(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 564 037 A1**

(12) EUROPEAN PATENT APPLICATION

(21) Application number: **93200885.7**

(51) Int. Cl.5: **B65D 51/00**

(22) Date of filing: **27.03.93**

(30) Priority: **02.04.92 US 862120**

(43) Date of publication of application:
06.10.93 Bulletin 93/40

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

(71) Applicant: **STERLING WINTHROP INC.**
90 Park Avenue
New York, NY 10016(US)

(72) Inventor: **Liebert, Richard T., c/o Sterling Winthrop Inc.**
81 Columbia Turnpike
Rensselaer New York 10016(US)

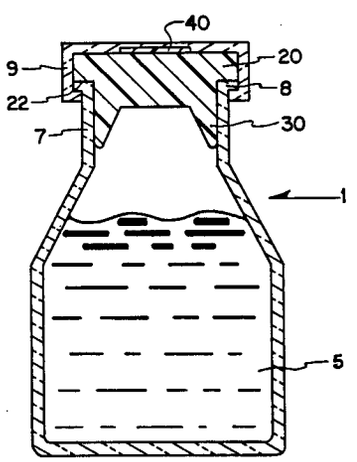
Inventor: **Brown, Neil H., Sterling Winthrop Inc.**
81 Columbia Turnpike,
Rensselaer
New York 10016(US)

(74) Representative: **Haile, Helen Cynthia et al**
Kodak Limited
Patent Department
Headstone Drive
Harrow, Middlesex HA1 4TY (GB)

(54) Abrasion resistant stopper to prevent generation of particles by piercing.

(57) An abrasion-resistant stopper (10) for a medical vial for containing a fluid therein comprising a stopper body of an elastomeric material having a head portion (20) and a fluid contactable leg portion (30), the leg portion (30) being adapted to be inserted into the medical vial for hermetically sealing the fluid therein and the head portion (20) comprising a top surface to receive a coating thereon, the top surface being coated with an abrasion-resistant coating (40) to prevent generation of particles upon piercing of the stopper (10) by a spike or a hypodermic needle. Preferably the coating (40) covers at least the centre, pierceable portion of the top surface and is advantageously polytetrafluoroethylene.

FIG.7



EP 0 564 037 A1

This invention relates to a stopper for a container and, more particularly, to an improved stopper for a container of parenteral solutions which is suitable for infusion spike penetration without producing unacceptable amounts of particulate matter.

Stopper systems for vials, bottles and the like are made of materials that are resistant to chemicals and pharmaceuticals such as corrosive materials, reagents, parenteral solutions and solid formulations reconstitutable with a solvent prior to use. The most commonly used stopper system for such products has been glass or plastic bottles and vials equipped with rubber stoppers made of elastomeric materials. The system appears to provide for good hermetical seal, safe storage and easy access to the content through the elastomeric stopper via the use of an infusion spike when withdrawal of the content is desired. The elastomeric stopper used comprises an elastomeric base, such as natural or synthetic rubber and an inert coating covering at least some portions of the stopper. The coating used heretofore includes chlorobutyl rubber, polymeric fluorocarbon resins such as polytetrafluoroethylene (TEFLON) and various thermoplastic films. The coating is intended to insulate the elastomeric stopper base from the content of the container in order to prevent contact and possible chemical reactions therebetween.

One of the major concerns in all products, and especially pharmaceutical parenteral products, is the generation of particulate foreign matter which may contaminate such products. In order to eliminate macroscopic and microscopic particulates, elaborate measures have been taken to remove them, such as filtration of the product and special washing and drying of the stopper system components. These steps help assure that the products meet the requirements and guidelines of the pharmaceutical industry, such as compendia guidelines, when the products reach the point of use. However, at the point of use, such as in the case of a parenteral product, new particulate matter is frequently generated by the practitioner when the stopper is penetrated by a needle or spike of an infusion set or an infusion spike. During such penetration a combination of elastic and plastic deformation of the stopper target area increases the stopper contact surface with the infusion spike as it is pressed into the stopper. Typically, untreated elastomeric stoppers offer a high degree of resistance against the exterior surface of the spike as the spike is being pushed into the penetration area. Most frequently, when stopper fragments are generated, they are the result of the elastomeric portion of the stopper being abraded off the upper surface of the stopper as it conforms to the shape of the penetrating spike. The fragments are then transported into the interior of the vial as the spike rolls and drags the fragments during penetration.

