

[Fig. 15B]

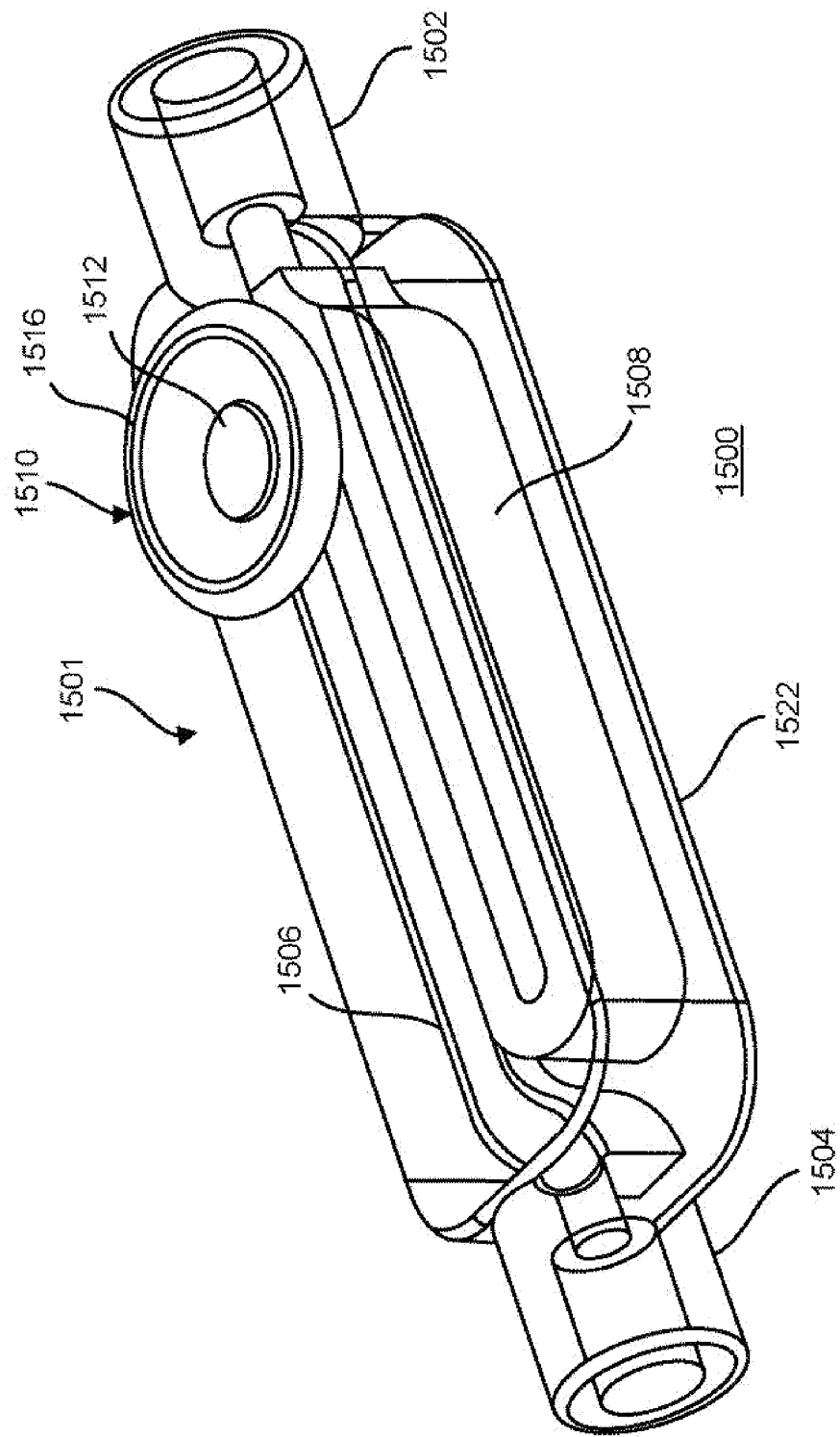


FIG. 15B

[Fig. 15C]

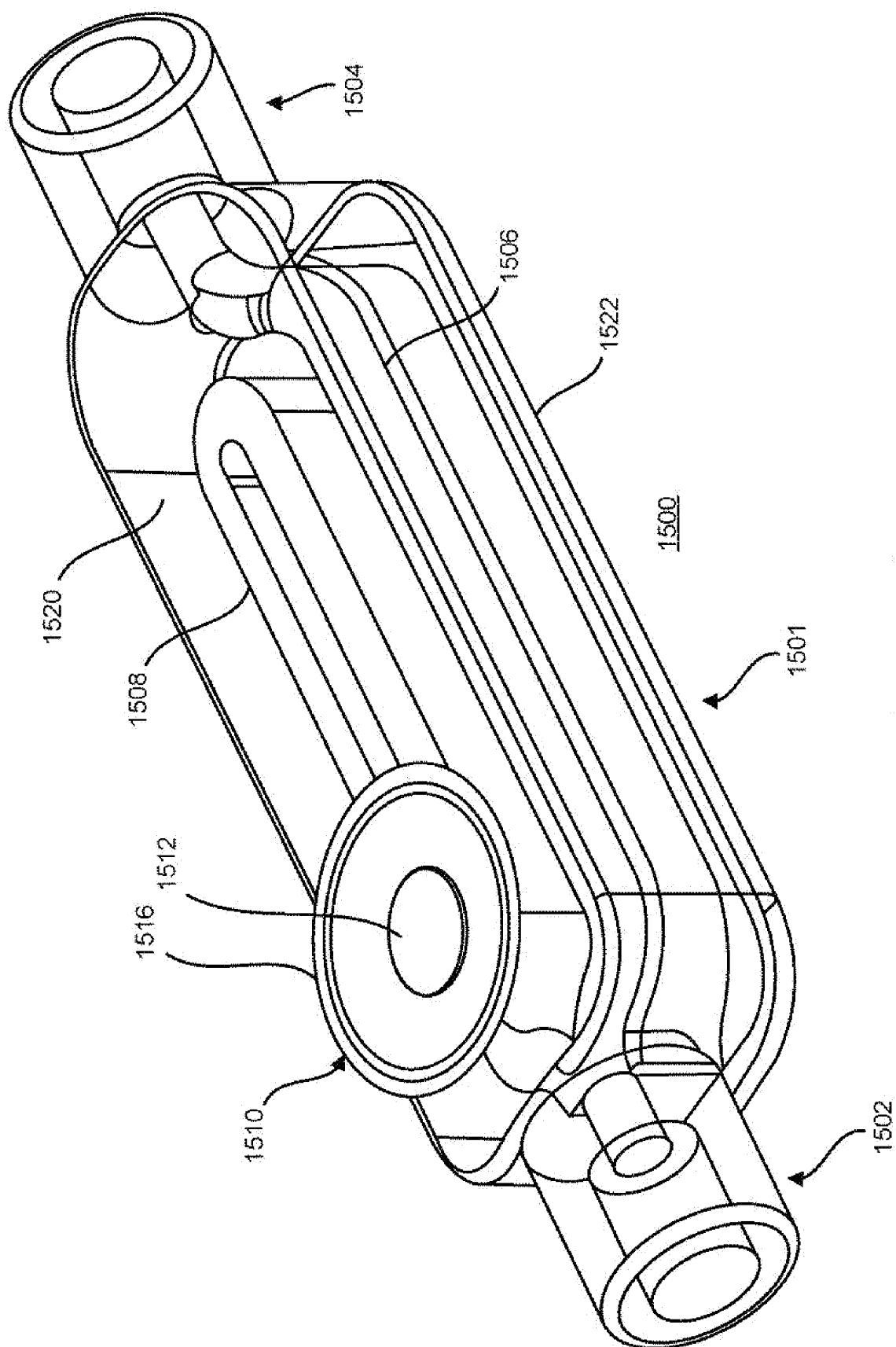


FIG. 15C

[Fig. 15D]

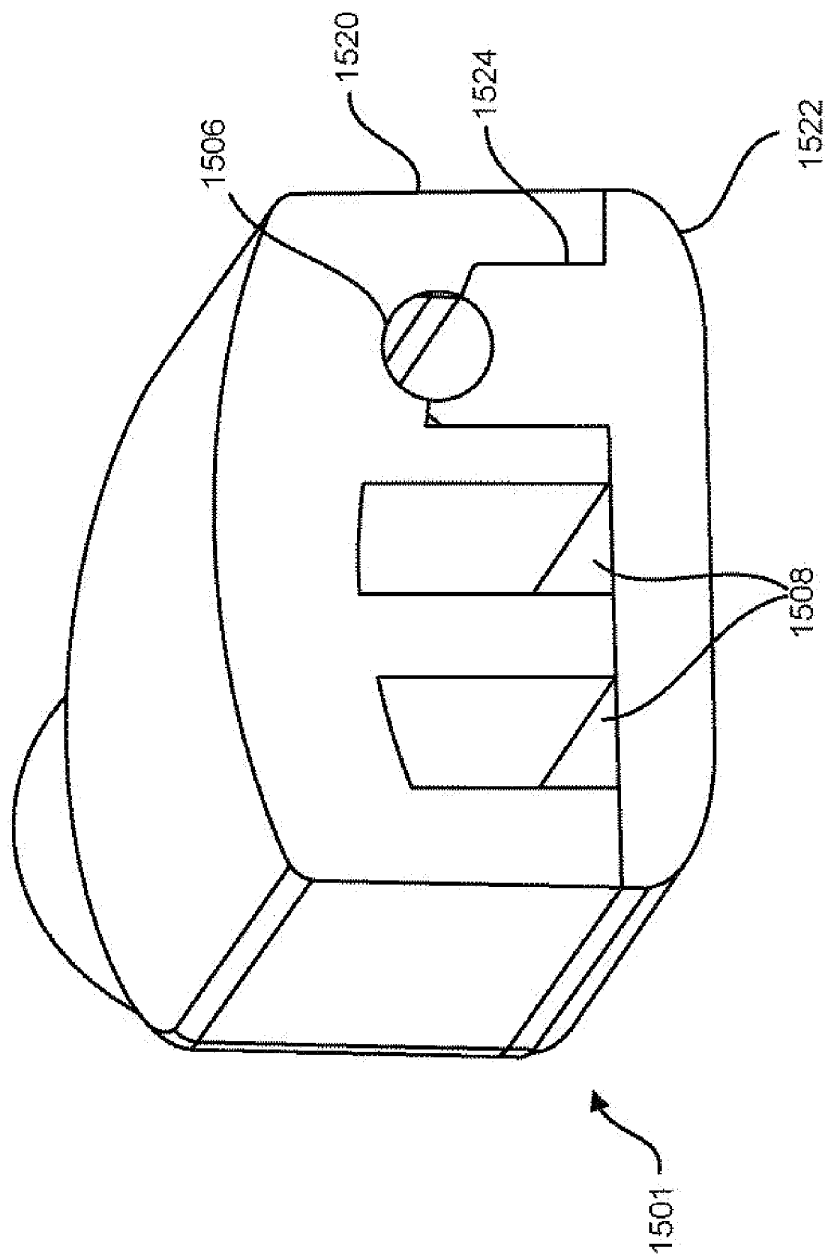


FIG. 15D

[Fig. 15E]

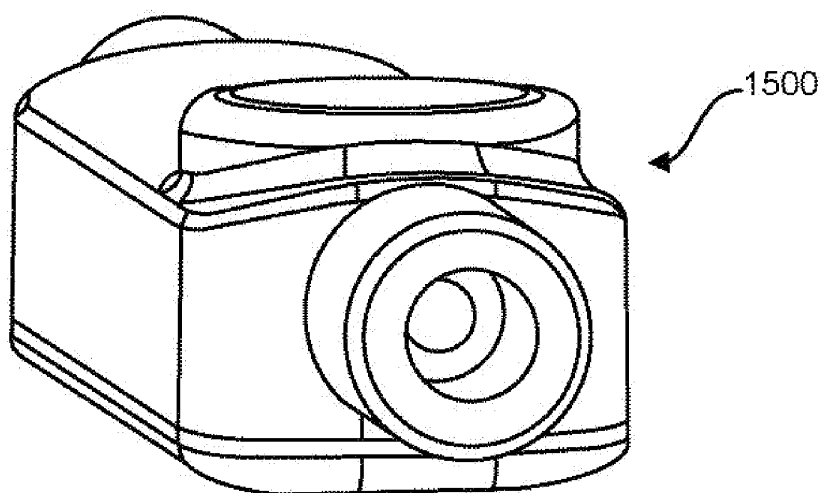
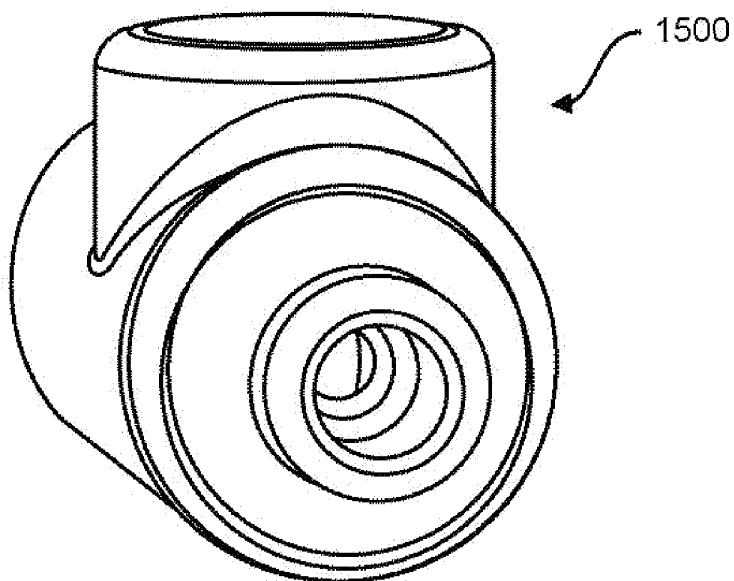


FIG. 15E

[Fig. 15F]

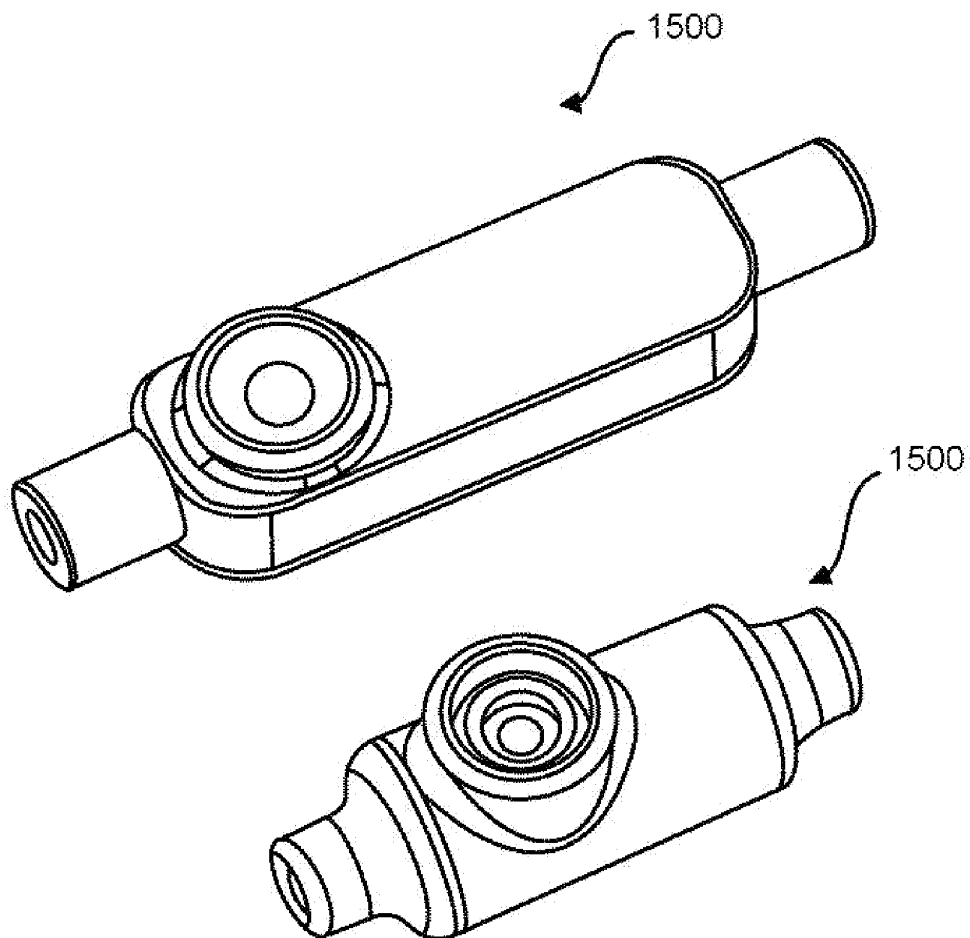


FIG. 15F

[Fig. 15G]

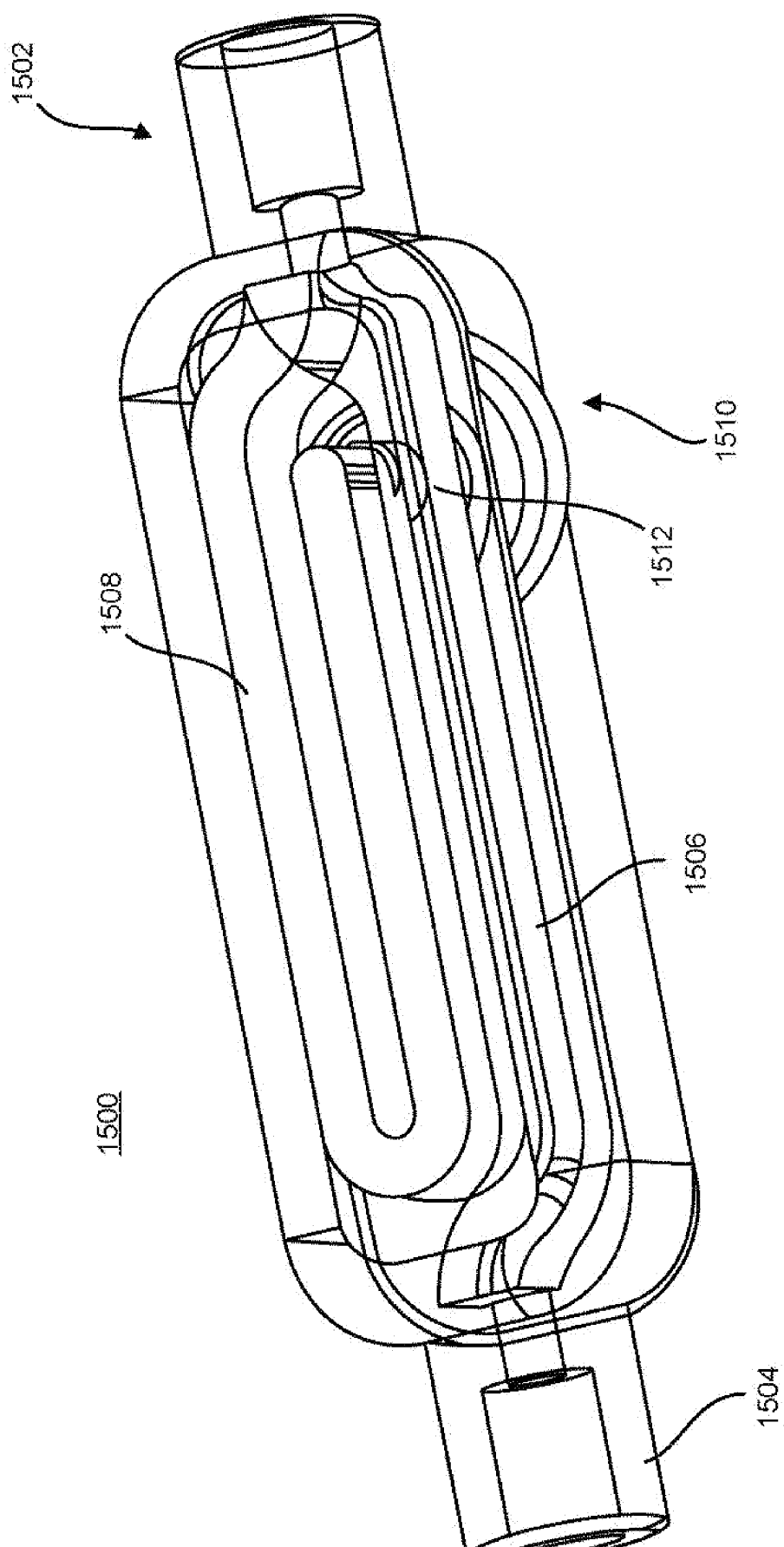


FIG. 15G

[Fig. 16A]

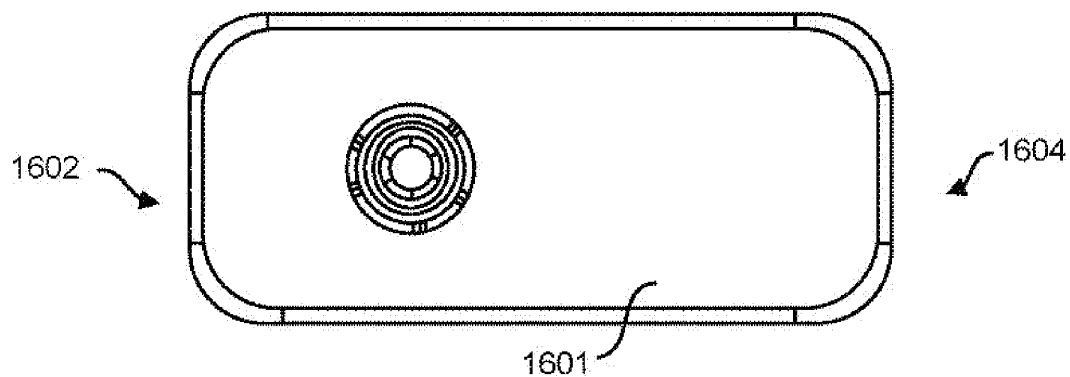


FIG. 16A

[Fig. 16B]

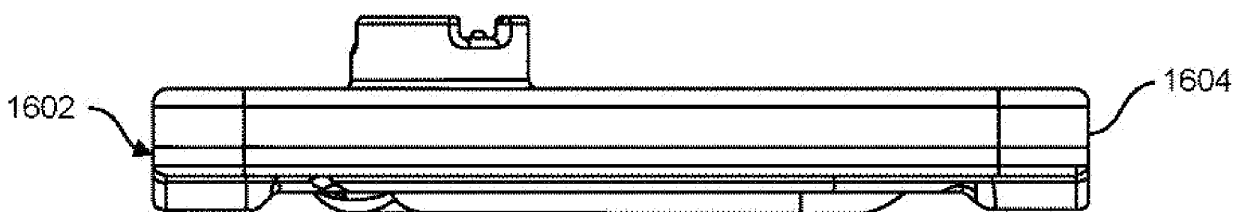


FIG. 16B

[Fig. 16C]

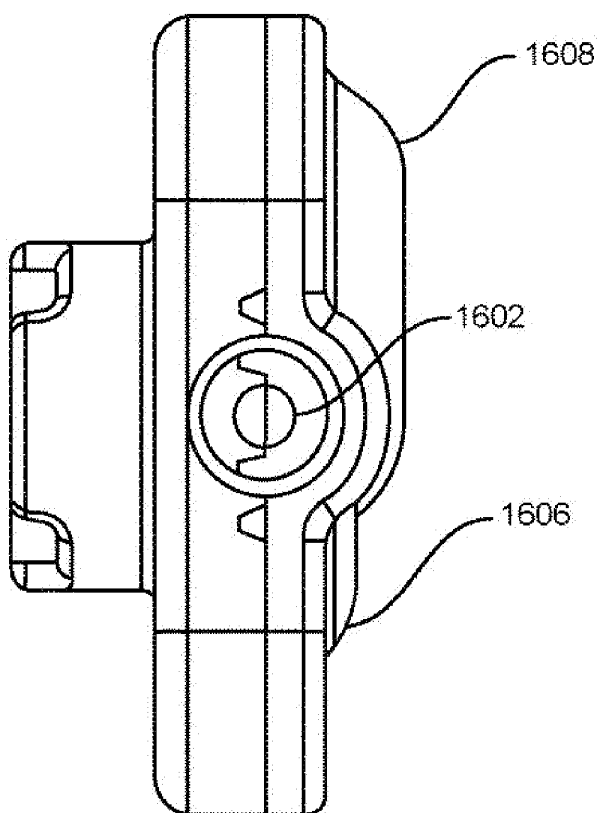


FIG. 16C

[Fig. 16D]

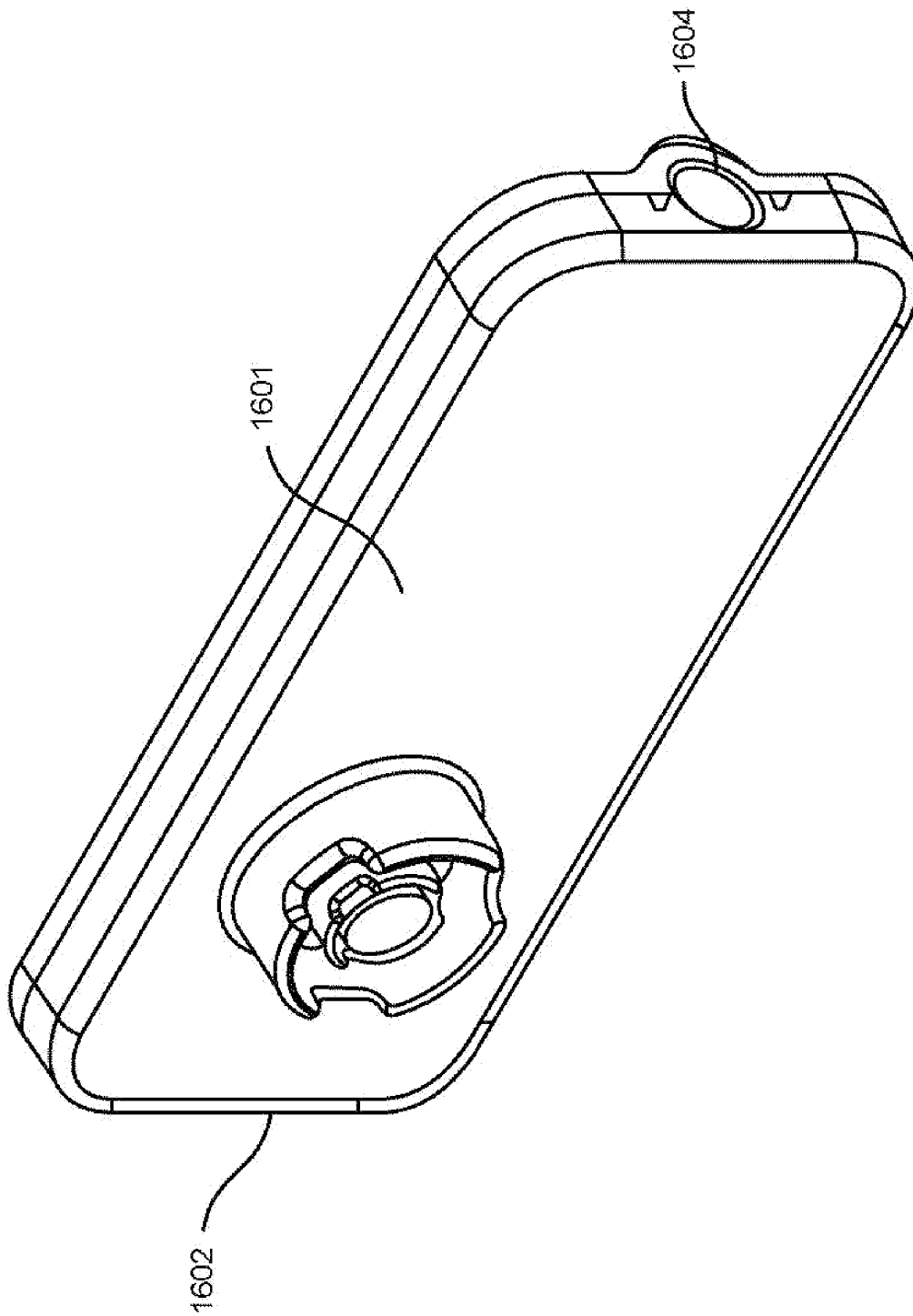


FIG. 16D

[Fig. 17A]

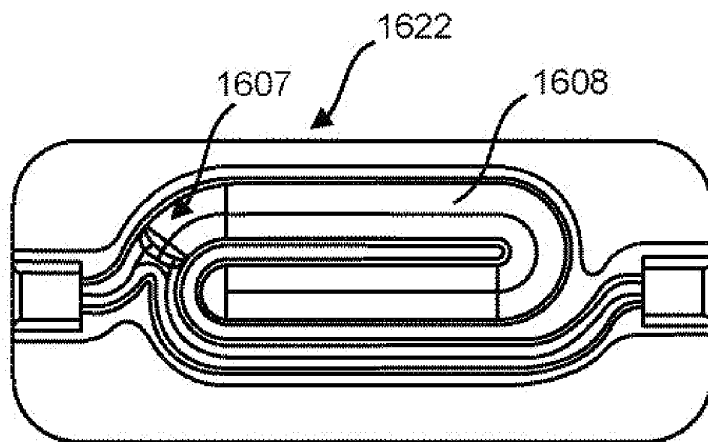


FIG. 17A

[Fig. 17B]

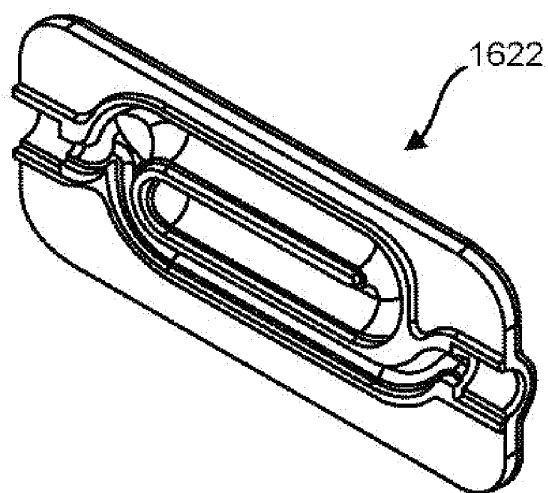


FIG. 17B

[Fig. 17C]

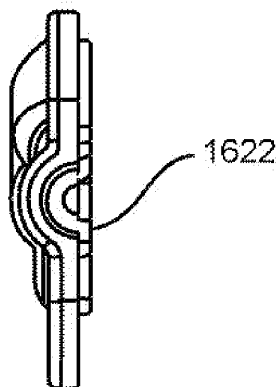


FIG. 17C

[Fig. 17D]

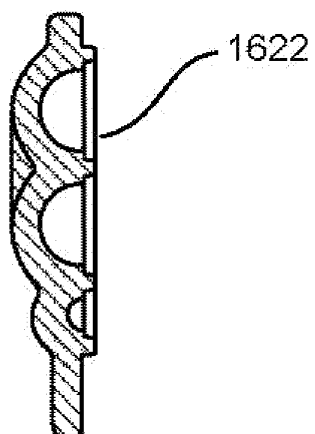


FIG. 17D

[Fig. 17E]

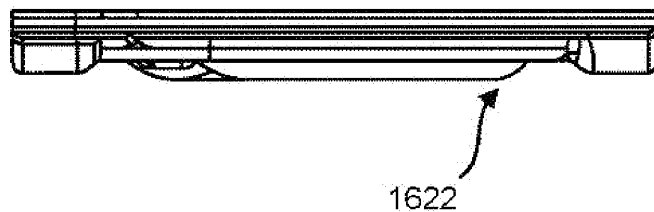


FIG. 17E

[Fig. 18A]

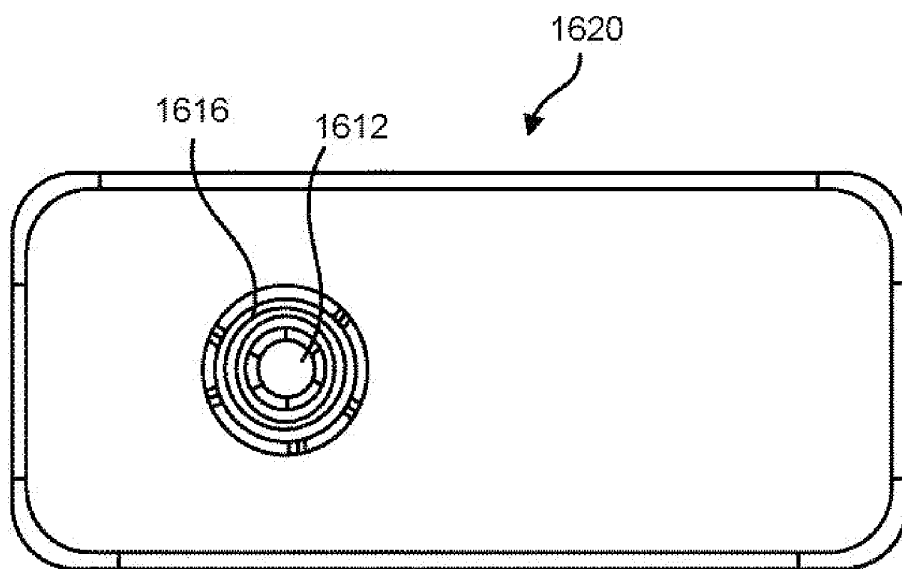


FIG. 18A

[Fig. 18B]

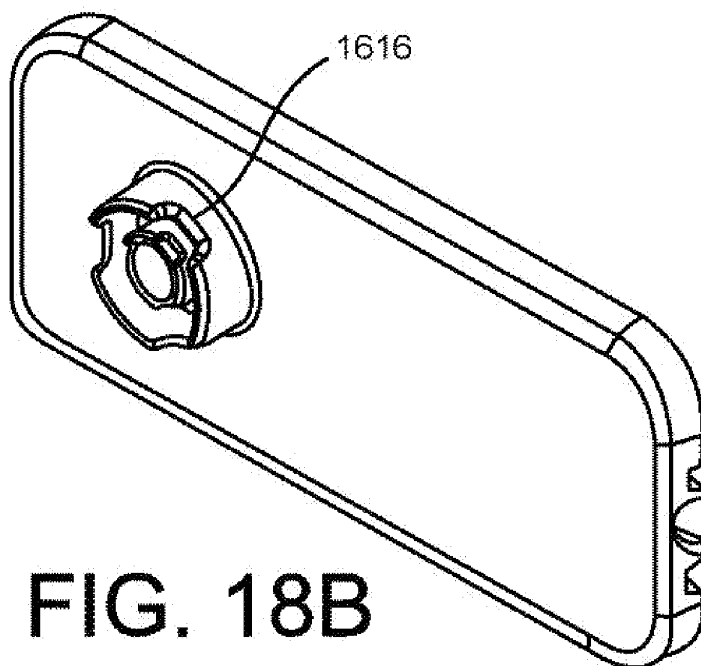


FIG. 18B

[Fig. 18C]

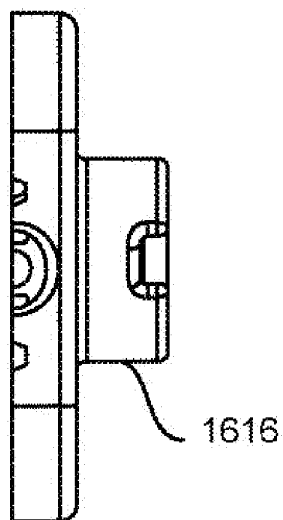
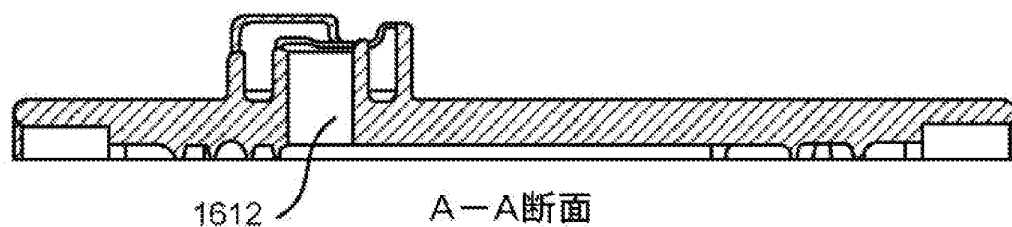
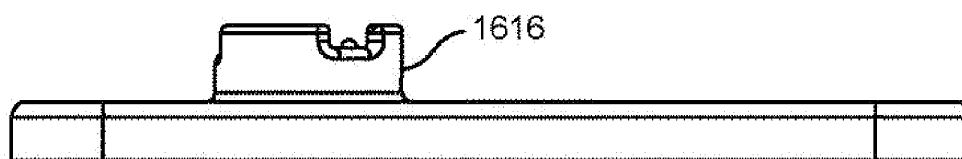


FIG. 18C

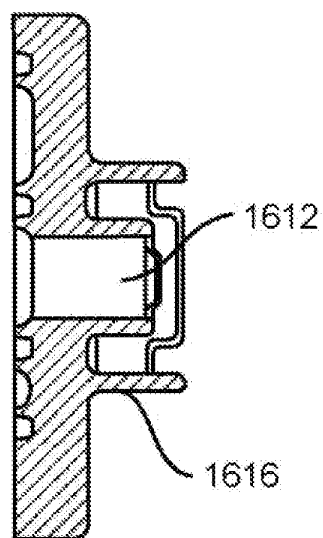
[Fig. 18D]

**FIG. 18D**

[Fig. 18E]

**FIG. 18E**

[Fig. 18F]



A-A断面

FIG. 18F

[Fig. 19A]

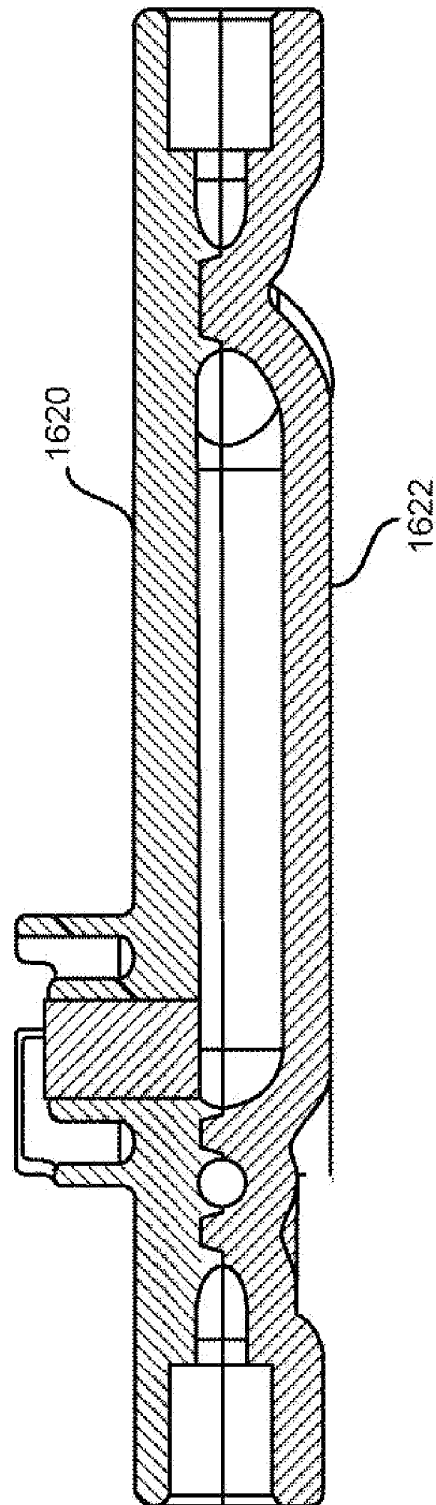


FIG. 19A

[Fig. 19B]

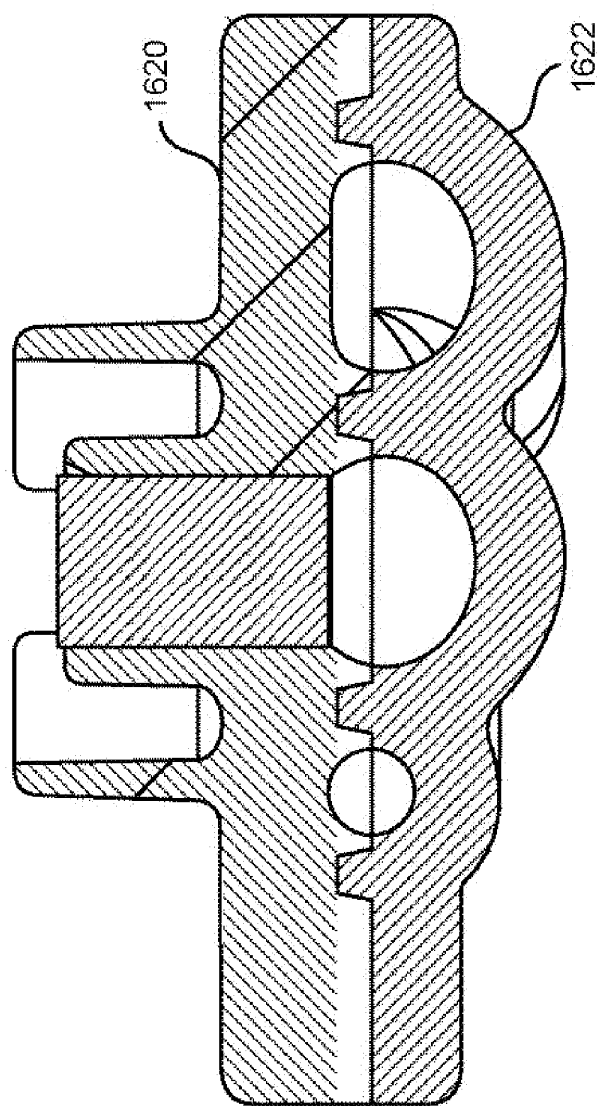


FIG. 19B

[Fig. 20]

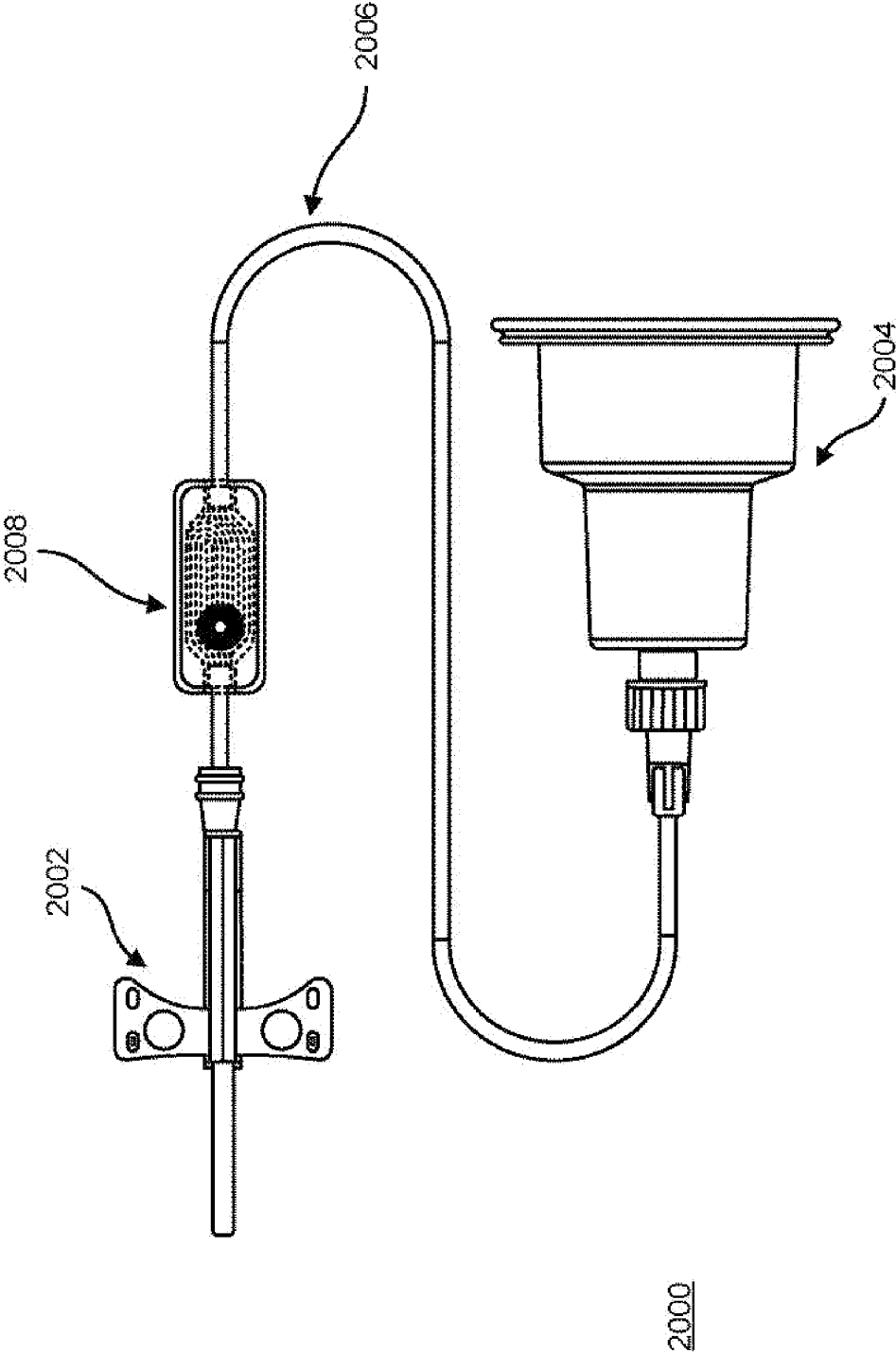


FIG. 20

[Fig. 21]

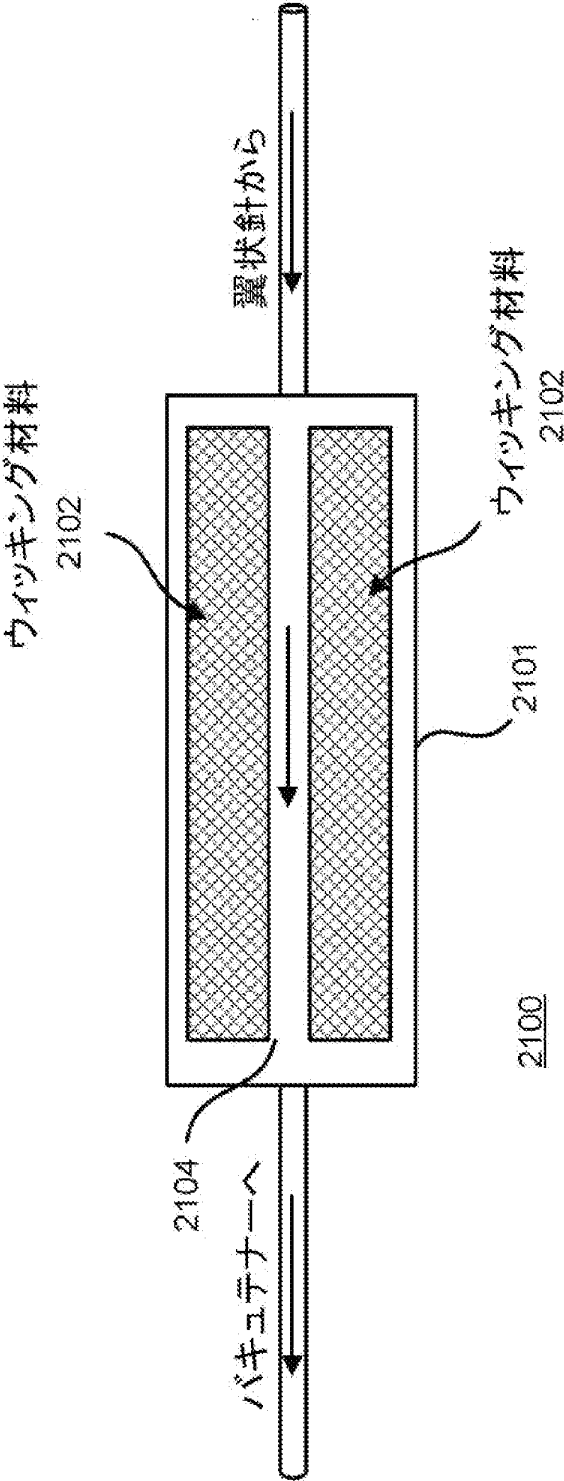


FIG. 21

[Fig. 22A]

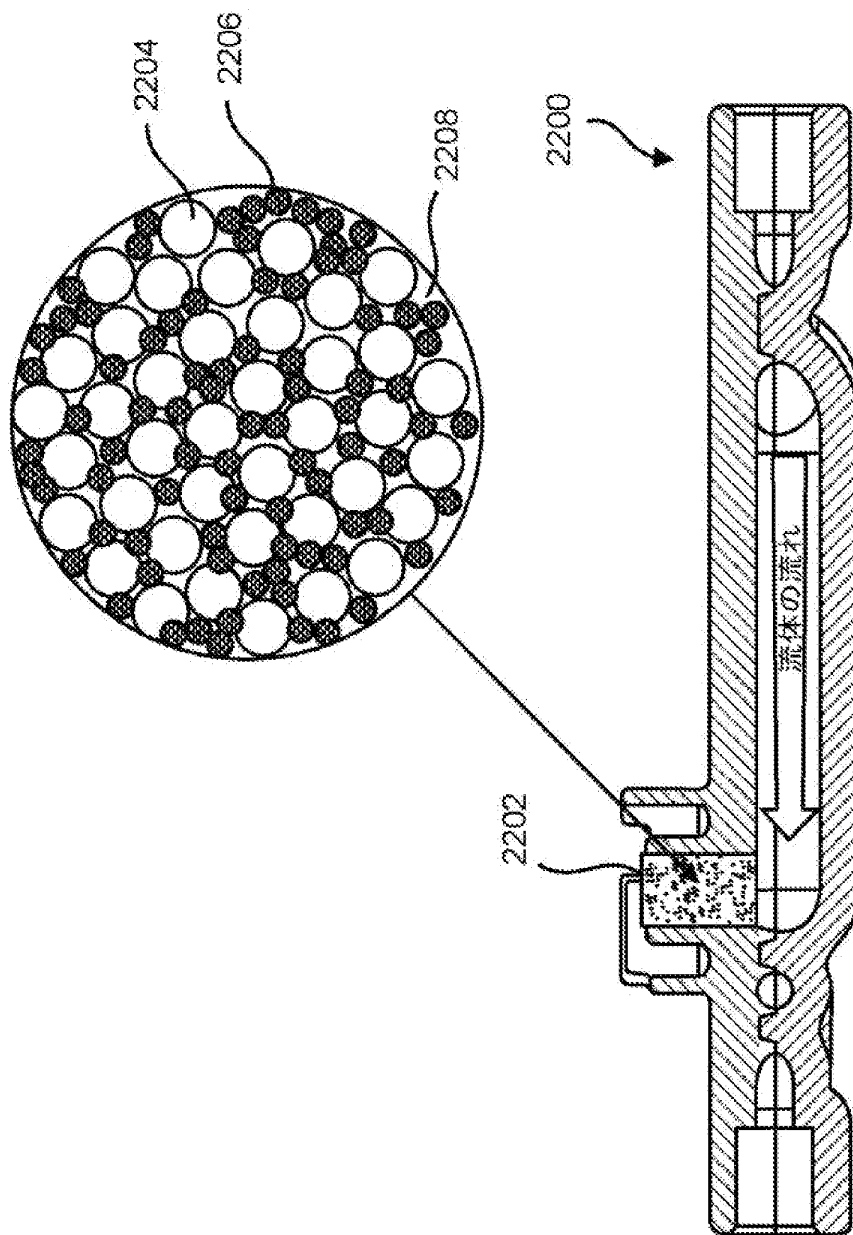


FIG. 22A

[Fig. 22B]

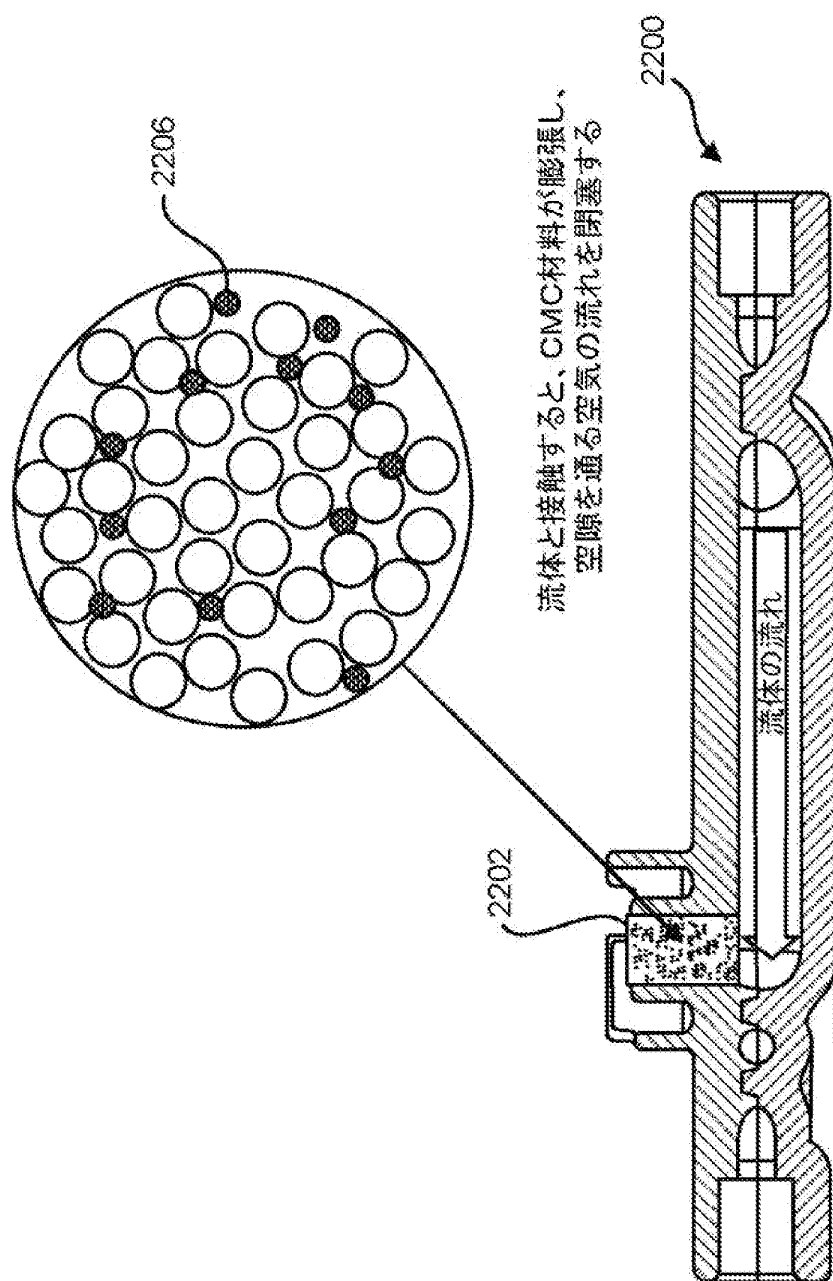


FIG. 22B

[Fig. 23A]

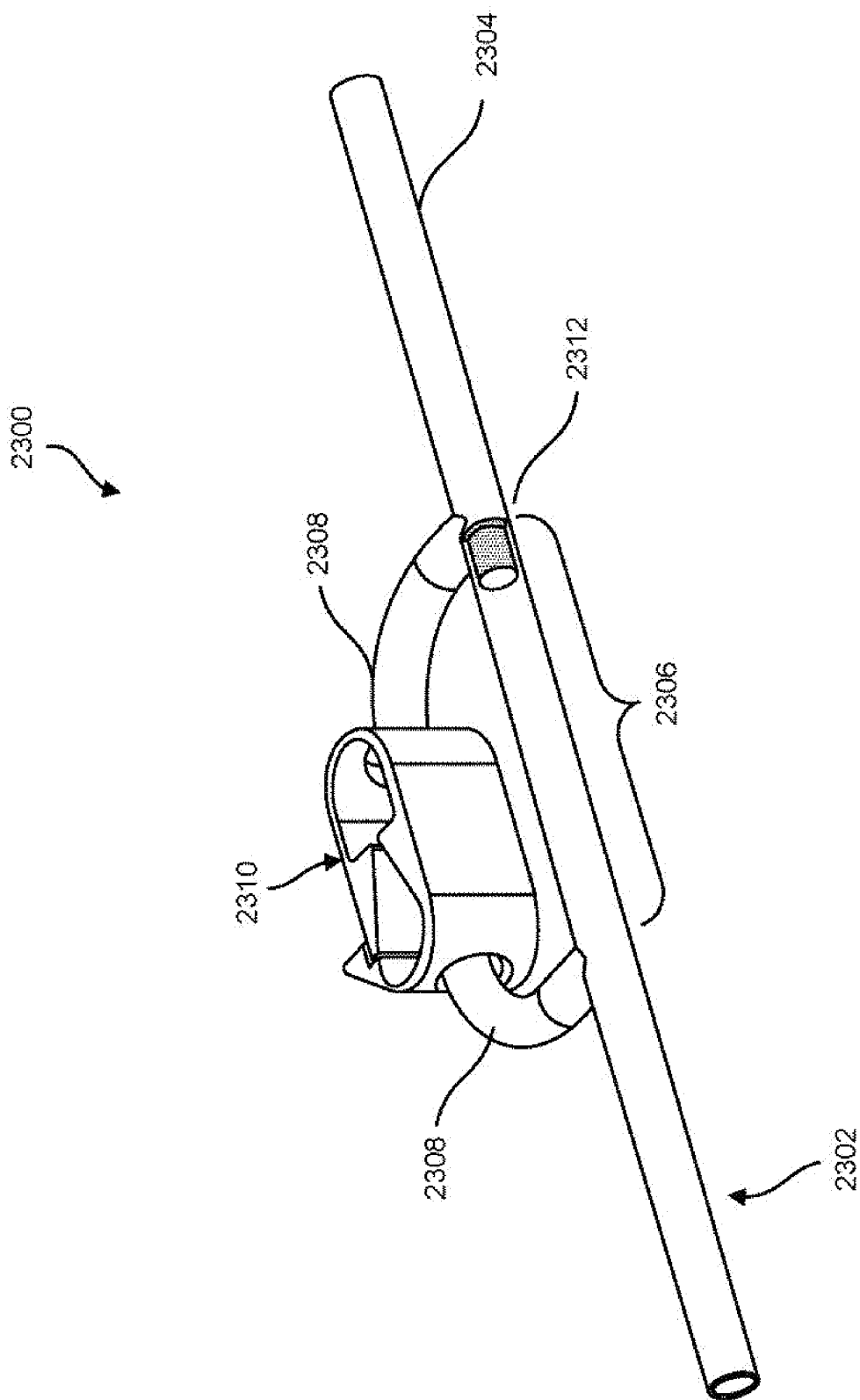


FIG. 23A

[Fig. 23B]

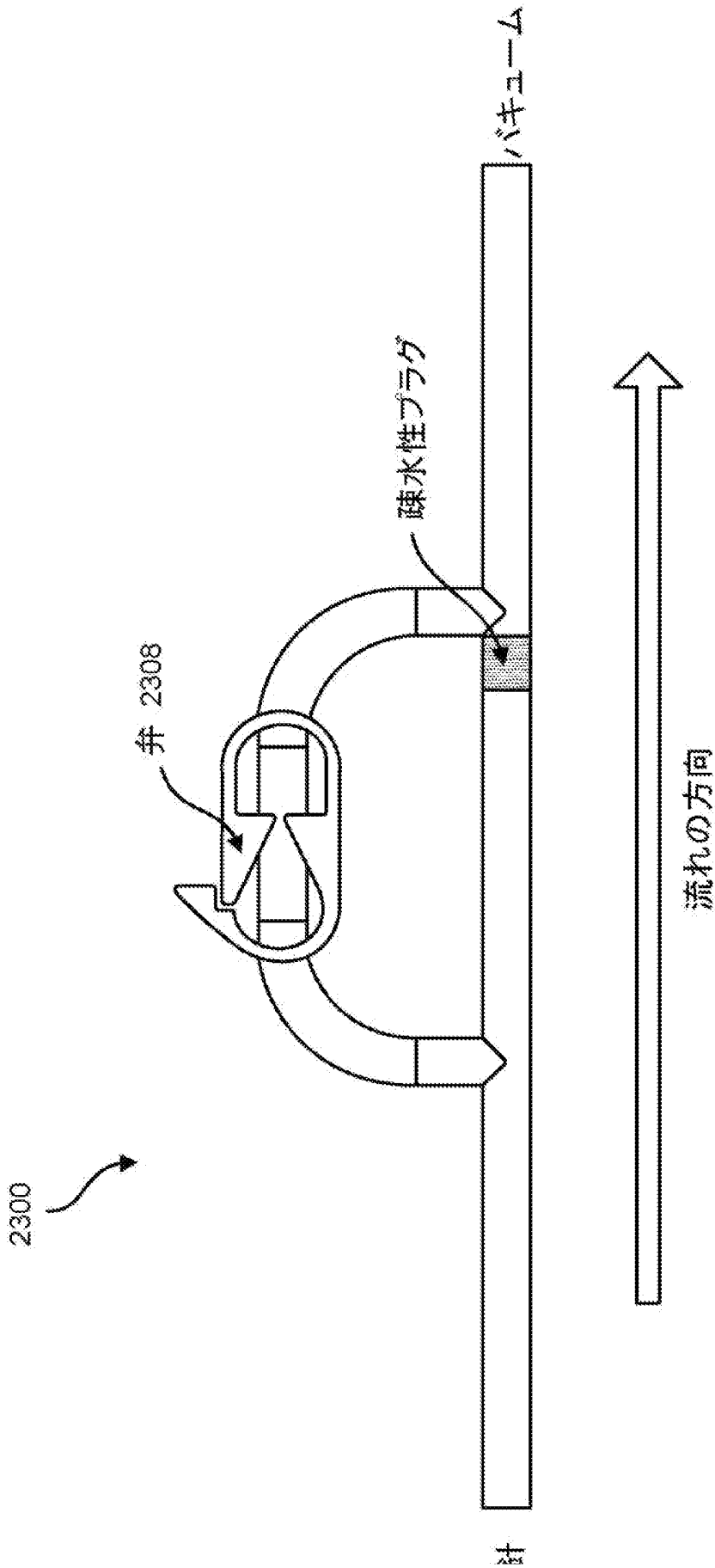


FIG. 23B

drawing

open

[1](#)[2](#)[3](#)[Four](#)[Five](#)[6](#)[7](#)[8A](#)[8B](#)[8C](#)[...](#)

Magnify and Rotate

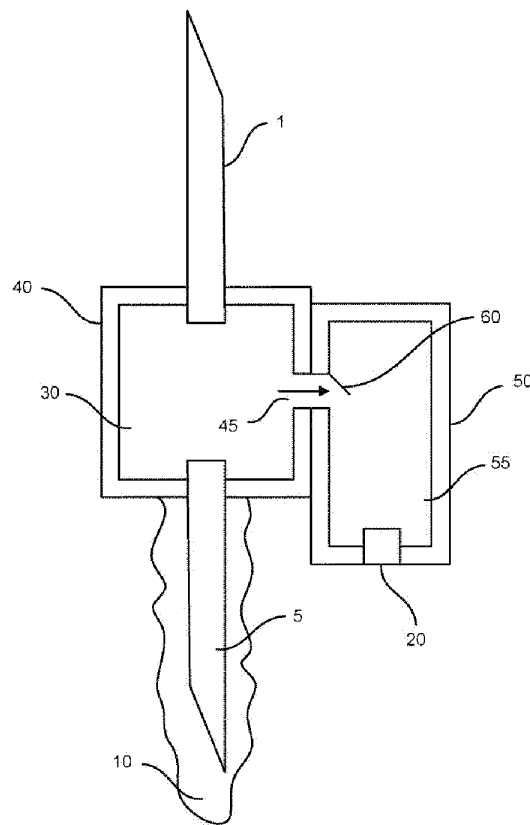
**FIG. 1**

Figure 1



1

/ 1

display



(19) 日本国特許庁(JP)

(12) 特 許 公 報(B2)

(11) 特許番号

特許第6734490号

(P6734490)

(45) 発行日 令和2年8月5日(2020. 8. 5)

(24) 登録日 令和2年7月13日(2020. 7. 13)

(51) Int. Cl.

F I

A 6 1 B 5/15 (2006. 01)

A 6 1 B 5/15 2 0 0

A 6 1 B 5/154 (2006. 01)

A 6 1 B 5/154 2 0 0

請求項の数 26 外国語出願 (全 39 頁)

(21) 出願番号 特願2020-340 (P2020-340)
(22) 出願日 令和2年1月6日(2020. 1. 6)
(62) 分割の表示 特願2018-523384 (P2018-523384)
の分割
原出願日 平成28年7月22日(2016. 7. 22)
(65) 公開番号 特開2020-96843 (P2020-96843A)
(43) 公開日 令和2年6月25日(2020. 6. 25)
審査請求日 令和2年1月31日(2020. 1. 31)
(31) 優先権主張番号 62/238, 636
(32) 優先日 平成27年10月7日(2015. 10. 7)
(33) 優先権主張国・地域又は機関
米国 (US)
(31) 優先権主張番号 62/318, 194
(32) 優先日 平成28年4月4日(2016. 4. 4)
(33) 優先権主張国・地域又は機関
米国 (US)

(73) 特許権者 518026730
クリン インコーポレイテッド
アメリカ合衆国 9 2 1 3 1 カリフォル
ニア州 サンディエゴ スクリップス ポ
ーウェイ パークウェイ 1 0 7 5 5 ナ
ンバー 2 5 7
(74) 代理人 100083806
弁理士 三好 秀和
(74) 代理人 100095500
弁理士 伊藤 正和
(74) 代理人 100111235
弁理士 原 裕子
(74) 代理人 100195257
弁理士 大淵 一志

最終頁に続く

(54) 【発明の名称】 血液隔離装置、体液隔離装置、及び血液隔離システム

【特許請求の範囲】

【請求項 1】

血液隔離装置であって、
入口ポートと、
出口ポートと、

隔離チャンバ及びサンプリング流路であって、前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記隔離チャンバは空気透過性血液バリアを含む通気口を有し、前記サンプリング流路は前記出口ポートと接続される遠位端を有する、隔離チャンバ及びサンプリング流路と、

前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含み、

前記隔離チャンバ、前記サンプリング流路、及び前記分岐点は、血液の第1部分が前記隔離チャンバ内での隔離のために前記空気透過性血液バリアに向かって前記隔離チャンバに流れ込み、血液の第2部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第1部分を迂回し、前記出口ポートに向かって前記サンプリング流路に向けられるように寸法設定され且つ構成される、血液隔離装置。

【請求項 2】

血液隔離装置であって、
入口ポートと、

出口ポートと、
空気透過性血液バリアを含む通気口を有する隔離チャンバと、
前記出口ポートと接続される遠位端を有するサンプリング流路と、
前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含み、

前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記分岐点は、血液の第1部分が前記隔離チャンバに流れ込み、前記空気透過性血液バリアを通して前記隔離チャンバ内の空気を追い出し、前記隔離チャンバ内に隔離されることを可能にし、血液の第2部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第1部分を迂回し、前記出口ポートに向かって前記サンプリング流路に向けられることを可能にするように寸法設定され且つ構成される、血液隔離装置。

【請求項3】

前記空気透過性血液バリアは、血液と接触すると少なくとも部分的に密封する空気透過性材料を含む、請求項1又は2に記載の血液隔離装置。

【請求項4】

前記隔離チャンバは、前記ハウジング内に画定された隔離流路を含む、請求項1又は2に記載の血液隔離装置。

【請求項5】

前記ハウジングは、上部部材と嵌合する下部部材を含み、前記下部部材及び前記上部部材のそれぞれは、前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路のそれぞれの一部を画定する、請求項1から3のいずれか一項に記載の血液隔離装置。

【請求項6】

患者針とサンプル採取装置とを有する採血経路と接続される血液隔離装置であって、
前記患者針と接続される入口ポートと、

隔離チャンバ及びサンプリング流路であって、前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記隔離チャンバは空気透過性血液バリアを含む通気口を有し、前記隔離チャンバ及び前記分岐点は、血液の第1部分を前記空気透過性血液バリアに向かって前記隔離チャンバに向けるように構成され、前記サンプリング流路は出口ポートと接続される遠位端を有し、前記サンプリング流路及び前記分岐点は、血液の第2部分が前記隔離チャンバ及び前記隔離チャンバ内に隔離された前記血液の第1部分を迂回し、前記出口ポートに向かって前記サンプリング流路に向けられることを可能にするように構成され、前記出口ポートは前記サンプル採取装置と接続される、隔離チャンバ及びサンプリング流路と、

前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含む、血液隔離装置。

【請求項7】

患者針とサンプル採取装置とを有する採血経路と接続される血液隔離装置であって、
前記患者針と接続される入口ポートと、

前記サンプル採取装置と接続される出口ポートと、

空気透過性血液バリアを含む通気口を有する隔離チャンバと、

前記出口ポートと接続される遠位端を有するサンプリング流路と、

前記入口ポート、前記出口ポート、前記隔離チャンバ、及び前記サンプリング流路を収容し且つ画定するハウジングと
を含み、

前記隔離チャンバ及び前記サンプリング流路のそれぞれが分岐点を介して前記入口ポートと接続され、前記分岐点は、血液の第1部分が前記隔離チャンバに流れ込み、前記空気透過性血液バリアを通して前記隔離チャンバ内の空気を追い出し、前記隔離チャンバ内に

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

【請求項 8】

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

【請求項 9】

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

【請求項 10】

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

【請求項 11】

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

【請求項 12】

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

【請求項 13】

体液隔離装置であって、
入口ポートと、
前記入口ポートと接続される出口ポートと、
分岐点を介して前記入口ポートと接続される隔離チャンバであって、空気透過性体液バリアを含む通気口を有する隔離チャンバと、
前記入口ポート、前記出口ポート、及び前記隔離チャンバを収容し且つ固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固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じ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 1 5】

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 1 3 又は 1 4 に記載の体液隔離装置。

【請求項 1 6】

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 3 又は 1 4 に記載の体液隔離装置。

【請求項 1 7】

前記入ロ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 部分を前記入ロポートから前記出ロポートに連ぶ、請求項 1 3 又は 1 4 に記載の体液隔離装置。

【請求項 1 8】

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、前記入ロポート、前記出ロポート、及び前記隔離チャンバのそれぞれの一部を固定する、請求項 1 3 又は 1 4 に記載の体液隔離装置。

【請求項 1 9】

前記分岐点を介して前記入ロ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 1 3 又は 1 4 に記載の体液隔離装置。

【請求項 2 0】

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、前記入ロポート、前記出ロポート、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固定する、請求項 1 9 に記載の体液隔離装置。

【請求項 2 1】

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ロポートと、
前記サンプル採取装置と接続される出ロポートと、
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、
前記出ロ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、
前記入ロポート、前記出ロポート、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ロポートと接続され、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、前記出ロ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 2 2】

前記入ロポートは、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 2 1 に記載の血液隔離システム。

【請求項 2 3】

前記出ロポートは、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 2 1 に記載の血液隔離システム。

【請求項 2 4】

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 2 1 に記載の血液隔離システム。

【請求項 2 5】

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、前記入ロ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広範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に加えられ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が必要とする。

【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パ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2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、銅、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」弁又はフラップ弁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、銅、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、バキューテナー（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を通し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し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。逗通経路の密封は、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～8F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を通し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されることができる。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されることができる。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 1 1 2 0 を含むことができる。採血装置 1 1 2 0 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 1 1 0 0 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 1 1 2 0 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。

【0 0 5 2】

図 1 2 A ~ 1 2 D 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 1 2 0 0 を示す。システム 1 2 0 0 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 1 2 0 4 に取り付けられるための血液隔離装置 1 2 0 2 を含む。血液隔離装置 1 2 0 2 は、バキュテナー (登録商標) 容器又はバイアルが採血装置 1 2 0 4 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 1 2 0 2 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。

【0 0 5 3】

一部の実施では、血液隔離装置 1 2 0 2 は、入口ポート 1 2 1 2 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 1 2 1 2 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 1 2 1 4 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 1 2 1 8 に分離する。

【0 0 5 4】

一部の実施では、隔離チャンバ 1 2 1 8 は、隔離装置 1 2 0 2 の本体内の流路として形成される。隔離チャンバ 1 2 1 8 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 1 2 0 2 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 1 2 A 及び 1 2 B に示すように、隔離装置 1 2 0 2 は、本体 1 2 0 6 とキャップ 1 2 0 8 とを含む。本体 1 2 0 6 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 1 2 0 8 から延びる 1 つ以上のアーム 1 2 1 0 が更に形成され、1 つ以上のアーム 1 2 1 0 は、本体 1 2 0 6 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。

【0 0 5 5】

図 1 3 A ~ 1 3 D 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 1 3 0 0 を示す。システム 1 3 0 0 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 1 3 0 4 に取り付けられるための血液隔離装置 1 3 0 2 を含む。血液隔離装置 1 3 0 2 は、バキュテナー (登録商標) 容器又はバイアルが採血装置 1 3 0 4 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 1 3 0 2 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。

【0 0 5 6】

血液隔離装置 1 3 0 2 は、入口ポート 1 3 1 4 と、主出口ポート 1 3 1 2 と、隔離流路ポート 1 3 1 6 とを有するハウジング 1 3 0 1 を含む。入口ポート 1 3 1 4 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 1 3 1 2 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 1 3 1 6 は、主入口ポート 1 3 1 4 から隔離チャンバ 1 3 1 8 に分離する。

【0 0 5 7】

図 1 3 A ~ 1 3 D に示す実施例では、隔離チャンバ 1 3 1 8 は、ハウジング 1 3 0 1 内の空洞又はチャンバとして形成され、又はハウジング 1 3 0 1 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つめ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偏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、ルーアーコネクタ（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に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る。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への開口部を固定し、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固定する出口ポート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で覆わ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

に曝されるのを阻上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を通過し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る。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】

入ロポート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、入ロポート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固定する出ロポート1604を更に含む。出ロポート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、入ロポート1602と出ロポート1604との間のサンプリング流路1606と、入ロポート1602と出ロポート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、最初のアリコーッ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、任意のナイズ、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、入ロポート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、入ロポート1602から出ロポート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、入ロポート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、互いに表合する上部部材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を通過し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 2 2 A 及び 2 2 B に示すように、血液隔離装置 2 2 0 0 の空気透過性血液バリア 2 2 0 2 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 2 2 0 4 を含むことができる。空気透過性血液バリア 2 2 0 2 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 2 2 0 6、又は他の密封材料を更に含む。空気透過性血液バリア 2 2 0 2 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 2 2 0 8 を更に含むことができる。図 2 2 B に示すように、流体と接触すると、自己密封材料 2 2 0 6 が膨張して空隙 2 2 0 8 を閉鎖し、空隙 2 2 0 8 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 2 3 A 及び 2 3 B は、患者針と接続するための入口ポート 2 3 0 2 と、血液サンプル採取装置と接続するための出口ポート 2 3 0 4 と、隔離チャンバ 2 3 0 6 と、隔離チャンバ 2 3 0 6 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 2 3 0 6 を迂回するサンプリング流路 2 3 0 8 とを有する、血液隔離装置 2 3 0 0 の更に別の実施を示している。隔離チャンバ 2 3 0 6 は、入口ポート 2 3 0 2 から最も遠い隔離チャンバ 2 3 0 6 の遠位端に疎水性プラグ 2 3 1 2 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 2 3 0 4 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 2 3 0 2 内に、そして隔離チャンバ 2 3 0 6 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 2 3 1 2 に接触し、最初のアリコートの血液を隔離チャンバ 2 3 0 6 に戻してそこで隔離させる。少量の血液が、最初は弁 2 3 0 8 によって閉鎖されているサンプリング流路 2 3 0 8 に入ることができる。弁 2 3 0 8 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 2 3 0 2 に流れ、隔離チャンバ 2 3 0 6 を迂回し、サンプリング流路 2 3 0 8 を通り抜けて出口ポート 2 3 0 4 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 2 3 0 8 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 2 3 0 8 は、最初のアリコートの血液が隔離チャンバ 2 3 0 6 内に隔離される前にサンプリング流路を挟み、膨へそらし、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。

【圖 1】

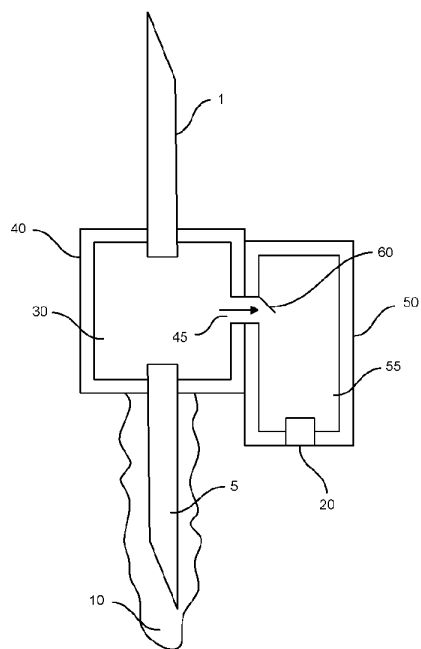


FIG. 1

【圖 2】

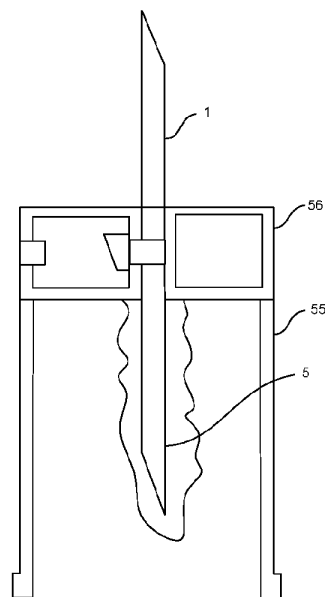


FIG. 2

【圖 3】

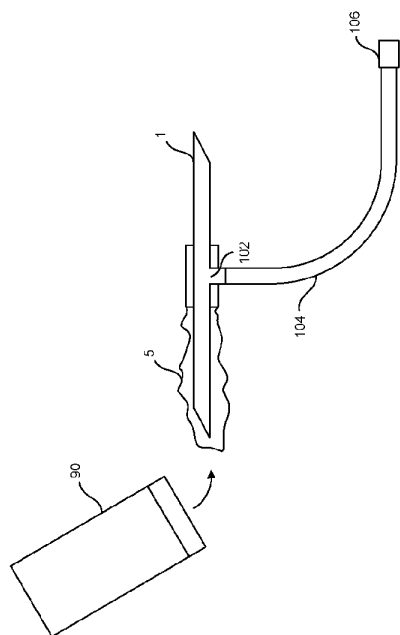


FIG. 3

【圖 4】

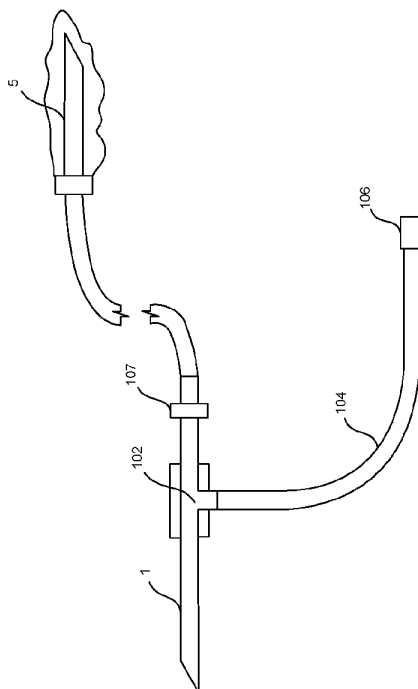


FIG. 4

【図 5】

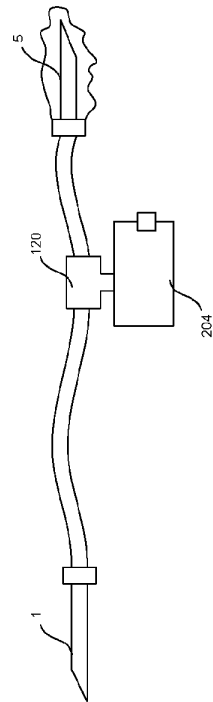


FIG. 5

【図 6】

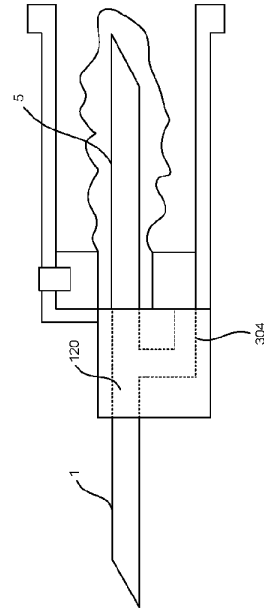


FIG. 6

【図 7】

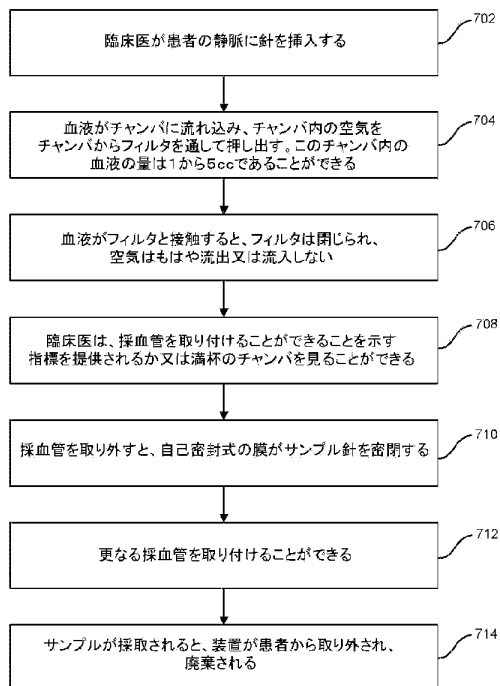


FIG. 7

【図 8 A】

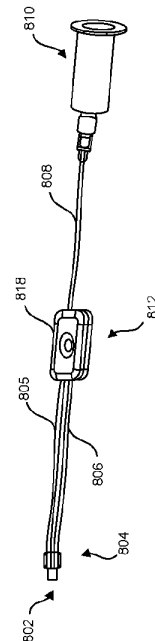


FIG. 8A

【 8 B 】

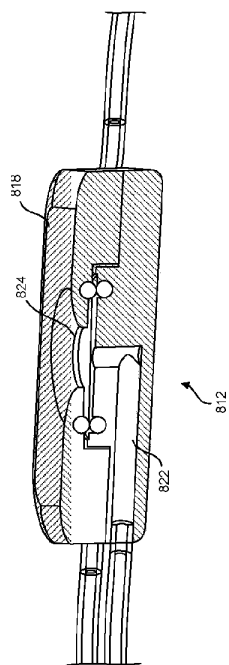


FIG. 8B

【 8 C 】

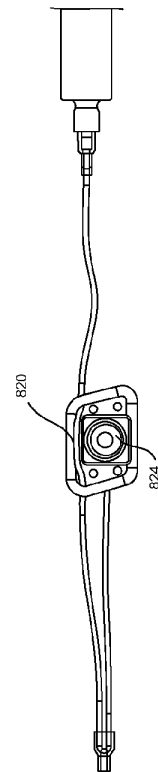


FIG. 8C

【 8 D 】

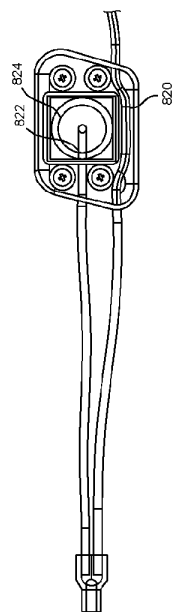


FIG. 8D

【 8 E 】

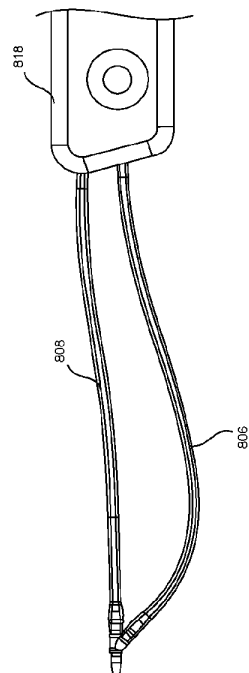
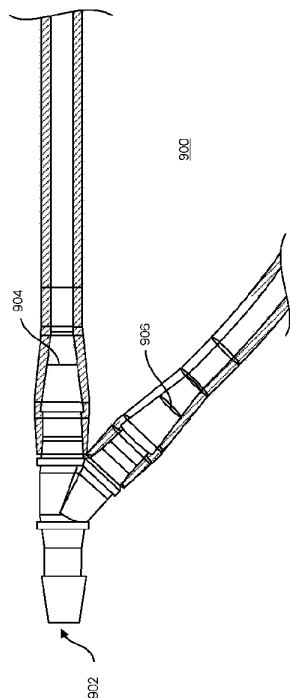


FIG. 8E

【図 9】



【図 10 A】

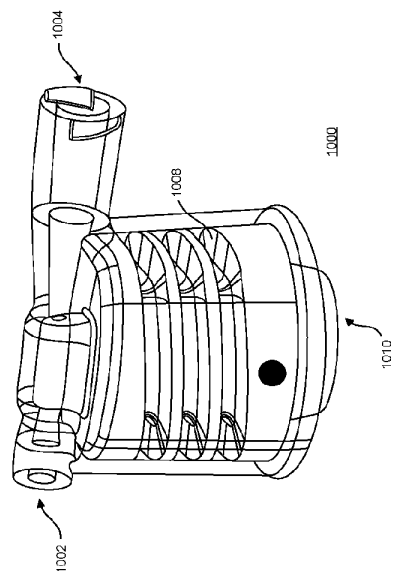


FIG. 9

FIG. 10A

【図 10 B】

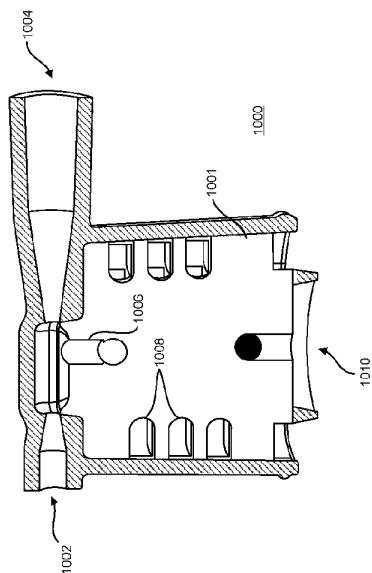


FIG. 10B

【図 10 C】

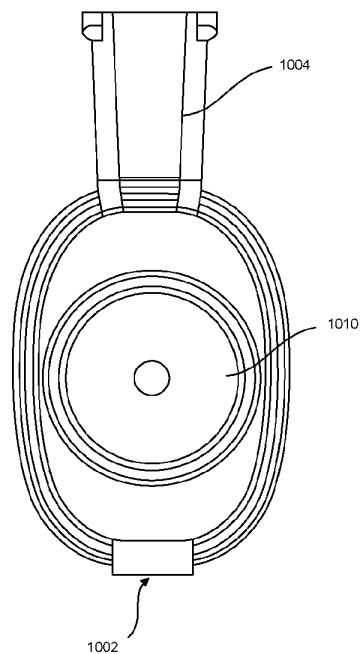


FIG. 10C

【図 10 D】

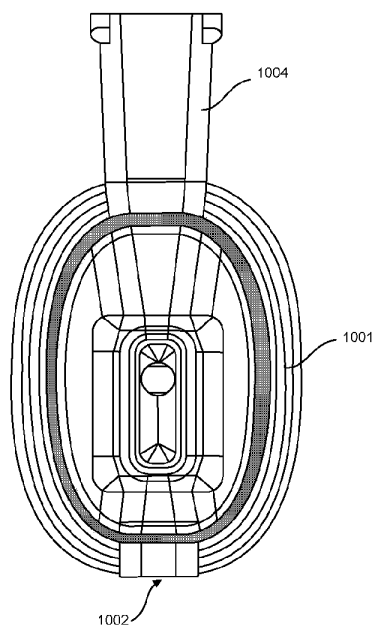


FIG. 10D

【図 11 A】

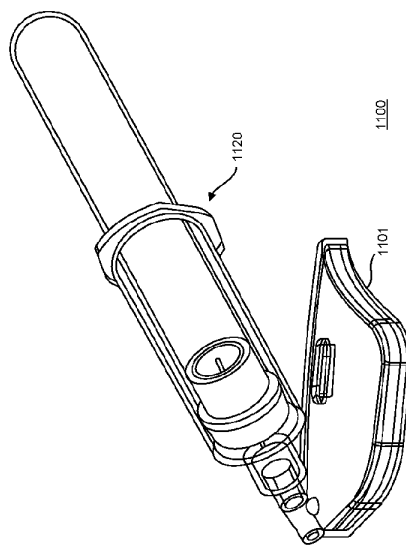


FIG. 11A

【図 11 B】

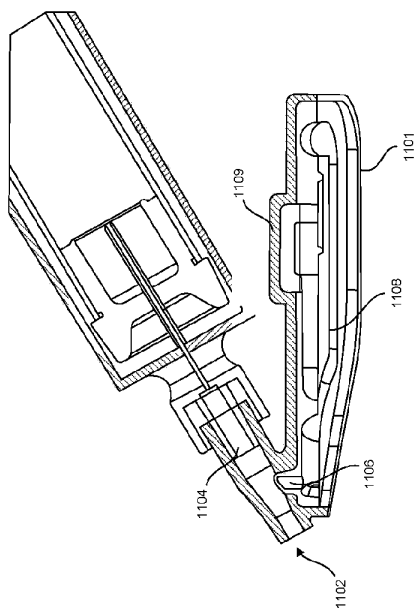


FIG. 11B

【図 11 C】

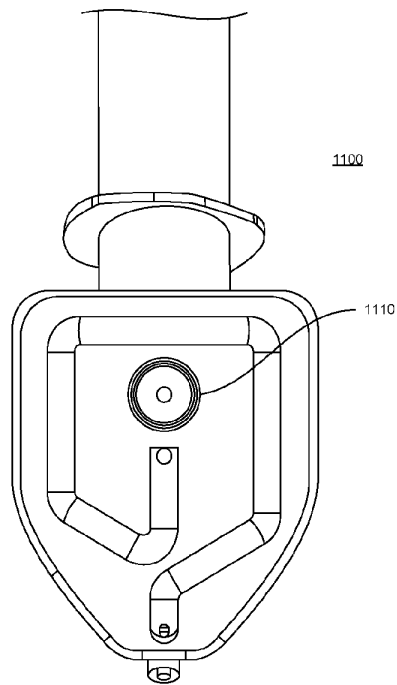


FIG. 11C

【図 11 D】

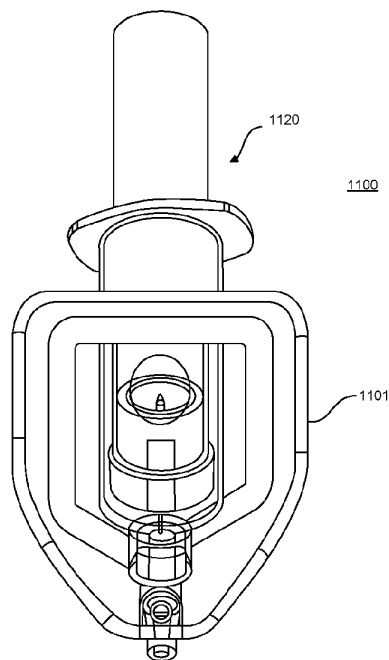


FIG. 11D

【図 11 E】

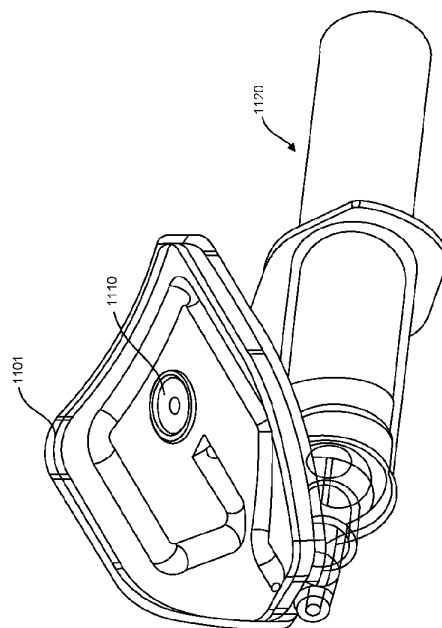


FIG. 11E

【図 12 A】

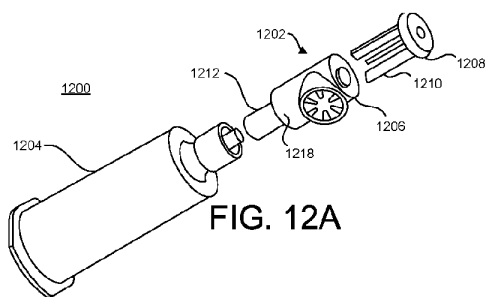


FIG. 12A

【図 12 B】

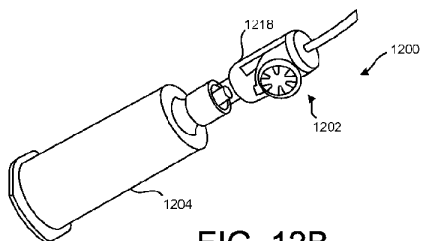


FIG. 12B

【図 12 C】

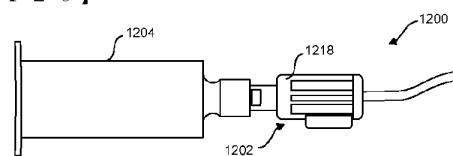


FIG. 12C

【図 12 D】

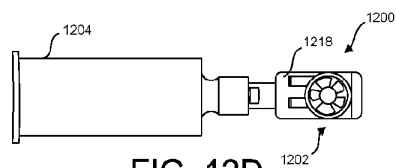


FIG. 12D

【図 13 A】

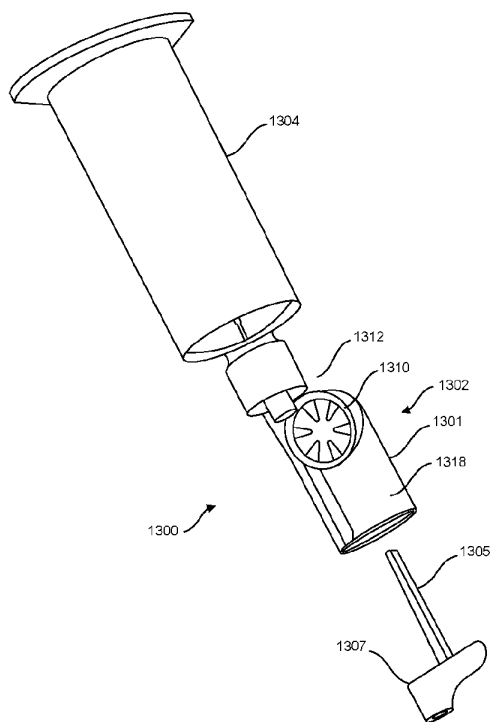


FIG. 13A

【図 13 B】

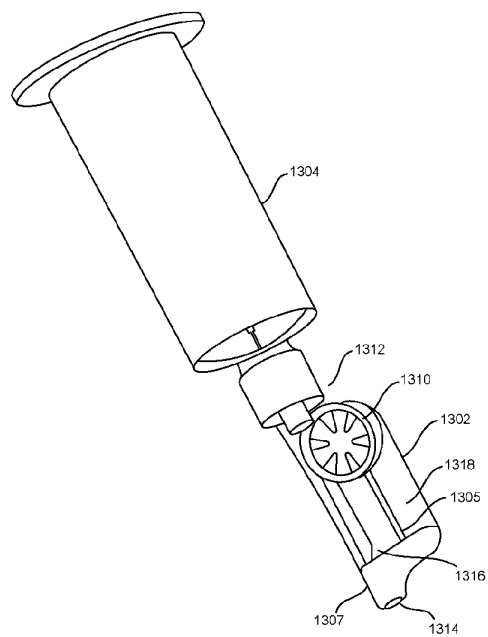


FIG. 13B

【図 13 C】

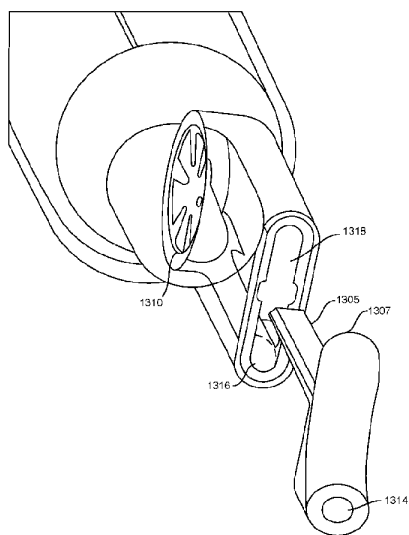


FIG. 13C

【図 13 D】

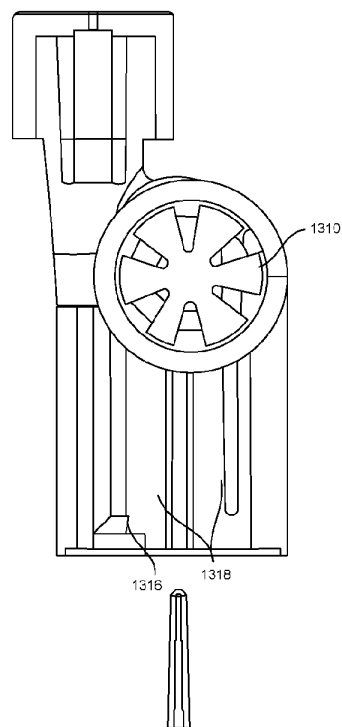


FIG. 13D

【図 14 A】

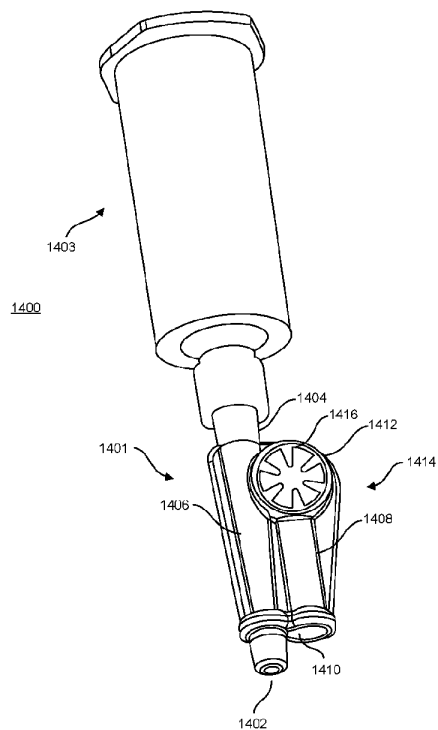


FIG. 14A

【図 14 B】

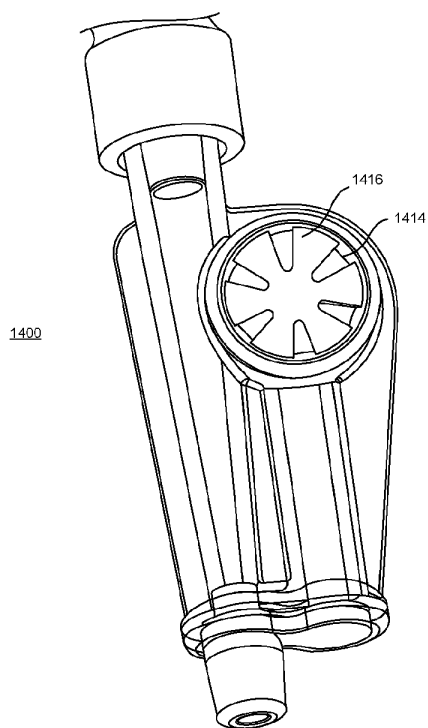


FIG. 14B

【図 14 C】

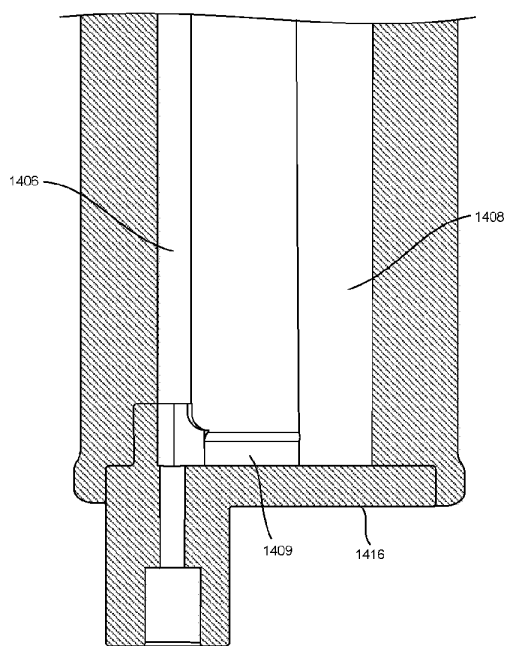


FIG. 14C

【図 14 D】

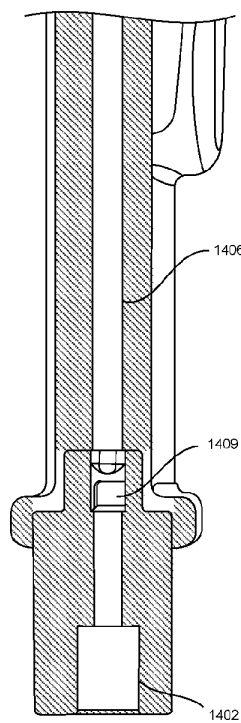


FIG. 14D

【図 14 E】

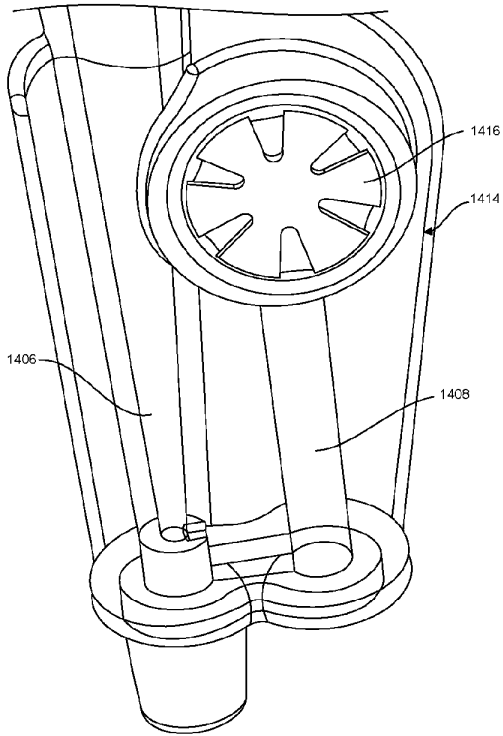


FIG. 14E

【図 15 A】

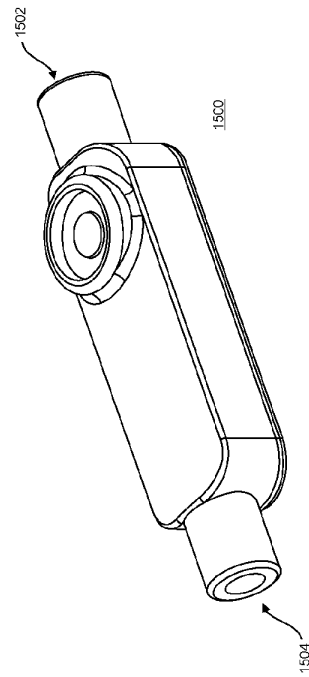


FIG. 15A

【図 15 B】

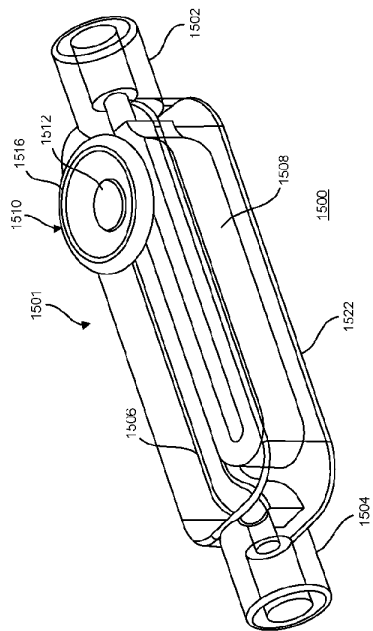


FIG. 15B

【図 15 C】

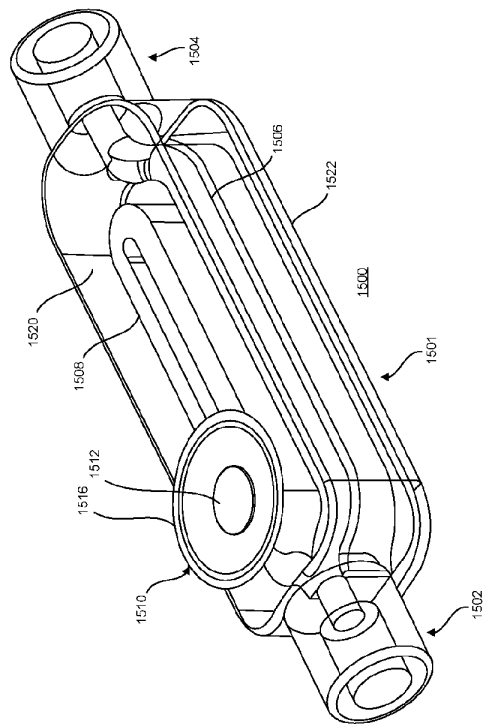


FIG. 15C

【図 15 D】

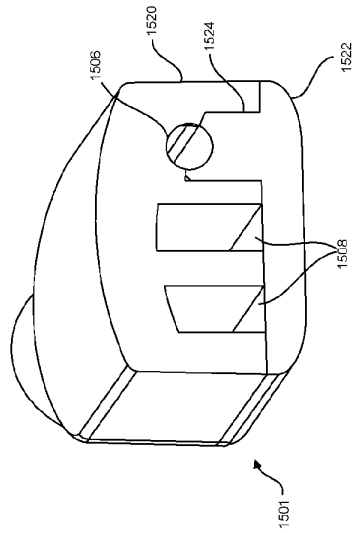


FIG. 15D

【図 15 E】

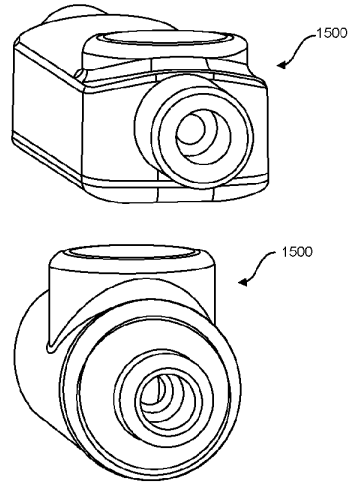


FIG. 15E

【図 15 F】

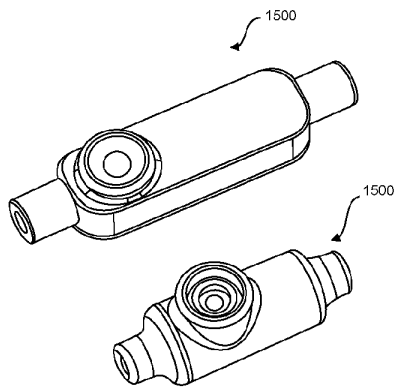


FIG. 15F

【図 15 G】

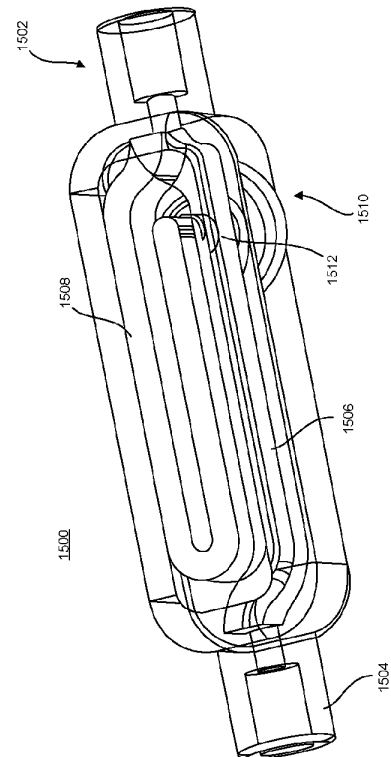


FIG. 15G

【図 16 A】

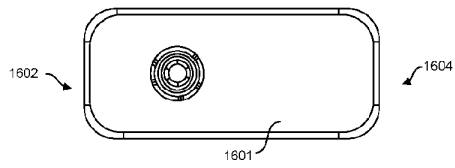


FIG. 16A

【図 16 B】

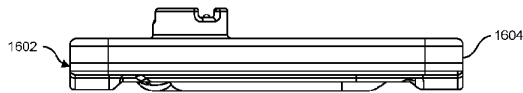


FIG. 16B

【図 16 C】

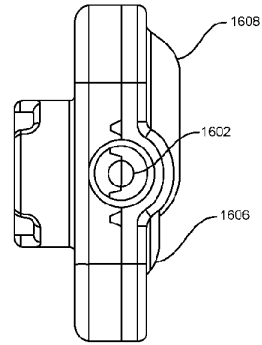


FIG. 16C

【図 16 D】

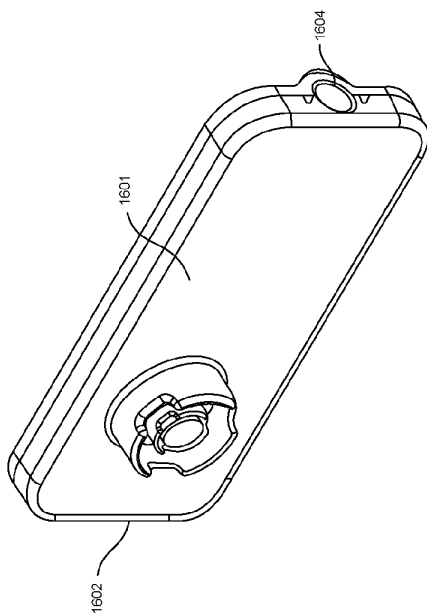


FIG. 16D

【図 17 A】

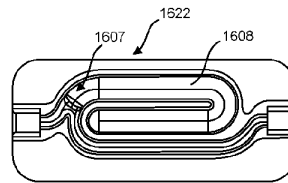


FIG. 17A

【図 17 B】

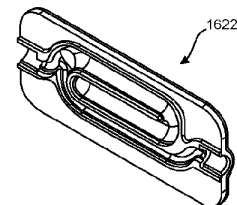


FIG. 17B

【図 17 C】

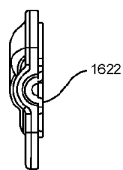


FIG. 17C

【図 17 D】

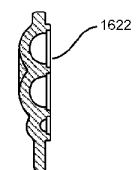


FIG. 17D

【図 17 E】

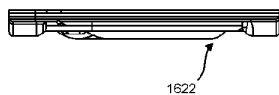


FIG. 17E

【図 18 C】

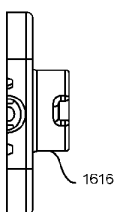


FIG. 18C

【図 18 D】

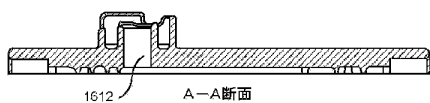


FIG. 18D

【図 18 E】

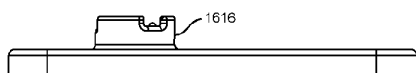


FIG. 18E

【図 18 A】

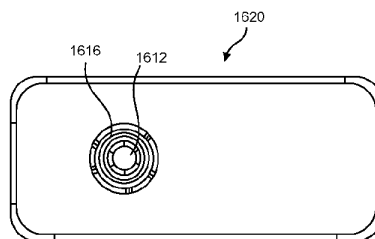


FIG. 18A

【図 18 B】

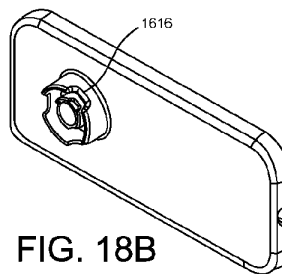
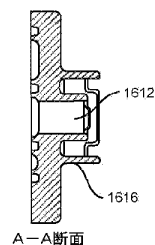


FIG. 18B

【図 18 F】



A-A断面

FIG. 18F

【図 2 2 A】

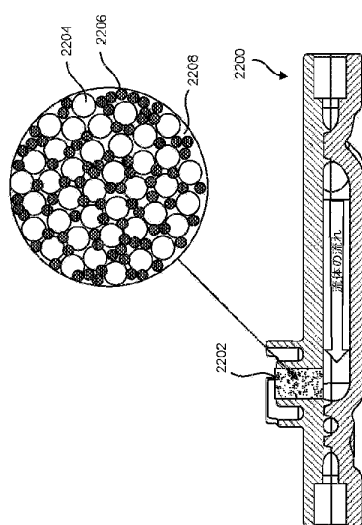


FIG. 22A

【図 2 2 B】

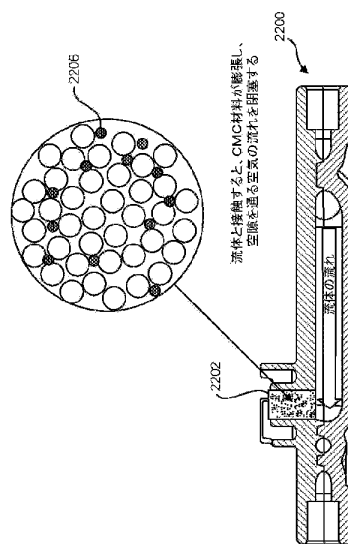


FIG. 22B

【図 2 3 A】

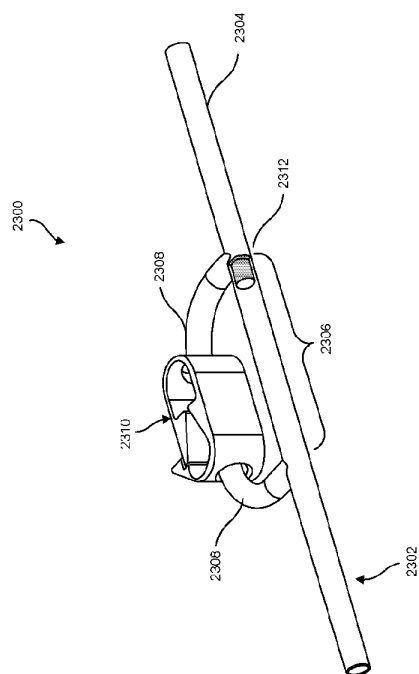


FIG. 23A

【図 2 3 B】

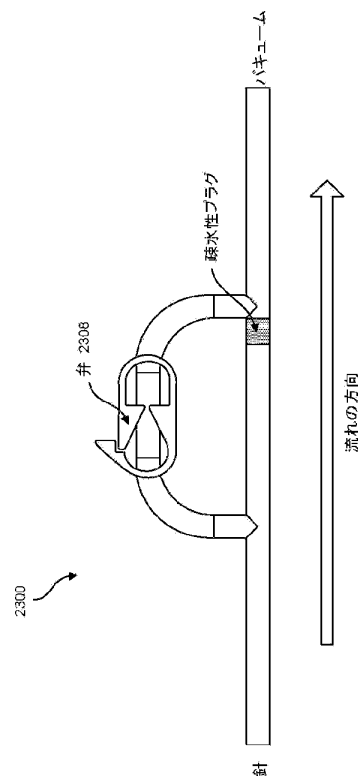


FIG. 23B

フロントページの続き

優先権主張番号

優先日 平成 年 月 日

優先権主張国・地域又は機関

米国

優先権主張番号

優先日 平成 年 月 日

優先権主張国・地域又は機関

米国

優先権主張番号

優先日 平成 年 月 日

優先権主張国・地域又は機関

米国

早期審査対象出願

発明者 ロジャーズ、 ボビー

アメリカ合衆国 92131 カリフォルニア州 サンディエゴ スクリップス ボーウェイ パークウェイ 10755 ナンバー 257

発明者 カン、 ジーノ

アメリカ合衆国 92131 カリフォルニア州 サンディエゴ スクリップス ボーウェイ パークウェイ 10755 ナンバー 257

発明者 デトロフ、 シコン

アメリカ合衆国 92131 カリフォルニア州 サンディエゴ スクリップス ボーウェイ パークウェイ 10755 ナンバー 257

審査官 清水 裕勝

参考文献 特開昭58-025146 (JP, A)

特開昭58-067238 (JP, A)

特開2012-016496 (JP, A)

特開昭57-089869 (JP, A)

特表平09-504726 (JP, A)

特開平02-224742 (JP, A)

特開2005-349196 (JP, A)

米国特許第04207870 (US, A)

米国特許出願公開第2013/0116599 (US, A1)

米国特許出願公開第2011/0306899 (US, A1)

調査した分野 , DB名

A61B 5/153-5/154

 Literature display

< 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 displayprimary 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

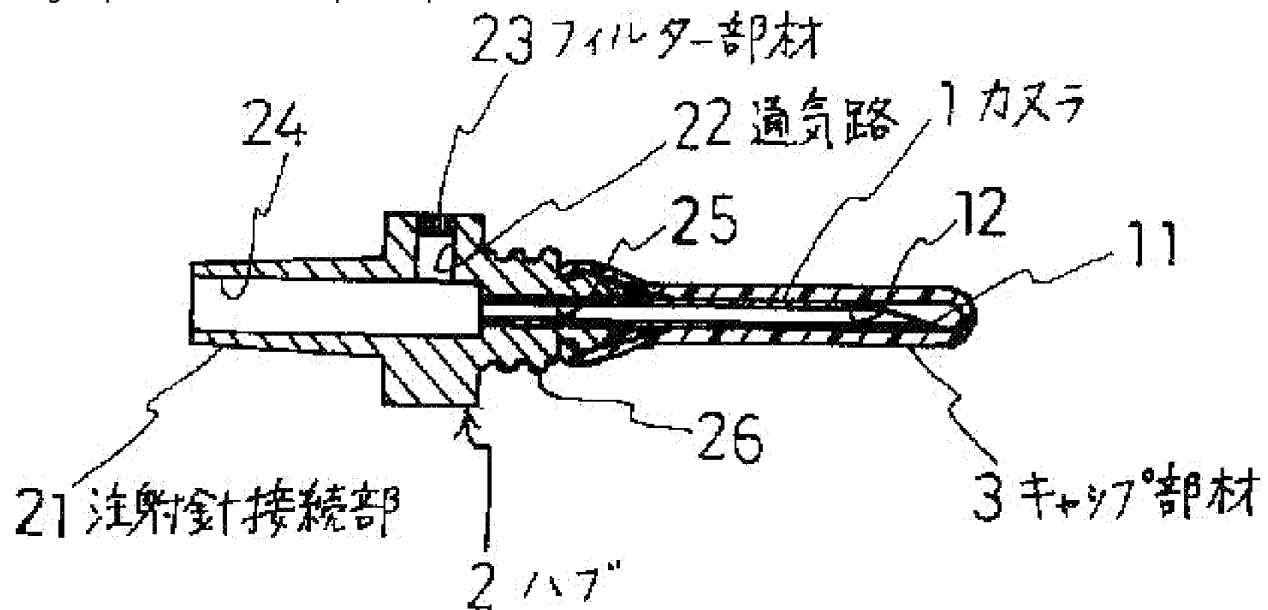
wrap up

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 causes 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 injection needle connecting portion 21 is provided at the rear end portion of the hub 2, and an air passage 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 obtained by connecting an injection needle 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 ventilation hole for communication between the inner cavity of the elastic tip and the outside atmosphere, 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 confirmed 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 to the ventilation hole of the transparent hub, it is necessary to confirm flashback. It takes a long time, and there is a problem that the blood collected inside the elastic tip may leak. SUMMARY OF THE INVENTION The present invention has been made in view of the above-mentioned circumstances

To provide a blood collecting adapter which enables confirmation of the insertion of a cutting edge 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 combination 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 end 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 end, 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 needle 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 removable blood collection adapter is used. In addition, a configuration in which an injection needle is connected to this blood collection adapter is adopted. Here, the injection needle connection part may be formed in a luer tip that can be fitted with the hub of the injection needle connected thereto, and the luer tip is concentrically threaded with the hub of the injection needle. 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 attached to the blood collection needle holder, the injection needle is connected to the injection needle connecting portion, and the injection needle is inserted into the blood vessel, the hollow portion of the injection needle and the blood collection are removed. Air existing in the hollow portion of the adapter passes through the gas-permeable filter member through the gas-permeable filter member by the inflowing blood, and is expelled to the outside. It flows into the hollow portion of the adapter and then through the air passage to reach the filter member. Therefore, by observing the air passage formed in the transparent hub, insertion of the injection needle into the blood vessel can be easily confirmed. Also, at this time, since the filter member is i

impermeable 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 embodiment 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. 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 hollow hub 2 supporting and fixing the rear end of this cannula 1 at its distal end. , the rubber elastic 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 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 hub 2 is a hollow member made of transparent synthetic resin such as polyethylene, polypropylene, 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 coupling means such as a male screw 26 is formed on the outer wall of the tip of the hub 2 so that it 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 generally external so that a hub 41 of the injection needle 4 can be fitted. It is formed into a so-called luer tip whose diameter is reduced in a tapered shape. For example, as shown in FIG. A hood-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 coupling means (not shown) is provided on the outer wall of the end portion of the hub 41 of the injection needle 4 . (not connected) may be threaded or luer connected. As the injection needle connecting 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 with an air passage 22 that communicates a hollow portion 24 with the outside air. ing. This filter member 23 is a gas-permeable and liquid-impermeable filter (hydrophobic filter), and as such a filter, a layered filter made of a polymer sintered body such as polypropylene or polyethylene 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 invention will be described with reference 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 the 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 pushed into the air passage of the blood collection adapter A by the inflowing blood. 22, it permeates the gas-permeable filter member 23 and is expelled to the outside. Then, the blood passes 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 passage 22 provided on the transparent hub 2, it is possible to easily confirm that the cutting edge 43 of the injection needle 4 has been inserted into the blood vessel. At this time, since the 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 blood 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 this has been pierced into the blood vessel, it is possible to eliminate the burden on the subject 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 embodiment 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 adapter 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

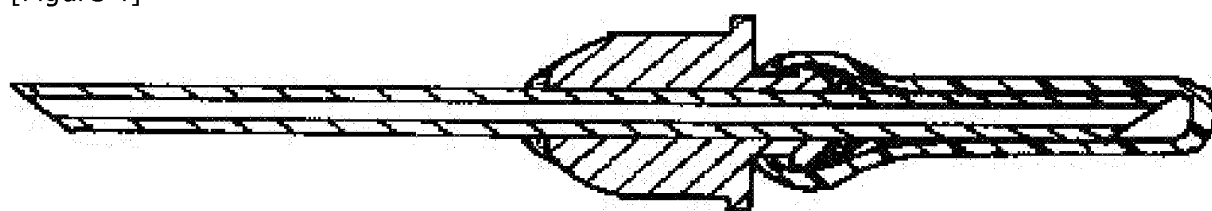
22 Air passage

- 23 Filter member
- 27 Female coupling means
- 3 Cap member
- 4 Injection needle
- A Blood collection adapter

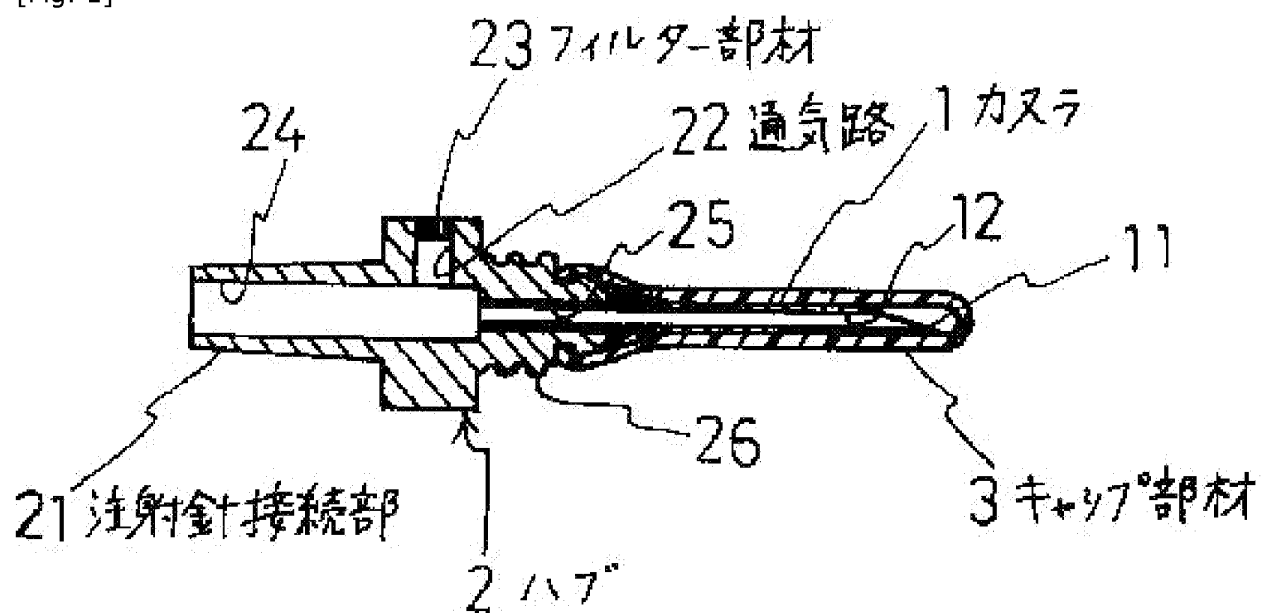
drawing

open

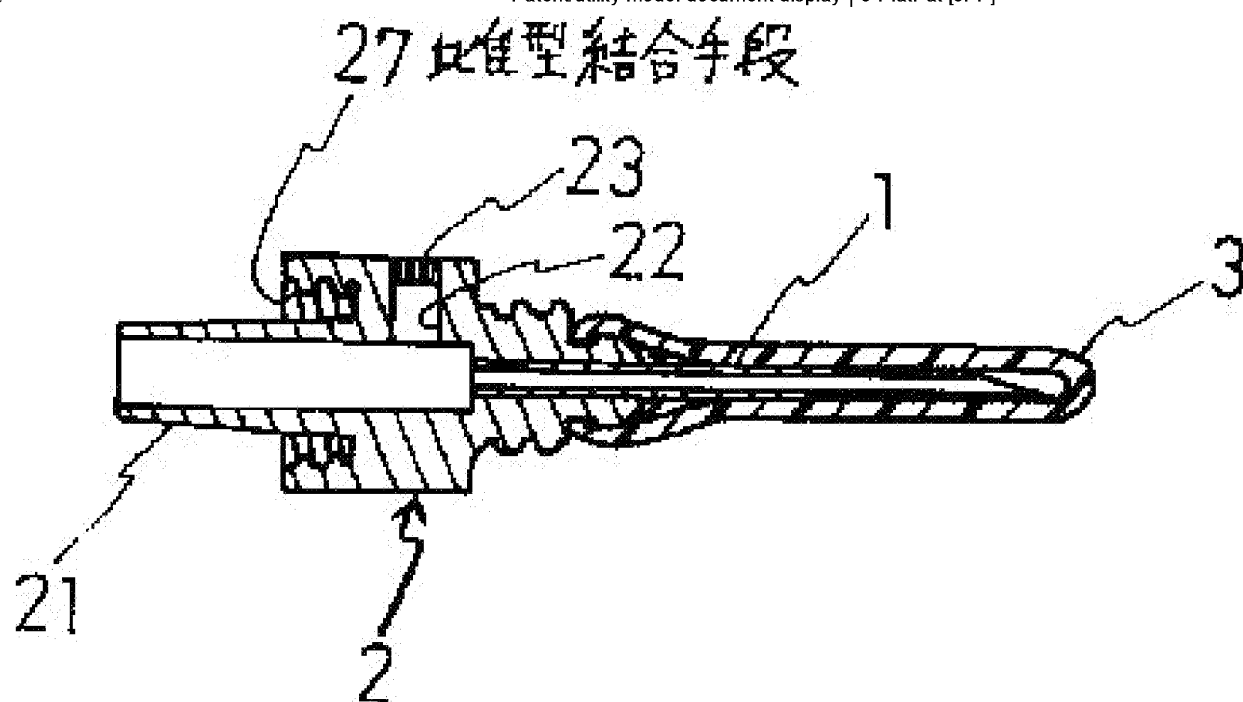
[Figure 4]



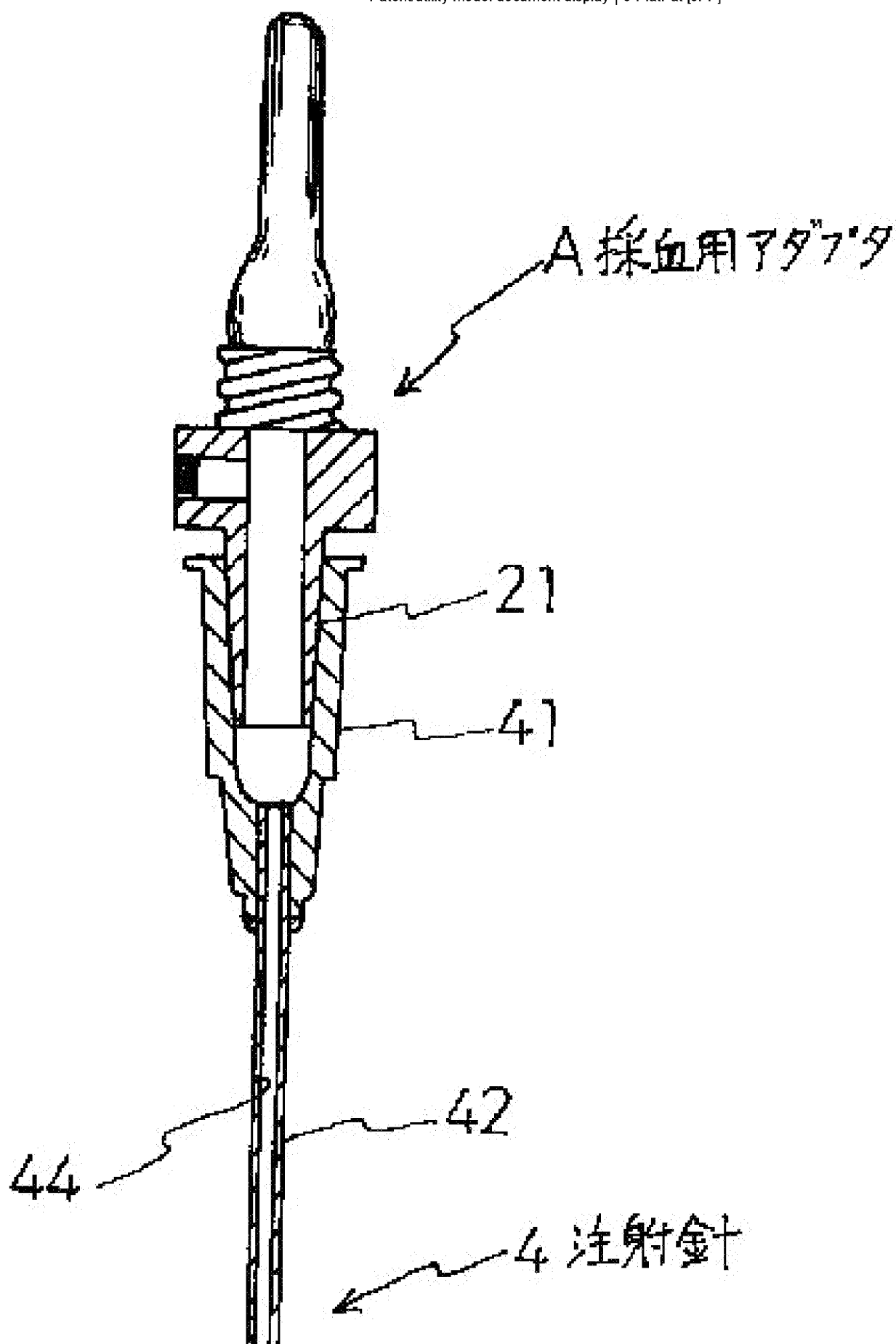
[Fig. 1]



[Figure 2]



[Figure 3]





close

Representative drawing

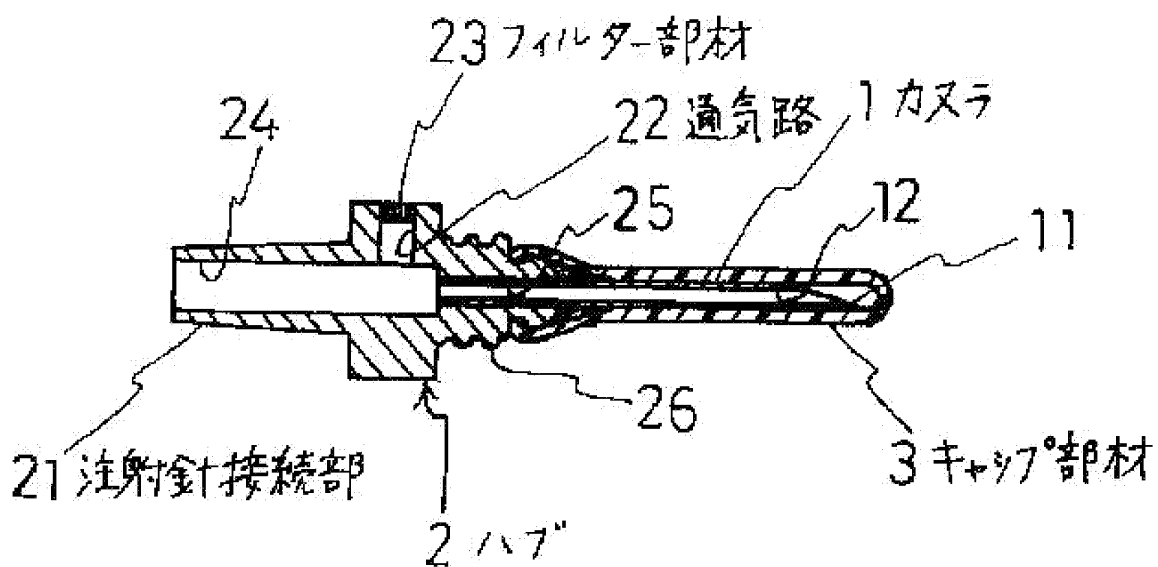
1

2

3

Four

Magnify and Rotate



Representative drawing

<

1

/ 1

display

>

(19) 日本国特許庁 (J P)

(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	F I	技術表示箇所
A 6 1 B 5/14	3 0 0	7638-2 J	A 6 1 B 5/14	3 0 0 E
A 6 1 M 5/32			A 6 1 M 5/32	

審査請求 未請求 請求項の数 4 O L (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

(71) 出願人 000135036

株式会社ニッショー

大阪府大阪市北区本庄西3丁目9番3号

(72) 発明者 桧垣 芳雄

群馬県館林市松原2丁目19番64号 ニプロ

医工株式会社内

(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

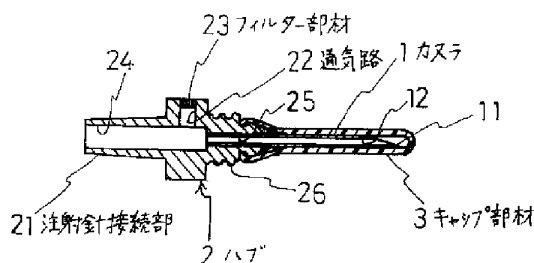
ニプロ内

(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を有する中空のカメラ1と、その先端部でこのカメラ1の後端部を支持し固定する透明な中空のハブ2と、カメラ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メラと、その先端部で該カメ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、前記カメ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メラと、その先端部で該カメ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、前記カメ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して採血用アダプタの中空部分に流入し、さらに通気路を通し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を有する中空のカメラ1と、その先端部でこのカメラ1の後端部を支持し固定する透明な中空のハブ2と、カメラ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メラ1の後端部が挿入され、接着剤で固定されており、このカメラ1にはゴム弾性体の例えば天然ゴムや、イソプレングム、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を嵌合できるように一般に外径がテーパ状に縮径された所謂ルーアチップに形成されている。ルーア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）と螺合またはルーア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の中間部は幅広の鐔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。まず、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を通して採血用アダプタAの中空部分24に流入し、さらに通気路22を通してフィルター部材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。

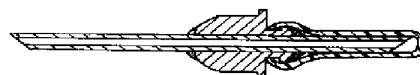
【図3】図1に示す採血用アダプタに注射針を取り付けた状態を示す図である。

【図4】従来の採血針を示す図である。

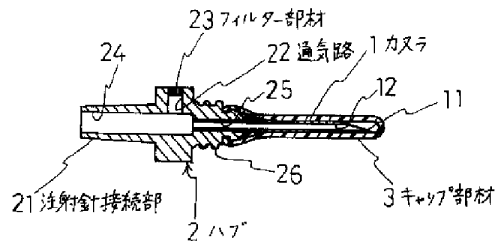
【符号の説明】

- 1 カメラ
- 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

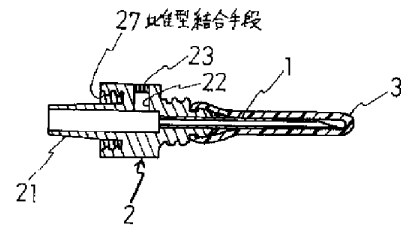
【図4】



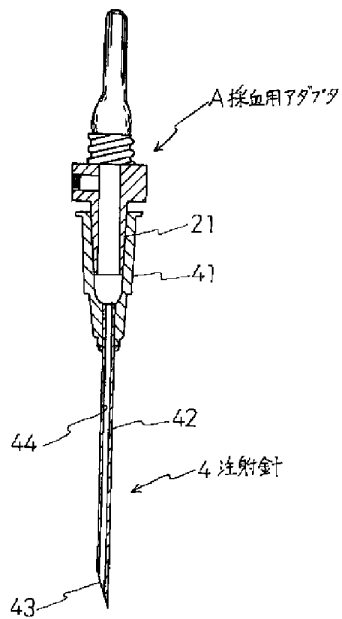
【図1】



【図2】



【図3】



(19)



(11) Veröffentlichungsnummer:

(11) Publication number: **EP 3 562 397 A0**

(11) Numéro de publication:

Internationale Anmeldung veröffentlicht durch die
Weltorganisation für geistiges Eigentum unter der Nummer:

WO 2018/125929 (Art. 153(3) EPÜ).

International application published by the World
Intellectual Property Organization under number:

WO 2018/125929 (Art. 153(3) EPC).

Demande internationale publiée par l'Organisation
Mondiale de la Propriété Intellectuelle sous le numéro:

WO 2018/125929 (art. 153(3) CBE).

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

(19) World Intellectual Property
Organization

International Bureau

(43) International Publication Date
05 July 2018 (05.07.2018)



(10) International Publication Number
WO 2018/125929 A1

(51) International Patent Classification:

A61B 5/15 (2006.01) *A61B 5/154* (2006.01)
A61B 5/153 (2006.01) *A61B 5/157* (2006.01)

(21) International Application Number:

PCT/US2017/068569

(22) International Filing Date:

27 December 2017 (27.12.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/439,426 27 December 2016 (27.12.2016) US

(71) Applicant: **KURIN, INC.** [US/US]; 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US).

(72) Inventors: **ROGERS, Bobby E.**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **KANG, Gino**; c/o Kurin, Inc., 10755

Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **STROUP, David Karl**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **COCHRAN, Jonas Dean**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **DEPTALA, Arthur**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **DETLOFF, John**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **POGUE, Lonnie**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **MACOWSKI, Brian**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US). **GARRETT, Chad**; c/o Kurin, Inc., 10755 Scripps Poway Parkway, No. 257, San Diego, California 92131 (US).

(74) Agent: **DEVERNOE, David** et al.; TROUTMAN SANDERS, LLP, 600 Peachtree Street NE, Suite 5200, Atlanta, Georgia 30308 (US).

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

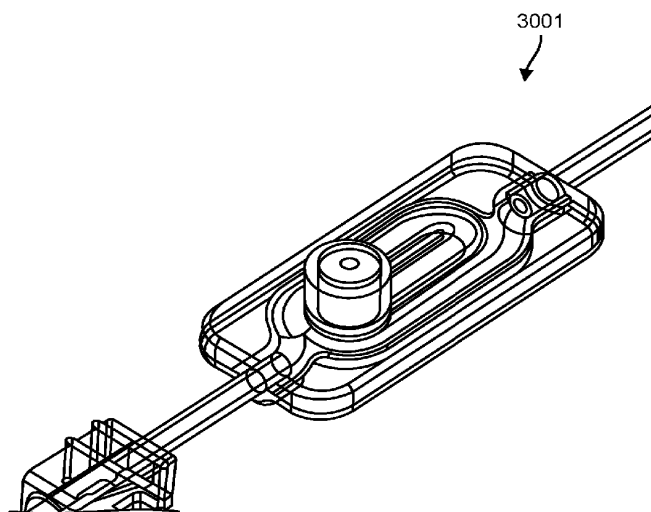


FIG. 30B

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

[Continued on next page]

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

BACKGROUND

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

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

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

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

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

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

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

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

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

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

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

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

SUMMARY

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

BRIEF DESCRIPTION OF THE DRAWINGS

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

- [0026] FIG. 1 illustrates a blood sample optimization system.
- [0027] FIG. 2 illustrates a blood sample optimization system in accordance with an alternative implementation.
- [0028] FIG. 3 illustrates a blood sample optimization system in accordance with another alternative implementation.
- [0029] FIG. 4 illustrates a blood sample optimization system in accordance with another alternative implementation.
- [0030] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.
- [0031] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.
- [0032] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.
- [0033] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.
- [0034] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.
- [0035] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.
- [0036] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.
- [0037] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.
- [0038] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.

[0039] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminants 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 contaminants in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. In some implementations, a blood sample optimization system includes a patient needle for vascular access to a patient's bloodstream, a sample needle for providing a blood sample to a blood collection container, such as an evacuated blood collection container or tube like a Vacutainer™ or the like, or other sampling device, and a blood sequestration device located between the patient needle and the sample needle. The blood sequestration device includes a sequestration chamber for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

[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 indicator or can see the full chamber, to indicate the evacuated blood collection tube, such as a Vacutainer™ can be attached. The indicator can include visibility into the primary chamber to see whether it is full, the blood barrier changing color, for example, or other indicator. The fill time of the sequestration chamber may be substantially instantaneous, so such indicator, if present, may be only that the sequestration chamber is filled.

[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

about 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 contaminants of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample. The blood sampling system 1400 includes a blood sequestration device 1401 that can be connected between a blood sample collection device 1403 and a patient needle (not shown). The blood sample collection device 1403 can be a Vacutainer or the like. The blood sequestration device 1401 includes an inlet port 1402 that can be connected with a patient needle that is inserted into a patient's vascular system for access to and withdrawing of a blood sample. The inlet port 1402 may also be connected with tubing or other conduit that is in turn connected with the patient needle.

[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 2406 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 2421 with 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 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.

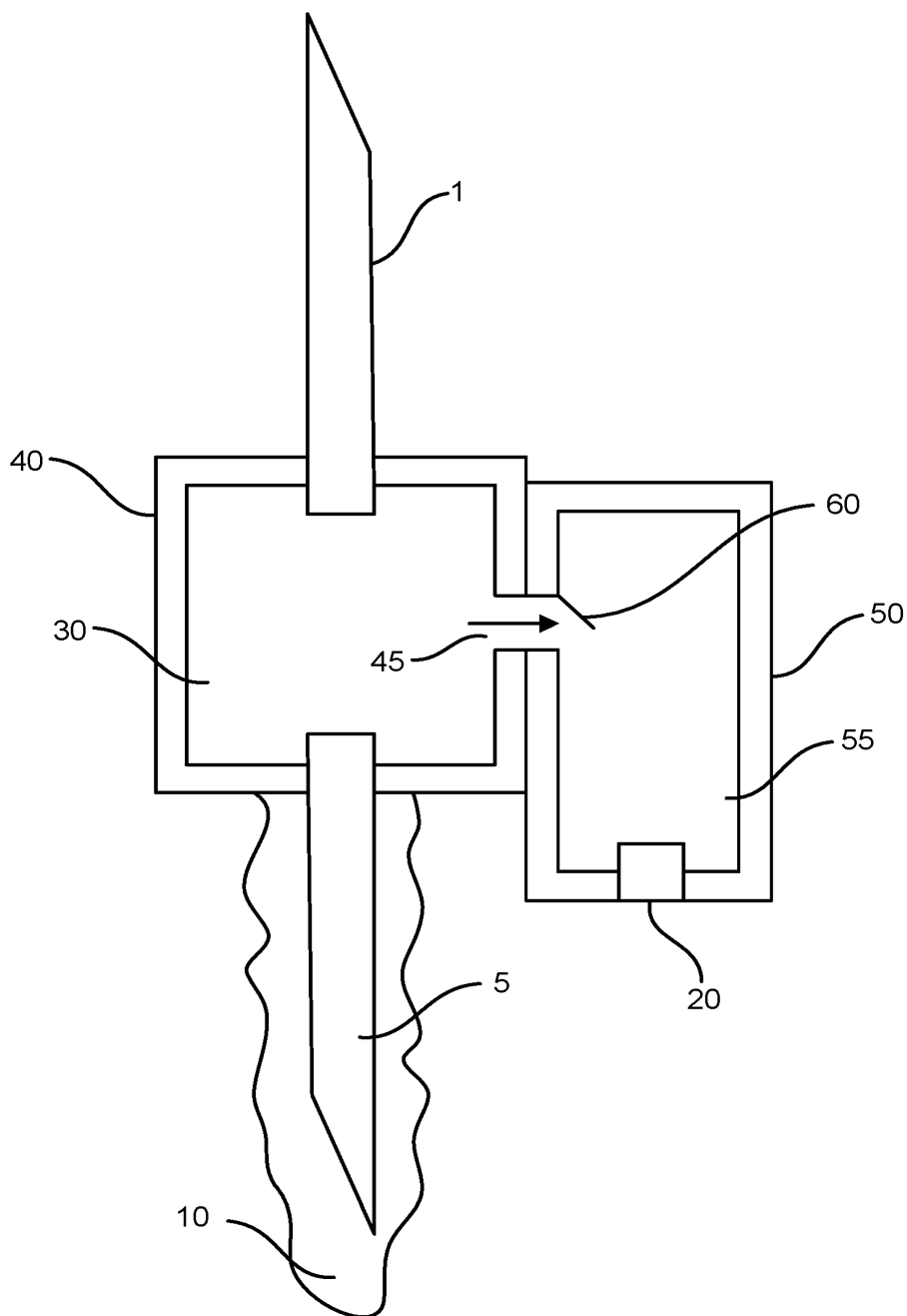


FIG. 1

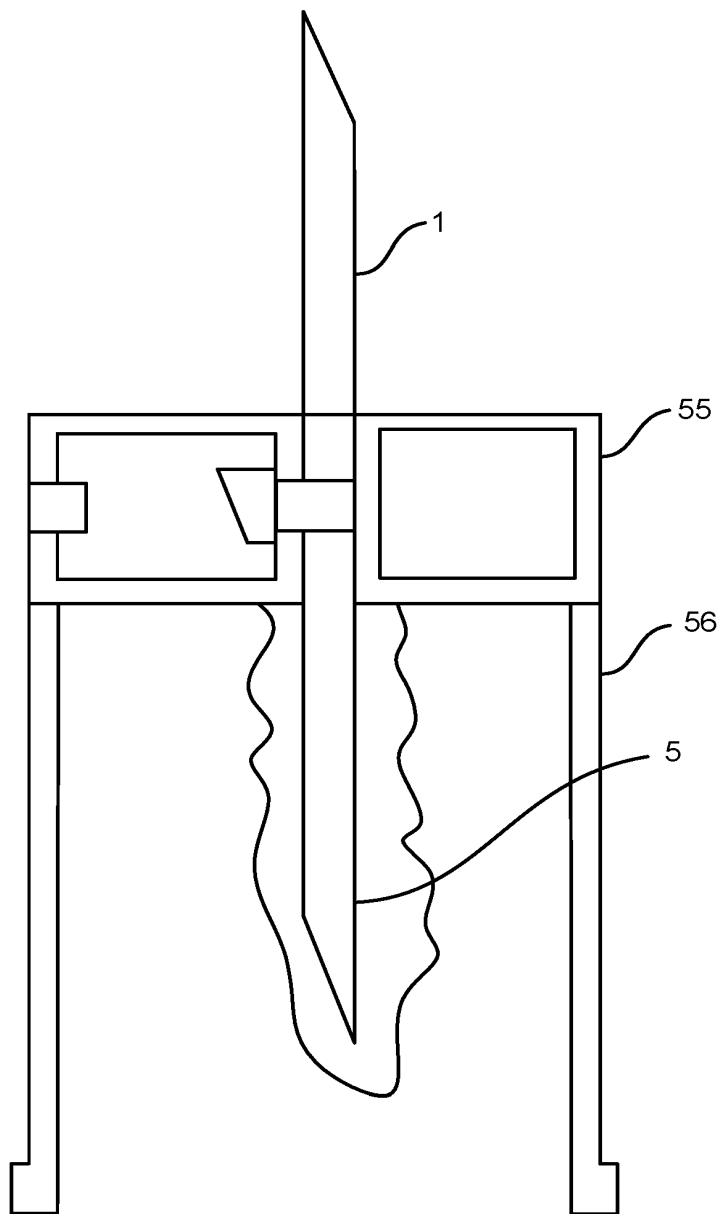


FIG. 2

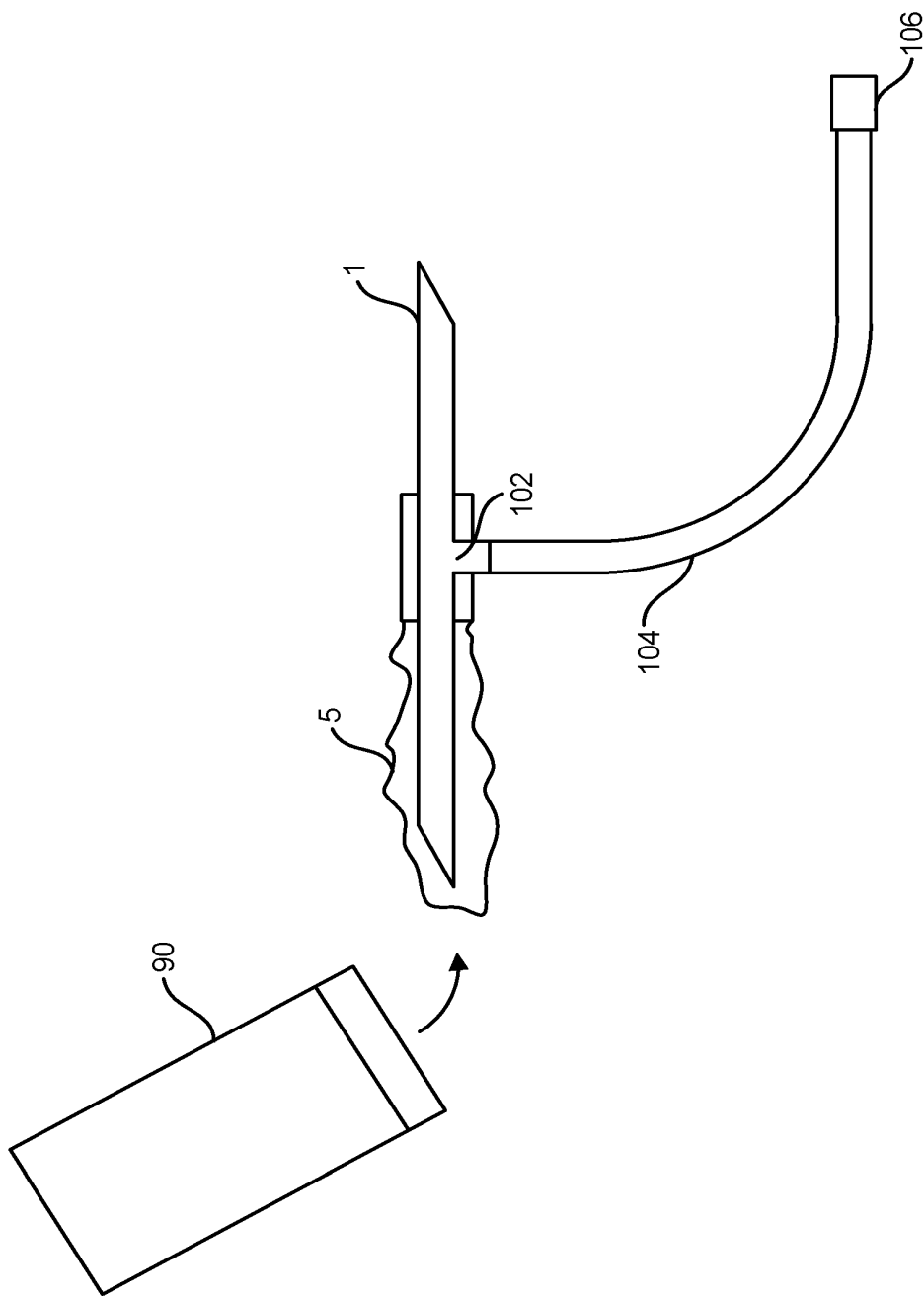


FIG. 3

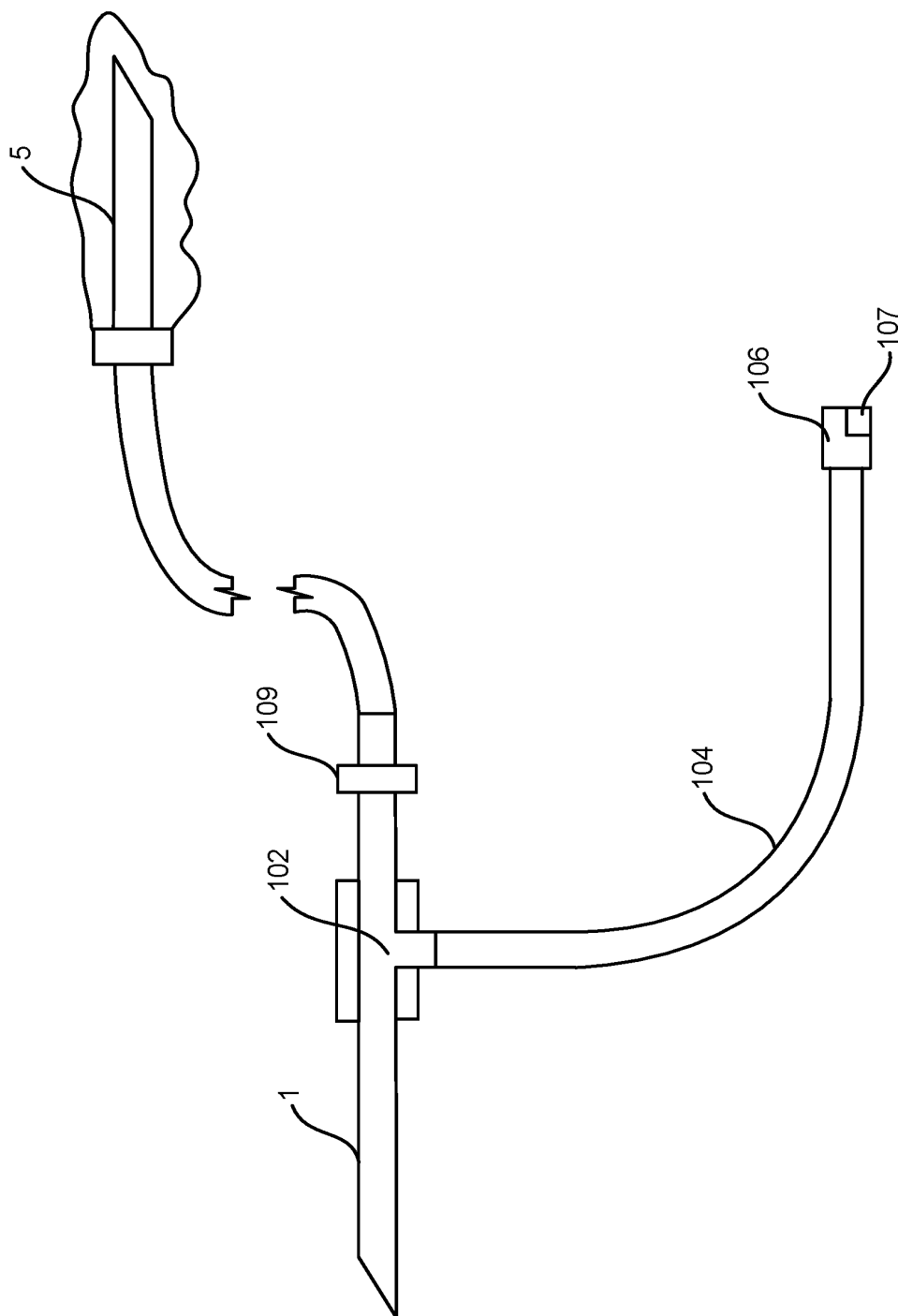


FIG. 4

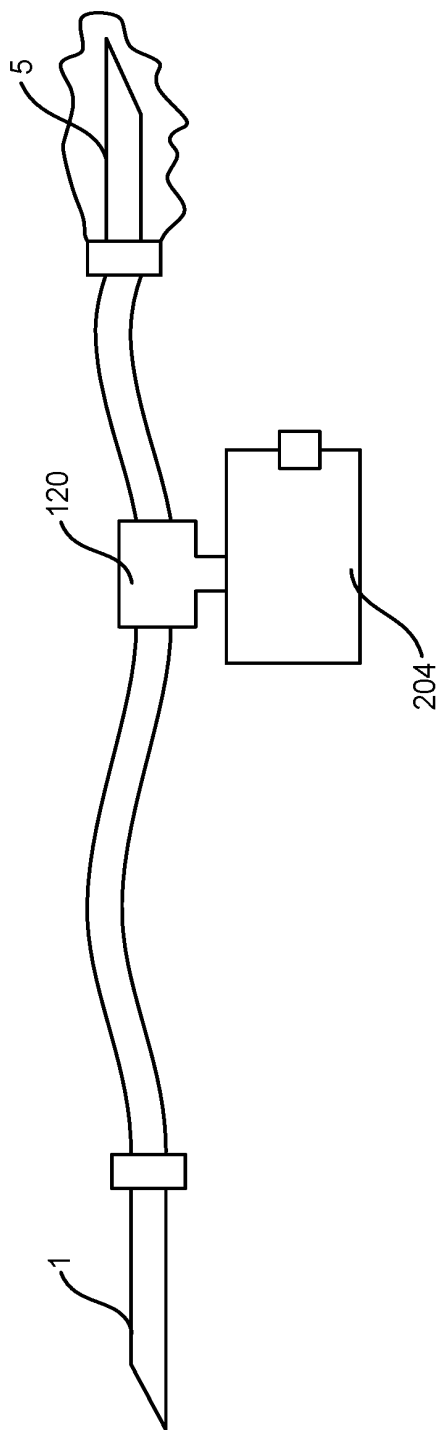


FIG. 5

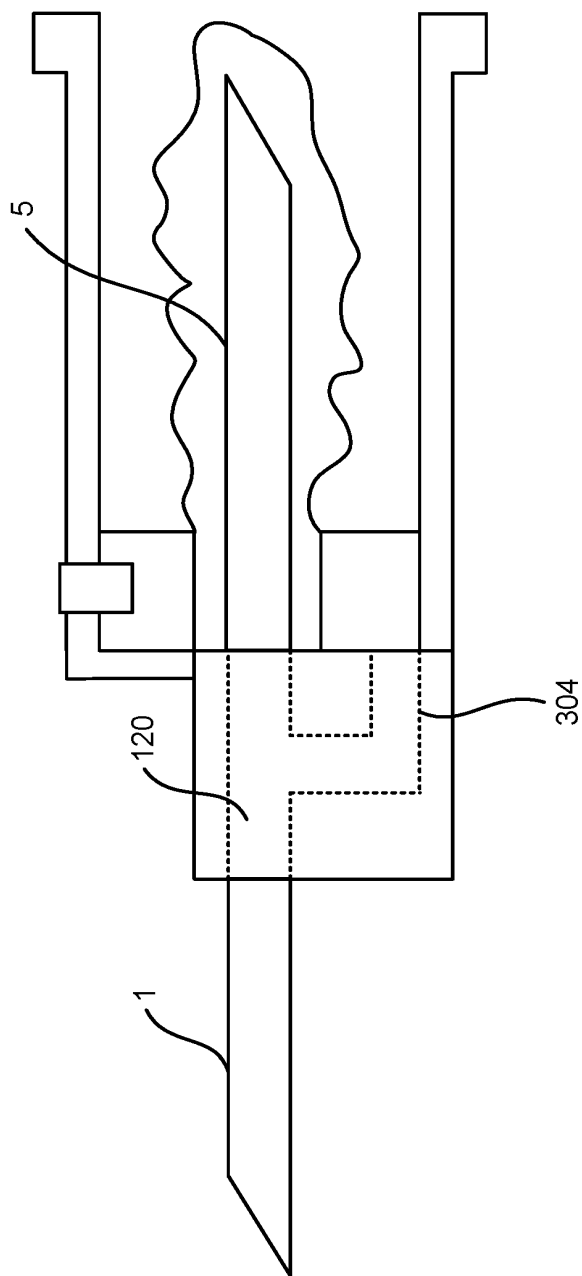


FIG. 6

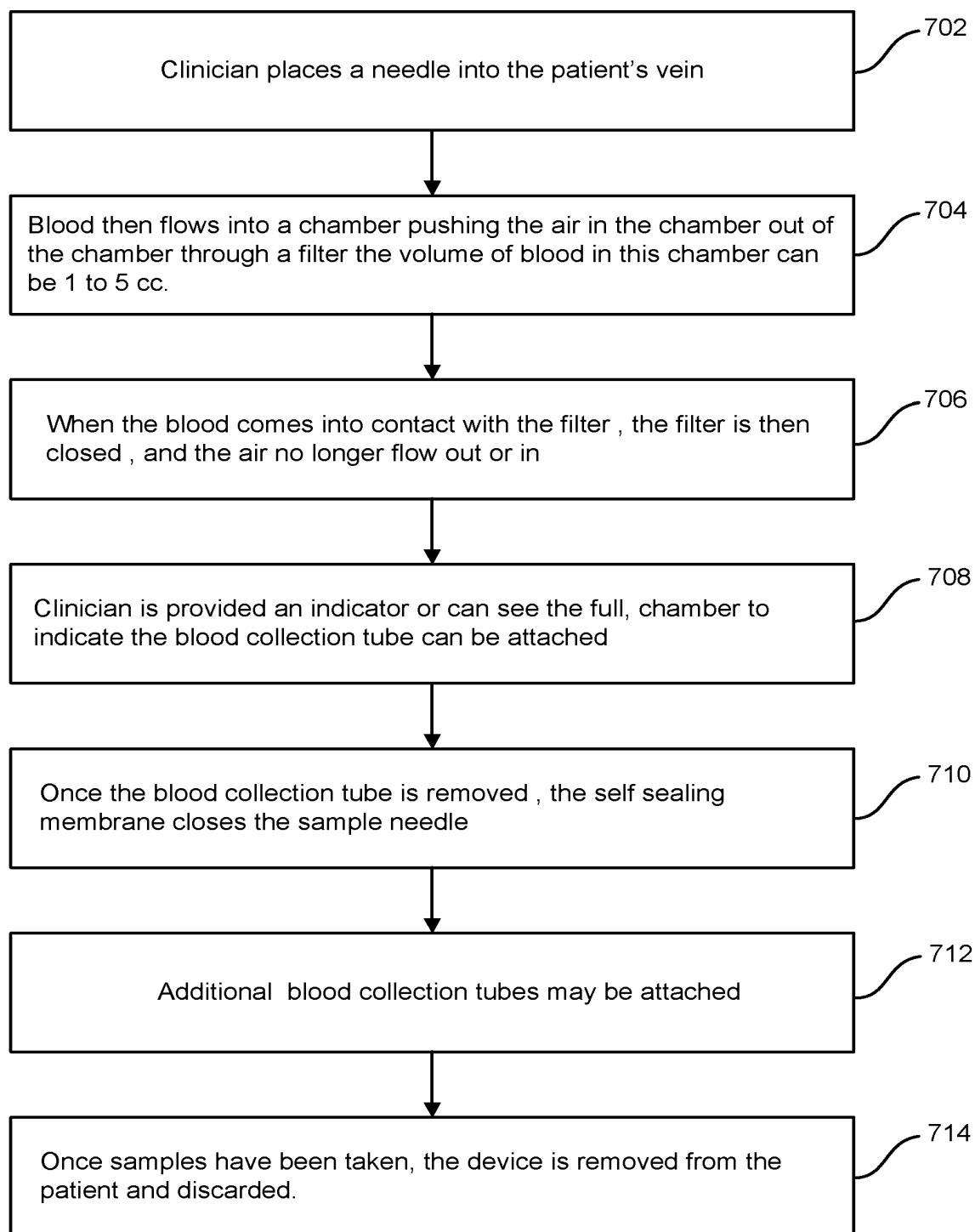
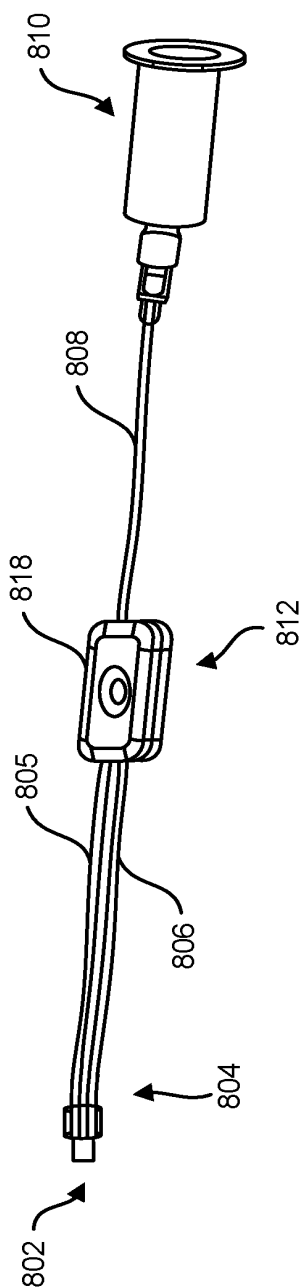


FIG. 7



800

FIG. 8A

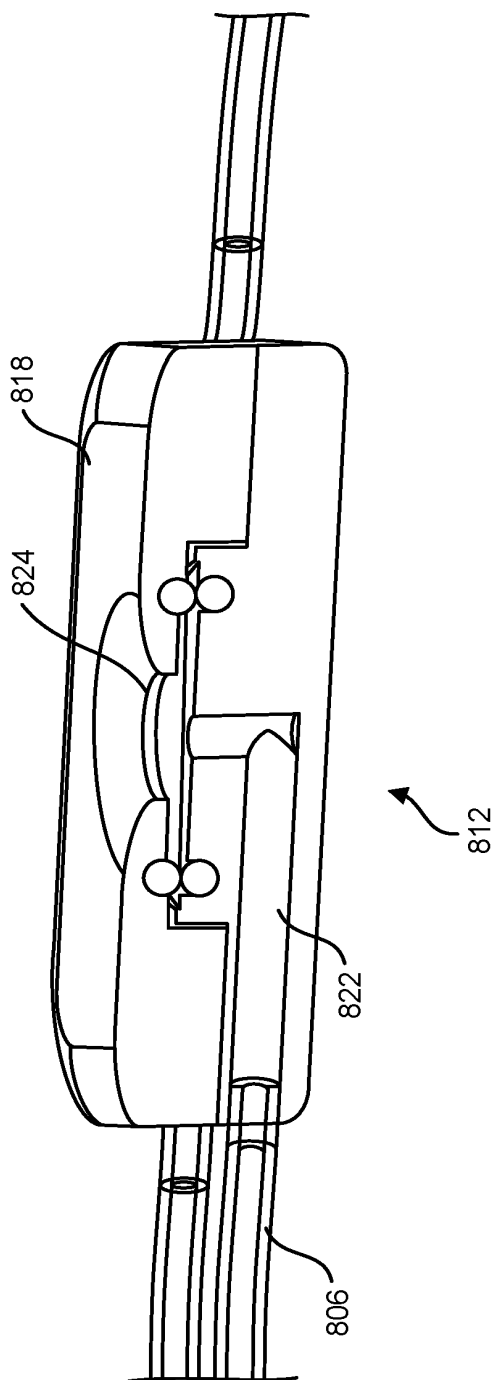


FIG. 8B

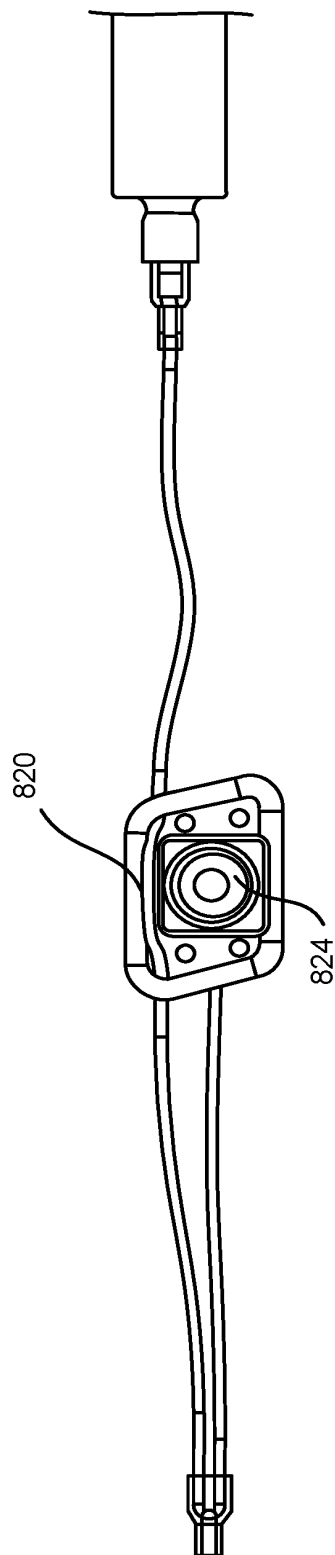


FIG. 8C

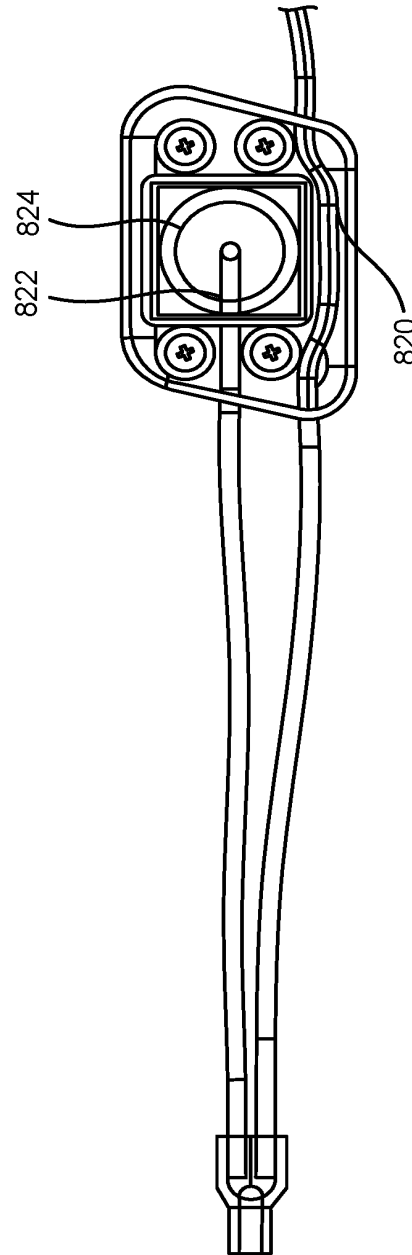


FIG. 8D

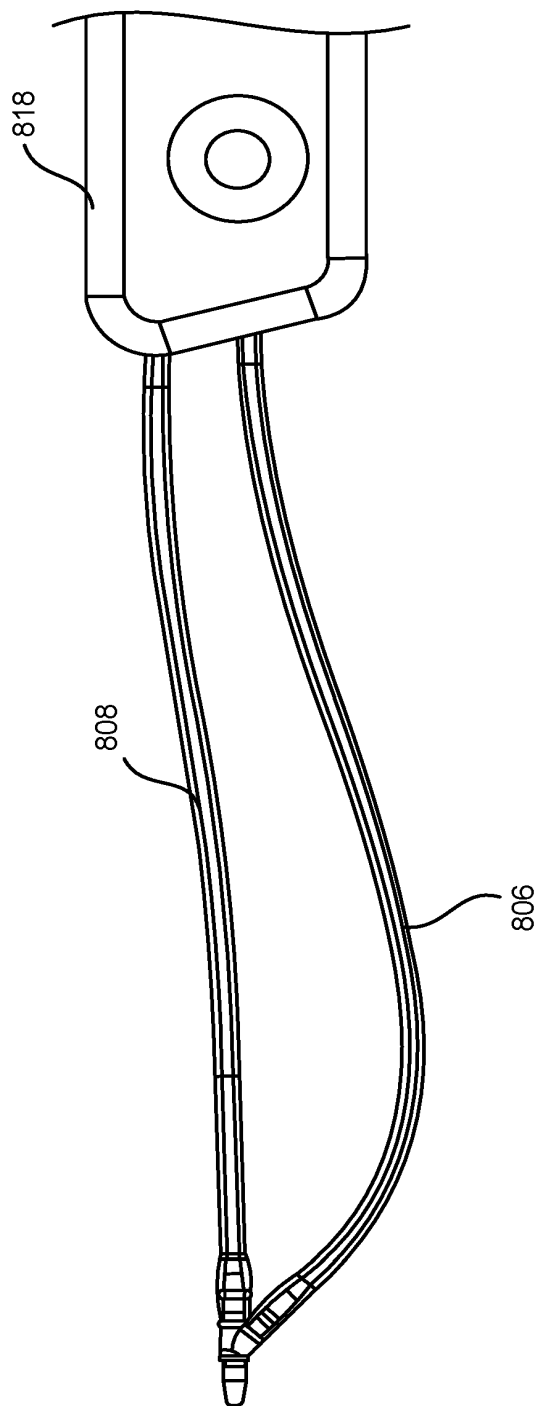


FIG. 8E

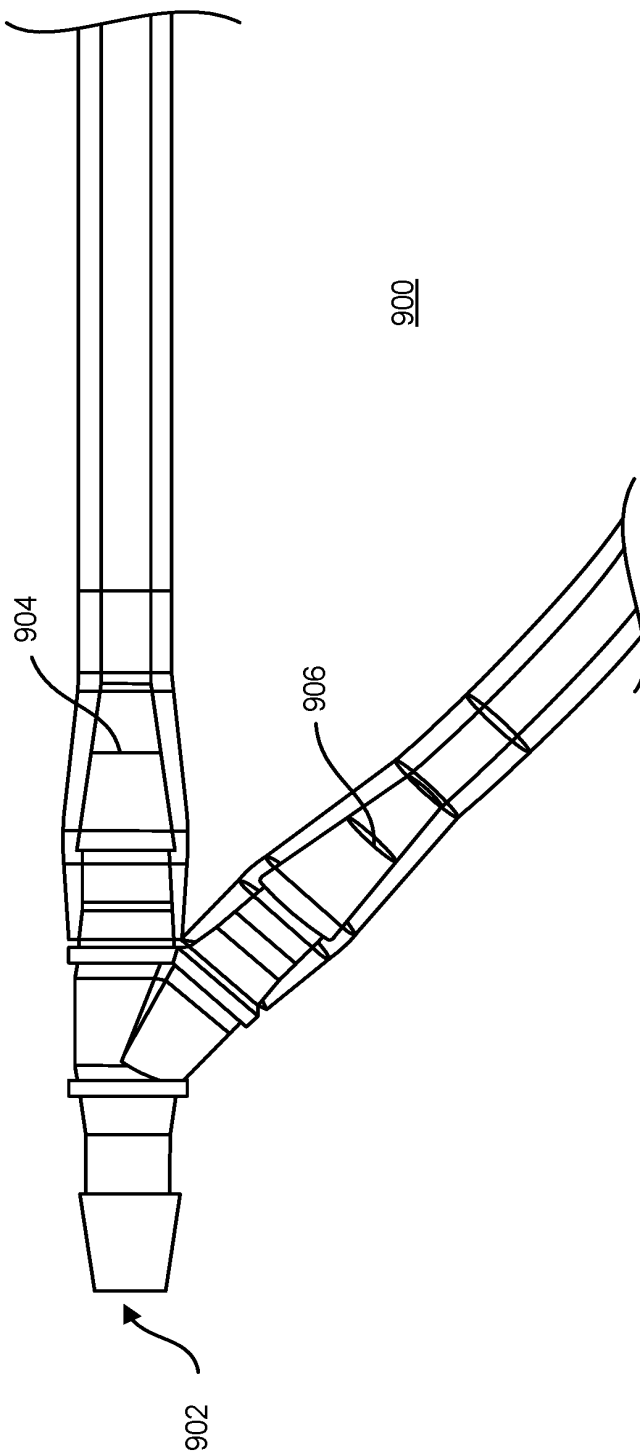


FIG. 9

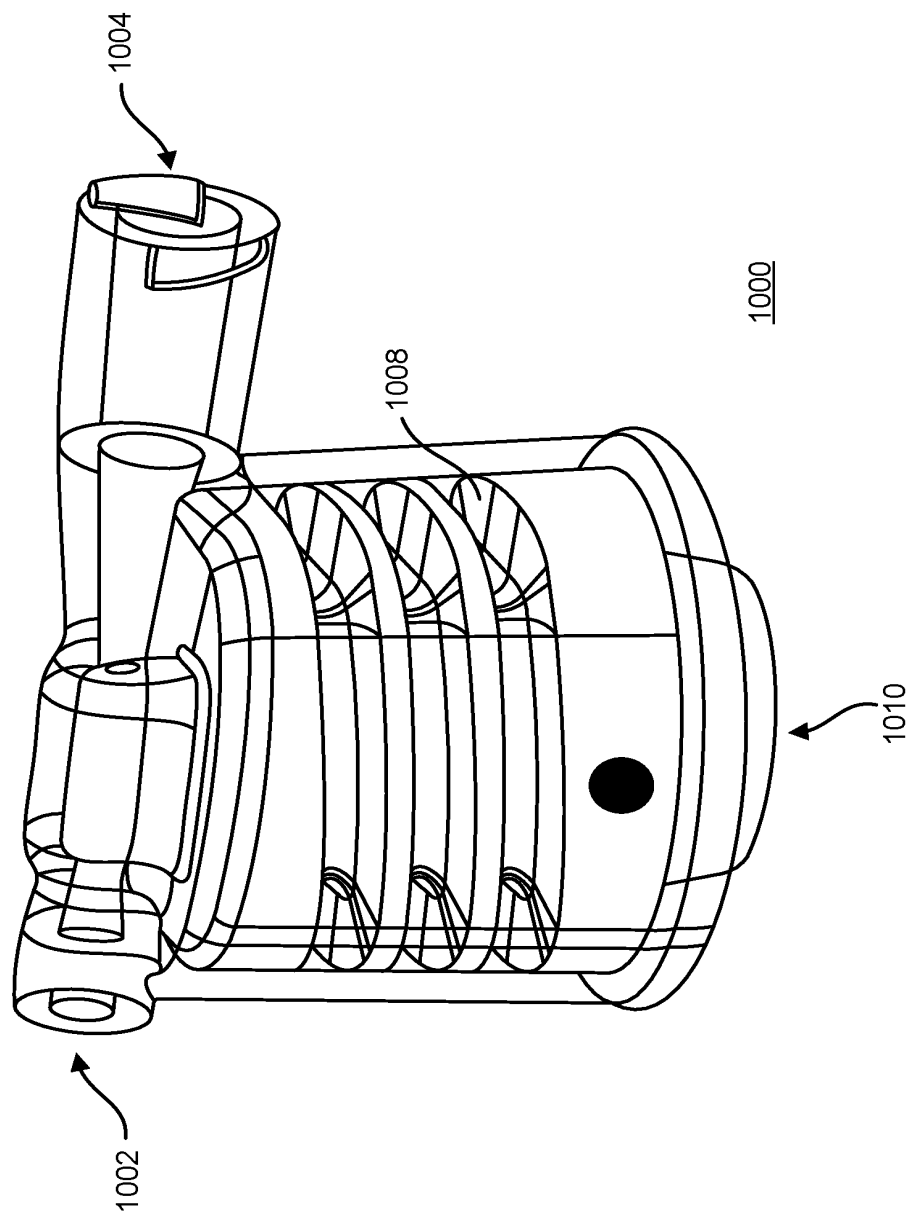


FIG. 10A

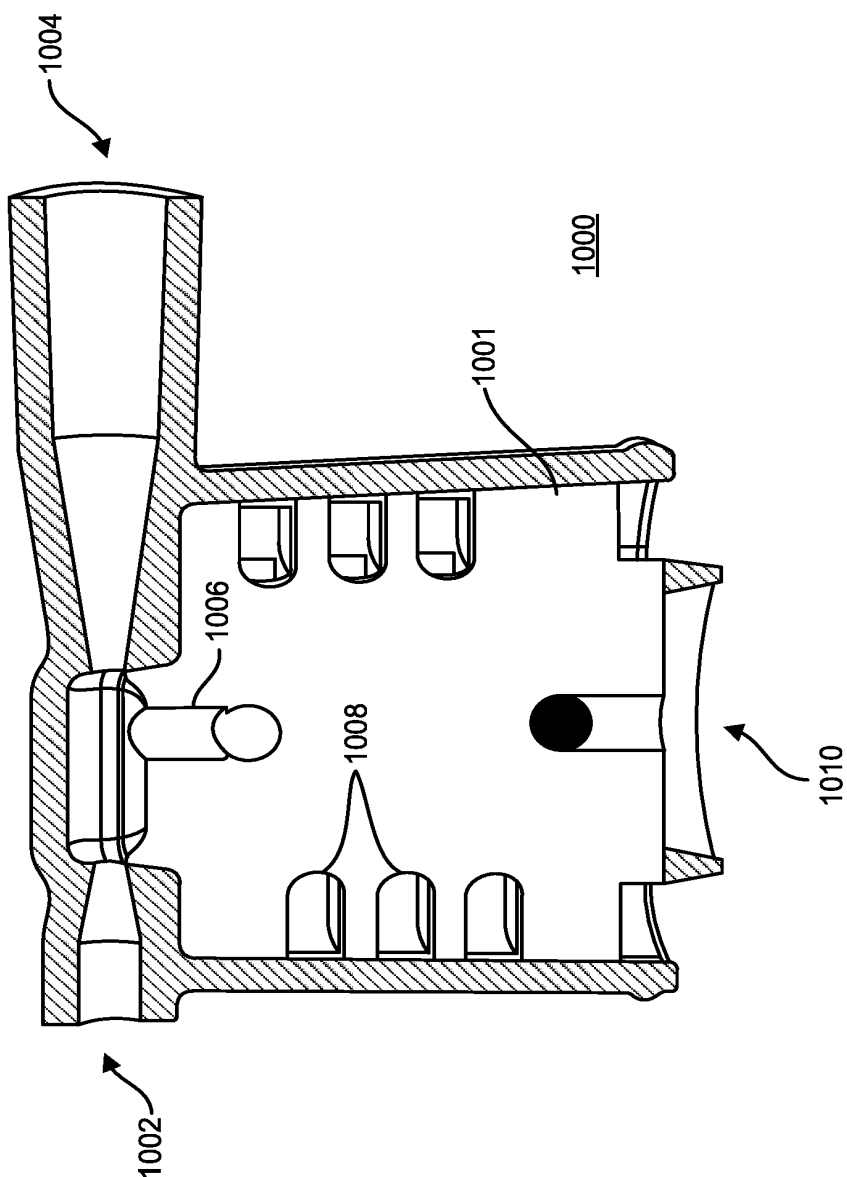


FIG. 10B

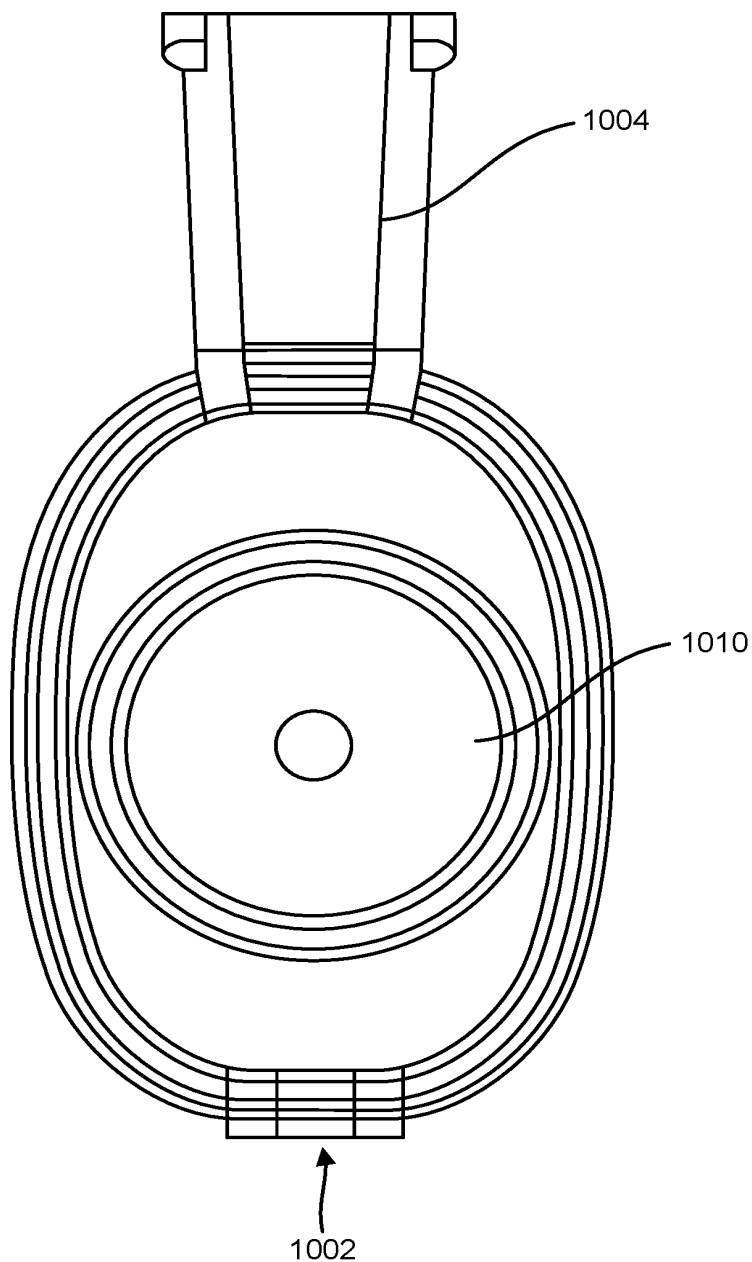


FIG. 10C

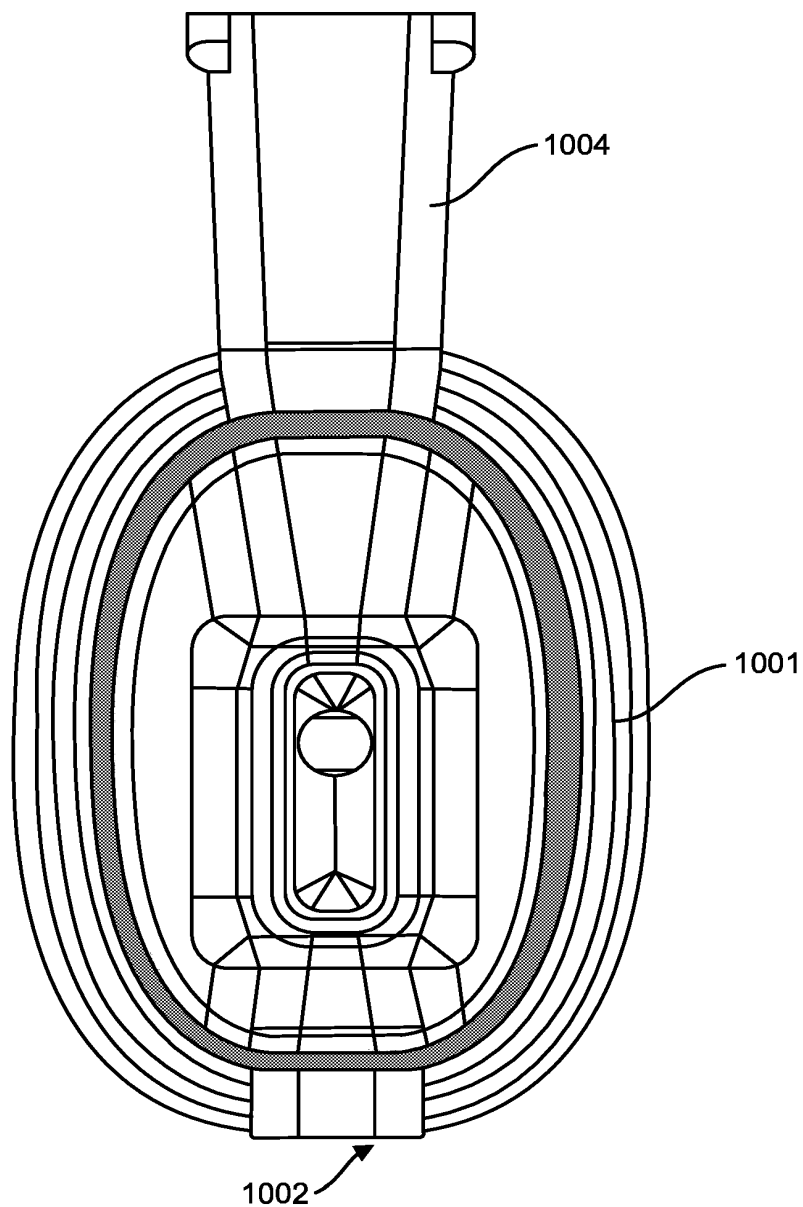


FIG. 10D

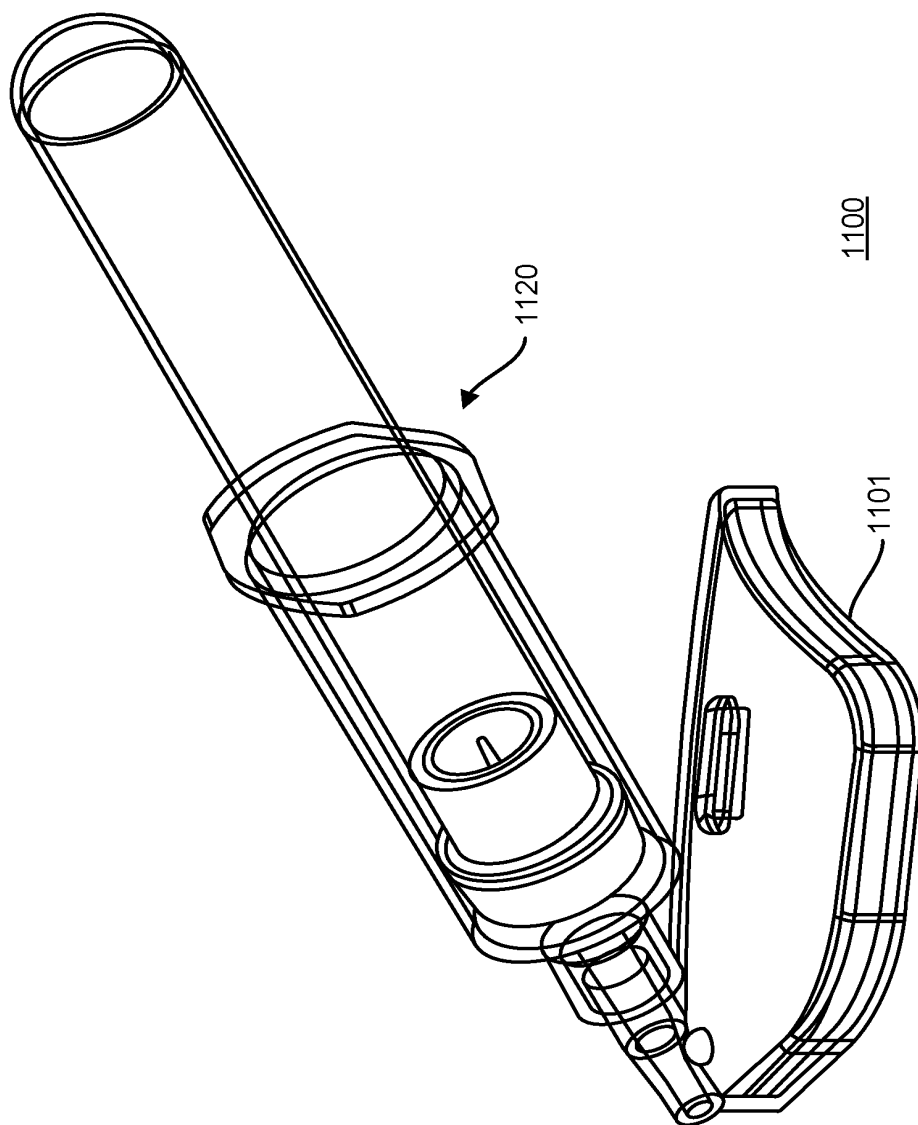


FIG. 11A

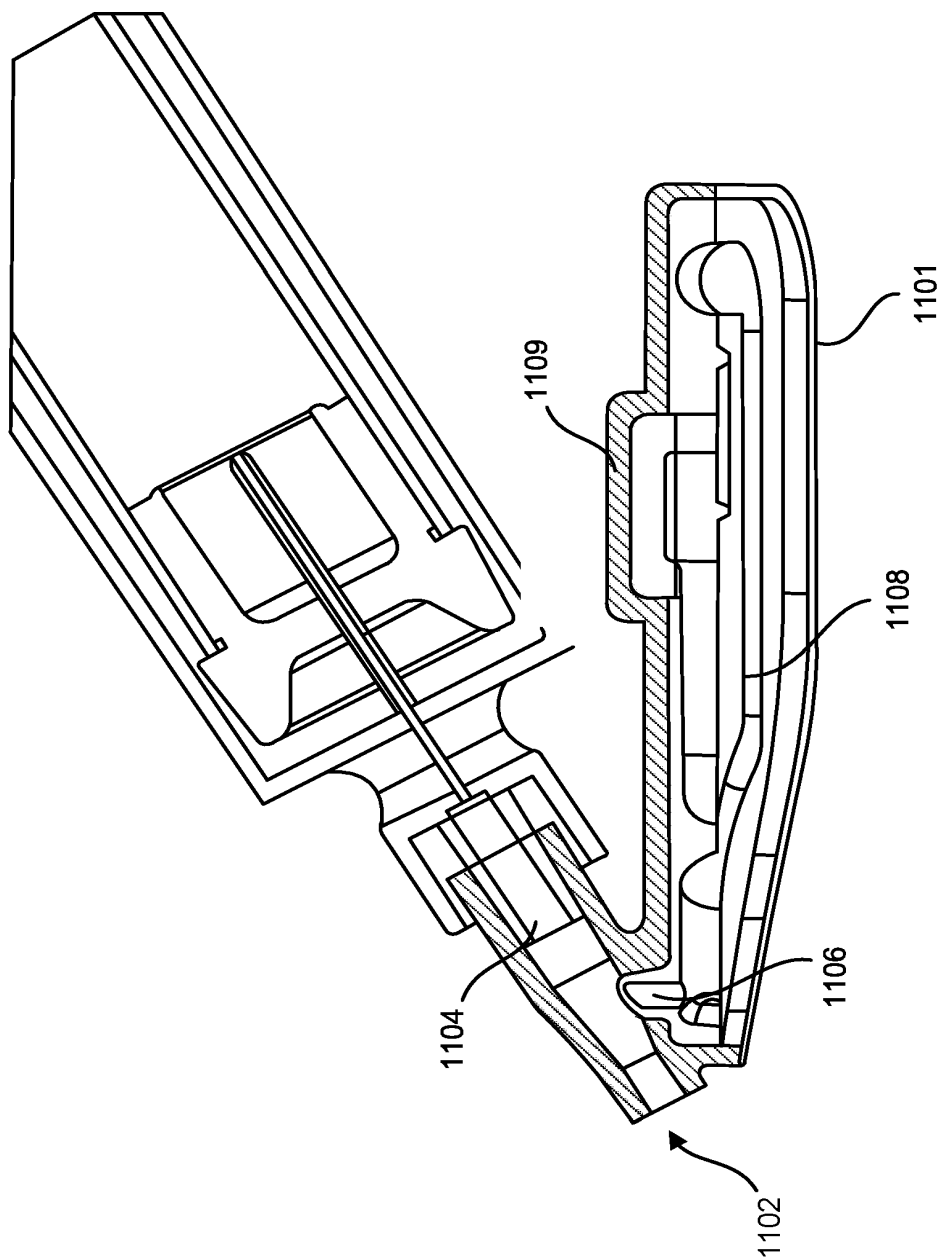


FIG. 11B

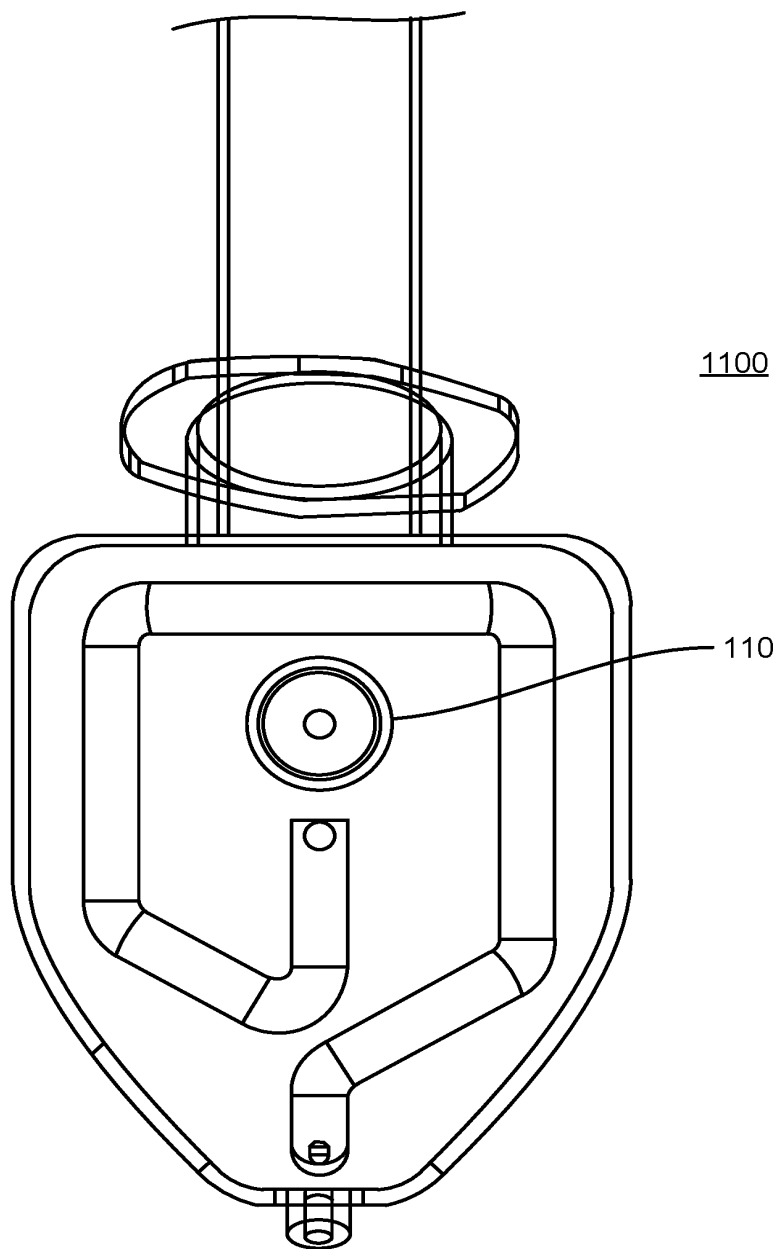


FIG. 11C

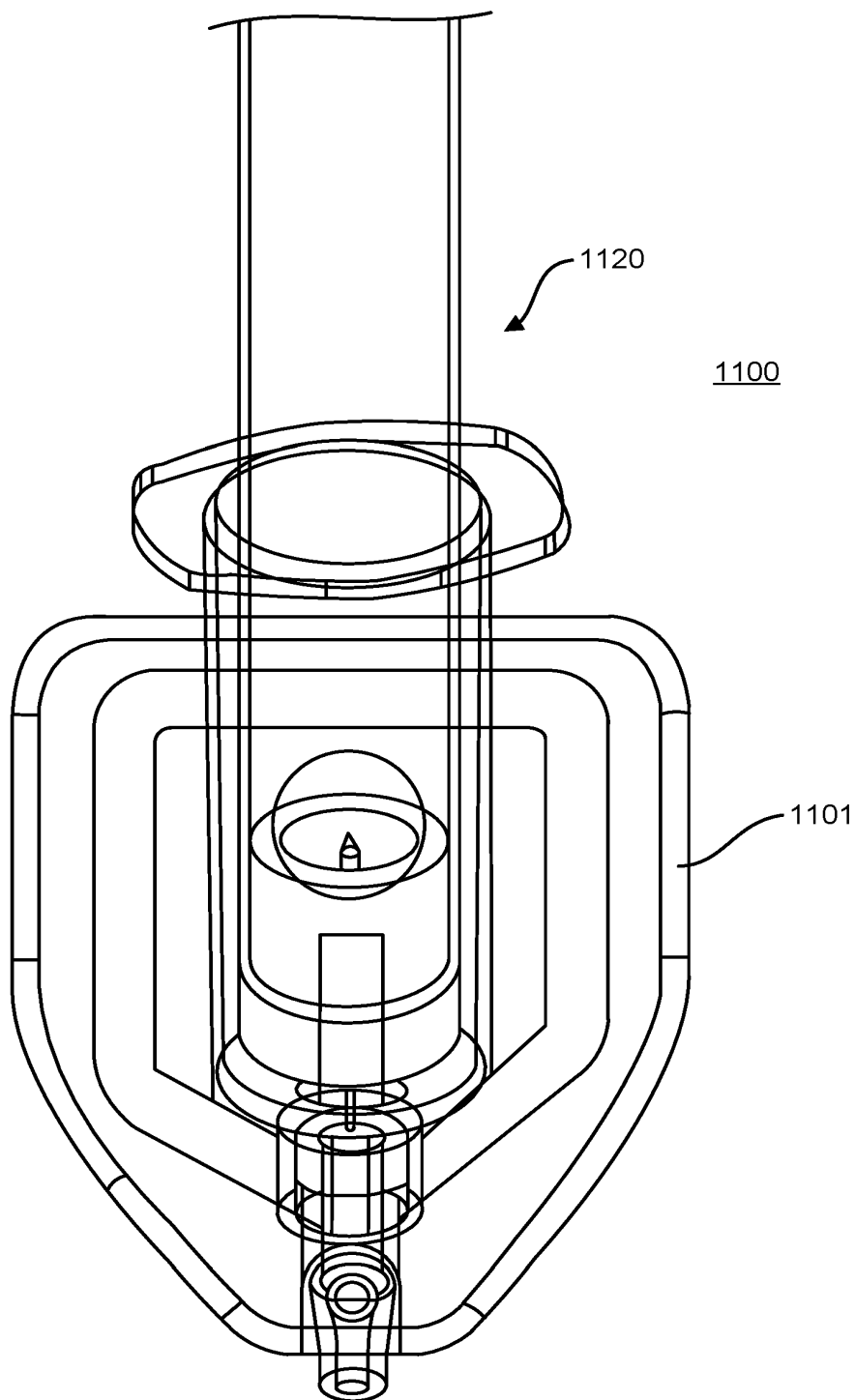
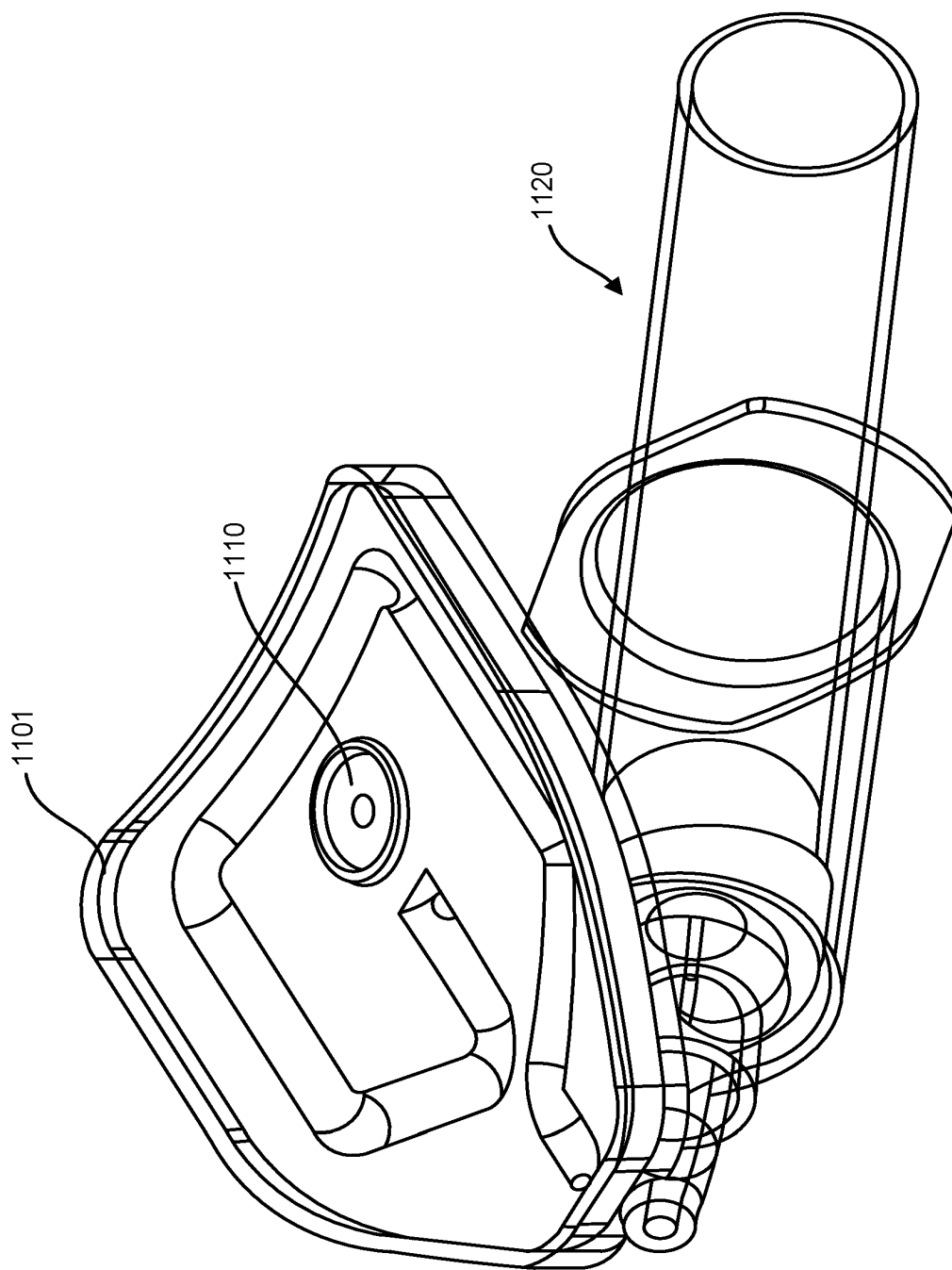


FIG. 11D



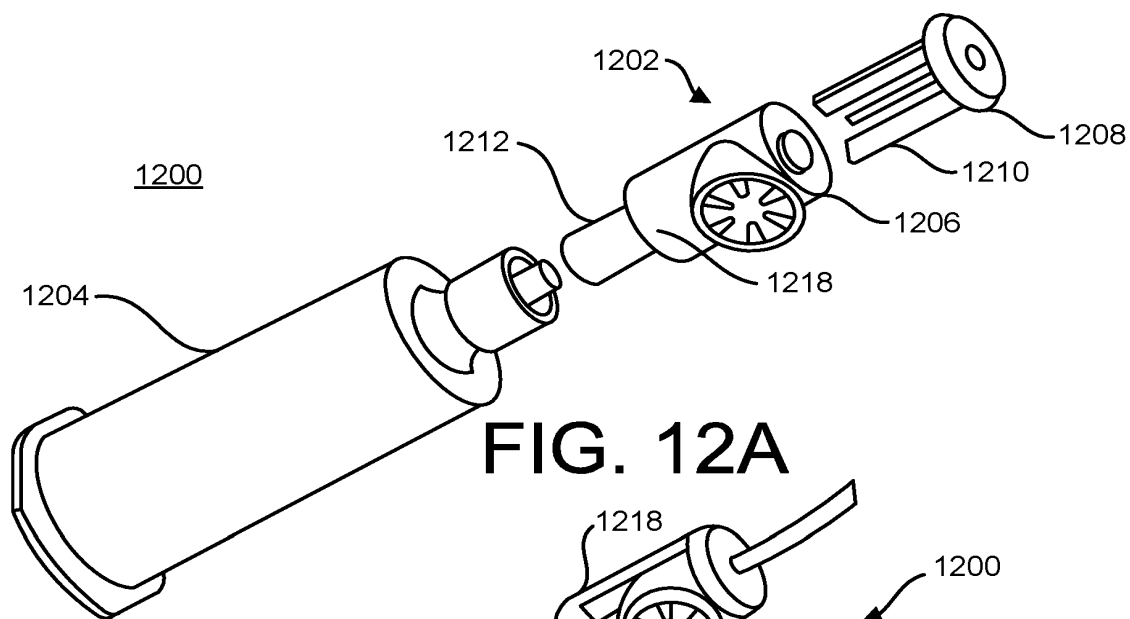


FIG. 12A

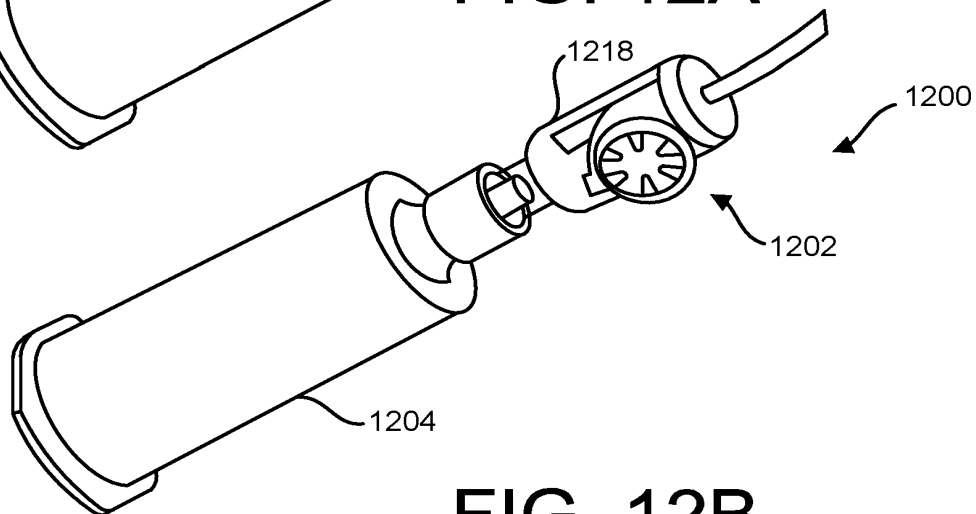


FIG. 12B

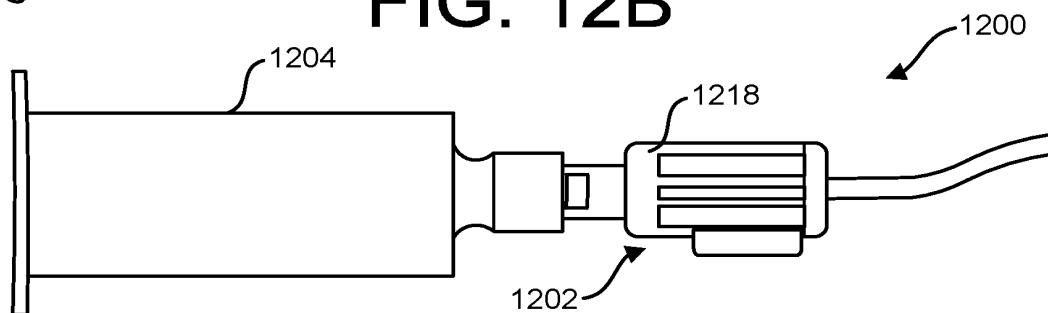


FIG. 12C

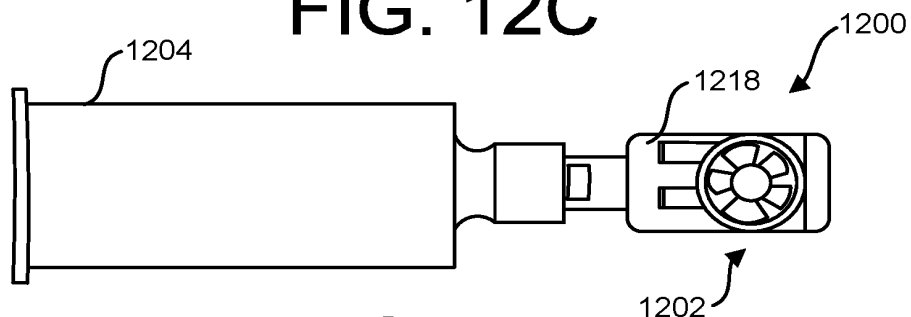


FIG. 12D

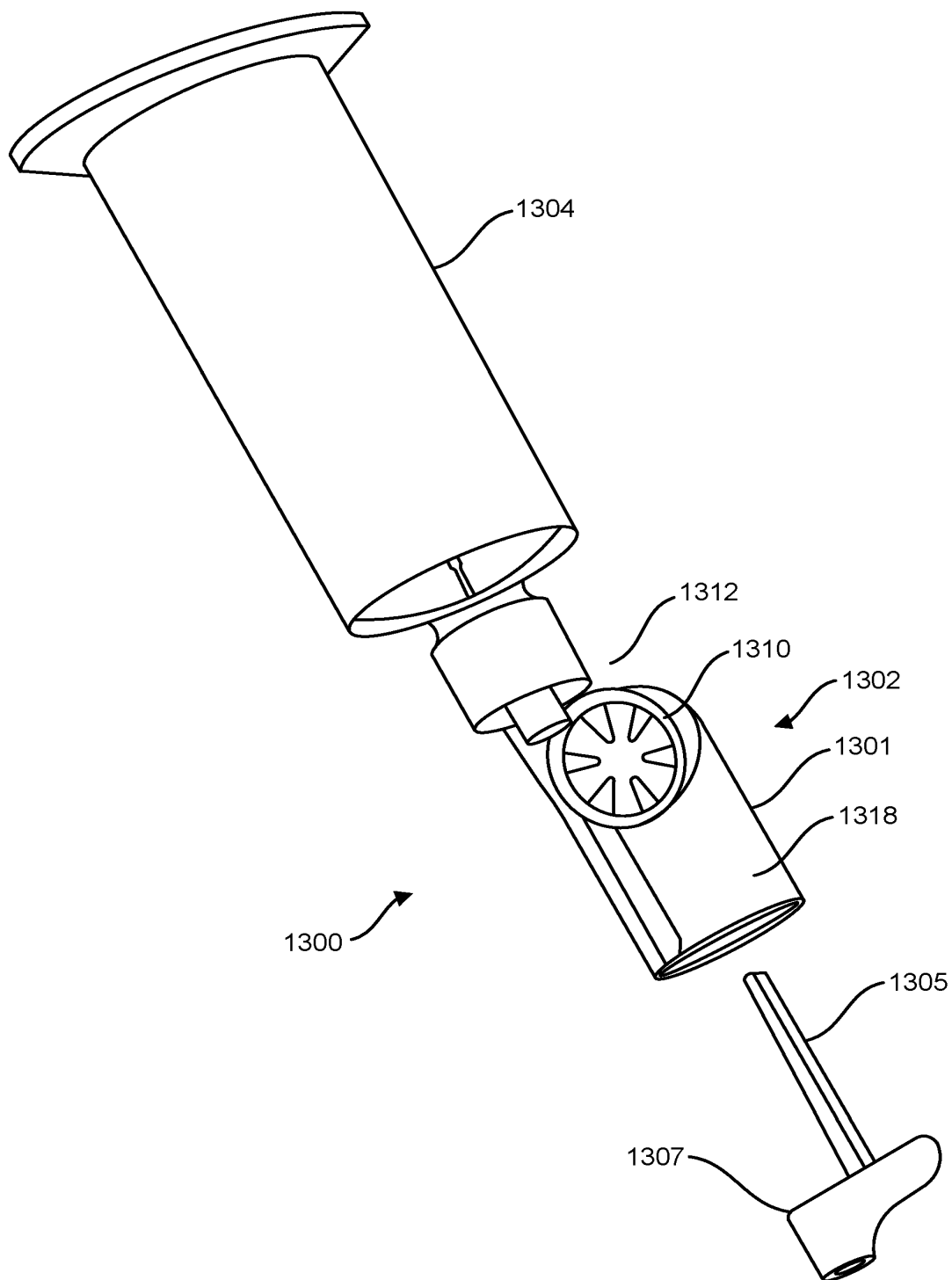


FIG. 13A

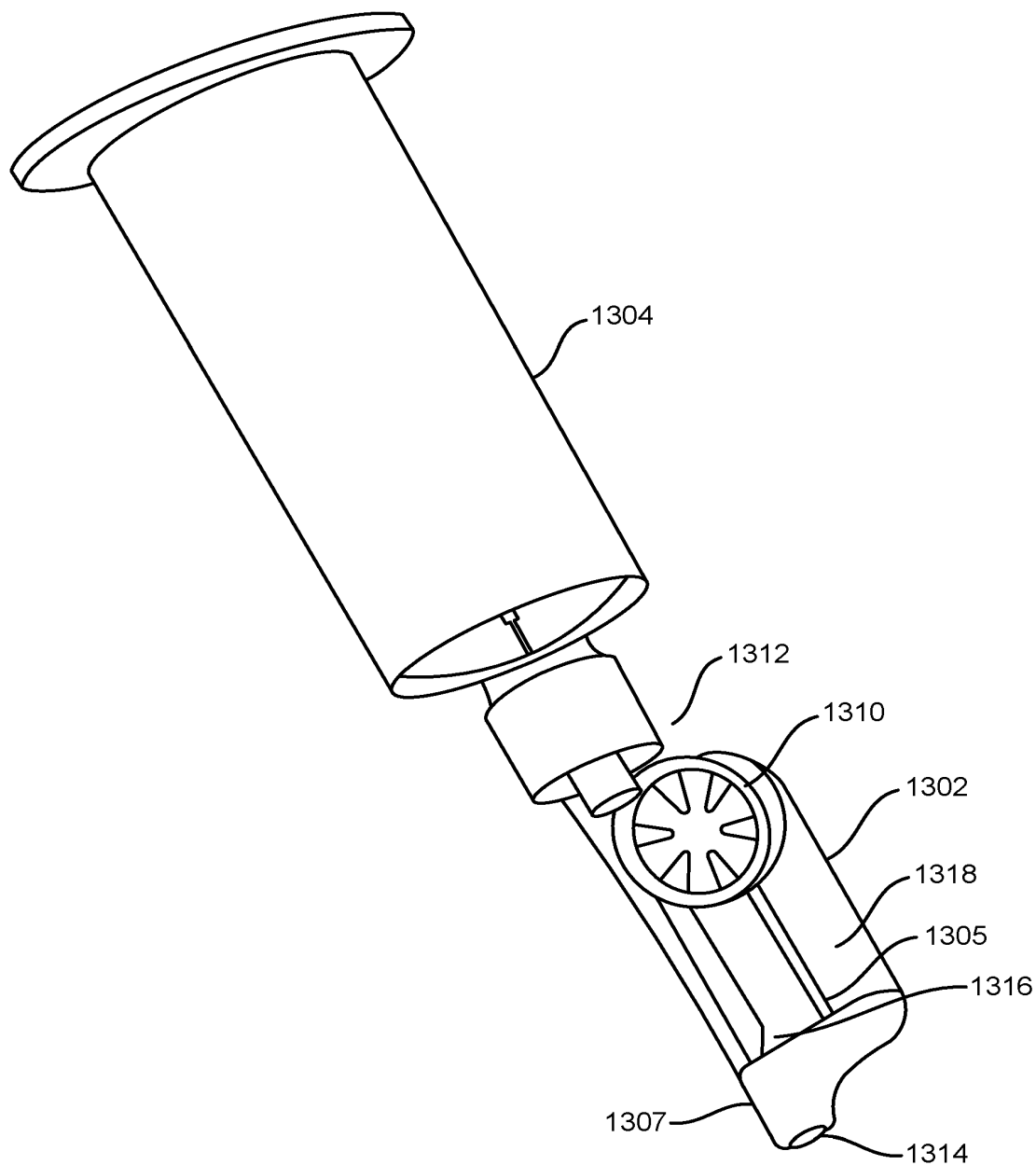


FIG. 13B

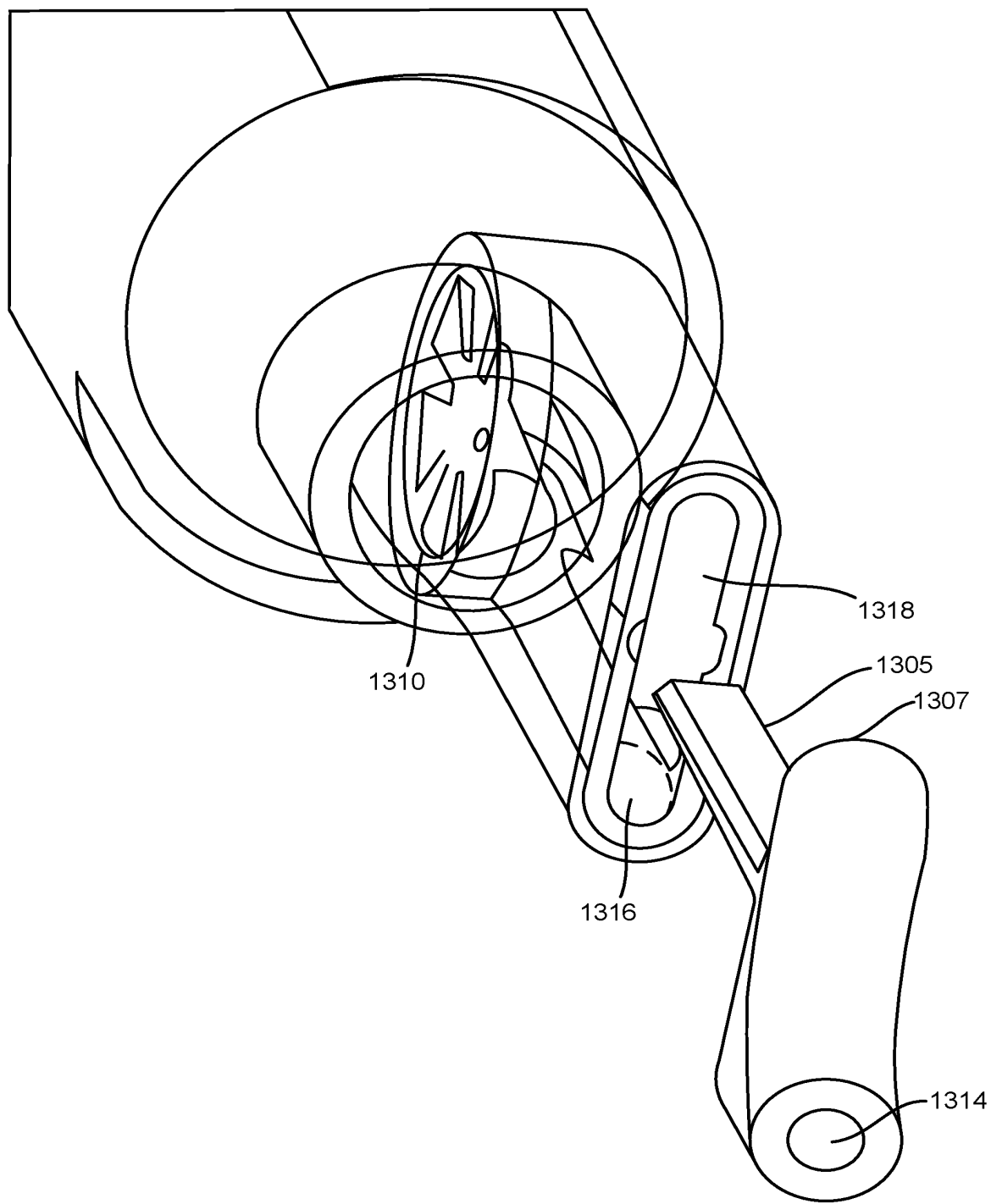


FIG. 13C

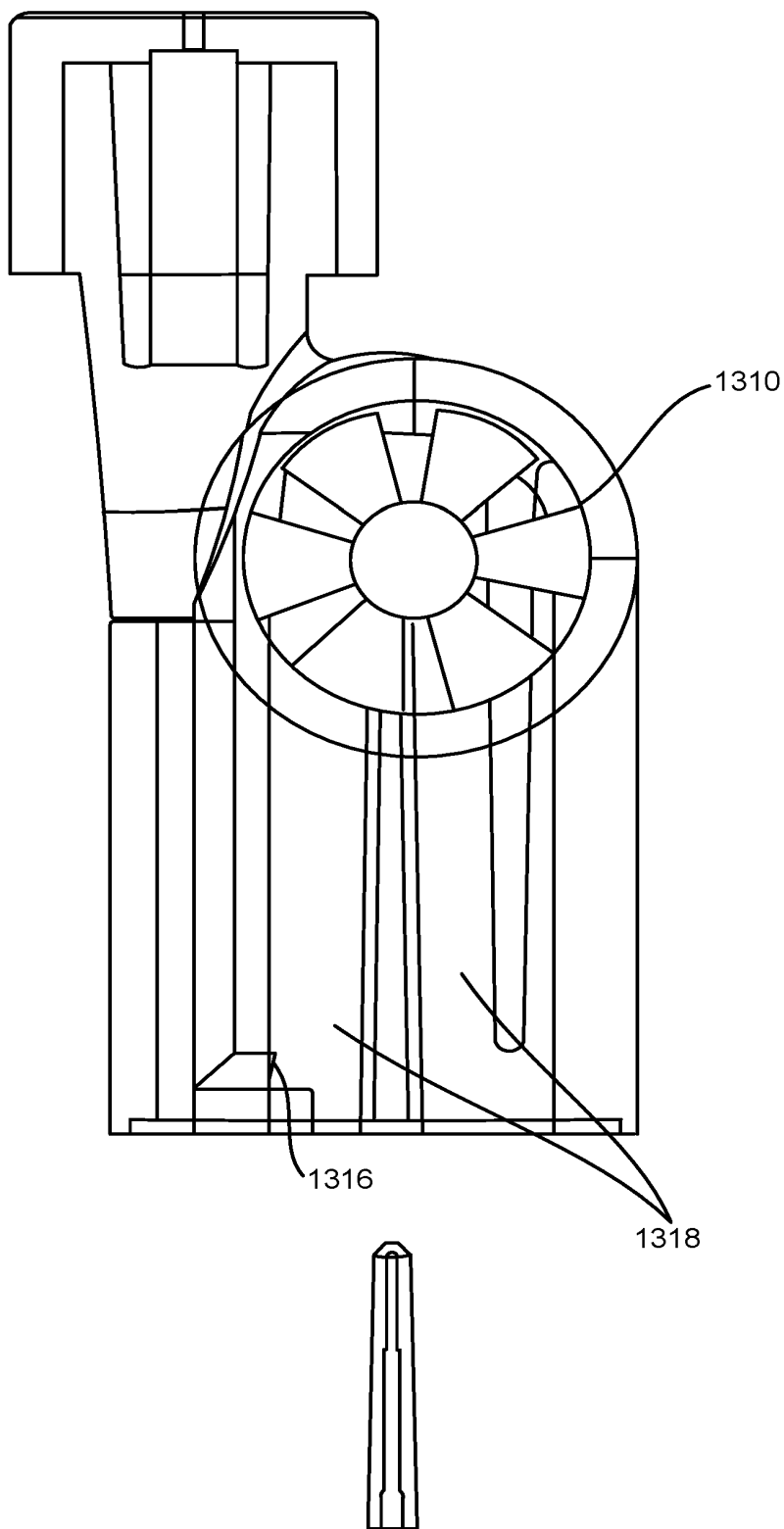


FIG. 13D

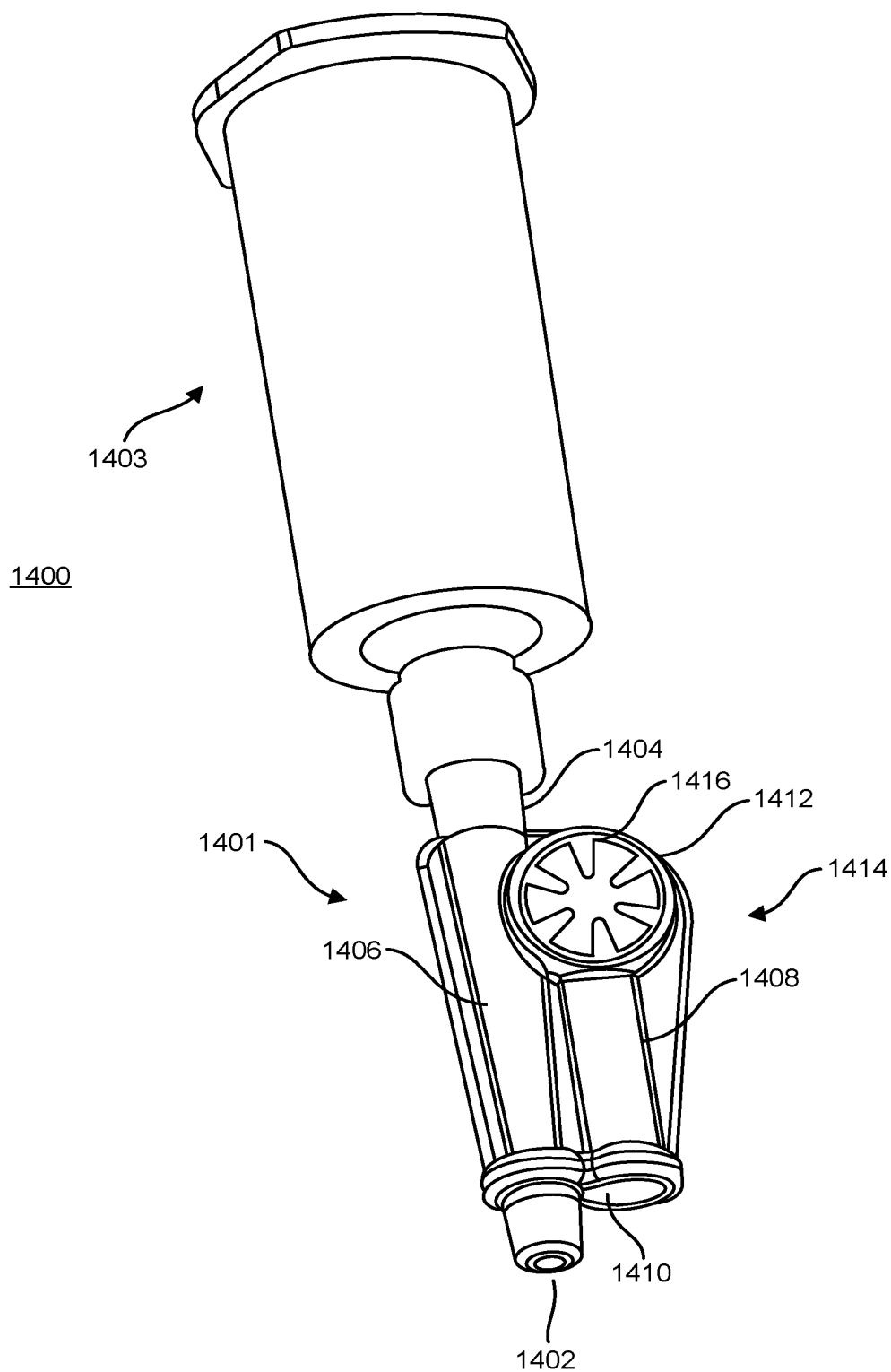


FIG. 14A

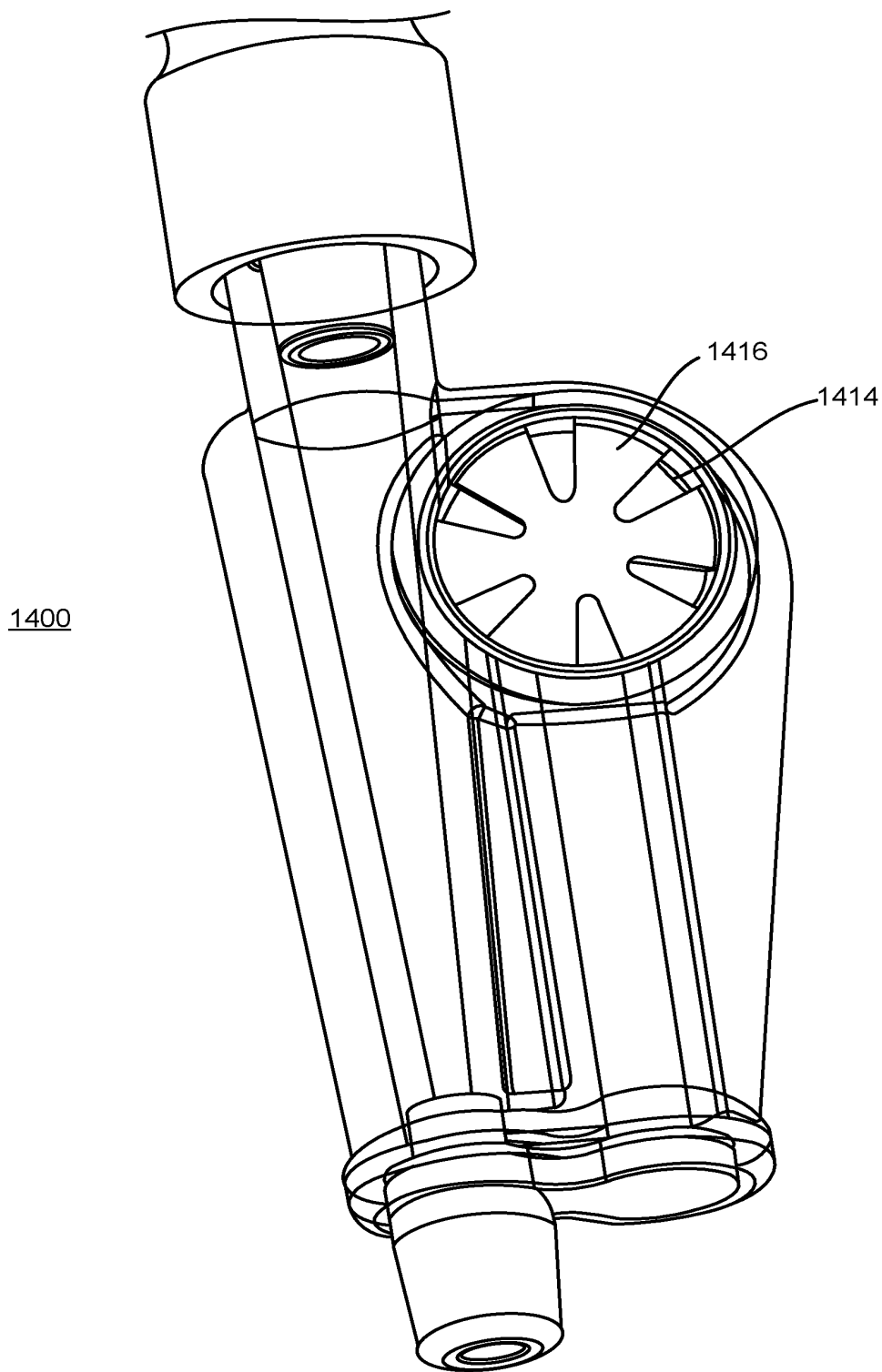


FIG. 14B

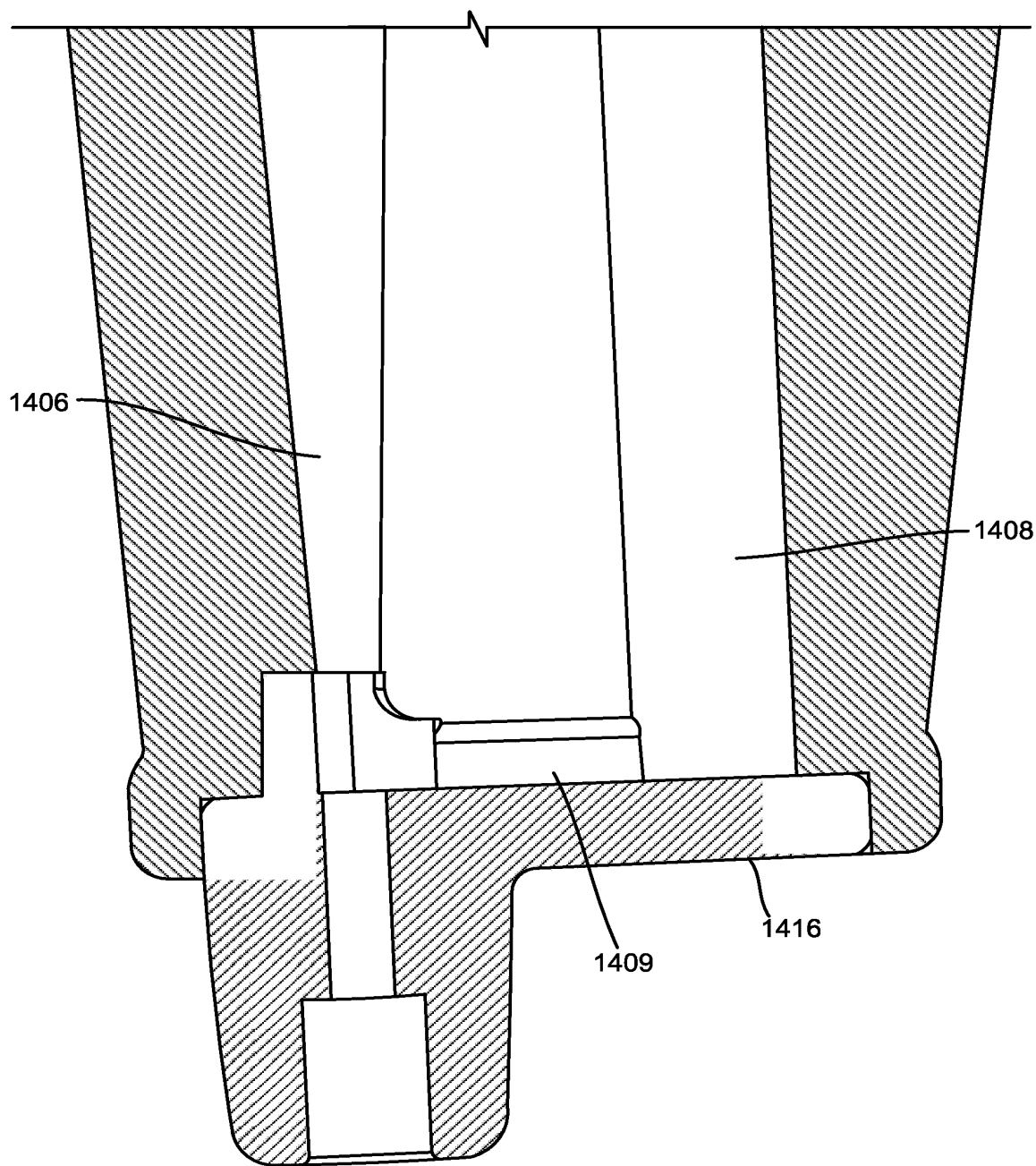


FIG. 14C

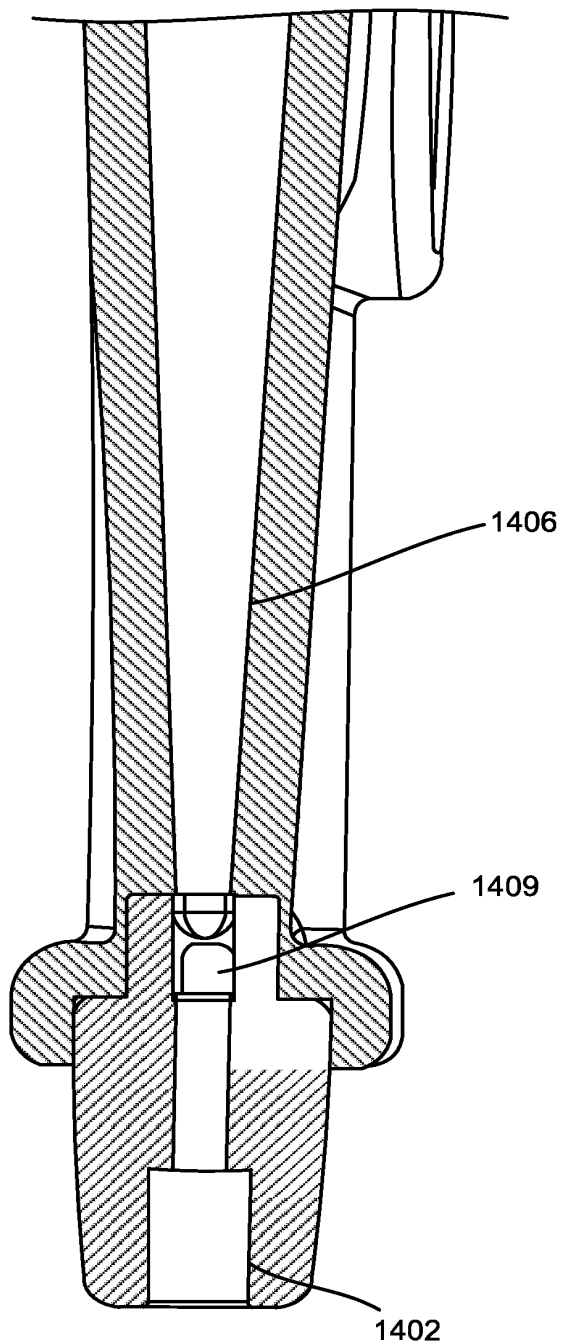


FIG. 14D

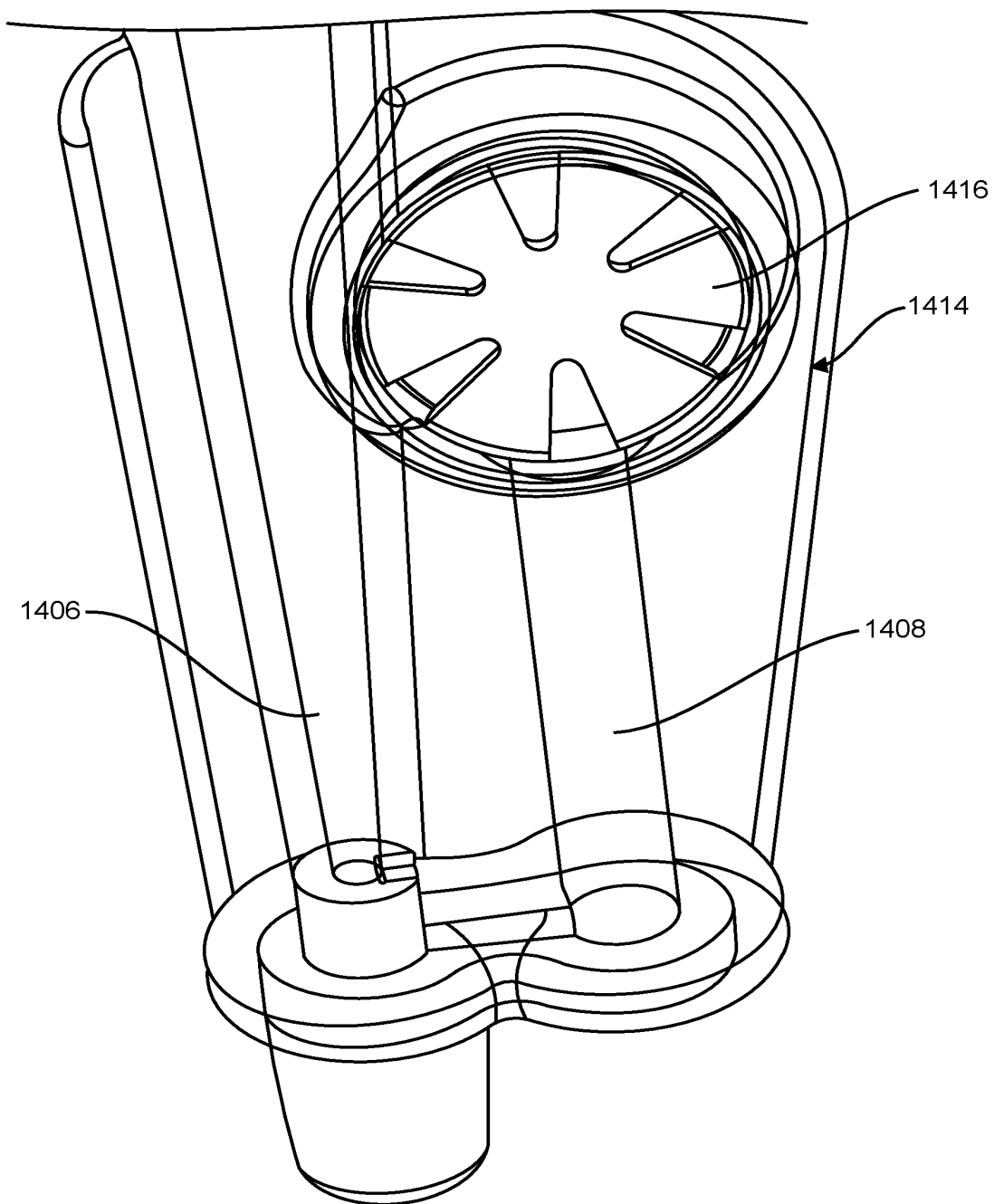


FIG. 14E

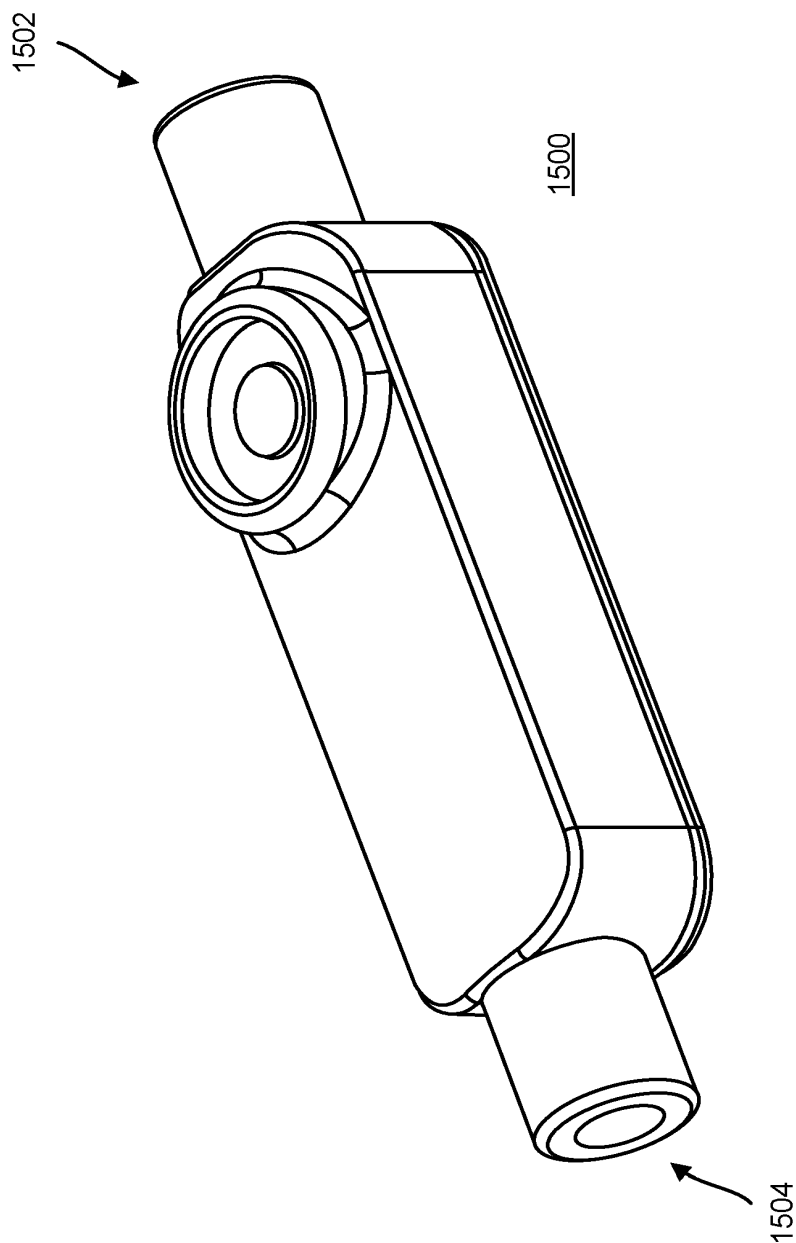


FIG. 15A

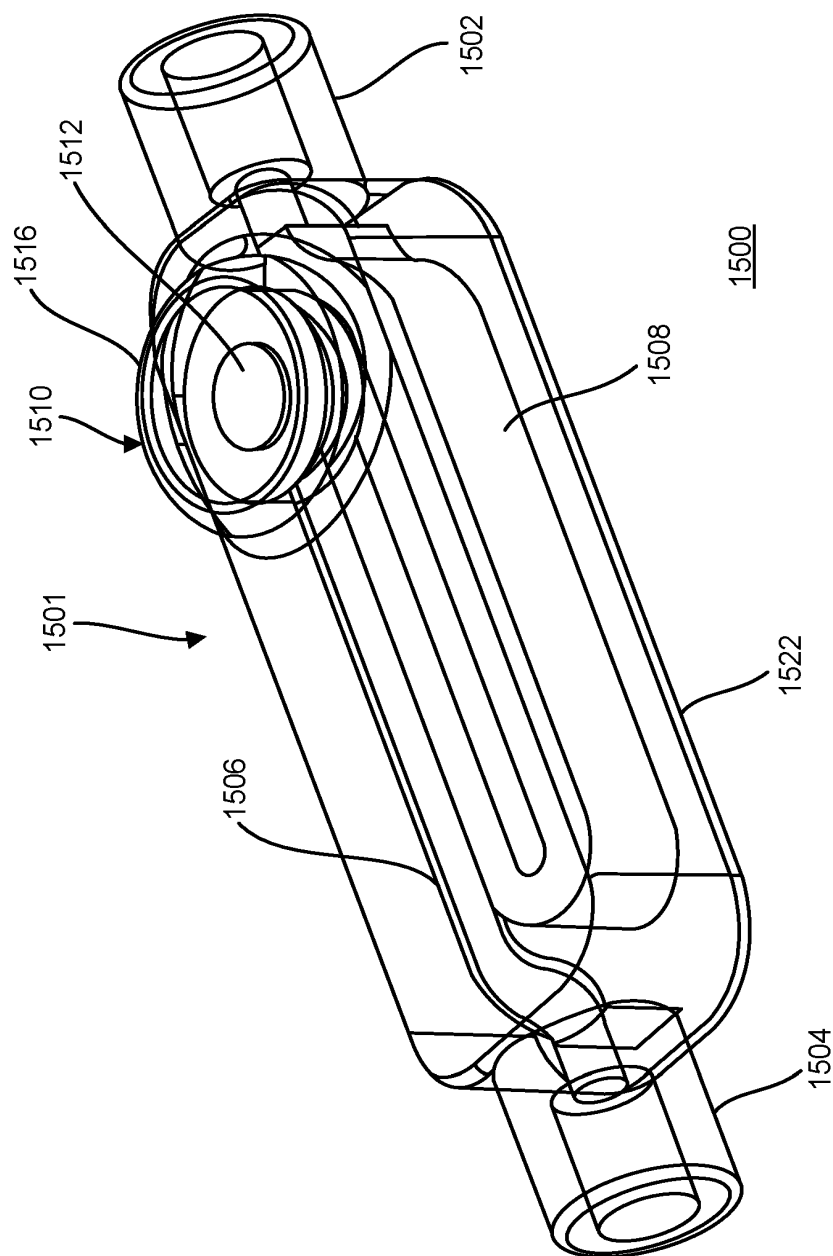


FIG. 15B

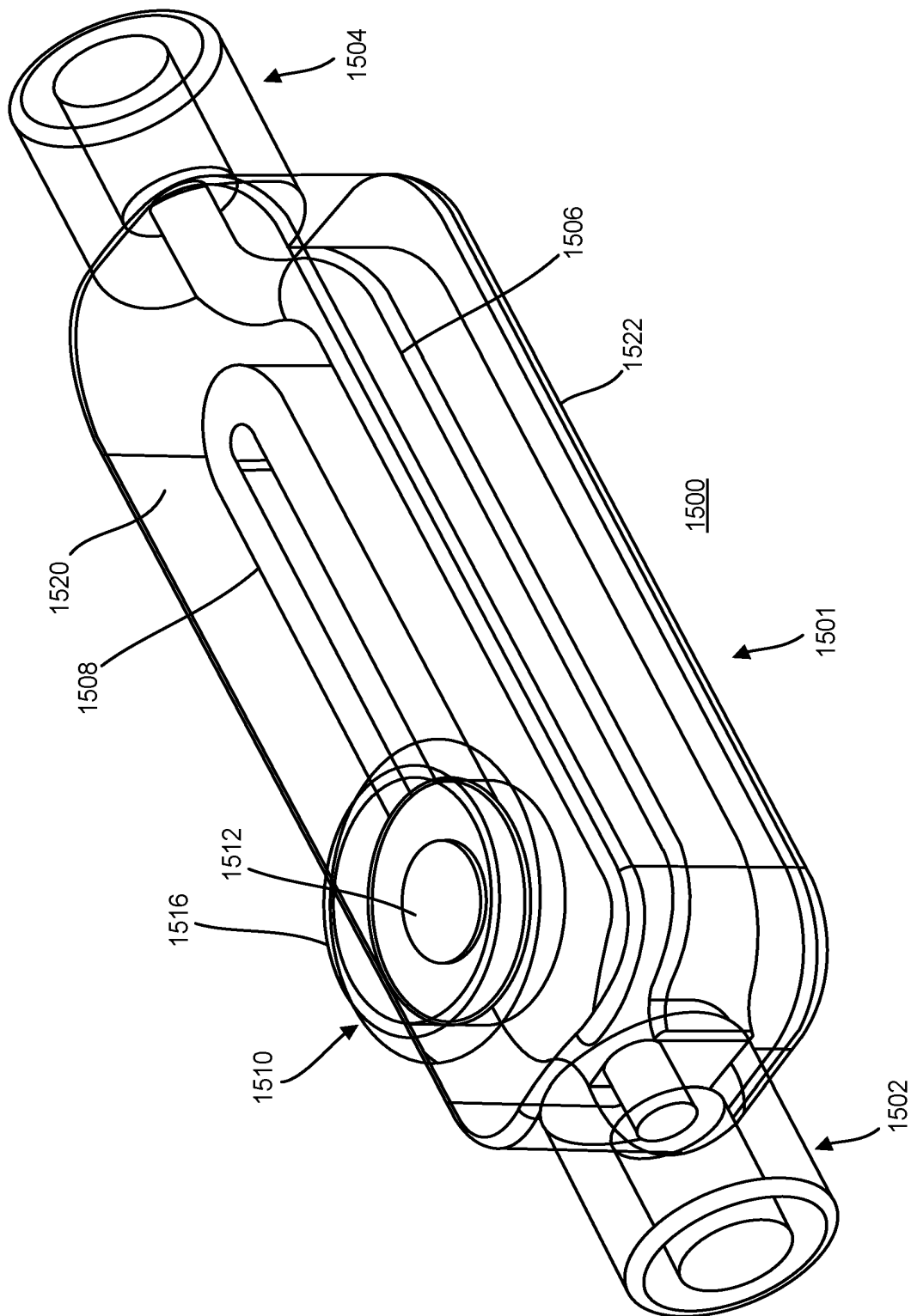


FIG. 15C

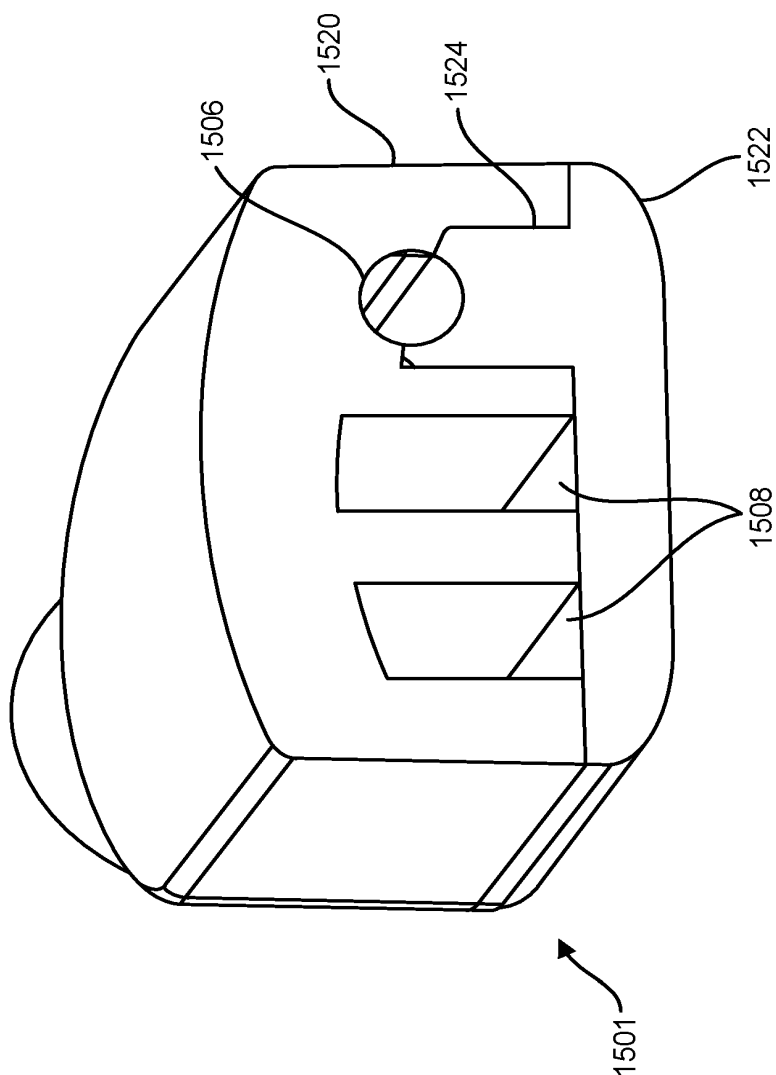


FIG. 15D

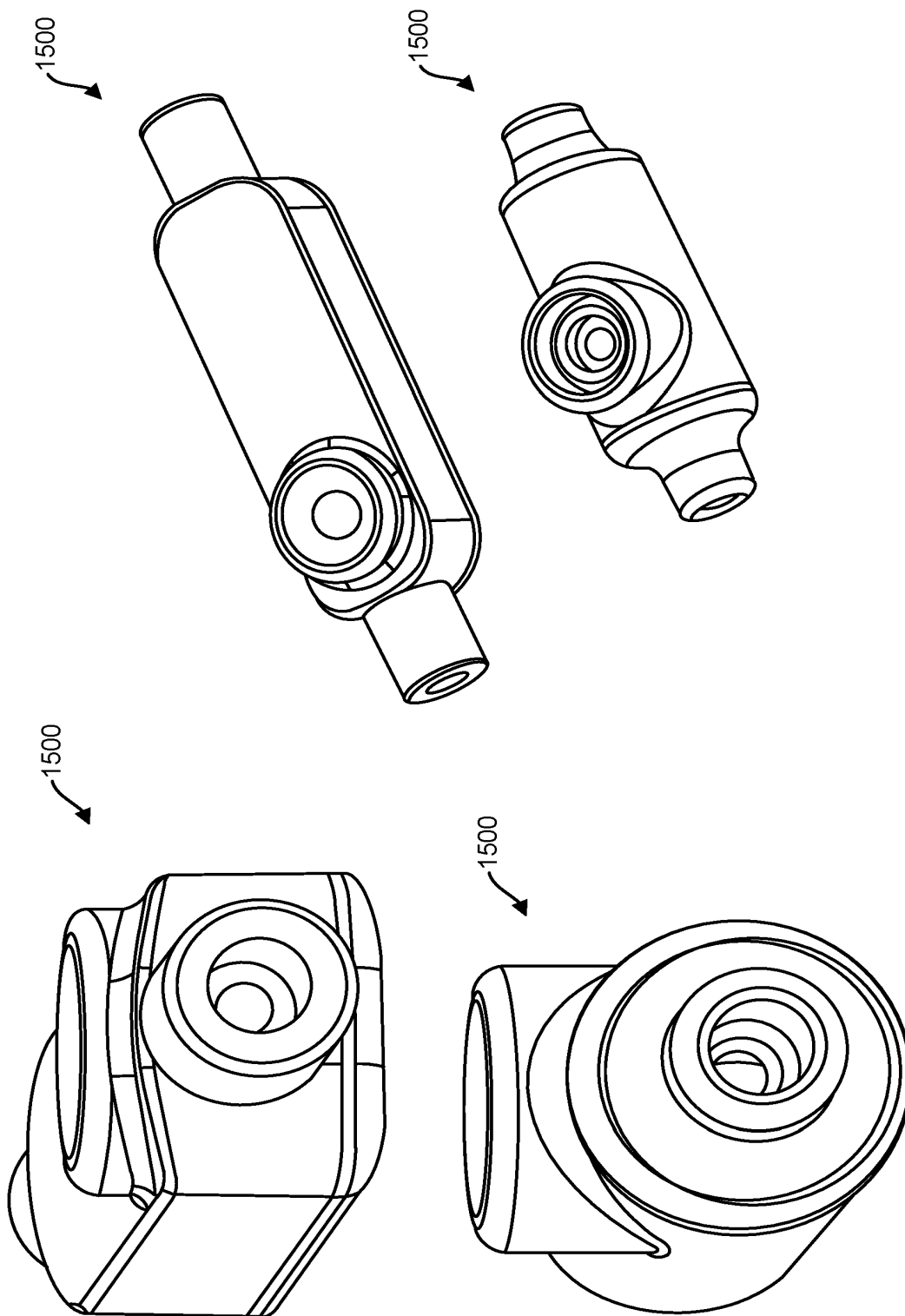


FIG. 15F

FIG. 15E

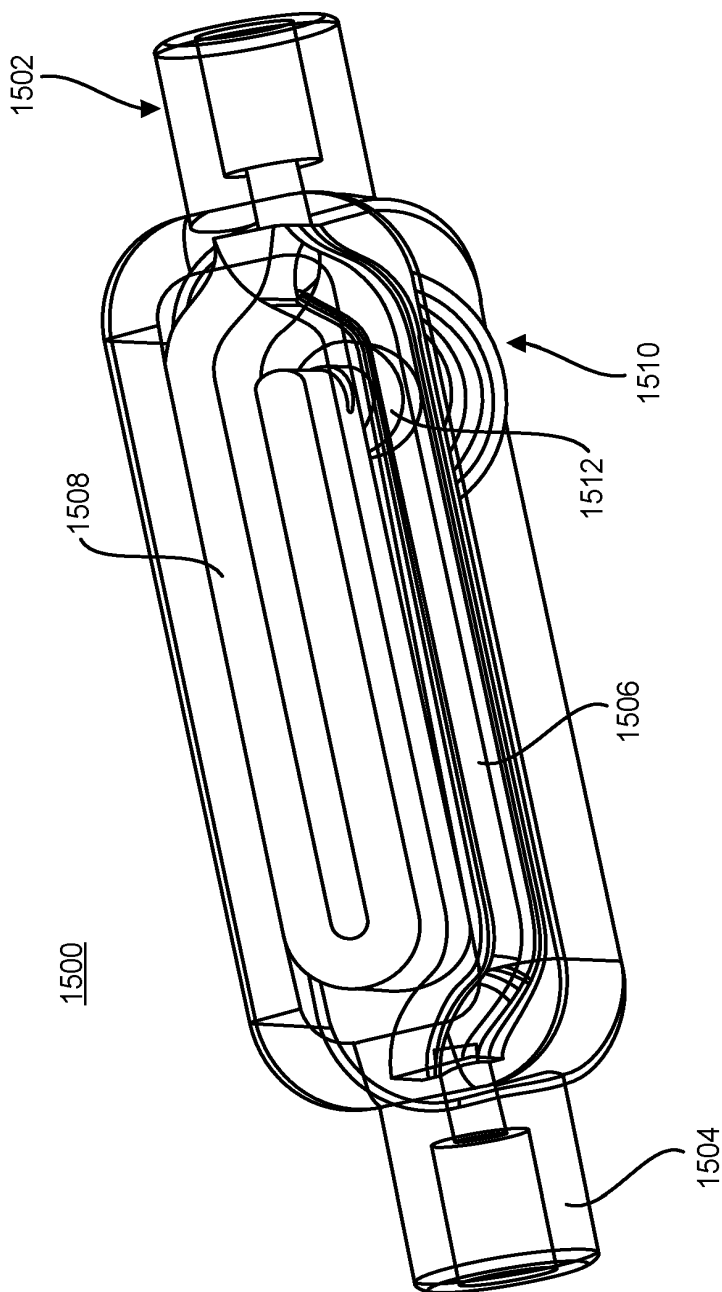


FIG. 15G

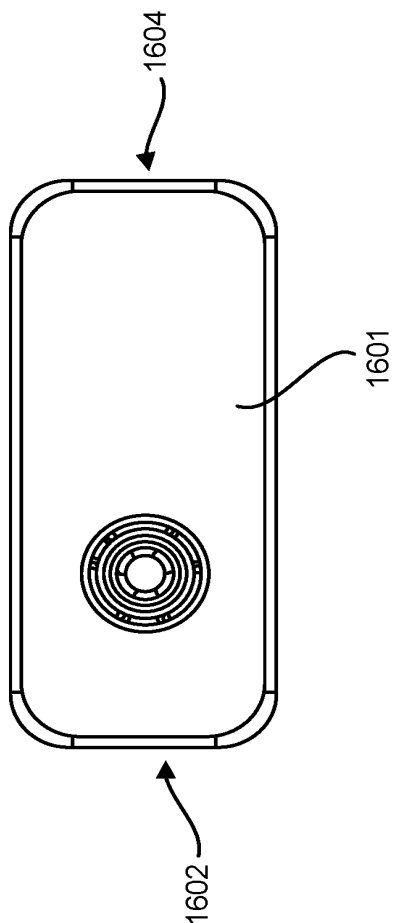


FIG. 16A

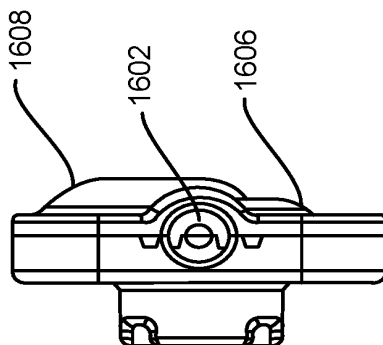


FIG. 16C

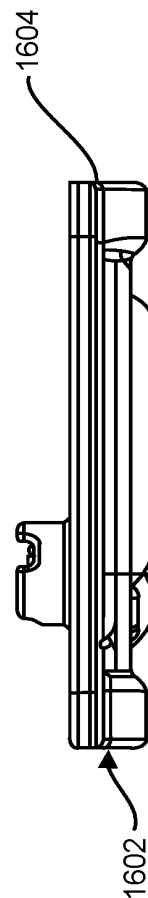


FIG. 16B

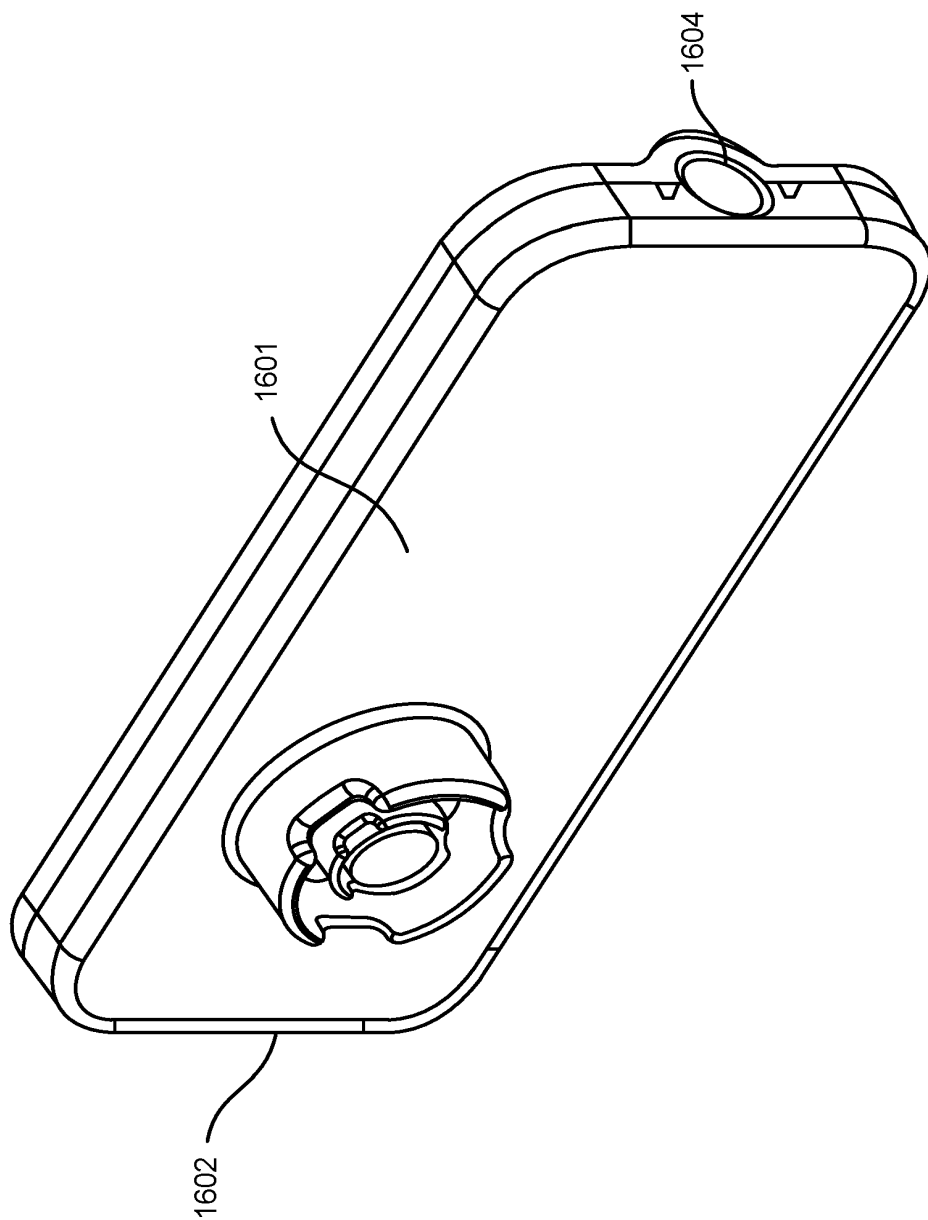


FIG. 16D

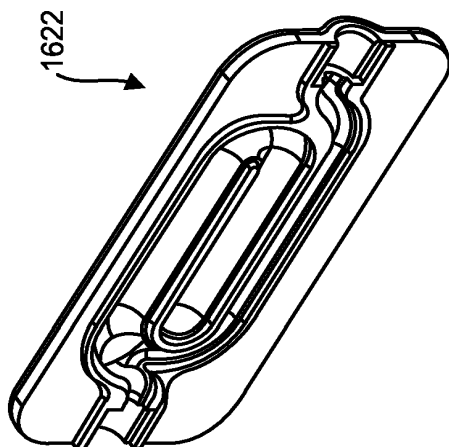


FIG. 17B

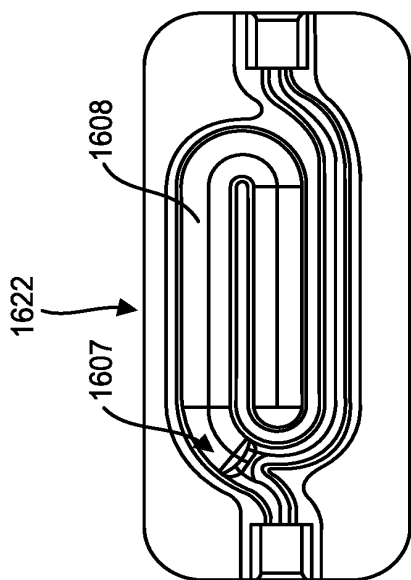


FIG. 17A

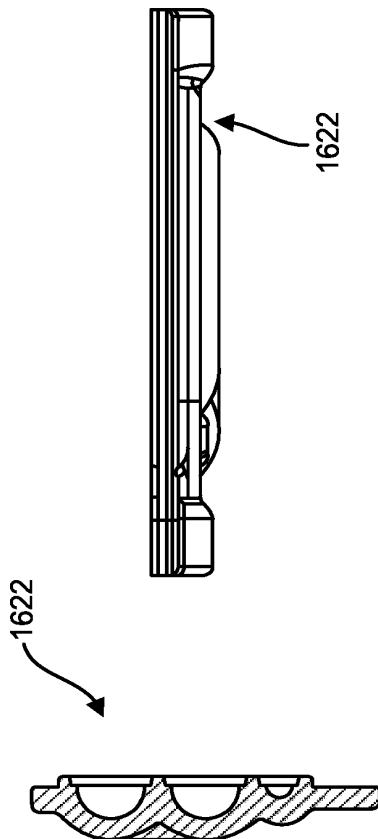


FIG. 17D

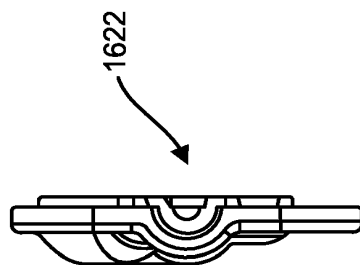


FIG. 17C

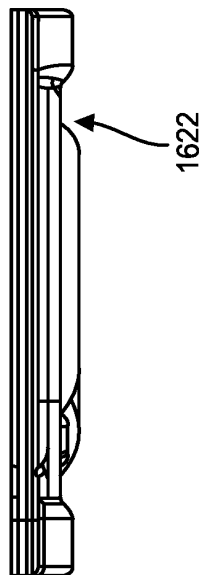


FIG. 17E

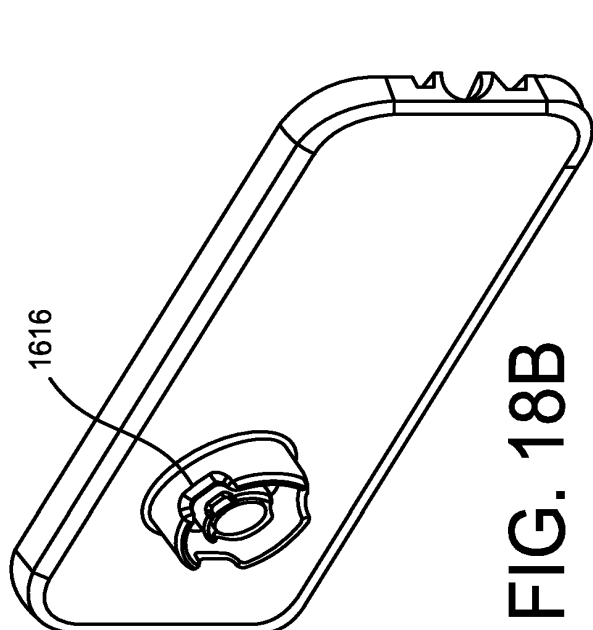


FIG. 18B

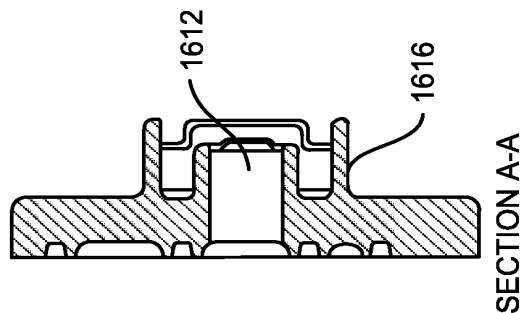


FIG. 18F

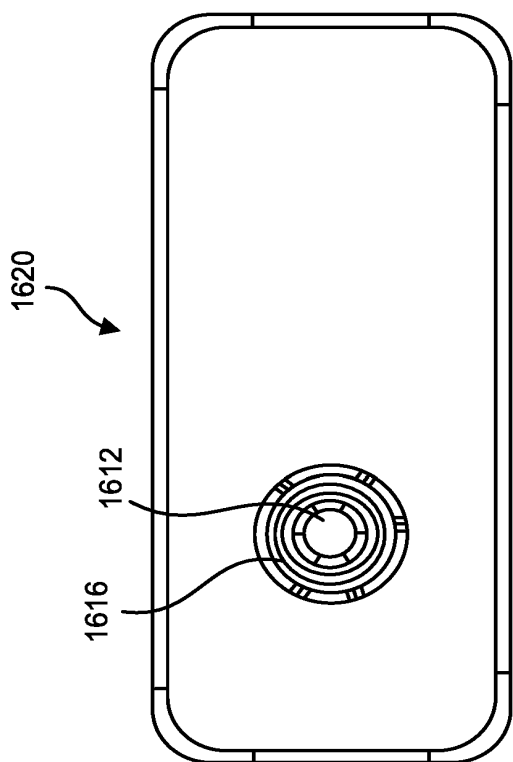


FIG. 18A

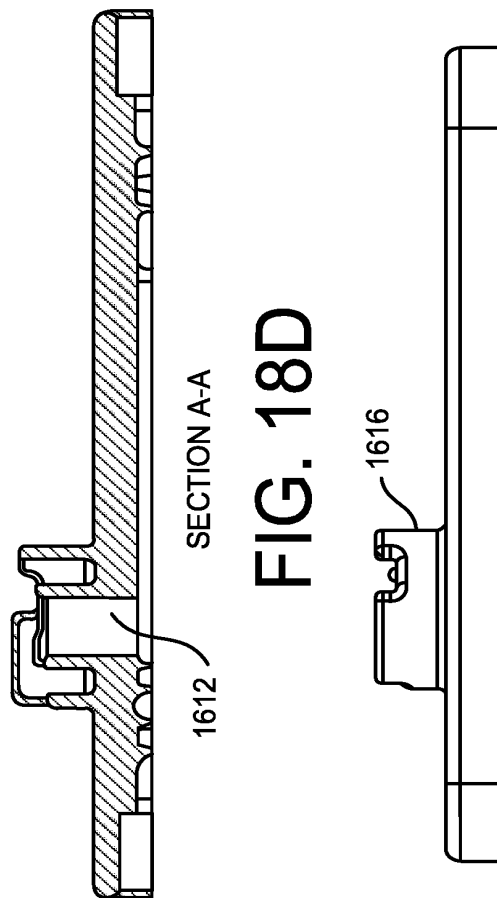


FIG. 18D

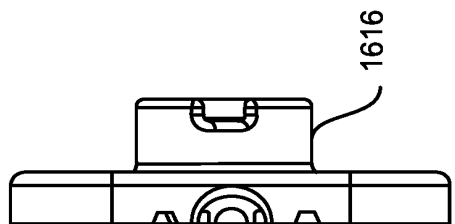


FIG. 18C

FIG. 18E

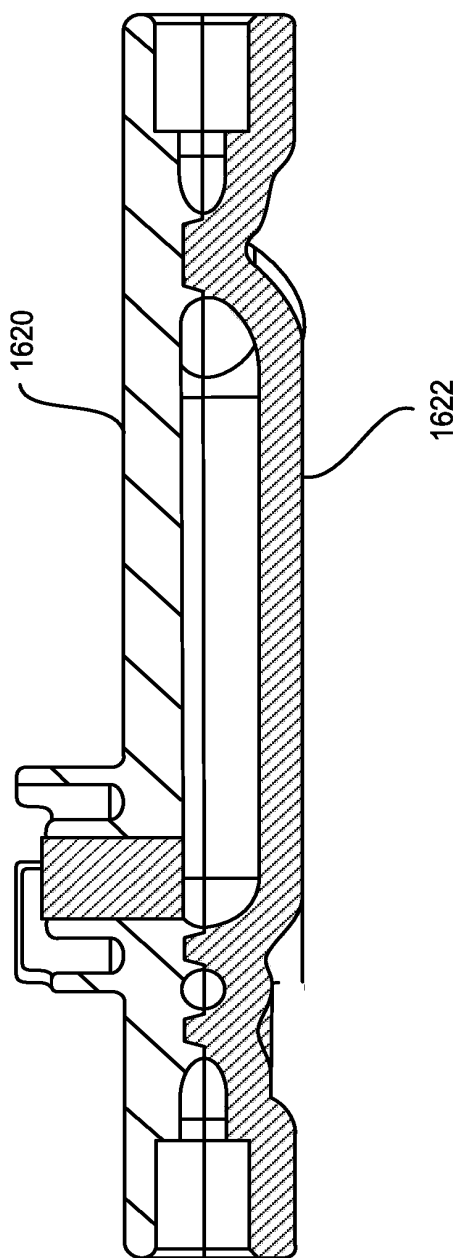


FIG. 19A

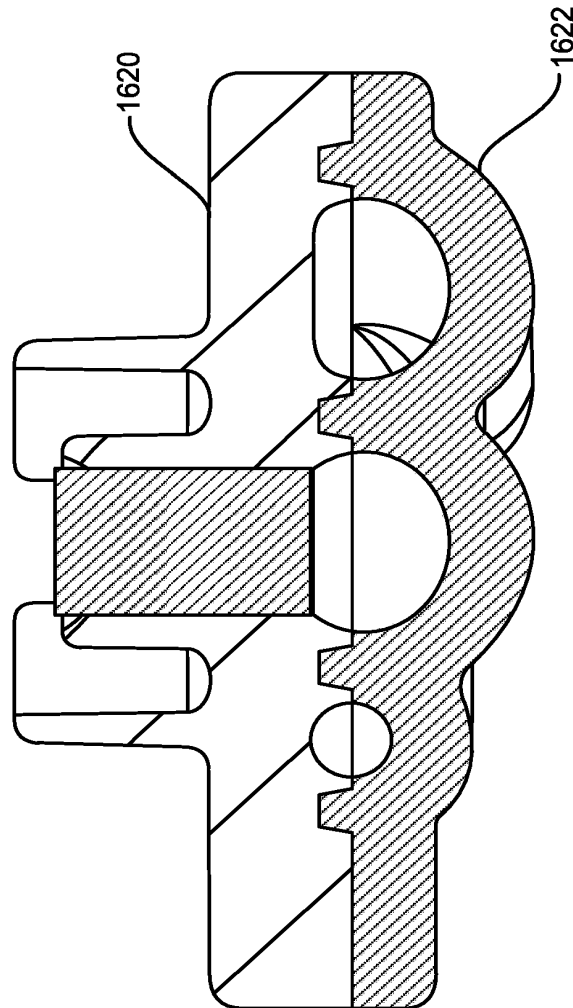


FIG. 19B

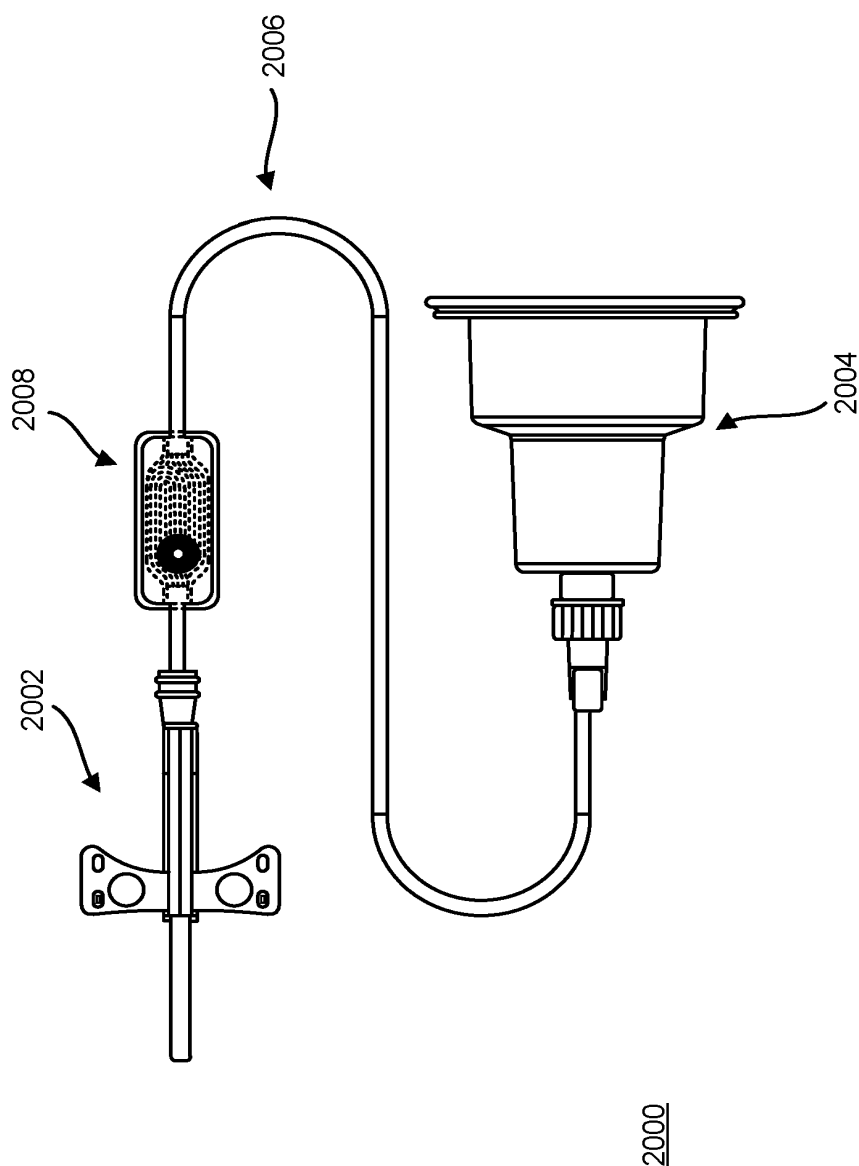


FIG. 20

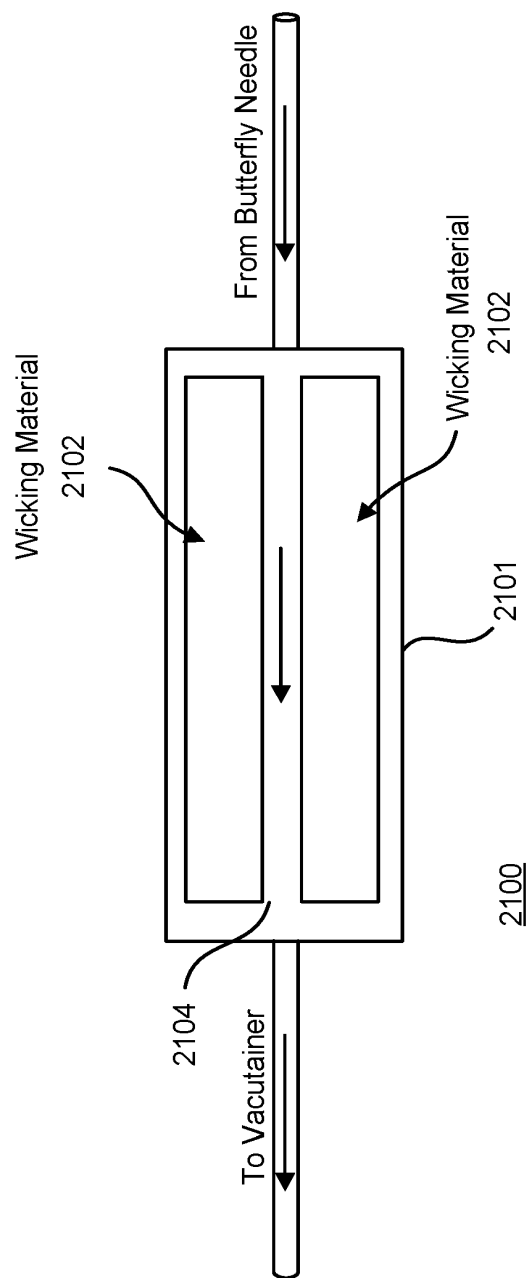


FIG. 21

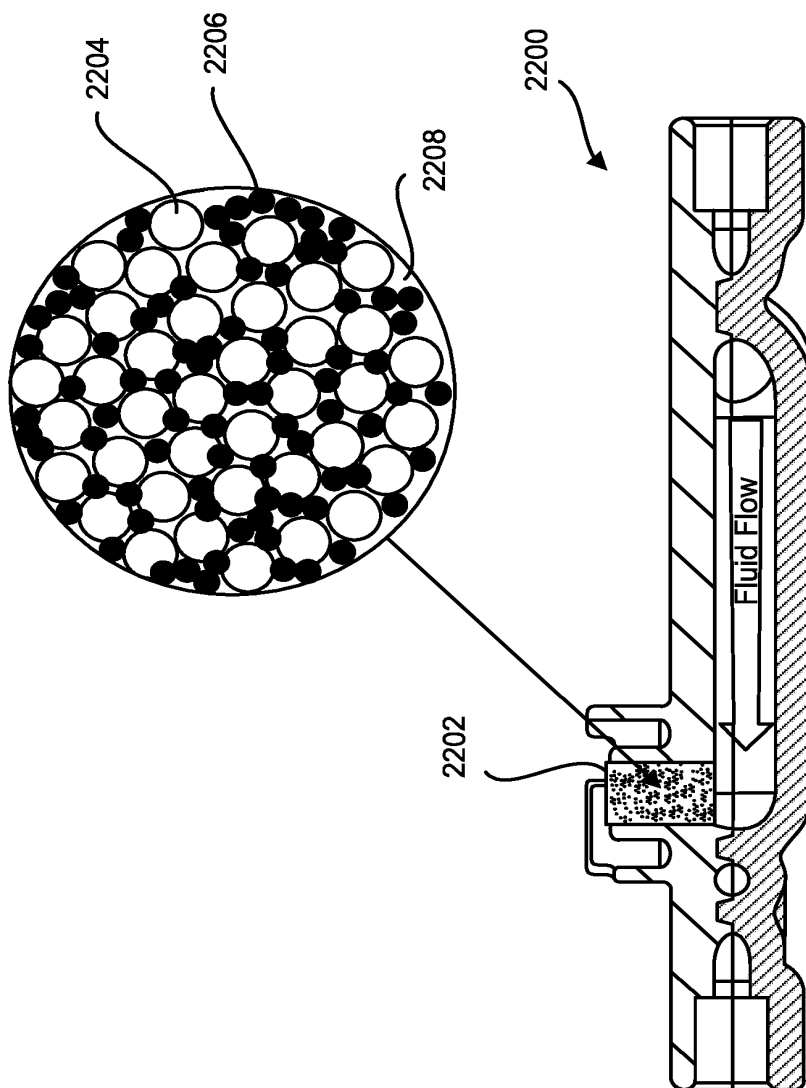


FIG. 22A

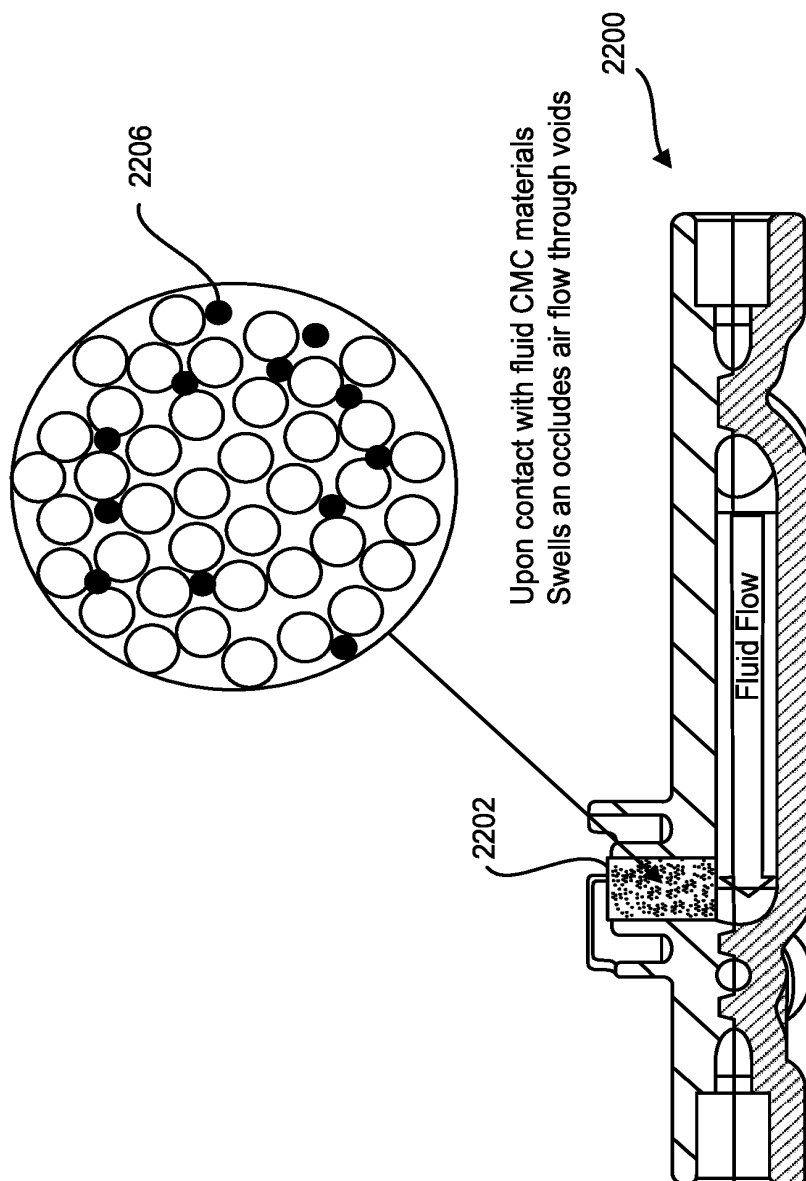


FIG. 22B

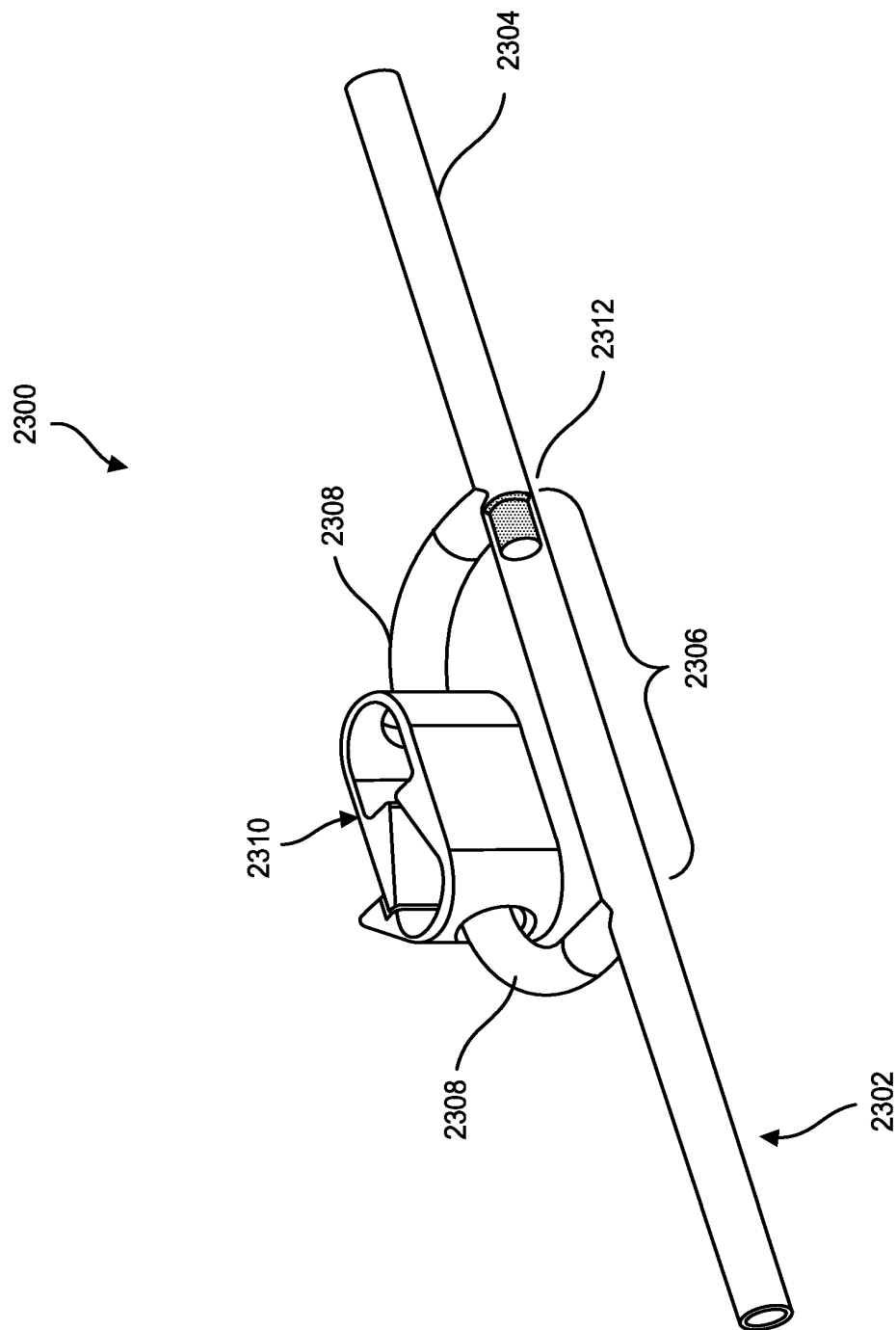


FIG. 23A

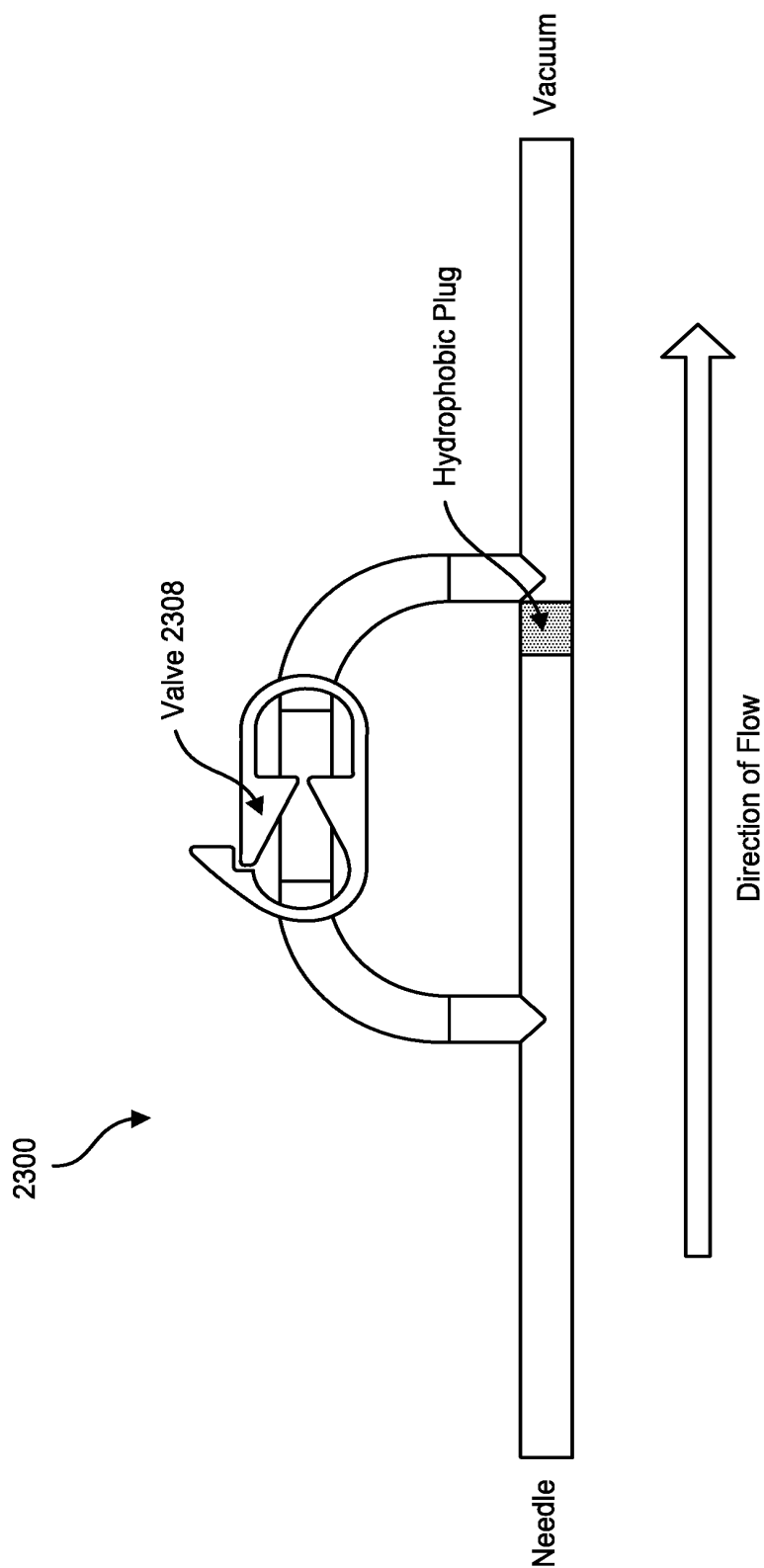
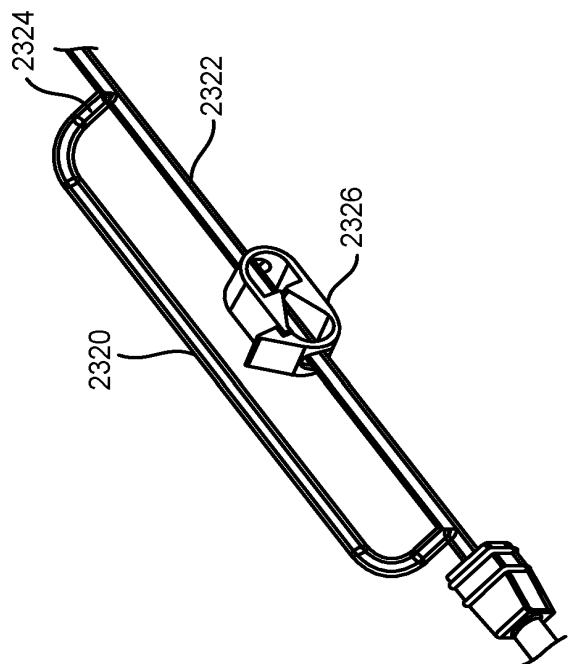
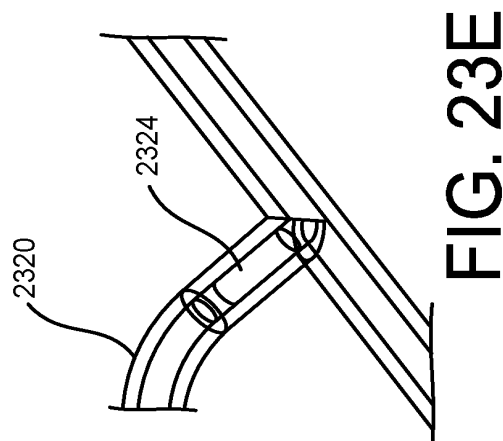
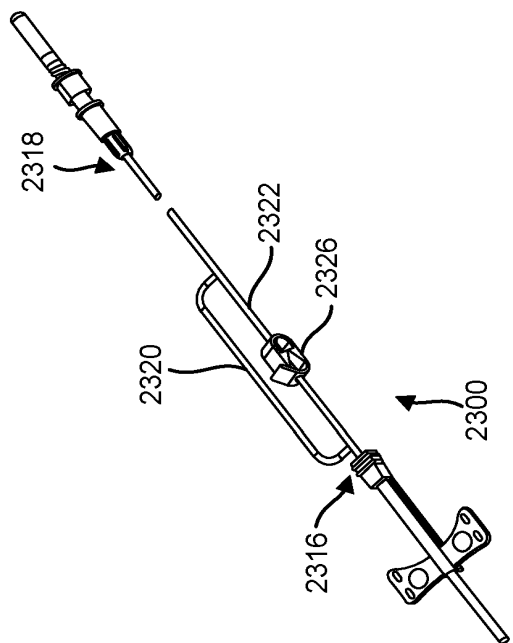


