Feb. 15, 1949. N. M. NESSET 2,461,837

METHOD OF HANDLING STERILE LIQUIDS

Filed Sept. 22, 1943 2 Sheets-Sheet 1

Fig. 1

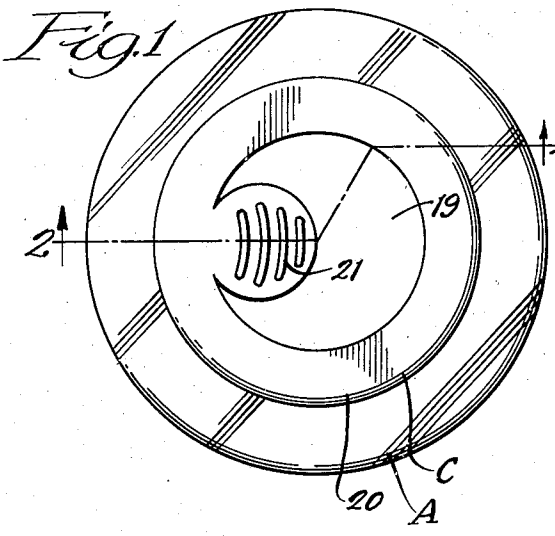


Fig. 2

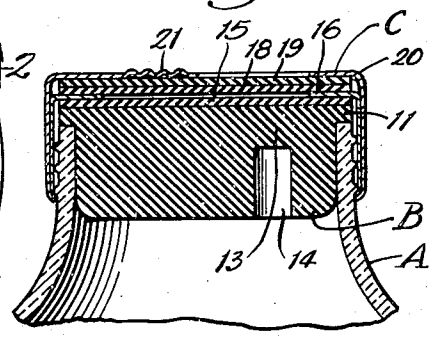


Fig. 3

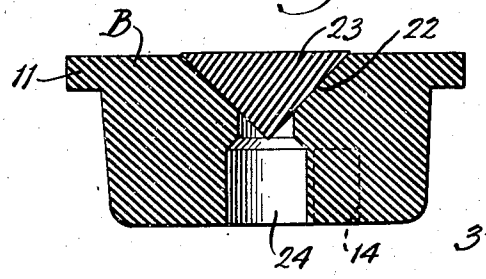


Fig. 4

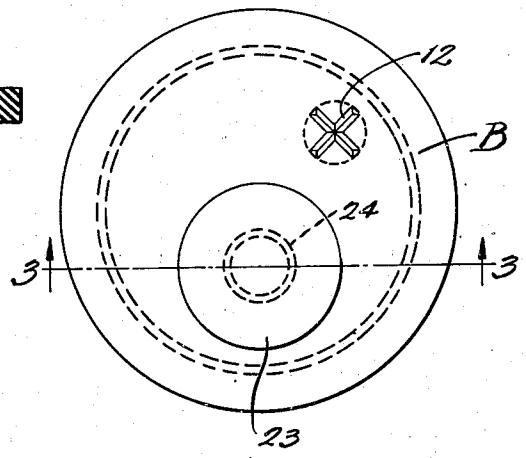
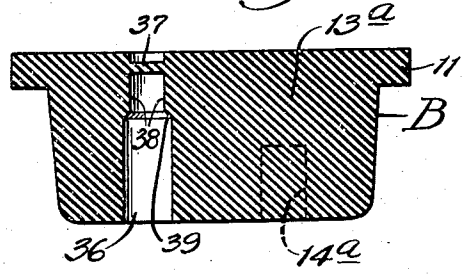


