所述第一流体路径的至少一部分。

9. 如权利要求 1 所述的设备，其中，所述转移机构包括被配置为将第二样本储存器流体耦接到所述转移机构的第三出口端口，并且限定被配置为使所述第三出口端口与所述入口端口流体连通的第三流体流路径。

10. 如权利要求 1 所述的设备，还包括：

限定第一内腔和第二内腔的流控制器，所述流控制器被配置为在第一配置和第二配置之间移动，在所述第一配置，所述第一内腔使所述第一流体流路径与所述入口端口流体连通，在所述第二配置，所述第二内腔使所述第二流体流路径与所述入口端口流体连通。

11. 如权利要求 10 所述的设备，其中，所述流控制器被配置为在所述第一体积的体液位于所述前样本储存器中之后从所述第一配置移动到所述第二配置。

12. 一种用于从患者获取体液样本的设备，所述设备包括：

前样本储存器，其被配置为接收从患者抽取的第一体积的体液；

转移机构，其包括入口端口、第一出口端口和第二出口端口，所述入口端口被配置为耦接到用于从患者接收体液的内腔限定装置，所述第一出口端口被配置为将所述前样本储存

器流体耦接到所述转移机构，并且所述第二出口端口被配置为将样本储存器流体耦接到所述转移机构；

流控制器，其至少部分地位于所述转移机构内，并且被配置为在第一配置和第二配置之间移动，在所述第一配置，所述流控制器限定在所述入口端口和所述第一出口端口之间的流体流路径的至少一部分，在所述第二配置，所述流控制器限定在所述入口端口和所述第二出口端口之间的流体流路径的至少一部分；以及

可移动构件，其能够移动地耦接到所述转移机构，并且被配置为在其中所述样本储存器与在所述入口端口和所述第二出口端口之间的流体流路径流体隔离的第一配置和其中所述样本储存器与在所述入口端口和所述第二出口端口之间的流体流路径流体连通的第二配置之间移动通过所述第二出口端口，所述样本储存器被配置为当所述流控制器处于其第二配置并且所述可移动构件处于其第二配置时接收从患者抽取的第二体积的体液。

13. 如权利要求 12 所述的设备，其中，所述第一体积的体液包括皮肤驻留的污染物，并且所述第二体积的体液基本不存在皮肤驻留的污染物。

14. 如权利要求 12 所述的设备，其中，所述流控制器相对于所述转移机构在其第一配置和其第二配置之间旋转。

15. 如权利要求 12 所述的设备，其中，所述流控制器相对于所述转移机构以线性运动方式移动。

16. 如权利要求 12 所述的设备，其中，所述流控制器被配置为当所述流控制器处于其第二配置时流体隔离所述前样本储存器。

17. 如权利要求 12 所述的设备，其中，所述可移动构件包括被配置为当所述可移动构件处于其第二配置时刺穿所述样本储存器的一部分的刺穿构件。

18. 如权利要求 12 所述的设备，其中，所述可移动构件耦接到被配置为至少暂时地保持所述可移动构件处于其第一配置的偏置构件。

19. 如权利要求 12 所述的设备，其中，所述转移机构包括被配置为将第二样本储存器流体耦接到所述转移机构的第三出口端口。

20. 如权利要求 19 所述的设备，其中，所述可移动构件是第一可移动构件，所述设备还包括：

第二可移动构件，其被配置为在所述第二样本储存器与被限定在所述入口端口和所述第三出口端口之间的流体流路径流体隔离的第一配置和所述第二样本储存器与被限定在所述入口端口和所述第三出口端口之间的流体流路径流体连通的第二配置之间移动通过所述第三出口端口，所述第二样本储存器被配置为当所述流控制器处于其第二配置并且所述第二可移动构件处于其第二配置时接收从患者抽取的第三体积的体液。

21. 一种用于从患者获取体液样本的设备，所述设备包括：

前样本储存器，其被配置为接收从患者抽取的第一体积的体液；

转移机构，其包括外壳和分配构件，所述外壳限定第一孔口和第二孔口，所述第一孔口与所述前样本储存器流体连通，所述分配构件至少部分地位于所述外壳内并限定与所述第二孔口流体连通的流体流通道，所述分配构件包括与所述流通道流体连通的耦接部分并且被配置为物理地和流体地耦接到样本储存器；以及

流控制器，其包括被配置为耦接到用于从患者接收体液的内腔限定装置的入口端口，

所述流控制器能够旋转地耦接到所述转移机构并且被配置为在其中所述入口端口与所述第一孔口流体连通的第一配置和其中所述入口端口与所述第二孔口流体连通的第二配置之间移动。

22. 如权利要求 21 所述的设备，其中，所述第一体积的体液包括皮肤驻留的污染物，并且所述第二体积的体液基本不存在皮肤驻留的污染物。

23. 如权利要求 21 所述的设备，其中，所述前样本储存器至少部分地由所述分配构件的一部分限定。

24. 如权利要求 21 所述的设备，其中，所述耦接部分包括被配置为刺穿所述样本储存器的一部分以使所述样本储存器与所述流体流通道流体连通的刺穿构件。

25. 如权利要求 24 所述的设备，其中，当所述流控制器处于其第二配置时，利用所述刺穿构件刺穿所述样本储存器的所述部分使体液开始从患者流过所述入口端口和所述流通道并流入所述样本储存器中。

26. 如权利要求 21 所述的设备，其中，所述第一体积的体液是第一预定体积的体液，所述流体流通道被配置为接收第二预定体积的体液，所述第二预定体积的体液与样本体积相关。

27. 如权利要求 26 所述的设备，其中，所述样本体积在约 10 毫升和约 50 毫升之间。

28. 如权利要求 26 所述的设备，其中，所述样本体积为约 30 毫升。

29. 如权利要求 21 所述的设备，其中，所述转移机构包括密封构件，当所述流控制器耦接到所述转移机构时，所述密封构件位于所述外壳和所述流控制器之间，从而使得所述密封构件与所述流控制器的表面和所述外壳的表面形成基本流体密封的密封结构，所述密封构件限定第一孔口和第二孔口，所述密封构件的第一孔口与所述外壳的第一孔口基本同心，并且所述密封构件的第二孔口与所述外壳的第二孔口基本同心。

30. 一种利用流计量传送装置从患者获取预定样本体积的体液的方法，所述流计量传送装置包括转移机构，所述转移机构包括被配置为选择性地与前样本储存器和样本储存器流体连通的入口端口，并且所述流计量传送装置包括被配置为计量从患者流至所述前样本储存器和所述样本储存器的体液流的流计量机构，所述方法包括：

在患者和所述流计量传送装置的端口之间建立流体连通；

在所述端口和所述前样本储存器之间建立流体连通；

计量从患者传送到所述前样本储存器的体液流；

经由所述流计量传送装置的所述流计量机构验证位于所述前样本储存器中的前样本体积的体液是预定前样本体积的体液；

使所述前样本储存器与所述端口流体隔离，以将所述前样本体积的体液隔绝在所述前样本储存器中；

在所述端口和所述样本储存器之间建立流体连通；

计量从患者传送到所述样本储存器的体液流；

经由所述流计量传送装置的所述流计量机构验证位于所述样本储存器中的样本体积的体液是预定样本体积的体液。

31. 如权利要求 30 所述的方法，其中，所述流计量传送装置包括被配置为在建立患者和所述前样本储存器之间的流体连通的第一配置和建立患者和所述样本储存器之间的流

体连通的第二配置之间移动的流控制器。

32. 如权利要求 30 所述的方法，其中，所述体液是血液。

33. 如权利要求 32 所述的方法，其中，所述样本储存器包括需氧培养介质或厌氧培养介质中的至少一种。

34. 如权利要求 30 所述的方法，其中，所述预定前样本体积在约 1 毫升和约 10 毫升之间。

35. 如权利要求 30 所述的方法，其中，所述预定样本体积在约 20 毫升和约 60 毫升之间。

36. 如权利要求 30 所述的方法，其中，所述预定样本体积为约 60 毫升。

37. 如权利要求 30 所述的方法，其中，所述样本储存器是第一样本储存器，并且所述样本体积是第一样本体积，所述方法还包括：

在验证所述第一样本储存器中的所述第一样本体积是所述预定样本体积之后，在所述端口和所述第二样本储存器之间建立流体连通；

计量从患者传送到所述第二样本储存器的体液流；以及

经由所述流计量传送装置的所述流计量机构验证位于所述第二样本储存器中的第二样本体积的体液是所述预定样本体积的体液。

38. 如权利要求 37 所述的方法，其中，所述第一样本体积和所述第二样本体积相等并都处于约 20 毫升和约 60 毫升之间。

39. 如权利要求 37 所述的方法，还包括：

在验证所述第二样本储存器中的所述第二样本体积是所述预定样本体积之后，在所述端口和所述第三样本储存器之间建立流体连通；

计量从患者传送到所述第三样本储存器的体液流；以及

经由所述流计量传送装置的所述流计量机构验证位于所述第三样本储存器中的第三样本体积的体液是所述预定样本体积的体液。

40. 如权利要求 39 所述的方法，其中，所述第一样本体积、所述第二样本体积和所述第三样本体积相等并都处于约 30 毫升和约 60 毫升之间。

41. 如权利要求 39 所述的方法，其中，所述第一样本体积、所述第二样本体积和所述第三样本体积都等于约 60 毫升。

无菌体液采集装置和方法

[0001] 相关申请的交叉引用

[0002] 本申请要求2012年12月4日提交的名称为“无菌体液采集装置和方法”的美国临时专利申请序列号61/733,199的优先权和利益，其全部公开内容通过引用合并于此。

背景技术

[0003] 本文描述的实施例总体涉及不经肠道获得体液样本，更具体地，涉及在减少微生物污染或体液源外部的其他污染物（诸如皮肤驻留的微生物）的情况下不经肠道获得体液样本的装置和方法。

[0004] 医疗保健行业从业者例行利用非经肠道获得的体液对患者进行各种类型的微生物测试。在一些情形中，测试患者样本（例如，体液）是否存在一种或多种潜在有害的微生物，诸如细菌、真菌或酵母属（例如，假丝酵母属）。微生物测试可包括在包含有助于微生物生长、实时诊断和/或基于PCR的方法的培养介质的一个或多个无菌器皿中培养患者样本。一般来说，当患者样本中存在这类微生物时，培养介质中的微生物随时间迅速增多。在可变的时间（例如，几小时至几天）之后，可通过自动的持续监控检测有机体的生长。这种自动监控可检测有机体生长所产生的二氧化碳。于是可测试培养介质中是否存在微生物。培养介质中微生物的存在表示从其获得样品的患者的体液中存在相同的微生物。因此，当确定培养介质中存在微生物时，患者的处方可以是一种或多种抗生素或者专门用于治疗或以其他方式去除患者体内的有害微生物的其他治疗方式。

[0005] 但是，患者样本可能在获得期间被污染和/或易于以其他方式导致错误的阳性结果。患者样本污染可能发生的一种方式是传送体表的微生物（例如，皮肤驻留的微生物），该微生物在针头插入患者期间被带走，随后被传送到具有患者样本的培养介质。体表和/或其他有害外部微生物可直接被带走，或经由组织碎片、毛囊、汗腺和其他附器结构被带走。另一种可能的污染源来自提取患者样本的人。例如，医生、采血师、护士等可将污染物从他们的身体（例如，手指、手臂等）传送到患者样本和/或传送到包含患者样本的仪器。进一步详述，在患者样本获得过程中（例如，患者至针头、针头/管至样本器皿等）使用的仪器和/或装置通常包括都可引入潜在的污染部位的多个流体分界面。这类仪器和/或装置的使用通常包括用以连接和/或流体耦接各个分界面的人工干预。由于这些分界面未被预组装和消毒为单个流体耦接系统，因此外部污染物可经由使用者（例如，医生、采血师等）和/或其他源（例如，环境空气、患者房间中的桌子和案台表面上的污染物、传送自亚麻织物或衣服的微生物等）被引入患者样本中。在一些情形中，这类污染物可在培养介质中存活并最终导致阳性微生物测试结果，由此错误地表明活体中存在这类微生物。

[0006] 在一些情形中，错误的阳性结果和/或错误的阴性结果可归因于患者样本的特定体积。例如，过度填充容积敏感的血液培养瓶可导致错误的阳性结果，如这类培养瓶的制造商提供的使用说明和/或警告标签以及相关的自动连续监控微生物检测系统提示的。在另一方面，作为另一例子，培养介质内不足的患者样本体积可导致错误的阴性结果。例如，在Mayo Clinic 2011年12月在Journal of Clinical Microbiology发表的名称为

"Optimized Pathogen Detection with 30-Compared to20-Milliliter Blood Culture Draws"的研究中,20 毫升 (mL) 的患者样本体积的结果是检测到患者样本中存在约 80%的细菌,40 毫升 (mL) 的患者样本体积的结果是检测到约 88%的细菌,60 毫升 (mL) 的患者样本体积的结果是检测到约 99%的细菌。

[0007] 在试图诊断或治疗可疑的疾病或情况时由污染、患者样本体积不足等导致的这种不准确的结果是一个顾虑。例如,微生物测试的错误阴性结果可导致误诊和 / 或延迟治疗患者的疾病,在一些情形中,这可能导致患者死亡。相反,微生物测试的错误阳性结果可导致患者不必要地经受一种或多种抗生素疗法,这会对患者产生严重的副作用,包括例如死亡,以及由于延长了患者住院时间和 / 或与错误治疗相关的其他并发症而给医疗保健系统带来不必要的负担和花费。错误,因这些错误的阳性结果而进行的诊断成像仪器的使用在成本方面以及患者安全方面 (因为不必要地暴露于与各种成像过程 (例如,CT 扫描) 相关的大剂量辐射对患者的长期健康具有许多已知的负面影响) 也是一个顾虑。

[0008] 因此,需要一种通过例如最小化患者样本和 / 或流体分界面暴露于周围的非无菌环境和 / 或其他外部污染源减少体液测试样本中的微生物污染的无菌"多合一"体液采集装置和方法。此外,这类体液采集装置需要包括准确计量、测量和 / 或其其他方式评估和确定从患者传送到样本储存器或培养介质的体液体积的装置,其可以是可视的、策略的或以其他方式与获得患者样本的医疗保健行业从业者基本实时地通信 (例如,在患者床边)。

发明内容

[0009] 本文描述了用于在减少体液源外部的微生物 (诸如皮肤驻留的微生物) 和 / 或其他有害外部污染物的情况下不经肠道获得体液样本的装置。在一些实施例中,用于从患者获取体液样本的设备包括前样本储存器、转移机构和流计量机构。前样本储存器被配置为接收从患者抽取的第一体积的体液。转移机构包括入口端口、第一出口端口和第二出口端口,并且限定第一流体流路径和第二流体流路径。所述入口端口可耦接到用于从患者接收体液的内腔限定装置。所述第一出口端口和第二出口端口被配置为将所述前样本储存器和样本储存器分别流体耦接到所述转移机构。第一流体流路径被配置为使所述第一出口端口与所述入口端口流体连通,并且第二流体流路径被配置为使所述第二出口端口与所述入口端口流体连通。流计量机构与所述第一流体流路径和所述第二流体流路径流体连通。所述流计量机构被配置为计量通过所述第一流体流路径流入所述前样本储存器的第一体积的体液流并计量通过所述第二流体流路径流入所述样本储存器的第二体积的体液流。所述流计量机构被配置为显示与第一体积和第二体积相关的体积指示。

附图说明

[0010] 图 1 是根据实施例的体液采集装置的示意图。

[0011] 图 2 是根据实施例的体液采集装置的立体图。

[0012] 图 3 是图 2 的体液采集装置的分解立体图。

[0013] 图 4 是沿图 3 的线 X_1-X_1截取的图 2 的体液采集装置中包括的外壳的剖视侧视图。

[0014] 图 5 是沿图 3 的线 X_2-X_2截取的图 2 的体液采集装置中包括的可移动构件的剖视图。

[0015] 图 6 和 7 分别是沿图 3 的线 X_3-X_3和 X_4-X_4截取的图 2 的体液采集装置中包括的流控制器的剖视图。

[0016] 图 8 是处于第一配置的图 2 的体液采集装置的顶视图。

[0017] 图 9 是沿图 8 的线 X_5-X_5截取的处于第一配置的图 2 的体液采集装置的剖视图。

[0018] 图 10 是处于第二配置的图 2 的体液采集装置的顶视图。

[0019] 图 11 是沿图 10 的线 X_6-X_6截取的处于第二配置的图 2 的体液采集装置的剖视图。

[0020] 图 12 和 13 分别是沿图 10 的线 X_6-X_6截取的处于第三配置和第四配置的图 2 的体液采集装置的剖视图。

[0021] 图 14 是根据实施例的体液采集装置的立体图。

[0022] 图 15 是沿图 14 的线 X_7-X_7截取的图 14 的体液采集装置的剖视侧视图。

[0023] 图 16 是根据实施例的体液采集装置的立体图。

[0024] 图 17 是图 16 的体液采集装置中包括的转移机构的分解立体图。

[0025] 图 18 是沿图 16 的线 X_8-X_8截取的图 16 的体液采集装置中包括的分配构件的剖视侧视图。

[0026] 图 19 是处于第一配置的图 16 的体液采集装置的顶视图。

[0027] 图 20 是沿图 19 的线 X_9-X_9截取的处于第一配置的图 16 的体液采集装置的一部分的剖视图。

[0028] 图 21 是处于第二配置的图 16 的体液采集装置的顶视图。

[0029] 图 22 是沿图 21 的线 X_{10}-X_{10}截取的处于第二配置的图 16 的体液采集装置的剖视图。

[0030] 图 23 是根据实施例的体液采集装置的立体图。

[0031] 图 24 是沿线 X_{11}-X_{11}截取的处于第一配置的图 23 的体液采集装置的一部分的剖视图。

[0032] 图 25 是沿线 X_{11}-X_{11}截取的处于第二配置的图 23 的体液采集装置的剖视图。

[0033] 图 26 是根据实施例的体液采集装置的立体图。

[0034] 图 27 的图 26 的体液采集装置中包括的转移机构的分解立体图。

[0035] 图 28 是沿图 27 的线 X_{13}-X_{13}截取的图 26 的体液采集装置中包括的分配构件的剖视图。

[0036] 图 29 是沿图 27 的线 X_{14}-X_{14}截取的图 26 的体液采集装置中包括的耦接构件的剖视图。

[0037] 图 30 是沿图 27 的线 X_{15}-X_{15}截取的图 26 的体液采集装置中包括的转盘的剖视图。

[0038] 图 31 是沿图 27 的线 X_{16}-X_{16}截取的图 26 的体液采集装置中包括的阀的剖视图。

[0039] 图 32 是沿线 X_{12}-X_{12}截取的处于第一配置的图 26 的体液采集装置的剖视图。

[0040] 图 33 是沿线 X_{12}-X_{12}截取的处于第二配置的图 26 的体液采集装置的剖视图。

[0041] 图 34 是根据实施例的体液采集装置的立体图。

[0042] 图 35 的图 34 的体液采集装置中包括的转移机构的分解立体图。

[0043] 图 36 是沿线 X_{17}-X_{17}截取的图 35 的转移机构中包括的分配构件的剖视图。

[0044] 图 37 是处于第一配置的图 34 的体液采集装置的一部分的顶视图。

[0045] 图 38 是沿线 X_{18}-X_{18}截取的处于第一配置的图 37 的体液采集装置的一部分的剖视

图。

[0046] 图 39 是处于第一配置的图 33 的体液采集装置的一部分的顶视图。

[0047] 图 40 是沿图 39 的线 X_{19}-X_{19}截取的处于第一配置的图 33 的体液采集装置的剖视图。

[0048] 图 41 是根据实施例的处于第一配置的体液采集装置的立体图。

[0049] 图 42 是图 41 的体液采集装置的一部分的分解立体图。

[0050] 图 43 是沿线 X_{20}-X_{20}截取的处于第一配置的图 41 的体液采集装置的剖视侧视图。

[0051] 图 44 是沿线 X_{20}-X_{20}截取的处于第二配置的图 41 的体液采集装置的剖视侧视图。

[0052] 图 45 是沿线 X_{20}-X_{20}截取的处于第三配置的图 41 的体液采集装置的剖视侧视图。

[0053] 图 46 是根据实施例的处于第一配置的体液采集装置的立体图。

[0054] 图 47 的图 45 的体液采集装置的一部分的分解立体图。

[0055] 图 48 是沿图 47 的线 X_{21}-X_{21}截取的图 46 的体液采集装置中包括的分配构件的剖视侧视图。

[0056] 图 49 是沿图 47 的线 X_{22}-X_{22}截取的图 46 的体液采集装置中包括的可移动构件的剖视图。

[0057] 图 50 是处于第一配置的图 46 的体液采集装置的顶视图。

[0058] 图 51 是沿图 50 的线 X_{23}-X_{23}截取的处于第一配置的图 46 的体液采集装置的一部分的剖视图。

[0059] 图 52 是处于第二配置的图 46 的体液采集装置的顶视图。

[0060] 图 53 是沿图 52 的线 X_{24}-X_{24}截取的处于第二配置的图 46 的体液采集装置的剖视图。

[0061] 图 54 是根据实施例的体液采集装置的立体图。

[0062] 图 55 是图 54 的体液采集装置的顶视图。

[0063] 图 56 是流程图，图示了利用根据实施例的采集装置获取减少污染的体液样本的方法。

具体实施方式

[0064] 本文描述了用于在减少体液源外部的微生物（诸如皮肤驻留的微生物）和 / 或其他有害外部污染物的情况下不经肠道获得体液样本的装置。在一些实施例中，用于从患者获取体液样本的设备包括前样本储存器、转移机构和流计量机构。前样本储存器被配置为接收从患者抽取的第一体积的体液。转移机构包括入口端口、第一出口端口和第二出口端口，并且限定第一流体流路径和第二流体流路径。所述入口端口可耦接到用于从患者接收体液的内腔限定装置。所述第一出口端口和第二出口端口被配置为将所述前样本储存器和样本储存器分别流体耦接到所述转移机构。第一流体流路径被配置为使所述第一出口端口与所述入口端口流体连通，并且第二流体流路径被配置为使所述第二出口端口与所述入口端口流体连通。流计量机构与所述第一流体流路径和所述第二流体流路径流体连通。所述流计量机构被配置为计量通过所述第一流体流路径流入所述前样本储存器的第一体积的体液流并计量通过所述第二流体流路径流入所述样本储存器的第二体积的体液流。所述流计量机构被配置为显示与第一体积和第二体积相关的体积指示。

[0065] 在一些实施例中，用于从患者获取体液样本的设备包括前样本储存器、转移机构、流控制器和可移动构件。前样本储存器被配置为接收从患者抽取的第一体积的体液。转移机构包括入口端口、第一出口端口和第二出口端口。所述入口端口可耦接到用于从患者接收体液的内腔限定装置。所述第一出口端口将所述前样本储存器流体耦接到所述转移机构，并且所述第二出口端口将样本储存器流体耦接到所述转移机构。流控制器至少部分地位于所述转移机构内，并且可在第一配置和第二配置之间移动，在所述第一配置，所述流控制器限定在所述入口端口和所述第一出口端口之间的流体流路径的至少一部分，在所述第二配置，所述流控制器限定在所述入口端口和所述第二出口端口之间的流体流路径的至少一部分。可移动构件可移动地耦接到所述转移机构，并且可在所述样本储存器与所述入口端口和所述第二出口端口之间的流体流路径流体隔离的第一配置和所述样本储存器与所述入口端口和所述第二出口端口之间的流体流路径流体连通的第二配置之间移动通过所述第二出口端口。所述样本储存器被配置为当所述流控制器处于其第二配置并且所述可移动构件处于其第二配置时接收从患者抽取的第二体积的体液。

[0066] 在一些实施例中，用于从患者获取体液样本的设备包括前样本储存器、转移机构和流控制器。前样本储存器被配置为接收从患者抽取的第一体积的体液。转移机构包括外壳和分配构件。所述外壳限定第一孔口和第二孔口，所述第一孔口与所述前样本储存器流体连通。所述分配构件至少部分地位于所述外壳内并限定与所述第二孔口流体连通的流体流通道。所述分配构件包括与所述流通道流体连通的耦接部分并且被配置为物理地和流体地耦接到样本储存器。流控制器包括可耦接到用于从患者接收体液的内腔限定装置的入口端口。所述流控制器可旋转地耦接到所述转移机构并且可在所述入口端口与所述第一孔口流体连通的第一配置和所述入口端口与所述第二孔口流体连通的第二配置之间移动。

