Title: AUTO INJECTOR WITH FLEXIBLE ELEMENTS PROVIDED IN THE HOUSING AND A CAP WITH A NEEDLE SHEATH

Abstract: There is provided an auto injector (1) for a syringe that is suitable for use in the injected delivery of drug to a patient. The auto injector comprises a housing (20) defining a housing cavity arranged for receipt of a syringe, and a needle delivery aperture (25) through which the hollow needle of the syringe protrudes during dispensing of the liquid drug formulation. The auto injector further comprises a needle sheath (70) for covering of the needle tip of the syringe, and a removable cap (60) for the needle delivery aperture of the housing. The removable cap defines an inwardly projecting needle sheath cover for covering the needle sheath that includes one or more gripping elements arranged for gripping of the needle sheath, and provided to the housing, one or more flexible elements (80) extending into said housing cavity thereof. The needle sheath cover and/or the one or more flexible elements are shaped for interaction with each other such that on moving the removable cap away from the capped position the one or more flexible elements are in urging contact with the needle sheath cover to thereby urge the one or more gripping elements into gripping contact with the needle sheath.
The present invention relates to an auto-injector device for receipt of a syringe that is suitable for use in the injected delivery of a drug formulation to a patient.

It is well-known to use syringes for the delivery of injectable liquid drug formulation to a patient. Traditional syringes rely on puncturing of the patient's skin by a hollow needle through which the injectable liquid drug (e.g. in solution or suspension form) is delivered to the muscle or tissue of the patient. It is also well-known to provide auto-injectors for use with syringes. Such auto-injectors typically comprise a body defining a housing for the syringe; and an actuating mechanism, which is triggered in use, to allow for automatic delivery of the liquid drug formulation from the syringe. The housing of the auto-injector typically defines a needle delivery aperture through which the hollow needle of the syringe protrudes during dispensing of the liquid drug formulation. A removable cap may also be provided to the housing, which in a capped position thereof acts to close off the needle delivery aperture, thereby preventing access to the syringe.

The syringe is typically provided with a needle sheath that is arranged in a rest configuration for sealing of the tip of the syringe needle. To maintain the sterility of the injectable liquid drug contents of the syringe it is essential that the integrity of the seal be maintained whilst the syringe is in the auto-injector and prior to injecting use thereof.

Auto-injectors have been suggested in which the removable cap defines an inwardly projecting needle sheath cover for covering the needle sheath, which cover includes one or more gripping elements (e.g. hooks) arranged for gripping
of the needle sheath. The needle sheath cover is arranged within the cap such that on removal of the cap the needle sheath is also removed to leave the needle tip of the syringe unsheathed and hence, ready for dispensing use.

Applicant has found that a problem can exist with providing sufficient gripping interaction between the gripping elements of the needle sheath cover and the needle sheath gripped thereby, such as to ensure that when the cap is removed the needle sheath is reliably and consistently also removed from the needle tip. Indeed, Applicant has found that in practice the gripping interaction may be insufficient or unreliable such that removal of the cap may result in only partial unsheathing or in extreme cases, no unsheathing at all of the needle tip (i.e. the needle sheath remains partly or wholly in sheathed relation to the needle tip).

In solution to this problem, Applicant has devised an auto-injector in which the housing is provided with one or more flexible elements extending into the housing cavity thereof. The needle sheath cover and/or the one or more flexible elements are shaped for interaction with each other such that on moving the removable cap from the capped position towards a cap removed position the one or more flexible elements are brought into urging contact with the needle sheath cover. Thereby the one or more gripping elements are urged into gripping contact with the needle sheath. Thus, the act of moving the cap from the capped to the uncapped position results in enhanced gripping contact between the needle sheath cover and the needle sheath such that unsheathing of the needle tip is more reliably and consistently achievable.

According to one aspect of the present invention there is provided an auto-injector comprising

a housing defining a housing cavity arranged for receipt of a syringe comprising
a barrel for containing a volume of a liquid drug formulation;

a hollow needle at a front end of said barrel, said hollow needle defining a needle tip for dispensing of said liquid drug formulation;

and

a plunger that is axially movable within the barrel,

wherein the housing defines a needle delivery aperture through which the hollow needle of the syringe protrudes during dispensing of the liquid drug formulation, the auto-injector further comprising

a needle sheath for covering of said needle tip of the syringe;

a removable cap that in a capped position acts to close off said needle delivery aperture of the housing, wherein said removable cap defines an inwardly projecting needle sheath cover for covering said needle sheath that includes one or more gripping elements arranged for gripping of the needle sheath; and

provided to the housing, one or more flexible elements extending into said housing cavity thereof,

wherein the needle sheath cover and/or the one or more flexible elements are shaped for interaction with each other such that on moving the removable cap away from the capped position the one or more flexible elements are in urging contact with the needle sheath cover to thereby urge the one or more gripping elements into gripping contact with the needle sheath.
These and other embodiments of the present invention are set forth in the later description, which describes for illustrative purposes only various embodiments thereof.

There is provided an auto-injector device that is arranged for use with a syringe that contains a liquid drug formulation. The syringe is arranged to be suitable for use in the injected delivery of the liquid drug formulation to a patient.

The auto-injector comprises a housing that defines a housing cavity (e.g. chamber form) that is arranged for receipt of the syringe and is therefore typically sized and shaped for this purpose.