Fig. 8



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Fig. 6

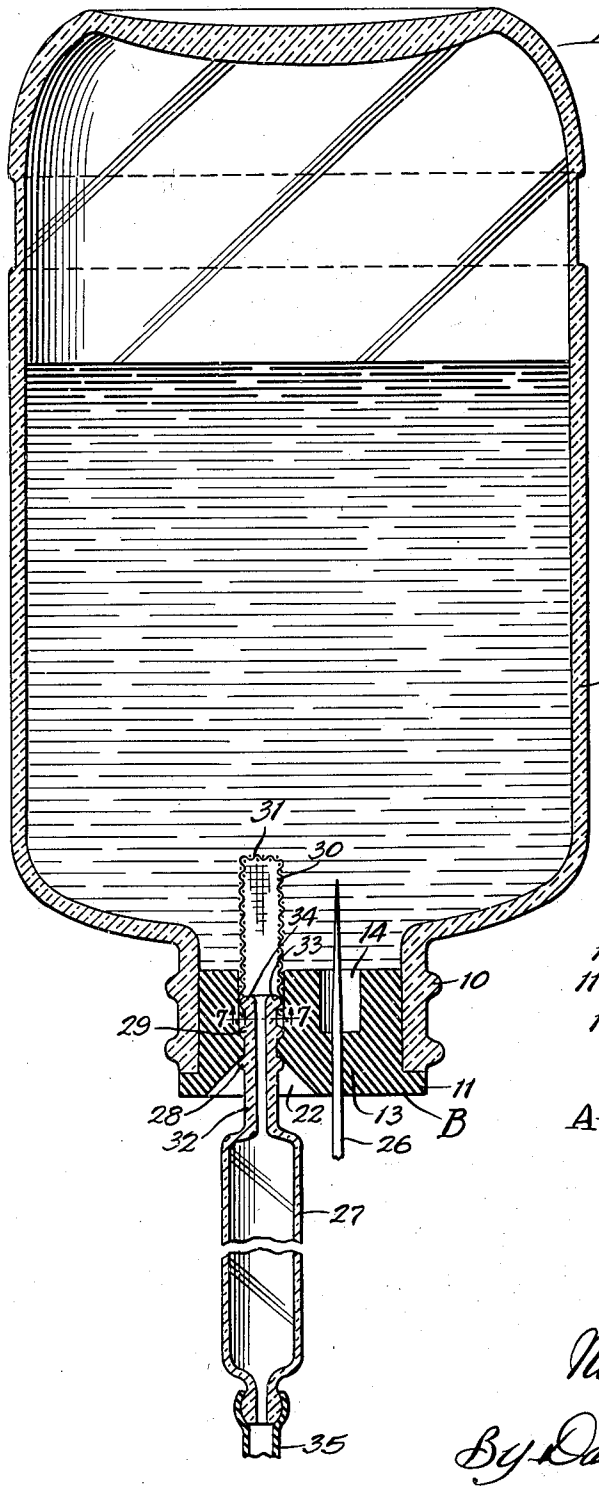


Fig. 7

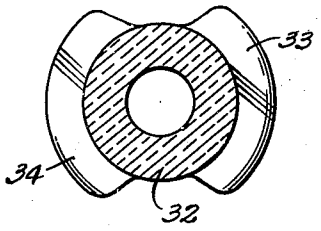
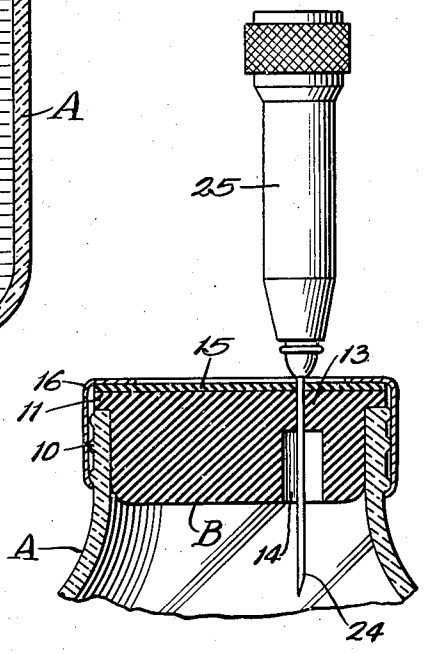


Fig. 5



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METHOD OF HANDLING STERILE LIQUIDS

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5 Claims. (Cl. 128—272)

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This invention relates to a method of handling sterile liquids, and more particularly to the handling and treating of liquids and maintaining the liquids in sterile condition in the course of handling and treatment.

