

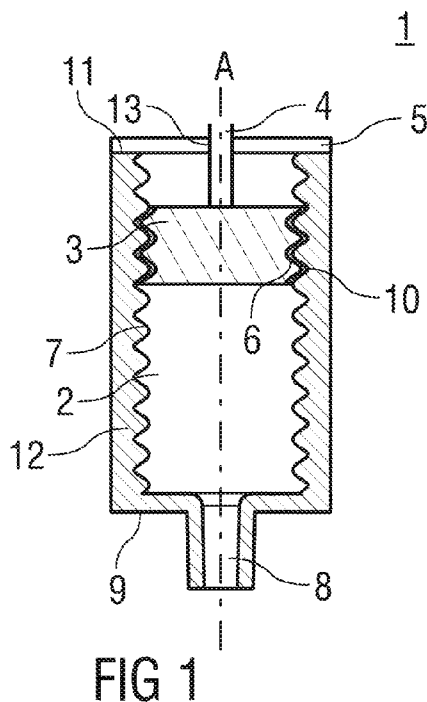


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[Continued on next page]

(54) **Title:** INJECTOR DEVICE



(57) **Abstract:** The invention relates to an injection device (1) with a compartment (2) for a substance to be dispensed by means of the injection device (1) and a stopper (3) sealing the compartment (2). The stopper (3) comprises a first thread (6) which cooperates with a complementary second thread (7) of another component (2, 4) of the injection device (1), such that the stopper (3) moves along a longitudinal axis (A) of the injection device (1) when the first thread (6) and the second thread (7) are rotated relatively to one another and thereby urges a substance contained in the compartment (2) to be dispensed.

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## INJECTOR DEVICE

### FIELD OF THE INVENTION

5 The present invention relates to an injection device with a compartment for a substance to be dispensed by means of the injection device and a stopper sealing the compartment. The substance to be dispensed may be a drug or a medicament.

### BACKGROUND OF THE INVENTION

10

Injection devices of this type are well known in the art. DE 10 2007 047 346 A1 discloses a syringe comprising a piston and a cylinder movable against each other in a direction of an axis of the syringe by the operation of an outer rotatable thread casing.

15

US 6004297 discloses an injection syringe for apportioning set doses of a medicine from a cartridge containing an amount of medicine sufficient for the preparation of a number of therapeutic doses. The injection syringe comprises a housing; a piston rod having a not circular cross-section and an outer thread, and a piston rod drive. The piston rod drive comprises a piston rod guide mating the not circular cross-section of  
20 the piston rod to allow axially displacement but not rotation of the piston rod in relation to said piston rod guide, and a nut member which is not axially displaceable in the housing and which has an inner thread mating the thread of the piston rod to form a self locking thread connection.

25

EP 2 050 477 A1 discloses an injection device with a compartment for a substance to be dispensed by means of the injection device and a stopper sealing the compartment. A piston rod comprises a first thread which cooperates with a complementary second thread of another component of the injection device, such that the stopper moves along a longitudinal axis of the injection device when the first thread and the  
30 second thread are rotated relatively to one another and thereby urges a substance contained in the compartment to be dispensed.

- 2 -

US 5 618 273 A discloses an injection device with a compartment for a substance to be dispensed by means of the injection device and a stopper sealing the compartment. A piston rod comprises a first thread which cooperates with a complementary  
5 second thread of another component of the injection device, such that the stopper moves along a longitudinal axis of the injection device when the first thread and the second thread are rotated relatively to one another and thereby urges a substance contained in the compartment to be dispensed.

10 EP 1 754 498 A1 discloses a drive arrangement for advancing a stopper in an ampoule. The drive arrangement comprises an advancing element composed of single members, who are consecutively inserted into the ampoule through a diverting area. The members may be threaded.

