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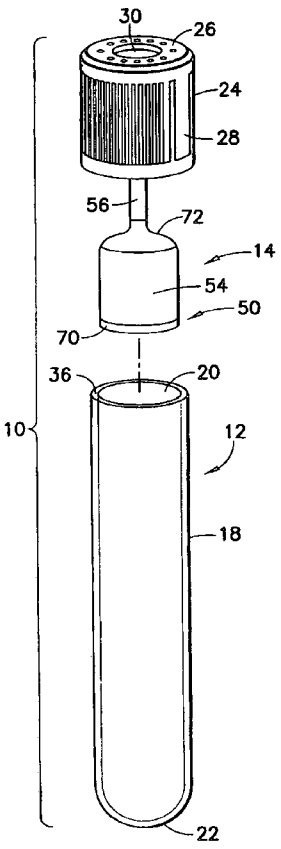

(57) Abstract: The fluid sample collection device is adapted to collect and separate a fluid sample into constituent parts such as separating plasma or serum from a blood sample. The device includes an evacuated outer container and an inner container. The outer container has a first open end and a second closed end. A pierceable closure closes the first open end thereby defining a first interior chamber. The inner container is contained within the outer container and separates the first interior chamber into an upper chamber portion and lower chamber portion in fluid communication. The inner container defines a second interior chamber separated from the lower chamber portion through a porous membrane. A port is provided for placing the second interior chamber in fluid communication with the first interior chamber. Another aspect of the device relates to a method of using the device to separate plasma or serum from a blood sample.

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MEMBRANE-BASED DOUBLE-LAYER TUBE FOR SAMPLE COLLECTIONS

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a fluid sample collection device and, more particularly, to a fluid sample collection device adapted to separate plasma or serum from a blood sample. More specifically, the present invention relates to an evacuated fluid sample collection device capable of separating plasma or serum from the cellular material in a blood sample through a porous filter also referred to as a membrane herein.

Description of Related Art

Plasma is the liquid portion of blood and is primarily comprised of water, proteins, glucose, amino acids, vitamins, inorganic salts, metabolites, and metabolic waste products. The generally solid portion of blood is comprised of a variety of cells including red cells, white cells, and platelets. Plasma is freely transferable with cells of the body. As a whole, plasma provides the medium to suspend white blood cells, red blood cells, and other cellular components for transport throughout a human or animal. If a plasma sample is desired, its separation from blood cells must occur well before blood coagulation. An anti-coagulation reagent may be added to a blood collection device to prevent coagulation. If blood is allowed to coagulate, the remaining liquid portion of the collected blood sample is called serum, which is devoid of some protein components of plasma. Separation of plasma/serum from blood cells is typically achieved by centrifugation.

Because plasma contains a rich source of components available for diagnostic analysis, medical devices have been devised for separating plasma from a whole blood sample. Several known blood collection devices are provided as evacuated multi-chamber devices that incorporate a filter or membrane that is used to remove or separate plasma from a collected blood sample. In some devices, the devices include a detachable chamber allowing a user to access the separated plasma specimen. Typically, in these known blood sample collection and separating devices the separating filter or membrane has a sufficiently small pore size to prevent cellular components from passing through the filter or membrane while allowing the passage of liquid. However, such filters or membranes often become clogged during a blood collection and plasma separation procedure thereby rendering typical vacuum forces generated by the evacuated device inadequate to draw plasma from a collected blood

sample. Several examples of known blood collection and separation devices are discussed hereinafter.

U.S. Patent No. 6,506,167 (Ishimito et al.) discloses a blood separating tube that includes an upstream tube separated by a filter from a downstream tube. The tubes are attachable to and detachable from each other and are initially provided in an evacuated state. During blood collection, blood is removed from a patient through intravenous puncture and transferred into the upstream tube through blood pressure and negative pressure inside the tube. In operation, a pressure differential is created between the upstream tube and the downstream tube as the blood contacts the filter between the two tubes. Several filter types are disclosed in this reference, including a membrane, glass fiber, filter paper with large pores and impregnated with anti-hemocyte antibodies, a filter impregnated with a cationic macromolecular substance to aggregate cells, and a laminated multi-layer filter. One problem associated with the device described in this patent is that blood cells often clog the filter during plasma separation resulting in inadequate vacuum force being present between the upstream tube and downstream tube during blood collection. A further problem with the device described in this patent is that the collected plasma in the downstream tube may be exposed to contaminants should the downstream tube be removed from the upstream tube.

U.S. Patent No. 6,471,069 (Lin et al.) discloses a device adapted to separate plasma/serum from blood cells and includes a flexible collapsible inner container disposed within a substantially rigid outer container. A closure seals the open top end of the outer container. A filter assembly is mounted to the open top end of the inner container. The filter assembly includes a filter that permits lighter fractions of a collected fluid sample to pass therethrough, while blocking the heavier fractions. The filter assembly further includes a filter support including a slit valve that opens in response to fluid pressure created by the lighter fractions for permitting the lighter fractions to flow therethrough. In use, a fluid sample is delivered to the inner container and the device is subjected to centrifugation which causes the filter assembly to move toward the bottom end of the outer container and allow the lighter fraction of the fluid sample to flow through the slit valve and into the space between the inner and outer containers. U.S. Patent No. 6,471,069 is incorporated herein by reference in its entirety.

U.S. Patent No. 6,659,288 (Amano et al.) discloses a plasma/serum collection device which includes a filtering unit. The device is constructed with a space above the filtering unit to preserve the blood cells, and defines a space below the filter into which plasma/serum is drawn under negative pressure. U.S. Patent 4,639,316 (Eldegheidy) discloses an automatic

liquid component separator which utilizes a cross-flow filtration area together with vacuum force to cause separation of a cell-free fraction from a cell fraction in a fluid sample. Other prior art in which plasma separation through a filter within a container is achieved through a pressure differential is disclosed in U.S. Patent Nos.: 3,682,596; 3,687,296; 3,701,434; 3,814,079; 4,131,549; and 4,639,316.

The foregoing blood collection and separation devices each utilize a pressure differential as the motive force to cause plasma separation from a whole blood sample. However, certain disadvantages are present in these devices, namely there is often insufficient differential pressure for complete plasma/serum separation, the separation filters easily become clogged with cellular material, and the separated plasma/serum is easily contaminated during removal from the device. Accordingly, there is a general need for a device and method that allow for rapid separation of plasma/serum from a blood sample ideally at the same location or a close proximity to the site of sample collection.

SUMMARY OF THE INVENTION

The present invention overcomes many of the deficiencies present in the prior art and allows a medical practitioner to both collect a bodily fluid sample, typically blood, and effect, for example, plasma/serum separation from the sample at or near the site of blood sample collection. In one embodiment, a device is provided for collecting and separating a fluid sample and generally comprises an evacuated outer container and an inner container. The outer container has a first open end and a second closed end. A pierceable closure closes the first open end thereby defining a first interior chamber. The inner container is contained within the outer container and separates the first interior chamber into an upper chamber portion in fluid communication with a lower chamber. The inner container defines a second interior chamber separated from the lower chamber portion of the first interior chamber through a porous membrane. A port is provided for placing the second interior chamber in fluid communication with the first interior chamber.

The fluid sample to be collected may comprise blood. Plasma or serum of the blood drawn within the first interior chamber passes through the porous membrane and into the second interior chamber of the inner container based on a pressure differential between the first interior chamber and the second interior chamber established by the blood contacting the porous membrane proximate the lower chamber portion. The porous membrane desirably prevents transfer of blood cells therethrough.

In one embodiment, the porous membrane may comprise filter paper, for example, one or more pieces of filter paper. The pore size of the porous membrane may be of a size to control the passing of desired molecules through the membrane. For example, the porous membrane may prevent molecules of 60,000 Daltons or higher from passing into the inner container. Additionally, the porous membrane may be capable or removing albumin, immunoglobulin, or other large molecules from the plasma or serum fraction of a blood sample. In another example, the porous membrane may prevent molecules of 10,000 Daltons or higher from passing into the inner container. Further, the porous membrane may have a pore size to enable peptide extraction from a blood sample. Moreover, the porous membrane may prevent molecules 2,000 Daltons or higher from passing into the inner container. Furthermore, the porous membrane may have a pore size to enable separation of metabolites and other small molecules from a blood sample.

The pore size of the porous membrane may also be between 0.1 μm to 2 μm. For example, the porous membrane may be a 0.22 μm membrane which may be used to remove virus particles for bio-safety plasma or serum sample collection as examples. In another example, the porous membrane may be a 0.45-1.0 μm membrane which may be used for platelet-free plasma or serum sample collection as examples. Further, the porous membrane may enable platelet-free plasma or serum sample collection.

In one variation, the inner container may be suspended within the outer container. In another variation, the inner container may be releasably connected with the pierceable closure. As a result, release of the inner container from the pierceable closure may open the port of the inner container and places the second interior chamber of the inner container in fluid communication with the first interior chamber. In a still further variation, the inner container may be movably supported within the first interior chamber of the outer container. As a result, movement of the inner container within the first interior chamber may open the port of the inner container and place the second interior chamber of the inner container in fluid communication with the first interior chamber. The outer container may support the inner container within the first interior chamber. Such support may occur after movement of the inner container within the first interior chamber.

The outer container may comprise an additive such agglutinating agents or anticoagulants. The porous membrane may be made of high density polyethylene, high density polypropylene, ceramic, porous metal, porous glass, glass fibers, polyvinyl polymers, paper, natural fibers, and combinations of the foregoing.

In another embodiment, the device is provided for separating plasma or serum from a blood sample and generally comprises an evacuated collection assembly comprising an outer container and an inner container. The outer container comprises a pierceable closure at one end. The inner container is contained within the outer container and the interior of the inner container is separated from the outer container by a porous membrane on the bottom of the inner container. The inner container comprises a port in fluid communication with the inner container. The port is desirably releasably connected to the pierceable closure.

The inner container may be entirely accommodated within the outer container. The port may be in fluid communication with the outer container, for example, when disconnected from the pierceable closure. The release of the port from the pierceable closure may enable opening of the port to unrestricted fluid communication with the outer container. The inner surface of the outer container may maintain a position of the inner container relative to the outer container. In operation, a pressure differential established between the outer container and the inner container upon entry of the blood sample into the outer container may be used to facilitate transportation of plasma or serum through the porous membrane into the inner container, while preventing the transfer of blood cells therethrough

In another aspect a method for separating plasma or serum from a blood sample is provided. The method may comprise a step of providing an evacuated collection assembly comprising an outer container having a pierceable closure at one end, an inner container contained within the outer container and defining an interior chamber therein, and a porous membrane separating the interior chamber of the inner container from the outer container. The method may further comprise a step of collecting a blood sample within the outer container of the assembly, thereby creating a pressure differential between the outer container and the inner container. The pressure differential generally causes plasma or serum from the blood sample to flow into the interior chamber of the inner container through the porous membrane. The plasma or serum flows into the inner container in a direction generally opposite to the direction of blood particle flow into the outer container during the blood sample collecting. Once collected, the plasma or serum may be removed from the inner container after the sample collection is complete. The inner container may comprise a port, and the method may further comprise a step of placing the port in fluid communication with the interior chamber of the outer container.

