



HU000029364T2

(19) **HU**(11) Lajstromszám: **E 029 364**(13) **T2****MAGYARORSZÁG**
Szellemi Tulajdon Nemzeti Hivatala**EURÓPAI SZABADALOM**
SZÖVEGÉNEK FORDÍTÁSA(21) Magyar ügyszám: **E 12 762612**(51) Int. Cl.: **A61M 5/24** (2006.01)(22) A bejelentés napja: **2012. 09. 27.****A61M 5/31** (2006.01)**A61M 53/15** (2006.01)

(96) Az európai bejelentés bejelentési száma:

EP 20120762612

(86) A nemzetközi (PCT) bejelentési szám:

PCT/EP 12/069032

(97) Az európai bejelentés közzétételi adatai:

EP 2760507 A1 **2013. 04. 04.**

(87) A nemzetközi közzétételi szám:

WO 13045527

(97) Az európai szabadalom megadásának meghirdetési adatai:

EP 2760507 B1 **2016. 04. 06.**

(30) Elsőbbségi adatok:

11183300 **2011. 09. 29.** **EP**

(73) Jogosult(ak):

Sanofi-Aventis Deutschland GmbH, 65929
Frankfurt am Main (DE)

(72) Feltaláló(k):

HELMER, Michael, 65926 Frankfurt am Main (DE)
EISENGARTHEN, Christoph, 65462 Ginsheim (DE)
HUTHMACHER, Winfried, 60389 Frankfurt (DE)
MOSEBACH, Carsten, 55128 Mainz (DE)

(74) Képvisező:

Danubia Szabadalmi és Jogi Iroda Kft.,
Budapest

(54)

Gyógyszeradagoló eszköz

Az európai szabadalom ellen, megadásának az Európai Szabadalmi Közlönyben való meghirdetésétől számított kilenc hónapon belül, felszólalást lehet benyújtani az Európai Szabadalmi Hivatalnál. (Európai Szabadalmi Egyezmény 99. cikk(1))

A fordítást a szabadalmas az 1995. évi XXXIII. törvény 84/H. §-a szerint nyújtotta be. A fordítás tartalmi helyességét a Szellemi Tulajdon Nemzeti Hivatala nem vizsgálta.



(11) **EP 2 760 507 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention
of the grant of the patent:
06.04.2016 Bulletin 2016/14

(51) Int Cl.:
A61M 5/24 (2006.01) A61M 5/315 (2006.01)
A61M 5/31 (2006.01)

(21) Application number: **12762612.5**

(86) International application number:
PCT/EP2012/069032

(22) Date of filing: **27.09.2012**

(87) International publication number:
WO 2013/045527 (04.04.2013 Gazette 2013/14)

(54) **DRUG DELIVERY DEVICE AND METHOD FOR A DRUG DELIVERY DEVICE**

MEDIKAMENTENABGABEVORRICHTUNG UND VERFAHREN ZUM ZUSAMMENBAUEN EINER
MEDIKAMENTENABGABEVORRICHTUNG

DISPOSITIF D'ADMINISTRATION DE MÉDICAMENTS ET PROCÉDÉ D'ASSAMBLAGE D'UN
DISPOSITIF D'ADMINISTRATION DE MÉDICAMENTS

(84) Designated Contracting States:
**AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO RS SE SI SK SM TR**

(30) Priority: **29.09.2011 EP 11183300**

(43) Date of publication of application:
06.08.2014 Bulletin 2014/32

(73) Proprietor: **Sanofi-Aventis Deutschland GmbH
65929 Frankfurt am Main (DE)**

(72) Inventors:
• **HELMER, Michael
65926 Frankfurt am Main (DE)**
• **EISENGARTHEN, Christoph
65462 Ginsheim (DE)**
• **HUTHMACHER, Winfried
60389 Frankfurt (DE)**
• **MOSEBACH, Carsten
55128 Mainz (DE)**

(56) References cited:
WO-A1-2010/063707 WO-A1-2011/039236
WO-A2-2011/039206 WO-A2-2011/051365

EP 2 760 507 B1

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

Description

[0001] This disclosure relates to a drug delivery device and a method for assembling a drug delivery device.

[0002] In a drug delivery device, often, a bung within a cartridge containing a plurality of doses of a drug is displaced by a piston rod. Thereby, a dose of the drug is expelled from the cartridge.

[0003] A drug delivery device is described in document WO 2008/058666 A1, for example.

[0004] WO 2010/063707 A1 discloses a medication delivery device comprising a housing, a cartridge for holding a medication, a movable piston retained within the cartridge, a drive member movable in a proximal direction with respect to the housing for setting a dose of medication to be delivered and in the distal direction for delivering the dose, a piston rod adapted to drive the piston in the distal direction with respect to the cartridge for delivering the dose, and a resilient member, which is arranged to move the drive member in the proximal direction after dose delivery, thereby reducing pressure of the piston rod on the piston.

[0005] WO 2011/051365 A2 discloses a method of assembling a drug delivery device, wherein a cartridge holder sub-assembly with a product-containing cartridge, in which a piston is movably arranged, and a drive unit in a housing sub-assembly, which is connectable to the cartridge holder sub-assembly, are provided. After the determination of the size of an axial clearance or gap between the piston rod and the piston, a correspondingly sized distance spacer is attached to the piston rod or the piston before the subassemblies are interconnected.

[0006] It is an object of the present invention to simplify the handling of a drug delivery device in an initial state. Furthermore, it is an object of the present invention to provide a method for assembling a drug delivery device for simplified handling in an initial state.

[0007] This object is achieved by the subject matter of the independent claims. Advantageous embodiments and refinements are subject matter of the dependent claims.

[0008] One aspect relates to an assembly for a drug delivery device. The assembly comprises a housing. The housing comprises a distal end and a proximal end. The assembly further comprises a cartridge. The cartridge is adapted and arranged to contain at least one dose of a drug, preferably a plurality of doses of the drug. A bung is movably arranged within the cartridge. In an initial state of the device, the bung is arranged in a proximal end position with respect to the cartridge. The cartridge may be fully filled in the initial state, e.g. no drug has been dispensed yet from the cartridge. The initial state of the device may be state before setting and dispensing a first dose of drug from the cartridge. The initial state may be the state of the device as supplied from the manufacturer. The assembly further comprises a piston rod. The piston rod is adapted and arranged to move the bung in the distal direction with respect to the cartridge for delivering

a dose of the drug. The assembly comprises a mechanism. Said mechanism is operable such that, after a dose delivery operation was completed, the piston rod is moved, preferably automatically moved, into the proximal direction with respect to the bung or away from the bung by a back off distance. Thereby, pressure of the piston rod onto the bung may be reduced. In the initial state, a distance between a distal end of the piston rod and a proximal end of the bung is greater than zero. The distance between the piston rod and the bung in the initial state is defined by the back off distance.

[0009] The mechanism ensures that, after a dose delivery operation was completed, the piston rod is positioned at the back off distance, from the bung. Pressure onto the bung, which may lead to droplets can thus be reduced or even avoided. In particular, the deformed bung may be allowed to relax in the proximal direction after the dose delivery operation was completed. Uncontrolled relaxation of the bung in the distal direction which may result in unintentional waste of the drug from the cartridge can be avoided in this way.

[0010] The mechanism may be further configured such that, in the initial state, the piston rod and the bung are separated by a predetermined initial distance. The predetermined initial distance may be equal to the back off distance or may be less than the back off distance. In particular, the mechanism may define the predetermined initial distance between the piston rod and the bung in the initial state to amount to a predefined initial value which depends from the value of the back off distance. The predefined initial value may be in the range of 0.1 mm to 1.0 mm. The predefined initial value may be 0.2 mm, for example. Adjustment or priming steps of the user, for arranging the piston rod at a predetermined distance from the bung before setting and dispensing a first dose from the device may be redundant. Underdosing may be prevented in this way. In particular, if a user skipped a necessary priming step and injected the priming volume instead, this would result in a significant underdose. By making the priming step redundant, this underdosing may be prevented and, thus, dose accuracy may be increased. Furthermore, this may help to reduce the risk of erroneous operation by inexperienced users and, thus, also waste of drug. Also, some over-cautious users tending to carry out a priming step prior to every dose, would not only waste the first dose of drug, but would unnecessarily empty the cartridge, so that that the device cannot deliver the required number of doses. Making the priming step redundant may help avoiding all of these problems.

[0011] In the initial state, there is a distance between the piston rod and the bung, the cartridge is not pressurized. Accordingly, if a needle is mounted to the cartridge, there won't be droplets of drug which emerges from the needle due to pressure in the cartridge. Some drugs may be harmful for the user, if they get in contact with the user's skin. The risk of exposing the skin to the drug due to droplets may be reduced or even avoided by the dis-

tance between the piston rod and the bung in the initial state.

[0012] A further aspect relates to a method for assembling a drug delivery device. The device is the device as described above. In a first step, a cartridge unit is provided. The cartridge unit may comprise a cartridge holder. The cartridge unit comprises a cartridge. The cartridge may be retained in the cartridge holder. The cartridge holds at least one dose of a drug, preferably a plurality of doses of the drug. A bung is movably arranged within the cartridge. Preferably, the bung is arranged in a proximal end position with respect to the cartridge. In particular, the cartridge may be in a completely filled state. In a next step, a drive unit is provided. The drive unit may be releasable or non-releasably connectable to the cartridge unit. The drive unit comprises a piston rod. The drive unit further comprises a mechanism. The mechanism is configured to move the piston rod by a back off distance when the mechanism switches from an activated state into a deactivated state. In a next step, the mechanism is activated. In a next step, the position of the proximal end of the bung with respect to a predetermined reference point on the cartridge unit, e.g. a mark on the cartridge holder in which the cartridge is retained, is measured, in particular when the mechanism is activated. In a next step, the position of the distal end of the piston rod with respect to a predetermined reference point on the drive unit, e.g. a mark on a housing, is measured. In a next step, information indicative for a relative position of the distal end of the piston rod and the proximal end of the bung is derived from the results of the previous measurements. In a next step, the mechanism is deactivated such that the piston rod is displaced by the back off distance. In a next step, the cartridge unit and the drive unit are connected to one another such that the piston rod and the bung are arranged at an initial distance from one another when the mechanism is deactivated.

[0013] In one embodiment, deriving the information comprises determining from the results of the measurements a connecting position for a connection of the cartridge unit and the drive unit such that if the units are connected in the connecting position, the piston rod and the bung are arranged at the initial distance from one another when the mechanism is deactivated. In this case, the cartridge unit and the drive unit may be connectable to one another by a weld. Thereby, the cartridge unit and the drive unit can be brought into variable relative positions for connecting the cartridge unit and the drive unit to one another. In particular, neither the cartridge unit nor the drive unit may comprise a connecting means having a fixed position with respect to the respective unit for connecting the cartridge unit and the drive unit to one another.

[0014] According to a further embodiment, deriving the information comprises determining from the results of the measurements a relative position of the proximal end of the bung and the distal end of the piston rod if the cartridge unit and the drive unit were connected by connect-

ing means provided on the cartridge unit and the drive unit. In this embodiment, the cartridge unit and the drive unit may be connectable to one another by a snap-fit connection or a thread. In this case, the cartridge unit and the drive unit may each comprise a connecting means having a fixed position with respect to the respective unit for connecting the cartridge unit to the drive unit. The connecting means of the cartridge unit may comprise a pin, for example. The connecting means of the drive unit may comprise an indentation, for example. Alternatively, the cartridge unit may comprise an indentation and the drive unit may comprise a pin for establishing the snap-fit connection between the cartridge unit and the drive unit. Alternatively, the cartridge unit may comprise a thread and the drive unit may comprise a mating thread.

