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[Continued on next page]

(54) Title: BLOOD COLLECTION TUBE WITH SEPARATION BARRIER

(57) Abstract: The invention relates to improved fluid collection containment devices and methods, utilizing a porous material separator that provides no or an acceptable level of interference with common diagnostic analytes. According to an aspect of the invention, the porous material separator is disposed in the tube in a predetermined position after centrifugation with a geometry that facilitates a sufficient separation of a blood sample while enabling usage in diagnostic blood testing.

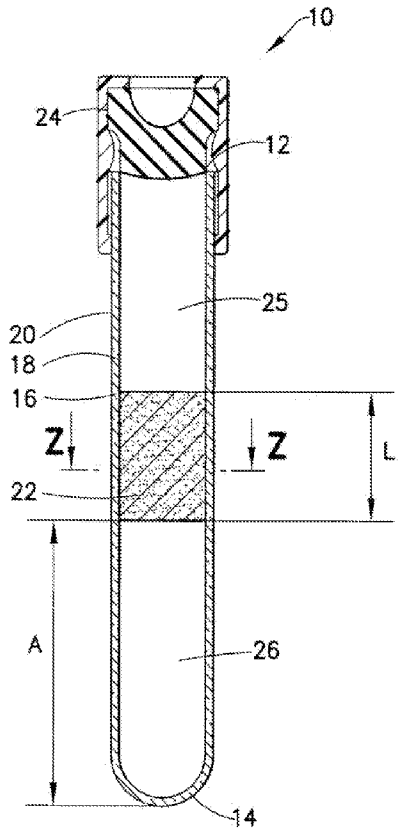

FIG.1

WO 2011/069145 A2

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PATENT APPLICATION

FOR: BLOOD COLLECTION TUBE WITH SEPARATION BARRIER

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates to body fluid collection containment devices and methods, in particular improved blood collection tubes and methods, capable of separating phases of different density using a porous separating medium.

Discussion of the Related Art

Fluid collection tubes containing a thixotropic gel for separating phases of different densities, e.g., in blood, are well known. See, e.g., U.S. Patents Nos. 3,997,442, 4,257,886, 4,426,290, 4,770,779, and 6,238,578. The gel is selected to have a density between the phases of blood which are to be separated. Upon centrifugation of a collected blood sample, the force of centrifugation causes movement of the gel from a substantially non-flowing state to a flowable state. In the flowable state, the gel migrates to a position between the two phases, e.g., between plasma / serum and hematocrit /clot portions. Upon cessation of centrifugation, the gel becomes substantially non-flowable, thereby maintaining the separation between phases. Therefore gel separators can be described as dynamic separators as they move during centrifugation. Gel movement, i.e., getting adequate movement and positioning of the gel upon centrifugation, and resolution or degree of separation within the liquid portions of biological samples can sometimes be an issue for the in-vitro diagnostic field. These devices also require special manufacturing equipment to prepare the gel and to fill the tubes.

US 3,972,812 discloses another type of dynamic separator in which a porous disc is inserted into the top of a collection tube containing a previously collected and clotted blood sample. The porous disc has a specific density such that it descends down the tube during centrifugation until it reaches the serum-clot interface. The disc filters the clotted portions of blood (fibrin and cellular material) from the serum portion of blood. The insertion of the porous disc after collection of the sample exposes the operator to the blood sample. In addition getting adequate movement of the porous disc upon centrifugation relies on the porous disc having a specific density (1.03 to 1.09 g/cc) intermediate to the materials to be separated.

SUMMARY OF THE INVENTION

The various embodiments of the present invention are directed to an improved fluid collection container such as a blood collection tube, containing a porous material separation medium which provides a barrier to maintain separation of a sample such as blood after centrifugation, with minimal or no interference with common diagnostic analytes.

According to one embodiment of the present invention, a blood collection tube comprises a first end and a second end and a sidewall between the first and second end having inner and outer walls. A separator made from a porous material and a pierceable closure to seal the first end. The porous material having a pore size such that all components of whole blood can flow through the separator.

In an additional embodiment of the present invention, a blood collection tube comprises a first end and a second end and a sidewall between the first and second end having inner and outer walls and a separator comprising a porous material and a pierceable closure to seal the first end. The porous material having a pore size greater than the particle size of all components of whole blood.

In another embodiment of the present invention, a blood collection tube comprises a first end and a second end and a sidewall between the first and second end having inner and outer walls and a separator affixed to the inner wall of the sidewall such that the separator does not substantially move in relation to said blood collection tube during centrifugation. The separator is composed of a porous material greater than the particle size of all components of whole blood. A pierceable closure seals the first end, wherein the blood collection tube is partially evacuated.

In a further embodiment of the present invention, a blood collection tube comprises a first end and a second end and a sidewall between the first and second end having inner and outer walls and a separator comprising a porous material having a pore size that is greater than the particle size of all components of whole blood. A pierceable closure seals the first end, wherein the separator moves from a first position to a second position along the longitudinal axis of the blood collection tube during centrifugation and wherein the blood collection tube is partially evacuated.

In a further embodiment of the present invention, a blood collection tube comprises a first end and a second end and a sidewall between the first and second end having inner and

outer walls, a separator and a pierceable closure to seal the first end. The separator having a static component having a top end and bottom end and a lumen extending therethrough, which is fixed to the inner wall of the side wall such that the static component remains substantially immobile during centrifugation, and a dynamic component which moves from a first position above the static component to a second position overlaying the top end of the static component during centrifugation. The separator further comprising a porous material.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a cross sectional view of an evacuated blood collection tube containing a separator of porous material according to an embodiment of the invention.

Fig. 2 is a cross sectional view of an evacuated blood collection tube containing a separator of porous material from the perspective of Z-Z as shown in Fig. 1 according to an embodiment of the invention.

Fig. 3 is a cross sectional view of a blood collection tube containing a separator of porous material after sample collection but before centrifugation according to an embodiment of the invention.

Fig. 4 is a cross sectional view of a blood collection tube containing a separator of porous material after centrifugation according to an embodiment of the invention.

Fig. 5 is a cross sectional view of a blood collection tube containing a dynamic separator in the first collection position according to an embodiment of the invention.

Fig. 6 is a cross sectional view of the blood collection tube in Fig. 5 after centrifugation, with the dynamic separator in the second separation position.

Fig. 7 is a cross sectional view of an alternate embodiment of a blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 8 is a cross sectional view of the blood collection tube of Fig. 7 after centrifugation, with the dynamic separator in the second separation position.

Fig. 9 is a partial cross sectional view of a blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 10 is a cross sectional view of a blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 11 is a cross sectional and plan view of the dynamic separator of Fig. 10 in the undeformed state.

Fig. 12 is a cross sectional view of an alternate embodiment of a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 13 is a cross sectional view of the dynamic separator of Fig. 12 during collection.

Fig. 14a is a cross sectional view of an alternate embodiment of a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 14b is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 14a in the second separation position.

Fig. 15a is a cross sectional view of an alternate embodiment of a dynamic separator, in accordance with an embodiment of the invention, just after launch during centrifugation.

Fig. 15b is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 15a in the second separation position.

Fig. 16 is a perspective view of an alternate embodiment of a dynamic separator.

Fig. 17 is a cross sectional view of the dynamic separator of Fig. 16.

Fig. 18 is a cross sectional view of a dynamic separator, in accordance with another embodiment of the invention.

Fig. 19 is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 16 in the first collection position.

Fig. 20 is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 16 in the second separation position.

Fig. 21 is a plan view of an alternate embodiment of a dynamic separator, in accordance with an embodiment of the present invention.

Fig. 22 is a cross sectional view of a portion of a blood collection tube having a dynamic separator of Fig. 21 in the first collection position.

Fig. 23 is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 21 in the second separation position.

Fig. 24 is a perspective view of an alternate embodiment of a dynamic separator, in accordance with an embodiment of the present invention.

Fig. 25 is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 24 in the first collection position.

Fig. 26 is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 21 in the second separation position prior to closure of the diverter valve.

Fig. 27 is a cross sectional view of a blood collection tube having a dynamic separator of Fig. 21 in the second separation position after closure of the diverter valve.

Fig. 28 is a perspective view of a blood collection tube having a dynamic separator, in accordance with an embodiment of the present invention.

Fig. 29 is a perspective view of an alternate embodiment of a dynamic separator of the present invention.

Fig. 30 is a perspective view of an alternate embodiment of a dynamic separator of the present invention.

Fig. 31 is a cross sectional view of a blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 32 is a cross sectional view of a blood collection tube, having a dynamic separator of Fig. 31 after sample collection but before centrifugation.

Fig. 33 is a cross sectional view of blood collection tube having a dynamic separator of Fig. 31 in the second separation position.

Fig. 34 is a cross sectional view of an alternate embodiment of a dynamic separator, in accordance with an embodiment of the present invention.

Fig. 35 is a cross sectional view of an alternate embodiment of a dynamic separator, in accordance with an embodiment of the present invention.

Fig. 36 is a cross sectional view of a blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 37 is a cross sectional view of blood collection tube having a dynamic separator of Fig. 36 after centrifugation, in the second separation position.

Fig. 38 is a cross sectional view of a blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the present invention.

Fig. 39 is a cross sectional view of blood collection tube having the dynamic separator of Fig. 38 after centrifugation, in the second separation position.

Fig. 40 is a cross sectional view of blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 41 is a cross sectional view of a blood collection tube having the dynamic separator of Fig. 40 after centrifugation, in the second separation position.

Fig. 42 is a cross sectional view of a blood collection tube having a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 43 is a cross sectional view of a blood collection tube having the dynamic separator of Fig. 42 after centrifugation, in the second separation position.

Fig. 44 is a cross sectional view of an alternate embodiment of a dynamic separator in the first collection position, in accordance with an embodiment of the invention.

Fig. 45 is a cross sectional view of a dynamic separator, in accordance with an embodiment of the present invention.

Fig. 46 is a cross sectional view of an alternate embodiment of a dynamic separator of the present invention in the first collection position.

Fig. 47 is a cross sectional view of a tube containing a separator which functions by a combination of both dynamic and static modes in, a first collection position, according to an embodiment of the invention.

Fig. 48 is a cross sectional view of the combination dynamic and static separator of Fig. 47 after centrifugation, in the second separation position.

Fig. 49 is a side view of an alternate embodiment of a combination dynamic and static separator in a first collection position, in accordance with an embodiment of the invention.

Fig. 50 is a side view of the combination dynamic and static separator of Fig. 49 after centrifugation, in the second separation position.

Fig. 51 is a cross sectional view of the combination dynamic and static separator of Fig. 50 in the first collection position.

Fig. 52 is a cross sectional view of the combination dynamic and static separator of Fig. 50 in the second separation position.

Fig. 53 is a cross sectional view of a blood collection tube having an alternate embodiment of a separator, in accordance with an embodiment of the present invention.

Fig. 54 is a cross sectional view of the blood collection tube of Fig. 53 during centrifugation.

Fig. 55 is a cross sectional view of a blood collection tube having a separator, in accordance with an embodiment of the present invention.

Fig. 56 is a cross sectional view of a blood collection tube of Fig. 53, wherein the separator is in the second separation position.

Fig. 57 shows a bar chart of Platelet counts (PLT) for prototype tubes and a control tube after centrifugation at 1300 x g for 10 minutes, in accordance with an embodiment of the invention.

Fig. 58 shows a table of various clinical parameters for prototype tubes and a control tube, under various centrifuge conditions, in accordance with an embodiment of the invention.

Fig. 59 shows a bar chart of Platelet count (PLT) results as shown in Fig. 58 for prototype tubes and a control tube after centrifugation at 1500 x g for 10 minutes, in accordance with an embodiment of the invention.

DETAILED DESCRIPTION OF THE INVENTION

It will be readily understood that the components of the present disclosure, as generally described and further illustrated in the figures herein, could be arranged and designed in a wide variety of different configurations. Thus, the following more detailed description, as represented in the figures, is not intended to limit the scope of the disclosure, but is merely a representation of exemplary combinations of the components.

A collection container such as a blood collection tube in accordance with an embodiment of the invention is shown in Figure 1. The tube 10 contains an open upper end 12, a lower closed end 14, and sidewalls 16 having an inner wall 18 and an outer wall 20. A separator 22 of length L is fixed to the inner wall 18 within the container, thereby forming an upper 25 and lower reservoir 26.

The tube 10 is provided with a closure such as a pierceable closure or stopper 24, which may be pierced by the non-patient end of a blood collection needle such as a double-ended blood collection needle commonly available in the art. The tube 10 may be evacuated, such that upon piercing by such a needle, blood is drawn from a patient's vasculature and into the tube 10. Details of evacuated and non-evacuated blood collection tubes and blood collection are well known to those skilled in the art.

As noted above, following sample collection, the tube is centrifuged causing portions of the blood sample to migrate based on their relative densities or specific gravities. Typically, upon sufficient centrifugation forces and duration, the blood sample separates into two phases of the blood sample, e.g., a generally acellular plasma and a cellular portion, typically inclusive of erythrocytes (red blood cells), granulocytes, lymphocytes and monocytes as is commonly known in the art.

The various embodiments of the invention provide a separator in a blood collection tube which provides an improved separation of a blood sample and an inert barrier which shows acceptable or no levels of assay interference and that confers therapeutic drug monitoring capability when compared to a gel separation medium.

According to embodiments of the invention, the separator is typically a porous material made of e.g. an open cell foam, a foamed rubber, a fleece, a mat, a honeycomb-like material or the like. The separator may be a monolithic single piece of porous material or can be an component containing a porous material. The porous material is inert (e.g. chemically and biologically), which means that it will have no or minimal effect on the blood or plasma or serum sample which would result in an analysis which would differ beyond clinically acceptable limits from that made on the same sample if the porous material was not used. The pore size of the porous material separator is sized and configured such that all the components of whole blood (including the largest e.g. the cellular components desired to be removed from the upper reservoir) may pass through the pores of the separator into the lower

reservoir. This includes by way of example a separator comprising a minimum pore size of e.g. 10 microns and in the range of 100 to 250 microns, preferably 190 to 220 microns. Thus, the porous material does not act as a filter, wherein a retentate and a filtrate are distinguished from each other. Examples of suitable materials are Basotect® V 3012 and Basotect® UF Melamine based (e.g. a formaldehyde-melamine-sodium bisulfite copolymer) open cell foams available from BASF or foam S6050HY by KOEPP Schaum GmbH, Germany available in reticulated and non-reticulated form, or Polydamp® Hydrophobic Melamine (PHM) Foam available from Polymer Technologies, Inc. Newark, Delaware.

The tube 10 can be made of glass, plastic or other suitable materials. Some preferred materials used to manufacture blood collection tube 10 include polypropylene, polyethylene, polyethyleneterephthalate, polystyrene, polycarbonate and cellulosics. More expensive plastics such as polytetrafluoroethylene and other fluorinated polymers may also be used. In addition to the materials mentioned above, examples of other suitable materials include polyolefins, polyamides, polyesters, silicones, polyurethanes, epoxies, acrylics, polyacrylates, polysulfones, polymethacrylates, PEEK, polyimide and fluoropolymers such as PTFE Teflon®, FEP Teflon®, Tefzel®, polyvinylidene fluoride (PVDF) and perfluoroalkoxy resins. Glass products including silica glass may also be used to manufacture the collection devices. One exemplary glass product is PYREX® (available from Corning Glass, Corning, New York). Ceramic collection devices can be used in accordance with embodiments of the invention. Cellulosic products such as paper and reinforced paper containers can also be used to form collection devices according to the invention.

The tube of the invention typically goes through additional processing steps either before or after the separator is inserted into the tube. For example, additives useful in blood or urine analysis, e.g., procoagulants or anticoagulants may be disposed into the tube. As known in the art, blood analysis is often performed on serum, and procoagulants are typically used to enhance the rate of clotting. Such procoagulants include silica particles or enzyme clot activators such as elagic acid, fibrinogen and thrombin. If plasma is desired for analysis, an anticoagulant is generally used to inhibit coagulation, such that blood cells can be separated by centrifugation. Such anticoagulants include oxalates, citrate, EDTA, EGTA, BAPA, and BAPTA, heparin and Boophilin. Additives are disposed in the containers in any suitable manner, liquid or solid, including dissolution in a solvent, or disposing in powdered, crystallized, or lyophilized form.

It should be noted that a porous material (e.g. an open cell foam), may be used to cause the activation of the coagulation process instead of or together with the use of a procoagulant additive. The porous material is placed in the fluid path of blood collection, such that contact with the porous material enhances activation (intrinsic pathway) of platelets, thus accelerating clotting needed for serum collection. The porous material may or may not need to act as a separator in such an embodiment.

Then, after any such additional additives are put into the tube, the tube (or group of tubes) is subjected to an evacuated chamber with a pressure below atmospheric pressure. A seal such as an elastomeric stopper or pierceable membrane is applied, and the tube is sterilized by a process such as irradiation (e.g., with cobalt 60 radiation), ethylene oxide gas exposure, or electron-beam exposure. (Note that several of these steps may be performed in an order other than that presented above).

In accordance with an embodiment of the invention, the blood collection tubes are capable of being formed in various shapes and in any desired size. For example, standard blood collection tubes with OD's of 13mm and 16 mm and lengths of 75mm, and 100mm are contemplated.

Figure 3 shows the axial separation position of a separator 22 along the longitudinal axis of the tube after centrifugation such that the separator is located at or near the expected limit of the hematocrit content 34 i.e. the position at which the interface between the hematocrit (the cellular portion) and plasma or serum (non-cellular liquid portion) occurs after centrifugation of a whole blood sample. For example, Dimension A (as shown in Figure 1) can be in the range of 10-60 mm, for example. In Figure 1 Dimension A is approximately 45 mm for a blood collection tube having an inner diameter (ID) of approximately 7.5mm, OD of 13mm, length of 100mm and a draw volume of 4.5 mls of blood.

Length L of a separator is typically proportional to the internal volume of the tube. For example, a separator length range of 6 to 50mm may be used for tube having an ID of approximately 7.5 mm, length of 100mm and a draw volume of 4.5 mls of blood.

The separators of various embodiments of the invention function by a dynamic mode, a static mode, or a combination of both dynamic and static modes, in order to form a barrier after centrifugation at the axial separation position along the longitudinal axis of the tube at

which interface between the generally acellular plasma and a cellular portion of the separated blood sample occurs.

A static separator or passive barrier is fixed at the axial separation position prior to collection or centrifugation and as such does not substantially move along the longitudinal axis of the blood collection tube during centrifugation. In contrast, to dynamic separators, the immobility of a static separator means that the overall density of the static separator may be independent of (and not intermediate of) the materials to be separated. Thus, the density of a static separator can be less than 1.03 g/cc (for example Basotect® V 3012 foam has a density of 0.009 g/cc) or greater than 1.09 g/cc and still function as a separator of whole blood.

A dynamic separator or active barrier moves during centrifugation from a first collection position to the axial separation position along the tube length. This dynamic mode necessitates that the overall density of a dynamic separator typically has a specific density in the range of 1.03 to 1.09 g/cc to be intermediate to that of the materials to be separated such as whole blood for example, in order to function.

Separators which function using a combination of dynamic and static modes will have a fixed static component or subcomponent and a dynamic component or sub component.

Figures 1 to 4 show an embodiment of a static separator. The static separator 22 is preferably fixed to the inner wall 18 within the blood collection tube by for example a frictional, chemical and/or mechanical interaction or configuration such that the separator 22 does not substantially move in relation to the blood collection tube during centrifugation of a sample. For example, the separator is substantially stationary or immobile along the longitudinal axis of the blood collection tube during collection and separation of a sample. A chemical interaction includes for example adhesives, however care must be taken in the selection of a suitable adhesive which must be capable of adhering the separator to the inner wall 18 while also remaining inert in the same manner as previously described for the porous material. A mechanical configuration includes for example using a friction force exerted between the inner wall 18 and the separator 22 sufficient to prevent axial movement of the separator towards the bottom of the tube during centrifugation. An example includes using a separator with an outer diameter (OD) that is larger than the internal diameter (ID) of tube (e.g. a separator of OD 10mm may be used with a tube ID of 7.5mm) which may also have a modulus of elasticity sufficient to provide an axial force and/or coefficient of friction to resist

or prevent axial movement as described above. Additional mechanical configurations may comprise interference engagement between the separator and a portion of the tube or structure attached or fixed thereto, for example a separator may be placed in the blood collection tube mold prior to molding of the blood collection tube, and the blood collection tube then molded around it. Other examples include the use of flanges or posts circumferentially spaced on the tube inner wall 18 on which the separator can rest or engage. Furthermore, the blood collection tube may be formed such that the separator is integral with the blood collection tube.

Figure 2 shows an intimate contact around the entire circumference of the OD of the separator along its length (L) with the inner wall 18 of the blood collection tube such that there are effectively no gaps between separator and the inner wall. Thus, the inner wall 18 occludes a portion of the pores in the separator due to for example an interference fit between the separator 22 and the inner wall 18 and a sample cannot flow from the upper reservoir 25 to the lower reservoir 26 or from the lower reservoir 26 to the upper reservoir 25 without passing through the separator.

Figure 3 shows the tube after collection and prior to centrifugation. During collection the whole blood sample 30 flows into the upper reservoir 25 and through the separator 22 into the lower reservoir 26 of the tube (thus the separator does not filter the blood) until the desired volume of blood has been collected as dictated by the level of evacuation according to an embodiment of the invention. A densometric separation of the whole blood components occurs during centrifugation, in which all species are free to move through the porous material until an appropriate equilibrium position is attained as dictated by the density of each component entity. Thus the cellular based components of the highest density (e.g. red blood cells and white blood cells) of whole blood pass through the pores of the porous material to the lower reservoir thereby forming the hematocrit region. In addition, the separator is positioned such that the lower density blood component species such as platelets have a centrifugation equilibrium position which is in inside the pores of the separator.