Further details and advantages of the invention will become clear upon reading the following detailed description in conjunction with the accompanying drawing figures, wherein like parts are designated with like reference numerals throughout.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is an exploded perspective view of a fluid sample collection device pursuant to one embodiment.

FIG. 2 is an exploded cross-sectional view of the device shown in **FIG. 1**.

FIG. 3 is a perspective view of a closure and inner container of the device shown in **FIG. 1**.

FIG. 4 is an assembled cross-sectional view of the device shown in **FIG. 1**.

FIG. 5 is an assembled cross-sectional view of the device shown in **FIG. 1**, showing the device in use during a fluid sample collection procedure.

FIG. 6 is an assembled cross-sectional view of the device shown in **FIG. 1**, showing initial fluid sample separation occurring within the device.

FIG. 7 is an assembled cross-sectional view of the device shown in **FIG. 1**, showing detachment of the inner container from the closure and resulting completion of fluid sample separation within the device.

FIG. 8 is an exploded perspective view of the fluid sample collection device pursuant to another embodiment.

FIG. 9 is a perspective view of the closure and inner container of the device shown in **FIG. 8**.

FIG. 10 is an assembled cross-sectional view of device shown in **FIG. 8**, showing the device accessed to accept a fluid sample for separation.

FIG. 11 is a top end view of the device shown in **FIG. 8**.

FIG. 12 is an assembled view of the fluid sample collection device pursuant to further embodiment, showing the device accessed to accept a fluid sample for separation.

FIG. 13 is an assembled cross-sectional view of the device shown in **FIG. 1** with an alternative closure for the device.

FIG. 14 is an assembled cross-sectional view of the device shown in **FIG. 1** with another alternative closure for the device

DESCRIPTION OF PREFERRED EMBODIMENTS

For purposes of the description hereinafter, spatial orientation terms, if used, shall relate to the referenced embodiment as it is oriented in the accompanying drawing figures or otherwise described in the following detailed description. However, it is to be understood that the embodiments described hereinafter may assume many alternative variations and embodiments. It is also to be understood that the specific devices illustrated in the

accompanying drawing figures and described herein are simply exemplary and should not be considered as limiting.

In one embodiment, a fluid sample collection device suitable for the collection of a blood sample and the separation of plasma, serum, or other fluid specimens from the cellular material (i.e., blood cells) of the blood sample is disclosed. However, the device described herein is generally applicable for separating solution (i.e., liquids) from solids like a filtration device. In particular, in one form, the device is adapted for collection of a blood sample through conventional sampling techniques and subsequent separation thereof by use of an assembly of components generally including an inner container, an outer container, and a closure member. The inner container generally draws plasma, serum, or other liquid specimens through a porous membrane, filter, or like separating member from the outer evacuated container to separate the plasma, serum, and/or other liquid specimen from the sample.

Referring initially to **FIGS. 1-4**, a device **10** for collecting and separating a fluid sample is generally shown. Device **10** is an assembly of components, namely a first or outer container or tube **12**, a second or inner container or tube **14**, and a closure **16** for sealing outer and inner containers **12**, **14**. Outer and inner containers **12**, **14** together form, pursuant to one embodiment, an evacuated collection assembly. Generally, outer container **12** encompasses inner container **14**, typically entirely accommodating the inner container **14** therein. Outer container **12** may be any container or vessel capable of containing a fluid sample, typically a blood sample, therein, and is desirably in the form of a conventional blood collection tube or vessel that may be evacuated by conventional means. Outer container **12** may be constructed of any known material, such as glass or molded plastic material and, in one particular embodiment, is constructed of polyethylene terephthalate (PET). Closure **16** is provided to make an air-tight seal with the outer container **12** and enclose inner container **14** within outer container **12**. Closure **16** is also used to support inner container **14** within outer container **12**, for example, in a suspended manner within the outer container **12**.

Outer container **12** is a generally cylindrical-shaped structure comprising a tubular sidewall **18** defining a first open or top end **20** and further forming a second closed or bottom end **22** of the outer container **12**. The closed end **22** may have a rounded or arcuate form as a conventional blood collection tube. Outer container **12** is sealed at open end **20** by closure **16** which is a pierceable component formed of rubber or molded plastic material but may be made of any pierceable elastomeric material. While closure **16** is generally akin to rubber or plastic tube stoppers known in the medical art, closure **16** possess several novel features in its

own right as discussed herein. Closure **16** is surrounded, at least in part, by a cap structure or member **24** which is included for protecting the closure **16** when seated within the open end **20** of outer container **12**. Cap member **24** is formed with an annular end wall **26** and a depending sidewall or skirt **28** which is configured to extend downward along sidewall **18** of outer container **12** when closure **16** is seated within the open end **20** of the outer container **12**. As discussed herein, closure **16** includes an insertable portion which is seated within the open end **20** of outer container **12** and which is held therein by frictional engagement with the inner surface or side of sidewall **18** and/or with an adhesive. Sidewall **28** of cap member **24** extends downward along the outer surface or side of sidewall **18** of outer container **12** to protect the exposed portion of closure **16** extending outward from the open end **20** of the outer container **12**. Annular end wall **26** defines a central aperture **30** to expose a portion of closure **16** to allow access to the interior of outer container **12**, which is typically accessed by a piercing element, such as a needle cannula, which is inserted through the pierceable closure **16** as described in greater detail herein.

Closure **16** is typically a unitary structure or body formed of rubber, plastic or another similar polymeric material, as described previously, and is generally an elastomeric closure element that is formed of suitable material capable of forming a substantially gas and liquid-tight seal with the open end **20** of outer container **12**. Additionally, the body of closure **16** is desirably capable of being punctured with a puncturing device, such as a needle cannula, as described previously. Such a needle cannula may be part of a blood collection device used to transfer blood into outer container **12**. Closure **16** is formed with a flanged head or cap portion **32** and a depending and integrally molded plug portion **34**. Cap portion **32** is adapted to seat or rest on a rim **36** defined by sidewall **18** of outer container **12** at the open end **20** of the outer container **12**. Plug portion **34** is generally adapted to be inserted into the open end **20** of outer container **12** and extend inward into the outer container **12** and form a substantially gas and liquid-tight seal with the inner surface or side of sidewall **18**. Thus, with plug portion **34** of closure **16** seated within the open end **20** of outer container **12**, a first interior chamber **38** is defined or formed within the outer container **12**. First interior chamber **38** may be placed under negative (i.e., vacuum) pressure with respect to external atmospheric pressure prior to sealing closure **16** in the open end **20** of outer container **12**, such that the interior of outer container **12** is under negative (i.e., vacuum) pressure. For example, after assembly of device **10** wherein inner container **14** is inserted in outer container **12**, the outer container **12** may be evacuated and subsequently sealed with closure **16** thereby placing first

interior chamber **38** under negative (i.e., vacuum) pressure and simultaneously placing the interior of inner container **14** under negative (i.e., vacuum) pressure.

Another aspect of device **10** relates to inner container **14** being movable within outer container **12** to accomplish full separation of the collected fluid sample. As shown in **FIG. 2**, an internal limiting structure **40** is provided within first interior chamber **38** which is used to limit internal movement of inner container **14** within outer container **12**, as discussed further herein. In the embodiment illustrated, limiting structure **40** is in the form of a circumferential flange or tab that extends inward from sidewall **18** of outer container **12** and, thus, is typically formed integrally with the body of outer container **12**. However, the specific movement-limiting structure illustrated in **FIG. 2** as limiting structure **40** should not be considered to limit the possible range of variations for limiting structure **40**. Such variations may take many forms, such as a circumferential restriction (i.e., narrowing) formed in sidewall **18** of outer container **12**, a sleeve structure disposed within outer container **12** and extending upward from the closed end **22** thereof, a platform extending upward from the closed end **22** of outer container **12**, one or more posts or tabs extending radially inward from sidewall **18** of outer container **12**, and like structures.

Cap portion **32** of closure **16** defines a top surface **42** which is typically partially enclosed by the annular end wall **26** of cap member **24**. Top surface **42** is exposed in the open area defined by central aperture **30** in cap member **24**, and this exposed area of top surface **42** is where a user of device **10** inserts a needle cannula or like piercing element to access the interior of outer container **12** and first interior chamber **38** in particular. Accordingly, to provide a blood sample to the first interior chamber **38**, a needle cannula or like piercing element of a blood collection device is used to penetrate the exposed portion of the top surface **42** of cap portion **32** of closure **16** which places the first interior chamber **38** in fluid communication with a needle inserted into a patient's vein for blood collection purposes. Since first interior chamber **38** is sealed and under negative (i.e., vacuum) pressure, blood flows from the vein, through the blood collection device, and into the first interior chamber **38** via the needle cannula inserted through closure **16**. If desired, the top surface **42** of cap portion **32** of closure may be recessed or otherwise shaped to provide a visual indication or cue of where to insert a needle cannula to appropriately penetrate the closure **16** and access the interior of outer container **12** without striking inner container **14**. This recessed or shaped area is designated by reference numeral **44** in **FIGS. 1-7** and is desirably part of the area of top surface **42** left exposed by central aperture **30** defined in the annular end wall **26** of cap member **24**. Further, plug portion **34** defines a bore or tubular

shaped recess **46** which is provided to support inner container **14** within outer container **12**, with inner container **14** depending or being suspended from plug portion **34** and extending into the first interior chamber **38** defined by outer container **12** and closure **16**.

Second or inner container **14** is a generally tubular or cylindrical structure in analogous manner to outer container **12** but may take other forms. Inner container **14** is desirably contained fully within outer container **12** and is initially associated with and supported by closure **16** to extend into the outer container **12**. In one embodiment, inner container **14** is a generally bell-shaped structure or unitary body which includes a first or distal end **50** and a second or proximal end **52**. Inner container **14** is generally comprised by a bell-shaped containment portion **54** defining or forming the distal end **50** and a tubular structure or conduit **56** that extends upward from containment portion **54** and defines or forms the proximal end **52** of the inner container **14**. Tubular conduit **56** forming the proximal end **52** of inner container **14** is adapted to engage the bore **46** defined in plug portion **34** of closure **16** whereby the inner container **14** may be suspended within outer container **12**. Containment portion **54** is hollow and defines a second interior chamber **58** which is in fluid communication with the upward-extending tubular conduit **56**.

