



**Declarations under Rule 4.17:**

— *of inventorship (Rule 4.17(iv))*

**Published:**

— *with international search report (Art. 21(3))*

## DRUG DELIVERY DEVICE WITH UNIDIRECTIONAL COUPLING

## 5 Technical Field

The present patent disclosure is generally directed to pen-type injection devices and specifically to the dose setting mechanisms for such drug delivery devices. Such devices provide for self-administration of a medicinal product from a multi-dose cartridge and permit a user to set the  
10 delivery dose. The present disclosure may find application in both disposable and reusable type drug delivery devices. However, aspects of the invention may be equally applicable in other scenarios as well.

## 15 Background

Pen-type drug delivery devices have application where regular injection by persons without formal medical training occurs. This is increasingly common among patients having diabetes where self-treatment enables such patients to conduct effective management of their disease. Diabetes has been shown to cause certain problems. For example, people with diabetes can  
20 get high blood pressure, kidney disease, nerve damage, heart disease, and even in certain circumstances blindness. The damage caused by these problems may occur in patients whose blood sugar has been out of control for years. Keeping blood sugar under control, by way of effective insulin administration, is one method that can help prevent this damage from occurring.

25 In addition, people with diabetes can go into "diabetic coma" if their blood sugar is too high. They can also develop blood sugar that is too low (i.e. hypoglycemia) if they don't get enough food, or they exercise too much without adjusting insulin or food. Both diabetic coma and hypoglycemia can be very serious, and even fatal, if not treated quickly. Closely watching blood sugar, being aware of the early signs and symptoms of blood sugar that is too high or too low,  
30 and treating those conditions early can prevent these problems from becoming too serious.

Pen-type drug delivery devices have been designed and developed to help patients suffering from diabetes and other disease states so as to prevent such problems from occurring. The circumstances identified above highlight a number of design considerations and criteria for drug  
35 delivery devices, especially those that may be used to treat diabetes. As just one example, one requirement is that the drug delivery device must be robust in construction. The drug delivery device must also be easy to use both in terms of the drug delivery device manipulation and

understanding of the device's operation. Diabetics, for instance, have to inject themselves repeatedly with insulin solution and the volume of insulin to be injected may vary from patient to patient and even from injection to injection. For at least this reason, certain diabetics may require drug delivery devices that allow the patient to inject successive measured dosages of the same or perhaps different present volumes of insulin solution accurately and with minimum dexterity challenges. This presents a further design challenge since, in the case of certain diabetics, users may have impaired vision and/or may be physically infirm with limited dexterity.

Generally, pen-type injection devices include a cartridge having a slid able piston and containing a multi-dose quantity of liquid medication. A lead screw extending from the dose setting mechanism of the injector pen is moveable in a forward (i.e. distal or delivery direction) to advance the piston within the cartridge in such a manner as to dispense the contained medication from an outlet at the opposite cartridge end, typically through a needle that penetrates a stopper or septum at that opposite end. In disposable or prefilled pens where the cartridge is permanently sealed within the pen housing, after a pen has been utilized to exhaust the supply of medication within the cartridge, the entire pen is then discarded. In reusable pens, after a pen has been utilized to exhaust the supply of medication within the cartridge, the pen is disassembled to allow replacement of the spent cartridge with a fresh cartridge, and then the pen is reassembled for its subsequent use.

A number of pen-type injection devices are commercially available and unfortunately a number of those devices suffer from one or more design flaws that may result in the improper use of the injection device or the delivery of an inaccurate dosing of the medicament. Inaccurate dose setting could lead to fatal results. Other design flaws allow the possibility that a counterfeiter can disassemble a disposable pen and insert bogus medicament cartridge. This pen is then reassembled and sold as new. Such design flaws may not be realized when a pen is first commercialized and may only become apparent after the injection device has been in commercial use by patients for an extended period of time. As such, there exists a need to evaluate existing pen designs to identify the design flaws and then take corrective action, which typically would include redesigning certain original mechanisms within the injection device.

One such pen injector lending itself to design improvements is described in WO 2005/018721 A1. The following describes a number of such design flaws and presents corrective solutions to eliminate these flaws.

Summary

In most, if not all, pen injection type devices dose accuracy is significantly affected if the distal end of the lead screw, through an associated bearing, is not in continuous engagement with the proximal end or face of the cartridge piston prior to the user setting a dose. Stated another way, in some dosing mechanism designs there is one or more flaws that allows the lead screw to  
5 move or otherwise translate off the piston proximally after a dose is injected and before a subsequent dose is set. In these cases the bearing is no longer in contact with the proximal end of the piston, thus creating a gap or void space between the distal face of the bearing and the proximal face of the piston. When a next dose is set and delivered, the lead screw would necessarily traverse this unintended gap before contacting and moving the piston. Because  
10 there is no movement of the piston during this gap closure and, hence, no expulsion of medicament from the cartridge, the actual dose delivered will be less than that set by an amount directly proportional to the size of the gap. Accordingly, it is of prime importance to prevent any unintended proximal movement of the lead screw between dose delivery and the setting of the next dose. Stated differently, the dosing mechanism must include structures to prevent any  
15 proximal movement of the lead screw relative to the cartridge piston.

A physical examination of the commercial pen injection device that is generally described in WO 2005/018721 A1 shows that, if a user pushes the dose knob in the distal direction and simultaneously rotates the dose knob in either direction (clockwise or counter clockwise), the  
20 lead screw is advanced in either the proximal and distal direction. For example, such a situation can develop as follows. The user begins to set a dose by rotating the dose knob, thereby causing the number sleeve to translate out proximally from the body of the injection device. Then, the user grips the number sleeve, thereby preventing the number sleeve from rotating. Afterwards, the user continues to rotate the dose knob while at the same time pushes the dose  
25 knob axially in the distal direction, i.e. towards the injection site. This causes the clutch to disengage from the dial link/dose knob, thereby allowing a relative rotation between the dial link/dose knob connection and the clutch. Because the existing pen injection device is configured with the dose knob permanently attached to the dial link, rotation of the dose knob necessarily rotates the dial link. Since the dial link is rotationally engaged with the drive nut  
30 through the extending fingers, the drive nut also rotates. Rotation of the drive nut while preventing the number sleeve, and hence, the inner sleeve, from moving will cause the drive nut to rotate in a fixed axial position. Since the drive nut is prevented from translating or screwing up/down along the lead screw, the lead screw, which is rotationally fixed by the mid-body, will be forced to translate axially relative to the threaded connection with the drive nut in either the  
35 distal or the proximal direction depending on which way the user turns the dose knob.

If the lead screw translates distally, is it possible to push the cartridge piston distally causing unwanted expulsion of medicament from the cartridge. Alternatively, if the lead screw is caused to translate proximally, this proximal movement will cause the lead screw bearing to disengage from the proximal face of the piston creating an undesired gap that will lead to an inaccurate  
5 dose. To solve this problem, the present invention modifies the original design of dosing mechanism to prohibit undesired motion of the lead screw.

#### Problem to be solved

10 A problem to be solved by the present disclosure is to provide a drug delivery device with increased dose accuracy and/or safety.

For example, in one arrangement, a modification is made to both the dial link and the clutch to include features that co-operate as a unidirectional coupling. Such a unidirectional coupling  
15 allows for rotation of the uncoupled dial link/dose knob and clutch in one direction while preventing the uncoupled dial link/dose knob and clutch from rotating in the opposite direction, thereby preventing the unwanted lead screw translation as described above.

More specifically, in one exemplary arrangement, a proximal portion of the dial link comprises a  
20 plurality of elongated serrations or edges that extend along an outer surface. For example, such elongated serrations or edges may comprise an asymmetric configuration, having two surfaces of different slopes. An interior surface of the modified clutch may be provided with a plurality of co-operating flexible arms that extend radially inwardly of the clutch. The serrations or edges and the co-operating flexible arms are preferably configured in such a way that they do not  
25 engage or co-operate with one another when the dial link/dose knob are clutched or engaged with one another. However, when the dial link/dose knob connection is pushed in a distal direction (typically to administer a set dose) so as to disengage the clutch from the dial link, the modified link and, hence, its elongated serrations or edges will move axially into engagement with the corresponding clutch counterpart flexible arms. In this manner, the modified dial link  
30 and modified clutch will function as a unidirectional coupling. That means in one rotational direction, the dial link/dose knob and the clutch are combined and in the other, opposite direction, the dial link and the clutch are decoupled. Therefore, while injecting with this modified dial link and clutch combination, the decoupled dial link clutch situation is needed because the number sleeve and, hence, the clutch must translate back distally into the housing so as to  
35 rotationally return to its starting position while preventing rotation in the opposite direction.

The pen-type drug delivery device including the above described design improvement includes a housing, a lead screw having a threaded shaft is rotatably fixed during dose setting and injecting that only moves axially in a distal direction relative to the housing during dose administration and is always prevented from moving proximally. The device also has a fluid container or cartridge defining a medicine-filled reservoir with a moveable piston at one end and an outlet at the other end, where the piston is engaged by a bearing connected to the distal end of the lead screw. The piston is advanced toward the outlet or distal end of the cartridge when the lead screw is moved distally during dose administration.

5 A drive nut is threadedly engaged with the threads on the lead screw and can rotate and move proximally relative to the lead screw and housing during dose setting. A number sleeve is threadedly engaged with the housing and is screwed outwardly in the proximal direction relative to the housing during dose setting. A dial link is slidably and rotationally engaged with the drive nut and is axially moveable and rotatably fixed relative to the drive nut. The dial link is rotatably fixed with the number sleeve through a clutch when the dial link and number sleeve are in a first, in particular axial, arrangement and when in a second, in particular axial, arrangement, the clutch and, hence, the number sleeve, are disengaged from the dial link and the number sleeve becomes rotatable relative to the dial link. An inner sleeve is threadedly engaged with the number sleeve, where the inner sleeve is axially moveable but rotatably fixed relative to the housing. During dose setting, the dial link and the number sleeve are in the first axial arrangement, whereby a screwing motion of the dose knob that is connected to the dial link and number sleeve relative to the housing screws the dial link and the number sleeve a first axial distance from a home position causing the number sleeve to extend in the proximal direction outwardly from the housing or body of the device. The screwing motion of the dial link screws the drive nut along the lead screw threaded shaft a second axial distance different from the first axial distance.

During dose dispensing, the dial link and the number sleeve element are in the second axial arrangement, whereby a screwing motion of the number sleeve relative to the housing back or inward towards the home position advances the inner sleeve without rotation in the distal direction to axially advance the drive nut and, thereby, the lead screw and the fluid container piston to dispense medicine from the outlet. The pen injector disclosed herein can be provided with a mechanical advantage that makes it easier for the user to push the dose knob during the dispensing of medication, which mechanical advantage can be very high and conveniently selected by the manufacturer during apparatus design. This mechanical advantage allows the number sleeve to travel a greater axial distance than the lead screw it advances, thus allowing for small doses to be delivered.

According to one aspect, a drug delivery device is provided. The device may be a pen-type device. The device may be a pen-type injector. The device may comprise a housing. The device may further comprise a lead screw. The lead screw may be configured to operate through the housing of the device for delivering a dose of drug or medicine or fluid from the device. The lead screw may be rotatably fixed with respect to the housing during dose setting and during dose delivery. The term "rotatably fixed" may mean in this context that any relative rotation between the lead screw and the housing is prevented. The lead screw may be axially moveable in a delivery direction relative to the housing for dose delivery. The lead screw may be prevented from being moveable in a direction opposite to the delivery direction.

The device may further comprise a cartridge. The cartridge may be adapted and arranged to contain a plurality of doses of the drug or medicine or fluid. The cartridge may comprise a distal end and a proximal end. The cartridge may comprise a piston. The piston may be slideably arranged in an interior of the cartridge. Before setting and dispensing a first dose from the cartridge, the piston may be arranged in a proximal end section of the cartridge. For dose delivery, the piston may be moveable by the lead screw with respect to the cartridge in the delivery direction. Preferably, throughout the operation of the device, the lead screw may be in abutment with the piston.

The device may further comprise a number sleeve. The number sleeve may be threadedly engaged with the housing. For this purpose, the housing may comprise a thread arranged on an inner surface of the housing. The number sleeve may comprise a thread arranged on the outer surface of the number sleeve. Due to mechanical cooperation of the threads, the number sleeve and the housing may be threadedly engaged. Due to mechanical cooperation of the threads, the number sleeve may be screwable with respect to the housing.