An object of the invention is to provide methods for the reception, storage and dispensing of sterile liquids. Another object is to provide methods for introducing sterile liquids into containers, maintaining the liquids within the containers in sterile condition, and dispensing the sterile liquids from the containers. A further object is to provide a method for receiving blood, storing the same in sterile condition, and thereafer dispensing the blood. Yet another object is to provide for the handling of parenteral solutions and for the storage and dispensing of such solutions.

Another object of the invention is to provide a method for the drying and storing of products, such as biologics, and the re-forming of such products as solutions, and the dispensing of the solutions. Yet another object is to provide in such a method for the maintaining of the solutions under sterile conditions. Still a further object is to provide a method for introducing solid materials into solutions which have been maintained in sterile condition prior to the dispensing of the solutions.

Another object of the invention is to provide a method for the handling and treatment of sterile liquids in which the material being treated is maintained in sterile condition throughout a series of operations and in which the liquid is introduced into a container through a closure having a self-sealing diaphragm and is withdrawn from the container through a passage in the closure which is opened by removing a removable plug from the passage.

Other features and advantages will appear from the following specification and drawings, in which—

Fig. 1 is a plan view of the closure in position on a container; Fig. 2 is a vertical sectional view taken along the line 2—2 of Fig. 1; Fig 3 is a vertical sectional view taken through another portion of the closure and along the line 3—3 of Fig. 4; Fig. 4 is a plan view of the closure alone; Fig. 5 is a vertical sectional view of the closure in position on a container and showing a needle extending therethrough for the introduction of liquids into the container; Fig. 6 is a vertical sectional view of a container having the closure therein and arranged for the dispensing of blood from the container; Fig. 7 is a transverse sectional view taken along the line 7—7 of Fig. 6;

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and Fig. 8 is a vertical sectional view of a modified form of closure.

In the embodiment of the invention shown in Figs. 1 to 7, A designates a container; B, a resilient closure for the neck of the container; and C, a removable sealing means.

The container A may be of any suitable type. As illustrated, the container is of glass and is of the general type shown in Baxter Patent No. 2,004,027, the bottom of the container being adapted to receive and support a bail member (not shown) by which the container can be supported in inverted position for the withdrawal of liquids.

The container neck A may be provided with beads or threads for the purpose of confining a cap thereon. In the specific illustration given, the container neck is provided with threads 10 and a bead.

The closure B may be of any suitable construction and resilient material. I prefer to employ a resilient rubber material which is quite elastic and which forms a good seal with the neck of the container A. The plug B is provided on its upper side with an integral flange 11 which rests upon the top of the container neck. An interrupted or short passage 14 extends partially through the blood and is closed by a thick integral diaphragm 13 which extends across the upper portion of the plug and across the top of the passage 14. The corresponding aligned portion of the plug immediately over the passage 14 may be marked at 12 with an X or some other indicating means to enable the operator to locate the passage 14 from above and pass a needle through the plug into the passage 14.

The thick integral diaphragm 13 which extends across the portion of the plug B above the passage 14 should be self-sealing after being punctured with a hypodermic needle. Thus, when the integral diaphragm 13 is punctured with an 18 gauge steel needle and the needle is withdrawn therefrom, the diaphragm 13 effectively closes the opening which was formd by the needle and seals such opening against the passage of air therethrough. In this manner, the diaphragm by virtue of its self-sealing qualities is effective to maintain a vacuum within the container after the withdrawl of a needle from the diaphragm.

The sealing means C may also be of any suitable construction. In the illustration given, I provide a thin flexible and resilient sealing member 15 directly over the plug B. The seal 15 is maintained against plug B, and also plug B is thereby maintained in position within the container by

means of the clamp member 16 which may be formed from aluminum or other metal and which is spun into the position shown. It will be observed that the clamp member on its lower side engages the lower bead whereby it is firmly locked in position. If desired, the threads 10 may be omitted and beads employed only near the lower portion of the bottle neck. With this construction, the inner seal 15 can be removed by tearing and, if desired, a portion of clamp 16 may be cut away along its upper flange to facilitate the grasping of the seal 15 to aid in its removal. If desired, the inner clamp 16 may also be provided with a tear flap to enable it to be separated from the container neck.