In the embodiment illustrated in **FIGS. 1-4**, tubular conduit **56** is coaxially aligned and extends upward from containment portion **54** to engage bore **46** which is further desirably coaxially aligned with central aperture **30** in cap member **24**. However, the diameter of tubular conduit **56** and, thus, bore **46** is desirably smaller than central aperture **30** to allow a user to insert a needle cannula through closure **16** in an area radially outward from the proximal end **52** of inner container **14** and, hence, radially outward from tubular conduit **56**. As a result, the inserted needle cannula is inserted generally parallel to tubular conduit **56**, and is not inserted directly into tubular conduit **56**. The proper insertion of a needle cannula through closure **16** is shown in **FIG. 5** discussed herein. It will be appreciated from the foregoing that inner container **14** and outer container **12** are also coaxially aligned by the coaxial engagement of tubular conduit **56** in bore **46** in plug portion **34** of closure **16**. In other embodiments discussed herein, inner container **14** and closure **16** may be configured such that inner container **14** is radially offset from a central axis **L** of outer container **12**, as shown in **FIGS. 8-12** discussed herein.

As described previously, in one embodiment, inner container **14** depends (i.e., is suspended) from closure **16** and is supported to closure **16** by frictional and/or adhesive engagement of tubular conduit **56** in bore **46** defined in plug portion **34** of the closure **16**. Thus, with the foregoing engagement, the proximal end **52** of inner container **14** is secured to

closure **16** with the distal end **50** projecting into the first interior chamber **38** when the closure **16** is inserted into and secured in the open end **20** of outer container **12**. As shown in **FIG. 4**, for example, the distal end **50** of inner container **14** is spaced a distance "**a**" from limiting structure **40** which extends radially inward from the sidewall **18** of outer container **12**. The positioning of inner container **14** within outer container **12** further separates or segregates the first interior chamber **38** into an upper chamber portion **60** and a lower chamber portion **62**. Upper chamber portion **60** is generally defined by the area above bell-shaped containment portion **54** and the lower chamber portion **62** is generally defined by the area below the containment portion **54** (i.e., the area below distal end **50**). Containment portion **54** has an outer diameter that is less than the inner diameter of outer container **12** to allow fluid to flow downward to lower chamber portion **62** from upper chamber portion **60** along the inner surface of the sidewall **18** of the outer container **12** once introduced into the upper chamber portion **60** via, for example, a needle cannula. Thus, annular spacing "**S**" between the outer diameter of containment portion **54** and the inner diameter of outer container **12** is sufficient to allow the free flow of liquid, such as blood, from the upper chamber portion **60** to the lower chamber portion **62**.

Tubular conduit **56** of inner container **14** further acts as a port which, during use of device **10**, is adapted to selectively place the second interior chamber **58** defined by containment portion **54** of inner container **14** in fluid communication the first interior chamber **38** defined by the confines defined by outer container **12** and closure **16**. Such a port is generally defined by an opening or port **64** at the end of tubular conduit **56** and, hence, at the proximal end **52** of inner container **14**. To allow "outlet" port or opening **64** to be in fluid communication with the interior of outer container **12**, tubular conduit **56** is desirably releasably disposed in bore **46** in plug portion **34** of closure **16** and thereby releasably connected to closure **16**. Thus, in order for outlet port or opening **64** to be in fluid communication with the fist interior chamber **38**, tubular conduit **56** must first be released of engagement with closure **16**. Once released of engagement, inner container **14** moves downward within outer container **12** under the force of gravity and/or by force exerted by a user of device **10** as described herein. However, the length of downward movement is limited by limiting structure **40** disposed within outer container **12**. In particular, the interference engagement between the distal end **50** of inner container **14** and limiting structure **40** limits downward movement of the inner container **14** within outer container **12** to distance **a**. Distal end **50** of inner container **14** is desirably fully open so that containment portion **54** defines an end opening **66** for admittance of fluid into the containment portion **54**.

End opening **66** may be the diameter of containment portion **54** or have a smaller diameter than the containment portion **54**.

The second interior chamber **58** defined by inner container **14** and, in particular, by containment portion **54** is separated from the first interior chamber **38** defined by outer container **12** and closure **16** by a porous member or filter element **70**. Typically, porous membrane **70** is adapted to separate plasma or serum from a whole blood sample, as will be discussed in more detail herein. Porous membrane **70** is disposed in or over end opening **66** in containment portion **54** and fully covers end opening **66** on an opposite side of a top end or side **72** of the containment portion **54**. Additionally, porous membrane **70** may be formed as a disk-shaped structure with a filtering center area which is secured to the distal end **50** of inner container **14** and fully covers end opening **66** in containment portion **54**, thereby also forming the distal end of containment portion **54**. Porous membrane **70** may be constructed of any suitable material including pores which are large enough to draw plasma or serum therethrough under a normal negative (i.e., vacuum) pressure of a conventional evacuated blood collection tube, but small enough to prevent blood cell cells, including red cells, white blood cells, platelets, etc., and aggregates such as blood clots from passing therethrough. As examples, porous membrane **70** may be comprised of high density polyethylene, high density polypropylene, ceramic, porous metal, porous glass, glass fibers, polyvinyl polymers, paper, natural fibers, and combinations thereof. As used herein, the terms "porous membrane" and "filter" or "filter element" are used interchangeably and can relate further to a column-like filter, a filter paper (i.e., Whateman paper), two or more stacked filter papers, a single membrane, or multiple membranes. Variations of the structural shape or supporting structure of porous membrane **70** are therefore contemplated and are within the skill of those skilled in the art. In general, filter paper used for porous membrane **70** is suitable for separating cells from plasma/serum and a membrane **70** with a selected pore size according to the molecular weights of proteins may be used to separate proteins which are smaller than the selected pore size from a collected blood sample.

The pore size of porous membrane **70** may be varied according to the required selectivity need by the user in separating a fluid sample. For example, the pore size of porous membrane **70** may be selected to achieve a selectivity according to the molecular weight of molecules desired to pass through the membrane. A pore size of 60,000 Daltons is used to prevent proteins or other macormolecules with 60,000 or higher molecular weight from passing to the second interior chamber **58**. Alternatively, porous membrane **70** may be adapted to remove albumin, immunoglobulin, and/or other large molecules from the collected

plasma or serum. Further, porous membrane **70** may be a molecular weight cut-off membrane of 10,000 Daltons or less for peptide extraction from the blood sample, or a molecular weight cut-off membrane of 2,000 Daltons or less to separate metabolites and other small molecules for biochemical analysis.

A porous membrane **70** having a pore size smaller than 50,000 Daltons allows only molecules smaller than 50,000 Daltons to pass through the porous membrane **70** so that, in addition to cells and clots, albumin, antibodies, and other large molecules remain in outer container **12** and do not pass to inner container **14**. This is important in the context of biomarker discovery, as albumin and many other large molecules in high abundance in blood often are not meaningful and can, thus, be easily removed. A porous membrane **70** of 3,000-10,000 in pore size allows only peptides less than about 3,000-10,000 Daltons to pass through. These peptides are ready for proteomic and diagnostic analysis. For general plasma or serum collection, a regular filter paper or porous membrane with a 0.45-1.0 μm pore size can be used for porous membrane **70**. This porous membrane **70** can remove all blood cells including platelets and, therefore, the collected plasma or serum in inner container **14** is a platelet-free sample. As a further example, when a porous membrane **70** with a pore size of about 0.22 μm is used, bacteria cells and viral particles, such as HIV, in addition to all blood cells, will not pass to inner container **14** and will be retained in lower chamber portion **62**. As a result, the plasma or serum collected in inner container **14** will be free of infection, providing bio-safety plasma or serum samples for downstream laboratory analysis. A desirable pore size range for the removal of bacteria cells and viral particles is about 0.1 μm to 2 μm. Membranes with pore sizes of 3,000, 10,000, 30,000, 50,000, 100,000, and 200,000 Daltons are commercially available.

It is contemplated that outer container **12** may include cell metabolism regulators, an agglutinating agent, and/or an anticoagulant therein. Agglutinating agents are used to create large aggregates of cells, which facilitates the filtering process. Suitable agglutinating agents include, but are not limited to, lectins, such as potato or wheat lectins. Alternative agglutinating agents may include antibodies with an affinity for blood cells attached to microbeads. The agglutinating agent may also be in the form of a solution, pellet, pill, or lyophilized specimen, such as granules, coated on a separate structure or coated on an inner surface of outer container **12**, and/or both outer and inner surfaces of inner container **14**. An anticoagulant such as heparin, EDTA, sodium citrate, or other known compound for preventing coagulation of blood can also be used. The term "agglutinating agent" is used to denote the use of an agglutinating agent alone to form cell aggregates, or the use of an

agglutinating agent in combination with a structure that can impart desired properties to the cellular aggregates. For example, the structure may be a microbead of a particular density, coated with an agglutinating agent. In another example, the structure can have a specific geometry, such as a string or cylinder, to impart a desired shape to the aggregates, such as a shape that is less densely packed than cellular aggregates without the structure, and which permits plasma to pass through the aggregates. The foregoing examples are not intended to be limiting, and any structure having the desired properties may be used as the starting particles for forming the cellular aggregates. In all embodiments described herein, the term "agglutinating agent" will refer to the use of an agglutinating agent alone, or in combination with a structure as described hereinabove, which has been coated with an agglutinating agent.

Inner container **14** may also optionally include an additive or additives similar to those in outer container **12** but which can interact only with the separated liquid, typically plasma or serum. Many additives have been found to cause hemolysis and other damage to blood cells. Accordingly, a benefit of the provided by the dual outer and inner containers **12**, **14** structure described in the foregoing description is the ability to place distinct additives in inner container **14** where they will not come into contact with blood cells present in the whole sample (i.e., in first interior chamber **38**) thereby reducing any adverse effects to the blood cells. Examples of additives include anticoagulants, detergents, preservatives, and enzymatic inhibitors such as protease inhibitors such as 4-(2-Aminoethyl)-benzenesulfonyl fluoride hydrochloride (AEBSF).

The overall size of outer and inner containers **12**, **14** are varied to provide predetermined relative differences in volume between the outer and inner containers **12**, **14** and, correspondingly, predetermined relative differences between the upper and lower chamber portions **60**, **62**. These predetermined relative differences can be chosen according to known characteristics of the collected fluid sample, typically blood. For example, the volume of the lower chamber portion **62** may be designed to be about 5X ml of fluid sample (i.e., blood), while the volume of inner container **14** (including containment portion **54** and tubular conduit **56**) is about 3X ml resulting in a ratio of volumes of about 5:3 which corresponds to the volume ratio of cells-pellets to plasma in whole blood. "X" in the foregoing can be any whole number or fraction (i.e., 0.05-10) and can be changed according to the total volume of the first interior chamber **38** in outer container **12**. The total volume of the upper chamber portion **60** is about 6X ml and the total sample volume available in device **10** is about 8X ml in the foregoing example.