[0015] The previously described mechanism may be configured such that, when the mechanism is in the activated state and the device is fully assembled, the distal end of the piston rod abuts the proximal end of the piston or is arranged at a distance with respect to the proximal end. The mechanism may be configured such, when the mechanism is in the activated state, the bung may be not deformed or compressed or it may be only slightly compressed by the piston rod. The mechanism may be configured such that, when the mechanism is in the activated state, mutual abutment of the bung and the piston rod may be such that the piston rod does not yet apply substantial pressure or thrust to the bung in order to prevent generation of droplet. Droplets may occur if the drug in the cartridge is pressurized and a needle unit is connected to the cartridge unit, thereby establishing fluid communication between the cartridge unit and the environment.

[0016] When the mechanism is in the activated state, play between elements of the drive unit may be reduced to a minimum, e.g. because all of the components are pushed distally with respect to the housing. Accordingly, the measurement is very reliable as all components comprise a well defined or biased position during the measurement. Accordingly, the relative positions of the components after the assembly was completed will also be well defined. Additionally, user operated priming steps may be redundant as the initial distance between the piston rod and the bung may be adjusted very precisely during the assembly process.

[0017] When the device is fully assembled and in the initial state with the mechanism being deactivated, there may be no abutment between the piston rod and the bung. In particular, the bung and the piston rod may be arranged at a predetermined initial distance from one another. The predetermined initial distance may be smaller than or equal to the back off distance. By arranging the piston rod at the predetermined initial distance, a user-performed priming step in order to ensure, that the bung and the piston rod are located at a predetermined position with respect to each other, thus ensuring, that with a first dose setting and a subsequent dose dispensing step, a predefined amount of the drug is dispensed, may be re-

dundant. Dose accuracy of the device may be increased.

[0018] According to a preferred embodiment, a drug delivery device is provided comprising:

- a housing comprising a distal end and a proximal end,
- a cartridge adapted and arranged to contain at least one dose of a drug, a bung being movably arranged within the cartridge, wherein in an initial state of the device, the bung is arranged in a proximal end position with respect to the cartridge,
- a piston rod adapted and arranged to move the bung in the distal direction with respect to the cartridge for delivering a dose of the drug.

[0019] The device further comprises a mechanism operable such that, after a dose delivery operation was completed, the piston rod is moved into the proximal direction with respect to the bung by a back off distance, and wherein in the initial state, a distance between a distal end of the piston rod and a proximal end of the bung is greater than zero, with the distance between the piston rod and the bung in the initial state being defined by the back off distance.

[0020] According to a preferred embodiment, a method for assembling a drug delivery device is provided, the method comprising the following steps:

- A) providing a cartridge unit comprising a cartridge which holds at least one dose of a drug, a bung being movably arranged within the cartridge,
- B) Providing a drive unit which is connectable to the cartridge unit, the drive unit comprising a piston rod and a mechanism, wherein the mechanism is configured to move the piston rod by a back off distance when the mechanism switches from an activated state into a deactivated state,
- C) activating the mechanism,
- D) measuring the position of the proximal end of the bung with respect to a predetermined reference point on the cartridge unit,
- E) measuring the position of the distal end of the piston rod with respect to a predetermined reference point on the drive unit,
- F) deriving, from the results of the measurements performed in steps D) and E), information indicative for a relative position of the distal end of the piston rod and the proximal end of the bung
- G) deactivating the mechanism such that the piston rod is displaced by the back off distance,
- H) connecting the cartridge unit and the drive unit to one another such that the piston rod and the bung are arranged at an initial distance from one another when the mechanism is deactivated.

[0021] By means of the activated mechanism, play between moveable components of the device may be removed. Accordingly, a very reliable measurement is en-

abled which results in a device of high dose accuracy without a priming step which has to be carried out by the user.

[0022] Of course, features described above in connection with different aspects and embodiments may be combined with each other and with features described below.

[0023] Further features and refinements become apparent from the following description of the exemplary embodiments in connection with the accompanying figures.

Figure 1 schematically shows a sectional side view of a drug delivery device,

Figure 2 schematically shows a sectional side view of the drug delivery device of Figure 1 after a dose setting operation was performed,

Figure 3 schematically shows a sectional side view of the drug delivery device of Figure 1 during assembly,

Figure 4 schematically shows the drug delivery device of Figure 3 after assembly was completed,

Figure 5 schematically shows a perspective side view of the assembled drug delivery device of Figure 5,

Figures 6A to 6C schematically show a sectional side view of parts of the drug delivery device of Figure 1 in different states of operation,

Figures 7A and 7B schematically show a perspective side view of parts of the drug delivery device of Figure 1,

Figure 7C schematically shows a sectional side view of the parts of the drug delivery device shown in Figures 7A and 7B,

Figure 7D schematically shows a bottom view of the parts of the drug delivery device shown in Figures 7A to 7C.

[0024] Like elements, elements of the same kind and identically acting elements may be provided with the same reference numerals in the figures.

[0025] In Figures 1 and 2 a drug delivery device 1 is shown. The drug delivery device 1 comprises a housing 4. The drug delivery device 1 and the housing 4 have a distal end and a proximal end. The distal end is indicated by arrow 17. The proximal end is indicated by arrow 18. 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 of the device 1.

[0026] The drug delivery device 1 comprises a cartridge holder 2. The drug delivery device 1 comprises a cartridge 3. The cartridge 3 is retained within the cartridge holder 2. The cartridge holder 2 stabilizes the position of the cartridge 3 mechanically. The cartridge holder 2 is connectable, e.g. by a threaded engagement, by a weld or by a snap-fit, to the housing 4. The cartridge holder 2 and the housing 4 are irreleasably connected to one another. A cap 6 can be secured to the drug delivery device 1 for protecting the device 1, and, in particular, the cartridge holder 2 or the cartridge 3 from environmental influences, e.g. when the device 1 is not used.

[0027] The cartridge 3 contains a drug 16, preferably a plurality of doses of the drug 16. The term "drug", as used herein, means 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 protein, a polysaccharide, a vaccine, a DNA, a RNA, an enzyme, an antihousehold 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,

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.

[0028] 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.

[0029] 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-(ω -carboxyheptadecanoyl)-des(B30) human insulin and B29-N-(ω -carboxyheptadecanoyl) human insulin.

[0030] 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-Ser-NH₂.

[0031] Exendin-4 derivatives are for example selected from the following list of compounds:

H-(Lys)4-des Pro36, des Pro37 Exendin-4(1-39)-NH₂,

H-(Lys)5-des Pro36, des Pro37 Exendin-4(1-39)-NH₂,

des Pro36 Exendin-4(1-39),

des Pro36 [Asp28] Exendin-4(1-39),

des Pro36 [IsoAsp28] Exendin-4(1-39),

des Pro36 [Met(0)14, Asp28] Exendin-4(1-39),

des Pro36 [Met(0)14, IsoAsp28] Exendin-4(1-39),

des Pro36 [Trp(02)25, Asp28] Exendin-4(1-39),

des Pro36 [Trp(02)25, IsoAsp28] Exendin-4(1-39),

des Pro36 [Met(0)14 Trp(02)25, Asp28] Exendin-4(1-39),

des Pro36 [Met(0)14 Trp(02)25, IsoAsp28] Exendin-4(1-39); or

des Pro36 [Asp28] Exendin-4(1-39),

des Pro36 [IsoAsp28] Exendin-4(1-39),

des Pro36 [Met(0)14, Asp28] Exendin-4(1-39),

des Pro36 [Met(0)14, IsoAsp28] Exendin-4(1-39),

des Pro36 [Trp(02)25, Asp28] Exendin-4(1-39),

des Pro36 [Trp(02)25, IsoAsp28] Exendin-4(1-39),

des Pro36 [Met(0)14 Trp(02)25, Asp28] Exendin-4(1-39),

des Pro36 [Met(0)14 Trp(02)25, IsoAsp28] Exendin-4(1-39),

wherein the group -Lys6-NH₂ may be bound to the C-terminus of the Exendin-4 derivative;

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,

H-Asn-(Glu)5des 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(02)25, Asp28] Exendin-4(1-39)-Lys6-NH₂,
 H-des Asp28 Pro36, Pro37, Pro38 [Trp(02)25] Exendin-4(1-39)-NH₂,
 H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(02)25, Asp28] Exendin-4(1-39)-NH₂,
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(02)25, Asp28] Exendin-4(1-39)-NH₂,
 des Pro36, Pro37, Pro38 [Trp(02)25, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
 H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(02)25, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(02)25, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
 H-(Lys)6-des Pro36 [Met(0)14, Asp28] Exendin-4(1-39)-Lys6-NH₂,
 des Met(0)14 Asp28 Pro36, Pro37, Pro38 Exendin-4(1-39)-NH₂,
 H-(Lys)6-des Pro36, Pro37, Pro38 [Met(0)14, Asp28] Exendin-4(1-39)-NH₂,
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(0)14, Asp28] Exendin-4(1-39)-NH₂,
 des Pro36, Pro37, Pro38 [Met(0)14, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
 H-(Lys)6-des Pro36, Pro37, Pro38 [Met(0)14, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
 H-Asn-(Glu)5 des Pro36, Pro37, Pro38 [Met(0)14, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
 H-Lys6-des Pro36 [Met(0)14, Trp(02)25, Asp28] Exendin-4(1-39)-Lys6-NH₂,
 H-des Asp28 Pro36, Pro37, Pro38 [Met(O)14, Trp(02)25] Exendin-4(1-39)-NH₂,
 H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH₂,
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(0)14, Trp(02)25, Asp28] Exendin-4(1-39)-NH₂,
 des Pro36, Pro37, Pro38 [Met(0)14, Trp(02)25, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
 H-(Lys)6-des Pro36, Pro37, Pro38 [Met(0)14, Trp(02)25, Asp28] Exendin-4(S1-39)-(Lys)6-NH₂,
 H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(02)25, Asp28] Exendin-4(1-39)-(Lys)6-NH₂;

or a pharmaceutically acceptable salt or solvate of any one of the afore-mentioned Exendin-4 derivative.

[0032] 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, Choriogonadotropin, Menotropin), Somatotropine (Somatotropin), Desmopressin, Terlipressin, Gonadorelin, Triptorelin, Leuprorelin, Buserelin, Nafarelin,

Goserelin.

[0033] 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 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.

[0034] Antibodies are globular plasma proteins (~150 kDa) that are also known as immunoglobulins which share a basic structure. As they have sugar chains added to amino acid residues, they are glycoproteins. The basic functional unit of each antihousing 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.

[0035] 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 β sheets create a "sandwich" shape, held together by interactions between conserved cysteines and other charged amino acids.

[0036] There are five types of mammalian Ig heavy chain denoted by α , δ , ϵ , γ , and μ . The type of heavy chain present defines the isotype of antihousing; these chains are found in IgA, IgD, IgE, IgG, and IgM antibodies, respectively.

[0037] Distinct heavy chains differ in size and composition; α and γ contain approximately 450 amino acids and δ approximately 500 amino acids, while μ and ϵ have approximately 550 amino acids. Each heavy chain has two regions, the constant region (C_H) and the variable region (V_H). 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 γ , α and δ have a constant region composed of three tandem Ig domains, and a hinge region for added flexibility; heavy chains μ and ϵ 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.

[0038] In mammals, there are two types of immunoglobulin light chain denoted by λ and κ . 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 antihousing contains two light chains that are always identical; only one type of light chain, κ or λ , is present per antihousing in mammals.

[0039] Although the general structure of all antibodies is very similar, the unique property of a given antihousing 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.

[0040] An "antihousing fragment" contains at least one antigen binding fragment as defined above, and exhibits essentially the same function and specificity as the complete antihousing 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 $F(ab')_2$ fragment containing both Fab pieces and the hinge region, including the H-H interchain disulfide bond. $F(ab')_2$ is divalent for antigen binding. The disulfide bond of $F(ab')_2$ 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).

[0041] 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^+ , or K^+ , or Ca^{2+} , or an ammonium ion $N^+(R1)(R2)(R3)(R4)$, 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.

[0042] Pharmaceutically acceptable solvates are for example hydrates.

