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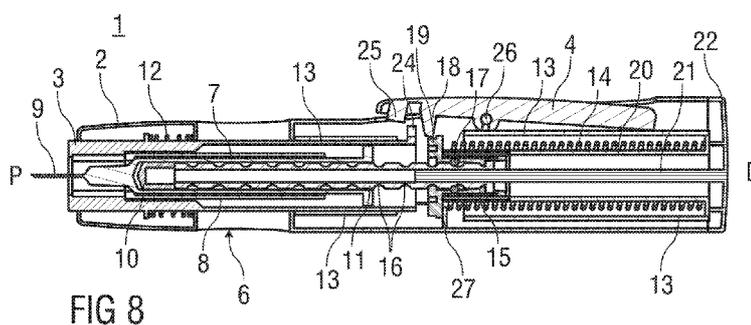
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(54) **Title:** AUTO-INJECTOR WITH A TORSION SPRING



(57) **Abstract:** The invention relates to an auto-injector (1) for administering a dose of a liquid medicament (M), comprising: - an elongate housing (2) arranged to contain a syringe (7) with a hollow needle (9) and a bung (10) for sealing the syringe (7) and displacing the medicament (M), the elongate housing (2) having a distal end (D) and a proximal end (P) with an orifice intended to be applied against an injection site, wherein the syringe (7) is slidably arranged with respect to the housing (2), - spring means (14) capable of, upon activation, pushing the needle (9) from a covered position inside the housing (2) into an advanced position through the orifice and past the proximal end (P) as well as operating the syringe (7) to supply the dose of medicament (M), - activating means (4) arranged to lock the spring means (14) in a pressurized state prior to manual operation and capable of, upon manual operation, releasing the spring means (14) for injection. The spring means (14) is a torsion spring (14) grounded at one end in the housing (2) and at the other end in a first gear member (15) rotatable about a longitudinal axis but axially fixed wherein the first gear member (15), upon rotation, is arranged for translatively moving a second gear member (11), the second gear member (11) prevented from rotating and coupled to the bung (10) in order to push it towards the proximal end (P), wherein the first gear member (15) is engaged with the activating means (4) prior to manual operation in a manner to prevent rotation and disengaged from the activating means (4) upon manual operation.



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AUTO-INJECTOR WITH A TORSION SPRING

Technical Field

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The invention relates to an auto-injector for administering a dose of a liquid medicament according to the preamble of claim 1.

Background of the Invention

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Administering an injection is a process which presents a number of risks and challenges for users and healthcare professionals, both mental and physical.

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Injection devices (i.e. devices capable of delivering medicaments from a medication container) typically fall into two categories - manual devices and auto-injectors.

20

In a manual device - the user must provide the mechanical energy to drive the fluid through the needle. This is typically done by some form of button / plunger that has to be continuously pressed by the user during the injection. There are numerous disadvantages to the user from this approach. If the user stops pressing the button / plunger then the injection will also stop. This means that the user can deliver an underdose if the device is not used properly (i.e. the plunger is not fully pressed to its end position). Injection forces may be too high for the user, in particular if the patient is elderly or has dexterity problems.

25

The extension of the button/plunger may be too great. Thus it can be inconvenient for the user to reach a fully extended button. The combination of injection force and button extension can cause trembling / shaking of the hand which in turn increases discomfort as the inserted needle moves.

30

Auto-injector devices aim to make self-administration of injected therapies easier for patients. Current therapies delivered by means of self-administered injections include drugs for diabetes (both insulin and newer GLP-1 class drugs), migraine, hormone therapies, anticoagulants etc.

Auto-injectors are devices which completely or partially replace activities involved in parenteral drug delivery from standard syringes. These activities may include removal of a protective syringe cap, insertion of a needle into a patient's skin, injection of the medicament, removal of the needle, shielding of the needle and preventing reuse of the device. This overcomes many of the disadvantages of manual devices. Injection forces / button extension, hand-shaking and the likelihood of delivering an incomplete dose are reduced. Triggering may be performed by numerous means, for example a trigger button or the action of the needle reaching its injection depth. In some devices the energy to deliver the fluid is provided by a spring.

US 2002/00951 20 A 1 discloses an automatic injection device which automatically injects a pre-measured quantity of fluid medicine when a tension spring is released. The tension spring moves an ampoule and the injection needle from a storage position to a deployed position when it is released. The content of the ampoule is thereafter expelled by the tension spring forcing a piston forward inside the ampoule. After the fluid medicine has been injected, torsion stored in the tension spring is released and the injection needle is automatically retracted back to its original storage position.

US 2006/287630 A 1 discloses an injection device including a torsion spring with a mid-axis and an output element with a longitudinal axis which can be displaced along its longitudinal axis by the torsion spring, the mid-axis of the torsion spring being generally parallel with the longitudinal axis of the output element.

WO 2009/037141 A 1 discloses an injection device comprising a housing, a container holder arranged within said housing having a container adapted to contain medicament to be delivered through a needle, plunger drive means, an energy accumulating member adapted to accumulate and transfer energy to said plunger drive means wherein said device further comprises container driver means arranged and designed to be connected to the plunger drive means and to the container holder for holding the container and its needle stationary within said housing before said energy is provided to the drive means and for urging the container towards the proximal end of the device

when said energy is provided to the drive means whereby a needle penetration and respectively an injection are performed.

5 WO 2009/098502 A2 discloses an autoinjector device comprising a drive housing and a syringe housing which can be disconnected to allow insertion of a syringe. A drive mechanism in the drive housing is cocked by means of a cord connected between the drive housing and the syringe housing. The drive mechanism comprises a drive gear rotatably mounted in the drive housing and acting as a rotary crank connected by a connecting rod to a plunger. In use the drive gear is driven by a torsion spring so that
10 the drive mechanism extends the syringe from the syringe housing and expels a dose and then retracts the syringe back into the housing. A firing button releases the drive gear to be driven by the torsion spring but is also engageable as a brake on the rim of the drive gear.

15 EP 1 728 529 A 1 discloses a device for the delivery of predetermined doses of liquid medicament to a patient, which medicament is intended to be inhaled by the patient or intended to be injected into the body of the patient. The device is adapted to be in a medicament delivery state and in a medicament non-delivery state. When the device is in a medicament delivery state, said device is adapted to drive a piston into a cartridge
20 containing the liquid medicament to be delivered, with a force that is above or equal to a predetermined minimum force value and below a predetermined maximum force value. The minimum force value is the lowest force value needed to deliver the predetermined dose and the maximum force value is the first force value at which it exists a risk of damaging the cartridge or the components of the device.

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Summary of the Invention

It is an object of the present invention to provide an improved auto-injector.

30 The object is achieved by an auto-injector according to claim 1.

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

An auto-injector for administering a dose of a liquid medicament according to the invention comprises:

- 5 - an elongate housing arranged to contain a syringe with a hollow needle and a bung for sealing the syringe and displacing the medicament, the elongate housing having a distal end and a proximal end with an orifice intended to be applied against an injection site, wherein the syringe is slidably arranged with respect to the housing,
- spring means capable of, upon activation, pushing the needle from a covered position inside the housing into an advanced position through the orifice and past the proximal 10 end as well as operating the syringe to supply the dose of medicament,
- activating means arranged to lock the spring means in a pressurized state prior to manual operation and capable of, upon manual operation, releasing the spring means for injection.

15 In the context of this patent application the term proximal refers to the direction pointing towards the patient during an injection while the term distal refers to the opposite direction pointing away from the patient.

According to the invention the spring means is a torsion spring grounded at one end in 20 the housing and at the other end in a first gear member rotatable about a longitudinal axis but axially fixed. The first gear member, upon rotation, is arranged for translatively moving a second gear member. The second gear member is prevented from rotating and coupled to the bung in order to push it towards the proximal end. The first gear member is engaged with the activating means prior to manual operation in a manner to 25 prevent rotation and disengaged from the activating means upon manual operation. The torsion spring is preferably loaded or wound during manufacturing of the auto-injector. When the torsion spring is released by operating the activating means the first gear member starts rotating.

30 The single torsion spring is used for both, inserting the needle and fully emptying the syringe. A major advantage of the torsion spring is that force is exerted on the bung and syringe in a smooth manner, whereas a conventional compression spring exhibits a

rather abrupt force deployment which may spoil a glass syringe or other parts of the auto-injector.