To assemble device **10**, inner container **14** is affixed to closure **16** by inserting tubular conduit **56** into bore **46** in plug portion **34** of the closure **16** forming an assembly structure comprised of inner container **14** and closure **16**, with inner container **14** suspended or depending from closure **16**. Outer container **12** and the assembly of inner container **14** and closure **16** are placed into an evacuator and, when a desired vacuum level is reached, inner container **14** and closure **16** are inserted into the open end **20** of outer container **12**. Once this assembly is disposed in outer container **12**, plug portion **34** of closure **16** is inserted into the open end **20** of outer container **12** which engages the inner surface of sidewall **18** of the outer container **12** and forms a gas and liquid-tight seal with the inner surface of the sidewall **18**. Cap portion **32** of closure **16** rests on the rim **36** of outer container **12**. Typically, cap member **24** is preassembled to closure **16**, with annular end wall **26** engaged with the top surface **42** of cap portion **32** of the closure **16** and the sidewall **28** of the cap portion **32** extending around the circumference of closure **16**. With closure **16** sealed in the open end **20** of outer container **12**, both the first interior chamber **38** defined by outer container **12** and the second interior chamber **58** defined by inner container **14** are at negative (i.e., vacuum) pressure. Device **10** is now ready for a fluid collection and separation procedure.

Referring further to **FIGS. 5-7** in addition to **FIGS. 1-4**, operational use of device **10** in the collection and separation of a whole blood sample will now be discussed. As indicated immediately above, device **10** is initially provided in an evacuated state with inner container **14** depending from closure **16** and extending into outer container **12** and both containers **12**, **14** in an evacuated state. The first interior chamber **38** is in fluid communication with the second interior chamber **58** through porous membrane **70** which is adapted to separate plasma or serum from the cellular components of a whole blood sample. A blood sample **B** is introduced into outer container **12** via a needle cannula **N** which is inserted through closure **16** and into the first interior chamber **38** in outer container **12**. Needle cannula **N** may be associated with a conventional blood collection device or set as described previously. Needle cannula **N** is inserted into the top surface **42** of closure **16** in the area left exposed by central aperture **30** in cap member **24**, with the recessed area **44** in the top surface **42** providing a visual indication or cue of where to insert the needle cannula **N** to appropriately penetrate the closure **16** and access the interior of outer container **12** without striking or entering inner container **14**. Blood sample **B** is drawn into the first interior chamber **38** in outer container **12** based on the negative (i.e., vacuum) pressure therein, and flows downward from the upper chamber portion **60** to the lower chamber portion **62** of the first interior chamber **38** through circumferential spacing or gap **S** between the inner container **14** and outer container **12**.

Blood sample **B** fills the lower chamber portion **62** to a level where it reaches porous membrane **70**. When the blood sample **B** reaches porous membrane **70**, the pressure in inner container **14** is approximately equal to that of outer container **12**. As additional blood sample **B** fills outer container **12**, it covers the outer or exposed surface of porous membrane **70** until the outer container **12** (i.e., into upper chamber portion **60**) is filled with the total volume of the sample to be taken, based upon the vacuum pressure available within the outer container **12**. At this point, no further sample can be drawn as the negative (i.e., vacuum) pressure within the first interior chamber **38** is exhausted or insufficient to continue sample collection and collection of blood sample **B** ceases. Additionally, the level of blood sample **B** in outer container **12** is above the inlet to inner container **14** (i.e., above porous membrane **70**) and a pressure differential exists between the outer and inner containers **12, 14**. A residual negative (i.e., vacuum) pressure is present within inner container **14** after blood sample **B** collection which adds to the pressure differential present between the outer and inner containers **12, 14** due to the liquid height differential between the outer and inner containers **12, 14**.

With the level of blood sample **B** in outer container **12** being above porous membrane **70** and a residual vacuum being present within inner container **14**, a pressure differential exists between the outer container **12** and inner container **14**, with the first interior chamber **38** in the outer chamber **12** being at a higher pressure than the second interior chamber **58** in inner container **14**. This pressure differential forces the liquid portion of the collected blood sample **B**, which is plasma or serum (hereinafter "**P/S**"), through filtering porous membrane **70**. In particular, plasma or serum **P/S** passes through porous filter **70** in the direction of arrow A_1 and enters the second interior chamber **58** defined by inner container **14** and containment portion **54** of inner container **14** in particular, while the blood sample **B** moves in the opposite direction to arrow A_1 (i.e., downward) in outer container **12**. Porous membrane **70** prevents cellular material and platelets (hereinafter "**C/P**") from entering the second interior chamber **58** defined by inner chamber **14** and containment portion **54** in particular. At this point, as illustrated in **FIG. 6**, only a portion of blood sample **B** is filtered with a partially recovered or separated portion of the plasma or serum **P/S** present within the second interior chamber **58** defined by inner chamber **14** and containment portion **54** thereof, as the residual vacuum in inner container **14** is now substantially exhausted. Additional plasma or serum **P/S** is present in blood sample **B** but the remaining pressure differential present between the height level of blood sample **B** in the first interior chamber **38** (i.e., in upper chamber portion **60**) in outer container **12** and the height level of plasma or serum **P/S**

in the second interior chamber **58** in inner container **14** (i.e., in containment portion **54**) is insufficient to cause further separation.

Referring now in particular to **FIG. 7**, additional separation of blood sample **B** can be effected by increasing the pressure differential between the level of blood sample **B** in the first interior chamber **38** in outer container **12** and the level of plasma or serum **P/S** in the second interior chamber **58** in inner container **14**. This is accomplished by a user of device **10** pressing downward on the top surface **42** of closure **16** in the open area defined by annular end wall **26** which has the effect of releasing inner container **14** from the closure **16**. In particular, the user presses down on closure **16** in the direction of arrow A_2 which causes tubular conduit **56** to be released from bore **46** defined in the plug portion **34** of the closure **16**. Once released of engagement with the plug portion **34** of closure **16**, port **64** in tubular conduit **56** places the second interior chamber **58** in inner container **14** in fluid communication with the upper chamber portion **60** of the first interior chamber **38** in outer container **12**. Additionally, substantially simultaneously, inner container **14** moves downward in outer container **12** under the force applied in the direction of arrow A_2 and/or by the force of gravity. This downward movement is interrupted when the distal end **50** of inner container **14** comes into interference contact with limiting structure **40** in outer container **12**. Thus, inner container **14** is movably supported within outer container **12**.

With the disengagement of inner container **14** from closure **16** as just described, an air pressure equalization is now present between the upper chamber portion **60** of the first interior chamber **38** in outer container **12** and the second interior chamber **58** in inner container **14**. However, with the downward movement of inner container **14** within outer container **12**, additional height differential exists between the level of blood sample **B** in the upper chamber portion **60** of the first interior chamber **38** and the level of separated plasma or serum **P/S** in the second interior chamber **58**. This height differential provides additional pressure differential which "presses" additional plasma or serum through porous membrane **70**. Separation of plasma or serum **P/S** continues until the level of plasma or serum **P/S** in the second interior chamber **58** in inner container **14** substantially equalizes with the level of cellular material/platelets **C/P** in the first interior chamber **38** in outer container **12**, as substantially shown in **FIG. 7**. At this point, the first interior chamber **38** and, primarily, the lower chamber portion **62** thereof contains cellular material/platelets **C/P** while the second interior chamber **58** contains plasma or serum **P/S**. Separation can also be accomplished by disconnecting inner container **14** from outer container **12** in the manner just described and then placing device **10** in a centrifuge and spinning at a proper G-force for 10-30 minutes. It

will be appreciated that closure **16** is desirably made of an elastomeric material with sufficient resiliency to allow a user of device **10** to press down on the closure **16** and cause sufficient expansion of bore **46** in the plug portion **34** of the closure **16** with finger pressure alone to cause tubular conduit **56** to become disengaged from the bore **46**. Moreover, this finger pressure alone may be sufficient to simply eject tubular conduit **56** from bore **46** in the plug portion **34** of the closure **16**.

As will be appreciated from the foregoing blood collection and separation example, closure **16** may be removed and inner container **14** removed from outer container **12**. Plasma or serum **P/S** present in the second interior chamber **58** in inner container **14** can then be accessed for downstream tests. Additionally, the first interior chamber **38** in outer container **12** contains primarily cellular material and platelets **C/P** which again can be removed for downstream testing.

Referring to **FIGS. 8-11**, another embodiment of device **10a** is shown. Device **10a** is similar in most respects to device **10** discussed previously but includes certain modifications to inner container **14a** and closure **16a**. In device **10a**, tubular conduit **56a** extending from containment portion **54a** of inner container **14a** is offset radially from a central axis of the containment portion **54a**. As a result, the top end or side **72a** of containment portion **54a** is tapered or angled to form the transition to the tubular conduit **56a**. As tubular conduit **56a** is no longer coaxially aligned with containment portion **54a**, inner container **14a** itself cannot be mounted to closure **16a** in the manner described previously. Closure **16a** is now formed to accommodate the offset axis configuration of tubular conduit **56a** of inner container **14a**. In particular, bore **46a** in the plug portion **34a** of closure **16a** is offset radially from the central axis of the closure **16a** and, thus, from the central axis **L** of outer container **12a** when the closure **16a** is seated in the open end **20a** of the outer container **12a**. Accordingly, tubular conduit **56a** lies along an axis offset radially and generally parallel to the central axis **L** of outer container **12a** when the tubular conduit **56a** is joined to closure **16a** and the closure **16a** is seated in the open end **20a** of the outer container **12a**. As will be appreciated from **FIG. 10**, containment portion **54a** of inner container **14a** lies generally coaxially aligned with the central axis **L** of outer container **12a**, only tubular conduit **56a** is offset radially from the central axis **L**.

The radially offset configuration of tubular conduit **56a** provides additional clearance to one side of the tubular conduit **56a** for insertion of needle cannula **N** into outer container **12a**, as shown in **FIG. 10**. This additional clearance provides a user of device **10a** with additional space for inserting needle cannula **N** into outer container **12a** and helps minimize

the possibility of inserting the needle cannula N directly into tubular conduit **56a** by mistake. To further aid the user in inserting needle cannula N correctly into outer container **12a**, closure **16a** is slightly modified as shown in **FIGS. 10** and **11** and, in particular, slightly modified over closure **16** discussed previously. Modified closure **16a** includes a generally planar top surface **42a** which features two markings. One or a first marking **74** denotes the appropriate location for the user of device **10a** to insert or pierce closure **16a** with needle cannula N while a second marking **76** denotes the location of the end of tubular conduit **56a**, which is also the proximal end **52** of the inner container **14a**. As a result, the user is made aware of the location of tubular conduit **56a** and, further, the appropriate location to pierce closure **16a** with needle cannula N. If desired, the central aperture **30a** in the annular end wall **26a** of cap member **24a** may be made larger to provide a greater degree of separation between the first marking **74** denoting the location for insertion of needle cannula N and the second marking **76** denoting the location of tubular conduit **56a**. Second marking **76** also aids the user in locating his or her finger(s) to apply the force necessary to dislodge tubular conduit **56a** from bore **46a** during a fluid sample collection and separation procedure. Other than the foregoing differences, device **10a** is similar in all respects to device **10** and operates in an analogous manner to device **10** as detailed previously.