[0043] A bung 5 is slideably retained within the cartridge 3. The bung 5 seals the cartridge 3 proximally. Movement of the bung 5 in the distal direction with respect

to the cartridge 3 causes the drug 16 to be dispensed from the cartridge 3. In an initial state of the device 1, i.e. the state as supplied from the manufacturer before setting and dispensing a first dose, the bung 5 is arranged in a proximal end position with respect to the cartridge 3. The cartridge 3 may be fully filled in the initial state, e.g. no drug 16 has been dispensed yet from the cartridge 3.

[0044] The drug delivery device 1 may be a pen-type device, in particular a pen-type injector. The device 1 is preferably configured for dispensing fixed doses of the drug 16, i.e. doses which may not be varied by a user. The device 1 is a re-usable device, which means that the cartridge 3 can be replaced, in particular during a reset operation, by a replacement cartridge for dispensing a plurality of doses from the replacement cartridge. Alternatively, the device 1 may be a disposable device 1 which means that the cartridge 3 is non-releasably connected to the cartridge holder 2.

[0045] The device 1 comprises a drive mechanism 7A, 7B, 13, 14. The drive mechanism is used for setting and dispensing a dose of the drug 16. For details of the drive mechanism, it is referred to the previously mentioned document WO 2008/058666 A1.

[0046] The device 1 comprises a piston rod 9. The piston rod 9 is configured to operate through the housing 4 of the device 1.

[0047] In one embodiment (see Figures 1, 2 and 7A to 7D) of the device 1, the length of the piston rod 9 can be varied. This may be achieved by means of an adjusting member 10. The adjusting member 10 may be part of the piston rod 9. The adjusting member 10 may be displaceably disposed on the piston rod 9. The adjusting member 10 may be arranged at the distal end of the piston rod 9. The adjusting member 10 may be connected to the piston rod 9 and can be displaced with respect to the piston rod 9, preferably along the piston rod's longitudinal axis, e.g. in axial direction for enlarging or reducing the length of the piston rod 9 prior to final assembly of the device 1, which is described later on in more detail. In an alternative embodiment, the length of the piston rod 9 is fixed (see embodiment of Figure 5).

[0048] In the embodiment where the length of the piston rod 9 is variable, the adjusting member 10 is interconnected with a distal end section of the piston rod 9 facing towards the bung 5. Consequently, the at least one adjusting member 10 is to be arranged between the piston rod 9 and the bung 5. The adjusting member 10 therefore serves as a kind of interface member intended to compensate variations of the mutual distance and/or relative position of piston rod 9 and the bung 5 that may occur, for instance, due to manufacturing and/or assembly tolerances. The piston rod 9 may further comprise at least one interlock means. The interlock means is adapted to interact with the adjusting member 10 and/or with the piston rod 9 for mutually locking in position the adjusting member 10 and the piston rod 9 in an arbitrary relative position to each other. In particular, the adjusting

member's 10 axial position relative to the piston rod 9 can be continuously modified, preferably for eliminating said manufacturing and assembly tolerances. Once the adjusting member 10 has been positioned in a tolerance-eliminating configuration with the piston rod 9, its relative position to the piston rod 9 can be either permanently or releasably locked by way of the at least one interlock means. During a tolerance eliminating procedure, e.g. during the assembly process as described below, the adjusting member 10 and piston rod 9 are mutually displaceable with respect to each other. In other words, they may be telescopically shiftable in axial direction. Once a tolerance-eliminating configuration has been attained, adjusting member 10 and piston rod 9 can be mutually interlocked in such a way, that the piston rod 9 is enabled to transfer a respective thrust or force to the bung 5 required for displacing the bung 5 in distal direction. By having the piston rod 9 and the adjusting member 10 displaceably attached or connected thereto, the overall axial dimension and extension of the piston rod 9 becomes variable, in particular for the purpose of tolerance elimination.

[0049] In another preferred embodiment (see Figures 7A to 7C), the adjusting member 10 and the piston rod 9 are threadedly engaged in order to axially displace the piston rod 9 and the adjusting member 10 relative to each other. The adjusting member 10 and the piston rod 9 are threadedly engaged by mechanical cooperation of an inner thread 23 of the adjusting member (see Figure 7C) and an outer thread 12 of the piston rod (see Figures 7A and 7C). The tread is preferably self-locking. By way of a threaded engagement of adjusting member 10 and piston rod 9, the overall axial dimensions of the piston rod 9 can be modified in a continuous way. Here, the interlock means is further adapted to inhibit self-acting relative rotation of piston rod 9 and adjusting member 10. Hence, the interlock means prevents, that the adjusting member 10 autonomously rotates with respect to the piston rod 9 and vice versa. By way of the threaded engagement, axially directed forces and thrust can be transferred, e.g. from the drive mechanism via the piston rod 9 to the adjusting member 10 and finally to the bung 5.

[0050] Since the interlock means is designed for inhibiting self-acting relative rotation of piston rod 9 and adjusting member 10, the interlock means itself may not have to withstand those comparatively large axial forces or respective thrust, which is required to displace the bung 5 in the distal direction.

[0051] In a further preferred aspect (see Figure 7C), the adjusting member 10 comprises a threaded receptacle, which is adapted to receive a correspondingly threaded distal socket portion of the piston rod 9.

[0052] In an alternative embodiment (not explicitly shown), the piston rod 9 comprises a threaded receptacle at its distal end section, which is adapted to receive a correspondingly threaded proximal socket portion of the adjusting member 10. Hence, the threaded engagement of piston rod 9 and adjusting member 10 can be generally

implemented either way.

[0053] In another preferred aspect (see Figure 7D), the interlock means comprises at least one resiliently biased tongue member 24 which is adapted to engage with a corrugated surface portion 25 of the adjusting member 10 or of the piston rod 9. Preferably, the interlock means may positively engage with a side wall of the receptacle of either the adjusting member 10 or the piston rod 9. Additionally, the interlock means is preferably arranged on that part or component comprising the socket portion.

[0054] In another preferred embodiment, the tongue member 24 is arranged laterally offset with respect to the socket portion. With respect to the transverse plane of the piston rod 9 that extends perpendicular to the piston rod's longitudinal axis, the axially protruding socket portion is typically arranged on the centre of the adjusting member 10. Here, the resiliently biased tongue member 24 is arranged and displaced with a lateral or radial offset with respect to the socket portion. Hence, mutual arrangement of socket portion and tongue member 24 is such that a gap is formed there between adapted to receive a side wall section of the receptacle.

[0055] In a further preferred embodiment, the radially inwardly facing side wall section of the receptacle is threaded in order to provide threaded engagement with the correspondingly threaded socket portion. The side wall section of the receptacle at its outwardly facing side is preferably corrugated or comprises a ribbed structure, by way of which a kind of positive or frictional engagement of the receptacle and the tongue member can be established in order to inhibit self-acting relative rotation of the receptacle relative to the socket portion.

[0056] In alternative embodiments it is also conceivable, that an outwardly facing side wall section of the receptacle is threaded and wherein an inwardly facing side wall section of said receptacle is corrugated or comprises a ribbed surface structure. In such embodiments, the resiliently biased tongue members are preferably arranged radially inward with respect to the threaded engagement of adjusting member 10 and piston rod 9.

[0057] Mutual engagement and interaction of resiliently biased tongue members and the corrugated surface provides a kind of snap-in feature. Depending on the overall number of longitudinally extending ribs or corrugations and the pitch of the thread a fine adjustment of piston rod and adjusting member 10 in a sub-millimetres range, preferably in a range of 1/10 mm or even 1/100-mm can be attained.

[0058] In a further preferred embodiment (not explicitly shown), threaded and corrugated side wall sections of the receptacle are arranged at least partially offset with respect to each other in axial direction. Moreover, the corrugations or the ribs of said wall section comprise an axial extension substantially corresponding with an overall axial extension of the mutually corresponding threads of receptacle and socket portion.

[0059] According to a further embodiment (not explicitly shown), the piston rod 9 comprises at least two tongue

members arranged at the piston rod 9 and being axially displaced in proximal direction with respect to the piston rod's distal end section. Here, the tongue members, that are preferably arranged opposite to each other in the transverse plane comprise radially inwardly pointing lug portions that are adapted to engage with the corrugated or ribbed outer side wall section of a proximal end of the adjusting member 10 comprising a cupped receptacle.

[0060] In a further aspect (see Figures 1 and 2), it is intended, that the adjusting member 10 comprises a contact surface at its distal end section that faces towards a proximal end section of the bung 5 if the drug delivery device 1 is in the initial state. The contact or abutment surface is of substantially plane shape and preferably extends in the transverse plane, hence perpendicular to the axial or longitudinal extension of the piston rod. Preferably, the distally facing outer surface of the cupped receptacle of the adjusting member 10 serves as a contact surface.

[0061] In the following, with abutment of the piston rod 9 and the bung 5, it may be meant that the adjusting member 10 abuts the bung 5.

[0062] The previously described embodiments of the piston rod 9, the adjusting member 10 and/or the interlock means result in a piston rod with adjustable length, which may be used to compensate manufacturing tolerances as described below. As already described further above, in an alternative embodiment of the device 1, the length of the piston rod 9 may be fixed. In this case, the previously described embodiments may be redundant and tolerances may be compensated by adjusting the position of a connection between the cartridge holder 2 and the housing 4. The elimination of tolerances results in a defined initial position of the piston rod 9 relative to the bung 5 after connection of the cartridge holder 2 and the housing 4 was completed and before the first dose of drug is dispensed from the cartridge 3.

[0063] The device 1 comprises a mechanism, in particular a back off mechanism. The mechanism comprises a spring member 15, e.g. a helical coil spring. The spring member 15 is axially secured within the housing 4. The spring member 15 is flexibly mounted within the housing. The spring member 15 is flexible in the axial direction. The spring member 15 is unitarily formed with the housing 4 or with a part 7A of the drive mechanism or with an insert of the housing. By means of the back-off mechanism, the piston rod 9 is moved proximally by a back off distance D after a dose delivery operation was performed, which is described later on in more detail. The back off distance D may be less than 1.0 mm. Preferably, the back off distance D is less than 0.5 mm. The back off distance D may be greater than 0.1 mm. The back off distance D preferably amounts to 0.3 mm, for example.

[0064] In the initial state of the device, the distal end of the piston rod 9 is arranged at a predetermined initial distance from the proximal end of the bung 5. The predetermined initial distance is equal to or smaller than the back off distance D. In particular, the predetermined initial

distance may be defined by the back off distance D, which is described in connection with the assembly process of the device 1. The predetermined initial distance amounts to 0.2 mm, for example. Accordingly, in the initial state of the device 1, the piston rod 9 and the bung 5 are arranged at a predetermined initial position with respect to one another. User operated steps, e.g. priming steps, for arranging the piston rod 9 and the bung 5 at a predetermined relative position are redundant.

[0065] The device 1 comprises an actuation member 14. The actuation member 14 is arranged at least partly within the housing 4 of the device 1. The actuation member 14 may comprise a dose button. The actuation member 14 may comprise a drive member. The actuation member 14 is displaceable with respect to the housing 4. The actuation member 14 can be positioned in a first position (see Figure 6A) with respect to the housing 4. The first position may be the most distal position of the actuation member 14 with respect to the housing 4. Alternatively, the actuation member 14 can be positioned in a second position with respect to the housing 4 (see Figure 6B). The second position of the actuation member 14 may be a back-off or initial position. Alternatively, the actuation member 14 can be positioned in a third position (see Figure 6C) with respect to the housing 4. The third position may be the most proximal position of the actuation member 14 with respect to the housing 4. The second position is arranged more proximal with respect to the housing 4 than the first position. The third position is arranged more proximally with respect to the housing 4 than the second position.

[0066] The actuation member 14 is positioned in the first position after a dose delivery operation was fully completed (see Figure 1). When the actuation member 14 is in the first position, the mechanism is activated. The actuation member 14 is positioned in the second position before a dose setting operation is initiated, e.g. in the initial state (see Figure 2). When the actuation member 14 is in the second position, the mechanism is deactivated. The actuation member 14 is positioned in the third position after a dose setting operation was completed. When the actuation member 14 is in the third position, the mechanism is deactivated.