15 EP 1 974 760 A1 discloses an injection device with a compartment for a substance to be dispensed by means of the injection device and a stopper sealing the compartment. The stopper comprises a first thread which cooperates with a complementary  
20 second thread of another component of the injection device, such that the stopper moves along a longitudinal axis of the injection device when the first thread and the second thread are rotated relatively to one another and thereby urges a substance contained in the compartment to be dispensed. The Stopper has an essentially cylindrical opening and the first thread is an internal thread on the surface of the opening.  
US 3 082 914 A and US 2 349 726 A disclose similar injection devices.

## 25 SUMMARY OF THE INVENTION

It is an object of the present invention to provide an injection device according to the preamble of claim 1 which reduces slip-stick tendency and improves dose accuracy.

30 The object is achieved by an injection device according to claim 1.

Preferred embodiments of the invention are given in the dependent claims.

According to the present invention there is provided an injection device with a compartment for a substance to be dispensed, for example a drug or a medicament, by means of the injection device and a stopper sealing the compartment. The stopper comprises a first thread which cooperates with a complementary second thread of another component of the injection device, such that the stopper moves along a longitudinal axis of the injection device when the first thread and the second thread are rotated relatively to one another and thereby urges a substance contained in the compartment to be dispensed.

The cooperation of the first and the second thread thus allows the stopper to be moved along the longitudinal axis by rotating these threads relative to one another in order to dispense the substance. This has several advantages as compared to standard translational movement of a stopper.

A first advantage is that the amount of the substance to be dispensed can be very accurately dosed as a function of the angle of the relative rotation of the threads.

A second advantage is that the effects of an accidental release of the injection device causing dispensing of substance are reduced, since large translational motions of the stopper are much easier caused by forces acting directly in the direction of the translation than indirectly via a relative rotation of the two threads.

An important third advantage of moving the stopper translationally by relative rotation of the two threads is that it avoids, or at least substantially reduces, a so-called stick-slip-effect caused by the friction between an outer surface of the stopper and an inner surface of a wall of the compartment for the substance. Typically, the static friction between these two surfaces exceeds the kinetic friction. If an applied force is large enough to overcome the static friction, then the reduction of the friction to the kinetic friction can cause a sudden jump in the relative motion of the stopper and the wall of

the compartment. This effect will usually increase with increasing storage period of the injection device, during which the stopper is not moved relatively to the walls of the compartment, since the stopper often almost glues at the wall of the compartment after some time. This stick-slip-effect applies usually to any relative motion of the stopper  
5 relative to the compartment wall. However, a sudden jump in this relative motion will dispense a smaller amount of the substance when it is a jump in a relative rotational motion of the two threads as compared to a sudden jump in a direct translational motion of the stopper along the longitudinal axis of the injection device. Therefore, a translational motion of the stopper caused by a relative rotational motion of the two  
10 threads can efficiently reduce undesirable stick-slip-effects.

A fourth advantage is that by moving the stopper translationally by relative rotation of the two threads, the stopper is less exposed to forces tending to compress it in the direction of the translational motion than by exerting to it a force directly in the translational direction. This reduces the compression of the stopper in the direction of its  
15 translational motion and the danger of its subsequent expansion during its translational motion which can influence the dose of the substance to be dispensed by the injection device in an undesirable and uncontrollable manner. In particular this further improves the dose accuracy of the injection device. Furthermore, the undesirable  
20 stick-slip-effect is reduced.

Preferentially at least one of the two threads is coated with a deformable coating sealing a contact area of the first thread and the second thread to prevent the substance from pervading the contact area.  
25

A deformable coating of one of the threads provides an efficient and simple means to prevent the substance from pervading the contact area since the contact pressure between cooperating pitches of the two threads will deform the coating so that it seals the contact area of the threads.  
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- 5 -

According to the invention, the stopper has an essentially cylindrical outer surface whose cylinder axis lies on the longitudinal axis of the injection device and the first thread is an external thread on this outer surface.

- 5 Accordingly, the compartment for the substance has a cylindrical inner surface corresponding to the outer surface of the stopper and the second thread is a structure on the inner surface of the compartment for the substance.