FIG. 23B



Replacement Sheet
52/69

Docket No. KURIN3PCT
PCT/US2017/068569

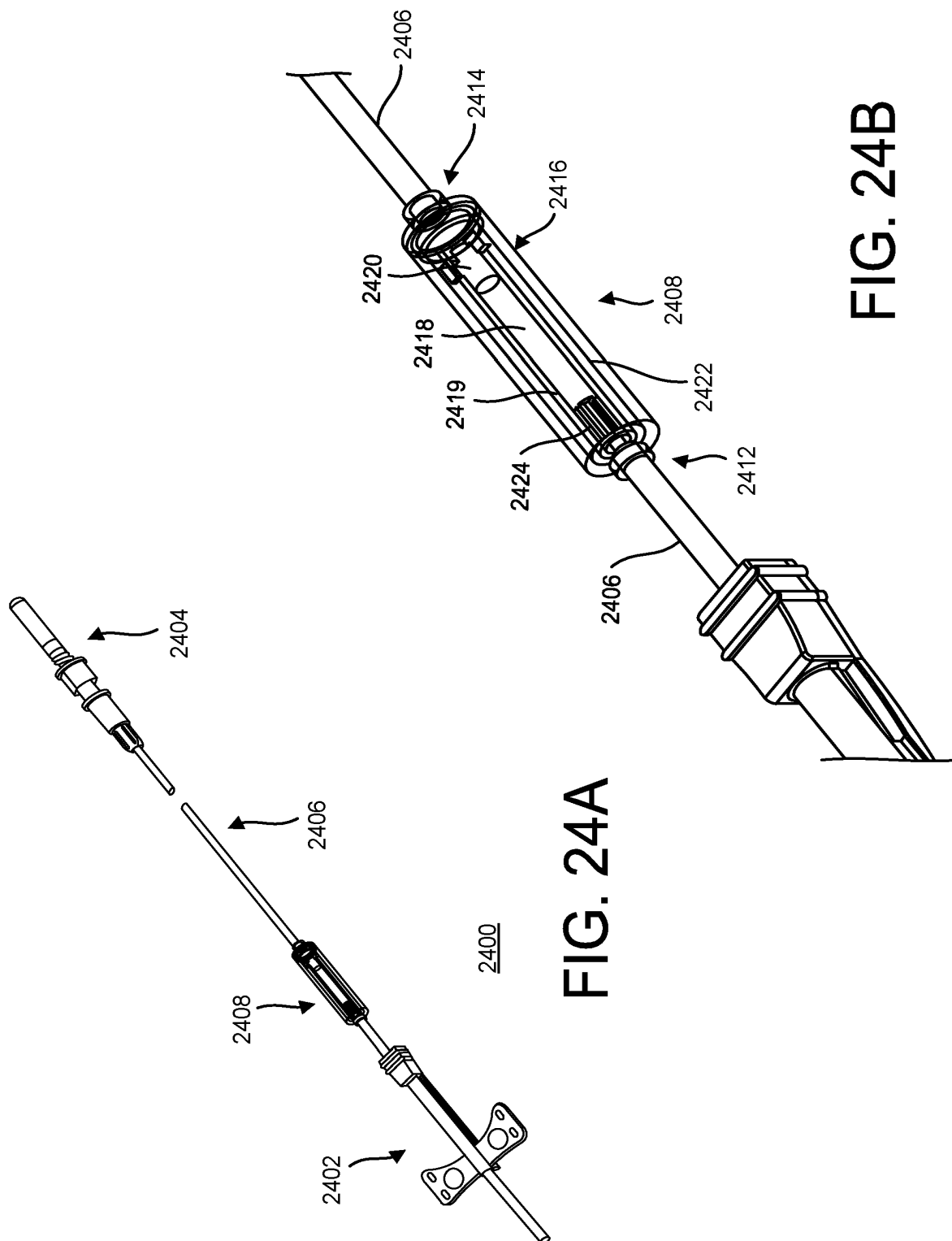


FIG. 24B

FIG. 24A

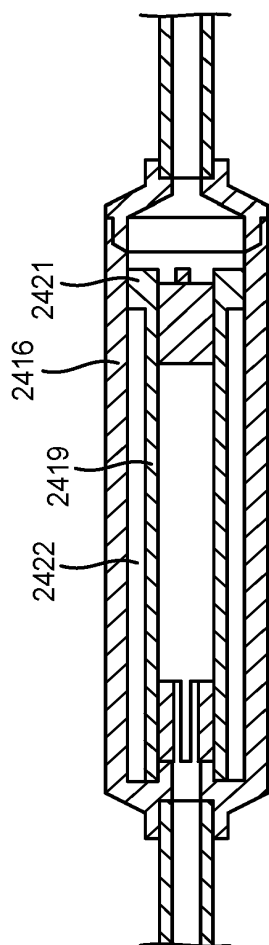


FIG. 24C

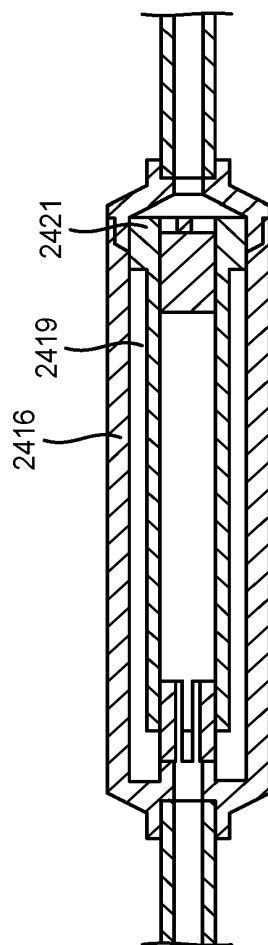


FIG. 24D

Replacement Sheet
54/69

Docket No. KURIN3PCT
PCT/US2017/068569

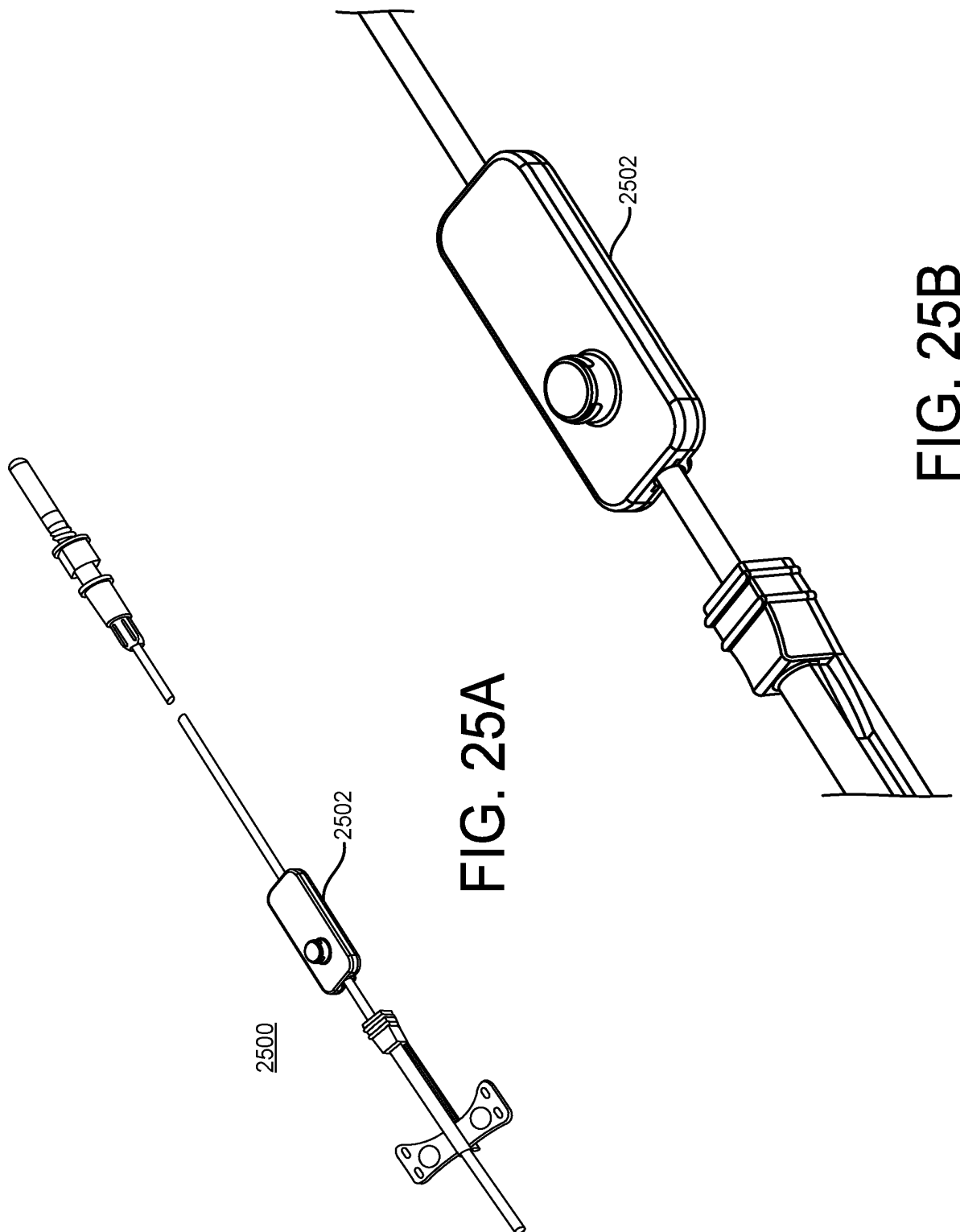


FIG. 25A

FIG. 25B

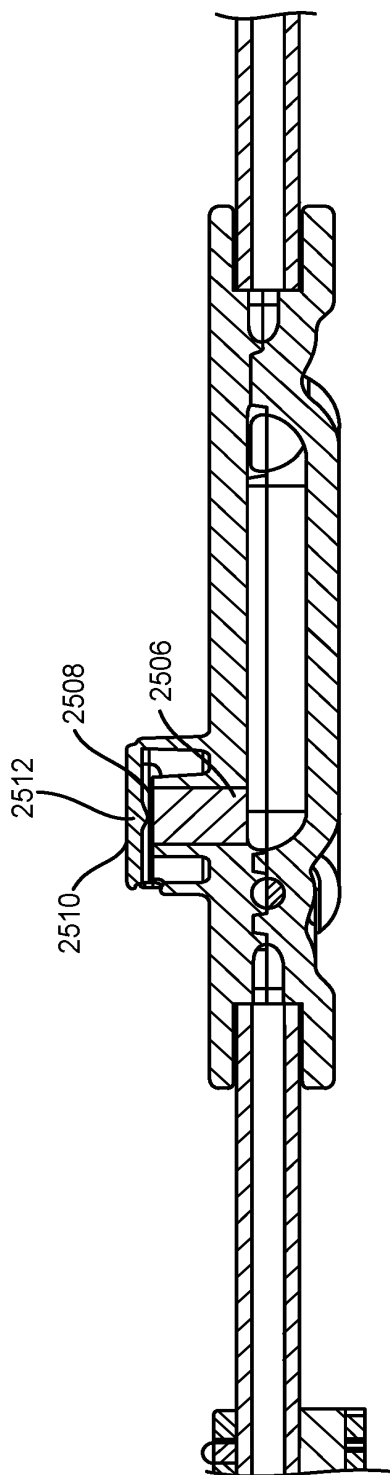


FIG. 25C

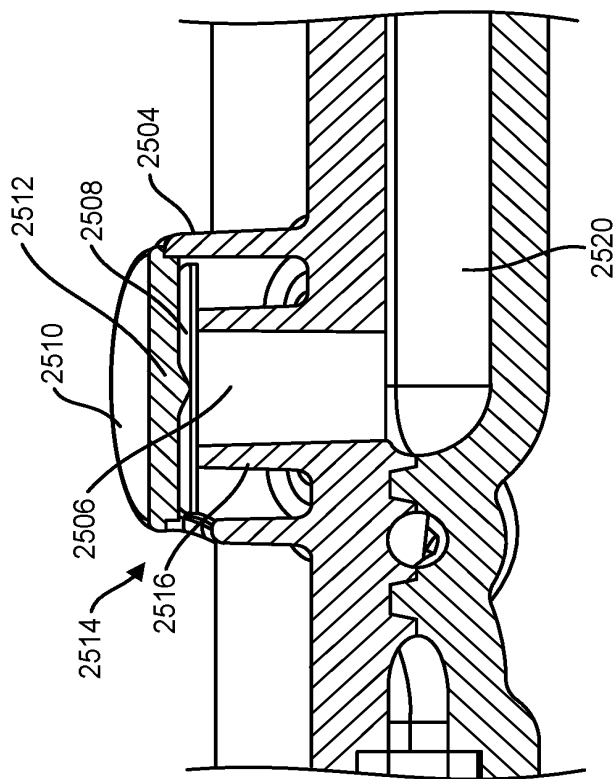


FIG. 25D

Replacement Sheet
56/69

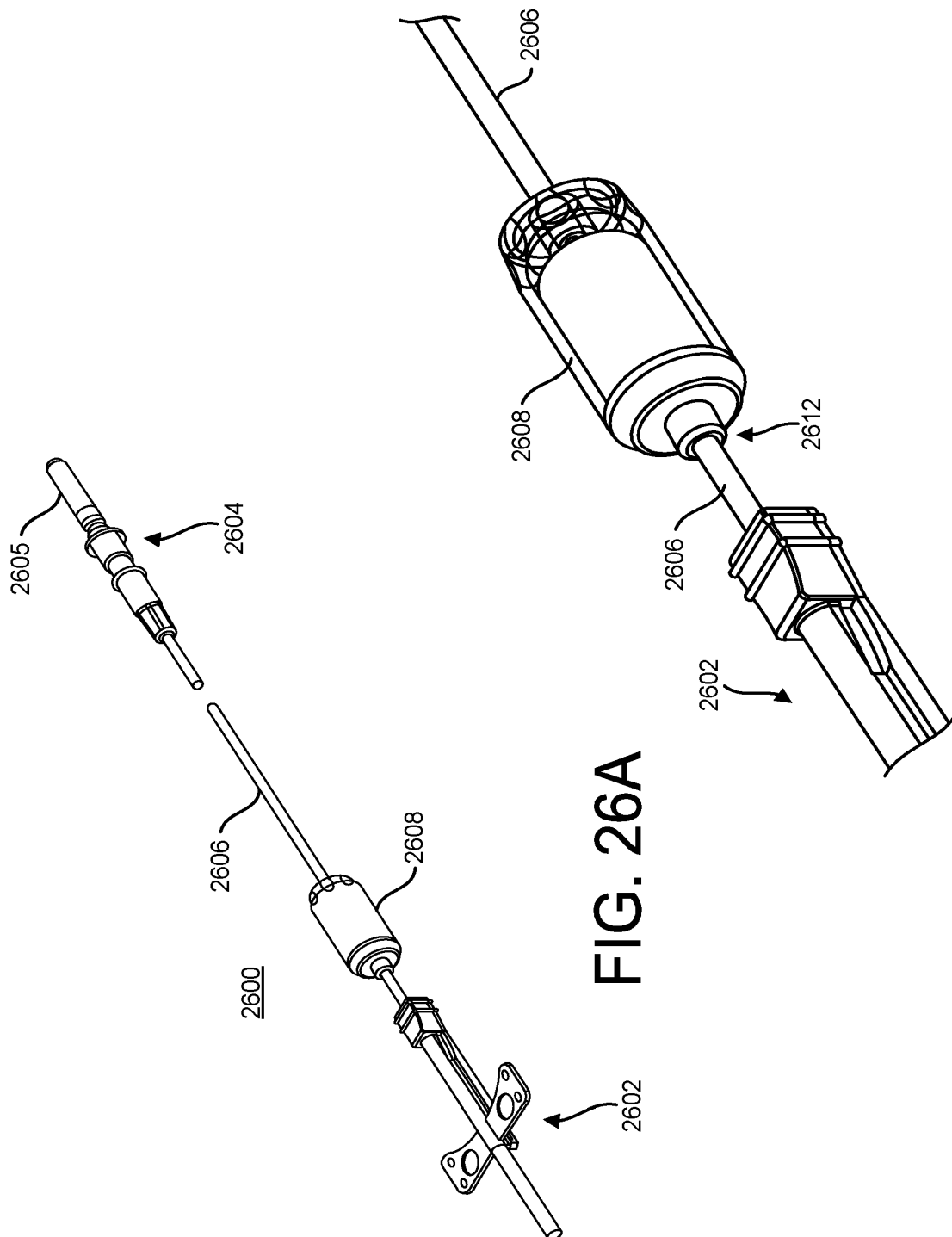


FIG. 26A

FIG. 26B

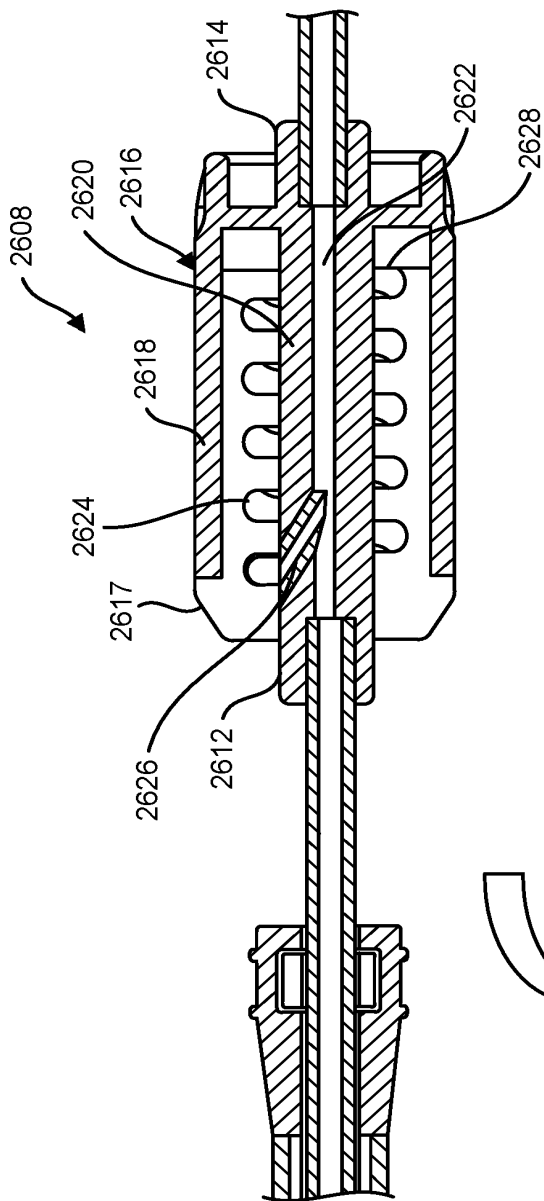


FIG. 26C

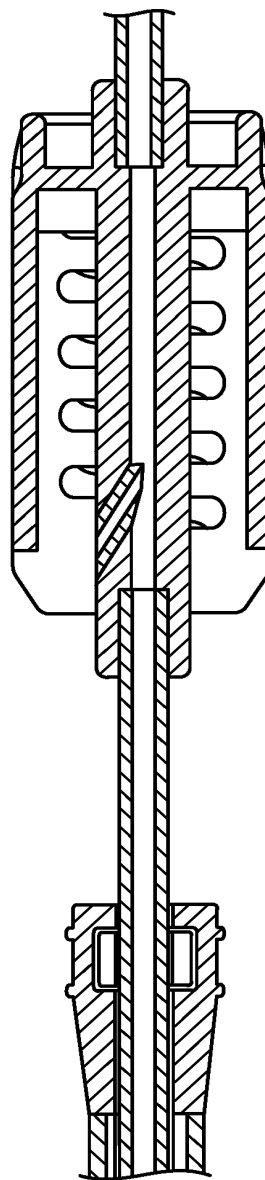


FIG. 26D

Replacement Sheet
58/69

Docket No. KURIN3PCT
PCT/US2017/068569

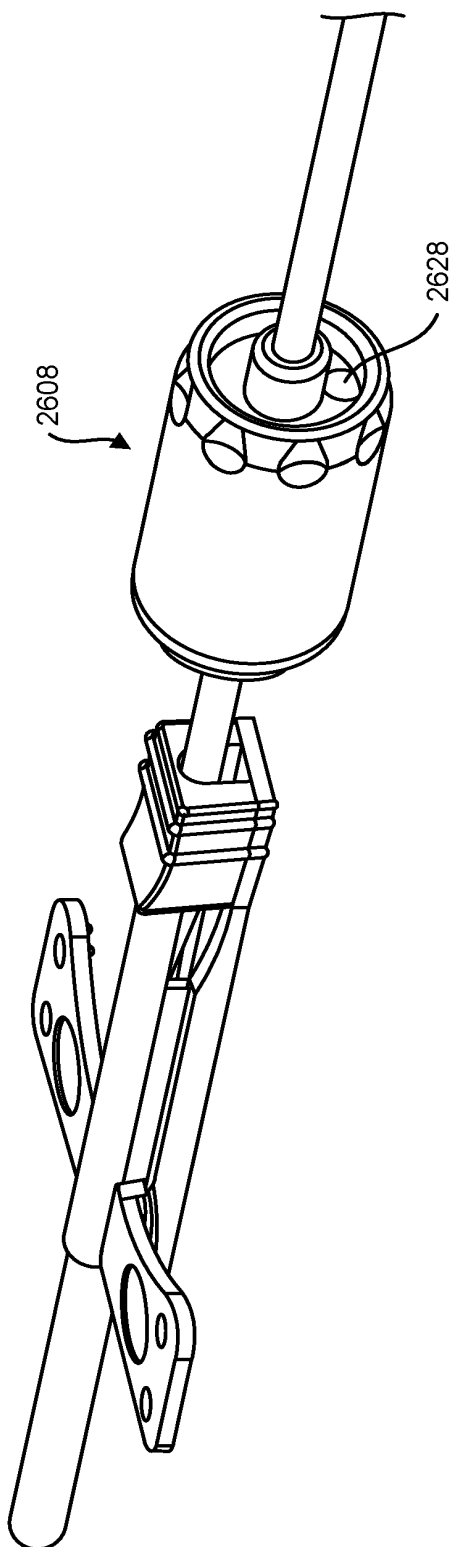
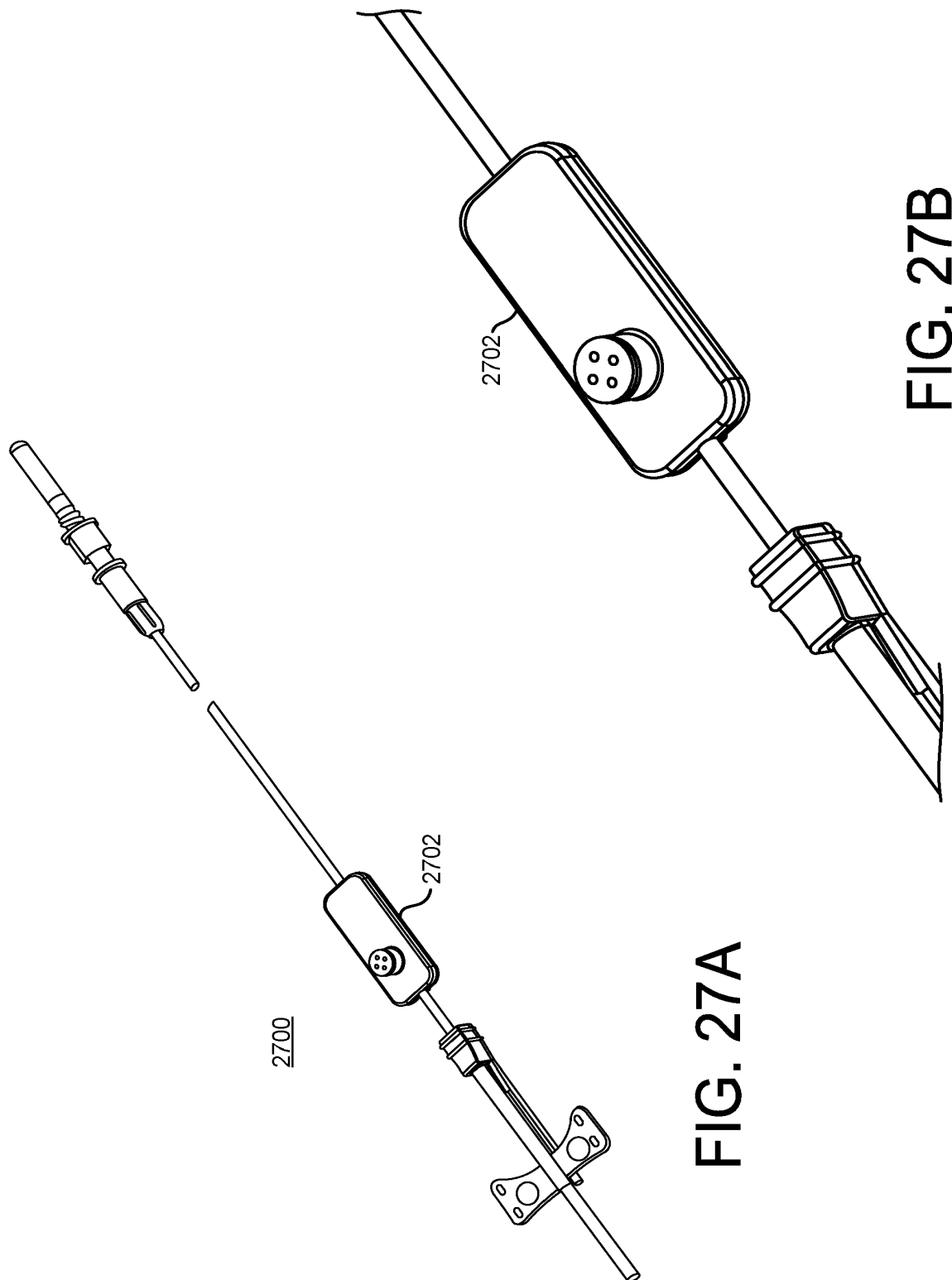


FIG. 26E



Replacement Sheet
60/69

Docket No. KURIN3PCT
PCT/US2017/068569

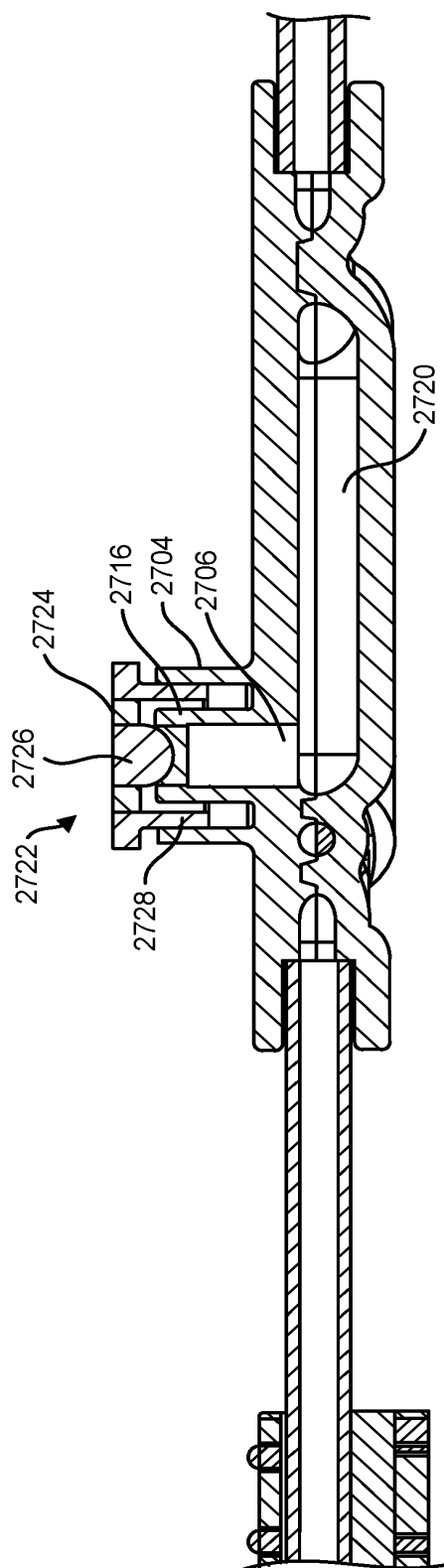


FIG. 27C

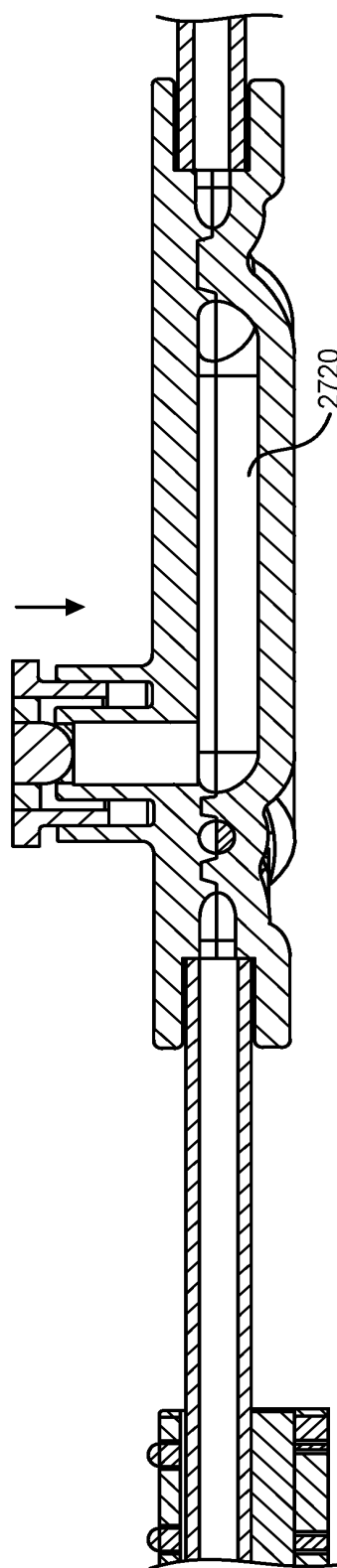
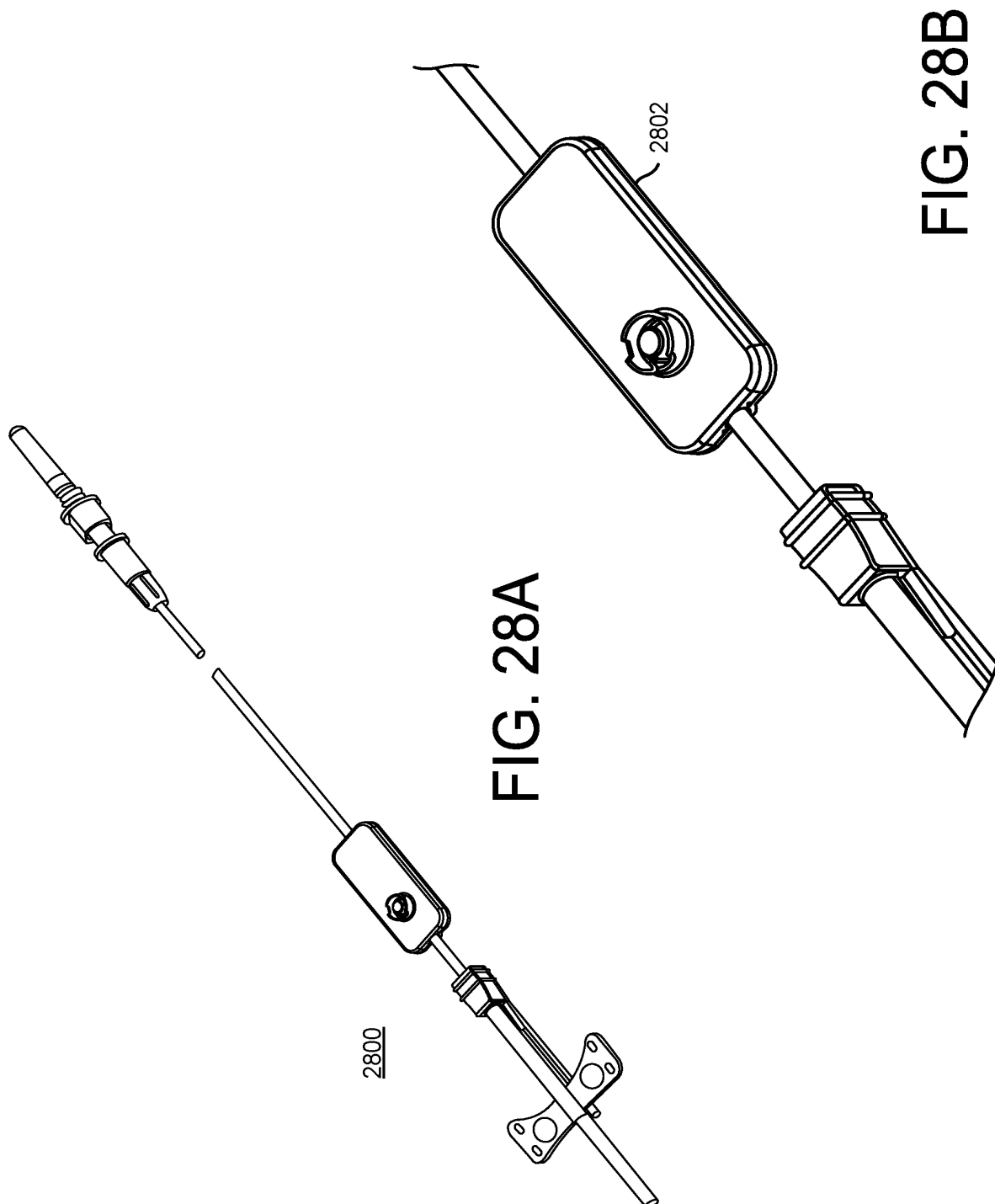


FIG. 27D



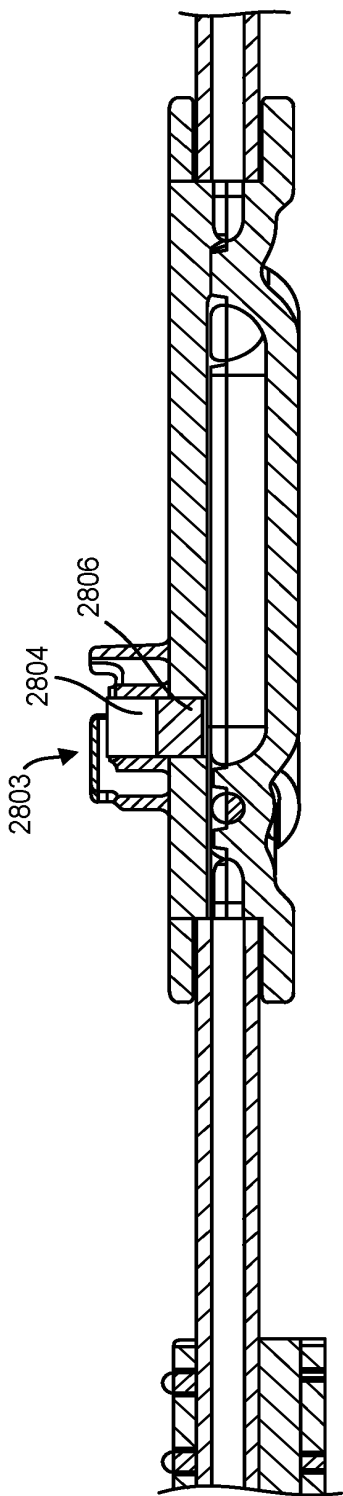


FIG. 28C

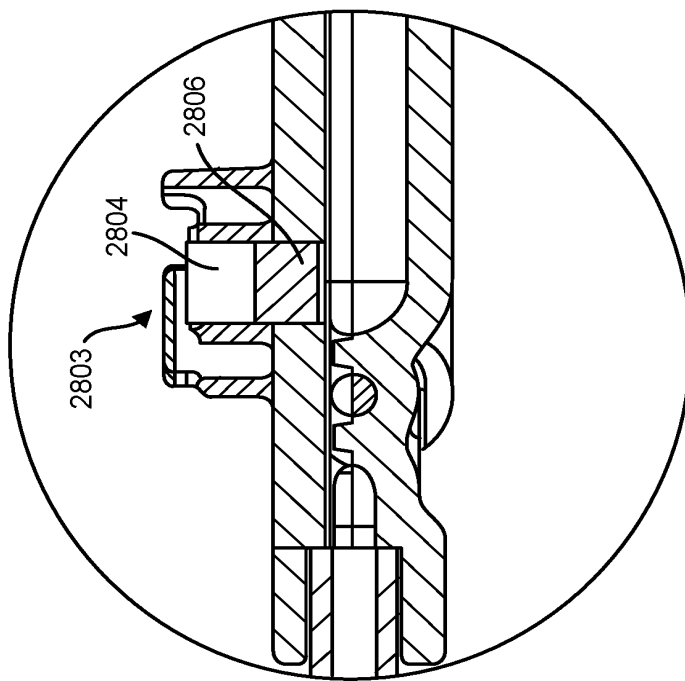


FIG. 28D

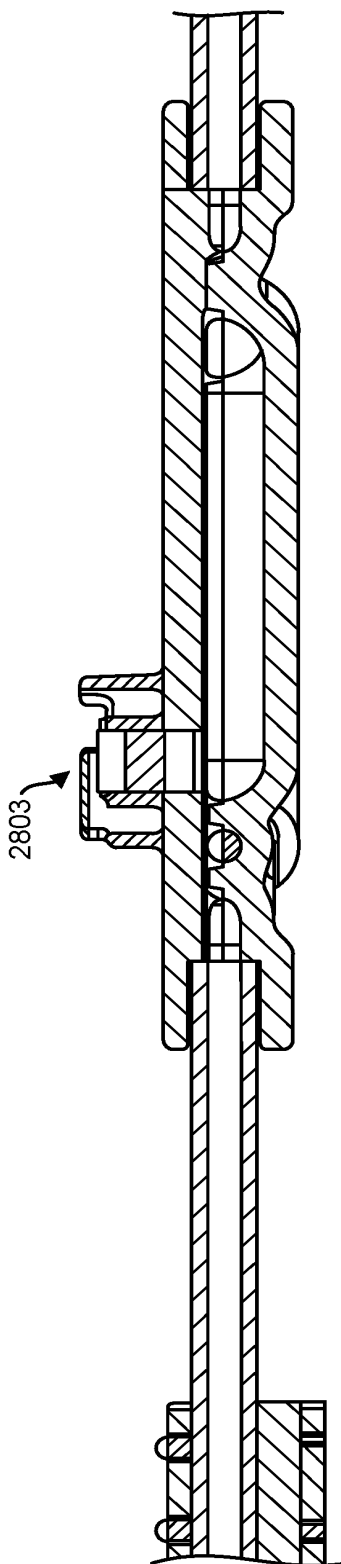


FIG. 28E

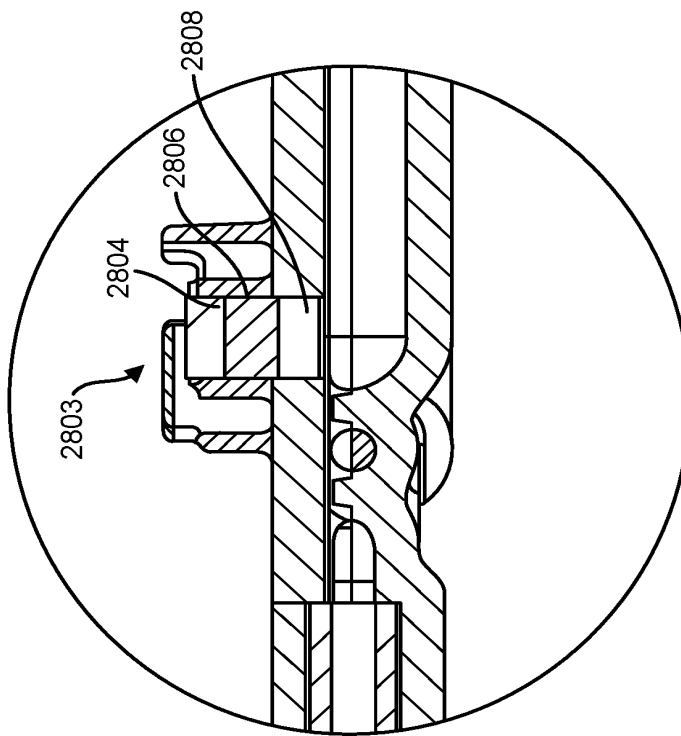
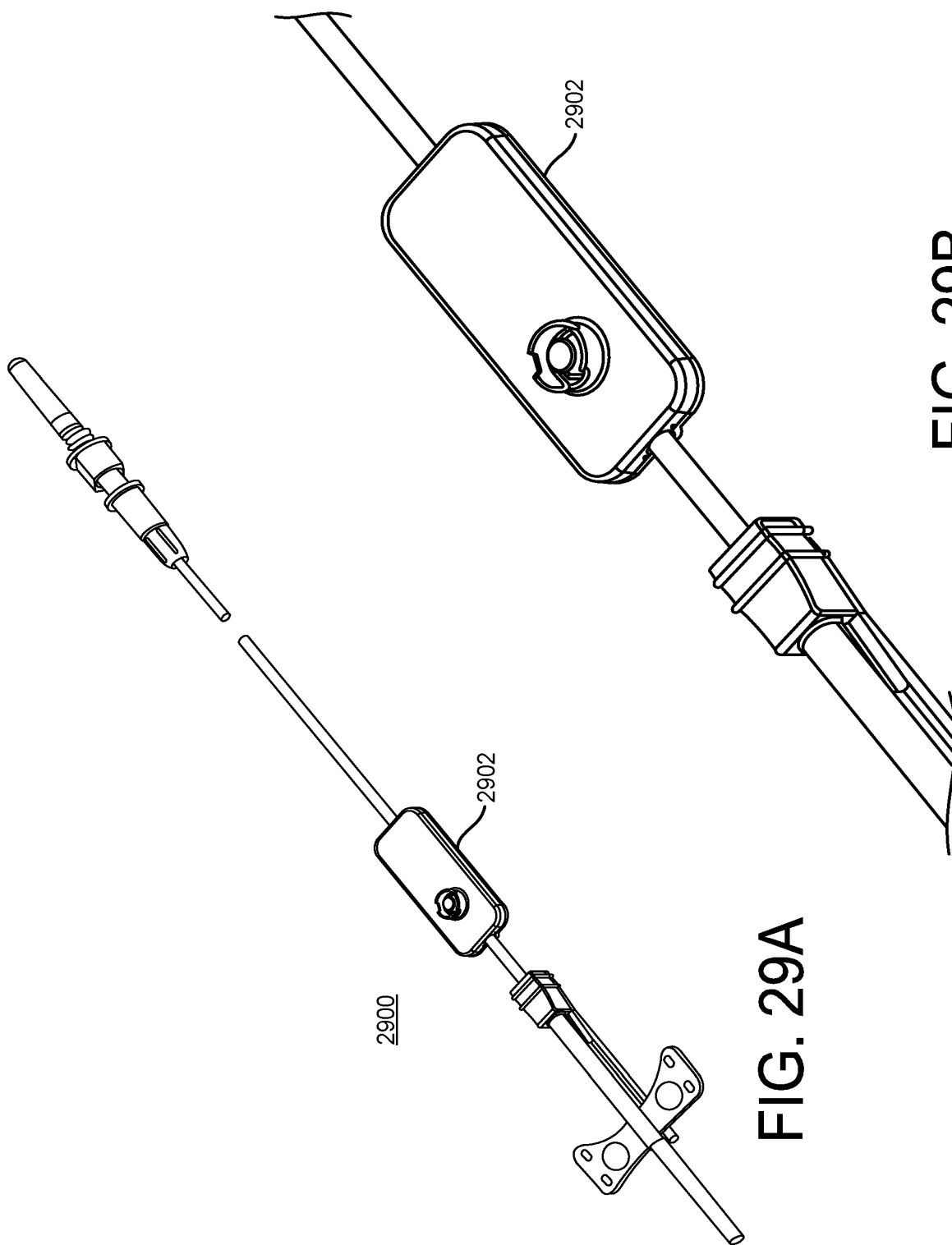


FIG. 28F

Replacement Sheet
64/69



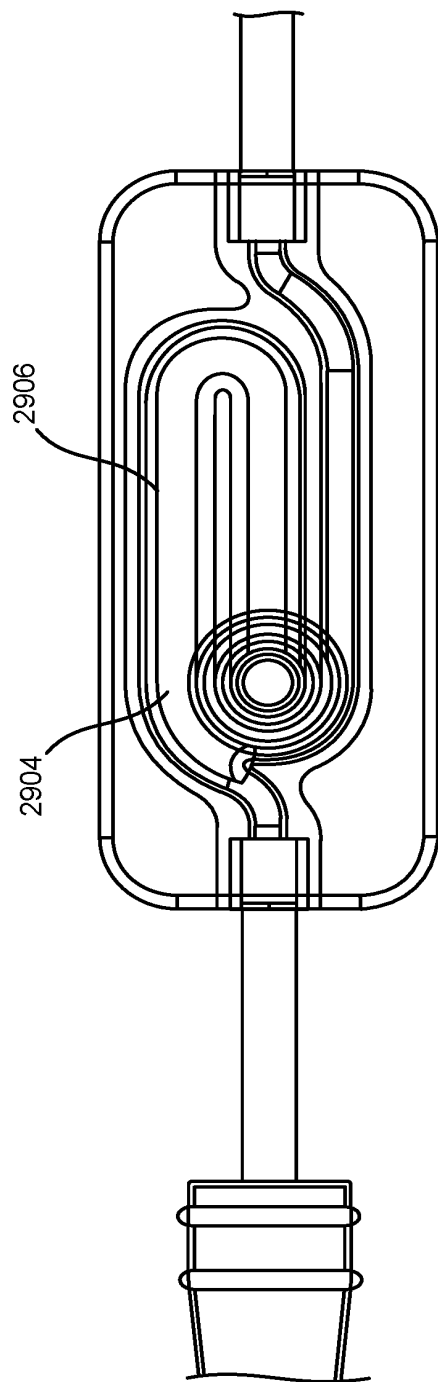


FIG. 29C

Replacement Sheet
66/69

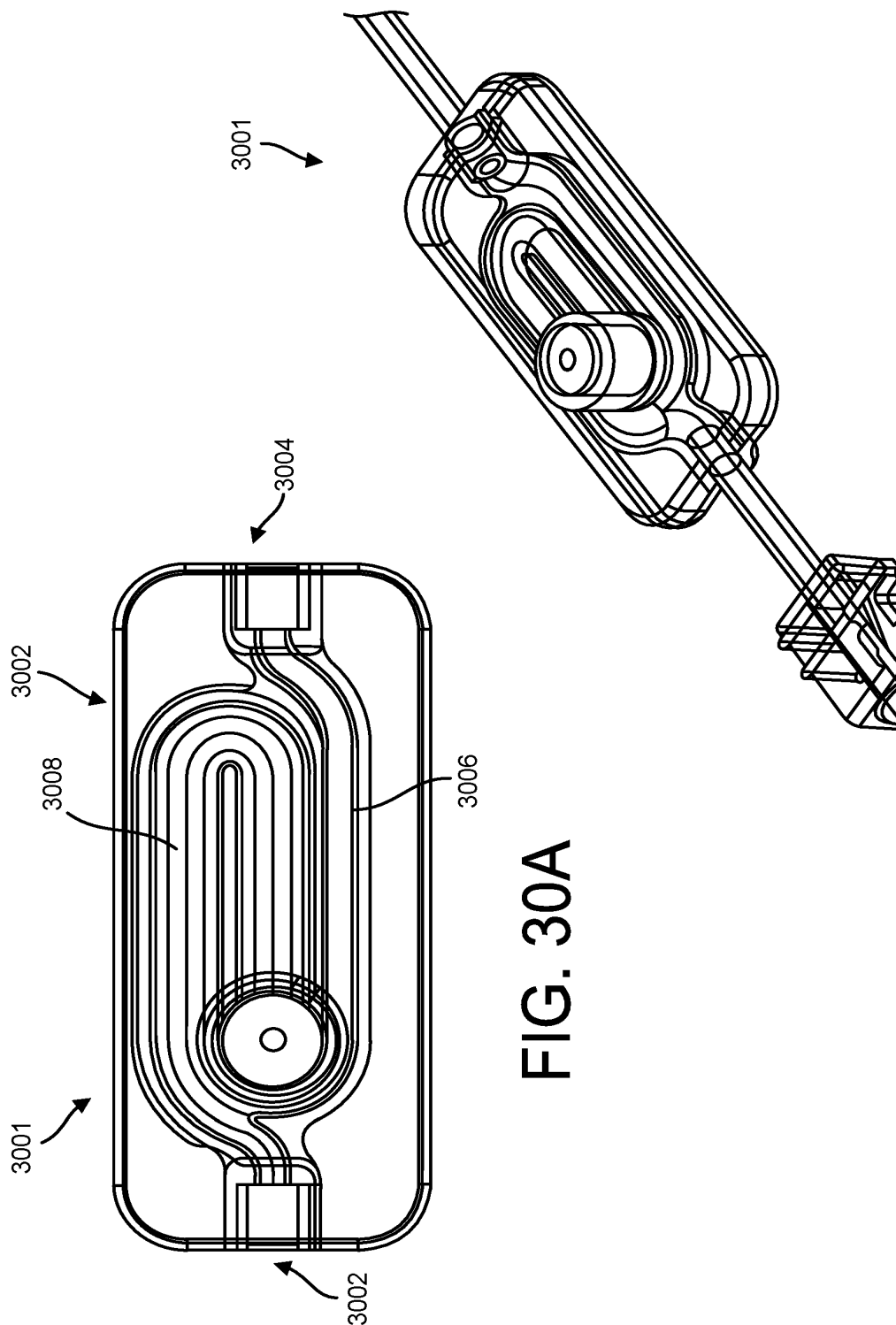


FIG. 30B

FIG. 30A

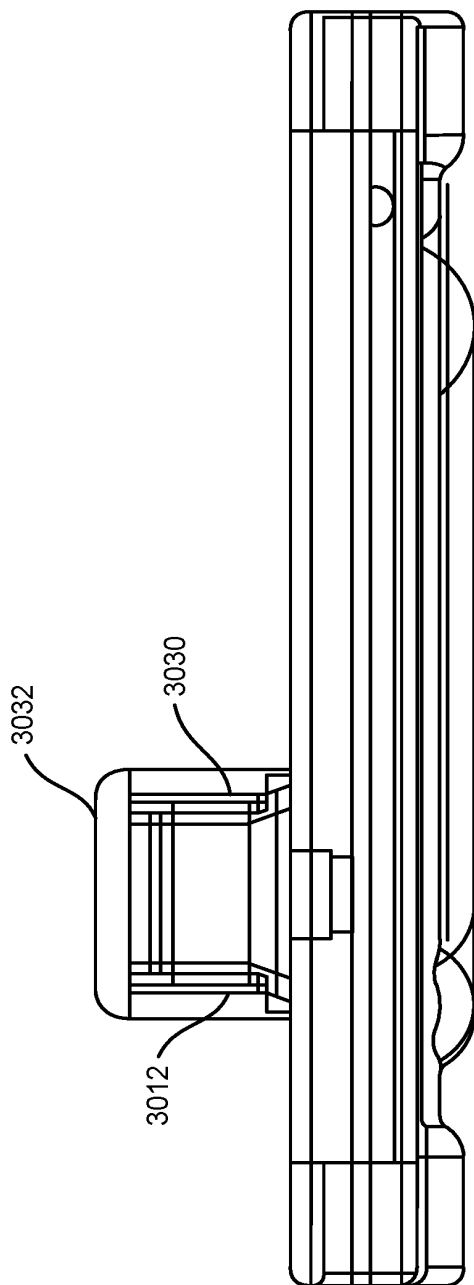


FIG. 30C

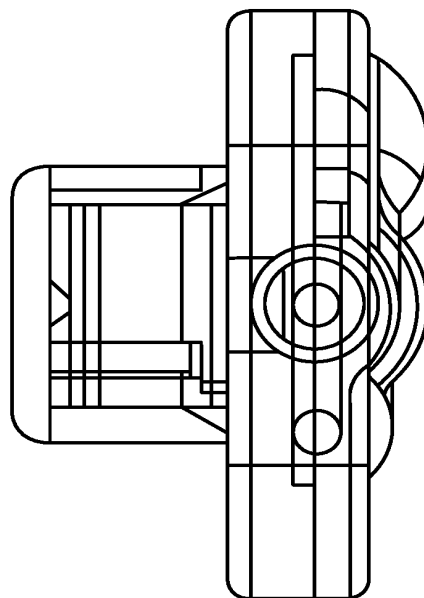
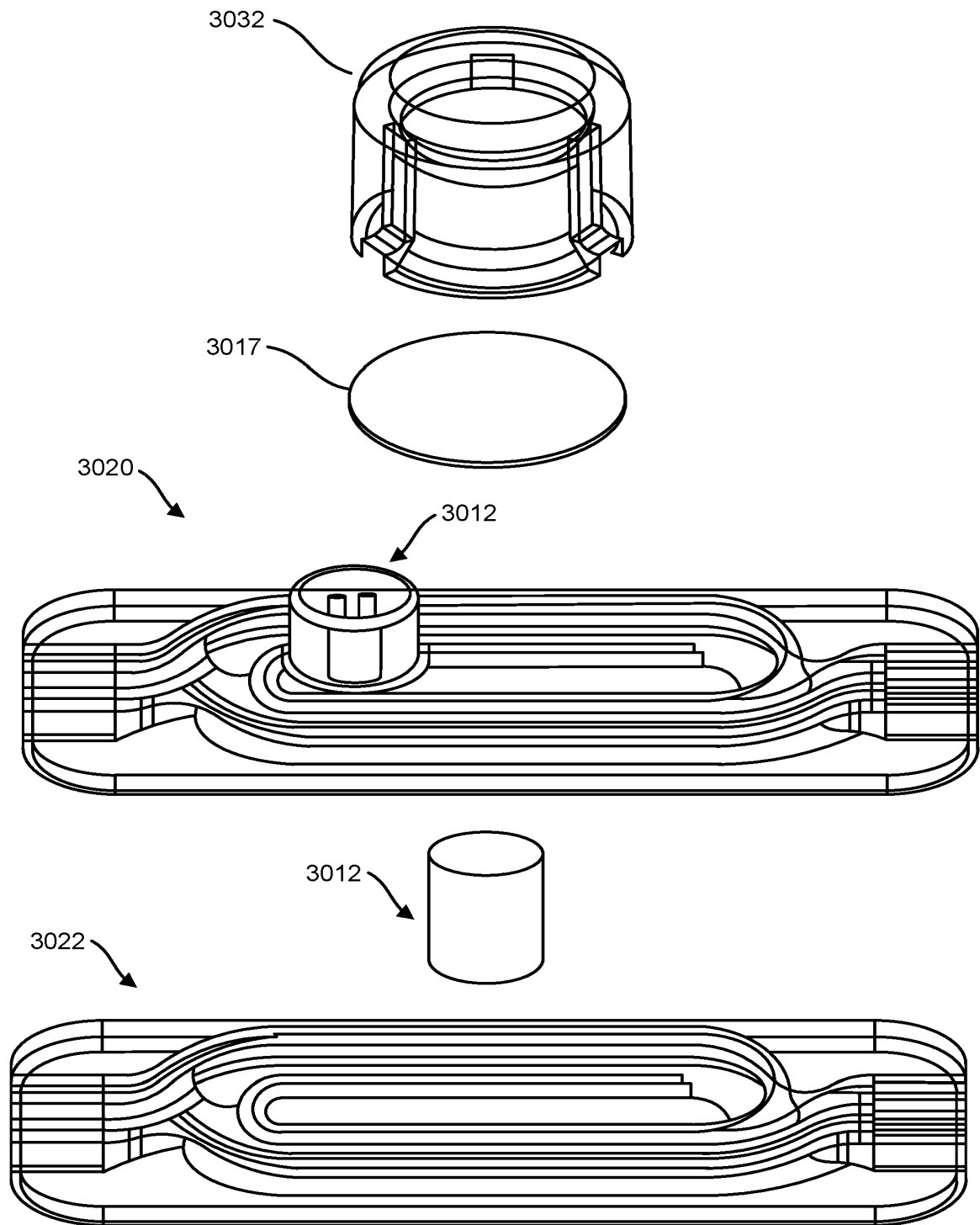


FIG. 30D

Replacement Sheet
68/69



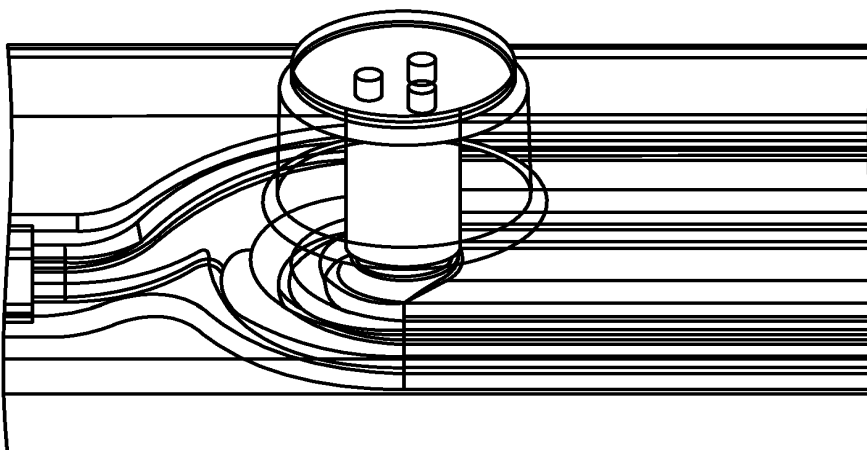


FIG. 30F

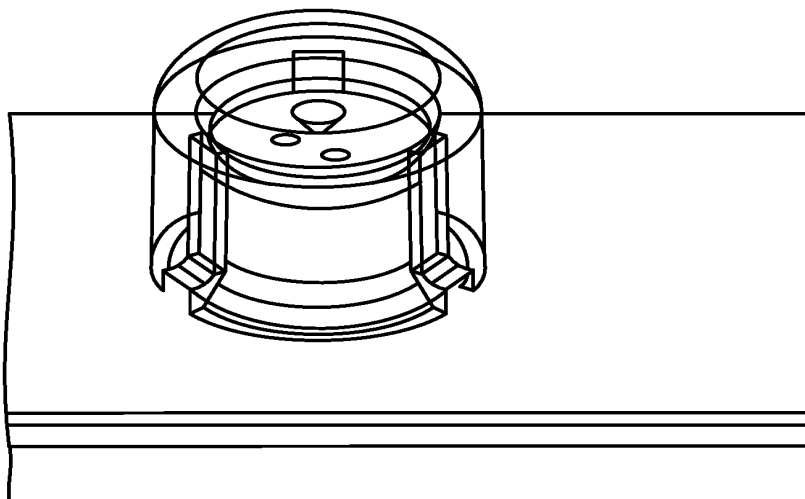


FIG. 30G

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

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

☒ See patent family annex.

* Special categories of cited documents :

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

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

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

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

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

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

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

29 March 2018

Date of mailing of the international search report

25/04/2018

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Nielsen, Michael

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	<p>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 -----</p>	1-20

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

 Literature display

< 1 / 1 display >

JP 2001-000424

 Document unit PDF progress information OPD search key URLs

Display format of the document display screen:

☒ text display ☐ PDF displayprimary literature | [Correction/correction](#) | [PAJ](#)

bibliography

close

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

(72) [Inventor]

[Name] Tsuguo Fujii

(72) [Inventor]

[Name] Suzuki Issei

[Theme code (reference)]

4C038

[F term (reference)]

4C038 TA06 UJ02 UJ06

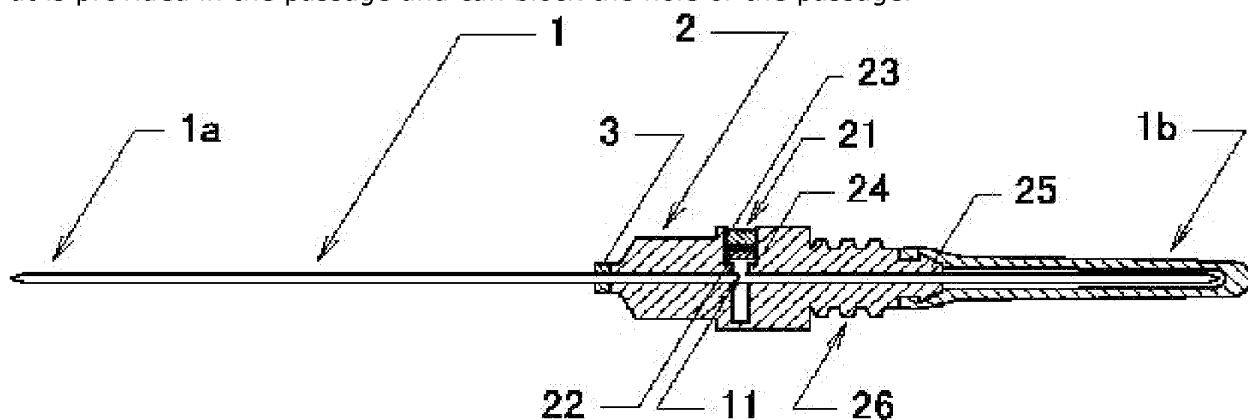
wrap up

close

(57) [Summary]

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

A needle tube (A) having a hole in at least a part of its side wall and having blade surfaces at both ends, and a passage provided so as to cover the hole and communicating between the outside and the inside of the needle tube through the hole. an air-permeable, blood-impermeable member (C) engaged with the open end of the passageway; and a needle tube support member (C) engaged with the needle tube support so as to seal one end of the needle tube. A blood collection needle having a rubber-like cap (D) that is closed and a sealing member (E) that is provided in the passage and can block the hole or the passage.



The scope of the claims

open

What is claimed is

: 1. A needle tube (A) having a hole in at least a part of its side wall and having blade surfaces at both ends; an air-permeable blood-impermeable member (C) secured to the open end of

the passageway, and one end of the needle tube so as to seal, a rubber-like cap (D) engaged with the needle tube support, and a sealing member (E) provided in the passage and capable of closing the hole or the passage.

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

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

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

detailed description

open

Description: BACKGROUND OF THE INVENTION

1.

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

2.

Description of the Related Art Conventionally, when collecting blood using a vacuum blood collection tube, there has been a blood collection needle that can confirm that the needle has definitely punctured the vein of a subject, that is, so-called flashback, before attaching the vacuum blood collection tube. is proposed. As such a conventional blood collection needle, for example, JP-A-61-64234 discloses a housing having a front end portion, a rear end portion, and a sample collection chamber provided with a passage for communicating with the outside air; A blood collection needle is disclosed having a cannula extending from the rear end and a tablet that expands upon contact with blood and blocks communication with the atmosphere. However, with this blood collection needle, when a vacuum blood collection tube is attached, negative pressure is applied to the tablet, and outside air may flow into the blood collection needle. [0003] Further, Japanese Patent Application Laid-Open No. 4-132541 discloses an elastic tip having a ventilation hole for communication between the inner cavity and the outside atmosphere, and an air-permeable filter provided at the outer opening of the ventilation hole. Also disclosed are blood collection needles with translucent hubs or elastic tips that allow flashback to

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

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

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

[0006] That is, the present invention provides a needle tube (A) having a hole in at least a part of its side wall and blade surfaces at both ends, a needle tube (A) provided so as to cover the hole, and communicating the outside and the inside of the needle tube through the hole. an air-permeable blood-impermeable member (C) secured to the open end of the passageway; and one end of the needle tube is sealed so as to seal the needle tube. A blood collection needle having a rubber-like cap (D) engaged with a support and a sealing member (E) provided in the passage and capable of closing the hole or the passage. BEST MODE FOR CARRYING OUT THE INVENTION Next, the present invention will be described in detail with reference to the drawings

FIG. 1 is a sectional view showing one embodiment of the blood collection needle of the present invention. The needle tube 1 is preferably made of stainless steel. One end 1a is a blade surface and is formed so as to pierce the blood vessel of the subject, and the other end 1b is also a blade surface and is formed so as to be inserted into a vacuum blood collection tube (not shown).

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

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

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

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

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

As shown in FIG. 2, when one end 1a of the needle tube 1 is punctured into the subject, the blood that has flowed from the inside of the needle tube 1 through the hole 11 into the passage 21 flows through the sealing member 22 and the needle tube support. It passes through the gap with the body 2 and is blocked by the air permeable blood impermeable member 23. After that, when the vacuum blood collection tube is attached to the other end 1b of the needle tube 1, the negative pressure of the vacuum blood collection tube pulls the sealing member 22 toward the needle tube 1 and closes the passage 21, as shown in FIG. As a result, negative pressure is not directly applied to the air-permeable blood-impermeable member 23, so that a predetermined amount of blood can be collected. Further, considering the sealing performance inside the needle tube 1, it is more preferable that the passage 21 is provided with a protrusion 24 for locking the sealing member 22 therein. As for the shape of the projection 24, in addition to the L-shaped cross section shown in FIG. etc.

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

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

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

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

Brief description of the drawing

open

BRIEF DESCRIPTION OF THE DRAWINGS

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

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

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

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

[Description of Symbols]

1 Needle tube

11 Hole

2 Needle tube support

21 Passage

22 Sealing member

23 Air-permeable blood-impermeable member

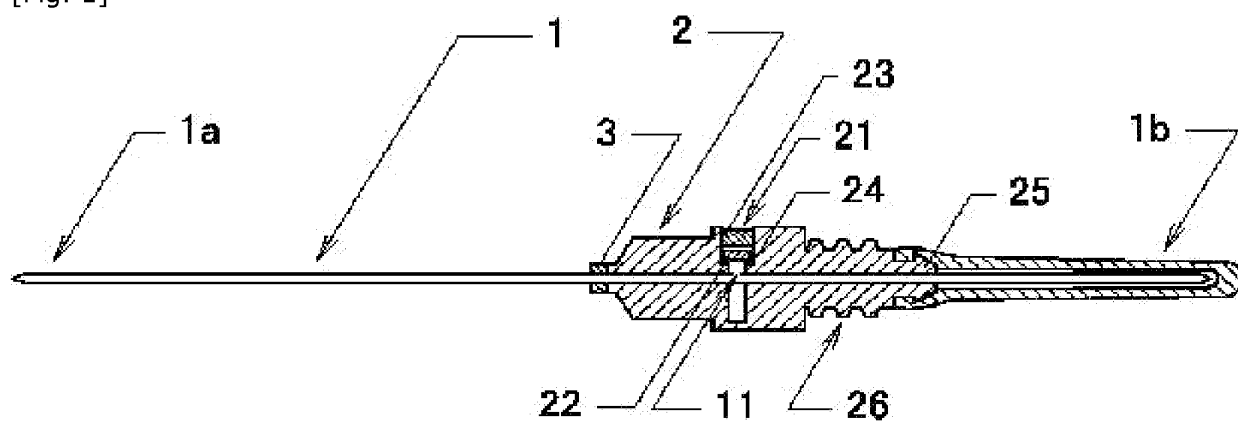
24 Convex portion

4 Rubber-like cap

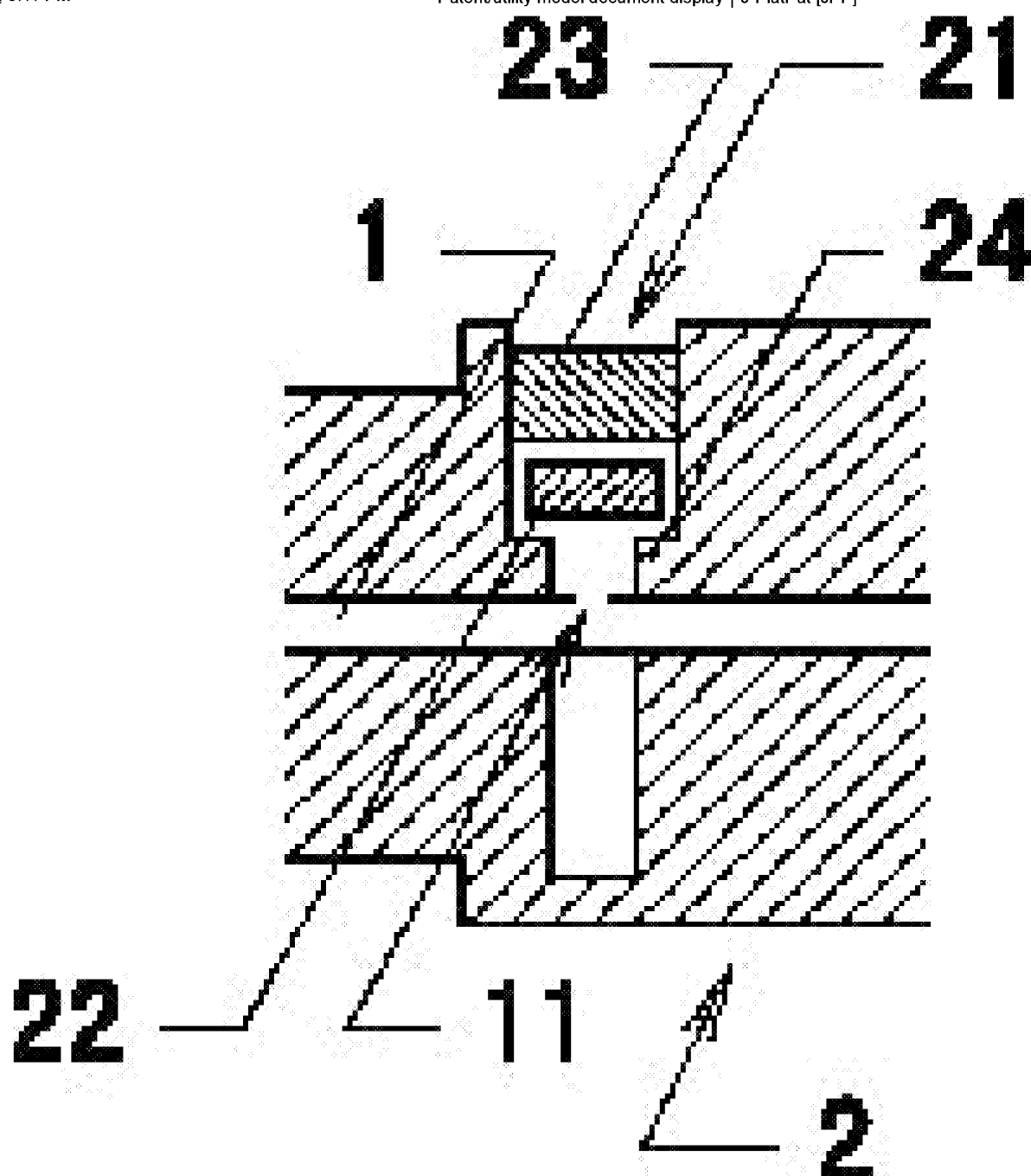
drawing

open

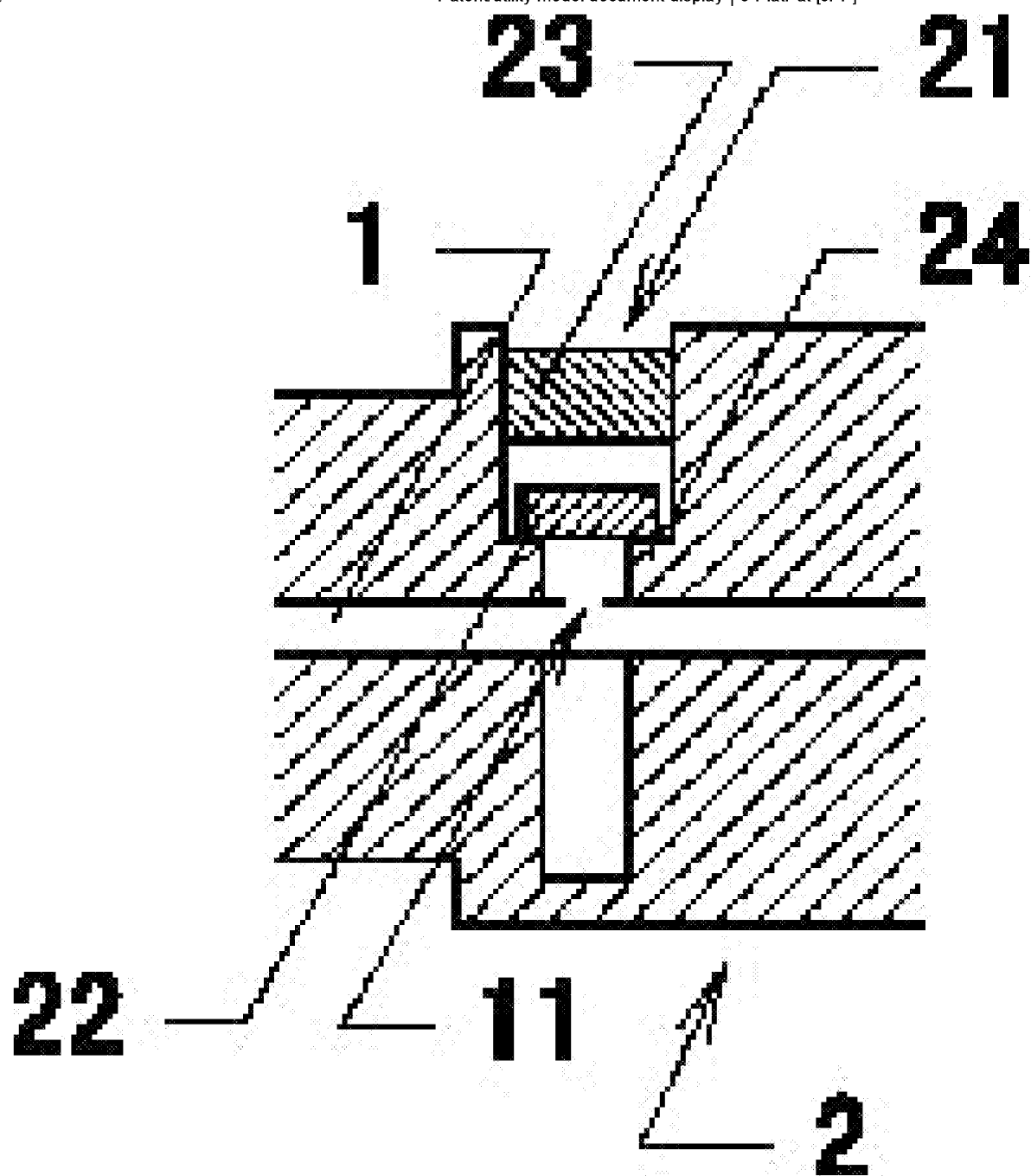
[Fig. 1]



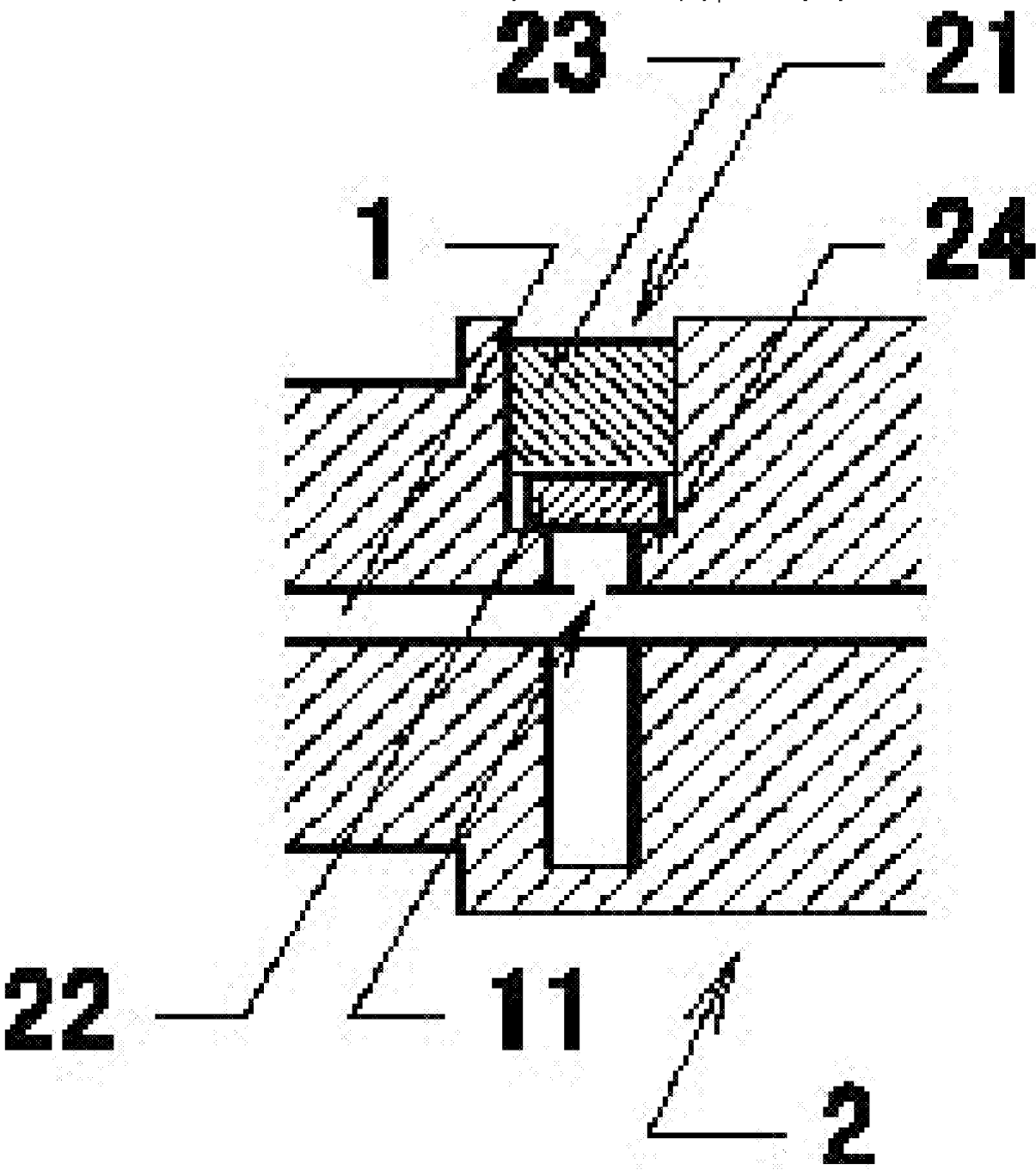
[Figure 2]



[Figure 3]



[Figure 4]

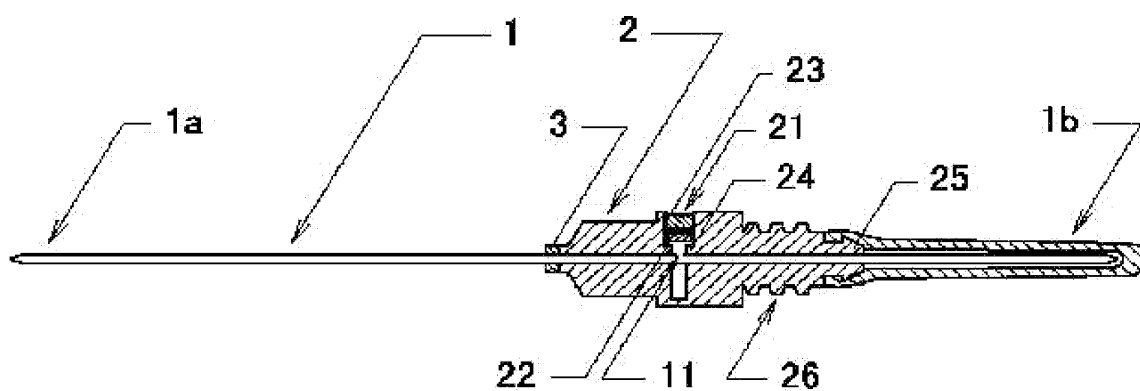


drawing

open

Representative drawing | 1 | 2 | 3 | Four

Magnify and Rotate



Representative drawing

(19) 日本国特許庁 (J P)

(12) 公 開 特 許 公 報 (A)

(11) 特許出願公開番号

特開2001-424

(P2001-424A)

(43) 公開日 平成13年1月9日(2001.1.9)

(51) Int.Cl.⁷

識別記号

F I

デマコト⁺(参考)

A 6 1 B 5/15

A 6 1 B 5/14

3 0 0 H 4 C 0 3 8

審査請求 未請求 請求項の数4 O L (全 3 頁)

(21) 出願番号 特願平11-174400

(22) 出願日 平成11年6月21日(1999.6.21)

(71) 出願人 000135036

株式会社ニッショー

大阪府大阪市北区本庄西3丁目9番3号

(72) 発明者 藤井 嗣雄

大阪市北区本庄西3丁目9番3号 株式会社ニッショー内

(72) 発明者 鈴木 一肇

神奈川県大和市深見3211-17

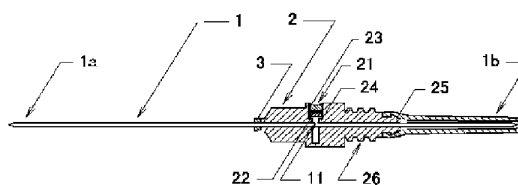
Fターム(参考) 4C038 TA06 UJ02 UJ06

(54) 【発明の名称】 採血針

(57) 【要約】

【課題】 採血時に針が確実に被検者の静脈に穿刺されたことを穿刺後、直ちに確認できる採血針を提供する。

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



【特許請求の範囲】

【請求項1】 側壁の少なくとも一部に孔を有し、両端が刃面である針管(A)、該孔を覆うように設けられ、該孔を通じて外部と針管の内部とを連通した通路を備えた針管支持体(B)、該通路の外部への開放端に係止された空気透過性血液不透過性部材(C)、針管の一方の端を密封するように、前記針管支持体に係止されてなるゴム状キャップ(D)、および前記通路内に設けられ、前記孔あるいは通路を塞ぎ得る封止部材(E)とを有する採血針。

【請求項2】 通路が封止部材に係止する凸部を有する請求項1記載の採血針。

【請求項3】 空気透過性血液不透過性部材が膨潤物質である請求項1、または2記載の採血針。

【請求項4】 針管支持体が透明または半透明である請求項1、2、または3記載の採血針。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】本発明は採血針に関し、さらに詳細にはその一端が被検者の血管に穿刺し、他端を真空採血管内に連通させて、真空採血管内の負圧に応じた量の血液を採取できるようにした採血針に関する。本発明の採血針によれば、他端を真空採血管に連通させる前に一端が被検者の静脈に穿刺されたことを確認できる。

【0002】

【従来の技術】従来から真空採血管による採血に際して、真空採血管を取り付ける前に、針が確実に被検者の静脈に穿刺されたこと、いわゆるフラッシュバックを確認できるような採血針が提案されている。このような従来の採血針としては、例えば、特開昭61-64234号公報には、前端部と後端部および外気と流通する通路を備えた試料収集室を有するハウジングと、その前端部および後端部から延設されたカニューレと、血液と接触して膨張し、外気との流通を遮断するタブレットを備えた採血針が開示されている。しかし、この採血針は、真空採血管を取り付けた時、タブレットに陰圧がかかるため、採血針内部に外気が流入するおそれがあり、既定の採血量が得られないことがある。

【0003】また、特開平4-132541号公報には、弾性チップ内腔部と外部雰囲気とを連通させる通気孔を有し、該通気孔の外部口部に通気性フィルタを備えており、透明ないし半透明のハブまたは弾性チップによりフラッシュバックを確認できる採血針が開示されている。しかしながら、この採血針の弾性チップは、採血針ホルダー内部に収納され、しかも、その上から手で保持されるため、弾性チップによるフラッシュバックの確認は非常に困難である。また、一端が被検者の静脈に穿刺したときに静脈圧により針管内部に侵入した血液は、弾性チップ内腔部に充満したあと、通気孔に侵入する構造を有しているため、ハブによりフラッシュバックを確認

するまでに時間を要する。

【0004】

【発明が解決しようとする課題】本発明は上記事情に鑑みてなされたもので、真空採血管取り付け時、フィルタ部(以下、空気透過性血液不透過性部材と呼ぶ)に陰圧がかからず、採血針の一端が静脈に穿刺された後、直ちにフラッシュバックを確認できる採血針を提供することを目的とする。

【0005】

【課題を解決するための手段】本発明者らは種々鋭意検討の結果、針管の側壁に孔を設け、その孔を通じて外部と針管内部とを連通させるような通路を設け、さらに真空採血管取り付け時に、針管内部を外部から遮断するような機構を設けた採血針が、上記課題を解決するものであることを見出し、本発明に到達した。

【0006】すなわち本発明は、側壁の少なくとも一部に孔を有し、両端が刃面である針管(A)、該孔を覆うように設けられ、該孔を通じて外部と針管の内部とを連通した通路を備えた針管支持体(B)、該通路の外部への開放端に係止された空気透過性血液不透過性部材(C)、針管の一方の端を密封するように、前記針管支持体に係止されてなるゴム状キャップ(D)、および前記通路内に設けられ、前記孔あるいは通路を塞ぎ得る封止部材(E)とを有する採血針である。

【0007】

【発明の実施の形態】次に本発明を図面に基づいて詳細に説明する。図1は本発明の採血針の一実施例を示す断面図である。針管1はステンレス製であるのが好ましい。その一端1aは刃面であり被検者の血管を刺すように形成されており、他端1bも刃面であり、真空採血管(図示せず)に差し込むように形成される。

【0008】前記針管1の側壁には孔11が設けられている。該孔11は針管支持体2内であれば、針管1のどの部分に設けられていてもよい。該針管1には前記孔11を覆うように、透明または半透明の針管支持体2が設けられる。該針管支持体2は針管1の一端1a側で、針管1と例えば接着剤3により密封的に固着されている。

【0009】この針管支持体2内には、前記孔11を通じて外部と針管1の内部とを連通した通路21が形成されている。該通路21は、外部と連通していれば、その外部への開放端はどこに設けられていてもよい。前記通路21により、針管1の一端1aの刃面が被検者の静脈に穿刺したとき、針管1内部に侵入した血液は、孔11を通して前記通路21に侵入し、侵入した血液を針管支持体2の側面から目視することで、フラッシュバックを確認することができる。

【0010】前記通路21内には、封止部材22が設けられている。該封止部材22としては、ポリプロピレン、テフロン(登録商標)およびシリコンゴムなどのプラスチック材料を使用することができるが、ステンレス

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

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

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

【0013】また、空気透過性血液不透過性部材23としては、アクリル酸系共重合体、スターチおよびゼラチンなどの膨潤物質を、単独あるいは他の化合物と混合して使用することができる。針管1の一端1aを被検者に穿刺したとき、流入してきた血液によって膨張した空気透過性血液不透過性部材23は、封止部材22を直接針管1に、あるいは図4に示すように通路21内の凸部24に押しつけ、孔11または通路21を塞ぐ。これにより、フラッシュバックを確認したあと、すぐに針管1内

部が密封される。また、真空採血管取り付け時には、真空採血管の陰圧により、さらに封止部材22は針管1、あるいは凸部24に密着するので、針管1内部の密封性はより高くなる。

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

【0015】

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

【図面の簡単な説明】

【図1】本発明の一実施例の採血針を示す断面図である。

【図2】図1の採血針における針管支持体部分の拡大断面図である。

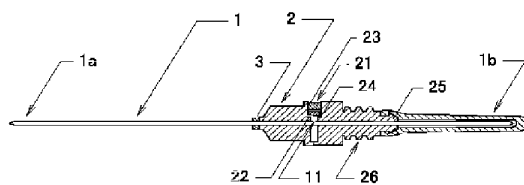
【図3】真空採血管取り付け時の、図1の採血針における、針管支持体部分の拡大断面図である。

【図4】本発明の他の採血針における、針管支持体部分の拡大断面図である。

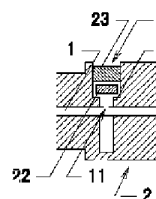
【符号の説明】

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

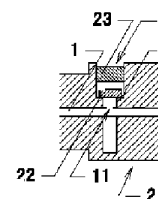
【図1】



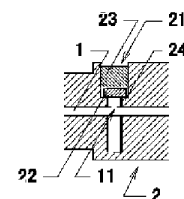
【図2】



【図3】



【図4】



Quality control of bacterial contamination of blood components: the feasibility of diversion system testing

Marcello Napolitano, Giulia Micciulli, Emilio Leone

Centro Trasfusionale, Ospedale Civile di Castrovillari, Cosenza, Italia

Quality controls and retrospective investigations indicate that the majority of bacterial strains isolated from platelet concentrates (PC) derives from bacterial flora contaminating the skin^{1,2}, while about 50% of cases of bacterial contamination of red cell concentrates (RCC) are caused by transitory episodes of asymptomatic bacteraemia in the donor³. For the recipient, the risk of receiving PC contaminated by bacteria is 10-1,000 higher than the combined risk of receiving product contaminated by viruses such as HBV, HCV and HIV. The available epidemiological data show that 1: 2-3,000 PC can be contaminated by bacteria and that the risk of severe sepsis is about 1 case for every 1:50,000 platelet transfusions¹. The risk of severe sepsis from transfusion of RCC is estimated to be about 1:500,000⁴. In the United States bacterial contamination of blood components is the second cause, after human error, of transfusion-related deaths².

The recognized preventive measures include: careful selection of the donor in order to avoid periods of possible bacteraemia (recent dental procedures or diarrhoea), scrupulous disinfection of the venipuncture site with appropriate disinfectants not contaminated by bacteria, diversion – for diagnostic purposes – of the first millilitres of donated blood. Widespread use of pathogen inactivation is currently only available for plasma. Assessment of microbiological contamination of blood components by automated culture systems is increasing and is the subject of considerable debate.

Microbiological cultures of blood components have two aims: to avoid assigning contaminated blood components and to control the quality of the process of producing the blood components themselves. Given the low prevalence of potentially contaminated blood components, preventive bacteriological screening should include all blood components produced: this is an onerous and demanding strategy. Again, in consideration of the low prevalence of contamination, the efficacy of the bacteriological controls on samples can be challenged. Nevertheless, statistically and epidemiologically interesting results can be obtained from co-operation among centres which share the same investigation methods and aims.

We analyzed the technical feasibility of a study on microbiological contamination, using a simple system of diversion into a satellite bag, which allows the blood component to be sampled without compromising its clinical usefulness.

The system allows samples of the contents of the primary bag to be analysed, so the results are applicable to all the blood components produced by fractionating that unit of whole blood, or to conserve the satellite bag in the same conditions as those of the blood component to test, thus exactly reproducing the times and methods of storing the component.

Triple or quadruple bags with SAG-M are used. After having carried out the fractionation and having detached the plasma bag, the SAG-M is allowed to flow into the bag with the red blood cells. After mixing, about 20 mL of the product are allowed to flow into the bag containing SAG-M. This bag is then destined for sampling for microbiological tests.

We used this system to investigate microbial contamination of RCC. The satellite bags were stored in the blood bank in the same conditions as those used for

Received: 30 April 2004 - Revision accepted: 31 May 2004

Correspondence:

Dott. Marcello Napolitano

Centro Trasfusionale

Ospedale Civile

Viale del Lavoro

87012 Castrovillari (CS), Italia

E-mail: manop@libero.it

the RCC to be transfused. The samples were taken in a sterile environment, under a laminar flow hood, on day + 16 of storage (this being the mean time of use of RCC in our centre) and on day + 42 (expiry date). The cultures were carried out with the MiniVITAL system (BioMerieux SA, Marcy-l'Etoile, France).

The presence of aerobic and anaerobic bacteria and mycetes was investigated. The sampling was carried out using two blood culture bottles with 5 mL of sample in each bottle. Overall, 340 cultures were set up for 170 units of RCC. One blood culture was positive for *Micrococcus spp.*, a saprophytic skin contaminant, weakly pathogenic

for humans. This positive culture was found in the group of samples taken on day + 42. Our results, indicating a higher than expected percentage of contamination, support the fact that the most prevalent type of contamination is that from the skin; the data are also of interest with the aim of controlling the production process of blood components⁵. It goes without saying that the number of investigations carried out is too low to attribute any statistical significance to the results.

We believe that it would be worthwhile building a multicentre collaboration on the basis of our methodological approach and in the light of our results.

References

- 1) Blajchman MA, Goldman M, Baeza F. Improving the bacteriological safety of platelet transfusion. *Transf Med Rev* 2004; **18**: 11-24.
- 2) Hillery CD, Josephson CD, Blajchman MA, et. al. Bacterial contamination of blood components: risks, strategies, and regulation. *Hematology (Am Soc Hematol Educ Program)* 2003; **i**: 575-89.
- 3) Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and intervention. *Vox Sang* 2004; **86**: 157-63.
- 4) Blajchman MA. Incidence and significance of the bacterial contamination of blood components. *Dev Biol (Basel)* 2002; **108**: 59-67.
- 5) McDonald CP, Roy A, Mahaian P, et. al. Relative values of the intervention of diversion and improved donor-arm disinfection to reduce the bacterial risk from blood transfusion. *Vox Sang* 2004; **86**: 178-82.

6. Morley C, Miller N, Bangham AD, Davis JA: Dry artificial surfactant and its effect on very premature babies. *Lancet* 1:64, 1981.
7. Johnson JWC, Permutt S, Sipple JH, Salem ES: Effect of intra-alveolar fluid on pulmonary surface tension properties. *J Appl Physiol* 19:769, 1964.
8. Krauss AN, Auld P: Measurement of functional residual capacity in distressed neonates by helium rebreathing. *J PEDIATR* 77:228, 1970.
9. Ivey HH, Kattwinkel J, Roth S: Nebulization of sonicated phospholipids for treatment of respiratory distress syndrome of infancy. In Tom B, Six H, editors: *Liposomes and immunobiology*. New York, 1980, Elsevier North-Holland, pp 301-314.

Fibronectin (cold insoluble globulin) in the neonate

Dorothy Ruth Barnard, M.D., and Mary Maureen Arthur Halifax, N.S., Canada

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

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

MATERIALS AND METHODS

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

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

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

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

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

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

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

From the Department of Pediatrics, School of Medicine, Dalhousie University.

Supported by Grant Ma-6645 from the Medical Research Council of Canada.

Reprint requests: D. R. Barnard, M.D., Department of Pediatrics, School of Medicine, Dalhousie University, Halifax, N.S., Canada B3J 3G9.

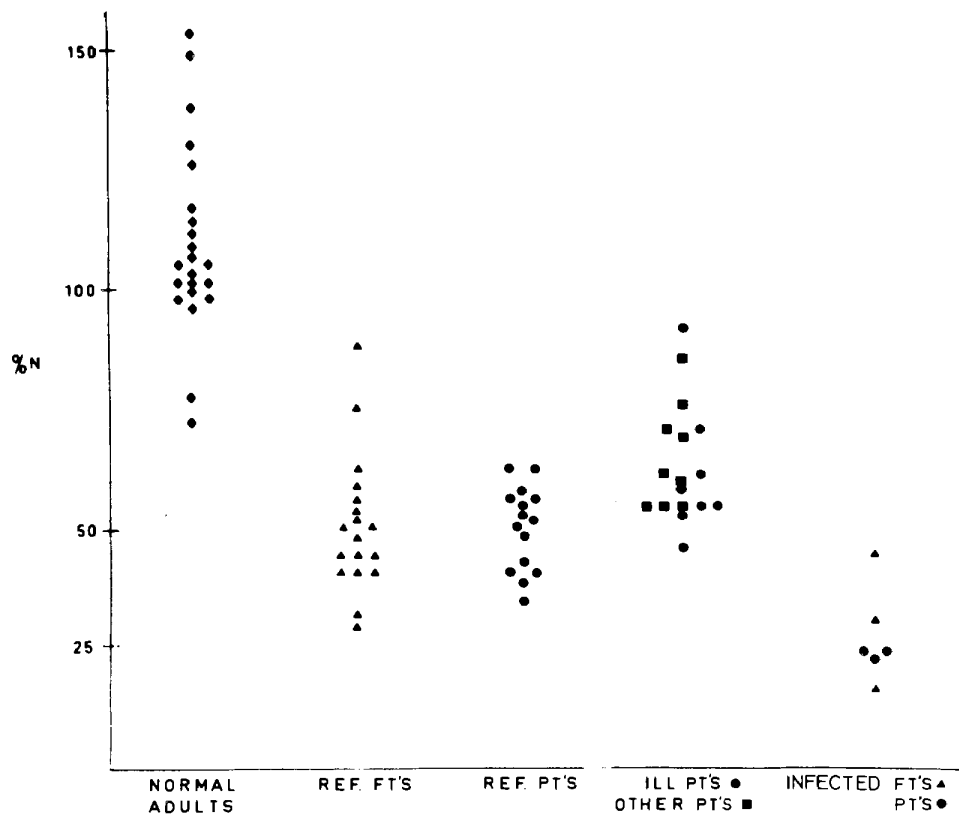


Figure. Fibrinogen values in adults, in infected infants, and in healthy infants. FT, Full-term; PT, preterm.

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

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

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

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

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

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

RESULTS

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

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

DISCUSSION

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

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

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

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

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

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

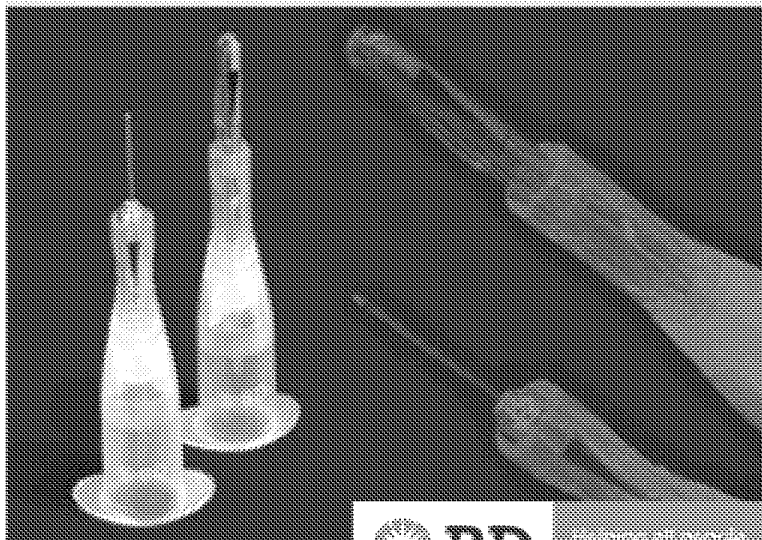
We acknowledge the excellent cooperation of the nurses and physicians of the Grace Maternity Hospital in obtaining cord blood specimens, and Drs. R. A. Bortolussi, A. Allen, D. Stinson, and E. Rees for blood specimens from septic infants.

REFERENCES

1. Mosher DF: Fibronectin. *Prog Hemost Thromb* 5:111, 1980.
2. Ruoslahti E, Engvall E, Hayman E: Fibronectin: Current concepts of its structure and functions. *Coll Res* 1:95, 1980.
3. MacDonald JA, Baum BJ, Rosenberg DM, et al: Destruction of a major extracellular adhesive glycoprotein (fibronectin) of human fibroblasts by neutral proteases from polymorphonuclear leucocyte granules. *Lab Invest* 40:350, 1979.
4. Ganrot PO: Variation of the concentrations of some plasma proteins in normal adults, in pregnant women and in newborns. *Scand J Clin Lab Invest* 29(suppl 124):83, 1972.
5. Saba TM, Blumenstock FA, Weberg PB, et al: Physiologic role of cold insoluble globulin in systemic host defence: Implications of its characterization as the opsonic alpha-2-surface binding protein. *Ann NY Acad Sci* 312:43, 1978.
6. Laurell CB: Electroimmunoassay. *Scand J Clin Invest* 29(suppl 124):21, 1972.
7. Mosesson MW, Amrani DL: The structure and biologic activities of plasma fibronectin. *Br J Haematol* 56:145, 1980.
8. Pearlstein E, Gold LI, Garcia-Pardo A: Fibronectin: A review of its structure and biological activity. *Mol Cell Biochem* 29:103, 1980.
9. Saba TM, Jaffa E: Plasma fibronectin (opsonic glycoprotein): Its synthesis by vascular endothelial cells and role in cardiopulmonary integrity after trauma as related to reticuloendothelial function. *Am J Med* 68:577, 1980.
10. Scovill WA, Annet SJ, Saba TM, et al: Cardiovascular hemodynamics after opsonic alpha-2-surface binding glycoprotein therapy in injured patients. *Surgery* 86:284, 1979.

Venous Blood Collection

BD Vacutainer® Passive Shielding
Blood Collection Needle



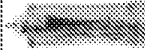
Helping all people
live healthy lives

*A New Generation of Safety from BD,
the leader in safety-engineered technology*

The BD Vacutainer® Passive Shielding Blood Collection Needle is designed to provide the highest amount of protection against needlesticks during a blood draw. The needle's safety shield releases automatically upon insertion of the first tube, providing protection from the time the first tube is inserted through product disposal.

BD Vacutainer® Passive Shielding Blood Collection Needle

Ordering Information

368617	Passive Shielding Blood Collection Needle	21g x 1" needle	25/Box 200/Case	
368617	Passive Shielding Blood Collection Needle	22g x 1" needle	25/Box 200/Case	



A part of the
BD Vacutainer®
Family of Venous Blood
Collection Products

CAUTION: Handle all biological samples and blood collection "sharps" (syringes, needles, lancet adapters, and blood collection sets) in accordance with the policies and procedures of your facility. Obtain appropriate medical attention in the event of any exposure to biological samples (e.g., through a puncture injury) since samples may transmit viral hepatitis, HIV (AIDS), or other infectious diseases. Unlike any safety-engineered feature if the blood collection device provides one. Discard all blood collection "sharps" in biohazard containers approved for their disposal.

BD Global Technical Services:

1.800.631.9174

BD Customer Service:

1.828.237.7762

www.bd.com/vacutainer



BD Diagnostics

Preanalytical Systems

1 Becton Drive

Franklin Lakes, NJ 07417

BD, BD Logo and all other trademarks are property of Becton, Dickinson and Company.

©2005 BD. Printed in USA 01/05 VS7355

PATENT SPECIFICATION (11)

1 378 602

1 378 602

- (21) Application No. 20920/73 (22) Filed 2 May 1973 (19)
 (31) Convention Application No. 266 996 (32) Filed 28 June 1972 in
 (33) United States of America (US)
 (44) Complete Specification published 27 Dec. 1974
 (51) International Classification A61B 5/14
 (52) Index at acceptance
 A5R 33D
 F2V D4X E1L2 E3B2 J2D M1F
 (72) Inventor WALDEMAR ALEXANDER AYRES



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

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

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

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

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

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

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

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

[P]

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

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

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

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

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

An example of a needle assembly in ac- 105
 cordance with our invention will now be de-
 scribed with reference to the accompanying
 drawings in which:—

Figure 1 is a side elevation of a needle as- 110
 sembly attached to a holder and with an
 evacuated container in a position ready for
 coupling with the needle assembly;

Figure 2 is an enlarged fragmentary sec- 115
 tion of the apparatus shown in Figure 1 after
 it has been used to achieve a venapuncture
 prior to the initial closure of a valve mem-
 ber;

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

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

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

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

permit blood to flow from a vein to the container;

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

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

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

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

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

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

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

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

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

65 The rear end of the cannula 25 extends

rearwardly from the housing 21 and has a pointed tip 43 for penetration through the stopper 41 of the evacuated container 39. The cannula 25 is slidably mounted in the bore 42 and has a forward blunt end 44 extending into the chamber 26. Adjacent the forward end of the cannula 25 is a side opening 45 which is movable into and out of the chamber 26 as the cannula 25 slides through the bore 42. The elastomeric sealing disc 30 rests against a rear wall of the chamber 26 and has a central hole, the diameter of which is smaller than the external diameter of the cannula 25, so that the elastomeric sealing disc 30 maintains a seal with the external surface of the cannula 25 as it slides through the disc 30. Thus the chamber is liquid-tight so that liquid flow into and out of the chamber 26 only occurs through the cannulae 24 and 25. The sealing disc 30 is held in place by the rigid disc 29 which is a 'push fit' in the rear of the housing 21. The sealing disc 30 is sandwiched between the disc 29 and the rear wall of the housing 21. An annular bead 46 projecting from the rear wall of the housing engages with the under surface of the disc 30 to ensure a seal between the disc 30 and the rear wall of the chamber and prevent leakage from the chamber 26 through the bore 42 in the rear part 23.

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

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

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

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

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

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

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

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

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

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

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

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

then positioned for use as depicted in Figure 3.

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

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

the penetration of the stopper 41 by the cannula 25.

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

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

WHAT WE CLAIM IS:—

1. A needle assembly for use with appar- 130

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- closed position and thereby prevent the back flow of fluid from the rear end of the assembly to the blood vessel when a predetermined pressure differential exists between the forward and rearward end of the assembly, the means for automatically blocking the blood flow due to venous pressure while changing from one container to a successive container including a second valve means adapted to permit or prevent the flow of blood through the rearward end and into the evacuated container as successive containers are filled with successive blood samples.
16. A needle assembly according to claim 1 constructed substantially as described with reference to the accompanying drawings.
- 5
- 10
- 15

For the Applicants,
GILL, JENNINGS & EVERY,
Chartered Patent Agents,
53/64 Chancery Lane,
London, WC2A 1HN.

Printed for Her Majesty's Stationery Office by Burgess & Son (Abingdon), Ltd.—1974.
Published at The Patent Office, 25 Southampton Buildings, London, WC2A 1AY
from which copies may be obtained.

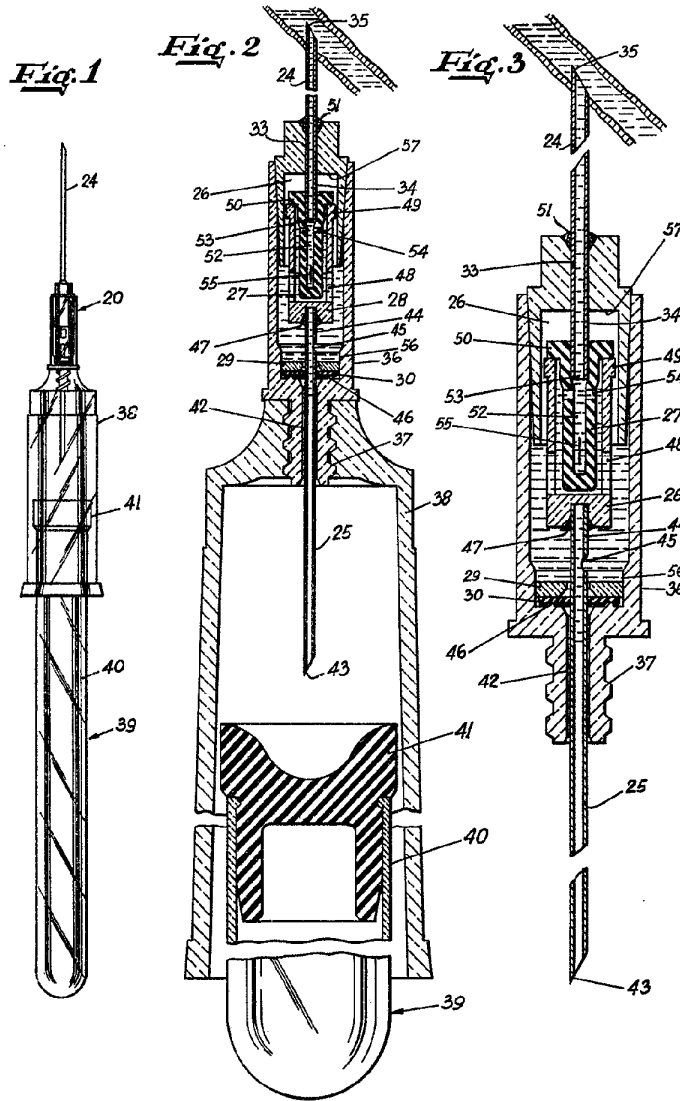


Fig. 4

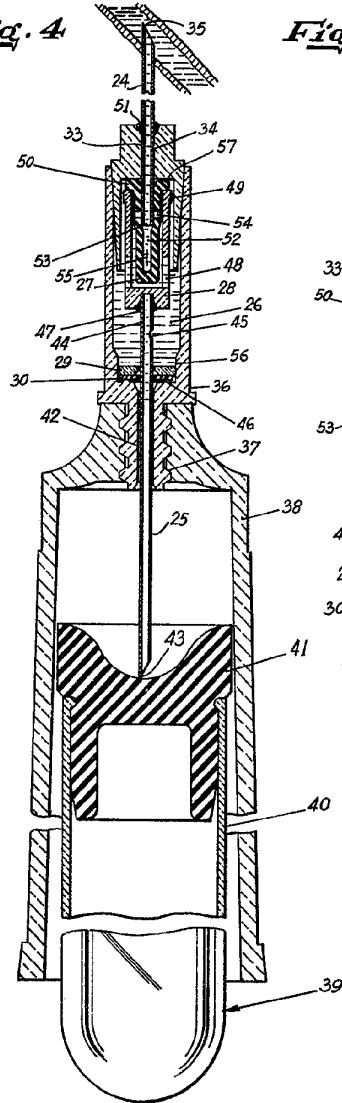


Fig. 5

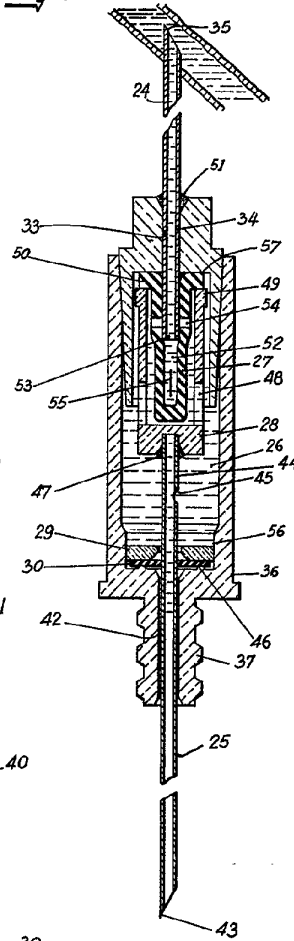


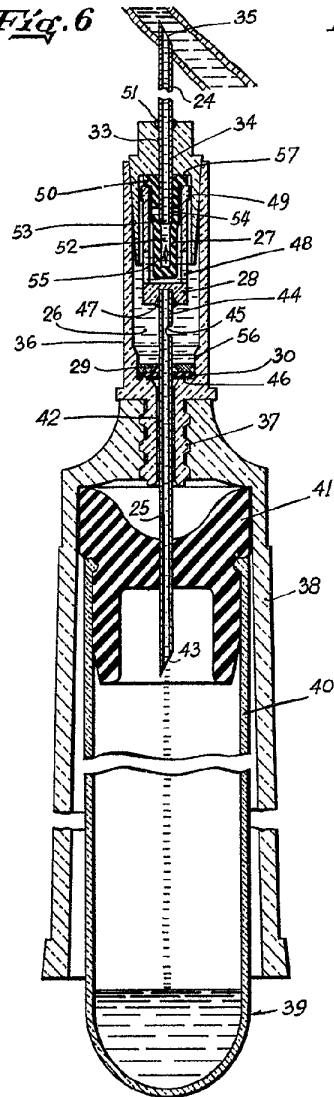
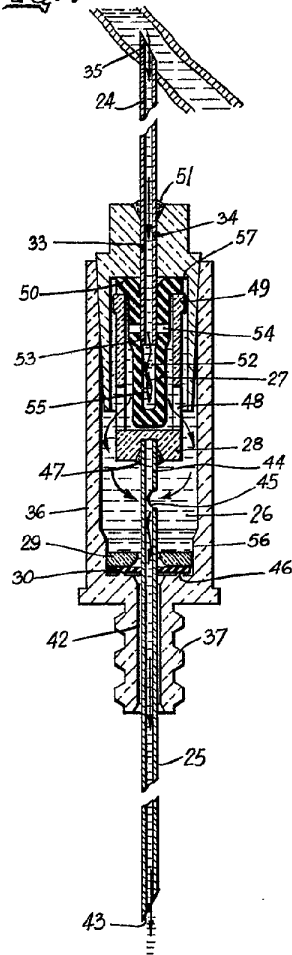
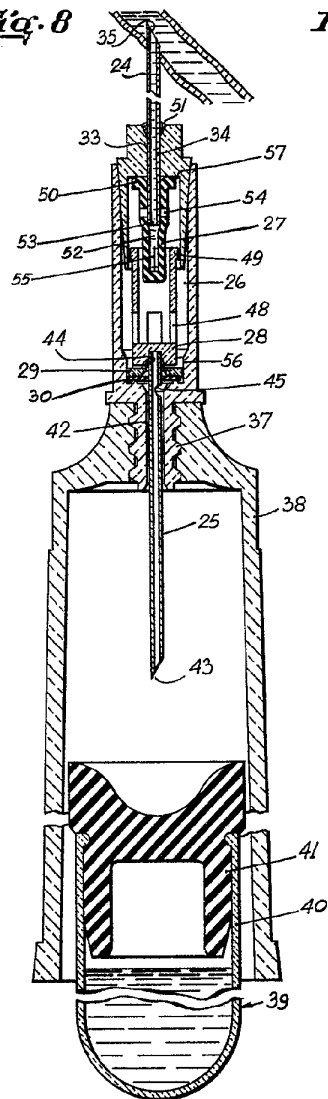
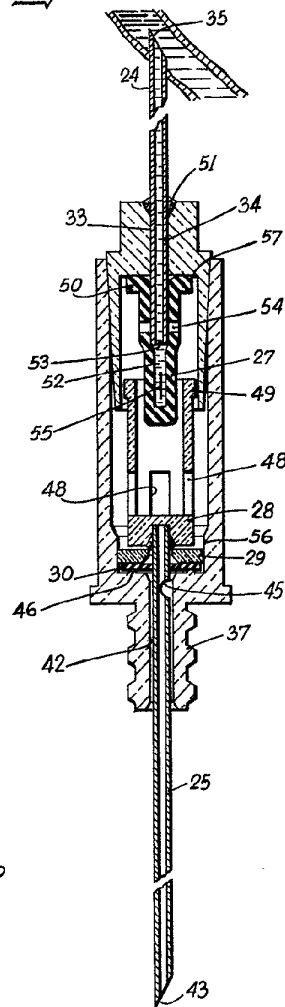
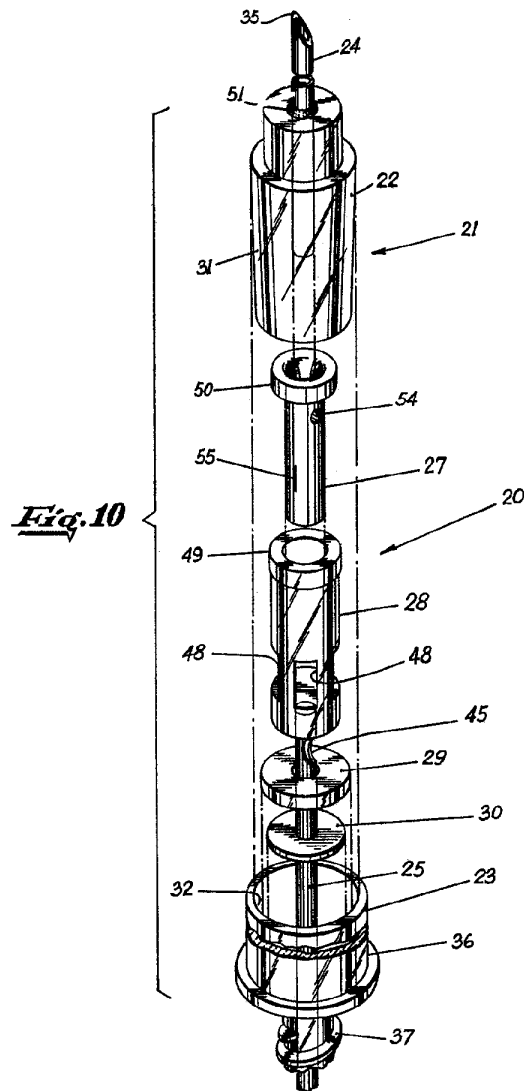
Fig. 6*Fig. 7*

Fig. 8*Fig. 9*



 Literature display


< 1 / 1 display >

Special table 2019-534792

[Registration Gazette](#)
[Document unit PDF](#)
[progress information](#)
[CPD](#)
[search key](#)
[URLs](#)

Display format of the document display screen:

☒ text display ☐ PDF display

primary literature

bibliography

close

(19) [Country of issue] Japan Patent Office (JP)
 (12) [Type of publication] Published patent publication (A)
 (11) [Publication number] Special table 2019-534792 (P2019-534792A)
 (43) [Publication date] December 5, 2019 (2019.12.5)
 (54) [Title of Invention] Cooling of Rolls in Rolling Stands
 (51) [International Patent Classification]
 B21B 27/10 (2006.01)
 [FI]
 B21B 27/10 A
 B21B 27/10 C
 B21B 27/10 D
 [Request for examination] Yes
 [Request for preliminary examination] Not yet requested
 [Total number of pages] 21
 (21
) 22) [Filing date] October 12, 2017 (2017.10.12)
 (85) [Translation submission date] June 13, 2019 (2019.6.13)

(86) [International application number] PCT/ EP2017/076000

(87) [International publication number] WO2018/073086 (87) [International publication date] April 26, 2018 (2018.4.26) (31) [Priority claim number] 16194099.4 (32) [Priority date] October 17, 2016 (2016.10.17) (33) [Country/region or organization claiming priority] European Patent Office (EP)

(81) [Designated countries/regions] AP (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), EA (AM, AZ, BY, KG, KZ, RU, TJ, TM), EP (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OA (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG), AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT

(71) [Applicant]

[Identification number] 515153152

[Name] Primetals Technologies Austria GmbH

(74) [Agent]

[Identification number] 100133400 [

Patent attorney]

[Name] Tatsuhiko Abe

(74) [Agent]

[Identification number] 100110364

[Patent Attorney]

[Name] Shinya Sanehiro

(72) [Inventor]

[Name] Alois Seilingner

(72) [Inventor]

[Name] Erich Orpits

(72) [Inventor]

[Name] Lucas Pichler

wrap up

close —

(57) [Summary]

The present invention relates to a cooling device (7) for cooling the rolls (5) of the rolling stand (1). The cooling device (7) comprises cooling beams (13) for receiving and discharging coolant. The cooling beam (13) has a plurality of full jet nozzles (21) arranged on the discharge side (19) of said cooling beam (13), said side facing the roll (5).) extending parallel to the roll axis (17). A jet of coolant with a substantially constant jet diameter can be sprayed through each of the full jet nozzles from the cooling beam (13) towards the roll (5) in the discharge direction (23).

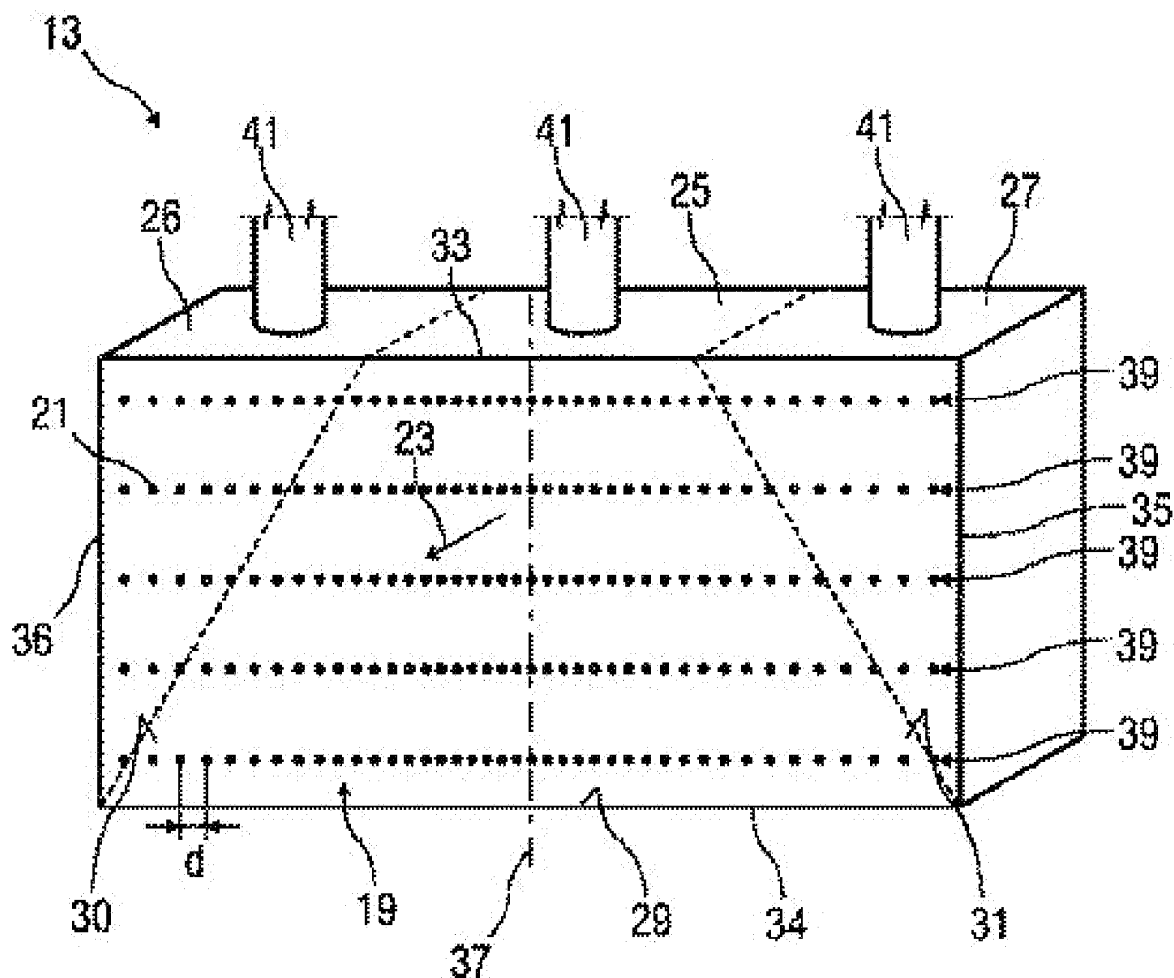


FIG 2

The scope of the claims

open

We claim:

1.

A cooling device (7) for cooling rolls (5) of a rolling stand (1) comprising cooling bars (13) for receiving and discharging a coolant, wherein

said cooling rod (13) has a plurality of full jet nozzles (21) arranged on a discharge side (19) of said cooling rod (13), said discharge side facing a roll (5), extending parallel to the roll axis (17) of said roll (5) and sending coolant jets of substantially constant jet diameter through each of the full jet nozzles from said cooling rods (13) to said roll. A cooling device (7) capable of discharging in a discharge direction (23) towards (5).

2.

The cooling rod (13) is divided into at least two mutually separated coolant chambers (25-27) for receiving coolant, each coolant chamber (25-27) comprising: Corresponding sub-regions (29-31) of said discharge side (19) of said cooling rod (13) where a plurality of full-jet nozzles (21) are arranged, through each of said full-jet nozzles (21), coolant Cooling device (7) according to claim 1, characterized in that a jet can be discharged from the coolant chamber (25-27) towards the roll (5).

3.

A first coolant chamber (25) corresponds to a first partial area (29) of said discharge side (19) of said cooling rod (13), said first partial area (29) is mirror symmetrical with respect to the centerline (37) of the discharge side (19) of the cooling rod (13), the axis being perpendicular to the roll axis (17). 3. Cooling device (7) according to claim 2.

[Claim 4]

characterized in that the extent of the first sub-region (29) parallel to the center line (37) varies along the direction of said roll axis (17) and is greatest along said center line (37). A cooling device (7) according to claim 2 or 3, wherein

5.

A cooling device (7) according to any one of claims 2 to 4, characterized in that the first partial area (29) is polygonal.

6.

Each coolant chamber (25-27) is connected to a coolant supply line (41) for supplying coolant into said coolant chamber (25-27), said coolant supply line (41) opens into said coolant chamber (25-27) substantially perpendicular to said discharge direction (23) of said coolant. A cooling device (7) according to claim 1.

7.

The amount of coolant supplied into the coolant chambers (25-27) is controlled independently of each other by respective control valves (43) and/or respective pumps (45). A cooling device (7) according to any one of claims 2 to 6, characterized in that it is capable of

8. A

system according to any one of claims 2 to 7, characterized by an automated system for controlling the amount of coolant fed into the coolant chamber (25-27). Cooling device (7).

9.

Characterized in that the nozzle spacing (d) of full jet nozzles (21) adjacent to each other along a direction parallel to said roll axis (17) varies along said direction. A cooling device (7) according to any one of claims 1 to 8.

[Claim 10]

10. Cooling device (7) according to claim 9, characterized in that said nozzle spacing (d) is narrowest in a central region of said discharge side (19) of said cooling rod (13).

11.

The nozzle spacing (d) is between about 25 mm and about 50 mm.

Cooling device (7) according to claim 9 or 10.

12. The method

according to any one of claims 1 to 11, characterized in that said full jet nozzles (21) are arranged in a plurality of mutually parallel nozzle rows (39). A cooling device (7) as described.

13.

Characterized in that said cooling rod (13) has a nozzle opening for each full jet nozzle (21) to which said full jet nozzle (21) is detachably fixed. A cooling device (7) according to any one of claims 1 to 12.

14.

A wiper (15) for wiping coolant from said roll (5), characterized by a wiper (15) which can be pivoted together with said cooling rod (13). A cooling device (7) according to any one of claims 1 to 13.

15. A

rolling stand (1) with rolls (5) and two cooling devices (7) each designed as claimed in any one of claims 1 to 13. A rolling stand (1), wherein said two cooling devices (7) are arranged on either side of said rolls (5).

detailed description

open

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to a cooling device for cooling the rolls of a rolling stand. BACKGROUND OF THE INVENTION Rolling stands for rolling rolling stock have rolls which are cooled with a cooling liquid, generally cooling water. [0003] US Pat. No. 6,200,000 discloses a stiff, concave shell that allows low-pressure cooling liquid to be applied to the rolls of a rolling stand. [0004] US Pat. No. 6,300,000 discloses fluid cooling of work rolls

of a roll stand by means of movable articulated cooling shells. In this case, the cooling liquid is applied mainly at low pressure using the cooling shell, but in addition the cooling liquid is applied at high pressure to produce a sufficient cooling effect. [0005] US Pat. No. 5,300,202 discloses a cooling device for cooling the work rolls of a rolling stand, which device comprises a stationary spray that is slightly narrower than the narrowest strip produced with the relevant rolling stand. It has axially displaceable spray bars for cooling only those portions of the work rolls which have bars and which correspond to the width of the strip being rolled at the time. [0006] US Pat. No. 6,200,403 discloses a method for cooling the work rolls of a rolling stand, in which cooling water is sprayed onto the work rolls at low pressure rather than high pressure, but at the same time The range that can be used is widened. [0007]

US Pat. No. 5,300,003 discloses a spray bar for cooling rolled stock, the spray bar extending transversely to the direction of travel of the rolled stock and having a central region and two edge regions. , the cooling medium can be supplied to each of them separately.

[0008]

[Patent Document 1] [US Patent Application Publication No. 2010/0089112](#) [Patent Document 2] [German Patent Application Publication No. 102009053074](#)

[Patent Document 3] [JP-A-6-170420](#) [Patent Document 4] [JP-A-59-156506](#) [Patent Document 5] [International Publication No. 2014/170139](#) [Outline of the Invention] [Problem to be Solved by the Invention] [SUMMARY OF THE INVENTION It is a principal object of the present invention to identify an improved cooling device for cooling the rolls of a rolling stand. [0010] According to the invention , this object is achieved by the features of claim 1 . Advantageous embodiments of the invention form the subject matter of the dependent claims . A cooling de

vice according to the invention for cooling the rolls of a rolling stand comprises cooling rods for receiving and discharging coolant. The cooling rod has a plurality of full jet nozzles located on the discharge side of the cooling rod, said side facing the roll and extending parallel to the roll axis of the roll. A coolant jet of coolant of substantially constant jet diameter can be discharged through each full jet nozzle from the cooling rod toward the roll in the discharge direction. [0013]

A full jet nozzle shall mean a nozzle capable of delivering a substantially straight jet of coolant with a substantially constant jet diameter. By virtue of the concentrated coolant discharge, the full jet nozzle produces a higher roll impact pressure at the same coolant pressure at the cooling rod than the conventionally used fan jet nozzle. Due to the large amount of coolant applied throughout, there is always a specific coolant film, typically a few millimeters to a few centimeters thick, by impinging coolant jets for good heat dissipation. Since this film should be penetrated as completely as possible, a higher impact pressure has a direct positive effect on the cooling action at the roll surface. Thanks to the high impact pressure of the coolant jets on the rolls produced by the full-jet nozzles, the coolant pressure in the cooling rods can be significantly reduced compared to when fan-jet nozzles are used, thereby increasing the cooling system. It is advantageous to be able to significantly reduce the energy consumption and operating costs of

[0014]

Since the coolant is discharged through a full-jet nozzle, the distance from the roll to the spray bar is also less critical over a wider range and therefore does not have to be adapted to the roll diameter. Thus, for example, a substantially straight coolant jet can cool the roll surface to be cooled at distances between 50 mm and 500 mm without any significant change in the cooling effect of the coolant jet.

[0015]

Since the reduction in coolant pressure is also associated with reduced loading and consequent wear on the nozzles, this also results in reduced maintenance costs as a result of reduced coolant pressure in the cooling rods, which is another advantage of using a full jet nozzle.

[0016]

In one embodiment of the invention, it is envisioned that the cooling rod is divided into at least two mutually separated coolant chambers for receiving coolant. Each coolant chamber corresponds to a sub-region of the discharge side of the cooling rod with a plurality of full-jet nozzles arranged through each of the full-jet nozzles to discharge a coolant jet from the coolant chamber toward the roll. Dividing the cooling rod into a plurality of mutually separated coolant chambers corresponding to different subregions of the discharge side of the cooling rod controls the coolant pressure in the subregions independently of each other, resulting in it is advantageous to be able to control the cooling effect of the subregions independently of each other by controlling the coolant flow rate delivered by the . Thereby, depending on the position, the roll

It is advantageous to be able to influence the cooling and ensure that the more strongly heated areas of the roll surface, for example the central area of the roll surface, are cooled more strongly than the less intensely heated areas. . A development of the above-described embodiment of the invention is that the first coolant chamber corresponds to a first partial area of the discharge side of the cooling rod, the first partial area being the discharge side of the cooling rod

is assumed to be mirror-symmetrical about the centerline of the roll, and its axis is perpendicular to the roll axis. For example, the extent of the first subregion parallel to the centerline varies along the direction of the roll axis and is greatest along the centerline. For example, the first partial area is polygonal. Embodiments in which the first sub-region is mirror-symmetrical about the center line take into account the fact that the rolls are generally also heated symmetrically about the center line. The fact that the extent of the first subregion parallel to the center line varies along the direction of the roll axis and has a maximum extent along the center line means that the roll is generally heated most strongly at the center and the heating of the roll decreases towards the edge region. A corresponding configuration of the first subregion thus makes it possible to adapt the cooling of the rolls to the position-dependent thermal load of the rolls by means of the first subregions.

[0018]

In another embodiment of the invention, each coolant chamber is connected to a coolant supply line for supplying coolant into the coolant chamber, the coolant supply line supplying coolant into the coolant chamber. It is assumed that the opening is substantially perpendicular to the ejection direction of the . The coolant supply lines open into the cooling rods substantially perpendicular to the direction of discharge, so that the pressure distribution of the coolant in each coolant chamber can be substantially uniform. Advantageously, the pressure gradient be

tween the full jet nozzle near the opening and the full jet nozzle away from the opening is thereby eliminated.

[0019]

Another embodiment of the invention envisions that the amount of coolant supplied into the coolant chambers can be controlled independently of each other by respective control valves and/or respective pumps. This allows the cooling effectiveness of the coolant jets discharged from the individual coolant chambers to be controlled independently of each other, as described above. If, for example, a conventional coolant supply system present at any given time can be used in the relevant rolling system, for example a water supply system that normally delivers cooling water at a pressure of 4 bar, the control It is particularly advantageous to control the amount of coolant by means of a valve. In this case, complex and expensive pressure boost systems can be dispensed with for roll cooling. By controlling the amount of coolant by the pumps, if appropriate in conjunction with control valves, individual pumps can be turned off or turned on during breaks between rolling or in the case of rolling operations requiring only a low cooling capacity. Power can be lowered, thereby reducing energy consumption. Another embodiment of the present invention contemplates an automated system for controlling the amount of coolant supplied into the coolant chamber

Thereby, it is advantageous to be able to automatically control the volumetric flow rate of the coolant discharged from the coolant chamber onto the roll in order to adapt the volumetric flow rate to the temperature distribution of the roll surface. In this case, the amount of coolant supplied into the coolant chamber is preferably controlled by an automated system through controlling the control valves and/or pumps mentioned above.

[0021]

In another embodiment of the invention, it is envisaged that the nozzle spacing of full jet nozzles adjacent to each other along a direction parallel to the roll axis varies along said direction. In this case, the nozzle spacing is preferably the narrowest in the central region of the discharge side of the cooling rod. For example, the nozzle spacing along the direction parallel to the roll axis is between about 25mm and about 50mm. These embodiments of the present invention also allow the nozzle spacing along the direction parallel to the roll axis to be varied according to the position-dependent thermal load of the roll surface, so that the placement of the full-jet nozzles can also be adapted to this thermal load. The minimum nozzle spacing in the central region of the discharge side of the cooling rods takes into account the fact that the central region of the roll surface generally experiences the greatest heat load.

Another

embodiment of the present invention envisions that the full jet nozzles are arranged in parallel rows of nozzles. Advantageously, this allows the coolant to be applied to the roll over a wider area and evenly as the roll rotates.

Another

embodiment of the invention envisions that the cooling rod has a nozzle opening for each full jet nozzle to which the full jet nozzle is removably secured. Advantageously, this embodiment of the present invention allows for easy replacement of defective jet nozzles.

In another embodiment of the invention, a wiper is provided for wiping coolant from

the roll, and the wiper and cooling bar can be pivoted together. For example, wipers direct excess coolant to the rolled stock and/or to the roll nip where the rolled stock is guided between two rolls to reduce friction between the rolled stock and the rolls. It is advantageous to be able to prevent the lubricant from washing away. Advantageously, the ability to pivot the wiper and cooling rods together obviates the need for additional equipment to move the cooling rods. In this case, the advantages of using full-jet nozzles already mentioned above are also in effect here. That is, by using a full-jet nozzle, the distance between the spray bar and the roll becomes less critical over a wider range and therefore no longer needs to be adapted to the roll diameter. Furthermore, the present invention is also particularly suitable as a retrofit to existing rolling systems with wipers, for example only conventional high pressure spray rods need to be replaced with cooling rods according to the invention.

[0025]

The rolling stand according to the invention comprises rolls and two cooling devices according to the invention, the two cooling devices being arranged on opposite sides of the rolls. The advantages of the rolling stand according to the invention result from the advantages of the cooling device according to the invention already mentioned above.

The above-described properties, features, and advantages of the present invention, as well as the manner in which

they are achieved, will become clearer and will be clearly understood.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027]

FIG. 1 is a schematic view of a rolling stand with cooling device;

2 is a schematic perspective view of a first exemplary embodiment of a cooling rod; FIG.

3 shows the volumetric flow rate of coolant delivered by the cooling rods shown in FIG. 2 as a function of position; FIG.

FIG. 4 is a discharge side view of a second exemplary embodiment of a cooling rod;

FIG. 5 is a discharge side view of a third exemplary embodiment of a cooling rod;

FIG. 6 is a discharge side view of a fourth exemplary embodiment of a cooling rod;

FIG. 7 is a view of the discharge side of the fifth exemplary embodiment of the cooling rod;

FIG. 8 is a view of the discharge side of the sixth exemplary embodiment of the cooling rod;

FIG. 9 is a view of the discharge side of the seventh exemplary embodiment of the cooling rod;

FIG. 10 is a discharge side view of an eighth exemplary embodiment of a cooling rod;

FIG. 11 is a discharge side view of a ninth exemplary embodiment of a cooling rod;

FIG. 12 is a discharge side view of a tenth exemplary embodiment of a cooling rod;

[Mode for carrying out the invention]

[0028]

In all drawings, the same parts are provided with the same reference numerals.

[0029]

FIG. 1 is a schematic diagram of a rolling stand 1 for rolling a rolling stock 3. FIG. The rolling stand 1 comprises two rolls 5 designed as work rolls and two cooling devices 7 for each roll 5, said devices being arranged on either side of the rolls 5. The rolls 5 are spaced apart by a roll nip 9 and pass the rolling stock 3 through the roll nip 9 in the rolling direction 11 to form the rolled stock 3. Each cooling device 7 comprises cooling bars 13 and wipers 15. Each cooling rod 13 is designed to receive and discharge coolant

.
For discharging the coolant, the cooling rod 13 has a plurality of full jet nozzles 21 arranged on the discharge side 19 of the cooling rod 13, said side facing the respective roll 5 and the roll of the roll 5. A coolant jet extending parallel to axis 17 and having a substantially constant jet diameter can be discharged in discharge direction 23 from cooling rod 13 towards roll 5 through each of the full-jet nozzles. Coolant may be supplied into the cooling rods 13 via coolant supply lines 41, the amount of coolant supplied into the cooling rods 13 being controlled by a control valve 43 and/or a frequency controlled pump 45, for example. can be controlled by A coolant is, for example, water. Each wiper 15 is designed to wipe coolant from the respective roll 5 and can be pivoted toward and away from the roll 5

.
The cooling rods 13 and wipers 15 of each cooling device 7 are fixed to the pivoting device of the cooling device 7, thus pivoting the cooling rods 13 and wipers 15 together toward and away from the rolls 5. Preferably, it can be moved.

[0032]

FIG. 2 is a schematic perspective view of a first exemplary embodiment of cooling rods 13 for delivering coolant to rolls 5. FIG. The cooling rod 13 is divided into three mutually separated coolant chambers 25-27 to receive coolant. Each coolant chamber 25-27 corresponds to a sub-region 29-31 of the discharge side 19 in which a plurality of full jet nozzles 21 are arranged to roll coolant jets from the coolant chambers 25-27 through each of the full jet nozzles. 5 can be discharged in the discharge direction 23. The discharge side 19 is rectangular with two longitudinal sides 33, 34 parallel to the roll axis 17 and two lateral sides 35, 36 perpendicular to the roll axis 17. The first coolant chamber 25 corresponds to a first partial area 29 of the discharge side 19 of the cooling rod 13 forming the central area of the discharge side 19

.
The first partial region 29 is mirror-symmetrical to the centerline 37 of the discharge side 19 of the cooling rod 13, said axis being perpendicular to the roll axis 17 and arranged on the first longitudinal side 33. It is a trapezoid with four vertices and two vertices each located at the endpoint of the second longitudinal side 34.

[0034]

The full jet nozzles 21 are arranged on the discharge side surface 19 in a plurality of nozzle rows 39 each extending parallel to the roll axis 17. In this case, the nozzle spacing d between the adjacent full jet nozzles 21 of each nozzle row 39 varies symmetrically with respect to the center line 37, so that the nozzle spacing d is narrowest at and widens towards the edge region of the outlet side 19, for example parabolically. In the exemplary embodiment shown in FIG. 2, the nozzle spacing d is twice as large at the ends of each nozzle row 39 as it is at the center of the nozzle row 39. The nozzle spacing d varies, for example, between 25mm and 50 mm. The nozzle rows 39 extend substantially evenly over the entire extent of the discharge side 19 and thus produce a relatively uniform cooling effect on the roll surface of the roll 5. A further development of the exemplary embodiment shown in FIG. 2 envisions arranging the nozzle rows 39 staggered with respect to each other, so that the full jet nozzles 21 of the various nozzle rows 39 are arranged in roll

It is not arranged along a direction perpendicular to the axis 17. A "cooling channel" extends perpendicular to the row of nozzles 39 where no coolant is ejected onto the roll 5, resulting in a reduced cooling effect, but this "cooling channel" can be avoided, so that the nozzle row 39 has a particularly uniform

Advantageously, a good cooling effect is achieved. Furthermore, the full jet nozzles 21 very close to or on the boundary between two adjacent sub-regions 29-31 in FIG

Displaced with respect to the arrangement, they are arranged to fall into one of the adjacent sub-regions 29-31, which subdivide into the coolant chambers 25-27 inside the cooling tube 13 by the separating plate such a boundary line. because it extends along Each full jet nozzle 21 is removably attached to the nozzle opening of the cooling rod 13, for example by a threaded joint

Each full jet nozzle 21 has a minimum diameter nozzle cross-section of, for example, about 4 mm. Each coolant chamber 25-27 is connected to a coolant supply line 41 for supplying coolant into the coolant chambers 25-27

, it is open substantially perpendicular to the discharge direction 23 of the coolant. The cross-sections of the coolant supply lines 41 each have a diameter of, for example, between 100 mm and 150 mm. The amount of coolant supplied into coolant chambers 25-27 via coolant supply line 41 is controlled by respective control valves 43 (not shown in FIG. 2) and/or respective pumps

can be controlled independently of each other by 45 (not shown in FIG. 2). Advantageously, this allows the amount of coolant discharged from the coolant chambers 25-27 to be adapted to

o different heat loads in different regions of the roll surface.

FIG. 3 shows, by way of example, the volume flow rate V_1

of three coolants discharged from the cooling rod 13 shown in FIG., V_2 , V_3 as a function of the position y along the direction parallel to the roll axis 17. Here, the volumetric flows V_1 , V_2 , V_3 are expressed as a percentage of the rated flow.

The rated

flow is the first volumetric flow V_1 at the center position y_m . A first volumetric flow rate V_1 occurs when coolant is fed into all three coolant chambers 25-27 at the same specified pressure rating for all coolant chambers 25-27. The first volume flow rate V_1 has a parabolic shape with a maximum at the central position y_m and decreases from the central position y_m towards the two end regions to half the value of the central position y_m . Become. The reason for this shape of the first volumetric flow rate V_1 is that from the center of the nozzle row 39 to the two ends, the nozzle spacing d of the full jet nozzles 21 along the nozzle row 39 doubles, a parabolic increase in the nozzle spacing d is assumed. Second volumetric flow rate V_2

supplies coolant into the first coolant chamber 25 at a coolant pressure of approximately twice the rated pressure and into the other two coolant chambers 26, at a coolant pressure of approximately half the rated pressure. 27 when supplied to each of them. The third volume flow rate V_3 supplies coolant into the first coolant chamber 25 at a coolant pressure approximately half the rated pressure and supplies coolant at a coolant pressure approximately twice the rated pressure

into each of the other two coolant chambers 26, 27. FIG. 3 illustrates the volumetric flow rates V_1 , V_2 , V_3 with different patterns of dependence on position y along the direction parallel to the roll axis 17 at different coolant pressures in the coolant chambers 25-27, so that the volume flows V_1 , V_2 , V_3 discharged from the cooling rods 13 can be adapted to the temperature distribution of the roll surfaces. The coolant pressure in each coolant chamber 25-27 is set by a respective control valve 43 and/or a respective pump 45. FIGS. 4-12 each show the discharge side 19 of another exemplary embodiment of the cooling rod 13. FIG. these

differs from the exemplary embodiment shown in FIG. 2 only in the shape and number of the coolant chambers 25-27 and the corresponding partial areas 29-31 of the discharge side 19. FIG. As in the exemplary embodiment shown in FIG. 2, the full jet nozzles 21 are each arranged in a plurality of nozzle rows 39, with the nozzle spacing d in each case extending from the center along it to the two ends. increase towards the part. Therefore, the full jet nozzle 21 of FIGS. 4-12 will not be described here again. Due to the distribution of the full jet nozzles 21 of

n the discharge side 19 similar to the exemplary embodiment shown in FIG. 2, each of the exemplary embodiments shown in FIGS. V₁, V₂, V₃ can be produced. Like the exemplary embodiment shown in FIG. 2, the exemplary embodiments shown in FIGS. 4-10 each correspond to three coolant chambers 25-27 and a discharge side 19.

It has partial regions 29-31. Similar to the exemplary embodiment shown in FIG. 2, the first subregion 29 is mirror-symmetrical about the centerline 37 of the discharge side 19 of the cooling rod 13, perpendicular to the roll axis 17, and the other two partial areas 30, 31 adjoin the first partial area 29 and on different sides of the centerline 37.

FIG.

4 shows that the first partial area 29 is trapezoidal with two vertices located on the first longitudinal side 33 and two vertices located on the second longitudinal side 34. 1 illustrates an exemplary embodiment;

[0048]

FIG. 5 shows that the first partial region 29 has one vertex arranged at the intersection of the centerline 37 and the first longitudinal side 33 and two corners arranged at the end of the second longitudinal side 34. 2 shows an exemplary embodiment that is a triangle with four vertices.

FIG.

6 shows that the first partial area 29 has one vertex located at the intersection of the centerline 37 and the first longitudinal side 33 and two corners located at the second longitudinal side 34. 2 shows an exemplary embodiment that is a triangle with four vertices.

FIG.

7 shows an exemplary embodiment in which the first partial area 29 is a rectangle with vertices located on the longitudinal sides 33, 34. In this exemplary embodiment, no coolant is discharged via the two outer partial regions 30, 31, so that the discharge of coolant can only occur from the central region of the discharge side 19. This exemplary embodiment is therefore particularly suitable for rolling rolling blanks 3 of different widths.

FIG.

8 shows that the second partial area 30 and the third partial area 31 each have a vertex on the first longitudinal side 33 and a vertex located at one end of the first longitudinal side 33, and vertices located on the lateral sides 35, 36. FIG.

FIG.

9 shows that the first partial region 29 has two vertices on the first longitudinal side 33 and two vertices located at the ends of the second longitudinal side 34, respectively. Figure 10 shows an exemplary embodiment that is a hexagon with vertices on its short sides 35, 36.

[0053]

FIG. 10 shows that the first partial regions 29 are arranged at one vertex arranged at the intersection of the centerline 37 and the first longitudinal side 33 and at the end of the second longitudinal side 34.

ngitudinal side 34 respectively. An exemplary embodiment is shown that is a pentagon with two vertices and one vertex on each of the short sides 35,36. The exemplary embodiments shown in FIGS. 11 and 12 each have two coolant chambers 25, 26 and corresponding subregions 29, 30 of the discharge side 19

.

Both partial regions 29 are mirror-symmetrical with respect to a centerline 37 of the discharge side 19 of the cooling rod 13 perpendicular to the roll axis 17.

FIG.

11 shows that the first partial area 29 is triangular with one vertex located at the centerline 37 and two vertices located at the ends of the second longitudinal sides 34 respectively. show s an exemplary embodiment

.

FIG.

12 shows that the first partial area 29 has one vertex located on the centerline 37 and two vertices located respectively at the ends of the second longitudinal sides 34 and each short edge. 4 shows an exemplary embodiment that is a pentagon with vertices on hand sides 35,36.

Although the present invention has been illustrated and described in more detail by way of preferred exemplary embodiments, the present invention is not limited to the disclosed examples, and a person skilled in the art can fully understand the scope of protection of the present invention

.

Other variations can be obtained from these without exceeding.

[Description of Symbols]

1

Rolling stand

3 Rolling material, rolling material

5 Roll

7 Cooling device

9 Roll gap

11 Rolling direction 13

Cooling bar

15 Wiper

17 Roll shaft

19 Discharge side surface

21 Full jet nozzle

23 Discharge direction

25-27 Cooling Agent chambers

29 to 31 Partial areas

33, 34 Longitudinal sides

35, 36 Short side
37 Center line
39 Nozzle row
41 Coolant supply line
43 Control valve
45 Pump
d Nozzle spacing

drawing

open

[Fig. 1]

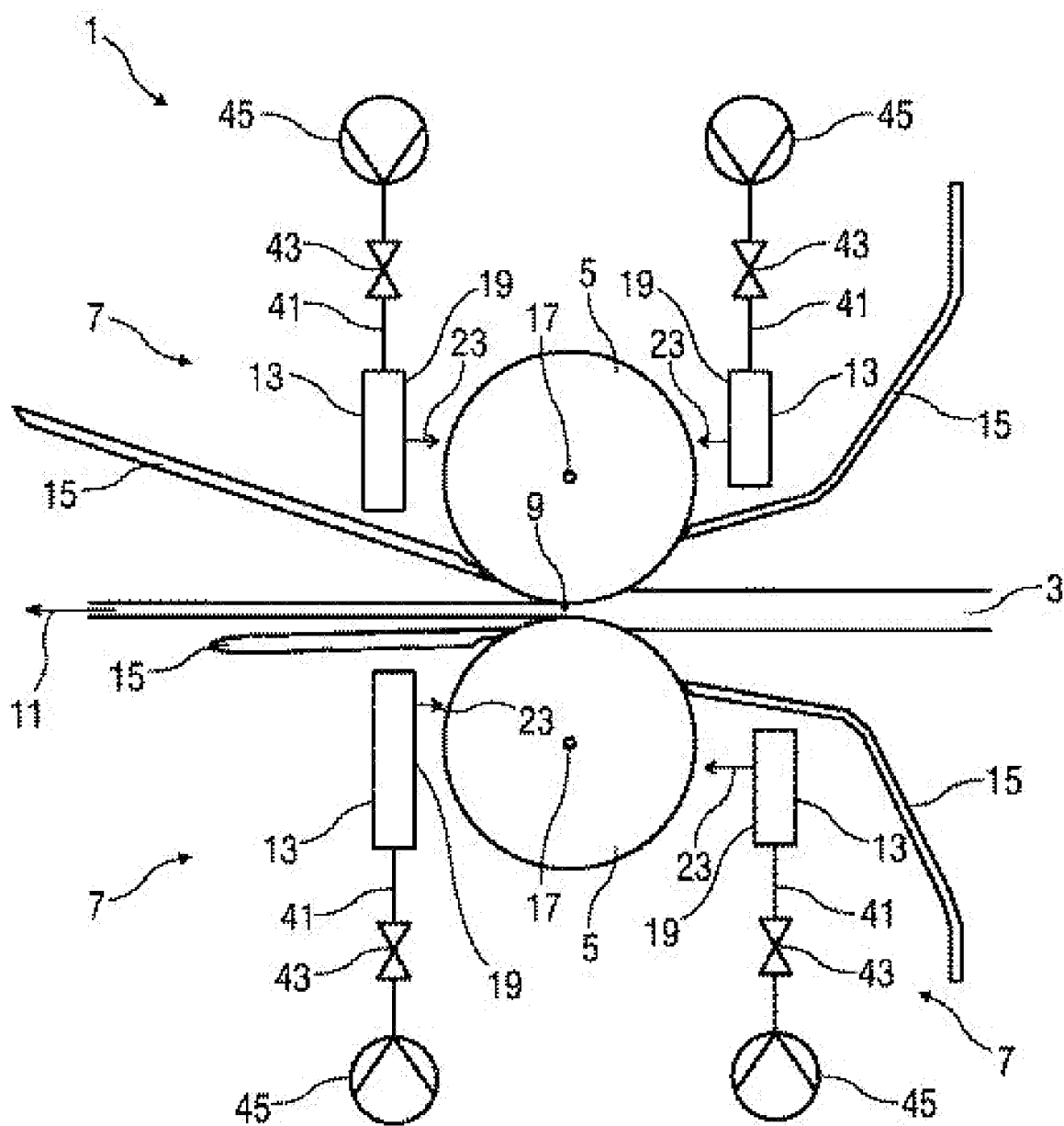


FIG 1

[Figure 2]

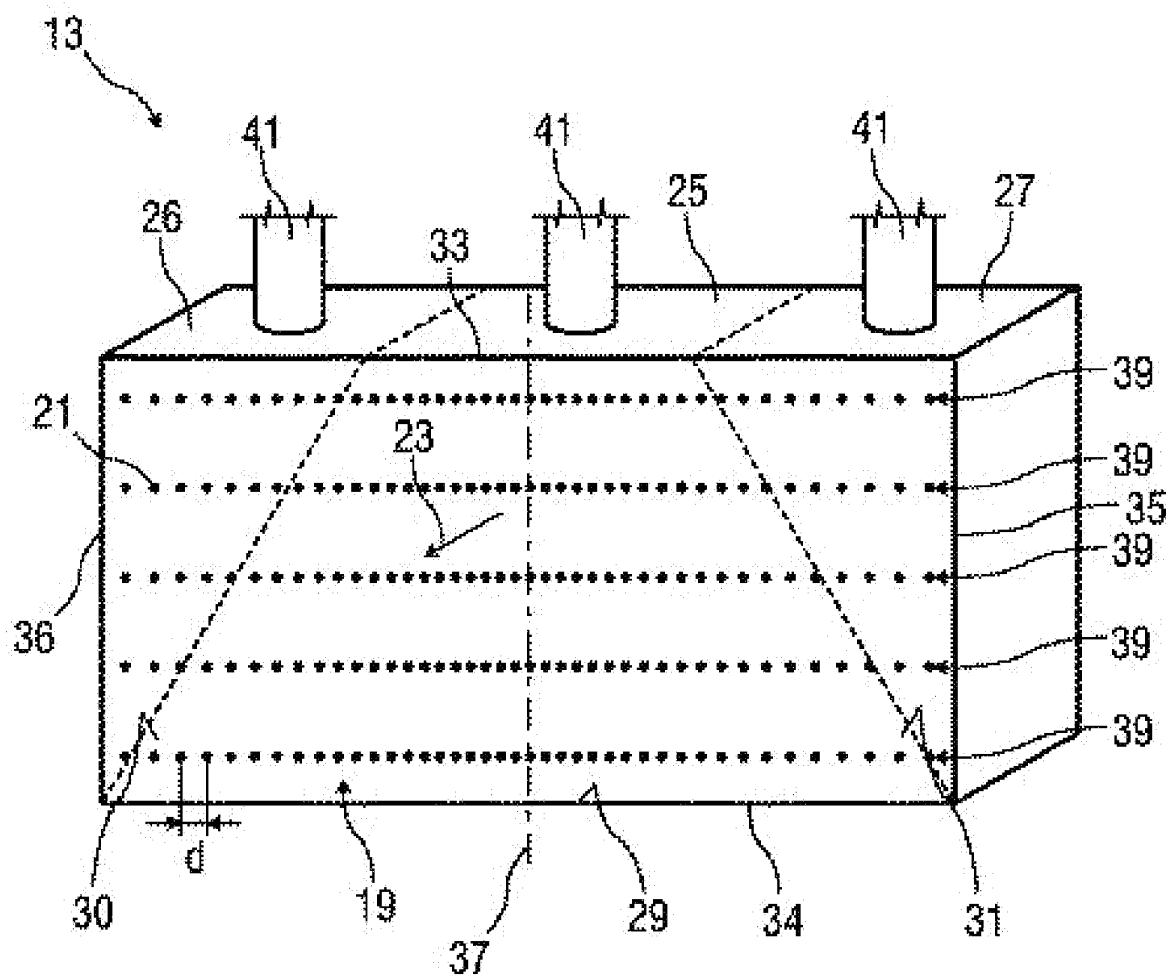


FIG 2

[Figure 3]

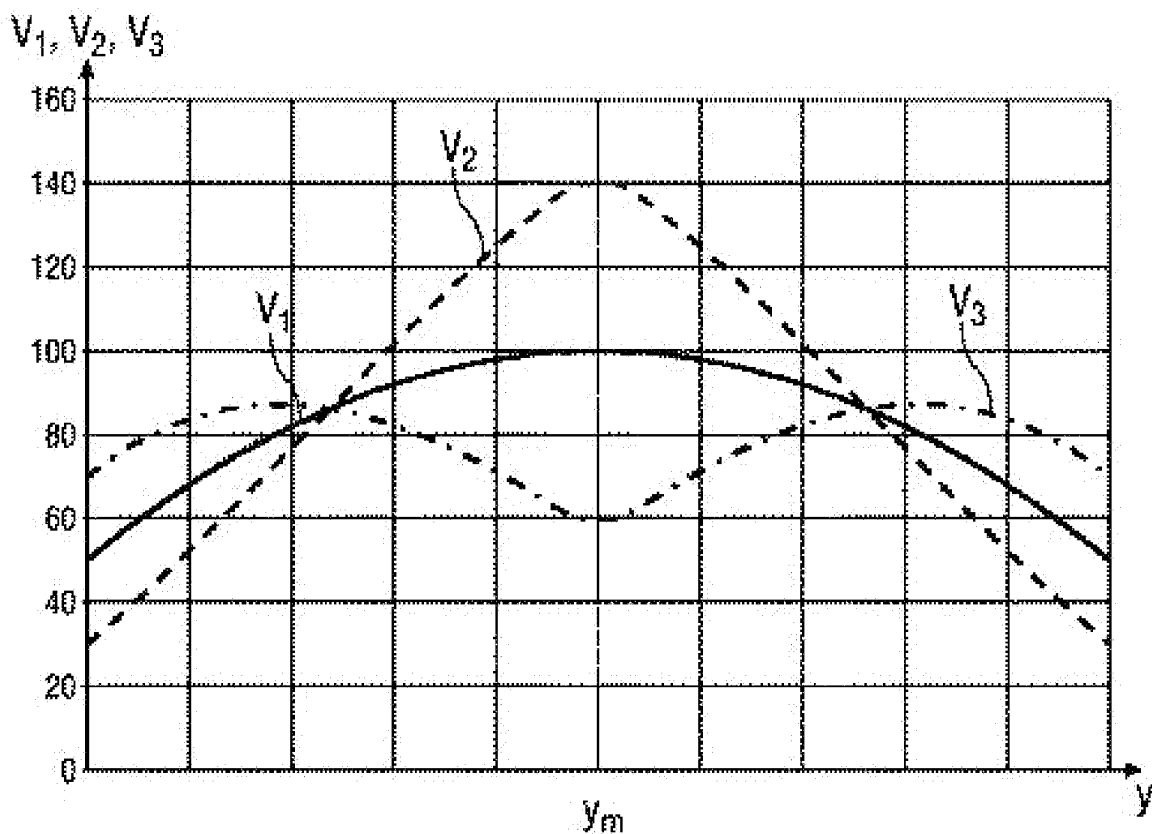


FIG 3

[Figure 4]

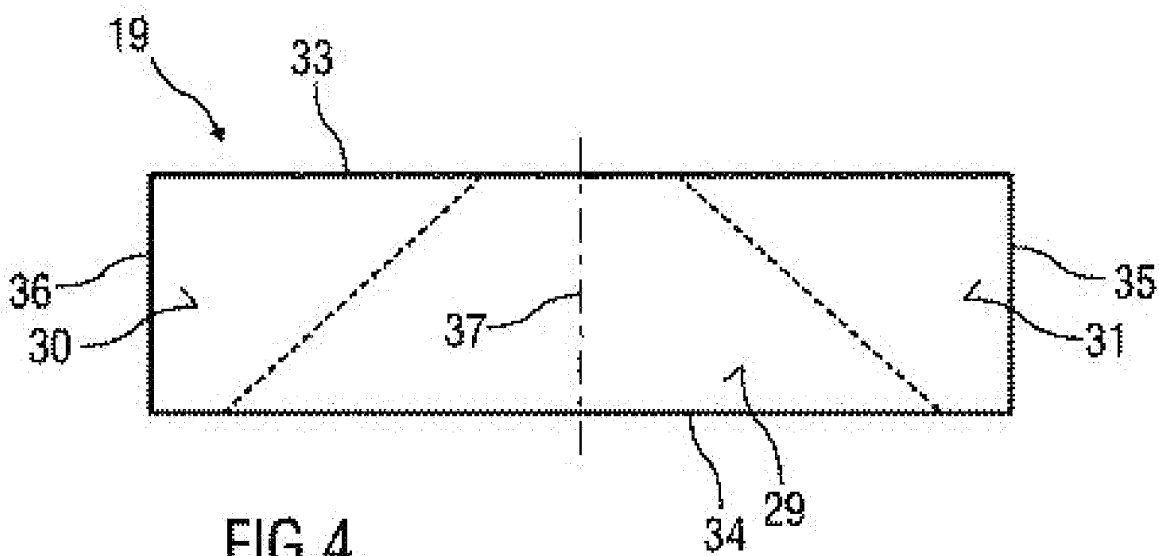
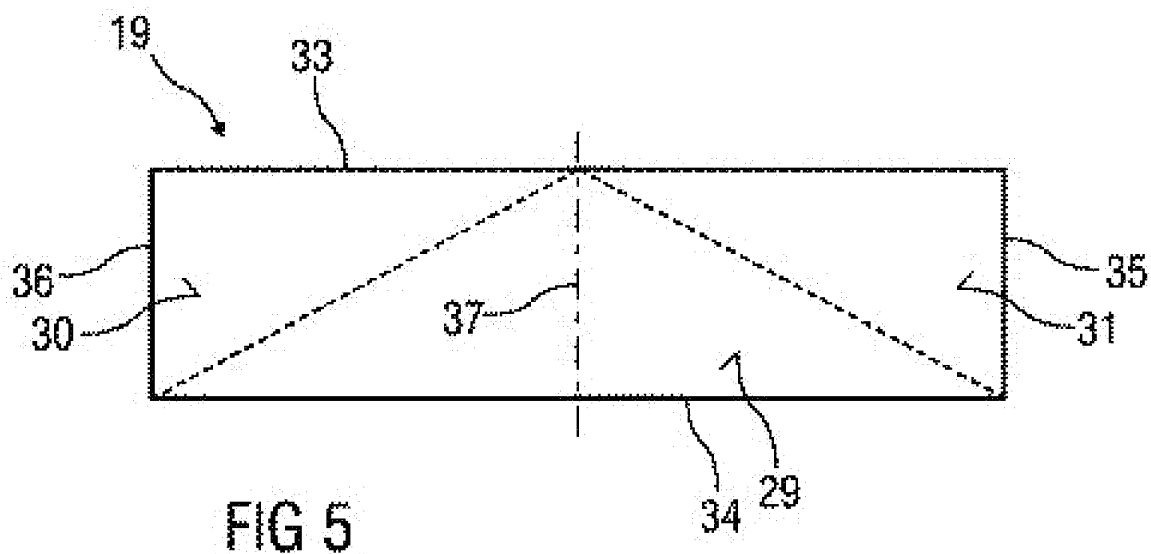
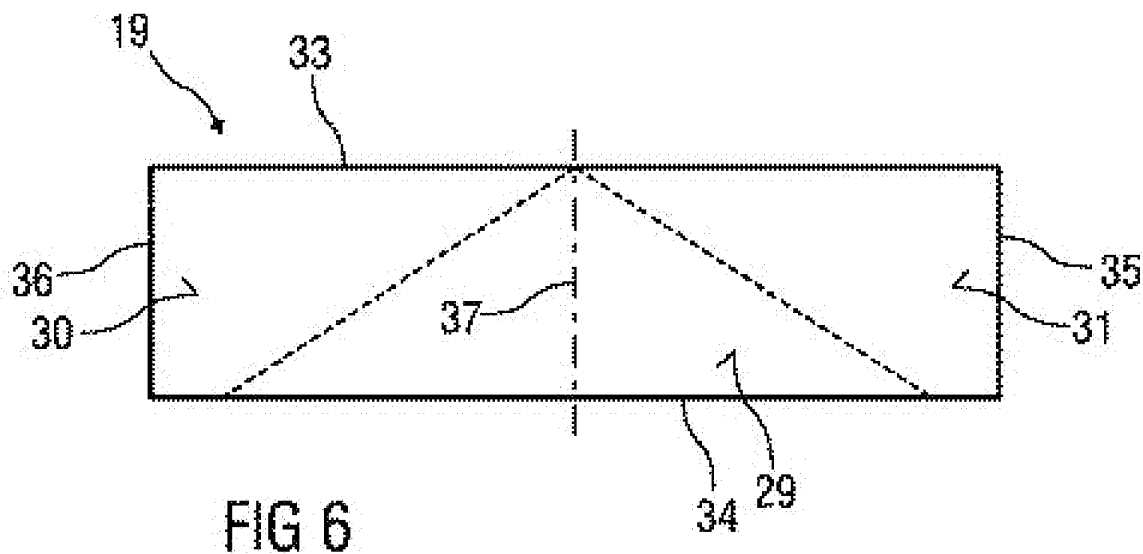


FIG 4

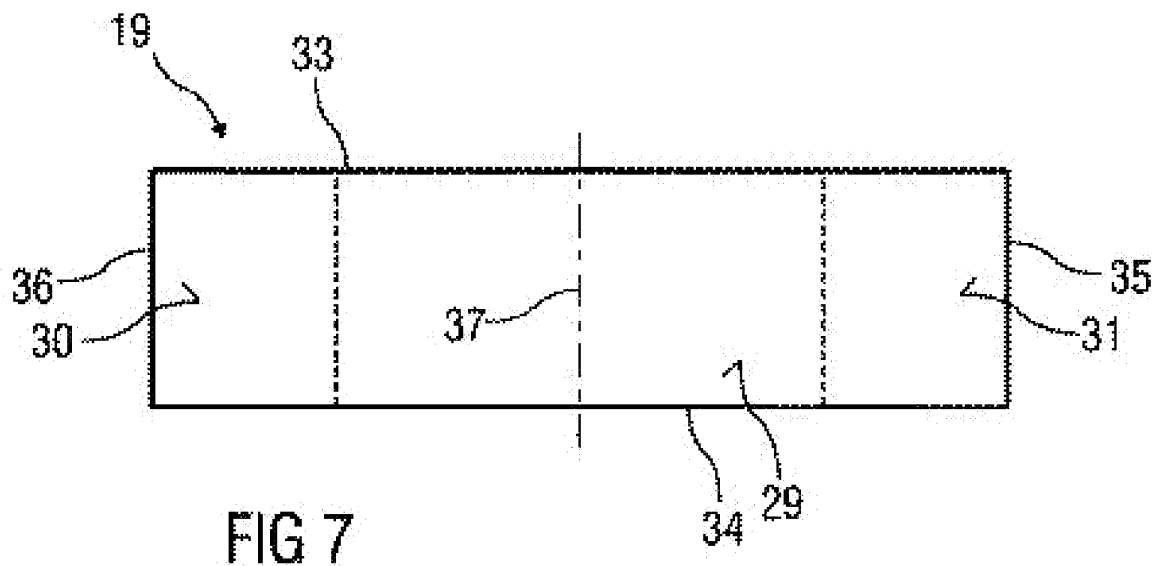
[Figure 5]



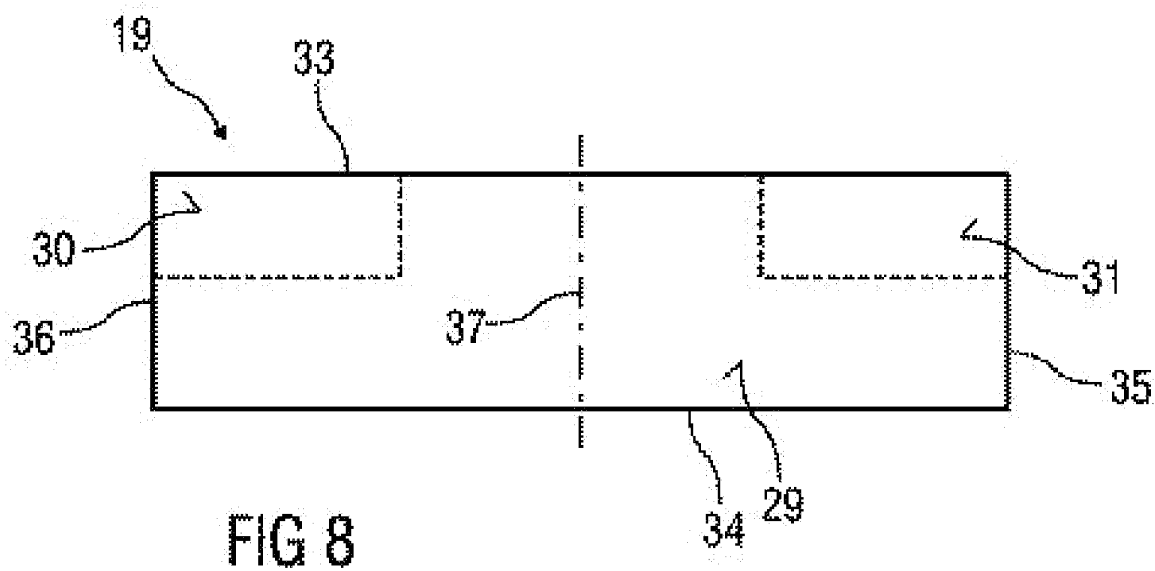
[Fig. 6]



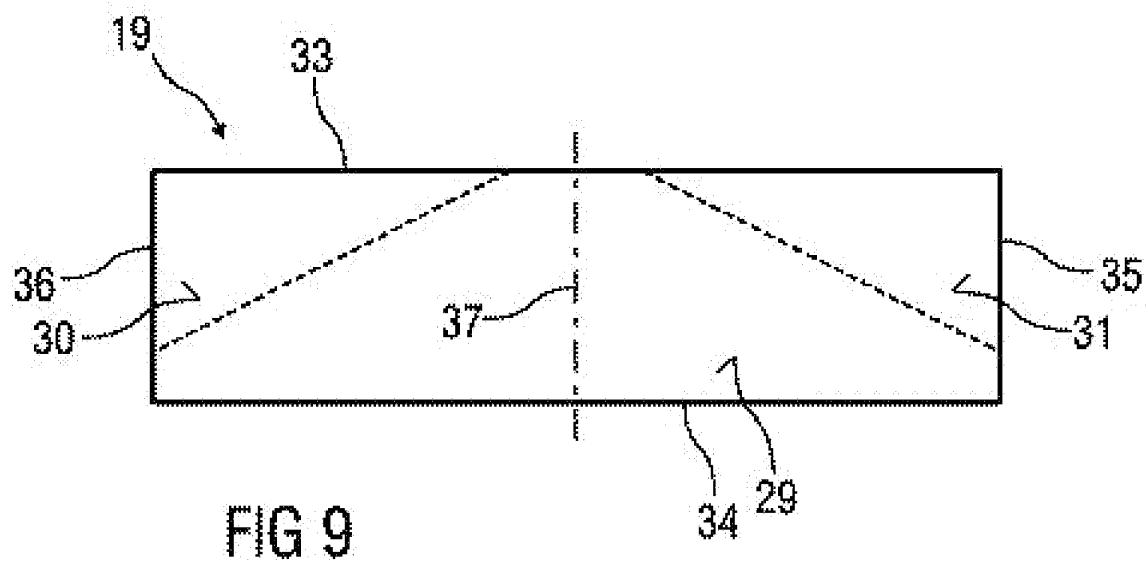
[Fig. 7]



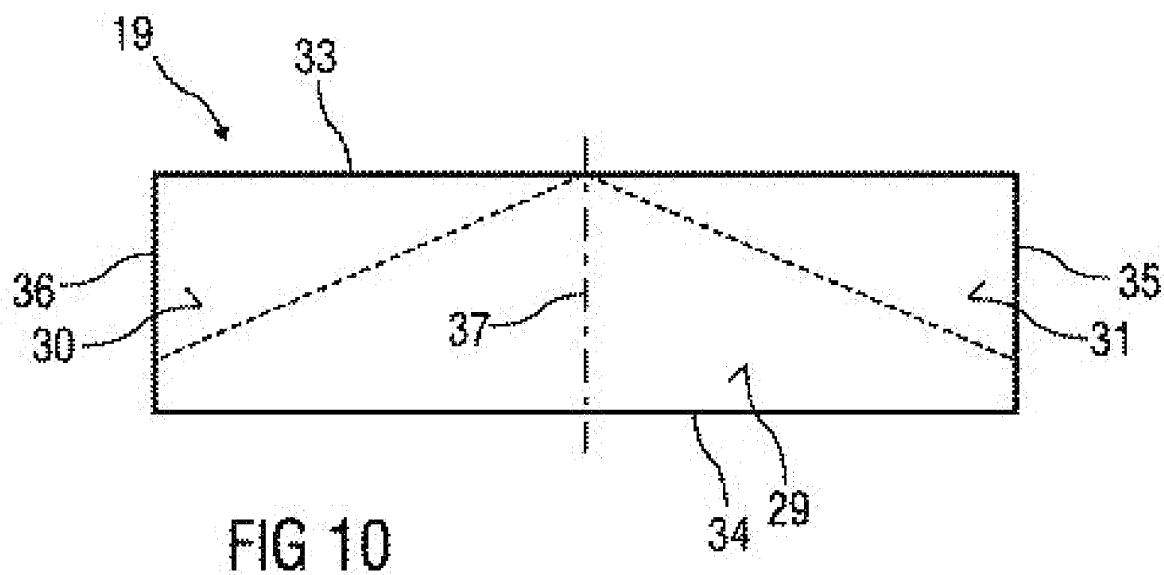
[Fig. 8]



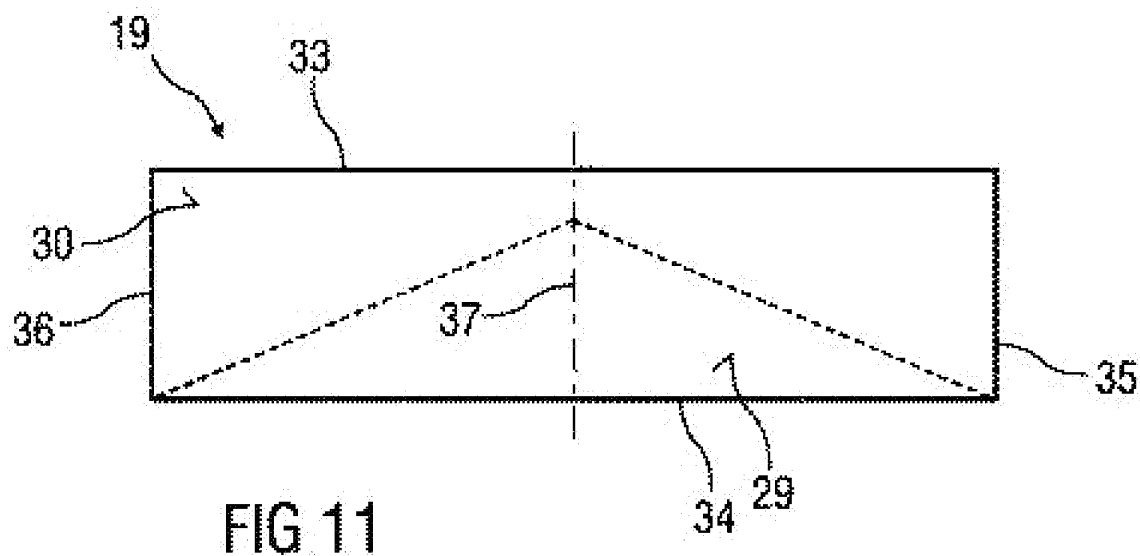
[Fig. 9]



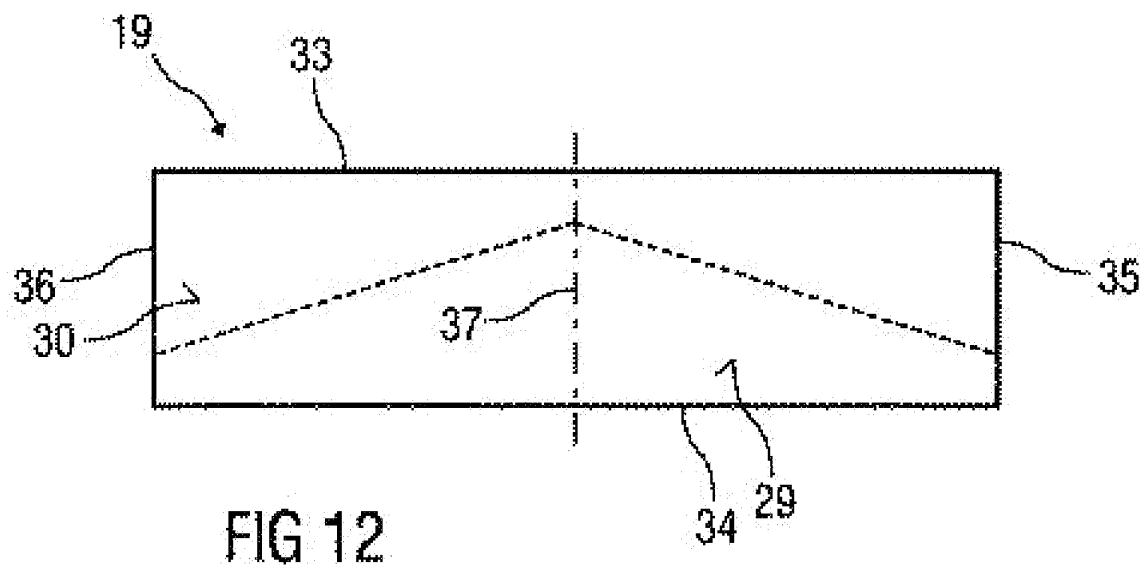
[Fig. 10]



[Fig. 11]



[Fig. 12]



search report

open +

drawing

open —

Representative drawing

1

2

3

Four

Five

6

7

8

9

...

Magnify and Rotate

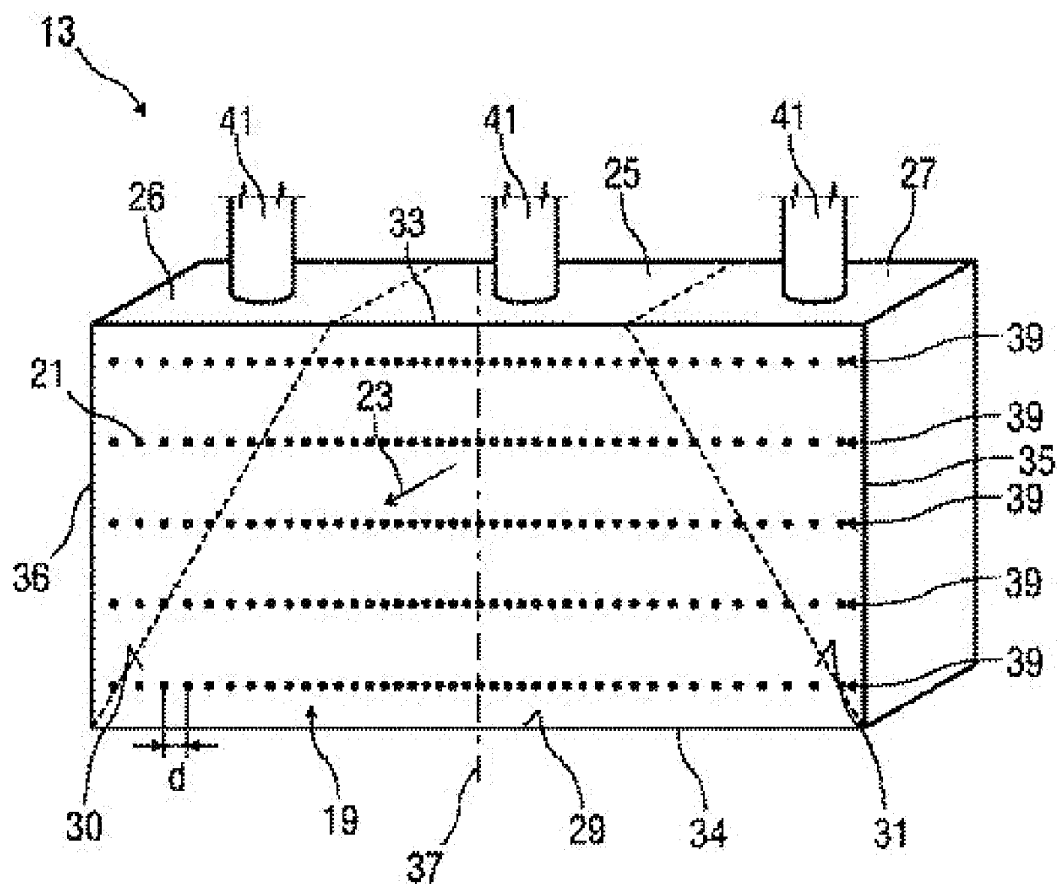


FIG 2

Representative drawing

1 / 1 display



Copyright JPO and INPIT

(P0200)

(19) 日本国特許庁(JP)

(12) 公表特許公報(A)

(11) 特許出願公表番号

特表2019-534792

(P2019-534792A)

(43) 公表日 令和1年12月5日(2019.12.5)

(51) Int.Cl.

B 2 1 B 27/10 (2006.01)

F I

B 2 1 B 27/10

A

B 2 1 B 27/10

C

B 2 1 B 27/10

D

テーマコード(参考)

審査請求 有 予備審査請求 未請求 (全 21 頁)

(21) 出願番号 特願2019-520550 (P2019-520550)
 (86) (22) 出願日 平成29年10月12日(2017.10.12)
 (85) 翻訳文提出日 令和1年6月13日(2019.6.13)
 (86) 国際出願番号 PCT/EP2017/076000
 (87) 国際公開番号 WO2018/073086
 (87) 国際公開日 平成30年4月26日(2018.4.26)
 (31) 優先権主張番号 16194099.4
 (32) 優先日 平成28年10月17日(2016.10.17)
 (33) 優先権主張国・地域又は機関 欧州特許庁(EP)

(71) 出願人 515153152
 ブライメタルズ・テクノロジーズ・オース
 トリア・ゲーエムベーハー
 オーストリア・4031・リンツ・ツーム
 シュトラッセ・44
 (74) 代理人 100133400
 弁理士 阿部 達彦
 (74) 代理人 100110364
 弁理士 実広 信哉
 (72) 発明者 アロイス・ザイリンガー
 オーストリア・4040・リンツ・ハーゼ
 ルグラーベンヴェーク・17
 (72) 発明者 エリッヒ・オービッツ
 オーストリア・7123・メンヒーフ・
 アンガーガッセ・46

最終頁に続く

(54) 【発明の名称】 圧延スタンドのロールの冷却

【要約】

本発明は、圧延スタンドのロールを冷却するための冷却装置に関する。冷却装置は、冷却剤を受け入れて吐出するための冷却ビームを備える。冷却ビームは、前記冷却ビームの吐出側面に配置された複数のフルジェットノズルを有し、前記側面は、ロールに面してロールのロール軸に平行に延在する。ほぼ一定のジェット径を有する冷却剤のジェットを、フルジェットノズルのそれぞれを通して、冷却ビームからロールに向けて吐出方向に噴霧することができる。

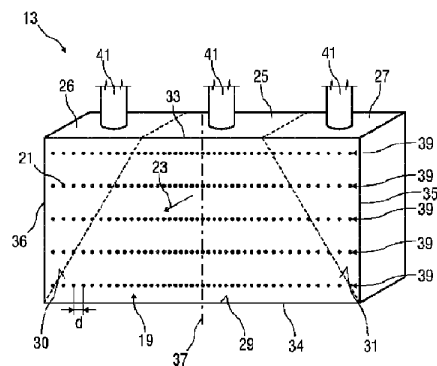


FIG 2

【特許請求の範囲】

【請求項 1】

冷却剤を受け入れて吐出するための冷却棒（13）を備えた、圧延スタンド（1）のロール（5）を冷却するための冷却装置（7）であって、

前記冷却棒（13）が、前記冷却棒（13）の吐出側面（19）に配置された複数のフルジェットノズル（21）を有し、前記吐出側面が、ロール（5）に面して前記ロール（5）のロール軸（17）に平行に延在し、ほぼ一定のジェット径の冷却剤の冷却剤ジェットを、フルジェットノズルのそれぞれを通して、前記冷却棒（13）から前記ロール（5）に向けて吐出方向（23）に吐出することができる、冷却装置（7）。

【請求項 2】

前記冷却棒（13）が、冷却剤を受け入れるための、相互に分離した少なくとも2つの冷却剤室（25～27）に分割され、各冷却剤室（25～27）が、複数のフルジェットノズル（21）が配置された前記冷却棒（13）の前記吐出側面（19）の部分領域（29～31）に対応し、前記フルジェットノズル（21）のそれぞれを通して、冷却剤ジェットを前記冷却剤室（25～27）から前記ロール（5）に向けて吐出することができることを特徴とする、請求項1に記載の冷却装置（7）。

【請求項 3】

第1の冷却剤室（25）が、前記冷却棒（13）の前記吐出側面（19）の第1の部分領域（29）に対応し、前記第1の部分領域（29）が、前記冷却棒（13）の前記吐出側面（19）の中心線（37）に対して鏡面对称であり、軸が前記ロール軸（17）に垂直であることを特徴とする、請求項2に記載の冷却装置（7）。

【請求項 4】

中心線（37）に並行する第1の部分領域（29）の範囲が、前記ロール軸（17）の方向に沿って変化し、前記中心線（37）に沿って最大であることを特徴とする、請求項2または3に記載の冷却装置（7）。

【請求項 5】

第1の部分領域（29）が多角形であることを特徴とする、請求項2から4のいずれか一項に記載の冷却装置（7）。

【請求項 6】

各冷却剤室（25～27）が、前記冷却剤室（25～27）内に冷却剤を供給するための冷却剤供給ライン（41）に接続され、前記冷却剤供給ライン（41）が、前記冷却剤室（25～27）内に、前記冷却剤の前記吐出方向（23）に実質的に垂直に開口していることを特徴とする、請求項2から5のいずれか一項に記載の冷却装置（7）。

【請求項 7】

前記冷却剤室（25～27）内に供給される前記冷却剤の量を、それぞれの制御弁（43）、および／または、それぞれのポンプ（45）によって互いに独立して制御することができることを特徴とする、請求項2から6のいずれか一項に記載の冷却装置（7）。

【請求項 8】

前記冷却剤室（25～27）内に供給される前記冷却剤の量を制御するための自動化システムによって特徴付けられた、請求項2から7のいずれか一項に記載の冷却装置（7）。

【請求項 9】

前記ロール軸（17）に平行な方向に沿って相互に隣り合うフルジェットノズル（21）のノズル間隔（d）が、前記方向に沿って変化していることを特徴とする、請求項1から8のいずれか一項に記載の冷却装置（7）。

【請求項 10】

前記ノズル間隔（d）が、前記冷却棒（13）の前記吐出側面（19）の中央領域において最も狭いことを特徴とする、請求項9に記載の冷却装置（7）。

【請求項 11】

前記ノズル間隔（d）が、約25mmから約50mmの間であることを特徴とする、請

求項 9 または 10 に記載の冷却装置（7）。

【請求項 12】

前記フルジェットノズル（21）が、相互に平行な複数のノズル列（39）になるように配置されていることを特徴とする、請求項 1 から 11 のいずれか一項に記載の冷却装置（7）。

【請求項 13】

前記冷却棒（13）が、前記フルジェットノズル（21）が取り外し可能に固定された、各フルジェットノズル（21）のためのノズル開口を有していることを特徴とする、請求項 1 から 12 のいずれか一項に記載の冷却装置（7）。

【請求項 14】

前記ロール（5）から冷却剤をぬぐい取るためのワイパ（15）であって、前記冷却棒（13）と一緒に駆動させることができるワイパ（15）によって特徴付けられた、請求項 1 から 13 のいずれか一項に記載の冷却装置（7）。

【請求項 15】

ロール（5）と、請求項 1 から 13 のいずれか一項に記載されたようにそれぞれ設計された 2 つの冷却装置（7）と、を備えた圧延スタンド（1）であって、前記 2 つの冷却装置（7）が、前記ロール（5）の両側に配置されている、圧延スタンド（1）。

【発明の詳細な説明】

【技術分野】

【0001】

本発明は、圧延スタンドのロールを冷却するための冷却装置に関する。

【背景技術】

【0002】

圧延素材を圧延するための圧延スタンドは、冷却液体、一般的には冷却水を用いて冷却されるロールを有する。

【0003】

特許文献 1 には、低圧の冷却液体を圧延スタンドのロールにかけることができる、剛性の高い凹状のシェルが開示されている。

【0004】

特許文献 2 には、移動可能な関節式冷却シェルによる圧延スタンドのワークロールの流動冷却が開示されている。この場合、冷却液体は、冷却シェルを用いて主として低圧でかけられるが、さらに、冷却液体は、高圧でかけられて十分な冷却効果を生じる。

【0005】

特許文献 3 には、圧延スタンドのワークロールを冷却するための冷却装置が開示されており、この装置は、関係する圧延スタンドを用いて生産される最も狭い片よりもやや狭い固定スプレー棒を有し、そのときに圧延されている片の幅に対応するワークロールのこれらの部分のみを冷却するための、軸方向に移動可能なスプレー棒を有する。

【0006】

特許文献 4 には、圧延スタンドのワークロールを冷却するための方法が開示されており、この方法では、冷却水が、高圧ではなく低圧でワークロールに噴霧されるが、同時に、かけられる範囲が広くされている。

【0007】

特許文献 5 には、圧延材を冷却するためのスプレー棒が開示されており、このスプレー棒は、圧延材の移動方向に横断して延在し、中央領域および 2 つの縁領域を有して、冷却媒体をそれらのそれぞれに別々に供給することができる。

【先行技術文献】

【特許文献】

【0008】

【特許文献 1】 米国特許出願公開第 号

【特許文献 2】 独国特許出願公開第 号

【特許文献3】特開平 号
【特許文献4】特開昭 号
【特許文献5】国際公開第 号

【発明の概要】

【発明が解決しようとする課題】

【0009】

圧延スタンドのロールを冷却するための改善された冷却装置を特定することが本発明の基本的な目的である。

【課題を解決するための手段】

【0010】

本発明によれば、この目的は、請求項 の特徴によって達成される。

【0011】

本発明の有利な実施形態は、従属請求項の主題を形成する。

【0012】

圧延スタンドのロールを冷却するための本発明による冷却装置は、冷却剤を受け入れて吐出するための冷却棒を備える。冷却棒は、冷却棒の吐出側面に配置された複数のフルジェットノズルを有し、前記側面は、ロールに面してロールのロール軸に平行に延在する。ほぼ一定のジェット径の冷却剤の冷却剤ジェットを、各フルジェットノズルを通して、冷却棒からロールに向けて吐出方向に吐出することができる。

【0013】

フルジェットノズルとは、ほぼ一定のジェット径で実質的に直線状の冷却剤ジェットを吐出することができるノズルを意味するものとする。冷却剤を集中させて吐出するおかげで、フルジェットノズルは、従来使用されてきたファンジェットノズルよりも、冷却棒での同じ冷却剤圧力でより高いロールへの衝撃圧を生じる。全体にかけられた大量の冷却剤の量により、典型的には、数ミリメートルから数センチメートルの厚さの特定の冷却剤膜が常により、良好な放熱のために冷却剤ジェットを衝突させることによって、この膜はできるだけ完全に貫通されるべきであるので、より高い衝撃圧は、ロール表面での冷却作用に直接良い効果を生じる。フルジェットノズルによって生じた、ロールへの冷却剤ジェットの高い衝撃圧のおかげで、冷却棒の冷却剤圧力は、ファンジェットノズルを使用した場合に比べて大きく下げることができ、それによって、冷却装置のエネルギー消費および運用コストを大きく下げることができることは有利である。

【0014】

冷却剤はフルジェットノズルを通して吐出されるので、ロールからスプレー棒までの間隔はさらに、広い範囲にわたってそれほど重要ではなくなり、したがって、ロール直径に適合させる必要はない。したがって、例えば、実質的に直進する冷却剤ジェットによって、冷却剤ジェットの冷却効果に何ら大きな変化もなしに、 から の間の距離で、冷却されるべきロール表面を冷却することができる。

【0015】

冷却剤圧力の低下はまた、負荷の低減、その結果としてノズルの摩耗の低減に関係するので、これもまた、冷却棒の冷却剤圧力の低下の結果、保守費用が低減され、これがフルジェットノズルの使用の別の利点である。

【0016】

本発明の一実施形態では、冷却棒が、冷却剤を受け入れるための、相互に分離した少なくとも一つの冷却剤室に分割されることが想定されている。各冷却剤室は、複数のフルジェットノズルが配置された冷却棒の吐出側面の部分領域に対応し、フルジェットノズルのそれぞれを通して、冷却剤ジェットを冷却剤室からロールに向けて吐出することができる。冷却棒の吐出側面の異なる部分領域に対応する、相互に分離した複数の冷却剤室に、冷却棒を分割すると、互いに独立して、部分領域の冷却剤圧力を制御し、その結果、部分領域によって吐出される冷却剤流量を制御することによって、部分領域の冷却効果を互いに独立して制御することができることは有利である。それによって、位置に応じてロールの

冷却に影響を与えることが可能となり、ロール表面のより強く加熱された領域、例えば、ロール表面の中央領域を、それほど強く加熱されていない領域よりも確実に強く冷却することができることは有利である。

【0017】

本発明の上記の実施形態の展開としては、第 1 の冷却剤室が、冷却棒の吐出側面の第 1 の部分領域に対応し、第 2 の部分領域が、冷却棒の吐出側面の中心線に対して鏡面对称であり、その軸がロール軸に垂直であることが想定されている。例えば、中心線に並行する第 1 の部分領域の範囲は、ロール軸の方向に沿って変化し、中心線に沿って最大である。例えば、第 1 の部分領域は多角形である。第 2 の部分領域が中心線に対して鏡面对称の実施形態は、ロールが概ね同様に、中心線に対して対称的に加熱されるという事実を考慮している。中心線に並行する第 2 の部分領域の範囲がロール軸の方向に沿って変化し、中心線に沿って最大範囲を有することは、ロールが、一般に、中心において最も強く加熱され、ロールの加熱が縁領域に向けて減少するという事実を考慮している。したがって、これに対応した第 2 の部分領域の構成は、第 1 の部分領域によって、位置に依存したロールの熱負荷にロールの冷却を適合させることを可能にする。

【0018】

本発明の別の実施形態では、各冷却剤室が、冷却剤室内に冷却剤を供給するための冷却剤供給ラインに接続され、冷却剤供給ラインが、冷却剤室内に、冷却剤の吐出方向に実質的に垂直に開口していることが想定されている。冷却剤供給ラインが、冷却棒内に、吐出方向に実質的に垂直に開口していることによって、各冷却剤室内の冷却剤の圧力分布をほとんど均一にすることができる。それによって、開口近くフルジェットノズルと開口から離れたフルジェットノズルとの間の圧力勾配がなくなることは有利である。

【0019】

本発明の別の実施形態では、冷却剤室内に供給される冷却剤の量を、それぞれの制御弁、および／または、それぞれのポンプによって互いに独立して制御することができることが想定されている。これによって、上記のように、個々の冷却剤室から吐出される冷却剤ジェットの冷却効果を互いに独立して制御することができる。例えば、通常、10 bar の圧力で冷却水を送出する水供給システムなどの、例えば、いかなるときにも存在する従来の冷却剤供給システムを、関連する圧延システムにおいて使用することができる場合には、制御弁によって冷却剤の量を制御することが特に有利である。この場合、ロール冷却をするために複雑で高価な昇圧システム無しで済ませることができる。適当であれば、制御弁と共に、ポンプによって冷却剤の量を制御することによって、圧延間の休止時、または、低い冷却能力しか必要でない圧延作業の場合に、個々のポンプを止める、またはポンプの動力を下げることができ、それによって、エネルギー消費を低減することができる。

【0020】

本発明の別の実施形態では、冷却剤室内に供給される冷却剤の量を制御するための自動化システムが想定されている。それによって、体積流量をロール表面の温度分布に適合させるために、冷却剤室からロールに吐出される冷却剤の体積流量を自動的に制御することができることは有利である。この場合、冷却剤室内に供給される冷却剤の量は、上記の制御弁および／またはポンプを制御することを通じて、自動化システムによって制御されることが好ましい。

【0021】

本発明の別の実施形態では、ロール軸に平行な方向に沿って相互に隣り合うフルジェットノズルのノズル間隔が前記方向に沿って変化していることが想定されている。この場合、ノズル間隔は、冷却棒の吐出側面の中央領域において最も狭いことが好ましい。例えば、ロール軸に平行な方向に沿うノズル間隔は、約 10 mm から約 20 mm の間である。本発明のこれらの実施形態によって、また、ロール軸に平行な方向に沿うノズル間隔が位置に依存したロール表面の熱負荷に従って変えられるので、フルジェットノズルの配置をこの熱負荷に適合させることもできる。最小のノズル間隔が冷却棒の吐出側面の中央領域にあるのは、ロール表面の中央領域が一般に、最大の熱負荷を受けるという事実を考慮している。

【0022】

本発明の別の実施形態では、フルジェットノズルが、相互に平行な複数のノズル列になるように配置されていることが想定されている。これによって、冷却剤をより広い範囲にわたって、かつ、ロールが回転することと併せて、均一にロールにかけることができることは有利である。

【0023】

本発明の別の実施形態では、冷却棒が、フルジェットノズルが取り外し可能に固定された、各フルジェットノズルのためのノズル開口を有していることが想定されている。本発明のこの実施形態によって、不良なジェットノズルを容易に交換することができることは有利である。

【0024】

本発明の別の実施形態では、ロールから冷却剤をぬぐい取るためのワイバが提供され、ワイバと冷却棒と一緒に駆動させることができる。例えば、ワイバによって、過剰な冷却剤が、圧延材に、および／または、圧延材が一つのロール間を案内されるロール間隙に導かれて、圧延材とロールとの間の摩擦を低減するための潤滑剤を洗い流すことを防ぐことができることは有利である。ワイバと冷却棒と一緒に駆動することができることによって、冷却棒を動かすための追加の装置の必要が除かれることは有利である。この場合、上記ですでに言及したフルジェットノズルを使用する利点は、この場合にもまた効果がある。すなわち、フルジェットノズルを使用することによって、スプレー棒とロールとの間の距離は、広い範囲にわたってそれほど重要ではなくなり、したがって、ロール直径に適合させる必要がなくなる。さらに、本発明はまた、ワイバを有する既存の圧延システムに対しては改造策として特に適しており、例えば、従来の高圧スプレー棒のみを本発明による冷却棒に交換するだけでよい。

【0025】

本発明による圧延スタンドは、ロール、および本発明による一つの冷却装置を備え、一つの冷却装置は、ロールの反対側に配置される。本発明による圧延スタンドの利点は、上記ですでに言及した、本発明による冷却装置の利点から生じる。

【0026】

この発明の上記の特性、特徴、および利点、ならびにこれらを達成する態様は、図面と併せてより詳細に説明される例示的な実施形態の以下の説明と関連して、より明確かつ明瞭に理解されるであろう。

【図面の簡単な説明】

【0027】

【図1】冷却装置を有する圧延スタンドの概略図である。

【図2】冷却棒の第1の例示的な実施形態の概略斜視図である。

【図3】図1に示した冷却棒によって吐出される冷却剤の体積流量を位置の関数として示した図である。

【図4】冷却棒の第1の例示的な実施形態の吐出側面の図である。

【図5】冷却棒の第2の例示的な実施形態の吐出側面の図である。

【図6】冷却棒の第3の例示的な実施形態の吐出側面の図である。

【図7】冷却棒の第4の例示的な実施形態の吐出側面の図である。

【図8】冷却棒の第5の例示的な実施形態の吐出側面の図である。

【図9】冷却棒の第6の例示的な実施形態の吐出側面の図である。

【図10】冷却棒の第7の例示的な実施形態の吐出側面の図である。

【図11】冷却棒の第8の例示的な実施形態の吐出側面の図である。

【図12】冷却棒の第9の例示的な実施形態の吐出側面の図である。

【発明を実施するための形態】

【0028】

すべての図面で、同じ部品には同じ参照符号が付けられている。

【0029】

図 は、圧延素材 を圧延するための圧延スタンド の概略図である。圧延スタンド は、ワークロールとして設計された つのロール 、および各ロール に対して つの冷却装置 を備え、前記装置は、ロール の両側に配置されている。ロール は、ロール間隙 だけ間隔を置いて配置され、圧延材 を形成するために、圧延素材 をロール間隙 に圧延方向に通す。各冷却装置 は、冷却棒 およびワイパ を備える。

【 0 0 3 0 】

各冷却棒 は、冷却剤を受け入れて吐出するように設計されている。冷却剤を吐出するために、冷却棒 は、冷却棒 の吐出側面 に配置された複数のフルジェットノズル を有し、前記側面は、それぞれのロール に面してロール のロール軸 に平行に延在し、ほぼ一定のジェット径の冷却剤ジェットを、フルジェットノズルのそれぞれを通して、冷却棒 からロール に向けて吐出方向 に吐出することができる。冷却剤は、冷却剤供給ライン を経て冷却棒 内に供給することができ、冷却棒 内に供給される冷却剤の量は、制御弁 、および／または、例えば周波数制御のポンプ によって制御することができる。冷却剤は、例えば、水である。

【 0 0 3 1 】

各ワイパ は、それぞれのロール から冷却剤をぬぐい取るように設計され、ロール に向かうように、またこれから離れるように枢動させることができる。各冷却装置 の冷却棒 およびワイパ は、冷却装置 の枢動装置に固定され、したがって、冷却棒 およびワイパ をロール に向かうように、またロール から離れるように一緒に枢動させることができることが好ましい。

【 0 0 3 2 】

図 は、ロール に冷却剤を吐出するための冷却棒 の第 の例示的な実施形態の概略斜視図である。冷却棒 は、相互に分離した つの冷却剤室 ～ に分割されて、冷却剤を受け入れる。各冷却剤室 ～ は、複数のフルジェットノズル が配置された吐出側面の部分領域 ～ に対応し、冷却剤ジェットを冷却剤室 ～ からフルジェットノズルのそれぞれを通してロール に向けて吐出方向 に吐出することができる。吐出側面 は、ロール軸 に平行な つの長手方向辺 、 、およびロール軸 に垂直な つの短手方向辺 、 を有する長方形である。

【 0 0 3 3 】

第 の冷却剤室 は、吐出側面 の中央領域を形成する、冷却棒 の吐出側面 の第 の部分領域 に対応する。第 の部分領域 は、冷却棒 の吐出側面 の中心線 に対して鏡面对称であり、前記軸はロール軸 に垂直であり、第 の長手方向辺 に配置された つの頂点と、第 の長手方向辺 の端点にそれぞれ配置された つの頂点とを有する台形である。

【 0 0 3 4 】

フルジェットノズル は、それぞれがロール軸 に平行に延在する複数のノズル列 になって、吐出側面 に配置されている。この場合、各ノズル列 の相互に隣り合うフルジェットノズル のノズル間隔 d は、中心線 に対して対称的に変化しており、その結果、ノズル間隔 d は、吐出側面 の中央領域において最も狭く、吐出側面 の縁領域に向かって、例えば、放物線状に広がっている。図 に示した例示的な実施形態では、ノズル間隔 d は、各ノズル列 の端部ではノズル列 の中心での間隔の 倍大きくなっている。ノズル間隔 d は、例えば、 から の間を変化する。ノズル列 は、吐出側面 の全範囲にわたって実質的に等間隔に延在し、したがって、ロール のロール表面に比較的均一な冷却効果を生じる。

【 0 0 3 5 】

図 に示した例示的な実施形態のさらなる展開としては、ノズル列 を互いに対してずらして配置することが想定され、したがって、様々なノズル列 のフルジェットノズルが、ロール軸 に垂直な方向に沿って配置されていない。「冷却チャネル」は、ノズル列 に垂直に延在して、そこでは、ロール に冷却剤が吐出されず、その結果、冷却効果が低下するが、この「冷却チャネル」を避けることができるので、ノズル列 の特に均一

な冷却効果が達成されることは有利である。

【0036】

さらに、図の隣り合うつの部分領域～間の境界線に非常に近い、または境界線上にあるフルジェットノズルは、完全に省かれるか、または、図に示した配置に対してずらされて、隣接した部分領域～のつに入るように配置され、それは分離板による冷却筒の内部の冷却剤室～への細分がこのような境界線に沿って延在するからである。

【0037】

各フルジェットノズルは、冷却棒のノズル開口に、例えば、ねじ込み継手によって取り外し可能に取り付けられる。フルジェットノズルはそれぞれ、例えば、約の最小直径のノズル断面を有する。

【0038】

各冷却剤室～は、冷却剤室～内に冷却剤を供給するための冷却剤供給ラインに接続され、冷却剤供給ラインは、冷却剤室～内に、冷却剤の吐出方向に実質的に垂直に開口している。冷却剤供給ラインの断面はそれぞれ、例えば、からの間の直径を有する。

【0039】

冷却剤供給ラインを経て冷却剤室～内に供給される冷却剤の量を、それぞれの制御弁図には示されていない、および／または、それぞれのポンプ図には示されていないによって互いに独立して制御することができる。これによって、冷却剤室～から吐出される冷却剤の量を、ロール表面の様々な領域の異なる熱負荷に対して適合させることができることは有利である。

【0040】

図は、一例として、図に示した冷却棒から吐出されるつの冷却剤の体積流量、 Q_1 、 Q_2 を、ロール軸に平行な方向に沿う位置 y の関数として示す。ここで、体積流量 Q_1 、 Q_2 は定格流量に対する比率で示されている。

【0041】

定格流量は、中央位置 y における第の体積流量である。第の体積流量は、冷却剤が、すべての冷却剤室～に対して同じ与定の定格圧力で、すべてのつの冷却剤室～内に供給された場合に生じる。第の体積流量は、中央位置 y で最大となる放物線の形状を有し、中央位置 y からつの端部領域に向かって減少して、中央位置 y の値の半分になる。第の体積流量がこのような形状になる理由は、ノズル列の中心から2つの端部へ、ノズル列に沿うフルジェットノズルのノズル間隔 d が倍になるからであり、ノズル間隔 d の放物線状の増大が仮定される。

【0042】

第の体積流量は、定格圧力のほぼ倍の冷却剤圧力で冷却剤を第の冷却剤室内に供給し、定格圧力のほぼ半分の冷却剤圧力で冷却剤を他のつの冷却剤室、内のそれぞれに供給した場合に生じる。

【0043】

第の体積流量は、定格圧力のほぼ半分の冷却剤圧力で冷却剤を第の冷却剤室内に供給し、定格圧力のほぼ倍の冷却剤圧力で冷却剤を他のつの冷却剤室、内のそれぞれに供給した場合に生じる。

【0044】

図は、ロール軸に平行な方向に沿う位置 y への依存性が異なるパターンを有する体積流量 Q_1 、 Q_2 を、冷却剤室～の異なる冷却剤圧力によって生じさせることができ、その結果、冷却棒から吐出される体積流量 Q_1 、 Q_2 を、ロール表面の温度分布に適合させることができることを示している。各冷却剤室～の冷却剤圧力は、それぞれの制御弁および／またはそれぞれのポンプによって設定される。

【0045】

図～図はそれぞれ、冷却棒の別の例示的な実施形態の吐出側面を示す。これら

の例示的な実施形態は、図 1 に示した例示的な実施形態とは、冷却剤室 100 ～ 102、およびそれに対応する吐出側面 100 の部分領域 100 の形状および数だけが異なる。図 1 に示した例示的な実施形態のように、フルジェットノズル 100 はそれぞれ、複数のノズル列 100 になるように配置され、それぞれの場合のノズル間隔 d は、それに沿って中央から 100 の端部に向かって増大する。したがって、図 1 ～図 1 のフルジェットノズル 100 はここでまた説明することはしない。吐出側面 100 のフルジェットノズル 100 の、図 1 に示した例示的な実施形態と同様な分布によって、図 1 ～図 1 に示される例示的な実施形態のそれぞれで、図 1 と同様な体積流量 100、100 を生じさせることができる。

【 0 0 4 6 】

図 1 に示した例示的な実施形態のように、図 1 ～図 1 に示した例示的な実施形態はそれぞれ、100 の冷却剤室 100、および吐出側面 100 にそれに対応する部分領域 100 を有する。図 1 に示した例示的な実施形態と同様に、第 100 の部分領域 100 は、冷却棒 100 の吐出側面 100 の、ロール軸 100 に垂直な中心線 100 に対して鏡面对称であり、他の 100 の部分領域 100、100 は、第 100 の部分領域 100 と中心線 100 の異なる側で隣接する。

【 0 0 4 7 】

図 1 は、第 100 の部分領域 100 が、第 100 の長手方向辺 100 に配置された 100 の頂点と、第 100 の長手方向辺 100 に配置された 100 の頂点とを有する台形である例示的な実施形態を示す。

【 0 0 4 8 】

図 1 は、第 100 の部分領域 100 が、中心線 100 と第 100 の長手方向辺 100 との交点に配置された 100 の頂点と、第 100 の長手方向辺 100 の端部に配置された 100 の頂点とを有する三角形である例示的な実施形態を示す。

【 0 0 4 9 】

図 1 は、第 100 の部分領域 100 が、中心線 100 と第 100 の長手方向辺 100 との交点に配置された 100 の頂点と、第 100 の長手方向辺 100 に配置された 100 の頂点とを有する三角形である例示的な実施形態を示す。

【 0 0 5 0 】

図 1 は、第 100 の部分領域 100 が、頂点 100 が長手方向辺 100、100 に配置された長方形である例示的な実施形態を示す。この例示的な実施形態では、100 の外側の部分領域 100、100 を経て冷却剤を吐出しないので、冷却剤の吐出を吐出側面 100 の中央領域からのみ生じさせることができる。したがって、この例示的な実施形態は、異なる幅の圧延素材 100 を圧延するのに特に適している。

【 0 0 5 1 】

図 1 は、第 100 の部分領域 100 および第 100 の部分領域 100 がそれぞれ、第 100 の長手方向辺 100 上の頂点と、第 100 の長手方向辺 100 の一端に配置された頂点と、短手方向辺 100、100 に配置された頂点とを有する長方形である例示的な実施形態を示す。

【 0 0 5 2 】

図 1 は、第 100 の部分領域 100 が、第 100 の長手方向辺 100 上の 100 の頂点と、第 100 の長手方向辺 100 の端部にそれぞれ配置された 100 の頂点と、それぞれの短手方向辺 100、100 上の頂点とを有する六角形である例示的な実施形態を示す。

【 0 0 5 3 】

図 1 は、第 100 の部分領域 100 が、中心線 100 と第 100 の長手方向辺 100 との交点に配置された 100 の頂点と、第 100 の長手方向辺 100 の端部にそれぞれ配置された 100 の頂点と、それぞれの短手方向辺 100、100 上の 100 の頂点とを有する五角形である例示的な実施形態を示す。

【 0 0 5 4 】

図 1 および図 1 に示した例示的な実施形態はそれぞれ、100 の冷却剤室 100、100、およびそれに対応する、吐出側面 100 の部分領域 100、100 を有する。両方の部分領域 100 は、冷却棒 100 の吐出側面 100 の、ロール軸 100 に垂直な中心線 100 に対して鏡面对称である。

【 0 0 5 5 】

図 1 は、第 100 の部分領域 100 が、中心線 100 に配置された 100 の頂点と、第 100 の長手方向辺 100 の端部にそれぞれ配置された 100 の頂点とを有する三角形である例示的な実施形態を示す。

。

【 0 0 5 6 】

図 は、第 の部分領域 が、中心線 に配置された つの頂点と、第 の長手方向辺の端部にそれぞれ配置された つの頂点と、それぞれの短手方向辺 、 上の頂点とを有する五角形である例示的な実施形態を示す。

【 0 0 5 7 】

本発明を、好ましい例示的な実施形態によって、より詳細に例示および説明したが、本発明は、開示した例に限定されるものではなく、当業者は、本発明の保護の範囲を超えずにこれらから他の変形を得ることができる。

【符号の説明】

【 0 0 5 8 】

圧延スタンド
圧延素材、圧延材
ロール
冷却装置
ロール間隙
圧延方向
冷却棒
ワイパ
ロール軸
吐出側面
ノルジェットノズル
吐出方向
～ 冷却剤室
～ 部分領域
、 長手方向辺
、 短手方向辺
中心線
ノズル列
冷却剤供給ライン
制御弁
ポンプ
ノズル間隔

【 図 1 】

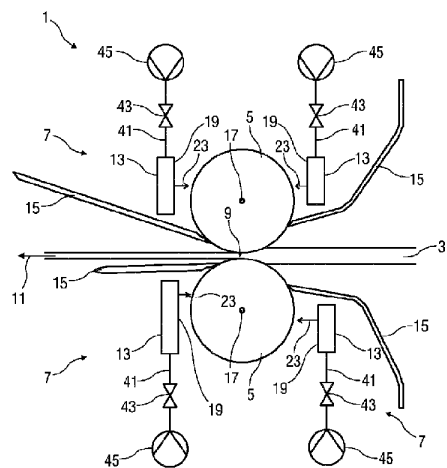


FIG 1

【 図 2 】

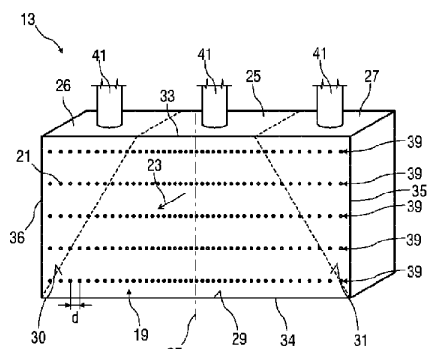


FIG 2

【 図 3 】

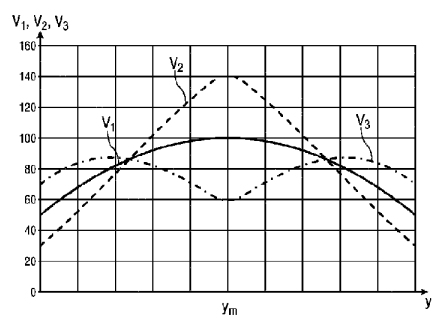


FIG 3

【 図 5 】

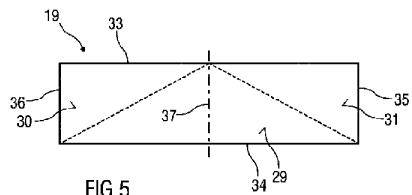


FIG 5

【 図 6 】

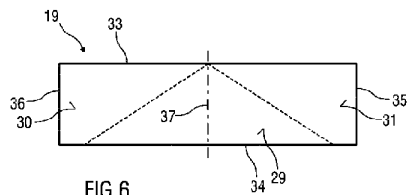


FIG 6

【 図 7 】

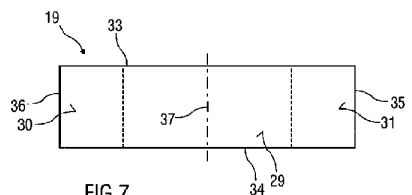


FIG 7

【 図 4 】

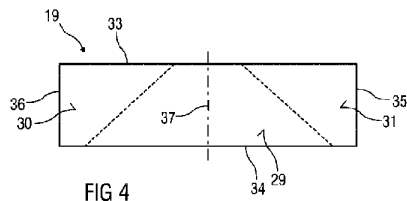
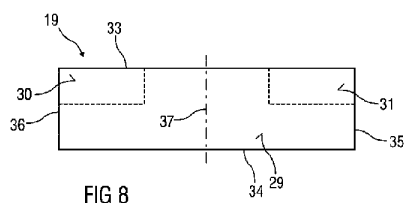
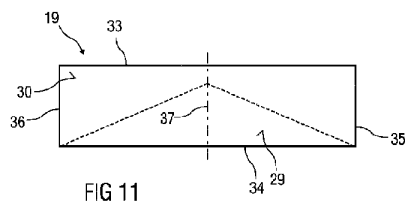


FIG 4

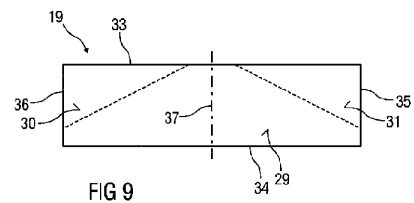
【 8 】



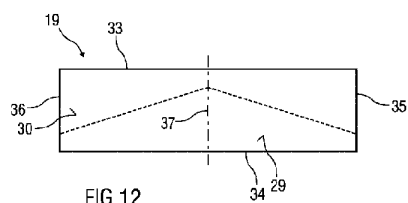
【 1 1 】



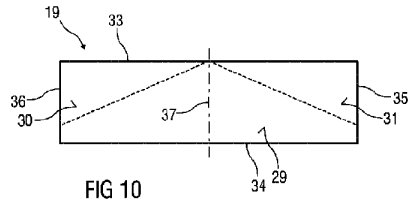
【 9 】



【 1 2 】



【 1 0 】



INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2017/076000

A. CLASSIFICATION OF SUBJECT MATTER INV. B21B27/10 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPO		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) B21B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31 August 2000 (2000-08-31)	1,15
Y	page 5, paragraph 3 - page 7, paragraph 3	2-5
X	WO 2008/149195 A1 (ARCELOMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11 December 2008 (2008-12-11)	1,15
Y	page 3, line 20 - page 4, line 12; figures 1,2	2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22 October 2014 (2014-10-22)	2-5
	paragraph [0017] - paragraph [0027]; figures 1-3	
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6 August 2015 (2015-08-06)	1
	page 4, line 8 - line 17	
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
11 January 2018		06/03/2018
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2260 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Frisch, Ulrich

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

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

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

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims, it is covered by claims Nos.:
1-5, 15

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/076000

The International Searching Authority has found that the international application contains multiple (groups of) inventions, as follows:

1. Claims 1-5, 15

Cooling device for cooling a roller, wherein two coolant chambers are provided which are separated from each other.

2. Claims 1, 6-8

Cooling device for cooling a roller, wherein the feed/control of the coolant is further defined.

3. Claims 1, 9-13

Cooling device for cooling a roller, wherein the distance of the nozzles is defined.

4. Claims 1, 14

Cooling device for cooling a roller, wherein an additional stripper is defined.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2017/076000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 20006508	U1	31-08-2000	DE 20006508 U1 31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195	A1	11-12-2008	AU 2008259470 A1 11-12-2008
		BR P10812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428	A1	22-10-2014	CN 105188975 A 23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832	A1	06-08-2015	DE 102014001146 A1 06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

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

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES INV. B21B27/10 ADD.		
Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC		
B. RECHERCHIERTE GEBIETE Recherchierte Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole) B21B		
Recherchierte, aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen		
Während der Internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe) EPO-Internal, WPI Data		
C. ALS WESENTLICH ANGESEHENE UNTERLAGEN		
Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	DE 200 06 508 U1 (ACHENBACH BUSCHHUETTEN GMBH [DE]) 31. August 2000 (2000-08-31)	1,15
Y	Seite 5, Absatz 3 - Seite 7, Absatz 3	2-5
X	WO 2008/149195 A1 (ARCELORMITTAL FRANCE [FR]; VANDERSCHUEREN DIRK [BE]; VAN POECKE PATRIC) 11. Dezember 2008 (2008-12-11)	1,15
Y	Seite 3, Zeile 20 - Seite 4, Zeile 12; Abbildungen 1,2	2-5
Y	EP 2 792 428 A1 (SIEMENS VAI METALS TECH GMBH [AT]) 22. Oktober 2014 (2014-10-22)	2-5
	Absatz [0017] - Absatz [0027]; Abbildungen 1-3	
A	WO 2015/113832 A1 (LOI THERMPROCESS GMBH [DE]) 6. August 2015 (2015-08-06)	1
	Seite 4, Zeile 8 - Zeile 17	
☐ Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen ☒ Siehe Anhang Patentfamilie		
* Besondere Kategorien von angegebenen Veröffentlichungen : "A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist "E" frühere Anmeldung oder Patent, die bzw. das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist "L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Recherchenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt) "O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausübung oder andere Maßnahmen bezieht "P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist "T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist "X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann allein aufgrund dieser Veröffentlichung nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden "Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist "&" Veröffentlichung, die Mitglied derselben Patentfamilie ist		
Datum des Abschlusses der internationalen Recherche 11. Januar 2018		Absenddatum des internationalen Recherchenberichts 06/03/2018
Name und Postanschrift der internationalen Recherchenbehörde Europäisches Patentamt, P.B. 5818 Patentaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016		Bevollmächtigter Bediensteter Frisch, Ulrich

2

Formblatt PCT/ISA210 (Blatt 2) (April 2005)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2017/076000

Feld Nr. II Bemerkungen zu den Ansprüchen, die sich als nicht recherchierbar erwiesen haben (Fortsetzung von Punkt 2 auf Blatt 1)

Gemäß Artikel 17(2)a) wurde aus folgenden Gründen für bestimmte Ansprüche kein internationaler Recherchenbericht erstellt:

1. ☐ Ansprüche Nr. weil sie sich auf Gegenstände beziehen, zu deren Recherche diese Behörde nicht verpflichtet ist, nämlich
2. ☐ Ansprüche Nr. weil sie sich auf Teile der internationalen Anmeldung beziehen, die den vorgeschriebenen Anforderungen so wenig entsprechen, dass eine sinnvolle internationale Recherche nicht durchgeführt werden kann, nämlich
3. ☐ Ansprüche Nr. weil es sich dabei um abhängige Ansprüche handelt, die nicht entsprechend Satz 2 und 3 der Regel 6.4 a) abgefasst sind.

Feld Nr. III Bemerkungen bei mangelnder Einheitlichkeit der Erfindung (Fortsetzung von Punkt 3 auf Blatt 1)

Diese Internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere Erfindungen enthält:

siehe Zusatzblatt

1. ☐ Da der Anmelder alle erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht auf alle recherchierbaren Ansprüche.
2. ☐ Da für alle recherchierbaren Ansprüche die Recherche ohne einen Arbeitsaufwand durchgeführt werden konnte, der zusätzliche Recherchengebühr gerechtfertigt hätte, hat die Behörde nicht zur Zahlung solcher Gebühren aufgefordert.
3. ☐ Da der Anmelder nur einige der erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser internationale Recherchenbericht nur auf die Ansprüche, für die Gebühren entrichtet worden sind, nämlich auf die Ansprüche Nr.
4. ☒ Der Anmelder hat die erforderlichen zusätzlichen Recherchengebühren nicht rechtzeitig entrichtet. Dieser internationale Recherchenbericht beschränkt sich daher auf die in den Ansprüchen zuerst erwähnte Erfindung; diese ist in folgenden Ansprüchen erfasst:
1-5, 15

Bemerkungen hinsichtlich eines Widerspruchs

- ☐ Der Anmelder hat die zusätzlichen Recherchengebühren unter Widerspruch entrichtet und die gegebenenfalls erforderliche Widerspruchsgebühr gezahlt.
- ☐ Die zusätzlichen Recherchengebühren wurden vom Anmelder unter Widerspruch gezahlt, jedoch wurde die entsprechende Widerspruchsgebühr nicht innerhalb der in der Aufforderung angegebenen Frist entrichtet.
- ☐ Die Zahlung der zusätzlichen Recherchengebühren erfolgte ohne Widerspruch.

WEITERE ANGABEN

PCT/ISA/ 210

Die internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere (Gruppen von) Erfindungen enthält, nämlich:

1. Ansprüche: 1-5, 15

Kühlvorrichtung zur Kühlung einer Walze, wobei zwei voneinander getrennte Kühlmittelkammern vorgesehen sind.

2. Ansprüche: 1, 6-8

Kühlvorrichtung zur Kühlung einer Walze, wobei die Zuleitung / Steuerung des Kühlmittels weiter definiert wird.

3. Ansprüche: 1, 9-13

Kühlvorrichtung zur Kühlung einer Walze, wobei der Abstand der Düsen definiert wird.

4. Ansprüche: 1, 14

Kühlvorrichtung zur Kühlung einer Walze, wobei ein zusätzlicher Abstreifer definiert wird

INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Akkordzeichen

PCT/EP2017/076000

Im Recherchenbericht angeführtes Patentedokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie	Datum der Veröffentlichung
DE 20006508 U1	31-08-2000	DE 20006508 U1	31-08-2000
		EP 1142652 A2	10-10-2001
		JP 2001347307 A	18-12-2001
		US 2001027672 A1	11-10-2001
WO 2008149195 A1	11-12-2008	AU 2008259470 A1	11-12-2008
		BR P10812201 A2	25-11-2014
		CA 2690098 A1	11-12-2008
		CN 101702888 A	05-05-2010
		EP 2014379 A1	14-01-2009
		EP 2164651 A1	24-03-2010
		JP 5380438 B2	08-01-2014
		JP 2010528870 A	26-08-2010
		KR 20100020462 A	22-02-2010
		RU 2009149178 A	20-07-2011
		SI 2164651 T1	30-08-2013
		UA 99295 C2	10-08-2012
		US 2010180657 A1	22-07-2010
		WO 2008149195 A1	11-12-2008
		ZA 200908405 B	28-07-2010
EP 2792428 A1	22-10-2014	CN 105188975 A	23-12-2015
		EP 2792428 A1	22-10-2014
		EP 2986400 A1	24-02-2016
		JP 6110015 B2	05-04-2017
		JP 2016515474 A	30-05-2016
		KR 20150143746 A	23-12-2015
		RU 2015141167 A	17-05-2017
		US 2016052033 A1	25-02-2016
		WO 2014170139 A1	23-10-2014
WO 2015113832 A1	06-08-2015	DE 102014001146 A1	06-08-2015
		EP 3099829 A1	07-12-2016
		WO 2015113832 A1	06-08-2015

Formblatt PCT/ISA210 (Anhang Patentfamilie) (April 2005)

フロントページの続き

指定国・地域

発明者 ルーカス・ビヒラー

オーストリア・4 0 4 0・リンツ・シュトラウムリングヴェーク・7



Australian Government
IP Australia

29 April 2020



Delivering a world leading IP system

www.ipaustralia.gov.au

ABN: 38 113 072 755

Examination report No. 1 for standard patent application

Griffith Hack
GPO Box 4164
Sydney NSW 2001
Australia

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

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

Dear Griffith Hack,

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

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

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

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

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

Yours sincerely,

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



Report details

Basis of the report

In examining this application I have considered:

- the PCT pamphlet as originally filed

Summary of novelty, inventive step and patentable subject matter

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

Detailed objections on issues that have been identified

Documents cited or considered relevant

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

[1] Cited in WO 2017019552

Special categories of cited documents:

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

Novelty and inventive step

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

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

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

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

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

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

END OF REPORT

United States District Court,
E.D. Texas, Marshall Division.

RETRACTABLE TECHNOLOGIES, INC., and Thomas J. Shaw,
Plaintiffs.

v.

BECTON DICKINSON & CO,
Defendant.

Civil Action No. 2:07-CV-250 (DF)

Jan. 20, 2009.

Bradley Carroll Weber, Paul Featherstone Schuster, Locke Liddell & Sapp, George E. Bowles, Mark Richard Backofen, Michael V. Powell, Monty Lee Ross, Roy William Hardin, Locke Lorde Bissell & Liddell LLP, Dallas, TX, Deborah J. Race, Otis W. Carroll, Jr., Ireland Carroll & Kelley, Tyler, TX, G. William Lavender, Lavender Law, Texarkana, AR, for Plaintiffs.

Robert A. Atkins, Jacqueline Pilar Rubin, Paul Weiss Rifkind Wharton & Garrison, Alexandra B. McTague, Wilmer Cutler Pickering Hale & Dorr, New York, NY, Alistair Byrne Dawson, David J. Beck, Beck Redden & Secrest, Houston, TX, Heath A. Brooks, Mark L. Rienzi, Stephanie K. Wood, William G. McElwain, Los Angeles, CA, Lisa J. Pirozzolo, William F. Lee, Wilmer Cutler Pickering Hale & Dorr, Boston, MA, William David Carter, Sr., Mercy Carter Tidwell, L.L.P., Texarkana, TX, for Defendant.

Stephen David Wilson, Locke Lord Bissell & Liddell LLP, Dallas, TX.

CLAIM CONSTRUCTION ORDER

Construing Terms in U.S. Patent Nos. 5,632,733, 6,090,077, and 7,351,224

DAVID FOLSOM, **District Judge.**

Before the Court are RTI's Opening Brief on Claim Construction (Dkt. No. 111), BD's Opening Claim Construction Brief (Dkt. No. 112), RTI's Reply Brief on Claim Construction (Dkt. No. 113) and BD's Notice of Supplemental Authority (Dkt. No. 116). Also before the Court are the Local Patent Rule (LPR) 4-3 Joint Claim Construction and Prehearing Statement (Dkt. No. 110) and the LPR 4-5 Joint Claim Construction Chart (Dkt. No. 114). A claim-construction hearing, in accordance with *Markman v. Westview Instruments*, 52 F.3d 967 (Fed.Cir.1995) (en banc), *aff'd*, 517 U.S. 370 (1996), was held in Texarkana on December 4, 2008. *See* Dkt. No. 118 (hearing transcript). After hearing the arguments of counsel and reviewing the relevant pleadings, presentation materials, other papers, and case law, the Court finds the disputed terms of the patents-in-suit should be construed as set forth herein.

TABLE OF CONTENTS

I.	BACKGROUND	-1-
II.	LEGAL PRINCIPLES	-1-
III.	PATENTS-IN-SUIT	-2-
IV.	U.S. PATENT NO. 5,632,733	-3-

A.	Overview	-3-
B.	Claim Construction	-5-
1.	"body"	-5-
2.	"barrel"	-6-
3.	"nose"/"nose portion"	-9-
4.	"transition zone"	-
		10-
5.	"inwardly facing surface"	-
		11-
6.	"retraction mechanism sealingly disposed in the nose"	-
		12-
7.	"retainer member"	-
		12-
8.	"bridging portion"	-
		16-
9.	"releaseably installed by sliding engagement of said retainer member and said inwardly facing surface"	-
		18-
10.	"sliding engagement producing a holding force"	-
		20-
11.	"outwardly facing surface"	-
		20-
V.	U.S. PATENT NO. 6,090,077	-
		21-
A.	Overview	-
		21-
B.	Claim Construction	-
		22-
1.	"body"/"barrel"	-
		22-
2.	"vent"	-
		22-
3.	"the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger"	-
		22-
4.	"a front end configured to operate the retraction mechanism"	-
		23-
VI.	U.S. PATENT NO. 7,351,224	-
		23-
A.	Overview	-
		23-
B.	Claim Construction	-
		24-
1.	"body"/"barrel"/"bridging portion"/"retainer member"	-
		24-
2.	"continuous retainer member surrounding the inner head"	-2
		5-
3.	"end cap"	-
		25-
4.	"wherein the continuous retainer member is releasable from the inner head"	-
		27-

I. BACKGROUND

In the present lawsuit, Retractable Technologies, Inc. and Thomas Shaw (collectively "RTI") contend certain safety syringes made by Becton, Dickinson and Co. ("BD") infringe claims of U.S. Patent Nos. 5,578,011 ("the '011 Patent"), 5,632,733 ("the '733 Patent"), 6,090,077 ("the '077 Patent"), and 7,351,224 ("the '224 Patent"). Both the '011 and '733 Patents are entitled "Tamperproof retractable syringe," while the '077 Patent is entitled "Syringe plunger assembly and barrel," and the '224 Patent is entitled "Retractable syringe assembly designed for one use." All three later patents are continuations-in-part of the '011 Patent. '733 at [63]; '077 at [63]; '224 at [63]. FN1

FN1. The parties have agreed on the construction of one term in the '011 Patent. The parties agree that "frictionally held retraction mechanism" will be construed as "a retraction mechanism held by friction." The Court has no reason to disagree and therefore adopts the parties' construction. Because no terms from the '011 Patent are in dispute this Claim Construction Order will not address the '011 Patent further.

II. LEGAL PRINCIPLES

A determination of patent infringement involves two steps: first, the patent claims are construed, and, second, the claims are compared to the allegedly infringing device. *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1455 (Fed.Cir.1998) (en banc). The legal principles of claim construction were reexamined by the Federal Circuit in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed.Cir.2005) (en banc). The Federal Circuit in *Phillips* expressly reaffirmed the principles of claim construction as set forth in *Markman v. Westview Instruments, Inc.*, 52 F.3d 967 (Fed.Cir.1995) (en banc), *aff'd*, 517 U.S. 370 (1996), *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576 (Fed.Cir.1996), and *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111 (Fed.Cir.2004). Claim construction is a legal question for the courts. *Markman*, 52 F.3d at 979.

The Court, in accordance with the doctrines of claim construction that it has outlined in the past, will construe the claims of the RTI Patents below. *See Pioneer v. Samsung*, No. 2:07-CV-170, Dkt. No. 94, at 2-8 (E.D. Tex. filed Mar. 10, 2008) (claim-construction order).

