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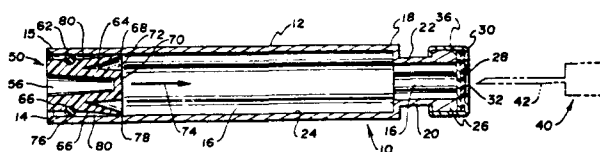
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⑤④ **Ampule for long-term storage of polymerizable substances.**

⑤⑦ An ampule for long-term storage of a polymerizable substance, such as a monomer of an aliphatic cyanoacrylate. First sealing means (28), for sealing the ampule, provides access to the enclosed contents by means of a needle (42). Second sealing means (50) comprising piston means engages the ampule interior wall (24). The piston means is constructed and arranged to inhibit catalyzation of the polymerizable substance contained in the ampule.



AMPULE FOR LONG-TERM STORAGE
OF POLYMERIZABLE SUBSTANCES

I. DESCRIPTION

BACKGROUND OF PRIOR ART

5 The present invention is directed to an improved
ampule construction for long-term storage and for ready
ultimate use of polymerizable substances such as a monomer
of methyl cyanoacrylate (MCA). The ampule prevents setup
or polymerization of the polymerizable substance while it
10 is stored in or used from the ampule. Methyl cyanocrylate
(MCA) is a well-known chemical product that has found
wide use in the medical field for a variety of purposes as
a tissue adhesive and is of particular and preferred
interest herein. More recently, MCA has found application
15 in the field of permanent sterilization of human females.
Sterilization in the female is accomplished by introduction
of small quantities of MCA into the fallopian tubes. Its
contact there with body moisture polymerizes the MCA and
blocks the fallopian tube. With passage of time, fibrous
20 tissue growth replaces the MCA and permanent sterilization
results. This use and procedure is described in the U.S.
Patent Nos. 3,822,702 and 3,948,259.

 Since MCA is the preferred polymerizable substance
insofar as this invention is concerned, the following des-
25 cription will refer to MCA in particular. However, the
invention is not limited to MCA as the only polymerizable
substance to be stored in ampules constructed according to
this invention. Rather, the invention is concerned with
the construction of ampules as set forth herein. Related
30 polymerizable substances are described in U.S. Patents

2,763,677; 3,483,870; 3,527,841; 3,564,078; 3,699,076;
3,759,264 and British Patent 1,159,548. An article appear-
ing in the Society of Plastics Engineers Journal 15 (No. 5),
(1959) entitled "Chemistry and Performance of Cyanoacrylate

5 Adhesive" also describes related polymerizable substances.
The term "polymerizable substances" is intended to be
inclusive of all such equivalent substances or compositions,
which are readily catalyzed by moisture, heat, light,
radiation, and the active sites provided by various organic
10 materials and caused to polymerize.

The property of polymerization which makes these
substances useful for many purposes also makes them diffi-
cult to store. For example, the very properties which make
MCA desirable for use as an adhesive for medical purposes,
15 such as the binding of wound edges together, make it a
difficult material to sterilize and store. MCA polymerizes
under a variety of conditions including exposure to even
trace amounts of moisture, heat, high energy radiation,
and virtually any active site organic, as do the other
20 polymerizable substances referred to hereinabove. It is
also difficult to store MCA for any period of time due
to its tendency to autocatalyze itself into a solid cured
polymer in storage. It is known that one can add quanti-
ties of inhibitor substances (generally in a range of
25 100-600 ppm) to the MCA to greatly reduce any tendency to
autocatalyze itself during the storage. However, in order
to prevent polymerization during sterilization (which
generally entails the use of elevated temperatures),
relatively large amounts of such inhibitors must be util-
30 ized. This problem of sterilization of the MCA has been
overcome by the invention entitled "Method of Bacterially
Purifying Methyl Cyanoacrylate," U.S. Patent Application
Ser. No. 784,956, filed April 6, 1977.

