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**A61M 5/315** (2006.01) A61M 5/28 (2006.01)

(52) UK CL (Edition X ):
**A5R** RGM RGP

(56) Documents Cited:
**GB 1275565 A**
**FR 002729573 A**
**US 5520642 A**
**US 2524362 A**
**EP 1386628 A2**
**JP 2002172166 A**
**US 4936830 A**

(58) Field of Search:
UK CL (Edition X ) **A5R**
INT CL[7] **A61M**
Other:

(54) Abstract Title: **Injection device with a piston having needle and plunger attachments.**

(57) The invention relates to an injection device that may be used with standard pharmaceutical vials, or other similar type of container, for the dispensing, or administration of the contents of the container without the use of a syringe. When assembled, the injection device includes a container 2 having a base and an open neck. An internal piston 10 is located within the container 2 and has an orifice 28. A needle 22 is releasably secured to the main body 14 of the internal piston 10 in fluid communication with the orifice 28. A plunger rod 26 is also releasably secured to the main body 14. Both the needle 22 and the plunger rod 26 extend in the same direction through the open neck of the container 2. Movement of the internal piston towards the base of the container 2 therefore forces that part of the contents of the container that is below the internal piston 10 though the orifice and out of the needle 22.

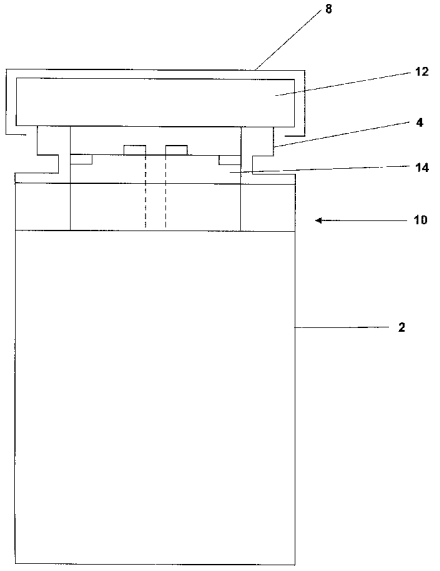


Figure 4

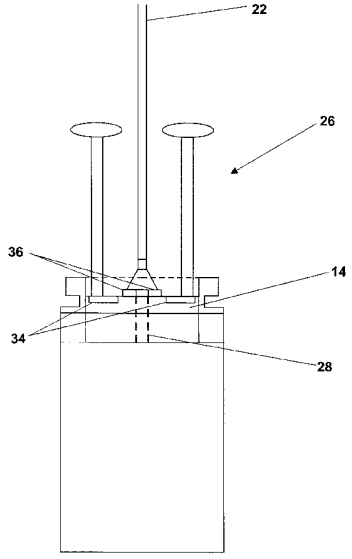


Figure 6

At least one drawing originally filed was informal and the print reproduced here is taken from a later filed formal copy.

This print takes account of replacement documents submitted after the date of filing to enable the application to comply with the formal requirements of the Patents Rules 1995



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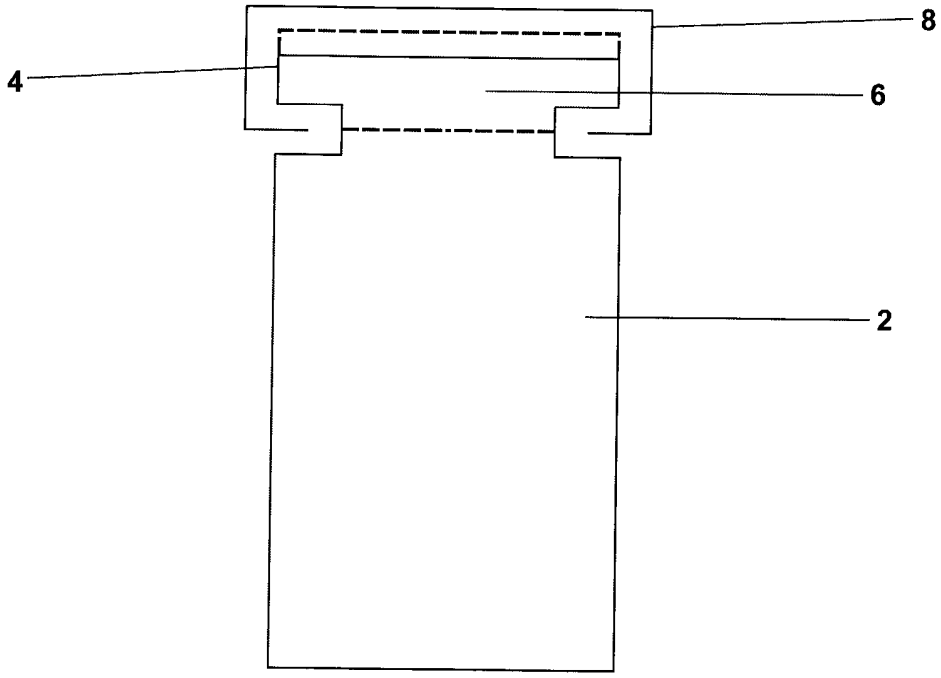


