Aug. 4, 1953 A. D. HOLMES 2,647,513

LYOPHILIZATION CONTAINER

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FIG. 1

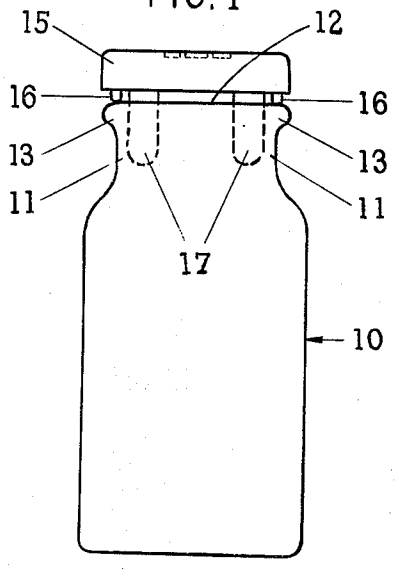


FIG. 2

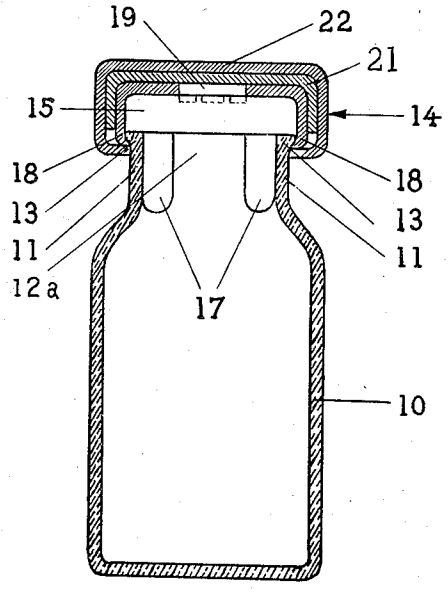
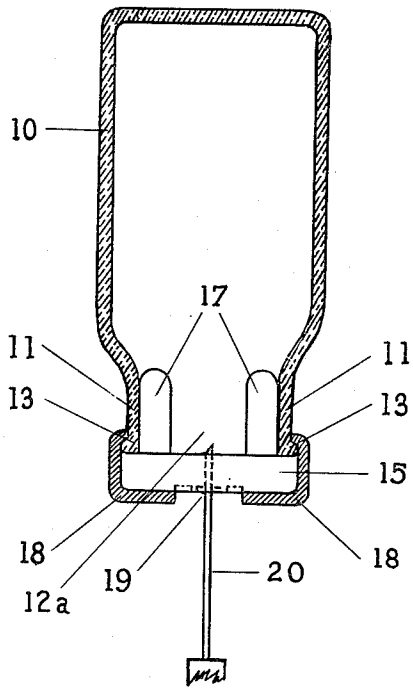


FIG. 3



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LYOPHILIZATION CONTAINER

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4 Claims. (Cl. 128—272)

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My invention relates to containers, and particularly to specially adapted closures and receptacles for drying, lyophilizing, and storing materials aseptically. My invention relates especially to containers for material which is unstable to heat in the presence of water, and which may be administered with a hypodermic syringe or the like.

My containers may be used in the conventional drying processes employing heat or a vacuum or both. As well as this, my containers are peculiarly suited for use in lyophilizing heat-labile materials such as animal tissue. Lyophilization consists in withdrawing moisture from water-bearing materials under the effect of a high vacuum and a certain amount of heat. This moisture may be loosely associated in these materials, and it may also occur in more tightly bound forms, such as water of hydration. In a typical lyophilization process, a fresh sample of a given heat-labile material is frozen and is then subjected to an extremely high vacuum until the moisture is withdrawn. It is then possible to preserve this material in a dry atmosphere for a long period of time without appreciably impairing its desired activity. This lyophilic material may be utilized as needed either in dry form or in solution.