However, the problem of storage in and use from
35 ampule of polymerizable substances such as sterilized MCA
has not been eliminated merely by sterilizing the MCA. A
storage problem still exists due to the fact that some of

the materials used in the construction of prior art ampules causes catalyzation of the polymerizable substance, such as MCA, which is stored in the ampules. The prior art ampule comprises a tube made, for example, of a material such as polyethylene, which is generally sealed at one end with a stopped or diaphragm of rubber or the like, and, at the other end, a movable piston of rubber or the like is provided for sealing the ampule while moving toward the stopper as the polymerizable substance is withdrawn from the ampule, such as by the needle of a hypodermic syringe passed through the stopper in a fashion similar to that normally used in removing drug solutions from ampules. The problem which occurs is that the rubber, and similar materials used in the stopper and piston, usually contains active sites which cause catalyzation of the polymerizable substances stored in the ampule, such as MCA. Experience has shown that such rubber-sealed ampules are acceptable for very short-term storage but that, upon overnight storage at approximately 50°C, the resin MCA, for example, polymerizes or "sets up" to a complete solid form. Because the rubber of the seals contains catalytically active sites, contact between the rubber parts and the MCA inside the ampule causes polymerization of the MCA in an unacceptably short period of time. This creates a very serious problem in the storage and use of polymerizable substances, particularly MCA, and makes it impossible to realize the full benefits of substances such as MCA, some uses of which are described in U.S. Patents 3,822,702 and 3,948,259. For example, where storage facilities may not be available for maintaining the MCA at a sufficiently low temperature to prevent polymerization while stored in the ampules, polymerization may take place unexpectedly.

One solution to the above-described problem would be to coat both the surfaces of the rubber stopper and the rubber piston which contact the polymerizable substances stored in an ampule with a protective coating, such as a conventional polyteleofluorelbylene (PTFE or TEFLON)

material. One such process utilizes a thin PTFE coating to be bonded to the rubber surface at the same time the rubber is being vulcanized. This is a relatively costly process and utilizes relatively expensive materials. Also,
5 any of the polymerizable substance which escapes past the PTFE coated portion of the piston contacts the rubber portion of the piston and polymerizes. This causes the "set up" of the balance of the polymerizable substance in the ampule.

10 It has been determined that polymerizable substances, such as bacterially purified MCA monomer, may be effectively stored in an ampule constructed in accordance with this invention without requiring expensive processing and coatings. In addition, the present invention permits
15 the use of a low level of inhibitor content in the polymerizable substance, which is desirable in the finished product to prevent autocatalyzation during storage. The ampule of the present invention may be made of relatively inexpensive materials and allows relatively long-term storage of polymerizable substances such as MCA with reduced
20 risk that polymerization may occur even though the ampule experiences elevated temperature conditions such as those found in tropical areas. Desirably, the ampule of the present invention and its contents will be maintained at low
25 temperatures where possible to further reduce the possibilities of unintended polymerization.

Another advantage of the present invention is that both the piston and stopper may be made of inexpensive materials and are of such construction that the polymer-
30 izable substance is not permitted to contact those portions of the piston and stopper which in prior art ampules have come into contact with the substance. Therefore, the piston and stopper construction of the present invention are such that catalyzation of the substance is prevented. The
35 construction of the ampule of the present invention also allows the ampule and its contents to be frozen thus preserving the contents over a longer period of time.

BRIEF SUMMARY OF THE INVENTION

This invention provides an ampule for long-term storage of a polymerizable substance such as a monomer of an aliphatic cyanoacrylate and comprises an ampule body
5 for holding a quantity of such a substance, first sealing means for sealing one portion of the ampule body and constructed and arranged to permit access to the inside thereof by a needle to permit draining of the substance and second sealing means including piston means situated
10 within the ampule for sealing another portion thereof and for inhibiting catalyzation of substances stored in the ampule.