Above the clamp 16, I provide another resilient seal 18, which is identical to seal 15 and which provides an uncontaminated and sterile surface on the seal so that the sterile hollow needle may be passed through plug B and seal 15 without becoming contaminated and thus obviating the danger of contaminating the interior of the container. Above the seal 18 is a metal disk 19, and above the disk 19 is an outer cap 20. Cap 20 is provided with a tear tab 21 and it has its lower portion spun about the lower bead of the threads 10 so as to confine it in position.

In addition to the passages described, the container B is provided with a cone-shaped seat 22 adapted to receive a correspondingly shaped cone valve 23. Below the seat 22, a passage 24 establishes communication with the interior of the container. It will be noted that the valve body 23 fits loosely within the seat 22 and may be lifted slightly under vacuum to permit the escape of vapors, etc. On the other hand, it has a smooth junction with the seat 22 so as to form an airtight seal therewith when pressure is exerted upon member 23.

Liquid may be introduced into the container by passing a hollow needle 24 through the self-sealing diaphragm 13 above the passage 14. For this operation, the cap 20 and metal disk 19 are removed from the closure. As seen in Fig. 5, the needle may be mounted on a valve 25 or any suitable or conventional construction for controlling the flow of blood through the needle and into the container A.

In the dispensing of liquids from the container A, as seen particularly in Figs. 6 and 7, the clamp 16, the cap 20, the metal disk 19, and the resilient seals 18 and 15 may be removed from the plug B. The valve plug 23 may also be removed from the plug B. A needle 26 may be passed through the self-sealing diaphragm 13 above the passage 14 so that the needle extends into the passage and into the container.

A dispensing adapter or fitting 27 may be provided adjacent its end with a pair of spaced enlargements 28 and 29 and at its end with a filter 30 of suitable construction. As illustrated, the filter 30 may be in the form of a stainless mesh filter, cylindrical in shape and having one end of the cylindrical portion thereof closed by the mesh as at 31. The filter may be equipped with a bead at the open end thereof which is adapted to be received in relasable locking engagement with the end of the adapter 27. As illustrated in Fig. 7, the end 32 of the adapter 27 may be provided with a pair of opposed flanges 33 and 34 which may be engaged by the bead on the filter 30. To the adapter 27 may be attached rubber tubing 35 or other suitable means for conducting the liquid from the adapter.

In the construction and arrangement illustrated in Fig. 6, the needle 26 serves to introduce air into the container while the blood is withdrawn through the filter 30 and adapter 27 to the rubber tubing 35.

In the modified form of the invention shown in Fig. 8, the closure plug B is equipped with a passage 36 therein and a thin integral diaphragm 37 extending across the upper portion of the passage. Preferably, as illustrated, the thin integral diaphragm 37 is spaced very slightly below the upper surface of the plug. The walls of the passage 36 may be constricted as at 38 below the diaphragm 37 so as to provide a shoulder 39 therebelow. In this construction, the plug may be provided with a passage 14^a and a thick integral diaphragm 13^a thereover corresponding exactly to the passage and self-sealing diaphragms shown in Figs. 1 to 7. This plug may also be provided with a passage and a removable valve plug corresponding exactly to the passage 24 and valve plug 23 shown in the embodiment of Figs. 1 to 7. Thus, the closure plug B, shown in Fig. 8, may be of exactly the same construction as the plug shown in Figs. 1 to 7 except for the provision of the additional passage 36 therein.

The method of receiving, storing, and dispensing sterile liquids in accordance with the present invention may utilize the apparatus described herein. To illustrate the method of the invention, the handling of blood will be described as a specific example. In the handling of blood, the container is sealed under vacuum with a conventional anti-coagulant solution therein. The closure is in position on the container, as shown in Figs. 1 and 2. If desired, the vacuum may be created in the container by heating the anti-coagulant solution therein while the valve plug 23 is loosely seated on the seat provided by the plug B. Air and moisture vapor may escape about the removable plug 23. When the heating is stopped, the plug 23 will be seated and, as the moisture vapor within the container condenses, a vacuum will be formed therein. The plug 23 will effectively seal the container to maintain this vacuum. The remaining closure equipment may then be applied.

