

AUSTRALIA

PATENTS ACT 1990

NOTICE OF ENTITLEMENT

I, David L. Reynolds of 305 Knowlton Road, P.O. Box 600, Lac Brome, Quebec
J0E 1V0, Canada being the applicant and nominated person in respect of
Application No. 67913/94, state the following:-

I am the actual inventor.

I am the applicant of the application listed in the declaration under Article 8 of the
PCT.

The basic application listed in the declaration made under Article 8 of the PCT is
the first application made in a Convention country in respect of the invention

DAVID L. REYNOLDS

By his Patent Attorneys

CULLEN & CO.


RON HALIDAY

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SYRINGE FOR INFUSION
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- (56) Prior Art Documents
US 5041094
EP 385916
- (57) Claim

1. A syringe having a piston (6) which is formed in two separate parts in longitudinal tandem within a syringe body (2), characterized in that the piston parts are a detached imperforate front part (6A) formed essentially of elastomeric material and nearer a forward end of the syringe body and an initially abutting rear part (6B) formed with a passageway (20) for establishing fluid communication between rear and front surfaces of that part, only the rear part (6B) having provision (18) for mechanical connection to a syringe actuator (38), in that a retainer (14) is engaged with a rear end of the syringe body to restrain the rear part (6B) against expulsion from the syringe body, and in that the provision for mechanical connection to a syringe actuator provides for alternative connection of said rear part to one of a mechanical actuator and a fluid pressure actuator communicable with said passageway (20).

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8. A method of discharging contents of a syringe, adapted for conventional actuation by a mechanical actuator, by a fluid pressure actuator, characterized by forming a piston of the syringe in two separable parts, namely a detached imperforate front part formed essentially of elastomeric material, and a rear part formed with a passageway for establishing fluid communication between rear and front surfaces of that part, only the rear part having provision for mechanical connection to a syringe actuator, and actuating said piston by connecting said fluid pressure actuator to the rear part and introducing pressurized fluid through said passageway from said actuator while restraining said rear part against rearward motion.



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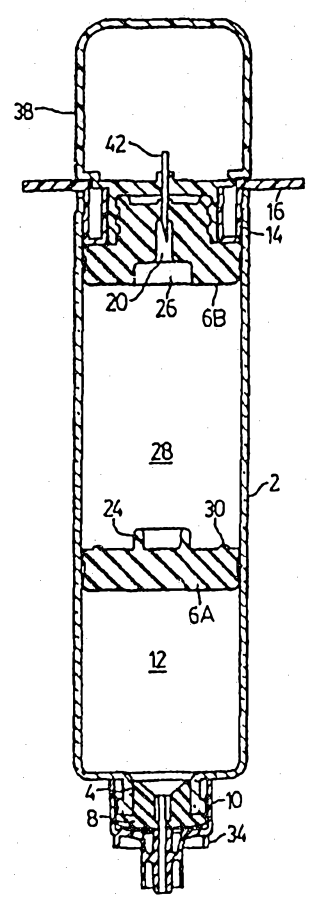
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(54) Title: SYRINGE FOR INFUSION

(57) Abstract

A syringe is modified to permit gradual administration of its contents with reduced problems due to seizing or stiction of its piston by dividing its piston (6) axially into two parts, a front detached part (6A) and a rear part (6B) which is the only part having provision for attachment to a syringe actuator. The rear part has a passage (20) through which fluid can be gradually introduced from an actuator (38) into a chamber (28) between the parts so as to force the front part forward while the rear part is restrained against rearward movement. The passage may be initially closed by a septum (22) which is penetrated by a cannula (42) on the actuator. If the syringe actuator is a plunger, the syringe can be used conventionally.



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SYRINGE FOR INFUSION

This invention relates to syringes, particularly prefilled syringes, such as are utilized for the dispensing
5 of pharmaceutical and personal care products.