The syringe that is received within the housing cavity comprises a barrel for holding a volume of the liquid drug formulation; a hollow needle at a front end of the barrel, the hollow needle defining a needle tip for dispensing of said liquid drug formulation; and a plunger (e.g. in the form of a rubber stopper) that is axially movable within the barrel. The plunger is movable axially within the barrel so as to enable the liquid drug formulation to be expelled from the barrel and thence through the hollow needle via the dispensing tip for injection into the patient. The syringe barrel is typically, comprised of glass but may also be comprised of a relatively hard plastic polymer such as hardened polyethylene, polycarbonate or cyclic olefin polymers.

In more detail, the barrel is selected such as to define a barrel chamber for containing a suitable volume of the liquid drug formulation. In aspects, that suitable volume is selected to correspond to a single dose of the drug formulation to be delivered to the patient. In other words, delivery of that single dose involves expelling all of the liquid drug formulation contents of the barrel chamber through the hollow needle for injection into the patient.
The hollow needle defines a needle bore, which is most typically of circular cross-section and of selected bore diameter. It may be appreciated that in aspects, the bore diameter may affect the force required to expel the liquid drug formulation through the needle and also the velocity at which the liquid drug formulation is expelled.

The selected needle bore may also, in aspects affect the degree of patient discomfort during injection. Smaller bore diameters, typically provide more patient comfort, whereas larger bore diameters enable more rapid / lower force delivery of the liquid through the needle. A compromise is therefore needed in selecting needle bore to provide acceptable patient comfort and liquid delivery through the needle characteristics.

Examples of typical needles that are suitable for use therein include 12.5mm ("half inch") long thin wall needles of grade 23G, 25G or 27G. These have a needle bore of from about 0.2 to 0.4mm such as from 0.25 to 0.35mm. Other examples include both regular and thin wall needles used in conventional syringes including those with bevels such as 3 and 5 bevels.

The housing of the auto-injector is shaped to define a housing cavity within which the syringe is receivable. The housing cavity is typically cylindrical in form, thereby matching the typically cylindrical outer profile of a syringe. The housing cavity may be further shaped with any manner of grooves, indentations or other shaping or surface details to define a 'lock and key' relationship between the housing and the syringe. Colour guides, arrows and any other surface markings may also be employed. The housing also defines a needle delivery aperture through which the hollow needle of the syringe protrudes during dispensing of the liquid drug formulation.
Typically, the housing of the auto-injector is provided with a barrel receiving part for receiving the barrel of the syringe; a plunger receiving part for receiving the plunger of the syringe; and a needle receiving part for receiving the hollow needle of the syringe.

In embodiments, the plunger receiving part of the housing allows the plunger to be received thereby and for the plunger to be movable (e.g. axially) therein from a first position, in which it is somewhat withdrawn from the barrel to a second position, in which it is moved somewhat into the barrel.

Typically, the needle receiving part of the auto-injector housing includes the needle delivery aperture through which the hollow needle may protrude from the housing, for example during expelling of the liquid drug formulation through the hollow needle and its needle tip for delivery to the patient.

In embodiments, the auto-injector housing is provided with a removable cap that fits over and thereby, acts in a capped position such as to close off, the needle delivery aperture. It may therefore, be appreciated that when in the capped position, the removable cap acts such as to prevent ingress of contaminants into the needle receiving part of the housing.

The auto-injector further comprises a needle sheath (e.g. as part of a needle cover) arranged in a rest configuration for sealing of the needle tip.

In embodiments, the needle sheath is comprised of a (e.g. resiliently) compressible material such as a natural or synthetic rubber material. In the rest configuration, the needle tip sticks into (e.g. is spiked or staked into) the needle sheath such that sealing of the needle tip is achieved. Usually, at least the first 3 to 4mm of the needle tip end is so sheathed. It will be appreciated that for clinical reasons, the sealing of the needle tip is preferably such as to prevent
passage of contaminant, bacterial or otherwise, through the needle tip and thus into the needle bore and syringe barrel chamber. Sterile sealing is preferred.

The removable cap defines an inwardly projecting needle sheath cover for covering the needle sheath. By 'inwardly projecting' it is meant that the needle sheath cover projects within the volume enclosed by the cap and away from the inner top surface of the cap, that is to say which projects, in the capped position towards the needle-receiving part of the housing cavity and hence, towards the needle of the syringe. Thus, the needle sheath cover is provided to (e.g. fixed to or integral with) the removable cap for the housing. The needle cover projects within the cap such that when the removable cap is in the capped position the needle sheath cover and needle sheath therewithin projects towards the needle tip of the syringe. In such embodiments, when in the capped position, the needle tip is sheathed by the needle sheath, and when the cap is removed the needle sheath cover and needle sheath within are also removed such as to thereby, unsheathe the needle tip.

In embodiments, the removable cap defines an essentially cylindrical cap chamber, optionally tapering, and the needle sheath cover is provided along the axis of that cylindrical chamber. In embodiments, the needle sheath cover defines a cylindrical needle sheath-receiving chamber. In embodiments, the cylindrical needle sheath-receiving chamber has at least partly tapering form.

The needle sheath cover includes one or more gripping elements (e.g. hooks or other projecting features) arranged for gripping of the needle sheath. In embodiments, the needle sheath is provided with one or more features arranged for receipt of the one or more gripping elements such as one or more indents, grooves or cavities.
The housing is provided with one or more (e.g. resiliently) flexible elements that extend (e.g. protrude) into the housing cavity. In embodiments, the one or more (e.g. resiliently) flexible elements are provided as one or more separate parts that attach or fix to an inner wall of the housing or are otherwise suitably held within the housing. In other embodiments, the one or more (e.g. resiliently) flexible elements are provided integrally with the housing (e.g. formed as an integral moulding therewith). The one or more flexible elements are typically provided to the needle receiving part of the auto-injector housing.

