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**Injection system**

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(56) Related Art  
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**WO 92/11897**  
**WO 95/12425**



## Injection System

The invention relates to an injection system for preparing a mixture of a solvent and a medicament and for subsequent dosed injection of the mixture, the system comprising:

5 a syringe from which set doses are apportioned from a cylinder ampoule having a first end closed by a pierceable membrane and a second end closed by a piston which can by a piston rod, which is successively advanced in a distal direction by the injection of set doses, be forced into the ampoule to press out a dose of a medicament stored in the ampoule between the membrane and the piston through  
10 an injection needle piercing the rubber membrane,

an ampoule with a solvent fitting into the syringe, and

15 a needle mounted in a needle hub and having an injection part projecting from a distal side of the hub and a back needle piercing the membrane of an ampoule when the needle hub is mounted on the syringe.

Whereas many medicaments are supplied as a solution or a suspension in pre-filled cylinder ampoules of the kind mentioned above, some kinds of medicine has a low storability when they are solved. Therefore these types of medicine are mainly stored  
20 in a vial as a lyophilised powder which is dissolved in a solvent which is injected in the vial by the user immediately before he is going to load his syringe with a new ampoule. The solution obtained in the vial is transmitted to a cylinder ampoule which is then ready to be mounted in a syringe of the above mentioned kind.

25 By the mixing it is important that a precisely measured amount of solvent is used for dissolving the powder in the vial as else the concentration of the mixture in the ampoule will be wrong so that the user loose his control with his medication. A precise mixing may be obtained by storing the solvent in the cylinder ampoule which is going to be used for the mixture. From the manufacturer the ampoule may contain a very  
30 precise amount of solvent which may be injected into the vial through a double ended needle penetrating the closing membranes of as well the ampoule as the vial.

When the powder in the vial is dissolved in the solvent injected in the vial, the mixture obtained is sucked back into the ampoule by drawing the piston of this ampoule outward and if the total amount of solvent was not injected in the vial the exceeding solvent will be mixed up in the mixture of medicine and solvent transmitted from the vial back into  
5 the ampoule.

When the piston of the ampoule is drawn outward to suck up the mixture in the ampoule it is very important that the piston is not drawn out of the ampoule as it may be difficult to put back again and will inevitably cause spill and contamination of the medicament.  
10

Any discussion of the prior art throughout the specification should in no way be considered as an admission that such prior art is widely known or forms part of common general knowledge in the field.

15 From WO 95/12425 is known a device for filling a cylinder ampoule for use in a syringe of the above mentioned kind. This apparatus comprises a holder in which an ampoule containing a measured amount of solvent may be mounted. At its front end the holder is equipped with a connecting device coupling the outlet end of the ampoule to a vial into which the solvent shall be injected to solve a lyophilised medicament. To the rear end of  
20 the holder a support is mounted in which a piston rod may be moved in the axial direction of the ampoule. The distal end of the piston rod is screwed into the piston and the proximal end of the piston rod projects from said support. The solvent in the ampoule may be pressed through a needle which from the front end of the ampoule forms a channel to the interior of the vial. The solvent is transmitted from the ampoule  
25 to the vial by pressing the projecting end of the piston rod which then presses the piston into the ampoule. The mixture obtained in the vial is thereafter sucked back into the ampoule by drawing the piston outward. This outward drawing is made possible by the fact that a rear end of the piston is provided with a hole with an inner thread which is engaged by an outer thread at the distal end of the piston rod. The piston rod support  
30 which forms a stop preventing the piston from being drawn out of the ampoule is fixed to the ampoule holder in such a way that it cannot be unfixed unless the screw connection between the piston and the piston rod is brought out of engagement. This way the risk for inadvertently drawing out the piston is eliminated.



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From US 3 336 924 is known a syringe package set comprising a vial containing a medication, an ampoule which has a first end closed by a pierceable membrane and a second end closed by a piston and containing a solvent in the space between the piston and the membrane, a needle on the ampoule through which the content of the ampoule can be  
5 injected into the vial to be mixed with the content of said vial, a piston rod fixed to the piston of the ampoule by which the piston rod the piston can be drawn outward in the ampoule to aspirate the mixture from the vial and by which the piston can again be pressed into the ampoule to give of the mixture from the ampoule through the needle. What is provided is a single use  
10 syringe containing a solvent which can be injected from the syringe into a vial from which a produced solution can be sucked back into the syringe and subsequently be injected by this syringe



AMENDED SHEET

However, the described solution implies that different devices must be carried and used. First the filling device must be taken apart and the ampoule mounted into said device. Then a filling procedure must be run through. Thereafter the device must be taken apart again to remove the filled ampoule, which must then be installed in the syringe by which  
5 a dose may be set and injected.