III. PATENTS-IN-SUIT

The patents-in-suit are directed to particular features of a retractable syringe. The '773 Patent issued on May 27, 1997 from an application filed on September 29, 1995. The '773 Patent is a continuation-in-part of U.S. Patent App. No. 438,954, which was eventually issued as the '011 Patent. '733 at [63]. The '773 Patent abstract reads:

A tamperproof retractable non-reusable syringe has a one piece hollow outer body with a barrel for a slidable plunger, a transition zone and a smaller diameter nose portion. An elongated needle holder and spring combination is installable from the rear of the outer body, guided into the nose portion and held by cooperating inwardly and outwardly facing surfaces oriented in the direction of retraction at the most constricted part of the transition zone where the nose begins. The plunger has an opening with a dislodgable stopper for receiving parts of the retraction mechanism. The stopper and the head of the needle holder are of significantly reduced diameter from the injection fluid chamber to resist blowing out prematurely. In one embodiment the head of the needle holder is surrounded by a separable retainer member which is slidingly removed by contact with the tip of the plunger after the stopper is mostly or fully removed to avoid cumulation of force required for retraction after the injection. In a second embodiment the head of the

needle holder is clamped and held by constricting forces imposed by stress on the outer body induced by interference fit. Release occurs by slight expansion on the barrel by contact of the plunger tip with a small internal ramp in the outer barrel. Both embodiments have a plunger cap configured to enter an opening in the outer body to provide an additional tamperproof feature.

'773 Patent at [57].

The '077 Patent issued July 18, 2000 from an application filed on April 25, 1997. The '077 Patent is a continuation-in-part of both the '773 and '011 Patents. '077 at [63]. The abstract from the '077 Patent mirrors that of the '773 Patent, but contains one additional sentence: "The retraction cavity is provided with venting structure to assure that all uninjected fluid is retained within the syringe body." Id. at [57].

The '224 Patent issued April 1, 2008 from an application filed July 17, 2000. The '224 Patent is a continuation-in-part of the '007, '773, and '011 Patents. '224 at [63]. The '773 Patent abstract reads:

A syringe assembly having a retractable needle, the syringe assembly being rendered unusable after a single injection and having a hollow syringe body, a retraction mechanism with a spring disposed in the front portion of the syringe and an inner head, a continuous retainer member surrounding the inner head, and a bridging portion disposed between the continuous retainer member and the inner head, wherein the bridging portion couples the continuous retainer member and the inner head to form a fluid seal between a fluid passageway and the barrel prior to retraction, and a plunger reciprocally disposed inside the barrel and forming a variable chamber between the plunger and the needle holder prior to and during retraction, wherein the continuous retainer member is releasable from the inner head of the needle holder when the plunger is further depressed inside the barrel following injection.

Id. at [57].

IV. U.S. PATENT NO. 5,632,733

A. Overview

RTI has asserted claims 1, 24, and 36 of the '733 Patent against BD in this lawsuit. Dkt. No. 114. For reference, asserted claims 1 and 24 are reproduced below (terms to be construed emphasized):

1. A tamperproof retractable syringe for injecting fluid wherein the syringe has a one piece **body** and a retraction mechanism assembleable from the rear which resists high blowout pressure during an injection but can be retracted with low plunger force after injection comprising:

a one piece hollow outer **body** having a longitudinally extending wall, comprising an elongated **barrel** and **nose**, with a **transition zone** connecting the **barrel** and **nose**, the **nose** having a reduced cross sectional area relative to the **barrel** and an **inwardly facing surface** in the wall at the most constricted part of the **transition zone** where the nose begins;

a plunger assembly disposed partially within the elongated **barrel**, the plunger having a head in slidable sealed contact with the interior of the outer **body**, a forward portion and a retraction cavity therein for receiving parts of a retraction mechanism;

a **retraction mechanism sealingly disposed in the nose**, the retraction mechanism having a retractable part comprising a needle holder having an elongated **body** having a needle holding tip portion in front and a head in back, a passageway defining a fluid path into a variable fluid chamber in the **barrel** below the plunger, and a spring applying retraction force to the retractable part, said retractable part being configured to be able to retract into the retraction cavity of the plunger when retraction is initiated;

the retraction mechanism further including a nonretractable part comprising a **retainer member** surrounding the head of the needle holder, the retainer member and said head of the needle holder being removably coupled by a **bridging portion** between them;

the needle holder and spring being installable into the **nose** from the rear of the **barrel** and **releaseably installed by sliding engagement of said retainer member and said inwardly facing surface** while compressing said spring, said **sliding engagement producing a holding force** in opposition to the retraction force applied to the needle holder by said spring; and

the plunger being depressible to a first position which comprises the end of an injection cycle whereby fluid previously drawn into the variable chamber is expelled through said fluid path, and a retraction position beyond said first position wherein retraction is initiated by the forward portion of the plunger head moving through the **transition zone** in the **nose** to release the needle holder by uncoupling the **retainer member** and needle holder at said **bridging portion** thereby reducing the holding force to an amount less than the retraction force on the needle holder to cause retraction of the retractable part into the retraction cavity of the plunger.

24. A method of assembling a tamperproof retractable syringe which is well suited for automated assembly;

providing a one piece hollow syringe **body** having a longitudinally extending wall with an open back end, comprising an elongated **barrel** and **nose portion** of reduced cross sectional area relative to the **barrel**, and an **inwardly facing surface** in the wall at the most constricted part of a **transition zone** between the **barrel** and **nose** where the **nose** begins;

providing a plunger assembly having a front portion and a back portion, the front portion including a head configured for sliding sealed contact with the interior of the elongated **barrel**, said head having a retraction cavity and a leading end configured to contact and remove a **retainer member** from a needle holder to be mounted in the **nose**;

providing a needle holder having an elongated **body** portion in front and a head in back with a fluid path therethrough, the head of the needle holder having a **retainer member** which can be separated from the head of the

needle holder by contact with the leading end of the plunger, the **retainer member** having an **outwardly facing surface** configured to slidably and frictionally engage said **inwardly facing surface** in the **nose** and hold the needle holder against a retraction force provided by the spring when the spring is compressed within the **nose**;

loading the spring followed by the needle holder into the back opening in the **barrel** part of the syringe **body** and positioning at least the forward portion of the spring and a portion of the elongated body of the needle holder within the **nose**;

moving the head end of the needle holder and the **retainer member** into the most constricted part of the transition zone where the **nose** begins; and

installing the needle holder and **retainer member** in the **nose** by sliding engagement of the **outwardly facing surface** of the **retainer member** with the **inwardly facing surface** in the wall while compressing the spring within the **nose**.

'733, 14:65-15:49, 16:64-17:37 (emphasis added).

B. Claim Construction

1. "body"

a. Parties' Positions

The parties propose the following constructions for "body," which is present in each of the asserted claims as well as the two other patents-in-suit. Dkt. No. 114. The primary dispute between the parties is whether the syringe body must be limited to a one-piece structure.

RTI	BD
A hollow outer structure that houses the syringe's components	A one-piece hollow outer structure that houses the syringe's components

RTI contends this term should not contain a one-piece limitation because many of the claims in the '733 Patent already contain such a limitation. Dkt. No. 111 at 22. To add this limitation to the definition of body itself would render the additional claim language meaningless. *Id.* RTI also contends the patentee expressly used a one-piece limitation in the '733 Patent while no such limitation is generally present in the '077 or '224 Patents. *Id.* at 23. In fact, the patentee in the '224 patent used the limitation to differentiate between certain claims. *Compare* '224, 22:38-40 (claim 43), *with* 24:23-25 (claim 57-"The syringe assembly of claim 43 wherein the body comprises a one-piece barrel.").

Judge Davis previously construed this term in connection with the '011 and '077 Patents. *See RTI v. New Medical Techs.*, Civil Action No. 4:02-CV-34, Dkt. No. 110 at 6-9 (E.D.Tex. March 8, 2008). Judge Davis, like RTI, found significant the fact that the patentee in this family of patents included the phrase "one piece" in some claims, but not in others. *Id.* at 7. As such, Judge Davis found it improper to limit the term to a preferred embodiment containing only a one-piece body. *Id.* at 8-9.

b. Court's Construction

At the outset, this Court notes that certain terms, such as barrel, pervade all of the patents-in-suit. Because all of these patents are related-the latter patents being continuations-in-part of earlier patents and patent applications-this Court finds that terms should be construed consistently throughout absent some evidence to the contrary. In addition, the specifications and claims of each patent within this family may provide guidance when construing such pervasive terms.

Regardless of whether collateral estoppels applies to the construction of this term, the Court finds no reason to deviate from Judge Davis' previous construction. *See Id.* at 6-9. Accordingly, this Court finds that "body" means "a hollow outer structure that houses the syringe's components."

2. "barrel"

a. Parties' Positions

The parties propose the following constructions for "barrel," which is present in each of the asserted claims as well as the other two patents-in-suit. Dkt. No. 114. The primary dispute between the parties is whether the syringe barrel must be cylindrical in shape.

RTI	BD
The elongated part of the syringe body including a portion within which the plunger moves during	The elongated cylindrical portion of the syringe body through which the plunger moves during

injection

injection

RTI contends the claimed barrel could take a number of conceivable shapes and should not be limited to a cylindrical form. Dkt. No. 111 at 26-27. RTI further argues that the '224 specification specifically contemplates a non-cylindrical barrel. *Id.* (citing '224, 10:47-50). Moreover, the principle of claim differentiation supports RTI's broad construction as certain claims specifically contain a cylindrical limitation while others do not. *Id.* at 27 (citing '224, 20:22-23 (claim 25)). Finally, RTI contends that it is improper to limit the claimed barrel to the portion of the syringe through which the plunger moves. *Id.* Instead, some claims within the '224 and '077 Patent suggest that the term may encompass other structures through which the plunger does not move; specifically, the term may also define the front end portion of the syringe, including the nose portion and retraction mechanism. *Id.* at 27-28 (citing *inter alia* '224, 22:37-40 (claim 43) & '077, 22:13-15).

In response, BD relies on numerous dictionaries, which suggest that a barrel is limited to a cylindrical shape. Dkt. No. 112 at 30-31. BD also maintains that every figure in this family of patents shows a cylindrical barrel and expressly labels the non-cylindrical parts of the syringe as a 'nose' or 'transition zone'. *Id.* Thus, BD argues that the patent figures make clear that the term is limited to a cylindrical shape and does not include narrow parts in the front end of the syringe. *Id.* In addition, BD contends that the terms barrel, nose, and transition zone should each be given distinct meanings because they are given different names and labels throughout the patent-to do otherwise would render the different labels superfluous. *Id.*

b. Court's Construction

The Federal Circuit has made it clear that when the specification discloses only a single preferred embodiment, limitations from that embodiment generally should not be imported into the claim language. *Phillips v. AWH Corp.*, 415 F.3d at 1323 (rejecting the contention that "if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment"). Limitations from the specification may be imported into the claims where it is clear that the patentee intended for the "claims and embodiments in the specification to be strictly coextensive." *Id.* (citing *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed.Cir.2001)). Such intention is evidenced by the manner in which the patentee uses a term within the specification and the claims. *Id.* (citing *Snow v. Lake Shore & M.S. Ry. Co.*, 121 U.S. 617, 630 (1887) (it was clear from the specification that there was "nothing in the context to indicate that the patentee contemplated any alternative" embodiment to the one presented)).

RTI is correct that all figures in the patents-in-suit generally depict syringes having a cylindrical barrel. The specification of the '224 Patent, however, makes it clear that the patentee contemplated alternative shapes. Specifically, the patent states that the "head of the needle holder is preferably circular but could conceivably be another shape with the retainer member correspondingly configured to conform to it." '224, 10:47-50. As the '224 Patent generally depicts a syringe having a barrel and needle holder having similar shape, such a statement evidences the patentee's belief that both the needle holder and related barrel could have a non-circular shape. Thus, the patentee may have contemplated a non-cylindrical barrel.

Moreover, claim 25 of the '224 Patent specifically recites a "substantially cylindrical barrel," which strongly suggests that the term is not inherently cylindrical. Furthermore, the absence of this "substantially cylindrical" limitation in other claims suggests that it should not be read into claims in which it is not present. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1326 (Fed.Cir.2003) ("when a patent claim does not contain a certain limitation and another claim does, that limitation cannot be read into the former claim"). The Court therefore finds that the term barrel should not be limited to a cylindrical shape.

Finally, although this Court believes that the terms barrel, nose, and transition zone are generally distinct

components within the patents-in-suit, the patents also suggest that the barrel may encompass some portion of the syringe through which the plunger does not move. Specifically, claim 25 of the '077 Patent recites a "barrel having a front end portion containing a retraction mechanism." If this front end portion of the claimed barrel contains the retraction mechanism, then it cannot logically also be a portion through which the plunger moves. Although the plunger will assuredly move through some portion of the barrel, this Court finds that it would be improper to limit the barrel to that portion.

Accordingly, this Court finds that "barrel means "the elongated part of the syringe body including a portion through which the plunger moves during injection."

3. "nose"/"nose portion"

The parties have agreed on a meaning for the term "nose," which appears in each asserted claim. The proposed construction is "the portion of the syringe at the injection end that has a reduced diameter relative to the barrel." Dkt. No. 110 at 1. The parties have further agreed that these claims require the "nose" to be distinct from the barrel and transition zone.

The parties have also agreed on a meaning for the term "nose portion," which appears in claims 24 and 36. The proposed construction is "section of the syringe body that has a reduced diameter relative to the barrel portion of the body." *Id.*

The Court has no reason to disagree and therefore adopts the parties' constructions.

4. "transition zone"

a. Parties' Positions

The parties propose the following constructions for "transition zone," which is present in each asserted claim. Dkt. No. 114.

RTI	BD
Portion of the syringe located between the barrel and the nose	Portion of the syringe with varied inner diameter located between the barrel and the nose

RTI contends this term should not be limited to the preferred embodiment, which identifies a transition zone with a sloping inner wall. Dkt. No. 111 at 21. While RTI concedes that the transition zone has a "constricted portion," it believes that the patent does not require that the transition zone have a varied inner diameter. *Id.* BD counters by arguing that the phrase "most constricted part of the transition zone" pertains to the whole invention and requires a varied inner diameter. Dkt. No. 112 at 28 (citing '733, 14:8-10).

Judge Davis previously construed this term in connection with the '011 and '077 Patents. *See RTI v. New Medical Techs.*, Civil Action No. 4:02-CV-34, Dkt. No. 110 at 15 (E.D.Tex. March 8, 2008). Judge Davis did not limit the term to a varied inner diameter. *Id.*

b. Court's Construction

Once again, the Court finds no reason to deviate from Judge Davis' previous construction. *See RTI v. New Medical Techs.*, Civil Action No. 4:02-CV-34, Dkt. No. 110 at 13-14 (E.D.Tex. March 8, 2008). In addition, the Court finds no reason to limit the term to the preferred embodiment. Accordingly, this Court finds that term "transition zone" means "portion of the syringe located between the barrel and the nose."

5. "inwardly facing surface"

a. Parties' Positions

The parties propose the following constructions for "inwardly facing surface," which is present in each asserted claim. Dkt. No. 114.

RTI	BD
A surface that faces the inside of the syringe	A surface in the wall that faces toward the center of the syringe and is parallel to the direction of the plunger motion

RTI contends this term should not be restricted to a surface that is parallel to the motion of the plunger, as such would improperly restrict the term to a preferred embodiment. Dkt. No. 111 at 29. RTI contends that the '733 specification attaches no significance to the fact that the preferred embodiment's surfaces happen to be parallel to the plunger's motion. *Id.* Additionally, RTI contends that claim differentiation precludes such a limitation, as the patentee chose to specifically align these surfaces in certain claims of the '011 Patent. *Id.* (citing '011, 13:40-43 (claim 3)).

In response, BD contends that every embodiment described or depicted in the ' 733 Patent demonstrates surfaces that are parallel to the vertical direction of the plunger motion. Dkt. No. 112 at 23-24. In addition, the Summary of the Invention within the '733 Patent also aligns these surfaces with the plunger motion. *Id.* (citing '733, 2:64-65 (inwardly and outwardly facing surfaces meet "along an interface oriented in the direction of retraction")). Alternatively, BD argues that during prosecution RTI took a narrower view of the scope of this term to overcome prior art. *Id.* As such, BD argues that RTI has surrendered broader, non-parallel coverage. *Id.*

b. Court's Construction

As discussed above, limitations from the preferred embodiment generally should not be imported into the claim language, unless the claims and the embodiments in the specification were meant to be strictly coextensive. Phillips, 415 F.3d at 1323. While the descriptions and depictions of the invention in the '733 Patent generally show an inwardly facing surface that is parallel to the plunger motion, this Court finds no evidence that such embodiments are strictly coextensive with the claimed invention. Indeed, the ' 011 Patent, from which the '733 Patent is a continuation-in-part, expressly claims such an orientation. '011, 13:40-43 (claim 3: "The tamperproof retractable syringe of claim 2 wherein said frictional holding [inwardly and outwardly facing] surfaces comprise a linear interface aligned in the direction of retraction."). Thus, when the patentee wished to limit the alignment of surfaces, he expressly claimed such. Accordingly, this Court finds that it would be improper to import an alignment limitation into claims where such is not expressly present.

Accordingly, this Court finds that the term "inwardly facing surface" means "a surface that faces toward the center of the syringe."

6. "retraction mechanism sealingly disposed in the nose"

The parties have agreed on a meaning for the term "retraction mechanism sealingly disposed in the nose," which appears in claim 1. The proposed construction is "a retraction mechanism sealed in the nose." Dkt. No. 110 at 1. The Court has no reason to disagree and therefore adopts the parties' construction.

7. "retainer member"

a. Parties' Positions

The parties propose the following constructions for "retainer member," which is present in each asserted claim and the '224 Patent. Dkt. No. 114. The primary dispute between the parties is whether the retainer

member must operate by means of a frictional force.

RTI	BD
A nonretractable part of the retraction mechanism that retains the retraction mechanism	A nonretractable part of the retraction mechanism, separate from the needle holder, that retains the retraction mechanism by frictional force with the wall of the syringe

RTI contends that BD's construction would not only limit the patent to a preferred embodiment, but would also limit the patent to RTI's particular commercial product, the VanishPoint(R)-syringe. Dkt. No. 111 at 8-10. The construction proposed by BD would read a frictional holding force limitation into the term. RTI believes this improper because some claims do not require any engagement or holding force, much less some kind of frictional force. *Id.* at 10 (citing '224, 20:46-54 (claim 43)). Moreover, RTI contends that the patentee explicitly stated in some claims that frictional forces were required, raising the implication that claims without such explicit statements are not limited to friction. *Id.* (comparing '733, 14:32-37 (claim 1) with 17:18-21 (claim 24) and 18:38-41 (claim 36)). RTI also contends that the specification expressly contemplates embodiments that operate using something other than friction to hold the retainer member in place. *Id.* at 11-13. Specifically, the patents teach that the holding force used in the invention, while preferably frictional, may instead rely on tack welding, sonic welding, adhesive, or clamping forces. *Id.* at 12-13 (citing '733, 9:50-53, 10:4-8, 6:47-55, and 11:49-52).

RTI also believes that BD's proposed construction is improper in another regard, it requires that the retainer member and needle holder be separate parts. *Id.* at 16-18. While one preferred embodiment teaches that the two components are separate parts, RTI argues that there is nothing in either the claims or the specification that requires such. *Id.* To the contrary, an alternative embodiment suggests that the two are welded together to form a single structure. *Id.* at 17 (citing '733, 9:7-27). Therefore, RTI contends that-despite being two components-the patents contemplate that the retainer member and needle holder may be formed into a single structure. *Id.*

In response, BD contends that the specification repeatedly describes the invention as a retracting syringe in which the needle holder is engaged and released by sliding surfaces, and therefore, friction. Dkt. No. 112 at 17. BD identifies numerous points in the specification where the holding force used in the invention is identified as a frictional force. *Id.* at 17-18 (citing '733, 2:67-3:6, 3:11-13, and 3:61). BD also contends that the specification uses the terms 'holding force' and 'frictional holding force' interchangeably, thus demonstrating that they are intended to have the same meaning. *Id.* (citing *Tate Access Floors, Inc. v. Maxcess Techs., Inc.*, 222 F.3d 958, 968 (Fed.Cir.2000)). Moreover, BD argues that the specification criticizes syringes in the prior art that operate without friction and rely instead on flexing, breaking, or penetration. *Id.* at 18 (citing '733, 1:48-54, 2:18-35). Specifically, BD contends the specification asserts that the invention was new and different because it "relies entirely on clamping force or friction...." *Id.* (quoting '733, 2:20-21).

In connection with the second issue regarding this term, that is whether the needle holder and retainer member must be separate parts, BD argues that the '733 claims suggest that the two components are inherently separate parts. *Id.* at 25. BD argues that a single, unitary structure cannot couple with itself or surround itself. *Id.* In addition, BD contends that the patent specification, specifically the Summary of the Invention, explains that the retraction mechanism has a "two part head." *Id.* (citing '733, 3:25-26). Finally, BD argues that melting or tacking two parts together do not make them a single part; instead, such coupling is further evidence that they are indeed two separate parts. *Id.* at 25-26.

b. Court's Construction

First, this Court finds that nothing in the specification requires the needle holder and retainer member be two separate parts. The specification states that in " *one embodiment*, the head of the holder is a two part head

comprising an inner head surrounded by a separable retainer" '733, 3:19-22 (emphasis added). This statement is explicitly limited to a single, preferred embodiment, thus suggesting that other embodiments of the invention may utilize a unitary structure. Such a structure is contemplated in an alternative embodiment in which the two components are initially welded together and later "ruptured or separated." *Id.* at 9:7-13.

Second, this Court finds that the invention operates through the use of a frictional or clamping force, and that the retainer member must utilize these forces. Although the claims by themselves may seem broad enough to encompass other methods of operation, the patent as a whole disavows such methods and limits itself to frictional or clamping forces. The Federal Circuit has stated that where "the general summary or description of the invention describes a feature of the invention ... and criticizes other products ... that lack the same feature, this operates as a clear disavowal of these other products..." *Astrazeneca AB v. Mutual Pharm. Co.*, 384 F.3d 1333, 1340 (Fed.Cir.2004), *see also* *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed.Cir.2001) ("Where the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims ... even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question.").

RTI is correct in asserting that some claims of the '733 Patent are explicitly limited to a frictional force while others do not. Claim differentiation would ordinarily require that all claims not be so limited. The specification, however, makes clear that the invention does not include the use flexing, breaking, or penetration as methods of operation. It does so by expressly criticizing other methods used in retractable syringes:

Other problems with the prior art are dependence on flexing or breaking of internal parts by the plunger in order to release the retraction mechanism and use of a diaphragm at the end of the plunger which must be penetrated by a needle holding member and spring. These structures present serious quality control and assembly problems.

'733, 1:48-54. In contrast to these less preferable methods, the specification asserts that the present invention is superior because it relies entirely on clamping or frictional forces: "The prior art has not recognized a retraction mechanism with separable parts that *relies entirely* on clamping force or friction...." '733, 2:18-20. By distinguishing itself from the prior art in such absolute terms, the patent has limited itself to a certain type of holding force-clamping or friction.

Finally, the varied embodiments in the invention demonstrate that this holding force may be utilized in different manners within the syringe. In one embodiment, a pair of frictional holding forces function to retain the needle in the projecting position: a frictional force between the wall of the syringe and the retainer member, and another between the retainer member and the needle holder. *See* '733, 6:56-67, 3:8-24. In another embodiment, the needle holder and retainer member are welded or tack molded together as discussed above. *See* '733, 9:50-53, 10:4-8, and 11:49-52. Although this weld or tack mold holds the needle holder and retainer member together, there is still a clamping or frictional force between the wall of the syringe and the retainer member. Without this force between the wall of the syringe and the retainer member, the syringe would be inoperable-it would be unable to retain the needle in a projecting position. Thus, the retainer member can only function through the use of a frictional or clamping force.

Accordingly, this Court finds that the term "retainer member" means "a non-retractable part of the retraction mechanism that uses some clamping or frictional force to keep the needle in the projecting position until released."

8. "bridging portion"

a. Parties' Positions

The parties propose the following constructions for "bridging portion," which is present in claim 1 and in the '224 Patent. Dkt. No. 114. The primary dispute between the parties is whether the bridging portion must be limited to a ridge-like structure.

RTI	BD
The structure that joins the retainer member and the head of the needle holder	A ridge on one of the facing surfaces that joins the retainer member and the head of the needle holder

RTI contends that BD's construction improperly limits the invention to a preferred embodiment. Dkt. No. 111 at 28. While the embodiment in Figure 8 admittedly depicts a raised ridge between facing surfaces, RTI argues that nothing in the specification limits the bridging portion to such a structure. *Id.* Instead, the specification states that the bridging portion may be joined to needle holder by a tack weld, or "by providing any other form of frangible bridging portion that holds the separable ring member and needle holder together." *Id.* at 28-29 (citing '733, 9:37-40).

In response, BD argues that the specification defines the bridging portion as a "small ridge" or "raised portion" joining facing surfaces. Dkt. No. 112 at 27 (citing '733, 3:43 and '077, 10:38-39). While the bridging portion may admittedly be made of various materials, BD contends that it must have some definable structure, which the patent identifies as a ridge on one of the facing surfaces. *Id.*

b. Court's Construction

The specification describes the bridging portion as a ridge-like structure that may take the form of a single "very small raised portion" or a "series of horizontally spaced apart raised portions ." While the preferred embodiment describes the bridging portion as such ridge-like structures, the Court finds no evidence that the patentee intended to limit the term to that structure. *See* Phillips, 415 F.3d at 1323 (claims should not be limited to particular embodiments unless the inventor has indicated such a narrow construction). Additionally, the bridging portion is part of an embodiment depicted in Figure 8, which the specification distinguishes from those embodiments depicted in Figures 1-3. *See* '733, 9:7-17. It is thus apparent that Figures 1-3 do not contain the claimed bridging portion, as the adjoining surfaces of the retainer member and needle holder in those embodiments are flush with one another. Thus, if two surfaces are completely flush with one another they cannot logically be joined by a bridging portion. As such, the claimed bridging portion, whatever the form it takes, must be a distinguishable structure that both joins the two components and provides some separation between them. The separation may take the form of a "small gap between them all around" ('733, 9:30-31) as depicted in Figure 8. Conversely, the bridging portion could take the form of a "frangible web" (Dkt. No 111 at 29), the gaps of which separate the two surfaces.

Accordingly, as the Court previously ruled, the term "bridging portion" means "a structure that spans the gap between and connects the retainer member and needle holder."

9. "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface"

a. Parties' Positions

The parties propose the following constructions for "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface," which is present in claim 1. Dkt. No. 114.

RTI	BD
Releaseably installed by sliding the retainer member along the inwardly facing surface to engage it with the wall of the syringe	Installed and released by sliding the retainer member along the inwardly facing surface to create and the release a frictional force with the wall of the syringe

As above, this term concerns the nature of the force involved in the invention. In addition, however, the parties also dispute the meaning of the words "releaseably installed" in this term. BD contends that "releaseably installed by sliding engagement" has two functional meanings. Dkt. No. 112 at 20. First, the phrase refers to the creation of a frictional force. *Id.* Second, the word "releaseably" requires that the retainer member be releaseable in the same way that it was installed. *Id.* at 20-21. BD contends that if the retraction mechanism is "installed by sliding engagement," then it must be released in the same manner-by sliding the retainer member away from the inwardly facing surface. *Id.* at 21.

RTI disagrees and contends that the term is not so limited. Dkt. No. 111 at 14. Instead, RTI argues that one of the alternate methods of release taught by the patent could achieve the release-namely by spreading the syringe wall and allowing a one-piece needle holder to retract. *Id.* at 14-15 (citing '733, 11:49-52).

b. Court's Construction

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or fictional force. This Court, however, is not persuaded that the claimed release must be accomplished in the same manner as the installation. The patent teaches alternative methods for providing release of the holding force. Specifically, the patent allows the holding force to be released by spreading the barrel apart slightly, thus releasing the retraction mechanism. *See* '733, 11:49-52 ("The barrel is flexible and is spread outwardly a slight among to the position of FIG. 6 just prior to retraction. Here the mating surfaces are separated an amount which reduces the clamping force on the needle holder."). Therefore, although the holding force is created by sliding engagement in this claim, the Patent contemplates another method of its release.

Accordingly, the Court finds that the term "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface" means "installed by sliding the retainer member along the inwardly facing surface to engage it with the wall of the syringe, which creates a clamping or frictional force that can be released at a later time."

10. "sliding engagement producing a holding force"

The parties propose the following constructions for "sliding engagement producing a holding force," which is present in claim 1. Dkt. No. 114.

RTI	BD
Sliding the retainer member along the inwardly facing surface of the body to produce a force that maintains the needle holder in the projected position	Sliding the retainer member along the inwardly facing surface of the body produces a frictional force that maintains the needle holder in the projected position

Once again, the dispute between the parties center on whether the holding force must be a frictional force. RTI and BD proffer the same arguments as those discussed above in connection with the term "retainer member." Dkt. Nos. 111 at 18 & 112 at 16-20.

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or fictional force. Accordingly, the Court finds that the term "continuous retainer member surrounding the inner head" means "sliding the retainer member along the inwardly facing surface of the body produces a clamping or frictional force that maintains the needle holder in the projected position."

11. "outwardly facing surface"

The parties propose the following constructions for "outwardly facing surface," which is present in claims

RTI	BD
A surface that faces toward the outside of the syringe	A surface that faces away from the center of the syringe and is parallel to the direction of the plunger motion

The parties present arguments similar to those presented in connection to the term "inwardly facing surface." For the same reasons as stated above in connection with inwardly facing surfaces, the Court finds that the claimed outwardly facing surfaces should not be limited to a direction parallel to the plunger motion.

Accordingly, this Court finds that the term "outwardly facing surface" means "a surface that faces away from the center of the syringe."

V. U.S. PATENT NO. 6,090,077

A. Overview

RTI has asserted claims 10 and 25 of the '077 Patent against BD in this lawsuit. Dkt. No. 114. For reference, the asserted claims are reproduced below (terms to be construed emphasized):

10. A syringe plunger handle assembly and syringe barrel combination for use in a retractable syringe for injecting fluids, comprising:

a hollow syringe **body** having an elongated tubular wall comprising an elongated **barrel** portion having an open back end;

an elongated plunger disposed for reciprocation in sliding sealed contact with the **barrel** portion of the **body**, the plunger having a tubular wall defining a head portion in front, a back end portion carrying a thumb cap and hollow interior comprising a retraction cavity located between the head portion and thumb cap;

the thumb cap having an outer side adapted to reside in close association with the open back end of the plunger **barrel** when the plunger is nearly fully depressed; and

the plunger having a **vent** in fluid communication with the retraction cavity, to allow airflow from the retraction cavity.

25. A tamperproof retractable syringe structure designed for one use, comprising:

a hollow syringe **body** comprising a syringe **barrel** having an open back end, **the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger;**

a plunger reciprocatably mounted in sliding sealed contact with the **barrel**, the plunger having a thumb cap at its back end for working the plunger relative to the **barrel** and **a front end configured to operate the retraction mechanism;**

the plunger having a tactile first position felt by a user pressing the thumb cap at the end of free travel of the plunger in the **barrel** when the plunger is moved forward to a stop, the plunger having a length relative to the length of the **barrel** whereby in the tactile first position of the plunger a portion of the plunger and the thumb cap extend behind the **barrel** for grasping in order to draw fluid into the **barrel** by partially withdrawing the plunger from the **barrel**;

the plunger having a retraction position obtained by pressing the thumb cap to move the plunger forward beyond the tactile first position and thereby operating the retraction mechanism and simultaneously lodging the thumb cap in the open back end of the **barrel** thereby rendering the thumb cap inaccessible for grasping.

'007 Patent, 19:33-50, 20:48-21:7 (emphasis added).

B. Claim Construction

1. "body"/"barrel"

The Court construed these terms as part of its analysis of the '733 Patent, of which the '077 Patent is a continuation-in-part. The Court finds no reason to deviate from its prior constructions.

2. "vent"

The parties have agreed on a meaning for the term "vent," which appears in claim 10. The proposed construction is "an aperture that provides an opportunity or means of escape, passage, or release ." Dkt. No. 110 at 1-2. While the Court has does not disagree with the overall construction, it does believe that the word "aperture" would be unnecessarily confusing to the jury. Thus, the Court finds that the term "vent" should be construed as "an opening that provides an opportunity or means of escape, passage, or release."

3. "the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger"

The parties have agreed on a meaning for the term "the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger," which appears in claim 25. The proposed construction is "the section of the barrel at the injection end has a retraction mechanism that is configured to be operated by a plunger." Dkt. No. 110 at 1-2. The Court has no reason to disagree and therefore adopts the parties' construction.

4. "a front end configured to operate the retraction mechanism"

The parties have agreed on a meaning for the term "a front end configured to operate the retraction mechanism," which appears in claim 25. The proposed construction is "portion of the plunger closer to the injection end of the syringe that operates the retraction mechanism." Dkt. No. 110 at 1. The Court has no reason to disagree and therefore adopts the parties' construction.

VI. U.S. PATENT NO. 7,351,224

A. Overview

RTI has asserted claims 43, 47, 55, 60, and 61 of the '224 Patent against BD in this lawsuit. Dkt. No. 114. Claim 43 is an independent claim, upon which claims 47, 55, 60, and 61 depend. For reference, the asserted claims are reproduced below (terms to be construed emphasized):

43. A syringe assembly having a retractable needle that is rendered unusable after a single injection of fluid into a patient, the assembly comprising:

a hollow syringe **body** comprising a **barrel** and having a front end portion and a back end portion, the back end portion further comprising at least one radially extending member providing finger grips for the syringe **body**;

a retraction mechanism disposed in the front end portion, the retraction mechanism further comprising a

needle holder having a head portion, an elongated needle holding portion, and a longitudinally extending fluid passageway through the head portion and the elongated needle holding portion, the head portion further comprising an inner head, **a continuous retainer member surrounding the inner head**, and a **bridging portion** disposed between the continuous **retainer member** and the inner head, wherein said **bridging portion** couples the continuous **retainer member** and the inner head to form a fluid seal between the fluid passageway and the **barrel** prior to retraction, and a compressed retraction spring surrounding at least part of the elongated needle holding portion and biasing the inner head toward the back end portion prior to retraction;

a retractable needle extending into the front end portion of the **body** through an opening in the front end portion of the **body**, the retractable needle being held in fixed relation to the elongated needle holding portion of the needle holder and in fluid communication with the longitudinally extending fluid passageway through the head portion and the needle holding portion;

a plunger reciprocally disposed inside the **barrel** and forming a variable chamber between the plunger and the needle holder prior to and during injection, the plunger being receivable into the **barrel** through the back end portion of the **body** and comprising an outer wall, a retraction cavity disposed inwardly of the outer wall, a plunger seal element providing sliding, sealed engagement between the plunger and the **barrel** and preventing fluid leakage between the plunger and the **barrel**, the plunger seal element being restrained from sliding longitudinally along the outer wall of the plunger, and a back end with an **end cap** having an outer periphery; and

a barrier disposed in the front end portion of the **body** that limits forward motion of the needle holding portion and the retractable needle relative to the **body** as the plunger is depressed inside the barrel during injection and retraction;

wherein the continuous retainer member is releasable from the inner head of the needle holder when the plunger is further depressed inside the barrel following injection.

47. The syringe assembly of claim 43 wherein the **body** further comprises a collar having an open back end, the collar extending rearwardly behind the at least one radially extending member and longitudinally separating the at least one radially extending member from the open back end, and wherein the outer periphery of the **end cap** is in close proximity to the back end of the collar following injection and during retraction.

55. The syringe assembly of claim 43 wherein the retraction cavity is **vented** behind the plunger seal element.

60. The syringe assembly claim 43 wherein the continuous retaining member has an outside mating surface making a fluid seal with the **barrel**.

The syringe assembly of claim 43 wherein the **body** and the elongated needle holder cooperate as a spring guide during compression of the retraction spring.

'224 Patent, 22:35-23:19, 23:32-39, 24:18-19, 24:33-35, 24:36-38 (emphasis added).

B. Claim Construction

1. "body"/"barrel"/"bridging portion"/"retainer member"

The Court construed these terms as part of its analysis of the '733 Patent, of which the '224 Patent is a continuation-in-part. The Court finds no reason to deviate from its prior constructions.

2. "continuous retainer member surrounding the inner head"

The parties propose the following constructions for "continuous retainer member surrounding the inner head," which is present in claim 43. Dkt. No. 114.

RTI	BD
A nonretractable part of the retraction mechanism that encircles the inner head of the needle holder, and retains the retraction mechanism	A nonretractable part of the retraction mechanism, separate from the needle holder, that encircles the inner head of the needle holder, and retains the retraction mechanism by frictional force with the wall of the syringe

RTI and BD proffer the same arguments as those discussed above in connection with the term "retainer member." Dkt. Nos. 111 at 13-14. Once again, the dispute between the parties is two-fold: (1) whether the holding force must be a frictional force, and (2) whether the needle holder and retainer member must be separate parts.

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or frictional force and that there is no requirement that two components be separate parts. Accordingly, the Court finds that the term "continuous retainer member surrounding the inner head" means "a non-retractable part of the retraction mechanism that encircles the inner head of the needle holder and uses some clamping or frictional force to keep the needle in the projecting position until released."

3. "end cap"

a. Parties' Positions

The parties offer the following constructions for "end cap," which is present in claims 43 and 47. Dkt. No. 114.

RTI	BD
Back end of the plunger	A separate piece that caps the open end of the plunger

RTI contends that BD's proposed construction improperly limits this term. Dkt. No. 111 at 30-31. RTI believes that nothing in the specification requires the end cap be a separate piece or that it cap the open end of the plunger. *Id.* Instead, RTI contends that the "force fit plug" is the separate piece that caps the end of the plunger, while the end cap is a part of the plunger itself. *Id.* (citing '224, 7:22-24 & Figs. 1-7). In addition, one claim specifically recites that "the end cap has an opening and a closure is installed in the opening." *Id.* (citing '224, 24:16-17 (claim 54)).

In response, BD contends that RTI's proposed construction does not make sense in light of the claim language. Dkt. No. 112 at 32. Specifically, the claims require a "back end with an end cap," and BD believes that RTI's construction would make this requirement nonsensical—a back end with a back end. *Id.* (citing '224, 22:65-23:9 (claim 43)).

b. Court's Construction

The Patent figures depict the end cap as a part of the plunger rather than a separate piece. *See* '224, Figs. 1-7. The Federal Circuit has held that an interpretation of a claim, which would not include a preferred embodiment disclosed in the specification, is "rarely, if ever, correct." Vitronics, 90 F.3d at 1583. This Court finds no reason to require the end cap to be a separate piece, as such a construction would not include the

embodiments depicted in Figures 1-7. This Court, however, also finds no reason to limit the term to these embodiments, in which the end cap is a part of the plunger. The Patent could conceivably cover an alternative embodiment in which the end cap was a separate piece.

In addition, the Patent states that it is the "force fit plug" rather than the end cap that closes the retraction cavity-the open end-at the back of the plunger. '224, 7:33-36. The end cap itself has a "central opening for permanently receiving [the] force fit plug." *Id.* As such, the end cap, in contradiction with the plain meaning of the word "cap," does not necessarily close the open end of the plunger. Instead, it allows the force fit plug to accomplish that function once it is permanently installed within the end cap's opening. This Court, however, also finds no reason to limit the term to this one preferred embodiment-it is possible that the Patent could cover a syringe in which the end cap and force fit plug were a single piece, rather than two separate parts.

Finally, because it is located at the back of the plunger, the Patent describes the end cap as a portion of the plunger with which the thumb contacts during depression. *Id.* ("Plunger has an end cap for depression of the plunger by the thumb.").

Accordingly, the Court finds that the term "end cap" means "a component at the back of the plunger, which may be contacted by the thumb during depression."

4. "wherein the continuous retainer member is releasable from the inner head"

a. Parties' Positions

The parties offer the following constructions for the term "wherein the continuous retainer member is releasable from the inner head," which appears in claim 43. Dkt. No. 114.

RTI	BD
The plunger releases the continuous retainer member from the inner head as the plunger is further depressed in the barrel	The plunger releases the continuous retainer member from the inner head by pushing the continuous retainer member off of the inner head as the plunger is depressed in the barrel to reduce the frictional force with the wall of the syringe

The parties' arguments in connection with this term closely mirror those proffered in connection with the term "releaseably installed by sliding engagement of said retainer member and said inwardly facing surface" construed above. *See* Dkt. Nos. 111 at 19-20 & 112 at 26-27.

b. Court's Construction

For the reasons stated above, this Court finds that the invention operates through the use of a clamping or frictional force. However, since the clamping or frictional forces are already part of this Court's construction of "continuous retainer member," this Court finds that it would be unnecessarily confusing and duplicative to include a reference to those forces in this term's construction. As also discussed above, this Court finds that the holding force may be released by some other manner than that with which it was installed.

Accordingly, the Court finds that the term "wherein the continuous retainer member is releasable from the inner head" means "the plunger releases the continuous retainer member from the inner head as the plunger is further depressed in the barrel."

VII. CONCLUSION

The Court hereby **ORDERS** the claim terms addressed herein construed as indicated. The table below summarizes the Court's constructions:

Term	Court's Construction
'773 Patent	
body	"a hollow outer structure that houses the syringe's components." A hollow outer structure that houses the syringe's components
barrel	The elongated part of the syringe body including a portion through which the plunger moves during injection
nose	The portion of the syringe at the injection end that has a reduced diameter relative to the barrel.
nose portion	Section of the syringe body that has a reduced diameter relative to the barrel portion of the body.
transition zone	Portion of the syringe located between the barrel and the nose
inwardly facing surface	A surface that faces toward the center of the syringe
retraction mechanism sealingly disposed in the nose	A retraction mechanism sealed in the nose.
retainer member	A non-retractable part of the retraction mechanism that uses some clamping or frictional force to keep the needle in the projecting position until released
bridging portion	A structure that spans the gap between and connects the retainer member and needle holder
releaseably installed by sliding engagement of said retainer member and said inwardly facing surface	Installed by sliding the retainer member along the inwardly facing surface to engage it with the wall of the syringe, which creates a clamping or frictional force that can be released at a later time
sliding engagement producing a holding force	Sliding the retainer member along the inwardly facing surface of the body produces a clamping or frictional force that maintains the needle holder in the projected position
outwardly facing surface	A surface that faces away from the center of the syringe
'077 Patent	
body	Same as above
barrel	Same as above
vent	An opening that provides an opportunity or means of escape, passage, or release
the barrel having a front end portion containing a retraction mechanism configured for operation by a plunger	The section of the barrel at the injection end has a retraction mechanism that is configured to be operated by a plunger.
a front end configured to operate the retraction mechanism	Portion of the plunger closer to the injection end of the syringe that operates the retraction mechanism.
'224 Patent	
body	Same as above
barrel	Same as above
retainer member	Same as above
bridging portion	Same as above
continuous retainer member surrounding the inner head	A non-retractable part of the retraction mechanism that encircles the inner head of the needle holder and uses some clamping or frictional force to keep the needle in the projecting position until released
end cap	A component at the back of the plunger, which may be contacted by the thumb during depression
wherein the continuous retainer member is releasable from the inner head	The plunger releases the continuous retainer member from the inner head as the plunger is further depressed in the barrel

IT IS SO ORDERED.

E.D.Tex.,2009.

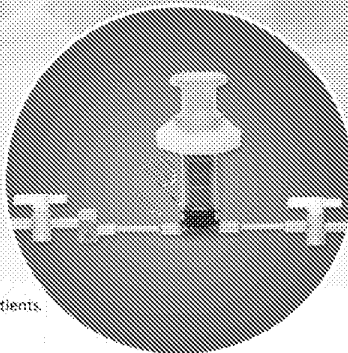
Retractable Technologies, Inc. v. Becton Dickinson & Co.

Produced by Sans Paper, LLC.

Conservation. Safety. Simplicity. Edwards VAMP and VAMP Jr. Systems.

VAMP System

Venous Arterial blood Management Protection System



VAMP Jr. System

for pediatric and neonatal patients.



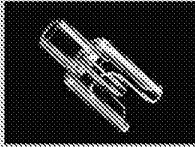


Figure 1: Cannula

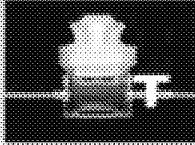


Figure 2: VAMP reservoir

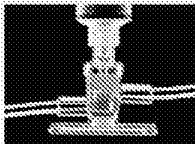


Figure 3: Z-site sampling port

VAMP Kits.

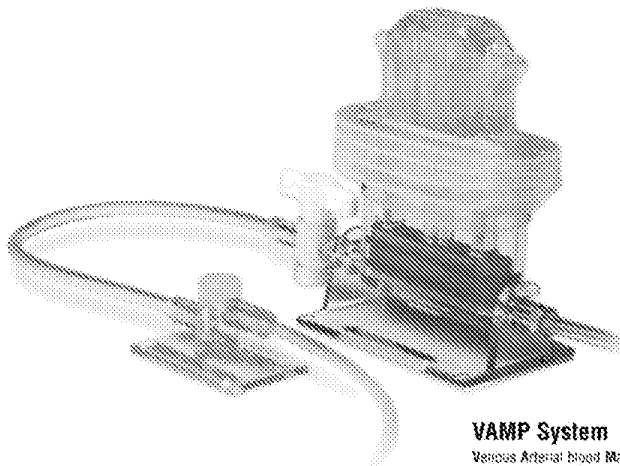
The closed blood sampling system—the perfect partner to the Edwards TruWave Disposable Pressure Transducer. The Edwards VAMP system provides the safety and patient comfort of needleless blood sampling. The blunt cannula design (Figure 1) provides safety by eliminating the needlesticks associated with blood sampling.

It's the only system with the VAMP reservoir—a unique design that conserves blood and ensures consistent blood sampling (Figure 2).

Another unique design that enables the collection of undiluted samples while greatly reducing residual blood buildup, is our Z-site sampling port (Figure 3). The VAMP system was designed with the benefits of a closed system in mind. From the self-sealing sampling port that replaces stopcocks to our patented reservoir and shut-off valve, we're dedicated to providing safe and convenient blood sampling for your patients.

The VAMP system is easy, safe, and convenient for your patient. And it works best with TruWave Disposable Pressure Transducers.

An Easy, Convenient System... An Accurate System



VAMP System

Venous Arterial blood Management Protection System

The safe way to perform pediatric and neonatal blood sampling.

Because it's just the right size for pediatric and neonatal care, the Edwards VAMP Jr. system makes blood sampling easier and safer for you and your special patients. Completely closed, which may provide greater protection against nosocomial infections, the VAMP Jr. system reduces the loss of patient blood while providing consistent clearing volumes, safer reinsertion and undisturbed accurate blood samples. The needleless system also reduces the threat of needlesticks.

A unique in-line reservoir puts safety first.

Blood conservation and consistent sampling are critical for optimal pediatric and neonatal care. The VAMP Jr. reservoir is designed with "ic" markings to help you select the appropriate clearing volumes based on the size of your patient and the samples required. And since the volume is held in the in-line reservoir and not set aside in a syringe to be returned later, the potential for contamination may be reduced. After sampling, the plunger is pushed closed, wiping the walls clean and safely reinfusing all the blood to the patient. Plus, VAMP Jr.'s special contamination hood and one way in line shut-off valves may reduce the risk of

exposure from touch and/or airborne contaminants.

The VAMP Jr. system fits the special needs of your special patients.

The VAMP Jr. system is designed to require decreased volume with a smaller reservoir for more accurate sampling and flushing in pediatric and neonatal patients. For the added convenience of accurate pressure monitoring, the VAMP Jr. system is available preassembled with TruWave disposable pressure transducers (DPTs) in kit configurations to meet the special needs of your special patients.

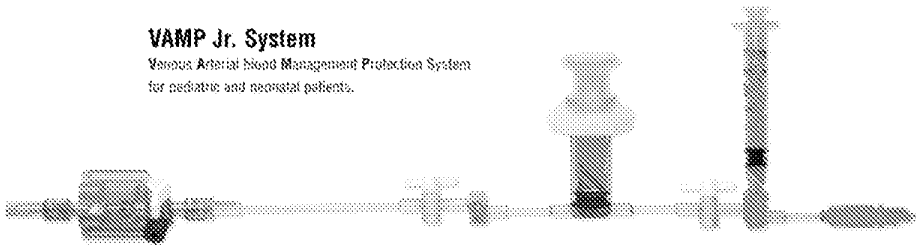
To learn more about the VAMP Jr. system contact your Edwards Lifesciences Corporation Representative at 1-801-424-1278.



tem... And with VAMP Kits, A Complete System

VAMP Jr. System

Vascular Arterial blood Management Protection System for pediatric and neonatal patients.



VAMP System Venous Arterial blood Management Protection

TruWave/VAMP Combination Kits	Case Qty.	Model No.
80" VAMP System with Arm-mount Reservoir	10	PXVAMP130
80" VAMP System with Arm-mount Reservoir	10	PXVAMP160
72" VAMP System with Arm-mount Reservoir	10	PXVAMP172
64" VAMP System with Arm-mount Reservoir	10	PXVAMP184
80" VAMP System with Pole-mount Reservoir	10	PXVAMP260
72" VAMP System with Pole-mount Reservoir	10	PXVAMP272
64" VAMP System with Pole-mount Reservoir	10	PXVAMP284
80" VAMP System with Arm-mount Reservoir on the arterial line with:	10	PXVAMP2K21
<ul style="list-style-type: none"> • Two TruWave Disposable Pressure Transducers with two 3 ml/hr flush devices • Bifurcated IV set instructions • One set of 48" and 12" pressure taping • Three 3-way stopcocks 		
80" VAMP System with Pole-mount Reservoir on the arterial line with:	10	PXVAMP2K22
<ul style="list-style-type: none"> • Two TruWave Disposable Pressure Transducers with two 3 ml/hr flush devices • Bifurcated IV set instructions • One set of 48" and 12" pressure taping • Three 3-way stopcocks 		

Please contact your local sales representative for VAMP combination kit information and model numbers.

VAMP Jr. System

VAMP Jr.	VAMP Jr./DPT Combo Kits
VAMP306 2" proximal, 4" distal for neonatal application	VAMP306PX Don TruWave DPT with 2" proximal, 4" distal VAMP Jr. for neonatal application
VAMP408 3" proximal, 3" distal for pediatric application	VAMP408PX Don TruWave DPT with 3" proximal, 3" distal VAMP Jr. for pediatric application
VAMP425 12" proximal, 16" distal for pediatric application	VAMP425PX Don TruWave DPT with 12" proximal, 16" distal VAMP Jr. for pediatric application
VAMP448 18" proximal, 28" distal for pediatric application	VAMP448PX Don TruWave DPT with 18" proximal, 28" distal VAMP Jr. for pediatric application



Edwards Lifesciences, Edwards, the stylized E logo and TruWave are trademarks of Edwards Lifesciences Corporation. © 2019 Edwards Lifesciences Corporation. All rights reserved. Edwards Lifesciences Corporation and its approved distributors, agents and dealers are ISO 13485.

Caution: Please refer to current product packaging for instructions, contraindications, warnings, precautions and other important information.

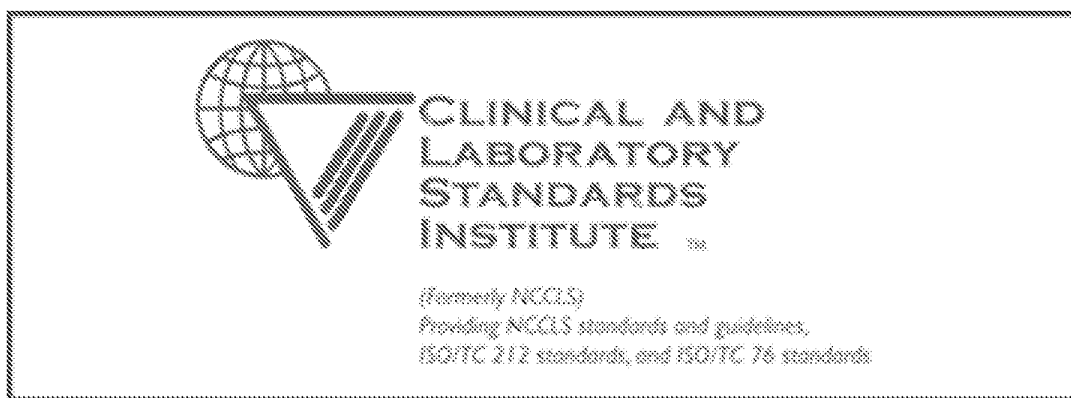
© 2019 Edwards Lifesciences LLC. All rights reserved. 1358-1300-11.



Edwards Lifesciences

Edwards Lifesciences LLC • One Edwards Way • Irvine, CA 92614 USA • 949.255.2500 • 800.454.3278 • www.edwards.com
 Edwards Lifesciences (Canada) Inc. • 1380 Centre Parkway West, Suite 300 • Mississauga, Ontario • Canada L5T 4G9 • Phone 905.585.3278 • 800.298.3903
 Edwards Lifesciences S.A. • Ch. du Gigan 6 • 1150 Saint-Pierre • Switzerland • Phone 41.21.825.8360
 Edwards Lifesciences Japan • 2-1-1 Rokusancho • Chiyoda-ku, Tokyo 100-0305 • Japan • Phone 81.3.5213.0755

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



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

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



NCCLS...

Serving the World's Medical Science Community Through Voluntary Consensus

NCCLS is an international, interdisciplinary, nonprofit, standards-developing, and educational organization that promotes the development and use of voluntary consensus standards and guidelines within the healthcare community. It is recognized worldwide for the application of its unique consensus process in the development of standards and guidelines for patient testing and related healthcare issues. NCCLS is based on the principle that consensus is an effective and cost-effective way to improve patient testing and healthcare services.

In addition to developing and promoting the use of voluntary consensus standards and guidelines, NCCLS provides an open and unbiased forum to address critical issues affecting the quality of patient testing and health care.

PUBLICATIONS

An NCCLS document is published as a standard, guideline, or committee report.

Standard A document developed through the consensus process that clearly identifies specific, essential requirements for materials, methods, or practices for use in an unmodified form. A standard may, in addition, contain discretionary elements, which are clearly identified.

Guideline A document developed through the consensus process describing criteria for a general operating practice, procedure, or material for voluntary use. A guideline may be used as written or modified by the user to fit specific needs.

Report A document that has not been subjected to consensus review and is released by the Board of Directors.

CONSENSUS PROCESS

The NCCLS voluntary consensus process is a protocol establishing formal criteria for:

- the authorization of a project
- the development and open review of documents
- the revision of documents in response to comments by users
- the acceptance of a document as a consensus standard or guideline.

Most NCCLS documents are subject to two levels of consensus—"proposed" and "approved." Depending on

the need for field evaluation or data collection, documents may also be made available for review at an intermediate (i.e., "tentative") consensus level.

Proposed An NCCLS consensus document undergoes the first stage of review by the healthcare community as a proposed standard or guideline. The document should receive a wide and thorough technical review, including an overall review of its scope, approach, and utility, and a line-by-line review of its technical and editorial content.

Tentative A tentative standard or guideline is made available for review and comment only when a recommended method has a well-defined need for a field evaluation or when a recommended protocol requires that specific data be collected. It should be reviewed to ensure its utility.

Approved An approved standard or guideline has achieved consensus within the healthcare community. It should be reviewed to assess the utility of the final document, to ensure attainment of consensus (i.e., that comments on earlier versions have been satisfactorily addressed), and to identify the need for additional consensus documents.

NCCLS standards and guidelines represent a consensus opinion on good practices and reflect the substantial agreement by materially affected, competent, and interested parties obtained by following NCCLS's established consensus procedures. Provisions in NCCLS standards and guidelines may be more or less stringent than applicable regulations. Consequently, conformance to this voluntary consensus document does not relieve the user of responsibility for compliance with applicable regulations.

COMMENTS

The comments of users are essential to the consensus process. Anyone may submit a comment, and all comments are addressed, according to the consensus process, by the NCCLS committee that wrote the document. All comments, including those that result in a change to the document when published at the next consensus level and those that do not result in a change, are responded to by the committee in an appendix to the document. Readers are strongly encouraged to comment in any form and at any time on any NCCLS document. Address comments to the NCCLS Executive Offices, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

VOLUNTEER PARTICIPATION

Healthcare professionals in all specialties are urged to volunteer for participation in NCCLS projects. Please contact the NCCLS Executive Offices for additional information on committee participation.

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

Charles F. Arkin, M.D.
J. David Bessman, M.D.
Roger R. Calam, Ph.D., DABCC
Dennis J Ernst, M.T.(ASCP)
Gary T. Parish
Diane I. Szamosi, M.A., M.T.(ASCP), SH
David J. Warunek, Ph.D.
Joan D. Wiseman, M.T.(ASCP)CT

Abstract

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

NCCLS. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition*. NCCLS document H3-A5 (ISBN 1-56238-515-1). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2003.

THE NCCLS consensus process, which is the mechanism for moving a document through two or more levels of review by the healthcare community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of NCCLS documents. Current editions are listed in the *NCCLS Catalog*, which is distributed to member organizations, and to nonmembers on request. If your organization is not a member and would like to become one, and to request a copy of the *NCCLS Catalog*, contact the NCCLS Executive Offices. Telephone: 610.688.0100; Fax: 610.688.0700; E-Mail: exoffice@nccls.org; Website: www.nccls.org



This publication is protected by copyright. No part of it may be reproduced, stored in a retrieval system, transmitted, or made available in any form or by any means (electronic, mechanical, photocopying, recording, or otherwise) without prior written permission from NCCLS, except as stated below.

NCCLS hereby grants permission to reproduce limited portions of this publication for use in laboratory procedure manuals at a single site, for interlibrary loan, or for use in educational programs provided that multiple copies of such reproduction shall include the following notice, be distributed without charge, and, in no event, contain more than 20% of the document's text.

Reproduced with permission, from NCCLS publication H3-A5—*Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition* (ISBN 1-56238-515-1). Copies of the current edition may be obtained from NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA.

Permission to reproduce or otherwise use the text of this document to an extent that exceeds the exemptions granted here or under the Copyright Law must be obtained from NCCLS by written request. To request such permission, address inquiries to the Executive Director, NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA.

Copyright ©2003. The National Committee for Clinical Laboratory Standards.

Suggested Citation

(NCCLS. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition*. NCCLS document H3-A5 [ISBN 1-56238-515-1]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2003.)

Proposed Standard

August 1977

Approved Standard—Fourth Edition

June 1998

Tentative Standard

February 1979

Approved Standard—Fifth Edition

December 2003

Approved Standard

March 1980

Approved Standard—Second Edition

April 1984

Approved Standard—Third Edition

July 1991

ISBN 1-56238-515-1

ISSN 0273-3099

Committee Membership

Area Committee on Hematology

Charles F. Arkin, M.D.

Chairholder

Lahey Clinic

Burlington, Massachusetts

Bruce H. Davis, M.D.

Vice-Chairholder

Maine Medical Center Research

Institute

Scarborough, Maine

J. David Bessman, M.D.

University of Texas Medical Branch

Galveston, Texas

Berend Houwen, M.D., Ph.D.

Beckman Coulter, Inc.

Brea, California

Frank M. LaDuca, Ph.D.

International Technidyne

Corporation

Edison, New Jersey

Ginette Y. Michaud, M.D.

FDA Center for Devices/Rad.

Health

Rockville, Maryland

Onno W. van Assendelft, M.D.,

Ph.D.

Centers for Disease Control and

Prevention

Atlanta, Georgia

Advisors

Dorothy M. Adcock, M.D.

Esoterix Coagulation

Aurora, Colorado

Sheila Clover, CPT (ASCP) (NCA)

Phlebotomy West

Brentwood, California

Dennis J. Ernst, M.T.(ASCP)

Center for Phlebotomy Education

Ramsey, Indiana

J. Heinrich Joist, M.D., Ph.D.

St. Louis University Health Science

Center

St. Louis, Missouri

John A. Koepke, M.D.

Durham, North Carolina

Francis Lacombe, M.D., Ph.D.

Laboratoire d'Hematologie

Pessac, France

Samuel J. Machin, MB, Ch.B,

FRCPath

The University College London

Hospital

London, United Kingdom

Richard A. Marlur, Ph.D.

Denver VA Medical Center

Denver, Colorado

Diane L. Szamosi,

M.A.,M.T.(ASCP)SH

Greiner Bio-One, VACUETTE

North America, Inc.

Monroe, North Carolina

Luc Van Hove, M.D., Ph.D.

Abbott Laboratories

Abbott Park, Illinois

Staff

Tracy A. Dooley, M.L.T.(ASCP)

Staff Liaison

NCCLS

Wayne, Pennsylvania

David E. Sterry, M.T.(ASCP)

Project Manager

NCCLS

Wayne, Pennsylvania

Donna M. Wilhelm

Editor

NCCLS

Wayne, Pennsylvania

Melissa A. Lewis

Assistant Editor

NCCLS

Wayne, Pennsylvania

Acknowledgement

NCCLS gratefully acknowledges the working group for their help in preparing the approved-level, fifth edition of this standard.

Charles F. Arkin, M.D.

Lahey Clinic

J. David Bessman, M.D.

University of Texas Medical Branch

Roger R. Calam, Ph.D., DABCC

St. John Hospital

Dennis J. Ernst, M.T.(ASCP)

Center for Phlebotomy Education

Gary T. Parish

Sarstedt, Inc.

Diane I. Szamosi, M.A.,

M.T.(ASCP), SH

Greiner Bio-One, VACUETTE

North America, Inc.

David J. Warunek, Ph.D., M.B.A.

BD VACUTAINER Systems

Joan D. Wiseman, M.T.(ASCP), CT

Consultant

Bernardsville, New Jersey

Contents

Abstract.....	i
Committee Membership.....	iii
Foreword.....	vii
1 Scope.....	1
2 Introduction.....	1
3 Standard Precautions.....	1
4 Definitions	1
5 Factors That Affect Laboratory Values	2
6 Facilities.....	2
6.1 Venipuncture Chairs.....	2
6.2 Hospital Area.....	3
7 Supplies.....	3
7.1 Utility Carts	3
7.2 Blood Collecting Trays.....	3
7.3 Gloves.....	3
7.4 Needles and Holders.....	4
7.5 Sterile Syringes.....	4
7.6 Venous Blood Collection Tubes.....	4
7.7 Tourniquets.....	4
7.8 Antiseptics	5
7.9 Gauze Pads	5
7.10 Puncture-Resistant Disposal Container	5
7.11 Ice	5
7.12 Adhesive Bandages.....	5
7.13 Warming Devices	5
7.14 Test Reference Manual.....	5
8 Venipuncture Procedure.....	5
8.1 Step 1: Prepare Accession Order.....	6
8.2 Step 2: Approach and Identify the Patient.....	6
8.3 Step 3: Verify Patient Diet Restrictions and Latex Sensitivity.....	8
8.4 Step 4: Assemble Supplies	8
8.5 Step 5: Position Patient.....	9
8.6 Step 6: Apply Tourniquet	10
8.7 Step 7: Put on Gloves	13
8.8 Step 8: Cleanse Venipuncture Site	13
8.9 Step 9: Perform Venipuncture	13
8.10 Step 10: Order of Draw	17
8.11 Step 11: Release the Tourniquet.....	17
8.12 Step 12: Place the Gauze Pad	17
8.13 Step 13: Remove and Dispose of the Needle.....	18
8.14 Step 14: Bandage the Arm.....	18

Contents (Continued)

8.15	Step 15: Label Blood Collection Tubes and Record Time of Collection	18
8.16	Step 16: Chill the Specimen	19
8.17	Step 17: Send Blood Collection Tubes to the Proper Laboratories	19
9	Venipuncture in Children and Difficult Collections	19
9.1	Procedure	19
9.2	Equipment	19
10	Additional Considerations	19
10.1	Monitoring Blood Volume Collected	19
10.2	Hematoma	20
10.3	Hemolysis	20
11	Special Situations	20
11.1	Timed Intervals	20
11.2	Specific Collection Techniques	20
11.3	Indwelling Lines or VADs	21
11.4	Heparin or Saline Locks	22
11.5	Fistula	22
11.6	Intravenous Fluids	22
11.7	Isolation	23
11.8	Emergency Situations	24
	References	26
	Summary of Comments and Subcommittee Responses	27
	Summary of Delegate Comments and Working Group Responses	28
	The Quality System Approach	34
	Related NCCLS Publications	35

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

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.

(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.³

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.

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.

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).

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 cultures⁷ (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.

- 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.

- (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.

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.).

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 H11—*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.

- (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.

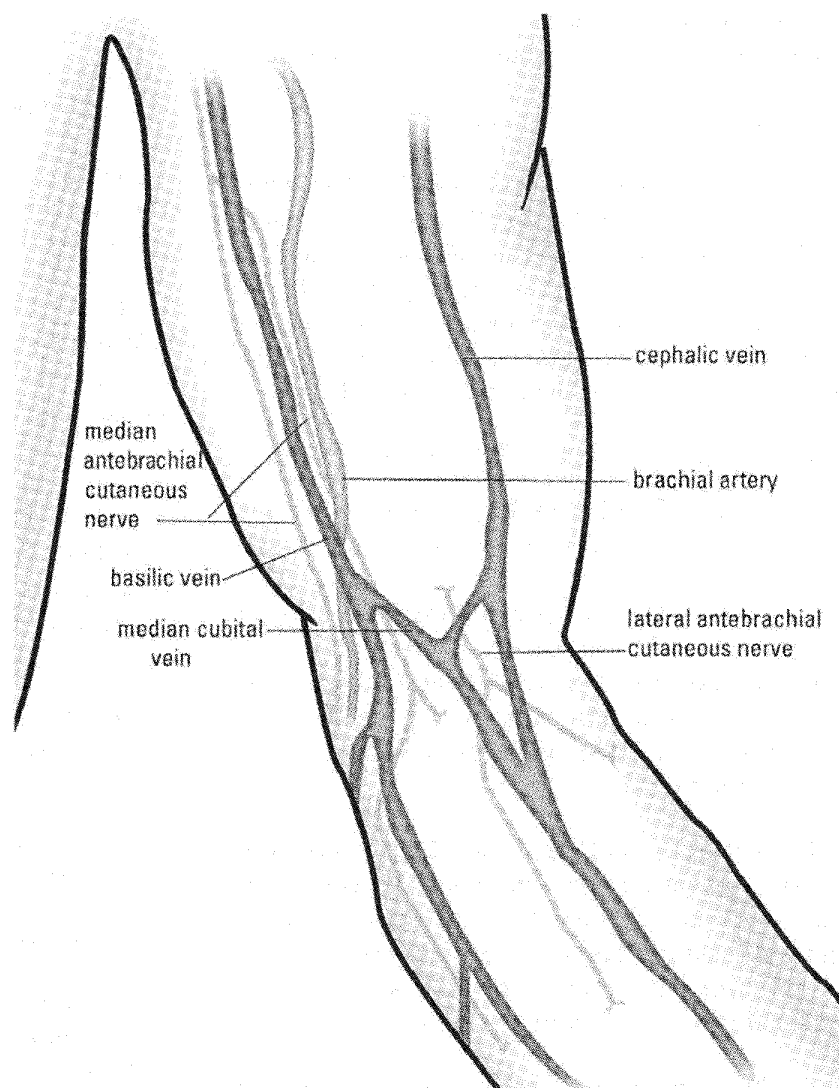


Figure 1. Superficial Veins of the Anterior Surface of the Upper Extremity (From Ernst DJ, Ernst C. Phlebotomy tools of the trade: Part 2—Surveying the antecubital area. *Home Healthcare Nurse*. 2002;20:402-403. Reprinted with permission from Lippincott Williams & Wilkins.)

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.

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,

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.

- (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."

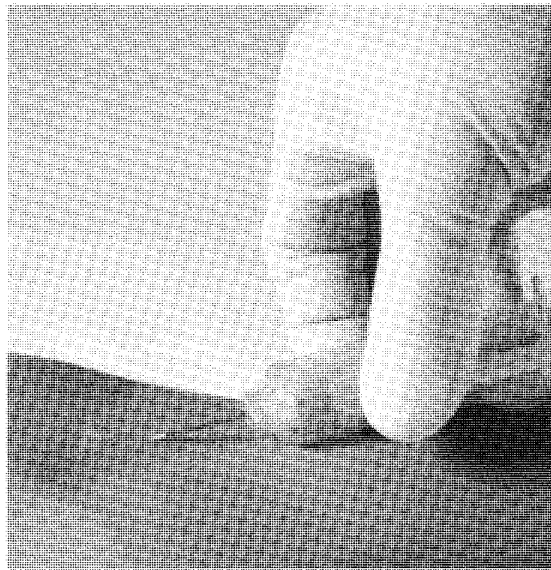


Figure 2. Proper Angle of Insertion (Figure contributed by the Center for Phlebotomy Education, Inc.)

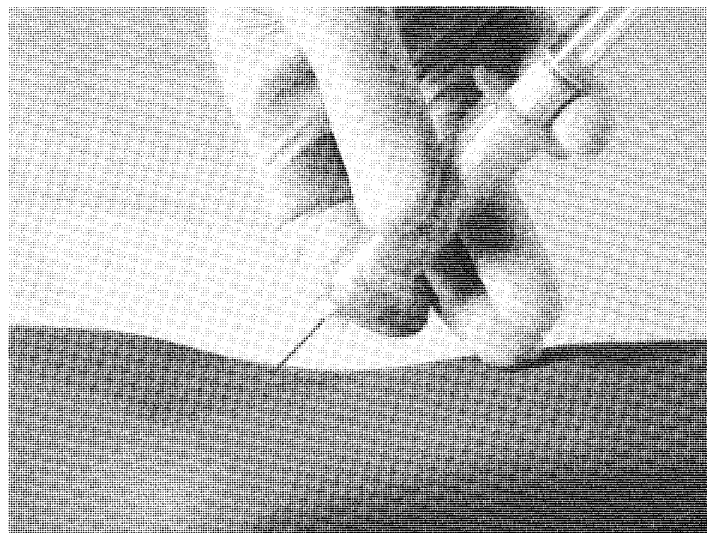


Figure 3. Improper Angle of Insertion (Figure contributed by the Center for Phlebotomy Education, Inc.)

- (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).

- (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.

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.

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

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.

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.)

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

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.

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 precautions²⁷:

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

There are three types of transmission based isolation precautions²³:

- 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.

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:

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

Menglin Tang, RN, BSN¹, Mei Feng, RN, MSN, Lijun Chen, RN, BSN, Jinmei Zhang, RN, BSN, Peng Ji, MM and Shuhua Luo, PhD

Author Affiliations

Author Affiliations

Corresponding author: Menglin Tang, RN, BSN, Department of Pediatric Intensive Care Unit, West China Hospital of Sichuan University, No. 37 Wai Nan Guo Xue Xiang, Chengdu, Sichuan, China (e-mail: menglin_tang@163.com).

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 studies⁶⁻⁸ indicated a low risk for infections associated with use of arterial catheters, recent studies⁹⁻¹¹ 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 al²¹ 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.

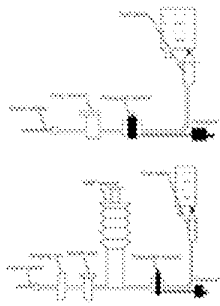
Samples and Randomization

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



View larger version:
 * In this page * In a new window

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 46 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 264 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).

View this table: ✱ In this window ✱ In a new window	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).

View this table: ✱ In this window ✱ In a new window	Table 2 Results of microbiological analysis of the 2 types of arterial catheter systems
--	---

View this table: ✱ In this window ✱ In a new window	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.

View this table:
* In this window * In a new window

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 guidelines²² 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 study²⁵ 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 studies⁹⁻¹¹ 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 al²¹ 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 al³² 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

Acknowledgments

We thank Mr Kuita Huang for the schematic diagrams of the 2 arterial catheter systems

We are also grateful to Dr Yabo Wang and Dr Da Zhu for their useful comments.

Footnotes

To purchase electronic or print reprints, contact the American Association of Critical-Care Nurses, 101 Columbia, Aliso Viejo, CA 92656. Phone, (800) 899-1712 or (949) 362-2050 (ext 532); fax, (949) 362-2049; e-mail, reprints@aacn.org.

Financial Disclosures

This research was supported by West China Hospital Research Funding H1212134.

eLetters

Now that you've read the article, create or contribute to an online discussion about this topic using eLetters. Just visit www.ccnonline.org and select the article you want to comment on. In the full-text or PDF view of the article, click "Responses" in the middle column and then "Submit a response."

dotmore

To learn more about reducing the risk for catheter-related infections, read "Simulation-Based Training for Nurses in Sterile Techniques During Central Vein Catheterization" by Gerolemcu et al in the *American Journal of Critical Care*, January 2014;23:40–48. Available at www.ajcconline.org.

©2014 American Association of Critical-Care Nurses

References

1. Paol J, Hanna M, Maki D. Intravascular catheter-related infections: advances in diagnosis, prevention, and management. *Lancet Infect Dis*. 2007;7(10):645–657. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
2. Frasca D, Dahyot-Fizelier C, Mimoz O. Prevention of central venous catheter-related infection in the intensive care unit. *Crit Care*. 2010;14(2):212.. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
3. Halton K, Graves N. Economic evaluation and catheter-related bloodstream infections. *Emerg Infect Dis*. 2007;13(6):815–823. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
4. Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. *Crit Care Med*. 2006;34(8):2084–2089. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
5. Neusch JE, Belli PL, Lake MD, et al. Reducing catheter-associated bloodstream infections in the pediatric intensive care unit: business case for quality improvement. *Pediatr Crit Care Med*. 2010;11(5):579–587. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
6. Ducharme EM, Guithrie M, Lacroix L, Lafleur L. Incidence of infection related to arterial catheterization in children: a prospective study. *Crit Care Med*. 1988;16(3):272–276. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
7. Lavente J, Jiménez A, Martín MM, Jiménez H, Triharran H, Marrs M, Laver. Arterial catheter-related infection in brachial than in femoral access. *Am J Infect Control*. 2010;38(9):e40–e42. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
8. Lavente J, Villanar J, Martín MM, Jiménez A, Marrs M, Laver. Catheter-related infection in critically ill patients. *Intensive Care Med*. 2004;30(8):1681–1684. » [Medline](#) » [Google Scholar](#)
9. Pilander PL, Van Wilgenboord E, Wilmer A, Bontemans WE. Use of full sterile barrier precautions during insertion of arterial catheters: a randomized trial. *Clin Infect Dis*. 2003;36(6):743–774. » [Abstract/FREE Full Text](#)
10. Lucet JC, Bouadma L, Zahar JR, et al. Infectious risk associated with arterial catheters compared with central venous catheters. *Crit Care Med*.

11. Couradman JP, Linman J, Richard CM. Assessment of peripheral arterial catheters as a source of sepsis in the critically ill: a narrative review. *J Hosp Infect.* 2010;75(1):12-18. »CrossRef »Medline »Google Scholar
12. Richards ML, Edwards JP, Culbreth DM, Gaurer BD. Nosocomial infections in pediatric intensive care units in the United States. *Pediatrics.* 1999; 102:A1620.
»»»<http://pediatrics.aappublications.org/content/103/4/e39.long>.
»Abstract/FREE Full Text
13. Gray C, Fowler SA, Cheney David C, King RM. Microbial contamination of arterial infusions used for hemodynamic monitoring: a randomized trial of contamination with sampling through conventional stopcock versus a novel closed system. *Infect Control Hosp Epidemiol.* 1989;10(12): 557-561.
»CrossRef »Medline »Google Scholar
14. Bouza E, Muñoz P, López Rodríguez, et al. A needleless closed system device (CLAVE) protector from intravascular catheter tip and hub colonization: a prospective randomized study. *J Hosp Infect.* 2003;54(4):279-287. »CrossRef »Medline »Google Scholar
15. Eneanya C, Courbier M, Lacroix J, Madaou D, Laffont J, Mathuyn S. Arterial catheter related infections in children: a 3 year cohort analysis. *Am J Dis Child.* 1991;145(9):1037-1042. »CrossRef »Medline »Google Scholar
16. Ots J, Imanishi H, Kanno M, Nakatani E, Nishimura M. A prospective clinical trial on prevention of catheter contamination using the hub protection cap for needleless injection device. *Am J Infect Control.* 2011; 39(4):309-313.
»CrossRef »Medline »Google Scholar
17. Casey AL, Burnell S, Whinn H, Worthington T, Farouqi MH, Elliott TS. A prospective clinical trial to evaluate the microbial barrier of a needleless connector. *J Hosp Infect.* 2007;65(3):212-218. »CrossRef »Medline »Google Scholar
18. Casey AL, Worthington T, Lambart BA, Quinn D, Farouqi MH, Elliott TS. A randomized, prospective clinical trial to assess the potential infection risk associated with the PeriFlow needleless connector. *J Hosp Infect.* 2003;54(4):286-293. »CrossRef »Medline »Google Scholar
19. Váheenen JC, Sauer C, Salazar M, et al. Safety of positive pressure valve connector in arterial catheters inserted into critically ill patients. *J Hosp Infect.* 2008;70(4):341-345. »CrossRef »Medline »Google Scholar
20. Mukhopadhyay A, Vin US, Baskarajumma D, et al. The use of a blood concentration device to reduce red blood cell transfusion requirements: a before and after study. *Crit Care.* 2010;14(1):R7.. »CrossRef »Medline »Google Scholar
21. Ots J, Nakatani E, Ueda M, et al. Comparison of bacterial contamination of blood concentration system and stopcock system arterial sampling lines used in critically ill patients. *Am J Infect Control.* 2012;40:531-537.
»Google Scholar
22. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis.* 2002; 35(11):1281-1307. »Abstract/FREE Full Text
23. Blet C, Nitenberg C, Chachaty E, et al. Diagnosis of catheter-related bacteraemia: a prospective comparison of the time to positivity of hub-blood versus peripheral blood cultures. *Lancet.* 1999;354(9184):1071-1077. »CrossRef »Medline »Google Scholar
24. Maki DG, Wiles CE, Sarrin DM. A semiquantitative culture method for identifying intravascular catheter-related infection. *Am J Med.* 1977;296:1305-1309. »CrossRef »Medline »Google Scholar
25. Tenover C, Lintley J, Scavoline R. Prospective study of arterial and central venous catheter colonization and of arterial and central venous catheter-related bacteraemia in intensive care units. *Crit Care Med.* 2005;33(6): 1276-1280. »CrossRef »Medline »Google Scholar
26. Bennett DM, Collins DB, McCannan CI, Backbath AD. The 100,000 Lives Commission: setting a goal and a deadline for improving health care quality. *JAMA.* 2006;295(3):324-327. »CrossRef »Medline »Google Scholar
27. Lacroix J, Santarrou D, Martin MM, Jiménez A, Mira JJ. Arterial catheter-related infection of 7040 catheters. *Crit Care.* 2006;10:R83. »CrossRef »Medline »Google Scholar
28. Esteban E, Buñol M, Pérez VL, et al. Bacteraemia related with arterial catheter in critically ill patients. *J Infect.* 2011;63(2):139-143. »CrossRef »Medline »Google Scholar
29. Thomas S, Thomas AM. The use of a blood concentration pressure transducer system in critically ill patients. *Anaesthesia.* 2000;55(1):27-31. »CrossRef

» [Medline](#) » [Google Scholar](#)

30. Ford Jones EL, Munderoff CM, Langley JM, et al. Epidemiologic study of 4684 hospital-acquired infections in pediatric patients. *Pediatr Infect Dis J*. 1989;8:668-675. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
31. Raymond J, Aulard Y. Nosocomial infection in pediatric patients: a European, multicenter prospective study. *Infect Control Hosp Epidemiol*. 2000;21(4):260-263. » [CrossRef](#) » [Medline](#) » [Google Scholar](#)
32. Clodi PL, Corrado M, Salzman CL. Quantitative culture of intravenous catheters and other intravascular inserts. *J Infect Dis*. 1980;141(6):781-786. » [Abstract/FREE Full Text](#)

We recommend

Chlorhexidine-Impregnated Dressings and Prevention of Catheter-Associated Bloodstream Infections in a Pediatric Intensive Care Unit

Drayga Stamez Ditzkaya et al., *Crit Care Nurs*

Arterial catheter setup for glucose control in critically ill patients: a randomized controlled trial.

Marta Pauwels-Torredó et al., *Am J Crit Care*

Evaluation of the use of a stabilization device to improve the quality of care in patients with peripherally inserted central catheters.

Jennifer Wallerhouse et al., *AACN Adv Crit Care*

Density of microbial colonization on external and internal surfaces of concurrently placed intravascular devices.

David Boon Choi Koh et al., *Am J Crit Care*

Using A Criteria-Based Reminder To Reduce Use Of Indwelling Urinary Catheters And Decrease Urinary Tract Infections

Yin-Yin Chen et al., *Am J Crit Care*

Antibiotic-Coated Central Venous Catheters ☑

Christine Campbell-Reardon et al., *Medscape*

Cluster-randomized trial of devices to prevent catheter-related bloodstream infection ☑

Bronelli SM et al., *MDLinx*

Hepatitis C: Why Was Your Medicaid Patient Rejected for Treatment? ☑

Insights Into Hepatitis

Non-inferiority of open passive drains compared with closed suction drains in pancreatic surgery outcomes: A prospective observational study ☑

Marchisiani G et al., *MDLinx*

Arterial Catheter for Glucose Control in Critically Ill ☑

Marta Pauwels-Torredó et al., *Medscape*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference KURIN4PCT		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US 20/23617	International filing date (day/month/year) 19 March 2020 (19.03.2020)	(Earliest) Priority Date (day/month/year) 13 March 2020 (13.03.2020)	
Applicant KURIN, INC.			

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

This international search report consists of a total of 2 sheets.

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

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed.
☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (see Box No. II).

3. ☐ Unity of invention is lacking (see Box No. III).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. 35
☐ as suggested by the applicant.
☐ as selected by this Authority, because the applicant failed to suggest a figure.
☒ as selected by this Authority, because this figure better characterizes the invention.
- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/23617

A. CLASSIFICATION OF SUBJECT MATTER IPC - A61B 5/15, A61B 5/153, A61B 5/154, A61B 5/157 (2020.01) CPC - A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) See Search History document Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched See Search History document Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) See Search History document		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2018/0177445 A1 (Kurin, Inc.) 28 June 2018 (28.06.2018), entire document	1-4, 10-12, 18

Y		5-9, 13-17, 19-20
Y	US 4,349,035 A (Thomas et al.) 14 September 1982 (14.09.1982), entire document	5-6, 8-9, 13-14, 16-17, 19-20
Y	US 5,401,262 A (Karwoski et al.) 28 March 1995 (28.03.1995), entire document	5, 7, 13, 15
A	US 2018/0271425 A1 (Kurin, Inc.) 27 September 2018 (27.09.2018), entire document	1-20
A	US 2018/0353117 A1 (Magnolia Medical Technologies, Inc.) 13 December 2018 (13.12.2018), entire document	1-20
☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "D" document cited by the applicant in the international application "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 07 JUNE 2020		Date of mailing of the international search report 19 JUN 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300		Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

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 43bis.1)

Date of mailing
(day/month/year)

19 JUN 2020

Applicant's or agent's file reference

KURIN4PCT

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US 20/23617

International filing date (day/month/year)

19 March 2020 (19.03.2020)

Priority date (day/month/year)

13 March 2020 (13.03.2020)

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

IPC - A61B 5/15, A61B 5/153, A61B 5/154, A61B 5/157 (2020.01)

CPC - A61B 5/15003, A61B 5/150213, A61B 5/150251, A61B 5/150992, A61B 5/150206, A61B 5/150221, A61B 5/150946

Applicant KURIN, INC.

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

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

2. FURTHER ACTION

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

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

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

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Date of completion of this opinion

07 JUNE 2020

Authorized officer

Lee Young

PCT Help Desk

Telephone No. 571-272-4300

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/23617

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed.
 - ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(b)).
3. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/23617

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement			
1. Statement				
Novelty (N)	Claims	5-9, 13-20	YES	
	Claims	1-4, 10-12	NO	
Inventive step (IS)	Claims	none	YES	
	Claims	1-20	NO	
Industrial applicability (IA)	Claims	1-20	YES	
	Claims	none	NO	
2. Citations and explanations:				
Claims 1-4 and 10-12 lack novelty under PCT Article 33(2) as being anticipated by US 2018/0177445 A1 to Kurin, Inc. (hereinafter Kurin).				
<p>Regarding claim 1, Kurin teaches a blood sequestration device (see fig. 30A-G; para [0156]) comprising; an inlet path (fig. 30A see inlet path 3002; para [0156]); an outlet path (fig. 30A see outlet path 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first portion of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A-D see vent 3010; para [0161]; para [0163]-[0165]), the junction being configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, it is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see para[0156], [0160]-[0161], [0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first amount of blood is received by the sequestration chamber (para [0160]-[0170]).</p> <p>Regarding claim 2, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction is angled from the inlet path toward the sequestration chamber (fig. 30A; fig. 17A see junction 3007 is angled from the inlet path to the sequestration chamber; para [0160]).</p> <p>Regarding claim 3, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction has a cross-sectional area that is smaller than a cross-sectional area of the inlet path (fig. 30A; fig. 17A see junction 3007 has a cross-sectional area closest to the inlet path that is smaller than a cross-sectional area of the inlet path below where it meets the junction; para [0160]).</p> <p>Regarding claim 4, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the junction has a cross-sectional area that is larger than a cross-sectional area of the inlet path (fig. 30A; fig. 17A see junction 3007 has a cross-sectional area near the sequestration chamber 3008 that is larger than a cross-sectional area of the inlet path where the inlet path opens to the junction; para [0160]; para [0163] junction cross-sectional area widens towards the sequestration chamber to direct blood).</p> <p>Regarding claim 10, Kurin teaches the blood sequestration device in accordance with claim 1, wherein the vent includes two or more vent apertures (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060] air permeable blood barrier may comprise a mesh, a mesh inherently comprises two or more vent apertures).</p> <p>Regarding claim 11, Kurin teaches a blood sequestration device (see fig. 30A-G; para [0156]) comprising; a housing (fig. 30A see housing 3001; para [0161]) having an inlet port (fig. 30A see inlet path 3002 has port opening in housing 3001; para [0156]; para [0161]) and an outlet port (fig. 30A see outlet path 3004 has outlet opening in housing 3001; para [0159]; para [0161]), the housing containing; an inlet path connected to the inlet port (fig. 30A see inlet path 3002; para [0156]); an outlet path connected with the outlet port (fig. 30A see outlet path 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first amount of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A see vent 3010; para [0161]; para [0163]-[0165]), the vent further being further configured to close upon the sequestration chamber being filled with the first portion of blood (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060]; para [0160]-[0170]), the junction being configured to inhibit a return of the first portion of blood out of the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, it is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see also para[0156], [0160]-[0161], [0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first portion of blood is received by the sequestration chamber (para [0160]-[0170]).</p>				
-Continued in Supplemental Box-				

Form PCT/ISA/237 (Box No. V) (revised January 2019)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 20/23617

Box No. VIII Certain observations on the international application

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

Regarding claim 18, the claim language is confusing and lacks clarity. Specifically, the recitation "the patient needle and the sample needle", lack proper antecedent basis. In order to give meaning to this claim and to give proper antecedent basis, based on the specification (para [0063]), this recitation has been interpreted as the following: "and a blood sequestration device connected along the blood sampling pathway between a patient needle and a sample needle, wherein the venipuncture apparatus includes the patient needle and the reservoir includes the sample needle".

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

-Box V.2 - Citations and Explanations-*

Regarding claim 12, Kurin teaches the blood sequestration device in accordance with claim 11, wherein the vent further comprises a closure mechanism that inhibits air from reentering the sequestration chamber after it has been displaced (para [0161] vent 3010 comprises air permeable blood barrier 3012 as previously described; para [0060]).

Claim 18 lacks an inventive step under PCT Article 33(3) as being obvious over Kurin.

Regarding claim 18, Kurin teaches a blood sample optimization system (fig. 30A-G; para [0156]) comprising: a blood sampling system (para [0156]) comprising: a venipuncture apparatus configured for venipuncture of a patient to access a sample of blood of a patient (para [0156] inlet port 3002 with opening connects to patient needle, needle is a suitable venipuncture apparatus); a blood sampling pathway connected with the venipuncture apparatus for conveying the sample of blood (fig. 30A see system 3000 comprises blood sampling pathway from inlet 3002 to outlet 3004 through sampling channel 3006; para [0156]); and a reservoir (fig. 30A see reservoir 3004; para [0158]); and a blood sequestration device connected along the blood sampling pathway between a patient needle and the reservoir (see fig. 30A-G; para [0156]), wherein the venipuncture apparatus includes the patient needle (para [0156] inlet port 3002 with opening connects to patient needle), the blood sequestration device comprising: an inlet path connected with the patient needle (fig. 30A see inlet path 3002; para [0156]); an outlet path connected with the reservoir (fig. 30A see outlet path through outlet reservoir 3004; para [0158]); a sequestration chamber (fig. 30A see sequestration chamber 3008; para [0160]) connected with the inlet path by a junction (fig. 30A see junction 3007; para [0160]; see fig. 17A-B) and being configured to receive a first portion of blood through the inlet path (para [0160]; para [0163]-[0164]), the sequestration chamber having a vent that allows air to be displaced by the first portion of blood (fig. 30A see vent 3010; para [0161]; para [0163]-[0165]), the junction being configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (intended use - see para [0160] "the diverter junction 3007 is configured such that the flow out of the inlet port 3002 is preferentially directed toward the sequestration chamber 3008" - since the junction is configured to direct flow away from the inlet port, is is thereby considered capable of inhibiting a return to the inlet path of any of the first portion of blood received by the sequestration chamber; see para[0156], [0160]-[0161], [0061],[0067]); and a sampling channel connected between the inlet path and the outlet path (fig. 30A see sampling channel 3006; para [0159]-[0160]), the sampling channel being configured to convey subsequent amounts of blood between the inlet path and the outlet path after the first amount of blood is received by the sequestration chamber (para [0160]-[0170]); but Kurin does not explicitly teach wherein the reservoir is configured for receiving an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood, nor wherein reservoir and connected outlet path comprise a sample needle. However, in another embodiment, Kurin teaches a sample needle at an outlet path of a blood sample collection device facilitates connection to an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood (fig. 1 see sample needle 5; para [0065]; see fig. 7). Combining embodiments is within the ordinary skill of a person within the art. Accordingly, it would have been obvious to a person having ordinary skill in the art to have provided a sample needle such that the reservoir is configured for receiving an evacuated blood collection tube to collect and contain at subsequent portion of the sample of blood in order to provide blood collection means with the blood sampling device.

Claims 5-6, 8-9, 13-14, 16-17 and 19-20 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 4,349,035 A to Thomas et al. (hereinafter Thomas).

Regarding claim 5, Kurin teaches the blood sequestration device in accordance with claim 1, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, in 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, in 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, in 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, in 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 6, Kurin in view of Thomas teaches the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a conical baffle having a tapered end directed toward the sequestration chamber (see Thomas fig. 4-5 passive structure tapers to a point towards chamber, thus restricting flow; see column 5, in 13-17).

Regarding claim 8, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a divider wall extending across a cross-section of the junction (see Thomas fig. 4-5 divider wall 25; column 6, in 7-13).

-*-Continued in next Supplemental Box-*

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

-*-Supplemental Box - Box V.2 - Citations and Explanations.-*-

Regarding claim 9, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 5, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a flow director extending from an inner surface of the junction (see Thomas fig. 4-5 valve 22 is a flow director; column 4, In 23-38; column 5, In 13-17), the flow director being configured to control a flow of blood (see Thomas column 4, In 23-28 flow director valve 22 controls flow by directing into chamber 21 and preventing backflow).

Regarding claim 13, Kurin teaches the blood sequestration device in accordance with claim 11, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, In 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, In 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, In 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, In 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 14, Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a conical baffle having a tapered end directed toward the sequestration chamber (see Thomas fig. 4-5 passive structure tapers to a point towards chamber, thus restricting flow; see column 5, In 13-17).

Regarding claim 16 Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a divider wall extending across a cross-section of the junction. (see Thomas fig. 4-5 divider wall 25; column 6, In 7-13).

Regarding claim 17 Kurin in view of Thomas teach the blood sequestration device in accordance with claim 13, and Kurin modified by Thomas further teaches wherein the one or more passive structures include a flow director extending from an inner surface of the junction (see Thomas fig. 4-5 valve 22 is a flow director; column 4, In 23-38; column 5, In 13-17), the flow director being configured to control a flow of blood (see Thomas column 4, In 23-28 flow director valve 22 controls flow by directing into chamber 21 and preventing backflow).

Regarding claim 19, Kurin teaches the blood sample optimization system in accordance with claim 18, but does not explicitly teach wherein the junction of the blood sequestration device includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Thomas teaches a blood collection device (see fig. 1; column 4, In 20-24) comprising an inlet path (fig. 5 see cannula 19; column 4, In 23-38) and a chamber connected by a junction (fig. 4-5 see junction 22 leads to chamber 21; column 4, In 23-38). Kurin further teaches wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber (fig. 4-5 see junction 22 comprises one-way valve to prevent backflow; column 4, In 32-38). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structure as taught by Thomas in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 20, Kurin in view of Thomas teach the blood sample optimization system in accordance with claim 19, and Kurin modified by Thomas further teaches wherein the one or more passive structures includes a wall extending from an inner surface of the junction to control a flow of the first portion of blood (see Thomas fig. 4-5 divider wall 25; column 6, In 7-13).

-*-Continued in next Supplemental Box.-*-

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/23617

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

-*-Supplemental Box - Box V.2 - Citations and Explanations-*

Claim 5, 7 and 13, 15 lack an inventive step under PCT Article 33(3) as being obvious over Kurin in view of US 5,401,262 A to Karwoski et al. (hereinafter Karwoski).

Regarding claim 5, Kurin teaches the blood sequestration device in accordance with claim 1, but does not explicitly teach wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Karwoski teaches a blood collection device (see fig. 1; column 4, In 20-40). Karwoski further teaches wherein a pathway of the blood collection devices includes one or more passive structures configured to inhibit a return to an inlet path of any of a sample of blood (fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structures as taught by Karwoski in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 7, Kurin in view of Karwoski teach the blood sequestration device in accordance with claim 5, and Kurin modified by Karwoski further teaches wherein the one or more passive structures include two or more staggered baffles extending from an inner surface of the junction (Karwoski fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65).

Regarding claim 13, Kurin teaches the blood sequestration device in accordance with claim 11, wherein the junction includes one or more passive structures configured to inhibit a return to the inlet path of any of the first portion of blood received by the sequestration chamber. However, in similar art, Karwoski teaches a blood collection device (see fig. 1; column 4, In 20-40). Karwoski further teaches wherein a pathway of the blood collection devices includes one or more passive structures configured to inhibit a return to an inlet path of any of a sample of blood (fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65). Passive structures for preventing backflow are well known in the art for improved blood collection by preventing contaminated blood from returning to a patient. Accordingly, it would have been obvious to a person having ordinary skill in the art to have included a passive structures as taught by Karwoski in the device taught by Kurin in order to prevent return flow to the patient for improved blood sampling.

Regarding claim 15, Kurin in view of Karwoski teach the blood sequestration device in accordance with claim 13, and Kurin modified by Karwoski further teaches wherein the one or more passive structures include two or more staggered baffles extending from an inner surface of the junction (Karwoski fig. 1 see baffles 112a-f direct flow through pathway and assist in fluid retention; column 18, In 1-24; column 21, In 55-65).

Claims 1-20 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used by industry.

SEARCH HISTORY

Application Number	PCT/US 20/23617
Search Conducted By	EAW
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)
<p style="text-align: center;">Search Logic:</p> <p>blood sampling sequestration device prevent backflow</p> <p>blood sampling sequestration device baffle directs flow</p> <p>blood sampling collection device prevent backflow</p> <p>blood sampling device valve restricts backflow controls flow</p>	

blood sequestration junction prevents backflow
blood sequestration junction flow restriction

Electronic Database Searched	Google
Files Searched	Web
Date Conducted	7 June 2020 (07.06.2020)
<p>Search Logic:</p> <p>blood sampling sequestration device prevent backflow</p> <p>blood sampling sequestration device baffle directs flow</p> <p>blood sampling collection device prevent backflow</p> <p>blood sampling device valve restricts backflow controls flow</p> <p>blood sequestration junction prevents backflow</p> <p>blood sequestration junction flow restriction</p>	



BD Saf-T-Intima™ closed IV cat ▼



BD Saf-T-Intima™ closed IV catheter system

The BD Saf-T-Intima™ closed IV catheter system incorporates preattached extension tubing to help support reduction in blood exposure.

About

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

[Configure](#) [Accept](#)

A removable PRN adapter allows the use of an ISO-compliant needleless connector.

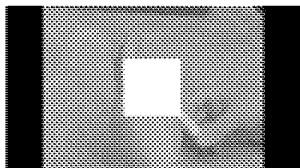
Closed system

Preattached extension tubing offers a closed system to minimize blood exposure during catheter insertion.

BD Vialon™ biomaterial

The system is constructed with BD Vialon biomaterial, a proprietary catheter material that softens in the vein.

Related Videos



BD Saf-T-Intima™ Closed IV Catheter...

Related Products



BD Nexiva™ closed IV catheter system



BD Nexiva™ Diffusics™ closed IV catheter system

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

[Configure](#)

[Accept](#)

Do you like this? Share it:

Contact Sales

Contact Support

DOWNLOADS

-  BD Saf-T-Intima™ directions for use
-  BD Saf-T-Intima™ points to practice in-service material
-  IV catheters/devices brochure

RESOURCES

Infusion Resource Library

Notes

* Compared to a nontapered tip

OFFERINGS

Capabilities
Brands
Integrated solutions
Catalogs

COMPANY

Contact us

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

Configure Accept

[Video gallery](#)

CLINICAL EXCELLENCE

[Case studies](#)

[Events](#)

[Webcasts](#)

[Training](#)

SUPPORT

[Technical support](#)

[Product security and privacy](#)

[Live chat](#)

[Customer portals](#)

[Alerts and notices](#)

[Electronic Instructions for Use](#)



© 2019 BD. All rights reserved. Unless otherwise noted, BD, the BD Logo and all other trademarks are property of Becton, Dickinson and Company.

[Privacy Policy](#) | [Terms of Use](#) | [Cookie Options](#)

This site uses cookies. If you click accept cookies then all cookies will be written. Please review our cookies policy and configure your cookies for your experience.

[Configure](#) [Accept](#)

 Literature display

< 1 / 1 display >

Japanese Patent Laid-Open No. 58-025146

Registration Gazette

public notice

 Document unit PDF progress information OPD search key URLs

Display format of the document display screen:

☒ text display ☐ PDF display

primary literature

bibliography

close



(19) [Country of issue] Japan Patent Office (JP)
(12) [Type of publication] Unexamined patent publication (A)
(11) [Publication number] JP-A-58-25146
(43) [Published date] 1983 (1983) February 15
(54) [Title of Invention] Blood vessel puncture display type multi-sample needle assembly
(51) [International Patent Classification 5th edition]
A61B 5/14
[FI]
A61B 5/14
[Request for examination] Yes
[Total number of pages] 9
(21) [Application number] Japanese Patent Application Showa 57-126629
(22) [Filing date] July 20, 1982
(31) [Priority claim number] 284894
(32) [Priority date] July 20, 1981
(33) [Country claiming priority] United States of America (US)
(71) [Applicant]

[Identification number] 9999999999
 [Name] Becton, Ditzkinson & Company
 (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 not 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, the chamber being translucent surrounding at least the chamber for user perception. a first puncture 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 the chamber and outwardly from the rear end. a second puncture needle extending outward and penetrating into the vacuum container for blood sample collection; an air permeable blood impermeable 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 outside 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 from the second needle; A sample needle assembly with a blood vessel puncture indicator, characterized by:
 2. 3. The assembly of claim 1, wherein said valve is a sleeve in airtight slidable contact over the 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 portion that fits over the outer diameter of the second puncture needle and covers at least one of the

he lateral holes in airtight contact.

5. The means for permitting blood flow includes a cavity formed in the sleeve and having a diameter greater than the fitting diameter, the length of the cavity extending inwardly toward the trailing end of the sleeve. ToWhen slid, the lateral holes are covered so that blood flows from the lateral hole closer to the chamber, through the cavity, back through the other lateral hole, 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 against 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 material.

9. 2. The assembly according to claim 1, wherein said first and second puncture needles are coupled within said chamber, and both puncture needles communicate with said chamber through 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 vacuum vessel to said housing.

12. 12. An assembly according to claim 11, comprising a holder for a vacuum vessel connected 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 puncture needle that feeds a collection device through a piercing device; a device mounted within the lumen of the second piercing needle that permits gas and liquid to pass through the second piercing needle; and a device for operatively collecting fluid from the second puncture needle 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 puncture needle and covers the lateral hole in the closed position. and a resiliently movable valve 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 lateral hole. 14. The assembly of claim 13 collected.

15. 14. The assembly according to claim 13, wherein said first and second puncture needles are integrally formed to form one puncture needle device, and a common lateral hole communicating with said chamber is provided.

16. 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

which is translucent to allow the assembly user to view the chamber. a housing; a first piercing 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 lumen 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 contact to prevent outflow of blood from the second puncture needle in the stationary mounting position, and the inner diameter of the sleeve is the same as that of the second puncture needle. The airtight contact is caused as a fit on the outer diameter, the sleeve is provided with a cavity 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 chamber bypassing the plug, enters the cavity, returns through the other lateral hole, and passes through the second puncture needle. Generating a continuous flow to allow collection, characterized in that the non-cavity portion of the sleeve is compressible towards the trailing end when the sleeve is slid during collection of blood from the second puncture needle. A multi-sample 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 like, and more particularly to collecting multiple samples of blood from a patient in multiple evacuated 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 patient's blood vessel.

It is now standard practice to collect multiple samples of fluid, such as blood, from a patient in a single procedure. Once the needle is inserted into the patient's blood vessel, the evacuated blood collection tube is then inserted into the holder. A holder is configured to connect to the needle and accommodate the vacuum tube. The needle remains inserted in the patient's vessel as each filled tube is removed from the holder. Various valves are currently in use to prevent blood from flowing out of the holder during removal of a filled tube and insertion of the next evacuated tube for subsequent sample collection. An elastomeric sleeve surrounding the inner needle is commonly used as this valve. Although the valve for this multi-sample needle assembly 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 blood vessel. Blood flow within the collection device is often minimal due to difficulty in locating the vessel or other reasons when collecting blood from the patient. In this case, it is most desirable 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 device during a single collection procedure by well-known techniques for multiple sample collection.

A problem that arises during the vascular puncture process is air pockets. This is found in various needle assemblies used for multi-sample blood collection. When a vascular puncture is performed and a vacuum blood collection container has not yet been attached to the other end of the needle device, pockets of air may prevent blood from flowing into the needle assembly. That is, the pocket remains within the needle assembly under steady atmospheric pressure. Therefore, even if a vascular puncture is performed, venous pressure may not allow blood to flow through the intravascular needle and into the collection device, and if a vacuum blood container is attached, the vacuum force will be sufficient within the needle assembly. Acts as a force of attraction. As recognized by the inventors in US Pat. No. 4,207,870, this air block problem prevents blood from flowing through the blood immersion needle to a point visible to the user. The device of this patent combines a porous evacuation device with a bypass valve through 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 Vascular 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 valve and air exclusion device, but are subject to further improvement. The present invention improves upon this device so that air is evacuated from the needle assembly and blood can flow directly into the needle assembly by evacuating the air.

A multi-sample needle assembly according to the present invention is useful for collecting liquid samples from a liquid supply. The needle assembly has a housing with a chamber and a puncture 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 fluid through a chamber to a collection device. A device is provided within the lumen of the second 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 with a front end, a rear end and an interior chamber. The housing surrounds at least the chamber and is translucent so that a user of the assembly can view the chamber. A first puncture ne

needle 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 collection 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 inserted into the space between the lateral holes of the lumen of the second puncture needle. A resilient 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 from flowing out of the second puncture needle. The valve is slidable to an open position, allowing blood to flow out of a lateral port near the chamber and into a second means are provided for 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 different from devices for the same purpose. In particular, the present invention mounts the anti-flow device directly into the second puncture needle. One or more lateral holes are provided in the 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 port to control liquid flow bypassing the liquid impermeable plug. Known devices place liquid-impermeable members in the chamber. There are no valves or liquid-impermeable plugs in the chamber with the configuration of the present invention. Thus, the user can easily see blood entering the chamber during the vascular puncture procedure. By using a gas permeable plug member in the second puncture needle, air is evacuated from within the assembly as blood enters the chamber, eliminating the problem of air blocking in the absence of the gas permeable member. Of particular advantage, during a multi-sample blood collection procedure, the present invention prevents blood leakage during blood collection container changes while the needle assembly 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 descriptions of various embodiments are illustrative of the principles of the invention and are not intended 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 puncture 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 piercing needle 15 to which internal threads 20 at the front end of the container holder 19 are threaded to attach the holder 19. The vacuum container 16 is slid into the holder 19 and the second puncture needle 15 penetrates the penetrable stopper 21 at the front end of the container 16. 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 pieces 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 formed in the rear end and is sized to fit the puncture needle 14. The puncture needle 14 is inserted into the hole 29, the inner end slightly entering the chamber 28 and communicating with the chamber. The tip of puncture needle 14 protrudes outward from end 25. After positioning the 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 outwardly extending piercing needle. A needle shield, not shown, normally surrounds the outward extension of the puncture needle and likewise has internal ribs. An engagement rib between the needle shield and the needle assembly facilitates the user's insertion and removal of the needle assembly into and out of the tube holder. A portion 34 of the front end surrounding the chamber 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 a translucent or transparent material to facilitate manufacturing and minimize the variety of materials 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 port is sealed to prevent leakage of blood entering chamber 28 when the needle enters the vessel. 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 desired 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 second puncture needle 15 in this embodiment. The end opposite the rear end is formed with external 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 second 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 joined. The second puncture needle 15 is fixed in the hole 38 with an adhesive or the like. A large hole 40 extends a short dimension into rear end 25 and communicates with hole 38. A sleeve valve 41 is slidable around the outward extension of the second puncture needle 15. The sleeve 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 portion slide into the bore 40 and the flange 45 contacts the inner wall of the rear end of the housing. Furthermore, a cavity portion 46 is provided in the thick wall portion 42. The inner diameter of the sleeve valve 41 is fitted to the outer diameter of the second puncture needle 15 except for the cavity portion. The inner diameter of the cavity 46 is larger than the inner diameter

r of the sleeve and larger than the outer diameter of the puncture needle. Functional differences 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 extension 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 makes an airtight contact over the bore 48 in the steady position. At the same time cavity 46 surrounds 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, blood impermeable, porous plug. A plug 52 is placed in the space between holes 48,50. Blood passing through the second puncture needle 15 is therefore blocked by the blood impermeable properties 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 and 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 and front ends of the housing. To ensure the required fluid flow within the housing, an elastomeric ring 55 is interposed between the flanges 35, 54 in the example shown. When assembling the front and rear ends, the flanges 35, 54 are fixed by a required fixing means such as an adhesive.

The sleeve valve 41 is compressible toward the rear end 25 when a thin walled portion 44 slides the valve as described below. The thick walled portion of the sleeve valve 41 has a cavity 46 and is not axially compressed like the thin walled portion. Further, the cavity 46 is of a length that communicates both bores 48, 50 together when the sleeve valve is slid inward toward the rearward end. Various materials can be used to manufacture the sleeve valve, but elastomeric materials are preferred.

For the porous plug 52, a porous material, such as sintered polyethylene, having an average pore 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 has elements similar to those shown in FIG. 2, and has similar characteristics, so that similar elements 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 single 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 puncture needle portion 15a extends outward from the rear end portion 25a. A common fluid outlet hole 62 is formed in the central portion of the puncture needle 61 and communicates with the chamber 28a. In the example of FIG. 3, blood flows through the lateral hole 62 and fills the chamber 28a when the sleeve valve is closed. This provides a visual indication to the user that

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-sample 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 rest and the sleeve valve is in fluid tight contact over the lateral bore 48. At steady venous pressure, blood from the patient is forced into the puncture needle 14 and into the chamber 28 through the front end 24 of the housing. Incoming blood expels air that was originally in chamber 28 through porous plug 52. Plug 52 is air permeable, blood impermeable. Air exits the open end of the second puncture needle. Blood flows through the first puncture needle 14 and fills the chamber 28 through the internal opening 30 shown in FIG. 2 or the transverse hole 62 shown in FIG. At least front end 24 or a portion thereof, such as wall 34, is translucent so that a user of the needle assembly can perceive if blood has entered chamber 28. FIG. If the user sees blood in the chamber, it is an indication that a vascular puncture has been performed. Conversely, if the puncture needle 14 is inserted into the patient and no blood is visible in the chamber 28, it indicates an inadequate vascular puncture. This feature eliminates the need for the user to attach the evacuated blood collection container to the second puncture needle 15 in the holder 19 until viewing the vascular puncture indication. Since the blood impermeable plug 52 and the sleeve valve 41 prevent blood flow from the second puncture needle, no blood will flow from the second puncture needle. When the user is satisfied with the vessel puncture, evacuated blood collection container 16 is slid into holder 19 and second puncture needle 15 penetrates 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 blood collection container ready to supply blood. A resilient sleeve valve 41 slides along the outer surface of the puncture needle and is compressed against the trailing end 25 as the puncture needle 15 penetrates the penetrable stopper 21. An enlarged view of the compressed sleeve valve 41 is shown in FIG. As shown, the thin walled portion 44 is compressed in an accordion 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 lateral holes 48 and 50, and neither hole becomes a liquid impermeable block. As a result, the blood 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 bypasses 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 the blood fills the blood collection container, the filled container is removed from the holder 19 while the puncture needle 14 remains punctured within the patient's blood vessel. Removal of the blood collection container simultaneously removes the compressive force against t

the slidable sleeve 41 and the sleeve slides outward back to the position shown in FIG. This position is the valve closed 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 needle. In particular, no blood leakage occurs between exchanges of the evacuated blood collection container. Therefore, blood flows from the patient's vessel into chamber 28, the next blood collection container is inserted into the holder, and the inward compression movement of the slidable valve is repeated as described above. Once the multi-sample blood collection is complete, the puncture needle 14 is removed from the patient and the entire needle assembly discarded.

Various modifications are possible for the present invention. The embodiment shown in Figures 8 and 9 prevents blood from flowing out of the puncture needle during valve closure and allows air to pass through for evacuation purposes. In the embodiment of FIG. 8, the multiple sample needle assembly 70 is largely similar to the previous embodiment, except that the piercing needle 71 pierces the penetrable stopper 72 of the blood collection container and leaves on only one side hole 74. prepare. The location of this lateral hole at the puncture needle 71 is significantly away from the rear end 75 of the needle assembly and close to the open end 76 of the 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 substantially similar to sleeve valve 41 previously described, but is somewhat longer to contact crossbore 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 provided with the thick wall portion 81 and the thin wall portion 82 in the illustrated example, this is 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 through the air permeable plug 78 and blood does not pass through the plug. Furthermore, the sleeve 80 effectively closes the lateral hole 74 so that no blood can escape. FIG. 9 shows the compressed position of sleeve valve 80 and is similar to FIG. Needle 71 penetrates a puncture is made in the possible stopper 72 and the lateral hole 74 is in the blood collection container. The sleeve valve 80 is slid and compressed toward the rear end 75 of the needle assembly. Since the lateral hole 74 is exposed, blood in the lumen 79 flows through the lateral hole 74 directly into the blood collection container. As shown in FIG. 9, blood bypasses plug 78 and diverts to lateral hole 74 and does not flow out the open end of the puncture needle. Once the blood collection container is full, the container is removed from the holder and the sleeve valve 80 is slid back to the position shown in FIG. This prevents blood from flowing out of the puncture needle between exchanges of the blood collection container.

As noted above, a multi-sample needle assembly according to the present invention controls the flow of liquids, such as blood, therethrough. To prevent blood from leaking out of the assembly during exchange of blood collection containers between multiple sample collection processes. 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 collection.

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 patient; FIG. FIG. 3 is an enlarged cross-sectional view of the multi-sample needle assembly taken along line 2-2, FIG. 3 is an enlarged cross-sectional view showing another embodiment of the 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 flowing through the puncture needle; FIG. 8 is another embodiment of the present invention shown in FIG. 4 and FIG. 9 is a sectional view showing a similar valve closed position, and FIG. 9 is a sectional view showing the valve open position of the embodiment of FIG.

Reference Signs List 10 Multi-sample needle assembly

12 Housings

14, 15 Puncture needle

16 Vacuum blood collection container

19 Container holder 24

Front end

25 Rear end

28 Chamber

41 Sleeve valve

42 Thick wall portion

44 Thin Wall portion

46... Cavities

48, 50... Lateral hole

52... Porous plug

Copyright JPO and INPIT

(P0200)

⑨ 日本国特許庁 (JP)

⑪ 特許出願公開

⑫ 公開特許公報 (A)

昭58—25146

⑤ Int. Cl.³
A 61 B 5/14

識別記号

庁内整理番号
6530—4C

⑬ 公開 昭和58年(1983)2月15日

発明の数 3
審査請求 未請求

(全 9 頁)

⑭ 血管穿刺表示器付き多サンプル針組立体

⑯ 特 願 昭57—126629

⑰ 出 願 昭57(1982)7月20日

優先権主張 ⑱ 1981年7月20日 ⑲ 米国(US)
⑳ 284894

㉑ 発 明 者 ジョセフ・カウフマン
アメリカ合衆国ニュージャージー
州エマーソン・クレスト・ロ

ード10

㉒ 出 願 人 ベクトン・ディツキンソン・ア
ンド・カンパニー
アメリカ合衆国ニュージャージー
州07652パラマス・マツク・
センター・ドライブ(番地な
し)

㉓ 代 理 人 弁理士 湯浅恭三 外2名

明 細 書

1. [発明の名称]

血管穿刺表示器付き多サンプル針組立体

2. [特許請求の範囲]

1. 患者から血液を収集する時に血管穿刺を認識し得る多サンプル針組立体であつて、前端部と後端部と内部の室とを有し少なくとも室を囲んで半透明として使用者が室を認識し得るようにしたハウジングと、上記室に流体連通し上記前端部から外方に延長して患者内に挿入可能な第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な弁とを備え、

上記弁は閉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ャビティーを含み、上記キャビティ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。

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な第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

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ー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ず横孔と、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、上記弁が閉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

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閉位置に滑動して上記キャビティ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する、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法が探求されている。

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過して収集装置内に流入しないことがあり、真空血液収集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過して流出する。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設して液を第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な弁を設け、弁の開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

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、はゞ穿刺針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

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の基本的な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、はゞ穿刺針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

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にキャビティ部46を設ける。スリーブ弁41の内径はキャビティ部を除いて第2の穿刺針15の外径に嵌合させる。キャビティ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。同時にキャビティ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の穿刺針の先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の穿刺針の先端から流出する。

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の厚壁部はキャビティ46を有し、薄壁部のように軸線方向には圧縮されない。更にキャビティ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内に貫通させる。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を通過してスリーブ弁が閉鎖した時に室28α内に充填する。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が血管穿刺手臓間に患者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を通過して排出する。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を通過して流れ第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に充填する。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

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填すれば、充填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

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内でアコーディ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の滑動によつてキャビティー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, キャビティー46を通過して流れ、プラグ52をバイパスする。血液はキャビティーから横孔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

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とは同様であるがいくらか長くして横孔74を液不透過に接触する。更にスリーブ弁80には前述のスリーブ弁41に記したキャビティーを必要としない。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図の位置即ち閉鎖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を通過して流れ、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

特開昭58- 25146(7)

可能ストツバ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を通過し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。

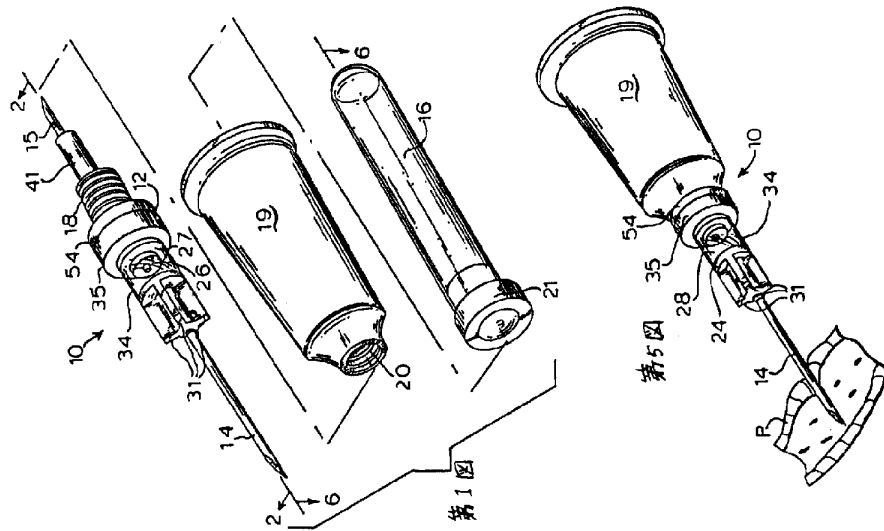
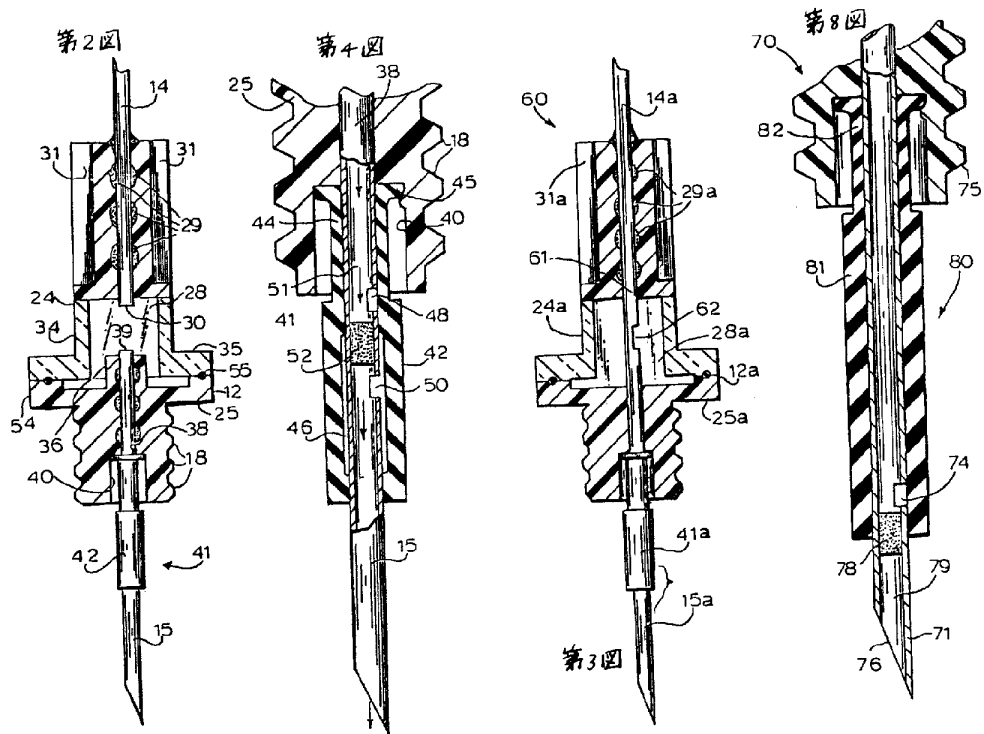
上述した通り、本発明による多サンプル針組立体は中を通る血液等の液の流れを制御する。多サンプル収集過程間の血液収集容器の交換の間に血液が組立体外に漏洩するのを防ぐ。更に、本発明は使用者に対する目視表示を行ない、血液収集のために血管内に穿刺された時に直に認識し得る。上述の特性は針組立体を多サンプル収集用として有効に使用するために貢献する。

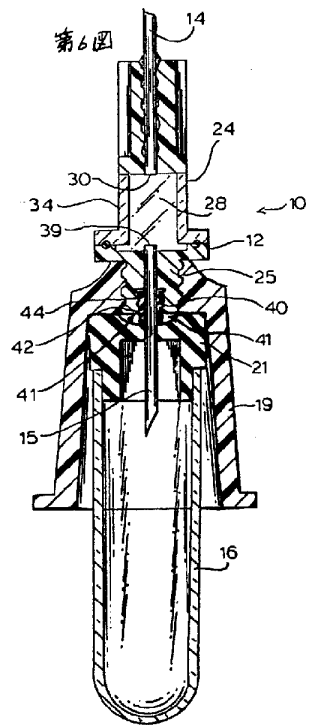
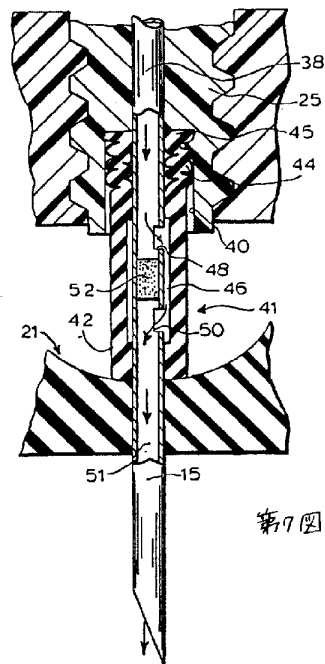
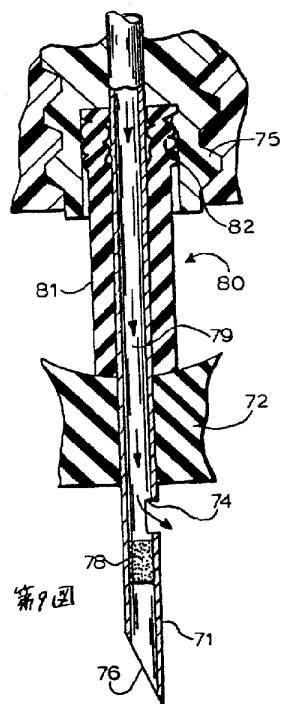
4. [図面の簡単な説明]

25 … 後端部
28 … 室
41 … スリーブ弁
42 … 厚壁部
44 … 薄壁部
46 … キャビティ
48, 50 … 横孔
52 … 多孔性プラグ

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}側面図、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図はホルダー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





**Espacenet****Bibliographic data: DE10134913 (C2) — 2003-06-26**

DEVICE AND METHOD FOR PREPARING BLOOD

Inventor(s): ECK MICHAEL [DE] ± (ECK, MICHAEL)

Applicant(s): HIBERNA AG [DE] ± (HIBERNA AG)

Classification: - **international:** **A61M1/02**; (IPC1-7): A61J1/00; A61M1/00; A61M1/36; B04B5/04
- **cooperative:** **A61M1/0209 (EP); A61M1/029 (EP, US)**

Application number: DE20011034913 20010718

Priority number(s): DE20011034913 20010718

Also published as: DE10134913 (A1) AU2002331254 (A1) WO03008012 (A2)
WO03008012 (A3) WO03008012 (A8)

Abstract not available for DE10134913 (C2)

Abstract of corresponding document: WO03008012 (A2)

The invention relates to a preparation device (100) for treating suspension samples, especially for preparing blood cryobanks. Said device comprises an arrangement of at least two containers for receiving suspension samples, sample parts and/or additives. Said containers are formed as chambers (13 to 15, 90) having fixed walls and are arranged in a fixed manner in relation to each other. A transfer device comprising at least one connecting line (22) is provided, by which means the chambers (13 to 15) can be interconnected.



Espacenet

Description: DE10134913 (C2) — 2003-06-26

DEVICE AND METHOD FOR PREPARING BLOOD

Description of DE10134913 (C2)

A high quality text as facsimile in your desired language may be available amongst the following family members:

WO03008012 (A2)

The EPO does not accept any responsibility for the accuracy of data and information originating from other authorities than the EPO; in particular, the EPO does not guarantee that they are complete, up-to-date or fit for specific purposes.

[0001] Die Erfindung betrifft eine Vorrichtung zur Probenpräparation, insbesondere eine Vorrichtung zur Handhabung und Behandlung von Blutproben, wie z. B. zum Trennen von Blutproben durch Zentrifugation und zur Modifizierung von Blutproben durch Zusatzstoffe zur Vorbereitung einer Kryokonservierung der Blutproben sowie eine Präparationsstation und ein Verfahren zur Blutpräparation, insbesondere zur Vorbereitung von Blutproben für die Kryokonservierung.

[0002] Es ist bekannt, zur Kryokonservierung von Blutproben zunächst aus einer Blutspende eine Blutkonserve für den einfrierfertigen Zustand zu präparieren. Die Präparation umfasst insbesondere erstens eine Auftrennung der Blutspende in eine Erythrozytensuspension, die kryokonserviert werden soll, und Restbestandteile und zweitens den Zusatz eines Kryoadditives zur Erythrozytensuspension. Bei herkömmlichen Verfahren erfolgt die Handhabung der Blutproben unter Verwendung von flexiblen Blutbeuteln, wie es schematisch in Fig. 6 illustriert ist. Eine Blutspende wird in einem ersten Blutbeutel 1' bereitgestellt und zentrifugiert. Nach dem Zentrifugieren ist die Blutspende in das Sediment und den Überstand (Plasma) getrennt. Der Überstand wird ggf. in einen Abfallbehälter 4' abgezogen. Die Erythrozytensuspension wird in einen weiteren Blutbeutel 2' umgefüllt, dem zur Bereitstellung der einfrierfertigen Konserve ein Kryoaditiv zugesetzt wird. Die illustrierte Verwendung von Blutbeuteln, die bspw. in DE 298 05 538 und WO 00/38762 beschrieben wird, besitzt die folgenden Nachteile.

[0003] Ein Hauptproblem betrifft die Handhabung der Blutbeutel. Da die Blutbeutel keine feste Form besitzen, muss insbesondere zur Erhaltung der Phasengrenze nach der Zentrifugation ein schonender Umgang mit den Blutbeuteln vorgesehen sein. Bei den genannten herkömmlichen Systemen sind zwar Vorrichtungen zur Halterung und zum Transport der Blutbeutel vorgesehen. Diese Vorrichtungen sind jedoch nur sehr eingeschränkt automatisierbar. Es müssen eine manuelle Beschickung der

Vorrichtungen und eine laufende Überwachung des Betriebes erfolgen. Des Weiteren sind die Blutbeutel bei den herkömmlichen Vorrichtungen über flexible Schläuche miteinander verbunden. Zur Trennung von Erythrozytensuspension und Überstand muss die Phasengrenze am Blutbeutel oder am Schlauch detektiert werden. Wegen der Flexibilität der jeweiligen Behältnisse besteht das Risiko einer Fehldetektion und damit einer Fehlfunktion bei der Präparation.

[0004] Weitere Nachteile ergeben sich aus Sterilitätsproblemen beim Umgang mit den Blutbeuteln. Die Schlauchverbindungen müssen steril an die Blutbeutel angeschlossen und nach dem jeweiligen Verfahrensschritt abgetrennt und verschweißt werden. Bei jedem Präparationsschritt müssen aufwendige Vorkehrungen zur Erhaltung der Sterilität und Pyrogenfreiheit der Blutproben getroffen werden.

[0005] Die herkömmliche Blutbeutelpräparation ist auch wegen der Verwechslungsgefahr problematisch. Wenn während der Präparation ein Blutbeutel verwechselt wird oder eine Kreuzkontamination zwischen Blutbeuteln auftritt, so kann dies verheerende Folgen für den Empfänger der Blutspende haben. Zum Ausschluss der Verwechslungsgefahr müssen bei herkömmlichen Systemen aufwendige Sicherheitsmaßnahmen realisiert werden.

[0006] Ein weiterer Nachteil der in WO 00/38762 beschriebenen Technik besteht in deren spezifischen Zuschnitt auf die Stammzellenpräparation. Bei der Trennung von Stammzellen aus biologischen Flüssigkeitsproben ist lediglich ein sehr geringer Stammzellengehalt aus den Proben abzutrennen. Dies ermöglicht den Einsatz spezieller Zentrifugationstechniken und eine geringere Empfindlichkeit in Bezug auf die Verwendung von Blutbeuteln.

[0007] In der modernen Medizin und im Katastrophenschutz besteht ein Interesse an vergrößerten Blutbanken mit einem breiten Spektrum verschiedenster Bluttypen. Zur Herstellung moderner Blutbanken ist eine Automatisierung der Konservenpräparation erforderlich. Wegen des Automatisierungsbedarfes ist die Anwendbarkeit herkömmlicher Präparationsvorrichtungen eingeschränkt.

[0008] Die illustrierten Probleme bei der Handhabung von Blutproben bestehen nicht nur bei der Vorbereitung von Konserven für die Kryokonservierung. Ein entsprechender Bedarf nach steriler, automatisierter und sicherer Probenhandhabung besteht auch bei der Bearbeitung von biologischen Zellsuspensionen für therapeutische Zwecke.

[0009] Die Aufgabe der Erfindung ist es, eine verbesserte Vorrichtung zur Präparation suspendierter biologischer Proben bereitzustellen, mit der die Nachteile herkömmlicher Systeme überwunden werden und die insbesondere für eine automatisierbare und sichere Handhabung einer Vielzahl von Proben geeignet ist. Ferner soll ein verbessertes System zur Präparation von Kryokonserven, wie z. B. Blut-Kryokonserven geschaffen werden sowie ein neuartiges Verfahren zur Handhabung biologischer suspendierter Proben, das insbesondere automatisierbar und sicher durchführbar ist.

[0010] Diese Aufgaben werden mit einer Präparationsvorrichtung, eine Präparationsstation und einem Verfahren mit den Merkmalen gemäß den Patentansprüchen 1, 9 und 11 gelöst. Vorteilhafte Ausführungsformen und Anwendungen der Erfindung ergeben sich aus den abhängigen Ansprüchen.

[0011] Die Grundidee der Erfindung ist es, eine Präparationsvorrichtung bereitzustellen, die mindestens zwei Behältnisse zur Aufnahme der zu behandelnden Suspensionsproben aufweist, wobei die Behältnisse im Unterschied zu herkömmlichen

Systemen durch relativ zueinander ortsfest positionierte Kammern mit festen Wänden gebildet werden. Die Kammern sind über einzeln betätigbare Leitungsverbindungen miteinander verbunden oder mit Anschlussstücken zur optionalen Ausbildung von Leitungsverbindungen zwischen den Kammern ausgestattet. Die erfindungsgemäße Präparationsvorrichtung ist gemäß einer ersten Ausführungsform durch einen integralen Aufbau gebildet, bei dem die Kammern in einem Kammerkörper geformt sind, an dessen einem Ende die Leitungsverbindungen ansetzbar oder einstellbar sind. Gemäß einer zweiten Ausführungsform umfasst die Präparationsvorrichtung ein Rahmengestell, in das die Kammern einzeln einsetzbar sind. Die Anschlussstücke der einzelnen Kammern sind sämtlich auf einer (z. B. unteren) Seite des Rahmengestells angeordnet. Je nach Bedarf werden die zunächst mit einem Septum verschlossenen Anschlussstücke geöffnet und über Leitungsverbindungen paarweise in Verbindung gebracht. Die Gestaltung mit einzelnen Kammern ist gemäß einer dritten Ausführungsform derart ausgebildet, dass das Rahmengestell mit einer Ventilplatte mit Leitungsverbindungen ausgestattet ist, über die die einzelnen Kammern paarweise verbunden werden können. Die Ausbildung der Präparationsvorrichtung als integraler Aufbau oder als Gestellaufbau mit mindestens zwei Kammern besitzt die Vorteile, dass die Präparationsvorrichtung im Rahmen eines automatisierten Verfahrensablaufes einen sicher greif- und manipulierbaren Gegenstand darstellt und dass die Probenhandhabung, insbesondere die unabhängige Vorbefüllung der Kammern, die Behandlung von Proben in den Kammern und die Überführung der Proben zwischen den Kammern, vereinfacht wird. Bei Anwendung der erfindungsgemäßen Präparationsvorrichtung zur Herstellung von Blutproben für die Kryokonservierung sind vorzugsweise mindestens drei Kammern vorgesehen.

[0012] Gemäß der genannten ersten Ausführungsform der Erfindung sind die Kammern vorzugsweise in Form von geraden Kreiszylindern in einem Kunststoffkörper gebildet, an dessen einem Ende eine Ventilplatte angebracht ist, die mindestens eine Leitungsverbindung zur Kopplung von jeweils zwei Kammern enthält. Der Aufbau mit einem integralen Kunststoffkörper besitzt den Vorteil, dass die Präparationsvorrichtung als Einwegprodukt herstellbar ist, so dass Sterilitäts- und Verwechslungsprobleme ausgeschlossen werden können. Als weiterer Vorteil ergibt sich eine hohe Stabilität der Präparationsvorrichtung insbesondere bei Zentrifugationsvorgängen.

[0013] Die genannten zweiten und dritten Ausführungsformen der Erfindung stellen jeweils einen modularen Aufbau dar. Die Kammern können als Einwegprodukte verwendet werden. Als zusätzlicher Vorteil ergibt sich beim Rahmenaufbau ein relativ geringes Gewicht.

[0014] Die Übertragung von Proben zwischen den Kammern erfolgt vorzugsweise durch einen hydrostatischen Druck, der als Gasdruck oder vorzugsweise mit Druckstempeln ausgeübt wird, die jeweils in den Kammern angeordnet sind. Alternativ ist es möglich, den Druck mit einem mechanisch betätigbaren Kolben zu übertragen (z. B. mit einem Pleuelgestänge). Die Kammern der erfindungsgemäßen Präparationsvorrichtung bilden bei dieser Gestaltung Kolben- Druckerzeuger, die sowohl zur Aufnahme der jeweiligen Proben als auch zur Übertragung der Proben in benachbarte Kammern eingerichtet sind.

[0015] Gemäß einer weiteren bevorzugten Gestaltung besteht die Präparationsvorrichtung, insbesondere die Kammern als Hauptkomponenten, zumindest teilweise aus einem transparenten Kunststoffmaterial. Bei Verwendung von nicht-transparentem Material besitzen die Kammern vorzugsweise mindestens ein transparentes Fenster zur optischen Detektion. Es wird eine zuverlässige und reproduzierbare optische Detektion von Probeneigenschaften, insbesondere der Lage

der Phasengrenze nach einer Zentrifugation, ermöglicht.

[0016] Gegenstand der Erfindung ist auch eine Präparationsstation, die mit der erfindungsgemäßen Präparationsvorrichtung ausgestattet ist und des Weiteren eine Druckeinrichtung zur Probenübertragung zwischen den Kammern, eine Detektoreinrichtung zur Messung von Probeneigenschaften in den Kammern und eine Stalleinrichtung zur selektiven Kopplung von Kammern aufweist.

[0017] Gegenstand der Erfindung ist auch ein Verfahren zur Präparation von Suspensionen, die biologisch relevante Komponenten, wie z. B. Zellen, Zellbestandteile oder Makromoleküle, enthalten, unter Verwendung der erfindungsgemäßen Präparationsvorrichtung. Das Verfahren zeichnet sich insbesondere dadurch aus, dass alle Präparationsschritte mit der gesamten Präparationsvorrichtung durchgeführt werden, die verschiedene Kammern zur Aufnahme von Proben in verschiedenen Präparationsstadien enthält.

[0018] Die Erfindung besitzt die folgenden Vorteile für die Probenpräparation, insbesondere für die Herstellung von Blut- Kryokonserven. Der Präparationsprozess ist zur Erhöhung der Produktivität bei der Konservenherstellung, d. h. zur Erzielung eines möglichst hohen Konservendurchsatzes, automatisierbar, wobei gleichzeitig die Herstellungsqualität gesteigert und unabhängig von der Handfertigkeit eines Bedieners aufrechterhalten wird. Eine erfindungsgemäß hergestellte Blutkonserve erfährt bereits durch die Verwendung der Präparationsvorrichtung eine Qualitätssteigerung, ohne dass die Präparation wesentlich verteuert wird.

[0019] Die erfindungsgemäße Präparationsvorrichtung ist während der Präparationsprozedur nach außen hin absolut abgeschlossen. Sie tritt lediglich einmalig jeweils beim Befüllen und beim Entleeren in Kontakt mit der Umgebung. Beispielsweise erfolgt die Vorbehandlung einer Konserve bis zum Erlangen des einfrierfertigen Zustandes absolut steril. Vorteilhafterweise wird das Öffnen, Verbinden und Verschließen von Beuteln und Verbindungsschläuchen entsprechend den herkömmlichen Systemen vermieden. Die Suspensionsprobe verlässt während der Präparationsschritte nicht die Präparationsvorrichtung. Eine Verwechslung z. B. von Blut verschiedener Spender oder eine Kontamination durch Fremdblut oder Mikroorganismen sind ausgeschlossen. Die Identität des Spenderblutes ist garantiert. Der Präparationsvorgang wird stark beschleunigt, da Arbeitsschritte, die bei herkömmlichen Systemen ggf. mehrfach notwendig sind, erfindungsgemäß vollständig entfallen können. Ein teilweiser oder vollständiger Probenverlust oder eine Kontamination der Arbeitsumgebung einschließlich des Laborpersonals durch undichte Schlauchverbindungen werden bei der erfindungsgemäßen Präparationsvorrichtung ausgeschlossen.

[0020] Die erfindungsgemäße Präparationsvorrichtung bildet ein festes Behältnis, das im Vergleich mit herkömmlich verwendeten Blutbeuteln ein definiertes und reproduzierbares Greifen und Handhaben der Vorrichtung und der an dieser angebrachten Ventile und/oder Stutzen ermöglicht. Das Greifen oder Positionieren und Klemmen von Verbindungsschläuchen entfällt, wenn die mindestens eine Verbindungsleitung in die Präparationsvorrichtung integriert ist und somit ein reproduzierbares und mehrfaches Verbinden der einzelnen Kammern auf kürzestem Weg ermöglicht. Durch die kurzen Wege und die Wahl eines geeigneten Querschnittes der jeweiligen Verbindungsleitung lässt sich die Transferzeit zur Übertragung von Proben zwischen den Kammern optimieren. Der Aufbau der Vorrichtung ermöglicht ein definiertes Positionieren der mindestens einen Verbindungsleitung. Ein versehentliches Verbinden von aktuell nicht kooperierenden Kammern wird ausgeschlossen. Ein

Deformieren oder Quetschen der Kammern wird erfindungsgemäß vermieden. Eine z. B. durch Zentrifugation eingestellte Phasentrennung von Probenbestandteilen kann durch einen Greifvorgang nicht verwischt werden.

[0021] Die feste und vorzugsweise symmetrische Anordnung der Kammern in einer erfindungsgemäßen Präparationsvorrichtung ermöglicht ein schnelles und definiertes Positionieren der jeweils interessierenden Kammer in einem Präparationssystem unabhängig vom Verfahrensschritt. Alle Sensoren und Aktoren sind automatisch korrekt positioniert. Es wird ein erhöhter, fehlerfreier Durchsatz erzielt. Beispielsweise lassen sich mit einer erfindungsgemäß Präparationsvorrichtung rund dreifach mehr Kryokonserven pro Zeileinheit präparieren. Die Präparationsvorrichtung ermöglicht eine freie Materialwahl und Dimensionierung der Außenform der Kammeranordnung. Vorteilhafterweise kann die Vorrichtung ohne Weiteres mit herkömmlichen Zentrifugiereinrichtungen verwendet werden.

[0022] Durch die Herstellung der Präparationsvorrichtung aus kostengünstigen Kunststoffmaterialien können große Stückzahlen der Vorrichtung in Spritzgieß- oder Extrusionstechniken hergestellt werden. Dies ist für die erfindungsgemäße Verwendung der fest bewandeten Kammern als Einwegprodukte von Vorteil.

[0023] Insbesondere bei der Präparation von Blutproben ergeben sich zusätzlich die folgenden Vorteile. Für Blutspendedienste entsteht bei Einsatz der erfindungsgemäßen Präparationsvorrichtung kein wesentlicher Zusatzaufwand. Es werden keine Mehrfachbeutelsysteme erforderlich. Die Präparationsvorrichtung kann direkt mit einem einfachen Spendebeutel (Einfachblutbeutel) gekoppelt werden. Der bei herkömmlichen Verfahren ggf. in den Abfall gelangende oder nur mit großem Aufwand gewinnbare Überstand (Plasma und "Buffy Coat") steht erfindungsgemäß bei Bedarf als zusätzliches Endprodukt zur Verfügung. Die Präparationsvorrichtung liefert auch Vorteile bei der nach der Präparation vorgesehenen Befüllung von Einfrierbeuteln. Ein befüllter Einfrierbeutel kann im angedockten Zustand an der Präparationsvorrichtung mit dieser einfach und steril entlüftet werden, in dem die jeweilige Kammer mit einem Unterdruck beaufschlagt wird.

[0024] Weitere Vorteile und Einzelheiten der Erfindung ergeben sich aus der folgenden Beschreibung der beigefügten Zeichnungen. Es zeigen:

[0025] Fig. 1 eine schematische Phantomansicht einer Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung in teilweise auseinander gezogenem Zustand,

[0026] Fig. 2 eine Illustration der Einbindung der Präparationsvorrichtung gemäß Fig. 1 in eine Vorrichtung zur Herstellung von Blutkonserven,

[0027] Fig. 3 eine vergrößerte Teilansicht eines Kammerendes der Präparationsvorrichtung gemäß Fig. 1,

[0028] Fig. 4 Illustration einer abgewandelten Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung,

[0029] Fig. 5 eine schematische Schnittansicht einer erfindungsgemäß verwendeten Einzelkammer, und

[0030] Fig. 6 eine Illustration einer herkömmlichen Präparationstechnik (Stand der Technik).

[0031] In Fig. 1 ist eine Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung 100 in schematischer Phantomansicht dargestellt. Die Präparationsvorrichtung 100 umfasst einen Kammerkörper 10, in dem drei Kammern zur Aufnahme von Suspensionsproben gebildet sind, eine Übertragungseinrichtung 20, bestehend aus einer Ventilplatte 22 und mindestens einer Verbindungsleitung 22, eine Stempel­einrichtung 30 mit mehreren Druckstempeln 31 bis 33 und eine Deckplatte 40, die den oberen Abschluss des Kammerkörpers 10 bildet. Der Kammerkörper 10 ist einstückig aus einem transparenten Kunststoffmaterial (z. B. PMMA, Cycloolefin-Copolymere, Polyamid, Polycarbonat, PCHP, Polyester oder Polysulfone) geformt. Er besitzt die äußere Form eines geraden Kreiszylinders mit einer ebenen Oberseite 11 und einer ebenen Unterseite 12. Im Inneren des Kammerkörpers 10 sind die drei zylinderförmigen Kammern 13, 14 und 15 zur Probenaufnahme gebildet. Am oberen Ende des Kammerkörpers 10 münden die Kammern frei in die Oberseite 11. Am unteren Ende besitzt jede Kammer eine Verjüngung 16 mit einem Anschlussstutzen 17, wie es vergrößert in Fig. 3 illustriert ist. Der Anschlussstutzen 17 mündet jeweils in die Unterseite 12 des Kammerkörpers 10.

[0032] Zur Anwendung bei der Präparation von Blutproben besitzt die Präparationsvorrichtung 100 bspw. einen Durchmesser von ca. 18 bis 20 cm, wobei die Höhe des Kammerkörpers 10 ca. 10 bis 12 cm beträgt und die Kammern 13 bis 15 jeweils einen Innendurchmesser von ca. 6 bis 8 cm besitzen. Eine Kammer besitzt vorzugsweise ein Volumen im Bereich von 400 ml bis 600 ml. Die Kammern 13 bis 15 sind vorzugsweise relativ zur Achse des Kammerkörpers 10 symmetrisch verteilt angeordnet.

[0033] Die Übertragungseinrichtung 20 ist zur Übertragung von Proben zwischen den Kammern 13 bis 15 eingerichtet. Die Ventilplatte 21 ist drehbar an der Unterseite 12 des Kammerkörpers 10 befestigt. In die ebenfalls aus Kunststoffmaterial hergestellte Ventilplatte 21 ist die Verbindungsleitung 22 integriert, die einen Überströmkanal bildet. An den Mündungen der Verbindungsleitungen 22 auf der inneren Seite der Verbindungsplatte 21, die an die Unterseite 12 des Kammerkörpers 10 angrenzt, oder an den Anschlussstutzen 17 der einzelnen Kammern (siehe Fig. 3) sind Dichtungsringe aus einem elastischen Material (z. B. PTFE) angebracht. Neben der Dichtfunktion können die Dichtungsringe (nicht dargestellt) auch als Rasteinrichtungen dienen. Bei Drehung der Verbindungsplatte 21 rasten die Dichtungsringe an den gewünschten Positionen der Anschlussstutzen oder der Mündung der Verbindungsleitung 22 ein, wenn diese gerade zueinander ausgerichtet sind.

[0034] Die Ventilplatte 21 besitzt eine Ventulfunktion, da in der Regel Flüssigkeit immer nur in einer Richtung von einer Kammer zur benachbarten Kammer gepumpt wird. Zum Ausschluss einer Fehlbedienung kann an der Ventilplatte 21 oder am Kammerkörper 10 eine Vorrichtung zur erzwungenen Vorgabe einer bestimmten Drehrichtung und/oder eine Wiederhol­sperr­e vorgesehen sein. Diese Vorrichtung umfasst bspw. eine Verzahnung, die eine Rückwärtsdrehung ausschließt, und/oder eine zusätzliche Arretierhilfe.

[0035] Der Aufbau der Ventilplatte 21 kann anwendungsabhängig abgewandelt werden (siehe Fig. 4). Es können mehrere Verbindungsleitungen vorgesehen sein. Die mindestens eine Verbindungsleitung kann mit einer Sperr- oder Ventileinrichtung ausgestattet sein. In der Ventilplatte können vorzugsweise zusätzliche Durchgangsöffnungen zur Beschickung der Kammern vorgesehen sein. Die Beschickung kann aber auch von der oberen Seite her erfolgen.

[0036] Zum Probentransport zwischen den Kammern werden die Proben mit einem Druck beaufschlagt. Unter der Wirkung eines Überdruckes in der Kammer, von der die Übertragung ausgeht, wird die Probe über den Überströmkanal in der Ventilplatte 21 übertragen. Der Übertragungsdruck wird mit einer Druckeinrichtung aufgebracht, die Teil der Präparationsstation (siehe Fig. 2) ist, in der die erfindungsgemäße Präparationsvorrichtung vorzugsweise verwendet wird. Gemäß einer vorteilhaften Ausführungsform der Erfindung wird der Druck mit einer Stempelinrichtung 30 übertragen, die in den Kammern 13 bis 15 jeweils einen Druckstempel 31 bis 33 aufweist. Die Druckstempel 31 bis 33 bestehen aus Kunststoffkörpern z. B. in Zylinderform, die formschlüssig in die jeweilige Kammer eingepasst sind. Jeder Druckstempel weist mindestens eine umlaufende Dichtlippe auf, die ggf. auftretende Spalte zwischen den Druckstempeln und den Kammerinnenwänden abdichtet. Die Dichtlippen verhindern ein Durchlaufen des Kolbens durch die flüssigen Proben bei Druckbeaufschlagung. Die Kolben mit den Dichtlippen bestehen aus einem Kunststoffmaterial (z. B. PTFE). Der Einsatz der Druckstempel 31 bis 33 in den Kammern besitzt den Vorteil, dass bei einer Bewegung der Präparationsvorrichtung 100 eine Probenbewegung in den Kammern verhindert wird, wenn die Druckstempel jeweils auf den Flüssigkeiten aufgesetzt sind. Nach einer Zentrifugation wird vorteilhafterweise eine Aufhebung der Phasengrenze zwischen den Fraktionen vermieden.

[0037] Die Druckstempel 31 bis 33 können gemäß einer bevorzugten Ausführungsform jeweils eine zentrale Bohrung (gestrichelt eingezeichnet) mit einem Verschluss (z. B. einem Septum) aufweisen. Dies ermöglicht einen Zugriff zu den Proben oder Zusatzflüssigkeiten in den Kammern von der Oberseite der Vorrichtung 100 her.

[0038] Gemäß einer abgewandelten Ausführungsform der Erfindung kann auf die Verwendung der Druckstempel auch verzichtet werden. In diesem Fall wird der Übertragungsdruck direkt auf die Flüssigkeitsoberfläche in der jeweiligen Kammer gegeben. Bei dieser Gestaltung sind die oberen Enden der Kammern an der Oberseite vorzugsweise mit einem Sterilfiltereinsatz ausgestattet, der nur für das jeweilig verwendete sterile Druckmedium (z. B. Luft, inertes Gas) durchlässig ist. Der Aufbau ohne Druckstempel besitzt die Vorteile eines vergrößerten Innenvolumens und vereinfachten Aufbaus der Kammern und damit einer Kostenersparnis.

[0039] Die obere Deckplatte 40 dient dem Abschluss der Präparationsvorrichtung 100. Sie ist fest auf dem Kammerkörper 10 angebracht und besitzt Durchtrittsöffnungen oder Anschlussstutzen 41, die jeweils mit den oberen Enden der Kammern 13 bis 15 ausgerichtet sind. Die Anschlussstutzen 41 dienen der Verbindung von einzelnen oder gleichzeitig allen Kammern mit der Druckeinrichtung und/oder Beschickungseinrichtungen.

[0040] Der Verfahrensablauf zur Herstellung einer Blut-Kryokonserven unter Verwendung einer erfindungsgemäßen Präparationsvorrichtung wird im Folgenden unter Bezug auf Fig. 2 erläutert. Fig. 2 zeigt die Präparationsvorrichtung 100 analog zur Darstellung gemäß Fig. 1 in Kombination mit Teilen der Präparationsstation.

[0041] Die Komponenten der Präparationsvorrichtung 100 sind mit den gleichen Bezugszeichen wie in Fig. 1 versehen.

[0042] Zur Präparationsstation gehören insbesondere die Druckeinrichtung 50, eine Detektoreinrichtung 60, eine Stempelinrichtung 70 und eine Steuereinrichtung 80. Die Druckeinrichtung 50 umfasst vorzugsweise einen Druckerzeuger 51 mit einem Motor 52 und einem Pumpenteil 53. Alternativ umfasst die Druckeinrichtung 50 eine

Hebeleinrichtung mit einer Pleuelstange. Die mechanische Kraftübertragung besitzt den Vorteil, dass die Positionierung der Druckstempel mit einer erhöhten Präzision erfolgen kann. Gemäß alternativen Ausführungsformen der Erfindung kann der Druckerzeuger auch durch eine Druckquelle (z. B. Druckgasflasche) mit einem Regelventil gebildet werden.

[0043] Die Detektoreinrichtung 60 umfasst insbesondere mindestens ein lichtempfindliches Element 61 zur Erkennung der Phasengrenze. Das lichtempfindliche Element 61 kann anwendungsabhängig mit (nicht dargestellten) Filtereinrichtungen ausgestattet sein. Es können auch mehrere lichtempfindliche Elemente entsprechend den Positionen der Kammern angeordnet sein. Anwendungsabhängig können auch andere Detektoren zur Erfassung von Probeneigenschaften vorgesehen sein, wie sie an sich aus der Analytik bekannt sind (z. B. Spektralphotometer, Widerstandsmesser zur Dichtebestimmung). Die Kammern können auch eine sich jeweils über ihre Länge erstreckende Skalierung zur optischen Kontrolle des Füllstandes, der Position der Druckstempel oder der Position der Phasengrenze aufweisen. Die Detektoren können ferner an anderen Komponenten der Präparationsvorrichtung, z. B. an einer Verbindungsleitung in der Ventilplatte, vorgesehen sein.

[0044] Zur Verstellung der oben erläuterten Ventilplatte 21 umfasst die Stelleinrichtung 70 ein Betätigungselement 71 und einen Stellmotor 72. Das Betätigungselement 71 besitzt die Form einer Platte mit mindestens einem Vorsprung 73, der mit mindestens einer entsprechenden Ausnehmung (nicht dargestellt) auf der Unterseite der Ventilplatte 21 zusammenwirkt. Der Vorsprung 73 greift in die Ausnehmung ein und verdreht die Ventilplatte 21 bei Betätigung des Stellmotors 72 in die gewünschte Position, so dass jeweils eine Kammer geöffnet oder geleert werden kann, jeweils zwei Kammern über die Verbindungsleitung 22 verbunden sind oder alle drei Kammern verschlossen sind.

[0045] Die Steuereinrichtung 80 ist mit den Komponenten 50, 60 und 70 des Präparationssystems verbunden. Je nach Betriebszustand und dem von der Detektoreinrichtung 60 gelieferten Detektorsignal werden in der folgenden Weise der Druckerzeuger 50 und die Stelleinrichtung 70 betätigt. Bei halbautomatischem oder manuellem Betrieb werden die entsprechenden Schritte zumindest teilweise durch einen Bediener durchgeführt.

[0046] In einem Startzustand sind die Kammern der erfindungsgemäßen Präparationsvorrichtung 100 wie folgt beschickt. In der ersten Kammer 13 befindet sich eine Blutspende. Die Blutspende wird aus einem Spenderbeutel in die erste Kammer 13 gefüllt, was ggf. unter Ausübung eines unterstützenden Unterdruckes erfolgt. Die zweite Kammer 14 ist mit einer Waschlösung gefüllt. In der dritten Kammer 15 befindet sich ein Kryoadditiv. Im Startzustand ist die erste Kammer 13 vollständig gefüllt, während die übrigen Kammern 14, 15 lediglich teilweise befüllt sind. In diesen Kammern ist so viel Volumen frei, wie es zur Übernahme der Erythrozytensuspension nach der Zentrifugation (siehe unten) erforderlich ist. Die Ventilplatte 21 wird nach dem Startzustand (alle verschlossen) so eingestellt, dass bspw. die erste und zweite Kammer 13, 14 verbunden sind. Vorteilhafterweise ist trotz der Verbindung im druckfreien Zustand über die Verbindungsleitung im Wesentlichen kein Flüssigkeitsaustausch gegeben.

[0047] In einem ersten Präparationsschritt wird der Kammerkörper mit den befüllten Kammern mit einer Zentrifugationseinrichtung zentrifugiert. Die (nicht dargestellte) Zentrifugationseinrichtung besitzt die Bauform einer an sich bekannten Großzentrifuge mit einzelnen Zentrifugenbechern, in denen eine Vielzahl von

Präparationsvorrichtungen gleichzeitig zentrifugiert werden können. Während der Zentrifugation erfolgt lediglich die Auftrennung der Blutspende in die Fraktionen. Eine Verschiebung der Druckstempel 31 bis 33 erfolgt nicht. Während der Zentrifugation sind die Kammern verschlossen.

[0048] Der Zustand der Präparationsvorrichtung nach der Zentrifugation ist in Fig. 2 dargestellt. In der ersten Kammer 13 sind die gebildeten Fraktionen der Blutspende mit dem Erythrozytensediment 1 der sog. "Buffy Coat"-Schicht 2 und dem Plasmaüberstand 3 illustriert. Das Erythrozytensediment 1 umfasst betriebsabhängig einen Volumenanteil von ca. 45% der Kammer 13. Der Volumenanteil hängt insbesondere von der Zentrifugationsgeschwindigkeit ab. Bei einer höheren Geschwindigkeit ergibt sich eine höhere Packungsdichte der Erythrozyten und damit ein geringerer Volumenanteil. Die "Buffy-Coat"-Schicht 2 ist ein thrombozyten- und leukozytenhaltiger Belag mit einer gräulichen Färbung, der sich nach der Zentrifugation zwischen den tiefroten Erythrozytensediment 1 und dem hellroten Plasmaüberstand 3 ausbildet.

[0049] Nach der Zentrifugation wird die Präparationsvorrichtung 100 in die Präparationsstation eingesetzt. Die Ventilplatte 21 wird in Durchlassrichtung zwischen die erste und zweite Kammer 13, 14 gedreht. Dies erfolgt manuell, z. B. mit einem Noppenschlüssel oder mit der Stelleinrichtung 70 (siehe oben). Die erste Kammer 13 wird mit einem Überdruck beaufschlagt. Unter der hydrostatischen oder mechanischen Druckeinwirkung bewegen sich der Druckstempel 31 nach unten und der Druckstempel 32 nach oben. Die aufgetrennte Blutspende wird in die zweite Kammer 14 übertragen. Dieser Präparationsschritt wird beendet, sobald die am unteren Ende der ersten Kammer 13 angeordnete Detektoreinrichtung 60 die "Buffy Coat"-Schicht 2 erfasst. In diesem Zustand ist sichergestellt, dass in dem verjüngtem Bereich 16 (siehe Fig. 3) und der Verbindungsleitung noch ausschließlich Erythrozytensediment vorhanden ist. Wenn die "Buffy Coat"-Schicht 2 erfasst worden ist, wird die Druckübertragung gestoppt. Danach wird die Ventilplatte in Verschlussstellung gebracht. Dies erfolgt entweder unmittelbar bei Detektion der Schicht 2 oder zeitlich verzögert, so dass Konzentratrete aus dem verjüngten Bereich 16 noch in die Verbindungsleitung gelangen können.

[0050] Die in die zweite Kammer 14 übertragenen Erythrozyten vermengen sich mit der Waschlösung. Die Waschlösung umfasst bspw. physiologische Kochsalzlösung. Es folgt eine weitere Zentrifugation, in deren Ergebnis sich die behandelten Erythrozyten als Konzentrat wiederum im unteren Teil der zweiten Kammer 14 sammeln, während die übrige Waschlösung den Überstand bildet.

[0051] In einem weiteren Präparationsschritt wird analog zu der beschriebenen Weise das gewaschene Erythrozytensediment in die dritte Kammer 15 übertragen. Hierzu wird die Ventilplatte 21 so verdreht, dass die Verbindungsleitung 22 zwischen der zweiten und dritten Kammer 14, 15 angeordnet ist. Außerdem wird der Druckverteiler 56 entsprechend verstellt. Die Druckübertragung wird wiederum in Abhängigkeit vom Detektorsignal der Detektoreinrichtung 60 gesteuert. Es kann an der zweiten Kammer 14 ein weiterer Sensor (nicht dargestellt) vorgesehen sein. Alternativ ist es möglich, die Präparationsvorrichtung 100 zu dem Sensor 61 hin zu verdrehen, so dass die Phasengrenze in der zweiten Kammer 14 erfasst werden kann.

[0052] Nach Übertragung des gewaschenen Erythrozytensedimentes in die dritte Kammer 15 erfolgt dort die Vermengung mit dem Kryoadditiv. Als Kryoadditiv werden die an sich bekannten Zusatzstoffe verwendet. Das Kryoadditiv umfasst bspw. eine Lösung aus wasserlöslichem Stärkederivat.

[0053] Nach Übertragung der gewaschenen Erythrozyten in die dritte Kammer 15 und Vermengung mit dem Kryoadditiv ist die Kryokonserven einfrüherfertig. Es folgt die Übertragung in den anwendungsabhängig gewählten Behälter, z. B. einen Kryobeutel, in dem der Einfriervorgang erfolgt. Vorteilhafterweise ist nach Abschluss der Präparation in der ersten Kammer 13 der Plasmaüberstand als spenderspezifisches Restprodukt vorhanden. Anwendungsabhängig kann das Plasma einer weiteren Verwendung zugeführt werden.

[0054] Einzelheiten einer gegenüber Fig. 1 abgewandelten Gestaltung der erfindungsgemäßen Präparationsvorrichtung sind in Fig. 4 dargestellt. Die Unterschiede beziehen sich auf die Ausbildung der Ventilplatte 21. Im obersten Teilbild von Fig. 4 ist die Unterseite 12 des Kammerkörpers 10 mit den Kammern 13 bis 15 illustriert. Jede Kammer besitzt eine Ein- und Auslassöffnung in Form eines Anschlussstutzens 17 (siehe Fig. 3). An jedem Anschlussstutzen 17 ist ein O-Dichtring 18 vorgesehen. In der Mitte des Kammerkörpers 10 befindet sich entsprechend der Zylinderachse eine Gewindebohrung 19 zur Befestigung der Ventilplatte 21.

[0055] Im mittleren Teilbild von Fig. 4 ist die Ventilplatte 21 einzeln dargestellt. Bei dieser Gestaltung sind zwei Verbindungsleitungen (oder Überströmkanäle) 22, 23 vorgesehen, die so angeordnet sind, dass mit einer der Verbindungsleitungen 22 oder 23 jeweils zwei Kammern verbunden werden können, während die jeweils andere Verbindungsleitung 22 oder 23 verschlossen ist. Die Verwendung von zwei Verbindungsleitungen besitzt den Vorteil geringerer Verstellwege bei der Einstellung der Kammervverbindungen bei den einzelnen Präparationsschritten. In der Ventilplatte sind drei Ein- und Auslassbohrungen 24 vorgesehen, die so angeordnet sind, dass wenn eine der Ein- und Auslassbohrungen 24 mit einem der Anschlussstutzen 17 ausgerichtet ist, die anderen Anschlussstutzen jeweils verschlossen bleiben.

[0056] Die Ventilplatte 21 besitzt einen umlaufenden O-Dichtring 25, der eine zusätzliche Dichtung gegenüber der Unterseite 12 des Kammerkörpers 10 bereitstellt. Das Bezugszeichen 26 bezieht sich auf die Drehachse und das Lager der Ventilplatte 21.

[0057] Im unteren Teilbild von Fig. 4 ist die Ventilplatte 21 und die Unterseite 12 des Kammerkörpers 10 im zusammenmontierten Zustand dargestellt. Wird die Ventilplatte 21 vom dargestellten Zustand nach links gedreht, so werden zunächst mit der Verbindungsleitung 22 die Kammern 13 und 14 verbunden und bei der weiteren Verstellung werden die Kammern 14 und 15 über die Verbindungsleitung 23 verbunden. Damit können mit einem kurzen Stellweg die beiden oben erläuterten Präparationsschritte ausgeführt werden.

[0058] Die in den Fig. 1 bis 4 illustrierte Ausführungsform der Erfindung kann je nach Aufgabenstellung vielfältig modifiziert werden. So können bspw. zur Durchführung weiterer Präparationsschritte im Kammerkörper weitere Kammern zur Aufnahme weiterer Zusatzstoffe vorgesehen sein. Anstelle der 120°-Anordnung können die Kammern auch anderweitig im Kammerkörper oder einem Rahmengestell (siehe unten) angeordnet werden. Die Beschickung der Kammern kann anwendungsabhängig von der Ober- oder Unterseite her erfolgen. Dies erfolgt vorzugsweise unter Verwendung von Schlauch- oder Pipettiersystemen. Gemäß einer bevorzugten Gestaltung der Erfindung sind die Einlassöffnungen der Kammern gerade an die Außendurchmesser von standardisierten Flüssigkeitspipetten oder Schlauchadapter angepasst, so dass diese zur Beschickung einfach angesetzt und betätigt werden können. Die Präparationsvorrichtung kann anwendungsabhängig in ihrer Größe

beliebig skaliert werden. Die Übertragungseinrichtung mit der Ventilplatte kann durch eine fest eingestellte Anordnung mehrerer Verbindungsleitungen mit betätigbaren Ventilen ersetzt werden.

[0059] An der Außenseite des Kammerkörpers können zusätzliche Greif- oder Befestigungseinrichtungen zur Handhabung des Kammerkörpers und/oder zum Einsatz in eine Zentrifuge vorgesehen sein.

[0060] Der Kammerkörper mit den integrierten Kammern kann erfindungsgemäß durch eine Anordnung einzelner Kammern in einem Rahmengestell ersetzt werden. Diese Gestaltung besitzt Vorteile in Bezug auf eine separate Befüllung der einzelnen Kammern vor der Zusammensetzung zur Präparationsvorrichtung und die Entsorgung der Kammern nach Verwendung. Als Rahmengestell kann jede geeignete Struktur verwendet werden, in die die Kammern entsprechend der gewünschten Anordnung fixiert einsetzbar sind und die eine genügende Stabilität bei der Zentrifugation besitzt. Je nach der Gestaltung der Kammern ist die Struktur des Rahmengestells angepasst.

[0061] Werden als Kammern fertige Kolbenspritzen mit geeigneten Kolbendurchmessern verwendet, so besitzt das Rahmengestell Ausnehmungen zur Aufnahme der Spritzenkolben. Wenn die Einzelkammern durch gerade Rohrkörper gebildet sind, werden die Ausnehmungen des Rahmengestells entsprechend angepasst. Am Boden des Rahmengestells sind ggf. konisch vorgeformte Kammerböden vorgesehen, wie dies in Fig. 5 illustriert ist.

[0062] Fig. 5 zeigt eine Einzelkammer in schematischer Schnittansicht. Zwei oder mehr derartige Einzelkammern (z. B. entsprechend der obigen Gestaltung drei Einzelkammern) sind an einem Rahmengestell (nicht dargestellt) vorgesehen. Die Einzelkammer 90 umfasst eine Kammerwand 91 in Form eines geraden Kreiszylinders und einen sich verjüngenden Teilbereich 92, der in einem entsprechend geformten Stützsockel 93 ruht, der Teil des Rahmengestells ist. Im Inneren der Einzelkammer 90 befindet sich der Druckstempel (siehe oben). Der Druckstempel ist bei dieser Gestaltung nicht zylinderförmig, sondern als Stempelplatte 94 mit einem außen umlaufenden Dichtring 97 ausgebildet. Die Stempelplatte 94 besteht beispielsweise aus PMMA. Der Dichtring 97 ist ein z. B. aus PTFE bestehendes Formteil, das formschlüssig über den äußeren Rand der Stempelplatte 94 gezogen ist. Der Querschnitt des Dichtringes 97 besitzt eine U-Form, deren offenen Enden zwei Dichtlippen bilden. Durch diese Formgebung wird ein dichtendes Anlegen der Dichtlippen an die Kammerwand sicherstellt. Die Oberseite der Einzelkammer 90 ist mit einer Deckplatte 95 verschlossen, die eine Durchtrittsöffnung 96 zum Durchlass des Druckmediums aufweist.

[0063] Die Einzelkammer 90 besitzt bspw. ein Volumen von 470 ml bei einem Durchmesser von ca. 80 mm, einer Länge der Kammerwand 91 von ca. 110 mm und einer Höhe des Stützsockels 93 von ca. 30 mm. Der Teilbereich 92 grenzt ein Teilvolumen von ca. 30 ml ab.

[0064] Bei einem erfindungsgemäßen Verfahren zur Blutpräparation kann abweichend von der oben erläuterten Zentrifugation der gesamten Präparationsvorrichtung die folgende Einzelkammerzentrifugation vorgesehen sein. Dabei wird die jeweils interessierende Einzelkammer (z. B. gemäß Fig. 5) aus dem Rahmengestell entnommen und separat zentrifugiert. Vor oder nach der Zentrifugation ist die Einzelkammer im Rahmengestell zur Durchführung der übrigen Schritte der Probenpräparation angeordnet. Dieses Verfahren ist besonders vorteilhaft, falls zur

Zentrifugation keine passende Zentrifuge zur Verfügung steht.

Notice

This translation is machine-generated. It cannot be guaranteed that it is intelligible, accurate, complete, reliable or fit for specific purposes. Critical decisions, such as commercially relevant or financial decisions, should not be based on machine-translation output.

CLAIMS DE10134913C2

1.

¹³ Preparation device (100) for the treatment of suspension samples, in particular for the preparation of cryopreserved blood, with an arrangement of at least two containers for receiving the suspension samples, sample parts and/or additives, characterized in that the containers as chambers (13 to 15, 90) are formed with solid walls and are arranged stationary relative to each other and a transmission device (20) is provided with at least one connecting line (22) via which the chambers (13 to 15) can be connected to one another.

2.

²² Preparation device according to Claim 1, characterized in that the chambers (13 to 15) are formed in a one-piece chamber body (10).

3.

²⁷ Preparation device according to Claim 1, characterized in that the chambers (90) are detachably fastened as individual chambers in a framework.

4.

³² Preparation device according to one of the preceding claims, characterized in that the walls of the chambers or the chamber bodies (10) consist of a transparent material.

5.

³⁷ Preparation device according to one of the preceding claims 1 or 2, characterized in that the

chambers (13 to 15) have the shape of straight hollow cylinders which run from an upper side (11) to an underside (12) of the chamber body (10), with the underside (12) of each chamber (13 to 15) has a connecting piece (17) to which one end of the at least one connecting line (22) can be connected.

6.

⁴⁵ Preparation device according to one of the preceding claims, characterized in that a pressure plunger (31 to 33) is provided in each chamber.

7.

⁵⁰ Preparation device according to Claim 6, characterized in that each pressure plunger (31 to 33) has a circumferential sealing lip.

8.

⁵⁵ Preparation device according to one of the preceding claims, characterized in that the transmission device (20) is formed by a valve plate (21) in which at least one connecting line (22) is integrated, the valve plate (21) being rotatably arranged.

9.

⁶¹ Preparation station for the preparation of suspension samples, having: at least one preparation device (100) according to one of the preceding claims, a pressure device (50) which is set up to generate an overpressure or underpressure in one of the chambers (13 to 15), a detector device (60) for detecting a phase boundary in one of the chambers (13 to 15), an actuating device (70) which has an actuating element (71) with which the transmission device (20) can be adjusted in such a way that two chambers each via the at least one connecting line (22) and a control device which is connected to the printing device (50), the detector device (60) and the actuating device (70) and for actuating the printing device (50) and the actuating device (70) as a function of a detector signal from the detector device (60) is established.

10.

⁷³ Preparation station according to Claim 9, characterized in that the pressure device (50) has a pneumatic pressure generator or a mechanical pressure generator with connecting rods.

11.

⁷⁸ Method for preparing suspension samples or cryopreserved blood using a preparation device (100) according to one of Claims 1 to 8, characterized in that a treatment of a sample in at least

one of the chambers (13 to 15, 90) and a transfer at least part of the sample between two chambers.

12.

85 Method according to Claim 11, characterized in that the sample treatment comprises centrifugation of the sample and/or treatment of the sample with additives.

13.

90 Method according to Claim 12, characterized in that the entire preparation device (100) or an individual chamber (90) is centrifuged during the centrifugation of the sample.



①⑨ **BUNDESREPUBLIK
DEUTSCHLAND**



**DEUTSCHES
PATENT- UND
MARKENAMT**

①⑫ **Patentschrift**
①⑩ **DE 101 34 913 C 2**

⑤① Int. Cl.⁷:
A 61 M 1/00
A 61 M 1/36
A 61 J 1/00
B 04 B 5/04

②① Aktenzeichen: 101 34 913.0-35
②② Anmeldetag: 18. 7. 2001
④③ Offenlegungstag: 20. 2. 2003
④⑤ Veröffentlichungstag
der Patenterteilung: 26. 6. 2003

DE 101 34 913 C 2

Innerhalb von 3 Monaten nach Veröffentlichung der Erteilung kann Einspruch erhoben werden

⑦③ Patentinhaber:
Hiberna AG, 97232 Giebelstadt, DE

⑦④ Vertreter:
v. Bezold & Sozien, 80799 München

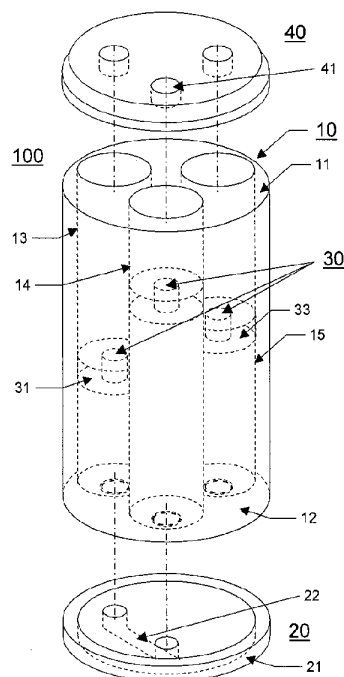
⑦② Erfinder:
Eck, Michael, 97074 Würzburg, DE

⑤⑥ Für die Beurteilung der Patentfähigkeit in Betracht
gezogene Druckschriften:

DE 298 05 538 U1
WO 00 38 762

⑤④ **Vorrichtung und Verfahren zur Blutpräparation**

⑤⑦ Präparationsvorrichtung (100) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme der Suspensionsproben, von Probenteilen und/oder von Zusatzstoffen, dadurch gekennzeichnet, dass die Behältnisse als Kammern (13 bis 15, 90) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind und eine Übertragungseinrichtung (20) mit mindestens einer Verbindungsleitung (22) vorgesehen ist, über die die Kammern (13 bis 15) miteinander verbindbar sind.



DE 101 34 913 C 2

[0001] Die Erfindung betrifft eine Vorrichtung zur Probenpräparation, insbesondere eine Vorrichtung zur Handhabung und Behandlung von Blutproben, wie z. B. zum Trennen von Blutproben durch Zentrifugation und zur Modifizierung von Blutproben durch Zusatzstoffe zur Vorbereitung einer Kryokonservierung der Blutproben sowie eine Präparationsstation und ein Verfahren zur Blutpräparation, insbesondere zur Vorbereitung von Blutproben für die Kryokonservierung.

[0002] Es ist bekannt, zur Kryokonservierung von Blutproben zunächst aus einer Blutspende eine Blutkonserve für den einfrierfertigen Zustand zu präparieren. Die Präparation umfasst insbesondere erstens eine Auftrennung der Blutspende in eine Erythrozytensuspension, die kryokonserviert werden soll, und Restbestandteile und zweitens den Zusatz eines Kryoadditives zur Erythrozytensuspension. Bei herkömmlichen Verfahren erfolgt die Handhabung der Blutproben unter Verwendung von flexiblen Blutbeuteln, wie es schematisch in Fig. 6 illustriert ist. Eine Blutspende wird in einem ersten Blutbeutel 1' bereitgestellt und zentrifugiert. Nach dem Zentrifugieren ist die Blutspende in das Sediment und den Überstand (Plasma) getrennt. Der Überstand wird ggf. in einen Abfallbehälter 4' abgezogen. Die Erythrozytensuspension wird in einen weiteren Blutbeutel 2' umgefüllt, dem zur Bereitstellung der einfrierfertigen Konserve ein Kryoadditiv zugesetzt wird. Die illustrierte Verwendung von Blutbeuteln, die bspw. in DE 298 05 538 und WO 00/38762 beschrieben wird, besitzt die folgenden Nachteile.

[0003] Ein Hauptproblem betrifft die Handhabung der Blutbeutel. Da die Blutbeutel keine feste Form besitzen, muss insbesondere zur Erhaltung der Phasengrenze nach der Zentrifugation ein schonender Umgang mit den Blutbeuteln vorgesehen sein. Bei den genannten herkömmlichen Systemen sind zwar Vorrichtungen zur Halterung und zum Transport der Blutbeutel vorgesehen. Diese Vorrichtungen sind jedoch nur sehr eingeschränkt automatisierbar. Es müssen eine manuelle Beschickung der Vorrichtungen und eine laufende Überwachung des Betriebes erfolgen. Des Weiteren sind die Blutbeutel bei den herkömmlichen Vorrichtungen über flexible Schläuche miteinander verbunden. Zur Trennung von Erythrozytensuspension und Überstand muss die Phasengrenze am Blutbeutel oder am Schlauch detektiert werden. Wegen der Flexibilität der jeweiligen Behältnisse besteht das Risiko einer Fehldetektion und damit einer Fehlfunktion bei der Präparation.

[0004] Weitere Nachteile ergeben sich aus Sterilitätsproblemen beim Umgang mit den Blutbeuteln. Die Schlauchverbindungen müssen steril an die Blutbeutel angeschlossen und nach dem jeweiligen Verfahrensschritt abgetrennt und verschweißt werden. Bei jedem Präparationsschritt müssen aufwendige Vorkehrungen zur Erhaltung der Sterilität und Pyrogenfreiheit der Blutproben getroffen werden.

[0005] Die herkömmliche Blutbeutelpräparation ist auch wegen der Verwechslungsgefahr problematisch. Wenn während der Präparation ein Blutbeutel verwechselt wird oder eine Kreuzkontamination zwischen Blutbeuteln auftritt, so kann dies verheerende Folgen für den Empfänger der Blutspende haben. Zum Ausschluss der Verwechslungsgefahr müssen bei herkömmlichen Systemen aufwendige Sicherheitsmaßnahmen realisiert werden.

[0006] Ein weiterer Nachteil der in WO 00/38762 beschriebenen Technik besteht in deren spezifischen Zuschnitt auf die Stammzellenpräparation. Bei der Trennung von Stammzellen aus biologischen Flüssigkeitsproben ist lediglich ein sehr geringer Stammzellengehalt aus den Proben ab-

zutrennen. Dies ermöglicht den Einsatz spezieller Zentrifugationstechniken und eine geringere Empfindlichkeit in Bezug auf die Verwendung von Blutbeuteln.

[0007] In der modernen Medizin und im Katastrophenschutz besteht ein Interesse an vergrößerten Blutbanken mit einem breiten Spektrum verschiedenster Bluttypen. Zur Herstellung moderner Blutbanken ist eine Automatisierung der Konservenpräparation erforderlich. Wegen des Automatisierungsbedarfes ist die Anwendbarkeit herkömmlicher Präparationsvorrichtungen eingeschränkt.

[0008] Die illustrierten Probleme bei der Handhabung von Blutproben bestehen nicht nur bei der Vorbereitung von Konserven für die Kryokonservierung. Ein entsprechender Bedarf nach steriler, automatisierter und sicherer Probenhandhabung besteht auch bei der Bearbeitung von biologischen Zellsuspensionen für therapeutische Zwecke.

[0009] Die Aufgabe der Erfindung ist es, eine verbesserte Vorrichtung zur Präparation suspendierter biologischer Proben bereitzustellen, mit der die Nachteile herkömmlicher Systeme überwunden werden und die insbesondere für eine automatisierbare und sichere Handhabung einer Vielzahl von Proben geeignet ist. Ferner soll ein verbessertes System zur Präparation von Kryokonserven, wie z. B. Blut-Kryokonserven geschaffen werden sowie ein neuartiges Verfahren zur Handhabung biologischer suspendierter Proben, das insbesondere automatisierbar und sicher durchführbar ist.

[0010] Diese Aufgaben werden mit einer Präparationsvorrichtung, eine Präparationsstation und einem Verfahren mit den Merkmalen gemäß den Patentansprüchen 1, 9 und 11 gelöst. Vorteilhafte Ausführungsformen und Anwendungen der Erfindung ergeben sich aus den abhängigen Ansprüchen.

[0011] Die Grundidee der Erfindung ist es, eine Präparationsvorrichtung bereitzustellen, die mindestens zwei Behältnisse zur Aufnahme der zu behandelnden Suspensionsproben aufweist, wobei die Behältnisse im Unterschied zu herkömmlichen Systemen durch relativ zueinander ortsfest positionierte Kammern mit festen Wänden gebildet werden. Die Kammern sind über einzeln betätigbare Leitungsverbindungen miteinander verbunden oder mit Anschlussstücken zur optionalen Ausbildung von Leitungsverbindungen zwischen den Kammern ausgestattet. Die erfindungsgemäße Präparationsvorrichtung ist gemäß einer ersten Ausführungsform durch einen integralen Aufbau gebildet, bei dem die Kammern in einem Kammerkörper geformt sind, an dessen einem Ende die Leitungsverbindungen ansetzbar oder einstellbar sind. Gemäß einer zweiten Ausführungsform umfasst die Präparationsvorrichtung ein Rahmengestell, in das die Kammern einzeln einsetzbar sind. Die Anschlussstücke der einzelnen Kammern sind sämtlich auf einer (z. B. unteren) Seite des Rahmengestells angeordnet. Je nach Bedarf werden die zunächst mit einem Septum verschlossenen Anschlussstücke geöffnet und über Leitungsverbindungen paarweise in Verbindung gebracht. Die Gestaltung mit einzelnen Kammern ist gemäß einer dritten Ausführungsform derart ausgebildet, dass das Rahmengestell mit einer Ventilplatte mit Leitungsverbindungen ausgestattet ist, über die die einzelnen Kammern paarweise verbunden werden können. Die Ausbildung der Präparationsvorrichtung als integraler Aufbau oder als Gestellaufbau mit mindestens zwei Kammern besitzt die Vorteile, dass die Präparationsvorrichtung im Rahmen eines automatisierten Verfahrensablaufes einen sicher greif- und manipulierbaren Gegenstand darstellt und dass die Probenhandhabung, insbesondere die unabhängige Vorbefüllung der Kammern, die Behandlung von Proben in den Kammern und die Überführung der Proben zwischen den Kammern, vereinfacht wird. Bei Anwendung der erfindungsgemäßen Präparationsvorrichtung zur Herstellung von Blutproben für die Kryokonservierung sind

vorzugsweise mindestens drei Kammern vorgesehen.

[0012] Gemäß der genannten ersten Ausführungsform der Erfindung sind die Kammern vorzugsweise in Form von geraden Kreiszylindern in einem Kunststoffkörper gebildet, an dessen einem Ende eine Ventilplatte angebracht ist, die mindestens eine Leitungsverbindung zur Kopplung von jeweils zwei Kammern enthält. Der Aufbau mit einem integralen Kunststoffkörper besitzt den Vorteil, dass die Präparationsvorrichtung als Einwegprodukt herstellbar ist, so dass Sterilitäts- und Verwechslungsprobleme ausgeschlossen werden können. Als weiterer Vorteil ergibt sich eine hohe Stabilität der Präparationsvorrichtung insbesondere bei Zentrifugationsvorgängen.

[0013] Die genannten zweiten und dritten Ausführungsformen der Erfindung stellen jeweils einen modularen Aufbau dar. Die Kammern können als Einwegprodukte verwendet werden. Als zusätzlicher Vorteil ergibt sich beim Rahmenaufbau ein relativ geringes Gewicht.

[0014] Die Übertragung von Proben zwischen den Kammern erfolgt vorzugsweise durch einen hydrostatischen Druck, der als Gasdruck oder vorzugsweise mit Druckstempeln ausgeübt wird, die jeweils in den Kammern angeordnet sind. Alternativ ist es möglich, den Druck mit einem mechanisch betätigbaren Kolben zu übertragen (z. B. mit einem Pleuelgestänge). Die Kammern der erfindungsgemäßen Präparationsvorrichtung bilden bei dieser Gestaltung Kolben-Druckerzeuger, die sowohl zur Aufnahme der jeweiligen Proben als auch zur Übertragung der Proben in benachbarte Kammern eingerichtet sind.

[0015] Gemäß einer weiteren bevorzugten Gestaltung besteht die Präparationsvorrichtung, insbesondere die Kammern als Hauptkomponenten, zumindest teilweise aus einem transparenten Kunststoffmaterial. Bei Verwendung von nicht-transparentem Material besitzen die Kammern vorzugsweise mindestens ein transparentes Fenster zur optischen Detektion. Es wird eine zuverlässige und reproduzierbare optische Detektion von Probeneigenschaften, insbesondere der Lage der Phasengrenze nach einer Zentrifugation, ermöglicht.

[0016] Gegenstand der Erfindung ist auch eine Präparationsstation, die mit der erfindungsgemäßen Präparationsvorrichtung ausgestattet ist und des Weiteren eine Druckeinrichtung zur Probenübertragung zwischen den Kammern, eine Detektoreinrichtung zur Messung von Probeneigenschaften in den Kammern und eine Stelleinrichtung zur selektiven Kopplung von Kammern aufweist.

[0017] Gegenstand der Erfindung ist auch ein Verfahren zur Präparation von Suspensionen, die biologisch relevante Komponenten, wie z. B. Zellen, Zellbestandteile oder Makromoleküle, enthalten, unter Verwendung der erfindungsgemäßen Präparationsvorrichtung. Das Verfahren zeichnet sich insbesondere dadurch aus, dass alle Präparations-schritte mit der gesamten Präparationsvorrichtung durchgeführt werden, die verschiedene Kammern zur Aufnahme von Proben in verschiedenen Präparationsstadien enthält.

[0018] Die Erfindung besitzt die folgenden Vorteile für die Probenpräparation, insbesondere für die Herstellung von Blut-Kryokonserven. Der Präparationsprozess ist zur Erhöhung der Produktivität bei der Konservenherstellung, d. h. zur Erzielung eines möglichst hohen Konservendurchsatzes, automatisierbar, wobei gleichzeitig die Herstellungsqualität gesteigert und unabhängig von der Handfertigkeit eines Bedieners aufrechterhalten wird. Eine erfindungsgemäß hergestellte Blutkonserve erfährt bereits durch die Verwendung der Präparationsvorrichtung eine Qualitätssteigerung, ohne dass die Präparation wesentlich verteuert wird.

[0019] Die erfindungsgemäße Präparationsvorrichtung ist während der Präparationsprozedur nach außen hin absolut

abgeschlossen. Sie tritt lediglich einmalig jeweils beim Befüllen und beim Entleeren in Kontakt mit der Umgebung. Beispielsweise erfolgt die Vorbehandlung einer Konserve bis zum Erlangen des einfrierfertigen Zustandes absolut steril. Vorteilhafterweise wird das Öffnen, Verbinden und Verschließen von Beuteln und Verbindungsschläuchen entsprechend den herkömmlichen Systemen vermieden. Die Suspensionsprobe verlässt während der Präparationsschritte nicht die Präparationsvorrichtung. Eine Verwechslung z. B. von Blut verschiedener Spender oder eine Kontamination durch Fremdblut oder Mikroorganismen sind ausgeschlossen. Die Identität des Spenderblutes ist garantiert. Der Präparationsvorgang wird stark beschleunigt, da Arbeitsschritte, die bei herkömmlichen Systemen ggf. mehrfach notwendig sind, erfindungsgemäß vollständig entfallen können. Ein teilweiser oder vollständiger Probenverlust oder eine Kontamination der Arbeitsumgebung einschließlich des Laborpersonals durch undichte Schlauchverbindungen werden bei der erfindungsgemäßen Präparationsvorrichtung ausgeschlossen.

[0020] Die erfindungsgemäße Präparationsvorrichtung bildet ein festes Behältnis, das im Vergleich mit herkömmlich verwendeten Blutbeuteln ein definiertes und reproduzierbares Greifen und Handhaben der Vorrichtung und der an dieser angebrachten Ventile und/oder Stutzen ermöglicht. Das Greifen oder Positionieren und Klemmen von Verbindungsschläuchen entfällt, wenn die mindestens eine Verbindungsleitung in die Präparationsvorrichtung integriert ist und somit ein reproduzierbares und mehrfaches Verbinden der einzelnen Kammern auf kürzestem Weg ermöglicht. Durch die kurzen Wege und die Wahl eines geeigneten Querschnittes der jeweiligen Verbindungsleitung lässt sich die Transferzeit zur Übertragung von Proben zwischen den Kammern optimieren. Der Aufbau der Vorrichtung ermöglicht ein definiertes Positionieren der mindestens einen Verbindungsleitung. Ein versehentliches Verbinden von aktuell nicht kooperierenden Kammern wird ausgeschlossen. Ein Deformieren oder Quetschen der Kammern wird erfindungsgemäß vermieden. Eine z. B. durch Zentrifugation eingestellte Phasentrennung von Probenbestandteilen kann durch einen Greifvorgang nicht verwischt werden.

[0021] Die feste und vorzugsweise symmetrische Anordnung der Kammern in einer erfindungsgemäßen Präparationsvorrichtung ermöglicht ein schnelles und definiertes Positionieren der jeweils interessierenden Kammer in einem Präparationssystem unabhängig vom Verfahrensschritt. Alle Sensoren und Aktoren sind automatisch korrekt positioniert. Es wird ein erhöhter, fehlerfreier Durchsatz erzielt. Beispielsweise lassen sich mit einer erfindungsgemäß Präparationsvorrichtung rund dreifach mehr Kryokonserven pro Zeiteinheit präparieren. Die Präparationsvorrichtung ermöglicht eine freie Materialwahl und Dimensionierung der Außenform der Kammeranordnung. Vorteilhafterweise kann die Vorrichtung ohne Weiteres mit herkömmlichen Zentrifugiereinrichtungen verwendet werden.

[0022] Durch die Herstellung der Präparationsvorrichtung aus kostengünstigen Kunststoffmaterialien können große Stückzahlen der Vorrichtung in Spritzgieß- oder Extrusionstechniken hergestellt werden. Dies ist für die erfindungsgemäße Verwendung der fest bewandeten Kammern als Einwegprodukte von Vorteil.

[0023] Insbesondere bei der Präparation von Blutproben ergeben sich zusätzlich die folgenden Vorteile. Für Blutspendedienste entsteht bei Einsatz der erfindungsgemäßen Präparationsvorrichtung kein wesentlicher Zusatzaufwand. Es werden keine Mehrfachbeutelssysteme erforderlich. Die Präparationsvorrichtung kann direkt mit einem einfachen Spendebeutel (Einfachblutbeutel) gekoppelt werden. Der

bei herkömmlichen Verfahren ggf. in den Abfall gelangende oder nur mit großem Aufwand gewinnbare Überstand (Plasma und "Buffy Coat") steht erfindungsgemäß bei Bedarf als zusätzliches Endprodukt zur Verfügung. Die Präparationsvorrichtung liefert auch Vorteile bei der nach der Präparation vorgesehenen Befüllung von Einfrierbeuteln. Ein befüllter Einfrierbeutel kann im angedockten Zustand an der Präparationsvorrichtung mit dieser einfach und steril entlüftet werden, in dem die jeweilige Kammer mit einem Unterdruck beaufschlagt wird.

[0024] Weitere Vorteile und Einzelheiten der Erfindung ergeben sich aus der folgenden Beschreibung der beigefügten Zeichnungen. Es zeigen:

[0025] Fig. 1 eine schematische Phantomansicht einer Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung in teilweise auseinander gezogenem Zustand, [0026] Fig. 2 eine Illustration der Einbindung der Präparationsvorrichtung gemäß Fig. 1 in eine Vorrichtung zur Herstellung von Blutkonserven,

[0027] Fig. 3 eine vergrößerte Teilansicht eines Kammerendes der Präparationsvorrichtung gemäß Fig. 1,

[0028] Fig. 4 Illustration einer abgewandelten Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung,

[0029] Fig. 5 eine schematische Schnittansicht einer erfindungsgemäß verwendeten Einzelkammer, und

[0030] Fig. 6 eine Illustration einer herkömmlichen Präparationstechnik (Stand der Technik).

[0031] In Fig. 1 ist eine Ausführungsform einer erfindungsgemäßen Präparationsvorrichtung 100 in schematischer Phantomansicht dargestellt. Die Präparationsvorrichtung 100 umfasst einen Kammerkörper 10, in dem drei Kammern zur Aufnahme von Suspensionsproben gebildet sind, eine Übertragungseinrichtung 20, bestehend aus einer Ventilplatte 22 und mindestens einer Verbindungsleitung 22, eine Stempelinrichtung 30 mit mehreren Druckstempeln 31 bis 33 und eine Deckplatte 40, die den oberen Abschluss des Kammerkörpers 10 bildet. Der Kammerkörper 10 ist einstückig aus einem transparenten Kunststoffmaterial (z. B. PMMA, Cycloolefin-Copolymere, Polyamid, Polycarbonat, PCHP, Polyester oder Polysulfone) geformt. Er besitzt die äußere Form eines geraden Kreiszylinders mit einer ebenen Oberseite 11 und einer ebenen Unterseite 12. Im Inneren des Kammerkörpers 10 sind die drei zylinderförmigen Kammern 13, 14 und 15 zur Probenaufnahme gebildet. Am oberen Ende des Kammerkörpers 10 münden die Kammern frei in die Oberseite 11. Am unteren Ende besitzt jede Kammer eine Verjüngung 16 mit einem Anschlussstutzen 17, wie es vergrößert in Fig. 3 illustriert ist. Der Anschlussstutzen 17 mündet jeweils in die Unterseite 12 des Kammerkörpers 10. [0032] Zur Anwendung bei der Präparation von Blutproben besitzt die Präparationsvorrichtung 100 bspw. einen Durchmesser von ca. 18 bis 20 cm, wobei die Höhe des Kammerkörpers 10 ca. 10 bis 12 cm beträgt und die Kammern 13 bis 15 jeweils einen Innendurchmesser von ca. 6 bis 8 cm besitzen. Eine Kammer besitzt vorzugsweise ein Volumen im Bereich von 400 ml bis 600 ml. Die Kammern 13 bis 15 sind vorzugsweise relativ zur Achse des Kammerkörpers 10 symmetrisch verteilt angeordnet.

[0033] Die Übertragungseinrichtung 20 ist zur Übertragung von Proben zwischen den Kammern 13 bis 15 eingerichtet. Die Ventilplatte 21 ist drehbar an der Unterseite 12 des Kammerkörpers 10 befestigt. In die ebenfalls aus Kunststoffmaterial hergestellte Ventilplatte 21 ist die Verbindungsleitung 22 integriert, die einen Überströmkanal bildet. An den Mündungen der Verbindungsleitungen 22 auf der inneren Seite der Ventilplatte 21, die an die Unterseite 12 des Kammerkörpers 10 angrenzt, oder an den Anschluss-

stutzen 17 der einzelnen Kammern (siehe Fig. 3) sind Dichtungsringe aus einem elastischen Material (z. B. PTFE) angebracht. Neben der Dichtfunktion können die Dichtungsringe (nicht dargestellt) auch als Rasteinrichtungen dienen.

Bei Drehung der Verbindungsplatte 21 rasten die Dichtungsringe an den gewünschten Positionen der Anschlussstutzen oder der Mündung der Verbindungsleitung 22 ein, wenn diese gerade zueinander ausgerichtet sind.

[0034] Die Ventilplatte 21 besitzt eine Ventilfunktion, da in der Regel Flüssigkeit immer nur in einer Richtung von einer Kammer zur benachbarten Kammer gepumpt wird. Zum Ausschluss einer Fehlbedienung kann an der Ventilplatte 21 oder am Kammerkörper 10 eine Vorrichtung zur erzwingenden Vorgabe einer bestimmten Drehrichtung und/oder eine Wiederhol Sperre vorgesehen sein. Diese Vorrichtung umfasst bspw. eine Verzahnung, die eine Rückwärtsdrehung ausschließt, und/oder eine zusätzliche Arretierhilfe.

[0035] Der Aufbau der Ventilplatte 21 kann anwendungsabhängig abgewandelt werden (siehe Fig. 4). Es können mehrere Verbindungsleitungen vorgesehen sein. Die mindestens eine Verbindungsleitung kann mit einer Sperr- oder Ventileinrichtung ausgestattet sein. In der Ventilplatte können vorzugsweise zusätzliche Durchgangsöffnungen zur Beschickung der Kammern vorgesehen sein. Die Beschickung kann aber auch von der oberen Seite her erfolgen.

[0036] Zum Proben transport zwischen den Kammern werden die Proben mit einem Druck beaufschlagt. Unter der Wirkung eines Überdruckes in der Kammer, von der die Übertragung ausgeht, wird die Probe über den Überströmkanal in der Ventilplatte 21 übertragen. Der Übertragungsdruck wird mit einer Druckeinrichtung aufgebracht, die Teil der Präparationsstation (siehe Fig. 2) ist, in der die erfindungsgemäße Präparationsvorrichtung vorzugsweise verwendet wird. Gemäß einer vorteilhaften Ausführungsform der Erfindung wird der Druck mit einer Stempelinrichtung 30 übertragen, die in den Kammern 13 bis 15 jeweils einen Druckstempel 31 bis 33 aufweist. Die Druckstempel 31 bis 33 bestehen aus Kunststoffkörpern z. B. in Zylinderform, die formschlüssig in die jeweilige Kammer eingepasst sind. Jeder Druckstempel weist mindestens eine umlaufende Dichtlippe auf, die ggf. auftretende Spalte zwischen den Druckstempeln und den Kammerinnenwänden abdichtet. Die Dichtlippen verhindern ein Durchlauf des Kolbens durch die flüssigen Proben bei Druckbeaufschlagung. Die Kolben mit den Dichtlippen bestehen aus einem Kunststoffmaterial (z. B. PTFE). Der Einsatz der Druckstempel 31 bis 33 in den Kammern besitzt den Vorteil, dass bei einer Bewegung der Präparationsvorrichtung 100 eine Probenbewegung in den Kammern verhindert wird, wenn die Druckstempel jeweils auf den Flüssigkeiten aufgesetzt sind. Nach einer Zentrifugation wird vorteilhafterweise eine Aufhebung der Phasengrenze zwischen den Fraktionen vermieden.

[0037] Die Druckstempel 31 bis 33 können gemäß einer bevorzugten Ausführungsform jeweils eine zentrale Bohrung (gestrichelt eingezeichnet) mit einem Verschluss (z. B. einem Septum) aufweisen. Dies ermöglicht einen Zugriff zu den Proben oder Zusatzflüssigkeiten in den Kammern von der Oberseite der Vorrichtung 100 her.

[0038] Gemäß einer abgewandelten Ausführungsform der Erfindung kann auf die Verwendung der Druckstempel auch verzichtet werden. In diesem Fall wird der Übertragungsdruck direkt auf die Flüssigkeitsoberfläche in der jeweiligen Kammer gegeben. Bei dieser Gestaltung sind die oberen Enden der Kammern an der Oberseite vorzugsweise mit einem Sterilfiltereinsatz ausgestattet, der nur für das jeweilig verwendete sterile Druckmedium (z. B. Luft, inertes Gas) durchlässig ist. Der Aufbau ohne Druckstempel besitzt die

Vorteile eines vergrößerten Innenvolumens und vereinfachten Aufbaus der Kammern und damit einer Kostenersparnis. [0039] Die obere Deckplatte 40 dient dem Abschluss der Präparationsvorrichtung 100. Sie ist fest auf dem Kammerkörper 10 angebracht und besitzt Durchtrittsöffnungen oder Anschlussstutzen 41, die jeweils mit den oberen Enden der Kammern 13 bis 15 ausgerichtet sind. Die Anschlussstutzen 41 dienen der Verbindung von einzelnen oder gleichzeitig allen Kammern mit der Druckeinrichtung und/oder Beschickungseinrichtungen.

[0040] Der Verfahrensablauf zur Herstellung einer Blut-Kryokonserven unter Verwendung einer erfindungsgemäßen Präparationsvorrichtung wird im Folgenden unter Bezug auf Fig. 2 erläutert. Fig. 2 zeigt die Präparationsvorrichtung 100 analog zur Darstellung gemäß Fig. 1 in Kombination mit Teilen der Präparationsstation.

[0041] Die Komponenten der Präparationsvorrichtung 100 sind mit den gleichen Bezugszeichen wie in Fig. 1 versehen.

[0042] Zur Präparationsstation gehören insbesondere die Druckeinrichtung 50, eine Detektoreinrichtung 60, eine Stelleinrichtung 70 und eine Steuereinrichtung 80. Die Druckeinrichtung 50 umfasst vorzugsweise einen Druckerzeuger 51 mit einem Motor 52 und einem Pumpenteil 53. Alternativ umfasst die Druckeinrichtung 50 eine Hebeleinrichtung mit einer Pleuelstange. Die mechanische Kraftübertragung besitzt den Vorteil, dass die Positionierung der Druckstempel mit einer erhöhten Präzision erfolgen kann. Gemäß alternativen Ausführungsformen der Erfindung kann der Druckerzeuger auch durch eine Druckquelle (z. B. Druckgasflasche) mit einem Regelventil gebildet werden.

[0043] Die Detektoreinrichtung 60 umfasst insbesondere mindestens ein lichtempfindliches Element 61 zur Erkennung der Phasengrenze. Das lichtempfindliche Element 61 kann anwendungsabhängig mit (nicht dargestellten) Filtereinrichtungen ausgestattet sein. Es können auch mehrere lichtempfindliche Elemente entsprechend den Positionen der Kammern angeordnet sein. Anwendungsabhängig können auch andere Detektoren zur Erfassung von Probeneigenschaften vorgesehen sein, wie sie an sich aus der Analytik bekannt sind (z. B. Spektralphotometer, Widerstandsmesser zur Dichtebestimmung). Die Kammern können auch eine sich jeweils über ihre Länge erstreckende Skalierung zur optischen Kontrolle des Füllstandes, der Position der Druckstempel oder der Position der Phasengrenze aufweisen. Die Detektoren können ferner an anderen Komponenten der Präparationsvorrichtung, z. B. an einer Verbindungsleitung in der Ventilplatte, vorgesehen sein.

[0044] Zur Verstellung der oben erläuterten Ventilplatte 21 umfasst die Stelleinrichtung 70 ein Betätigungselement 71 und einen Stellmotor 72. Das Betätigungselement 71 besitzt die Form einer Platte mit mindestens einem Vorsprung 73, der mit mindestens einer entsprechenden Ausnehmung (nicht dargestellt) auf der Unterseite der Ventilplatte 21 zusammenwirkt. Der Vorsprung 73 greift in die Ausnehmung ein und verdreht die Ventilplatte 21 bei Betätigung des Stellmotors 72 in die gewünschte Position, so dass jeweils eine Kammer geöffnet oder geleert werden kann, jeweils zwei Kammern über die Verbindungsleitung 22 verbunden sind oder alle drei Kammern verschlossen sind.

[0045] Die Steuereinrichtung 80 ist mit den Komponenten 50, 60 und 70 des Präparationssystems verbunden. Je nach Betriebszustand und dem von der Detektoreinrichtung 60 gelieferten Detektorsignal werden in der folgenden Weise der Druckerzeuger 50 und die Stelleinrichtung 70 betätigt. Bei halbautomatischem oder manuellem Betrieb werden die entsprechenden Schritte zumindest teilweise durch einen Bediener durchgeführt.

[0046] In einem Startzustand sind die Kammern der erfindungsgemäßen Präparationsvorrichtung 100 wie folgt beschickt. In der ersten Kammer 13 befindet sich eine Blutspende. Die Blutspende wird aus einem Spenderbeutel in die erste Kammer 13 gefüllt, was ggf. unter Ausübung eines unterstützenden Unterdruckes erfolgt. Die zweite Kammer 14 ist mit einer Waschlösung gefüllt. In der dritten Kammer 15 befindet sich ein Kryoadditiv. Im Startzustand ist die erste Kammer 13 vollständig gefüllt, während die übrigen Kammern 14, 15 lediglich teilweise befüllt sind. In diesen Kammern ist so viel Volumen frei, wie es zur Übernahme der Erythrozytensuspension nach der Zentrifugation (siehe unten) erforderlich ist. Die Ventilplatte 21 wird nach dem Startzustand (alle verschlossen) so eingestellt, dass bspw. die erste und zweite Kammer 13, 14 verbunden sind. Vorteilhafterweise ist trotz der Verbindung im druckfreien Zustand über die Verbindungsleitung im Wesentlichen kein Flüssigkeitsaustausch gegeben.

[0047] In einem ersten Präparationsschritt wird der Kammerkörper mit den befüllten Kammern mit einer Zentrifugationseinrichtung zentrifugiert. Die (nicht dargestellte) Zentrifugationseinrichtung besitzt die Bauform einer an sich bekannten Großzentrifuge mit einzelnen Zentrifugenbechern, in denen eine Vielzahl von Präparationsvorrichtungen gleichzeitig zentrifugiert werden können. Während der Zentrifugation erfolgt lediglich die Auftrennung der Blutspende in die Fraktionen. Eine Verschiebung der Druckstempel 31 bis 33 erfolgt nicht. Während der Zentrifugation sind die Kammern verschlossen.

[0048] Der Zustand der Präparationsvorrichtung nach der Zentrifugation ist in Fig. 2 dargestellt. In der ersten Kammer 13 sind die gebildeten Fraktionen der Blutspende mit dem Erythrozytensediment 1 der sog. "Buffy Coat"-Schicht 2 und dem Plasmaüberstand 3 illustriert. Das Erythrozytensediment 1 umfasst betriebsabhängig einen Volumenanteil von ca. 45% der Kammer 13. Der Volumenanteil hängt insbesondere von der Zentrifugationsgeschwindigkeit ab. Bei einer höheren Geschwindigkeit ergibt sich eine höhere Packungsdichte der Erythrozyten und damit ein geringerer Volumenanteil. Die "Buffy-Coat"-Schicht 2 ist ein thrombozyten- und leukozytenhaltiger Belag mit einer gräulichen Färbung, der sich nach der Zentrifugation zwischen den tiefroten Erythrozytensediment 1 und dem hellroten Plasmaüberstand 3 ausbildet.

[0049] Nach der Zentrifugation wird die Präparationsvorrichtung 100 in die Präparationsstation eingesetzt. Die Ventilplatte 21 wird in Durchlassrichtung zwischen die erste und zweite Kammer 13, 14 gedreht. Dies erfolgt manuell, z. B. mit einem Noppenschlüssel oder mit der Stelleinrichtung 70 (siehe oben). Die erste Kammer 13 wird mit einem Überdruck beaufschlagt. Unter der hydrostatischen oder mechanischen Druckeinwirkung bewegen sich der Druckstempel 31 nach unten und der Druckstempel 32 nach oben. Die aufgetrennte Blutspende wird in die zweite Kammer 14 übertragen. Dieser Präparationsschritt wird beendet, sobald die am unteren Ende der ersten Kammer 13 angeordnete Detektoreinrichtung 60 die "Buffy Coat"-Schicht 2 erfasst. In diesem Zustand ist sichergestellt, dass in dem verjüngtem Bereich 16 (siehe Fig. 3) und der Verbindungsleitung noch ausschließlich Erythrozytensediment vorhanden ist. Wenn die "Buffy Coat"-Schicht 2 erfasst worden ist, wird die Druckübertragung gestoppt. Danach wird die Ventilplatte in Verschlussstellung gebracht. Dies erfolgt entweder unmittelbar bei Detektion der Schicht 2 oder zeitlich verzögert, so dass Konzentratreste aus dem verjüngten Bereich 16 noch in die Verbindungsleitung gelangen können.

[0050] Die in die zweite Kammer 14 übertragenen Erythrozyten vermengen sich mit der Waschlösung. Die Wasch-

lösung umfasst bspw. physiologische Kochsalzlösung. Es folgt eine weitere Zentrifugation, in deren Ergebnis sich die behandelten Erythrozyten als Konzentrat wiederum im unteren Teil der zweiten Kammer **14** sammeln, während die übrige Waschlösung den Überstand bildet.

[0051] In einem weiteren Präparationsschritt wird analog zu der beschriebenen Weise das gewaschene Erythrozytensediment in die dritte Kammer **15** übertragen. Hierzu wird die Ventilplatte **21** so verdreht, dass die Verbindungsleitung **22** zwischen der zweiten und dritten Kammer **14**, **15** angeordnet ist. Außerdem wird der Druckverteiler **56** entsprechend verstellt. Die Druckübertragung wird wiederum in Abhängigkeit vom Detektorsignal der Detektoreinrichtung **60** gesteuert. Es kann an der zweiten Kammer **14** ein weiterer Sensor (nicht dargestellt) vorgesehen sein. Alternativ ist es möglich, die Präparationsvorrichtung **100** zu dem Sensor **61** hin zu verdrehen, so dass die Phasengrenze in der zweiten Kammer **14** erfasst werden kann.

[0052] Nach Übertragung des gewaschenen Erythrozytensedimentes in die dritte Kammer **15** erfolgt dort die Vermengung mit dem Kryoadditiv. Als Kryoadditiv werden die an sich bekannten Zusatzstoffe verwendet. Das Kryoadditiv umfasst bspw. eine Lösung aus wasserlöslichem Stärkederivat.

[0053] Nach Übertragung der gewaschenen Erythrozyten in die dritte Kammer **15** und Vermengung mit dem Kryoadditiv ist die Kryokonserven einfrüherfertig. Es folgt die Übertragung in den anwendungsabhängig gewählten Behälter, z. B. einen Kryobeutel, in dem der Einfriervorgang erfolgt. Vorteilhafterweise ist nach Abschluss der Präparation in der ersten Kammer **13** der Plasmaüberstand als spenderspezifisches Restprodukt vorhanden. Anwendungsabhängig kann das Plasma einer weiteren Verwendung zugeführt werden.

[0054] Einzelheiten einer gegenüber **Fig. 1** abgewandelten Gestaltung der erfindungsgemäßen Präparationsvorrichtung sind in **Fig. 4** dargestellt. Die Unterschiede beziehen sich auf die Ausbildung der Ventilplatte **21**. Im obersten Teilbild von **Fig. 4** ist die Unterseite **12** des Kammerkörpers **10** mit den Kammern **13** bis **15** illustriert. Jede Kammer besitzt eine Ein- und Auslassöffnung in Form eines Anschlussstutzens **17** (siehe **Fig. 3**). An jedem Anschlussstutzen **17** ist ein O-Dichtring **18** vorgesehen. In der Mitte des Kammerkörpers **10** befindet sich entsprechend der Zylinderachse eine Gewindebohrung **19** zur Befestigung der Ventilplatte **21**.

[0055] Im mittleren Teilbild von **Fig. 4** ist die Ventilplatte **21** einzeln dargestellt. Bei dieser Gestaltung sind zwei Verbindungsleitungen (oder Überströmkanäle) **22**, **23** vorgesehen, die so angeordnet sind, dass mit einer der Verbindungsleitungen **22** oder **23** jeweils zwei Kammern verbunden werden können, während die jeweils andere Verbindungsleitung **22** oder **23** verschlossen ist. Die Verwendung von zwei Verbindungsleitungen besitzt den Vorteil geringerer Verstellwege bei der Einstellung der Kammerverbindungen bei den einzelnen Präparationsschritten. In der Ventilplatte sind drei Ein- und Auslassbohrungen **24** vorgesehen, die so angeordnet sind, dass wenn eine der Ein- und Auslassbohrungen **24** mit einem der Anschlussstutzen **17** ausgerichtet ist, die anderen Anschlussstutzen jeweils verschlossen bleiben.

[0056] Die Ventilplatte **21** besitzt einen umlaufenden O-Dichtring **25**, der eine zusätzliche Dichtung gegenüber der Unterseite **12** des Kammerkörpers **10** bereitstellt. Das Bezugszeichen **26** bezieht sich auf die Drehachse und das Lager der Ventilplatte **21**.

[0057] Im unteren Teilbild von **Fig. 4** ist die Ventilplatte **21** und die Unterseite **12** des Kammerkörpers **10** im zusammenmontierten Zustand dargestellt. Wird die Ventilplatte **21** vom dargestellten Zustand nach links gedreht, so werden zu-

nächst mit der Verbindungsleitung **22** die Kammern **13** und **14** verbunden und bei der weiteren Verstellung werden die Kammern **14** und **15** über die Verbindungsleitung **23** verbunden. Damit können mit einem kurzen Stellweg die beiden oben erläuterten Präparationsschritte ausgeführt werden.

[0058] Die in den **Fig. 1** bis **4** illustrierte Ausführungsform der Erfindung kann je nach Aufgabenstellung vielfältig modifiziert werden. So können bspw. zur Durchführung weiterer Präparationsschritte im Kammerkörper weitere Kammern zur Aufnahme weiterer Zusatzstoffe vorgesehen sein. Anstelle der 120°-Anordnung können die Kammern auch anderweitig im Kammerkörper oder einem Rahmengestell (siehe unten) angeordnet werden. Die Beschickung der Kammern kann anwendungsabhängig von der Ober- oder Unterseite her erfolgen. Dies erfolgt vorzugsweise unter Verwendung von Schlauch- oder Pipettiersystemen. Gemäß einer bevorzugten Gestaltung der Erfindung sind die Einlassöffnungen der Kammern gerade an die Außendurchmesser von standardisierten Flüssigkeitspipetten oder Schlauchadapter angepasst, so dass diese zur Beschickung einfach angesetzt und betätigt werden können. Die Präparationsvorrichtung kann anwendungsabhängig in ihrer Größe beliebig skaliert werden. Die Übertragungseinrichtung mit der Ventilplatte kann durch eine fest eingestellte Anordnung mehrerer Verbindungsleitungen mit betätigbaren Ventilen ersetzt werden.

[0059] An der Außenseite des Kammerkörpers können zusätzliche Greif- oder Befestigungseinrichtungen zur Handhabung des Kammerkörpers und/oder zum Einsatz in eine Zentrifuge vorgesehen sein.

[0060] Der Kammerkörper mit den integrierten Kammern kann erfindungsgemäß durch eine Anordnung einzelner Kammern in einem Rahmengestell ersetzt werden. Diese Gestaltung besitzt Vorteile in Bezug auf eine separate Befüllung der einzelnen Kammern vor der Zusammensetzung zur Präparationsvorrichtung und die Entsorgung der Kammern nach Verwendung. Als Rahmengestell kann jede geeignete Struktur verwendet werden, in die die Kammern entsprechend der gewünschten Anordnung fixiert einsetzbar sind und die eine genügende Stabilität bei der Zentrifugation besitzt. Je nach der Gestaltung der Kammern ist die Struktur des Rahmengestells angepasst.

[0061] Werden als Kammern fertige Kolbenspritzen mit geeigneten Kolbendurchmessern verwendet, so besitzt das Rahmengestell Ausnehmungen zur Aufnahme der Spritzenkolben. Wenn die Einzelkammern durch gerade Rohrkörper gebildet sind, werden die Ausnehmungen des Rahmengestells entsprechend angepasst. Am Boden des Rahmengestells sind ggf. konisch vorgeformte Kammerböden vorgesehen, wie dies in **Fig. 5** illustriert ist.

[0062] **Fig. 5** zeigt eine Einzelkammer in schematischer Schnittansicht. Zwei oder mehr derartige Einzelkammern (z. B. entsprechend der obigen Gestaltung drei Einzelkammern) sind an einem Rahmengestell (nicht dargestellt) vorgesehen. Die Einzelkammer **90** umfasst eine Kammerwand **91** in Form eines geraden Kreiszylinders und einen sich verjüngenden Teilbereich **92**, der in einem entsprechend geformten Stützsockel **93** ruht, der Teil des Rahmengestells ist. Im Inneren der Einzelkammer **90** befindet sich der Druckstempel (siehe oben). Der Druckstempel ist bei dieser Gestaltung nicht zylinderförmig, sondern als Stempelplatte **94** mit einem außen umlaufenden Dichtring **97** ausgebildet. Die Stempelplatte **94** besteht beispielsweise aus PMMA. Der Dichtring **97** ist ein z. B. aus PTFE bestehendes Formteil, das formschlüssig über den äußeren Rand der Stempelplatte **94** gezogen ist. Der Querschnitt des Dichtringes **97** besitzt eine U-Form, deren offenen Enden zwei Dichtlippen bilden.

Durch diese Formgebung wird ein dichtendes Anlegen der Dichtlippen an die Kammerwand sicherstellt. Die Oberseite der Einzelkammer **90** ist mit einer Deckplatte **95** verschlossen, die eine Durchtrittsöffnung **96** zum Durchlass des Druckmediums aufweist.

[0063] Die Einzelkammer **90** besitzt bspw. ein Volumen von 470 ml bei einem Durchmesser von ca. 80 mm, einer Länge der Kammerwand **91** von ca. 110 mm und einer Höhe des Stützsockels **93** von ca. 30 mm. Der Teilbereich **92** grenzt ein Teilvolumen von ca. 30 ml ab.

[0064] Bei einem erfindungsgemäßen Verfahren zur Blutpräparation kann abweichend von der oben erläuterten Zentrifugation der gesamten Präparationsvorrichtung die folgende Einzelkammerzentrifugation vorgesehen sein. Dabei wird die jeweils interessierende Einzelkammer (z. B. gemäß **Fig. 5**) aus dem Rahmengestell entnommen und separat zentrifugiert. Vor oder nach der Zentrifugation ist die Einzelkammer im Rahmengestell zur Durchführung der übrigen Schritte der Probenpräparation angeordnet. Dieses Verfahren ist besonders vorteilhaft, falls zur Zentrifugation keine passende Zentrifuge zur Verfügung steht.

Patentansprüche

1. Präparationsvorrichtung (**100**) zur Behandlung von Suspensionsproben, insbesondere zur Präparation von Blut-Kryokonserven, mit einer Anordnung von mindestens zwei Behältnissen zur Aufnahme der Suspensionsproben, von Probeteilen und/oder von Zusatzstoffen, **dadurch gekennzeichnet**, dass die Behältnisse als Kammern (**13 bis 15, 90**) mit festen Wänden gebildet und relativ zueinander ortsfest angeordnet sind und eine Übertragungseinrichtung (**20**) mit mindestens einer Verbindungsleitung (**22**) vorgesehen ist, über die die Kammern (**13 bis 15**) miteinander verbindbar sind.
2. Präparationsvorrichtung nach Anspruch 1, dadurch gekennzeichnet, dass die Kammern (**13 bis 15**) in einem einstückigen Kammerkörper (**10**) gebildet sind.
3. Präparationsvorrichtung nach Anspruch 1, dadurch gekennzeichnet, dass die Kammern (**90**) als Einzelkammern lösbar in einem Rahmengestell befestigt sind.
4. Präparationsvorrichtung nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass die Wände der Kammern oder der Kammerkörper (**10**) aus einem transparenten Material bestehen.
5. Präparationsvorrichtung nach einem der vorhergehenden Ansprüche 1 oder 2, dadurch gekennzeichnet, dass die Kammern (**13 bis 15**) die Gestalt gerader Hohlzylinder besitzen, die von einer Oberseite (**11**) bis zu einer Unterseite (**12**) des Kammerkörpers (**10**) verlaufen, wobei an der Unterseite (**12**) jede Kammer (**13 bis 15**) einen Anschlussstutzen (**17**) aufweist, mit dem jeweils ein Ende der mindestens einen Verbindungsleitung (**22**) verbunden werden kann.
6. Präparationsvorrichtung nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass in jeder Kammer ein Druckstempel (**31 bis 33**) vorgesehen ist.
7. Präparationsvorrichtung nach Anspruch 6, dadurch gekennzeichnet, dass jeder Druckstempel (**31 bis 33**) eine umlaufende Dichtlippe aufweist.
8. Präparationsvorrichtung nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass die Übertragungseinrichtung (**20**) durch eine Ventilplatte (**21**) gebildet ist, in der mindestens eine Verbindungsleitung (**22**) integriert ist, wobei die Ventilplatte (**21**) verdrehbar angeordnet ist.

9. Präparationsstation zur Präparation von Suspensionsproben, mit:

mindestens einer Präparationsvorrichtung (**100**) nach einem der vorhergehenden Ansprüche,
einer Druckeinrichtung (**50**), die zur Erzeugung eines Über- oder Unterdruckes in einer der Kammern (**13 bis 15**) eingerichtet ist,
einer Detektoreinrichtung (**60**) zur Erkennung einer Phasengrenze in einer der Kammern (**13 bis 15**),
einer Stelleinrichtung (**70**), die ein Betätigungselement (**71**) aufweist, mit dem die Übertragungseinrichtung (**20**) derart einstellbar ist, dass jeweils zwei Kammern über die mindestens eine Verbindungsleitung (**22**) verbunden sind, und
einer Steuereinrichtung, die mit der Druckeinrichtung (**50**), der Detektoreinrichtung (**60**) und der Stelleinrichtung (**70**) verbunden und zur Betätigung der Druckeinrichtung (**50**) und der Stelleinrichtung (**70**) in Abhängigkeit von einem Detektorsignal der Detektoreinrichtung (**60**) eingerichtet ist.

10. Präparationsstation nach Anspruch 9, dadurch gekennzeichnet, dass die Druckeinrichtung (**50**) einen pneumatischen Druckerzeuger oder einen mechanischen Druckerzeuger mit Pleuelstangen aufweist.

11. Verfahren zum Präparieren von Suspensionsproben oder von Blut-Kryokonserven unter Verwendung einer Präparationsvorrichtung (**100**) nach einem der Ansprüche 1 bis 8, dadurch gekennzeichnet, dass abwechselnd eine Behandlung einer Probe in mindestens einer der Kammern (**13 bis 15, 90**) und eine Übertragung mindestens eines Teils der Probe zwischen zwei Kammern erfolgt.

12. Verfahren nach Anspruch 11, dadurch gekennzeichnet, dass die Probenbehandlung eine Zentrifugation der Probe und/oder eine Behandlung der Probe mit Zusatzstoffen umfasst.

13. Verfahren nach Anspruch 12, dadurch gekennzeichnet, dass bei der Zentrifugation der Probe die gesamte Präparationsvorrichtung (**100**) oder eine Einzelkammer (**90**) zentrifugiert wird.

Hierzu 5 Seite(n) Zeichnungen

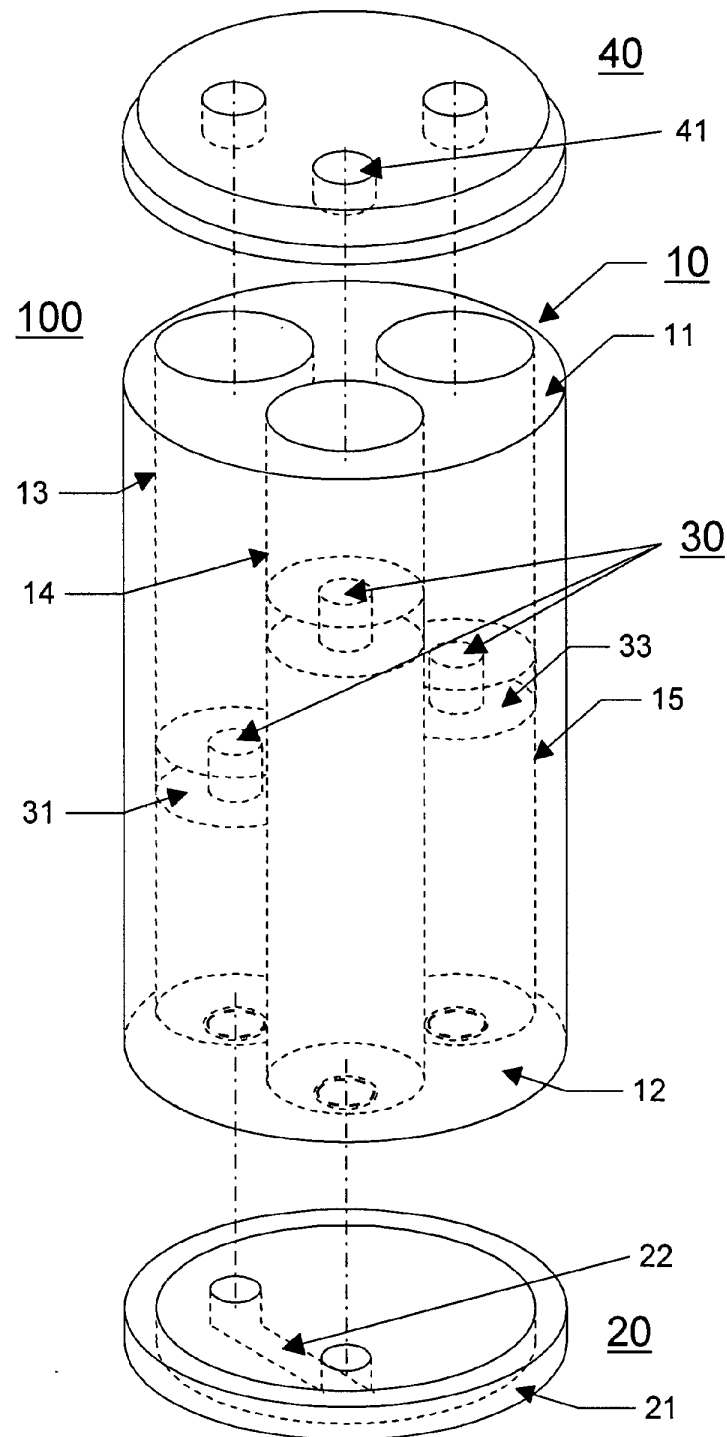


Fig. 1

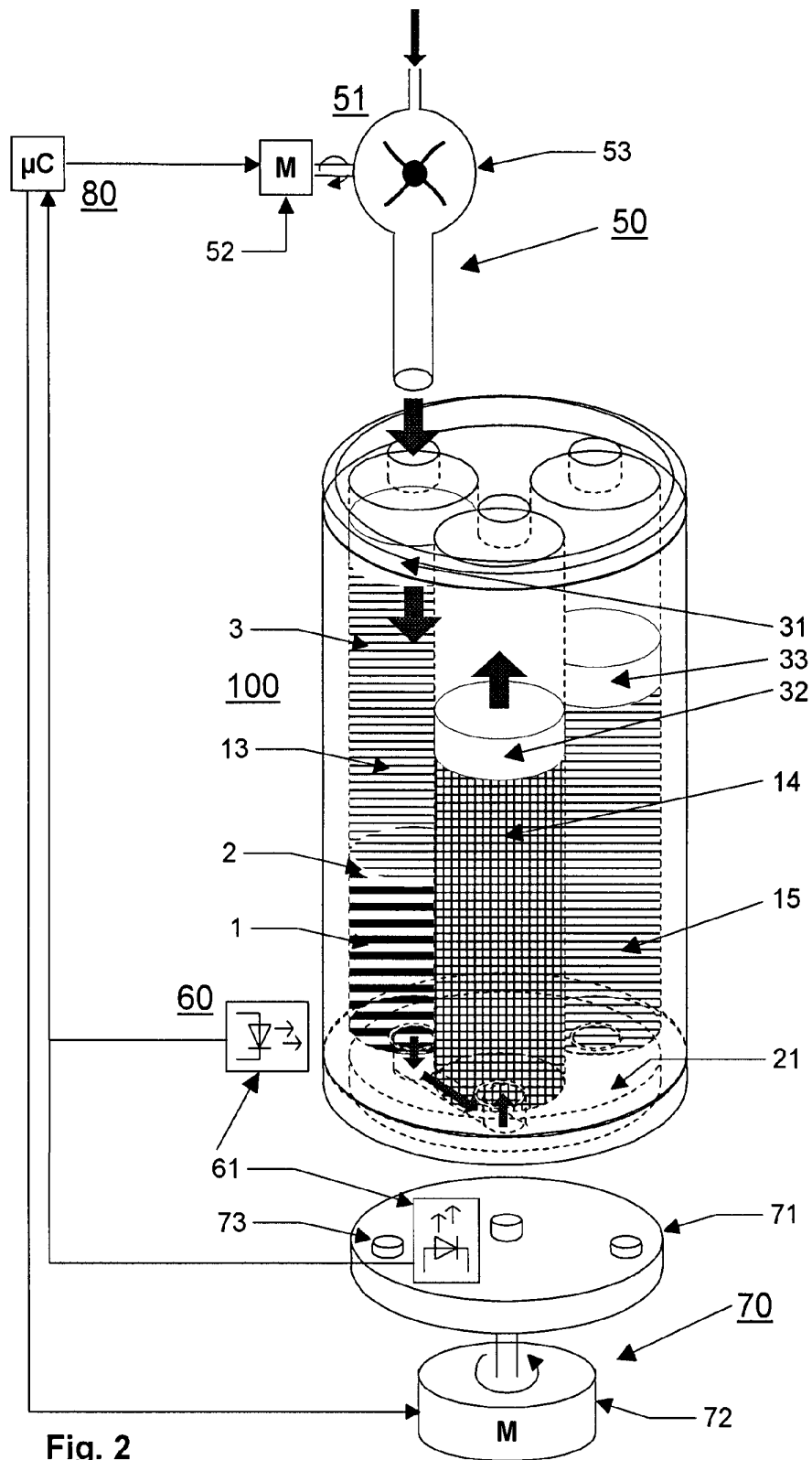


Fig. 2

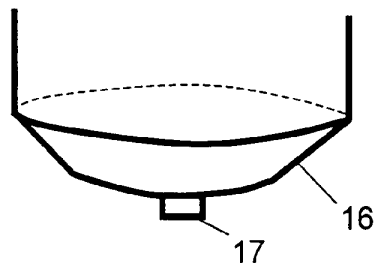


Fig. 3

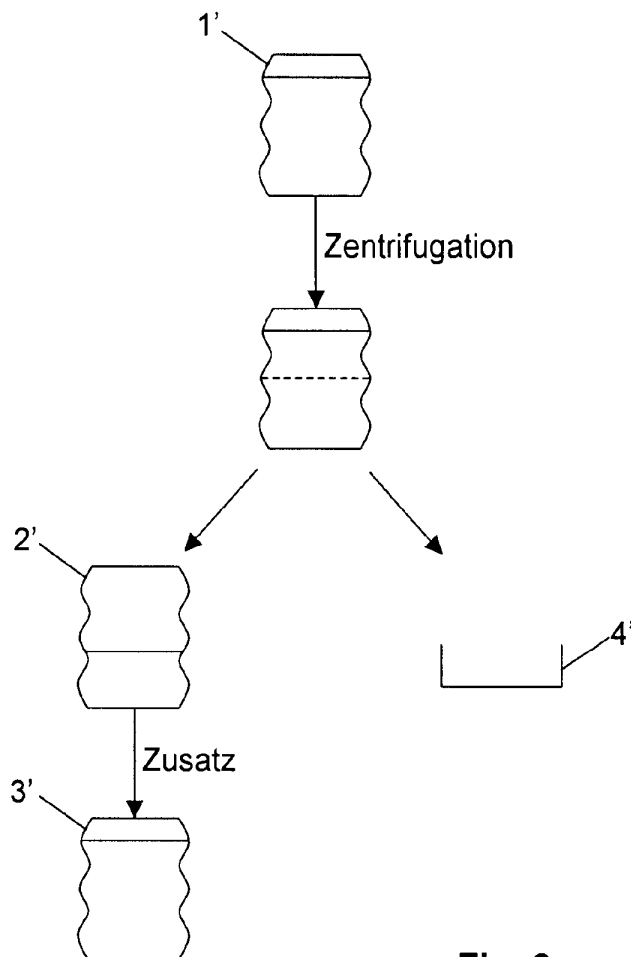


Fig. 6
(Stand der Technik)

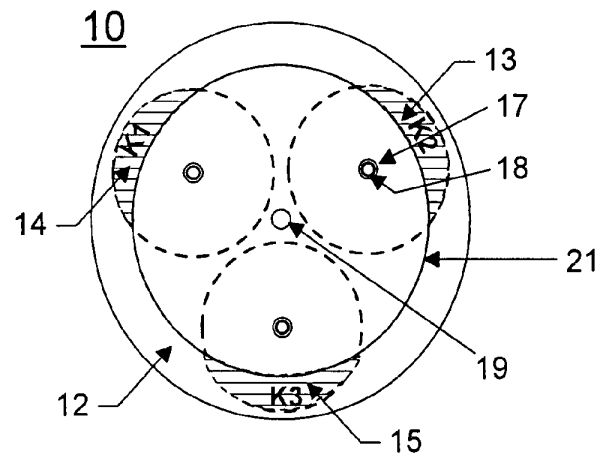
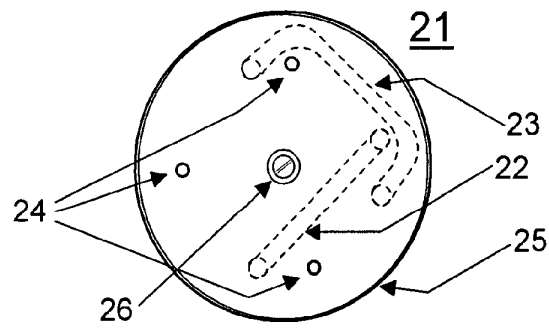
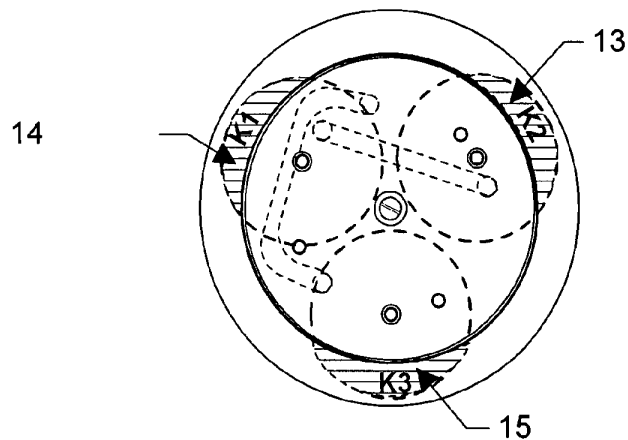


Fig. 4

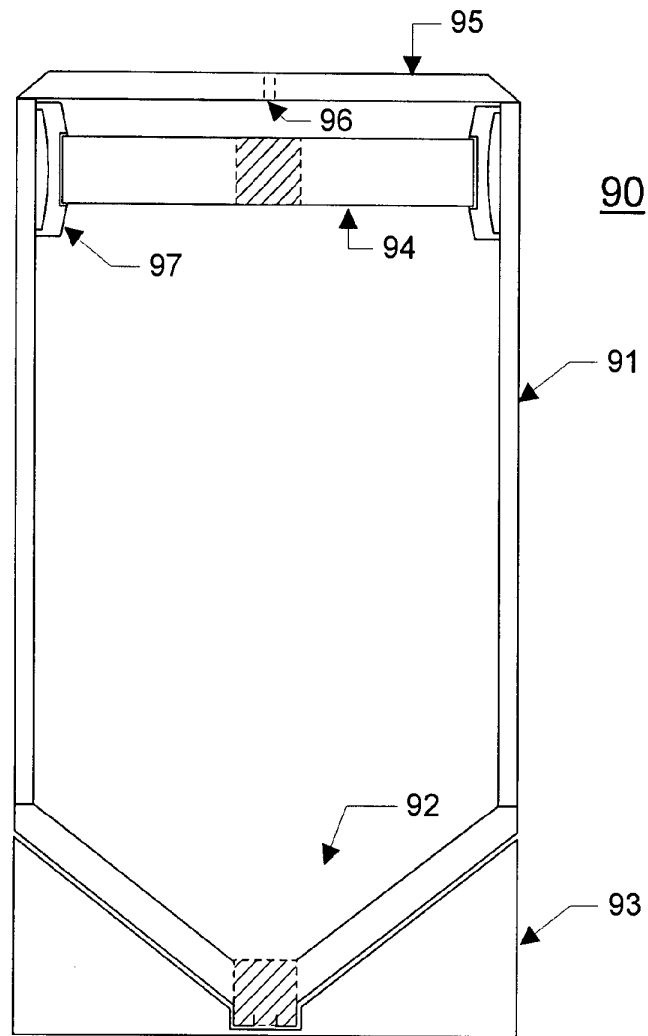


Fig. 5

 Literature display


< 1 / 1 display >

Patent 5789869

publication

 Document unit PDF progress information OPD search key URLs

Display format of the document display screen:

☒ text display ☐ PDF display

primary literature

bibliography

close



(19) [Country of issue] Japan Patent Office (JP)
 (12) [Type of publication] Patent publication (B2)
 (11) [Patent number] Patent No. 5789869 (P5789869)
 (24) [Registration date] 2015 August 14 (2015.8.14)
 (45) [Date of Issue] October 7, 2015 (2015.10.7)
 (54) [Title of Invention] Auxiliary Plate for Polishing Pad and Equipped with Auxiliary Plate for Polishing Pad Polishing Apparatus
 (51) [International Patent Classification]
 B24B 37/12 (2012.01)
 [FI]
 B24B 37/04 A
 [Number of Claims] 11
 [Total Number of Pages] 21
 (21) [Application Number] Patent Application 2011-165360 (P2011-165360)
 (22) [Application date] July 28, 2011 (2011.7.28)
 (65) [Publication number] JP-A-2013-27951 (P2013-27951A) (43) [Publication date] 2013 February 7, 2013 (February 7, 2013) [Date of request for examination] June 25, 2014 (June 25,

2014) [Matters to be stated regarding results of research commissioned by the government] (report by applicant) commissioned by the government Patent application related to research results (FY2010 Ministry of Economy, Trade and Industry "Strategic Fundamental Technology Advancement Support Project" commissioned research, patent application subject to Article 19 of the Industrial Technology Enhancement Act) (73) [Patentee] [Identification number] 599 096053

[Name] Toho Engineering Co., Ltd.

(74) [Agent]

[Identification Number] 100103252 [

Patent Attorney]

[Name] Yoshitaka Kasai

(74) [Agent]

[Identification Number] 100147717

[Patent Attorney]

[Name] Or name] Mie Nakane

(72) [Inventor]

[Name] Tatsutoshi Suzuki

(72) [Inventor]

[Name] Eiji Suzuki

[Examiner] Takashi Kameda

(56) [References] [Reference] Japanese Patent Application

Laid- Open No. 08- 118231 (JP.A) [Reference] JP-A-07-328915 (JP.A) (58) [Field investigate d] (Int.Cl., DB name) B24B 37/12 H01L 21/304...

The scope of the claims

open

(57) [Scope of Claims]

[Claim 1] A

polishing pad auxiliary plate mounted on a rotating surface plate of a polishing apparatus for detachably attaching a polishing pad to the rotating surface plate, wherein

:

a first fixing means for fixing the lower auxiliary plate to the rotating surface plate; and
a pad supporting surface on which the polishing pad is superimposed and fixed. an upper auxiliary plate superimposed on the upper surface of the lower auxiliary plate;

second fixing means for fixing the upper auxiliary plate to the lower auxiliary plate;

the lower auxiliary plate and the upper side; positioning means for aligning the center axis of the lower auxiliary plate with respect to the rotating surface

plate of the polishing apparatus, and the lower auxiliary plate is fixed by the first fixing means to the rotating surface plate of the polishing apparatus. By removing the upper auxiliary plate from the lower auxiliary plate held and fixed to the rotating surface plate, the polishing pad is rotated while being fixed to the pad supporting surface of the upper auxiliary plate. The upper auxiliary plate can be removed from the surface plate, and the removed upper auxiliary plate can be fixed and attached again to the lower auxiliary plate while being aligned by the positioning means, and,

the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is smaller than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means;

Auxiliary plate for a polishing pad, characterized in that :

[Claim 2]

2. The auxiliary plate for a polishing pad according to claim 1 , wherein said positioning means is located inside the outer peripheral surfaces of said lower auxiliary plate and said upper auxiliary plate.

3. The positioning means

includes an engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate and protruding toward the other, and the lower auxiliary plate and the upper auxiliary plate. 3. An auxiliary plate for a polishing pad according to claim 2 , wherein said auxiliary plate for a polishing pad comprises an engaging concave portion provided on the other side thereof and with which said engaging convex portion is engaged .

4. The polishing pad according to claim 3

, wherein said engaging projections and said engaging recesses are formed with engaging portions located on the outer peripheral portions of said lower auxiliary plate and said upper auxiliary plate. Auxiliary plate. 5. An annular engagement in which the engaging portions of the engaging protrusion and the engaging recess extend continuously in the circumferential direction of the lower auxiliary plate and the upper auxiliary plate and are fitted to each other. 5.

The auxiliary plate for a polishing pad according to claim 4 , comprising an outer peripheral surface and an engaging inner peripheral surface . 6. At a plurality of locations on the circumfe

rence of the outer peripheral portions of the lower auxiliary plate and the upper auxiliary plate, the lower auxiliary plate and the upper auxiliary plate are overlapped on one side toward the other. The engaging concave portion that opens and the engaging convex portion that protrudes toward one side of the other of the mutual overlapping surfaces of the lower auxiliary plate and the upper auxiliary plate are formed at positions corresponding to each other, wherein said engaging portion is formed by fitting said engaging convex portion into said engaging concave portion.

5. The polishing pad auxiliary plate according to 4.

7.

The engaging protrusions projecting from a plurality of locations on the circumference of one of the lower auxiliary plate and the upper auxiliary plate toward the other are formed of an elastic material, and The engagement portion is formed by engaging the tip of the engagement projection with the engagement recess provided in the outer peripheral surface of the other of the side auxiliary plate and the upper auxiliary plate. 5. The polishing pad auxiliary plate according to claim 4.

8. A polishing pad auxiliary plate according to claim 3

, wherein said engaging projections and said engaging recesses are provided on the central axes of said lower auxiliary plate and said upper auxiliary plate. 9. An outer peripheral surface of said engaging projection and an inner peripheral surface of said engaging recess are formed with screw grooves for engaging with each other, and said engaging projection and said engaging portion constituting said positioning means are formed with thread grooves for engaging with each other. 9. The auxiliary plate for a polishing pad according to claim 8, wherein said second fixing means is formed by screwing with said mating recess. 10. The engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate is formed of the same material as one of the lower auxiliary plate and the upper auxiliary plate. The auxiliary plate for a polishing pad according to any one of claims 3, 4, 5, 6, 8 and 9.

11. The auxiliary plate for a polishing pad according to any one of claims 1 to 10 is mounted on the upper surface of a rotating surface plate, and a protective member is provided on the outer peripheral side of the rotating surface plate with a gap

therebetween. 11. The positioning means according to any one of claims 1 to 10, wherein the positioning means is disposed on the inner peripheral side of the outer peripheral end faces of the rotating platen and the polishing pad auxiliary plate. 2. A polishing apparatus comprising

g the polishing pad auxiliary plate according to 1 or 2 above.

detailed description

open

Description: BACKGROUND OF THE INVENTION 1.

Field of the Invention The present invention relates to the polishing of substrates such as silicon wafers, semiconductor substrates, glass substrates, etc., which are workpieces requiring high flatness accuracy. It relates to a related technology, and more particularly to a technology that makes it possible to reuse a polishing pad used in polishing the surface of such a substrate.

is. 2.

Description of the Related Art As is well known, in manufacturing a semiconductor, a polishing process is performed to flatten the surface of a substrate such as a silicon wafer, a semiconductor substrate, a glass substrate, or the like. Such a polishing process generally involves fixing a disc-shaped polishing pad made of a resin material or the like directly on a rotating surface plate of a polishing apparatus with a double-sided tape, and supplying a polishing liquid containing abrasive grains to the polishing pad. Polishing is performed by rotating the substrates relative to each other. [0003] Polishing pads for carrying out such a polishing process are made of foamed or non-foamed urethane or the like, as described in Japanese Patent Application Laid-Open No. 2002-11630 (Patent Document 1). A resin pad is used. Further, in many cases, the polishing surface of such a polishing pad is provided with grooves such as concentric circles, grids, or radial grooves, or the bubbles of foamed resin are opened. [0004] By the way, when performing a polishing process using a polishing pad, when changing the type of substrate to be polished, the polishing pad used for the polishing process is peeled off from the rotating platen and replaced with another polishing pad. sometimes you have to. Also, for example, when a polishing pad that has deteriorated due to polishing is to be re-processed, such as by grooving the surface, with another processing device for the purpose of reusing the polishing pad, the polishing pad is removed from the rotating platen. Needs to be pulled off. [0005]

However, since the thin disk-shaped polishing pad is firmly fixed to the rotating surface plate of the polishing apparatus with an adhesive tape, when the polishing pad is peeled off from the rotating surface plate, Damage such as bending, breaking, wrinkling, and tearing is likely to occur. Therefore, due to such damage, there is often a problem that such polishing pads cannot be reused and must be discarded even though their service life has not expired.

[0006]

Moreover, the work of peeling off the polishing pad from the rotating surface plate while paying close attention not to damage it requires skill and caution, and there is also the problem of placing a heavy burden on the operator. In addition, since it takes a considerable amount of time to peel off the polishing pad from the rotating surface plate, the polishing apparatus, which is expensive and valuable equipment, must be stopped for a long time, which shortens the operation time of the equipment. There was also the problem that the

[0007]

Therefore, the present inventor previously described in Japanese Patent Application Laid-Open No. 2010-214579 (Patent Document 2) that an auxiliary plate is attached to the back surface of the polishing pad, and the polishing pad is rotated by the polishing apparatus through this auxiliary plate. We proposed a polishing pad with an auxiliary plate that is fixed to the surface plate with double-sided tape. In such a polishing pad with auxiliary plate, since the polishing pad is attached to and detached from the rotary surface plate while being supported by the auxiliary plate, damage to the polishing pad during attachment and detachment is reinforced by the auxiliary plate. Therefore, it is possible to attach and detach the polishing pad to and from the rotating surface plate with good workability while preventing the polishing pad from being damaged.

[0008]

However, as a result of further studies and studies by the present inventors, it has been found that it is difficult to say that the polishing pad with an auxiliary plate proposed in Patent Document 2 is easily compatible with all polishing apparatuses.

[0009]

That is, when the polishing pad is overlaid and fixed to the rotating surface plate, it is necessary to align the center of the polishing pad with the rotation center of the rotating surface plate. Accuracy is required for center alignment. If the number of attachment/detachment of the polishing pad to/from the rotating platen increases by adopting the auxiliary plate as described above, it becomes more difficult and labor-intensive to align the center position when attaching the polishing pad to the rotating platen.

It becomes a problem. Further, in the polishing pad with auxiliary plate proposed in Patent Document 2, in order to detachably attach the auxiliary plate while aligning the center of the auxiliary plate with respect to the rotary surface plate, the following are provided between the auxiliary plate and the rotary surface plate

:

For example, fixing means such as an outer peripheral ring may be provided on the outer peripheral surface of the rotating platen. On the other hand, in some polishing apparatuses, a protective cover or the like is attached to the outer peripheral side of the rotary platen, so that the space on the outer peripheral side of the rotary platen is extremely narrow. Therefore, if such an outer peripheral ring were to be adopted, and a polishing device with a narrow space on the outer peripheral side of the rotating surface plate was used, there was a possibility that the polishing device would need to be modified. of.

[Prior Art Documents]

[Patent Documents]

[0011]

[Patent Document 1] [Japanese Unexamined Patent Application Publication No. 2002-11630](#) [Patent Document 2] [Japanese Unexamined Patent Application Publication No. 2010-214579](#) [Summary of the Invention] [Problems to be Solved by the Invention] SUMMARY OF THE INVENTION It is an object of the present invention to provide a polishing pad which can be easily attached to and detached from a rotating surface plate while sufficiently securing the fixing force of the polishing pad to the rotating surface plate. For a polishing pad with a novel structure, which can prevent damage to the polishing pad when the polishing pad is removed from the rotating platen, and which can be advantageous for reuse of the polishing pad, for example. To provide an auxiliary plate. [0013]

In addition, according to the present invention, the work of aligning the center when mounting the polishing pad on the rotating surface plate can be performed easily and accurately, and the labor burden can be reduced. Another object of the present invention is to provide an auxiliary plate for a polishing pad with an improved structure, which can be easily and advantageously applied to a rotating surface plate in a polishing machine without requiring any special modification. A further object of the present invention is to provide a polishing apparatus having such a novel polishing pad auxiliary plate

. Means for Solving the Problems In order to solve the above problems, a first aspect of the present invention relating to an auxiliary plate for a polishing pad is: (A) mounted on a rotating surface plate of a polishing apparatus; A polishing pad auxiliary plate for detachably attaching a pad to the rotary platen, comprising: (B) a lower auxiliary plate disposed on the upper surface of the rotary platen; and (C) the lower auxiliary plate. and (D) a pad supporting surface on which the polishing pad is superimposed and fixed, which is superimposed on the upper s

surface of the lower auxiliary plate. (E) a second fixing means for fixing the upper auxiliary plate to the lower auxiliary plate; The lower auxiliary plate is held in a fixed state by the first fixing means to the rotating surface plate of the polishing apparatus, and is fixed to the rotating surface plate. Further, by removing the upper auxiliary plate from the lower auxiliary plate, the polishing pad can be removed from the rotating surface plate while being fixed to the pad supporting surface of the upper auxiliary plate. At the same time, it is possible to attach the removed upper auxiliary plate to the lower auxiliary plate by fixing it again in a state of being aligned by the positioning means.

and the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is stronger than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means. It features a smaller auxiliary plate for the polishing pad. In the polishing pad auxiliary plate constructed according to the present invention, the polishing pad is composed of the upper auxiliary plate and the upper auxiliary plate

It is fixedly attached to the rotating surface plate via the lower auxiliary plate. Thereby, the upper auxiliary plate can be removed from the lower auxiliary plate while the lower auxiliary plate is fixed to the rotating surface plate, and the polishing pad can be removed from the rotating surface plate while being fixed to the upper auxiliary plate. becomes possible. Therefore, in a state in which the polishing pad is reinforced and protected by the upper auxiliary plate, the polishing pad can be removed from the rotating surface plate while preventing damage to the polishing pad, and the thin polishing pad can be easily handled

becomes. For example, when the polishing pad is repeatedly attached and detached when the object to be polished or the polishing conditions are changed, or when the worn polishing pad is detached and reattached after reprocessing, the attachment and detachment of the polishing pad to and from the rotating platen and the polishing are difficult. It is also possible to easily perform operations such as reproduction processing for pads. Moreover, since the lower auxiliary plate still fixed to the rotating surface plate and the upper auxiliary plate removed together with the polishing pad are aligned with each other by the positioning means, the position on the rotating surface plate can be easily adjusted

The attachment and detachment work of the polishing pad, which requires alignment, can be performed more easily. In particular, since the positioning means is provided between the lower auxiliary plate and the upper auxiliary plate, there is no need to apply special processing or the like to the rotating surface plate. In addition, it is possible to prevent such positioning me

ans from protruding to the outer peripheral side of the rotating surface plate. It can be applied without applying. In the polishing pad auxiliary plate according to the first aspect of the present invention

, the fixing force between the lower auxiliary plate and the upper auxiliary plate by the second fixing means is smaller than the fixing force between the rotating platen and the lower auxiliary plate by the first fixing means; A certain aspect is adopted. According to the first aspect, the fixing forces of the first and second fixing means are mutually adjusted, so that the upper auxiliary plate to which the polishing pad is fixed can be rotated

. This makes it easier to remove the lower auxiliary plate that is still fixed to the surface plate. In short, there is no need for a special operation or the like to keep the lower auxiliary plate fixed to the rotating platen, and the polishing pad can be attached to the upper supporting plate while the lower auxiliary plate remains fixed to the rotating platen. It becomes possible to easily remove the plate from the rotating surface plate while it is fixed to the plate. According to a second aspect of the present invention, in the polishing pad auxiliary plate according to the first aspect, the positioning means is arranged on the inner peripheral side of the outer peripheral surfaces of the lower auxiliary plate and the upper auxiliary plate. It is located and provided. [0022] In the polishing pad auxiliary plate of this aspect, the projection of the upper and lower auxiliary plates to the outer peripheral side of the positioning means is completely avoided. Therefore, for example, even when the outer diameter of the upper and lower auxiliary plates is set to be the same as or slightly smaller than the outer diameter of the rotating surface plate, the supporting surface of the polishing pad can be secured sufficiently large and the It is possible to prevent the positioning means from protruding to the outer peripheral side, and even if a protective cover or the like is installed on the outer peripheral side of the rotating surface plate, it will not become an obstacle when applying the polishing pad auxiliary plate according to the present invention. Avoided.

According to a third aspect

of the present invention, in the polishing pad auxiliary plate according to the second aspect, the positioning means is provided on one of the lower auxiliary plate and the upper auxiliary plate and on the other. It is composed of an engaging projection projecting toward and an engaging recess provided in the other of the lower auxiliary plate and the upper auxiliary plate with which the engaging projection is engaged. With the polishing pad auxiliary plate of this aspect, it is possible to easily obtain a mechanically large positioning force based on the mutual engagement between the engaging projections and the engaging recesses. Further, by adjusti

ng the shape, size, number, etc. of the engaging projections and engaging recesses, it is possible to easily set the direction and acting force of the positioning action with a large degree of freedom.

A fourth aspect

of the present invention is the auxiliary plate for a polishing pad according to the third aspect, wherein the engaging projections and the engaging recesses are located on the outer peripheries of the lower auxiliary plate and the upper auxiliary plate. It is formed with an engaging portion located in the portion. In the polishing pad auxiliary plate of this aspect, the engagement outer peripheral surface of the engagement projection and the engagement recess are positioned in the outer peripheral portion away from the center of the polishing pad auxiliary plate and are engaged with each other in a concave-convex manner. By forming the engagement inner peripheral surface of the upper and lower auxiliary plates, the relative positioning accuracy, particularly the radial positioning accuracy, can be improved. As shown in the sixth and seventh aspects below, the engaging outer peripheral surface of the engaging convex portion and the engaging inner peripheral surface of the engaging concave portion are arranged around the center of the polishing pad auxiliary plate. It may extend in the circumferential direction along the outer peripheral edge of the polishing pad auxiliary plate, or it may extend on the circumference like the engaging protrusions and engaging recesses formed on the outer peripheral portion of the polishing pad auxiliary plate. It may be in a partially positioned form.

A fifth aspect of the present invention is the auxiliary plate for a polishing pad according to the fourth aspect, wherein the engaging portions of the engaging projections and the engaging recesses correspond to the lower auxiliary plate and the It is composed of an annular engaging outer peripheral surface and an engaging inner peripheral surface that extend continuously in the circumferential direction of the upper auxiliary plate and are fitted to each other. [0028]

In the polishing pad auxiliary plate of this aspect, more preferably, the engaging concave portion and the engaging convex portion are formed with an annular inner and outer peripheral engaging surface that spreads around the central axis of the polishing pad auxiliary plate. Therefore, when the upper auxiliary plate is attached to the lower auxiliary plate, it is not necessary to align the upper auxiliary plate with each other in the circumferential direction, and the work can be performed easily and quickly. A sixth aspect of the present invention is a polishing pad auxiliary plate according to the fourth aspect, wherein the lower auxiliary plate and the upper auxiliary plate are provided at a plurality of locations on the periphery of the outer perip

heral portions of the lower auxiliary plate and the upper auxiliary plate. The engaging recess opening toward the other on one of the overlapping surfaces of the lower auxiliary plate and the upper auxiliary plate, and the other of the mutually overlapping surfaces of the lower auxiliary plate and the upper auxiliary plate and the engaging projection projecting toward one side are formed at positions corresponding to each other, and the engaging portion is formed by fitting the engaging projection into the engaging recess. is. In the polishing pad auxiliary plate of this mode, the mutual positioning of the upper and lower auxiliary plates can be easily realized not only in the direction perpendicular to the axis but also in the circumferential direction around the central axis. In a seventh aspect of the present invention, in the polishing pad auxiliary plate according to the fourth aspect, the outer peripheral portion of one of the lower auxiliary plate and the upper auxiliary plate has a plurality of points on the circumference of the other. The engaging convex portion protruding toward the upper auxiliary plate is formed of an elastic material, and engages with the engaging concave portion provided in an opening on the outer peripheral surface of the other of the lower auxiliary plate and the upper auxiliary plate. The engaging portion is configured by engaging the tip of the engaging projection.

In the polishing pad auxiliary plate of this aspect, it is possible to form the engaging portions so as to be exposed on the outer peripheral surfaces of the upper and lower auxiliary plates. can be confirmed. In addition, in this aspect, the engagement state of the engagement portion can be stably maintained by utilizing the elasticity of the engagement convex portion. An eighth aspect of

the present invention is the polishing pad auxiliary plate according to the third aspect, where in the engaging projections and the engaging recesses are located at the centers of the lower auxiliary plate and the upper auxiliary plate. It is provided on the shaft. In the polishing pad auxiliary plate of this aspect, the engaging projections and the engaging recesses are formed on the central axis of the upper and lower auxiliary plates.

By providing this, it becomes possible to align the central axes of the upper and lower auxiliary plates with one engaging portion. Further, when the engaging projections and the engaging recesses provided on the central axis are aligned with each other, it is not necessary to align the upper and lower auxiliary plates with each other in the circumferential direction. can be ea

sily brought into engagement. According to a ninth aspect of the present invention, in the polishing pad auxiliary plate according to the eighth aspect, the outer peripheral surface of the engaging projection and the inner peripheral surface of the engaging recess are screwed together

. A groove is formed, and the second fixing means is formed by screwing the engaging projection and the engaging recess that constitute the positioning means. [0036] In the polishing pad auxiliary plate of this mode, the fixing force between the upper auxiliary plate and the lower auxiliary plate can be obtained by the positioning means. Therefore, it is possible to configure the second fixing means only by such positioning means, or to configure the fixing force between the upper and lower auxiliary plates by the second fixing means as an auxiliary means by the positioning means. A tenth aspect of the present invention is the third, fourth, fifth, sixth, eighth and ninth

2. In the polishing pad auxiliary plate according to any one of the above aspects, the engaging projection provided on one of the lower auxiliary plate and the upper auxiliary plate is arranged between the lower auxiliary plate and the upper auxiliary plate. It is made of the same material as the one. In the polishing pad auxiliary plate of this aspect, it is possible to prevent the support characteristics of the polishing pad of the auxiliary plates superimposed one on top of the other from greatly differing locally at the portions where the engaging projections are formed

. Therefore, when a pressing force acts on the surface of the polishing pad during pad polishing, the pressure reaction force and the elasticity of the polishing pad are reduced at the formation portions of the engaging convex portions and the engaging concave portions of the upper and lower auxiliary plates that support the polishing pad. It is possible to reduce or avoid defects such as polishing accuracy caused by local differences in such characteristics. Further, according to the present invention, the auxiliary plate for a polishing pad according to any one of the first to tenth aspects of the present invention is mounted on the upper surface of a rotating platen, and is attached to the outer peripheral side of the rotating platen

. A polishing apparatus in which a protective member is arranged with a gap in between, and the positioning means is provided on the inner peripheral side of the outer peripheral end surfaces of the rotating platen and the polishing pad auxiliary plate, Characterized by EFFECTS OF THE INVENTION By adopting the polishing pad auxiliary plate structured according to the present invention or using the polishing apparatus structured according to the present invention, the polishing pad can be prevented from being damaged and polished. can be easily removed from and attached to the rotating surface plate, and positioning of the polishing pad on the ro

tating surface plate can be performed easily and accurately. [Brief Description of the Drawings]

FIG. 1 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a first embodiment of the present invention;

2 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 1; FIG.

FIG. 3 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a second embodiment of the present invention;

4 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 3; FIG.

FIG. 5 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a third embodiment of the present invention;

6 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 5; FIG.

FIG. 7 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a fourth embodiment of the present invention;

8 is an explanatory view of a longitudinal section showing a state in which the polishing pad is removed in the polishing apparatus shown in FIG. 7; FIG.

FIG. 9 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to a fifth embodiment of the present invention;

10 is a side view of a lower auxiliary plate that constitutes the polishing pad auxiliary plate shown in FIG. 9; FIG.

11 is a plan view of the lower auxiliary plate shown in FIG. 10; FIG.

FIG. 12 is a longitudinal sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a sixth embodiment of the present invention;

FIG. 13 is a vertical cross-sectional view showing the essential parts of a polishing apparatus equipped with a polishing pad auxiliary plate according to a seventh embodiment of the present invention;

FIG. 14 is a vertical cross-sectional view showing a main part of a polishing apparatus equipped with a polishing pad auxiliary plate according to an eighth embodiment of the present invention;

FIG. 15 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a ninth embodiment of the present invention is removed;

FIG. 16 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate is removed according to a tenth embodiment of the present invention;

FIG. 17 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to an eleventh embodiment of the present invention is removed;

FIG. 18 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a twelfth embodiment of the present invention is removed;

FIG. 19 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a thirteenth embodiment of the present invention is removed;

FIG. 20 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a fourteenth embodiment of the present invention is positioned;

FIG. 21 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a fifteenth embodiment of the present invention is positioned;

FIG. 22 is an explanatory view of a longitudinal section showing a state in which a polishing pad auxiliary plate according to a sixteenth embodiment of the present invention is removed;

DETAILED DESCRIPTION OF THE INVENTION Embodiments of the present invention will be described below

below

with reference to the drawings. First, FIGS. 1 and 2 show a polishing pad auxiliary plate 10 as a first embodiment of the present invention. This polishing pad auxiliary plate 10 is used by being attached to a rotary surface plate 14 of a polishing apparatus 12, and a polishing pad 16 is detachably attached to the rotary surface plate 14. As shown in FIG.

The polishing apparatus is used ,

for example, as a CMP apparatus as described in Japanese Patent Application Laid-Open No. 2010-141155, for example. A rotating shaft extending vertically is rotatably supported by the main body of the apparatus fixedly installed above, and a disk-shaped rotating platen 14 is fixed to the upper end of the rotating shaft. The rotating surface plate 14 has a flat upper surface 18 extending horizontally, and the upper surface 18 serves as a support surface for the polishing pad 16. The rotating shaft is connected to the rotating output shaft of an electric motor, and the driving force of the electric motor is transmitted so that the rotating shaft and thus the rotating surface plate 14 are rotated about the central axis. there is A nozzle for supplying polishing slurry is arranged above the upper surface 18 supporting the polishing pad 16, and a wafer or the like to be polished (an object to be polished) is held and rotated while being moved to the polishing pad 16. A polishing head is provided for polishing by pressing. In such a

polishing apparatus, the polishing pad auxiliary plate 10 mounted on the rotating platen 14 is

includes a lower auxiliary plate 20 and an upper auxiliary plate 22 . A lower auxiliary plate 20 is fixed to the upper surface 18 of the rotating platen 14 by first fixing means 24 , and an upper auxiliary plate 22 is attached to the upper surface of the lower auxiliary plate 20 . It is fixed by two fixing means 26 . That is, the lower auxiliary plate 20 and the upper auxiliary plate 22 are overlapped and fixed to each other via the second fixing means 26, thereby forming the polishing pad auxiliary plate 10 having a two-layer structure as a whole. , and is attached to the upper surface 18 of the rotating surface plate 14 by the first fixing means 24 .

Each of the lower auxiliary plate 20 and the upper

auxiliary plate 22 has a thin, substantially circular flat plate shape, and has a flat front surface (upper surface) and a rear surface (lower surface). These upper and lower auxiliary plates 22 and 20 are desirably made of a harder material than the polishing pad 16 to which it is attached, or having a higher member rigidity than the polishing pad 16 . Although it depends on the method of use, as will be described later, the lower auxiliary plate 20 can be used without being repeatedly attached and detached after being attached to the rotary surface plate 14, while the upper auxiliary plate 22 can be attached and detached after being attached to the rotary surface plate 14. is expected to be repeated, it is desirable that at least the upper auxiliary plate 22 should have higher member rigidity than the polishing pad 16 .

[0046]

Of course, the upper auxiliary plate 22 supports the polishing pad 16 and provides the strength, rigidity, and rigidity required for various treatments such as polishing, cleaning, and re-grinding of the polishing pad surface, in addition to polishing by the polishing device 12 . Any material that satisfies shape stability and accuracy may be used, and its material and thickness are not limited. In particular, not only the lower auxiliary plate 20 but also the upper auxiliary plate 22 alone bears the supporting strength and rigidity of the polishing pad 16. Since the lower surface is supported by the rotating surface plate 14 by being superimposed on each other and used, the strength and rigidity of the single unit are not required so much. Therefore, in addition to metals such as stainless steel, synthetic resins, fiber-reinforced resins, and the like can be employed as materials for forming the lower auxiliary plate 20 and the upper auxiliary plate 22 . In particular, synthetic resin materials are lighter than metal materials and easier to process and handle. . In order to obtain a stable supporting force over the entire polishing pad 16, it is desirable to set the outer diameter dimension of the upper auxiliary plate 22 to be equal to or larger than the outer diameter dimension of the polishing pad 16, and

It is desirable to set the outer diameter of the lower auxiliary plate 20 to be equal to or larger than the outer diameter of the upper auxiliary plate 22, and set the outer diameter of the lower auxiliary plate 20 to be equal to or smaller than the outer diameter of the rotating surface

plate 12. should be set to In particular, as shown in FIGS. 1 and 2, the outer diameters of the lower auxiliary plate 20 and the upper auxiliary plate 22 are made substantially the same, and the outer diameter of the rotating surface plate 14 to be mounted is also substantially the same. By doing so, it becomes possible to ensure a sufficiently large support area for the polishing pad 16. As a result, the polishing pad 16 having approximately the same size as the rotating surface plate 14 can be attached to the rotating surface plate 14 with approximately the same supporting force over the entirety thereof.

[0048]

Furthermore, as the first fixing means 24 and the second fixing means 26, the lower auxiliary plate 20 and the upper auxiliary plate 22 are fixed to the upper surface 18 of the rotating plate 14 against the external force exerted during polishing. It is not particularly limited as long as it can be held at. Specifically, an adhesive, a pressure-sensitive adhesive, or a double-sided tape having an adhesive or a pressure-sensitive adhesive attached to both sides of a base sheet may be employed as the first and second fixing means 24, 26. In addition, negative pressure suction using negative pressure air or the like, or magnetic suction using a permanent magnet or an electromagnet can be employed. In addition, it is desirable that the fixing means made of adhesive or the like apply substantially uniform fixing force over substantially the entire surface of the flat overlapping surfaces of the lower auxiliary plate 20 and the upper auxiliary plate 22. Adhesive strength can be obtained, and problems such as locally different support characteristics of the polishing pad 16 on the surface of the polishing pad auxiliary plate 10 can be avoided.

For example ,

the fixing force can be turned ON/OFF by negative pressure suction or an electromagnet. auxiliary

It is desirable to set the fixing force of the upper auxiliary plate 22 to the lower auxiliary plate 20 by the second fixing means 26 to be smaller than the fixing force of the plate 20. As a result, when the upper auxiliary plate 22 is peeled off from the lower auxiliary plate 20 and removed, the lower auxiliary plate 20 can be easily left fixed on the rotating surface plate 14.例文帳に追加 The specific realization of such a difference in adhesion force is achieved by differentiating the adhesion means itself such as the material of the adhesive and pressure-sensitive adhesive, as well as the adhesion area and the condition of the adhesion surface (surface roughness, presence or absence of plasma treatment, etc.) can also be realized by making the .

Further, the surface (upper surface) of the upper auxiliary plate 22 serves as a

polishing pad supporting surface, and the polishing pad 16 is superimposed and mounted thereon. As such a polishing pad 16, conventionally known various types of polishing pads can be employed. The back surface of the polishing pad 16 is fixed to the surface of the upper auxiliary plate 22 using a conventionally known adhesive tape or suitable adhesive for attaching the polishing pad.

It is desirable that the fixing means for fixing

the polishing pad 16 to the upper auxiliary plate 22 has a larger fixing force than the second fixing means 26 described above. As a result, when the upper auxiliary plate 22 is removed from the lower auxiliary plate 20 with the polishing pad 16 still fixed, the polishing pad 16 does not move from the upper auxiliary plate 22 even if the upper auxiliary plate 22 is bent or the like. It is possible to effectively prevent the peeling off. The outer diameter of the polishing pad 16 is generally a standard value, but in many cases it is set equal to or smaller than the outer diameter of the upper surface 18 of the rotating surface plate 14 to which it is mounted . [0053]

Further, for example, at least one of between the upper surface 18 of the rotating surface plate 14 and the lower auxiliary plate 20, between the lower auxiliary plate 20 and the upper auxiliary plate 22, and between the upper auxiliary plate 22 and the polishing pad 16 A suitable cushioning layer may be provided. By providing such a cushion layer, it becomes possible to achieve uniform polishing efficiency over the entire surface of the workpiece when polishing with the polishing pad 16 . [0054]

As such a cushion layer, for example, a resin sheet, an elastomer sheet, a rubber sheet, or the like to which a certain degree of compressibility is imparted by foaming can be suitably employed. A cushion layer can also be configured by the first fixing means 24 , the second fixing means 26 , and the means for fixing the polishing pad 16 to the upper auxiliary plate 22 . In order to prevent local distortion on the support surface of the polishing pad 16, the cushion layer is formed so as to have a size and a constant thickness over substantially the entire support area of the polishing pad 16. is desirable. Positioning means 28 are provided between the lower auxiliary plate 20 and the upper auxiliary plate 22 that constitute the polishing pad auxiliary plate 10 to align the centers of the plates with each other .

In the present embodiment, a circular stepped surface 30 is formed on the outer peripheral portion of the lower auxiliary plate 20 and extends around the central axis of the lower auxiliary plate 20 over the entire circumference. By reducing the thickness of the lower auxiliary plate 20 on the outer peripheral side of the stepped surface 30, the cutout cross-sectional shape that opens to the outer peripheral surface of the lower auxiliary plate 20 continues to the entire circumference in the circumferential direction. An annular engaging recess 32 that extends inward is formed integrally with the lower auxiliary plate 20 so as to protrude therefrom. [0056]

On the other hand, in the present embodiment, a circular stepped surface 34 is formed on the outer peripheral portion of the upper auxiliary plate 22 so as to extend around the central axis of the upper auxiliary plate 22 over the entire circumference. Since the thickness of the upper auxiliary plate 22 is increased on the outer peripheral side of the stepped surface 34, an a

nnular engagement continuously extends along the outer peripheral edge of the upper auxiliary plate 22 along the entire circumference in the circumferential direction. A mating projection 36 is integrally formed so as to protrude from the upper auxiliary plate 22. Incidentally, the engaging convex portion 36 and the engaging concave portion 32 may be formed on either of the upper and lower auxiliary plates 22 and 20.