An important object of my invention is the provision of an improved container, susceptible of economic manufacture, in which material may be either dried or lyophilized under reduced pressure and if desired, in an aseptic area. Another object of my invention is the provision of a container of this type having a single opening which may be partly covered by a closure so as to prevent the entrance of foreign contaminants and yet to permit the exit of gases and vapors during evacuation of the container atmosphere. Still another object of my invention is the provision of a container of the kind referred to, having a dispensing zone into which a hypodermic needle or the like may be unerringly inserted and from which liquid contents may be completely withdrawn without waste.

A specific embodiment of my invention is illustrated in the accompanying drawing wherein:

Fig. 1 is a side view of a receptacle and a cover having spacing means and aligning projections, showing the cover supported on the receptacle in a position suitable for evacuation;

Fig. 2 is a side view of the cover, and a vertical section of the receptacle and a collar-and-cap assembly showing the container in a position suitable for storage; and

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Fig. 3 is a side view of the cover and a hypodermic-type needle, and a vertical section of the receptacle and an inner collar showing the container in a position suitable for withdrawal of the contents.

Referring now to the drawing, numeral 10 designates a receptacle provided with a neck-portion 11 having a cylindrical wall. The top of the neck-portion 11 has an opening 12 bounded by a flange 13 which is disposed in a plane at right angles to the vertical axis of the receptacle 10. The receptacle 10 may take any convenient shape or form, while the neck-portion 11 of the receptacle 10 is desirably cylindrical in shape. A material such as glass or clear plastic is suitable for the construction of receptacle 10.

The numeral 14 refers to a closure structure which includes a flexible disc-like cover 15, a number of spacing knobs 16, aligning projections 17, an inner collar 18, a cap 21, and an outer collar 22.

The cover 15 is desirably flexible and resilient and yet is sufficiently firm so as to maintain a disc-like shape when placed upon the receptacle 10. When placed loosely on the receptacle 10, the cover 15 serves as a shield or dust-cap for the opening 12, and when pressed toward the receptacle 10, the cover 15 engages the flange 13 and closes the opening 12.

The knobs 16 are disposed in a suitable position between the cover 15 and the flange 13 so as to space the cover from the flange. Preferably, these knobs 16 are made of a collapsible material such as live rubber or material having like characteristics and are sufficiently bulky and firm so as to support the weight of the cover 15 and its aligning projections 17, yet are thinly constructed so that they may be collapsed to a substantially flat position by a downward force greater than the weight of 15 and 17. When the cover 15 is placed in a position over the opening 12, the knobs 16 engage the flange 13, support the weight of the cover 15 and its projections 17, and prevent 15 from seating flatly onto 13. In this position air space is provided between the bottom surface of 15 and the top surface of 13, so that the interior of the receptacle 10 is in open communication with the atmosphere surrounding the container. When the cover 15 is urged toward the receptacle 10 by a sufficiently strong exterior force, the knobs 16 collapse, the cover 15 moves toward the receptacle 10, conforms itself over the collapsed knobs 16 onto the flange 13, and closes the opening 12 in the receptacle 10. An equivalent result is obtained if the knobs 16 are made

rigid and incompressible and if the cover 15 is made sufficiently pliant and flexible so that it may yield to a downward force and conform itself about the knobs 16 and onto the flange 13.

It is important to provide spacing means such as the knobs 16. The spacing means may be of either solid or hollow construction and may have a variety of shapes. For example, it may take the form of a hollow hemisphere or a thin strip but is not limited to these specific shapes.

Aligning projections 17, equally spaced at points equidistant from the center of the bottom surface of the cover 15, are attached to, and extend down lengthwise from, the bottom of the cover 15. These projections 17 are spaced apart from each other so that when inserted within the opening 12 of the receptacle 10, they slidably engage the cylindrical wall of the neck-portion 11 and prevent lateral movement of the cover 15. In this position a channel 12a, defined by the walls of the projections 17 and the wall of the neck-portion 11, is provided within the opening 12. It will be seen that an equivalent embodiment of these projections is a single cylindrical plug adapted to fill the zone within the neck-portion 11 except for a vertical channel bounded on one side by the wall of the neck-portion 11. This channel 12a serves as an outlet passage during evacuation and also provides a zone into which the contents may flow during the dispensing stage.