[0067] 在一些实施例中，一种利用流计量传送装置的方法，所述流计量传送装置具有转移机构，所述转移机构具有被配置为选择性地与前样本储存器和样本储存器流体连通的入口端口，并且所述流计量传送装置包括被配置为计量从患者流至所述前样本储存器和所述样本储存器的体液流的流计量机构，所述方法包括在患者和所述流计量传送装置的端口之间建立流体连通。然后，在所述端口和所述前样本储存器之间建立流体连通。计量从患者传送到所述前样本储存器的体液流。所述方法包括经由所述流计量传送装置的所述流计量机构验证位于所述前样本储存器中的前样本体积的体液是预定前样本体积的体液。在前样本体积位于前样本储存器中时，使所述前样本储存器与所述端口流体隔离，以将所述前样本体积的体液隔绝在所述前样本储存器中。当前样本储存器被流体隔离时，所述方法包括在所述端口和所述样本储存器之间建立流体连通。计量从患者传送到所述样本储存器的体液流。所述方法包括经由所述流计量传送装置的所述流计量机构验证位于所述样本储存器中的样本体积的体液是预定样本体积的体液。

[0068] 在一些实施例中，所述设备包括转移机构和流控制器。转移机构可限定入口端口、第一出口端口、第二出口端口和第三出口端口。第一出口端口流体耦接到前样本储存器，第二出口端口流体耦接到第一样本储存器，并且第三出口端口流体耦接到第二样本储存器，等等。所有流体储存器可彼此流体隔离。流控制器包括可容许沿特定方向的流体移动的各种流体通道并可被配置为可操作地耦接到转移机构。在使用时，当转移机构处于第一配置时，流控制器可容许体液流进入前样本储存器。转移机构可移动到第二配置，在该配置中，

流控制器可容许体液流进入第一样本储存器。此外，之后可将转移机构移动到第三配置，由此流控制器可容许体液流进入第二样本储存器。

[0069] 在一些实施例中，体液采集装置可被配置为在允许第二体积的体液流入第一样本储存器和/或第三体积的体液流入第二样本储存器之前选择性地将第一预定体积的体液转移到前样本储存器中。以此方式，第二和/或第三体积的体液可用于诊断或其他测试，同时隔离可能包含来自（从其获得样本的）患者的体表或体外的其他源的微生物的第一体积的体液。在一些实施例中，根据将执行的分析和/或测试方案，体液采集装置可包括额外的样本储存器（例如，3、4、5、6个或更多个）。

[0070] 在一些实施例中，体液采集装置可包括流计量装置，以确保从患者采集合适体积的体液和/或将合适体积的体液传送到特定的前样本和/或样本储存器中。体液采集装置可被配置为在采集了经计量体积的体液之后自动地转移和/或控制流体流。例如，在采集了第一计量前样本体积之后，转移机构可被配置为将体液流转移到第一样本储存器，然后在采集了第一计量样本体积之后，转移机构可被配置为将体液流转移到第二样本储存器，等等。在一些实施例中，体液采集装置可包括计量体积显示器，诸如，例如，液晶显示器(LCD)，以为使用者提供关于多少体液已经被采集到每个特定的单个样本储存器中的视觉指示。在一些实施例中，可提供多个显示器，以容许定制的前样本和/或样本体积采集。

[0071] 如在本说明书和所附权利要求中使用的，单数形式的冠词可包括复数个指示对象，除非上下文清晰地指示相反。因此，例如，用语“一个构件”意在表示单个构件或多个构件的组合，“一种材料”意在表示一种或多种材料或其组合。

[0072] 如在此使用的，“体液”可包括从患者身体获取的任何流体，包括但不限于，血液、脑脊液、尿液、胆汁、淋巴液、唾液、滑液、血清、胸膜液、羊水等，或其任意组合。

[0073] 如在此使用的，用语“第一预定量”、“第一量”和“第一体积”描述被配置为由第一储存器或前样本储存器接收或容纳的体液的量。虽然用语“第一量”和“第一体积”未明确描述预定量，但应该理解，第一量是第一预定量，除非存在明确的不同描述。

[0074] 如在此使用的，用语“第二量”和“第二体积”描述被配置为由第二储存器或样本储存器接收或容纳的体液的量。第二量可以是任何合适的体液量，不必是预定的。相反，当明确地如此描述时，第二储存器或样本储存器接收或容纳的第二量可以是第二预定量。

[0075] 如在此使用的，用语“组”可涉及多个特征或具有多个部分的单个特征。例如，当涉及一组壁时，一组壁可被认为是具有不同部分的一个壁，或者一组壁可为认为是多个壁。另一种类似的表述是，整体构造的项可包括一组壁。所述一组壁可包括例如彼此不连续的多个部分。一组壁还可由单独生产、之后接合在一起（例如，经由焊接、粘合剂或任何合适的方法）的多个项制成。

[0076] 如在此使用的，词语“近端”和“远端”分别涉及靠近和远离使装置与患者接触的使用者的方向。因此，例如，首先接触患者身体的装置端部将是远端，而装置的相反端（例如，使用者操纵的装置端部）将是装置的近端。

[0077] 如在此使用的，在与数值一起使用时，用语“约”、“近似”和“大体上”意在传达的是如此限定的值名义上是表述值。换言之，在与数值一起使用时，用语约、近似和大体上通常包括表述值±给定公差。例如，在一些情形中，合适的公差可以是表述值的±10%；因此，约0.5将包括0.45和0.55，约10将包括9至11，约1000将包括900至1100。在其他

情形中，合适的公差可以表述值的最后一位有效数字的 ± 可接受百分比。例如，合适的公差可以是最后一位有效数字的 ±10％；因此，约 10.1 将包括 10.09 和 10.11，约 25 将包括 24.5 和 25.5。这些变化可由制造公差或其他实际考虑（诸如，例如，与测量工具或可接受的人为误差等相关的公差）决定。

[0078] 当描述体液的预定体积和体液的采集体积之间的关系时，应该理解所述值包括合适的公差，诸如上文描述的那些。例如，当表述体液的采集体积大体上等于体液的预定体积时，采集体积和预定体积在合适的公差内名义上相等。在一些情形中，公差可由采集体积的体液的目的用途决定。例如，在一些情形中，当血液的采集体积在制造商（或最佳循证实践）的建议量的 1.0％至 5.0％内时血液培养物的化验的准确率可约为 99％。例如，体液化验的制造商建议量可为每个样本采集瓶 10 毫升 (mL)，总计使用四至六个采集瓶（即，总体积 40ml 至 60ml），对于约 99％的可信度 ±5％。因此，10.5mL 的采集体积将提供超过约 99％可信度的结果，而 11mL 的采集体积将提供小于约 99％可信度的结果。在其他情形中，合适的公差可以为 0.1％、0.5％、1.0％、2.0％、3.0％、4.0％、5.0％、6.0％、7.0％、8.0％、9.0％、10.0％或其之间的百分比的任何分数。在其他情形中，公差可大于 10.0％。因此，本文描述的任何实施例可包括被配置为计量流和 / 或以其他方式测量合适公差内的体液体积的任何合适的流计量机构和 / 或装置，和 / 或与这样的机构和 / 或装置一起使用。此外。流计量机构和 / 或装置可被布置为用以最小化或消除可由不准确的测量和 / 或人为误差等的组合导致的公差叠加。

[0079] 图 1 是根据实施例的体液采集装置 100 的一部分的示意图。一般来说，体液采集装置 100（在此被称作“流体采集装置”或“采集装置”）被配置为允许从患者抽取体液，从而使得第一部分或体积的抽取流体被转移远离将用作生物样本（诸如，为医疗诊断和 / 或治疗而进行测试）的第二和 / 或第三部分或体积的抽取流体。换言之，采集装置 100 被配置为将第一预定体积的体液传送到前样本采集储存器，并将第二和第三体积（或者，在一些实施例中，第四、第五等等）的体液传送到与前样本采集储存器流体隔离的一个或多个样本采集储存器，如本文更详细地描述的。

[0080] 采集装置 100 包括转移机构 120、流控制器 140、前样本储存器 170、第一样本储存器 180 和不同于第一样本储存器 180 的第二样本储存器 190。转移机构 120 包括入口端口 121 和至少两个出口端口，诸如第一出口端口 125 和第二出口端口 126，如图 1 所示。在一些实施例中，转移机构 120 可包括与前样本储存器和样本储存器的总数相等的一组出口端口。例如，当采集装置 100 具有一个前样本储存器和四个样本储存器时，转移机构 120 可包括五个出口端口。在一些实施例中，转移机构 120 能够可操作地耦接到致动器（图 1 未示出），其可辅助转移机构 120 在多个配置之间的移动。入口端口 121 被配置为流体耦接到用于限定将体液从患者抽取和 / 或输送到采集装置 100 的路径 X 的医疗装置上。例如，入口端口 121 可流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。以此方式，转移装置 120 可经由针头或任何其他内腔限定装置从患者接收体液。

[0081] 转移机构 120 的第一出口端口 125 可流体耦接到前样本储存器 170。在一些实施例中，前样本储存器 170 与第一出口端口 125 和 / 或转移机构 120 的一部分一体形成。在其他实施例中，前样本储存器 170 可经由粘合剂、阻力配合、机械紧固件、任意数量的配合凹口、螺纹耦接和 / 或任何其他合适的耦接或其组合而机械地和 / 或流体地耦接到转移机

构 120。另一种类似的表述是，前样本储存器 170 可物理地（例如，机械地）耦接到转移机构 120，从而使得前样本储存器 170 所限定的内部容积与转移机构 120 的第一出口端口 125 流体连通。在其他实施例中，前样本储存器 170 可经由中间结构（图 1 未示出），诸如柔性无菌管，可操作地耦接到转移机构 120 的第一出口端口 125。更具体地，该中间结构可限定被配置为使前样本储存器 170 与第一出口端口 125 流体连通的内腔。

[0082] 前样本储存器 170 被配置为接收和容纳第一预定体积的体液。在一些实施例中，前样本储存器 170 被配置为容纳第一体积的体液，从而使得第一体积与随后从患者抽取的第二和 / 或第三体积的体液（其可与第一体积的体液相同或不同）流体隔离开。前样本储存器 170 可以是用于容纳体液的任何合适的储存器，诸如，2012 年 6 月 12 日公布的名称为“Systems and Methods for Parenterally Procuring Bodily-Fluid Samples with Reduced Contamination”的美国专利 No.8,197,420（在下文中称作“‘420 专利”）中详细描述的前样本储存器，该专利的全部公开内容通过引用合并于此。

[0083] 在一些实施例中，转移机构 120 的第二出口端口 126 被配置为流体耦接到内腔限定装置上，该内腔限定装置可耦接到第一样本储存器 180 和第二样本储存器 190。可选地，在其他实施例中，转移机构 120 的第二出口端口 126 可耦接到第一样本储存器 180，并且转移机构 120 可具有耦接到第二样本储存器 190 上的第三出口端口（未示出）。在一些实施例中，第一样本储存器 180 可与第二出口端口 126 和 / 或转移机构 120 的一部分一体形成。在其他实施例中，第一样本储存器 180 可机械耦接到第二出口端口 126 或经由中间结构（诸如，上文参照前样本储存器 170 描述的）可操作地耦接到第二出口端口 126。第一样本储存器 180 被配置为接收和容纳第二体积的体液。例如，第二体积的体液可以是在抽取第一前样本体积之后从患者抽取的量。在一些实施例中，第一样本储存器 180 被配置为以第二体积与第一体积的前样本体液流体隔离的方式容纳第二体积的体液。

[0084] 第一样本储存器 180 和第二样本储存器 190 可以是用于容纳体液的任何合适的无菌储存器，包括例如上文通过引用合并的‘420 专利中描述的样本储存器。在一些实施例中，第二体积可以是任何合适的体液体积并且不需要是预定的。在一些实施例中，将体液传送到第一样本储存器 180 和 / 或第二样本储存器 190 可被计量等，从而使得第二体积是第二预定体积。

[0085] 第二样本储存器 190 可以是任何合适的样本储存器。在一些实施例中，第二样本储存器 190 可大体上类似于上述第一样本储存器 180。第二样本储存器 190 可如上所述地流体耦接到第二出口端口 126。第二出口端口 126 与第二样本储存器 190 的流体耦接可大体上类似于第二出口端口 126 与第一样本储存器 180 的流体耦接。因此，在此不进一步详细描述这些部分，并且应该认为大体上类似，除非存在明确的不同描述。此外，转移机构 120 的其他出口端口和样本储存器（图 1 未示出）可大体上类似于第二出口端口 126 和第一样本储存器 180。

[0086] 在一些实施例中，前样本储存器 170、第一样本储存器 180 和第二样本储存器 190 可以类似方式耦接到转移机构 120（或与其形成在一起）。在其他实施例中，前样本储存器 170、第一样本储存器 180 和第二样本储存器 190 不必以类似方式耦接到转移机构 120。例如，在一些实施例中，前样本储存器 170 可与转移机构 120（例如，第一出口端口 124）一体形成，并且第一样本储存器 180 和 / 或第二样本储存器 190 可经由诸如柔性无菌管或其任

意组合的中间结构可操作地耦接到转移机构 120（例如，第二出口端口 126）。

[0087] 在一些实施例中，采集装置 100 可还包括致动器（图 1 未示出）和限定第一流体流路径 142、第二流体流路径 144 和可选的其他流体流路径（图 1 未示出）的流控制器 140。在一些实施例中，致动器可包括在转移机构 120 中或以其他方式可操作地耦接到转移机构 120。以此方式，致动器可被配置为控制流控制器 140 内的流体移动（例如，在不同配置之间）。例如，致动器可在对应于流控制器 140 的第一配置的第一位置、与第一位置不同的对应于流控制器 140 的第二配置的第二位置等等之间移动。在一些实施例中，致动器可被配置为单向移动。例如，致动器可从其第一位置移动到其第二位置，但不能从其第二位置移动到其第一位置。类似地，致动器可从其第二位置移动到第三位置，但不能从其第三位置移动返回其第二位置。以此方式，防止流控制器 140 在移动到其第一配置之前移动到其第二或第三配置，因此需要将第一量体液引导到前样本储存器 170 中，而非被设计为容纳将用作生物样本（诸如，为医疗诊断和 / 或治疗而进行测试）的第二和 / 或第三部体积的抽取流体的样本储存器 180 和 / 或 190 中。

[0088] 流控制器 140 被配置为使得，当处于第一配置时，第一流体流路径 142 将入口端口 121 流体耦接到第一出口端口 125，并且当处于第二配置时，第二流体流路径 144 将入口端口 121 流体耦接到第二出口端口 126。在一些实施例中，如上所述的致动器可被配置为在第一配置和第二配置以及可选的第三或第四配置之间以平移方式移动流控制器 140。例如，在一些实施例中，当流控制器 140 相对于采集装置 100 处于远端位置时，流控制器 140 可处于第一配置。在这类实施例中，致动器可被致动，以相对于采集装置 100 沿近端方向将流控制器 140 移动到近端位置，由此使流控制器 130 处于第二配置。在其他实施例中，致动器也可被致动，以在第一配置和第二配置或可选的第三或第四配置之间以旋转运动方式移动流控制器 140。

[0089] 因此，当流控制器 140 处于第一配置时，第二出口端口 126（以及耦接到相同储存器的可选的其他出口端口）与入口端口 121 流体隔离。类似地，当流控制器 140 处于第二配置时，第一出口端口 125 与入口端口 121 流体隔离。并且可选地，如果流控制器 140 处于第三配置（图 1 未示出），则第一出口端口 125 和第二出口端口 126 与入口端口 121 流体隔离。以此方式，当流控制器 140 处于第一配置时，流控制器 140 可经由第一出口端口 125 将第一量的体液引导或转移到前样本储存器 170，并且当流控制器 140 处于第二配置时，流控制器 140 可经由第二出口端口 126 将第二量的体液引导或转移到第一样本储存器 180。

[0090] 在一些实施例中，致动器的至少一部分可以可操作地耦接到前样本储存器 170。以此方式，致动器（或至少致动器的所述部分）可被配置为在“前样本”流体储存器 170 内引入真空或以其他方式促进真空的产生，由此，当转移机构 120 处于其第一配置时，使体液开始通过采集装置 100 流入前样本流体储存器 170 中。致动器可包括用于促使液体流入采集装置 100 的任何合适的机构，诸如，例如，旋转盘、活塞、滑块、转盘、按钮、手柄、杠杆和 / 或任何其他合适的机构或其组合。在此参照特定实施例更详细地描述合适的致动器的例子。

[0091] 在一些实施例中，转移机构 120 可被配置为需要在转移机构 120 允许第二量的体液流通过转移机构 120 被输送到第一样本流体储存器 180 和 / 或第二样本流体储存器 190 之前将第一量体液输送到前样本流体储存器 170。以此方式，转移机构 120 的特征可被描绘为需要医疗保健行业从业者服从在采集第二和 / 或第三量（例如，样本）体液之前采集第

一预定量（例如，前样本）。另一种类似的表述是，转移机构 120 可被配置为防止医疗保健行业从业者在未首先将第一量或前样本体液转移到前样本储存器 170 的情况下将第二量或样本体液采集到第一样本储存器 180 中。以此方式，防止医疗保健行业从业者将第一量体液包括（无论是有意的还是无意的）在用于分析的体液样本中，该第一量体液更可能含有体表微生物和 / 或其他有害外部污染物。在其他实施例中，流体采集装置 100 不需要包括强制服从特征或部件。

[0092] 在一些实施例中，转移机构 120 可具有与第一、第二和第三配置不同的第四配置（图 1 未示出）。当处于第四配置时，转移机构 120 可同时将入口端口 121 与第一出口端口 125、第二出口端口 126 和可选的第三出口端口流体隔离。因此，当转移机构 120 处于其第四配置时，防止体液从入口端口 121 流到前样本储存器 170、第一样本储存器 180 和第二样本储存器 190。在使用时，例如，可致动（例如，手动地或自动地）转移机构 120，以使转移机构 120 处于第一配置，从而使得体液从入口端口 121 流到前样本储存器 170，然后移动到第二配置，从而使得体液可从入口端口 121 流到第一样本储存器 180，并可选地移动到第三配置，从而使得体液可从入口端口 121 流到第二样本储存器 190，然后移动到第四配置，以使体液停止流入和 / 或流过转移机构 120。以此方式，装置被有效地“锁定”并独立地处于第四配置，从而防止装置 100 中任何残留的体液被污染和 / 或以其他方式使医疗保健行业从业者和 / 或患者暴露于潜在的危险流体。此可选的安全特征可防止暴露于可能感染诸如 HIV、丙型肝炎等病原体的体液样本。

[0093] 在一些实施例中，采集装置 100 的一个或多个部分可位于外壳（图 1 未示出）内。例如，在一些实施例中，转移机构 120、第一前样本储存器 170 及样本储存器 180 和 190 中的一个或多个的至少一部分可位于外壳内。在这种实施例中，转移机构 120 的至少一部分可通过外壳，以容许使用者致动流控制器 140，从而控制体液从患者（例如，血管）流到采集装置 100。在此参照特定实施例更详细地描述合适的外壳的例子。

[0094] 在一些实施例中，采集装置 100 可以可选地包括可计量通过采集装置的体液流的一个或多个流计量装置。例如，流计量装置可与第一流体流路径 142 和 / 或第二流体流路径 144 流体连通，以计量通过它们的体液流。在其他实施例中，流计量装置可与第一端口 125 和 / 或第二端口 126 流体连通和 / 或位于其中。流计量装置可包括指示器等（例如，转盘、显示器、颜色、触觉输出装置、电信号输出装置，诸如无线电信号、蓝牙无线电信号等），其可被配置为向使用者提供与传送到前样本储存器 170、第一样本储存器 180 和 / 或第二样本储存器 190 相关的指示。在一些实施例中，流计量装置可以可操作地耦接到例如致动器等，诸如上文描述的那些。在这类实施例中，流计量装置可致动致动器，以基于已流过流计量装置的期望量体液使流控制器 140 在其第一配置和其第二配置之间移动。因此，流计量装置可用于确保期望量的体液被传送到前样本储存器 170、第一样本储存器 180 和 / 或第二样本储存器 190，这继而可防止在例如患者样本等的微生物测试中产生不足的、不准确的和 / 或错误的结果。

[0095] 现在参照图 2-13，采集装置 200 包括转移机构 220、流控制器 240、前样本储存器 270、第一样本储存器 280 和与第一样本储存器 280 不同的第二样本储存器 290。如在此进一步描述的，采集装置 200 可在第一、第二和第三配置之间移动，以传递大体上不存在体外微生物（诸如，例如，皮肤驻留的微生物和 / 或其他有害外部污染物）的体液流。采集装置

200 可具有任何合适的形状、尺寸或配置。例如，尽管图 2-13 示出了样本储存器 280 和 / 或 290 相对于外壳 201 垂直地定向，但采集装置 200 的样本储存器 280 和 / 或 290 可定向在外壳 201 的平面中或相对于外壳 201 成圆锥形地放置，等等。

[0096] 转移机构 220 包括外壳 201 和可移动构件 250 和 250'。如图 2-4 所示，外壳 201 耦接到前样本储存器 270、第一样本储存器 280 和第二样本储存器 290。外壳 201 包括入口端口 221、第一出口端口 230、第二出口端口 231、第三出口端口 232，并限定内部流通道 235，流通道 235 可限定从患者采集体液的流体流路径。入口端口 221 可选择性地与内部流通道 235 流体连通。更具体地，入口通道 221 可限定可与内部流通道 235 流体连通的入口内腔 202。以此方式，入口端口 221 从外壳 201 的一部分延伸出，从而使得内部流通道 235 可经由入口内腔 202 与大体在外壳 201 外的空间流体连通。入口端口 221 可流体耦接到限定将体液从患者抽取和 / 或输送到采集装置 200 的流体流路径的医疗装置（未示出）。例如，入口端口 221 可直接地或经由适配器 204 间接地流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。另一种类似的表述是，当内腔限定装置耦接到入口端口 221 时，入口端口 221 限定的入口内腔 202 与内腔限定装置限定的内腔流体连通。进一步详述，当内腔限定装置位于患者身体的一部分内（例如，在患者的血管或脊柱腔内）时，外壳 201 的内部流通道 235 可与患者身体的该部分流体连通。

[0097] 外壳 201 限定的内部流通道 235 是中心内腔，其沿外壳 201 的长度延伸并且可在静脉穿刺（用于获取体液的其他方法）之后与患者的体液流体连通，如在此描述的。内部流通道 235 形成用于在入口端口 221 和第一出口端口 230、第二出口端口 231 及第三出口端口 232 之间传送体液的流体流路径。更具体地，当内部流通道 235 与患者（经由耦接到入口端口 221 的医疗装置）流体连通时，第一出口端口 230、第二出口端口 231 和第三出口端口 232 可选择性地与内部流通道 235 流体连通，以容许体液流入前样本储存器 270、第一样本储存器 280 或第二样本储存器 290 中的至少一个。在一些实施例中，在预定体积的体液被采集在前样本储存器 270 中之前，阻止体液流到第二出口端口 231 和第三出口端口 232。在一些实施例中，第二出口端口 231 和第三出口端口 232 可同时与内部流通道 235 流体连通。在一些实施例中，第二出口端口 231 和第三出口端口 232 可依次与内部流通道 235 流体连通。

[0098] 可移动构件 250、250' 被配置为被使用者从相对于外壳 201 的第一位置致动到第二位置，以将流体流引导到第一样本储存器 280 和第二样本储存器 290 中。可移动构件 250、250' 大体相同，并因此参照单个可移动构件 250 进行描述。如图 5 所示，可移动构件 250 包括限定内部腔 252 的凸台 251、入口端口 253、第一出口端口 254 和限定流体耦接到内部腔 252 的内腔 256 的刺穿构件 255。入口端口 253 和出口端口 254 延伸通过限定可移动构件 250 的内部腔 252 的凸台 251 的壁。可移动构件 250 被配置为被安装在外壳 201 的支撑件 257（见图 4）上，从而使得凸台 251 位于孔眼 258（见图 4）内并且可移动构件 250 的至少一部分被容纳在环形腔 260 中。可选地，偏置构件 259（例如，弹簧）可位于环形腔 260 中，以使可移动构件 250 在被使用者致动之后返回其第一位置。在一些实施例中，可移动构件 250、环形腔 260、孔眼 258 或凸台 251 可包括被配置为在被使用者致动之后将可移动构件 250 承托在第二位置（例如，下压位置）的机械锁定特征。

