

Our Ref 349055

631270 FORM 1

AUSTRALIA  
Patents Act

APPLICATION FOR A STANDARD PATENT

Ciba-Geigy AG, of Klybeckstrasse 141, 4002 BASLE, SWITZERLAND

hereby applies for the grant of a standard patent for an invention entitled

Apparatus for removing preservatives from solutions

which is described in the accompanying complete specification.

Details of basic application(s):

Basic Application: Country:

461,988

UNITED STATES OF AMERICA

Date:

8 January 1990

The address for service is:

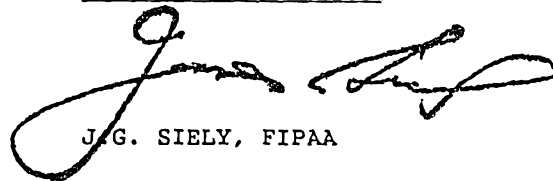
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DATED this SECOND day of JANUARY 1991

Ciba-Geigy AG

By Its Patent Attorneys

ARTHUR S. CAVE & CO.



J.G. SIELY, FIPAA

TO:

The Commissioner of Patents  
COMMONWEALTH OF AUSTRALIA

FEE: 458.00

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COMMONWEALTH OF AUSTRALIA

Patents Act 1952 - 1969

DECLARATION IN SUPPORT OF A CONVENTION APPLICATION FOR A PATENT

In support of the Convention Application made by CIBA-GEIGY AG for a patent for an invention entitled:

Apparatus for removing preservatives from solutions

I, Werner Waldegg of CIBA-GEIGY AG, Klybeckstrasse 141, 4002 Basle, Switzerland do solemnly and sincerely declare as follows:

1. I am authorised by the applicant for the patent to make this declaration on its behalf.
2. The basic application(s) as defined by Section 141 on the Act was (were) made in USA  
on January 8, 1990

by Barbara L. Heyl, Lynn C. Winterton, Kai C. Su and Jack C. White

3. Barbara L. Heyl, 516 Sidney Ave., Atlanta, GA 30312, USA,  
Lynn C. Winterton, 1445 Parkmont Dr., Roswell, GA 30076, USA,  
Kai C. Su, 13090 Hopewell Rd., Alpharetta, GA 30201, USA and  
Jack C. White, 321 Malley Dr., Stone Mountain, GA 30087, USA

~~is~~ (are) the actual inventor(s) of the invention and the facts upon which the applicant is entitled to make the application are as follows: The said applicant is the assignee of the actual inventor(s).

4. The basic application(~~s~~) referred to in paragraph 2 of this Declaration was (~~were~~) the first application(~~s~~) made in a Convention country in respect of the invention the subject of the application.

DECLARED at Basle, Switzerland on  
December 12, 1990

CIBA-GEIGY AG

  
Werner Waldegg

Single Signature, by special power

To: The Commissioner of Patents

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(12) PATENT ABRIDGMENT      (11) Document No. AU-B-68607/91  
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(54) Title  
APPARATUS FOR REMOVING PRESERVATIVES FROM SOLUTIONS

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461988      08.01.90      US UNITED STATES OF AMERICA

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(56) Prior Art Documents  
US 4002168  
US 3346146  
US 2761833

(57) Claim

*for removing a preservative from a solution*  
1. A dispensing device, comprising:

a) a container body defining a solution retaining chamber therein, said container having a container outlet for dispensing said solution from said chamber; and

b) means for removing a preservative from said solution as said solution is dispensed from said chamber through said container outlet.

2. The device of Claim 1, wherein said removing means comprise a scavenging material provided within the path of said solution as said solution travels from said chamber to said container outlet.

23. A fitment for removing a preservative from a solution dispensed from the outlet of a container, comprising:

a) a body portion having one of its ends capable of being in flow communication with said container outlet, a fitment outlet at its other end and a passageway

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interconnecting said ends;

b) means on said fitment for engaging said fitment to  
said container; and

c) means within said passage for removing a  
preservative from said solution as said solution passes from  
said container outlet to said fitment outlet.