5 According to the invention an essentially tube-shaped needle shroud is arranged around the syringe in the housing. The needle shroud is slidable between at least a drawn back position with the needle shroud almost hidden inside the housing and an advanced position with the needle shroud protruding from the proximal end and covering the hollow needle in its advanced position. The needle shroud is biased by a second spring means towards the advanced position and locked in the drawn back position by a
10 locking means which is releasable by rotary movement transmitted from the first gear member through a clutch mechanism which is engaged by the second gear member shortly before the second gear member is fully advanced during an injection stroke. Hence, once the dose is complete, the second spring means returns the needle shroud over the needle. This makes the device safer than an equivalent manual injection with
15 respect to needlestick injuries.

In a particularly preferred embodiment an interlock mechanism is arranged for locking the activating means and preventing it from accidental operation. The interlock mechanism may be coupled to the needle shroud. The interlock mechanism may be
20 releasable by pushing the needle shroud a small distance into the housing from the needle shroud's retracted position. Thus, the device cannot be used until the needle shroud is depressed. In normal use this would occur by pushing the device against an injection site, i.e. a patient's skin.

25 The activating means may be a trigger button laterally arranged at the housing and operable by being pressed transversally with respect to the longitudinal axis. Conventional auto-injectors have the trigger button at their distal end. The advantage of having the trigger button on the side is that the user is less likely to incur an injury should they be confused as to which end the needle will appear from.

30

The trigger button may have a locking pin engageable with at least one dog tooth provided on the first gear member for preventing rotation thereof in order to lock the

spring means or keep it locked in a pressurized state. The dog teeth may be circumferentially arranged at the first gear member thus allowing for stopping the rotation and consequently the injection at any point in time by releasing the trigger button. The trigger button may therefore be biased by a return spring.

5

The shroud locking means may have the shape of a bayonet fit between the needle shroud and an outer rear tube, which is arranged around the torsion spring. The needle shroud is guided in the housing in a manner to prevent relative rotation, e.g. by at least one spline engaging a respective slot in the housing. The outer rear tube is coupled to the clutch mechanism and may therefore be rotated by the torsion spring. The bayonet fit comprises a bayonet pin and a corresponding pin track arranged between the outer rear tube and the needle shroud. The pin may be held behind a track shoulder in order to hold the needle shroud in its retracted position. In order to release the needle shroud the outer rear tube is rotated by a small angle thus turning the bayonet pin away from the track shoulder (or vice versa) and into a straight longitudinal part of the pin track so the compression spring may forward the needle shroud as soon as the auto-injector is removed from the injection site.

10

15

The second gear member may be a piston rod having an external lead screw thread. The piston rod may have an axial bore for slidably arranging the piston rod on a shaft attached to the housing. The axial bore and the shaft may have corresponding non-circular profiles in order to prevent relative rotation, e.g. square profiles or profiles with at least one spline or flat. The shaft may be directly or indirectly attached to the housing, e.g. by an end cap. However, the shaft has to be secured against rotation relative to the housing.

20

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The first gear member may be a lead nut engaged with the external lead screw thread of the second gear member. The lead nut may have an internal lead screw thread or a pin guided in the external lead screw thread of the piston rod. Preferably the lead nut is equipped with at least one ball bearing in order to achieve a low friction contact.

30

In one embodiment the external lead screw thread may have a variable pitch. Thus, speed and force of the needle insertion and injection of the medicament may be adapted to user convenience and to the fact that the torque of the torsion spring is highest when it is fully loaded and lowest near the end of the injection stroke. E.g. the pitch of the thread may be adapted to ensure a quick needle insertion and a relatively slow injection of the medicament in order to cause the least possible pain for the patient.

The interlock mechanism may comprise respective catches provided on the needle shroud and the trigger button. The catches may have the shape of hooks gearing into each other when the needle shroud is in an initial retracted position. As soon as the needle shroud is pushed in a small distance from the retracted position the hook shaped catches are laterally shifted out of engagement and the trigger button may be operated. In order to allow the needle shroud to be pushed back from the retracted position a small clearance may be provided in the pin track behind the track shoulder.

In a preferred embodiment the syringe is arranged in a syringe carrier and supported by the syringe carrier at a proximal end. Supporting the syringe at its proximal end rather than at its flanges avoids damaging the syringe under load since the flanges are more fragile, in particular in a glass syringe. The syringe carrier is slidably arranged in the needle shroud. An abutment is provided in the needle shroud defining a maximum forward position of the syringe carrier. This allows for defining an injection depth, e.g. for a subcutaneous or intramuscular injection.

The clutch mechanism for releasing the needle shroud towards the end of the injection may comprise a circumferential shoulder arranged on the second gear member, e.g. at its distal end, and at least one resilient clutch finger or a number of resilient clutch fingers with respective inclined inner surfaces arranged on a distal end of the first gear member. The shoulder is arranged for increasingly pressing against the inclined surfaces when forwarded thereby flexing the clutch fingers outward near the end of an injection stroke. The clutch mechanism further comprises an inner rear tube arranged around the clutch fingers inside the torsion spring and attached to the outer rear tube at

their distal ends. The inner rear tube has a number of internal longitudinal splines for engaging the flexed-out clutch fingers. Prior to being flexed out by the shoulder the first gear member, i.e. the lead nut and its clutch fingers spin without engaging the longitudinal splines of the inner rear tube. When the clutch fingers are flexed out radially they engage with the longitudinal splines in the inner rear tube. Thus the rotation of the first gear member is forwarded to the bayonet fit so the bayonet pin comes clear of the track shoulder and gets into the straight longitudinal part of the pin track thus allowing the needle shroud to slide forward when removed from the injection site. The clutch fingers may have respective external teeth protruding radially outwardly in order to provide a defined engagement with the longitudinal splines.

In a preferred embodiment the internal longitudinal splines are arranged in a manner to form a ratchet when engaged with the clutch fingers. This allows for continued rotation of the lead nut even after the outer rear tube has been rotated and consequently the bayonet pin has hit the side of the longitudinal part of the pin track so the bung may be further forwarded until it bottoms out in the syringe so dead volume is avoided. This is particularly advantageous as it ensures improved dose accuracy and no wastage of expensive medicaments as the syringe or cartridge is fully emptied. By contrast a purely positive locking engagement between the clutch fingers and the longitudinal splines would stall the rotary movement as soon as the bayonet pin hits the side of the longitudinal part of the pin track. Furthermore the ratchet style engagement provides an acoustic feedback for the user announcing the upcoming end of the injection. During this time, e.g. ten seconds the user is asked to keep pressure on the injection site.

As the user withdraws the auto-injector from the injection site after the end of injection the needle shroud is pushed over the needle by the compression spring into its advanced position. A locking mechanism may be provided for locking the needle shroud in its advanced position so the needle cannot be re-exposed and needle stick injuries with the now contaminated needle are avoided.

The housing may have at least one viewing window for inspecting the syringe.

The auto-injector may preferably be used for subcutaneous or intra-muscular injection, particularly for delivering one of an analgetic, an anticoagulant, insulin, an insulin derivate, heparin, Lovenox, a vaccine, a growth hormone, a peptide hormone, a proteine, antibodies and complex carbohydrates.

5

The term „medicament", as used herein, means a pharmaceutical formulation containing at least one pharmaceutically active compound,

10 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,
20 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,

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

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-NH₂.

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

20 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 [Asp₂₈] Exendin-4(1-39),
 des Pro₃₆ [IsoAsp₂₈] Exendin-4(1-39),
 25 des Pro₃₆ [Met(O)₁₄, Asp₂₈] Exendin-4(1-39),
 des Pro₃₆ [Met(O)₁₄, IsoAsp₂₈] Exendin-4(1-39),
 des Pro₃₆ [Trp(O₂)₂₅, Asp₂₈] Exendin-4(1-39),
 des Pro₃₆ [Trp(O₂)₂₅, IsoAsp₂₈] Exendin-4(1-39),
 des Pro₃₆ [Met(O)₁₄ Trp(O₂)₂₅, Asp₂₈] Exendin-4(1-39),
 30 des Pro₃₆ [Met(O)₁₄ Trp(O₂)₂₅, IsoAsp₂₈] 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
 10 derivative;

or an Exendin-4 derivative of the sequence
 H-(Lys)6-des Pro36 [Asp28] Exendin-4(1 -39)-Lys6-NH2,
 des Asp28 Pro36, Pro37, Pro38Exendin-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-desPro36, Pro37, Pro38 [Met(O)1 4, 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-NH2,

H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
H-Asn-(Glu)5 des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
H-Lys6-des Pro36 [Met(O)14, Trp(O₂)25, Asp28] Exendin-4(1-39)-Lys6-NH₂,
H-des Asp28 Pro36, Pro37, Pro38 [Met(O)14, Trp(O₂)25] Exendin-4(1-39)-NH₂,
5 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, Trp(O₂)25, Asp28] Exendin-4(1-39)-
NH₂,
des Pro36, Pro37, Pro38 [Met(O)14, Trp(O₂)25, Asp28] Exendin-4(1-39)-(Lys)6-NH₂,
H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O₂)25, Asp28] Exendin-4(S1-39)-
10 (Lys)6-NH₂,
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O₂)25, Asp28] Exendin-4(1-39)-
(Lys)6-NH₂;

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

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

A polysaccharide is for example a glucosaminoglycane, a hyaluronic acid, a heparin, a
low molecular weight heparin or an ultra low molecular weight heparin or a derivative
25 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.