Figure 1

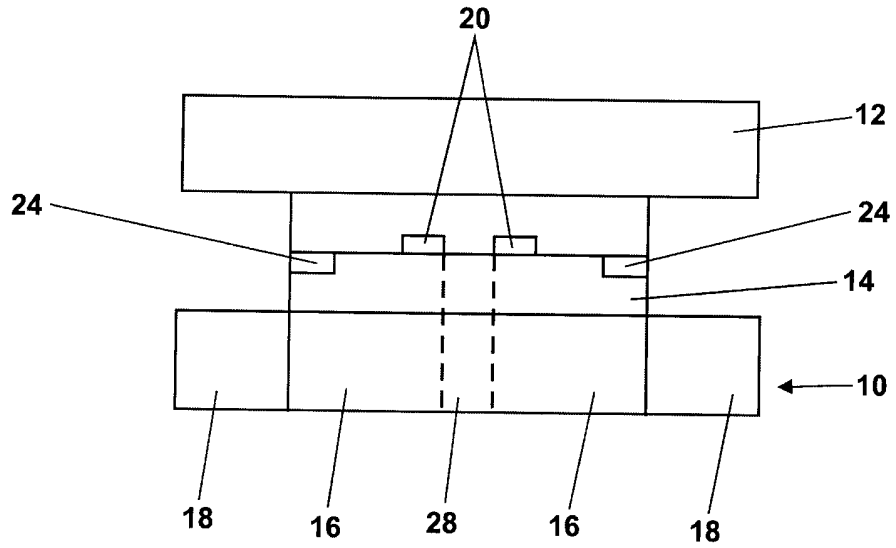


Figure 2

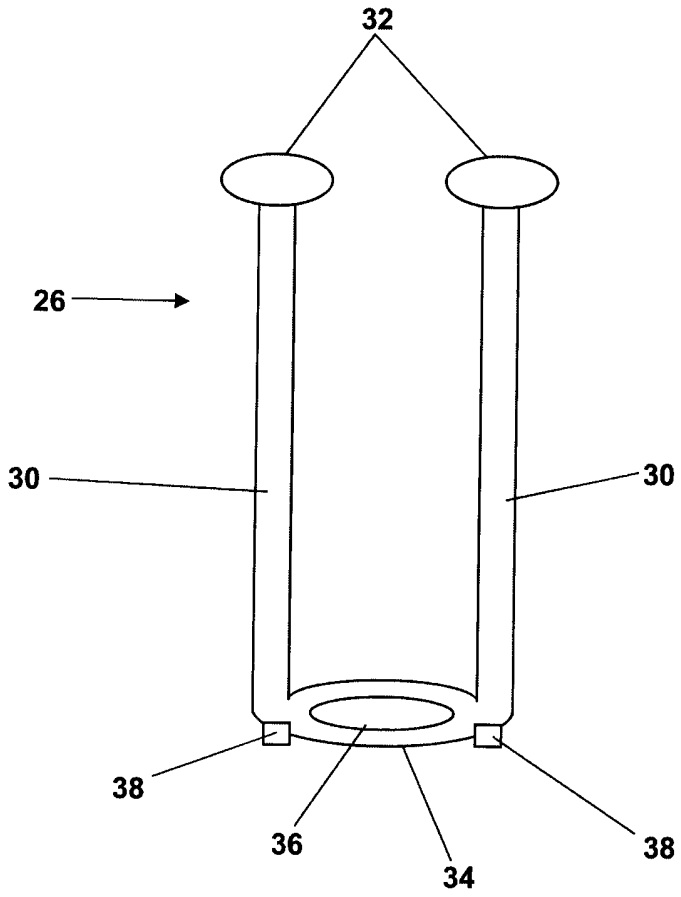


Figure 3

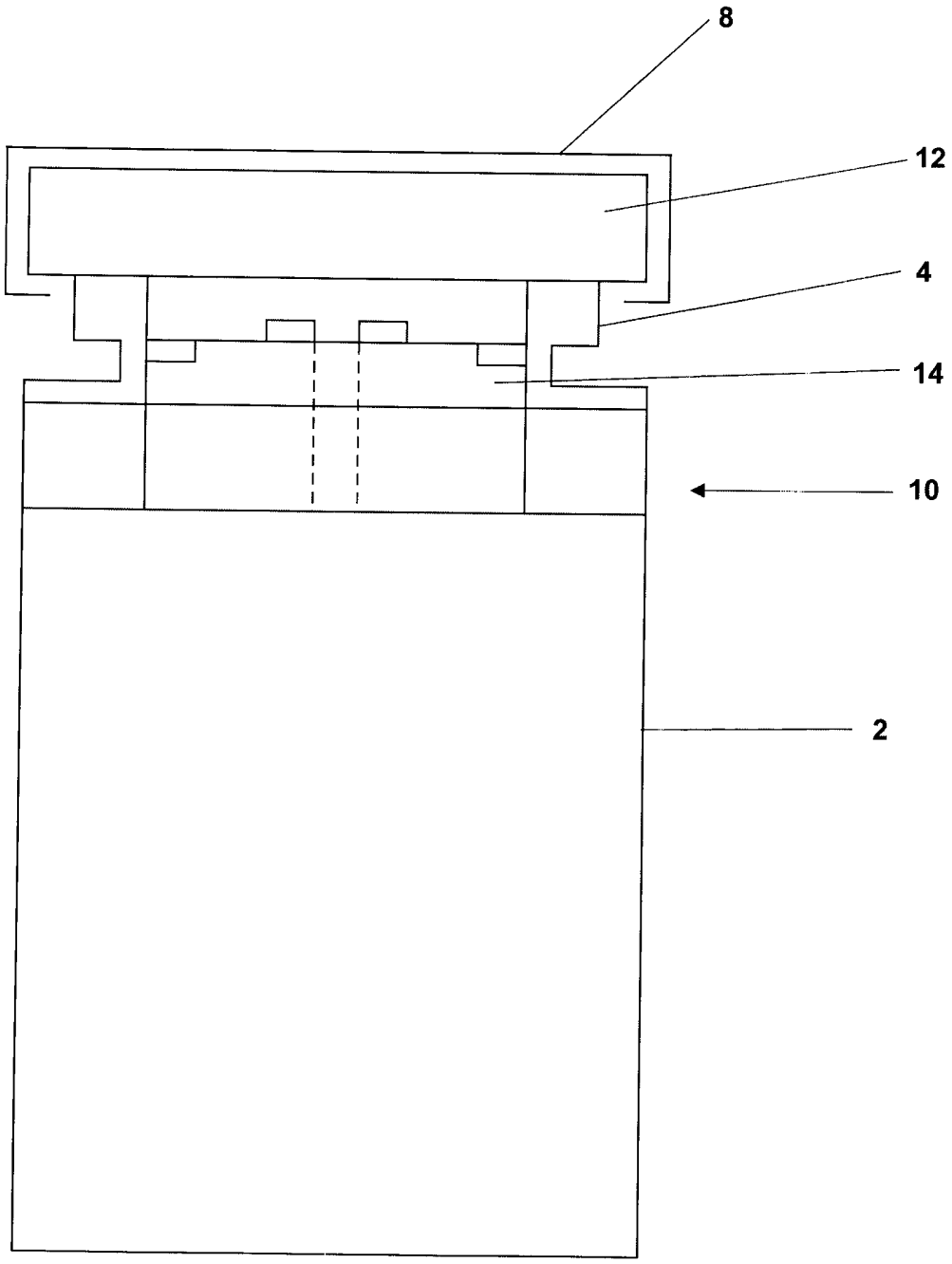


Figure 4

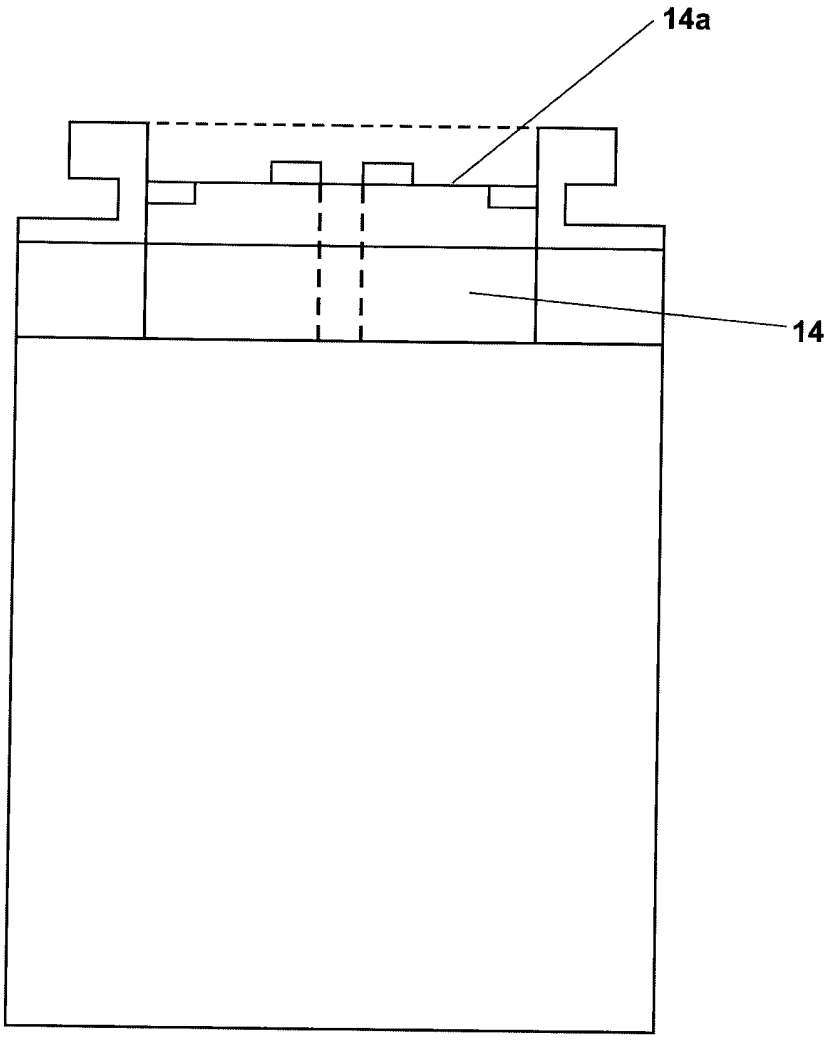


Figure 5

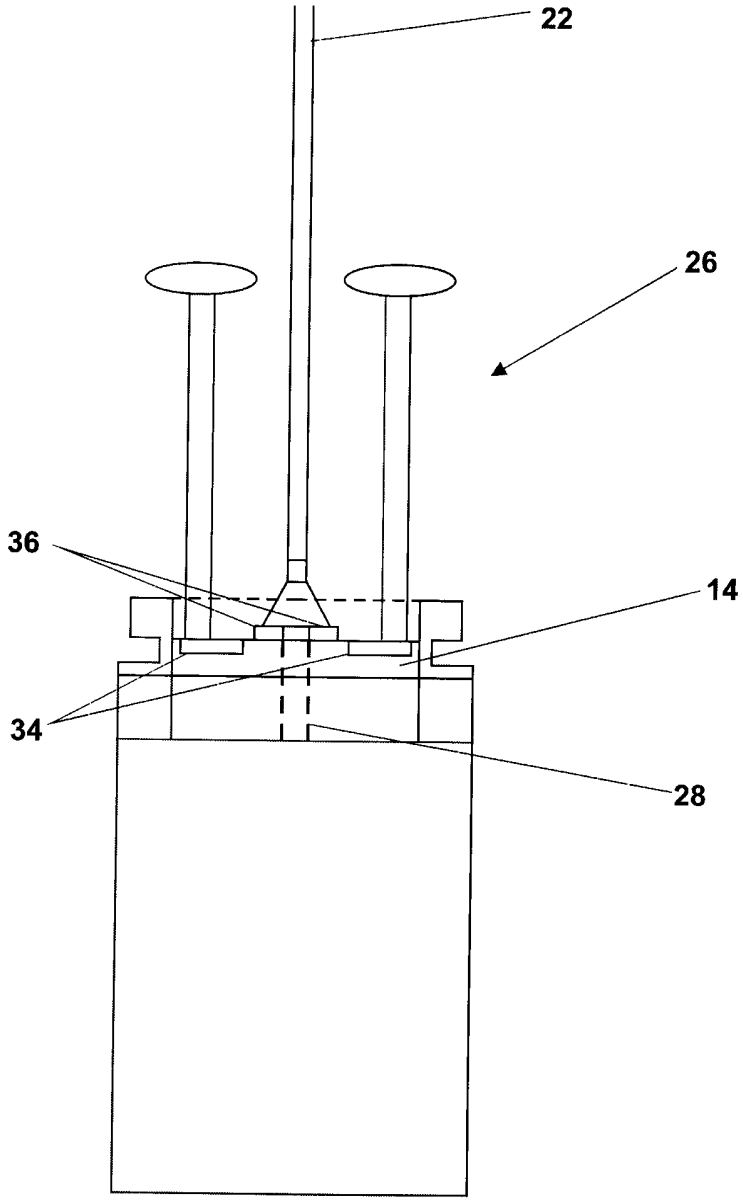


Figure 6