[0099] 如在此描述的，在第一配置，以使得可移动构件 250 与内部流通道 235 分隔开的

方式放置可移动构件 250。在这种配置中，不会在患者身体的一部分（例如，血管、脊柱腔等）和样本储存器 280 和 / 或 290 之间建立流体流路径。换言之，当可移动构件 250 处于其第一配置时，第一样本储存器 280 和第二样本储存器 290 与外壳 201 所限定的内部流通道 235 流体隔离开。使用者可致动可移动构件 250，以将可移动构件 250 从第一配置移动到第二配置并与内部流通道 235 对齐。使用者施加的力可足以使偏置构件 259 变形（例如，压缩），由此容许刺穿构件 255 插入样本储存器 280 和 / 或 290 中。在第二配置，入口端口 253 和出口端口 254 与内部流通道 235 大体对齐，使得内部腔 252 与内部流通道 235 流体连通。因此，当可移动构件 250 处于第二配置时，在内部流通道 235、内部腔 252、刺穿构件 255 的内腔 256 和样本储存器 280 之间建立流体流路径。换言之，在这种配置中，体液可从患者（例如，血管、脊柱腔等）通过转移机构 220 流入第一样本储存器 280 和 / 或第二样本储存器 290 中，如在此更详细地描述的。

[0100] 前样本储存器 270 可以是用于容纳体液的任何合适的储存器，诸如，例如，一次性可丢弃式采集管和 / 或基于真空的采集管等。前样本储存器 270 被配置为以任何合适的方式流体耦接到采集装置 200 的第一出口端口 230（直接地或经由中间结构，诸如无菌柔性管）。例如，在一些实施例中，前样本储存器 270 的一部分可在第一出口端口 230 的一部分内形成摩擦配合。在其他实施例中，前样本储存器 270 可经由螺纹耦接、粘合剂、卡扣配合、机械紧固件和 / 或任何其他合适的耦接方法耦接到第一出口端口 230。在一些实施例中，前样本储存器 270 可与万科 201 一体形成。前样本储存器 270 可被配置为保持（前样本储存器 270）内部处于负压状态（真空状态），这可容许经由真空吸力通过出口端口 230 将体液从入口端口 221 抽入前样本储存器 270。前样本储存器 270 被配置为包含第一量体液，其中，第一量体液可以是预定或未定量，使得第一量体液与随后从患者抽取的第二和 / 或第三量体液流体隔离。

[0101] 样本储存器 280 和 / 或 290 可以是用于容纳体液的任何合适的储存器，诸如，例如，一次性可丢弃式采集管、基于真空的采集管和 / 或通过引用合并的 '420 专利中描述的样本储存器等。在一些实施例中，样本储存器 280 和 / 或 290 可以大体类似于或等同于已知的样本容器，诸如，例如，**Vacutainer®** 等。样本储存器 280 和 / 或 290 分别包括样本容器 282 和 292，并分别包括真空密封件 284 和 294。真空密封件 284 或 294 分别保持样本容器 282 或 292 内的负压状态（真空状态），这可容许经由真空吸力将体液分别从内部流通道 235 抽入本容器 282 或 292。样本储存器 280 和 / 或 290 可被配置为以任何合适的方式分别流体耦接到采集装置 200 的第二出口端口 231 和第三出口端口 232（直接地或经由中间结构，诸如无菌柔性管）。可相对于出口端口 231 和 / 或 232 移动样本储存器 280 和 / 或 290，以使样本储存器 280 和 / 或 290 与出口端口 231 和 / 或 232 流体连通。样本储存器 280 和 290 可被配置为包含第二或第三量的体液。第二或第三量的体液可以是预定或未定量，使得第二或第三量的体液与从患者抽取的第一量体液流体隔离。在一些配置中，样本储存器 280 和 / 或 290 可通过以与前样本储存器 270 类似的方式与外壳 201 一体形成而耦接到采集装置 200，因此在此不详细描述。在一些情形中，样本储存器 280 和 / 或 290 可以是透明的，从而使得使用者可具有视觉反馈，以确认流入样本储存器 280 和 / 或 290 的体液流。

[0102] 在一些实施例中，样本储存器 280 和 290 及转移机构 220（和 / 或采集装置 200 的

除样本储存器 280 和 290 之外的部分）单独形成（例如，非一体形成）并在例如制造期间耦接在一起。在一些情形中，可在大体上无菌或密封环境（例如，填充乙撑氧等的环境）中，将样本储存器 280 和 290 耦接到转移机构 220。因此，样本储存器 280 和 290 与转移机构 220 之间的接触面在使用之前大体是无菌的。此外，可以以预组装方式运输和 / 或存储采集装置 200，从而保持样本储存器 280 和 290 与转移机构 220 之间的接触面大体无菌。

[0103] 如图 6 和 7 所示，流控制器 240 包括第一构件 241 和第二构件 245。第一构件 241 被配置为位于外壳 201 的凹口 266（例如，见图 4）中，并且可由生物兼容的任意数量的材料制成，诸如，例如，钛、石墨、热解碳、聚酯、聚碳酸酯、聚亚安酯和 / 或弹性体材料等。在一些实施例中，第二构件 245 用作将第一构件 241 从第一配置移动到第二配置的致动器。更具体地，当第一构件 241 位于凹口 266 中时，第二构件 245 可在第一位置和第二位置之间移动，以在第一和第二配置之间移动流控制器 240。在一些实施例中，外壳 201 可选择性地限制第二构件 245 从其第一位置到其第二位置的移动。在一些实施例中，外壳 201 可被配置为一旦第二构件 245 已经移动到第二位置就阻止其移动。换言之，外壳 201 可包括阻止第二构件 245 从第二位置移动返回第一位置的锁定构件。第二构件 245 和 / 或外壳 201 还可包括机械棘爪和 / 或提供视觉或触觉反馈以确保精确地定位第二构件 245 的其他指示器。

[0104] 第一构件 241 可包括用于在静脉穿刺（和 / 或其他获得患者体液的方法）之后引导流体流的多个通道。例如，如图 6 和 7 所示，第一构件 241 包括第一流通道 242 和第二流通道 244。当第二构件 245 处于第一位置时（例如，见图 8 和 9），流控制器 240 处于第一配置，并且第一流通道 242 在入口端口 221 和第一出口端口 230 之间建立流体连通，同时使入口端口 221 和内部流通道 235 流体隔离。当第二构件 245 处于第二位置时（例如，见图 10-13），流控制器 240 处于第二配置，并且第二流通道 244 在入口端口 221 和内部流通道 235 之间建立流体连通，同时使入口端口 221 和第一出口端口 230 流体隔离。可包括与额外的第一构件 241 的流通道和 / 或流控制器 240 配置相对应的额外第二构件 245 位置，以在患者和采集装置 200 之间进一步引导 / 隔离流体。例如，第二构件 245 可具有与流控制器 240 的第三配置相对应的第三位置，其大体上完全阻止患者和采集装置 200 之间的流体流。换言之，在一些实施例中，在从患者获取了全部体液样本之后，可将转盘移动到第三位置，以相对于外部环境大体上密封采集装置 200 中的样本。

[0105] 在操作时，采集装置 200 可用于从患者采集减少污染（来自皮肤驻留的微生物和 / 或其他有害外部污染物）的体液（例如，血液）。例如，采集装置 200 的入口端口 221 经由适配器 204 流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。在静脉穿刺（或其他体液获得方法）之后，旋转第二构件 245，直到它达到如图 8 和 9 所示的第一位置。替代性地，第二构件 245 可被预设在第一位置，并且采集装置 200 可以其他方式被密封，以保持前样本储存器 270 中的真空和采集装置 200 的无菌性。例如，入口端口 221 和 / 或适配器 204 可包括当采集装置 200 耦接到针头或其他内腔限定装置时打开的阀。

[0106] 如上所述，当第二构件 245 处于第一位置时，流控制器 240 处于第一配置，并且第一构件 241 的第一流通道 242 在入口端口 221 和第一出口端口 230 之间建立流体连通，同时使入口端口 221 和内部流通道 235 流体隔离。此外，在第一配置中，第一和第二样本储存器 280 和 290 与入口端口 221 流体隔离，并且在患者身体的一部分（例如，血管）和前样本储存器 270 之间限定流体流路径，如图 9 的箭头 AA 所示。如上所述，采集装置 200 中使用

的流体储存器，诸如，前样本储存器 270 及样本储存器 280 和 290，可被配置为限定负压（例如，小于采集装置 200 正在从其抽取体液的身体部分的流体压力的压力），从而使得一旦在患者身体的一部分（例如，血管）和前样本储存器 270 之间建立流体连通，前样本储存器 270 内的负压就会使前样本储存器 270 和患者身体的所述部分之间的压力差将体液抽入样样本储存器 270。在此第一配置，流控制器 240 还使前样本储存器 270 与内部流通道 235 流体隔离。因此，第一量（预定的或未定的）体液可在静脉穿刺（例如）之后立即被容纳到前样本储存器 270 中并与随后的样本隔离。以此方式，采集装置 200 可用于防止第一量体液（其最可能含有体表微生物和 / 或其他有害的外部污染物）污染随后量的体液样本，这些体液样本被采集并用于可受污染物影响的诊断或其他测试。

[0107] 在前样本储存器 270 中采集了所述体积的体液前样本之后，可旋转第二构件 245 直到它达到其第二位置，如图 10 和 11 所示。当第二构件 245 处于第二位置时，流控制器 240 处于第二配置，并且第一构件 241 的第二流通道 244 在入口端口 221 和内部流通道 235 之间建立流体连通，同时使第一出口端口 230（即，前样本储存器 270）与入口端口 221 流体隔离。换言之，在第二配置，流控制器 240 经由第二流通道 244 在患者身体的一部分（例如，血管）和内部流通道 235 之间建立流体流路径，如图 11 的箭头 BB 所示。

[0108] 当流控制器 240 处于第二配置时，使用者可将可移动构件 250 和 / 或 250’从第一位置致动（即，按压）到第二位置，以在患者身体的一部分（例如，血管）与第一样本储存器 280 和 / 或第二样本储存器 290 之间建立流体连通。更具体地，将可移动构件 250 从其第一位置移动到其第二配置，从而使刺穿构件 255 以刺穿构件 255 可穿透位于样本容器 282 内的第一样本储存器 280 的真空密封件 284 的方式穿过出口端口 231，如图 12 的箭头 CC 所示。当处于第二位置时，可移动构件 250 的入口端口 253 和出口端口 254 与内部流通道 235 大体对齐并流体连通，这容许体液从内部流通道 235 流入可移动构件 250 的内部腔 252 并离开刺穿构件 255 的内腔 256 进入第一样本储存器 280。样本储存器 280 和内部流通道 235 之间的压力差（例如，真空或负压）将体液抽入样本储存器 280。换言之，在第二配置，可移动构件 250 在内部流通道 235 和第一样本储存器 280 之间建立流体流路径，如图 12 的箭头 DD 所示。一旦期望量的体液（例如，第二量）被采集在第一样本储存器 280 中，使用者就可释放可移动构件 250，容许偏置构件 259 将按钮 250 移动回其第一位置。当可移动构件 250 返回其第一位置时，刺穿构件 255 被移离第一样本储存器 280，并且密封件 284（例如，独立密封隔膜）使第一样本储存器 280 与内部流通道 235 流体隔离。

[0109] 以类似方式，当流控制器 240 处于第二配置时，使用者可将可移动构件 250’从其第一位置致动（即，按压）到其第二位置，如图 13 的箭头 EE 所示。以此方式，以与上述可移动构件 250 和第一样本储存器 280 类似的方式，在患者身体的一部分（例如，血管）和第二样本储存器 290 之间（经由出口端口 232）建立流体连通。换言之，在第二配置，可移动构件 250’在内部流通道 235 和第二样本储存器 290 之间建立流体流路径，如图 13 的箭头 FF 所示。一旦期望量的体液（例如，第三量）被采集在第二样本储存器 290 中，使用者就可释放可移动构件 250’，容许偏置构件 259’将按钮 250’移动回其第一位置。尽管被示出和描述为按顺序的过程，但不必要求填充顺序和 / 或排序（即，不必必须在样本储存器 290 之前填充样本储存器 280，等等）。换言之，一旦流控制器 240 被移动到第二配置，就可按任何顺序、在同一时刻（例如，同时）和 / 或以重叠的时间间隔填充第一样本储存器 280 和第

二样本储存器 290（和任何额外的样本储存器）。例如，使用者可开始填充第一样本储存器 280，然后在部分地填充第一样本储存器 280 之后，使用者可按压可移动构件 250'，以填充第二样本储存器 290，而第一样本储存器 280 填充完成。此外，通过反复致动（插入）可移动构件 250 和 / 或 250' 可调整样本储存器 280 和 / 或 290 中采集的体液的体积。如上所述，第二构件 245 可具有与流控制器 240 的第三配置相对应的第三位置，其可大体上完全阻止患者和采集装置 200 之间的流体流，以相对于外部环境大体上密封采集装置 200 中的样本。

[0110] 尽管图 2-13 未示出，但采集装置 200 可包括可被配置为计量被传送到前样本储存器 270、第一样本储存器 280 和 / 或第二样本储存器 290 的体液体积的流计量装置等。例如，在一些实施例中，流控制器 240 的第一构件 241 可包括与第一流通道 242 和第二流通道 244 流体连通的流计量装置。在其他实施例中，流计量装置可位于可移动构件 250 和 / 或 250' 的内部腔 252 内。因此，可计量和 / 或控制被传送到和位于第一样本储存器 280 和第二样本储存器 290 中的体液样本的体积，从而使得位于每个样本储存器 280 和 290 中的体液的体积是预定体积，诸如，例如，10mL、20mL、30mL 等。

[0111] 尽管采集装置 200 被示出和描述为包括第一样本储存器 280 和第二样本储存器 290，但在其他实施例中，采集装置可包括任意数量的前样本和 / 或样本储存器。例如，图 14 和 15 图示了根据实施例的采集装置 300。如图所示，采集装置 300 的某些方面可与以上参照图 2-13 描述的采集装置 200 的相应方面大体类似。因此，在此不进一步详细描述类似的方面。

[0112] 如图 14 和 15 所示，采集装置 300 包括转移机构 320、流控制器 340、前样本储存器 370、第一样本储存器 380、第二样本储存器 380'、第三样本储存器 390 和第四样本储存器 390'。前样本储存器 370 可大体类似于上文详细描述的前样本储存器 270。在一些实施例中，样本储存器 380、380'、390 和 390' 可大体类似于上文详细描述的样本储存器 280 和 290。在一些实施例中，样本储存器 380、380'、390 和 390' 可具有大体相同的形状和尺寸并包括例如大体相同的培养介质。在其他实施例中，样本储存器 380、380'、390 和 390' 可具有大体相同的形状和尺寸并包括需氧培养介质或厌氧培养介质中的一种。例如，在一些实施例中，第一样本储存器 380 和第三样本储存器 390 可包括需氧培养介质，而第二样本储存器 380' 和第四样本储存器 390' 可包括厌氧培养介质。在其他实施例中，样本储存器 380、380'、390 和 390' 可各自包括处于任何布置或组合的需氧或厌氧培养介质。

[0113] 转移机构 320 包括外壳 301 和一组可移动构件 350、350'、350"、350"'。可移动构件 350、350'、350"、350"' 例如大体类似于上文参照图 5 描述的可移动构件 250。因此，可移动构件 350、350'、350"、350"' 可相对于外壳 301 在第一位置和第二位置之间移动，以分别与样本储存器 380、380'、390 和 390' 流体连通。外壳 301 包括和 / 或限定入口端口 321、被配置为与前样本储存器 370 流体连通的第一出口端口 330、被配置为与第一样本储存器 380 流体连通的第二出口端口 331、被配置为与第二样本储存器 380' 流体连通的第三出口端口 332、被配置为与第三样本储存器 390 流体连通的第四出口端口 333 和被配置为与第四样本储存器 390' 流体连通的第五出口端口 334。此外，外壳 301 限定内部流通道 335，流通道 335 可以与上文参照外壳 201 的内部流通道 235 描述的类似方式选择性地与入口端口 321 和出口端口 331、332、333 和 334 流体连通。

[0114] 例如，流控制器 340 大体类似于上文参照图 6-13 描述的流控制器 240。因此，流控制器 340 可在第一配置和第二配置之间旋转，以选择性地限定患者和前样本储存器 370 或样本储存器 380、380'、390 和 390' 之间的流体流路径的一部分。以此方式，使用者可用与上文参照图 8-13 中的采集装置 200 描述的类似方式操纵采集装置 300。因此，第一体积的体液可被传送到并位于前样本储存器 370 中，并且随后体积的体液可被传送到并位于样本储存器 380、380'、390 和 390' 中。

[0115] 图 16-22 图示根据实施例的采集装置 400。采集装置 400 包括转移机构 420、流控制器 440 和样本储存器 480、480'、490 和 490'。如在此进一步描述的，采集装置 400 可在第一、第二、第三、第四和第五配置之间移动，以传递大体上不存在体外微生物（诸如，例如，皮肤驻留的微生物和 / 或其他有害外部污染物）的体液流。采集装置 400 可具有任何合适的形状、尺寸或配置。例如，尽管图 16-22 示出了样本储存器 480、480'、490 和 490' 相对于外壳 401 垂直地定向，但采集装置 400 的样本储存器 480、480'、490 和 490' 可相对于外壳 401 定向在任何合适的平面中或相对于外壳 401 成圆锥形地放置，等等。

[0116] 样本储存器 480、480'、490 和 490' 在形式和功能上大体类似于或等同于采集装置 200 的样本储存器 280 和 / 或 290，因此这里不详细描述。如上所述，样本储存器 480、480'、490 和 490' 保持负压状态（真空状态），这可容许经由吸力将体液从患者抽入样本储存器 480、480'、490 和 490'。在一些实施例中，样本储存器 480 和 480' 可以是需氧培养瓶，样本储存器 490 和 490' 可以是厌氧培养瓶，并且采集装置 400 可用于通过单次静脉穿刺采集多个需氧和多个厌氧血液培养样本。如在此进一步详细描述的，样本储存器 480、480'、490 和 490' 可各自与转移机构 420 的至少一部分流体连通，以接收一定体积的体液样本。体液样本的体积可以是预定或未定的量。此外，一旦期望量的体液位于样本储存器 480、480'、490 和 490' 中，每个样本储存器 480、480'、490 和 490' 就可与转移机构 420 的至少一部分流体隔离，如在此进一步详细描述的。

[0117] 转移机构 420 包括外壳 401 和分配构件 429。转移机构 420 的外壳 401 物理地和流体地耦接到分配构件 429，并提供和 / 或限定用于从患者采集体液的一组流体流路径。外壳 401 限定凹口 466 和一组出口孔口 403。凹口 466 被配置为容纳包括在流控制器 440 中的密封构件 441，如在此进一步详细描述的。该组出口孔口 403 包括第一出口孔口 403a、第二出口孔口 403b、第三出口孔口 403c、第四出口孔口 403d 和第五出口孔口 403e，它们各自被配置为限定与分配构件 429 的不同部分流体连通的不同流体流路径。更具体地，分配构件 429 限定和 / 或形成与第一出口孔口 403a 流体连通的前样本储存器 470 的至少一部分以及与第二出口孔口 403b 流体连通的第一流通道 435a、与第三出口孔口 403c 流体连通的第二流通道 435b、与第四出口孔口 403d 流体连通的第三流通道 435c 和第五出口孔口 403e 流体连通的第四流通道 435。

[0118] 如图 17 和 18 所示，分配构件 429 限定腔或空间，所述腔或空间限定前样本储存器 470 的至少一部分。前样本储存器 470 被配置为容纳体液，诸如，例如，血液、血浆和 / 或尿液等。外壳 401 的第一出口孔口 403a 可与前样本储存器 470 的开口部分大体对齐，以容许前样本储存器 470 接收来自患者的体液流。例如，前样本储存器 470 可接收和容纳第一量或体积的体液，其中，体液的第一量可以是预定的或未定的量。此外，转移机构 420 的布置可使得前样本储存器 470 保持与流通道 435a、435b、435c 和 435d 和 / 或随后从患者抽取的

多部分体液流体隔离，如在此进一步详细描述的。尽管上文将前样本储存器 270 和 370 描述为保持负压，但前样本储存器 470 不保持负压状态（真空状态），因而其他机制，诸如，例如，重力可用于将体液抽入前样本储存器 470 中。

[0119] 流通道 435a-435d 从分配构件 429 的中心沿径向延伸并被布置为使得每个流通道 435a、435b、435c 和 435d 与前样本储存器 470 和其他流通道流体隔离。以此方式，流通道 435a、435b、435c 和 435d 可引导和 / 或以其他方式限定第一端部（分别与出口孔口 403b、403c、403d 和 403e 大体对齐）和第二端部之间的流体流路径。如图 17 和 18 所示，分配构件 429 限定位于第一流通道 435a 的第二端部处的第一出口端口 431、位于第二流通道 435b 的第二端部处的第二出口端口 432、位于第三流通道 435c 的第二端部处的第三出口端口 433 和位于第四流通道 435d 的第二端部处的第四出口端口 434。此外，分配构件 429 包括第一刺穿构件 455a、第二刺穿构件 455b、第三刺穿构件 455c、第四刺穿构件 455d，它们分别物理地和流体地耦接到第一出口端口 431、第二出口端口 432、第三出口端口 433、第四出口端口 434。因此，刺穿构件 455a-355d 可用于穿透样本储存器 480、480'、490 和 490'的真空密封件，这可使体液开始流动，如在此进一步详细描述的。尽管图 17 和 18 未示出，但样本储存器 480、480'、490 和 490'可以任何合适的方式物理地耦接到分配构件 429 的一部分上（直接地或经由中间结构，诸如无菌柔性管），这可容许样本储存器 480、480'、490 和 490' 分别与出口端口 431、432、433 和 434 流体连通。

[0120] 流控制器 440 包括转盘 445 和密封构件 441。密封构件 441 位于外壳 401 的凹口 466（例如，见图 20）中。更具体地，流控制器 440 可耦接到外壳 401，从而使得密封构件 441 位于限定凹口 466 的外壳 401 的表面和转盘 445 的表面之间并与两个表面接触。此外，密封构件 441 可具有这样的尺寸和形状，即，当流控制器 440 耦接到外壳 401 时，使得密封构件 441 与转盘 445 的表面和限定凹口 466（例如，见图 20）的外壳 401 的表面形成大体流体密封的密封结构，如在此进一步详细描述的。密封构件 441 可由任意数量的生物兼容材料制成，诸如，例如，硅酮、聚乳酸、聚乙交酯、聚乳酸 - 羟基乙酸共聚物 (PLGA)、聚酸酐、聚原酸酯、聚醚、聚已酸内酯、聚酰胺酯、聚丁酸、聚戊酸、聚氨酯、尼龙、聚酯、聚碳酸酯、聚丙烯酸酯、醋酸乙烯酯和其他酰基取代纤维素乙酸酯的聚合物、聚苯乙烯、聚氯乙烯、聚氟乙烯、聚乙烯咪唑、聚烯烃氯磺酸、聚环氧乙烷和 / 或其共混物和共聚物。

[0121] 如图 17 所示，密封构件 441 限定可在静脉穿刺（或其他获得体液的方法）之后引导体液流的一组孔口 444。例如，由密封构件 441 限定的该组孔口 444 包括第一孔口 444a、第二孔口 444b、第三孔口 444c、第四孔口 444d 和第五孔口 444e。密封构件 441 的布置使得，当密封构件 441 处于凹口 466 中时，第一孔口 444a、第二孔口 444b、第三孔口 444c、第四孔口 444d 和第五孔口 444e 分别与外壳 401 的第一出口孔口 403a、第二出口孔口 403b、第三出口孔口 403c、第四出口孔口 403d 和第五出口孔口 403e 大体对齐。

[0122] 流控制器 440 的转盘 445 可旋转地耦接到外壳 401 上并且可相对于外壳 401 在第一位置、第二位置、第三位置、第四位置和第五位置之间移动。转盘 445 包括限定内腔 402 的入口端口 421。入口端口 421 可流体耦接到限定用于将体液从患者抽取和 / 或输送到采集装置 400 的流体流路径的医疗装置（未示出）。例如，入口端口 421 可直接地或经由适配器 404 间接地流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。另一种类似的表述是，当内腔限定装置耦接到入口端口 421 时，入口端口 421 限定的入口内腔 402 与内腔限

定装置限定的内腔流体连通。以此方式，入口端口 421 可被配置为选择性地使前样本储存器 470、第一样本储存器 480、第二样本储存器 480'、第三样本储存器 490 和第四样本储存器 490' 与患者流体连通，如在此进一步详细描述的。