When the blood is to be introduced into the container, the cap 20 and metal disk 19 are removed and, as seen in Fig. 5, a needle is passed through the self-sealing diaphragm 13 into the passage 14 and the container A. Blood from a donor or other source may then flow through the valve 25 and needle 24 into the container A, the vacuum within the container being used to draw the blood thereinto.

After the blood has been drawn into the container, the valve 24 is removed from the plug B and the self-sealing diaphragm 13 closes the opening so as to effectively seal the container. The blood is then maintained under sterile conditions and the container remains sealed under the residual vacuum which remains after drawing the blood into the container.

When the blood is to be withdrawn from the container, the apparatus shown in Fig. 6 may be used. The cap 20, metal disk 19, the rubber seals 18 and 15, and clamping members 16 may all be removed from the plug B. A needle 26 may then be passed through the self-sealing insert 13. The removable valve plug 23 is removed from the plug B and the adapter 27 is introduced into the passage 24 in the plug B. The spaced enlargements 28 and 29 engage the portions of the plug B at the base of the seat for the valve 23 which has been removed. The filter on the end of the

adapter 27 serves to filter blood which passes from the container into the adapter. The container is placed in inverted position and air flows inwardly through the needle 26 while the blood flows outwardly through the filter 30 and adapter 27.

With this equipment, the blood may be handled under completely sterile conditions. It may be introduced into the container, maintained in sterile condition during storage, and withdrawn also under sterile conditions.

The method may be applied in a similar manner for the dispensing of parenteral solutions. The parenteral solution may be placed in the container and sterilized therein. The heating of the solution within the container to sterilize it permits the creation of a vacuum within the container by reason of the flow of air and moisture vapor past the removable valve plug 23. When the container and solution are cooled, a vacuum is formed therein.

When the solution is to be dispensed, a fitting or adapter, such as the adapter 27, may be placed in the passage 24 from which the plug 23 is removed. In the case of parenteral solutions, the filter 30 on the end of the adapter may be omitted. The needle 26 may be passed through the self-sealing diaphragm 23 to introduce air into the container.

A similar method may be utilized in connection with the modified form of plug B, shown in Fig. 8, which may be used for the handling of parenteral solutions, and if the plug is not to be reused the passage 36 may be used for the introduction of air into the container. In this case, the thin diaphragm 37 will be ruptured by an air tube of suitable or conventional construction which may be placed therein. If desired, an air tube may be placed within the container itself and may extend into the passage 36 and against the shoulder 39. In this case, the diaphragm 37 is ruptured, and air flows inwardly through the opening formed thereby.

Another application of the invention lies in the drying of biologics or other material. When it is desired to dry biologics, the closure cap and upper rubber seal 18 are removed. The liquid biologic is then drawn into the container through a hollow needle which is passed through the sealing member 15, the plug B, and into an opening into passage 14 in the plug. Since a vacuum is furnished within the container, the liquid can be readily drawn at a controlled rate through a tube connected with the hollow needle until a desired amount is obtained within the container. When it is desired to dry the material now within the container, the remaining rubber seal 15 is removed and the top surface of the rubber plug and the cone valve 23 is sterilized with a suitable antiseptic, such as iodine, alcohol, and the like. The filled unit is then placed in the evacuated chamber, which is subsequently subjected to a high vacuum, the differential in pressures on the inside of the container and of the evacuated chamber being automatically adjusted by the same mechanism that obtained in the creation of a partial pressure in the first assembling of the container. Heat is applied and under the influence of temperature and the reduced pressure, the liquid portion of the contents is removed, leaving the solid material within the container. The vapors from the liquid during this operation escape through the vertical passage around the cone valve 23 in exactly the same manner as heretofore described for the removal

of air. Upon sudden release of the high vacuum in the evacuated chamber, the rubber cone seal is again firmly seated, hermetically sealing the container. The unit is then removed from the chamber, the top surface being sterilized and a new sterile rubber seal 15 placed upon the top of the closure plug, followed with a metal disk, and the metal band spun into position, thus re-sealing the package for storage and transportation.

All of the above steps are accomplished in a desirable aseptic manner, permitting ease in handling and an absolute minimum possibility of contamination, all of which are extremely important in the preparation of dried biologics.