30 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 Ca²⁺, 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.

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Pharmaceutically acceptable solvates are for example hydrates.

Further scope of applicability of the present invention will become apparent from the detailed description given hereinafter. However, it should be understood that the detailed description and specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

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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 limitive of the present invention, and wherein:

25 Figure 1 is a perspective view of an auto-injector with a needle shroud and a lateral trigger button,

 Figure 2 is a longitudinal section of the auto-injector in a prior to use state,

30 Figure 3 is a perspective detail view of the longitudinal section of figure 2 with the needle shroud and the trigger button interlocked,

- Figure 4 is a perspective detail view with the trigger button released from the interlock by pressing the needle shroud against an injection site,
- Figure 5 is a perspective detail view with the trigger button pressed,
- 5 Figure 6 is a longitudinal section of the auto-injector with a syringe and an injection needle advanced in order to pierce a patient's skin,
- Figure 7 is a detail view of the longitudinal section of figure 6,
- 10 Figure 8 is a longitudinal section of the auto-injector with a piston rod advancing a bung in order to expel a liquid medicament from the syringe,
- Figure 9 is a detail view of figure 8 with a clutch mechanism,
- 15 Figure 10 shows perspective views of two alternative clutch mechanisms,
- Figure 11 is a perspective view of the auto-injector with a bayonet fit between the needle shroud and an outer rear tube, the needle shroud prevented
- 20 from moving forward,
- Figure 12 is a perspective view of the auto-injector with the bayonet fit, the outer rear tube rotated in order to allow the needle shroud to move forward,
- 25 Figure 13 is a perspective view of the auto-injector with the bayonet fit, the needle shroud pushed forward by means of a bias spring, and
- Figure 14 is a longitudinal section of the auto-injector with the needle shroud fully advanced and locked in forward position in order to protect the needle.
- 30

Corresponding parts are marked with the same reference symbols in all figures.

Detailed Description of Preferred Embodiments

Figure 1 shows a perspective view of an auto-injector 1 with an elongate housing 2 and a needle shroud 3 for protecting a needle (not shown). A lateral trigger button 4 may be transversally pressed in order to trigger an automatic injection. The trigger button 4 is interlocked with the needle shroud 3 so it cannot be pressed until the needle shroud 3 is pushed into the housing 2 by placing it on an injection site, e.g. a patient's skin and applying pressure. The needle shroud 3 has longitudinal splines 5 engaged in corresponding grooves in the housing 1 for preventing relative rotation of the needle shroud 3 with respect to the housing 1. A viewing window 6 allows for viewing and inspecting a syringe held in the auto-injector 1.

Figure 2 shows a longitudinal section of the auto-injector 1 in a prior to use state. A syringe 7 is partially surrounded and supported at a front end by a syringe carrier 8. Attached at the front end of the syringe 7 is a hollow needle 9 for piercing a patient's skin and delivering a liquid medicament M stored inside the syringe 7. Near the distal end of the syringe 7 a bung 10 is arranged for sealing and containing the medicament. The bung 10 may be advanced by a piston rod 11 in order to expel the medicament M from the syringe 7. The syringe carrier 8 is slidably arranged inside the needle shroud 3. The needle shroud 3 is biased by a compression spring 12 towards a proximal end P. A bayonet fit (shown in figure 11) between the needle shroud 3 and an outer rear tube 13 serves for holding the needle shroud 3 in a retracted position against the bias of the compression spring 12 prior to use, thus enabling the patient to grab and remove the rubber needle shield (not shown).

A torsion spring 14 is arranged inside the outer rear tube 13 and with one end attached to a distal end D of the housing 2 so torque from the torsion spring 14 is reacted into the housing 2. The other end of the torsion spring 14 is coupled to a lead nut 15 which is rotatably mounted around the piston rod 11. The piston rod 11 has an external lead screw thread 16 engaged with the lead nut 15. The lead nut 15 is equipped with at least one ball bearing 17 for this engagement. It could alternatively have at least one pin. In the prior to use state shown in figure 2 the lead nut 15 is biased by the torsion spring 14

but kept from rotating by a locking pin 18 arranged at the trigger button 4 engaged with a dog tooth 19 arranged at the lead nut 15. An inner rear tube 20 is arranged inside the torsion spring 14 and around the piston rod 11 and part of the lead nut 15. The piston rod 11 is guided along a shaft 21 arranged in an axial bore of the piston rod 11. The axial bore and the shaft 21 both have a non-circular profile in order to keep the piston rod 11 from rotating, e.g. a square profile or a profile with at least one spline or flat. The shaft 21 is attached to an end cap 22 arranged at the distal end D of the auto-injector 1.

A protective needle shield (not shown) may be provided which has to be removed prior to use by a user resulting in the situation of figure 1. In this situation the needle 9 is a safe distance back within the needle shroud to protect the user from accidental needlestick injuries.

Figure 3 shows a perspective detail view of the longitudinal section of figure 2 with the needle shroud 3 and the trigger button 4 interlocked by catches 24, 25 provided at the needle shroud 3 and the trigger button 4, respectively.

In order to prepare for an injection the user pushes the proximal end P of the auto-injector 1 against the injection site. Thus the needle shroud 3 is moved into the auto-injector 1 by a small distance big enough to release the interlocking catches 24, 25 from each other. This situation is shown in figure 4. The compression spring 12 opposes the motion of the needle shroud 3 but is specified such that its spring rate and preload are low enough to feel natural for the user. The trigger button 4 may now be operated.

Figure 5 shows the distal end of the trigger button 4 being pressed thus rotating the trigger button 4 about a trigger pivot 26 in the housing 2, raising the proximal end of the trigger button 4 and moving the locking pin 18 out of the engagement with the dog tooth 19 of the lead nut 15. Thus the lead nut 15 is released and torque from the torsion spring 14 causes the lead nut 15 to rotate. Since the lead nut 15 abuts against a thrust face 27 in the housing 2 it is kept from moving in distal direction D due to the load applied to the piston rod 11 while rotating.

Instead, as shown in figure 6, the piston rod 11, kept from rotating by the shaft 21, is pushed forward in proximal direction P due to the engagement of the lead nut 15 and the lead screw thread 16. The advancing piston rod 11 pushes against the bung 10 which in turn advances the syringe 7 by virtue of the friction between the bung 10 and the syringe wall and due to the thin fluid channel inside the hollow needle 9 opposing the displacement of the medicament M. The advancing syringe 7 also causes the needle 9 to protrude beyond the proximal end P of the auto-injector 1 into the injection site, e.g. the patient's skin. Since the syringe 7 is supported at its proximal end by an orifice of the syringe carrier 8 the syringe carrier 8 is also advanced with the syringe 7 until the syringe carrier 8 abuts against an abutment in the needle shroud 3 as shown in figure 6. This contact sets the injection depth relative to the needle shroud 3.

Figure 7 is a detail view of the longitudinal section of figure 6.

After the syringe carrier 8 has hit the abutment of the needle shroud 3 the syringe 7 is kept from advancing further. With the lead nut 15 still rotating and pushing the piston rod 11 the bung 10 overcomes the friction and the hydraulic resistance of the medicament M and advances inside the syringe 7 thereby displacing the medicament M and delivering it through the fluid channel of the hollow needle 9 into or through the patient's skin. This situation is shown in figure 8.