It is an object of the present invention to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

10 Accordingly, the present invention relates to an injection system which makes a special filling device superfluous.

According to a first aspect, the present invention provides an injection for preparing a mixture of a solvent and a medicament and for subsequent dosed injection of the  
15 mixture, the system comprising:

an ampoule which has a first end closed by pierceable membrane and a second end closed by a piston and containing a solvent in the space between the piston and the  
20 membrane,

a syringe with a dose setting and injection mechanism by which doses can be set and apportioned from the cylinder ampoule by successfully advancing a piston rod in a distal direction to push the piston into the cylinder ampoule.

25 a needle mounted in a needed hub and having an injection part projecting from a distal side of the hub and a back needle by which the membrane of the ampoule can be pierced when the needle hub is mounted on the syringe.

wherein means are provided which even when an ampoule is mounted in the syringe  
30 allows the piston rod to be released from the dose setting and injection mechanism so that this piston rod can be drawn in a proximal direction, and that the piston of the ampoule and the piston rod have a co-operating coupling means by which the piston can be coupled to the piston rod to follow movements of said piston rod in both axial directions.



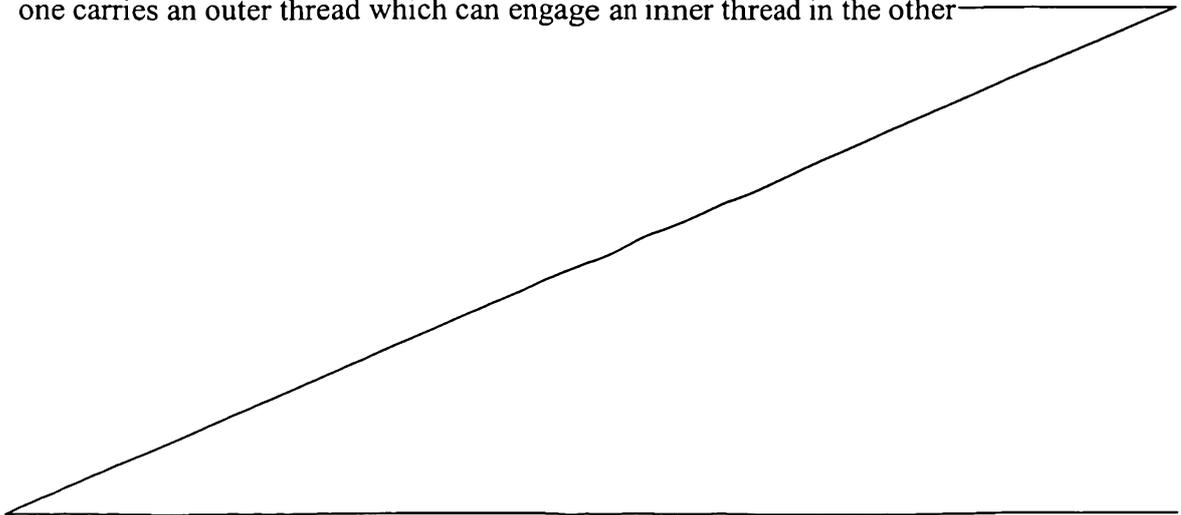
According to a second aspect, the present invention provides an ampoule for an injection system according to claim 1 or claim 2, wherein the ampoule is adapted to fit into the syringe for apportioning of set doses, the piston being provided with coupling means designed for co-operation with coupling means on the piston rod of the syringe.

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In such a syringe an ampoule with solvent may be mounted with the distal end of the piston rod engaging the piston of the ampoule, and through a needle mounted in the common way on the syringe the solvent may be injected into a vial by repetitively setting a dose and injecting this dose through the closing rubber membrane of the vial

10 until the ampoule is emptied. An adapter may be mounted between the syringe and the vial to keep these elements in position during said operation and during the next operation which is to draw the piston rod in a proximal direction whereby due to its engagement with the piston in the ampoule it will draw this piston outward in the ampoule. Thereby the mixture prepared in the vial by the injection of the solvent will be  
15 sucked into the ampoule from where it may now be apportioned in doses which may be individually set by the dose setting mechanism.