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FORM 10

COMPLETE SPECIFICATION

(ORIGINAL)

Application Number:  
Lodged:

Complete Specification Lodged:  
Accepted:  
Published:

Priority:  
Related Art:

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Applicant(s): Ciba-Geigy AG  
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Complete specification for the invention entitled

"Apparatus for removing preservatives from  
solutions".

The following statement is a full description of this invention, including the  
best method of performing it known to me:-

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APPARATUS FOR REMOVING PRESERVATIVES FROM SOLUTIONS

The present invention relates to an apparatus for removing preservatives from solutions, in particular from ophthalmic solutions applied in contact lens care.

Many solutions are available for making contact lenses more comfortable, safer, and easier to wear. For example, wetting solutions facilitate the wetting of a lens, soaking solutions serve as anti-microbial storage medium and prevent dehydration and distortion of the lens, and cleaning solutions remove accumulated eye secretions and other contaminants from lenses. A large number of other solutions are also used by contact lens patients. These ophthalmic solutions are typically marketed in squeezable plastic containers or aerosol cans having a nozzle through which the solution is dispensed.

Because these solutions come in contact either directly or indirectly with the eye, it is very important that they be free of microbial growth. To this end, it is common practice for preservatives to be provided in these solutions. Among the preservatives used in ophthalmic solutions are polymoxin B sulfate, quaternary ammonium compounds, chlorobutanol, organic mercurials, p-hydroxybenzoic acid esters, and certain phenyls and substituted alcohols.

A problem exists, however, in that the preservatives used in the ophthalmic solutions can cause eye irritation if used in high concentrations. For example, benzalkonium chloride (BAK) is used as a preservative in ophthalmic solutions and has broad anti-bacterial and anti-fungal activity when used with other components, such as disodium ethylene diaminetetraacetic acid

(EDTA). However, it has been reported that repeated use of BAK can denature the corneal protein and cause irreversible eye damage. Also, in addition to chemical sensitivity, a number of contact lens wearers have allergic reactions to the preservatives used in ophthalmic solutions, even at relatively low concentrations.

The typical remedy for overcoming chemical sensitivity and allergic reactions to preservatives in ophthalmic solutions entails switching the patients to an unpreserved solution. However, unpreserved solutions present problems in marketing, as well as in home storage, in that once the container housing the solution is opened, the solution quickly becomes contaminated and unsuitable for further use. They also tend to be very expensive to produce.

Therefore, there exists a need for an apparatus which removes preservatives, as well as other components, from a solution as the solution is dispensed to a patient.

There exists a further need for such an apparatus which is easily manufactured and economical to use.

There exists a further need for an apparatus which may be attached to a standard solution container.

The present invention provides a device for removing a preservative from ophthalmic and other solutions as the solution is dispensed from a container, <sup>as defined in the claims.</sup> The device preferably comprises a container having squeezable sidewalls defining a solution retaining chamber, but may also be an aerosol can or other container. The container also preferably includes a neck portion and a dispensing head having a container outlet on its



end through which the solution is dispensed. Means for removing the preservative from the solution as the solution is dispensed from the chamber through the container outlet are also provided.

In a first embodiment, the means for removing a preservative from the solution comprise a scavenging material provided within the path of the solution as the solution is dispensed. In this embodiment, the device is a standard solution container housing a solution having the component to be removed, and the scavenging material is held within the dispensing head.

The scavenging material may have a positive charge for scavenging negatively charged preservatives or it may have a negative charge for scavenging positively charged preservatives or it may be a material which selectively scavenges components by a size exclusion mechanism or it may comprise any other means for removing a component from solution.

In an alternative embodiment, a fitment may be utilized having a fitment body which is releasably engagable with a standard solution container. The fitment includes passage means within its body for allowing passing of the solution from the container to a fitment outlet. In this embodiment, the means for removing a preservative may comprise a scavenging material provided within the fitment so as to be within the path of the solution as the solution is dispensed from the container outlet to the fitment outlet. The fitment has the advantage of being able to be adapted to standard solution containers.