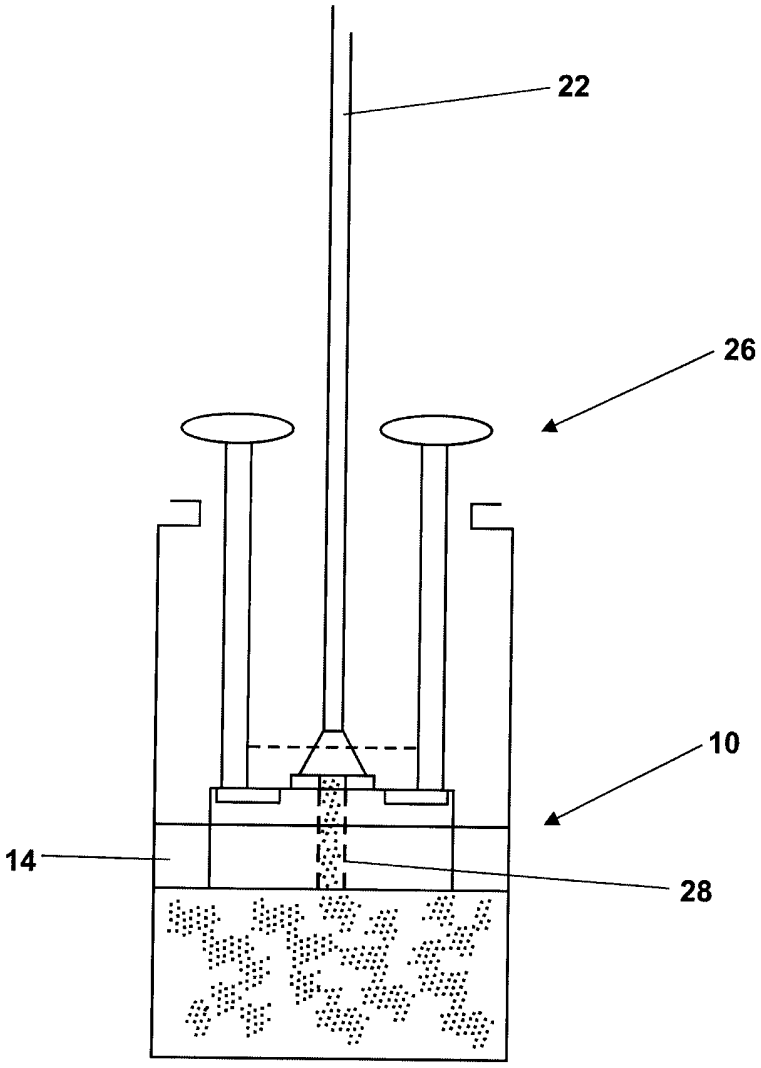


Figure 7

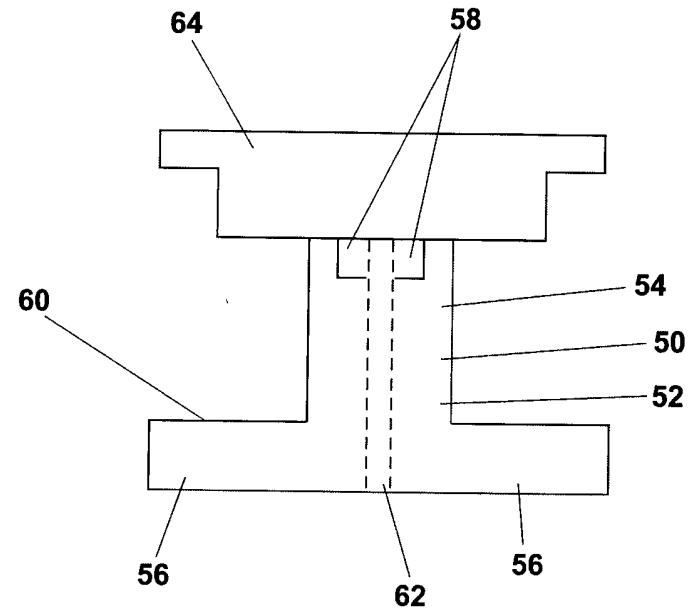


Figure 8

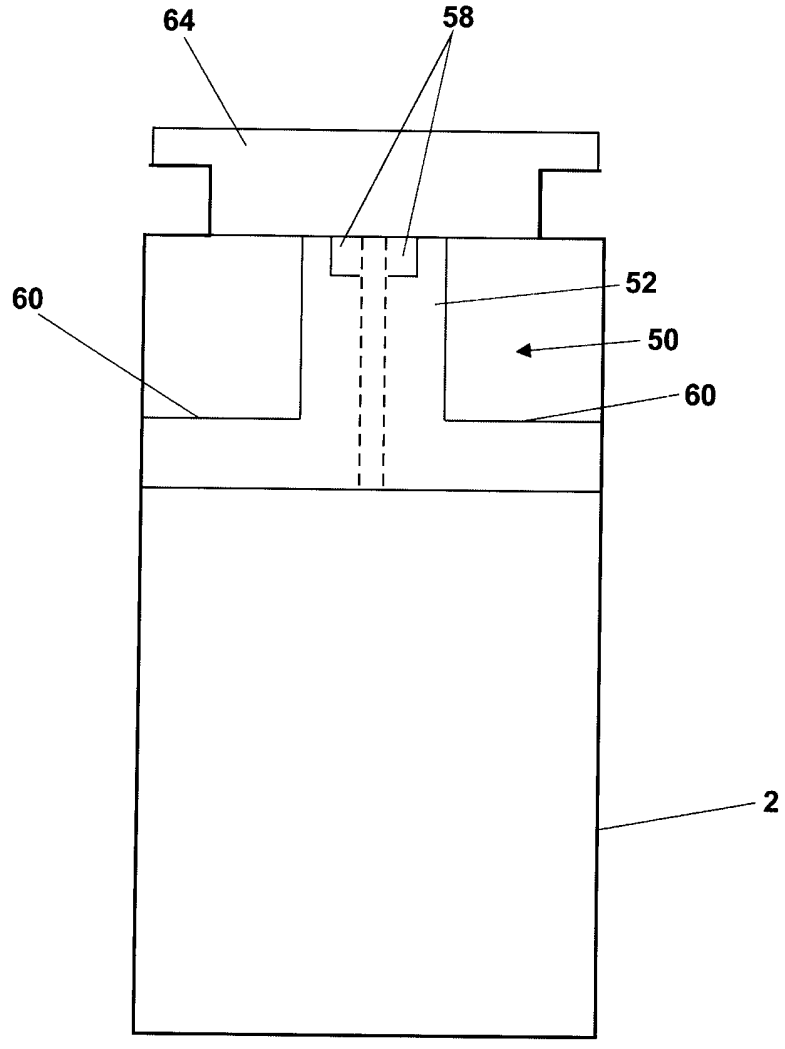


Figure 9

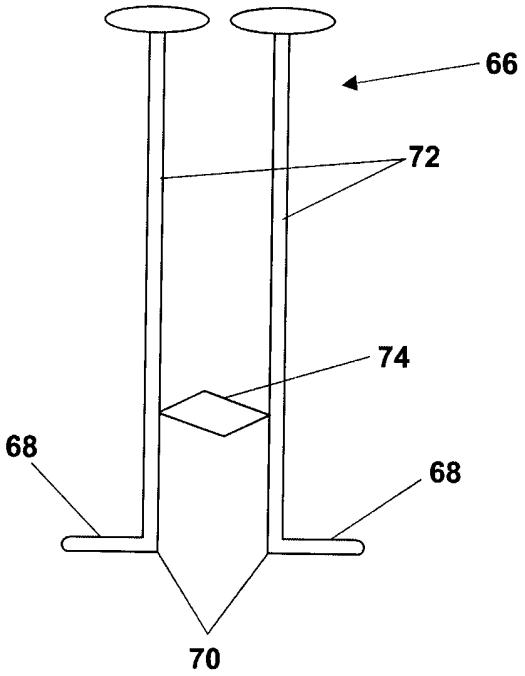


Figure 10

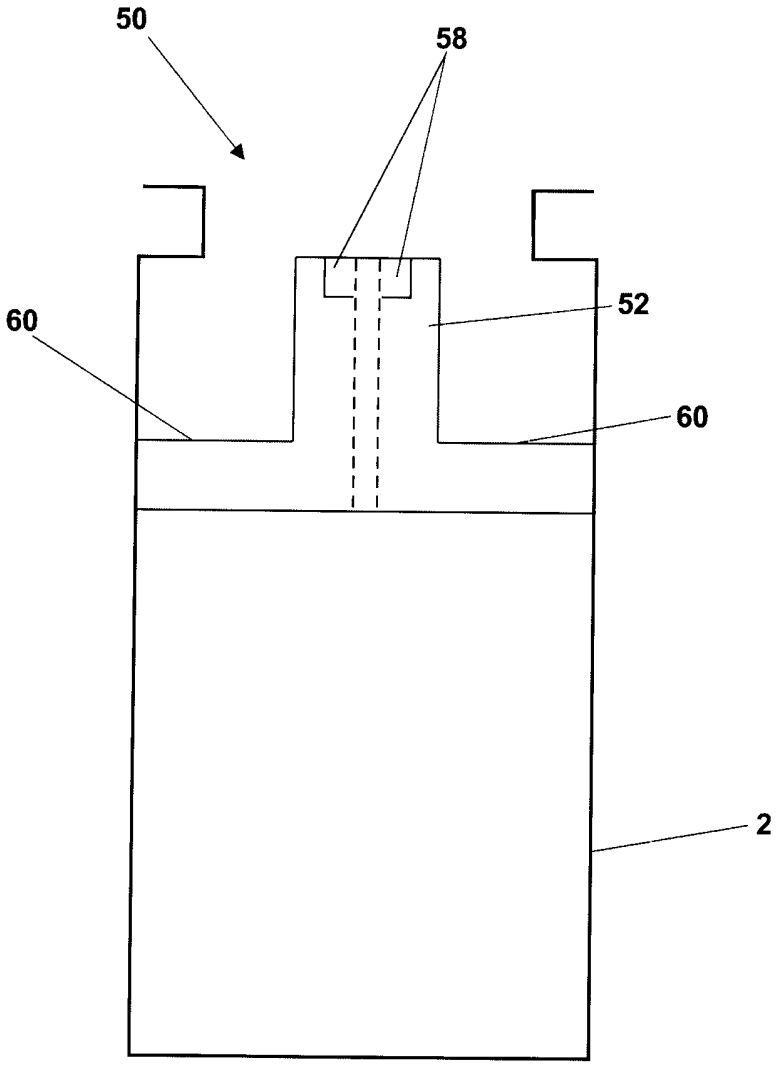


Figure 11