The device may further comprise a dial link. The dial link may be axially moveable with respect to the housing. The dial link may be axially moveable for setting and dispensing a dose. The dial link may be rotatable with respect to the housing for dose setting. The dial link may be prevented from rotation with respect to the housing for dose delivery. The dial link may be rotatably fixed with the number sleeve when the dial link and the number sleeve are in a first arrangement, preferably a first axial arrangement. The term "rotatably fixed" may mean in this context that any relative rotational movement between the number sleeve and the dial link is prevented. In the first arrangement, the number sleeve and the dial link may be coupled, e.g. due to mechanical cooperation of a clutch with the dial link. The dial link may be rotatably fixed with the number sleeve for dose setting. In particular, rotation of the number sleeve during dose

setting may be transferred into rotation of the dial link. The number sleeve and the dial link may be - in a limited fashion - rotatable with respect to one another when the dial link and the number sleeve are in a second arrangement, preferably a second axial arrangement. For example, the number sleeve may be rotatable relative to the dial link when the dial link and the number sleeve are in the second arrangement for dispensing a set dose. In the second arrangement, the number sleeve and the dial link may be - at least partly - uncoupled. The number sleeve and the dial link may become uncoupled for dose delivery, in particular for moving the lead screw in the delivery direction. This uncoupling may enable relative rotation of the number sleeve with respect to the dial link in the delivery direction.

10 The device may further comprise a coupling, in particular a unidirectional coupling. The term "unidirectional" may mean that the coupling may enable relative rotational movement of two components, e.g. the number sleeve and the dial link, in one direction while preventing relative rotational movement of the two components in an opposite direction. In particular, the unidirectional coupling may be adapted and arranged to allow a relative rotation between the dial link and the number sleeve in a first direction when the dial link and the number sleeve are in the second arrangement. The first direction may be the clockwise direction, for example. The unidirectional coupling may be adapted and arranged to prevent relative rotation between the dial link and the number sleeve in a direction opposite to the first direction when the dial link and the number sleeve are in the second arrangement. The direction opposite to the first direction may be anti-clockwise direction.

By means of the unidirectional coupling, the number sleeve may be rotatable with respect to the dial link for enabling movement of the lead screw in the delivery direction for dose delivery. However, the number sleeve may be prevented from relative rotation with respect to the dial link in the direction opposite to the first direction, e.g. the anti-clockwise direction. Also, the dial link may be prevented from relative rotation with respect to the number sleeve in the direction opposite to the first direction, e.g. the anti-clockwise direction. Accordingly, any rotational movement which would result in an axial movement of the lead screw in a direction opposite to the delivery direction may be prevented. Accordingly, the unidirectional coupling prevents that the lead screw is moved away from the piston between subsequent dose delivery steps. In this way, underdosing, which may have fatal consequences for the user can be prevented. Dose accuracy and safety of the device are increased.

35 According to one embodiment, the device further comprises a clutch. The clutch may be adapted and arranged to be axially and rotationally locked to the number sleeve. The clutch may be coupleable to the dial link. The dial link may be arranged at least partly within the clutch.

The clutch may provide a rotational coupling between the number sleeve and the dial link in the first arrangement. The clutch may be adapted and arranged to mechanically cooperate with the dial link such that the dial link and the number sleeve are rotationally coupled when the dial link and the number sleeve are in the first arrangement.

5

The unidirectional coupling may comprise at least one arm. The coupling may comprise two, three, four or more arms. The arm may be flexible in a radial direction. The arm may be provided on the clutch. Thus, the clutch may fulfill two functions. Firstly, it may rotationally couple the number sleeve and the dial link in the first arrangement, e.g. for dose setting.

10 Secondly, it may enable a unidirectional coupling between the number sleeve and the dial link in the second arrangement, e.g. for dose delivery. Further components, which would make the device more complicated are, thus, superfluous. Hence, a cost-effective and easily working device is provided.

15 According to one embodiment, the unidirectional coupling further comprises at least one edge or protrusion. The edge may be arranged on the dial link. The edge may protrude from the dial link in a radial direction. The edge may be adapted and arranged to interact with the flexible arm provided on the clutch. By means of the edge and the arm a reliable and easily-working unidirectional coupling may be provided between the number sleeve and the dial link. The  
20 flexible arm and the edge may be adapted and arranged to form a radially effective unidirectional coupling. Alternatively, the flexible arm and the edge may be adapted and arranged to form an axially effective unidirectional coupling.

25 According to one embodiment, the device is adapted and arranged such that, when the dial link and the number sleeve are in the first arrangement, the edge and the flexible arm are free from mechanical cooperation with one another. In the first arrangement, there may be no unidirectional coupling between the dial link and the number sleeve. Rather, there may be a coupling between the number sleeve and the dial link due to mechanical cooperation of dial link and the clutch, which coupling may prevent any rotation between the dial link and the number  
30 sleeve. Accordingly, the unidirectional coupling may not influence a dose setting operation of the device.

When the dial link and the number sleeve are brought in the second arrangement, the edge and the flexible arm may be brought in mechanical cooperation with one another. In particular, the  
35 edge and the arm may become engaged when the number sleeve and the dial link are brought in the second arrangement. The device may further comprise a dose knob. The dose knob may be connected, preferably permanently connected to the dial link. Thus, axial and rotational

movement of the dose knob may be transferred into axial and rotational movement of the dial link. The dose knob may be adapted and arranged to set and deliver a dose. The user may depress the dose knob for initiating a dose delivery operation. The device and, in particular the dose knob, may be configured such that, when the dose knob is moved in the delivery direction for performing a delivery operation, the flexible arm and the edge are brought in mechanical cooperation with one another. In other words, movement of the dose knob in the delivery direction may bring the number sleeve and the dial link in the second arrangement. Further, movement of the dose knob in the delivery direction may establish the unidirectional coupling between the number sleeve and the dial link.

10 Accordingly, when the dial link and the number sleeve are in the second arrangement, the edge and the flexible arm mechanically cooperate with one another. Thus, the unidirectional coupling may be provided in the second arrangement only, i.e. during a dose delivery operation. By means of the unidirectional coupling, any movement of the piston rod in the direction opposite to the delivery direction may be effectively prevented.

20 According to one embodiment, the flexible arm is arranged on an inner surface of the clutch. The arm may protrude radially inwardly and towards the dial link from the inner surface of the clutch. The edge may be provided on an outer surface of the dial link. The edge may protrude radially outwardly and towards the clutch from the outer surface of the dial link.

25 According to one embodiment, the edge is shaped asymmetrically. In particular, the edge may comprise a first surface. The first surface may have a first slope. The edge may comprise a second surface. The second surface may have a second slope. The first slope may have a different angle as compared to the second slope. The first surface may have a greater inclination than the second surface. By means of the asymmetric edge, rotation of the number sleeve in the first direction with respect to the dial link may be enabled while rotation of the number sleeve in the second direction may be prevented.

30 According to one embodiment, the unidirectional coupling comprises a plurality of flexible arms. The unidirectional coupling may comprise a plurality of edges. The arms and edges may be adapted and arranged to interact with one another when the dial link and the number sleeve are in the second arrangement. In particular, one respective arm may be configured to mechanically cooperate with one respective edge. In this way, a very effective unidirectional coupling may be provided.

35

According to one embodiment, the unidirectional coupling may be adapted and arranged to allow a relative rotation between the dial link and the number sleeve in a clockwise direction. However, relative rotation between the dial link and the number sleeve in the anti-clockwise direction may be prevented. In this way, rotation of the number sleeve with respect to the dial link in the distal or delivery direction for dispensing the drug may be enabled. Accordingly, the delivery operation of the device may not be hampered by the unidirectional coupling.

According to one embodiment, the device further comprises an inner sleeve. The inner sleeve may be arranged within the housing of the device. The inner sleeve may be axially moveable with respect to the housing. The inner sleeve may be axially moveable in the proximal direction for setting a dose. The inner sleeve may be axially moveable in the distal or delivery direction for dispensing the set dose. The proximal direction may be opposite to the distal or delivery direction. The inner sleeve may be rotatably fixed relative to the housing throughout the operation of the device. The inner sleeve may be threadedly engaged with the number sleeve. The device may further comprise a drive nut. The lead screw may comprise a threaded shaft. The drive nut may be, preferably permanently, threadedly engaged with the threaded shaft. For dose delivery, the drive nut may be adapted to advance the lead screw with respect to the housing to dispense fluid from the cartridge. The dial link may be connected with the drive nut. The dial link may be permanently connected to the drive nut. The dial link may be axially moveable with respect to the drive nut. The dial link may be rotatably fixed relative to the drive nut.

According to one embodiment, the device is adapted such that, during dose setting, the dial link and the number sleeve are in the first axial arrangement. A screwing motion of the dial link and the number sleeve relative to the housing may be adapted to screw the dial link and the number sleeve a first axial distance away from a home position with respect to the housing. The number sleeve and the dial link may be screwed in the direction opposite to the delivery direction, i.e. the proximal direction, with respect to the housing. The home position may be that position with respect to the housing in which the number sleeve and the dial link are positioned when the device is supplied from the manufacturer. The screwing motion of the dial link may be configured to screw the drive nut along the lead screw for a second axial distance. The second axial distance may be different from the first axial distance. The second axial distance may be smaller than the first axial distance. The drive nut may be moved in the proximal direction due to mechanical cooperation with the dial link.

The device may further be adapted such that, during dose delivery, the dial link and the number sleeve may be in the second axial arrangement. In the second axial arrangement, the number

sleeve may be rotatable with respect to the dial link in the delivery direction. In the second axial arrangement, the dial link may be prevented from rotation but may be axially moveable in the delivery direction. A screwing motion of the number sleeve relative to the housing back towards the home position may be adapted to advance the inner sleeve in the delivery direction. The screwing motion of the number sleeve relative to the housing back towards the home position may be adapted to advance the dial link without rotation in the delivery direction to axially advance the drive nut. Thus, the lead screw and the moveable piston may be advanced in the delivery direction to dispense fluid from the cartridge due to mechanical cooperation of the drive nut and the lead screw.

According to one embodiment, the device further comprises a mid-body. The mid-body may be axially fixed inside of the housing. The mid-body may be prevented from any movement with respect to the housing due to mechanical cooperation with the housing. The lead screw may comprise a spline. The spline may comprise a keyway. The spline may be arranged along the threaded shaft. The spline may extend along a whole length of the lead screw. The mid-body may comprise at least one protrusion, e.g. a tab. The mid-body may comprise a plurality of protrusions or tabs. The tabs may slidably fit within the keyway in the lead screw. The tabs may be adapted and arranged to prevent a rotation of the lead screw with respect to the housing.

According to one embodiment, the inner sleeve is splined to the mid-body. The inner sleeve may be axially moveable relative to the mid-body. The inner sleeve may be rotatably fixed relative to the mid-body. The inner sleeve may be axially moveable and rotatably fixed relative to the mid-body by means of at least one lug of the mid-body. The lug may slidably fit within at least one slot formed in the inner sleeve.

According to one embodiment, the number sleeve comprises a threading for threaded engagement with the housing. The threading or thread may be an outer thread of the number sleeve. The threading of the number sleeve to the housing may be of a first lead. The number sleeve may comprise a threading for threaded engagement with the inner sleeve. Said threading or thread may be an inner thread of the number sleeve. The threading of the number sleeve to the inner sleeve may be of a second lead. The lead screw may comprise a threading, in particular an outer threading. The threading of the lead screw may be of a third lead. The first lead, the second lead and the third lead may be different from one another.

According to one aspect, a drug delivery device is provided comprising:

- a housing;
- a lead screw having a longitudinal axis, a distal end and a proximal end that is rotatably fixed during dose setting and dose delivery and axially movable in a distal direction relative to the

housing, the lead screw including a threaded shaft and a bearing foot connected to the distal end, wherein the lead screw has a smooth keyway positioned parallel to the longitudinal axis;

- a cartridge with a movable piston at one end and an outlet at the other end, the piston engagable by the lead screw bearing to be advanced toward said outlet when the lead screw is moved distally;
- a drive nut threadedly engaged and screwable along the lead screw threaded shaft;
- a number sleeve threadedly engaged with the housing to be screwable relative to the housing;
- a dial link connected with the drive nut and axially movable and rotatably fixed relative to the drive nut, the dial link rotatably fixed with number sleeve when the dial link and number sleeve are in a first axial arrangement, the number sleeve rotatable relative to the dial link when the dial link and number sleeve are in a second axial arrangement;
- an inner sleeve threadedly engaged with the number, the inner sleeve axially movable and rotatably fixed relative to the housing;
- a mid-body fixed inside of the housing, the mid-body comprising tabs (31) that slidably fit within the keyway in the lead screw to prevent rotation of the lead screw within the housing, the mid-body further comprising at least one metal ratchet arm configured to prevent the lead screw from moving in the proximal direction;

wherein the inner sleeve is axially movable and rotatably fixed relative to the mid-body by at least one lug of the mid-body that slidably fits within at least one slot formed in the inner sleeve;

and wherein the threading of number sleeve to the housing is of a first lead, the threading of the inner sleeve to the number sleeve is of a second lead, and the threading of the lead screw threaded shaft is of a third lead, and the first lead, the second lead and the third lead are not equal;

wherein during dose setting, the dial link and the number sleeve are in the first axial arrangement, whereby a screwing motion of dial link and number sleeve relative to the housing screws the dial link and the number sleeve a first axial distance from a home position, which screwing motion of dial link screws said drive nut along the lead screw threaded shaft a second axial distance that is different than the first axial distance;

wherein during dose delivery, the dial link and number sleeve are in said second axial arrangement, whereby a screwing motion of the number sleeve relative to the housing back toward the home position advances the inner sleeve without rotation in the distal direction to axially advance the drive nut that is axially fixed to the inner sleeve and thereby the lead screw and the movable piston to dispense fluid from the cartridge outlet, and wherein a unidirectional coupling is provided that allows relative rotation between the dial link and the number sleeve in only a first direction.