Also, means for providing a control of the flow of solution out of the container may be provided. For example, a check valve may be provided within the final dispensing outlet to prevent backflow of solution into the container following use. Additionally, means for regulating the flow of air into the container, namely, a second check valve, may be placed within the neck portion of a squeezable container for allowing air to flow into a depressed container, thereby restoring the container to its original shape. This embodiment will minimize the incidence of microbial growth in the area of the dispensing head proximate the final dispensing outlet.

Therefore, it is an object of the present invention to provide an apparatus which removes preservatives, as well as other components, from a solution as the solution is dispensed to a patient.

It is also an object of the present invention to provide such an apparatus which is easily manufactured and economical to use.

It is also an object of the present invention to provide such an apparatus which may be adapted to a standard solution container. These and other objects and advantages will be more apparent from the following detailed description of the invention.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an exploded view of a first embodiment of the present invention in which scavenging material is provided

within a container;

Figure 2 is a partial cross-sectional view of a first embodiment of the present invention in which scavenging material is provided within a container;

Figure 3 is an exploded view of a second embodiment of the present invention in which scavenging material is provided within a fitment;

Figure 4 is a partial cross-sectional view of a second embodiment of the present invention in which scavenging material is provided within a fitment;

Figure 5 is a partial cross-sectional view of an embodiment of the present invention in which the dispensing head is snap-fitted onto a container; and

Figure 6 is a partial cross-sectional view of an embodiment of the present invention having means for providing one-directional flow of solution out of a container.

Referring to the figures, a device 10 for removing components, such as preservatives, from solutions, such as an ophthalmic solution, is shown. The device 10 includes a container 12, preferably constructed of molded plastic, having resilient sidewalls 14 which define a solution retaining chamber and which preferably may be deformed by inward pressure to produce a pressure within the container 12 for using and dispensing its contents. The container 12 is provided with an upstanding neck portion 16 having external threads 18 thereabout. A dispensing head 20 is provided atop the neck portion 16, either integrally, as shown in Figs. 1-4, by threading engagement, or by snap-fitting engagement as shown in

Figs. 5 and 6. A flange portion 22 is provided between the dispensing head 20 and the container neck 16. The dispensing head 20 has passage means, such as a duct or other passageway, through its length which in turn has a first end in communication with the chamber and a container outlet 24 at the other end.

In a first embodiment of the present invention, shown in Figs. 1 and 2, means for removing preservatives or other components are placed directly within the dispenser head 20. In its preferred form, the preservative removing means comprise scavenging material 26 provided intermediate the chamber and the container outlet 24, so as to be within the path of the solution as the solution is dispensed from the container 12. The material 26 should be positioned as close as possible to the outlet 24 to minimize empty space in the upper portion of the dispensing head 20. The material 26 may be compressed into a porous mass which is preferably insert molded into the dispensing head 20. However, any other means of maintaining the material in the path of the solution may also be used. Alternatively, as shown in Fig. 2, the material 26 may be in the form of fine particles and held in place by porous supporting members 28 and 30. The members 28 and 30 may be made from porous plastic, such as porous polyethylene. In either case, it is important that the solution pass through the scavenging material 26 as it exits the container 12 so that the component is removed upon contact with the scavenging material 26.

A second embodiment of the invention, shown in Figs. 3

and 4, includes a fitment 32 having a body 34 which is affixable to a standard-size container 12, such as described above but without the scavenging material 26 within its dispensing head 20. The lower portion 36 of the fitment 32 is provided with internal threads 38 which complementarily mate with threads 18 on the outer surface of the neck portion 16 so that the fitment 32 may be releasably matable to the container 12. As seen in Fig. 4, when the fitment 32 is in threaded relationship with the container neck portion 16, an internal flange 40 of the fitment 32 rests atop the neck portion 16 to provide a seal between the fitment 32 and container 12. The fitment 32 has a fitment outlet 42 atop a tapered upper section 44, as well as a passage or duct through its length. The passage is preferably adjacent to and in flow registration with the container outlet 24 at one end and opens to the fitment outlet 42 at its other end. In this alternative embodiment, the scavenging material 26 is provided within the fitment 32, and removes the component, such as preservative, from the solution as the solution passes from the container outlet 24 to the fitment outlet 42. As in the first embodiment, the scavenger material 26 may be in solid mass or powder or other form.