10 The corresponding cylindrical shapes of the outer surface of the stopper and the inner surface of the compartment with cooperating threads allow advantageously a rotation of these threads relative to one another causing a translational motion of the stopper along the longitudinal axis of the injection device.

15 In combination with an above-mentioned deformable coating, the injection device according to the invention allows one to make the stopper out of a comparatively firm material since the stopper itself need not be elastic in order to seal the compartment, as the contact area of the thread is sealed by the deformable coating. The use of a firm stopper has the advantage that the stopper is less compressed by the internal pressure in the compartment which improves the dose accuracy, as explained  
20 above.

The stopper is preferentially firmly connected in a force-fitting and/or form-fitting and/or integrally joined manner to a rod member which extends from the stopper along the longitudinal axis of the injection device.

25 A firm connection of the stopper to a rod member which extends from the stopper along the longitudinal axis of the injection device has the advantage that the stopper can be rotated around the longitudinal axis of the injection device by rotating the rod member around its longitudinal axis.

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In a non-inventive second-embodiment the stopper has an essentially cylindrical opening and the first thread is an internal thread on the surface of the opening.

5 Furthermore, in the second embodiment the stopper is preferentially coupled to a rod member which extends along the longitudinal axis of the injection device and has a cylindrical section corresponding to the opening in the stopper and the second thread is an external thread on this section.

10 The corresponding cylindrical shapes of the opening in the stopper and the section of the rod element with cooperating threads allow advantageously a rotation of these threads relative to one another causing a translational motion of the stopper along the longitudinal axis of the injection device. Hence, in contrast to the first embodiment, the stopper rotates relative to the rod member, without necessarily rotating relative to the compartment for the substance. Therefore, in this embodiment the outer surface of the  
15 stopper and the inner surface of the compartment wall need not be of cylindrical shape. In fact, they may have, for instance, rectangular cross sections in a plane orthogonal to the longitudinal axis of the injection device. This may be advantageous for uses of the injection device where a non-cylindrical shape of the injection device is better suited than a cylindrical shape. For instance, when a medical syringe is used  
20 within the injection device, the syringe normally needs to be prevented from rotating within the injection device and that can be easily achieved when the injection device has a rectangular cross section.

25 In the second embodiment, the injection device preferentially comprises fixing means preventing the rod member to move along the longitudinal axis of the injection device.

Such fixing means thus fix the position of the rod member relative to the compartment for the substance. This has the advantage that the translational motion of the stopper is controlled solely by the rotation of the rod member around its longitudinal axis, and  
30 not additionally by the translational motions of the rod member.



In both embodiments the injection device comprises preferentially bearing means constraining the position of the rod member to the longitudinal axis of the injection device and allowing the rod member to rotate around the longitudinal axis of the injection device.

5

Such bearing means advantageously stabilize the position of the rod member and thus facilitate and improve the use of the injection device. Furthermore they prevent misuse of the injection device caused by tilting the rod member relative to the longitudinal axis of the injection device which may damage the injection device.

10

In both embodiments the injection device comprises preferentially stopping means preventing the stopper from leaving the compartment for the substance.

Such stopping means prevent advantageously the substance from leaking accidentally from the compartment by restraining the stopper from leaving the compartment.

15

An injection device according to the invention is particularly suited to be used in a pen injector.

## 20 BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will become more fully understood from the detailed description given hereinbelow and the accompanying drawings which are given by way of illustration only, and thus, are not limitative of the present invention. These and other objects, features, aspects, and advantages of the present invention will become more apparent from the following detailed description of preferred embodiments and accompanying drawings, in which

25

Fig. 1 illustrates schematically a longitudinal section of a first embodiment of an injector comprising a stopper with an external thread, and

30

Fig. 2 illustrates schematically a longitudinal section of a non-inventive second embodiment of an injection device comprising a stopper with an internal thread.

## DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

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Figure 1 illustrates schematically a longitudinal section of a first embodiment of an injection device 1 according to the invention. The injection device 1 comprises a compartment 2 for a substance to be dispensed, for example a drug or a medicament, by means of the injection device 1, a stopper 3 sealing the compartment 2, a rod member 4 firmly connected to the stopper 3, and a closure head 5.

10

The stopper 3 is of cylindrical shape and comprises a first thread 6 formed as an external thread on its outer surface. The cylinder axis of the stopper 3 lies on a longitudinal axis A of the injection device 1.

15

The compartment 2 is also of cylindrical shape and has an inner cylinder diameter that corresponds to the cylinder diameter of the stopper 3. The compartment 2 has a second thread 7 on its inner surface. The second thread 7 corresponds to the first thread 6 on the outer surface of the stopper 3 and cooperates with the latter so that the stopper 3 moves along the longitudinal axis A when it is rotated around the longitudinal axis A.

20

The compartment 2 comprises a conical nozzle 8 through which a substance contained in the compartment 2 can be dispensed and which extends from a central area of a bottom surface 9 of the compartment 2.

25

The first thread 6 is coated with a deformable coating 10 sealing a contact area of the first thread 6 and the second thread 7 to prevent a substance contained in the compartment 2 from pervading the contact area.

30

The rod member 4 extends from the stopper 3 along the longitudinal axis A out of the compartment 2 so that it can be used to rotate the stopper 3 from the outside of the compartment 2 by rotating the rod member 4 around its longitudinal axis.

5 The closure head 5 closes the compartment 2 at a top side and is firmly connected to a top edge 11 of a side wall 12 of the compartment 2. It comprises a recess 13 for the rod member 4 which extends through this recess 13. The closure head 5 serves as stopping means preventing the stopper 3 from leaving the compartment 2 and the recess 13 serves as bearing means constraining the position of the rod member 4 to the  
10 longitudinal axis A and allowing the rod member 4 to rotate around the longitudinal axis A.

Figure 2 illustrates schematically a longitudinal section of a non-inventive second embodiment of an injection device 1 according to the invention. The injection device 1  
15 comprises a compartment 2 for a substance to be dispensed by means of the injection device 1, a stopper 3 sealing the compartment 2, a rod member 4 coupled to the stopper 3, and a closure head 5.

The compartment 2 is of cylindrical shape and has a flat inner surface. As in the first  
20 embodiment it comprises a conical nozzle 8 through which a substance contained in the compartment 2 can be dispensed and which extends from a bottom surface 9 of the compartment 2. However, the nozzle 8 now does not extend from a central area of the bottom surface 9 but from an area closer to a circumference of the bottom surface 9.

25 The stopper 3 is also of cylindrical shape with a cylinder diameter that corresponds to the inner cylinder diameter of the compartment 2. The stopper 3 features a cylindrical opening 14 in a central area around a longitudinal axis A of the injection device 1 and a first thread 6 which is formed as an internal thread on the surface of the opening 14.  
30 The cylindrical outer surface of the stopper 3 is flat and made out of an elastic material which contacts the inner surface of the compartment 2, thereby retaining a sub-

stance contained in the compartment 2 to pervade a contact area of the stopper 3 and the inner surface of the compartment 2.

5 The closure head 5 is formed and located as in the first embodiment illustrated in figure 1. In particular it features a recess 13 for the rod member 4.

10 The rod member 4 is of cylindrical shape with a cylinder diameter corresponding to the cylinder diameter of the opening 14 in the stopper 3. It comprises a second thread 7 which is formed as an external thread on its surface. The second thread 7 corresponds to the first thread 6 on the surface of the opening 14 in the stopper 3 and cooperates with the first thread 6 so that the stopper 3 moves along the longitudinal axis A when the rod member 4 is rotated around the longitudinal axis A.