FIG. 12 shows a further embodiment of device **10b** which is similar in most respects to devices **10a** just discussed and includes the same modifications to inner container **14b** and closure **16b** as found in inner container **14a** and closure **16a**. Device **10b** differs from device **10a** in that limiting structure **40a** found on the sidewall **18a** of outer container **12a** of device **10a** is not present in outer container **12b**. In device **10b**, closed end **22b** of outer container **12b** forms the limiting structure for limiting downward movement of inner container **14b** in outer container **12b** during a fluid sample collection and separation procedure involving device **10b**. As the closed end **22b** forms the movement limiting structure for inner container **14b**, it will be apparent from **FIG. 12** that tubular conduit **56b** is elongated over tubular conduit **56a** detailed previously. Other than the two foregoing differences, device **10b** is similar in all respects to device **10a** and operates in an analogous manner as device **10b** with a few minor differences as detailed herein.

In use, device **10b** collects a fluid sample in the manner described previously. Such a collection procedure begins with the insertion of needle cannula N through closure **16b** and the depositing of a fluid sample in the first interior chamber **38b** in outer container **12b**. Separation of the fluid sample commences as described previously in connection with device **10**. As shown in **FIG. 12**, the distal end **50b** of inner container **14b** is separated by a distance

"**b**" from the closed end **22b** of outer container **12b**. Distance **b** is approximately the same distance as distance or length **a** described previously in connection with device **10**. When it is desired to "complete" the fluid sample separation, the user of device **10b** initiates the detachment or disengagement of tubular conduit **56b** from closure **16b** in the manner described previously, but inner container **14b** is limited in its downward movement by interference contact between the distal end **50b** of the inner container **14b** and the closed end **22b** of the outer container **12b**. Final fluid sample separation occurs when the distal end **50b** of inner container **14b** abuts against the closed end **22b** of outer container **12b** which forms the limiting structure limiting movement of the inner container **14b** within the outer container **12b** in this embodiment. This final separation procedure is similar to the final fluid sample separation which occurs when inner container **14** is released of engagement with closure **16** and moves downward to contact limiting structure **40** within outer container **12** in device **10**.

FIGS. 13-14 show two modifications to closure **16** which may be used in any of the embodiments of device **10, 10a, 10b** described hereinabove. In **FIG. 13**, closure **16** includes a depending portion **78** which depends from plug portion **34** and which is intended to replace bore **46** as the carrying structure for tubular conduit **56** of inner container **14**. Accordingly, depending portion **78** extends into the end opening **66** in tubular conduit **56** and frictionally engages the inner surface or side of the sidewall of tubular conduit **56** to suspend inner container **14** from closure **16**. As further shown in **FIG. 13**, a needle guide slot **80** may be defined in closure **16** and which extends through cap portion **32** and partially through plug portion **34** to help guide a user in locating a needle cannula (not shown) at the proper location to puncture or pierce the closure **16** to admit a fluid sample into the first interior chamber **38** in outer container **12**. Such a needle guide slot **80** is applicable to all the closures **16, 16a, 16b** described previously. The central aperture **30** defined by annular end wall **26** of cap member **24** may be sized (i.e., enlarged) in a similar manner to central aperture **30a** defined by annular end wall **26a** of cap member **24a** so that additional radial clearance may be provided between the needle guide slot **80** the proximal end **52** of inner container **14**.

In **FIG. 14**, closure **16** includes a circumferential rim **82** which is formed as part of cap portion **32** and is configured to overlap and extend downward along the sidewall **18** of outer container **12**. Rim **82** extends downward along the sidewall **18** of outer container **12** in a similar manner to sidewall **28** of cap member **24**. Sidewall **28** of cap member **24** is now generally coextensive with cap portion **32** and rim **82** of closure **16**. Rim **82** provides additional sealing on the outside of outer container **12** thereby providing more robust sealing between closure **16** and the open end **20** of outer container **12**.

While several embodiments of a fluid sample collection device and method were described in the foregoing detailed description, those skilled in the art may make modifications and alterations to these embodiments without departing from the scope and spirit of the invention. Accordingly, the foregoing description is intended to be illustrative rather than restrictive. The invention described hereinabove is defined by the appended claims and all changes to the invention that fall within the meaning and the range of equivalency of the claims are embraced within their scope.

WHAT IS CLAIMED IS:

1. A device for collecting and separating a fluid sample comprising:

an evacuated outer container having a first open end and a second closed end with a pierceable closure closing the first open end and defining a first interior chamber therein; and

an inner container contained within the outer container and separating the first interior chamber into an upper chamber portion in fluid communication with a lower chamber portion, the inner container defining a second interior chamber separated from the lower chamber portion of the first interior chamber through a porous membrane and including a port adapted to place the second interior chamber in fluid communication with the first interior chamber.

2. A device as claimed in Claim 1, wherein the porous membrane comprises filter paper.

3. A device as claimed in Claim 1, wherein the porous membrane has a pore size that controls the passing of desired molecules.

4. A device as claimed in Claim 3, wherein the porous membrane prevents molecules of 60,000 Daltons or higher from passing into the inner container.

5. A device as claimed in Claim 3, wherein the porous membrane is capable of removing albumin, immunoglobulin or other large molecules from a blood sample.

6. A device as claimed in Claim 3, wherein the porous membrane prevents molecules of 10,000 Daltons or higher from passing into the inner container.

7. A device as claimed in Claim 6, wherein the porous membrane prevents molecules of 2,000 Daltons or higher from passing into the inner container.

8. A device as claimed in Claim 3, wherein the porous membrane has a pore size to enable peptide extraction from a blood sample.

9. A device as claimed in Claim 3, wherein the porous membrane has a pore size to enable separation of metabolites and other small molecules from a blood sample.

10. A device as claimed in Claim 1, wherein the pore size of the porous membrane is between 0.1 μm to 2 μm.

11. A device as claimed in Claim 10, wherein the porous membrane is a 0.22 μm membrane.

12. A device as claimed in Claim 10, wherein the porous membrane enables removal of virus particles for bio-safety plasma or serum sample collection.

13. A device as claimed in Claim 10, wherein the porous membrane is a 0.45-1.0 μm membrane.

14. A device as claimed in Claim 10, wherein the porous membrane enables platelet-free plasma or serum sample collection.

15. A device as claimed in Claim 1, wherein the inner container is suspended within the outer container.

16. A device as claimed in Claim 1, wherein the inner container is releasably connected with the pierceable closure.

17. A device as claimed in Claim 16, wherein release of the inner container from the pierceable closure opens the port of the inner container and places the second interior chamber of the inner container in fluid communication with the first interior chamber.

18. A device as claimed in Claim 1, wherein the inner container is movably supported within the first interior chamber of the outer container.

19. A device as claimed in Claim 18, wherein movement of the inner container within the first interior chamber opens the port of the inner container and places the second interior chamber of the inner container in fluid communication with the first interior chamber.

20. A device as claimed in Claim 19, wherein the outer container comprises structure therein to support the inner container within the first interior chamber after movement of the inner container within the first interior chamber.

21. A device as claimed in Claim 1, wherein the outer container supports the inner container within the first interior chamber.

22. A device as claimed in Claim 1, wherein the outer container comprises an additive selected from the group consisting of agglutinating agents and anticoagulants.

23. A device as claimed in Claim 1, wherein the porous membrane comprises a material selected from the group consisting of high density polyethylene, high density polypropylene, ceramic, porous metal, porous glass, glass fibers, polyvinyl polymers, paper, natural fibers, and combinations thereof.

24. A device for separating plasma or serum from a blood sample comprising:

an evacuated collection assembly comprising an outer container and an inner container;

the outer container including a pierceable closure at one end; and

the inner container contained within the outer container, the interior of the inner container separated from the outer container by a porous membrane on the bottom of the inner container, and the inner container comprising a port in fluid communication with the inner container and the inner container releasably connected to the pierceable closure.

25. The device as claimed in Claim 24, wherein the inner container is entirely accommodated within the outer container.

26. The device as claimed in Claim 24, wherein the port is in fluid communication with the outer container when the inner container is disconnected from the pierceable closure.

27. The device as claimed in Claim 24, wherein release of the inner container from the pierceable closure opens the port to unrestricted fluid communication with the outer container.

28. The device as claimed in Claim 24, further comprising structure on the inner surface of the outer container for maintaining a position of the inner container relative to the outer container.

29. The device as claimed in Claim 24, wherein a pressure differential established between the outer container and the inner container upon entry of the blood sample into the outer container facilitates transportation of plasma or serum through the porous membrane into the inner container, while preventing the transfer of blood cells therethrough

30. A method for separating plasma or serum from a blood sample comprising the steps of:

providing an evacuated collection assembly comprising an outer container having a pierceable closure at one end, an inner container contained within the outer container and defining an interior chamber therein, and a porous membrane separating the interior chamber of the inner container from the outer container; and

collecting a blood sample within the outer container of the assembly, thereby creating a pressure differential between the outer container and the inner container, the pressure differential causing plasma or serum from the blood sample to flow into the interior chamber of the inner container through the porous membrane.

31. The method of claim 30, wherein the plasma or serum flows into the inner container in a direction generally opposite to the direction of blood particle flow into the outer container during the collecting.

32. The method of claim 30, wherein the plasma or serum is removable from the inner container after the blood sample collection is complete.

33. The method of claim 30, wherein the inner container comprises a port, and the method further comprises placing the port in fluid communication with the interior chamber of the outer container.