[0123] 如上所述，转盘 445 可在第一、第二、第三、第四和第五位置之间移动。当转盘 445 处于第一位置时，流控制器 440 处于第一配置，并且入口端口 421 可与密封构件 441 的第一孔口 444a 和外壳 401 的第一出口孔口 403a 大体对齐。以此方式，密封构件 441 的第一孔口 444a 在入口端口 421 和第一出口孔口 403a 之间建立流体连通，同时使入口端口 421 与出口端口 403b、403c、403d 和 403e 流体隔离，这继而使入口端口 421 与流通道 435a-335d 流体隔离。当第一出口端口 403a 与前样本储存器 470 的开口部分对齐时，第一孔口 444a 和第一出口孔口 403a 在入口端口 421 和前样本储存器 470 之间建立流体连通。当转盘 445 被旋转（或被致动）到第二位置时，流控制器 440 处于第二配置，并且第二出口孔口 444b 在入口端口 421 和第二出口孔口 403b 之间建立流体连通，同时使入口端口 421 与出口端口 403a、403c、403d 和 403e 流体隔离。当第二出口孔口 403b 与第一流通道 435a 的第一端部对齐时，第二孔口 444b 和第二出口孔口 403b 在入口端口 421 和第一流通道 435a 之间建立流体连通。

[0124] 当转盘 445 被旋转到第三、第四和第五位置时，采集装置 400 以类似方式工作。因此，当入口内腔 402 与患者（例如，经由耦接到入口端口 421 的医疗装置）流体连通时，第一出口端口 430、第二出口端口 431、第三出口端口 432、第四出口端口 433 和第五出口端口 434 可选择性地与入口内腔 402 流体连通，以容许全部体液流入样本储存器 480、480'、490 和 490' 中的一个或多个或前样本储存器 470 中的至少一者。在一些实施例中，可包括与额外的密封出口孔口和 / 或流控制器 440 的配置相对应的额外的转盘 445 的位置，以在患者和采集装置 400 之间进一步引导 / 隔离流体流。例如，转盘 445 可具有对应于流控制器 440 的第六配置的第六位置，其大体完全阻止患者和采集装置 400 之间的流体流。换言之，在一些实施例中，在从患者获取全部体液样本之后，转盘 445 可移动到第六位置，以相对于外部环境大体密封采集装置 400 中的样本。

[0125] 在一些实施例中，防止体液流到与样本储存器相连的出口端口（例如，出口端口 431-434），直到在前样本储存器 470 中采集了预定体积的体液。在一些实施例中，与样本储存器相连的出口端口（例如，出口端口 431-434）仅能依次与入口内腔 402 流体连通（例如，出口端口 431 必须在出口端口 432 之前与入口内腔 402 流体连通，等等）。在一些实施例中，与随后的样本储存器相连的出口端口（例如，出口端口 432-434）仅能在已经采集确定体积的体液之后与入口内腔 402 流体连通。在一些实施例中，与样本储存器相连的出口端口（例如，出口端口 431-434）可按任何随机方式、对顺序没有任何偏好地与入口内腔 402 流体连通（例如，出口端口 434 可在出口端口 431 之前与入口内腔 402 流体连通，出口端口 432 可在出口端口 433 之前与入口内腔 402 流体连通，等等）。

[0126] 在一些实施例中，外壳 401 可选择性地限制转盘 445 从其第一位置到其第二、第三、第四和第五位置的移动。在一些实施例中，外壳 401 可被配置为一旦转盘 445 已经移动到第五位置就阻止其移动。换言之，外壳 401 可包括阻止转盘 445 从第五位置移动返回第一位置的锁定机构。转盘 445 和 / 或外壳 401 还可包括机械棘爪和 / 或提供视觉或触觉反馈以确保相对于外壳 401 的出口孔口 403a-403e 精确地定位转盘 445 的其他指示器。

[0127] 在操作时，采集装置400可用于从患者采集减少污染的体液（例如，血液、血浆和/或尿液等）。例如，采集装置400的入口端口421流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。在静脉穿刺（或其他体液获得方法）之后，致动（或旋转）转盘445，直到它达到如图19和20所示的第一位置。替代性地，转盘445可被预设在第一位置，并且采集装置400可以其他方式被密封，以保持采集装置400的无菌性。例如，入口端口421可包括当采集装置400耦接到针头或其他内腔限定装置时打开的阀。

[0128] 如上所述，当转盘445处于第一位置时，流控制器440处于第一配置，并且密封构件441的第一孔口444a在入口端口421和第一出口端口430（包括在外壳401中）之间建立流体连通，同时使入口端口421和四个流通道435a-335d流体隔离。此外，在第一配置中，样本储存器480、480'、490和490'与入口端口421流体隔离，并且在患者身体的一部分（例如，血管）和前样本储存器470之间限定流体流路径，如图20的箭头GG所示。在此第一配置，体液（例如，通过重力、真空等）从患者身体的一部分通过入口端口421的入口内腔402、密封构件441的第一孔口444a、第一出口端口430流入前样本储存器470。在第一配置，流控制器440还使前样本储存器470与流通道435a-335d流体隔离。因此，第一量（预定的或未定的）体液可在静脉穿刺（例如）之后立即被容纳到前样本储存器470中并与随后的样本隔离。以此方式，采集装置400可用于防止第一量体液（其最可能含有体表微生物和/或其他有害的外部污染物）污染随后量的体液样本，这些体液样本被采集并用于可受污染物影响的诊断或其他测试。

[0129] 在前样本储存器470中采集了体液前样本之后，可致动（或旋转）转盘445直到它达到其第二位置，如图21和22所示。当转盘445处于第二位置时，流控制器440处于第二配置，并且密封构件441的第二孔口444b在入口端口421和流通道435a之间建立流体连通，同时使前样本储存器470与入口端口421流体隔离。换言之，在第二配置，流控制器440在患者身体的一部分（例如，血管）和流通道435a之间建立流体流路径，如图22的箭头HH所示。当流控制器440处于第二配置时，使用者可将样本储存器480从第一配置致动到第二配置（例如，推动刺穿构件455a），以在患者身体的一部分（例如，血管）与第一样本储存器480之间建立流体连通。

[0130] 如上所述，将样本储存器480移动到第二配置会致使刺穿构件455a穿透样本储存器480的真空密封件，位于样本储存器480内的。在此第二配置，患者身体的所述部分（例如，血管）暴露于来自样本储存器480的由其中的负压状态（真空）产生的真空吸力下。样本储存器480和患者身体的所述部分之间的压力差（例如，真空或负压）将体液抽入样本储存器480。体液从患者身体的所述部分通过入口端口421的入口内腔402、密封构件441的第二孔口444b、外壳401的第二出口孔口403b流入第一流通道435a。真空吸力经由第二出口端口431和刺穿构件455a通过第一流通道435a将体液流抽入样本储存器480。换言之，在第二配置，流控制器440在入口端口421和样本储存器480之间建立流体流路径。一旦期望量的体液（例如，第二量）被采集在样本储存器480中，使用者就可将流控制器440致动（旋转）到第三位置和/或将样本储存器480移回其第一配置，以使样本储存器480与流通道435a隔离。当样本储存器480返回其第一配置时，刺穿构件455a被移离样本储存器480，并且样本储存器480的密封件（例如，独立密封隔膜）使第一样本储存器480与流通道435a流体隔离。当流控制器440分别位于第三、第四和第五配置时，以类似方式填

充其他样本储存器。

[0131] 应该注意，不必要求填充顺序和/或排序（即，不必必须在样本储存器490之前填充样本储存器480，等等）。换言之，可按任何顺序填充第一样本储存器480和第二样本储存器490（和任何额外的样本储存器）。例如，使用者可开始填充第一样本储存器480，然后在部分地填充第一样本储存器480之后，使用者可填充第二样本储存器490。此外，通过反复填充样本储存器480和/或490可调整样本储存器480和/或490中采集的体液的体积。但是，在其他实施例中，可机械地操纵填充顺序，从而使得在确定特定量的体液已经位于第一储存器之前不能进入第二样本储存器，等等。如上所述，转盘445可具有与流控制器440的第六配置相对应的第六位置，其可大体上完全阻止患者和采集装置400之间的流体流，以相对于外部环境大体上密封采集装置400中的样本。

[0132] 尽管采集装置400被示出和描述为包括和/或耦接到一组四个样本储存器（例如，第一样本储存器480、第二样本储存器480'、第三样本储存器490和第四样本储存器490'），但在其他实施例中，采集装置可包括和/或耦接到任意合适数量的样本储存器。例如，图23-25图示了根据实施例的采集装置500。如图所示，采集装置500的某些方面可与以上参照图16-22描述的采集装置500的相应方面大体类似。因此，在此不进一步详细描述类似的方面。

[0133] 采集装置500包括转移机构520、流控制器540和第一样本储存器580和第二样本储存器590。样本储存器580和590可与上文详细描述的样本储存器大体类似。在一些实施例中，样本储存器580和590可具有大体相同的形状和尺寸并可包括大体相同的培养介质。在其他实施例中，样本储存器580和590可具有大体相同的形状和尺寸并可包括需氧培养介质或厌氧培养介质中的一种。在其他实施例中，第一样本储存器580的第一尺寸可大体大于第二样本储存器590的尺寸。

[0134] 如图24和25所示，转移机构520包括外壳501和分配构件529。转移机构520的外壳501物理地和流体地耦接到分配构件529，并提供和/或限定用于从患者采集体液的一组流体流路径。如以上参照外壳401描述的，外壳501可限定凹口以及第一出口孔口503a、第二出口孔口503b和第三出口孔口503c。凹口被配置为容纳包括在流控制器540中的密封构件541，如上文详细描述的。第一出口孔口503a、第二出口孔口503b和第三出口孔口503c在形式和功能上可分别大体类似于外壳401限定的第一出口孔口403a、第二出口孔口403b和第三出口孔口403c。类似地，分配构件529限定与包括在转移机构429中的前样本储存器470、第一流通道435a和第二流通道435b大体类似的前样本储存器570、第一流通道535a和第二流通道535b。因此，前样本储存器570与第一出口孔口503a流体连通，第一流通道535a与第二出口孔口503b流体连通，并且第二流体流通道535b与第三出口孔口503c流体连通，如上文参照转移机构420描述的。如图25所示，分配构件529限定与第一流通道535a和第一刺穿构件555a流体连通的第一出口端口531和与第二流通道535b和第二刺穿构件555b流体连通的第二出口端口532。如上所述，刺穿构件555a和555b可用于穿透样本储存器580和590的真空密封件，这可使体液开始流动，如在此进一步详细描述的。

[0135] 流控制器540包括转盘545和密封构件541。密封构件541位于外壳501的凹口中，如上所述。以此方式，当流控制器540耦接到外壳501时，密封构件541与转盘545的

表面和限定凹口的外壳 501 的表面形成大体流体密封的密封结构。如图 24 和 25 所示，密封构件 541 限定分别与第一出口孔口 503a、第二出口孔口 503b 和第三出口孔口 503c 大体对齐的第一孔口 544a、第二孔口 544b 和第三孔口 544c，如参照密封构件 441 详细描述的。

[0136] 流控制器 540 的转盘 545 在形式和功能上可大体类似于转盘 445，同时具有适于耦接到外壳 501 的尺寸。因此，转盘 545 可以可旋转地耦接到外壳 501 上并且可相对于外壳 501 在第一位置、第二位置和第三位置之间移动。转盘 545 包括限定内腔 502 的入口端口 521，并且入口端口 521 可流体耦接到限定用于将体液从患者抽取和 / 或输送到采集装置 500 的流体流路径的医疗装置（未示出）。以此方式，入口端口 521 可被配置为选择性地设置前样本储存器 570、第一样本储存器 580 和第二样本储存器 590。更具体地，当转盘 545 处于第一位置时，流控制器 540 处于第一配置，并且入口端口 521 可与密封构件 541 的第一孔口 544a 和外壳 501 的第一出口孔口 503a 大体对齐。以此方式，密封构件 541 的第一孔口 544a 在入口端口 521 和第一出口孔口 503a 之间建立流体连通，并因而使入口端口 521 与前样本储存器 570 流体连通，如上文参照采集装置 400 详细描述的。类似地，当转盘 545 被旋转（或被致动）到第二位置时，流控制器 540 处于第二配置，并且第二出口孔口 544b 在入口端口 521 和第二出口孔口 503b 之间建立流体连通，并因而在入口端口 521 和第一流通道 535a 之间建立流体连通；并且当转盘 545 被旋转到第三位置时，流控制器 540 处于第三配置，并且第三出口孔口 544c 在入口端口 521 和第三出口孔口 503c 之间建立流体连通，并因而在入口端口 521 和第二流通道 535a 之间建立流体连通。以此方式，采集装置 500 可用于将第一体积的体液传送到前样本储存器 570，随后用于分别将第二体积和第三体积的体液传送到第一样本储存器 580 和第二样本储存器 590，如上文参照采集装置 400 详细描述的。

[0137] 图 26-33 图示了根据实施例的采集装置 600。采集装置 600 包括转移机构 620、流控制器 640 和样本储存器 680、680’、690 和 690’。如在此进一步描述的，采集装置 600 可在第一、第二、第三、第四和第五配置之间移动，以传递大体上不存在体外微生物（诸如，例如，皮肤驻留的微生物和 / 或其他有害外部污染物）的体液流。采集装置 600 可具有任何合适的形状、尺寸或配置。例如，采集装置 600 的多个方面和 / 或部分在在形式和 / 或功能上大体类似于上述采集装置 100、200、300、400 和 / 或 500 中任何装置的相应方面和 / 或部分。因此，在此不进一步详细描述这类类似的方面和 / 或部分。例如，在一些实施例中，采集装置 600 的样本储存器 680、680’、690 和 690’在形式和 / 或功能上可分别大体类似于和 / 或等同于图 16-22 的采集装置 400 中包括的样本储存器 480、480’、490 和 490’。

[0138] 转移机构 620 包括分配构件 629 和一组耦接构件 637a、637b、637c 和 637d（例如，见图 27）。分配构件 629 与耦接构件 637a、637b、637c 和 637d 流体连通，并被配置为提供和 / 或限定用于从患者采集体液的一组流体流路径。如图 27 和 28 所示，分配构件 629 限定和 / 或形成与前样本储存器 670 流体连通的第一出口端口 630、与第一耦接构件 637a 流体连通的第二出口端口 631、与第二耦接构件 637b 流体连通的第三出口端口 632、与第三耦接构件 637c 流体连通的第四出口端口 633、与第四耦接构件 637d 流体连通的第五出口端口 634。

[0139] 如图 28 所示，分配构件 629 限定腔或空间，所述腔或空间限定前样本储存器 670 的至少一部分。前样本储存器 670 被配置为容纳体液，诸如，例如，血液、血浆和 / 或尿液等。例如，前样本储存器 670 可接收和容纳来自患者的第一量或体积的体液，其中，体液的第一

量可以是预定的或未定的量。此外，转移机构 620 和流控制器 640 的布置可使得前样本储存器 670 保持与耦接构件 637a、637b、637c 和 637d 和 / 或随后从患者抽取的多部分体液流体隔离，如在此进一步详细描述的。以此方式，出口端口 631、632、633 和 634 可在流控制器 640 与各个耦接构件 637a、637b、637c 和 637d 之间引导和 / 或限定流体流路径，如在此进一步详细描述的。在一些实施例中，第一出口端口 630 和前样本储存器 670 的布置在形式和功能上可大体类似于前样本储存器 470 和 / 或 570。因此，这里不进一步详细描述前样本储存器 670。

[0140] 如图 29 所示，第一耦接构件 637a 限定与刺穿构件 655a 流体耦接的流通道 638a。如上所述，耦接构件 637a 可物理地和流体地耦接到分配构件 629。例如，流通道 638a 可接纳分配构件的第二出口端口 631 的一部分，以将耦接构件 637a 物理地和流体地耦接到其上。在一些实施例中，第二出口端口 631 的表面可与限定流通道 638a 的耦接构件 637a 的内表面形成大体流体密封的密封结构（例如，可形成大体气密的密封结构的摩擦配合）。耦接部分 637a 的刺穿构件 655a 在形式和功能上可大体类似于图 16-22 的采集装置 400 中包括的刺穿构件 455a。因此，这里不进一步详细描述刺穿构件 655a。类似地布置第二耦接构件 637b、第三耦接构件 637c 和第四耦接构件 637d。因此，第二耦接构件 637b、第三耦接构件 637c 和第四耦接构件 637d 各自分别包括刺穿构件 655b、655c 和 655d，并各自分别限定流通道 638b、638c 和 638d。如在此进一步详细描述的，第一耦接构件 637a、第二耦接构件 637b、第三耦接构件 637c 和第四耦接构件 637d 可用于选择性地使转移机构 620 分别与第一样本储存器 680、第二样本储存器 680'、第三样本储存器 690 和第四样本储存器 690' 流体连通。

[0141] 如图 30 和 31 所示，流控制器 640 包括转盘 645 和密封构件 641。流控制器 640 的转盘 645 可旋转地位于分配构件 629 内（例如，见图 32 和 33）并且可在第一位置、第二位置、第三位置和第四位置之间移动。转盘 645 包括各自与内部容积 646（例如，见图 30）流体连通的入口端口 621、第一出口端口 647 和第二出口端口 648。内部容积 646 被配置为接纳密封构件 641 的一部分，如在此进一步详细描述的。入口端口 621 可流体耦接到限定用于将体液从患者抽取和 / 或输送到采集装置 600 的流体流路径的医疗装置（未示出）。例如，入口端口 621 可直接地或经由适配器 604（例如，见图 26 和 27）间接地流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。第一出口端口 647 与前样本储存器 670 流体连通。例如，第一出口端口 647 可以可旋转地位于分配构件 629 的第一出口端口 630 中。当转盘 645 分别位于其第一位置、第二位置、第三位置和第四位置时，第二出口端口 648 可选择性地与第二出口端口 631、第三出口端口 632、第四出口端口 633 和第五出口端口 634 流体连通。以此方式，转盘 645 的内部容积 646 可选择性地与前样本储存器 670、第一样本储存器 680、第二样本储存器 680'、第三样本储存器 690 和第四样本储存器 690' 与流体连通，如在此进一步详细描述的。

[0142] 流控制器 640 的密封构件 641 的至少一部分可旋转地位于转盘 645 的内部容积 646 中并可在第一位置和第二位置之间移动。此外，密封构件 641 可具有这样的尺寸和形状，即，使得密封构件 641 的外表面与限定内部容积 646 的至少一部分的转盘 645 的内表面形成大体流体密封的密封结构。如图 31 所示，密封构件 641 限定第一流通道 642 和第二流通道 644。当密封构件 641 处于其在内部容积 646 内的第一位置时，第一流通道 642 在入

口端口 621 和第一出口端口 647 之间建立流体连通，同时使入口端口 621 与第二出口端口 648 流体隔离。类似地，当密封构件 641 处于其在内部容积 646 内的第二位置时，第二流通道 644 在入口端口 621 和第二出口端口 648 之间建立流体连通，同时使入口端口 621 与第一出口端口 647 流体隔离。当转盘 645 旋转到分配构件 629 内的第二、第三和第四位置时，采集装置 600 以类似方式工作。因此，当入口端口 621 与患者（例如，经由耦接到入口端口 621 和 / 或适配器 604 的医疗装置）流体连通时，分配构件 629 的第一出口端口 630、第二出口端口 631、第三出口端口 632、第四出口端口 633 和第五出口端口 634 可选择性地与入口端口 621 流体连通，以容许体液分别流入前样本储存器 670、第一样本储存器 680、第二样本储存器 680'、第三样本储存器 690 和第四样本储存器 690'。

[0143] 在操作时，采集装置 600 可用于从患者采集减少污染的体液（例如，血液、血浆和 / 或尿液等）。例如，采集装置 600 的入口端口 621 流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。在静脉穿刺（或其他体液获得方法）之后，可致动（或旋转）密封构件 641，直到它处于如图 32 所示的第一位置。替代性地，密封构件 641 可被预设在第一位置，并且采集装置 600 可以其他方式被密封，以保持采集装置 600 的无菌性。当密封构件 641 处于其第一位置时，流控制器 640 在入口端口 621 和分配构件 629 的第一出口端口 630 之间建立流体连通，同时使入口端口 621 与耦接构件 637a、637b、637c 和 637d 流体隔离。因此，如图 32 的箭头 II 所示，可按上文参照采集装置 400 描述的类似方式将体液从患者通过入口端口 621、第一流通道 642、转盘 645 的第一出口端口 647 和分配构件 629 的第一出口端口 630 流入前样本储存器 670。

[0144] 在前样本储存器 670 中采集了体液前样本之后，可相对于转盘 645 将密封构件 641 从其第一位置致动（或旋转）到其第二位置。类似地，可相对于分配构件 629 致动（或旋转）转盘 645，直到它达到第二位置，如图 33 所示。当密封构件 641 和转盘 645 处于第二位置时，流控制器 640 处于第二配置，并且密封构件 641 的第二流通道 644 在入口端口 621 和第一耦接构件 637a 的流通道 638a 之间建立流体连通，同时使前样本储存器 670 与入口端口 621 流体隔离。当流控制器 640 处于第二配置时，使用者可将样本储存器 680 从第一配置致动到第二配置（例如，推动刺穿构件 655a），以在患者身体的一部分（例如，血管）与第一样本储存器 680 之间建立流体连通。如上所述，将样本储存器 680 移动到第二配置会致使刺穿构件 655a 穿透样本储存器 680 的真空密封件，位于样本储存器 680 内的。在此第二配置，患者身体的所述部分（例如，血管）暴露于来自样本储存器 680 的由其中的负压状态（真空）产生的真空吸力下。体液从患者身体的所述部分通过入口端口 621、第二流通道 641、第二出口端口 631、流通道 638a 和第一耦接构件 637a 的刺穿构件 655a 进入第一样本储存器 680，如图 33 的箭头 JJ 所示。

[0145] 一旦期望量的体液（例如，第二量）被采集在样本储存器 680 中，使用者就可将流控制器 640 致动（旋转）到第三位置和 / 或将样本储存器 680 移回其第一配置，以使第一样本储存器 680 与第二流通道 644 隔离。当样本储存器 680 返回其第一配置时，刺穿构件 655a 被移离样本储存器 680，并且样本储存器 680 的密封件（例如，独立密封隔膜）使第一样本储存器 680 与流通道 635a 流体隔离。当流控制器 640 分别位于第三、第四和第五配置时，以类似方式填充其他样本储存器。

[0146] 图 34-40 描绘根据实施例的采集装置 700。采集装置 700 包括转移机构 720、流控

制器 740 以及样本储存器 780 和 790（尽管描绘了用于四个样本储存器的托架，但为了清楚起见图中仅包括两个样本储存器，并且额外的样本储存器（例如，第五、第六等）可被包括作为采集装置 700 的一部分）。如在此进一步描述的，采集装置 700 可在第一、第二、第三、第四和第五配置之间移动，以传递大体上不存在体外微生物（诸如，例如，皮肤驻留的微生物和 / 或其他有害外部污染物）的体液流。采集装置 700 可具有任何合适的形状、尺寸或配置。例如，采集装置 700 的一些方面和 / 或部分在形式和功能上可大体类似于采集装置 100、200、300、400、500 和 / 或 600 中任何装置的相应方面和 / 或部分。因此这里不进一步详细描述这些类似的方面和 / 或部分。例如，采集装置 700 的样本储存器 780 和 790 在形式和功能上可大体类似于图 16-22 的采集装置 400 中包括的样本储存器 480 和 490。

[0147] 转移机构 720 包括外壳 701、分配构件 729 和基板 771。如上文参照采集装置 400 描述的，外壳 701 限定第一出口孔口 703a、第二出口孔口 703b、第三出口孔口 703c、第四出口孔口 703d 和第五出口孔口 703e，它们各自被配置为与分配构件 729 的不同部分流体连通。更具体地，分配构件 729 限定和 / 或形成与第一出口孔口 703a 流体连通的前样本储存器 770 的至少一部分以及与第二出口孔口 703b 流体连通的第一流体腔 735a、与第三出口孔口 703c 流体连通的第二流体腔 735b、与第四出口孔口 703d 流体连通的第三流体腔 735c 和第五出口孔口 703e 流体连通的第四流体腔 735d。此外，外壳 701 限定被配置为可移动地接纳流控制器 740 的至少一部分的凹口 766，如在此进一步详细描述的。