[0067] The actuation member 14 is moveable from the second or the third position into the first position for activating the mechanism of the device 1. The actuation member 14 is moveable from the third position into the first position for delivering a set dose of the drug 16. Movement of the actuation member 14 from the third position into the first position is transferred to the piston rod 9 by mechanical cooperation of the actuation member 14 and the piston rod 9.

[0068] The actuation member 14 is moveable from the first position, i.e. the most distal position, into the second position, i.e. the back-off or initial position, for deactivating the mechanism of the device 1. Movement of the actuation member 14 for being displaced from the first position into the second position is transferred to the piston

rod 9 for displacing the piston rod 9 by the back off distance D, which is described later on in more detail.

[0069] The actuation member 14 is further moveable from the second position into the third position for setting a dose of the drug 16. Movement of the actuation member 14 for being displaced from the second position into the third position is prevented from being transferred to the piston rod 9 by mechanical cooperation of the housing 4 and the piston rod 9.

[0070] Operation of the back off mechanism is described in the following in connection with the assembly and the operation of the device 1.

[0071] For assembling the device 1, the following steps are performed. The steps may be, but need not necessarily be performed in the order given below. Note that the subsequently described steps apply for the case that the length of the piston rod is adjustable. This is in the following referred to as embodiment "A". The case in which the position of a connection between the housing 4 and the cartridge holder 2 may be varied to compensate tolerances which does not require a piston rod 9 with adjustable length is in the following referred to as embodiment "B" and is described later on.

[0072] A.1) In a first step, the cartridge holder 2 containing the cartridge 3 is provided. The cartridge 3 is in a completely filled state. In particular, the bung 5 is arranged in the proximal end position with respect to the cartridge 3.

[0073] A.2) In a second step, the housing 4 with the actuation member 14, the spring member 15 and the piston rod 9 being retained therein is provided. The actuation member 14 is in the second position, the mechanism thus being deactivated. In particular, the spring 15 is in a relaxed state. The housing 4 is not yet connected to the cartridge holder 2.

[0074] A.3) In a next step, the previously mentioned back off mechanism is activated. This is achieved by moving the actuation member 14 distally from the second position into the first position. The distance by which the actuation member 14 is moved distally amounts to 0.6 mm, for example. The distance may be greater than 0.1 mm. The distance may be smaller than 2.0 mm. The actuation member 14 is moved against a proximally directed force provided by the spring member 15. Accordingly, the spring member 15 is biased when the actuation member 14 is moved distally. When the actuation member 14 is moved into the first position, the piston rod 9 is moved distally, as well. The piston rod 9 is moved distally by half of the distance by which the actuation member 14 is moved distally, for example. The piston rod 9 is moved distally by 0.3 mm, for example. Accordingly, the mechanical advantage of the device 1 amounts to 2:1 (see embodiments of "rack and pinion" in document WO 2008/058666 A1). When the actuation member 14 is positioned in the first position, the back off mechanism is fully activated.

[0075] A.4) In a next step, the position of the proximal end of the bung 5 with respect to a predetermined refer-

ence point on the cartridge unit is measured. The reference point can be located on the cartridge 3 or on the cartridge holder 2, for example (see Figure 3).

[0076] A.5) In a next step, the position of the distal end of the piston rod 9 with respect to a predetermined reference point 19 on the housing 4 is measured (see Figure 3).

[0077] A.6) In a next step, the relative position which the proximal end of the bung 5 and the distal end of the piston rod 9 would have when the cartridge holder 2 and the housing 4 were connected, with the mechanism being activated is calculated from the results of the measurements performed in the two previous steps (steps A.4) and A.5)), e.g. based on the known and reliable dimensions of the cartridge holder 2 and the housing 4, the measured values and the position of the marks on the cartridge holder 2 and the housing 4. This relative position is preferably such that, when the mechanism is activated and the device 1 is fully assembled, the bung 5 is not compressed or only minimally compressed by the piston rod 9. The relative position is preferable such that, when the mechanism is activated and the device 1 is fully assembled, the bung 5 and the piston rod 9 just abut one another, or there is a small distance between them.

[0078] A.7) In a next step, the mechanism is deactivated. This is achieved by releasing the actuation member 14. Once released, the actuation member 14 is automatically moved from the first position into the second position due to the proximally directed force exerted onto the actuation member 14 by the spring member 15. Movement of the actuation member 14 from the first position into the second position is transferred to the piston rod 9 such that piston rod 9 is displaced by the back off distance D. The piston rod 9 is displaced by a back off distance D which amounts to 0.3 mm, for example. When the actuation member 14 is in the second position, the mechanism is fully deactivated.

[0079] A.8) In a next step, it is checked whether the relative position calculated in step A.6) corresponds to a predetermined relative position. The predetermined relative position may be chosen such that, when the mechanism is activated and the device 1 is fully assembled, the bung 5 is not compressed or only slightly compressed by the piston rod 9. Hence, the predetermined relative position should be chosen such that mutual abutment of the bung 5 and the piston rod 9 is such that the piston rod 9 does not yet apply substantial pressure or thrust to the bung 5 in order to prevent generation of droplet.

[0080] A.9) If the relative position which was calculated in step A.6) does not correspond to the predetermined relative position (see step 8)), the length of the piston rod 9 may be varied as described above.

[0081] If the relative position which was calculated in step A.6) is such that there would be a gap between the distal end of the piston rod 9 and the proximal end of the bung 5 when the mechanism is activated and the device 1 finally assembled, the length of the piston rod 9 is enlarged by screwing the adjusting member 10 in the distal

direction with respect to the piston rod 9. Otherwise underdosing could occur, which could have lethal or even fatal consequences for the user.

[0082] If, on the other hand, the relative position which was calculated in step A.6) is such that the distance between the proximal end of the bung 5 and the distal end of the piston rod 9 was too small when the device 1 is assembled, the piston rod 9 would strongly compress the bung 5. This could lead to droplets of the drug 16 or even overdosing. Accordingly, in this case the length of the piston rod 9 is reduced by screwing the adjusting member 10 in the proximal direction with respect to the piston rod 9.

[0083] After adjusting the length of the piston rod 9, steps A.3) to A.8) are repeated. If then, again, the relative position which was calculated in step A.6) does not correspond to the predetermined relative position, step A.8) is repeated again.

[0084] A.10) If, after having performed step A.8) and, optionally, step A.9) the relative position which was calculated in step A.6) corresponds to the predetermined relative position, the cartridge holder 2 and the housing 4 are moved towards each other (arrow 21 in Figure 4) and connected to one another (see Figure 4). Thereby, the cartridge holder 2 and the housing 4 are irreleasably connected by threading or snap-fitting to the cartridge holder 2 and the housing 4 to one another. Thereby, the connection means, e.g. two mating threads or two mating snap-fit elements, are arranged at a fixed position with respect to the housing 4 and the cartridge holder 2.

[0085] In the following, the steps for assembling the device 1 according to embodiment "B" are described. In embodiment "B", the length of the piston rod 9 may be fixed and the piston rod 9 can not be used to compensate the tolerances.

[0086] Concerning the steps B.1) to B.5) it is referred to the steps A.1) to A.5), which also apply for the case that the length of the piston rod 9 is not adjustable.

[0087] B.6) In a next step, a connecting position for a connection of the cartridge holder 2 and the housing 4 is determined from the results of the measurements performed in steps B.4) and B.5), e.g. based on the known and reliable dimensions of the cartridge holder 2 and the housing 4, the measured values and the position of the marks on the cartridge holder 2 and the housing 4. Thereby, the connecting position is chosen such that if the housing 4 and the cartridge holder 2 are connected in the connecting position, the piston rod 9 and the bung 5 are arranged at a predetermined initial distance from one another when the mechanism is deactivated. In particular, it is calculated from the measurements performed in steps B.4) and B.5) which connecting position the cartridge holder 2 and the housing 4 should have to achieve the initial distance between the bung 5 and the piston rod 9 when the device 1 is fully assembled. This distance is preferably such that, when the mechanism is activated and the device 1 is fully assembled, the bung 5 is not compressed or only minimally compressed by the piston

rod 9. The distance between piston rod 9 and bung 5, when the mechanism is activated, may be zero or greater than zero. The distance is preferably such that, when the mechanism is activated and the device 1 is fully assembled, the bung 5 and the piston rod 9 just about one another, or there is a small distance between them.

[0088] B.7) In a next step, the mechanism is deactivated. Regarding step B.7) it is referred to step A.7) which applies also for the embodiment where the length of the piston rod 9 is not necessarily adjustable.

[0089] B.8) In a next step, the cartridge holder 2 and the housing 4 are moved towards each other and connected to one another. Thereby, the cartridge holder 2 and the housing 4 are irreleasably connected by a weld, for example, which is shown in Figure 5. The cartridge holder 2 and the housing 4 are welded to one another by a laser, for example. The cartridge holder 2 and the housing 4 are welded to one another via a welding surface 22, for example (Figure 5). This has the advantage that the cartridge holder 2 and the housing 4 can be brought into variable relative positions when connecting the cartridge holder 2 and the housing 4 to one another. Accordingly, the piston rod 9 and the bung 5 can be brought at variable relative initial positions. In particular, by welding the cartridge holder 2 and the housing 4 to one another, variable predetermined initial distances between the piston rod 9 and the bung 4 can be established. This is possible as the welding surface 22 can be applied to various places on the outer surface of the housing 4 and the cartridge holder 2. Accordingly, in this case, adjustment of the length of the piston rod 9 is redundant.

[0090] When the cartridge holder 2 and the housing 4 are connected, in particular after having performed step A.10) for embodiment "A", or step B.8) for embodiment "B", the device 1 is fully assembled. Now, the device 1 is in the previously described initial state. The initial distance between the distal end of the piston rod 9 and the proximal end of the bung 5 is greater than zero. The initial distance is defined by the back off distance D the piston rod 9 was moved proximally when the actuation member 14 was moved from the first position into the second position during the assembly process. The distance in the initial state may correspond to the back off distance D.

[0091] The device 1 is supplied to the user in the initial state. For operating the device 1, the following steps are performed:

For setting a dose of the drug 16, the user moves the actuation member 14 from the second position into the third position (see Figure 2). The piston rod 9 is held in its position by mechanical cooperation with the housing 4. The piston rod 9 is arranged at the predetermined initial distance from the bung 5, which, in Figure 2 corresponds to the back off distance.

For delivering the dose, the user moves the actuation member 14 from the third position into the first posi-

tion. Movement of the actuation member 14 is thereby transferred to the piston rod 9 for dispensing the dose. When the actuation member 14 is moved distally, the spring member 15 is biased, the mechanism thus being activated. When the actuation member 14 is in the first position, the mechanism is activated. The dose delivery operation is completed when the actuation member 14 is in the first position. This state is depicted in Figure 1.

[0092] The user now releases the actuation member 14. The actuation member 14 is automatically moved from the first into the second position by the spring member 15. Thereby, the mechanism is deactivated. When the actuation member 14 is moved into the second position, the piston rod 9 is moved proximally by the back off distance D. The back off distance D is less than the distance by which the piston rod 9 is moved distally during a dose delivery operation, i.e. when the actuation member 14 is moved from the third position into the first position. The back off distance D amounts preferably to less than 30% of the distance by which the piston rod 9 is moved distally during a dose delivery operation. Now, the device 1 is ready for setting and dispensing a further dose of the drug 16.