In the preferred embodiment of the present invention, the first sealing means includes a stopper or
15 diaphragm member which has an inexpensive protective coating on the portion of the member which contacts the monomer inside the ampule body. This coating prevents the stored substance from contacting the first seal means even when a needle is passed through the seal member into the ampule
20 body for draining the monomer. The second sealing means includes a piston of a material similar to that of the ampule body in that it does not foster polymerization of the stored substance upon contact. The piston has an "O" ring sealing member which acts as a secondary seal and a
25 flared interior end section which provides a seal. The flared end section of the piston fits within the container means and bears against the inside wall of the container to sealingly engage it so as to prevent the leakage of the polymerizable substance from the container. The "O" ring
30 acts as a secondary seal such that in the event any stored substance does pass the primary seal provided by the flared end section, it will be trapped in the space between the flared end section, the "O" ring, and the inner wall of the ampule body and held separate from the remaining
35 polymerizable substance within the ampule. This trapping action inhibits the "O" ring from causing the polymerizable substance stored inside the ampule from being catalyzed by contact with the "O" ring.

These and other objects and advantages of the invention will more fully appear from the following description made in connection with the accompanying drawings, wherein like reference characters refer to similar parts
5 throughout the separate views.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a perspective view of the preferred embodiment of the ampule of the present invention;

Fig. 2 shows a cross-sectional view of the ampule
10 shown in Fig. 1 taken across lines 2-2 shown in Fig. 1;
and,

Fig. 3 is a perspective view of the piston utilized in the ampule of the present invention shown in Figs. 1 and 2.

15 DETAILED DESCRIPTION OF INVENTION

Figs. 1 and 2 show an ampule 10 of the present invention which includes a tubular body or member 12 having a beveled end portion 14 at one end 15 thereof and having a cylindrical opening 16 of slightly decreasing
20 diameter forming an apertured passage therethrough from beveled end portion 14 to opposite end portion 18 thereby defining a chamber. In the preferred embodiment member 12 is a cylindrical tube but it could have other configurations, with appropriate modifications in the other components of ampule 10. The opening 16 at end 18 is smaller
25 in cross-sectional diameter than is the cross-sectional diameter of member 12 at the beveled end portion 14. The end 18 of member 12 has a neck portion 20 affixed thereto. Neck portion 20 has an opening 22 passing completely
30 through the neck portion 20. Opening 22 communicates both with opening 16 and the space outside member 12. Member 12 and neck portion 20 are preferably made of a water tight, noncatalyzing plastic material such as polyethylene or polypropylene. Opening 16 of member 12 has a very
35 smooth inner wall 24 so that the polymerizable substance

contained within ampule 10 will have less tendency to leave a layer on the inner surface or wall 24. Located on the end of neck portion 20 opposite end 18 of member 12 is a lip or raised portion 26. Neck 20 and lip 26 are made of the same material as member 12 and may be integrally molded together as a single unit. As noted, opening 16 is provided with a slightly decreasing cross-sectional diameter, and ampule 10 may be readily molded as a single piece.

Sealing neck portion 20 is a fixed seal means including a body such as a stopper, plug, or preferably a diaphragm-type member as shown at 28 which is provided as a closure to seal the opening 16 at end 32 of member 12. A rim or cap 30 fitted over the end of neck portion 20 partially extending over end 32 and member 28 is provided to retain member 28 in sealing position. A coating such as a sprayed-on PTFE coating 36 is provided over the inner surface of member 28 so as to render it inert to the contents thereof. Member 28 is preferably made of a high modulus rubber material such as butyl, natural, buna, neoprene, or any other appropriate high modulus rubber. Such high modulus rubbers have the appropriate characteristics for allowing a device such as that disclosed in U.S. Patents 3,822,702 and 3,948,259 such as that shown in phantom at 40 having a needle 42 to puncture member 28 and be used for draining from the ampule chamber defined by opening 16. The high modulus rubber materials allow needle 42 to puncture member 28 without coring the member and also allowing the member to reseal once needle 42 is withdrawn from the ampule. Coating 36 is provided because it is inert to the polymerizable substance contained within ampule 10 and is not a catalyst for polymerization. By providing coating 36, any reactive sites are shielded from the ampule contents since coating 36 prevents contact between the contents and the inner surface of member 28 prior to needle 42 being passed therethrough to drain contents out of the chamber.