Figure 4 shows that after collection and centrifugation the various species in the hematocrit region 33 remain in their density equilibrium position in the lower reservoir 26 and are effectively prevented from traveling above the separator 22 by gravity, density and the length of the tortuous flow path present in the porous material. In accordance with an embodiment of the invention, the species which are located within the separator are retained

within the pores or captured by porous material and are prevented from flowing into the upper reservoir. Thus the porous material forms a passive barrier after centrifugation, which improves the separation of plasma from the remainder of the whole blood sample such as platelets, red blood cells, white blood cells.

It is generally desirable to direct blood into the blood collection tube such that the blood is able to travel beneath the separator, since serum tubes for some applications require the red blood cells to be below the separator (e.g., where the red blood cells clot and are to be separated from the serum). (This may be less important for plasma tubes.) Such an outcome may be difficult if the separator starts on the bottom of the tube.

Another embodiment of the static separator (as shown in Figs. 1 to 3) provides a solution for this problem by locating / applying the procoagulant (such as silica) in the lower reservoir 26 only (not shown) such that the collected red blood cells would only contact the procoagulant beneath separator 22.

Another solution to this problem is to use a dynamic separator which is designed to be secured at the top of the blood collection tube, in a first collection position, such that the non-patient end of the needle can be inserted through the separator into the tube interior. The separator would thus be formed of a material pierceable by such a needle, and of a size/shape to allow the needle to pass completely through. Securement of the separator at the top end of the tube could be attained by molding in a feature that mates with a corresponding feature of the tube closure, or by utilizing a friction force /interference fit that holds the separator at the top of the tube prior to centrifugation, and the like. The forces experienced by the separator during centrifugation overcome the securement forces thereby allowing the separator to launch and migrate down the tube to the second separation position.

Figures 5 to 46 show various dynamic separators, according to embodiments of the invention. The overall density of a dynamic separator is typically in the range of 1.03 to 1.09 g/cc to be intermediate to that of the materials to be separated such as whole blood for example, in order to effectively move during centrifugation to the axial separation position along the tube length.

These embodiments utilize a collection container such as a blood collection tube 10, comprising an open end 12, a second end 14 and sidewalls 16 having an inner wall 18 and an outer wall 20 therebetween, and a pierceable closure 24 enclosing at least the open end.

Figures 5 and 6 show a dynamic separator in accordance with an embodiment of the invention. Separator 122 is made from a porous material plug or cylinder 121 and at least one ballast weight/mass 123 attached or embedded within porous material plug 121. Figure 5 shows that during collection of blood, the non-patient end of cannula 99 penetrates pierceable cap 24 and is embedded within separator 122. As described above the pore size of porous material plug 121 is such that the blood components can easily flow through the separator to the reservoir 13 without filtration of the unclotted blood components or a back flow due to a flow restriction occurring. The dynamic nature means that the overall density of a separator such as separator 122 has a specific density in the range of 1.03 to 1.09 g/cc to be intermediate to that of the materials to be separated such as whole blood for example. Thus, each ballast weight/mass 123 is made from a high density material (e.g. glass, delrin, polystyrene) and is attached to or embedded in the porous material plug 121 (e.g. Basotect® V 3012 foam having a density of 0.009 g/cc) in order to obtain an overall separator 122 specific density in the desired range. Prior to centrifugation separator 122 may be retained at the upper end 12 of tube 10 by securement to pierceable cap 24 (by for example a temporary adhesive bond), and/or inner wall 18 (by for example a sufficient friction force).

Upon centrifugation and immersion of the separator 122 in the fluid, the lower density porous material plug 121 provides a buoyant upward force on the separator 122 relative to the fluid. Simultaneously, the higher density ballast weight(s)/mass 123 provide an axial force downward on the separator. The combined forces stretch and elongate porous material plug 121 axially, causing inward radial movement of the middle region. This radial movement pulls the porous material plug 121 out of contact with the inner wall 18 of the tube so that it is free to move axially. Alternatively, the porous material plug may not move radially inward, but allows for the centrifugal force to overcome the friction force, until the separator moves towards a position of equilibrium.

Therefore, multiple paths are developed both through the pores of porous material plug 121 and between the inner wall 18 of the tube and the OD of porous material plug 121 that permit the flow of the low-density serum component past the separator 122 as it migrates down the tube. Migration of the separator 122 terminates when it reaches the axial separation position between the lower density fluid component and higher density fluid or cellular/solid components, equal to its overall density. Upon terminating centrifugation, porous material plug 121 expands to its undeformed shape, sealing against the inner wall 18 of the tube,

thereby creating a barrier between the higher and lower density components of the sample fluid as shown in Figure 6. After centrifugation the various species in the hematocrit region 33 remain in their density equilibrium position in the lower reservoir 26 and are prevented from traveling above the separator 122 by gravity, density and the length of the tortuous flow path present in the porous material. The species which are located within the separator 122 are retained within the pores or captured by porous material and are restrained from flowing into the upper reservoir. Thus, the porous material forms a passive barrier after centrifugation, which improves the separation of serum or plasma from the remainder of the whole blood sample such as platelets, red blood cells, white blood cells.

Figures 7 and 8 show another embodiment of a dynamic separator which is similar to that shown in Figures 5 and 6. Separator 132 is another dynamic separator having a porous material plug 131 and at least one ballast weight/mass 133 attached or embedded within porous material plug 131. The difference to that of the previous embodiment is that a recess 135 is present in the lower end of porous material plug 131 to provide a reduced cross section and assist allowing the non patient cannula to completely penetrate separator 132 when in the first collection position. Thus, during collection, needle cannula 99 penetrates pierceable cap 24 and separator 132 allowing blood to flow directly into reservoir 13 of the tube through recess 135 as shown in Figure 7.

Figure 9 shows an embodiment of the invention in which a porous material dynamic separator is located adjacent a tube closure 224 of reduced cross sectional thickness when compared to conventional pierceable closure 24. The pierceable closure structure may be a foil or a combination of a pierceable closure and foil as shown in US Patent 5,061,263 for example. Dynamic separator 142 has the same composition as separator 122 in Figure 5 and likewise has overall separator specific density in the desired range. The reduced cross section of tube closure 224 together with the location of separator 142 adjacent tube closure 224 facilitates a greater depth of penetration of the non-patient cannula 99 either deep into separator 142 similar to that shown in Figure 5 or more preferably completely through the separator 142 during normal phlebotomy as shown in Figure 9.

Figures 10 and 11 show another embodiment of a dynamic separator. Dynamic separator 152 is made from a porous material plug 151 and a wiper 153. Wiper 153 has a disc portion 154 having holes 155 or slits through the cross section and a taper section 156 (that tapers toward the upper end 12 of the tube in an opening fashion) around the outer

circumference of disc portion 154. The disc portion 154 is bonded or attached to the lower surface of the porous material plug 151. Wiper 153 is made from an elastomer (such as for example bromo butyl rubber or a thermoplastic elastomer) and fulfills the same function as the ballast weight/mass element in the previous dynamic separator embodiments in order to ensure that the overall separator 152 specific density is in a desired range. The dynamic separator 152 is placed into the upper end 12 of tube 10, such that porous material plug 151 is projecting from the top of tube 12. Pierceable closure 24 is then inserted into and thereby seals upper end 12 in a manner that also compresses the porous material plug 151 to a reduced cross sectional thickness (L1) without moving the wiper 153. Wiper 153 is held in position by either a friction force or a temporary adhesive bond between taper section 156 and inner wall 18 of the tube 12.

On collection a non patient cannula is able to penetrate deep into the porous material plug 151 such that blood will flow along the pores of porous material plug 151, through the holes 155 of wiper 153, and into the reservoir 13 of tube 12. Upon centrifugation, the centrifugal forces stretch and elongate porous material plug 151 axially, causing inward radial movement such that the friction force between taper section 156 and inner wall 18 of the tube 12 is overcome and separator 152 begins to travel axially down the longitudinal axis of tube 12. Taper section 156 can maintain radial engagement or move out of contact with the inner wall 18 of the tube 12 during movement. Separator 152 continues to migrate down the tube until the separation position is reached as determined by the overall separator density. On completion of centrifugation, porous material plug 151 expands to its undeformed shape and cross-sectional thickness (L_2), thereby exerting taper section 156 to seal against the inner wall 18 of the tube, thereby creating another barrier in addition to the porous material plug 151.

Figures 12 and 13 show another embodiment of a dynamic separator. This embodiment comprises a separator 172, comprising a porous material plug 171 surrounded by a non-porous material (such as an elastomer) sleeve 173. The porous material plug 171 is preferably tapered from a larger diameter at the bottom to smaller diameter at the top, in a frusto-conical manner. A barrier cap 175 is secured to top of the porous material plug 171 which is made from a material prevents the porous material plug 171 from being penetrated by a cannula and forms a liquid seal with sleeve 173. The non-porous material of sleeve 173 has a specific gravity large enough to ensure the overall separator 172 specific density in the desired range, as well as providing sealing capability between the inner wall 18 within the

blood collection tube and the separator 172. The porous material plug 171 is in intimate contact with the sleeve 173 and may be bonded together, or held together by, for example a mechanical means at the lower portion of separator 172. Prior to collection separator 172 is in a first position within the internal reservoir of the blood collection tube adjacent to or towards the open end of the blood collection tube and pierceable closure. Upon collection, a non-patient needle 99 is inserted into and penetrates the pierceable closure of the tube (not shown) and impacts the barrier cap 175, causing partial compression of the porous material plug 171, breaking the fluid seal between barrier cap 175 and sleeve 173 thus allowing blood to flow both through porous material plug 171 and at the interface between the porous material plug 171 and sleeve 173, and into the lower chamber of the blood collection tube. Preferably, the force needed to compress the porous material plug 171 to a degree of compression substantial enough to allow for blood to flow through the separator 172 is less than the friction force between the sleeve 173 and the inner wall 18 of the tube 10.

During centrifugation, the magnitude of the barrier cap 175 specific density causes the porous material plug 171 to deform to allow the flow of blood components of lower density to flow through and above the separator 172. After centrifugation, porous material plug 171 recovers to the original undeformed state such that barrier cap 175 reforms a fluid seal with sleeve 173 to form a barrier at the second separation position between the cellular and non-cellular components of blood.

In an alternate embodiment the barrier cap may not completely occlude the top of the porous material plug such that the barrier cap does not form a complete fluid seal with sleeve in the undeformed state and a tortuous flow path would exist through the separator.

Figures 14 and 15 show an embodiment of the invention in which a cylindrical funnel structure 186 is engaged into the pierceable closure 324 of the blood collection tube 10, and at least partially extends into or completely through the length of dynamic separator 182 when dynamic separator 182 is positioned in a first position substantially adjacent pierceable closure 324 (See Figure 14a). Dynamic separator 182 has, for example the same composition as separator 122 in Figure 5. A slit or small opening through the cross section and along the center axis of the porous material plug, allows for cylindrical structure 186 to at least partially, preferably completely, extend into the separator 182. Separator 182 is retained on cylindrical structure 186 by friction or by a temporary adhesive bond. During collection, a non-patient needle 99 is inserted into the pierceable closure 324. The tip of the non-patient

needle protrudes through the pierceable closure 324, internal to the cylindrical structure 186, preferably through or bypassing separator 182 depending on the depth of penetration of the cylindrical structure 186 into separator 182. During centrifugation, the friction forces between the cylindrical structure 186 and the separator 182 are low enough to allow separator 182 to launch from the first position and to the second separation position, wherein the separator 182 overlays the partially formed cellular material of the sample (See Figure 14b).

A fully cored inner section 187 of the porous material plug along the center axis can be removed from the separator in place of a slit. However the removal of a core from the separator 182a requires that the inner wall 318 of the tube 10 to be tapered or comprise ramps that provide for tapering from a larger inside diameter to a smaller inside diameter when moving from the open end to the second end of the tube. Thus, during centrifugation, as the separator 182a moves from the first position to the second separation position (See Figure 15a), the taper of the sidewall of the tube provides for radial compression of the separator, wherein the slit or cored opening compresses, thereby restricting flow of cellular material through the separator to the pore structure of the porous material only (See Figure 15b).

Figures 16 to 20 show two versions of an embodiment of a dynamic separator. Figure 17 shows a separator 192a in which a ballast mass 193a has a conical shaped lumen 195a therethrough and is enclosed by a cylindrical sleeve of porous material 191a which seals against the inner wall 18 of blood collection tube 10. Upon collection a non-patient needle 99 of a blood collection needle penetrates the pierceable closure 24 and aligns with conical lumen 195a, blood then funnels through the separator 192a via lumen 195a, and into the bottom section of the blood collection tube. Blood may transfer through the base of separator 192a, by mechanisms such as fluid pressure causing temporary distortion for blood to transfer, or a one-way valve (not shown) such as a duckbill valve located at the base of the conical lumen 195a. Blood is then forced to pass through the cylindrical sleeve of porous material 191a during centrifugation as the one way valve mechanism prevents any back flow of blood up the conical lumen 195a.

Figure 18 shows a separator 192b in which an annular ballast mass 193b is attached to the upper surface of a porous material plug 191b which has a conical shaped lumen 195b extending almost completely through. Upon collection a non-patient needle 99 of a blood collection needle penetrates the pierceable closure 24 and aligns with conical lumen 195b, the majority of blood flow then occurs through the separator 192b via lumen 195b, and into the

bottom section of the blood collection tube. Blood may also transfer through separator 192b by diffusion through the pores of the porous material plug 191b.

The dynamic separators 192a and 192b have an overall separator specific density in the desired range to ensure movement of the separator under centrifugation forces from a first position (Figure 19) near the open end and pierceable closure to the second separation position (Figure 20).

Figures 21 to 23 show a different embodiment of a dynamic separator which uses a rotational movement to form a barrier during separation. Separator 212 is made from a porous material plug 211 and at least one ballast weight/mass 213 attached to the porous material plug 211. During collection, separator 212 is located at a first position in the tube wherein ballast mass 213 is attached to the side of porous material plug 211 and thus interposed between inner wall 18 of the blood collection tube 10 and porous material plug 211 (see Figures 23 and 24). Therefore collected blood can flow through the separator 212 via flow channels 215 and 216. The dimensions W and Y of porous material plug 211 (when undeformed) are greater than the internal diameter of blood collection tube 10 such that it will not fit unless compressed into the tube opening, wherein the friction and radial compression forces between the separator 212 and inner wall 18 maintain the separator 212 in the first collection position. The off-center location of ballast mass 213 causes the center of mass to be offset from the centroid of the separator 212. Thus, during centrifugation a moment is created which overcomes the forces holding separator 212 in the first collection position, which allows for rotation of the separator 212, wherein the mass 213 moves first and then the porous material plug 211 follows, thereby rotating the separator 212 by 90° into a second separation position (See Figure 23). Once the separator is in the second separation position, there is intimate contact around the entire circumference of the outer diameter of the porous material plug 211 along dimension W with the inner wall 18 of the blood collection tube such that there are no gaps between porous material plug 211 and the inner wall 18, wherein the friction and radial compression forces generated due to the magnitude of dimension Y between the separator 212 and inner wall 18 maintain the separator 212 in the second separation position.

Figures 24 to 30 show various embodiments of a three part dynamic separator. Figure 24 shows a separator 222 comprising a porous material cylinder 221, a funnel shaped valve body 223, and a diverter valve 225 that may resemble a valve pin sealing element or

arrangement. Porous material cylinder 221 surrounds the central portion of valve body 223 and contacts inner wall 18 of blood collection tube 10. On collection the separator 222 is in a first position adjacent tube closure 24. Lumen 227 comprises a funnel shaped upper end that guides blood drawn through tube closure 24 to a channel 228 axially oriented with the diverter valve 225, such that blood flows through separator 222 and exits out of diverter valve 225. Separator 222 is retained in the first position via securement of the top of the valve body 223 to the tube closure and/or a friction force between the outer surface of porous material cylinder 221 on the inner wall 18 of blood collection tube 10.

Upon centrifugation, separator 222 moves downwards to the second separation position (See Figure 26) as the overall separator specific density in the desired range as previously described. Upon arriving at the separation position diverter valve 225 hits either or both of a cellular portion of the blood sample, or a feature of the tube such as the bottom of the tube, causing the diverter valve 225 to move to the closed position (See Figure 29) which blocks channel 228 such fluid flow from beneath to above separator 222 can only occur by passing through porous material cylinder 221 either between inner wall 18 and the outer surface of valve body 223 or through one of the windows 229 in the sidewall of lumen 227. A number of projections 230 from the diverter valve 225 externally engage external portions of the funnel in a cam-follower type of arrangement. The diverter valve 225 is designed to not re-open once it has closed under normal operating conditions unless an external manual force is applied to both the valve body 223 and the diverter valve 225.

Figures 28 to 30 shows additional embodiments (225a, 225b, 225c) of diverter valve design which may have a concave lower surface 225a, an extended length and a concave lower surface 225b, or an extended length and a spherical ball with a flange 225b wherein the OD of the flange is equal to the internal diameter of blood collection tube 10 a point towards the lower end 14.

Figures 31 to 33 show another embodiment of a dynamic separator. Separator 232 has a porous material plug 231 and at least one ballast weight/mass (not shown) attached to or embedded within porous material plug 231, in addition a flexible and liquid permeable inner container 235 is affixed to the separator 232. Inner container 235 has an open top which is attached to the OD of porous material plug 231, a closed bottom end and a flexible collapsible sidewall extending therebetween. An additive such as e.g. procoagulant or anticoagulant can be spray dried inside inner container 235. Prior to and upon collection

separator 232 is located at a first collection position adjacent the pierceable closure 24 (with the inner container 235 hanging beneath) so that a non-patient needle will either completely or deeply penetrate separator 232 to deliver whole blood 30 into the inner container 235 and mix with the additive present (see Figure 32).

Upon centrifugation, separator 232 moves down the longitudinal axis of tube 10 under the relative centrifugal force whilst compressing the inner container 235, resulting in the expulsion of the fluid component of the blood through the until such time that no more fluid can be expressed and the separator 232 rests at the second separation position on top of the hematocrit region 33 or cellular mass resulting in the separation of serum or plasma 32 from the cellular components of whole blood.

One advantage of this embodiment of collecting blood into a permeable inner container is the minimization or elimination adherence of blood cells, red cells in particular to the tube wall which can result in interferences with a number of diagnostic tests. It may also eliminate the need of using surfactants on the inner surface of the collection tube for minimizing red cell adherence.

Figures 34 to 46 show dynamic separators having a porous material plug and various embodiments of ballast weights/ masses. Figure 34 shows a separator 242 comprising a porous material plug 241 and a cylindrical ring ballast mass 243 circumscribing the porous material plug 241. The ring 243 provides density and mass to enable the movement of the separator system under centrifugal forces against the forces of buoyancy and friction between the open-cell foam and the sidewall of the tube. In one embodiment, the porous material plug has a diameter larger than that of the internal diameter of the tube. The ring 243 comprises an outside diameter smaller than the internal diameter of the tube, and the inside diameter of the ring causes "mushrooming" of the porous material plug, thereby establishing interference engagement with the inner wall 18 of the tube. Figure 35 shows another embodiment in which the porous material plug 241a may be formed with a cutout portion 246 such that the ring 243 surrounds the porous material plug 241, without causing "mushrooming" of the porous material plug to engage the inner wall 18 of the tube.

Figures 36 to 39 show two embodiments of a dynamic separator 252 comprising a porous material plug 251 and one or more bead ballast masses 253. The bead ballast masses 253 are affixed to the porous material plug 251 via friction fit, interference fit, and/or

chemical bonding. The beads may be affixed to the top surface of porous material plug 251 (Figures 36 and 37) or sandwiched between two foam portions 251a 251b, (Figures 38 and 39) which in some cases may involve foams of differing diameters, material, or pore size.

Figures 40 and 41 show a dynamic separator having a ballast weight/ mass ring 263 positioned on top of the porous material plug 261 via friction fit, interference fit, and/or chemical bonding. The ballast mass ring 263 may comprise an annular hole, such that the ring does not interfere with the non-patient needle on collection. Porous material plug 261 may also have an annular recess on the upper surface (not shown) to receive ring 263 such that the top surface of the separator is flat.

Figures 42 and 43 show a dynamic separator 272 positioned directly inside pierceable closure 724 of the tube, and mechanically or chemically engaged or interfaced to the pierceable closure 724 and not the inner wall 18 of the tube 10. The engagement of separator 272 to the underside of the pierceable closure 724 at the first collection position in this embodiment provides for the possibility of the top surface of the separator being devoid of cells resting on it upon the launch of the separator 272 during centrifugation.

Figures 44 and 45 show more embodiments of a dynamic separator directly mechanically or chemically engaged or interfaced to the pierceable closure but also in contact with the inner wall of the tube. Separator 282 has a feature 285 that mates with a corresponding feature 287 of the tube closure 824 to retain separator 282 in the first collection position. However centrifugal forces can override the retention features 285 and 287 such that separator 282 may migrate to the second separation position. Figure 45 shows a separator 292 having a first upper porous material section 294 and a lower porous material plug section 291 with a plurality of ballast mass beads 293 sandwiched between the sections. Separator 292 is retained in the first collection position by mating features 295 and 297. During centrifugation first upper porous material section 294 may remain engaged to the bottom portion of the pierceable closure 924, while lower porous material plug section 291 and the ballast mass beads 293 launch to act as a dynamic separator. In an alternate embodiment, the first upper porous material section or lower porous material plug section may be partially perforated such that it tears to facilitate the launch of the dynamic separator portion.