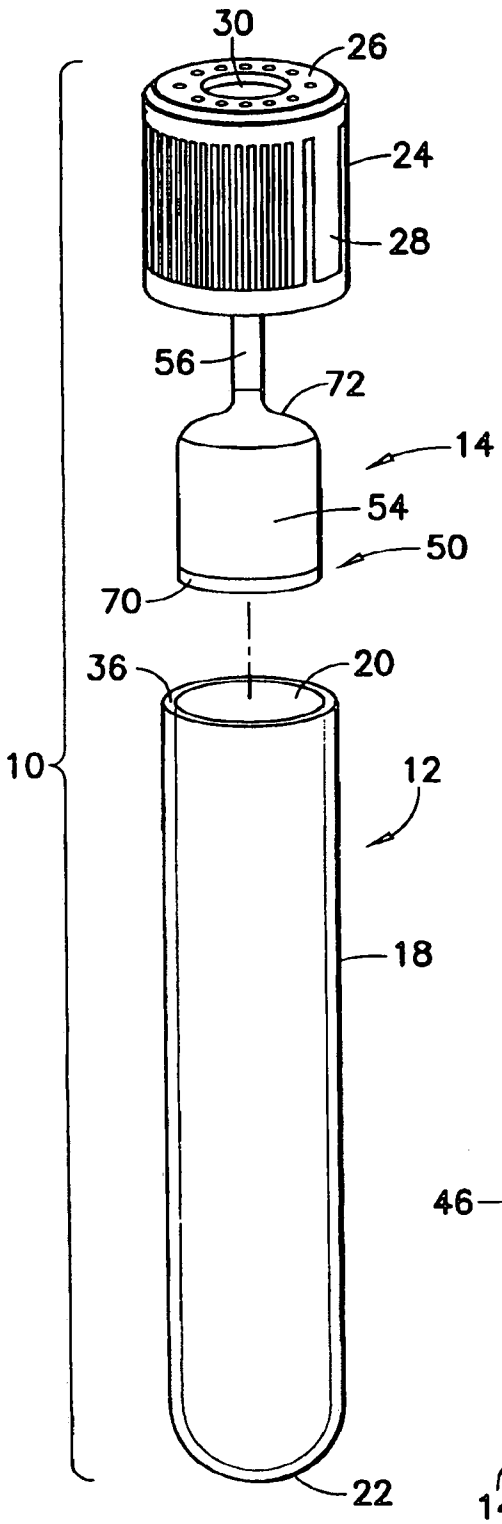


FIG. 1

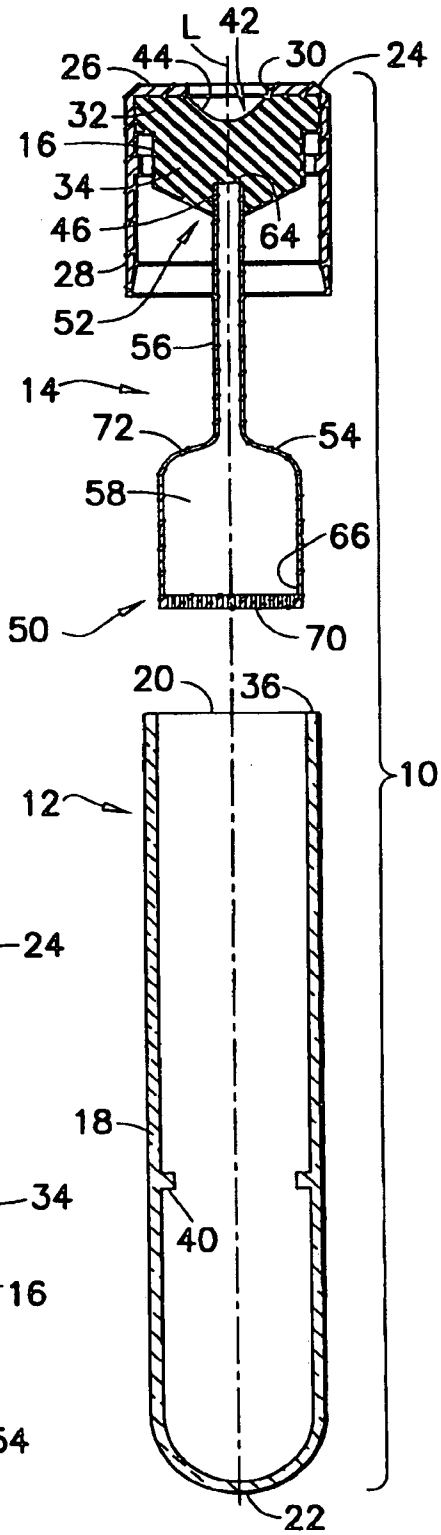


FIG. 2

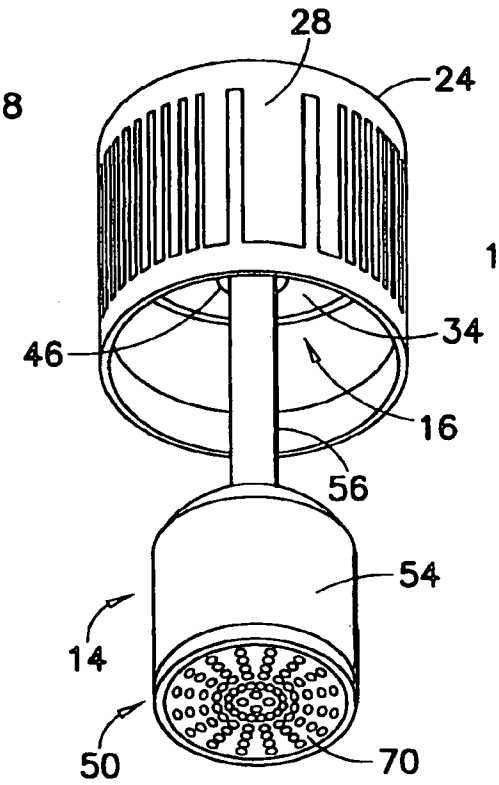


FIG. 3

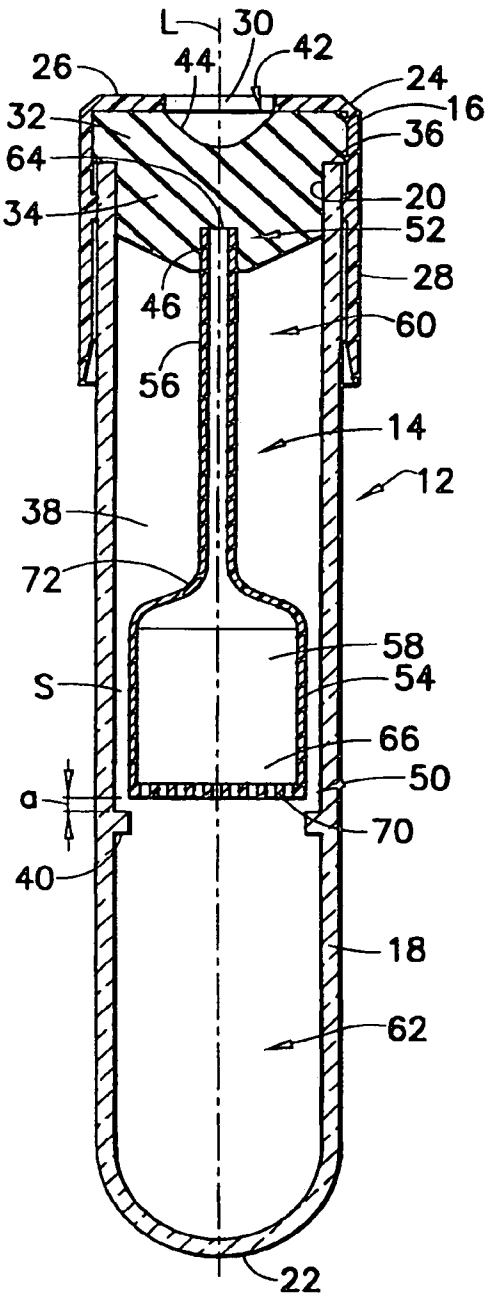

L
30
42
44
26
24
16
32
36
64
20
34
52
28
46
60
56
14
12
38
72
58
S
54
66
50
a
70
40
18
62
22