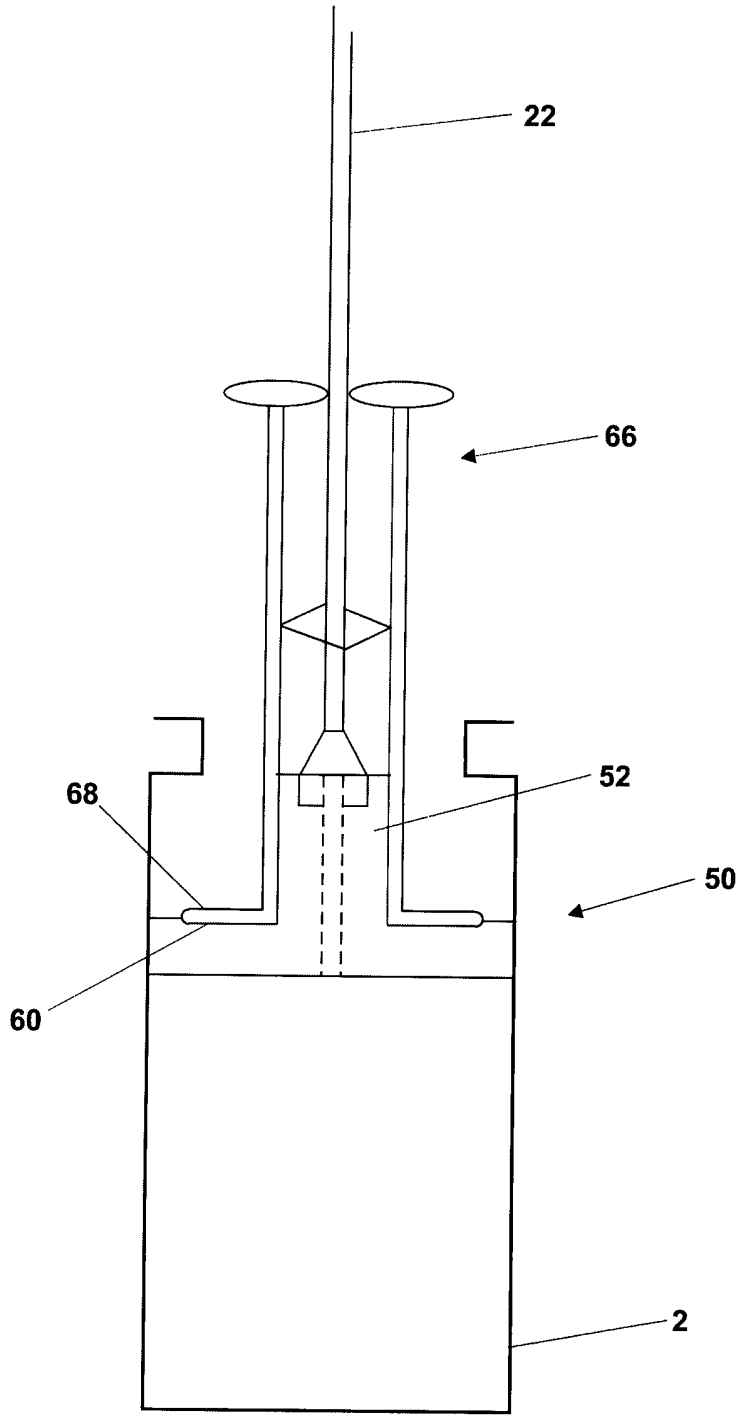


Figure 12

# TITLE

Injection devices

# DESCRIPTION

## Technical Field

The invention relates to the administration of drugs to a patient, and in particular to the administration of drugs by injection directly from a pre-filled vial or container, without the need for the use of a syringe. The term "drug" refers to any biologically active substance that needs to be delivered into the bloodstream of a patient, whether therapeutic or not, for example pharmaceuticals, vaccines and proteins. The patient may be human or animal.