The coupling means of the piston rod and the piston may appropriately be parts of which one carries an outer thread which can engage an inner thread in the other



part. However other kinds couplings allowing transmission of axial movements in both axial direction may be used so as snap couplings or bayonet couplings.

In some syringes the piston may be mowed in both axial directions against the resistance of friction in a piston rod guidance whereas other syringes are provided with a unidirectional coupling which allows only a movement of the piston rod and the piston in a distal direction when an ampoule is mounted in the syringe. When the ampoule is dismounted the unidirectional coupling is released and the piston rod may be moved in the proximal direction to a retracted position which it takes up when a full ampoule is mounted. In such syringes means may be provided which even when an ampoule is mounted in the syringe can be operated to set the piston free to be moved in a proximal direction.

According to a preferred embodiment of the invention the dosing mechanism of the syringe comprises a dose setting and injecting member which to set a dose is rotated from a stop an angle which is proportional with the set dose and which to inject the set dose is rotated back to the stop, an inner thread in a tubular housing of the syringe, an outer thread provided on elements forming a part of a piston rod assembly, which outer thread is in engagement with the inner thread of the housing, a unidirectional coupling between the dose setting and injecting member which only by injecting transmits the rotation to the piston rod to screw this rod in a distal direction through the housing, which syringe may according to the invention be characterised in that the means setting the piston rod free are means drawing the elements carrying the external thread out of engagement with the inner thread of the housing. In such a syringe the means setting the piston rod free may be means drawing the elements carrying the external thread of the piston rod out of engagement with the inner thread of the housing.

An ampoule according to the invention is an ampoule designed to fit into a syringe for apportioning of set doses and which ampoule has a piston provided with coupling means designed for co-operation with coupling means on the piston rod of said syringe to secure said piston to said piston rod.



In the following the invention is described in further details with reference to the drawing, wherein

- 5     Figure 1     shows a sectional view of a syringe according to the invention,
- Figure 2     shows in an enlarged scale the proximal part of the syringe shown in figure 1,
- 10    Figure 3     shows a perspective view of a carrier in the syringe according to figure 1 and 2,
- Figure 4     shows perspective view of a piston rod assembly for the syringe shown in figure 1 and 2,
- 15    Figure 5     shows a perspective view of a piston rod driver for the syringe shown in figure 1 and 2,
- Figure 6     shows an expanded view of the piston rod assembly shown in figure 4,
- 20    Figure 7     shows a sectional view of the piston rod assembly, and
- Figure 8     shows the distal end of a syringe coupled to a vial.

25

The syringe in figure 1 has a tubular housing 1 with an inner tubular housing 2. The distal ends of the end of the housings form a cartridge holder and the proximal ends accommodate mechanisms by which mixing of a medicament, dose setting and injection are controlled.

30

A piston rod 3 is at its distal end provided with an outer thread 4 which fits into an inner thread 5 in a piston 6 of an ampoule 7 which is at its distal end closed by a membrane 8. By mounting of the ampoule this ampoule is rotated so that the thread 4 of the piston rod 3 engages the thread 5 of the piston in the ampoule 7. A flange 9 near the distal end of the piston rod 3 defines the distance the piston rod 3 may be screwed into the piston 6 so that the piston rod 3 is not wedged in the piston 6. Her  
5 the connection between piston and piston rod is shown as a thread connection but other connections so as bayonet couplings may be used to secure the piston to the piston rod in such a way that the piston will follow the piston rod during axial move-  
10 ments thereof in both directions.

When the piston 3 of the ampoule 7 is attached to the piston rod 3 the cartridge holder is closed by an end stopper 10 screwed on the distal end of the inner housing 2. The membrane 8 of the ampoule is sealed on this ampoule by a member having a  
15 threaded opening in which a needle hub 11 with a double pointed needle 12 may be received so that one end of the needle 12 penetrates the rubber membrane 8 of the ampoule 7 whereas the other end of the needle may be inserted through the skin of a person who shall receive an injection. When the syringe is not in use the needle receiving part with the needle may be covered by a cap 13 so that nobody is hurt by  
20 the needle.