According to one embodiment, the unidirectional coupling comprises a plurality of flexible arms provided on an inner surface of a clutch.

5 According to one embodiment, the unidirectional coupling further comprises a plurality of edges that interact with the plurality of flexible arms provided on the inner surface of the clutch.

According to one embodiment, the plurality of edges are provided on an outer surface of the dial link.

10 According to one embodiment, the plurality of edges comprise asymmetrical edges, each asymmetrical edge comprising a first surface having a first slope and a second surface having a second slope, the first slope having a different angle than the second slope.

15 According to one embodiment, the unidirectional coupling allows relative rotation between the dial link and the number sleeve in only a clockwise direction.

20 These as well as other advantages of the various aspects of the improved drug delivery device, and the manner of attaining them, will become apparent to those of ordinary skill in the art by reading the following detailed description, with appropriate reference to the accompanying figures.

The scope of the invention is defined by the content of the claims. The invention is not limited to specific embodiments but comprises any combination of elements of different embodiments. Moreover, the invention comprises any combination of claims and any combination of features  
25 disclosed by the claims.

#### Brief description of the Figures

30 Exemplary embodiments are described herein with reference to the drawings, in which:  
Figure 1 is an illustration of one embodiment of the present invention showing the assembled pen-type medication dispensing apparatus where the cap has been removed to reveal the cartridge container affixed to the dose setting mechanism;

35 Figure 2 is a close up view of the cartridge container and the pen needle that can be attached to the cartridge container for injection of the medicament;

Figure 3 is an exploded view of the embodiment from Figure 1 showing each of the individual parts arranged relative to each other as they exist in the fully assembled device;

Figure 4 is a perspective view of one embodiment of a modified dial link configuration;

5

Figure 5 is a perspective view of one embodiment of a modified clutch configuration;

Figure 6 is a perspective view of the modified dial link configuration of Figure 4 and the modified clutch configuration of Figure 5 in a state where the unidirectional coupling prevents rotation in a first direction;

10

Figure 7 is a cross-sectional view of the embodiment of the modified dial link configuration of Figure 4 in an engaged position with the modified clutch configuration of Figure 5; and

15

Figure 8 is a cross-sectional view of the embodiment illustrated in Figure 7.

Corresponding reference characters indicate corresponding parts throughout the several views. Although the drawings represent embodiments of the present invention, the drawings are not necessarily to scale, and certain features may be exaggerated or omitted in some of the drawings in order to better illustrate and explain the present invention.

20

#### Detailed Description

Referring first to Figures 1 to 3, there is shown a drug delivery device 1 as an injector pen, which pen has an elongated, substantially writing instrument-like form, although other forms are within the scope of the invention. In other words, the drug delivery device 1 may be a pen-type device. The drug delivery device 1 comprises a housing having a cartridge holder 2, and a main (exterior) body or housing 4.

25

The drug delivery device 1 and the housing have a distal end and a proximal end. The term "distal end" designates that end of the drug delivery device 1 or a component thereof which is or is to be arranged closest to a dispensing end of the drug delivery device 1. The term "proximal end" designates that end of the device 1 or a component thereof which is or is to be arranged furthest away from the dispensing end of the device 1. The distal end and the proximal end are spaced apart from one another in the direction of an axis. The axis may be the longitudinal axis or rotational axis of the device 1.

30  
35

The proximal end of the cartridge holder 2 and the distal end of the main housing 4 are secured together by appropriate retaining features depending on whether the pen injector is designed as a reusable device or as a disposable device. In the latter case, the retaining feature would be permanent using the connection means described below. If the device is reusable, the retaining  
5 meaning would be a screw-type connection, a Luerlok, snap fit, bayonet, or the like type or combination of fittings that allow the user to easily disassemble the device to replace the empty cartridge with a fresh new cartridge. In this illustrated arrangement, the cartridge holder 2 is secured within the proximal end of the main body 4.

10 A cartridge 8 from which a number of doses of a medicinal product may be dispensed is provided in the cartridge holder 2. Preferably, the cartridge 8 contains a type of medicament that must be administered often, such as once or more times a day. One such medicament is insulin. A piston 10 shown in Fig. 2 is initially retained in the proximal end of the cartridge 8 and as each injection is completed gradually moves distally to the empty cartridge position. A removable cap  
15 14 is releasably retained connected to the main body 4 covering the cartridge holder 2.

The dose setting mechanism of the drug delivery device illustrated in Figures 1-3 may be utilized as either for a disposable or reusable drug delivery device. Where the drug delivery device 1 comprises a disposable drug delivery device, the cartridge 8 cannot be removed from  
20 the device 1 without destroying the device 1. In a disposable device, the proximal end of the cartridge holder 2 can be fixedly mounted or secured, via adhesives, ultrasonic welding or in another suitable manner, to the dose setting mechanism housing when the injector pen is assembled by the manufacturer. Alternatively, where the drug delivery device 1 comprises a reusable drug delivery device, the cartridge 8 is removable and may be removed from the  
25 device 1 without destroying the device 1. In the drug delivery device 1 illustrated in Figures 1-3, the device 1 is illustrated as a disposable drug delivery device. However, those of ordinary skill in the art will recognize that the dose setting mechanism could also be used on reusable drug delivery devices as well, while in the case of a reusable pen, wherein the cartridge holder 2 may be reusable, such that the proximal end can be removably mounted or secured, for example via  
30 a threaded, bayonet, or snap fit connection, to a reusable dose setting mechanism having a resettable lead screw.

The previously mentioned removable or replaceable cap 14 is used to cover the cartridge holder 2 extending from the main housing 4. Preferably, the outer dimensions of the replaceable cap  
35 14 are similar to or identical to the outer dimensions of the main housing 4 so as to provide an impression of a unitary whole part when the replaceable cap 14 is in position covering the cartridge holder 2. In use, the removable cap 14 is removed and a pen needle assembly 16

comprising a double-ended needle mounted in a hub may be screwed or pushed onto the distal end of the cartridge holder 2 or, alternatively, may be snapped onto this distal end.

5 Cartridge 8 is of conventional design and defines a medicine-filled reservoir that is closed at its proximal end by the piston 10 that is axially slidably and sealably engaged with the cartridge interior wall to hold the fluid medication within the reservoir. The distal, outlet end of the cartridge reservoir is sealed by a septum 11 held by a cap 13 that is secured to a stepped-down diameter neck portion 15 of the cartridge 8. When the pen needle assembly 16 is mounted on the distal end of the cartridge holder 2, the proximal point of the injection needle passes through  
10 a central opening in the distal end of the cartridge holder 2, an opening in the cap 13, and penetrates the cartridge septum 11 to provide a fluid flow outlet by which medicine within the cartridge reservoir can be dispensed from the distal needle tip during operations of injector pen 1. The fluid medicine cartridge 8 shown and described above is illustrative and not intended to be limiting as other constructions may be employed within the scope of this invention.

15 Main body 4 of injector pen 1 houses an axially advanceable lead screw 22, a drive nut 23, a inner sleeve 29, a dial link 25, a number sleeve 24, a clutch 26, and a compression spring 27. A dose knob 28 is connected to the dial link 25 and is used to set the dose and then to inject the set dose. Housing or main body 4 is formed from a lightweight material, such as injection  
20 molded plastic. The housing 4 may be molded as a single, tubular piece for robustness. A window 51 in the housing 4 near its proximal end can be filled with a magnifying lens that snaps fits to the housing 4 and allows dosage indicating markings (not shown) on the number sleeve 24 to be readily visible during use.

25 Near the interior distal end of the housing 4 is mounted a mid-body 20 that is formed with a central opening having an inward facing anti-rotation mechanism formed from a pair of diametrically opposed elements or tabs 31 having squared off inward ends that each slidably fit within longitudinal keyways 32 in the lead screw 22. In alternate embodiments, features other than tabs and keyways, for instance a lead screw with flats that fits within a complementarily  
30 shaped hole in a collar, may be used to prevent rotation. The tabs 31 prevent the lead screw 22 from rotating within the housing 4 during pen use, but permit the lead screw 22 to be shifted longitudinally, such as in the distal direction towards the cartridge 8. A snap fit or sonic welding connection of the mid-body 20 to the tubular housing 4 can be used to prevent axial and rotational relative motion of the mid-body 20 to the housing 4.

35 The lead screw 22 is in the form of a screw that is axially translatable and rotatably fixed during dosing and injecting. The term "rotatably fixed" shall mean in this context that the lead screw 22

is prevented from rotation during dosing and injecting. The lead screw 22 includes a shaft with a helical threading 33 along its length, which threading 33 is interrupted by the longitudinally extending keyways or grooves 32. A thread stop 34 shown at the proximal end of the threading 33 is provided and is used in preventing the pen from being set by a user to deliver a dose of medicine larger than remains in cartridge 8. Other forms of stopping the screw motion may be substituted within the scope of the invention, for example, the threading at the proximal screw end could stop near the proximal end where it cannot be cammed in, and such solid screw with thread stop better ensures the nut 23 will not be torqued off the screw during dose setting. The distal end of lead screw 22 includes an enlarged, disc-shaped foot or bearing 21 to distribute loading on the cartridge piston 10 that the bearing 21 contacts and thereby directly engages during the piston 10 advancing. The separate bearing foot 21 can be attached, such as with a snap fit 20 that may permit relative rotation, to the lead screw 22. The lead screw 22 is shown as being a one-piece plastic injection molding, but alternate materials of construction and multiple pieces are possible.

The drive nut 23 includes a cylindrical, tube-shaped body with flexible fingers 36 and clicker teeth 35. The distal region of the drive nut 23 is formed with an internal threading 37 that threadedly engages in a friction locking fashion the threading 33 on the lead screw 22. Threadings 33 and 37 are shown as a double start threading but may be differently formed while still providing suitable friction locking capabilities, such as a single start threading or another multiple start threading. The drive nut 23 is located within the inner sleeve 29 and is axially, but not rotationally fixed, to the inner sleeve 29. As the drive nut 23 is rotated relative to inner sleeve 29 during dose setting, the clicker teeth 35 engage in a ratchet fashion flexible arms 38 that project radially on the inside of the inner sleeve 29. As the drive nut 23 rotates, the flexible arms 38 ride over the teeth 35 creating an audible clicking noise. The teeth 35 are configured so that each click is equal to one dose volume being set. As few as one flexible clicker arm 38 may be provided, but the use of four equally angularly spaced arms 38 aids in centering the drive nut 23 within the inner sleeve 29. The hollow interior of the drive nut body 23 located proximally of the threading 37 allows free passage of the proximal end of the lead screw 22. The exterior surface of the drive nut 23 is designed to cooperatively engage with the dial link 25 so that the dial link 25 is axially free and rotatably fixed relative to the drive nut 23. Thus, during use the dial link 25 is axially moveable relative to, but rotatably locked with, the threaded drive nut 23. This connection is possible because of the cooperation of the proximally extending fingers 36 on the drive nut 23 and the distally extending fingers 43 of the dial link 25. These two sets of fingers 36, 43 move axially relative to each other but engage each other rotationally during dose setting when the dial link 25 is rotated by turning the dose knob 28, which is fixed to

the dial link 25. The drive nut 23 is shown as being a one-piece plastic injection molding, but other constructions are within the scope of the invention.

5 In the shown embodiment, the dial link 25 is formed in one piece of an injection molded plastic and which fits within the body 4. A flange 40 that rings a central region of the dial link body includes splines or teeth 39 that extend from the distal face of the flange 40, and teeth 41 that extend from the proximal face of the flange 40. A stepped-down portion of the proximal end of the dial link 25 forms an axially and proximally extending stem 42. The distal end of the dial link body includes the pair of fingers 43 that fit with the fingers 36 of the drive nut 23 to allow axial  
10 motion but not rotational motion of the drive nut 23 relative to the dial link 25, thereby rotationally locking the pieces together within the same annular space. Fingers 36 and 43 extend sufficiently axially to ensure they do not disengage during the setting of the maximum pen dose for injection.

