

[54] **LYOFLO-STOPPER**

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Related U.S. Application Data

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[52] U.S. Cl. **34/5, 34/92**

[51] Int. Cl. **F26b 5/06**

[58] Field of Search **34/5, 15, 92**

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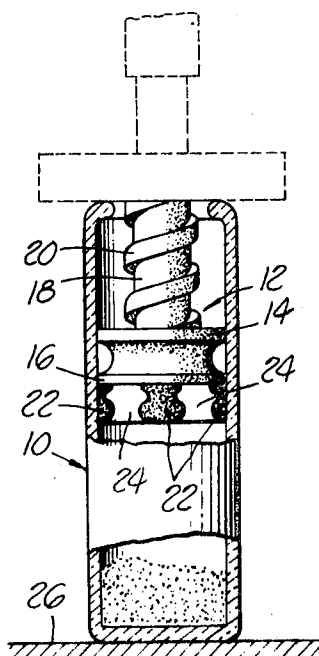
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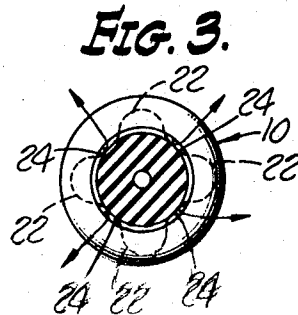
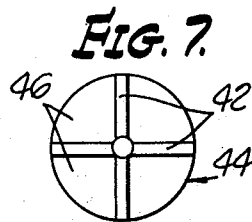
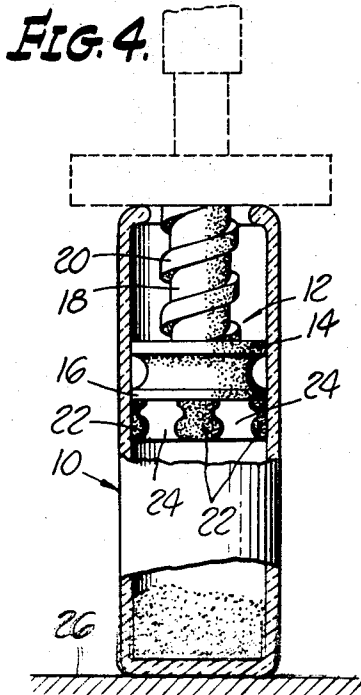
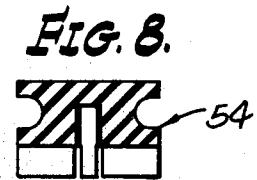
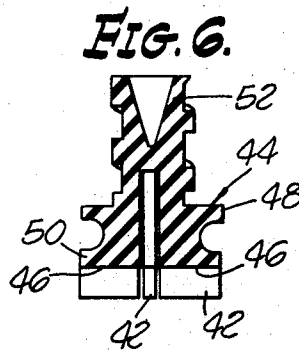
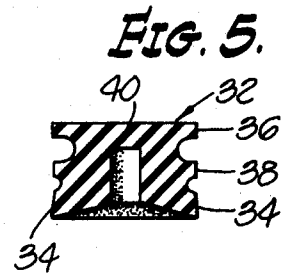
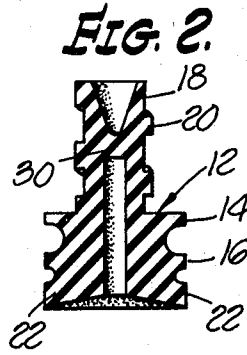
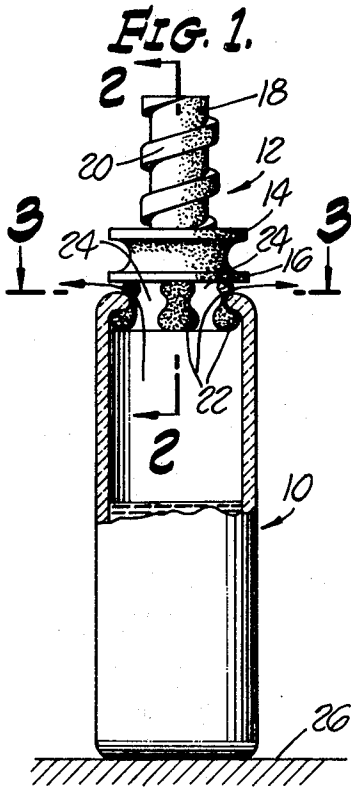
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[57] **ABSTRACT**

This patent describes a novel resilient lyophilizing stopper for use in a vial or other medicament container having an open end, said stopper comprising an upper portion having one or more sealing rings adapted to form a seal on the inside walls of said vial and act as a piston therein, and a lower portion comprising a series of interruptions around the periphery of the lower portion, said interruptions forming a force compression fit with the walls of the vial and the spaces between the interruptions being adapted to provide a gas passage from the interior of the vial to the exterior when said sealing rings are held beyond the end of the vial by said interruptions.