In its withdrawn position as shown in figure 1 the piston rod 3 is accommodated in the proximal part of the inner housing where it is surrounded by a carrier 14 which is shown in figure 3 and is a longitudinal tubular member having three longitudinal slots  
25 15 in approximately its full length and a flange 16 at its distal end. At its proximal end the carrier 14 has a part with a not round cross section and which is snapped into a correspondingly not round opening in a driver 17 through which rotation is transmitted to the carrier during injection operation of the syringe as it will be described below. The carrier 14 may be rotated about its axis but a ratchet 18 coupled between  
30 the carrier 14 and the inner housing 2 has the effect that the carrier is rotatable in only one direction.

The proximal part of the housing 1 is surrounded by a cap 19 which may rotate on said proximal part. An edge of the cap 19 is provided with a dose indicating scale 20 which may by rotation of the cap be moved relative to an arrow 21 on the housing 1 at the transition between the proximal and the distal part. On the outer wall of the housing 1 a stop 22 is provided against which a not shown protrusion in the cap abuts. When the cap is rotated in a direction away from the stop a circular surface with saw tooth shaped steps having a steep and an inclined edge provided on the inner side of the end bottom 23 of the cap 19 slides over a corresponding surfaced provided on the driver 17. The surfaces are forced against each other by a spring 24 so that a click is heard each time the top of the steps on one of the surfaces fall down in the bottom of the steps on the other surface. When the cap is rotated back until its protrusion abuts the stop 22 on the outer wall of the housing 1 the end bottom 23 will transmit the rotation to the driver 17 as the steep edge of the steps on the circular surfaces of the end bottom 23 will now abut the steep edges of the steps on the driver 17. The driver 17 is then rotated and its rotation is transmitted to the carrier 14 the ratchet 18 being so oriented that it allows this rotation.

Figure 5 shows a piston rod driver 25 comprising a disc 26 from the edge of which three 120° displaced flexible arms 27 extend in an axial direction. At the outer ends of the arms 27 members 28 are provided each carrying a thread 30 which may engage a matching thread 29 on the inner side of the proximal part of the inner housing 2 when the members 28 are supported so that the flexible arms 27 do not bend away so that the threads 30 and 29 are disengaged.

The piston rod 3 which at its distal end is provided with the tread 4 for engagement with a thread in the piston 6 of an ampoule is a part of a piston rod assembly which is shown in figure 4, 5 and 6 in perspective, as an expanded view, and a sectional view, respectively. The piston rod 3 is tubular and is at its proximal end provided with three axial, 120° displaced slots dividing the end of the piston rod into three tongues 31. At the bottom end of each of the slots the piston rod is provided with a protrusion

30



32 which engages the slots 15 of the carrier 14. The piston rod driver 25 is mounted with its disc 26 abutting the end of the tongues 31, its arms 27 engaging the slots between the tongues 31, and the free ends of its threaded members 28 abutting the proximal ends of the protrusions 32. The protrusions 32 and the threaded members 5 28 of the piston rod driver protrude through the slots 15 of the carrier and this way rotation of the carrier will be transmitted to the piston rod 3 and the piston rod driver 25 whereas piston rod 3 and piston rod driver 25 may be axially displaced relative to the carrier 14. A support member having protrusions 33 engaging the slots between the tongues 31 of the piston rod 3 is against the force of a spring 34 axially displace- 10 able in the piston rod 3 from a position near the distal end of said slots to a position near the free end of the tongues 31. In the position near the bottom end of the slots the protrusions 33 will support the members 28 and keep their threads 30 in engagement with the thread 29 of the housing, but when the protrusion are moved to their position near the end of the tongues 31 the arms 27 of the piston rod driver is 15 supported near the disc 26 and the members 28 may due to the oblique sides of the engaging threads 29 and 30 be pressed inward toward the axis so that they may be moved axially with their threads 30 scratching over the thread 29 in the housing.