FIG.4

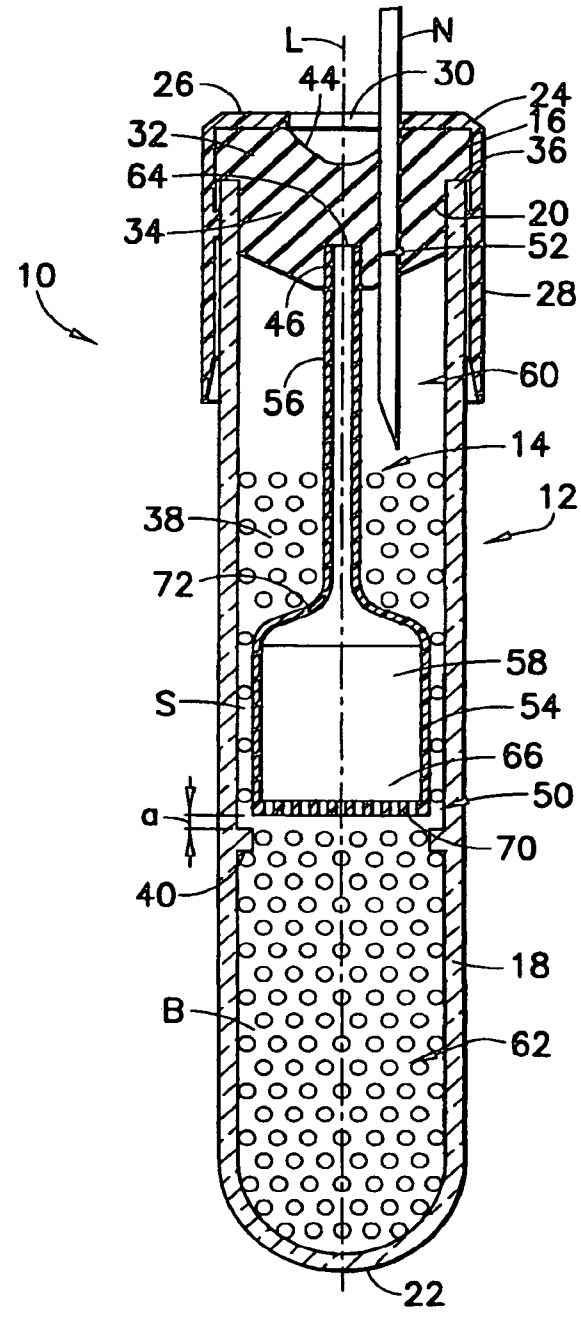

10
L
N
30
44
26
24
16
32
36
64
20
34
52
28
46
60
56
14
12
38
72
58
S
54
66
50
a
70
40
18
B
62
22

FIG.5

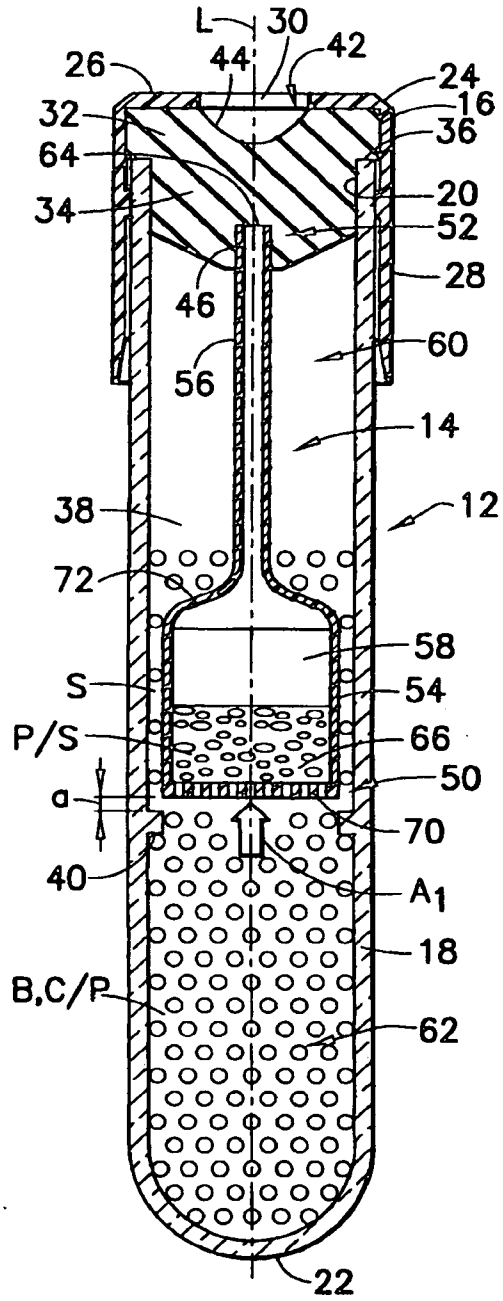

L
30
42
44
26
24
32
16
36
64
20
34
52
28
46
60
56
14
38
12
72
58
S
54
P/S
66
50
a
70
40
A1
18
B,C/P
62
22

FIG.6

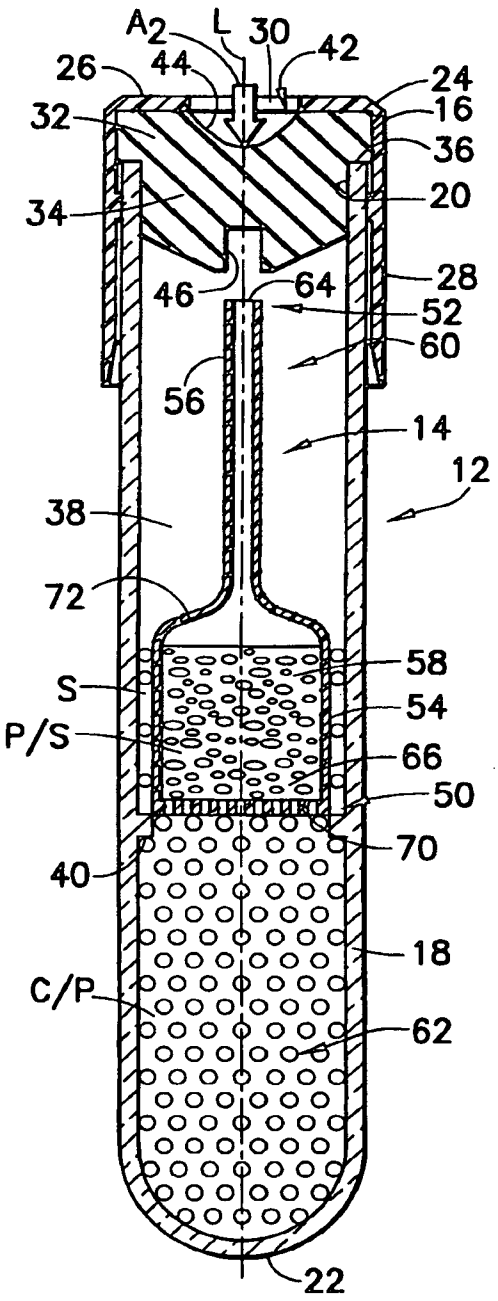

A2
L
30
42
44
26
24
32
16
36
20
34
28
46
64
52
60
56
14
12
38
72
58
S
54
P/S
66
50
70
40
18
C/P
62
22

FIG.7

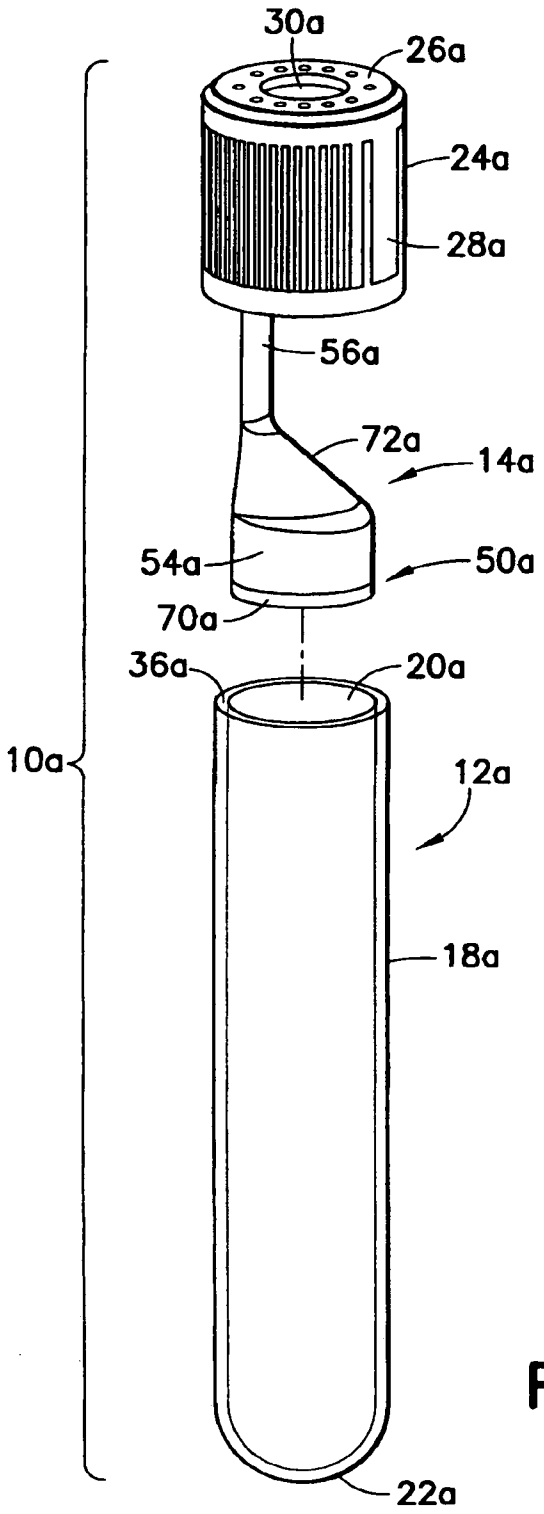


FIG.8

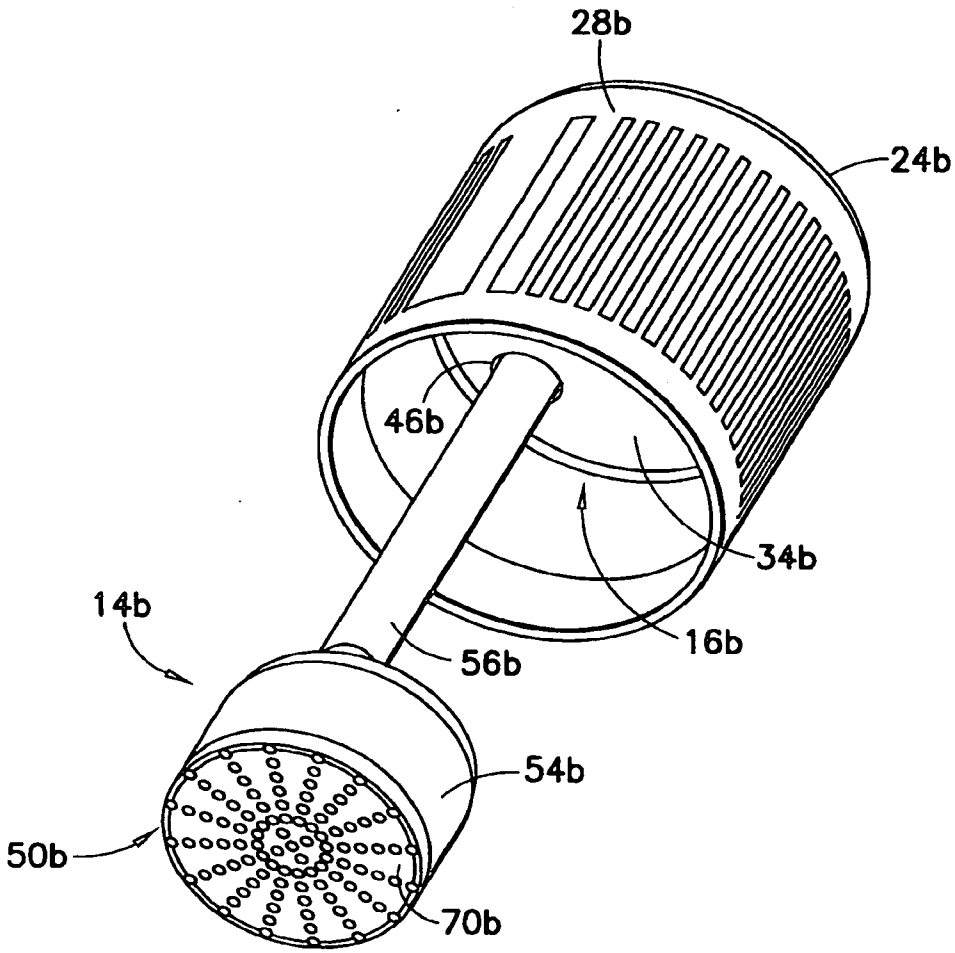
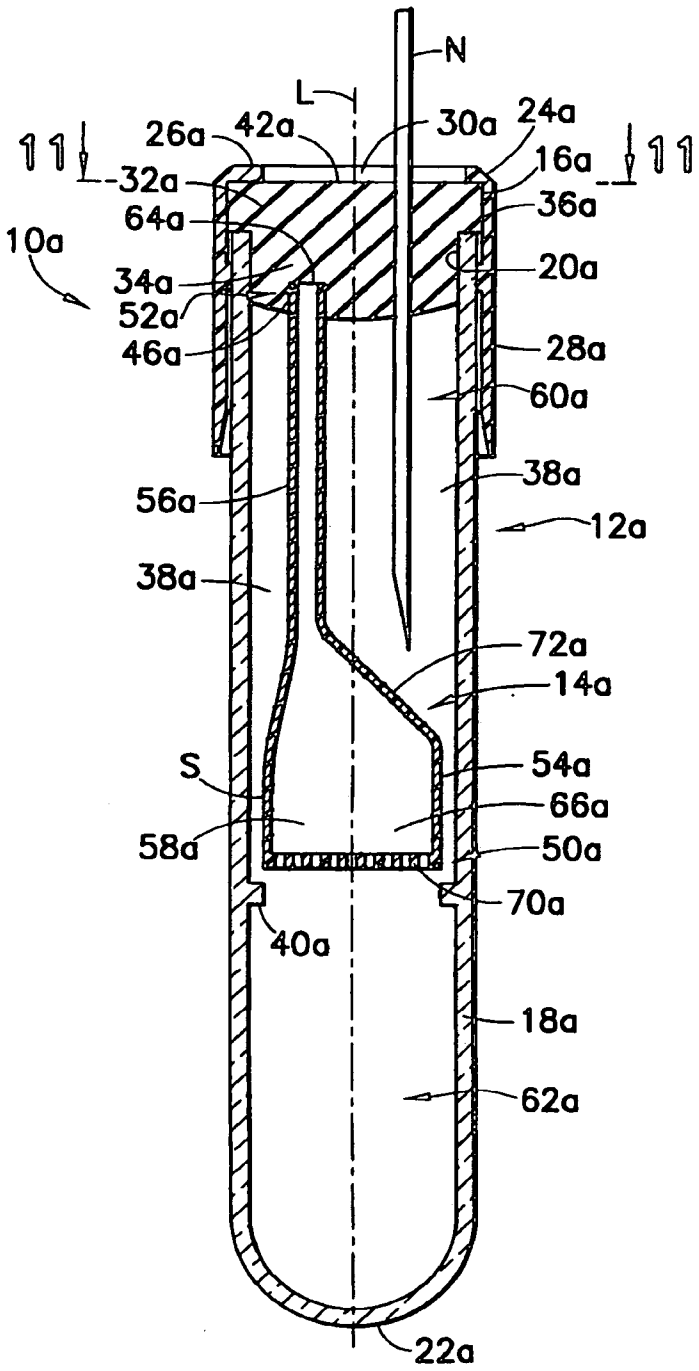