15 An injection molded plastic dose knob 28 with a proximal face, and having a distally facing and centrally located bearing collar and alignment post is provided. The stem 42 of the of the dial link 25 receives the dose knob alignment post and can be ultrasonically welded within the bearing collar during manufacturing assembly, so as to axially and rotatably fix together the dose knob 28 and the dial link 25. The term "rotatably fix" shall mean in this context that any  
20 relative rotational movement between the dose knob 28 and the dial link 25 is prevented. A dose knob skirt 50 distally extends from the radial periphery of the dose knob distal face to serve as a grip portion for a user during dose setting.

Coaxially mounted around the dial link 25 is the number sleeve 24. The number sleeve 24 has a  
25 cylindrical exterior surface 30 with a threading 52 formed as a helical groove that engages a corresponding threading 62 formed on the interior surface of body 4 to threadedly engage the number sleeve 24 to the pen housing. Threadings 52 and 62 are shown as a single start threading but may be differently formed. Threading 62 abuts an end 63 of threading 52 on the the number sleeve 24 at the maximum pen dose, assuming the cartridge 8 is sufficiently full for  
30 such a maximum dose. A stop surface 64 on the distal end of the outer surface of the number sleeve 24 is positioned in slightly spaced apart relationship with a projecting stop at the zero dose position, and another stop surface is to be abutted by the stop if a user attempts to manually screw the screw element below a zero dose position. A hollow interior 65 of the number sleeve 24 is defined by a cylindrical interior surface provided with a helical threading 67.

35

The outside diameter of the number sleeve 24 is selected such that it can fit inside the dose knob 28. A proximal end region of the number sleeve 24 includes a number of notches 70 and

corresponding windows 71 that are alternately spaced around the circumference. The number sleeve 24 includes around its exterior surface 30 suitable indicia of therapeutic dose size as visible through the body opening 51. A clutch 26 fits within the open proximal end of the number sleeve 24. Ears 72 on the clutch 26 fit within the notches 70 and assembly fingers (not explicitly shown in the Figures) snap lock into the windows 71 to axially and rotatably lock the number sleeve 24 and the clutch 26 together during manufacturing assembly. A ring of axially extending teeth 54 on the clutch 26 formed in the interior surface of a flange cooperate with the dial link teeth 41 proximally facing on the dial link 25.

10 Disposed between the clutch 26 and the inside portion of the dose knob 28 is the compression or biasing spring 27 that urges the clutch 26 to engage the teeth 41 on the dial link 25. During injection, when a user manually applies a plunging force onto the proximal face of the dose knob 28, the spring 27 is elastically compressed, thus disengaging the clutch 26 and the number sleeve 24 from the dial link 25. Flange teeth 41 on the dial link 25 and clutch teeth 54  
15 mesh when the spring 27 has biased the clutch 26 and attached the number sleeve 24 to the dose knob 28 and the dial link 25. The dose knob 28 and the dial link 25 are not meshed with the clutch 26 and the number sleeve 24 when the spring 27 has been sufficiently compressed during injecting. While a helically coiled metal wire spring is shown, other forms of commonly known biasing elements may be substituted.

20 The inner sleeve 29 is injection molded from plastic and includes a tubular body that fits into the hollow 65 of the number sleeve 24. The inner sleeve 29 has a helical threading 75 on its outer surface that engages the internal threading 67 on the inside surface of the number sleeve 24. Threadings 67 and 75 are shown as a single start threading, but may be differently formed. The proximal most portion of the end of inner sleeve 24, which end is partially helically shaped  
25 corresponding to the threading, is notched to form a partial ring of axially projecting teeth 76 that, when meshed with dial link distally facing teeth 39, serve to rotatably lock together the dial link 25 and the inner sleeve 29. The inner sleeve 29 is keyed to the pen body 4 through the intermediate mid-body 20 that is axially and rotationally fixed to the body 4. The distal end of the  
30 inner sleeve 29 has a pair of ridge-defined slots 77 on the periphery of the inner sleeve 29 which axially, slidably receive lugs 78 radially inwardly projecting from the mid-body 20.

Openings molded into the inner sleeve 29 define four resilient fingers 38 having radially inwardly projecting teeth that are axially oriented and shaped to project into a recess in the distal end of  
35 the drive nut 23 that has radially projecting teeth or ridges 35 such that the inwardly projecting teeth click over, in either rotational direction, teeth 35 during dose setting. The fingers 38 with

teeth cooperate with the recess on the drive nut 23 to hinder the nut 23 from coming off the inner sleeve 29 after being assembled thereto during manufacture.

To facilitate back-driving during dose delivery, the threaded connections of the number sleeve 24 and the body 4, and the number sleeve 24 and the inner sleeve 29, are non-binding and provided by projecting 60° face angle threads that slide within correspondingly designed recessed grooves. With these threadings, it is preferred that the mechanical advantage is 3.4 or greater, and the screw lead of the drive member or drive nut 23 is 0.108 inch.

Figure 4 illustrates a perspective view of a modified dial link configuration 25a providing a unidirectional coupling feature. As illustrated, in this modified embodiment, the dial link 25a has certain similarities with the dial link 25 illustrated in Figure 3. For example, this modified dial link 25a is formed in one piece of an injection molded plastic and fits within the body 4. The dial link 25a comprises a flange 40 that rings a central region 88 of the dial link body. A distal portion of this central region 88 comprises splines or teeth 39 that extend from the distal face of the flange 40. In addition, teeth 41 extend from the proximal face of the flange 40. In addition, a proximal portion of this central region 88 of the dial link 25a is configured to comprise a plurality of elongated serrations or edges 82. These features may be equally spaced around an outer surface of the proximal portion of the dial link 25a. As described below, in one preferred arrangement, these serrations or edges 82 comprise two non-symmetrical sloping surfaces, a first sloping surface having a greater inclination or slope as compared to the second sloping surface. For example, Figure 8 illustrates a cross sectional view of the modified dial link 25a engaged with the modified clutch 26a so as to form a unidirectional coupling 100. As illustrated in Figure 8, a first sloping surface 84 of a first serration or edge 82a comprises a greater inclination than a second surface 86 of this serration or edge 82a.

As will be described in greater detail below, these serrations or edges 82 are configured to interact with corresponding features of the modified clutch 26a when the dose knob 28 is pushed in the distal direction. That is, these features interact such that, when the modified clutch 26a becomes disengaged from the modified dial link 25a and the dial link splines 41 move out of engagement with the axially extending teeth 54 on the modified clutch 26a, this unidirectional coupling 100 allows the clutch 26a and, hence, the number sleeve 24 to rotate in only one direction vis-à-vis the dial link 25a. Preferably, this is the rotational direction wherein the number sleeve 24 translates distally, back into the housing 4 during a dose dispense step.

Similar to the dial link 25 illustrated in Figure 3, the modified dial link 25a illustrated in Figure 4 comprises a stepped-down portion of the proximal end of dial link 25a which forms an axially

and proximally extending stem 42. The distal end of the dial link body includes a pair of fingers 43 that fit with the fingers 36 of the drive nut 23 to allow axial motion but not rotational motion of the drive nut 23 relative to the dial link 25a, thereby rotationally locking the pieces together within the same annular space. The fingers 36 and 43 extend sufficiently axially to ensure that they do not disengage during the setting of the maximum pen dose for injection.

Figure 5 illustrates a perspective view of a modified clutch 26a. As illustrated, this modified clutch 26a is similar to the clutch 26 illustrated in Figure 3. That is, this modified clutch 26a fits within the open proximal end of the number sleeve 24. Ears 72 on the modified clutch 26a fit within notches the 70 and assembly fingers (not explicitly shown in the Figures) snap lock into the windows 71 of the number sleeve 24 to axially and rotatably lock the number sleeve 24 and the modified clutch 26a together during manufacturing assembly. A ring of axially extending teeth 54 on the modified clutch 26a formed in the interior surface of the flange cooperate with the dial link teeth 41 proximally facing on modified dial link 25a. Disposed between the clutch 26a and the inside portion of the dose knob 28 is the previously mentioned spring 27 that urges the clutch 26a to engage teeth 41 on the modified dial link 25a. During injection, when a user manually applies a plunging force onto the proximal face of the dose knob 28, the spring 27 is elastically compressed, thus disengaging the modified clutch 26a and the number sleeve 25 from the dial link 25a. The flange teeth 41 on the modified dial link 25a and the teeth 54 of the modified clutch 26a mesh when the spring 27 has biased the modified clutch 26a and the attached number sleeve 24 to the dose knob 28 and the modified dial link 25a. The dose knob 28 and the modified dial link 25a are not meshed with the modified clutch 26a and the number sleeve 24 when the spring 27 has been sufficiently compressed during injecting.

The modified clutch 26a further comprises a plurality of inwardly extending flexible arms 80 provided along a distal portion of an inner surface 96 (see Figure 8) of the clutch 26a. For example, as illustrated in cross sectional view provided by Figure 8, the clutch 26a comprises three inwardly extending flexible arms 80a-c that extend inwardly away from the inner surface 96 of the clutch 26a. Figure 7 illustrates a cross sectional view of the flange teeth 41 on the dial link 25a meshed with the clutch teeth 54 when the spring 27 is in an uncompressed state (Figure 7 shows the compressed situation).

Utilizing the modified dial link 25a and clutch 26a, the flange teeth 41 on the dial link 25a and the clutch teeth 54 mesh when the spring 27 has biased the clutch 26a and the attached number sleeve 24 to the dose knob 28 and dial link 25a. For example, as illustrated in Figure 6, the modified dial link 25a is not meshed with the clutch 26a (and, hence, the number sleeve 24) when the spring 27 has been sufficiently compressed during injecting. As can be seen from

Figure 6, the proximal flange teeth 41 on the modified dial link 25a are no longer meshed with the axially extending clutch teeth 54. However, as the modified dial link 25a is axially moved in the distal direction, now the elongated serrations or edges 82 along the distal end of the dial link 25a slide into or become engaged with the corresponding inner flexible arms 80 of the modified clutch 26a. It is in this position that the elongated serrations or edges 82 and the flexible arms 80 form a unidirectional coupling 100.

As such, in this modified configuration, the unidirectional coupling 100 is established between the modified dial link 25a and the modified clutch 26a. This can be seen in Figure 8.

In this illustrated arrangement of Figure 8, as the modified clutch 26a rotates in a first direction 90, the flexible arms 80a-c ride over the first sloping surfaces 82a of the serrations or edges 82 such that the flexible arms 80 can move from one edge to the next neighbouring edge or edges provided along the inner surface 96 of the clutch 26a. The first direction may be the clockwise direction. However, because of the slope of the second sloping face 82b, the flexible arms 80 are prevented from rotating in a second direction 92. The second direction may be opposite to the first direction. The second direction may be anti-clockwise.

Consequently, with this unidirectional coupling 100 between the modified dial link 25a and the modified clutch 26a, as a user begins to set a dose by rotating the dose knob 28 and, thereby, causing the number sleeve 24 to translate out proximally from the body 4 of the injection device and, then, and the user grips the number sleeve 24, thereby preventing the number sleeve 24 from rotating, the user will be prevented from rotating the dose knob 28 in the second direction 92 while at the same time pushing the dose knob 28 axially in the distal direction – i.e. towards the injection site. As such, with this unidirectional coupling 100, disengagement of the clutch 26a from the dial link 25a/dose knob 28 will no longer allow a relative rotation between the dial link 25a/dose knob 28 connection and the clutch 26a in the undesired direction so as to allow rotation of the modified dial link 25a and, hence, of the drive nut 23.

The operation of the above described embodiment will now be explained. The pen 1 with a needle 16 attached should first be primed to remove any trap air in the cartridge 8 and to ensure the bearing 21 is in contact with the proximal end of the cartridge stopper or piston 10. In particular, typically while clutching the pen body 4 in one hand, a user manually grips the dose knob skirt 50 and then begins to turn the knob 28 relative to the body 4. At the zero dose arrangement, and as long as the knob 28 is not also being plunged which is improper, the knob 28 can only be rotated in a dose increasing direction due to the number sleeve 24 not being further movable distally. A user stops the rotating after a short amount of number 24 sleeve

travel that is associated with a small delivery volume, such as one or two units, which is indicated by markings visible through a window 51. Then, and after removing the cap 14 and any other needle cap present, and while pointing the needle tip upward, the user applies a plunging force on the dose knob 28 to drive it distally until the number sleeve 24 returns to the zero dose position, at which the number sleeve threading 52 has reached the distal end of the body threading 62, during which plunging action the piston 10 is shifted forward within the cartridge 8. If a user sees that the piston movement has caused liquid to reach the needle distal tip, the priming process is complete. If no liquid is visible at the needle tip, the priming steps are repeated as needed. After priming, the pen 1 is ready to be used for an actual injection.

First, a user prepares the pen by setting the desired dose, as visible in the window 51, by turning of the knob 28. If the user dials up too large of a dose, and without expelling any medicine, the user can rotate down the dial by turning the knob 28 in the opposite direction, all the way back to zero if desired. To set a dose, the knob 28 is turned in a clockwise direction.