[0148] 如图 36 所示，分配构件 729 限定腔或空间，所述腔或空间形成前样本储存器 770 的至少一部分。前样本储存器 770 被配置为容纳体液，诸如，例如，血液、血浆和 / 或尿液等。外壳 701 的第一出口孔口 703a 可与前样本储存器 770 的开口部分大体对齐，以容许前样本储存器 770 接收来自患者的体液流，如上文详细描述的。进一步详述，分配构件 729 包括一组壁 736，它们可例如将分配构件 729 的内部容积划分成彼此流体隔离的多个部分和 / 或空间。例如，如图 36 所示，该组壁 736 可将分配构件 729 的内部容积划分成前样本储存器 770、第一流体腔 735a、第二流体腔 735b、第三流体腔 735c 和第四流体腔 735d。在一些实施例中，壁 736 可均等地限定和 / 或形成前样本储存器 770 和流体腔 735a-735d。在其他实施例中，前样本储存器 770 限定的空间可不同于流体腔 735a-735d 限定的空间。

[0149] 分配构件 729 还包括第一刺穿构件 755a、第二刺穿构件 755b、第三刺穿构件 755c、第四刺穿构件 755d，它们分别与第一流体腔 735a、第二流体腔 735b、第三流体腔 735c 和第四流体腔 735d。因此，刺穿构件 755a-355d 可用于穿透样本储存器 780 和 790（以及图 34-40 中未示出的相应样本储存器）的真空密封件，这可使体液开始流动，如在此进一步详细描述的。

[0150] 采集装置 700 的流控制器 740 包括转盘 745 和密封构件 741。密封构件 741 位于外壳 701 的凹口 766（例如，见图 38 和 40）中。更具体地，流控制器 740 可耦接到外壳 701，从而使得密封构件 741 位于限定凹口 766 的外壳 701 的表面和转盘 745 的表面之间并与两个表面接触。密封构件 741 可被配置为与转盘 745 的表面和限定凹口 766 的外壳 701 的表面形成大体流体密封的密封结构，如上文详细描述的。如图 35 所示，密封构件 741 限定第一孔口 744a、第二孔口 744b、第三孔口 744c、第四孔口 744d 和第五孔口 744e。密封构件 741 的布置使得，当密封构件 741 处于凹口 766 中时，第一孔口 744a、第二孔口 744b、第三孔口 744c、第四孔口 744d 和第五孔口 744e 分别与外壳 701 的第一出口孔口 703a、第二出口孔口

703b、第三出口孔口 703c、第四出口孔口 703d 和第五出口孔口 703e 大体对齐。

[0151] 流控制器 740 的转盘 745 可旋转地耦接到外壳 701 上并且可相对于外壳 701 在第一位置、第二位置、第三位置、第四位置和第五位置之间移动。转盘 745 包括入口端口 721，入口端口 721 可（直接地或经由适配器 704 间接地）流体耦接到限定用于将体液从患者抽取和/或输送到采集装置 700 的流体流路径的医疗装置。以此方式，入口端口 721 可被配置为选择性地使前样本储存器 770、第一样本储存器 780、第二样本储存器 780'、第三样本储存器 790 和第四样本储存器 790' 与患者流体连通，如在此进一步详细描述的。当转盘 745 处于第一位置时，流控制器 740 处于第一配置，并且入口端口 721 可与密封构件 741 的第一孔口 744a 和外壳 701 的第一出口孔口 703a 大体对齐。以此方式，密封构件 741 的第一孔口 744a 在入口端口 721 和第一出口孔口 703a 之间建立流体连通，同时使入口端口 721 与出口端口 703b、703c、703d 和 703e 流体隔离，这继而使入口端口 721 与流体腔 735a-335d 流体隔离。当转盘 745 被旋转（或被致动）到第二位置时，流控制器 740 处于第二配置，并且第二出口孔口 744b 在入口端口 721 和第二出口孔口 703b 之间建立流体连通，同时使入口端口 721 与前样本储存器 770 和流体腔 735b-735d 流体隔离。当转盘 745 被旋转到第三、第四和第五位置时，采集装置 700 以类似方式工作。因此，当入口内腔 721 与患者（例如，经由耦接到入口端口 721 的医疗装置）流体连通时，第一出口孔口 703a、第二出口孔口 703b、第三出口孔口 703c、第四出口孔口 703d 和第五出口孔口 703e 可选择性地与入口端口 721 流体连通，以容许全部体液流入前样本储存器 770、第一样本储存器 780 或第二样本储存器 790（或与其耦接的任何其他流体储存器）中的至少一个。

[0152] 在一些实施例中，外壳 701 可选择性地限制转盘 745 从其第一位置到其第二、第三、第四和第五位置的移动。在一些实施例中，外壳 701 可被配置为一旦转盘已经移动到第五位置就阻止其移动。换言之，外壳 701 可包括阻止转盘 745 从第五位置移动返回第一位置的锁定机构。此特征可降低流体腔 735b-735d 和/或样本储存器 780 和 790 中采集的体液被前样本储存器 770 中容纳的体液（其具有包含表面束缚微生物和/或其他有害外部污染物的高风险）污染的风险。此锁定机构还可保护医疗保健行业从业者，防止其暴露于患者样本中的血源性病原体，其可包括 HIV、丙型肝炎等。转盘 745 和/或外壳 701 还可包括机械棘爪和/或提供视觉或触觉反馈以确保相对于出口端口 703b 和外壳 701 的出口孔口 703a-703d 精确地定位转盘 745 的其他指示器。

[0153] 与图 16-22 描绘的采集装置 400 的实施例类似，采集装置 700 包括前样本储存器 770，其是包含在分配构件 729 内的腔。前样本储存器 770 可包含体液，诸如，例如，血液、血浆和/或尿液等。前样本储存器 770 被配置为流体耦接到采集装置 700 的第一出口端口 703a（位于外壳 701 中）。在采集装置 700 的操作期间，当流控制器 740 处于第一位置时，体液从患者身体的一部分（例如，血管）经由入口端口 721 被抽入前样本储存器 770、用于前样本储存器的位于密封构件 741 中的孔口 744a 和第一出口端口 703a。前样本储存器 770 被配置为包含从患者抽取的第一量的体液，其中体液的第一量可以是预定或未定量，从而使得第一量体液与随后从患者抽取的第二和/或第三和/或第四和/或第五量体液流体隔离。

[0154] 在操作时，采集装置 700 可用于从患者采集减少污染的体液（例如，血液、血浆、尿液等）。例如，采集装置 700 的入口端口 721 流体耦接到针头或其他内腔限定装置（例如，

柔性无菌管）。在静脉穿刺之后，旋转转盘 745，直到它达到如图 37 和 38 所示的第一位置。替代性地，转盘 745 可被预设在第一位置，并且采集装置 700 可以其他方式被密封，以保持采集装置 700 的无菌性，如上所述。当转盘 745 处于第一位置时，流控制器 740 处于第一配置，并且密封构件 741 的第一出口孔口 744a 在入口端口 721 和第一出口端口 703a（包括在外壳 701 中）之间建立流体连通，同时使入口端口 721 和四个样品流通道 735a-735d 流体隔离。在此第一配置，体液从患者身体的一部分通过入口端口 721、密封构件 741 的第一出口孔口 744a、外壳 701 的第一出口端口 703a 流入分配构件 770 限定的前样本储存器 770，如图 38 的箭头 KK 所示。因此，第一量（预定的或未定的）体液可在静脉穿刺之后立即被接纳到前样本储存器 770 中并与随后的样本隔离，如上文详细描述的。

[0155] 在前样本储存器 770 中采集了体液前样本之后，可致动（或旋转）转盘 745 直到它达到第二位置，如图 39 和 40 所示。当转盘 745 处于第二位置时，流控制器 740 处于第二配置，并且密封构件 741 的第二出口孔口 744a 在入口端口 721 和第一流体腔 735a 之间建立流体连通，同时使前样本储存器 770 与入口端口 721 流体隔离。一旦第一流体腔 735a 被填充以体液，流控制器 740 就可移动到第三位置，以相对于外部环境隔离和密封第一流体通道 735a。此外，可将样本储存器 780 从第一配置致动到第二配置，以将体液从第一流体腔 735a 传送到样本储存器 780。例如，可通过使用者或自动地将样本储存器 780 从第一配置致动（推动刺穿构件 755a）到第二配置，以在患者身体的一部分（例如，血管）和样本储存器 780 之间建立流体连通。如上所述，将样本储存器 780 移动至第二配置会致使刺穿构件 755a 穿透样本储存器 780 的真空密封件并位于样本储存器 780 中。在第二配置，患者身体的所述部分（例如，血管）暴露于来自样本储存器 780 的由某些实施例中样本储存器 780 内存在的负压状态（真空）产生的真空吸力。因此，体液从患者身体的所述部分通过入口端口 721、密封构件 741 的第二出口孔口 744b、外壳 701 的第二出口孔口 703b、第二流体腔 735b 流入第一样本储存器 780，如图 40 的箭头 LL 所示。

[0156] 一旦期望量的体液（例如，第二量）被采集在样本储存器 780 中，使用者就可将流控制器 740 致动（旋转）到第三位置和 / 或将样本储存器 780 移回其第一配置，以使样本储存器 780 与入口端口 721 隔离。当样本储存器 780 返回第一配置时，刺穿构件 755a 被移离样本储存器 780，并且样本储存器 780 的密封件（例如，独立密封隔膜）使第一样本储存器 780 与第二流体腔 735b 及外部环境流体隔离。当流控制器 740 分别位于第三、第四和第五配置时，以相同方式填充其他样本储存器。

[0157] 在一些实施例中，采集装置 700 可被构造为不存在分隔分配构件 729 中的不同流体腔 735a-735d 的一组壁 736（见图 16 的详细剖视图）。在这类实施例中，分配构件 729 被划分在前样本储存器 770 和组合式流体腔 735（即，流体腔未被壁 736 分隔成四个单独的部段）之间。在这类实施例中，使用者可通过同时将转盘 745 致动（旋转）到各个第二、第三、第四或第五位置来填充全部四个样本储存器。

[0158] 本文描述的任何实施例都可与例如计量装置一起使用，计量装置可用于计量（例如，量化）流入前样本储存器和 / 或样本储存器的体液流。在一些情形中，实验室标准实践不能确保一致地遵从精确的体液（例如，血液样品）移入体积，因为实际上填充体积是临床医生和、或采血师视觉地确定的并因此存在人为误差。血液采集瓶上的体积指示器在被抓握时难以读数并且在抽取过程期间常常未竖直地抓握采集瓶的事实也可导致从患者接收

的体液样本的体积不准确。不足的样本体积（例如，低于制造商的建议值）可降低培养测试的敏感度，导致错误的阴性结果。此外，超过制造商建议值的填充体积可导致错误的阳性结果，如在用于特定类型的测试供给和设备（例如，被设计为与制造商生产的自动微生物检测系统一起使用的血液培养瓶，制造商诸如为新泽西州富兰克林湖的 Becton Dickinson）的概述材料和使用说明中指示的。因此，流计量和体积显示特征可容许实验室技术人员和/或医疗保健行业从业者（例如，采血师）根据需要如何处理样本在将样本储存器放入培养器或放入其他实验室测试仪器之前确认各个单个样本储存器中采集的体液的体积。实验室技术人员和/或采血师还可记录（例如，在病历卡、数据库、电子表格等中）精确的体积信息，以便临床医生在收到结果时评估，由此帮助降低错误地解释错误的阴性和/或错误的阳性结果的可能性。

[0159] 例如，图 41-45 图示可包括一个或多个计量装置的采集装置 800。采集装置 800 包括转移机构 820、流控制器 840、显示器 875 和样本储存器 880。如在此进一步描述的，采集装置 800 可在第一、第二和第三配置之间移动，以传递大体上不存在体外微生物（诸如，例如，皮肤驻留的微生物和/或其他有害外部污染物）的体液流。采集装置 800 可具有任何合适的形状、尺寸或配置。例如，采集装置 600 的一些方面和/或部分在形式和功能上可大体类似于上述采集装置 100、200、300、400、500、600 和/或 700 中任何装置的相应方面和/或部分。因此，这里不进一步详细描述这些类似的方面和/或部分。例如，在一些实施例中，采集装置 800 的样本储存器 880 在形式和功能上可大体类似于和/或等同于图 16-22 的采集装置 400 中包括的样本储存器 480。

[0160] 如图 41-43 所示，转移机构 820 包括致动器部分 822（例如，第一部分）、医疗部分 823（例如，第二部分）和耦接部分 824（例如，第三部分）。转移机构 820 的致动器部分 822 的大体圆柱形的，包括限定内部容积 806 的一组环形壁。更具体地，致动器部分 822 包括大体闭合的第一端部和与第一端部相反、大体开口以容许进入内部容积 806 的第二端部。以此方式，致动器部分 822 可以可移动地接纳流控制器 840 的至少一部分，如在此进一步详细描述的。致动器部分 822 还包括入口端口 821 和出口端口 831。入口端口 821 可流体耦接到限定用于将体液从患者抽取和/或输送到采集装置 800 的流体流路径的医疗装置（直接地或经由适配器 804 间接地），如上文详细描述的。

[0161] 致动器部分 822 的出口端口 831 可选择性地使致动器部分 822 的内部容积 806 与医疗部分 823 限定的内部容积 807 流体连通。如图 43 所示，医疗部分 823 位于致动器部分 822 和耦接部分 824 之间。尽管图 41-45 中未示出，但医疗部分 823 可包括计量装置，其可被配置为计量被传送到例如样本储存器 880 的体液的体积。例如，在一些实施例中，流计量装置可流体耦接到出口端口 831，以计量流过的体液流。如图 41 和 42 所示，医疗部分 823 包括显示器 875，其可为使用者提供与例如已流过出口端口 831 的体积相关的视觉指示和/或信息。在其他实施例中，流计量装置可被放置在转移机构 820 中或沿转移机构 820 的任何其他位置。

[0162] 耦接部分 824 可物理地和流体地耦接到医疗部分 823。例如，在一些实施例中，耦接部分 824 可部分地位于医疗部分 823 的内部容积 807 中并经由摩擦配合、压装配合、卡扣配合、螺纹耦接和/或粘合剂至少暂时地耦接到其上。耦接部分 824 被配置为接纳样本储存器 880 的一部分，并包括刺穿构件 855，其可用于穿透样本储存器 880 的真空密封件，这容

许体液开始流动，如上文详细描述的。

[0163] 采集装置 800 的流控制器 840 至少部分地位于致动器部分 822 限定的内部容积 806 中，并且可在第一配置、第二配置和第三配置之间移动。如图 42 和 43 所示，流控制器 840 包括具有第一密封构件 861、第二密封构件 862 和第三密封构件 863 的可移动构件 850 及偏置构件 859（例如，弹簧等）。密封构件 861、862 和 863 与限定内部容积 806 的致动器部分 822 的内表面接触。因此，密封构件 861、862 和 863 可各自与所述内表面形成大体流体密封的密封结构，例如，这可将致动器部分 822 的内部容积 806 划分成流体隔离的多个部分，如在此进一步详细描述的。

[0164] 可移动构件 850 可在内部容积 806 内在第一位置、第二位置和第三位置之间移动。可移动构件 850 的布置可使得当可移动构件 850 在其第一、第二和第三位置之间移动时，密封构件 861、862 和 863 可在内部容积 806 内选择性地移动。更具体地，当可移动构件 850 在其第一、第二和第三位置之间移动时，第一密封构件 861 可与可移动构件 850 同时移动。第二密封构件 862 和第三密封构件 863 可牢固地耦接到彼此（例如，彼此相距固定距离地放置）并且关于可移动构件 850 的一部分可滑动地放置，这可容许可移动构件 850 从其第一位置（例如，见图 43）移动至其第二位置（例如，见图 44），同时第二密封构件 862 和第三密封构件 863 相对于致动器部分 822 保持处于大体固定的位置。例如，当可移动构件 850 在其第一位置和第二位置之间移动时，第二密封构件 862 和第三密封构件 863 可保持处于大体固定的位置，从而使得入口端口 821 位于第二密封构件 862 的第一侧上，而出口端口 831 位于第二密封构件 862 的与第一侧相反的第二侧上。因此，当可移动构件 850 处于其第一位置（图 43）和其第二位置（图 44）时，入口端口 821 与被限定在第一密封构件 861 和第二密封构件 862 之间的内部容积 806 部分流体连通，并且出口端口与被限定在第二密封构件 862 和第三密封构件 863 之间的内部容积 806 部分流体连通，如在此进一步详细描述的。

[0165] 流控制器 840 的布置可使得，当可移动构件 850 从其第一位置移动到其第二位置时，第一密封构件 861 相对于第二密封构件 862 和第三密封构件 863 移动。第一密封构件 861 相对于第二密封构件 862 的移动可使得限定在其之间的空间增大，这可形成和 / 或以其他方式限定前样本储存器 870。此外，当密封构件 861 和 862 与致动器部分 822 的内表面形成大体流体密封的密封结构时，被限定在第一密封构件 861 和第二密封构件 862 之间的前样本储存器 870 与内部容积 806 的其他部分流体隔离。因此，当可移动构件 850 从其第一位置移动到其第二位置时，入口端口 821 可与前样本储存器 870 流体连通。当可移动构件 850 从其第二位置（例如，见图 44）移动到其第三位置（例如，见图 45）时，可移动构件 850 的一部分可接触第三密封构件 863，以在内部容积 806 内同时移动第一密封构件 861、第二密封构件 862 和第三密封构件 863。因此，可相对于入口端口 821 移动第二密封构件 862，从而使得入口端口 821 和出口端口 831 都与被限定在第二密封构件 862 和第三密封构件 863 之间的内部容积 806 的一部分流体连通，如在此进一步详细描述的。

[0166] 在操作时，采集装置 800 可用于从患者采集减少污染的体液（例如，血液、血浆、尿液等）。例如，采集装置 800 的入口端口 821 可流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。当入口端口 821 耦接到内腔限定装置时，可将流控制器 840 从其第一配置移动到其第二配置。以此方式，使用者可施加将可移动构件 850 从其第一位置移动到其第二位置的力，如图 44 的箭头 MM 所示。如上所述，第一密封构件 861 与可移动构件 850 同

时移动，从而增大被限定在第一密封构件 861 和第二密封构件 862 之间的空间，由此形成和 / 或限定前样本储存器 870。当第一密封构件 861 和第二密封构件 862 与限定内部容积 806 的致动器部分 822 的内表面形成大体流体密封的密封结构时，第一密封构件 861 和第二密封构件 862 之间空间的增大会在前样本储存器 870 中产生负压。因此，一旦在患者身体的一部分（例如，血管）和前样本储存器 870 之间建立了流体连通（例如，经由图 44 中的入口端口 821），在前样本储存器 870 和患者身体的所述部分之间限定的负压差就会通过入口端口 821 将体液抽入前样本储存器 870，如图 44 的箭头 NN 所示。在此第一配置中，流控制器 840 还使前样本储存器 870 与出口端口 831 流体隔离。因此，第一量（预定的或未定的）体液可在静脉穿刺（例如）之后立即被容纳到前样本储存器 870 中并与随后的样本隔离。以此方式，采集装置 800 可用于防止第一量体液（其最可能含有体表微生物和 / 或其他有害的外部污染物）污染随后量的体液样本，这些体液样本被采集并用于可受污染物影响的诊断或其他测试。在一些实施例中，计量装置可计量位于前样本储存器 870 中的体液的体积，并在显示器 875 上显示与体积相关的值。

[0167] 在前样本储存器 870 中采集了所述体积的体液前样本之后，将可移动构件 850 从其第二位置移动到其第三位置，以使流控制器处于其第三配置，如图 45 的箭头 OO 所示。如上所述，当将可移动构件 850 从其第二位置移动到其第三位置时，可移动构件 850 的所述部分与第三密封构件 863 接触。因此，可移动构件 850 可在内部容积 806 内大体同时地移动第一密封构件 861、第二密封构件 862 和第三密封构件 863。因此，可相对于入口端口 821 移动第二密封构件 862，从而使得入口端口 821 和出口端口 831 都与被限定在第二密封构件 862 和第三密封构件 863 之间的内部容积 806 的一部分流体连通，如在此进一步详细描述的。此外，当所述体积的体液被流体隔离在前样本储存器 870 中时，第二密封构件 862 和第三密封构件 863 沿第一密封构件 861 方向的移动受到限制（即，体液的基本不可压缩的流体）。以此方式，前样本体积的体液被隔绝在前样本储存器 870 中，并且被限定在第二密封构件 862 和第三密封构件 863 之间的空间限定在入口端口 821 和出口端口 831 之间的流体流路径。此外，流控制器 840 的布置使得，当处于其第三配置时，第一密封构件 861 与偏置构件 859 接触，并且使用者施加在可移动构件 850 上的力的至少一部分能够使偏置构件 859 变形、收缩、弯曲和 / 或以其他方式改变形状。因此，偏置构件 859 可在第一密封构件 861 上施加抵抗流控制器 840 从其第二配置移动到其第三配置的反作用力，如在此进一步详细描述的。

[0168] 相对于采集装置 800 放置样本储存器 880，从而使得刺穿构件 855 穿透样本储存器 880 的真空密封件，以位于样本储存器内，如上文详细描述的。样本储存器 880 和患者身体的所述部分之间的压力差（例如，真空或负压）将体液抽入样本储存器 880。换言之，在第二配置，流控制器 840 和转移机构 820 建立流体流路径，从而使得体液可通过入口端口 821、被限定在第二密封构件 862 和第三密封构件 863 之间的内部容积 806 部分和致动器部分 822 的出口端口 831，通过医疗部分 823 和耦接部分 824 的刺穿构件 855 从患者被抽入样本储存器 880 中，如图 45 的箭头 PP 所示。如上所述，计量装置（未示出）可计量被传送通过例如出口端口 831 的体液的体积，并且可在显示器 875 上显示与体积相关的值。

[0169] 一旦期望量的体液（例如，第二量）被采集在样本储存器 880 中，使用者就可去除和 / 或减小施加在可移动构件 850 上的力，由此容许偏置构件 859 将第一密封构件 861 和

可移动构件 850 从它们的第三位置移向它们的第二位置。此外，由于前样本储存器 870 中的体液基本不可压缩，因此第一密封构件 861 的移动会通过所述体积的体液传送力，以将第二密封构件 862 和第三密封构件 863 从它们的第三位置移向它们的第二位置。在一些实施例中，偏置构件 859 可在第一密封构件 861 上施加力，所述力能够相对于致动器部分 822 将第二密封构件 862 移动至可例如大体上阻塞入口端口 821 的第四位置。因此，入口端口 821 可与致动器部分 822 的内部容积 806 流体隔离。此外，可从样本储存器 880 移开刺穿构件 855，并且和密封件（例如，独立密封隔膜）可使体液样本与样本储存器 880 外的空间流体隔离。通过将刺穿构件 855 放入样本储存器并将流控制器 840 移动至第三位置以容许液体从患者流至样本储存器，可类似地填充随后的样本储存器。

[0170] 图 46-53 图示根据实施例的采集装置 900。采集装置 900 包括转移机构 920、流控制器 940 和样本储存器 980、980’、990 和 990’。如在此进一步描述的，采集装置 900 可在第一、第二、第三、第四和第五配置之间移动，以传递大体上不存在体外微生物（诸如，例如，皮肤驻留的微生物和 / 或其他有害外部污染物）的体液流。采集装置 900 可具有任何合适的形状、尺寸或配置。例如，采集装置 900 的一些方面和 / 或部分在形式和功能上可大体类似于上述采集装置 100、200、300、400、500、600、700 和 / 或 800 中任何装置的相应方面和 / 或部分。因此，这里不进一步详细描述这些类似的方面和 / 或部分。例如，在一些实施例中，采集装置 900 的样本储存器 980、980’、990 和 990’ 在形式和功能上可分别大体类似于和 / 或等同于图 26-33 的采集装置 600 中包括的样本储存器 680、680’、690 和 690’。。

[0171] 转移机构 920 包括外壳 901、分配构件 929 和可移动构件 950a、950b、950c 和 950d。外壳 901 物理地和流体地耦接到分配构件 929，并提供和 / 或限定用于从患者采集体液的一组流体流路径。外壳 901 包括一组显示器 975’（例如，液晶显示器 (LCD) 等），它们可被包括在流计量装置中和 / 或以其他方式耦接（例如，电气地和 / 或机械地）到流计量装置，如在此进一步详细描述的。外壳 901 限定凹口 966、出口孔口 903a、903b、903c、903d、903e 和可移动构件开口 950a、950b、950c、950d（在此也被称作“开口”）。凹口 966 被配置为容纳包括在流控制器 940 中的密封构件 941，如在此进一步详细描述的。第一出口孔口 903a、第二出口孔口 903b、第三出口孔口 903c、第四出口孔口 903d 和第五出口孔口 903e 各自被配置为限定与分配构件 929 的不同部分流体连通的不同流体流路径。更具体地，分配构件 929 限定和 / 或形成与第一出口孔口 903a 流体连通的前样本储存器 970 的至少一部分，以及与第二出口孔口 903b 流体连通的第一流通道 935a、与第三出口孔口 903c 流体连通的第二流通道 935b、与第四出口孔口 903d 流体连通的第三流通道 935c 和第五出口孔口 903e 流体连通的第四流通道 935d。