The one or more (e.g. resiliently) flexible elements are arranged for interaction with the needle sheath cover during an uncapping (i.e. cap removal operation).

Thus, the needle sheath cover and/or the one or more flexible elements are shaped for interaction with each other such that on moving the removable cap away from the capped position (i.e. during uncapping and when the cap is moved to an uncapped position) the one or more flexible elements are in (e.g. move into or are brought into) urging contact with the needle sheath cover to thereby urge the one or more gripping elements into gripping contact with the needle sheath.

Thus, in essence the effect of the user removing the cap from its capped position on the housing is that (as a result of the interaction between the needle sheath cover and/or the one or more flexible elements) the one or more gripping elements of the needle sheath cover are in (e.g. are brought into or move into) urged gripping relationship with the needle sheath. The needle sheath is therefore more tightly gripped and hence, more likely to be removed from its sheathing relationship with the needle tip as the cap and its inwardly projecting needle sheath cover are moved away from the capped position.
It will be appreciated that the need for gripping of the needle sheath is most pronounced during the earlier stages of the unsheathing of the needle tip since this corresponds to the point at which the frictional contact between needle sheath and hollow needle is also likely to be most pronounced. It will also be appreciated that once the needle sheath had been removed (i.e. the needle tip unsheathed) then the need for gripping is reduced.

In embodiments, the interaction between the needle sheath cover and/or the one or more flexible elements during relative movement thereof during an uncapping operation may be optimised to ensure consistent and reliable removal of the needle sheath as a result of removal of the cap. The presence of a relative tapering relationship between the needle sheath cover and/or the one or more flexible elements during at least part of such relative movement has been found to be beneficial.

Thus, in embodiments the needle sheath cover defines a tapering surface at an outer part thereof arranged for contact with the one or more flexible elements. In other embodiments, the one or more flexible elements define a tapering surface arranged for contact with an outer part of the needle sheath cover.

In embodiments, the one or more (e.g. resiliently) flexible elements may also be arranged to perform two further separate functions.

In a first further function, in the capped configuration, in which the needle sheath locates to seal off the needle tip, Applicant has found that it is beneficial if the one or more (e.g. resiliently) flexible elements at least lightly contact the needle cover to restrict (e.g. prevent) movement thereof. Thus, movement of the needle cover is restricted by the action of the (e.g. resiliently) flexible elements, which in embodiments engage with the needle cover to hold it, and thereby restrict
movement thereof. Such restriction of movement assists in maintaining the integrity of the seal relationship between the needle tip and the needle sheath.

In embodiments, in the capped position the one or more flexible elements contact the needle sheath cover to thereby bring the one or more gripping elements into at least light contact with the needle sheath.

In the use configuration, the needle cover is removed from the needle tip during an uncapping operation such as to unseal that tip. In a second further function, in this use configuration, the one or more (e.g. resiliently) flexible elements flex into the housing cavity to provide a barrier surface. This barrier surface acts such as to obstruct the exit of the syringe barrel from the housing cavity. Such obstructing function is particularly important in the instance of fracture (i.e. breakage) of the syringe, which is generally comprised of glass material. In this instance, the barrier surface acts such as to obstruct the exit of fractured parts (e.g. glass shards) of the syringe from the housing cavity. The patient is thereby, protected from coming into contact with such fractured parts, and thus potential injury in the event of such a syringe fracture event occurring.

In embodiments, the one or more (e.g. resiliently) flexible elements comprise a ring comprised of a (e.g. resiliently) flexible material such as a plastic polymer or natural or synthetic rubber material. That ring (e.g. an O-ring) is generally provided to an inner wall of the (cylindrical) housing such that the outer ring circumference thereof attaches to the inner wall of the housing. In the rest configuration, the inner ring circumference thereof contacts the needle cover (e.g. the needle sheath or a needle sheath cover provided thereto) and is somewhat compressed inwards as a result of that contact, the effect of which is to restrict movement of the needle cover. In the use configuration, the needle cover is removed, and in the absence of compressive contact with the needle cover, the ring expands outwards into the housing cavity to provide a barrier
surface, which acts such as to obstruct the exit of the syringe barrel from the housing cavity. Preferably, the diameter of the uncompressed inner ring circumference of the ring is less than that of the syringe barrel such that when the ring is in its uncompressed state the syringe barrel may not pass through the ring.

In embodiments, each of the one or more (e.g. resiliently) flexible elements comprises a flexible finger element comprised of a (e.g. resiliently) flexible material such as a plastic polymer. Each finger element is generally provided to an inner wall of the (cylindrical) housing such that the finger base thereof attaches to the inner wall of the housing. Typically, an arrangement (e.g. circular arrangement) of flexible finger elements is employed such as from three to eight finger elements. In the rest configuration, the finger tip of each finger element contacts the needle cover (e.g. the needle sheath or a needle sheath cover provided thereto) and is somewhat flexed inwards as a result of that contact, the effect of which is to restrict movement of the needle cover. In the use configuration, the needle cover is removed, and in the absence of the compressive contact with the needle cover, the flexible finger element(s) flex into the housing cavity to provide a barrier surface, which acts such as to obstruct the exit of the syringe barrel from the housing cavity. Where the flexible finger elements are provided as a circular arrangement, it is preferable that the diameter of the inner circumferential aperture defined by the extremes of the finger tips thereof is less than that of the syringe barrel such that when the finger elements of that circular arrangement flex outwards the syringe barrel may not pass through the inner circumferential aperture defined thereby.