Because the dose knob 28 and the dial link 25a are fixed rotationally, the dial link 25a is rotated causing the distally facing fingers 43 to engage the proximally facing fingers 36 of the drive nut 23 to thereby turn the drive nut 23 in same direction. Rotation of the drive nut 23 causes the nut 23 to rotate relative to the stationary lead screw 22 whereby the nut 23 moves or climbs up the lead screw 22 in the proximal direction. The drive nut 23 rotates relative to the inner sleeve 29 that is held rotationally fixed relative to the body 4 through the splined connection to the mid-body 20. Because the drive nut 23 and the inner sleeve 29 are axially fixed, proximal axial movement of the drive nut 23 causes the inner sleeve 29 to slide proximally relative to the mid-body 20. Because the clutch 26a is rotationally fixed with the dial link 25a during dose setting, the clutch 26a rotates causing the number sleeve 24 to rotate and to spin out proximally away from body 4. Because the pitch of the threads on the number sleeve 24 are greater than the pitch of the threads on the inner sleeve 29, the number sleeve 24 and the dial link 25a will translate a larger axial distance as compared to the inner sleeve 29 and the drive nut 23.

To inject the dose, after pen 1 is manipulated so the injection needle distal tip properly penetrates, for example, a user's skin, an axial, distal plunging force is applied to the knob face 53 to force the dial link 25a axially in the distal direction towards the body 4, such as with a thumb or index finger of the hand which grasps the housing 4. Initially during injecting, the dial link 25a is shifted axially, which shifting motion compresses the biasing spring 27 to close the gap between the knob surface and the proximal end of the number sleeve 24. The biasing spring 27 is designed to compress prior to the number sleeve 24 moving relative to the body 4. When the dial link 25a shifts relative to the number sleeve 24 to the axial arrangement of the drive nut 23, the clutch teeth 54 and dial link teeth 42 disengage to allow a backdriving rotation

of the number sleeve 24 relative to the dial link 25a. Thus, the dial link 25a and the clutch 26a and, thus, the number sleeve 24, are disengaged. During the axial movement of the dial link 25a, the drive nut 23 does not move axially or rotationally. When the number sleeve 24 and the clutch 26a rotatably uncouple from the dial link 25a, as the dial link 25a is continued to be axially plunged without rotation by the user by the plunging of the knob 28, the number sleeve 24 screws into the body 4 as it spins relative to the knob 28 and the dose markings on the number sleeve 24 that indicate the amount still remaining to be injected are visible through the window 51.

As it screws down, the number sleeve 24 causes the inner sleeve 29 to in essence screw up the internal thread inside of the number sleeve threading as the inner sleeve 29 advances distally a lesser distance than the number sleeve 24. The advancement of the inner sleeve 29, due to the abutting or direct engagement with the distal end of the drive nut 23, advances the drive nut 23 without rotation, which due to its threaded connection with the lead screw 22 advances the lead screw 22 axially without rotation, which lead screw advancement shifts the cartridge piston 10 to expel medication from the cartridge reservoir. The injection is completed when the number sleeve threading 52 has reached the distal end of the body 4, at which time pen 1 is once again arranged in the ready state or zero dose position.

Pen 1 can continue to be used to deliver any desired dose until the medicine remaining in the cartridge 8 is insufficient for a proper dosing. This insufficiency is indicated to the user by the inability to fully set the desired dose due to drive nut threading 37 abutting the thread stop 34 of the lead screw 22, at which time the drive nut 23 and the dial link 25a cannot be rotated proximally any farther. When insufficient medicine remains, the pen 1 is to be disposed of and replaced with a similar but entirely new pen.

The terms „medicament“ or „medicinal product“, as used herein, preferably mean a pharmaceutical formulation containing at least one pharmaceutically active compound,

wherein in one embodiment the pharmaceutically active compound has a molecular weight up to 1500 Da and/or is a peptide, a proteine, a polysaccharide, a vaccine, a DNA, a RNA, , an enzyme, an antibody or a fragment thereof, a hormone or an oligonucleotide, or a mixture of the above-mentioned pharmaceutically active compound,

wherein in a further embodiment the pharmaceutically active compound is useful for the treatment and/or prophylaxis of diabetes mellitus or complications associated with diabetes

mellitus such as diabetic retinopathy, thromboembolism disorders such as deep vein or pulmonary thromboembolism, acute coronary syndrome (ACS), angina, myocardial infarction, cancer, macular degeneration, inflammation, hay fever, atherosclerosis and/or rheumatoid arthritis,

5

wherein in a further embodiment the pharmaceutically active compound comprises at least one peptide for the treatment and/or prophylaxis of diabetes mellitus or complications associated with diabetes mellitus such as diabetic retinopathy,

wherein in a further embodiment the pharmaceutically active compound comprises at least one human insulin or a human insulin analogue or derivative, glucagon-like peptide (GLP-1) or an analogue or derivative thereof, or exendin-3 or exendin-4 or an analogue or derivative of exendin-3 or exendin-4.

Insulin analogues are for example Gly(A21), Arg(B31), Arg(B32) human insulin; Lys(B3), Glu(B29) human insulin; Lys(B28), Pro(B29) human insulin; Asp(B28) human insulin; human insulin, wherein proline in position B28 is replaced by Asp, Lys, Leu, Val or Ala and wherein in position B29 Lys may be replaced by Pro; Ala(B26) human insulin; Des(B28-B30) human insulin; Des(B27) human insulin and Des(B30) human insulin.

Insulin derivatives are for example B29-N-myristoyl-des(B30) human insulin; B29-N-palmitoyl-des(B30) human insulin; B29-N-myristoyl human insulin; B29-N-palmitoyl human insulin; B28-N-myristoyl LysB28ProB29 human insulin; B28-N-palmitoyl-LysB28ProB29 human insulin; B30-N-myristoyl-ThrB29LysB30 human insulin; B30-N-palmitoyl-ThrB29LysB30 human insulin; B29-N-(N-palmitoyl-Y-glutamyl)-des(B30) human insulin; B29-N-(N-lithocholyl-Y-glutamyl)-des(B30) human insulin; B29-N-( $\omega$ -carboxyheptadecanoyl)-des(B30) human insulin and B29-N-( $\omega$ -carboxyheptadecanoyl) human insulin.

Exendin-4 for example means Exendin-4(1-39), a peptide of the sequence H-His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH<sub>2</sub>.

Exendin-4 derivatives are for example selected from the following list of compounds:

H-(Lys)<sub>4</sub>-des Pro<sub>36</sub>, des Pro<sub>37</sub> Exendin-4(1-39)-NH<sub>2</sub>,  
 H-(Lys)<sub>5</sub>-des Pro<sub>36</sub>, des Pro<sub>37</sub> Exendin-4(1-39)-NH<sub>2</sub>,  
 des Pro<sub>36</sub> Exendin-4(1-39),  
 des Pro<sub>36</sub> [Asp<sub>28</sub>] Exendin-4(1-39),

- des Pro36 [IsoAsp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14, Asp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14, IsoAsp28] Exendin-4(1-39),  
 des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39),  
 5 des Pro36 [Trp(O2)25, IsoAsp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14 Trp(O2)25, Asp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14 Trp(O2)25, IsoAsp28] Exendin-4(1-39); or
- des Pro36 [Asp28] Exendin-4(1-39),  
 10 des Pro36 [IsoAsp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14, Asp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14, IsoAsp28] Exendin-4(1-39),  
 des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39),  
 des Pro36 [Trp(O2)25, IsoAsp28] Exendin-4(1-39),  
 15 des Pro36 [Met(O)14 Trp(O2)25, Asp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14 Trp(O2)25, IsoAsp28] Exendin-4(1-39),
- wherein the group -Lys6-NH2 may be bound to the C-terminus of the Exendin-4 derivative;
- 20 or an Exendin-4 derivative of the sequence  
 des Pro36 Exendin-4(1-39)-Lys6-NH2 (AVE0010),  
 H-(Lys)6-des Pro36 [Asp28] Exendin-4(1-39)-Lys6-NH2,  
 des Asp28 Pro36, Pro37, Pro38 Exendin-4(1-39)-NH2,  
 H-(Lys)6-des Pro36, Pro38 [Asp28] Exendin-4(1-39)-NH2,  
 25 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-NH2,  
 des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-(Lys)6-NH2,  
 H-(Lys)6-des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-(Lys)6-NH2,  
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-(Lys)6-NH2,  
 H-(Lys)6-des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39)-Lys6-NH2,  
 30 H-des Asp28 Pro36, Pro37, Pro38 [Trp(O2)25] Exendin-4(1-39)-NH2,  
 H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-NH2,  
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-NH2,  
 des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,  
 H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,  
 35 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2, H-  
 (Lys)6-des Pro36 [Met(O)14, Asp28] Exendin-4(1-39)-Lys6-NH2,  
 des Met(O)14 Asp28 Pro36, Pro37, Pro38 Exendin-4(1-39)-NH2,

H-(Lys)6-desPro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH<sub>2</sub>,  
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH<sub>2</sub>,  
 des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH<sub>2</sub>,  
 H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH<sub>2</sub>,  
 5 H-Asn-(Glu)5 des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH<sub>2</sub>,  
 H-Lys6-des Pro36 [Met(O)14, Trp(O<sub>2</sub>)25, Asp28] Exendin-4(1-39)-Lys6-NH<sub>2</sub>,  
 H-des Asp28 Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)25] Exendin-4(1-39)-NH<sub>2</sub>,  
 H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH<sub>2</sub>,  
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)25, Asp28] Exendin-4(1-39)-NH<sub>2</sub>,  
 10 des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)25, Asp28] Exendin-4(1-39)-(Lys)6-NH<sub>2</sub>,  
 H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)25, Asp28] Exendin-4(S1-39)-(Lys)6-NH<sub>2</sub>,  
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)25, Asp28] Exendin-4(1-39)-(Lys)6-  
 NH<sub>2</sub>;  
 or a pharmaceutically acceptable salt or solvate of any one of the afore-mentioned Exendin-4  
 15 derivative.

Hormones are for example hypophysis hormones or hypothalamus hormones or regulatory  
 active peptides and their antagonists as listed in Rote Liste, ed. 2008, Chapter 50, such as  
 Gonadotropine (Follitropin, Lutropin, Choriongonadotropin, Menotropin), Somatotropine  
 20 (Somatropin), Desmopressin, Terlipressin, Gonadorelin, Triptorelin, Leuprorelin, Buserelin,  
 Nafarelin, Goserelin.

A polysaccharide is for example a glucosaminoglycane, a hyaluronic acid, a heparin, a low  
 molecular weight heparin or an ultra low molecular weight heparin or a derivative thereof, or a  
 25 sulphated, e.g. a poly-sulphated form of the above-mentioned polysaccharides, and/or a  
 pharmaceutically acceptable salt thereof. An example of a pharmaceutically acceptable salt of a  
 poly-sulphated low molecular weight heparin is enoxaparin sodium.

Antibodies are globular plasma proteins (~150 kDa) that are also known as immunoglobulins  
 30 which share a basic structure. As they have sugar chains added to amino acid residues, they  
 are glycoproteins. The basic functional unit of each antibody is an immunoglobulin (Ig)  
 monomer (containing only one Ig unit); secreted antibodies can also be dimeric with two Ig units  
 as with IgA, tetrameric with four Ig units like teleost fish IgM, or pentameric with five Ig units, like  
 mammalian IgM.

35 The Ig monomer is a "Y"-shaped molecule that consists of four polypeptide chains; two identical  
 heavy chains and two identical light chains connected by disulfide bonds between cysteine

residues. Each heavy chain is about 440 amino acids long; each light chain is about 220 amino acids long. Heavy and light chains each contain intrachain disulfide bonds which stabilize their folding. Each chain is composed of structural domains called Ig domains. These domains contain about 70-110 amino acids and are classified into different categories (for example, variable or V, and constant or C) according to their size and function. They have a characteristic immunoglobulin fold in which two  $\beta$  sheets create a "sandwich" shape, held together by interactions between conserved cysteines and other charged amino acids.

There are five types of mammalian Ig heavy chain denoted by  $\alpha$ ,  $\delta$ ,  $\epsilon$ ,  $\gamma$ , and  $\mu$ . The type of heavy chain present defines the isotype of antibody; these chains are found in IgA, IgD, IgE, IgG, and IgM antibodies, respectively.

Distinct heavy chains differ in size and composition;  $\alpha$  and  $\gamma$  contain approximately 450 amino acids and  $\delta$  approximately 500 amino acids, while  $\mu$  and  $\epsilon$  have approximately 550 amino acids. Each heavy chain has two regions, the constant region (CH) and the variable region (VH). In one species, the constant region is essentially identical in all antibodies of the same isotype, but differs in antibodies of different isotypes. Heavy chains  $\gamma$ ,  $\alpha$  and  $\delta$  have a constant region composed of three tandem Ig domains, and a hinge region for added flexibility; heavy chains  $\mu$  and  $\epsilon$  have a constant region composed of four immunoglobulin domains. The variable region of the heavy chain differs in antibodies produced by different B cells, but is the same for all antibodies produced by a single B cell or B cell clone. The variable region of each heavy chain is approximately 110 amino acids long and is composed of a single Ig domain.

