United States Patent

[11] 3,543,967

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[54] **DEVICE FOR PACKAGING TWO SEPARATE SUBSTANCES**
5 Claims, 5 Drawing Figs.

[52] **U.S. Cl.** **222/136,** 222/145, 222/386
[51] **Int. Cl.** **B67d 5/52**
[50] **Field of Search** ..... 222/386, 136, 145; 128/218(M)

[56] **References Cited**

UNITED STATES PATENTS

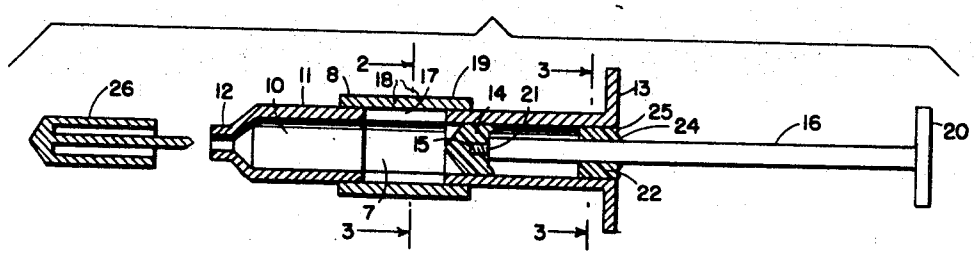
3,016,896	1/1962	Van Sickle	128/218(M)UX
3,058,467	10/1962	Faure	128/218(MX)
3,164,303	1/1965	Trautmann	222/386X
3,291,128	12/1966	O'Neil	222/386X
3,330,282	7/1967	Visser et al.	128/218(MX)
3,348,546	10/1967	Roberts et al.	222/386X

FOREIGN PATENTS

1,099,362	3/1955	France	128/218(M)UX

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ABSTRACT: In a storage device, particularly a hypodermic syringe, the barrel wall is provided at a midpoint with at least two channels which permits passage of the contents from one chamber to the other. The chambers are separated by the piston which is positively locked to a plunger and in storage the piston is sealed to the barrel wall by a breakable seal. The plunger passes through a proximal plug and plunger and plug are sealed with a breakable seal, the construction of plunger and plug enabling rotation of the plunger to break the various seals.