In addition to the problem of particulate matter produced and carried into the vial during the spiking procedure, there are two other, although less frequently occurring, anomalies: stopper push-through into the vial and spike blow-out caused by residual elastic tension of the stopper against the spike which urges the spike outward.

The most common solution to these problems has been the application of silicone lubricant to the stopper and/or the spike to reduce the frictional drag between the stopper and the spike. While silicone does reduce particle generation from the spiking procedure, it also increases the risk of product contamination from its own composition.

Another approach proposed in the prior art to reduce the tendency of the stopper to generate particulate matter during manufacturing and storage is to coat the elastomeric core of the stopper with a thermoplastic film on the fluid-contacting side thereof. We have found, however, that the use of such construction is less than satisfactory to solve the problem.

The present invention addresses the need to eliminate or at least greatly reduce the particle generation from surface erosion of the stopper during spike penetration. In addition, the invention reduces the risk of the push-through and blow-out tendency by minimizing frictional drag and residual elastic tension during spike penetration. These advantages are achieved without the use of a lubricant, such as silicone oil, which could contaminate the product contained in the vial or bottle.

We have found surprisingly that if a non-reactive, inert, coating which is highly resistant to abrasion is applied to the upper surface of an elastomeric stopper where spike penetration will take place, particle generation during spiking is all but eliminated and the tendency of push-through as well as blow-out of the spike is greatly reduced.

Accordingly this invention provides an abrasion-resistant stopper for a medical vial for containing a fluid therein comprising:

a stopper body of an elastomeric material having a head portion and a fluid contactable leg portion,

said leg portion being adapted to be inserted into said medical vial for hermetically sealing said fluid therein, and

said head portion comprising a top surface to receive a coating thereon, said top surface being coated with an abrasion-resistant coating to prevent generation of particles upon piercing of the stopper by a spike or a hypodermic needle.

Preferably the coating covers at least the centre, pierceable portion of the top surface for spike or needle penetration of the stopper when withdrawal of fluid is desired.

In use, the coating on the top surface of the stopper conforms to the deformation of the stopper caused by the spike penetration procedure. It appears that, upon piercing, the spike is not in contact with the elastomeric stopper body but only with the abrasion-resistant coating thereby circumventing abrasion and eliminating the formation of elastomeric particulate materials.

The invention will now be more fully described with reference to the following drawings in which

FIG. 1 is a perspective view of one embodiment of the stopper of the present invention;

FIG. 2 is a plan view of the stopper shown in FIG. 1;

FIG. 3 is a cross-sectional view of the stopper shown in FIG. 2 taken along the line a - a;

FIG. 4 is a perspective view of another embodiment of the stopper of the present invention;

FIG. 5 is a plan view of the stopper shown in FIG.4;

FIG. 6 is a cross-sectional view of the stopper shown in FIG. 2 taken along the line b - b; and

FIG. 7 is a cross-section of a vial containing an injectable liquid closed with the stopper of the present invention.

Referring to FIGS. 1, 2 and 3, numeral 10 shows one embodiment of the stopper of the present invention comprising: a head portion 20 and a leg portion 30. Head portion 20 comprises a flange 22 which is adapted to cover a corresponding planar, circular mouth portion of a medical vial, while leg portion 30 is adapted for insertion into the neck of the vial to tightly seal the content therein. Numeral 40 shows an abrasion-resistant film mounted on the centre part of the head portion 20 which serves as the piercing area for insertion and withdrawal of a spike or hypodermic needle.

Referring to FIGS. 4, 5 and 6, numeral 10' shows another embodiment of the stopper of the present invention comprising: a head portion 20' and a leg portion 30'. Head portion 20' comprises a flange 22' which is adapted to cover a corresponding planar, circular mouth portion of a medical vial, while leg portion 30' is adapted for insertion into the neck of the vial to tightly seal the content therein. Numeral 40' shows an abrasion-resistant film mounted on the top part of the head portion 20'. In this embodiment recess 32' extends toward the top surface of the head portion 20' forming a thin portion 34' in head portion 20' for facilitating piercing of the stopper by a spike.

FIG. 7 illustrates a stopper 10 having an abrasion-resistant film 40 covering vial 1. Vial 1, containing an injectable fluid 5, is sealed by stopper (10 or 10') by inserting leg portion 30 of the stopper into the neck 7 of the vial 1. Flange portion 22 of head portion 20 tightly seals the mouth 8 of vial 1. A thin metal foil 9 is crimped over head portion 20 and flange portion 22 of stopper (10 or 10') to tightly seal and securely hold the stopper in vial 1.