Figure 6 shows an expanded view of the piston rod assembly. It is seen that the 20 piston rod assembly is provided by combining a tubular part forming the actual piston rod 3 and provided with a thread 4 the active length of which is limited by a flange 9 provided by a ring mounted on the piston rod. The protrusions 32 are provided on a part 35 added to form a part of the piston rod 3. The same way the slotted part of the piston rod is added as an individual part. Between the slotted part and the 25 rest of the piston rod a ring 35 is mounted forming an abutment for the spring 34 which is inserted between said ring and a flange on a tubular sleeve 36 in which an end of the supporting element is secured. A spindle 37 extends all the way through the piston rod, the supporting element and the disc of the piston driver and has at its distal end a head 39 having a diameter which is larger than the diameter of the bore 30 in the sleeve 36 so that this head will engage the flanged end of the sleeve 36 if the spindle is drawn in the proximal direction and will against the force of the spring 34

move the supporting element on which the sleeve 36 is secured to a position wherein its protrusions lies near the free ends of the tongues 31. The spindle 37 further projects through the driver 17, the end bottom 23 of the cap 19 and into a button 38. By a thread 39 the spindle is secured to the driver 17 and to the button 39 whereas the diameter of the opening through the end bottom 23 of the cap 19 is large enough to let the spindle 37 pass freely.

Due to the ratchet 18 the carrier may only be rotated in a direction by which the piston driver is rotated relative to the housing in such a direction that said piston driver is screwed in a direction towards the distal end of the syringe to press out the content of an ampoule mounted in the syringe. A dose may therefore be set by rotating the cap away from the stop 22 in the opposite direction to make the coupling between the driver 17 and the end bottom 23 of the cap 19 click over a number of teeth corresponding to the size of the wanted dose this way giving an audible indication of the size of the set dose. During the clicking the button 6 will sink and jump back at each click to give a tactile indication of the size of the set dose. Thereafter the set dose may be injected by rotating the cap 19 back to abutment with the stop. During this rotation the coupling between the end bottom of the cap and the driver 17 will transmit the rotation to the driver 17 which will again rotate the carrier 14 which transmits the rotation to the piston driver to screw it along the housing 2 a distance proportional with the angle of rotation.

When the syringe is going to be used for injection of a medicament which has to be mixed from two or more components immediately before the use, an ampoule with a solvent component is mounted in the syringe, a needle is mounted and the free end of this needle is inserted in a vial containing another possibly solid component of the medicament. In figure 8 this insertion is illustrated by a vial 40 which is closed by a stopper 41 through which the needle 12 is inserted. It is further illustrated how an adapter 42 may be placed on the vial 40 which adapter has a socket to which the distal end of the syringe may be mounted using the coupling which normally is used for fixing the needle protection cap 13. With the needle inserted in the vial repetitive

dose setting and injection rotations of the cap is performed whereby the piston is successively moved into the ampoule until the full content thereof is injected into the vial 40.

5 Hereafter the vial may be turned upside down still with the needle inserted through the stopper of the vial. Now the piston in the ampoule may be drawn back to its position corresponding to a full ampoule whereby the mixture provided in the vial may be sucked back into the ampoule. This is obtained by drawing the cap in a proximal direction which means that the spindle 37 is pulled in this direction. Hereby the driver  
10 which is secured to the spindle and snap locked onto the carrier 14 will first be lifted off said carrier where after the spindle may be moved freely until its head 39 abuts the sleeve 36. Further movement of the spindle 37 will cause a compression of the spring 34 and the protrusions of the support member will be moved to their position near the free end of the tongues 31 where the piston threaded members 28 of the  
15 piston driver 25 is no longer supported. The axial pull of the spindle is now transmitted to the piston rod which is restrained in moving due to the engagement between the inner thread in the housing and the threaded members 28 of the piston drive. However, due to the lacking support of the members 28 these may be bend inward towards the axis and the engagement between the threads 29 and 30 may be re-  
20 leased so that the piston rod 3 may be drawn backward with the piston drive members scratching over the thread 29 in the housing. Due to the engagement between the thread 4 at the distal end of the piston rod 3 and the thread in the piston 6 of the ampoule 7 said piston is drawn outwards in the ampoule and the content from the vial 40 is sucked over into the ampoule 7. When the spindle 37 thereafter is moved  
25 back to its original position the spring 34 is released and the support member is moved back so that its protrusions 33 support the threaded members of the piston rod driver 25 to keep the tread of these members in engagement with the inner thread 29 of the housing. Finally the driver 17 is snapped onto the carrier 14 again and the syringe is ready for use as a syringe by which a dose may be set and in-  
30 jected.