The inner collar 18 engages the cover 15 and the flange 13 and holds the cover 15 flat upon the flange 13 with sufficient force to seal the opening 12 in the receptacle 10. The inner collar 18 desirably is provided with an aperture 19 adjacent the center of the top surface of the cover 15. The visible portion of the cover 15 seen through the aperture 19 may be punctured with a hypodermic needle 20 which may be thrust into an open zone within the container between or among the projections 17. The area of the cover 15 outlined by the aperture 19 is purposely arranged opposite an open zone within the container so that when the cover 15 is punctured vertically at a point within this area, it is virtually impossible to contact the projections 17, the flange 13, or the neck-portion 11. In the case of a cover 15 having a single projection of the plug type referred to above, the needle 20 may be inserted into the vertical channel.

In the embodiment of the invention shown in the drawing I provide the cap 21 and the outer collar 22 for my container. The cap 21 covers the aperture 19 and slidably engages the sides of the inner collar 18. This cap 21 serves to protect the cover 15 from accidental rupture. The outer collar 22 engages the cap 21 and the inner collar 18 and prevents the cap 21 from sliding off the inner collar 18. The outer collar 22 also serves to strengthen the seal and protect the inner seal members. The outer collar 22 may be provided with a tear strip which may be easily detached so as to permit the ready removal of the collar 22 from the container.

While I prefer to fabricate the cover 15, knobs 16 and aligning projections 17 from a single piece of live rubber stock, any suitable material may serve for the construction of 15 and 17. The inner collar 18, cap 21 and outer collar 22 may be made of a pliable metal or a plastic material.

In operation, I place the cover 15 over the opening 12 in receptacle 10 containing a substance which is to be dried or lyophilized. This is accomplished by inserting the aligning projections 17 downward within the opening 12 until the knobs 16 engage the flange 13. The aligning projections 17 loosely contact the wall of the neck-portion 11 and serve to center the cover 15 over the opening 12. In this position the weight of the cover 15 is supported by the knobs 16 which bear upon the flange 13 and provide an air passage between 15 and 13. Although the cover 15 is spaced from the flange 13 sufficiently far to permit the passage of effluent vapors, yet it is disposed sufficiently close to the flange 13 so as to effectively impede dust, airborne bacteria, and the like from entering the receptacle 10 by way of the opening 12.

The assembly as shown in Fig. 3 is then placed in a suitable evacuating chamber and subjected to a sustained high vacuum. As a result, the water associated with the substance within the receptacle 10 vaporizes or sublimes and passes between the projections 17 through the opening 12 in the receptacle 10 and out of the container by way of the passage between the cover 15 and the flange 13. This evacuation step is continued until the desired degree of desiccation is attained, at which point the vacuum is broken by introducing air within the chamber. If atmospheric pressure is restored within the chamber rapidly, the sudden surge of incoming air forces the cover 15 down onto the flange 13 thereby collapsing the spacing knobs 16 and sealing the opening 12 in the receptacle 10. At this point, the pressure within the container is subatmospheric, with the result that the cover 15 is constantly being pressed down and held firmly by the pressure differential. The cover 15 remains in this position as long as the pressure differential is maintained. If atmospheric pressure is restored within the chamber slowly, air enters the receptacle 10 by way of the space afforded by the knobs 16 and the aligning projections 17 until the pressure is uniform throughout the chamber and the receptacle 10.

Material which is to be lyophilized, rather than merely dried, is first frozen in order to preserve its activity and structure and, inadvertently, some of the material is sometimes frozen onto the flange 13 or the adjacent parts of the cover 15. When this occurs with a container which is not provided with spacing knobs 16, the cover 15 occasionally is frozen shut upon the opening 12.