The stepped surface 30 and the engaging recess 32 of the lower auxiliary plate 20 are aligned with the stepped surface 34 and the engaging projection 36 of the upper auxiliary plate 22. It constitutes an engagement outer peripheral surface and an engagement inner peripheral surface. When the upper auxiliary plate 22 is superimposed on the lower auxiliary plate 20, the engaging convex portion 36 is fitted into the engaging concave portion 32, and the stepped surface 34 is superimposed on the stepped surface 30 in the radial direction. is formed. As a result, the engaging concave portion 32 and the engaging convex portion 36 constitute the positioning means 28, and the lower auxiliary plate 20 and the upper side support plate 20 are aligned in the radial direction with their central axes aligned with each other. Auxiliary plates 22 are superimposed. In addition, the positioning means 28 is positioned on the inner peripheral side of the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20, thereby preventing the upper and lower auxiliary plates 22 and 20 and the polishing apparatus 12 from becoming large. . In the polishing apparatus 12 provided with the polishing pad auxiliary plate 10 having such a structure, the upper and lower auxiliary plates 22 are mounted on the upper surface 18 of the rotating platen 14 as shown in FIG

, 20 is fixedly attached, and the polishing pad 16 is fixedly supported on the upper surface of the upper auxiliary plate 22. Then, the rotating platen 14 is driven to rotate, and the substrate or the like is processed. CMP (Chemical Mechanical Polishing) is applied to objects. The polishing apparatus 12 can exhibit the following special technical effects by being provided with the polishing pad auxiliary plate 10 having a specific structure.

[0059]

First, as shown in FIG. 2, while the polishing pad 16 is fixed to the upper surface of the upper auxiliary plate 22, the upper auxiliary plate 22 is fixed to the rotating surface plate 14 by the first fixing means 24. By removing the side auxiliary plate 20, the polishing pad 16 can be removed from the rotating surface plate 14. - 特許庁 Even when the surface (polishing surface) of the polishing pad 16 is removed from the rotating platen 14 and cleaned or reprocessed, the polishing pad 16 can be kept fixed to the upper surface of the upper auxiliary plate 22. As a result, the upper auxiliary plate 22 provides reinforcement not only when the polishing pad 16 is attached to and detached from the rotating surface plate 14, when the polishing pad 16 is cleaned and reprocessed, but also when the polishing pad 16 is transported or stored. By this action, the polishing pad 16 can be prevented from being bent or damaged, and the polishing pad 16 can be kept in good condition.

Further

, even when the polishing pad 16 is removed from the rotating surface plate 14 together with the upper auxiliary plate 22, the lower auxiliary plate 20 remains on the upper surface 18 of the rotating surface plate 14. When the polishing pad 16 is again mounted on the rotating platen 14, the positioning means 28 provided between the upper auxiliary plate 22 and the lower auxiliary plate 20 moves the upper auxiliary plate 22 and thus the polishing pad 16 to the lower auxiliary plate. The central axis of the plate 20 and thus the rotating platen 14 can be aligned with high precision and easily.

[0061]

Here, since the engaging concave portion 32 and the engaging convex portion 36 constituting the positioning means 28 are overlapped with almost no gap in a mutually fitted state, the supporting characteristics of the polishing pad 16 are improved. can be prevented from adversely affecting Of the outer peripheral portions of the upper and lower auxiliary plates 22 and 20, particularly in the present embodiment, an engaging portion, in other words, a positioning means 28, is formed on the outer peripheral edge portion, and the diameter of the polishing pad 16 that serves as the main region for polishing is formed. Since it is out of the middle part in the direction, even if there is a slight gap between the engaging concave portion 32 and the engaging convex portion 36, the supporting characteristics of the polishing pad 16 are such that a serious problem occurs in the polishing characteristics. can be avoided. Moreover, the engaging concave portion 32 and the engaging convex portion 36 constituting the positioning means 28 are formed on the superimposed surfaces of the upper and lower auxiliary plates 22 and 20, in other words, on the outer circumferences of the rotating surface plate 14 and the polishing pad auxiliary plate 10

Since it is formed on the inner peripheral side of the end face, the upper and lower auxiliary plates 22 and 20 can be prevented from projecting onto the outer peripheral surface. Therefore, as shown in FIGS. 1 and 2, for example, even when the protective member 38 is installed close to the outer peripheral side of the rotating surface plate 14 in the polishing apparatus 12, the protective member 38 cannot be protected. Polishing provided with upper and lower auxiliary plates 22, 20 provided with positioning means 28 while avoiding interference

A device 12 is made possible. Furthermore, as described above, while preventing damage to the polishing pad 16, the polishing pad 16 can be quickly attached to and detached from the rotating platen 14 with accurate positioning accuracy

The operating time of the expensive polishing equipment is not unnecessarily limited for such work, and the operating efficiency of the polishing equipment can be improved, and thus the production efficiency of substrates and the like (polishing work efficiency) can be improved.

In addition ,

since the polishing pad 16 can be easily attached to and detached from the rotating surface

plate 14, the reuse of the polishing pad 16 can be realized on a practical level without special skill or knowledge. That is, for example, the polishing pad 16 once removed from the rotating platen 14 can be reused when changing the type of the object to be polished such as a substrate, or the polishing pad 16 can be re-processed by another processing device such as surface grooving as a countermeasure against deterioration. It is also possible to consider reusing the polishing pad 16 once removed from the rotating surface plate 14 after reprocessing at a practical level. Although the first embodiment of the present invention has been described above, the specific structure of the present invention should not be construed as limited by the first embodiment.

A plurality of other embodiments of the present invention having different positioning means between the upper and lower auxiliary plates 22 and 20 are illustrated below, but these embodiments are not intended to limit the configuration of the present invention. In the following embodiments, members and parts having the same structure as in the first embodiment are denoted by the same reference numerals as those in the first embodiment in the corresponding parts in each figure. , their detailed description is omitted. 3 and 4 show a polishing apparatus 42 provided with a polishing pad auxiliary plate 40 as a second embodiment of the present invention.

In this polishing pad auxiliary plate 40, an engaging recess 44 is formed by an annular groove continuously extending in the circumferential direction on the outer peripheral portion of the upper surface of the lower auxiliary plate 20. As shown in FIG. On the other hand, on the outer peripheral portion of the lower surface of the upper auxiliary plate 22, an engagement convex portion 46 is formed by an annular protrusion extending continuously in the circumferential direction. The engaging projection 46 may be formed integrally with the upper auxiliary plate 22, or may be formed separately as illustrated. That is, in this embodiment, an annular circumferential groove 48 that opens in the lower surface of the upper auxiliary plate 22 and extends in the circumferential direction is formed. block is fitted and fixed at one end in the axial direction to form an engagement convex portion 46. The engaging concave portion 44 of the lower auxiliary plate 20 and the engaging convex portion 46 of the upper auxiliary plate 22 are both formed at corresponding radial positions around the central axis.

are overlapped, the engagement projections 46 are fitted into the engagement recesses 44, thereby aligning the upper and lower auxiliary plates 22 and 20 with each other in the radial direction. In the present embodiment, two side walls of the engaging recess 44 of the lower auxiliary plate 20 and the inner and outer peripheral surfaces of the engaging protrusion 46 of the upper auxiliary plate 20 are superimposed on each other in the corresponding radial direction.

n. A pair of inner and outer engagement surfaces are provided. 5 and 6 show a polishing apparatus 52 provided with a polishing pad auxiliary plate 50 as a third embodiment of the present invention

. [0070]

In this polishing pad auxiliary plate 50, the lower auxiliary plate 20 has a stepped surface 54 as a circular engagement inner peripheral surface extending all around the central axis on the outer peripheral portion thereof. By increasing the thickness of the lower auxiliary plate 20 on the outer peripheral side of the stepped surface 54, an annular shape continuously extends along the outer peripheral edge of the lower auxiliary plate 20 along the entire circumference in the circumferential direction. The engaging convex portion 56 of

It is formed integrally with the side auxiliary plate 20. On the other hand, on the outer peripheral portion of the upper auxiliary plate 22, there is formed a stepped surface 58 as a circular engagement outer peripheral surface extending all around the central axis

. Since the thickness of the upper auxiliary plate 22 is reduced on the outer peripheral side of the step surface 58, the upper auxiliary plate 22 has a notched cross-sectional shape that opens to the outer peripheral surface and extends continuously along the entire circumference in the circumferential direction. An annular engaging recess 60 is formed integrally with the upper auxiliary plate 22.

Further, the step surface 54 of the lower auxiliary plate 20 is formed with

female threads, while the step surface 58 of the upper auxiliary plate 22 is formed with male threads. Then, the female thread of the stepped surface 54 of the lower auxiliary plate 20 is screwed with the male thread of the stepped surface 58 of the upper auxiliary plate 22 so that the stepped surface 54 of the lower auxiliary plate 20 and the stepped surface 58 of the upper auxiliary plate 22 are screwed together. are superimposed on each other in the radial direction, the upper auxiliary plate 22 is superimposed on the upper surface of the lower auxiliary plate 20. Further, in such a superimposed state, the screwing structure of the stepped surfaces 58, 54 of the upper and lower auxiliary plates 22, 20 constitutes a second fixing means 62 for detachably fixing the upper and lower auxiliary plates 22, 20. The direction of the male and female threads in such a threaded structure is set in consideration of the rotational reaction force exerted on the rotating surface plate 14 of the polishing device 12 during polishing so that the screws do not loosen

. It is desirable that

FIGS.

7 and 8 show a polishing apparatus 66 having a polishing pad auxiliary plate 64 as a fourth embodiment of the present invention.

[0075]

In this polishing pad auxiliary plate 64, a cylindrical engaging convex portion 68 projecting upward is formed at the central portion of the upper surface of the lower auxiliary plate 20. The engaging projection 68 may be formed integrally with the lower auxiliary plate 20, or may be formed separately as shown in the drawing. That is, in this embodiment, a circular fitting recess 70 is formed on the central axis of the lower auxiliary plate 20, and a cylindrical block formed separately from the fitting recess 70 is provided. An engaging convex portion 68 is formed by being fitted and fixed at one end in the axial direction. On the other hand, in the central portion of the lower surface of the upper auxiliary plate 22, there is formed a bottomed circular engaging recess 72 that opens to the lower surface on the central axis. Incidentally, the engaging convex portion 68 and the engaging concave portion 72 may be formed on either of the upper and lower auxiliary plates 22 and 20. As shown in FIG. 9, when the upper and lower auxiliary plates 22 and 20 are superimposed, the engaging convex portion 68 is fitted into the engaging concave portion 72, thereby aligning the upper and lower auxiliary plates 22 and 20 with each other in the radial direction.

It is designed to be In this embodiment, the engagement outer peripheral surface and the engagement inner peripheral surface are formed by the outer peripheral surface of the engaging protrusion 68 of the lower auxiliary plate 20 and the inner peripheral surface of the engaging recess 72 of the upper auxiliary plate 22. It is configured.

FIG.

9 shows a polishing apparatus 76 provided with a polishing pad auxiliary plate 74 as a fifth embodiment of the present invention.

[0078]

In this polishing pad auxiliary plate 74, a cylindrical engaging convex portion 78 projecting upward is formed on the outer peripheral portion of the upper surface of the lower auxiliary plate 20. This engaging projection 78 may be formed integrally with the lower auxiliary plate 20, or may form a fitting recess in the lower auxiliary plate 20 like the engaging projection in the fourth embodiment. Alternatively, a separate pin or the like may be fixed by press-fitting or the like. Also, as shown in FIGS. 10 and 11, a plurality of such engaging projections 78 are formed independently of each other at the outer peripheral portion of the lower auxiliary plate 20 at predetermined intervals in the circumferential direction. Particularly preferably, the plurality of engaging protrusions 78 are formed at regular intervals in the circumferential direction and positioned on the same circle on the central axis.

On the other hand, on the outer peripheral portion of the lower surface of the upper auxiliary plate 22, bottomed circular engagement grooves are provided at positions corresponding to the formation positions of the plurality of engaging projections 78 on the lower auxiliary plate 20, respectively. A concave portion 80 is formed to open downward. Incidentally, the engagin

g convex portion 78 and the engaging concave portion 80 may be formed on either of the upper and lower auxiliary plates 22 and 20. As shown in FIG. When the upper and lower auxiliary plates 22 and 20 are superimposed, the engaging convex portions 78 are fitted into the engaging concave portions 80, respectively, so that the upper and lower auxiliary plates 22 and 20 are positioned radially relative to each other

are designed to be matched. In the present embodiment, the outer circumferences of the lower auxiliary plate 20 and the upper auxiliary plate 22 are formed by the outer circumference of the engagement projection 78 of the lower auxiliary plate 20 and the inner circumference of the engagement recess 80 of the upper auxiliary plate 22. An engaging outer peripheral surface and an engaging inner peripheral surface located in a portion are configured. In particular, as in this embodiment, by adopting positioning means consisting of a plurality of engaging projections 78 and engaging recesses 80 independent in the circumferential direction, the superimposed upper and lower auxiliary plates 22, 20 can be diametrically aligned

Mutual positioning is possible not only in the direction but also in the circumferential direction. Instead of the plurality of independent engaging recesses 80 formed in the upper auxiliary plate 22,

a circumferential groove continuously extending circularly in the circumferential direction around the central axis of the upper auxiliary plate 22 may be employed. Alternatively, as shown in the sixth embodiment of the present invention in FIG. 12, a circular stepped surface 82 is formed around the central axis of the outer peripheral portion of the upper auxiliary plate 22 and extends over the entire circumference. By making the thickness dimension of the outer peripheral side smaller than 82, it is also possible to form an annular engagement concave portion 83 that has a notched cross-sectional shape that opens to the outer peripheral surface of the upper auxiliary plate 22 and that extends continuously all around in the circumferential direction. It is possible.

[0083]

In this way, in the upper auxiliary plate 22, the engaging surfaces of the engaging projections 78 of the lower auxiliary plate 20 are formed continuously over the entire circumference, so that when the upper and lower auxiliary plates 20 and 22 are superimposed, the upper and lower auxiliary plates 20 and 22 can be overlapped. Since it is no longer necessary to align the auxiliary plates 20 and 22 with each other in the circumferential direction, the mounting work can be easily performed.

FIG.

13 shows a polishing pad auxiliary plate 84 as a seventh embodiment of the present invention.

In this polishing pad auxiliary plate 84, the upper portion of the outer peripheral surface of the lower auxiliary plate 20 and the lower portion of the outer peripheral surface of the upper

auxiliary plate 22 are each provided with a small diameter portion. By superimposing the upper and lower auxiliary plates 22 and 20, the small diameter portions of the upper and lower auxiliary plates 22 and 20 form an annular ring that extends across the entire circumference in the circumferential direction by widening a predetermined width across the upper and lower auxiliary plates 22 and 20. A shaped receiving recess 86 is formed. A groove-shaped engaging recess 88 is formed at the lower end of the small diameter portion of the lower auxiliary plate 20.

The engagement recess 88 opens to the outer peripheral surface of the lower auxiliary plate 20 at the bottom surface of the accommodation recess 86. Here, the bottom surface of the accommodation recess 86 refers to an annular surface extending over the upper and lower auxiliary plates 22 and 20 and extending in the vertical direction in FIG. On the other hand, a plate-shaped engaging projection 90 made of an elastic material is attached to the small-diameter portion of the upper auxiliary plate 22 that constitutes the accommodation recess 86 so that its proximal end is fixed by a fixing pin 92. The engaging protrusions 90 are accommodated in accommodation recesses 86 formed on the outer peripheral surfaces of the upper and lower auxiliary plates 22, 20 and extend from the upper auxiliary plate 22 onto the outer peripheral surface of the lower auxiliary plate 20. There is an engaging claw portion 94 formed at the tip portion of the engaging projection portion 90 is engaged with an engaging recess portion 88 formed in the small diameter portion of the lower auxiliary plate 20, and the engaging projection portion 90 is locked. It is held in a locked state based on elasticity.

Furthermore, a plurality of such engaging projections 90 are provided on the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20 at predetermined intervals in the circumferential direction. And attached to the outer peripheral surface of the upper auxiliary plate 22

Each of the engaging projections 90 is elastically pressed against the outer peripheral surface of the lower auxiliary plate 20, thereby forming positioning means for positioning the upper and lower auxiliary plates 22, 20 relative to each other on the central axis. Further, by engaging the engaging claw portion 94 of the engaging convex portion 90 with the engaging concave portion 88, a fixing means is also configured to hold the upper and lower auxiliary plates 22 and 20 in a superimposed state and apply a fixing force. There is. Instead of the engaging protrusions 90 having the engaging claws 94 that engage with the engaging recesses 88 as described above, for example, an eighth embodiment of the present invention shown in FIG

In addition, a connecting plate 100 extending across the upper and lower auxiliary plates 22 and 20 and superimposed on the bottom surface of the housing recess 86 is adopted, and both ends of the connecting plate 100 are connected to one of the upper and lower auxiliary plates 22 and 20. It is also possible to fix to the outer peripheral surface of the by connecting pins 1

02, 102. At least one of the connecting pins 102, 102 is detachable from the lower auxiliary plate 20 or the upper auxiliary plate 22, so that the connection of the upper and lower auxiliary plates 22, 20 by the connecting plate 100 can be released. , the attachment and detachment of the upper auxiliary plate 22 to which the polishing pad 16 is fixed with respect to the lower auxiliary plate 20 is permitted. The first fixing means 24 and the second fixing means 26 made of double-faced tape or the like shown in the first to eighth embodiments are used when removing the upper and lower auxiliary plates 22 and 20 and the rotating surface plate 14

In addition, it is desirable to be held on the fixing surface on the side of a specific member. This facilitates handling of the upper and lower auxiliary plates 22, 20 and the first and second fixing means 24, 26 in a detached state. In addition, the fixing surfaces on which the first and second fixing means 24 and 26 remain are determined by making the fixing force of both surfaces of the first fixing means and the second fixing means 24 and 26 themselves different from each other. It is possible to set by differentiating the surface roughness, material, etc. of the fixed upper and lower auxiliary plates 22 and 20 and the rotating platen 14 from each other. In particular, it

is desirable that the first fixing means 24 is held on the fixing surface on the side of the lower auxiliary plate 20 when the lower auxiliary plate 20 is removed. becomes easier. On the other hand, as shown in FIG. 2 in the first embodiment, the second fixing means 26 is held on the fixing surface on the side of the upper auxiliary plate 22 when the upper auxiliary plate 22 is removed. Alternatively, it may remain on the upper surface of the lower auxiliary plate 20 as in the ninth embodiment of the present invention shown in FIG. By holding the second fixing means 26 on the fixing surface on the side of the upper auxiliary plate 22, the removed upper auxiliary plate 22 can be attached to the rotating surface plate of the device for reprocessing such as grooving of the polishing pad 16. At the time of mounting, it is also possible to use the second fixing means 26 held by the upper auxiliary plate 22 for mounting. On the other hand, by holding the second fixing means 26 on the fixing surface of the lower auxiliary plate 20, when mounting another upper auxiliary plate 22 with another polishing pad 16 mounted thereon to the lower auxiliary plate 20, It is also possible to attach using the second fixing means 26 held by the lower auxiliary plate 20 .

Further, the engaging recesses 32, 44, 60, 72, 80, (83), 88 and the engaging projections 36, 46, 56,

70, 78, 90 shown in the first to seventh embodiments may be provided on opposite sides of the lower auxiliary plate 20 side and the upper auxiliary plate 22 side. For example, as the tenth embodiment of the present invention is shown in FIG. The stepped surface 30 and the engaging recess 32 may be formed on the upper auxiliary plate 22 , while the stepped surface 34 and the engaging convex portion 36 forming the inner peripheral surface of the engagement may be formed on the lower auxiliary plate 20 . It is possible.

[0092]

Furthermore, the engaging recesses 32, 44, 60, 72, 80, (83) and the engaging protrusions 36, 46, 56, 70, 78 shown in the first to sixth embodiments are overlapped with each other. It is also possible to form an inclination angle with respect to the outer peripheral surface of the engaging projection and the inner peripheral surface of the engaging recess for positioning the upper and lower auxiliary plates 22 and 20 by using the upper and lower auxiliary plates 22 and 20 as shown in FIG. For example, as an eleventh embodiment of the present invention is shown in FIG. On the other hand, while the engaging convex portion 36 is tapered in the inclined direction in which it gradually tapers in the projecting direction,

A stepped surface 30 serving as an engaging outer peripheral surface of an engaging recess 32 formed in the outer peripheral portion of the upper auxiliary plate 22 can be tapered at an inclination direction and an inclination angle corresponding to the stepped surface 34. As a result, the operation of fitting the engaging convex portion 36 into the engaging concave portion 32 and overlapping the upper and lower auxiliary plates 22, 20 can be further facilitated by using the tapers provided on both the stepped surfaces 34, 30 as guide surfaces. This can be done easily. Incidentally, as shown in the twelfth embodiment of the invention shown in FIG. 18 and the thirteenth embodiment of the invention shown in FIG.

Even when adopting a plurality of projection-shaped engaging projections 78 formed independently in the direction and a plurality of hole-shaped engaging recesses 80 formed at respective corresponding positions of the upper auxiliary plate 22, the engagement A tapered portion 104 having a tapered shape can be formed by giving an inclination angle to the outer peripheral surface of the projecting tip portion of the convex portion 78. In FIG. 19, an engagement pin 106 formed separately is press-fitted into a fitting hole 105 formed in the lower auxiliary plate 20 to form the engagement convex portion 78. The lower end of the locking pin 106 also has a tapered portion 104 similar to the upper end. As a result, the locking pin 106 has no directivity and is easy to handle, and the operation of press-fitting it into the fitting hole 105 is also facilitated.

[0094]

Further, in the fourteenth embodiment of the present invention shown in FIG. 20, a straddle between the upper and lower auxiliary plates 22, 20 is used as a kind of positioning means for aligning the central axis of the upper and lower auxiliary plates 22, 20 in a superimposed state. A locating sleeve 108 is thus shown fitted over. The positioning sleeve 108 has an inner diameter that is the same as or slightly larger than the outer diameter of the upper and lower auxiliary plates 22 and 20, which are disk-shaped and have substantially the same outer diameter. Such a positioning sleeve 108 is used when superimposing the upper and lower auxiliary plates 22 and 20, and by superimposing the upper and lower auxiliary plates 22 and 20 within the positioning sleeve 108, the central axes of the upper and lower auxiliary plates 22 and 20 are aligned. They can be axially superimposed and secured to each other with a second securing means 26. Therefore, the positioning sleeve 108 can be removed after the upper a

nd lower auxiliary plates 22 and 20 are superimposed and fixed to each other, thereby positioning the upper and lower auxiliary plates 22 and 20 so as to protrude on the outer peripheral surface. It is possible to attach them to each other without any means and in precise alignment.

[0095]

Furthermore, in the fifteenth embodiment of the present invention shown in FIG. 21, a slit-shaped engagement groove 110 is formed extending across the overlapping direction when the upper and lower auxiliary plates 22 and 20 are overlapped. The engaging grooves 110 are open to the outer peripheral surfaces of the upper and lower auxiliary plates 22 and 20 and have a predetermined depth radially inward. It is A plate-shaped engaging plate 112 is fitted into the engaging groove 110 from the opening of the outer peripheral surface, so that the upper and lower auxiliary plates 22 and 20 are positioned by the engaging plate 112 and is in a connected state. Although the engaging plate 112 is formed separately from the upper and lower auxiliary plates 22 and 20, it may be formed integrally with one of the upper and lower auxiliary plates 22 and 20 so as to protrude toward the other. In that case, the engagement groove 110 is formed only in the other auxiliary plate.

Furthermore, in the sixteenth embodiment of the present invention shown in FIG. 22 ,

a fitting recess 114 is formed as an engaging recess opening in the lower surface of the upper auxiliary plate 22 . In particular, in this embodiment, the fitting recess 114 is formed as an annular groove extending continuously in the circumferential direction around the central axis of the upper auxiliary plate 22 . On the other hand, the lower auxiliary plate 20 has a fitting convex portion 116 as an engaging convex portion that protrudes upward on the upper surface that overlaps with the upper auxiliary plate 22 . In addition, in this embodiment, the fitting protrusion 116 is formed as an annular protrusion corresponding to the fitting recess 114 . When the upper and lower auxiliary plates 22 and 20 are superimposed, the fitting convex portion 116 is positioned so as to enter the fitting concave portion 114 .

[0097]

The fitting projection 116 has a hollow structure, and the inside of the fitting projection 116 is provided with an external space.

A fluid reservoir 118 is formed which is sealed between them. Further, at least the inner peripheral wall and the outer peripheral wall of the wall portion of the fitting convex portion 116 that defines the fluid reservoir 118 are bulged and deformable in the radial direction. Specifically, for example, by forming the fitting convex portion 116 with a rubber elastic material or the like, it is possible to realize an inner peripheral wall that can bulge radially inward and an outer peripheral wall that can bulge radially outward. Further, the lower auxiliary plate 22 is formed with a fluid passage 120 that communicates with the fluid reservoir 118 and extends radially outward and opens to the outer peripheral surface.

A pressure screw 122 is screwed into the end opening. In addition, a sealed area composed of

the fluid passage 120 and the fluid reservoir 118 sealed by the pressurizing screw 122 is filled with an incompressible fluid such as oil.

Thus

, by screwing the pressure screw 122, the internal pressure of the fluid reservoir 118 can be increased through the fluid passage 120, and the inner and outer peripheral walls of the fluid reservoir 118 can be bulged outward. As a result, the fitting convex portion 116 is expanded and pressed against the inner surface of the fitting concave portion 114, so that the upper and lower auxiliary plates 22 and 20 can be positioned and fixed to each other by mutual frictional force. there is

When removing the upper auxiliary plate 22 from the lower auxiliary plate 20 ,

the pressure screw 122 is rotated in the direction of loosening and moved to the outer peripheral side of the lower auxiliary plate 20, whereby the fluid reservoir 118 is removed. can be reduced to release the pressing force of the fitting protrusion 116 against the fitting recess 114 .

[0101]

In addition, although not listed individually, the present invention can be implemented with various changes, modifications, improvements, etc. based on the knowledge of those skilled in the art. It is also possible to attach an O-ring or a sealing material to the portion to prevent foreign matter from entering the overlapping surfaces of the upper and lower auxiliary plates.

In addition to the auxiliary plates 20 and 22 having the two-layer structure described above, it

is also possible to add additional auxiliary plates in a laminated state and fixed by fixing means. By adopting the auxiliary plate of the third layer in this way, it becomes possible to realize an elastic support state or to dispose of the intermediate layer.

[Description of Reference Symbols]

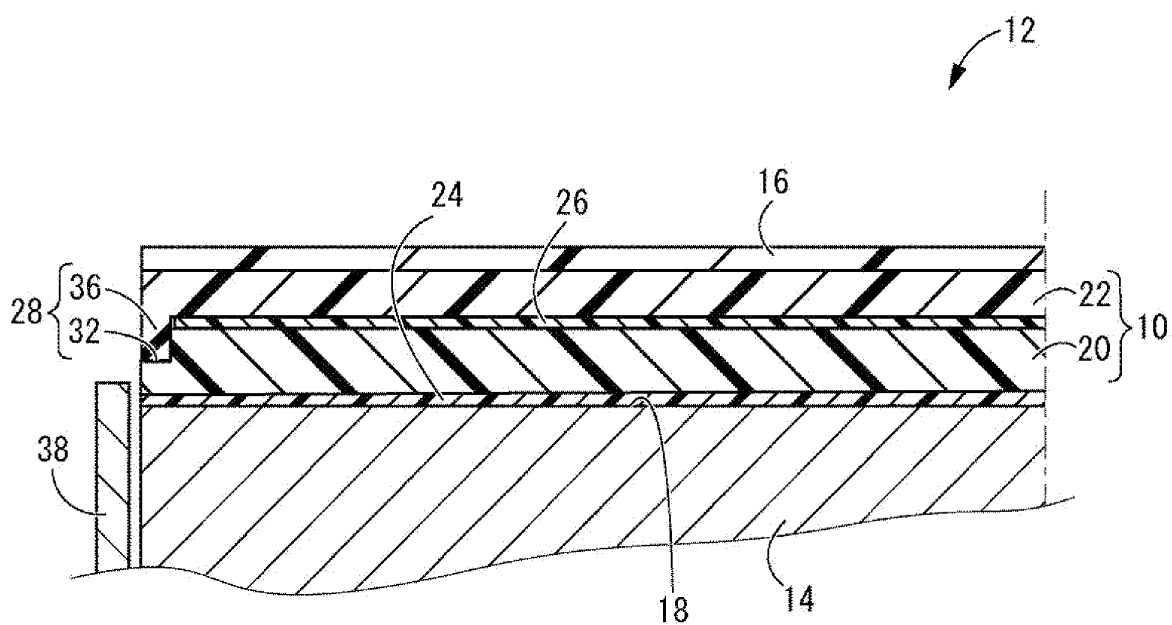
10

, 40, 50, 64, 74, 84: polishing pad auxiliary plate, 12, 42, 52, 66, 76: polishing device, 14: rotating platen, 16: polishing pad, 18: upper surface, 20: lower auxiliary plate, 22: upper auxiliary plate, 24: first fixing means, 26, 62: second fixing means, 28: positioning means, 30, 58: step surface (engagement outer circumference surface), 32, 44, 60, 72, 80, 88: engagement concave portion, 34, 54: step surface (engagement inner peripheral surface), 36, 46, 56, 68, 78, 90: engagement convex portion, 38: Protective member

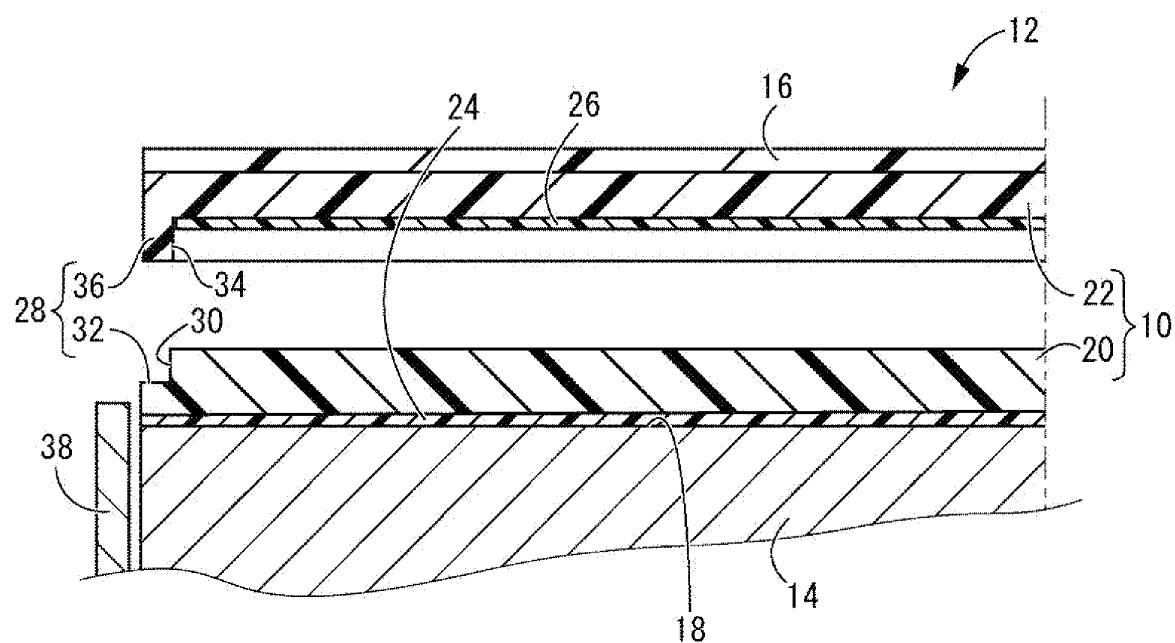
drawing

open

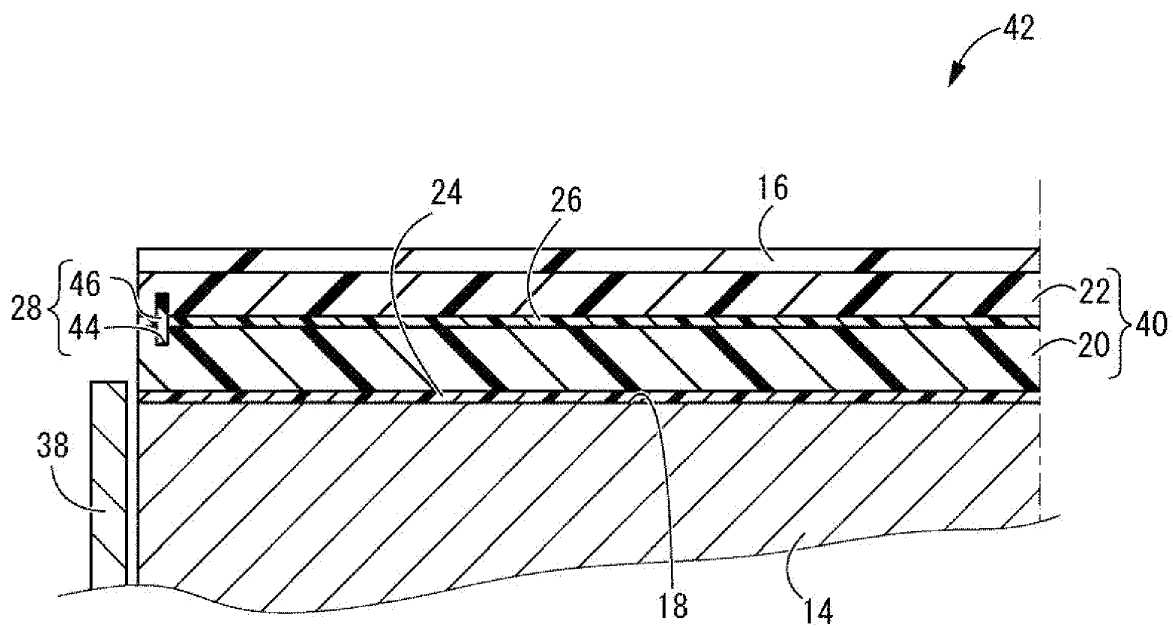
[Fig. 1]



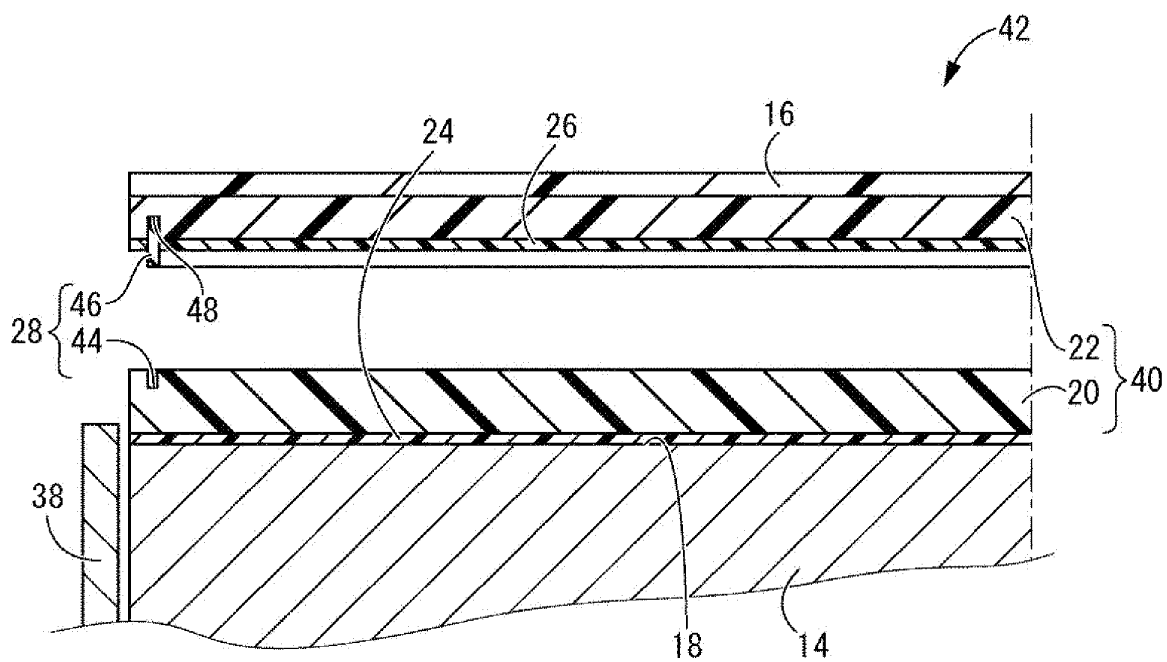
[Figure 2]



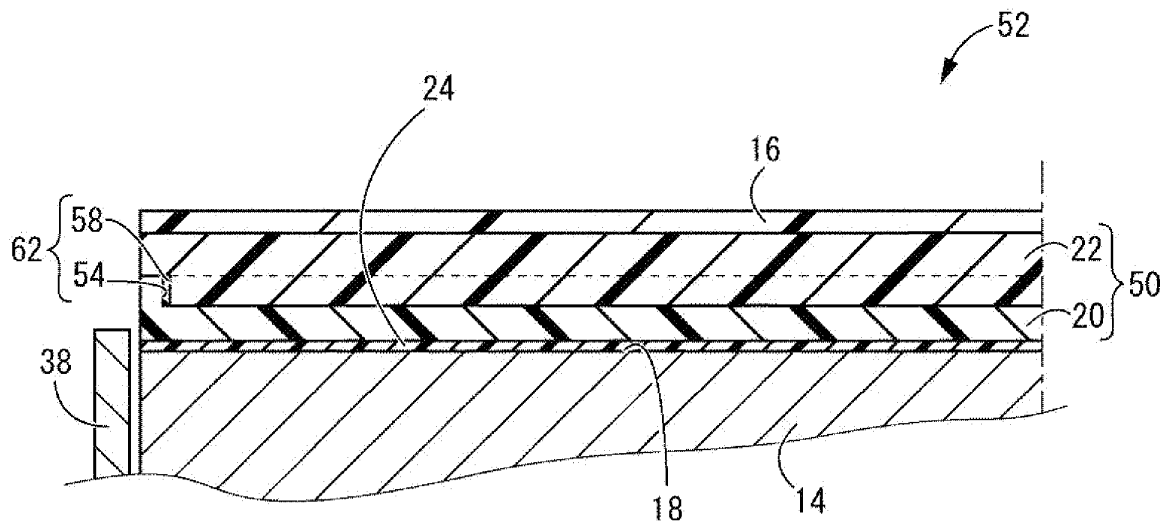
[Figure 3]



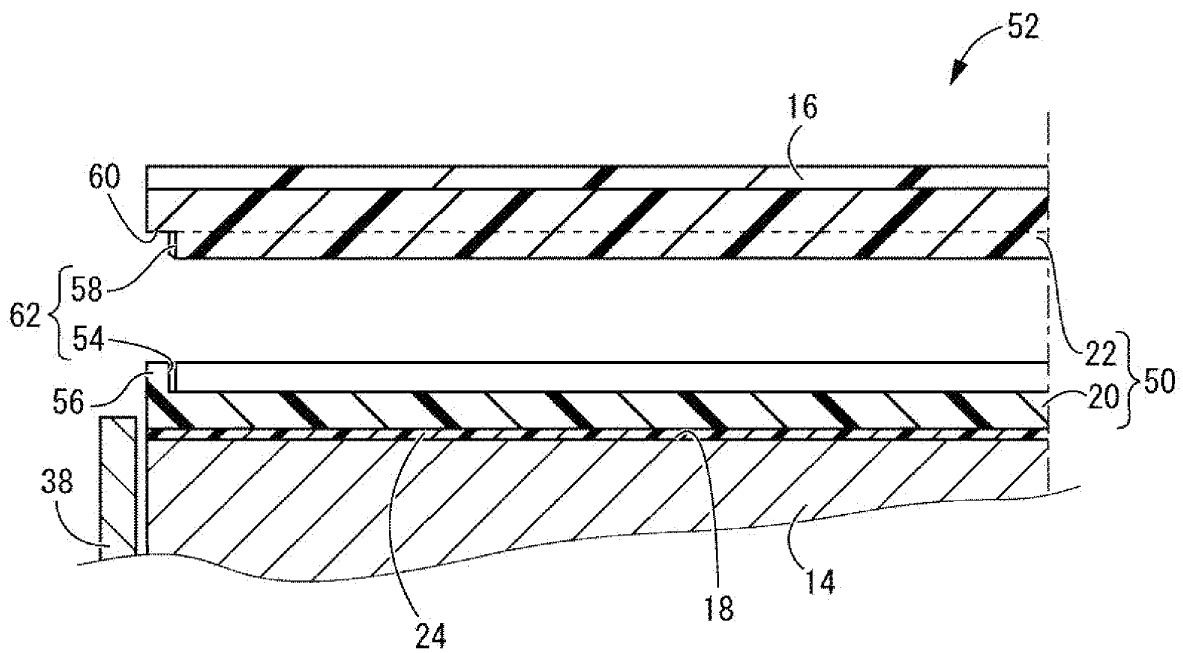
[Figure 4]



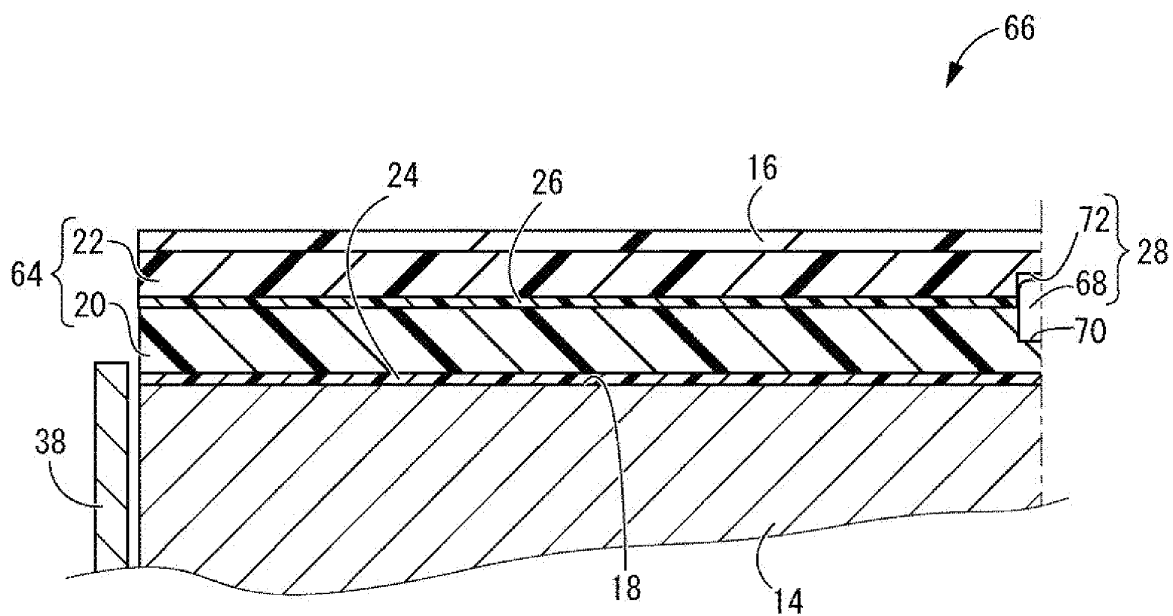
[Figure 5]



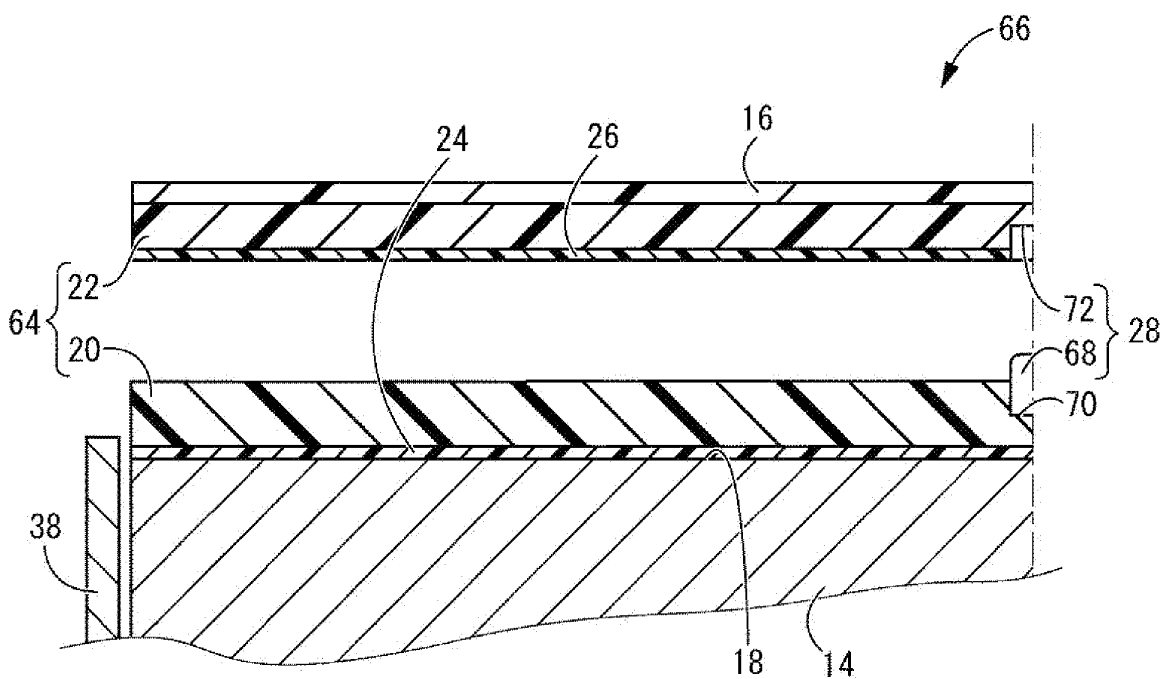
[Fig. 6]



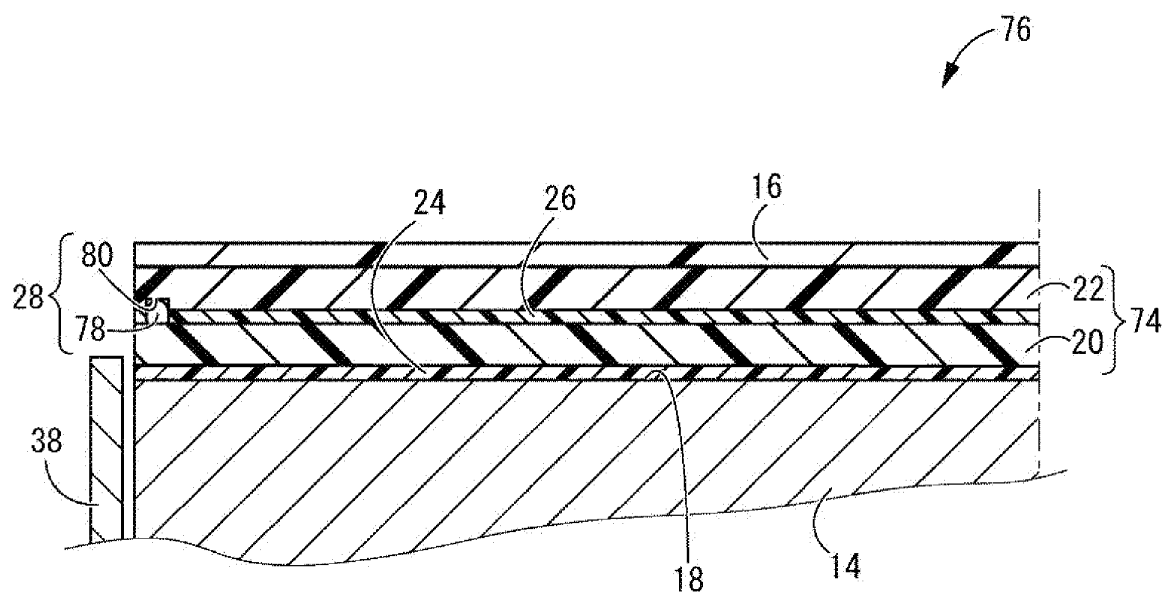
[Fig. 7]



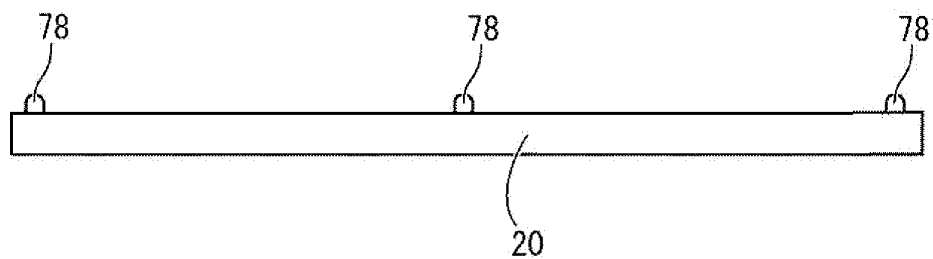
[Fig. 8]



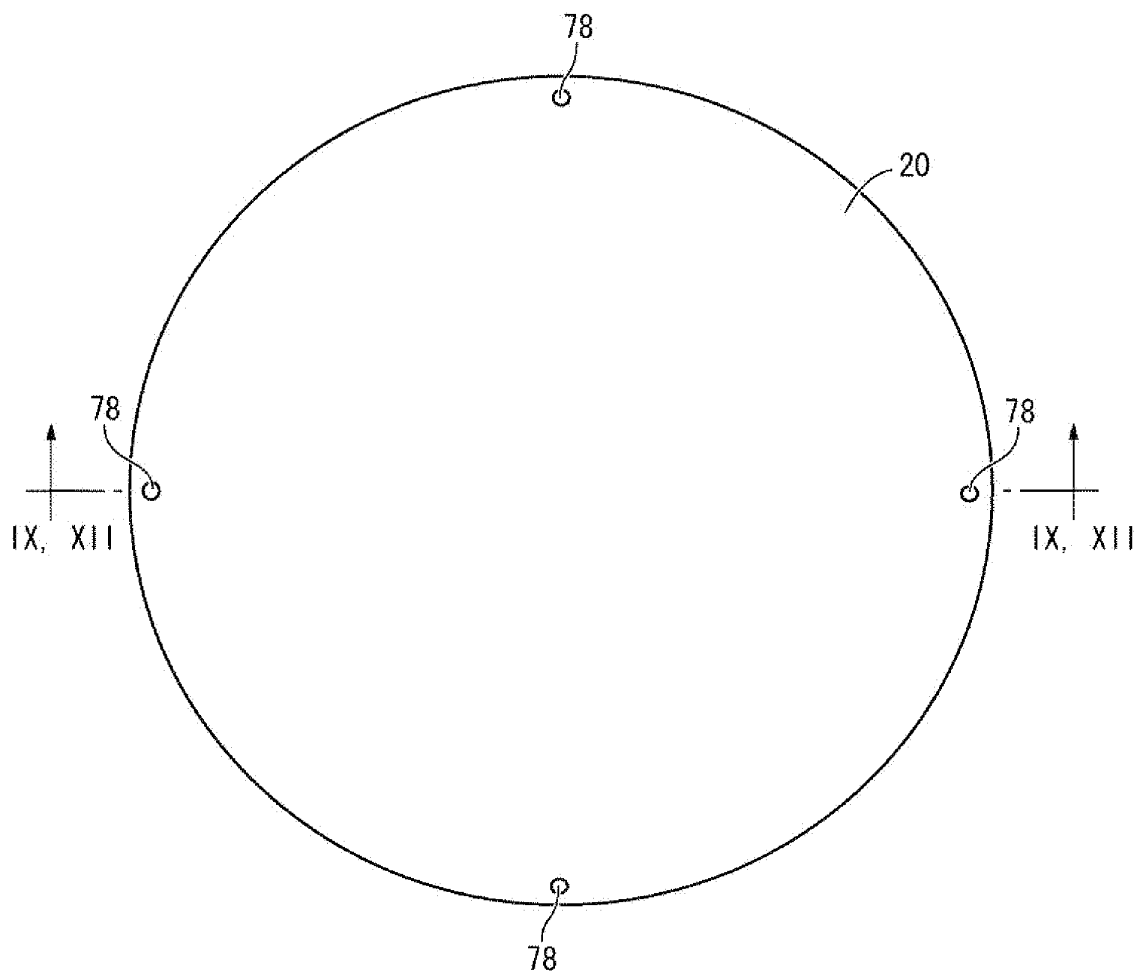
[Fig. 9]



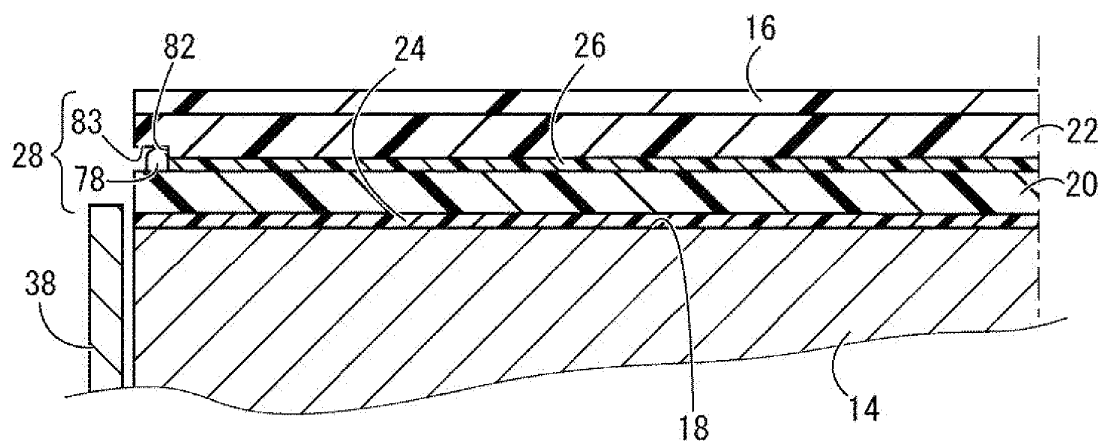
[Fig. 10]



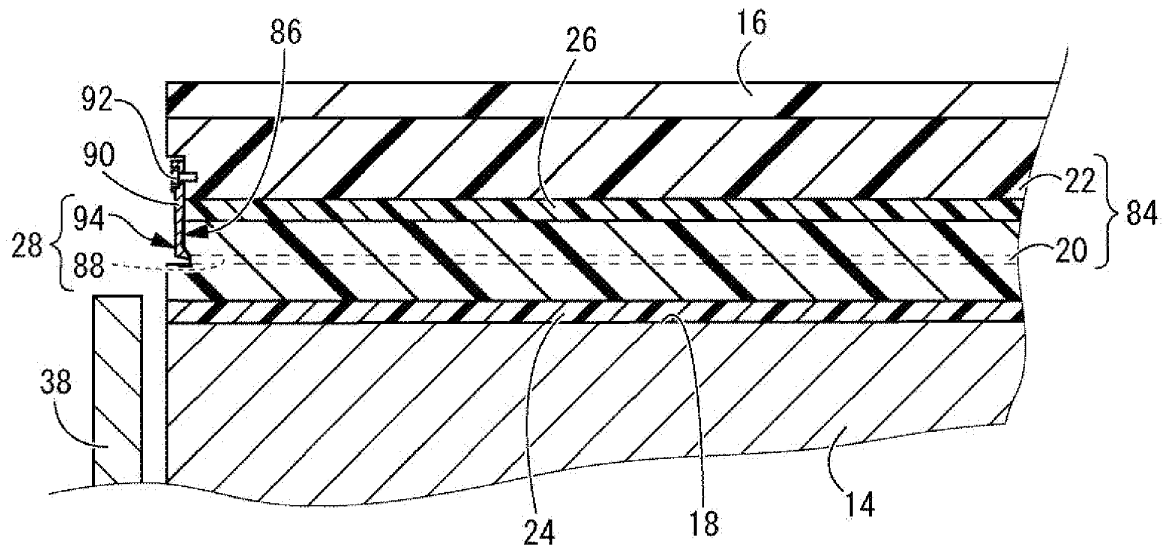
[Fig. 11]



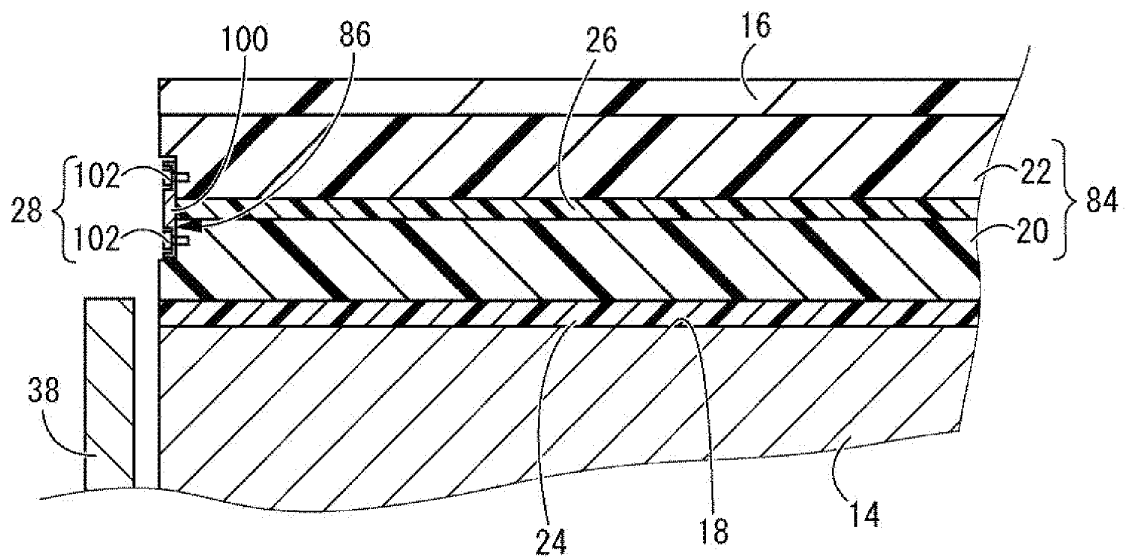
[Fig. 12]



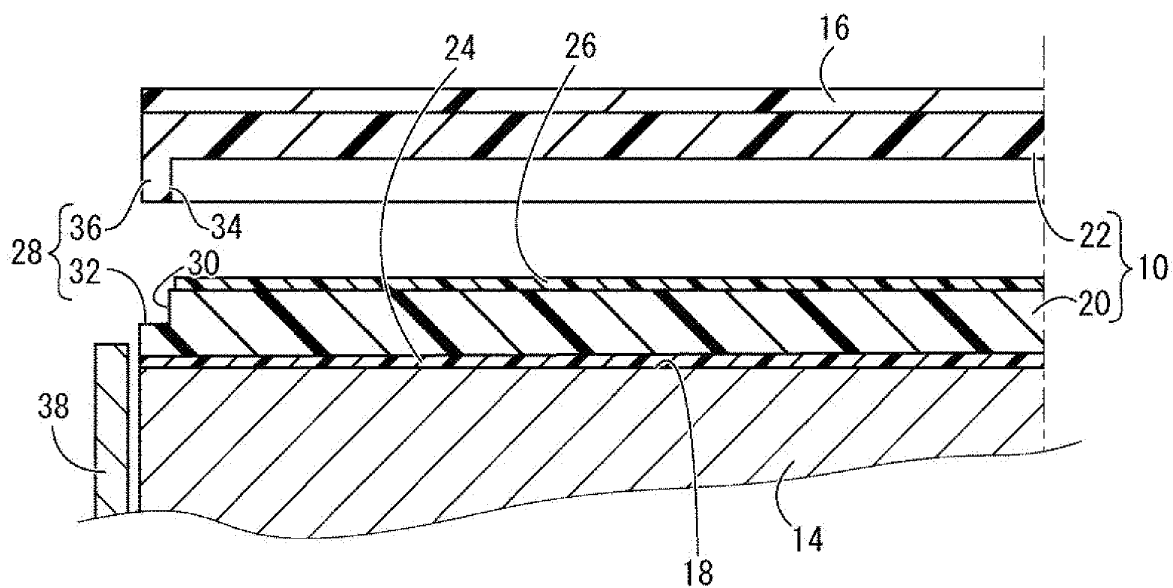
[Fig. 13]



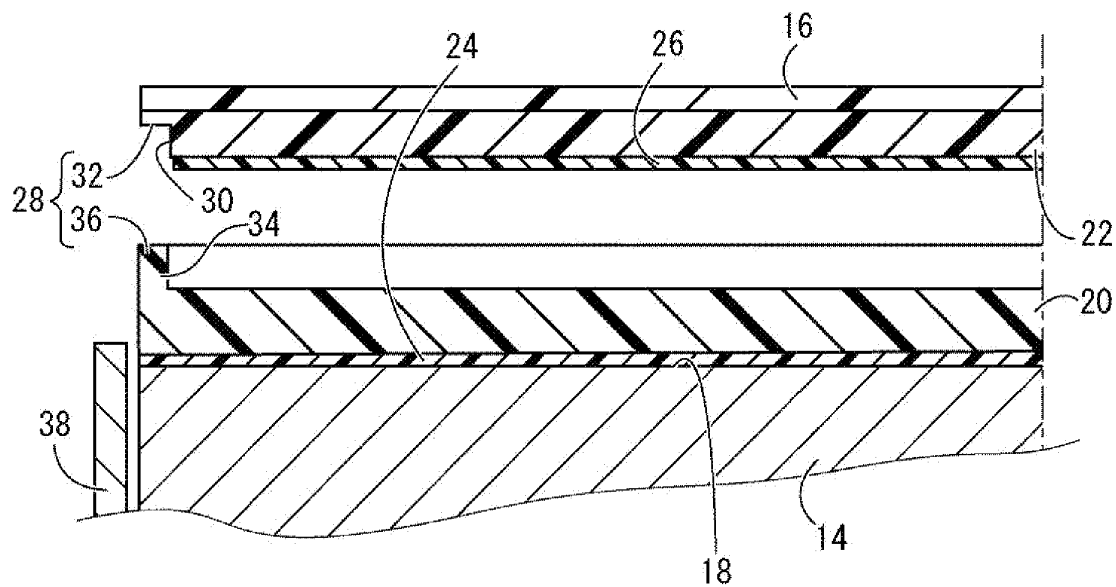
[Fig. 14]



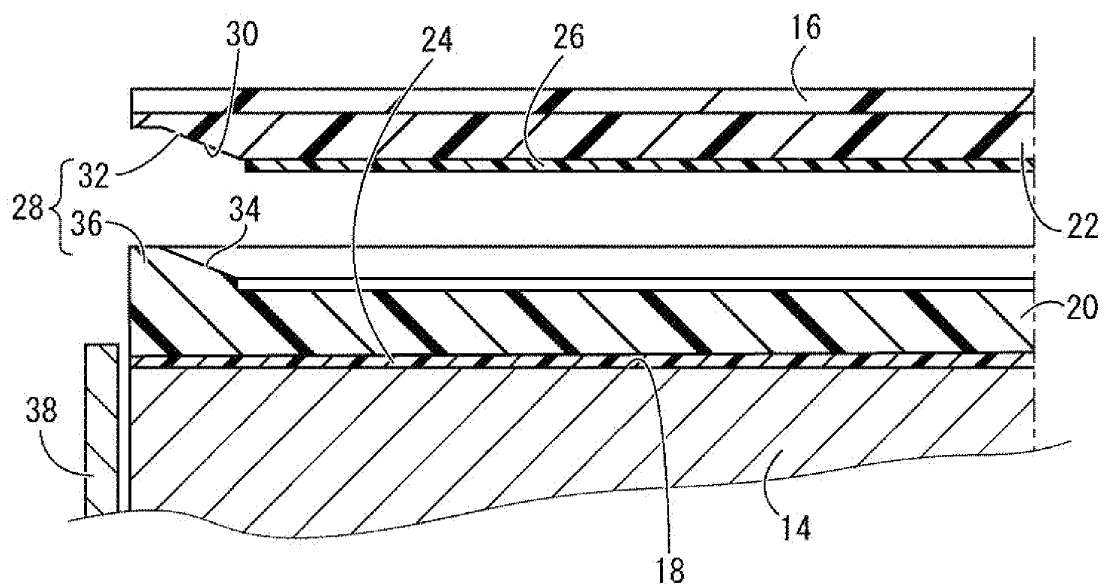
[Fig. 15]



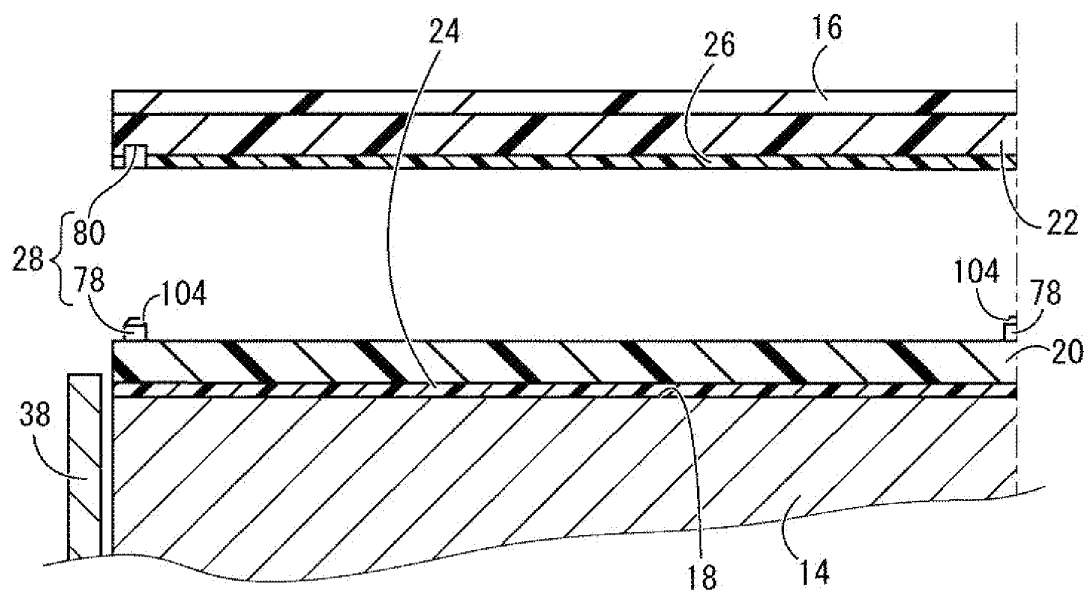
[Fig. 16]



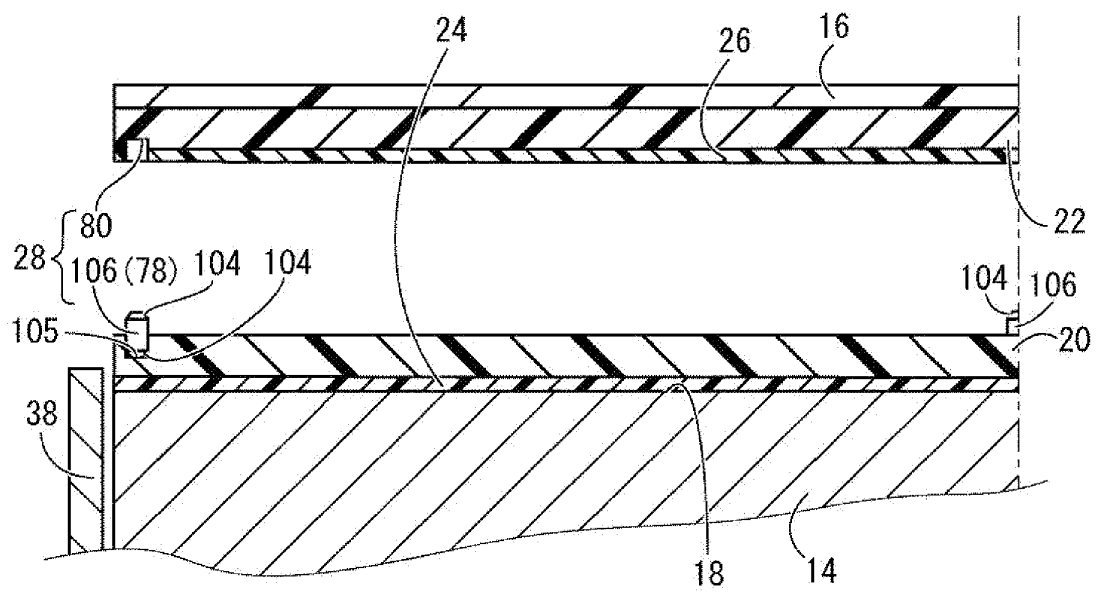
[Fig. 17]



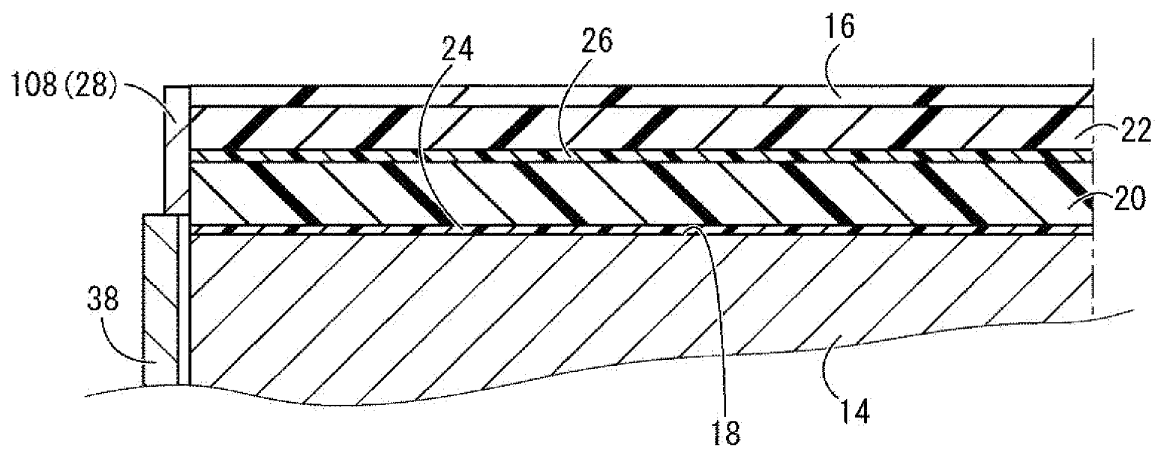
[Fig. 18]



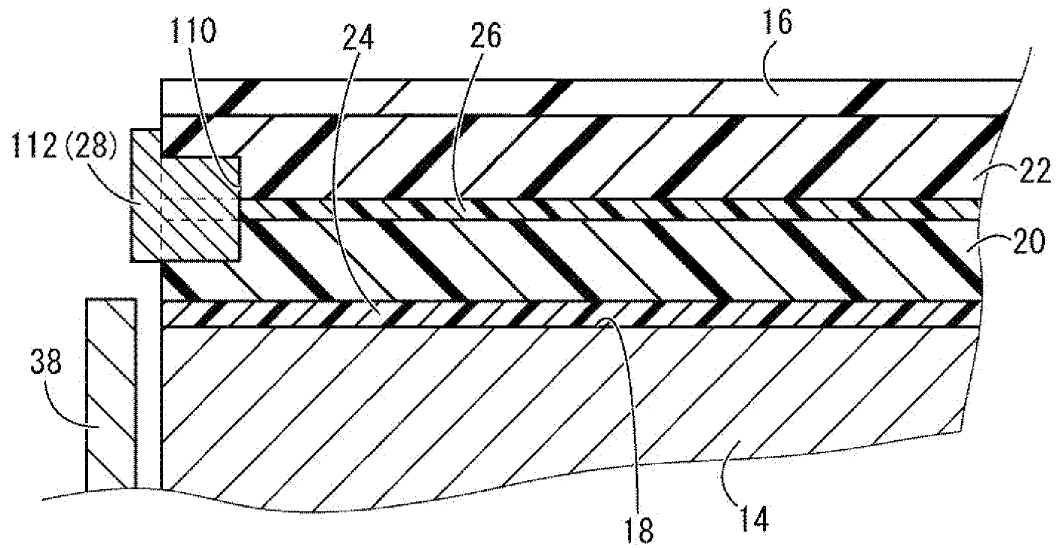
[Fig. 19]



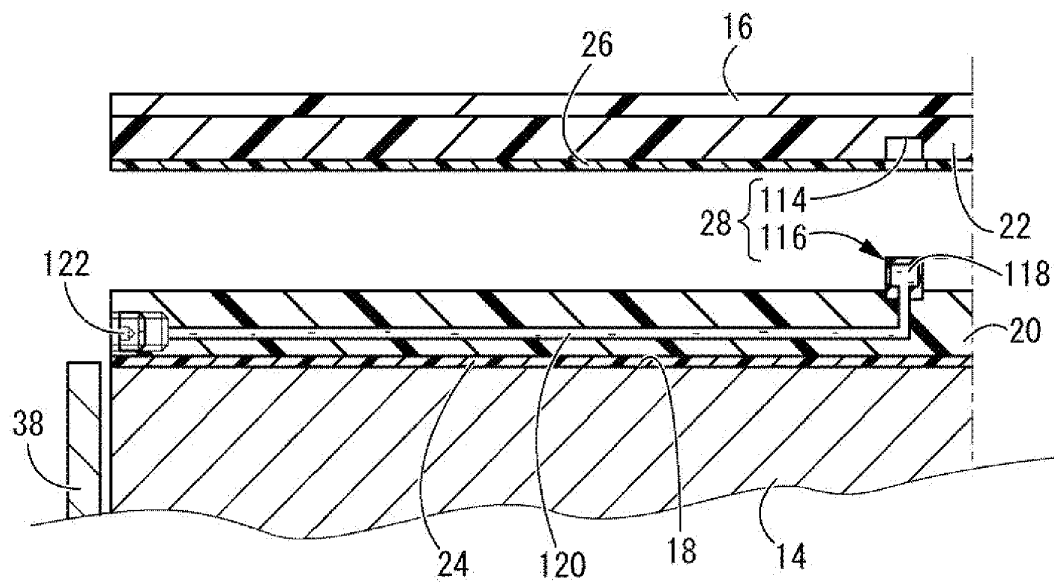
[Fig. 20]



[Fig. 21]



[Fig. 22]



drawing

close

1 2 3 Four Five 6 7 8 9 Ten ...

Magnify and Rotate

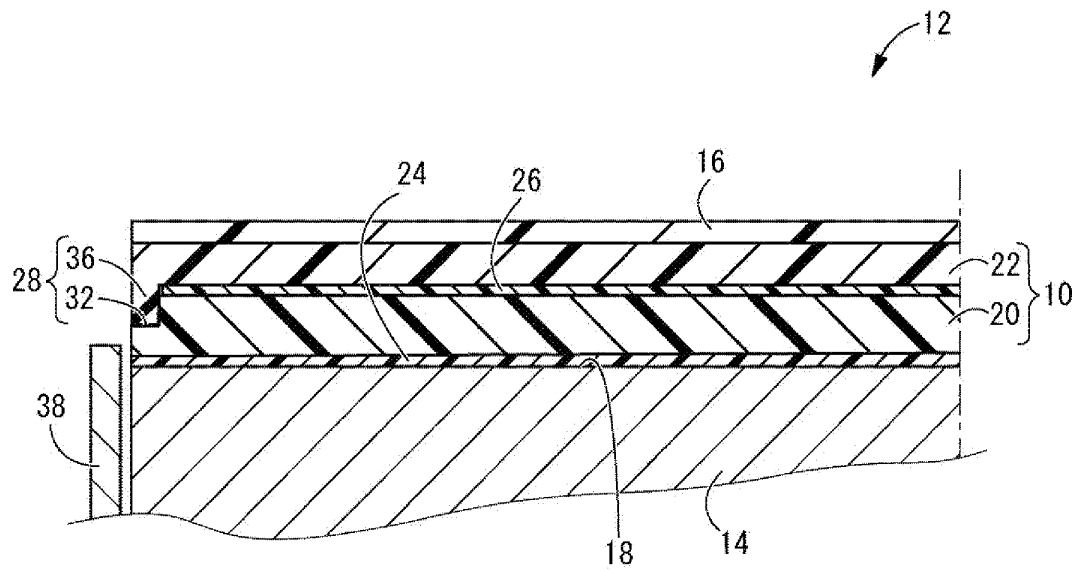


Figure 1

(19) 日本国特許庁(JP)

(12) 特 許 公 報(B2)

(11) 特許番号

特許第5789869号

(P5789869)

(45) 発行日 平成27年10月7日(2015. 10. 7)

(24) 登録日 平成27年8月14日(2015.8.14)

(51) Int. Cl.

F 1

B 2 4 B 37/12 (2012.01)

B 2 4 B 37/04

A

請求項の数 11 (全 21 頁)

(21) 出願番号	特願2011-165360 (P2011-165360)	(73) 特許権者	599096053
(22) 出願日	平成23年7月28日(2011. 7. 28)		東邦エンジニアリング株式会社
(65) 公開番号	特開2013-27951 (P2013-27951A)		三重県四日市市山分町字川之下4 4 3
(43) 公開日	平成25年2月7日(2013. 2. 7)	(74) 代理人	100103252
審査請求日	平成26年6月25日(2014. 6. 25)		弁理士 笠井 美孝
(出願人による申告) 国等の委託研究の成果に係る特許出願(平成22年度経済産業省「戦略的基盤技術高度化支援事業」委託研究、産業技術力強化法第19条の適用を受ける特許出願)		(74) 代理人	100147717
			弁理士 中根 美枝
		(72) 発明者	鈴木 辰俊
			三重県四日市市山分町字川之下4 4 3 東邦エンジニアリング株式会社内
		(72) 発明者	鈴木 英賢
			三重県四日市市山分町字川之下4 4 3 東邦エンジニアリング株式会社内
		審査官	亀田 貴志
		最終頁に続く	

(54) 【発明の名称】 研磨パッド用補助板および研磨パッド用補助板を備えた研磨装置

(57) 【特許請求の範囲】

【請求項1】

研磨装置の回転定盤に装着されて、研磨パッドを該回転定盤に対して着脱可能に取り付ける研磨パッド用補助板において、

前記回転定盤の上面に重ね合わされて配される下側補助板と、

該下側補助板を該回転定盤に固着する第一の固着手段と、

前記研磨パッドが重ね合わされて固着されるパッド支持面を備えており、該下側補助板の上面に重ね合わされて配される上側補助板と、

該上側補助板を該下側補助板に固着する第二の固着手段と、

該下側補助板と該上側補助板とを相互に位置決めして中心軸を合わせる位置決め手段とを、有しており、前記研磨装置の前記回転定盤に対して前記下側補助板が前記第一の固着手段による固着状態に保持されて、該回転定盤に固着された該下側補助板から前記上側補助板を取り外すことにより、該上側補助板の前記パッド支持面に固着されたままの状態の前記研磨パッドを該回転定盤から取り外すことが可能とされていると共に、取り外した該上側補助板を該下側補助板に対して前記位置決め手段による位置合わせ状態で再び固着せしめて取り付けることが可能とされており、且つ、

前記第二の固着手段による前記下側補助板と前記上側補助板との固着力が、前記第一の固着手段による前記回転定盤と該下側補助板との固着力よりも小さくされていることを特徴とする研磨パッド用補助板。

【請求項2】

10

20

前記位置決め手段が、前記下側補助板および前記上側補助板の外周面よりも内周側に位置して設けられている請求項 1 に記載の研磨パッド用補助板。

【請求項 3】

前記位置決め手段が、

前記下側補助板と前記上側補助板との一方に設けられて他方に向かって突出する係合凸部と、該下側補助板と前記上側補助板との他方に設けられて該係合凸部が係合せしめられる係合凹部とによって構成されている請求項 2 に記載の研磨パッド用補助板。

【請求項 4】

前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の外周部分に位置する係合部をもって形成されている請求項 3 に記載の研磨パッド用補助板。

10

【請求項 5】

前記係合凸部および前記係合凹部における前記係合部が、前記下側補助板および前記上側補助板の周方向に連続して延びて相互に嵌め合わされる環状の係合外周面および係合内周面によって構成されている請求項 4 に記載の研磨パッド用補助板。

【請求項 6】

前記下側補助板および前記上側補助板の外周部分における周上の複数箇所において、前記下側補助板と前記上側補助板との相互の重ね合わせ面の一方において他方に向かって開口する前記係合凹部と、該下側補助板と前記上側補助板との相互の重ね合わせ面の他方において一方に向かって突出する前記係合凸部とが、互いに対応する位置に形成されており、該係合凹部に対する該係合凸部の嵌まり込みによって前記係合部が構成されている請求項 4 に記載の研磨パッド用補助板。

20

【請求項 7】

前記下側補助板と前記上側補助板との一方の外周部分における周上の複数箇所から他方に向かって突出する前記係合凸部が弾性材によって形成されており、該下側補助板と前記上側補助板との他方における外周面に開口して設けられた前記係合凹部に対して該係合凸部の先端が係合されることにより前記係合部が構成されている請求項 4 に記載の研磨パッド用補助板。

【請求項 8】

前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の中心軸上に設けられている請求項 3 に記載の研磨パッド用補助板。

30

【請求項 9】

前記係合凸部の外周面と前記係合凹部の内周面とにおいて互いに螺合するねじ溝が形成されており、前記位置決め手段を構成する該係合凸部と該係合凹部との螺合により前記第二の固着手段が構成されている請求項 8 に記載の研磨パッド用補助板。

【請求項 10】

前記下側補助板と前記上側補助板との一方に設けられた前記係合凸部が、該下側補助板と該上側補助板との一方と同じ材質で形成されている請求項 3、4、5、6、8、9 の何れか 1 項に記載の研磨パッド用補助板。

【請求項 11】

請求項 1 ～ 10 の何れか 1 項に記載の研磨パッド用補助板が回転定盤の上面に装着されると共に、該回転定盤の外周側に隙間を隔てて保護部材が配設されており、該回転定盤および該研磨パッド用補助板の外周端面よりも内周側に位置して、前記位置決め手段が設けられていることを特徴とする請求項 1 ～ 10 の何れか 1 項に記載の研磨パッド用補助板を備えた研磨装置。

40

【発明の詳細な説明】

【技術分野】

【0001】

本発明は、シリコンウエハや半導体基板、ガラス基板等のような高い平坦加工精度が要求される被加工物である基板を対象とする研磨に関連する技術に係り、特に、かかる基板の表面を研磨する際に用いられる研磨パッドの再使用を実現可能とする技術に関するもの

50

である。

【背景技術】

【0002】

良く知られているように、半導体の製造に際しては、構成材となるシリコンウエハや半導体基板、ガラス基板等の基板の表面を平坦化する研磨処理が行われている。かかる研磨処理は、一般に、樹脂材等からなる円板形状の研磨パッドを研磨装置の回転定盤の上に両面テープで直接固定し、砥粒を含んだ研磨液を供給しつつ、研磨パッドと基板を相対的に回転運動させて研磨を行うことによって実施されている。

【0003】

そして、このような研磨処理を実施するための研磨パッドとしては、特開2002-11630号公報（特許文献1）等に記載されているように、発泡又は無発泡のウレタン等からなる樹脂パッドが採用されている。また、かかる研磨パッドの研磨表面には、多くの場合、同心円状や格子状、放射状等の溝加工が施されたり、発泡樹脂の気泡が開口される等している。

【0004】

ところで、研磨パッドを用いた研磨加工を行う場合には、研磨対象である基板の品種切り替え等に際して、研磨加工に使用する研磨パッドを回転定盤から引き剥がして別の研磨パッドに交換しなければならない場合がある。また、例えば、研磨加工に伴って劣化した研磨パッドを、その再使用等を目的として、別の加工装置で表面溝入れ等の再加工するような場合等においても、研磨パッドを回転定盤から引き剥がすことが必要となる。

【0005】

ところが、薄肉円板形状の研磨パッドは、研磨装置の回転定盤に対して粘着テープで強固に固着されていることから、この研磨パッドを回転定盤から引き剥がす際に、研磨パッドに対して曲がりや折れ、シワ、破れ等の損傷が発生し易い。それ故このような損傷が原因で、かかる研磨パッドを、寿命がきていないにもかかわらず、再使用できずに廃棄せざるを得なくなることが多いという問題があった。

【0006】

しかも、損傷しないように細心の注意を払いつつ研磨パッドを回転定盤から引き剥がす作業は、熟練と注意を要することから作業者に大きな負担をかけるという問題もあった。加えて、研磨パッドを回転定盤から引き剥がす作業に相当の時間が必要となることから、高価で貴重な設備である研磨装置を長時間に亘って停止させなければならず、設備の稼働時間が制限されてしまうという問題もあった。

【0007】

そこで、本発明者は、先に特開2010-214579号公報（特許文献2）において、研磨パッドの裏面に補助板を取り付け、この補助板を介して、研磨パッドを研磨装置の回転定盤に対して両面テープ等で固着するようにした補助板付き研磨パッドを提案した。かかる補助板付き研磨パッドでは、研磨パッドが補助板で支持されたままの状態を保ちつつ回転定盤に対して着脱されることから、着脱に際しての研磨パッドの損傷が補助板で補強される。それ故、研磨パッドの損傷を防止しつつ、回転定盤に対して研磨パッドを良好な作業性をもって着脱することが可能となる。

【0008】

ところが、本発明者が更なる研究と検討を重ねたところ、特許文献2で提案した補助板付き研磨パッドでは、必ずしも全ての研磨装置への対応が容易であると言えないことがわかった。

【0009】

すなわち、研磨パッドを回転定盤に重ね合わせて固着する際には、研磨パッドの中心を回転定盤の回転中心に位置合わせする必要がある、特に研磨表面に溝等が施された研磨パッドでは中心位置合わせに精度が要求される。そして、上述の如き補助板を採用することで回転定盤に対する研磨パッドの着脱回数が増加すると、より一層、研磨パッドを回転定盤に装着する際の中心位置合わせの作業が難しくて労力負担が大きいのことが大きな

問題となるのである。

【0010】

また、特許文献2で提案した補助板付き研磨パッドでは、補助板を回転定盤に対して中心位置合わせしつつ着脱可能に取り付けるために、補助板と回転定盤との間において、例えば回転定盤の外周面上に外周リングなどの固着手段が設けられる場合がある。一方、研磨装置のなかには、回転定盤の外周側に保護カバー等が装着されて、回転定盤の外周側のスペースが非常に狭くなっているものもある。それ故、仮に、そのような外周リングを採用しようとした場合に、たまたま回転定盤の外周側のスペースが狭い研磨装置を用いる際には、研磨装置の改造が必要となるおそれもあったのである。

【先行技術文献】

10

【特許文献】

【0011】

【特許文献1】特開2002-11630号公報

【特許文献2】特開2010-214579号公報

【発明の概要】

【発明が解決しようとする課題】

【0012】

本発明は上述の如き事情を背景として為されたものであり、回転定盤に対する研磨パッドの固着力を十分に確保しつつ、回転定盤に対する研磨パッドの着脱を容易に行うことを可能と為し、特に回転定盤から研磨パッドを取り外すに際しての研磨パッドの損傷を防止することが出来て、例えば研磨パッドの再利用の実現にも有利とされ得る、新規な構造の研磨パッド用補助板を提供することにある。

20

【0013】

それに加えて、本発明は、研磨パッドを回転定盤に装着する際の中心合わせの作業を容易に且つ精度良く行うことが出来て、労力負担も軽減され得ると共に、従来の各種仕様の研磨装置における回転定盤にも特別な改造を必要とすることなく容易に且つ有利に適用され得る、改良された構造の研磨パッド用補助板を提供することも、目的とする。

【0014】

さらに、本発明は、かかる新規な構造とされた研磨パッド用補助板を備えた研磨装置を提供することも、目的とする。

30

【課題を解決するための手段】

【0015】

かかる課題を解決するために、研磨パッド用補助板に関する本発明の第一の態様は、(A) 研磨装置の回転定盤に装着されて、研磨パッドを該回転定盤に対して着脱可能に取り付ける研磨パッド用補助板において、(B) 前記回転定盤の上面に重ね合わされて配される下側補助板と、(C) 該下側補助板を該回転定盤に固着する第一の固着手段と、(D) 前記研磨パッドが重ね合わされて固着されるパッド支持面を備えており、該下側補助板の上面に重ね合わされて配される上側補助板と、(E) 該上側補助板を該下側補助板に固着する第二の固着手段と、(F) 該下側補助板と該上側補助板とを相互に位置決めして中心軸を合わせる位置決め手段とを、有しており、前記研磨装置の前記回転定盤に対して前記下側補助板が前記第一の固着手段による固着状態に保持されて、該回転定盤に固着された該下側補助板から前記上側補助板を取り外すことにより、該上側補助板の前記パッド支持面に固着されたままの状態の前記研磨パッドを該回転定盤から取り外すことが可能とされていると共に、取り外した該上側補助板を該下側補助板に対して前記位置決め手段による位置合わせ状態で再び固着せしめて取り付けることが可能とされており、且つ、前記第二の固着手段による前記下側補助板と前記上側補助板との固着力が、前記第一の固着手段による前記回転定盤と該下側補助板との固着力よりも小さくされている研磨パッド用補助板を特徴とする。

40

【0016】

本発明に従う構造とされた研磨パッド用補助板では、研磨パッドを、上側補助板および

50

下側補助板を介して、回転定盤に固着して装着することとなる。これにより、下側補助板を回転定盤に固着したまま、下側補助板から上側補助板を取り外すことが出来、研磨パッドを上側補助板に固着されたままの状態での回転定盤から取り外すことが可能となる。

【0017】

それ故、研磨パッドが上側補助板で補強および保護された状態で、研磨パッドの損傷を防止しつつ、研磨パッドを回転定盤から取り外すことが出来、薄肉の研磨パッドの取り扱いも容易となる。そして、例えば研磨対象物や研磨条件の変更等に際して研磨パッドの着脱を繰り返す際や、磨耗した研磨パッドを取り外して再生処理後に再装着する際などにおいて、回転定盤への研磨パッドの着脱や研磨パッドに対する再生処理等の作業を容易に行うことも可能となる。

10

【0018】

しかも、回転定盤に固着されたままの下側補助板と、研磨パッドと共に取り外される上側補助板とが、位置決め手段により相互に中心軸合わせされることから、回転定盤への位置合わせが必要となる研磨パッドの着脱作業を一層容易に行うことができる。特に、かかる位置決め手段が、下側補助板と上側補助板との間に設けられていることから、回転定盤に対して特別な加工等を施す必要がない。また、かかる位置決め手段が、回転定盤よりも外周側に大きく突出することが回避され得、例えば回転定盤の外周側に保護カバー等が設けられている研磨装置などにも、特別な改造を施すことなく適用可能とされる。

【0019】

上記本発明の第一の態様に係る研磨パッド用補助板においては、前記第二の固着手段による前記下側補助板と前記上側補助板との固着力が、前記第一の固着手段による前記回転定盤と該下側補助板との固着力よりも小さくされている態様が、採用されている。

20

【0020】

このような第一の態様に従えば、第一及び第二の固着手段における固着力を相互に調整して設定したことにより、研磨パッドが固着されたままの上側補助板を、回転定盤に固着されたままの下側補助板から取り外す作業が一層容易となる。要するに、下側補助板を回転定盤に対して固着状態に保つための特別な操作等を必要とすることなく、下側補助板を回転定盤への固着状態に残しつつ研磨パッドを上側補助板に固着されたままの状態での回転定盤から容易に取り外すことが可能になる。

【0021】

本発明の第二の態様は、前記第一の態様に係る研磨パッド用補助板において、前記位置決め手段が、前記下側補助板および前記上側補助板の外周面よりも内周側に位置して設けられているものである。

30

【0022】

本態様の研磨パッド用補助板では、位置決め手段における上下補助板の外周側への突出が完全に回避される。それ故、例えば上下補助板の外径寸法を回転定盤の外径寸法と同じか僅かに小さく設定して装着する場合でも、研磨パッドの支持面を十分に大きく確保しつつ、回転定盤から外周側に位置決め手段が突出することを回避することが出来、回転定盤の外周側に保護カバー等が設置されていても、本発明に係る研磨パッド用補助板の適用に際して障害となることが回避される。

40

【0023】

本発明の第三の態様は、前記第二の態様に係る研磨パッド用補助板において、前記位置決め手段が、前記下側補助板と前記上側補助板との一方に設けられて他方に向かって突出する係合凸部と、該下側補助板と前記上側補助板との他方に設けられて該係合凸部が係合せしめられる係合凹部とによって構成されているものである。

【0024】

本態様の研磨パッド用補助板では、係合凸部と係合凹部との相互係合作用に基づいて、機械的に大きな位置決め力を容易に得ることが可能となる。また、係合凸部や係合凹部の形状や大きさ、数などを調節することにより、位置決め作用の方向や作用力を大きな自由度で容易に設定することも可能となる。

50

【0025】

本発明の第四の態様は、前記第三の態様に係る研磨パッド用補助板において、前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の外周部分に位置する係合部をもって形成されているものである。

【0026】

本態様の研磨パッド用補助板では、研磨パッド用補助板の中央から離れた外周部分に位置して、相互に凹凸嵌合せしめられる係合凸部の係合外周面と係合凹部の係合内周面とを形成することにより、上下補助板の相対的な位置決め精度、特に径方向の位置決め精度の向上が図られ得る。なお、後述の第六及び第七の態様にも示されているように、係合凸部の係合外周面および係合凹部の係合内周面は、研磨パッド用補助板の中心周りで研磨パッド用補助板の外周縁部に沿って周方向に延びる形態であっても良いし、研磨パッド用補助板の外周部分に形成された係合凸部と係合凹部のように周上で部分的に位置する形態であっても良い。

10

【0027】

本発明の第五の態様は、前記第四の態様に係る研磨パッド用補助板において、前記係合凸部および前記係合凹部における前記係合部が、前記下側補助板および前記上側補助板の周方向に連続して延びて相互に嵌め合わされる環状の係合外周面および係合内周面によって構成されているものである。

【0028】

本態様の研磨パッド用補助板において、より好適には、研磨パッド用補助板の中心軸回りに広がる環状の係合内外周面をもって係合凹部と係合凸部が形成されることとなり、それによって、上側補助板の下側補助板への装着時に周方向での相互の位置合わせが不要なくなり、容易且つ速やかに作業することが可能となる。

20

【0029】

本発明の第六の態様は、前記第四の態様に係る研磨パッド用補助板であって、前記下側補助板および前記上側補助板の外周部分における周上の複数箇所において、前記下側補助板と前記上側補助板との相互の重ね合わせ面の一方において他方に向かって開口する前記係合凹部と、該下側補助板と前記上側補助板との相互の重ね合わせ面の他方において一方に向かって突出する前記係合凸部とが、互いに対応する位置に形成されており、該係合凹部に対する該係合凸部の嵌まり込みによって前記係合部が構成されているものである。

30

【0030】

本態様の研磨パッド用補助板では、上下補助板の相互の位置合わせを軸直角方向だけでなく中心軸回りの周方向でも容易に実現することが可能となる。

【0031】

本発明の第七の態様は、前記第四の態様に係る研磨パッド用補助板において、前記下側補助板と前記上側補助板との一方の外周部分における周上の複数箇所から他方に向かって突出する前記係合凸部が弾性材によって形成されており、該下側補助板と前記上側補助板との他方における外周面に開口して設けられた前記係合凹部に対して該係合凸部の先端が係合されることにより前記係合部が構成されているものである。

【0032】

本態様の研磨パッド用補助板では、上下補助板の外周面上に係合部を露出させて形成することが可能であり、それによって係合部の係合状態を目視等で容易に確認することが可能となる。また、本態様では、係合凸部の弾性を利用して係合部における係合状態が安定して保たれ得る。

40

【0033】

本発明の第八の態様は、前記第三の態様に係る研磨パッド用補助板において、前記係合凸部および前記係合凹部が、前記下側補助板および前記上側補助板の中心軸上に設けられているものである。

【0034】

本態様の研磨パッド用補助板では、上下補助板の中心軸上に係合凸部および係合凹部を

50

設けたことにより、一つの係合部によって上下補助板の中心軸合わせを行うことが可能になる。また、中心軸上に設けられた係合凸部と係合凹部の相互の位置合わせに際しては、上下補助板の周方向での相互の位置合わせが必要なく、それら係合凸部と係合凹部を容易に係合状態とすることも可能になる。

【0035】

本発明の第九の態様は、前記第八の態様に係る研磨パッド用補助板において、前記係合凸部の外周面と前記係合凹部の内周面とにおいて互いに螺合するねじ溝が形成されており、前記位置決め手段を構成する該係合凸部と該係合凹部との螺合により前記第二の固着手段が構成されているものである。

【0036】

本態様の研磨パッド用補助板では、位置決め手段により、上側補助板と下側補助板との固着力を得ることができる。それ故、かかる位置決め手段のみによって第二の固着手段を構成したり、第二の固着手段による上下補助板間の固着力を位置決め手段で補助的に構成することも可能となる。

【0037】

本発明の第十の態様は、前記第三、四、五、六、八、九の何れかの態様に係る研磨パッド用補助板において、前記下側補助板と前記上側補助板との一方に設けられた前記係合凸部が、該下側補助板と該上側補助板との一方と同じ材質で形成されているものである。

【0038】

本態様の研磨パッド用補助板では、上下で重ね合わされた補助板における研磨パッドの支持特性が、係合凸部の形成部分で局所的に大きく異なることを防止することが可能となる。それ故、パッド研磨加工に際して押圧力が研磨パッド表面に作用した際、かかる研磨パッドを支持している上下補助板における係合凸部や係合凹部の形成部位において、押圧反力や研磨パッド弾性などの特性が局部的に異なることに起因する研磨精度などの不具合を軽減乃至は回避することが可能になる。

【0039】

さらに、本発明は、前記第一～十の何れかの態様に記載の本発明に係る研磨パッド用補助板が回転定盤の上面に装着されると共に、該回転定盤の外周側に隙間を隔てて保護部材が配設されており、該回転定盤および該研磨パッド用補助板の外周端面よりも内周側に位置して、前記位置決め手段が設けられている研磨装置も、特徴とする。

【発明の効果】

【0040】

本発明に従う構造とされた研磨パッド用補助板を採用し、または本発明に従う構造とされた研磨装置を用いることによって、研磨パッドの損傷を防止しつつ、研磨パッドを回転定盤から容易に取り外したり装着したりすることが可能となるのであり、研磨パッドの装着に際しての回転定盤への位置合わせも容易に且つ精度良く行うことが可能となる。

【図面の簡単な説明】

【0041】

【図1】本発明の第一の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図2】図1に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図3】本発明の第二の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図4】図3に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図5】本発明の第三の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図6】図5に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図 7】本発明の第四の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 8】図 7 に示された研磨装置において研磨パッドを取り外した状態を示す縦断面の説明図。

【図 9】本発明の第五の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 10】図 9 に示された研磨パッド用補助板を構成する下側補助板の側面図。

【図 11】図 10 に示された下側補助板の平面図。

【図 12】本発明の第六の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 13】本発明の第七の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 14】本発明の第八の実施形態としての研磨パッド用補助板を装着した研磨装置の要部を示す縦断面図。

【図 15】本発明の第九の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 16】本発明の第十の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 17】本発明の第十一の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 18】本発明の第十二の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 19】本発明の第十三の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【図 20】本発明の第十四の実施形態としての研磨パッド用補助板を位置決めした状態を示す縦断面の説明図。

【図 21】本発明の第十五の実施形態としての研磨パッド用補助板を位置決めした状態を示す縦断面の説明図。

【図 22】本発明の第十六の実施形態としての研磨パッド用補助板を取り外した状態を示す縦断面の説明図。

【発明を実施するための形態】

【0042】

以下、本発明の実施形態について、図面を参照しつつ説明する。先ず、図 1～2 には、本発明の第一の実施形態としての研磨パッド用補助板 10 が示されている。この研磨パッド用補助板 10 は、研磨装置 12 の回転定盤 14 に装着されて用いられ、回転定盤 14 に対して研磨パッド 16 を着脱可能に取り付けるようになっている。

【0043】

研磨装置は、例えば特開 2010-141155 号公報等に記載されているように例えば CMP 装置として用いられるものであって、基本構造は周知であるが要部を説明すると、先ず基礎ベース上に固定設置された装置本体によって鉛直方向に延びる回転軸が回転可能に支持されており、この回転軸の上端部に円盤形状の回転定盤 14 が固設されている。かかる回転定盤 14 は、水平方向に広がる平坦な上面 18 を有しており、この上面 18 が研磨パッド 16 の支持面とされている。また、回転軸には、電気モータの回転出力軸が連結されており、電気モータの駆動力が伝達されることで回転軸ひいては回転定盤 14 が中心軸回りに回転駆動されるようになっている。なお、研磨パッド 16 を支持する上面 18 の上方には、研磨用スラリを供給するノズルが配置されると共に、研磨対象（被研磨物）であるウェハ等を保持して回転させつつ研磨パッド 16 に押し付けることで研磨加工を施す研磨ヘッドが配設されている。

【0044】

このような研磨装置において、その回転定盤 14 に装着された研磨パッド用補助板 10

10

20

30

40

50

は、下側補助板 20 および上側補助板 22 を含んでいる。そして、回転定盤 14 の上面 18 に対して、下側補助板 20 が第一の固着手段 24 で固着されており、更に、下側補助板 20 の上面に対して、上側補助板 22 が第二の固着手段 26 で固着されている。即ち、下側補助板 20 と上側補助板 22 は、第二の固着手段 26 を介して相互に重ね合わされて固着されることにより、全体として二層構造とされた研磨パッド用補助板 10 を構成しており、第一の固着手段 24 により回転定盤 14 の上面 18 に取り付けられている。

【0045】

下側補助板 20 および上側補助板 22 は、何れも、薄肉の略円形平板形状とされており、平坦な表面（上面）と裏面（下面）を有している。これらの上下補助板 22, 20 は、装着される研磨パッド 16 よりも硬質材料であるものや、研磨パッド 16 よりも部材剛性が大きいものが望ましい。使用方法にもよるが、後述するように下側補助板 20 は回転定盤 14 への取り付け後に着脱を繰り返さない使用も可能である一方、上側補助板 22 は回転定盤 14 への取り付け後に着脱を繰り返すことが予定されることから、少なくとも上側補助板 22 は、研磨パッド 16 よりも部材剛性が大きいものを採用することが望ましい。

【0046】

尤も、上側補助板 22 は、研磨パッド 16 を支持せしめて、研磨装置 12 による研磨加工の他、研磨パッド表面へのドレッシング、清掃、再溝入などの各種の処理に際して要求される強度や剛性、形状安定性及び精度を満足するものであれば良く、その材質や厚さ寸法は限定されるものでない。特に、下側補助板 20 だけでなく上側補助板 22 も、それ単体で、研磨パッド 16 の支持強度や剛性等を負うものでなく、例えば研磨加工に際しては研磨装置 12 の回転定盤 14 の上に重ね合わされて使用されることで、回転定盤 14 で下面を支持されるものであることから、単体での強度や剛性がそれ程迄に要求されるものでない。それ故、ステンレス鋼等の金属の他、合成樹脂や繊維強化樹脂等も、下側補助板 20 や上側補助板 22 の形成材料として採用され得る。特に、合成樹脂材は金属材に比して軽量で加工や取扱いが容易であり、例えばポリカーボネート等は、厚さ寸法精度の安定性や温度変化に対する低歪み特性にも優れているといった利点がある。

【0047】

また、研磨パッド 16 の全体に亘って安定した支持力を得るためには、上側補助板 22 の外径寸法を研磨パッド 16 の外径寸法の値以上に設定することが望ましく、且つ下側補助板 20 の外径寸法を上側補助板 22 の外径寸法の値以上に設定することが望ましく、更に下側補助板 20 の外径寸法を回転定盤 12 の外径寸法の値以下に設定することが望ましい。特に、図 1, 2 に示されているように、下側補助板 20 および上側補助板 22 の外径寸法を略同じにすると共に、装着される回転定盤 14 の外径寸法とも略同じとすることにより、研磨パッド 16 の支持面積を十分に大きく確保することが可能になる。これにより、回転定盤 14 と略同じ大きさの研磨パッド 16 を、その全体に亘って略同じ支持力をもって回転定盤 14 に装着することが可能となる。

【0048】

更にまた、第一の固着手段 24 および第二の固着手段 26 としては、研磨に際して及ぼされる外力に対抗して、回転定盤 14 の上面 18 へ下側補助板 20 および上側補助板 22 を固着状態に保持し得るものであればよく、特に限定されるものでない。具体的には、接着剤や粘着剤、または基材シートの両面に接着剤や粘着剤が付着等された両面テープなどが、第一及び第二の固着手段 24, 26 として採用され得るが、その他、負圧エア等を利用した負圧吸引や、永久磁石又は電磁石を利用した磁力吸引なども採用可能である。また、これらの接着剤等からなる固着手段は、下側補助板 20 や上側補助板 22 において平坦な重ね合わせ面の略全面に亘って略均一に固着力を及ぼすことが望ましく、それによって、大きな固着力を得ることが出来ると共に、研磨パッド用補助板 10 の表面において研磨パッド 16 の支持特性が局所的に異なる不具合等を回避できる。

【0049】

例えば負圧吸引や電磁石では固着力を ON/OFF できるが、接着剤等のように一定の固着力が及ぼされる場合には、第一の固着手段 24 による回転定盤 14 に対する下側補助

板 2 0 の固着力に比して、第二の固着手段 2 6 により下側補助板 2 0 に対する上側補助板 2 2 の固着力が小さくなるように設定されることが望ましい。これにより、上側補助板 2 2 を下側補助板 2 0 から引き剥がして取り外す際、下側補助板 2 0 を回転定盤 1 4 上に固着せしめたまま残置させておくことが容易に実現可能となる。このような固着力の相違の具体的な実現は、接着剤や粘着剤の材質など固着手段そのものを相互に異ならせる他、固着面積や固着面の状態（面粗さやプラズマ等の処理有無など）を相互に異ならせること等によっても実現可能である。

【0050】

さらに、上側補助板 2 2 の表面（上面）は研磨パッド支持面となっており、研磨パッド 1 6 が重ね合わされて取り付けられている。かかる研磨パッド 1 6 は、従来から公知の各種の研磨パッドを採用することが出来る。そして、この研磨パッド 1 6 の裏面が、上側補助板 2 2 の表面に対して、研磨パッド貼付用として従来公知の粘着テープや適当な接着剤等を利用して固着されている。

【0051】

なお、研磨パッド 1 6 の上側補助板 2 2 への固着手段は前述の第二の固着手段 2 6 よりも、大きな固着力を設定することが望ましい。これにより、研磨パッド 1 6 が固着されたままの状態の上側補助板 2 2 を下側補助板 2 0 から取り外す際に、上側補助板 2 2 が湾曲等しても研磨パッド 1 6 が上側補助板 2 2 から予期せずに剥がれることが効果的に防止され得る。

【0052】

また、研磨パッド 1 6 の外径寸法は、一般に規格値とされるが、多くの場合、装着される回転定盤 1 4 の上面 1 8 の外径寸法と同じか小さく設定される。

【0053】

さらに、例えば回転定盤 1 4 の上面 1 8 と下側補助板 2 0 との間、下側補助板 2 0 と上側補助板 2 2 との間、上側補助板 2 2 と研磨パッド 1 6 との間の少なくとも一つにおいて、適当なクッション層を設けても良い。このようなクッション層を設けることにより、研磨パッド 1 6 による研磨加工に際して、被加工物に対する研磨効率の全面に亘る均一化を図ることが可能となる。

【0054】

かかるクッション層としては、例えば発泡によってある程度の圧縮性が付与された樹脂シートや、エラストマーシート、ゴムシート等が好適に採用され得る。また、第一の固着手段 2 4 や第二の固着手段 2 6、研磨パッド 1 6 の上側補助板 2 2 への固着手段によって、クッション層を構成することも可能である。なお、クッション層は、研磨パッド 1 6 の支持面における局所的な歪を防止するために、研磨パッド 1 6 の支持領域の略全体に亘る大きさをもって一定厚さで存在するように、形成されることが望ましい。

【0055】

また、研磨パッド用補助板 1 0 を構成する下側補助板 2 0 と上側補助板 2 2 との間には、相互に位置決めして中心軸を合わせる位置決め手段 2 8 が設けられている。本実施形態では、下側補助板 2 0 の外周部分に、下側補助板 2 0 の中心軸回りで全周に亘って延びる円形の段差面 3 0 が形成されている。そして、この段差面 3 0 よりも外周側では下側補助板 2 0 の厚さ寸法が小さくされることで、下側補助板 2 0 の外周面に開放する切欠断面形状をもって周方向の全周に連続して延びる環状の係合凹部 3 2 が、下側補助板 2 0 に突出して一体形成されている。

【0056】

一方、本実施形態では、上側補助板 2 2 の外周部分には、上側補助板 2 2 の中心軸回りで全周に亘って延びる円形の段差面 3 4 が形成されている。そして、この段差面 3 4 よりも外周側では上側補助板 2 2 の厚さ寸法が大きくなることで、上側補助板 2 2 の外周端縁に沿って周方向の全周に連続して延びる環状の係合凸部 3 6 が、上側補助板 2 2 に突出して一体形成されている。なお、係合凸部 3 6 および係合凹部 3 2 は、上下補助板 2 2、2 0 のどちらに形成されていても良い。

【0057】

上述の下側補助板20の段差面30および係合凹部32は、上側補助板22の段差面34および係合凸部36に対して相互に位置合わせされており、本実施形態において係合外周面および係合内周面を構成している。そして、下側補助板20に上側補助板22が重ね合わされる際、係合凹部32に係合凸部36が嵌まり込み、段差面30に段差面34が径方向で重ね合わされ、係合部が形成される。これにより、係合凹部32と係合凸部36とによって位置決め手段28が構成されており、中心軸が相互に一致させられて径方向で位置合わせされた状態で、下側補助板20と上側補助板22が重ね合わされるようになっている。なお、位置決め手段28は、上下補助板22、20の外周面よりも内周側に位置して設けられ、それにより、上下補助板22、20、ひいては研磨装置12が大型化しないようにしている。

10

【0058】

このような構造とされた研磨パッド用補助板10を備えた研磨装置12にあっては、図1に示されているように、回転定盤14の上面18に上下の補助板22、20からなる研磨パッド用補助板10を固着せしめて装着すると共に、上側補助板22の上面に研磨パッド16を固着支持せしめた状態で、回転定盤14を回転駆動させて基板等の被加工物に対してCMP（化学機械研磨）を施すようにされる。そして、かかる研磨装置12は、特定構造の研磨パッド用補助板10を備えていることにより、以下の如き特別な技術的效果を発揮し得る。

【0059】

20

先ず、図2に示されているように、研磨パッド16を上側補助板22の上面に固着させたまま、上側補助板22を、第一の固着手段24により回転定盤14に固着された下側補助板20から取り外すことにより、研磨パッド16を回転定盤14から取り外すことが出来る。そして、回転定盤14から取り外して研磨パッド16の表面（研磨面）をクリーニングや再加工等する場合でも、研磨パッド16を上側補助板22の上面に固着させたままで行うことが出来る。これにより、回転定盤14に対する研磨パッド16の着脱の際や、研磨パッド16のクリーニングや再加工の際などは勿論、研磨パッド16の移送時や保存時等においても、上側補助板22による補強作用により研磨パッド16の曲がりや損傷を防止できて、研磨パッド16を良好な状態に保つことが出来る。

【0060】

30

また、研磨パッド16を上側補助板22と共に回転定盤14から取り外した際にも、回転定盤14の上面18には下側補助板20が残置される。そして、研磨パッド16を再び回転定盤14に装着する際、上側補助板22と下側補助板20との間に設けられた位置決め手段28により、上側補助板22ひいては研磨パッド16が下側補助板20ひいては回転定盤14に対して高精度に且つ容易に中心軸合わせされ得る。

【0061】

ここにおいて、かかる位置決め手段28を構成する係合凹部32と係合凸部36は、相互に嵌合された状態で殆ど隙間なく重ね合わされるようになっていることから、研磨パッド16の支持特性への悪影響が防止され得る。また、上下補助板22、20の外周部分のうち特に本実施形態では外周端縁部に係合部、言い換えると位置決め手段28が形成されており、研磨パッド16において研磨用の主たる領域となる径方向中間部分を外れていることから、係合凹部32と係合凸部36の嵌合部分に多少の隙間があっても、研磨特性に大きな問題が発生する程の研磨パッド16の支持特性への悪影響が回避され得る。

40

【0062】

しかも、位置決め手段28を構成する係合凹部32と係合凸部36は、上下補助板22、20の重ね合わせ面、換言すると、回転定盤14および研磨パッド用補助板10の外周端面よりも内周側に形成されており、上下補助板22、20の外周面上への突出が回避され得る。それ故、例えば図1、2に示されているように、研磨装置12において回転定盤14の外周側に近接して保護部材38が設置されている場合でも、そのような保護部材38への干渉を回避しつつ、位置決め手段28を備えた上下補助板22、20を備えた研磨

50

装置 12 が実現可能とされる。

【0063】

さらに、上述のように研磨パッド 16 の損傷を防止しつつ、正確な位置合わせ精度で速やかに研磨パッド 16 を回転定盤 14 に対して着脱することが出来る結果、研磨パッド 16 の着脱等の作業のために高価な研磨設備の稼働時間が不必要に制限されることがなくなり、研磨設備の稼働効率の向上ひいては基板等の生産効率（研磨作業効率）の向上が達成され得る。

【0064】

また、研磨パッド 16 の回転定盤 14 に対する着脱が容易に実現されることから、特別な熟練や知識がなくとも研磨パッド 16 の再利用が実用レベルで実現可能となる。即ち、例えば、基板等の被研磨物の品種切り替え等に際して一旦回転定盤 14 から外した研磨パッド 16 を再利用したり、劣化対策として別の加工装置で表面溝入れ等の再加工するのに一旦回転定盤 14 から取り外した研磨パッド 16 を再加工後に再利用したりすることなども、実用化レベルで検討することが可能となるのである。

【0065】

以上、本発明の第一の実施形態について説明してきたが、本発明の具体的構造はかかる第一の実施形態によって限定的に解釈されるものでない。上下補助板 22, 20 間において別構造の位置決め手段を備えた、本発明の別の実施形態の複数を以下に例示するが、これらの実施形態も本発明の構成を限定的に示すものでない。なお、以下の実施形態において、第一の実施形態と同様な構造とされた部材および部位については、それぞれ、第一の実施形態と同一の符号を各図中の対応する部位に記載することにより、それらの詳細な説明を省略する。

【0066】

図 3～4 には、本発明の第二の実施形態としての研磨パッド用補助板 40 を備えた研磨装置 42 が示されている。

【0067】

この研磨パッド用補助板 40 においては、下側補助板 20 の上面の外周部分を周方向に連続して延びる円環形状の溝によって係合凹部 44 が形成されている。一方、上側補助板 22 の下面の外周部分には、周方向に連続して延びる円環形状の突起によって係合凸部 46 が形成されている。この係合凸部 46 は、上側補助板 22 に一体形成されていても良いが、図示されているように、別体形成されていても良い。即ち、本実施形態では、上側補助板 22 の下面に開口して周方向に延びる円環形状の周溝 48 が形成されており、この周溝 48 に対して、別体形成された円環形状のブロックが軸方向一端側で嵌め込まれて固着されることにより係合凸部 46 が形成されている。

【0068】

下側補助板 20 の係合凹部 44 と、上側補助板 22 の係合凸部 46 は、何れも中心軸回りで対応する径方向位置に形成されており、上下補助板 22, 20 が重ね合わされた際、係合凹部 44 に対して係合凸部 46 が嵌め入れられることにより、上下補助板 22, 20 が相互に径方向で位置合わせされるようになっている。なお、本実施形態では、下側補助板 20 の係合凹部 44 における両側壁面と、上側補助板の係合凸部 46 における内外周面との、各対応する径方向の重ね合わせ面によって、二組の係合内周面および係合外周面が構成されている。

【0069】

図 5～6 には、本発明の第三の実施形態としての研磨パッド用補助板 50 を備えた研磨装置 52 が示されている。

【0070】

この研磨パッド用補助板 50 においては、下側補助板 20 の外周部分には、中心軸回りで全周に亘って延びる円形の係合内周面としての段差面 54 が形成されている。そして、この段差面 54 よりも外周側では下側補助板 20 の厚さ寸法が大きくされることで、下側補助板 20 の外周端縁に沿って周方向の全周に連続して延びる環状の係合凸部 56 が、下

側補助板 20 に一体形成されている。

【0071】

一方、上側補助板 22 の外周部分には、中心軸回りで全周に亘って延びる円形の係合外周面としての段差面 58 が形成されている。そして、この段差面 58 よりも外周側では上側補助板 22 の厚さ寸法が小さくされることで、上側補助板 22 の外周面に開放する切欠断面形状をもって周方向の全周に連続して延びる環状の係合凹部 60 が、上側補助板 22 に一体形成されている。

【0072】

さらに、下側補助板 20 の段差面 54 には雌ねじが形成されている一方、上側補助板 22 の段差面 58 には雄ねじが形成されている。そして、下側補助板 20 の段差面 54 の雌ねじに対して上側補助板 22 の段差面 58 の雄ねじを螺合させて、下側補助板 20 の段差面 54 と上側補助板 22 の段差面 58 とを径方向に重ね合わせることで、下側補助板 20 の上面に上側補助板 22 が重ね合わされるようになっている。また、かかる重ね合わせ状態では、上下補助板 22, 20 の段差面 58, 54 の螺着構造により、上下補助板 22, 20 を取り外し可能に固着する第二の固着手段 62 が構成されている。

【0073】

なお、このような螺着構造における雌雄ねじは、研磨装置 12 の回転定盤 14 に対して及ぼされる研磨時の回転反力を考慮して、ねじが緩まないようにねじ方向が設定されることが望ましい。

【0074】

図 7～8 には、本発明の第四の実施形態としての研磨パッド用補助板 64 を備えた研磨装置 66 が示されている。

【0075】

この研磨パッド用補助板 64 においては、下側補助板 20 の上面の中央部分で上方に向かって突出する円柱形状の係合凸部 68 が形成されている。この係合凸部 68 は、下側補助板 20 に一体形成されていても良いが、図示されているように、別体形成されていても良い。即ち、本実施形態では、下側補助板 20 の中心軸上に円形の嵌着凹所 70 が形成されており、この嵌着凹所 70 に対して、別体形成された円柱形状のブロックが軸方向一端側で嵌め込まれて固着されることにより係合凸部 68 が形成されている。一方、上側補助板 22 の下面の中央部分には、中心軸上で下面に開口する有底円形の係合凹部 72 が形成されている。なお、係合凸部 68 および係合凹部 72 は上下補助板 22, 20 のどちらに形成されていても良い。

【0076】

そして、上下補助板 22, 20 が重ね合わされた際、係合凹部 72 に対して係合凸部 68 が嵌め入れられることにより、上下補助板 22, 20 が相互に径方向で位置合わせされるようになっている。なお、本実施形態では、下側補助板 20 の係合凸部 68 の外周面と上側補助板 22 の係合凹部 72 の内周面とによって、係合外周面と係合内周面とが構成されている。

【0077】

図 9 には、本発明の第五の実施形態としての研磨パッド用補助板 74 を備えた研磨装置 76 が示されている。

【0078】

この研磨パッド用補助板 74 においては、下側補助板 20 の上面の外周部分で上方に向かって突出する円柱形状の係合凸部 78 が形成されている。この係合凸部 78 は、下側補助板 20 に一体形成されていても良いし、前記第四の実施形態における係合凸部のように入側補助板 20 に嵌着凹所を形成して別体のピンなどを圧入等で固着しても良い。また、図 10～11 に示されているように、かかる係合凸部 78 は、下側補助板 20 の外周部分で周方向で所定距離を隔てて互いに独立して複数形成されている。特に好適には、周方向で等間隔に且つ中心軸上の同一円上に位置して、それら複数の係合凸部 78 が形成される。

。

【0079】

一方、上側補助板22の下面の外周部分には、下側補助板20における複数の係合凸部78の形成位置に対して各対応する位置に、それぞれ、有底円形の係合凹部80が下方に向かって開口して形成されている。なお、係合凸部78および係合凹部80は上下補助板22、20のどちらに形成されていても良い。

【0080】

そして、上下補助板22、20が重ね合わされた際、係合凹部80に対してそれぞれ係合凸部78が嵌め入れられることにより、上下補助板22、20が相互に径方向で位置合わせされるようになっている。なお、本実施形態では、下側補助板20の係合凸部78の外周面と上側補助板22の係合凹部80の内周面とによって、下側補助板20および上側補助板22の外周部分に位置する係合外周面と係合内周面とが構成されている。

10

【0081】

特に本実施形態のように、周方向で独立した複数の係合凸部78と係合凹部80とからなる位置決め手段を採用することにより、重ね合わされた上下補助板22、20を径方向だけでなく周方向においても相互に位置決めすることが可能となる。

【0082】

なお、上側補助板22に形成される独立した複数の係合凹部80に代えて、上側補助板22の中心軸回りで周方向に連続して円形に延びる周溝を採用したり、或いは図12における本発明の第六の実施形態に示されているように、上側補助板22の外周部分を中心軸回りで全周に亘って延びる円形の段差面82を形成し、この段差面82よりも外周側の厚さ寸法を小さくすることで、上側補助板22の外周面に開放する切欠断面形状をもって周方向の全周に連続して延びる環状の係合凹部83を形成することも可能である。

20

【0083】

このように上側補助板22において、下側補助板20の係合凸部78の係合面を全周に亘って連続して形成することにより、上下補助板20、22の重ね合わせに際して、上下補助板20、22を相互に周方向で位置合わせする必要がなくなって装着作業を容易に行うことが可能となる。

【0084】

図13には、本発明の第七の実施形態としての研磨パッド用補助板84が示されている。

30

【0085】

この研磨パッド用補助板84においては、下側補助板20の外周面上の上側部分と、上側補助板22の外周面の下側部分とに、それぞれ小径部が設けられている。そして、これら上下補助板22、20が重ね合わされることにより、それぞれの小径部によって、上下補助板22、20間に跨がって所定幅で広がって周方向の全周に亘って延びる円環形状の收容凹所86が形成されている。

【0086】

また、下側補助板20の小径部下端には、溝状の係合凹部88が形成されている。この係合凹部88は、收容凹所86の底面において、下側補助板20の外周面に開口せしめられている。ここで、收容凹所86の底面とは、收容凹所86を構成する面のうち、上下補助板22、20に跨り、図13の上下方向に広がる環状の面を指す。一方、收容凹所86を構成する上側補助板22の小径部には、弾性材からなる板状の係合凸部90が、その基端部において固定ピン92で固定されて取り付けられている。この係合凸部90は、上下補助板22、20の外周面に形成された收容凹所86に收容配置されており、上側補助板22から下側補助板20の外周面上に延び出している。そして、係合凸部90の先端部分に形成された係合爪部94が、下側補助板20の小径部に形成された係合凹部88に対して係止され、係合凸部90の弾性に基づいて係止状態に保持されるようになっている。

40

【0087】

更にまた、このような係合凸部90が、上下補助板22、20の外周面上で周方向に所定距離を隔てて複数設けられている。そして、上側補助板22の外周面に取り付けられた

50

各係合凸部 90 が、下側補助板 20 の外周面に対して弾性的に押し付けられることで、上下補助板 22、20 が中心軸上で相互に位置決めする位置決め手段が構成されている。また、係合凸部 90 の係合爪部 94 が係合凹部 88 に係止されることにより、上下補助板 22、20 を重ね合わせ状態に保持せしめて固着力を及ぼす固着手段も構成されている。

【0088】

なお、上述の如き係合凹部 88 に係合する係合爪部 94 を備えた係合凸部 90 に代えて、例えば図 14 に示された本発明の第八の実施形態のように、上下補助板 22、20 間に跨がって延びて収容凹所 86 の底面に重ね合わされる連結板 100 を採用し、かかる連結板 100 の両端部分を上下補助板 22、20 の各一方の外周面に対して連結ピン 102、102 で固着することも可能である。なお、連結ピン 102、102 の少なくとも一方は下側補助板 20 又は上側補助板 22 に対して着脱可能とされることにより、上下補助板 22、20 の連結板 100 による連結が解除可能とされて、研磨パッド 16 が固着された上側補助板 22 の下側補助板 20 に対する着脱が許容されることとなる。

【0089】

また、第一～八の実施形態に示された両面テープ等からなる第一の固着手段 24 や第二の固着手段 26 は、上下補助板 22、20 や回転定盤 14 を取り外す際に、特定の部材側の固着面に保持されることが望ましい。これにより、取り外した状態での上下補助板 22、20 や第一及び第二の固着手段 24、26 の取り扱いが容易となるからである。なお、第一及び第二の固着手段 24、26 が何れの固着面に残るかは、第一の固着手段や第二の固着手段 24、26 自体における両面の固着力を相互に異ならせる他、固着される上下補助板 22、20 や回転定盤 14 の面粗度や材質等を相互に異ならせることなどによって設定することが可能である。

【0090】

特に、第一の固着手段 24 は、下側補助板 20 を取り外す際に下側補助板 20 側の固着面に保持されることが望ましく、それによって回転定盤 14 の上面 18 のメンテナンスが容易となる。一方、第二の固着手段 26 は、第一の実施形態における図 2 に示されているように、上側補助板 22 を取り外す際に上側補助板 22 側の固着面に保持されるようになっていても良いし、例えば図 15 に示す本発明の第九の実施形態のように、下側補助板 20 の上面に残るようにしても良い。なお、第二の固着手段 26 を上側補助板 22 側の固着面に保持させることにより、研磨パッド 16 の溝入れなどの再加工用装置の回転定盤に対して、取り外した上側補助板 22 を装着する際に、上側補助板 22 に保持された第二の固着手段 26 を利用して取り付けることも可能となる。一方、第二の固着手段 26 を下側補助板 20 側の固着面に保持させることにより、別の研磨パッド 16 を装着した別の上側補助板 22 を下側補助板 20 に装着する際に、下側補助板 20 に保持された第二の固着手段 26 を利用して取り付けることも可能となる。

【0091】

また、第一～七の実施形態に示された係合凹部 32、44、60、72、80、(83)、88 と係合凸部 36、46、56、70、78、90 は、下側補助板 20 側と上側補助板 22 側とにおいて相互に反対側に設けられていても良い。例えば本発明の第十の実施形態が図 16 に示されているように、第一の実施形態として図 1～2 に示された研磨パッド用補助板 10 に対して、その係合外周面を構成する段差面 30 と係合凹部 32 とを上側補助板 22 に形成する一方、係合内周面を構成する段差面 34 と係合凸部 36 とを下側補助板 20 に形成することも可能である。

【0092】

更にまた、第一～六の実施形態に示された係合凹部 32、44、60、72、80、(83) と係合凸部 36、46、56、70、78 において、相互に重ね合わされて上下補助板 22、20 を位置決めする係合凸部の外周面と係合凹部の内周面とに対して傾斜角を付すことも可能である。例えば本発明の第十一の実施形態が図 17 に示されているように、下側補助板 20 の外周部分に突出形成した係合凸部 36 の係合内周面としての段差面 34 に対して、係合凸部 36 が突出方向で次第に先細となる傾斜方向のテーパを付す一方、

上側補助板２２の外周部分に形成した係合凹部３２の係合外周面としての段差面３０に対して、段差面３４に対応する傾斜方向および傾斜角度のテーパを付すことができる。これにより、係合凸部３６を係合凹部３２に嵌め入れて上下補助板２２、２０を重ね合わせる作業を、両段差面３４、３０に付されたテーパを案内面として利用することで、一層容易に行うことが可能となる。

【００９３】

因みに、図１８に記載の本発明の第十二の実施形態や、図１９に記載の本発明の第十三の実施形態に示されているように、下側補助板２０の周方向で独立して複数形成される突起形状の係合凸部７８と、上側補助板２２の各対応する位置に形成される複数の穴形状の係合凹部８０とを採用する場合でも、係合凸部７８の突出先端部分の外周面に対して傾斜角を付して、先細形状のテーパ部１０４を形成することができる。なお、図１９では、下側補助板２０に形成された嵌着穴１０５に対して、別体形成された係止ピン１０６が圧入等で固着されて係合凸部７８が構成されており、かかる係止ピン１０６の下端にも、上端と同様なテーパ部１０４が付されている。これにより、係止ピン１０６に方向性が無くなって取り扱いが容易となると共に、嵌着穴１０５への圧入作業も容易となる。

【００９４】

また、図２０に示された本発明の第十四の実施形態では、上下補助板２２、２０の重ね合わせ状態で中心軸を合わせる位置決め手段の一種として、それら上下補助板２２、２０間に跨がって外挿される位置決めスリーブ１０８が示されている。この位置決めスリーブ１０８は、互いに略同じ外径寸法の円板形状とされた上下補助板２２、２０の外径寸法と同じか僅かに大きな内径寸法を有しており、金属材や合成樹脂材によって形成されている。このような位置決めスリーブ１０８を、上下補助板２２、２０の重ね合わせに際して用いて、位置決めスリーブ１０８内で上下補助板２２、２０を重ね合わせるとにより、上下補助板２２、２０を中心軸合わせしつつ軸方向に重ね合わせて、第二の固着手段２６で相互に固着することができる。それ故、上下補助板２２、２０を重ね合わせて相互に固着せしめた後で、位置決めスリーブ１０８を取り外すことが出来るのであり、それによって、上下補助板２２、２０を、外周面上に突出する位置決め手段を有しない状態で且つ正確な位置合わせ状態で相互に固着することが可能となる。

【００９５】

更にまた、図２１に示された本発明の第十五の実施形態では、上下補助板２２、２０の重ね合わせ状態で重ね合わせ方向に跨がって延びるスリット状の係合溝１１０が形成されている。この係合溝１１０は、上下補助板２２、２０の外周面に開口して径方向内方に所定深さを有しており、上下補助板２２、２０の周方向で互いに独立して複数設けられている。そして、かかる係合溝１１０に対して、外周面の開口部からプレート形状の係合板１１２が嵌め入れられることにより、かかる係合板１１２で上下補助板２２、２０が相互に位置決めされると共に、相互に連結状態とされている。なお、かかる係合板１１２は、上下補助板２２、２０と別体形成されているが、例えば上下補助板２２、２０の何れか一方において他方に向かって突出する形状をもって一体形成されていても良い。その場合には、係合溝１１０は、当該他方の補助板にだけ形成されることとなる。

【００９６】

さらに、図２２に示された本発明の第十六の実施形態では、上側補助板２２の下面に開口する係合凹部としての嵌合凹部１１４が形成されている。特に本実施形態では、かかる嵌合凹部１１４が、上側補助板２２の中心軸回りで周方向に連続して延びる環状溝として形成されている。一方、下側補助板２０には、上側補助板２２に重ね合わされる上面において上方に突出する係合凸部としての嵌合凸部１１６が形成されている。なお、本実施形態では、かかる嵌合凸部１１６が、嵌合凹部１１４に対応する環状凸部として形成されている。そして、上下補助板２２、２０の重ね合わせ状態で、嵌合凸部１１６が嵌合凹部１１４に入り込んで位置せしめられるようになっている。

【００９７】

また、嵌合凸部１１６は中空構造とされており、嵌合凸部１１６の内部において外部空

間に対して密閉された流体溜 1 1 8 が形成されている。更に、この流体溜 1 1 8 を画成する嵌合凸部 1 1 6 の壁部は、少なくとも内周壁と外周壁が径方向に向かって膨出変形可能にされている。具体的には、例えば嵌合凸部 1 1 6 をゴム弾性体などで形成することによって、径方向内方に膨出可能な内周壁と径方向外方に膨出可能な外周壁とが実現可能である。

【0098】

更にまた、下側補助板 2 2 には、流体溜 1 1 8 に連通して、径方向外方に延び出し外周面に開口する流体通路 1 2 0 が形成されていると共に、この流体通路 1 2 0 の外周端開口部に加圧ねじ 1 2 2 がねじ込まれている。また、加圧ねじ 1 2 2 で封止された流体通路 1 2 0 と流体溜 1 1 8 からなる密閉領域には、オイルなどの非圧縮性流体が充填されている。

10

【0099】

これにより、加圧ねじ 1 2 2 をねじ込むことにより、流体通路 1 2 0 を通じて流体溜 1 1 8 の内圧を上昇させて、流体溜 1 1 8 の内周壁および外周壁を外方に膨出させることが出来る。その結果、嵌合凸部 1 1 6 が拡張されて、嵌合凹部 1 1 4 の内面に押し付けられ、相互の摩擦等によって上下補助板 2 2, 2 0 を相互に位置決めすると共に固着力も及ぼし得るようになっている。

【0100】

なお、上側補助板 2 2 を下側補助板 2 0 から取り外すに際しては、加圧ねじ 1 2 2 を緩ませる方向に回転操作して下側補助板 2 0 の外周側に移動させることにより、流体溜 1 1 8 の圧力を低下させて嵌合凸部 1 1 6 の嵌合凹部 1 1 4 への押し付け力を解除することができる。

20

【0101】

その他、一々列挙はしないが、本発明は当業者の知識に基づいて種々なる変更、修正、改良などを加えて実施することが可能であり、例えば、係合凸部と係合凹部の係合部分に Oリングやシール材を装着して上下補助板の重ね合わせ面等への異物の侵入を防止することも可能である。

【0102】

また、上述の二層構造の補助板 2 0, 2 2 に加えて、更に補助板を積層状態で且つ固着手段で固着せしめて追加することも可能である。このように第三層の補助板を採用することで、弾性支持状態を実現したり、或いは中間層を使い捨てる等の態様も可能となる。

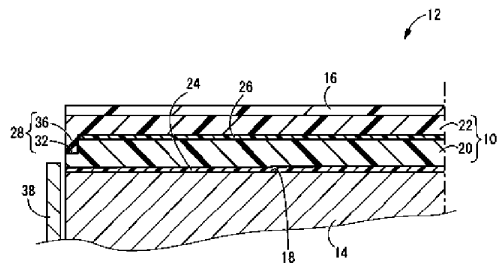
30

【符号の説明】

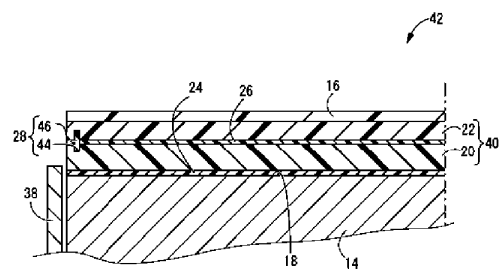
【0103】

1 0, 4 0, 5 0, 6 4, 7 4, 8 4 : 研磨パッド用補助板、1 2, 4 2, 5 2, 6 6, 7 6 : 研磨装置、1 4 : 回転定盤、1 6 : 研磨パッド、1 8 : 上面、2 0 : 下側補助板、2 2 : 上側補助板、2 4 : 第一の固着手段、2 6, 6 2 : 第二の固着手段、2 8 : 位置決め手段、3 0, 5 8 : 段差面 (係合外周面)、3 2, 4 4, 6 0, 7 2, 8 0, 8 8 : 係合凹部、3 4, 5 4 : 段差面 (係合内周面)、3 6, 4 6, 5 6, 6 8, 7 8, 9 0 : 係合凸部、3 8 : 保護部材

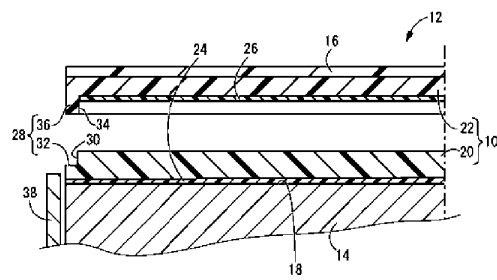
【図 1】



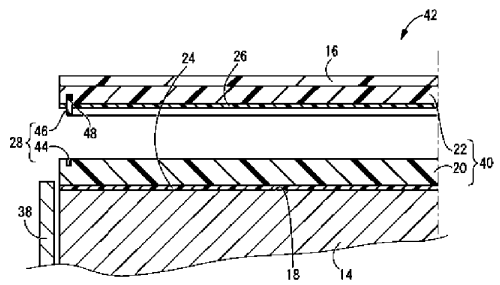
【図 3】



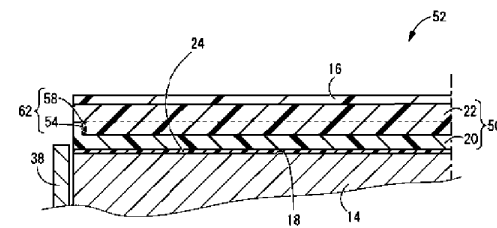
【図 2】



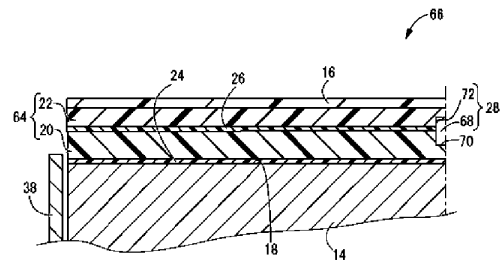
【図 4】



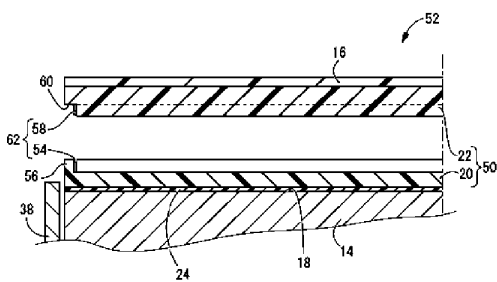
【図 5】



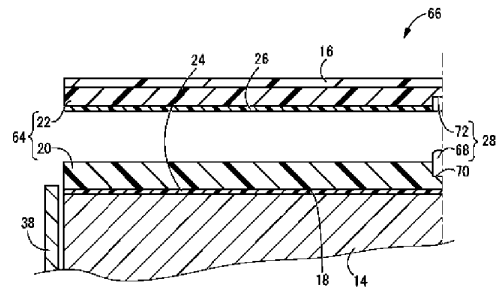
【図 7】



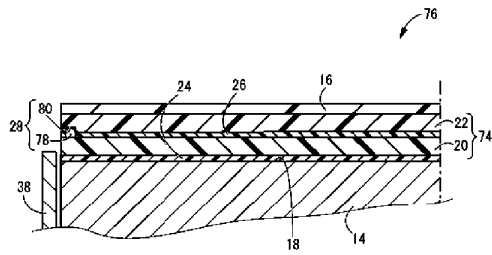
【図 6】



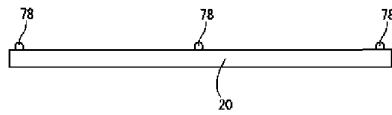
【図 8】



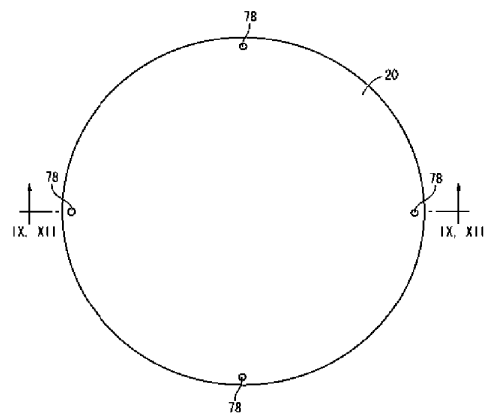
【図 9】



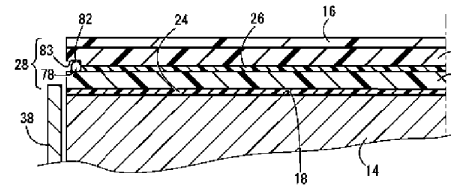
【図 10】



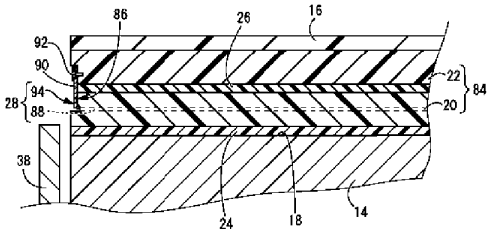
【図 11】



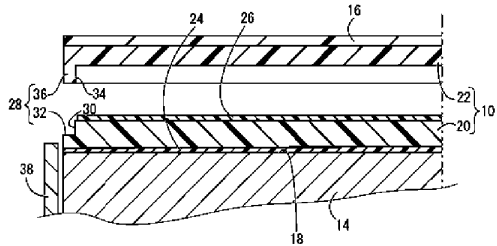
【図 12】



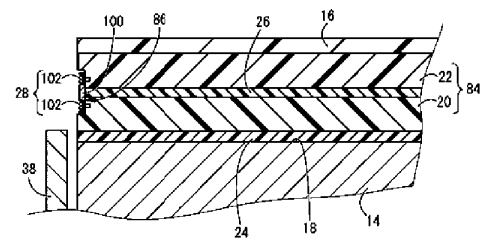
【図 13】



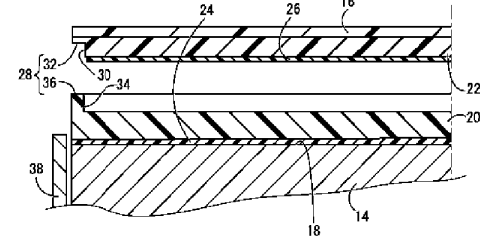
【図 15】



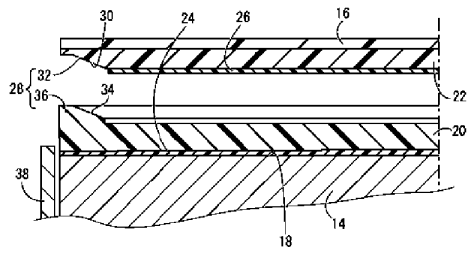
【図 14】



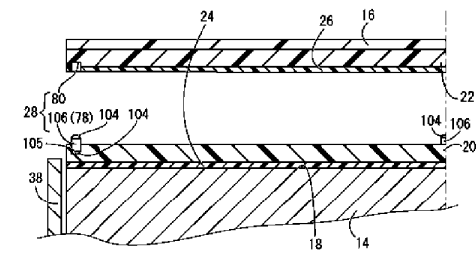
【図 16】



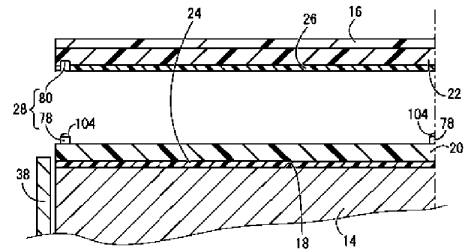
【图 17】



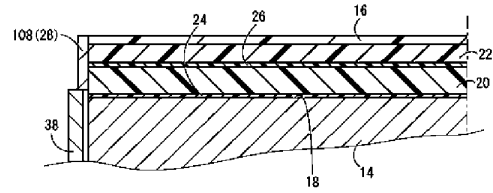
【图 19】



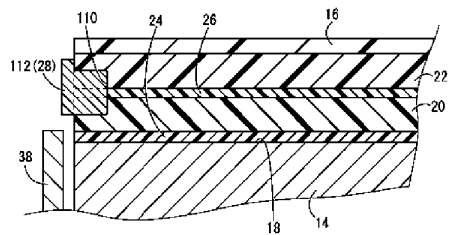
【 例 1 8 】



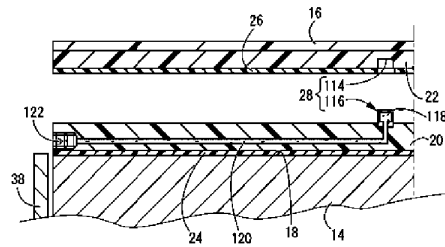
【图 20】



【图 2-1】



【图 2-2】



フロントページの続き

(56)参考文献 特開平08-118231 (JP, A)
特開平07-328915 (JP, A)

(58)調査した分野(Int. Cl., DB名)
B24B 37/12
H01L 21/304

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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

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

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

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

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

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☐ the text is approved as submitted by the applicant
☒ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 15C
☒ 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 contaminants in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2016/043709

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61B5/15 A61B5/153 A61B5/154
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHER LLOYD [US]; BR) 29 December 2011 (2011-12-29) paragraph [0070] figure 15 abstract	1-5, 7-13, 15-20
A	----- 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
	----- -/-	



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

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

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

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

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

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

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

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

11 October 2016

Date of mailing of the international search report

19/10/2016

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Schultz, Ottmar

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2016/043709

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures -----	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures -----	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14 -----	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures -----	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18 -----	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2016/043709

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

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.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.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.
PCT/US2016/043709

International filing date (day/month/year)
22.07.2016

Priority date (day/month/year)
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 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will 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 notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

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

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

Name and mailing address of the ISA:



European Patent Office
Gitschiner Str. 103
D-10958 Berlin
Tel. +49 30 25901 - 0
Fax: +49 30 25901 - 840

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Schultz, Ottmar

Telephone No. +49 30 25901-0



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/043709

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 43bis.1(a))
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/043709

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	<u>2, 6, 7, 11, 14</u>
	No: Claims	<u>1, 3-5, 8-10, 12, 13, 15-20</u>
Inventive step (IS)	Yes: Claims	<u>6, 14</u>
	No: Claims	<u>1-5, 7-13, 15-20</u>
Industrial applicability (IA)	Yes: Claims	<u>1-20</u>
	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]; FISCHER 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 and 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.

+++++

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

Alonna Norberg, MD

Norman C. Christopher, MD

Maria L. Ramundo, MD

John R. Bower, MD

Shirley A. Berman, RN

FEVER IS THE PRIMARY COMPLAINT in up to 20% of children presenting to emergency departments,¹ and bacteremia is the source of fever in 1.5% to 2.3% of these patients.^{2,3} Blood culture is the criterion standard for identifying children with bacteremia⁴⁻⁷; however, false-positive blood cultures are common and may add significantly to health care costs.⁸⁻¹¹ High rates of contamination are common among pediatric patients, likely related to difficulties inherent to phlebotomy in young patients.¹² To minimize the number of venipunctures in children, blood culture specimens are obtained simultaneously with intravenous catheter placement in many emergency departments. The impact of using intravenous catheters to obtain blood cultures is unclear.¹³⁻¹⁶ We hypothesized that the blood culture contamination rate would be less when blood culture specimens were obtained from a remote site rather than through a newly inserted intravenous catheter.

METHODS

A preintervention and postintervention observational study of patients who had a blood culture obtained as part of their routine emergency department course

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

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

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

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

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

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

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

JAMA. 2003;289:726-729

www.jama.com

was conducted. Patients 18 years old or younger who presented to the emergency department at a free-standing tertiary care children's hospital that evaluates more than 65 000 children annually and required a blood culture as part of their routine care were eligible. Pa-

tients were identified by computerized search of the hospital database.

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

Author Affiliations: Divisions of Emergency Medicine (Drs Norberg, Christopher, Ramundo, and Ms Berman) and Infectious Diseases (Dr Bower), Department of Pediatrics, Children's Hospital Medical Center of Akron, Akron, Ohio; and Departments of Emergency Medicine and Pediatrics, Northeastern Ohio

Universities College of Medicine, Rootstown (Drs Norberg, Christopher, Ramundo, and Bower).

Corresponding Author and Reprints: Norman C. Christopher, MD, Division of Emergency Medicine, Children's Hospital Medical Center, One Perkins Square, Akron, OH 44308 (e-mail: Nchristopher@CHMCA.org).

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

Baseline Phase

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

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

Postintervention Phase

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

Classification of Blood Culture Isolates

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

Table 1. Patient Demographics

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

Abbreviation: IQR, interquartile range.

month of the study ([number of contaminated specimens $\times$ 100]/[number of blood cultures obtained]). The mean blood culture contamination rate and the upper and lower control limits were established based on the preintervention data, with control limits representing ± 3 SD from the mean.¹⁶⁻¹⁸

RESULTS

RESULTS

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

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

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

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

Data Analysis

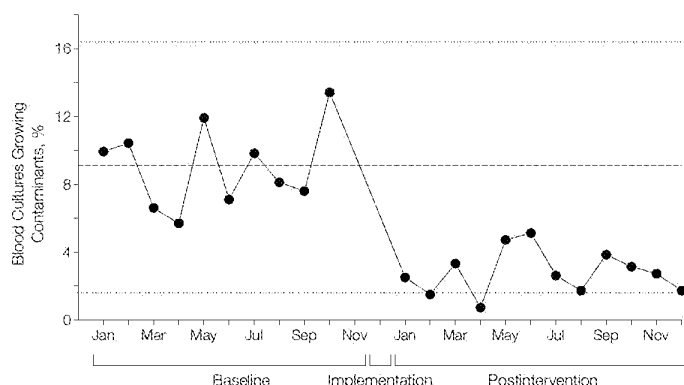
Data were analyzed using STATA Version 7.0 (Dallas, Tex, 2001). Univariate analysis was performed unless stated otherwise. Pearson χ^2 was used to analyze categorical data. Descriptive analysis of continuous data was performed. $P < .05$ was the level of significance.

Statistical process control methodology was also used to examine the impact of the intervention over time. A run chart was constructed showing the blood culture contamination rate for each

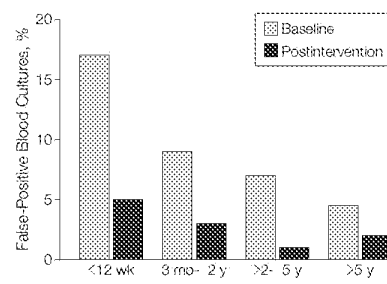
Table 2. Blood Culture Contaminants in the Baseline and Postintervention Periods of Study

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

*There were 191 contaminated specimens growing 243 organisms in the baseline phase and 58 contaminated specimens growing 65 organisms in the postintervention phase of the study.

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

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

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

postintervention period was 2.8%, with a true-positive rate of 2.3%. Using a 2-sample test of proportions, the contaminated blood culture rate in the postintervention phase is significantly

decreased when compared with the baseline phase ($P < .001$). The increase in true-positive rates did not reach statistical significance ($P = .20$).

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

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

COMMENT

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

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

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

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

site suggest that the 2 techniques are essentially equivalent. Smart and Baggoley²² failed to show a difference in the contamination rate in 940 adult patients randomized to phlebotomy by either venipuncture or by placement of an intravenous catheter. Isaacman and Karasic¹⁴ prospectively evaluated a convenience sample of 99 pediatric patients, each of whom had 2 blood cultures obtained, one by venipuncture and one through a newly inserted intravenous catheter. The authors demonstrated a low contamination rate with both techniques, concluding that newly inserted intravenous catheters offer an alternative to a separate venipuncture procedure in patients requiring blood culture. The small number of patients enrolled and the impact of the nursing staff's awareness of the study protocol may have biased the results.

On the other hand, a study by Ramsbook et al¹⁵ suggested that blood culture contamination rates were decreased when using dedicated phlebotomy compared with those obtained through a newly inserted intravenous catheter. Importantly, this study demonstrated the highest contamination rates in patients younger than 3 months of age, regardless of the collection method used, a finding confirmed in our study. Because staff members were aware of ongoing data collection, the potential effect on their phlebotomy technique is unknown.

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

control group was included to account for secular temporal changes.

Obtaining blood cultures from a separate site requires the patient to undergo an additional procedure for phlebotomy, but the overall benefit in terms of costs associated with a high contamination rate is likely to be substantial. During the baseline period, there were 6 contaminated specimens for every true-positive blood culture, compared with a ratio of 1.2:1 after implementation of the intervention. If subsequent patient management is based on preliminary blood culture results, false-positive test results will result in repeat emergency department visits, unnecessary medical interventions, unnecessary antibiotic therapy, and even hospital admission. One study⁹ found that 26% of children followed as outpatients who had false-positive blood cultures were hospitalized unnecessarily, and that unnecessary use of antibiotics was significantly increased in the presence of false-positive blood culture results. Additional costs that are more difficult to quantify include staff effort and time required to arrange follow-up for patients, exposure of patients to unnecessary procedures, and cost and inconvenience related to repeat emergency department and/or hospital visits.^{10,24}

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

REFERENCES

- Nelson ES, Walsh K, Fleisher GR. Spectrum and frequency of pediatric illness presenting to a general community hospital emergency department. *Pediatrics*. 1992;90:5-10.
- Alpern ER, Alessandrini EA, Bell LM, et al. Occult bacteremia from a pediatric emergency department: current prevalence, time to detection, and outcome. *Pediatrics*. 2000;106:505-511.
- Lee GM, Harper MB. Risk of bacteremia for febrile young children in the post-Haemophilus influenza type B era. *Arch Pediatr Adolesc Med*. 1998;152:624-628.
- Baraff LJ, Bass JW, Fleisher GR, et al. Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. *Ann Emerg Med*. 1993;22:1188-1210.
- Kupperman N. Occult bacteremia in young febrile children. *Pediatr Clin North Am*. 1999;46:1073-1109.
- Downs SM, McNutt RA, Margolis PA. Management of infants at risk for occult bacteremia: a decision analysis. *J Pediatr*. 1991;118:11-20.
- Yamamoto LG, Worthley RG, Melish ME, et al. A revised decision analysis of strategies in the management of febrile children at risk for occult bacteremia. *Am J Emerg Med*. 1998;16:193-207.
- Weinbaum FI, Lavie S, Danek M, et al. Doing it right the first time: quality improvement and the contaminant blood culture. *J Clin Microbiol*. 1997;35:563-565.
- Thuler LCS, Jenicek M. Impact of a false positive blood culture result on the management of febrile children. *Pediatr Infect Dis J*. 1997;16:846-851.
- Bates DW, Goldman L. Contaminant blood culture and resource utilization: the true consequences of false-positive results. *JAMA*. 1991;265:365-369.
- Lieu TA, Schwartz JS. Strategies for diagnosis and treatment of children at risk for occult bacteremia: clinical effectiveness and cost effectiveness. *J Pediatr*. 1991;118:21-29.
- Campos JM. Detection of blood stream infections in children. *Eur J Clin Microbiol Infect Dis*. 1989;8:815-824.
- Tonnesen A, Feuier MA, Lockwood WR. Cultures of blood drawn by catheter vs venipuncture. *JAMA*. 1976;235:1877-1879.
- Isaacman DJ, Karasic RB. Utility of collecting blood cultures through newly inserted intravenous catheters. *Pediatr Infect Dis J*. 1990;9:815-818.
- Ramsbook C, Childers K, Cron SG, Nirken M. Comparison of blood culture contamination rates in a pediatric emergency room: newly inserted intravenous catheters versus venipuncture. *Infect Control Hosp Epidemiol*. 2000;21:649-651.
- Schwab RA, DelSordo SA, Cunningham MR, Craven K, Watson WA. Using statistical process control to demonstrate the effect of operational interventions on quality indicators in the emergency department. *J Healthc Qual*. 1999;21:38-41.
- Benneyan JC. Statistical quality control methods in infection control and hospital epidemiology, part I: introduction and basic theory. *Infect Control Hosp Epidemiol*. 1998;19:194-214.
- Benneyan JC. Statistical quality control methods in infection control and hospital epidemiology, part II: chart use, statistical properties, and research issues. *Infect Control Hosp Epidemiol*. 1998;19:265-283.
- Humble C. Caveats regarding the use of control charts. *Infect Control Hosp Epidemiol*. 1998;19:865-868.
- Mylotte JA, White D, McDermott C, Hodan C. Nosocomial bloodstream infection at a veterans hospital: 1979-1987. *Infect Control Hosp Epidemiol*. 1989;10:455-464.
- Koska MT. Using CQI methods to lower postsurgical wound infection rates. *Hospitals*. 1992;66:62-64.
- Smart D, Baggoley C. Effect of needle changing and intravenous cannula collection on blood culture contamination rates. *Ann Emerg Med*. 1993;22:1164-1168.
- Komberg A. Evaluation of false positive blood cultures: guidelines for early detection of contaminated cultures in febrile children. *Pediatr Emerg Care*. 1994;10:20-23.
- Segal GS, Chamberlain JA. Resource utilization and contaminated blood cultures in children at risk for occult bacteremia. *Arch Pediatr Adolesc Med*. 2000;154:469-473.



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**

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." Thereaf-

ter, the American Association of Blood Banks (AABB) proposed new standards to help mitigate transfusion of units that were contaminated with bacteria. Adopted with a final implementation date of March 1, 2004, the AABB Standard reads "*The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components.*"

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

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

* Christopher D. Hillyer, MD, Emory University School of Medicine, Atlanta, GA
Cassandra D. Josephson, MD, Emory University School of Medicine, Atlanta, GA
Morris A. Blajchman, MD, FRCP(C), McMaster University and Canadian Blood Services, Hamilton, Ontario, Canada
Jaroslav G. Vostal, MD, PhD, Center for Biologics Evaluation and Research, FDA
Jay S. Epstein, MD, Center for Biologics Evaluation and Research, FDA
Jesse L. Goodman, MD, MPH, Center for Biologics Evaluation and Research, FDA

including improving donor skin disinfection, removal of first aliquot of donor blood, pre-transfusion detection of bacteria, reducing recipient exposure, and pathogen reduction/inactivation. In the final sections, Drs. Vostal, Epstein and Goodman describe the regulations and regulatory approaches critical to the appropriate implementation of a bacterial contamination screening and limitation program including their and/or the FDA's input on prevention of bacterial contamination,

Bacterial 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 96-06³ at www.AABB.org), proposed new standards (December 2002) to help mitigate transfusion of units that were

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.

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-

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 Cross¹⁸ 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 Scale²² 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

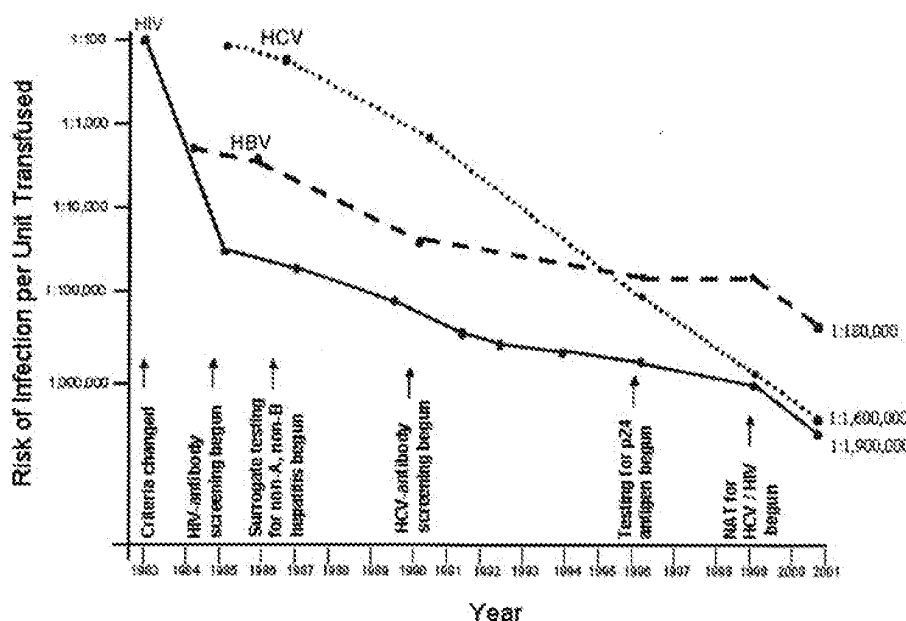


Figure 1. New test implementation and declining risk of viral infections from transfusion.²⁰

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

Modified by M.P. Busch from table in AuBuchon JP, Birmeyer 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.

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

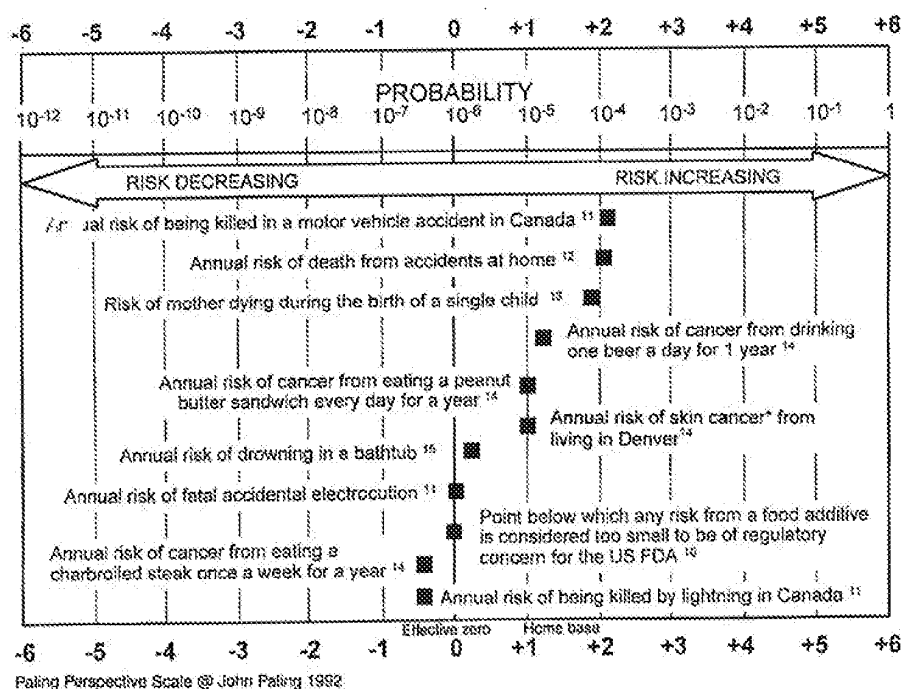
Term Used	Risk Range	Example	Risk Estimate
High	> 1:100	(A) Transmission to susceptible household contacts of measles and chickenpox (A) Transmission of HIV from mother to child (Europe)	1:1–1:2 1:6
Moderate	1:100–1:1,000	(D) Smoking 10 cigarettes per day (D) All natural causes, age 40	1:200 1:850
Low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

fusion (often termed NiSHOTS; see **Table 2**) which dramatically outweigh the residual risk of TT-infectious diseases.²⁴ However, the agents that are known to be transfusion transmitted, and those that “might be” are described in **Table 3**, for it is only upon this backdrop that a decision can be made on the relative value of new technologies and their ability to abrogate the agents,

**Figure 2. Risks with which the public is comfortable.**

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

Abbreviations: FDA, Food and Drug Administration.²²

Reprinted with permission from Lee DH, Paling JE, Blajchman MA. A new tool for communicating transfusion risk information. *Transfusion*. 1998;38:184-188.

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 10⁶/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

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

Agent	Transfusion Transmission
Parasites	
Malaria	Rare cases
Babesia	Occasional cases, endemic
<i>T. cruzii</i>	Occasional cases, US
<i>T. gondii</i>	Rare cases
Leishmania	Rare cases (< 5 worldwide)
Bacteria	
Contaminants	Approximately 1:3,000 platelet units
Specific Agents	
<i>T. pallidum</i>	Rare cases
<i>B. burgdorferi</i>	No known cases
<i>E. chaffeensis</i>	No known cases
<i>E. cytophagophila</i>	One possible case
<i>R. rickettsii</i>	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 lymphotropic 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.

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 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 Product 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	Dziedzickowski 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	Dziedzickowski et al ³⁹	1 per 7,080	0
Overall	<i>n</i> = 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 (10⁶) 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.

(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, contami-

nation 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

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 CO₂ production by bacteria.
 7. Measure O₂ 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.

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-de-

rived 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 $\mu\text{mol/L}$ 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

alcohol followed by tincture of iodine that have been thought to be superior to those using povidone 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 ⁵¹Cr or ¹¹¹In 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

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 (Bio-Merieux, 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 CO₂ in the sample culture, while the other detects a decrease in pO₂. *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

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

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

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

Regulatory summary

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

Concluding Comments

Septic transfusion reactions associated with the use of contaminated blood products remain a very significant adverse event. Nonetheless, clear-cut approaches to reduce the frequency of such events are appearing. A

wide variety of measures have been proposed in order to reduce the frequency of transfusion-associated septic reactions and many of these measures are being actively investigated, and in some countries being instituted.^{15,76} Thus, the potential reduction in the risk of transfusion-associated septic reactions is a realistic possibility in the foreseeable future.

REFERENCES

1. Jacobs MR, Palavecino E, Yamotvian R. Don't bug me: The problem of bacterial contamination of blood components—challenges and solutions. *Transfusion*. 2001;41:1131-1134.
2. Goodnough LT, Shander A, Brecher ME. Transfusion medicine: looking to the future. *Lancet*. 2003;361:161-169.
3. Association Bulletin #96-6: Bacterial contamination of blood components. AABB Faxnet, No. 294, American Association of Blood Banks, Bethesda, MD 1996.
4. Dykstra A, Jacobs J, Yamotvian R. Prospective microbiologic surveillance (PMS) of random donor (RDP) and single donor apheresis platelets (SDP). *Transfusion*. 1998;38:104S.
5. Ness PM, Braine HG, King K, et al. Single donor platelets reduce the risk of septic transfusion reactions. *Transfusion*. 2001;41:857-861.
6. Yomtovian R, Lazarus HM, Goodnough LT, et al. A prospective microbiologic surveillance program to detect and prevent the transfusion of bacterially contaminated platelets. *Transfusion*. 1993;33:902-909.
7. Dodd RY. Adverse consequence of blood transfusion: quantitative risk estimates. In: Nance ST, ed. *Blood supply: risks, perceptions and prospects for the future*. Bethesda, MD: American Association of Blood Banks; 1994:1-24.
8. Klein HG, Dodd RY, Ness PM, Fratantoni JA, Nemo GJ. Current status of microbial contamination of blood components: summary of a conference. *Transfusion*. 1997;37:95-101.
9. FDA workshop. Bacterial Contamination of Platelets. 1999. Available at: <http://www.fda.gov/cber/minutes/bact092499.pdf>. Accessed 7/20/03.
10. FDA workshop. Safety and Efficacy of Methods for Reducing Pathogens in Cellular Blood Products Used in Transfusion. 2002; Available at: <http://www.fda.gov/cber/minutes/pathtrans080702.pdf>.
11. Kuehnert MJ, Roth VR, Haley NR, et al. Transfusion-transmitted bacterial infection in the United States, 1998 through 2000. *Transfusion*. 2001;41:1493-1499.
12. Blajchman MA. Bacterial contamination and proliferation during the storage of cellular blood products. *Vox Sang*. 1998;74:155-159.
13. Dodd RY. Bacterial contamination and transfusion safety: experience in the United States. *Transfus Clin Biol*. 2003;10:6-9.
14. Brecher ME, Hay SN. The role of bacterial testing of cellular blood products in light of new pathogen inactivation technologies. *Blood Therapies Med*. 2003;3:49-55.
15. Blajchman MA. Incidence and significance of the bacterial contamination of blood components. *Dev Biol*. 2002;108:59-67.
16. Association Bulletin #02-8: Update on Bacterial Contamination of Platelet Units. American Association of Blood Banks, Bethesda, MD 2002.
17. AdvaMed. Ensuring blood safety and availability in the U.S.: technological advances, cost, and challenges to payment. Lewin Group. *Transfusion (Suppl)*. 2003; 43:41S-46S.
18. American Red Cross: Blood Safety and Availability. 2002;

- Available at: <http://www.redcross.org/services/biomed/blood/supply/intro.html>. Accessed 7/20/03.
19. Dodd RY, Notari EP, Stramer SL. Current prevalence and incidence of infectious disease markers and estimated window-period risk in the American Red Cross blood donor population. *Transfusion*. 2002;42:975-979.
 20. AuBuchon JP, Birkmeyer JD, Busch MP. Safety of the Blood Supply in the United States: Opportunities and Controversies. *Ann Intern Med*. 1997;127:904-909.
 21. Calman KC. Cancer: science and society and the communication of risk. *BMJ*. 1996; 313:799-802.
 22. Lee DH, Paling JE, Blajchman MA. A new tool for communicating transfusion risk information. *Transfusion*. 1998;38:184-188.
 23. Hunter N, Foster J, Chong A, et al. Transmission of prion diseases by blood transfusion. *J Gen Virol*. 2002;83:2907-2914.
 24. Association Bulletin #01-4: Non-infectious Serious Hazards of Transfusion—NiSHOTs. American Association of Blood Banks; Bethesda, MD 2001.
 25. Hillyer CD, Lankford KV, Roback JD, Gillespie TW, Silberstein LE. Transfusion of the HIV-seropositive patient: immunomodulation, viral reactivation, and limiting exposure to EBV (HHV-4), CMV (HHV-5), and HHV-6, 7, and 8. *Transfus Med Rev*. 1999;13:1-17.
 26. Brecher ME, Holland PV, Pineda AA, Tegtmeier GE, Yomtovian R. Growth of bacteria in inoculated platelets: implications for bacteria detection and the extension of platelet storage. *Transfusion*. 2000;40:1308-1312.
 27. Borden CW, Hall WH. Fatal transfusion reactions from massive bacterial contamination of blood. *N Engl J Med*. 1951;245:760-765.
 28. Goldman M, Blajchman MA. Bacterial contamination. In: Popovsky M, ed. *Transfusion Reactions*. 2nd ed. Bethesda, MD: AABB; 2001:133-159.
 29. Sazama K. Reports of 355 transfusion-associated deaths: 1976 through 1985. *Transfusion*. 1990;30:583-590.
 30. Honig CL, Bove JR. Transfusion-associated fatalities: Review of Bureau of Biologics reports 1976-1978. *Transfusion*. 1980;20:653-661.
 31. Blajchman MA, Ali AM. Bacteria in the blood supply: An overlooked issue in transfusion medicine. In: Nance, SJ, ed. *Blood Safety: Current Challenges*. Bethesda, MD: AABB; 1992: 213-228.
 32. Morrow JF, Braine HG, Kickler TS, et al. Septic reactions to platelet transfusions. *JAMA*. 1991;266:555-558.
 33. Barrett BB, Anderson JW, Anderson KC. Strategies for the avoidance of bacterial contamination of blood components. *Transfusion*. 1993;33:228-233.
 34. Yomtovian R, Lazarus HM, Goodnough LT, et al. A prospective microbiologic surveillance program to detect and prevent the transfusion of bacterially contaminated platelets. *Transfusion*. 1993;33:902-909.
 35. Chiu EKW, Yuen KY, Lie AKW, et al. A prospective study on symptomatic bacteremia from platelet transfusion and its management. *Transfusion*. 1994;34:950-965.
 36. Blajchman MA, Ali A, Lyn P, et al. A prospective study to determine the frequency of bacterial contamination in random donor platelet concentrates [abstract]. *Blood*. 1994;84(suppl):529.
 37. Leiby DA, Kerr KL, Compos JM, Dodd RY. A prospective analysis of microbial contaminants in outdated random-donor platelets from multiple sites. *Transfusion*. 1997;37:259-263.
 38. Blajchman MA, Ali A, Lyn P, et al. Bacterial surveillance of platelet concentrates: quantitation of bacterial load. [Abstract]. *Transfusion*. 1997;37(suppl):74S.
 39. Dzieczkowski JS, Barrett BB, Nester D, et al. Characterization of reactions after exclusive transfusion of white cell-reduced cellular blood components. *Transfusion*. 1995;35:20-25.
 40. Aubuchon JP, Cooper LK, Leach MF, et al. Experience with universal bacterial culturing to detect contamination of apheresis platelet units in a hospital transfusion service. *Transfusion*. 2002;42:855-861.
 41. Perez P, Salmi LR, Follea G, et al. Determinants of transfusion-associated bacterial contamination: Results of the French BACTHEM Case-Control Study. *Transfusion*. 2001;41:862-872.
 42. Grossman BJ, Kollins P, Lau PM, et al. Screening blood donors for gastrointestinal illness: a strategy to eliminate carriers of *Yersinia enterocolitica*. *Transfusion*. 1991;31:500-501.
 43. Theakston EP, Morris AJ, Streat SJ, et al. Transfusion-transmitted *Yersinia enterocolitica* infection in New Zealand. *Aust N Z J Med* 1997; 127:62-67.
 44. Beresford AM. Transfusion reaction due to *Yersinia enterocolitica* and review of other reported cases. *Pathology*. 1995;27:133-135.
 45. Goldman M, Blajchman MA. Blood product-associated bacterial sepsis. *Transfus Med Rev*. 1991;5:73-83.
 46. Schiffman RB, Pindur A. The effect of skin disinfection materials on reducing blood culture contamination. *Am J Clin Pathol*. 1993;99:536-538.
 47. Gibson T and Norris W. Skin fragments removed by injection needles. *Lancet*. 1958;2:983-985.
 48. Anderson KC, Lew MA, Gorgone BC, et al. Transfusion-related sepsis after prolonged platelet storage. *Am J Med*. 1986;81:405-411.
 49. McDonald CP, Hartley S, Orchard K, et al. Fatal *Clostridium perfringens* sepsis from a pooled platelet transfusion. *Trans Med*. 1998;8:19-22.
 50. Hogman CF, Engstrand L. Serious bacterial complications from blood components—how do they occur? *Trans Med*. 1998;8:1-3.
 51. Hogman CF, Fritz H, Sandberg L. Posttransfusion *Serratia marcescens* septicemia. *Transfusion*. 1993;33:189-191.
 52. Goldman M, Roy G, Frechette N, et al. Evaluation of donor skin disinfection methods. *Transfusion*. 1997;37:309-312.
 53. McDonald CP, Lowe P, Roy A, et al. Evaluation of donor arm disinfection techniques. *Vox Sang*. 2001;80:135-141.
 54. Bruneau C, Perez P, Chassaigne M et al. Efficacy of a new collection procedure for preventing bacterial contamination of whole-blood donations. *Transfusion*. 2001;41:74-81.
 55. de Korte D, Marcelis JH, Soeterboek AM. Determination of the degree of bacterial contamination of whole-blood collections using an automated microbe-detection system. *Transfusion*. 2001;41:815-818.
 56. Wagner SJ, Robinette D, Friedman LI, Miripol J. Diversion of initial blood flow to prevent whole-blood contamination by skin surface bacteria: an in vitro model. *Transfusion*. 2000;40:335-338.
 57. Ben-Hur E, Moor ACE, Margolis-Nunno H, et al. The photo-decontamination of cellular blood components: Mechanisms and use of photosensitization in transfusion medicine. *Transfus Med Rev*. 1997;10:15-22.
 58. Corash L. Inactivation of viruses, bacteria, protozoa, and leukocytes in platelet concentrates: Current research perspectives. *Transfus Med Rev*. 1999;13:18-30.
 59. Chapman J. Progress in improving the pathogen safety of red cell concentrates. *Vox Sang*. 2000;78(suppl 2):203-204.
 60. Goodrich RP. The use of riboflavin for the inactivation of

- pathogens in blood products. *Vox Sang.* 2000;78(suppl 2):211-215.
61. Lin L, Cook DN, Wieseahn GP et al. Photochemical inactivation of viruses and bacteria in platelet concentrates by use of a novel psoralen and long-wavelength ultraviolet light. *Transfusion.* 1997;37:423-435.
 62. FDA Blood Products Advisory Committee, December. 2002. Available at: <http://www.fda.gov/ohrms/dockets/ac/02/transcripts/3913t1.rtf>. 7/20/03
 63. de Korte D, Marcelis JH, Verhoeven AJ, Soeterboek AM. Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections. *Vox Sang.* 2002;83:13-16.
 64. Kopko PM, Holland PV. Mechanisms of severe transfusion reactions. *Transfusion Clin Bio.* 2001;8:278-281.
 65. Brecher ME, Means N, Jere CS, Heath DG, Rothenberg SJ, Stutzman LC. Evaluation of an automated culture system for detecting bacterial contamination of platelets: an analysis with 15 contaminating organisms. *Transfusion.* 2001;41:477-482.
 66. Vostal JG, Mondoro TH. Liquid cold storage of platelets: a revitalized possible alternative for limiting bacterial contamination of platelet products. *Trans Med Rev.* 1997;11:286-295.
 67. Hoffmeister KM, Felbinger TW, Falet H, et al. The clearance mechanism of chilled blood platelets. *Cell.* 2003;112:87-97.
 68. FDA draft guidance. For platelet testing and evaluation of platelet substitutes. 1999; Available at: <http://www.fda.gov/cber/gdlns/platelet.htm>. 7/20/03
 69. Wagner SJ, Robinette D. Evaluation of swirling, pH, and glucose tests for the detection of bacterial contamination in platelet concentrates. *Transfusion.* 1996;36:989-993.
 70. Brecher ME, Wong EC, Chen SE, Vampola C, Rocco RM. Antibiotic-labeled probes and microvolume fluorimetry for the rapid detection of bacterial contamination in platelet components: a preliminary report. *Transfusion.* 2000;40:411-413.
 71. Brecher ME, Hogan JJ, Boothe G, et al. Platelet bacterial contamination and the use of a chemiluminescence-linked universal bacterial ribosomal RNA gene probe. *Transfusion.* 1994;34:750-755.
 72. AuBuchon JP, Cooper LK, Leach MF, Zuaro DE, Schwartzman JD. Experience with universal bacterial culturing to detect contamination of apheresis platelet units in a hospital transfusion service. *Transfusion.* 2002;42:809-811.
 73. Winslow RM. Current status of blood substitute research: towards a new paradigm. *J Intern Med.* 2003;253:508-517.
 74. Wagner SJ, Moroff G, Katz AJ, Friedman LI. Comparison of bacteria growth in single and pooled platelet concentrates after deliberate inoculation and storage. *Transfusion.* 1995;35:298-302.
 75. FDA Blood Products Advisory Committee, March. 2003. Available at: <http://www.fda.gov/ohrms/dockets/ac/03/transcripts/3940t1.htm>. 7/20/03
 76. Engelfriet CP, Reesink HW, Blajchman MA, et al. International Forum: Bacterial contamination of blood components. *Vox Sang.* 2000;78:59-67.

New Closed IV Catheter System

A. VAN ZUNDERT

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

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

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

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

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

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

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

A. van Zundert, M.D., Ph.D., F.R.C.A., Catharina Hospital – Brabant Medical School, Eindhoven, The Netherlands.

Correspondence address: Prof. dr. A. van Zundert, Department of Anesthesiology, ICU & Pain Therapy, Catharina Hospital – Brabant Medical School, Michelangelolaan 2, Eindhoven, 5623 EJ, The Netherlands. E-mail: zundert@jae.nl.

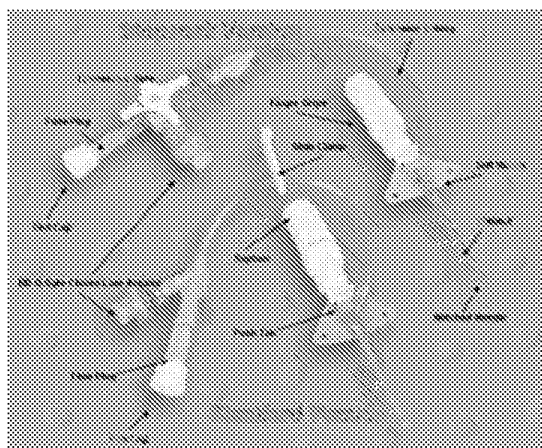


Fig. 1. — The new integrated completely closed IV catheter system (BD Nexiva™). Shown are two versions: the top one has a three-way valve to which the Q-Syte™ is attached; the bottom one, with the Q-Syte™ closed Luer Lok access. Both devices have a flow plug for venting out the air during insertion.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

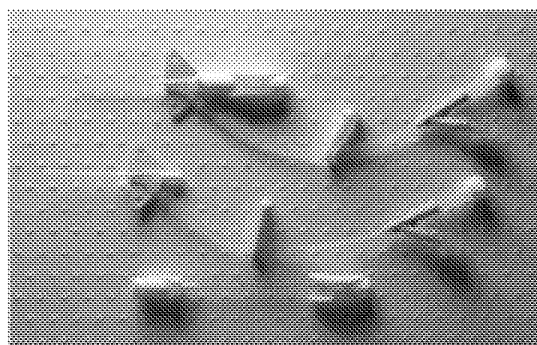


Fig. 2. — Non-activated (top) and activated (bottom) versions of the BD Nexiva™.

The white portion (catheter body) is used for gripping the device. Once inserted into the vein, the catheter body is withdrawn completely and the needle is automatically sheathed (see lower picture), thus protecting from accidental needle stick injuries.

Table 1

Characteristics of IV needles

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

Table 2

Advantages of new IV cannula over previous IV catheters

<ul style="list-style-type: none"> • rapid reliable blood flashback via notched needles • reduced pain to patient* • lower infection and thrombotic risks** • simplicity in dressing, resistant to snagging • needle-less access to ports • more closed to bacterial entry • reduced needlestick risk • minimal blood exposure for the user

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

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

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

Once the needle is withdrawn and has been shielded it cannot be inserted into the cannula again. Furthermore, the hub, after needle with-

drawal, cannot be accessed by any device (e.g. syringe, tubing, plug). At this point, the extension line has to be clamped before removing the vent plug and either connecting the infusion line or flushing and attaching the white cap. The three-way stopcock version (Fig. 1) does not have a clamp. The valve serves this function.

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

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

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

In conclusion, our experience with the BD Nexiva™ peripheral IV catheter indicates that it provides better IV access to peripheral veins, with less pain to patients and with rapid and clearly visible primary and secondary flashback of blood. By

having all the add-ons (valve, extension tube, stopcock) already integrated into the device, infection risk should be reduced. Above all this IV cannula prevents needlestick and blood exposure, which is a dramatic improvement in an era where risks of infections are increasingly due to blood exposure.

References

1. Peters J. L., Fisher C., Mehtar S., *Intravenous stopcocks and injection ports (letter)*, LANCET, **II**, 701-702, 1980.
2. Oberhammer E. P., *Contamination of injection ports on intravenous cannulae (letter)*, LANCET, **II**, 1027-1028, 1980.
3. Pilsworth R., *Risk from cannulae used to maintain intravenous access (letter)*, BR. MED. J., **282**, 222-223, 1981.
4. Gaukroger P. B., Roberts J. G., Manners T. A., *Infusion thrombophlebitis: A prospective comparison of 645 vialon and teflon cannulae in anaesthetic and postoperative use*, ANESTH. INTENS. CARE, **16**, 265-271, 1988.
5. Jaquot C., Fauvage B., Bru J. P., Croize J., Calop J., *Effect of type of material on thrombophlebitis risk with peripheral venous catheters*, ANN. FR. ANAESTH. REANIM., **8**, 3-7, 1989.
6. McKee J. M., Shell J. A., Warren T. A., Campbell V. P., *Complications of intravenous therapy: A randomised prospective study - vialon vs teflon*, J. INTRAVEN. NURS., **129**, 288-295, 1989.

Effect of Portal Venous Blood Flow Diversion on Portal Pressure

David S. Zimmon, Richard E. Kessler

J Clin Invest. 1980;65(6):1388-1397. <https://doi.org/10.1172/JCI109803>.

Research Article

To anticipate the hepatic vascular response to portacaval anastomosis, we studied portal pressure during diversion of portal blood through a temporary extracorporeal umbilical vein to saphenous vein shunt. The relationship of portal pressure to shunted flow was approximately linear. In five schistosomiasis patients (controls) portal diversion to 1,250 ml/min gave portal pressure-shunted flow curve slopes ranging from 0.13 to 0.57 cm water/100 ml per min (0.31 ± 0.18 , mean $\pm$ SD). In 17 cirrhotic patients with portal hypertension a continuum of slopes was observed from within mean ± 2 SD of control (type A) to larger slopes (type B) indicating failure of portal pressure regulation. When portal flow was augmented by shunting from saphenous vein to portal vein, cirrhotic patients who had slopes less than mean ± 2 SD of controls during diversion (type A) exhibited a compliant system with small increases in portal pressure, whereas type B patients had significantly greater pressure increases. Selective investigations suggested that changes in portal pressure provoked compensatory changes in hepatic arterial blood flow that tended to maintain portal pressure at a set point. Type B patients demonstrated failure of this mechanism to varying degrees.

After end-to-side portacaval shunt, seven type A cirrhotic patients maintained residual intrahepatic venous pressure unchanged from prior portal pressure, whereas six type B patients had a significant decrease. Residual intrahepatic venous pressure was measured after portacaval shunt [...]

Find the latest version:

<http://jci.me/109803-pdf>



Effect of Portal Venous Blood Flow Diversion on Portal Pressure

DAVID S. ZIMMON and RICHARD E. KESSLER, *Medical Service, Gastroenterology
Section and the Surgical Service, New York Veterans Administration Medical
Center, and the New York University School of Medicine, New York 10010*

ABSTRACT To anticipate the hepatic vascular response to portacaval anastomosis, we studied portal pressure during diversion of portal blood through a temporary extracorporeal umbilical vein to saphenous vein shunt. The relationship of portal pressure to shunted flow was approximately linear. In five schistosomiasis patients (controls) portal diversion to 1,250 ml/min gave portal pressure-shunted flow curve slopes ranging from 0.13 to 0.57 cm water/100 ml per min (0.31 ± 0.18 , mean $\pm$ SD). In 17 cirrhotic patients with portal hypertension a continuum of slopes was observed from within mean ± 2 SD of control (type A) to larger slopes (type B) indicating failure of portal pressure regulation. When portal flow was augmented by shunting from saphenous vein to portal vein, cirrhotic patients who had slopes less than mean ± 2 SD of controls during diversion (type A) exhibited a compliant system with small increases in portal pressure, whereas type B patients had significantly greater pressure increases. Selective investigations suggested that changes in portal pressure provoked compensatory changes in hepatic arterial blood flow that tended to maintain portal pressure at a set point. Type B patients demonstrated failure of this mechanism to varying degrees.

After end-to-side portacaval shunt, seven type A cirrhotic patients maintained residual intrahepatic venous pressure unchanged from prior portal pressure, whereas six type B patients had a significant decrease. Residual intrahepatic venous pressure was measured after portacaval shunt in 40 cirrhotic patients who were followed

for as long as 9 yr (median survival 4.0 yr). The 13 patients who developed chronic encephalopathy had significantly lower pressure (21.1 ± 4.4 cm, mean $\pm$ SD) and shorter survival (median 0.6 yr) than the other 27 patients (32.6 ± 5.3 cm, 5.0 yr). The preoperative estimation of portal pressure-diverted portal flow curve slope anticipates the hepatic vascular response to portacaval anastomosis and identifies a group of patients in whom loss of portal blood flow results in a low residual intrahepatic venous pressure that is associated with early death and chronic encephalopathy.

INTRODUCTION

The increase in hepatic vascular resistance accompanying liver disease raises portal pressure and diminishes portal venous flow to the liver. Prograde portal flow may cease or even become retrograde as portal-systemic collaterals divert portal flow (1, 2). Increased hepatic arterial flow is presumed to compensate for reduced portal flow and account for normal values of total hepatic flow observed occasionally in cirrhotic patients with portal hypertension and portal systemic collateral circulation (3-6). An abrupt compensatory increase in hepatic arterial flow has been documented during acute portal flow diversion at the creation of a portacaval anastomosis (7-9). These facts imply homeostatic activity of the splanchnic vascular system to maintain portal pressure and/or hepatic blood flow when portal blood flow decreases (10-12). To evaluate the splanchnic hemodynamic response to portal blood flow diversion, we studied the response of portal pressure to acute incremental diversion of portal venous blood through a temporary extracorporeal umbilical vein to saphenous vein portal-systemic shunt (13).

METHODS

Subjects. In the schistosomiasis patients (Table I) described here, portal pressure and liver function tests including Bromsulfalein retention were normal. These patients were assumed to have normal splanchnic hemodynamics. They

This work was presented in part at the annual meetings of the American Association for the Study of Liver Disease, 4 November 1970, 1 November 1972, and 8 November 1978, Chicago Illinois; of the American Federation of Clinical Research, 12 May 1971 and 29 April 1973; and of the American College of Surgery, 14 November 1969. Abstracts were published in *Gastroenterology*, **60**: 169 (1970), **64**: 166 (1973), **75**: 996 (1978); *Clin. Res.* **19**: 406 (1971), **21**: 529 (1973); and *Surg. Forum*, **22**: 351-352 (1971), **23**: 334-336 (1972). Address reprint requests to Dr. Zimmon.

Received for publication 11 April 1977 and in revised form 31 January 1980.

were studied after heparinization, but before the administration of tartar emetic (13). The initial 17 cirrhotic patients (Table I) with documented esophageal varices were studied after umbilical vein catheterization for measurement of portal pressure (14), for umbilical vein angiography before portal-systemic shunt surgery (15), or for the establishment of an extracorporeal portal-systemic shunt to reduce portal pressure and control life threatening variceal hemorrhage (16). Subsequent patients evaluated before and after or during portacaval shunt received internal therapeutic end-to-side portacaval anastomosis after endoscopically documented variceal hemorrhage (17). In our institution umbilical vein catheterization is the preferred method for evaluating the portal circulation because of its safety and reliability (18). Informed consent was obtained from all subjects. These studies were performed under a research protocol approved by the Research Committee of the Veterans Administration Medical Center, New York, and the New York University School of Medicine.

Except where specifically indicated all procedures were performed under local anesthesia. The umbilical vein was catheterized extraperitoneally (19) and connected to a saphenous catheter by a silicon rubber tube with an occluding roller pump (solid state varistaltic pump; Manostat Corp., New York) and cannulating square wave electromagnetic flow meter (model E-3000; Statham Instruments Inc., Oxnard, Calif.). The umbilical vein catheter has an integral molded wire to prevent collapse and a second 1-mm lumen within its wall to allow continuous recording of portal pressure (model 1956 SP-BJBI, U. S. Catheter and Instrument Co., Glen Falls, N. Y.). Pres-

ures were recorded using Statham P37 perfused strain gauges that permitted a continuous infusion of heparin (0.1 mg/min). Electrical mean pressures were used to obviate respiratory fluctuation. Zero pressure level was taken as 12 cm above the couch.

The hepatic vein was catheterized from an antecubital vein (20, 21). The achievement of a wedged position was confirmed by the demonstration of an arterial pulse in the pressure recording, by the identity of wedged hepatic venous pressure and portal pressure, and by injection of radiopaque contrast at the completion of a study.

Flow through the extracorporeal shunt was monitored by the cannulating square wave flow meter calibrated for zero flow with the shunt occluded. In vitro calibration for flow rates to 3,000 ml/min with pumped whole blood and occluding roller pump yields an accuracy of $\pm 5\%$. The pumping circuit was primed with 200 ml of normal saline.

Procedure. After catheter placement and shunt construction, portal pressure was recorded and portal to systemic shunting initiated at 100 ml/min. Stabilization of pump rate required 5–10 s. By that time, pressures were stable and were recorded. Shunting was increased in 100 ml/min increments. When maximum hepatofugal flow was achieved as evidenced by portal vein flutter, shunting was stopped and pressure recorded. Systemic to portal shunting was then begun in 100 ml/min increments until limited by saphenous vein flutter. The shunting portion of the procedure required 15–20 min.

The response of portal pressure to shunting at different

TABLE I
Effect of Portal Venous Flow Diversion or Augmentation on Portal Pressure

Case	Diagnosis etiology	Documentation	Ascites (-4+)	Direction portal flow	Basal PP	Hepatofugal pumping			Hepatopetal pumping		
						Max flow	Pressure change	Pressure-flow slope	Max flow	Pressure change	Pressure-flow slope
					cm	ml/min	cm	cm/100 ml	ml/min	cm	cm/100 ml
1	C,A	Biopsy	0	Prograde	37	1,100	0	0.00	500	+2	+0.40
2	S	—	—	Prograde	15	750	-1	-0.13			
3	S	—	—	Prograde	11	1,200	-2	-0.17			
4	C,A	Biopsy	+1	Prograde	35	1,450	-3	-0.20			
5	S	—	—	Prograde	15	1,250	-3.5	-0.28			
6	C	Biopsy	3+	Prograde	27	1,600	-6	-0.38	1,000	+3	+0.30
7	S	—	—	Prograde	14	1,100	-5	-0.43			
8	C,A	Biopsy	0	Retrograde	37	900	-4	-0.44			
9	C,A	Biopsy	0	Prograde	36	1,000	-5	-0.50	700	+1	+0.14
10	S	—	—	Prograde	8	700	-4	-0.57	1,100	0	0.0
11	C,A	Biopsy	2+	Retrograde	39	1,700	-10	-0.59	1,200	+1	+0.08
12	C,A	W,biopsy	0	Prograde	35	2,500	-15	-0.60	900	+2.5	+0.27
13	C,HEM	Biopsy	+1	Prograde	29	1,500	-9	-0.60	600	+3	+0.50
14	C,A	Biopsy	0	Prograde	39	1,500	-13	-0.87	1,000	+16	+1.6
15	C,A	W,biopsy	2+	Prograde	42	600	-6	-1.00	1,400	+6	+0.43
16	C,A	Biopsy	1+	Prograde	26	1,000	-10	-1.00	750	+9	+1.20
17	C,CR	Biopsy	1+	Prograde	29	850	-18	-2.11			
18	C,A	Autopsy	0	Prograde	37	900	-28	-3.10	700	+11	+1.57
19	C,A	Biopsy	2+	Prograde	39	900	-31	-3.44	700	+9	+1.28
20	C,A	Biopsy	4+	Prograde	35	800	-31	-3.87			
21	C,A,HEP	Biopsy	0	Prograde	55	1,100	-48	-4.36			
22	C,A	Biopsy	0	Prograde	35	500	-30	-6.00	500	+18	+3.6

Abbreviations used in this table: C, cirrhosis; S, schistosomiasis; A, alcoholism; HEM, hemachromatosis; HEP, hepatoma; CR, cryptogenic; W, wedged hepatic venous pressure; PP, portal pressure; max, maximum.

vascular volumes was studied after phlebotomy accomplished by draining the extracorporeal circuit into a sterile infusion bottle containing 20 mg of heparin. 1 liter of blood was withdrawn in 3 min. After studying the response of portal pressure to shunting the blood was reinfused. Then, for volume expansion 5% dextran or blood was infused. Final volume was dictated by the patient's clinical status (22). Since the elapsed time for phlebotomy and volume expansion was <15 min, vascular volume shifts were considered to be negligible. Therefore, changes in blood volume were calculated from the measured quantity withdrawn or infused.

At the completion of a study the direction of portal venous flow (prograde or retrograde) was determined by observing the course of a gentle hand injection of 50% sodium diazotrate (Hypaque, Winthrop Laboratories, Sterling Drug Co., New York) through the primary lumen of the umbilical vein catheter (3). Radiopaque contrast media were not administered before pressure or flow measurements because of their effect on systemic and splanchnic hemodynamics (23). Finally, a pressure injection with serial x rays was used to visualize the portal vasculature (15).

Definition of residual intrahepatic venous pressure. Wedged hepatic venous pressure and portal pressure measured by umbilical vein catheterization are identical in patients with cirrhosis when the portal circulation is intact (24). Simultaneous measurement of wedged hepatic venous pressure and umbilical portal pressure in two cirrhotic patients during shunting of portal flow agreed within ± 1 cm water (Fig. 1). After disconnection of the extrahepatic portal venous system from the liver by end-to-side portacaval shunt, residual intrahepatic venous pressure was measured by wedged hepatic venous catheterization or by umbilical vein catheterization of the intrahepatic portal vein. The extrahepatic portal venous system drains into the vena cava.

Construction of portal pressure-shunted portal flow curves. Curves constructed for controls with *Schistosoma mansoni* infections and cirrhotic patients with portal pressure-shunted portal flow curve slopes < -0.67 cm water/100 ml per min diverted flow were linear (Figs. 1 and 2) and allow a simple arithmetic expression of slope as change in pressure/100 ml per min shunted flow. Cirrhotic patients with steep slopes have a smaller range of flow and curves that are increasingly convex (Figs. 2 and 3). For the purpose of this paper, the arithmetic portal pressure-shunted portal flow curve slope is derived from the sum change in pressure divided by maximum flow before vein flutter was detected by palpation of the shunt or pumping was stopped because of increased portal pressure. As indicated, certain patients were studied at laparotomy under anesthesia or during resuscitation from hemorrhage. These circumstances provide unique opportunities to gain physiologic insights in man but undoubtedly influence to a greater or lesser extent the data obtained. Therefore, we confined data in Table I describing the control (schistosomiasis) patients and values in cirrhotic patients with portal hypertension for portal pressure-shunted portal flow curve slope to subjects studied without anesthesia or laparotomy when hemodynamically stable.

Statistical significance was determined with the Wilcoxon two sample ranked test, unpaired *t* test, and log rank test (25, 26).

RESULTS

Schistosomiasis (control) subjects

During portal to systemic shunting averaging 1,000 ml/min (range, 700–1,350) in five schistosomiasis pa-

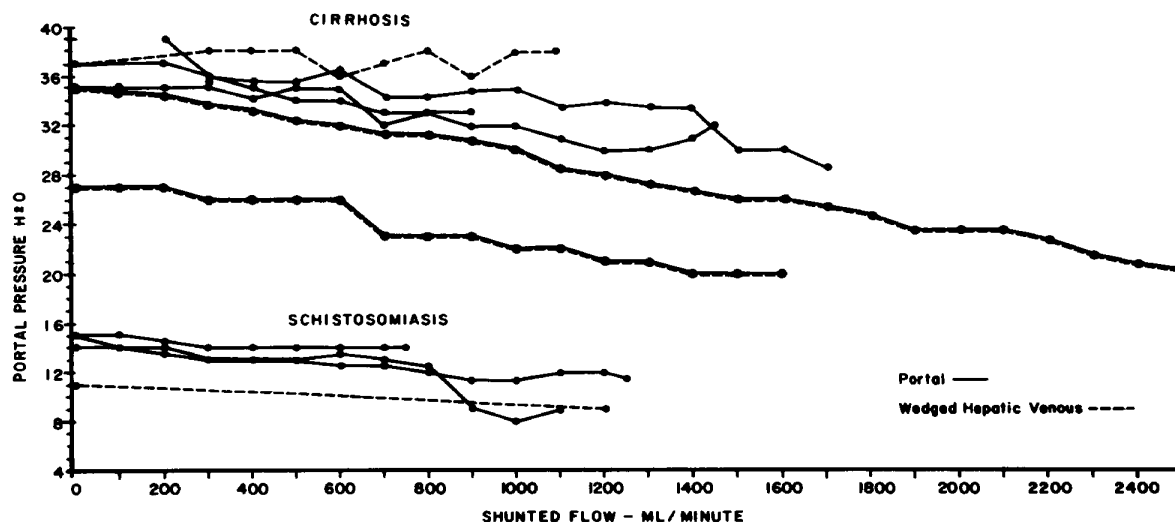


FIGURE 1 Response of portal pressure to portal venous blood flow diversion in type A cirrhotic patients and control subjects. Portal pressure (centimeters water) is plotted against volume of shunted portal venous flow (milliliters per minute) diverted through an umbilicosaphenous shunt. Six representative cirrhotic patients are shown in order of decreasing basal portal pressure (case Nos. 11, 1, 8, 4, 12, and 6, Table I). Four representative controls (2, 5, 7, and 3, Table I) are shown in order of decreasing basal portal pressure. The solid line indicates portal pressure measured through an umbilical vein catheter in the left portal vein. The interrupted line indicates portal pressure measured by wedged hepatic venous catheterization. The combined solid and interrupted lines in two cirrhotic patients (11, 1, Table I) indicate simultaneous measurement of portal and wedged hepatic venous pressures.

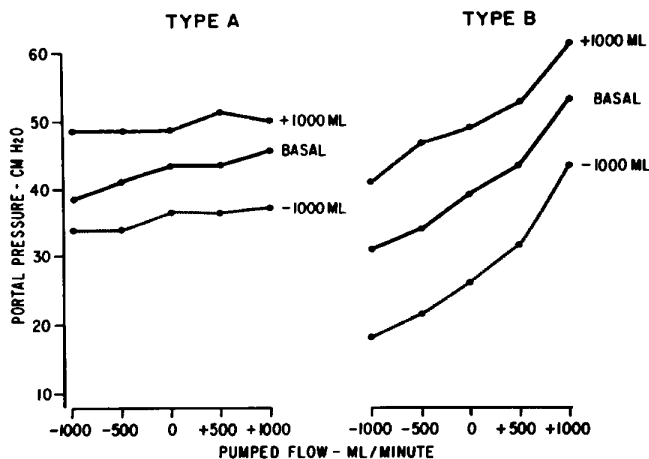


FIGURE 2 Effect of changes in blood volume on portal pressure and portal pressure-shunted flow curve slope. In a single type A patient (left) basal portal pressure of 43 cm was reduced to 36 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000 ml-volume load in addition to replacement of the 1,000-ml phlebotomy, whereas portal pressure-shunted flow slope varied from 0.35 to 0.15 to 0.10 cm/100 ml per min shunted flow, respectively. In a single type B patient, a basal portal pressure of 39 cm was reduced to 26 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000-ml volume load after replacement of the phlebotomy, whereas portal pressure-shunted flow curve slope varied from 1.15 to 1.25 to 1.05, respectively.

tients portal pressure decreased an average of 3.1 cm water (range, 1–4). Portal pressure-shunted portal flow slope averaged -0.31 ± 0.18 (mean $\pm$ SD) cm water/100 ml per min diverted flow (range -0.13 to -0.57) (Table I).

Cirrhotic patients

In cirrhotic patients ($n = 17$) with portal hypertension, the response to portal diversion was varied and the portal pressure-shunted portal flow slope ranged from -0.0 to -6.0 . In patient 1 (Table I) portal pressure was unchanged by portal diversion of 1,000 ml/min, whereas in patient 22 (Table I) portal pressure fell to central venous levels with diversion of only 500 ml/min (Table I). A histogram (Fig. 4, upper) of portal pressure-shunted portal flow slope during diversion in cirrhotic patients with portal hypertension shows a continuum from slopes similar to *S. mansoni* patients with normal portal pressure (Fig. 4, hatched bars) to extremely high values. A relationship between basal portal pressure and portal pressure-shunted portal flow slope is not apparent (Table I). The lack of correlation between portal pressure and portal pressure-shunted portal flow slope arises, in part, from the influence of blood volume on portal pressure (Fig. 2). Increasing or decreasing blood volume produces a corresponding shift in portal pressure (22) with little change in portal pressure-shunted portal flow slope.

Definition of type A and B cirrhotic patients

Type A cirrhotic patients (Figs. 1 and 2) are defined as those with portal pressure-shunted portal flow slopes < -0.67 cm/100 ml per min (control mean $\pm$ 2 SD). Type B cirrhotic patients have portal pressure-shunted portal flow slopes in excess of -0.67 cm/100 ml per min diverted flow (Table I, Figs. 2 and 3). In the initial 17 patients studied (Table I) the mean basal portal pressure (34.4 ± 4.2 cm of water, mean $\pm$ SD) of eight cirrhotic patients with portal pressure-shunted flow slopes for portal flow diversion within the mean $\pm$ 2 SD of the five control (schistosomiasis) patients was not significantly different from the mean basal portal pressure (37.4 ± 8.3 cm) of the nine cirrhotic patients with greater slopes. Similarly, in a group of 13 patients clinically considered candidates for portacaval anastomosis (Fig. 5), the basal portal pressures of seven type A patients were not significantly different from the six type B patients. The 23 cirrhotic patients with endoscopically documented bleeding esophageal varices classified as type A or type B when hemodynamically stable under local anesthesia had basal portal pressure ranging from 55 to 26 cm. The 55-cm value (Table I, No. 21) occurred in a patient with hepatoma. Although the three highest values (55, 45, and 42 cm) and the two lowest values (26 and 28 cm) were found in type B patients, the pressures of type A patients were not significantly different (Wilcoxon rank test) from type B.

Mechanism for maintenance of portal pressure during portal venous flow diversion

Hepatic arterial response to extracorporeal portal diversion. Hepatic arterial flow was measured at laparotomy for portacaval anastomosis by noncannulating square wave electromagnetic flow meter in two type A cirrhotic patients before and during diversion of 1 liter/min. Hepatic arterial flow increased 40 and 46%.

Spontaneous total retrograde portal flow in type A portal hypertension. Two (Nos. 8 and 11) of 17 cirrhotic patients described had total retrograde portal venous flow (Table I) (3). Both had type A portal hypertension with portal pressure-shunted portal flow slopes of 0.44 and 0.59 cm/100 ml per min. The presence of total retrograde portal flow implies sufficient portal-systemic collateral vessels for egress from the splanchnic chamber of all splenic and mesenteric inflow and a portion of hepatic arterial flow. The most likely source for additional splanchnic inflow to maintain portal pressure during portal diversion in this situation is the hepatic artery.

Portal pressure response to portal flow augmentation by systemic to portal shunting. In portal hypertension an added load should increase portal pressure, since mechanisms for reducing splanchnic inflow or in-

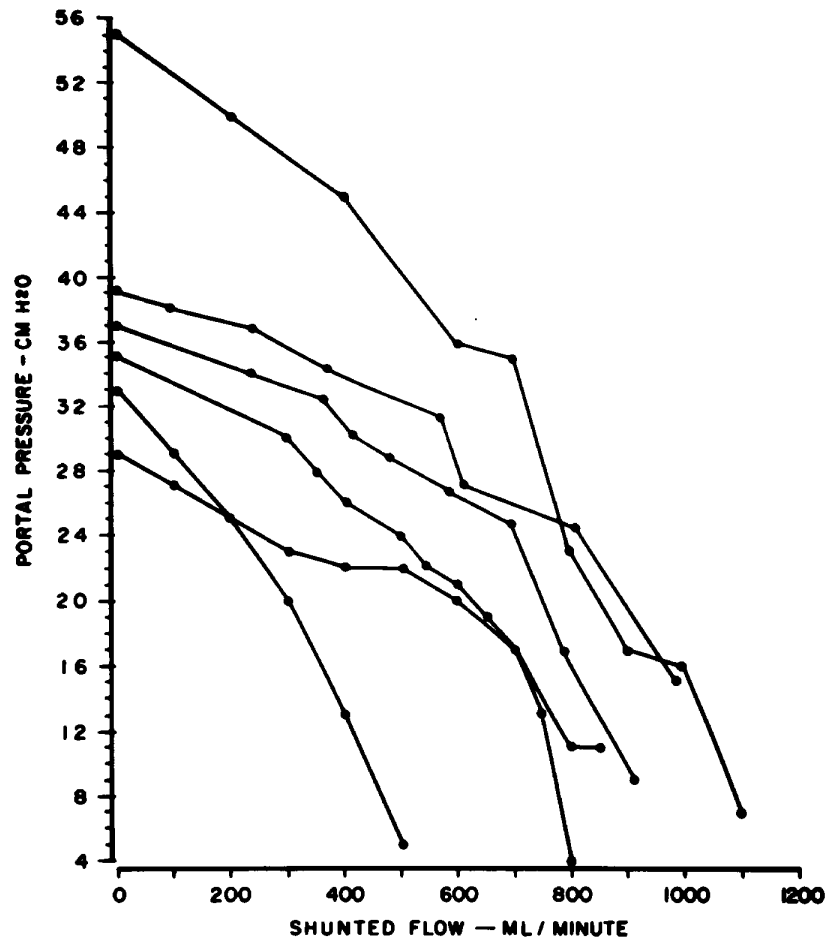


FIGURE 3 Response of portal pressure to portal diversion in type B cirrhotic patients. Portal pressure (centimeters water) is plotted against volume of portal venous flow diverted through the umbilicosaphenous shunt. Six representative type B cases in order of decreasing basal portal pressure (case Nos. 21, 19, 18, 20, 22, and 17, Table I) are shown.

creasing outflow already would be activated by existing portal hypertension. Type A patients accommodate their portal pressure as well to portal flow augmentation as diversion (Table I, Figs. 2 and 4). Portal pressure-shunted portal flow curve slopes are more varied for augmentation but are similar to slopes (Table I) for diversion in the 12 patients where both maneuvers were performed (Fig. 4).

Type A cirrhotic subjects who during portal diversion had portal pressure-shunted portal flow slopes less than the mean ± 2 SD of control exhibit a compliant system in that relatively small increases in portal pressure were observed (range, $+0.08$ to $+0.50$, mean $\pm$ SD, 0.3 ± 1.6 cm/100 ml per min, $n = 6$). Cirrhotic patients with steep type B slopes during portal diversion demonstrated steep slopes during augmentation (range, $+0.43$ to $+3.60$, mean $\pm$ SD, 1.6 ± 1.1 cm/100 ml per min, $n = 6$) that were increased ($P < 0.01$) when compared to the

compliant group. The basal portal pressures of the eight cirrhotic patients with type A slopes (34.4 ± 4.2 cm water, mean $\pm$ SD) were not significantly different from the nine cirrhotic patients with type B slopes (37.4 ± 8.3 cm water).

Induced retrograde portal flow during portal venous flow diversion. If increasing hepatic arterial flow, rather than changing portal-systemic collateral, splenic, or mesenteric inflow, accounts for the maintenance of portal pressure during portal diversion, sampling of indocyanine green from the umbilicosaphenous shunt during diversion should demonstrate extraction of indocyanine green from portal blood when increased hepatic arterial flow reverses through hepatic sinusoids to enter the extracorporeal circuit. At laparotomy for portacaval shunt with 750 ml/min portal diversion, prograde portal flow was evidenced by absence of extraction. Retrograde flow of hepatic arterial blood into the

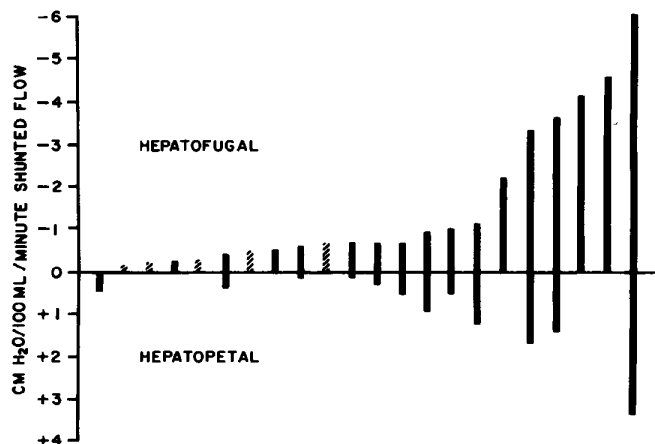


FIGURE 4 Histogram of portal pressure-shunted portal venous flow slope. Patients 1 (left) through 22 (right) are presented in order of increasing slope (Table I). The upper bars refer to the slope for portal diversion (hepatofugal shunting). The lower bars refer to the slope for portal blood flow augmentation (hepatopetal shunting) performed in 12 patients. Hatched bars indicate schistosomiasis patients (controls).

portal vein with extraction occurred at diversion rates in excess of 1,000 ml/min. This type A patient (Table IIA) accommodated to 1,000 ml/min portal diversion or augmentation (portal pressure-shunted portal flow slope -0.3 , $+0.0$) with little change in portal pressure.

Portal pressure and intrahepatic venous pressure response to occlusion of hepatic artery or portal vein. Intraoperative occlusion of hepatic artery or portal vein before and during diversion of blood from the hepatic side of the occluded portal vein was studied in two patients to compare hepatic artery and portal venous (splenic and mesenteric) capacity to sustain intrahepatic venous pressure (Table II). Intrahepatic venous pressure was measured and blood was shunted through the umbilical catheter on the hepatic side of the occluded portal vein.

The type A patient maintained intrahepatic venous pressure with flow from either hepatic artery or portal vein (Table II experiments 5A and 6A). Portal venous flow alone maintained portal venous pressure when the hepatic artery was occluded (experiment 5A) suggesting adequate portal flow to support pressure. When portal flow is stopped, hepatic artery flow is adequate to prevent a reduction in intrahepatic venous pressure (experiment 6A). The response to 1,000 ml/min portal to systemic shunting between the site of portal vein occlusion and the liver (experiment 7A) shows the hepatic artery to have a greater capacity to support intrahepatic venous pressure than mesenteric and splenic vessels, since pressure falls less when the portal vein is occluded and the hepatic artery supplies the liver (experiment 8A) than when the hepatic artery is

occluded and the portal vein supplies liver (experiment 7A). This suggests that increased hepatic artery flow is the most important mechanism in maintaining portal pressure during portal diversion in this type A patient.

In a type B patient (Table II) occlusion of the portal vein precipitated an 11-cm decrease in intrahepatic venous pressure (experiment 6B) indicating the failure of hepatic artery flow to maintain pressure. This inadequacy was exaggerated by simultaneous portal vein occlusion and portal diversion (Experiment 8B). This type B patient relies on portal flow to sustain intrahepatic venous pressure. The failure of hepatic artery occlusion to reduce portal pressure (experiment 5B) indicates a small hepatic artery contribution to maintenance of portal pressure in this patient. The steep portal pressure-shunted portal flow slope when the portal vein is patent (experiment 2B) demonstrates the failure of portal-systemic collateral flow to compensate for increasing or decreasing portal flow.

Maintenance of residual intrahepatic venous pressure after end-to-side portacaval anastomosis. If the portal pressure-shunted portal flow slope estimates he-

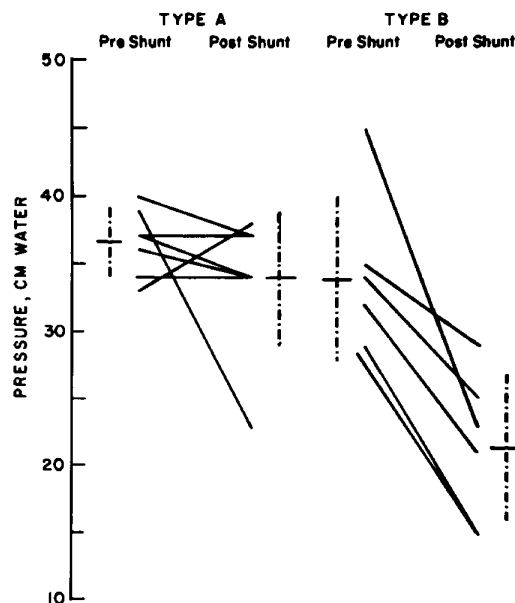


FIGURE 5 Effect of total portal venous flow diversion by end-to-side portacaval anastomosis on intrahepatic venous pressure in type A and type B patients. The horizontal solid bar indicates the mean. The vertical interrupted line indicates SD. Preoperative portal pressures for type A and type B patients were not significantly different. After portacaval shunt mean intrahepatic venous pressure in type B patients (21.3 ± 5.6 , $n = 6$) is significantly decreased ($P < 0.01$) when compared to preshunt portal pressure or postshunt intrahepatic venous pressure in type A patients (33.9 ± 5.0 , $n = 7$). Four type A and four type B patients shown here had portal pressure-shunted portal flow slope determined under anesthesia at laparotomy for portacaval anastomosis and are excluded from Table I.

TABLE II
*Response of Intrahepatic Venous Pressure to Occlusion
of Hepatic Artery and Portal Vein*

Experiment	Hemodynamic type	A	B
1	Basal portal pressure	46	29
2	Portal pressure during diversion, 1,000 ml/min	43	16
3	Portal pressure during augmen- tation, 1,000 ml/min	46	37
4	Pressure-flow slope (cm water/100 ml per min) diversion	-0.3	-1.3
	augmentation	+0.0	+0.8
5	Portal pressure with hepatic artery occluded	44	31
6	Intrahepatic pressure with portal vein occluded	44	18
7	Portal pressure with hepatic artery occluded plus diversion, 1,000 ml/min	35	22
8	Intrahepatic pressure portal vein occluded plus diversion, 1,000 ml/min	39	3

patic vascular capacity to sustain portal pressure during portal venous diversion, the residual intrahepatic venous pressure after end-to-side portacaval anastomosis when the hepatic artery alone supplies the liver should correlate with the preoperative portal pressure and postoperative intrahepatic venous pressure. In 13 patients undergoing end-to-side portacaval anastomosis (Fig. 5) after determination of portal pressure-shunted portal flow slope preoperative portal pressure in seven type A patients (36.6 ± 2.5 cm, mean $\pm$ SD) was not significantly different from six type B patients (33.8 ± 6.1 cm). After end-to-side portacaval anastomosis in type A patients intrahepatic venous pressure was not significantly changed (33.9 ± 5.0) indicating hepatic vascular compensation for loss of portal venous flow. Type B patients suffered a decrease in intrahepatic venous pressure (21.3 ± 5.6) that was significant when compared to their preoperative portal pressure ($t = 3.38$, $P < 0.01$) or to the postoperative intrahepatic venous pressure of the type A patients ($t = 3.90$, $P < 0.01$).

Residual intrahepatic venous pressure after end-to-side portacaval shunt and prognosis. Our initial clinical observations suggested that type B patients in whom residual intrahepatic venous pressure fell after portacaval anastomosis (Fig. 5) frequently died shortly after surgery or suffered from chronic encephalopathy. Therefore, residual intrahepatic venous pressure was measured in 40 patients with cirrhosis associated with

ethanol abuse shortly after interval end-to-side portacaval anastomosis when they were hemodynamically stable. The patients were followed clinically for as long as 9 yr (median, 4.0 yr). 13 patients developed chronic hepatic encephalopathy defined as diminished mental function that was improved by and required continued dietary protein restriction and antibiotic or lactulose therapy. Six of these died within 1 mo of surgery and were classified as early deaths (Fig. 6). The mean residual intrahepatic venous pressure of these 13 patients (21.1 ± 4.4 cm) was significantly less ($P < 0.001$) than the 27 patients that did not have chronic encephalopathy (32.6 ± 5.3 cm).

Life table analysis (25, 26) demonstrated a significantly ($P < 0.01$) shorter survival (median, 0.6 yr) for the 13 patients with lower pressures when compared to the other patients (median, 5.0 yr) (Fig. 7). None of the 27 patients with relatively favorable postoperative courses had a residual intrahepatic venous pressure < 25 cm. 6 of 8 patients who died within 1 mo, 8 of 10 patients who died within 1 yr, and 6 of 7 patients who survived the postoperative period, but suffered from chronic encephalopathy, were unable to maintain residual intrahepatic venous pressure above 25 cm. These findings suggest that 25 cm is a critical lower limit of pressure, below which hepatic function is not maintained and chronic encephalopathy with early death supervenes.

DISCUSSION

A lesser fall in portal pressure than would be expected for a given quantity of portal blood flow diversion indicates a compensatory vascular mechanism. Therefore, the steepest portal pressure-shunted portal flow slope observed (Table I, patient 22) most clearly approaches the absence of this postulated mechanism. Lesser slopes result from its activity. The failure of the portal pressure-shunted portal flow slope to be altered by changing blood volume, portal pressure, and presumably cardiac output (27) points to a splanchnic rather than systemic origin of the proposed mechanism. The small portal pressure-shunted portal flow slopes recorded in control subjects may reflect both low and variable hepatic resistance to flow (28, 29). Similarly, a lesser increase in portal pressure than expected during portal blood flow augmentation by systemic to portal shunting in the presence of portal hypertension suggests a compensatory decrease in arterial inflow to the splanchnic chamber since hepatic and portal-systemic collateral outflow resistance should be limiting when cirrhosis and portal hypertension are present (30-32). Failure or absence of this mechanism in some patients with cirrhosis is indicated by the continuum of portal pressure-shunted portal flow slopes observed.

An increase of mesenteric and splenic venous flow

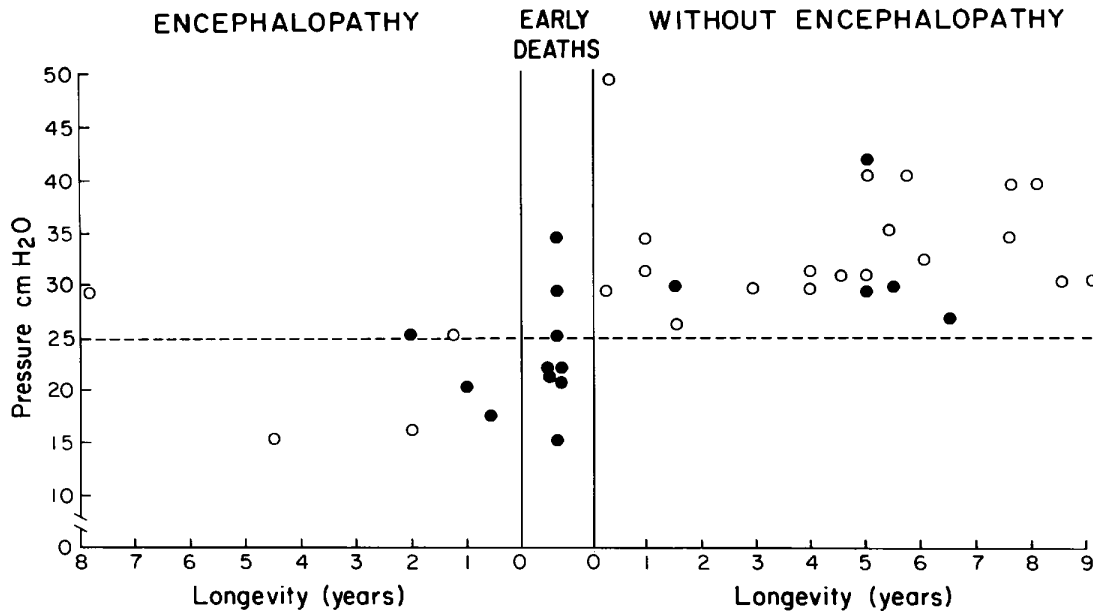


FIGURE 6 Relationship of survival and clinical status (encephalopathy) to residual intrahepatic venous pressure after end-to-side portacaval anastomosis (open circle, alive; closed circle, dead). The 13 patients with encephalopathy (left) had significantly lower pressures than those without encephalopathy (right, $n = 27$) and a significantly shorter survival (median, 0.6 vs. 5.0 yr). Early mortality is defined as death within 1 mo of surgery.

in response to reduced portal pressure is suggested by the maintenance of portal pressure despite hepatic artery occlusion (Table II) and published studies demonstrating an increase in portal and splenic flow after

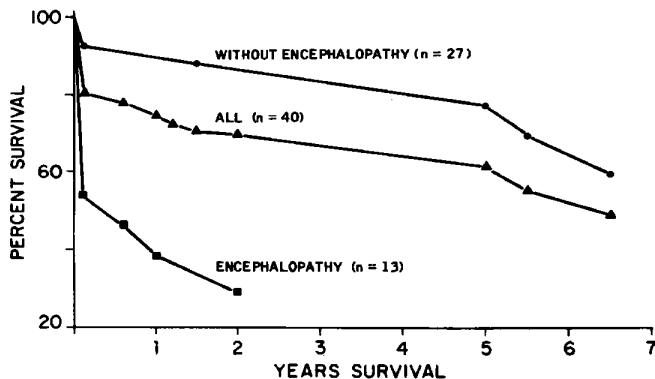


FIGURE 7 Life table analysis of 40 patients followed for up to 9 yr after end-to-side portacaval anastomosis (center curve, all patients). The 13 patients with chronic encephalopathy had a lower residual intrahepatic venous pressure and reduce median survival (0.6 yr, lower curve) when compared to the 27 patients with residual intrahepatic venous pressure > 25 cm and median survival 5.0 yr who did not have chronic encephalopathy (highest curve). The highest and lowest curves are significantly different (log rank test, $P = 0.01$). Cumulative survival for the 13 patients in the lower curve was not carried beyond 2 yr because experience was limited to only two patients surviving beyond this point.

portacaval anastomosis (10, 33). Hepatic (9, 34–36), mesenteric, and splenic (33) arteries may all contribute to maintenance of portal pressure in type A patients when the portal circulation is intact. Conversely, the steep portal pressure-shunted portal flow slopes in type B patients indicate a limited response of all these vessels to changing portal flow and suggests a widespread defect in vascular function.

Abnormal vascular responses in the cardiac (37, 38), pulmonary (39), renal (40), integumentary (41), and splanchnic (36) systems have been demonstrated in patients with liver disease. The increased cardiac output (37) functional renal failure (42) and portal hypertension (43) of liver disease may be reversible. The portal hypertension of cirrhotic patients in this study consisting of an elevated portal pressure setpoint and a variable limitation of the response to changing portal flow also, at least in part, may be a reversible alteration in vascular responsiveness (44) rather than a consequence of the presumed fixed anatomic hepatic outflow block previously conceived as the cause of portal hypertension (45).

Alternatively, the continuum of response to changing portal flow could result from anatomic alterations in the hepatic artery associated with cirrhosis (46, 47). Herrick (48), and later Dock (49), perfused the livers of alcoholic hypertrophic cirrhotic patients in vitro and demonstrated a reciprocal relationship between hepatic arterial pressure and portal pressure. They speculated on the role

of relatively increased hepatic arterial flow as a factor in the portal hypertension of cirrhosis associated with alcoholism. The investigations reported here were based upon their early studies and imply similar conclusions.

Moreno et al. (1) and Burchell et al. (9) have studied portal and hepatic arterial blood flow at laparotomy for portacaval anastomosis. They demonstrated an elevated setpoint for portal pressure of 40 cm of water since this pressure was found despite wide variation in portal blood flow (10). Attempts to correlate portal or hepatic arterial flow measured before or immediately after portacaval anastomosis with prognosis failed (9).

After our initial publications, Reynolds (50) attempted and failed to correlate wedge hepatic venous pressure measured after portacaval shunt with prognosis. His data were drawn retrospectively from studies of hepatic blood flow after portacaval shunt (51, 52) and, therefore, excluded patients who died early or had poor liver function that precluded blood flow measurement. Furthermore, the additional variable of inferior vena caval pressure was introduced by subtracting inferior vena caval pressure from the wedged hepatic venous pressure. Subsequently, Burchell et al. (53) retrospectively correlated a limited increment in hepatic arterial flow occurring after portacaval shunt with early death and encephalopathy. Patients with less than a 200 ml/min increase in hepatic arterial flow after diversion of portal flow by portacaval shunt accounted for 90% of the patients with encephalopathy or early mortality. Unfortunately, their hemodynamic data did not include residual intrahepatic venous pressure. Nevertheless, their retrospective analysis of intraoperative data and correlation of hemodynamic response to long-term prognosis confirms the data presented here.

The prolonged survival and absence of hepatic encephalopathy in patients with residual intrahepatic pressures >25 cm suggests that this is the minimum pressure required to sustain hepatic function. The elevated portal pressure set point of 40 cm, maintained in these patients before portacaval shunt when they were at risk for variceal hemorrhage, is on the average 15 cm greater. This 15-cm excess of portal pressure appears to increase the risk of variceal hemorrhage without serving an essential role in maintaining hepatic perfusion.

There is general agreement that prior hemodynamic measurements have been of "inconsistent value in selecting the proper shunt to be done or in predicting its physiologic outcome" (54). The preoperative hemodynamic classification presented here allows a prospective quantitative stratification of cirrhotic patients that identifies the type B patients who require portal blood flow to maintain hepatic perfusion and the type A patients who tolerate the loss of portal flow produced by portacaval anastomosis relatively well.

ACKNOWLEDGMENTS

We wish to express our deep appreciation for the sustained support of Dr. Norton Spritz without which this work would not have been possible. We also wish to thank Mr. Sonny Marty and Miss Rubell Smith for expert technical and secretarial assistance. Dr. Joseph G. Feldman supervised the analysis of life table data and provided expert statistical advice.

This work was supported by Veterans Administration Research Funds.

REFERENCES

- Warren, W. D., J. J. Fomon, M. Viamonte, L. O. Martinez, and M. Kalsner. 1968. Spontaneous reversal of portal venous blood flow in cirrhosis. *Surg. Gynecol. Obstet.* **126**: 315-323.
- Kessler, R. E., D. A. Tice, and D. S. Zimmon. 1969. Retrograde flow of portal vein blood in patients with cirrhosis. *Radiology*. **92**: 1038-1042.
- Shaldon, S., L. Chiandussi, L. Guevara, J. Caesar, and S. Sherlock. 1961. The estimation of hepatic blood flow and intrahepatic shunted blood flow by colloidal heat denatured human serum albumin labeled with ^{131}I . *J. Clin. Invest.* **40**: 1346-1354.
- Imanaga, H., S. Yamamoto, and Y. Kuroyanagi. 1962. Surgical treatment of portal hypertension according to state of intrahepatic circulation. *Ann. Surg.* **155**: 42.
- Price, J. B., A. B. Voorhees, and R. C. Britton. 1967. Operative hemodynamic studies in portal hypertension. *Arch. Surg.* **95**: 843-852.
- Fuchs, W. A., R. Preisig, E. Voegeli, and J. Bircher. 1972. Hepatic arteriography in cirrhosis of the liver and portal hypertension. *Invest. Radiol.* **8**: 369-377.
- Schenk, W. G., J. C. McDonald, K. McDonald, and T. Drapanas. 1962. Direct measurement of hepatic blood flow in surgical patients: with related observations on hepatic flow dynamics in experimental animals. *Ann. Surg.* **156**: 463-471.
- Ferguson, D. J. 1963. Hemodynamics in surgery for portal hypertension. *Ann. Surg.* **158**: 383-386.
- Burchell, A. R., A. H. Moreno, W. F. Panke, and T. F. Nealon, Jr. 1974. Hemodynamic variables and prognosis following portacaval shunts. *Surg. Gynecol. Obstet.* **138**: 359-369.
- Moreno, A. H., A. R. Burchell, L. M. Rousselot, W. F. Panke, S. F. Slafsky, and J. H. Burke. 1967. Portal blood flow in cirrhosis of the liver. *J. Clin. Invest.* **46**: 436-444.
- Betz quoted by F. C. Herrick. 1907. An experimental study into the cause of the increased portal pressure in portal cirrhosis. *J. Exp. Med.* **9**: 93-104.
- Tystrup, N., K. Winkler, K. Mellemegaard, and M. Andreassen. 1962. Determination of the hepatic arterial blood flow and oxygen supply in man by clamping the hepatic artery during surgery. *J. Clin. Invest.* **41**: 447-454.
- Kessler, R. E., J. H. Amadeo, D. A. Tice, and D. S. Zimmon. 1970. Filtration of schistosomes in unanesthetized man. *JAMA (J. Am. Med. Assoc.)*. **214**: 510-524.
- Kessler, R. E., E. Santoni, D. A. Tice, and D. S. Zimmon. 1969. The effect of lymph drainage on portal pressure and bleeding esophageal varices. *Gastroenterology*. **56**: 538-547.
- Kessler, R. E., and D. S. Zimmon. 1966. Umbilical vein angiography. *Radiology*. **87**: 841-844.
- Kessler, R. E., D. A. Tice, and D. S. Zimmon. 1969. Effect of umbilico-systemic shunting on portal pressure and bleeding varices. *Surg. Forum*. **20**: 376-377.

17. Jackson, F. C., E. B. Perrin, W. R. Felix, and A. G. Smith. 1971. A clinical investigation of the portacaval shunt. V. survival analysis of the therapeutic operation. *Ann. Surg.* **174**: 672-701.
18. Kessler, R. E., D. A. Tice, and D. S. Zimmon. 1973. Value, complications, and limitations of umbilical vein catheterization. *Surg. Gynecol. Obstet.* **136**: 529-535.
19. Kessler, R. E., and D. S. Zimmon. 1967. Umbilical vein catheterization in man. *Surg. Gynecol. Obstet.* **124**: 594-598.
20. Meyers, J. D., and W. J. Taylor. 1951. An estimation of portal venous pressure by occlusive catheterization of the hepatic venule. *J. Clin. Invest.* **30**: 662-663.
21. Reynolds, T. B., A. G. Redeker, and H. M. Geller. 1957. Wedged hepatic venous pressure. *Am. J. Med.* **22**: 341-349.
22. Zimmon, D. S., and R. E. Kessler. 1974. The portal pressure-blood volume relationship in cirrhosis. *Gut.* **15**: 99-101.
23. Williams, R., D. S. Zimmon, E. Thompson, and S. Sherlock. 1964. The estimation of segmental hepatic venous flow in man. *Gastroenterology.* **46**: 525-530.
24. Viallet, A., J. G. Joly, D. Marleau, and P. Lavoie. 1970. Comparison of free portal venous pressure and wedged hepatic venous pressure in patients with cirrhosis of the liver. *Gastroenterology.* **59**: 372-375.
25. Peto, R., M. C. Pike, P. Armitage, N. E. Breslow, D. R. Cox, S. V. Howard, N. Mantel, K. McPherson, J. Peto and P. G. Smith. 1976. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. I. Introduction and design. *Br. J. Cancer.* **34**: 585-612.
26. Peto, R., M. C. Pike, P. Armitage, N. E. Breslow, D. R. Cox, S. V. Howard, N. Mantel, K. McPherson, J. Peto, and P. G. Smith. 1977. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. *Br. J. Cancer.* **35**: 1-39.
27. De Freitas, F. M., E. Z. Faraco, D. F. de Azevedo, J. Zaduchliver, and I. Lewin. 1965. Behavior of normal pulmonary circulation during changes of total blood volume in man. *J. Clin. Invest.* **44**: 366-378.
28. Wade, O. L., B. Coombs, A. M. Childs, H. O. Wheeler, A. Cournand, and S. E. Bradley. 1956. The effect of exercise on the splanchnic blood flow and splanchnic blood volume in normal man. *Clin. Sci.* **15**: 457-464.
29. Price, H. L., S. Deutsch, B. E. Marshall, G. W. Stephen, M. G. Behar, and G. R. Neufeld. 1966. Hemodynamic and metabolic effect of hemorrhage in man, with particular reference to the splanchnic circulation. *Circ. Res.* **28**: 469-474.
30. Kely, R. H., A. H. Baggenstoss, and H. R. Butt. 1950. The relation of the regenerated hepatic nodule to the vascular bed in cirrhosis. *Proc. Mayo Clinic.* **25**: 17-26.
31. Hales, M. R., J. S. Allan, and E. M. Hall. 1959. Injection-corrosion studies of normal and cirrhotic livers. *Am. J. Pathol.* **35**: 909-941.
32. Edwards, E. A. 1951. Functional anatomy of the portasystemic communications. *Arch. Int. Med.* **88**: 137-154.
33. Gitlin, N., G. R. Grahame, L. Kreel, H. S. Williams, and S. Sherlock. 1970. Splenic blood flow and resistance in patients with cirrhosis before and after portacaval anastomoses. *Gastroenterology.* **59**: 208-213.
34. Greenway, C. V., and R. D. Stark. 1971. Hepatic vascular bed. *Physiol. Rev.* **2**: 23-65.
35. Viamonte, M., W. D. Warren, J. J. Fomon, and L. O. Martinez. 1970. Angiographic investigations in portal hypertension. *Surg. Gynecol. Obstet.* **130**: 37-53.
36. Kreel, L., N. Gitlin, and S. Sherlock. 1970. Hepatic artery angiography in portal hypertension. *Am. J. Med.* **48**: 618-623.
37. Murray, J. F., A. M. Dawson, and S. Sherlock. 1958. Circulatory changes in chronic liver disease. *Am. J. Med.* **24**: 358-367.
38. Kontos, H. A., W. Shapiro, H. P. Mauck, and J. I. Patterson. 1964. General and regional circulatory alterations in cirrhosis. *Am. J. Med.* **37**: 526-535.
39. Daoud, F. S., J. T. Reeves, J. W. Schaefer. 1972. Failure of hypoxic pulmonary vasoconstriction in patients with liver cirrhosis. *J. Clin. Invest.* **51**: 1076-1079.
40. Kew, M. C., R. R. Varma, H. S. Williams, P. W. Brunt, K. J. Hourigan, and S. Sherlock. 1971. Renal and intrarenal blood flow in cirrhosis of the liver. *Lancet.* **II**: 504-510.
41. Lünzer, M., S. P. Newman, and S. Sherlock. 1973. Skeletal muscle blood flow and neurovascular reactivity in liver disease. *Gut.* **14**: 354-359.
42. Koppel, M. H., J. W. Coburn, M. M. Mims, H. Goldstein, J. D. Boyle, and M. E. Rubini. 1969. The transplantation of cadaveric kidneys from patients with hepato-renal syndrome. Evidence for the functional nature of renal failure in advanced liver disease. *N. Engl. J. Med.* **280**: 1367-1371.
43. Reynolds, T. B., H. M. Geller, O. T. Kuzma, and A. G. Redeker. 1960. Spontaneous decrease in portal pressure with clinical improvement in cirrhosis. *N. Engl. J. Med.* **263**: 734-739.
44. Zimmon, D. S. 1977. The hepatic vasculature and its response to hepatic injury: a working hypothesis. *Yale J. Biol. Med.* **50**: 497-506.
45. Bradley, S. E. 1958. Methods of evaluation of the splanchnic circulation. In *Circulation Proceedings of the Harvey Tercentenary Congress*. J. McMichael, editor. Blackwell Scientific Publications Ltd., Oxford, England. 255-265.
46. Rappaport, A. M., and J. H. Schneiderman. 1976. The function of the hepatic artery. *Rev. Physiol. Biochem. Pharmacol.* **76**: 130-175.
47. Takahashi, T., and F. Tezuka. 1974. Hepatic arteries and arterial circulation in liver cirrhosis. *Tohoku J. Exp. Med.* **113**: 113-128.
48. Herrick, F. C. 1907. An experimental study into the cause of the increased portal pressure in portal cirrhosis. *J. Exp. Med.* **9**: 93-104.
49. Dock, W. 1942. The role of hepatic arterial flow in the portal hypertension of cirrhosis. *Trans. Assoc. Amer. Physicians.* **57**: 302-305.
50. Reynolds, T. B. 1974. The role of hemodynamic measurements in Selection of patients for portasystemic shunt. *Arch. Surg.* **108**: 276-281.
51. Redeker, A. G., H. M. Geller, and T. B. Reynolds. 1958. Hepatic wedge pressure, blood flow, vascular resistance and oxygen consumption before and after end-to-side portacaval shunt. *J. Clin. Invest.* **37**: 606-613.
52. Redeker, A. G., C. T. Kunelis, S. Yamamoto, and T. B. Reynolds. 1964. Assessment of portal and hepatic hemodynamics after side-to-side portacaval shunt in patients with cirrhosis. *J. Clin. Invest.* **43**: 1464-1471.
53. Burchell, A. R., A. H. Moreno, W. F. Panke, and T. F. Nealon, Jr. 1976. Hepatic artery flow improvement after portacaval shunt: A single hemodynamic clinical correlate. *Ann. Surg.* **184**: 289-302.
54. Malt, R. A., D. C. Nabseth, M. J. Orloff, and S. Stipa. 1979. Portal hypertension 1979. *N. Engl. J. Med.* **301**: 617-618.

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

Giancarlo Maria Liumbruno^{1,2}, Liviana Catalano¹, Vanessa Piccinini¹, Simonetta Pupella¹, Giuliano Grazzini¹

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

Introduction

The level of safety of transfusion therapy is now very high thanks to the combination of serological methods and genomic amplification used to screen for transmissible diseases and the meticulous care with which repeat, voluntary, unpaid donors are selected¹⁻⁴.

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 caused 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 2004⁷, 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 2003¹¹⁻¹⁹. 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 tests²⁰, 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 cells²³. 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 cells²¹.

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 transfused²¹.

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 equipment²¹.

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

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
	Yontovian 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
<i>Total</i>			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
	Yontovian R ¹²	1993	0	2,476	0.0
	Dziczekowski JS ¹⁸	1995	1	5,197	19.2
	AuBuchon JP ¹⁹	2002	1	2,678	37.3
<i>Total</i>			21	34,334	61.2
Red blood cell concentrates	Barrett BB ¹¹	1993	1	31,385	3.2
	Dziczekowski JS ¹⁸	1995	1	7,080	14.1
<i>Total</i>			2	38,465	5.2
Overall total			67	159,725	41.9

the context of different national epidemiological situations²¹.

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 cases²⁹, 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 bags³⁰. Furthermore, it is even more difficult to achieve satisfactory disinfection of a skin surface that has become irregular due to scars from previous donations²⁸.

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 onwards³³⁻⁴⁷.

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 mL³⁴; indeed, diversion of the first part of the donation guaranteed an 88% reduction in the percentage of bacterial contamination²⁸.

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 collected³⁵.

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 log³⁶. 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 Bruncau's group in France published the results of a multicentre study³⁷ 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 collected³⁸; contemporaneously, in the Netherlands,

Bos *et al.* obtained a 53% reduction of contamination of the same blood component³⁹.

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 diversion⁴¹; 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 year⁴².

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 pools⁴³. 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" (isopropyl 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 2004⁴⁴; 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,

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 contamination⁴⁵.

A statistically significant reduction ($p = 0.005$) in bacterial contamination of PCs from whole blood was also found in a Canadian study by Robillard⁴⁶, 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 bacteria¹⁷.

In a study recently performed in the USA on bacterial contamination of platelets from apheresis³³, 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 A 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 blood¹³, reported in a study from 1994, to the considerably lower value of 1 case per 73,000 transfusions of platelets from single donors²⁴, reported in a study from 2001. This latter result is completely in line with the findings of the American Red Cross³³ 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 introduced⁵⁰.

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 components⁴⁹; in the same year, this measure was made obligatory in Germany⁵¹ and other countries, including France, the Netherlands and Canada, subsequently adopted

this modification of the production process of blood components^{3,16,52}, 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, 2007⁵³; 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 them⁵¹; 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 bacteria²³, 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 components⁵⁵ and, during the selection process, encouraging donors to report any changes of health that occur in the period immediately after the donation⁵⁴.

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 France⁵², 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

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 - bioMérieux 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 Andreau⁵², as well as diagnostic tests and could also exploit pathogen inactivation methods, but remains dependent on appropriate use of transfusion therapy.

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

References

- 1) AuBuchon JP, Birkmeyer JD, Busch MP. Safety of the blood supply in the United States: opportunities and controversies. *Ann Intern Med* 1997; **127**: 904-9.
- 2) Hillyer CD, Josephson CD, Blajchman MA, et al. Bacterial contamination of blood components: risks, strategies, and regulation: joint ASH and AABB educational session in transfusion medicine. *Hematology Am Soc Hematol Educ Program* 2003; 575-89.
- 3) Stramer LS. Current risks of transfusion-transmitted agents: a review. *Arch Pathol Lab Med* 2007; **131**: 702-7.
- 4) Dodd RY. Current risk for transfusion transmitted infections. *Curr Opin Hematol* 2007; **14**: 671-6.
- 5) Blajchman MA, Beckers EAM, Dickmeiss E, et al. Bacterial detection of platelets: current problems and possible resolutions. *Transfus Med Rev* 2005; **19**: 259-72.
- 6) O'Brien SF, Yi QL, Fan W, et al. Current incidence and estimated residual risk of transfusion-transmitted infections in donations made to Canadian Blood Services. *Transfusion* 2007; **47**: 316-25.
- 7) Blajchman MA. Bacterial contamination of cellular blood components: risks, sources and control. *Vox Sang* 2004; **87** (Suppl 1): S98-103.
- 8) American Association of Blood Banks. Guidance On Implementation Of New Bacterial Reduction And Detection Standard. Bethesda, MD: AABB; August 29, 2003. Association Bulletin 03-10.
- 9) Alter HJ. Pathogen reduction: a precautionary principle paradigm. *Transfus Med Rev* 2008; **22**: 97-102.
- 10) Blajchman MA. Incidence and significance of the bacterial contamination of blood components. *Dev Biol (Basel)* 2002; **108**: 59-67.
- 11) Barrett BB, Anderson JW, Anderson KC. Strategies for the avoidance of bacterial contamination of blood components. *Transfusion* 1993; **33**: 228-33.
- 12) Yomtovian R, Lazarus HM, Goodnough LT, et al. A prospective microbiologic surveillance program to detect and prevent the transfusion of bacterially contaminated platelets. *Transfusion* 1993; **33**: 902-9.
- 13) Chiu EKW, Yuen KY, Lie AKW, et al. A prospective study of symptomatic bacteremia following platelet transfusion and of its management. *Transfusion* 1994; **34**: 950-4.
- 14) Blajchman MA, Ali A, Lyn P, et al. A prospective study to determine the frequency of bacterial contamination in random donor platelet concentrates [abstract]. *Blood* 1994; **84**: 529.
- 15) Leiby DA, Kerr KL, Compos JM, Dodd RY. A retrospective analysis of microbial contaminants in outdated random-donor platelets from multiple sites. *Transfusion* 1997; **37**: 259-63.
- 16) Blajchman MA, Ali A, Lyn P, et al. Bacterial surveillance of platelet concentrates: quantitation of bacterial load [abstract]. *Transfusion* 1997; **37** (Suppl): 74S.
- 17) Blajchman MA, Ali AM. Bacteria in the blood supply: an overlooked issue in transfusion medicine. In: Nance SJ, editor. *Blood Safety: Current Challenges*. Bethesda, MD: AABB; 1992. p.213-28.
- 18) Dzieczkowski JS, Barrett BB, Nester D, et al. Characterization of reactions after exclusive transfusion of white cell-reduced cellular blood components. *Transfusion* 1995; **35**: 20-5.
- 19) AuBuchon JP, Cooper LK, Leach MF, et al. Experience

- with universal bacterial culturing to detect contamination of apheresis platelet units in a hospital transfusion service. *Transfusion* 2002; **42**: 855-61.
- 20) Beckers EAM. Effects of bacterial testing: what risks are remaining? *ISBT Science Series* 2007; **2**: 30-4.
 - 21) Brecher ME, Hay SN. Bacterial contamination of blood components. *Clin Microbiol Rev* 2005; **18**: 195-204.
 - 22) Reading FC, Brecher ME. Transfusion-related bacterial sepsis. *Curr Opin Hematol* 2001; **8**: 380-8.
 - 23) Kuehnert MJ, Roth VR, Haley NR, et al. Transfusion-transmitted bacterial infection in the United States, 1998 through 2000. *Transfusion* 2001; **41**: 1493-9.
 - 24) Ness P, Braine H, King K, et al. Single-donor platelets reduce the risk of septic platelet transfusion reactions. *Transfusion* 2001; **41**: 857-61.
 - 25) Council of Europe. Guide to the Preparation, Use and Quality Assurance of Blood Components. Recommendation No R (95) 15 on the Preparation, Use and Quality Assurance of Blood Components, 14th ed, Strasbourg, Council of Europe Press; 2008.
 - 26) Decreto del Ministro della Salute 3 Marzo 2005. Caratteristiche e modalità per la donazione di sangue e di emocomponenti. *Gazzetta Ufficiale della Repubblica Italiana* n. 85, 13 Aprile 2005.
 - 27) Vasconcelos E, Seghatchian J. Bacterial contamination in blood components and preventative strategies: an overview. *Transfus Apher Sci* 2001; **31**: 155-63.
 - 28) McDonald CP. Bacterial risk reduction by improved donor arm disinfection, diversion and bacterial screening. *Transfus Med* 2006; **16**: 381-96.
 - 29) Gibson T, Norris W. Skin fragments removed by injection needles. *Lancet* 1958; **2**: 983-5.
 - 30) Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and interventions. *Vox Sang* 2004; **86**: 157-63.
 - 31) Kojima K, Togashi T, Hasegawa K, Kawasaki H. Subcutaneous fatty tissue can stray into a blood bag [abstract]. *Vox Sang* 1998; **74** (Suppl 1): 1205.
 - 32) Butchta C, Nedorost N, Regele H, et al. Skin plugs in phlebotomy puncture for blood donation. *Wien Klin Wochenschr* 2005; **117**: 141-4.
 - 33) Eder AJ, Kennedy JM, Dy BA, et al. Bacterial screening of apheresis platelets and the residual risk of septic transfusion reactions: the American Red Cross experience (2004-2006). *Transfusion* 2007; **47**: 1134-42.
 - 34) Olthuis H, Puyllaart C, Verhagen C, Valk L. Method for removal of contaminating bacteria during venapuncture [abstract]. *Proceedings V Regional ISBT Congress* 1995; 77.
 - 35) Figueroa PI, Yoshimori R, Nelson E, et al. Distribution of bacteria in fluid passing through an inoculated collection needle [abstract]. *Transfusion* 1995; **35** (Suppl 1): 11S.
 - 36) Wagner SJ, Robinette D, Friedman LI, Miripol J. Diversion of initial blood flow to prevent whole-blood contamination by skin surface bacteria: an in vitro model. *Transfusion* 2000; **40**: 335-8.
 - 37) Bruneau C, Perez P, Chassaigne M, et al. Efficacy of a new collection procedure for preventing bacterial contamination of whole-blood donations. *Transfusion* 2001; **41**: 74-81.
 - 38) Schneider T, Tunez T, Fontaine O. Benefits of the pre-donation sampling pouch in order to reduce bacterial contamination of pooled platelet concentrates [abstract]. *Vox Sang* 2002; **83** (Suppl 2): 162.
 - 39) Bos H, Yedema TH, Luten M. Reduction of the incidence on bacterial contamination by pre-donating drawing blood for safety tests [abstract]. *Vox Sang* 2002; **83** (Suppl 2): 6.
 - 40) Yedema T, Curvers J, De Kort W, Bos II. Reduction of the incidence of bacterial contamination of thrombocyte concentrates [abstract]. *Transfusion* 2003; **43** (Suppl): 51A.
 - 41) de Korte D, Marcelis JH, Verhoeven AJ, Soeterboek AM. Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections. *Vox Sang* 2002; **83**: 13-6.
 - 42) de Korte D, Curvers J, Beckers E, Marcelis J. Bacterial contamination of platelet concentrates: status after implementation of diversion in the Netherlands [abstract]. *Transfusion* 2005; **45** (Suppl): 26A.
 - 43) de Korte D, Curvers J, de Kort WLAM, et al. Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands. *Transfusion* 2006; **46**: 476-85.
 - 44) de Korte D, Curvers J, Beckers E, Marcelis JH. 5 years bacterial screening of PC in the Netherlands [abstract]. *Transfusion* 2007; **47** (Suppl 3): 197A-98A.
 - 45) McDonald CP, Roy A, Mahajan P, et al. Relative values of the interventions of diversion and improved donor-arm disinfection to reduce the bacterial risk from blood transfusion. *Vox Sang* 2004; **86**: 178-82.
 - 46) Robillard P, Nawej K, Delage G. Platelet bacterial contaminations and effectiveness of diverting the first 40 mls at whole blood donation [abstract]. *Transfusion* 2005; **45** (Suppl): 25A.
 - 47) Delage G, Itaj NK, Robillard P. Cumulative effect of preventive measures on incidence of bacterial infections in platelet recipients [abstract]. *Transfusion* 2006; **46** (Suppl 2): 33A.
 - 48) Stainsby D, Jones H, Asher D, et al. Serious hazards of transfusion: a decade of hemovigilance in the UK. *Transfus Med Rev* 2006; **20**: 273-82.
 - 49) Serious Hazards Of Transfusion (SHOT). Reports and summaries. Available at: <http://www.shotuk.org/SHOT%20reports%20&%20Summaries.htm>.
 - 50) Murphy WG, Foley M, Doherty C, et al. Screening platelet concentrates for bacterial contamination: low numbers of bacteria and slow growth in contaminated units mandate an alternative approach to product safety. *Vox Sang* 2008; **95**: 13-9.
 - 51) Walther-Wenke G, Doerner R, Montag T, et al. Bacterial contamination of platelet concentrates prepared by different methods: results of standardized sterility testing in Germany. *Vox Sang* 2006; **90**: 177-82.
 - 52) Andreau G, Caldani C, Morel P. Reduction of septic transfusion reactions related to bacteria contamination without implementing bacteria detection. *ISBT Science Series* 2008; **3**: 124-32.

- 53) Decreto Legislativo 9 novembre 2007, n. 208. Attuazione della direttiva 2005/62/CE che applica la direttiva 2002/98/CE per quanto riguarda le norme e le specifiche comunitarie relative ad un sistema di qualità per i servizi trasfusionali. Gazzetta Ufficiale della Repubblica Italiana - Serie Generale n. 261 del 9-11-2007 - Supplemento Ordinario n. 228.
- 54) Rao PL, Strausbaugh LJ, Liedtke LA, et al. Bacterial infections associated with blood transfusion: experience and perspective of infectious diseases consultants. *Transfusion* 2007; **47**: 1206-11.
- 55) Decreto del Ministro della Salute 3 Marzo 2005. Protocolli per l'accertamento della idoneità del donatore di sangue e di emocomponenti. Gazzetta Ufficiale della Repubblica Italiana n. 85, 13 Aprile 2005.
- 56) Yomtovian R, Tomasulo P, Jacobs MR. Platelet bacterial contamination: assessing progress and identifying quandaries in a rapidly evolving field [editorial]. *Transfusion* 2007; **47**: 1340-6.
- 57) Yomtovian R. Bacterial contamination of blood: lessons from the past and road map for the future. *Transfusion* 2004; **44**: 450-60.
- 58) Benjamin RJ. Bacterial culture of apheresis platelet products and the residual risk of sepsis. *ISBT Science Series* 2008; **3**: 133-8.
- 59) Benjamin RJ, Wagner S. The residual risk of sepsis: modeling bacterial detection in a two bottle culture system and an analysis of sampling error. *Transfusion* 2007; **47**: 1381-9.
- 60) Cole B, Smith T. PASSPORT Post Approval Surveillance Study of Platelet Outcomes, Release Tested. January 29, 2008. Available at: <http://www.passportstudy.com/documents/PassportLetter.pdf>. Downloaded on July 7, 2008.

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

Effects of skin disinfection method, diversion bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands

Dirk de Korte, Joyce Curvers, Wim L.A.M. de Korte, Tiny Hoekstra, Cees L. van der Poel, Erik A.M. Beckers, and Jan H. Marcelis

BACKGROUND: Bacterial contamination of blood products is a great hazard for development of fatal transfusion reactions. Bacterial screening of platelet concentrates (PC) by aerobic and anaerobic culturing (BacT/ALERT, bioMérieux) was introduced in the Netherlands in October 2001.

STUDY DESIGN AND METHODS: In November 2002, a nationwide, uniform skin cleansing method was introduced with a double-swab disinfection with 70 percent isopropyl alcohol. One location routinely used an integrated diversion bag to collect the first 20 to 30 mL.

RESULTS: Over the calendar years 2002 and 2003, in total 113,093 PCs derived from pooled buffy coats were screened. After introduction of the new disinfection method, 0.35 percent were initially positive. This was a small reduction compared to the previous disinfection methods under which 0.95 percent were initially positive. The location with use of the diversion bag showed a significantly lower frequency of bacterial contamination, with 0.50 percent before and 0.37 percent after introduction of 70 percent isopropyl alcohol. In addition 8000 apheresis PCs were also screened, showing 24 initially positive samples (0.30%).

CONCLUSION: The use of the diversion bag and, to a lesser extent, the use of double swabs with 70 percent isopropyl alcohol, led to a reduction of contamination. As expected, predominant contamination with resident skin bacteria was reduced. The combination of diversion bag and new disinfection led to a frequency of initial positive results for pooled five-donor PCs, which is similar to that of single-donor apheresis PCs. Furthermore, the bacterial detection system and associated product recall procedures have been shown to be effective in preventing transfusion of contaminated PCs and/or related red cells, especially for rapidly growing bacteria.

Since the dramatic reduction of transfusion-transmitted viral infections through screening for various blood-borne viruses, transfusion-related bacterial infections have become one of the major risks of transfusion. Bacterial contamination is considered to be, after clerical errors, the second most common cause of death from transfusion, with mortality rates for platelet (PLT)-related sepsis ranging from 1 in 20,000 to 1 in 100,000 donor exposures.¹⁻³ In contrast, the current frequencies of virus transmission via blood components are estimated as 1 in 1,800,000 for hepatitis C virus, 1 in 220,000 for hepatitis B virus, and 1 in 2,300,000 for human immunodeficiency virus.^{4,5} Therefore, additional screening of blood products for bacterial contamination is under consideration or has already been implemented in many countries, both in Europe and in North America.⁶

Because of their storage at room temperature, PLT products are most sensitive for bacterial contamination and thus a logical choice to start screening. In the Neth-

ABBREVIATIONS: CNS = coagulase-negative staphylococci; IPA = isopropyl alcohol; PC(s) = platelet concentrate(s); T5 = PCs prepared from pools of five buffy coats; TTBI = transfusion-transmitted bacterial infection.

From Sanquin Research, Amsterdam; Sanquin Blood Bank Region Southeast, Nijmegen; Sanquin Blood Supply Foundation, Amsterdam; Sanquin Blood Bank Region Southwest, Rotterdam; and Elisabeth Hospital, Tilburg, the Netherlands.

Address correspondence to: D. de Korte, PhD, Sanquin Research, Department of Blood Cell Research, Plesmanlaan 125, 1066 CX Amsterdam, the Netherlands; e-mail: D.deKorte@Sanquin.nl.

Received for publication May 26, 2005; revision received July 15, 2005, and accepted July 17, 2005.

doi: 10.1111/j.1537-2995.2006.00746.x

TRANSFUSION 2006;46:476-485.

erlands, nationwide screening for bacterial contamination in 100 percent of PLT products was introduced at the end of 2001. All Dutch blood banks use the BacT/ALERT culturing system (bioMérieux [formerly Organon Teknika], Boxtel, the Netherlands), with a standardized protocol.

It has previously been shown that in the majority of positive cultures, bacterial contamination is a result of resident skin flora⁷ most likely originating from the venipuncture plug.^{8,9} Although hygienic precautions are taken to prevent contamination during collection, a further reduction of the number of products with bacterial contamination is desirable. To reduce the risk of contamination by skin flora two strategies can be used: 1) diversion of the first aliquot of the donation and 2) improvement of skin disinfection.

Regarding the first method we, as well as others, have previously shown that diversion of the first 10 mL of a whole-blood donation reduces the incidence of bacteria in the remaining whole-blood unit.^{8,10,11} The effect of this diversion, however, on bacterial contamination of the final product, PLT concentrates (PCs) prepared from pooled buffy coats, has not yet been reported.

Considering skin disinfection, iodine is the most effective disinfectant. Because it is considered to be a donor-unfriendly agent, however, isopropyl alcohol (IPA) is the next best choice. McDonald and coworkers¹² have shown that improved skin disinfection methods drastically reduced the number of remaining bacteria on the phlebotomy puncture site—especially those methods with a double-swab method, with the best results for the combination of IPA and iodine. For this approach too, the final effect on bacterial contamination of buffy coat-derived PCs has not yet been reported.

From January 2002, at collection centers of the Sanquin Blood Bank Region Southeast (Nijmegen, the Netherlands), a collection system with an integrated diversion bag was used to divert the first 20 to 30 mL of the whole-blood donation. This volume was subsequently used for infection disease and immunohematology testing. All other collection centers of the Sanquin Blood Banks used standard whole-blood collection systems without a diversion bag. In October 2002, a standardized skin disinfection method, with 70 percent IPA in a double-swab method, was introduced in all the collection centers of the Sanquin Blood Banks (including Nijmegen). During the whole period all apheresis PCs were collected with a diversion pouch included in the system.

In this report we evaluate data on bacterial contamination in the Netherlands for all apheresis PCs and PCs prepared from pools of five buffy coats (T5), collected in 2002 and 2003. The large numbers enable us to make a reliable judgment of the effect of diversion and/or changed disinfection method on the final degree of bacterial contamination of PC.

MATERIALS AND METHODS

Blood collection with or without diversion

Whole blood was collected under standard blood banking conditions with either a four-bag top and bottom citrate phosphate dextrose (CPD)-saline adenine glucose mannitol (SAGM) red cell (RBC) inline filter system (Compoflex, Fresenius Hemocare, NPBI International, Emmer-Compascuum, the Netherlands) or a comparable system (Baxter PL146-CPD-70 mL 3-Optipure, Baxter, Utrecht, the Netherlands).

Sanquin Blood Bank Region Southeast (Nijmegen, the Netherlands) used a five-bag top and bottom CPD-SAGM RBC inline filter system (Compoflex, Fresenius Hemocare, NPBI International) including an integrated sample bag (T3941, Fresenius Hemocare), in which diversion of the first 20 to 30 mL of the donation was performed. After collection of the first volume, a clamp was set and the sample bag was sealed. Donation proceeded normally in the collection bag with CPD. All other collection centers collected blood for infectious diseases and immunohematology testing after donation was completed via a sampling site attached to the collection system.

Processing to PCs

Whole blood is processed similarly at all collection centers after collection, with rapid cooling to 20°C and overnight storage at this temperature.¹³ Briefly, after a hard centrifugation of the whole blood, the buffy coats are collected. Five buffy coats (same blood group) are pooled and mixed with either 300 mL of plasma or additive solution (AS; PAS I, Baxter). The pooled buffy coats are centrifuged again (soft centrifugation) to produce T5 products. Preparation procedures for T5 varied slightly between regions, but these differences (type of leukodepletion filter and storage container) are not likely to cause variations in the degree of bacterial contamination.

The blood bank locations of Rotterdam (Region Southwest), Utrecht (Region Northwest), and Nijmegen (Region Southeast) used PAS II as AS in the T5 products; all other blood bank locations used plasma for pooling.

Skin disinfection

Before October 2002 skin disinfection was performed with various methods in the Sanquin collection centers, referred to as the "old skin disinfection method." Most centers (>95% of total collections) used a single swab method with 70 percent alcohol–0.5 percent chlorhexidine or 70 percent IPA, but some small centers used single swabs with iodine tincture, whereas one small center used a double-swab method with 70 percent alcohol–0.5 percent chlorhexidine. Because no differences were found between the various centers for the old methods,

the data for the old methods have been pooled (with and without exclusion of the center with the diversion bag). Starting from October 2002, a uniform disinfection method was introduced nationwide with a 30-second spaced double-swab method with 70 percent IPA. Sanquin Blood Bank Region Southwest introduced this new disinfection method in October 2002, the Regions North-east and Southeast did so in November 2002, and Region Northwest introduced it in January 2003.

Screening on bacterial contamination

For the screening on bacterial contamination, within 2 hours after preparation of a T5 (this is 16-22 hr after collection) or within 12 hours after collection of the apheresis product, both aerobic and anaerobic culture bottles were inoculated (approx. 7.5 mL per bottle; range, 5-10 mL). Inoculation was performed under aseptic conditions with a laminar airflow cabinet, as reported previously.⁷

Culture bottles were incubated at 35°C in the BacT/ALERT system until flagged positive or up to 7 days if negative (also in those cases were the corresponding bottle became positive). Positively flagged bottles were sent to regional reference laboratories for determination by plating the sample. PCs and RBCs related to an initially positive bottle were taken out of inventory or recalled. Corresponding RBCs, if available from stock or recall, were cultured in the BacT/ALERT (for 7 days; both aerobic and anaerobic bottle), and positively flagged bottles were also sent to the reference laboratories for determination.

Study design and statistical analysis

Both initial culture test results and data on the microbiologic determination have been included in analyses of the results over the complete calendar years 2002 and 2003. The results were used to test the effects of the new disinfection method and/or the diversion on the degree of contamination. The results of the center with the diversion bag were compared to the pooled results of all other centers not with the diversion bag.

Data showing a positive initial test, but without determination results, have been labeled as missing. If the determination test could not detect microorganisms, the initial test result has been labeled as negative determination culture.

Because the hypothesis was that the contamination degree would be decreased after introduction of diversion and/or new disinfection, differences in frequency of bacterial contamination between the (sub)groups were tested with a one-sided chi-square test unless indicated otherwise. Logistic regression was used to calculate the odds ratios (OR) for risk of bacterial contamination with the different methods (diversion and disinfection). Multivariate logistic regression was performed to correct for

possible confounding effects, such as seasonal effects and AS.

All statistical analyses were performed with computer software (SPSS, version 11.0, SPSS Inc., Chicago, IL).

RESULTS

Number of contaminated products

In 2002 and 2003, a total of 122,907 PCs were tested in the BacT/ALERT system, with an aerobic and an anaerobic bottle per product, each inoculated with 7.5 mL of PC. The majority of these PCs were T5, but 1814 products were made by pooling three buffy coats, with an initially positive signal rate of 0.39 percent ($n = 7$). A total of 8000 apheresis PCs were tested, with 0.30 percent ($n = 24$) initially positive in the BacT/ALERT system. Because of their small numbers, the products made by pooling three buffy coats are left out of further analysis, and the apheresis products are presented as separate group, with limited data analyses, leaving 113,093 T5 products.

In approximately 10 percent of initially positive results, with some variation per region, no microorganism could be cultured from the positive bottle. Infrequently, however, a microorganism could be isolated from one of the associated RBCs (9 of 106). For a limited number of initially positive samples no information was reported regarding determination culture (these are labeled as missing), but for the large majority (98%) data on determination were available.

Effects of diversion and disinfection methods

In Table 1 the frequency of bacterial contamination for the different collection methods is shown. Diversion was associated with a significant reduction of bacterial contamination from 0.95 to 0.50 percent (chi-square test, $p = 0.002$) with the old skin disinfection method and from 0.85 to 0.37 percent (chi-square test, $p = 0.001$) when the new disinfection method was applied. For collections without diversion, the new skin disinfection method compared to the old methods resulted in a mild reduction in initially positive samples from 0.95 to 0.85 percent (chi-square test, $p = 0.049$). For collections with diversion, the new skin disinfection method compared to the old method also resulted in a reduction in initially positive samples from 0.50 to 0.37 percent (chi-square test, $p = 0.18$).

Calculated on initially positive samples, diversion resulted in an OR of 0.47 (95% CI, 0.35-0.63; $p < 0.001$) with univariate logistic regression. Multivariate logistic regression, with correction for disinfection method, time of screening (season), and AS resulted in an OR of 0.49 (95% CI, 0.36-0.67; $p = 0.003$).

For the new disinfection, the OR was 0.88 (95% CI, 0.77-1.00; $p = 0.05$) in univariate analysis and 0.87 (95% CI,

TABLE 1. Degree of contamination in subsets of T5 products*

Collection method	No diversion	Diversion	Total
Old skin disinfections			
Total tested	42,582	4,362	46,944
Initially positive (%)	405 (0.95)	22 (0.50)	427 (0.91)
Positive determination culture (%)	373 (0.88)	18 (0.41)	391 (0.84)
Negative determination culture (%)	26 (0.06)	4 (0.09)	30 (0.06)
Missing subculture data	6	0	6
70 percent IPA skin disinfection			
Total tested	59,400	6,749	66,149
Initially positive (%)	505 (0.85)	25 (0.37)	530 (0.80)
Positive determination culture (%)	427 (0.72)	17 (0.25)	444 (0.67)
Negative determination culture (%)	68 (0.11)	8 (0.12)	76 (0.11)
Missing subculture data	10	0	10
Total test period			
Total tested	101,982	11,111	113,093
Initially positive (%)	910 (0.89)	47 (0.43)	957 (0.85)
Positive determination culture (%)	800 (0.78)	35 (0.32)	835 (0.74)
Negative determination culture (%)	94 (0.09)	12 (0.11)	106 (0.09)
Missing subculture data	16	0	16

* Absolute numbers, within parentheses: percentages of total tested.

0.76-0.99; $p = 0.03$) with multivariate analysis corrected for time of screening (season), AS, and diversion. Because of the study design, correction for the region was not possible, but no significant differences between the regions were found. Removing individual centers from the analysis did not alter any of the conclusions and only marginally affected estimated effect sizes and CIs.

The effects of the various interventions have been evaluated, either with the percentages of initially positive samples or with the percentage of positive samples resulting in a positive determination culture. The percentage of initially positive samples determines the effect of the interventions on the numbers of PCs and related RBCs blocked by the screening and thus the consequences for blood banking logistics. The positive determination cultures reflect the effect of the interventions on the final degree of bacterially contaminated PCs. The ORs were slightly lower (with lower p values) when calculated on the number of positive determination cultures, owing to the increase in negative determination cultures after introduction of diversion and/or the new disinfection method.

Plasma compared to AS

At three collection centers (Rotterdam in Region Southwest, Utrecht in Region Northwest, and Nijmegen in Region Southeast), T5 products were prepared in a mixture of PLT AS (PAS II, Baxter) and plasma (65:35 ratio, vol/vol; $n = 35\,812$). We have compared the contamination in PAS II products without diversion with plasma products without diversion to evaluate the effect of AS on the degree of contamination.

The frequency of bacterial contamination was slightly reduced in PAS II PLT products (0.36%) compared to plasma products (0.91%; chi-square test, $p = 0.44$, not sig-

nificant). This difference did not change after the introduction of the 70 percent IPA.

Determination results

Table 2 summarizes the different species found in the contaminated T5 products, with classification in some origin-related groups. The majority of detected microorganisms were skin bacteria, mainly diphtheroids or coagulase-negative staphylococci (CNS; and other Gram-positive cocci). The other bacteria belong either to the transient skin bacteria or to the gastrointestinal tract.

After diversion, contamination with skin flora (Table 2; both diphtheroids [chi-square test, $p < 0.001$] and the CNS plus group [chi-square test, $p = 0.001$]) was significantly reduced, whereas the other groups were not significantly reduced. The fact that no bacteria belonging to the gastrointestinal tract were found after diversion is probably due to their low frequency in combination with the relatively small numbers tested. The fraction of initially positive bottles with a negative determination culture was higher with diversion, although not significantly so (chi-square test, $p = 0.36$).

When comparing the old disinfection method with the new disinfection method (without diversion), a significant reduction of the CNS plus group was found (Table 2; chi-square test, $p < 0.001$), but no reduction of diphtheroids. Contamination with other bacteria was slightly reduced; however, this difference was significant only for *Staphylococcus aureus* (chi-square test, $p = 0.02$). As for diversion, an increase in the fraction with a negative determination culture was observed (chi-square test, $p = 0.002$).