In the syringe described the piston rod is bound to be moved in the distal direction by the dosing mechanism due to the ratchet 18 which provides a one way coupling which ensures that the piston rod is only movable in said distal direction as long as it is coupled to the dosing mechanism. In other types of syringes the piston rod is prevented from being moved in a proximal direction by detent mechanisms comprising a pawl which secured to the housing engages a tothing along the piston rod or comprising a leaf spring which secured to the housing cuts into the piston rod. To realise the invention such a pawl engagement or cutting engagement may by appropriate members be operated to be disengaged to set the piston free to be moved in a proximal direction.

In the above description the mutual engaging threads of the piston rod and the piston are provided as an outer thread at the end of the piston rod which engage an inner thread in a bore in the piston. Alternatively the piston can be provided with a threaded stud engaging an inner thread in a bore in the end of the piston rod.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. An injection system for preparing a mixture of a solvent and a medicament and for subsequent dosed injection of the mixture, the system comprising:

5 an ampoule which has a first end closed by pierceable membrane and a second end closed by a piston and containing a solvent in the space between the piston and the membrane,

a syringe with a dose setting and injection mechanism by which doses can be set and  
10 apportioned from the cylinder ampoule by successfully advancing a piston rod in a distal direction to push the piston into the cylinder ampoule.

a needle mounted in a needed hub and having an injection part projecting from a distal side of the hub and a back needle by which the membrane of the ampoule can be pierced  
15 when the needle hub is mounted on the syringe.

wherein means are provided which even when an ampoule is mounted in the syringe allows the piston rod to be released from the dose setting and injection mechanism so that this piston rod can be drawn in a proximal direction, and that the piston of the  
20 ampoule and the piston rod have co-operating coupling means by which the piston can be coupled to the piston rod to follow movements of said piston rod in both axial directions.

2. A system according to claim 1, wherein the coupling means of the piston rod and  
25 the piston are mutual engaging threads.

3. A syringe according to claim 1 or claim 2, wherein the dose setting and injection mechanism comprises a dose setting and injecting member which to set a dose is rotatable from a stop an angle which is proportional with the set dose and which to inject  
30 the set dose is rotated back to the stop, an inner thread in a tubular housing of the syringe, an outer thread provided on elements forming a part of a piston rod assembly, which outer thread can be engaged with the inner thread of the housing, a unidirectional coupling between the dose setting and injecting member so that the rotation of said unidirectional coupling is only by injection transmittable to the piston rod to screw this



rod in a distal direction through the housing, wherein the means for setting the piston rod free are means for drawing the elements carrying the external thread out of engagement with the inner thread of the housing.

5 4. An ampoule for an injection system according to claim 1 or claim 2, wherein the ampoule is adapted to fit into the syringe for apportioning of set doses, the piston being provided with coupling means designed for co-operation with coupling means on the piston rod of the syringe.

10 5. An injection system for preparing a mixture of a solvent and a medicament, substantially as herein described with reference to the accompanying drawings.

15 6. An ampoule for an injection system for preparing a mixture of a solvent and a medicament, substantially as herein described with reference to the accompanying drawings.

DATED this 16<sup>th</sup> Day of January 2002  
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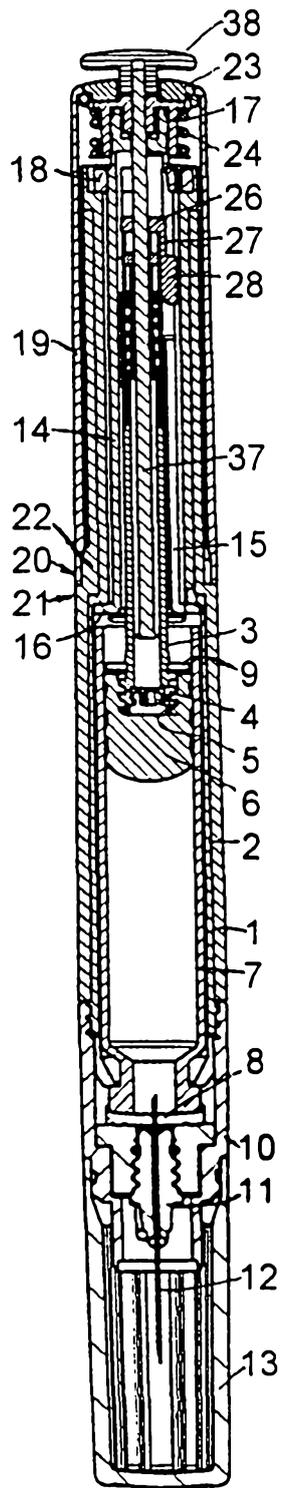