For ease of assembly, Applicant has realized that it is advantageous if the one or more (e.g. resiliently) flexible elements are arranged such that during a capping operation when the needle sheath cover is projected (i.e. inserted) into the housing for sheathing of the needle tip, part thereof interacts with the one or
more (e.g. resiliently) flexible elements such that these flex (or compress) towards the inner wall of the housing. On completion of that insertion step (i.e. in the capped position) the one or more (e.g. resiliently) flexible elements are thus, in a somewhat tensed state, which better acts such as to impact on thus, restrict movement of the needle sheath cover.

In terms of function, the auto-injector is arranged to allow for actuation of the syringe. Thus, the auto-injector is typically provided with an actuating mechanism for actuating the syringe (e.g. typically by plunging the plunger axially into the barrel thereof) to deliver the liquid formulation to the patient.

The actuating mechanism typically includes an energy store for storing energy that can then be released to allow for actuation of the syringe. In aspects, the energy store comprises a mechanical energy store such as a spring (e.g. a compression or torsion spring). In other aspects, the energy store may be provided by a container of compressed liquid or gas propellant that on release provides a source of jet energy propulsion.

The energy store is in embodiments, able to exert a force of up to 60N on the plunger of the syringe. Where the energy store is a compression spring the force exerted typically varies over the actuation profile such as from a range of 60 to 40N at the start of actuation to from 40 to 20N at the end of the actuation profile. Where the energy store is a compressed liquid or gas propellant a more constant force is typically exerted over the actuation profile.

In preferred embodiments, actuation of the actuating mechanism is responsive to a trigger (e.g. a user-actuable trigger). In embodiments, the trigger comprises a button, switch or lever arrangement. In other embodiments, a press actuation mechanism that is actuable in response to pressing of the housing of the device against the skin is also envisaged.
In embodiments, a reset mechanism is provided for resetting the firing mechanism after actuation thereof. The reset mechanism may for example, comprise a spring, motor, mechanical arrangement or a reset coupling.

For safety and hygiene reasons, it is desirable that the needle does not protrude from (i.e. outwith) the housing other than when expelling the liquid drug formulation during an injection procedure. Thus embodiments are envisaged in which, the housing is arranged such that the needle receiving part thereof allows for the needle of the syringe to be axially moveable therein from a first (i.e. rest) position in which the needle is wholly housed by the needle receiving part to a second (i.e. use) position in which at least the tip of the needle protrudes from that needle receiving part of the housing. In aspects, the housing includes biasing means (e.g. a spring) arranged such that the needle is normally biased towards the first (i.e. rest) position, wherein such biasing means are overcome during the actuation of the syringe by the actuating mechanism to allow for movement of the needle to the second (i.e. use) position.

In embodiments, a needle retraction mechanism is provided for retracting the needle back into the needle receiving part of the housing after the injection procedure, that is to say retracting the needle from the second (i.e. use) position to a retracted position thereof. The retraction mechanism may for example, comprise a spring, motor, mechanical arrangement or a reset coupling.

In embodiments, the auto-injector is provided with child-resistant features to prevent undesirable actuation of the actuating mechanism by a young child.

In embodiments, the auto-injector is provided with a visual indicator that is arranged to provide the user with a visual indication of the temperature state of the auto-injector, and particularly of the syringe and its contents (i.e. the liquid drug formulation), which at least allows the user to differentiate between a 'too cold to use' state and a 'sufficiently warm to use' state. Such visual indicators are described in Applicant's co-pending PCT patent application no. WO2008/146,021, which claims priority from UK patent application no. 0710433.4 filed on 31st May 2007, the contents of both of which are incorporated herein by reference.

In embodiments, the syringe of the auto-injector herein contains a liquid drug formulation, which is designed for refrigerated rest (e.g. at from 2-8°C) and for injected delivery at room temperature (e.g. at or about 18-30°C). In embodiments, the viscosity of the liquid drug formulation is less than 120 mPa.s (120 centipoise), preferably less than 100 mPa.s (100 centipoise) at a delivery temperature of 20°C.

Applicant has appreciated that the concept of using a ring comprised of a (e.g. resiliently) flexible material such as a plastic polymer or natural or synthetic rubber material as a barrier surface is more generally applicable.

In embodiments, the ring is typically not provided (e.g. directly) to the housing. That is to say, the ring does not fix or attach to the housing or is not provided as an integral part thereof. The ring is comprised of a (e.g. resiliently) flexible material such as a plastic polymer or natural or synthetic rubber material, and is embodiments of O-ring form.
In embodiments, a ring is provided to the auto-injector such that in the rest configuration, the ring contacts the needle cover to restrict movement thereof, and wherein in a use configuration the needle cover is removed from the needle tip such that the ring extends into the housing cavity to provide a barrier surface for obstructing exit of the syringe barrel therefrom.

In embodiments, the needle barrel is provided with a barrel sleeve that is arranged to fit over part or all of the length of the needle barrel, and the ring is provided to that sleeve (e.g. by attaching or fixing thereto or as an integral part thereof). In these embodiments, the ring (e.g. an O-ring) is generally provided to an inner wall of the (cylindrical) barrel sleeve such that the outer ring circumference thereof attaches to the inner wall of the barrel sleeve. The barrel sleeve may also extend out beyond the syringe barrel to wholly or partly enclose a length of the end-shoul er of the syringe barrel and of the hollow needle that extends from (the end-shoulder) of the syringe barrel.