Figure 46 shows an embodiment of a dynamic separator 312 which utilizes spikes 313 through portions of a porous material plug 311, as a means of attachment to the lower surface

of pierceable closure 324 of the blood collection tube 10 to retain separator 312 in the first collection position. The spikes 313 can also function as the ballast mass for the separator 312 or a dedicated ballast mass can be present in addition to the spikes 313 in order to give a separator overall density in the desired range. In embodiments where the spikes 313 also function as the ballast mass, the forces required to remove the spikes 313 from the porous material plug 311 are larger than the force required to remove the spikes 313 from the pierceable closure 324.

Figures 47 to 56 show a number of separator embodiments which function using a combination of dynamic and static modes. Each embodiment has a fixed static component/sub assembly and a dynamic component/sub assembly.

Figures 47 and 48 show an embodiment of a separator 412 which has a static component 425 and a dynamic component 426. Static component 425 comprises a cylinder of a porous material having a top and bottom end and a lumen 430 along the center axis to provide for a flow path coaxial with the axis of the outside diameter of the cylinder, and the tube. Static component 425 is preferably fixed to the inner wall 18 within the blood collection tube by for example a frictional, chemical and/or mechanical interaction or configuration such that the static component 425 does not substantially move in relation to the blood collection tube during centrifugation of a sample. Dynamic component 426 comprises a separate and detached plug 431 that shares a similar diameter with that of the static component 425 and a ballast mass 433 that fits within the inside diameter of lumen 430 in the static component 425. Ballast mass 433 such as a glass bead may be attached via adhesive to plug 431. Plug 431 may be made from a porous material such as open cell foam or a non-porous material such as a closed cell foam, or polymer. The overall density of dynamic component 426 is in the specified range for a dynamic separator.

Prior to and upon collection, dynamic component 426 is secured to inner wall 18 by an adhesive above static component 425 in the first collection position. The tip of a non-patient needle protrudes through the pierceable closure and blood flow driven by the pressure conditions of the evacuated tube allows for blood to be drawn around dynamic component 426, and generally through the lumen 430 of static component 425. Upon centrifugation, the cellular material of the blood is driven below and into static component 425, and finally, dynamic component 426 launches from the first collection position (Figure 47) and moves to the second separation position (Figure 48), wherein the plug 431 overlays the top end of static

component 425 with ballast mass 433 occluding lumen 430 to form separator 412. Plug 431 may form a liquid seal with the inner wall 18 if made from a non-porous material or a greater length of torturous path barrier if formed from a porous material.

A laminated sheet of material may be used to adhere plug 431 to inner wall 18 instead of adhesive. However the strength of the bond between laminated sheet and inner wall 18 has to be greater than that between plug 431 and laminated sheet such that the laminated sheet remains on inner wall 18 after the launch of dynamic sub-component 426.

Figures 49 to 52 show an embodiment of a separator 512 which has a static component 525 and a dynamic component 526 similar to that shown in Figures 47 and 48. The only difference to that of the previous embodiment is that a dynamic component 526 is unitary to static component 525, such that plug 531 is connected by a living hinge to static component 525. Therefore prior to and upon collection ballast mass 533 rests at the top of lumen 530 in the static component 525 causing plug 531 to be raised in a partially open manner, in the first collection position (See Figures 49 and 51). Thus, collected blood driven by the pressure conditions of the evacuated tube flows around plug 531 and ballast mass 533, and generally through the lumen 530 of the static component 525. Upon centrifugation, the cellular material is driven below and into the static component 525, and finally, the dynamic component 526 pivots from the first position and moves to the second separation closed position (See Figures 50 and 52), wherein the plug 531 overlays the top end of the static component 525 and ballast mass 533 occludes lumen 530. Plug 531 may form a liquid seal with the inner wall 18 if made from a non-porous material or a greater length of torturous path barrier if formed from a porous material.

Figures 53 and 54 show an embodiment of a separator 612 comprising a porous material plug 611 which is suitable for use as a dynamic or static separator. The upper surface 614 of separator 612 is concave, with the concavity having a funnel shaped profile. This may provide for the separator to be used in fixed-angle centrifuges, wherein the tube may rotate about the axis of a centrifuge's rotor in a manner where the axis of the tube is not completely perpendicular to the centrifuge (See Figure 54).

Separator 612 is affixed to inner wall 18 when used as a static separator. A ballast mass is attached to porous material plug 611 for use as a dynamic separator in order to

provide the required overall specific density to allow for movement during centrifugation to the separation position.

The advantage of the concave profile for the upper surface relates to utilizing a minimum length of porous material needed to provide for an effective barrier, that if parallel on both upper and lower surfaces sides like a uniform plug of foam, would otherwise not be able to be used with fixed angle centrifuges without providing for a larger thickness such that the cell/cell-free interface would extend through the barrier (and normal to the axis of centrifugation) in both fixed and swing bucket centrifuges.

Figures 55 and 56 show an embodiment of a separator 712 comprising a porous material plug 711 which is suitable for use as a dynamic or static separator. Separator 712 comprises a porous material plug 711 and a higher density cylindrical straw like structure 713. Cylinder 713 is as long if not longer than the porous material plug 711, and interposed between the inner wall 18 of the blood collection tube 10 and the sidewall of the porous material plug 711 to be held in an interference engagement. Upon collection separator 712 is intermediately positioned inside the blood collection tube 10, such that blood when introduced through the pierceable closure via a non-patient needle, blood rests on the top of the separator 712, and flows through the lumen 715 of cylinder 714 under a combination of vacuum (that diminishes while filling) and gravity driving forces. Upon centrifugation, cylinder 713, being of a higher density and having less frictional resistance between the porous material plug 711 and inner wall 18 launches downward to the bottom of the blood collection tube 10, thereby allowing porous material plug 711 to function as the barrier structure with intimate contact with inner wall 18 established around the entire outer circumference.

In static embodiments porous material plug 711 remains in the separation position and does not substantially move during centrifugation. In dynamic embodiments, the porous material plug 711 moves before and after the cylindrical structure 713 launches from the porous material plug 711. An additional ballast mass (not shown) adhered to the porous material plug 711 causes the separator to finally position itself at the cell / cell-free interface.

In an alternative dynamic embodiment the cylindrical structure is disposed in a fully cored inner section of the porous material plug along the center axis. However the removal of a core from the porous material plug requires that the inner wall of the blood collection tube

to be tapered or comprise ramps that provide for tapering from a larger inside diameter to a smaller inside diameter when moving from the open end to the second end of the tube. Thus, during centrifugation, (after launch of the cylindrical structure) as the separator moves from the first position to the second separation position, the taper of the sidewall of the tube provides for radial compression of the separator, wherein the cored opening compresses, thereby restricting flow of cellular material through the separator to the pore structure of the porous material only.

EXAMPLES

The following examples are intended to illustrate embodiments of the invention and are not intended to limit the invention.

Example 1

Initial Evaluation of Open Cell Foam

Prototype tubes were fabricated with three types of foam (Basotect® V3012 and Basotect® UF Melamine based open cell foams available from BASF and Polydamp® Hydrophobic Melamine Foam PHM foam available from Polymer Technologies Inc) cut into 10mm OD circular tubes and inserted into unevacuated Lithium-Heparin tubes. These prototypes included two different lengths (L= 25 or 50mm) of separator and two positions (A= 0 or 12 mm) tubes. Citrated sheep's blood (5 mls) was dispensed into each of the tubes. The tubes were then centrifuged at 1300 x g for 10 minutes and the separator performance was then evaluated.

Whole blood was observed in the lower reservoir for each type of foam prior to centrifugation. A barrier between hematocrit and plasma was formed by each type of foam, however the positioning of the foam separator was critical to barrier formation as each foam located at the bottom of the tube (A=0) did not form a barrier. In addition a separator length L of 50mm at a position of A= 12mm prevented the addition of 5mls of blood to the tube.

Example 2

First Evaluation of Open Cell Foam using Evacuated Tubes with Human Blood

Method; Prototype tubes were fabricated with two types of foam (Basotect® V 3012 and Basotect® UF Melamine based open cell foams available from BASF) cut into 10mm OD circular tubes and inserted into Lithium-Heparin tubes of approximately 7.5mm ID and

13mm OD at a fixed position approximately 45 mm from the bottom of the tube (the expected position of the plasma/hematocrit interface). These prototypes included two different lengths (L= 6 or 12mm) of separator. The prototype tubes were then evacuated to give a 4.5ml fill. The prototype tubes and a control (Plasma Separation Tube (PST) Gel Tube from Becton Dickinson and Company) were then filled using an indirect blood draw procedure from 5 subjects and centrifuged at 1300 x g for 10 minutes. The tubes were then compared visually and for a range of clinical chemistry parameters.

Results; Foam integrity was unaffected by evacuation and the separator in each prototype tube remained immobile upon centrifugation. All the prototype separators formed a barrier between the plasma and hematocrit. Some hemolysis was also observed within the L=12mm Basotect® V 3012 foam separator and within the gel layer of the control tube. No apparent difference observed between the prototype foam separator tubes and the Gel "Control" tube for CA (calcium), MG (magnesium), K+ (potassium), CHOL (cholesterol), ALB (albumin) or Folate within each subject. A slightly high bias was observed for LDH (lactate dehydrogenase) from tubes with foam separator, however, the results were within expected normal range.

Example 3

Second Evaluation of Open Cell Foam using Evacuated Tubes with Human Blood

Method; Prototype tubes were fabricated with two types of foam (Basotect® V 3012 (W) and Basotect® UF (G) Melamine based open cell foams available from BASF) cut into 10mm OD circular tubes, with a length L= 12mm, and inserted into Lithium-Heparin tubes of approximately 7.5mm ID and 13mm OD at a fixed position approximately 45 mm from the bottom of the tube (the expected position of the plasma/hematocrit interface). The prototype tubes were then evacuated to give a 4.5ml fill. The prototype tubes and a control (Plasma Separation Tube (PST) Gel Tube from Becton Dickinson and Company) were then filled using an indirect blood draw procedure from 5 subjects and centrifuged at 1300 x g for 10 minutes. The tubes were then compared visually and evaluated for a range of clinical chemistry parameters. In addition cell counts were performed using the Beckman Coulter LH750 analyzer on each tube to evaluate separation performance. In addition, each tube was inverted 8 times 60-90 minutes after centrifugation and a second set of cell counts conducted to evaluate the barrier properties of each separator.

Results; No apparent differences were observed between the foam separator tubes and Gel "Control" tubes for White Blood Cell (WBC), Red Blood Cell (RBC), Hemoglobin (HGB) and Platelet (PLT) counts within a given subject.

Figure 57 shows that mixing of separated plasma by inversion of the tube 8 times after centrifugation resulted in elevated platelet counts when compared to the initial post centrifugation platelet count. However, a similar increase in platelet counts was observed in the foam separator tubes and the gel control tubes.

Within a subject, no apparent differences were observed between the Foam Separator tubes and the Gel Control tubes for GLUC (glucose), BUN (blood urea nitrogen), CREA (creatinine), K+ (potassium), CL (chloride), Fe (iron), Ca (calcium), Mg (magnesium), Phos (phosphate), Chol (cholesterol), Trig (triglycerides), Uric (uric acid), TP (total protein), ALB (albumin), AST (aspartate aminotransferase), ALT (alanine aminotransferase), LD (lactate dehydrogenase), GGT (gamma glutamyl transferase), ALKP (alkaline phosphatase) or TBIL (total bilirubin).

Example 4

Effect of Centrifugation Parameters on Residual Cell Counts

Method; Prototype tubes were fabricated with a separator made from Basotect® V 3012 (Melamine based open cell foam available from BASF) cut into 10mm OD circular tubes, with a length L= 12mm, and inserted into Lithium-Heparin tubes of approximately 7.5mm ID and 13mm OD at a fixed position approximately 45 mm from the bottom of the tube (the expected position of the plasma/hematocrit interface). The prototype tubes were then evacuated to give a 4.5ml fill. The prototype tubes for 2 of the subjects (8 and 9) to be tested were sterilized using irradiation. The prototype tubes and a control (Plasma Separation Tube (PST) Gel Tube from Becton Dickinson and Company) were then filled using an indirect blood draw procedure from 10 subjects. The prototype tubes were then centrifuged at 1500 x g, 3000 x g, or 4500 x g for 3, 5 or 10 minutes while the control gel tubes were centrifuged at 1500 x g for 10 minutes. Cell counts using the standard procedures were then conducted to evaluate separation performance under each of the centrifuge conditions. In addition, each tube was inverted 10 times 60-90 minutes after centrifugation and a second set of cell counts conducted to evaluate the barrier properties of each separator.

Results; The integrity of all the foam separators were unaffected by evacuation. Upon centrifugation, all prototype tubes formed good barriers.

A summary of the cell count results is shown in Figure 58. Overall WBC, RBC and HGB counts did not show a significant difference across all the iterations of testing. However the results did show that at a given centrifugation speed, the longer the centrifugation time, the fewer number of contaminating Platelets present in the supernatant plasma for the foam separator tubes. However, centrifugation for 3 minutes for 1500 x g may not be enough to give plasma of the requisite purity. The results suggest that not only the foam separator works as an effective barrier, but may also as a capture for the residual platelets in its infrastructure at the plasma-foam interface. Irradiation of the tubes (sterilization) does not appear to affect the performance of the foam separator tube.

Figure 59 shows a comparison of the platelet counts at the BD recommended centrifugation parameters (1500 x g for 10 minutes) for gel tube centrifugation with foam separator tubes. It can be seen that immediately following centrifugation, the PLT levels in the foam separator tubes are equivalent to the gel control tubes. It should be noted that subjects 5 through 10 were actually analyzed 24 hours after initial draw due to reagent availability. Following 10 inversions of the tubes, the PLT counts in the foam separator tubes increased slightly (maximum = 33) compared to the Gel Control Tube (min = 80, max = 190). These results show a better performance of the foam separator tubes compared to the gel control tubes.

This improvement in separation of the foam separator over the gel separator can be explained by location of platelets after centrifugation. In the foam separator tubes the platelets are trapped or captured within the pores of the separator after centrifugation, thus the 10 inversions of the tubes fails to cause the platelets to flow out of the separator. In the gel separator tube, platelets may be present on the upper surface of the gel barrier after centrifugation as a result of having a lower density than the gel or due to premature barrier formation of the gel (before complete separation), thus the 10 inversions of the gel tubes causes platelets to mix with the plasma, giving a lower separation performance.

Example 5

Recovery of Digoxin spiked into an Open Cell Foam Separator

Prototype tubes were fabricated with a separator made from Basotect® V 3012 (Melamine based open cell foam available from BASF) cut into 10mm OD circular tubes, with a length L= 12mm, and inserted into Lithium-Heparin tubes of approximately 7.5mm ID and 13mm OD at a fixed position approximately 45 mm from the bottom of the tube (the expected position of the plasma/hematocrit interface). Digoxin High Calibrator (0.5 mls) was spiked onto the foam. The prototype tubes were then evacuated to give a 4.5ml fill. The tubes were filled using an indirect draw procedure from 1 subject, mixed and centrifuged at 1500 x 'g' for 10 minutes. The Digoxin High Calibrator was assayed on the Elecsys neat, 1:10 dilution and 1:20 dilution. The prototype tubes were also assayed for Digoxin on the Elecsys 2010 in triplicate 4 hours after the sample draw.

The results for the Digoxin High Calibrator are shown in Table 1:

Table 1

Replicate	ng/ml
1	3.56
2	5.71
3	5.73
4	4.02
5	3.90
6	4.00
Average	**4.49**

The Calibrator average result is 4.49 ng/ml; therefore 2.24 ng of Digoxin was added to the foam separator. Since the blood sample volume was 4.5ml, then 2.24 ng of Digoxin was distributed into this volume, thus giving a concentration of 0.499 ng/ml Digoxin in the tube.

Table 2 shows the concentration of the Digoxin within the samples recovered from the prototype tubes.

Table 2

Replicate	Sample 1 (ng/ml)	Sample 2 (ng/ml)
1	.519	.487
2	.512	.501
3	.494	.508
Average	**0.508**	**0.499**

Therefore the overall average recovery for both the samples (same subject) was 0.504 ng/ml. Thus, Digoxin was quantitatively recovered from the two prototype foam separator tubes.

Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein.

What is claimed is:

1. A blood collection tube comprising,

a first end and a second end and a sidewall between said first and second end having inner and outer walls; and

a separator further comprising a porous material;

a pierceable closure to seal said first end:

wherein said porous material has a pore size such that all components of whole blood can flow through said separator.

2. The blood collection tube of claim 1, wherein said separator is positioned at location of a plasma/hematocrit interface after centrifugation of a whole blood sample in said blood collection tube.

3. The blood collection tube of claim 1, wherein said separator is positioned in the range of 10 to 60 mm from said second end of said blood collection tube after centrifugation of a whole blood sample in said blood collection tube.

4. The blood collection tube of claim 1, wherein said separator has a length in the range of 6 to 50 mm.

5. The blood collection tube of claim 1, wherein said separator is fixed to said inner wall of said side wall such that said separator remains substantially immobile during centrifugation.

6. The blood collection tube of claim 5, wherein said separator is fixed to said inner wall of said side wall by a frictional configuration.

7. The blood collection tube of claim 5, wherein said separator is fixed to said inner wall of said side wall by a mechanical configuration.

8. The blood collection tube of claim 7, wherein said mechanical configuration comprises an interference engagement between said separator and said inner wall of said side wall.

9. The blood collection tube of claim 7, wherein said mechanical configuration comprises at least one flange or post circumferentially spaced on said inner wall of said blood collection tube on which said separator can rest.

10. The blood collection tube of claim 5, wherein said separator is fixed to said inner wall of said side wall by a chemical interaction.

11. The blood collection tube of claim 10, wherein said chemical interaction further comprises an adhesive.

12. The blood collection tube of claim 1, wherein said blood collection tube is partially evacuated.

13. The blood collection tube of claim 1, wherein said porous material is an open cell foam, a foamed rubber, a fleece, a mat, or a honeycomb-like material.

14. The blood collection tube of claim 1, wherein said porous material is an open cell foam.

15. The blood collection tube of claim 14, wherein said open cell foam further comprises a polymer containing melamine.

16. The blood collection tube of claim 1, wherein said separator is substantially inert with respect to a blood sample.

17. The blood collection tube of claim 1, wherein said porous material is substantially inert with respect to a blood sample.

18. The blood collection tube of claim 1, wherein said separator moves from a first position to a second position along the longitudinal axis of said blood collection tube during centrifugation.

19. The blood collection tube of claim 18, wherein said second position is positioned at the location of a plasma/hematocrit interface after centrifugation of a whole blood sample in said blood collection tube.

20. The blood collection tube of claim 18, wherein the overall density of said separator is in the range of 1.03 to 1.09 g/cc.

21. The blood collection tube of claim 18, wherein said separator is retained in said first position by frictional configuration with said inner wall of said side wall.

22. The blood collection tube of claim 18, wherein said separator is retained in said first position by mechanical configuration with said inner wall of said side wall.

23. The blood collection tube of claim 22, wherein said mechanical configuration comprises an interference engagement between said separator and said inner wall of said side wall.

24. The blood collection tube of claim 18, wherein said separator is retained in said second position by frictional configuration with said inner wall of said side wall.

25. The blood collection tube of claim 18, wherein said separator is retained in said second position by mechanical configuration with said inner wall of said side wall.

26. The blood collection tube of claim 25, wherein said mechanical configuration comprises an interference engagement between said separator and said inner wall of said side wall.

27. The blood collection tube of claim 18, said separator further comprising a porous material plug and at least one ballast mass.

28. The blood collection tube of claim 27, said porous material plug further comprising a recess in a lower surface.

29. The blood collection tube of claim 18, said separator further comprising a porous material plug and a wiper.

30. The blood collection tube of claim 29, said wiper further comprising a disc portion having holes through the cross section and a taper section around the outer circumference of said disc portion.

31. The blood collection tube of claim 18, said separator further comprising a porous material frusto-conical plug surrounded by a non-porous material sleeve.

32. The blood collection tube of claim 31 said porous material frusto-conical plug further comprising a barrier cap secured to the top of said porous material frusto-conical plug.

33. The blood collection tube of claim 18, wherein said pierceable closure further comprises a cylindrical structure wherein said cylindrical structure extends through said separator when said separator is in said first position.

34. The blood collection tube of claim 18, said separator further comprising a ballast mass having a conical shaped lumen enclosed by a cylindrical sleeve of porous material.

35. The blood collection tube of claim 18, said separator further comprising a porous material plug having a conical shaped lumen and a ballast mass ring attached to the upper surface of said porous material plug.

36. The blood collection tube of claim 18, wherein the movement of said separator from said first to said second position includes a rotational movement of said separator.

37. The blood collection tube of claim 27, wherein said at least one ballast mass is attached to a sidewall of said porous material plug when said separator is in said first position.

38. The blood collection tube of claim 18, said separator further comprising a valve body having a lumen therethrough, a porous material cylinder surrounding a portion of said valve body, and a diverter valve, wherein said diverter valve allows fluid to flow along said lumen when open and occludes said lumen when closed.

39. The blood collection tube of claim 38, wherein said diverter valve is open when said separator is in said first position.

40. The blood collection tube of claim 39, wherein said diverter valve closes upon contact with said second end of said blood collection tube.

41. The blood collection tube of claim 39, wherein said diverter valve closes upon contact with said hematocrit interface after centrifugation of a whole blood sample in said blood collection tube.