As a consequence, such a container cannot be smoothly evacuated, if at all, until the cover 15 thaws out so that air within the container can move out into the vacuum zone. In these cases when the cover 15 does thaw, the air is sometimes released with almost explosive violence, and material within the receptacle 10 is often carried out by the air and lost. The purpose of the knobs 16 is to avoid these ill effects by spacing the cover 15 from the flange 13 so that this undesirable pressure differential is not established.

After air has been introduced into the receptacle 10 containing the dried material, the inner collar 18 is fitted over the cover 15 and flange 13. This collar 18 is pressed downward upon the cover 15 so as to seal the opening 12, and is held in this position by crimping the lower portion of the collar 18 under the flange 13. Here, the cover 15 may advantageously serve as a gasket. Of course, a tight seal may be undesirable for certain purposes, and in these cases it would be advisable to fasten the inner collar 17 loosely as with a loose, partial crimp or without the gasket effect. The cap 21 is placed upon the inner collar

18, and in turn the outer collar 22 is placed upon the cap 21 so as to envelop the exposed surfaces of the cap 21 and the collar 18. The outer collar 22 is held in position by crimping its lower portion under the flange 13. The container may now be held in storage.

The contents of my container are removed through the cover 15 with a hypodermic needle 20 and syringe. In order to expose the cover 15 for injection, the outer collar 22 and cap 21 are removed. After the collar 22 has been removed, the cap 21 readily slides off of the inner collar 18 and exposes the top surface of the cover 15 through the aperture 19 in the collar 18.

The hypodermic needle 20 is inserted through the cover 15 and a suitable solvent is injected within the receptacle 10 so as to dissolve the contents. When the material has dissolved, the container is inverted and the liquid is withdrawn through the needle 20. In draining to the tip of the needle 20 the liquid is free to move between the aligning projections 17 to the surface of the disc-like cover 15. When the bottom surface of the cover 15 is held in a horizontal position, substantially all of the liquid may be withdrawn conveniently and without delay.

Other modifications of my container as herein described, all within the spirit of my invention, will readily occur to those skilled in the art.

I claim:

1. A container comprising a receptacle having a neck-portion provided with an opening bounded by a flange, a cover for said opening, spacing means disposed between said cover and flange to provide an air passage therebetween, said spacing means being collapsible to permit closing of said opening when said cover is pressed toward said flange, and means projecting from said cover to align said cover over said opening, said aligning means extending at right angles from said cover into said opening and neck-portion, said aligning means providing a channel within said neck-portion for the free passage of material into and from said receptacle, said channel communicating with at least part of said opening whereby said channel is in open communication with said air passage when said cover is spaced with respect to said flange.

2. A container comprising a receptacle having a neck-portion provided with an opening bounded by a flange, a cover for said opening, spacing means disposed between said cover and flange to provide an air passage therebetween, said spacing means being collapsible to permit closing of said opening when said cover is pressed toward said flange, and a plurality of projections extending at right angles from said cover into said opening and neck-portion, said projections providing a channel within said neck-portion for the free passage of material into and from said receptacle, said channel communicating with said opening whereby said channel is in open communication with said air passage when said cover is spaced with respect to said flange.

3. A container comprising a receptacle having a neck-portion provided with an opening bounded by a flange, a cover for said opening, spacing means disposed between said cover and flange to provide an air passage therebetween, said spacing means being collapsible to permit closing of said opening when said cover is pressed toward said flange, means projecting from said cover to align said cover over said opening, said aligning means extending at right angles from said cover into said opening and neck-portion, said aligning means providing a channel within said neck-portion for the free passage of material into and from said receptacle, said channel communicating with at least part of said opening whereby said channel is in open communication with said air passage when said cover is spaced with respect to said flange, and a collar to engage said cover and flange and adapted to press and to hold said cover upon said flange.

4. The container as in claim 3 wherein said collar has an aperture adjacent the top surface of said cover to permit the insertion of a hollow needle through said cover.

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