Fig. 6 shows a device 10 of the present invention which includes means for providing one-directional flow of solution out of the container, such as a check valve 50. Preferably, the valve 50 is a deformable, polymeric valve that is positioned within the container outlet 24 so as to be in flow communication with the interior portion of the dispensing head

20 at one end and with the atmosphere at a second end. In its normal or closed position, the valve 50 does not allow air or solution to flow into or out of the container 12. However, as a result of the pressure exerted onto the container 12 during use, the valve 50 moves to an open position that allows the solution to pass through to the atmosphere. When the pressure on the container 12 is stopped, the valve 50 closes and any solution remaining atop the valve 50 cannot be pulled back inside the container 12, thereby minimizing the incidence of organisms re-entering the container 12 after use.

Also, when a squeezable container 12 is used, means for drawing air into the container 12 may be provided for returning the container 12 to its original shape. Preferably, a second one way check valve 52 is provided within the neck portion 16 and below the scavenging material 26. Upon release of the container 12 by the user, air is drawn into the container 12 by the valve 52, thereby restoring the container 12 to its proper shape. Also, because the valve 52 is one-directional, solution from within the container 12 cannot leak out to the atmosphere through the valve 52. Furthermore, because the second valve 52 is below the scavenging material 26, any organism which should happen to be withdrawn into the container will be deposited into the preserved solution and killed.

Both the dispensing head 20 of the first embodiment and the fitment 32 of the second embodiment may include a closure cap 46. The closure cap 46 may have internal threads 48 capable of matingly engaging with either the threads 18 of the neck portion 16, as shown in Fig. 1, or the external threads 50

of the fitment 32, as shown in Fig. 3, and resting on flange 22.

Of course, containers other than squeezable plastic types may be utilized. The scavenging material may be placed within an aerosol type dispenser, a solid bottle, or some other container.

Virtually any type of scavenging material 26 for removing a preservative or other component from solution may be used. For example, removal of benzalkonium chloride or other quaternary ammonium compounds can be accomplished by an ionic exchange mechanism. The scavenging material 26 would preferably be an inert material with a negative charge, and the positively charged quaternary ammonium compound would adhere to the material 26 as it flows through the fitment 32 or dispensing head 20, depending on the embodiment. Examples of products capable of removing positively charged preservatives such as BAK include AG-50X-8, AG-50X-16, BIO-BS-SM2, and BIO REX 70, all available from BIO-RAD Laboratories, Richmond, California and Acropor 5A-6404 available from Gelman Sciences, Ann Arbor, Michigan. Similarly, negatively charged components, such as acids, may be removed by using positively charged scavenging material 26. Examples of such scavenging material includes AG-1, AG-2X8, and AG-10 Alumina from BIO-RAD Laboratories. For example, it has been found that scavenging material 26 comprising Chelex 100 from Bio Rad will remove Thimerosal from solution. Alternatively, the scavenging material may be porous plastic, such as porous polyethylene, imbedded with a cross-linked styrene divinyl benzene which is sulfonated to produce either a positively charged hydrogen form

or a negatively charged sodium form. Other scavenging materials useful in the present invention are those relating to chemical affinity techniques, such as immunoassay, active site binding and affinity chromatography.

As one particular example, it has been found that a scavenging material comprised of a mixture of "Bio Rex 5" and "AG-4", both Bio Rad products, in a 75 to 25 ratio will almost completely remove .1% sorbic acid from a solution and raise the pH of the solution from 4.0 to 7.0. This is important since sorbic acid is a commonly used preservative in contact lens solutions. In addition, sorbic acid is normally stored at pH = 7.0, where it is not stable. At pH = 4.0, it is very stable but cannot be instilled into the eye. The present invention will therefore allow solution to be stored at low pH and the pH raised to an ocularly acceptable level as the solution is administered.