[0172] 如图 47 和 48 所示，分配构件 929 限定腔或空间，所述腔或空间限定前样本储存器 970 的至少一部分。前样本储存器 970 被配置为容纳体液，诸如，例如，血液、血浆和 / 或尿液等。外壳 901 的第一出口孔口 903a 可与前样本储存器 970 的开口部分大体对齐，以容许前样本储存器 970 接收来自患者的体液流，如上文参照图 16-22 的前样本储存器 470 详细描述的。流通道 935a-935d 从分配构件 929 的中心沿径向延伸并被布置为使得每个流通道 935a、935b、935c 和 935d 与前样本储存器 970 及其他流通道流体隔离。以此方式，流通道 935a、935b、935c 和 935d 可引导和 / 或以其他方式限定第一端部（限定分别与出口孔口 903b、903c、903d 和 903e 大体对齐的开口）和第二端部（限定被配置为分别接纳可移动构

件 950a、950b、950c、950d 的开口或端口）之间的流体流路径。尽管图 47 和 48 示出了分配构件 929 包括大体闭合的流通道 935a-935d，但在其他实施例中，流通道 935a-935d 可以是大体开放的，如上文参照图 17 和 18 的分配构件 429 示出和描述的。因此，采集装置 900 的分配构件 929 可以与采集装置 400 的分配构件 429 大体类似的方式起作用。

[0173] 可移动构件 950a、950b、950c 和 950d 可以可移动地位于外壳 901 的各个开口 905a、905b、905c 和 905d 中，以及由分配构件 929 的第二端部限定的相应开口中。尽管图 46-53 中未示出，但在一些实施例中，可移动构件 950a、950b、950c 和 950d 可以可操作地耦接到偏置构件等，如上文参照采集装置 200 的可移动构件 250 和 250' 详细描述的。以此方式，使用者可相对于外壳 901 和分配构件 929 从第一位置和第二位置致动（例如，移动）可移动构件 950a、950b、950c 和 950d，以将流体流分别引导入第一样本储存器 980、第二样本储存器 980'、第三样本储存器 990 和第四样本储存器 990'。可移动构件 950a、950b、950c 和 950d 大体相同，并因此参照图 49 中的单个可移动构件 950 进行描述。此外，可移动构件 950 的一些部分可大体类似于上述可移动构件 250 和 350。因此，这里不进一步详细描述可移动构件 950 的一些部分。可移动构件 950 限定与入口端口 953 和刺穿构件 955 流体连通的内部腔 952。刺穿构件大体类似于上文详细描述的那些。入口端口 953 延伸通过限定内部腔 952 的一组壁，以使可移动构件 950 的内部容积 952 与相应的流通道 935a、935b、935c 或 935d 流体连通。

[0174] 如图 49 所示，可移动构件 950 包括可旋转地位于内部容积 952 中并与入口端口 953 大体直接地流体连通的流控制机构 967。流计量机构 967 可以是例如可包括一组辐条或翅片的轮等。以此方式，体液可进入可移动构件 950 的入口端口 953 并流过流计量装置 967，这继而可致使流计量装置 967 相对于可移动构件 950 旋转。因此，流计量装置 967 的旋转特征可用于确定被传送到可移动构件 950 的内部容积 952 中的体液的体积和 / 或体积流率等。尽管图 46-53 中未示出，但可移动构件 950 的流控制机构 967 可操作地耦接到外壳 901 的显示器 975' 上。因此，当体液被传送到例如样本储存器 980、980'、990 和 / 或 990' 时，与体液流相关的体积信息可显示在显示器 975' 上。以此方式，使用者可操纵采集装置 900 从患者采集体液样本并且可使至少一个显示器 975' 可视化，以确定被传送到例如样本储存器 980 的体液样本的准确体积。

[0175] 采集装置 900 的流控制器 940 包括转盘 945 和密封构件 941。密封构件 941 位于外壳 901 的凹口 966 中。更具体地，流控制器 940 可耦接到外壳 901，从而使得密封构件 941 位于限定凹口 966 的外壳 901 的表面和转盘 945 的表面之间并与两个表面接触。密封构件 941 可被配置为与转盘 945 的表面和限定凹口 966 的外壳 901 的表面形成大体流体密封的密封结构，如上文详细描述的。如图 47 所示，密封构件 941 限定第一孔口 944a、第二孔口 944b、第三孔口 944c、第四孔口 944d 和第五孔口 944e。密封构件 941 的布置使得，当密封构件 941 处于凹口 966 中时，第一孔口 944a、第二孔口 944b、第三孔口 944c、第四孔口 944d 和第五孔口 944e 分别与外壳 901 的第一出口孔口 903a、第二出口孔口 903b、第三出口孔口 903c、第四出口孔口 903d 和第五出口孔口 903e 大体对齐。

[0176] 流控制器 940 的转盘 945 可旋转地耦接到外壳 901 上并且可相对于外壳 901 在第一位置、第二位置、第三位置、第四位置和第五位置之间移动。转盘 945 包括入口端口 921，其可流体耦接到限定用于将体液从患者抽取和 / 或输送到采集装置 900 的流体流路径的医

疗装置（直接地或经由适配器 904 间接地）。以此方式，入口端口 921 可被配置为选择性地使前样本储存器 970、第一样本储存器 980、第二样本储存器 980'、第三样本储存器 990 和第四样本储存器 990'与患者流体连通，如在此进一步详细描述的。转盘 945 可被配置为以与上文参照采集装置 400 的转盘 445 描述的大体类似的方式旋转通过第一位置、第二位置、第三位置、第四位置和第五位置，并且因此，这里不进一步详细描述。

[0177] 如图所示，转盘 945 可还包括显示器 975，其可被配置为显示与体液流相关的体积信息。例如，尽管图 46-53 中未示出，但转盘可包括流计量装置等，诸如可移动构件 950 包括的流计量装置 967。以此方式，流计量装置可计量流过例如入口端口 921 的体液流并且可以可操作地耦接到显示器 975，从而在转盘 945 的显示器 975 上显示通过入口端口 921 的体液流。

[0178] 在操作时，采集装置 900 可用于从患者采集减少污染的体液（例如，血液、血浆和/或尿液等）。例如，采集装置 900 的入口端口 921 可流体耦接到针头或其他内腔限定装置（例如，柔性无菌管）。在静脉穿刺（或其他体液获得方法）之后，致动（或旋转）转盘 945，直到它达到如图 50 和 51 所示的第一位置。替代性地，转盘 945 可被预设在第一位置，并且采集装置 900 可以其他方式被密封，以保持采集装置 900 的无菌性。

[0179] 如上所述，当转盘 945 处于第一位置时，流控制器 940 处于第一配置，并且密封构件 941 的第一孔口 944a 在入口端口 921 和第一出口端口 930（包括在外壳 901 中）之间建立流体连通，同时使入口端口 921 和四个流通道 935a-335d 流体隔离。此外，在第一配置中，样本储存器 980、980'、990 和 990'与入口端口 921 流体隔离，并且在患者身体的一部分（例如，血管）和前样本储存器 970 之间限定流体流路径，如图 51 的箭头 QQ 所示。在此第一配置，体液（例如，通过重力、真空等）从患者身体的一部分通过入口端口 921、密封构件 941 的第一孔口 944a、外壳 901 的第一出口端口 903a 流入前样本储存器 970。在第一配置，流控制器 940 还使前样本储存器 970 与流通道 935a-935d 流体隔离。因此，第一量（预定的或未定的）体液可在静脉穿刺（例如）之后立即被容纳到前样本储存器 970 中并与随后的样本隔离。以此方式，采集装置 900 可用于防止第一量体液（其最可能含有体表微生物和/或其他有害的外部污染物）污染随后量的体液样本，这些体液样本被采集并用于可受污染物影响的诊断或其他测试。此外，显示器 975 可显示例如从流控制机构（未示出）接收的与传送到前样本储存器 970 的体液体积相关的信息。因此，准确体积的体液可被传送到前样本储存器并被流体隔离在其中。

[0180] 在前样本储存器 970 中采集了体液前样本之后，可致动（或旋转）转盘 945 直到它达到第二位置，如图 52 和 53 所示。当转盘 945 处于第二位置时，流控制器 940 处于第二配置，并且密封构件 941 的第二孔口 944b 在入口端口 921 和流通道 935a 之间建立流体连通，同时使前样本储存器 970 与入口端口 921 流体隔离。当流控制器 940 处于第二配置时，使用者可将可移动构件 950a 从第一位置致动（例如，按压）到第二位置，以在患者（例如，血管）与第一样本储存器 880 之间建立流体连通。此外，可将可移动构件 950 从其第一位置移动到其第二配置，以使刺穿构件 955 穿过第一样本储存器 980 的真空密封件，以位于其中，如图 53 的箭头 RR 所示。

[0181] 当处于第二位置时，可移动构件 950 的入口端口 953 与第一流通道 935a 大体对齐并流体连通，这容许体液从第一流通道 935a 流入可移动构件 950 的内部腔 952，并从刺穿构

件 955 流入第一样本储存器 980。样本储存器 980 和第一流通道 935a 之间的压力差（例如，真空或负压）将体液抽入样本储存器 980。换言之，在第二配置，流控制器 940 和可移动构件 950a 在转盘 945 入口端口 921 和样本储存器 980 之间建立流体流路径，如图 53 的箭头 SS 所示。此外，流过可移动构件 950a 的体液流使流计量机构 967 相对于可移动构件 950 旋转。因此，流计量机构 967 的旋转可用于确定被传送到样本储存器 980 的体液样本的体积。此外，显示器 975’可显示例如从流控制机构 967 接收的与传送到样本储存器 980 的体液体积相关的信息。因此，准确体积的体液可被传送到样本储存器 980。例如，在一些情形中，采集装置 900 可用于分别在第一样本储存器 980、第二样本储存器 980’和第三样本储存器 990 中采集三个 20mL 体积的样本（即，采集的样本总体积为 60mL）。

[0182] 一旦期望量的体液（例如，第二量）被采集在第一样本储存器 980 中，使用者就可释放可移动构件 950，容许偏置构件（未示出）移回其第一位置。当可移动构件 950 返回其第一位置时，刺穿构件 955 被移离第一样本储存器 980，并且密封件（例如，独立密封隔膜）使第一样本储存器 980 与内部流通道 935 流体隔离。采集装置 900 可用于通过分别将转盘 945 旋转到其第三位置、第四位置和第五位置，将第二样本体积传送到第二样本储存器 980’、将第三样本体积传送到第三样本储存器 990 以及将第四样本体积传送到第四样本储存器 990’。

[0183] 在一些情形中，体液采集装置 900 可容许临床医生和 / 或采血师打开包含体液采集装置 900 的包装并仅移除外壳 901（其包含分配构件 929）并将外壳 901 拿到患者床边。临床医生和 / 或采血师可利用任何标准化技术对患者身体的所述部分（例如，血管）执行静脉穿刺（或采用任何其他获得患者体液的方法）。在静脉穿刺之后，临床医生和 / 或采血师可采集全部样本所需的总血液体积。例如，临床医生和 / 或采血师可采集 2.5mL 前样本转移体积并为四个样本储存器中的每个采集 10mL 样本体积，总计采集 42.5mL 体液（例如，血液）。在采集了期望量的体液之后，可从患者身体的所述部分（例如，血管）移走皮下注射针头，并且临床医生和 / 或采血师可将外壳 901（其包含体液）放置在 4 组式（或 2 组式）预消毒的样本储存器上方，所述样本储存器具有被预先放置在匹配外壳 901 的几何形状的定制托盘中的隔膜顶部。通过利用这种预消毒的一组样本储存器，临床医生不必执行用消毒试剂“擦拭”样本储存器顶部的过程步骤，由此减小的污染的可能性（例如，如果不适当地和不足地消毒储存器的顶部的话）。然后，临床医生和 / 或采血师可在准确地控制体积的情况下启动将体液自动移入样本储存器。在某些实施例中，在完成样本储存器的移入之后，可将显示每个单独样本储存器的体积信息的整个装置 900 送到实验室以便分析。在其他实施例中，样本储存器 980 和 / 或 990 可被单独移开并被送到实验室以便分析。

[0184] 尽管参照图 46-53 示出和描述了采集装置 900 包括可显示与被传送通过采集装置的一部分的体液的体积相关的体积数据的一组显示器 975 和 975’，但在其他实施例中，采集装置可包括具有任何合适的输出指示器的任何合适的流计量机构。例如，图 54 和 55 图示了根据实施例的转移机构 1020 和流控制器 1040。转移机构 1020 和流控制器 1040 在形式和功能上可分别与转移机构 920 和流控制器 940 大体类似。因此，在此不进一步详细描述类似部分。但是，转移机构 1020 和流控制器 1040 可在一组显示器 1075 的布置上不同。例如，转移机构 1020 包括被配置为可移动地接纳一组可移动构件 1050a、1050b、1050c 和 1050d 的外壳 1001，可移动构件可各自包括上文参照可移动构件 950 描述的流计量机构。因

此，可移动构件 1050a、1050b、1050c 和 1050d 可用于确定从其中传送通过的体液的准确体积。如图 55 所示，外壳 1001 的显示器 1075 可包括一组三个灯，第一灯对应小体积（例如，5mL）、第二灯对应中间体积（例如，20mL），并且第三灯对应可接受的和 / 或大体积（例如，40mL）。以此方式，当体液流通过流控制器 1040 和转移机构 1020 被传送到例如第一可移动构件 1050a 时，包括在其中的流计量机构可向显示器发送信号灯，显示器能够根据传送通过可移动构件 1050 的体液的体积点亮第一灯、第二灯和 / 或第三灯。

[0185] 在其他实施例中，可移动构件 1050a、1050b、1050c 和 1050d 可相对于外壳 1001 从第一位置移动到第二、第三或第四位置。在这类实施例中，位置可与例如待被传送到样本储存器的体液的目的体积相关。例如，在一些实施例中，使用者可将可移动构件 1050a 从其第一位置致动（例如，移动）到其第二位置。在这类实施例中，第二位置可与例如待被传送到样本储存器的小体积体液（例如，10mL）相关。在一些实施例中，外壳 1001 和 / 或可移动构件 1050a 可包括棘爪、锁、搭扣、突起和 / 或凹口等，它们可暂时保持可移动构件 1050a 处于第二位置，直到所述小体积的样本已被传送到样本储存器。此外，一旦位于第二位置，显示器 1075 就可被配置为点亮与小体积相关的第一灯，以向使用者指示待传送到样本储存器的体液的预设体积。一旦期望体积的体液被传送到样本储存器并被流体隔离在其中，转移机构 1020 就可被配置为使可移动构件 1050a 自动返回其第一位置。以此方式，转移机构 1020 和流控制器 1040 可物理地和流体地耦接到任意数量的样本储存器并用于将准确体积的体液传送到每个样本储存器。

[0186] 图 56 是图示利用流计量传送装置从患者获得预定样本体积的体液的方法 1190 的流程图。流计量传送装置可以是本文描述的任何传送装置（在此也被称作“采集装置”）。例如，在一些实施例中，传送装置可以是上文参照图 46-53 描述的采集装置 900。因此，传送装置可包括具有被配置为与患者选择性地流体连通的入口端口的转移机构、前样本储存器和样本储存器以及被配置为计量从患者流到前样本储存器和样本储存器的体液流的流计量机构。方法 1190 包括在步骤 1191 在患者和流计量传送装置之间建立流体连通。例如，端口可流体耦接到针头或其他内腔限定装置（例如，柔性无菌管），其继而可插入患者（例如，静脉穿刺事件或其他获得体液的方法）。

[0187] 当端口与患者流体连通时，在步骤 1192，在端口和前样本储存器之间建立流体连通。在一些实施例中，流计量传送装置可包括流控制器等（例如，诸如，采集装置 900 中包括的流控制器 940），流控制器等可被致动和 / 或被操纵（例如，旋转）到在端口和前样本储存器之间建立流体连通的位置（例如，第一位置）。在一些实施例中，致动流控制器可使得流控制器和转移机构共同限定端口和前样本储存器之间的流体流路径的至少一部分。在一些实施例中，前样本储存器可包括负压等，其可例如使体液流开始从患者流入前样本储存器。在其他实施例中，可以任何其他合适的方式（例如，重力等）使体液流开始流动。

[0188] 在步骤 1193，计量从患者传送到前样本储存器的体液流。例如，在一些实施例中，端口可包括可计量穿过端口的体液流的流控制机构（例如，以与上文参照采集装置 900 的流控制机构 967 描述的方式类似的方式）。因此，前样本体积的体液被传送到前样本储存器。方法 1190 包括在步骤 1194 包括经由流计量传送装置的流计量机构验证位于前样本储存器中的前样本体积的体液是预定前样本体积的体液。例如，流计量机构可以包括类似的显示器和 / 或可以可操作地耦接类似的显示器（例如，采集装置 900 的显示器 975 和 / 或

975’）。流计量机构可被配置为在显示器上显示体积信息，如上所述。

[0189] 在步骤 1195，一旦前样本体积的体液位于前样本储存器中，就使前样本储存器与端口流体隔离，以将前样本体积的体液隔绝在前样本储存器中。例如，在一些情形中，可将流控制器和 / 或转移机构从第一位置和 / 或配置致动（或旋转）到第二位置和 / 或第二配置。当流控制器和 / 或转移机构处于第二配置时，前样本储存器与前样本储存器外的空间流体隔离。在一些实施例中，在步骤 1196，当流控制器和 / 或转移机构被致动到其第二位置和 / 或配置时，在端口和样本储存器之间建立流体连通。例如，在一些实施例中，流计量传送装置可包括可移动构件（例如，可移动构件 950）等，其可包括被配置为刺穿样本储存器的一部分（例如，隔膜等）的刺穿构件。因此，当流控制器和 / 或转移机构处于其第二位置和 / 或配置时，刺穿样本储存器的所述部分会使样本储存器与端口流体连通。如上所述，样本储存器可包括可例如使体液流开始从患者流入样本储存器的负压等。

[0190] 在步骤 1197，计量从患者传送到前样本储存器的体液流。例如，如上所述，端口可包括可计量穿过端口的体液流的流控制机构（例如，以与上文参照采集装置 900 的流控制机构 967 描述的方式类似的方式）。在一些实施例中，流控制机构可包括在例如可移动构件等中，诸如图 49 的可移动构件 950。因此，样本体积的体液被传送到样本储存器。方法 1190 包括在步骤 1198 包括经由流计量传送装置的流计量机构验证位于样本储存器中的样本体积的体液是预定样本体积的体液。例如，显示器等可被配置为显示体积信息，如上所述。

[0191] 以此方式，采集了可包含例如外部驻留微生物的预定前样本体积的体液。例如，在一些实施例中，预定前样本体积可以是约 0.1mL、约 0.3mL、约 0.5mL、约 1.0mL、约 2.0mL、约 3.0mL、约 4.0mL、约 5.0mL、约 10.0mL、约 20mL、约 50mL 和 / 或其之间的任何体积或分数体积。在其他实施例中，前样本体积可大于 50mL 或小于 0.1mL。在其他实施例中，预定前样本体积可在约 2mL 和约 5mL 之间。在一个实施例中，预定前样本体积可为约 3mL。此外，通过采集预定前样本体积，位于一个或多个样本储存器中的预定样本体积可大体不存在外部驻留微生物。在一些实施例中，预定样本体积可在 10mL 和 60mL 之间。在其他实施例中，预定样本体积可在 30mL 和 60mL 之间。在其他实施例中，预定样本体积可为 60mL。尽管上文描述了将样本体积的体液传送到单个样本储存器，但在其他实施例中，流计量传送装置可用于将预定样本体积传送到多于一个样本储存器。例如，在一些实施例中，可将预定前样本体积的体液采集和流体隔离在前样本储存器中，如上所述。当前样本体积被流体隔离时，流计量传送装置可用于将预定样本体积传送到第一样本储存器，将预定样本体积传送到第二样本储存器以及将预定样本体积传送到第三样本储存器。在这类情形中，预定样本体积可以是例如 20mL，从而使得位于第一、第二和第三样本储存器中的总样本体积为 60mL。

[0192] 本文描述的体液采集装置的各个实施例可容许利用单次静脉穿刺采集两（或更多）组体液（例如，血液）样本。当前的医疗水平规定利用从不同的单独体液获取位置获得的样本（例如，经由两次单独的静脉穿刺，经由导管和静脉穿刺和 / 或其任意组合）进行某些测试（例如，血液培养）。本文描述的实施例可帮助从单个体液获取位置（例如，静脉穿刺）获得用于特定诊断测试（例如，血液培养测试）的多个样本，这可将获得这些样本所需的静脉穿刺年度次数降至原来的 1/2。这以类似的方式有益于患者和医疗保健行业从业者。减少静脉穿刺（和 / 或其他体液获得过程）的次数可显著降低针头刺伤医疗保健行业从业者的风险，并减少由这些过程导致的患者的相关并发症（例如，血肿、血栓、静脉炎、感

染等）。此外，减少体液获得过程（例如，静脉穿刺）的数量减少了与这些过程相关的补给、人力和废物。医疗保健系统实现的成本降低是重大的并且给出了更高效地使用资源以及改进患者结果的机会，这是因为提高了样本的完整性，由此产生更准确的患者诊断，鼓励治疗计划的形成和执行。体液采集装置还显著降低了在采集后分析中产生错误阳性结果的可能性。本文描述的体液采集装置还可简化体液采集过程并减少手动步骤和“接触点”的数量，由此降低外部污染的可能性。本文描述的装置还可最小化实验室技术人员和/或采血师被针头刺伤和感染的风险。

[0193] 在一些实施例中，本文描述的体液采集装置（例如，100、200、300、400、500、600、700、800 和 900）可包括抗菌饱和材料和/或部分地由该材料形成（例如，外壳 401）。当前水平依靠医疗保健行业从业者将各个抗菌材料（例如，异丙醇棉签）放置在各个样本储存器（例如，480、480’、490 和 490’）顶部。为了确保服从此准则，装置 400（例如）可包括位于装置 400 内的抗菌材料，从而使得当外壳 401 位于 4 组式（或 2 组式）瓶的顶部时，如图 16 所示，外壳 401 与样本储存器 480、480’、490 和 490’ 的顶部最先接触的点是抗菌材料。以此方式，可确保在将体液移入样本储存器之前合适地消毒样本储存器 480、480’、490 和 490’ 的顶部。

[0194] 尽管已经具体地示出和描述了各种实施例，但可对形式和细节进行各种改变。例如，尽管参照图 19-22 示出和描述了沿单个方向选择转盘 445（致动器），但在其他实施例中，可沿第一方向和与第一方向相反的第二方向旋转转盘 445（致动器）。在这类实施例中，沿第二方向的旋转可被配置为使采集装置移动通过任意数量的配置。在其他实施例中，可限制致动器沿第二方向的旋转。在一些实施例中，转盘可包括机械止动件或锁，以流体隔离从患者接收的第一体积的体液（即，受污染的样本）。换言之，一旦第一储存器（前样本储存器）被填充以预定体积的体液并且使用者已经旋转转盘（致动器）以开始抽入额外的样本，转盘（致动器）就不能向后移动以与第一样本体积（包含在前样本储存器中）建立流体连通。

[0195] 尽管上文已经描述了实施例，但是应该理解，它们仅是以举例方式给出的，并且不受限制。虽然各个实施例已经被描述为具有特定的特征和/或部件的组合，但其他实施例可具有来自本文描述的任何实施例的任何特征和/或部件的任意组合或子组合。例如，尽管参照图 34-40 示出和描述了采集装置 700 具有第一、第二、第三、第四或第五配置，但在其他实施例中，本文描述的采集装置可具有更多或更少的配置。此外，尽管参照图 2-13 示出和描述了采集装置 200 具有作为前样本储存器 270 的基于真空的采集管，但在其他实施例中，采集装置 200 可具有被容纳在外壳 201 中的腔，类似于图 16-22 给出的实施例的采集装置 400，其包括作为被容纳在分配构件 429 内的腔的前样本储存器 470，反之亦然。