In the context of this invention the term "syringe" is used broadly to refer to a container, having a tubular body usually of cylindrical cross-section, and liquid contents which are dispensed through a relatively small
10 tubulation present or introduced at one otherwise closed end, hereinafter referred to as the forward end, of the body upon displacement of piston longitudinally within the body. By "prefilled" is meant either prefilled with a liquid which is dispensed, or prefilled with a liquid soluble or miscible
15 component of such a liquid which can be reconstituted by addition of a second liquid diluent, solvent or carrier component immediately prior to use. The body of such a syringe is usually but not necessarily of glass or synthetic plastic material, and usually but not necessarily
20 transparent.

It is important that the contents of a prefilled syringe be secure against leakage or contamination during storage, and in many cases during terminal sterilization which is required prior to storage. This entails that the
25 piston makes a seal with the body which is hermetic or near

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hermetic. At least the peripheral walls of such pistons are usually formed of elastomeric material in compressive engagement, typically in plural longitudinally spaced annular zones, with an inside wall of the syringe body, in order to
5 maintain the necessary seal. Despite various remedial measures which may be utilized, such as the use of silicone lubricants, this extensive engagement can give rise to significant problems when the time comes for the piston to be displaced.

10 There is sufficient frictional engagement between the piston and the wall of the body that substantial force may be required to move the piston, whilst "stiction" effects mean that the force required to initiate piston movement will usually be significantly greater than that required to
15 maintain it. Since the piston will have some longitudinal resilience, stiction effects can make it very difficult to obtain smooth discharge of the contents of syringes at low rates. These problems are often aggravated by the tendency for the piston to "seize" during storage, with the material
20 of the piston forming a more or less tenacious bond to the wall of the body. Such seizure may require considerable force to be applied to the piston to break the bond and permit initial movement of the piston.

 When a plunger is utilized to activate the piston
25 and expel the contents of a syringe at a fairly rapid rate, sufficient force can usually readily be applied to the piston through the plunger to overcome stiction or seizure provided that known remedial measures have been utilized, but difficulties arise when the contents of the syringe are to be
30 dispensed slowly or in small quantities over a considerable period of time. When a pharmaceutical is to be infused slowly into a patient, available techniques include the use of syringe pumps, which incorporate an electric motor which slowly advances the piston by means of a plunger, and IV bag
35 and minibag systems in which the pharmaceutical is discharged

from the syringe into a flexible bag of fluid and is thence
 infused into the patient at a controlled rate. Syringe
 pumps are expensive and cannot always prevent
 irregularities of discharge due to stiction effects,
 5 particularly at very low discharge rates. Bag based
 systems cannot readily be set up to provide very low
 discharge rates and require an extra stage of preparation
 as well as more dilution of the pharmaceutical than may be
 appropriate in some cases.

10

It has been proposed to provide syringes with two part
 pistons. In EP 03663338A, a mixing syringe utilizes
 pistons attached to a common plunger the front piston and
 the plunger having passageways which can be used in
 15 conjunction with a secondary plunger to provide a desired
 mixing action. In GB 2205750A, a two part piston, of which
 the front part is attached to a syringe plunger and has
 fluid non-return valves in it, is utilized to render a
 syringe non-refillable. In EP 0254765A, the plunger is
 20 again connected to the front part of the piston, with a
 space initially between the piston parts being evacuated
 through a one way valve in the plunger.

It is an object of the present invention to provide a
 25 syringe which addresses the problems discussed above and is
 better suited to applications in which the syringe contents
 are to be discharged at a low rate or in small quantities,
 whilst maintaining normal functionality. While it uses a
 two part piston, it does so in a manner quite different
 30 from the prior art discussed above.