In mammals, there are two types of immunoglobulin light chain denoted by  $\lambda$  and  $\kappa$ . A light chain has two successive domains: one constant domain (CL) and one variable domain (VL). The approximate length of a light chain is 211 to 217 amino acids. Each antibody contains two light chains that are always identical; only one type of light chain,  $\kappa$  or  $\lambda$ , is present per antibody in mammals.

Although the general structure of all antibodies is very similar, the unique property of a given antibody is determined by the variable (V) regions, as detailed above. More specifically, variable loops, three each the light (VL) and three on the heavy (VH) chain, are responsible for binding to the antigen, i.e. for its antigen specificity. These loops are referred to as the Complementarity Determining Regions (CDRs). Because CDRs from both VH and VL domains contribute to the antigen-binding site, it is the combination of the heavy and the light chains, and not either alone, that determines the final antigen specificity.

An "antibody fragment" contains at least one antigen binding fragment as defined above, and exhibits essentially the same function and specificity as the complete antibody of which the fragment is derived from. Limited proteolytic digestion with papain cleaves the Ig prototype into three fragments. Two identical amino terminal fragments, each containing one entire L chain and about half an H chain, are the antigen binding fragments (Fab). The third fragment, similar in size but containing the carboxyl terminal half of both heavy chains with their interchain disulfide bond, is the crystalizable fragment (Fc). The Fc contains carbohydrates, complement-binding, and FcR-binding sites. Limited pepsin digestion yields a single F(ab')<sub>2</sub> fragment containing both Fab pieces and the hinge region, including the H-H interchain disulfide bond. F(ab')<sub>2</sub> is divalent for antigen binding. The disulfide bond of F(ab')<sub>2</sub> may be cleaved in order to obtain Fab'. Moreover, the variable regions of the heavy and light chains can be fused together to form a single chain variable fragment (scFv).

Pharmaceutically acceptable salts are for example acid addition salts and basic salts. Acid addition salts are e.g. HCl or HBr salts. Basic salts are e.g. salts having a cation selected from alkali or alkaline, e.g. Na<sup>+</sup>, or K<sup>+</sup>, or Ca<sup>2+</sup>, or an ammonium ion N<sup>+</sup>(R1)(R2)(R3)(R4), wherein R1 to R4 independently of each other mean: hydrogen, an optionally substituted C1-C6-alkyl group, an optionally substituted C2-C6-alkenyl group, an optionally substituted C6-C10-aryl group, or an optionally substituted C6-C10-heteroaryl group. Further examples of pharmaceutically acceptable salts are described in "Remington's Pharmaceutical Sciences" 17. ed. Alfonso R. Gennaro (Ed.), Mark Publishing Company, Easton, Pa., U.S.A., 1985 and in Encyclopedia of Pharmaceutical Technology.

Pharmaceutically acceptable solvates are for example hydrates.

While this invention has been shown and described as having various designs, the present invention may be modified within the spirit and scope of this disclosure. For example, to deliver a fixed dose, the pen would preferably be modified such that the maximum that the dial could be screwed out to prepare the pen for injection would correspond to the fixed dose. Such a fixed dose pen could eliminate numerical dosage indicating marking, and instead provide user cues in the form of, for example, instructions and a graphical dosing indicator. This disclosure is therefore intended to cover any variations, uses or adaptations of the invention using its general principles. Further, this disclosure is intended to cover such departures from the present disclosure as come within known or customary practice in the art to which this invention pertains.

35

## List of Reference Numerals

1. Pen injection drug delivery device assembled
2. Cartridge holder
- 5 4. housing or body
8. cartridge
10. piston
11. septum
13. cartridge cap
- 10 14. removable cap
15. neck portion
16. injection needle
17. distal end of cartridge holder
20. mid-body
- 15 21. bearing
22. lead screw
23. drive nut
24. number sleeve
25. dial link
- 20 25a. modified dial link
26. clutch
- 26a. modified clutch
27. compression spring
28. dose knob
- 25 29. inner sleeve
30. exterior surface of number sleeve
31. tabs
32. keyways
33. helical threading
- 30 34. threaded stop
35. clicker teeth
36. proximally extending fingers
37. threading on drive nut
38. flexible arm
- 35 39. dial link teeth extending distally
40. flange
41. dial link teeth extending proximally

- 42. dial link stem
- 43. dial link fingers
- 50. dose knob skirt
- 51. window
- 5 52. threading on exterior surface of number sleeve
- 53. dose knob face
- 54. axially extending teeth on clutch
- 55. alignment post
- 62. threading on inside of body
- 10 63. end of threading on number sleeve
- 64. stop surface
- 65. hollow interior of number sleeve
- 67. helical threading on inside of number sleeve
- 70. notches
- 15 71. windows on number sleeve
- 72. ears
- 75. helical threading on inner sleeve
- 76. axially projecting teeth on inner sleeve
- 77. ridged defined slots
- 20 78. lugs
- 80. flexible arms
- 82. serrations/edges
- 84. first sloping surface
- 86. second sloping surface
- 25 88. dial link central region
- 90. first direction
- 92. second direction
- 96. clutch inner surface
- 100. unidirectional coupling

## Claims

- 5 1. A drug delivery device (1) comprising:
- a housing (4),
  - a lead screw (22) that is rotatably fixed with respect to the housing (4) during dose setting and during dose delivery and that is axially moveable in a delivery direction relative to the housing (4) for dose delivery,
  - 10 - a number sleeve (24) threadedly engaged with the housing (4) to be screwable relative to the housing (4),
  - a dial link (25a) which is adapted and arranged to be axially moved and rotated with respect to the housing (4) for dose setting and which is prevented from rotation with respect to the housing (4) for dose delivery,
- 15 wherein the dial link (25) is rotatably fixed with the number sleeve (24) when the dial link (25a) and the number sleeve (24) are in a first arrangement, and wherein the number sleeve (24) and the dial link (25a) are rotatable with respect to one another when the dial link (25a) and the number sleeve (24) are in a second arrangement,
- wherein the device (1) further comprises a unidirectional coupling (100) which is adapted and arranged to allow a relative rotation between the dial link (25a) and the number sleeve (24) in a first direction while preventing relative rotation between the dial link (25a) and the number sleeve (24) in a direction opposite to the first direction when the dial link (25a) and the number sleeve (24) are in the second arrangement.
- 20
- 25 2. The drug delivery device (1) according to claim 1, further comprising a clutch (26a), wherein the clutch (26a) is adapted and arranged to be axially and rotationally locked to the number sleeve (24), wherein the unidirectional coupling (100) comprises at least one flexible arm (80) provided on the clutch (26a).
- 30 3. The drug delivery device (1) according to claim 2, wherein the unidirectional coupling (100) further comprises at least one edge (82) adapted and arranged to interact with the flexible arm (80) provided on the clutch (26a).
4. The drug delivery device (1) according to claim 3,
- 35 wherein the device (1) is adapted such that, when the dial link (25a) and the number sleeve (24) are in the first arrangement, the edge (82) and the flexible arm (80) are free from mechanical cooperation with one another and, when the dial link (25a) and the number sleeve (24) are

brought in the second arrangement, the edge (82) and the flexible arm (80) are brought in mechanical cooperation with one another to prevent relative rotation between the dial link (25a) and the number sleeve (24) in the direction opposite to the first direction.

- 5 5. The drug delivery device (1) according to claim 4,  
wherein the device (1) further comprises a dose knob (28), wherein the dose knob (28) is  
connected to the dial link (25a) and is adapted and arranged to set and deliver a dose, wherein  
the device (1) is configured such that, when the dose knob (28) is moved in the delivery  
direction for performing a delivery operation, the flexible arm (80) and the edge (82) are brought  
10 in mechanical cooperation with one another.
6. The drug delivery device (1) according to any of claims 3 to 5,  
wherein the flexible arm (80) is arranged on an inner surface of the clutch (26a) and, wherein  
the edge (82) is provided on an outer surface of the dial link (25a).  
15
7. The drug delivery device (1) according to any of claims 3 to 6,  
wherein the edge (82) is shaped asymmetrically, the edge (82) comprising a first surface (84)  
having a first slope and a second surface (86) having a second slope, the first slope having a  
different angle than the second slope.  
20
8. The drug delivery device (1) according to claim 7,  
wherein the first surface (84) has a greater inclination than the second surface (86).
9. The drug delivery device (1) according to any of the previous claims,  
25 wherein the unidirectional coupling (100) comprises a plurality of flexible arms (80) and a  
plurality of edges (82), the arms (80) and edges (82) being adapted and arranged to interact  
with one another when the dial link (25a) and the number sleeve (24) are in the second  
arrangement.
- 30 10. The drug delivery device (1) according to any of the previous claims,  
wherein the unidirectional coupling (100) is adapted and arranged to allow a relative rotation  
between the dial link (25a) and the number sleeve (24) in a clockwise direction.
11. The drug delivery device (1) according to any of the previous claims,  
35 further comprising  
- a cartridge (8) comprising a piston (10), wherein, for dose delivery, the piston (10) is moveable  
with respect to the cartridge (8) in the delivery direction by the lead screw (22),

- an inner sleeve (29) which is axially moveable and rotatably fixed relative to the housing (4), wherein the inner sleeve (29) is threadedly engaged with the number sleeve (24),  
- a drive nut (23), wherein the lead screw (22) comprises a threaded shaft, wherein the drive nut (23) is threadedly engaged with the threaded shaft, and wherein, for dose delivery, the drive nut (23) is adapted to advance the lead screw (22) with respect to the housing (4) to dispense fluid from the cartridge (8), wherein the dial link (25a) is axially moveable with respect to the drive nut (23) and rotatably fixed relative to the drive nut (23).

12. The drug delivery device (1) according to claim 11,  
wherein the device (1) is adapted such that, during dose setting, the dial link (25a) and the number sleeve (24) are in the first arrangement, whereby a screwing motion of the dial link (25a) and the number sleeve (24) relative to the housing (4) screws the dial link (25a) and the number sleeve (24) a first axial distance away from a home position with respect to the housing (4), wherein the screwing motion is configured to screw the drive nut (23) along the lead screw (22) a second axial distance that is different than the first axial distance, and wherein the device (1) is adapted such that, during dose delivery, the dial link (25a) and the number sleeve (24) are in the second axial arrangement, whereby a screwing motion of the number sleeve (24) relative to the housing (4) back towards the home position advances the inner sleeve (29) without rotation in the delivery direction to axially advance the drive nut (23) that is axially fixed to the inner sleeve (29) and, thereby, the lead screw (22) and the moveable piston (10) to dispense fluid from the cartridge (8).

13. The drug delivery device (1) according to any of the previous claims,  
further comprising a mid-body (20) which is axially fixed inside of the housing (4), wherein the lead screw (22) comprises a keyway (32) arranged along the lead screw (22), and wherein the mid-body (20) comprises tabs (31) that slidably fit within the keyway (32) in the lead screw (22) to prevent rotation of the lead screw (22) with respect to the housing (4).

14. The drug delivery device (1) according to any of claims 11 or 12 and claim 13,  
wherein the inner sleeve (29) is axially moveable and rotatably fixed relative to the mid-body (20) by at least one lug (78) of the mid-body (20) that slidably fits within at least one slot (77) formed in the inner sleeve (29).

15. The drug delivery device (1) according to any of claims 11 to 14,  
wherein the number sleeve (24) comprises a threading for threaded engagement with the housing (4), the threading of number sleeve (24) to the housing (4) being of a first lead, and wherein the number sleeve (24) comprises a threading for threaded engagement with the inner

sleeve (29), the threading of the inner sleeve (29) to the number sleeve (24) being of a second lead, and wherein the lead screw (22) comprises a threading, the threading of the lead screw (22) being of a third lead, wherein the first lead, the second lead and the third lead are different from one another.