In embodiments, the ring is provided to a forward part of the barrel sleeve (e.g. corresponding to a part that extends out beyond the syringe barrel). In embodiments thereof, in the rest configuration, the inner ring circumference contacts the needle cover (e.g. the needle sheath or a needle sheath cover provided thereto) and is somewhat compressed inwards as a result of that contact, the effect of which is to restrict movement of the needle cover. In the use configuration, the needle cover is removed, and in the absence of compressive contact with the needle cover, the ring expands outwards into the housing cavity to provide a barrier surface, which acts such as to obstruct the exit of the syringe barrel from the barrel sleeve, and preferably hence also from the housing cavity. Preferably, the ring provides the only such barrier surface and the barrel sleeve is not provided with any other barrier surface-providing elements such as flexible fingers or flanges. Preferably, the diameter of the
uncompressed inner ring circumference of the ring is less than that of the syringe barrel such that when the ring is in its uncompressed state the syringe barrel may not pass through the ring.

According to a further aspect of the present invention there is provided a kit of parts comprising an auto-injector as described above; and a syringe containing a liquid drug formulation.

According to a further aspect of the present invention there is provided a kit of parts comprising an auto-injector as described above; and packaging therefor; and optionally a syringe containing a liquid drug formulation.

Suitable packaging typically comprises a container for the auto-injector and syringe. In aspects, the packaging comprises a compartment for the auto-injector pre-loaded with the syringe. In aspects, the packaging comprises a separate compartment for a 'kit' of the auto-injector and the syringe.

The invention will now be described further with reference to the accompanying drawings in which:

Figure 1 is a sectional view from the side of a first auto-injector in accord with the present invention shown in the 'at rest position' with removable cap and needle cover in place;

Figure 2a is a sectional view from the side of the first auto-injector of Figure 1 shown in the 'uncapped position' with removable cap and needle cover now removed from the housing;

Figure 2b is a sectional view from the side of the removable cap and needle cover of Figure 1 as now removed therefrom;
Figure 3 is a sectional view from the side of the first auto-injector of Figure 1 with the needle cover partly removed therefrom;

Figure 4 is a sectional view from the side of the first auto-injector of Figure 1 in 'the ready to inject position' with the needle cover removed therefrom; the trigger released; and the syringe thereof advanced with needle tip protruding;

Figure 5 is a sectional view from the side of the first auto-injector of Figure 1 in 'the post-injection position' with the syringe thereof advanced with needle tip protruding; and the syringe plunger plunged deep within the syringe barrel;

Figure 6 is a sectional view from the side of the first auto-injector of Figure 1 in 'syringe retracted and locked position' with the syringe retracted back into the housing and locked into place therein;

Figure 7 is a sectional view from the side of an alternative removable cap and needle cover for use with the first auto-injector of Figure 2;

Figure 8 is a sectional view of the front part of a second auto-injector herein, as shown absent any needle cover;

Figure 9 is a sectional view of the front part of a third auto-injector herein, as shown absent any needle cover;

Figure 10 is a sectional view of the front part of a fourth auto-injector herein, as shown absent any needle cover;

Figure 11 is a perspective view of the outer housing of a fifth auto-injector herein;
Figure 12 is a sectional cut-away view in perspective of the fifth auto-injector of Figure 11 with removable cap and needle cover in place;

Figure 13 is a sectional view from the side of the fifth auto-injector of Figure 11 with removable cap and needle cover in place;

Figure 14 is a sectional cut-away view in perspective of detail of the forward part of the fifth auto-injector of Figure 11 with removable cap and needle cover in place;

Figure 15 is a perspective view of a detail of inner parts of the fifth auto-injector of Figure 11, as shown with removable cap, needle cover, outer housing and inner housing sleeve removed;

Figure 16 is a second perspective view of a detail of inner parts of the fifth auto-injector of Figure 11, as shown with removable cap, needle cover, outer housing and inner housing sleeve removed;

Figure 17 is a perspective view of the syringe plunger and collet assembly of the fifth auto-injector of Figure 11;

Figure 18 is a second perspective view of the syringe plunger and collet assembly of the fifth auto-injector of Figure 11;

Figure 19 is a perspective view of the syringe plunger of the fifth auto-injector of Figure 11 and for use in the syringe plunger and collet assembly of Figure 18;

Figure 20 is a side view of a rear collet for use in the syringe plunger and collet assembly of Figure 18;
Figure 21 is a perspective view of a detail of the relationship between plunger rod, collet and return spring within the inner housing sleeve and outer housing of the fifth auto-injector of Figure 11;

Figure 22 is a side view of the inner housing sleeve of the fifth auto-injector of Figure 11;

Figure 23 is a part cut-away side view of the relationship between the inner housing sleeve and the plunger rod and collet assembly of Figure 18 in the fifth auto-injector of Figure 11;

Figures 24a to 24e show sectional views from the side of the fifth auto-injector of Figure 11 during sequential use steps thereof;

Figures 25a and 25b show top views of an expanding collet for use in alternative coupling/decoupling mechanisms of auto-injectors herein with the lugs thereof respectively shown in the 'lugs in' and 'lugs out' positions;

Figures 26a and 26b show top views of an expanding collet of Figures 25a and 25b as respectively shown in the 'lugs in' and 'lugs out' positions;

Figure 27 shows in sectional and perspective views details of a slot and key mechanism for orienting a plunger rod for use in an auto-injector herein;

Figures 28a to 28c show part cut-away side views of an alternative inner housing sleeve and its relationship with the plunger rod and collet assembly of an auto-injector herein during sequential use steps thereof;
Figure 29 shows an exploded part-sectional view of the front part of the fifth auto-injector device of Figure 11 during an assembly step thereof; and

Figure 30 shows in sectional and perspective views details of an alternative slot and key mechanism for orienting a plunger rod for use in an auto-injector herein.