## Background

Drugs have been administered to patients by intravenous injection and infusion dating back to 1670. The first syringe and needle combination able to pierce skin was developed by Charles Gabriel Parvaz, a French surgeon, and Alexander Wood, a Scottish physician, in 1853. Its first use was to inject Morphine as a painkiller. Between 1949 and 1950 Arthur E. Smith received 8 US patents for a disposable syringe, and in 1954 Becton, Dickinson and Company developed the first mass produced glass syringe with needle. This was used for the administration of Salk polio vaccine to a million American children. In 1955, Roehr Products developed the first plastic disposable hypodermic syringe called the Monoject, and in 1956 Colin Murdoch, a Pharmacist from Timaru, New Zealand patented a plastic disposable syringe to replace the glass syringe. The first mass produced plastic disposable syringes were introduced under the brand 'Plastipak', by Beckton Dickinson in 1961.

The primary advantages offered by syringes for the administration of drugs include:

- The immediate delivery of the drug into the blood stream, hence immediate onset of therapeutic action.
- By-passing the first-pass metabolism of drugs that take place in the liver where drugs are administered by routes such as oral administration.

- Drugs inactivated by gastrointestinal enzymes or gastrointestinal pH can be delivered directly into the systemic circulation.
- Easy to predict pharmacokinetic profiles, thus therapeutic efficacy of administered dose.

Drugs are generally administered using needles by removing the required dose from containers filled with the appropriate drug. These containers are usually glass vials or glass ampoules. In the case of ampoules the neck of the ampoule is snapped open, a needle is attached to a syringe and the required dose is drawn into the syringe. Any excess product and air is removed and the dose is injected into the patient. In the case of vials, the needle is used to pierce the rubber septum that separates the product from the external environment and the product is drawn into the syringe and administered in the same way as described for ampoules.

Some of the problems associated with the use of conventional syringes are as follows:

- There are a number of steps involved for administering the drug using a syringe, from a vial or ampoule. This has the potential for introducing contamination and compromising the aseptic integrity of the product.
- There is potential for dosing errors in that the physician or nurse or patient is required to measure out the required dose.
- In most cases the vials or ampoules must be over-filled by up to 25% in order to ensure the desired dose may be withdrawn. In the case of high value drugs, or scarce biologics, this could be cost-prohibitive and economically unsound.

These problems can be overcome by the use of pre-filled syringes which contain the requisite dose for administration and generally already have a needle assembled (aseptically) such that aseptic integrity of the product or container is not compromised during or prior to administration. Some of the advantages of pre-filled syringes are as follows:

- Accurate dosing.
- Single/reduced operation steps, thus allowing for rapid administration in emergencies.
- Reduced risk of microbiological contamination.
- Significant reductions in degree of over-fill required.
- Generally non-re-usable thus minimizing risk of disease transmission.

There are currently numerous manufacturers and suppliers of pre-filled syringes to the pharmaceutical industry for the packaging of drugs. The following are examples of some of the types of pre-filled syringes that are currently available.

- Lovenox Prefilled Syringe with an automatic safety device, in compliance with the Needlestick Safety and Prevention Act. The device allows single handed activation, and is the best selling low-molecular-weight heparin administration system in the world.
- AVONEX pre-filled syringes providing once a week dosing of Interferon beta-1a for the treatment of Multiple Sclerosis.
- Beckton Dickinson:
    - BD Uniject – Pre-fill injection device, easy to use, single use, non-reusable system;
    - BD Hypak – Glass pre-fillable syringe;
    - BD Readyfill - Glass pre-fillable syringe with baked silicon and needle isolation;
    - BD Hypoint – Pre-fillable syringe with attachable needle, and tamper evident;
    - BD Sterifill – Plastik pre-fillable syringe composed of high purity amorphous plastic material; and
    - BD Intera – Spring based retracting syringe with a detachable needle.

Despite the advantages imparted by the use of pre-filled syringes, one of the major limitations has been the huge investments in new technology required for processing drugs into pre-filled syringes rather than into conventional ampoules or vials.

Furthermore, for existing marketed products the move to pre-filled syringes requires a plethora of re-validation work to ascertain that the move to new packaging components and materials does not adversely affect the drug. These materials generally include new types of elastomeric materials from which syringe plunger tips are composed, and silicone films applied to impart lubricity. Vials and stoppers for example do not have any silicone on them thus it is necessary to determine what effect this has on the drug where pre-filled syringes are used.

In an attempt to minimise the huge investments in processing equipment, Duoject Medical Systems Incorporated of Quebec Canada, took on the challenge of developing a system that allows pre-filled syringes to be filled using existing processing technologies, thus negating the need for new processing technologies and installations. This was achieved by developing the Vari-Vial™ system where the bottom of the traditional vial is replaced with an elastomeric stopper that functions as a plunger or internal piston and seals the drug in the vial. The vial is filled and capped using standard processing equipment. On administration, a needle is securely attached to the top of the vial, and a plunger rod is attached to the base of the vial so that the system can be operated like a standard syringe.

**The Invention**

The invention provides an injection device as described in claim 1 to allow the administration of drugs into patients by injection directly from a pre-filled vial or container, and without the use of a syringe. The injection device also allows for the processing of the pre-filled container using standard drug filling and processing technologies. However, it will be readily appreciated that the injection device may also be processed using specialist filling technologies that are designed specifically for the use with the present invention.

Further, preferred features of the invention are defined in the subclaims.

The injection device can be used to administer any type of drug, therapeutic, agent, vaccine, biotechnology derived protein or macromolecule, to humans or animals,

intended for administration by injection. Furthermore, the injection device may be used for the purpose of dispensing any desired volume of the contents of the appropriate container for purposes of further processing, which could include product reconstitution.

**The drawings**

Figure 1 is a diagram of a standard vial or container used as a primary package for drugs intended for administration by injection.

Figure 2 is a schematic of a first type of internal piston that forms part of the injection device of the present invention and shown in combination with a stopper.

Figure 3 is a schematic of a plunger rod for use with the internal piston of Figure 2.

Figure 4 is a schematic of the internal piston of Figure 2 inserted into a standard container.

Figure 5 is a schematic of the internal piston of Figure 2 inserted into a standard container and with the outer cap of the standard container and the inner stopper removed.

Figure 6 is a schematic of the internal piston of Figure 2 inserted into a standard container and with the plunger rod of Figure 3 and a needle attached.

Figure 7 is a schematic of the internal piston of Figure 2 inserted into a standard container with the plunger rod depressed.

Figure 8 is a schematic of a second type of internal piston that forms part of the injection device of the present invention and shown in combination with a stopper.

Figure 9 is a schematic of the internal piston of Figure 8 inserted into a standard container.

Figure 10 is a schematic of an alternative plunger rod for use with the internal piston of Figure 9.