1 Claim, 8 Drawing Figures





LYOFLO-STOPPER

This application is a division of Ser. No. 791,727, filed Jan. 16, 1969 and now U.S. Pat. No. 3,578,195.

BACKGROUND OF THE INVENTION

Many medicament devices are packaged in a lyophilizer which is a device for the removal of moisture from those medicaments which must necessarily be stored in dry form due to instability problems in the presence of moisture. The lyophilizer comprises a chamber adapted to be closed and maintain a vacuum in which there is provided a cold surface upon which the container carrying the material to be lyophilized can rest during the lyophilizing process. When the chamber is closed and vacuum applied the vapor present in the medicament within the vial is carried off leaving the dry medicament. The ordinary non-reciprocating closures for such vials can be inserted in the end of the vial at the end of the lyophilization cycle while the vial is still in the lyophilizer. The seating of the non-reciprocating stopper within the lyophilizer is relatively simple since the stopper has a peripheral flange which abuts the edges of the wall of the open end of the vial when the stopper is seated. However, the piston or reciprocating type vial stoppers do not have any flange to act as a stop against the travel of the stopper. In the case of the piston stopper, the normal practice is to remove the vial containing the medicament from the lyophilizer at the end of the cycle and insert the piston stopper in the open end to maintain a seal until the material is ready for use. The difficulty with this practice is that the removal of the medicament and vial from the lyophilizer, and the exposure of the medicament to air after lyophilization can result in contamination of the medicament. The present invention is believed to represent a substantial advance in the art in that for the first time there is provided a piston stopper for a vial wherein the stopper is basically capable of fitting in the open end of the vial in two different positions. In one position, the stopper is aligned with the vial bore, but so situated and so constructed that the vapor from the medicament can be withdrawn by the vacuum of the lyophilizer. The piston stopper is also provided with sealing rings which can be easily sealed by mechanical force within the lyophilizer. Thus, the present invention for the first time provides the completion, that is, the closure of the vial with a piston stopper within the lyophilizer so that contamination of the medicament by exposure to air after lyophilization is effectively precluded.

SUMMARY OF THE INVENTION

Briefly, the present invention comprises a novel resilient lyophilizing piston stopper for use in a vial or other medicament container having an open end, said stopper comprising an upper portion having one or more sealing rings adapted to form a seal on the inside walls of said vial and act as a piston therein, and a lower portion comprising a series of interruptions around the periphery of the lower portion, said interruptions forming a slidable force compression fit with the walls of the vial and the spaces between the interruptions being adapted to provide a gas passage from the interior of the vial to the exterior when said sealing rings are held beyond the end of the vial by said interruptions.

Accordingly, it is a principal object of the present invention to provide a novel piston stopper for use in a

medicament vial which permits the completion of the lyophilization cycle within the lyophilizer.

More specifically, it is an object of the present invention to avoid the possibility of contamination of the lyophilized medicament which is inherent in the present normal practice wherein the insertion of the stopper in the vial is completed outside the lyophilizer.

Still another object of the present invention is to provide a novel type of plug for use in a vial to permit both lyophilization and sealing depending upon the position of the stopper within the vial.

These and other objects and advantages of the present invention will be apparent from the more detailed description which follows taken in conjunction with the accompanying drawings.

DESCRIPTION OF PREFERRED EMBODIMENTS

Turning to the drawings:

FIG. 1 shows a side view of a vial having the novel stopper of the present invention positioned therein in the lyophilizing position;

FIG. 2 is a sectional view of the stopper shown in FIG. 1 and taken along the line 2—2;

FIG. 3 is a sectional view taken along the line 3—3 of FIG. 1;

FIG. 4 shows the vial of FIG. 1 after completion and seating of the stopper;

FIG. 5 is a sectional view of another embodiment of the lyophilizing stopper of the present invention;

FIG. 6 shows still another embodiment of the lyophilizing stopper of the present invention in sectional view;

FIG. 7 is a plan view of the stopper of FIG. 6; and

FIG. 8 is a sectional view of yet another embodiment of the lyophilizing stopper of the present invention.