Referring now to the drawings, Figure 1 shows a first auto-injector device 1 herein that is arranged for use with a syringe 10 that contains a liquid drug formulation 5. As shown at Figure 1, the device 1 is provided with a removable cap 60 that is shown in the capped position. Figure 2a shows the auto-injector device 1 with the cap 60 removed, which cap 60 is shown separately and in more detail in Figure 2b.

The auto-injector device 1 comprises a generally cylindrical form housing 20 that is arranged for receipt of the syringe 10 and is sized and shaped for this purpose.

The syringe 10 comprises a barrel 12 for holding the liquid drug formulation 5; a hollow needle 14 at one end of the barrel 12; and a syringe plunger 18 in the form of a rubber stopper that is arranged for axial movement (e.g. in response to plunging motion of plunger 16) within the barrel 12 such as to enable the liquid drug formulation 5 to be expelled through the hollow needle 14. The hollow needle 14 defines a needle bore, which is of circular cross-section (e.g. 23G, 25G or 27G bore diameter) and a needle tip 15.

The housing 20 of the auto-injector device 1 defines a housing cavity within which the syringe 10 is received. In more detail, the housing 20 of the auto-injector defines a barrel receiving cavity 22, plunger receiving cavity 23 and needle receiving cavity 24. The needle receiving cavity 24 is provided with a needle delivery aperture 25 through which in use, the hollow needle 14 of the
syringe 10 may protrude from the housing 20. It may be seen that the inner wall 26 of needle receiving cavity 24 part of the housing 20 tapers inwardly to define a needle delivery aperture 25 of reduced diameter compared to the diameter of the needle receiving cavity 24.

In a subtle aspect, the housing 20 may be seen to comprise initially separate front 27 and rear 28 parts that mate at screw-threaded fitting 29. In alternative embodiments, a snap-fitting may instead be employed between the front 27 and rear 28 housing parts. Such a two-part 27, 28 initial structure has been found to be useful from an assembly standpoint in that it allows for ready assembly of parts into the housing 20. However, in both rest and use modes of operation the separate housing parts 27, 28 are joined together and indeed, the screw-fitting 29 may in aspects, be configured for permanent attachment to prevent any dis-assembly thereof. The housing 20 also comprises inner housing sleeve 21.

Referring now in particular to Figure 2b, the removable cap 60 may be appreciated to function such as to close off, the needle delivery aperture 25 (i.e. as shown at Figure 1). Projecting into the cap 60 interior, from the top inner surface 61 thereof, there is provided a needle cover 70 comprising a natural or synthetic rubber needle sheath 72 that is arranged in the rest configuration of Figure 1 for sheathed sealing of the needle tip 15. That needle sheath 72 is also provided with a sheath shell 74 (e.g. of polypropylene), one purpose of which is to add rigidity and to reduce the tendency of the needle sheath 72 to flex away from the axis defined by the needle 14. The needle sheath 72 and sheath shell 74 are further provided with a needle sheath cover 76 that at its forward end projects away from the top inner surface 61 of the cap 60 and at its rear end defines hooks 77 arranged for gripped receipt of the sheath shell 74 and needle sheath 72. Thus overall, the needle cover 70 comprises needle sheath 72; needle sheath shell 74; and needle sheath cover 76 parts, all of which are defined as an inner extending part of the removable cap 60. The needle sheath
72 is also provided with a polypropylene end ring 78, which comprises an integral moulded part of needle sheath shell 74 and which assists in maintaining rigidity of the rear end portion thereof.

The needle receiving cavity part 24 of the housing 20 is provided at the inner wall thereof with a flexible element in the form of an O-ring 80 comprised of a plastic polymer or natural or synthetic rubber material. An outer ring circumference of that O-ring 80 attaches to the inner wall of the housing 20. In the rest configuration of Figure 1, the inner ring circumference 82 thereof contacts the needle sheath cover 76 part of the needle cover 70 and is somewhat compressed (i.e. tensed) inwards as a result of that contact, the effect of which contact is to thereby restrict movement of the needle cover 70. In the 'cap removed' configuration of Figure 2a, the cap 60 and needle cover 70 are removed to open up the needle delivery aperture 25. In the absence of compressive contact with the needle cover 70, the O-ring 80 expands outwards into the needle receiving cavity 24 to provide a barrier surface 83 at its syringe-facing wall. The barrier surface 83 may thus, act such as to obstruct the exit of the syringe barrel 12 from the housing cavity 24. This barrier function is assisted by the fact that the diameter of the uncompressed (i.e. as in the 'ready to use' configuration of Figure 2a) inner ring circumference 82 of the O-ring 80 is less than the diameter of the syringe barrel 12 such that the syringe barrel 12 is unable to pass through the uncompressed O-ring 80. In the event of fracture of the syringe 10, the O-ring 80 thus, acts to obstruct passage of any syringe 10 fragments through the needle delivery aperture 25, and thereby protects the patient from harm.