Other preservatives that are not directly charged, such as chlorhexadine, could also be removed by the present invention. For example, a size exclusion mechanism may be utilized for removing certain types of preservative compounds. Overall, the term "scavenging material" as used herein refers to all material which will remove or change the nature of preservatives or other components in a solution exiting the container.

From the foregoing description of the invention, it should be seen that the present invention provides the ability to dispense preservative-free solutions from containers housing solutions that are preserved. Whereas the present invention

has been described with respect to specific embodiments thereof, it should be understood that various changes and modifications will be suggested to one skilled in the art and it is intended that Bio Rad will remove Thimerosal from solution. Alternatively, the scavenging material may be porous plastic, such as porous polyethylene, imbedded with a cross-linked styrene divinyl benzene which is sulfonated to produce either a positively charged hydrogen form or a negatively charged sodium form. Other scavenging materials useful in the present invention are those relating to chemical affinity techniques, such as immunoassay, active site binding and affinity chromatography.

As one particular example, it has been found that a scavenging material comprised of a mixture of "Bio Rex 5" and the invention encompass such changes and modifications that will fall within the scope of the appended claims.

The claims defining the invention are as follows:

1. *for removing a preservative from a solution*  
A dispensing device, comprising:
  - a) a container body defining a solution retaining chamber therein, said container having a container outlet for dispensing said solution from said chamber; and
  - b) means for removing a preservative from said solution as said solution is dispensed from said chamber through said container outlet.
2. The device of Claim 1, wherein said removing means comprise a scavenging material provided within the path of said solution as said solution travels from said chamber to said container outlet.
3. The device of Claim 1, and further comprising a dispensing head on said container having passage means therethrough, said passage means having a first end in communication with said chamber and said container outlet being at the other end thereof, said removing means located intermediate said first end and said container outlet.
4. The device of Claim 3, wherein said dispensing head is integrally formed on said container body.
5. The device of Claim 2, wherein said scavenging material has a negative charge and said preservative has a positive charge.
6. The device of Claim 2, wherein said scavenging material has a positive charge and said preservative has a negative charge.
7. The device of Claim 2, wherein said scavenging material is fumed silica and said preservative is a quaternary ammonium



compound.

8. The device of Claim 2, wherein said scavenging material is a size exclusion material for selectively removing said preservative based upon the size thereof.

9. The device is Claim 3, wherein said removing means is insert-molded into said dispensing head.

10. The device of Claim 2, wherein said solution is an ophthalmic solution applied in contact lens care.

11. The device of Claim 2, wherein said scavenging material is in the form of a porous mass.

12. The device of Claim 1, and further comprising a fitment releasably engagable with said container body and having a passage therethrough, one end of said passage being in flow communication with said container outlet and a fitment outlet through which said solution may be dispensed from said container being at the other end of said passage, and wherein said removing means is provided within said passage.

13. The device of Claim 12, wherein said container body has a dispensing head having a duct therethrough, said duct having one end in flow registration with said chamber and said container outlet being at the other end thereof, and wherein said device further comprises means for releasably mating said fitment with said dispensing head.

14. The device of Claim 13, wherein said mating means comprises a threaded neck portion on said dispensing head and wherein said fitment has a threaded base portion complementarily threaded to said neck portion.

15. The device of Claim 2, wherein said scavenging material

is porous plastic embedded with sulfonated cross-linked styrene divinyl benzene.

16. The device of Claim 3, wherein said dispensing head is threadingly matable onto said container body.

17. The device of Claim 3, wherein said dispensing head is snap fittingly engagable onto said container body.

18. The device of Claim 1, wherein said container body is an aerosol can.

19. The device of Claim 1, and further comprising means on said container body for controlling the direction of flow of solution from said container body.

20. The device of Claim 20, wherein said means for controlling the direction of flow of solution from said container body comprise a first check valve provided in said container outlet.

21. The device of Claim 20, and further comprising means on said container body for regulating the flow of air into said chamber below said preservative removing means.