Reference numerals

[0093]

1	Drug delivery device
2	Cartridge holder
3	Cartridge
4	Housing
5	Bung
6	Cap
7A	Insert
7B	Drive mechanism
9	Piston rod
10	Adjusting member
11	Bearing surface
12	Thread
13	Drive mechanism
14	Actuation member
15	Spring member
16	Drug
17	Distal end
18	Proximal end
19	Reference point
20	Distance
22	Welding plane
D	Back off distance
23	Inner thread
24	Tongue member
25	Surface portion

Claims

1. A drug delivery device (1) comprising:

- 5 - a housing (4) comprising a distal end and a proximal end,
- a cartridge (3) adapted and arranged to contain at least one dose of a drug (16), a bung (5) being movably arranged within the cartridge (3), wherein in an initial state of the device (1), the bung (5) is arranged in a proximal end position with respect to the cartridge (3),
- 10 - a piston rod (9) adapted and arranged to move the bung (5) in the distal direction with respect to the cartridge (3) for delivering a dose of the drug (16),

wherein the device (1) comprises a mechanism operable such that, after a dose delivery operation was completed, the piston rod (9) is moved into the proximal direction with respect to the bung (5) by a back off distance (D),

characterized in that

in the initial state, a distance between a distal end of the piston rod (9) and a proximal end of the bung (5) is greater than zero, with the distance between the piston rod (9) and the bung (5) in the initial state being defined by the back off distance (D).

- 20
- 25
- 30 2. The device according to claim 1, further comprising an actuation member (14) which is moveable with respect to the housing (4), wherein, the actuation member (14) is moveable between a first position and a second position, and wherein movement of the actuation member (14) for being displaced from the first position into the second position is transferred to the piston rod (9) for displacing the piston rod (9) by the back off distance (D).
- 35
- 40 3. The device according to claim 1 or claim 2, wherein the back off distance (D) is greater than or equal to the distance between the distal end of the piston rod (9) and the proximal end of the bung (5) in the initial state.
- 45
- 50 4. The device according to claim 2 or claim 3, wherein the actuation member (14) is further moveable between the second position and a third position, in which the actuation member (14) is positioned after a dose setting operation was completed, wherein the third position is arranged more proximally with respect to the housing (4) than the second position.
- 55 5. The device according to any of claims 2 to 4, comprising a spring member (15) which is mounted within the housing (4), wherein the spring member (15) is configured and arranged to exert a force onto the actuation member (14) to move the actuation

member (14) from the first position into the second position, thereby moving the piston rod (9) proximally by the back off distance (D).

6. The device according to claim 5, wherein the back off distance (D) is in the range of 0.1 to 1.0 mm.
7. The device according to claim 5 or claim 6, wherein the back off distance (D) is less than the distance by which the piston rod (9) is moved distally during a dose delivery operation.
8. The device according to any of the previous claims, wherein the piston rod (9) is configured such that the axial dimension of the piston rod (9) can be varied.
9. A method for assembling a drug delivery device (1), the method comprising the following steps:

A) Providing a cartridge unit comprising a cartridge (3) which holds at least one dose of a drug (16), a bung (5) being movably arranged within the cartridge (3),

B) providing a drive unit which is connectable to the cartridge unit, the drive unit comprising a piston rod (9) and a mechanism, wherein the mechanism is configured to move the piston rod (9) by a back off distance (D) when the mechanism switches from an activated state into a deactivated state,

C) activating the mechanism,

characterized in that

the following steps are performed:

D) measuring the position of the proximal end of the bung (5) with respect to a predetermined reference point on the cartridge unit,

E) measuring the position of the distal end of the piston rod (9) with respect to a predetermined reference point on the drive unit,

F) deriving, from the results of the measurements performed in steps D) and E), information indicative for a relative position of the distal end of the piston rod (9) and the proximal end of the bung (5) when the cartridge holder and the housing are connected,

G) deactivating the mechanism such that the piston rod (9) is displaced by the back off distance (D),

H) connecting the cartridge unit and the drive unit to one another such that the piston rod (9) and the bung (5) are arranged at an initial distance from one another when the mechanism is deactivated.

10. The method of claim 9, wherein

deriving the information comprises determining from the results of the measurements a connecting position for a connection of the cartridge unit and the drive unit such that if the units are connected by the connection in the connecting position, the piston rod (9) and the bung (5) are arranged at the initial distance from one another when the mechanism is deactivated.

11. The method of claim 9 or claim 10, wherein the connection is a weld.
12. The method of claim 9, wherein deriving the information comprises determining from the results of the measurements a relative position of the proximal end of the bung (5) and the distal end of the piston rod (9) if the cartridge unit and the drive unit were connected by connecting means provided on the cartridge unit and the drive unit.
13. The method of claim 12, further comprising the step of checking whether the relative position of the proximal end of the bung (5) and the distal end of the piston rod (9) corresponds to a predetermined relative position of the proximal end of the bung (5) and the distal end of the piston rod (9).
14. The method of claim 13, wherein if the relative position does not correspond to the predetermined relative position, modifying the axial dimension of the piston rod (9) such that the relative position corresponds to the predetermined relative position.
15. The method according to claim 13 or claim 14, wherein the predetermined relative position is chosen such that the initial distance between the proximal end of the bung (5) and the distal end of the piston rod (9) is equal to or slightly greater than zero when the device (1) has been assembled and the mechanism is activated.

Patentansprüche

1. Medikamenten-Verabreichungsvorrichtung (1), umfassend:

- ein Gehäuse (4), umfassend ein distales Ende und ein proximales Ende,

- eine Kartusche (3), die ausgelegt und angeordnet ist, um wenigstens eine Dosis eines Arzneimittels (16) zu enthalten, wobei ein Stopfen (5) beweglich in der Kartusche (3) angeordnet ist, wobei der Stopfen (5) in einem Anfangszustand der Vorrichtung (1) in einer proximalen Endstellung bezüglich der Kartusche (3) ange-

ordnet ist,

- eine Kolbenstange (9), die ausgelegt und angeordnet ist, um den Stopfen (5) in die distale Richtung bezüglich der Kartusche (3) zur Abgabe einer Dosis des Arzneimittels (16) zu bewegen,

wobei die Vorrichtung (1) einen Mechanismus umfasst, der so betätigbar ist, dass nach einem beendeten Dosisverabreichungsvorgang die Kolbenstange (9) in die proximale Richtung bezüglich des Stopfens (5) über eine Rücksetzstrecke (D) bewegt wird, **dadurch gekennzeichnet, dass** im Anfangszustand ein Abstand zwischen einem distalen Ende der Kolbenstange (9) und einem proximalen Ende des Stopfens (5) größer als Null ist, wobei der Abstand zwischen der Kolbenstange (9) und dem Stopfen (5) in dem Anfangszustand durch die Rücksetzstrecke (D) definiert wird.

2. Vorrichtung nach Anspruch 1, ferner umfassend ein Betätigungselement (14), das bezüglich des Gehäuses (4) bewegbar ist, wobei das Betätigungselement (14) zwischen einer ersten Stellung und einer zweiten Stellung bewegbar ist und wobei die Bewegung des Betätigungselements (14) zur Verschiebung aus der ersten Stellung in die zweite Stellung auf die Kolbenstange (9) übertragen wird, um die Kolbenstange (9) über die Rücksetzstrecke (D) zu verschieben.
3. Vorrichtung nach Anspruch 1 oder Anspruch 2, wobei die Rücksetzstrecke (D) größer als der oder gleich dem Abstand zwischen dem distalen Ende der Kolbenstange (9) und dem proximalen Ende des Stopfens (5) im Anfangszustand ist.
4. Vorrichtung nach Anspruch 2 oder Anspruch 3, wobei das Betätigungselement (14) ferner zwischen der zweiten Stellung und einer dritten Stellung bewegbar ist, in der das Betätigungselement (14) nach einem beendeten Dosis-einstellungsvorgang angeordnet ist, wobei die dritte Stellung bezüglich des Gehäuses (4) weiter proximal als die zweite Stellung angeordnet ist.
5. Vorrichtung nach einem der Ansprüche 2 bis 4, umfassend ein Federelement (15), das in dem Gehäuse (4) angebracht ist, wobei das Federelement (15) ausgelegt und angeordnet ist, um eine Kraft auf das Betätigungselement (14) auszuüben, um das Betätigungselement (14) aus der ersten Stellung in die zweite Stellung zu bewegen, wodurch die Kolbenstange (9) proximal über die Rücksetzstrecke (D) bewegt wird.
6. Vorrichtung nach Anspruch 5, wobei die Rücksetzstrecke (D) im Bereich von 0,1

bis 1,0 mm liegt.

7. Vorrichtung nach Anspruch 5 oder Anspruch 6, wobei die Rücksetzstrecke (D) kleiner als die Strecke ist, um welche die Kolbenstange (9) distal während eines Dosisverabreichungsvorgangs bewegt wird.
8. Vorrichtung nach einem der vorhergehenden Ansprüche, wobei die Kolbenstange (9) so ausgebildet ist, dass die axiale Abmessung der Kolbenstange (9) variiert werden kann.
9. Verfahren zum Zusammenbauen einer Medikamenten-Verabreichungsvorrichtung (1), wobei das Verfahren die folgenden Schritte umfasst:
 - A) Bereitstellen einer Kartuscheneinheit, umfassend eine Kartusche (3), die wenigstens eine Dosis eines Arzneimittels (16) enthält, wobei ein Stopfen (5) beweglich in der Kartusche (3) angeordnet ist,
 - B) Bereitstellen einer Antriebseinheit, die mit der Kartuscheneinheit verbindbar ist, wobei die Antriebseinheit eine Kolbenstange (9) und einen Mechanismus umfasst, wobei der Mechanismus ausgelegt ist, um die Kolbenstange (9) über eine Rücksetzstrecke (D) zu bewegen, wenn der Mechanismus von einem aktivierten Zustand in einen deaktivierten Zustand umschaltet,
 - C) Aktivieren des Mechanismus,

dadurch gekennzeichnet, dass die folgenden Schritte durchgeführt werden:

 - D) Messen der Stellung des proximalen Endes des Stopfens (5) bezüglich eines vorbestimmten Bezugspunkts auf der Kartuscheneinheit,
 - E) Messen der Stellung des distalen Endes der Kolbenstange (9) bezüglich eines vorbestimmten Bezugspunkts auf der Antriebseinheit,
 - F) Ableiten, aus den Ergebnissen der in den Schritten D) und E) durchgeführten Messungen, von Informationen, die auf eine relative Stellung des distalen Endes der Kolbenstange (9) und des proximalen Endes des Stopfens (5) hinweisen, wenn der Kartuschenhalter mit dem Gehäuse verbunden ist,
 - G) Deaktivieren des Mechanismus, so dass die Kolbenstange (9) über die Rücksetzstrecke (D) verschoben wird,
 - H) Verbinden der Kartuscheneinheit und der Antriebseinheit miteinander, so dass die Kolbenstange (9) und der Stopfen (5) in einen Anfangsabstand voneinander angeordnet sind, wenn der Mechanismus deaktiviert wird.

10. Verfahren nach Anspruch 9, wobei das Ableiten der Informationen das Bestimmen, aus den Ergebnissen der Messungen, einer Verbindungsstellung für eine Verbindung der Kartuscheneinheit und der Antriebseinheit umfasst, so dass, wenn die Einheiten über die Verbindung in der Verbindungsstellung miteinander verbunden werden, die Kolbenstange (9) und der Stopfen (5) in dem Anfangsabstand voneinander angeordnet sind, wenn der Mechanismus deaktiviert wird.
11. Verfahren nach Anspruch 9 oder Anspruch 10, wobei die Verbindung eine Schweißverbindung ist.
12. Verfahren nach Anspruch 9, wobei das Ableiten der Informationen das Bestimmen, aus den Ergebnissen der Messungen, einer relativen Stellung des proximalen Endes des Stopfens (5) und des distalen Endes der Kolbenstange (9) umfasst, wenn die Kartuscheneinheit und die Antriebseinheit über ein Verbindungsmittel, das auf der Kartuscheneinheit und der Antriebseinheit bereitgestellt ist, miteinander verbunden wären.
13. Verfahren nach Anspruch 12, ferner umfassend die folgenden Schritte
Überprüfen, ob die relative Stellung des proximalen Endes des Stopfens (5) und des distalen Endes der Kolbenstange (9) einer vorbestimmten relativen Stellung des proximalen Endes des Stopfens (5) und des distalen Endes der Kolbenstange (9) entspricht.
14. Verfahren nach Anspruch 13, wobei, wenn die relative Stellung nicht der vorbestimmten relativen Stellung entspricht, die axiale Abmessung der Kolbenstange (9) so modifiziert wird, dass die relative Stellung der vorbestimmten relativen Stellung entspricht.
15. Verfahren nach Anspruch 13 oder Anspruch 14, wobei die vorbestimmte relative Stellung so gewählt wird, dass der Anfangsabstand zwischen dem proximalen Ende des Stopfens (5) und dem distalen Ende der Kolbenstange (9) Null entspricht oder etwas größer als Null ist, wenn die Vorrichtung (1) zusammengebaut wurde und der Mechanismus aktiviert ist.