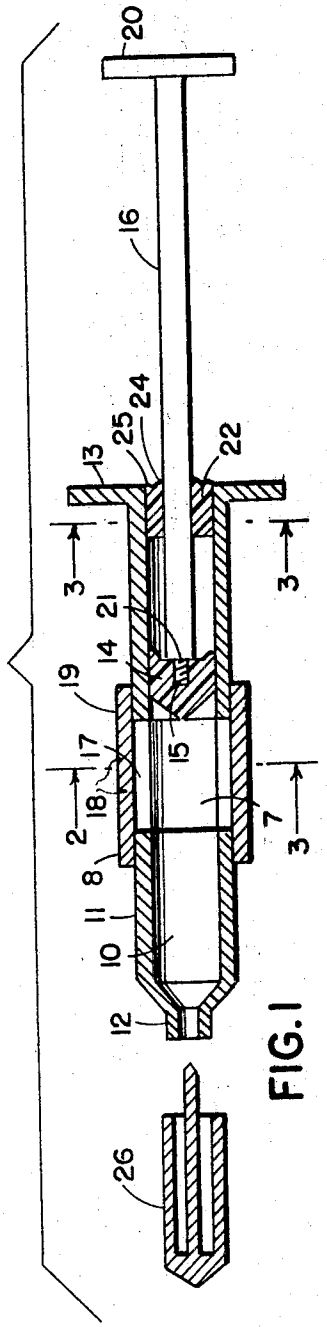


FIG. 1

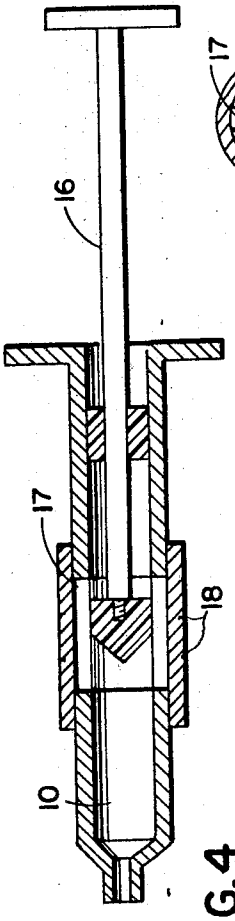


FIG. 4

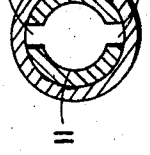


FIG. 2

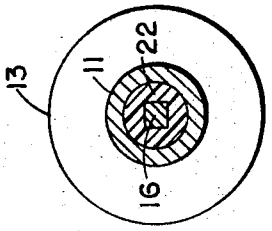


FIG. 3

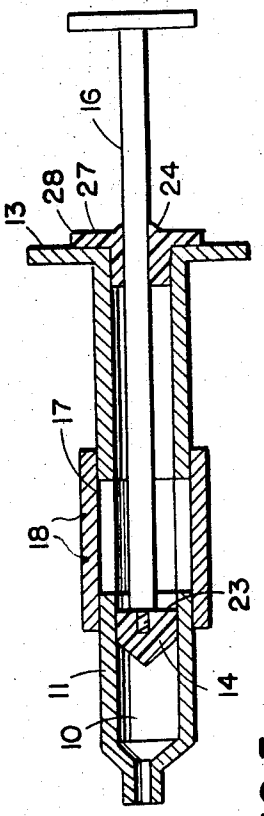


FIG. 5

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DEVICE FOR PACKAGING TWO SEPARATE SUBSTANCES

This invention relates to a device for packaging two separate substances and for intermixing them when desired prior to dispersing the mixture.

While the invention is capable of wider application, it is primarily intended for the manufacture of disposable hypodermic syringes used in injecting various pharmaceutical materials. The disclosure of the present embodiments of the invention will provide guidance for those skilled in the art who may have occasion to apply the invention for other specific purposes.

The giving by injection of pharmaceutical materials can be a complex procedure when a solution of a material, e.g. a drug has to be administered. The contents of sterile vials of drug and solvent have to be transferred from one vial to the other by means of a hypodermic syringe provided with graduations by means of one needle, mixed, withdrawn back into the syringe and a further needle fitted for making the injection; accurate measurements are required to provide the correct dosage. In some cases, the drug can be packaged in single dose cartridges which require special syringes or disposable syringes but this is only practicable for a limited range of materials since few drugs are stable for any length of time in solution or suspension.

Two compartment syringes have been suggested which would contain predetermined amounts of two components for instance drug and diluent. These have the advantage of limiting the number of units, controlling asepsis, permitting precontrolled dosages and avoiding mixture of compatible drugs and diluents until actually required for use.

Such hypodermic syringes have included arrangements in which tow chambers are provided to store separately components prior to use and have a means for passing a liquid component from one chamber to the other immediately prior to use. Thus, in U.S. Pat. No. 2,591,046 an auxiliary floating piston separates the two chambers and grooves are provided in the wall to permit passage of liquid past the piston when the piston moves down the barrel.

Such arrangements have proved difficult to manufacture and, more important, have not provided a satisfactory means of ensuring adequate separation of the two chambers over long periods to prevent escape of a liquid component.

Thus, one requirement for such a syringe, if intended to be disposable, is that the construction be suitable for mass production at relatively low cost. Another requirement is that the device may be relied upon to confine the two components effectively in complete isolation from one another for storage, shipment and shelf life prior to use. It would also be desirable to have a device adapted for easy filling with the two components. Desirably the method of filling should permit the packaging of a wide range of predetermined proportions of two ingredients without altering the essential technique of filling. A further requirement is that the device not only be efficient in mixing the two components but have a simple and obvious mode of operation.

For different uses, the device should desirably be capable of use with various nozzles or needles of specialized configuration.

Hitherto these various requirements have tended to be antagonistic. In particular, the necessity for effective separation of the components has led to increasingly complex structures.