Figure 7 shows another form of removable cap 160 and needle cover 170 arranged for use with the first auto-injector device 1 of Figure 2a (i.e. as an alternative to the removable cap of Figure 2b). Some of the features of that device are also visible in Figure 7.
As previously, the removable cap 160 may be appreciated to function such as to
close off, the needle delivery aperture 25 of the device 1. Projecting into the cap
160 interior, from the top inner surface 161 thereof, there is provided a needle
cover 170 comprising a natural or synthetic rubber needle sheath 172 that is
arranged in the rest configuration (as shown at Figure 7) for sheathed sealing of
the needle tip 15. That needle sheath 172 is also provided with a polypropylene
sheath shell 174, one purpose of which is to add rigidity and to reduce the
tendency of the needle sheath 172 to flex away from the axis defined by the
needle 14. The needle sheath 172 and sheath shell 174 are further provided
with a needle sheath cover 176 that at its forward end projects away from the
top inner surface 161 of the cap 160 and at its rear end defines hooks 177
arranged for gripped receipt of a polypropylene end ring 178 provided to the
needle sheath 172. It is this different gripping arrangement of the hooks 177 that
mainly distinguishes this cap 160 over that shown in Figure 2b. Overall, the
needle cover 170 comprises needle sheath 172; needle sheath shell 174; and
needle sheath cover 176 parts, all of which are defined as an inner extending
part of the removable cap 160. Again, as previously described, in the use
configuration the needle cover 170 contacts the O-ring 80, which compresses
(i.e. tenses) inwards and thereby, acts such as to restrict movement of the
needle cover 170.

Figures 8 to 10 show views of the detail of front parts of second to fourth auto-
injector devices herein as shown absent any needle cover, which differ from the
first auto-injector device 1 of Figure 1 only in that alternative arrangements or
types of flexible element, are used instead of the O-ring 80 shown at the
position of Figure 1.

Thus, in Figure 8 the housing 220 is again provided with a flexible element in the
form of an O-ring 280 comprised of a natural or synthetic rubber material, but
that O-ring 280 locates in the needle receiving cavity 224 of the housing 220 at a position that is further away from the needle delivery aperture 225 and closer to the barrel 216 of the syringe 210. As before, in the use configuration as shown in Figure 8, the O-ring 280 extends outwards into the needle receiving cavity 224 to provide a barrier surface 283 at its syringe-facing wall.

In Figure 9 the housing 320 is provided with a flexible element in the form of an protruding limb 380 with 'lollipop' head 381 that is suitably comprised of a natural or synthetic rubber material. That protruding limb 380 locates in the needle receiving cavity 324 of the housing 320 at a position that is spaced from the needle delivery aperture 325 and relatively close to the barrel 316 of the syringe 310. As before, in the use configuration as shown in Figure 9, the limb 380 extends into the needle receiving cavity 324 such as to provide a barrier surface 383 at the syringe-facing part of the head thereof.

In Figure 10 the housing 420 is provided with a flexible element in the form of a flexible finger 480 that is suitably comprised of a plastic polymer material. That flexible finger 480 locates in the needle receiving cavity 424 of the housing 420 at a position that is spaced from the needle delivery aperture 425 and relatively close to the barrel 416 of the syringe 410. As before, in the use configuration as shown in Figure 10, the flexible finger 480 extends into the needle receiving cavity 424 such as to provide a barrier surface 483 at the syringe-facing part of the finger tip end 483 thereof.

It will be appreciated that for ease of assembly the flexible elements 80; 280; 380; 480 of each of the first to fourth devices 1 are arranged such that when a needle cover 70; 170 is inserted into the housing 20; 220; 320; 420 for sheathing of the needle tip 15, part thereof interacts with the flexible elements 80; 280; 380; 480 such that these flex (or compress) towards the inner wall of the housing. On completion of that insertion step (i.e. in the rest configuration)
the flexible elements 80; 280; 380; 480 are thus, in a somewhat tensed state, which better acts such as to impact on thus, restrict movement of the needle cover 70; 170. Conversely, on removal of the needle cover 70; 170 during a use operation the flexible elements 80; 280; 380; 480 flex (or compress) away from the inner wall of the housing 20; 220; 320; 420, and thus further into the housing cavity.

Returning now to Figures 1 and 2a, the rear part 28 of the housing 20 may be seen to be provided with an inner housing sleeve 21 that screw or snap fixes to the front part 27 of the housing. A barrel sleeve 30 having front tapered 31 and rear 32 flanges is provided within the inner housing sleeve 21 at a position corresponding to the barrel receiving part 22. The barrel sleeve 30 is cylindrical and arranged for receipt of the syringe barrel 12, wherein an end circular barrel lip 13 of the syringe barrel 12 seats between the rear flange 32 thereof and a washer 34 provided to the inner housing sleeve 21. In embodiments, the barrel lip 13 may be of truncated circular or other suitable form. Light compression return spring 36 fits over a rearmost part of the barrel sleeve 30 such that a first spring end thereof contacts the rear flange 32 of the barrel sleeve 30 and a second spring end thereof contacts a rigid washer 35 provided exterior to the barrel sleeve 30 and interior to the inner housing sleeve 21. In the 'at rest' configuration (e.g. of Figure 1), the rigid washer 35 also seats up against the rear perpendicular face of tapered flange 38, which protrudes from the inner housing sleeve 21. Overall, the effect is that in the rest configuration, the barrel sleeve 30 may reciprocate within the inner housing sleeve 21 under the influence of the return spring 36. As is described in more detail hereinafter, during actuation of the syringe 10 the biasing action of the light compression return spring 36 is overcome and the syringe barrel 12 and needle 14 move axially such that the tip 15 of the needle 14 protrudes out through the delivery aperture 25 of the needle-receiving part 24 of the housing 20 to enable the liquid drug formulation 5 to be delivered by injection to a patient.
The syringe barrel 12 is provided with a syringe plunger 18, which abuts but is not otherwise connected to the forward end 17 of plunger rod 16. It may be appreciated that in general terms, actuation of the syringe 10 occurs in response to plunging of the plunger rod 16 against the rubber plunger 18, thereby plunging both 16, 18 of the parts into the barrel 12 of the syringe 10, which cause the liquid drug formulation 5 to be expelled through the tip 15 of the hollow needle 14. By not physically attaching the plunger rod 16 to the rubber plunger 18 it means that the syringe 10 can move in the housing 20 with respect to the plunger rod 16, but without risk of pulling the rubber plunger 18 from the syringe barrel 12, which may risk breach of sterility or leakage of liquid drug formulation 5 contents therefrom.