42. The blood collection tube of claim 38, said valve body further comprising at least one window through the sidewall of said lumen.

43. The blood collection tube of claim 42, wherein fluid flow through said separator only occurs by passing through said porous material cylinder between said inner wall of said blood collection tube and the outer surface of said valve body and through said at least one window through the sidewall of said lumen when said diverter valve is closed.

44. The blood collection tube of claim 18, said separator further comprising a porous material plug, at least one ballast mass attached to said porous material plug, and a flexible liquid permeable inner container having an open top attached to said porous material plug, a closed bottom and a flexible sidewall extending therebetween.

45. The blood collection tube of claim 18, said separator further comprising a porous material plug and a ring ballast mass circumscribing said porous material plug.

46. The blood collection tube of claim 45, wherein the internal diameter of said ring ballast mass is smaller than the outer diameter of said porous material plug, thereby establishing an interference engagement between said porous material plug and said inner wall of said blood collection tube.

47. The blood collection tube of claim 18, said separator further comprising a porous material plug having a recessed portion around the outer diameter and a ring ballast mass positioned in said recessed portion.

48. The blood collection tube of claim 18, said separator further comprising a porous material plug and a plurality of ballast masses.

49. The blood collection tube of claim 18, wherein said separator is retained in said first position by a frictional, mechanical or chemical engagement with said pierceable closure.

50. The blood collection tube of claim 18, said separator further comprising a porous material plug and at least one spike.

51. The blood collection tube of claim 50, wherein said at least one spike retains said separator in said first position by engagement with said pierceable closure.

52. The blood collection tube of claim 50, wherein said at least one spike functions is a ballast mass.

53. The blood collection tube of claim 1, wherein said separator further comprises:

a static component having a top end and bottom end and a lumen extending therethrough, which is fixed to said inner wall of said side wall such that said static component remains substantially immobile during centrifugation, and

a dynamic component which moves from a first position above said static component to a second position overlaying said top end of said static component during centrifugation.

54. The blood collection tube of claim 54, wherein said dynamic component further comprising a porous material plug having a similar outer diameter to the internal diameter of said blood collection tube and a ballast mass attached to the lower surface of said porous material plug.

55. The blood collection tube of claim 53, wherein said ballast mass occludes said lumen of said static component when said dynamic component is in said second position.

56. The blood collection tube of claim 53, wherein said static component further comprising a cylinder of porous material.

57. The blood collection tube of claim 53, wherein said static component and said dynamic components are distinct units.

58. The blood collection tube of claim 53, wherein said static component and said dynamic components are unitary.

59. The blood collection tube of claim 1, wherein said separator further comprises a porous material plug having a concave upper surface.

60. The blood collection tube of claim 1, wherein said separator further comprises a monolithic porous material plug.

61. The blood collection tube of claim 60, further comprising a cylindrical structure extending through said monolithic porous material plug prior to centrifugation.

62. The blood collection tube of claim 61, wherein said cylindrical structure launches from said monolithic porous material plug during centrifugation.

63. A blood collection tube comprising,

a first end and a second end and a sidewall between said first and second end having inner and outer walls; and

a separator further comprising a porous material;

a pierceable closure to seal said first end:

wherein said porous material having a pore size greater than the particle size of all components of whole blood.

64. A blood collection tube comprising, a first end and a second end and a sidewall between said first and second end having inner and outer walls, a separator affixed to said inner wall of said sidewall such that said separator does not substantially move in relation to said blood collection tube during centrifugation, said separator further comprising a porous material, and a pierceable closure to seal said first end, wherein said porous material having a

pore size greater than the particle size of all components of whole blood, and wherein said blood collection tube is partially evacuated.

65. A blood collection tube comprising, a first end and a second end and a sidewall between said first and second end having inner and outer walls, a separator comprising a porous material, and a pierceable closure to seal said first end, wherein said separator moves from a first position to a second position along the longitudinal axis of said blood collection tube during centrifugation, and wherein said porous material having a pore size greater than the particle size of all components of whole blood, and wherein said blood collection tube is partially evacuated.

66. A blood collection tube comprising, a first end and a second end and a sidewall between said first and second end having inner and outer walls, a separator having a static component having a top end and bottom end and a lumen extending therethrough, which is fixed to said inner wall of said side wall such that said static component remains substantially immobile during centrifugation, and a dynamic component which moves from a first position above said static component to a second position overlaying said top end of said static component during centrifugation, said separator further comprising a porous material, and a pierceable closure to seal said first end, wherein said porous material having a pore size greater than the particle size of all components of whole blood.

67. A blood collection tube comprising, a first end and a second end and a sidewall between said first and second end having inner and outer walls; and a monolithic separator comprising a porous material and disposed between the first and second ends; a pierceable closure to seal said first end: wherein said porous material consists of a melamine based open cell foam.

68. A blood collection tube comprising, a first end and a second end and a sidewall between said first and second end having inner and outer walls; and a separator comprising a porous material and disposed between the first and second ends; and a pierceable closure to seal said first end wherein said porous material further comprises a copolymer of formaldehyde-melamine and sodium bisulfite.

69. A method of manufacturing a blood collection tube, comprising: providing a blood collection tube comprising a first end and a second end and a sidewall between said first and

second end having inner and outer walls, the blood collection tube having an inner cavity, wherein said first end is open; inserting a separator comprising a porous material into the blood collection tube, the separator inserted at a location defining an upper volume between the first end and the separator as well as a lower volume between the first end and the separator; depressurizing the inner cavity to a pressure lower than atmosphere; and sealing hermetically the first end with a pierceable closure wherein said porous material has a pore size such that all components of whole blood can flow through said separator.

70. The method of claim 69, wherein disposing the separator into the blood collection tube requires compression of the separator prior to insertion.

71. The method of claim 70, further comprising disposing an additive into the blood collection tube.

72. A method of separating blood comprising the steps of: providing a blood collection tube comprising, a first end and a second end and a sidewall between said first and second end having inner and outer walls; a separator further comprising a porous material having a pore size such that all components of whole blood can flow through said separator; and a pierceable closure to seal said first end: collecting a sample of blood through said pierceable closure and into said blood collection tube subjecting said blood collection tube to centrifugation; and terminating said centrifugation such that said separator is at a separation position forming a barrier between said the cellular portion and non-cellular liquid portion of said blood sample.

73. The method of claim 72, wherein the collection a sample of blood includes providing a needle that penetrates said pierceable closure whereby the sample enters the tube through the needle.

74. The method of claim 73, further comprising removing the needle from said pierceable closure whereby said closure self-seals.

75. The method of claim 72, wherein said separator is fixed to said inner wall of said side wall at said separation position such that said separator remains substantially immobile during centrifugation.

76. The method of claim 72, wherein said blood collection tube is partially evacuated.

77. The method of claim 72, wherein said porous material is an open cell foam, a foamed rubber, a fleece, a mat, or a honeycomb-like material.

78. The method of claim 72, wherein said porous material is an open cell foam.

79. The method of claim 78, wherein said open cell foam further comprises a polymer containing melamine.

80. The method of claim 72, wherein said separator moves from a first position to said separation position along the longitudinal axis of said blood collection tube during centrifugation.

81. The method of claim 80, wherein said separator is located towards said pierceable closure when in said first position.

82. The method of claim 80, wherein said collection of a sample of blood includes providing a needle that penetrates said pierceable closure and said separator whereby the sample enters the tube through the needle when said separator is in said first position.

83. The method of claim 80, said separator further comprising a porous material plug and at least one ballast mass attached or embedded within said porous material plug.

84. The method of claim 83, wherein on collection said separator is held in said first position by a friction force between said porous material plug and said inner wall of said tube and a non patient cannula is able to penetrate deep into said porous material plug such that blood flows through the pores of said porous material plug, and into the reservoir of said tube.

85. The method of claim 84, wherein during centrifugation, the centrifugal forces stretch and elongate said porous material plug axially, causing inward radial movement such that said friction force between said porous material plug and inner wall of said tube is overcome and said separator moves axially down the longitudinal axis of said tube.

86. The method of claim 80, said separator further comprising a porous material plug and a wiper, said wiper having a disc portion having holes through the cross section and a taper section around the outer circumference of said disc portion.

87. The method of claim 86, wherein on collection said separator is held in said first position by a friction force between said inner wall of said tube said porous material plug and said taper section and a non patient cannula is able to penetrate deep into said porous material

plug such that blood flows through the pores of said porous material plug, said holes of said wiper, and into the reservoir of said tube.

88. The method of claim 87, wherein during centrifugation, the centrifugal forces stretch and elongate said porous material plug axially, causing inward radial movement such that said friction force which holds said separator in said first position is overcome and said separator travels axially down the longitudinal axis of said tube.

89. The method of claim 88, wherein on termination of centrifugation, said porous material plug expands to its undeformed shape, thereby causing said porous material plug and said taper section to seal against said inner wall of the tube, such that said wiper forms another barrier in addition to said porous material plug.

90. The method of claim 80, wherein the movement of said separator from said first position to said separation position includes a rotational movement of said separator.

91. The method of claim 80, said separator further comprising, a valve body having a lumen therethrough, a porous material cylinder surrounding a portion of said valve body, and a diverter valve, wherein said diverter valve allows fluid to flow along said lumen when open and occludes said lumen when closed.

92. The method of claim 91, wherein said separator is retained in said first position on collection of a blood sample by a releasable securement of said valve body to said pierceable closure and a friction force between an outer surface of said porous material cylinder and said inner wall of said tube.

93. The method of claim 92, wherein the collection a sample of blood includes providing a needle that penetrates said pierceable closure whereby the blood sample enters the tube through the needle and passes through the separator by flowing along said lumen and out of said diverter valve.

94. The method of claim 93, wherein during centrifugation said diverter valve closes on reaching said separation position by contact with either said cellular portion of said blood sample or the bottom of said tube.

95. The method of claim 94, wherein blood flow from beneath to above said separator can only occur by passing through said porous material cylinder when said diverter valve is closed.

96. The method of claim 72, wherein said separator further comprises: a static component having a top end and bottom end and a lumen extending therethrough, which is fixed to said inner wall of said side wall at said separation position, and a dynamic component moveable from a first position above said static component to a second position overlaying said top end of said static component.

97. The method of claim 96, wherein said static component further comprising a cylinder of porous material.

98. The method of claim 97, wherein the collection a sample of blood includes providing a needle that penetrates said pierceable closure whereby the blood sample enters the tube through the needle and passes through said static component by flowing along said lumen.

99. The method of claim 98, wherein during centrifugation said static component remains substantially immobile.

100. The method of claim 99, wherein said dynamic component further comprising a porous material plug having a similar outer diameter to the internal diameter of said blood collection tube and a ballast mass attached to the lower surface of said porous material plug.

101. The method of claim 100, wherein during centrifugation said dynamic component moves from said first position to said second position such that said ballast mass occludes said lumen of said static component, thereby forming said barrier between said the cellular portion and non-cellular liquid portion of said blood sample.