According to the invention, a syringe has a piston
 which is formed in two separate but initially abutting parts
 in longitudinal tandem within and in sealing relationship
 35 with a syringe body, namely a detached imperforate front
 part nearer the forward end of the body and preferably of
 relative smaller axial extent, and a rear part preferably



of relatively greater axial extent, and formed with passageway means, which may be initially obturated, for establishing fluid communication between rear and front surfaces of that part. Only the rear part of the piston

5 has provision for mechanical connection to a syringe actuator. A retainer ring is engaged with a rear end of the syringe body to restrain the rear part of the piston against expulsion from the syringe body. A rear surface of the front part normally abuts and is supported by a front

10 surface of the rear part, and the two parts cooperate to provide a high degree of sealing between the piston and the body. The provision for mechanical connection to a syringe actuator provides both for connection to a mechanical actuator, and for connection with a fluid pressure actuator

15 communicable with the passageway. By passing fluid through the passageway, from the rear to the front of the rear part, into a chamber between the two parts, the front part may be displaced forwardly relative to the rear part, thus in turn applying pressure to the syringe contents to expel

20 the latter, but the frictional engagement between the front part and the wall of the body will be much reduced as compared with the piston as a whole, since the degree of engagement of the front part with the wall is reduced compared with the piston as a whole. "Stiction" effects

25 are also greatly reduced, as is the force required to overcome seizing, not only because of the reduced wall engagement, but because, for material of a given hardness, the transverse flexibility of the usually disc-like front part alone will be much increased as compared to a one

30 piece piston. Any stiction or seizing will result in pressure behind the front portion bowing the latter forward, thus reducing its engagement with the body wall and overcoming the stiction or seizing. The overall effect is to greatly reduce the pressure needed to ensure

35 displacement of the syringe contents, whilst at the same time attaining much smoother movement even at very low displacement rates. Rearward expulsion of the rear part of

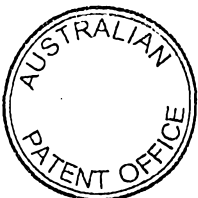


the piston is present by the retainer, and the rear part thus forms a reaction surface against which the fluid pressure may act to.

5 Further features of the invention are set forth in the appended claims, and will become apparent from the following description of an exemplary embodiment of the invention with reference to the accompanying drawings in which:

10 Figure 1 is a longitudinal cross-sectional view of a syringe in accordance with the invention, during dispensing of the syringe contents by means of a gas-generator coupled to the syringe;

15 Figure 2 is a similar but partially exploded view of components of a similar syringe prior to filling, together



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with an alternative cannula arrangement for applying fluid to operate the syringe;

Figure 3 is a side elevational view of components of a piston of the syringe.

5 Referring to the drawings, the syringe is based on a "bottomless vial" constructed and filled generally as described in European Published Patent Application No. 0298585. It has a generally cylindrical glass (or synthetic plastic) body 2 having a narrower neck 4 at one front or top
10 end, and an open bottom closed by an elastomeric piston 6. The body is filled with a pharmaceutical or personal care preparation through the neck 4, which is then closed by an elastomeric closure 8 and an annular cap 10, using conventional vial filling and capping machinery, although it
15 should be understood that techniques utilized to fill the syringe with its contents 12 forms no part of the present invention. The piston 4 is retained within the syringe body by a retainer ring 14 which also provides a flange 16 providing a finger grip or reaction component enabling the
20 syringe to be actuated in a conventional manner using a plunger attached to a screw threaded extension 18 formed at the back of the piston 6, either manually or by means of a syringe pump. The retainer ring is engaged with the syringe body in a manner somewhat similar to that described in WO
25 92/05507, but the details of the securement of the retainer ring do not form part of the present invention. The fitting of the ring 14 does however provide a support for the piston enabling the syringe to be terminally sterilized without danger of the piston being ejected by internal pressure
30 developed within the body.

As compared to the pistons shown in the above-mentioned European patent application, the piston in the present embodiment is axially separated into two parts, a front part 6A nearer the forward end of the syringe body, and
35 a rear part 6B. The rear part 6B is formed with an axially

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extending passage 20, which is initially closed at its rear end by a septum 22. A flange 24 on a rear surface of the portion 6A enters a recess 26 on a front surface of the portion 6B to enclose an initially small chamber 28, and
5 pimples 30 on the rear surface of the portion 6A engage the front surface of the portion 6B. Both portions have annular ridges 32 on their outer periphery which engage the inside wall of the body 2.