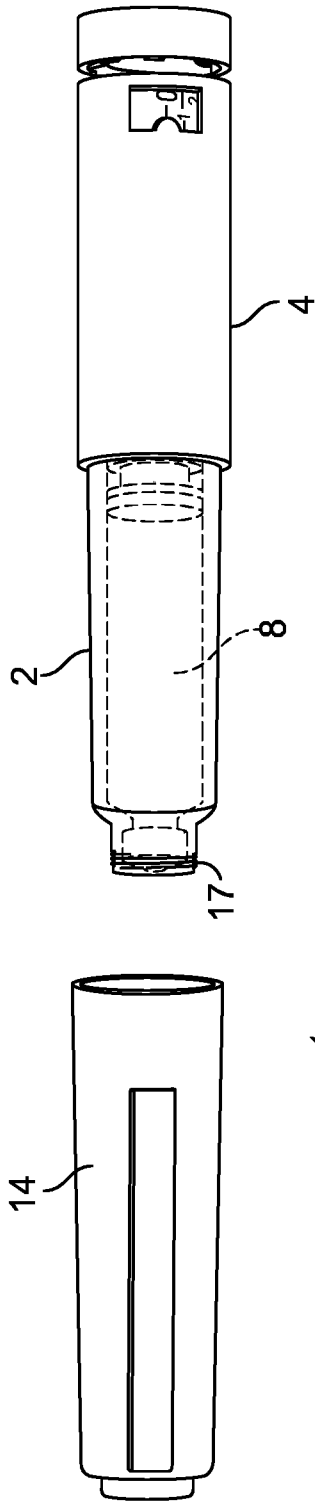


FIG. 1

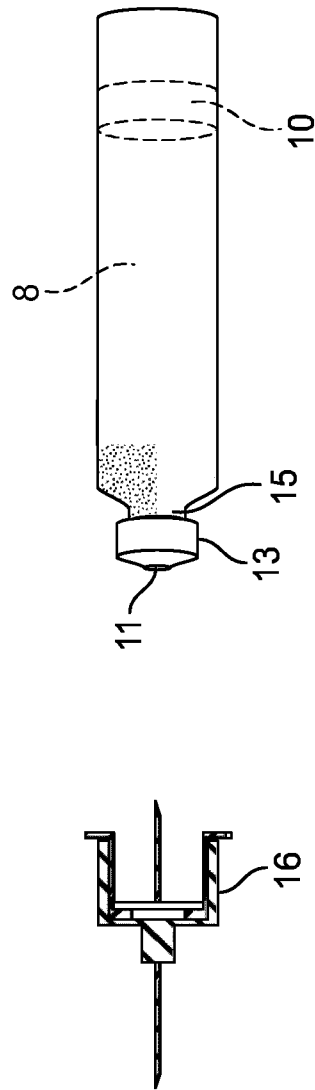


FIG. 2

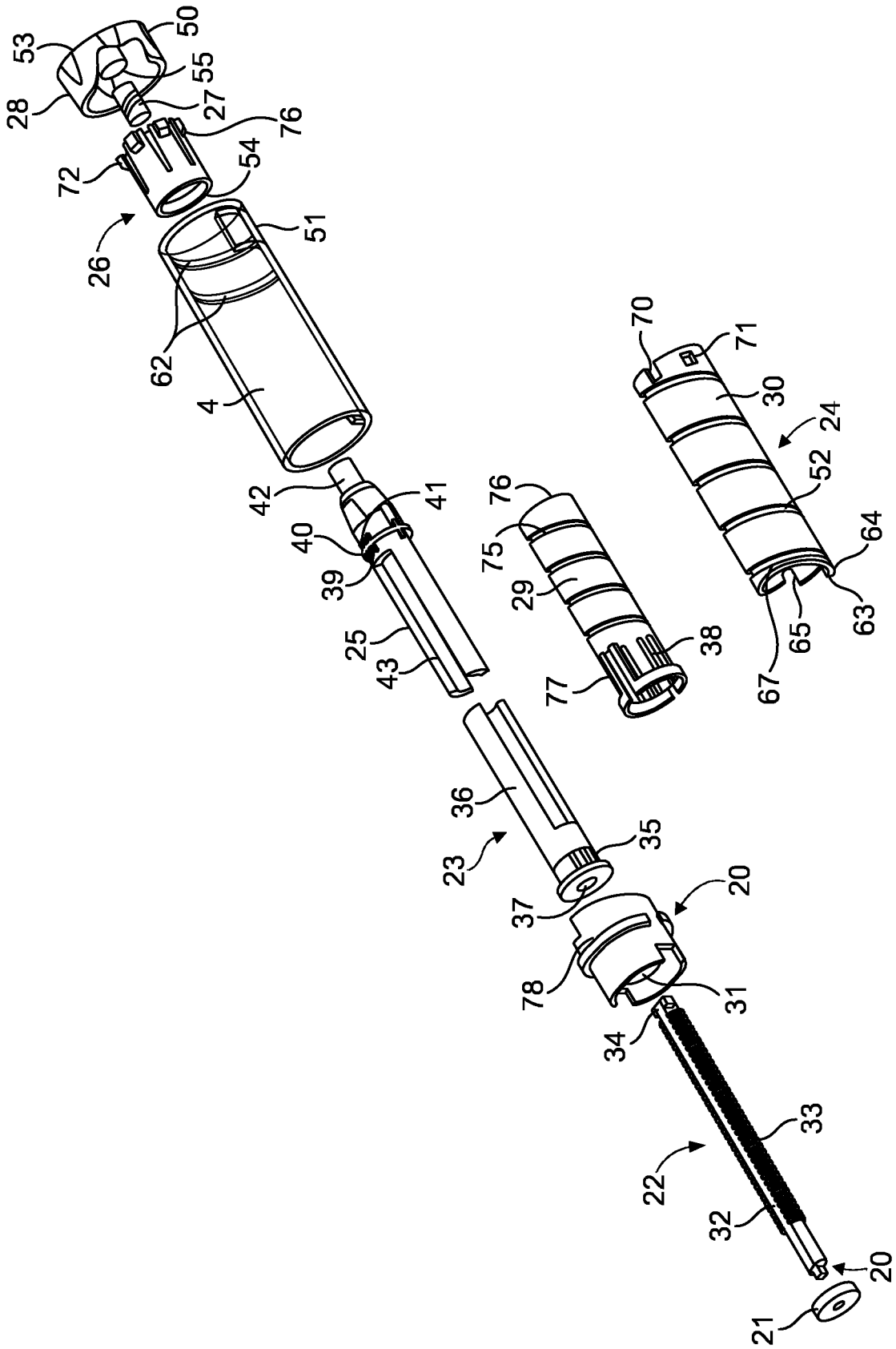


FIG. 3

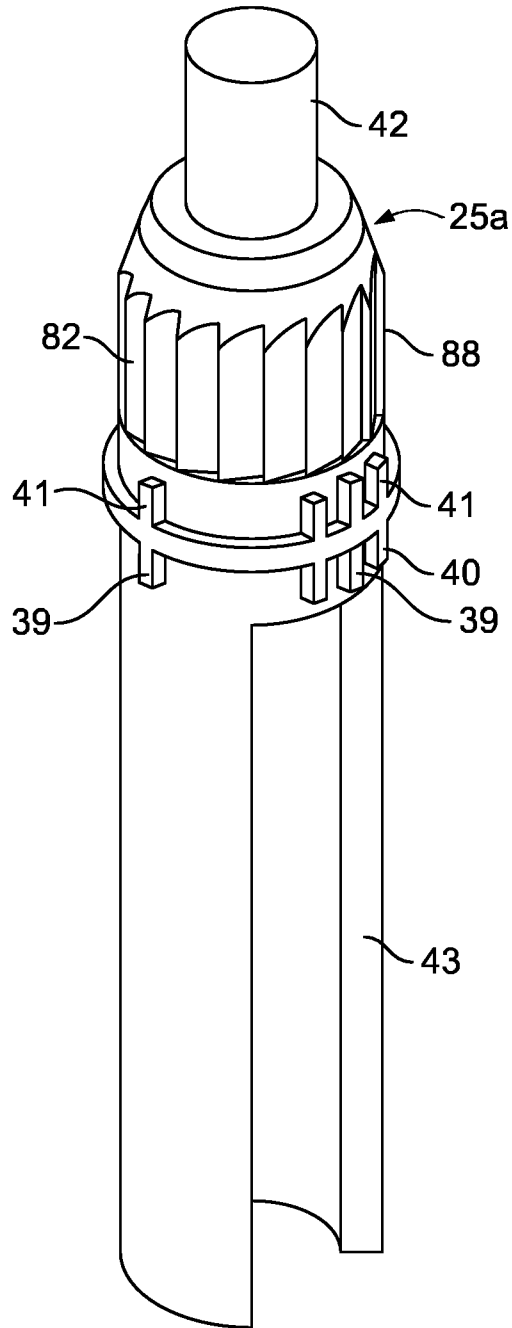


FIG. 4

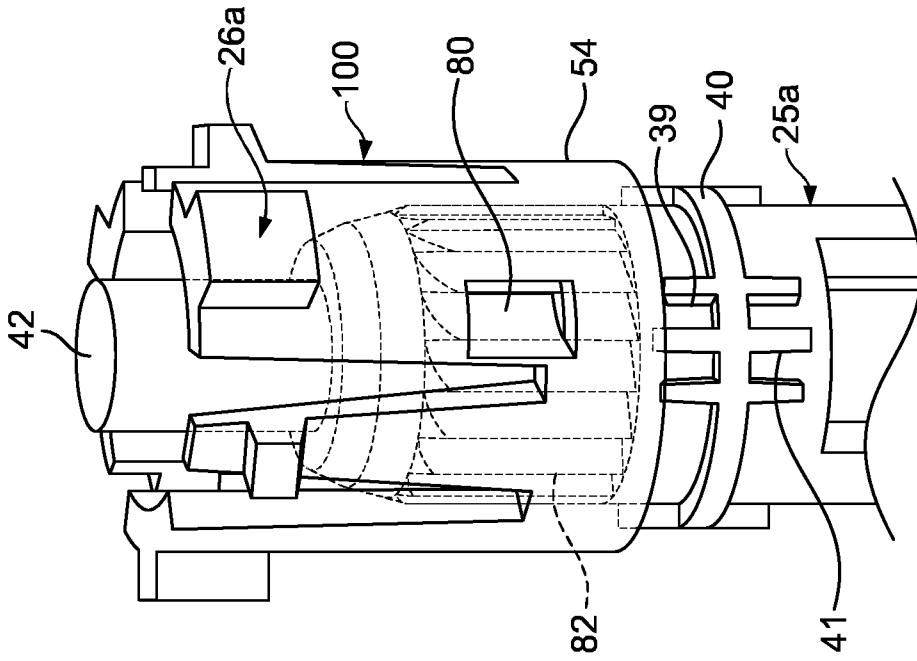


FIG. 6

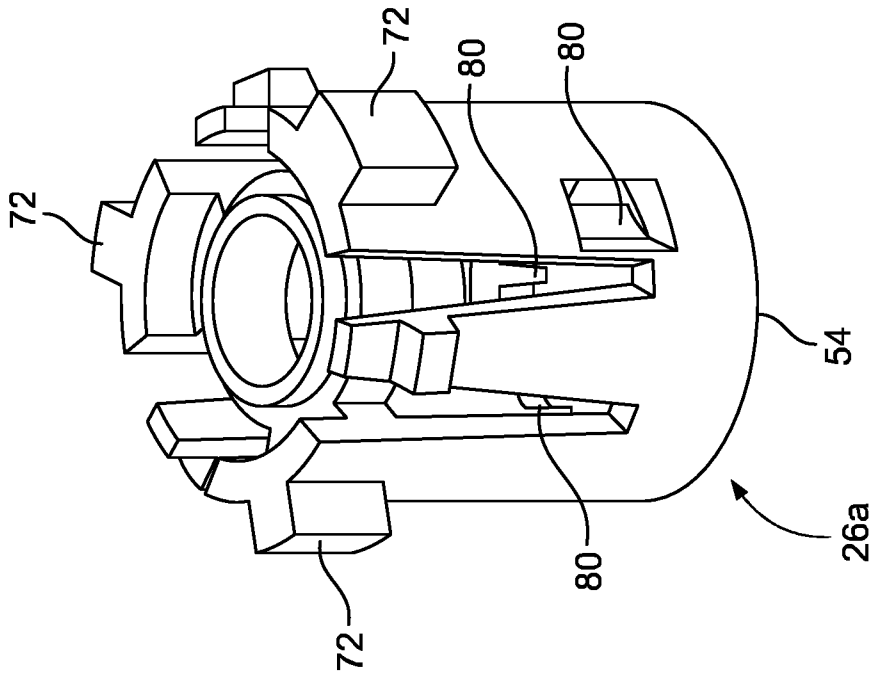


FIG. 5

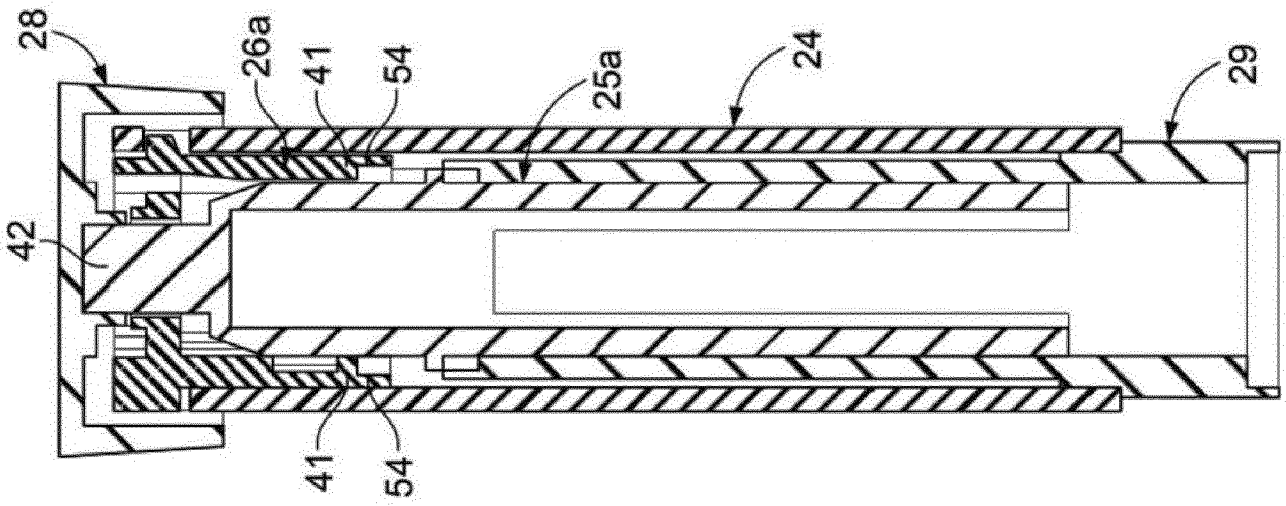


FIG. 7

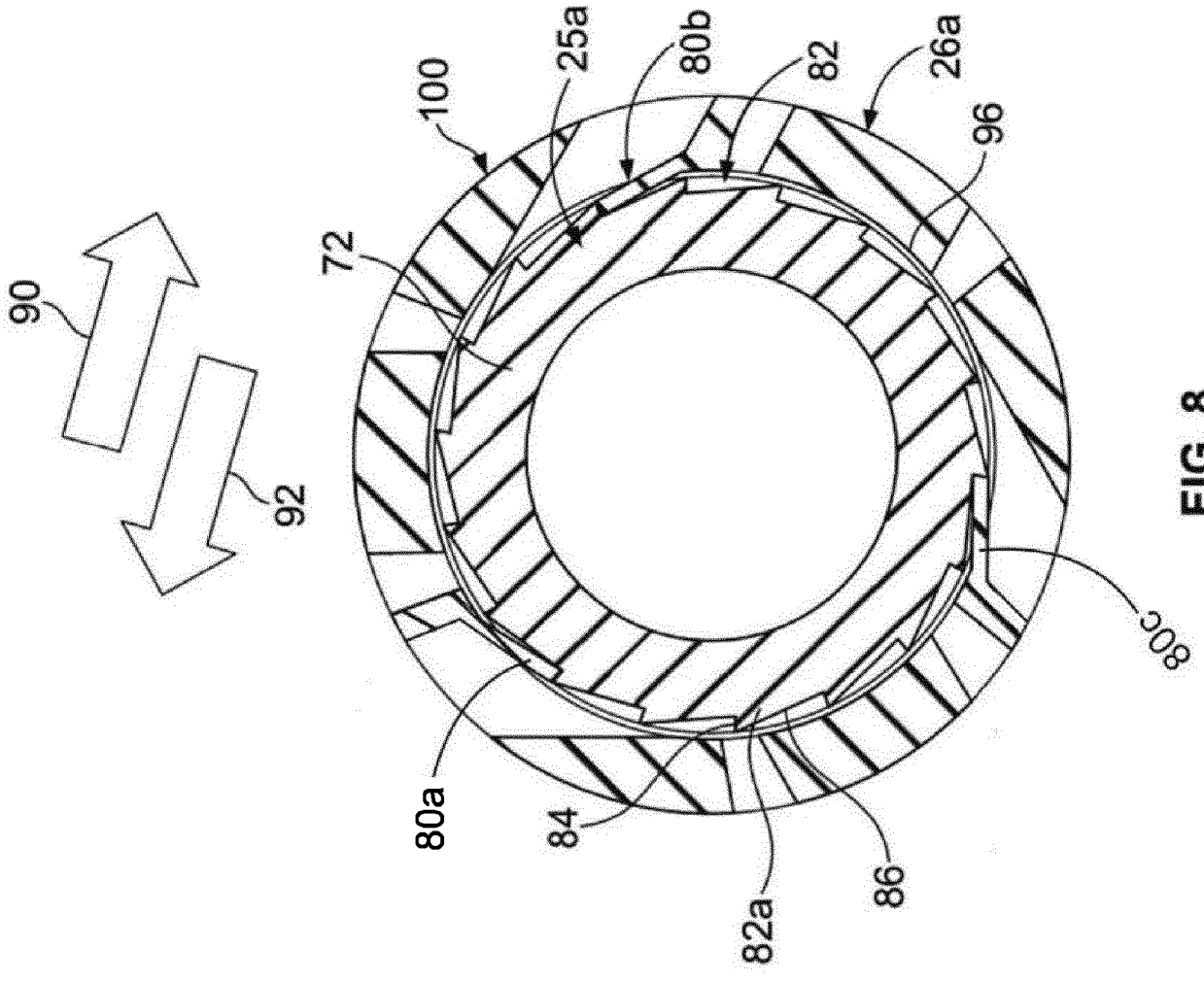


FIG. 8

INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2014/074705

A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61M5/315  
ADD.  
  
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)  
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 practicable, search terms used)  
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/267207 A1 (VEASEY ROBERT FREDERICK [GB] ET AL) 30 December 2004 (2004-12-30) paragraph [0068] - paragraph [0084] -----	1-15
X	WO 2004/078242 A2 (DCA DESIGN INT LTD [GB]) 16 September 2004 (2004-09-16) the whole document -----	1-15
X	WO 2011/039236 A1 (SANOFI AVENTIS DEUTSCHLAND [DE]; KOUYOUMJIAN GAREN [GB]; VEASEY ROBERT) 7 April 2011 (2011-04-07) the whole document -----	1-15
X	US 2013/211342 A1 (RAAB STEFFEN [DE] ET AL) 15 August 2013 (2013-08-15) the whole document -----	1-15
	-/--	

Further documents are listed in the continuation of Box C.

See patent family 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 application or patent 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  18 December 2014	Date of mailing of the international search report  07/01/2015
---	--

Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Neiller, Frédéric
--	---

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2014/074705

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/139629 A1 (SANOFI AVENTIS DEUTSCHLAND [DE]; PLUMPTRE DAVID [GB]) 9 December 2010 (2010-12-09) the whole document -----	1-15

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/074705

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 2004267207	A1	30-12-2004	AR 043458 A1	27-07-2005
			AT 405310 T	15-09-2008
			AT 474614 T	15-08-2010
			AU 2004216828 A1	16-09-2004
			AU 2004216831 A1	16-09-2004
			BR PI0408090 A	14-02-2006
			BR PI0408112 A	01-03-2006
			CA 2518009 A1	16-09-2004
			CA 2518015 A1	16-09-2004
			CL 2004000425 A1	22-04-2005
			CN 1780653 A	31-05-2006
			CN 1816363 A	09-08-2006
			CY 1108581 T1	09-04-2014
			DK 1601395 T3	08-11-2010
			DK 1601397 T3	05-01-2009
			EP 1601395 A2	07-12-2005
			EP 1601397 A2	07-12-2005
			EP 1944050 A2	16-07-2008
			EP 2221077 A2	25-08-2010
			ES 2312975 T3	01-03-2009
			ES 2349130 T3	28-12-2010
			HK 1092083 A1	27-11-2009
			HK 1094544 A1	24-12-2009
			HR P20050767 A2	31-10-2006
			HR P20050769 A2	31-10-2006
			IL 170481 A	30-12-2010
			IL 170618 A	28-04-2011
			JP 4699355 B2	08-06-2011
			JP 4939211 B2	23-05-2012
			JP 2006519075 A	24-08-2006
			JP 2006519078 A	24-08-2006
			KR 20060010721 A	02-02-2006
			KR 20060010722 A	02-02-2006
			MX PA05009124 A	20-10-2005
			MX PA05009185 A	18-10-2005
			PT 1601395 E	25-10-2010
			PT 1601397 E	02-12-2008
			SI 1601395 T1	30-11-2010
			SI 1601397 T1	28-02-2009
			TW I323180 B	11-04-2010