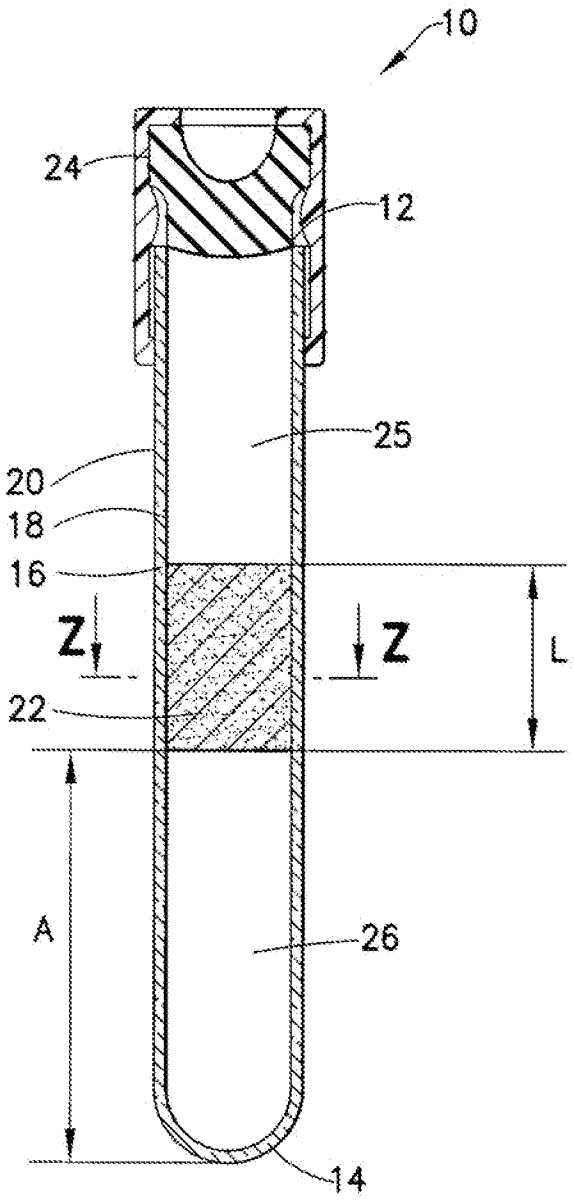

FIG.1

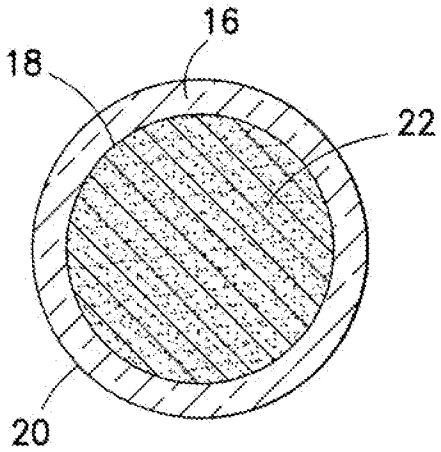

FIG.2

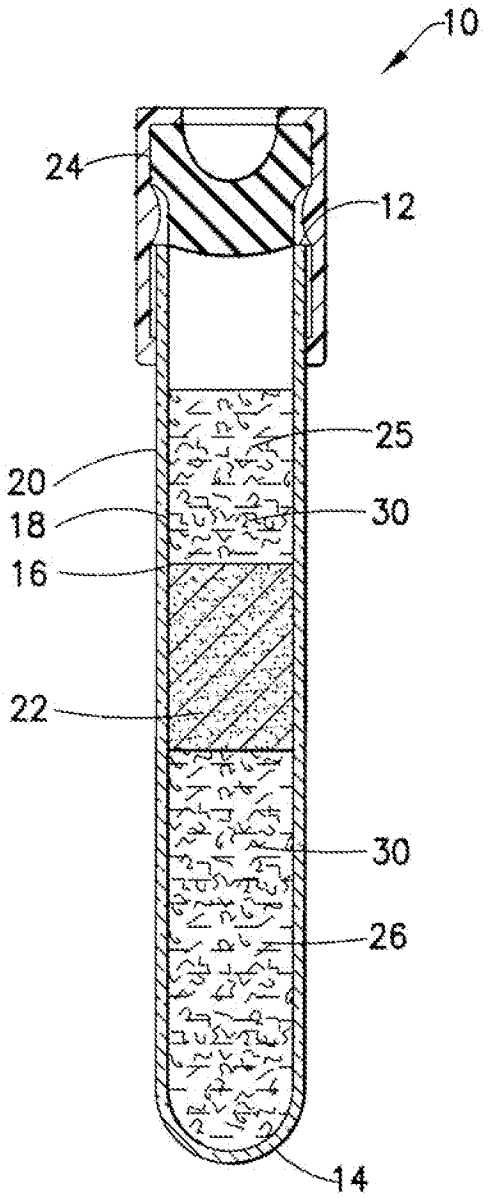

FIG.3

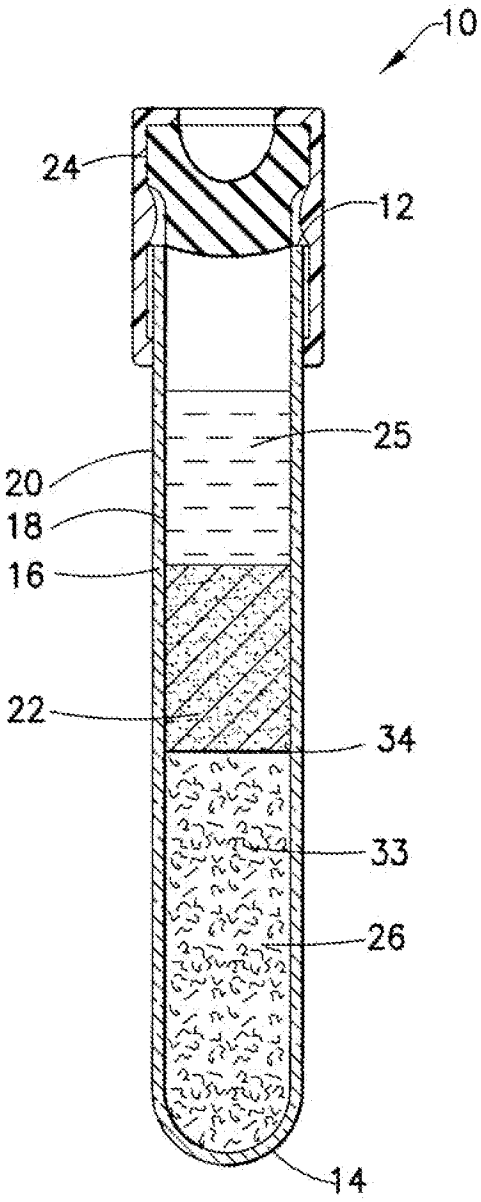

FIG.4

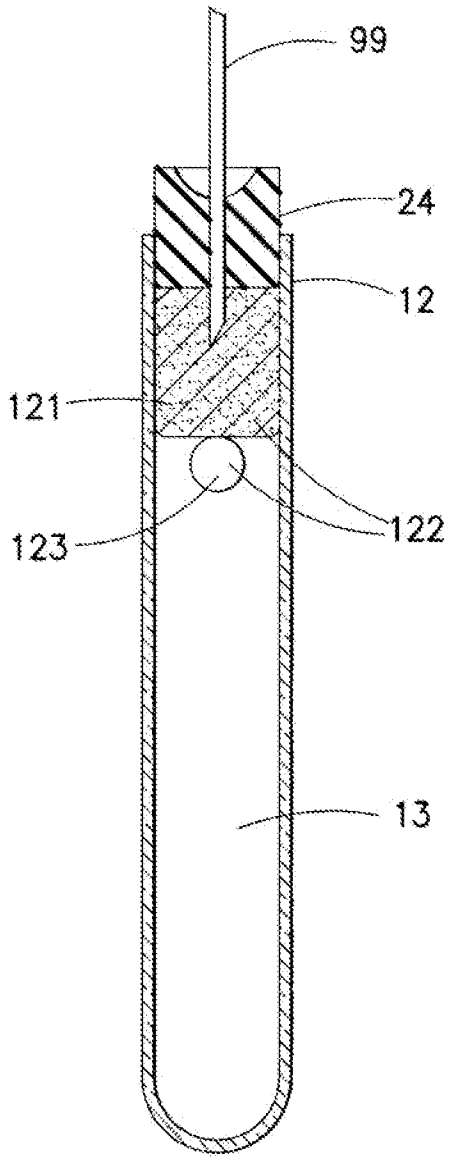

FIG.5

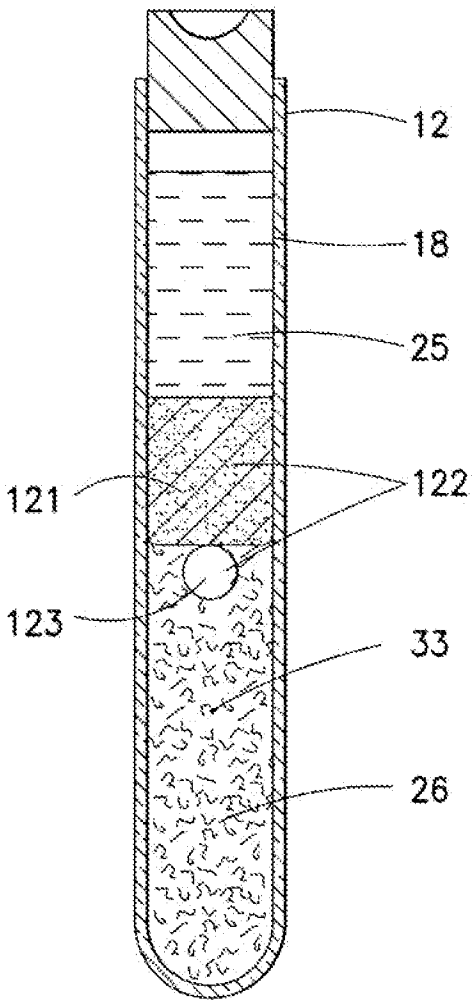

FIG.6

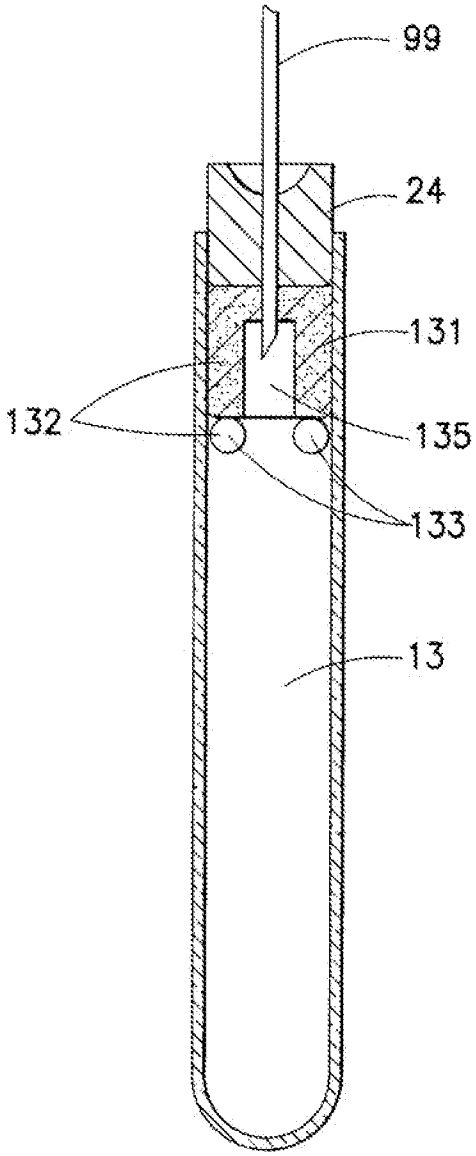

FIG.7

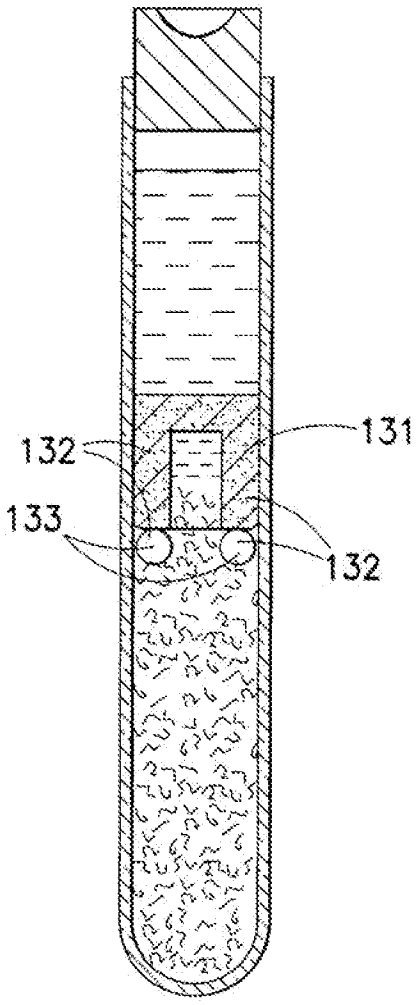

FIG.8

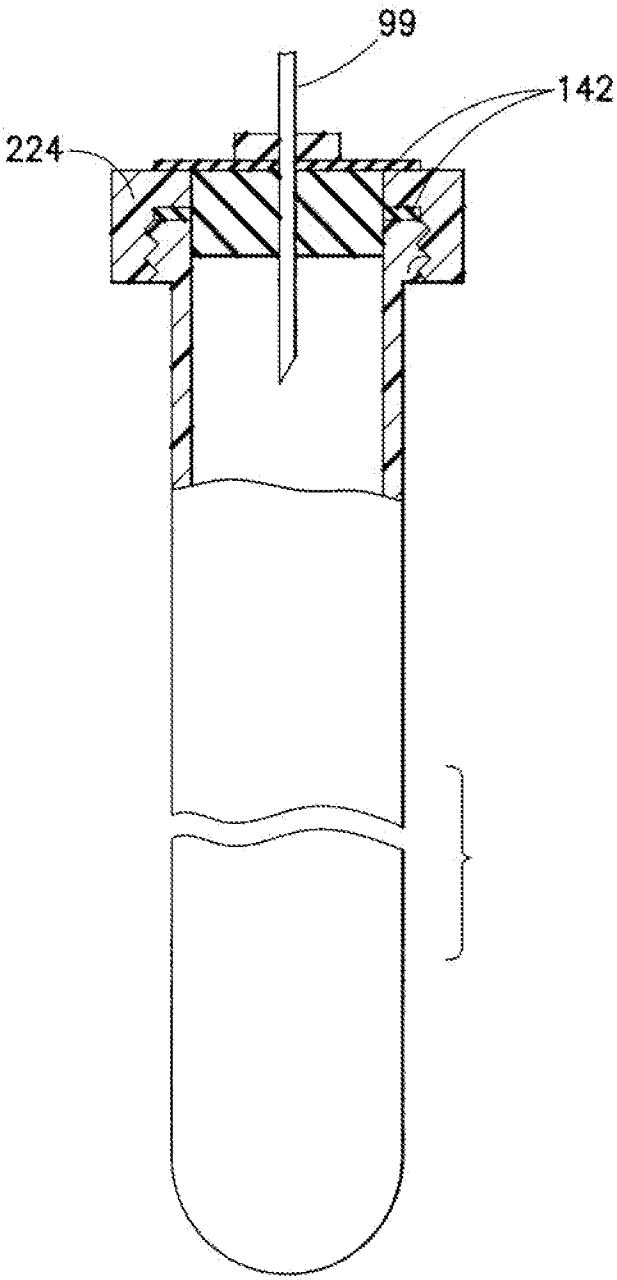

FIG.9

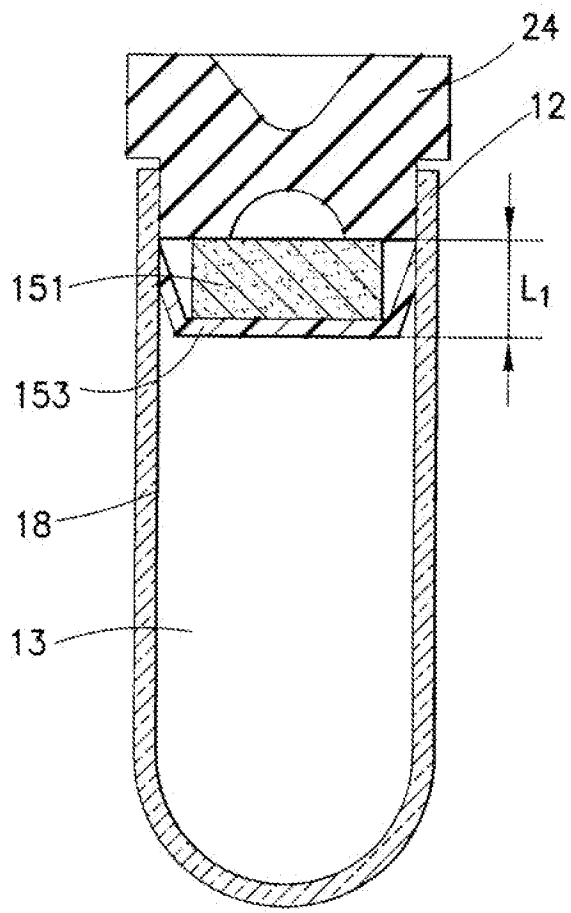

FIG.10

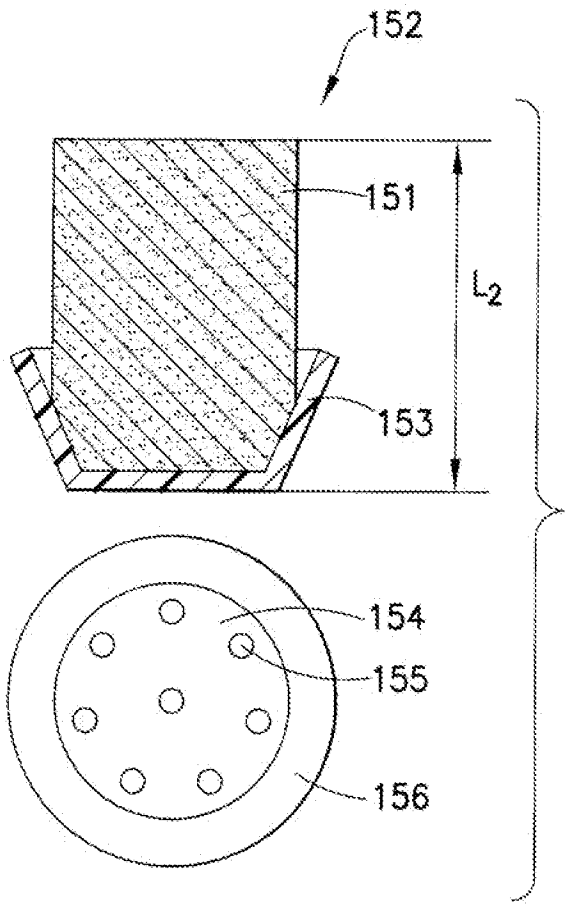

FIG.11

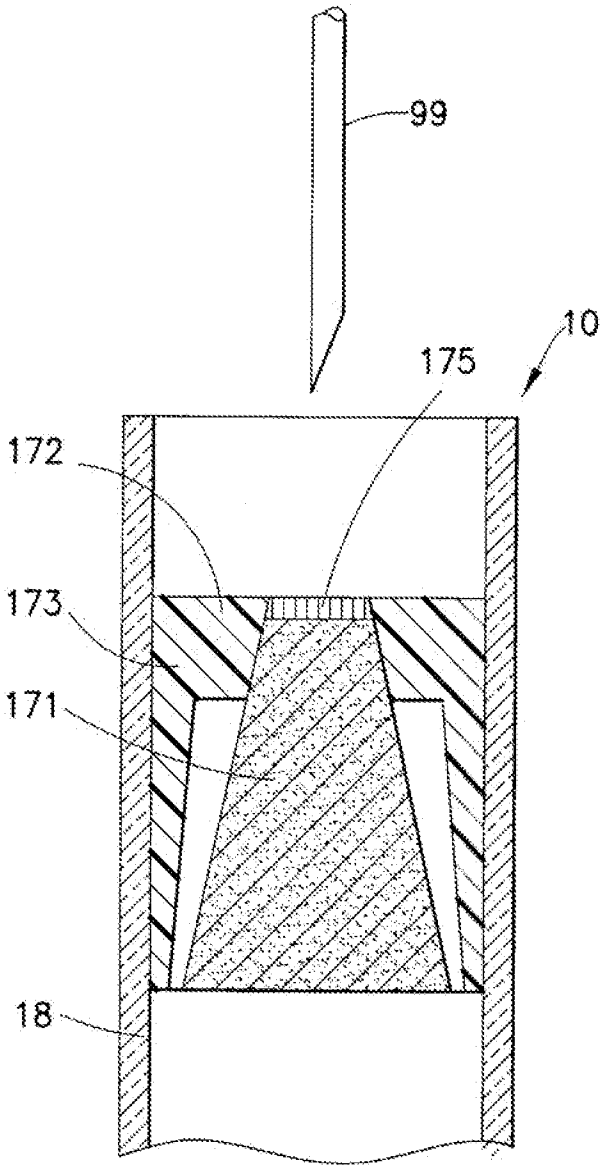

FIG.12

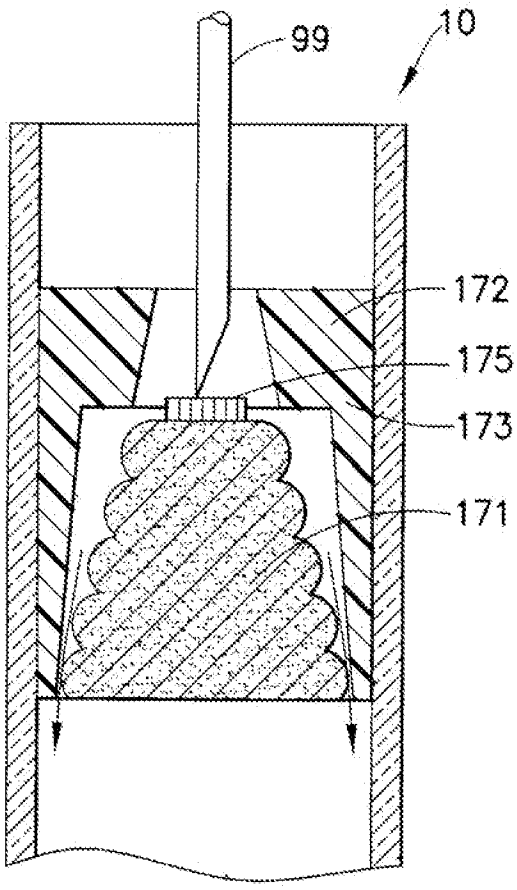

FIG.13

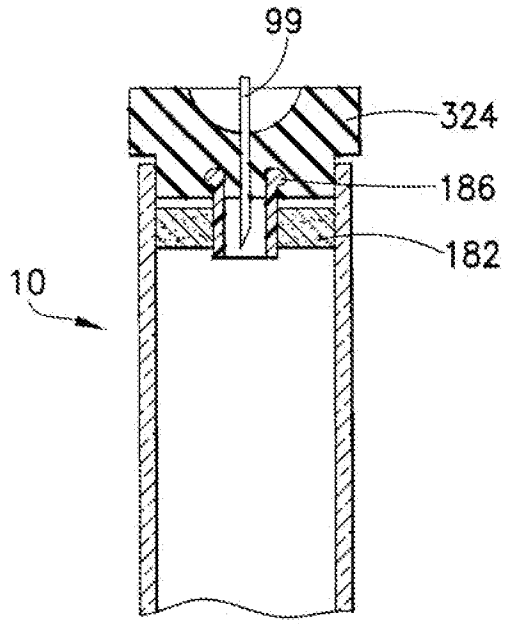

FIG.14a

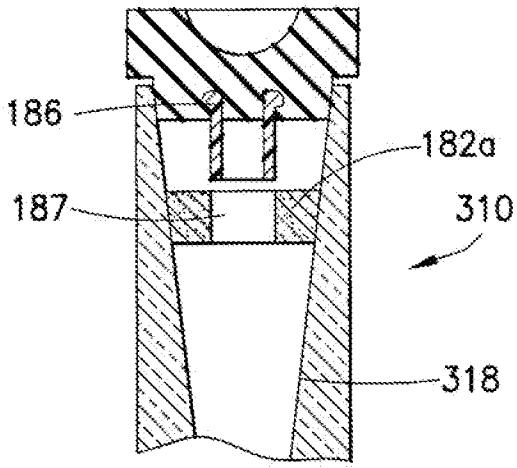

FIG.15a

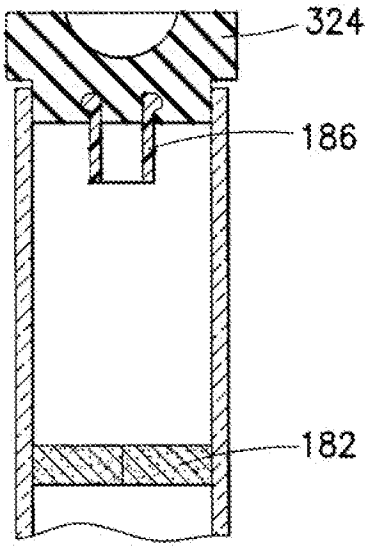

FIG.14b

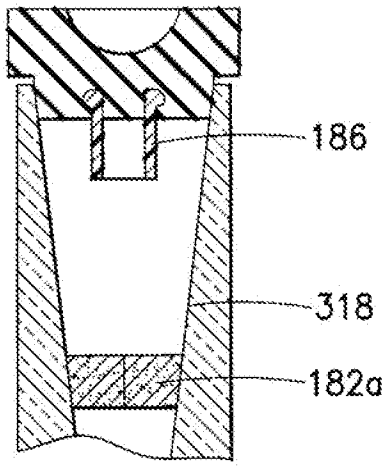

FIG.15b

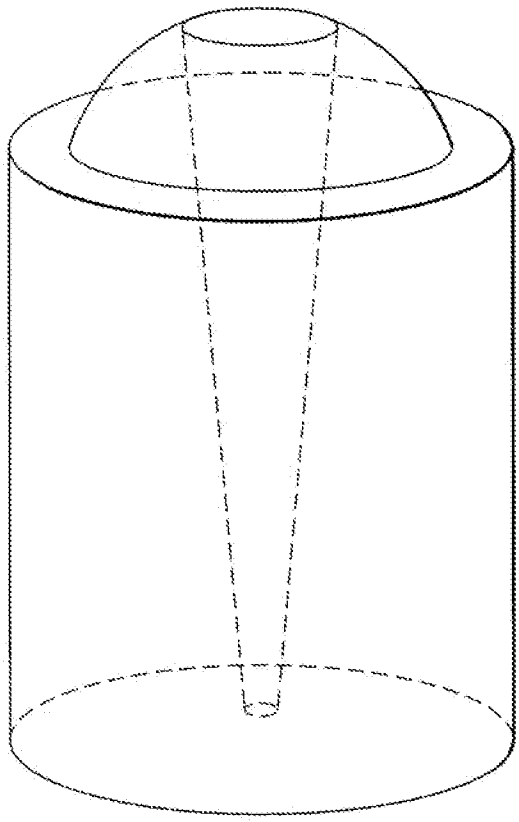

FIG.16

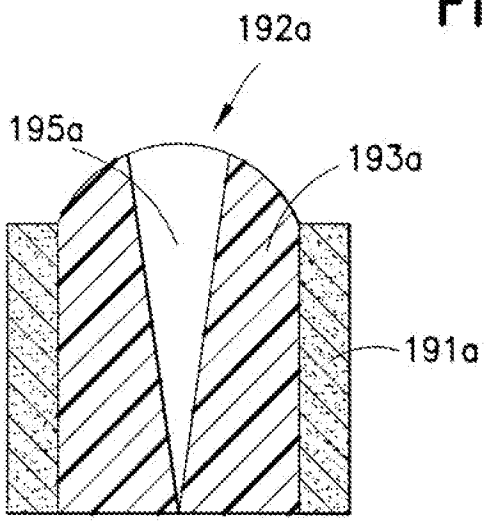

FIG.17

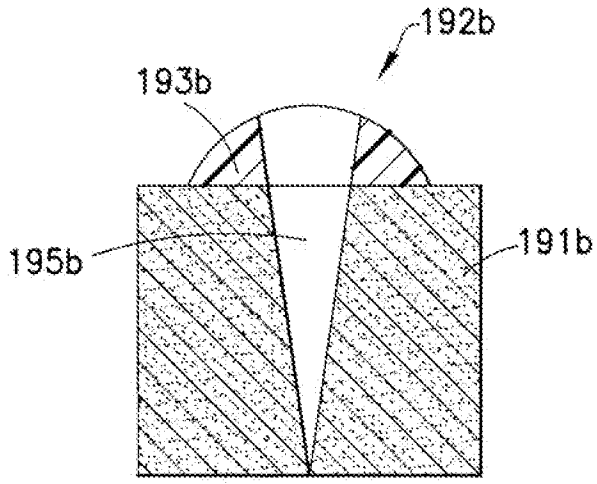

FIG.18

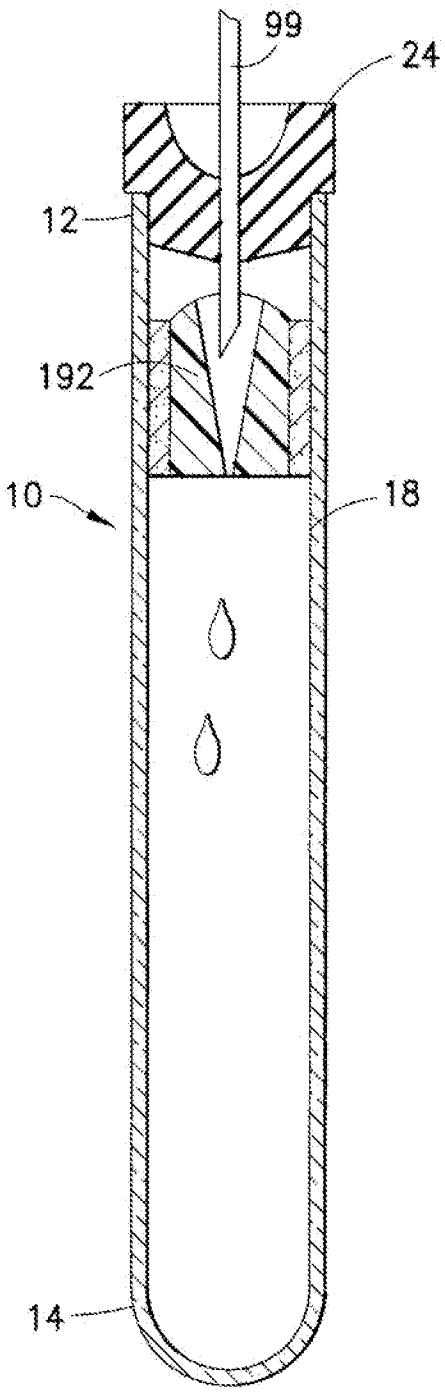

FIG.19

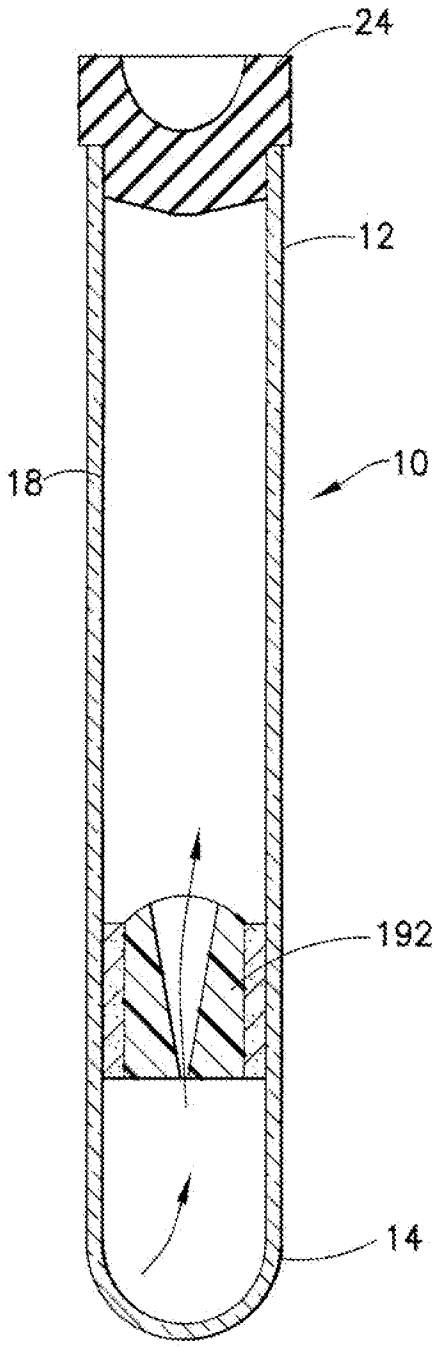

FIG.20

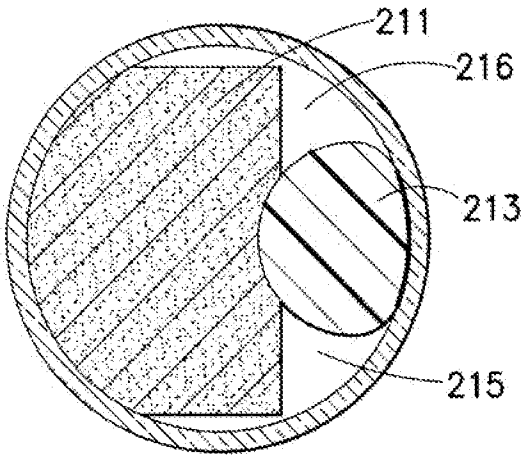

FIG.21

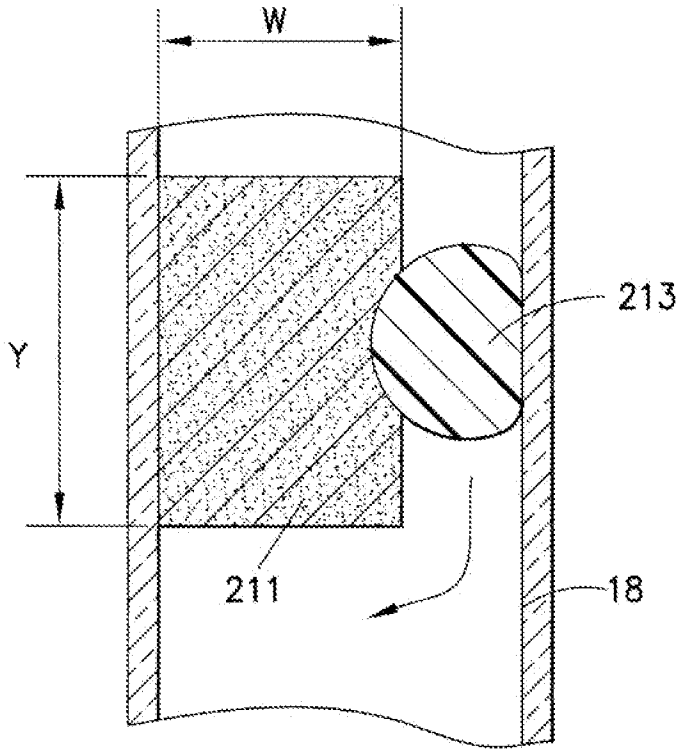

FIG.22

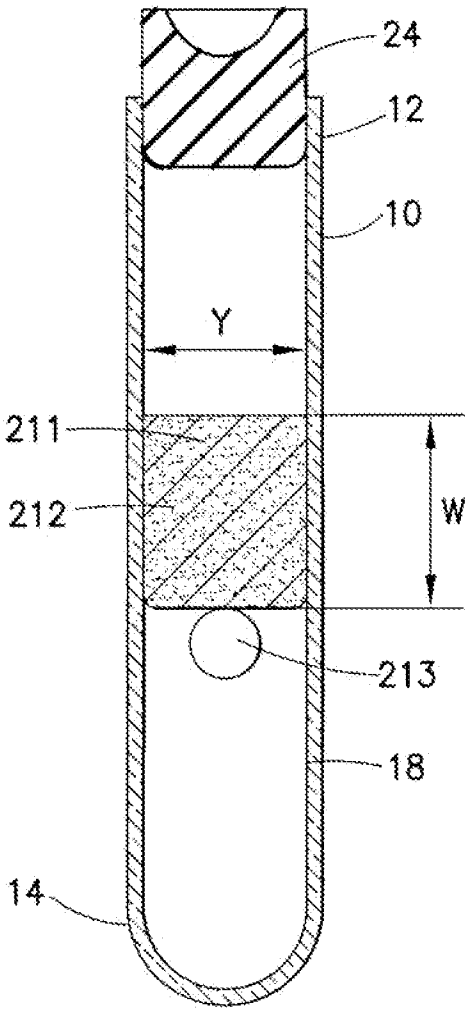

FIG.23

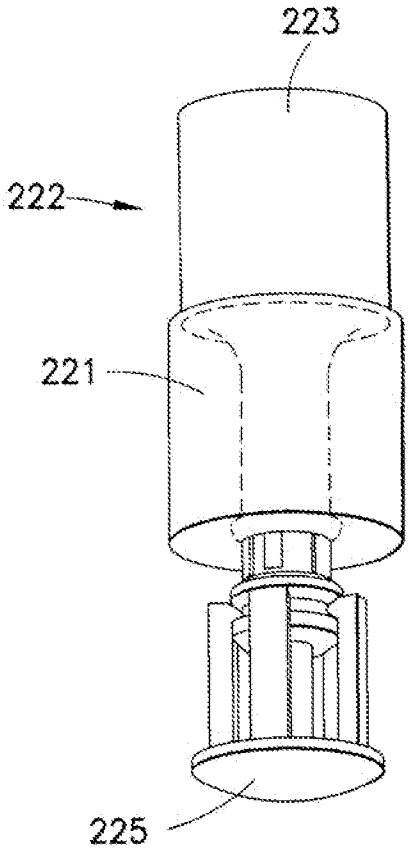

FIG.24

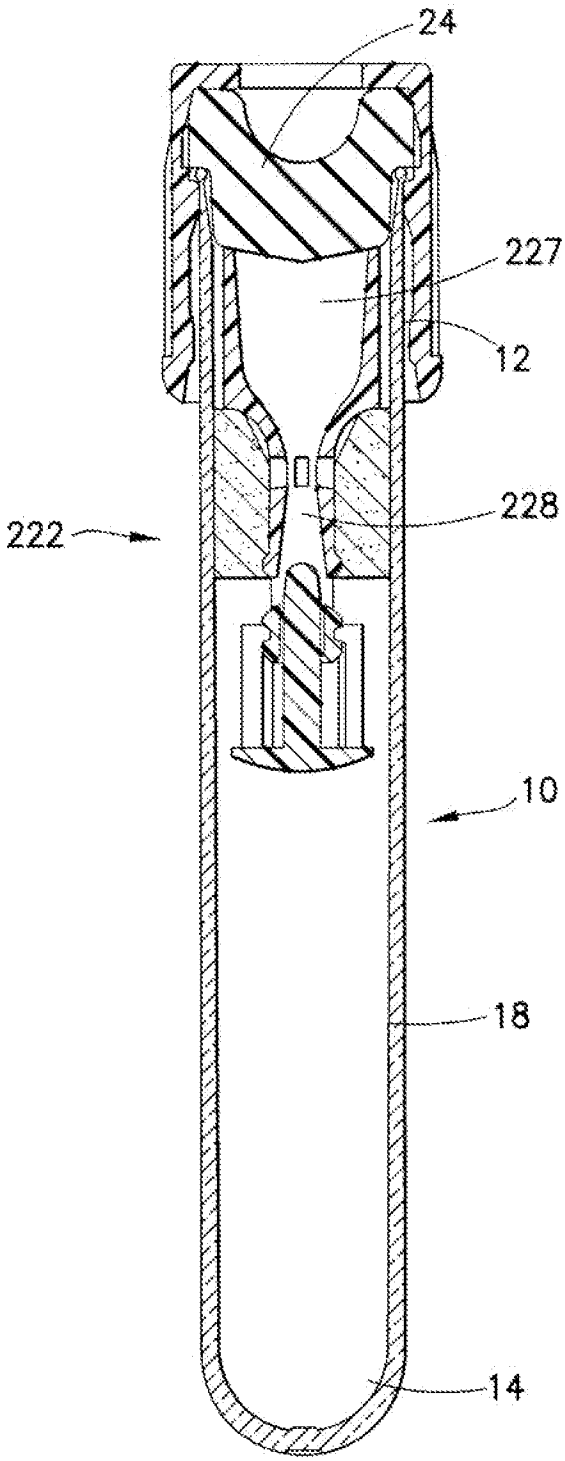

FIG.25

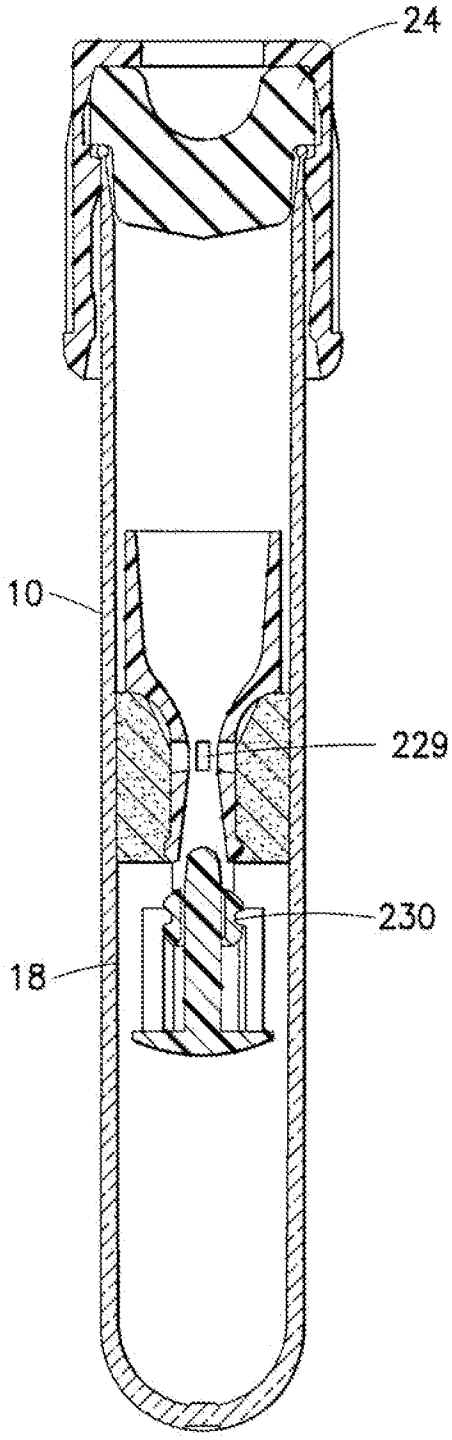

FIG.26

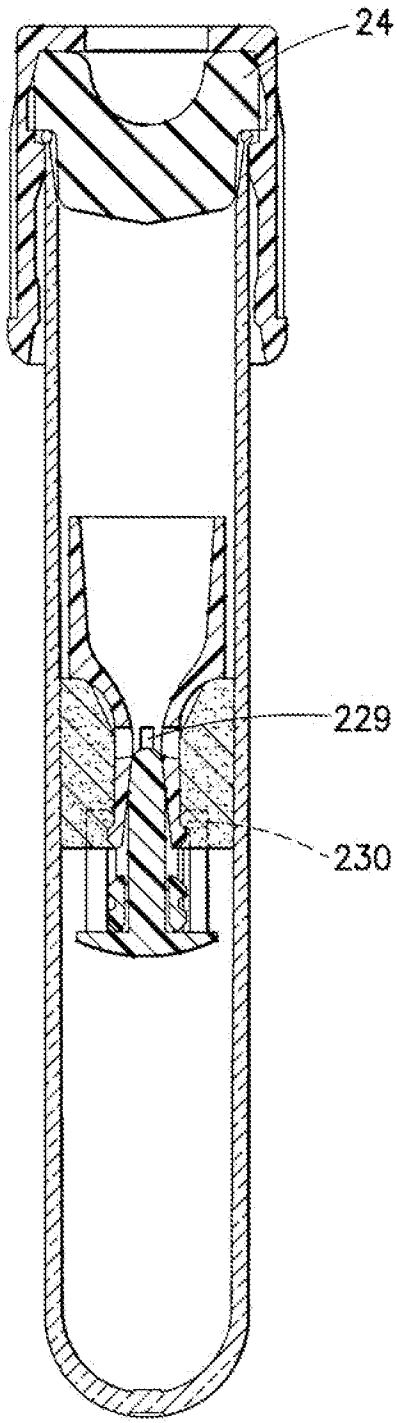

FIG.27

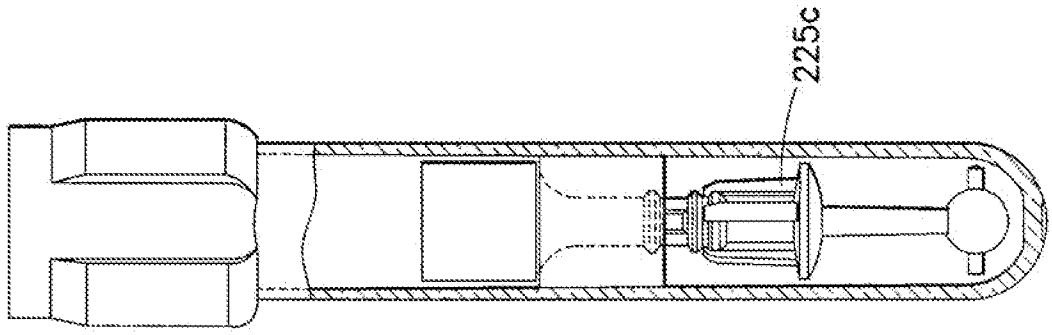

FIG.30

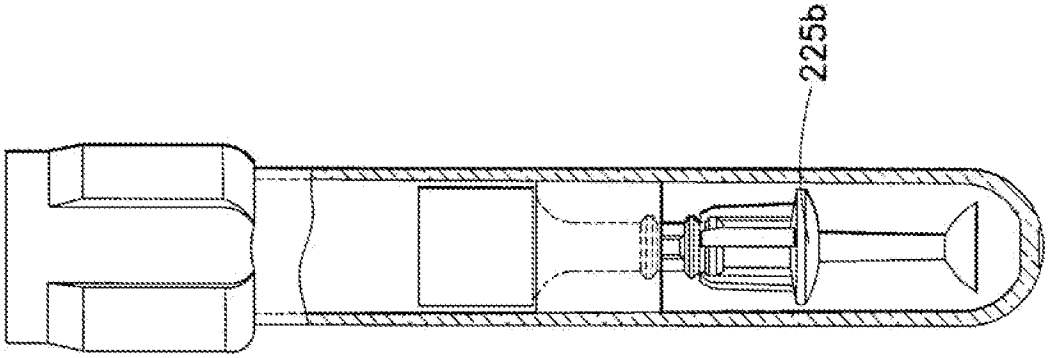

FIG.29

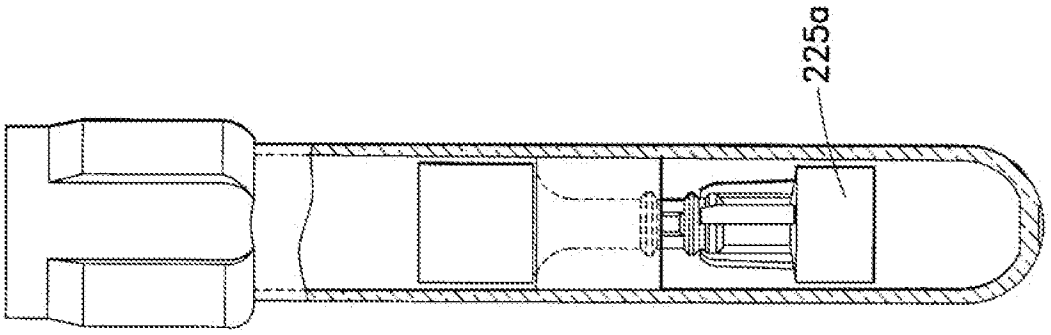

FIG.28

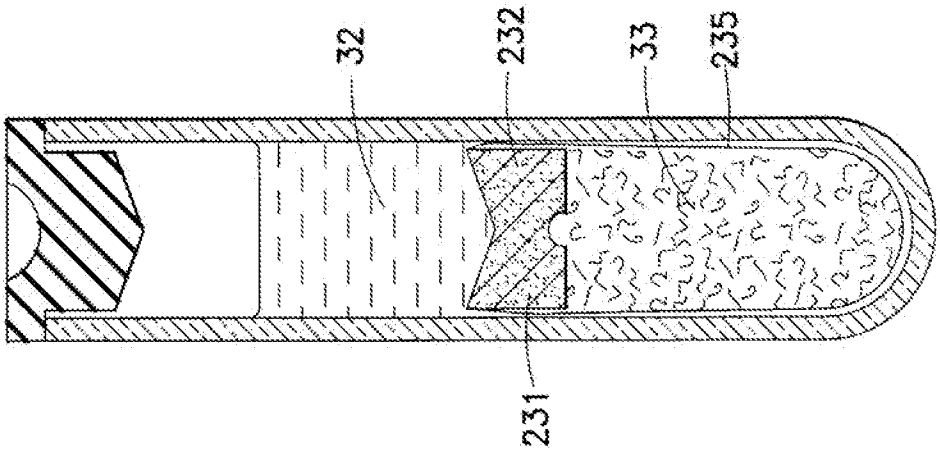

FIG.33

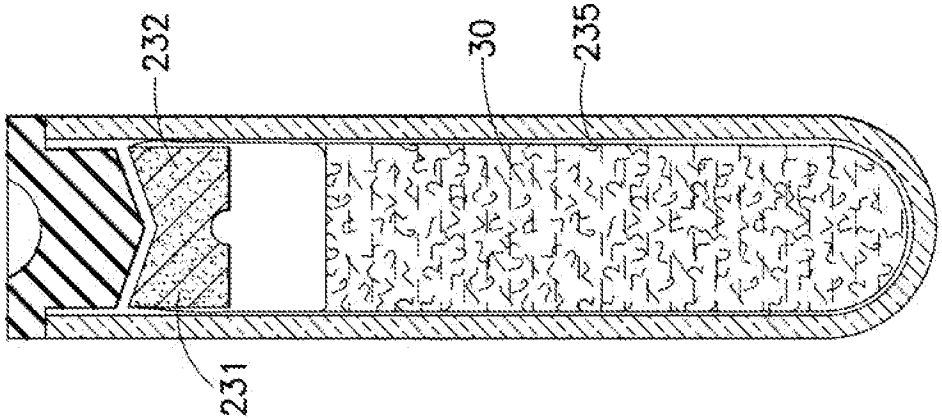

FIG.32

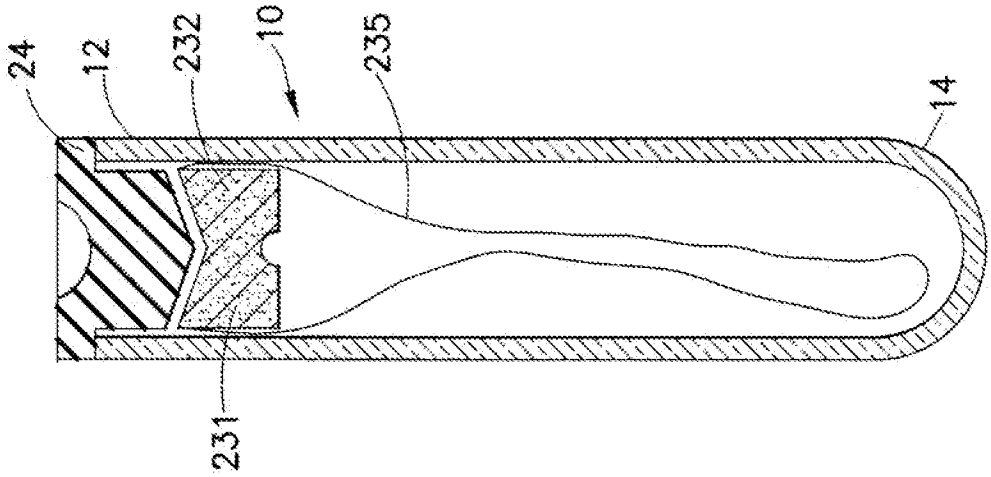

FIG.31

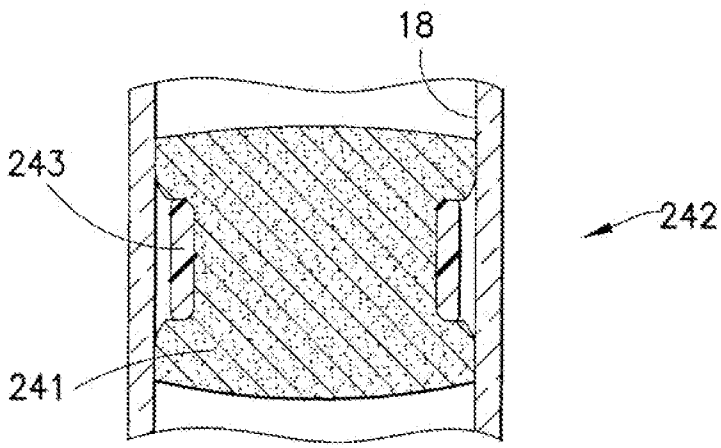

FIG.34

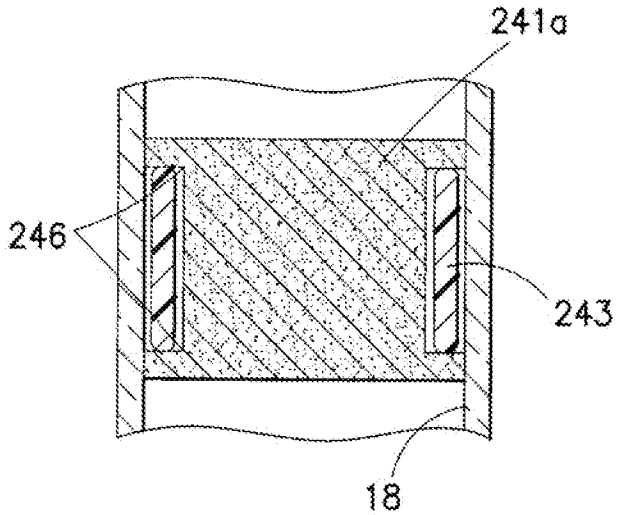

FIG.35

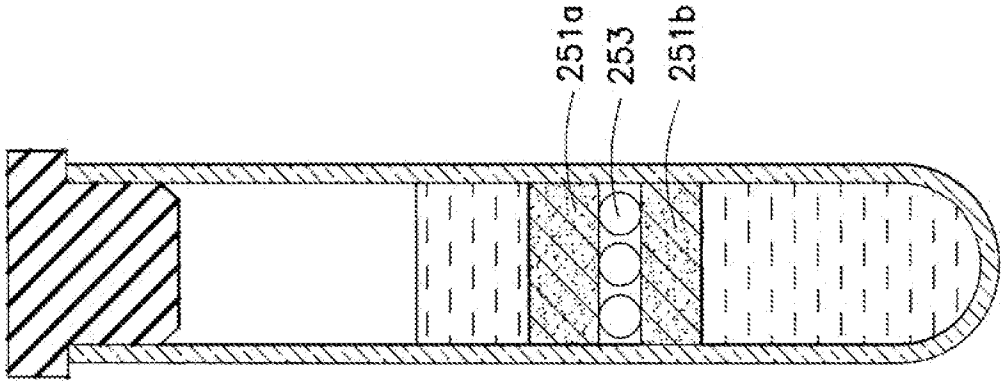