Figure 11 is a schematic of the internal piston of Figure 8 with the inner stopper removed.

Figure 12 is a schematic of the internal piston of Figure 8 inserted into a standard container and with the alternative plunger rod of Figure 10 and needle attached.

**Detailed description of the drawings**

Figure 1 shows a standard vial or container 2 for holding a drug or other product for administration by injection. The container 2 can be made of glass or a plastics material. The container 2 will generally be manufactured by moulding a tube of glass or plastics material to the desired shape using high temperature burners. The shape of the container 2 may be altered by changing the tooling used in the manufacturing process. The container 2 has an open neck 4 that is shaped to allow the secure seating of an elastometic closure or stopper 6. A cap 8 (usually made of aluminium) is placed over the neck 4 of the container 2 and crimped into position to secure the stopper 6. The stopper 6 provides a barrier between the drug or other product inside the container 2 and the ingress of gasses or microbes from the external environment. The stopper 6 also prevents the seepage of the drug or other product from the container 2.

Figure 2 shows an internal piston 10 that is used in conjunction with an elastomeric stopper to seal the neck of a standard container. The internal piston 10 can be used with existing processing technologies with only minor adjustments being needed to the closure feed bowl, feed track and insertion arm (the latter being responsible for inserting the stopper in to the neck of the container).

The internal piston 10 is used in combination with a standard elastomeric stopper 12 of the type shown in Figure 1. However, it will be readily appreciated that the stopper can be specially designed for use with the internal piston. The stopper 12 cushions the outer aluminium cap 8 (Figure 4) and provides an additional seal. The stopper 12 is releasably secured to the main body 14 of the internal piston using an adhesive. The stopper 12 can therefore be removed from the main body 14 by applying a moderate force to break the adhesive. The stopper may also be secured using a mechanical means such as an interlocking connection, for example. In this case, the stopper can be removed from the main body by manually unlocking the two components parts.

The main body 14 of the internal piston 10 includes a rigid core 16 and a flexible peripheral or edge region 18. Accordingly, the internal piston 10 is constructed such

that it can be inserted into the neck of a standard container with only moderate force. The edge region 18 will flex to allow the internal piston 10 to pass through the neck of the container and then deform back to its original shape to form a seal with the inner wall of the container 2.

The internal piston 10 can be formed as a single construction or from several parts adhered together to allow the formation of the rigid core 16 and flexible peripheral edge region 18. The internal piston 10 will be sized and shaped so as to allow minimal excess fill in the container, and the maximum volume of contents to be expelled from the container, on activation of the internal piston.

The main body 14 of the internal piston 10 includes needle attachment points 20 to which a needle 22 (Figure 6) can be releasably attached. The needle attachment points 20 can allow the secure attachment of a standard commercially available needle 22. Alternatively they may allow the attachment of a needle specially designed for use with the injection device.

The main body 14 also includes plunger rod attachment points 24 to which a plunger rod 26 (Figures 3 and 6) can be releasably attached.

An axially extending orifice 28 is formed in the main body 14. The orifice 28 may be open, or may contain a plug (not shown) that is removed from the external side of the internal piston 10 prior to use. The plug is preferably made of a suitable material, which may be of natural or synthetic origin, and is compatible with the contents of the container. It will be readily appreciated that the needle 22 is mounted such that its proximal end is in fluid communication with the orifice 28.

With reference to Figure 3, the plunger rod 26 includes a pair of elongate arms 30 that terminate in flanges 32. The base part 34 of the plunger rod 26 includes an opening 36 through which the needle 22 (Figure 6) may extend when it is attached to the main body 14 of the internal piston 10. A pair of connectors 38 are used to releasably connect the plunger rod 26 to the main body 14 by means of the plunger rod

attachment points 24. The plunger rod 26 can be attached to main body 14 of the internal piston 10 by a suitable mechanism, which could include a leur slip, leur lock or other type of system. The objective is to ensure the plunger rod 26 is securely attached to the internal piston 10, such that it may function as a plunger rod support, with flanges 32 that allow it to be held firmly and for pressure to be applied. The plunger rod 26 may be suitably graduated to allow variable doses to be accurately dispense/administered or may be actuated to allow the entire contents of the container to be expelled (less any nominal hold volumes). The actuation may be effected manually or via a suitable automated system or device.

Figure 4 shows the internal piston 10 inserted into a standard container 2. The main body 14 is seated under the neck 4 of the container 2 and the stopper 12 is seated on the neck of the container. An aluminium cap 8 covers the top of the container 2 and may be a conventional tear-off cap that can be removed manually.

The method of using the internal piston 10 will now be explained with reference to Figures 5 to 7. First of all, the aluminium cap 8 is removed and the stopper 12 is pulled away from the main body 14 of the internal piston 10 to expose the upper surface 14a. The plunger rod 26 and needle 22 are then attached to the main body 14 at their respective attachment points. Figure 6 shows how the needle 22 extends through the opening 36 in the base part 34 of the plunger rod 26.

The attachment of a needle 22 and plunger rod 26 to the main body 14 results in a single integrated container-syringe injection device, whereby the contents of the container 2 may be expelled or administered into a patient. When the plunger rod 26 is held firmly and the plunger rod and the base of the container 2 are moved in opposing directions, or the plunger rod is held firmly and the base of the container is depressed firmly, the main body 14 of the internal piston 10 moves towards the base of the container. This axial movement displaces the contents of the container, which flow through the orifice 28 and exit through the needle 22 as shown in Figure 7.

Figures 8 to 12 represent an alternative embodiment of the internal piston with a modified plunger rod which allows for the even distribution of pressure over the flexible peripheral edge region of the internal piston such that the plunger rod does not warp or deform in any way resulting in variability in the contents that are dispensed from the container.

The internal piston 50 includes a main body 52 having a rigid core 54 and a flexible peripheral or edge region 56. The main body 52 of the internal piston 50 also includes needle attachment points 58 to which a needle 22 (Figure 12) can be releasably attached, and plunger rod seating areas 60. An axially extending orifice 62 is formed in the main body 52. The orifice 62 may be open, or may contain a plug (not shown) that is removed from the external side of the internal piston 50 prior to use. The plug is preferably made of a suitable material, which may be of natural or synthetic origin, and is compatible with the contents of the container. The internal piston 50 is covered by a stopper 64 as described above.

Figure 9 shows the internal piston 50 inserted into a container 2. To use the internal piston 50, the stopper 64 is pulled away from the main body 52 as shown in Figure 11 to expose the needle attachment points 58 and the plunger rod seating areas 60.