15 The first thread 6 is coated with a deformable coating 10 sealing a contact area of the first thread 6 and the second thread 7 to prevent a substance contained in the compartment 2 from pervading this contact area.

20 The rod member 4 extends from a cavity 15 in a bottom wall 16 through the opening 14 in the stopper 3 and through the recess 13 in the closure head 5 out of the compartment 2.

25 The cavity 15 is ball-shaped with a maximal cross-section in the interior of the bottom wall 16. It mounts an end piece 17 of the rod member 4 of corresponding shape and size so that the end piece 17 can rotate around the longitudinal axis A but cannot leave the cavity 15. The cavity 15 thus serves both as fixing means preventing the rod member 4 to move along the longitudinal axis A of the injection device 1 and, in cooperation with the recess 13 in the closure head 5 and the opening 14 in the stopper 3, as bearing means constraining the position of the rod member 4 to the longitudinal axis A and allowing the rod member 4 to rotate around the longitudinal axis A.

30

In both embodiments illustrated in figures 1 and 2 the compartment 2 and the rod member 4 are made out of glass or plastics, e.g. as injection moulding parts, the stopper 3 and the closure head 5 are made out of plastics, e.g. as injection moulding parts.

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The term “drug or “medicament“, as used herein, means a pharmaceutical formulation containing at least one pharmaceutically active compound,

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

15

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,

20

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,

25

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 exedin-3 or exedin-4 or an analogue or derivative of exedin-3 or exedin-4.

30

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.

5

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

10

15

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

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

20

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

25

des Pro<sub>36</sub> [Met(O)<sub>14</sub>, Asp<sub>28</sub>] Exendin-4(1-39),  
 des Pro<sub>36</sub> [Met(O)<sub>14</sub>, IsoAsp<sub>28</sub>] Exendin-4(1-39),  
 des Pro<sub>36</sub> [Trp(O<sub>2</sub>)<sub>25</sub>, Asp<sub>28</sub>] Exendin-4(1-39),  
 des Pro<sub>36</sub> [Trp(O<sub>2</sub>)<sub>25</sub>, IsoAsp<sub>28</sub>] Exendin-4(1-39),  
 des Pro<sub>36</sub> [Met(O)<sub>14</sub> Trp(O<sub>2</sub>)<sub>25</sub>, Asp<sub>28</sub>] Exendin-4(1-39),

30

des Pro<sub>36</sub> [Met(O)<sub>14</sub> Trp(O<sub>2</sub>)<sub>25</sub>, IsoAsp<sub>28</sub>] Exendin-4(1-39); or

des Pro36 [Asp28] Exendin-4(1-39),  
 des Pro36 [IsoAsp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14, Asp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14, IsoAsp28] Exendin-4(1-39),  
 5 des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39),  
 des Pro36 [Trp(O2)25, IsoAsp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14 Trp(O2)25, Asp28] Exendin-4(1-39),  
 des Pro36 [Met(O)14 Trp(O2)25, IsoAsp28] Exendin-4(1-39),  
 wherein the group -Lys6-NH2 may be bound to the C-terminus of the Exendin-4 de-  
 10 rivative;

or an Exendin-4 derivative of the sequence

H-(Lys)6-des Pro36 [Asp28] Exendin-4(1-39)-Lys6-NH2,

des Asp28 Pro36, Pro37, Pro38 Exendin-4(1-39)-NH2,

15 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,

20 H-(Lys)6-des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39)-Lys6-NH2,

H-des Asp28 Pro36, Pro37, Pro38 [Trp(O2)25] Exendin-4(1-39)-NH2,

H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-NH2,

H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-NH2,

des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,

25 H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,

H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-  
 NH2,

H-(Lys)6-des Pro36 [Met(O)14, Asp28] Exendin-4(1-39)-Lys6-NH2,

des Met(O)14 Asp28 Pro36, Pro37, Pro38 Exendin-4(1-39)-NH2,

30 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(O)14, Asp28] Exendin-4(1-39)-NH2,

des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH<sub>2</sub>,  
H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH<sub>2</sub>,  
H-Asn-(Glu)5 des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-  
NH<sub>2</sub>,