Figure 8 shows the piston rod 11 and the bung 10 almost fully advanced and the syringe 7 almost entirely emptied but for a small residue. Referring now to figures 9 and 10a and 10b showing different detail views of the cutout marked in figure 8, just before the bung 10 bottoms out in the syringe 7 a shoulder 28 on the distal end of the piston rod 11 behind the lead screw thread 15 is pushed into clutch fingers 29 on the distal end of the lead nut 15 thereby bending the clutch fingers 29 radially outward. Each clutch finger 29 has an external tooth 30 which now engages with a respective internal longitudinal spline 31 provided in the proximal end of the inner rear tube 20, causing the inner rear tube 20 to rotate along with the lead nut 15. The splines 31 are arranged in a ratchet manner in figure 10a.

Figure 10b shows an alternative embodiment with rounded finger teeth 30. In both embodiments (fig 10a and 10 b) the clutch mechanism is arranged to let the clutch fingers 29 generate enough torque on the longitudinal splines 31 to partially rotate the outer rear tube 13 to release a bayonet fit described below in figure 11. However the torque generated has to be low enough to let the lead nut 15 continue rotating with the spring arms jumping over the splines 31 and making a rattling noise indicating that the injection has been nearly finished. The inner rear tube 20 is coupled with the outer rear tube 13 near the distal end D of the auto-injector 1 (cf. fig. 8). Thus the outer rear tube 13 is also rotated. The outer tube 13 has a circumferential slot (not illustrated) to allow the distal end of the torsion spring to pass through to the housing 2 for grounding the torsion spring 14. The circumferential slot has to be long enough to allow a partial rotation of the outer rear tube 13 in order to disengage the bayonet fit described below in figure 11.

Figure 11 shows a perspective view of the auto-injector 1 just before the engagement of the clutch fingers 29 with the internal longitudinal splines 31. The bayonet fit between a pin 32 of the needle shroud 3 and a pin track 33 of the outer rear tube 13 is still in a state with the pin 32 behind a track shoulder 34 so the needle shroud 3 would be held in position against the bias of the compression spring 12 if the still depressed needle shroud 3 was released. A small axial clearance behind the track shoulder 34 allows the needle shroud 3 to be pushed in distal direction D just enough to disengage the interlock between the button 4 and the needle shroud 3 as described above.

When the clutch fingers 29 are engaged with the internal longitudinal splines 31 the outer rear tube 13 is rotated so as to disengage the bayonet fit by the pin 32 coming clear of the track shoulder 34 so the needle shroud 3 may be pushed forward by the compression spring 12 (see fig. 12). At this point the user is asked to keep pressure with the auto-injector 1 at the injection site for a short period of time, e.g. ten seconds. During this time the lead nut 15 is still rotating and forwarding the piston rod 11 and bung 10 until the bung 10 bottoms out at the proximal end of the syringe 7 thereby virtually entirely displacing the rest of the medicament M from the syringe 7.

As the user withdraws the auto-injector 1 from the injection site the needle shroud 3 is pushed over the needle 9 in proximal direction P by the compression spring 12. This situation is shown in figures 13 and 14. A locking mechanism, such as a unidirectional barb or other known to those skilled in the art, may be provided to lock the needle shroud 3 in this forward position in order to prevent re-exposure of the needle.

The auto-injector 1 may preferably be used for delivering one of an analgetic, an anticoagulant, insulin, an insulin derivate, heparin, Lovenox, a vaccine, a growth hormone, a peptide hormone, a proteine, antibodies and complex carbohydrates.

List of References

	1	auto-injector
	2	housing
5	3	needle shroud
	4	trigger button, activating means
	5	spline
	6	viewing window
	7	syringe, medicament container
10	8	syringe carrier
	9	hollow needle
	10	bung
	11	piston rod, second gear member
	12	compression spring, second spring means
15	13	outer rear tube
	14	torsion spring, spring means
	15	lead nut, first gear member
	16	lead screw thread
	17	ball bearings
20	18	locking pin
	19	dog tooth
	20	inner rear tube
	21	shaft
	22	end cap
25	23	button pivot
	24	catch
	25	catch
	26	trigger pivot
	27	thrust face
30	28	shoulder
	29	clutch finger
	30	external tooth

- 31 internal longitudinal spline
- 32 bayonet pin
- 33 pin track
- 34 track shoulder

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- D distal direction, distal end
- M medicament
- P proximal direction, proximal end

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Claims

1. Auto-injector (1) for administering a dose of a liquid medicament (M), comprising:
- 5 - an elongate housing (2) arranged to contain a syringe (7) with a hollow needle (9) and a bung (10) for sealing the syringe (7) and displacing the medicament (M), the elongate housing (2) having a distal end (D) and a proximal end (P) with an orifice intended to be applied against an injection site, wherein the syringe (7) is slidably arranged with respect to the housing (2),
- 10 - spring means (14) capable of, upon activation, pushing the needle (9) from a covered position inside the housing (2) into an advanced position through the orifice and past the proximal end (P) as well as operating the syringe (7) to supply the dose of medicament (M),
- activating means (4) arranged to lock the spring means (14) in a pressurized state
- 15 prior to manual operation and capable of, upon manual operation, releasing the spring means (14) for injection,
- wherein the spring means (14) is a torsion spring (14) grounded at one end in the housing (2) and at the other end in a first gear member (15) rotatable about a longitudinal axis but axially fixed, wherein the first gear member (15), upon rotation,
- 20 is arranged for translatively moving a second gear member (11), the second gear member (11) being prevented from rotating relative to the housing and coupled to the bung (10) in order to push it towards the proximal end (P), wherein the first gear member (15) is engaged with the activating means (4) prior to manual operation in a manner to prevent rotation and disengaged from the activating means (4) upon
- 25 manual operation, wherein an essentially tube-shaped needle shroud (3) is arranged around the syringe (7) in the housing (2), the needle shroud (3) slidable between at least a retracted position with the needle shroud (3) almost hidden inside the housing (2) and an advanced position with the needle shroud (3) protruding from the proximal end (P) and covering the hollow needle (9) in its advanced position,
- 30 wherein the needle shroud (3) is biased by a second spring means (12) towards the advanced position, characterized in that the needle shroud (3) is locked in the retracted position by a locking means which is releasable by rotary movement

transmitted from the first gear member (15) through a clutch mechanism which is engaged by the second gear member (11) shortly before the second gear member (11) is fully advanced during an injection stroke..

- 5 2. Auto-injector (1) according to claim 1, characterized in that an interlock mechanism is arranged for locking the activating means (4) and preventing it from being manually operated, wherein the interlock mechanism is coupled to the needle shroud (3), wherein the interlock mechanism is releasable by pushing the needle shroud (3) a small distance into the housing (2) from the needle shroud's (3)
- 10 retracted position.
3. Auto-injector (1) according to one of the preceding claims, characterized in that the activating means (4) is a trigger button (4), laterally arranged at the housing (2) and operable by being pressed transversally with respect to the longitudinal axis.
- 15 4. Auto-injector (1) according to claim 3, characterized in that the trigger button (4) has a locking pin (18) engageable with at least one dog tooth (19) provided at the first gear member (15) for preventing rotation thereof in order to lock the spring means (14) in its pressurized state.
- 20 5. Auto-injector (1) according to one of the claims 1 to 4, characterized in that the locking means has the shape of a bayonet fit between the needle shroud (3) and an outer rear tube (13) arranged around the torsion spring (14), wherein the needle shroud (3) is guided in the housing (2) in a manner to prevent relative rotation and
- 25 wherein the outer rear tube (13) is coupled to the clutch mechanism, wherein the bayonet fit comprises a bayonet pin (32) arranged at one of the outer rear tube (13) or the needle shroud (3) and a pin track (33) arranged in the other one of the outer rear tube (13) or the needle shroud (3).
- 30 6. Auto-injector (1) according to one of the preceding claims, characterized in that the second gear member (11) is a piston rod (11) having an external lead screw thread (16), the piston rod (11) having an axial bore for slidably arranging the piston rod

(11) on a shaft (21) attached to the housing (2), the axial bore and the shaft (21) having corresponding non-circular profiles, wherein the first gear member (15) is a lead nut (15) engaged with the external lead screw thread (16).