In order to exploit the features of the invention,
10 the chamber 28 is placed in communication with a source of fluid (gas or liquid) through the rear of the piston by penetrating the septum 22: in some cases, particularly where sterility is not at a premium, the septum may not be needed, or it may be replaced by some other means of obturating the
15 passage. A pressure differential is set up as between this source of fluid and the pressure of the contents 12 of the syringe, which are placed in communication with a destination through a tubulation represented in this example by a connector cap 34 incorporating a cannula 36 which penetrates
20 the closure 8. This connector may for example be coupled to a tube through which the content of the syringe is administered to a patient.

As pressure in the chamber 28 rises above the pressure in front of the portion 6A, a forward force will be
25 applied to that portion. If there is any stiction or seizing to the wall of the body, the elasticity of the disc-shaped portion 6A will result in its bowing forward in the middle thus tending to release the ridges 32 from the body wall and providing some displacement of the syringe contents until the
30 peripheral portions of the disc follow the centre portion.

If the syringe is raised above the level of discharge from the elastic end of the tube connected to the cap 34, a column of liquid in the tube will result in a negative pressure (relative to atmospheric) within the

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syringe body in front of the piston, and the mere rupture of the septum 22 to provide an air passage will result in the pressure in the chamber 28 rising above that within the body. Even quite a limited elevation of the syringe, comparable to
5 that used in conventional IV administration, can be sufficient to result in smooth displacement of the piston portion 6A. The rate of displacement will depend on the capacity of the tube, and if microbore tube is used, a slow and controlled administration of the content of the syringe
10 can be obtained over an extended period.

For many purposes a more positively controlled displacement will be desirable. One exemplary means of achieving this is to couple an electrochemical gas generator 38 of the type disclosed in U.S. Patent No. 4,522,698 (Maget)
15 to the rear portion 6B of the piston as shown in Figure 1. The generator is switched on, and coupled by means of screw coupling 40 to the extension 18 so that a cannula 42 which forms the gas outlet of the device penetrates the septum 22 and communicates with the chamber 28. Electrochemical gas
20 generators are commercially available which generate gas when activated at a very low and controlled rate so as to provide controlled displacement of the piston portion 6A. Rather than a gas generator, the unit 38 could be a compressed gas cartridge provided with a suitable pressure or flow rate
25 regulator valve, or the cannula 42 could be secured in a threaded mounting 44 and provided with a coupling 46 for connection to a source of liquid such as water (which source need not be sterile) through appropriate flow or pressure regulating means. By storing such liquid used for
30 displacement in a graduated container, an accurate indication may be provided thereby of quantity of liquid displaced from the syringe, without resorting to graduation of the syringe. In yet another variant, the syringe contents may be pumped from the syringe through the cannula 36, and the septum 22 is
35 either absent, or ruptured by inserting a cannula 42 open to the atmosphere at its outer end, so that atmospheric pressure

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will move the piston portion 6A to compensate for liquid removed from the syringe without the necessity for admitting air into the syringe body ahead of the piston.