5 H-Lys6-des Pro36 [Met(O)14, Trp(O<sub>2</sub>)<sub>25</sub>, Asp28] Exendin-4(1-39)-Lys6-NH<sub>2</sub>,  
H-des Asp28 Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)<sub>25</sub>] Exendin-4(1-39)-NH<sub>2</sub>,  
H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH<sub>2</sub>,  
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)<sub>25</sub>, Asp28] Exendin-4(1-  
39)-NH<sub>2</sub>,

10 des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)<sub>25</sub>, Asp28] Exendin-4(1-39)-(Lys)6-NH<sub>2</sub>,  
H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)<sub>25</sub>, Asp28] Exendin-4(S1-39)-  
(Lys)6-NH<sub>2</sub>,  
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O<sub>2</sub>)<sub>25</sub>, Asp28] Exendin-4(1-  
39)-(Lys)6-NH<sub>2</sub>;

15

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

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

25 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 polysac-  
charides, and/or a pharmaceutically acceptable salt thereof. An example of a pharma-  
30 ceutically acceptable salt of a poly-sulphated low molecular weight heparin is enoxa-  
parin sodium.



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

Pharmaceutically acceptable solvates are for example hydrates.

## LIST OF REFERENCES

	1	injection device
	2	compartment
5	3	stopper
	4	rod member
	5	closure head
	6	first thread
	7	second thread
10	8	conical nozzle
	9	bottom surface
	10	coating
	11	top edge
	12	side wall
15	13	recess
	14	opening
	15	cavity
	16	bottom wall
	17	end piece
20	A	longitudinal axis

## CLAIMS

- 5 1. Injection device (1) with a compartment (2) for a substance to be dispensed by means of the injection device (1) and a stopper (3) sealing the compartment (2), the stopper (3) comprising a first thread (6) which cooperates with a complementary second thread (7) of another component (2, 4) of the injection device (1), such that the stopper (3) moves along a longitudinal axis (A) of the injection device (1) when the first thread (6) and the second thread (7) are rotated relatively to one another and thereby urges a substance contained in the compartment (2) to be dispensed, wherein the stopper (3) has an essentially cylindrical outer surface whose cylinder axis lies on the longitudinal axis (A) of the injection device (1), wherein the compartment (2) has a cylindrical inner surface corresponding to the outer surface of the stopper (3),
- 10 characterized in that the first thread (6) is an external thread on the outer surface of the stopper (3) and that the second thread (7) is a structure on the inner surface of the compartment (2).
- 15
- 20 2. Injection device (1) according to claim 1, characterized in that the first thread (6) is coated with a deformable coating (10) sealing a contact area of the first thread (6) and the second thread (7) to prevent the substance from pervading the contact area.
- 25 3. Injection device (1) according to claim 1 or 2, characterized in that the second thread (7) is coated with a deformable coating (10) sealing a contact area of the first thread (6) and the second thread (7) to prevent the substance from pervading the contact area.
- 30 4. Injection device (1) according to one of the claims 1 to 3, characterized in that the stopper (3) is firmly connected in a force-fitting and/or

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form-fitting and/or integrally joined manner to a rod member (4) which extends from the stopper (3) along the longitudinal axis (A).

5. Injection device (1) according to claim 4,  
5 characterized by bearing (13, 14, 15) means constraining the position of the rod member (4) to the longitudinal axis (A) of the injection device (1) and allowing the rod member (4) to rotate around the longitudinal axis (A) of the injection device (1).
- 10 6. Injection device (1) according to any one of the preceding claims, characterized by stopping means (5) preventing the stopper (3) from leaving the compartment (2).
- 15 7. Pen injector with an injection device (1) according to any one of the preceding claims.