Fig. 1

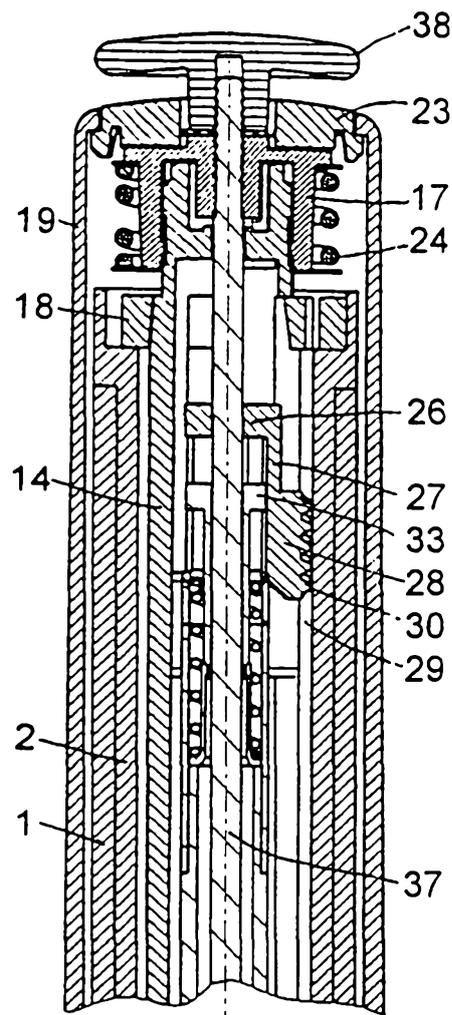


Fig. 2

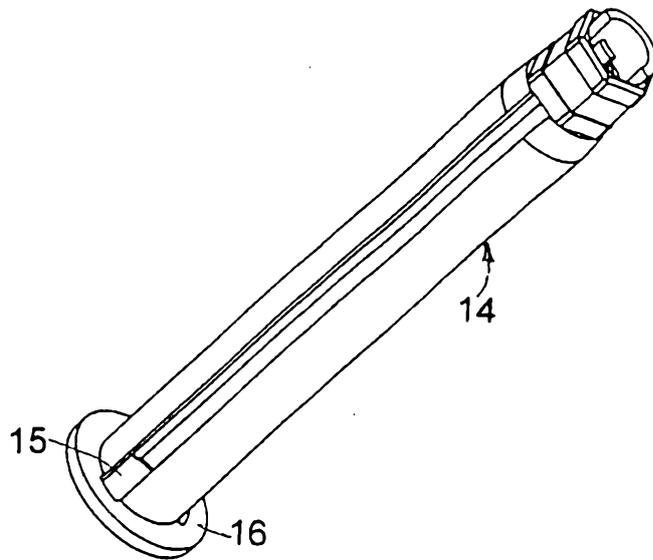


Fig. 3

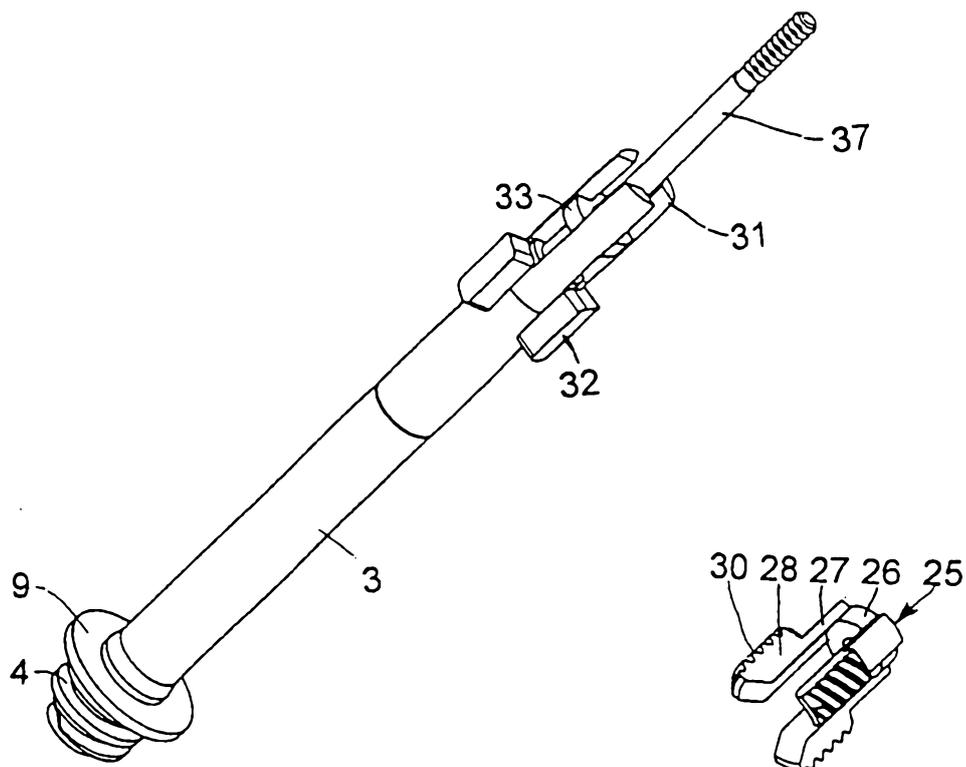


Fig. 4