During storage, or conventional usage as a plunger
5 operated syringe, the portion 6A is supported by the portion
6B to provide fully effective sealing of the syringe
contents. The front portion 6A need only have sufficient
axial extent to maintain its alignment in the body during
10 displacement, and will usually have a lesser overall axial
extent from the portion 6B. The passage 20 may be formed as
part of the chamber 28, or in the rear surface of the portion
6B, or in any other way which permits fluid communication to
be established readily between the front and rear surfaces of
the portion 6B. The septum 22 or equivalent sealing
15 structure will normally be desirable, but could in some cases
be dispensed with or replaced by a removable or frangible
seal over the rear end of the syringe body. Provided that at
least the portion 6A of the piston is formed essentially of
elastomeric material, the portion 6B could be formed of non-
20 elastomeric material or be of composite construction. The
pimples 30 limit contact between the piston parts so as to
allow fluid pressure to be developed between them and avoid
the risk of unwanted adhesion between the parts. The pimples
or equivalent protuberances could of course be formed on
25 either or both parts.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A syringe having a piston (6) which is formed in two separate parts in longitudinal tandem within a syringe body (2), characterized in that the piston parts are a detached
 5 imperforate front part (6A) formed essentially of elastomeric material and nearer a forward end of the syringe body and an initially abutting rear part (6B) formed with a passageway (20) for establishing fluid communication between rear and front surfaces of that part, only the rear part (6B) having
 10 provision (18) for mechanical connection to a syringe actuator (38), in that a retainer (14) is engaged with a rear end of the syringe body to restrain the rear part (6B) against expulsion from the syringe body, and in that the provision for mechanical connection to a syringe actuator
 15 provides for alternative connection of said rear part to one of a mechanical actuator and a fluid pressure actuator communicable with said passageway (20).
2. A syringe according to claim 1, characterized in that
 20 the piston parts (6A, 6B) cooperate to form a chamber (28) between said parts with which said passageway (20) communicates.
3. A syringe according to claim 1 or 2, characterized in
 25 that the front part (6A) of the piston is of generally disc-shaped configuration, and thin enough to bow under the application of differential fluid pressures to front and rear surfaces thereof.
- 30 4. A syringe according to claim 1, 2 or 3, characterized in that the front part (6A) of the piston is of lesser axial extent than the rear part (6B).
5. A syringe according to anyone of the preceding claims,
 35 characterized in that the retainer (14) is a ring lodged within the rear end of the syringe body and defining a passage through which the rear part (6B) is mechanically



connected to a syringe actuator.

6. A syringe according to anyone of the preceding claims, wherein the passageway is closed by a septum (22) perforable by a cannula (42) attached to a syringe actuator.

7. A syringe according to anyone of the preceding claims, characterized in that at least one of the piston parts is formed with protuberance (30) to limit contact with the other part.

8. A method of discharging contents of a syringe, adapted for conventional actuation by a mechanical actuator, by a fluid pressure actuator, characterized by forming a piston of the syringe in two separable parts, namely a detached imperforate front part formed essentially of elastomeric material, and a rear part formed with a passageway for establishing fluid communication between rear and front surfaces of that part, only the rear part having provision for mechanical connection to a syringe actuator, and actuating said piston by connecting said fluid pressure actuator to the rear part and introducing pressurized fluid through said passageway from said actuator while restraining said rear part against rearward motion.

9. A method according to claim 8, characterized in that the fluid pressure actuator is a gas generator.

10. A method according to claim 8, characterized in that the fluid pressure actuator is a coupling to a tube linked to a source of fluid pressure.

11. A method according to anyone of claims 8 - 10, characterized in that the step of coupling a fluid pressure actuator to the rear part includes penetration of a septum in the passageway by a cannula on the actuator.



12. A method according to anyone of claims 8-11, in which the front part of the piston is disk shaped and sufficiently flexible such that it will bow under pressure, and causing said front part to bow by the introduction of said 5 pressurized fluid so as to overcome stiction effects.