22. The device of Claim 21, wherein said regulating means comprise a second check valve.

23. A fitment for removing a preservative from a solution dispensed from the outlet of a container, comprising:

a) a body portion having one of its ends capable of being in flow communication with said container outlet, a fitment outlet at its other end and a passageway interconnecting said ends;

b) means on said fitment for engaging said fitment to said container; and

c) means within said passage for removing a preservative from said solution as said solution passes from said container outlet to said fitment outlet.

24. The fitment of Claim 23, wherein said removing means comprise scavenging material provided within the path of said solution.

25. The fitment of Claim 24, wherein said scavenging material has a negative charge and said preservative is positively charged.

26. The fitment of Claim 24, wherein said scavenging material has a positive charge and said preservative is negatively charged.

27. The fitment of Claim 24, wherein said scavenging material is fumed silica and said preservative is a quaternary ammonium compound.

28. The fitment of Claim 24, wherein said scavenging material selectively scavenges said preservative by a size exclusion mechanism.

29. The fitment of Claim 23, wherein said container has a dispensing head having said container outlet therethrough, and wherein said fitment body is releasably engagable with said dispensing head.

30. The fitment of Claim 29, wherein said dispensing head has a threaded neck portion and wherein said fitment body has a threaded base portion threadingly matable to said neck portion for engaging said fitment body with said container.

31. The fitment of Claim 23, wherein said solution is an ophthalmic solution.

32. The fitment of Claim 23, wherein said scavenging material is comprised of porous plastic embedded with sulfonated cross-linked styrene divinyl benzene.

33. The fitment of Claim 30, wherein said dispensing head is threadingly matable onto said container.

34. The fitment of Claim 30, wherein said dispensing head is integral with said container.

35. The fitment of Claim 30, wherein said dispensing head is snap fittingly engagable onto said container.

36. The fitment of Claim 23, and further comprising means on said container body for controlling the direction of flow of said solution from said container body.

37. The fitment of Claim 23, wherein said means for controlling the direction of flow of solution from the container body comprises a first check valve provided in said container outlet.

38. The fitment of Claim 23, and further comprising means on said container body for regulating the flow of air into said chamber below said component removing means.

39. The fitment of Claim 38, wherein said regulating means comprise a second check valve.

40. A dispensing device substantially as herein described with reference to any one or more of the drawings.

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41. A fitment for removing a preservative from a solution dispensed from the outlet of a container, substantially as herein described with reference to any one or more of the drawings.

DATED this 20th day of February, 1991.

CIBA-GEIGY AG  
By Its Patent Attorneys  
ARTHUR S. CAVE & CO.

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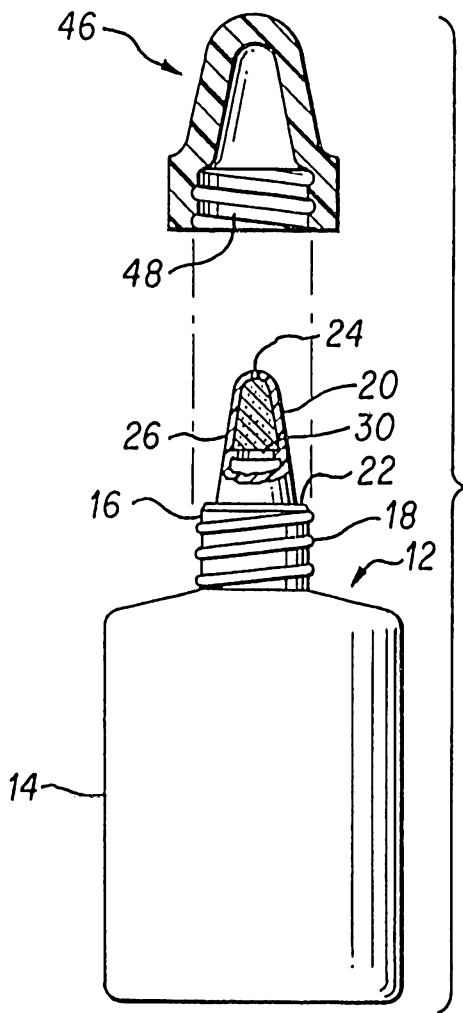