FIG.39

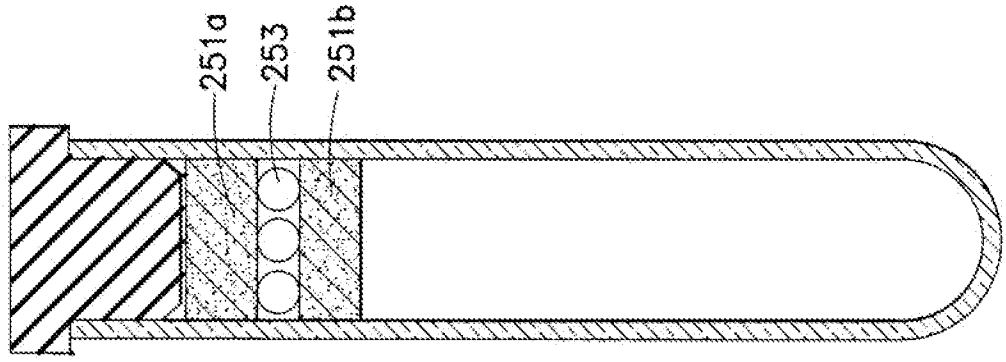

FIG.38

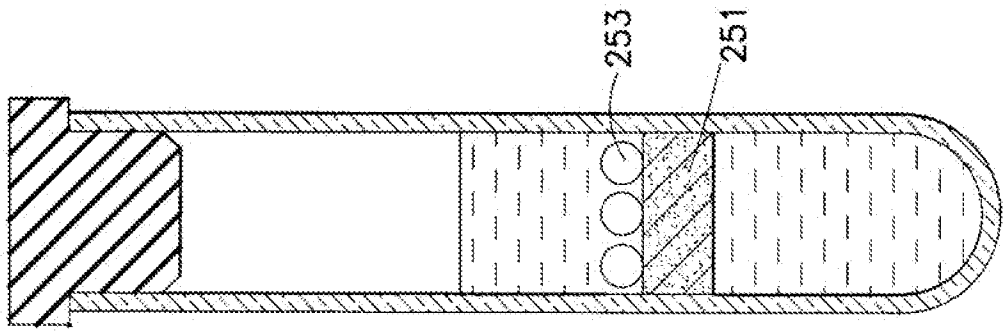

FIG.37

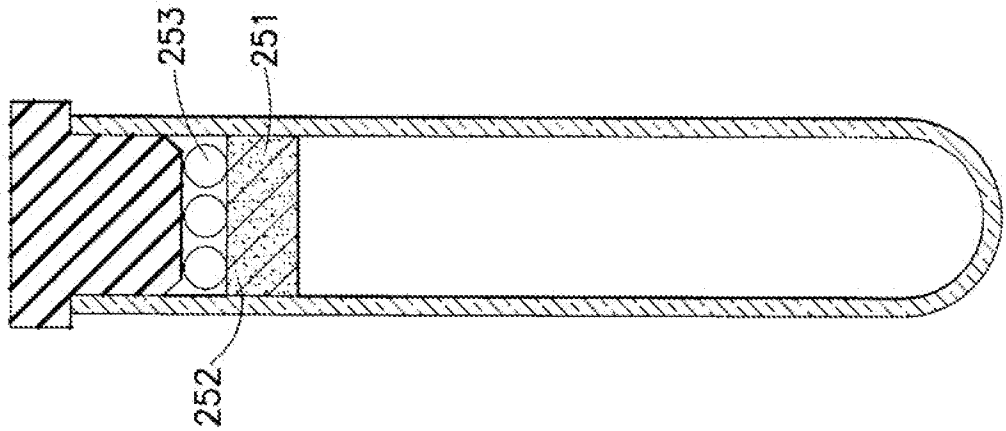

FIG.36

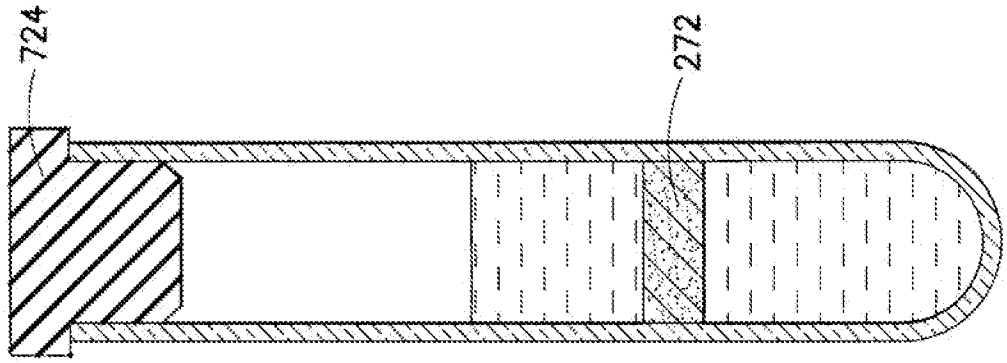

FIG.43

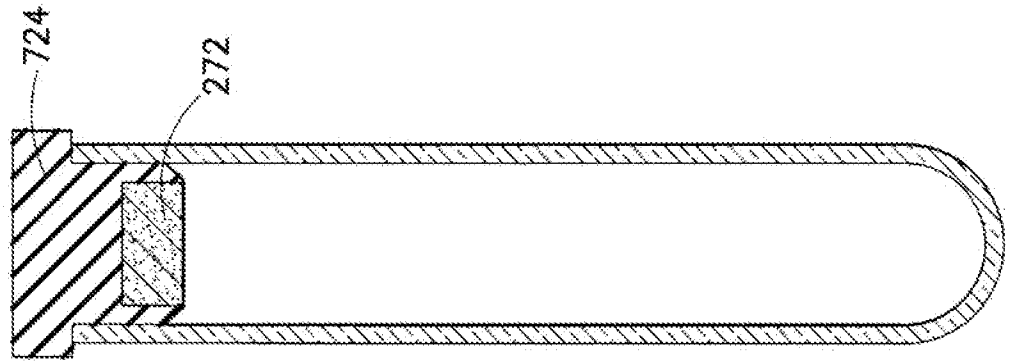

FIG.42

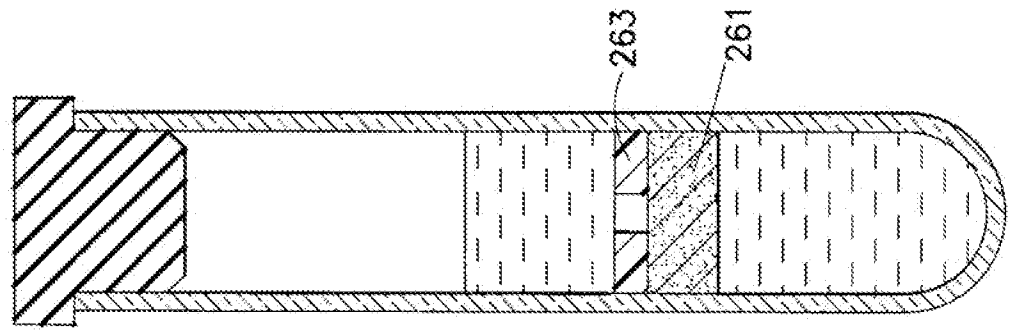

FIG.41

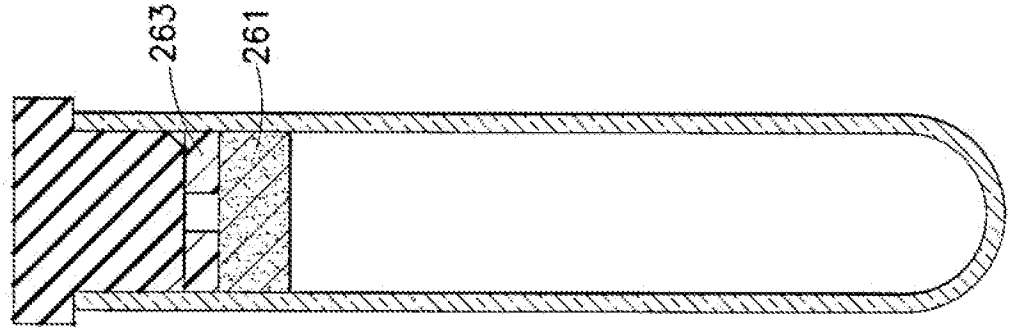

FIG.40

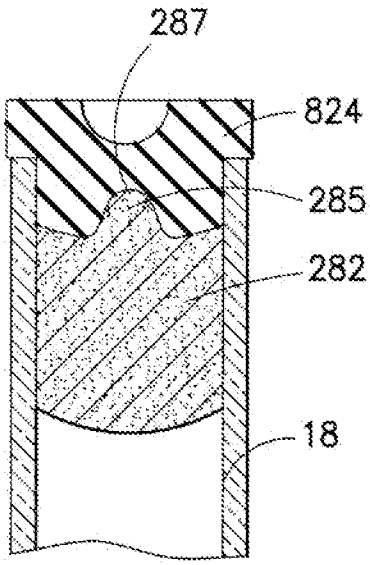

FIG.44

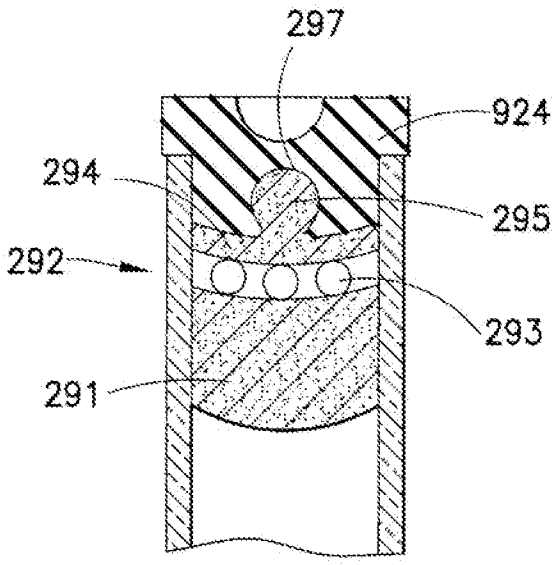

FIG.45

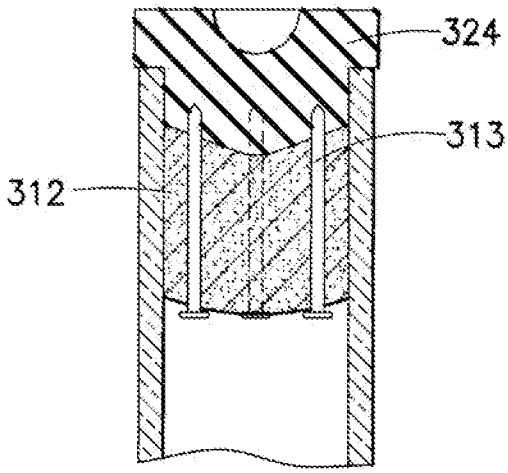

FIG.46

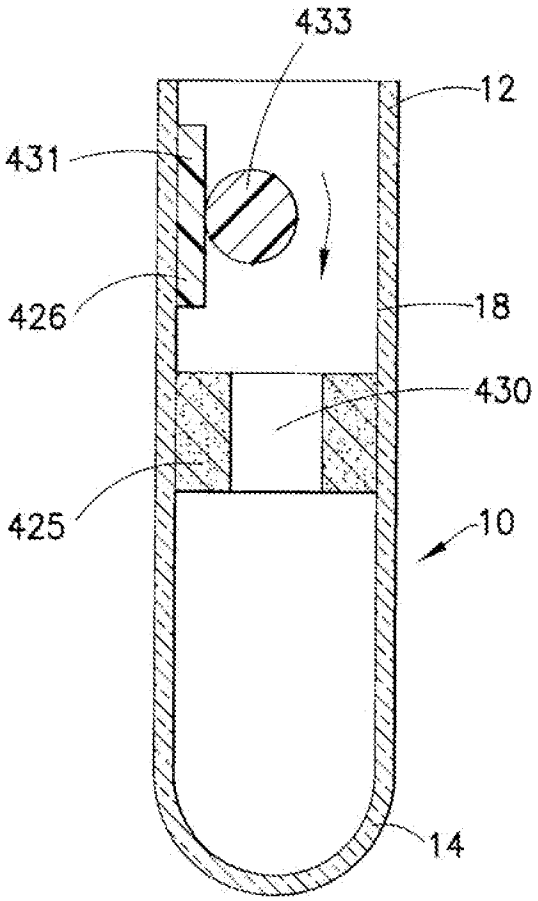

FIG.47

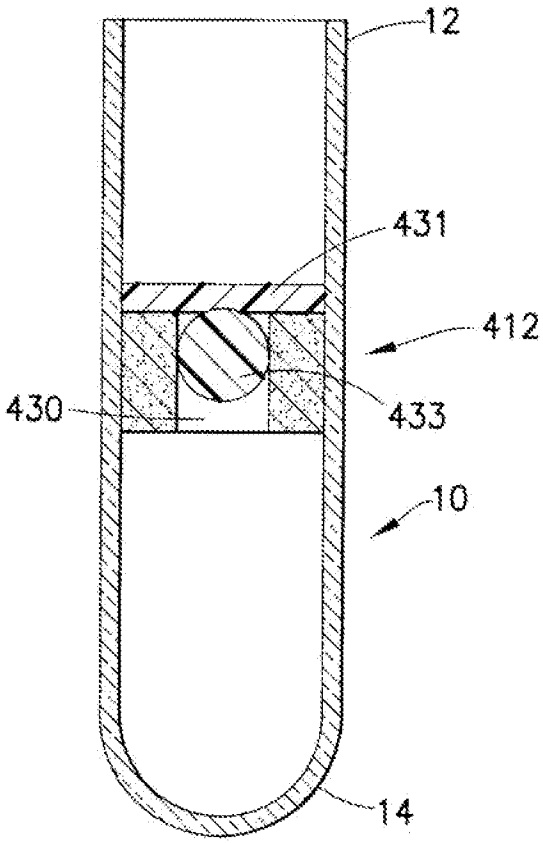

FIG.48

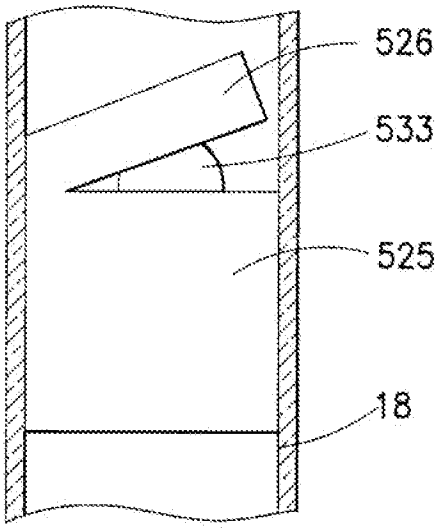

FIG.49

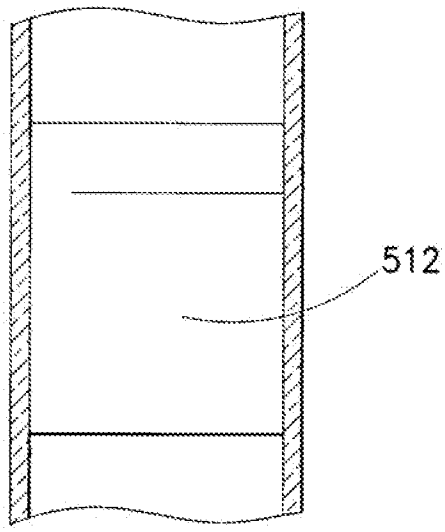

FIG.50

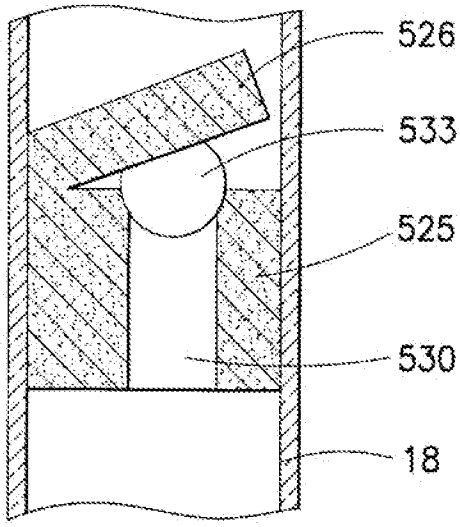

FIG.51

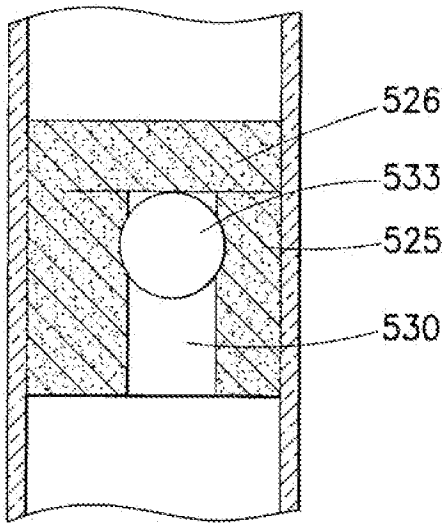

FIG.52

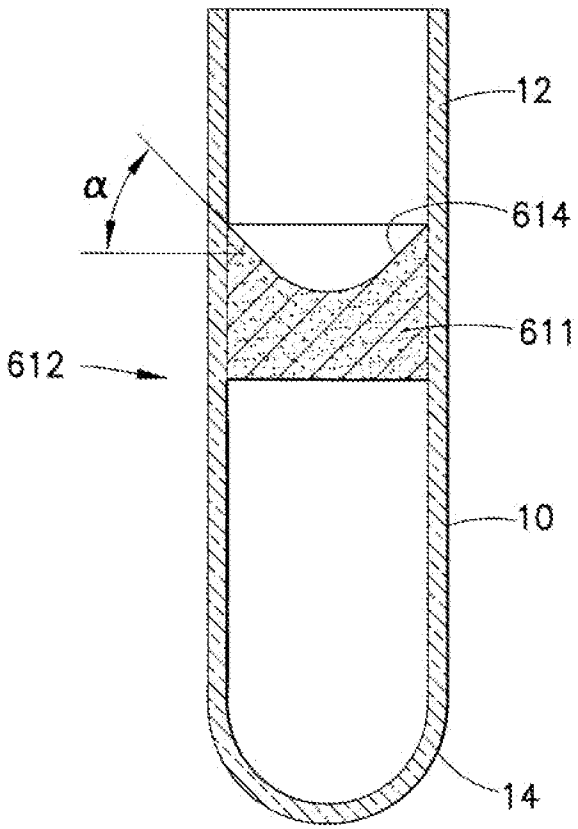

FIG.53

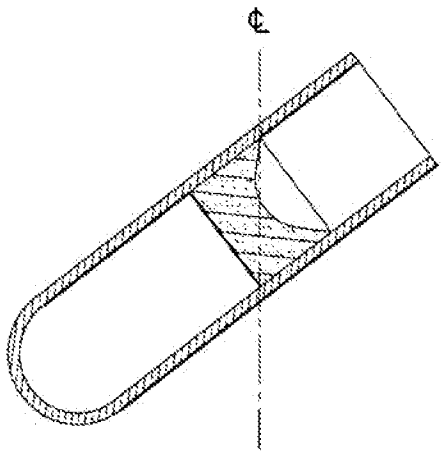

FIG.54

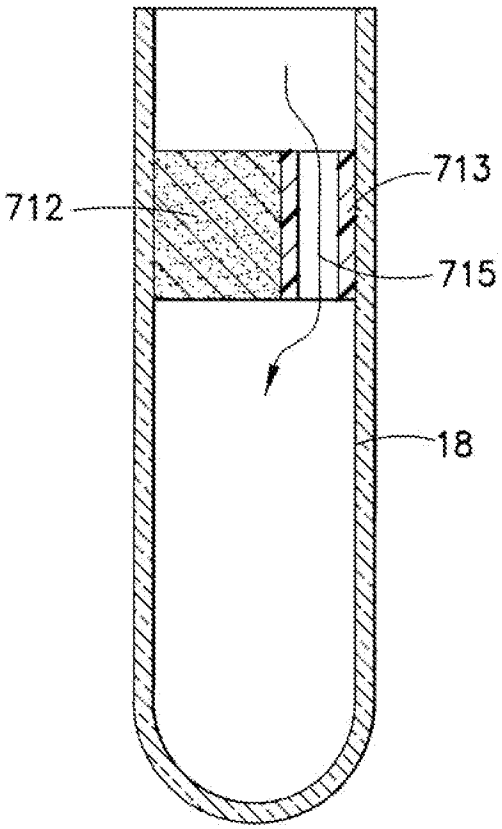

FIG.55

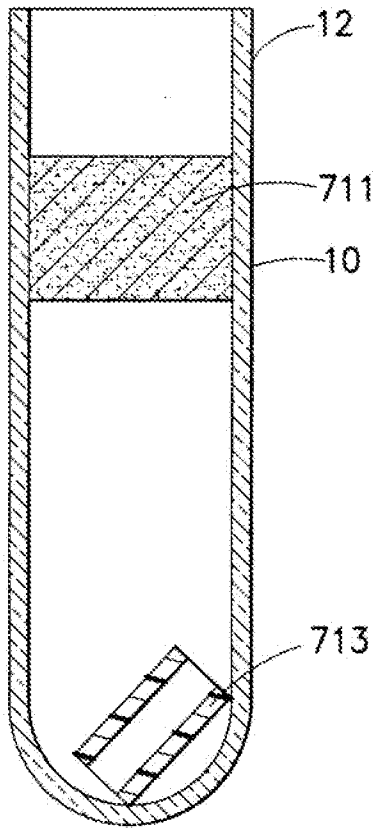

FIG.56

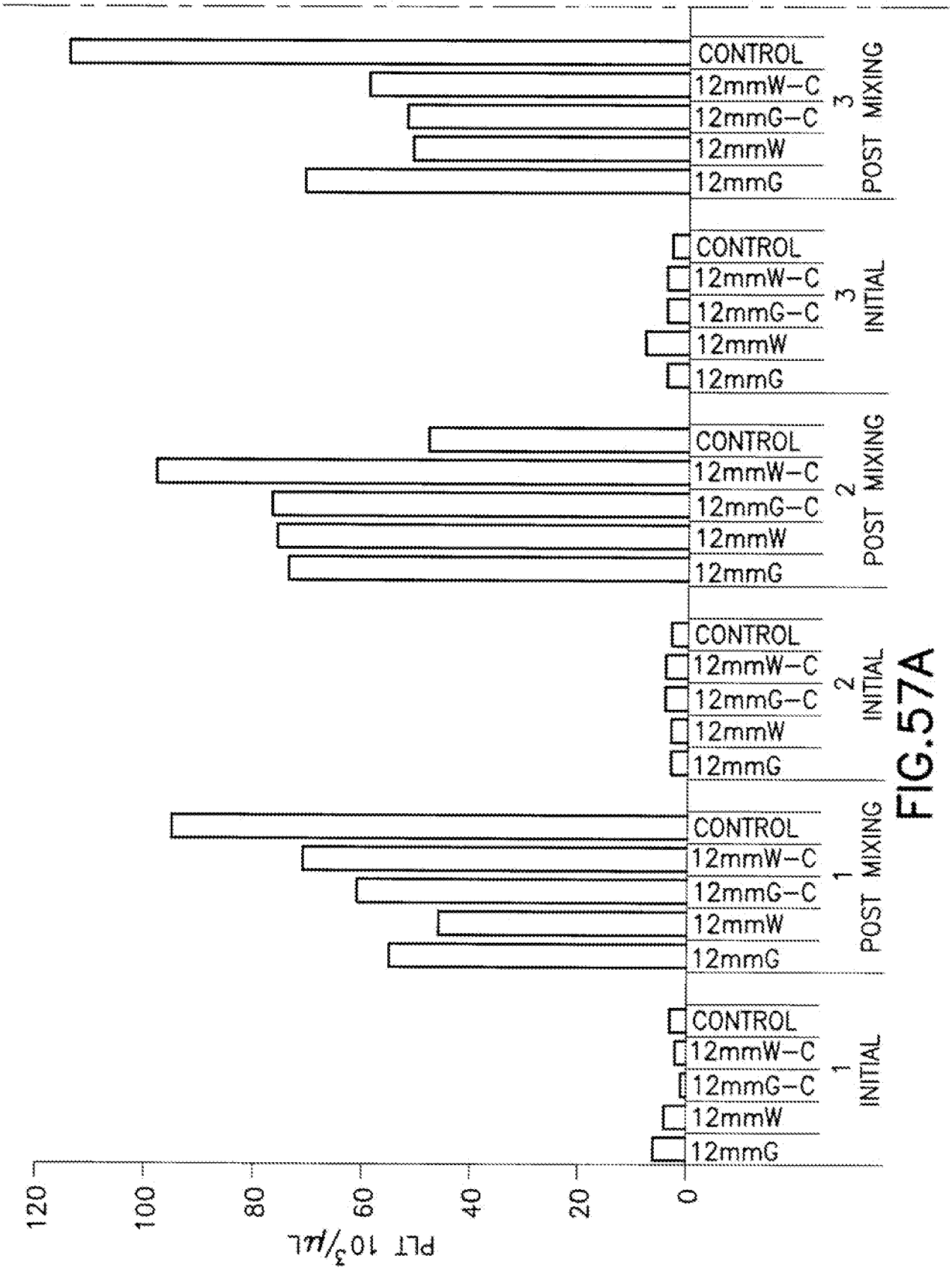
CONTROL
12mmW-C
12mmG-C
12mmW
12mmG
3 POST MIXING
3 INITIAL
2 POST MIXING
2 INITIAL
1 POST MIXING
1 INITIAL
120
100
80
60
40
20
0
PLT $10^3/\mu L$

FIG.57A

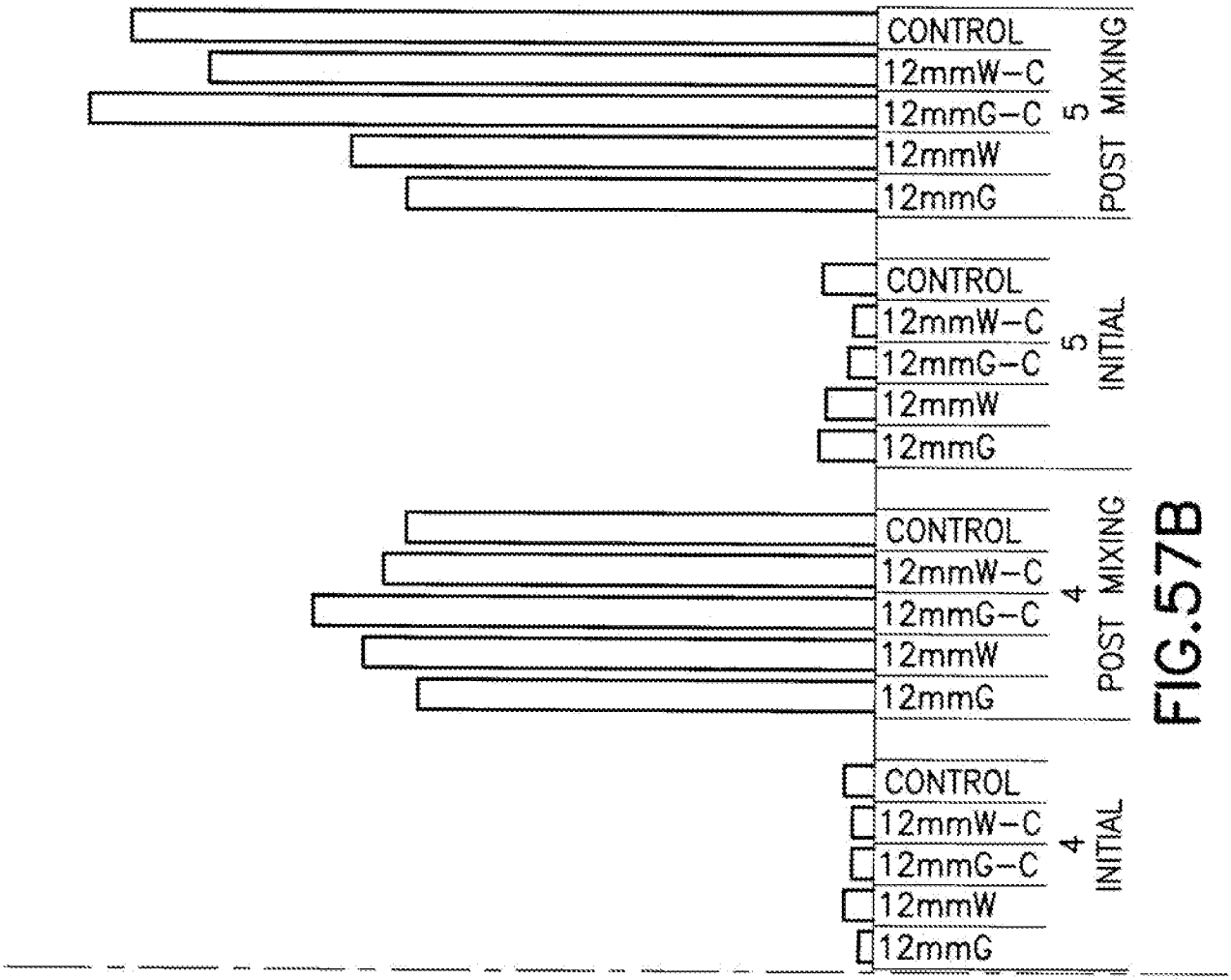

FIG.57B

FIG.57A FIG.57B

FIG.57

SUBJECT		CELL COUNTS	PROTOTYPE FOAM SEPARATOR TUBES									CONTROL
			1500 x 'g'			3000 x 'g'			4500 x 'g'			1500 x 'g'
			3min	5min	10min	3min	5min	10min	3min	5min	10min	10min
1	INITIAL	WBC 10^3/μl	0.1	0	0	0	0	0	0	0	0	0
		RBC 10^6/μl	0.02	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
		PLT 10^3/μl	10	7	2	3	3	3	5	4	4	2
	POST-MIXING	WBC 10^3/μl	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	1
		RBC 10^6/μl	0	0	0	0	0	0	0	0	0	0.01
		HGB g/dL	0.2	0.2	0.2	0.2	0.2	0.3	0.2	0	0.2	0.2
		PLT 10^3/μl	23	16	24	13	18	13	19	15	12	162
2	INITIAL	WBC 10^3/μl	0	0	0	0	0	0	0	0	0	0.1