Cylindrical member 12 is also provided with a generally cylindrical piston 50, shown in perspective view in Fig. 3. Piston 50 is introduced into opening 16 via the beveled end portion 14 of member 12 and is seated within the apertured passage formed by opening 16 at end 15. Piston 50 is of a material inert to the ampule contents and is preferably of a material similar to member 12, i.e., a polyethylene or polypropylene or any other suitable material to which the polymerizable substances to be contained in the ampule will have a relatively low tendency to adhere and which does not catalyze the polymerization of the ampule contents. Piston 50 has a cylindrical portion 52 located at one end thereof and a frusto-conical or flared section 54 formed integrally with and adjacent cylindrical portion 52. Piston 50 is provided with a hole 56 extending partially therethrough and tapering in cross-sectional diameter with its largest dimension being at end 58 of piston 50. Tapered hole 56 is provided to allow piston 50 to be integrally molded of a plastic material of the type described above as a single member. Located around the outer surface of cylindrical portion 52 of piston 50 is an annular peripheral seal or groove 60 which carries snugly therein an "O" ring 62 which is preferably made of the same materials as member 28. Inwardly thereof is a frusto-conical or flared section 54 which flares outwardly beginning at the point of connection 66 with cylindrical portion 52. Flared portion 54 together with end 70 of cylindrical portion 52 defines an annular groove on the flare of end 70 as a space 72, the purpose of which is explained below. The outer diameter of "O" ring 62 and the maximum diameter of outwardly flared frusto-conical section 54 at point 68 are such that when piston 50 is introduced into opening 16 of member 12 at the beveled end portion 14, both the "O" ring 62 and end point 68 of flared portion 54 will be compressed by the inner wall 24 of opening 16 resulting in two areas of sealing engagement, i.e., first and second seal means on

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the piston. By providing space 72, flared portion 54 may be readily compressed as piston 50 moves in the direction of arrow 74 toward member 28 as the contents of the ampule are being withdrawn by means of needle 42. Since flared
5 portion 54 and "O" ring 62 bear snugly against inner wall 24 of opening 16, as piston 50 moves, a seal is provided both at end point 68 of flared portion 54 where it contacts inner wall 24 and also at the area of contact between the "O" ring 62 and inner wall 24. These seals,
10 shown at points 76 and 78 for the position of piston 50 as shown in Fig. 2, and the body of piston 50 define or provide a trapping space 80 all the way around piston 50 between "O" ring 62 and end 68 of flared portion 54. By providing beveled end portion 14, the introduction of
15 piston 50 is greatly facilitated with end 68 of flared portion 54 being the leading portion introduced into the opening 16 in member 12. If end 15 of member 12 were not beveled as at portion 14, because of the relatively tight fit between end 68 of flared portion 54 and inner wall 24,
20 it would be difficult to introduce piston 50 into opening 16 of member 12.

Ampule 10 operates as follows. For filling the chamber provided by opening 16 in ampule 10 with the polymerizable substance to be stored, a standard type automatic filling machine may be used (not shown). Piston 50
25 is positioned within opening 16 so as to eliminate any space not occupied by the polymerizable substance which is introduced through opening 22 in neck portion 20. Once the space between piston 50 and end 18 of member 12 is
30 completely filled with the substance, member 28 is seated in opening 22 and cap 30 is automatically affixed in position leaving a small portion of end 32 of stopper 28 exposed for access by needle 42. Ampule 10 is thus sealed at both ends, and with coating 36 over the inner surface
35 of member 28 and with the construction of piston 50, the contents of ampule 10 can be stored for long periods without "O" ring 62 or member 28 providing any catalyzation which would cause polymerization thereof.