Some significant differences in the type of microorganisms were detected between plasma and PAS II PLT

TABLE 2. Determination of initially positive samples*

Variable	Old disinfection, no diversion	New disinfection, no diversion	Diversion (both disinfections)	Totals
Number of PCs tested	42,582	59,400	11,111	113,093
Initially positive bottles	405	505	47	957
Missing determination	6	10	0	16
Skin flora				
Diphtheroids†	160 (0.38)	230 (0.39)	18 (0.16)	406
CNS plus‡	153 (0.36)	119 (0.20)	12 (0.11)	284
<i>S. aureus</i> §	9 (0.02)	3 (0.005)	1 (0.01)	13
Transient skin flora				
<i>Bacillus</i> spp.	25 (0.06)	35 (0.06)	4 (0.04)	64
Gastrointestinal tract flora				
Gram-negative rods¶	8 (0.02)	9 (0.02)	0	17
Streptococci	5 (0.01)	1 (0.002)	0	6
Peptostreptococci	9 (0.02)	15 (0.03)	0	24
Residual group				
Others	4 (0.01)	15 (0.03)	0	19
No microorganism	26 (0.06)	68 (0.11)	12 (0.11)	106

* Values given as absolute numbers (percentage of total tested samples), with an additional column adding up absolute numbers.

† Diphtheroids include: *Propionibacterium* spp. (mainly acnes), *Corynebacterium* spp., and unspecified diphtheroid rods or Gram-positive rods (not spore forming).

‡ CNS plus include all coagulase-negative *Staphylococcus* subspecies (mainly epidermidis) and Gram-positive cocci (less than 10% of the total; aerococci [2], micrococci [5], and unspecified [16]).

§ Although there are limited reports on *S. aureus* contamination originating from endogenous bacteremia in the donor.

|| *Bacillus* spp. (roughly 50% *B. cereus*), including some unspecified spore formers (12).

¶ Various species, i.e., *Pseudomonas* (1), *Brevundimonas* (1), *Flavomonas* (2), *Bacterioides* spp. (4), *Salmonella* (1), *Proteus vulgaris* (1), and some unspecified (6 aerobic, 1 anaerobic).

products. Both *S. aureus* and Gram-negative rods had a significantly lower frequency in PAS II products (chi-square test, $p = 0.01$, two-sided). Moreover, the frequency of initially positive bottles with a negative determination culture was lower in PAS II (chi-square test, $p = 0.01$, two-sided). These differences might be explained by a lower initial load with bacteria, because less potentially contaminated whole blood-derived material is used.

Aerobic and anaerobic bottles

Table 3 shows the mean time until the aerobic and anaerobic bottles became positive, in relation to the determination result. In general, aerobic bottles became positive sooner than anaerobic bottles. From the positive aerobic bottles only 35 (11%) turned positive after 5 days, whereas from the positive anaerobic bottles 221 (35%) turned positive after 5 days. Except for diphtheroid (more particularly the *Propionibacterium* spp.) and peptostreptococci species, most bacteria did not show a preference for either the aerobic or the anaerobic bottles (Table 3). This is in agreement with the results of spiking studies by Brecher and colleagues¹⁴ showing for most bacteria growth in both the aerobic and the anaerobic bottle. During the test period, only 46 positively flagged units were reported to become positive in both the aerobic and the anaerobic bottle. It must be kept in mind that every negative bottle (also in case the corresponding bottle became positive) was cultured for 7 days.

Apheresis products

Table 4 shows some details for the 8000 apheresis PCs, all collected with an apheresis set including a diversion pouch. Owing to small numbers, the 95 percent CIs overlap, and no significant differences were found between the old and new disinfection methods. As for the T5, the percentage of positively flagged bottles without microorganism in the determination culture was higher after introduction of the new disinfection method (chi-square test, $p = 0.26$). In the apheresis PCs in two cases a Gram-negative rod was detected (0.03%; an *Escherichia coli* and a *Bacteroides* spp.), in one case a *Bacillus* spp. (0.01%), and in two cases a *Streptococcus* (0.03%). In eight cases the bacteria belonged to the CNS plus group (0.1%), in three cases the bacteria belonged to the diphtheroids group (0.04%), and in seven cases a negative determination culture was obtained (0.09%). These frequencies were comparable to those found in the T5 products after diversion (Table 2), except for diphtheroids (0.04% vs. 0.16% in T5).

Follow-up procedures after positive flagging

PCs. For 790 (83% of total) positively flagged T5, data on recall procedures were available (Table 5). From these units, 386 (49%) units had to be recalled and 404 units were still at the blood bank. The majority (88%) of the recalled products had already been transfused and only 45 of the recalled products could be prevented from being transfused (Table 5). Positively flagged units, which were

TABLE 3. Growth characteristics for different bacteria species

Variable	Total number of bottles	No data on time until positive	Both bottles positive	Aerobic bottle		Anaerobic bottle	
				Time until positive*	Number	Time until positive*	Number
Total	957	38	46	1.8	330	4.0	635
Skin flora							
Diphtheroids†	408	5	4	3.7	45	5.0	362
CNS plus‡	284	2	26	1.1	165	2.6	143
<i>S. aureus</i> §	13	0	0	0.9	6	1.3	7
Transient skin flora							
<i>Bacillus</i> spp.	64	1	7	1.7	41	2.1	29
Gastrointestinal tract flora							
Gram-negative rods¶	17	0	0	1.9	10	2.9	7
Streptococci	6	0	3	2.8	4	3.0	5
Peptostreptococci	24	1	0		0	3.9	23
Residual group							
Others	19		3	1.3	9	4.0	13
No microorganism	106	13	3	2.3	50	2.4	46
Missing determination	15	16					

* Mean time in days until positive signal with BacT/ALERT.

† Diphtheroids include: *Propionibacterium* spp. (mainly *acnes*), *Corynebacterium* spp., and unspecified diphtheroid rods or Gram-positive rods (not spore forming).

‡ CNS plus include all coagulase-negative *Staphylococcus* subspecies (mainly *epidermidis*) and Gram-positive cocci (less than 10% of the total; aerococci [2]; micrococci [5], and unspecified [16]).

§ Although there are limited reports on *S. aureus* contamination originating from endogenous bacteremia in the donor.

|| *Bacillus* spp. (roughly 50% *B. cereus*), including some unspecified spore formers (12).

¶ Various species, i.e., *Pseudomonas* (1), *Brevundimonas* (1), *Flavomonas* (2), *Bacterioides* spp. (4), *Salmonella* (1), *Proteus vulgaris* (1), and some unspecified (6 aerobic, 1 anaerobic).

TABLE 4. Degree of contamination in subsets of apheresis products*

Variable	Old skin disinfections	70% IPA skin disinfection	Total test period
Total number tested	3037	4963	8000
Initially positive (%)	7 (0.23)	17 (0.34)	24 (0.30)
Positive determination culture (%)	6 (0.20)	12 (0.24)	18 (0.23)
Negative determination culture (%)	1 (0.03)	5 (0.10)	6 (0.08)
Missing subculture	0	1	1

* Absolute numbers, within parentheses: percentages of total tested. All apheresis products were collected with a set with diversion pouch.

already transfused at the moment of detection, had a mean time until detection of 4.7 days, whereas for the units still in the blood bank the mean time until detection was 2.2 days. Of 345 units with a positive signal in the first 48 hours of culture, only 27 units had already been transfused.

Table 5 also shows the recall information in relation to the various microorganisms. For the rapidly growing bacteria, most of the PCs were still in the blood bank inventory or could successfully be recalled. The majority of already transfused PCs were contaminated with diphtheroids, mainly flagging positive between Day 4 and Day 7 of culture.

During this surveillance period, no severe clinical effects of units flagged positive after transfusion were reported to Sanquin or the Dutch hemovigilance system (Transfusion Reactions in Patients; TRIP). Over the entire period, there were 165 follow-up reports (for every case a

report was asked, but only in 40% a response was received) of transfused products corresponding to cultures flagged positive after release. In two cases mild clinical symptoms (fever) were reported, but no direct relation with the PLT transfusion was established. During the same period, two cases of sepsis were reported after transfusion of PCs with a negative signal in the screening¹⁵ (also after 7 days of cul-

turing). In both cases *Bacillus cereus* was identified as the causative microorganism, but it remains unclear whether this microorganism could have entered the PC during preparation or storage, due to pinholes in the bag, or whether it was definitely a false-negative result of the screening system (present in the sample, but not resulting in a positive flagging of the culture).

Related RBCs. In case of a positive signal in the bacterial screening of a pooled PLT product, corresponding RBCs were cultured. Data on RBC recall and cultures were available for 94 percent (901/957) of the initially positive flagged T5 units. In 40 percent of these cases there was a positive signal from the BacT/ALERT for one of the RBC units. In 85 percent of positive RBC units, the same microorganism as in the corresponding PC was found (majority diphtheroids). In the majority of cases where the microorganism was of different species, it belonged to the same group. Only in 27 cases was the microorganism found in

TABLE 5. Recall and transfusion details with respect to corresponding PCs and RBC units

Variable	Corresponding PC units				Related RBC units			
	Total number of PCs	Unknown*	Recall†	Transfused‡	Total number of RBC units	Unknown*	Recall†	Transfused‡
Total	957	167	386	341	4785	375	741	138
Skin flora								
Diphtheroids§	408	57	256	234	2040	76	553	113
CNS plus	284	54	57	42	1420	85	92	12
<i>S. aureus</i> ¶	13	0	0	0	65	2	0	0
Transient skin flora								
<i>Bacillus</i> spp.**	64	10	16	12	320	15	28	2
Gastrointestinal tract flora								
Gram-negative rods††	17	0	3	3	85	25	2	1
Streptococci	6	1	1	1	30	0	1	0
Peptostreptococci	24	3	14	12	120	2	16	3
Residual group								
Others	19	3	11	9	95	0	6	1
No microorganism	106	23	28	28	530	90	43	6
Missing determination	16	16			80	80		

* No data on recall available.
† Recall of products already released to hospitals.
‡ Already transfused at time of recall.
§ Diphtheroids include: *Propionibacterium* spp. (mainly acnes), *Corynebacterium* spp., and unspecified diphtheroid rods or Gram-positive rods (not spore forming).
|| CNS plus include all coagulase-negative *Staphylococcus* subspecies (mainly epidermidis) and Gram-positive cocci (less than 10% of the total; aerococci [2]; micrococci [5], and unspecified [16]).
¶ Although there are limited reports on *S. aureus* contamination originating from endogenous bacteremia in the donor.
** *Bacillus* spp. (roughly 50% *B. cereus*), including some unspecified spore formers (12).
†† Various species, i.e., *Pseudomonas* (1), *Brevundimonas* (1), *Flavomonas* (2), *Bacterioides* spp. (4), *Salmonella* (1), *Proteus vulgaris* (1), and some unspecified (6 aerobic, 1 anaerobic).

the RBCs totally unrelated to the organism as found in the PCs. This number included the 9 cases with no determination culture for the PC, whereas a microorganism could be isolated from one of the associated RBC units. The bacterial species in these cases were CNS plus (4), diphtheroids (4), and *Bacillus* spp. (1).

Of a total of 4505 RBC units (901 PCs each with 5 related RBC units), 741 RBC units had already been released and had to be recalled for culturing. The recall was successful in 68 percent of the cases. A total of 234 units were not available for culture, including 138 RBC units (relating to 99 PC units) that had already been transfused. For 69 of these 138 cases, one of the other related RBC units contained the same bacterium as found in the culture from the PC. From this it might be concluded that only in the remaining 69 cases possibly contaminated RBCs were transfused. These were mainly related to positive PLT cultures in which diphtheroids found (66/69). Because RBCs are stored at 4°C, however, it is not likely that these transfused RBCs contained harmful quantities of bacteria. This is supported by the fact that no transfusion reactions were reported for these units.

DISCUSSION

Based on the results of two calendar years (2002 and 2003) of bacterial screening of all PCs in the Netherlands, it can be concluded that interventions to reduce bacterial con-

tamination were very effective, resulting in a reduction of initially positive cultures for pooled T5 products from 0.95 percent (no interventions) to 0.37 percent (two interventions: diversion and new skin disinfection). The 50 percent reduction in frequency upon diversion is very similar to that found in our previous whole-blood diversion study¹⁰ and also corresponds with the reduction in contamination reported by McDonald and coworkers.¹⁶ The double-swab 70 percent IPA disinfection method slightly enhanced the reducing effect on bacterial contamination of diversion, although this is of marginal significance and without synergy. The final frequency of 0.37 percent (95% CI, 0.24-0.55) positive cultures found for pooled T5 products after introduction of both diversion and new disinfection method is not significantly different from the 0.30 percent contamination rate for single donor apheresis PC (95% CI, 0.19-0.45), whereas the differentiation profile is also similar. This suggests that the relation between number of donor units and degree of bacterial contamination of the final PC, as described by Ness and colleagues,¹ no longer exists if special care is taken to avoid introduction of bacteria during collection. The finding that contamination is reduced to such a large extent by diversion has led to the introduction of the diversion pouch throughout the Netherlands, starting from July 2004.

Our current screening system for bacterial contamination of PC is highly sensitive by use of two bottles. The

fact that in less than 5 percent of positively flagged units both bottles were positive suggests that positive units have an initial bacterial contamination around the lower detection limit of the culture system. Owing to the high sensitivity, the percentage of initially positive units is relatively high in our screening system compared to other reported rates of bacterial contamination. Most likely, this is due to the fact that other studies use only one culture bottle, with lower inoculation volumes and shorter culture times. Wagner and Robinette¹⁷ showed that higher inoculation volumes lead to shorter detection times. Our results are very similar to those in Belgium, where a similar screening approach is used.^{18,19} When reanalyzing our results according to the system used in Denmark, that is, only the aerobic bottle and 5 days of culture, our result of 0.4 percent initially positive for T5 (with double-swab disinfections and without diversion) is very comparable to the Danish results.²⁰ Also for apheresis units, the recalculated initially positive rate of 0.1 percent (only aerobic bottle, 5 days culturing) resembles the values reported by other groups¹ taken into account that our inoculated volume is larger.

The selectivity of a screening system should be as high as possible, because false-positive samples result in unnecessary recalls and false-negative samples result in possible transfusion of positive units. For some as yet unknown reason, the rate of negative determination cultures is increased after the introduction of interventions for disinfection and diversion. The fraction of negative determination cultures is 0.047 percent of total tested bottles (two per unit), which is in agreement with data from Belgium and Denmark.^{18,20} This would result in a false-positive rate by system failure of about 1 of 2000 cultures. Given that in 9 percent of cases with a negative determination culture for PCs, one of the RBC units contained a microorganism, it remains questionable whether a negative determination culture really should be flagged false-positive. Another possibility would be that in some cases the microorganism still has growth capacity (positive signal in BacT/ALERT), but no colony-forming properties (negative determination culture). This possibility is not hypothetical, because experiments from our group showed that after UV-C illumination the survival of bacteria is much higher (about 1.5 log) when measured in liquid culture, compared to measurement of colony formation on solid media (unpublished results). Based on these results, we intend to implement a follow-up procedure for negative determination cultures, with additional attempts to obtain a subculture.

The effect of introducing a standardized double-swab 70 percent IPA disinfection method showed borderline significance in both univariate and multivariate statistical testing with respect to reduction of bacterial contamination. This is in contrast to literature results. McDonald and colleagues¹⁶ reported a possible reduction of approxi-

mately 50 percent by the introduction of double-swab disinfection. These results, however, were obtained with a first swab with IPA and a second swab with iodine tincture, which might explain differences in the results. Lee and coworkers²¹ recently also reported a significant reduction of the degree of bacterial contamination of PCs prepared from whole blood by the PLT-rich plasma method, as a result of a changed disinfection method. With respect to skin flora, however, as expected, our new disinfection method has a highly significant reducing effect on the CNS plus group, but no effect on diphtheroids. This can be explained by the fact that diphtheroids especially colonize the interior of the sebaceous glands²² whereas Gram-positive cocci, including CNS, are more on the skin surface. Surface disinfection will therefore be less adequate to remove diphtheroids, whereas diversion will reduce all kind of skin flora, as found in our study.

The various bacteria species detected in 2 years of bacterial screening of PCs in the Netherlands are classified as skin flora, transient skin flora, or gastrointestinal tract flora, with some very rough subclassification. Within the skin flora, the relatively slowly growing diphtheroids (either anaerobic *Propionibacterium* or aerobic *Corynebacterium*) represent the largest group. These bacteria are usually not considered being a clinical hazard^{14,23} but there are some reports describing transfusion-transmitted bacterial infection (TTBI) with *Propionibacterium*.^{24,25} Diphtheroids also are among the Gram-positive bacteria that can colonize prosthetic valves and intravascular implants, causing infections that are difficult to treat.²⁶ Upon prolongation of storage time to 7 days or longer, and without a screening system able to detect these bacteria, one should be aware of transmission of slow-growing bacteria, such as *Propionibacterium* spp. This problem is currently not encountered, because PCs containing these bacteria are generally transfused before reaching the threshold for inducing TTBI in the recipient.

The second largest group are the Gram-positive cocci not being *S. aureus* (CNS plus). These commensal skin flora are not considered very pathogenic either. Gram-positive cocci, however, are a regular cause of TTBI^{24,27} but seldom responsible for septic fatalities.²⁸ The small subgroup of *S. aureus* is the type of skin flora with a high clinical hazard profile¹ but all 13 cases found in our surveillance had a positive culture before the products were released.

The *Bacillus* spp. belongs to the transient skin flora and this group includes some not further determined spore formers. Owing to the etiology of infection (we are only considering transmission via transfusion), no further distinction was made between *B. cereus* (known from food poisoning) and other *Bacillus* spp. The new disinfection method has no effect on the frequency of this group, as expected, because spores are not inactivated by 70 percent IPA. Diversion is expected to result in a reduc-

tion for spore formers, but the observed reduction is not significant, likely because of the low numbers. Because spore formers remain a risk to cause TTBI even with bacterial culturing in place, further research should be focused on improved disinfection also effective in inactivating spores.

Approximately 5 percent of all initial positive samples were determined as normally belonging to the gastrointestinal tract flora, although these bacteria can also be encountered as transient skin flora. The largest subgroup are the anaerobic *Peptostreptococci* spp. (associated with abdominal wound infections) and some *Streptococcus* spp., which are often reported in transfusion-associated sepsis.²⁸

The group of Gram-negative rods is very heterogeneous, with *Bacteroides* spp. and *Salmonella* spp. highly likely to have come from the donor's blood circulation. The aerobic Gram-negative rods, although we did not fully determine the species in all cases, are most probably non-fermentative bacilli and are highly likely to have been introduced as transient skin flora. The Gram-negative rods are well known as causative agents for TTBI, especially those cases related to septic fatalities.^{1,2,24,25,28} In our study most products positive for the presence of Gram-negative rods were prevented from entering the transfusion chain. In the single case with a transfused RBC unit, the culture turned positive after 5 days.

Among the remaining group, one remarkable microorganism is found, a *Nocardia* spp., well known as transient skin flora present in soil and causing pneumonia, especially in immunocompromised patients or in chronic lung disease.

Despite the absence of a quarantine period, in the Dutch practice more than 90 percent of the units that flagged positive within 2 days could be prevented from being transfused, including the majority of those contaminated with the more dangerous bacteria like Gram-negative bacteria, *B. cereus* and *S. aureus*. Ninety percent of units flagged positive after being released had a positive signal after more than 2 days of culturing. These units were mainly found to be contaminated with diphtheroids, especially *Propionibacterium* spp. and the majority of these units had already been transfused. During the period of the study, two mild transfusion reactions were reported due to transfusion of such units. In general, however, underreporting is noticed in hemovigilance systems, emphasizing the need for improvement. Extension of the storage period of PCs from 5 to 7 days allows for an initial quarantine period as proposed by Munksgaard and colleagues²⁰ but this will have a very limited impact on the number of PCs already transfused at the time of a positive culture.

In conclusion, it is shown that introduction of diversion and improvement of skin disinfection are effective in reducing the frequency of contaminated blood products.

Still, the remaining risk is high enough to warrant screening for bacterial contamination. The screening system in place in the Netherlands proves to be successful in preventing the seriously contaminated PCs from entering the transfusion chain, a similar conclusion to that reported for Belgium¹⁹ with a similar screening system.

ACKNOWLEDGMENT

The authors thank M.P. Janssen, PhD (Julius Center for Health Sciences and Primary Care, UMC, Utrecht, the Netherlands), for help with the statistical analysis.

REFERENCES

1. Ness PM, Braine HG, King K, et al. Single-donor platelets reduce the risk of septic platelet transfusion reactions. *Transfusion* 2001;41:857-61.
2. Kuehnert MJ, Roth VR, Haley NR, et al. Transfusion-transmitted bacterial infection in the United States, 1998 through 2001. *Transfusion* 2001;41:1493-9.
3. Morrow JF, Braine HG. Septic reactions to platelet transfusion: a persistent problem. *JAMA* 1991;266:555-8.
4. Dodd RY, Notari EP, Stramer SL. Current prevalence and incidence of infectious disease markers and estimated window-period risk in the American Red Cross blood donor population. *Transfusion* 2002;42:975-9.
5. Bush MP, Glynn SA, Stramer SL, et al. A new strategy for estimating risks of transfusion-transmitted viral infections based on rates of detection of recently infected donors. *Transfusion* 2005;45:254-64.
6. Standards for blood banks and transfusion services. 22nd ed. Bethesda; American Association of Blood Banks; 2004.
7. de Korte D, Marcelis JH, Soeterboek AM. Determination of the degree of bacterial contamination of whole-blood collections using an automated microbe-detection system. *Transfusion* 2001;41:815-8.
8. Bruneau C, Perez P, Chassaigne M, et al. Efficacy of a new collection procedure for preventing bacterial contamination of whole-blood donations. *Transfusion* 2001;41:74-81.
9. Wagner SJ, Robinette D, Friedman IL, et al. Diversion of initial blood flow to prevent whole-blood contamination by skin surface bacteria: an in vitro model. *Transfusion* 2000;40:335-8.
10. Olthuis H, Puylaart C, Verhagen C, Valk L. Methods for removal of contaminating bacteria during venapuncture. *Proceedings V Regional ISBT Congress, Venice* 77; 1995.
11. de Korte D, Marcelis JH, Verhoeven AJ, et al. Diversion of first blood Volume results in a reduction of bacterial contamination for whole-blood collections. *Vox Sang* 2002;83:13-6.
12. McDonald CP, Lowe P, Roy A, et al. Evaluation of donor arm disinfection techniques. *Vox Sang* 2001;80:135-41.

13. Pietersz RNI, de Korte D, Reesink HW, et al. Storage of whole blood for up to 24 h at ambient temperature prior to component preparation. *Vox Sang* 1989;56:145-50.
14. Brecher ME, Means N, Jere CS, et al. Evaluation of an automated culture system for detecting bacterial contamination of platelets: an analysis with 15 contaminating organisms. *Transfusion* 2001;41:477-82.
15. Te Boekhorst TA, Beckers EA, Vos M, Verneij H, van Rhenen DJ. Clinical significance of bacteriologic screening in platelet concentrates. *Transfusion* 2005;45:514-9.
16. McDonald CP, Roy A, Mahajan P, et al. Relative values of the interventions of diversion and improved donor-arm disinfection to reduce the bacterial risk from blood transfusion. *Vox Sang* 2004;86:178-82.
17. Wagner SJ, Robinette D. Evaluation of an automated microbiologic blood culture device for detection of bacteria in platelet components. *Transfusion* 1998;38:674-9.
18. Schelstraete B, Bijneens BJ, Wuyts G. Prevalence of bacteria in leukodepleted pooled platelet concentrates and apheresis platelets: a 3 years experience. *Transfusion* 2000;40(Suppl):12S.
19. Van Haute I, Van Vooren M, Lootens N, Claeys H, Vandekerckhove B. Screening of platelet concentrates for bacterial growth. *Transfusion* 2000;40(Suppl):70S.
20. Munksgaard L, Albjerg L, Lillevang ST, et al. Detection of bacterial contamination of platelet components: six years' experience with the BacT/ALERT system. *Transfusion* 2004;44:1166-73.
21. Lee CK, Hin PL, Mak A, et al. Impact of donor arm skin disinfection on the bacterial contamination rate of platelet concentrates. *Vox Sang* 2002;83:204-8.
22. Sneath PH, Mair NS, Sharpe ME, Holt JG. Genus *Propionibacterium*. In: Cummins CS, Johnson JL, editors. *Bergey's manual of systematic bacteriology*. Baltimore: Williams & Wilkins; 1986. p. 1346-53.
23. Kunishima S, Inoue C, Kamiya T, et al. Presence of *Propionibacterium acnes* in blood components. *Transfusion* 2001;41:1126-9.
24. Sazama K. Reports on 355 transfusion-associated deaths, 1976 through 1985. *Transfusion* 1990;30:583-90.
25. Perez P, Salmi LR, Follea G, et al. Determinants of transfusion-associated bacterial contamination: results of the French BACTHEM Case-Control Study. *Transfusion* 2001;41:862-72.
26. Threlkeld MG, Cobbs CG. Infectious disorders of prosthetic valves and intravascular devices. In: Mandel GL, Bennett JE, Dolin R, editors. *Principles and practice of infectious diseases*. New York: Churchill Livingstone; 1995. p. 783-93.
27. Wagner SJ, Friedman LJ, Dodd RY. Transfusion-associated bacterial sepsis. *Clin Microbiol Rev* 1994;7:290-302.
28. Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and interventions. *Vox Sang* 2004;86:157-63. ■

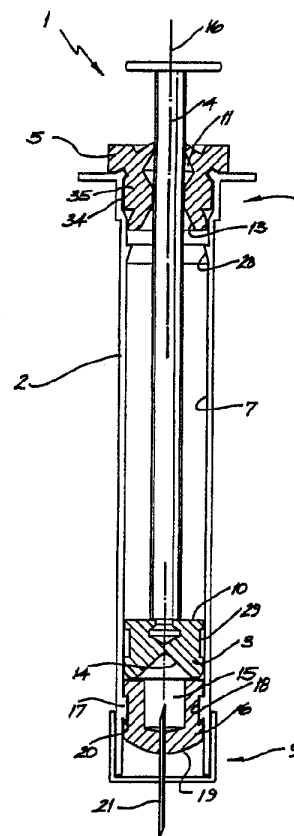


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : A61B 5/14	A1	(11) International Publication Number: WO 92/16144 (43) International Publication Date: 1 October 1992 (01.10.92)
(21) International Application Number: PCT/AU92/00105 (22) International Filing Date: 10 March 1992 (10.03.92) (30) Priority data: PK 5140 15 March 1991 (15.03.91) AU (71) Applicant (for all designated States except US): GOLD-SPILL PTY. LTD. [AU/AU]; 8 Eagle Street, Alderley, QLD 4051 (AU). (72) Inventor; and (75) Inventor/Applicant (for US only) : ROBB, Darryl, Gordon [AU/AU]; 10 Chapple Lane, Gympie, QLD 4570 (AU). (74) Agent: F.B. Rice & Co.; 28A Montague Street, Balmain, NSW 2041 (AU).		(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European patent), NO, PL, RO, RU, SD, SE, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent), US. Published <i>With international search report.</i>

(54) Title: BODY FLUID EXTRACTION DEVICE**(57) Abstract**

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



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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

- 1 -

BODY FLUID EXTRACTION DEVICEField of the Invention

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

Background

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

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

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

- 2 -

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

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

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

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

Summary of the Invention

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

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

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

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

- 3 -

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

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

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

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

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

- 4 -

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

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

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

In this way, a body fluid extraction device is

- 5 -

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

Brief Description of the Drawings

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

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

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

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

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

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

- 6 -

device;

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

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

Detailed Description of the Preferred Embodiment

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

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

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

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

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

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

- 7 -

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

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

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

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

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

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

- 8 -

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

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

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

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

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

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

- 9 -

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

Sealing means 5 is constructed from a compressible 10 elastic material such that any attempt to deform its outer surface results in a variation of an internal pressure within the compressible elastic material. Plunger 4 passes through hole 11 in sealing means 5 so that the internal pressure is communicated as a pressure of sealing 15 means 5 on plunger 4. This results in a frictional force between sealing means 5 and plunger 4 which retards its rate of movement.

Sealing means 5 can be rotated within portion 34 of the tubular body 2 about longitudinal axis 16. When 20 sealing means 5 is rotated relative to portion 34 of tubular body 2 such that large dimensions 26 and 24 are substantially collinear. The internal pressure in sealing means 5 is a minimum. However, when sealing means 5 is rotated relative to portion 34 of tubular body 2 such that 25 large dimension 26 is substantially collinear with small dimension 30, the internal pressure in sealing means 5 is a maximum.

Thus, by varying an angle of rotation of sealing means 5 relative to tubular body 2, a user of the device 30 can control the amount of pressure exerted by sealing means 5 on plunger 4. This results in a controllable frictional force between sealing means 5 and plunger 4 which controllably retards the rate of movement of plunger 4, the rate of movement of piston 3, and the rate 35 of body fluid extraction.

- 10 -

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

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

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

- 11 -

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

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

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

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

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

- 12 -

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

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

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

Plug 114 will serve to prevent the complete removal of piston head 95, after removal of the cannular the cap
25 112 is replaced over sleeve 111, and the sample of blood or other fluid, is now ready for safe and convenient transportation or storage.

- 13 -

CLAIMS:-

1. A device for extracting body fluid comprising:
a tubular body having a proximal end, a distal end, and a bore;
5 a piston disposed within the bore, the piston having a proximal face, a distal face, and an outer face, the outer face being in slidable contact with the bore;
a plunger mounted slidably at the proximal end of the tubular body and removably attached to the proximal face
10 of the piston for pushing the piston from the proximal end of the tubular body towards the distal end of the tubular body during a preparatory stroke in which an external pressure is applied to the plunger, the plunger having a shank;
15 sealing means for slidably sealing the proximal end of the tubular body to the shank of the plunger so as to form a first chamber defined by the bore, the shaft, the sealing means, and the proximal face of the piston, so that a pressure reduction is formed in the first chamber
20 during the preparatory stroke of the plunger;
closure means to close the distal end of the tubular body so as to form a second chamber defined by the bore, the distal face of the piston and the closure means;
the closure means is adapted to cooperate with
25 filling means for placing the body fluid in fluid communication with the second chamber so that, after the external pressure is removed from the plunger, the pressure reduction in the first chamber causes the piston to move towards the proximal end of the tubular body and
30 to draw body fluid into the second chamber.
2. A device for extracting body fluid as claimed in claim 1 in which the closure means comprises
a bung situated within the bore between the piston and the distal end of the tubular body, the bung having an
35 outer wall in slidable contact with the bore, so as to

- 14 -

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

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

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

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

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

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

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

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

- 15 -

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

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

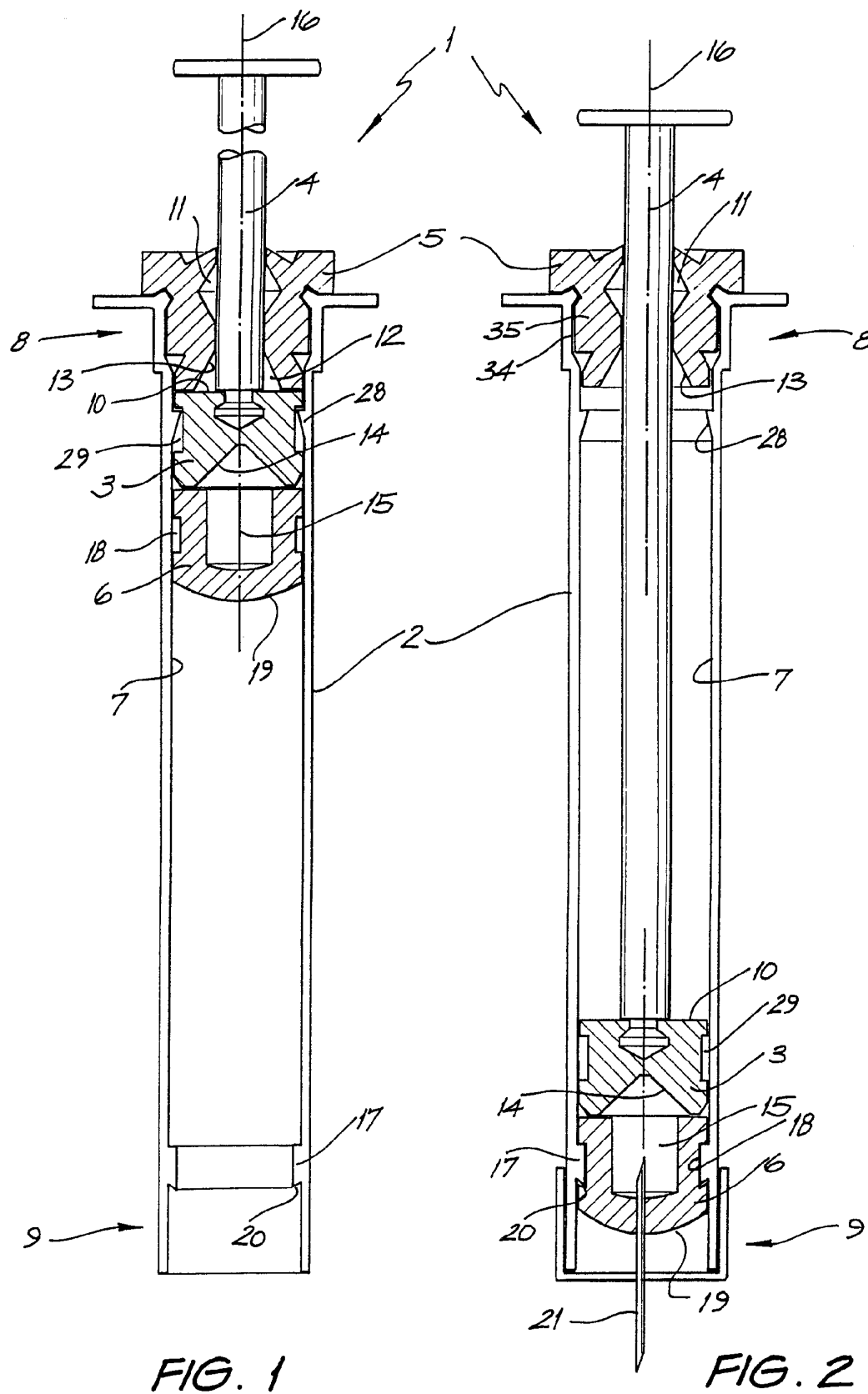
5 a circumferential groove around the outer wall of bung so that, at the end of the preparatory stroke, the circumferential rib is substantially aligned with the circumferential groove so as to impede a movement of the bung towards the proximal end of the tubular body.

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

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

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

1/3



2/3

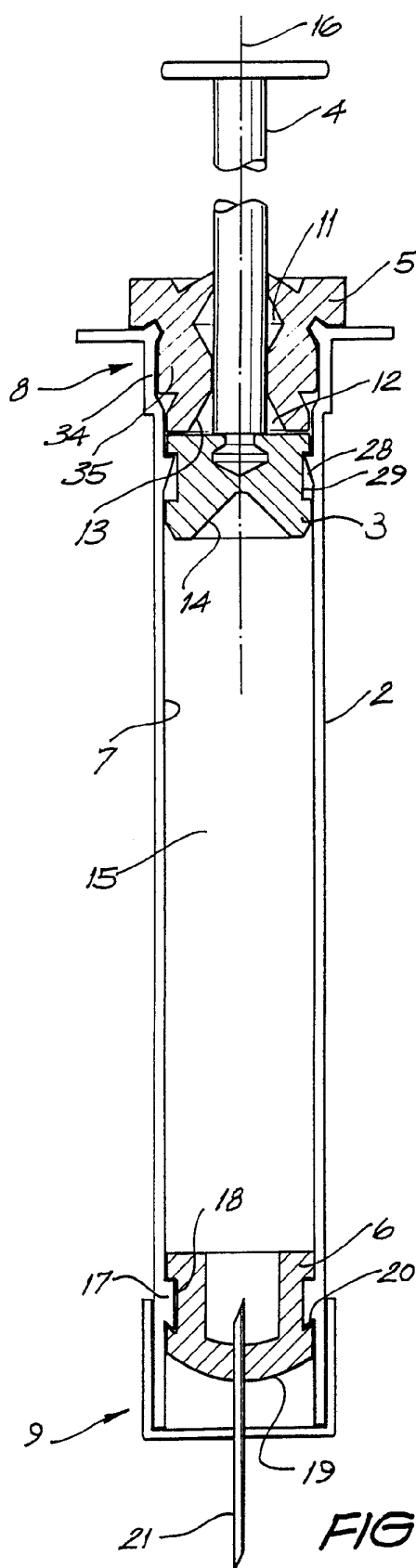


FIG. 3

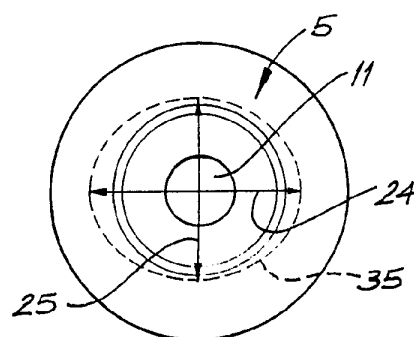


FIG. 4

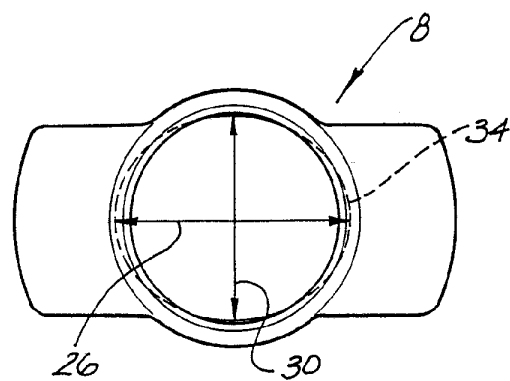


FIG. 5

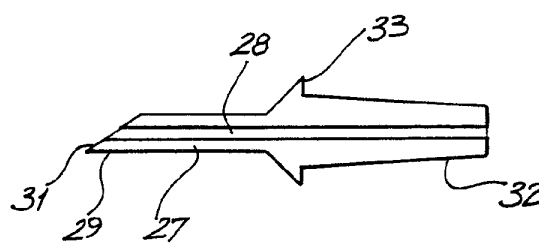


FIG. 6

INTERNATIONAL SEARCH REPORT

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent classification (IPC) or to both National Classification and IPC Int. Cl. ⁸ A61B 5/14		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC	A61B 5/14	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
AU:IPC as above		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹		
Category [*]	Citation of Document, ¹¹ with indication, where appropriate of the relevant passages ¹²	Relevant to Claim No ¹³
X,Y	EP,A,0279956 (VAN-TEC INCORPORATED) 31 August 1988 (31.08.88) See whole document, particularly claim 1.	(1,9-10)
Y	US,A,4361155 (ANASTASIO) 30 November 1982 (30.11.82) See column 3, lines 40-45.	(9)
Y	US,A,3930492 (HATSUNO et al) 6 January 1976 (06.01.76) See column 2.	(9-10)
A	US,A,4041934 (GENESE) 16 August 1977 (16.08.77)	
(continued)		
<div> <div> [*] Special categories of cited documents : ¹⁰ </div> <div> <p>"A" Document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div> <p>"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</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"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</p> <p>"&" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search 22 May 1992 (22.05.92)		Date of Mailing of this International Search Report 2 June 1992 (02.06.92)
International Searching Authority AUSTRALIAN PATENT OFFICE		Signature of Authorized Officer A HENDRICKSON 

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET		
A	US,A,4215702 (AYER) 5 August 1980 (05.08.80)	A US,A,4215702
A	US,A,4257426 (BAILEY) 24 March 1981 (24.03.81)	
A	GB,A,2218076 (BATES) 8 November 1989 (08.11.89)	
V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE ¹		
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:		
1. ☐ Claim numbers ..., because they relate to subject matter not required to be searched by this Authority, namely:		
2. ☐ Claim numbers ..., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:		
3. ☐ Claim numbers ..., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4a		
VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING ²		
This International Searching Authority found multiple inventions in this international application as follows:		
1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.		
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:		
3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:		
4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.		
Remark on Protest		
☐ The additional search fees were accompanied by applicant's protest.		
☐ No protest accompanied the payment of additional search fees.		

**ANNEX TO THE INTERNATIONAL SEARCH REPORT ON
INTERNATIONAL APPLICATION NO. PCT/AU 92/00105**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member	
US	4361155		
EP	279956	JP 63246145	US 4766908
US	3930492		

END OF ANNEX

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

FREDRIC I. WEINBAUM,^{1,2*} SOL LAVIE,³ MARGARET DANEK,² DIANE SIXSMITH,⁴
GEORGE F. HEINRICH,⁵ AND STEPHEN S. MILLS⁵

*Departments of Surgery,¹ Pathology,³ Emergency Medicine,⁴ Quality Management,² and Administration,⁵
The New York Hospital Medical Center of Queens, Flushing, New York†*

Received 12 July 1996/Returned for modification 20 August 1996/Accepted 5 December 1996

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

* Corresponding author. Mailing address: The New York Hospital Medical Center of Queens, 56-45 Main St., Flushing, NY 11355. Phone: (718) 670-1817. Fax: (718) 670-1196.

† The New York Hospital Medical Center of Queens is an affiliate of the New York Hospital-Cornell Medical Center and a member of The New York Hospital Care Network.

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	<i>P</i> value	Duration of study (mo)	No. of contaminated cultures/total no. of cultures (%)	<i>P</i> 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

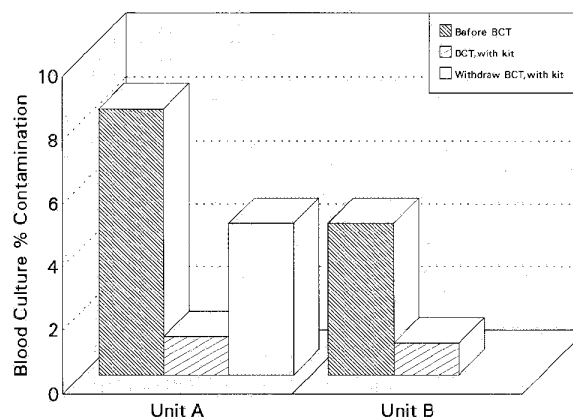


FIG. 1. Effect of BCT and commercial prep kits on rate of blood culture contamination.

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.

ACKNOWLEDGMENTS

We acknowledge James Rahal for critical review of the manuscript, Moises Malowany for suggestions and support, Susan Luca for excellent secretarial assistance, and finally, our Clinical Support Quality Assessment and Improvement Committee for its contribution to the project.

REFERENCES

1. Bates, D. W., and T. H. Lee. 1992. Rapid classification of positive blood cultures: prospective validation of a multivariate algorithm. *JAMA* 267: 1962-1966.
2. Bates, D. W., L. Goldman, and T. H. Lee. 1991. Contaminant blood cultures and resource utilization: the true consequences of false-positive results. *JAMA* 265:365-369.
3. Berwick, D. M. 1989. Sounding board: continuous improvement as an ideal in health care. *N. Engl. J. Med.* 320:53-56.
4. Crosby, P. B. 1979. *Quality is free: the art of making quality certain*. McGraw-Hill Book Company, New York, N.Y.
5. Crosby, P. B. 1984. *Quality without tears: the art of hassle-free management*. McGraw-Hill Book Company, New York, N.Y.
6. Dunagan, W. C., R. S. Woodward, G. Medoff, et al. 1989. Antimicrobial misuse in patients with positive blood cultures. *Am. J. Med.* 87:253-259.
7. Juran, T. M. 1992. *Juran on quality by design*. The Free Press, Macmillan, Inc., New York, N.Y.
8. Reller, L. B., P. R. Murray, and J. O. MacLowry. 1982. Cumitech 1A, Blood cultures II. Coordinating ed., J. A. Washington II. American Society for Microbiology, Washington, D.C.
9. Schiffman, R. B., and A. Pindur. 1993. The effect of skin disinfection materials on reducing blood culture contamination. *Am. J. Clin. Pathol.* 99:536-538.
10. Strand, C. L., R. R. Wajsbort, and K. Sturmann. 1993. Effect of Iodophor vs. iodine tincture skin preparation on blood culture contamination rate. *JAMA* 269:1004-1006.



Espacenet

Bibliographic data: WO2017019552 (A1) — 2017-02-02

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Inventor(s): ROGERS BOBBY [US]; KANG GINO [US]; DETLOFF JOHN [US] ± (ROGERS, Bobby, ; KANG, Gino, ; DETLOFF, John)

Applicant(s): KURIN INC [US] ± (KURIN, INC)

Classification: - international: A61B5/15; A61B5/153; A61B5/154
- cooperative: A61B5/15003 (EP, IL, US); A61B5/150213 (EP, IL, US); A61B5/150221 (IL, US); A61B5/150389 (EP, IL, US); A61B5/150473 (EP, IL, US); A61B5/150572 (EP, IL, US); A61B5/150992 (IL, US); A61B5/153 (EP, IL, US); A61B5/154 (EP, IL, US); A61M39/04 (IL, US); A61M39/0693 (IL, US); A61M2039/0202 (IL, US); A61M2039/0633 (IL, US); A61M2039/068 (IL, US)

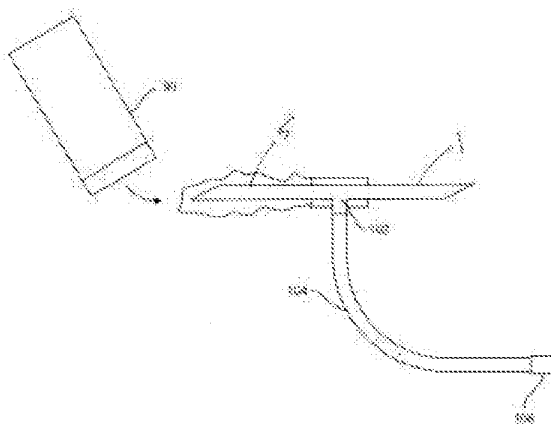
Application number: WO2016US43709 20160722 Global Dossier

Priority number(s): US201562196797P 20150724 ; US201562238636P 20151007 ; US201662318194P 20160404 ; US201615140448 20160427 ; US201615140443 20160427

Also published as: AU2016297849 (A1) AU2021202622 (A1) CA2993646 (A1) EP3324845 (A1) EP3324845 (B1) more

Abstract of WO2017019552 (A1)

Blood sample optimization systems and methods are described that reduce or eliminate contaminants in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (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.



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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
2 February 2017 (02.02.2017)



(10) International Publication Number
WO 2017/019552 A1

(51) International Patent Classification:
A61B 5/15 (2006.01) *A61B 5/154* (2006.01)
A61B 5/153 (2006.01)

(21) International Application Number:
PCT/US2016/043709

(22) International Filing Date:
22 July 2016 (22.07.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/196,797 24 July 2015 (24.07.2015) US
62/238,636 7 October 2015 (07.10.2015) US
62/318,194 4 April 2016 (04.04.2016) US
15/140,448 27 April 2016 (27.04.2016) US
15/140,443 27 April 2016 (27.04.2016) US

(71) Applicant: KURIN, INC. [US/US]; 10755 Scripps Poway
Parkway No. 257, San Diego, CA 92131 (US).

(72) Inventors: ROGERS, Bobby; 10755 Scripps Poway Park-
way No. 257, San Diego, CA 92131 (US). KANG, Gino;
10755 Scripps Poway Parkway No. 257, San Diego, CA
92131 (US). DETLOFF, John; 10755 Scripps Poway
Parkway No. 257, San Diego, CA 92131 (US).

(74) Agents: CLEARY, James, P. et al.; Mintz Levin Cohn
Ferris Glovsky And Popeo, P.C., 3580 Carmel Mountain
Road, Suite 300, San Diego, CA 92130-6768 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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

Published:

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

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

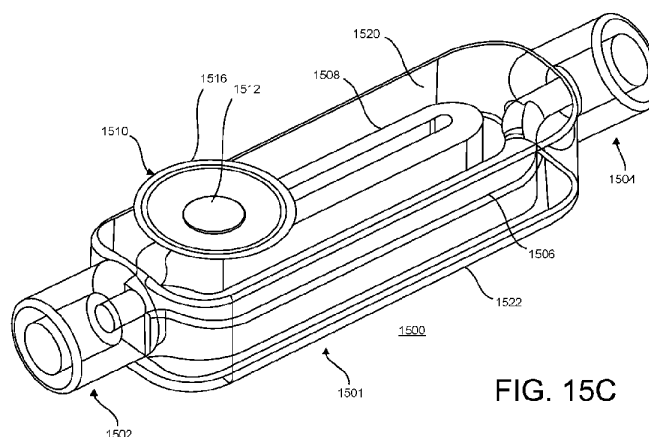


FIG. 15C

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

WO 2017/019552 A1

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

CROSS-REFERENCE TO RELATED APPLICATIONS

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

BACKGROUND

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

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

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

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

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

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

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

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

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

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

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

SUMMARY

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

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

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

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

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

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

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

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

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

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

BRIEF DESCRIPTION OF THE DRAWINGS

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

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

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

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

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

- [0028] FIG. 5 illustrates a blood sample optimization system in accordance with another alternative implementation.
- [0029] FIG. 6 illustrates a blood sample optimization system in accordance with an alternative implementation.
- [0030] FIG. 7 is a flowchart of a method for optimizing a quality of a blood culture.
- [0031] FIGS. 8A – 8E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with some implementations.
- [0032] FIG. 9 illustrates a pathway splitter for use in a blood sequestrations system.
- [0033] FIGS. 10A – 10D illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with alternative implementations.
- [0034] FIGS. 11A – 11E illustrate a blood sequestration system for non-contaminated blood sampling, in accordance with other alternative implementations.
- [0035] FIGS. 12A-12D illustrate a blood sample optimization system including a blood sequestration device in accordance with yet other alternative implementations.
- [0036] FIGS. 13A-13D illustrate a blood sample optimization system 1300 in accordance with yet another alternative implementations.
- [0037] FIGS. 14A-14E illustrate yet another implementation of a blood sampling system to sequester contaminants of an initial aliquot or sample to reduce false positives in blood cultures or tests performed on a patient's blood sample.
- [0038] FIGS. 15A-15G illustrate a blood sequestration device and method of using the same, in accordance with yet another implementation.
- [0039] FIGS. 16A-16D illustrate a blood sequestration device in accordance with yet another implementation.

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

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

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

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

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

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

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

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

DETAILED DESCRIPTION

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

or fluid-tight connector or connection, such as threading or Luer fitting, or the like.

Accordingly, as discussed above, the blood sequestration device 1600 can be fabricated and sold with the patient needle and/or tubing and the blood sample collection device as a single unit, eliminating the need for connecting the patient needle and the blood sample collection device to the blood sequestration device 1600 at the time of blood draw or sampling.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

CLAIMS

1. A blood sequestration device comprising:
an inlet port;
an outlet port;
a sequestration chamber connected with the inlet port, the sequestration chamber having a vent comprising an air permeable blood barrier;
a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port; and
a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.
2. The blood sequestration device in accordance with claim 1, wherein the air permeable blood barrier includes an air permeable material that seals at least partially upon contact with blood.
3. The blood sequestration device in accordance with claim 1, wherein the sequestration chamber includes a sequestration channel defined in the housing.
4. The blood sequestration device in accordance with claim 3, further comprising a blood sampling pathway connected with the inlet port, and wherein the inlet port defined by the housing has a cross-sectional geometry consistent with the blood sampling pathway.
5. The blood sequestration device in accordance with claim 3, wherein the sampling channel defined by the housing has a cross-sectional geometry consistent with the inlet port.
6. The blood sequestration device in accordance with claim 1, wherein the sequestration chamber and the sampling channel are connected with the inlet port by a junction that is configured to direct a first portion of blood to the sequestration chamber.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

an outlet port connected with a distal end of the sampling channel for conveying the second portion of the blood sample to the sample needle; and
a housing that houses and defines the inlet port, the outlet port, the sequestration chamber, and the sampling channel.

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

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

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

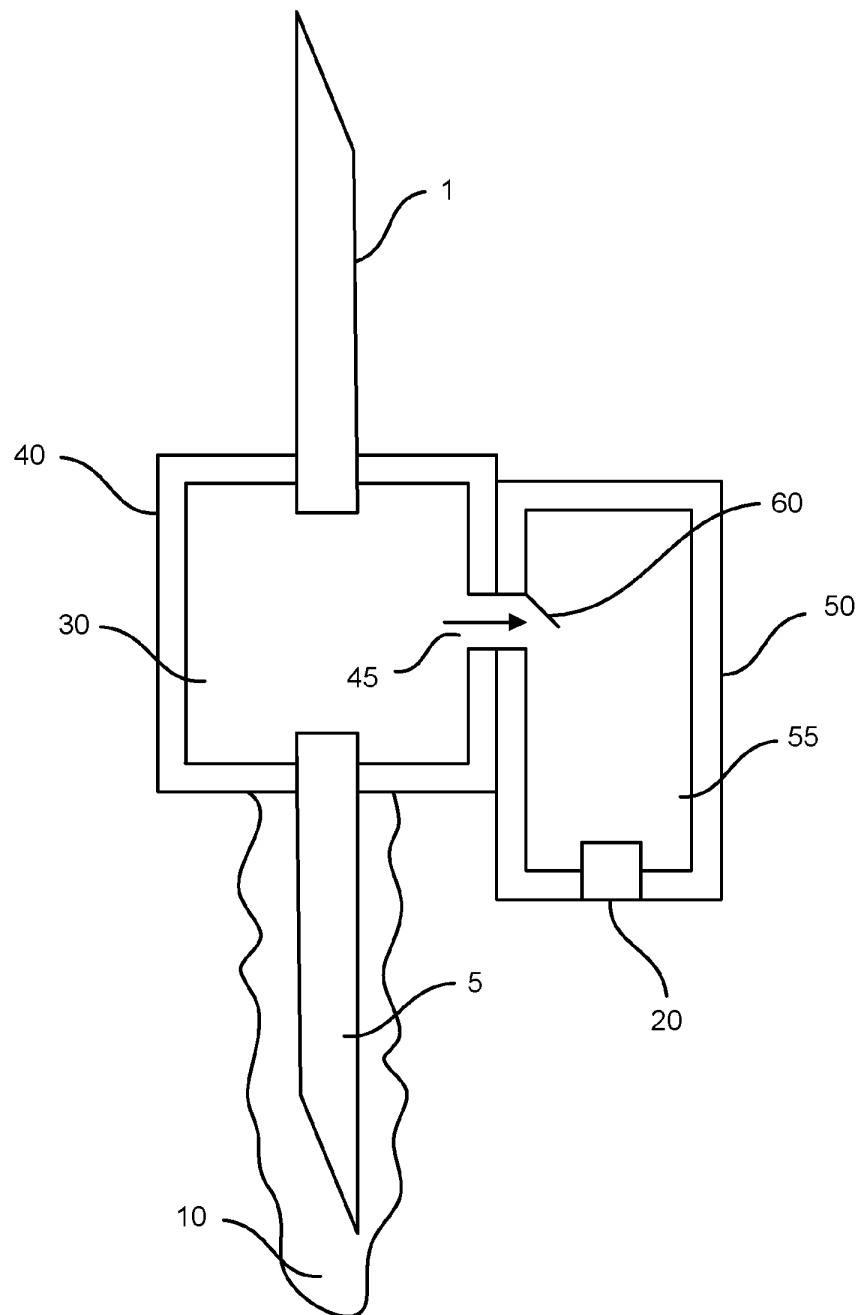


FIG. 1

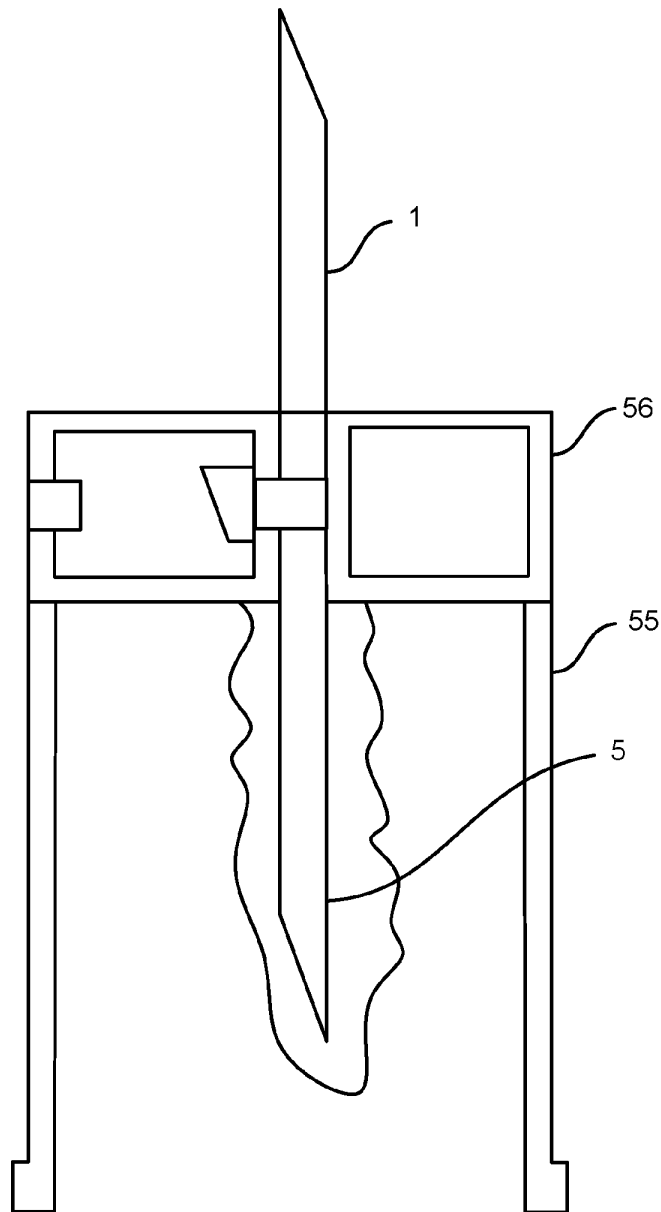


FIG. 2

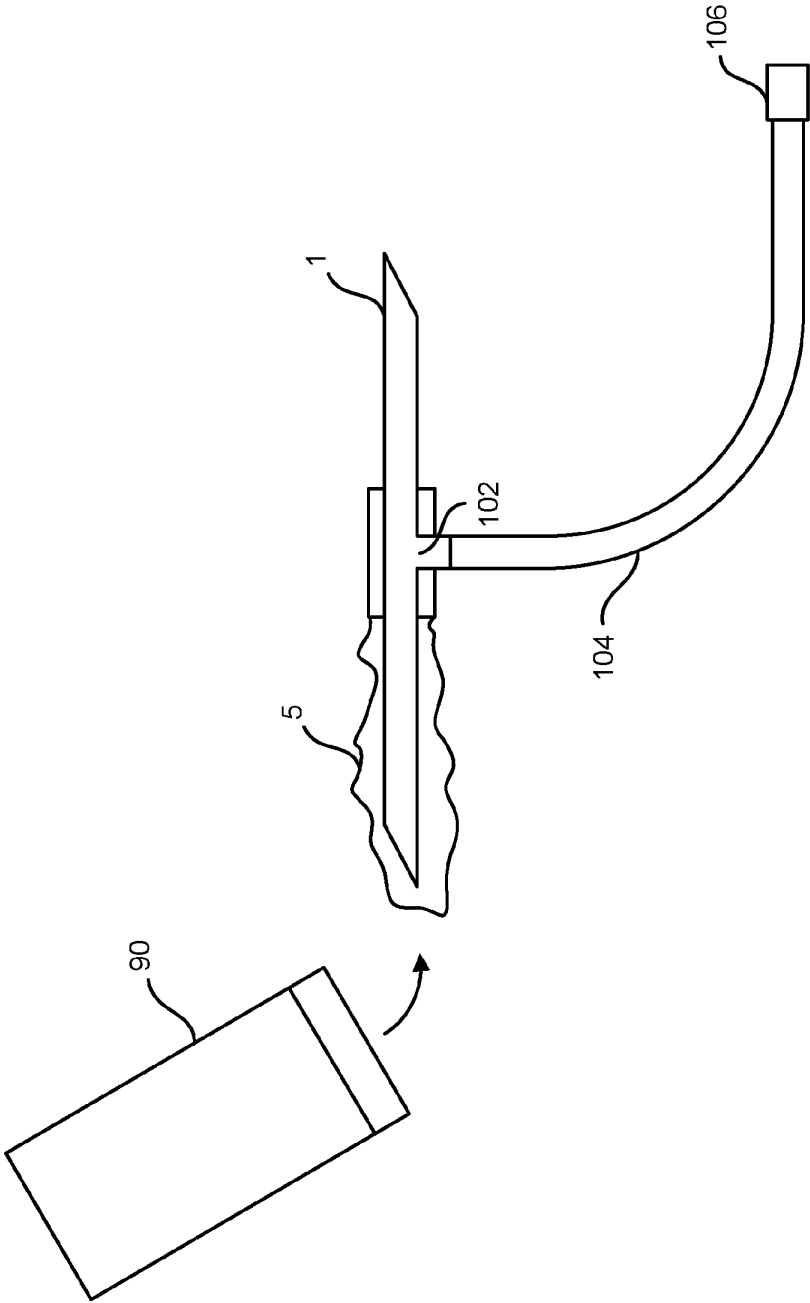


FIG. 3

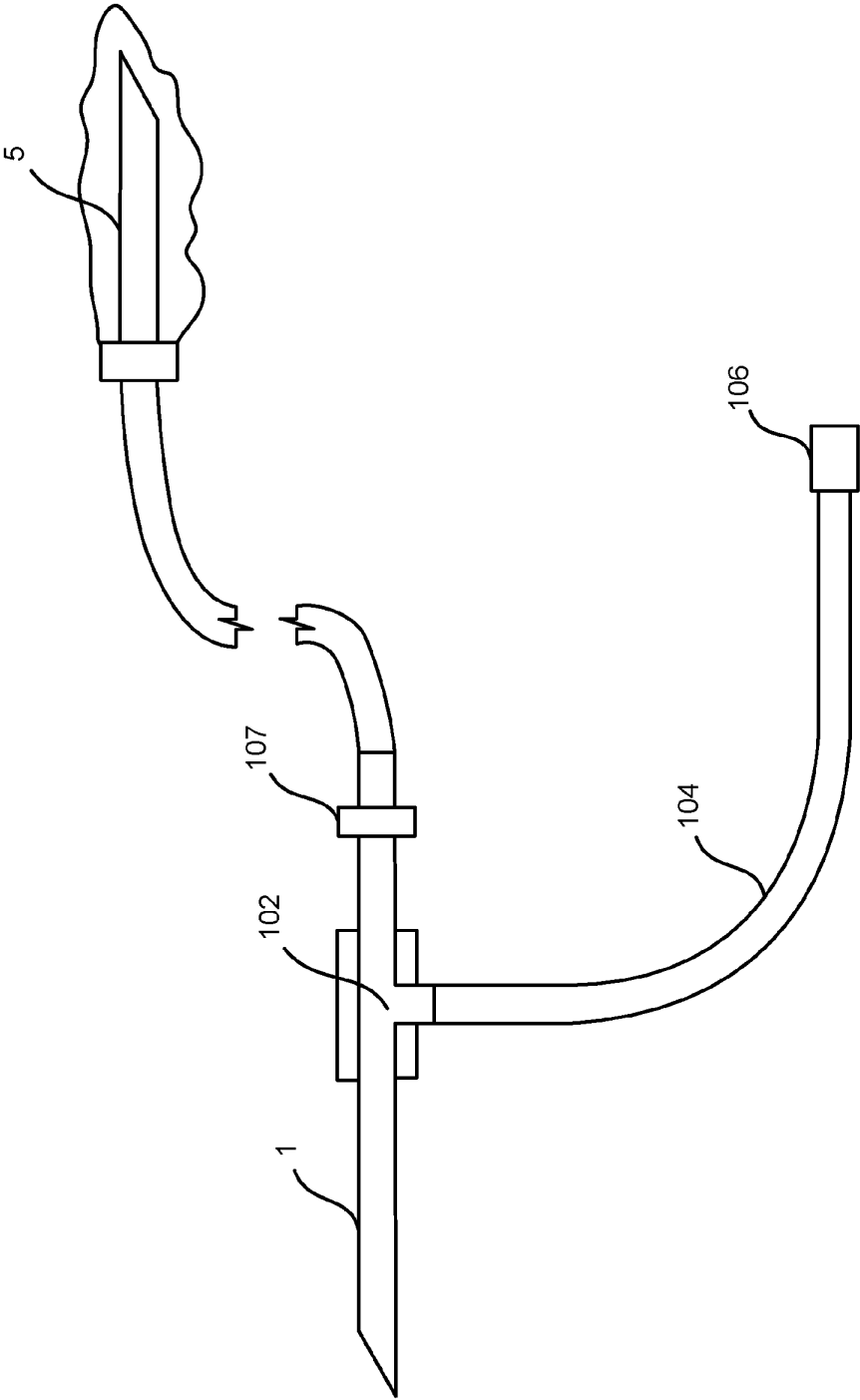


FIG. 4

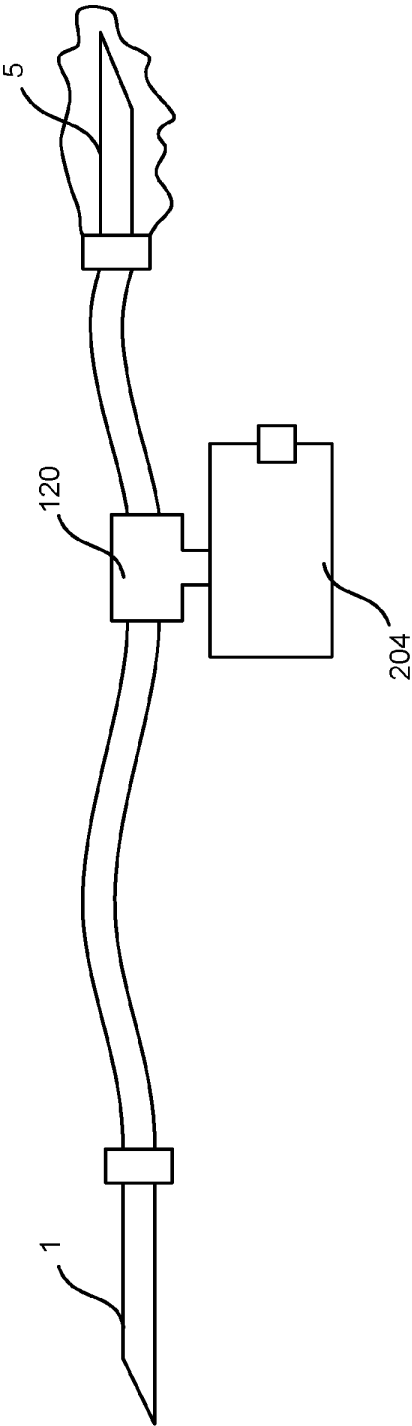


FIG. 5

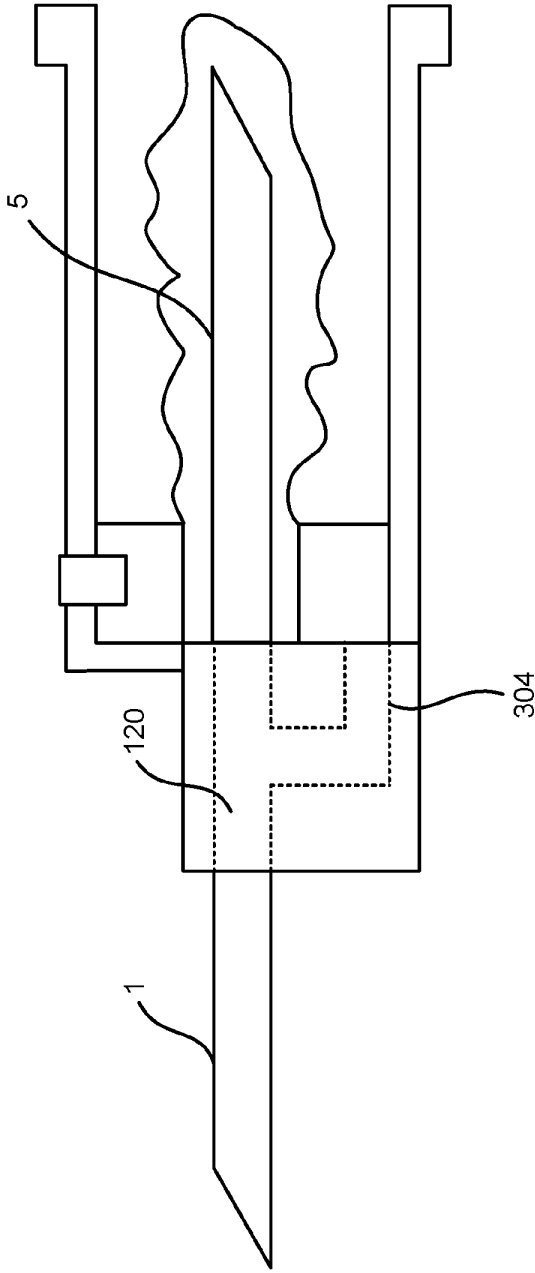
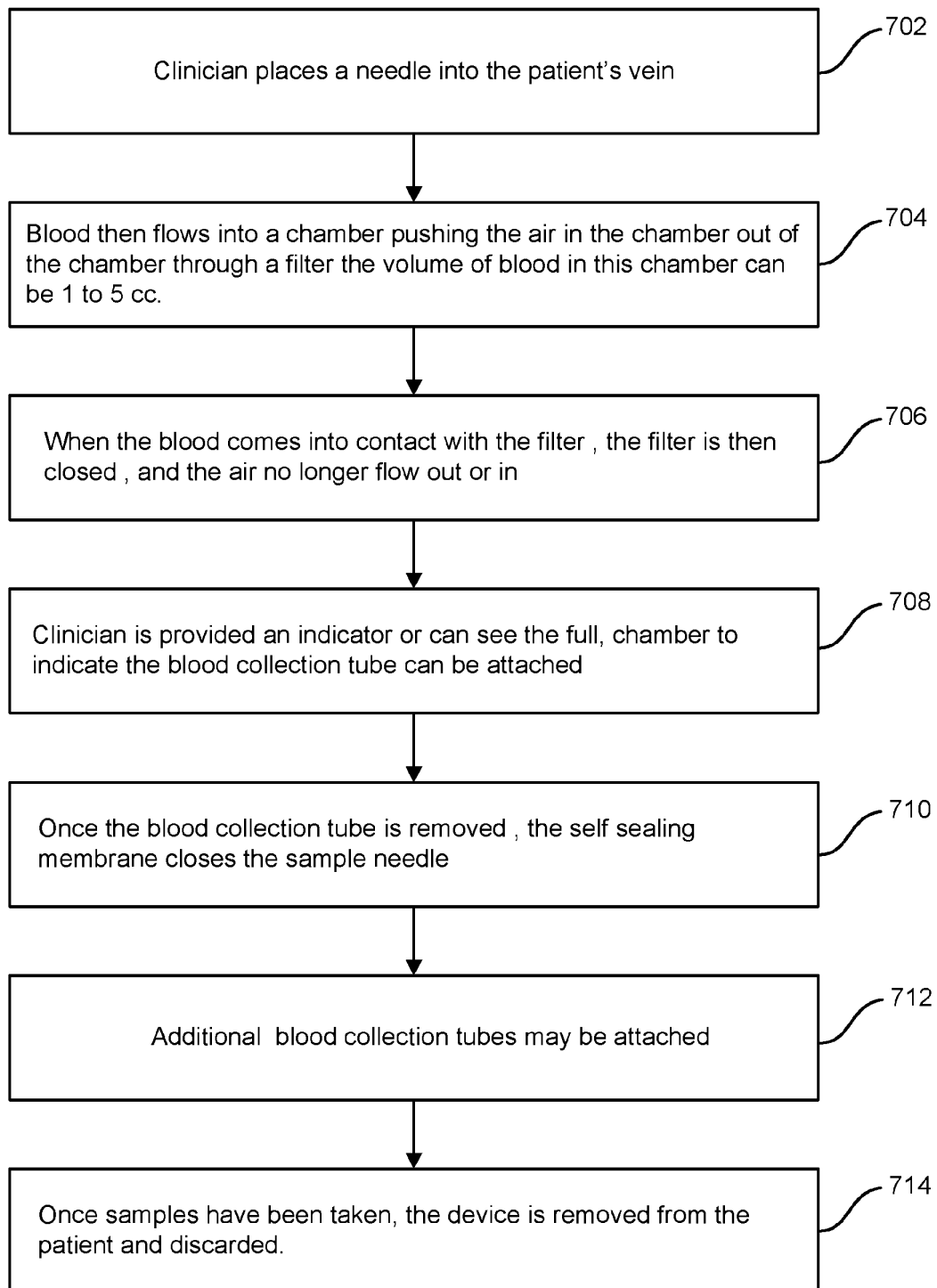
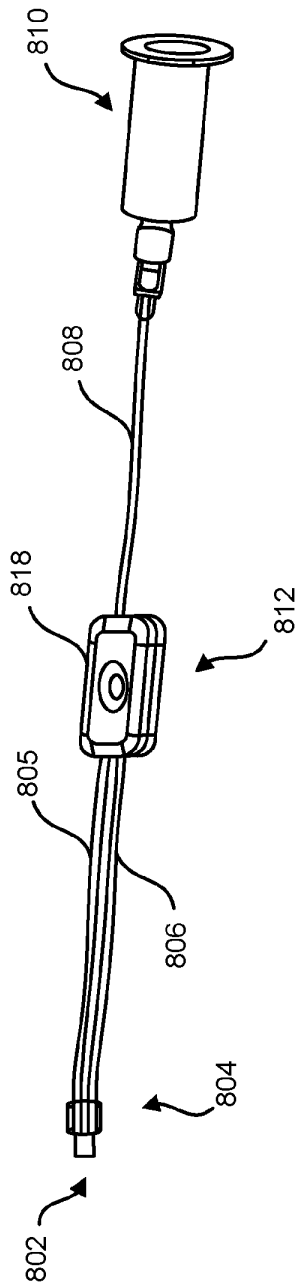


FIG. 6

**FIG. 7**



800

FIG. 8A

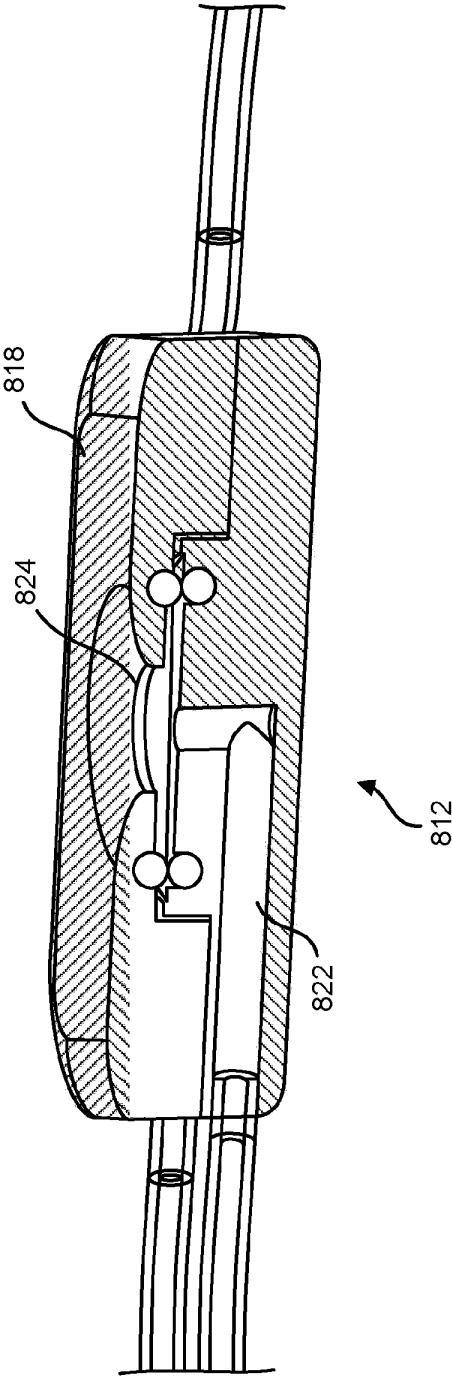


FIG. 8B

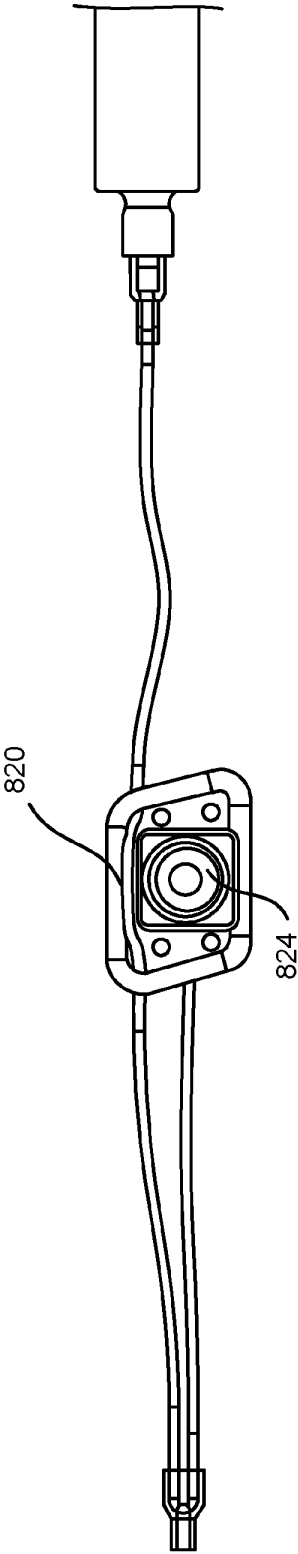


FIG. 8C

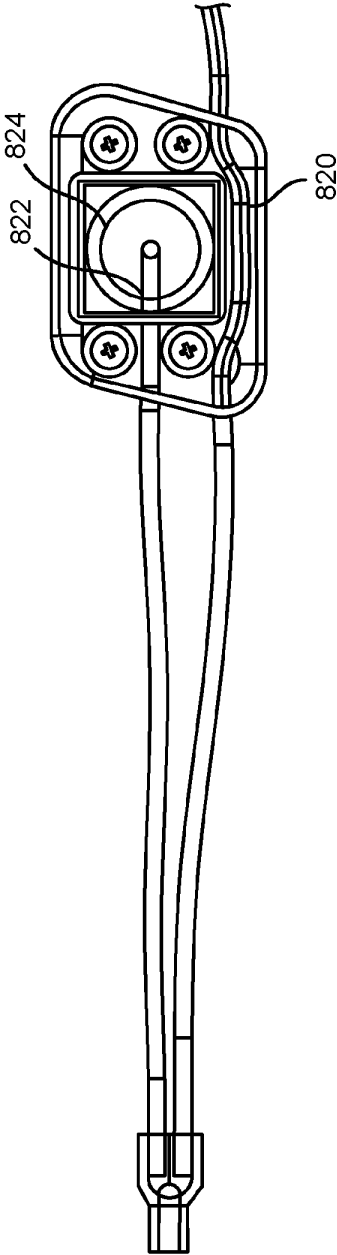


FIG. 8D

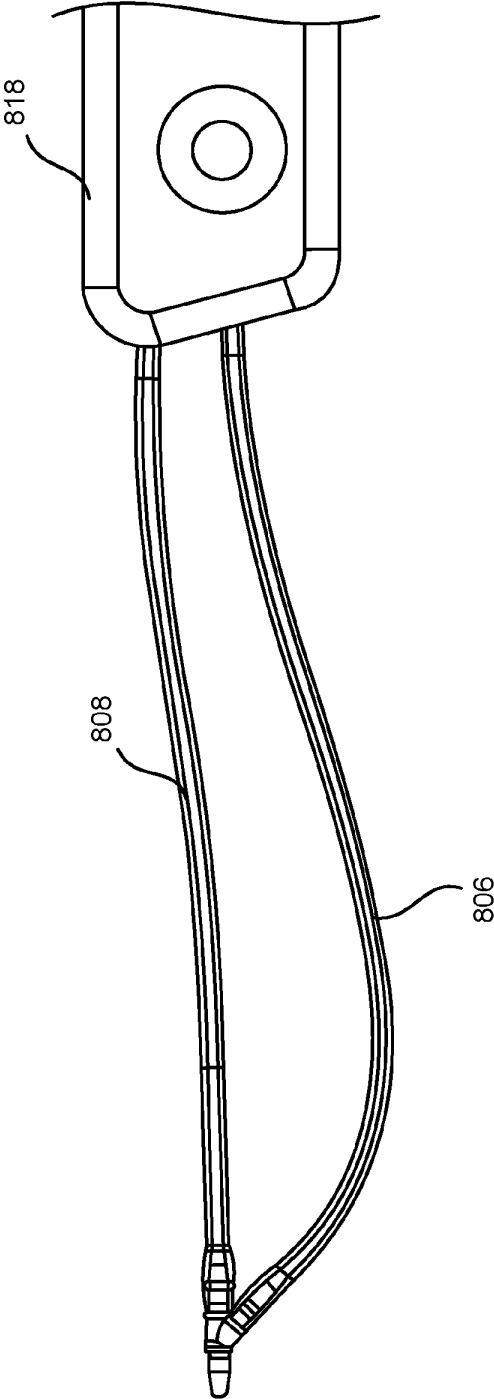


FIG. 8E

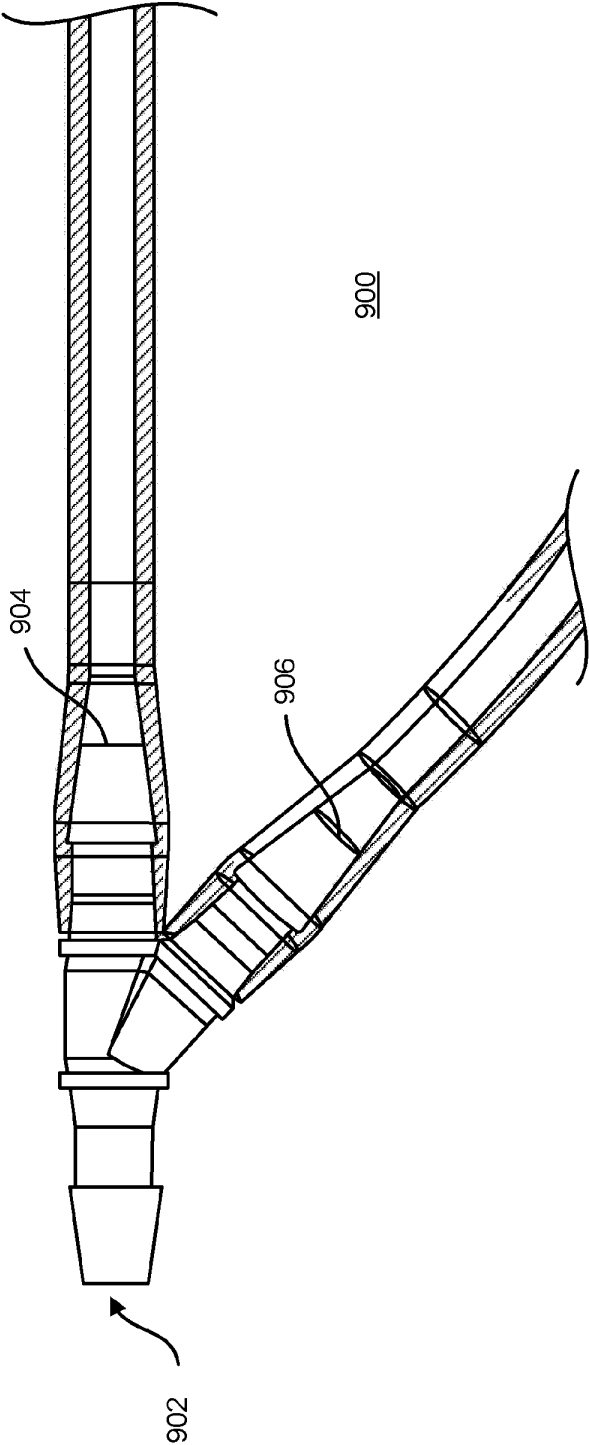


FIG. 9

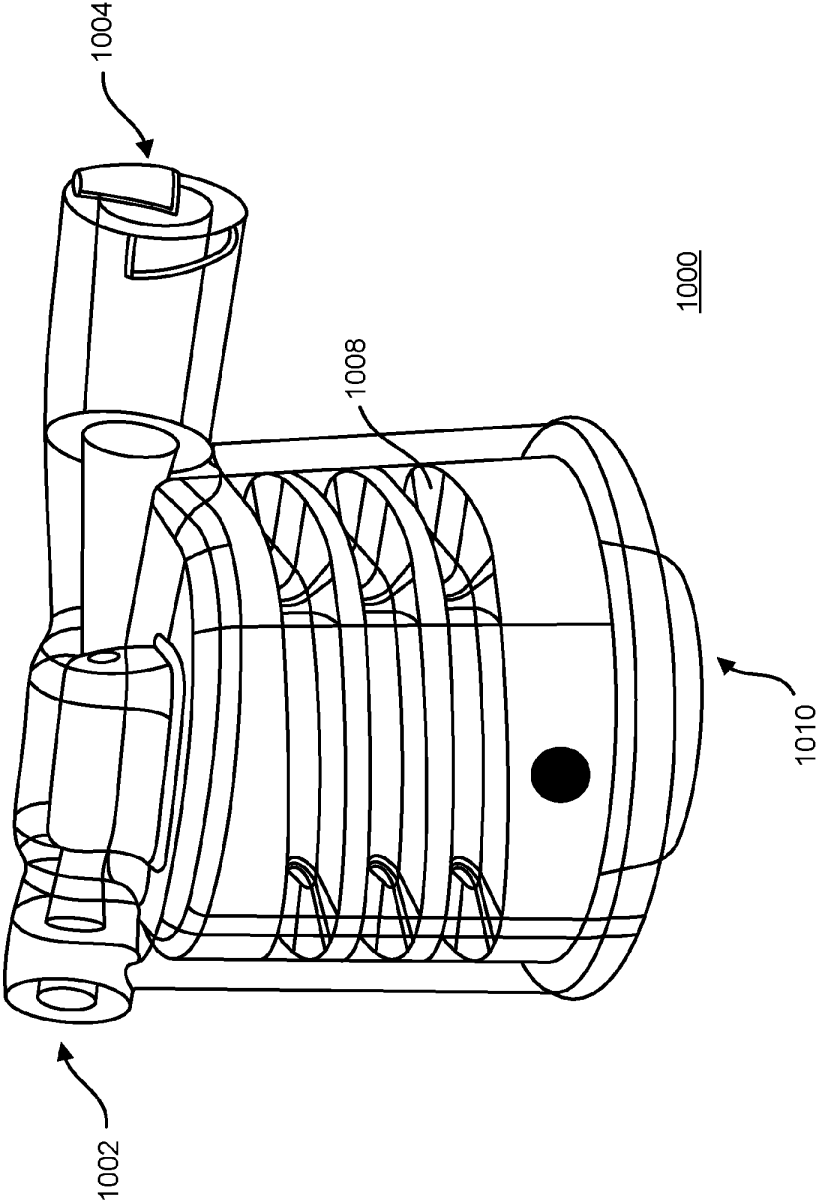


FIG. 10A

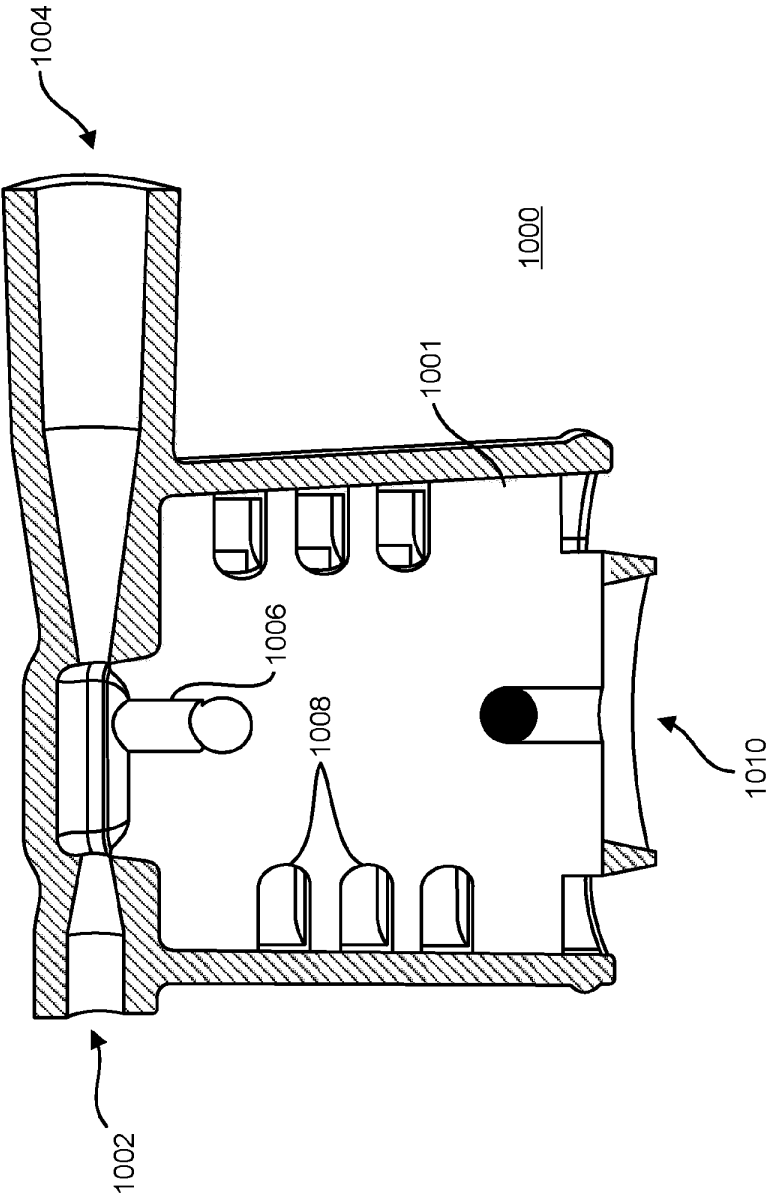


FIG. 10B

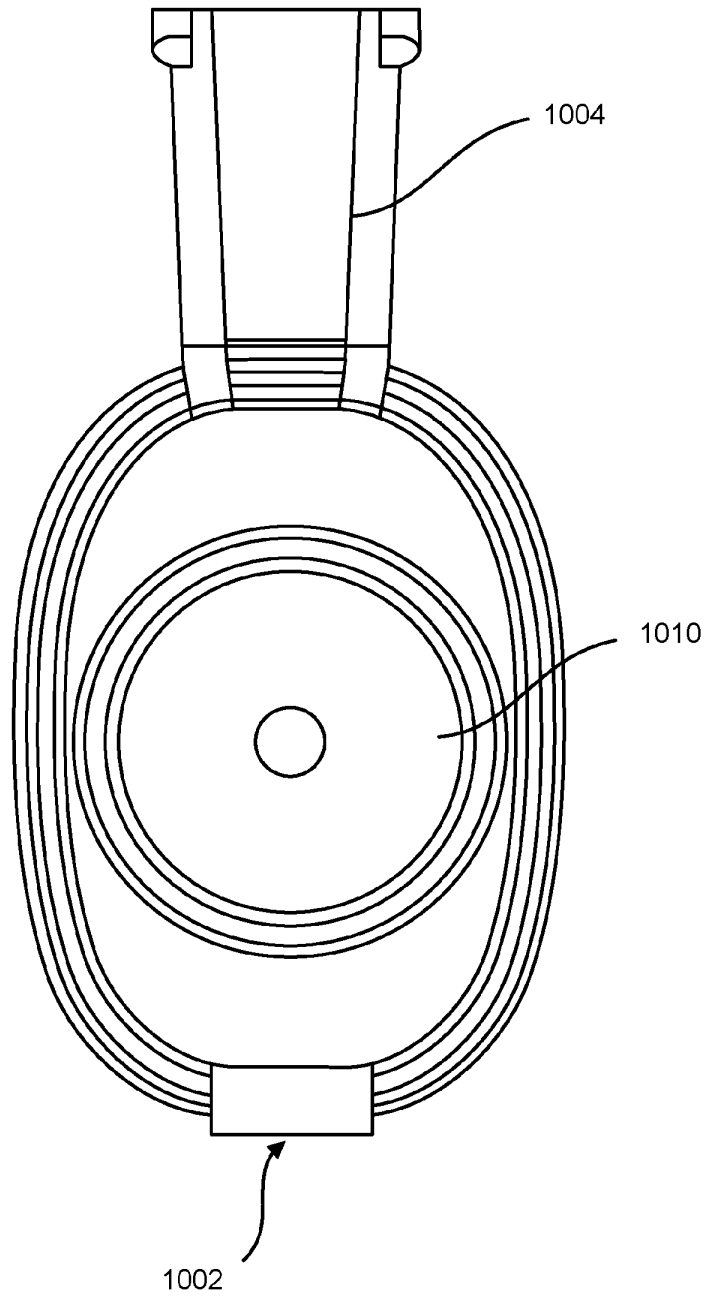


FIG. 10C

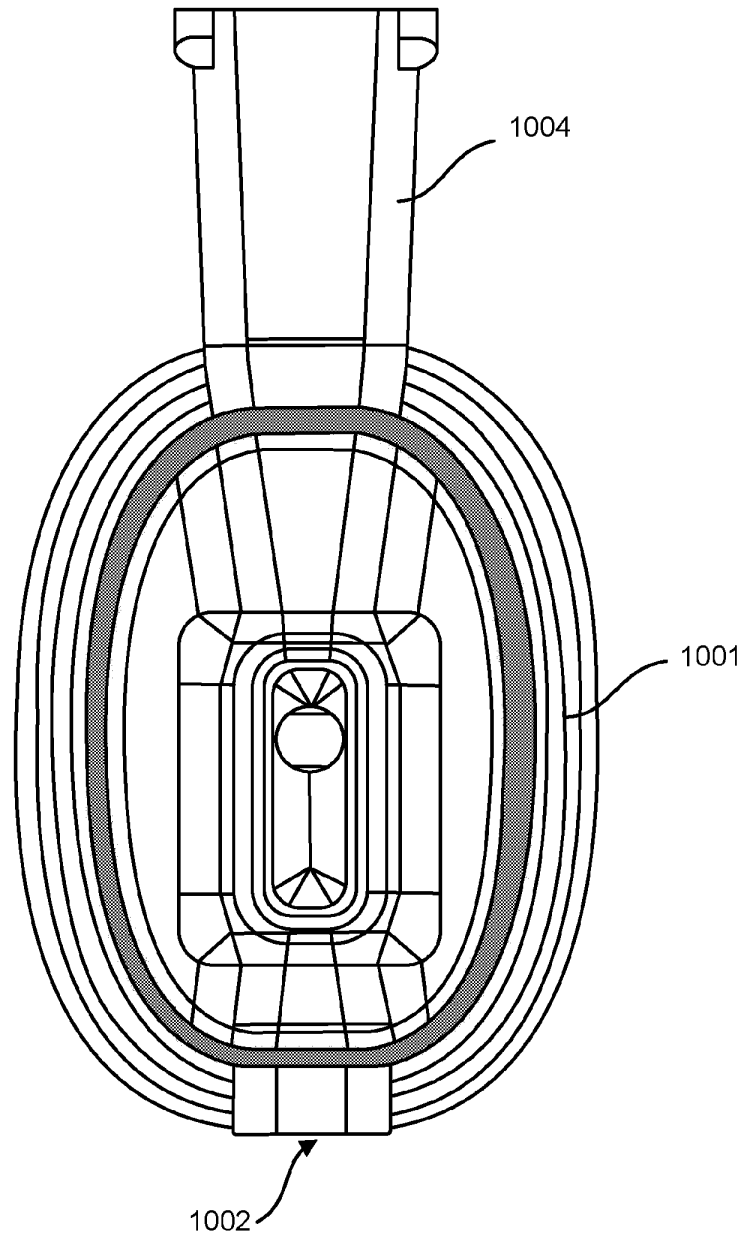


FIG. 10D

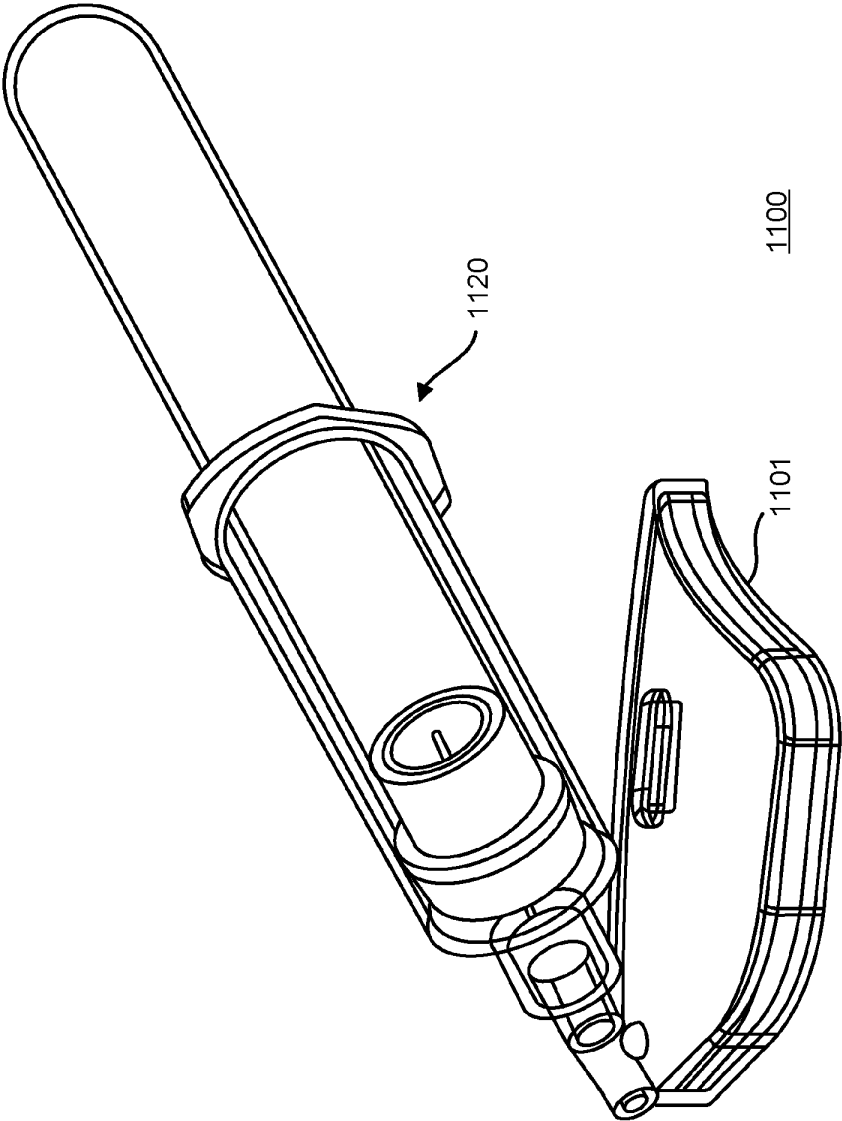


FIG. 11A

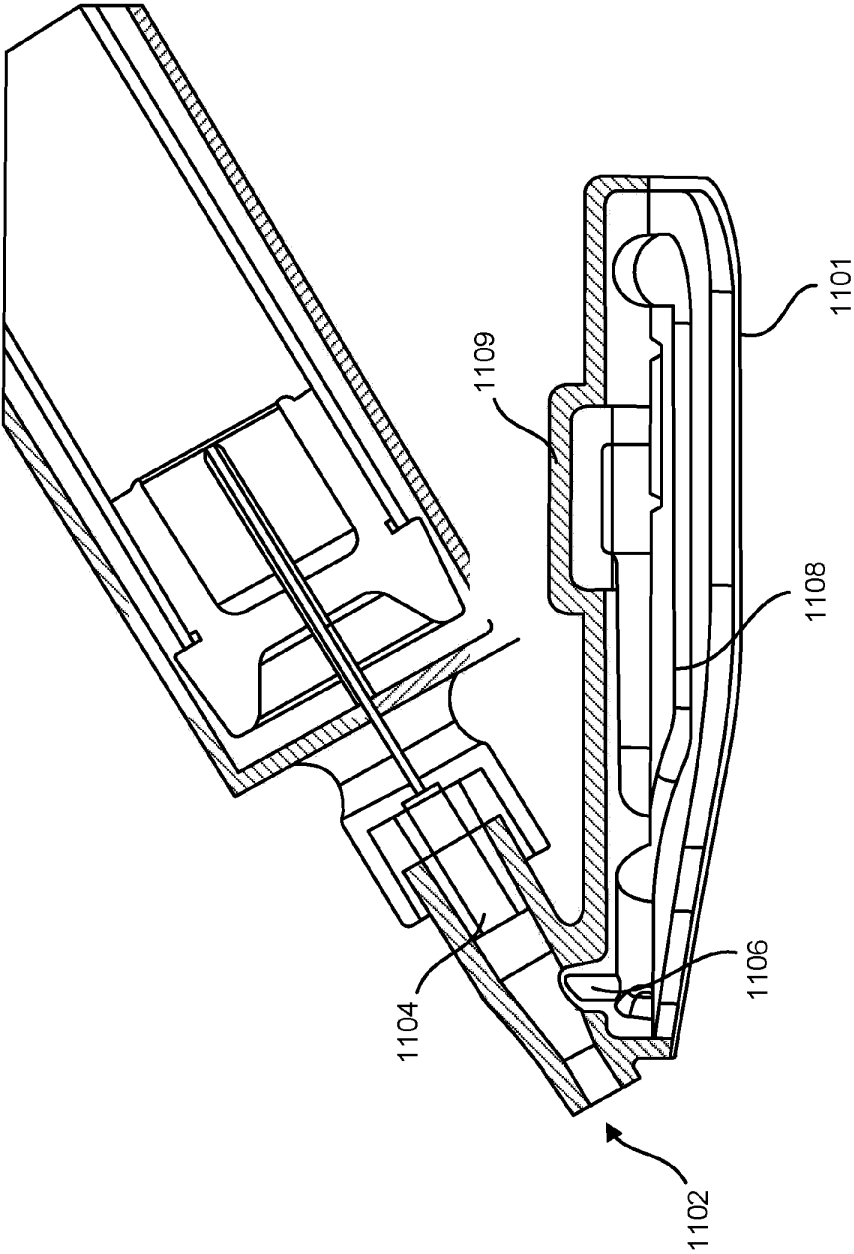


FIG. 11B

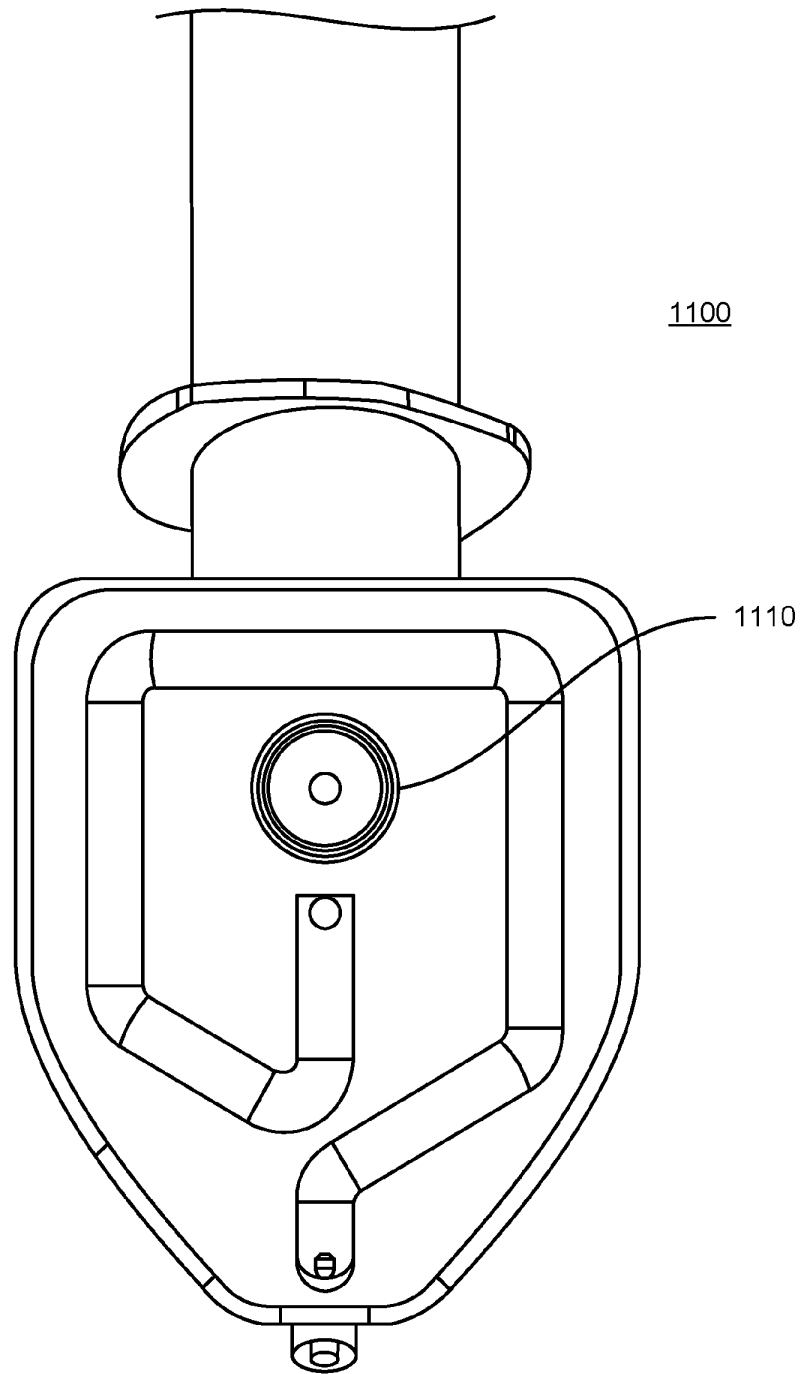


FIG. 11C

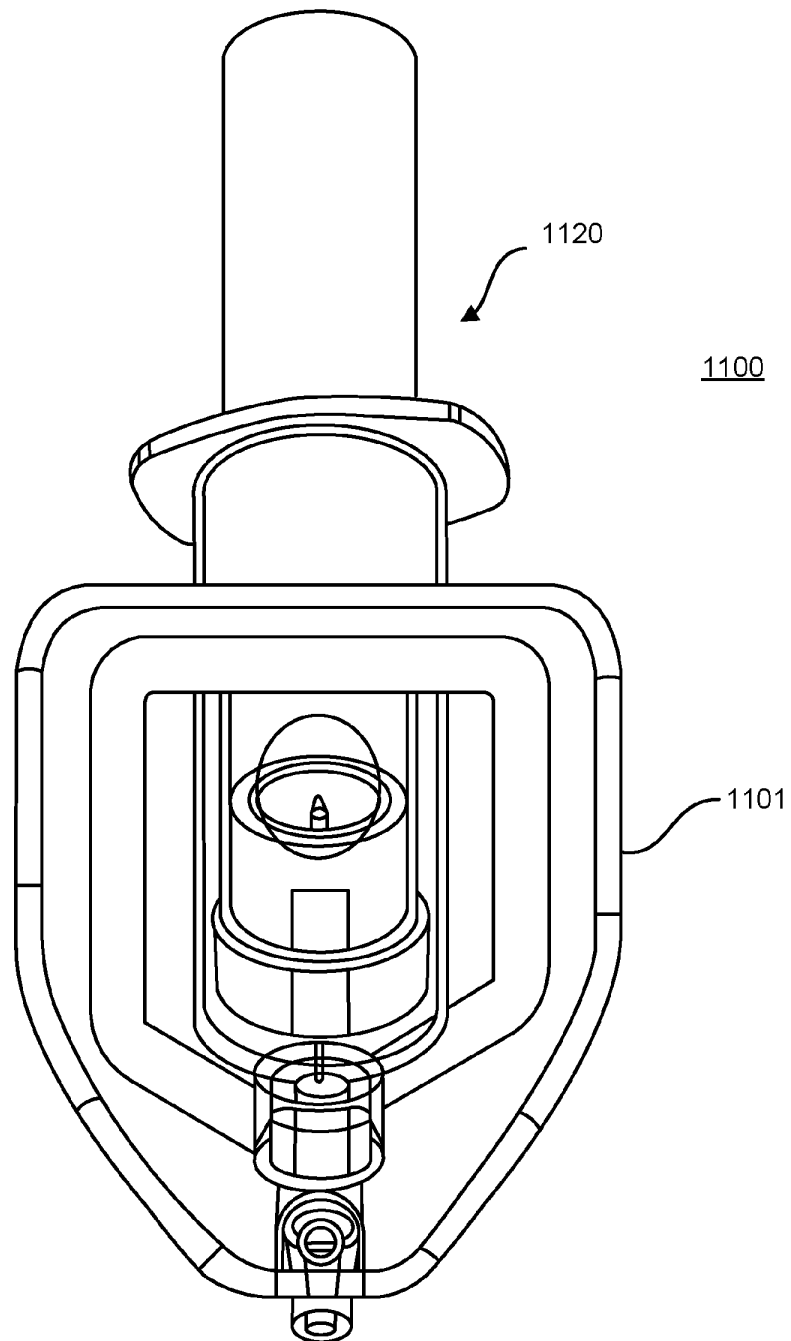


FIG. 11D

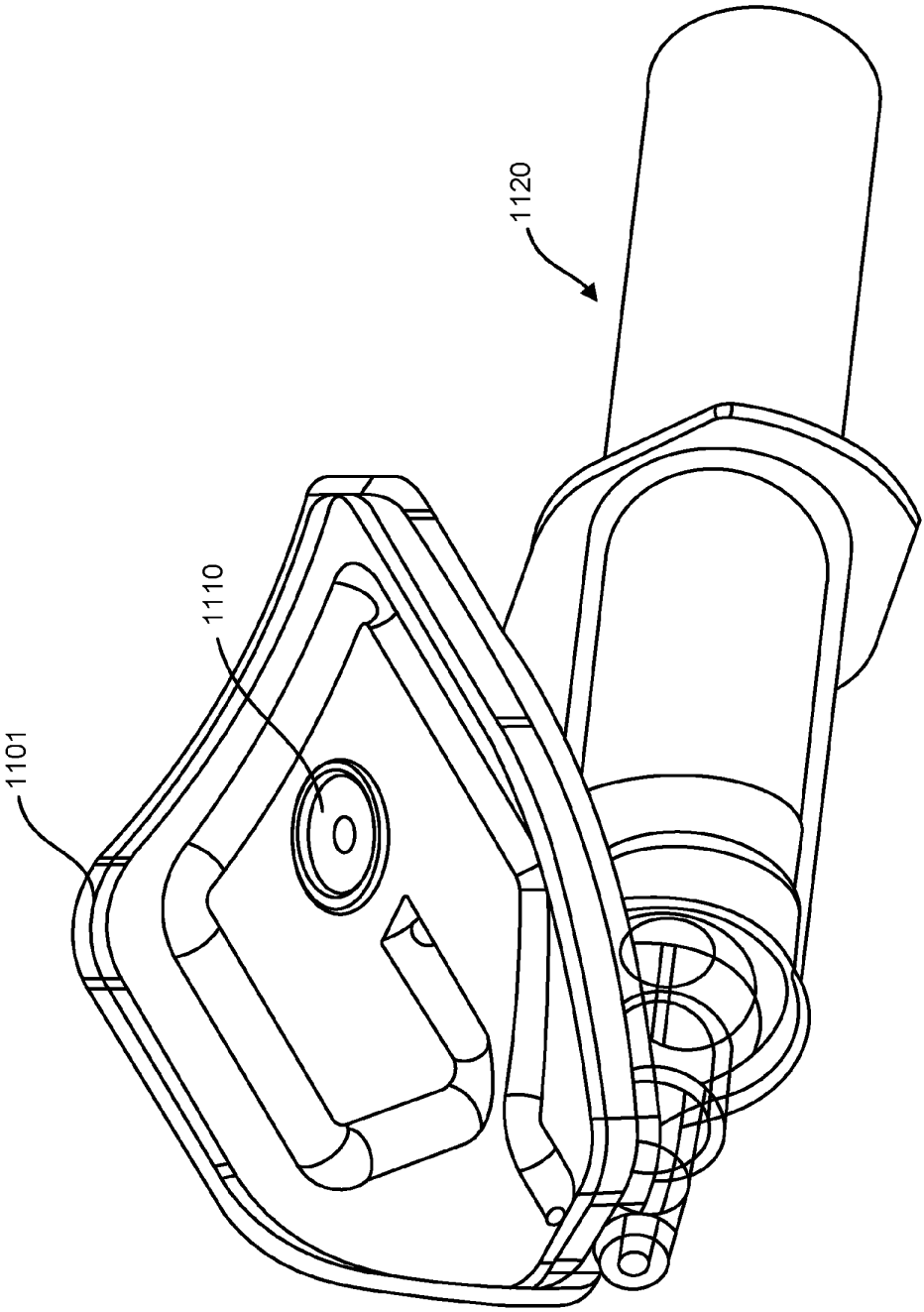


FIG. 11E

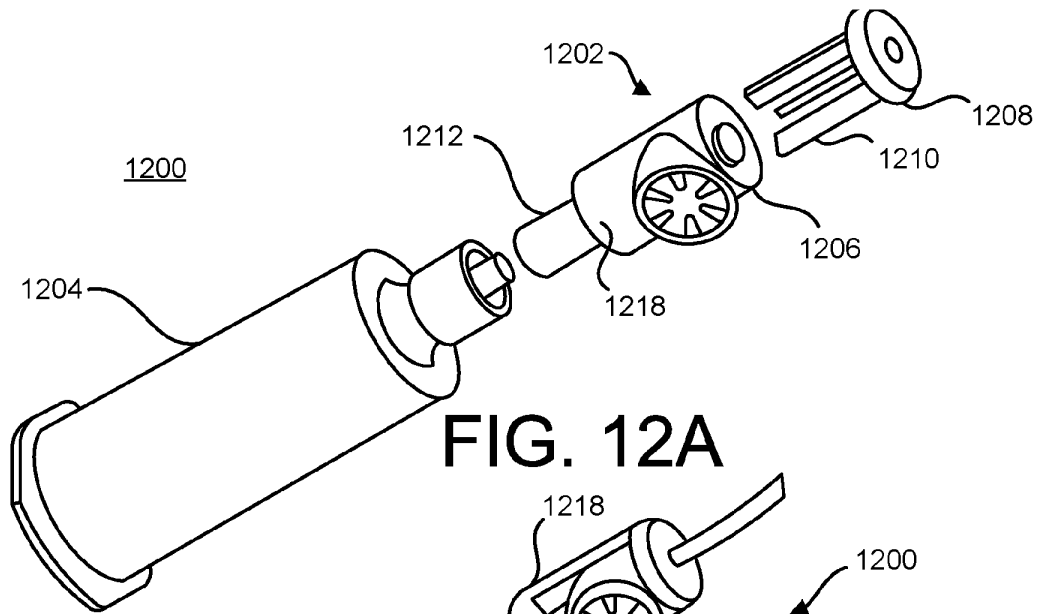


FIG. 12A

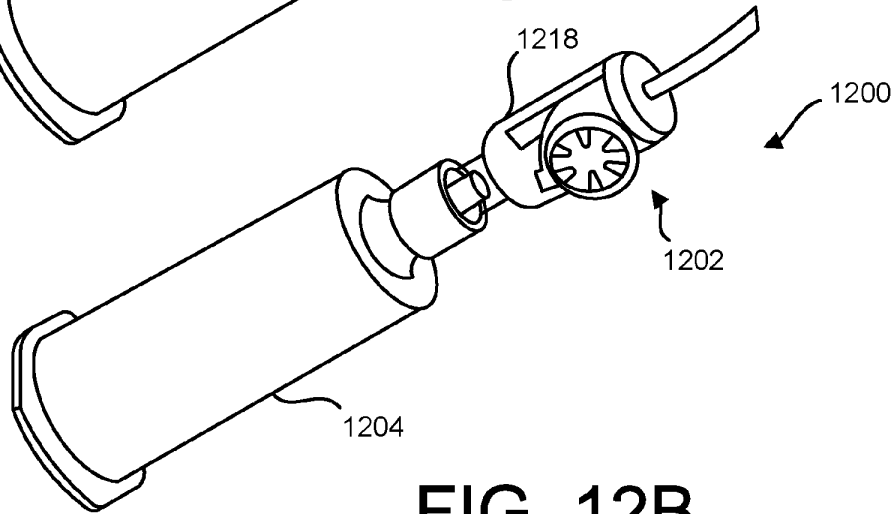


FIG. 12B

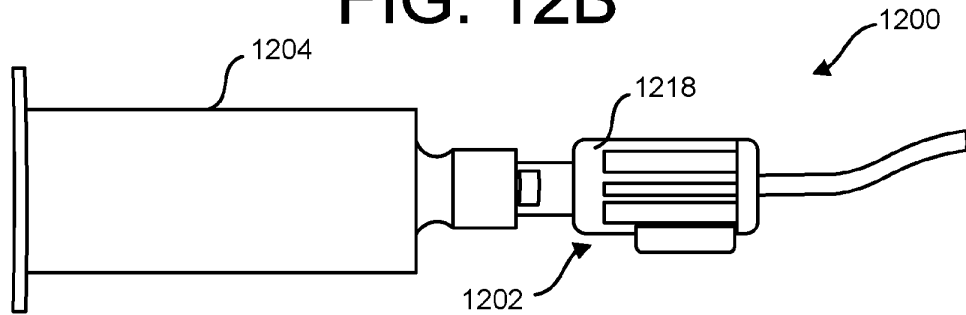


FIG. 12C

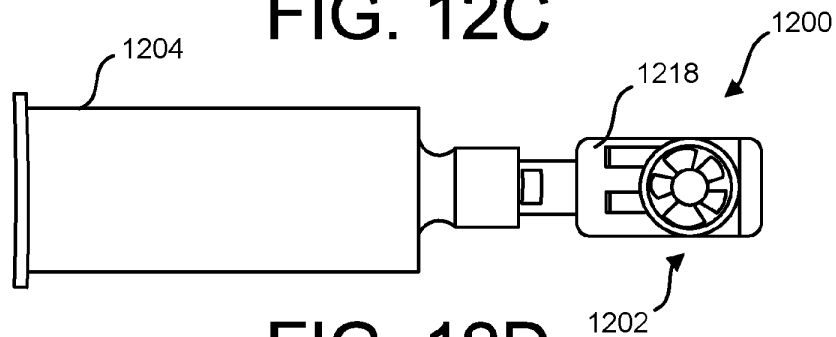


FIG. 12D

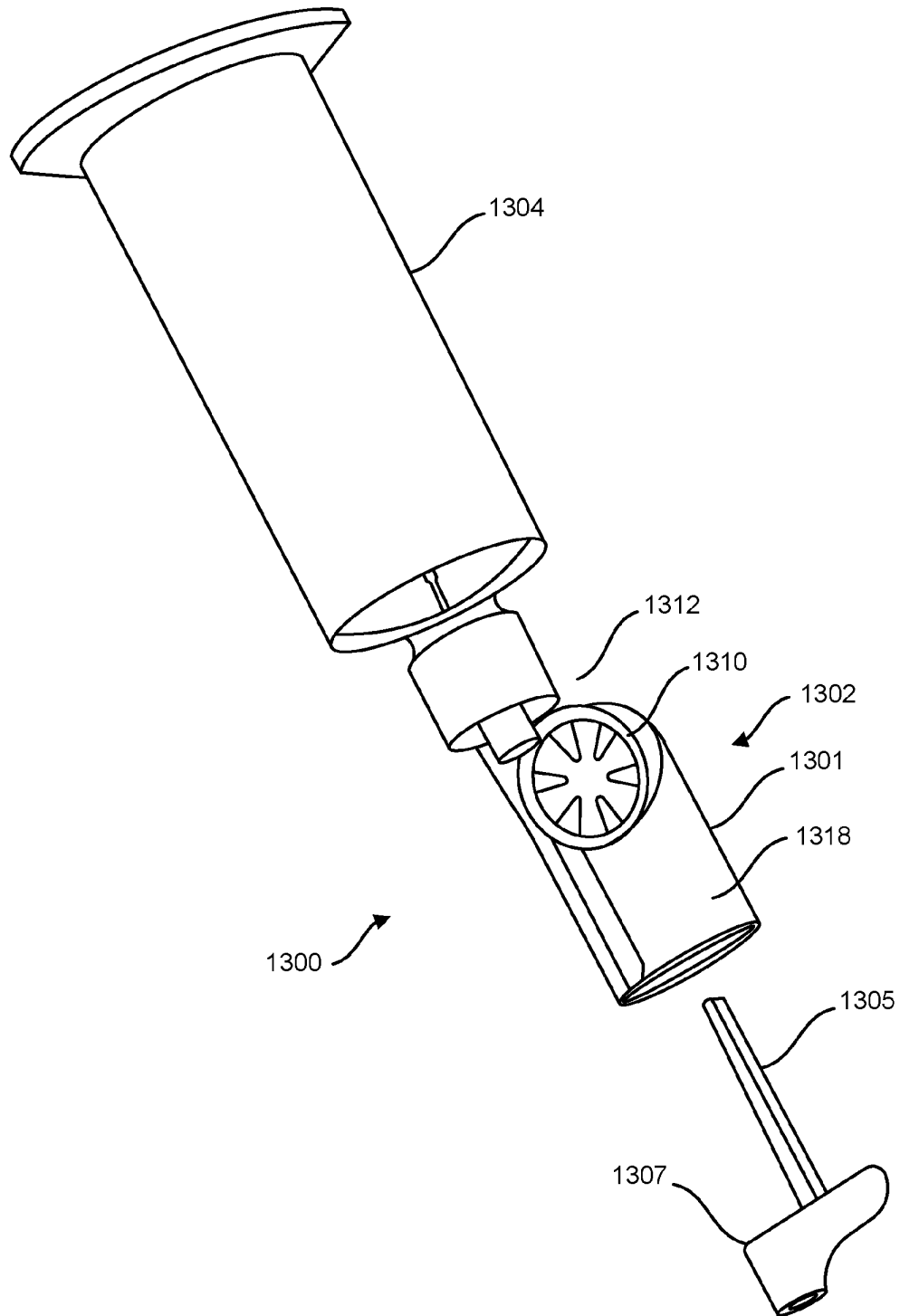


FIG. 13A

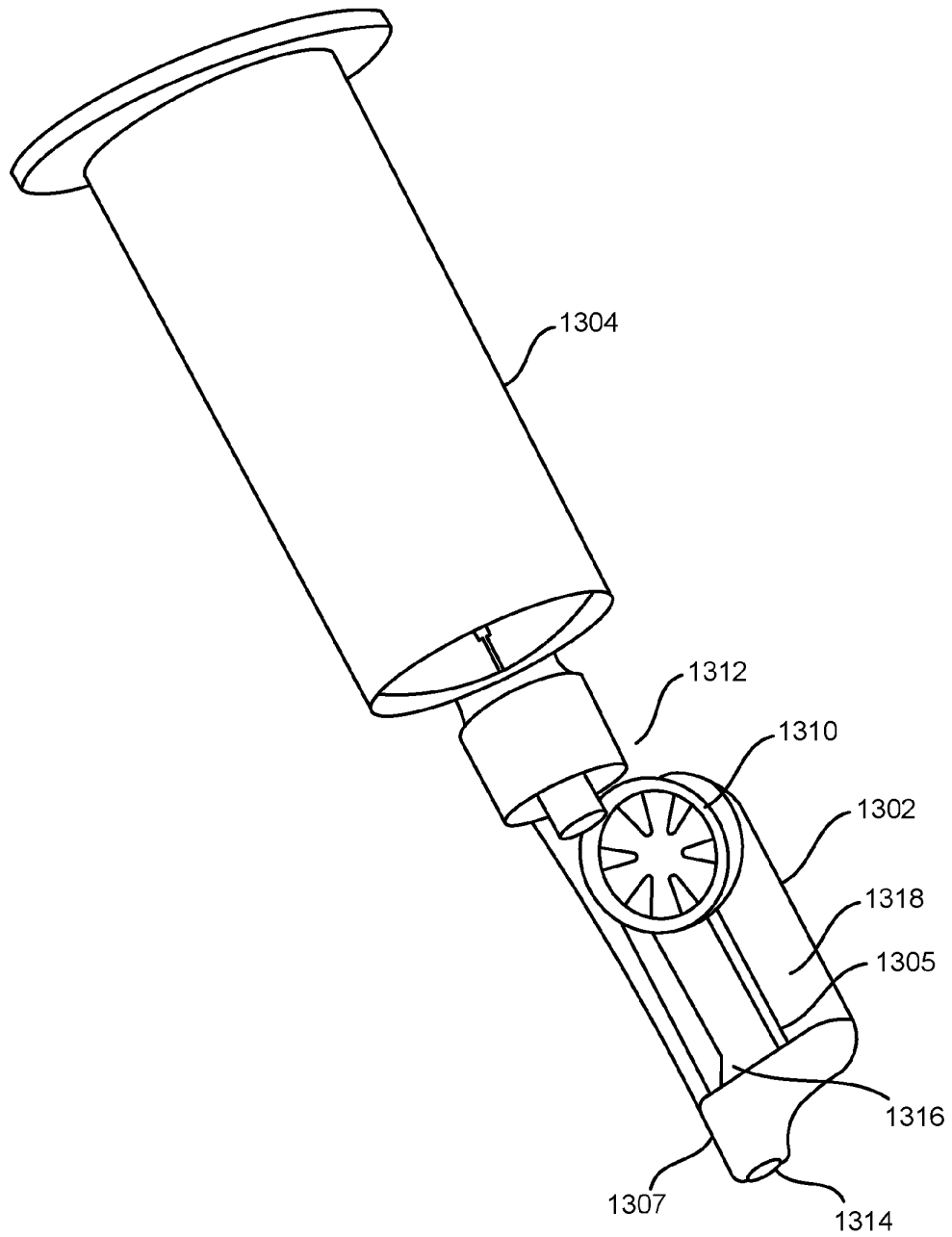


FIG. 13B

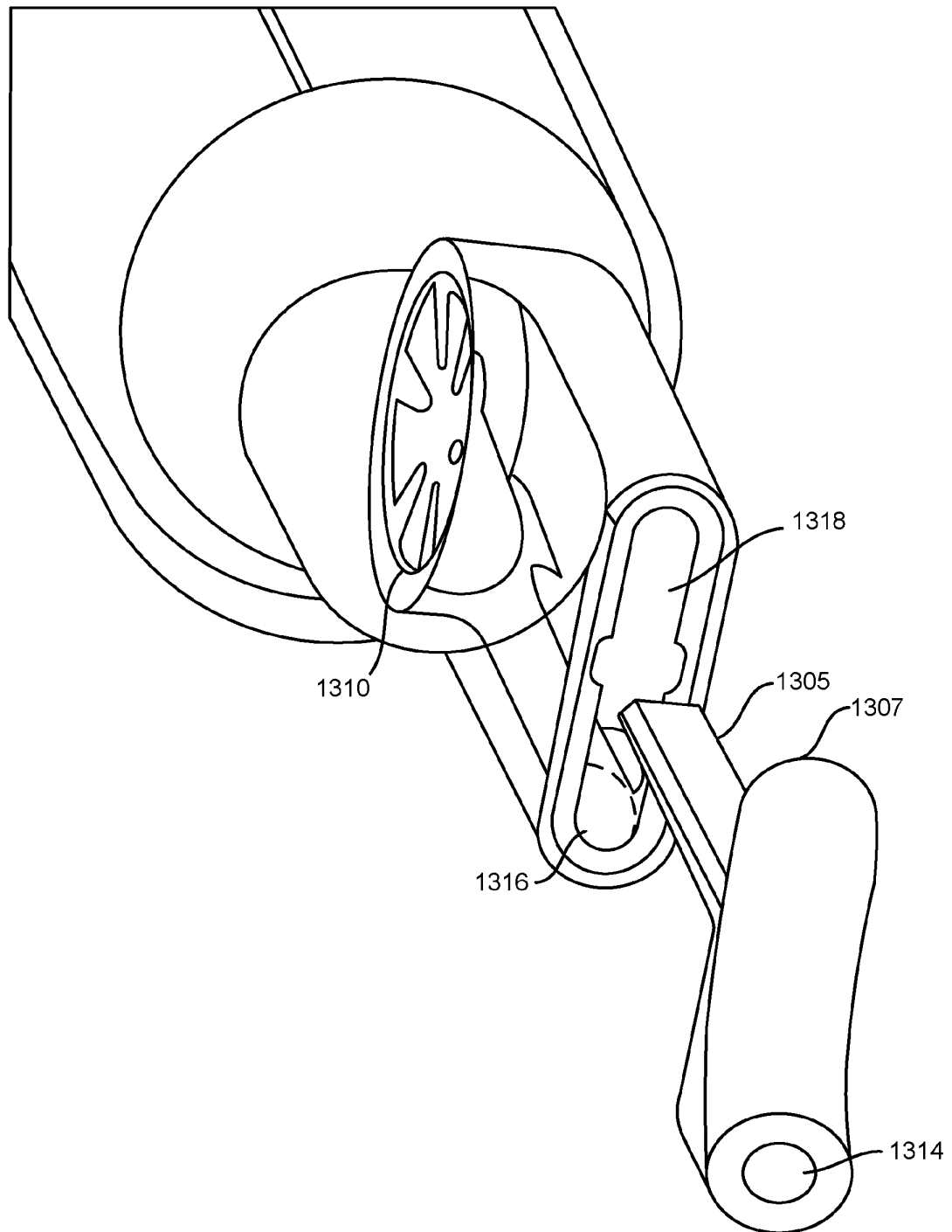


FIG. 13C

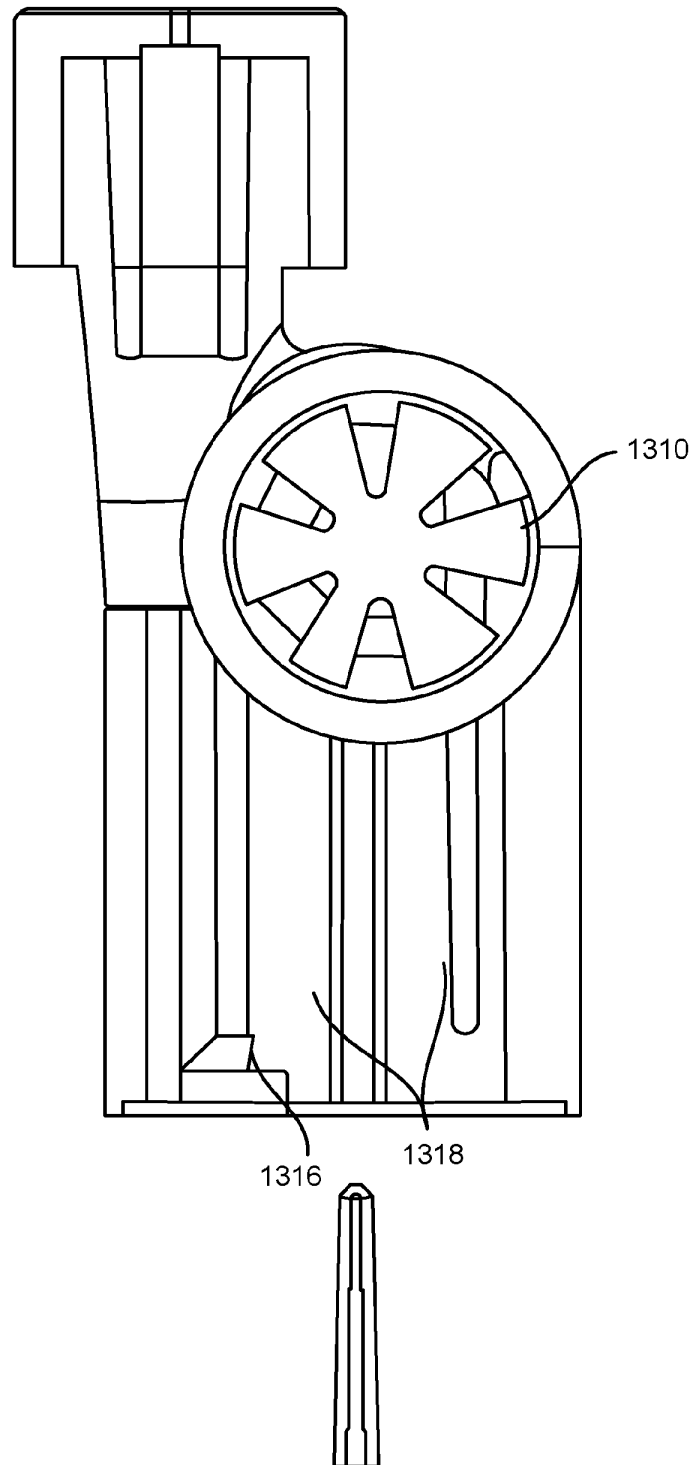


FIG. 13D

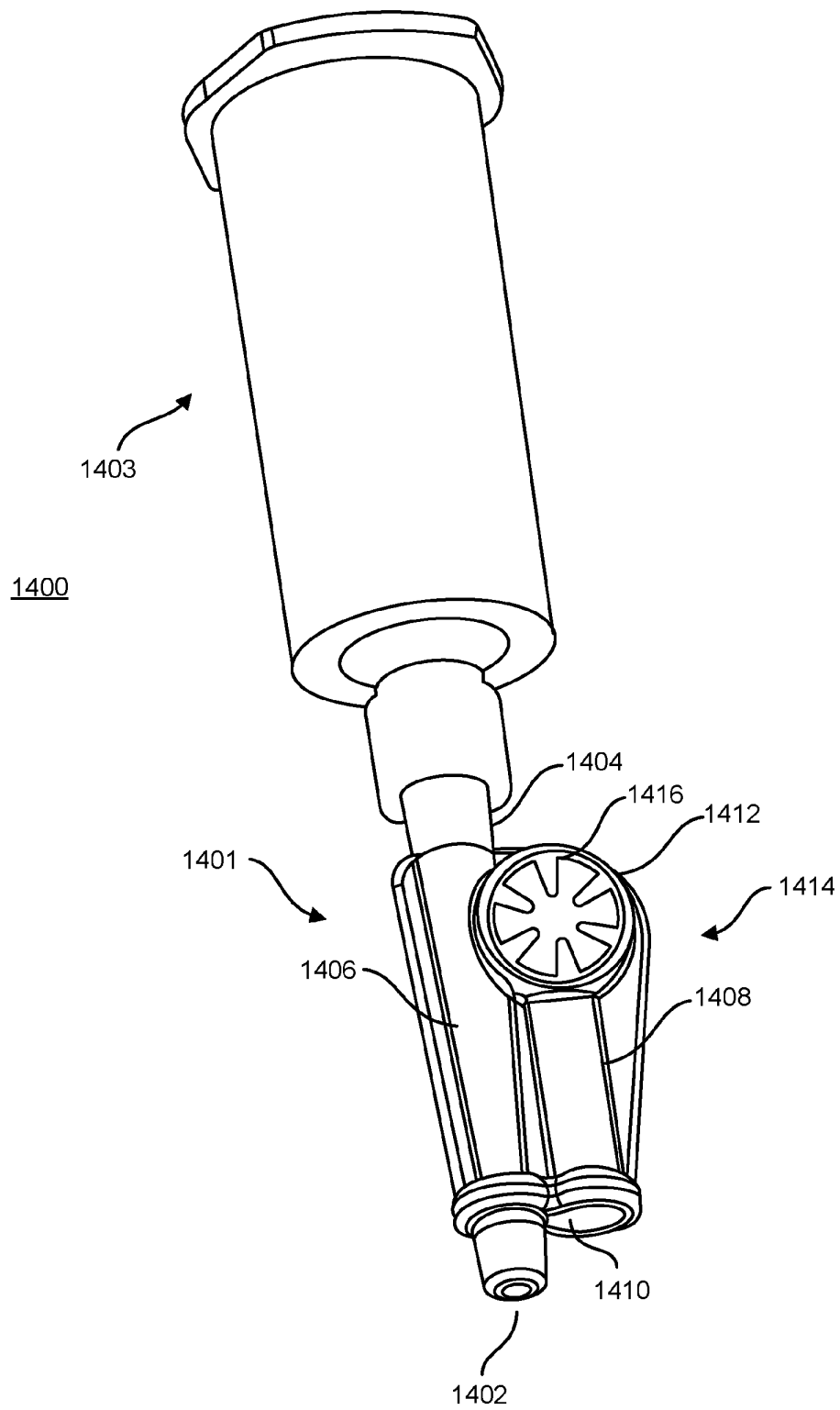


FIG. 14A

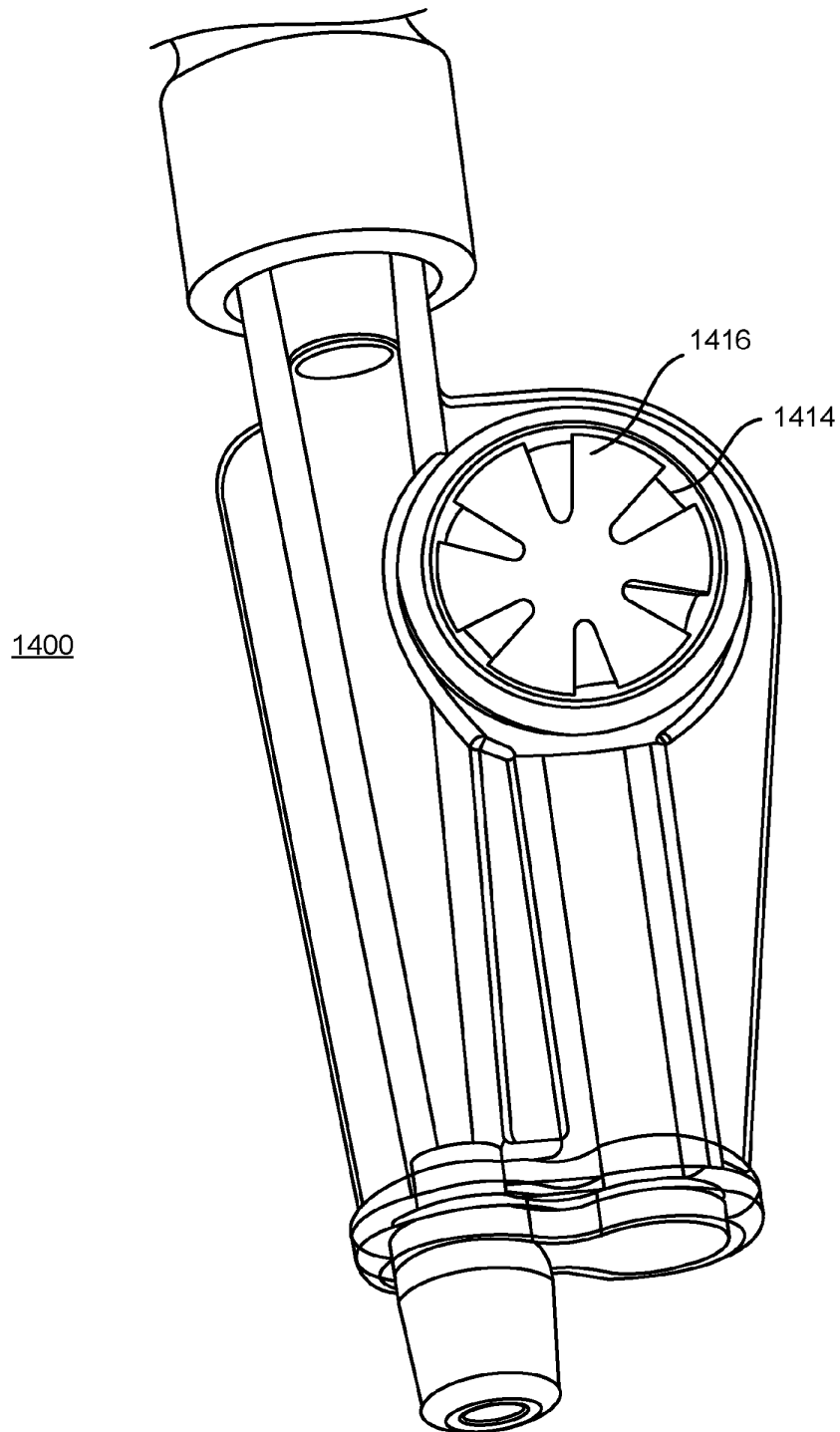


FIG. 14B

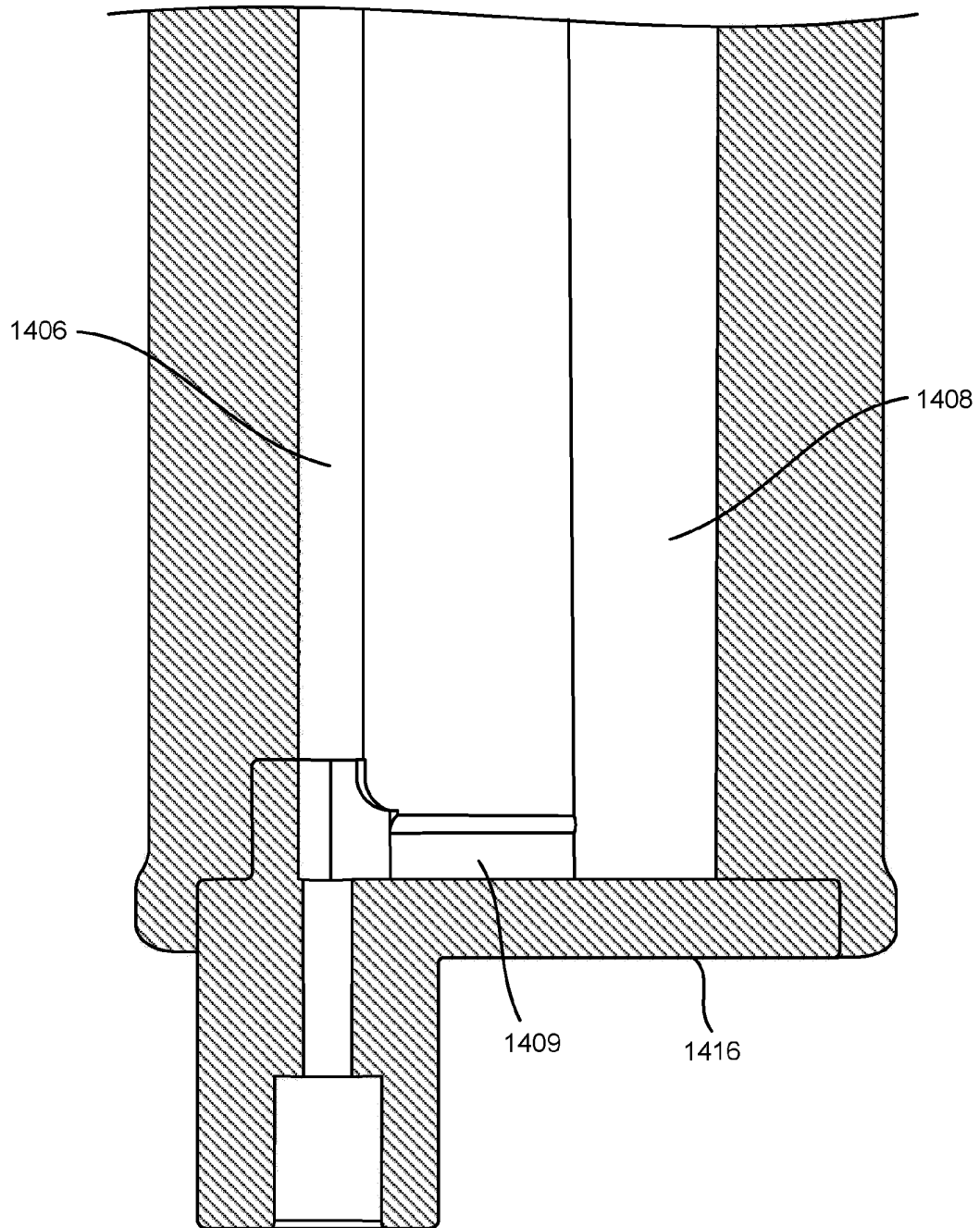


FIG. 14C

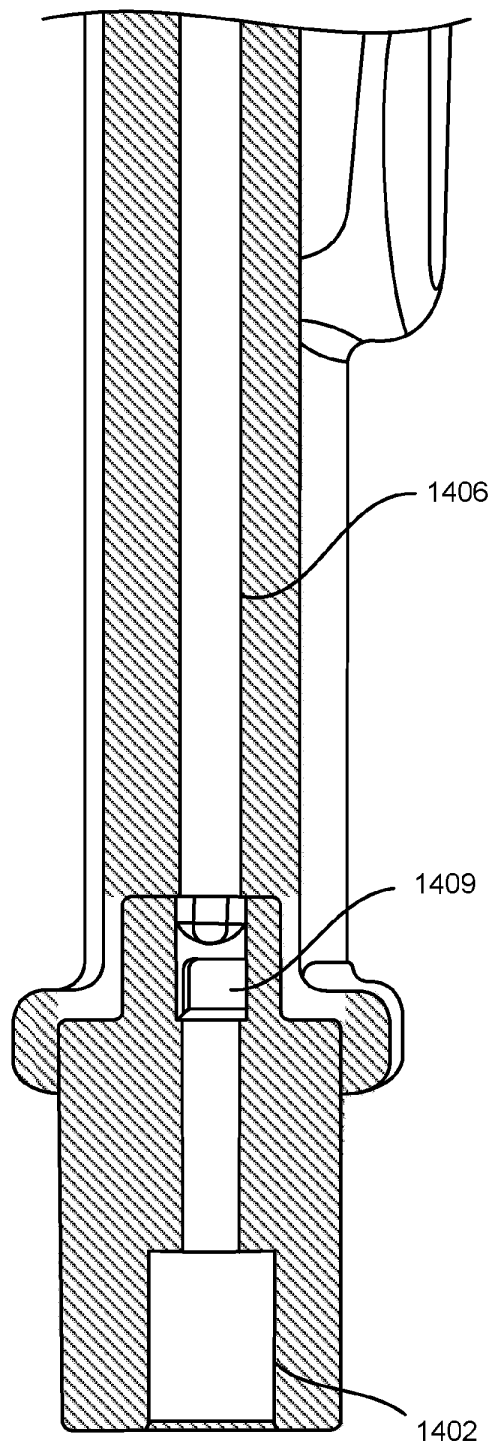


FIG. 14D

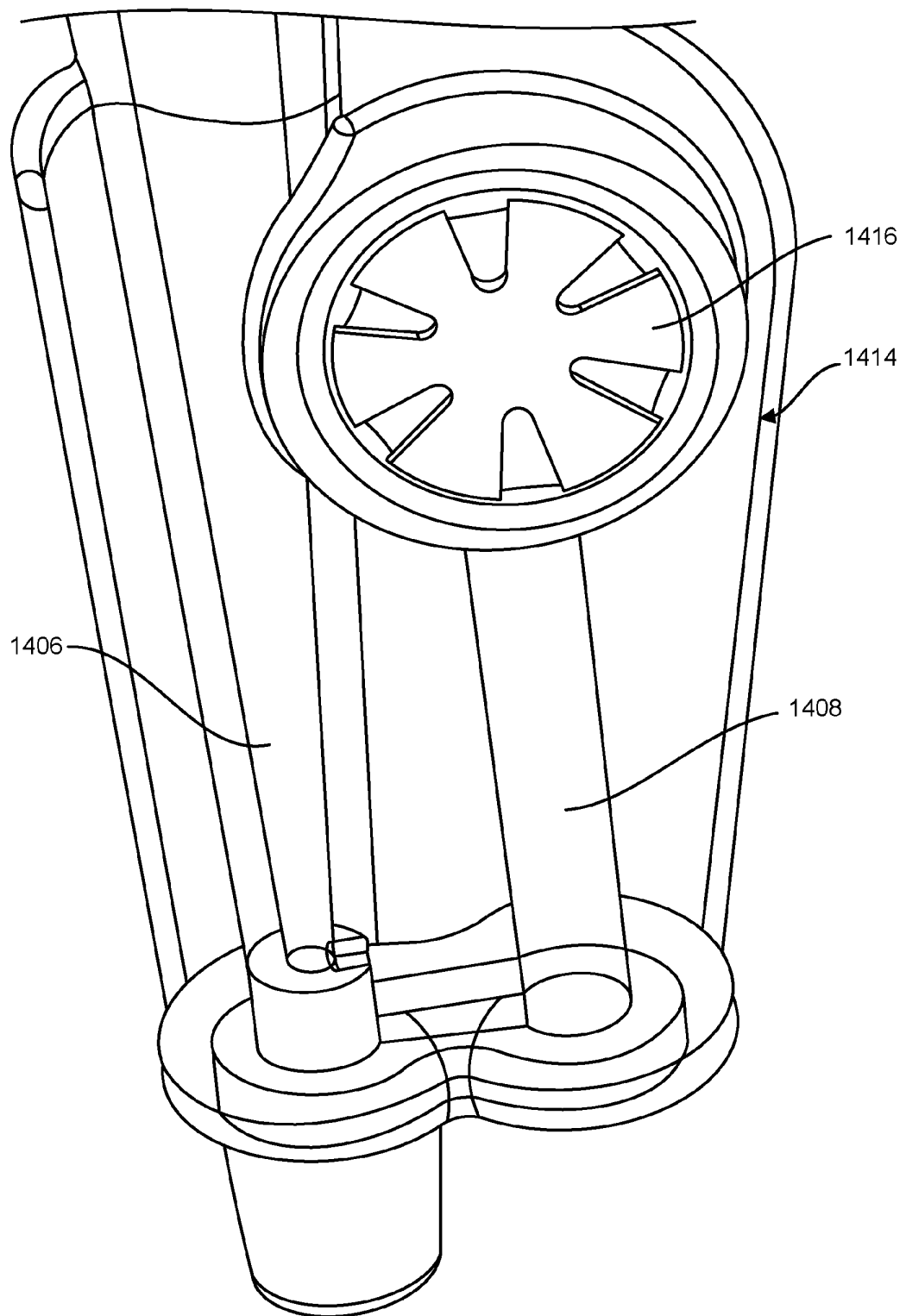


FIG. 14E

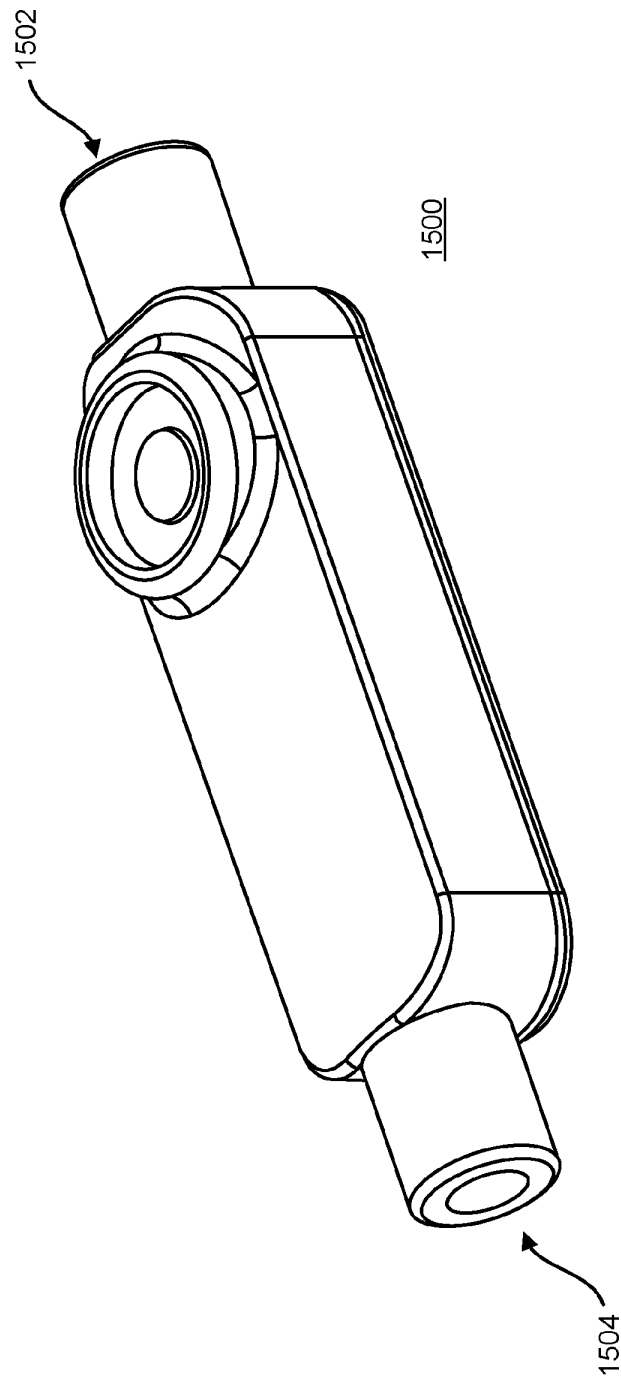


FIG. 15A

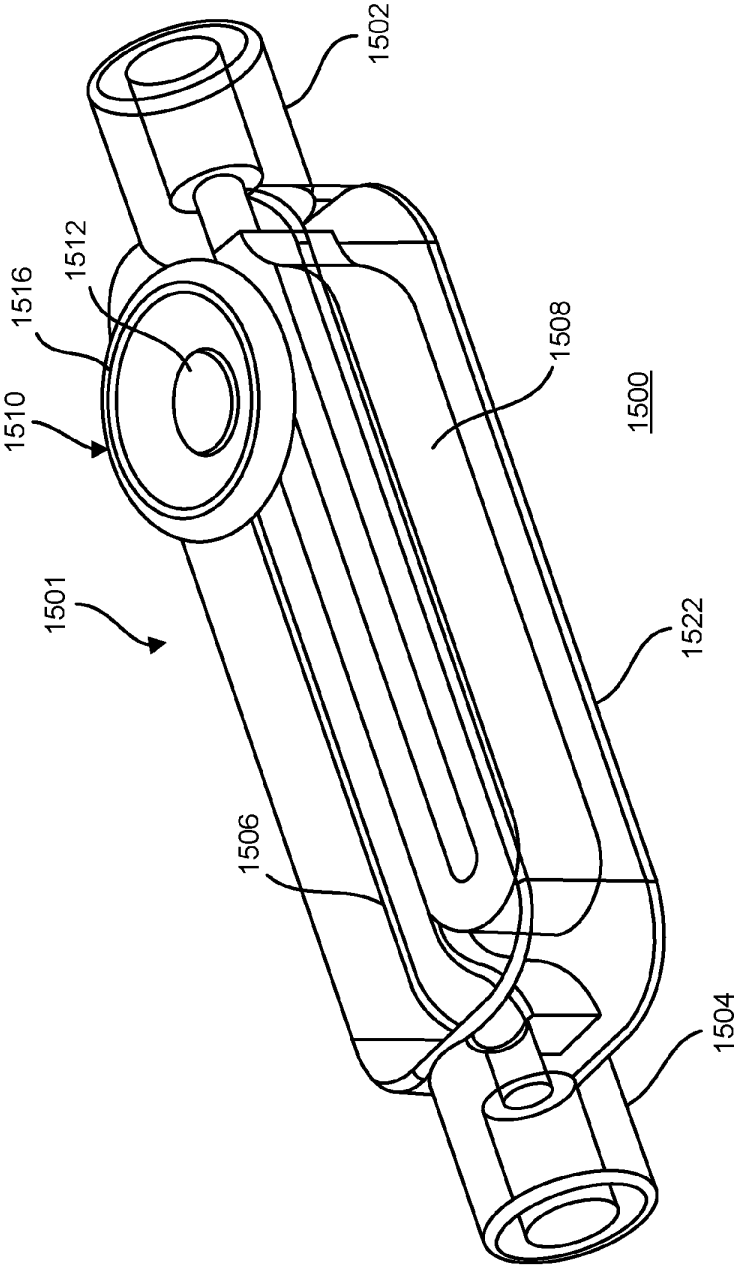


FIG. 15B

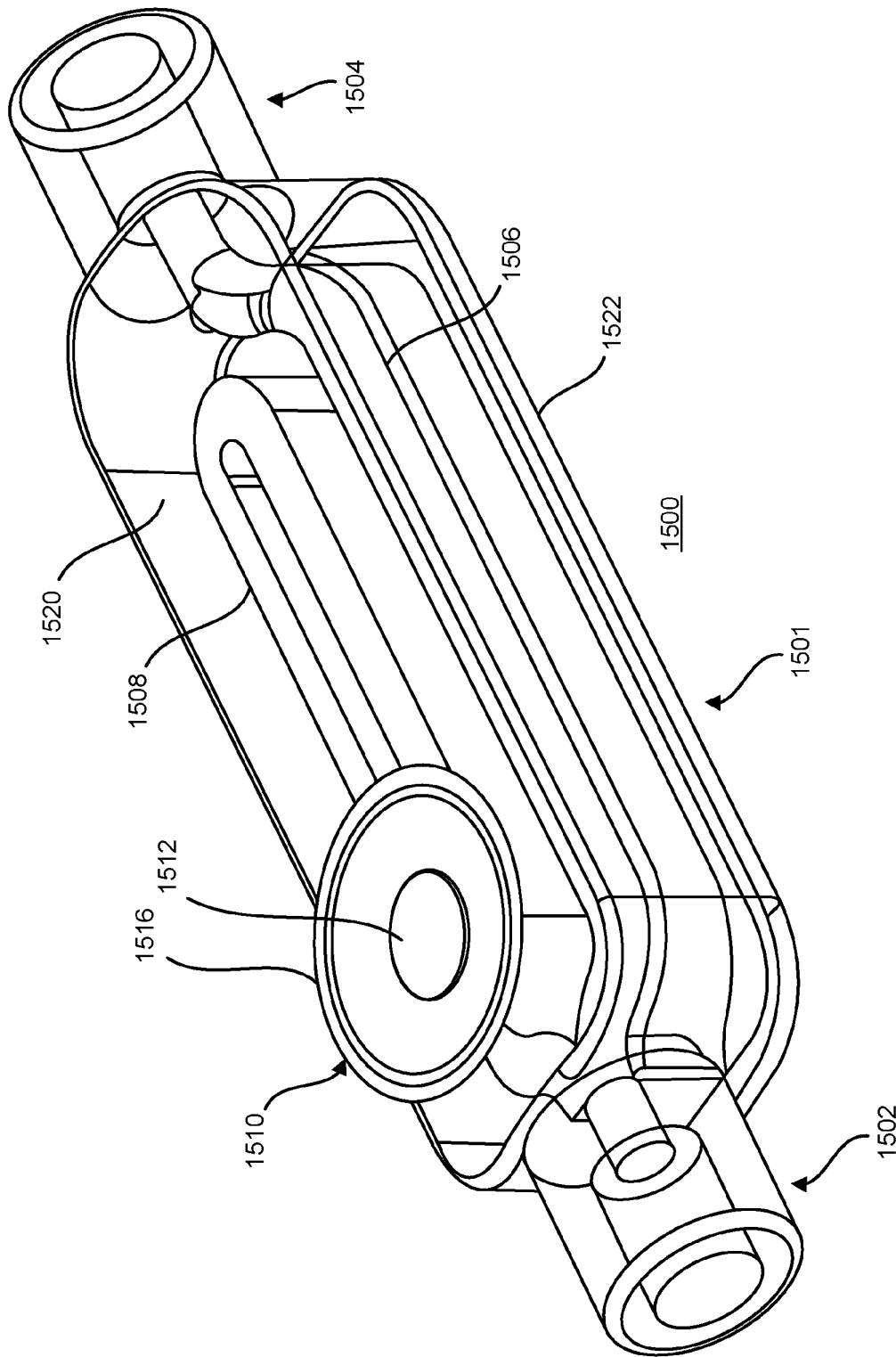


FIG. 15C

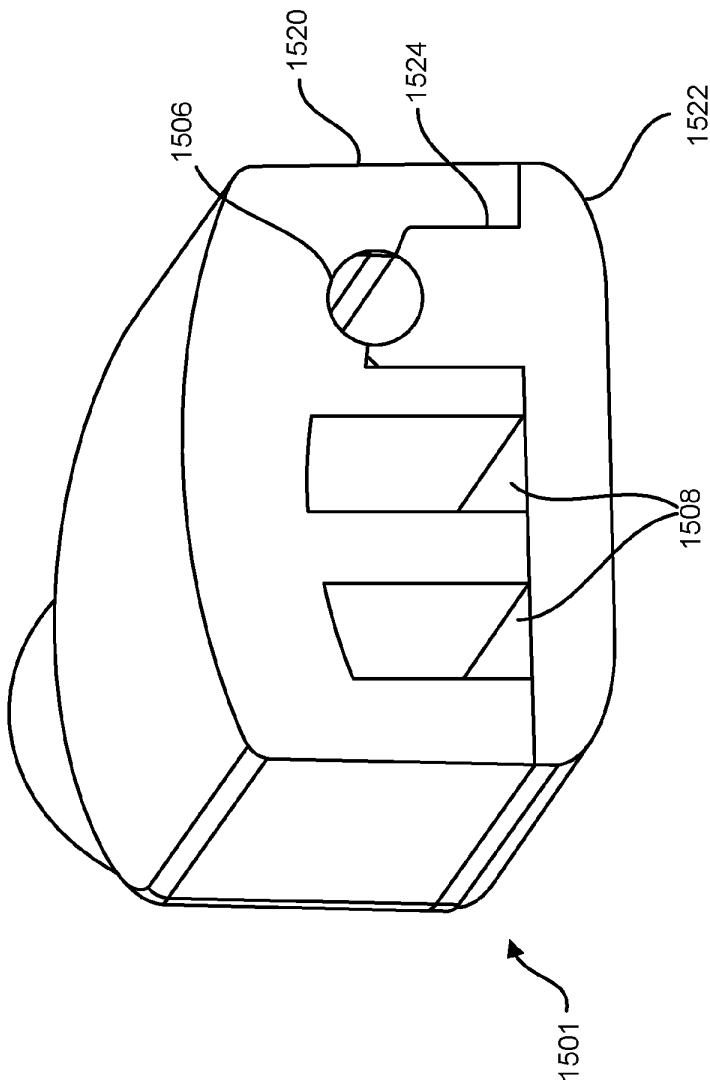


FIG. 15D

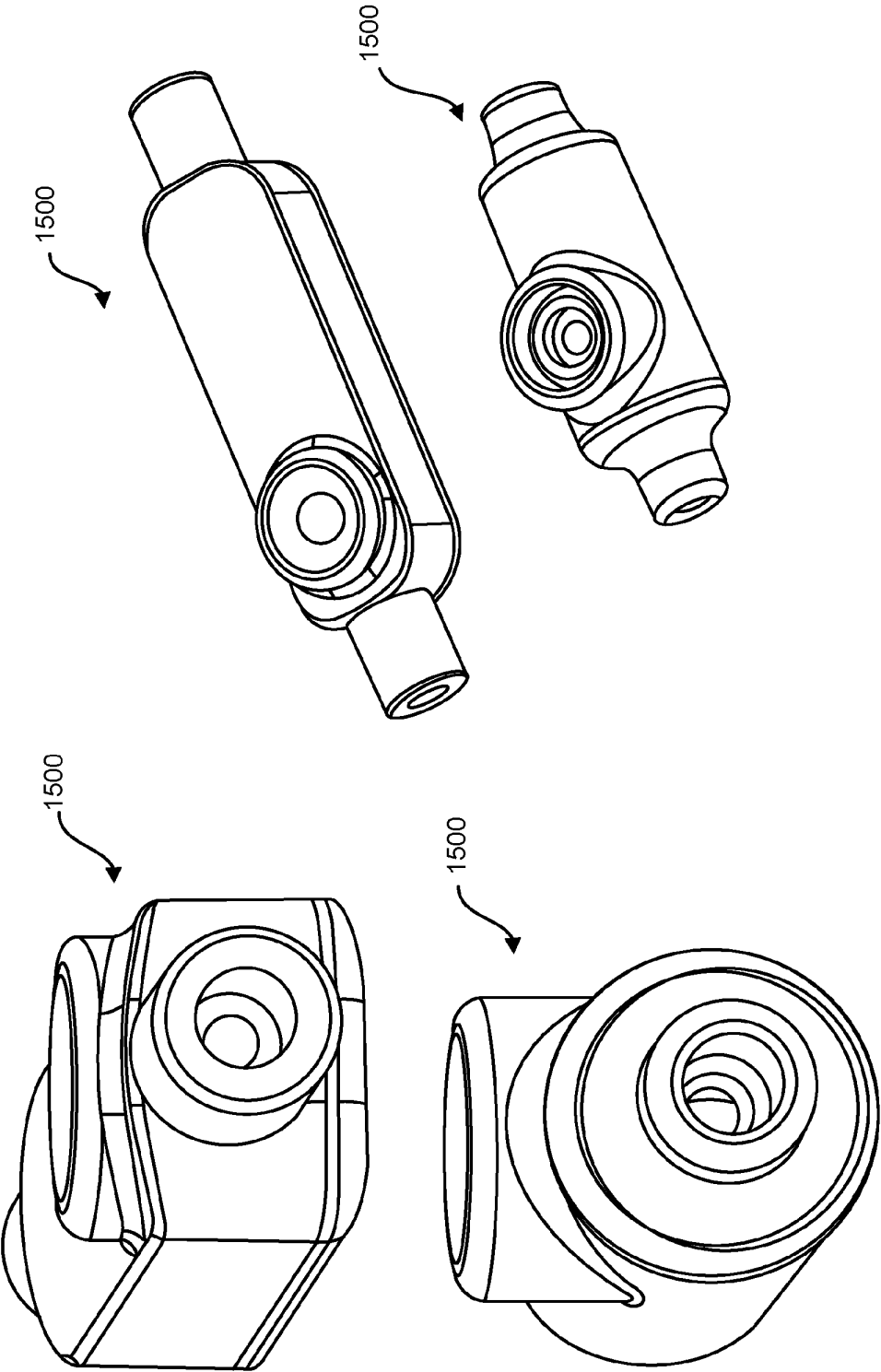


FIG. 15F

FIG. 15E

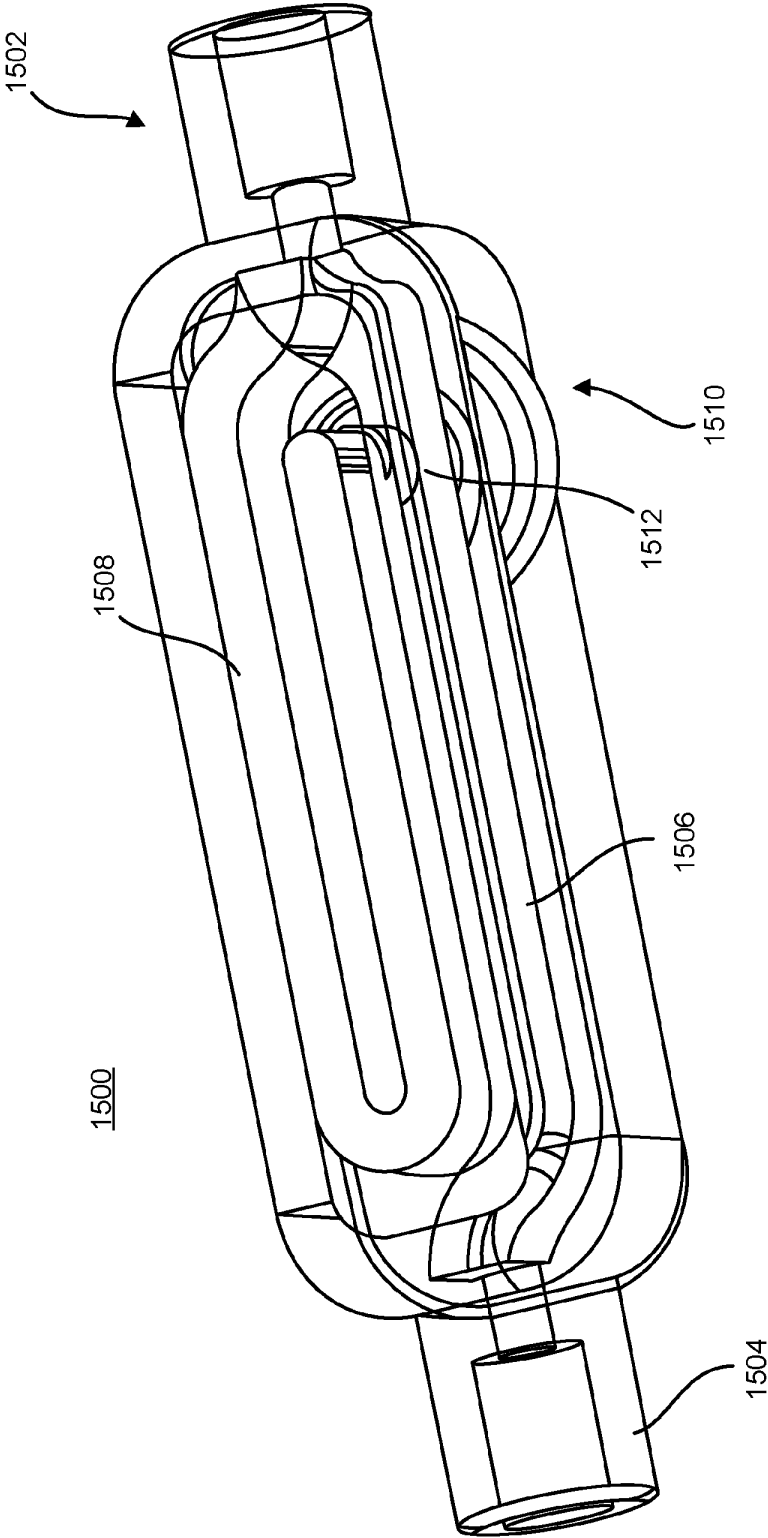


FIG. 15G

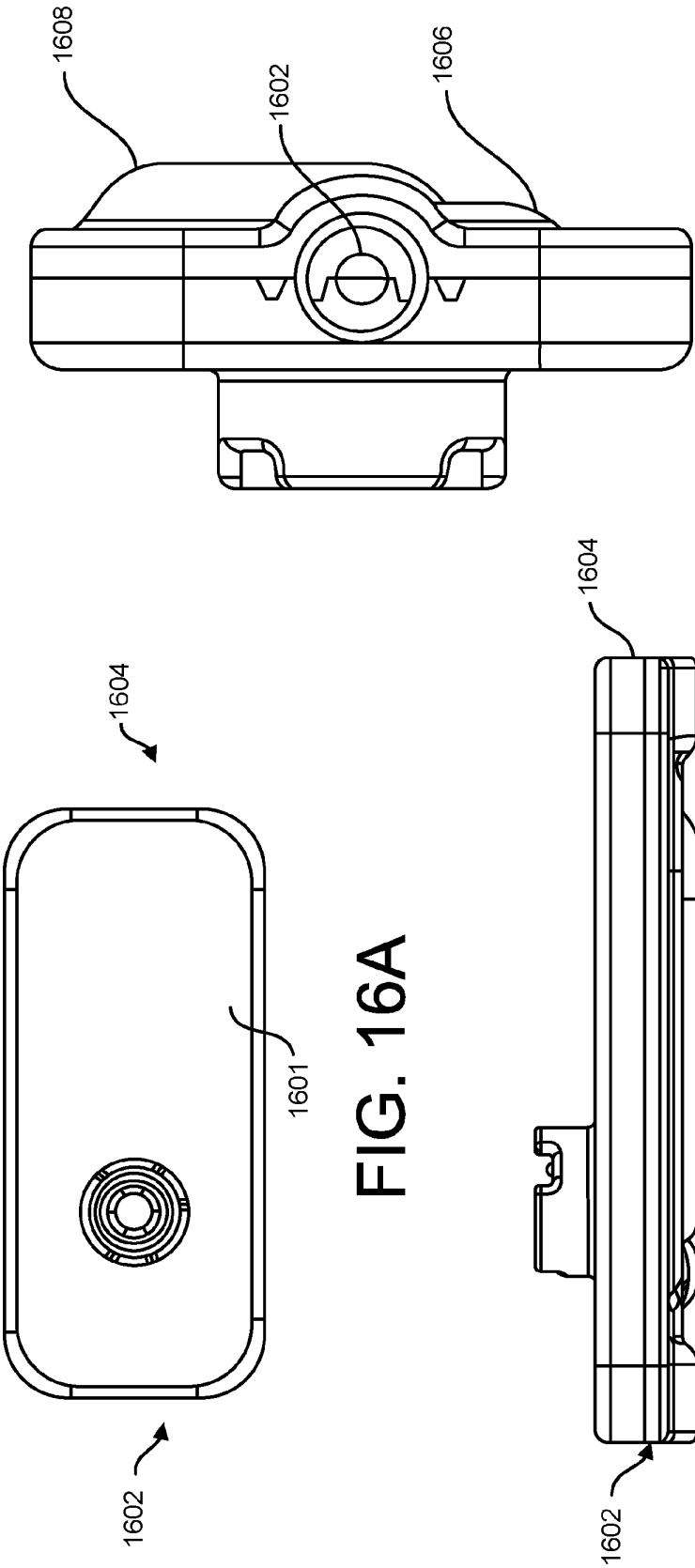


FIG. 16A

FIG. 16B

FIG. 16C

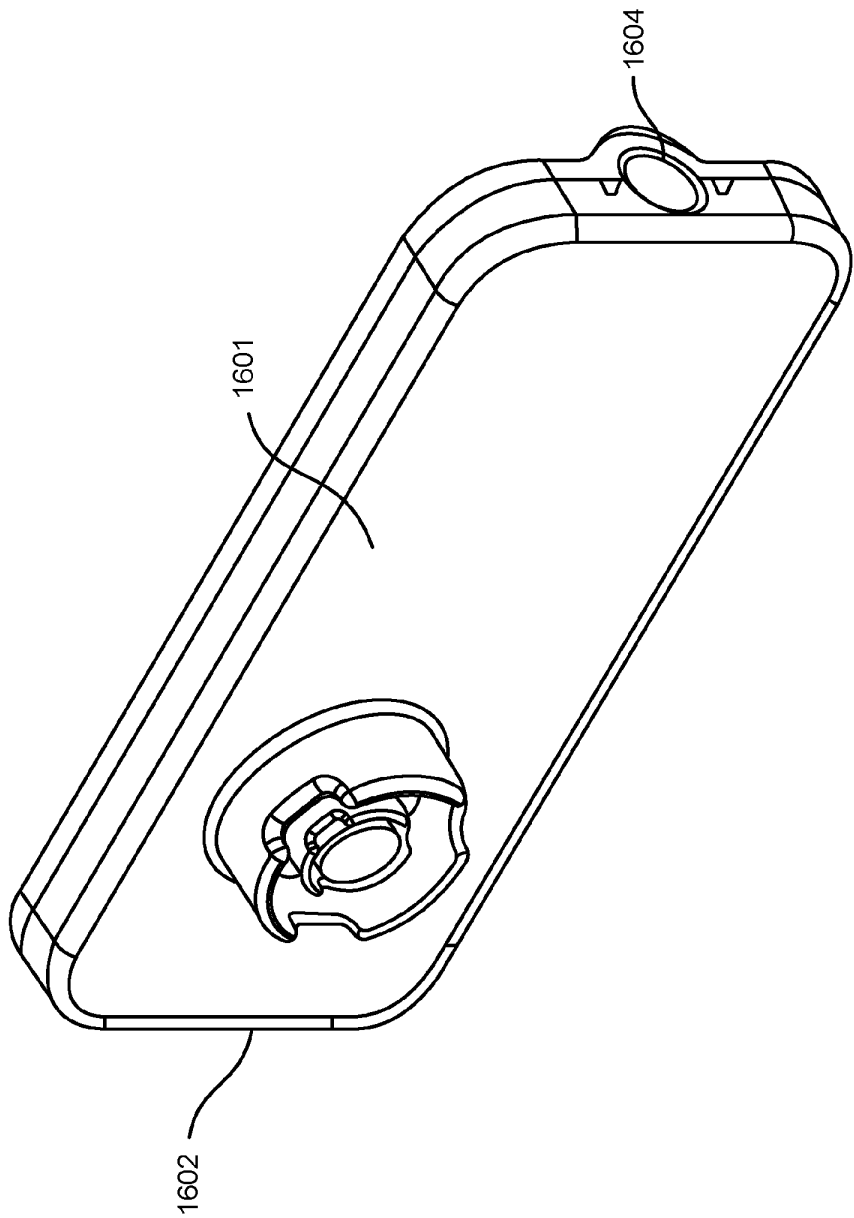


FIG. 16D

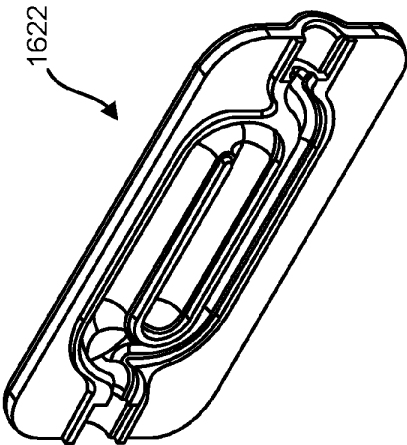


FIG. 17B

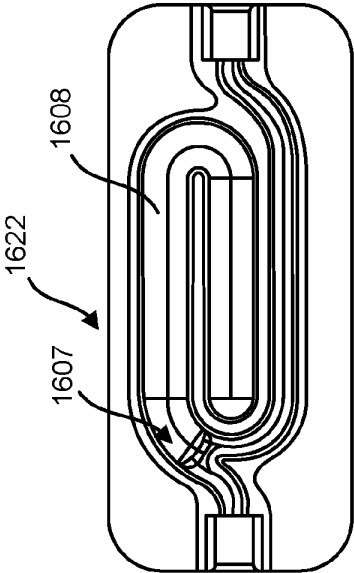


FIG. 17A

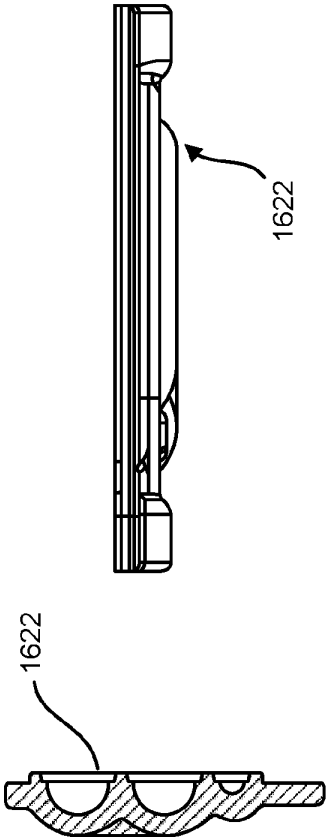


FIG. 17D

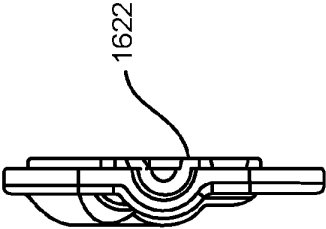


FIG. 17C



FIG. 17E

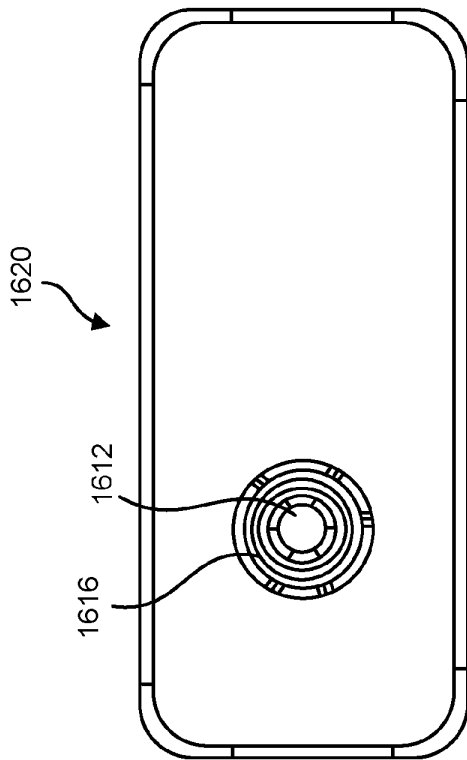


FIG. 18A

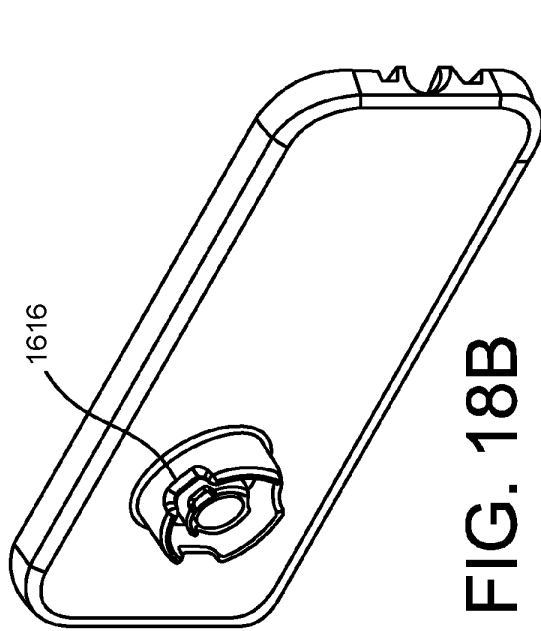


FIG. 18B

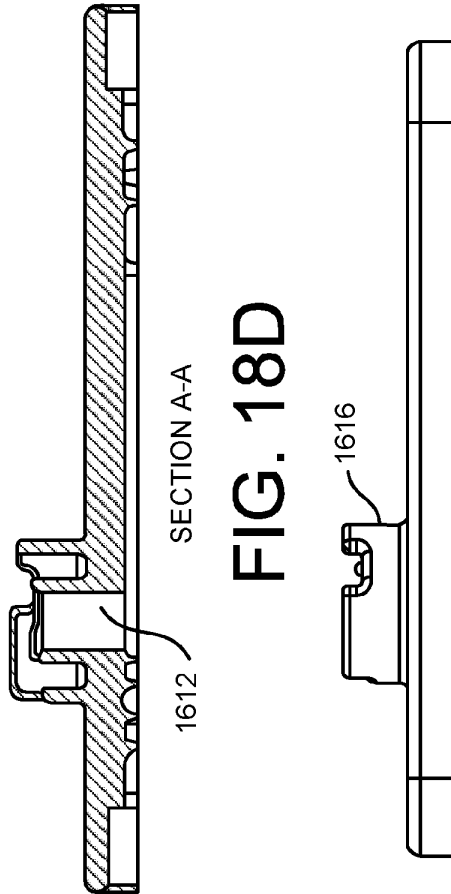


FIG. 18D

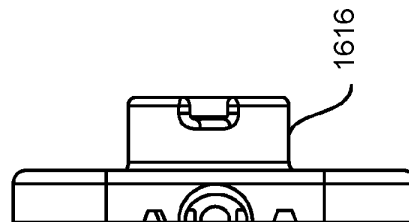


FIG. 18C

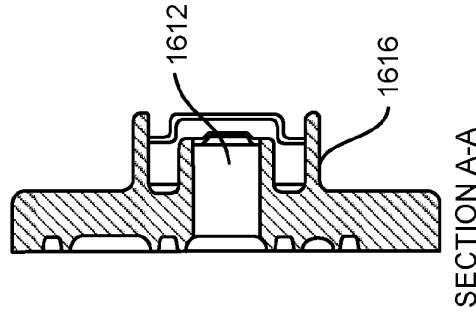


FIG. 18F

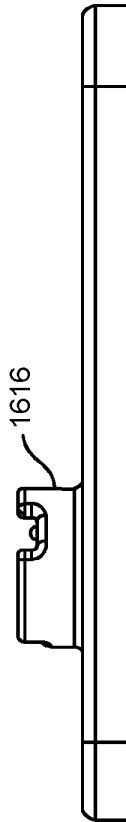


FIG. 18E

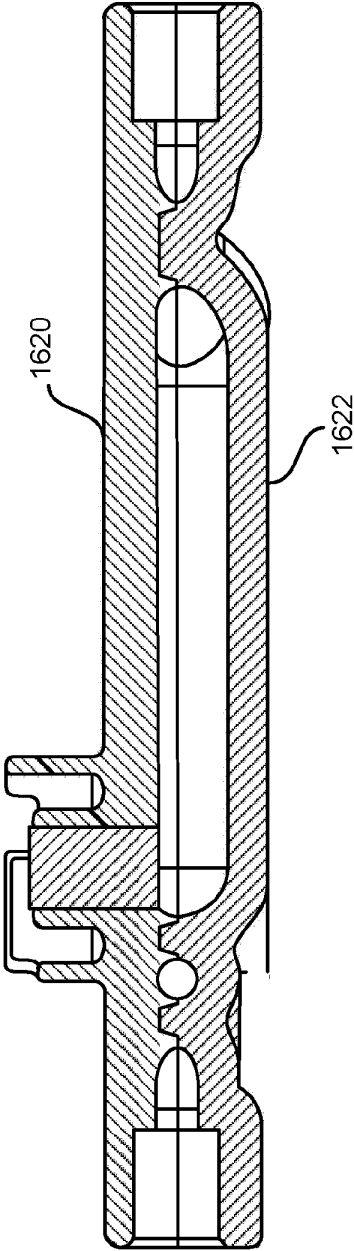


FIG. 19A

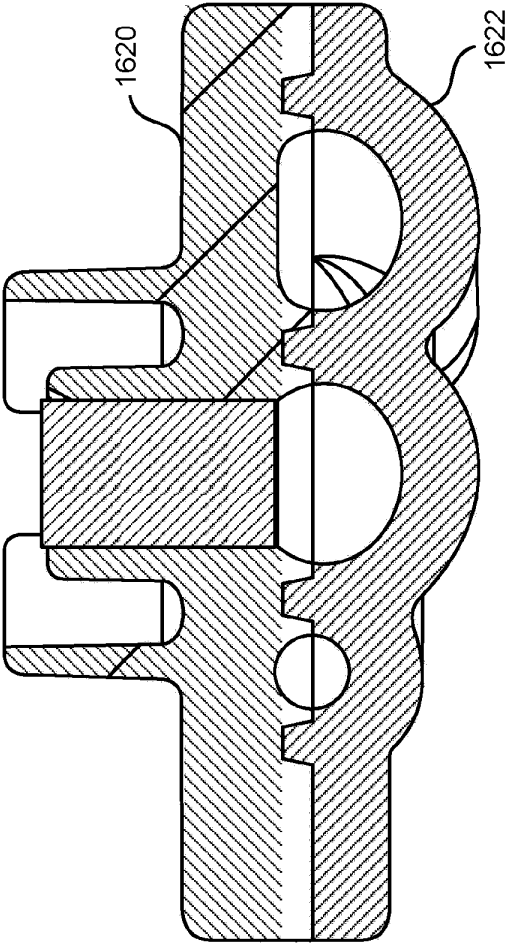


FIG. 19B

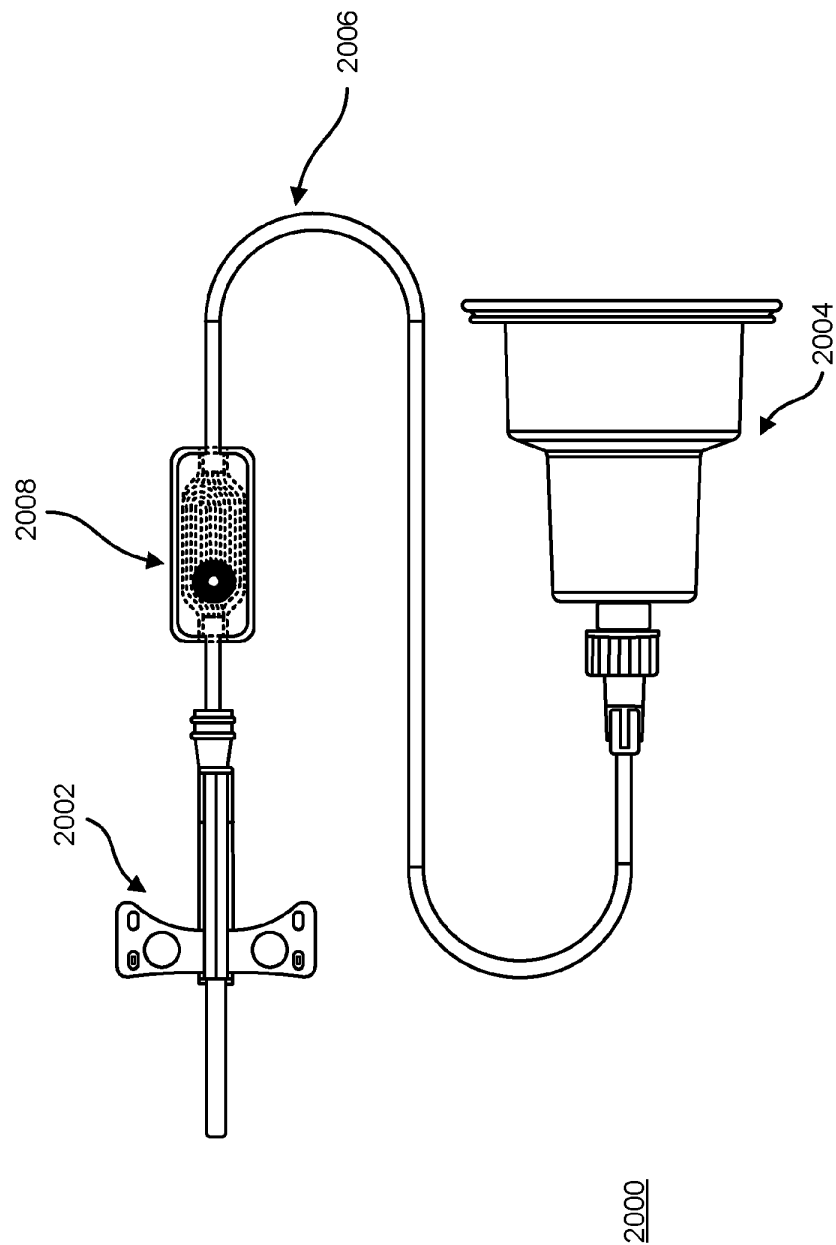


FIG. 20

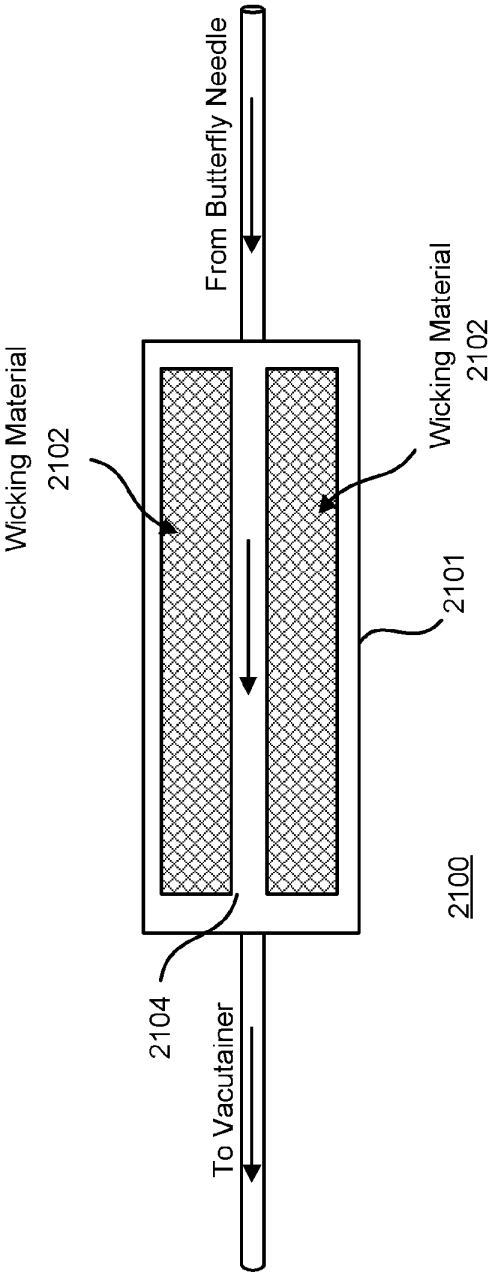


FIG. 21

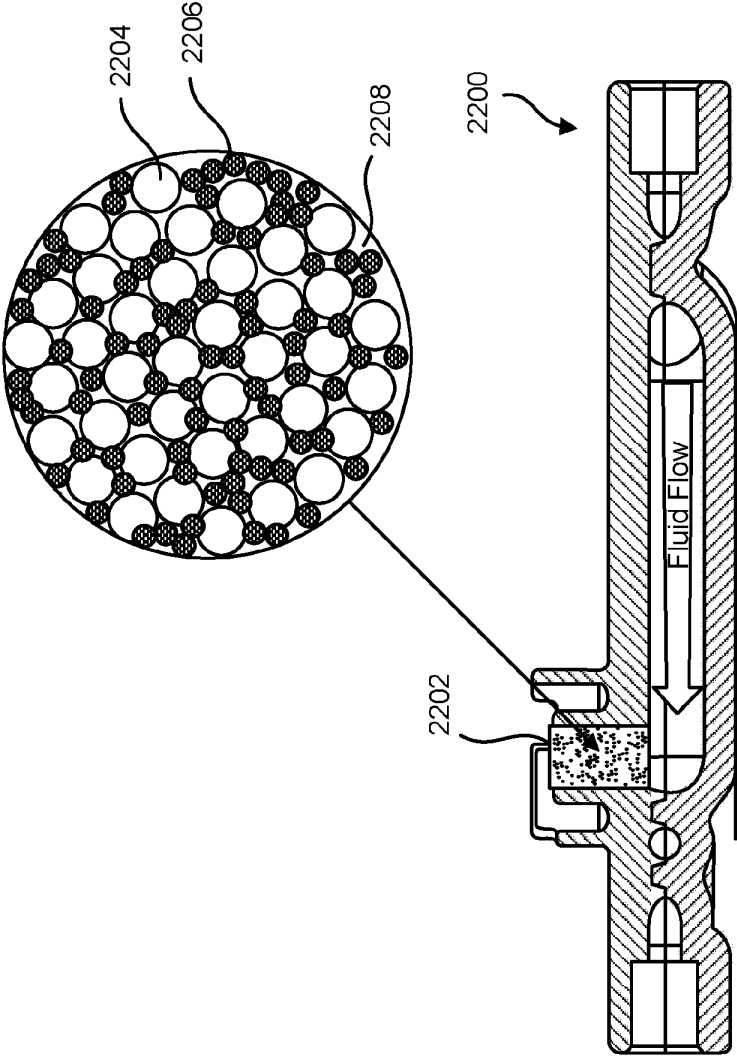


FIG. 22A

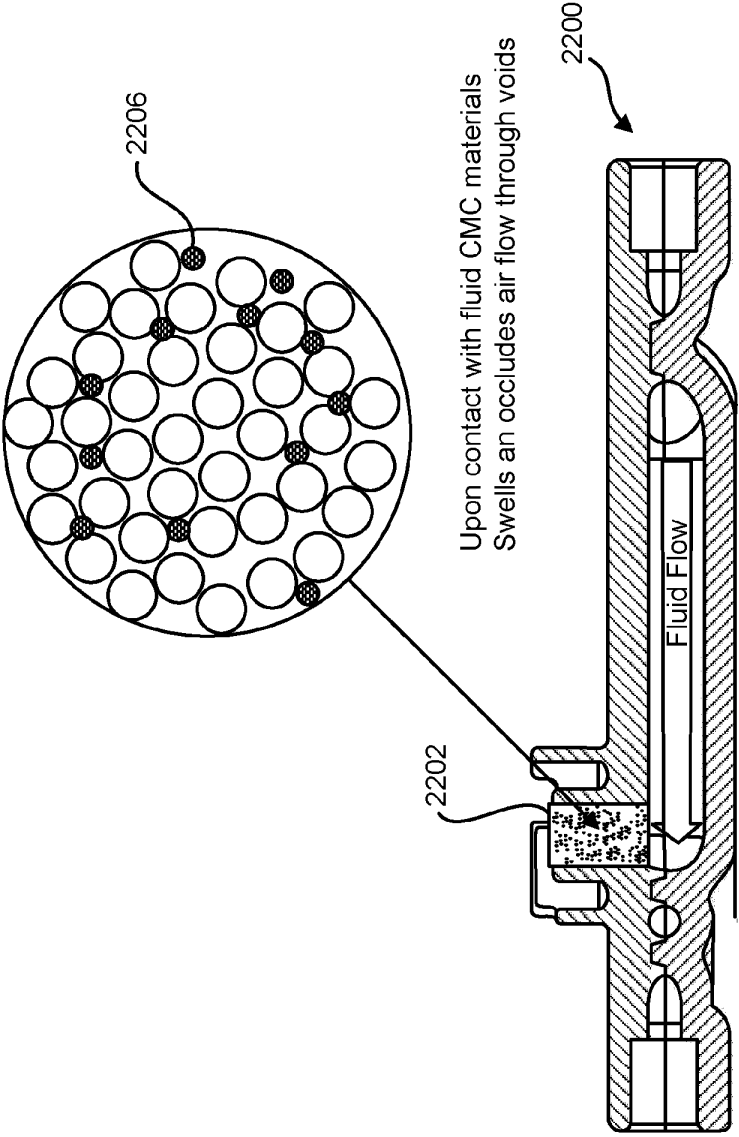


FIG. 22B

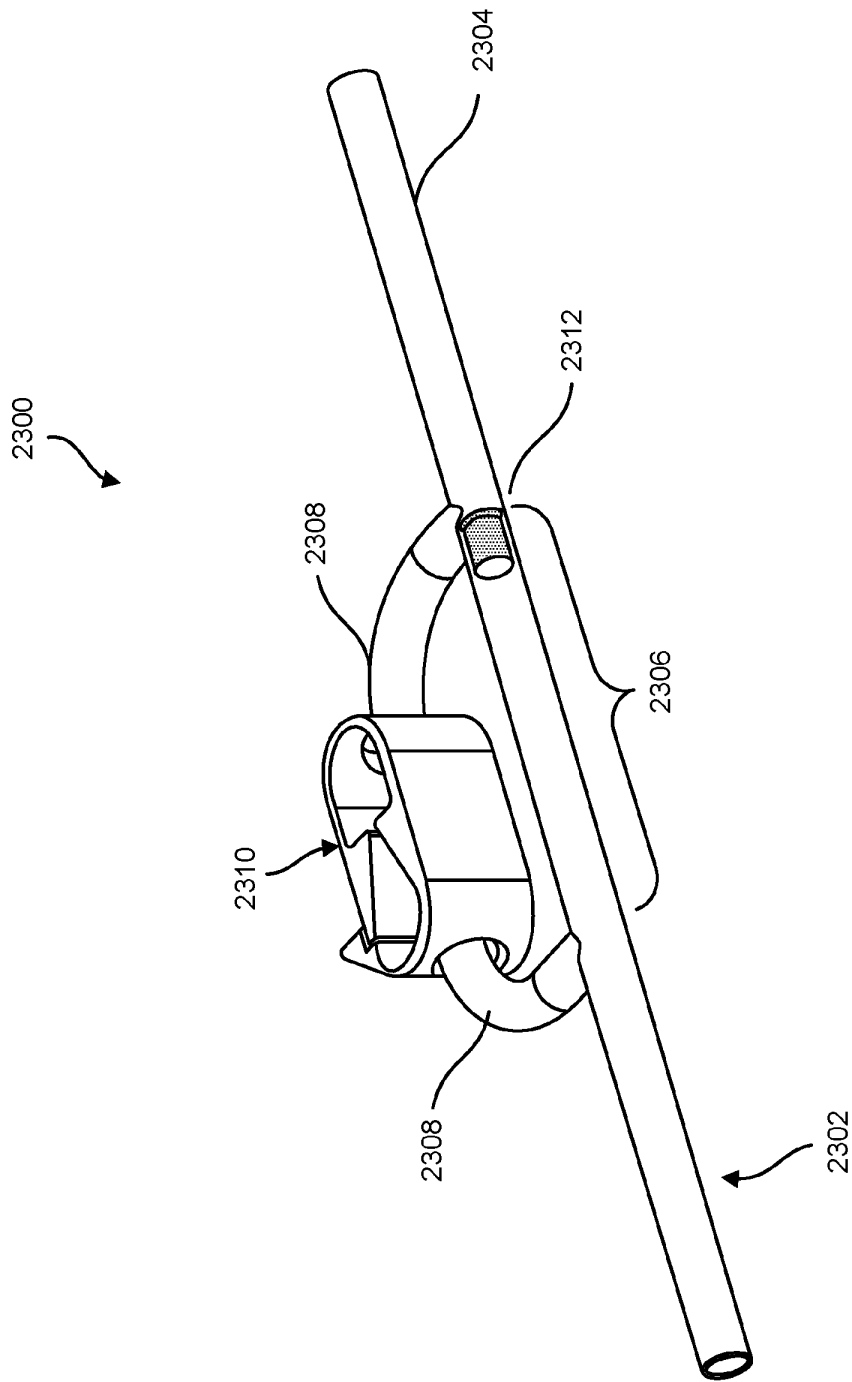


FIG. 23A

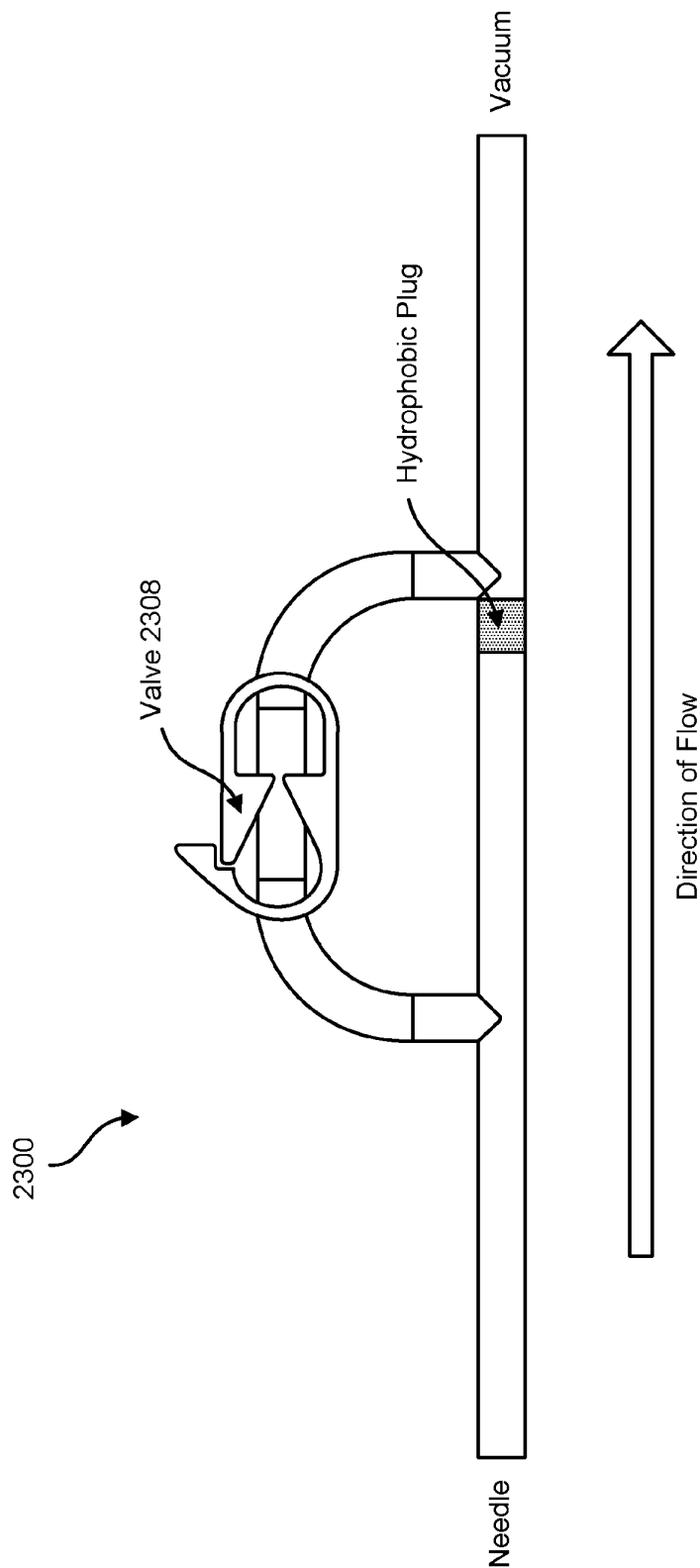


FIG. 23B

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2016/043709

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'	Quotation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/162772 A1 (CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHER LLOYD [US]; BR) 29 December 2011 (2011-12-29)	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

11 October 2016

Date of mailing of the international search report

19/10/2016

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer _____

Schultz, Ottmar

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures -----	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures -----	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14 -----	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures -----	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18 -----	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2016/043709

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 P10505336 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

PCT

WORLD INTELLECTUAL PROPE
International Bu

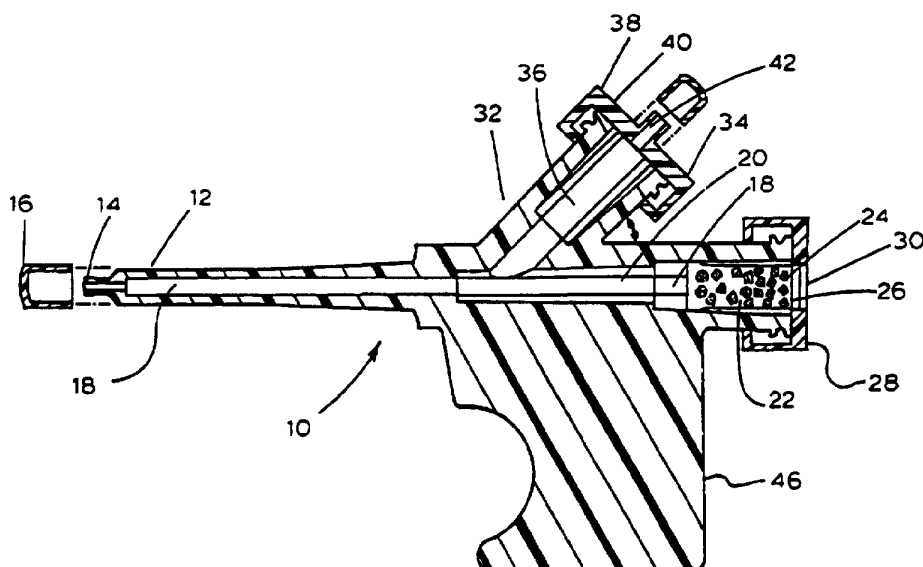


INTERNATIONAL APPLICATION PUBLISHED UNDER

WO 9605875A1

(51) International Patent Classification ⁶ : A61M 5/00		A1	(11) International Publication Number: WO 96/05875
			(43) International Publication Date: 29 February 1996 (29.02.96)
(21) International Application Number: PCT/US95/10702			(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
(22) International Filing Date: 22 August 1995 (22.08.95)			
(30) Priority Data: 08/296,207 25 August 1994 (25.08.94) US			
(71) Applicant: BAXTER INTERNATIONAL INC. [US/US]; One Baxter Parkway, Deerfield, IL 60015 (US).			
(72) Inventors: DESECKI, Vincent, C.; 28420 West Big Hollow Road, Ingleside, IL 60041 (US). BROWNE, Glennie; 944 Hidden Lake Drive, Buffalo Grove, IL 60089 (US).			
(74) Agents: NICHOLS, Jeffrey, C. et al.; One Baxter Parkway, Deerfield, IL 60015 (US).			Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

(54) Title: CLOSED SYSTEM BLOOD SAMPLING DEVICE



(57) Abstract

The invention comprises a closed system blood sampling device comprising a bifurcated capillary tube (10) which has a first branch (12) having a cannula shaped end (14) for withdrawing and conveying blood to a communicating blood collection zone. The second branch of the bifurcated capillary tube (32) is connected to and is in fluid communication with the blood collection zone. It terminates in an opening adapted to receive a blood withdrawal device.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

CLOSED SYSTEM BLOOD SAMPLING DEVICE

FIELD OF THE INVENTION

The invention relates to closed system blood sampling devices.

5 BACKGROUND OF THE INVENTION

Arterial blood gas sampling is a standard procedure often used to help assess respiratory function in the critically ill. In some cases, samples can be drawn as many as 20 times a day.

For the typical neonatal patient weighing 1000 grams and
10 having approximately 85 cc of total body fluid capacity, the volume of blood samples becomes a critical factor.

A technique called the 3 drop method is gaining substantial clinical acceptance in neonatal units across the country. This method calls for inserting a blunt hypodermic
15 needle as far as possible into a standard sleeve stoppered T-Connector. Three drops of blood estimated to be approximately .06 cc are allowed to drip onto a gauge pad, thereby clearing the cannula of heparinized or non-circulating blood while providing a fresh arterial sample to the surface. 3 more drops
20 are then collected in a micro container followed by cannula withdrawal. Blood cannula contents within the cannula lumen and the previously collected micro container sample are then aspirated into a tuberculin type syringe for transport to the blood lab for testing. A flush of the T-Connector to eliminate residual
25 blood then ensues. This procedure provides the ability to withdraw a controlled blood volume; .06 cc as necessary

-2-

discard and .12 cc to perhaps .20 cc for actual blood gas testing.

Several opportunities for procedural improvement exist. One challenge is the open environment method of collection which could foster blood contamination and/or the spread of infectious diseases. Secondly, the collection process in regard to volume accuracy is difficult to control and highly sensitive to variations in clinician technique, catheter positioning and arterial pressure. If a device can be designed for closed system collection which could also insure consistency of sample volume time after time, treatment of neonatal patients where blood volume levels are critical, accuracy improvements could be a major clinical benefit.

THE DRAWINGS

Fig. 1 is a horizontal cut away side view showing the closed system blood sampling device of the invention.

Fig. 2 is a vertical, partial schematic view showing the closed system blood sampling device connected to an injection site which, in turn, is fitted into a venipuncture device used to withdraw arterial blood.

In the drawings, like parts have like numbers.

THE INVENTION

The invention is a closed system blood sampling device comprising a bifurcated capillary tube which has a first branch having a cannula shaped end for withdrawing and conveying blood to a communicating blood collection zone. The blood

-3-

collection zone is for storing a quantity of withdrawn blood. It also feeds an initial fraction of withdrawn blood to a communicating blood disposal chamber which has an air permeable liquid sealed end.

5 The second branch of the bifurcated capillary tube is connected to and is in fluid communication with the blood collection zone. It terminates in an opening adapted to receive a blood withdrawal device.

10 In preferred embodiments the closed system blood sampling device the cannula shaped end is blunt, the blood disposal chamber has its end fitted with a cap containing an air permeable hydrophobic membrane, and the blood disposal chamber contains a porous blood adsorbent. The second branch has an interior angle not greater than 90 degrees and preferably
15 the interior angle is 60 degrees. It is also desirable that the cannula shaped end be tapered so that it snugly fits into the preferred injection sites more fully described hereafter.

20 Preferably, the closed system blood sampling device is removed from the injection site before the blood sample is withdrawn therefrom by means such as a tuberculum syringe or aspirated directly into a blood gas analyzer.

 While the closed blood sampling device is particularly suited for obtaining neonatal blood samples it is readily adapted to obtain samples from a variety of patient types.

-4-

DETAILED DESCRIPTION OF THE INVENTION

In Fig. 1 the closed system blood sampling device is designated generally by the numeral 10. It is preferably constructed of a clear chemically inert non-toxic plastic such as polycarbonate. It comprises a blood withdrawal cannula shaped end 12. The cannula tip 14 is blunt and necked down to prevent injection site from blood flash back during arterial sampling. To maintain sterility the cannula tip is fitted with a removable cap 16 which is removed just before the blood sampling device is to be used.

Fig. 1 shows the cannula shaped end 12 to be tapered. This particular configuration was selected so that the cannula may engage and generally mate with a particular injection site, the details of which will be more fully described hereafter. The interior bore 18 of the cannula shaped end is dimensioned to allow withdrawn blood to move along the bore by means of capillary action driven by normally positive arterial blood pressure.

The interior capillary bore 18 connects with and continues into a larger outer diameter lumen 20. The continuous bore 18 of the cannula 12 and the lumen 20 comprise a blood collection zone. Bore 18 as it exits the lumen 20 empties into blood disposal chamber 22. In a preferred embodiment of the invention, blood disposal chamber 22 contains a blood retaining means such as adsorbing material 24 which may be rayon or cellulosic wadding. The open end 26 of the blood disposal

- 5 -

chamber 22 is closed with a cap 28 that has its top fitted with a liquid tight, air permeable hydrophobic membrane 30 which allows air to be evacuated from the blood sampling device 10 of the invention. A suitable membrane material is sheet
5 polytetrafluoroethylene having a thickness of about 0.8 microns.

Fitted to the lumen 20, and in fluid communication therewith, is the second branch or port 32. It is positioned so as to have an interior angle 34 not exceeding 90 degrees. The interior angle is preferably about 60 degrees. The bore 36
10 connects with and corresponds in dimension with bore 18. Port 32 terminates and is sealed by adapter cap 38 whose top 40 is fitted with a capillary luer 42. The capillary luer is protected from contamination by means of protective cap 44 which is removed just prior to blood being withdrawn from the closed
15 blood sampling device. The port 32 and its bore 36 form a part of the blood collection zone previously described. For convenience of use, the closed blood sampling device is fitted with pistol grip handle 46.

The blood collection zone has a larger liquid capacity than
20 the liquid capacity of the blood disposal chamber. If the closed blood sampling device described were to be used in neonatal blood sampling, the liquid capacity of the blood collection zone might be 0.12 cc and the liquid capacity of the blood disposal chamber 22 would be about 0.06 cc.

25 The use of the closed blood sampling device of the invention to withdraw and sample blood is illustrated in Fig. 2 which shows artery 48 in communication with a venipuncture

- 6 -

device 50 which was inserted through subcutaneous tissue 52. The neck 54 of the venipuncture device 50 is adapted to receive an injection site 56. While conventional injection sites may be used as such or adapted to be used in the practice of the invention, it is preferred that the injection site be of the type having a resilient resealable septum which is preferably pre-slit. An injection site of this type is available from Baxter Healthcare Corporation and is a Neonatal T-Connector Luer sold under the brand name, InterLink, a registered trademark of Baxter Healthcare Corporation.

Such pre-slit, resilient, resealable injection sites and their method of fabrication are described in U.S. 5,188,620 the disclosure of which is incorporated herein by reference. The pre-slit resilient resealable injection sites described in this patent are designed to receive blunt cannulas. Another injection site related to the injection sites detailed in U.S. 5,188,620 is described in U.S. 5,300,034. This patent also details numerous publications and references which describe the preferred injection sites used in the practice of this invention. This patent and the publications listed therein also are incorporated herein by reference.

The injection site 56 is fitted with T-connector 58 which, in turn, is fitted with microbore tubing which, through female luer 62, is connected to IV line 64. The distal end 64 of the injection site 56 is connected to the neck 54 of the venipuncture device 50. The proximal end 66 of the injection site 56 is fitted with a pre-slit resilient resealing septum 68 adapted to receive

-7-

the blood withdrawal cannula 12 which is dimensioned to fit snugly into the injection site. Inserted into the second branch or
160 port 32 is a conventional syringe 70, such as a tuberculum blood draw syringe, or an arterial blood gas loss of resistance syringe.

The device's cannula 12 would be inserted through the septum 68 of the injection site 56 and positioned so that the tip
165 14 of the cannula 12 was fully inserted into the injection site adjacent to the venipuncture device. In doing so, the residual volume of the actual T-Housing would be eliminated as a measurable factor in blood draw volume. Arterial pressure would cause blood flow to enter and flow up the device via
170 capillary action. As blood moved up the hydrophobic membrane 30 of the device, air would escape via the upstream hydrophobic membrane 30. Original blood first present in the catheter would be pushed beyond the luer bifurcation for retention in the device and eventual disposal. The device would
175 be withdrawn from the T-Connector as soon as visual confirmation of the blood filled lumen was made. The vented removal cap 44 would be removed from the bifurcated luer 42 and replaced by the syringe 70 which would be aspirated to remove the arterial blood sample. Residual blood volume
180 upstream of the bifurcation would remain in the device for subsequent disposal.

-8-

WE CLAIM:

1. A closed system blood sampling device comprising a bifurcated capillary tube comprising:

- 5 a. a first branch having a cannula shaped end for withdrawing and conveying blood to a communicating;
- b. blood collection zone for storing a quantity of withdrawn blood and feeding an initial fraction of withdrawn blood to a communicating;
- 10 c. blood disposal chamber having an air permeable liquid sealed end; and,
- d. a second branch connected to and in fluid communication with the blood collection zone which terminates in an opening adapted to
15 receive a blood withdrawal device.

2. The closed system blood sampling device of Claim 1 where the cannula shaped end is blunt, the blood disposal chamber has its end fitted with a cap containing an air permeable hydrophobic membrane, and the blood disposal
5 chamber contains a porous blood adsorbent.

3. The closed system blood sampling device of Claim 1 where the second branch has an interior angle not greater than 90 degrees.

4. The closed system blood sampling device of Claim 3 where the second branch has an angle of about 60 degrees.

-9-

5. The closed system blood sampling device of Claim 2 where the cannula shaped end is tapered.

6. The closed system blood sampling device of Claim 2 where the blunt cannula shaped end is adapted to be received by a injection site which contains a resilient resealing means.

7. The closed system blood sampling device of Claim 6 where the injection site is a pre-slit injection site.

8. The closed system blood sampling device of Claim 2 where the blood collection zone has a volume greater than the volume of the blood disposal chamber.

-10-

9. A method of sampling blood from a patient having an artery fitted with a venipuncture device which is attached to an injection site containing the closed blood sampling device of Claim 1 which comprises the steps of:

- 5 a. withdrawing blood through the cannula shaped end of the closed blood sampling device thereby sequentially filling the blood disposal chamber and then the blood collection zone;
- 10 b. withdrawing through the opening in the second branch the blood contained in the blood collection zone for subsequent processing; and, then,
- c. discarding the closed system blood sampling device

10. The method of Claim 9 where the cannula is blunt, the blood disposal chamber has its end fitted with a cap containing an air permeable hydrophobic membrane, and contains a porous blood adsorbent.

11. The method of Claim 9 where the second branch has an interior angle not greater than 90 degrees.

12. The method Claim 11 where the second branch has an angle of about 60 degrees.

13. The method of Claim 10 where the cannula shaped end is tapered.

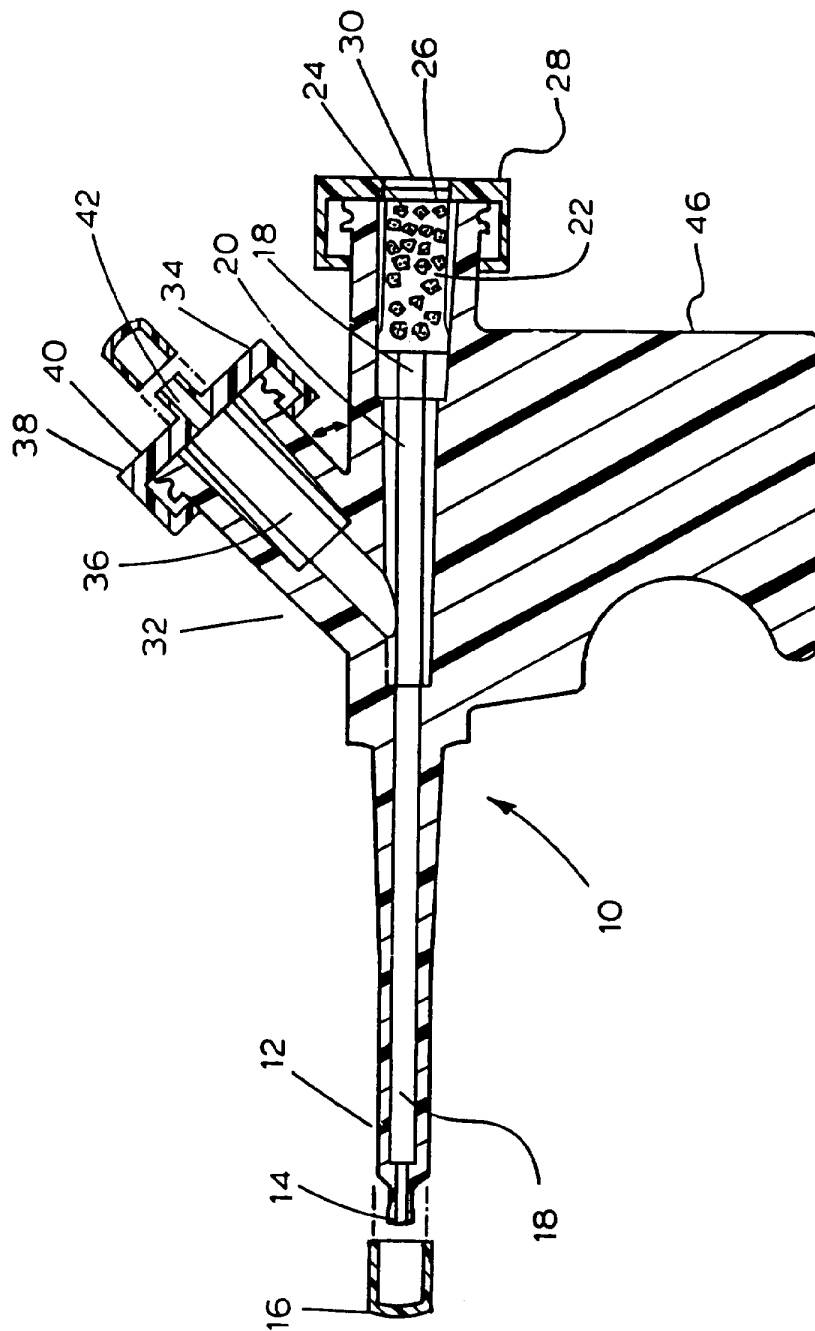
-11-

14. The method of Claim 10 where the blunt cannula shaped end is adapted to be received by a injection site which contains a resilient resealing means.

15. The method of Claim 14 where the injection site is a pre-slit injection site.

16. The method of Claim 10 where the blood collection zone has a volume greater than the volume of the blood disposal chamber.

1/2



SUBSTITUTE SHEET (RULE 26)

FIG. 1

2/2

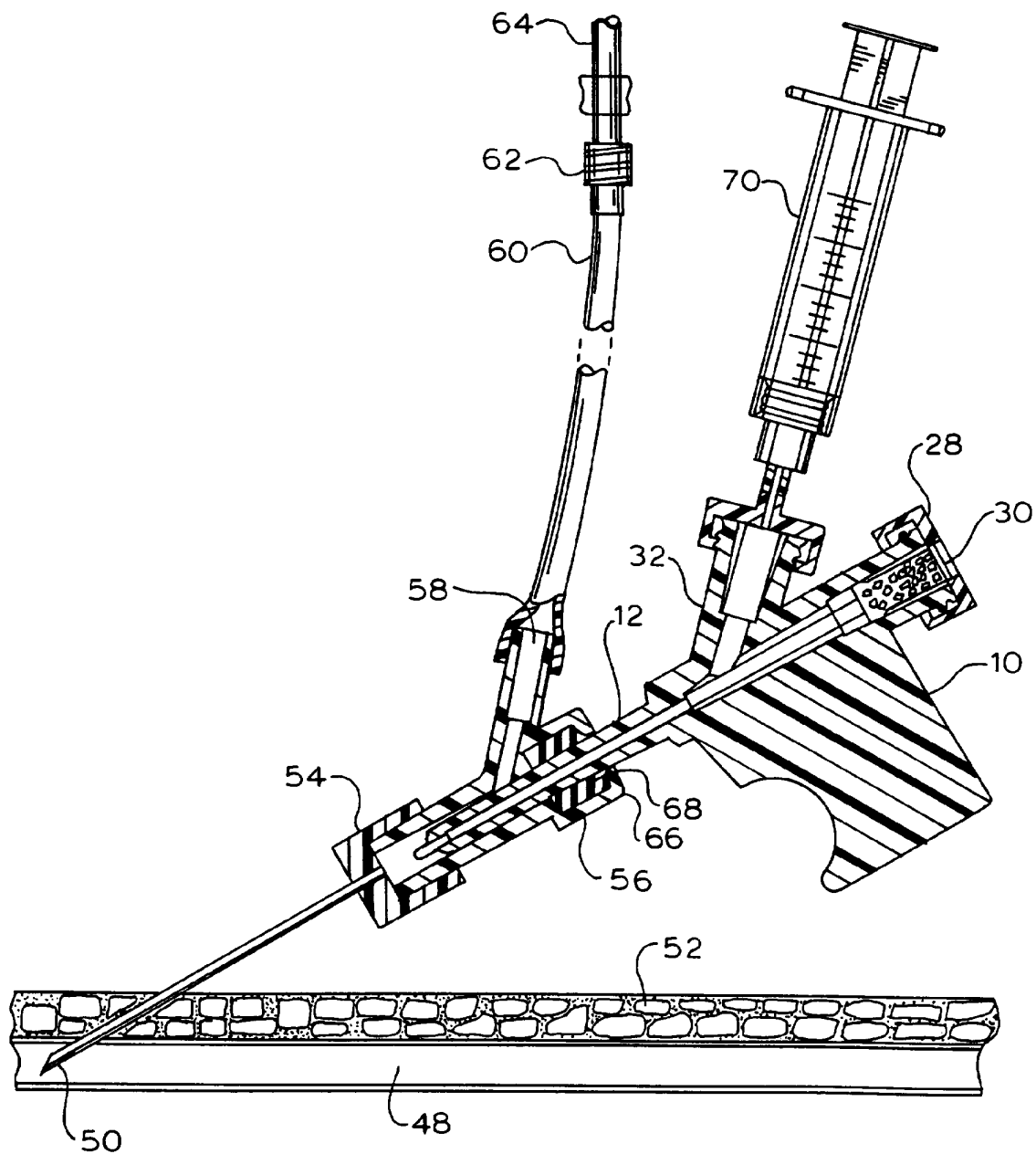


FIG. 2
SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/10702

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A 61M 5/00

US CL : 604/122

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

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

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

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

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



Espacenet

Bibliographic data: WO2011162772 (A1) — 2011-12-29

BLOOD DRAWING DEVICE WITH FLASH DETECTION

Inventor(s): FISCHEL LLOYD [US]; BROWN LEROY [US] ± (FISCHEL, LLOYD, ; BROWN, LEROY)

Applicant(s): CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC [US]; FISCHEL LLOYD [US]; BROWN LEROY [US] ± (CLEARVIEW PATIENT SAFETY TECHNOLOGIES, LLC, ; FISCHEL, LLOYD, ; BROWN, LEROY)

Classification: - international: A61M5/36
- cooperative: [A61B5/15003 \(EP\)](#); [A61B5/150213 \(EP\)](#); [A61B5/150389 \(EP\)](#); [A61B5/150496 \(EP\)](#); [A61B5/150572 \(EP\)](#); [A61B5/150732 \(EP\)](#); [A61B5/15074 \(EP\)](#); [A61B5/150992 \(EP\)](#); [A61B5/1545 \(EP\)](#); [A61B5/150473 \(EP\)](#)

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

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

Abstract of WO2011162772 (A1)

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

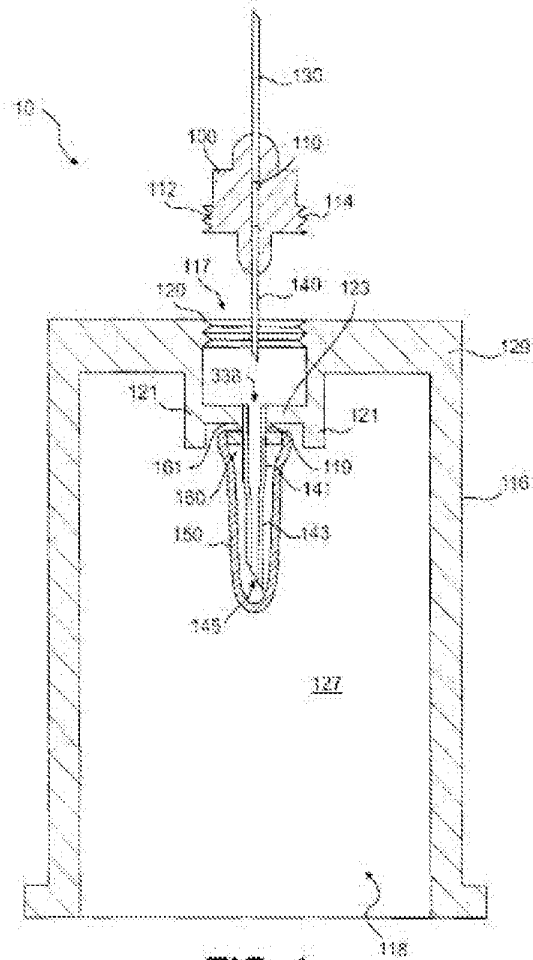


FIG. 1



(51) International Patent Classification:
A61M 5/36 (2006.01)

(21) International Application Number:
PCT/US2010/040030

(22) International Filing Date:
25 June 2010 (25.06.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
12/822,931 24 June 2010 (24.06.2010) US

(71) Applicant (for all designated States except US):
CLEARVIEW PATIENT SAFETY TECHNOLOGIES, LLC [US/US]; 20 N. Lanikai Place, Haiku, HI 96708 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FISCHEL, Lloyd** [US/US]; 20 N. Lanikai Place, Haiku, HI 96708 (US).

BROWN, Leroy [US/US]; 9393 River Oaks Lane, Orangevale, CA 95662 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK,

[Continued on next page]

(54) Title: BLOOD DRAWING DEVICE WITH FLASH DETECTION

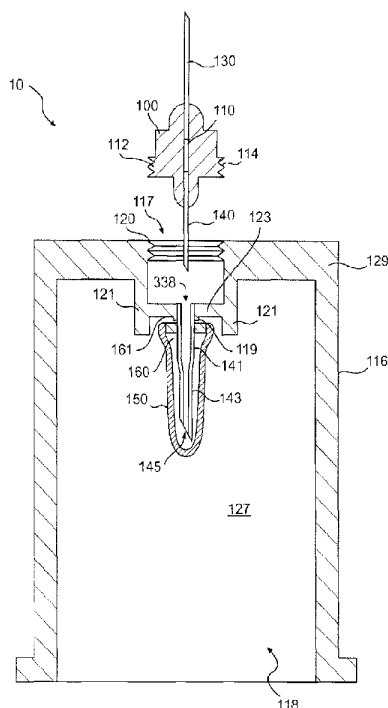


FIG. 1

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



SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

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

BLOOD DRAWING DEVICE WITH FLASH DETECTION

FIELD OF THE INVENTION

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

BACKGROUND OF THE INVENTION

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

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

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

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

SUMMARY OF THE INVENTION

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

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

BRIEF DESCRIPTION OF THE DRAWINGS

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

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

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

after connection to the blood drawing needle.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

sleeve.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

WHAT IS CLAIMED IS:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

20. The guide tube of Claim 15 further comprising:

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

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

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

(150) are transparent or translucent.

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

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

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

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

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

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

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

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

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

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

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

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

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

29. The guide tube of Claim 22 further comprising:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

47. The device of Claim 1, further comprising:

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

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

48. The device of Claim 1, further comprising:

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

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

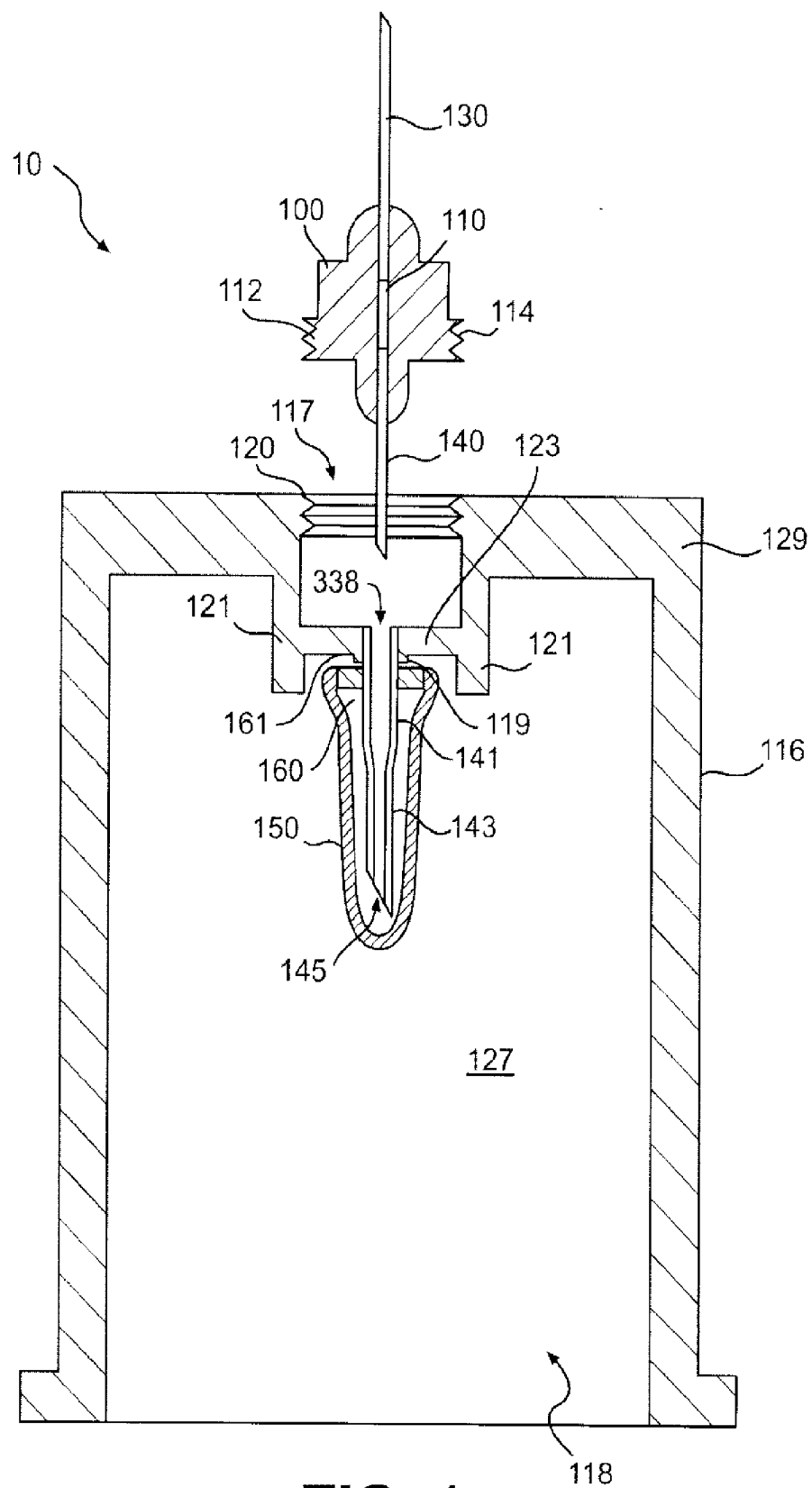


FIG. 1

SUBSTITUTE SHEET (RULE 26)

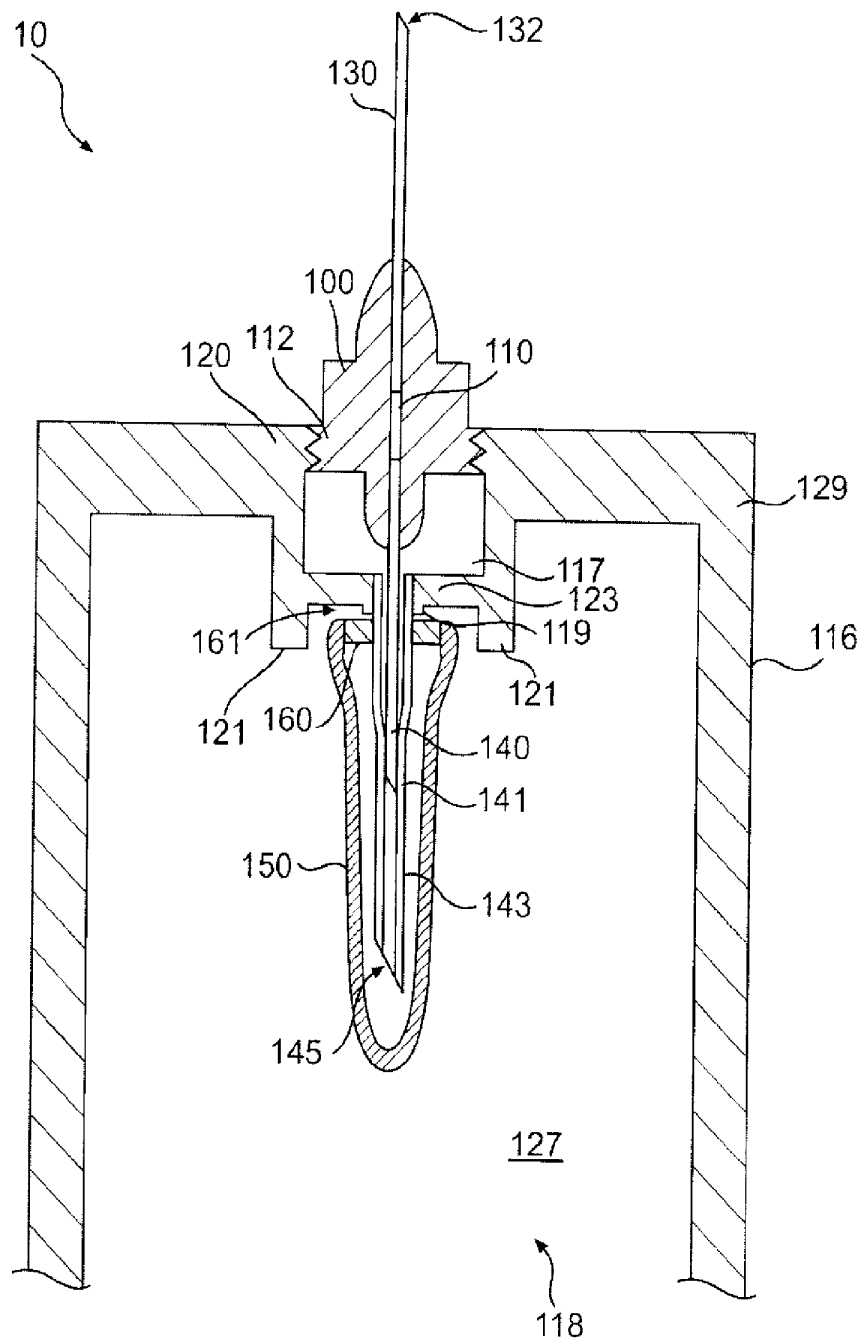


FIG. 2

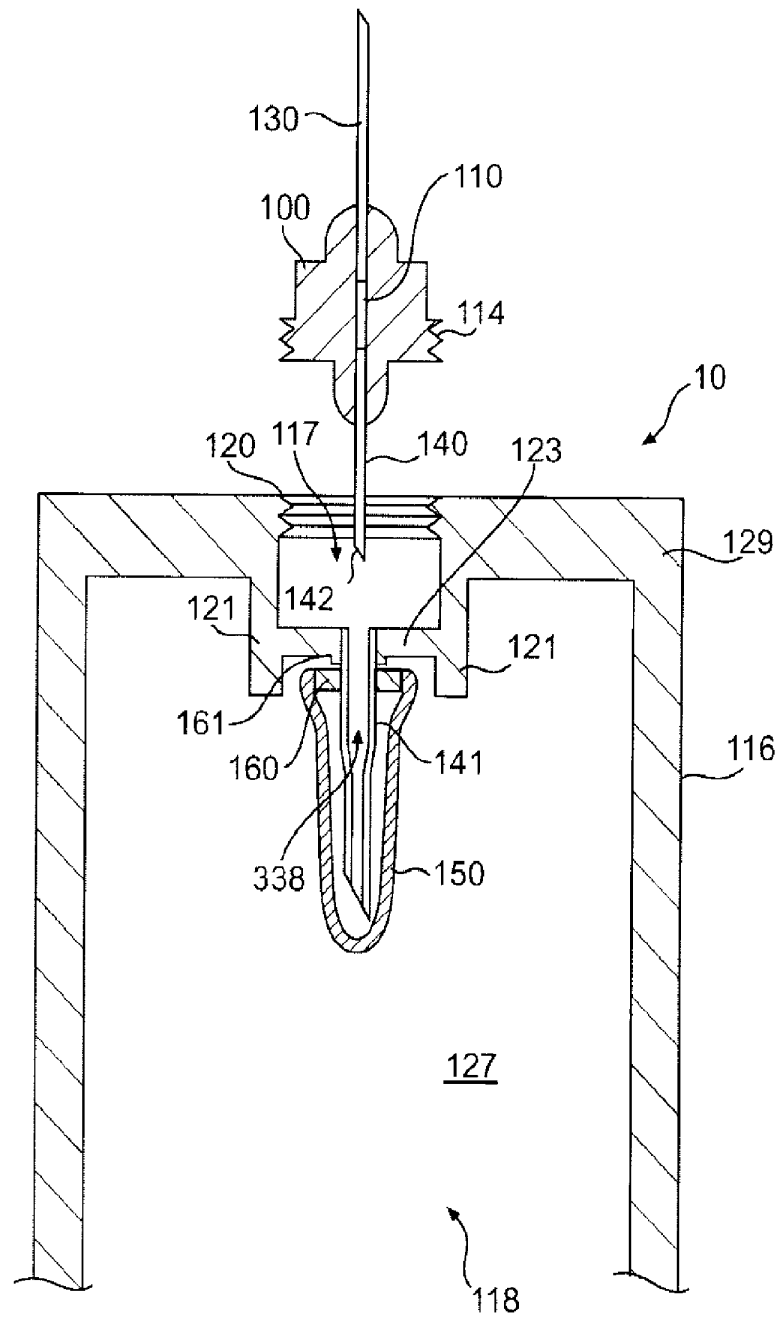


FIG. 3

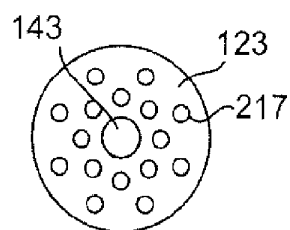


FIG. 4

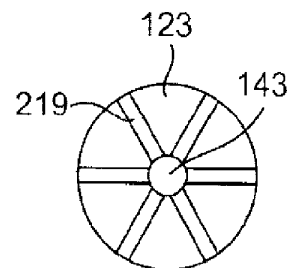
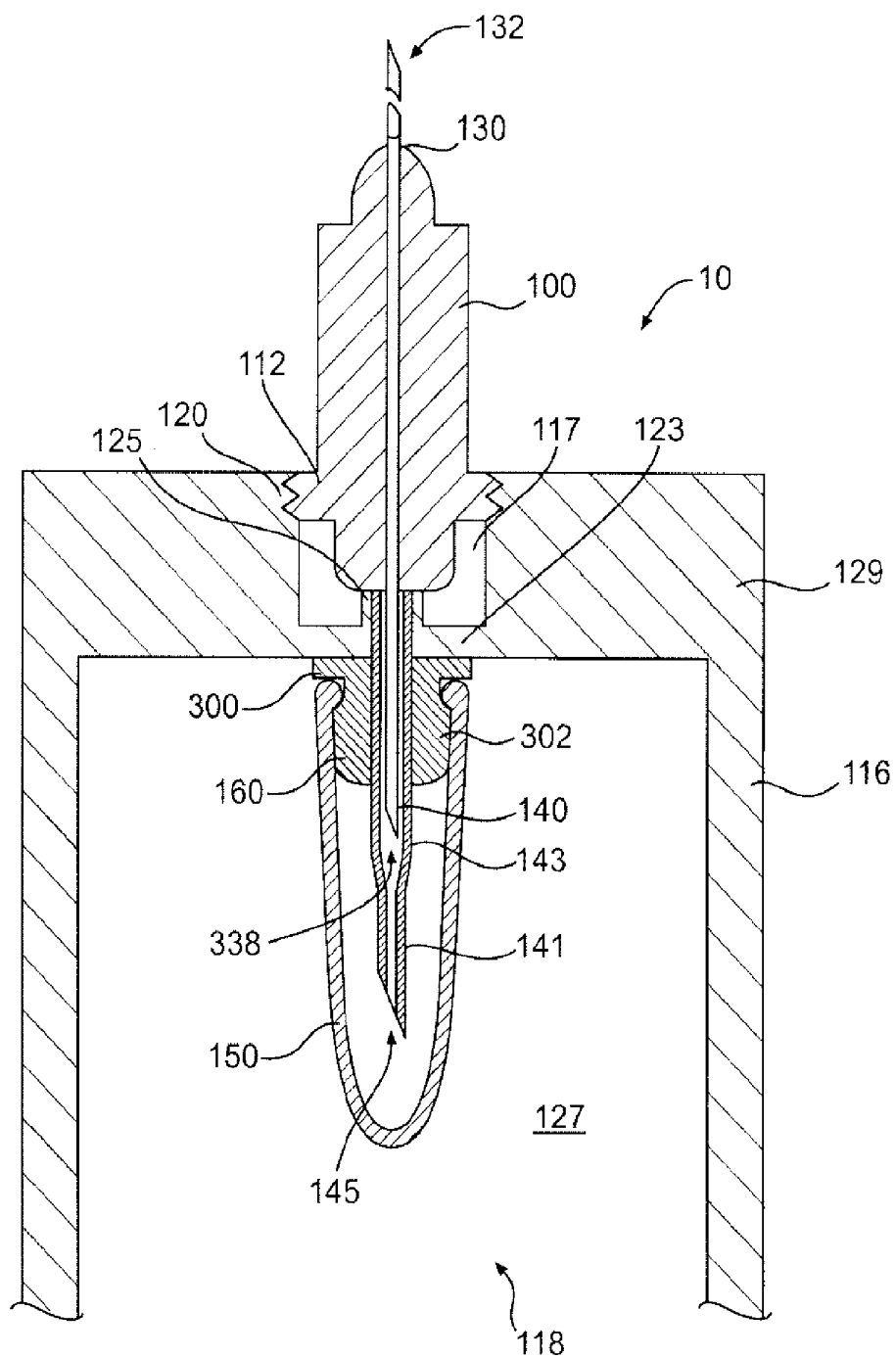


FIG. 5

**FIG. 6**

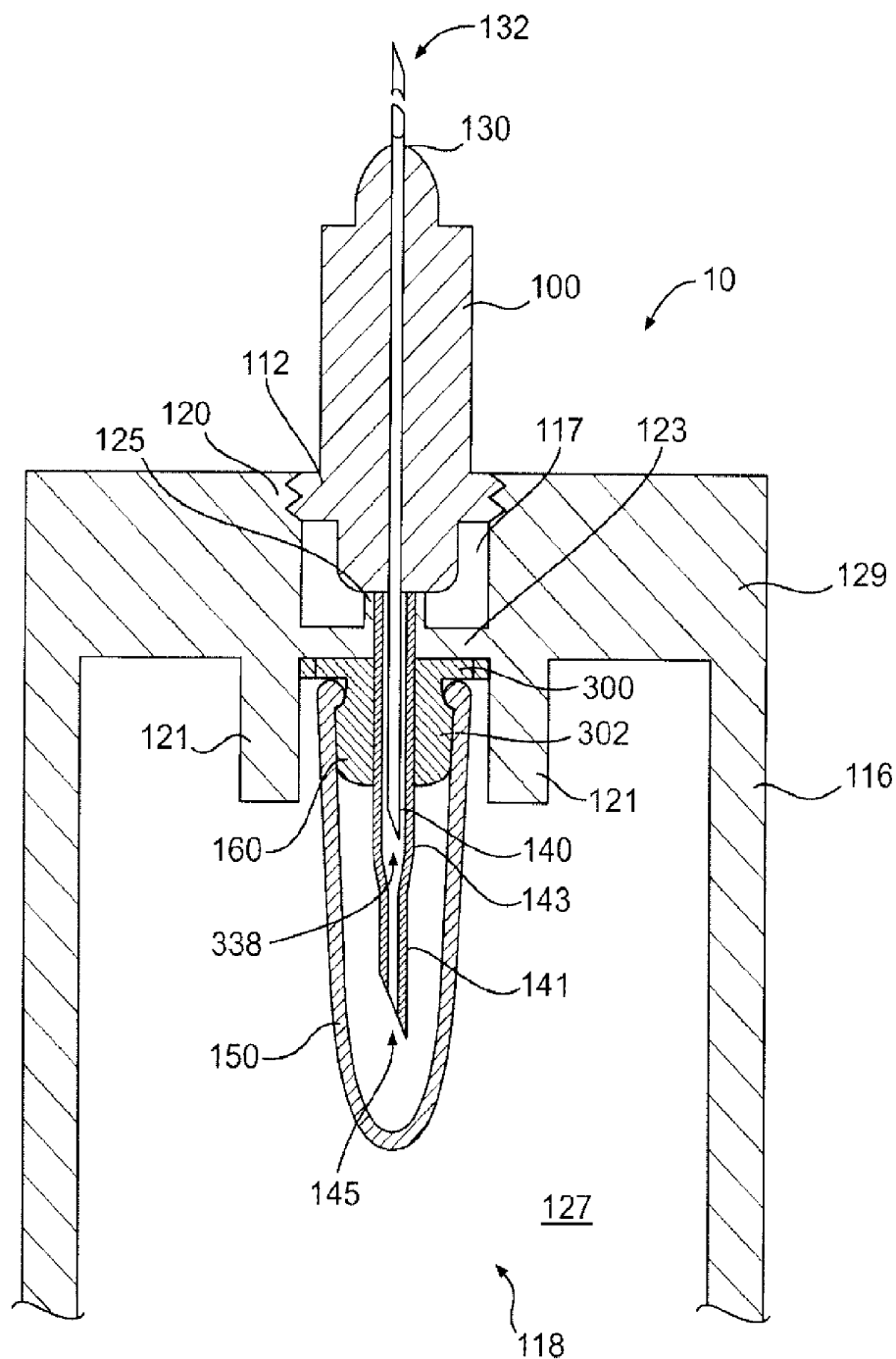
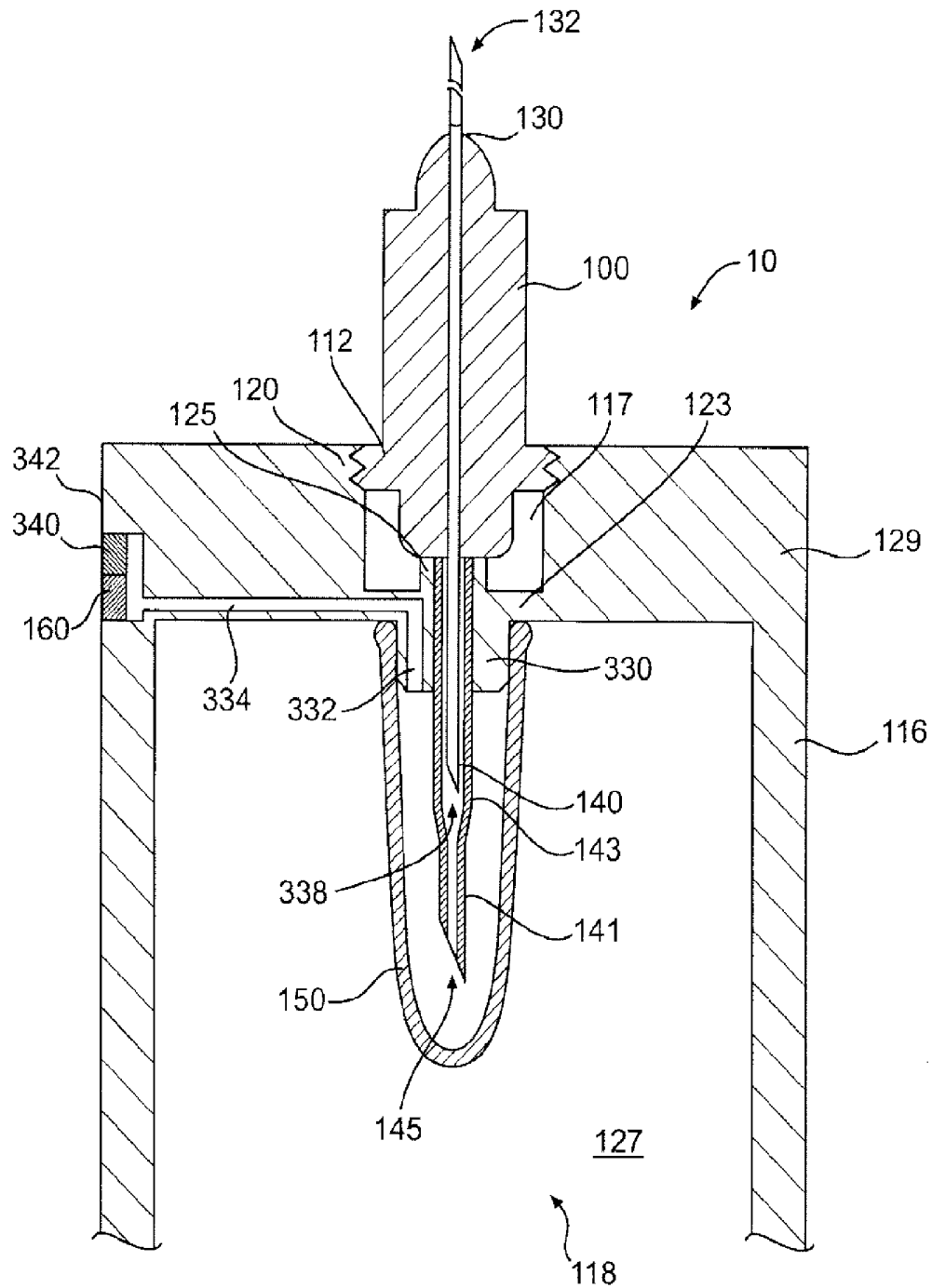
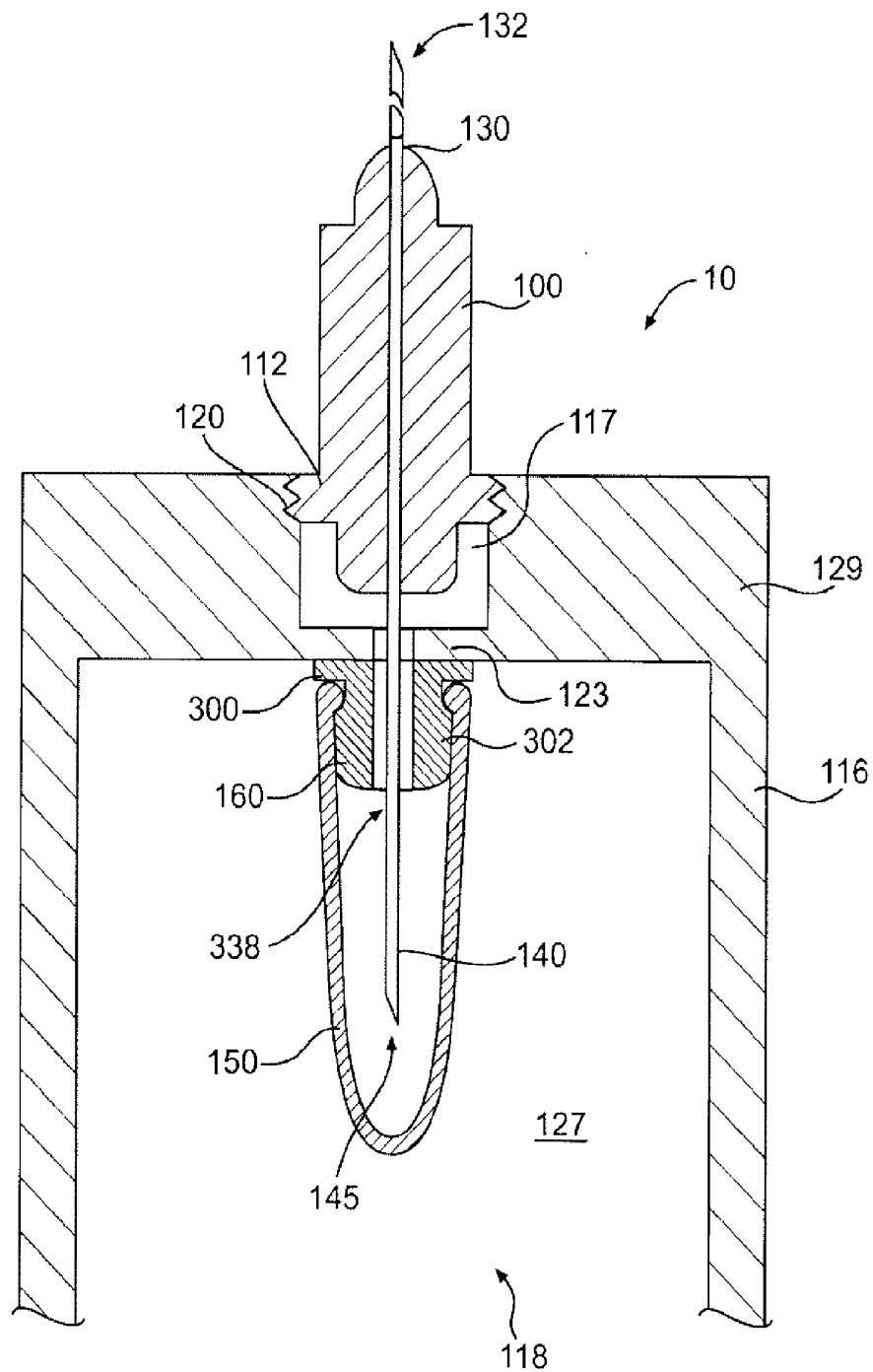


FIG. 7



**FIG. 10**

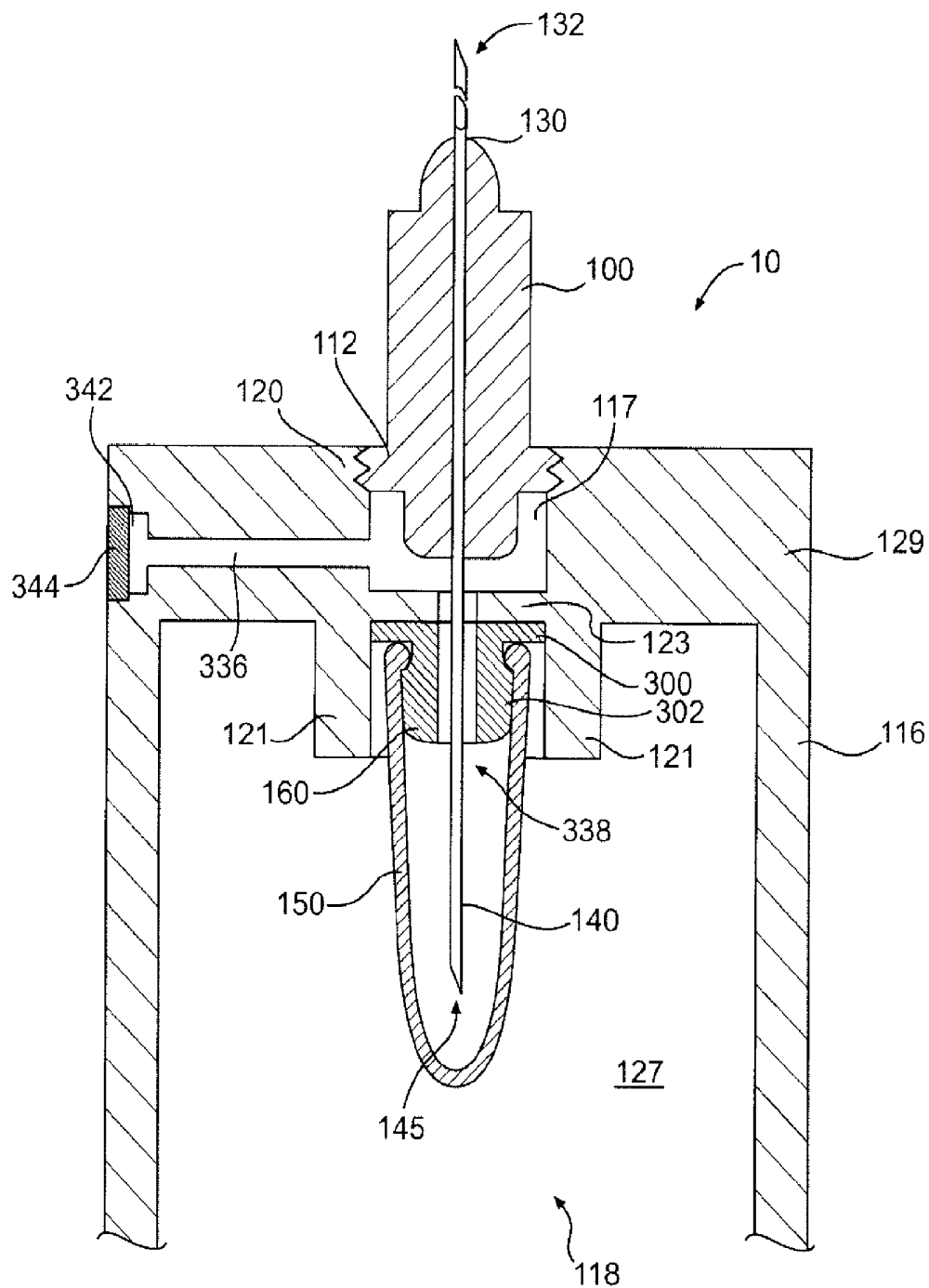
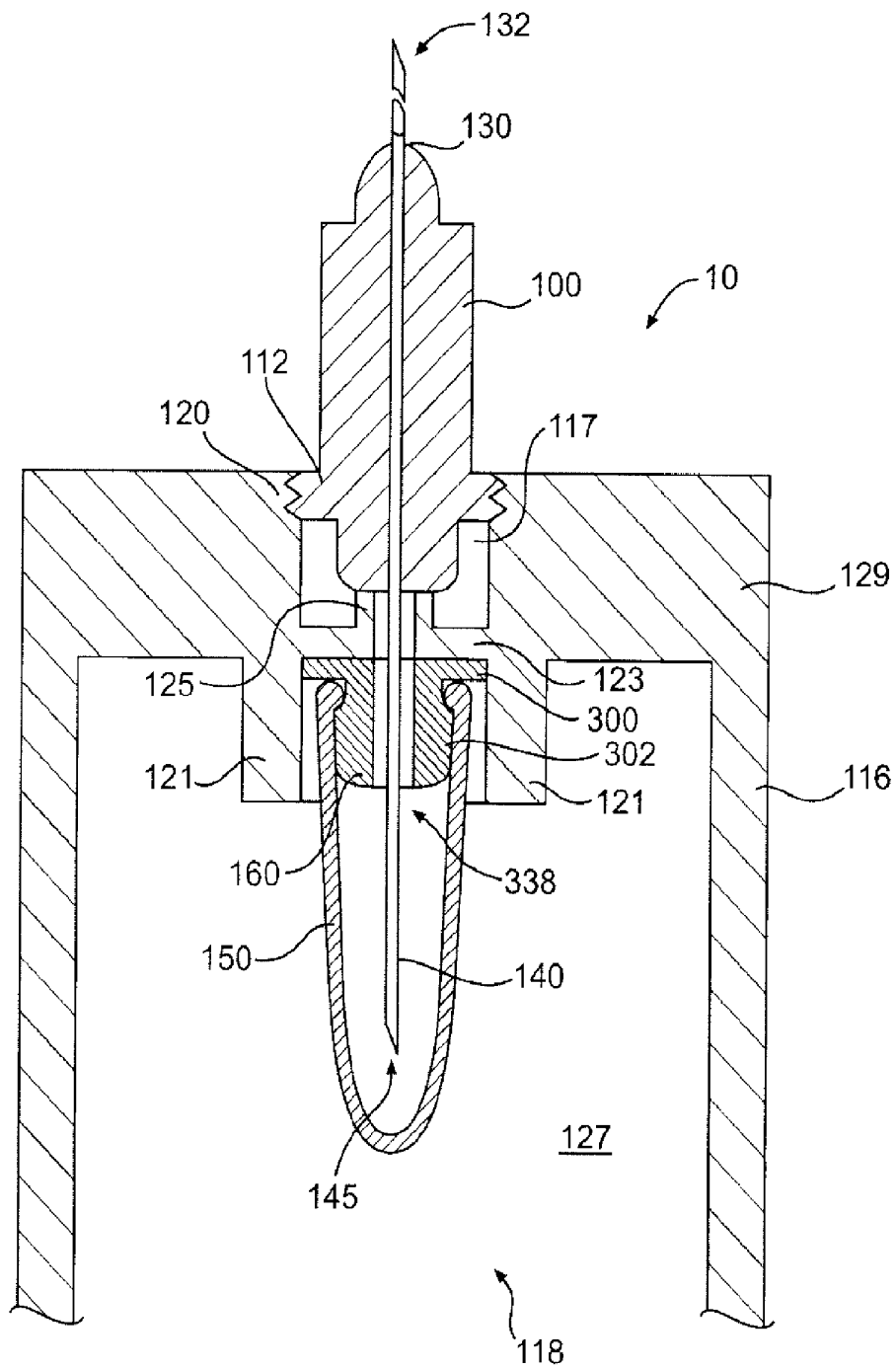


FIG. 12

**FIG. 13**

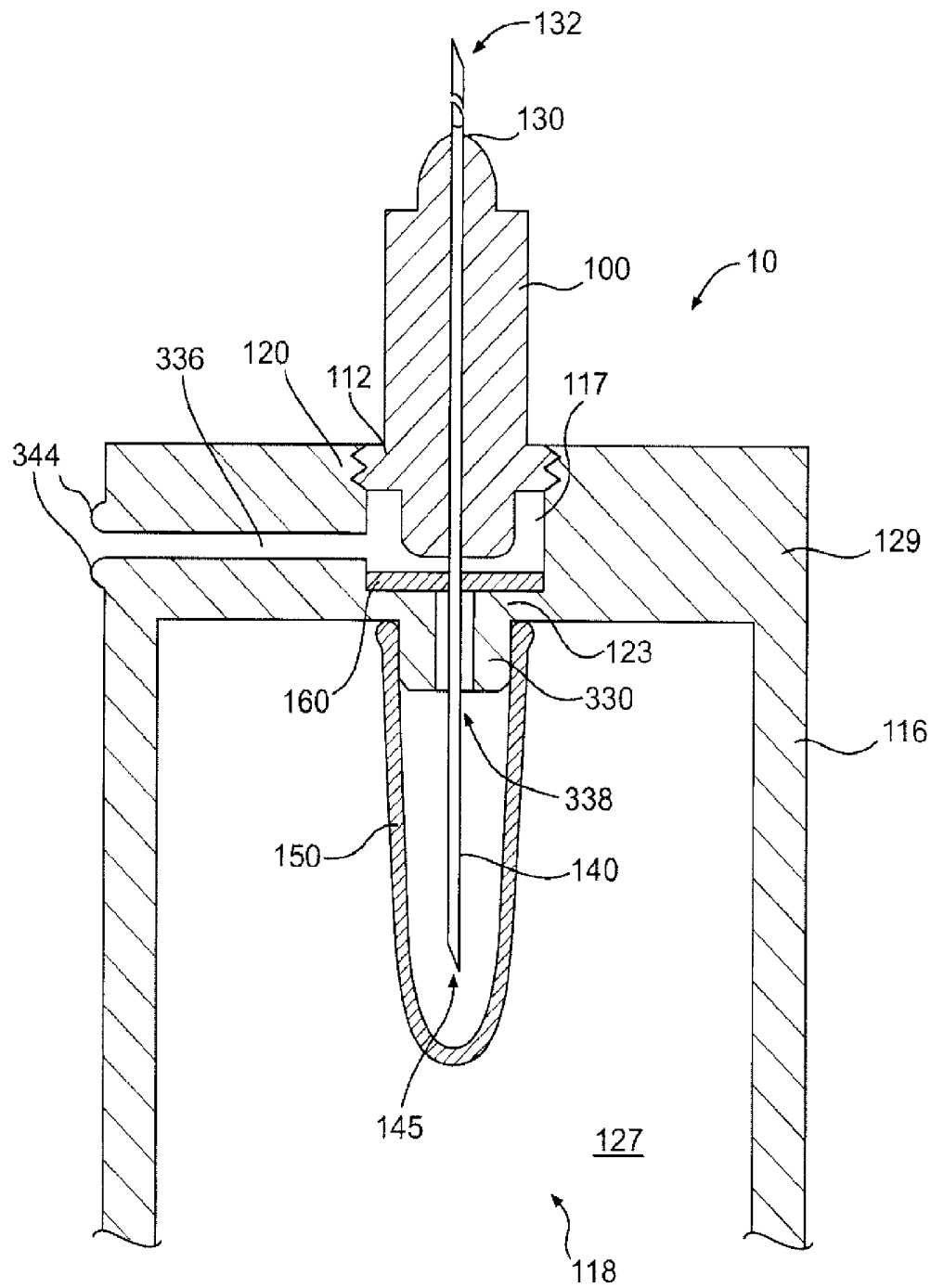


FIG. 16

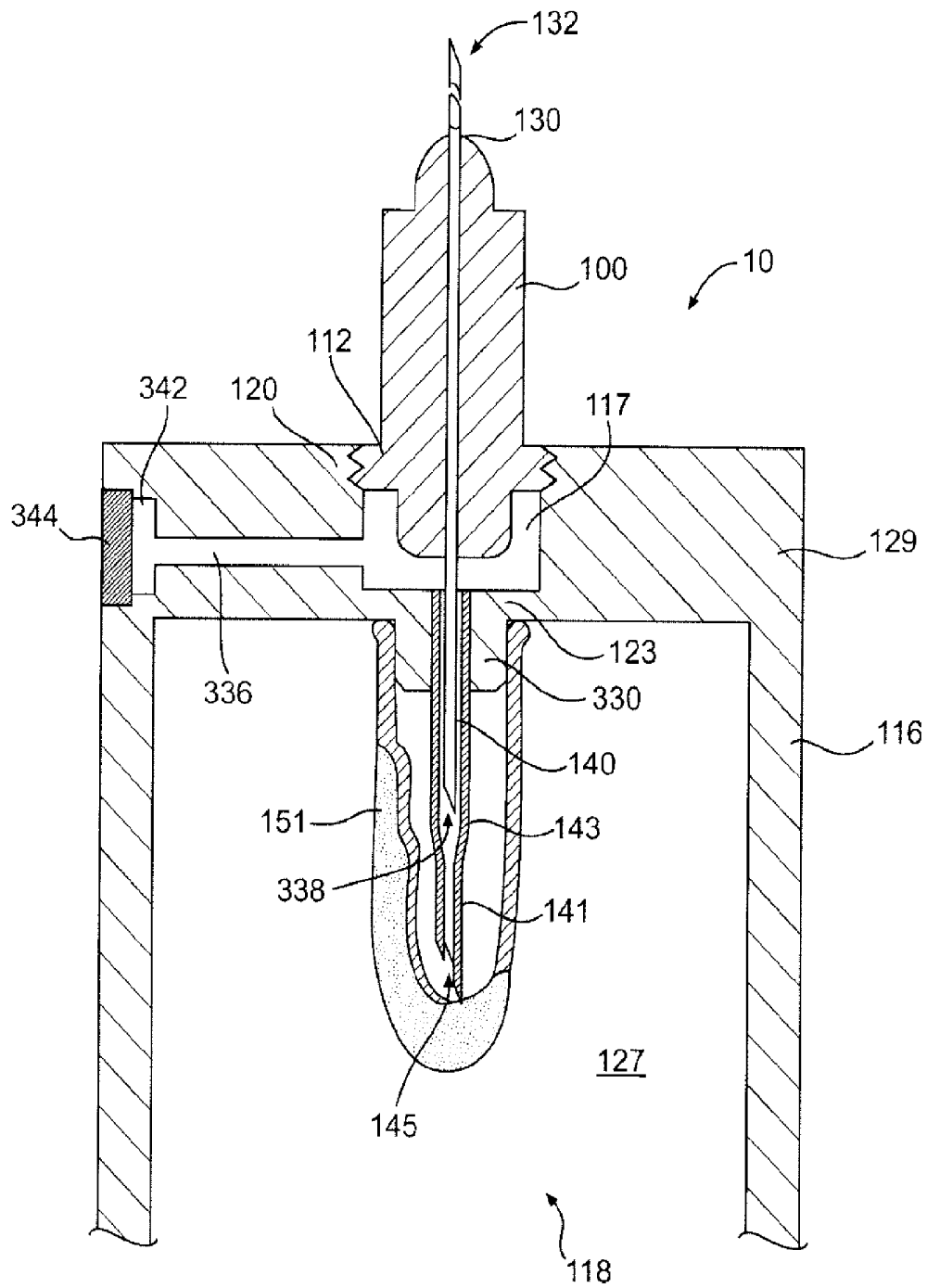


FIG. 18

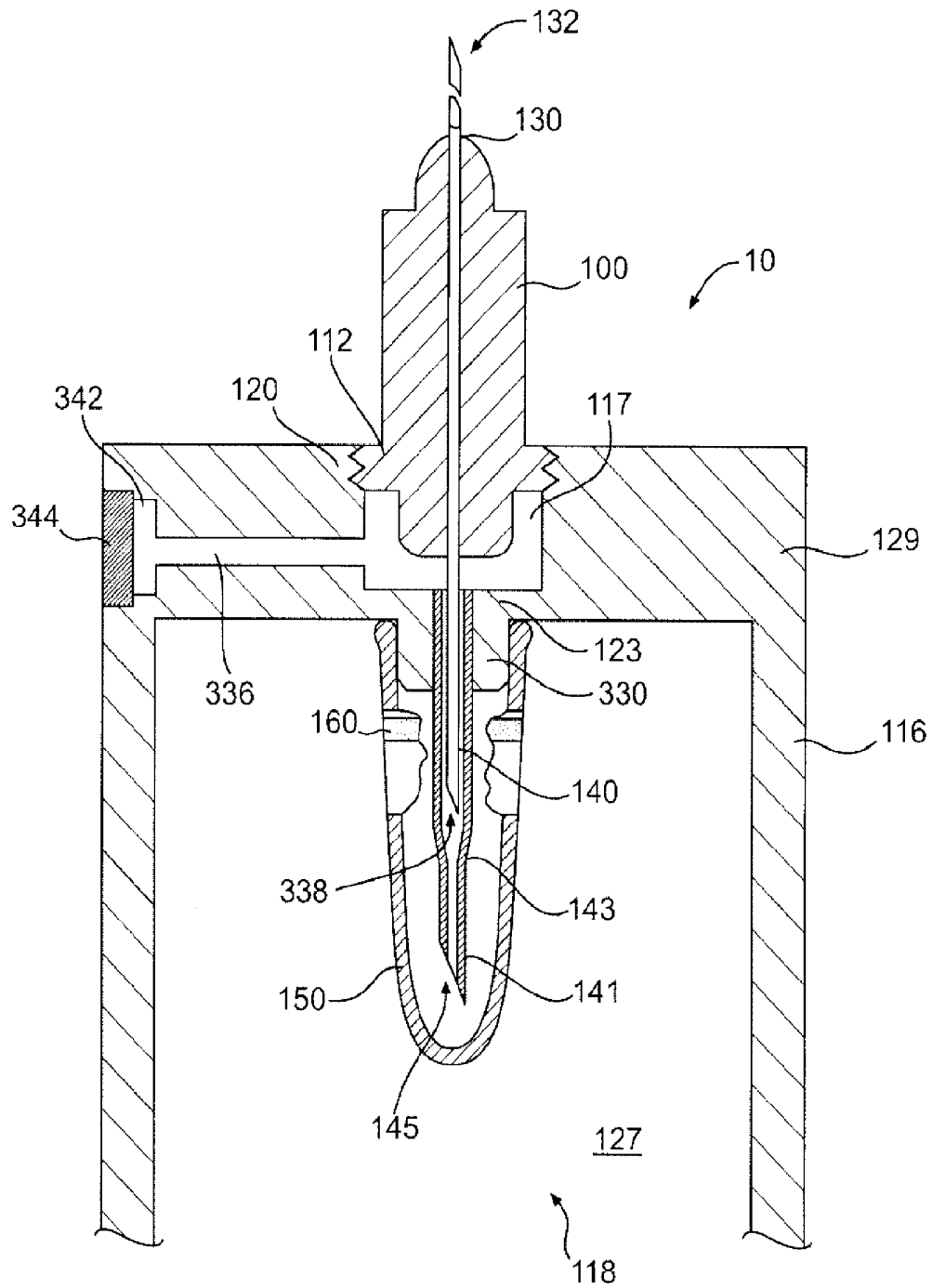


FIG. 19

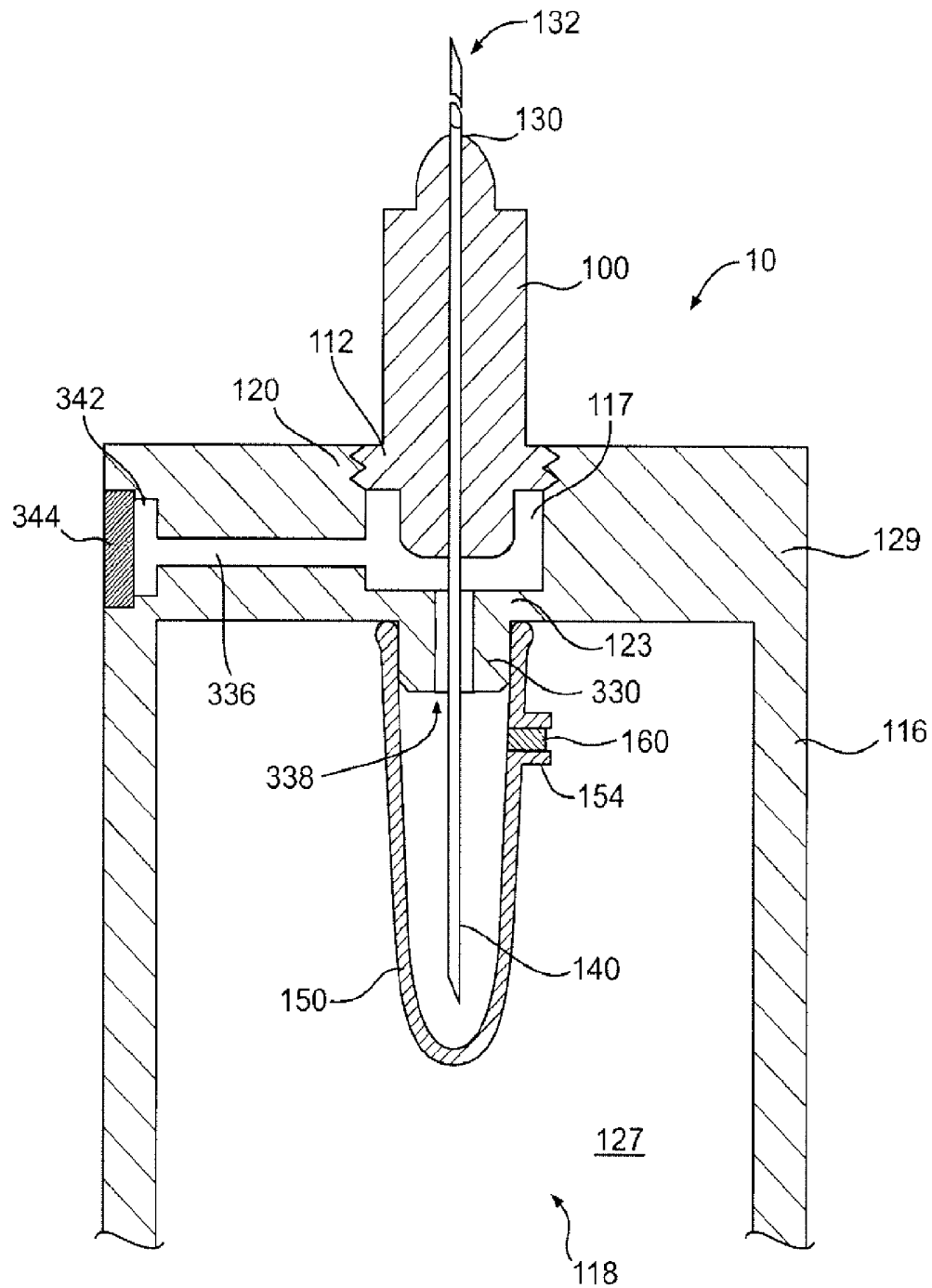


FIG. 20

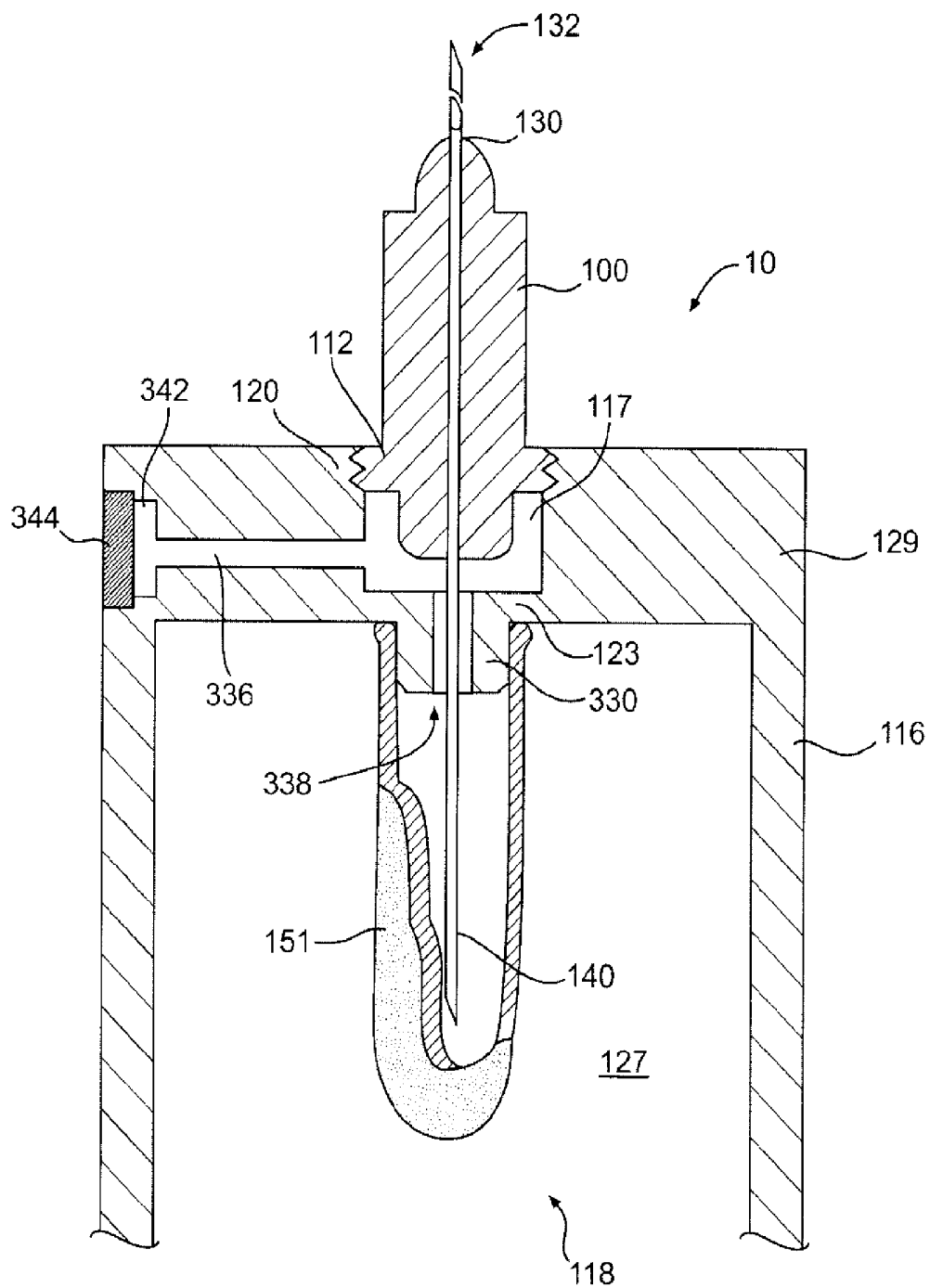


FIG. 21

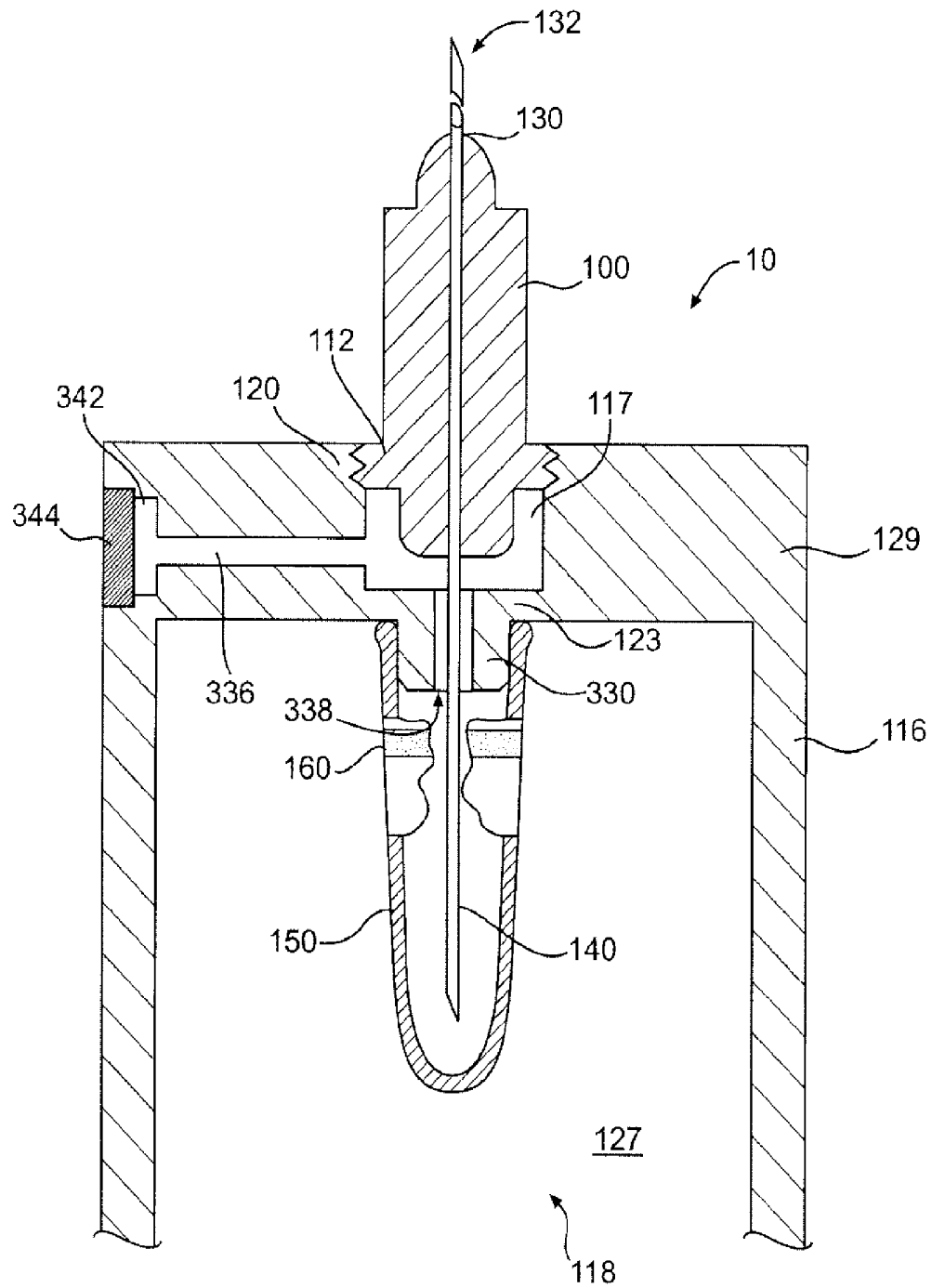


FIG. 22

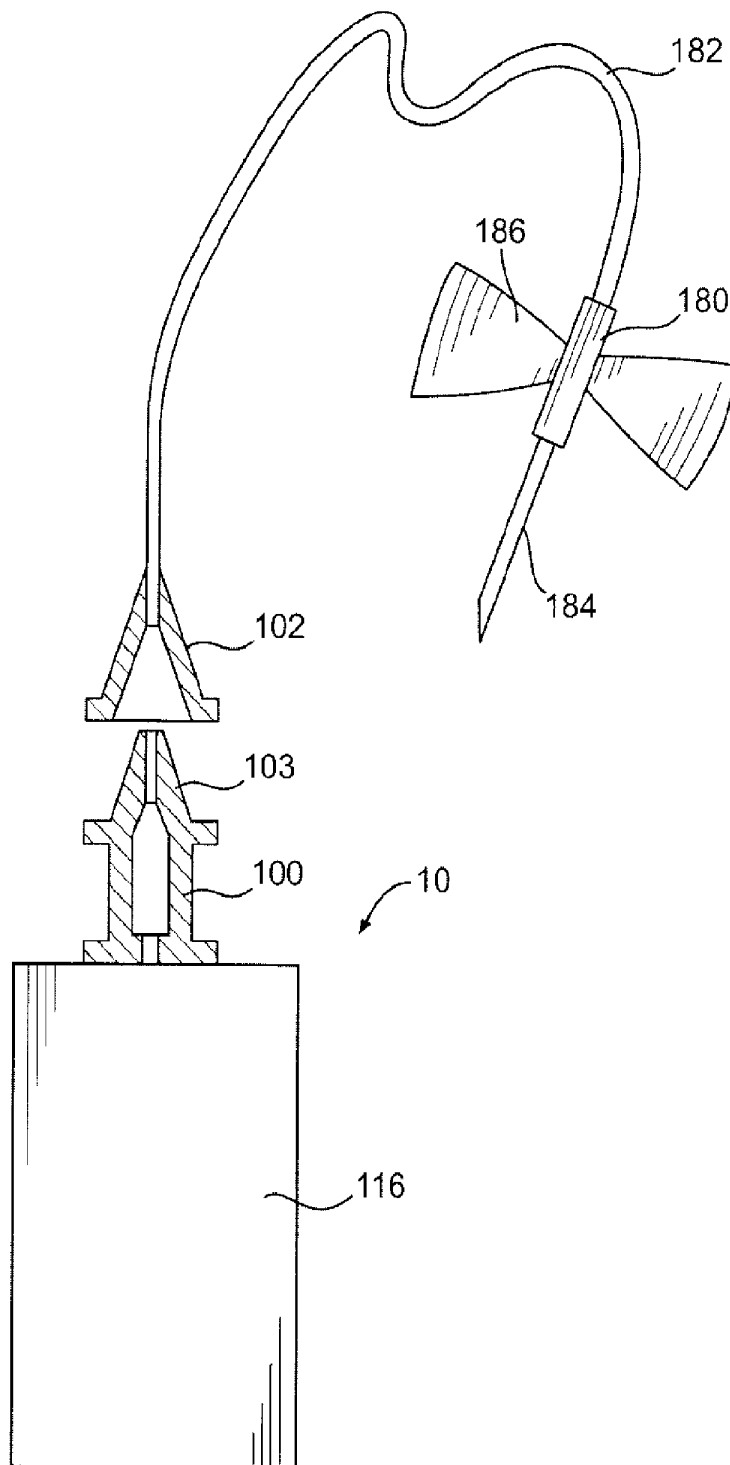


FIG. 23

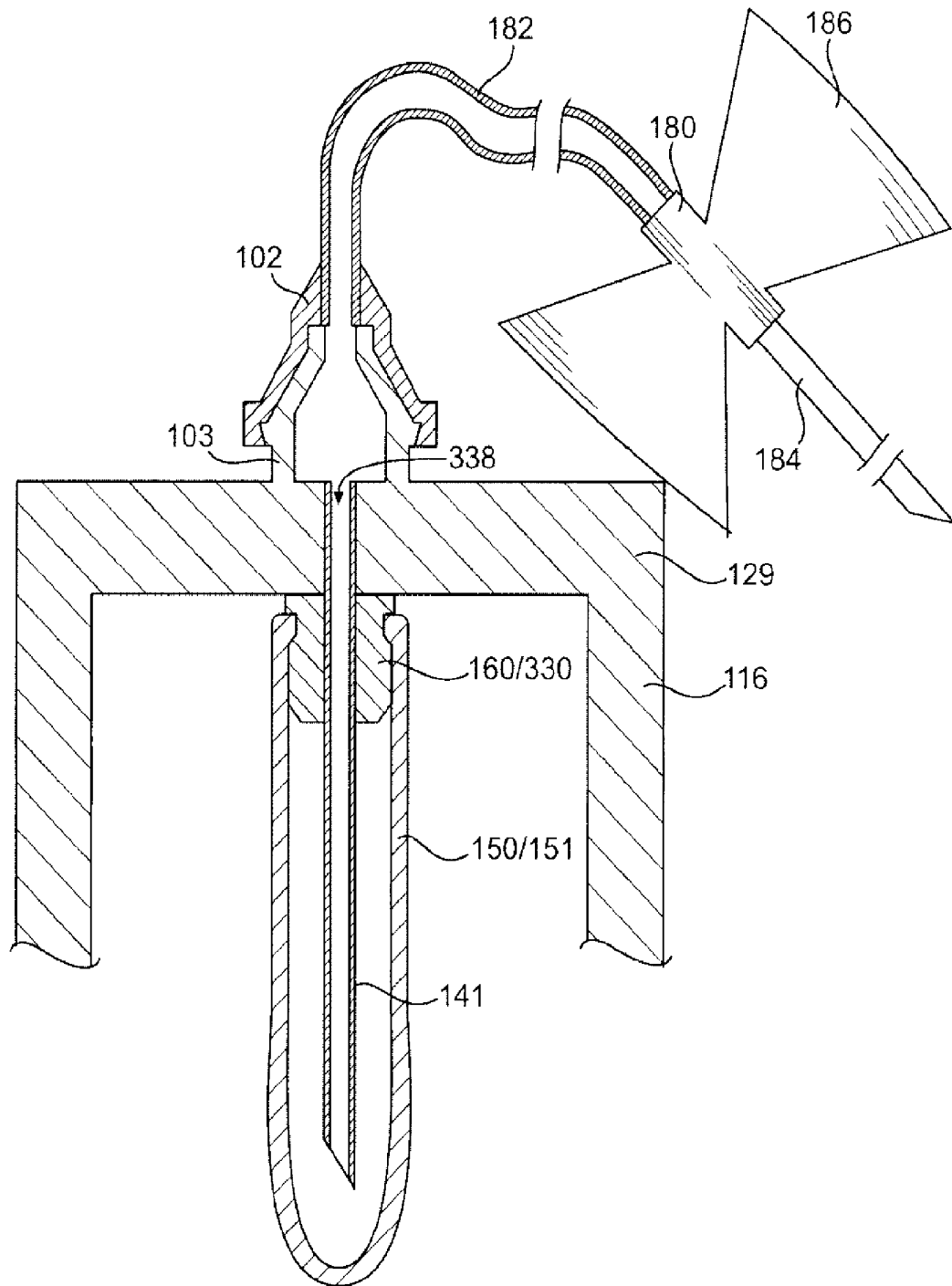


FIG. 24

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2010/040030

A. CLASSIFICATION OF SUBJECT MATTER

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

USPC - 604/122

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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

USPC - 604/122, 164

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

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

MicroPatent, Freepatentsonline, Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

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


* Special categories of cited documents:

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

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

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

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

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

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

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"G" document member of the same patent family

Date of the actual completion of the international search

12 August 2010

Date of mailing of the international search report

30 AUG 2010

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer:

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

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

 Literature display


< 1 / 1 display >

Patent 5867238

publication

 Document unit PDF progress information OPD search key URLs

Display format of the document display screen:

☒ text display ☐ PDF display

primary literature

bibliography

close



(19) [Country of issue] Japan Patent Office (JP)
 (12) [Type of publication] Patent gazette (B2)
 (11) [Patent number] Patent No. 5867238 (P5867238)
 (24) [Registration date] 2016 January 15 (2016.1.15)
 (45) [Issue date] February 24, 2016 (2016.2.24)
 (54) [Title of the invention] Auto scaling method, auto scaling program and computer node
 (51) [International Patent Classification]
 G06F 9/50 (2006.01)
 [FI]
 G06F 9/46 462A
 [Number of Claims] 6
 [Total Number of Pages] 22
 (21) [Application Number] Patent Application 2012-78501 (P2012-78501)
 (22) [Application date] March 30, 2012 (2012.3.30)
 (65) [Publication number] [JP 2013-210683](#) (P2013-210683A) (43) [Publication date] October
 10, 2013 (2013.10.10) [Date of request for examination] January 6, 2015 (2015.1.6) (73) [P
 atent holder] [Identification number] 000005223 [Name] Fujitsu Limited (74) [Agent] [Iden



fication Number] 100111822 [Patent Attorney] [Name] Akihiko Watabe

(74) [Agent]

[Identification number] 100119161

[Patent attorney]

[Name] Keiko Shigehisa

(72) [Inventor]

[Name] Kiyonobu Sato

(72) [Inventor]

[Name] Kazumi Shinozaki

(72) [Inventor]

[Name] Hiroaki Kubota

[Examiner] Yukio Tanaka

(56) [Reference]

[Reference] JP-A-2009-265778 (JP.A) [Reference] JP-A-2008-015958 (JP.A) (58)) [Investigated field] (Int.Cl., DB name) G06F 9/50 ..