Turning to the drawings in greater detail, in FIGS. 1—4, the vial 10 is provided with the stopper of basically cylindrical cross-section indicated generally as 12. This stopper is provided with sealing rings 14 and 16 and a threaded extension 18 having thereon male threads 20. At the lower end of the stopper 12 there are provided a series of four tabs or bump-like projections or interruptions 22. Between the projections 22 there are openings 24 to provide vapor passage as indicated. In operation, the stopper 12 is initially positioned in the vial 10 in the manner shown in FIG. 1 and inserted in a lyophilizer having a chilled surface 26. Lyophilizing is then carried out in conventional manner until the medicament contained within the vial is dry. Then, by mechanical means within the lyophilizer the plug 12 is depressed into the end of the vial 10 until sealing rings 14 and 16 form a seal on the inside walls of vial 10, as shown in FIG. 4. Thereafter gas can be bled into the lyophilizer. The pressure of a gas on the exterior of the vial will cause the stopper to move in a piston-like fashion down into the inside of the vial. The exact position at which the vial will stop depends upon the amount of interference between the rings and a vial wall. If it is desired to stop the plug at any particular point after lyophilization, this can be accomplished by providing a restriction or ring in the inside wall of the vial which has a greater interference with the rings on the stopper than can be overcome by atmospheric pressure. Another way of establishing the stopping of the stopper at any given point is to permit the introduction of some sterile

gas into the lyophilizer prior to the pressing of the stopper into the position where the rings 14 and 16 seal on the inside of the vial. After a certain amount of gas pressure has been thus established, the mechanical pressure is then applied to the end of the stopper 12 to cause the sealing rings to seal on the inside of the vial. Then the atmospheric pressure is restored to the inside of the lyophilizer which will cause the vial to move a certain distance inside the vial. The amount of gas introduced prior to the seating of the rings will determine the final rest point of the stopper and here again this can be determined empirically by very simple testing. Obviously, the precise stop point selected in any given situation will depend upon the requirements of the given situation; i.e., the amount of lyophilized material in the vial.

The threaded extension 18 on the vial shown in FIGS. 1-4 is adapted to be made up with a medicament injector of the type described in applicant's previously issued U.S. Pat. No. 3,376,866, issued Apr. 9, 1968, the disclosure of which is expressly incorporated herein by reference. When the vial is assembled with the injector, the diaphragm 30 is punctured, and the diluent can be aspirated into vial 10 to form the medicament solution. The device is then used to inject the patient. During aspiration the plug 12 acts as a piston within the vial and serves to expel all of the contents of the vial.

However, it is not necessary that the stopper of the present invention be provided with a threaded extension. For example, a simple plain face stopper 32 such as shown in FIG. 5 may also be provided with the lyophilizing feature at the lower end by virtue of spaced projections or interruptions 34. Sealing rings 36 and 38 function as previously described. In this case, the contents of the vial can be removed at the time of use by simply injecting a diluent with a normal syringe by piercing the thin diaphragm portion 40 of the stopper with the needle injecting the liquid, shaking the vial to dissolve the medicament, and then removing the medicament solution with the syringe and administering the same in conventional fashion. As the solution is removed by the syringe, the piston stopper slides downwardly within the vial as a result of the vacuum created within the vial by the removal of solution.

The projections or interruptions 22 and 34 on the stopper are of a maximum diameter slightly greater

than the inside diameter of the vial. This is of particular value in that it permits lyophilization because the stopper is maintained in an aligned position with respect to the bore of the vial by the interference or compression fit of the projections in the end of the vial.

The projections can take many forms. For example, as shown in FIGS. 6 and 7, the projections are four up-standing ridges 42 on the face of stopper 44, disposed at right angles to each other, and terminating at the periphery of the stopper so as to function in a manner similar to the projections 22 previously described. The vapor passage space is provided by areas 46 between the ridges 42. The sealing rings 48 and 50, and threaded extension 52 are identical to those on the stopper of FIGS. 1-5.

FIG. 8 shows a stopper 54 which is the same as that of FIGS. 6 and 7 except that no threaded extension is provided.

The stoppers of this invention may be molded or otherwise formed from any resilient material such as rubber so that the projections will hold the stopper in aligned position while lyophilizing, and the sealing rings will form a seal on the inside of the vial after completion.

Having fully described the invention it is intended that it be limited only by the lawful scope of the appended claims.

I claim:

1. The method of lyophilizing which comprises placing a material to be lyophilized within a vial comprising a cylinder having an open end and a closed end, placing in said open end a resilient lyophilizing piston stopper provided with an upper portion having one or more sealing rings, and a lower portion comprising a series of interruptions around the periphery of the lower portion, said interruptions forming a force compression fit with the walls of the vials and the spaces between the interruptions being adapted to provide a gas passage from the interior of the vial to the exterior, said stopper being initially positioned in said vial so that said sealing rings are held beyond the end of the vial by said interruptions, placing said vial in a lyophilizer, lyophilizing said material, and applying force to said stopper while said vial is in said lyophilizer to cause said sealing rings to seal on the inside walls of said vial.

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