Fig. 5

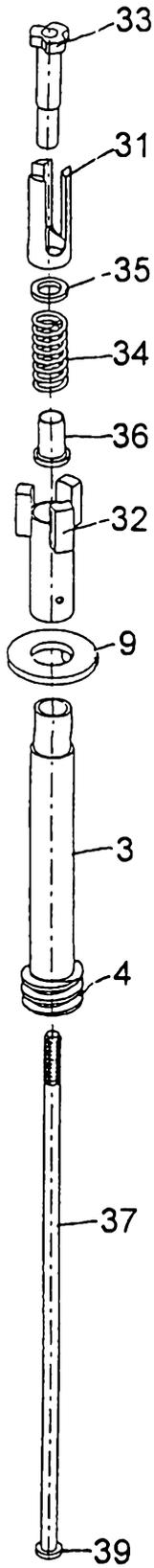


Fig. 6

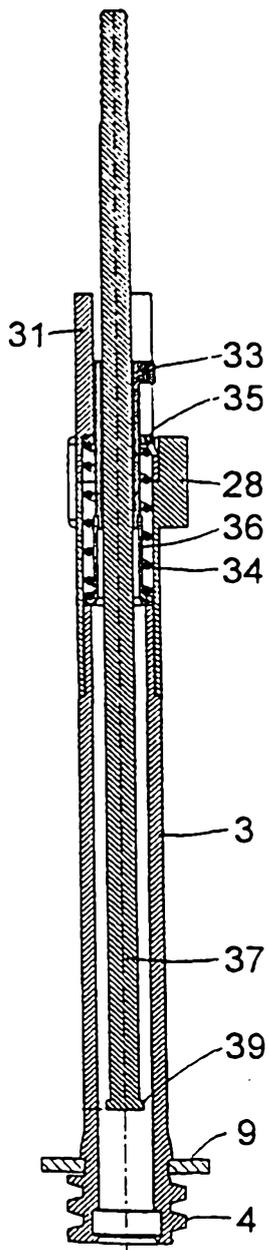


Fig. 7

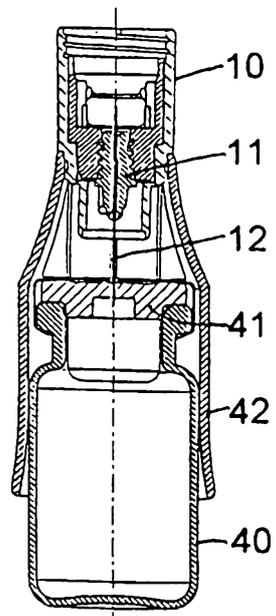


Fig. 8