		RBC 10^6/μl	0	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.3	0.2	0.2	0.2	0.3	0.3	0.2	0.2	0.2	0.2
		PLT 10^3/μl	11	7	3	5	7	3	8	4	3	8
	POST-MIXING	WBC 10^3/μl	0.3	0.3	0.3	0.2	0.2	0.1	0.2	0.2	0.2	0.6
		RBC 10^6/μl	0	0	0	0	0	0	0	0	0	0.01
		HGB g/dL	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
		PLT 10^3/μl	29	25	18	23	21	15	24	26	24	81
3	INITIAL	WBC 10^3/μl	0	0	0	0	0	0	0	0	0.1	0
		RBC 10^6/μl	0.01	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.2	0.1
		PLT 10^3/μl	17	12	4	8	7	4	11	26	56	11
	POST-MIXING	WBC 10^3/μl	0.3	0.3	0.2	0.2	0.2	0.2	0.3	0.2	0.2	0.7
		RBC 10^6/μl	0.01	0	0	0	0	0	0	0	0	0.01
		HGB g/dL	0.2	0.1	0.2	0.2	0.1	0.1	0.1	0.2	0.2	0.2
		PLT 10^3/μl	28	24	18	19	20	18	94	26	58	158

FIG.58A

FIG.58A
FIG.58B
FIG.58C FIG.58

4	INITIAL	WBC 10^3/μl	0.1	0.1	0	0	0	0	0.1	0	0	0.1
		RBC 10^6/μl	0	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
		PLT 10^3/μl	15	10	6	6	4	3	6	4	4	17
	POST-MIXING	WBC 10^3/μl	0.3	0.5	0.2	0.4	0.2	0.2	0.2	0.3	0.2	0.5
		RBC 10^6/μl	0	0.01	0	0	0	0	0	0	0	0.01
		HGB g/dL	0.2	0.2	0.2	0.3	0.3	0.2	0.2	0.2	0.2	0.1
		PLT 10^3/μl	24	26	19	19	16	21	21	19	20	145
5	INITIAL	WBC 10^3/μl	0	0	0	0	0	0	0	0.2	0	0.1
		RBC 10^6/μl	0.01	0	0	0	0	0	0	0.01	0	0
		HGB g/dL	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
		PLT 10^3/μl	14	11	4	10	7	4	6	57	5	9
	POST-MIXING	WBC 10^3/μl	0.3	0.4	0.2	0.2	0.2	0.2	0.2	0.3	0.2	1.4
		RBC 10^6/μl	0.01	0.01	0	0	0	0	0	0.01	0	0.02
		HGB g/dL	0	0.2	0.2	0.2	0.2	0.2	0.3	0.2	0.2	0.2
		PLT 10^3/μl	45	34	18	24	23	17	41	66	23	105
6*	INITIAL	WBC 10^3/μl	0.1	0.1	0	0	0	0	0	0	0	0
		RBC 10^6/μl	0.03	0.01	0	0	0	0	0	0	0	0
		HGB g/dL	0.3	0.3	0.3	0.3	0.3	0.3	0.2	0.3	0.3	0.3
		PLT 10^3/μl	20	9	3	6	7	6	6	5	7	3
	POST-MIXING	WBC 10^3/μl	0.3	0.3	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.5
		RBC 10^6/μl	0.01	0.01	0	0	0	0	0	0	0	0.02
		HGB g/dL	0.3	0.3	0.3	0.2	0.3	0.3	0.3	0.3	0.3	0.3