The present invention meets these requirements by providing a positively controlled piston which can be readily positioned and breakably sealed at a given position within a syringe body or shell to separate the body into two compartments. Hereinafter this position will be referred to as the sealed position. A rearward or proximal compartment through which passes a plunger positively locked to the piston is closed at the outer or proximal end by a plug, the plug and plunger being adapted to permit rotation of at least the plunger. One or more breakable seals seal either or both of the plunger and plug. To permit movement from one compartment to another of the component, there is provided in the barrel at a section

spaced from the ends of the barrel and in other than the sections at which the piston is sealed, two or more channels in the wall of length greater than the axial thickness of the piston. Movement of the piston from the sealed position to the channels then permits flow of a component past the piston and thereafter forward movement of the piston past the channels will close the access to the channels and force the contents forward.

The piston can be formed from rubber or a polymeric material or metal and should be a close sliding fit in the barrel to avoid as far as possible escape of components past the piston even after the seals are broken other than by the channels.

The locking of the plunger to the piston can be effected by formation as an integral unit, by forming respective threaded male and female couplings or by any other locking or joining technique which ensures that the plunger is capable of rotating the piston to break the seal.

A breakable seal is provided around the circumference of the piston to seal the piston to the wall of the barrel.

To close the rear compartment there is provided an appropriate proximally located plug which can be an internal plug (i.e. wholly within the barrel) or a flanged plug, the flange surrounding the outer wall. The latter plug is preferred when rearward movement of the plunger is required in operation and can be firmly sealed to the barrel. This plug can be of similar composition to the piston. The plunger can be of circular or noncircular cross section though a circular cross section is necessary with the flanged plug. When a plunger of noncircular cross section is employed with an internal plug, said plug must also be provided with a breakable seal to permit rotation of the plug. The plug will tend to move along the barrel with the plunger assisting in urging of the contents of the rear compartment forwardly.

The plunger is sealed to the rearward plug and the rearward plug is sealed to the barrel wall. When the rearward plug is an internal plug, the seals must be such as to permit rotation of the plunger. Thus, a plunger of round cross section could be breakably sealed to the plug and the plug firmly sealed to the barrel wall. For convenience, however, the same sealing material will be employed to seal the plunger to the plug and the plug to the barrel wall.

The forward or distal end of the barrel can be sealed by any means suitable to a hypodermic syringe for instance an injection cannula can be formed by a needle permanently mounted and a protective cover thereover with a breakable seal. Alternatively, an occlusive cap of appropriate construction can be provided to close the forward end of the barrel.

The breakable seal which is an essential feature of the invention can be provided by any of the techniques at present available in the art. At present, breakable seals are widely used for instance in sealing a protective sheath to hypodermic syringes having attached needles. Such seals have been suggested for sealing of plungers of disposable syringes to the plugs sealing the ends of the barrels. However, there has not, hitherto, been disclosed the sealing of an internal portion of a syringe with a view to preventing escape of a component past the piston. A tight fit between barrel and piston has been described in the art as a "sealing relationship" but where relative movement is permitted there can never be a sufficient hermetic sealing between compartments as is required for storage. The positive seal of the present invention is required. The seal is generally readily formed by application of a solution in a readily evaporable organic solvent of a polymer which is usually a synthetic polymeric material to the point to be sealed. On evaporation of the solvent, a thin layer of the polymer is left which is resistant to rupture except by the rotation of the piston. Other methods of applying the seals are readily apparent to those skilled in the art. The choice of the polymer will depend on the location of the seal and the materials with which it is to be in contact but generally it will be inert and resistant to passage of vapor in film form. Different polymers could be used for seals at different places in the

device. The essential feature of all of the seals whether breakable or permanent is that they provide a hermetic sealing for the contents of the barrel and can maintain said contents sterile.

The channels in the walls of the barrel are generally located at a midpoint in the length of the barrel and the ends of the channels are sufficiently spaced from the ends of the barrel to permit the piston in the sealed position to form a sealed chamber either forward or rearward of the channels and, when the device is ready to eject the contents from the barrel, to permit the piston in moving forward to close off channels to form a forward closed portion sufficient to hold the contents to be ejected. The lengths of the channels must be greater than the axial length of the piston.