The scope of the claims

open

(57) [Claims]

[Claim 1] In a system that distributes and executes

requested processing to a plurality of virtualized

computer nodes, a computer node that manages tasks executed in the system comprises: When a processing request with a specified delivery date is received, the management information stored in the storage unit for managing the tasks executed by the computer nodes of the system is referred to, and the task of the processing request is assigned to the computer node



A simulation is performed, and

the simulation of the assignment shows that there is no computer node that can complete 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 method characterized by executing a process of 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. 2. The computer node that manages the task further refers to the management 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 that 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 nodes can also complete the processing within the deadline. move the task,

2. The autoscaling method of claim 1, further comprising removing from the system computer 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 simulating the movement so that the number of tasks to be executed is equal to or less than a predetermined number. If it is determined that a computer node can be prepared to meet the processing request, tasks that can be completed within the deadline are moved to other computer nodes, and computer

nodes with a predetermined number or less of tasks to be executed are assigned to the processing request task.

3. The auto-scaling method according to claim 2, further comprising executing a process of setting 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 excluded 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. [00

09] In one aspect, the object of the present invention is to provide a technique that enable



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 delivery date, the computer node that is stored in the storage unit is referring to management information for managing tasks to be executed, executing a simulation of allocating the task of the 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 the 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, processing is executed to increase the number of computer nodes in the system

m. EFFECTS OF THE INVENTION [0011] According to one aspect, it is possible to operate a system with good billing efficiency. BRIEF DESCRIPTION OF THE DRAWINGS [0012] FIG. 1 is a diagram explaining a problem of a system realized on-premises; 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 embodiment; FIG. 5 is a diagram showing an example of a virtual machine system that implements a node according to this embodiment; FIG. 6 is a diagram illustrating an example of a simulation of assignment of processing-requested tasks by a scheduler in a master node according 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 according 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 according 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 according 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 rescheduling 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 rescheduling 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 according to the embodiment;

16 is a processing flowchart when a processing request is received by the master node according 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 below with reference to the drawings. [0014] FIG. 1 is a diagram for explaining problems of a system implemented on-premise. In the example shown in FIG. 1, the vertical length of a graphic representing a task indicates the resource consumption of the task, and the horizontal length indicates the processing time of the task. In the example shown in FIG. 1, the vertical axis of the graph indicates the resource consumption of the system, and the horizontal axis indicates the passage of time. t_0 _



$\sim t_3$ 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.

indicates 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 t_0 . 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 t_3 . As shown in FIG. 1B, the processing end time of task #3, which has the earliest processing end time, is t_1 , so if task #4 is scheduled after task #3, the processing end time of task #4 is t_3 , 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 t_3 , 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 technique 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 example, 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 fulfilled. Be able to complete tasks on time.

[0024]

However, since the resources that can be scaled up are limited to the resources of the physical machines that implement the nodes, which are virtual machines, there is a limit to how much nodes can be scaled up. In addition, usually multiple virtual machine nodes are arranged on one physical machine, and if there is no surplus after allocating the resources of the physical 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-tenant environment, multiple tenants' virtual machines are running on a single physical machine, 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 scale-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 technique for changing the amount of system resources

.

Scale-out is a technique for adding nodes to a system. Scale shrink is a technique for removing nodes from a system. By using scale-out technology, it is almost certain that all requested processing 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 task, and the horizontal length indicates the processing time of the task. In the example shown in 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



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 t_0 . 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 t_3 . 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 pro

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-shrunked at the same time as the processing of task #3 ends, the processing of task #4 will be forcibly terminated. In this way, if scale shrinkage is determined just by looking at resource consumption as in the above-mentioned IaaS vendor service, for example, 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 composed of virtual machine nodes provided from the IaaS side in cloud computing. The system 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 (Local Area Network) or the Internet. The system 100 comprises a master node 110 and slave nodes 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 that 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 one 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 the 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 120c, 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 200 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 communication section 115 , a rescheduling processing section 116 and a scale shrink processing 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 communication unit 111 passes it to the schedule processing unit 112. FIG. If the processing of the received request cannot be processed within the system 100, the client communication unit 111 responds to that effect to the client 200. FIG. Processes that cannot be executed within the system 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 machine 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 the processing result received from the slave node 120 . When the client communication unit 111 receives a processing request with a specified delivery date, the schedule processing unit 112 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 managing 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 complete 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 that 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 processing 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 here. 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 112
In step 2, the slave node 120 that has become free due to the movement of the task is determined as the target slave node 120 to which the task of the processing request is to be assigned. If the schedule processing unit 112 cannot prepare a slave node 120 capable of completing the processing of the requested task within the delivery date even if the task is moved, the schedule processing unit 112 unlocks the locked slave node 120 if any

For example, it is determined whether the processing of the requested task can be completed within the deadline. When it is determined that the processing of the requested task can be completed within the due date by unlocking, the schedule processing unit 112 unlocks the locked slave node 120. The schedule processing unit 112 determines the unlocked slave node 120 as the target slave node 120 to which the task of the processing request is to be assigned.

[0049]

If the slave node 120 to which the task of the processing request is to be assigned is not found in the processing up to this point, the schedule processing unit 112 determines that the slave node 120 should be added to the system 100 by scale-out.

The scale-out processing unit 114 performs processing for

adding computer nodes to the system 100 by scale-out. More specifically, the scale-out processing unit 114 accesses the management computer on the IaaS side using an interface prepared by the IaaS side and requests scale-out to the own system 100.

[0051]

The slave communication unit 115 communicates with the slave node 120. For example, the slave communication unit 115 requests the slave node 120 to which the task of the received processing request is to be assigned to process the task. The slave communication unit 115 also receives the processing result of the requested task from the slave node 120 as a response. When a task is moved, the slave communication unit 115 notifies the source slave node 120 of the stop of the task, and notifies the destination slave node 120 of the execution of the task.



- . The rescheduling processing unit 116, for example, periodically refers to the management information stored in the schedule information storage unit 113, and targets slave nodes 120 that do not have tasks to be executed
- . The rescheduling processing unit 116 also refers to the management information stored in the schedule information storage unit 113 and executes a simulation of migrating a task running on a certain slave node 120 to another slave node 120 . . The rescheduling processing unit 116 detects tasks that can be completed within the deadline even if they are moved to another slave node 120 . [0054]

The rescheduling processing unit 116 determines whether or not the slave node 120 having no task to be executed can be prepared by moving the detected task. If it is determined that a slave node 120 that does not have a task to be executed can be prepared by moving the task, the rescheduling processing unit 116 transfers the task to another slave node 120 via the slave communication unit 115. to run. The movement of tasks is the same as in the case of the schedule processing unit 112 described above. The rescheduling unit 116 targets the slave node 120, which no longer has tasks to be executed due to the movement of tasks, for scale shrink.

The rescheduling processing unit 116 also determines whether or not it

is possible to prepare a slave node 120 in which the number of tasks to be executed is equal to or less than a predetermined number by moving the detected tasks. If it is determined that a slave node 120 can be prepared in which the number of tasks to be executed by task movement is equal to or less than a predetermined number, the rescheduling processing unit 116 performs the process of moving the corresponding task to another slave node 120 via slave communication. 115. Reschedule processing part

116 sets a lock on the slave node 120 for which the number of tasks to be executed due to task movement is equal to or less than a predetermined number. As a general rule, the locked slave node 120 is not assigned a task with a new processing request, so it becomes the target of scale shrink after the processing of the remaining tasks is completed. The scale shrink processing unit 117 performs processing for deleting the target slave node 120 from the system 100 by scale shrink

.

More specifically, the scale shrink processing unit 117 uses an interface prepared by the IaaS side to access the management computer on the IaaS side and request scale shrinking of the target slave node 120 . The slave node 120 has a master communication section 121 and an application 122

.



As shown in FIG. 4, the slave node 120 can run multiple types of applications 122a, b, . When the task of the processing request is assigned, the task processing is executed by the application 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 the 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 result response to the master node 110 .

FIG.

5 is a diagram showing an example of a virtual machine system that implements a node according 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 system 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 master 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 often 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 10 . A virtual machine 30 including the master node 110 and slave node 120 can be constructed 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 example, an external storage device such as a HDD (Hard Disk Drive) or an auxiliary storage device. The medium reading/writing device 15 is, for example, a CD-R (Compact Disc Recordable) drive or a DVD-R (Digital Versatile Disc Recordable) drive. The input device 16 is, for example, a keyboard/mouse. The output device 17 is, for example, a display device such as a display. Note that the hardware configuration of the computer 10 can be arbitrarily designed as required.

The master node 110, slave node 120, and functional units provided in each node shown in FIG. 4 can be realized by hardware such as the CPU 11 and memory 12 provided in the computer 10, and software programs . A program executable by the computer 10

The program is stored in the storage device 13, for example, read out to the memory 12 when



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 t_3 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 the



e database. As for the resource consumption of a task, for example, if a value is determined for each application 122 that processes the task, that value can be used. The resource consumption amount may be inquired of the slave node 120. In addition, various well-known techniques can be used.

In the master node 110, when the schedule processing unit 112 receives a processing request, it

first verifies whether the task of the processing request can be assigned to the slave node 120 under the current circumstances.

FIG.

7(A) shows the execution of the process request task X at #a so that the process execution is started at time t_0 .

An example of verification assigned to a slave node 120a is shown. Also, FIG. 7B shows an example 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 t_0 . In either case, the resource consumption 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 task A#1 executed by slave node 120a of #a, which finishes processing the earliest, is completed. In this case, the verification result is NG because the processing end time of the processing request task X exceeds the due date t_3 . Next, the schedule processing unit 112 performs verification to move a task whose processing can be completed by the due date even if the task is 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 slave node 120a in terms of resource consumption. Processing can be completed by the due date even if the system is restarted. FIG. 8(B) shows an example of verification in which the processing request task X is assigned to the #b slave node 120b whose resource consumption has 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 verification 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 120c added by the scale-out processing unit 114. As described above, the master 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 operated 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 this embodiment.

FIG .

10 shows the schedule of tasks executed by the slave nodes 120a, 120b, and 120c of the system 100 at time t_0 . As shown in FIG. 10, at this point, the system 100 has three slave nodes 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 rescheduling 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 restarted 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 delivery date t_2 , so the verification result will be NG. The rescheduling unit 116 determines that it is not possible 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 restarted by slave node 120a of #a. As shown in FIG. 11B, task C#1 can be completed by the deadline t_3 even if the slave node 120a of #a is restarted. Furthermore, when task C#1 is moved 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 116 instructs the #C slave node 120c to stop task C#1 and the #A slave node 120a to execute task 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 rescheduling unit 116 targets the #C slave node 120c for scale shrink. The scale shrink processing unit 117 executes scale shrink processing for the #C slave node 120c.

[0084]



In this way, the master node 110 according to the present embodiment actively creates slave nodes 120 that do not have tasks to be executed by moving tasks to other slave nodes 120, and executes scale shrink. As a result, it is possible to positively delete useless slave nodes 120, so that it is possible to operate the system 100 efficiently without unnecessary billing. FIG. 12 and 13 are diagrams for explaining an example of setting a lock on a slave node by the rescheduling processor in the master node of this embodiment.

FIG. 12 shows the schedule of tasks executed by the slave nodes 120a and 120b of the system 100 at time t_0 . As shown in FIG. 12, the system 100 has two slave nodes 120 at this time: #a slave node 120a and #b slave node 120b. In the master node 110, when the slave node 120 that has no tasks to be executed cannot be prepared even if the tasks are moved, the rescheduling processing unit 116 reduces the number of tasks to be executed by moving the tasks to a predetermined number or less. Verifies whether the slave node 120 can be prepared. For example, the predetermined number is 1 here. FIG. 13A shows an example of verification in which task B#2 executed by the #b slave node 120b is restarted by the #a slave node 120a. As shown in FIG. 13(A), task B#2 has a deadline of t_3 even if the slave node 120a of #a is restarted.

Processing can be completed by Even if task B#1 executed by slave node 120b of #b is to be restarted by slave node 120a of #a, task B#1 will be moved because the processing end time will exceed the due date t_2 . Can not.

Assuming that task B#2 is

moved to #a slave node 120a, as shown in FIG. . At this time, the rescheduling processing unit 116 instructs the #B slave node 120b to stop the task B#2 and instructs the #A slave node 120a to execute the task B#2 via the slave communication unit 115. do.

Also, as shown in FIG. 13(B), a lock is set for the slave node 120b of #b, for which the only task to be executed is B#1. Information on the slave node 120 that has set the lock is recorded in a storage unit such as the schedule information storage unit 113 that can be accessed by the schedule processing unit 112. As a general rule, the #b slave node 120b is not assigned a new processing request task. can be deleted. As described above, the master node 110 according to the present embodiment moves tasks to other slave nodes 120, actively creates slave nodes 120 with fewer tasks to be executed, and creates new slave nodes 120 for those slave nodes 120.



Suppress task allocation for processing requests. As a result, the environment of the system 100 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 processing 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 FIG. 6(C) from the client 200 in the state shown in FIG. 13(B). At this time, the schedule processing unit 112 attempts to allocate the processing request task X to the unlocked #a slave node 120a as shown in FIG. Cannot be allocated because it would exceed the resource limit. Furthermore, 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 120b 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 request 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 to another slave node 120. As a result, it is possible to suppress the occurrence of scale-out while maintaining an environment that facilitates scale-shrinking to the very limit, so that the system 100 can be operated efficiently without unnecessary billing.

The master node 110 according to the present embodiment gives top priority to completing task 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 processing 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 processing request is not acceptable (NO in step S11), the client

The communication unit 111 responds to the client that the processing request cannot be accepted (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 o



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 slave node 120 to which the task of the processing request is assigned (step S15). The slave communication unit 115 requests the determined slave node 120 to process the task of the processing 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, moves the existing task, and a simulation of assigning tasks is performed (step S16). Here, for example, as shown in FIG. 8, if there is an existing task that can be completed within the delivery date even if it is moved to another slave node 120 and re-executed, the existing task is moved 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 the processing request by moving the existing task (step S17). If the task of the processing request can be assigned (YES in step S17), the schedule processing unit 112 moves the corresponding existing task (step S18). More specifically, the schedule processing unit 112 requests, via the slave communication unit 115, the slave node 120 from which the existing task is moved to stop the task. Also, the schedule processing unit 112 requests the slave node 120 to which the existing task is moved to execute the task via the slave communication unit 115. The slave 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 schedule 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 processing request can be assigned (step S19). If the lock is released and it becomes possible to allocate 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 shown 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. The 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 communication unit 115 responds with the processing result to the processing request from the slave node 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 node 110, the rescheduling processing section 116 starts this processing at a predetermined timing

. The rescheduling processing unit 116 refers to the management information in the schedule information storage unit 113 and determines whether there is a slave node 120 that currently has no task to be executed (step S30). If there is a slave node 120 that does not have a task to be executed (YES in step S30), the scale shrink processing unit 117 executes scale shrink 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 information 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 within the deadline even if it is moved to another slave node 120 and re-executed, there is no task to move and execute the task. It is verified whether the slave node 120 can be created. For 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 tasks are moved and executed. It is verified whether the following slave nodes 120 can be generated. [0110]

The rescheduling unit 116 determines whether it is possible to generate a slave node 120 that does not have a task to be executed by moving the task, that is, whether it is possible to move the task and perform scale shrinking (step S33). If scale shrinking becomes possible by moving 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 which the task is moved to stop the task via the slave communication unit 115 . Also, the resche



uling processing unit 116 requests the slave node 120 to which the task is moved to execute the 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 movement of the tasks (step S35). The scale shrink removes the slave node 120 from the system 100 .

[0111]

If the scale shrink is not possible even if the task is moved (NO in step S33), the rescheduling processing unit 116 moves the task, and if there is a slave node 120 where the number of tasks to be executed is less than the predetermined number, It is determined whether or not (step S36). If there is no slave node 120 for which the number of tasks to be executed is equal to or less than the predetermined number even if the tasks are moved (NO in step S36), the rescheduling processing unit 116 ends the processing.

[0112]

If there is a slave node 120 in which the number of tasks to be executed by migrating tasks is equal to or less than the predetermined number (YES in step S36), the rescheduling processing 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 communication unit 115 . Also, the rescheduling processing unit 116 requests the slave node 120 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 be 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 S31.

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 the 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 communication unit 116 Reschedule processing unit 117 Scale shrink processing unit 120 Slave node 121 Master Communication unit 122 Application 200 Client 300 Network



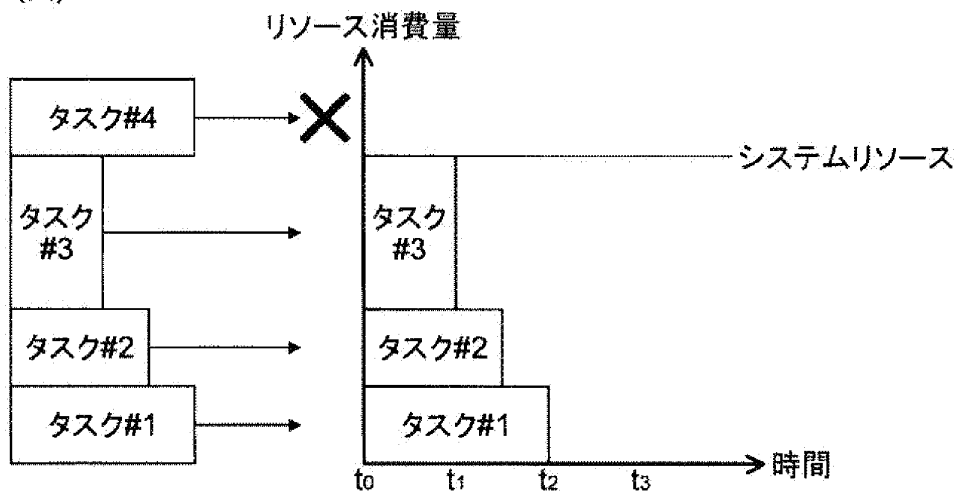
drawing	open 



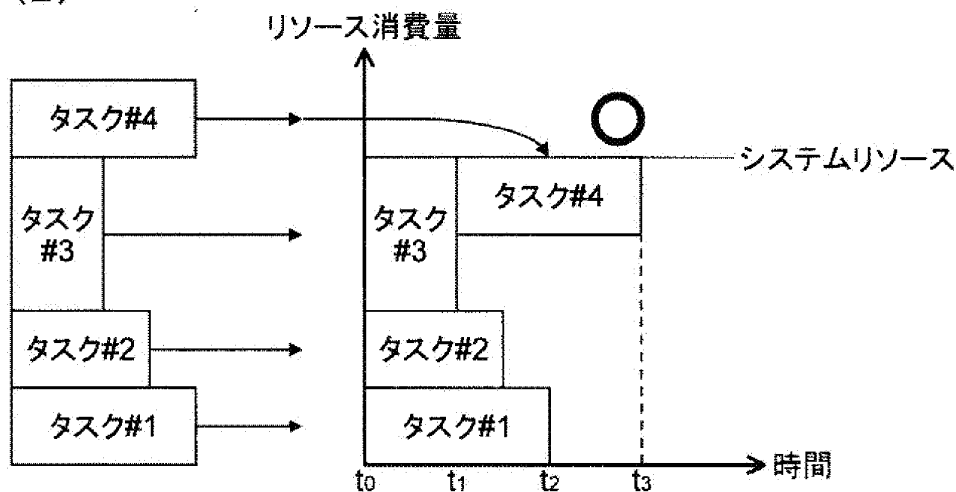
[Fig. 1]



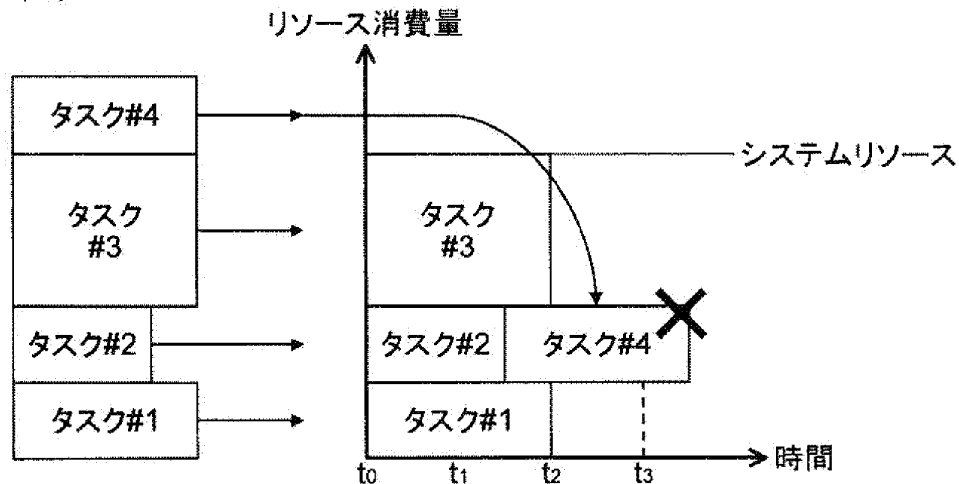
(A)



(B)



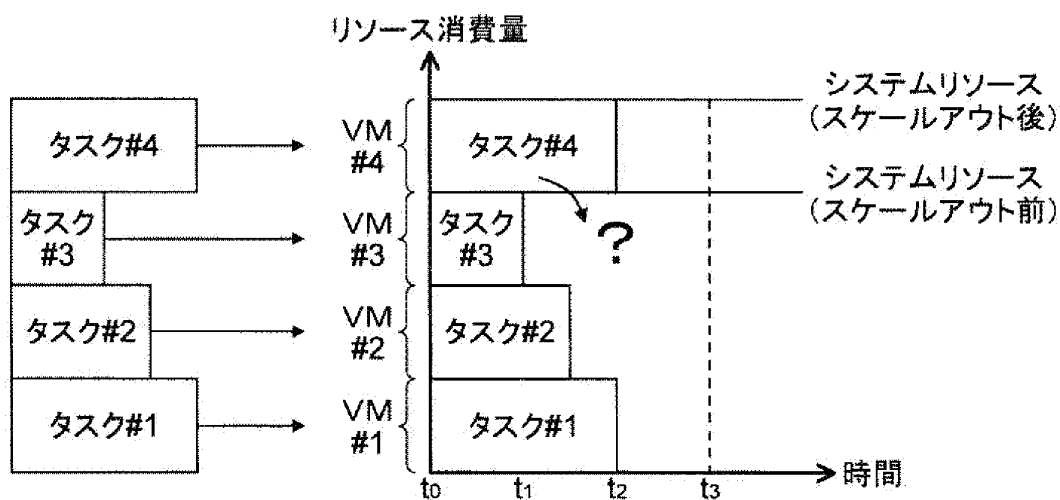
(C)



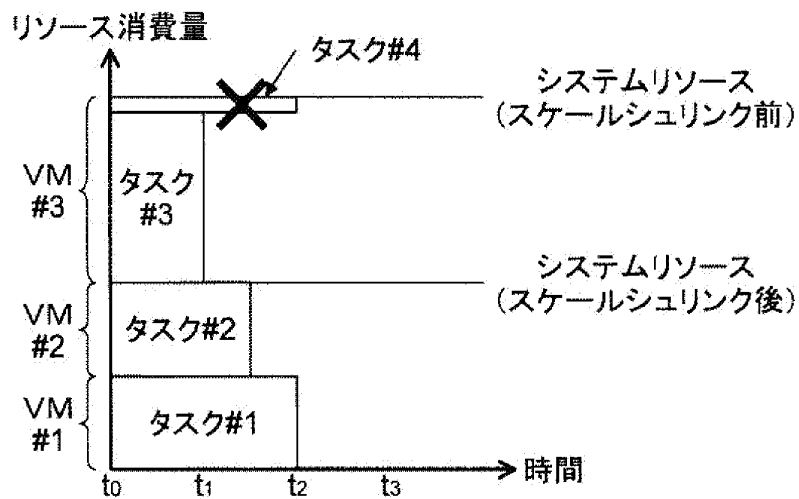
[Figure 2]



(A)

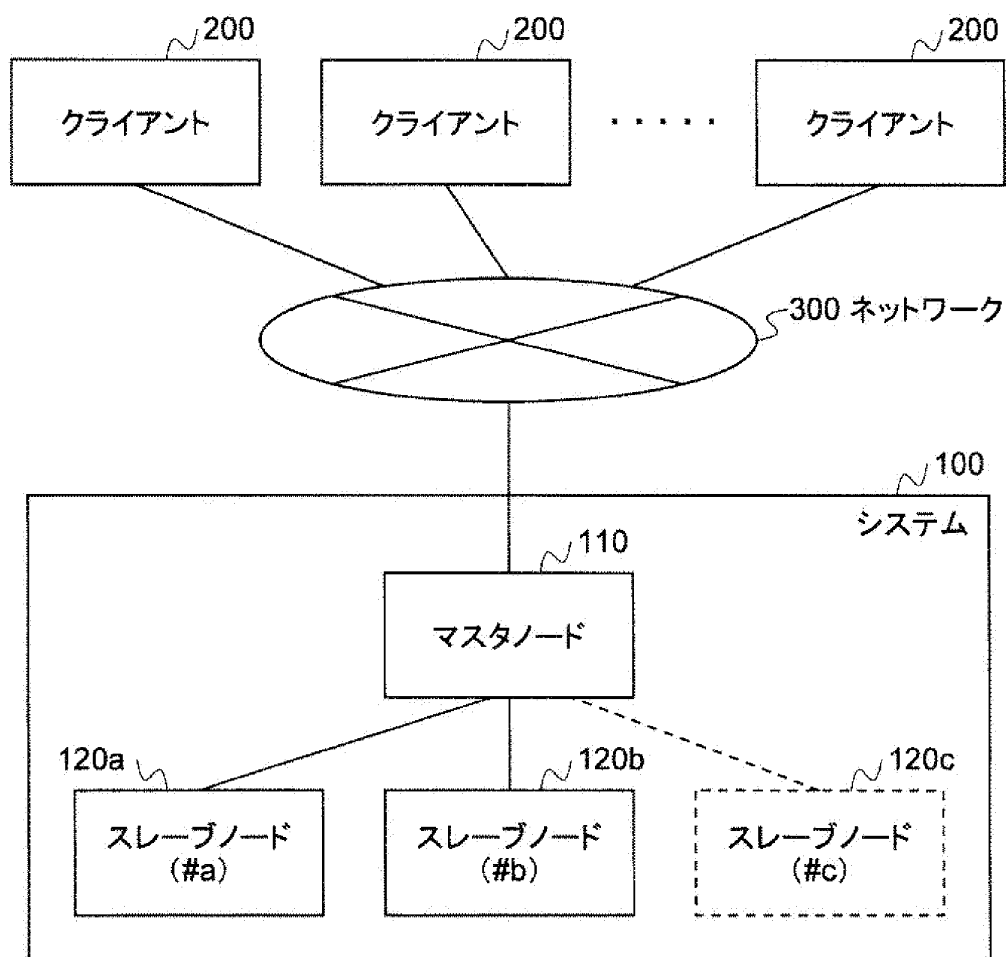


(B)



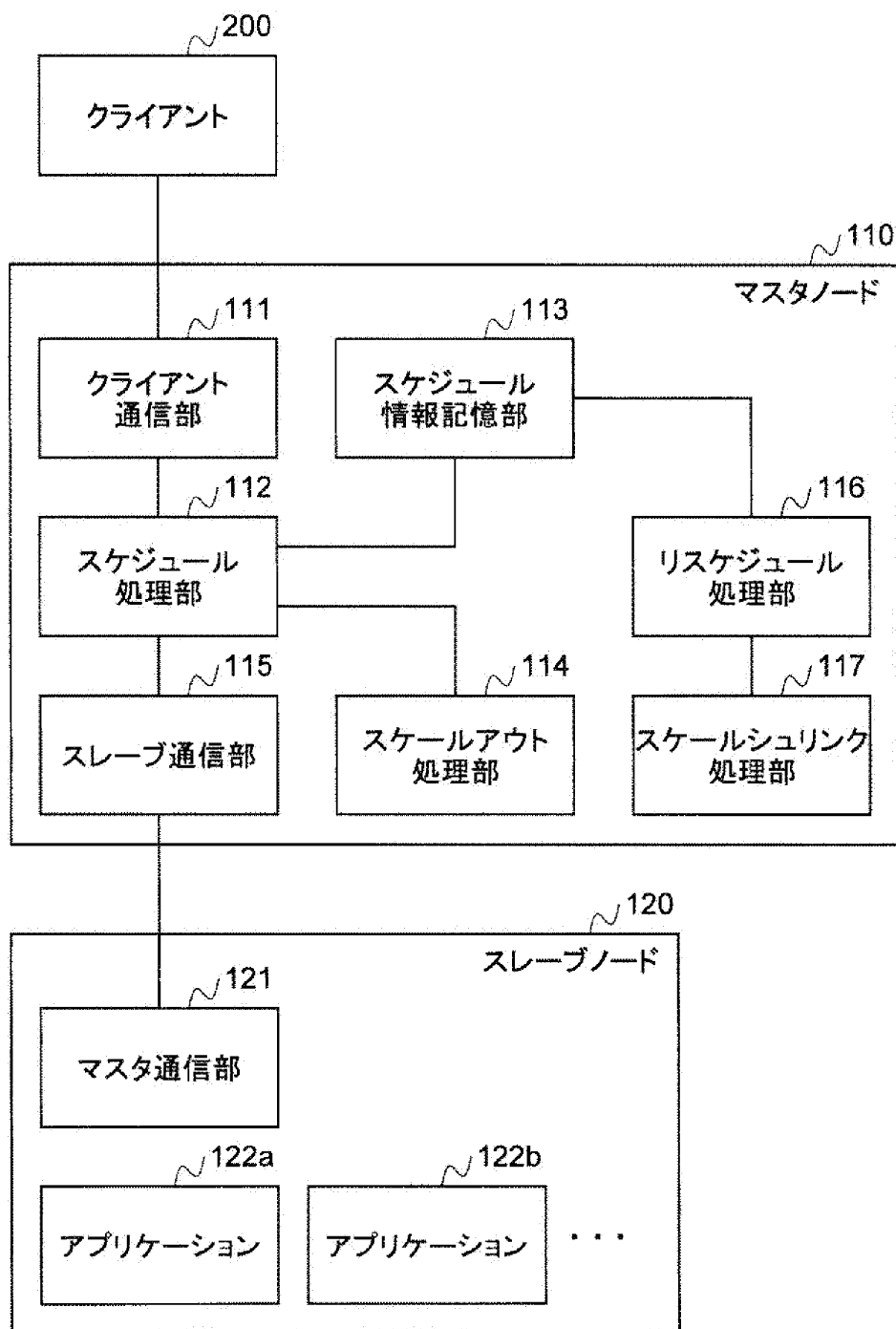
[Figure 3]



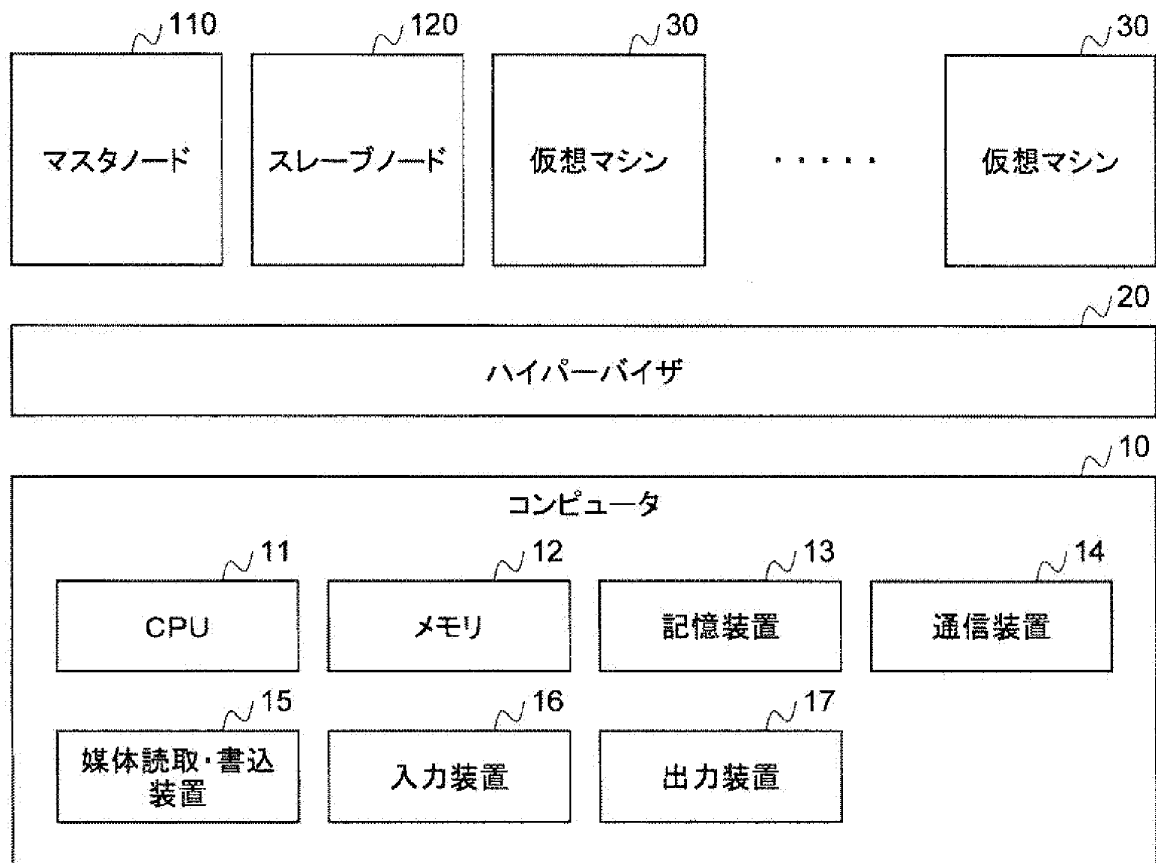


[Figure 4]



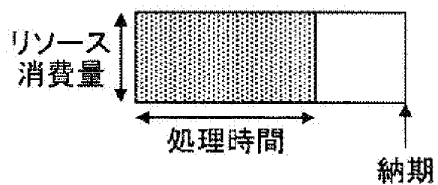


[Figure 5]

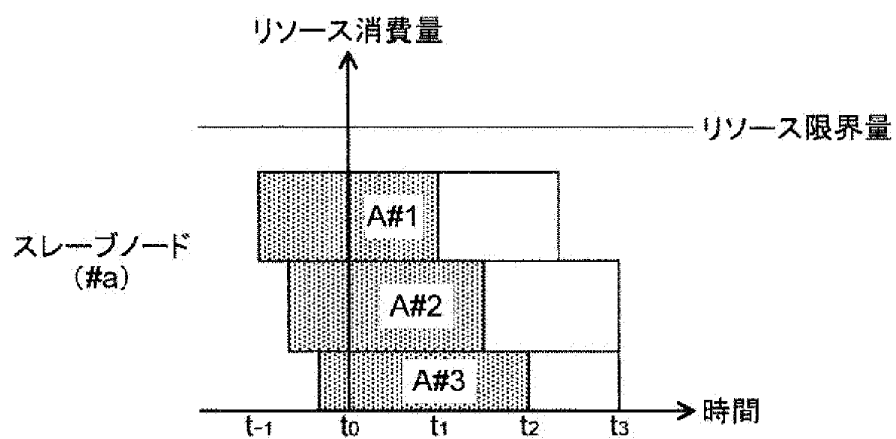
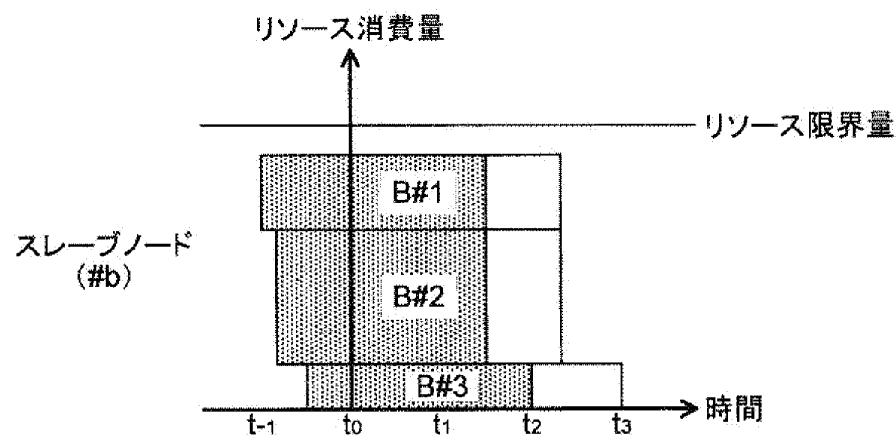


[Fig. 6]

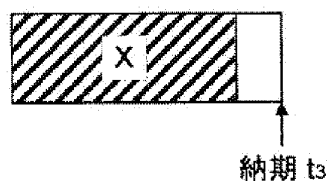
(A)



(B)



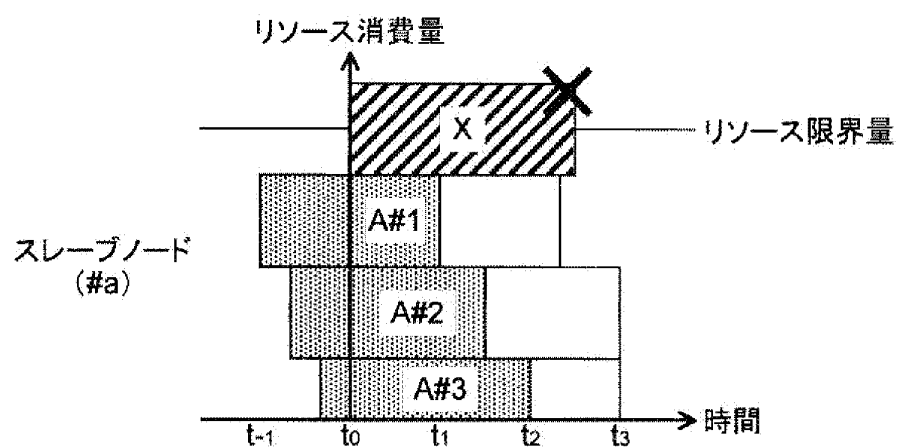
(C)



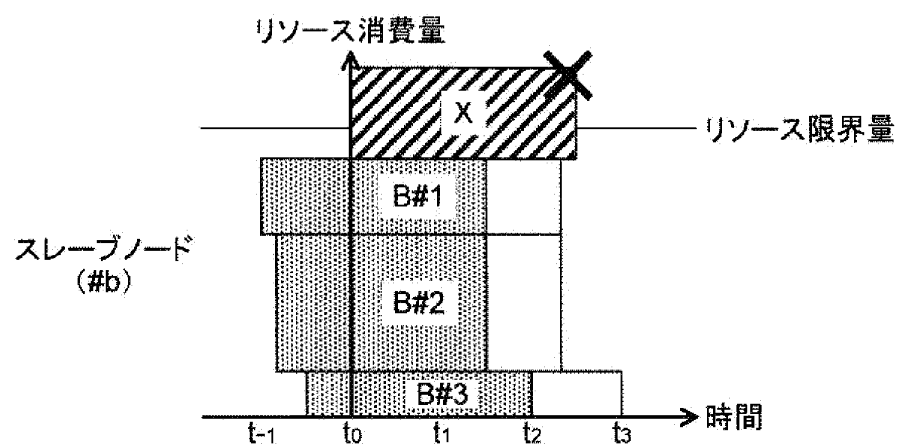
[Fig. 7]



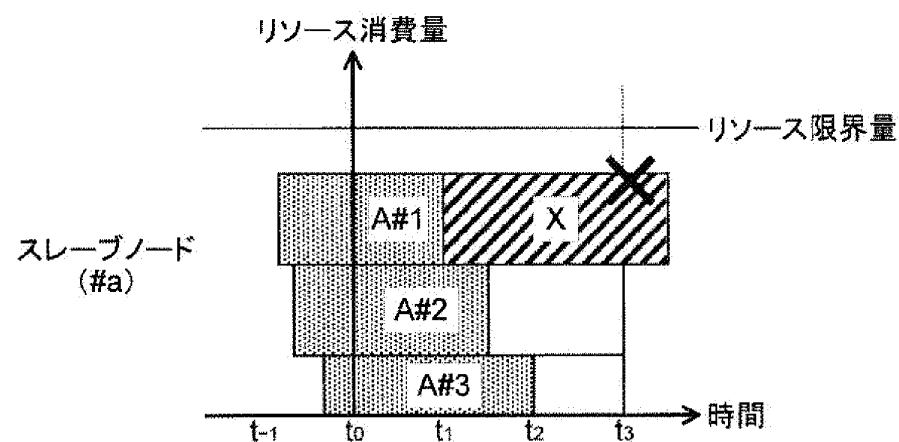
(A)



(B)



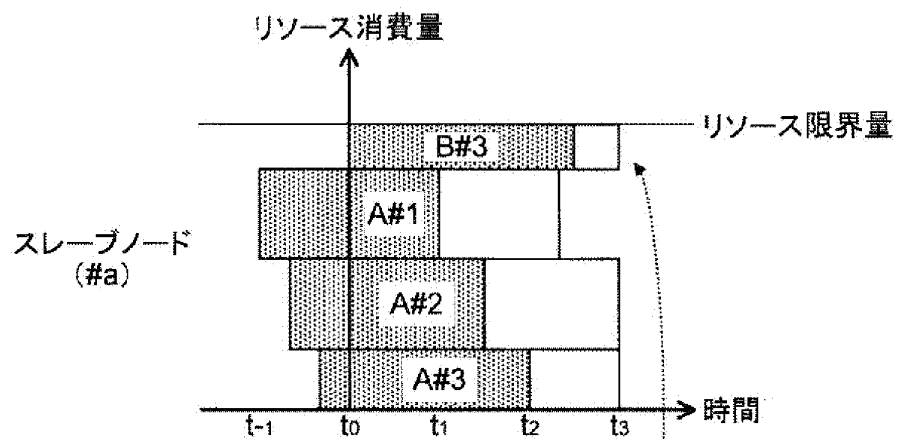
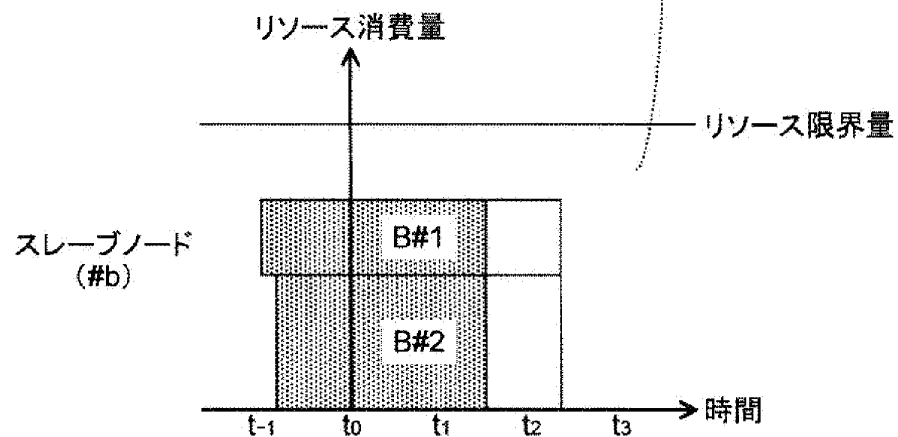
(C)



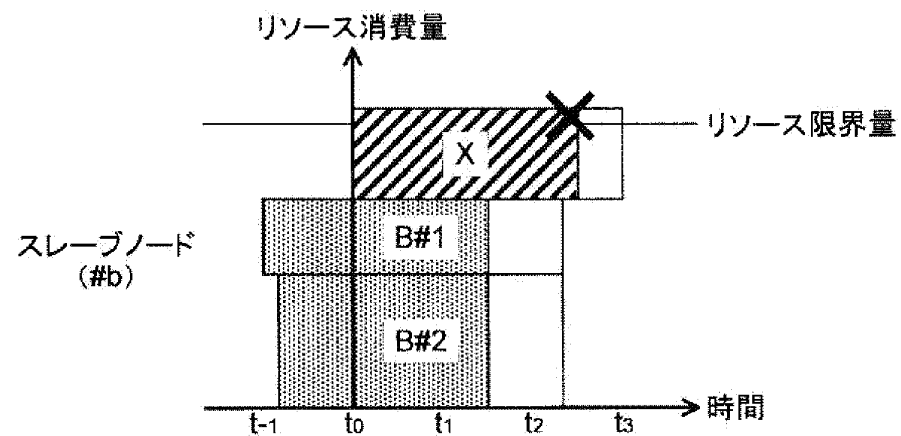
[Fig. 8]



(A)

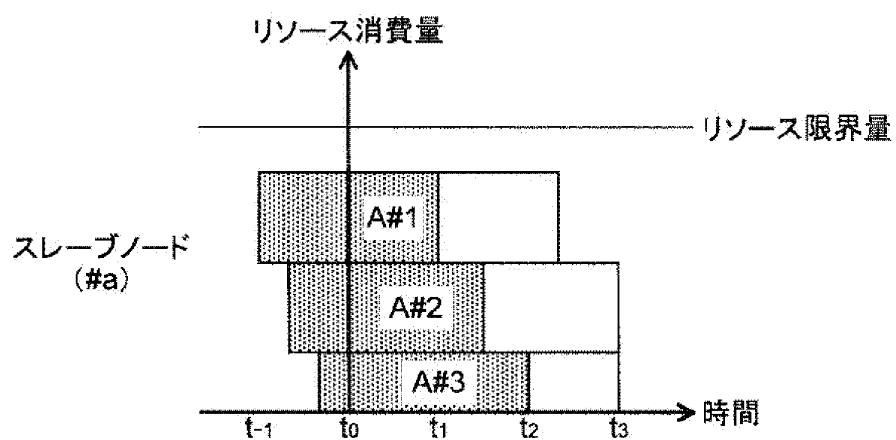
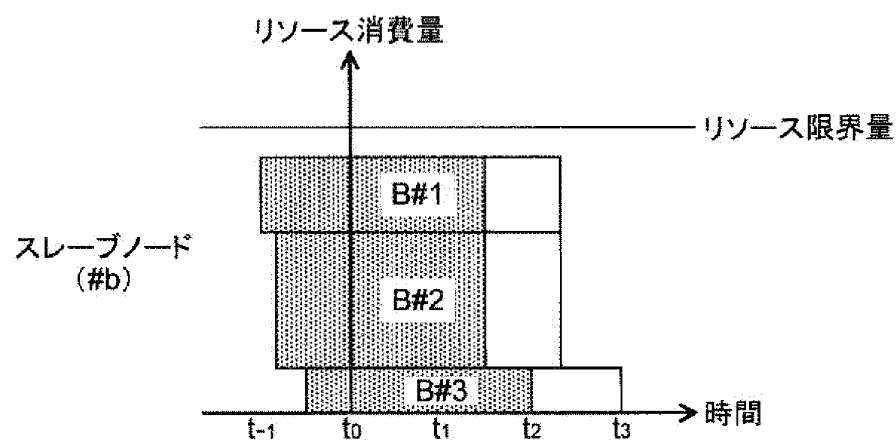
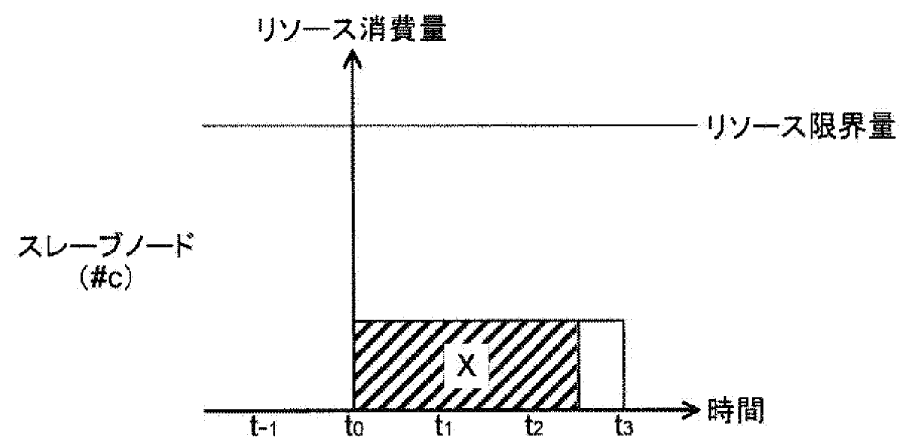


(B)



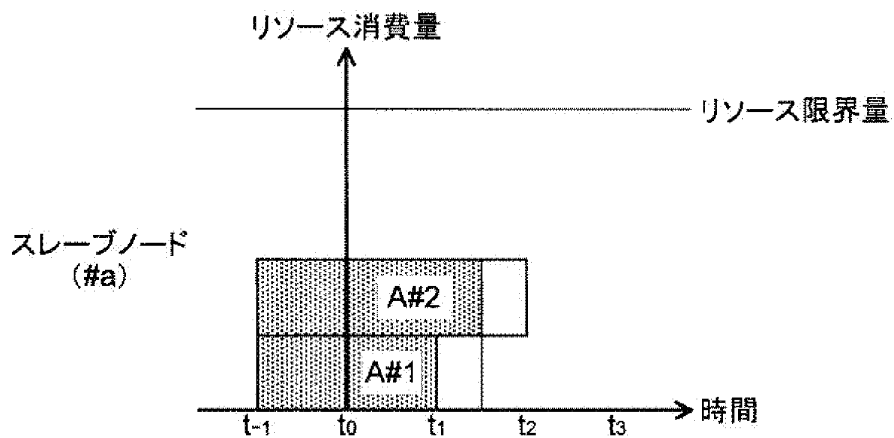
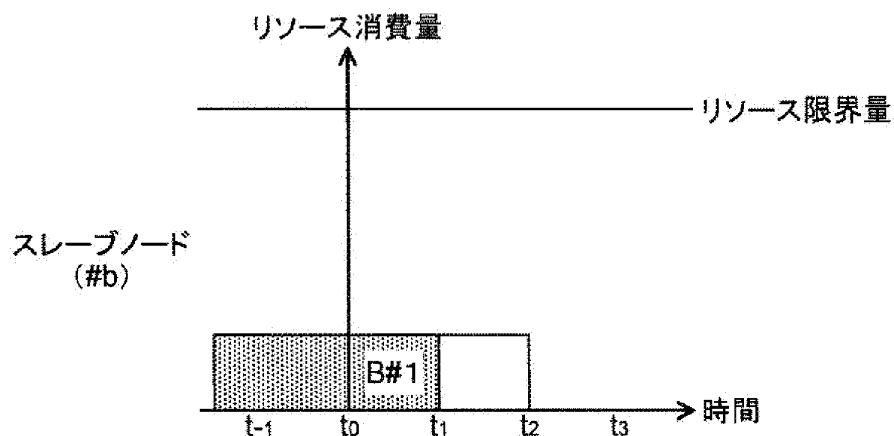
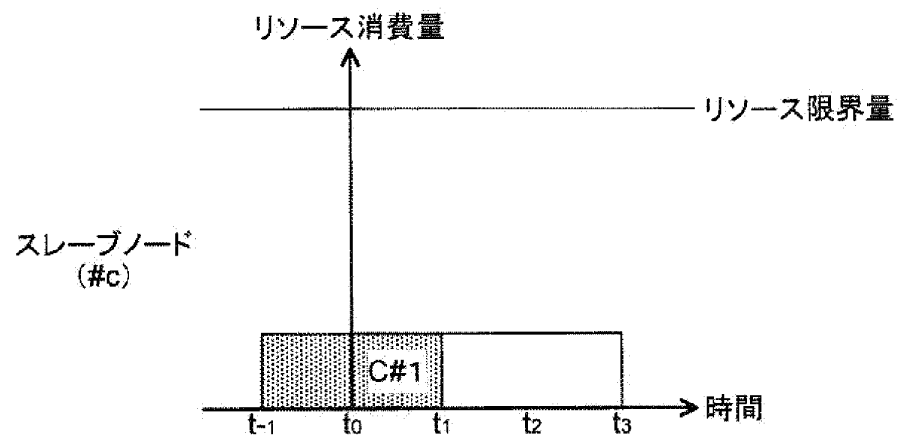
[Fig. 9]





[Fig. 10]

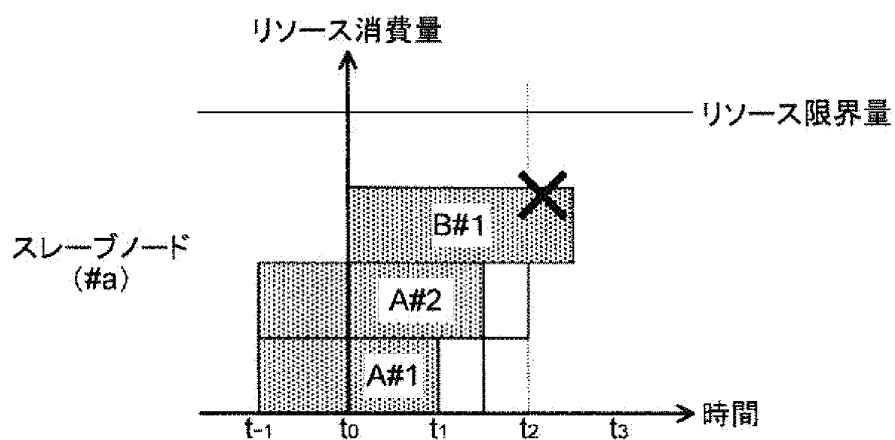




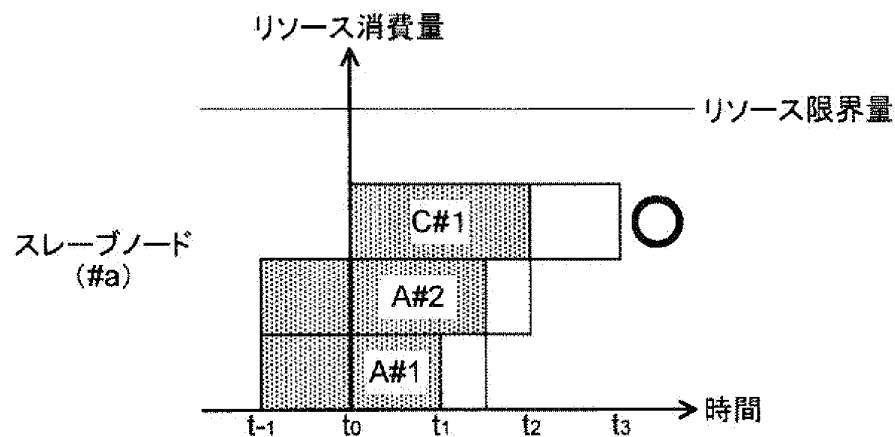
[Fig. 11]



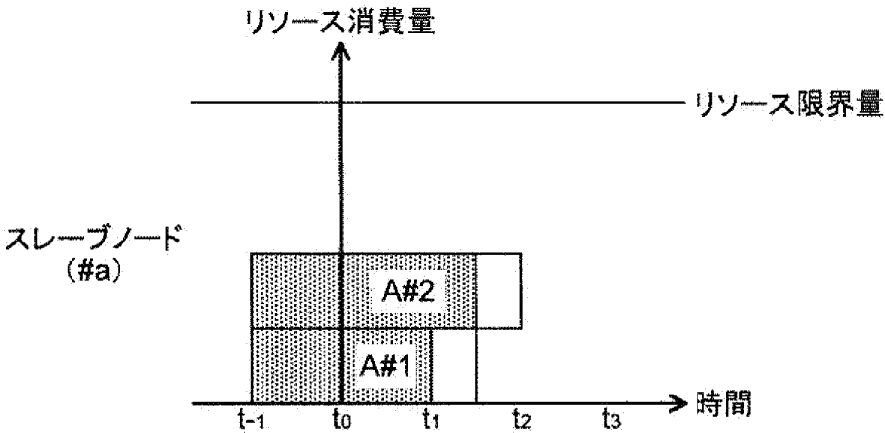
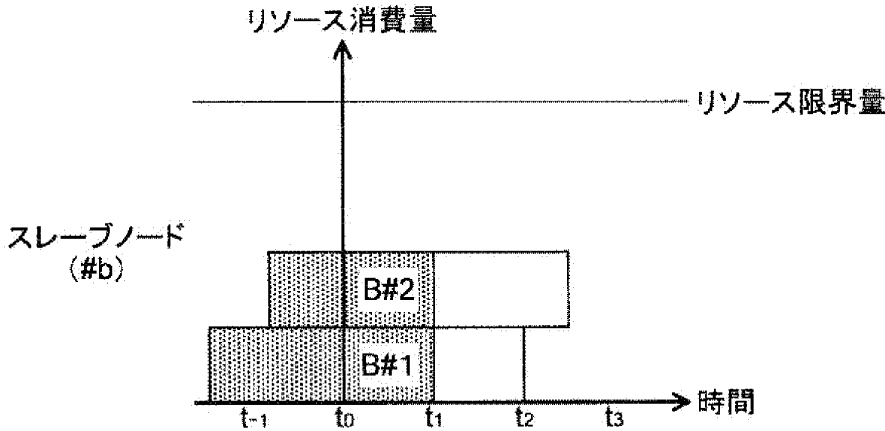
(A)



(B)



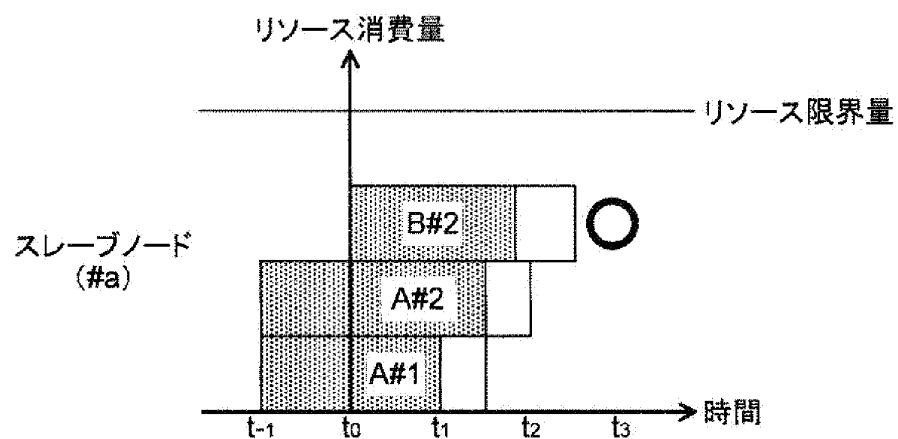
[Fig. 12]



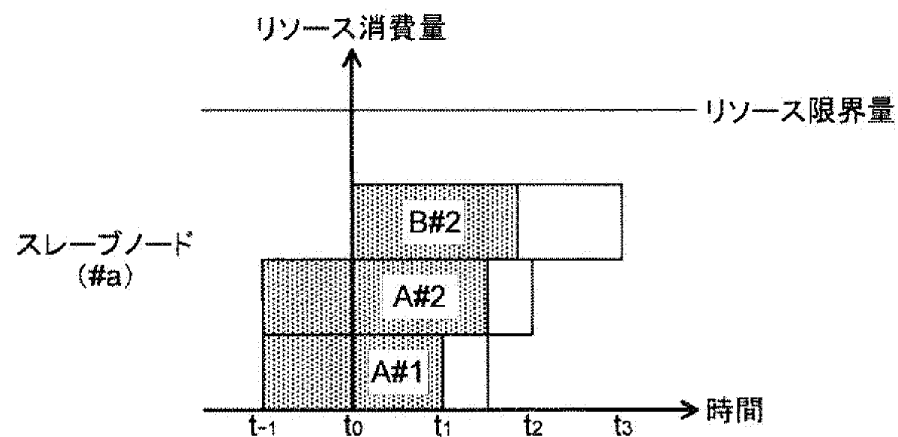
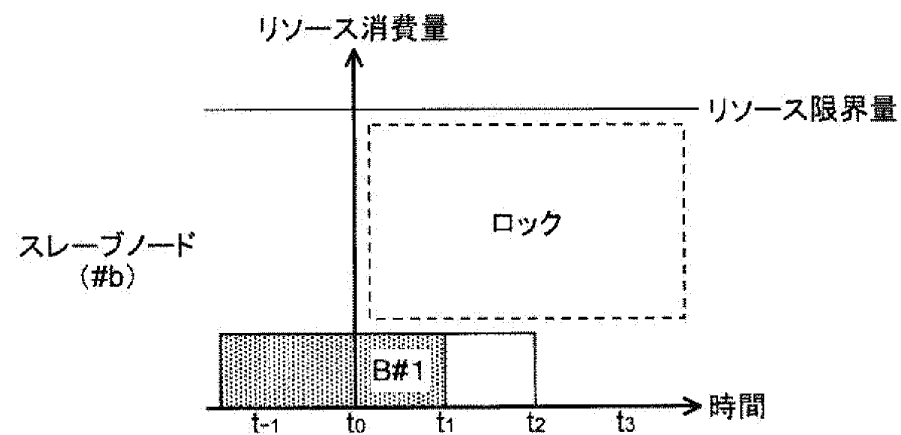
[Fig. 13]



(A)

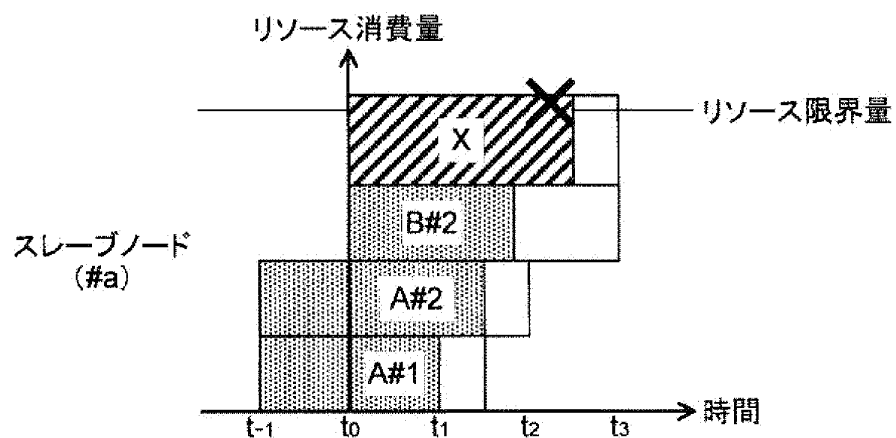


(B)

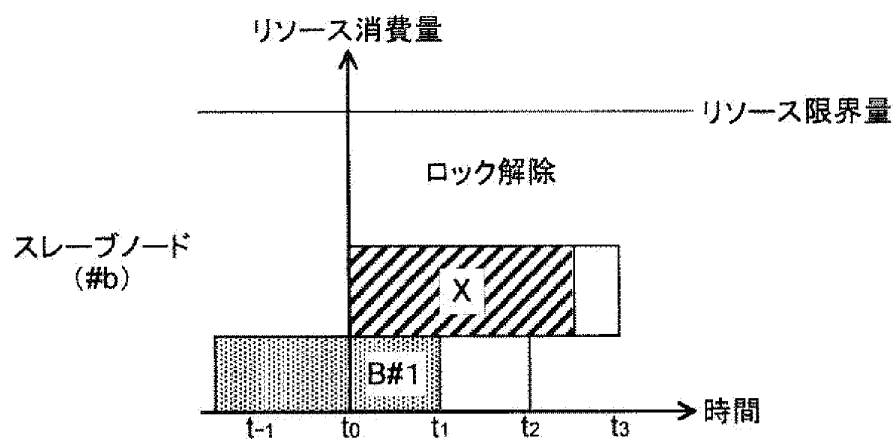


[Fig. 14]

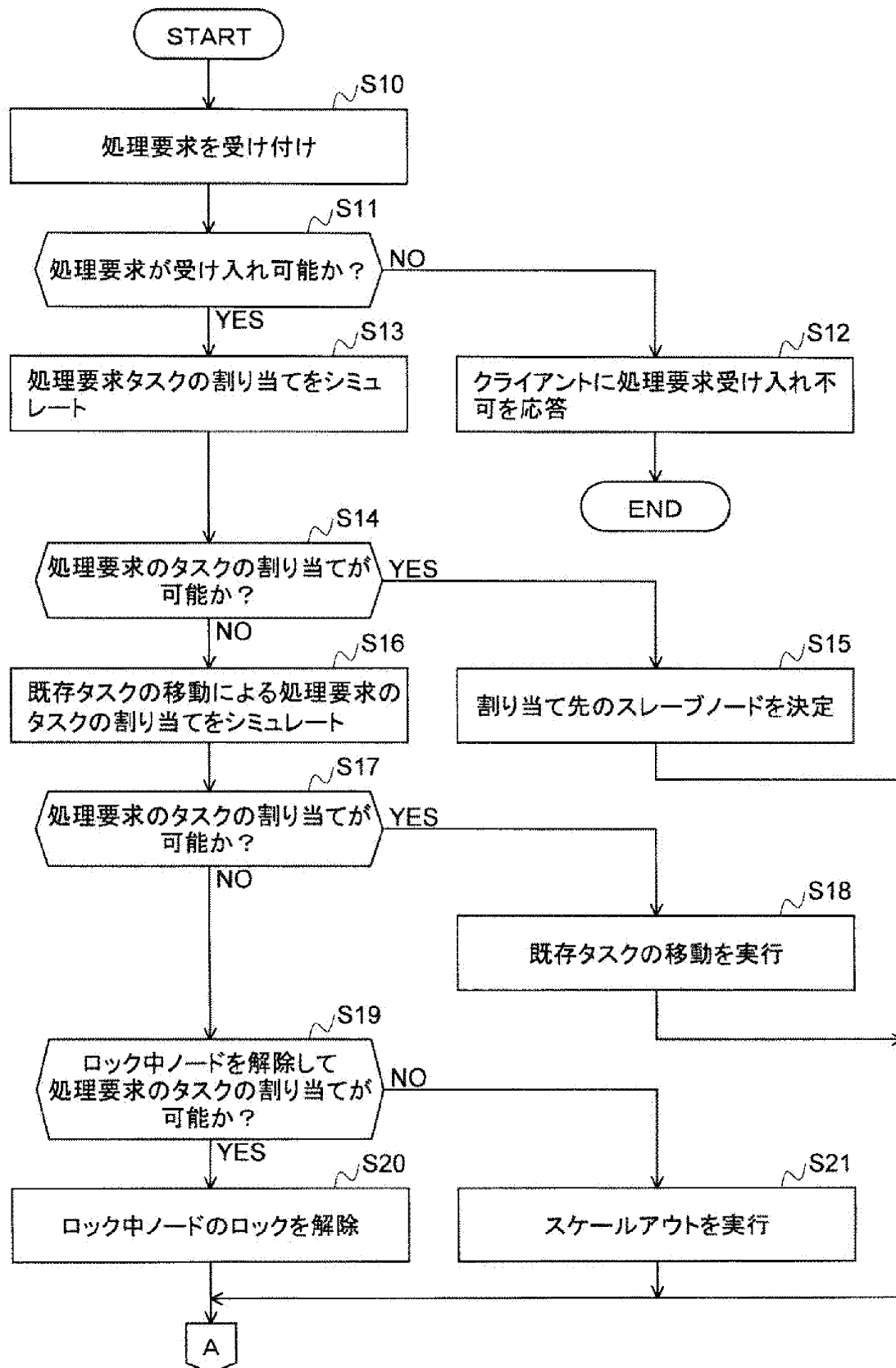
(A)



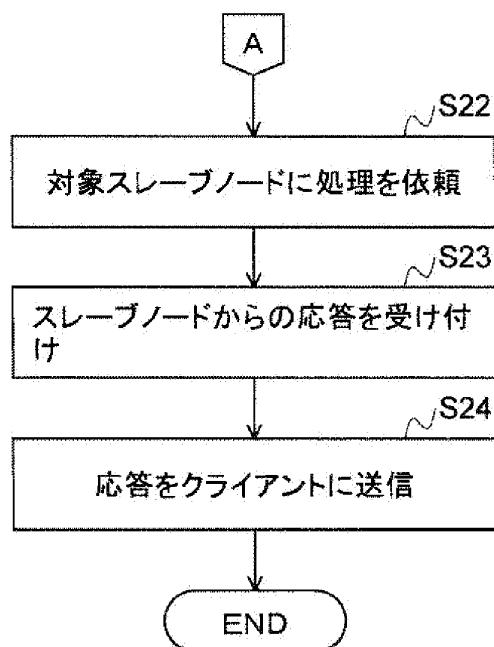
(B)



[Fig. 15]

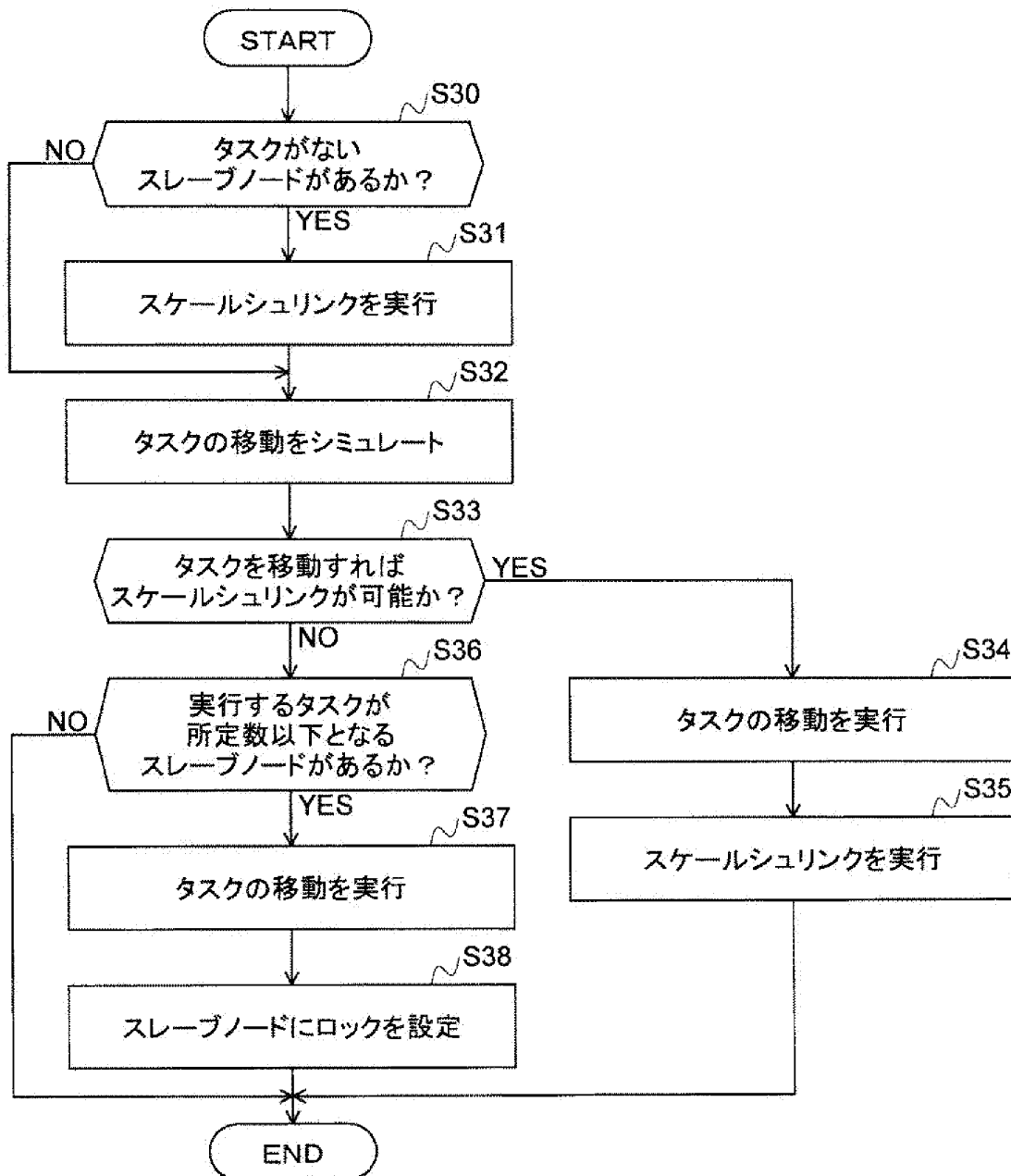


[Fig. 16]



[Fig. 17]





drawing

open

1 2 3 Four Five 6 7 8 9 Ten ...

Magnify and Rotate

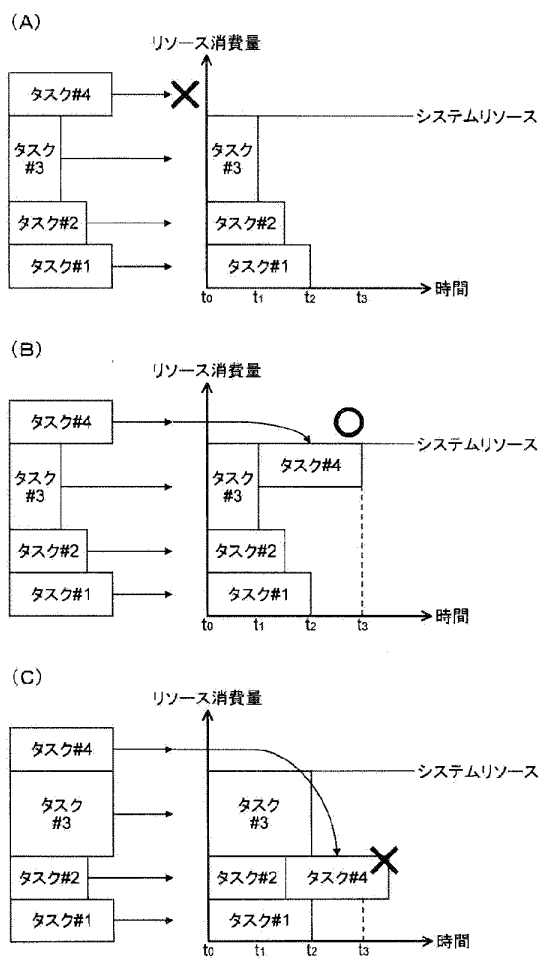


Figure 1

< 1 / 1 display >



(19) 日本国特許庁(JP)

(12) 特 許 公 報(B2)

(11) 特許番号
特許第5867238号
(P5867238)

(45) 発行日 平成28年2月24日(2016.2.24)

(24) 登録日 平成28年1月15日(2016.1.15)

(51) Int. Cl. F 1
G 0 6 F 9 / 5 0 (2 0 0 6 . 0 1) G 0 6 F 9 / 4 6 4 6 2 A

請求項の数 6 (全 22 頁)

(21) 出願番号	特願2012-78501 (P2012-78501)	(73) 特許権者	000005223
(22) 出願日	平成24年3月30日 (2012.3.30)		富士通株式会社
(65) 公開番号	特開2013-210683 (P2013-210683A)		神奈川県川崎市中原区上小田中4丁目1番1号
(43) 公開日	平成25年10月10日 (2013.10.10)	(74) 代理人	100111822
審査請求日	平成27年1月6日 (2015.1.6)		弁理士 渡部 章彦
		(74) 代理人	100119161
			弁理士 重久 啓子
		(72) 発明者	佐藤 清伸
			神奈川県川崎市中原区上小田中4丁目1番1号 富士通株式会社内
		(72) 発明者	篠崎 和美
			神奈川県川崎市中原区上小田中4丁目1番1号 富士通株式会社内
最終頁に続く			

(54) 【発明の名称】 オートスケーリング方法、オートスケーリングプログラムおよびコンピュータノード

(57) 【特許請求の範囲】

【請求項1】

要求された処理を複数の仮想化されたコンピュータノードに分散して実行するシステムにおいて、該システムで実行するタスクの管理を行うコンピュータノードが、

納期が指定された処理要求を受け付けた際に、記憶部に記憶された、前記システムが備えるコンピュータノードが実行するタスクを管理する管理情報を参照して、該処理要求のタスクをコンピュータノードに割り当てるシミュレーションを実行し、

前記割り当てのシミュレーションにより、前記処理要求のタスクを納期内に処理終了可能なコンピュータノードがなく、さらに他のコンピュータノードでも納期内に処理終了可能なタスクを移動しても前記処理要求のタスクを納期内に処理終了可能なコンピュータノードを用意できないと判定された場合に、前記システムのコンピュータノードの数を増加する処理を実行する

ことを特徴とするオートスケーリング方法。

【請求項2】

前記タスクの管理を行うコンピュータノードが、さらに、

前記管理情報を参照して、あるコンピュータノードで動作するタスクを、他のコンピュータノードに移動するシミュレーションを実行し、

前記移動のシミュレーションにより、他のコンピュータノードでも納期内に処理終了可能なタスクを移動して、実行するタスクがないコンピュータノードを用意できると判定された場合に、該他のコンピュータノードでも納期内に処理終了可能なタスクを移動し、

10

20

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。

10

【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。

20

【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】

30

【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。

40

【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

50

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、課金の効率が良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。

10

【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。

20

【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。

30

【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】

40

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。 $t_0 \sim t_3$ 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越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

50

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。

10

【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】

20

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】

30

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。

40

【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

50

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。 $t_0 \sim t_3$ 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上がるため、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】

ただし、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 2 0 0 がシステム 1 0 0 内部のノードであってもよい。

【 0 0 4 1 】

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。

【 0 0 4 2 】

マスタノード 1 1 0 は、クライアント通信部 1 1 1、スケジュール処理部 1 1 2、スケジュール情報記憶部 1 1 3、スケールアウト処理部 1 1 4、スレーブ通信部 1 1 5、リスケジュール処理部 1 1 6、スケールシュリンク処理部 1 1 7 を備える。

【 0 0 4 3 】

クライアント通信部 1 1 1 は、クライアント 2 0 0 からの処理要求を受け付ける。クライアント通信部 1 1 1 は、受け付けた要求の処理がシステム 1 0 0 内で実行可能なものであれば、スケジュール処理部 1 1 2 に渡す。クライアント通信部 1 1 1 は、受け付けた要求の処理がシステム 1 0 0 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 2 0 0 に応答する。システム 1 0 0 内で処理実行不可能な処理は、例えばスレーブノード 1 2 0 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 1 2 0 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 1 1 1 は、スレーブノード 1 2 0 から受け取った処理結果をクライアント 2 0 0 に通知する。

【 0 0 4 4 】

スケジュール処理部 1 1 2 は、クライアント通信部 1 1 1 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 1 1 3 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 1 2 0 に割り当てるシミュレーションを実行する。

【 0 0 4 5 】

スケジュール情報記憶部 1 1 3 は、システム 1 0 0 が備えるスレーブノード 1 2 0 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 1 1 3 に記憶された管理情報には、すべてのスレーブノード 1 2 0 で実行するタスクのスケジュールが記録されている。

【 0 0 4 6 】

より具体的には、スケジュール処理部 1 1 2 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 1 2 0 の検出を行う。ここでは、スケジュール処理部 1 1 2 は、即時に処理実行可能なスレーブノード 1 2 0 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 1 2 0 も検出する。スケジュール処理部 1 1 2 は、ここで検出されたスレーブノード 1 2 0 から、処理要求のタスクを割り当てるスレーブノード 1 2 0 を選択する。なお、ここでは、ロック中のスレーブノード 1 2 0 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 1 2 0 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。

【 0 0 4 7 】

スケジュール処理部 1 1 2 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 1 2 0 がなければ、他のスレーブノード 1 2 0 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 1 1 2 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 1 2 0 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 1 2 0 を用意できると判定される場合、スケジュール処理部 1 1 2 は、該タスクを他のスレーブノード 1 2 0 に移動する処理を、スレーブ通信部 1 1 5 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 1 2 0 で停止し、移動先のスレーブノード 1 2 0 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 1 2 0 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 1 2 0 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 1 2 0 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 1 1

10

20

30

40

50

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。

10

【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に対して該タスクの実行を通知する。

20

【0052】

リスク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。

30

【0053】

また、リスク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。リスク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】

リスク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、リスクスケジュール処理部116は、該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。リスク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。

40

【0055】

また、リスク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、リスクスケジュール処理部116は、該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。リスクスケジュール処理部

50

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。

10

【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。

20

【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。

30

【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。

40

【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

50

グラムは、例えば、記憶装置 1 3 に記憶され、その実行時にメモリ 1 2 に読み出され、CPU 1 1 により実行される。

【0064】

コンピュータ 1 0 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 1 0 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 1 1 0 による処理について、より具体的な例を用いて説明する。 10

【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 2 0 0 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。 20

【0068】

図 6 (B) は、クライアント 2 0 0 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 1 0 0 が備える各スレーブノード 1 2 0 a, 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 1 0 0 が備えるスレーブノード 1 2 0 は、# a のスレーブノード 1 2 0 a と # b のスレーブノード 1 2 0 b の 2 つである。なお、スケジュール情報記憶部 1 1 3 には、例えば図 6 (B) のグラフに示すようなシステム 1 0 0 が備えるスレーブノード 1 2 0 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。 $t_{-1} \sim t_3$ は、等間隔の時刻を示す。 30

【0069】

図 6 (C) は、時刻 t_0 の時点でクライアント 2 0 0 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 1 2 2 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 1 2 0 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。 40

【0071】

マスタノード 1 1 0 において、スケジュール処理部 1 1 2 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 1 2 0 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 50

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

10

20

30

40

50

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。

10

【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。

20

【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。

30

【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。

40

【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。

50

【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、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がしやすい環境となり、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高いシステム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高いシステム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）。

10

【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。

20

【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）。

30

【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。

40

【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

50

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 S 3 8）。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 1 2 0 は、その後のステップ S 3 0, S 3 1 の処理でスケールシュリンクの対象となる。

【0 1 1 3】

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】

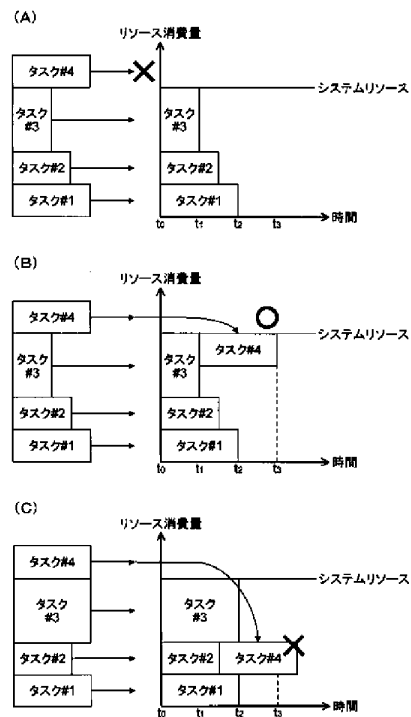
【0 1 1 4】

- 1 0 0 システム
- 1 1 0 マスタノード
- 1 1 1 クライアント通信部
- 1 1 2 スケジュール処理部
- 1 1 3 スケジュール情報記憶部
- 1 1 4 スケールアウト処理部
- 1 1 5 スレーブ通信部
- 1 1 6 リスケジュール処理部
- 1 1 7 スケールシュリンク処理部
- 1 2 0 スレーブノード
- 1 2 1 マスタ通信部
- 1 2 2 アプリケーション
- 2 0 0 クライアント
- 3 0 0 ネットワーク

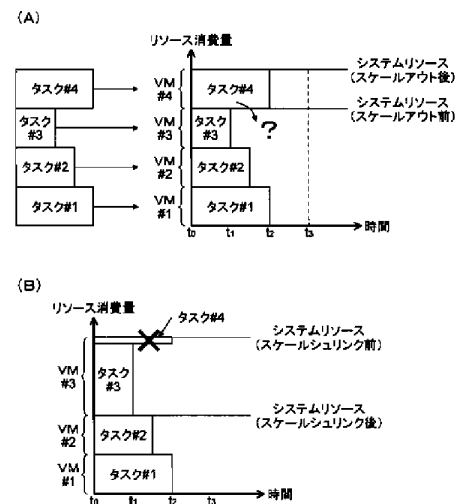
10

20

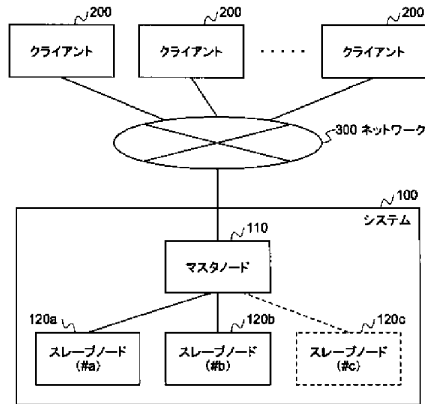
【図 1】



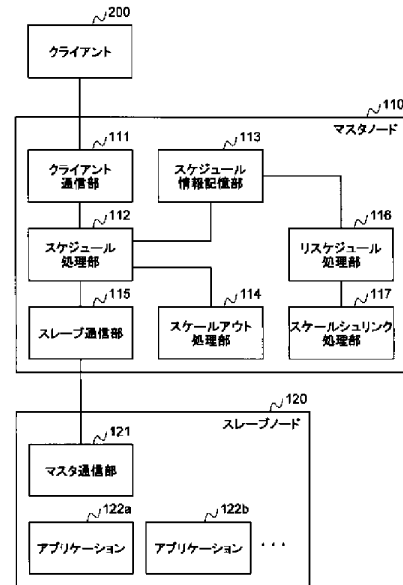
【図 2】



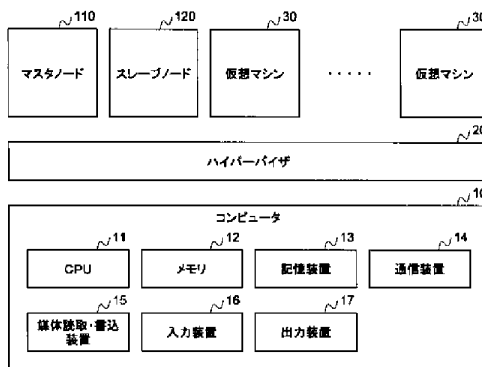
【図 3】



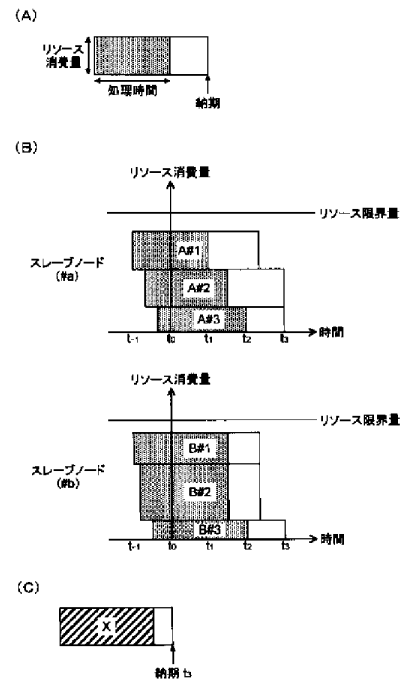
【図 4】



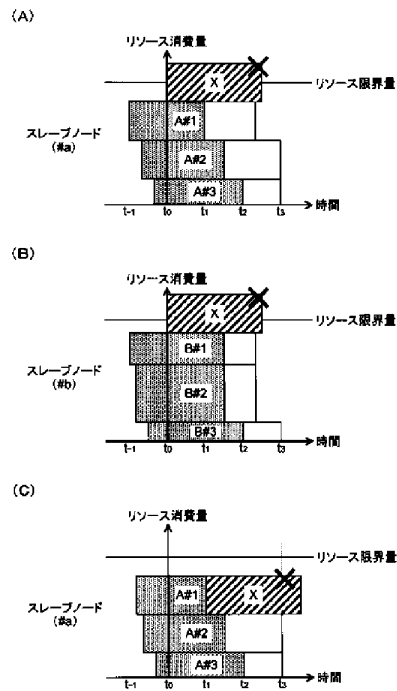
【図 5】



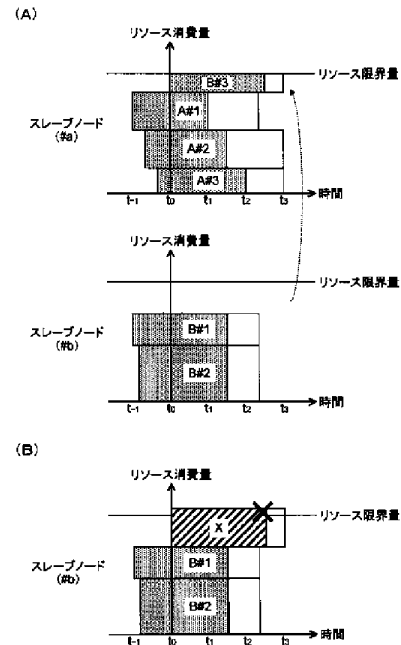
【図 6】



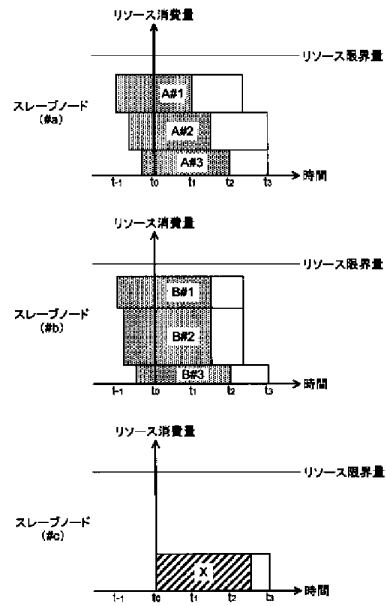
【図 7】



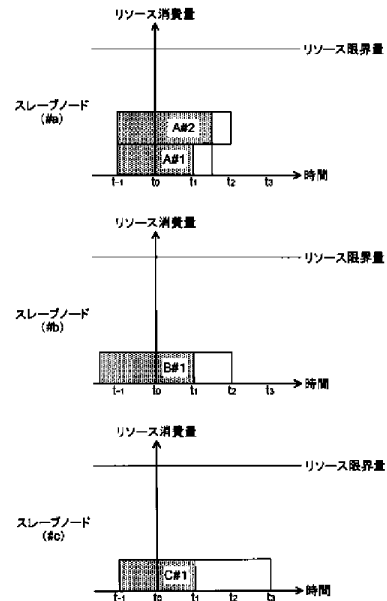
【図 8】



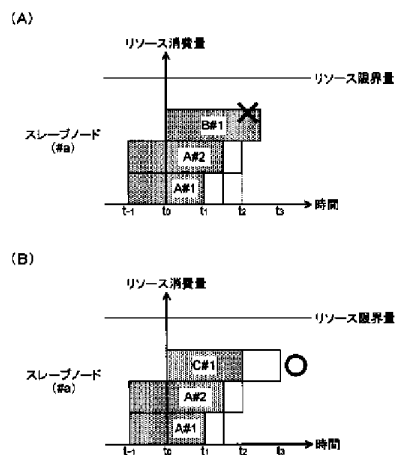
【図 9】



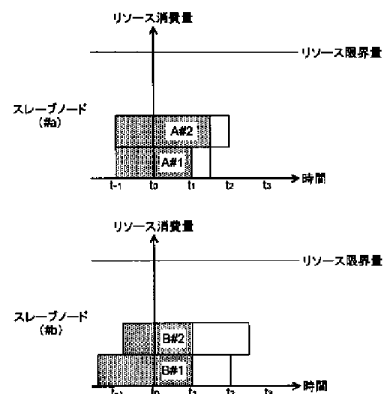
【図 10】



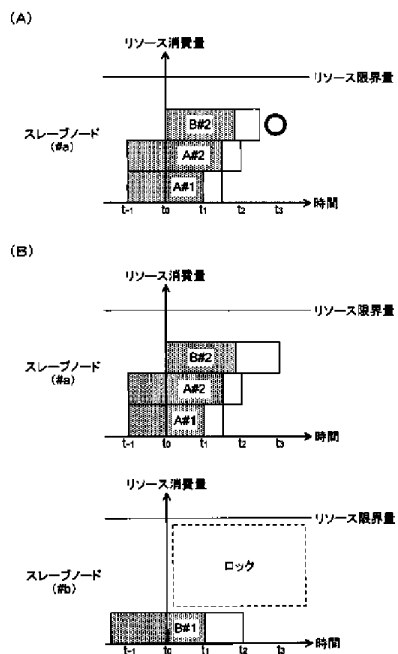
【図 1 1】



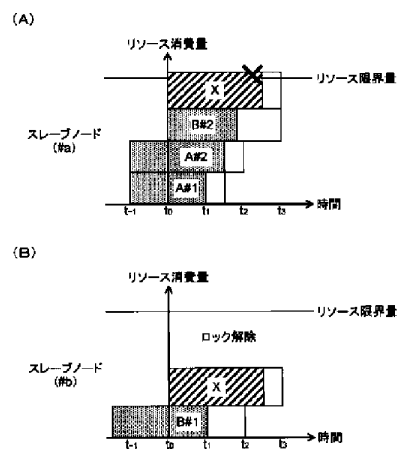
【図 1 2】



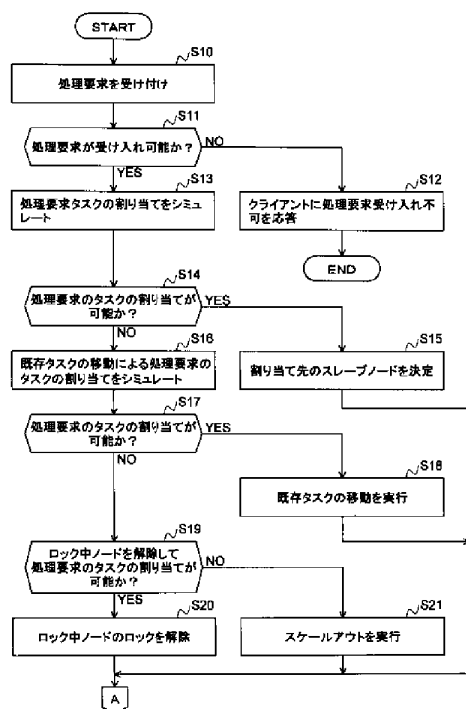
【図 1 3】



【図 1 4】



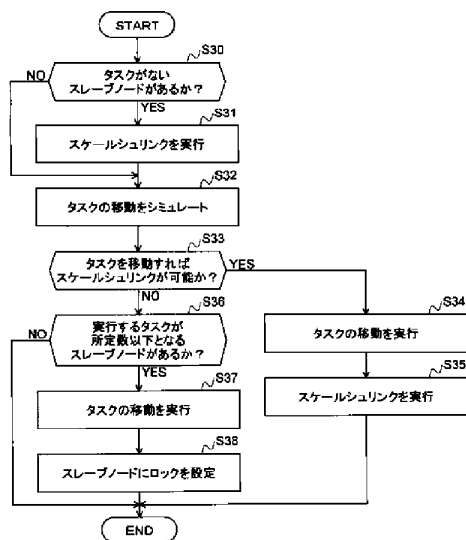
【図15】



【図16】



【図17】



フロントページの続き

(72)発明者 久保田 博昭

神奈川県川崎市中原区上小田中4丁目1番1号 富士通株式会社内

審査官 田中 幸雄

(56)参考文献 特開2009-265778 (JP, A)

特開2008-015958 (JP, A)

(58)調査した分野(Int.Cl., DB名)

G06F 9/50

 Literature display


< 1 / 1 display >

Patent 6643474

publication

 Document unit PDF progress information OPD search key URLs

Display format of the document display screen:

☒ text display
 ☐ PDF display

primary literature

bibliography

close



(19) [Country of issue] Japan Patent Office (JP)
 (12) [Type of publication] Patent publication (B2)
 (11) [Patent number] Patent No. 6643474 (P6643474)
 (24) [Registration date] Reiwa 2 January 8, 2020 (2020.1.8)
 (45) [Issue date] February 12, 2020 (2020.2.12)
 (54) [Title of the invention] Blood sample optimization system and blood isolation device
 (51) [International Patent Classification]
 A61B 5/15 (2006.01)
 A61B 5/154 (2006.01)
 [FI]
 A61B 5/15 200
 A61B 5/154 200
 [Number of Claims] 16
 [Total Number of Pages] 39
 (21) [Application No.] Patent application 2018-523384 (P2018-523384)
 (86) (22) [Application date] July 22, 2016 (2016.7.22)
 (65) [Publication number] Special table 2018-525191 (P2018-525191A) (43) [Publication date]

e] September 6, 2018 (2018.9.6) (86) [International application number] PCT/US2016/04370
9 (87) [International publication number] WO2017/019552 (87) [International publication Dat
e] February 2, 2017 (2017.2.2)

[Date of request for examination] May 20, 2019 (2019.5.20)

(31) [Priority claim number] 62/238,636

(32) [Priority date] October 7, 2015 (2015.10.7)

(33) [Country/region or organization claiming priority] United States (US)

(31) [Priority claim number] 62/318,194

(32) [Priority date] April 4, 2016 (2016.4.4)

(33) [Priority claiming country/region or organization] United States (US)

(31) [Priority claim number] 62/196,797

(32) [Priority date] July 24, 2015 (2015.7.24)

(33) [Priority Country/Territory or Organization] United States (US)

(31) [Priority claim number] 15/140,448

(32) [Priority date] April 27, 2016 (2016.4.27)

(33) [Priority claim Country/region or organization] United States (US)

(31) [Priority claim number] 15/140,443

(32) [Priority date] April 27, 2016 (2016.4.27)

(33) [Priority claim country/ Region or institution] United States (US)

[Application subject to accelerated examination]

(73) [Patent holder]

[Identification number] 518026730

[Name] Klin Inc.

(74) [Agent]

[Identification number] 100083806

[Patent attorney]]

[Name] Hidekazu Miyoshi

(74) [Agent]

[Identification number] 100095500

[Patent attorney]

[Name] Masakazu Ito

(74) [Agent]

[Identification number] 100111235 [

Patent attorney]

[Name or name] Yuko Hara

(74) [Agent]

[Identification number] 100195257

[Patent Attorney]

[Name] Kazushi Obuchi

(72) [Inventor]

[Name] Rogers, Bobby

(72) [Inventor]

[Name] Kan, Gino

(72) [Inventor]

[Name] Detrov, John

[Examiner] Hirokatsu Shimizu

(56) [Reference]

[Reference] Japanese Patent Application [Laid-Open No. 58-025146 \(JP, A\)](#) [Reference] [Japanese Patent Application Laid-Open No. 58-067238 \(JP, A\)](#) [Reference] Japanese Patent Application on Laid-Open No. [2012-016496 \(JP, A\)](#) [Reference] [JP-A-57-089869 \(JP, A\)](#) [Reference] [National Publication of International Patent Application No. 09-504726 \(JP, A\)](#) [Reference] [JP-A-02-224742 \(JP, A\)](#) [Reference] [United States Patent No. 04207870 \(US, A\)](#)

(58) [Investigated field] (Int.Cl., DB name)

A61B 5/153-5/154

The scope of the claims

open

(57) [Claims]

[Claim 1]

A blood sample optimization system, a blood collection system,
a patient configured for venipuncture of a patient to allow withdrawal of a patient blood sample. a needle,
a blood collection path connected to said patient needle and configured to carry said blood sample, and a
sample configured to receive an evacuated blood collection tube for collecting and containin

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 needle, the inlet port

configured to receive the blood sample

; An isolation chamber connected to the inlet port and having a vent including an air permeable 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 sampling flow path having a proximal end connected to the inlet port and configured to receive a subsequent portion of the blood sample; the passageway and the inlet port are connected to the blood sample

bypassing the isolation chamber and a first portion of the blood sample isolated in the isolation 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 sample into the evacuated blood collection tube, the inlet port, the outlet port, the isolation chamber and

the

blood sample optimization system, further comprising a housing containing and defining a sampling flow path; and a blood isolation device .

2.

The isolation chamber of the blood isolation device is at ambient air pressure, and wherein the isolation chamber receives a first portion of the blood sample by patient blood pressure overcoming the ambient air pressure within the isolation chamber. 2. The blood sample optimization system of claim 1. 3. The blood of claim 2, wherein said sample needle includes a seal pierced by said evacuated blood collection tube to open access to said patient needle via said blood 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 device permits a subsequent portion of said blood sample to enter said inlet port under vacuum pressure by said evacuated blood collection tube opening said sample needle. blood sample optimization system.

5.

The blood sample optimization system of claim 1, wherein said air permeable blood barrier of said blood isolation device comprises an air permeable material that seals upon contact with

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 sample needle, wherein the sample needle is unsealed and the blood sample adapted to be removed from the patient. a blood isolation device connected to a blood collection system comprising 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 chamber 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 isolate a first portion of the blood sample before it is opened by a blood vessel; and a proximal end 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 subsequent 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 to 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 isolation chamber and said sampling channel.

[Claim 8]

8. The blood isolation device of claim 7, wherein the isolation chamber is at ambient air pressure 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 an air permeable material that seals upon contact with blood.

10.

The blood isolation device of claim 7, wherein said isolation chamber includes an isolation channel 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 collection path configured to carry said blood sample; and a sample needle

configured to receive an evacuated blood collection tube for withdrawing and containing a subsequent portion of said blood sample; A blood isolation device connected along the blood collection path between a patient needle and the sample needle, the inlet port configured to receive the blood sample, and a sample needle of the inlet port and the blood collection system. 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 removing 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 receive a subsequent portion of said blood sample, said isolation chamber, said sampling channel 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 subsequent portion of the blood sample to a distal end of the sampling channel; and a blood isolation device configured to direct the outlet port connected to a

blood vessel and further comprising a housing containing and defining the inlet port, the outlet 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 the isolation chamber receives a first portion of the blood sample by patient blood pressure overcoming the ambient air pressure within the isolation chamber. 12. The blood sample optimization system according to 11.

13.

The blood sample optimization system of claim 11, wherein said sample needle includes a seal pierced by said evacuated blood collection tube to open access to said patient needle via said 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 with 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 comprises 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 "Blood Sample Optimization System and Blood Contaminant Isolation Apparatus and Method," filed April 27, 2016. and U.S. nonprovisional application Ser. and both of these U.S. nonprovisional applications, U.S. Provisional Patent Application No. 62/196,797 entitled "Blood Culture Improvement System and Method," filed on July 24, 2015, dated October 7, 2015; U.S. Provisional Application No. 62/238,636, entitled "Blood Sequestration System for Clean Blood Collection," 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 incorporated by reference in its entirety.

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 within hospitals or other medical 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 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.

[0006]

One consequence of the collection of blood cultures 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, especially for the patient's condition. Such venous collapse is dangerous and very difficult to control because such a condition is impossible to know 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 disinfection can reduce contamination concerns, but more than 20% of the skin's microorganisms are located deep in the dermis and are not affected by disinfection. 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 drawn 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

[

0013]

The present specification presents systems and methods for reducing blood culture contamination, 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 attach 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 implementations of the systems and methods disclosed herein, blood sampling is accomplished passively through the use of the patient's own blood pressure, thereby reducing the risk of venous collapse and reducing current practice

.

eliminates further user steps beyond The system and method can be adapted to suit short-path direct puncture or butterfly venipuncture systems. It can also be used with samples taken through 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 connected to the inlet port and the outlet port.

ected to the inlet port, the isolation chamber having a vent including an air permeable blood barrier. The blood isolation device has a proximal end connected with the inlet port and a distal end 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 collection path. The blood collection path has a patient needle and a sample collection device. The blood isolation device includes an entry port connected to the patient needle and an isolation chamber connected to the entry port, 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 to the inlet port, and an outlet port connected to the distal end of the sampling channel and the sample collection device.

[0017]

In yet another aspect, a blood isolation device is described that interfaces with a blood collection 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 evacuated blood collection tube. A blood isolation device includes an inlet port connected to a patient needle for receiving a blood sample from a patient. A blood isolation device is an isolation chamber connected to an inlet port and having a vent containing an air permeable blood barrier for receiving and receiving an initial portion of a blood sample before the sample needle is opened 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 connected to the inlet port for 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 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 collection system for enabling and obtaining one or more samples of a patient's blood and false positive identification of pathogens in the patient's blood that may have been contaminated by the venipuncture process. a blood isolation device for receiving and isolating an initial portion of one or more samples of the patient's blood 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 the patient needle for carrying the blood sample, and a blood sample. and a sample needle configured to receive an evacuated blood collection container for collecting and containing a subsequent 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 implementations;

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 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 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 implementation.

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

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

FIG. 14C shows yet another implementation of a blood collection system that isolates contaminants in the initial aliquot or sample to reduce false positives in blood cultures or tests performed on patient blood samples.

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

FIG. 14E further illustrates a blood collection system that isolates contaminants of an initial aliquot 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 another implementation.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

DETAILED DESCRIPTION OF THE INVENTION

[0024]

The present specification provides a blood sample optimization system that reduces or eliminates contaminants in a blood sample taken, thereby reducing or eliminating false positive readings in blood cultures or other tests of the blood sample taken. and methods. 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 isolation device includes an isolation chamber for isolating a first aliquot of blood that may be contaminated, and after the first aliquot of blood is isolated 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 uncontaminated blood may also be included.

FIG .

1 shows a blood sample optimization system according to some implementations. The system 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 valve

e, or another sampling interface.

or with a sample needle (i.e., a Vacutainer®, etc.) that can be housed within the device and initially 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 pushed by or around the sample needle 5 by using a Vacutainer® bottle (not shown) for collecting 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, channels, passages for receiving and holding an initial aliquot of patient blood, which can be of a predetermined 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 contain 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 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 implemented. 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 greater 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 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, 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 allows air to exit the isolation chamber 55. As used herein, the term "air permeable blood barrier" means an air permeable but substantially blood impermeable substance, material or structure. Representative examples are hydrophobic membranes and hydrophobic coatings, hydrophilic membranes or hydrophilic 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 more materials that allow air to pass through until it contacts liquid, such materials being air permeable. and/or completely or partially sealed to prevent or block the passage of 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.

[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 donor 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 o

r indicators, respectively, for sensing and/or indicating when a predetermined 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 isolation chamber 55 can be of any size or shape and can include any type of material 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 agents, coagulants, and 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 blood collection bottle is attached to the sample needle.

[0033]

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 to patient needle 1 . 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 flow 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

The isolation chamber 104 can be formed from a tube or formed by a rigid housing and is initially filled with air. The isolation chamber 104 receives blood flowing out of the patient automatically, ie, under pressure due to the patient's own blood pressure. 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 and to minimize or eliminate mixing of the initial aliquot of blood with the main blood sample. Minimize 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 attached to any length of tubing whose opposite end is connected to a T or Y connector 102, as shown in FIG

can be done. The isolation chamber 104 can be of any shape or volume so long as the initial aliquot contains a predetermined amount of blood sample. The T or Y connector 102 can also include 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 predetermined 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 to

o pinch and prevent fluid flow through the tube. Once the air permeable blood barrier and primary chamber are sealed, the first aliquot of blood is confined to the isolation chamber 104 and a vacuum blood collection tube, such as a Vacutainer® bottle, is attached to the sample needle to obtain a sample

.

5 is attached. The blood collection tube can be removed and the sample needle 5 resealed. Any number of subsequent blood collection tubes can be attached for additional blood draws or samples. 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 needle. 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 implementations in which an isolation chamber 304 configured as the primary collection flow path receives 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 barrier 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 sample optimization system is first sealed and the first aliquot is transferred to an isolation chamber 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 chamber, force air through the air permeable blood barrier, and replace the air in the isolation chamber with blood.

[0040]

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 chamber, forcing 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 be 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 automatically flows into the isolation chamber before being drawn into or otherwise entering the bottle.

As the isolation chamber fills, blood collects or otherwise contacts an air permeable blood barrier 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 primary chamber 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. 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 allowing air to re-enter the system through isolation

do not. 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 show an exemplary blood sample optimization system 800 for non-contaminated blood collection, according to some implementations. 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. A sample collection tube 808 receives a blood sample once the isolation chamber tube 806 is filled. 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

or connected at either end to a non-contaminated 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 .

[0045]

Blood isolation device 812 further includes an isolation chamber 822 or other chamber connected with isolation chamber tube 806 . Isolation chamber 822 terminates in air permeable blood barrier 824 . The air permeable blood barrier 824 can also include a coloring agent that changes 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 lights, sound generating mechanisms, etc. can be used. In some implementations, the air permeable blood barrier is positioned perpendicular to the orientation of isolation chamber 822, but 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-rigid material or range of materials.

FIG.

9 illustrates a path splitter for use in, for example, blood sequestration systems such as those shown in FIGS. 8A-8E.

900 is shown. 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 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 Vacutainer® base or housing, or directly 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 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 906 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 according to the mechanisms and techniques described herein, subsequent blood samples can flow into inlet port 902 and pass unobstructed. It flows out directly from the main conduit outlet port 904 . 10A-10D show blood isolation device 1000 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 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, substantially as described above. Air within the isolation chamber 1008 is expelled by the first aliquot 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. Blood 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 chamber 1108. The flow path can 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 in contact with blood.

[0051]

In some implementations, the blood isolation device 1100 can include a blood collection device 1120, such as a normally closed needle, Vacutainer® shield, or other collection device. Blood 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. Accordingly, the blood collection device 1120 can collect and ensure a clean blood sample so as to reduce the risk of false positive tests.

[0052]

Figures 12A-12D show a blood sample optimization system 1200 according to yet another alternative 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 device. Blood isolation 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 initial aliquot or volume to blood isolation device 1202. Constructed and arranged 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 patient

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 containers or vacutainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be connected to a device. The isolation flow port separates the isolation chamber 1218 from the main 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-shaped 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 therein. 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 are 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 port 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 another alternative implementation. System 1300 includes a blood isolation device 1302 for attachment 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® container or vial is attached to the collection needle of blood collection device 1304. within the isolation 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 needle 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 vacutainers, associated tubing, luer connectors, syringes, luer actuated valves. It can be connected to a device. An isolation flow port 1316 separates from the main inlet port 1314 into an isolation chamber 1318. In the embodiment shown in FIGS. 13A-13D, isolation chamber 1318 is formed as a cavity or chamber within housing 1301 or is formed by walls defining housing 1301.

The isolation chamber 1318 is a tortuous flow path such as a U-shaped flow path, an S-shaped 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 be

e embedded with various channels, openings or grooves, and can extend from cap 1307 at any 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 formed by the tortuous flow path within the isolation chamber 1318. Isolate the first aliquot or volume 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 isolation chamber 1318 is expelled through the air permeable blood barrier 1310 by the first aliquot of blood supplied into the isolation chamber 1318 by the patient's blood pressure. Once the isolation chamber 1318 has been filled and the air within the isolation chamber 1318 has been displaced, a force such as a vacuum or other pressure such as that provided by a blood sampling device such as the 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. 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 isolation chamber 1318 along with the blood of the first aliquot.

[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 cultures or tests performed on patient blood samples. Blood collection system 1400 includes a blood 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 Vacutainer® or the like. Blood isolation device 1401 includes an entry port 1402 that can be connected to a patient needle that is inserted into the patient's vasculature for access to and collection of a blood sample. Inlet port 1402 can also be connected to a tube or other conduit that is also connected to a patient needle.

Inlet port 1402

defines an opening to blood isolation device 1401, which opening 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 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 opening 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 1403. The exit port 1404 has a connector device such as an unthreaded interference or glue joint for attachment to a variety of devices including, but not limited to, threaded caps, luer connectors (male or female), tubing, and the like. can further include

[0061]

Blood isolation device 1401 further includes a sampling channel 1406 between inlet port 1402 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 configuration. In some implementations, sampling channel 1406 has a cross-sectional area substantially similar to the opening of inlet port 1402. In other implementations, sampling channel 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 port 1402 and outlet port 1404. redirected, but preferably connected to the proximal end of sampling channel 1406 near inlet port 1402 and from the proximal end.

separated or diverted from the The isolation chamber 1408 is initially maintained at atmospheric 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 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 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 air 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 surrounding fluids or droplets. This can be done in a variety of mechanical ways including, but not limited to, adding a hydrophobic membrane to the protective cover. As shown in FIGS. 14C and 14D, the sampling channel 1406 may be cylindrical or frusto-conical in shape from a smaller 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 1402 through diverting path 1409 into isolation chamber 1408. Diversion pathway 1409 can have 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 by 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 lower member that sealably mates with the upper member. One or both of the lower and upper members can include a sampling channel 1406 and an isolation chamber 1408 as well as a diverting passageway 1409, an inlet port 1402 and an outlet port 1404. In some other implementations, one or more of diverting path 1409, inlet port 1402, and/or outlet port 1404 are at

east partially closed by a cap member connected to either end of housing 1414 . can be formed in In some implementations, the upper and lower members and the cap member can be connected together by laser welding, heat sealing, gluing, snapping, screwing, bolting, or the like. In other implementations, some or all of the interior surfaces of the diversion pathway 1409 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 chamber 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 the 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 connection with other collection devices such as evacuated blood collection containers or vacutainers, associated tubing, luer connectors, syringes, luer actuated valves, and the like. It can be connected to a device.

[0066]

Blood isolation device 1500 includes an entry port 1502 that can be connected to a patient needle that is inserted into the patient's vasculature for access to and collection of a blood sample. Entry port 1502 can also be connected to a tube or other conduit that is also connected to a patient needle. Entry port 1502 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 patient needle itself. For example, the opening has a diameter of approximately 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 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 integrated with the entry port 1502, such as by co-molding, gluing, laser welding, or heat bonding the parts together. This allows the blood isolation device 1500 to be manufactured and sold 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 port 1504 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 connection such as a threaded 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 isolation

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 1502 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 configuration. In some implementations, sampling channel 1506 has a cross-sectional area substantially similar to the opening of inlet port 1502. In other implementations, sampling channel 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 port 1502 and outlet port 1504. Although diverted, it is preferably connected to and disconnected or diverted from the proximal end of sampling channel 1506 near inlet port 1502. In some implementations, the diversion channel includes a Y-junction. The isolation chamber 1508 is preferably maintained at atmospheric pressure and includes a vent 1510 at or near the distal end 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 aliquot 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 blood barrier 1512 with their fingers or other external instruments while still allowing the patient's own blood pressure to force the isolation chamber 1508 into contact. Allowing air to exit the air permeable blood barrier 1512 as the air is forced out of the isolation chamber by forcing blood into it. The protective cover 1516 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.

FIG.

15B is a perspective view of blood isolation device 1500 from the top of housing 1501, including 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 the device is empty.

Filling the separation chamber 1508 is shown. Figure 15G is a perspective view of the blood isolation device 1500 from the bottom of the housing 1501 and the exit port 1504 of the blood isolation device 1500, showing the initial flow while the sampling channel 1506 is empty before the sample collection device is activated. An aliquot of blood is shown filling the isolation chamber 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 remaining within isolation chamber 1508. FIG. Blood is drawn through sampling channel 1506 during the period of time.

FIG .

15D is a cross-sectional view of blood isolation device 1500 according to some implementations, 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 configured 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 implementations, 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 example, an injection molding process or by etching, cutting, or molding. It has grooves, channels, locks, conduits or other pathways pre-formed by perforations or the like. The upper member 1520 may be attached by any mating or connecting mechanism, such as using laser welding, thermal bonding, ultrasonic welding, adhesives, screws, rivets, bolts, etc., or latches, grooves, tongues, pins, flanges. Other mating mechanisms, such as, can connect with lower member 1522 . In some implementations, the upper member 1520 can include grooves, channels, locks, conduits or other pathways, while the lower member 1522 is the upper member 1520, 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 grooves or partial channels, for example, to complete the formation of either sampling channel 1506 and/or isolation chamber 1508 . In some implementations, the protrusions 1524 can be formed 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 1520 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 by 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-translucent material. In other implementations, the housing 1501 can be largely opaque or non-transparent, but the housing surfaces immediately adjacent the sampling channel 1506 and/or the isolation 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 that the sequestered blood is then released while a clean blood sample is drawn through the sampling channel 1506. 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 in to 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 a 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 connected to a patient needle. Entry port 1602 defines an opening to blood isolation device 1600, which opening 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 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

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, gluing, laser welding, or heat bonding the parts together. Blood isolation device 1600 is thereby manufactured and sold 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 or 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 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 connection such as a threaded 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 device such that the patient needle and blood sample collection device are connected to blood isolation during blood collection or sampling. The need to connect to device 1600 can be eliminated.

[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 sampling channel 1606. and an isolation chamber 1608 that is isolated or diverted from. 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 i

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 inlet port 1602 is preferentially directed into isolation chamber 1608, as shown in FIGS. 17A-17B. The isolation chamber 1608 can also include or form a bend or ramp to move the initial blood 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 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 member 1622 that fit together. Blood isolation device 1600 includes 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 gasket or sealing member. FIG. 17A-17D show the lower member 1622 of the housing for the blood isolation device 1600. The lower member 1622 includes pre-formed grooves, channels, locks, conduits, such as 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, 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 welding, thermal bonding, gluing, screws, rivets, bolts, etc., or latches, grooves, tongues, pins, flanges. Upper member 1620 is shown connectable with lower member 1622 by other mating mechanisms such as. 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.

[0090]

In some implementations, sampling channel 1606 and isolation chamber 1608 are formed by 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 from a transparent or translucent material, or from an opaque or non-translucent material. In other

her 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. There may be first a visual cue or sign that the isolation chamber 1608 is filled to the required or desired degree, and/or a subsequent isolation while a clean blood sample 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, but are not limited to, contact, penetration, or partial penetration of blood, causing the air permeable blood barrier 1612 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.

[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 prevent a user from touching air permeable blood barrier 1612 with their fingers or other external 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 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.

.

Both pathways are initially filled with air at atmospheric pressure, but the sampling channel 1606 is initially sealed by a Vacutainer® or other such sealed blood collection device at the outlet port 1604. , the isolation chamber 1608 terminates in a vent 1610 to the atmosphere that includes 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 passes through inlet port 1602 of blood isolation device 1600. do. This initial volume of potentially contaminated blood preferentially enters isolation chamber 1608 by finding the path of least resistance. The patient's own blood pressure overcomes the atmospheric pressure in the vented isolation chamber 1608 and expels the air in the isolation chamber 1608 through the air permeable 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 effects 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 blood barrier 1612. When blood contacts 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 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 blood 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 blood 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 optimization 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 that includes a sealed collection needle such that once a sealed vacuum container is placed on the collection needle and the container is pierced once by the collection needle, the patient needle is exposed to the patient needle. A blood sample is drawn from 2002 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.

FIG.

21 shows a non-vented blood isolation device 2100 that uses wicking material chambers. Blood isolation device 2100 includes a housing 2101 having a sampling channel 2104 at least partially 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 immediately escapes into the wicking material of the isolation chamber 2102. The wicking material 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 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.

[0100]

As described herein, air permeable blood barriers can be made using a wide variety of different structures and materials. As shown in Figures 22A and 22B, an air permeable blood barrier 2202 of a blood isolation device 2200 can include a polymeric bead matrix 2204 that has been 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 cellulose 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. Self-sealing 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 channel 2308 that bypasses the isolation chamber 2306 once the isolation chamber is filled to the first aliquot of blood that may be present. Isolation chamber 2306 includes a hydrophobic plug 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 is 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 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 inlet port 2302, bypasses 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 geometry 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 the sampling channel before the first aliquot of blood is sequestered in sequestration chamber 2306. can.

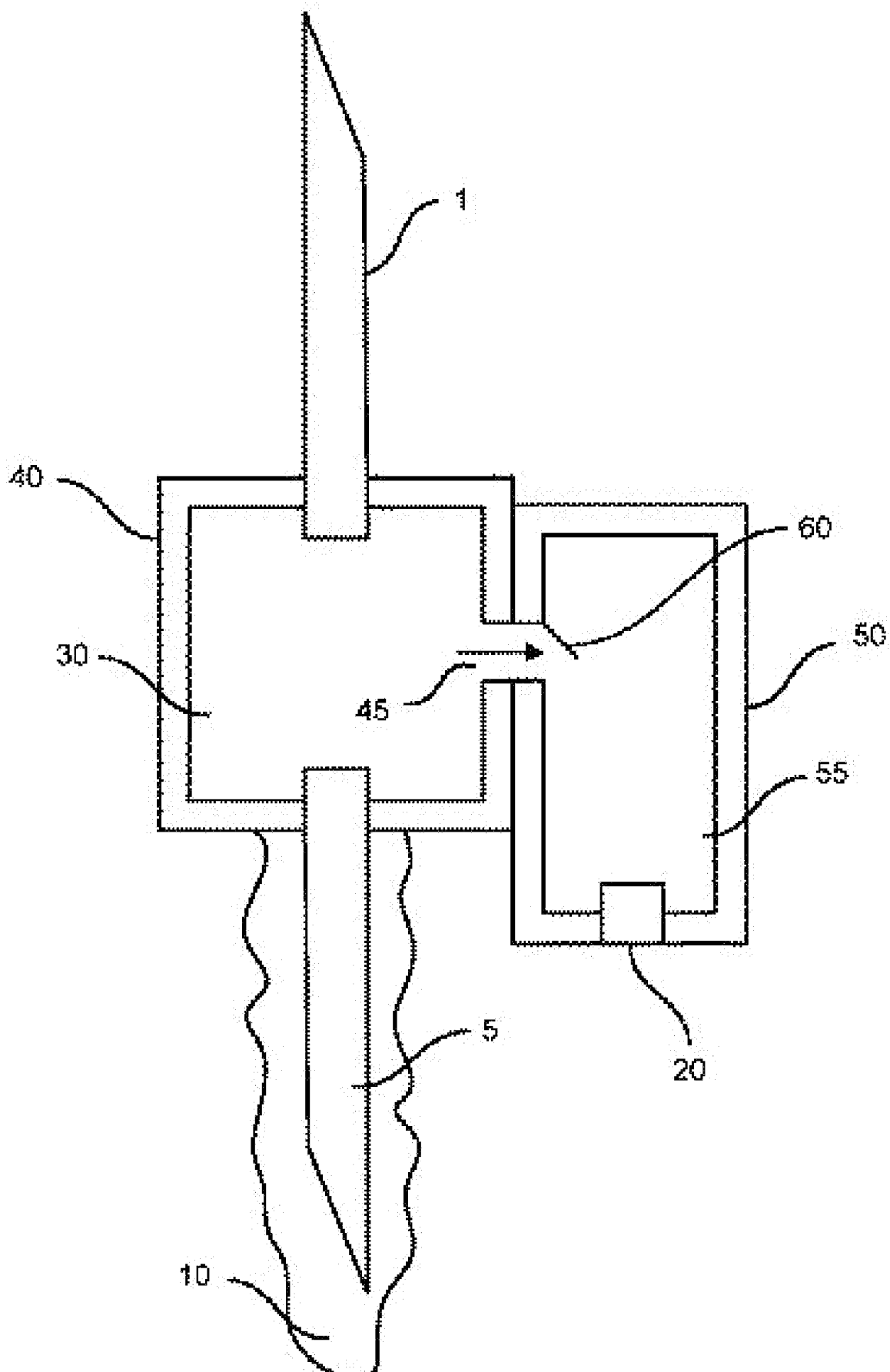
[0103]

While various embodiments have been described in detail above, other modifications are possible. Other embodiments may be within the scope of the following claims.

drawing

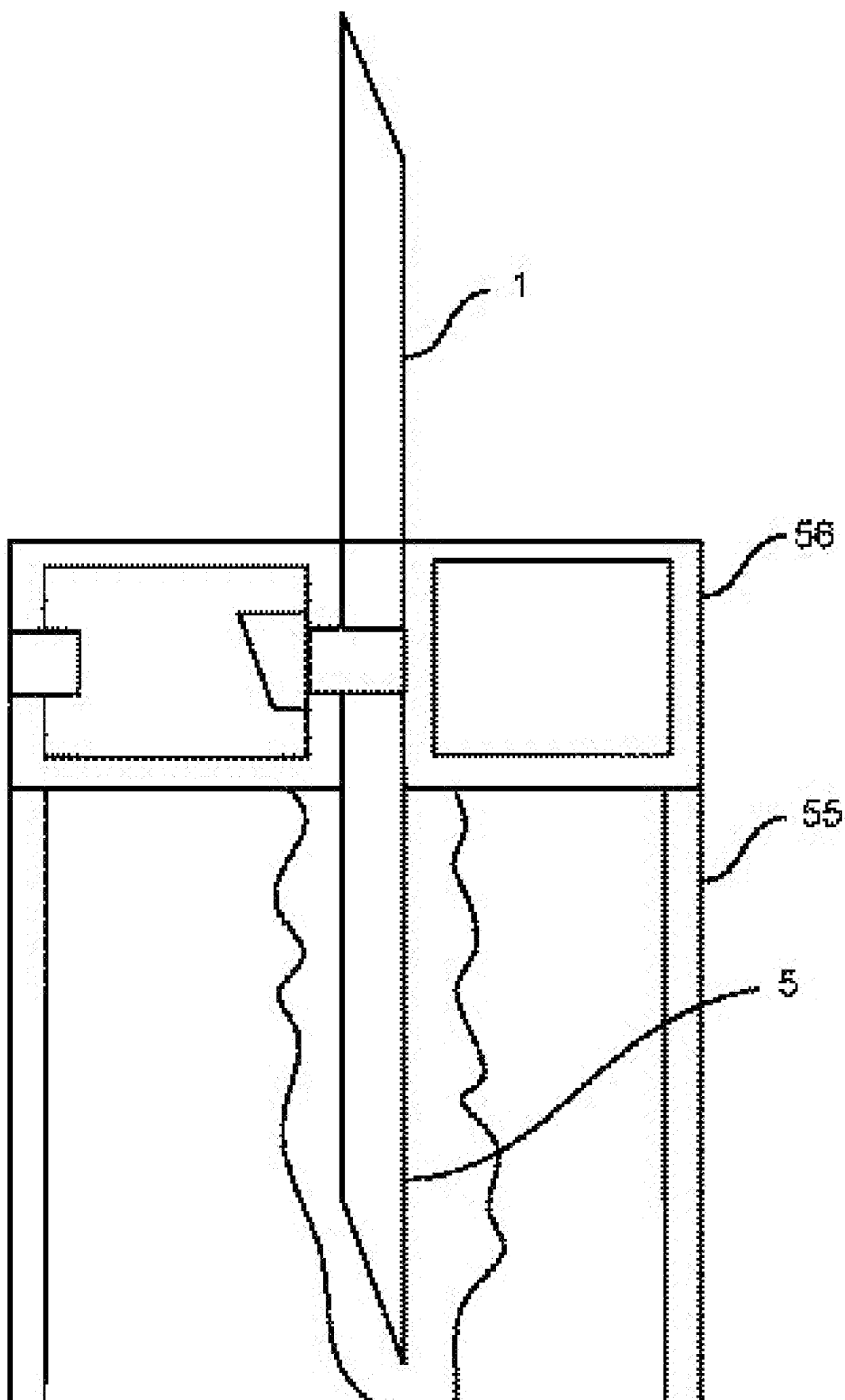
open

[Fig. 1]



[Figure 2]

FIG. 1



[Figure 3]

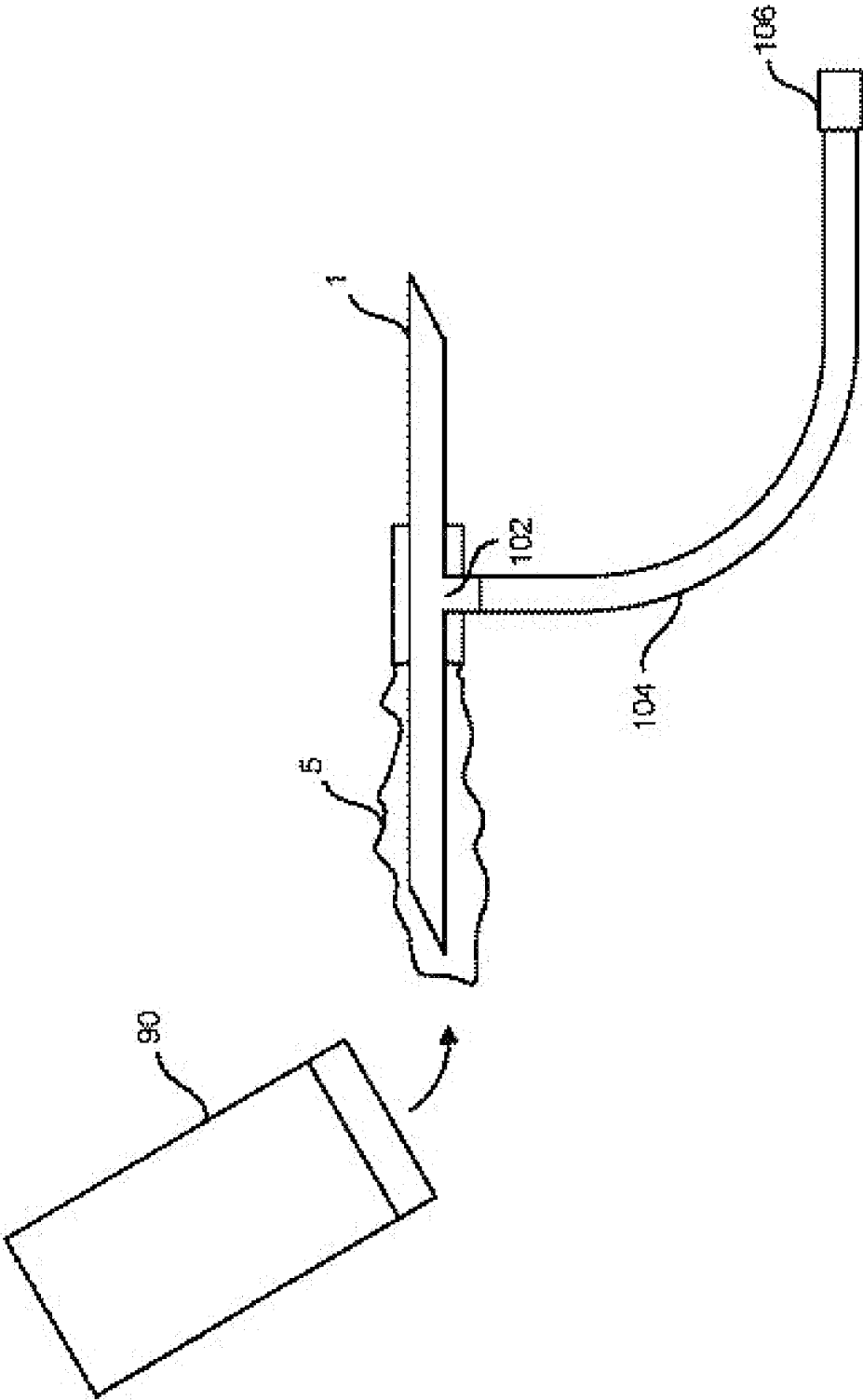


FIG. 3

[Figure 4]

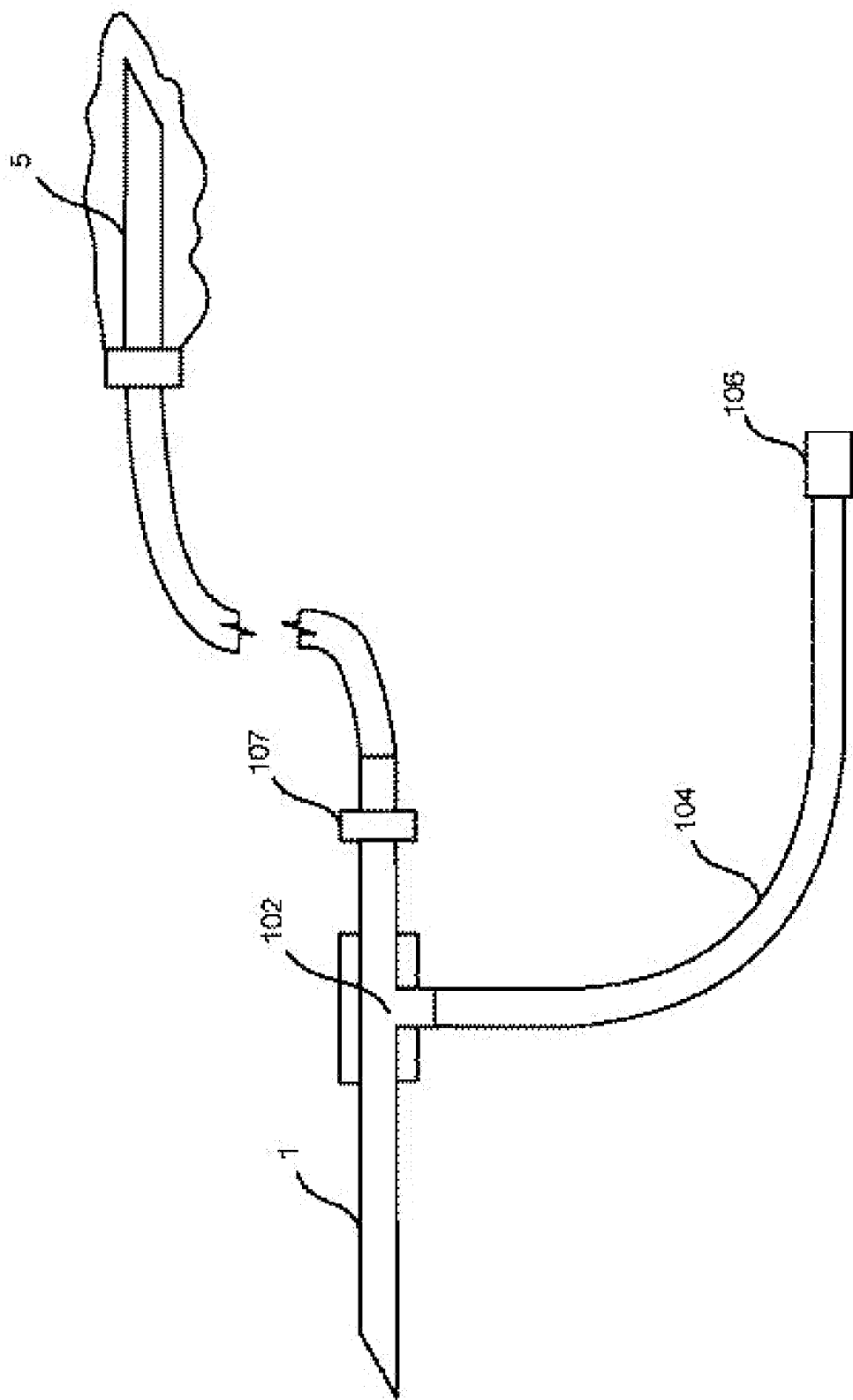


FIG. 4

[Figure 5]

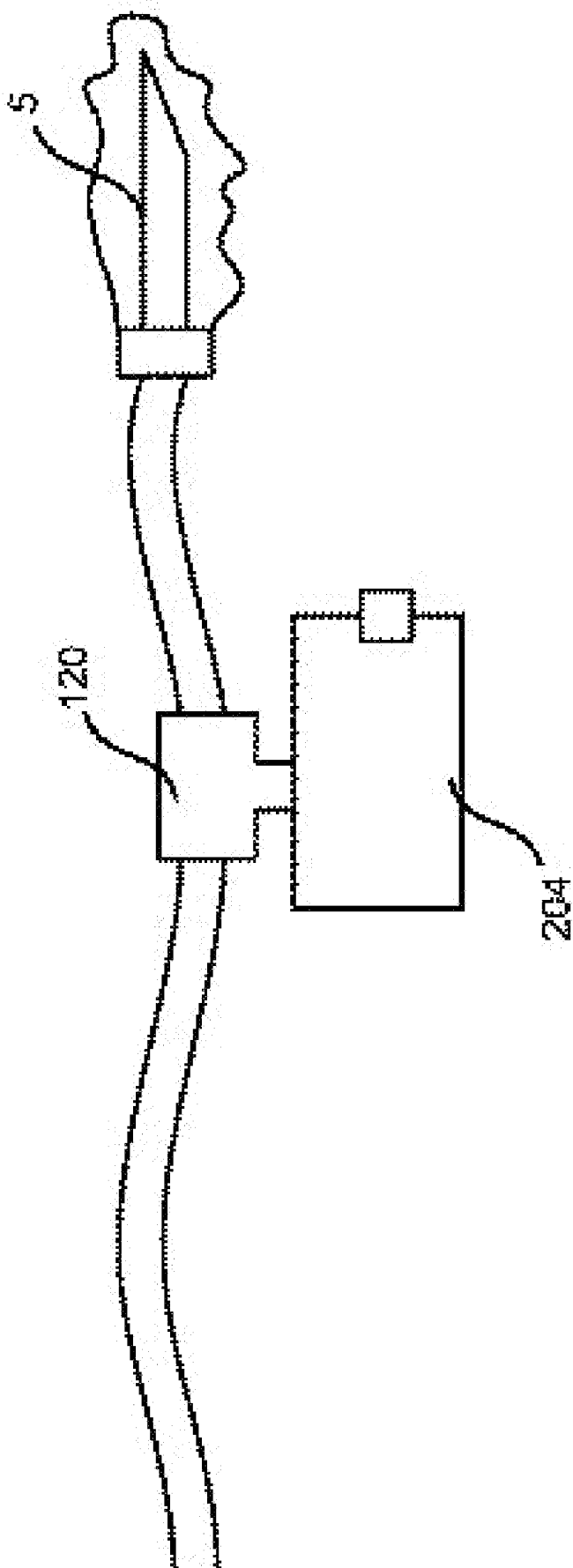
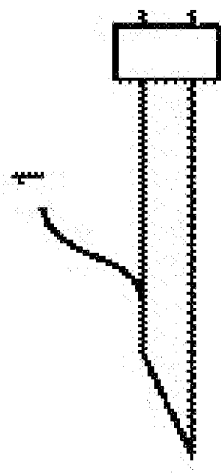
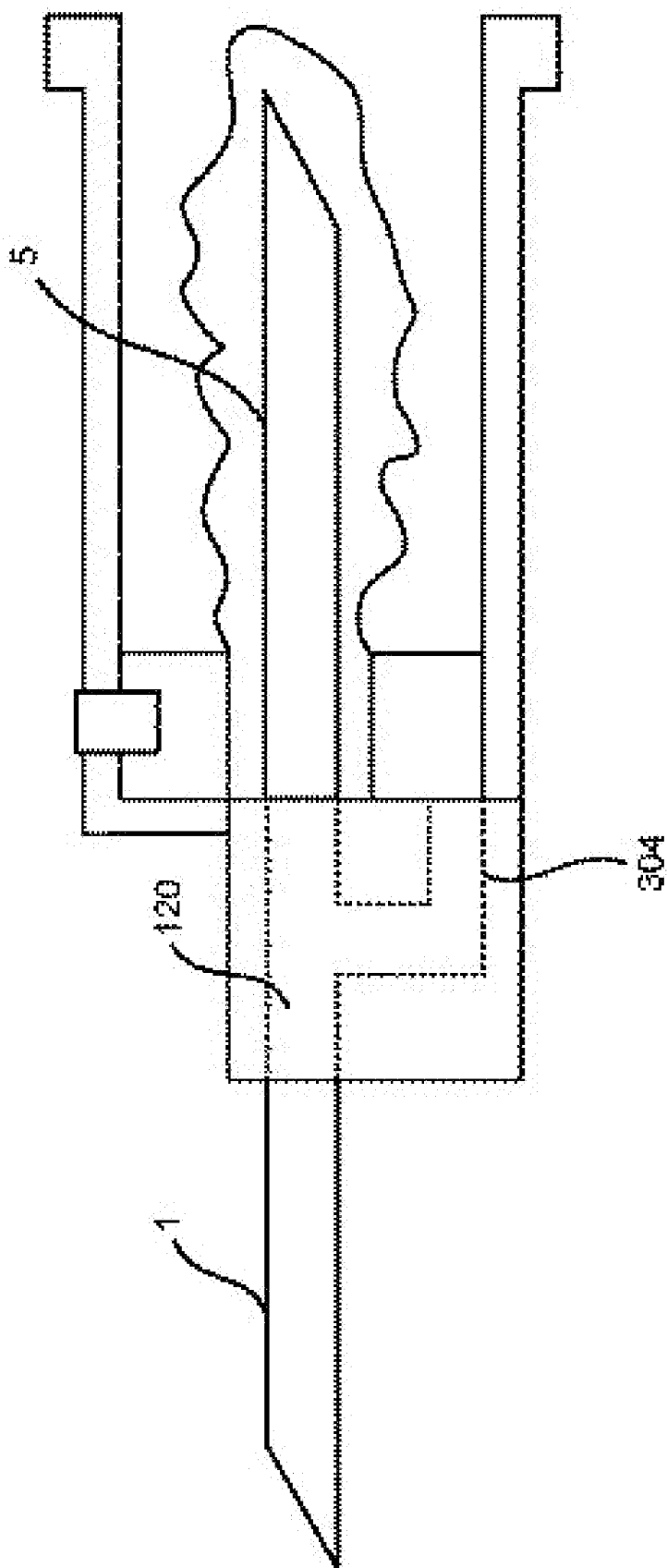


FIG. 5

[Fig. 6]



**FIG. 6**

[Fig. 7]

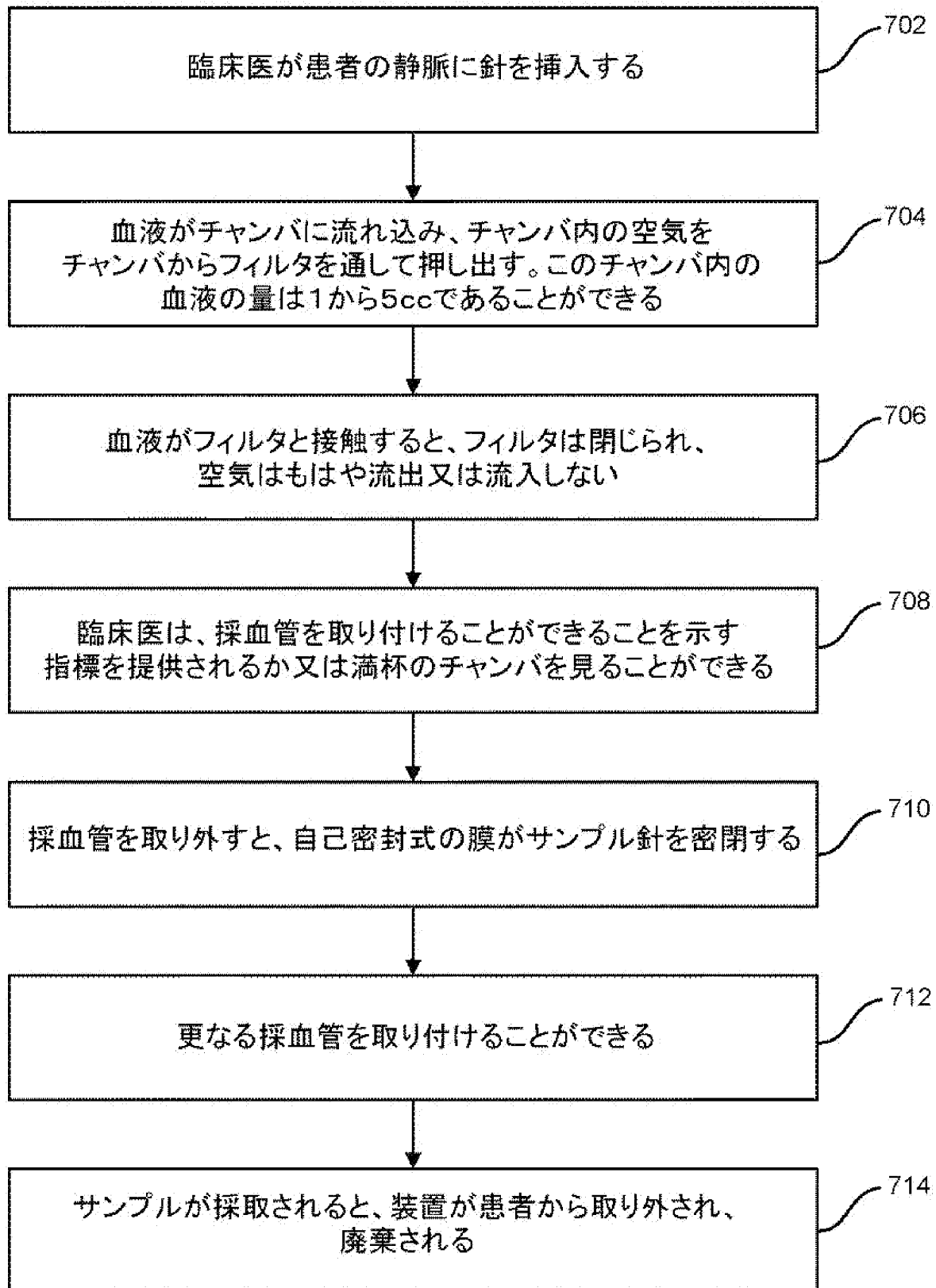


FIG. 7

[Fig. 8A]

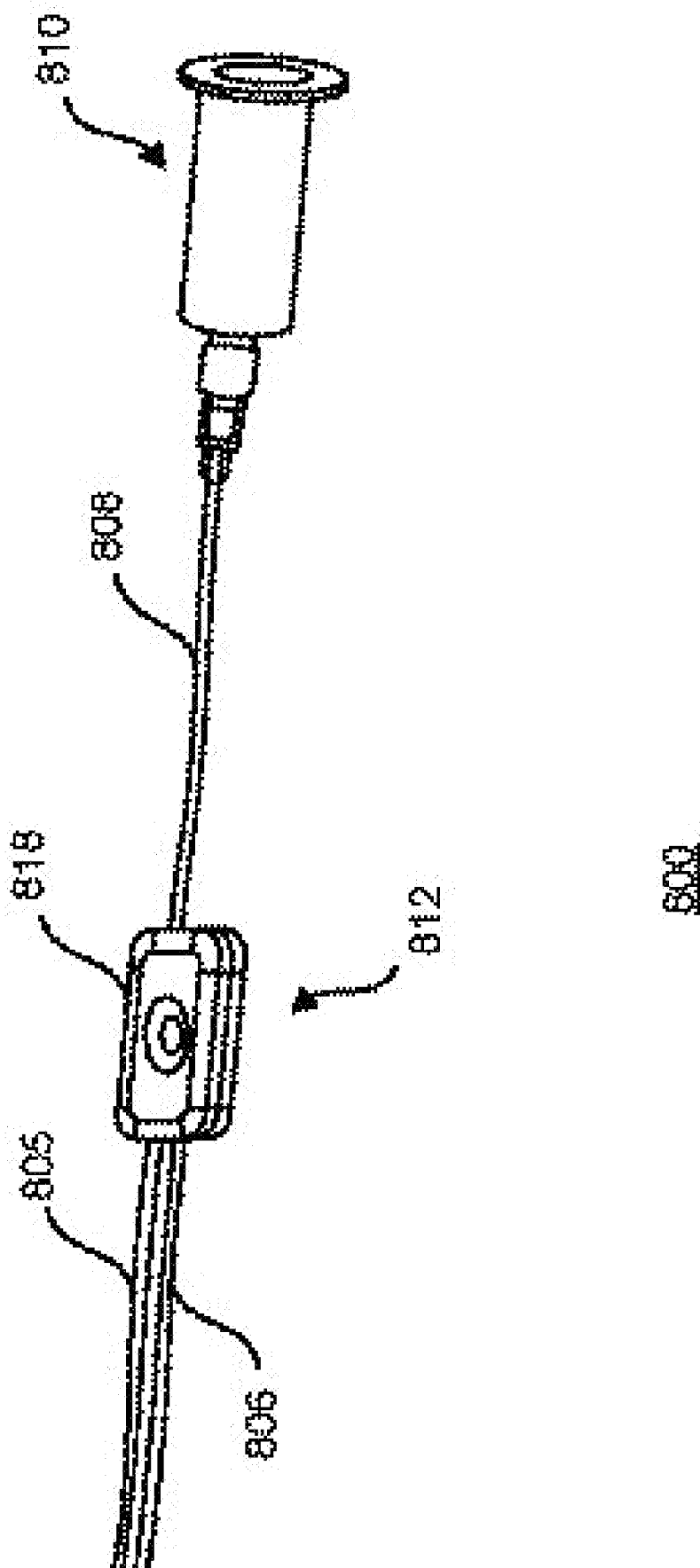
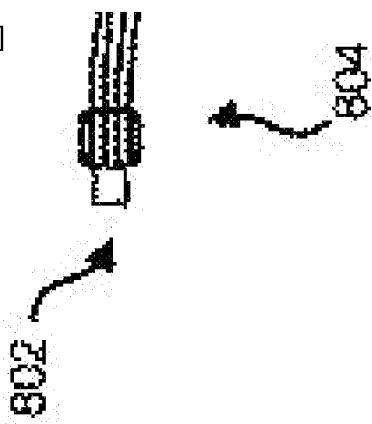


FIG. 8A

[Fig. 8B]



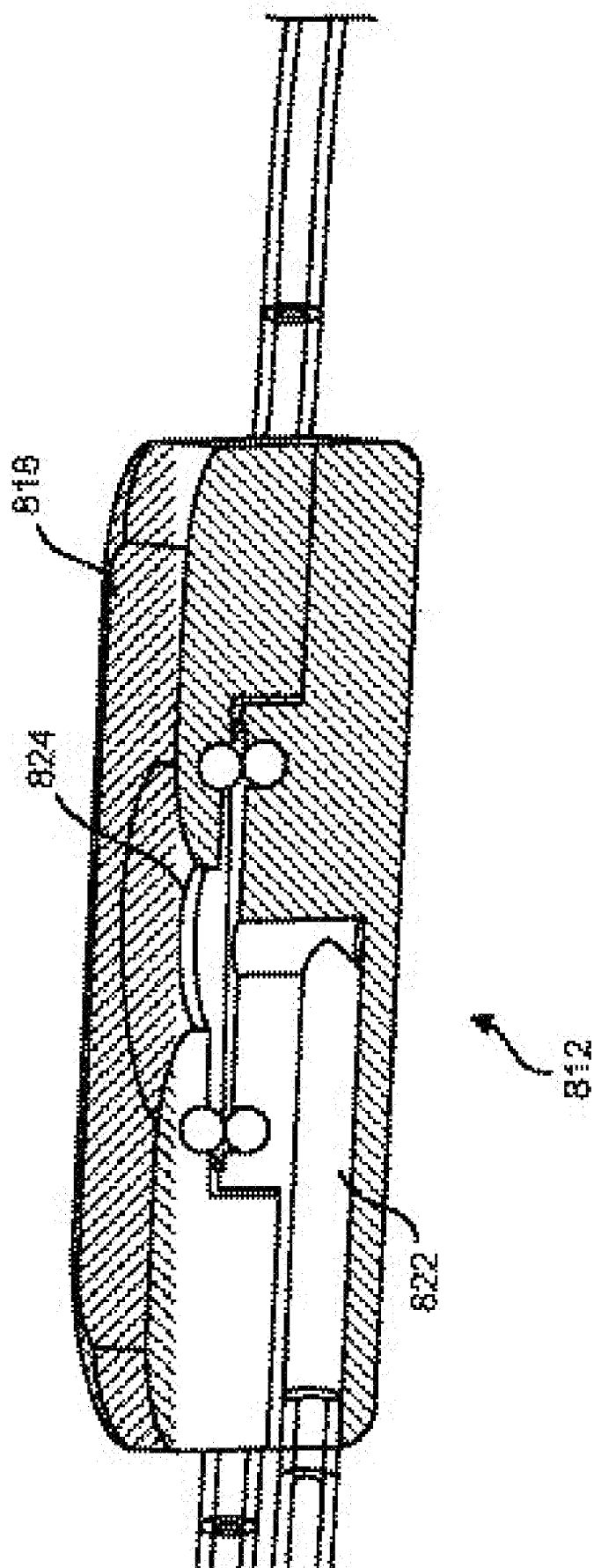


FIG. 8B

[Fig. 8C]



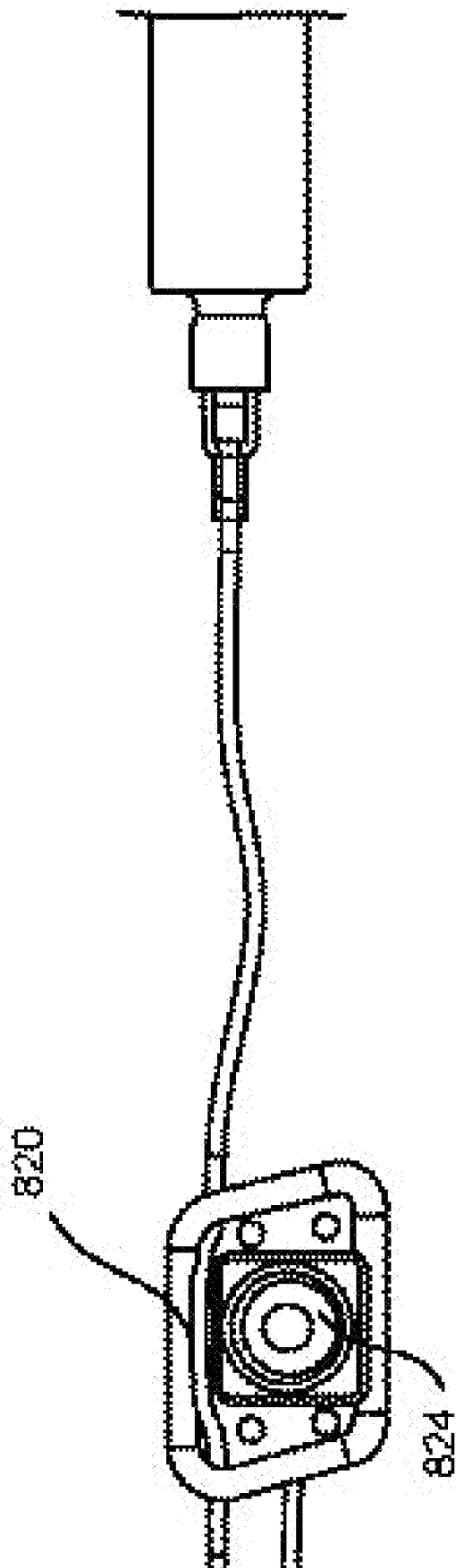
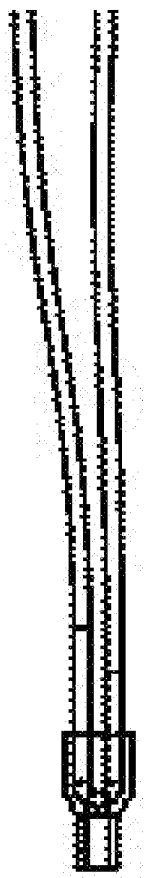


FIG. 8C

[Fig. 8D]



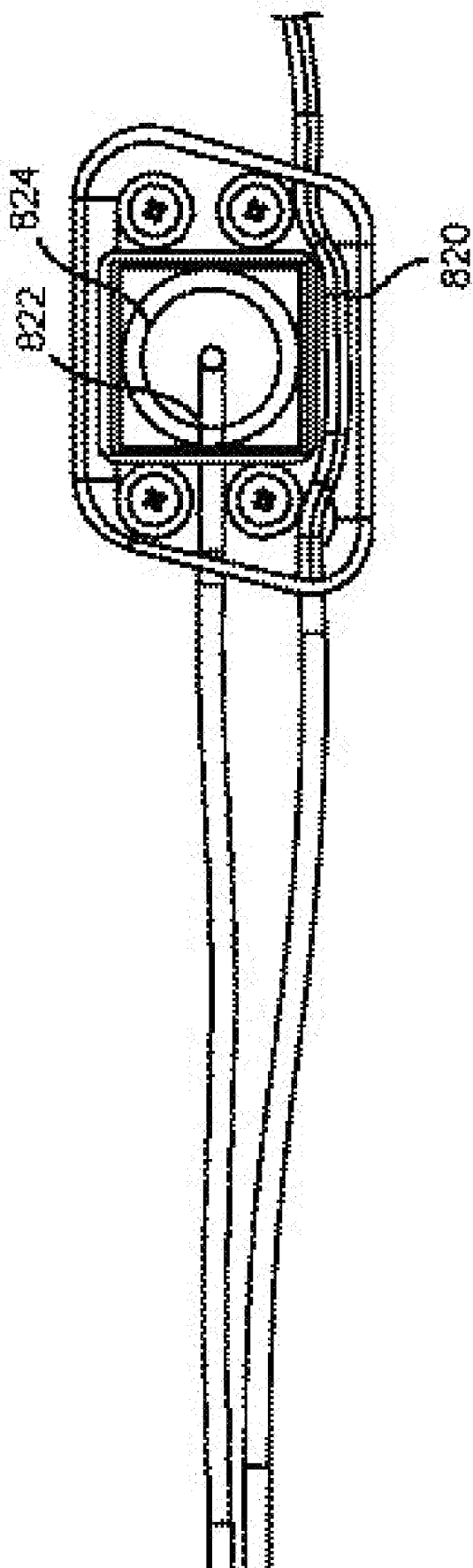


FIG. 8D

[Fig. 8E]



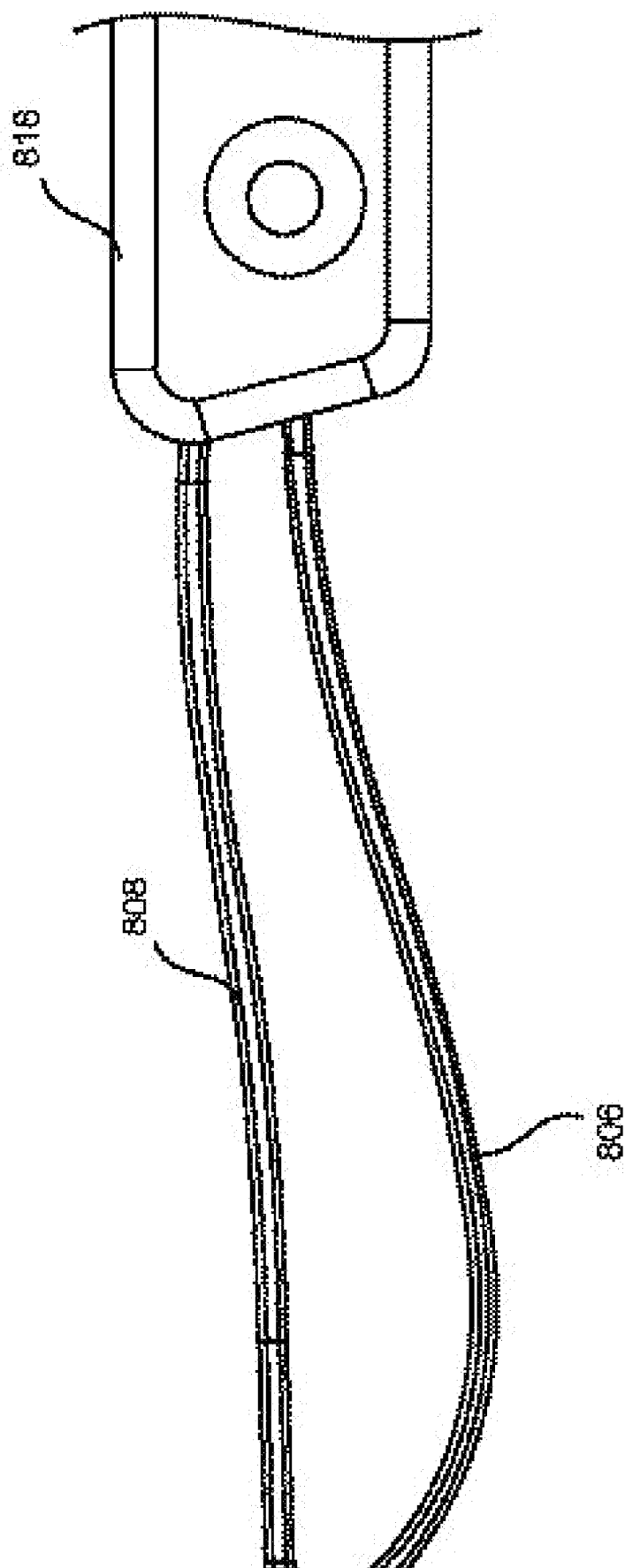
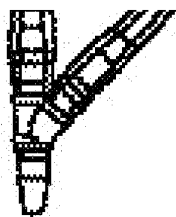


FIG. 8E

[Fig. 9]



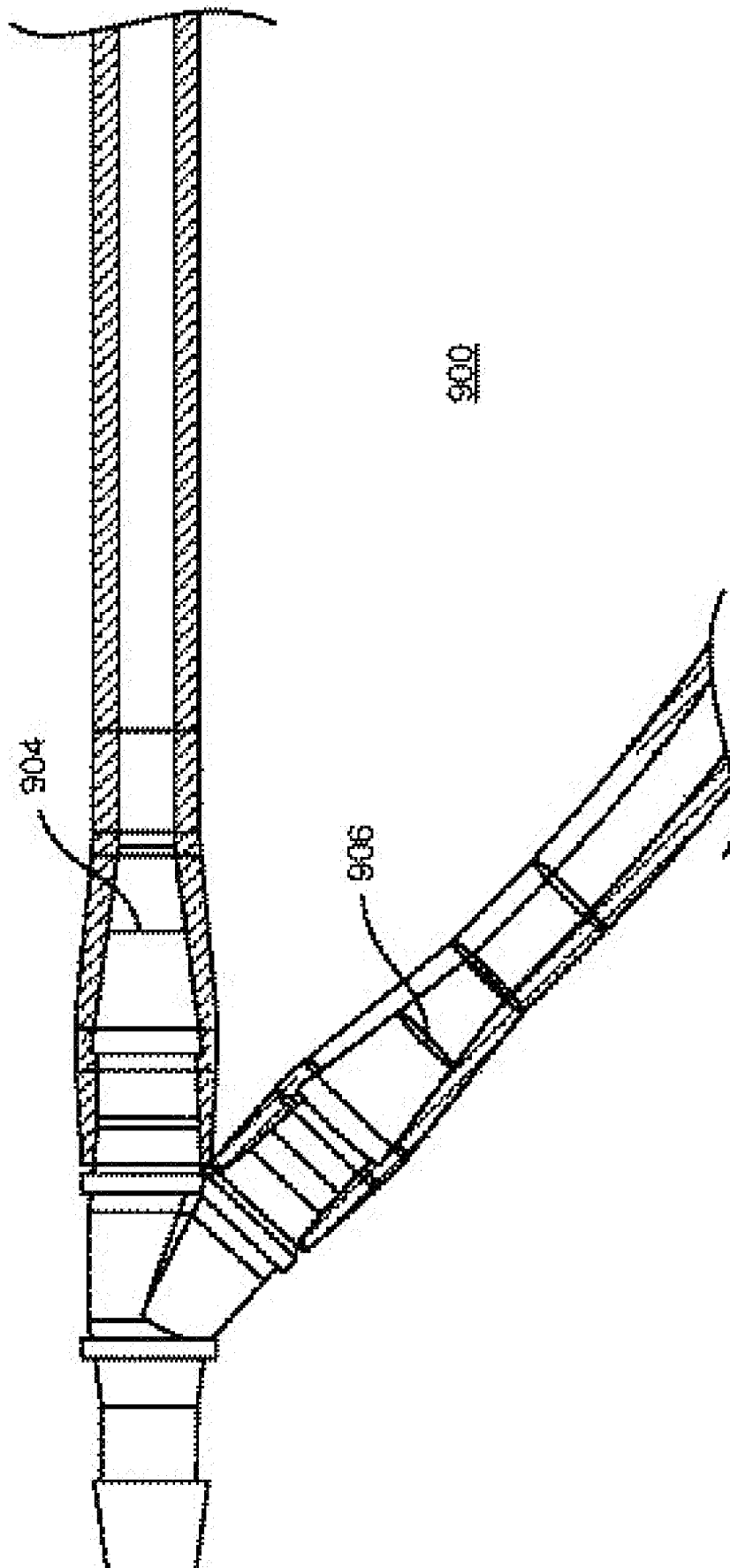


FIG. 9

[Fig. 10A]

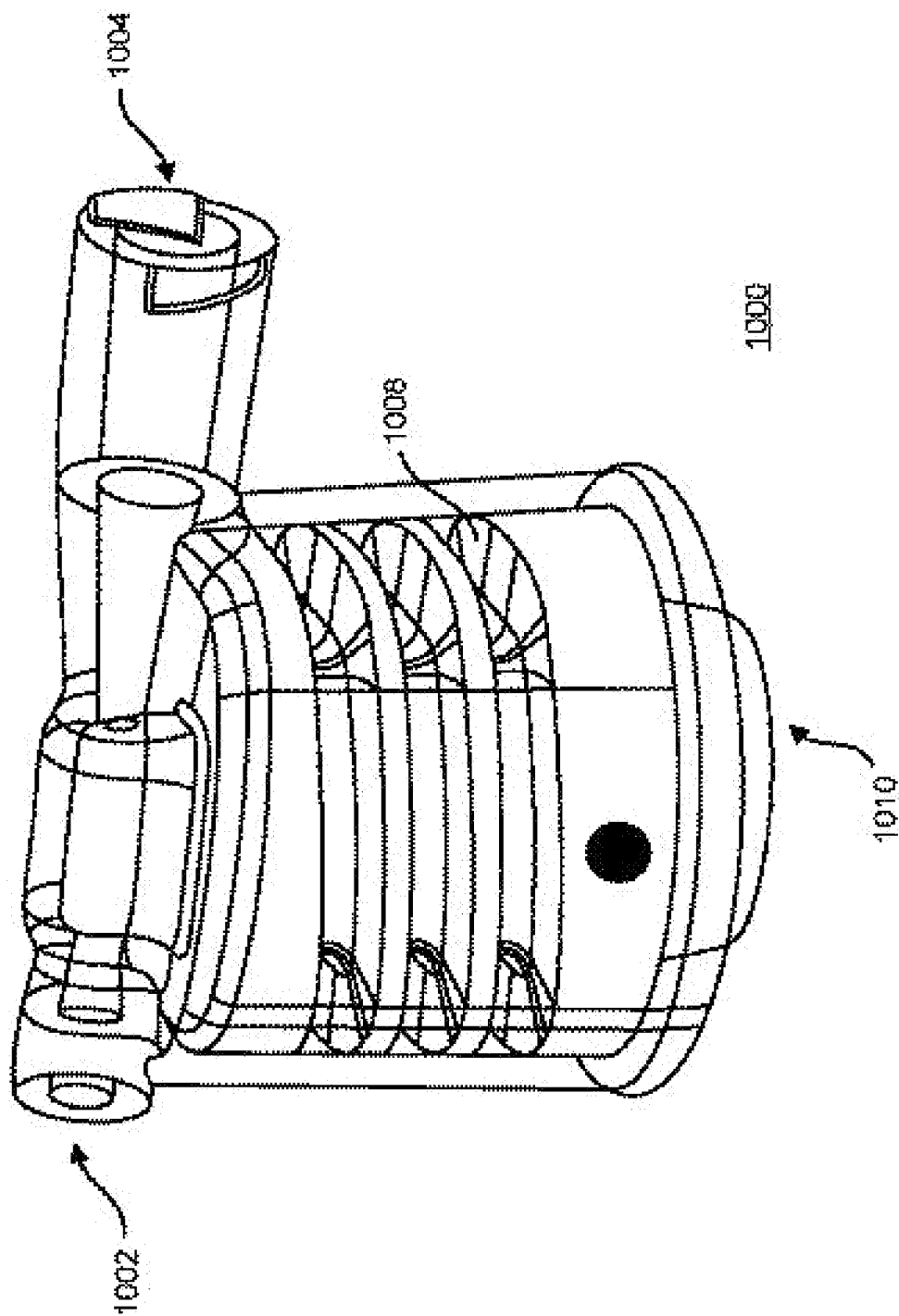


FIG. 10A

[Fig. 10B]

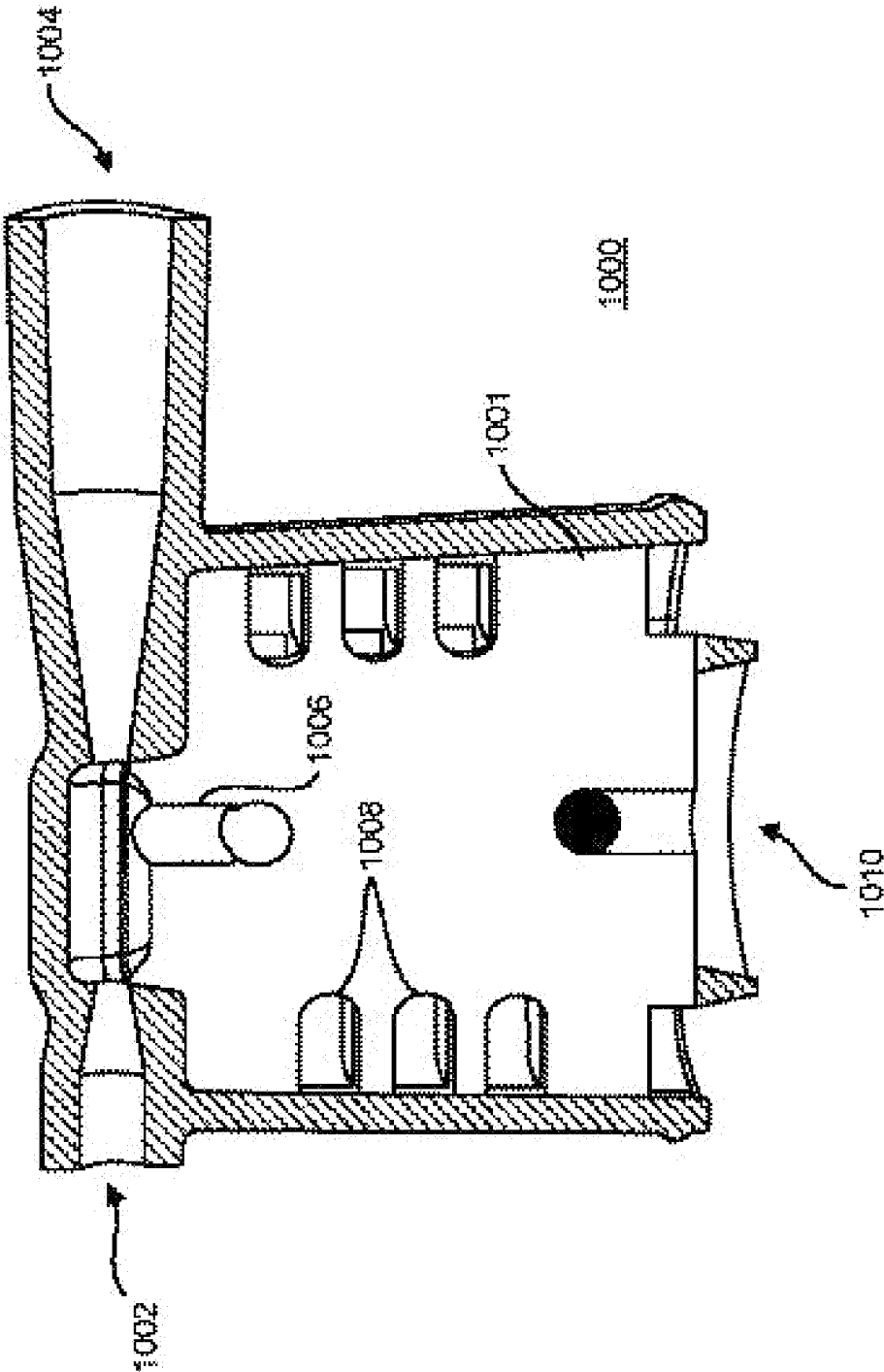
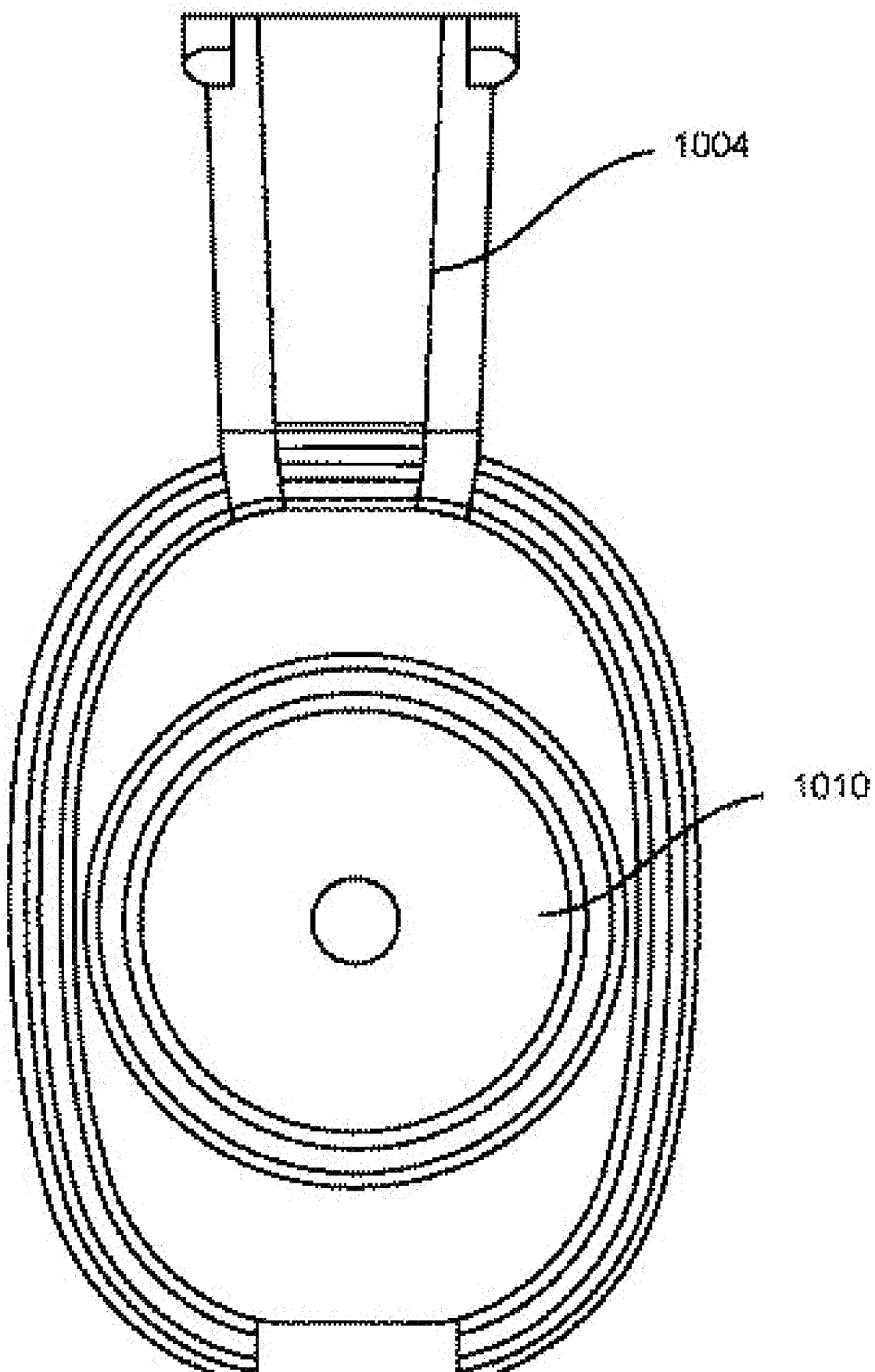


FIG. 10B

[Fig. 10C]



[Fig. 10D]

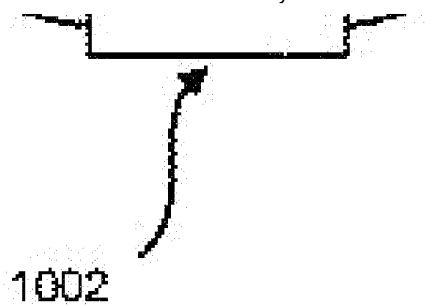
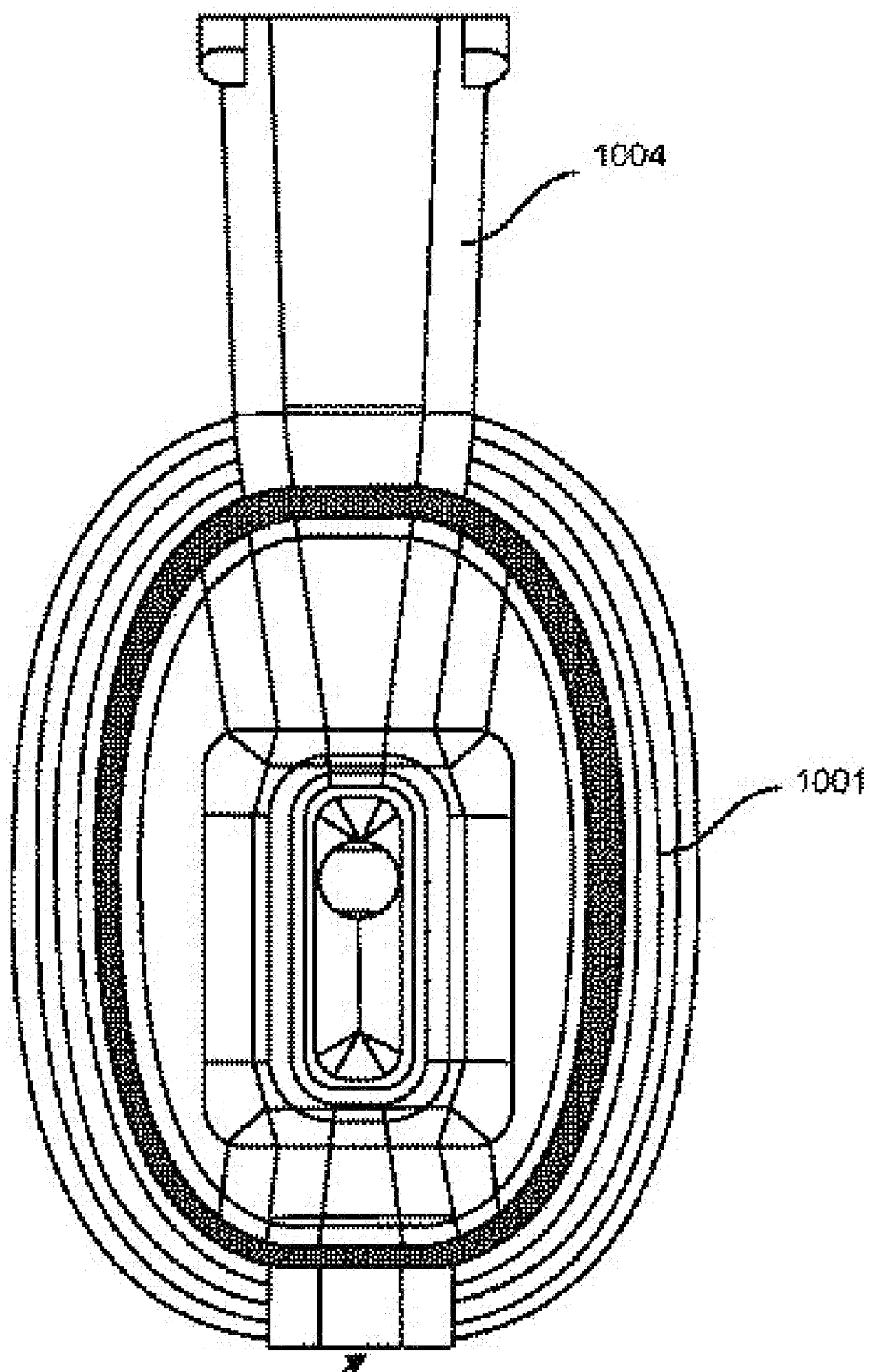


FIG. 10C



[Fig. 11A]

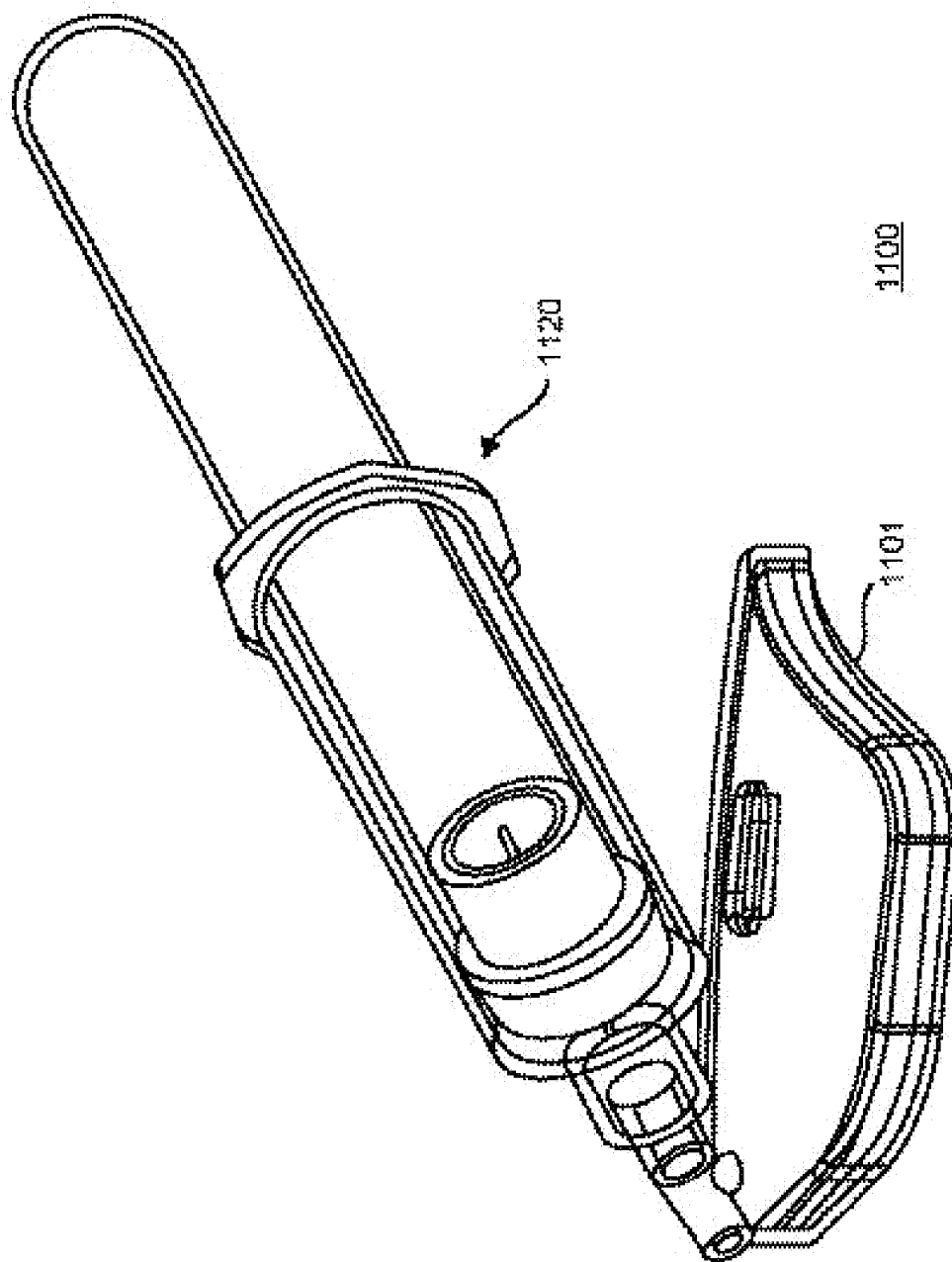


FIG. 11A

[Fig. 11B]

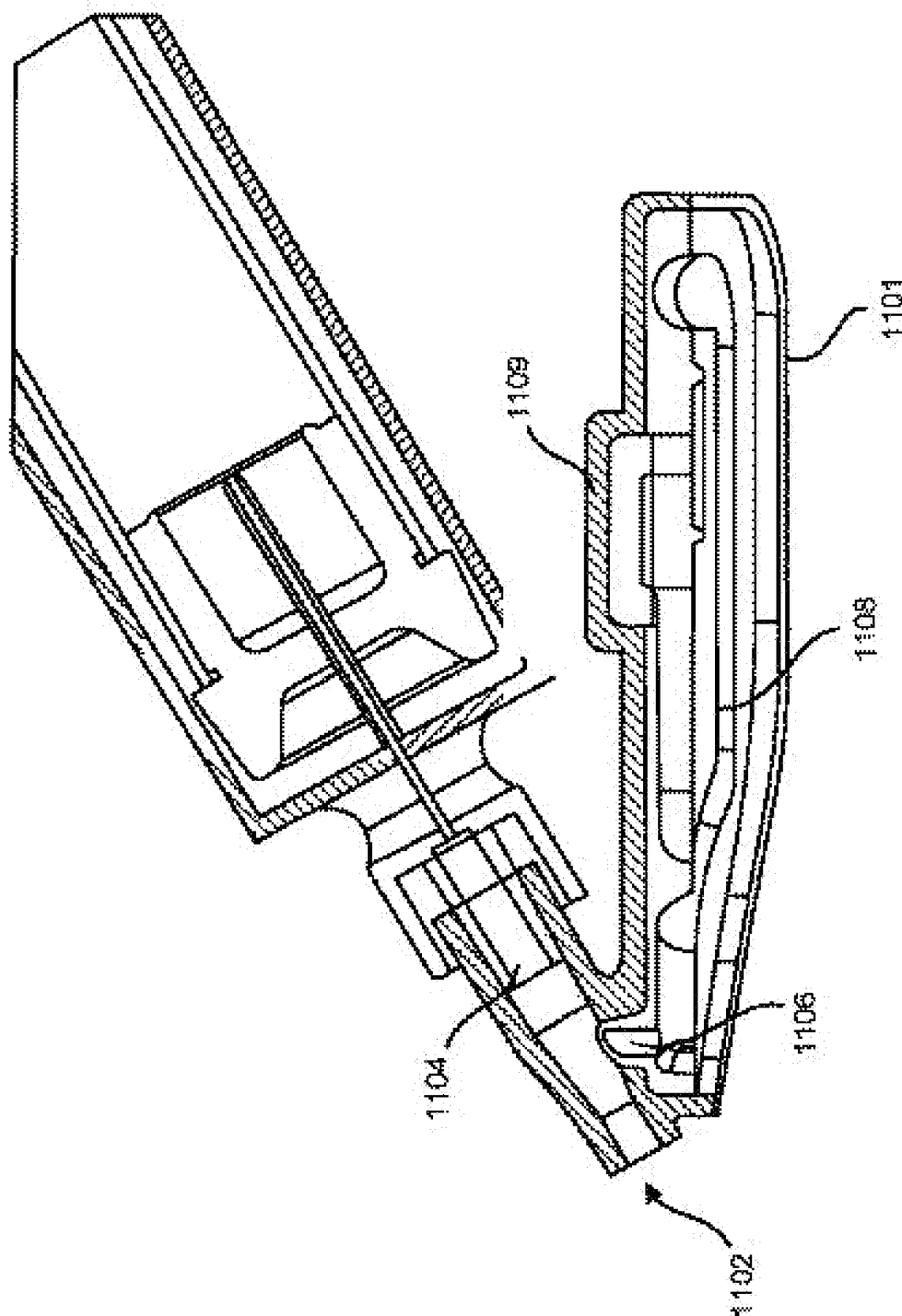
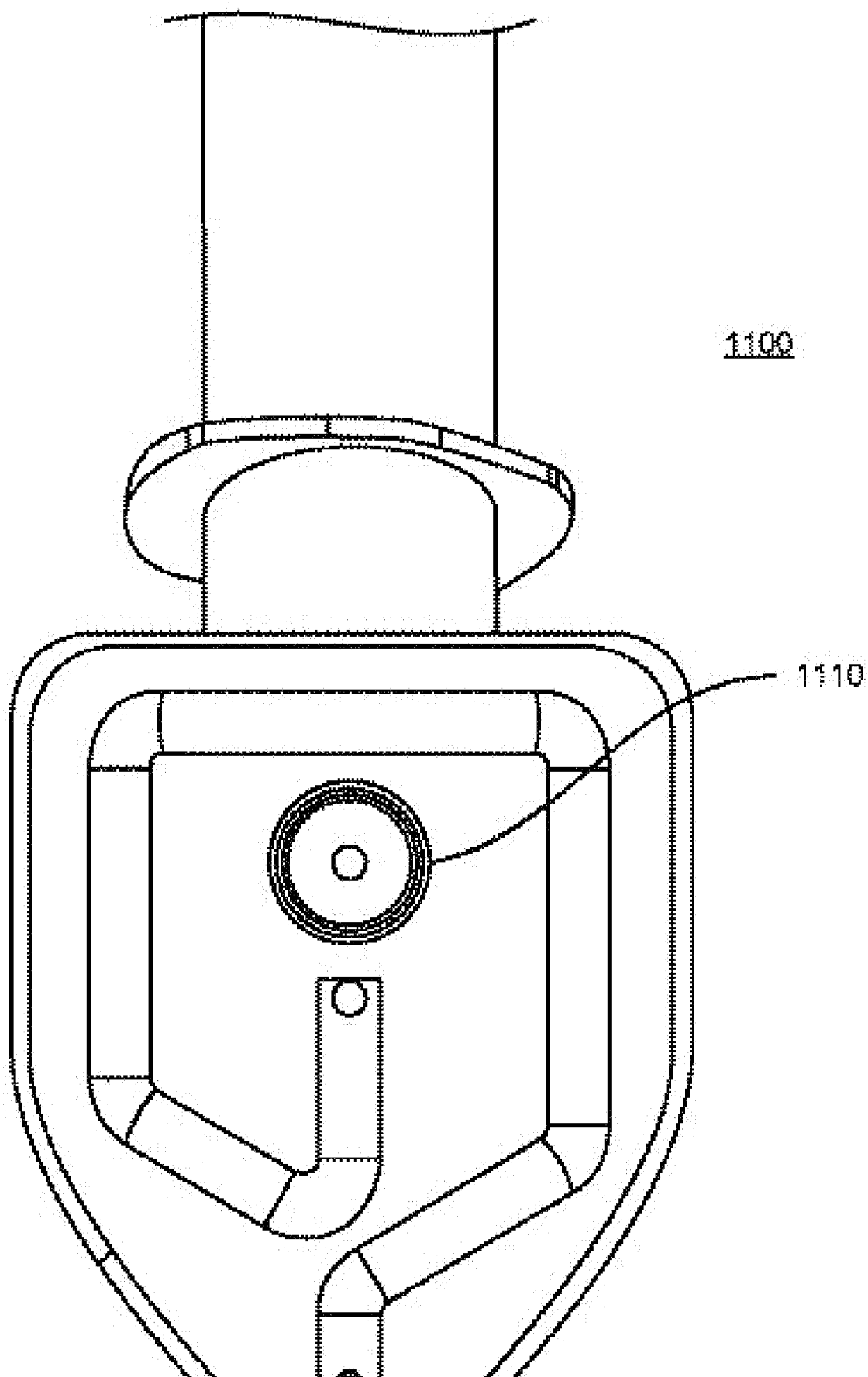


FIG. 11B

[Fig. 11C]



[Fig. 11D]

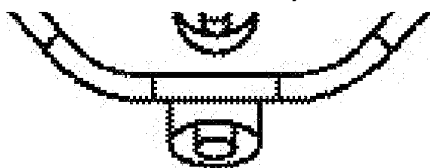
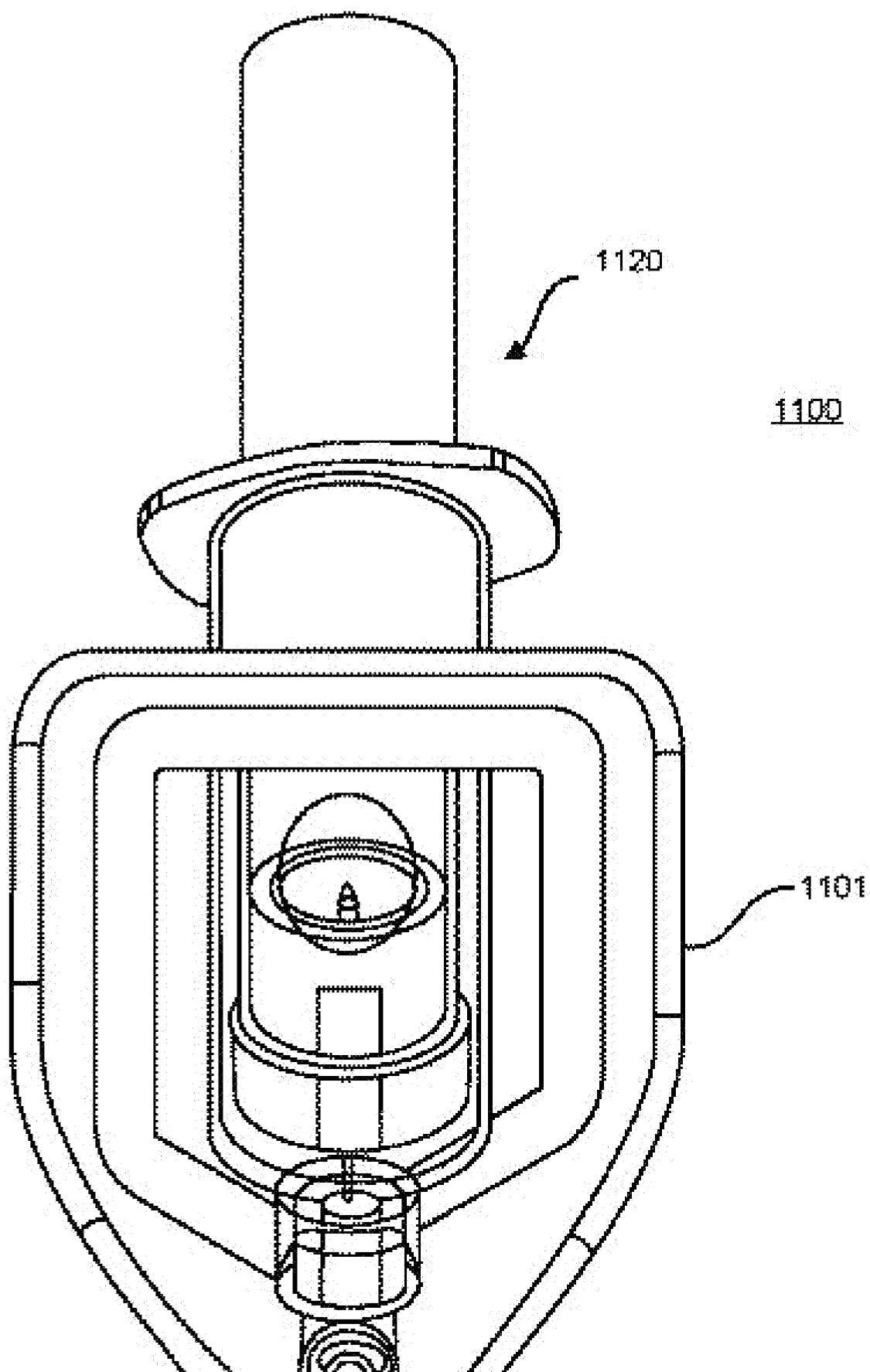


FIG. 11C



[Fig. 11E]

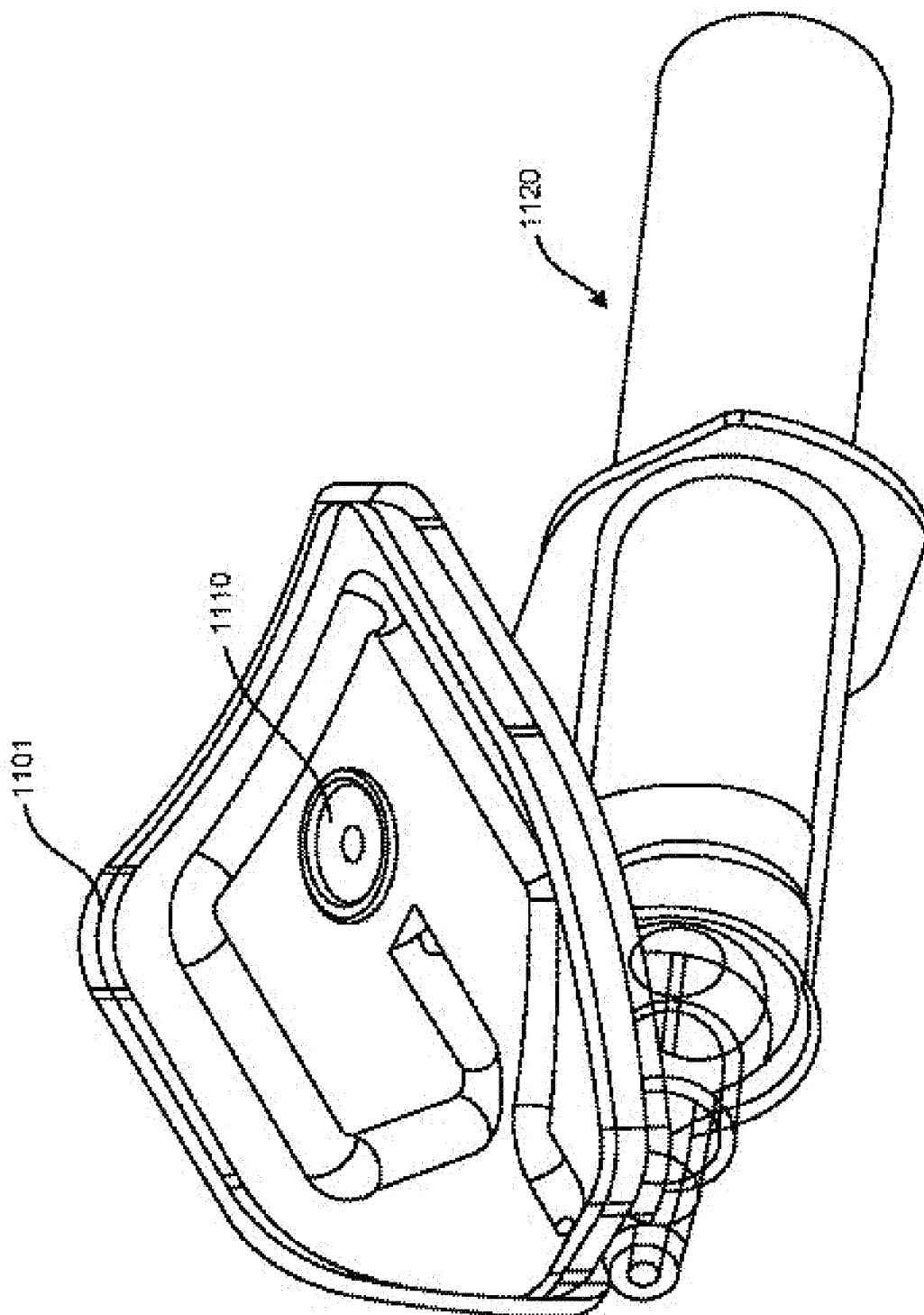
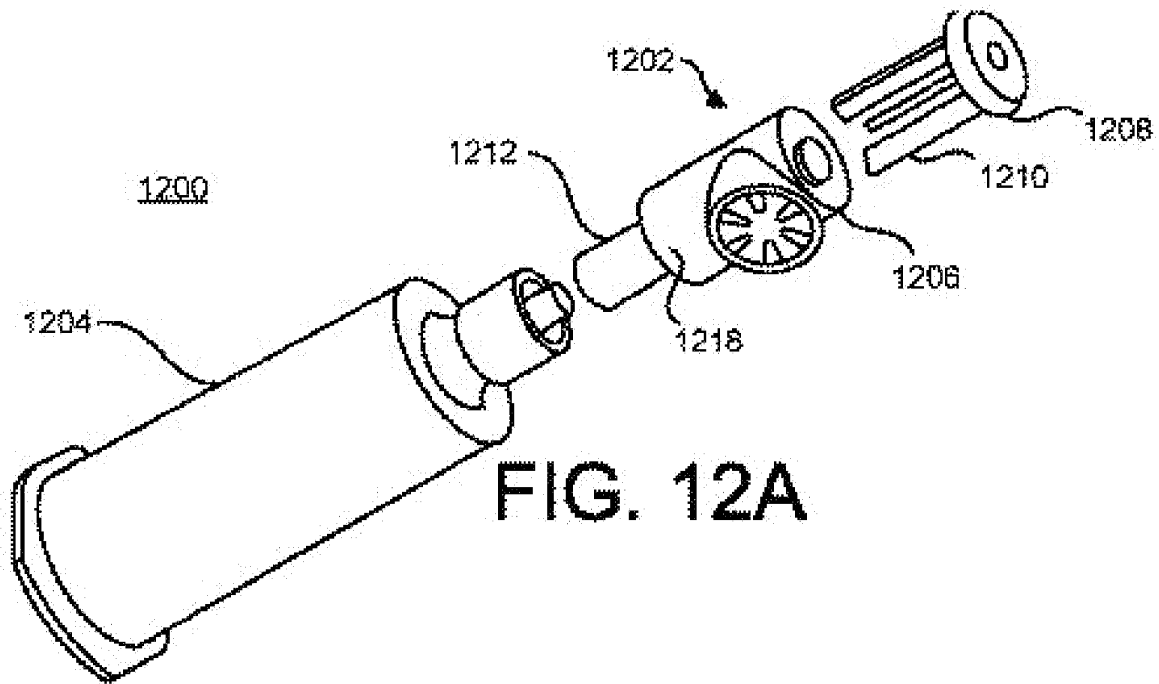
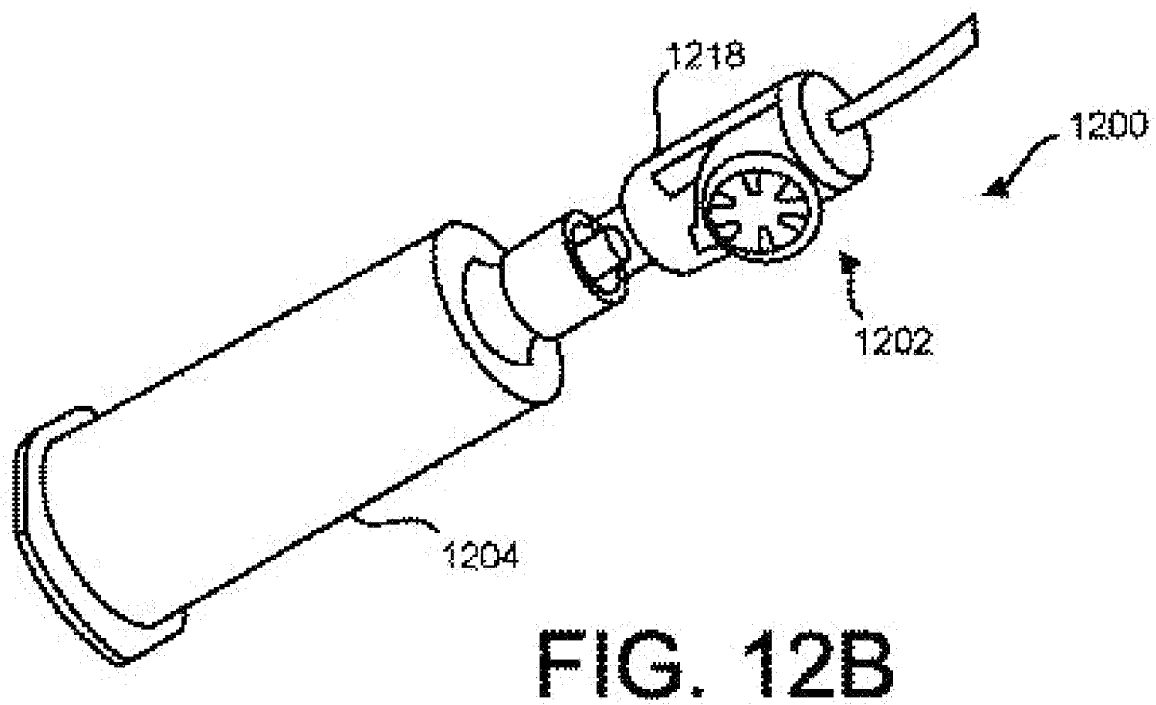


FIG. 11E

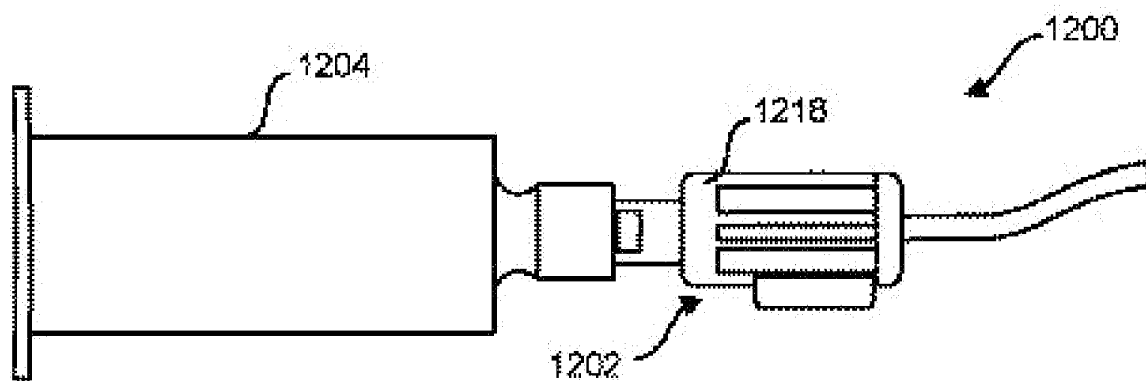
[Fig. 12A]



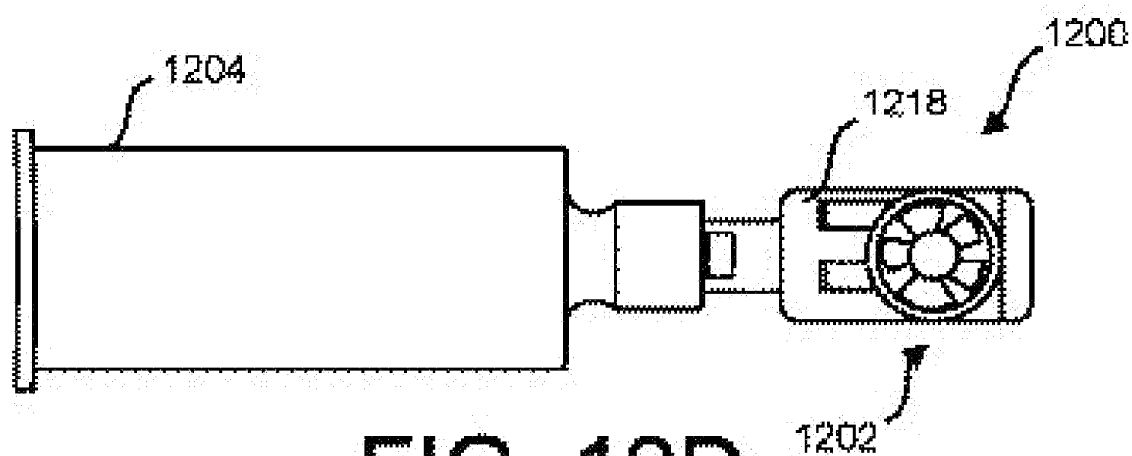
[Fig. 12B]



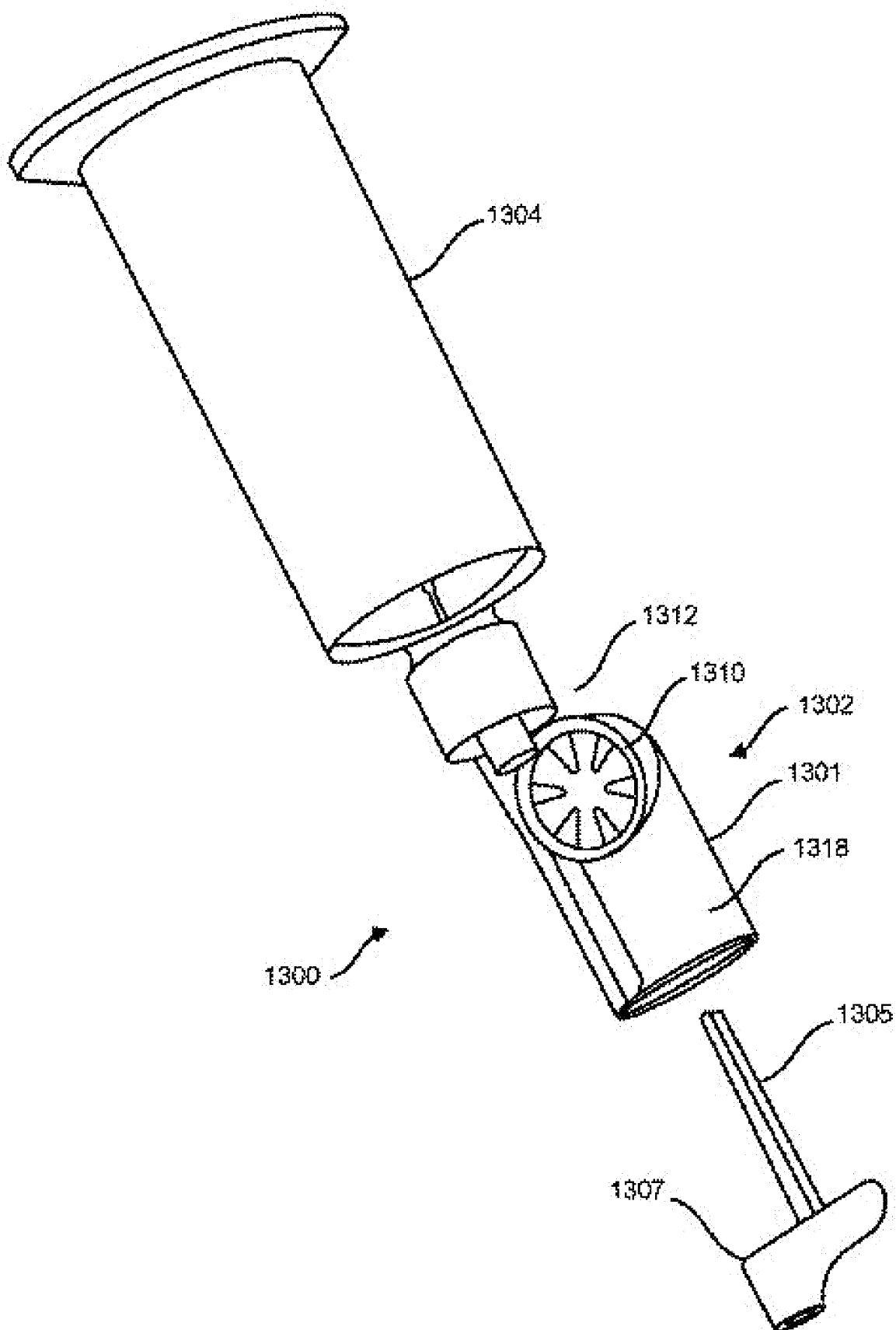
[Fig. 12C]



[Fig. 12D]

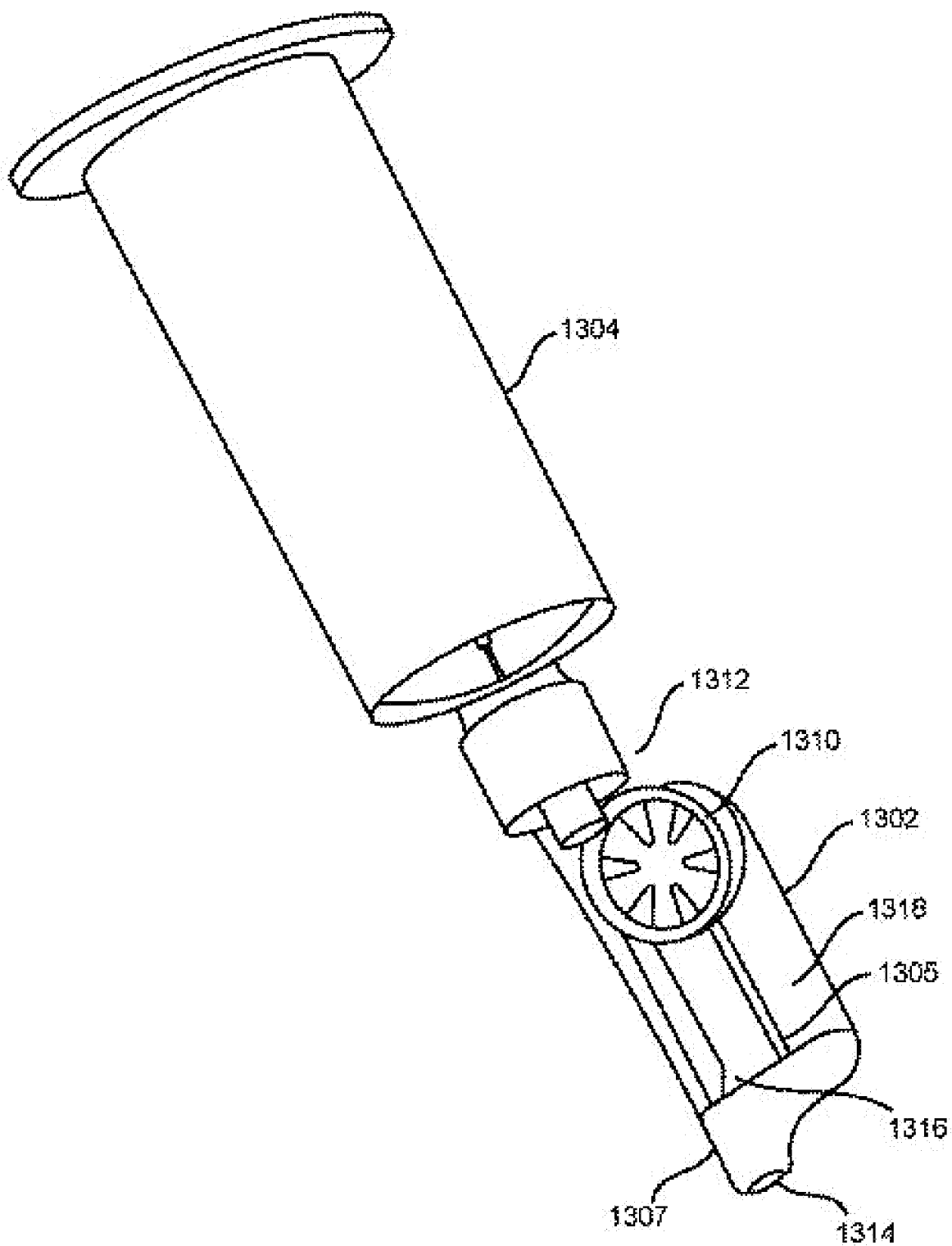


[Fig. 13A]

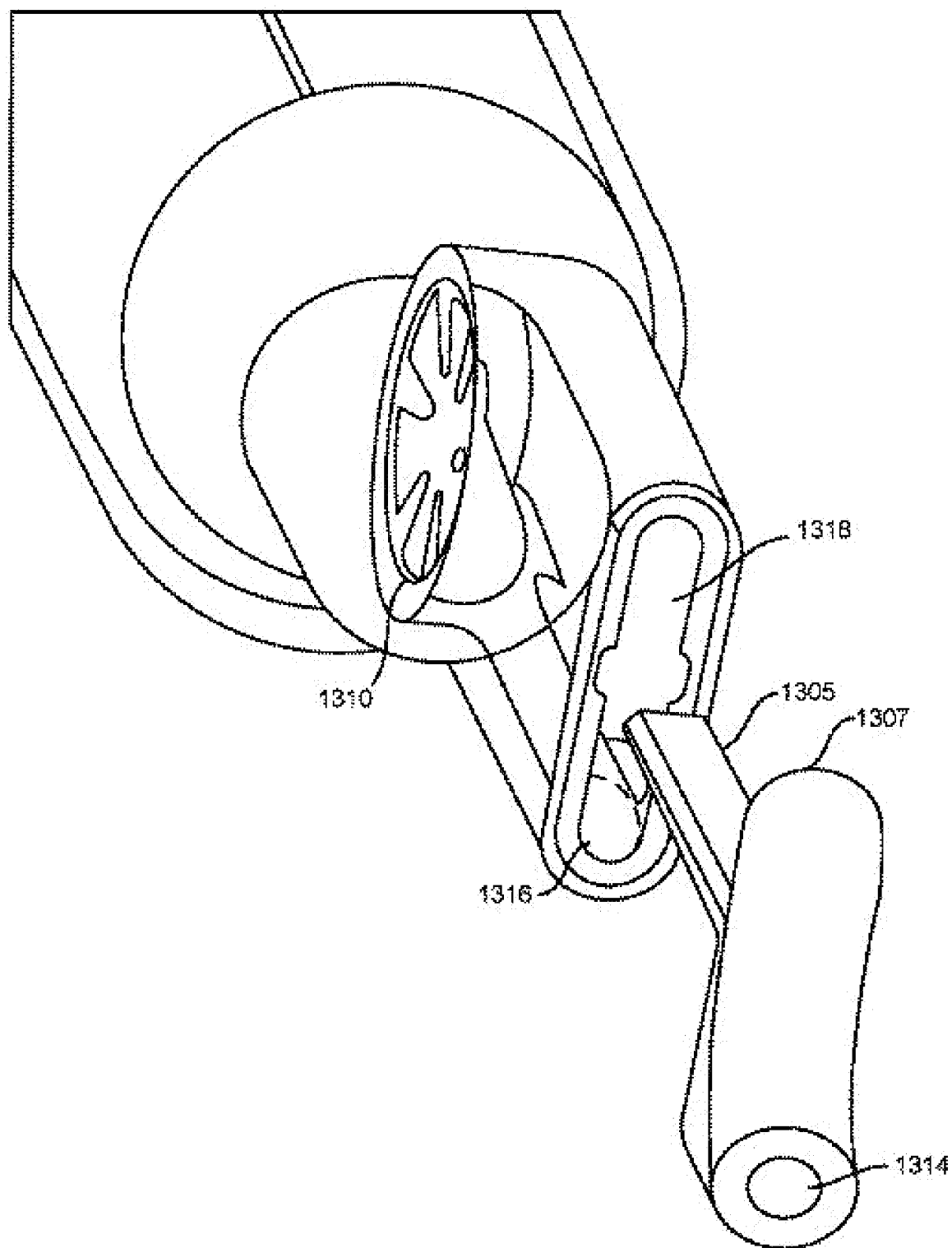


[Fig. 13B]

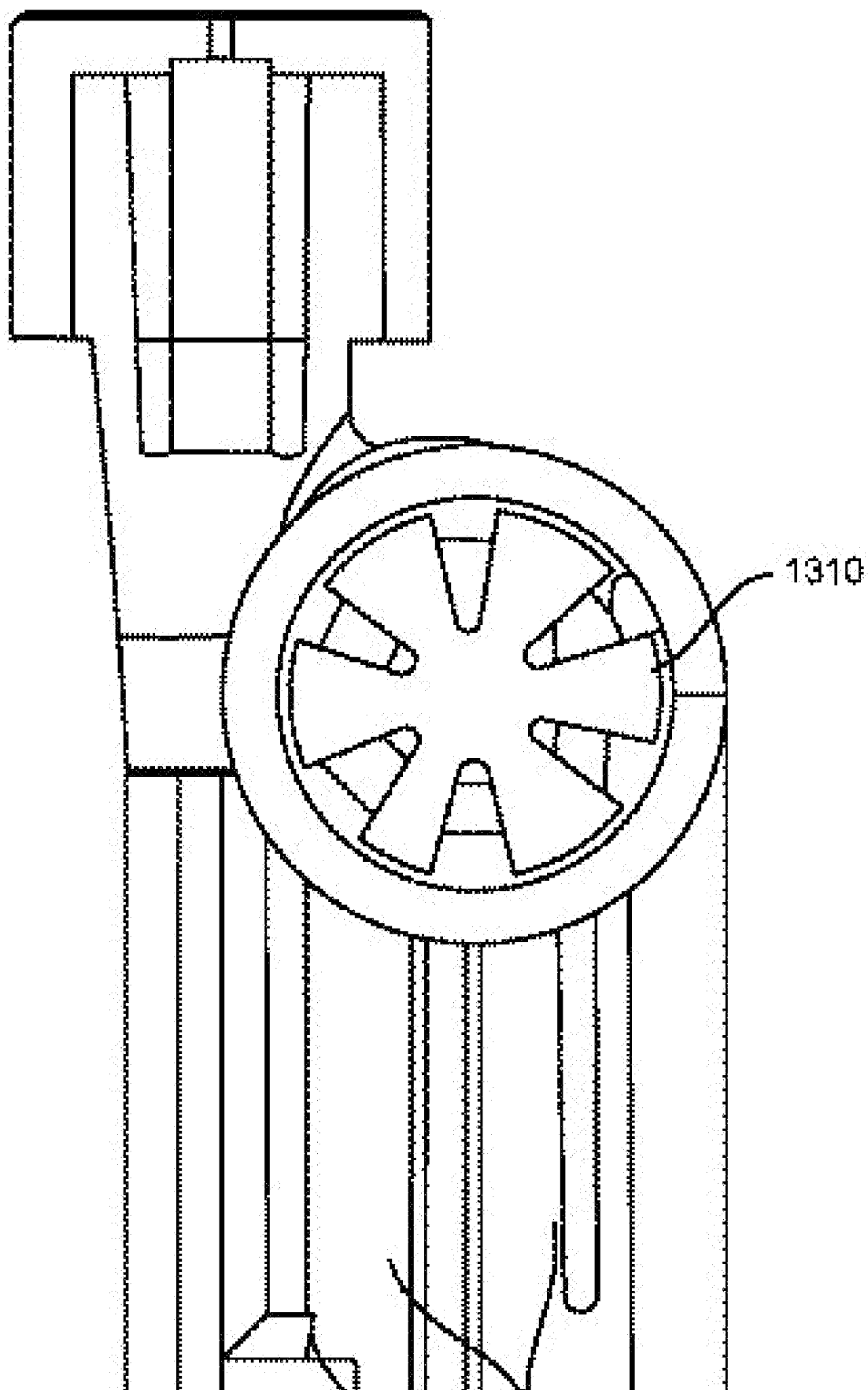
FIG. 13A

**FIG. 13B**

[Fig. 13C]

**FIG. 13C**

[Fig. 13D]



[Fig. 14A]

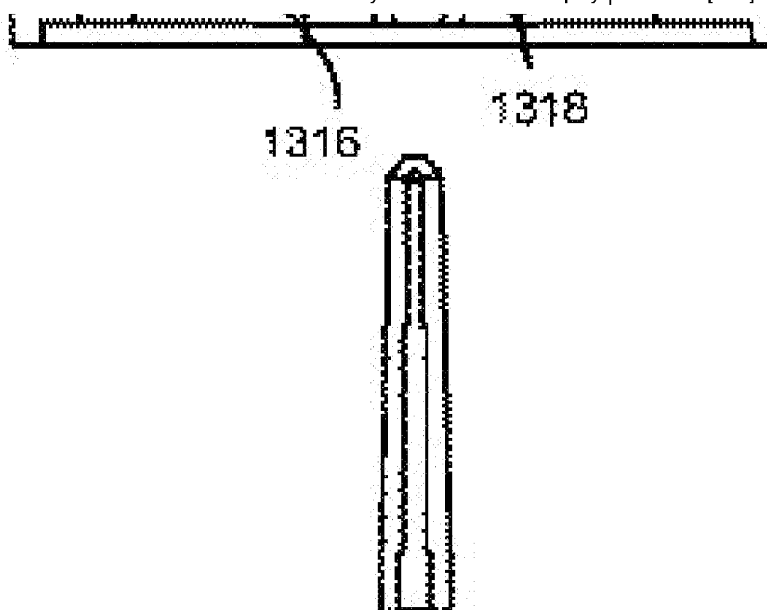
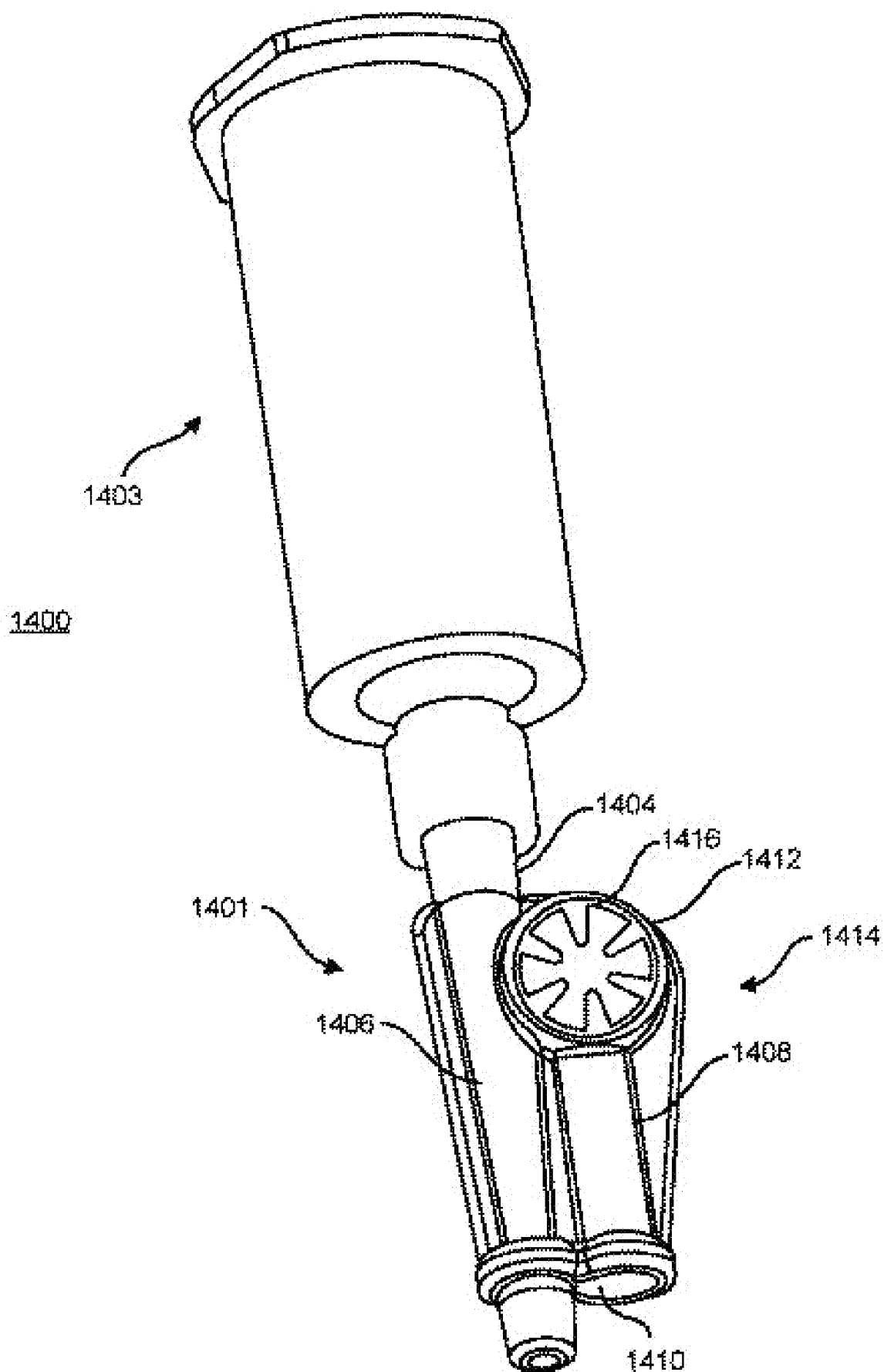


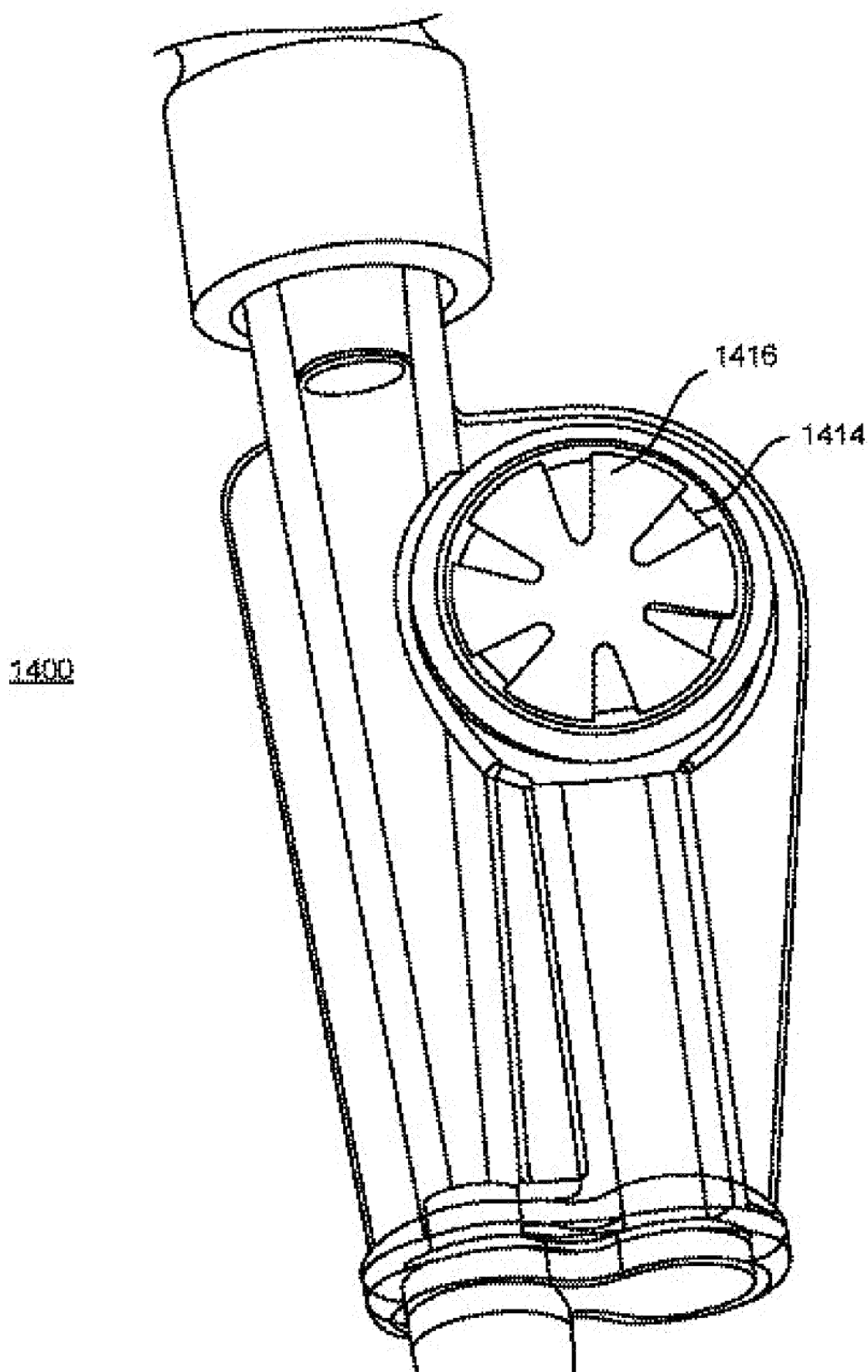
FIG. 13D



[Fig. 14B]

1402

FIG. 14A



[Fig. 14C]



FIG. 14B

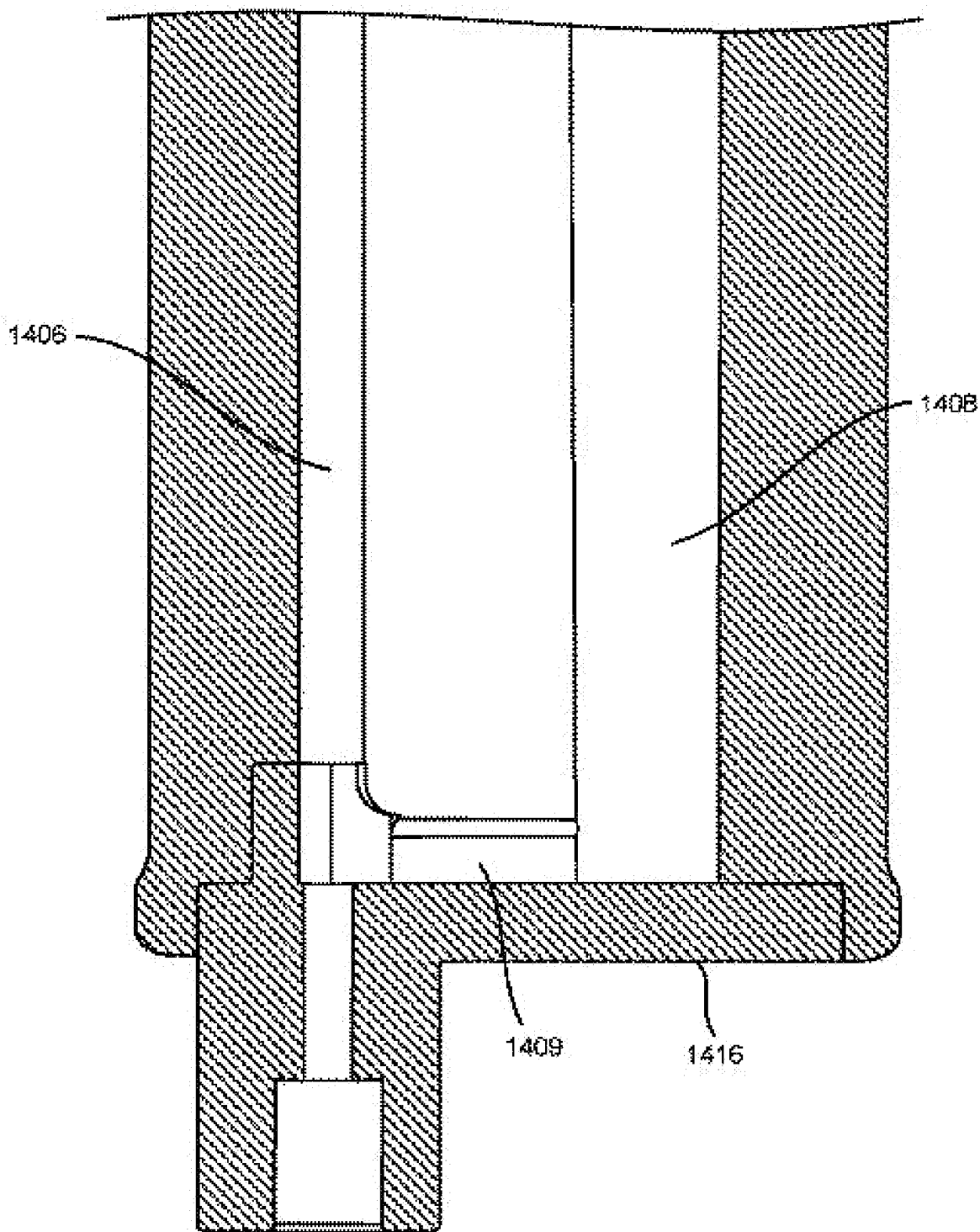
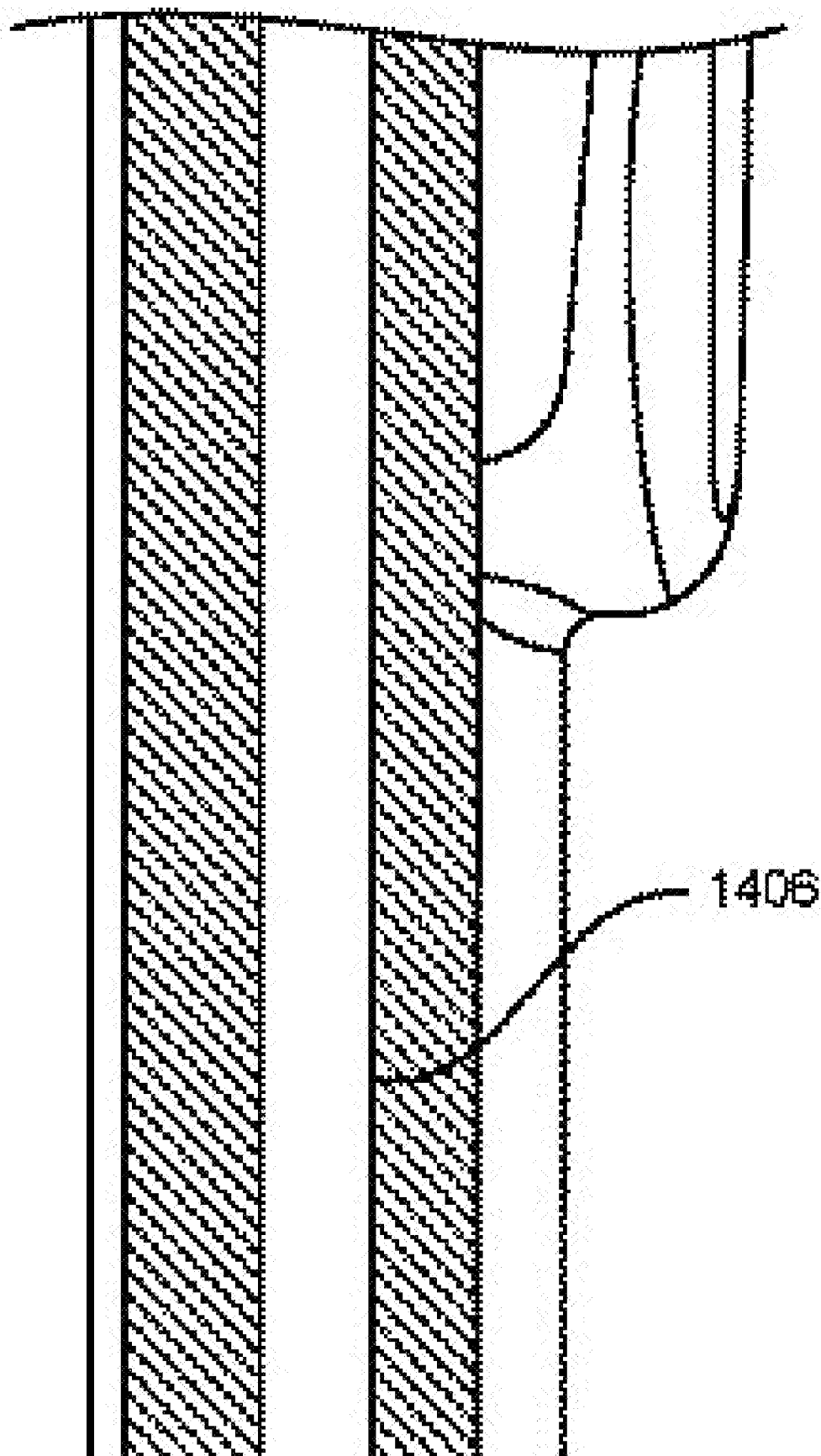


FIG. 14C

[Fig. 14D]



[Fig. 14E]