FIG. 1

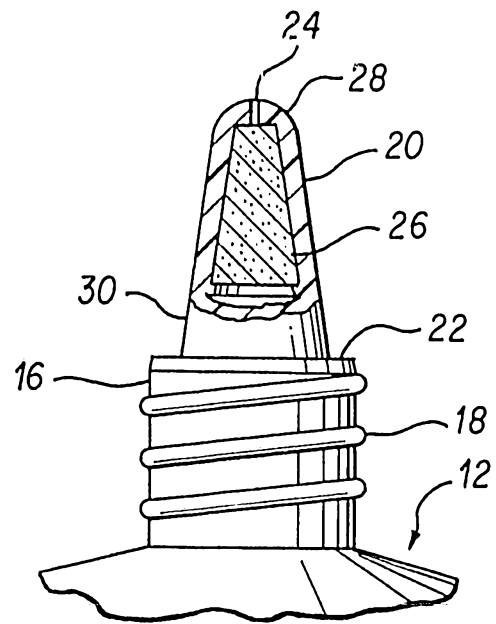
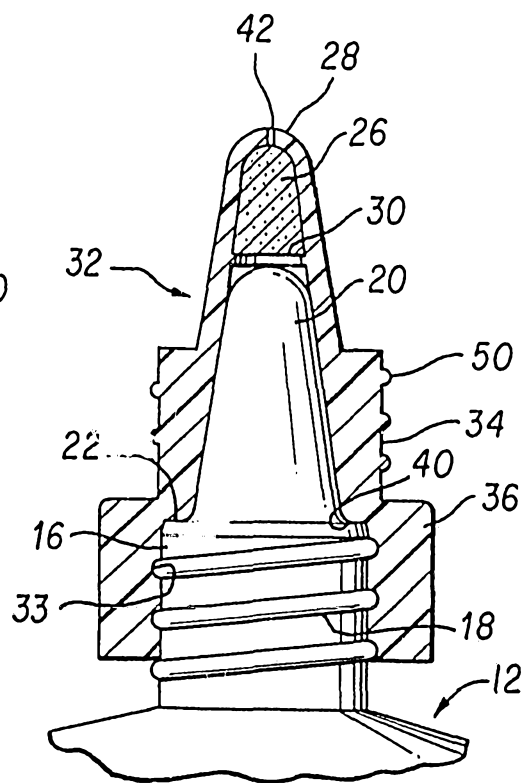
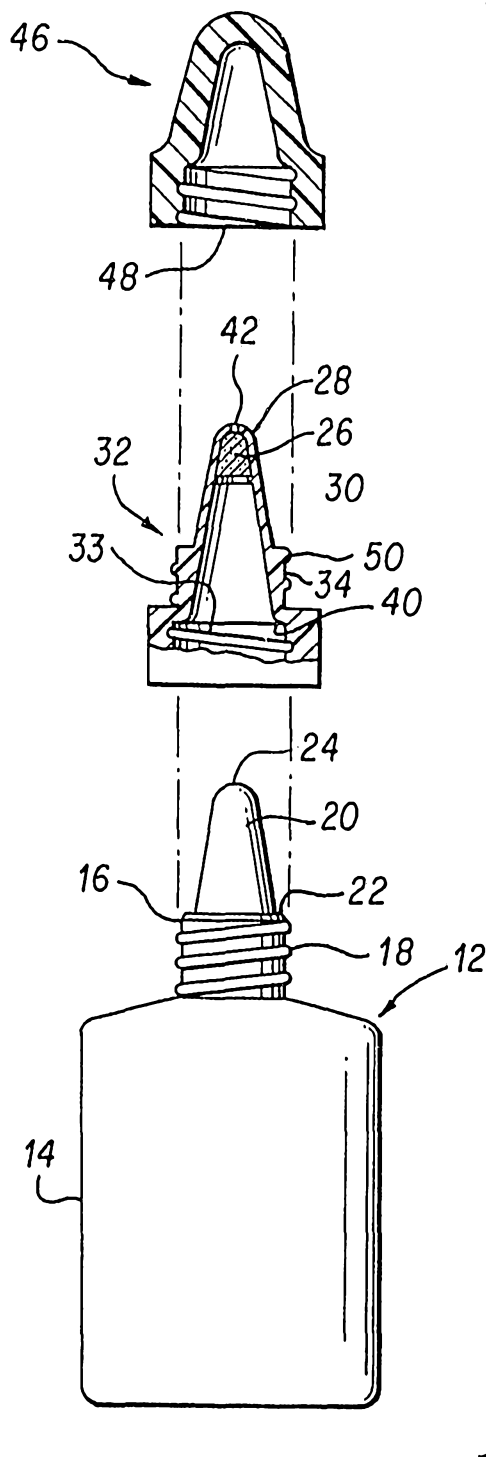