The channels can be formed as an integral part of the barrel in the manufacture thereof but in a preferred feature of the invention the channels can be formed by forming or cutting slots on the walls of the barrel which are sealed externally most suitably by a sleeve.

Further features of the invention will appear from the following description of specific embodiments which are only, however, intended to be illustrative of the invention.

In the drawings:

FIG. 1 is longitudinal sectional view of one embodiment of the invention;

FIG. 2 is a transverse section on the line 2–2 of FIG. 1 showing the channelled section;

FIG. 3 is a transverse section on the line 3–3 of FIG. 1 showing the occlusive plug;

FIG. 4 is longitudinal section of the embodiment of FIG. 1 showing the parts during operation at the time of mixing.

FIG. 5 is a longitudinal section of an alternative embodiment of the invention.

The principal parts of the device include a rigid cylindrical barrel 10 with walls 11 shaped at the forward i.e. distal end to a hub 12 that will accommodate a standard hypodermic needle of the "push-on" or "lock" type. The walls can be formed of glass or of plastic materials customary in the art. Alternatively a hollow needle may be permanently fused onto the hub or tip. The indicated friction-joint structure for attachment of a needle to the needle hub could be replaced by an external screw thread on the hub with complementary screw threads on a needle or dispensing tip. Other and functional equivalent mating means such as snap-on joints or bayonet joints can be provided. The rearward or proximal end of the barrel is open and surrounded by a flange 13 to accommodate the fingers during injection. If desired, this flange can be omitted or an alternative structure provided to be gripped by the fingers. The barrel is divided into two separate compartments by a piston 14 of soft resilient material such as rubber or suitable plastic. One of the compartments can be storage of a powdered drug component, the other for storage of a liquid drug component. A blind aperture 15 opens into the rearward face of the piston 14 and is internally threaded or otherwise formed to key with a complementary formation on the distal end of a plunger 16 so that the respectively female and male couplings of piston and plunger can be readily and firmly locked together during assembly and filling of the device.

Appropriately placed in the walls 11 of the barrel and parallel with its main axis are two diametrically opposed channels 17 whose axial lengths are longer than the axial length of the piston 14, typically about one-and-a-half times the piston length. Their width and depth are not critical providing they are sufficient to permit ready ready passage of liquid from one compartment to the other, and the free flow of air in the opposite direction when the piston is moved to a position midway in the channels as shown in FIG. 4. More than two channels could be employed if desired for any reason. Two is usually an adequate number. For ease in positioning, this position for the piston may be suitably indicated by scribe marks 18 on the barrel wall. These channels could be constructed by moulding them integrally with the barrel itself. However, in the preferred embodiment illustrated they are readily constructed by cutting slots and sealing. Two diametrically opposed slots of suitable length and breadth as described above are molded or cut through the entire thickness of the barrel wall 11; they are then covered by slipping over the barrel as sleeve 19 that can be fused or otherwise permanently fixed in place. This method of construction provides a depth of each channel identical to the thickness of the barrel wall.

In FIG. 2 there is shown a cross section of the barrel in the region of the channels showing their diametrically opposed positions, their formation from apertures extending through the barrel wall and the sleeve properly positioned around the barrel externally and fused or otherwise fixed there.

In the filled device, one or other of the drug components, usually the dry powder, is placed in the forward part of the barrel. The piston 14 is located within the barrel in a position either rearward (most usually) or forward (less usually) of the channels, so as to close the forward compartment completely.

At one end of the plunger 16 is a pushbutton 20 or flange to accommodate the thumb while making the injection. At the other end is the threaded (or other suitably formed) tip 21 that can be made readily to lock with the piston 14 as described above. The length of the plunger must be such that it can be used to push the piston all the way down to the forward tip of the syringe barrel to eject the contents for instance in making an injection. Alternatively, the length of the piston can be such as just to extend to the outer edge of the plug with means provided to lock an extension to the plunger immediately prior to use to provide the desired length. The cross section of the plunger (as illustrated in FIG. 3) may be of any convenient or desired shape.