With reference to Figure 10, the modified plunger rod 66 contains flanges 68 at the base part 70. Moreover, the two arms 72 of the plunger rod 66 are attached by a flexible spring type mechanism 74 allowing the arms to be squeezed together so that the flanges 68 can be inserted through the neck of the container 2. When inserted through the neck of the container 2, the base flanges 68 of the plunger rod 66 rest evenly on the plunger rod seating areas 60 of the main body 52 of the internal piston 50 as shown in Figure 12.

Using the same principle, alternative geometries and shapes may be used to achieve the same end goal of expelling the contents of the container 2. Furthermore, the internal piston 50 may be used with specially designed vials or containers with geometries that allow for optimal performance.

Once the needle 22 and the plunger rod 66 are attached to the main body 52 of the internal piston 50, the contents of the container 2 can be expelled or administered into a patient in the same way as described above.

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## CLAIMS

1. An injection device comprising:

a container having a base and an open neck; and

an internal piston located within the container, the internal piston having an orifice, needle attachment means for mounting a needle in fluid communication with the orifice such that the needle can extend through the open neck of the container, and plunger rod attachment means for mounting a plunger rod such that the plunger rod can extend through the open neck of the container, and wherein movement of the internal piston towards the base of the container forces the contents of the container through the orifice.

2. An injection device according to claim 1, wherein the internal piston includes a rigid core and a flexible peripheral region.

3. An injection device according to claim 1 or claim 2, further comprising a plug for sealing the orifice.

4. An injection device according to any preceding claim, further comprising a needle releasably secured to the needle attachment means of the internal piston such that the needle is in fluid communication with the orifice.

5. An injection device according to any preceding claim, further comprising a plunger rod having means for releasably securing the plunger rod to the plunger rod attachment means of the internal piston.

6. An injection device according to claim 5, wherein the plunger rod includes a base part and a pair of plunger arms.

7. An injection device according to claim 6, wherein each of the plunger arms terminates in a flange.

8. An injection device according to claim 6 or claim 7, wherein the plunger arms are connected together by a flexible spring mechanism.

9. An injection device according to any of claim 6 to 8, wherein the base part of the plunger rod includes an aperture.

10. An injection device according to any of claims 5 to 9, wherein the means for relcasably securing the plunger rod to the internal piston includes a leur slip or leur lock.

11. An injection device according to any preceding claim, further comprising a stopper located in the open neck of the container and releasably secured to the internal piston.

12. An injection device according to claim 11, wherein the stopper is releasably secured to the internal piston by an adhesive.

13. An injection device according to claim 11, wherein the stopper is releasably secured to the internal piston by mechanical means.

14. An injection device according to any preceding claim, wherein the internal piston is made of a plastics material.

15. An injection device according to any preceding claim, wherein the container is made of glass.

16. An injection device according to any of claims 1 to 14, wherein the container is made of a plastics material.

17. An injection device substantially as herein described and with reference to the drawings.

## Amendments to the claims have been filed as follows

**CLAIMS**

1. An injection device comprising:

a container having a base, a cylindrical sidewall extending from the base and an open neck having a diameter less than the diameter of the sidewall; and

an internal piston located within the container, the internal piston having an orifice, needle attachment means for mounting a needle in fluid communication with the orifice such that the needle can extend through the open neck of the container, and plunger rod attachment means for mounting a plunger rod such that the plunger rod can extend through the open neck of the container, and wherein movement of the internal piston towards the base of the container forces the contents of the container through the orifice.

2. An injection device according to claim 1, wherein the internal piston includes a rigid core and a flexible peripheral region.

3. An injection device according to claim 1 or claim 2, further comprising a plug for sealing the orifice.

4. An injection device according to any preceding claim, further comprising a needle releasably secured to the needle attachment means of the internal piston such that the needle is in fluid communication with the orifice.

5. An injection device according to any preceding claim, further comprising a plunger rod having means for releasably securing the plunger rod to the plunger rod attachment means of the internal piston.

6. An injection device according to claim 5, wherein the plunger rod includes a base part and a pair of plunger arms.

7. An injection device according to claim 6, wherein each of the plunger arms terminates in a flange.

8. An injection device according to claim 6 or claim 7, wherein the plunger arms are connected together by a flexible spring mechanism.

9. An injection device according to any of claim 6 to 8, wherein the base part of the plunger rod includes an aperture.

10. An injection device according to any of claims 5 to 9, wherein the means for releasably securing the plunger rod to the internal piston includes a leur slip or leur lock.

11. An injection device according to any preceding claim, further comprising a stopper located in the open neck of the container and releasably secured to the internal piston.

12. An injection device according to claim 11, wherein the stopper is releasably secured to the internal piston by an adhesive.

13. An injection device according to claim 11, wherein the stopper is releasably secured to the internal piston by mechanical means.

14. An injection device according to any preceding claim, wherein the internal piston is made of a plastics material.

15. An injection device according to any preceding claim, wherein the container is made of glass.

16. An injection device according to any of claims 1 to 14, wherein the container is made of a plastics material.

17. An injection device substantially as herein described and with reference to Figures 2 to 12.

INVESTOR IN PEOPLE

**Application No:** GB0421977.0 **Examiner:** Mr Alex Robinson

**Claims searched:** 1 to 16 **Date of search:** 26 January 2005

# Patents Act 1977: Search Report under Section 17

**Documents considered to be relevant:**

| Category | Relevant to claims | Identity of document and passage or figure of particular relevance |
|---|---|---|
| X | 1, 2, 4 to 10 and 14 to 16. | EP 1386628 A2 (MDC Investment Holding) Whole document. |
| X | 1 to 5 and 14 to 16. | JP 2002172166 A (Shionogi) Figures and abstract, see in particular figure 7. |
| X | 1, 5 and 11 to 16. | US 5520642 A (Bigagli) Whole document. |
| X | 1 to 3, 5 and 14 to 16. | US 4936830 A (Verlier) Whole document. |
| X | 1 to 4 and 14 to 16. | GB 1275565 A (Sterling) Whole document. |
| X | 1, 4, 5 and 14 to 16. | US 2524362 A (Smith) Whole document. |
| X | 1, 4, 5 and 14 to 16. | FR 2729573 A (Brunel) Figures and abstract. |

Categories:

| | | | |
|---|---|---|---|
| X | Document indicating lack of novelty or inventive step | A | Document indicating technological background and/or state of the art. |
| Y | Document indicating lack of inventive step if combined with one or more other documents of same category. | P | Document published on or after the declared priority date but before the filing date of this invention |
| & | Member of the same patent family | E | Patent document published on or after, but with priority date earlier than, the filing date of this application |

## Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC$^{X}$ :

A5R

Worldwide search of patent documents classified in the following areas of the IPC$^{07}$

A61M

The following online and other databases have been used in the preparation of this search report

EPODOC, WPI, JAPIO.