Revendications

1. Dispositif (1) d'administration de médicaments comportant :
- un logement (4) comportant une extrémité distale et une extrémité proximale,
 - une cartouche (3) conçue et disposée pour contenir au moins une dose d'un médicament

(16), un bouchon (5) étant disposé de manière mobile à l'intérieur de la cartouche (3), dans lequel dans un état initial du dispositif (1), le bouchon (5) est disposé dans une position d'extrémité proximale par rapport à la cartouche (3),
- une tige (9) de piston conçue et disposée pour déplacer le bouchon (5) dans la direction distale par rapport à la cartouche (3), destinée à administrer une dose du médicament (16),

dans lequel le dispositif (1) comporte un mécanisme fonctionnant de sorte que, après que l'opération d'administration d'une dose ait été terminée, la tige (9) de piston soit déplacée dans la direction proximale par rapport au bouchon (5) d'une distance (D) de recul,

caractérisé en ce que

dans l'état initial, une distance entre une extrémité distale de la tige (9) de piston et une extrémité proximale du bouchon (5) est supérieure à zéro, la distance entre la tige (9) de piston et le bouchon (5) dans l'état initial étant délimitée par la distance (D) de recul.

2. Dispositif selon la revendication 1, comportant en outre un élément (14) d'actionnement qui est mobile par rapport au logement (4), dans lequel, l'élément (14) d'actionnement est mobile entre une première position et une deuxième position, et dans lequel le mouvement de l'élément (14) d'actionnement lorsqu'il est déplacé d'une première position à la deuxième position est transféré à la tige (9) de piston pour déplacer la tige (9) de piston de la distance (D) de recul.
3. Dispositif selon la revendication 1 ou la revendication 2, dans lequel la distance (D) de recul est supérieure ou égale à la distance entre l'extrémité distale de la tige (9) de piston et l'extrémité proximale du bouchon (5) dans l'état initial.
4. Dispositif selon la revendication 2 ou la revendication 3, dans lequel l'élément (14) d'actionnement est en outre mobile entre la deuxième position et une troisième position, dans laquelle l'élément (14) d'actionnement est positionné après qu'une opération de réglage de dose a été terminée, la troisième position étant disposée de manière plus proximale par rapport au logement (4) que la deuxième position.
5. Dispositif selon l'une quelconque des revendications 2 à 4, comportant un élément (15) ressort qui est monté à l'intérieur du logement (4), dans lequel l'élément (15) ressort est configuré et disposé pour exercer une force sur l'élément (14) d'actionnement afin de dé-

- placer l'élément (14) d'actionnement de la première position à la deuxième position, déplaçant ainsi la tige (9) de piston proximale de la distance (D) de recul.
6. Dispositif selon la revendication 5, dans lequel la distance (D) de recul est de l'ordre de 0,1 à 1,0 mm.
7. Dispositif selon la revendication 5 ou la revendication 6, dans lequel la distance (D) de recul est inférieure à la distance à laquelle la tige (9) de piston est déplacée distalement durant une opération d'administration de dose.
8. Dispositif selon l'une quelconque des revendications précédentes, dans lequel la tige (9) de piston est configurée de sorte que la dimension axiale de la tige (9) de piston puisse être variée.
9. Procédé destiné à assembler un dispositif (1) d'administration de médicaments, le procédé comportant les étapes suivantes :
- A) fournir une unité de cartouche comportant une cartouche (3) qui contient au moins une dose de médicament (16), un bouchon (5) étant disposé de manière mobile à l'intérieur de la cartouche (3),
- B) fournir une unité d'entraînement qui peut être reliée à l'unité de cartouche, l'unité d'entraînement comportant une tige (9) de piston et un mécanisme, le mécanisme étant configuré pour déplacer la tige (9) de piston d'une distance (D) de recul lorsque le mécanisme change d'un état activé à un état désactivé,
- C) activer le mécanisme,
- recul,
- H) relier l'unité de cartouche et l'unité d'entraînement l'une à l'autre de sorte que la tige (9) de piston et le bouchon (5) soient disposés à une distance initiale l'un de l'autre lorsque le mécanisme est désactivé.
10. Procédé selon la revendication 9, dans lequel l'obtention des informations consiste à déterminer, à partir des résultats des mesures, une position de liaison pour une liaison de l'unité de cartouche et de l'unité d'entraînement de sorte que si les unités sont reliées par la liaison dans la position de liaison, la tige (9) de piston et le bouchon (5) soient disposés à la distance initiale l'un de l'autre lorsque le mécanisme est désactivé.
11. Procédé selon la revendication 9 ou la revendication 10, dans lequel la liaison est une soudure.
12. Procédé selon la revendication 9, dans lequel l'obtention des informations consiste à déterminer, à partir des résultats des mesures, une position relative de l'extrémité proximale du bouchon (5) et de l'extrémité distale de la tige (9) de piston si l'unité de cartouche et l'unité d'entraînement étaient reliées par un moyen de liaison fourni sur l'unité de cartouche et l'unité d'entraînement.
13. Procédé selon la revendication 12, comportant en outre l'étape consistant à vérifier si la position relative de l'extrémité proximale du bouchon (5) et de l'extrémité distale de la tige (9) de piston correspond à une position relative prédéterminée de l'extrémité proximale du bouchon (5) et de l'extrémité distale de la tige (9) de piston.
14. Procédé selon la revendication 13, dans lequel si la position relative ne correspond pas à la position relative prédéterminée, la dimension axiale de la tige (9) de piston doit être modifiée de sorte que la position relative corresponde à la position relative prédéterminée.
15. Procédé selon la revendication 13 ou la revendication 14, dans lequel la position relative prédéterminée est choisie de sorte que la distance initiale entre l'extrémité proximale du bouchon (5) et l'extrémité distale de la tige (9) de piston soit égale ou légèrement supérieure à zéro lorsque le dispositif (1) a été assemblé et le mécanisme est activé.
- D) mesurer la position de l'extrémité proximale du bouchon (5) par rapport à un point de référence prédéterminé sur l'unité de cartouche,
- E) mesurer la position de l'extrémité distale de la tige (9) de piston par rapport à un point de référence prédéterminé sur l'unité d'entraînement,
- F) obtenir, à partir des résultats des mesures réalisées aux étapes D) et E), des informations indiquant une position relative de l'extrémité distale de la tige (9) de piston et de l'extrémité proximale du bouchon (5) lorsque le support de cartouche et le logement sont reliés,
- G) désactiver le mécanisme de sorte que la tige (9) du piston soit déplacée de la distance (D) de