At the rearward end of the barrel, i.e. proximal end, is provided an internal plug 22. This internal plug can be made of similar material to that used in manufacture of the piston 14 and may indeed have the same general form except that it has a through aperture to accommodate passage of the plunger. The type of plug just described is particularly suitable where the piston has to be pushed into the channelled region. Where the storage position of the piston is forward of the bypass as depicted in FIG. 5, the alternative type of end closure or plug also shown in FIG. 5 and described below is to be preferred.

In FIG. 3 is shown in cross section through the barrel wall, rear plug and plunger after assembly has been completed.

The shape of through aperture in the rearward plug corresponds exactly with the cross section of the plunger. Where the cross section of the plunger and the corresponding aperture in the plug are other than circular any twisting or rotation of the piston rod will be accompanied by a corresponding movement of the plug shown in FIG. 1.

When the device is filled with the components a seal 23 is provided about the circumference of the piston to seal to the barrel wall 11. This breakable seal is a readily breakable seal of the type commercially available and is obtained, for instance by application of a solution of a vinyl polymer in an ethyl acetate solvent and drying. The plunger is sealed to the rearward plug 22 by a seal 24 and the plug is sealed to the barrel by a breakable seal 25.

The device is filled by first sealing the distal end either by a needle or the closure 26 which is hermetically sealed. If prior to assembly and filling of the device a hypodermic needle is fitted to the hub of the syringe the needle should be covered by a protective sheath, lightly sealed in place with a breakable seal, to protect the needle point and maintain sterility. If a hypodermic needle is not to be fitted during filling and assembly, then the syringe hub should, before filling of the forward chamber, be covered with the occlusive cap 26 which incorporates an integral stylet to plug the relatively large orifice in the syringe tip and prevents loss or contamination of the drug component. This occlusive cap is also of course hermetically sealed in place with a breakable seal as described for the alternative needle sheath. The component for the forward compartment is then loaded through the rear end of the barrel. The piston 14 either mounted on the plunger 16 or unmounted, usually the latter, is then inserted and the piston

located on the barrel either forwardly or rearwardly of the channels.

A sealing material is then applied about the piston to form the breakable hermetic seal **24** between the piston and barrel wall. Thus, the device provides a simple method of loading one compartment and closing while giving access to the rear of the piston to effect sealing. After the forward compartment of the device has been filled with the drug component, with the piston placed in position to separate the two compartments and hermetically sealed there in the manner described, the second and final part of the filling and assembly process for the device can be completed. Where the plunger is not already mounted in the piston, the end plug is slipped on to the plunger and drawn well back toward the thumb pushbutton **10**. The threaded tip is then lightly screwed into the threaded aperture in the properly positioned and sealed piston **4**. For different construction of plunger and piston this procedure would be modified. The rear compartment is then filled with the remaining drug component and the end plug is then slid forward along the plunger into position just inside the rear opening of the syringe barrel. If the liquid drug component is to occupy the rear chamber (as may be preferred in most instances) the said liquid may be filled into the rear compartment as a first step, and then the screw tip of the plunger inserted and mated with the piston after which the end plug is slid into position as before. The joints between the end plug and the barrel wall, and between the plug and the plunger are hermetically sealed with a suitable sealant material as was used for sealing the piston or a different sealant can be used. The light seal thus provided between the plug and the barrel wall can of course readily be broken by twisting or rotating the plunger when the device is about to be used for making an injection.

FIG. **5** shows an alternative embodiment with similar items labeled with the same numbers. Only the principal items and differing features are indicated. The piston **14** is positioned forward of the channels **17**: in this assembly the piston has to be drawn backwards into the channeled region to allow mixing of the drug components when the syringe is being brought into use. If an end plug such as the one described above and pictured in FIG. **1** were to be used there would be a serious risk of pulling it out of the syringe barrel while drawing the piston backward into the mixing position, this causing spillage and loss of drug component. To obviate this possibility the alternate type of end closure shown in FIG. **5** should be employed. This closure consists of a flanged plug **27** with a through aperture for passage of the plunger **16**. The stopper flange **28** is firmly sealed to the syringe flange **13** with an unbreakable seal after filling, so that the stopper cannot accidentally be pulled out.