The elastomeric material of the stopper body must be a fluid-impervious, resilient and inert material without leachable additives therein in order to prevent any alteration of the product contained in the vial. It may be of a single component or a blend of components. Examples of materials include synthetic or natural rubber, such as butyl rubber, isoprene rubber, butadiene rubber, silicone rubber, halogenated rubber, ethylene propylene therpolymer and the like. Specific examples of a synthetic elastomeric rubber include the CH_2CF_2-C_3F_6 (C_3F_5H) and the C_2F_4-$C_2F_3OCF_3$ series of elastomers made by duPont under the trade names of VITON® and CARLEZ®; the fluoro-silicone rubbers, such as those made by Dow Corning under the name of SILASTIC®; and polyisobutylenes, such as VISTANEX MML-100 and MML-140; and halogenated butyl rubber, such as CHLOROBUTYL 1066, made by Exxon Chemical Company.

These or other suitable elastomers may be made into the desired stopper configuration by known methods. Such methods conventionally include the use of a curing agent, a stabilizer and a filler and comprise a primary and secondary curing step at elevated temperatures.

The abrasion-resistant coating for covering the top portion of the stopper, but at least the centre, pierceable portion thereof, may be: a polyvinyl, such as polystyrene, polyvinyl acetate (PVA), polyvinyl chloride (PVC), polyvinylidene chloride (PVDC), a copolymer of PVC and PVDC, polyvinyl fluoride, polyvinylidene fluoride, polychlorotrifluoroethylene and polytetrafluoroethylene ; a polyolefine, such as polypropylene and polymethylpentene; an ether, such a polymethylene oxide, polyphenylene oxide and polyphenylene sulphone; an ester, such as polyethylene terephthalate (PET), polycarbonate and copolyesters; an ester, such as polycaprolactam (Nylon 6), polyhexamethylene adipamide (Nylon 66) and polyundecanoamide (Nylon 11).

The abrasion-resistant coating covering at least the centre, pierceable portion of the top surface of the stopper is preferably polytetrafluoroethylene sold under the trade name TEFLON by duPont.

The coating thickness will be in the range of about 0.002 to 1.0 mm, and preferably about 0.02 to 0.5 mm. The coating may be applied or bonded to the stopper body in any suitable manner known in the art, such as, but not limited to, by the use of adhesives, solvents, spray applications, radio waves, infrared,

microwaves, ultrasonics and heat or a combination thereof.

The preferred stopper of the present invention comprising an elastomeric material and a TEFLON coating on the top centre portion thereof was tested against another stopper of the same elastomeric material but without the TEFLON coating thereon.

The vials were capped with the stoppers. Each stopper was pierced with a spike and then the spike was removed. The vials were examined for the presence of elastomeric particles caused by the piercing. The result of the spiking is shown in Table 1.

TABLE 1

Stopper	No. of Samples	Mean Particle Count
Present Invention	25	0.6
Elastomeric (Control)	25	15.4

The present invention has been described in connection with the preferred embodiments shown in the drawings but is in no way limited thereto. It is to be noted that various changes and modifications are apparent to those skilled in the art.

Claims

1. An abrasion-resistant stopper for a medical vial for containing a fluid therein comprising:

a stopper body of an elastomeric material having a head portion and a fluid contactable leg portion,

said leg portion being adapted to be inserted into said medical vial for hermetically sealing said fluid therein, and

said head portion comprising a top surface to receive a coating thereon, said top surface being coated with an abrasion-resistant coating to prevent generation of particles upon piercing of the stopper by a spike or a hypodermic needle.

2. A stopper as claimed in claim 1 wherein said coating covers the centre, pierceable portion of said top surface.

3. A stopper as claimed in either of the preceding claims wherein said coating is applied to said top surface by the use of an adhesive, solvent, spray application, radio waves, infrared, microwaves, ultrasonics, heat or a combination thereof.

4. A stopper as claimed in any one of claims 1 to 3 wherein said coating is a polyvinyl.

5. A stopper as claimed in claim 4 wherein the coating is selected from the group consisting of polystyrene, polyvinyl acetate, polyvinyl chloride, polyvinylidene chloride, a copolymer of polyvinyl chloride and polyvinylidene chloride, polyvinyl fluoride, polyvinylidene fluoride, polychlorotrifluoroethylene and polytetrafluoroethylene.