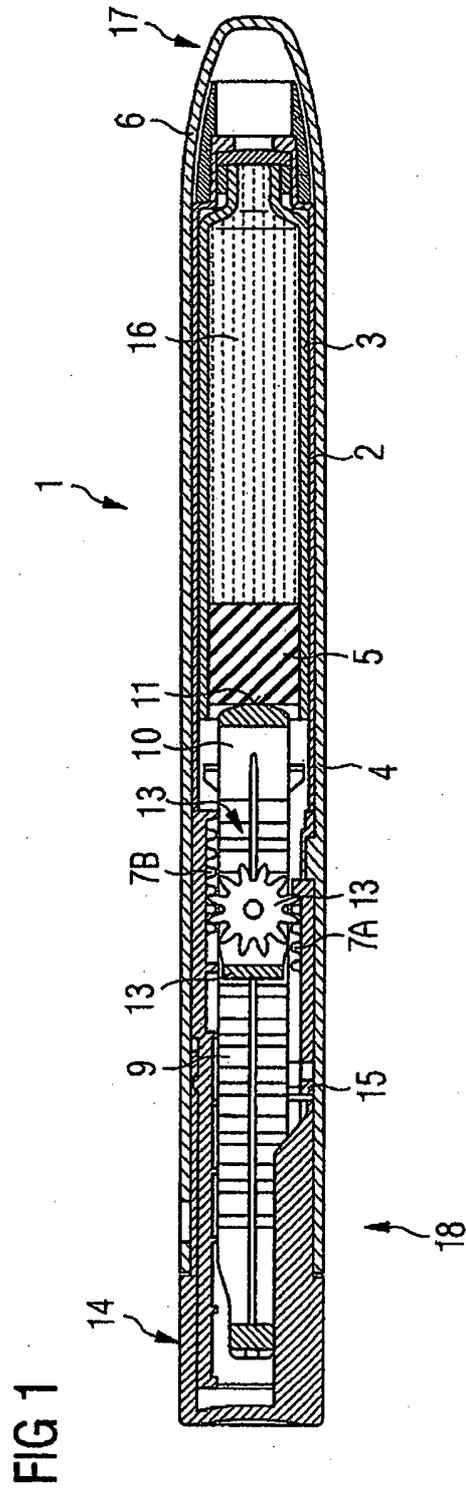


FIG 2

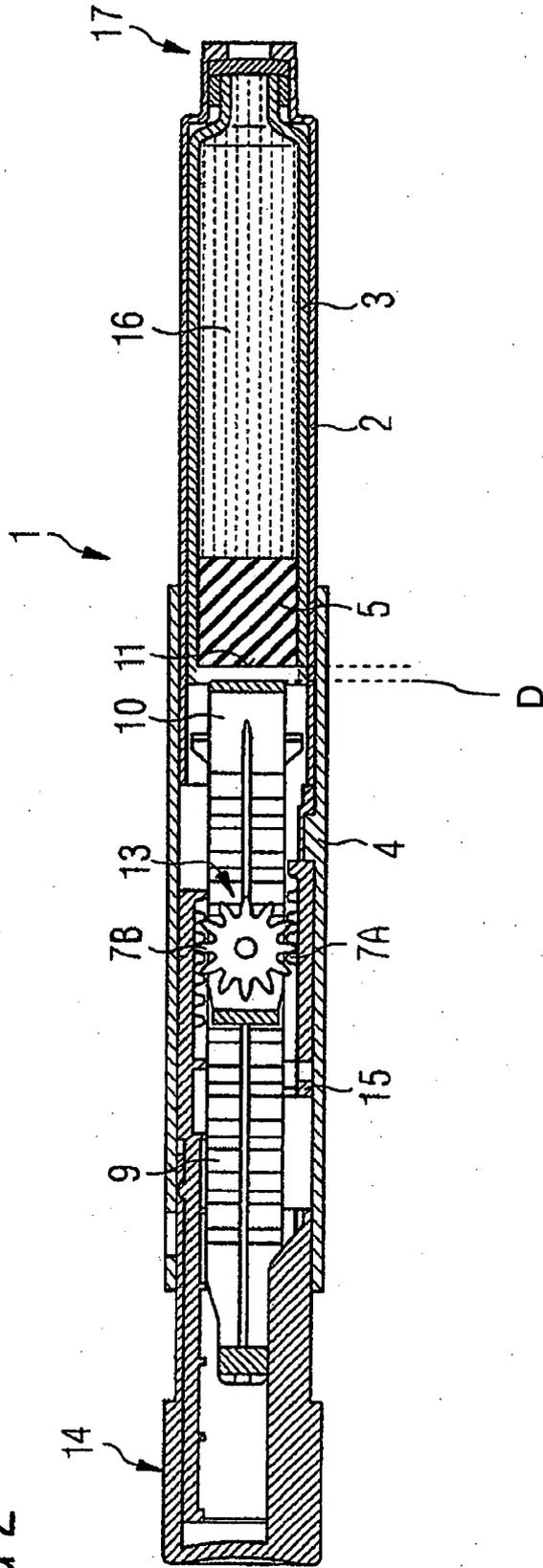
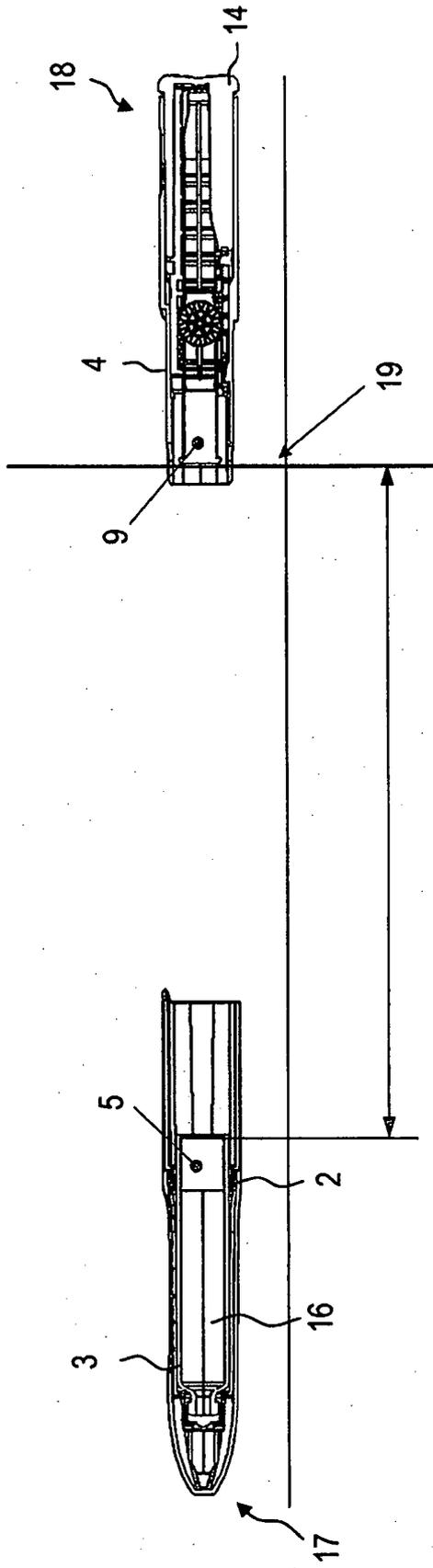
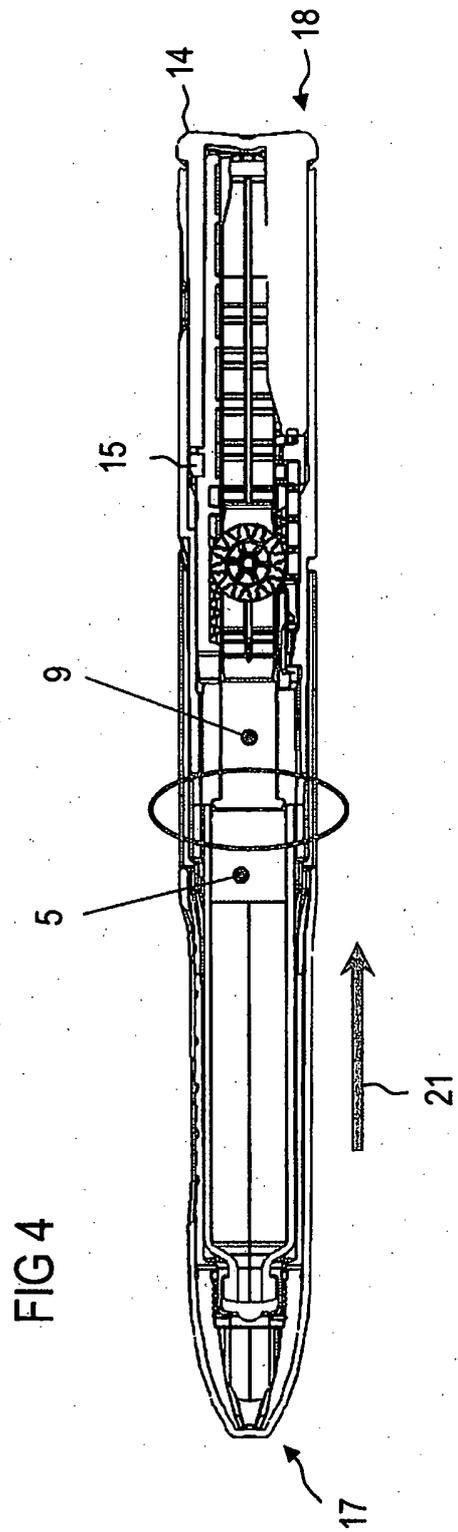
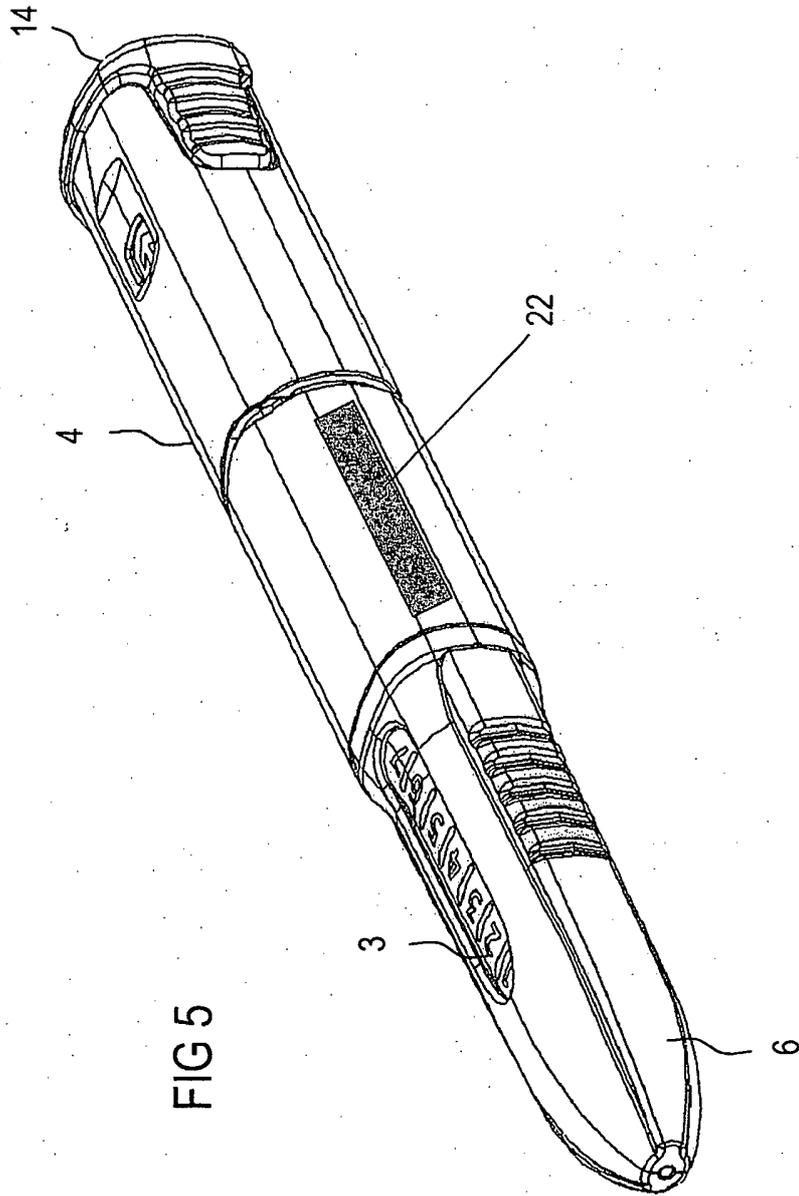
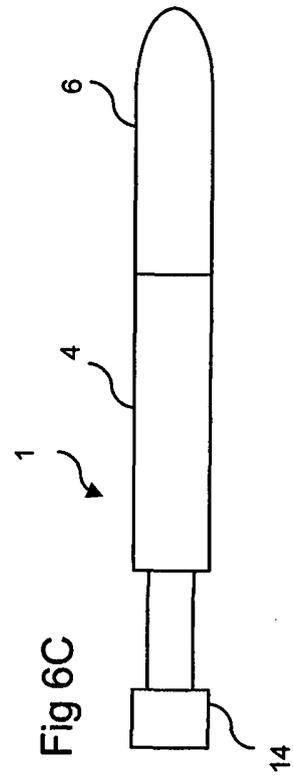
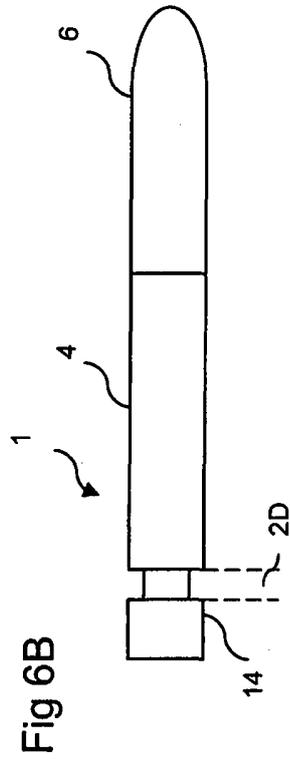
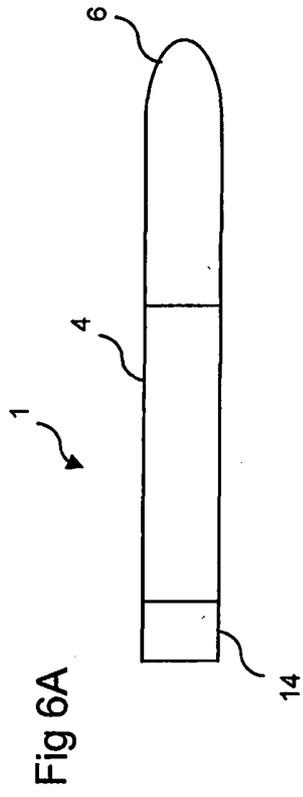