		PLT 10^3/μl	27	28	14	19	24	21	19	19	22	133
7*	INITIAL	WBC 10^3/μl	0	0	0	0.1	0	0	0	0	0	0
		RBC 10^6/μl	0.01	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.2	0.2	0.2	0.1	0.2	0.2	0.2	0.2	0.2	0.1
		PLT 10^3/μl	15	15	9	9	8	5	7	7	7	4
		WBC 10^3/μl	0.4	0.4	0.2	0.2	0.2	0.2	0.2	0.3	0.2	1

FIG.58B

	POST-MIXING	RBC 10^6/μl	0.01	0.01	0.01	0	0	0	0	0	0	0.01
		HGB g/dL	0.2	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.1	0.2
		PLT 10^3/μl	34	30	21	23	23	22	20	20	25	147
8*	INITIAL	WBC 10^3/μl	0	0	0	0	0	0	0	0	0	0
		RBC 10^6/μl	0	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2
		PLT 10^3/μl	14	10	7	8	10	10	8	8	7	12
	POST-MIXING	WBC 10^3/μl	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.1	1.1
		RBC 10^6/μl	0.01	0	0.01	0	0	0	0	0	0	0.01
		HGB g/dL	0.2	0.1	0.1	0.2	0.1	0.2	0.1	0.1	0.1	0.1
		PLT 10^3/μl	31	24	24	22	25	26	21	21	26	190
9*	INITIAL	WBC 10^3/μl	0	0	0	0	0	0	0	0.2	0.2	0
		RBC 10^6/μl	0	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.2
		PLT 10^3/μl	17	15	10	14	9	8	9	10	10	11
	POST-MIXING	WBC 10^3/μl	0.4	0.2	0.3	0.2	0.2	0.2	0.2	0.3	0.3	0.7
		RBC 10^6/μl	0.01	0	0	0.01	0	0.01	0	0	0	0.01
		HGB g/dL	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
		PLT 10^3/μl	36	31	33	32	25	27	31	27	26	154
10*	INITIAL	WBC 10^3/μl	0	0	0	0	0	0	0	0	0	0
		RBC 10^6/μl	0	0	0	0	0	0	0	0	0	0
		HGB g/dL	0.2	0.1	0.1	0.2	0.1	0.2	0.1	0.1	0.1	0.1
		PLT 10^3/μl	29	12	3	19	8	3	9	5	3	3
	POST-MIXING	WBC 10^3/μl	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0
		RBC 10^6/μl	0.01	0	0	0	0	0	0	0	0	0.01
		HGB g/dL	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.2	0.1	0.1
		PLT 10^3/μl	43	19	14	31	17	12	19	16	17	95

FIG.58C

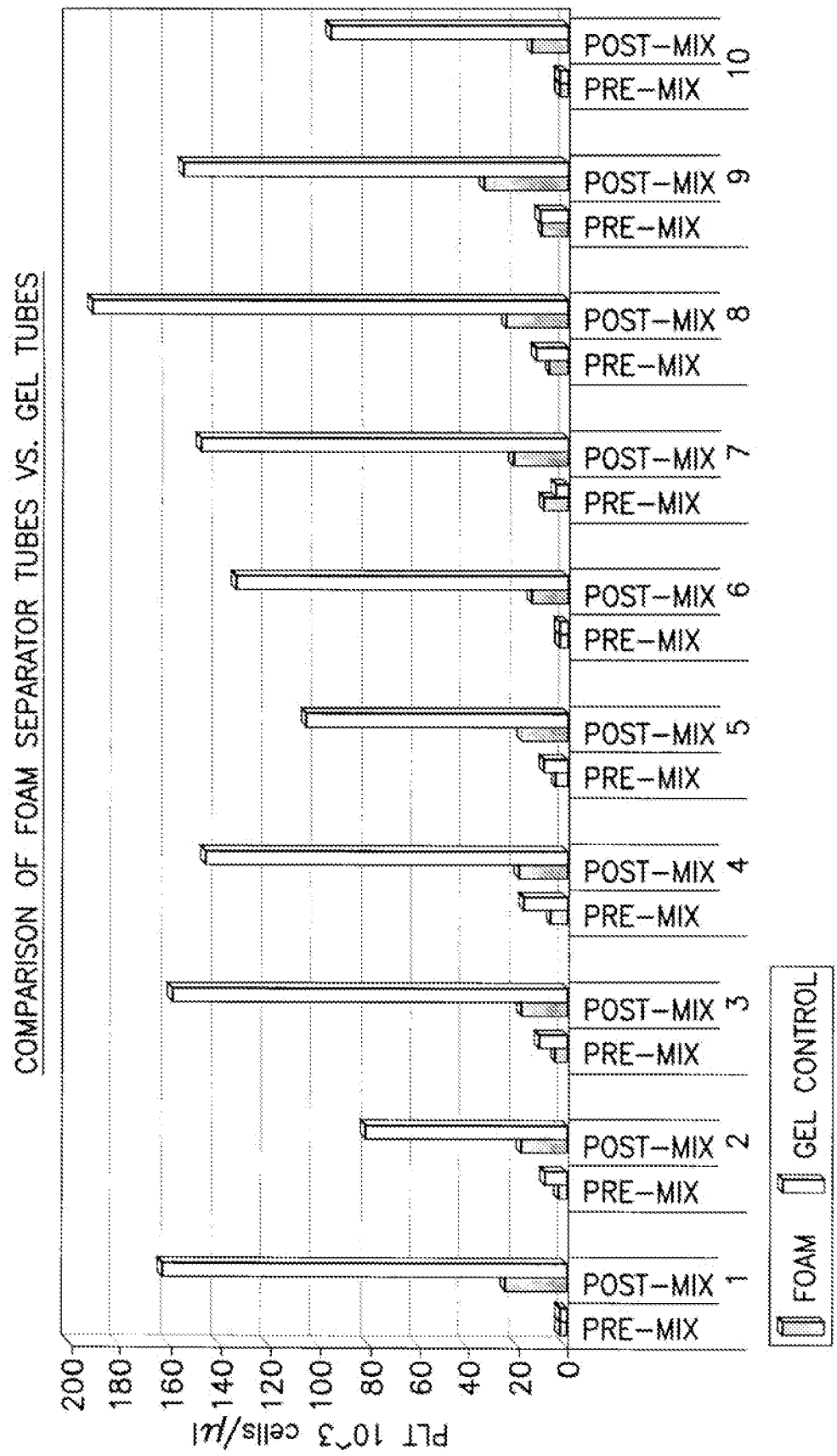
COMPARISON OF FOAM SEPARATOR TUBES VS. GEL TUBES
PLT 10^3 cells/μl
200
180
160
140
120
100
80
60
40
20
0
POST-MIX
PRE-MIX
10
9
8
7
6
5
4
3
2
1
FOAM
GEL CONTROL

FIG.59