[0196] 还可以改变各个部件的特定配置。例如，各个部件的尺寸和特定形状可与所示实施例不同，但仍提供如本文所述的功能。更具体地，可具体选择各个部件的尺寸和形状，以使体液流以期望速率流入流体储存器。此外，尽管图 49 具体示出了流计量机构 967，但本文描述的任何采集装置可与任何合适的流计量机构一起使用。例如，在一些实施例中，采集装置可包括流计量机构和/或被配置为测量体液的体积特征的任何其他机构、装置或方法，诸如，例如，压力传感器、电压传感器、光学传感器、速度传感器、流计量器、应变仪、阀、涡轮机、浮子、位移分析、密度分析、重量分析、光学分析、超声波分析、热能分析、多普勒分析、电

磁场 (emf) 分析、反射分析、障碍分析、面积分析、文丘里管分析、科里奥利分析、视觉分析和 / 或任何其他合适的传感器、分析法和 / 或计算法 (例如，应用和 / 或利用例如波义耳定律、理想气体定律和 / 或力计算法 (力＝质量＊加速度))。

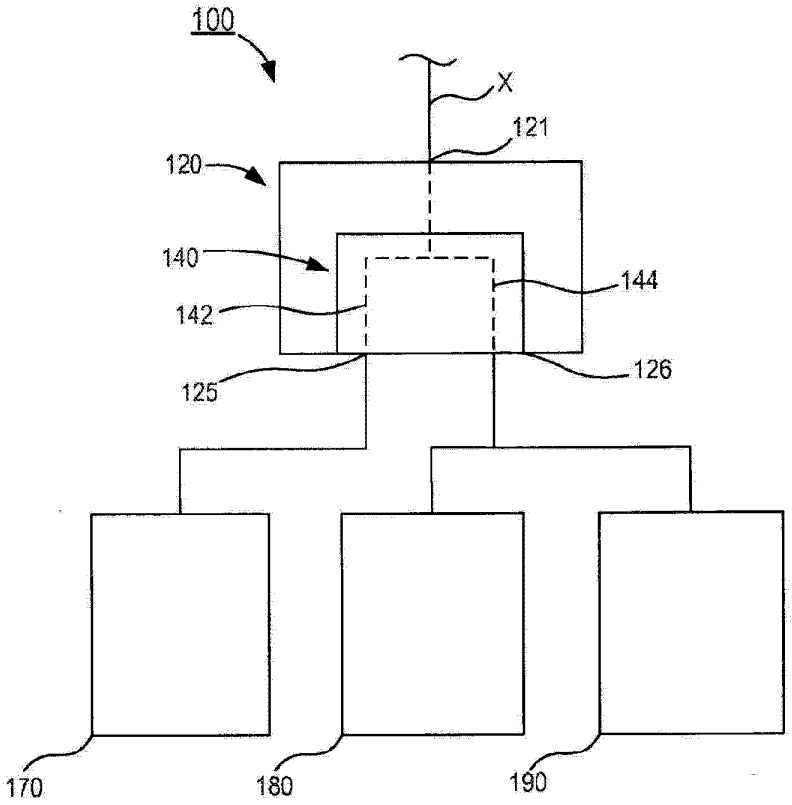


图 1

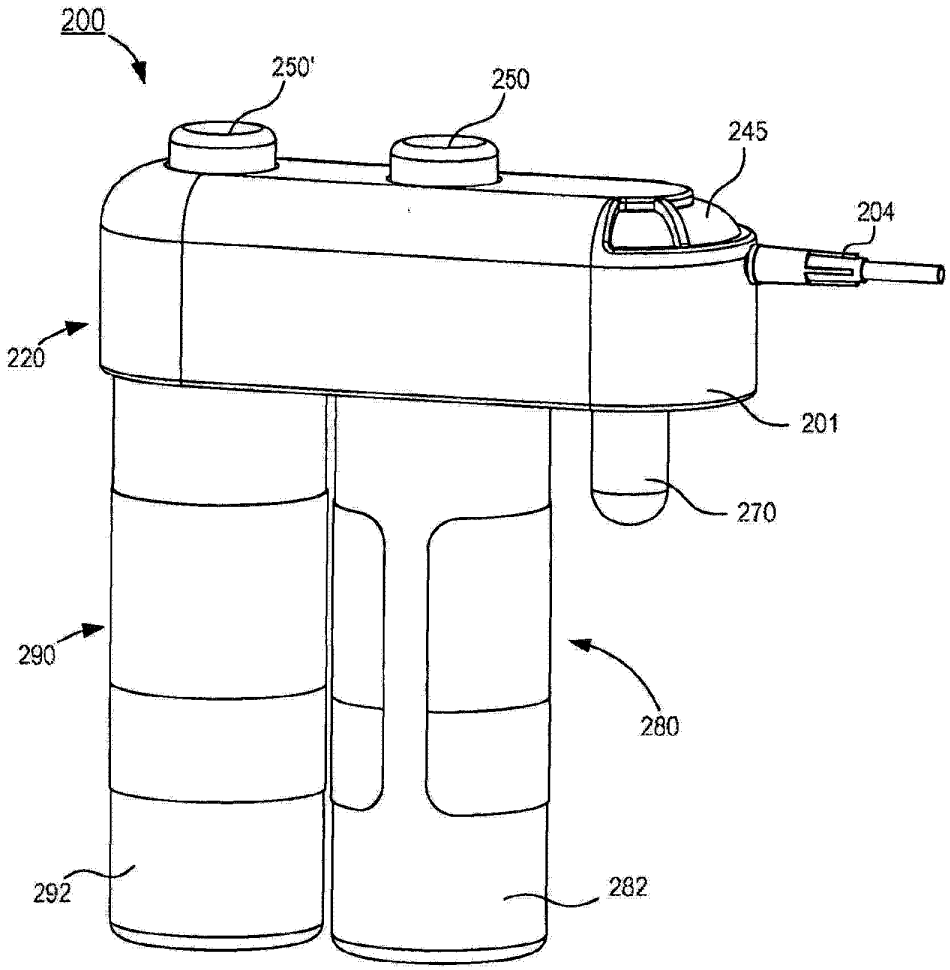


图 2

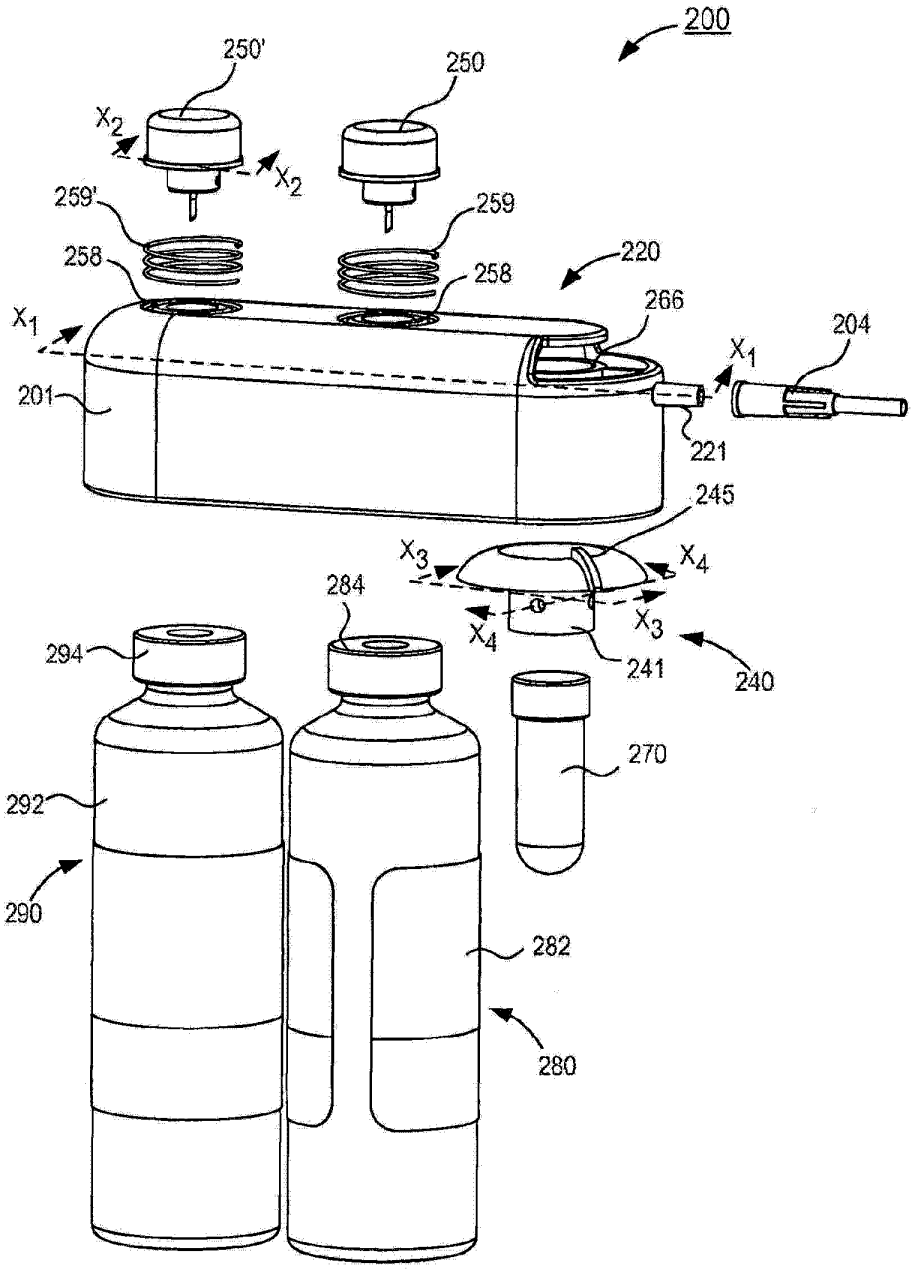

200
250'
250
X2
X2
259'
259
258
258
220
266
X1
X1
204
201
221
245
X3
X4
284
X4
X3
294
241
240
270
292
290
282
280

图 3

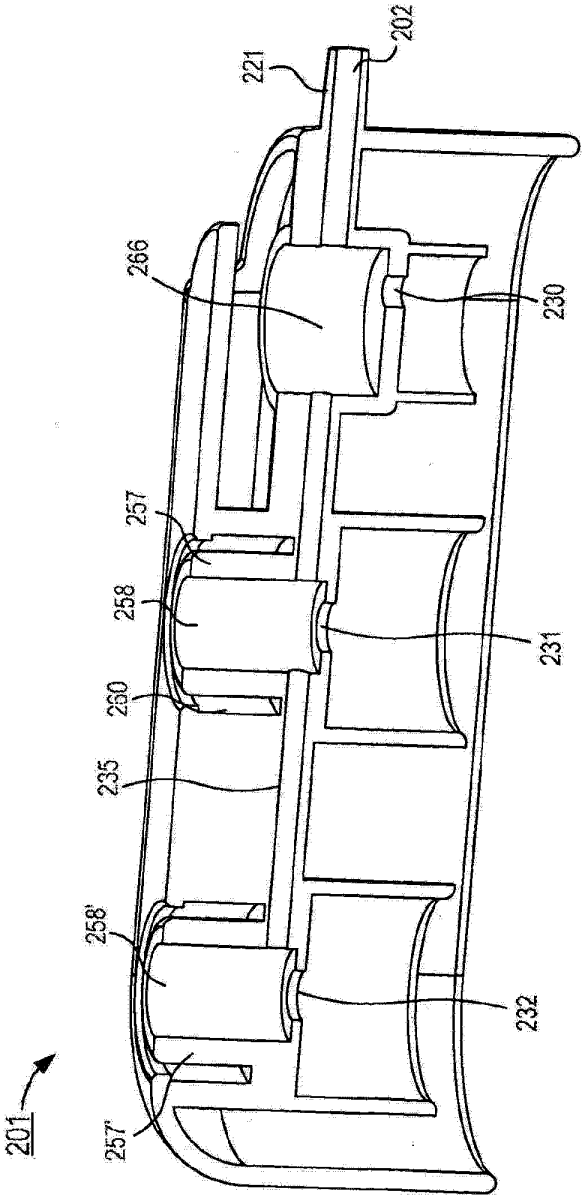


图 4

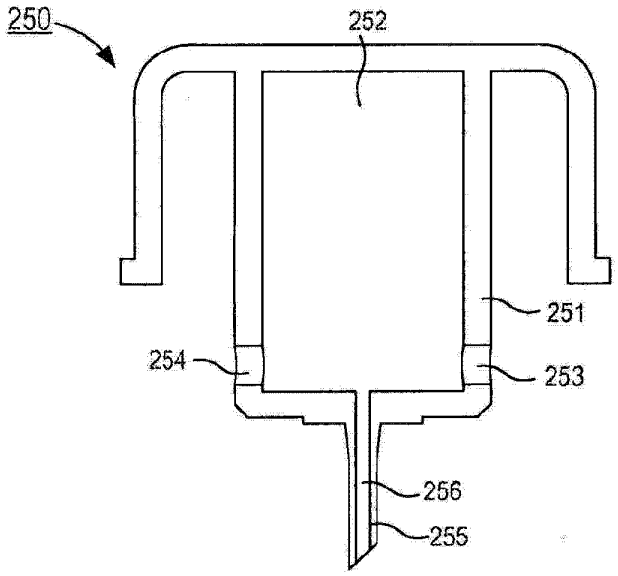


图 5

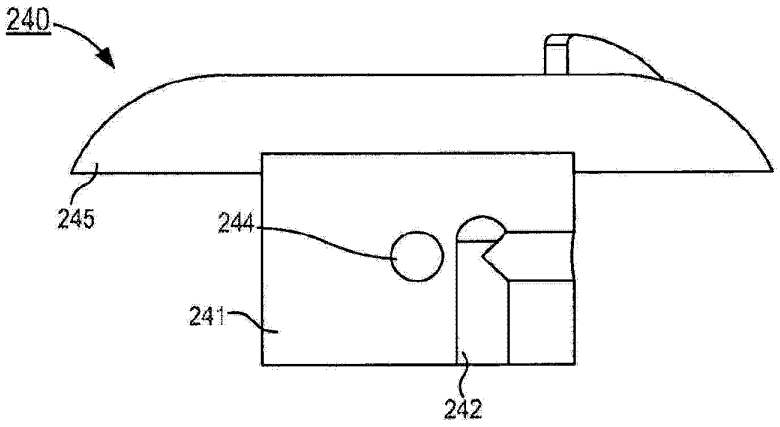


图 6

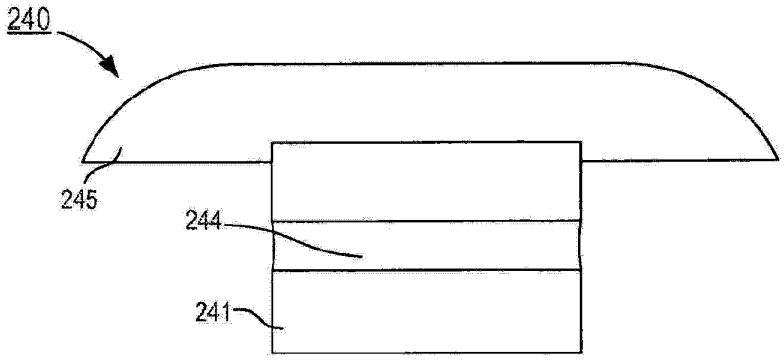


图 7

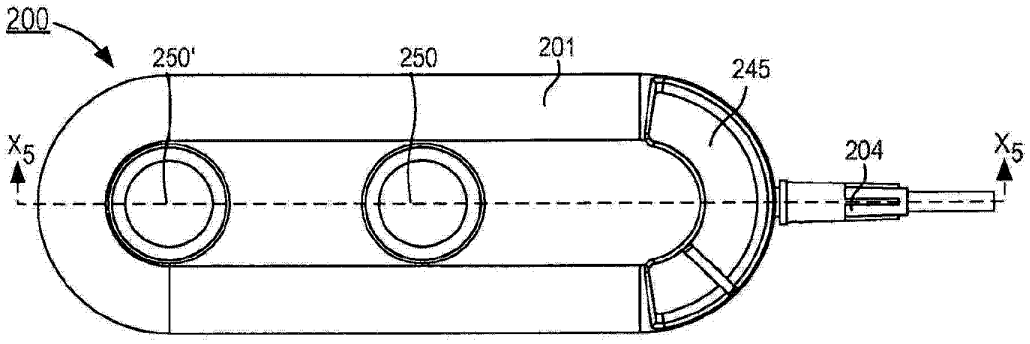


图 8

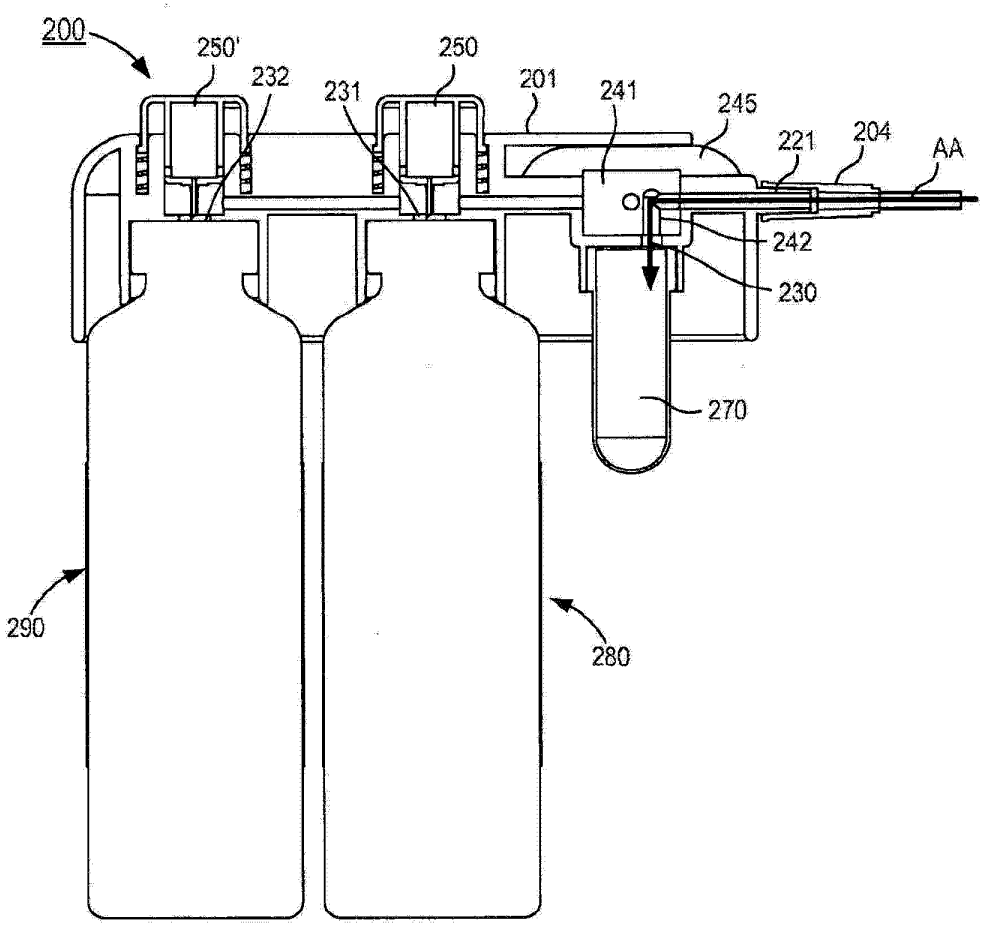

200
250'
232
231
250
201
241
245
221
204
AA
242
230
270
290
280

图 9

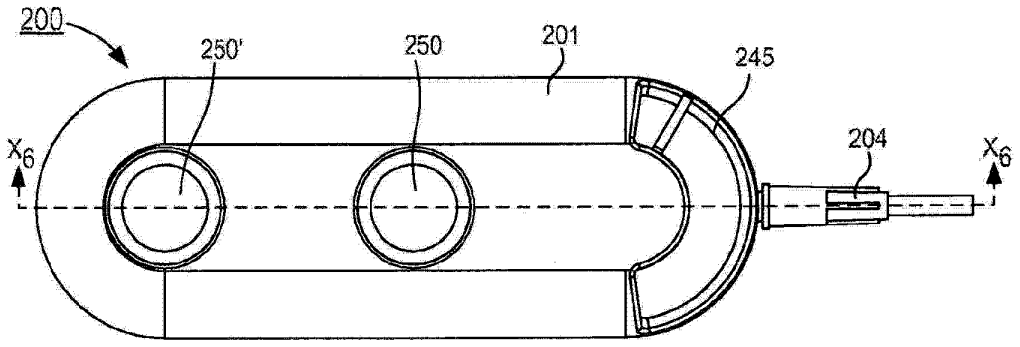

200
250'
250
201
245
204
X6