Thus, with opening 16 filled with a desired amount of polymerizable substance, coating 36 on member 28 prevents contact between the contents and inner surface of member 28. At the same time, end 68 of flared portion 54 on piston 50 provides a primary seal to prevent leakage of the contents out of end 15 of member 12. Since piston 50 is made of materials which do not affect the polymerizable substances, the bulk of the contents of the chamber provided by opening 16 is prevented from reaching "O" ring 62. Therefore, no reaction can occur between the active sites of "O" ring 62 and the polymerizable substance contained within opening 16. In the event that a slight amount of substance does leak past point 68 of flared portion 54, such substance is trapped in space 80 defined by "O" ring 62, flared portion 54, and inner wall 24 of member 12. "O" ring 62 provides a secondary seal for preventing leakage of the monomer material out of end 15 of the member 12.

If it is desired to withdraw or drain stored polymerizable substance from within opening 16, needle 42 is passed through member 28 and through coating 36. Material may then be drained from opening 16 through needle 42. As the draining occurs, piston 50 moves toward end 18 of member 12 eliminating any space not occupied by stored contents as it is being withdrawn from member 12. In moving in the direction of arrow 74, since the opening 16 is tapering down or decreasing in diameter as piston 50 moves toward end 18 of member 12, the inner wall 24 of member 12 continues to further compress portion 68 of flared portion 64, as well as further compressing the outer surface of "O" ring 62. In this manner, any material, which may escape past the primary seal provided by end point 68 of flared portion 64, will be trapped in space 80 between flared portion 64, the secondary seal provided by "O" ring 62 and the surface of inner wall 24. Thus, there is no way for either piston 50 or member 28 to cause catalyzation of the ampule contents. The construction of ampules of the present invention is such that once filled

with stored substance, ampule 10 may be frozen so as to preserve the contents thereof over a long period of time.

5 It should be understood that the ampule construction of the present invention may be utilized with various forms of polymerizable substances. That is, the invention is not limited to the storage of monomeric methyl cyanoacrylate but can be utilized in the storage of all polymerizable substances as defined hereinabove but particularly in the storage of the monomeric esters of aliphatic cyanoacrylates described in U.S. Patent Nos. 2,763,677 and
10 3,659,264. For purposes of the description of the invention, MCA is utilized as an example only. The term monomeric polymer as used herein is intended to include the monomer and mixtures therewith of dimers or trimers where
15 these mixtures are substantially monomers and are liquid substances at room temperatures.

It will, of course, be understood that various changes, as well as those mentioned above, may be made in the form, details, arrangements, and proportions of
20 the various parts without departing from the scope of the present invention.

II. CLAIMS

1. An ampule comprising:
 - a body defining a chamber for holding a substance to be stored, at least a portion of the chamber having a cylindrical walled opening for receiving a sealing member; and
 - a sealing member positioned in the opening, closing it off and sealing the chamber, the member including an inner and an outer sealing portion;
 - the outer sealing portion defining an annular peripheral seal normal to the opening wall for receiving an "O" ring,
 - an "O" ring in the seat,
 - the inner sealing portion defining an outwardly flaring conical inner end,
 - both the "O" ring and the flaring inner end sealingly engaging the opening wall and forming an isolated trapping space therebetween.
2. The ampule of Claim 1 wherein the body is cylindrical, the chamber is an extension of the opening and is generally cylindrically shaped, and the opening is located at one end of the body.
3. The ampule of Claim 1 wherein the body and the sealing member are formed of the same material.
4. The ampule of Claim 1 wherein the aperture opening in the end of the body is beveled at its inner periphery for receiving the sealing member.
5. In an ampule of the type having a tubular hollow body sealed at opposite ends, the first seal at one end comprising a fixed body into which a hypodermic syringe may be inserted for withdrawing varying amounts of the ampule contents, the second seal at the other end of the

body comprising a sliding piston sealingly received in the hollow body for sliding into the body as the ampule contents are withdrawn at the other end, the improvement comprising first and second spaced sealing means carried
5 by the piston;

the first sealing means comprising a seated "O" ring on the piston and positioned between the piston and the interior wall of the hollow body forming a seal therebetween,
10 the second sealing means comprising an outwardly flaring conical end portion at the inner end of the piston, the flared end portion sealingly engaging the interior wall of the hollow body, the first and second spaced sealing means forming a
15 trapping space therebetween.