- 5 7. Auto-injector (1) according to claim 6, characterized in that the external lead screw thread (16) has a variable pitch.
8. Auto-injector (1) according to one of the claims 3 to 7, characterized in that the interlock mechanism comprises respective catches (24, 25) provided at the needle
10 shroud (3) and the trigger button (4).
9. Auto-injector (1) according to one of the claims 1 to 8, characterized in that the syringe (7) is arranged in a syringe carrier (8) and supported by the syringe carrier (8) at a proximal end, wherein the syringe carrier (8) is slidably arranged in the
15 needle shroud (3) and wherein an abutment is provided in the needle shroud (3) defining a maximum forward position of the syringe carrier (8).
10. Auto-injector (1) according to one of the claims 1 to 7, characterized in that the clutch mechanism comprises a circumferential shoulder (28) arranged at the second
20 gear member (11) and at least one resilient clutch finger (29) with a respective inclined inner surface arranged at a distal end of the first gear member (15), the shoulder (28) arranged for increasingly pressing against the inclined surface thereby flexing the clutch fingers (29) outward near the end of an injection stroke, wherein the clutch mechanism further comprises an inner rear tube (20) arranged around the
25 clutch fingers (29) inside the torsion spring (14) and attached to the outer rear tube (13) at their distal ends, the inner rear tube (14) having a number of internal longitudinal splines (31) for engaging the flexed-out clutch fingers (29).
11. Auto-injector (1) according to claim 10, characterized in that the internal longitudinal
30 splines (31) are arranged in a manner to form a ratchet when engaged with the clutch fingers (29).

12. Auto-injector (1) according to one of the claims 1 to 11, characterized in that a locking mechanism is provided for locking the needle shroud (3) in its advanced position.
- 5 13. Auto-injector (1) according to one of the preceding claims, characterized in that at least one viewing window (6) for inspecting the syringe (7) is provided in the housing (2).
- 10 14. Auto-injector (1) according to one of the claims 6 to 13, characterized in that the lead nut (15) is provided with at least one pin or with a ball bearing (17) for engaging the external lead screw thread (16).