The joint between the stopper and the plunger is hermetically sealed with a breakable seal **24** as before. It will be apparent that for this type of assembly a plunger of circular cross section must be employed. The piston is sealed by seal **23** to the wall **11** of the barrel.

Whichever method of assembly is adopted (FIG. **1** or FIG. **5**) the syringe is operated as follows:

With the barrel **10** grasped firmly between the fingers of one hand and the plunger **16** firmly grasped in the other the plunger **16** is twisted in a clockwise direction for approximately half a turn. Because the piston **14** is positively locked to and functionally integral with the plunger the seal **23** maintaining the piston in the storage position is broken simultaneously by this clockwise twisting of the plunger. Depending on the construction of plunger and rearward plug a seal either **24** or **25** is also broken to permit forward movement of the plunger. With the seals broken, the piston can then be moved easily into position intermediate between the ends of the channels **17** as illustrated in FIG. **4**, enabling the liquid drug component to flow via the lower channel into the chamber containing the powdered drug which will dissolve or become suspended as the case may be; at the same time air is vented via the upper channel between the two chambers. Because the piston, which is also the dividing wall between the two chambers, is under positive control at all times it is very simple to move the piston into the exact correct position in relation to the bypasses for mixing of the drugs to take place (indicated by scribed lines **18** on the barrel wall as shown in FIG. **1**), or if the mark is accidentally overshot it is a very simple matter to make the necessary fine readjustment or correction instead of having to abandon as useless and spoiled both the syringe and its contents.

Depending upon the sequence in which the drug components were stored in the syringe mixing will take place in either the forward or in the rear compartment. If in the rear, the mixed solution or suspension is simply flowed through a channel into the forward compartment, ready to make the injection. The occlusive cap **26** or a needle sheath is removed from the tip of the syringe as the case may be, by twisting off; a hypodermic needle is attached if not already fitted, and after pushing the piston forward to expel any air trapped with the injectable contents, as is standard practice the injection is completed in the usual way and the syringe container can be discarded.

I claim:

1. A hypodermic syringe body for separately storing two components permitting mixing in the syringe body and dispensing, comprising:

a barrel with a distal portion to receive a dispensing means, said barrel having at least two slots in the walls thereof, the ends of said slots being spaced from the ends of the barrel;

a piston slideably mounted within said barrel, of axial length shorter than the axial distance between the ends of the slots and positioned to separate said barrel into two non-communicating chambers said piston having a close sliding fit in said barrel and when adjacent to said slots permitting ready flow of a liquid therethrough;

a sleeve sealed to the outer wall to close said slots, the channel formed by said slots being of dimensions permitting ready flow of a liquid past the piston;

a rupturable hermetic positive seal of polymeric material applied to seal the piston to the barrel and resistant to rupture except by rotation of the piston;

a plunger positively locked to said piston, extending proximal thereof;

a proximal plug through which said plunger extends said plug and said plunger being constructed to permit rotation of at least said plunger in said barrel;

a hermetic seal between said plunger and said plug; and

a hermetic seal between said plug and said barrel, at least one of said last two seals being a rupturable seal of polymeric material applied to form said seal.

2. A hypodermic syringe body according to claim **1** wherein the proximal plug lies within the barrel and the seal between said plug and the barrel is rupturable.

3. A hypodermic syringe body according to claim **1** wherein said seal between said proximal plug and said barrel is an unbreakable seal, and said plunger is of circular cross section.

4. A hypodermic syringe body according to claim **3** wherein a flange extends circumferentially around the proximal end of the barrel, a flange is provided on said plug to lie adjacent to said barrel flange and an unbreakable seal is provided between said barrel flange and said plug flange.

5. A hypodermic syringe body according to claim **1** wherein the barrel has two slots diametrically opposed.