When the dried material within the container is to be used, the outer cover may be removed along with the metal and rubber disks. Using again the hollow needle connected to a hollow tube, the desired fluid for causing a re-solution of the dried material is drawn into the container, utilizing the partial vacuum which was left in the container at the conclusion of the drying step. Inasmuch as all of the vacuum which was in the container is not utilized for drawing in the solvent, the residual partial pressure provides sufficient means for holding the cone seal in a sealing position so that when the tube and needle are removed after drawing in the solvent, there is still a hermetically sealed package which preserves the inherent asepsis and permits subsequent storage and transportation of the regenerated biologic.

For the dispensing of the regenerated material, the rubber cone seal 23 is readily removed, exposing a free hole into which is inserted the proper connection for withdrawal, and the container is inverted to permit the liquid to be dispensed. A proper air inlet into the unit for dispensation is created by puncturing the thin rubber stopper 13 in passage 12.

The above steps are illustrative of steps which may be employed with the new type of closure wherein the valve permits the withdrawal of air, moisture, vapors, etc., while at the same time by reason of its smooth connection with the cone seat, permits a quick re-sealing and the maintenance of vacuum within the container. It will be understood, however, that the closure has a great number of other uses which can be here enumerated. For example, the wide opening permits the introduction of certain solid materials into a container holding parenteral fluids for solution immediately prior to dispensation. Due to the fact that certain solid drugs are unstable when in solution, precluding the possibility of making up such materials well in advance of requirement, the present closure offers a simple method for introducing such drugs into the container just before dispensation. Similarly, certain drugs do not withstand heat sterilization. With the present closure, the diluent may be sterilized first and then such drugs may be aseptically introduced through the opening controlled by valve 23 into the container. It will further be noted that the container readily permits automatic creation of a heat vacuum in a container, permitting the outflow of heated gases, etc., and then quickly closing the opening upon the application of an atmospheric pressure to the outside of the container closure.

This application is a continuation-in-part of my co-pending application Serial No. 393,395, filed May 14, 1941, for Closure and method of using same, now abandoned.

While in the foregoing specification, I have set forth certain details of structure and certain steps

as illustrative of the uses to which the structure may be put, it will be understood that such details of structure and such method steps may be widely varied without departing from the spirit of my invention.

I claim:

1. A method of handling blood, comprising heating a water solution of an anticoagulant within a container having an opening to sterilize the solution and cause water vapor to be withdrawn through the opening, sealing said opening, evacuating said container, and introducing blood into the evacuated container while the same is sealed against the ingress of air.

2. In a method of drying biologics and the like, the steps of drawing the liquid material to be dried into an evacuated container provided with an opening, sealing said opening against the ingress of air while permitting the escape of vapors, heating and further evacuating the container to dry the material therein and to cause the vapors to escape through said opening, and subjecting the exterior of said container to atmospheric pressure to maintain said opening sealed against the ingress of air.

3. In a method of drying biologics and the like, the steps of drawing the liquid material to be dried into an evacuated container having an opening, sealing said opening against the ingress of air while permitting the escape of vapors, subjecting the exterior of the container to vacuum and heat to cause the vapors of the material therein to be withdrawn through said opening, and then subjecting the exterior of the container to atmospheric pressure to seal said opening against the ingress of air.

4. In a method of drying biologics and the like, the steps of drawing the liquid material to be dried into an evacuated container provided with an opening, heating the container to cause vapors therein to pass through said opening, subjecting the exterior of said container to vacuum, then after the drying operation sealing said opening, and thereafter introducing liquid under the influence of the vacuum within the container into the vacuum to regenerate the dried material while maintaining the container in sealed condition.

5. In a method of drying biologics and the like, the steps of drawing the liquid material to be dried into an evacuated container provided with an opening, heating the container to cause vapors to pass through said opening, subjecting the exterior of said container to vacuum, then after the drying operation sealing said opening, thereby maintaining the interior of said container under vacuum, and introducing liquid under the influence of the vacuum within the container into the container to regenerate the dried material while maintaining the container in sealed condition.

NAURICE M. NESSET.

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