X6

图 10

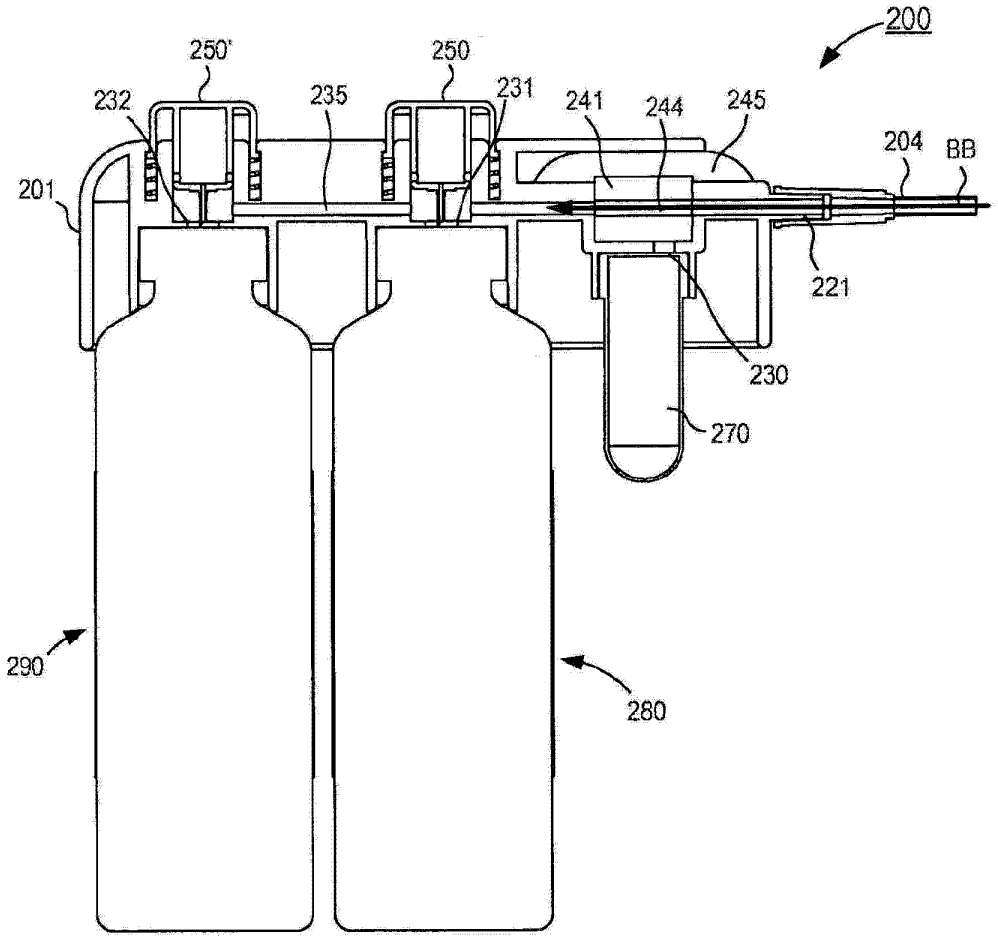

200
250'
250
232
235
231
241
244
245
204
BB
201
221
230
270
290
280

图 11

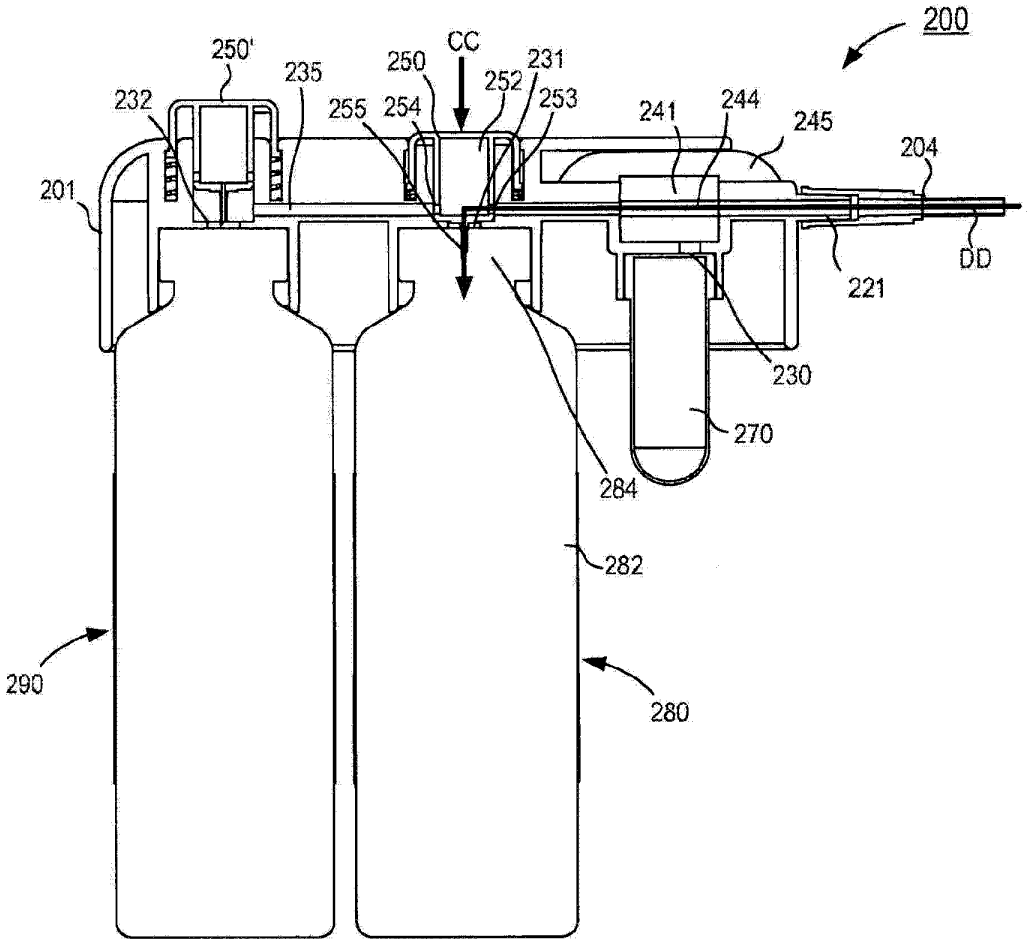

200
250'
235
CC
250
231
252
253
232
255
254
241
244
245
204
201
DD
221
230
270
284
282
290
280

图 12

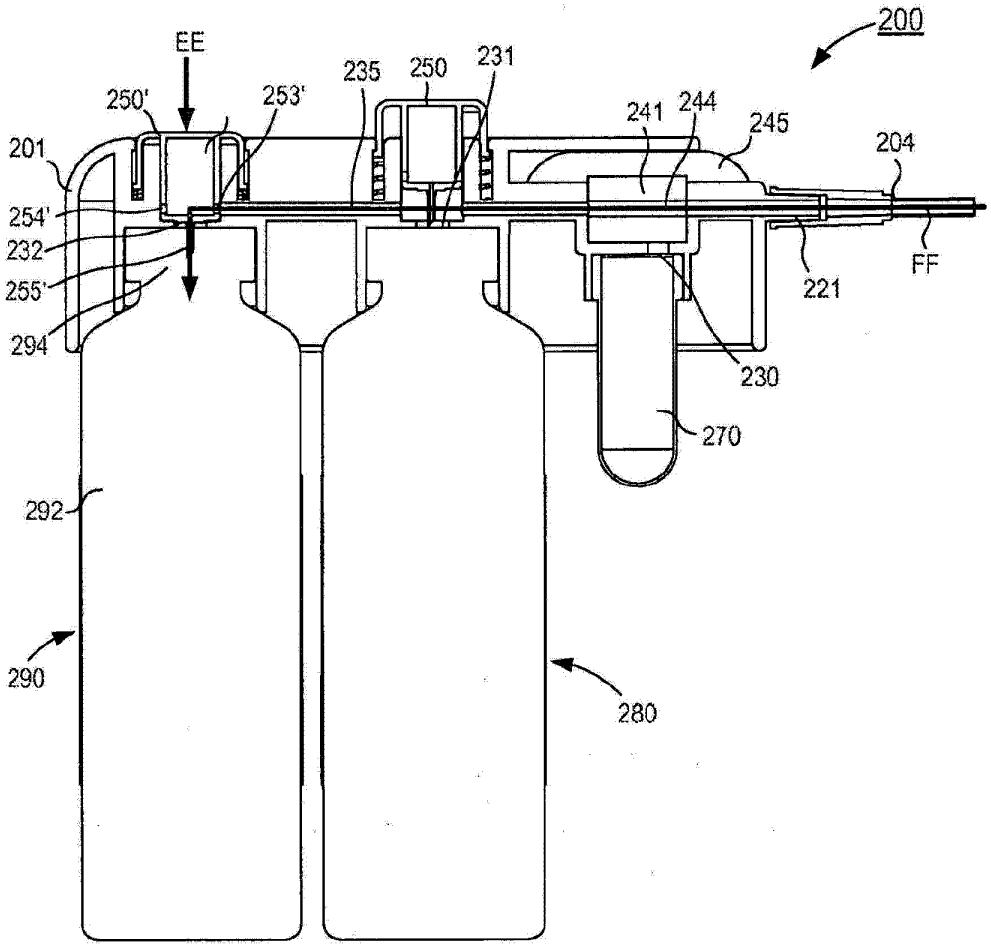

200
EE
250'
253'
235
250
231
241
244
245
204
201
254'
232
255'
294
221
FF
230
270
292
290
280

图 13

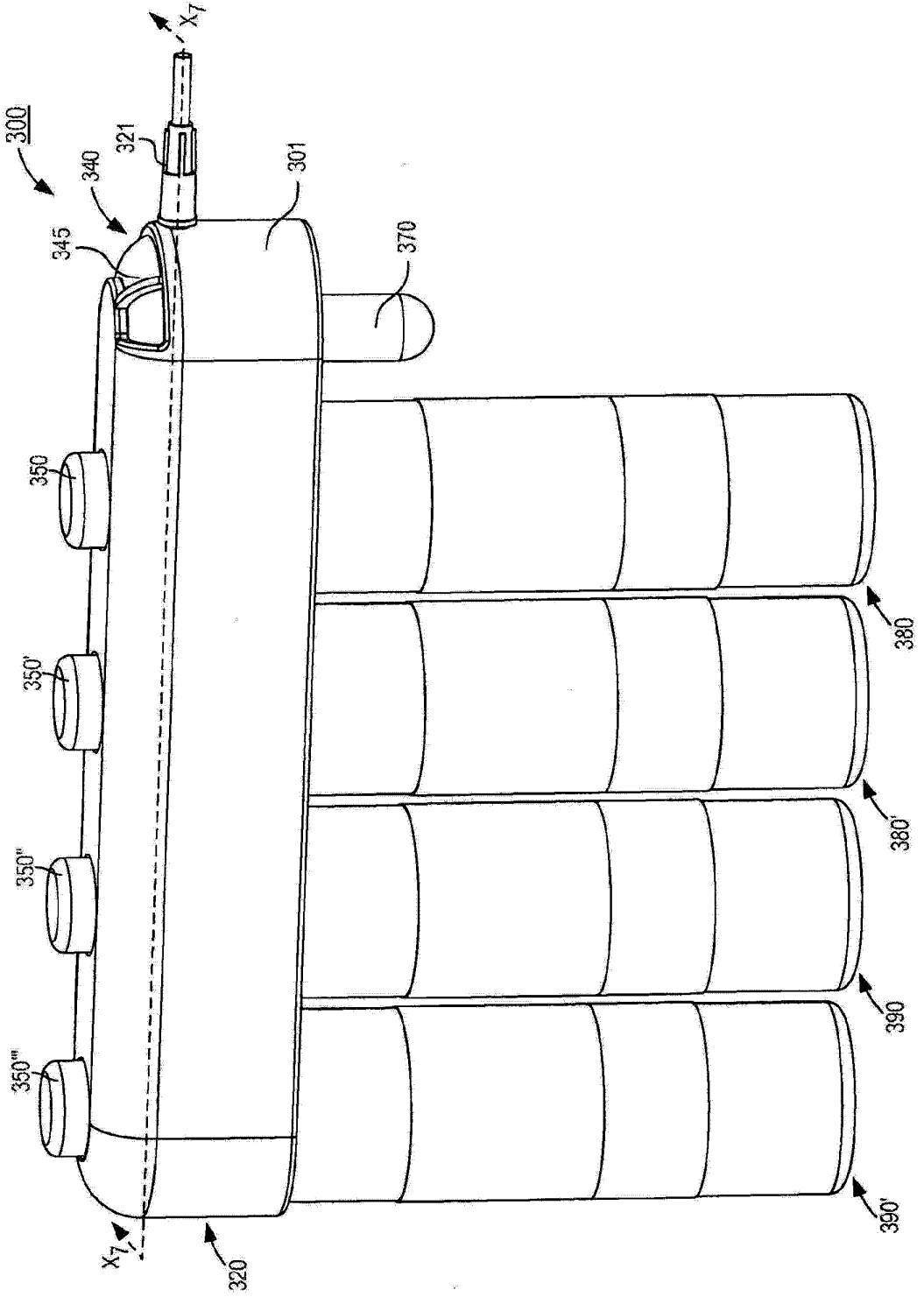


图 14

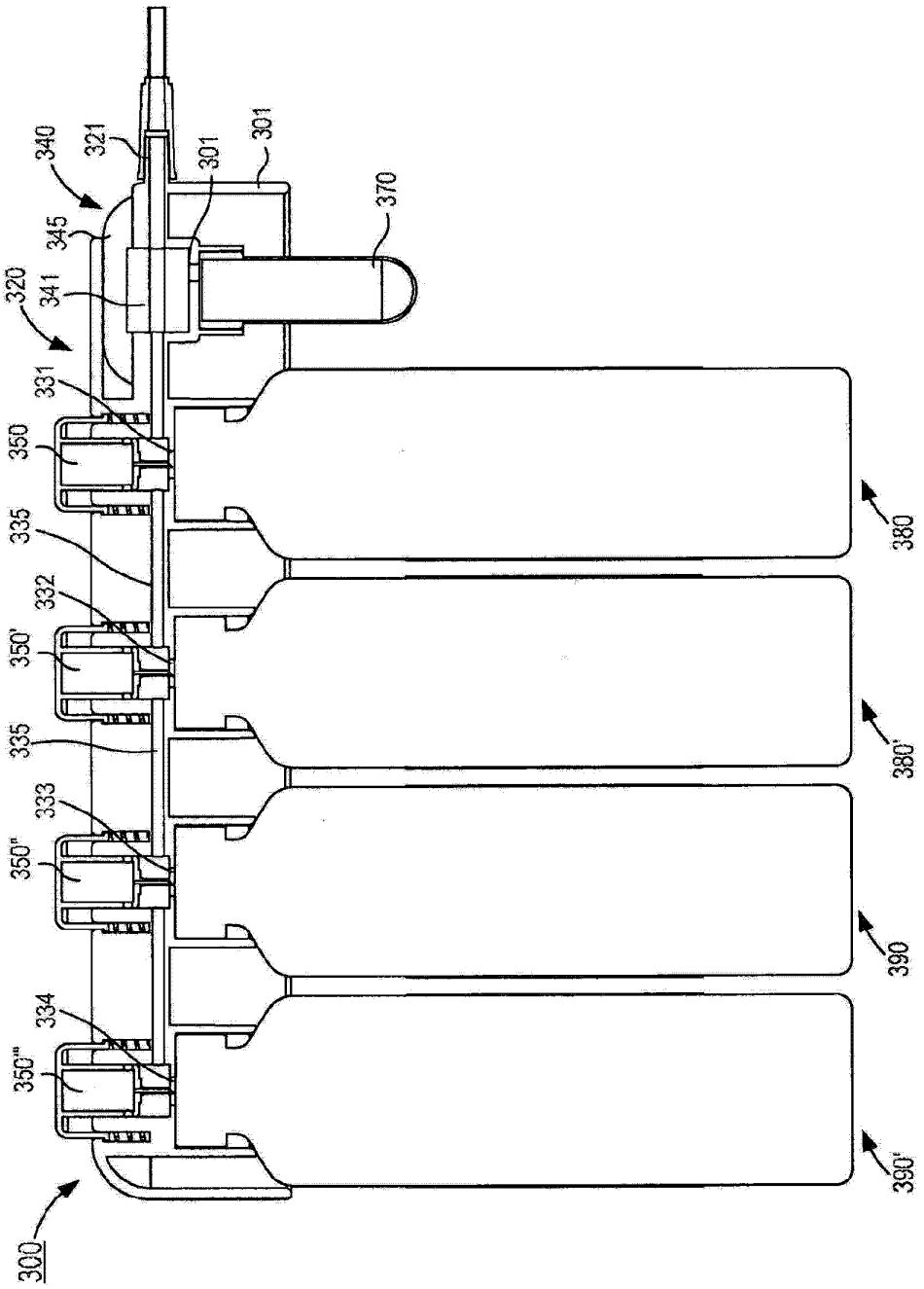

340
321
301
301
370
345
320
341
331
350
335
332
350'
335
333
350"
334
350'"
300
380
380'
390
390'

图 15

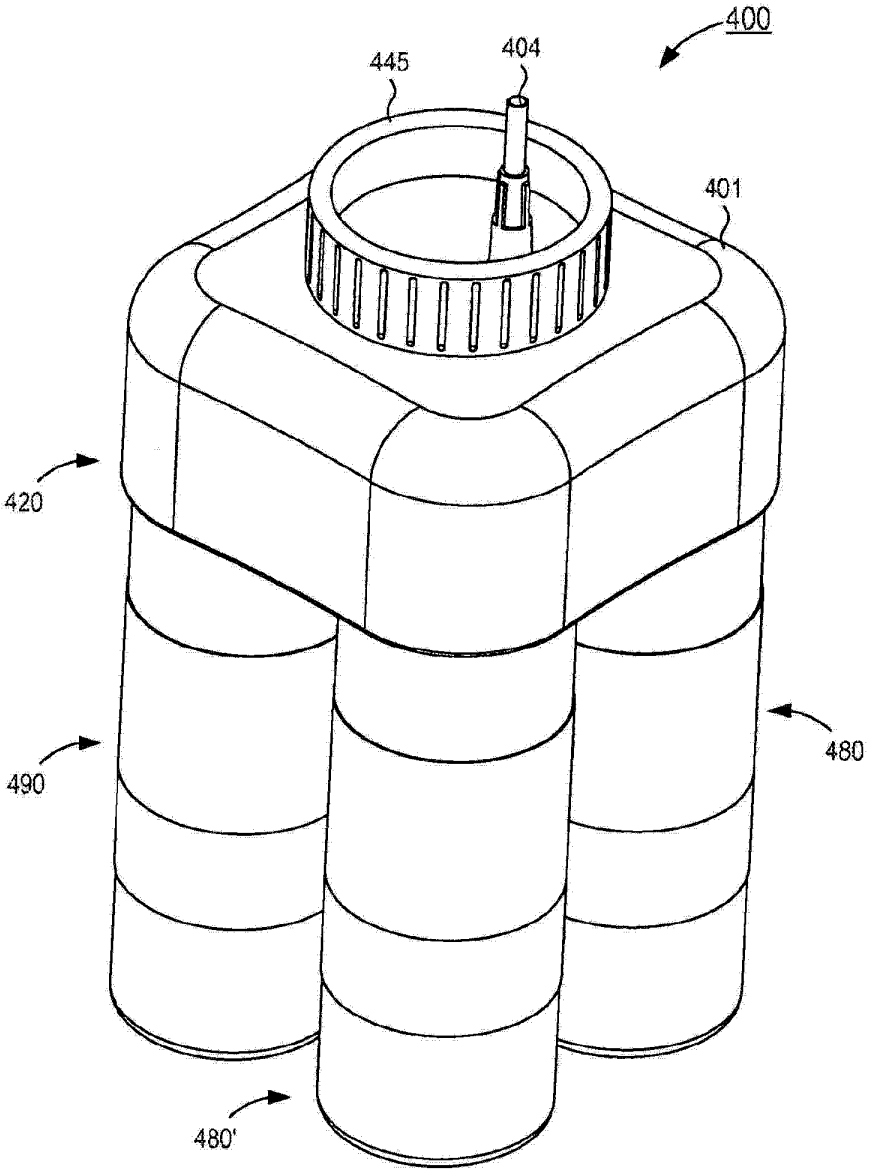


图 16

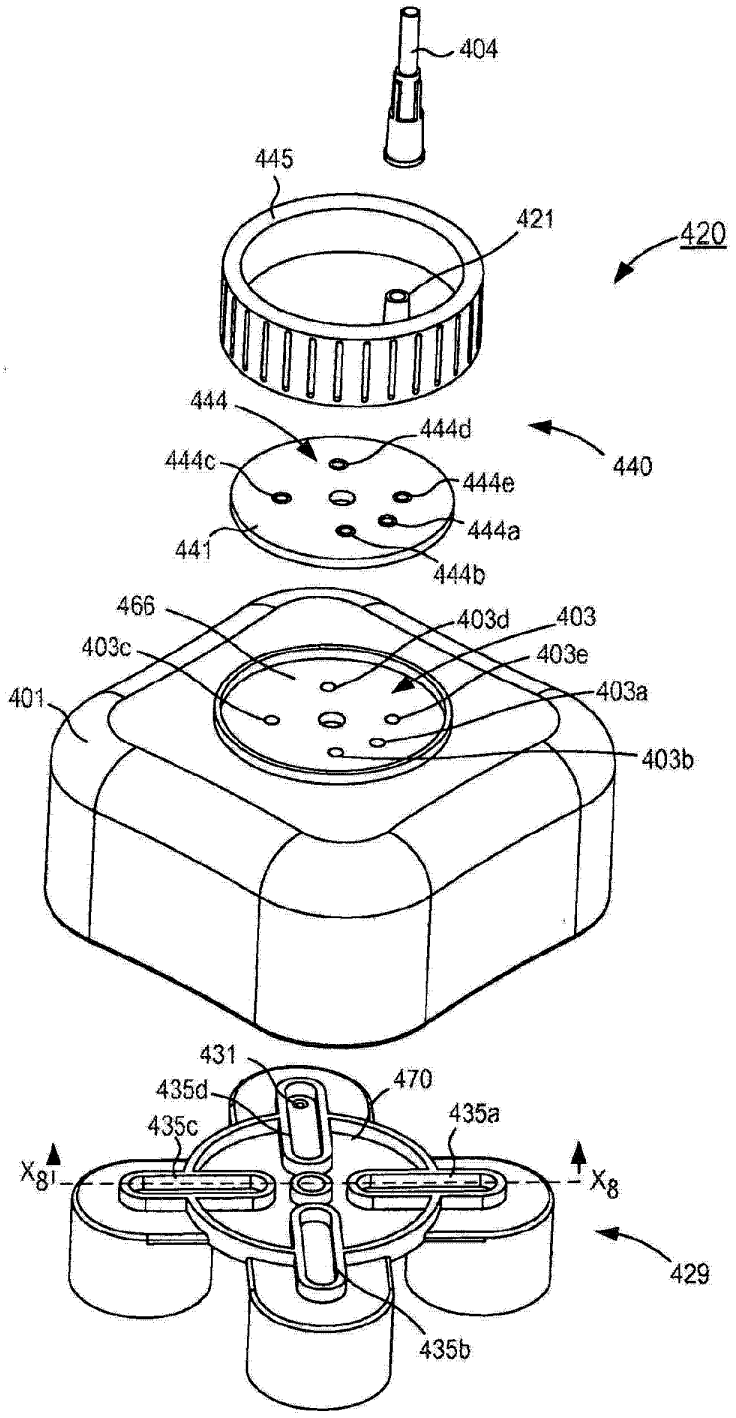

404
445
421
420
444
444d
440
444c
444e
444a
441
444b
466
403d
403
403c
403e
401
403a
403b
431
435d
470
435c
435a
X8
X8
429
435b

图 17

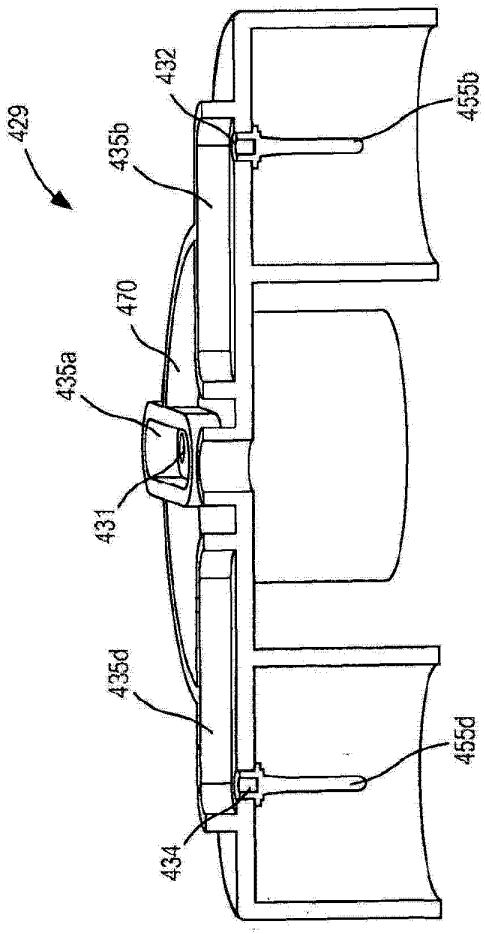


图 18

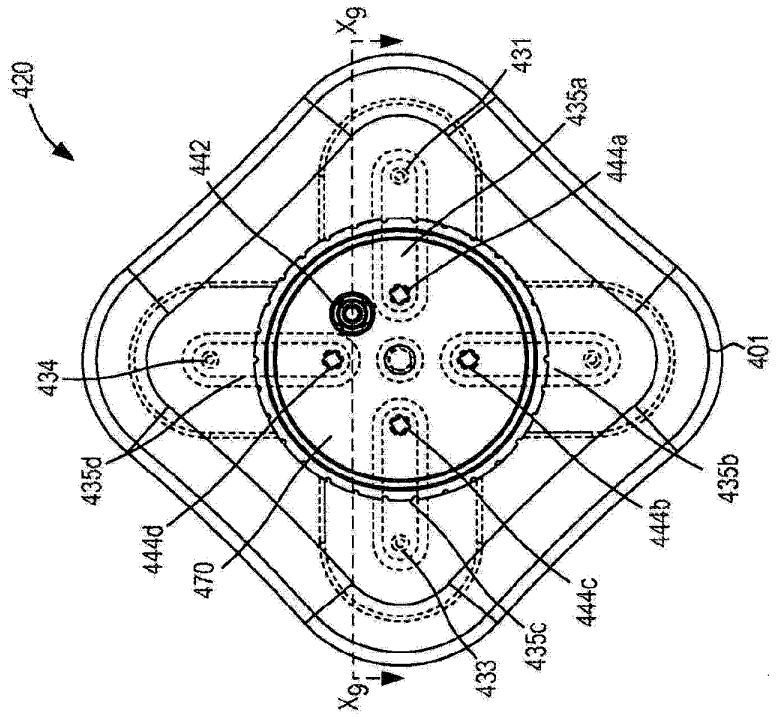

X9
420
431
435a
444a
442
434
401
435d
435b
444d
444b
470
444c
435c
433
X9r

图 19

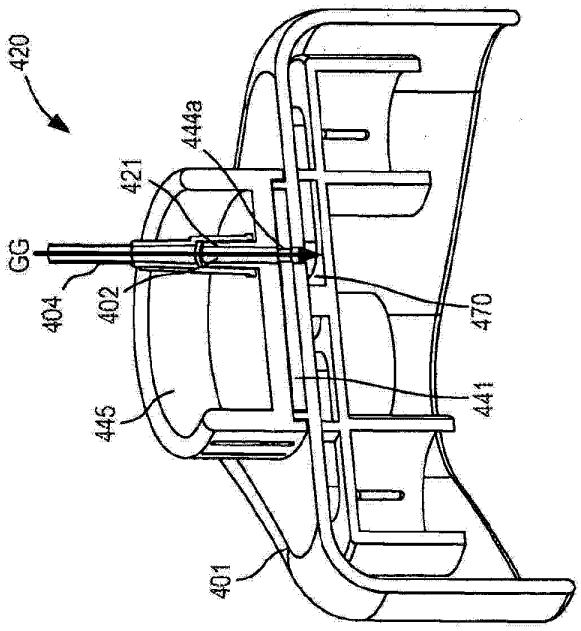

420
444a
421
GG
404
402
470
441
445
401

图 20