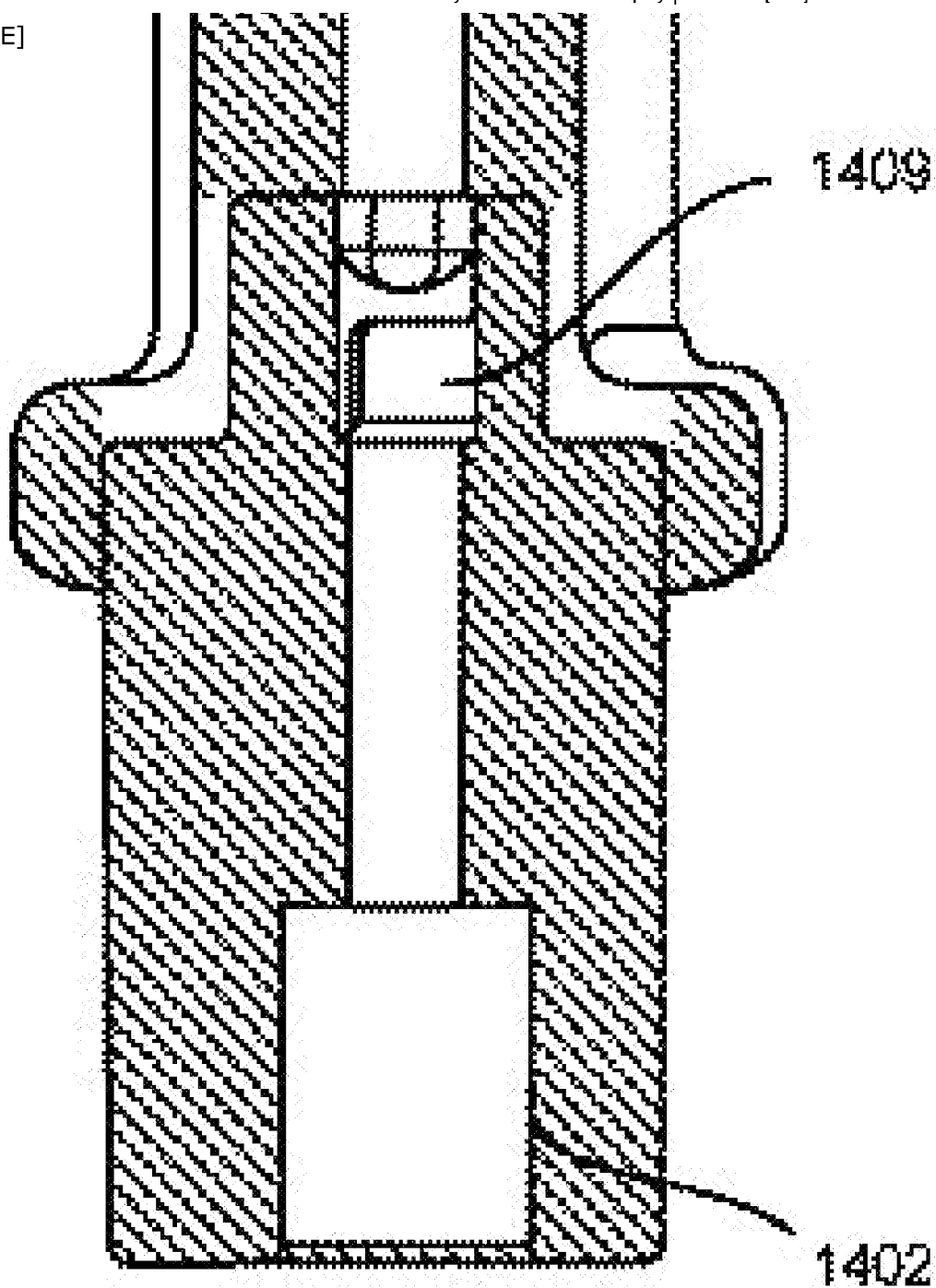


FIG. 14D

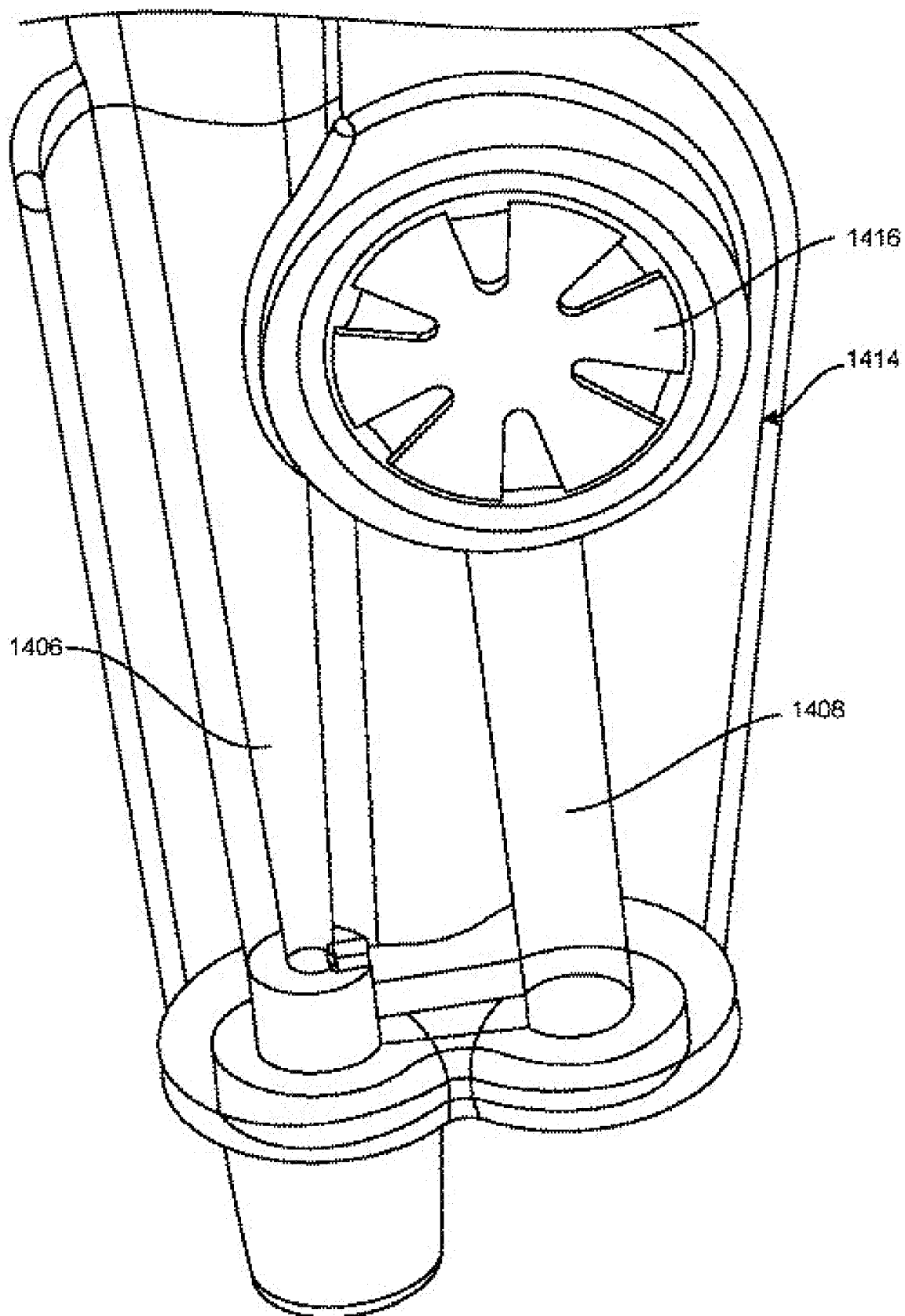


FIG. 14E

[Fig. 15A]

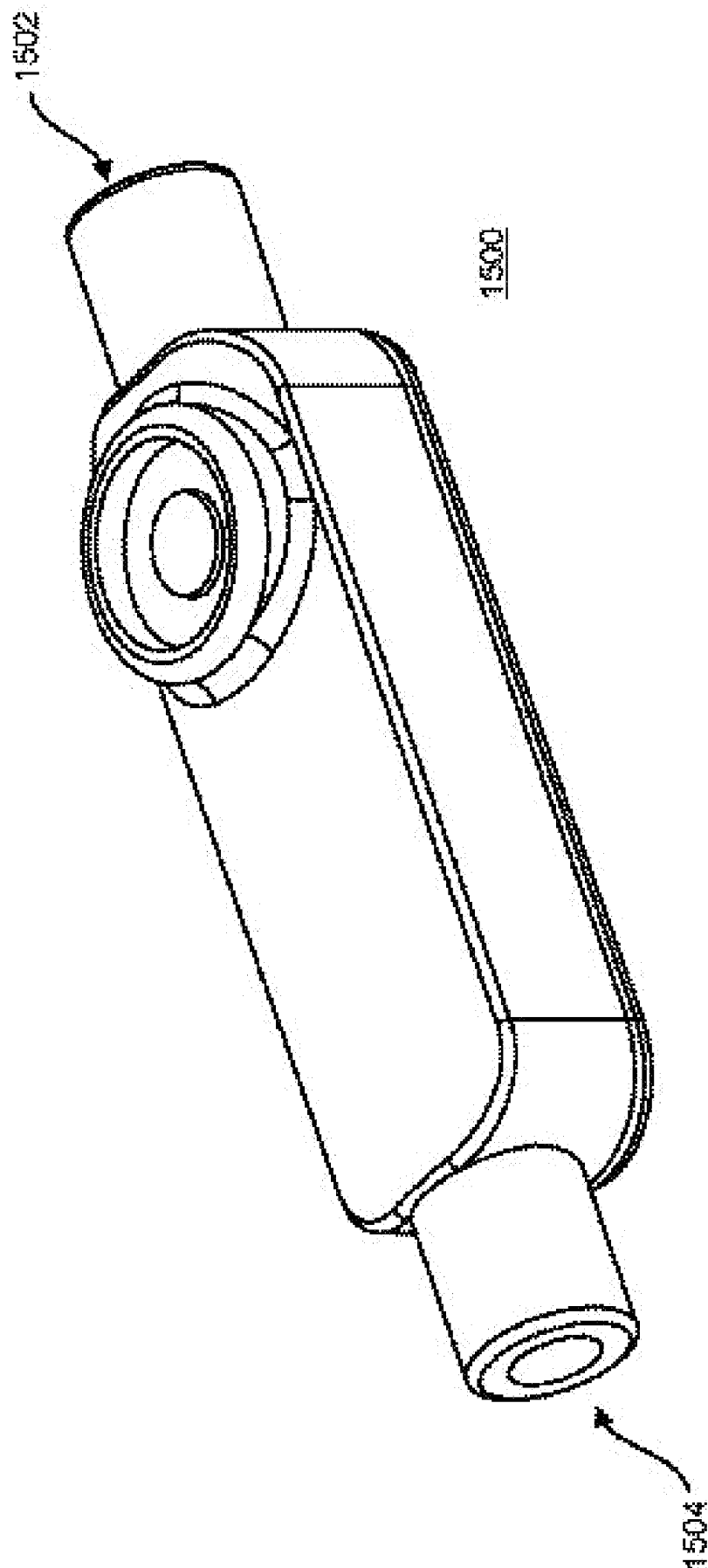


FIG. 15A

[Fig. 15B]

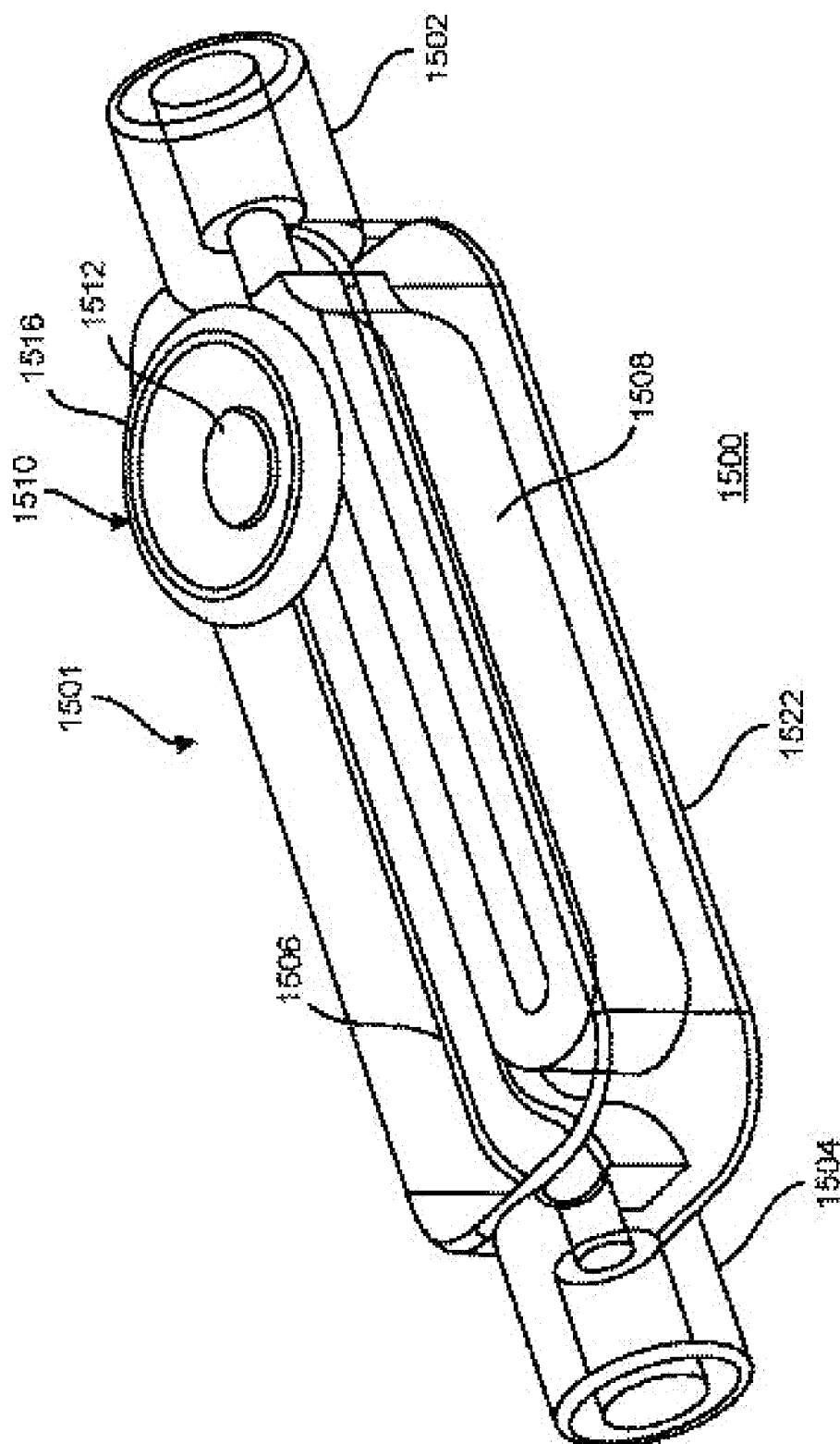


FIG. 15B

[Fig. 15C]

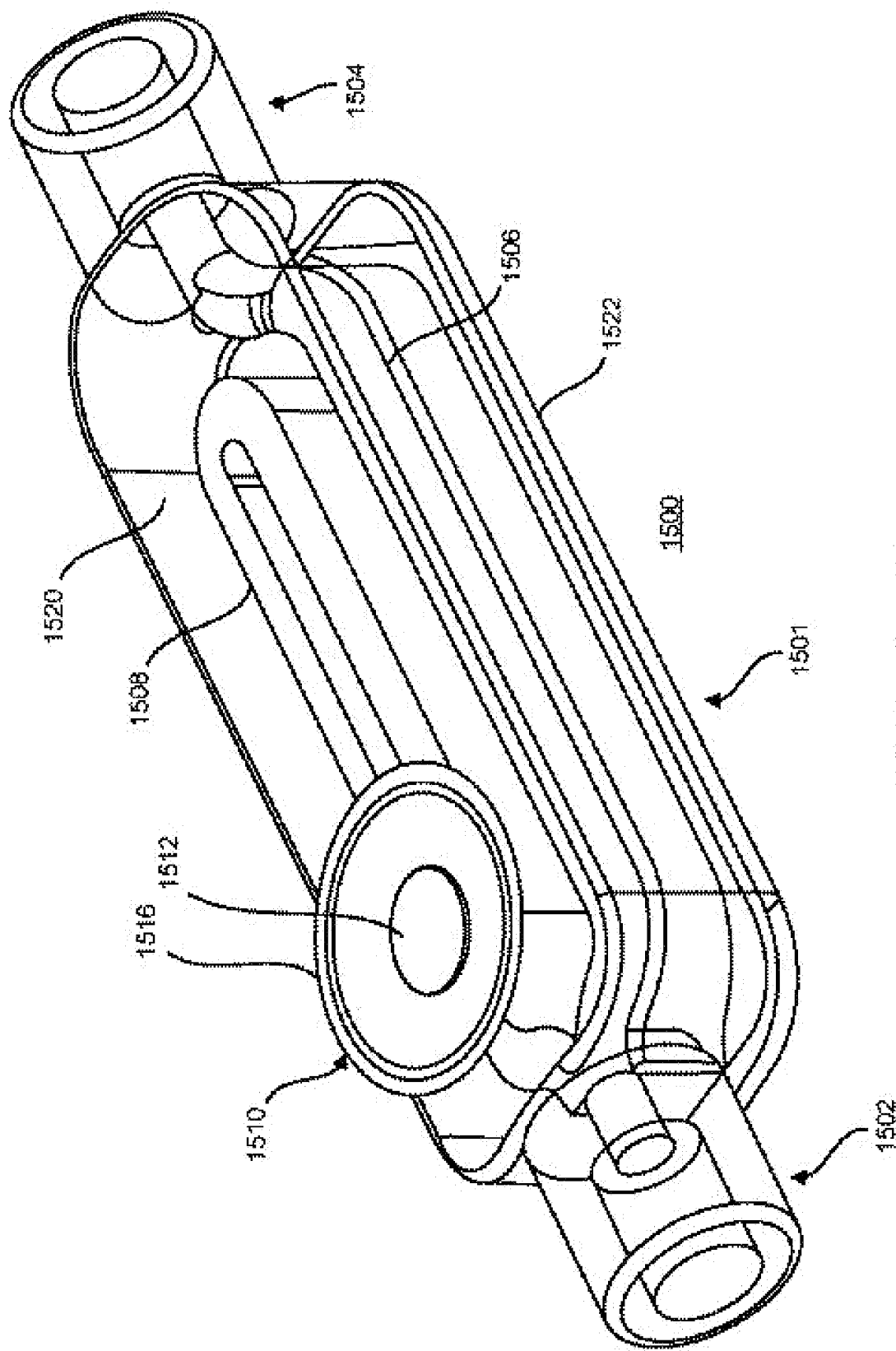


FIG. 15C

[Fig. 15D]

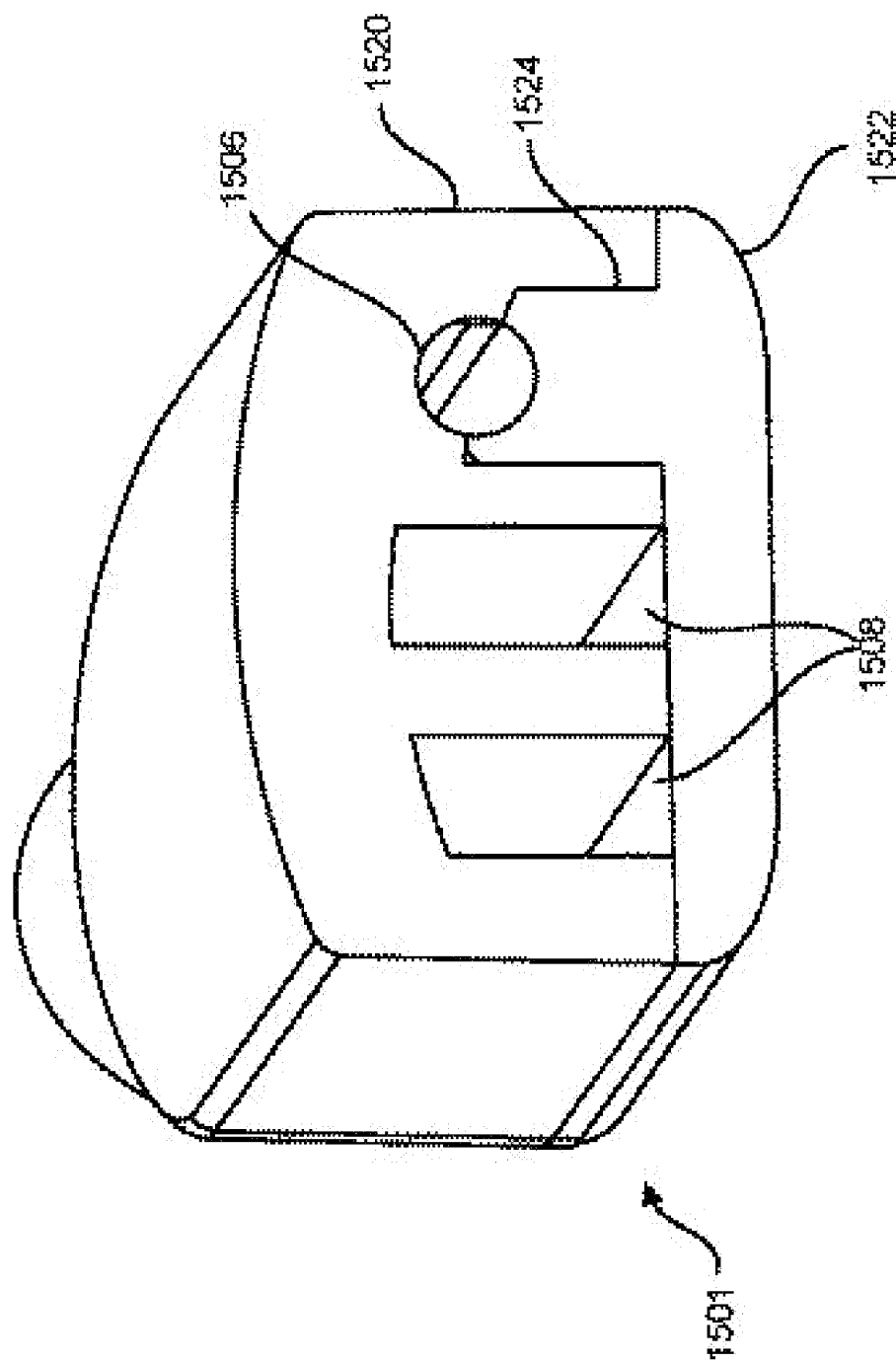


FIG. 15D

[Fig. 15E]

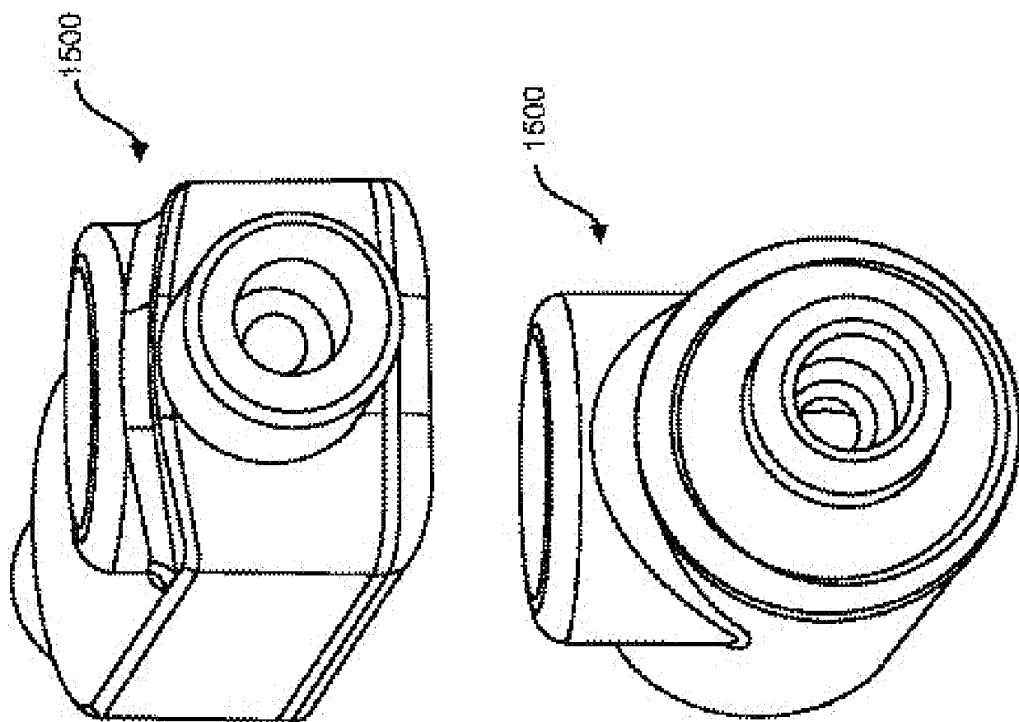
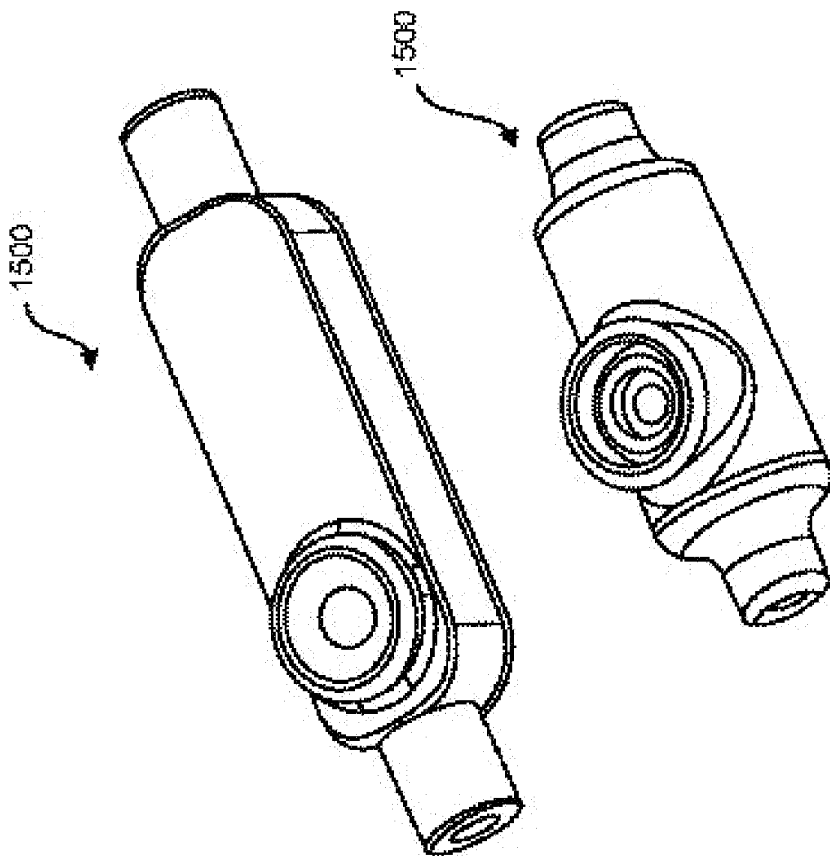


FIG. 15E

[Fig. 15F]



[Fig. 15G]

FIG. 15F

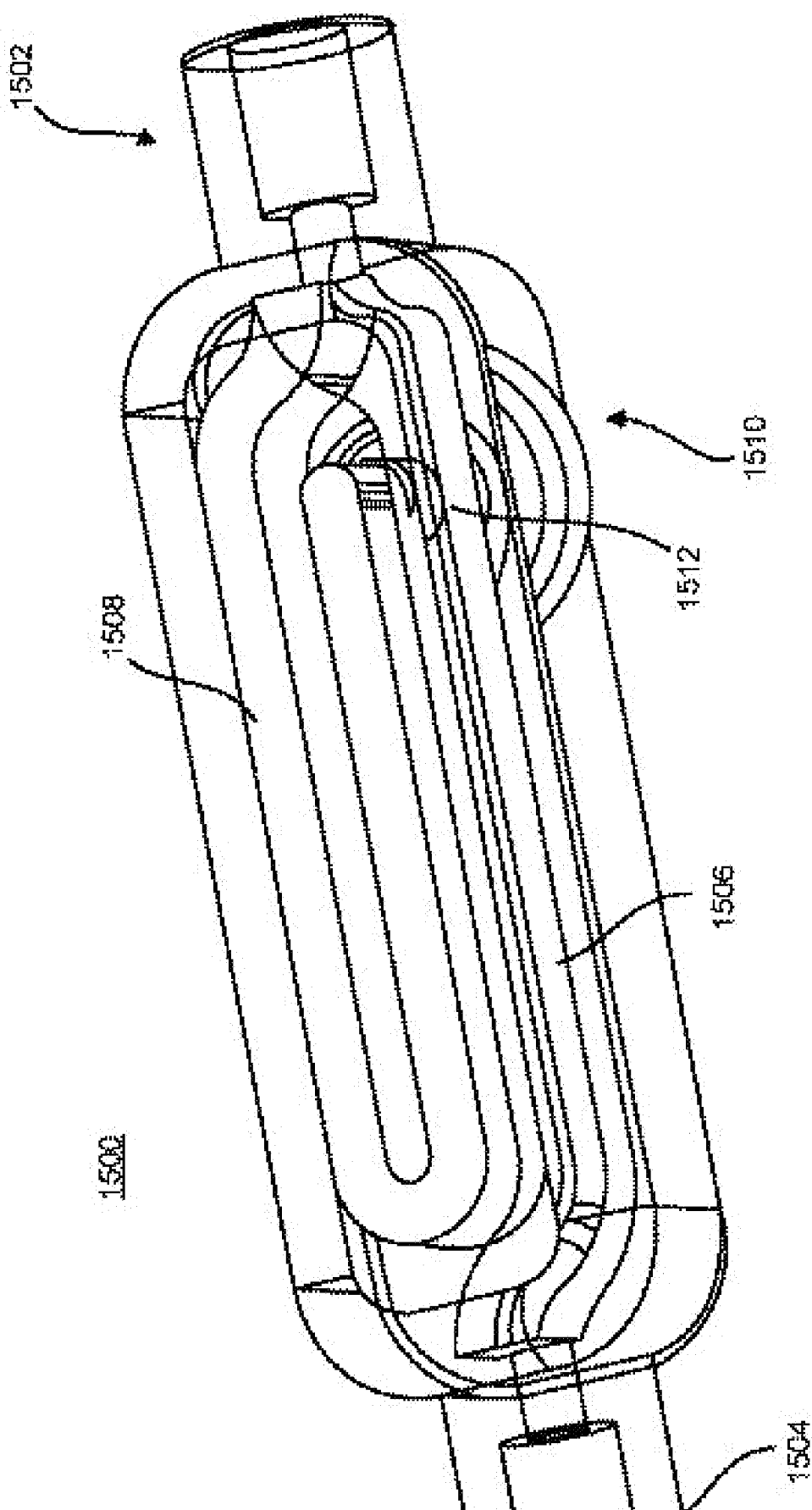


FIG. 15G

[Fig. 16A]



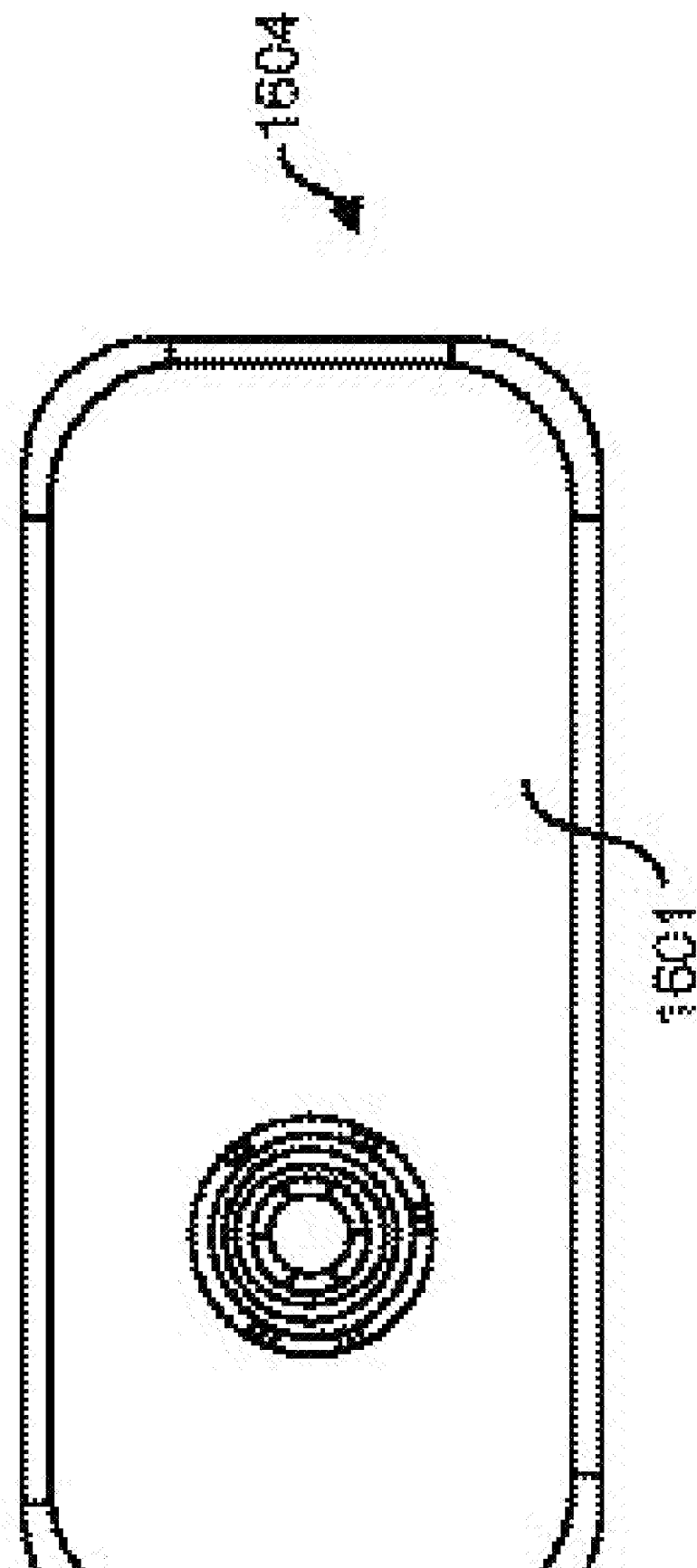
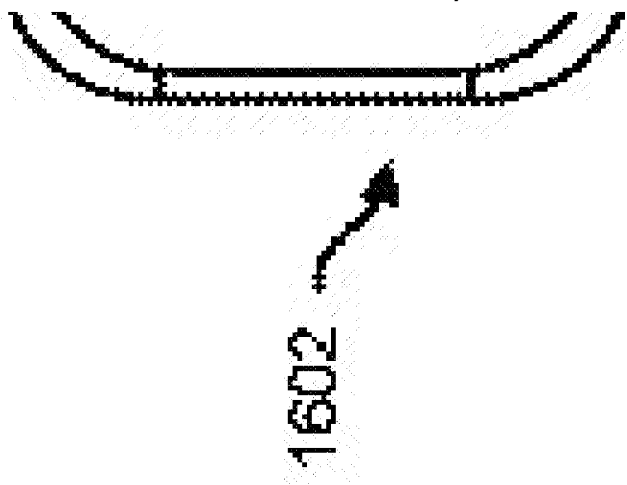


FIG. 16A

[Fig. 16B]



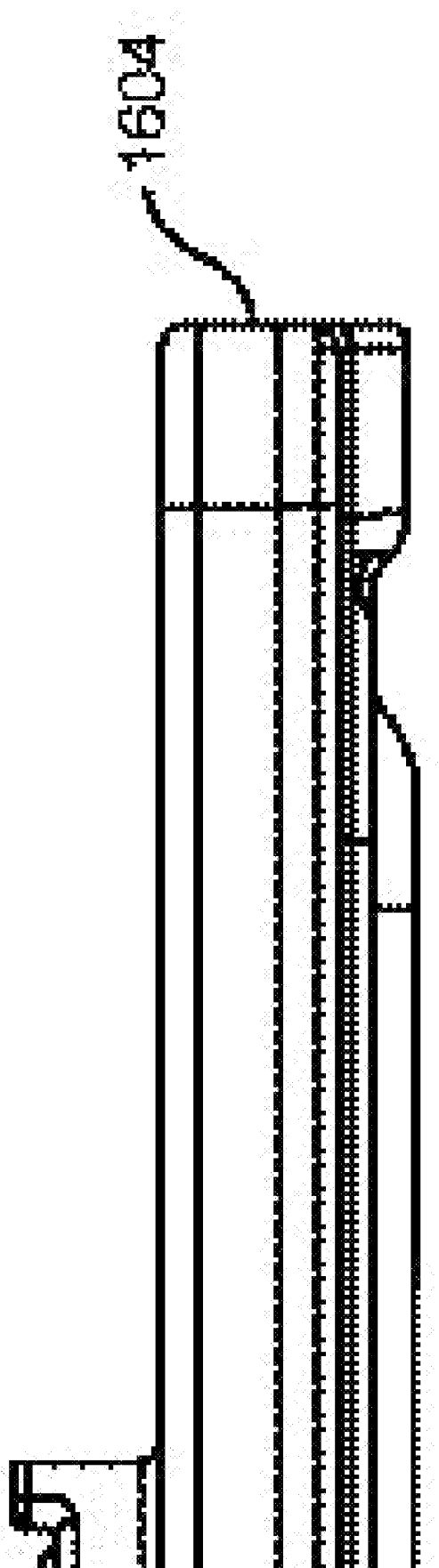


FIG. 16B

[Fig. 16C]

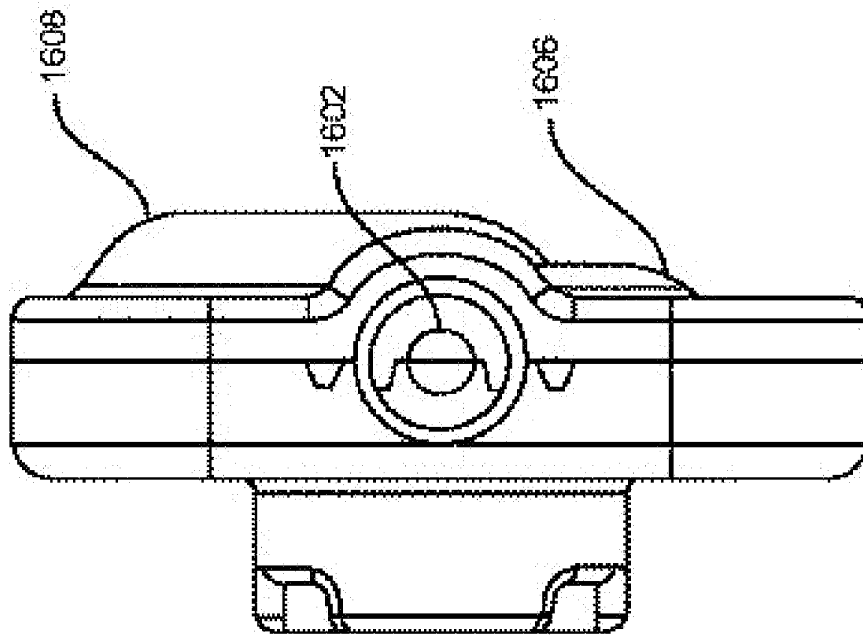


FIG. 16C

[Fig. 16D]

1602

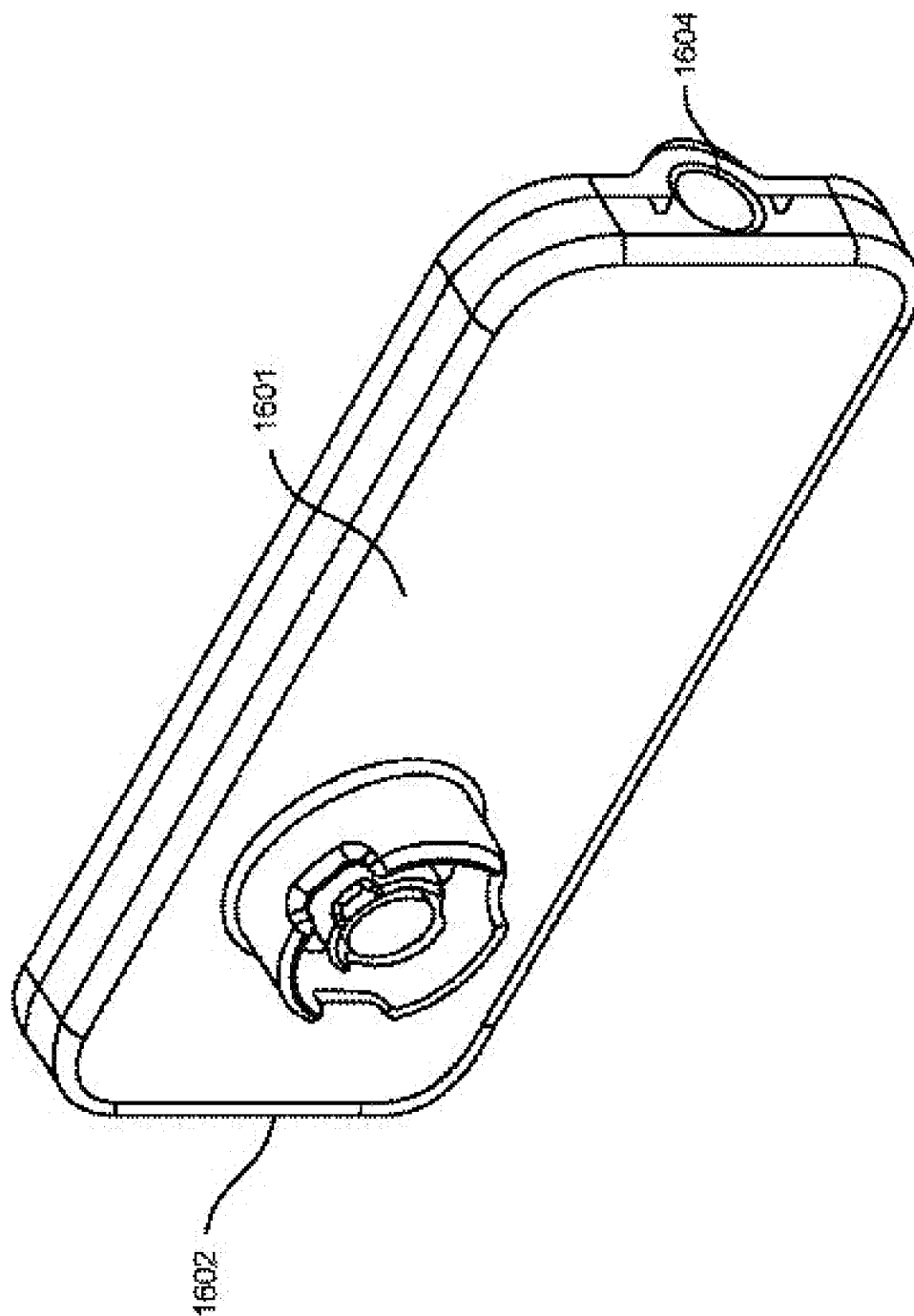


FIG. 16D

[Fig. 17A]

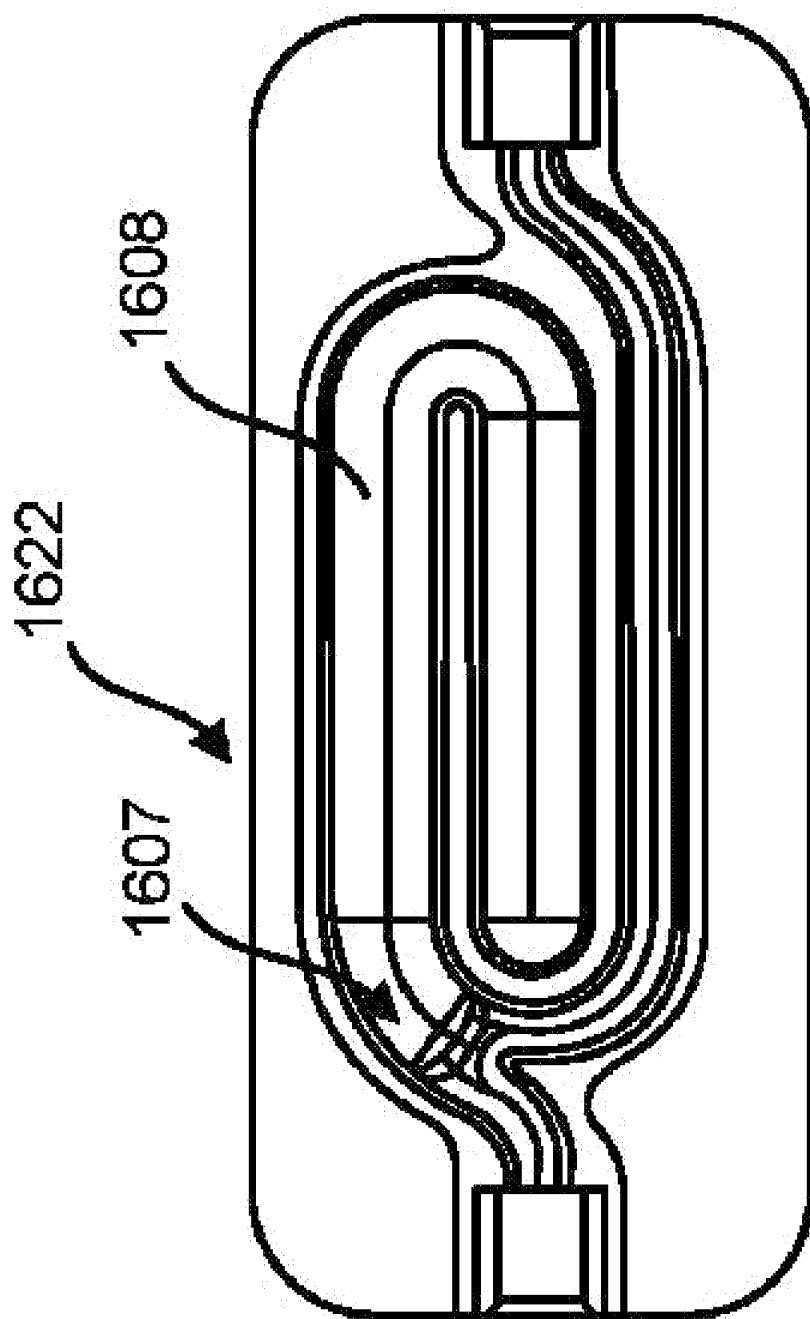


FIG. 17A

[Fig. 17B]

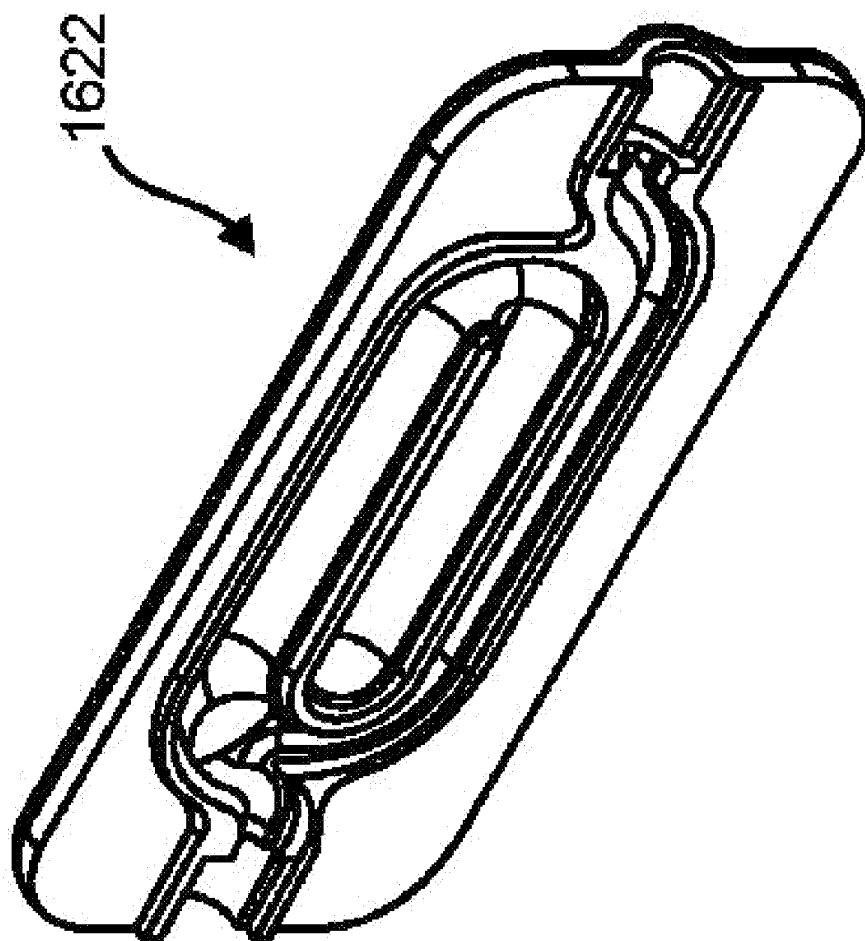


FIG. 17B

[Fig. 17C]

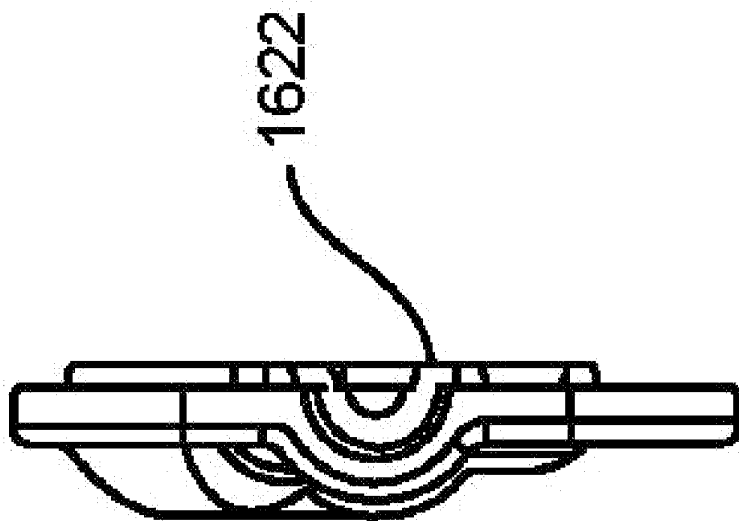
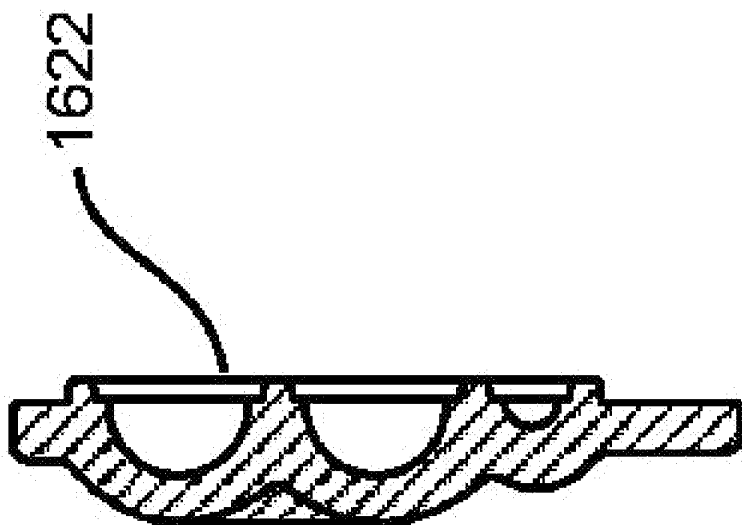


FIG. 17C

[Fig. 17D]



[Fig. 17E]

FIG. 17D



FIG. 17E

[Fig. 18A]

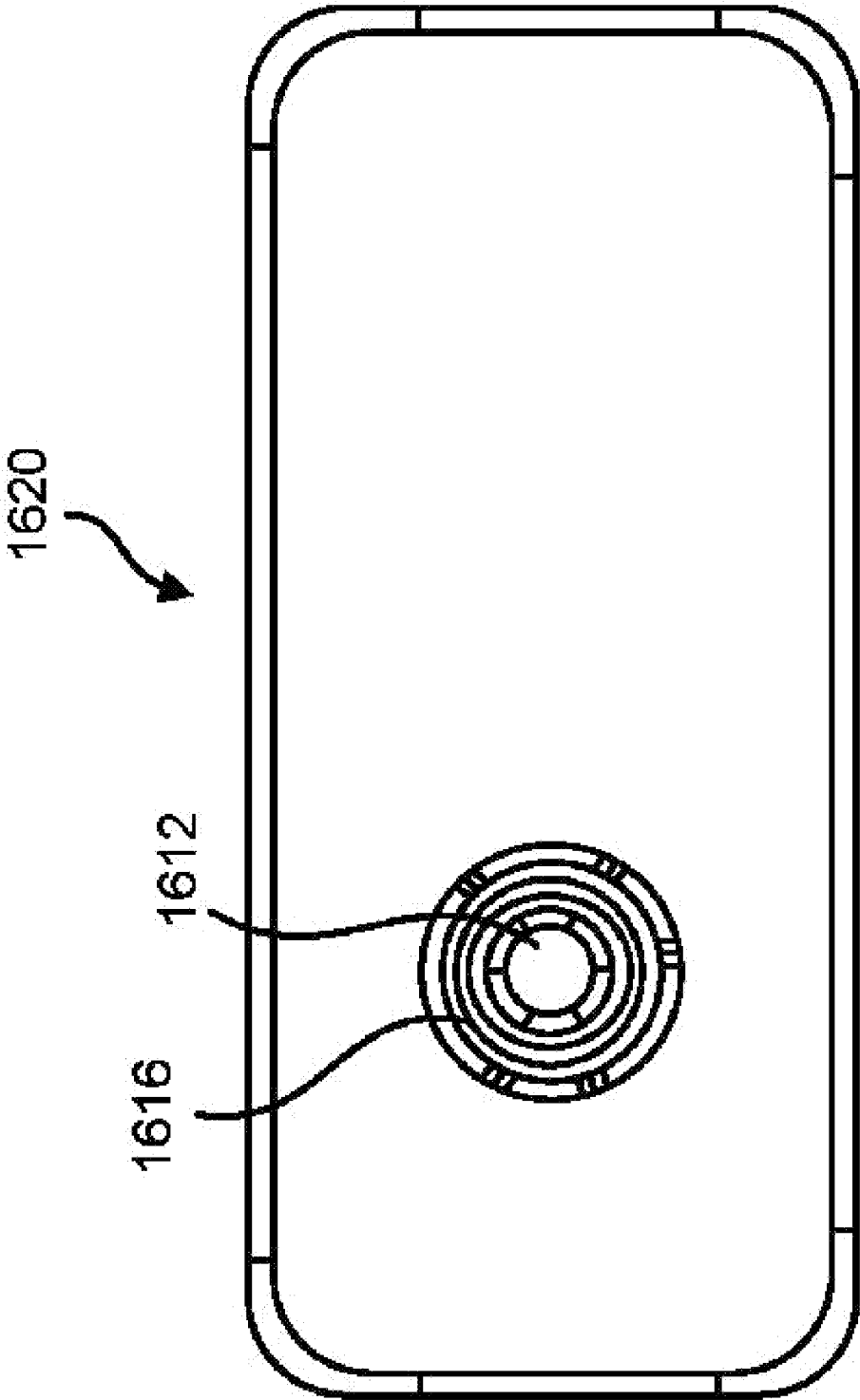


FIG. 18A

[Fig. 18B]

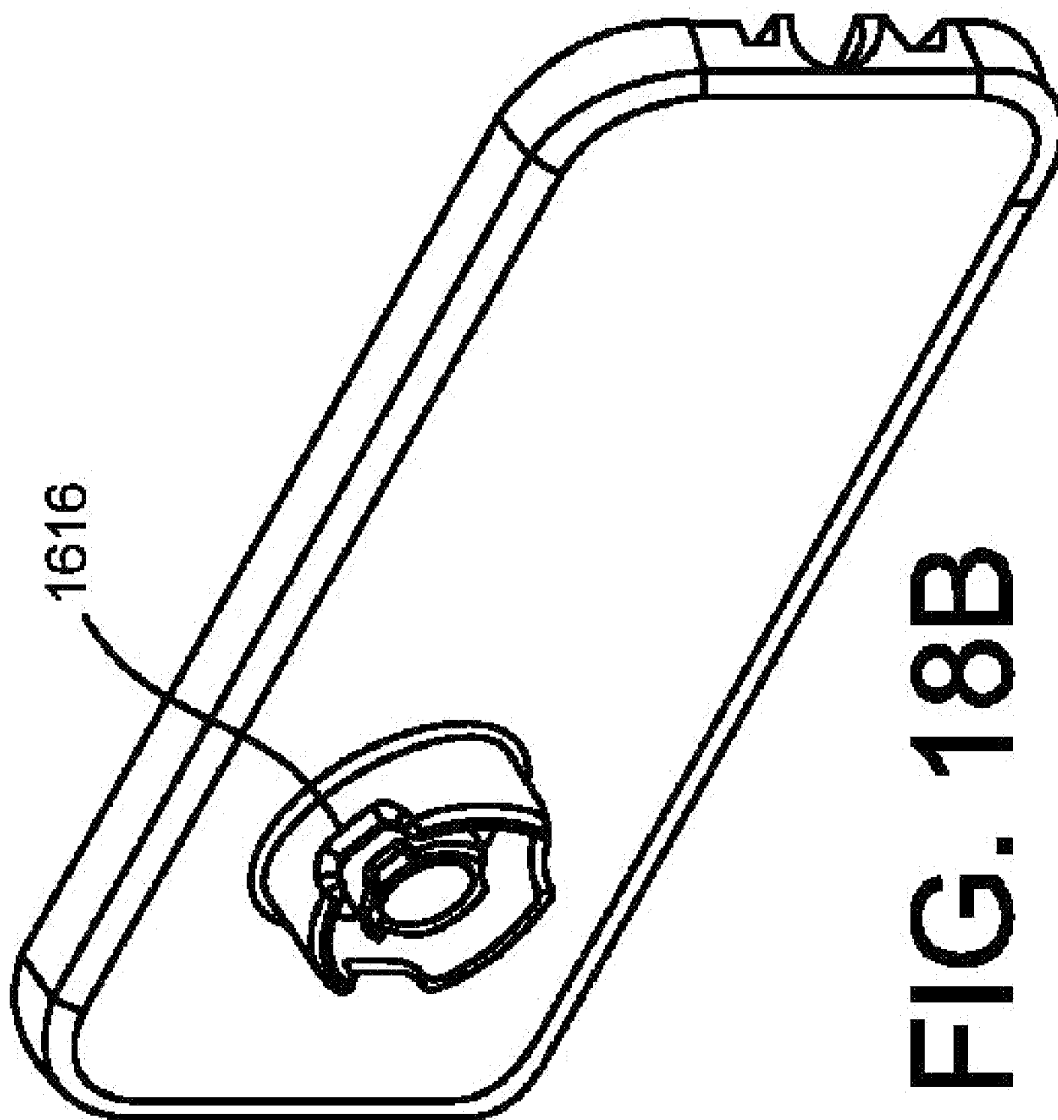


FIG. 18B

[Fig. 18C]

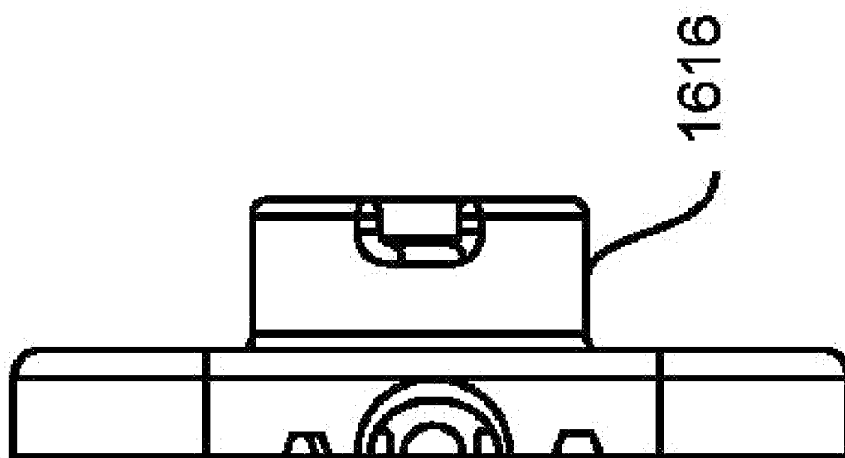


FIG. 18C

[Fig. 18D]

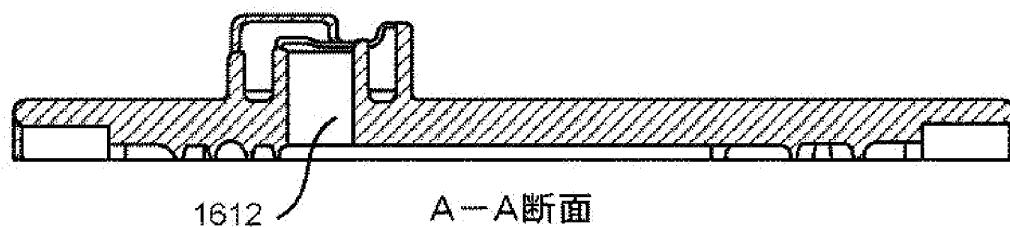
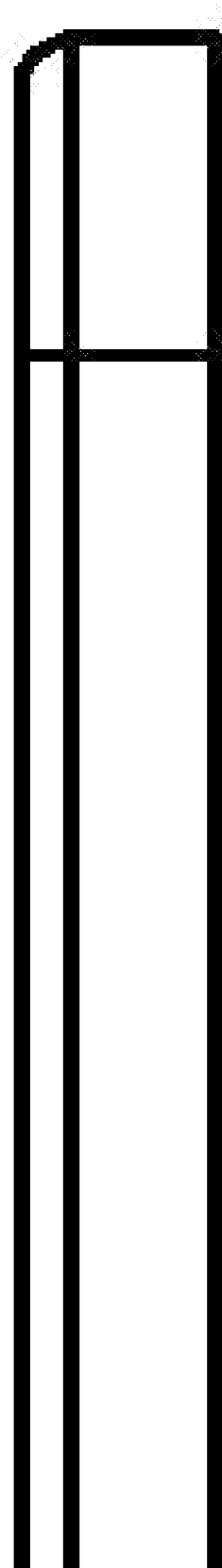
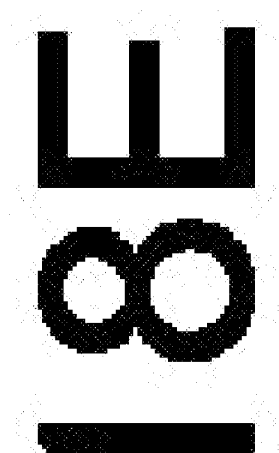


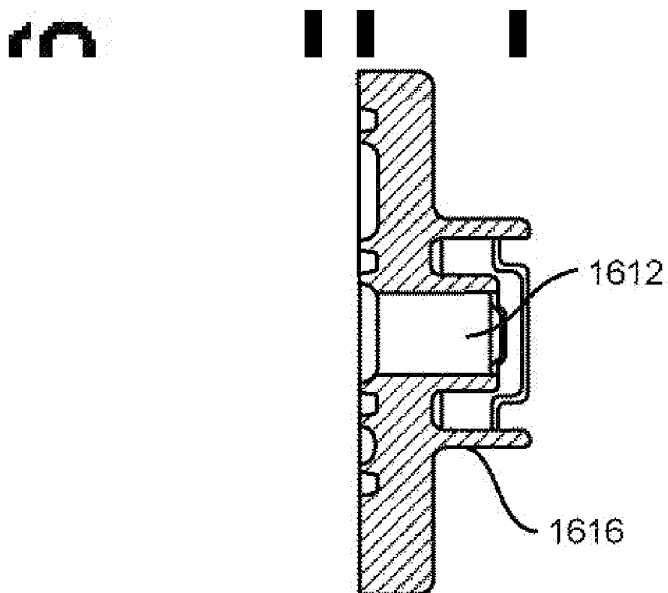
FIG. 18D

[Fig. 18E]

16



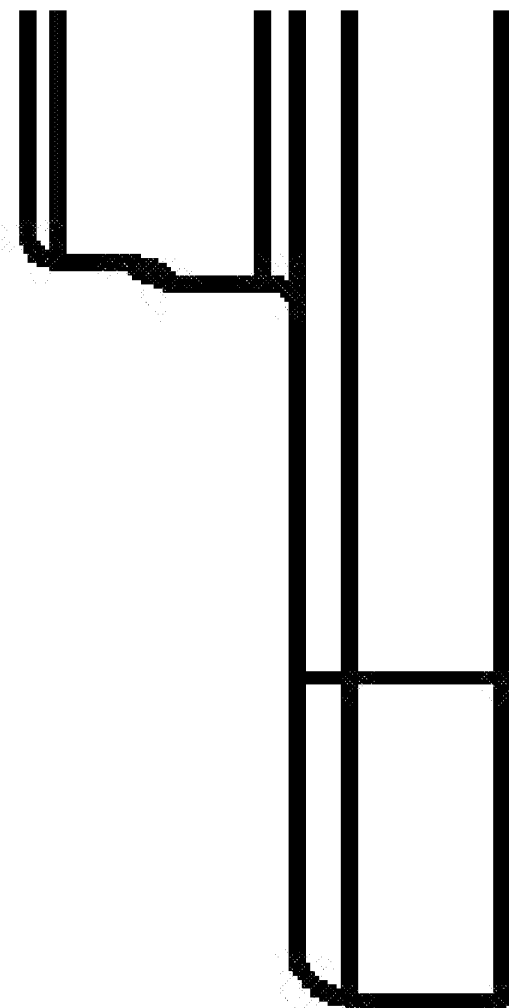
[Fig. 18F]



A-A断面

FIG. 18F

[Fig. 19A]



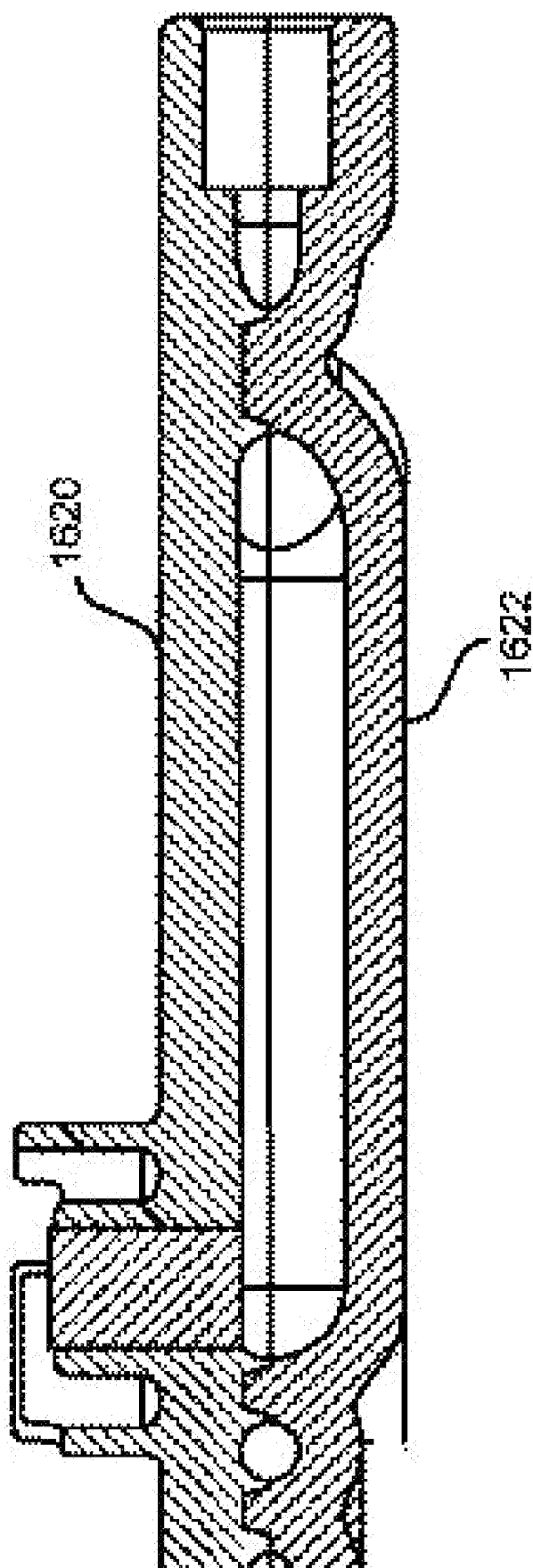


FIG. 19A

[Fig. 19B]

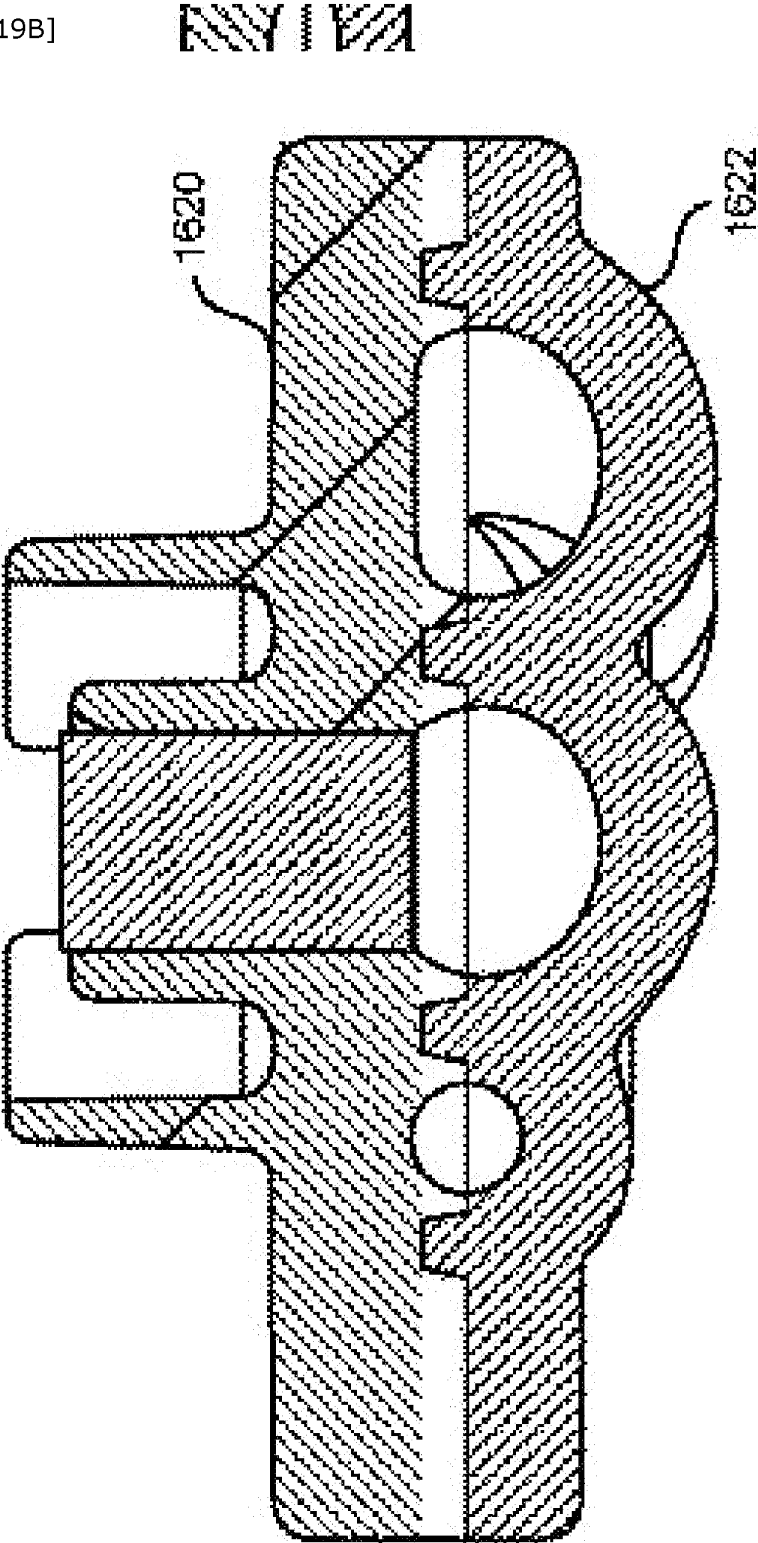


FIG. 19B

[Fig. 20]

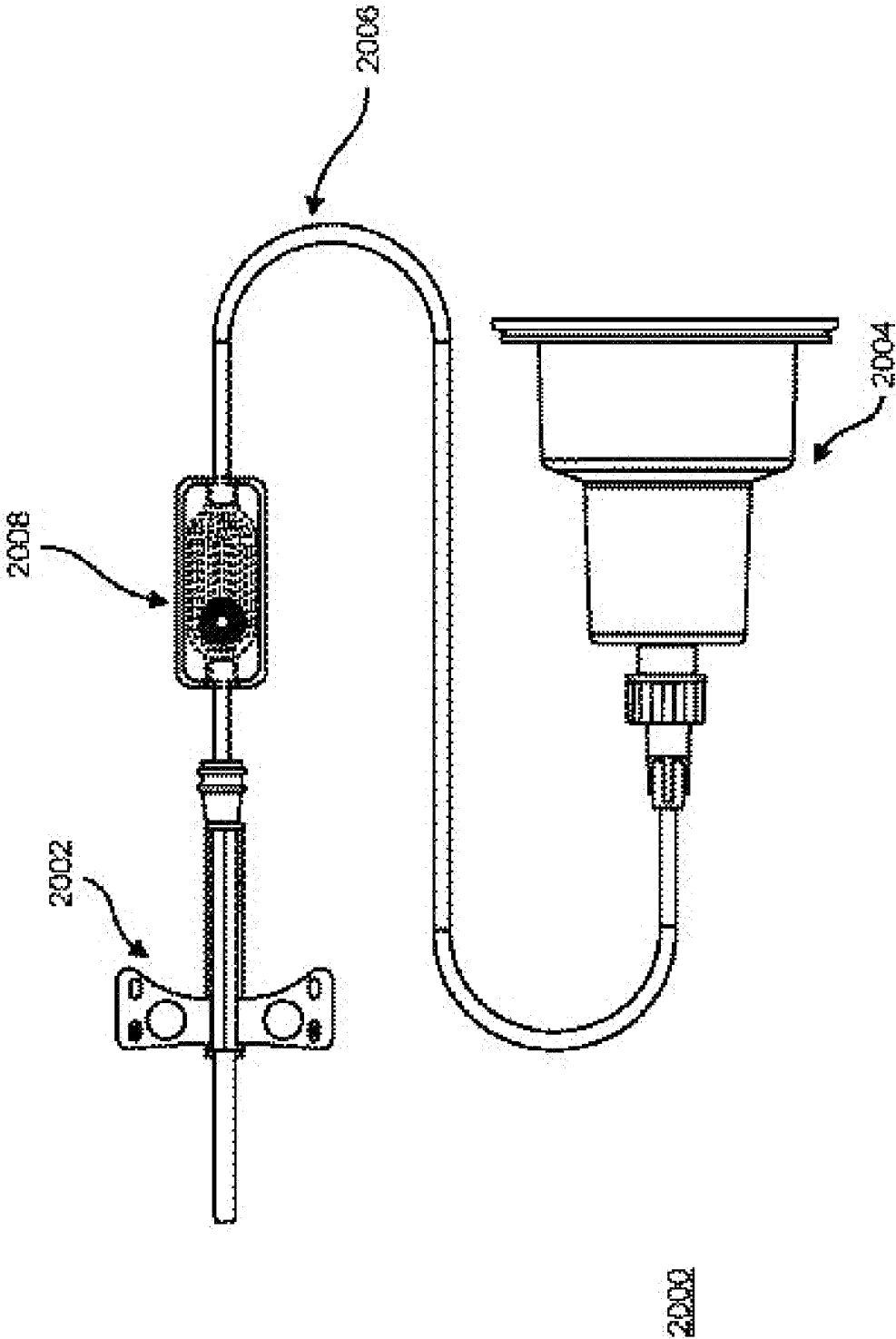


FIG. 20

[Fig. 21]

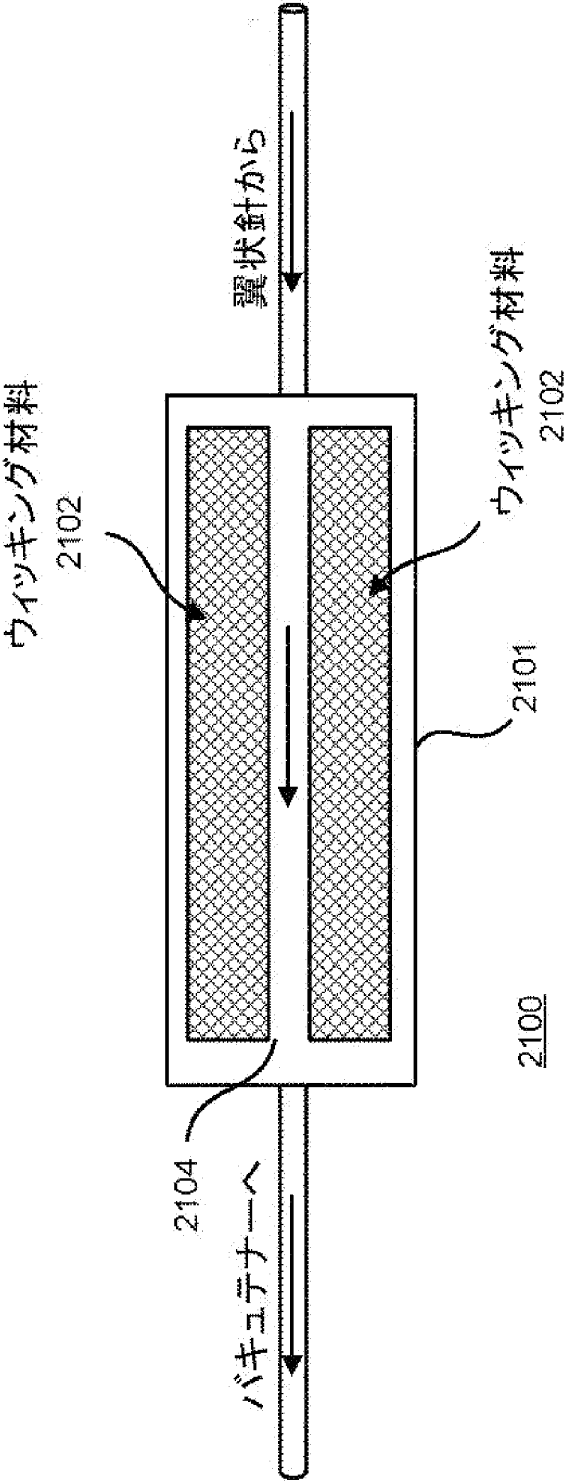


FIG. 21

[Fig. 22A]

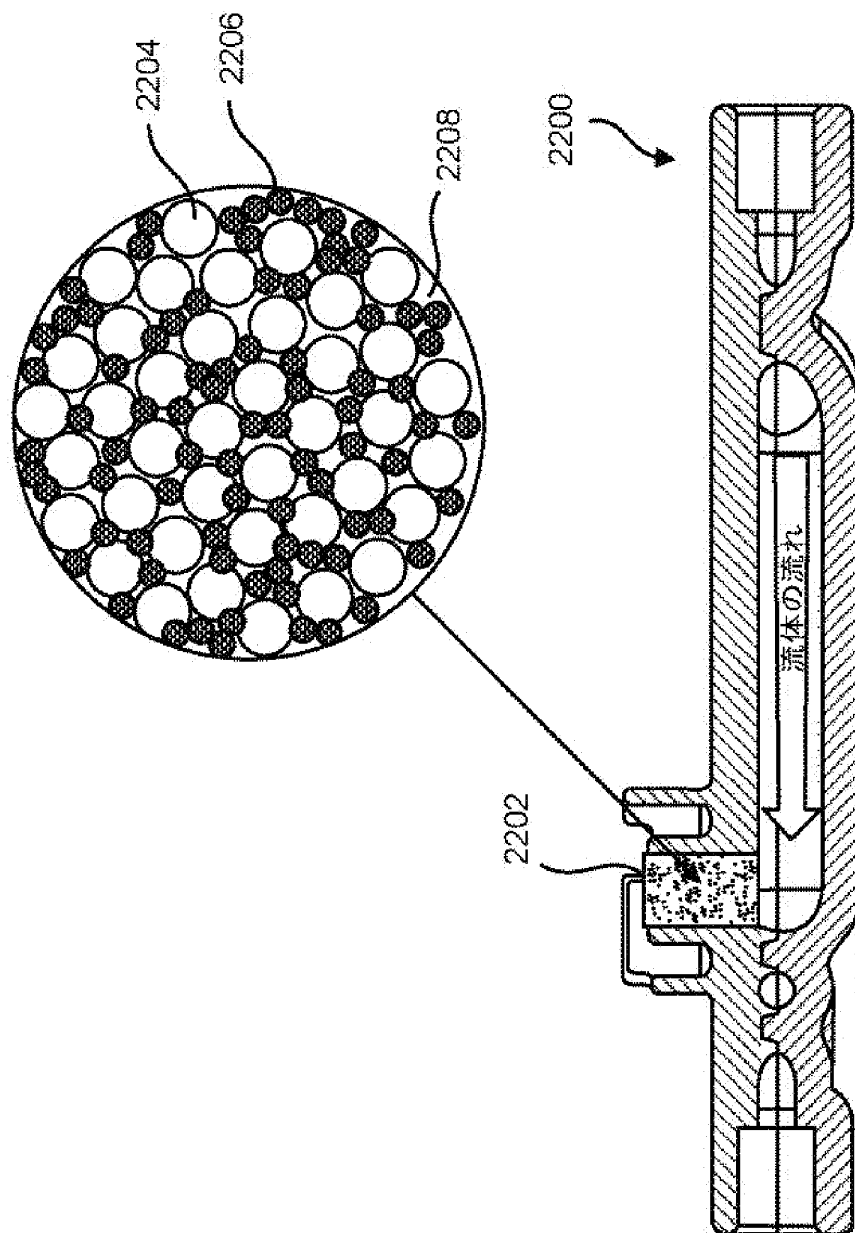


FIG. 22A

[Fig. 22B]

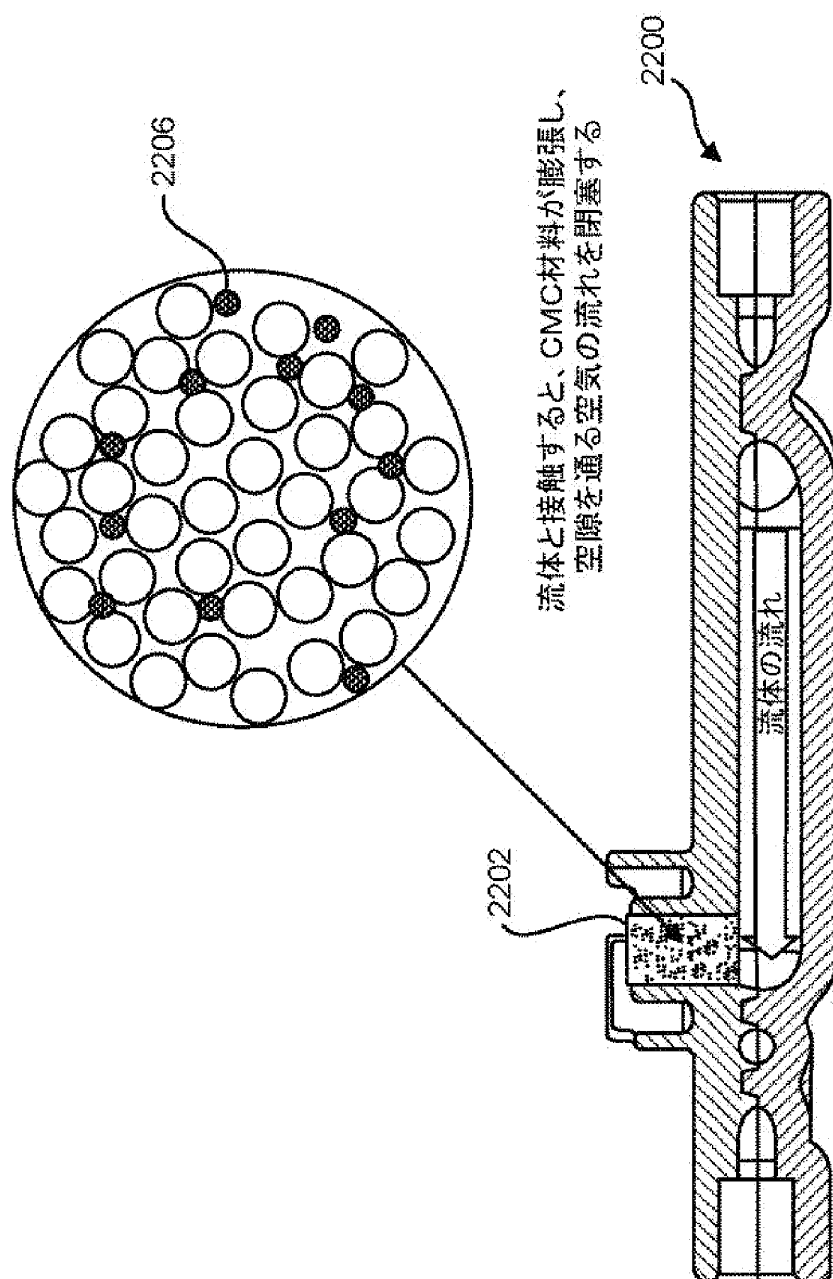


FIG. 22B

[Fig. 23A]

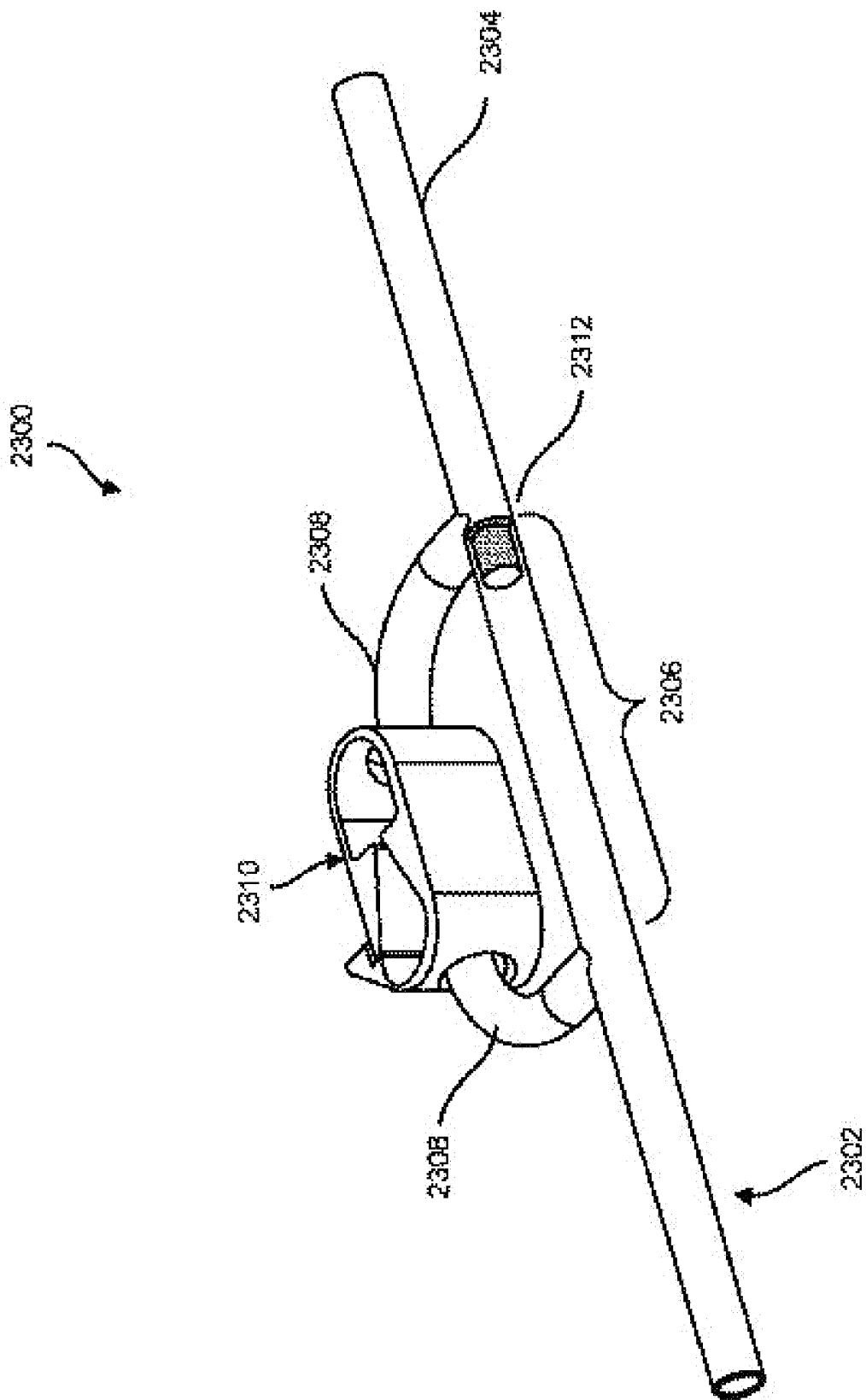


FIG. 23A

[Fig. 23B]

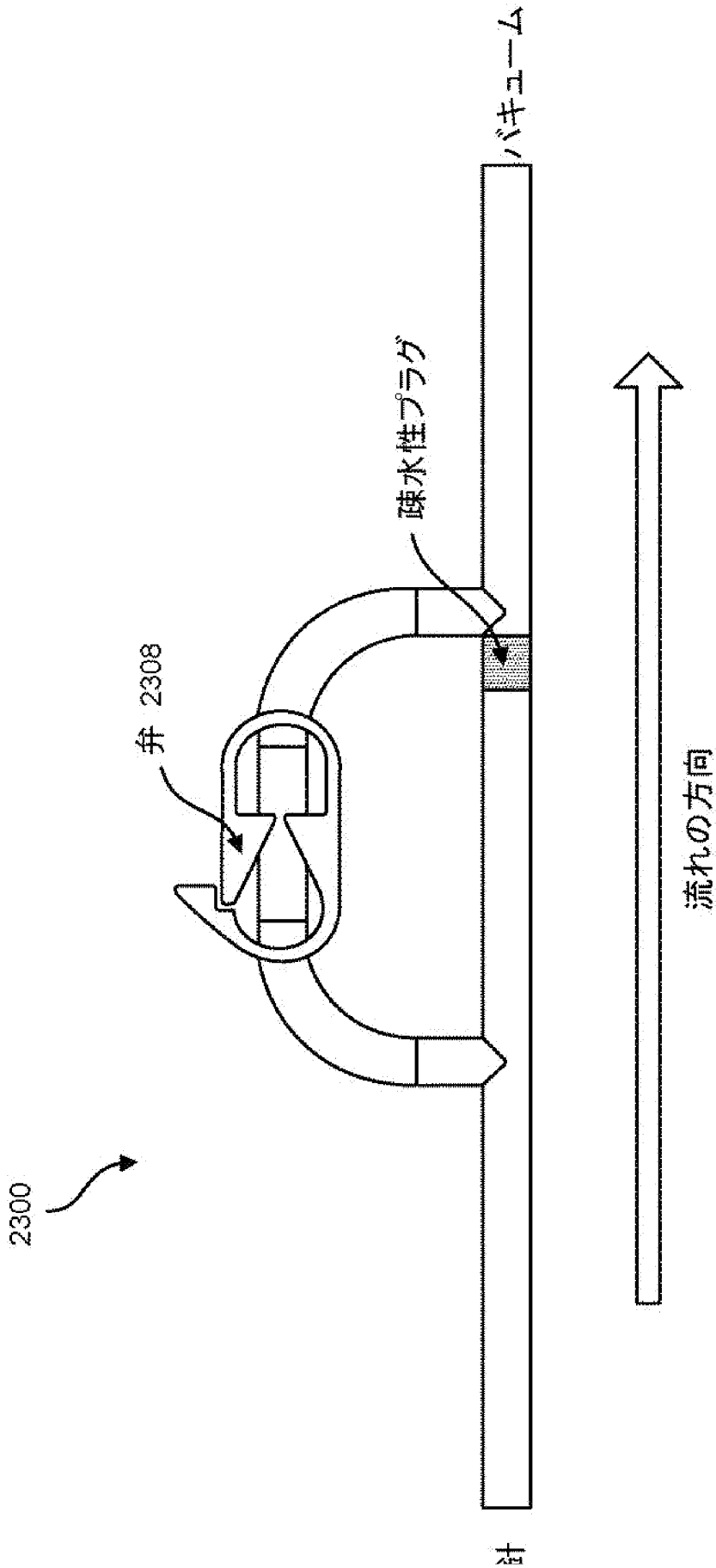


FIG. 23B

drawing

open

123FourFive678A8B8C

...

Magnify and Rotate

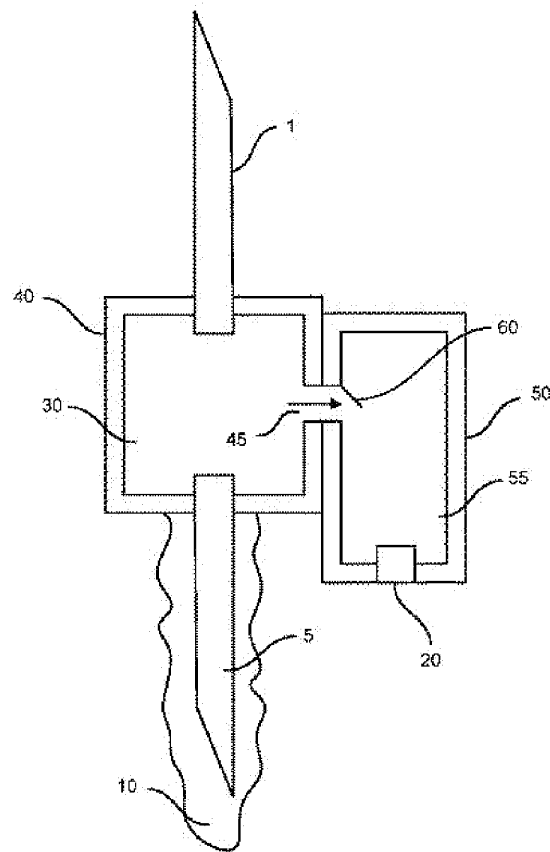
**FIG. 1**

Figure 1



1

/ 1

display



(19) 日本国特許庁 (JP)

(12) 特 許 公 報 (B2)

(11) 特許番号

特許第6643474号

(P6643474)

(45) 発行日 令和2年2月12日 (2020. 2. 12)

(24) 登録日 令和2年1月8日 (2020. 1. 8)

(51) Int. Cl.		F I	
A 6 1 B	5/15	(2006. 01)	A 6 1 B 5/15 2 0 0
A 6 1 B	5/154	(2006. 01)	A 6 1 B 5/154 2 0 0

請求項の数 16 (全 39 頁)

(21) 出願番号	特願2018-523384 (P2018-523384)	(73) 特許権者	518026730
(86) (22) 出願日	平成28年7月22日 (2016. 7. 22)		クリン インコーポレイテッド
(65) 公表番号	特表2018-525191 (P2018-525191A)		アメリカ合衆国 9 2 1 3 1 カリフォル
(43) 公表日	平成30年9月6日 (2018. 9. 6)		ニア州 サンディエゴ スクリップス ポ
(86) 国際出願番号	PCT/US2016/043709		ーウェイ パークウェイ 1 0 7 5 5 ナ
(87) 国際公開番号	W02017/019552		ンバー 2 5 7
(87) 国際公開日	平成29年2月2日 (2017. 2. 2)	(74) 代理人	100083806
審査請求日	令和1年5月20日 (2019. 5. 20)		弁理士 三好 秀和
(31) 優先権主張番号	62/238, 636	(74) 代理人	100095500
(32) 優先日	平成27年10月7日 (2015. 10. 7)		弁理士 伊藤 正和
(33) 優先権主張国・地域又は機関	米国 (US)	(74) 代理人	100111235
(31) 優先権主張番号	62/318, 194		弁理士 原 裕子
(32) 優先日	平成28年4月4日 (2016. 4. 4)	(74) 代理人	100195257
(33) 優先権主張国・地域又は機関	米国 (US)		弁理士 大淵 一志

最終頁に続く

(54) 【発明の名称】 血液サンプル最適化システム及び血液隔離装置

(57) 【特許請求の範囲】

【請求項 1】

血液サンプル最適化システムであって、

採血システムであって、

患者の血液サンプルを取り出せるようにするために患者の静脈穿刺用に構成された患者針と、

前記患者針に接続され、前記血液サンプルを運ぶように構成された採血経路と、

前記血液サンプルの後続の部分を採用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

10

20

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。

10

【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。

20

【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、

30

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む、

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、

40

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】

50

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 1 0】

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 1 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の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 1 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 1 に記載の血液サンプル最適化システム。

【請求項 1 3】

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 1 1 に記載の血液サンプル最適化システム。

【請求項 1 4】

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 1 に記載の血液サンプル最適化システム。

【請求項 1 5】

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 1 に記載の血液サンプル最適化システム。

【請求項 1 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 1 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。

10

【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污染源である。

20

【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。

30

【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。

40

【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】

50

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。

10

【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。

20

【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が必要とする。

【発明の概要】

30

【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ることもできる。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。

40

【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

50

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】

【 0 0 2 3 】

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 8 A】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。

10

【図 8 B】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 8 C】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 8 D】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 8 E】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 10 A】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 10 B】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 10 C】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 10 D】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。

20

【図 11 A】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 11 B】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 11 C】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 11 D】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 11 E】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 12 A】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 12 B】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 12 C】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。

30

【図 12 D】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 13 A】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 13 B】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 13 C】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 13 D】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 14 A】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 14 B】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。

40

【図 14 C】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 14 D】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 14 E】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。

50

別の実施を示す。

【図 1 5 A】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 1 5 B】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 1 5 C】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 1 5 D】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 1 5 E】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 1 5 F】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 1 5 G】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 1 6 A】更に別の実施に従う血液隔離装置を示す。

【図 1 6 B】更に別の実施に従う血液隔離装置を示す。

【図 1 6 C】更に別の実施に従う血液隔離装置を示す。

【図 1 6 D】更に別の実施に従う血液隔離装置を示す。

【図 1 7 A】血液隔離装置用のハウジングの下部部材を示す。

【図 1 7 B】血液隔離装置用のハウジングの下部部材を示す。

【図 1 7 C】血液隔離装置用のハウジングの下部部材を示す。

【図 1 7 D】血液隔離装置用のハウジングの下部部材を示す。

【図 1 7 E】血液隔離装置用のハウジングの下部部材を示す。

【図 1 8 A】血液隔離装置用のハウジングの上部部材を示す。

【図 1 8 B】血液隔離装置用のハウジングの上部部材を示す。

【図 1 8 C】血液隔離装置用のハウジングの上部部材を示す。

【図 1 8 D】血液隔離装置用のハウジングの上部部材を示す。

【図 1 8 E】血液隔離装置用のハウジングの上部部材を示す。

【図 1 8 F】血液隔離装置用のハウジングの上部部材を示す。

【図 1 9 A】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 1 9 B】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 2 0】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 2 1】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 2 2 A】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 2 2 B】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 2 3 A】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 2 3 B】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】

【0 0 2 4】

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。

【0 0 2 5】

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 1 0、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内に保持する一方方向フラップ又は一方方向弁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への一方方向の血液の流れのための「ダックビル」弁又はフラップ弁60などを含むことができる。空気透過性血液バリア20は、空気が出ることの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。

10

【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。

20

【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、バキューテナー（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を通過し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。

30

【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過し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。

40

【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

50

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

10

【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。

20

【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。

30

【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。

40

50

【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。

10

【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。

20

30

【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を通し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。

40

【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

50

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されることができる。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。

10

【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。

20

【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。

30

【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。

40

【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】

50

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。

10

【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。

20

【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。

30

【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。

40

【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

50

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、ルーアコネクタ（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まで徐々に広げることができる。

【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。

10

【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。

20

【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。

30

【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、ルーアコネクタ、注射器、ルーア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。

40

【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

50

る円形であることができるが、0. 01インチ（0. 254 mm）から0. 2インチ（5. 08 mm）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で覆わ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

10

20

30

40

50

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を通し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 人口ポート 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。

10

【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。

20

【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。

30

【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（1.143 mm）の直径を有する円形であることができるが、0.01 インチ（0.254 mm）から 0.2 インチ（5.08 mm）又はそれ以上の直径を有することができる。

40

【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、

50

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ることができる。

【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ることができる。

10

【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、最初のアリコーッ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。

20

【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。

30

【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。

40

【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

50

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。

10

【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。

20

【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。

30

【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。

40

【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

50

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を通過し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

10

20

30

40

50

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。バキューテナー（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。

10

【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。

20

【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】

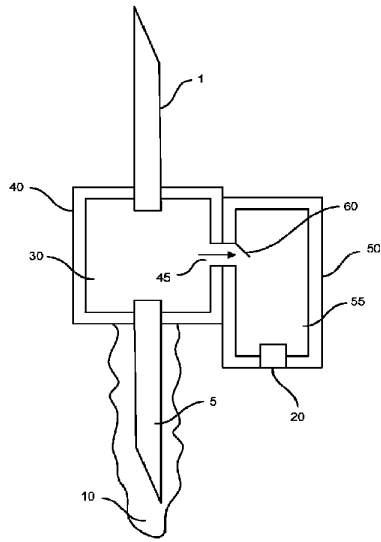


FIG. 1

【図 2】

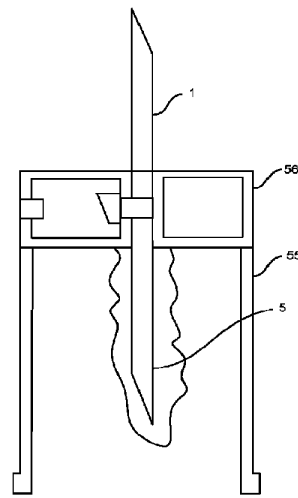


FIG. 2

【図 3】

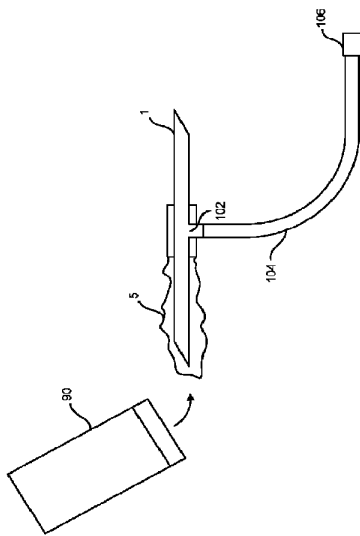


FIG. 3

【図 4】

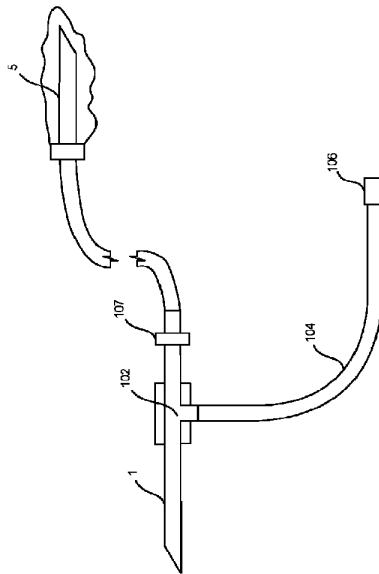


FIG. 4

【図 5】

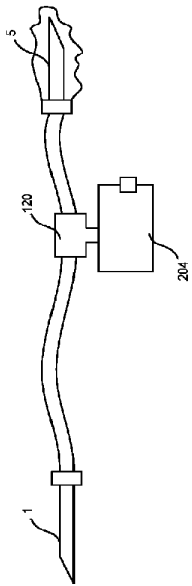


FIG. 5

【図 6】

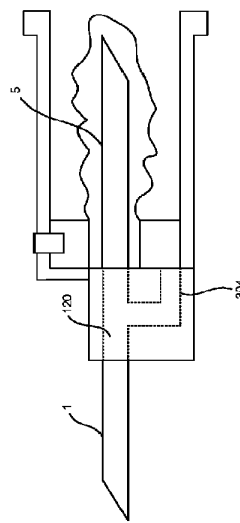


FIG. 6

【図 7】

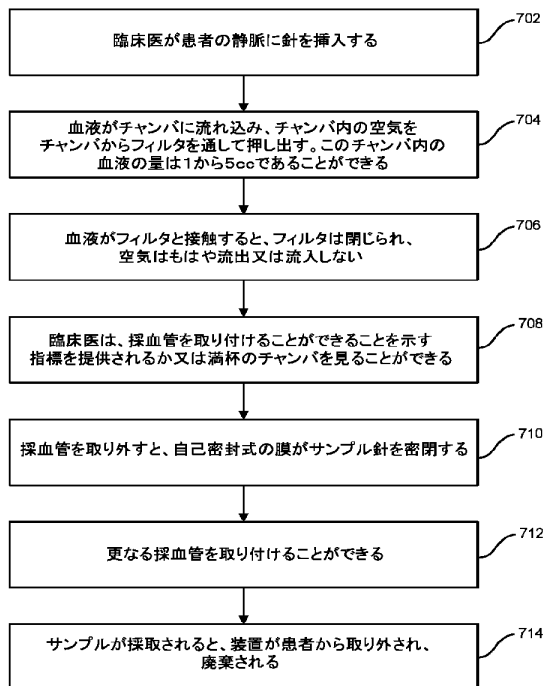


FIG. 7

【図 8 A】

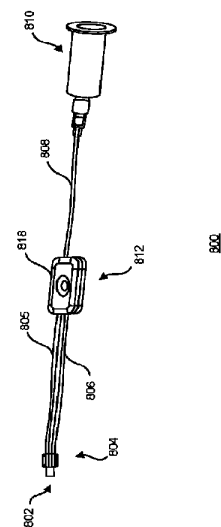


FIG. 8A

【図 8 B】

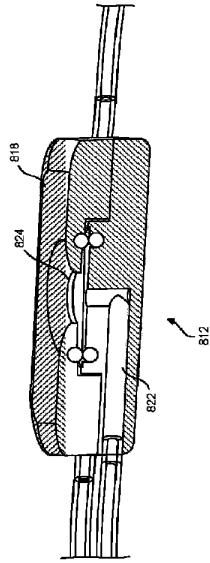


FIG. 8B

【図 8 C】

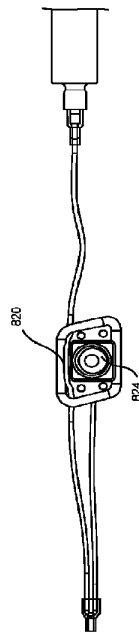


FIG. 8C

【図 8 D】

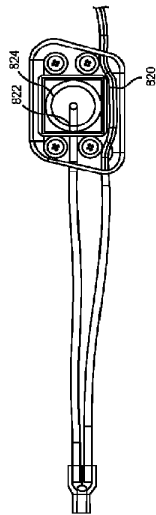


FIG. 8D

【図 8 E】

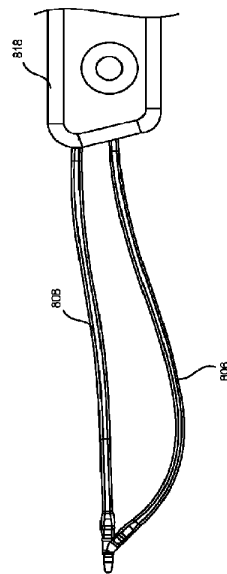


FIG. 8E

【図 9】

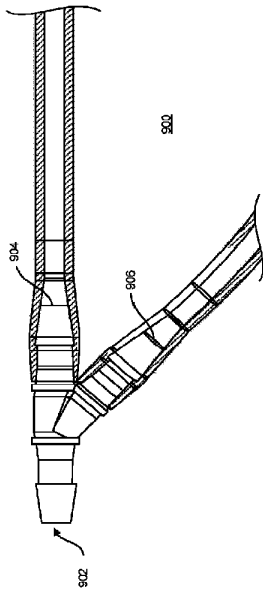


FIG. 9

【図 10 A】

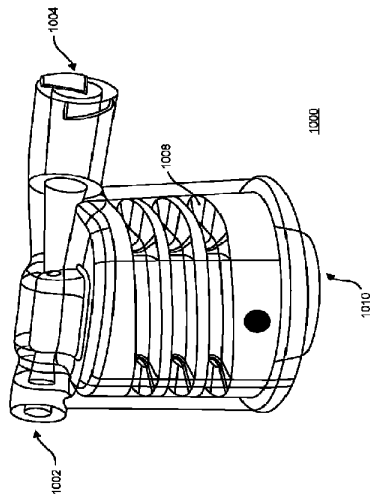


FIG. 10A

【図 10 B】

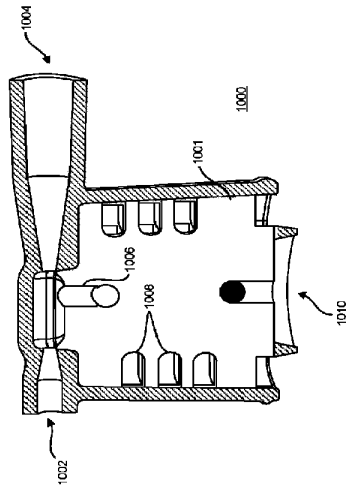


FIG. 10B

【図 10 C】

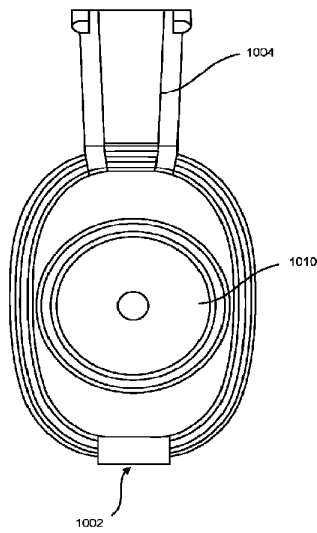


FIG. 10C

【図 10 D】

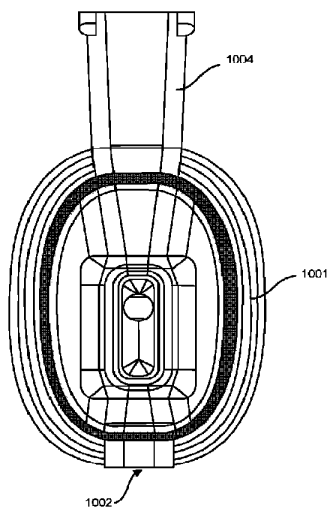


FIG. 10D

【図 11 A】

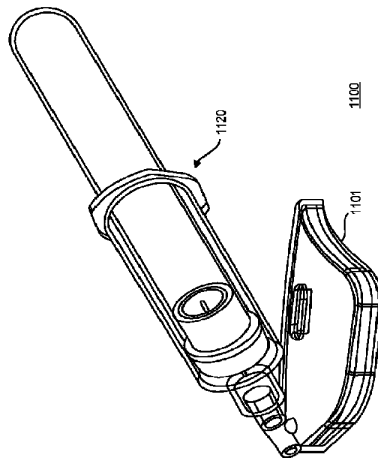


FIG. 11A

【図 11 B】

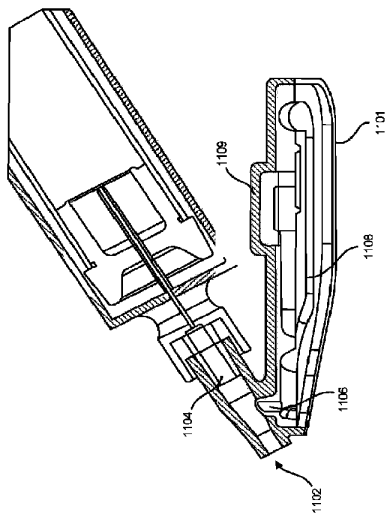


FIG. 11B

【図 11 C】

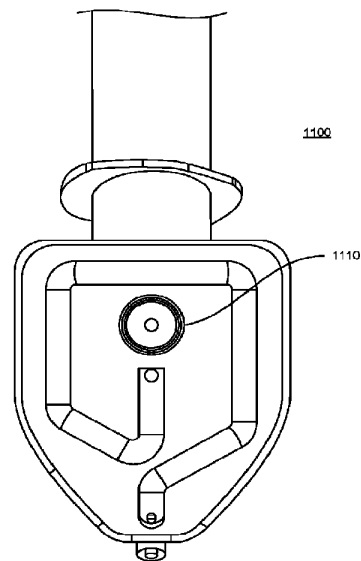


FIG. 11C

【図 11 D】

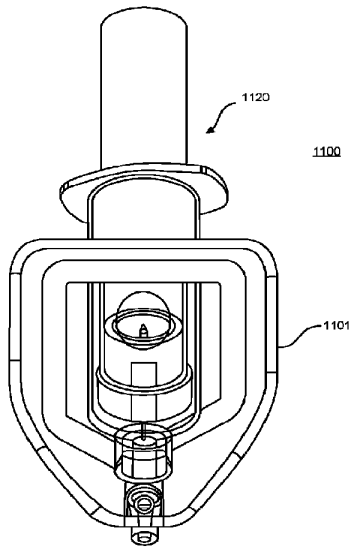


FIG. 11D

【図 11 E】

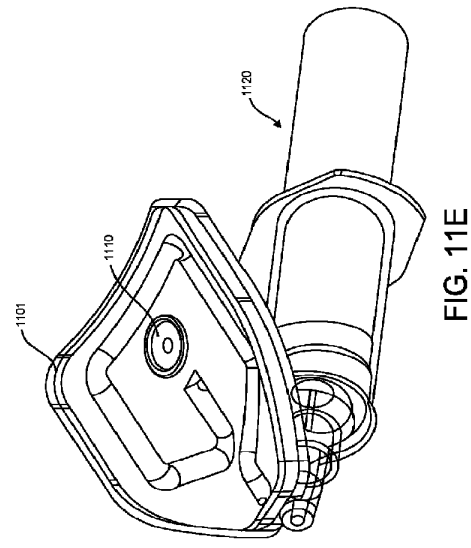


FIG. 11E

【図 12 A】

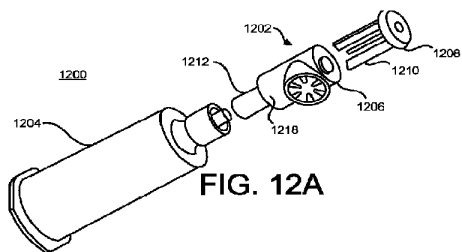


FIG. 12A

【図 12 B】

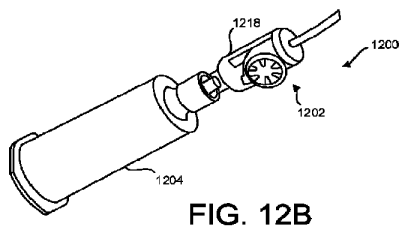


FIG. 12B

【図 12 C】

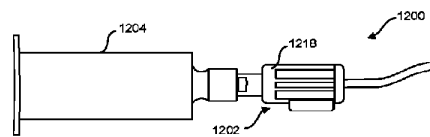


FIG. 12C

【図 12 D】

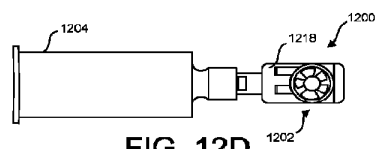


FIG. 12D

【図 13 A】

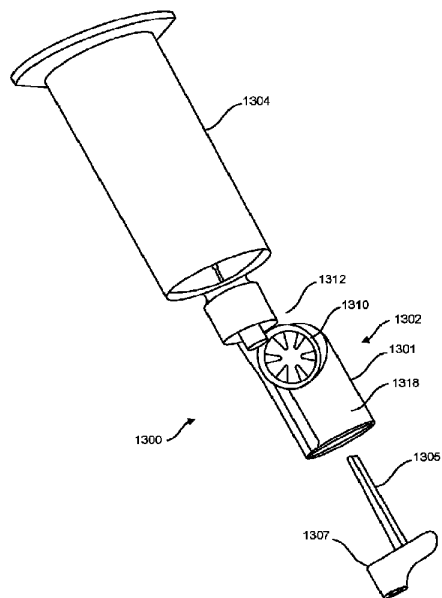


FIG. 13A

【図 13 B】

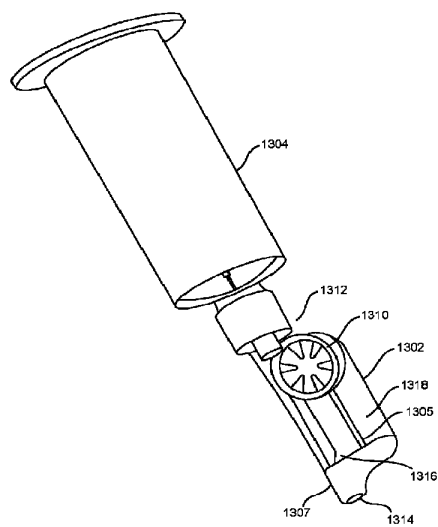


FIG. 13B

【図 13 C】

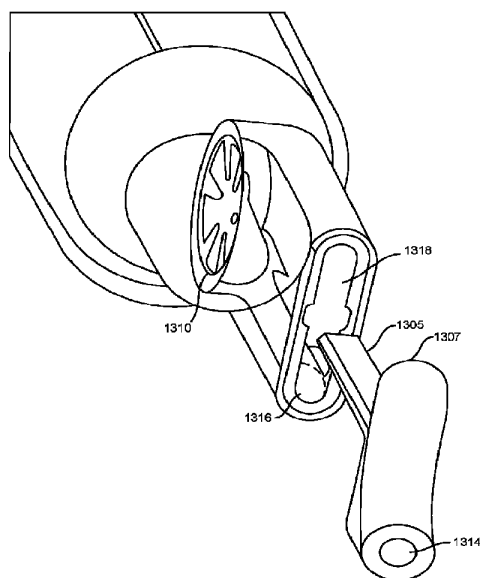


FIG. 13C

【図 13 D】

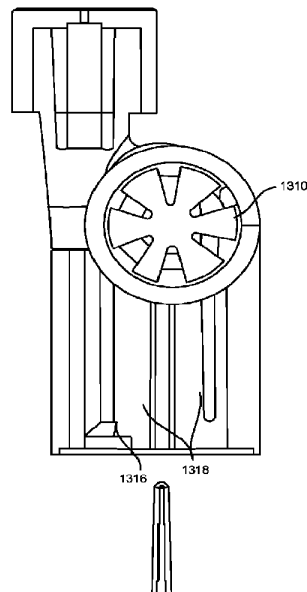


FIG. 13D

【図 14 A】

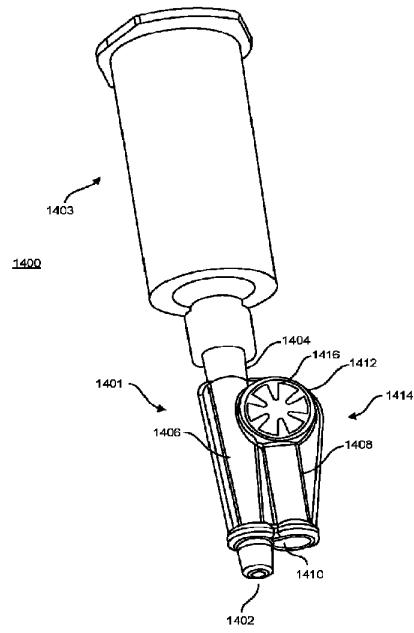


FIG. 14A

【図 14 B】

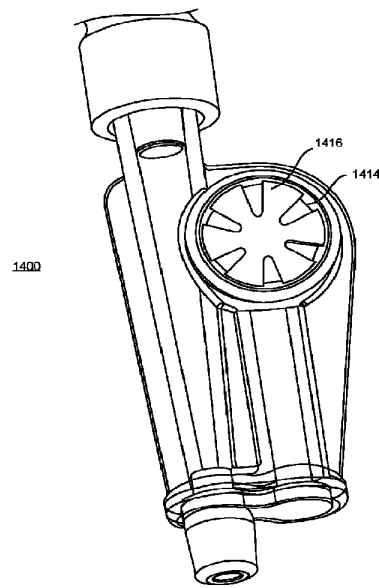


FIG. 14B

【図 14 C】

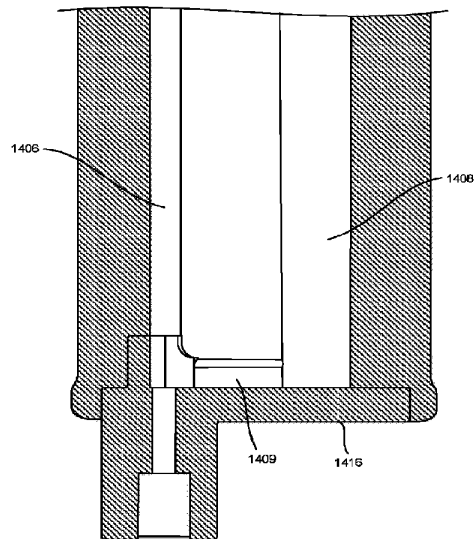


FIG. 14C

【図 14 D】

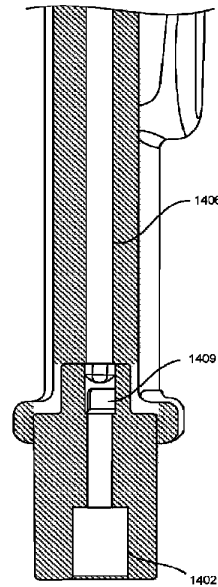


FIG. 14D

【図 14 E】

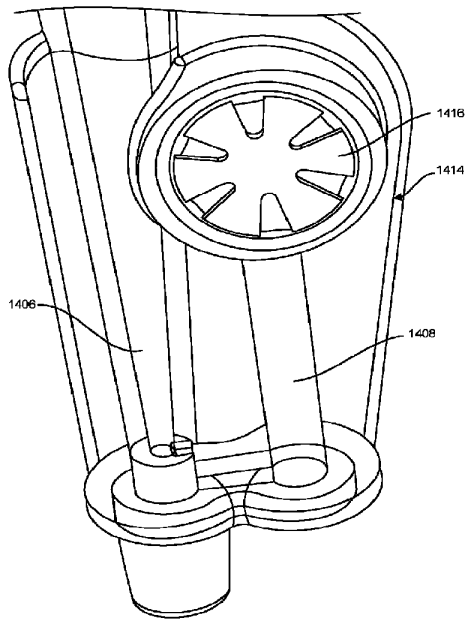


FIG. 14E

【図 15 A】

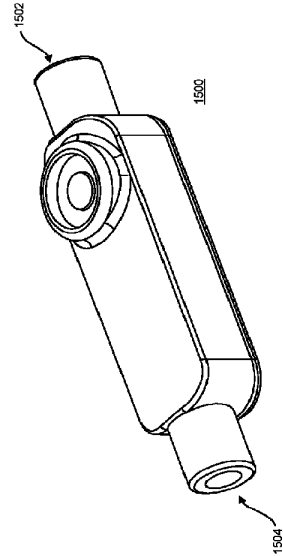


FIG. 15A

【図 15 B】

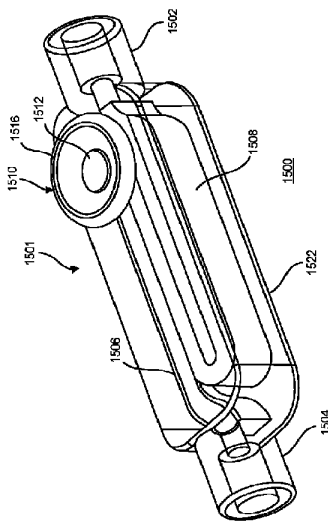


FIG. 15B

【図 15 C】

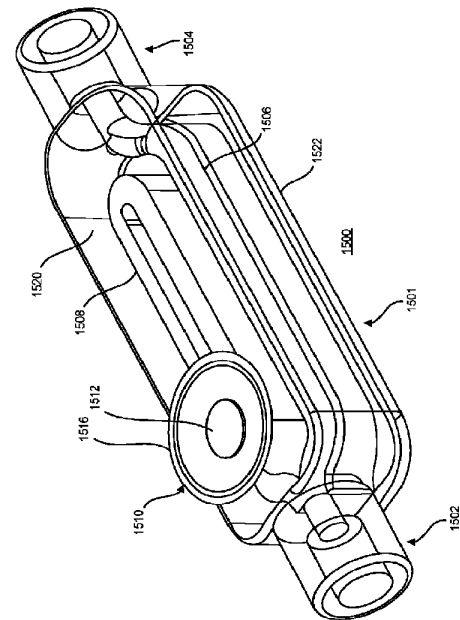


FIG. 15C

【図 15 D】

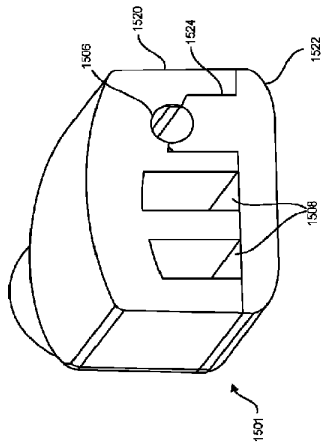


FIG. 15D

【図 15 E】

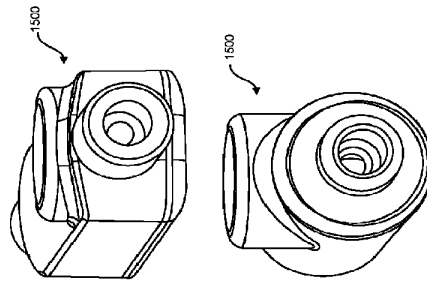


FIG. 15E

【図 15 F】

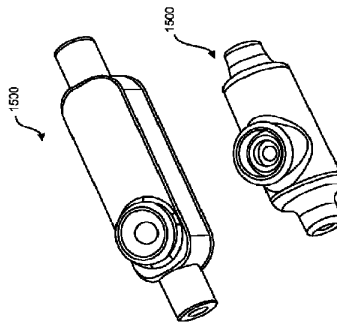


FIG. 15F

【図 15 G】

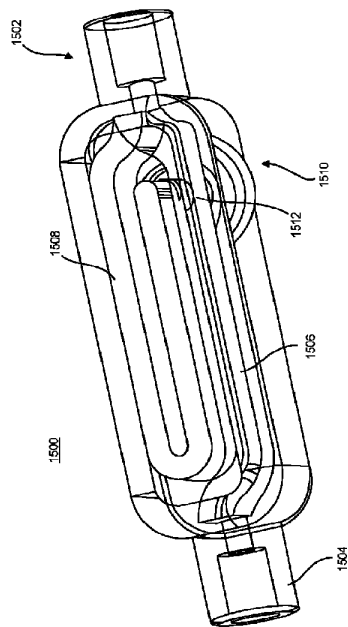


FIG. 15G

【図 16 A】

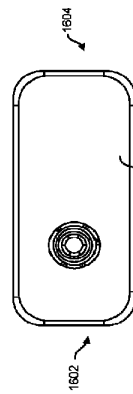


FIG. 16A

【図 16 B】

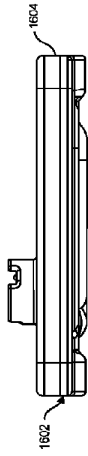


FIG. 16B

【図 16 D】

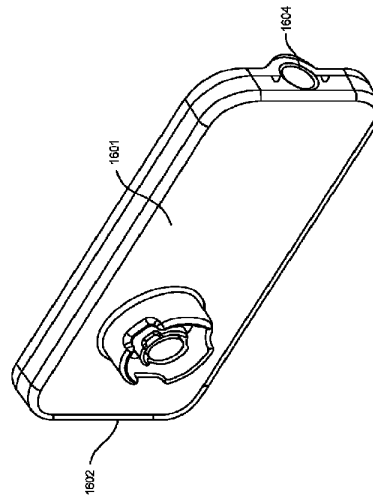


FIG. 16D

【図 16 C】

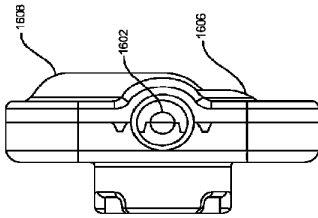


FIG. 16C

【図 17 A】

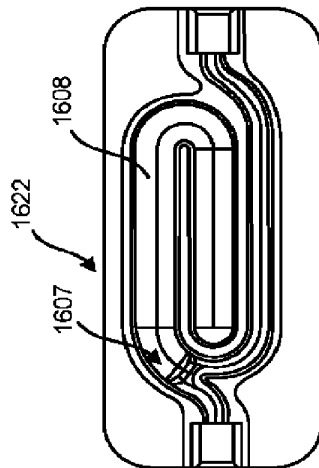


FIG. 17A

【図 17 B】

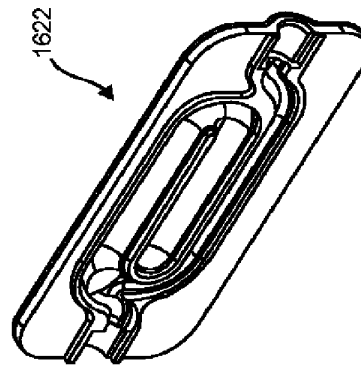


FIG. 17B

【図 17 C】

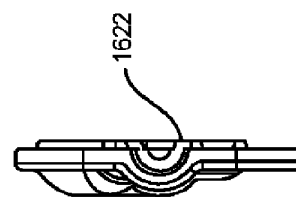


FIG. 17C

【図 17 D】

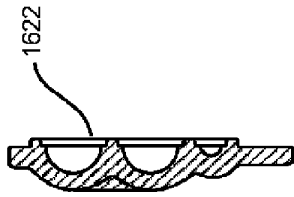


FIG. 17D

【図 17 E】



FIG. 17E

【図 18 A】

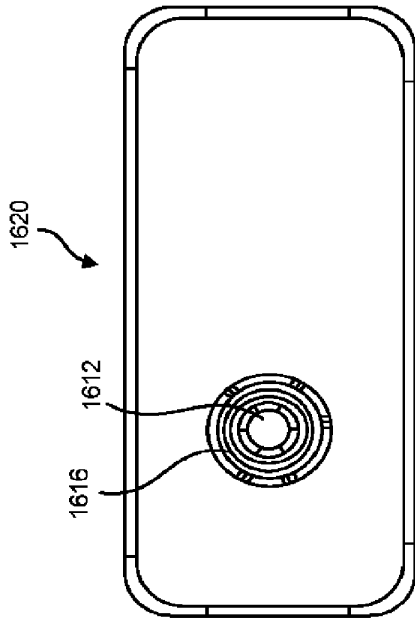


FIG. 18A

【図 18 B】

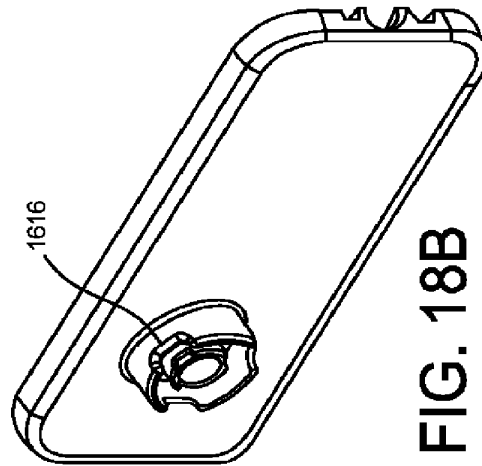


FIG. 18B

【図 18 C】

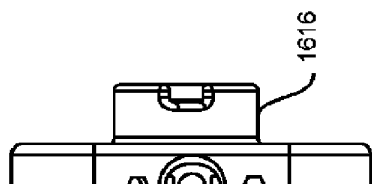


FIG. 18C

【図 18 E】

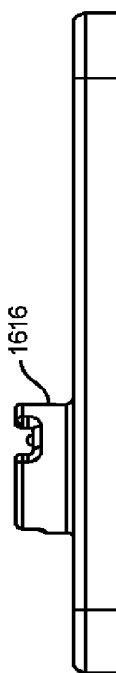


FIG. 18E

【図 18 D】

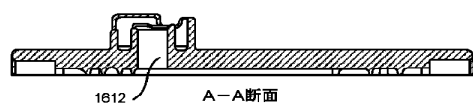


FIG. 18D

【図 18 F】

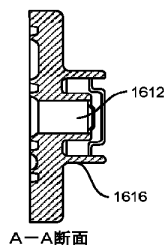


FIG. 18F

【図 19 A】

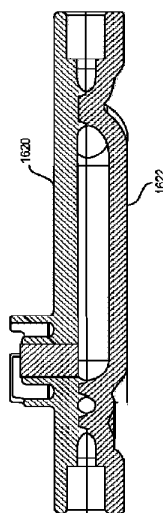


FIG. 19A

【图 19 B】

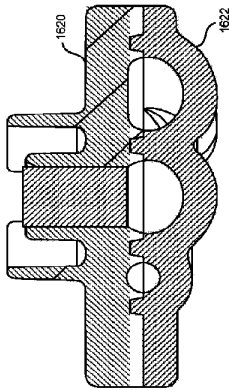


FIG. 19B

【 図 2 0 】

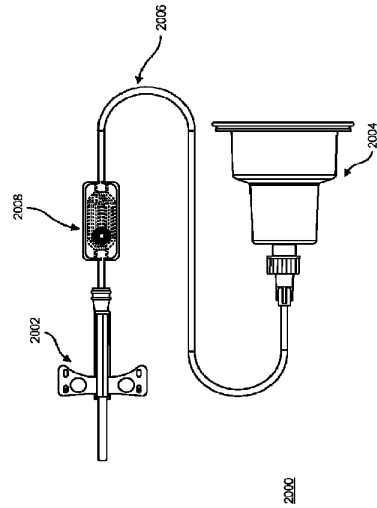


FIG. 20

【 図 2 1 】

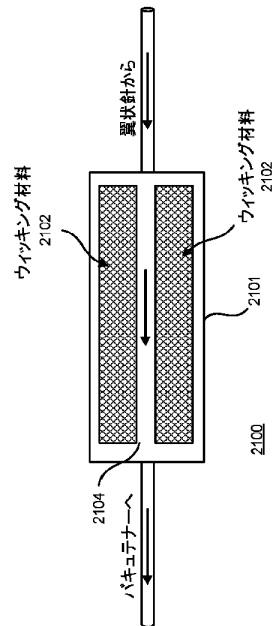


FIG. 21

【图 2 2 A】

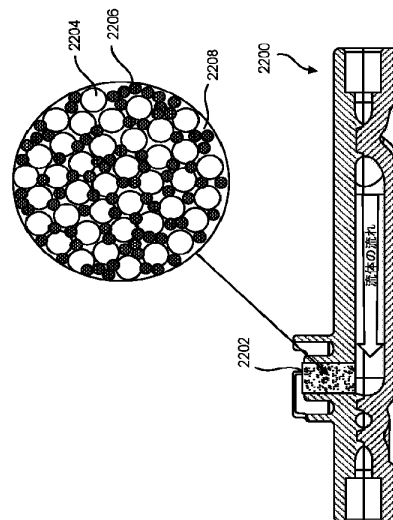


FIG. 22A

【図 2 2 B】

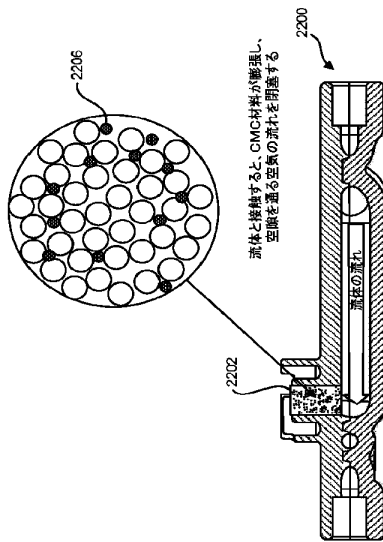


FIG. 22B

【図 2 3 A】

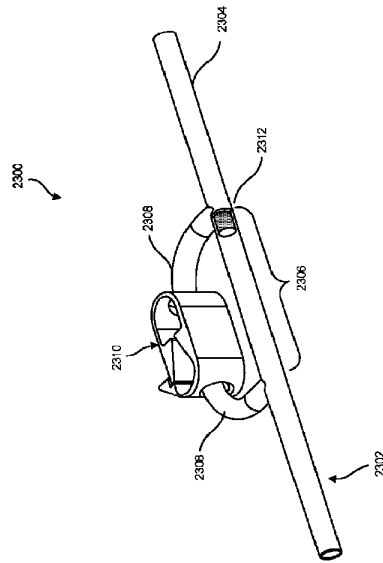


FIG. 23A

【図 2 3 B】

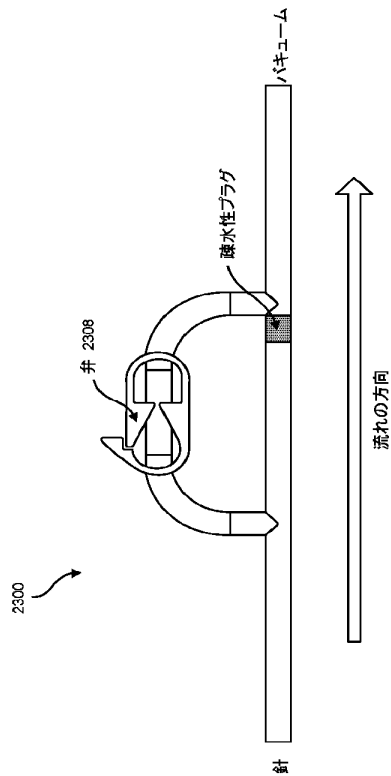


FIG. 23B

フロントページの続き

- (31) 優先権主張番号 62/196, 797
(32) 優先日 平成27年7月24日 (2015. 7. 24)
(33) 優先権主張国・地域又は機関
米国 (US)
(31) 優先権主張番号 15/140, 448
(32) 優先日 平成28年4月27日 (2016. 4. 27)
(33) 優先権主張国・地域又は機関
米国 (US)
(31) 優先権主張番号 15/140, 443
(32) 優先日 平成28年4月27日 (2016. 4. 27)
(33) 優先権主張国・地域又は機関
米国 (US)

早期審査対象出願

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

審査官 清水 裕勝

- (56) 参考文献 特開昭58-025146 (JP, A)
特開昭58-067238 (JP, A)
特開2012-016496 (JP, A)
特開昭57-089869 (JP, A)
特表平09-504726 (JP, A)
特開平02-224742 (JP, A)
米国特許第04207870 (US, A)

- (58) 調査した分野(Int.Cl., DB名)
A61B 5/153-5/154

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 5736-PCT	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US 2015/035870	International filing date (<i>day/month/year</i>) 15 June 2015 (15.06.2015)	(Earliest) Priority Date (<i>day/month/year</i>) 13 June 2014 (13.06.2014)
Applicant GARRET, Chad et al.		

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

This international search report consists of a total of 2 sheets.

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

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

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

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

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

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

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the drawings to be published with the abstract is Figure No. 1

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 2015/035870

A. CLASSIFICATION OF SUBJECT MATTER
A61B 5/15 (2006.01)
A61M 25/01 (2006.01)
G01N 33/48 (2006.01)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B 5/15, A61M 5/19, 25/01 G01N 33/48

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

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

PatSearch, Espacenet, USPTO, Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2013/082301 A1 (TELEFLEX MEDICAL, INC.) 06.06.2013	1-9
Y	claims, [0006]-[0008], [0037], [0041], [0044]-[0054], fig. 1-5	10-13, 15-16, 18-19
Y	JP 2009131273 A (CSL BEHRING GMBH) 18.06.2009 abstract	10-13
X	EP 2593169 A1 (BECTON DICKINSON CO) 22.05.2013 abstract, [0006]-[0013]	14, 17
Y		15-16, 18-19



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

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

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

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

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

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

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

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

19 October 2015 (19.10.2015)

Date of mailing of the international search report

05 November 2015 (05.11.2015)

 Name and mailing address of the ISA/RU:
 Federal Institute of Industrial Property,
 Berezhevskaya nab., 30-1, Moscow, G-59,
 GSP-3, Russia, 125993
 Facsimile No: (8-495) 531-63-18, (8-499) 243-33-37

Authorized officer

E. Kazak

Telephone No. 8 (495) 531 64 81

Form PCT/ISA/210 (second sheet) (January 2015)

PATENT COOPERATION TREATY

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

From the INTERNATIONAL SEARCHING AUTHORITY

To:

HARMS, Donn K.
12702 Via Cortina, Suite 100
Del Mar, CA 92014
United States of America

Date of mailing (*day/month/year*)
05 November 2015 (05.11.2015)

Applicant's or agent's file reference
5736-PCT

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/US 2015/035870

International filing date (*day/month/year*)
15 June 2015 (15.06.2015)

Priority date (*day/month/year*)
13 June 2014 (13.06.2014)

International Patent Classification (IPC) or both national classification and IPC
A61B 5/15 (2006.01)
A61M 25/01 (2006.01)
G01N 33/48 (2006.01)

Applicant
GARRET, Chad et al.

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

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

2. FURTHER ACTION

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

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

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

Name and mailing address of the ISA/RU:
Federal Institute of Industrial Property,
Berezhkovskaya nab., 30-1, Moscow, G-59,
GSP-3, Russia, 125993
Facsimile No: (8-495) 531-63-18, (8-499) 243-33-37

Date of completion of this opinion
19 October 2015 (19.10.2015)

Authorized officer
E. Kazak
Telephone No. 8 (495) 531 64 81

Form PCT/ISA/237 (cover sheet) (January 2015)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 2015/035870

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
☒ the international application in the language in which it was filed.
☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a)).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:
 - a. ☐ forming part of the international application as filed:
☐ in the form of an Annex C/ST.25 text file.
☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).
☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 2015/035870

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

1. Statement

Novelty (N)	Claims	10-13, 15-16, 18-19	YES
	Claims	1-9, 14, 17	NO
Inventive step (IS)	Claims		YES
	Claims	10-13, 15-16, 18-19	NO
Industrial applicability (IA)	Claims	1-19	YES
	Claims		NO

2. Citations and explanations:

D1 - WO 2013/082301 A1

D2 - JP 2009131273 A

D3 - EP 2593169 A1

D1 can be regarded as the closest prior art of test component for blood according to claim 1.

D1 (claims, [0006] - [0008]) discloses a substrate configured to generate a visually discernable reaction to the presence or a threshold level of a substance in said blood; said substrate adapted for positioning in a fluid communication pathway carrying blood from a flash chamber defined by a surrounding sidewall of a housing of an introducer; and said substrate generating said visually discernable reaction viewable by a user of said introducer, subsequent to a fluid communication of said blood from said flash chamber to said substrate.

Thus, the invention according to claim 1 does not meet the criterion of novelty.

D3 can be regarded as the closest prior art of the inventions according to independent claims 14, 17.

D3 (abstract, [0006] - [0013]) discloses an introducer for the introduction of a catheter into the vein or artery of a patient: said introducer having a needle in axial communication between a distal end and a flash chamber with a housing of said introducer; a testing substrate within a substrate housing, said substrate housing in a fluid communication with said flash chamber through a passage in a sidewall of said flash chamber; said testing substrate configured to generate a visually discernable result, to a substance contained within blood communicated through said needle to said flash chamber; and said testing substrate viewable through a cover of said substrate housing, whereby said user can concurrently introduce a catheter to a patient and view test results for the presence of said substance with said blood from said patient communicated to said flash chamber.

D3 (abstract, [0006] - [0013]) discloses a method of testing a patient's blood for a substance comprising the steps of: placing a substrate having a visually discernable reaction area thereon to a said substance, in a fluid communication with a flash chamber of an introducer employed for the insertion of a catheter into the vein or artery of a patient; puncturing the vein or artery of said patient with a needle engaged to said introducer; allowing blood from said vein or artery to communicate axially through said needle to a flash chamber in said introducer; allowing a portion of said blood to fluidly communicate with said substrate; and viewing said substrate to ascertain said visually discernable reaction.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of V:

Thus, the inventions according to independent claims 14, 17 do not meet the criterion of novelty.

The features of dependent claims 2-4, describing the fluid communication being through the microporous membrane disposed within the flash chamber, are disclosed in D1 ([0037], [0041], [0044], [0054]).

The features of dependent claims 5-6, indicating that positioned within a chamber of a substrate housing, said housing being engageable with an exterior of said sidewall of said substrate housing; and said fluid communication to said substrate communicating through an aperture in said sidewall, are disclosed in D1 ([0054]).

The features of dependent claims 7-9, indicating that substrate housing having a transparent cover in an engagement with a base having a passage aligned with said aperture in said sidewall; and providing for visually discernable reaction are disclosed in D1 ([0054], fig.1-5).

Thus, the invention according to dependent claims 2-9 does not meet the criterion of novelty.

The features of dependent claims 10-13, indicating that a clotting factor on or adjacent to said separation membrane generating a cessation of said fluid communication through said separation membrane subsequent to a duration of time sufficient to clot said blood at said separation membrane are disclosed in D2 (abstract).

The features of dependent claim 15 indicating that a separation membrane interposed between said flash chamber and said substrate; and said separation membrane allowing only blood plasma from said portion of blood therethrough to a said fluid communication with said substrate are disclosed in D1 ([0044], [0054]).

The features of dependent claim 16, indicating a plurality of said testing substrates, each located within separate said substrate housing, each said substrate housing in a fluid communication with said flash chamber through a passage in a sidewall of said flash chamber are also disclosed in D1 ([0044], [0054]).

The features of dependent claims 18, 19, indicating a visually discernable reaction area of substrate positioned in substrate housing are disclosed in D1 ([0044]).

Thus, the invention according to dependent claims 10-13, 15, 16, 18, 19 does not meet the criterion of inventive step.

The inventions according to claims 1-19 meet the criterion of industrial applicability.

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

In both the previously reported cases of myoclonic spasms following the administration of morphine and diamorphine, the drugs had been infused spinally in much smaller doses. The 100-fold difference in dose before the development of myoclonus is probably related to the concentration gradient between the intravenous and cerebrospinal compartments, this being a function of a lipid solubility of diamorphine. Terminally ill patients at the Hospice commonly receive comparable doses of

diamorphine and morphine to that initially given to this patient without developing myoclonic spasms, but ureteric obstruction leading to chronic renal insufficiency may have accelerated central neuronal toxicity in this patient as it would impair excretion of unconjugated active morphine.

Ashgate Hospice
Chesterfield

D. TURNER

References

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

Venous/arterial blood management protection system

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

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

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

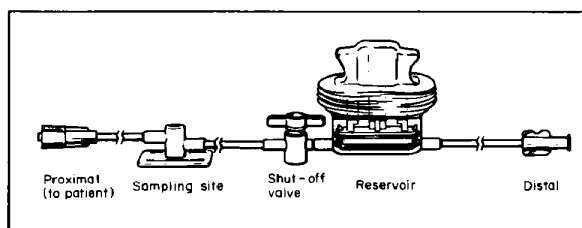


Fig. 1. Baxter venous/arterial blood management protection system (VAMPTM).

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

Queen Alexandra Hospital,
Portsmouth PO6 3LY

A. CHALLINER
G.B. SMITH
B.L. TAYLOR

References

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

Dural puncture and depth of the extradural space

We read with interest the article by Sutton and Linter (*Anaesthesia* 1991; **46**: 97-8) concerning the relative risk of dural puncture as a function of the depth of the extradural space. This study prompted us to examine our own data about the same subject. Since 1989, we have recorded

prospectively, and collected on standardised forms, the technical characteristics of all the epidurals performed in obstetric patients, either for labour or for elective Caesarean section. The depth of extradural space was one of the collected items, as well as the occurrence of dural

MINIREVIEW

Blood Culture Contamination: Persisting Problems and Partial Progress

Melvin P. Weinstein*

Departments of Medicine and Pathology, University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School, and Microbiology Laboratory, Robert Wood Johnson University Hospital, New Brunswick, New Jersey 08903-0019

Although it has been widely appreciated for many years among physicians and microbiologists that blood cultures are among the most important laboratory tests performed in the diagnosis of serious infections (35), it has become equally apparent in more recent years that contaminated blood cultures are common (25, 42), enormously costly (3, 29), and frequently confusing for clinicians (1, 12, 14, 26). Clinical studies of blood-stream infections over 3 decades have provided guidelines for differentiating true pathogens from contaminants or organisms of unknown significance (14, 18, 41, 42); however, a true “gold standard” for differentiating pathogens from contaminants does not exist (4, 25). Moreover, the most common blood culture contaminants, coagulase-negative staphylococci (CoNS), which were almost always such several decades ago (18, 41), now are pathogens more frequently (19, 25, 26, 42), and judging the clinical significance of this group of microorganisms in blood has proven to be especially problematic (1, 11, 22, 24, 26, 42; S. J. Peacock, I. C. Bowler, and D. W. Crook., Letter, *Lancet* **346**:191–192, 1995). This review focuses on how pathogen-contaminant decisions are made, the phenomenon of increasing contamination of blood cultures, potential methods for addressing high contamination rates, and practical laboratory approaches to the workup of likely contaminants.

TOOLS FOR INTERPRETING THE CLINICAL SIGNIFICANCE OF POSITIVE BLOOD CULTURES

A number of clinical and laboratory tools have been proposed to aid microbiologists and physicians in deciding whether a blood isolate is a pathogen or a contaminant. These include the identity of the microorganism itself; clinical features such as fever, leukocytosis, and results of imaging studies (available to the clinician but usually not to the microbiologist); the proportion of blood culture sets positive as a function of the number of sets obtained; the time it takes for growth to be detected once a blood culture is received in the laboratory; and the number of culture vials within a culture set that show growth. Some of these tools have proven to be quite useful, whereas others have not.

The identity of the microorganism that grows from a positive

blood culture provides important interpretative information. MacGregor and Beaty (18) documented this observation in the early 1970s, and studies by my colleagues and I confirmed and updated the earlier findings (41, 42). A predictive model that assessed multiple variables also documented microorganism identity as an independent predictor (4). Microorganisms that always or nearly always (>90%) represent true bacteremia or fungemia include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli* and other members of the *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Candida albicans* (42). Although published data from large studies with multiple isolates of the following organisms are lacking, it is my observation that *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, members of the *Bacteroides fragilis* group, *Candida* species other than *C. albicans*, and *Cryptococcus neoformans* always or virtually always represent true infection. In contrast, microorganisms such as *Corynebacterium* species, *Bacillus* species other than *B. anthracis*, and *Propionibacterium acnes* represent true bacteremia only rarely (42). Detection of CoNS, the most frequent of all blood culture isolates, can be especially vexing. These bacteria are most often contaminants, but they have taken on increased clinical importance as the etiologic agents of catheter-associated bacteremia and bacteremia in patients with vascular and other prostheses (19, 26, 42). Accordingly, one can no longer judge the clinical significance of a CoNS isolate solely on the basis of its identity. Similarly, the clinical significance of other microorganisms also cannot be judged based only their identity. For example, in a recent study, enterococci and viridans group streptococci were pathogens 78 and 38% of the time, respectively, and *Clostridium perfringens* most often (77%) was a contaminant, whereas other *Clostridium* species most often (80%) were pathogens (42).

The number of blood culture sets that grow microorganisms, especially when measured as a function of the total number obtained, has proved to be a useful aid in interpreting the clinical significance of positive blood cultures (18, 41, 42). In contrast to patients with endocarditis or other bloodstream infections, in whom all blood cultures or the majority thereof are positive, patients whose blood cultures grow contaminants usually have only a single blood culture (when two or more are obtained) that is positive (42). Although obvious, it bears emphasis that if only a single blood culture is obtained, the value

* Mailing address: Robert Wood Johnson Medical School, 1 Robert Wood Johnson Pl., New Brunswick, NJ 08903-0019. Phone: (732) 235-7713. Fax: (732) 235-7951. E-mail: weinstei@umdnj.edu.

of this tool ceases to exist; and this is but one reason (another being increased blood volume) that at least two blood culture specimens are recommended as standard practice (2, 23, 37). The value of obtaining more than a single blood culture is that it also assists in interpreting the clinical significance of positive results by virtue of the following calculation. If an institution has a baseline blood culture contamination rate of 3%, the probability of recovering the same organism in two culture sets from a patient, and of that organism being a contaminant, is less than 1 in 1,000 ($0.03 \times 0.03 = 0.0009$)!

A laboratory tool that has been used as an aid to differentiating clinically significant isolates from contaminants is assessment of the time necessary for microbial growth to occur (4). The underlying premise is that growth of pathogens, which are likely to be present in larger inocula, will be detected earlier than that of contaminants, which are likely to be present in much smaller quantities (18). Whereas this concept likely has validity, the degree of overlap in the detection times of true pathogens versus contaminants is such that this variable cannot be relied upon as a predictor of a true-positive culture (8). Moreover, with the wide use of continuously monitoring blood culture systems and the concomitant decrease in the time to detection of growth, the time difference between the detection of true pathogens and contaminants has been narrowed even further.

Some microbiologists and clinicians have used the number of culture bottles positive within a blood culture set as a guide to determine whether isolates represent true pathogens or contaminants. However, there now are published data, at least for CoNS, that show that this technique is not clinically useful (22; Peacock et al., letter). Although clinically significant CoNS may grow more often in multiple bottles within a set as opposed to a single bottle, and contaminants may more often grow in only one bottle of a set, the degree of overlap is such that for a given culture this information cannot predict clinical significance reliably (22; Peacock et al., letter). Accordingly, this criterion should not be used.

THE PARADOX OF INCREASING NUMBERS OF CONTAMINANTS

Despite numerous advances in blood culture methodology and systems in recent decades, some hospitals and laboratories have noted that an increasing proportion of blood culture isolates represent contamination compared with those in years past (42). There are several possible explanations for this unexpected observation. The newer continuously monitoring blood culture systems have improved algorithms for detecting microbial growth and may be detecting microorganisms present in low numbers that previously were missed. Moreover, several broth medium formulations such as the BACTEC Plus Resin media (Becton Dickinson, Sparks, Md.) and BacT/ALERT FN media (bioMérieux, Durham, N.C.) have been shown to have improved detection of staphylococci, including CoNS which most often are contaminants (10, 20, 28, 38, 40, 43, 45). Thus, the ability of new systems and media to detect these organisms, even when present in small numbers, may be responsible in part for the observed increase in the proportion of blood cultures with contaminants.

The increased use of central venous access catheters and

utilization of these devices for the purpose of obtaining blood specimens for culture may also be contributing to the increased numbers of contaminated blood cultures. Several studies have documented increased contamination when blood cultures are obtained in this fashion (5, 6, 7; R. B. Sivadas, B. Vazirani, S. Mirrett, and M. P. Weinstein, Abstr. 101st Gen. Meet. Am. Soc. Microbiol., abstr. C10, 2001), perhaps because it is more difficult to sterilize these devices than it is the skin before blood is obtained. Although physicians and nurses may believe they are saving patients the pain of an extra needle stick when blood cultures are obtained from catheters rather than by venipuncture, they may actually be doing their patients and the health care system a disservice if contaminants are grown from the culture resulting in the need for even more cultures, other diagnostic studies, unnecessary antibiotic therapy, and the associated incremental costs of care.

Prior to the human immunodeficiency virus (HIV) era, blood cultures traditionally were obtained by a two-needle technique, using a sterile needle and syringe to perform the venipuncture, then changing to a second sterile needle before inoculating the blood culture vial. The purpose of the two-needle technique was to reduce the chance that skin microorganisms that might be present on the needle used for the venipuncture would be inoculated into the blood culture vial, thereby resulting in a contaminated blood culture. As the knowledge of HIV as a bloodborne pathogen and the risks of needle stick transmission of HIV became evident, several studies were undertaken to determine whether contamination rates would be affected if only one needle was used for both venipuncture and inoculation of blood culture vials (9, 15, 16). The results of each of these studies showed no significant increase in contamination rates when the single-needle technique was used. Subsequently, however, a meta-analysis suggested that single-needle blood cultures were associated with contamination rates of 3.7% compared with 2.0% when a two-needle technique was used (30). Since the current standard of care continues to be the single-needle technique in order to reduce the risk of occupational needle stick injuries, slightly higher contamination rates may have to be tolerated.

REDUCING THE NUMBER OF CONTAMINATED BLOOD CULTURES

Although it is not possible to achieve contamination rates of zero or even close to zero (31), there are potential means by which contamination can be reduced. These include the use of collection methods that increase the chances for sterility, for example, obtaining blood via venipuncture rather than from an intravascular catheter or using a two-needle rather than a single-needle technique, as has already been mentioned. For the reasons already stated, the two-needle method is unlikely to return to widespread use; however, laboratories and institutions can and should actively promote blood cultures obtained from venipuncture rather than intravascular devices as a means of practicing evidence-based medicine.

There is also evidence that some antiseptic preparations may be more efficacious than others in reducing contamination rates. Povidone iodine preparations require 1.5 to 2 min of contact time to produce their maximum antiseptic effect, whereas iodine tincture requires approximately 30 s (13). Health care

workers who obtain blood cultures are often in a hurry, do not understand the importance of antiseptic preparation contact time, and are less likely to wait 1.5 to 2 min as opposed to half a minute before obtaining blood. At least two studies have documented a significantly lower contamination rate using iodine tincture compared with an iodophor (17, 31). Another report compared the use of 0.2% chlorine peroxide and 10% povidone iodine and demonstrated lower contamination rates when chlorine peroxide was used (29). Lastly, an alcoholic solution of 0.5% chlorhexidine gluconate used as an antiseptic prior to blood culture was associated with significantly lower contamination rates compared with a standard povidone-iodine preparation (21).

Several published studies have shown that trained phlebotomists or blood culture teams can reduce contamination rates in individual institutions (27, 32, 36), and this has been confirmed in my own institution (Sivadas et al., 101st Gen. Meet. Am. Soc. Microbiol.). At a New York City, N.Y., community teaching hospital, the contamination rate for blood cultures drawn by a blood culture team using a commercially available blood culture prep kit was approximately 1% compared with rates of 4.8% for blood cultures drawn by resident physicians using the same method (36). The contamination rate when residents did not use the commercial prep kit was even higher (8.4%) (36). In a large survey of over 600 hospitals sponsored by the College of American Pathologists, median contamination rates for institutions in which more than half of all blood cultures were collected by resident physicians was 3.9%, compared with 2.2% in the remaining institutions (27). In a pilot study at my institution, contamination of blood cultures obtained by phlebotomists trained and monitored monthly by microbiology laboratory staff was 3%, compared with nearly 11% for blood cultures obtained by resident physicians, non-degree nursing assistants, and nurses (M. P. Weinstein, unpublished observation). Subsequently, my colleagues and I assessed contamination in a larger study and again found that samples collected by phlebotomists had lower contamination rates than those collected by nondegree nursing assistants, nurses, and resident physicians (the last of whose samples had the highest contamination rates) (Sivadas et al., 101st Gen. Meet. Am. Soc. Microbiol.).

Whether or not commercially marketed blood culture prep kits are associated with reduced blood culture contamination rates remains controversial. Some studies have shown reduced contamination (27, 36) with commercial prep kits, whereas others have shown no difference (44). The manufacturer of at least one commercial prep kit has offered ongoing in-service education for personnel obtaining blood cultures (M. P. Weinstein, personal observation), which itself may be associated with reduced contamination rates.

LABORATORY WORKUP OF LIKELY BLOOD CULTURE CONTAMINANTS

In the real world of clinical microbiology laboratories, nearly half of all positive blood cultures represent contamination (42). Complete laboratory workup of contaminant isolates is associated with increased technologist workload and institutional cost. Therefore, some laboratories have developed algo-

ritms for dealing with this problem based, at least in part, on many of the studies reviewed in this article.

At the University of Iowa, for example, Richter et al. (25) tested, validated, and implemented an algorithm to minimize the workup of blood culture contaminants. CoNS, aerobic and anaerobic diphtheroids, *Micrococcus* spp., *Bacillus* spp., and viridans group streptococci are considered contaminants if certain criteria are met. If two or more blood cultures are obtained and only one is positive, the isolate is reported as a probable contaminant and susceptibility testing is not done unless the physician calls the laboratory. If only a single blood culture is obtained and grows one of the likely contaminants, a pathology resident reviews the patient's chart and judges the clinical significance of the isolate based on published data (42). Susceptibility testing is not done if the isolate is judged to be a contaminant. If two or more blood cultures are obtained and two cultures are positive within a 48-h period, one of two actions is taken. If the isolates are viridans group streptococci, they are presumed to be clinically significant and a full workup is done. If one of the other likely contaminants is present, the pathology resident reviews the patient's chart, and the laboratory workup proceeds according to the resident's judgment regarding clinical significance.

In my laboratory, a similar protocol is followed, but it is modified somewhat based on the fact that pathology residents are not always assigned to microbiology. The same microorganisms are considered likely contaminants. If two or more blood cultures are submitted and only one is positive, neither species identification nor susceptibility testing is done; the isolate is reported as a probable contaminant. If only one blood culture is submitted and it grows a likely contaminant, the workup is the same; the isolate is reported to be of indeterminate significance and the physician is advised to call the laboratory director if additional workup is needed. If two or more blood cultures grow a likely contaminant other than CoNS (see below) within a 48-h period, a full workup is done. If the isolates are the same, the identification and susceptibility results are reported. If the isolates are different, they are reported as probable contaminants without susceptibility results.

When two or more blood cultures grow CoNS, my laboratory undertakes species identification and reports susceptibility results. I find that the additional information assists in determining whether the isolates are clinically significant (12, 39). If the strains isolated have the same biochemical profile and antibiogram, it is probable that they are identical (although only molecular typing provides proof). This information increases the likelihood that the isolates represent clinically significant bacteremia, and identification and susceptibility results are reported to the clinician. However, if the biochemical profiles and antibiograms are not the same (i.e., two or more differences in biochemical results and susceptibilities [susceptible versus resistant]), the isolates are much more likely to represent contamination. In this instance, the laboratory reports that two different CoNS strains were identified, and susceptibility results are not provided. Although this technique has proven clinically useful in most circumstances, the algorithm is not foolproof. Two studies from the same center in Belgium have described polyclonal CoNS bacteremia (33, 34). Thus, in patients who have multiple positive blood cultures growing CoNS that appear to be different strains, the labora-

tory may need to perform additional testing if clinicians believe clinically significant infection is present.

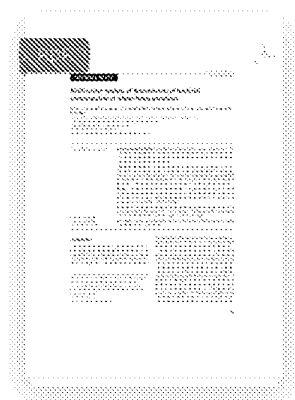
As is apparent from the foregoing discussion, the current state of the art remains suboptimal. Although progress has been made, the interpretation of the clinical significance of microorganisms that are common blood culture contaminants and the technical effort and institutional costs associated with working up probable contaminants remain problematic. Gold standards for solving these problems still are elusive.

REFERENCES

- Archer, G. L. 1985. Coagulase-negative staphylococci in blood cultures: the clinician's dilemma. *Infect. Control* 6:477-478.
- Aronson, M., and D. Bor. 1987. Blood cultures. *Ann. Intern. Med.* 106:246-253.
- Bates, D. W., L. Goldman, and T. H. Lee. 1991. Contaminant blood cultures and resource utilization: the true consequences of false-positive results. *JAMA* 265:365-369.
- Bates, D. W., and T. H. Lee. 1992. Rapid classification of positive blood cultures: prospective validation of a multivariate algorithm. *JAMA* 267:1962-1966.
- Bryant, J. K., and C. L. Strand. 1987. Reliability of blood cultures collected from intravascular catheter versus venipuncture. *Am. J. Clin. Pathol.* 88:113-116.
- DesJardin, J. A., M. A. Falagas, R. Ruthazer, J. Griffith, D. Wawrose, D. Schenkein, K. Miller, and D. R. Snyderman. 1999. Clinical utility of blood cultures drawn from indwelling central venous catheters in hospitalized patients with cancer. *Ann. Intern. Med.* 131:631-647.
- Everts, R. J., E. N. Vinson, P. O. Adholla, and L. B. Reller. 2001. Contamination of catheter-drawn blood cultures. *J. Clin. Microbiol.* 39:3393-3394.
- Hstrup, D. 1978. Sepsis: organisms from blood culture at the Mayo Clinic: 1968-1975, p. 23-25. *In* J. Washington II (ed.), *The detection of septicemia*. CRC Press, West Palm Beach, Fla.
- Isaacman, D., and R. Karasic. 1990. Lack of effect of changing needles on contamination of blood cultures. *Pediatr. Infect. Dis. J.* 9:274-278.
- Jorgensen, J. H., S. Mirrett, L. C. McDonald, P. R. Murray, M. P. Weinstein, J. Fune, C. W. Trippy, M. Masterson, and L. B. Reller. 1997. Controlled clinical laboratory comparison of BACTEC Plus Aerobic/F resin medium with BacT/Alert Aerobic FAN medium for detection of bacteremia and fungemia. *J. Clin. Microbiol.* 35:53-58.
- Khatib, R., K. M. Riederer, J. A. Clark, S. Khatib, L. E. Briski, and F. M. Wilson. 1995. Coagulase-negative staphylococci in multiple blood cultures: strain relatedness and determinants of same-strain bacteremia. *J. Clin. Microbiol.* 33:816-820.
- Kim S-D., L. C. McDonald, W. R. Jarvis, S. K. McAllister, R. Jerris, L. A. Carson, and J. M. Miller. 2000. Determining the significance of coagulase-negative staphylococci isolated from blood cultures at a community hospital: a role for species and strain identification. *Infect. Control Hosp. Epidemiol.* 21:213-217.
- King, T. C., and P. B. Price. 1963. An evaluation of iodophors as skin antiseptics. *Surg. Gynecol. Obstet.* 116:361-365.
- Kirchhoff, L. V., and J. N. Sheagren. 1985. Epidemiology and clinical significance of blood cultures positive for coagulase-negative staphylococcus. *Infect. Control* 6:479-486.
- Krumholz, H. M., S. Cummings, and M. York. 1990. Blood culture phlebotomy: switching needles does not prevent contamination. *Ann. Intern. Med.* 113:290-292.
- Leisure, M. K., D. M. Moore, J. D. Schwartzman, G. F. Hayden, and L. G. Donowitz. 1990. Changing the needle when inoculating blood cultures: a no-benefit and high-risk procedure. *JAMA* 264:2111-2112.
- Little, J. R., P. R. Murray, P. S. Traynor, and E. Spitznagel. 1999. A randomized trial of povidone-iodine compared with iodine tincture for venipuncture site disinfection: effects on rates of blood culture contamination. *Am. J. Med.* 107:119-125.
- MacGregor, R. R., and H. N. Beaty. 1972. Evaluation of positive blood cultures. Guidelines for early differentiation of contaminated from valid positive cultures. *Arch. Intern. Med.* 130:84-87.
- Martin, M. A., M. A. Pfaller, and R. P. Wenzel. 1989. Coagulase-negative staphylococcal bacteremia: mortality and hospital stay. *Ann. Intern. Med.* 110:9-16.
- McDonald, L. C., J. Fune, L. D. Guido, M. P. Weinstein, L. G. Reimer, T. M. Flynn, M. L. Wilson, S. Mirrett, and L. B. Reller. 1996. Clinical importance of the increased sensitivity of BacT/Alert FAN aerobic and anaerobic blood culture bottles. *J. Clin. Microbiol.* 34:2180-2184.
- Mimoz, O., A. Karim, A. Mercat, M. Cosseron, B. Falissard, F. Parker, C. Richard, K. Samii, and P. Nordmann. 1999. Chlorhexidine compared with povidone-iodine as skin preparation before blood culture: a randomized controlled trial. *Ann. Intern. Med.* 131:834-837.
- Mirrett, S., M. P. Weinstein, L. G. Reimer, M. L. Wilson, and L. B. Reller. 2001. Relevance of the number of positive bottles in determining clinical significance of coagulase-negative staphylococci in blood cultures. *J. Clin. Microbiol.* 39:3279-3281.
- Reimer, L. G., M. P. Weinstein, and M. L. Wilson. 1997. Update on the detection of bacteremia and fungemia. *Clin. Microbiol. Rev.* 10:444-465.
- Reller, L. B. 1996. Introduction. *Clin. Infect. Dis.* 23:38-39.
- Richter, S. S., S. E. Beekmann, J. L. Croco, D. J. Diekema, F. P. Koontz, M. A. Pfaller, and G. V. Doern. 2002. Minimizing the workup of blood culture contaminants: implementation and evaluation of a laboratory-based algorithm. *J. Clin. Microbiol.* 40:2437-2444.
- Rupp, M. E., and G. L. Archer. 1994. Coagulase-negative staphylococci: pathogens associated with medical progress. *Clin. Infect. Dis.* 19:231-243.
- Schifman, R. B., and A. Pindur. 1993. The effect of skin disinfection materials on reducing blood culture contamination. *Am. J. Clin. Pathol.* 99:536-538.
- Smith, J. A., E. A. Bryce, J. H. Ngui-yen, and F. J. Roberts. 1995. Comparison of BACTEC 9240 and BacT/Alert blood culture systems in an adult hospital. *J. Clin. Microbiol.* 33:1905-1908.
- Souvenir, D., D. E. Anderson, Jr., S. Palpant, H. Mroch, S. Askin, J. Anderson, J. Claridge, J. Eiland, C. Malone, M. W. Garrison, P. Watson, and D. M. Campbell. 1998. Blood cultures positive for coagulase-negative staphylococci: antiseptic, pseudobacteremia, and therapy of patients. *J. Clin. Microbiol.* 36:1923-1926.
- Spitalnic, S. J., R. H. Wollard, and L. A. Mermel. 1995. The significance of changing needles when inoculating blood cultures: a meta-analysis. *Clin. Infect. Dis.* 21:1003-1006.
- Strand, C. L., R. R. Wajsbort, and K. Sturmann. 1993. Effect of iodophor vs. iodine tincture skin preparation on blood culture contamination rate. *JAMA* 269:1004-1006.
- Surdulescu, S., D. Utamsingh, and R. Shekar. 1998. Phlebotomy teams reduce blood culture contamination rate and save money. *Clin. Perform. Qual. Health Care* 6:60-62.
- Van Eldere, J., W. E. Peetermans, M. Struelens, A. Deplano, and H. Bobbaers. 2000. Polyclonal staphylococcal endocarditis caused by genetic variability. *Clin. Infect. Dis.* 31:24-30.
- Van Wijngaerden, E., W. E. Peetermans, S. Van Lierde, and J. Van Eldere. 1997. Polyclonal staphylococcus endocarditis. *Clin. Infect. Dis.* 25:69-71.
- Washington, J. A. 1975. Blood cultures: principles and techniques. *Mayo Clin. Proc.* 50:91-97.
- Weinbaum, F. L., S. Lavie, M. Danek, D. Sixsmith, G. F. Heinrich, and S. S. Mills. 1997. Doing it right the first time: quality improvement and the contaminant blood culture. *J. Clin. Microbiol.* 35:563-565.
- Weinstein, M. P. 1996. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. *Clin. Infect. Dis.* 23:40-46.
- Weinstein, M. P., S. Mirrett, L. G. Reimer, M. L. Wilson, S. Smith-Elekes, C. R. Chuard, K. L. Joho, and L. B. Reller. 1995. Controlled evaluation of BacT/Alert standard aerobic and FAN aerobic blood culture bottles for detection of bacteremia and fungemia. *J. Clin. Microbiol.* 33:978-981.
- Weinstein, M. P., S. Mirrett, L. Van Pelt, M. McKinnon, B. L. Zimmer, W. E. Kloos, and L. B. Reller. 1998. Clinical importance of identifying coagulase-negative staphylococci from blood cultures: evaluation of MicroScan Rapid and Dried Overnight Gram-positive panels versus a conventional reference method. *J. Clin. Microbiol.* 36:2089-2092.
- Weinstein, M. P., S. Mirrett, M. L. Wilson, L. J. Harrell, C. W. Stratton, and L. B. Reller. 1991. Controlled evaluation of BACTEC Plus 26 and Roche Septi-Chek aerobic blood culture bottles. *J. Clin. Microbiol.* 29:879-882.
- Weinstein, M. P., L. B. Reller, J. R. Murphy, and K. A. Lichtenstein. 1983. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. *Rev. Infect. Dis.* 5:535-553.
- Weinstein, M. P., M. L. Towns, S. M. Quartey, S. Mirrett, L. G. Reimer, G. Parmagiani, and L. B. Reller. 1997. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. *Clin. Infect. Dis.* 24:584-602.
- Wilson, M. L., S. Mirrett, F. T. Meredith, M. P. Weinstein, V. Scotto, and L. B. Reller. 2001. Controlled clinical comparison of BACTEC Plus Anaerobic/F versus Standard Anaerobic/F blood culture bottles for the detection of bacteremia and fungemia in adults. *J. Clin. Microbiol.* 39:983-989.
- Wilson, M. L., M. P. Weinstein, S. Mirrett, L. G. Reimer, C. Fernando, F. T. Meredith, and L. B. Reller. 2000. Comparison of iodophor and alcohol pledgets versus the Medi-Flex Blood Culture Prep Kit II for preventing contamination of blood cultures. *J. Clin. Microbiol.* 38:4665-4667.
- Wilson, M. L., M. P. Weinstein, S. Mirrett, L. G. Reimer, S. Smith-Elekes, C. R. Chuard, and L. B. Reller. 1995. Controlled evaluation of BacT/Alert standard anaerobic and FAN anaerobic blood culture bottles for the detection of bacteremia and fungemia. *J. Clin. Microbiol.* 33:2265-2270.

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

✕ DOWNLOAD



Multivariate analysis of determinants of bacterial contamination of whole-blood donations

Vox Sanguinis, 2002

✎ Luc Noel ✎ P. Perez ✎ Paul Pérez



Download with Zotero



Download with Mendeley

or download with email

ORIGINAL PAPER

Vox Sanguinis [2002] 82, 55–60

© 2002 Blackwell Science

Multivariate analysis of determinants of bacterial contamination of whole-blood donations

P. Perez¹, C. Bruneau², M. Chassaigne², L. R. Salmi¹, L. Noel³, P. Allouch³, A. Audurier², C. Guilan⁴, G. Janus⁵, G. Boulard³ & P. de Micco¹¹Institut de Santé publique, d'Epidémiologie et de Développement, Université Victor Segalen Bordeaux 2, Bordeaux, France²EFS Centre-Atlantique and Faculté de Médecine, Université de Tours, Tours, France³Hôpital Mignot and EFS Ile-de-France, Versailles, France⁴EFS Alpes-Méditerranée, Marseille, France⁵Centre de Transfusion Sanguine des Armées Jean Julliard, Clamart, France

Vox Sanguinis

Background and Objectives Introduction of bacteria into blood components at the collection stage seems to be a frequent occurrence. We therefore assessed determinants of bacterial contamination of whole-blood donations to gain insight into contamination mechanisms and direct prevention.

Materials and Methods A cross-sectional study was carried out on donors accepted for whole-blood donation in four French blood banks. Each blood bank used its own two-stage procedure for phlebotomy site preparation. Contamination was identified by culturing two 15-ml samples (collected aseptically at the outset of donation) in a BacT/Alert 240® system. Determinants were assessed by logistic regression analysis.

Results Bacterial contamination, mainly by skin flora, occurred in 76 (2.2%) out of 3385 donations. Significant determinants were as follows: the blood bank (odds ratio [OR] range = 3.0–5.6, $P < 0.001$); lack of repetition of scrub (OR = 2.7, $P = 0.032$); and donor age > 35 years (OR = 1.8, $P = 0.036$).

Conclusion Systematic scrub repetition should be implemented to reduce bacterial contamination by skin flora at the collection stage. Further research is required to clarify the role of different antiseptic agents and of donor age.

Key words: adverse effects, bacterial infections, blood donors, blood transfusion, logistic models, prevention, risk factors.

Received: 14 May 2001,

revised: 16 October 2001,

accepted: 25 October 2001

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

[Download](#)

Introduction

Transfusion-associated bacterial contamination (TABC) is a potentially serious transfusion adverse event, reported to be responsible for 10% of transfusion-related fatalities reported in the USA from 1976 to 1999 [1], and for 22% in France from 1994 to 1999 [2]. TABC was considered by the United States

ing transfusion safety [3] and has been recently acknowledged as the most frequent transfusion-transmitted infection [4].

The most effective measures for preventing TABC would be systematic culture of every blood component or the application of bacterial inactivation steps during manufacture. However, bacterial inactivation methods are still under development [5], and techniques currently available for aseptic sampling and culture of cellular blood components may need further validation [6]. Other possible interventions may be aimed at avoiding or reducing the introduction of bacteria from all possible sources [7]. Contamination sources are rarely found, but that most frequently reported is the blood donor [7,8]. Bacteria may come from the bloodstream of infected but asymptomatic donors, or from the donor skin [8]. Despite well-conducted antisepsis, high concentrations of bacteria

Correspondence: Paul Perez, MD, PhD, Unité de Soutien Méthodologique à

la Recherche Clinique et Epidémiologique du Centre Hospitalier
Universitaire de Bordeaux, Unité INSERM 330, Case 11, Université V.
Segalen Bordeaux 2, 146 Léo-Saignat, 33076 Bordeaux Cedex, France
Tel.: (33) 5 57 57 14 42
Fax: (33) 5 57 57 15 78
E-mail: Paul.Perez@sped.u-bordeaux2.fr

55

56 P. Perez *et al.*

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 procedures to improve the safety of blood transfusion. Research on factors contributing to bacterial contamination 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: Etab-

lissement 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 Betadine® (chlorhexidine) but 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: *Staphylococcus aureus* CIP 53-156 (American Type Culture Collection [ATCC] 6538P; ATCC, Rockville, MD), *Clostridium sporogenes* CIP 79-03 (ATCC 19404), *Propionibacterium*

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

BOWLING

Determinants of donation bacterial contamination 57

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 specific form at the lab draw and transferred to the tree 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 quar-

tile: 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 origin-

ally from 76 donations. The most common bacterial species were CNS (66%). Gram-positive bacilli, mostly *Bacillus* species and *P. acnes*, accounted for 14%, and Gram-negative bacilli for 5%, of species.

The overall prevalence rate of bacterial contamination was 2.2% (95% CI: 1.8–2.8%).

Determinants of bacterial contamination

In the univariate analysis, characteristics significantly associated with bacterial contamination were the blood bank, period of collection, time since last meal, donor age and the presence of hairs at the phlebotomy site (Table 1). As the rate of contamination was more than twofold higher when donors were > 35 years, this characteristic was used as a binary variable.

Characteristics significantly associated with bacterial contamination in the final multivariate model were the blood bank, a donor age > 35 years and the lack of repetition of the antisepsis scrub stage (Table 1).

Discussion

Our study confirmed the high frequency of bacterial contamination of whole-blood donations and revealed a strong protective role of repeating the antisepsis scrub stage. Other main determinants were the collecting blood bank and donor age. Contaminating bacteria, isolated after culture, were most likely to have a skin origin.

Our estimation of bacterial contamination rates of blood donations is higher than those previously reported in whole-blood units, but consistent with those of the first few ml collected [20] and with blood-culture contamination rates reported in clinical settings, where the same mechanisms may be implicated [21,22].

The major influence of the collecting blood bank may be related to the agent used for antisepsis. The risk of bacterial contamination was the highest in the blood bank using non-alcoholic povidone-iodine. This is consistent with studies

© 2002 Blackwell Science Ltd. *Vox Sanguinis* (2002) 82, 55–60

58 P. Perez *et al.*

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)

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

 Blackwell Science

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	3.36	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.^bCI: confidence interval of odds ratio (OR).^cLikelihood ratio test.^dReference category for OR estimation.© 2002 Blackwell Science Ltd. *Vox Sanguinis* (2002) 82, 55–60

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

Download

A Multivariate analysis of determinants of bacterial contamination of whole-blood donations

[Download](#)

[About](#) [Press](#) [Blog](#) [People](#) [Papers](#) [Job Board](#) [Advertise](#) [We're Hiring!](#) [Help Center](#)

Find new research papers in: [Physics](#) [Chemistry](#) [Biology](#) [Health Sciences](#) [Ecology](#) [Earth Sciences](#) [Cognitive Science](#) [Mathematics](#) [Computer Science](#)

[Terms](#) [Privacy](#) [Copyright](#) Academia ©2019



European Patent Office
80298 MUNICH
GERMANY

Questions about this communication ?
Contact Customer Services at www.epo.org/contact



Thum, Bernhard
Wuesthoff & Wuesthoff
Patentanwälte PartG mbB
Schweigerstraße 2
81541 München
ALLEMAGNE

Date
09.12.20

Reference EPA-150 670	Application No./Patent No. 20197213.0 - 1132
Applicant/Proprietor Kurin, Inc.	

Communication

The extended European search report is enclosed.

The extended European search report includes, pursuant to Rule 62 EPC, the European search report (R. 61 EPC) or the partial European search report/ declaration of no search (R. 63 EPC) and the European search opinion.

Copies of documents cited in the European search report are attached.

☒ 0 additional set(s) of copies of such documents is (are) enclosed as well.

The following have been approved:

☐ Abstract

☐ Title

☒ The Abstract was modified and the definitive text is attached to this communication.

The following figure(s) will be published together with the abstract: 30B

Refund of search fee

If applicable under Article 9 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.

Should you wish to further prosecute this application in the examination phase, your attention is drawn to the provisions of Rule 70a EPC. An invitation to respond to the extended European search report will be issued once the date of publication of the European search report has been mentioned in the European Patent Bulletin (R. 69(1), R. 70(2) EPC).





European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840

Application No.:

20 197 213.0

The application and the invention to which it relates seem to meet the requirements of the EPC. Upon presence of a valid request for examination and consideration by the examining division, a communication under Rule 71(3) EPC may be issued.



EUROPEAN SEARCH REPORT

Application Number
EP 20 19 7213

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	US 2014/039348 A1 (BULLINGTON GREGORY J [US] ET AL) 6 February 2014 (2014-02-06) * the whole document *	1-7	INV. A61B5/15 A61B5/153 A61B5/154 A61B5/157
A	US 2014/107564 A1 (BULLINGTON GREGORY J [US] ET AL) 17 April 2014 (2014-04-17) * the whole document *	1-7	
A	US 4 813 433 A (DOWNEY JOHN M [US]) 21 March 1989 (1989-03-21) * the whole document *	1-7	
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) * abstract * * paragraph [0048] - paragraph [0075]; figures 2-12 *	1-7	
A	WO 2013/181352 A1 (MAGNOLIA MEDICAL TECHNOLOGIES INC [US]; BULLINGTON GREGORY J [US]; PAT) 5 December 2013 (2013-12-05) * abstract * * paragraph [1090]; figures 11,12 *	1-7	
			TECHNICAL FIELDS SEARCHED (IPC)
			A61B
The present search report has been drawn up for all claims			
Place of search Berlin		Date of completion of the search 19 November 2020	Examiner Nielsen, Michael
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			
T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

1
EPO FORM 1503 03/02 (P04001)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 20 19 7213

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

19-11-2020

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014039348 A1	06-02-2014	US 2014039348 A1	06-02-2014
		US 2016113560 A1	28-04-2016
		WO 2014022275 A1	06-02-2014

US 2014107564 A1	17-04-2014	EP 2906269 A1	19-08-2015
		EP 3318295 A1	09-05-2018
		US 2014107564 A1	17-04-2014
		US 2015367069 A1	24-12-2015
		US 2018177943 A1	28-06-2018
		US 2019151536 A1	23-05-2019
		WO 2014058945 A1	17-04-2014

US 4813433 A	21-03-1989	NONE	

US 2013317391 A1	28-11-2013	US 2013317391 A1	28-11-2013
		US 2015099996 A1	09-04-2015
		US 2015351678 A1	10-12-2015
		US 2018092584 A1	05-04-2018
		US 2019209066 A1	11-07-2019

WO 2013181352 A1	05-12-2013	AU 2013267448 A1	18-12-2014
		AU 2017216493 A1	07-09-2017
		AU 2019204941 A1	25-07-2019
		AU 2020213415 A1	27-08-2020
		CA 2875118 A1	05-12-2013
		CN 104902817 A	09-09-2015
		CN 107736901 A	27-02-2018
		EP 2854643 A1	08-04-2015
		EP 3173021 A1	31-05-2017
		EP 3549522 A1	09-10-2019
		JP 6242386 B2	06-12-2017
		JP 6695314 B2	20-05-2020
		JP 2015519145 A	09-07-2015
		JP 2018034009 A	08-03-2018
		JP 2020121167 A	13-08-2020
		US 2014155781 A1	05-06-2014
		US 2015351679 A1	10-12-2015
		US 2018116577 A1	03-05-2018
		US 2020359951 A1	19-11-2020
		WO 2013181352 A1	05-12-2013

EPO FORM P0453

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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

☒ 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. 15C
☒ 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 contaminants in collected blood samples, which in turn reduces or eliminates false positive readings in blood cultures or other testing of collected blood samples. A blood sample optimization system can include a blood sequestration device (1500) located between a patient needle and a sample needle. The blood sequestration device can include a sequestration chamber (1508) for sequestering an initial, potentially contaminated aliquot of blood, and may further include a sampling channel (1506) that bypasses the sequestration chamber to convey likely uncontaminated blood between the patient needle and the sample needle after the initial aliquot of blood is sequestered in the sequestration chamber.

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)

EP0-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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

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

☒ See patent family annex.

* Special categories of cited documents :

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

"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

11 October 2016

Date of mailing of the international search report

19/10/2016

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Schultz, Ottmar

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/043709

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 416 290 A (LUTKOWSKI LAWRENCE [US]) 22 November 1983 (1983-11-22) abstract; figures -----	1-20
A	US 3 648 684 A (BARNWELL CLEORA W ET AL) 14 March 1972 (1972-03-14) abstract; figures -----	1-20
A	EP 1 665 986 A1 (BECTON DICKINSON CO [US]) 7 June 2006 (2006-06-07) figures 13,14 -----	1-20
A	US 4 056 101 A (GEISSLER ULRICH C ET AL) 1 November 1977 (1977-11-01) abstract; figures -----	1-20
A	US 2013/317391 A1 (BULLINGTON GREGORY J [US] ET AL) 28 November 2013 (2013-11-28) paragraphs [0084] - [0094] figures 16-18 -----	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2016/043709

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

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.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.
PCT/US2016/043709

International filing date (day/month/year)
22.07.2016

Priority date (day/month/year)
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 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will 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 notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

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

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

Name and mailing address of the ISA:



European Patent Office
Gitschiner Str. 103
D-10958 Berlin
Tel. +49 30 25901 - 0
Fax: +49 30 25901 - 840

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Schultz, Ottmar

Telephone No. +49 30 25901-0



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/043709

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:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/043709

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

1. Statement

Novelty (N)	Yes: Claims	<u>2, 6, 7, 11, 14</u>
	No: Claims	<u>1, 3-5, 8-10, 12, 13, 15-20</u>
Inventive step (IS)	Yes: Claims	<u>6, 14</u>
	No: Claims	<u>1-5, 7-13, 15-20</u>
Industrial applicability (IA)	Yes: Claims	<u>1-20</u>
	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]; FISCHER 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 and 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.

+++++

Updated Review of Blood Culture Contamination

Keri K. Hall¹* and Jason A. Lyman²

Division of Infectious Diseases and International Health, Department of Internal Medicine,¹ and Division of Clinical Informatics, Department of Public Health Sciences,² University of Virginia School of Medicine, Charlottesville, Virginia 22908

INTRODUCTION	788
Prevalence and Significance	788
DETECTION OF CONTAMINATED BLOOD CULTURES	789
Identity of Organism	789
Number of Positive Blood Culture Sets	790
Number of Positive Blood Culture Bottles within a Blood Culture Set	792
Time to Growth (Time to Positivity)	792
Quantity of Growth per Culture Bottle	793
Clinical and Laboratory Clues	793
Source of Cultures (Catheter Drawn versus Percutaneous)	793
Role of Information Technology: Automated Classification of Positive Blood Cultures	794
PREVENTING CONTAMINATION	795
Skin Preparation	795
Culture Bottle Preparation	796
Single Needle versus Double Needle	796
Obtaining Cultures Percutaneously instead of via Vascular Catheters	796
Phlebotomy Team	796
Commercial Blood Culture Collection Kits	797
SUPPORTING OPTIMAL USE OF BLOOD CULTURES	797
Clinical Prediction Models	797
Population Studies of Bacteremia Prevalence	798
BLOOD CULTURE CONTAMINATION IN THE PEDIATRIC POPULATION	798
CONCLUSION	799
REFERENCES	799

INTRODUCTION

The blood culture represents a critical tool for the health care professional as a means of detecting the dangerous presence of living organisms in the bloodstream. A positive blood culture can suggest a definitive diagnosis, enable the targeting of therapy against the specific organism(s) in question, and provide prognostic value (22). Like any test, however, false-positive results can limit the utility of this important tool. In blood cultures, false positives arise due to contamination, which occurs when organisms that are not actually present in a blood sample are grown in culture. Contaminated cultures have been recognized as a troublesome issue for decades and continue to be a source of frustration for clinical and laboratory personnel alike. Faced with a positive blood culture result, clinicians must determine whether the organism represents a clinically significant infection associated with great risk of morbidity and mortality or a false-positive result of no clinical consequence. Further complicating the issue in recent years is the increasing use of central venous catheters (CVC) and other indwelling vascular access devices (5, 90). Interpretation of culture results for patients with these devices in place is particularly challenging because while these individuals are at

increased risk for bacteremia, such results may also indicate culture contamination or colonization of the line. The clinical uncertainty associated with the interpretation of ambiguous culture results is costly, as has been demonstrated in a number of studies of both adult and pediatric patients (13, 115, 125, 138).

Prevalence and Significance

While target rates for contamination have been set at 2 to 3% (30, 131), actual rates seem to vary widely between institutions, from as little as 0.6% to over 6% (13, 64, 67, 82, 89, 112, 113, 125, 131, 150). The College of American Pathologists (CAP) Q-Probes quality improvement study involved the prospective examination of 497,134 blood culture specimens from 640 U.S. health care institutions (113). While the median adult inpatient contamination rate was 2.5%, some organizations had a rate of less than 1.0%, while for other organizations, more than 5.0% of their blood cultures were contaminated. More recently, the CAP Q-Tracks study found an overall median contamination rate of 2.92% for data collected from 356 institutions from 1999 to 2003. There is also some evidence to suggest that in recent decades, these rates have been on the increase (150), although the Q-Tracks study found no increase over the 4-year time frame for their data. The suggested reasons for this increase include technological advances that allow the detection of smaller quantities of living microorganisms in the blood, the increased use of indwelling catheters for the

* Corresponding author. Mailing address: P.O. Box 800473, Department of Infection Control, University of Virginia Health System, Charlottesville, VA 22908. Phone: (434) 924-0260. Fax: (434) 924-1225. E-mail: kkh2n@virginia.edu.

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 blood-stream 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
<i>Corynebacterium</i> spp. (other than <i>C. jeikeium</i>)	33.4	96	Not reported	68–78
<i>Bacillus</i> spp.	0.8	91.7	Not reported	68–70 (other than <i>B. anthracis</i>)
<i>Propionibacterium acnes</i>	3.0	100	Not reported	84–85
Viridans group streptococci	4.5	49.3	Not reported	32–33
<i>Clostridium perfringens</i>	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

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 ≤ 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 Schiffman 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 an-

aerobic 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 ≤ 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 ± 1.4 days) from culture sets that differed by strain (1.9 ± 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).

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 $<36^{\circ}\text{C}$) or marked fever (temperature of $>40^{\circ}\text{C}$), leukocyte counts of $<4,000$ leukocytes/ μl or $>20,000$ leukocytes/ μl , and hypotension predicted true infection as opposed to contamination (155). However, another study found that fever at the onset of a blood culture positive for *Staphylococcus epidermidis* did not help differentiate true bacteremia from contamination in leukemic patients (68). Other studies have found similar results in which sepsis-like syndromes, including fever, did not help differentiate episodes thought to be contaminants from true bacteremias (118).

Clinical criteria combined with laboratory data have been used in several studies to differentiate contaminated cultures from clinically significant cultures (14, 30, 43, 51, 59, 125, 129, 155). Bates et al. developed a multivariate algorithm utilizing many predictors, one of which was a "clinical risk score," which consisted of fever, rigors, outcome, intravenous drug abuse, acute abdomen, and comorbidities as variables (14). This clinical risk score was found to be predictive of contamination, as was the organism type, days to culture positivity, and the presence of multiple positive cultures. Khatib et al.'s molecular analysis of 47 episodes of coagulase-negative staphylococcus-positive cultures found that strain relatedness was more frequent in patients who had a fever (15 [71.4%] of 21), an identifiable source (7 [77.8%] of 9), or a bacteremia that met

the definition of nosocomial acquisition (18 [50%] of 36) (57). The presence of an identifiable source, specifically, a central venous catheter, was found to be predictive of true bacteremia in another study as well (68).

National Nosocomial Infection Surveillance (NNIS) parameters and surveillance criteria often utilize the treating clinician's diagnosis of bloodstream infection to differentiate true bacteremia from contamination for common contaminants (43). However, one study that correlated cultures that grew the same strain of coagulase-negative staphylococci with the clinician's suspicion/treatment found that the classification of coagulase-negative staphylococcal bacteremias as the same strain correlated poorly with the clinical assessment utilizing the clinician's diagnosis (117). Furthermore, in another study, even though treating clinicians and reviewers who performed retrospective analyses agreed on 100% of coagulase-negative staphylococcal bacteremias and 95% of contaminations, one-half of patients with contaminated blood cultures were still treated with antibiotics, leading to vancomycin misuse in 34% of patients (125). Of course, this may be related to a lower threshold for interpreting an uncertain result as an infection until proven otherwise in the presence of a gravely ill patient rather than true disagreements about what represents contamination.

Other surrogate markers for infection have been studied as well, including the use of C-reactive protein measurements. In neonates, a single C-reactive protein obtained at least 12 h after the onset of symptoms has been found to be helpful to diagnose clinical sepsis (18, 98, 110). In another study of leukemic patients, the level of a single C-reactive protein did not help differentiate between contamination and bacteremia, but the median increase in C-reactive protein over 24 h from the first positive blood culture did help (68). Given these data, some neonatal intensive care unit (NICU) clinicians are beginning to utilize C-reactive protein for this purpose: a survey of 35 NICUs found that C-reactive proteins were routinely obtained at 23% of NICUs and by 30% of NICU clinicians (105).

Source of Cultures (Catheter Drawn versus Percutaneous)

When blood cultures drawn from a vascular catheter are positive, the results could indicate one of three possibilities: true bacteremia, catheter colonization, or culture contamination. Catheter colonization is not contamination, nor is it infection—it occurs when microorganisms grow on the surface of a catheter such that the colonizing organisms would be expected to grow in blood samples obtained from the catheter (in contrast to culture contamination). Catheter colonization may or may not progress to cause symptoms of infection or true bacteremia. Studies have shown that 15 to 25% of short-term central venous catheters are colonized, usually by coagulase-negative staphylococci, and most patients have no evidence of infection (46, 133). Therefore, cultures drawn from central lines could be expected to be positive due to colonization in a substantial number of patients.

Because of the uncertainties surrounding blood cultures obtained from vascular catheters, the clinical utility of these cultures has been evaluated. In one study that used blinded assessments by infectious disease experts to determine the presence of true bacteremia, catheter-drawn cultures had a

sensitivity of 89%, compared to 78% for peripheral cultures, with a positive predictive value of 63% for catheter-drawn cultures versus 73% for percutaneous cultures (34). The results of that study were similar to those of other studies, leading many to suggest that if cultures are obtained from a catheter, at least one set should be drawn percutaneously (13, 20, 38, 74, 76, 92). The advantage of drawing a percutaneous culture to aid the interpretation of catheter-drawn cultures was mathematically evaluated by Tokars in a modeling study of coagulase-negative staphylococcal bacteremia (139). Tokars found that when two of two cultures were positive, the positive predictive value would be 98% if both samples were obtained through the vein, 96% if one sample was obtained through a catheter and the other was obtained through a vein, and only 50% if both samples were obtained through a catheter (139). Other studies, however, have not found a significant difference between results of catheter-drawn and peripheral cultures (39, 125, 158). If it is in fact true that blood cultures obtained from vascular catheters are more likely to be contaminated than percutaneously obtained cultures, the reason may be that sterilizing catheters prior to accessing them is more difficult than sterilizing skin or that catheter colonization is confounding catheter-drawn culture results (151).

One instance in which multiple sets of cultures are often not obtained is in NICU infants for whom the removal of too much blood is of concern and difficulty obtaining peripheral cultures is a reality. Indeed, in a survey of 35 NICUs, 83% of clinicians drew only one blood culture when a catheter-drawn sample was unavailable (105). In that same study, if blood was able to be obtained from a catheter, 224 (80%) of 279 clinicians said that they would obtain at least two blood cultures, including at least one from a peripheral vein; 37 (13%) would obtain a single culture through the central venous catheter; and 18 (6%) would obtain a single blood culture from a peripheral vein. Because of these concerns in the NICU population, antimicrobials that are active against coagulase-negative staphylococci (usually vancomycin) are often overutilized in the NICU. When practice habits from 35 NICUs were evaluated, 47 to 85% of clinicians completed a full course of antimicrobials when a single blood culture was obtained and grew coagulase-negative staphylococci, whereas a significantly lower percentage (22 to 47%) completed a full course when one of two blood culture sets grew coagulase-negative staphylococci (105).

Role of Information Technology: Automated Classification of Positive Blood Cultures

In recent decades, health information technology has played an increasingly important role in the field of infectious disease. Infection control activities are extremely data intensive, and health care information technology offers tremendous potential for improvements in the efficiency of surveillance and reporting systems. Health care institutions are increasingly turning to data-warehousing technologies to support these activities (23, 47, 109, 157). With respect to the challenge of blood culture contamination, investigators have explored automated, computer-based approaches for the classification of culture results as likely contaminants or pathogens. Such an approach offers at least two potential benefits: assisting clinical

interpretation and decision-making in the face of ambiguous culture results and providing objective, reproducible, cost-efficient approaches to surveillance of nosocomial infections and bloodstream infection rates. In addition, such methods are almost always significantly faster, as they do not rely on manual identification of positive blood cultures or subsequent labor-intensive review of potentially incomplete or unavailable clinical data.

From the standpoint of surveillance, differentiating contamination from true bacteremia is essential for the accurate measurement of nosocomial bloodstream infection rates. Automated approaches to this task have been shown to perform very well compared with infection control practitioners (ICP) applying the traditional NNIS criteria (56, 141, 161). Yokoe et al. demonstrated that an automated approach for detecting nosocomial infections that relied solely upon microbiology data agreed with an NNIS-based retrospective assessment by ICP 91% of the time for cultures of adult patients (161). Disagreements were due primarily to situations in which only a single positive culture had been identified. In this scenario, CDC definitions rely on additional clinical data such as patient findings or treatment information, while the automated approach relied on a subsequent positive culture within a 5-day period. As a result of this difference in approach, 5/65 cultures were labeled as contaminated by the automated approach and as true bacteremia by the NNIS definition. In pediatric patients, agreement was found only 50% of the time, suggesting that its utility in this population may be limited. Graham et al. specifically studied the ability of a similar system in the neonatal population (47). They examined the performance of an automated system for detecting nosocomial bloodstream infections in two neonatal intensive care units in support of infection control activities. They found that their sensitivity and specificity for detecting such infections were 79% and 96%, respectively, although when coagulase-negative staphylococci were excluded, those numbers rose to 84% and 99%.

Trick et al. focused on the evaluation of a computer-based approach for detecting hospital-acquired, CVC-associated bloodstream infections (141). A comprehensive comparison of prospective ICP review, retrospective investigator assessment, and various computer algorithms was conducted on positive blood cultures from adult patients. Making this determination required several specific steps, including (i) the appropriate classification of hospital-acquired infection versus infection present upon admission, (ii) the correct ascertainment of true bacteremia versus contamination, (iii) distinguishing primary versus secondary infections, and (iv) detection of CVC use. The automated rules varied with respect to the inclusion of medication data and the time period over which data were used by a given rule. Those authors found that their computer-based algorithms performed at least as well as the ICP assessment and in fact outperformed them when combined with a manual determination of CVC use. When they looked specifically at the classification of pathogens versus contaminant organisms, a computer-based algorithm that included both microbiology data as well as pharmacy data had a sensitivity and specificity of 77% and 73%, respectively. The use of microbiology data only resulted in a drop of sensitivity to 55%.

Other investigators focused on the automated classification of blood culture results in order to provide clinical decision

support by estimating probabilities of contamination and displaying this information to clinicians at the point of care. Wang et al. utilized a previously validated prediction model (14) and revised it to include only readily available electronic data (146). By eliminating clinical data such as blood pressure, temperature, etc., they found only a slight degradation in the performance of the model. They then implemented a clinical rule into the laboratory information system to display the probability information along with blood culture results. In a subsequent house staff survey, they found that half of the respondents indicated that the results had influenced their assessment of the probability of true bacteremia, and 98% indicated a desire to continue to receive the reports. These findings suggest that computer-based approaches offer not only benefits for surveillance activities but also an opportunity to change physician behavior for individual patients. Other investigators have also shown that models that use only readily available electronic data perform well in correctly predicting contamination (100).

PREVENTING CONTAMINATION

By definition, the specificity of the blood culture is directly related to the rate of false-positive results, which are caused primarily by contamination. Reducing contamination rates would lead to improved specificity and better performance of this important test. Unfortunately, there has been a dearth of blinded, randomized, controlled trials that might provide clear and compelling guidance on the best methods for the prevention of contamination. While few would claim that the complete elimination of contamination is possible, a number of efforts to reduce contamination rates have been explored, advocated, and utilized. Factors that have been explored for reducing contamination include skin preparation, culture bottle preparation, single versus double needle for bottle inoculation, source of culture (catheter versus percutaneous), the use of dedicated phlebotomy teams, and the use of commercial blood culture collection kits.

Skin Preparation

The most common source of contaminated percutaneous blood cultures is often thought to be the skin of the patient at the site where the cultures are obtained. One study attempted to find the source of coagulase-negative staphylococcal contaminants by performing molecular analysis to compare each blood isolate to isolates obtained from swabs of the patient and from the individual who obtained the cultures (144). Of 19 patients with contaminated cultures, six of the isolates were able to be matched to swabs, and all six matching swabs came from the patient, implying that the most common source of contamination is the patient's own skin flora. However, it is important that no matching sources were found for 13 of the 19 isolates.

Skin antisepsis cannot entirely prevent the contamination of blood cultures from skin flora because as many as 20% of skin-associated bacteria have been found to survive disinfection, as found by culturing skin samples harvested with a sterile surgical technique (21, 116). These skin bacteria can be located in deep layers of the skin or in other structures that antiseptics

cannot penetrate. Nonetheless, inadequate skin preparation is thought to be the most common cause of blood culture contamination (30, 89, 147).

Many studies have been performed to determine the best skin antiseptic product to use for blood culturing. Perhaps the most commonly studied and traditionally used skin antiseptic for blood culturing is povidone-iodine, an iodophor. Three studies have found significantly lower contamination rates using iodine tincture compared with povidone-iodine (67, 113, 131), although two of those studies did not have standardized phlebotomy protocols and drying times for the antiseptics. The CAP Q-Probes study investigators found that the median contamination rate was significantly lower in settings where tincture of iodine was used (2.1%) versus an iodophor (2.6%) ($P = 0.036$), but these differences were not found in organizations that relied on a dedicated phlebotomy service, suggesting that contamination may be more related to technique than the actual antiseptic used (113). One study of chlorine peroxide versus povidone-iodine found contamination in 22 (1.3%) of 1,639 cultures in the chlorine peroxide group compared to 37 (2.3%) of 1,637 in the povidone-iodine group ($P = 0.065$) (125). Another study found that 0.5% chlorhexidine plus alcohol had significantly lower contamination rates than standard povidone-iodine (82). In contrast, two studies that compared chlorhexidine to tincture of iodine did not find a statistically significant difference in contamination rates between the two products (11, 140).

Alcohol-based products are also frequently utilized for skin preparation for blood cultures. Calfee and Farr performed a randomized comparative trial of four skin antiseptics for 12,692 percutaneous blood cultures—10% povidone iodine, 70% isopropyl alcohol, tincture of iodine, or povidone-iodine plus 70% ethyl alcohol (25). The overall contamination rate was 2.62% during the study period. The contamination rates were 2.93% with povidone-iodine, 2.58% with tincture of iodine, 2.50% with isopropyl alcohol, and 2.46% with povidone-iodine plus 70% ethyl alcohol ($P = 0.62$). Although there were no significant differences between the groups, those authors concluded that the antiseptics that contained alcohol may have had greater efficacy. Other studies that examined the difference between alcohol solutions and iodine were unable to detect a statistically significant difference in contamination rates (64, 119).

Several barriers can prevent the skin antiseptic 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

phlebotomy teams are increasingly common in the inpatient setting; in a study of 640 institutions, Schiffman 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, Yehezkeili 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. Ramscook et al. found similar results in a 6-month study of 2,431 pediatric blood cultures, with contamination rates of 3.4% for specimens collected via intravenous catheters versus 2.0% for those obtained by separate venipuncture ($P = 0.043$) (101). While

that study used a large sample size, details of the study design and methods are somewhat unclear, making it difficult to ascertain both internal and external validity. Other studies have shown no difference in contamination rates according to specimen collection routes (55, 124). Given pediatricians' disinclination to subject children and infants to unnecessary painful procedures, and the lack of clear evidence on which approach best prevents specimen contamination, the use of existing catheters for blood culture collection continues in this patient population (79). As described above, single blood cultures are particularly common in pediatric patients; this fact, combined with the increased utilization of catheter-based culture specimens, makes discrimination between true bacteremia and contamination challenging, particularly when coagulase-negative staphylococci are grown in culture (24). To combat this challenge, investigators have explored multiple avenues, including the use of C-reactive protein, time to positivity, quantity of growth, and clinical status (3, 18, 19, 32, 44, 98, 110, 129). While none of these factors have performed well enough individually to warrant widespread adoption, they continue to be under investigation.

CONCLUSION

Clearly, progress has been made on several fronts in the battle against blood culture contamination. Better strategies for preventing contamination in the first place are being established, and we are improving our ability to distinguish contamination from true bacteremia. New research on measures to estimate the pretest likelihood of bacteremia offers promise in reducing unnecessary blood culture utilization. Despite the progress that has been made, however, significant barriers remain. Without a gold standard for truly distinguishing contaminant organisms from true pathogens, studies that seek to measure the success of prevention strategies are inherently limited. Similarly, efforts to help establish the posttest probability of bacteremia given a positive result are restricted. Genomic and proteomic approaches for identifying bacteremia are being explored but remain in the early stages (96, 122, 123). There is evidence, however, to suggest that even these methods can be hampered by problems with contamination (95). Furthermore, additional research on the value of time to positivity and quantity of growth for differentiating culture contamination from bacteremia is necessary. Of the various prevention strategies, additional investigation would help to determine the relative effect of each strategy on overall contamination rates. In the meantime, information technology may have a role in facilitating the detection of contamination, assisting clinical decision-making, and enabling better systems for tracking contamination rates both within and between institutions. Additional research on how to make these tools more useful and more acceptable in the clinical work environment is needed. Similarly, while clinical prediction rules for bacteremia have received much scrutiny in the past 15 years, it remains unclear whether they perform at a level that is accurate enough to influence physician behavior and affect blood culture utilization. More research is needed to refine these models and test them in other settings. In the pediatric arena, additional studies are clearly needed to help physicians interpret the results of

single blood cultures that grow coagulase-negative staphylococci, a persistent challenge. Ultimately, blood culture contamination is a complex, challenging problem that requires a multidisciplinary approach. Well-conceived and effectively implemented strategies are important for reconciling the sometimes contradictory requirements of individual patient care, population health, and effective resource allocation.

REFERENCES

1. Alpern, E. R., E. A. Alessandrini, L. M. Bell, K. N. Shaw, and K. L. McGowan. 2000. Occult bacteremia from a pediatric emergency department: current prevalence, time to detection, and outcome. *Pediatrics* **106**: 505–511.
2. American Thoracic Society and the Infectious Disease Society of America. 2005. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am. J. Respir. Crit. Care Med.* **171**:388–416.
3. Ammann, R. A., A. Hirt, A. R. Luthy, and C. Aebi. 2003. Identification of children presenting with fever in chemotherapy-induced neutropenia at low risk for severe bacterial infection. *Med. Pediatr. Oncol.* **41**:436–443.
4. Ammann, R. A., A. Hirt, A. R. Luthy, and C. Aebi. 2004. Predicting bacteremia in children with fever and chemotherapy-induced neutropenia. *Pediatr. Infect. Dis. J.* **23**:61–67.
5. Anonymous. 1996. National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986–April 1996, issued May 1996. A report from the National Nosocomial Infections Surveillance (NNIS) System. *Am. J. Infect. Control* **24**:380–388.
6. Aronson, M. D., and D. H. Bor. 1987. Blood cultures. *Ann. Intern. Med.* **106**:246–253.
7. Ashdown, L. R. 1988. Blood culture collection techniques and bacterial contamination. *Pathology* **20**:397–398.
8. Bachur, R. G., and M. B. Harper. 2001. Predictive model for serious bacterial infections among infants younger than 3 months of age. *Pediatrics* **108**:311–316.
9. Bandyopadhyay, S., J. Bergholte, C. D. Blackwell, J. R. Friedlander, and H. Hennes. 2002. Risk of serious bacterial infection in children with fever without a source in the post-Haemophilus influenzae era when antibiotics are reserved for culture-proven bacteremia. *Arch. Pediatr. Adolesc. Med.* **156**:512–517. (Erratum, **156**:749.)
10. Baraff, L. J., J. W. Bass, G. R. Fleisher, J. O. Klein, G. H. McCracken, Jr., K. R. Powell, D. L. Schriger, et al. 1993. Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. *Ann. Emerg. Med.* **22**:1198–1210. (Erratum, **22**:1490.)
11. Barenfanger, J., C. Drake, J. Lawhorn, and S. J. Verhulst. 2004. Comparison of chlorhexidine and tincture of iodine for skin antisepsis in preparation for blood sample collection. *J. Clin. Microbiol.* **42**:2216–2217.
12. Bates, D. W., E. F. Cook, L. Goldman, and T. H. Lee. 1990. Predicting bacteremia in hospitalized patients. A prospectively validated model. *Ann. Intern. Med.* **113**:495–500.
13. Bates, D. W., L. Goldman, and T. H. Lee. 1991. Contaminant blood cultures and resource utilization. The true consequences of false-positive results. *JAMA* **265**:365–369.
14. Bates, D. W., and T. H. Lee. 1992. Rapid classification of positive blood cultures. Prospective validation of a multivariate algorithm. *JAMA* **267**: 1962–1966.
15. Bates, D. W., K. E. Pruess, and T. H. Lee. 1995. How bad are bacteremia and sepsis? Outcomes in a cohort with suspected bacteremia. *Arch. Intern. Med.* **155**:593–598.
16. Beekmann, S. E., D. J. Diekema, and G. V. Doern. 2005. Determining the clinical significance of coagulase-negative staphylococci isolated from blood cultures. *Infect. Control Hosp. Epidemiol.* **26**:559–566.
17. Bekeris, L. G., J. A. Tworek, M. K. Walsh, and P. N. Valenstein. 2005. Trends in blood culture contamination: a College of American Pathologists Q-Tracks study of 356 institutions. *Arch. Pathol. Lab. Med.* **129**:1222–1225.
18. Berger, C., J. Uehlinger, D. Ghelli, N. Blau, and S. Fanconi. 1995. Comparison of C-reactive protein and white blood cell count with differential in neonates at risk for septicemia. *Eur. J. Pediatr.* **154**:138–144.
19. Berger, R. M., M. Y. Berger, H. A. van Steensel-Moll, G. Dzolic-Danilovic, and G. Derksen-Lubsen. 1996. A predictive model to estimate the risk of serious bacterial infections in febrile infants. *Eur. J. Pediatr.* **155**:468–473.
20. Beutz, M., G. Sherman, J. Mayfield, V. J. Fraser, and M. H. Kollef. 2003. Clinical utility of blood cultures drawn from central vein catheters and peripheral venipuncture in critically ill medical patients. *Chest* **123**:854–861.
- 20a. Birnbaumer, D. M. 24 November 2004, posting date. Blood cultures aren't useful for managing immunocompetent CAP inpatients. *J. Watch Emerg. Med.* [Online.] <http://emergency-medicine.jwatch.org/cgi/content/full/2004/1124/1>.
21. Brown, E., R. P. Wenzel, and J. O. Hendley. 1989. Exploration of the microbial anatomy of normal human skin by using plasmid profiles of

- coagulase-negative staphylococci: search for the reservoir of resident skin flora. *J. Infect. Dis.* **160**:644–650.
22. Bryan, C. S. 1989. Clinical implications of positive blood cultures. *Clin. Microbiol. Rev.* **2**:329–353.
 23. Burke, J. P., D. C. Classen, S. L. Pestotnik, R. S. Evans, and L. E. Stevens. 1991. The HELP system and its application to infection control. *J. Hosp. Infect.* **18**(Suppl. A):424–431.
 24. Buttery, J. P. 2002. Blood cultures in newborns and children: optimising an everyday test. *Arch. Dis. Child. Fetal Neonatal Ed.* **87**:F25–F28.
 25. Calfee, D. P., and B. M. Farr. 2002. Comparison of four antiseptic preparations for skin in the prevention of contamination of percutaneously drawn blood cultures: a randomized trial. *J. Clin. Microbiol.* **40**:1660–1665.
 26. Campbell, S. G., T. J. Marrie, R. Anstey, S. Ackroyd-Stolarz, and G. Dickinson. 2003. Utility of blood cultures in the management of adults with community acquired pneumonia discharged from the emergency department. *Emerg. Med. J.* **20**:521–523.
 27. Campbell, S. G., T. J. Marrie, R. Anstey, G. Dickinson, and S. Ackroyd-Stolarz. 2003. The contribution of blood cultures to the clinical management of adult patients admitted to the hospital with community-acquired pneumonia: a prospective observational study. *Chest* **123**:1142–1150.
 28. Catton, J. A., B. M. Dobbins, P. Kite, J. M. Wood, K. Eastwood, S. Sugden, J. A. Sandoe, D. Burke, M. J. McMahon, and M. H. Wilcox. 2005. In situ diagnosis of intravascular catheter-related bloodstream infection: a comparison of quantitative culture, differential time to positivity, and endoluminal brushing. *Crit. Care Med.* **33**:787–791.
 29. Chalasani, N. P., M. A. Valdecana, A. K. Gopal, J. E. McGowan, Jr., and R. L. Jurado. 1995. Clinical utility of blood cultures in adult patients with community-acquired pneumonia without defined underlying risks. *Chest* **108**:932–936.
 30. Chandrasekar, P. H., and W. J. Brown. 1994. Clinical issues of blood cultures. *Arch. Intern. Med.* **154**:841–849.
 31. Chapnick, E. K., B. C. Schaffer, J. D. Graddon, L. I. Lutwick, S. A. Krigsmann, and M. Levi. 1991. Technique for drawing blood for cultures: is changing needles truly necessary? *Southern Med. J.* **84**:1197–1198.
 32. Chiu, Y. H., T. J. Chen, C. T. Chen, and C. C. Lu. 2005. Positive blood cultures in pediatric emergency department patients: epidemiological and clinical characteristics. *Acta Paediatr. Taiwan.* **46**:11–16.
 33. Corbo, J., B. Friedman, P. Bijur, and E. J. Gallagher. 2004. Limited usefulness of initial blood cultures in community acquired pneumonia. *Emerg. Med. J.* **21**:446–448.
 34. DesJardin, J. A., M. E. Falagas, R. Ruthazer, J. Griffith, D. Wawrose, D. Schenkein, K. Miller, and D. R. Snyderman. 1999. Clinical utility of blood cultures drawn from indwelling central venous catheters in hospitalized patients with cancer. *Ann. Intern. Med.* **131**:641–647.
 35. Dunagan, W. C., R. S. Woodward, G. Medoff, J. L. Gray III, E. Casabar, M. D. Smith, C. A. Lawrenz, and E. Spitznagel. 1989. Antimicrobial misuse in patients with positive blood cultures. *Am. J. Med.* **87**:253–259.
 36. Ernst, D. J. 2004. Controlling blood-culture contamination rates. *Med. Lab. Obs.* **36**:14–18; quiz, 20–21.
 37. Evans, M. R., A. L. Truant, J. Kostman, and L. Locke. 1991. The detection of positive blood cultures by the BACTEC NR660. The clinical importance of four-day versus seven-day testing. *Diagn. Microbiol. Infect. Dis.* **14**:107–110.
 38. Everts, R. J., E. N. Vinson, P. O. Adholla, and L. B. Reller. 2001. Contamination of catheter-drawn blood cultures. *J. Clin. Microbiol.* **39**:3393–3394.
 39. Felices, F. J., J. L. Hernandez, J. Ruiz, J. Meseguer, J. A. Gomez, and E. Molina. 1979. Use of the central venous pressure catheter to obtain blood cultures. *Crit. Care Med.* **7**:78–79.
 40. Fontanarosa, P. B., F. J. Kaerberlein, L. W. Gerson, and R. B. Thomson. 1992. Difficulty in predicting bacteremia in elderly emergency patients. *Ann. Emerg. Med.* **21**:842–848.
 41. Franklin, J. A., A. H. Gaur, J. L. Shenep, X. J. Hu, and P. M. Flynn. 2004. In situ diagnosis of central venous catheter-related bloodstream infection without peripheral blood culture. *Pediatr. Infect. Dis. J.* **23**:614–618.
 42. Galdhart, J. O., A. Morvan, N. Desplaces, and N. et Solh. 1999. Phenotypic and genomic variation among *Staphylococcus epidermidis* strains infecting joint prostheses. *J. Clin. Microbiol.* **37**:1306–1312.
 43. Garner, J. S., W. R. Jarvis, T. G. Emori, T. C. Horan, and J. M. Hughes. 1988. CDC definitions for nosocomial infections, 1988. *Am. J. Infect. Control* **16**:128–140. (Erratum, **16**:177.)
 44. Gaur, A. H., P. M. Flynn, D. J. Heine, M. A. Giannini, J. L. Shenep, and R. T. Hayden. 2005. Diagnosis of catheter-related bloodstream infections among pediatric oncology patients lacking a peripheral culture, using differential time to detection. *Pediatr. Infect. Dis. J.* **24**:445–449.
 45. Gibb, A. P., B. Hill, B. Chorea, and R. Brant. 1997. Reduction in blood culture contamination rate by feedback to phlebotomists. *Arch. Pathol. Lab. Med.* **121**:503–507.
 46. Gowardman, J. R., C. Montgomery, S. Thirlwell, J. Shewan, A. Idema, P. D. Larsen, and J. H. Havill. 1998. Central venous catheter-related bloodstream infections: an analysis of incidence and risk factors in a cohort of 400 patients. *Intensive Care Med.* **24**:1034–1039.
 47. Graham, P. L., III, P. San Gabriel, S. Lutwick, J. Haas, and L. Saiman. 2004. Validation of a multicenter computer-based surveillance system for hospital-acquired bloodstream infections in neonatal intensive care departments. *Am. J. Infect. Control* **32**:232–234.
 48. Haimi-Cohen, Y., S. Shafinoori, V. Tucci, and L. G. Rubin. 2003. Use of incubation time to detection in BACTEC 9240 to distinguish coagulase-negative staphylococcal contamination from infection in pediatric blood cultures. *Pediatr. Infect. Dis. J.* **22**:968–974.
 49. Han, X. Y., and A. L. Truant. 1999. The detection of positive blood cultures by the AccuMed ESP-384 system: the clinical significance of three-day testing. *Diagn. Microbiol. Infect. Dis.* **33**:1–6.
 50. Hardy, D. J., B. B. Hulbert, and P. C. Migneault. 1992. Time to detection of positive BacT/Alert blood cultures and lack of need for routine subculture of 5- to 7-day negative cultures. *J. Clin. Microbiol.* **30**:2743–2745.
 51. Herwaldt, L. A., M. Geiss, C. Kao, and M. A. Pfaller. 1996. The positive predictive value of isolating coagulase-negative staphylococci from blood cultures. *Clin. Infect. Dis.* **22**:14–20.
 52. Herz, A. M., T. L. Greenhow, J. Alcantara, J. Hansen, R. P. Baxter, S. B. Black, and H. R. Shinefield. 2006. Changing epidemiology of outpatient bacteremia in 3- to 36-month-old children after the introduction of the heptavalent-conjugated pneumococcal vaccine. *Pediatr. Infect. Dis. J.* **25**:293–300.
 - 52a. Houck, P. M., D. W. Bratzler, J. G. Bartlett, L. Mandell, M. S. Niederman. 27 April 2005, posting date. The CMS Blood Cultures for CAP Program: the architects speak out. *J. Watch Emerg. Med.* [Online.] <http://emergency-medicine.jwatch.org/cgi/content/full/2005/4/27/1>.
 53. Huang, A. H., J. J. Yan, and J. J. Wu. 1998. Comparison of five days versus seven days of incubation for detection of positive blood cultures by the Bactec 9240 system. *Eur. J. Clin. Microbiol. Infect. Dis.* **17**:637–641.
 - 53a. Innes, G., K. Roland, E. Grafstein, and J. M. Christenson. 2000. Utility of blood cultures in the emergency department. *Acad. Emerg. Med.* **7**:579.
 54. Isaacman, D. J., and R. B. Karasic. 1990. Lack of effect of changing needles on contamination of blood cultures. *Pediatr. Infect. Dis. J.* **9**:274–278.
 55. Isaacman, D. J., and R. B. Karasic. 1990. Utility of collecting blood cultures through newly inserted intravenous catheters. *Pediatr. Infect. Dis. J.* **9**:815–818.
 56. Kahn, M. G., S. A. Steib, V. J. Fraser, and W. C. Dunagan. 1993. An expert system for culture-based infection control surveillance, p. 171–175. In *Proceedings of the Annual Symposium on Computer Applications in Medical Care*. Hanley & Belfus, Inc., Philadelphia, Pa.
 57. Khatib, R., K. M. Riederer, J. A. Clark, S. Khatib, L. E. Briski, and F. M. Wilson. 1995. Coagulase-negative staphylococci in multiple blood cultures: strain relatedness and determinants of same-strain bacteremia. *J. Clin. Microbiol.* **33**:816–820.
 58. Kim, S. D., L. C. McDonald, W. R. Jarvis, S. K. McAllister, R. Jerris, L. A. Carson, and J. M. Miller. 2000. Determining the significance of coagulase-negative staphylococci isolated from blood cultures at a community hospital: a role for species and strain identification. *Infect. Control Hosp. Epidemiol.* **21**:213–217.
 59. Krause, R., R. Haberl, A. Wolfer, F. Daxböck, H. W. Auner, G. J. Krejs, C. Wenisch, and E. C. Reisinger. 2003. Molecular typing of coagulase-negative staphylococcal blood and skin culture isolates to differentiate between bacteremia and contamination. *Eur. J. Clin. Microbiol. Infect. Dis.* **22**:760–763.
 60. Krumholz, H. M., S. Cummings, and M. York. 1990. Blood culture phlebotomy: switching needles does not prevent contamination. *Ann. Intern. Med.* **113**:290–292. (Erratum, **113**:723.)
 61. Kuppermann, N., G. R. Fleisher, and D. M. Jaffe. 1998. Predictors of occult pneumococcal bacteremia in young febrile children. *Ann. Emerg. Med.* **31**:679–687.
 62. Kurlat, I., B. J. Stoll, and J. E. McGowan, Jr. 1989. Time to positivity for detection of bacteremia in neonates. *J. Clin. Microbiol.* **27**:1068–1071.
 63. Lee, G. M., G. R. Fleisher, and M. B. Harper. 2001. Management of febrile children in the age of the conjugate pneumococcal vaccine: a cost-effectiveness analysis. *Pediatrics* **108**:835–844.
 64. Lee, S., I. Schoen, and A. Malkin. 1967. Comparison of use of alcohol with that of iodine for skin antisepsis in obtaining blood cultures. *Am. J. Clin. Pathol.* **47**:646–648.
 65. Leibovici, L., S. Greenshtain, O. Cohen, F. Mor, and A. J. Wysebeek. 1991. Bacteremia in febrile patients. A clinical model for diagnosis. *Arch. Intern. Med.* **151**:1801–1806.
 66. Leisure, M. K., D. M. Moore, J. D. Schwartzman, G. F. Hayden, and L. G. Donowitz. 1990. Changing the needle when inoculating blood cultures. A no-benefit and high-risk procedure. *JAMA* **264**:2111–2112.
 67. Little, J. R., P. R. Murray, P. S. Traynor, and E. Spitznagel. 1999. A randomized trial of povidone-iodine compared with iodine tincture for venipuncture site disinfection: effects on rates of blood culture contamination. *Am. J. Med.* **107**:119–125.
 68. Lyytikäinen, O., V. Valtonen, V. J. Anttila, and P. Ruutu. 1998. Evaluation of clinical and laboratory findings in leukaemic patients with blood cultures positive for *Staphylococcus epidermidis*. *J. Hosp. Infect.* **38**:27.
 69. MacGregor, R. R., and H. N. Beaty. 1972. Evaluation of positive blood cultures. Guidelines for early differentiation of contaminated from valid positive cultures. *Arch. Intern. Med.* **130**:84–87.

70. Madsen, K., M. Rosenman, S. Hui, and P. P. Breitfeld. 2002. Value of electronic data for model validation and refinement: bacteremia risk in children with fever and neutropenia. *J. Pediatr. Hematol. Oncol.* **24**:256–262.
71. Magadia, R. R., and M. P. Weinstein. 2001. Laboratory diagnosis of bacteremia and fungemia. *Infect. Dis. Clin. N. Am.* **15**:1009–1024.
72. Makadon, H. J., D. Bor, G. Friedland, P. Dasse, A. L. Komaroff, and M. D. Aronson. 1987. Febrile inpatients: house officers' use of blood cultures. *J. Gen. Intern. Med.* **2**:293–297.
73. Mandell, L. A., J. G. Bartlett, S. F. Dowell, T. M. File, Jr., D. M. Musher, C. Whitney, et al. 2003. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. *Clin. Infect. Dis.* **37**:1405–1433.
74. Martinez, J. A., J. A. DesJardin, M. Aronoff, S. Supran, S. A. Nasraway, and D. R. Snyderman. 2002. Clinical utility of blood cultures drawn from central venous or arterial catheters in critically ill surgical patients. *Crit. Care Med.* **30**:7–13.
75. Masterson, K. C., and J. E. McGowan, Jr. 1988. Detection of positive blood cultures by the Bactec NR660. The clinical importance of five versus seven days of testing. *Am. J. Clin. Pathol.* **90**:91–94.
76. McBryde, E. S., M. Tilse, and J. McCormack. 2005. Comparison of contamination rates of catheter-drawn and peripheral blood cultures. *J. Hosp. Infect.* **60**:118–121.
77. McDonald, L. C., J. Fune, L. B. Gaido, M. P. Weinstein, L. G. Reimer, T. M. Flynn, M. L. Wilson, S. Mirrett, and L. B. Reller. 1996. Clinical importance of increased sensitivity of BacT/Alert FAN aerobic and anaerobic blood culture bottles. *J. Clin. Microbiol.* **34**:2180–2184.
78. McGowan, J. E., Jr., L. Bratton, J. O. Klein, and M. Finland. 1973. Bacteremia in febrile children seen in a "walk-in" pediatric clinic. *N. Engl. J. Med.* **288**:1309–1312.
79. McQuillen, K. K., K. A. Santucci, M. A. Conrad, D. G. Nelson, W. Lewander, S. J. Duffy, and A. C. Anderson. 1999. Intravenous catheter blood cultures: utility and contamination. *Pediatrics* **103**:e52.
80. Mellors, J. W., R. I. Horwitz, M. R. Harvey, and S. M. Horwitz. 1987. A simple index to identify occult bacterial infection in adults with acute unexplained fever. *Arch. Intern. Med.* **147**:666–671.
81. Metersky, M. L., A. Ma, D. W. Bratzler, and P. M. Houck. 2004. Predicting bacteremia in patients with community-acquired pneumonia. *Am. J. Respir. Crit. Care Med.* **169**:342–347.
82. Mimoz, O., A. Karim, A. Mercat, M. Cosseron, B. Falissard, F. Parker, C. Richard, K. Samii, and P. Nordmann. 1999. Chlorhexidine compared with povidone-iodine as skin preparation before blood culture. A randomized, controlled trial. *Ann. Intern. Med.* **131**:834–837.
83. Mirrett, S., L. B. Reller, C. A. Pettit, C. W. Woods, B. Vazirani, R. Sivasdas, and M. P. Weinstein. 2003. Controlled clinical comparison of BacT/ALERT standard aerobic medium with BACTEC standard aerobic medium for culturing blood. *J. Clin. Microbiol.* **41**:2391–2394.
84. Mirrett, S., M. P. Weinstein, L. G. Reimer, M. L. Wilson, and L. B. Reller. 2001. Relevance of the number of positive bottles in determining clinical significance of coagulase-negative staphylococci in blood cultures. *J. Clin. Microbiol.* **39**:3279–3281.
85. Mozes, B., D. Milatiner, C. Block, Z. Blumstein, and H. Halkin. 1993. Inconsistency of a model aimed at predicting bacteremia in hospitalized patients. *J. Clin. Epidemiol.* **46**:1035–1040.
86. Muller-Premru, M., and P. Cernelc. 2004. Molecular epidemiology of catheter-related bloodstream infections caused by coagulase-negative staphylococci in hematological patients with neutropenia. *Epidemiol. Infect.* **132**:921–925.
87. Murray, P. R., P. Traynor, and D. Hopson. 1992. Critical assessment of blood culture techniques: analysis of recovery of obligate and facultative anaerobes, strict aerobic bacteria, and fungi in aerobic and anaerobic blood culture bottles. *J. Clin. Microbiol.* **30**:1462–1468.
88. Mylotte, J. M., M. A. Pisano, S. Ram, S. Nakasato, and D. Rotella. 1995. Validation of a bacteremia prediction model. *Infect. Control Hosp. Epidemiol.* **16**:203–209.
89. Mylotte, J. M., and A. Tayara. 2000. Blood cultures: clinical aspects and controversies. *Eur. J. Clin. Microbiol. Infect. Dis.* **19**:157–163.
90. National Nosocomial Infections Surveillance System. 2004. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am. J. Infect. Control* **32**:470–485.
91. Niederman, M. S., L. A. Mandell, A. Anzueto, J. B. Bass, W. A. Broughton, G. D. Campbell, N. Dean, T. File, M. J. Fine, P. A. Gross, F. Martinez, T. J. Marrie, J. F. Plouffe, J. Ramirez, G. A. Sarosi, A. Torres, R. Wilson, V. L. Yu, et al. 2001. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. *Am. J. Respir. Crit. Care Med.* **163**:1730–1754.
92. Norberg, A., N. C. Christopher, M. L. Ramundo, J. R. Bower, and S. A. Berman. 2003. Contamination rates of blood cultures obtained by dedicated phlebotomy vs intravenous catheter. *JAMA* **289**:726–729.
93. Novis, D. A., J. C. Dale, R. B. Schiffman, S. G. Ruby, and M. K. Walsh. 2001. Solitary blood cultures: a College of American Pathologists Q-Probes study of 132,778 blood culture sets in 333 small hospitals. *Arch. Pathol. Lab. Med.* **125**:1290–1294.
94. Peacock, S. J., I. C. Bowler, and D. W. Crook. 1995. Positive predictive value of blood cultures growing coagulase-negative staphylococci. *Lancet* **346**:191–192.
95. Peters, R. P., T. Mohammadi, C. M. Vandenbroucke-Grauls, S. A. Danner, M. A. van Agtmael, and P. H. Savelkoul. 2004. Detection of bacterial DNA in blood samples from febrile patients: underestimated infection or emerging contamination? *FEMS Immunol. Med. Microbiol.* **42**:249–253.
96. Peters, R. P., M. A. van Agtmael, S. A. Danner, P. H. Savelkoul, and C. M. Vandenbroucke-Grauls. 2004. New developments in the diagnosis of bloodstream infections. *Lancet Infect. Dis.* **4**:751–760.
97. Poses, R. M., and M. Anthony. 1991. Availability, wishful thinking, and physicians' diagnostic judgments for patients with suspected bacteremia. *Med. Decis. Making* **11**:159–168.
98. Pourcyrous, M., H. S. Bada, S. B. Korones, V. Baselski, and S. P. Wong. 1993. Significance of serial C-reactive protein responses in neonatal infection and other disorders. *Pediatrics* **92**:431–435.
99. Rackoff, W. R., R. Gonin, C. Robinson, S. G. Kreissman, and P. B. Breitfeld. 1996. Predicting the risk of bacteremia in children with fever and neutropenia. *J. Clin. Oncol.* **14**:919–924.
100. Ram, S., J. M. Mylotte, and M. Pisano. 1995. Rapid classification of positive blood cultures: validation and modification of a prediction model. *J. Gen. Intern. Med.* **10**:82–88.
101. Ramscook, C., K. Childers, S. G. Cron, and M. Nirken. 2000. Comparison of blood-culture contamination rates in a pediatric emergency room: newly inserted intravenous catheters versus venipuncture. *Infect. Control Hosp. Epidemiol.* **21**:649–651.
102. Reimer, L. G., M. L. Wilson, and M. P. Weinstein. 1997. Update on detection of bacteremia and fungemia. *Clin. Microbiol. Rev.* **10**:444–465.
103. Reisner, B. S., and G. L. Woods. 1999. Times to detection of bacteria and yeasts in BACTEC 9240 blood culture bottles. *J. Clin. Microbiol.* **37**:2024–2026.
104. Rogers, M. S., and B. A. Oppenheim. 1998. The use of continuous monitoring blood culture systems in the diagnosis of catheter related sepsis. *J. Clin. Pathol.* **51**:635–637.
105. Rubin, L. G., P. J. Sanchez, J. Siegel, G. Levine, L. Saiman, W. R. Jarvis, et al. 2002. Evaluation and treatment of neonates with suspected late-onset sepsis: a survey of neonatologists' practices. *Pediatrics* **110**:e42.
106. Rubin, R. H., E. D. Shapiro, V. T. Andriole, R. J. Davis, W. E. Stamm, et al. 1992. Evaluation of new anti-infective drugs for the treatment of urinary tract infection. *Clin. Infect. Dis.* **15**(Suppl. 1):S216–S227.
107. Salfdar, N., and D. G. Maki. 2004. The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. *Intensive Care Med.* **30**:62–67.
108. Saito, T., K. Senda, S. Takakura, N. Fujihara, T. Kudo, Y. Iinuma, M. Tanimoto, and S. Ichiyama. 2003. Detection of bacteria and fungi in BacT/Alert standard blood-culture bottles. *J. Infect. Chemother.* **9**:227–232.
109. Samore, M., D. Lichtenberg, L. Saubermann, C. Kawachi, and Y. Carmeli. 1997. A clinical data repository enhances hospital infection control, p. 56–60. *In* Proceedings of the AMIA Annual Fall Symposium. Hanley & Belfus, Inc., Philadelphia, Pa.
110. Santolaya, M. E., J. Cofre, and V. Beresi. 1994. C-reactive protein: a valuable aid for the management of febrile children with cancer and neutropenia. *Clin. Infect. Dis.* **18**:589–595.
111. Schiffman, R. B., P. Bachner, and P. J. Howanitz. 1996. Blood culture quality improvement: a College of American Pathologists Q-Probes study involving 909 institutions and 289 572 blood culture sets. *Arch. Pathol. Lab. Med.* **120**:999–1002.
112. Schiffman, R. B., and A. Pindur. 1993. The effect of skin disinfection materials on reducing blood culture contamination. *Am. J. Clin. Pathol.* **99**:536–538.
113. Schiffman, R. B., C. L. Strand, F. A. Meier, and P. J. Howanitz. 1998. Blood culture contamination: a College of American Pathologists Q-Probes study involving 640 institutions and 497134 specimens from adult patients. *Arch. Pathol. Lab. Med.* **122**:216–221.
114. Scott, A. C. 1979. Blood-culture technique: two needles or one. *Lancet* **i**:1414.
115. Segal, G. S., and J. M. Chamberlain. 2000. Resource utilization and contaminated blood cultures in children at risk for occult bacteremia. *Arch. Pediatr. Adolesc. Med.* **154**:469–473.
116. Selwyn, S., and H. Ellis. 1972. Skin bacteria and skin disinfection reconsidered. *Br. Med. J.* **i**:136–140.
117. Seo, S. K., L. Venkataraman, P. C. DeGirolami, and M. H. Samore. 2000. Molecular typing of coagulase-negative staphylococci from blood cultures does not correlate with clinical criteria for true bacteremia. *Am. J. Med.* **109**:697–704.
118. Shafazand, S., and A. B. Weinacker. 2002. Blood cultures in the critical care unit: improving utilization and yield. *Chest* **122**:1727–1736.
119. Shahar, E., B. S. Wohl-Gottesman, and L. Shenkman. 1990. Contamination of blood cultures during venepuncture: fact or myth? *Postgrad. Med. J.* **66**:1053.

120. Shapiro, N. I., R. E. Wolfe, S. Wright, J. Spears, and D. W. Bates. 2003. Who needs a blood culture? A prospectively derived and validated clinical prediction rule. *Acad. Emerg. Med.* **10**:435-436.
121. Sharma, M., K. Riederer, L. B. Johnson, and R. Khatib. 2001. Molecular analysis of coagulase-negative Staphylococcus isolates from blood cultures: prevalence of genotypic variation and polyclonal bacteremia. *Clin. Infect. Dis.* **33**:1317-1323.
122. Siondalski, P., J. Siebert, A. Samet, M. Bronk, B. Krawczyk, and J. Kur. 2004. Usefulness of the PCR technique for bacterial DNA detection in blood of the patients after "opened heart" operations. *Pol. J. Microbiol.* **53**:145-149.
123. Sleight, J., R. Cursons, and M. La Pine. 2001. Detection of bacteraemia in critically ill patients using 16S rDNA polymerase chain reaction and DNA sequencing. *Intensive Care Med.* **27**:1269-1273.
124. Smart, D., C. Baggoley, J. Head, D. Noble, B. Wetherall, and D. L. Gordon. 1993. Effect of needle changing and intravenous cannula collection on blood culture contamination rates. *Ann. Emerg. Med.* **22**:1164-1168.
125. Souvenir, D., D. E. Anderson, Jr., S. Palpant, H. Mroch, S. Askin, J. Anderson, J. Claridge, J. Eiland, C. Malone, M. W. Garrison, P. Watson, and D. M. Campbell. 1998. Blood cultures positive for coagulase-negative staphylococci: antiseptics, pseudobacteremia, and therapy of patients. *J. Clin. Microbiol.* **36**:1923-1926.
126. Spitalnic, S. J., R. H. Woolard, and L. A. Merimel. 1995. The significance of changing needles when inoculating blood cultures: a meta-analysis. *Clin. Infect. Dis.* **21**:1103-1106.
127. Stamm, W. E. 1984. Quantitative urine cultures revisited. *Eur. J. Clin. Microbiol.* **3**:279-281.
128. Stamm, W. E., G. W. Counts, K. R. Running, S. Fihn, M. Turck, and K. K. Holmes. 1982. Diagnosis of coliform infection in acutely dysuric women. *N. Engl. J. Med.* **307**:463-468.
129. St. Geme, J. W., III, L. M. Bell, S. Baumgart, C. T. D'Angio, and M. C. Harris. 1990. Distinguishing sepsis from blood culture contamination in young infants with blood cultures growing coagulase-negative staphylococci. *Pediatrics* **86**:157-162.
130. Stoll, M. L., and L. G. Rubin. 2004. Incidence of occult bacteremia among highly febrile young children in the era of the pneumococcal conjugate vaccine: a study from a children's hospital emergency department and urgent care center. *Arch. Pediatr. Adolesc. Med.* **158**:671-675.
131. Strand, C. L., R. R. Wajsbort, and K. Sturmann. 1993. Effect of iodophor vs iodine tincture skin preparation on blood culture contamination rate. *JAMA* **269**:1004-1006.
- 131a. Sturmann, K. M., J. Bopp, D. Molinari, S. Akhtar, and J. Murphy. 1996. Blood cultures in adult patients released from an urban emergency department: a 15-month experience. *Acad. Emerg. Med.* **3**:768-775.
132. Surdulescu, S., D. Utamsingh, and R. Shekar. 1998. Phlebotomy teams reduce blood-culture contamination rate and save money. *Clin. Perform. Qual. Health Care* **6**:60-62.
133. Tacconelli, E., M. Tumbarello, M. Pittiruti, F. Leone, M. B. Lucia, R. Cauda, and L. Ortona. 1997. Central venous catheter-related sepsis in a cohort of 366 hospitalised patients. *Eur. J. Clin. Microbiol. Infect. Dis.* **16**:203-209.
134. Tan, L., J. C. Hawk III, and M. L. Sterling. 2001. Report of the Council on Scientific Affairs: preventing needlestick injuries in health care settings. *Arch. Intern. Med.* **161**:929-936.
135. Teele, D. W., S. I. Pelton, M. J. Grant, J. Herskowitz, D. J. Rosen, C. E. Allen, R. S. Wimmer, and J. O. Klein. 1975. Bacteremia in febrile children under 2 years of age: results of cultures of blood of 600 consecutive febrile children seen in a "walk-in" clinic. *J. Pediatr.* **87**:227-230.
136. Thamlikitkul, V., S. Chokloikaew, T. Tangtrakul, P. Siripoonkiat, N. Wongpreedee, and S. Danchaivijitr. 1992. Blood culture: comparison of outcomes between switch-needle and no-switch techniques. *Am. J. Infect. Control* **20**:122-125.
137. Theerthakara, R., W. El-Halees, M. Ismail, R. A. Solis, and M. A. Khan. 2001. Nonvalue of the initial microbiological studies in the management of nonsevere community-acquired pneumonia. *Chest* **119**:181-184.
138. Thuler, L. C., M. Jenicek, J. P. Turgeon, M. Rivard, P. Lebel, and M. H. Lebel. 1997. Impact of a false positive blood culture result on the management of febrile children. *Pediatr. Infect. Dis. J.* **16**:846-851.
139. Tokars, J. I. 2004. Predictive value of blood cultures positive for coagulase-negative staphylococci: implications for patient care and health care quality assurance. *Clin. Infect. Dis.* **39**:333-341.
140. Trautner, B. W., J. E. Clarridge, and R. O. Darouiche. 2002. Skin antiseptics kits containing alcohol and chlorhexidine gluconate or tincture of iodine are associated with low rates of blood culture contamination. *Infect. Control Hosp. Epidemiol.* **23**:397-401.
141. Trick, W. E., B. M. Zagorski, J. I. Tokars, M. O. Vernon, S. F. Welbel, M. F. Wisniewski, C. Richards, and R. A. Weinstein. 2004. Computer algorithms to detect bloodstream infections. *Emerg. Infect. Dis.* **10**:1612-1620.
142. Van Eldere, J., W. E. Peetermans, M. Struelens, A. Deplano, and H. Bobbaers. 2000. Polyclonal Staphylococcal endocarditis caused by genetic variability. *Clin. Infect. Dis.* **31**:24-30.
143. Van Wijngaerden, E., W. E. Peetermans, S. Van Lierde, and J. Van Eldere. 1997. Polyclonal staphylococcus endocarditis. *Clin. Infect. Dis.* **25**:69-71.
144. Viagappan, M., and M. C. Kelsey. 1995. The origin of coagulase-negative staphylococci isolated from blood cultures. *J. Hosp. Infect.* **30**:217-223.
145. Waltzman, M. L., and M. Harper. 2001. Financial and clinical impact of false-positive blood culture results. *Clin. Infect. Dis.* **33**:296-299.
146. Wang, S. J., G. J. Kuperman, L. Ohno-Machado, A. Onderdonk, H. Sandige, and D. W. Bates. 2000. Using electronic data to predict the probability of true bacteremia from positive blood cultures. p. 893-897. *In* Proceedings of the AMIA Annual Symposium. Hanley & Belfus, Inc., Philadelphia, Pa.
147. Washington, J. A., II, and D. M. Ilstrup. 1986. Blood cultures: issues and controversies. *Rev. Infect. Dis.* **8**:792-802.
148. Wasson, J. H., H. C. Sox, R. K. Neff, and L. Goldman. 1985. Clinical prediction rules. Applications and methodological standards. *N. Engl. J. Med.* **313**:793-799.
149. Waterer, G. W., and R. G. Wunderink. 2001. The influence of the severity of community-acquired pneumonia on the usefulness of blood cultures. *Respir. Med.* **95**:78-82.
150. Weinbaum, F. I., S. Lavie, M. Danek, D. Sixsmith, G. F. Heinrich, and S. S. Mills. 1997. Doing it right the first time: quality improvement and the contaminant blood culture. *J. Clin. Microbiol.* **35**:563-565.
151. Weinstein, M. P. 2003. Blood culture contamination: persisting problems and partial progress. *J. Clin. Microbiol.* **41**:2275-2278.
152. Weinstein, M. P. 1996. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. *Clin. Infect. Dis.* **23**:40-46.
153. Weinstein, M. P., S. Mirrett, L. Van Pelt, M. McKinnon, B. L. Zimmer, W. Kloos, and L. B. Reller. 1998. Clinical importance of identifying coagulase-negative staphylococci isolated from blood cultures: evaluation of MicroScan Rapid and Dried Overnight Gram-Positive panels versus a conventional reference method. *J. Clin. Microbiol.* **36**:2089-2092.
154. Weinstein, M. P., L. B. Reller, J. R. Murphy, and K. A. Lichtenstein. 1983. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. *Rev. Infect. Dis.* **5**:53-53.
155. Weinstein, M. P., M. L. Towns, S. M. Quartey, S. Mirrett, L. G. Reimer, G. Parmigiani, and L. B. Reller. 1997. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. *Clin. Infect. Dis.* **24**:584-602.
156. Wilson, M. L., M. P. Weinstein, S. Mirrett, L. G. Reimer, C. Fernando, F. T. Meredith, and L. B. Reller. 2000. Comparison of iodophor and alcohol pledgets with the Medi-Flex Blood Culture Prep Kit II for preventing contamination of blood cultures. *J. Clin. Microbiol.* **38**:4665-4667.
157. Wisniewski, M. F., P. Kieszowski, B. M. Zagorski, W. E. Trick, M. Sommers, and R. A. Weinstein. 2003. Development of a clinical data warehouse for hospital infection control. *J. Am. Med. Inform. Assoc.* **10**:454-462.
158. Wormser, G. P., I. M. Onorato, T. J. Preminger, D. Culver, and W. J. Martone. 1990. Sensitivity and specificity of blood cultures obtained through intravascular catheters. *Crit. Care Med.* **18**:152-156.
159. Wyllie, D. H., I. C. Bowler, and T. E. Peto. 2005. Bacteraemia prediction in emergency medical admissions: role of C reactive protein. *J. Clin. Pathol.* **58**:352-356.
160. Yehezkeili, Y., S. Subah, G. Elhanan, R. Raz, A. Porter, A. Regev, and L. Leibovici. 1996. Two rules for early prediction of bacteremia: testing in a university and a community hospital. *J. Gen. Intern. Med.* **11**:98-103.
161. Yokoe, D. S., J. Anderson, R. Chambers, M. Connor, R. Finberg, C. Hopkins, D. Lichtenberg, S. Marino, D. McLaughlin, E. O'Rourke, M. Samore, K. Sands, J. Strymish, E. Tamplin, N. Vallonde, and R. Platt. 1998. Simplified surveillance for nosocomial bloodstream infections. *Infect. Control Hosp. Epidemiol.* **19**:657-660.

Original Article

Quality of Processed Blood for Autotransfusion

Gerald Shulman, MD

University of Texas Medical Branch, Galveston, Texas

Keywords: red cell mass flow rate, speed, plasma washout, quality

Presented at the American Society of Extra-Corporeal Technology 37th International Conference, April 8–11, 1999, New Orleans, Louisiana

ABSTRACT

Centrifugal red blood cell washers for intraoperative autotransfusion process shed blood during surgery. In this study, the quality of processed fresh, human bank blood was assessed in a standardized laboratory setting during standard, medium, and high flow processing. Red cell recovery rates and plasma washout efficiencies were compared using three different devices. The accurate parameters measuring effectiveness and product quality were red cell mass (RCM) flow rate and the plasma washout efficiency. Cobe BRAT 2, a system with discontinuous flow (DF) and a cylindrical centrifuge bowl, permitted processing in standard and medium flow of 26 and 35 mL RCM/min, respectively, with washout of residual plasma albumin of 93.2 and 91.2%. The Medtronic Sequestra 1000, a DF system with a conical centrifuge bowl processed blood at 15 and 23 mL RCM/min and eliminated plasma albumin with 98.4 and 96.8% washout during standard and medium flow, respectively, with significant red cell loss occurring during medium flow. The respective speeds of high-flow programs with BRAT 2 and Sequestra 1000 were 15 and 22 mL RCM/min, related to a hematocrit in the holding bag, less than that of the incoming blood from the reservoir. Washout was 58.2 and 58.3%, respectively. Fresenius CATS, a continuous flow (CF) device, produced flow rates of 19, 24, and 43 mL RCM/min and plasma albumin elimination of 97.8, 94.4, and 93.3% in standard, medium, and high-flow, respectively. Holding bag hematocrits with CF exceeded that of DF. Standard, medium, and high-flow programs of CATS may be used without restriction.

Address correspondence to:
Gerald Shulman, MD
Blood Bank Division
Department of Pathology and Laboratory Medicine
Emory University School of Medicine
1364 Clifton Road NE
Atlanta, GA 30322

INTRODUCTION

The red blood cell recovery rate and washing efficiency of centrifugal devices used for intraoperative autologous transfusion (IAT) have an impact on the safety, purity, and potency of the processed product. Standard programs of most IAT devices have shown satisfactory performance during vascular surgery (1), cardiothoracic surgery (2), and major orthopedic surgery (3–7). However, accurate data on processing at high speeds are limited. The operating principles of centrifugal equipment are based either on discontinuous (DF) or continuous flow (CF). DF devices employ conical or cylindrical bowl geometries, which may affect results of the washing procedures. Manufacturers provide defined preprogrammed washing procedures with various washing speeds. In addition, operator-defined options are available, allowing for alteration of processing parameters of centrifuge speed and flow rates. Although changes that may affect the characteristics of the blood product are indicated, no exact data are provided.

The goal of this study is to perform a well-defined laboratory comparison of the processing speed and quality of the washed red cell product of three autotransfusion devices, each with operating principles based on different technology. Three speeds were studied in standard, medium, and high flow programs using nondistributable donor red cells reconstituted with compatible plasma and at three dilutions with saline, simulating conditions in the operating room.

MATERIALS AND METHODS

Washing programs were based on an ordinary requirement (standard flow), rapid (medium flow), and a very rapid (high flow), each representative of routine, rapidly processed, and emergency methods, respectively. The Cobe BRAT 2^a, the Fresenius CATS^b, and the Medtronic Sequestra 1000^c were employed during this study. Manufacturer-specified programs for DF using Sequestra 1000 with a conical centrifuge bowl and CATS with CF were selected as corresponding standard, medium, and high flow programs. The programs for comparable function on BRAT 2 with DF and a cylindrical centrifuge bowl were the standard flow program as specified by the manufacturer, medium and high flow are available as operator-defined procedures (Table 1).

Compatible fresh frozen plasma and nondistributable donor packed red cells, less than 5 days from the time of collection, were pooled to achieve a hematocrit (HCT) of approximately 40%. To simulate blood collected from a surgical field, an adjustment was made with normal saline to dilute pools with target HCT of approximately 30, 20, and 10%, each confirmed

before processing. After thorough mixing, the pool was divided into separate bags and used as blood reservoirs. The devices were used with the same disposable sets for each respective instrument in the three corresponding programs. Variability between individual lots are not expected to influence test results significantly because of the known high reproducibility of the manufacturing process involved. A fresh portion of the identical blood pool was processed on each device in three separate consecutive runs in the automatic modes. The processing times using the 250-mL bowl with BRAT 2 and the 225-mL bowl with Sequestra 1000 were recorded each for one completely filled bowl until the system stopped automatically; residual packed red blood cells in the emptying lines to the holding bags were transferred by activating the "Empty" routine twice more. The processing time with CATS was measured during accumulation of an equivalent volume of 225 mL packed red cells in the holding bag as measured by digital display on the instrument's control panel. To be consistent, the residual red cell volume in the emptying line to the holding bag was retained in the line. Volumes of blood from the reservoir and packed red cells in the holding bag were calculated from weights before and after processing. The weight differences were divided by densities according to measured HCT levels (8), respectively, to calculate volumes of blood drawn from reservoirs and packed red cells collected into holding bags. Volumes of five mL blood each were sampled from the reservoirs before and from holding bags after processing for CBC with the MAXM^d blood cell counter and tested within 2 hours. Similarly, separate samples were collected, the centrifuged supernatant separated and frozen at -30°C, pending batch analysis of plasma albumin measured immunochemically with the Behring BN Laser Nephelometer^e as the indicator for plasma washout.

Processing speeds, red cell recovery, rates of albumin elimination, and residual albumin transfusion were calculated as follows:

$$\text{blood flow rate from reservoir (mL/min)} = \frac{\text{blood volume processed}}{\text{processing time}}$$

$$\text{PRBC flow rate into holding bag (mL/min)} = \frac{\text{Volume of PRBC}}{\text{processing time}}$$

$$\text{RCM flow rate into holding bag (mL/min)} = \frac{\text{Volume PRBC} * \text{HCT}_{\text{PRBC}}}{\text{processing time}}$$

$$\begin{aligned} \text{RBC recovery rate in the holding bag (efficiency \%)} \\ = \frac{\text{PRBC volume} * \text{HCT}_{\text{PRBC}}}{\text{Blood volume} * \text{HCT}_{\text{blood}}} * 100 \end{aligned}$$

^a Cobe Laboratories, Inc., Arvada, CO 80004

^b Medtronic Inc., Parker, CO 80134

^c Fresenius Hemotechnology, Inc., Concord, CA 94520

^d Coulter, Miami, FL

^e Dade-Behring, Deerfield, IL

Table 1. Processing parameters of three autotransfusion devices tested in three different programs with reconstituted human bank whole blood in three saline dilutions

Program	Parameter	BRAT 2	CATS	Sequestra 1000
Standard flow	Fill speed (mL/min)	400	35 mL/min*	300
	Wash speed (mL/min)	800	WF = 5**	300
	Empty speed (mL/min)	600		300
	Wash volume (mL)	1000		1000
Medium flow	Fill speed (mL/min)	700	50 mL/min*	500
	Wash speed (mL/min)	1000	WF = 3**	500
	Empty speed (mL/min)	1000		500
	Wash volume (mL)	1000		1000
High flow	Fill speed (mL/min)	1300	100 mL/min*	1000
	Wash speed (mL/min)	1300	WF = 1**	1000
	Empty speed (mL/min)	1300		1000
	Wash volume (mL)	1000		750

*Default blood flow to holding bag (packed red blood cells).

**WF = wash factor = mL saline/mL packed red blood cells.

Table 2. Hematocrits (mean $\pm$ standard deviation %) of blood in the holding bags for three autotransfusion devices using three programs at reservoir hematocrits of 10, 20, and 30% and three replicate procedures in each

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
10% <i>N</i> = 3	49 $\pm$ 1	47 $\pm$ 1	9 $\pm$ 0.0	58 $\pm$ 0.0	54 $\pm$ 0.0	63 $\pm$ 0.0	55 $\pm$ 0.0	53 $\pm$ 1	5 $\pm$ 0.0
20% <i>N</i> = 3	45 $\pm$ 0.0	41 $\pm$ 1	16 $\pm$ 0.0	58 $\pm$ 1	54 $\pm$ 1	58 $\pm$ 0.0	53 $\pm$ 1	49 $\pm$ 2	11 $\pm$ 1
30% <i>N</i> = 3	44 $\pm$ 0.0	39 $\pm$ 0.0	24 $\pm$ 0.0	54 $\pm$ 0.0	53 $\pm$ 1	58 $\pm$ 0.0	52 $\pm$ 2	45 $\pm$ 1	18 $\pm$ 0.0
Average All <i>N</i> = 9	46 $\pm$ 2 o	42 $\pm$ 3 o	16 $\pm$ 6 o	57 $\pm$ 2 o*	54 $\pm$ 5 o*	59 $\pm$ 3 o*	53 $\pm$ 2 *	49 $\pm$ 3 *	11 $\pm$ 5 *

Average All = means of all hematocrits; o*| = $p < .05$ between corresponding programs.

$$\text{Albumin elimination rate (\%)} = \left[1 - \frac{\text{Total Albumin}_{\text{PRBC}}}{\text{Total Albumin}_{\text{blood}}} \right] * 100$$

$$= \left[1 - \frac{\text{Volume PRBC} * (1 - \text{HCT}_{\text{PRBC}}) * \text{Albumin}_{\text{PRBC}}}{\text{Volume Blood} * (1 - \text{HCT}_{\text{blood}}) * \text{Albumin}_{\text{blood}}} \right] * 100$$

Residual Albumin transfusion rate
(mg/dL RCM)

$$= \frac{\text{Albumin}_{\text{PRBC}} * (1 - \text{HCT}_{\text{PRBC}})}{\text{HCT}_{\text{PRBC}}}$$

Mean values and standard deviations were calculated for three replicates of each parameter and program based on three runs each using blood with a HCT of 10, 20, and 30% ($N = 9$). This represented the range of applications encountered clinically.

STATISTICS

Student's *t*-test for unpaired data was used and probability of $p < .05$ was considered significant. Statistically significant differences are indicated by the symbols o*| in the tables and figures for corresponding programs.

RESULTS

The differences between DF and CF are shown in Figure 1. In CF, blood from the reservoir was pumped into a rotating horizontal wash chamber, C-shaped like a spiral, hollow band. First, the red blood cells were concentrated on the outer aspect of the channel, then became resuspended in saline, reconcentrated on the outer aspect, and then transferred to the holding bag in a continuous flow of blood through the system. Plasma and saline wash waste were diverted to the waste bag.

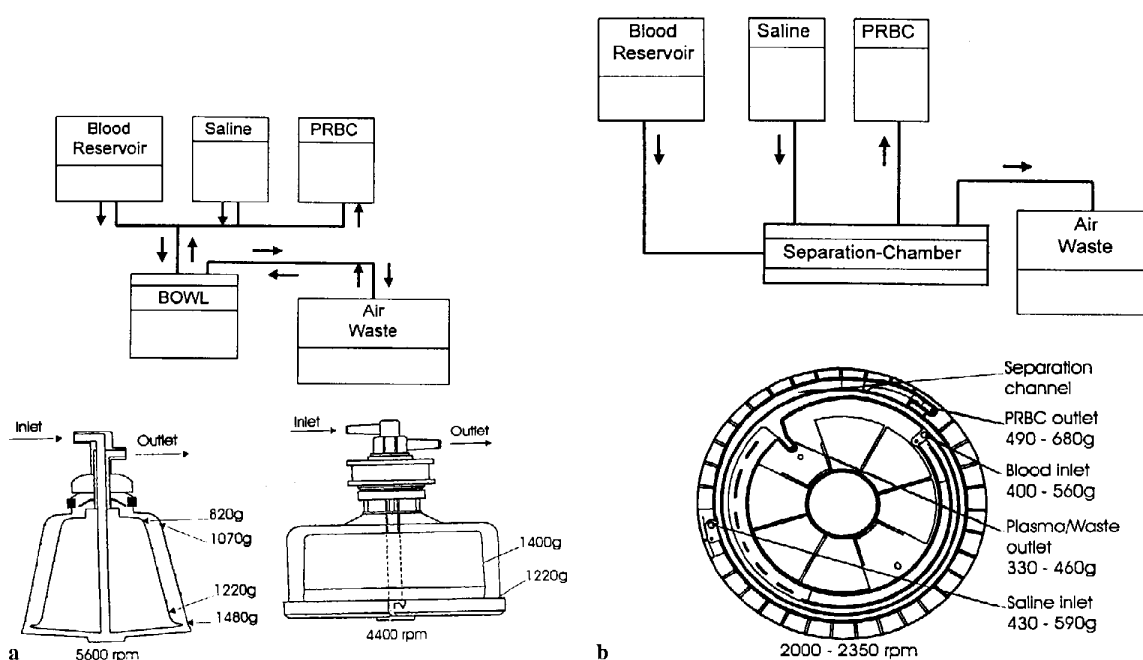


Figure 1: Diagrammatic representations of the flow in systems devised for intraoperative autologous transfusion in (a) discontinuous and (b) continuous flow procedures.

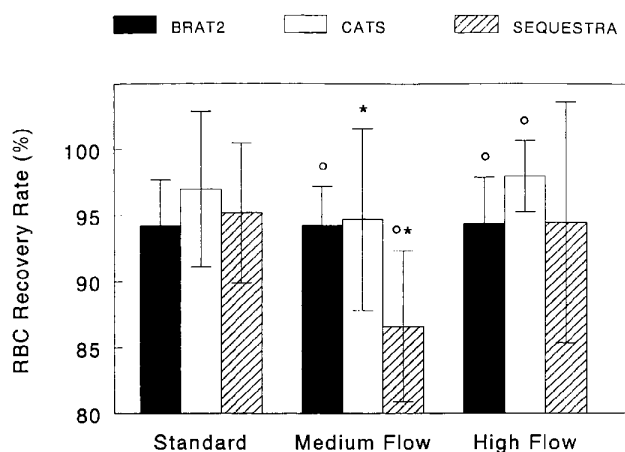


Figure 2: Mean red blood cell recovery rates $\pm$ standard deviations for three replicate processing runs using three autotransfusion devices in three programs; ° * = $p < .05$; $N = 9$.

HCT of the processed packed red cells was found to be consistently greatest in all CF (CATS) programs as compared with values obtained with the cylindrical DF (BRAT2) or the conical DF (Sequestra 1000) bowl systems. This was independent of the processing speed and HCT of the incoming blood. In DF, the HCT of packed red cells in the holding bag decreased progressively with greater processing speeds and with a greater HCT of the incoming blood (Table 2). High flow with BRAT 2 and Sequestra 1000 resulted in HCT even less than

that of the blood in the reservoir before processing. As the speed was increased during processing with both BRAT 2 and Sequestra 1000, the volume of saline used per mL RCM became increased because of an insufficient red cell content in the bowls. However, with CATS, the volume of saline used per mL RCM decreased significantly (Table 3).

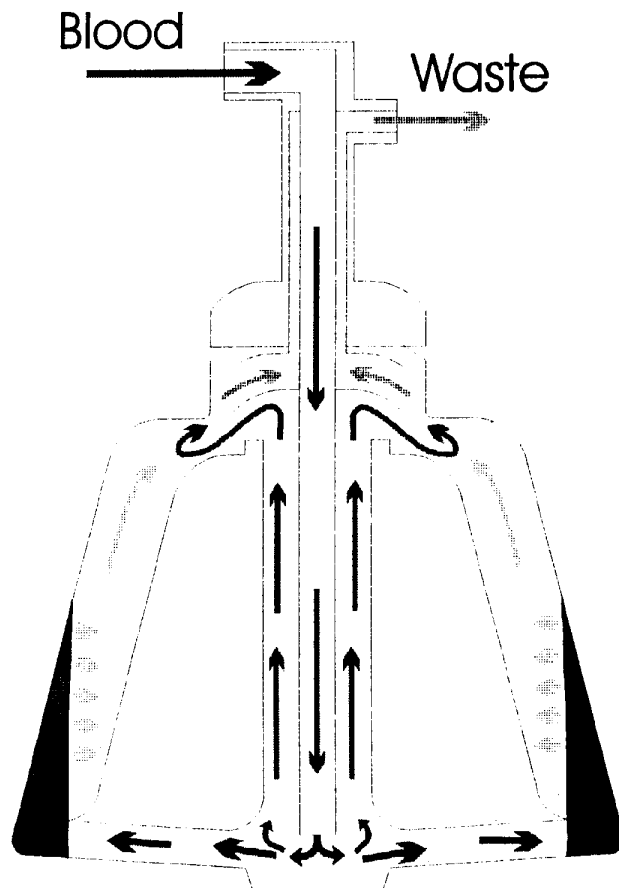
Apart from the medium flow program of Sequestra 1000, the range of red blood cell recovery rates was between 94 and 98% using all devices in all programs (Figure 2). During medium flow on Sequestra 1000, visible red cell loss to waste occurred with a diminished recovery rate of 86%. This was because of formation of an inverted saucer-shaped layer of red cells at the level of the rotating seal (Figure 3), caused by pressure diversion from the inlet port directly to the waste outlet. Red cell flow bypassed separation in the centrifugal field because of pressure buildup from force developed by rapid pump speeds once the bowl capacity was filled to about one-third.

In DF, processing reservoir samples with different HCT levels resulted in variation of the red cell mass flow rate into the holding bags (Table 4). Apart from incoming blood from the reservoir with high flow and an HCT of 10%, the red cell mass flow rate with CATS was found to be constant. The red cell mass flow rate into the holding bag increased progressively for all three devices from standard to medium flow. However, CATS high flow continued to show further increase in red cell mass flow rate, but both DF instruments showed a marked decline ($p < .0001$). The flow rates with high flow for both BRAT 2 and Sequestra 1000 were less than those of standard

Table 3. Saline volumes per red cell mass processed (mean $\pm$ standard deviation; mL saline/mL RCM processed) for three autotransfusion devices using three programs with three replicate procedures in each

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
Average All <i>N</i> = 9	8.9 $\pm$ 0.4 ○	9.8 $\pm$ 0.8 ○	30.1 $\pm$ 12.5 ○*	9.6 $\pm$ 0.5 ○*	6.4 $\pm$ 0.2 ○*	2.6 $\pm$ 0.8 ○*	8.7 $\pm$ 0.4 *	9.4 $\pm$ 0.6 *	36.8 $\pm$ 18.9 *

○*| = $p < .05$ between corresponding programs.

**Figure 3: Processing with the conical centrifuge bowl at high flow rates showing red cell loss to waste, presumably due to pressure buildup.**

flow because of premature triggering of the optical sensors by unseparated red blood cells. Wash cycles were initiated before filling the bowl properly, and the red cells were diluted further with saline wash solution. The CATS red cell mass high flow was 23% greater than the fastest program with the BRAT 2 (medium flow) and 87% greater than the fastest program of Sequestra 1000 (medium flow). Packed red blood cell flow rates proved to be misleading and erroneously indicated the

greatest processing speed with DF in the high-flow programs (Table 5).

There was no visible hemolysis on naked eye examination of the supernatants; however, samples from the BRAT 2 with its cylindrical centrifuge bowl had a pale yellow color consistent with residual plasma. The depth of color increased with greater processing speeds. The washout efficiency was evaluated by comparing initial plasma albumin contents of the reservoir blood supernatant volumes before processing with those of corresponding packed red blood cells in the holding bags after processing. The supernatant residual albumin concentrations of samples taken from the holding bags after processing (packed red cells) are summarized in Table 6. Residual albumin concentration of supernatants in the holding bags increased progressively with greater processing speeds using all devices. Residual albumin concentrations using BRAT 2 was greatest in all three flow programs. In standard flow, comparison of the average albumin elimination rate with CATS and Sequestra 1000 showed no difference (Table 7). Both were greater than those of BRAT 2 ($p < .05$). In medium flow, the average albumin elimination rate with BRAT 2 was less than Sequestra 1000 ($p < .05$). In high flow, CATS was greater than both Sequestra 1000 and BRAT 2 ($p < .0001$). In all systems and programs, the albumin elimination rate decreased with an increase in HCT of the incoming blood. The mean albumin transfusion rates (Figure 4) in standard, medium, and high flow, respectively, with BRAT 2 were 447 ± 340 mg/dL, 604 ± 514 mg/dL, and $2,738 \pm 167$ mg/dL; with CATS were 90 ± 44 mg/dL, 337 ± 284 mg/dL, and 346 ± 357 mg/dL; and with Sequestra 1000 were 69 ± 36 mg/dL, 217 ± 125 mg/dL, and $2,277 \pm 253$ mg/dL. Compared with CATS and Sequestra 1000, residual albumin transfusion rates for BRAT 2 ranged up to six times greater in standard flow programs ($p < .01$) and up to three times greater in medium flow ($p < .01$). In high flow, the albumin transfusion rate of BRAT 2 and Sequestra 1000 were up to eight times greater as compared to CATS ($p < .0001$).

DISCUSSION

In confirmation of the value of intraoperative autologous transfusion practice, post-transfusion survival of salvaged red

Table 4. Red cell mass (RCM) flow rates to the holding bags (mean $\pm$ standard deviation; mL/min) for three autotransfusion devices using three programs at reservoir hematocrits of 10, 20, and 30% as well as the means for all hematocrits

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
10% <i>N</i> = 3	19 $\pm$ 0.8	29 $\pm$ 1.2	12 $\pm$ 0.6	18 $\pm$ 0.3	23 $\pm$ 0.1	28 $\pm$ 0.4	11 $\pm$ 0.2	19 $\pm$ 0.7	7 $\pm$ 0.4
20% <i>N</i> = 3	27 $\pm$ 0.5	37 $\pm$ 0.8	22 $\pm$ 0.0	19 $\pm$ 0.3	25 $\pm$ 0.7	49 $\pm$ 3.5	17 $\pm$ 0.4	24 $\pm$ 1.2	14 $\pm$ 1.2
30% <i>N</i> = 3	32 $\pm$ 0.6	40 $\pm$ 0.3	34 $\pm$ 0.1	19 $\pm$ 1.4	24 $\pm$ 0.4	53 $\pm$ 1.7	18 $\pm$ 0.8	26 $\pm$ 2.8	24 $\pm$ 9.6
Average All <i>N</i> = 9	26 $\pm$ 5.6 ○*	35 $\pm$ 4.5 ○*	22 $\pm$ 9.0 ○*	19 $\pm$ 1.0 ○	24 $\pm$ 0.9 ○	43 $\pm$ 11.3 ○	15 $\pm$ 3.0 *○	23 $\pm$ 2.9 *	15 $\pm$ 7.0 *

Average All = three replicate procedures in each program; ○*| = $p < .05$ between corresponding programs.