FIG. 2

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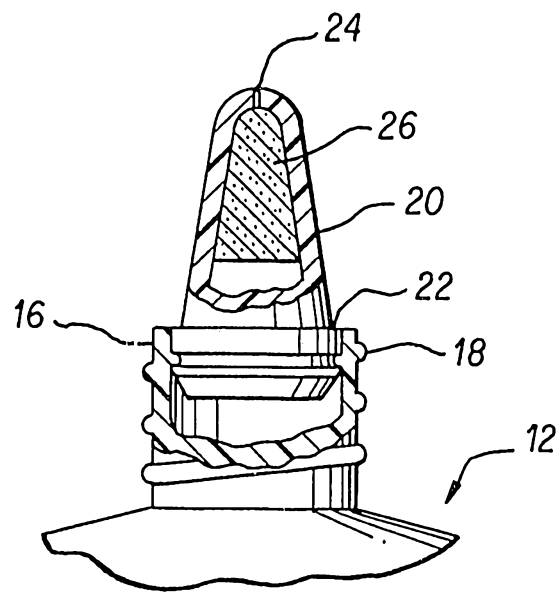


FIG. 5

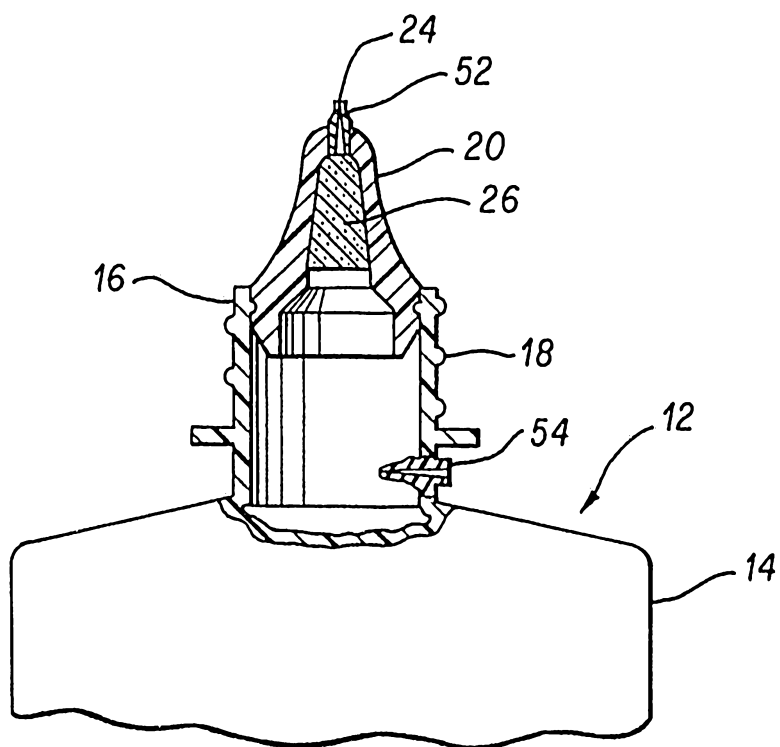


FIG. 6