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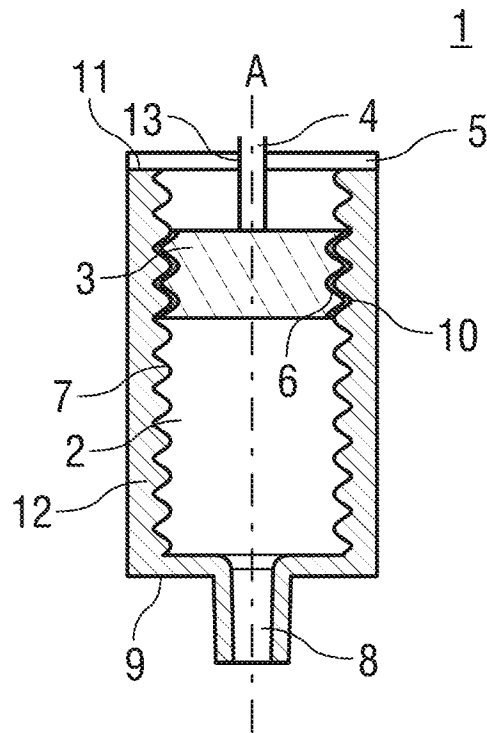


FIG 1

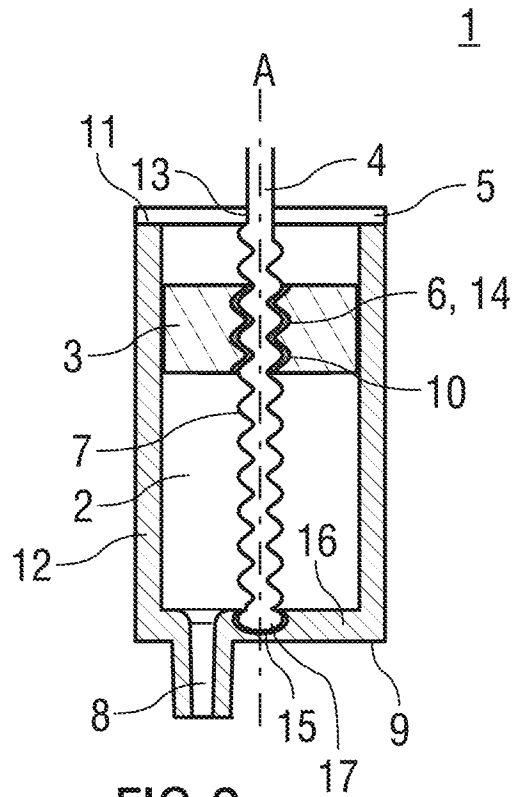


FIG 2

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2010/062151

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. . . A61M5/315      A61M5/31 ADD.:		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) <b>A61M</b>		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) <b>EPO-Internal</b>		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 2 050 477 A1 (HOFFMANN LA ROCHE [CH]; ROCHE DIAGNOSTICS GMBH [DE]) 22 April 2009 (2009-04-22) paragraph [0017]; figures	1-7
A	US 5 618 273 A (FISCHER DAVID V [US]) 8 April 1997 (1997-04-08) figures	1
X	EP 1 754 498 A1 (ROCHE DIAGNOSTICS GMBH [DE]; HOFFMANN LA ROCHE [CH]) 21 February 2007 (2007-02-21) paragraph [0038]; figures	2
X	US 2005/156981 A1 (SILVERBROOK KIA [AU] ET AL SILVERBROOK KIA [AU] ET AL) 21 July 2005 (2005-07-21) figure 104	1
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
* Special categories of cited documents :		
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family	
Date of the actual completion of the international search  <p style="text-align: center; font-weight: bold;">30 November 2010</p>	Date of mailing of the international search report  <p style="text-align: center; font-weight: bold;">06/12/2010</p>	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  <p style="text-align: center; font-weight: bold;">Ehrsam, Fernand</p>	

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Information on patent family members

International application No

PCT/EP2010/062151

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