Table 5. Packed red blood cell (PRBC) processing rate (mean $\pm$ standard deviation; mL/min) for three autotransfusion devices using three replicate procedures in three programs

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
Average All <i>N</i> = 9	58 $\pm$ 15 ○*	85 $\pm$ 17 ○*	136 $\pm$ 6 ○*	33 $\pm$ 2 ○	47 $\pm$ 5 ○	74 $\pm$ 21 ○	29 $\pm$ 5 *	48 $\pm$ 7 *	128 $\pm$ 6 *

Average all = means of all reservoir hematocrits; ○*| = $p < .05$ between corresponding programs.

Table 6. Washed packed red blood cell supernatant albumin concentrations (mean $\pm$ standard deviation; mg/dL) for three autotransfusion devices using three programs

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
Average All <i>N</i> = 9	358 $\pm$ 258 ○*	395 $\pm$ 310	558 $\pm$ 265 ○	114 $\pm$ 50 *	306 $\pm$ 212	474 $\pm$ 299	82 $\pm$ 45 ○	194 $\pm$ 94	297 $\pm$ 152 ○

Average All = means of all programs with three replicates in each; ○*| = $p < .05$ between corresponding programs.

blood cells shed during surgery was studied; the radio-labeled chromium half-lives of shed red cells were reported previously to be comparable with normal values (9). In this report, quality of processed blood shed during surgery was evaluated in a defined environment using a single pool of donor banked blood to minimize variation for comparing test results. Red cells, suspended in freshly thawed, compatible frozen donor plasma were used to simulate operating room conditions in terms of blood viscosity and hemoglobin level. Comparable programs for each of the three systems were evaluated by using the same pool of blood with triplicate testing, showing close reproducibility within each program. Of the parameters studied, processing speed was the greatest factor influencing HCT, red cell recovery, and washout quality. Progressively greater process-

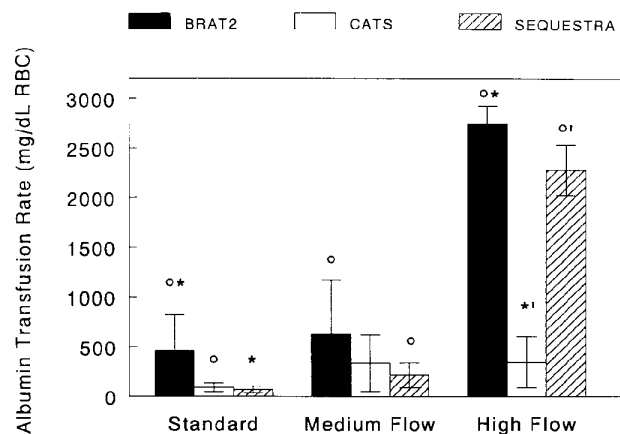
ing speeds with DF devices led to decreased HCT of the packed red cells (PRBC) collected into the holding bag, and removal rates of plasma were reduced with all the devices to a varying degree.

Processed RBC must be prepared with a suitable HCT to affect a proper post-transfusion increment. The standard flow program of BRAT 2 and the standard and medium flow programs of Sequestra 1000 achieved a satisfactory HCT. HCT of the red cell products was inversely related to filling rates and the HCT of shed blood. The medium flow of BRAT 2 and high flow of both BRAT 2 and Sequestra 1000 yielded products with unacceptably low HCT. Because the separation capacity, defined by the radius of the bowl and centrifuge rotations per minute, is constant in all DF washing programs, a slower filling

Table 7. Albumin elimination rates (mean $\pm$ standard deviation %) for three autotransfusion devices using three programs and three replicate procedures in each at 10, 20, 30%

Reservoir Hematocrit	Cobe BRAT 2			Fresenius CATS			Medtronic Sequestra		
	Stand	Med	High	Stand	Med	High	Stand	Med	High
10% <i>N</i> = 3	98.7 $\pm$ 0.4	98.4 $\pm$ 0.3	59 $\pm$ 0.4	99.4 $\pm$ 0.2	98.5 $\pm$ 0.5	98.3 $\pm$ 0.5	99.5 $\pm$ 0.04	98.6 $\pm$ 0.2	57.5 $\pm$ 2.9
20% <i>N</i> = 3	96.4 $\pm$ 2.5	96.1 $\pm$ 2.8	74.3 $\pm$ 18.2	98.3 $\pm$ 0.8	96.8 $\pm$ 0.2	94.7 $\pm$ 0.9	98.5 $\pm$ 0.5	98.0 $\pm$ 1.4	61.2 $\pm$ 2.0
30% <i>N</i> = 3	84.5 $\pm$ 0.7	79.3 $\pm$ 0.5	54.9 $\pm$ 2.8	96.2 $\pm$ 0.3	92.6 $\pm$ 1.2	86.8 $\pm$ 0.2	96.6 $\pm$ 0.1	93.3 $\pm$ 0.1	56.4 $\pm$ 1.0
Average All <i>N</i> = 9	93.2 $\pm$ 6.4 **	91.2 $\pm$ 8.7 o	62.8 $\pm$ 3.5 o	97.8 $\pm$ 1.4 o	94.4 $\pm$ 4.6	93.3 $\pm$ 4.8 **	98.4 $\pm$ 1.2 *	96.8 $\pm$ 2.3 o	58.3 $\pm$ 2.9 *

Average all = means for all hematocrits; ** $\dagger$ = $p < .05$ between corresponding programs.

**Figure 4:** Mean holding bag supernatant albumin transfusion rates $\pm$ standard deviations (mg/dL/RCM) for three replicate processing runs using three autotransfusion devices in three programs; * = $p < .05$; $N = 9$.

rate increases the time that the red blood cells settle in the centrifuge bowl, facilitating more concentration. With increased flow and increased HCT, packing of red blood cells is reduced and, at even greater flow, poorly separated red blood cells may trigger optical sensors, falsely detecting the appropriate PRBC filling level in the bowl and initiating a premature wash cycle. Residual air in the bowl is replaced with saline wash, further diluting red cell mass. Improper red blood cell sedimentation in respective centrifuge bowls of DF devices permits excess saline retention, leading to errors with false packed red blood cell flow rates and albumin concentration measurements.

HCT was maintained at a high level during progressively increased processing speeds with CATS (54–59%). As shown in previous clinical studies at standard flow, HCT using CATS was consistently greater than a variety of DF systems (1, 5, 7, 10). HCT was between 55 and 78% using the high flow wash

(2–4, 11), also confirmed in the author's operating room experience. While clinical experience with most DF equipment documented HCT results between 44 and 56% using standard flow (1, 5, 7, 10), no published data were found on the use of medium and high flow.

All laboratory and clinical data reviewed (1, 2, 5, 6) revealed no significant differences in RBC recovery using DF and CATS with standard flow programs. In medium flow of Sequestra 1000, diminished red cell recovery from red cell loss to waste was noted in the effluent line from the bowl, and was also noted in the author's operating room experience at flow rates higher than 500 mL/min; at 1000 mL/min there was almost complete red cell loss to waste. This observation was not seen with BRAT 2 and may be related to the design of the conical centrifuge bowl.

This study describes the importance of accuracy in reporting the data for red blood cell processing speeds. Packed red blood cell flow rates are invalid because of variability of HCT of samples from the holding bag. A system yielding packed red blood cells with a lower HCT seems to process blood more rapidly, but the RCM flow rate is low, and a salvaged red cell unit of inadequate potency results. The RCM flow rate is the accurate measurement. Although RCM flow increased significantly from standard to medium flow using all three systems evaluated, increased pump speeds with high flow actually failed to compensate for progressive decline in HCT of the packed red blood cells in DF systems. This was attributable to inadequate separation of red cells in the bowl of DF. Using CATS, there was progressive increase in RCM flow rates with greater processing speeds; in contrast the high flow programs of BRAT 2 and Sequestra 1000 showed markedly decreased RCM flow rates. The manufacturers of CATS claim that a constant packed red blood cell flow rate and HCT is related to preprogrammed specification of the various programs. This is substantiated in this study, even with high flow, as in the emergency wash procedure. In CATS, the RCM flow rate to the holding bag remains constant because of automatic varia-

tion of incoming blood flow resulting from instrument adaptation to HCT of the blood from the reservoir. The processing speed with CATS may be modified during operation by selecting a processing program deemed more applicable while good product quality is maintained. In contrast, parameters of DF devices, including blood and saline flow, wash volume, and centrifuge speed, independently may be modified by the operator to increase processing speed. As shown in this study, this may lead to poor PRBC quality, even if used within permissible ranges that are recommended by the manufacturers. Changing processing parameters of DF during operation on quality may necessitate more stringent manufacturer limitations for the ranges of adjustable parameters to prevent transfusion of PRBC with questionable potency and purity.

As an indicator of plasma washout, plasma albumin endogenous in the samples proved to be a suitable analyte, because sampling or hemolysis did not interfere. Immunochemical analysis is relatively inexpensive, readily available in most clinical laboratories, and may be deferred while samples of red cell supernatant are maintained in appropriately frozen storage. Although used by many (1-3, 6-8, 11-13), potassium concentration is unreliable as a marker for washout because of spurious concentration increases from hemolysis or delay in separating supernatant from red cells. In addition, because measurement with the potassium ion selective electrode is optimized for testing in a plasma or serum medium, reproducibility was poor when measuring saline supernatants. Flame photometry, the appropriate analytical method, is very seldom used in clinical laboratories. Free hemoglobin and heparin measurements were also used by many (1-6, 12) but, because of very high dilution requirements for measurement, these methods may be too insensitive for levels encountered in shed blood. Fibrinogen and activated factor XII also were used (6) but may be unreliable markers, because erratic changes in concentration may be associated with incomplete anticoagulation.

All systems showed decreased washing efficiency with greater processing speeds. In contrast with the supernatant albumin concentration, which increased only slightly with greater flow rates, the albumin elimination rates decreased, and residual albumin transfusion rates increased very significantly. This observation was characteristic of DF systems, especially when comparing standard and high flow programs. These findings indicate that contaminating plasma proteins, including activated clotting factors, are transfused in relatively high amounts and could be significant in patients enduring estimated blood losses of one liter and more. The albumin concentration of supernatant in the holding bags is misleading; the albumin elimination and transfusion rates also reflect the variation in HCT of the packed red blood cells and are the proper parameters of quality control. Using DF devices reduced plasma washout with progressively greater processing speed related to a decreased HCT of the packed red blood cells, which reflected improper filling of the bowls. In DF, the phase

of major elimination of plasma during red cell processing is when the plasma is separated to waste in a bowl that is filled properly. A respective separation of the plasma effluent during the filling cycle and the wash solution during the wash cycle into separate receptacles confirmed that 75% of plasma-free hemoglobin from shed blood was recovered in the separated plasma, and only 13% was found in the wash waste (9). Thus, the effect of the wash procedure in DF at the higher flow rates is minor and cannot compensate for insufficient plasma separation when bowls are filled incompletely.

The standard and medium flow programs of Sequestra 1000 may result in a satisfactory plasma protein elimination rate from shed blood in all surgical procedures. Using BRAT 2 with standard flow and parameters defined by the manufacturer, elimination of plasma is significantly less, and, in situations with poor blood quality, orthopedic surgery for example, using BRAT 2 may be questionable. In high-flow programs of the DF devices tested, the HCT and elimination of plasma are unacceptably low, and use of DF equipment is discouraged. All programs of CATS consistently yielded red cell products with preferred purity and potency. CATS provided red cell units with the greatest HCT, at the fastest processing speed and with the most elimination of plasma constituents, even when using high flow and may be recommended in all emergency situations without restriction. IAT is recommended as a viable transfusion option in a changing environment where autologous blood transfusion is accepted to be immunologically superior to allogeneic blood products and where costs and problems with the availability of blood products are increasing constantly.

REFERENCES

1. Holleufer RF, von Bormann B. Comparative study of the Fresenius CATS and the Dideco Autotrans autotransfusion systems in vascular surgery. In: World Apheresis Association 6th International Congress, 1996, Abstract Book. Scientific Press, Florence, Italy.
2. Walpoth BH, Eggensperger N, Walpoth-Aslan BN, et al. Qualitative assessment of blood washing with the continuous autologous transfusion system (CATS). *Int J Artif Organs*. 1997;20:234-239.
3. Florio G, Valbonesi M, Lercari G, et al. The Fresenius continuous autotransfusion system (CATS): Preliminary studies and application. *Int J Artif Organs*. 1996;19:431-434.
4. Breiting D, Frick U, Mauermann K, et al. Maschinelle intraoperative Autotransfusion (MAT): Qualitative Untersuchung Verschiedener Programme eines Kontinuierlichen Autotransfusionsverfahrens. *A I N S*. 1998;33 Suppl 3:FP-D 205.6.
5. Booke M, Fingerhut D, Greis A, et al. Intraoperative autotransfusion—A clinical study of two different blood pro-

- cessing techniques. *Infusionsther Transfusionsmed.* 1997; 24:190–336.
6. Lorentz A, Waibel H, Becker P. Qualitätskontrollen bei zwei maschinellen autotransfusionsgeräten (CATS/Cell-Saver V). *Haematologie, München, Sympomed.* 1997;16.
 7. Mertzlufft F, Bergum G, Seyfert UT. Maschinelle intraoperative Autotransfusion (MAT): Untersuchung zur qualitat verschiedener Autotransfusionssysteme. *Anaesthesist.* 1996;45;Suppl 2: FV 1313.
 8. Van Slyke DD, Phillips RA, Dole VP, et al. Calculation of hemoglobin from blood specific gravities. *J Biol Chem.* 1950;183:349.
 9. von Finck M, Schmidt R, Schneider W, et al. The quality of retransfused autologous red cells. Investigation on the elimination of plasma haemoglobin, osmotic fragility and survival rate of retransfused red cells. *Anaesthesist.* 1986; 35:686–692.
 10. Pipa A, Petersen J, Hergert M. Maschinelle Autotransfusion: Vergleich gewaschener erythrozytenkonzentrate mit biochemischen, haematologischen, und mikroskopischen verfahren. *Haematologie, München, Sympomed.* 1997.
 11. Schleinzner W, Singbartl G. Intraoperative Autotransfusion mit einem neuen Kontinuierlichen Autotransfusionssystem (Fresenius CATS). *Haematologie, München, Sympomed.* 1996;5:6–9.
 12. Santrach PJ, Willis EA, Mathison BA, et al. Performance characteristics of a modified centrifuge bowl for blood salvage. *Transfusion.* 1998;38, Suppl:77S.
 13. Santrach PJ, Willis EA, Mathison BA, et al. Potassium removal as a measure of processing efficiency in blood salvage. *Transfusion.* 1998;38, Suppl:79S.

Current Blood Culture Methods and Systems: Clinical Concepts, Technology, and Interpretation of Results

Melvin P. Weinstein

From the Departments of Medicine and Pathology, University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School; and the Microbiology Laboratory, Robert Wood Johnson University Hospital, New Brunswick, New Jersey

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.

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

Received 4 March 1996.

Reprints or correspondence: Dr. Melvin P. Weinstein, Robert Wood Johnson Medical School, 1 Robert Wood Johnson Place, New Brunswick, New Jersey 08903–0019.

Clinical Infectious Diseases 1996;23:40–6
© 1996 by The University of Chicago. All rights reserved.
1058–4838/96/2301–0004\$02.00

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 episodes 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

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 inservice 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

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. Comparisons 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 instrumented 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 CO₂ by growing microorganisms.

For the radiometric system, the instrument detects ¹⁴CO₂ in the bottle headspace, and for the nonradiometric system, CO₂ 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 CO₂ 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

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 CO₂ 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

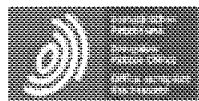
Blood cultures, as described herein, currently represent the “gold standard” for diagnosis of septicemia. Nonetheless, they have limitations. Positive results require hours to days of incubation. No one culture medium or system in use has been shown to be best suited to the detection of all potential 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.

References

1. Reller LB, Murray PR, MacLowry JD. Blood cultures II. In: Washington JA II, ed. Cumitech 1A. Washington, DC: American Society for Microbiology, 1982.
2. King TC, Price PB. An evaluation of iodophors as skin antiseptics. *Surg Gynecol Obstet* 1963;116:361–5.
3. Strand CL, Wajsbort RR, Sturmman K. Effect of iodophor vs. iodine tincture skin preparation on blood culture contamination rate. *JAMA* 1993;269:1004–6.
4. Schiffman RB, Pindur A. The effect of skin disinfection materials on reducing blood culture contamination. *Am J Clin Pathol* 1993;99:536–8.
5. Tonnesen A, Peuler M, Lockwood WR. Cultures of blood drawn by catheters vs. venipuncture. *JAMA* 1976;235:1877.

6. Felices FJ, Hernandez JL, Ruiz J, Meseguer J, Gómez JA, Molina E. Use of the central venous pressure catheter to obtain blood cultures. *Crit Care Med* 1979;7:78-9.
7. Tafuro P, Colbourn D, Gurevich I, et al. Comparison of blood cultures obtained simultaneously by venepuncture and from vascular lines. *J Hosp Infect* 1986;7:283-8.
8. Bryant JK, Strand CL. Reliability of blood cultures collected from intravascular catheter versus venipuncture. *Am J Clin Pathol* 1987;88:113-6.
9. Aronson MD, Bor DH. Blood cultures. *Ann Intern Med* 1987;106:246-53.
10. Isaacman DJ, Karasic RB. Utility of collecting blood cultures through newly inserted intravenous catheters. *Pediatr Infect Dis J* 1990;9:815-8.
11. Krumholz HM, Cummings S, York M. Blood culture phlebotomy: switching needles does not prevent contamination. *Ann Intern Med* 1990;113:290-2.
12. Leisure MK, Moore DM, Schwartzman JD, Hayden GF, Donowitz LG. Changing the needle when inoculating blood cultures: a no-benefit and high-risk procedure. *JAMA* 1990;264:2111-2.
13. Spitalnic SJ, Woolard RH, Mermel LA. The significance of changing needles when inoculating blood cultures: a meta-analysis. *Clin Infect Dis* 1995;21:1103-6.
14. Washington JA II. Blood cultures: principles and techniques. *Mayo Clin Proc* 1975;50:91-8.
15. Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. *Rev Infect Dis* 1983;5:35-53.
16. Weinstein MP, Joho KL, Quartey SM. Assessment of the third blood culture: does it increase detection of bacteremia [abstract no C150]. In: Program and abstracts of the 94th General Meeting of the American Society for Microbiology (Las Vegas). Washington, DC: American Society for Microbiology, 1994:517.
17. Strand CL. Blood cultures: consensus recommendations in 1988. Microbiology no. MB 88-1 (MB-172). American Society for Clinical Pathologists Check Sample Continuing Education Program. Chicago: American Society for Clinical Pathologists, 1988.
18. Li J, Plorde JJ, Carlson LG. Effects of volume and periodicity on blood cultures. *J Clin Microbiol* 1994;32:2829-31.
19. Wilson ML, Weinstein MP. General principles in the laboratory detection of bacteremia and fungemia. *Clin Lab Med* 1994;14:69-82.
20. Washington JA II, Ilstrup DM. Blood cultures: issues and controversies. *Rev Infect Dis* 1986;8:792-802.
21. Hall MM, Ilstrup DM, Washington JA II. Effect of volume of blood cultured on detection of bacteremia. *J Clin Microbiol* 1976;3:643-5.
22. Ilstrup DM, Washington JA II. The importance of volume of blood cultured in the detection of bacteremia and fungemia. *Diagn Microbiol Infect Dis* 1983;1:107-10.
23. Plorde JJ, Tenover FC, Carlson LG. Specimen volume versus yield in the BACTEC blood culture system. *J Clin Microbiol* 1985;22:292-5.
24. Tenney JH, Reller LB, Mirrett S, Wang W-LL, Weinstein MP. Controlled evaluation of the volume of blood cultured in detection of bacteremia and fungemia. *J Clin Microbiol* 1982;15:558-61.
25. Paisley JW, Lauer BA. Pediatric blood cultures. *Clin Lab Med* 1994;14:17-30.
26. Szymczak EG, Barr JT, Durbin WA, Goldmann DA. Evaluation of blood culture procedures in a pediatric hospital. *J Clin Microbiol* 1979;9:88-92.
27. Wilson ML. Introduction. *Clin Lab Med* 1994;14:1-7.
28. Auckenthaler R, Ilstrup DM, Washington JA II. Comparison of recovery of organisms from blood cultures diluted 10% (volume/volume) and 20% (volume/volume). *J Clin Microbiol* 1982;15:860-4.
29. Salvetti JF, Davies TA, Randall EL, Whitaker S, Waters JR. Effect of blood dilution on recovery of organisms from clinical blood cultures in medium containing sodium polyanethanol sulfonate. *J Clin Microbiol* 1979;9:248-52.
30. Reller LB, Lichtenstein KA, Mirrett S, Wang W-LL. Controlled evaluation of the ratio of blood to broth in the detection of bacteremia by blood culture [abstract 177]. In: Programs and abstracts of the Annual Meeting of the American Society for Microbiology (Las Vegas). Washington, DC: American Society for Microbiology, 1978:306.
31. Weinstein MP, Mirrett S, Wilson ML, Harrell LJ, Stratton CW, Reller LB. Controlled evaluation of BACTEC Plus 26 and Roche Septi-Chek aerobic blood culture bottles. *J Clin Microbiol* 1991;29:879-82.
32. Weinstein MP, Mirrett S, Reimer LG, et al. Controlled evaluation of BacT/Alert standard aerobic and FAN aerobic blood culture bottles for detection of bacteremia and fungemia. *J Clin Microbiol* 1995;33:978-81.
33. Wilson ML, Weinstein MP, Mirrett S, et al. Controlled evaluation of BacT/Alert standard anaerobic and FAN anaerobic blood culture bottles for the detection of bacteremia and fungemia. *J Clin Microbiol* 1995;33:2265-70.
34. Pohlman JK, Kirkley BA, Easley KA, Basile BA, Washington JA. Controlled clinical evaluation of BACTEC Plus Aerobic/F and BacT/Alert aerobic FAN bottles for detection of bloodstream infections. *J Clin Microbiol* 1995;33:2856-8.
35. Murray PR, Traynor P, Hopson D. Critical assessment of blood culture techniques: analysis of recovery of obligate and facultative anaerobes, strict aerobic bacteria, and fungi in aerobic and anaerobic blood culture bottles. *J Clin Microbiol* 1992;30:1462-8.
36. Dorsher CW, Rosenblatt JE, Wilson WR, Ilstrup DM. Anaerobic bacteremia: decreasing rate over a 15-year period. *Rev Infect Dis* 1991;13:633-6.
37. Lombardi DP, Engleberg NC. Anaerobic bacteremia: incidence, patient characteristics, and clinical significance. *Am J Med* 1992;92:53-60.
38. Morris AJ, Wilson ML, Mirrett S, Reller LB. Rationale for selective use of anaerobic blood cultures. *J Clin Microbiol* 1993;31:2110-3.
39. Sharp SE, McLaughlin JC, Goodman JM, et al. Clinical assessment of anaerobic isolates from blood cultures. *Diagn Microbiol Infect Dis* 1993;17:19-22.
40. Zaidi AKM, Knaut AL, Mirrett S, Reller LB. Value of routine anaerobic blood cultures for pediatric patients. *J Pediatr* 1995;127:263-8.
41. Evans MR, Truant AL, Kostman J, Locke L. The detection of positive blood cultures by the BACTEC NR660. The clinical importance of four-day versus seven-day testing. *Diagn Microbiol Infect Dis* 1991;14:107-10.
42. Hardy DJ, Hulbert BB, Migneault PC. Time to detection of positive BacT/Alert blood cultures and lack of need for routine subculture of 5- to 7-day negative cultures. *J Clin Microbiol* 1992;30:2743-5.
43. Masterson KC, McGowan JE Jr. Detection of positive blood cultures by the BACTEC NR660: the clinical importance of five versus seven days of testing. *Am J Clin Pathol* 1988;90:91-4.
44. Wilson ML, Mirrett S, Reller LB, Weinstein MP, Reimer LG. Recovery of clinically important microorganisms from the BacT/Alert blood culture system does not require testing for seven days. *Diagn Microbiol Infect Dis* 1993;16:31-4.
45. Washington JA. Collection, transport, and processing of blood cultures. *Clin Lab Med* 1994;14:59-68.
46. Wilson ML, Weinstein MP, Reimer LG, Mirrett S, Reller LB. Controlled comparison of the BacT/Alert and BACTEC 660/730 nonradiometric blood culture systems. *J Clin Microbiol* 1992;30:323-9.
47. Smith JA, Bryce EA, Ngui-Yen JH, Roberts FJ. Comparison of BACTEC 9240 and BacT/Alert blood culture systems in an adult hospital. *J Clin Microbiol* 1995;33:1905-8.
48. Kiehn TE, Cammarata R. Comparative recoveries of *Mycobacterium avium-M. intracellulare* from Isolator lysis-centrifugation and BACTEC 13A blood culture systems. *J Clin Microbiol* 1988;26:760-1.
49. Witebsky FG, Keiser JF, Conville PS, et al. Comparison of BACTEC 13A medium and DuPont Isolator for detection of mycobacteremia. *J Clin Microbiol* 1988;26:1501-5.

50. Pfaller MA, Sibley TK, Westfall LM, Hoppe-Bauer JE, Keating MA, Murray PR. Clinical laboratory comparison of a slide blood culture system with a conventional broth system. *J Clin Microbiol* 1982;16:525-30.
51. Henry NK, Grewell CM, McLimans CA, Washington JA II. Comparison of the Roche Septi-Chek blood culture bottle with a brain heart infusion biphasic medium bottle and with a tryptic soy broth bottle. *J Clin Microbiol* 1984;19:315-7.
52. Weinstein MP, Reller LB, Mirrett S, Stratton CW, Reimer LG, Wang W-LL. Controlled evaluation of the agar-slide and radiometric blood culture systems for the detection of bacteremia and fungemia. *J Clin Microbiol* 1986;23:221-5.
53. Weinstein MP, Mirrett S, Reimer LG, Reller LB. Effect of agitation and terminal subcultures on yield and speed of detection of the Oxoid signal blood culture system versus the BACTEC radiometric system. *J Clin Microbiol* 1989;27:427-30.
54. Murray PR, Niles AC, Heeren RL, Curren MM, James LE, Hoppe-Bauer JE. Comparative evaluation of the Oxoid Signal and Roche Septi-Chek blood culture systems. *J Clin Microbiol* 1988;26:2526-30.
55. Weinstein MP, Mirrett S, Reller LB. Comparative evaluation of Oxoid Signal and BACTEC radiometric blood culture systems for the detection of bacteremia and fungemia. *J Clin Microbiol* 1988;26:962-4.
56. Daley C, Lim I, Modra J, Wilkinson I. Comparative evaluation of nonradiometric BACTEC and improved Oxoid signal blood culture systems in a clinical laboratory. *J Clin Microbiol* 1990;28:1586-90.
57. Doern GV. Manual blood culture systems and the antimicrobial removal device. *Clin Lab Med* 1994;14:133-47.
58. Wilson ML, Weinstein MP, Reller LB. Automated blood culture systems. *Clin Lab Med* 1994;14:149-69.
59. Nolte FS, Williams JM, Jerris RC, et al. Multicenter clinical evaluation of a continuous monitoring blood culture system using fluorescent-sensor technology (BACTEC 9240). *J Clin Microbiol* 1993;31:552-7.
60. Krisher KK, Whyburn DR, Koepnick FE. Comparison of the BacT/Alert pediatric blood culture system, Pedi-BacT, with conventional culture using the 20-milliliter Becton-Dickinson supplemented peptone broth tube. *J Clin Microbiol* 1993;31:793-7.
61. Kirkley BA, Easley KA, Washington JA. Controlled clinical evaluation of Isolator and ESP aerobic blood culture systems for detection of bloodstream infections. *J Clin Microbiol* 1994;32:1547-9.
62. Kellogg JA, Bankert DA, Manzella JP, Parsey KS, Scott SL, Cavanaugh SH. Clinical comparison of isolator and thiol broth with ESP aerobic and anaerobic bottles for recovery of pathogens from blood. *J Clin Microbiol* 1994;32:2050-5.
63. Rohner P, Pepey B, Auckenthaler R. Comparison of BacT/Alert with Signal blood culture system. *J Clin Microbiol* 1995;33:313-7.
64. Welby PL, Keller DS, Storch GA. Comparison of automated Difco ESP blood culture system with biphasic BBL Septi-Chek system for detection of bloodstream infections in pediatric patients. *J Clin Microbiol* 1995;33:1084-8.
65. Hellinger WC, Cawley JJ, Alvarez S, et al. Clinical comparison of the Isolator and BacT/Alert aerobic blood culture systems. *J Clin Microbiol* 1995;33:1787-90.
66. Pohlman JK, Kirkley BA, Easley KA, Washington JA. Controlled clinical comparison of Isolator and BACTEC 9240 aerobic/F resin bottle for detection of bloodstream infections. *J Clin Microbiol* 1995;33:2525-9.
67. Zwadyk P Jr, Pierson CL, Young C. Comparison of Difco ESP and Organon Teknika BacT/Alert continuous-monitoring blood culture systems. *J Clin Microbiol* 1994;32:1273-9.
68. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization: the true consequences of false-positive results. *JAMA* 1991;265:365-9.
69. Towns ML, Quartey SM, Weinstein MP, Reimer LG, Reller LB. The clinical significance of positive blood cultures: a prospective, multicenter investigation [abstract C232]. In: Program and abstracts of the 93rd General Meeting of the American Society for Microbiology (Atlanta). Washington, DC: American Society for Microbiology, 1993:487.
70. Mirrett S, Weinstein MP, Reimer LG, Wilson ML, Reller LB. Interpretation of coagulase-negative staphylococci in blood cultures: does the number of positive bottles help? [abstract C69]. In: Program and abstracts of the 93rd General Meeting of the American Society for Microbiology (Atlanta). Washington, DC: American Society for Microbiology, 1993:458.
71. Peacock SJ, Bowler ICJW, Crook DWM. Positive predictive value of blood cultures growing coagulase-negative staphylococci [letter]. *Lancet* 1995;346:191-2.



Espacenet

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

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

Inventor(s):

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

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

Application number: DE19720003008U 19720127

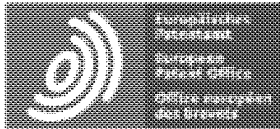
Priority number(s): AT19710009545 19711105

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

Abstract not available for DE7203008 (U)

Abstract of corresponding document: DE2203858 (B2)

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



Notice

This translation is machine-generated. It cannot be guaranteed that it is intelligible, accurate, complete, reliable or fit for specific purposes. Critical decisions, such as commercially relevant or financial decisions, should not be based on machine-translation output.

DESCRIPTION DE7203008U

[0001]

¹³ IMMUNO

[0002]

¹⁷ Public limited company for chemiscli-medizirii sclie

[0003]

²¹ Products Vienna (Austria.

²²)

[0004]

²⁶ Combined blood collection and infusion device

[0005]

³⁰ Plasmapheresis is used to obtain large quantities of plasma. This is a method in which blood is taken from the donor using a suitable blood-sucking device into a container partially filled with an anticoagulant, after which the container is centrifuged.

³³ The plasma which is left over after centrifugation is sucked off and the container with the erythrocytes is connected to an infusion device after it has been suspended in physiological saline solution and the erythrocytes are infused into the donor via the venipuncture needle which is still in the donor's vein.

³⁷ This process is repeated once when performing a so-called double plasmapheresis.

[0006]

41 The infusion devices previously used for plasmapheresis contained a drip chamber

[0007]

45 connecting line leading from a storage vessel to the single or double plasmapheresis bag and this has a further connecting line to the venipuncture needle. The devices for double plasmapheresis contained two

[0008]

51 ■■■. koi.i

[0009]

55 the corresponding connection lines to the venipuncture needle, which are also inextricably connected to the bags. This inextricable connection between the two bags and the venipuncture needle makes it more difficult and expensive to manufacture and use the devices and does not permit any variation in the work program.

59 E.g., it is not possible to collect centrifuged plasma in a reservoir without the bag intermediate stations. Wolters it is not possible with the known double bag devices to repeat the process of collection and reinfusion more than once, because in practice it is impossible in the device to be produced efficiently, which contains more than four bags which are inseparably connected to one another and to the venipuncture needle by means of corresponding connecting lines.

[0010]

67 The invention aims to avoid the disadvantages and difficulties described and consists in a blood collection and infusion device which has a reservoir for an infusion liquid, a connecting line leading via a drip chamber from the reservoir to the venipuncture needle and a further connection from the venipuncture needle to a blood reservoir, that the blood container provided with one or more connection points can be interchangeably connected to a line branching off from the connecting line between the reservoir and the venipuncture needle, which line is preferably provided with a shut-off element.

[0011]

77 The blood container can be designed as a single-chamber bag or as a two-chamber bag and can advantageously consist of flexible, transparent plastic material.

[0012]

82 As a result of the detachable connection of the ulutbehltex-s with the other parts of the device, the manufacture of the container is simpler and cheaper; the work program can be varied and modified in any way.

85 It is thus possible, after the contents of the blood container have been centrifuged, to convey the plasma into a second bag connected to the first bag or into another storage container.

87 It is also possible to repeat the process of removal and infusion not just twice but as often as you like, which z.

89 B. is essential in leukocytophoresis and thrombocytophoresis, in which cases the process is to be repeated up to 10 times.

91 Throughout the manipulation, the venipuncture can be left in the donor's vein

[0013]

95 The subject of the invention is explained in more detail using an exemplary embodiment in the drawing.

97 1 denotes the reservoir for an infusion liquid, with which the line 2 leading to the drip chamber 3 can be connected.

99 h

100 is a shut-off device in this line.

101 A branch piece 5, which is also a shut-off device

102 H

103 y

104 has, carries a coupling piece 6, which is connected to the blood container in the reinfusion phase in a manner to be described later.

106 From the drip chamber 3 leads the line 7, which is also a shut-off device

107 C''

108 has, to the venipuncture needle 8.

109 According to the invention, the line 9 branches off from this connecting line between the reservoir and the venipuncture needle and again has a shut-off element 4

111 nl

112 has and a coupling piece 10 has.

113 The blood container 11 designed as a single-chamber bag can be releasably connected to the line 9 via the attachment piece 12 and the coupling piece 10. The bag is preferably made of flexible and transparent plastic material

116 lk

117 are closable removal openings of the bag

[0014]

121 designated.

122 An embodiment of the invention consists in the fact that the bag 11 is connected to the bag 16, which is otherwise constructed in the same way, by means of a vesicle line; in this case, the blood container is designed as a two-chamber bag

[0015]

128 The function of the device is the following: After connecting the container 1 to the line 2, with the shut-off elements 4 and 4" open and the shut-off elements 4'" and 4M closed, the system is completely filled with physiological before inserting the venipuncture needle into the vein, avoiding air bubbles Saline solution filled. Then the shut-off element 4M in the line 7 is closed and the venipuncture needle inserted into the vein is connected to the B^ätsl 11 by connecting the coupling piece 10 to the attachment 12, the shut-off element 4Mt is opened and blood collection begins.

135 After the desired amount of blood has been removed, the shut-off element 4'" is closed and the container 11 is separated from the system.

137 Now another bag is connected to the coupling piece 10.

138 Then, with the shut-off element 4 still open, the shut-off element 4" is opened and a slow flow of physiological saline solution is infused into the donor's vein.

140 After removal from the system, the bag 11 is centrifuged and the supernatant plasma is separated from the sediment and collected.

142 The sediment remains in the blood bag 11 .

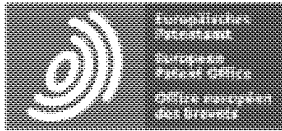
143 In the next phase, the shut-off device 4n in the line 7 is closed, the blood bag 11 is connected to one of the connectors 13 or 14 with the coupling piece 6 of the line 5, 4" is closed. 41 is opened and physiological saline solution is transferred into the bag 11 until a infusable suspension of erythrocytes in the physiological saline is formed.

147 Then the obturator 4 is

[0016]

151 closed, kopened and the suspension infused into the vein. The process can be repeated as often as desired, whereby, as mentioned earlier, the blood container can be designed either as a single or as a double bag.

154 As can be seen, the device is easy to use; Compared to the known devices, it also has the further great advantage that, to protect the donor during the plasmapheresis procedure, the blood group of the donor can be checked at any time by taking a blood sample at the coupling piece 10 in order to avoid mixing up the blood group when the erythrocytes are reinfused.



Notice

This translation is machine-generated. It cannot be guaranteed that it is intelligible, accurate, complete, reliable or fit for specific purposes. Critical decisions, such as commercially relevant or financial decisions, should not be based on machine-translation output.

CLAIMS DE7203008U

1.

¹³ * Uc/n sayings t

2.

¹⁷ 1. Combined blood collection and infusion device for carrying out single and multiple plasma.phereses or leukocyto- and thrombocytophereses, with a reservoir for an infusion liquid, a connecting line leading via a drip chamber from the storage vessel to the venipuncture needle and a further connection from the Venipuncture needle to a blood reservoir, characterized in that the blood reservoir (II), which is provided with one or more connection points, can be interchangeably connected to a line (9) branching off from the connecting line (7) between the reservoir (I) and the venipuncture needle (8), which preferably has a shut-off device (kn1) is provided, can be connected.

3.

²⁸ 2, Combined blood collection and infusion device according to Claim 1, characterized in that the blood container (II) is designed as a single-chamber bag or as a two-chamber bag and preferably consists of flexible, transparent plastic material.

DEUTSCHES GEBRAUCHSMUSTER

Bekanntmachungstag: 10. 5. 1972

A61m 1-00

7203008

30k 1-02

AT 27.01.72

Pr 05.11.71 Österreich A9545-71

Bez: Kombiniertes Blutabnahme- und
Infusionsgerät.

Anm: Immuno Aktiengesellschaft für che-
misch-medizinische Produkte, Wien;

Vtr: Glawe, R., Dr.-Ing.; Delfs, K.,
Dipl.-Ing.; Moll, W., Dipl.-Phys. Dr.
rer.nat; Pat.-Anwälte, 8000 München
und 2000 Hamburg;

lbm

Bitte beachten: Zutreffendes ankreuzen; stark umrandete Felder freilassen!

An das
Deutsche Patentamt
8000 München 2
Zweibrückenstraße 12

Ort: München
Datum: 26. Januar 1972
Eig. Zeichen: 4 34

(Bitte freilassen!)

Für den in den Anlagen beschriebenen Gegenstand (Arbeitsgerät oder Gebrauchsgegenstand oder Teil davon) wird die Eintragung in die Rolle für Gebrauchsmuster beantragt.

6 72 03 008.1

Anmelder:
(Vor- u. Zuname, b. Frauen auch Geburtsname;
Firma u. Firmensitz gem. Handelsreg.-Eintrag;
sonstige Bezeichnung des Anmelders)
in Postleitzahl, Ort, Str., Haus-Nr., ggf. auch
Postfach, bei ausländischen Orten auch Staat
und Bezirk)

Immuno Aktiengesellschaft für chemisch-
medizinische Produkte, 1220, Wien,
Industriestr. 72, Österreich

3891746 DE

Vertreter:
(Name, Anschrift mit Postleitzahl, ggf. auch
Postfach; Anwaltsvereinigungen in
Übereinstimmung mit der Vollmacht angeben)

Patentanwälte
Dr. Richard Glawe **Dipl.-Ing. Klaus Delfs** **Dr. Walter Moil**
München Hamburg München

1368

**Zustellungsbevollmächtigter,
Zustellungsanschrift**
(Name, Anschrift mit Postleitzahl, ggf. auch
Postfach)

Abholfach 13

Die Anmeldung ist eine ☐ **Ausscheidung aus der**
Gebrauchsmuster-Anmeldung Akt.Z.
Für die Ausscheidung wird als Anmeldetag der beansprucht

Die Bezeichnung lautet:
(kurze und genaue technische Bezeichnung des
Gegenstands, auf den sich die Erfindung
bezieht, übereinstimmend mit dem Titel der
Beschreibung;
keine Phantasiebezeichnung!)

Kombiniertes Blutabnahme- und Infusionsgerät

In Anspruch genommen wird die
Auslandspriorität der Voranmeldung
(Reihenfolge: Anmeldetag, Land, Aktenzeichen;
Ankreuzen 1 ankreuzen)
Ausstellungspriorität
(Reihenfolge: 1. Schaustellungstag, amtl.
Bestimmung und Ort der Ausstellung mit
Eröffnungstag;
Ankreuzen 2 ankreuzen)

5. November 1971, Österreich, A 9545/71

05.11.71 DE A 9545-71

Die Gebühr für die Gebrauchsmusteranmeldung in Höhe von 30,— DM

☐ ist entrichtet. ☒ wird entrichtet.*

Es wird beantragt, auf die Dauer von Monat(en) (max. 6 Monate ab Anmeldetag) die Eintragung und Bekanntmachung
anzusetzen.

Anlagen: (Die angekreuzten Unterlagen sind beigelegt)

- ☒ Ein weiteres Stück dieses Antrags
- ☒ Eine Beschreibung
- ☒ Ein Stück mit Schutzanspruch(en)
- ☒ Ein Satz Aktenzeichnungen mit Blatt
- ☒ Zwei vergrößerte Modelle
- ☒ Vertretervollmacht

- 1. ☒
- 2. ☒
- 3. ☒
- 4. ☒
- 5. ☒

Bitte freilassen

Von diesem Antrag und allen Unterlagen
wurden Abschriften zurückbehalten.

Raum für Gebührenmarken —

(bei Platzmangel auch Rückseite benutzen)

7203008 10.5.72

(Patentamt)

4

I M M U N O
Aktiengesellschaft für
chemisch-medizinische
Produkte
Wien (Österreich)

Kombiniertes Blutabnahme- und Infusionsgerät

Zur Gewinnung großer Plasma-Mengen wird die Plasmapherese angewendet. Dies ist eine Methode, bei der dem Spender mittels eines geeigneten Abnahmeapparates Blut in ein mit einem gerinnungshemmenden Mittel teilweise gefüllten Behälter abgenommen wird, worauf der Behälter zentrifugiert wird. Das nach dem Zentrifugieren überstehende Plasma wird abgesaugt und der Behälter mit den Erythrocyten wird nach Aufschwemmen mit physiologischer Kochsalzlösung an ein Infusionsgerät angeschlossen und die Erythrocyten werden über die noch in der Vene des Spenders befindliche Venenpunktionsnadel dem Spender infundiert. Dieser Vorgang wird bei Durchführung einer sogenannten Doppelplasmapherese einmal wiederholt.

Die für Plasmapheresen bisher verwendeten Infusionsgeräte enthielten eine über eine Tropfkammer führende Verbindungsleitung von einem Vorratsgefäß zum Einfach- oder Doppelplasmapheresebeutel und dieser besitzt eine weitere Verbindungsleitung zur Venenpunktionsnadel. Die Geräte für Doppelplasmapheresen enthielten zwei

7203008 10.5.72

miteinander unlösbar verbundene Blutabnahmebeutel mit den entsprechenden, ebenfalls mit den Beuteln unlösbar verbundenen Verbindungsleitungen zur Venenpunktionsnadel. Diese unlösbare Verbindung der beiden Beutel und der Venenpunktionsnadel untereinander erschwert und verteuert die Herstellung und Handhabung der Geräte und erlaubt keinerlei Variation im Arbeitsprogramm. Z.B. ist es nicht möglich, zentrifugiertes Plasma ohne die Beutelzwischenstationen in einem Vorratsbehälter zu sammeln. Weiters ist es mit den bekannten Doppelbeutelgeräten nicht möglich, den Vorgang der Abnahme und Reinfundierung mehr als einmal zu wiederholen, weil es in der Praxis unmöglich ist, ein Gerät rationell herzustellen, welches mehr als vier, durch entsprechende Verbindungsleitungen unlösbar miteinander und mit der Venenpunktionsnadel verbundene Beutel enthält.

Die Erfindung bezweckt die Vermeidung der geschilderten Nachteile und Schwierigkeiten und besteht bei einem Blutabnahme- und Infusionsgerät, welches einen Vorratsbehälter für eine Infusionsflüssigkeit, eine über eine Tropfkammer führende Verbindungsleitung vom Vorratsgefäß zur Venenpunktionsnadel und eine weitere Verbindung von der Venenpunktionsnadel zu einem Blutbehälter aufweist, darin, daß der mit einer oder mehreren Anschlußstellen versehene Blutbehälter austauschbar an eine von der Verbindungsleitung zwischen Vorratsbehälter und Venenpunktionsnadel abzweigenden Leitung, die vorzugsweise mit einem Absperrorgan versehen ist, anschließbar ist.

Der Blutbehälter kann als Einkammerbeutel, oder als Zweikammerbeutel ausgebildet sein und verteilhaft aus flexiblem transparentem Kunststoffmaterial, bestehen.

7203008

- 3 -

6

Infolge der lösbaren Verbindung des Blutbehälters mit den übrigen Teilen des Gerätes ist die Herstellung des Behälters einfacher und billiger; das Arbeitsprogramm kann in beliebiger Weise variiert und modifiziert werden. So ist es möglich, nach Zentrifugieren des Inhaltes des Blutbehälters das Plasma in einen mit dem ersten Beutel verbundenen zweiten Beutel oder in einen sonstigen Vorratsbehälter zu fördern. Es ist ferner möglich, den Vorgang der Abnahme und Infusion nicht nur zweimal sondern beliebig oft zu wiederholen, was z.B. wesentlich ist bei der Leukozyto- und Thrombozytopherese, in welchen Fällen der Vorgang bis zu 10 mal zu wiederholen ist. Während der gesamten Manipulation kann die Venenpunktionsnadel in der Vene des Spenders verbleiben.

Der Erfindungsgegenstand ist an einem Ausführungsbeispiel in der Zeichnung näher erläutert. Mit 1 ist der Vorratsbehälter für eine Infusionsflüssigkeit bezeichnet, mit dem die zur Tropfkammer 3 führende Leitung 2 verbindbar ist. 4 ist ein Absperrorgan in dieser Leitung. Ein Abzweigstück 5, welches ebenfalls ein Absperrorgan 4' aufweist, trägt ein Kupplungsstück 6, welches in später noch zu beschreibender Weise mit dem Blutbehälter in der Reinfusionsphase verbunden wird. Von der Tropfkammer 3 führt die Leitung 7, die ebenfalls ein Absperrorgan 4'' aufweist, zur Venenpunktionsnadel 8. Von dieser Verbindungsleitung zwischen Vorratsbehälter und Venenpunktionsnadel zweigt erfindungsgemäß die Leitung 9 ab, die wieder ein Absperrorgan 4''' aufweist und ein Kupplungsstück 10 besitzt. Der als Einkammerbeutel ausgebildete Blutbehälter 11 ist über das Ansatzstück 12 und das Kupplungsstück 10 lösbar mit der Leitung 9 verbindbar. Der Beutel besteht vorzugsweise aus flexiblem und transparentem Kunststoffmaterial. Mit 13 und 14 sind verschließbare Entnahmeöffnungen des Beutels

7203008 10.5.72

bezeichnet. Eine Ausführungsform der Erfindung besteht darin, daß der Beutel 11 durch eine Verbindungsleitung 15 mit dem sonst in gleicher Weise ausgebildeten Beutel 16 verbunden ist; in diesem Fall ist der Blutbehälter also als Zweikammerbeutel ausgebildet.

Die Funktion des Gerätes ist die folgende: Nach Verbinden des Behälters 1 mit der Leitung 2 wird bei geöffneten Absperrorganen 4 und 4" und geschlossenen Absperrorganen 4' und 4"' das System vor Einführen der Venenpunktionsnadel in die Vene unter Vermeidung von Luftblasen vollständig mit physiologischer Kochsalzlösung gefüllt. Dann wird das Absperrorgan 4" in der Leitung 7 geschlossen und die Venenpunktionsnadel in die Vene eingeführt. Dann wird durch Verbinden des Kupplungsstückes 10 mit dem Ansatzstück 12 der Beutel 11 angeschlossen, das Absperrorgan 4"' geöffnet und die Blutabnahme beginnt. Nach Entnahme der gewünschten Blutmenge wird das Absperrorgan 4"' geschlossen und der Behälter 11 vom System abgetrennt. Nun wird ein weiterer Beutel an das Kupplungsstück 10 angeschlossen. Sodann wird bei noch offenem Absperrorgan 4 das Absperrorgan 4" geöffnet und ein langsamer Fluß von physiologischer Kochsalzlösung in die Vene des Spenders infundiert. Der Beutel 11 wird nach Abnahme vom System zentrifugiert und das überstehende Plasma von dem Sediment getrennt und gesammelt. Im Blutbeutel 11 bleibt das Sediment übrig. In der nächsten Phase wird das Absperrorgan 4" in der Leitung 7 geschlossen, der Blutbeutel 11 mit einem der Anschlußstücke 13 oder 14 mit dem Kupplungsstück 6 der Leitung 5 verbunden, 4" geschlossen, 4' geöffnet und physiologische Kochsalzlösung in den Beutel 11 übergeführt, bis eine infundierbare Suspension von Erythrocyten in der physiologischen Kochsalzlösung gebildet ist. Dann wird das Absperrorgan 4 ge-

7203008 10.5.72

720172

- 5 -

8

geschlossen, 4" geöffnet und die Suspension in die Vene infundiert. Der Vorgang kann beliebig oft wiederholt werden, wobei, wie früher erwähnt, der Blutbehälter entweder als Einfach- oder als Doppelbeutel ausgeführt sein kann. Wie ersichtlich, ist das Gerät einfach zu bedienen; es hat gegenüber den bekannten Geräten auch noch den weiteren großen Vorteil, daß zum Schutz des Spenders während der Plasmaphereseprozedur jederzeit die Blutgruppe des Spenders durch Entnahme einer Blutprobe beim Kupplungsstück 10 kontrolliert werden kann, um eine Verwechslung der Blutgruppe bei der Reinfusion der Erythrocyten zu vermeiden.

7203008 10.5.72

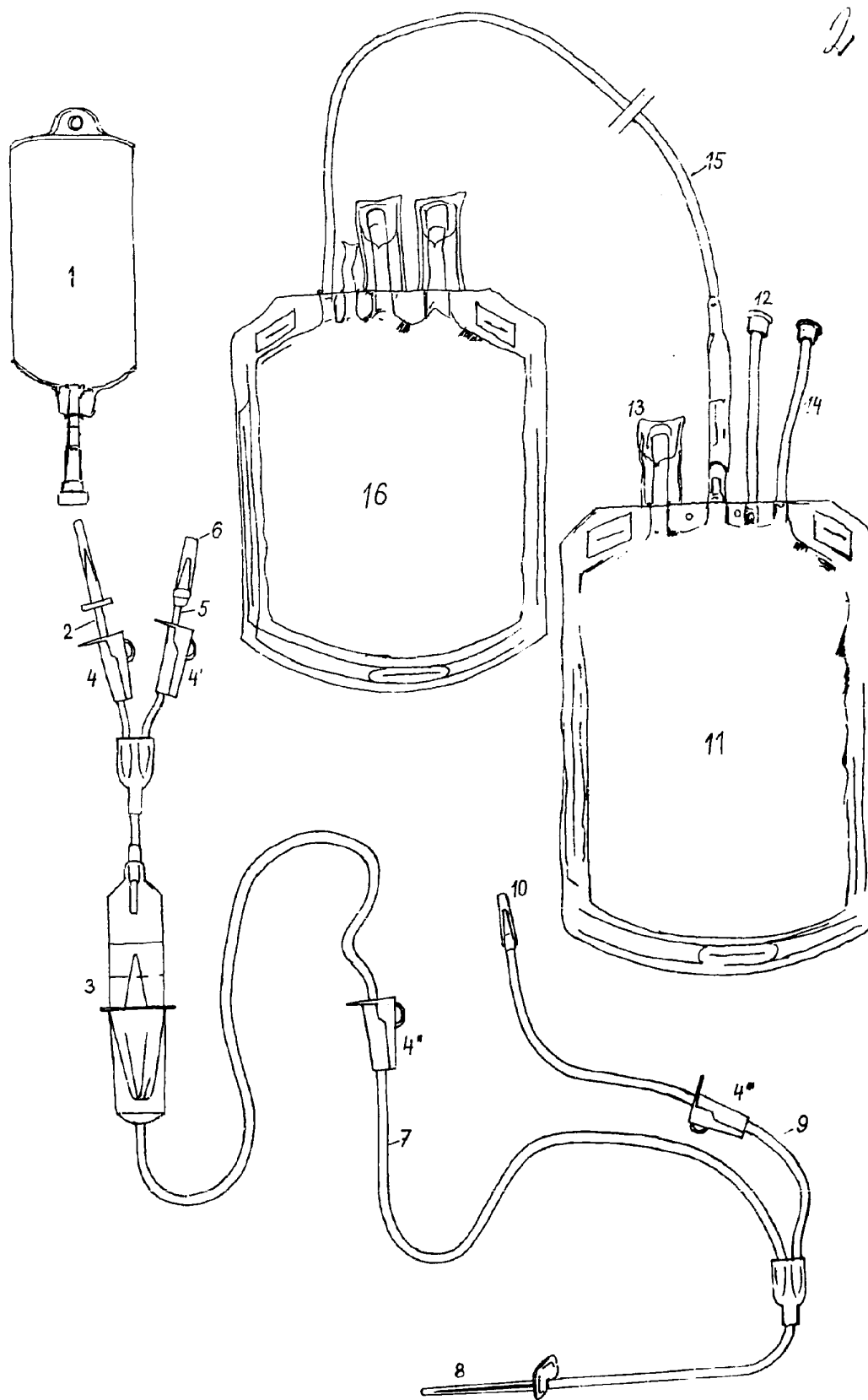
~~Patent~~ Ansprüche :

1. Kombiniertes Blutabnahme- und Infusionsgerät zur Durchführung von Einfach- und Mehrfachplasmapheresen bzw. von Leukozyto- und Thrombozytopheresen, mit einem Vorratsbehälter für eine Infusionsflüssigkeit, einer über eine Tropfkammer führenden Verbindungsleitung vom Vorratsgefäß zur Venenpunktionsnadel und einer weiteren Verbindung von der Venenpunktionsnadel zu einem Blutbehälter, dadurch gekennzeichnet, daß der mit einer oder mehreren Anschlußstellen versehene Blutbehälter (11) austauschbar an eine von der Verbindungsleitung (7) zwischen Vorratsbehälter (1) und Venenpunktionsnadel (8) abzweigenden Leitung (9), die vorzugsweise mit einem Absperrorgan (4'') versehen ist, anschließbar ist.
2. Kombiniertes Blutabnahme- und Infusionsgerät nach Anspruch 1, dadurch gekennzeichnet, daß der Blutbehälter (11) als Einkammerbeutel oder als Zweikammerbeutel ausgebildet ist und vorzugsweise aus flexiblem transparentem Kunststoffmaterial besteht.

7203008 10.5.72

1172

2



7203008 10.5.72



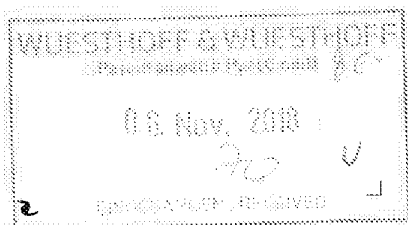
European Patent Office
10958 BERLIN
GERMANY
Tel: +49 30 2590 10
Fax: +49 30 2590 1840



Thum, Bernhard
Wuesthoff & Wuesthoff
Patentanwälte PartG mbB
Schweigerstraße 2
81541 München
ALLEMAGNE

Formalities Officer
Name: Schulze, Cornelia
Tel: +49 30 25901 - 701
or call
+31 (0)70 340 45 00

Substantive Examiner
Name: Schultz, Oltmar
Tel: +49 30 25901 - 566



Application No. 16 747 682.9 - 1132	Ref. EPA-142 451	Date 31.10.2018
Applicant KURIN, INC.		

Basel 28.02.19 uof/Pl.
WL 06.12.18 ✓
WV 28.01.19 ✓ uof
103

Communication pursuant to Article 94(3) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(2) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 126(2) and 131(2) and (4) EPC. One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (R. 50(1) EPC).

If filing amendments, you must identify them and indicate the basis for them in the application as filed. Failure to meet either requirement may lead to a communication from the Examining Division requesting that you correct this deficiency (R. 137(4) EPC).

In case you withdraw the application within the above-mentioned period, the examination fee will be refunded at a rate of 50% (Art. 11 (b) RFees).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Art. 94(4) EPC).



Schultz, Ottmar
Primary Examiner
For the Examining Division

Enclosure(s): 1 page/s reasons (Form 2906)

Datum
Date 31.10.2018
Date

Blatt
Sheet 1
Feuille

Anmelde-Nr:
Application No: 16 747 682.9
Demande n°:

The examination is being carried out on the following application documents

Description, Pages

1-33 as published

Claims, Numbers

1-20 as published

Drawings, Sheets

1/50-50/50 as published

+++++

An International Preliminary Report on Patentability has already been drawn up for the present application in accordance with the PCT. The deficiencies mentioned in that report give rise to objections under the corresponding provisions of the EPC.

+++++

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 50828-501001WO	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2016/043709	International filing date (<i>day/month/year</i>) 22 July 2016 (22.07.2016)	Priority date (<i>day/month/year</i>) 24 July 2015 (24.07.2015)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant KURIN, INC.			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| ☒ | Box No. I | Basis of the report |
| ☐ | Box No. II | Priority |
| ☐ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☒ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

		Date of issuance of this report 30 January 2018 (30.01.2018)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland		Authorized officer Lingfei Bai
Facsimile No. +41 22 338 82 70		e-mail: pct.team2@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.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.
PCT/US2016/043709

International filing date (day/month/year)
22.07.2016

Priority date (day/month/year)
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 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will 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 notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
Gitschiner Str. 103
D-10958 Berlin
Tel. +49 30 25901 - 0
Fax: +49 30 25901 - 840

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Schultz, Ottmar

Telephone No. +49 30 25901-0



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/043709

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 43bis.1(a))
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/043709

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>2, 6, 7, 11, 14</u>
	No: Claims	<u>1, 3-5, 8-10, 12, 13, 15-20</u>
Inventive step (IS)	Yes: Claims	<u>6, 14</u>
	No: Claims	<u>1-5, 7-13, 15-20</u>
Industrial applicability (IA)	Yes: Claims	<u>1-20</u>
	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]; FISCHER 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 and 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.

+++++

INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Application Number	18113710
	Filing Date	02/24/2023
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Client Number	069366
Page 1 of 1	Matter Number	0574153_KUR2C04US

<p align="center">GENERAL</p> <p>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.</p> <p>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.</p> <p>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.</p>

<p align="center">TIMING</p> <p>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.</p>
--

<p align="center">CERTIFICATION STATEMENT</p> <p>No certification statement is required. This Information Disclosure Statement is being filed in accordance with 37 CFR 1.97(b).</p>

<p align="center">FEE</p> <p>No fee is required. This Information Disclosure Statement is being filed in accordance with 37 CFR 1.97(b).</p>

<p align="center">ADDITIONAL COMMENTS</p>
--

SIGNATURE			
Signature	/ Benjamin F. Hudson /	Date	2023-05-10
Name	Benjamin F. Hudson	Registration Number	71,474

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Fri May 12 06:15:26 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new outgoing correspondence. This correspondence is now available for viewing in Patent Center.

The official date of notification of the outgoing correspondence will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:

The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	CTNF	05/12/2023	069366-0574153_KUR2C04US
18113710	892	05/12/2023	069366-0574153_KUR2C04US

To view your correspondence online, please sign in to [Patent Center](#) and then select Workbench/View correspondence. To update your email address(es), select Manage/Manage customer numbers.

If you have any questions, please contact the [Patent Electronic Business Center](#) (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/113,710	02/24/2023	Bobby E. ROGERS	069366-0574153_KUR2C04US

CONFIRMATION NO. 2715

27500

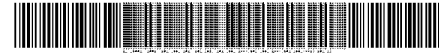
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)

ATTENTION: DOCKETING DEPARTMENT

P.O BOX 10500

McLean, VA 22102

PUBLICATION NOTICE



0000000059053970

Date Mailed: 07/06/2023

Title:BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION DEVICE AND METHOD

Publication No.US-2023-0210422-A1

Publication Date:07/06/2023

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently <http://www.uspto.gov/patft/>.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently <https://portal.uspto.gov/pair/> PublicPair. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Thu Jul 06 05:27:15 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new outgoing correspondence. This correspondence is now available for viewing in Patent Center.

The official date of notification of the outgoing correspondence will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:

The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	NTC.PUB	07/06/2023	069366-0574153_KUR2C04US

To view your correspondence online, please sign in to [Patent Center](#) and then select Workbench/View correspondence. To update your email address(es), select Manage/Manage customer numbers.

If you have any questions, please contact the [Patent Electronic Business Center](#) (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team



UNITED STATES
PATENT AND TRADEMARK OFFICE

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/113,710

RECEIPT DATE / TIME
08/09/2023 04:24:07 PM ET

ATTORNEY DOCKET #
069366-0574153_KUR2C04US

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION
DEVICE AND METHOD

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 2715

FILED BY Trent Tercenio

PATENT CENTER # 62588070

FILING DATE 02/24/2023

CUSTOMER # 27500

FIRST NAMED INVENTOR Bobby E. ROGERS

CORRESPONDENCE ADDRESS -

AUTHORIZED BY Benjamin Hudson

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0574153_KUR2C04US_Transmittal-Letter.pdf	1	Transmittal Letter	493 KB
069366-0574153_KUR2C04US_Response_to_Non-Final_Office_Action_rcvd_12MAY2023_4894-3293-1692_v1-APP.TEXT.docx	15	Application body structured text document	107 KB

Warning: All artifacts (SmartArt, Drawings, Charts, etc) have been replaced with images.
Bookmarks were found and have been removed.

069366-
0574153_KUR2C04US_PTO
_IDS-Form.pdf

4

Information Disclosure
Statement (IDS) Form (SB08)

1019 KB

Digest

DOCUMENT

MESSAGE DIGEST(SHA-512)

069366- 0574153_KUR2C04US_Transm ittal-Letter.pdf	95A651350248E F75B324D2905242B1639449C738BC8B4AA094 C8B06419E571DED03C9BDF A2E1AB6C2627CB9905A93873159 995105EEB87CB2D56D3B35C8BBD9F
069366- 0574153_KUR2C04US_Respon se_to_Non- Final_Office_Action_rcvd_12MA Y2023_4894-3293-1692_v1- APP.TEXT.docx	2F9C06AF46AB3C0A5D4D01E401C06700E12AF876A5588D491 25C01F3B53086426163F58E321A7A6474C8F4AE68BE869543B 34B870449A250992FE1B632971F7A
069366- 0574153_KUR2C04US_PTO_I DS-Form.pdf	D4E952972FB9CF9A72862215F156547F06F71778F3DA90F8100 748DB1B0174D0F43980A7E940A9497EEA033B6A423F55540CE 5C203A2B5D4FAFA2D256B9AD24C

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION # **18/113,710** RECEIPT DATE / TIME **08/09/2023 04:24:07 PM ET** ATTORNEY DOCKET # **069366-0574153_KUR2C04US**

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION
DEVICE AND METHOD

Application Information

APPLICATION TYPE Utility - Nonprovisional Application under 35 USC 111(a) PATENT # -
CONFIRMATION # 2715 FILED BY Trent Tercenio
PATENT CENTER # 62588070 AUTHORIZED BY Benjamin Hudson
CUSTOMER # 27500 FILING DATE 02/24/2023
CORRESPONDENCE ADDRESS - FIRST NAMED INVENTOR Bobby E. ROGERS

Payment Information

PAYMENT METHOD DA / 033975 PAYMENT TRANSACTION ID E202389G26527613 PAYMENT AUTHORIZED BY Trent Tercenio

FEE CODE	DESCRIPTION	ITEM PRICE(\$)	QUANTITY	ITEM TOTAL(\$)
2806	SUBMISSION OF AN INFORMATION DISCLOSURE STATEMENT	104.00	1	104.00
2202	EACH CLAIM IN EXCESS OF 20	40.00	9	360.00
TOTAL AMOUNT:				\$464.00

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d))

and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Application Number	18113710
	Filing Date	02/24/2023
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Client Number	069366
Page 1 of 1	Matter Number	0574153_KUR2C04US

<p align="center">GENERAL</p> <p>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.</p> <p>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.</p> <p>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.</p>

<p align="center">TIMING</p> <p>In accordance with 37 CFR 1.97(c), this Information Disclosure Statement is being filed after the period specified in 37 CFR 1.97(b) and before the mailing date of a Final Action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an Action that otherwise closes prosecution in the application.</p>
--

<p align="center">CERTIFICATION STATEMENT</p> <p>No certification statement is required. This Information Disclosure Statement is being filed in accordance with 37 CFR 1.97(c) and is accompanied by the fee set forth in 37 CFR 1.17(p).</p>

<p align="center">FEE</p> <p>This Information Disclosure Statement is being filed in accordance with 37 CFR 1.97(c), and is not accompanied by one of the certification statements of 37 CFR 1.97(e). Therefore, this Information Disclosure Statement is subject to the \$104 (small entity) fee set forth in 37 CFR 1.17(p).</p>

<p align="center">ADDITIONAL COMMENTS</p>
--

SIGNATURE			
Signature	/ Benjamin F. Hudson /	Date	2023-08-09
Name	Benjamin F. Hudson	Registration Number	71,474

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		18113710	
	Filing Date		2023-02-24	
	First Named Inventor	Bobby E. ROGERS		
	Art Unit	-		
	Examiner Name			
	Attorney Docket Number	069366-0574153_KUR2C04US		

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			
If you wish to add additional U.S. Patent citation information please click the Add button.							Add	
U.S. PATENT APPLICATION PUBLICATIONS							Remove	
Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear		
	1							
If you wish to add additional U.S. Published Application citation information please click the Add button.							Add	
FOREIGN PATENT DOCUMENTS							Remove	
Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ²	Kind Code ⁴	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear	T ⁵
	1							☐
If you wish to add additional Foreign Patent Document citation information please click the Add button.							Add	
NON-PATENT LITERATURE DOCUMENTS							Remove	
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.						T ⁵

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		18113710
	Filing Date		2023-02-24
	First Named Inventor	Bobby E. ROGERS	
	Art Unit	-	
	Examiner Name		
	Attorney Docket Number	069366-0574153_KUR2C04US	

	1		☐
--	---	--	--------------------------

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	18113710
	Filing Date	2023-02-24
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Examiner Name	
	Attorney Docket Number	069366-0574153_KUR2C04US

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)	2023-08-09
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent 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.

Application No. 18/113,710

Attorney's Docket No.: 069366-0574153_KUR2C04US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Bobby E. Rogers, et al.

Confirmation No: 2715

Application No.: 18/113,710

Art Unit: 3791

Filed: February 24, 2023

Examiner: May A. Abouelela

For: BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT
SEQUESTRATION DEVICE AND METHOD

Mail Stop Amendment

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

RESPONSE TO NON-FINAL OFFICE ACTION

Dear Examiner Abouelela:

This reply is responsive to the Non-Final Office Action mailed May 12, 2023, in the above-referenced matter (hereinafter “the Office Action”). Reconsideration and allowance of the application is requested in view of the following:

Amendments to the Specification beginning on page 2.

Listing of Claims beginning on page 3.

Remarks beginning on page 8.

Application No. 18/113,710

Attorney's Docket No.: 069366-0574153_KUR2C04US
(PATENT)

AMENDMENTS TO THE SPECIFICATION

Please amend the title of the application to be: Blood Sample Optimization Device

LISTING OF CLAIMS

This listing of claims replaces all prior versions of claims in the application:

1. (Original) A device comprising:

an inlet port;

an outlet port;

a chamber connected with the inlet port and configured to receive a first portion of blood,
the chamber including an air permeable material that seals at least partially upon contact with a
portion of the first portion of blood; and

a sampling channel having a proximal end connected with the inlet port and a distal end
connected with the outlet port.
2. (Original) The device in accordance with claim 1, wherein the device is configured such
that, when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into
the chamber.
3. (Original) The device in accordance with claim 2, wherein the device is further
configured such that an initial aliquot of blood will contact the air permeable material and back
up into the chamber.
4. (Original) The device in accordance with claim 3, wherein the device is further
configured such that follow-on amounts of blood will flow through the sampling channel
towards the outlet port.

5. (Original) The device in accordance with claim 1, wherein the air permeable material is located at a distal end of the chamber.
6. (Original) The device in accordance with claim 1, wherein the air permeable material is a hydrophobic plug.
7. (Original) The device in accordance with claim 1, wherein the air permeable material is a hydrophobic membrane.
8. (Original) The device in accordance with claim 1, wherein the air permeable material is a hydrophilic membrane.
9. (Original) The device in accordance with claim 1, wherein the sampling channel further comprises a valve configured to close off the sampling channel.
10. (Original) The device in accordance with claim 9, wherein the valve is a clip.
11. (Original) The device in accordance with claim 1, further comprising a junction configured to direct an initial blood flow into the chamber.
12. (Original) The device in accordance with claim 1, further comprising a junction configured such that flow out of the inlet port is preferentially directed toward the chamber.
13. (Original) The device in accordance with claim 1, wherein the chamber has a larger cross-sectional area than the sampling channel.
14. (Cancelled)

15. (Cancelled)
16. (Original) The device in accordance with claim 1, further comprising a patient needle and a sample collection device.
17. (New) A device comprising:
 - an inlet port for receiving a blood sample;
 - an outlet port;
 - a chamber connected with the inlet port and the outlet port, and configured to collect a first portion of the blood sample, the chamber including a material that is air permeable and blood impermeable; and
 - a sampling channel connected with the inlet port and configured to convey a subsequent portion of the blood sample to the outlet port while bypassing the chamber.
18. (New) The device in accordance with claim 17, wherein the device is configured such that, when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into the chamber.
19. (New) The device in accordance with claim 18, wherein the device is further configured such that an initial aliquot of blood will contact the material and back up into the chamber.
20. (New) The device in accordance with claim 17, wherein the material is located at a distal end of the chamber.
21. (New) The device in accordance with claim 17, wherein the material is a hydrophobic plug.

22. (New) The device in accordance with claim 17, wherein the material is a hydrophobic membrane.
23. (New) The device in accordance with claim 17, wherein the material is a hydrophilic membrane.
24. (New) The device in accordance with claim 17, wherein the sampling channel further comprises a valve configured to close off the sampling channel.
25. (New) The device in accordance with claim 24, wherein the valve is a clip.
26. (New) The device in accordance with claim 17, the device further comprising a junction connecting the inlet port and the sampling channel and the chamber.
27. (New) The device in accordance with claim 26, wherein the junction is configured to convey the subsequent portion of the blood sample to the outlet port while bypassing the chamber.
28. (New) The device in accordance with claim 17, wherein the chamber has a larger cross-sectional area than the sampling channel.
29. (New) The device in accordance with claim 17, further comprising a housing that defines the chamber and the sampling channel.
30. (New) The device in accordance with claim 29, 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 chamber, and the sampling channel.

31. (New) The device in accordance with claim 17, further comprising a patient needle and a sample collection device.

REMARKS

Claim Summary: Prior to this response, Claims 1-16 were pending. Claims 14 and 15 are cancelled and Claims 17-31 are new. After entry of this response, Claims 1-13 and 16-31 will be pending. No new matter is added with this amendment. Reconsideration and allowance of the current application are requested in light of the following remarks.

Summary of Rejections: The Office has rejected Claim 12 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite; Claims 1, 5, 8-14, and 16 under 35 U.S.C. §102 as allegedly being anticipated by Christensen (US 2010/0057004), hereinafter "Christensen;" Claims 2-4, 6 and 7 as allegedly being unpatentable under 35 U.S.C. §103 over Christensen (US 2010/0057004), hereinafter "Christensen," in view of Weilbacher (US 2008/0167577), hereinafter "Weilbacher;" Claim 15 as allegedly being obvious under 35 U.S.C. §103 over Christensen (US 2010/0057004), hereinafter "Christensen."

No Change in Scope of Claims: The Office is respectfully reminded that the scope of at least one claim has remained unchanged in this Response. If new grounds of rejection for an unchanged claim are presented in a subsequent action, per MPEP§706.07(a), that subsequent action cannot properly be made final.

Request for Interview: The present response is believed to be sufficient to overcome the pending rejections. However, if this paper is not deemed sufficient to result in a notice of allowance, or if any remaining issues can be more efficiently handled by telephone, the Examiner is respectfully requested to contact the undersigned by either phone or e-mail to schedule an interview at a mutually convenient time.

Rejections for Non-Statutory Double Patenting

The Office Action rejects Claims 1-16 on the grounds of non-statutory obviousness-type double patenting as allegedly being unpatentable over Claims 1-16 of U.S. Patent No. 10,010,282, Claims 1-16 of U.S. Patent No. 9,820,682, Claims 1-23 of U.S. Patent No. 10,143,412, and Claims 1-23 of U.S. Patent No. 11,118,266. In order to further prosecution of the present application and obtain allowance of the pending claims, Applicant submits herewith a terminal disclaimer to overcome the rejections.

However, the instant application has a filing date of April 27, 2016 based on the filing date of the oldest non-provisional parent application (now U.S. Patent No. 10,010,282) and predates the effective filing date of U.S. 11,311,219 (December 27, 2016 for its U.S. provisional application 62/439,426). Thus, the instant application will expire prior to the '219 patent is improper and therefore the double patenting rejection over the '219 patent is moot. As such, the instant response does not include a terminal disclaimer to overcome that double-patenting rejection.

In so doing, Applicant does not indicate agreement with the propriety of the rejections.

Claim interpretation under 35 U.S.C. §112(f)

The Office Action alleges that Claims 11 and 12 should be interpreted under 35 U.S.C. §112(f) as allegedly reciting functional language without sufficient structure to perform the recited function. Applicant respectfully disagrees.

MPEP § 2181 (I) (A) states that a term denotes structure (and therefore should not be interpreted under § 112(f)) when the specification provides sufficient description informing one of skill in the art that it denotes structure:

“To determine whether a word, term, or phrase coupled with a function denotes structure, examiners may check whether: (1) **the specification provides a**

description sufficient to inform one of ordinary skill in the art that the term denotes structure....”

In this case, the present specification clearly indicates that the term “junction” is a term that denotes structure. See, e.g., Paragraph [0109]:

[00109] “... junction 1607 may be substantially **Y-shaped, T-shaped, or U-shaped.**”

When something is described as *having a shape*, it is a structure, not a function.

For at least these reasons, withdrawal of the pending interpretations under §112(f) is respectfully requested.

Rejections under 35 U.S.C. §112 (b) (indefiniteness)

Claim 12 recites “flow out of the inlet port....” A person of skill in the art would understand the meaning of the term “flow out” when read in light of the specification. For example, the flow into the device can be of blood (as noted in claim 1) but may also be another bodily fluid besides blood. See, e.g., Paragraph [0079]:

“...a first aliquot or amount of blood, and to sequester that first aliquot or amount of blood **or other bodily fluid....”**

Claim 12 also recites “flow out of the inlet port is preferentially directed toward the chamber.” A person of skill in the art would understand the meaning of the term “preferentially” when read in light of the specification. For example, such preferential flow can be due to the chamber having a larger cross section than the sampling channel. See, e.g., Paragraph [0112]:

“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.”

Nowhere does the specification claim fluid flow positively/only can be directed to the chamber.

Moreover, the Oxford Languages dictionary defines “preferentially” as:

- a) in a way that involves preference or partiality; more favorably.
- b) with greater likelihood; to a greater degree.

In view of these considerations, and additional description throughout the present specification, it is respectfully submitted that a person of skill in the art would understand the meaning of the claim term. For at least these reasons, withdrawal of the pending rejections under §112 (b) is respectfully requested.

Rejections under 35 U.S.C. §102 / §103

The Office Action rejects Claim 1 as allegedly anticipated in view of Christensen.

However, Christensen fails to disclose or suggest at least the following elements of Claim 1:

“...an air permeable material that seals at least partially upon contact with a portion of the first portion of blood.”

None of Christensen's cited paragraphs [0048]-[0050] have this material, as alleged in the Office Action to be Christensen's “venting material.”

In Paragraph [0048], the venting material is not described as sealing in any way. In fact, this embodiment relies on closure of a rotation valve to stop air or other fluid from travelling through the vent:

“Airflow or gas flow will travel from the fluid path 28, through the venting material 32, and out the user-activated rotation valve 34 when the valve 34 is open. When the valve 34 is closed, no air or other fluid will travel through the vent 30.”

In Paragraph [0049], there is no disclosure of venting material. Instead, it discloses that a **user-activated seal is closed** to prevent gas or other fluid from escaping:

“...**user-activated seal 36 will close** the airflow channels adjacent the seal 36, preventing any further gas or other fluid from escaping.”

In Paragraph [0050], the first layer 46 of the described venting material is only described as able to be saturated rather than sealing at least partially upon contact [with blood].

Christensen goes even further to explicitly describe that blood can “seep or weep *through*” the first layer, rather than sealing as claimed:

“As blood or other liquid comes into contact with the first layer 46, **the liquid will seep or weep through the first layer 46**, saturating the first layer 46 of venting material.”

Christensen *also* fails to disclose or suggest the following elements of Claim 1:

“a **sampling** channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.”

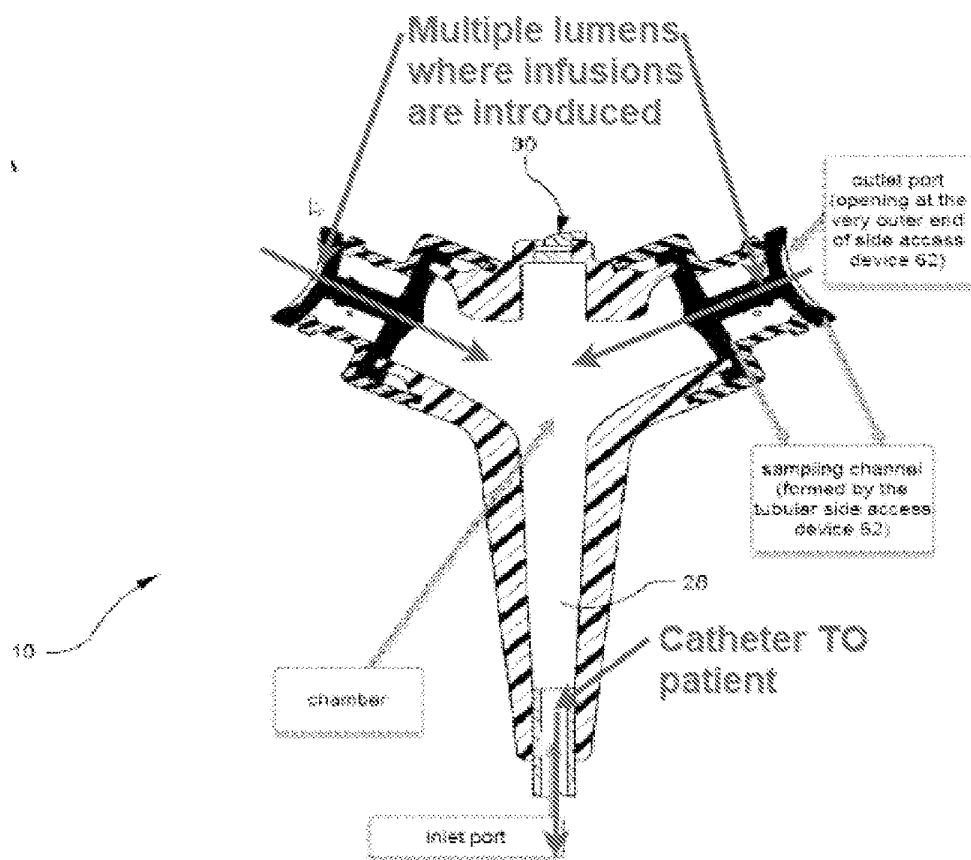
Christensen does not disclose “a sampling channel” because Christensen is not taking samples. Instead, Christensen’s system is used for *infusion* therapy (i.e., putting fluids *into* patients rather than taking samples out of them). See, e.g., Paragraph [0002]:

“The present disclosure relates to **infusion** therapy with vascular access devices... Hospitalized, home care, and other patients **receive** fluids, pharmaceuticals, and blood products via a vascular access device.”

The Office Action supported its assertion by providing an annotated Figure 2A alleging that its element 62 was an outlet port for taking samples (see illustration below further annotated by Applicant). However, element 62 is not an outlet, but rather an inlet to the vascular access device, where infusing fluids are introduced (in fact multiple different fluids can be introduced through the multiple lumens identified in the figure below). The fluids then go out of the vascular access device and into the patient’s vein through catheter 16 (catheter 16 is shown in Figure 1 and has been highlighted in yellow in the illustration below). See also Paragraphs [0003] and [0004]:

[0003] Infusion therapy is facilitated by a vascular access device. The vascular access device may access a patient’s peripheral or central vasculature.

[0004] A common vascular access device is a **catheter** that is inserted into a patient's vein... The catheter, or any other **vascular access device** attached thereto, **may have a single lumen or multiple lumens for infusion of many fluids simultaneously.**"



Christensen therefore fails to disclose or suggest an air permeable material that seals at least partially upon contact with a portion of the first portion of blood and also a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port.

Applicant respectfully asserts that the additional references cited by the Office Action in

the rejection of dependent Claims 2, 4, 7, and 15 fail to cure these deficiencies of Christensen.

For at least the reasons given above, the art of record fails to disclose or suggest each of the elements of Claim 1 and thus withdrawal of the pending rejection under §102 is respectfully requested.

New Independent Claim 17 recites a chamber (which includes the material that is air permeable and blood impermeable) that is specifically connected to both the inlet port and the outlet port. The claim is directed to subject matter differing in scope from Claim 1, but includes features related to the discussion above and is therefore believed to be allowable for the reasons described above.

Each of the remaining pending claims depends from one of independent Claims 1 or 17 and thus each is likewise patentable for at least the reasons discussed above.

CONCLUSION

On the basis of the foregoing remarks and/or amendments, allowance of the pending claims is respectfully requested. It is believed that all the pending rejections have been addressed in this paper. However, failure to address a specific rejection, issue or comment, does not signify agreement with or concession of that rejection, issue or comment. In addition, because any arguments made above are not intended to be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper.

No additional fees are believed to be due, however the Commissioner is authorized to

Application No. 18/113,710

Attorney's Docket No.: 069366-0574153_KUR2C04US
(PATENT)

charge any fees that may be due, or credit any overpayment of same, to Deposit Account
033975, Reference No. 069366-0574153_KUR2C04US. If there are any questions regarding
this submission, the Examiner is encouraged to contact the undersigned at the telephone number
provided below.

Respectfully submitted,
PILLSBURY WINTHROP SHAW PITTMAN LLP

Date: August 9, 2023

By: /Ben Hudson/

Benjamin F. Hudson, Ph.D.

Reg. No. 71,474

PO BOX 10500
McLean, Virginia 22102
Telephone: (858) 509-4000
Customer No. 27500

4894-3293-1692.v1



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/113,710	02/24/2023	Bobby E. ROGERS	069366-0574153_KUR2C04US	2715
27500 7590 08/25/2023 PILLSBURY WINTHROP SHAW PITTMAN LLP (CV) ATTENTION: DOCKETING DEPARTMENT P.O BOX 10500 McLean, VA 22102			EXAMINER ABOUELELA, MAY A	
			ART UNIT 3791	PAPER NUMBER
			NOTIFICATION DATE 08/25/2023	DELIVERY MODE 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

<i>Office Action Summary</i>	Application No. 18/113,710	Applicant(s) ROGERS et al.	
	Examiner MAY A ABOUELELA	Art Unit 3791	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 08/09/2023.
☐ 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) 1-13 and 16-31 is/are pending in the application.
 5a) Of the above claim(s) ____ is/are withdrawn from consideration.

6) ☒ Claim(s) 17-31 is/are allowed.

7) ☒ Claim(s) 1-13 and 16 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: _____

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 08/09/2023, and 05/10/2023. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.

Claim(s) 1, 5, 8-13 and 16 is/are rejected under 35 U.S.C. 102(1)(a) as being anticipated by Christensen et al (US 20100057004).

As to claim 1, Christensen discloses a device comprising:

an inlet port (catheter 14 and the frontal inlet port of device 10 where catheter 14 is connected/inserted therein, par.41-43 and par.47, fig.1-4);

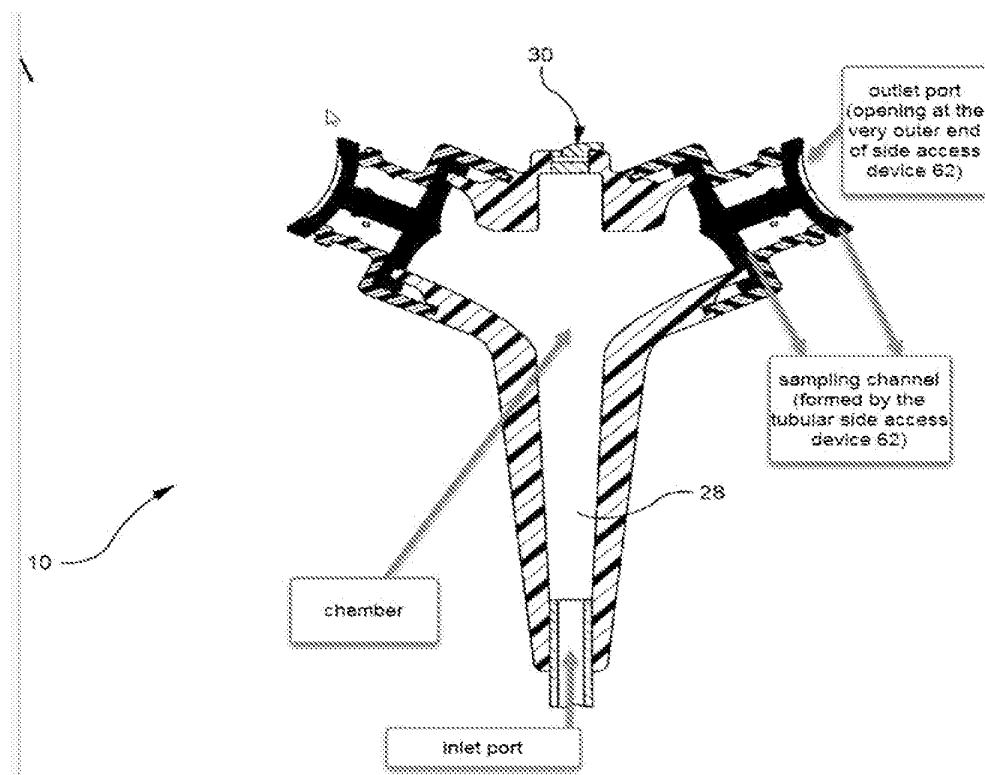
an outlet port (outlet opening at the very outer end of side access device 62 of device 10 where tube 16 is connected to and/or outlet port at the end of tube 16 connected to Y-adapter 18, par.41-43, par.53, fig.1-5);

a chamber (a fluid path 28 filling the interior of the extravascular system 10, par.47, fig.1-4) connected with the inlet port (fluid path 28 within the interior of device 10 is connected to catheter 14 and the frontal inlet port of device 10, fig.1-5) and configured to receive a first portion of blood (operator will insert the needle 12 into the vasculature of a patient and wait for flashback of blood to travel into the system 10 to confirm that the needle 12 is properly located within the vasculature of the patient, par.7, par.42, and blood travels into and along the catheter 14 and extension tubing 16 because a vent plug 22 permits air to escape the system 10 as blood enters the system 10, par.43)(The Examiner respectfully notes that flashback of blood, is considered the initial portion of blood),

the chamber including an air permeable material (venting material in vent 30, par.48-50, a removable filter plug 50 and a re-seal elastomer 52 in vent 30, par.51-53, or 114 that expands when exposed to liquid from bath 28, and thus seals the vent, par.71-72, fig.1-16, and/or curing material 108 of the vent 30 described with reference to FIGS. 13 and 14 provides a vent capable of venting gas from the system 10 without permitting the escape of liquid after the liquid has come into contact with the material 108, par.69, a porous membrane 110, par.70) that seals at least partially upon contact with a portion of the first portion of blood (par.48-53); and

a sampling channel (tubular channel formed by side access device 62 of device 10 and integrated extension tube 16, par.41-42, fig.1-6) having a proximal end connected with

the inlet port and a distal end connected with the outlet port (tubular channel formed by side access device 62 of device 10 having proximal end connected to frontal inlet port of device 10 at catheter 14, and having a distal end connected to the outlet opening at the very outer end of side access device 62 of device 10, as best seen in fig.1-6)(Examiner respectfully notes that since blood travels into and along the catheter 14 and extension tubing 16 because a vent plug 22 permits air to escape the system 10 as blood enters the system 10, par.43, so tubular channel formed by side access device 62 is configured to sample and convey blood to tubing 16).



As to claim 5, Christensen discloses the device, wherein the air permeable material is located at a distal end of the chamber (a vent may be placed at or near the start of the fluid path, or the vent may be placed at any point in between the start or end of the fluid path of the extravascular system, par.45, as best seen in fig.1-3).

As to claim 8, Christensen discloses the device, wherein the air permeable material is a hydrophilic membrane (vent 30 includes an expandable vent material 114 that is hydrophilic, par.71, fig.16).

As to claim 9, Christensen discloses the device, wherein the sampling channel further comprises a valve configured to close off the sampling channel (side clamp 20, par.41, slide clamp 20 on the integrated extension tubing 16 is provided to eliminate blood exposure when the vent plug 22 is replaced with another vascular access device, par.42, fig.1).

As to claim 10, Christensen discloses the device, wherein the valve is a clip (clamp 20, par.41, fig.1)

As to claim 11, Christensen discloses the device, further comprising a junction configured to direct an initial blood flow into the chamber (the longitudinal shape at the beginning of fluid path 28 formed in the interior of device 10 forces the flashback blood to enter the interior of device 10, par.43-48, and/or vent 30, vent 30 may be placed at or near the terminus of the system 10 in order to allow fluid, including gas, blood, saline,

and water, to fill the internal chamber of the fluid path directly adjacent any vascular access devices of the system 10, par.51-52, fig.1-6).

As to claim 12, Christensen discloses the device, further comprising a junction configured such that flow out of the inlet port is preferentially directed toward the chamber (the longitudinal shape at the beginning of fluid path 28 formed in the interior of device 10 forces the flashback blood to enter the interior of device 10, par.43-48, and/or vent 30, vent 30 may be placed at or near the terminus of the system 10 in order to allow fluid, including gas, blood, saline, and water, to fill the internal chamber of the fluid path directly adjacent any vascular access devices of the system 10, par.51-52, fig.1-6).

As to claim 13, Christensen discloses the device, wherein the chamber has a larger cross-sectional area than the sampling channel (the cross-sectional area of fluid path 28 of the interior of device 10 is larger than the side tubular channel and tube 16, as best seen in fig.1-3).

As to claim 16, Christensen discloses the device, further comprising a patient needle (needle 12, par.41-43, fig.1) and a sample collection device (Luer access device or port 24, par.41)(Examiner respectfully notes that the luer access device is a device that is connected to obtain blood sample in a sampling container, see link:

<https://www.medline.com/product/Blood-Transfer-and-Luer-Lock-Access-Device/Z05-PF253812#:~:text=Luer%20lock%20access%20devices%20%28LLAD%20and%20AC>

SD%29%20are,reduce%20the%20risk%20of%20transfer-related%20injuries%20and%20infections).

Claim Rejections - 35 USC § 103

4. 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) 2-4, 6 and 7 is/are rejected under 35 U.S.C. 103 as being obvious over Christensen et al (US 20100057004), in view of Weilbacher et al (US 2008/0167577).

As to claims 2-4, 6 and 7, Christensen discloses the device, wherein the device is further configured such that an initial aliquot of blood will contact the air permeable material and back up into the chamber (operator will insert the needle 12 into the vasculature of a patient and wait for flashback of blood to travel into the system 10 to confirm that the needle 12 is properly located within the vasculature of the patient. The blood travels into and along the catheter 14 and extension tubing. The fluid path 28 is in communication with a vent 30, and the vent 30 is capable of venting gas from the fluid path 28 of the system 10, par.47 and par.53), wherein the device is further configured such that follow-on amounts of blood will flow through the sampling channel towards the outlet port (blood travels into and along the catheter 14 and extension tubing 16

because a vent plug 22 permits air to escape the system 10 as blood enters the system 10, par.43).

Christensen discloses the invention substantially as above, but failed to explicitly teach wherein the device is configured such that, when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into the chamber, and wherein the air permeable material is a hydrophobic plug/membrane.

However Weilbacher discloses an analogous vascular access needle assembly (abstract, fig.1-3), when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into the chamber (collection tube 17 is maintained at a vacuum such that when distal needle portion 20 is properly positioned in a vein 38 of a patient and collection tube 17 is positioned within cavity 34 OF BODY 30, blood will flow through needle 10 into blood collection tube 17, par.33, fig.1)(the Examiner respectfully notes the vacuum applies blood drawing force), and wherein the air permeable material is a hydrophobic plug/membrane (filter material 116 disposed in chamber 112, wherein material includes a hydrophobic material. In an alternate embodiment, the material includes a hydrophilic wicking material. In yet another embodiment, the material includes a hydrophobic plug, par.11 and par.35, fig.2).

As these types of blood drawing force are well-known in the art, so it would have been obvious to one having an ordinary skill in the art before the effective filing date of the invention to maintain blood collection devices and/or luer accesses devices connected to port 24 taught by Christensen's invention under vacuum, as tube 17 taught by

Weilbacher's invention, to facilitated blood sampling and prevent unwanted blood exposure/spilling, as taught by Weilbacher's invention (par.33).

Still, as the hydrophobic air permeable filter/material are well known in the art to vent air, so it would have been obvious to one having an ordinary skill in the art before the effective filing date of the invention to substitute the hydrophilic material taught by Christensen's invention, with the hydrophobic material taught by Weilbacher's invention, for the same reason of venting air from sampling chamber, as taught by Weilbacher's invention (par.11 and par.35-36).

Allowable Subject Matter

5. Claims 17-31 are allowed.

6. The following is an examiner's statement of reasons for allowance: the most pertinent prior art Christensen et al (US 2010/0057004) teaches a device comprising: an inlet port for receiving a blood sample; an outlet port; a chamber connected with the inlet port and the outlet port, and configured to collect a first portion of the blood sample, the chamber including a material that is air permeable and blood impermeable.

The prior art does not teach, disclose and/or fairly suggest a sampling channel connected with the inlet port and configured to convey a subsequent portion of the blood sample to the outlet port while bypassing the chamber.

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."

Response to Arguments

7. Applicant's arguments claim objections/rejections and double patenting have been fully considered and are persuasive. The claim objections/rejections and double patenting have been withdrawn.

8. Applicant's arguments regarding Christensen's invention does not teach the claimed subject matter "an air permeable material that seals at least partially upon contact with a portion of the first portion of blood" in claim 1 have been fully considered but they are not persuasive, because Christensen's invention explicitly teaches hydrophilic air permeable material 114 that allows air to pass through vent 30, and then expands when exposed to liquid from fluid path 28, and thus seals the vent (par.71-72), similarly materials 108 and 110, par.69-70.

So, Christensen's invention explicitly teaches the claimed subject matter "an air permeable material that seals at least partially upon contact with a portion of the first portion of blood" in claim 1.

9. Still, regarding the Applicant's arguments that Christensen's invention does not teach "a sampling channel having a proximal end connected with the inlet port and a distal end connected with the outlet port" in claim 1 because Christensen's invention is not taking samples. Instead Christensen's invention is used for infusion therapy (see arguments page 5) have been fully considered but are not persuasive, because claim 1 broadly claims "A device comprising" in the preamble, and does not claim a blood sampling/collecting device. Under the broadest reasonable interpretation the claimed

subject matter "sampling channel" may be interpreted as sampling any type of tissue, fluid and/or infusion agents, and does not necessarily means sampling blood.

Device 10 taught by Christensen's invention comprises a fluid path 28 filling the interior of the extravascular system 10 (par.47) configured to receive a portion of blood (operator will insert the needle 12 into the vasculature of a patient and wait for flashback of blood to travel into fluid path 28 to confirm that the needle 12 is properly located within the vasculature of the patient (par.7, par.42), and blood travels into and along the catheter 14 and extension tubing 16 because a vent plug 22 permits air to escape the system 10 as blood enters the system 10 (par.43).

Examiner respectfully notes that since blood travels into and along the catheter 14 and extension tubing 16, so tubular channel formed by side access device 62 is configured to sample and convey blood to tubing 16.

So, it can be fairly interpreted that the tubular channel is a sampling channel that samples blood to and from tubing 16, as claimed in claim 1.

Conclusion

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure Burkholz et al (US 20120/016266).

11. **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 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

Application/Control Number: 18/113,710
Art Unit: 3791

Page 13

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

<i>Notice of References Cited</i>	Application/Control No. 18/113,710		Applicant(s)/Patent Under Reexamination ROGERS et al.	
	Examiner MAY A ABOUELELA		Art Unit 3791	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20160325085-A1	11-2016	Chelak; Todd	F16K7/20	1/1
*	B	US-20160262677-A1	09-2016	EBETSBERGER; Franz	A61B5/150251	1/1
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

<i>Index of Claims</i> 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS										
☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47										
CLAIM		DATE								
Final	Original	05/08/2023	08/22/2023							
	1	✓	✓							
	2	✓	✓							
	3	✓	✓							
	4	✓	✓							
	5	✓	✓							
	6	✓	✓							
	7	✓	✓							
	8	✓	✓							
	9	✓	✓							
	10	✓	✓							
	11	✓	✓							
	12	✓	✓							
	13	✓	✓							
	14	✓	-							
	15	✓	-							
	16	✓	✓							
	17		=							
	18		=							
	19		=							
	20		=							
	21		=							
	22		=							
	23		=							
	24		=							
	25		=							
	26		=							
	27		=							
	28		=							
	29		=							
	30		=							
	31		=							

<i>Search Notes</i> 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

CPC - Searched*		
Symbol	Date	Examiner
A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068	05/08/2023	MA
updated as above	08/22/2023	MA

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
text search, class/subclass search, inventor name search	05/08/2023	MA
updated as above	08/22/2023	MA

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	
--	--

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		18113710	
	Filing Date		2023-02-24	
	First Named Inventor	Bobby E. ROGERS		
	Art Unit	-		
	Examiner Name			
	Attorney Docket Number	069366-0574153_KUR2C04US		

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			
If you wish to add additional U.S. Patent citation information please click the Add button.							Add	
U.S.PATENT APPLICATION PUBLICATIONS							Remove	
Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear		
	1							
If you wish to add additional U.S. Published Application citation information please click the Add button.							Add	
FOREIGN PATENT DOCUMENTS							Remove	
Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ²	Kind Code ⁴	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T ⁵
	1							☐
If you wish to add additional Foreign Patent Document citation information please click the Add button							Add	
NON-PATENT LITERATURE DOCUMENTS							Remove	
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.						T ⁵

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

	1		☐
--	---	--	--------------------------

If you wish to add additional non-patent literature document citation information please click the Add button **EXAMINER SIGNATURE**

Examiner Signature	/MAY A ABOUELELA/	Date Considered	08/22/2023
--------------------	-------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

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)	2023-08-09
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent 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.

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	0	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/20 11:05 PM
L2	1	("20020099309").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 11:38 AM
L3	1	("14055232").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 11:39 AM
L4	1763	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 05:18 PM
L5	63	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:19 PM
L6	28	("2004/0073171").URP N.	(USPAT)	OR	OFF	OFF	2016/12/21 05:36 PM
L7	0	("1and(bloodnear4sequest\$5)").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 05:41 PM
L8	5225	1and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:42 PM
L9	7	L4 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:42 PM
L10	73	("20020002349" "20020183651" "20030055381" "20040010228" "20040054333" "20040147855" "20050004524" "20050240161" "20050245885" "20050281713" "20060287639" "2707953" "3013557" "3098016" "3382865" "3405706" "3494351" "3577980" "3648684" "3848579" "3937211" "4057050" "4133863" "4166450" "4340067" "4370987" "4444203" "4459997" "4509534" "4676256" "4865583" "4890627" "4988339" "5009847" "5097842" "5108927" "5122129" "5269317" "5360011" "5429610" "5450856" "5507299" "5577513" "5762633" "5882318" "5922551" "6016712" "6057105" "6159164" "6210909" "6364890" "6387086" "6403381"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:43 PM

L11	2	"6692479" "6746420" "6913580" "7044941" "7087047").PN. OR ("8197420").URPN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:44 PM
L12	77	("0453322" "0577682" "0729011" "1074965" "1110189" "1450016" "1521890" "2218899" "2688325" "2895773" "3176595" "3214069" "3236268" "3263874" "3486503" "3577980" "3754644" "3794221" "3834387" "3855997" "3937211" "3958570").PN. OR ("4057050").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:47 PM
L13	852	L4 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L14	46	L10 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L15	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:29 PM
L16	1	("20130317391").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:42 PM
L17	1254	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:43 PM
L18	1070	L17 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 06:43 PM
L19	265030	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:09 PM
L20	5653	L19 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L21	207	L20 and (seal near4 air)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L22	23	"2004087258"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 08:59 PM
L23	1	("20050004524").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 08:23 PM
L24	1	("20030105414").PN.	(US-PGPUB; USPAT;	OR	ON	ON	2017/04/11

L25	1	("5749857").PN.	USOCR) (US-PGPUB; USPAT; USOCR)	OR	ON	ON	08:24 PM 2017/04/11 08:26 PM
L26	13	("20040073171" "20040 147855" "20050240161 " "20130317391" "2016 0174888" "4057050" "8 197420" "8523826" "85 35241" "8540663" "856 8371" "8864684" "9138 572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 08:39 PM
L27	1	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 09:43 PM
L28	0	("4and(bloodnear4air)").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 10:01 PM
L29	3	L26 and (blood near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:01 PM
L30	6	L26 and vent\$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:02 PM
L31	5	("2013/0317391").URP N.	(USPAT)	OR	OFF	OFF	2017/04/11 10:06 PM
L32	48	("2005/0004524").URP N.	(USPAT)	OR	OFF	OFF	2017/04/11 10:17 PM
L33	1	("20120170037").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/12 04:11 PM
L34	1	("6139540").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:52 PM
L35	1	("20040116878").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:54 PM
L36	1	("20100152752").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:16 PM
L37	1	("6395003").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:20 PM
L38	5	("2013/0317391").URP N.	(USPAT)	OR	OFF	OFF	2017/04/13 01:43 PM
L39	1	("4444203").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:44 PM
L40	1	("20020004647").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:48 PM
L41	1	("3817240").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L42	1	("3874367").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L43	1	("3886930").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:58 PM
L44	1	("4106497").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM
L45	1	("4154229").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM
L46	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:00 PM

L47	292	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2017/04/13 02:01 PM
L48	1	("4412548").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:04 PM
L49	1	("5222502").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:11 PM
L50	1	("5520193").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:15 PM
L51	1	("20100057004").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:16 PM
L52	1	("20070088279").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:29 PM
L53	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/04/13 03:29 PM
L54	13	L53 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 03:52 PM
L55	1255	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 04:23 PM
L56	4	L55 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:23 PM
L57	272301	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L58	5898	L57 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L59	114	L58 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:29 PM
L60	2	("2007/0088279").URPN.	(USPAT)	OR	OFF	OFF	2017/04/13 05:58 PM
L61	1	("6358217").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/21 02:02 PM
L62	6	("2002/0004647").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 12:48 PM
L63	2	("14493796").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:21 PM
L64	2	("14494208").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:23 PM
L65	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/27 01:28 PM
L66	1	("20080145933").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:51 PM
L67	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 01:55 PM
L68	1	("20040054333").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:59 PM

L69	1	("20120109034").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:37 PM
L70	1	("20100228206").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:39 PM
L71	3	("2010/0228206").URP N.	(USPAT)	OR	OFF	OFF	2017/09/27 02:47 PM
L72	66	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:41 PM
L73	4	L72 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:42 PM
L74	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:58 PM
L75	845	L74 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:58 PM
L76	9	L75 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L77	86	("2007/0083162").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L78	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:59 PM
L79	9	("2008/0145933").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 02:04 PM
L80	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 02:20 PM
L81	1071	L80 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:20 PM
L82	78	L81 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:21 PM
L83	282596	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L84	6183	L83 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L85	387	L84 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:01 PM
L86	362	L85 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:02 PM
L87	12	("2005/0010189").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 04:03 PM
L88	1363	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:04 PM
L89	74	L88 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:05 PM
L90	21	("3965910" "3996923"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2017/09/28

		"4131127" "4301811" "4450854" "4506691" "4819684" "5147333" "5393035" "5636975").PN. OR ("6569117").URPN.	USOCR)				04:09 PM
L91	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:12 PM
L92	18	L91 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:12 PM
L93	9	("2008/0145933").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 04:13 PM
L95	67	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:23 PM
L96	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:25 PM
L97	4	L96 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:25 PM
L98	3	L97 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:26 PM
L99	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:50 PM
L100	13	L99 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:50 PM
L101	255	("1779451" "2004050" "2700385" "2836942" "2854976" "2953243" "3021942" "3073307" "3074542" "3255873" "3294231" "3323523" "3329146" "3333682" "3367488" "3382865" "3485239" "3537452" "3585984" "3610240" "3658061" "3664879" "3817240" "3828775" "3859998" "3874367" "3886930" "3890971" "3904033" "3934722" "3968876" "4106497" "4108175" "4113090" "4139009" "4154229" "4166450" "4175008" "4193400" "4207870" "4269186" "4300678" "4312362" "4317445" "4340068" "4375849" "4398544" "4409990" "4412548" "4416290" "4416291" "4418703" "4430082" "4436098" "4444203" "4592744"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/01/09 04:51 PM

		"4634428"	"4643722"				
		"4659330"	"4664249"				
		"4664654"	"4671408"				
		"4679571"	"4681567"				
		"4695274"	"4702738"				
		"4723943"	"4728320"				
		"4728321"	"4731059"				
		"4735311"	"4735618"				
		"4737144"	"4738663"				
		"4743233"	"4746008"				
		"4747836"	"4747837"				
		"4772272"	"4778453"				
		"4781697"	"4782841"				
		"4788986"	"4790828"				
		"4793484"	"4795432"				
		"4795443"	"4801295"				
		"4804372"	"4813426"				
		"4816022"	"4816024"				
		"4819659"	"4820277"				
		"4826490"	"4826491"				
		"4838871"	"4842587"				
		"4844089"	"4846796"				
		"4850968"	"4850976"				
		"4850977"	"4850978"				
		"4850994"	"4850996"				
		"4858607"	"4863434"				
		"4863435"	"4863436"				
		"4865592"	"4867746"				
		"4872552"	"4874383"				
		"4874384"	"4883469"				
		"4886072"	"4886503"				
		"4888001"	"4892107"				
		"4892521"	"4894052"				
		"4900309"	"4909791"				
		"4909792").PN. OR					
		("4921096"	"4927018"				
		"4944397"	"4966591"				
		"4971068"	"4976699"				
		"4982842"	"5011475"				
		"5011479"	"5030207"				
		"5032116"	"5033476"				
		"5055102"	"5069225"				
		"5078693"	"5078698"				
		"5092845"	"5112327"				
		"5116325"	"5120319"				
		"5122121"	"5135509"				
		"5137518"	"5139489"				
		"5151089"	"5154285"				
		"5181523"	"5188611"				
		"5197954"	"5201794"				
		"5207653"	"5217025"				
		"5222502"	"5232454"				
		"5232455"	"5242411"				
		"5242417"	"5277311"				
		"5290246"	"5295969"				
		"5303713"	"5306259"				
		"5312369"	"5401251"				
		"5405332"	"5423765"				

		"5450856" "5462534" "5485854" "5486163" "5490841" "5496281" "5509907" "5520193" "5533984" "5542932" "5584816" "5599313" "5599318" "5603699" "5632732" "5643219" "5662617" "5665075" "5669889" "5693022" "5697914" "5702369" "5733265" "5755701" "5807351" "5830190" "5836920" "5885249" "5893844" "5913846" "5984895" "5993426" "6059737" "6077244" "6077253" "6080137" "6096006" "6110160" "6120482" "6156010" "6190370" "6261263" "6511439" "6533760" "6964658" "7160267" "RE31086").PN. OR ("7615033").URPN.					
L102	215	L101 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:51 PM
L103	1347	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:11 PM
L104	17	L103 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L105	19	("2009/0312711").URP N.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L106	11	("2007/0106220").URP N.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L107	288967	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L108	6321	L107 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L109	121	L108 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:17 PM
L110	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:31 PM
L111	6	L110 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:31 PM
L113	71	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:31 PM
L114	0	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:38 PM

L115	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:38 PM
L116	2	(15/140448).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:40 PM
L117	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 01:56 PM
L118	854	L117 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:56 PM
L119	91	L118 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:57 PM
L120	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:06 PM
L121	1074	L120 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:06 PM
L122	80	L121 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:06 PM
L123	301210	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/07/24 02:11 PM
L124	6556	L123 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/07/24 02:11 PM
L125	3664	L124 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L126	12749	"19" and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L127	117	L125 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L128	1348	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:16 PM
L129	75	L128 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:17 PM
L130	1	("20120291564").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 02:21 PM
L131	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:25 PM
L132	18	L131 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:25 PM
L133	98	("20020002349" "20020183651" "20030055381" "20030208151" "20040010228" "20040054333" "20040147855" "20050004524"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:44 PM

		"20050240161" "20050245885" "20050281713" "20060287639" "20080108954" "20080145933" "2707953" "3013557" "3098016" "3382865" "3405706" "3494351" "3577980" "3648684" "3848579" "3937211" "4057050" "4133863" "4166450" "4340067" "4370987" "4444203" "4459997" "4509534" "4657160" "4676256" "4865583" "4890627" "4988339" "5009847" "5097842" "5108927" "5122129" "5269317" "5330464" "5360011" "5429610" "5450856" "5507299" "5577513" "5762633" "5865812" "5882318" "5922551" "6016712" "6057105" "6159164" "6210909" "6364890" "6387086" "6403381" "6626884" "6692479" "6746420" "6913580" "7044941" "7087047" "7335188" "7744573" "8197420" "8231546" "8337418").PN. OR ("8535241").URPN.					
L134	307	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:47 PM
L135	23	("4166450").PN. OR ("4412548").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L136	307	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L137	4	("2007/0088279").URP N.	(USPAT)	OR	ON	ON	2018/07/24 02:48 PM
L138	1	(14/990763).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 02:58 PM
L139	9	(blood and sequest\$5 and junction and first and portion and sampl\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 03:07 PM

L140	1	(15/287421).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/25 09:39 PM
L141	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/26 11:56 AM
L142	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:24 PM
L143	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:25 PM
L144	34	("20020004647" "20030105414" "20040054333" "20040073171" "20040147855" "20050004524" "20050240161" "20070088279" "20080145933" "20100057004" "20130317391" "20160174888" "3817240" "3874367" "3886930" "4057050" "4106497" "4154229" "4207870" "4412548" "5222502" "5520193" "5749857" "6569117" "8197420" "8523826" "8535241" "8540663" "8568371" "8864684" "9022951" "9060724" "9138572" "9204864").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 05:53 PM
L145	272	((("ROGERS") near3 ("Bobby")) OR ((("KANG") near3 ("Gino")) OR ((("STROUP") near3 ("David")) OR ((("COCHRAN") near3 ("Jonas")) OR ((("DEPTALA") near3 ("Arthur")) OR ((("DETLOFF") near3 ("John")) OR ((("POGUE") near3 ("Lonnie")) OR ((("MACOWSKI") near3 ("Brian")) OR ((("GARRETT") near3 ("Chad")))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/07 05:57 PM
L146	9	L145 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 05:58 PM
L147	34	("20020004647" "20030105414" "20040054333" "20040073171" "20040147855" "20050004524" "20050240161" "20070088279" "20080145933" "20100057004" "20130317391" "20160174888" "3817240" "38743	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 06:26 PM

		67" "3886930" "4057050" "4106497" "4154229" "4207870" "4412548" "5222502" "5520193" "5749857" "6569117" "8197420" "8523826" "8535241" "8540663" "8568371" "8864684" "9022951" "9060724" "9138572" "9204864").PN.					
L148	5	L147 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 06:29 PM
L149	6	("2010/0057004").URP N.	(USPAT)	OR	ON	ON	2019/11/07 06:40 PM
L150	0	L149 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:20 PM
L151	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:21 PM
L152	4	L151 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L153	1766	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:21 PM
L154	13	L153 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L155	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:22 PM
L156	48	L155 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:22 PM
L157	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L158	17	L157 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:43 PM
L159	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L160	6	L159 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L161	333030	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L162	6981	L161 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L163	139	L162 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L164	117	L163 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:45 PM
L165	1	L146 and (enclos\$3 near4 mechanism)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:51 PM
L166	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/08 04:57 PM

L167	1	(15/139716).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/11 12:09 PM
L168	1	(15/520430).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 11:02 AM
L169	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:11 PM
L170	1	("20120253321").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:13 PM
L171	1	(15/861959).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:14 PM
L172	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 02:17 PM
L173	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:14 PM
L174	1	("20080167577").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:19 PM
L175	4	("2008/0167577").URP N.	(USPAT)	OR	ON	ON	2019/12/09 03:30 PM
L176	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:31 PM
L177	39	(US-20040073171-\$ or US-20160174888-\$ or US-20050240161-\$ or US-20040147855-\$ or US-20130317391-\$ or US-20050004524-\$ or US-20030105414-\$ or US-20020004647-\$ or US-20100057004-\$ or US-20070088279-\$ or US-20080145933-\$ or US-20040054333-\$ or US-20100010372-\$ or US-20080319346-\$ or US-20080167577-\$).did. or (US-9138572-\$ or US-8568371-\$ or US-8540663-\$ or US-8523826-\$ or US-8197420-\$ or US-4057050-\$ or US-8864684-\$ or US-8535241-\$ or US-5749857-\$ or US-9060724-\$ or US-9204864-\$ or US-3817240-\$ or US-3874367-\$ or US-3886930-\$ or US-4106497-\$ or US-4154229-\$ or US-4207870-\$ or US-4412548-\$ or US-5222502-\$ or US-5520193-\$ or US-	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:37 PM

L178	8	9022951-\$ or US-6569117-\$ or US-3741197-\$ or US-8603009-\$).did. ("20040054333" "8197420" "9855001" "9861306" "10045724" "10028687" "8337418" "10028689").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:42 PM
L179	100	("20020002349" "20020183651" "20030055381" "20040010228" "20040054333" "20040147855" "20050004524" "20050240161" "20050245885" "20050281713" "20060287639" "2707953" "3013557" "3098016" "3382865" "3405706" "3494351" "3577980" "3648684" "3848579" "3937211" "4057050" "4133863" "4166450" "4340067" "4370987" "4444203" "4459997" "4509534" "4676256" "4865583" "4890627" "4988339" "5009847" "5097842" "5108927" "5122129" "5269317" "5360011" "5429610" "5450856" "5507299" "5577513" "5762633" "5882318" "5922551" "6016712" "6057105" "6159164" "6210909" "6364890" "6387086" "6403381" "6692479" "6746420" "6913580" "7044941" "7087047").PN. OR ("8197420").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 03:43 PM
L180	70	L179 and (blood near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 03:43 PM
L181	43	L180 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 03:44 PM
L182	270	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/12/09 04:13 PM

L183	335813	("Jay")) OR (("GAW") near3 ("Shan"))).INV. (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L184	7259	L183 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L185	325	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 04:33 PM
L186	594	L184 and (flash\$6 and seal\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L187	476	L186 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L188	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:14 PM
L189	1123	L188 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L190	1013	L189 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L191	10	L190 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:16 PM
L192	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:23 PM
L193	1143	L192 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L194	1038	L193 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L195	3	L194 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L196	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:24 PM
L197	618	L196 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L198	557	L197 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L199	1	(15/854273).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:25 PM
L200	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:31 PM
L201	219	L200 and ((blood or	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09

L202	199	fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4)) L201 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	05:33 PM 2019/12/09 05:33 PM
L203	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:36 PM
L204	44	L203 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:37 PM
L205	1	(15/508871).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/10 11:58 AM
L206	342199	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/03/16 12:53 PM
L207	4239	L206 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:53 PM
L208	146	L207 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:54 PM
L209	101	L208 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:55 PM
L210	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:38 PM
L211	1123	L210 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:38 PM
L212	1013	L211 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L213	22	L212 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L214	108	("20020193748" "20030093009" "20030105414" "20030220614" "20030229315" "20040059302" "20040092872" "20040193120" "20050004524" "20050065482" "20050124944" "20050187493" "20050245868" "20050245869" "20050245870" "20050245879" "20050245885"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 01:46 PM

L215	26	"20060036219" "20060224122" "20070106220" "20070106224" "20070167914" "20080086085" "20080177202" "20080319345" "20080319346" "20090204026" "20100262038" "4106497" "4207870" "4305406" "4572210" "4573976" "4641663" "4795443" "4840619" "4894055" "4900307" "4994046" "5015241" "5195985" "5215534" "5222502" "5242417" "5246428" "5256153" "5295970" "5303713" "5312372" "5336199" "5348544" "5356392" "5411492" "5439449" "5466223" "5501675" "5542932" "5599313" "5662617" "5665075" "5672161" "5676658" "5702369" "5704920" "5733265" "5755522" "5957892" "5984899" "6149629" "6224576" "6254575" "6261263" "6298541" "6344032" "6436086" "6440104" "6524277" "6533760" "6592556" "6623456" "6635032" "6648855" "6695819" "6699217" "6712792" "6780169" "6837877" "6869415" "6984223" "7001363" "7128726" "7147624" "7160267" "7163526" "7223258" "7226432" "7396343" "7428773" "7537581" "7766879" "D422700" "D442280" "D604836" "D604837" "D604838" "D604839" "D605287").PN. OR ("8603009").URPN. L214 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:47 PM
------	----	--	-------------------	----	-----	-----	------------------------

L216	27	("2008/0319346").URP N.	(USPAT)	OR	ON	ON	2020/03/16 01:47 PM
L217	23	("2003/0105414").URP N.	(USPAT)	OR	ON	ON	2020/03/16 01:48 PM
L218	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:52 PM
L219	1143	L218 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L220	25	L219 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L221	353695	((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:54 PM
L222	3643	L221 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L223	1926	L222 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L224	785	L223 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:56 PM
L225	7046	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 02:32 PM
L226	14	L225 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:35 PM
L227	1352	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:36 PM
L228	135	L227 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L229	19	L228 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L230	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:47 PM
L231	3	L230 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:47 PM
L232	19	("2008/0145933").URP N.	(USPAT)	OR	ON	ON	2020/03/16 02:48 PM
L233	795	(600/576).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:58 PM
L234	71	L233 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:58 PM

L235	57	L234 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:59 PM
L236	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 03:12 PM
L237	11	L236 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:12 PM
L238	45	("20040054333" "20050 240161" "4412548" "57 49857" "8197420" "985 5001" "9861306" "2002 0004647" "2010005700 4" "3741197" "2004007 3171" "3874367" "4057 050" "4106497" "81974 20" "8535241" "854066 3" "8603009" "8864684" "10045724" "3817240" "10028687" "20030105 414" "5222502" "55201 93" "6569117" "856837 1" "20040147855" "200 70088279" "200801459 33" "20100010372" "38 86930" "8523826" "906 0724" "9204864" "8337 418" "20050004524" "2 0080167577" "2008031 9346" "20130317391" " 4154229" "9022951" "1 0028689" "2016017488 8" "4207870" "9138572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:13 PM
L239	6	("2008/0167577").URP N.	(USPAT)	OR	ON	ON	2020/03/16 03:13 PM
L240	118	("3500828" "3670729" "3714945" "3977400" "3994293" "3995619" "4106491" "4200096" "4468224" "4531987" "4549554" "4735215" "4828548" "4874373" "4893635" "4894052" "4907599" "4944308" "4994042" "5129884" "5400798").PN. OR ("5749857").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 03:15 PM
L241	6	("2008/0167577").URP N.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 03:15 PM
L242	274	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR (("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2020/03/16 03:25 PM

L243	61	L242 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:25 PM
L244	1	(15/854273).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 03:47 PM
L245	0	(14/502498).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:11 PM
L246	1	("20110082383").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:24 PM
L247	1	("8150506").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:24 PM
L252	1	(15/057214).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/17 11:28 AM
L253	348964	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/06/10 05:22 PM
L254	7453	L253 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/06/10 05:22 PM
L255	155	L254 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:23 PM
L256	77	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 05:35 PM
L257	343953	(blood same (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:40 PM
L258	11	L256 and (blood same (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:41 PM
L259	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 05:50 PM
L260	121	("3500828" "3670729" "3714945" "3977400" "3994293" "3995619" "4106491" "4200096" "4468224" "4531987" "4549554" "4735215" "4828548" "4874373" "4893635" "4894052" "4907599" "4944308" "4994042" "5129884" "5400798").PN. OR ("5749857").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/06/10 06:19 PM
L261	32	L260 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:20 PM
L262	1	("3648684").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L263	1	("4056101").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L264	329	(600/577).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/06/10

L265	11	L264 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	06:39 PM 2020/06/10 06:39 PM
L266	29	("2008/0319346").URP N.	(USPAT)	OR	ON	ON	2020/06/10 06:40 PM
L267	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:40 PM
L268	72	L267 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:40 PM
L269	1767	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:44 PM
L270	31	L269 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:45 PM
L271	77	("4676249" "4787891" "4850960" "4874382" "4886067" "4886500" "4900307" "4904242" "4917102" "4950252" "4955862" "5046508" "5116353" "5125718" "5129884" "5163911" "5217435" "5290244" "5295974" "5314503" "5318585" "5330432" "5360410" "5366441" "5376075" "5395337" "5531692" "5695475" "5695479" "5702367" "5735813" "5749857" "5788654" "5800395" "5846226" "5871470" "5882342" "5919172" "5935108" "5935113" "5989220" "6050976" "6077244" "6099504" "6126641" "6162195").PN. OR ("6398743").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/06/10 06:46 PM
L272	18	L271 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:46 PM
L273	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:48 PM
L274	7050	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:49 PM
L275	14	L274 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:49 PM
L276	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:51 PM
L277	7	L276 and ((blood or	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10

L278	1368	fluid\$4) near4 (sequest\$5 or flash\$4)) (604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	06:51 PM 2020/06/10 06:52 PM
L279	135	L278 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:52 PM
L280	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 07:08 PM
L281	3	L280 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 07:08 PM
L282	20	("2008/0145933").URP N.	(USPAT)	OR	ON	ON	2020/06/10 07:08 PM
L286	1	("10045704").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 08:56 PM
L287	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:16 PM
L288	1	("10010282").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:17 PM
L289	100	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/01 09:17 PM
L290	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:36 PM
L291	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:39 PM
L292	180	((("ROGERS") near3 ("Bobby"))).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/03/02 12:19 PM
L293	11	L292 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 12:20 PM
L294	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:47 PM
L295	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:49 PM
L296	1	("20020048170").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:36 PM
L297	1	("20040174525").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:49 PM
L298	1	("10045704").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 03:09 PM
L299	27321	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/03/02 03:17 PM

L300	4594	A61B5/154 or A61B5/153 or A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc. L299 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:27 PM
L301	3762	L300 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:28 PM
L302	257	L301 and (air near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L303	420	L301 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L304	1	("20110167658").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 03:30 PM
L305	5	("2015/0306288").URP N.	(USPAT)	OR	ON	ON	2021/03/02 04:15 PM
L306	1	(16/208559).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 04:32 PM
L307	2	("2009/0043225").URP N.	(USPAT)	OR	ON	ON	2021/03/02 04:49 PM
L308	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/03/02 05:00 PM
L309	1363	L308 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:00 PM
L310	73	L309 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L311	73	L310 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L312	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:34 PM
L313	711	L312 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L314	58	L313 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L315	58	L314 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L316	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:42 PM
L317	277	L316 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:42 PM

L318	20	L317 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:43 PM
L319	336	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/03/02 05:44 PM
L320	210	L319 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L321	196	L320 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L322	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:48 PM
L323	1208	L322 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L324	73	L323 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L325	73	L324 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:49 PM
L326	1368	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:59 PM
L327	271	L326 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L328	10	L327 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L329	268	L327 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L330	182	(("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/07/08 02:22 PM
L331	27660	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/153 or A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/07/08 03:27 PM
L332	4684	L331 and ((blood or fluid\$4) near4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:28 PM

L333	3769	(sequest\$5 or sampl\$4 or flash\$4 or collect\$4)) L332 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L334	579	L333 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L335	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:54 PM
L336	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:56 PM
L337	337	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:19 PM
L338	211	L337 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L339	196	L338 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L340	37	L339 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L341	221	("20010021827" "20020004650" "20020055716" "20020072715" "20020103464" "20020103465" "20020107488" "20020151856" "20020193748" "20030028171" "20030036730" "20030050608" "20030055385" "20030078544" "20030093009" "20030105414" "20030114797" "20030120222" "20030176842" "20030181873" "20030191438" "20030199827" "20030216687" "20030220614" "20030229315" "20030229316" "20040024370" "20040059302" "20040092872" "20040102740" "20040111068" "20040193120"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"20040204681" "20040210197" "20050004524" "20050059936" "20050065482" "20050124944" "20050165353" "20050187493" "20050228345" "20050245868" "20050245869" "20050245870" "20050245879" "20050245885" "20050283093" "20060015073" "20060036217" "20060036219" "20060079847" "20060129064" "20060189934" "20060189936" "20060224122" "20060270947" "20060276756" "20070021724" "20070027430" "20070106220" "20070106224" "20070167914" "20070282275" "20080015513" "20080086085" "20080177202" "20080221528" "20080269691" "20080306452" "20080319345" "20080319346" "20090204026" "20090227896" "20100063455" "20100191189" "20100262038" "20110118674" "4106497" "4207870" "4305406" "4572210" "4573976" "4641663" "4795443" "4813426" "4840619" "4887998" "4894055" "4900307" "4923477" "4994046" "5015241" "5195985" "5215534" "5219333" "5222502" "5242417" "5246428" "5256153").PN. OR ("5295970" "5295975"				
--	--	---	--	--	--	--

		"5303713"	"5312372"				
		"5318547"	"5336199"				
		"5344408"	"5348544"				
		"5356392"	"5389085"				
		"5403286"	"5411492"				
		"5439449"	"5466223"				
		"5501675"	"5542932"				
		"5549558"	"5595566"				
		"5599313"	"5607402"				
		"5662617"	"5665075"				
		"5669889"	"5672161"				
		"5676658"	"5681295"				
		"5685855"	"5687740"				
		"5688241"	"5695474"				
		"5702369"	"5704920"				
		"5718239"	"5733265"				
		"5755522"	"5769826"				
		"5795336"	"5879337"				
		"5893845"	"5910130"				
		"5921964"	"5957892"				
		"5984899"	"6149629"				
		"6171284"	"6183445"				
		"6224576"	"6254575"				
		"6261263"	"6261265"				
		"6298541"	"6344032"				
		"6419658"	"6436086"				
		"6440104"	"6471677"				
		"6475191"	"6485469"				
		"6524277"	"6533760"				
		"6554807"	"6575939"				
		"6592556"	"6623456"				
		"6623461"	"6635032"				
		"6641555"	"6648855"				
		"6648856"	"6659983"				
		"6695819"	"6699217"				
		"6712792"	"6716199"				
		"6761704"	"6773419"				
		"6780169"	"6805689"				
		"6811545"	"6835190"				
		"6837877"	"6846302"				
		"6860872"	"6869415"				
		"6905483"	"6918891"				
		"6958054"	"6974423"				
		"6984223"	"6997913"				
		"7001363"	"7083600"				
		"7101355"	"7128726"				
		"7147624"	"7160267"				
		"7163526"	"7201740"				
		"7211065"	"7223258"				
		"7226432"	"7361159"				
		"7396343"	"7428773"				
		"7524308"	"7537581"				
		"7670320"	"7727190"				
		"7766879"	"7938808"				
		"8066679"	"8282605"				
		"8795198"	"D422700"				
		"D442280"					
		"D604836"	"D604837"				

L342	115	"D604838" "D604839" "D605287" "RE35539" "RE43473").PN. OR ("9615783").URPN. ("20020193748" "20030093009" "20030105414" "20030220614" "20030229315" "20040059302" "20040092872" "20040193120" "20050004524" "20050065482" "20050124944" "20050187493" "20050245868" "20050245869" "20050245870" "20050245879" "20050245885" "20060036219" "20060224122" "20070106220" "20070106224" "20070167914" "20080086085" "20080177202" "20080319345" "20080319346" "20090204026" "20100262038" "4106497" "4207870" "4305406" "4572210" "4573976" "4641663" "4795443" "4840619" "4894055" "4900307" "4994046" "5015241" "5195985" "5215534" "5222502" "5242417" "5246428" "5256153" "5295970" "5303713" "5312372" "5336199" "5348544" "5356392" "5411492" "5439449" "5466223" "5501675" "5542932" "5599313" "5662617" "5665075" "5672161" "5676658" "5702369" "5704920" "5733265" "5755522" "5957892" "5984899" "6149629" "6224576" "6254575" "6261263" "6298541" "6344032" "6436086" "6440104" "6524277" "6533760"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM
------	-----	---	-----------------------------	----	----	----	------------------------

L343	148	"6592556" "6623456" "6635032" "6648855" "6695819" "6699217" "6712792" "6780169" "6837877" "6869415" "6984223" "7001363" "7128726" "7147624" "7160267" "7163526" "7223258" "7226432" "7396343" "7428773" "7537581" "7766879" "D422700" "D442280" "D604836" "D604837" "D604838" "D604839" "D605287").PN. OR ("8603009").URPN. ("20020193748" "20030105414" "20030229315" "20040059302" "20040092872" "20050004524" "20050187493" "20050245868" "20050245869" "20050245870" "20050245885" "20060036219" "20070106220" "20070167914" "20080086085" "20080177202" "4106497" "4207870" "4305406" "4573976" "4641663" "4795443" "4840619" "4894055" "4900307" "4994046" "5015241" "5195985" "5215534" "5222502" "5242417" "5256153" "5295970" "5303713" "5312372" "5336199" "5348544" "5356392" "5411492" "5439449" "5466223" "5501675" "5542932" "5672161" "5676658" "5702369" "5704920" "5755522" "5984899" "6149629" "6261263" "6298541" "6436086" "6440104" "6524277" "6533760" "6592556" "6623456" "6635032" "6648855" "6699217" "6712792" "6780169" "6837877" "6869415" "6984223"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM
------	-----	---	-----------------------------	----	----	----	------------------------

L344	41	"7001363" "7128726" "7147624" "7160267" "7163526" "7223258" "7226432" "7396343" "7428773" "D422700" "D442280").PN. OR ("7766879").URPN. ("2735430" "2798487" "3187749" "3240209" "3585984" "3817240" "4166450" "4207870" "4295477" "4312362").PN. OR ("4436098").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:22 PM
L345	163	L341 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:22 PM
L346	163	L345 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:23 PM
L347	22	("2005/0283093").URP N.	(USPAT)	OR	ON	ON	2021/07/08 04:23 PM
L348	163	L345 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L349	163	L348 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L350	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/08 04:37 PM
L351	1363	L350 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:37 PM
L352	1346	L351 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L353	136	L352 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L354	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:41 PM
L355	711	L354 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L356	699	L355 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L357	123	L356 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L358	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:44 PM
L359	277	L358 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM

L360	260	or flash\$4 or collect\$4)) L359 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM
L361	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:46 PM
L362	1208	L361 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:46 PM
L363	1194	L362 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L364	1194	L363 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L366	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:05 PM
L367	319	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR ("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/02/02 03:14 PM
L368	1	(16/376745).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:35 PM
L369	190	((("ROGERS") near3 ("Bobby"))).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 03:36 PM
L370	2	(15/140448).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:41 PM
L371	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L372	1	("9060725").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L373	1	("9060724").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:43 PM
L374	1	("9022950").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L375	1	("9022951").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L376	1	("10292633").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:46 PM
L377	1	("10433779").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:47 PM
L378	1	("10436554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:48 PM
L379	1	("10736554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L380	1	("10912506").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L381	1	("10010282").PN.	(US-PGPUB; USPAT;	OR	OFF	OFF	2022/02/02

L382	1	(16/376745).APP.	USOCR) (US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	03:49 PM 2022/02/02 03:50 PM
L383	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:51 PM
L384	276	(600/579).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:52 PM
L385	204	L384 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 03:53 PM
L386	37427	(A61B5/150221 or A61B5/15003 or A61B5/150236 or A61B5/150244 or A61B5/150251 or A61B5/150389 or A61B5/150503 or A61B5/150992 or A61B5/153 or A61B5/155 or A61B10/0048 or A61B10/0051 or A61B10/007 or A61B2010/0061 or A61B2010/0077 or A61B2010/008).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 04:35 PM
L387	7279	L386 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L388	4442	L387 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L389	874	L388 and (seal\$4 near4 (member or mechanism\$4 or vent\$4 or elastic\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:38 PM
L390	26	("2008/0145933").URP N.	(USPAT)	OR	ON	ON	2022/02/02 04:52 PM
L391	44	("2008/0319346").URP N.	(USPAT)	OR	ON	ON	2022/02/02 04:59 PM
L392	385	L386 and ((blood or fluid) near4 (seal\$4 near4 (member or mechanism\$4 or vent\$4 or elastic\$4)))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM
L393	171	L392 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM
L394	355	(604/103).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 05:52 PM
L395	7	L394 and ((blood or fluid) near4 (seal\$4 near4 (member or mechanism\$4 or vent\$4 or elastic\$4)))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:52 PM

L396	1	(16/328127).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/03 12:00 PM
L397	0	"1020130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L398	8	"20130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L399	14	"2013021595"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:18 PM
L400	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/04 07:10 PM
L401	1	(15/746656).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/05 11:48 AM
L402	0	(17/388440).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/07 09:34 AM
L403	1	("20050048465").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2022/02/07 09:34 AM
L404	196	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:08 PM
L405	16	L404 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L406	16	L404 and ((blood or chamber) near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L407	16	L406 and (junct\$4 or bypass\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L408	16	L406 and junct\$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L409	22445	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:54 PM
L410	4525	L409 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4 or flush\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:55 PM
L411	3810	L410 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:56 PM
L412	820	L411 and ((vent\$4 or	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18

L413	22445	open\$4 or apertur\$4) near4 air) (A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	03:57 PM 2022/05/18 05:51 PM
L414	4603	L413 and ((blood or fluid\$4 or chamber) same (sequest\$5 or sampl\$4 or flash\$4 or collect\$4 or flush\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:51 PM
L415	511	L414 and ((junct\$4 or bypass\$4 or divert\$4) near4 (blood or fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:52 PM
L416	355	L415 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:53 PM
L417	1	(16/819033).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:10 PM
L418	1	(17/094692).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L419	1	(17/538990).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L420	1	("11311219").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:27 PM
L421	1	("11185266").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:30 PM
L422	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:31 PM
L423	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:32 PM
L424	331	((("BULLINGTON") near3 ("Gregory")) OR ((("PATTON") near3 ("Richard")) OR ((("MAZGA") near3 ("Jay")) OR ((("GAW") near3 ("Shan")))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/06/06 03:44 PM
L425	8944	(A61B5/150221 OR A61B5/15003 OR A61B5/150236 OR A61B5/150244 OR A61B5/150251 OR A61B5/150389 OR A61B5/150503 OR A61B5/150992 OR A61B5/153 OR A61B5/155 OR A61B10/0048 OR A61B10/0051 OR	(US-PGPUB; USPAT)	OR	ON	ON	2022/06/06 05:17 PM

L426	58747	A61B10/007 OR A61B2010/0061 OR A61B2010/0077 OR A61B2010/008).cpc. (A61B5/150221 OR A61B5/15003 OR A61B5/150236 OR A61B5/150244 OR A61B5/150251 OR A61B5/150389 OR A61B5/150503 OR A61B5/150992 OR A61B5/153 OR A61B5/155 OR A61B10/0048 OR A61B10/0051 OR A61B10/007 OR A61B2010/0061 OR A61B2010/0077 OR A61B2010/008).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/06/06 05:17 PM
L427	7420	426 AND ((blood OR fluid\$4) near4 (sequest\$5 OR saml\$4 OR flash\$4 OR collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/06/06 05:18 PM
L428	4441	427 AND @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/06/06 05:18 PM
L429	846	428 AND (seal\$4 near4 (member OR mechanism\$4 OR vent\$4 OR elastic\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/06/06 05:20 PM
L430	2	"17525682"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/06/06 05:46 PM
L431	547	426 AND (((blood OR fluid\$4) near4 (sequest\$5 OR bypass\$4 OR flash\$4)) AND seal\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/06/06 05:50 PM
L432	231	431 AND @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/06/06 05:50 PM
L433	1	18/113710	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/22 02:58 PM
L434	209	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	OFF	OFF	2023/08/22 03:09 PM
L435	21	434 AND (((blood OR fluid\$4) near4 (sequest\$5 OR bypass\$4 OR flash\$4)) AND seal\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/22 03:09 PM
L436	9	"20100057004"	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/22 03:11 PM
L437	49165	(A61B5/150992 OR A61B5/15003 OR	(US-PGPUB; USPAT; USOCR; FIT (AU, AP,	OR	ON	ON	2023/08/22 03:49 PM

L438	33727	A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068 OR A61B5/150251).cpc.	AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/08/22 03:51 PM
L439	36143	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/154 OR A61B5/153 OR A61M39/0693 OR A61M39/04 OR A61B5/150221 OR A61M2039/0633 OR A61M2039/0202 OR A61M2039/068 OR A61B5/150251).cpc. 438 AND @ad<"20150724"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2023/08/22 03:52 PM
L440	3944	439 AND ((blood OR fluid\$4) near4 (sequest\$5 OR bypass\$4 OR flash\$4 OR collect\$4 OR sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/22 03:52 PM
L441	1473	440 AND (seal\$4 near4 (member OR mechanism\$4 OR vent\$4 OR elastic\$4 OR filter\$4 OR material\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/22 03:53 PM

L442	8	"20080167577"	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/22 04:42 PM
L443	115	440 AND (seal\$4 near4(expos\$4 OR contact\$4) near5 (blood OR fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/22 04:58 PM
L444	116	440 AND (seal\$4 near4(expos\$4 OR contact\$4 OR absorb\$4) near5 (blood OR fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/22 04:59 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N94	1	(port and sequest\$5 and junction and chamber and sampl\$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:15 PM
N112	3	(port and sequest\$5 and chamber and sampl\$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:39 PM
N248	4	(blood and fluid\$4 and inlet and outlet and port and reservoir and allow and initial\$4 and sequest\$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N249	4	(blood and fluid\$4 and inlet and outlet and port and reservoir and allow\$4 and initial\$4 and sequest\$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N250	495	(blood and fluid\$4 and allow\$4 and initial\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N251	107	(blood and fluid\$4 and allow\$4 and initial\$4 and subsequent\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N283	9	((blood or fluid\$4) and sequestrat\$4 and chamber and sampl\$4 and vent\$4 and air\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N284	530	((blood or fluid\$4) and chamber and sampl\$4 and vent\$4 and air\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N285	84	((blood or fluid\$4) and chamber and cap and sampl\$4 and vent\$4 and air\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:32 PM

N365	6	(port and sequest\$5 and junction and chamber and sampl\$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:49 PM
N366	0	(blood AND seal\$4 AND sampl\$4 AND state AND transfer\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2022/06/06 03:50 PM
N367	41	(blood AND seal\$4 AND bypass\$4 AND transfer\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2022/06/06 03:51 PM
N368	396	(blood AND seal\$4 AND sampl\$4 AND transfer\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2022/06/06 05:13 PM
N369	172	(blood AND seal\$4 AND sampl\$4 AND transfer\$4 AND volume).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2022/06/06 05:13 PM
N370	5	(blood AND seal\$4 AND sampl\$4 AND transfer\$4 AND volume AND bypass\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2022/06/06 05:14 PM
N371	8944	(A61B5/150221 OR A61B5/15003 OR A61B5/150236 OR A61B5/150244 OR A61B5/150251 OR A61B5/150389 OR A61B5/150503 OR A61B5/150992 OR A61B5/153 OR A61B5/155 OR A61B10/0048 OR A61B10/0051 OR A61B10/007 OR A61B2010/0061 OR A61B2010/0077 OR A61B2010/008).cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2022/06/06 05:16 PM

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)

Approved for use through 11/30/2020. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	18113710
	Filing Date	2023-02-24
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Examiner Name	
	Attorney Docket Number	069366-0574153_KUR2C04US

U.S.PATENTS						Remove
--------------------	--	--	--	--	--	------------------------

Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

[Add](#)

U.S.PATENT APPLICATION PUBLICATIONS						Remove
--	--	--	--	--	--	------------------------

Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button.

[Add](#)

FOREIGN PATENT DOCUMENTS								Remove
---------------------------------	--	--	--	--	--	--	--	------------------------

Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ²ⁱ	Kind Code ⁴	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear	T ⁵
	1							

If you wish to add additional Foreign Patent Document citation information please click the Add button

[Add](#)

NON-PATENT LITERATURE DOCUMENTS				Remove
--	--	--	--	------------------------

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T ⁵

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

1	Ziegler, R., et al. "Controlled Clinical Laboratory Comparison of Two Supplemented Aerobic and Anaerobic Media Used in Automated Blood Culture Systems to Detect Bloodstream Infections," Journal of Clinical Microbiology, Mar. 1998, p. 657-661.
2	Pall Medical, "Leukotrap Filtration Systems for Whole Blood Derived Platelets, Leukotrap RC PL and Leukotrap PL Systems" literature, (2005) 8 pages.
3	Meissner, George F. , et al., "The Standard Clotting Time, A Method Based on the Use of Whole Venous Blood in Capillary Tubes," The American Journal of Clinical Pathology, Vol. 39, No. 3., pp. 321-323, March 1963.
4	Mayer, G.A. "A Method for the Reliable Determination of Clotting Time in Whole Blood," Canadian Medical Association Journal, June 15, 1955, Vol. 72, Pages 927-929.

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	/MAY A AROUELELA/	Date Considered	08/22/2023
--------------------	-------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-05-10
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent 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.

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	18113710
	Filing Date	2023-02-24
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Examiner Name	
	Attorney Docket Number	069366-0574153_KUR2C04US

U.S.PATENTS						Remove
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1	5200325		1993-04-06	BLATT JOEL M	
	2	5432084		1995-07-11	BRUBAKER DANIEL B	
	3	5972294		1999-10-26	SMITH JOHN L	
	4	6187347		2001-02-13	PATTERSON JAMES A	
	5	6599474		2003-07-29	EVTDIENKO VLADIMIR	
	6	8197420		2012-06-12	PATTON RICHARD G	
	7	8535241		2013-09-17	BULLINGTON GREGORY	
	8	9060724		2015-06-23	BULLINGTON GREGORY J	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

9	9155495		2015-10-13	BULLINGTON GREGORY J	
10	4412548		1983-11-01	HOCH LOUIS	
11	5222502		1993-06-29	KUROSE KATSUTOSHI	
12	5520193		1996-05-28	SUZUKI ISSEI	
13	9022951		2015-05-05	BULLINGTON GREGORY	
14	6569117		2003-05-27	ZIV DAVID	
15	3741197		1973-06-26	SANZ M	
16	8603009		2013-12-10	TAN ALVIN CHEE LEONG	
17	4207870		1980-06-17	ELDRIDGE WILLIAM N	
18	9877675		2018-01-30	BAID RISHI	
19	4444203		1984-04-24	ENGELMAN ALLAN	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

20	6398743		2002-06-04	HALSETH THOR R	
21	9022950		2015-05-05	BULLINGTON GREGORY	
22	4436098		1984-03-13	KAUFMAN JOSEPH	
23	9138572		2015-09-22	ZEYTOONIAN PAUL	
24	8568371		2013-10-29	SIOPEs WILLIAM	
25	8540663		2013-09-24	DAVEY CHRISTOPHER T	
26	8523826		2013-09-03	LAYTON JR RUSSELL K	
27	4057050		1977-11-08	SARSTEDT WALTER	
28	8864684		2014-10-21	BULLINGTON GREGORY J	
29	5749857		1998-05-12	CUPPY MICHAEL J	
30	9204864		2015-12-08	BULLINGTON GREGORY J	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

31	3874367		1975-04-01	AYRES WALDEMAR A	
32	3886930		1975-06-03	RYAN GEORGE R	
33	4106497		1978-08-15	PERCARPIO EDWARD P	
34	4154229		1979-05-15	NUGENT EDWARD L	
35	4980297		1990-12-25	HAYNES JOHN L	
36	9820682		2017-11-21	ROGERS BOBBY E	
37	10010282		2018-07-03	ROGERS BOBBY E	
38	10143412		2018-12-04	ROGERS BOBBY E	
39	11185266		2021-11-30	ROGERS BOBBY E	
40	10827964		2020-11-10	ROGERS BOBBY E	
41	11311219		2022-04-26	ROGERS BOBBY E	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

42	3817240	1974-06-18	AYRES W
43	3648684	1972-03-14	BARNWELL CLEORA W
44	4056101	1977-11-01	GEISSLER ULRICH C
45	4416290	1983-11-22	LUTKOWSKI LAWRENCE
46	3070725	2011-12-06	CHRISTENSEN KELLY D
47	4349035	1982-09-14	THOMAS JOSEPH J
48	4813433	1989-03-21	DOWNEY JOHN M
49	5401262	1995-03-28	KARWOSKI THEODORE
50	3859998	1975-01-14	THOMAS JOSEPH JOHN
51	4373535	1983-02-15	MARTELL MICHAEL D
52	4690154	1987-09-01	WOODFORD TIMOTHY

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

53	5097842		1992-03-24	BONN GINA B	
54	5865803		1999-02-02	MAJOR MIKLOS	
55	5873841		1999-02-23	BRANNON JAMES K	
56	6013037		2000-01-11	BRANNON JAMES K	
57	6913580		2005-07-05	STONE BENJAMIN CURTIS	
58	11213232		2022-01-04	VOSEVIC MILAN	
59	6626884		2003-09-30	DILLON JAGMOHANBIR SINGH	
60	4904240		1990-02-27	HOOVER ROCKLIN L	
61	4673386		1987-06-16	GORDON MARK G	
62	7461671		2008-12-09	EHWALD RUDOLF	
63	6506182		2003-01-14	ESTABROOK BRIAN K	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

64	3382865	1968-05-14	WORRALL JR ASHTON L
65	3848579	1974-11-19	VILLA REAL A
66	6106509	2000-08-22	LOUBSER PAUL G
67	3494352	1970-02-10	RUSSO RONALD D
68	6224561	2001-05-01	SWENDSON DAVID L
69	7055401	2006-06-06	PRYBELLA JOHN R
70	5135489	1992-08-04	UEPSON STEVEN C
71	5811658	1998-09-22	VAN DRIEL MICHAEL R
72	3604410	1971-09-14	WHITACRE GARY L
73	5772608	1998-06-30	DHAS V VARAPRABHU
74	4150089	1979-04-17	LINET MICHAEL S

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

75	4257416		1981-03-24	PRAGER DAVID	
76	4193400		1980-03-18	LOVELESS JAMES C	
77	6843775		2005-01-18	HYUN DONGCHUL D	
78	7666166		2010-02-23	EMMERT MICHAEL	
79	7479131		2009-01-20	MATHIAS JEAN-MARIE	
80	8377040		2013-02-19	BURKHOLZ JONATHAN KARL	
81	5417673		1995-05-23	GORDON MARK G	
82	6638252		2003-10-28	MOULTON WILLIAM G	
83	3945380		1976-03-23	DABNEY WILLIAM C	
84	5100394		1992-03-31	DUDAR THOMAS E	
85	8827958		2014-09-09	BIERMAN STEVEN F	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

86	8574203		2013-11-05	STOUT MARTY L	
87	6860871		2005-03-01	KURACINA THOMAS C	
88	6945948		2005-09-20	BAINBRIDGE MARLENE	
89	7306736		2007-12-11	COLLINS GREGORY R	
90	6691486		1997-11-25	BEHRINGER BRUCE E	
91	6980830		1999-11-09	SAVAGE DOUGLAS ROBERT	
92	6045185		1991-09-03	OHNAKA YUKIHIRO	
93	6632906		1997-05-27	ISHIDA NOBORU	
94	6695004		2004-02-24	RAYBUCK JOHN L	
95	6733433		2004-05-11	FELL CLAUDE	
96	7241281		2007-07-10	COELHO PHILIP H	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

97	8349254		2013-01-08	HOSHINO YOSHITERU	
98	5439450		1995-08-08	HAEDT LORI E	
99	6905483		2005-06-14	NEWBY C MARK	
100	5431811		1995-07-11	TUSINI ANDREA	
101	6736783		2004-05-18	BLAKE KEVIN R	
102	7052603		2006-05-30	SCHICK KARL G	
103	3835835		1974-09-17	THOMPSON R	

If you wish to add additional U.S. Patent citation information please click the Add button.

Add

U.S.PATENT APPLICATION PUBLICATIONS

Remove

Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1	20010044615		2001-11-22	AMANO YOSHIKAZU	
	2	20030082074		2003-05-01	JURIK FRANKLIN A	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

3	20030185707		2003-10-02	WAKI YOSHIHIDE	
4	20040116830		2004-06-17	TRUDEAU WILLIAM M	
5	20090299253		2009-12-03	HURSEY FRANCIS X	
6	20130158506		2013-06-20	HARRIS ADRIENNE ROSE	
7	20150246352		2015-09-03	BULLINGTON GREGORY J	
8	20150342510		2015-12-03	BULLINGTON GREGORY J	
9	20160361006		2016-12-15	BULLINGTON GREGORY J	
10	20170065733		2017-03-09	BULLINGTON GREGORY J	
11	20180140240		2018-05-24	BULLINGTON GREGORY J	
12	20140112841		2014-04-24	SCHOEN CHRISTIAN	
13	20180271425		2018-09-27	ROGERS BOBBY E	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

14	20080319346		2008-12-25	CRAWFORD JAMIESON	
15	20100057004		2010-03-04	CHRISTENSEN KELLY D	
16	20070088279		2007-04-19	SHUE MING-JENG	
17	20080145933		2008-06-19	PATTON RICHARD G	
18	20040054333		2004-03-18	THEEUWES FELIX	
19	20100010372		2010-01-14	BROWN LEROY R	
20	20080167577		2008-07-10	WEILBACHER EUGENE E	
21	20080086085		2008-04-10	BROWN LEROY R	
22	20070083162		2007-04-12	O'REAGAN JAMES	
23	20160008579		2016-01-14	BURKHOLZ JONATHAN KARL	
24	20120016266		2012-01-19	BURKHOLZ JONATHAN KARL	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

25	20130317391		2013-11-28	BULLINGTON GREGORY J	
26	20160174888		2016-06-23	BERTHIER ERWIN	
27	20050240161		2005-10-27	CRAWFORD JAMIESON W M	
28	20040147855		2004-07-29	MARSDEN STEWART	
29	20040073171		2004-04-15	ROGERS BOBBY E	
30	20050004524		2005-01-06	NEWBY C MARK	
31	20030105414		2003-06-05	LEONG ALVIN TAN CHEE	
32	20020004647		2002-01-10	LEONG ALVIN TAN CHEE	
33	20140155781		2014-06-05	BULLINGTON GREGORY J	
34	20030208151		2003-11-06	KRAUS MENACHEM	
35	20090227953		2009-09-10	TAN CHEE LEONG	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

36	20170020428		2017-01-26	ROGERS BOBBY E	
37	20170020427		2017-01-26	ROGERS BOBBY E	
38	20050005635		2005-01-13	LE METAIS MARC	
39	20050007524		2005-01-13	LUO FANG-CHEN	
40	20140039348		2014-02-06	BULLINGTON GREGORY J	
41	20140107564		2014-04-17	BULLINGTON GREGORY J	
42	20140155782		2014-06-05	BULLINGTON GREGORY J	
43	20140276578		2014-09-18	BULLINGTON GREGORY J	
44	20160017488		2016-01-21	KOBAYASHI MASAYUKI	
45	20180177445		2018-06-28	ROGERS BOBBY E	
46	20180353117		2018-12-13	BULLINGTON GREGORY J	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

47	20190159711		2019-05-30	ROGERS BOBBY E	
48	20050245885		2005-11-03	BROWN LEROY	
49	20110306899		2011-12-15	BROWN LEROY R	
50	20130116599		2013-05-09	BULLINGTON GREGORY J	
51	20050273019		2005-12-08	CONWAY HUGH	
52	20150351678		2015-12-10	BULLINGTON GREGORY	
53	20220160271		2022-05-26	VOSEVIC MILAN	
54	20050161112		2005-07-28	EHWALD RUDOLF	
55	20070119508		2007-05-31	WEST RICHARD L	
56	20220304600		2022-09-29	HAMMER JEREMY	

If you wish to add additional U.S. Published Application citation information please click the Add button.

Add

FOREIGN PATENT DOCUMENTS

Remove

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

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	2593169A1	EP		2013-05-22	BECTON DICKINSON CO		
	2	2009131273A	JP		2009-06-18	CSL BEHRING GMBH		×
	3	2010062734A1	WO		2010-06-03	UNIV MARYLAND		☐
	4	2013082301A1	WO		2013-06-06	TELEFLEX MEDICAL INC		☐
	5	1378602A	GB		1974-12-27	BECTON DICKINSON CO		☐
	6	2019055487A1	WO		2019-03-21	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	7	2019232196A1	WO		2019-12-05	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	8	H08257018	JP		1996-10-08	NISSHO KK		☒
	9	1665986	EP		2006-06-07	BECTON DICKINSON CO		☐
	10	2011162772A1	WO		2011-12-29	CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC		☐

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

11	2993646	CA	2017-02-02	KURIN INC	☐
12	3324845A1	EP	2018-05-30	KURIN INC	☐
13	3562397A1	EP	2019-11-06	KURIN INC	☐
14	3622890A1	EP	2020-03-18	KURIN INC	☐
15	5789869B2	JP	2015-10-07	TOHO ENGINEERING KK,	☒
16	5867238B2	JP	2016-02-24	FUJITSU LTD,	☒
17	6643474B2	JP	2020-02-12	クリン インコーポレイ テッド	☒
18	6734490	JP	2020-08-05	クリン インコーポレイ テッド	☒
19	2001000424	JP	2001-01-09	NISSHO KK	☒
20	2012016496A	JP	2012-01-26	TERUMO CORP	☒
21	2016504075	JP	2016-02-12	マグノリア メディカル テクノロジーズ, イン コーポレイテッド	☒

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

22	2019534792A	JP	2019-12-05	プライメタルズ・テクノロジー・オーストラリア・ゲーエムペーハー	☒
23	H09504726A	JP	1997-05-13	BAXTER INT	☒
24	9605875A1	WO	1996-02-29	BAXTER INT	☐
25	2013181352A1	WO	2013-12-05	MAGNOLIA MEDICAL TECHNOLOGIES INC	☐
26	2014058945	WO	2014-04-17	BULLINGTON GREGORY J	☐
27	2017019552A1	WO	2017-02-02	KURIN INC	☐
28	2018125929A1	WO	2018-07-05	KURIN INC	☐
29	S5825146A	JP	1983-02-15	BECTON DICKINSON CO	☒
30	S5867238A	JP	1983-04-21	BECTON DICKINSON CO	☒
31	5643474	JP	2014-12-17	ヴェロシス, インク.	☒
32	5825146B2	JP	2015-12-02	JVC KENWOOD CORP,	☒

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

33	2020000340A	JP	2020-01-09	TOSHO INC	☒
34	2013240628	JP	2013-12-05	COVIDIEN LP	☒
35	H02224742	JP	1990-09-06	SPACELABS INC	☒
36	S5789869	JP	1982-06-04	BECTON DICKINSON CO	☒
37	2005349196	JP	2005-12-22	BECTON DICKINSON CO	☒
38	10243129	DE	2004-04-01	RITTER GMBH	☒
39	7203008	DE	1972-05-10	IMMUNO AG FUER CHEM-MED PROD	☒
40	10038026	DE	2001-02-22	ZIERDEN PETER	☒
41	29913417	DE	2000-12-28	ZIERDEN PETER	☒
42	10134913	DE	2003-02-20	HIBERNA AG	☒
43	10134913C2	DE	2003-06-26	HIBERNA AG	☒

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

44	2541494	DE	1977-03-31	GUERRA LUIS A	☒
45	2008101025	WO	2008-08-21	EDWARDS LIFESCIENCES CORP	☐
46	0448795A2	EP	1991-10-02	BECTON DICKINSON CO	☐
47	199216144	WO	1992-10-01	GOLDSPILL PTY. LTD.	☐
48	2007033319A1	WO	2007-03-22	EDWARDS LIFESCIENCES CORP	☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

Add

NON-PATENT LITERATURE DOCUMENTS

Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T ⁵
	1	International Search Report and Written Opinion dated Nov. 5, 2015, for PCT application No. PCT/US2015/035870. 6 pages.	
	2	International Search Report and Written Opinion dated 16 July 2020 for PCT application no. PCT/US2020/026276. 9 pages.	
	3	Bullington, et al., Systems and Methods for Sample Collection with Reduced Hemolysis, Exhibit H in U.S. Appl. No. 62/517,681, dated Jun. 9, 2017, 131 pages.	
	4	Communication Under Rule 71(3) EPC dated Apr. 22, 2020 for EP application No. 17840467.9. 125 pages.	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

5	European Patent Application No. EP19200766.4 extended European Search Report dated Dec. 2, 2019, 11 pages.
6	European Patent Office, Extended European Search Report for European Patent Application 20197213.0-1132, dated Dec. 9, 2020, 6 pages.
7	European Patent Office; Communication pursuant to Article 94(3) EPC; dated Oct. 31, 2018; 11 pages.
8	Examination Report No. 1 dated Apr. 29, 2020, for Australian Patent Application No. 2016297849. 3 pages.
9	International Search Report and Written Opinion dated Jun. 19, 2020, for PCT application No. PCTUS2020/023617. 12 pages.
10	European Patent Office, International Search Report and Written Opinion for PCT/US16/43709, dated Oct. 19, 2016, 14 pages.
11	International Search Report/Written Opinion for PCT/US17/68569 dated Apr. 25, 2018. 9 pages.
12	European Patent Office, International Search Report/Written Opinion for PCT/US17/068569 dated Apr. 25, 2018, 9 pages.
13	International Search Report and Written Opinion for PCT/US16/43709, Dated October 19, 2016. 13 pages.
14	Retractable Techs., Inc. v. Becton Dickinson & Co., CA No. 2:07-CV-250, Claim Construction Order (E.D. Tex., Jan. 20, 2009). 20 pages.
15	Hillyer, Christopher D., et al. "Bacterial Contamination of Blood Components: Risks, Strategies and Regulation," Hematology, 2003, pp. 575-589.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

16	De Korte, Dirk, et al. "Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections." Vox sanguinis 83.1 (2002): 13-16.
17	Brecher, Mark E., et al. "Bacterial contamination of blood components." Clinical microbiology reviews 18.1 (2005): 195-204.
18	Van Zundert, Adrien. "New closed IV catheter system." Acta Anæsthesiologica Belgica 56.3 (2005): 283-285.
19	Hall, Keri K., et al. "Updated review of blood culture contamination." Clinical microbiology reviews 19.4 (2006): 788-802.
20	Li, Yiwen, et al. "Direct labeling and visualization of blood vessels with lipophilic carbocyanine dye Dil." Nature protocols 3.11 (2008): 1703-1708.
21	Page, Catherine, et al. "Blood conservation devices in critical care: a narrative review." Annals of intensive care 3 (2013): 1-6.
22	Abbott Point of Care, Cartridge and Test Information, Art: 714258-010; Rev. Date: 15-Aug-16, 1-6 pages.
23	Zimmon, David S. et al. "Effect of portal venous blood flow diversion on portal pressure." The Journal of Clinical Investigation 65.6 (1980): 1388-1397.
24	Patton, Richard G., et al. "Innovation for reducing blood culture contamination: initial specimen diversion technique." Journal of clinical microbiology 48.12 (2010): 4501-4503.
25	Tang, Menglin, et al. "Closed blood conservation device for reducing catheter-related infections in children after cardiac surgery." Critical Care Nurse 34.5 (2014): 53-60.
26	Ernst, Dennis J. et al. "NCCLS simplifies the order of draw: a brief history." MLO: medical laboratory observer 36.5 (2004): 1-5 pages.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

27	Gottlieb, T. "Hazards of bacterial contamination of blood products." Anaesthesia and intensive care 21.1 (1993): 20-23.
28	Norberg, Alonna, et al. "Contamination rates of blood cultures obtained by dedicated phlebotomy vs intravenous catheter." Jama 289.6 (2003): 726-729.
29	Quilici, Nathalie, et al. "Differential quantitative blood cultures in the diagnosis of catheter-related sepsis in intensive care units." Clinical infectious diseases 25.5 (1997): 1066-1070.
30	Napolitano, Marcello, et al. "Quality control of bacterial contamination of blood components: the feasibility of diversion system testing." Blood Transfus 2 (2004): 231-232.
31	De Korte, Dirk, et al. "Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands." Transfusion 46.3 (2006): 476-485.
32	Liumbruno, Giancarlo Maria, et al. "Reduction of the risk of bacterial contamination of blood components through diversion of the first part of the donation of blood and blood components." Blood Transfusion 7.2 (2009): 86.
33	NCCLS. Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition. H3-A5, Vol. 23, No. 32. Replaces H3-A4; Vol. 18, No. 7. 1-52 pages. http://demo.nextlab.ir/Organization/Documents/CLSI-Standards/CLSI-H3-A5.aspx
34	Challiner, A., et al. "Venous/arterial blood management protection system." Anaesthesia 47.2 (1992): 169-169.
35	Murphy, Michael F. "Better Blood Transfusion." Journal of the Intensive Care Society 4.3 (2003): 78-80.
36	Palavecino, Elizabeth L., et al. "Detecting bacterial contamination in platelet products." Clinical laboratory 52.9-10 (2006): 443-456.
37	Sheppard, Chelsea A., et al. "Bacterial contamination of platelets for transfusion: recent advances and issues." Laboratory Medicine 36.12 (2005): 767-770.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

38	Shulman, Gerald. "Quality of processed blood for autotransfusion." JOURNAL OF EXTRACORPOREAL TECHNOLOGY 32.1 (2000): 11-19.
39	Weinbaum, Fredric I., et al. "Doing it right the first time: quality improvement and the contaminant blood culture." Journal of Clinical Microbiology 35.3 (1997): 563-565.
40	Weinstein, Melvin P. "Blood culture contamination: persisting problems and partial progress." Journal of clinical microbiology 41.6 (2003): 2275-2278.
41	Weinstein, Melvin P., et al. "The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults." Clinical Infectious Diseases 24.4 (1997): 584-602.
42	Weinstein, Melvin P. "Current blood culture methods and systems: clinical concepts, technology, and interpretation of results." Clinical infectious diseases 23.1 (1996): 40-46.
43	Closed IV, BD Saf-T-Intima. "Catheter System, Becton, Dickinson and Company, Brochure." Retrieved from the Internet (August 23, 2019). 4 pages.
44	Perez, P., et al. "Multivariate analysis of determinants of bacterial contamination of whole-blood donations." Vox Sanguinis 82.2 (2002): 55-60.
45	McDonald, Carl P. "Interventions implemented to reduce the risk of transmission of bacteria by transfusion in the English National Blood Service." Transfusion Medicine and Hemotherapy 38.4 (2011): 255-258.
46	Lifesciences, Edwards. "Conservation. Safety. Simplicity. Edwards VAMP and VAMP Jr. Systems." (2002). 4 pages.
47	Sheppard, et al., Bacterial Contamination of Platelets for Transfusion: Recent Advances and Issues, LABMEDICINE, Vol. 36, No. 12, Dec. 2005 ("Sheppard 2005").
48	BD Diagnostics, "Venous Blood Collection, BD Vacutainer Passive Shielding Blood Collection Needle " literature (2005) 2 pages.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

49	Barnard, Dorothy R., et al. "Fibronectin (cold insoluble globulin) in the neonate," The Journal of Pediatrics, Vol. 102, Issue 3, March 1983, Pages 453-455.
----	--

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	/MAY A ABOUELELA/	Date Considered	08/22/2023
--------------------	-------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-05-10
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent 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.

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Fri Aug 25 05:09:57 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new outgoing correspondence. This correspondence is now available for viewing in Patent Center.

The official date of notification of the outgoing correspondence will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:

The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	CTFR	08/25/2023	069366-0574153_KUR2C04US
18113710	892	08/25/2023	069366-0574153_KUR2C04US
18113710	1449	08/25/2023	069366-0574153_KUR2C04US
18113710	1449	08/25/2023	069366-0574153_KUR2C04US
18113710	1449	08/25/2023	069366-0574153_KUR2C04US

To view your correspondence online, please sign in to [Patent Center](#) and then select Workbench/View correspondence. To update your email address(es), select Manage/Manage customer numbers.

If you have any questions, please contact the [Patent Electronic Business Center](#) (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team

Application No. 18/113,710

Attorney's Docket No.: 069366-0574153_KUR2C04US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Bobby E. Rogers, et al.

Confirmation No: 2715

Application No.: 18/113,710

Art Unit: 3791

Filed: February 24, 2023

Examiner: May A. Abouelela

For: Blood Sample Optimization Device

Mail Stop AF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO FINAL OFFICE ACTION

Dear Examiner Abouelela:

This reply is responsive to the Final Office Action mailed August 25, 2023, in the above-referenced matter (hereinafter “the Office Action”). Reconsideration and allowance of the application is requested in view of the following:

Listing of Claims beginning on page 2.

Remarks beginning on page 5.

LISTING OF CLAIMS

This listing of claims replaces all prior versions of claims in the application:

1-16. (Cancelled)

17. (Previously Presented) A device comprising:

an inlet port for receiving a blood sample;

an outlet port;

a chamber connected with the inlet port and the outlet port, and configured to collect a first portion of the blood sample, the chamber including a material that is air permeable and blood impermeable; and

a sampling channel connected with the inlet port and configured to convey a subsequent portion of the blood sample to the outlet port while bypassing the chamber.

18. (Previously Presented) The device in accordance with claim 17, wherein the device is configured such that, when a drawing force is applied at the outlet port, blood is drawn into the inlet port and into the chamber.

19. (Previously Presented) The device in accordance with claim 18, wherein the device is further configured such that an initial aliquot of blood will contact the material and back up into the chamber.

20. (Previously Presented) The device in accordance with claim 17, wherein the material is located at a distal end of the chamber.

21. (Previously Presented) The device in accordance with claim 17, wherein the material is a hydrophobic plug.

22. (Previously Presented) The device in accordance with claim 17, wherein the material is a hydrophobic membrane.

23. (Previously Presented) The device in accordance with claim 17, wherein the material is a hydrophilic membrane.

24. (Previously Presented) The device in accordance with claim 17, wherein the sampling channel further comprises a valve configured to close off the sampling channel.

25. (Previously Presented) The device in accordance with claim 24, wherein the valve is a clip.

26. (Previously Presented) The device in accordance with claim 17, the device further comprising a junction connecting the inlet port and the sampling channel and the chamber.

27. (Previously Presented) The device in accordance with claim 26, wherein the junction is configured to convey the subsequent portion of the blood sample to the outlet port while bypassing the chamber.

28. (Previously Presented) The device in accordance with claim 17, wherein the chamber has a larger cross-sectional area than the sampling channel.

29. (Previously Presented) The device in accordance with claim 17, further comprising a housing that defines the chamber and the sampling channel.

30. (Previously Presented) The device in accordance with claim 29, 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 chamber, and the sampling channel.

31. (Previously Presented) The device in accordance with claim 17, further comprising a patient needle and a sample collection device.

REMARKS

Claim Summary: Prior to this response, Claims 1-13 and 16-31 were pending. Claims 1-13 and 16 are cancelled. After entry of this response, Claims 17-31 will be pending. Reconsideration and allowance of the current application are requested in light of the following remarks.

Summary of Rejections: The Office has rejected Claims 1, 5, 8-13, and 16 under 35 U.S.C. §102 as allegedly being anticipated by Christensen (US 2010/0057004), hereinafter “Christensen,” Claims 2-4, 6 and 7 as allegedly being unpatentable under 35 U.S.C. §103 over Christensen in view of Weilbacher (US 2008/0167577), hereinafter “Weilbacher.”

Request for Interview: The present response is believed to be sufficient to overcome the pending rejections. However, if this paper is not deemed sufficient to result in a notice of allowance, or if any remaining issues can be more efficiently handled by telephone, the Examiner is respectfully requested to contact the undersigned.

Rejections under 35 U.S.C. §102 / §103

While Applicant does not concede the rejections of Claims 1-13 and 16, in an effort to advance prosecution and achieve an immediate allowance, Applicant herein cancels these claims, leaving only the subject matter identified as allowable in the present Office Action.

Allowable Subject Matter

The Office Action indicates that Claims 17-31 are allowable. With the present amendment, only Claims 17-31 are now pending. Accordingly, Applicant respectfully suggests that the application is in condition for allowance.

CONCLUSION

On the basis of the foregoing remarks, allowance of the pending claims is respectfully requested. It is believed that all the pending rejections have been addressed in this paper. However, failure to address a specific rejection, issue or comment, does not signify agreement with or concession of that rejection, issue or comment. In addition, because any arguments made above are not intended to be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper.

No additional fees are believed to be due, however the Commissioner is authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account 033975, Reference No. 069366-0574153_KUR2C04US. If there are any questions regarding this submission, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,
PILLSBURY WINTHROP SHAW PITTMAN LLP

Date: August 29, 2023

By: /Ben Hudson/

Benjamin F. Hudson, Ph.D.

Reg. No. 71,474

PO BOX 10500
McLean, Virginia 22102
Telephone: (858) 509-4000
Customer No. 27500

4894-3293-1692.v1



UNITED STATES
PATENT AND TRADEMARK OFFICE

Page 1 of 2

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/113,710

RECEIPT DATE / TIME
08/29/2023 03:27:03 PM ET

ATTORNEY DOCKET #
069366-0574153_KUR2C04US

Title of Invention

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD CONTAMINANT SEQUESTRATION
DEVICE AND METHOD

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 2715

FILED BY Trent Tercenio

PATENT CENTER # 62698434

FILING DATE 02/24/2023

CUSTOMER # 27500

FIRST NAMED INVENTOR Bobby E. ROGERS

CORRESPONDENCE ADDRESS -

AUTHORIZED BY Benjamin Hudson

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
069366-0574153_KUR2C04US_Resp onse_to_Final_Office_Action _rcvd_25AUG2023_4894- 3293-1692_v1- APP.TEXT.docx	6	Application body structured text document	41 KB

Warning: Bookmarks were found and have been removed. All artifacts (SmartArt,
Drawings, Charts, etc) have been replaced with images.

Digest

DOCUMENT**MESSAGE DIGEST(SHA-512)**

069366-	2A58257C3E FEF9283F0B416A1FCA2490725F19025B485A3EAD
0574153_KUR2C04US_Respon	4BD48BEC882C9FC1AAD00755D61FE0F6A5465DFF1BD33E56
se_to_Final_Office_Action_rcvd	A77ED2A18D69D7708C2F477F488A9F
_25AUG2023_4894-3293-	
1692_v1-APP.TEXT.docx	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875				Application or Docket Number 18/113,710		Filing Date 02/24/2023		☐ To be Mailed					
ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO													
APPLICATION AS FILED - PART I													
		(Column 1)		(Column 2)									
FOR		NUMBER FILED		NUMBER EXTRA		RATE (\$)		FEE (\$)					
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))		N/A		N/A		N/A							
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))		N/A		N/A		N/A							
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))		N/A		N/A		N/A							
TOTAL CLAIMS (37 CFR 1.16(j))		minus 20 =		*		x \$40 =							
INDEPENDENT CLAIMS (37 CFR 1.16(h))		minus 3 =		*		x \$ 192 =							
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))		If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).											
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))													
* If the difference in column 1 is less than zero, enter "0" in column 2.						TOTAL							
APPLICATION AS AMENDED - PART II													
		(Column 1)		(Column 2)		(Column 3)							
AMENDMENT	08/29/2023		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)		
	Total (37 CFR 1.16(i))		* 15		Minus ** 29		= 0		x \$ 40 =		0		
	Independent (37 CFR 1.16(h))		* 1		Minus *** 3		= 0		x \$ 192 =		0		
	☐ Application Size Fee (37 CFR 1.16(s))												
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))												
										TOTAL ADD'L FEE		0	
		(Column 1)		(Column 2)		(Column 3)							
AMENDMENT			CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)		
	Total (37 CFR 1.16(i))		*		Minus **		=		x \$ 0 =				
	Independent (37 CFR 1.16(h))		*		Minus ***		=		x \$ 0 =				
	☐ Application Size Fee (37 CFR 1.16(s))												
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))												
										TOTAL ADD'L FEE			
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.										LIE			
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".										/ZURIASHWORK ZENEBE/			
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".													
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.													

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

27500 7590 09/08/2023
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

EXAMINER

ABOUELELA, MAY A

ART UNIT PAPER NUMBER

3791

DATE MAILED: 09/08/2023

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/113,710	02/24/2023	Bobby E. ROGERS	069366-0574153_KUR2C04US	2715

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	12/08/2023

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 EFS-Web.

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 09/08/2023

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 EFS-Web 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.
-----------------	-------------	----------------------	---------------------	------------------

18/113,710 02/24/2023 Bobby E. ROGERS 069366-0574153_KUR2C04US 2715

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	12/08/2023

EXAMINER	ART UNIT	CLASS-SUBCLASS
ABOUELELA, MAY A	3791	600-577000

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 Patent Center or EFS-Web ☐ 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

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

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.

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.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/113,710	02/24/2023	Bobby E. ROGERS	069366-0574153_KUR2C04US	2715
27500	7590	09/08/2023	EXAMINER	
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)			ABOUELELA, MAY A	
ATTENTION: DOCKETING DEPARTMENT			ART UNIT	
P.O BOX 10500			PAPER NUMBER	
McLean, VA 22102			3791	

DATE MAILED: 09/08/2023

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. 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 disclosure of these records is required by the Freedom of Information Act.
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 inspection 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.

Notice of Allowability	Application No. 18/113,710	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 08/29/2023.
☐ 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 17-31. 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 _____.	5. ☐ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☒ Other <u>A.NE.</u>
---	---

/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 05/10/2023. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Allowable Subject Matter

3. Claims 17-31 are allowed.
4. The following is an examiner's statement of reasons for allowance: the most pertinent prior art Christensen et al (2010/0057004) teaches a device comprising: an inlet port for receiving a blood sample; an outlet port; a chamber connected with the inlet port and the outlet port, and configured to collect a first portion of the blood sample, the chamber including a material that is air permeable and blood impermeable.

The prior art does not teach, disclose and/or fairly suggest a sampling channel connected with the inlet port and configured to convey a subsequent portion of the blood sample to the outlet port while bypassing the chamber.

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

<i>Notice of References Cited</i>	Application/Control No. 18/113,710		Applicant(s)/Patent Under Reexamination ROGERS et al.	
	Examiner MAY A ABOUELELA		Art Unit 3791	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20160073937-A1	03-2016	Burkholz; Jonathan Karl	A61B5/150251	604/524
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

<i>Search Notes</i> 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

CPC - Searched*		
Symbol	Date	Examiner
A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068	05/08/2023	MA
updated as above	08/22/2023	MA
updated as above	08/31/2023	MA

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
text search, class/subclass search, inventor name search	05/08/2023	MA
updated as above	08/22/2023	MA
updated as above	08/31/2023	MA

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
as above		08/31/2023	MA

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	
--	--

<i>Search Notes</i> 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	
--	--

<i>Index of Claims</i> 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS										
☐ Claims renumbered in the same order as presented by applicant					☐ CPA		☐ T.D.		☐ R.1.47	
CLAIM		DATE								
Final	Original	05/08/2023	08/22/2023	08/31/2023						
	1	✓	✓	-						
	2	✓	✓	-						
	3	✓	✓	-						
	4	✓	✓	-						
	5	✓	✓	-						
	6	✓	✓	-						
	7	✓	✓	-						
	8	✓	✓	-						
	9	✓	✓	-						
	10	✓	✓	-						
	11	✓	✓	-						
	12	✓	✓	-						
	13	✓	✓	-						
	14	✓	-	-						
	15	✓	-	-						
	16	✓	✓	-						
1	17		=	=						
2	18		=	=						
3	19		=	=						
4	20		=	=						
5	21		=	=						
6	22		=	=						
7	23		=	=						
8	24		=	=						
9	25		=	=						
10	26		=	=						
11	27		=	=						
12	28		=	=						
13	29		=	=						
14	30		=	=						
15	31		=	=						

Issue Classification 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

CPC						
Symbol					Type	Version
A61B	/	5	/	150992	F	2013-01-01
A61M	/	39	/	04	I	2013-01-01
A61B	/	5	/	150221	I	2013-01-01
A61B	/	5	/	15003	I	2013-01-01
A61B	/	5	/	150213	I	2013-01-01
A61B	/	5	/	150389	I	2013-01-01
A61B	/	5	/	150473	I	2013-01-01
A61B	/	5	/	150572	I	2013-01-01
A61B	/	5	/	154	I	2013-01-01
A61B	/	5	/	153	I	2013-01-01
A61M	/	39	/	0693	I	2013-01-01
A61M	/	2039	/	0202	A	2013-01-01
A61M	/	2039	/	068	A	2013-01-01
A61M	/	2039	/	0633	A	2013-01-01

CPC Combination Sets					
Symbol				Type	Set

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	15	
/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	31 August 2023	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	17	23A

Issue Classification 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

INTERNATIONAL CLASSIFICATION			
CLAIMED			
A61B	/	5	/ 00
NON-CLAIMED			
/		/	

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	15	
/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791	31 August 2023	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	17	23A

Issue Classification 	Application/Control No. 18/113,710	Applicant(s)/Patent Under Reexamination ROGERS et al.
	Examiner MAY A ABOUELELA	Art Unit 3791

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47															
CLAIMS															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		10	3	19	12	28								
	2		11	4	20	13	29								
	3		12	5	21	14	30								
	4		13	6	22	15	31								
	5		14	7	23										
	6		15	8	24										
	7		16	9	25										
	8	1	17	10	26										
	9	2	18	11	27										

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 15	
/MAY A ABOUELELA/ Primary Examiner, Art Unit 3791 (Primary Examiner) _____ (Date) _____		31 August 2023 O.G. Print Claim(s) 17	O.G. Print Figure 23A

Application No. 18/113,710

Attorney's Docket No.: 069366-0574153_KUR2C04US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Bobby E. Rogers, et al.

Confirmation No: 2715

Application No.: 18/113,710

Art Unit: 3791

Filed: February 24, 2023

Examiner: May A. Abouelela

For: Blood Sample Optimization Device

09/06/2023

Mail Stop AF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

OK TO ENTER: /M.A.A/

RESPONSE TO FINAL OFFICE ACTION

Dear Examiner Abouelela:

This reply is responsive to the Final Office Action mailed August 25, 2023, in the above-referenced matter (hereinafter "the Office Action"). Reconsideration and allowance of the application is requested in view of the following:

Listing of Claims beginning on page 2.

Remarks beginning on page 5.

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	18113710
	Filing Date	2023-02-24
	First Named Inventor	Bobby E. ROGERS
	Art Unit	-
	Examiner Name	
	Attorney Docket Number	069366-0574153_KUR2C04US

U.S.PATENTS						Remove
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1	5200325		1993-04-06	BLATT JOEL M	
	2	5432084		1995-07-11	BRUBAKER DANIEL B	
	3	5972294		1999-10-26	SMITH JOHN L	
	4	6187347		2001-02-13	PATTERSON JAMES A	
	5	6599474		2003-07-29	EVTDIENKO VLADIMIR	
	6	8197420		2012-06-12	PATTON RICHARD G	
	7	8535241		2013-09-17	BULLINGTON GREGORY	
	8	9060724		2015-06-23	BULLINGTON GREGORY J	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

9	9155495		2015-10-13	BULLINGTON GREGORY J	
10	4412548		1983-11-01	HOCH LOUIS	
11	5222502		1993-06-29	KUROSE KATSUTOSHI	
12	5520193		1996-05-28	SUZUKI ISSEI	
13	9022951		2015-05-05	BULLINGTON GREGORY	
14	6569117		2003-05-27	ZIV DAVID	
15	3741197		1973-06-26	SANZ M	
16	8603009		2013-12-10	TAN ALVIN CHEE LEONG	
17	4207870		1980-06-17	ELDRIDGE WILLIAM N	
18	9877675		2018-01-30	BAID RISHI	
19	4444203		1984-04-24	ENGELMAN ALLAN	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

20	6398743		2002-06-04	HALSETH THOR R	
21	9022950		2015-05-05	BULLINGTON GREGORY	
22	4436098		1984-03-13	KAUFMAN JOSEPH	
23	9138572		2015-09-22	ZEYTOONIAN PAUL	
24	8568371		2013-10-29	SIOPEs WILLIAM	
25	8540663		2013-09-24	DAVEY CHRISTOPHER T	
26	8523826		2013-09-03	LAYTON JR RUSSELL K	
27	4057050		1977-11-08	SARSTEDT WALTER	
28	8864684		2014-10-21	BULLINGTON GREGORY J	
29	5749857		1998-05-12	CUPPY MICHAEL J	
30	9204864		2015-12-08	BULLINGTON GREGORY J	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

31	3874367		1975-04-01	AYRES WALDEMAR A	
32	3886930		1975-06-03	RYAN GEORGE R	
33	4106497		1978-08-15	PERCARPIO EDWARD P	
34	4154229		1979-05-15	NUGENT EDWARD L	
35	4980297		1990-12-25	HAYNES JOHN L	
36	9820682		2017-11-21	ROGERS BOBBY E	
37	10010282		2018-07-03	ROGERS BOBBY E	
38	10143412		2018-12-04	ROGERS BOBBY E	
39	11185266		2021-11-30	ROGERS BOBBY E	
40	10827964		2020-11-10	ROGERS BOBBY E	
41	11311219		2022-04-26	ROGERS BOBBY E	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

42	3817240	1974-06-18	AYRES W
43	3648684	1972-03-14	BARNWELL CLEORA W
44	4056101	1977-11-01	GEISSLER ULRICH C
45	4416290	1983-11-22	LUTKOWSKI LAWRENCE
46	3070725	2011-12-06	CHRISTENSEN KELLY D
47	4349035	1982-09-14	THOMAS JOSEPH J
48	4813433	1989-03-21	DOWNEY JOHN M
49	5401262	1995-03-28	KARWOSKI THEODORE
50	3859998	1975-01-14	THOMAS JOSEPH JOHN
51	4373535	1983-02-15	MARTELL MICHAEL D
52	4690154	1987-09-01	WOODFORD TIMOTHY

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

53	5097842		1992-03-24	BONN GINA B	
54	5865803		1999-02-02	MAJOR MIKLOS	
55	5873841		1999-02-23	BRANNON JAMES K	
56	6013037		2000-01-11	BRANNON JAMES K	
57	6913580		2005-07-05	STONE BENJAMIN CURTIS	
58	11213232		2022-01-04	VOSEVIC MILAN	
59	6626884		2003-09-30	DILLON JAGMOHANBIR SINGH	
60	4904240		1990-02-27	HOOVER ROCKLIN L	
61	4673386		1987-06-16	GORDON MARK G	
62	7461671		2008-12-09	EHWALD RUDOLF	
63	6506182		2003-01-14	ESTABROOK BRIAN K	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

64	3382865	1968-05-14	WORRALL JR ASHTON L
65	3848579	1974-11-19	VILLA REAL A
66	6106509	2000-08-22	LOUBSER PAUL G
67	3494352	1970-02-10	RUSSO RONALD D
68	6224561	2001-05-01	SWENDSON DAVID L
69	7055401	2006-06-06	PRYBELLA JOHN R
70	5135489	1992-08-04	UEPSON STEVEN C
71	5811658	1998-09-22	VAN DRIEL MICHAEL R
72	3604410	1971-09-14	WHITACRE GARY L
73	5772608	1998-06-30	DHAS V VARAPRABHU
74	4150089	1979-04-17	LINET MICHAEL S

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

75	4257416		1981-03-24	PRAGER DAVID	
76	4193400		1980-03-18	LOVELESS JAMES C	
77	6843775		2005-01-18	HYUN DONGCHUL D	
78	7666166		2010-02-23	EMMERT MICHAEL	
79	7479131		2009-01-20	MATHIAS JEAN-MARIE	
80	8377040		2013-02-19	BURKHOLZ JONATHAN KARL	
81	5417673		1995-05-23	GORDON MARK G	
82	6638252		2003-10-28	MOULTON WILLIAM G	
83	3945380		1976-03-23	DABNEY WILLIAM C	
84	5100394		1992-03-31	DUDAR THOMAS E	
85	8827958		2014-09-09	BIERMAN STEVEN F	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

86	8574203		2013-11-05	STOUT MARTY L	
87	6860871		2005-03-01	KURACINA THOMAS C	
88	6945948		2005-09-20	BAINBRIDGE MARLENE	
89	7306736		2007-12-11	COLLINS GREGORY R	
90	5691486		1997-11-25	BEHRINGER BRUCE E	
91	5980830		1999-11-09	SAVAGE DOUGLAS ROBERT	
92	5045185		1991-09-03	OHNAKA YUKIHIRO	
93	5632906		1997-05-27	ISHIDA NOBORU	
94	6695004		2004-02-24	RAYBUCK JOHN L	
95	6733433		2004-05-11	FELL CLAUDE	
96	7241281		2007-07-10	COELHO PHILIP H	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

97	8349254		2013-01-08	HOSHINO YOSHITERU	
98	5439450		1995-08-08	HAEDT LORI E	
99	6905483		2005-06-14	NEWBY C MARK	
100	5431811		1995-07-11	TUSINI ANDREA	
101	6736783		2004-05-18	BLAKE KEVIN R	
102	7052603		2006-05-30	SCHICK KARL G	
103	3835835		1974-09-17	THOMPSON R	

If you wish to add additional U.S. Patent citation information please click the Add button.

Add

U.S.PATENT APPLICATION PUBLICATIONS

Remove

Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1	20010044615		2001-11-22	AMANO YOSHIKAZU	
	2	20030082074		2003-05-01	JURIK FRANKLIN A	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

3	20030185707		2003-10-02	WAKI YOSHIHIDE	
4	20040116830		2004-06-17	TRUDEAU WILLIAM M	
5	20090299253		2009-12-03	HURSEY FRANCIS X	
6	20130158506		2013-06-20	HARRIS ADRIENNE ROSE	
7	20150246352		2015-09-03	BULLINGTON GREGORY J	
8	20150342510		2015-12-03	BULLINGTON GREGORY J	
9	20160361006		2016-12-15	BULLINGTON GREGORY J	
10	20170065733		2017-03-09	BULLINGTON GREGORY J	
11	20180140240		2018-05-24	BULLINGTON GREGORY J	
12	20140112841		2014-04-24	SCHOEN CHRISTIAN	
13	20180271425		2018-09-27	ROGERS BOBBY E	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

14	20080319346		2008-12-25	CRAWFORD JAMIESON	
15	20100057004		2010-03-04	CHRISTENSEN KELLY D	
16	20070088279		2007-04-19	SHUE MING-JENG	
17	20080145933		2008-06-19	PATTON RICHARD G	
18	20040054333		2004-03-18	THEEUWES FELIX	
19	20100010372		2010-01-14	BROWN LEROY R	
20	20080167577		2008-07-10	WEILBACHER EUGENE E	
21	20080086085		2008-04-10	BROWN LEROY R	
22	20070083162		2007-04-12	O'REAGAN JAMES	
23	20160008579		2016-01-14	BURKHOLZ JONATHAN KARL	
24	20120016266		2012-01-19	BURKHOLZ JONATHAN KARL	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

25	20130317391		2013-11-28	BULLINGTON GREGORY J	
26	20160174888		2016-06-23	BERTHIER ERWIN	
27	20050240161		2005-10-27	CRAWFORD JAMIESON W M	
28	20040147855		2004-07-29	MARSDEN STEWART	
29	20040073171		2004-04-15	ROGERS BOBBY E	
30	20050004524		2005-01-06	NEWBY C MARK	
31	20030105414		2003-06-05	LEONG ALVIN TAN CHEE	
32	20020004647		2002-01-10	LEONG ALVIN TAN CHEE	
33	20140155781		2014-06-05	BULLINGTON GREGORY J	
34	20030208151		2003-11-06	KRAUS MENACHEM	
35	20090227953		2009-09-10	TAN CHEE LEONG	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

36	20170020428		2017-01-26	ROGERS BOBBY E	
37	20170020427		2017-01-26	ROGERS BOBBY E	
38	20050005635		2005-01-13	LE METAIS MARC	
39	20050007524		2005-01-13	LUO FANG-CHEN	
40	20140039348		2014-02-06	BULLINGTON GREGORY J	
41	20140107564		2014-04-17	BULLINGTON GREGORY J	
42	20140155782		2014-06-05	BULLINGTON GREGORY J	
43	20140276578		2014-09-18	BULLINGTON GREGORY J	
44	20160017488		2016-01-21	KOBAYASHI MASAYUKI	
45	20180177445		2018-06-28	ROGERS BOBBY E	
46	20180353117		2018-12-13	BULLINGTON GREGORY J	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

47	20190159711		2019-05-30	ROGERS BOBBY E	
48	20050245885		2005-11-03	BROWN LEROY	
49	20110306899		2011-12-15	BROWN LEROY R	
50	20130116599		2013-05-09	BULLINGTON GREGORY J	
51	20050273019		2005-12-08	CONWAY HUGH	
52	20150351678		2015-12-10	BULLINGTON GREGORY	
53	20220160271		2022-05-26	VOSEVIC MILAN	
54	20050161112		2005-07-28	EHWALD RUDOLF	
55	20070119508		2007-05-31	WEST RICHARD L	
56	20220304600		2022-09-29	HAMMER JEREMY	

If you wish to add additional U.S. Published Application citation information please click the Add button.

Add

FOREIGN PATENT DOCUMENTS

Remove

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ²	Kind Code ⁴	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear	T ⁵
	1	2593169A1	EP		2013-05-22	BECTON DICKINSON CO		
	2	2009131273A	JP		2009-06-18	CSL BEHRING GMBH		×
	3	2010062734A1	WO		2010-06-03	UNIV MARYLAND		☐
	4	2013082301A1	WO		2013-06-06	TELEFLEX MEDICAL INC		☐
	5	1378602A	GB		1974-12-27	BECTON DICKINSON CO		☐
	6	2019055487A1	WO		2019-03-21	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	7	2019232196A1	WO		2019-12-05	MAGNOLIA MEDICAL TECHNOLOGIES INC		☐
	8	H08257018	JP		1996-10-08	NISSHO KK		☒
	9	1665986	EP		2006-06-07	BECTON DICKINSON CO		☐
	10	2011162772A1	WO		2011-12-29	CLEARVIEW PATIENT SAFETY TECHNOLOGIES LLC		☐

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

11	2993646	CA		2017-02-02	KURIN INC	☐
12	3324845A1	EP		2018-05-30	KURIN INC	☐
13	3562397A1	EP		2019-11-06	KURIN INC	☐
14	3622890A1	EP		2020-03-18	KURIN INC	☐
15	5789869B2	JP		2015-10-07	TOHO ENGINEERING KK,	☒
16	5867238B2	JP		2016-02-24	FUJITSU LTD,	☒
17	6643474B2	JP		2020-02-12	クリン インコーポレイ テッド	☒
18	6734490	JP		2020-08-05	クリン インコーポレイ テッド	☒
19	2001000424	JP		2001-01-09	NISSHO KK	☒
20	2012016496A	JP		2012-01-26	TERUMO CORP	☒
21	2016504075	JP		2016-02-12	マグノリア メディカル テクノロジーズ, イン コーポレイテッド	☒

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

22	2019534792A	JP		2019-12-05	プライメタルズ・テクノロジー・オーストラリア・ゲーエムベーハー	☒
23	H09504726A	JP		1997-05-13	BAXTER INT	☒
24	9605875A1	WO		1996-02-29	BAXTER INT	☐
25	2013181352A1	WO		2013-12-05	MAGNOLIA MEDICAL TECHNOLOGIES INC	☐
26	2014058945	WO		2014-04-17	BULLINGTON GREGORY J	☐
27	2017019552A1	WO		2017-02-02	KURIN INC	☐
28	2018125929A1	WO		2018-07-05	KURIN INC	☐
29	S5825146A	JP		1983-02-15	BECTON DICKINSON CO	☒
30	S5867238A	JP		1983-04-21	BECTON DICKINSON CO	☒
31	5643474	JP		2014-12-17	ヴェロシス, インク.	☒
32	5825146B2	JP		2015-12-02	JVC KENWOOD CORP,	☒

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

33	2020000340A	JP	2020-01-09	TOSHO INC	☒
34	2013240628	JP	2013-12-05	COVIDIEN LP	☒
35	H02224742	JP	1990-09-06	SPACELABS INC	☒
36	S5789869	JP	1982-06-04	BECTON DICKINSON CO	☒
37	2005349196	JP	2005-12-22	BECTON DICKINSON CO	☒
38	10243129	DE	2004-04-01	RITTER GMBH	☒
39	7203008	DE	1972-05-10	IMMUNO AG FUER CHEM-MED PROD	☒
40	10038026	DE	2001-02-22	ZIERDEN PETER	☒
41	29913417	DE	2000-12-28	ZIERDEN PETER	☒
42	10134913	DE	2003-02-20	HIBERNA AG	☒
43	10134913C2	DE	2003-06-26	HIBERNA AG	☒

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

44	2541494	DE	1977-03-31	GUERRA LUIS A	☒
45	2008101025	WO	2008-08-21	EDWARDS LIFESCIENCES CORP	☐
46	0448795A2	EP	1991-10-02	BECTON DICKINSON CO	☐
47	199216144	WO	1992-10-01	GOLDSPILL PTY. LTD.	☐
48	2007033319A1	WO	2007-03-22	EDWARDS LIFESCIENCES CORP	☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T ⁵
	1	International Search Report and Written Opinion dated Nov. 5, 2015, for PCT application No. PCT/US2015/035870. 6 pages.	
	2	International Search Report and Written Opinion dated 16 July 2020 for PCT application no. PCT/US2020/026276. 9 pages.	
	3	Bullington, et al., Systems and Methods for Sample Collection with Reduced Hemolysis, Exhibit H in U.S. Appl. No. 62/517,681, dated Jun. 9, 2017, 131 pages.	
	4	Communication Under Rule 71(3) EPC dated Apr. 22, 2020 for EP application No. 17840467.9. 125 pages.	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

5	European Patent Application No. EP19200766.4 extended European Search Report dated Dec. 2, 2019, 11 pages.
6	European Patent Office, Extended European Search Report for European Patent Application 20197213.0-1132, dated Dec. 9, 2020, 6 pages.
7	European Patent Office; Communication pursuant to Article 94(3) EPC; dated Oct. 31, 2018; 11 pages.
8	Examination Report No. 1 dated Apr. 29, 2020, for Australian Patent Application No. 2016297849. 3 pages.
9	International Search Report and Written Opinion dated Jun. 19, 2020, for PCT application No. PCTUS2020/023617. 12 pages.
10	European Patent Office, International Search Report and Written Opinion for PCT/US16/43709, dated Oct. 19, 2016, 14 pages.
11	International Search Report/Written Opinion for PCT/US17/68569 dated Apr. 25, 2018. 9 pages.
12	European Patent Office, International Search Report/Written Opinion for PCT/US17/068569 dated Apr. 25, 2018, 9 pages.
13	International Search Report and Written Opinion for PCT/US16/43709, Dated October 19, 2016. 13 pages.
14	Retractable Techs., Inc. v. Becton Dickinson & Co., CA No. 2:07-CV-250, Claim Construction Order (E.D. Tex., Jan. 20, 2009). 20 pages.
15	Hillyer, Christopher D., et al. "Bacterial Contamination of Blood Components: Risks, Strategies and Regulation," Hematology, 2003, pp. 575-589.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

16	De Korte, Dirk, et al. "Diversion of first blood volume results in a reduction of bacterial contamination for whole-blood collections." Vox sanguinis 83.1 (2002): 13-16.
17	Brecher, Mark E., et al. "Bacterial contamination of blood components." Clinical microbiology reviews 18.1 (2005): 195-204.
18	Van Zundert, Adrien. "New closed IV catheter system." Acta Anæsthesiologica Belgica 56.3 (2005): 283-285.
19	Hall, Keri K., et al. "Updated review of blood culture contamination." Clinical microbiology reviews 19.4 (2006): 788-802.
20	Li, Yiwen, et al. "Direct labeling and visualization of blood vessels with lipophilic carbocyanine dye Dil." Nature protocols 3.11 (2008): 1703-1708.
21	Page, Catherine, et al. "Blood conservation devices in critical care: a narrative review." Annals of intensive care 3 (2013): 1-6.
22	Abbott Point of Care, Cartridge and Test Information, Art: 714258-010; Rev. Date: 15-Aug-16, 1-6 pages.
23	Zimmon, David S. et al. "Effect of portal venous blood flow diversion on portal pressure." The Journal of Clinical Investigation 65.6 (1980): 1388-1397.
24	Patton, Richard G., et al. "Innovation for reducing blood culture contamination: initial specimen diversion technique." Journal of clinical microbiology 48.12 (2010): 4501-4503.
25	Tang, Menglin, et al. "Closed blood conservation device for reducing catheter-related infections in children after cardiac surgery." Critical Care Nurse 34.5 (2014): 53-60.
26	Ernst, Dennis J. et al. "NCCLS simplifies the order of draw: a brief history." MLO: medical laboratory observer 36.5 (2004): 1-5 pages.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

27	Gottlieb, T. "Hazards of bacterial contamination of blood products." Anaesthesia and intensive care 21.1 (1993): 20-23.
28	Norberg, Alonna, et al. "Contamination rates of blood cultures obtained by dedicated phlebotomy vs intravenous catheter." Jama 289.6 (2003): 726-729.
29	Quilici, Nathalie, et al. "Differential quantitative blood cultures in the diagnosis of catheter-related sepsis in intensive care units." Clinical infectious diseases 25.5 (1997): 1066-1070.
30	Napolitano, Marcello, et al. "Quality control of bacterial contamination of blood components: the feasibility of diversion system testing." Blood Transfus 2 (2004): 231-232.
31	De Korte, Dirk, et al. "Effects of skin disinfection method, deviation bag, and bacterial screening on clinical safety of platelet transfusions in the Netherlands." Transfusion 46.3 (2006): 476-485.
32	Liumbruno, Giancarlo Maria, et al. "Reduction of the risk of bacterial contamination of blood components through diversion of the first part of the donation of blood and blood components." Blood Transfusion 7.2 (2009): 86.
33	NCCLS. Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Fifth Edition. H3-A5, Vol. 23, No. 32. Replaces H3-A4; Vol. 18, No. 7. 1-52 pages. http://demo.nextlab.ir/Organization/Documents/CLSI-Standards/CLSI-H3-A5.aspx
34	Challiner, A., et al. "Venous/arterial blood management protection system." Anaesthesia 47.2 (1992): 169-169.
35	Murphy, Michael F. "Better Blood Transfusion." Journal of the Intensive Care Society 4.3 (2003): 78-80.
36	Palavecino, Elizabeth L., et al. "Detecting bacterial contamination in platelet products." Clinical laboratory 52.9-10 (2006): 443-456.
37	Sheppard, Chelsea A., et al. "Bacterial contamination of platelets for transfusion: recent advances and issues." Laboratory Medicine 36.12 (2005): 767-770.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

38	Shulman, Gerald. "Quality of processed blood for autotransfusion." JOURNAL OF EXTRACORPOREAL TECHNOLOGY 32.1 (2000): 11-19.
39	Weinbaum, Fredric I., et al. "Doing it right the first time: quality improvement and the contaminant blood culture." Journal of Clinical Microbiology 35.3 (1997): 563-565.
40	Weinstein, Melvin P. "Blood culture contamination: persisting problems and partial progress." Journal of clinical microbiology 41.6 (2003): 2275-2278.
41	Weinstein, Melvin P., et al. "The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults." Clinical Infectious Diseases 24.4 (1997): 584-602.
42	Weinstein, Melvin P. "Current blood culture methods and systems: clinical concepts, technology, and interpretation of results." Clinical infectious diseases 23.1 (1996): 40-46.
43	Closed IV, BD Saf-T-Intima. "Catheter System, Becton, Dickinson and Company, Brochure." Retrieved from the Internet (August 23, 2019). 4 pages.
44	Perez, P., et al. "Multivariate analysis of determinants of bacterial contamination of whole-blood donations." Vox Sanguinis 82.2 (2002): 55-60.
45	McDonald, Carl P. "Interventions implemented to reduce the risk of transmission of bacteria by transfusion in the English National Blood Service." Transfusion Medicine and Hemotherapy 38.4 (2011): 255-258.
46	Lifesciences, Edwards. "Conservation. Safety. Simplicity. Edwards VAMP and VAMP Jr. Systems." (2002). 4 pages.
47	Sheppard, et al., Bacterial Contamination of Platelets for Transfusion: Recent Advances and Issues, LABMEDICINE, Vol. 36, No. 12, Dec. 2005 ("Sheppard 2005").
48	BD Diagnostics, "Venous Blood Collection, BD Vacutainer Passive Shielding Blood Collection Needle " literature (2005) 2 pages.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

49

Barnard, Dorothy R., et al. "Fibronectin (cold insoluble globulin) in the neonate," The Journal of Pediatrics, Vol. 102, Issue 3, March 1983, Pages 453-455.

If you wish to add additional non-patent literature document citation information please click the Add button

Add

EXAMINER SIGNATURE

Examiner Signature	/MAY A ABOUELELA/	Date Considered	08/31/2023
--------------------	-------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	18113710
Filing Date	2023-02-24
First Named Inventor	Bobby E. ROGERS
Art Unit	-
Examiner Name	
Attorney Docket Number	069366-0574153_KUR2C04US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Benjamin F. Hudson/	Date (YYYY-MM-DD)	2023-05-10
Name/Print	Benjamin F. Hudson	Registration Number	71,474

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent 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.

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	0	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/20 11:05 PM
L2	1	("20020099309").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 11:38 AM
L3	1	("14055232").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 11:39 AM
L4	1763	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 05:18 PM
L5	63	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:19 PM
L6	28	("2004/0073171").URP N.	(USPAT)	OR	OFF	OFF	2016/12/21 05:36 PM
L7	0	("1and(bloodnear4sequest\$5)").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 05:41 PM
L8	5225	1and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:42 PM
L9	7	L4 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:42 PM
L10	73	("20020002349" "20020183651" "20030055381" "20040010228" "20040054333" "20040147855" "20050004524" "20050240161" "20050245885" "20050281713" "20060287639" "2707953" "3013557" "3098016" "3382865" "3405706" "3494351" "3577980" "3648684" "3848579" "3937211" "4057050" "4133863" "4166450" "4340067" "4370987" "4444203" "4459997" "4509534" "4676256" "4865583" "4890627" "4988339" "5009847" "5097842" "5108927" "5122129" "5269317" "5360011" "5429610" "5450856" "5507299" "5577513" "5762633" "5882318" "5922551" "6016712" "6057105" "6159164" "6210909" "6364890" "6387086" "6403381"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:43 PM

L11	2	"6692479" "6746420" "6913580" "7044941" "7087047").PN. OR ("8197420").URPN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:44 PM
L12	77	("0453322" "0577682" "0729011" "1074965" "1110189" "1450016" "1521890" "2218899" "2688325" "2895773" "3176595" "3214069" "3236268" "3263874" "3486503" "3577980" "3754644" "3794221" "3834387" "3855997" "3937211" "3958570").PN. OR ("4057050").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2016/12/21 05:47 PM
L13	852	L4 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L14	46	L10 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 05:47 PM
L15	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:29 PM
L16	1	("20130317391").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:42 PM
L17	1254	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2016/12/21 06:43 PM
L18	1070	L17 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2016/12/21 06:43 PM
L19	265030	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:09 PM
L20	5653	L19 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L21	207	L20 and (seal near4 air)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 07:10 PM
L22	23	"2004087258"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2016/12/21 08:59 PM
L23	1	("20050004524").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 08:23 PM
L24	1	("20030105414").PN.	(US-PGPUB; USPAT;	OR	ON	ON	2017/04/11

L25	1	("5749857").PN.	USOCR) (US-PGPUB; USPAT; USOCR)	OR	ON	ON	08:24 PM 2017/04/11 08:26 PM
L26	13	("20040073171" "20040 147855" "20050240161 " "20130317391" "2016 0174888" "4057050" "8 197420" "8523826" "85 35241" "8540663" "856 8371" "8864684" "9138 572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 08:39 PM
L27	1	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 09:43 PM
L28	0	("4and(bloodnear4air)").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/11 10:01 PM
L29	3	L26 and (blood near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:01 PM
L30	6	L26 and vent\$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/11 10:02 PM
L31	5	("2013/0317391").URP N.	(USPAT)	OR	OFF	OFF	2017/04/11 10:06 PM
L32	48	("2005/0004524").URP N.	(USPAT)	OR	OFF	OFF	2017/04/11 10:17 PM
L33	1	("20120170037").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/12 04:11 PM
L34	1	("6139540").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:52 PM
L35	1	("20040116878").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 12:54 PM
L36	1	("20100152752").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:16 PM
L37	1	("6395003").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:20 PM
L38	5	("2013/0317391").URP N.	(USPAT)	OR	OFF	OFF	2017/04/13 01:43 PM
L39	1	("4444203").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:44 PM
L40	1	("20020004647").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:48 PM
L41	1	("3817240").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L42	1	("3874367").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:57 PM
L43	1	("3886930").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:58 PM
L44	1	("4106497").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM
L45	1	("4154229").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 01:59 PM
L46	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:00 PM

L47	292	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2017/04/13 02:01 PM
L48	1	("4412548").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:04 PM
L49	1	("5222502").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:11 PM
L50	1	("5520193").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:15 PM
L51	1	("20100057004").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:16 PM
L52	1	("20070088279").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 02:29 PM
L53	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/04/13 03:29 PM
L54	13	L53 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 03:52 PM
L55	1255	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/13 04:23 PM
L56	4	L55 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:23 PM
L57	272301	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L58	5898	L57 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/04/13 04:29 PM
L59	114	L58 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/04/13 04:29 PM
L60	2	("2007/0088279").URPN.	(USPAT)	OR	OFF	OFF	2017/04/13 05:58 PM
L61	1	("6358217").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/04/21 02:02 PM
L62	6	("2002/0004647").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 12:48 PM
L63	2	("14493796").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:21 PM
L64	2	("14494208").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:23 PM
L65	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/27 01:28 PM
L66	1	("20080145933").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:51 PM
L67	9	("2008/0145933").URPN.	(USPAT)	OR	OFF	OFF	2017/09/27 01:55 PM
L68	1	("20040054333").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 01:59 PM

L69	1	("20120109034").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:37 PM
L70	1	("20100228206").PN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/27 02:39 PM
L71	3	("2010/0228206").URP N.	(USPAT)	OR	OFF	OFF	2017/09/27 02:47 PM
L72	66	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:41 PM
L73	4	L72 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:42 PM
L74	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:58 PM
L75	845	L74 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:58 PM
L76	9	L75 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L77	86	("2007/0083162").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 01:59 PM
L78	1	("15140443").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 01:59 PM
L79	9	("2008/0145933").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 02:04 PM
L80	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2017/09/28 02:20 PM
L81	1071	L80 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:20 PM
L82	78	L81 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 02:21 PM
L83	282596	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L84	6183	L83 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2017/09/28 04:01 PM
L85	387	L84 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:01 PM
L86	362	L85 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:02 PM
L87	12	("2005/0010189").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 04:03 PM
L88	1363	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:04 PM
L89	74	L88 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:05 PM
L90	21	("3965910" "3996923"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2017/09/28

		"4131127" "4301811" "4450854" "4506691" "4819684" "5147333" "5393035" "5636975").PN. OR ("6569117").URPN.	USOCR)				04:09 PM
L91	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2017/09/28 04:12 PM
L92	18	L91 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:12 PM
L93	9	("2008/0145933").URP N.	(USPAT)	OR	OFF	OFF	2017/09/28 04:13 PM
L95	67	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:23 PM
L96	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:25 PM
L97	4	L96 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:25 PM
L98	3	L97 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:26 PM
L99	1733	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 04:50 PM
L100	13	L99 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:50 PM
L101	255	("1779451" "2004050" "2700385" "2836942" "2854976" "2953243" "3021942" "3073307" "3074542" "3255873" "3294231" "3323523" "3329146" "3333682" "3367488" "3382865" "3485239" "3537452" "3585984" "3610240" "3658061" "3664879" "3817240" "3828775" "3859998" "3874367" "3886930" "3890971" "3904033" "3934722" "3968876" "4106497" "4108175" "4113090" "4139009" "4154229" "4166450" "4175008" "4193400" "4207870" "4269186" "4300678" "4312362" "4317445" "4340068" "4375849" "4398544" "4409990" "4412548" "4416290" "4416291" "4418703" "4430082" "4436098" "4444203" "4592744"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/01/09 04:51 PM

		"4634428"	"4643722"				
		"4659330"	"4664249"				
		"4664654"	"4671408"				
		"4679571"	"4681567"				
		"4695274"	"4702738"				
		"4723943"	"4728320"				
		"4728321"	"4731059"				
		"4735311"	"4735618"				
		"4737144"	"4738663"				
		"4743233"	"4746008"				
		"4747836"	"4747837"				
		"4772272"	"4778453"				
		"4781697"	"4782841"				
		"4788986"	"4790828"				
		"4793484"	"4795432"				
		"4795443"	"4801295"				
		"4804372"	"4813426"				
		"4816022"	"4816024"				
		"4819659"	"4820277"				
		"4826490"	"4826491"				
		"4838871"	"4842587"				
		"4844089"	"4846796"				
		"4850968"	"4850976"				
		"4850977"	"4850978"				
		"4850994"	"4850996"				
		"4858607"	"4863434"				
		"4863435"	"4863436"				
		"4865592"	"4867746"				
		"4872552"	"4874383"				
		"4874384"	"4883469"				
		"4886072"	"4886503"				
		"4888001"	"4892107"				
		"4892521"	"4894052"				
		"4900309"	"4909791"				
		"4909792").PN. OR					
		("4921096"	"4927018"				
		"4944397"	"4966591"				
		"4971068"	"4976699"				
		"4982842"	"5011475"				
		"5011479"	"5030207"				
		"5032116"	"5033476"				
		"5055102"	"5069225"				
		"5078693"	"5078698"				
		"5092845"	"5112327"				
		"5116325"	"5120319"				
		"5122121"	"5135509"				
		"5137518"	"5139489"				
		"5151089"	"5154285"				
		"5181523"	"5188611"				
		"5197954"	"5201794"				
		"5207653"	"5217025"				
		"5222502"	"5232454"				
		"5232455"	"5242411"				
		"5242417"	"5277311"				
		"5290246"	"5295969"				
		"5303713"	"5306259"				
		"5312369"	"5401251"				
		"5405332"	"5423765"				

		"5450856" "5462534" "5485854" "5486163" "5490841" "5496281" "5509907" "5520193" "5533984" "5542932" "5584816" "5599313" "5599318" "5603699" "5632732" "5643219" "5662617" "5665075" "5669889" "5693022" "5697914" "5702369" "5733265" "5755701" "5807351" "5830190" "5836920" "5885249" "5893844" "5913846" "5984895" "5993426" "6059737" "6077244" "6077253" "6080137" "6096006" "6110160" "6120482" "6156010" "6190370" "6261263" "6511439" "6533760" "6964658" "7160267" "RE31086").PN. OR ("7615033").URPN.					
L102	215	L101 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 04:51 PM
L103	1347	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:11 PM
L104	17	L103 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L105	19	("2009/0312711").URP N.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L106	11	("2007/0106220").URP N.	(USPAT)	OR	OFF	OFF	2018/01/09 05:11 PM
L107	288967	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L108	6321	L107 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/01/09 05:16 PM
L109	121	L108 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:17 PM
L110	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/01/09 05:31 PM
L111	6	L110 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:31 PM
L113	71	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:31 PM
L114	0	("15140443").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:38 PM

L115	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:38 PM
L116	2	(15/140448).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 01:40 PM
L117	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 01:56 PM
L118	854	L117 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:56 PM
L119	91	L118 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 01:57 PM
L120	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:06 PM
L121	1074	L120 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:06 PM
L122	80	L121 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:06 PM
L123	301210	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/07/24 02:11 PM
L124	6556	L123 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2018/07/24 02:11 PM
L125	3664	L124 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L126	12749	"19" and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L127	117	L125 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:12 PM
L128	1348	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:16 PM
L129	75	L128 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:17 PM
L130	1	("20120291564").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 02:21 PM
L131	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 02:25 PM
L132	18	L131 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/07/24 02:25 PM
L133	98	("20020002349" "20020183651" "20030055381" "20030208151" "20040010228" "20040054333" "20040147855" "20050004524"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:44 PM

		"20050240161" "20050245885" "20050281713" "20060287639" "20080108954" "20080145933" "2707953" "3013557" "3098016" "3382865" "3405706" "3494351" "3577980" "3648684" "3848579" "3937211" "4057050" "4133863" "4166450" "4340067" "4370987" "4444203" "4459997" "4509534" "4657160" "4676256" "4865583" "4890627" "4988339" "5009847" "5097842" "5108927" "5122129" "5269317" "5330464" "5360011" "5429610" "5450856" "5507299" "5577513" "5762633" "5865812" "5882318" "5922551" "6016712" "6057105" "6159164" "6210909" "6364890" "6387086" "6403381" "6626884" "6692479" "6746420" "6913580" "7044941" "7087047" "7335188" "7744573" "8197420" "8231546" "8337418").PN. OR ("8535241").URPN.					
L134	307	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:47 PM
L135	23	("4166450").PN. OR ("4412548").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L136	307	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2018/07/24 02:48 PM
L137	4	("2007/0088279").URP N.	(USPAT)	OR	ON	ON	2018/07/24 02:48 PM
L138	1	(14/990763).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/24 02:58 PM
L139	9	(blood and sequest\$5 and junction and first and portion and sampl\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2018/07/24 03:07 PM

L140	1	(15/287421).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/25 09:39 PM
L141	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2018/07/26 11:56 AM
L142	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:24 PM
L143	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 03:25 PM
L144	34	("20020004647" "20030105414" "20040054333" "20040073171" "20040147855" "20050004524" "20050240161" "20070088279" "20080145933" "20100057004" "20130317391" "20160174888" "3817240" "3874367" "3886930" "4057050" "4106497" "4154229" "4207870" "4412548" "5222502" "5520193" "5749857" "6569117" "8197420" "8523826" "8535241" "8540663" "8568371" "8864684" "9022951" "9060724" "9138572" "9204864").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 05:53 PM
L145	272	((("ROGERS") near3 ("Bobby")) OR ((("KANG") near3 ("Gino")) OR ((("STROUP") near3 ("David")) OR ((("COCHRAN") near3 ("Jonas")) OR ((("DEPTALA") near3 ("Arthur")) OR ((("DETLOFF") near3 ("John")) OR ((("POGUE") near3 ("Lonnie")) OR ((("MACOWSKI") near3 ("Brian")) OR ((("GARRETT") near3 ("Chad")))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/07 05:57 PM
L146	9	L145 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 05:58 PM
L147	34	("20020004647" "20030105414" "20040054333" "20040073171" "20040147855" "20050004524" "20050240161" "20070088279" "20080145933" "20100057004" "20130317391" "20160174888" "3817240" "38743	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 06:26 PM

		67" "3886930" "4057050" "4106497" "4154229" "4207870" "4412548" "5222502" "5520193" "5749857" "6569117" "8197420" "8523826" "8535241" "8540663" "8568371" "8864684" "9022951" "9060724" "9138572" "9204864").PN.					
L148	5	L147 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 06:29 PM
L149	6	("2010/0057004").URP N.	(USPAT)	OR	ON	ON	2019/11/07 06:40 PM
L150	0	L149 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:20 PM
L151	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:21 PM
L152	4	L151 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L153	1766	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:21 PM
L154	13	L153 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:21 PM
L155	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/07 07:22 PM
L156	48	L155 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:22 PM
L157	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L158	17	L157 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:43 PM
L159	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/07 07:43 PM
L160	6	L159 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L161	333030	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L162	6981	L161 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/11/07 07:44 PM
L163	139	L162 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:44 PM
L164	117	L163 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:45 PM
L165	1	L146 and (enclos\$3 near4 mechanism)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/11/07 07:51 PM
L166	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/08 04:57 PM

L167	1	(15/139716).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/11 12:09 PM
L168	1	(15/520430).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 11:02 AM
L169	1	("7637875").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:11 PM
L170	1	("20120253321").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:13 PM
L171	1	(15/861959).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/11/12 12:14 PM
L172	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 02:17 PM
L173	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:14 PM
L174	1	("20080167577").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:19 PM
L175	4	("2008/0167577").URP N.	(USPAT)	OR	ON	ON	2019/12/09 03:30 PM
L176	1	("8197420").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 03:31 PM
L177	39	(US-20040073171-\$ or US-20160174888-\$ or US-20050240161-\$ or US-20040147855-\$ or US-20130317391-\$ or US-20050004524-\$ or US-20030105414-\$ or US-20020004647-\$ or US-20100057004-\$ or US-20070088279-\$ or US-20080145933-\$ or US-20040054333-\$ or US-20100010372-\$ or US-20080319346-\$ or US-20080167577-\$).did. or (US-9138572-\$ or US-8568371-\$ or US-8540663-\$ or US-8523826-\$ or US-8197420-\$ or US-4057050-\$ or US-8864684-\$ or US-8535241-\$ or US-5749857-\$ or US-9060724-\$ or US-9204864-\$ or US-3817240-\$ or US-3874367-\$ or US-3886930-\$ or US-4106497-\$ or US-4154229-\$ or US-4207870-\$ or US-4412548-\$ or US-5222502-\$ or US-5520193-\$ or US-	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:37 PM

L178	8	9022951-\$ or US-6569117-\$ or US-3741197-\$ or US-8603009-\$).did. ("20040054333" "8197420" "9855001" "9861306" "10045724" "10028687" "8337418" "10028689").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 03:42 PM
L179	100	("20020002349" "20020183651" "20030055381" "20040010228" "20040054333" "20040147855" "20050004524" "20050240161" "20050245885" "20050281713" "20060287639" "2707953" "3013557" "3098016" "3382865" "3405706" "3494351" "3577980" "3648684" "3848579" "3937211" "4057050" "4133863" "4166450" "4340067" "4370987" "4444203" "4459997" "4509534" "4676256" "4865583" "4890627" "4988339" "5009847" "5097842" "5108927" "5122129" "5269317" "5360011" "5429610" "5450856" "5507299" "5577513" "5762633" "5882318" "5922551" "6016712" "6057105" "6159164" "6210909" "6364890" "6387086" "6403381" "6692479" "6746420" "6913580" "7044941" "7087047").PN. OR ("8197420").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 03:43 PM
L180	70	L179 and (blood near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 03:43 PM
L181	43	L180 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 03:44 PM
L182	270	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/12/09 04:13 PM

L183	335813	("Jay")) OR (("GAW") near3 ("Shan"))).INV. (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L184	7259	L183 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2019/12/09 04:22 PM
L185	325	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2019/12/09 04:33 PM
L186	594	L184 and (flash\$6 and seal\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L187	476	L186 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 04:40 PM
L188	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:14 PM
L189	1123	L188 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L190	1013	L189 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:15 PM
L191	10	L190 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:16 PM
L192	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:23 PM
L193	1143	L192 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L194	1038	L193 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L195	3	L194 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:23 PM
L196	811	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:24 PM
L197	618	L196 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L198	557	L197 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:24 PM
L199	1	(15/854273).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/09 05:25 PM
L200	1351	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:31 PM
L201	219	L200 and ((blood or	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09

L202	199	fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4)) L201 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	05:33 PM 2019/12/09 05:33 PM
L203	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2019/12/09 05:36 PM
L204	44	L203 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2019/12/09 05:37 PM
L205	1	(15/508871).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2019/12/10 11:58 AM
L206	342199	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/03/16 12:53 PM
L207	4239	L206 AND ((A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:53 PM
L208	146	L207 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:54 PM
L209	101	L208 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 12:55 PM
L210	1735	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:38 PM
L211	1123	L210 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:38 PM
L212	1013	L211 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L213	22	L212 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:39 PM
L214	108	("20020193748" "20030093009" "20030105414" "20030220614" "20030229315" "20040059302" "20040092872" "20040193120" "20050004524" "20050065482" "20050124944" "20050187493" "20050245868" "20050245869" "20050245870" "20050245879" "20050245885"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 01:46 PM

L215	26	"20060036219" "20060224122" "20070106220" "20070106224" "20070167914" "20080086085" "20080177202" "20080319345" "20080319346" "20090204026" "20100262038" "4106497" "4207870" "4305406" "4572210" "4573976" "4641663" "4795443" "4840619" "4894055" "4900307" "4994046" "5015241" "5195985" "5215534" "5222502" "5242417" "5246428" "5256153" "5295970" "5303713" "5312372" "5336199" "5348544" "5356392" "5411492" "5439449" "5466223" "5501675" "5542932" "5599313" "5662617" "5665075" "5672161" "5676658" "5702369" "5704920" "5733265" "5755522" "5957892" "5984899" "6149629" "6224576" "6254575" "6261263" "6298541" "6344032" "6436086" "6440104" "6524277" "6533760" "6592556" "6623456" "6635032" "6648855" "6695819" "6699217" "6712792" "6780169" "6837877" "6869415" "6984223" "7001363" "7128726" "7147624" "7160267" "7163526" "7223258" "7226432" "7396343" "7428773" "7537581" "7766879" "D422700" "D442280" "D604836" "D604837" "D604838" "D604839" "D605287").PN. OR ("8603009").URPN. L214 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:47 PM
------	----	--	-------------------	----	-----	-----	------------------------

L216	27	("2008/0319346").URP N.	(USPAT)	OR	ON	ON	2020/03/16 01:47 PM
L217	23	("2003/0105414").URP N.	(USPAT)	OR	ON	ON	2020/03/16 01:48 PM
L218	1258	(600/583).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 01:52 PM
L219	1143	L218 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L220	25	L219 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:52 PM
L221	353695	((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:54 PM
L222	3643	L221 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L223	1926	L222 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:55 PM
L224	785	L223 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 01:56 PM
L225	7046	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 02:32 PM
L226	14	L225 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:35 PM
L227	1352	(604/164.01).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:36 PM
L228	135	L227 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L229	19	L228 and (((vent\$4 or open\$5 or hole or aperture) near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:36 PM
L230	448	(435/294.1).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:47 PM
L231	3	L230 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:47 PM
L232	19	("2008/0145933").URP N.	(USPAT)	OR	ON	ON	2020/03/16 02:48 PM
L233	795	(600/576).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 02:58 PM
L234	71	L233 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:58 PM

L235	57	L234 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 02:59 PM
L236	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 03:12 PM
L237	11	L236 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:12 PM
L238	45	("20040054333" "20050 240161" "4412548" "57 49857" "8197420" "985 5001" "9861306" "2002 0004647" "2010005700 4" "3741197" "2004007 3171" "3874367" "4057 050" "4106497" "81974 20" "8535241" "854066 3" "8603009" "8864684" "10045724" "3817240" "10028687" "20030105 414" "5222502" "55201 93" "6569117" "856837 1" "20040147855" "200 70088279" "200801459 33" "20100010372" "38 86930" "8523826" "906 0724" "9204864" "8337 418" "20050004524" "2 0080167577" "2008031 9346" "20130317391" " 4154229" "9022951" "1 0028689" "2016017488 8" "4207870" "9138572").PN.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:13 PM
L239	6	("2008/0167577").URP N.	(USPAT)	OR	ON	ON	2020/03/16 03:13 PM
L240	118	("3500828" "3670729" "3714945" "3977400" "3994293" "3995619" "4106491" "4200096" "4468224" "4531987" "4549554" "4735215" "4828548" "4874373" "4893635" "4894052" "4907599" "4944308" "4994042" "5129884" "5400798").PN. OR ("5749857").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/03/16 03:15 PM
L241	6	("2008/0167577").URP N.	(US-PGPUB; USPAT)	OR	ON	ON	2020/03/16 03:15 PM
L242	274	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR (("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2020/03/16 03:25 PM

L243	61	L242 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:25 PM
L244	1	(15/854273).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 03:47 PM
L245	0	(14/502498).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:11 PM
L246	1	("20110082383").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:24 PM
L247	1	("8150506").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/16 04:24 PM
L252	1	(15/057214).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/03/17 11:28 AM
L253	348964	(blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/06/10 05:22 PM
L254	7453	L253 AND (A61B10/0096 OR A61B5/150022).CPC.)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2020/06/10 05:22 PM
L255	155	L254 and ((vent\$4 near4 air) and flash\$6)	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:23 PM
L256	77	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 05:35 PM
L257	343953	(blood same (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:40 PM
L258	11	L256 and (blood same (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 05:41 PM
L259	1	("5749857").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 05:50 PM
L260	121	("3500828" "3670729" "3714945" "3977400" "3994293" "3995619" "4106491" "4200096" "4468224" "4531987" "4549554" "4735215" "4828548" "4874373" "4893635" "4894052" "4907599" "4944308" "4994042" "5129884" "5400798").PN. OR ("5749857").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/06/10 06:19 PM
L261	32	L260 and (blood near4 (sequest\$5 or sampl\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:20 PM
L262	1	("3648684").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L263	1	("4056101").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:38 PM
L264	329	(600/577).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2020/06/10

L265	11	L264 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	06:39 PM 2020/06/10 06:39 PM
L266	29	("2008/0319346").URP N.	(USPAT)	OR	ON	ON	2020/06/10 06:40 PM
L267	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:40 PM
L268	72	L267 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:40 PM
L269	1767	(600/573).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:44 PM
L270	31	L269 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:45 PM
L271	77	("4676249" "4787891" "4850960" "4874382" "4886067" "4886500" "4900307" "4904242" "4917102" "4950252" "4955862" "5046508" "5116353" "5125718" "5129884" "5163911" "5217435" "5290244" "5295974" "5314503" "5318585" "5330432" "5360410" "5366441" "5376075" "5395337" "5531692" "5695475" "5695479" "5702367" "5735813" "5749857" "5788654" "5800395" "5846226" "5871470" "5882342" "5919172" "5935108" "5935113" "5989220" "6050976" "6077244" "6099504" "6126641" "6162195").PN. OR ("6398743").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2020/06/10 06:46 PM
L272	18	L271 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:46 PM
L273	1	(15/893518).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:48 PM
L274	7050	(600/300).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:49 PM
L275	14	L274 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:49 PM
L276	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 06:51 PM
L277	7	L276 and ((blood or	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10

L278	1368	fluid\$4) near4 (sequest\$5 or flash\$4)) (604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	06:51 PM 2020/06/10 06:52 PM
L279	135	L278 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:52 PM
L280	499	(435/294.1).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 07:08 PM
L281	3	L280 and ((blood or fluid\$4) near4 (sequest\$5 or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 07:08 PM
L282	20	("2008/0145933").URP N.	(USPAT)	OR	ON	ON	2020/06/10 07:08 PM
L286	1	("10045704").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/06/10 08:56 PM
L287	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:16 PM
L288	1	("10010282").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:17 PM
L289	100	((("ROGERS") near3 ("Bobby")) OR (("KANG") near3 ("Gino")) OR (("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/01 09:17 PM
L290	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:36 PM
L291	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/01 09:39 PM
L292	180	((("ROGERS") near3 ("Bobby"))).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/03/02 12:19 PM
L293	11	L292 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 12:20 PM
L294	2	(15/140443).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:47 PM
L295	1	(15/855439).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 12:49 PM
L296	1	("20020048170").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:36 PM
L297	1	("20040174525").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 01:49 PM
L298	1	("10045704").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 03:09 PM
L299	27321	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/03/02 03:17 PM

L300	4594	A61B5/154 or A61B5/153 or A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc. L299 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:27 PM
L301	3762	L300 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:28 PM
L302	257	L301 and (air near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L303	420	L301 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 03:29 PM
L304	1	("20110167658").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 03:30 PM
L305	5	("2015/0306288").URP N.	(USPAT)	OR	ON	ON	2021/03/02 04:15 PM
L306	1	(16/208559).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 04:32 PM
L307	2	("2009/0043225").URP N.	(USPAT)	OR	ON	ON	2021/03/02 04:49 PM
L308	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/03/02 05:00 PM
L309	1363	L308 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:00 PM
L310	73	L309 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L311	73	L310 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:01 PM
L312	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:34 PM
L313	711	L312 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L314	58	L313 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L315	58	L314 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:34 PM
L316	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:42 PM
L317	277	L316 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:42 PM

L318	20	L317 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:43 PM
L319	336	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/03/02 05:44 PM
L320	210	L319 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L321	196	L320 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:44 PM
L322	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:48 PM
L323	1208	L322 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L324	73	L323 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:48 PM
L325	73	L324 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 05:49 PM
L326	1368	(604/164.01).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/03/02 05:59 PM
L327	271	L326 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L328	10	L327 and ((air or gas\$4) near4 permeab\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L329	268	L327 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/03/02 06:00 PM
L330	182	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2021/07/08 02:22 PM
L331	27660	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/153 or A61M39/0693 or A61M39/04 or A61B5/150221 or A61M2039/0633 or A61M2039/0202 or A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2021/07/08 03:27 PM
L332	4684	L331 and ((blood or fluid\$4) near4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:28 PM

L333	3769	(sequest\$5 or sampl\$4 or flash\$4 or collect\$4)) L332 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L334	579	L333 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 03:29 PM
L335	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:54 PM
L336	1	("4207870").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 03:56 PM
L337	337	("2913000" "3817240" "3859998" "3864979" "4016879" "4046144").PN. OR ("4207870").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:19 PM
L338	211	L337 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L339	196	L338 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L340	37	L339 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:19 PM
L341	221	("20010021827" "20020004650" "20020055716" "20020072715" "20020103464" "20020103465" "20020107488" "20020151856" "20020193748" "20030028171" "20030036730" "20030050608" "20030055385" "20030078544" "20030093009" "20030105414" "20030114797" "20030120222" "20030176842" "20030181873" "20030191438" "20030199827" "20030216687" "20030220614" "20030229315" "20030229316" "20040024370" "20040059302" "20040092872" "20040102740" "20040111068" "20040193120"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM

		"20040204681" "20040210197" "20050004524" "20050059936" "20050065482" "20050124944" "20050165353" "20050187493" "20050228345" "20050245868" "20050245869" "20050245870" "20050245879" "20050245885" "20050283093" "20060015073" "20060036217" "20060036219" "20060079847" "20060129064" "20060189934" "20060189936" "20060224122" "20060270947" "20060276756" "20070021724" "20070027430" "20070106220" "20070106224" "20070167914" "20070282275" "20080015513" "20080086085" "20080177202" "20080221528" "20080269691" "20080306452" "20080319345" "20080319346" "20090204026" "20090227896" "20100063455" "20100191189" "20100262038" "20110118674" "4106497" "4207870" "4305406" "4572210" "4573976" "4641663" "4795443" "4813426" "4840619" "4887998" "4894055" "4900307" "4923477" "4994046" "5015241" "5195985" "5215534" "5219333" "5222502" "5242417" "5246428" "5256153").PN. OR ("5295970" "5295975"				
--	--	---	--	--	--	--

		"5303713"	"5312372"				
		"5318547"	"5336199"				
		"5344408"	"5348544"				
		"5356392"	"5389085"				
		"5403286"	"5411492"				
		"5439449"	"5466223"				
		"5501675"	"5542932"				
		"5549558"	"5595566"				
		"5599313"	"5607402"				
		"5662617"	"5665075"				
		"5669889"	"5672161"				
		"5676658"	"5681295"				
		"5685855"	"5687740"				
		"5688241"	"5695474"				
		"5702369"	"5704920"				
		"5718239"	"5733265"				
		"5755522"	"5769826"				
		"5795336"	"5879337"				
		"5893845"	"5910130"				
		"5921964"	"5957892"				
		"5984899"	"6149629"				
		"6171284"	"6183445"				
		"6224576"	"6254575"				
		"6261263"	"6261265"				
		"6298541"	"6344032"				
		"6419658"	"6436086"				
		"6440104"	"6471677"				
		"6475191"	"6485469"				
		"6524277"	"6533760"				
		"6554807"	"6575939"				
		"6592556"	"6623456"				
		"6623461"	"6635032"				
		"6641555"	"6648855"				
		"6648856"	"6659983"				
		"6695819"	"6699217"				
		"6712792"	"6716199"				
		"6761704"	"6773419"				
		"6780169"	"6805689"				
		"6811545"	"6835190"				
		"6837877"	"6846302"				
		"6860872"	"6869415"				
		"6905483"	"6918891"				
		"6958054"	"6974423"				
		"6984223"	"6997913"				
		"7001363"	"7083600"				
		"7101355"	"7128726"				
		"7147624"	"7160267"				
		"7163526"	"7201740"				
		"7211065"	"7223258"				
		"7226432"	"7361159"				
		"7396343"	"7428773"				
		"7524308"	"7537581"				
		"7670320"	"7727190"				
		"7766879"	"7938808"				
		"8066679"	"8282605"				
		"8795198"	"D422700"				
		"D442280"					
		"D604836"	"D604837"				

L342	115	"D604838" "D604839" "D605287" "RE35539" "RE43473").PN. OR ("9615783").URPN. ("20020193748" "20030093009" "20030105414" "20030220614" "20030229315" "20040059302" "20040092872" "20040193120" "20050004524" "20050065482" "20050124944" "20050187493" "20050245868" "20050245869" "20050245870" "20050245879" "20050245885" "20060036219" "20060224122" "20070106220" "20070106224" "20070167914" "20080086085" "20080177202" "20080319345" "20080319346" "20090204026" "20100262038" "4106497" "4207870" "4305406" "4572210" "4573976" "4641663" "4795443" "4840619" "4894055" "4900307" "4994046" "5015241" "5195985" "5215534" "5222502" "5242417" "5246428" "5256153" "5295970" "5303713" "5312372" "5336199" "5348544" "5356392" "5411492" "5439449" "5466223" "5501675" "5542932" "5599313" "5662617" "5665075" "5672161" "5676658" "5702369" "5704920" "5733265" "5755522" "5957892" "5984899" "6149629" "6224576" "6254575" "6261263" "6298541" "6344032" "6436086" "6440104" "6524277" "6533760"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM
------	-----	---	-----------------------------	----	----	----	------------------------

L343	148	"6592556" "6623456" "6635032" "6648855" "6695819" "6699217" "6712792" "6780169" "6837877" "6869415" "6984223" "7001363" "7128726" "7147624" "7160267" "7163526" "7223258" "7226432" "7396343" "7428773" "7537581" "7766879" "D422700" "D442280" "D604836" "D604837" "D604838" "D604839" "D605287").PN. OR ("8603009").URPN. ("20020193748" "20030105414" "20030229315" "20040059302" "20040092872" "20050004524" "20050187493" "20050245868" "20050245869" "20050245870" "20050245885" "20060036219" "20070106220" "20070167914" "20080086085" "20080177202" "4106497" "4207870" "4305406" "4573976" "4641663" "4795443" "4840619" "4894055" "4900307" "4994046" "5015241" "5195985" "5215534" "5222502" "5242417" "5256153" "5295970" "5303713" "5312372" "5336199" "5348544" "5356392" "5411492" "5439449" "5466223" "5501675" "5542932" "5672161" "5676658" "5702369" "5704920" "5755522" "5984899" "6149629" "6261263" "6298541" "6436086" "6440104" "6524277" "6533760" "6592556" "6623456" "6635032" "6648855" "6699217" "6712792" "6780169" "6837877" "6869415" "6984223"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:21 PM
------	-----	---	-----------------------------	----	----	----	------------------------

L344	41	"7001363" "7128726" "7147624" "7160267" "7163526" "7223258" "7226432" "7396343" "7428773" "D422700" "D442280").PN. OR ("7766879").URPN. ("2735430" "2798487" "3187749" "3240209" "3585984" "3817240" "4166450" "4207870" "4295477" "4312362").PN. OR ("4436098").URPN.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2021/07/08 04:22 PM
L345	163	L341 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:22 PM
L346	163	L345 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:23 PM
L347	22	("2005/0283093").URP N.	(USPAT)	OR	ON	ON	2021/07/08 04:23 PM
L348	163	L345 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L349	163	L348 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:27 PM
L350	1736	(600/573).CCLS.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/08 04:37 PM
L351	1363	L350 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:37 PM
L352	1346	L351 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L353	136	L352 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:38 PM
L354	812	(600/576).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:41 PM
L355	711	L354 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L356	699	L355 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L357	123	L356 and (vent\$4 near4 air)	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:41 PM
L358	371	(600/577).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:44 PM
L359	277	L358 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM

L360	260	or flash\$4 or collect\$4)) L359 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:45 PM
L361	1259	(600/583).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2021/07/08 04:46 PM
L362	1208	L361 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:46 PM
L363	1194	L362 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L364	1194	L363 and @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:47 PM
L366	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:05 PM
L367	319	((("BULLINGTON") near3 ("Gregory")) OR (("PATTON") near3 ("Richard")) OR (("MIAZGA") near3 ("Jay")) OR ("GAW") near3 ("Shan"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/02/02 03:14 PM
L368	1	(16/376745).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:35 PM
L369	190	((("ROGERS") near3 ("Bobby"))).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 03:36 PM
L370	2	(15/140448).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:41 PM
L371	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L372	1	("9060725").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:42 PM
L373	1	("9060724").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:43 PM
L374	1	("9022950").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L375	1	("9022951").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:45 PM
L376	1	("10292633").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:46 PM
L377	1	("10433779").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:47 PM
L378	1	("10436554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:48 PM
L379	1	("10736554").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L380	1	("10912506").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:49 PM
L381	1	("10010282").PN.	(US-PGPUB; USPAT;	OR	OFF	OFF	2022/02/02

L382	1	(16/376745).APP.	USOCR) (US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	03:49 PM 2022/02/02 03:50 PM
L383	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:51 PM
L384	276	(600/579).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 03:52 PM
L385	204	L384 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 03:53 PM
L386	37427	(A61B5/150221 or A61B5/15003 or A61B5/150236 or A61B5/150244 or A61B5/150251 or A61B5/150389 or A61B5/150503 or A61B5/150992 or A61B5/153 or A61B5/155 or A61B10/0048 or A61B10/0051 or A61B10/007 or A61B2010/0061 or A61B2010/0077 or A61B2010/008).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/02/02 04:35 PM
L387	7279	L386 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L388	4442	L387 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:36 PM
L389	874	L388 and (seal\$4 near4 (member or mechanism\$4 or vent\$4 or elastic\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 04:38 PM
L390	26	("2008/0145933").URP N.	(USPAT)	OR	ON	ON	2022/02/02 04:52 PM
L391	44	("2008/0319346").URP N.	(USPAT)	OR	ON	ON	2022/02/02 04:59 PM
L392	385	L386 and ((blood or fluid) near4 (seal\$4 near4 (member or mechanism\$4 or vent\$4 or elastic\$4)))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM
L393	171	L392 and @ad<"20120530"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:28 PM
L394	355	(604/103).CCLS.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/02 05:52 PM
L395	7	L394 and ((blood or fluid) near4 (seal\$4 near4 (member or mechanism\$4 or vent\$4 or elastic\$4)))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/02/02 05:52 PM

L396	1	(16/328127).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/03 12:00 PM
L397	0	"1020130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L398	8	"20130062845"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:17 PM
L399	14	"2013021595"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/02/04 04:18 PM
L400	2	(14/055232).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/04 07:10 PM
L401	1	(15/746656).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/05 11:48 AM
L402	0	(17/388440).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/02/07 09:34 AM
L403	1	("20050048465").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2022/02/07 09:34 AM
L404	196	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:08 PM
L405	16	L404 and (blood near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L406	16	L404 and ((blood or chamber) near4 sequest\$5)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:08 PM
L407	16	L406 and (junct\$4 or bypass\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L408	16	L406 and junct\$4	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:09 PM
L409	22445	(A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/05/18 03:54 PM
L410	4525	L409 and ((blood or fluid\$4) near4 (sequest\$5 or sampl\$4 or flash\$4 or collect\$4 or flush\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:55 PM
L411	3810	L410 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 03:56 PM
L412	820	L411 and ((vent\$4 or	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18

L413	22445	open\$4 or apertur\$4) near4 air) (A61B5/150992 or A61B5/15003 or A61B5/150213 or A61B5/150221 or A61B5/150389 or A61B5/150473 or A61B5/150572 or A61B5/154 or A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	03:57 PM 2022/05/18 05:51 PM
L414	4603	L413 and ((blood or fluid\$4 or chamber) same (sequest\$5 or sampl\$4 or flash\$4 or collect\$4 or flush\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:51 PM
L415	511	L414 and ((junct\$4 or bypass\$4 or divert\$4) near4 (blood or fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:52 PM
L416	355	L415 and @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/05/18 05:53 PM
L417	1	(16/819033).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:10 PM
L418	1	(17/094692).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L419	1	(17/538990).APP.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:25 PM
L420	1	("11311219").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:27 PM
L421	1	("11185266").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:30 PM
L422	1	("10143412").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:31 PM
L423	1	("9820682").PN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/05/18 06:32 PM
L424	252	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/10/13 01:41 PM
L425	38	424 AND (closur\$4 OR enclos\$4)	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 01:42 PM

L426	42781	(A61B5/150213 OR A61B5/15003 OR A61B5/150221 OR A61B5/150251 OR A61B5/150732 OR A61B5/15074 OR A61B5/150992 OR A61B5/153 OR A61B5/150389 OR A61B5/150503).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/13 01:47 PM
L427	5205	426 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 01:50 PM
L428	4803	427 AND ((blood OR fluid\$4) near4 (sequest\$5 OR sampl\$4 OR flash\$4 OR collect\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 01:51 PM
L429	519	428 AND ((closur\$4 OR enclos\$4 OR pug\$4) near5 (vent OR open\$4 OR air))	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 01:54 PM
L430	169	"5749857"	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 02:14 PM
L431	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13 02:14 PM
L432	346	427 AND ((junct\$4 OR bypass\$4 OR divert\$4) near4 (blood OR fluid))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 02:18 PM
L433	186	("3500828" "3670729" "3714945" "3977400" "3994293" "3995619" "4106491" "4200096" "4468224" "4531987" "4549554" "4735215" "4828548" "4874373" "4893635" "4894052" "4907599" "4944308" "4994042" "5129884" "5400798").pn. OR ("5749857").urpn. AND (PGPB USPT USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2022/10/13 02:32 PM
L434	124	433 AND ((blood OR fluid\$4) near4 (sequest\$5 OR sampl\$4 OR flash\$4 OR collect\$4 OR optimiz\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/10/13 02:34 PM
L435	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/10/13

L436	1	17/138056	(US-PGPUB; USPAT)	OR	ON	ON	02:34 PM 2022/10/19 11:35 AM
L437	253	((("ROGERS") near3 ("Bobby"))).INV.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/11/16 03:25 PM
L438	39	437 AND (closur\$4 OR enclos\$4)	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 03:25 PM
L439	35391	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/154 OR A61B5/15074).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2022/11/16 03:46 PM
L440	4100	439 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:48 PM
L441	3875	440 AND ((blood OR fluid\$4 OR urine) SAME (sequest\$5 OR sampl\$4 OR flash\$4 OR collect\$4 OR optimiz\$5))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:49 PM
L442	368	441 AND ((junct\$4 OR bypass\$4 OR divert\$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 03:50 PM
L443	7	"10827964"	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 04:13 PM
L444	1	16/819033	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 04:48 PM
L445	359	"4207870"	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 05:07 PM

L446	1	("4207870").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/11/16 05:07 PM
L447	3814	440 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flash\$4 OR collect\$4 OR optimiz\$5))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:17 PM
L448	366	447 AND ((junct\$4 OR bypass\$4 OR divert\$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:17 PM
L449	89	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 01:13 PM
L450	24	449 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5or flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:14 PM
L451	24	449 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5 OR flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:14 PM
L452	6634	(A61B5/150213 OR A61B5/15003 OR A61B5/150221 OR A61B5/150251 OR A61B5/150732 OR A61B5/15074 OR A61B5/150992 OR A61B5/153 OR A61B5/150389 OR A61B5/150503).cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 01:32 PM
L453	5326	452 AND @ad<"20170210"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:32 PM
L454	4928	453 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5 OR flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:32 PM
L455	371	454 AND ((junct\$4 OR bypass\$4 OR divert\$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 01:33 PM
L456	11	("2016/0361006").urpn. AND (PGPB USPT USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:03 PM
L457	1	17/094692	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 03:11 PM
L458	49	("20020004647" "20030	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11

		105414 "20040054333 "20040073171 "2004 0147855 "2005000452 4 "20050240161 "200 70083162 "200700882 79 "20080086085 "20 080145933 "20080167 577 "20080319346 "2 0100010372 "2010005 7004 "20120016266 "2 0130317391 "201600 08579 "20160174888" "3 741197 "3817240 "3 874367 "3886930 "40 57050 "4106497 "415 4229 "4207870 "4412 548 "4436098 "44442 03 "5222502 "552019 3 "5749857 "6398743" "6569117 "8197420" "8 8523826 "8535241 "8 540663 "8568371 "86 03009 "8864684 "902 2950 "9022951 "9060 724 "9138572 "91554 95 "9204864 "987767 5").PN.					03:18 PM
L459	13	458 AND ((junct\$4 OR bypass\$4 OR divert\$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:18 PM
L460	155	("2707953" "2992974" "3013557" "3098016" "3382865" "3405706" "3494351" "3577980" "3635798" "3648684" "3848579" "3890203" "3937211" "4057050" "4133863" "4166450" "4340067" "4370987" "4425235" "4444203" "4459997" "4509534" "4657160" "4676256" "4865583" "4890627" "4988339" "5009847" "5097842" "5108927" "5122129" "5269317" "5330464" "5360011" "5429610" "5450856" "5454786" "5485854" "5507299" "5577513" "5762633" "5865812" "5882318" "5922551" "6016712" "6057105" "6159164" "6210909" "6328726" "6364890" "6387086" "6403381"	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:21 PM

		"6520948" "6626884" "6692479" "6716187" "6746420" "6913580" "7044941" "7087047" "7335188" "7384416" "7744573" "8197420" "8231546" "8337418" "8535241" "8647286" "8864684" "8876734" "20020002349" "20020183651" "20030055381" "20030208151" "20040010228" "20040054283" "20040054333" "20040147855" "20050004524" "20050240161" "20050245885" "20050281713" "20060287639" "20080108954" "20080145933" "20100152681" "20120095367" "20120215131" "20130079604" "20130116599" "20130317391" "20140081172").pn. OR ("9060724").urpn. AND (PGPB USPT USOC).dbnm.					
L461	31	("2008/0145933").urpn. AND (PGPB USPT USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2023/04/11 03:30 PM
L462	1	("5749857").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 03:46 PM
L463	13	459 AND ((junct\$4 OR bypass\$4 OR divert\$4) near5 (blood OR fluid OR urine))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:47 PM
L464	4994	453 AND ((blood OR fluid\$4 OR urine OR semen) SAME (sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5 OR flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:58 PM
L465	968	464 AND ((junct\$4 OR bypass\$4 OR diver\$5) SAME (blood OR fluid OR urine OR semen))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 03:59 PM
L466	707	465 AND housing	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:50 PM

L467	2911	464 AND ((blood OR fluid\$4 OR urine OR semen) near5 (first OR second OR subsequent\$4 OR bypass))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L468	2954	464 AND ((blood OR fluid\$4 OR urine OR semen) near5 (first OR second OR subsequent\$4 OR convey\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L469	2891	464 AND ((blood OR fluid\$4 OR urine OR semen) near5 (first OR second OR subsequent\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:52 PM
L470	790	469 AND ((junct\$4 OR bypass\$4 OR diver\$5) SAME (blood OR fluid OR urine OR semen))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/04/11 04:53 PM
L471	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 12:35 PM
L472	164	((("ROGERS") near3 ("Bobby")).INV.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); EPO; JPO; DERWENT; IBM_TDB)	OR	OFF	OFF	2023/05/08 02:18 PM
L473	1	("4207870").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:23 PM
L474	1	("10827964").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:31 PM
L475	1	("11311219").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:32 PM
L476	1	"17094692"	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:34 PM
L477	2	"17730118"	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:34 PM
L478	1	("10012828").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:36 PM
L479	1	("10010282").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 03:36 PM
L480	48138	(A61B5/150992 OR A61B5/15003 OR	(US-PGPUB; USPAT; USOCR; FIT (AU, AP,	OR	ON	ON	2023/05/08 03:59 PM

		A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L481	5081	480 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 04:15 PM
L482	3947	481 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5 OR flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 04:17 PM
L483	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 04:17 PM
L484	1069	482 AND (air near5 (filter\$4 OR material\$4 OR membrane OR permeab\$4 OR vent\$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 04:32 PM
L485	203	("3500828" "3670729" "3714945" "3977400" "3994293" "3995619" "4106491" "4200096" "4468224" "4531987" "4549554" "4735215" "4828548" "4874373" "4893635" "4894052" "4907599" "4944308" "4994042" "5129884" "5400798").pn. OR ("5749857").urpn. AND (PGPB USPT USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/05/08 04:51 PM
L486	606	484 AND ((pressure OR vacuum) near5 (draw OR forc\$4 OR withdraw OR flow\$4)) SAME (blood OR fluid)	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 05:32 PM
L487	24	("2010/0057004").urpn. AND (PGPB USPT USOC).dbnm.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2023/05/08 05:35 PM
L488	3	487 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/05/08 05:55 PM
L489	49	((US-20080319346-A1 OR US-20100057004-	(US-PGPUB; USPAT; USOCR; FIT (AU, AP,	OR	ON	ON	2023/05/08 06:07 PM

		A1 OR US- 20070088279-A1 OR US-20080145933-A1 OR US-20040054333- A1 OR US- 20100010372-A1 OR US-20080167577-A1 OR US-20080086085- A1 OR US- 20070083162-A1 OR US-20160008579-A1 OR US-20120016266- A1 OR US- 20130317391-A1 OR US-20160174888-A1 OR US-20050240161- A1 OR US- 20040147855-A1 OR US-20040073171-A1 OR US-20050004524- A1 OR US- 20030105414-A1 OR US-20020004647- A1).did. AND PGPB.dbnm.) OR ((US- 4412548-A OR US- 5222502-A OR US- 5520193-A OR US- 9022951-B2 OR US- 6569117-B1 OR US- 3741197-A OR US- 8603009-B2 OR US- 4207870-A OR US- 9877675-B2 OR US- 4444203-A OR US- 6398743-B1 OR US- 9022950-B2 OR US- 9155495-B2 OR US- 4436098-A OR US- 9138572-B2 OR US- 8568371-B2 OR US- 8540663-B2 OR US- 8523826-B2 OR US- 8197420-B2 OR US- 4057050-A OR US- 8864684-B2 OR US- 8535241-B2 OR US- 5749857-A OR US- 9060724-B2 OR US- 9204864-B2 OR US- 3817240-A OR US- 3874367-A OR US- 3886930-A OR US- 4106497-A OR US- 4154229-A).did. AND USPT.dbnm.)	AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L490	25	489 AND (air near5 (filter\$4 OR material\$4	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:07 PM

L491	204	OR membrane OR permeab\$4 OR vent\$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:29 PM
L492	118	482 AND (hous\$4 SAME (inlet AND outlet AND channel))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:33 PM
L493	1	491 AND (hous\$4 near5 ((top OR upper) AND (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L494	0	489 AND (hous\$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L495	27	492 AND (hous\$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:39 PM
L496	172	484 AND (hous\$4 near5 ((top OR upper) SAME (lower OR bottom)))	(US-PGPUB; USPAT)	OR	ON	ON	2023/05/08 06:41 PM
L497	113	((("ROGERS") near3 ("Bobby")) OR ((("KANG") near3 ("Gino")) OR ((("DETLOFF") near3 ("John"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/07/05 01:58 PM
L498	26	497 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5 OR flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 01:58 PM
L499	4	15/855439	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 03:12 PM
L500	48306	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT;	OR	ON	ON	2023/07/05 03:36 PM

L501	5081	500 AND @ad<"20150724"	IBM_TDB) (US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 03:36 PM
L502	3947	501 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5 OR flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 03:37 PM
L503	1069	502 AND (air near5 (filter\$4 OR material\$4 OR membrane OR permeab\$4 OR vent\$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 03:37 PM
L504	3871	501 AND ((blood OR fluid\$4 OR urine) near5(divert\$4 OR direct\$4 OR flow\$4 OR bypass\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:18 PM
L505	3030	501 AND ((blood OR fluid\$4 OR urine) near5(divert\$4 OR direct\$4 OR flow\$4 OR bypass\$4 OR allow\$4)) SAME (channel\$4 OR chamber OR junct\$4 OR inlet OR outlet OR path\$4 OR contain\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:20 PM
L506	921	503 AND ((blood OR fluid\$4 OR urine) near5(divert\$4 OR direct\$4 OR flow\$4 OR bypass\$4 OR allow\$4)) SAME (channel\$4 OR chamber OR junct\$4 OR inlet OR outlet OR path\$4 OR contain\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/07/05 05:20 PM
L507	1	17/538990	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 06:04 PM
L508	1	16/961875	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 08:21 PM
L509	7	"20070148624"	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 01:02 PM
L510	43469	(A61B5/150992 OR A61B5/15003 OR A61B5/150213 OR A61B5/150221 OR A61B5/150389 OR A61B5/150473 OR A61B5/150572 OR A61B5/153 OR A61B5/154 OR A61M39/04 OR A61M39/0693 OR	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE,	OR	ON	ON	2023/08/31 01:28 PM

		A61M2039/0202 OR A61M2039/0633 OR A61M2039/068).cpc.	SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO)				
L511	5081	510 AND @ad<"20150724"	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/31 01:32 PM
L512	3947	511 AND ((blood OR fluid\$4 OR urine) near5(sequest\$5 OR sampl\$4 OR flush\$4 OR collect\$4 OR optimiz\$5 OR flash\$4))	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/31 01:32 PM
L513	2653	512 AND ((blood OR fluid\$4 OR urine) near5(divert\$4 OR direct\$4 OR flow\$4 OR bypass\$4 OR allow\$4)) SAME (channel\$4 OR chamber OR junct\$4 OR inlet OR outlet OR path\$4 OR contain\$4)	(US-PGPUB; USPAT)	OR	OFF	OFF	2023/08/31 01:32 PM
L514	921	513 AND (air near5 (filter\$4 OR material\$4 OR membrane OR permeab\$4 OR vent\$4))	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 01:33 PM
L515	1	18/113710	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 02:05 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N94	1	(port and sequest\$5 and junction and chamber and sampl\$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2017/09/28 04:15 PM
N112	3	(port and sequest\$5 and chamber and sampl\$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2018/01/09 05:39 PM
N248	4	(blood and fluid\$4 and inlet and outlet and port and reservoir and allow and initial\$4 and sequest\$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N249	4	(blood and fluid\$4 and inlet and outlet and port and reservoir and allow\$4 and initial\$4 and sequest\$5).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:30 PM
N250	495	(blood and fluid\$4 and allow\$4 and	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM

N251	107	initial\$4).clm. (blood and fluid\$4 and allow\$4 and initial\$4 and subsequent\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/03/16 03:31 PM
N283	9	((blood or fluid\$4) and sequestrat\$4 and chamber and sampl\$4 and vent\$4 and air\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N284	530	((blood or fluid\$4) and chamber and sampl\$4 and vent\$4 and air\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:31 PM
N285	84	((blood or fluid\$4) and chamber and cap and sampl\$4 and vent\$4 and air\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2020/06/10 06:32 PM
N365	6	(port and sequest\$5 and junction and chamber and sampl\$4 and vent and barrier).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2021/07/08 04:49 PM
N366	9	(blood AND fluid\$4 AND inlet AND outlet AND junct\$4 AND inhibit\$4).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:31 PM
N367	84	((blood OR fluid\$4) AND chamber AND sampl\$4 AND junction AND (inhibit\$4 OR prevent\$4)).clm.	(US-PGPUB; USPAT)	OR	OFF	OFF	2022/11/16 05:36 PM
N368	25	(blood AND chamber AND sampl\$4 AND junction AND inlet AND outlet AND port AND first).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:48 PM
N369	4	(blood AND chamber AND sampl\$4 AND junction AND inlet AND outlet AND port AND first AND hous\$4 AND subsequent).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:49 PM
N370	64902	"465" AND housing	(US-PGPUB; USPAT)	OR	ON	ON	2023/04/11 04:50 PM
N371	6	(inlet AND outlet AND junct\$4 AND channel AND sampl\$4 AND fluid\$4 AND vent AND air AND permeab\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:51 PM
N372	167	(inlet AND outlet AND junct\$4 AND channel AND sampl\$4 AND fluid\$4).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:52 PM

N373	23	(inlet AND outlet AND junction AND channel AND sample AND fluid AND bypass).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/07/05 05:53 PM
N374	33	(inlet AND outlet AND chamber AND blood AND sample AND bypass).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 02:35 PM
N375	18	(inlet AND outlet AND chamber AND blood AND sample AND bypass AND air AND permeable).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2023/08/31 02:36 PM

Bibliographic Data

Application No: 18/113,710

Foreign Priority claimed: ☐ Yes ☒ No

35 USC 119 (a-d) conditions met: ☐ Yes ☒ No ☒ Met After Allowance

Verified and Acknowledged: /MAY A ABOUELELA/

M.A.A

Examiner's Signature

Initials

Title:

BLOOD SAMPLE OPTIMIZATION SYSTEM AND BLOOD
CONTAMINANT SEQUESTRATION DEVICE AND METHOD

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
02/24/2023	600	3791	069366- 0574153_KUR2C04US
RULE			

APPLICANTS

Kurin, Inc.,

INVENTORS

Bobby E. ROGERS, Park City, UT, UNITED STATES

Gino KANG, Irvine, CA, UNITED STATES

John DETLOFF, San Diego, CA, UNITED STATES

CONTINUING DATA

This application is a CON of 17538990 11/30/2021

17538990 is a CON of 16208559 12/04/2018 PAT 11185266

16208559 is a CON of 15994559 05/31/2018 PAT 10143412

15994559 is a CON of 15140448 04/27/2016 PAT 10010282

15140448 has PRO of 62318194 04/04/2016

15140448 has PRO of 62238636 10/07/2015

15140448 has PRO of 62196797 07/24/2015 *

(*) Data provided by applicant is not consistent with PTO record

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

03/28/2023

** SMALL ENTITY **

STATE OR COUNTRY

UNITED STATES

ADDRESS

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)

ATTENTION: DOCKETING DEPARTMENT

P.O BOX 10500

McLean, VA 22102

UNITED STATES

FILING FEE RECEIVED

\$2,400

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Fri Sep 08 05:15:45 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new outgoing correspondence. This correspondence is now available for viewing in Patent Center.

The official date of notification of the outgoing correspondence will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:

The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	NOA	09/08/2023	069366-0574153_KUR2C04US
18113710	892	09/08/2023	069366-0574153_KUR2C04US
18113710	1449	09/08/2023	069366-0574153_KUR2C04US

To view your correspondence online, please sign in to [Patent Center](#) and then select Workbench/View correspondence. To update your email address(es), select Manage/Manage customer numbers.

If you have any questions, please contact the [Patent Electronic Business Center](#) (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
18/113,710	02/24/2023	3791	1024	069366-0574153_KUR2C04US	16	1

CONFIRMATION NO. 2715

REPLACEMENT FILING RECEIPT



0000000061859840

27500
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

Date Mailed: 09/14/2023

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Bobby E. ROGERS, Park City, UT;
Gino KANG, Irvine, CA;
John DETLOFF, San Diego, CA;

Applicant(s)

Kurin, Inc., San Diego, CA;

Assignment For Published Patent Application

Kurin, Inc., San Diego, CA

Power of Attorney: The patent practitioners associated with Customer Number 27500

Domestic Priority data as claimed by applicant

This application is a CON of 17/538,990 11/30/2021 *
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

(*) Data provided by applicant is not consistent with PTO records.

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: 03/28/2023

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/113,710**

Projected Publication Date: 07/06/2023

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

BLOOD SAMPLE OPTIMIZATION DEVICE

Preliminary Class

600

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign

page 2 of 4

patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER
Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Thu Sep 14 05:22:54 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new outgoing correspondence. This correspondence is now available for viewing in Patent Center.

The official date of notification of the outgoing correspondence will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:

The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	APP.FILE.REC	09/14/2023	069366-0574153_KUR2C04US

To view your correspondence online, please sign in to [Patent Center](#) and then select Workbench/View correspondence. To update your email address(es), select Manage/Manage customer numbers.

If you have any questions, please contact the [Patent Electronic Business Center](#) (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Bobby E. Rogers, et al.

Confirmation No: 2715

Application No.: 18/113,710

Art Unit: 3791

Filed: February 24, 2023

Examiner: May A. Abouelela

For: BLOOD SAMPLE OPTIMIZATION DEVICE

Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

COMMENTS ON EXAMINER'S STATEMENT OF REASONS FOR ALLOWANCE

Applicant thanks Examiner Abouelela for the Notice of Allowance and the Examiner's efforts in examining the above-referenced application.

Applicant received the Examiner's "Statement Of Reasons For Allowance" (hereafter the "Statement") along with the Notice and wishes to note that entry of this Statement should not be construed as Applicant necessarily agreeing with or acquiescing to the reasons stated therein.

Applicant recognizes that, in accordance with MPEP § 1302.14, the Statement need not set forth all of the details as to why claims are allowed and, respectfully, Applicant does not concede that the Statement contains the only reasons for which the pending claims are allowable. Each of the claims stands on its own merits and is patentable because of the combination it recites and not because of the presence or absence of any one particular element.

CONCLUSION

It is believed that no fees are due in connection with the filing of this paper. In the event that it is determined that fees are due, however, the Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account 033975, Reference No. 069366-0574153_KUR2C04US.

Respectfully submitted,
PILLSBURY WINTHROP SHAW PITTMAN LLP

Date: October 26, 2023 By: /Ben Hudson/
Benjamin F. Hudson, Ph.D.
Reg. No. 71,474

PO Box 10500
McLean, Virginia 22102
Telephone: (858) 509-4000
Customer No. 27500



ELECTRONIC PAYMENT RECEIPT

APPLICATION # 18/113,710	RECEIPT DATE / TIME 10/26/2023 04:51:31 PM ET	ATTORNEY DOCKET # 069366-0574153_KUR2C04US
------------------------------------	---	--

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	2715	FILED BY	Trent Tercenio
PATENT CENTER #	63089875	AUTHORIZED BY	Benjamin Hudson
CUSTOMER #	27500	FILING DATE	02/24/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Bobby E. ROGERS

Payment Information

PAYMENT METHOD DA / 033975	PAYMENT TRANSACTION ID E20230PG51529225	PAYMENT AUTHORIZED BY Trent Tercenio
-------------------------------	--	---

FEE CODE	DESCRIPTION	ITEM PRICE(\$)	QUANTITY	ITEM TOTAL(\$)
2501	UTILITY ISSUE FEE	480.00	1	480.00
TOTAL AMOUNT:				\$480.00

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage

submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



UNITED STATES
PATENT AND TRADEMARK OFFICE

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/113,710

RECEIPT DATE / TIME
10/26/2023 04:51:31 PM ET

ATTORNEY DOCKET #
069366-0574153_KUR2C04US

Title of Invention

BLOOD SAMPLE OPTIMIZATION DEVICE

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 2715

FILED BY Trent Tercenio

PATENT CENTER # 63089875

FILING DATE 02/24/2023

CUSTOMER # 27500

FIRST NAMED INVENTOR Bobby E. ROGERS

CORRESPONDENCE ADDRESS -

AUTHORIZED BY Benjamin Hudson

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
----------	-------	-------------	-----------

069366-0574153_KUR2C04US_Comments_on_Reasons_for_Allo wance-LET..docx	2	Miscellaneous Incoming Letter	32 KB
--	---	-------------------------------	-------

Warning: Text decorations have been removed.

069366-0574153_KUR2C04US_Issue _Fee_TBF.pdf	1	Issue Fee Payment (PTO-85B)	1204 KB
--	---	-----------------------------	---------

Digest

DOCUMENT**MESSAGE DIGEST(SHA-512)**

069366-	AA09114F66CD7714589463130795A2E4E5BC90FD30F49CF945
0574153_KUR2C04US_Comm	CFC3D5866EF6D013D8590DA4C877EDE106BEAB356A47985E
ents_on_Reasons_for_Allowanc	42CC001334E6D485A608CC34E62030
e-LET..docx	
069366-	13C2131F90673B0E63A8999EFCC12172F2C33B53F2284D4D16
0574153_KUR2C04US_Issue_	1ED85BF7FCAA9786A2C1FE9622B875F887076396DF9553F9B
Fee_TBF.pdf	BCD0DE67B22A7399B64736944C570

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

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 09/08/2023

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 EFS-Web 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.
-----------------	-------------	----------------------	---------------------	------------------

18/113,710 02/24/2023 Bobby E. ROGERS 069366-0574153_KUR2C04US 2715

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	12/08/2023

EXAMINER	ART UNIT	CLASS-SUBCLASS
ABOUELELA, MAY A	3791	600-577000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Pillsbury Winthrop Shaw Pittman LLP

2

3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE
KURIN, INC.

(B) RESIDENCE: (CITY and STATE OR COUNTRY)
SAN DIEGO, CALIFORNIA

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 Patent Center or EFS-Web ☐ 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. 03-3975

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

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.

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.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Ben Hudson/

Date October 26, 2023

Typed or printed name Benjamin F. Hudson

Registration No. 71,474



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/113,710	12/05/2023	11832944	069366-0574153_KUR2C04US	2715

27500

7590

11/15/2023

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at <https://patentcenter.uspto.gov/>. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at <https://certifiedcopycenter.uspto.gov/index.html>. The Certified Copy Center may be reached at (800)972-6382.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (<https://patentcenter.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PATENT CENTER site <https://patentcenter.uspto.gov> for additional inventors):

Bobby E. ROGERS, Park City, UT;
Gino KANG, Irvine, CA;
John DETLOFF, San Diego, CA;

APPLICANT(s) (Please see PATENT CENTER site <https://patentcenter.uspto.gov> for additional applicants):

Kurin, Inc., San Diego, CA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit [SelectUSA.gov](https://selectusa.gov).

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - Correspondence Notification for Customer Number 27500

Thu Nov 16 05:22:21 EST 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new outgoing correspondence. This correspondence is now available for viewing in Patent Center.

The official date of notification of the outgoing correspondence will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:

The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Document	Mailroom Date	Attorney Docket No.
18113710	ISSUE.NTF	11/15/2023	069366-0574153 KUR2C04US

To view your correspondence online, please sign in to [Patent Center](#) and then select Workbench/View correspondence. To update your email address(es), select Manage/Manage customer numbers.

If you have any questions, please contact the [Patent Electronic Business Center](#) (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/113,710	02/24/2023	Bobby E. ROGERS	069366-0574153_KUR2C04US	2715
27500	7590	12/05/2023		
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)			EXAMINER	
ATTENTION: DOCKETING DEPARTMENT			ABOUELELA, MAY A	
P.O BOX 10500				
McLean, VA 22102			ART UNIT	PAPER NUMBER
			3791	
			NOTIFICATION DATE	DELIVERY MODE
			12/05/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Docket_IP@pillsburylaw.com



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.
18/113,710	05-Dec-2023	11832944

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
McLean, VA 22102

EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at <https://patentcenter.uspto.gov>

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit <https://www.uspto.gov/electronicgrants>

TO: Docket_IP@pillsburylaw.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - eGrant Notification for Customer Number 27500

Tue Dec 05 06:08:03 EST 2023

Dear Patent Center Customer:

Correspondence Address:

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean,VIRGINIA,22102
UNITED STATES

This is a courtesy notification regarding the following USPTO patent application(s) associated with your Customer Number, 27500, that have new eGrant(s). The eGrant is now available for viewing in Patent Center.

The official date of the eGrant notification will be indicated on the form (e.g., PTOL-90) accompanying the correspondence.

Disclaimer:

The list of documents shown below are provided as a courtesy and is not part of the official file wrapper. The content of the images shown in the Image File Wrapper is the official record.

Application	Patent	Document	Mailroom Date	Attorney Docket No.
18113710	11832944	EGRANT.NTF	12/05/2023	069366-0574153_KUR2C04US

To examine your eGrant online, please access [Patent Center](#) then search using the listed application or patent number. To download, click on the eGrant link on the left-hand menu or select the "Download eGrant" link on the Application data page.

If you have any questions, please contact the [Patent Electronic Business Center](#) (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team