FIG 3









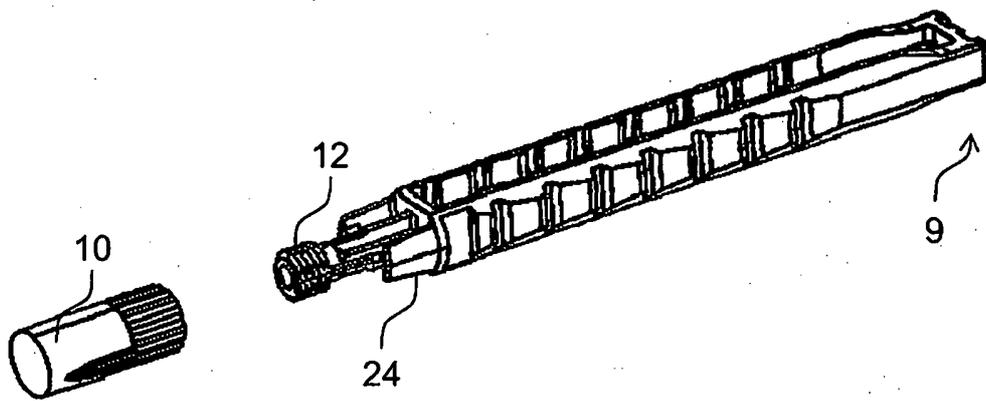


Fig. 7A

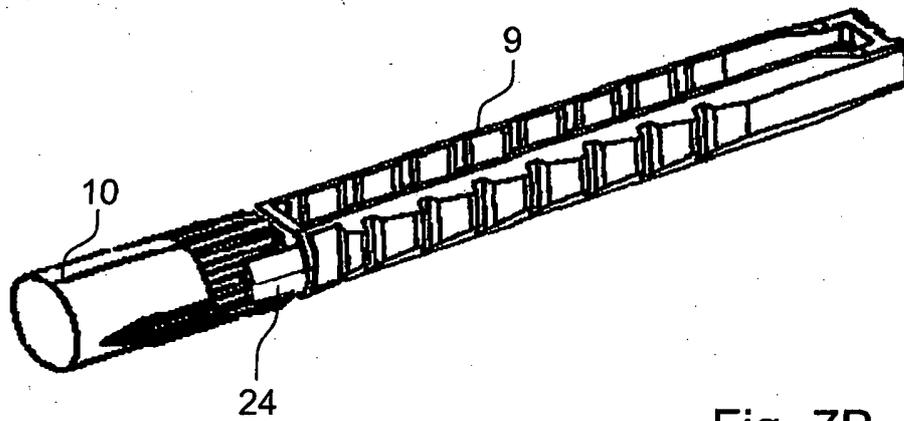


Fig. 7B

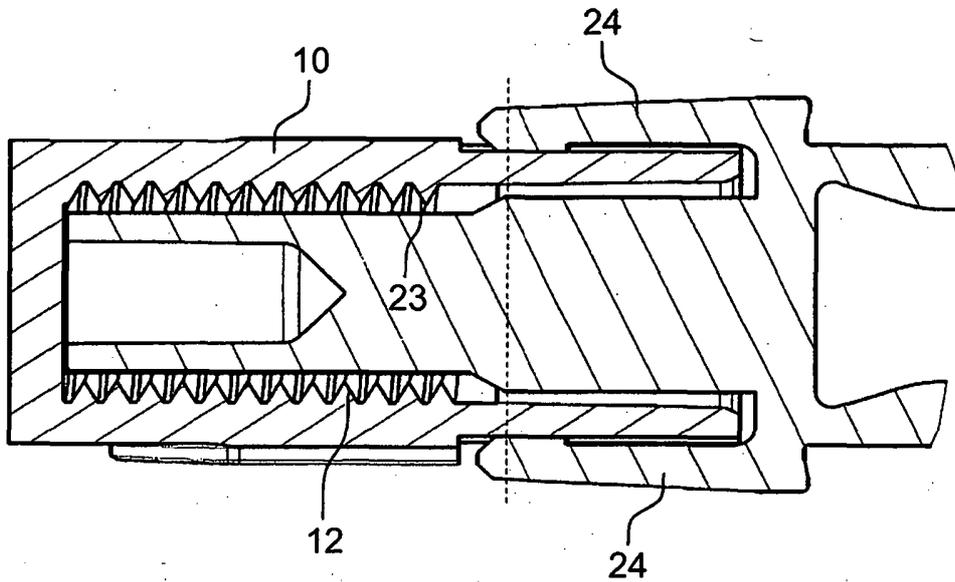


Fig. 7C

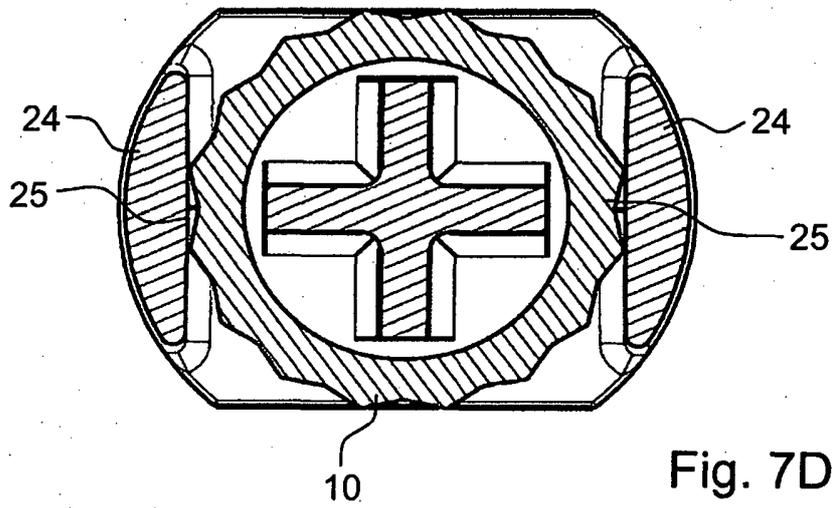


Fig. 7D

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- WO 2008058666 A1 [0003] [0045] [0074]
- WO 2011051365 A2 [0005]
- WO 2010063707 A1 [0004]

Non-patent literature cited in the description

- Remington's Pharmaceutical Sciences. Mark Publishing Company, 1985 [0041]
- Encyclopedia of Pharmaceutical Technology [0041]

GYÓGYSZERADAGOLÓ ESZKÖZ

SZABADALMI IGÉNYPONTOK

1. Gyógyszeradagoló eszköz (1), amely tartalmaz:
 - disztális véggel és proximális véggel rendelkező ház (4),
 - legalább egy gyógyszeradag (16) tárolására alkalmasan elrendezett betétet (3), egy dugó (5) elmozdíthatóan van elrendezve a betéten (3) belül, ahol az eszköz (1) kezdeti állapotában a dugó (5) a betét (3) képest proximálisvég-helyzetben van elrendezve,
 - a dugónak (5) a betét (3) képest disztális irányban történő elmozdítására alkalmasan elrendezett dugattyúrúd (9) a gyógyszeradag (16) beadagolására,ahol az eszköz (1) olyan szerkezetet tartalmaz, amely oly módon működtethető, hogy egy adag-adagoló művelet befejeztével a dugattyúrúd (9) a dugóhoz (5) képest proximális irányban egy utánengedő távolságnival (D) (back-off distance) van elmozdítva,
azzal jellemezve, hogy
a kezdeti állapotban a dugattyúrúd (9) disztális vége és a dugó (5) proximális vége közötti távolság nullánál nagyobb, úgy, hogy a dugattyúrúd (9) és a dugó (5) közötti távolságot a kezdeti állapotban az utánengedő távolság (D) határozza meg.
2. Az 1. igénypont szerinti eszköz, amely tartalmaz továbbá egy, a házhoz (4) képest elmozdítható működtető tagot (14), amely egy első helyzet és egy második helyzet között elmozdítható, ahol a működtető tag (14) mozgása az első helyzetből a második helyzetbe való áthelyezése érdekében átadódik a dugattyúrúdra (9) a dugattyúrúd (9) utánengedő távolságnival (D) történő áthelyezésére.
3. Az 1. vagy 2. igénypont szerinti eszköz, amelyben az utánengedő távolság (D) nagyobb vagy egyenlő a dugattyúrúd (9) disztális vége és a dugó (5) proximális vége közötti távolsággal a kezdeti állapotban.
4. A 2. vagy 3. igénypont szerinti eszköz, amelyben a működtető tag (14) továbbá elmozdítható a második helyzet és egy harmadik helyzet között, amelybe a működtető tag (14) egy adagbeállító művelet befejeztével van behelyezve, ahol a harmadik helyzet a második helyzetnél a házhoz (4) képest közelebb van elrendezve.
5. A 2-5. igénypontok bármelyike szerinti eszköz, amely a ház (4) belül beszerelt olyan rugós tagot (15) tartalmaz, amely a működtető tagon (14) erő kifejtésére alkalmasan van elrendezve a működtető tagnak (14) az első helyzetből a második helyzetbe mozgatására, ezáltal a dugattyúrúd (9) utánengedő távolságnival (D) való proximális mozgatására.
6. Az 5. igénypont szerinti eszköz, amelyben az utánengedő távolság (D) 0,1-1,0 mm között van.
7. Az 5. vagy 6. igénypont szerinti eszköz, amelyben az utánengedő távolság (D) kisebb, mint az a távolság, amellyel a dugattyúrúd (9) disztálisan el van mozdítva az adagkiadagolási művelet során.
8. Az előző igénypontok bármelyike szerinti eszköz, amelyben a dugattyúrúd (9) úgy van kialakítva, hogy a dugattyúrúd (9) tengelyirányú mérete változtatható.
9. Eljárás gyógyszeradagoló eszköz (1) összeállítására, amely eljárás a következő lépéseket tartalmazza:
 - A) előkészítünk egy betétegyeséget, amely legalább egy gyógyszeradagot (16) tartó betétet (3) tartalmaz, ahol egy dugó (5) elmozdíthatóan van elrendezve a betéten (3) belül,

- B) előkészítünk egy, a betétegységhez csatlakoztatható olyan meghajtó egységet, amely egy dugattyúrúdat (9), valamint egy olyan szerkezetet tartalmaz, amely a szerkezet aktivált állapotából az inaktívált állapotába kapcsolásakor a dugattyúrúdat (9) egy utánengedő távolságyival (D) (back-off distance) elmozdítóan van kialsakítva,
 - C) aktiváljuk a szerkezetet,
azzal jellemezve, hogy a következő lépéseket hajtjuk végre:
 - D) megmérjük a dugó (5) proximális végének helyzetét egy, a betétegységen előre meghatározott referenciaponthoz viszonyítva,
 - E) megmérjük a dugattyúrúd (9) disztális végének helyzetét egy, a meghajtó egységen előre meghatározott referenciaponthoz viszonyítva,
 - F) a D) és az E) lépés során végrehajtott mérések eredményeiből információkat nyerünk ki a dugattyúrúd (9) disztális végének és a dugó (5) proximális végének a betéttartó és a ház csatlakoztatott állapotában lévő viszonylagos helyzetére vonatkozóan,
 - G) inaktíváljuk a szerkezetet annak érdekében, hogy a dugattyúrúdat (9) az utánengedő távolságyival (D) áthelyezzük,
 - H) csatlakoztatjuk a betétegységet és a meghajtó egységet oly módon, hogy a dugattyúrúd (9) és a dugó (5) egymástól egy kezdeti távolságra legyenek elrendezve a szerkezet inaktíválása során.
10. A 9. igénypont szerinti eljárás, amelyben az információk kinyerése során a mérési eredmények alapján meghatározunk egy csatlakozási helyzetet a betétegység és a meghajtó egység csatlakoztatásához oly módon, hogy amennyiben az egységeket a csatlakozási helyzetben történő csatlakozás révén csatlakoztatjuk, a szerkezet inaktíválásakor a dugattyúrúdat (9) és a dugót (5) egymáshoz képest a kezdeti távolságra rendezzük el.
11. A 10. igénypont szerinti eljárás, amelyben a csatlakoztatást hegesztéssel hajtjuk végre.
12. A 9. igénypont szerinti eljárás, amelyben az információk kinyerése során a mérési eredmények alapján meghatározzuk a dugó (5) proximális végének, valamint a dugattyúrúd (9) disztális végének viszonylagos helyzetét, úgy mintha a betétegység és a meghajtó egység csatlakoztatva volna egy, a betétegységen és a meghajtó egységen felszerelt csatlakozató eszközzel.
13. A 12. igénypont szerinti eljárás, amely tartalmaz még egy olyan lépést, amelyben ellenőrizzük, hogy a dugó (5) proximális végének és a dugattyúrúd (9) disztális végének a viszonylagos helyzete megfelel-e a dugó (5) proximális vége és a dugattyúrúd (9) disztális vége egy előre meghatározott viszonylagos helyzetének.
14. A 13. igénypont szerinti eljárás, amelyben amennyiben a viszonylagos helyzet nem felel meg az előre meghatározott viszonylagos helyzetnek, módosítjuk a dugattyúrúd (9) tengelyirányú méretét annak érdekében, hogy a viszonylagos helyzet megfeleljen az előre meghatározott viszonylagos helyzetnek.
15. A 13. vagy 14. igénypont szerinti eljárás, amelyben az előre meghatározott viszonylagos helyzetet úgy választjuk meg, hogy a dugó (5) proximális vége és a dugattyúrúd (9) disztális vége közötti kezdeti távolság egyezzen meg vagy kissé nagyobb legyen nullánál az eszköz (1) összeállítását és a szerkezet aktiválását követően.