6. A stopper as claimed in claim 5 wherein the coating is polytetrafluoroethylene

7. A stopper as claimed in any one of claims 1 to 3 wherein said coating is a polyolefine.

8. A stopper as claimed in claim 7 wherein the coating is selected from the group consisting of polypropylene and polymethylpentene.

9. A stopper as claimed in any one of claims 1 to 3 wherein said coating is an ether.

10. A stopper as claimed in claim 9 wherein the coating is selected from the group consisting of polymethylene oxide, polyphenylene oxide and polyphenylene sulphone.

11. A stopper as claimed in any one of claims 1 to 3 wherein said coating is an ester.

12. A stopper as claimed in claim 11 wherein the coating is selected from the group consisting of polyethylene terephthalate, polycarbonate and copolyesters.

13. A stopper as claimed in claim 11 wherein the coating is selected from the group consisting of polycaprolactam, polyhexamethylene adipamide and polyundecanoamide.

14. A stopper as claimed in any one of the preceding claims wherein the coating has a thickness of about 0.002 to 1.0 mm.

15. A stopper as claimed in claim 14 wherein the coating has a thickness of about 0.02 to 0.5 mm.

FIG.1

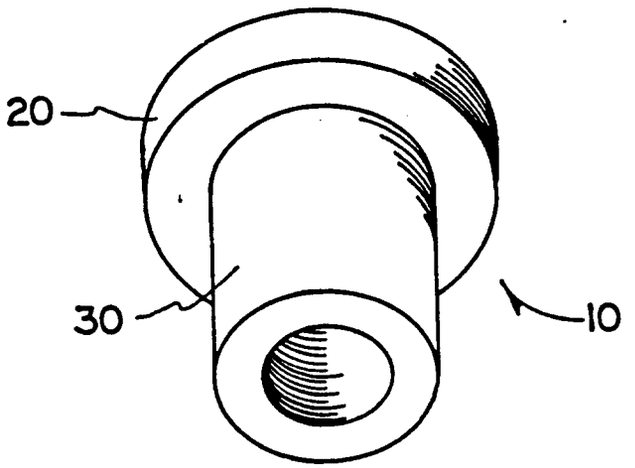


FIG. 2

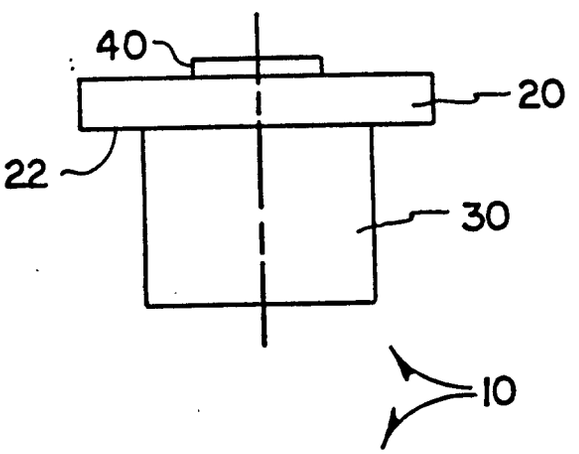


FIG.3

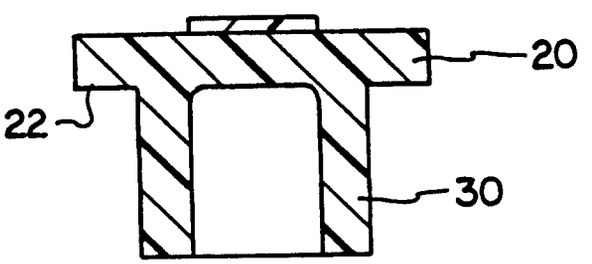


FIG.4

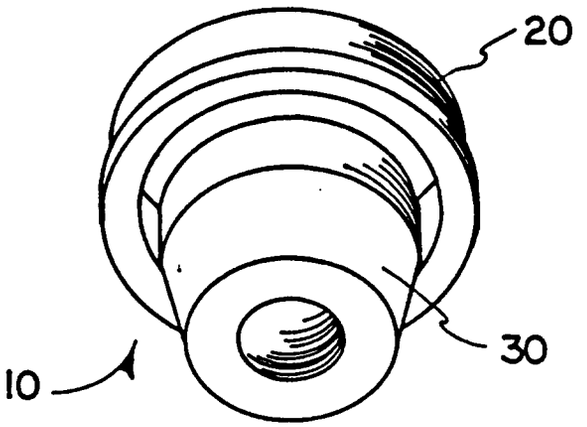


FIG. 5

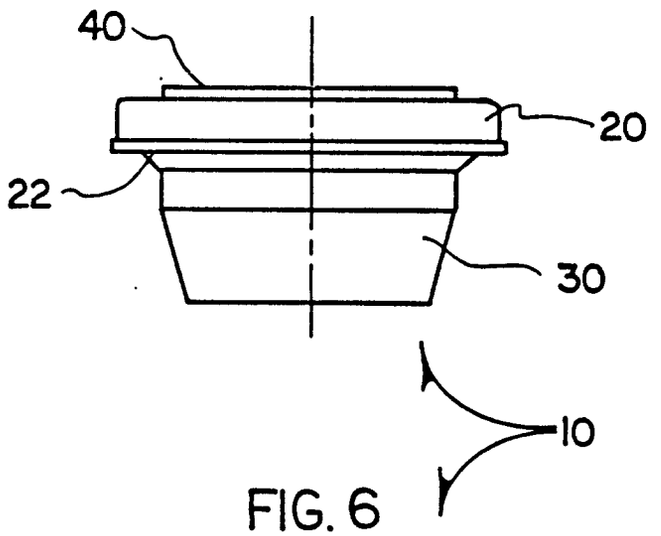


FIG. 6

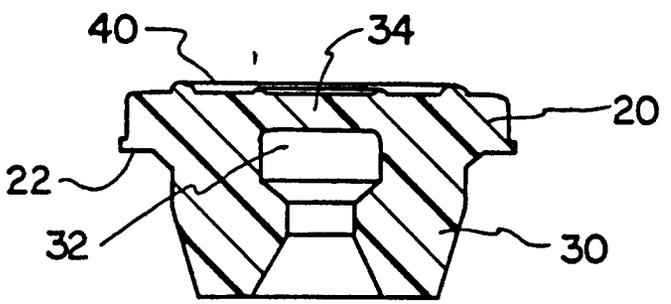
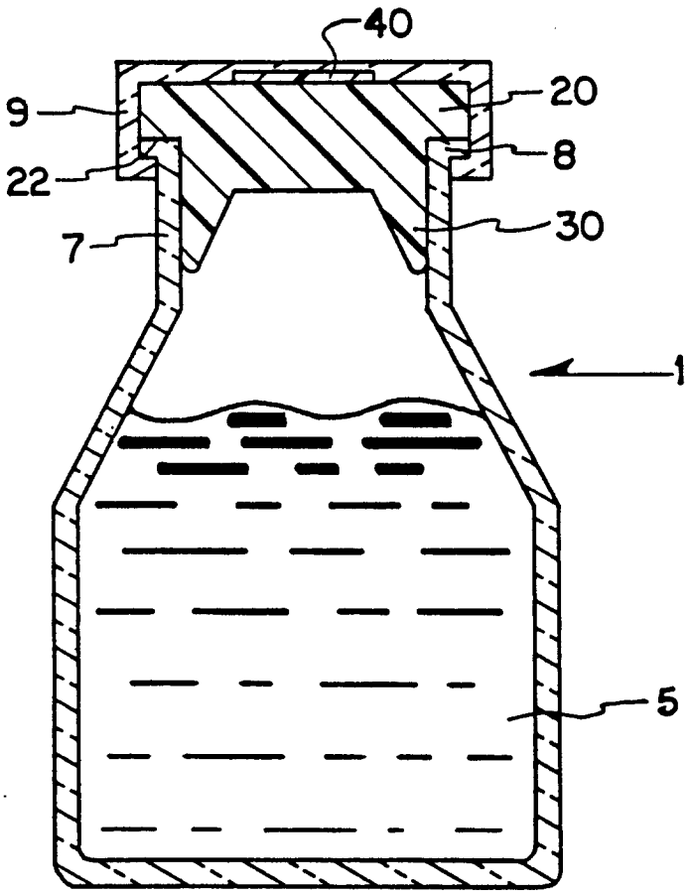


FIG. 7



European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 93 20 0885

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	EP-A-0 294 127 (DAIKYO GOMU SEIKO LTD.) * claims; figure 1 *	1-15	B65D51/00
X	US-A-4 499 148 (GOODALE ET AL.) * column 4, line 25 - line 40 * * figures 2-4 *	1-15	
X	DE-U-8 906 346 (PHARMA-GUMMI WIMMER WEST GMBH) * page 6, line 15 - line 23; figure 1 *	1-15	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

B65D
A61J

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	09 JUNE 1993	GODOT T.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P0401)