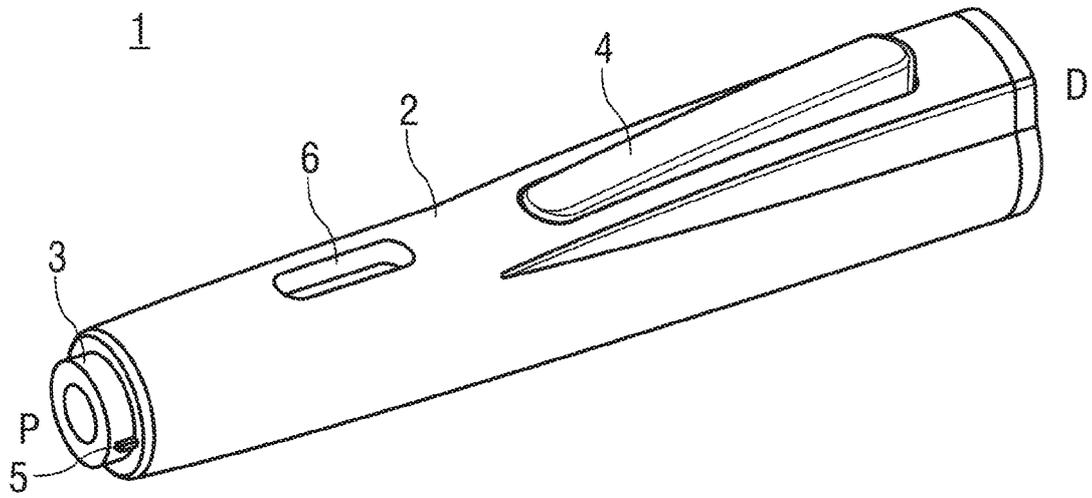


FIG 1

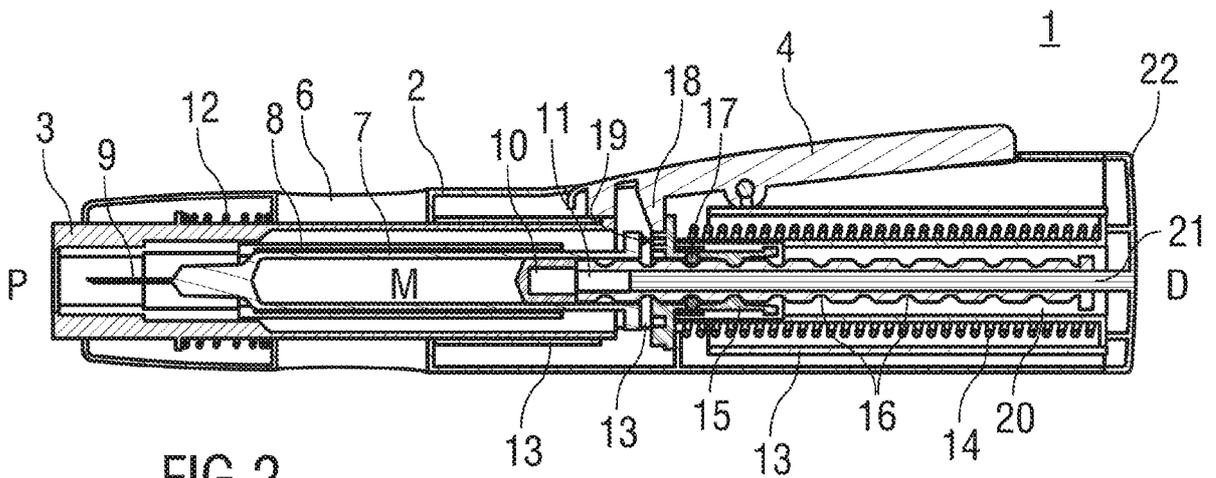


FIG 2

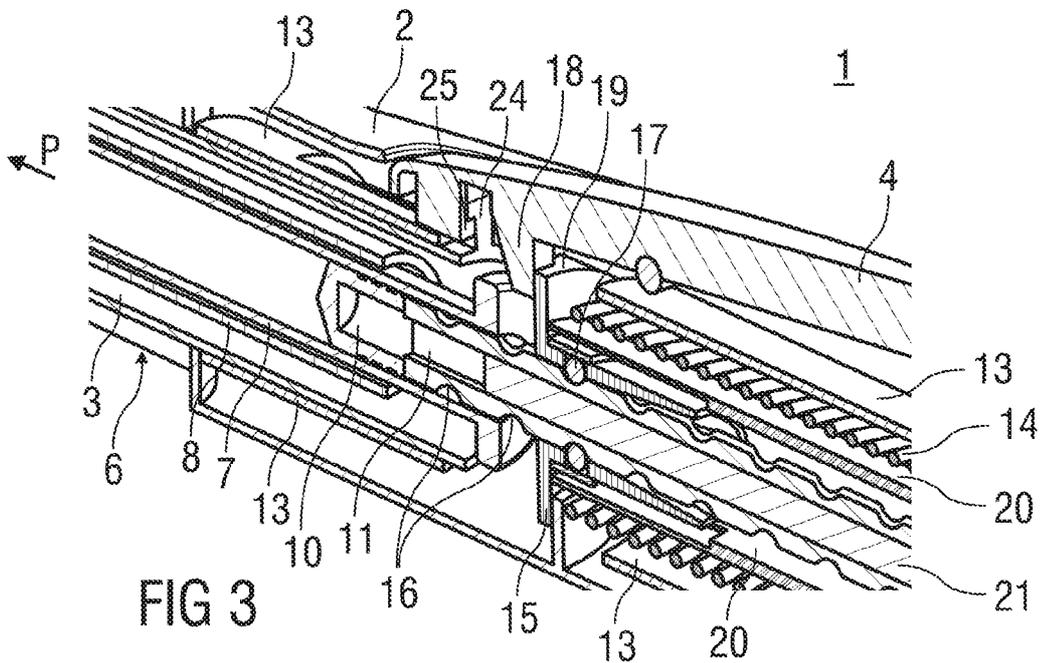
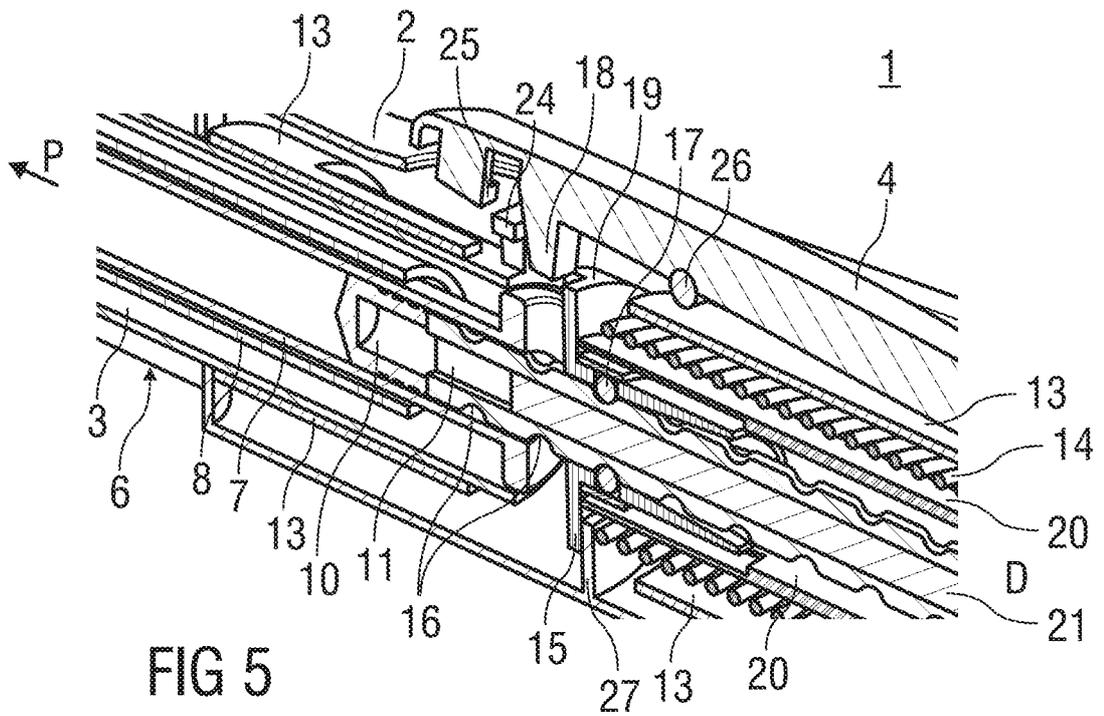
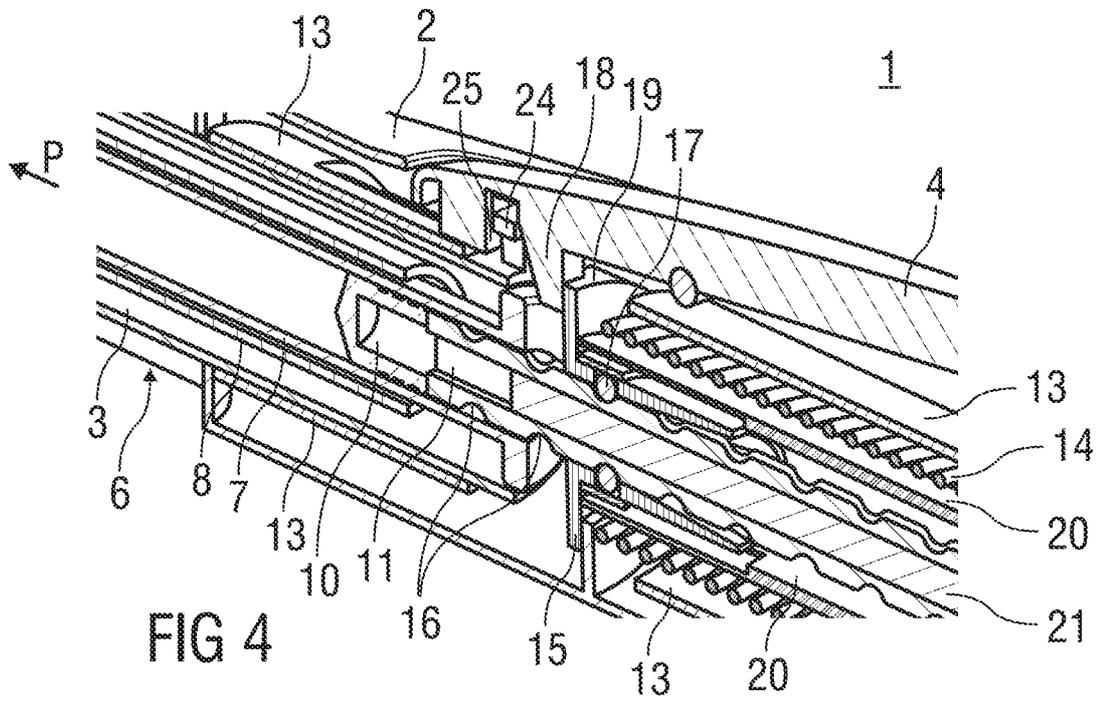