6. The ampule of Claim 5 wherein the inside diameter of the hollow body gradually decreases from the end receiving the piston to the end receiving the fixed stopper thereby providing a tapered chamber in the body.

20 7. The ampule of Claim 5 wherein the flared end of the piston has an annular groove on its end face for providing flexibility in the flared portion.

8. An ampule for storing polymerizable substances, such as MCA and other aliphatic cyanoacrylates,
25 the ampule comprising:

an elongated body of a material inert and non-catalytic to the ampule contents and having an axial passage extending completely therethrough defining a chamber for holding the substance to be
30 stored therein,

fixed seal means closing the passage at one end of the body, the seal means including a body of a material readily penetrable by a hypodermic syringe needle for withdrawing the contents of the ampule,
35 the interior facing surface of the seal means body

carrying a coating of a material inert and non-catalytic to the ampule contents,

5 piston seal means, of a material inert to the ampule contents, closing the passage at the other end of the body and being slidably received therein for moving into the chamber as the contents are depleted; sealing contact between the piston and the body chamber wall being established by an "O" ring seated on the piston and by an outwardly flaring
10 cone-like inner end portion on the piston.

9. The ampule of Claim 8 wherein the piston and the ampule body are of the same material.

10. The ampule of Claim 8 wherein the coating on the interior surface of the seal means body is PTFE.

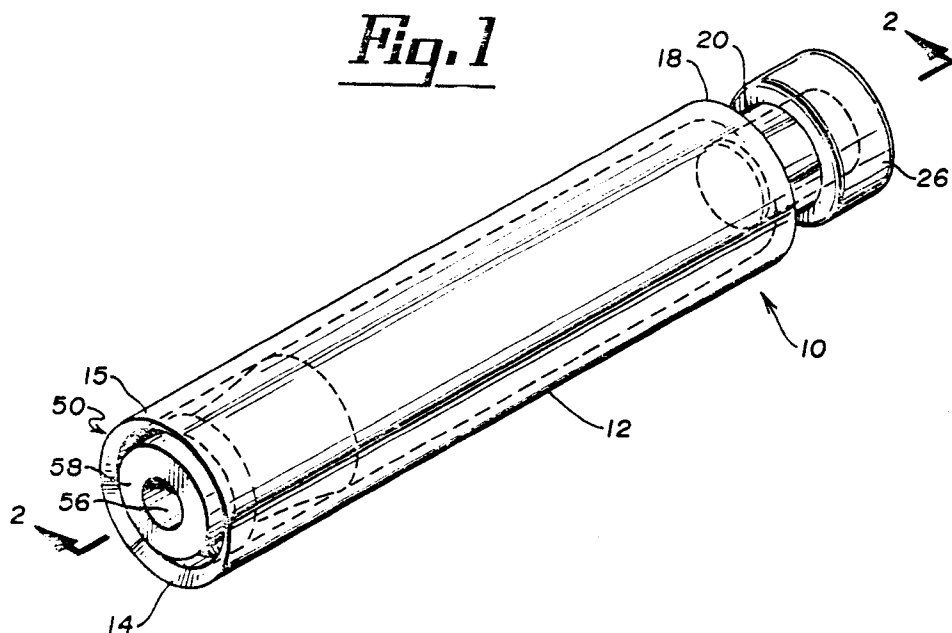
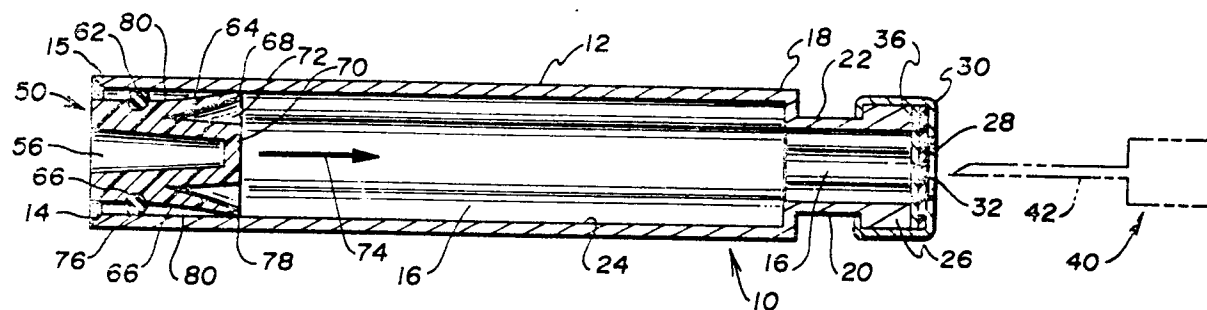
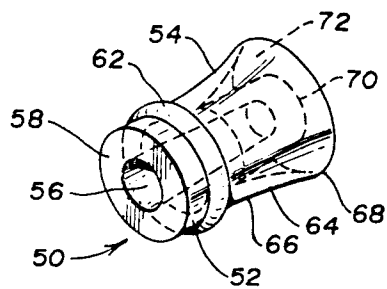
15 11. The ampule of Claim 8 wherein the passage opening for receiving the piston seal means into the body is beveled at its periphery.