FIG.9


N
L
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26a
42a
30a
24a
16a
11
32a
36a
64a
10a
20a
34a
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46a
60a
38a
56a
12a
38a
72a
14a
S
54a
66a
58a
50a
70a
40a
18a
62a
22a

FIG. 10

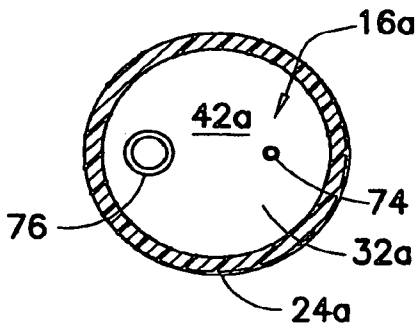
16a
42a
74
76
32a
24a

FIG. 11

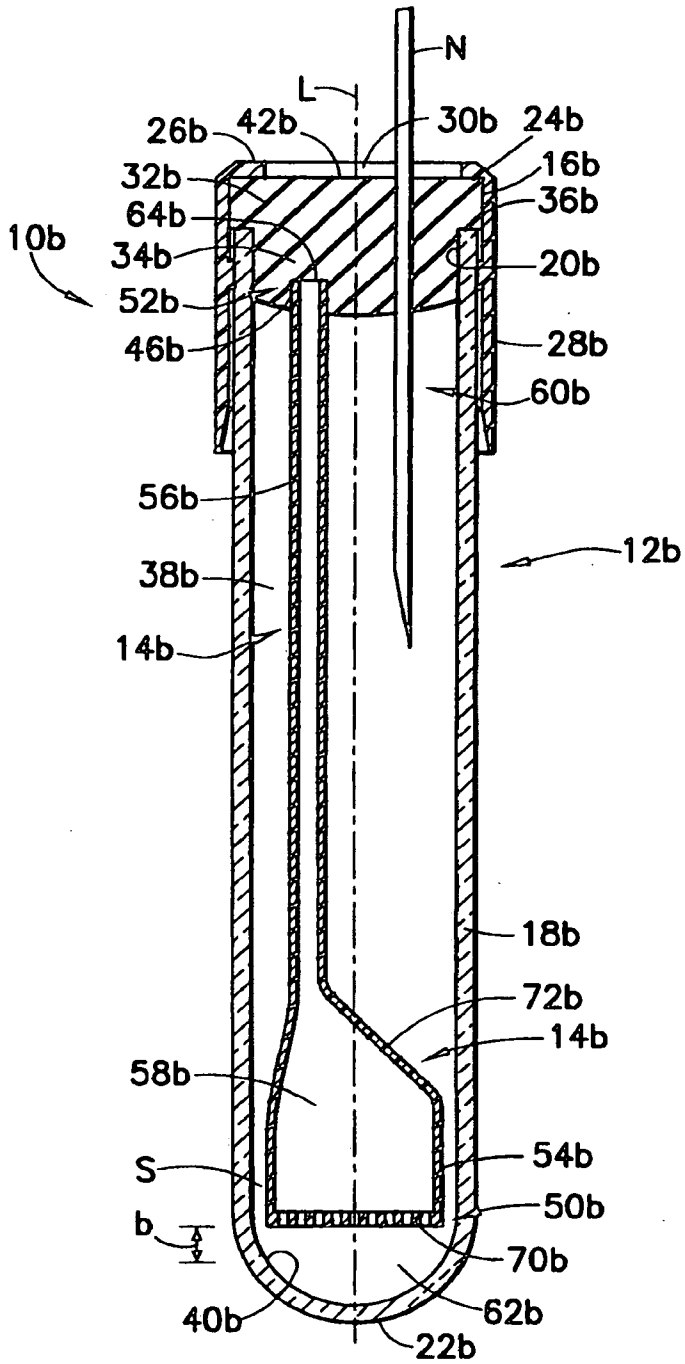
N
L
26b
42b
30b
24b
32b
16b
64b
36b
10b
34b
20b
52b
46b
28b
60b
56b
12b
38b
14b
18b
72b
14b
58b
54b
S
50b
b
70b
62b
40b
22b

FIG. 12

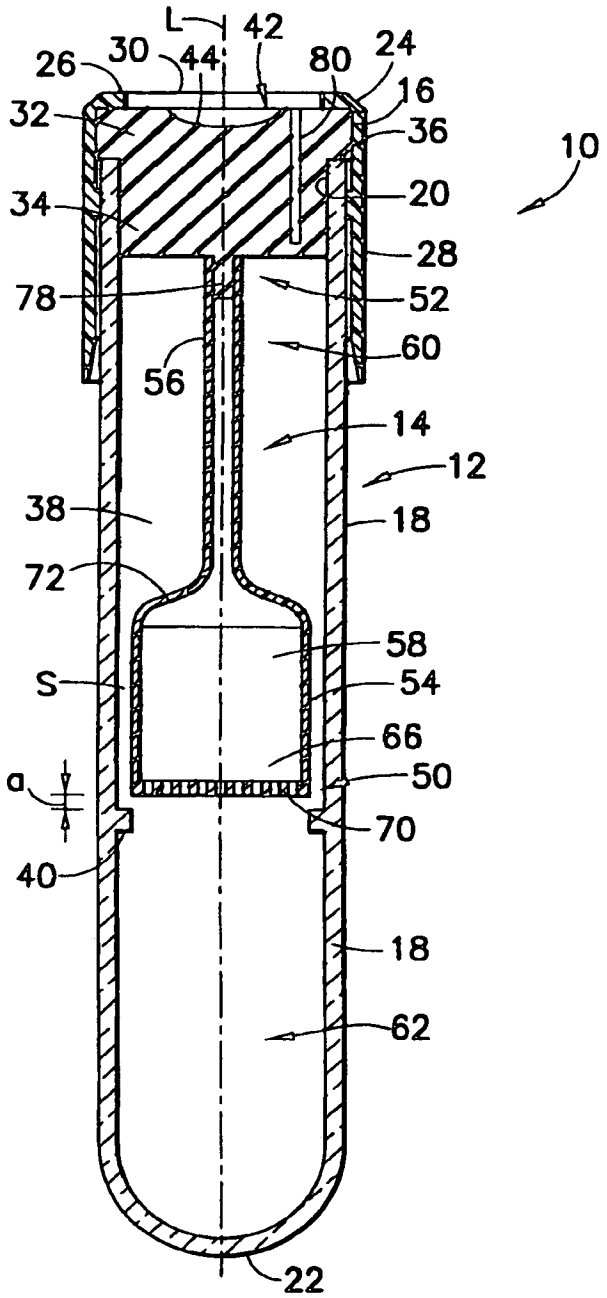
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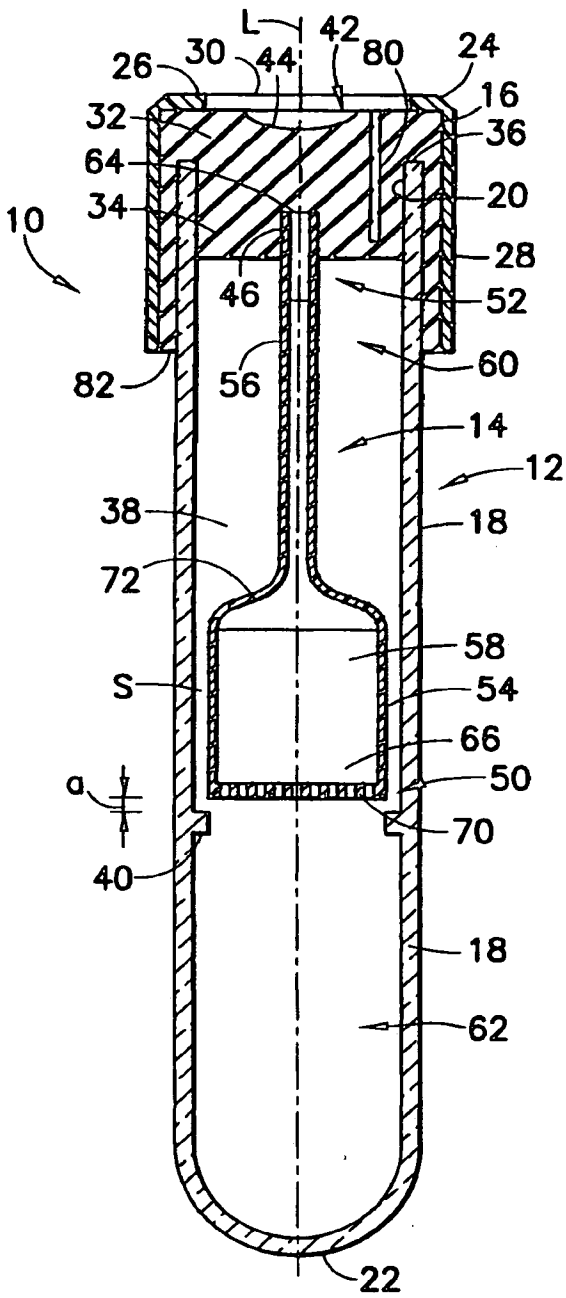
FIG. 13


L
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82
56
60
14
12
38
18
72
58
S
54
66
a
50
70
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18
62
22

FIG. 14