DATED this 10th day of August 1998

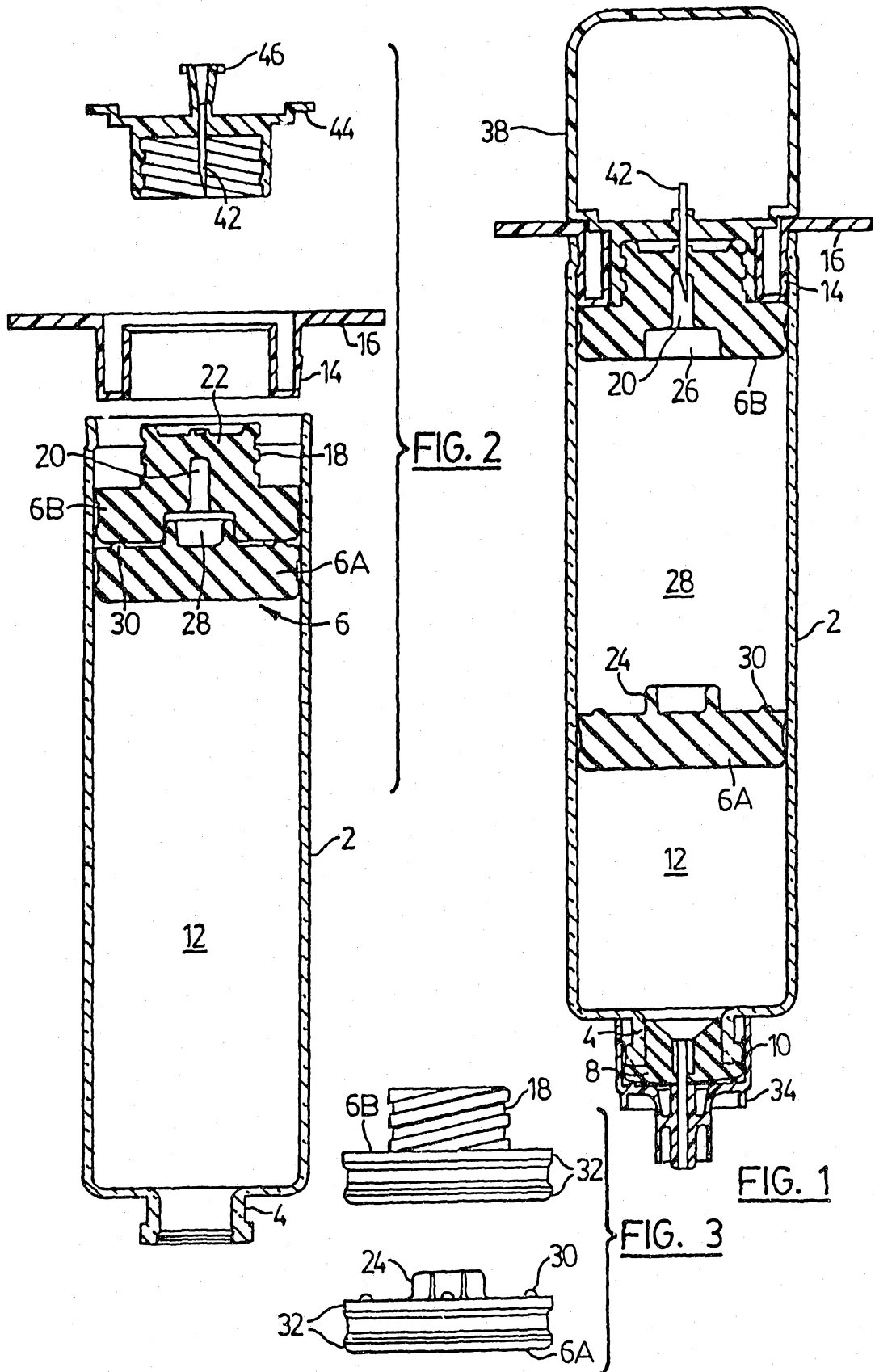
DAVID L REYNOLDS

By his Patent Attorneys

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 94/00277

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61M5/155

According to International Patent Classification (IPC) or to both national classification and IPC:

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,89 00866 (S.P.I.R.A.L.) 9 February 1989	1,2,6,8,10,11
Y	see page 11, line 10 - page 15, line 8; figures	3-5,9
Y	EP,A,0 385 916 (S.I. SCIENTIFIC INNOVATIONS LTD.) 5 September 1990 see column 3, line 19 - column 4, line 7; figures	3-5,9
X	US,A,2 605 765 (KOLLSMAN) 5 August 1952 see column 3, line 48 - column 4, line 68; figure 1	1-5,8,10
X	US,A,4 666 430 (BROWN ET AL) 19 May 1987 see the whole document	1-5,8-10

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

23 August 1994

31.08.94

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.
PCT/CA 94/00277

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-8900866	09-02-89	FR-A- 2618681	03-02-89
		DE-A- 3868321	19-03-92
		EP-A, B 0329784	30-08-89
		JP-T- 2500816	22-03-90
		US-A- 5041094	20-08-91

EP-A-0385916	05-09-90	DE-D- 69005857	24-02-94
		DE-T- 69005857	19-05-94
		US-A- 5062834	05-11-91

US-A-2605765		NONE	

US-A-4666430	19-05-87	US-A- 4759527	26-07-88