12. The ampule of Claim 8 wherein the ampule body and the piston seal means are of polyethylene and the
20 seal means body is of a rubber composition.

13. The ampule of Claim 8 wherein the ampule body and the piston seal means are of polypropylene and the seal means body is of a rubber composition.

14. The ampule of Claim 8 wherein the inside
25 diameter of the passage defining the chamber gradually decreases along the body length from the piston sealing means toward the fixed seal means.

15. The ampule of Claim 8 wherein the flared end of the piston means has an annular groove on its end
30 face.

Fig. 1Fig. 2Fig. 3



European Patent
Office

EUROPEAN SEARCH REPORT

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Application number

EP 78 10 1106

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl. ³)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
	<u>FR - A - 1 412 340</u> (THE AMALGAMATED DENTAL COMP.LTD) * Page 1, column 2, lines 24-38; figure *	1,2,5	A 61 J 1/06 B 65 D 35/30
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	<u>FR - A - 2 264 562</u> (COMPAGNIE GENERALE DE RADIOLOGIE) * Page 2, lines 10-15; page 5, lines 5-10; figure *	1,2,7,13	
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	<u>CH - A - 366 126</u> (SEDAT) * page 2, lines 4-9; figure 4 *	1,2,7,12	TECHNICAL FIELDS SEARCHED (Int.Cl. ³) A 61 J A 61 M B 65 D
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	<u>FR - A - 1 333 235</u> (NOGIER) * Page 1, column 2, lines 15-26; figures *	1,7,12	
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	<u>US - A - 3 151 617</u> (BAUM) * Column 2, lines 21-25; figures; claim *	1-3,9	
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	<u>GB - A - 811 398</u> (EVERETT) * Page 2, lines 71-74; figure 1 *	10	CATEGORY OF CITED DOCUMENTS X: particularly relevant A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention E: conflicting application D: document cited in the application L: citation for other reasons
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	<u>US - A - 3 540 444</u> (MORELAND) * Figure 8 *	4,7,11	
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	./.		&: member of the same patent family, corresponding document
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
The Hague	15-01-1979	VANRUNXT	