FIG 3



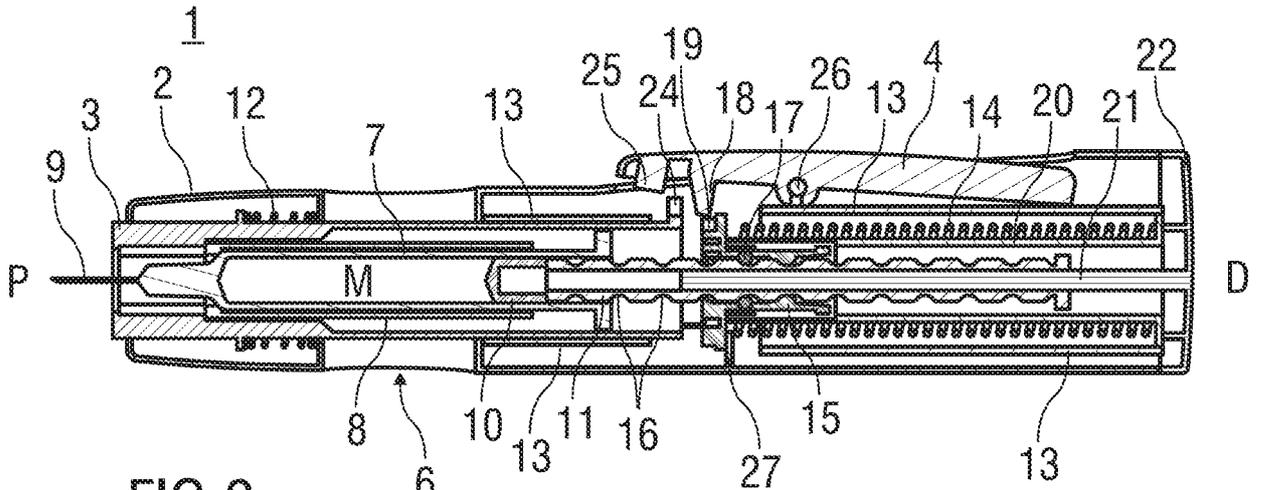


FIG 6

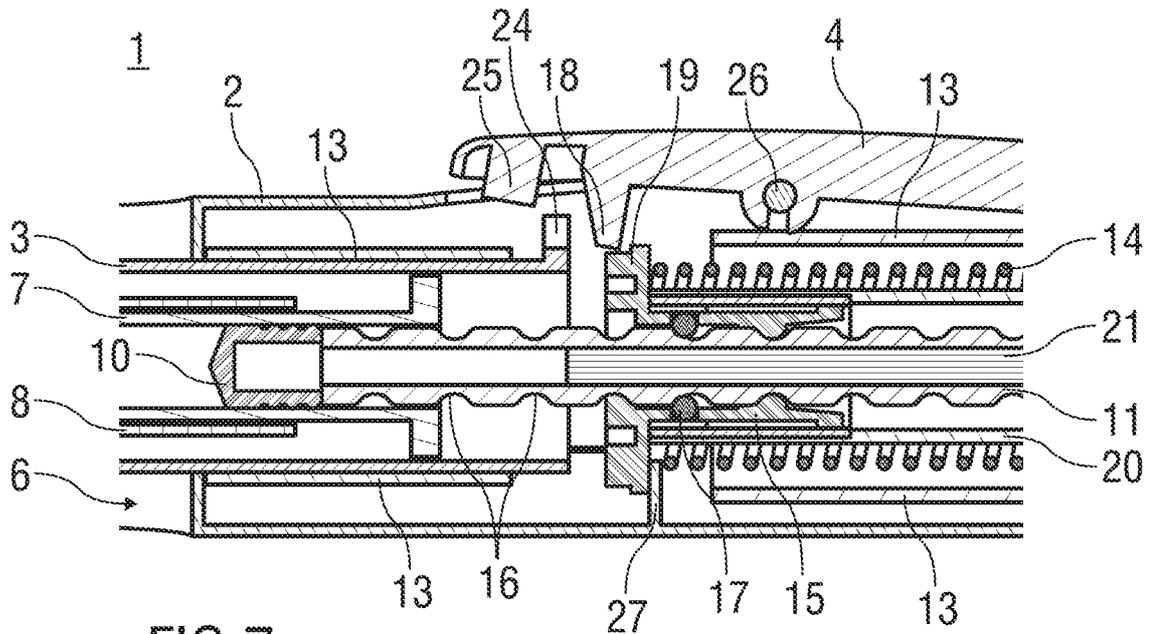


FIG 7

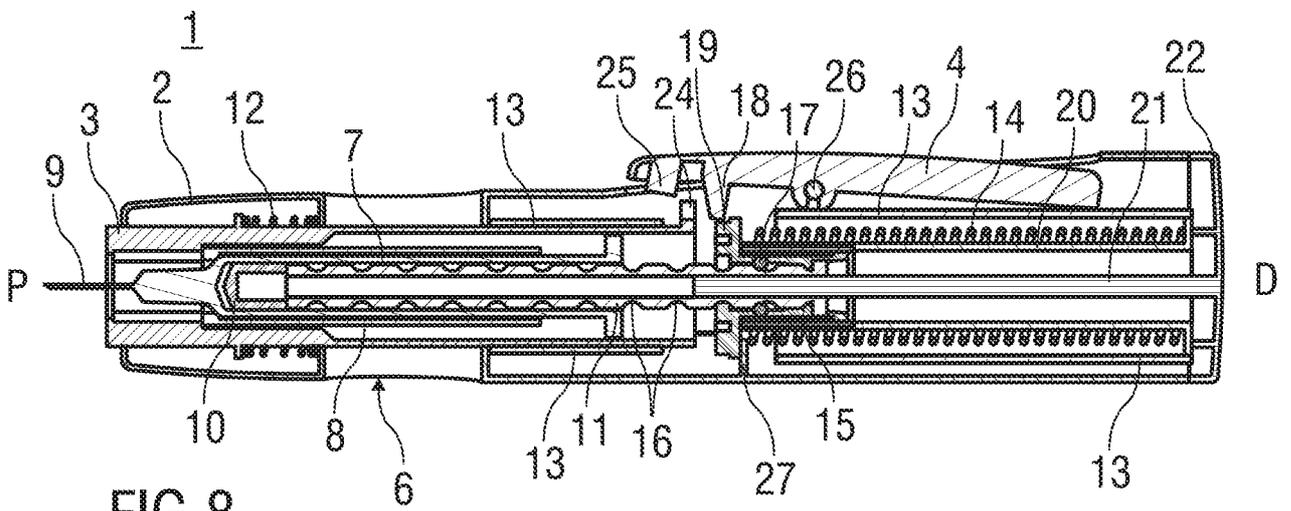


FIG 8

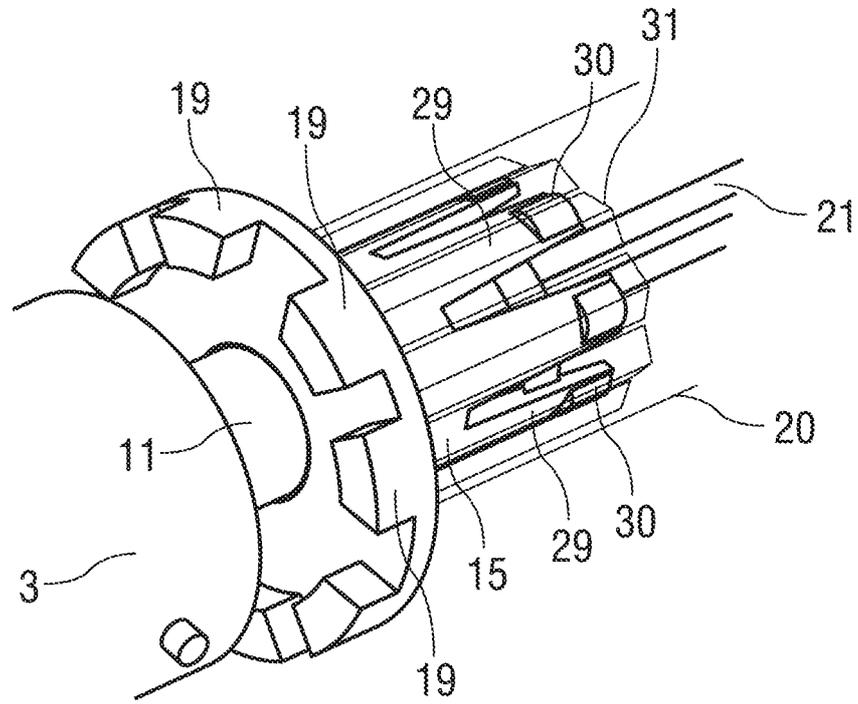


FIG 10B

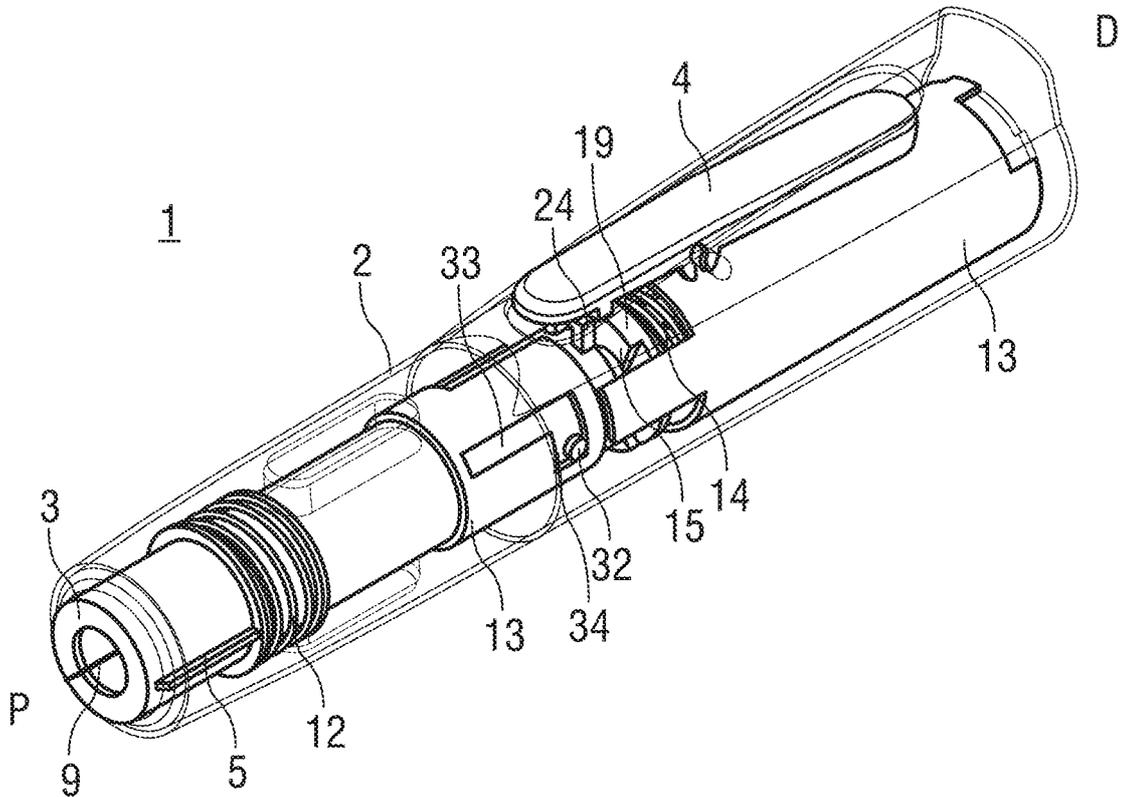


FIG 11

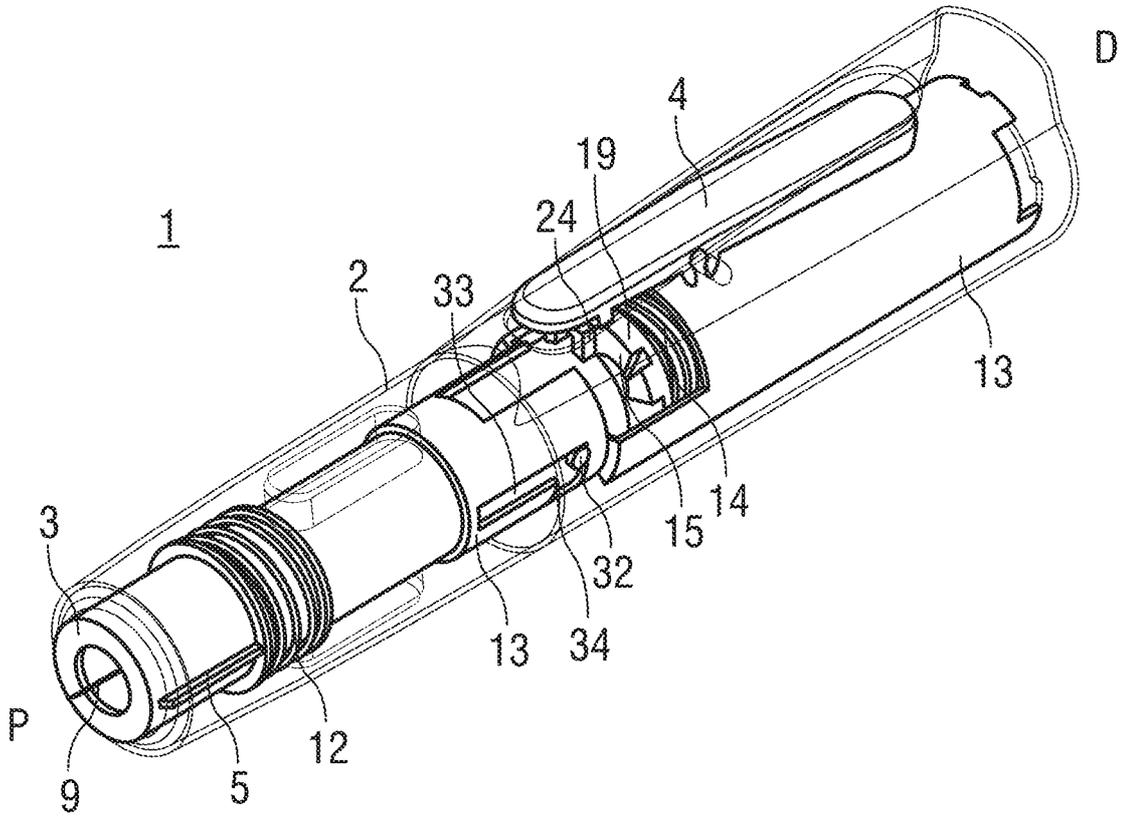


FIG 12

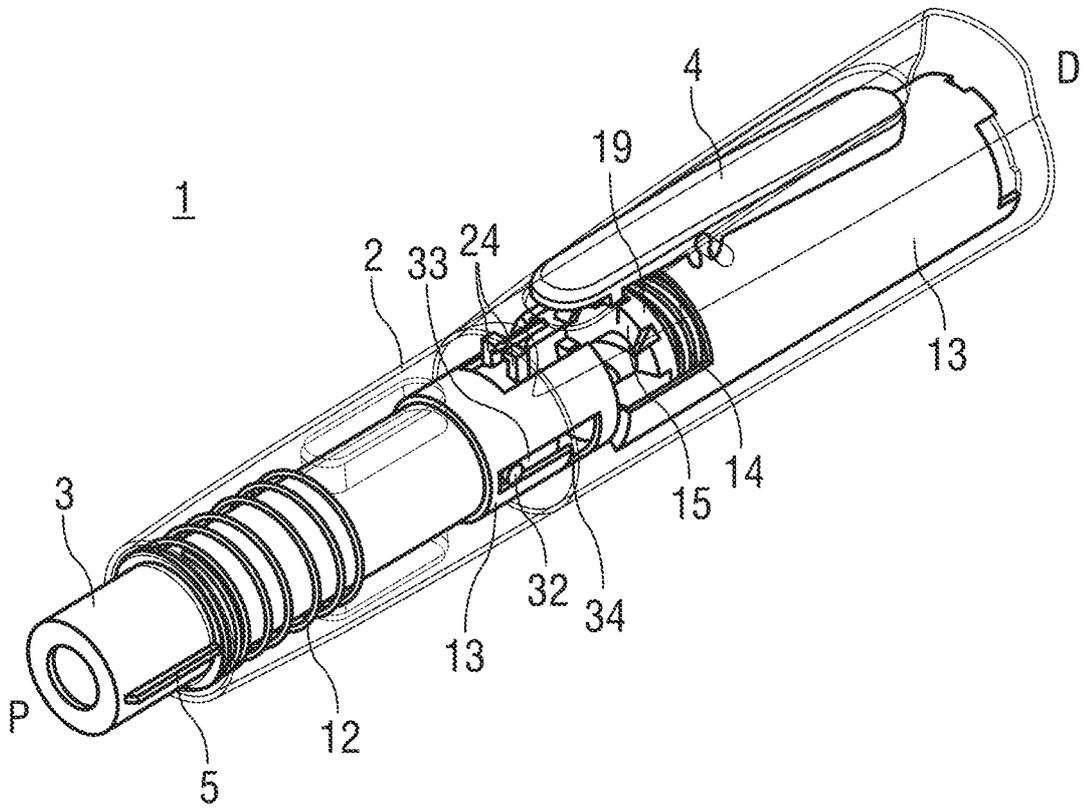


FIG 13

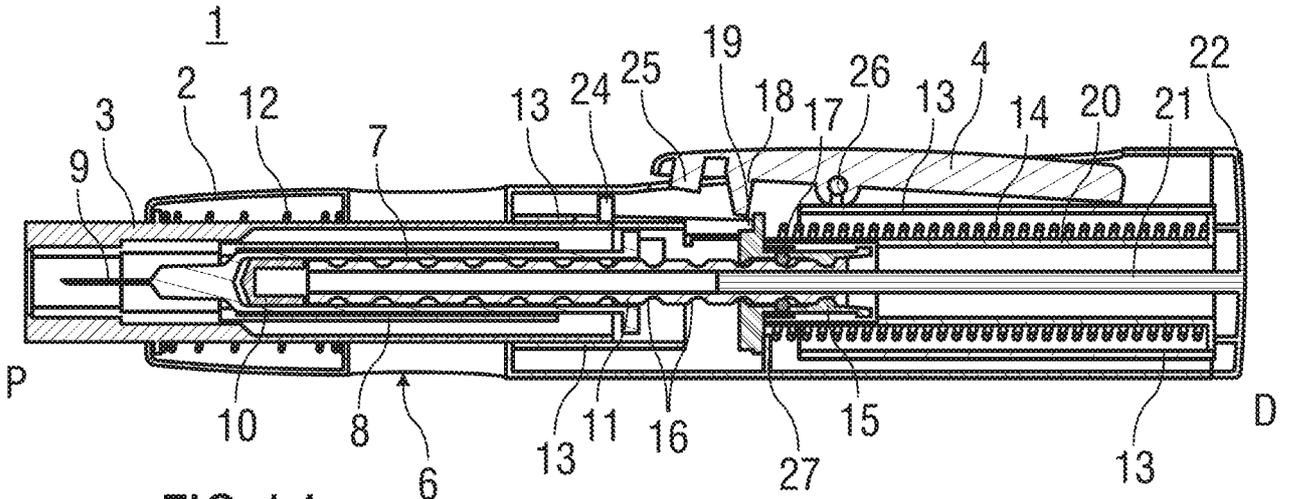


FIG 14

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2011/052297

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/20 A61M5/32
ADD. A61M5/00

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

B. FIELDS SEARCHED

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

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal , WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2006/287630 AI (HOMMANN EDGAR [CH]) 21 December 2006 (2006-12-21) figures 1-8 paragraph [0031] - paragraph [0039] -----	1-14
X	W0 2009/037141 AI (SHL GROUP AB [SE] ; KRONESTEDT VICTOR [SE]) 26 March 2009 (2009-03-26) figures 1-6 paragraph [0029] - paragraph [0044] -----	1,6,7 ,9, 12-14
X	EP 1 728 529 AI (SHL MEDICAL AB [SE]) 6 December 2006 (2006-12-06) paragraph [0036] ; figures 7-19 paragraph [0047] - paragraph [0071] ----- -/- .	1,6,7 ,9, 13

Further documents are listed in the continuation of Box C. See patent family annex.

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Date of the actual completion of the international search 26 April 2011	Date of mailing of the international search report 04/05/2011
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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 Reinbold, Sylvie
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2011/052297

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	wo 2009/098502 A2 (OWEN MUMFORD LTD [GB] ; COWE TOBY [GB]) 13 August 2009 (2009-08-13) page 7, line 23 - page 11, line 11; figures 1-13 -----	1-14

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Information on patent family members

International application No PCT/EP2011/052297

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