			TW I341739 B	11-05-2011
			US 2004267207 A1	30-12-2004
			US 2005113765 A1	26-05-2005
			US 2009287162 A1	19-11-2009
			US 2011028911 A1	03-02-2011
			US 2011301550 A1	08-12-2011
			US 2012041386 A1	16-02-2012
			US 2012215176 A1	23-08-2012
			US 2013102969 A1	25-04-2013
			US 2014018743 A1	16-01-2014
			US 2014316343 A1	23-10-2014
			WO 2004078240 A2	16-09-2004
			WO 2004078242 A2	16-09-2004
			ZA 200506658 A	26-07-2006
-----				
WO 2004078242	A2	16-09-2004	AR 043458 A1	27-07-2005
			AT 405310 T	15-09-2008
			AT 474614 T	15-08-2010

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/074705

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
		AU 2004216828 A1	16-09-2004	
		AU 2004216831 A1	16-09-2004	
		BR PI0408090 A	14-02-2006	
		BR PI0408112 A	01-03-2006	
		CA 2518009 A1	16-09-2004	
		CA 2518015 A1	16-09-2004	
		CL 2004000425 A1	22-04-2005	
		CN 1780653 A	31-05-2006	
		CN 1816363 A	09-08-2006	
		CY 1108581 T1	09-04-2014	
		DK 1601395 T3	08-11-2010	
		DK 1601397 T3	05-01-2009	
		EP 1601395 A2	07-12-2005	
		EP 1601397 A2	07-12-2005	
		EP 1944050 A2	16-07-2008	
		EP 2221077 A2	25-08-2010	
		ES 2312975 T3	01-03-2009	
		ES 2349130 T3	28-12-2010	
		HK 1092083 A1	27-11-2009	
		HK 1094544 A1	24-12-2009	
		HR P20050767 A2	31-10-2006	
		HR P20050769 A2	31-10-2006	
		IL 170481 A	30-12-2010	
		IL 170618 A	28-04-2011	
		JP 4699355 B2	08-06-2011	
		JP 4939211 B2	23-05-2012	
		JP 2006519075 A	24-08-2006	
		JP 2006519078 A	24-08-2006	
		KR 20060010721 A	02-02-2006	
		KR 20060010722 A	02-02-2006	
		MX PA05009124 A	20-10-2005	
		MX PA05009185 A	18-10-2005	
		PT 1601395 E	25-10-2010	
		PT 1601397 E	02-12-2008	
		SI 1601395 T1	30-11-2010	
		SI 1601397 T1	28-02-2009	
		TW I323180 B	11-04-2010	
		TW I341739 B	11-05-2011	
		US 2004267207 A1	30-12-2004	
		US 2005113765 A1	26-05-2005	
		US 2009287162 A1	19-11-2009	
		US 2011028911 A1	03-02-2011	
		US 2011301550 A1	08-12-2011	
		US 2012041386 A1	16-02-2012	
		US 2012215176 A1	23-08-2012	
		US 2013102969 A1	25-04-2013	
		US 2014018743 A1	16-01-2014	
		US 2014316343 A1	23-10-2014	
		WO 2004078240 A2	16-09-2004	
		WO 2004078242 A2	16-09-2004	
		ZA 200506658 A	26-07-2006	
-----				
WO 2011039236	A1	07-04-2011	CA 2773672 A1	07-04-2011
			EP 2482891 A1	08-08-2012
			JP 2013506466 A	28-02-2013
			US 2012289908 A1	15-11-2012
			WO 2011039236 A1	07-04-2011
-----				

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/EP2014/074705
---

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2013211342	A1	15-08-2013	AR 081598 A1 03-10-2012
			CA 2801635 A1 15-12-2011
			EP 2579920 A2 17-04-2013
			JP 2013528086 A 08-07-2013
			TW 201210648 A 16-03-2012
			US 2013211342 A1 15-08-2013
			WO 2011154482 A2 15-12-2011
-----			
WO 2010139629	A1	09-12-2010	AR 076608 A1 22-06-2011
			AU 2010255804 A1 22-12-2011
			CA 2762012 A1 09-12-2010
			CN 102458526 A 16-05-2012
			EP 2437819 A1 11-04-2012
			JP 2012528618 A 15-11-2012
			KR 20120028895 A 23-03-2012
			NZ 596699 A 31-01-2014
			RU 2011154136 A 20-07-2013
			SG 176079 A1 29-12-2011
			TW 201107006 A 01-03-2011
			US 2010324493 A1 23-12-2010
			US 2012157929 A1 21-06-2012
			WO 2010139629 A1 09-12-2010
-----			