The auto-injector device 1 is provided with both an actuating mechanism and an after use, locking mechanism, both of which are now described in more detail.

The actuating mechanism of the auto-injector device 1 comprises a strong drive compression spring 40 that fits around the rear end of the plunger rod 16 and seats at a rear spring end thereof against the end wall 21a of the inner sleeve housing and at a front end thereof against washer 43 and rear collet 42. The rear collet 42 mounts (but, in a de-mountable sense as described hereinafter) by peg elements 47 thereof to the plunger rod 16 such that spring force experienced thereby will cause plunging of the rod 16 towards the rubber plunger 18 of the syringe 10. Such movement of the plunger rod is normally prevented by push trigger release 48, which in a non-trigger released position (e.g. of Figures 1, 2a and 3) seats firmly within rear notch 19 of the plunger rod 16.

The plunger rod 16 is also provided with front collet 44, which mounts (but, in a de-mountable sense as described hereinafter) by peg elements 45 thereof to the
plunger rod 16 at a forward position thereof. In the rest position, the front collet 44 seats up against washer 34, which in turn seats against end circular barrel lip 13 of the syringe barrel 12. The effect is that during actuation, when the plunger rod 16 plunges forward the collet 44 (when so-mounted) also moves forward to drive the washer 34 and syringe barrel 12 forward.

The de-mounting mechanism of the front collet 44 is now described: Thus, the front collet 44 is provided with two or more lugs 50 disposed arranged around its circumference, which in the 'rest' configuration engage in tracks 52 (e.g. slot or groove form) provided to the inner sleeve housing 21. These tracks 52 define straight paths running parallel to the axis of the syringe 10 for the most of the length, but at the forward part thereof define a helical path, which serves to rotate the front collet 44 to disengage the peg elements 45 from the plunger rod 16 such that the front collet 44 is now dismounted from the plunger rod 16. The effect of this dismounting is that further forward plunging movement of the plunger rod 16 no longer results in forward movement of the washer 34 and syringe barrel 13, but rather only plunges the rubber syringe plunger 18 forward for expelling the liquid drug formulation 5 contents of the syringe barrel 12 through the tip 15 of the hollow needle 14. Once the front collet 44 dismounts from the plunger rod 16 it may engage in a further straight slot track (not visible) provided to the inner housing sleeve 21.

Thus overall, the front collet 44 and straight/helical track 52 mechanism described above facilitates a two-stage actuating process. In the first stage, when the front collet 44 mounts to the plunger rod 16, release of spring force from the strong spring 40 to move the rear collet 42, washer 43 and plunger rod 16 forward also causes the syringe 10 to be advanced to move the needle tip 15 thereof through the needle delivery aperture 25 to a delivery position. In the second stage, when the front collet 44 has become dismounted from the plunger rod 16, further forward movement of the plunger rod 16 only causes plunging of
the rubber plunger 18 within the syringe barrel 12 to cause delivery of liquid drug formulation 5 from the syringe 10.

In a detailed aspect, the rear collet 42 is also provided with two or more lugs 55 disposed arranged around its circumference, which in the rest configuration engage in tracks 56 (e.g. slot or groove form) provided to the inner sleeve housing 21. These tracks 56 define straight paths running parallel to the axis of the syringe 10 for the most of the length, but at the forward part thereof define a helical path, which serves to rotate the rear collet 42 to disengage the peg elements 47 from the plunger rod 16 at the end of the injection stroke such that the rear collet 44 is now dismounted from the plunger rod 16. It will be appreciated that the dismounting of the rear collet 44 occurs at a later stage (i.e. at end of injection stroke) than the similar dismounting of the front collet 42 (i.e. at the point at which the needle tip 15 protrudes from the needle delivery aperture 25, but prior to dispensing of liquid drug formulation 5 therefrom. Once both collets 42, 44 are dismounted the plunger rod 16 is released from the influence of the strong drive spring 40, and the syringe 10 may thus, be returned to its rest position or beyond under the action of the return spring 36.

Further details of exemplary straight/helical track 52, 56; 552; 556; 852; 856 mechanisms are described later by reference to Figures 22, 23 and 28a to 28c in relation to other auto-injectors herein. These track arrangements 552; 556; 852; 856 may in embodiments, be applied to the first auto-injector of Figures 1 to 6 and variants thereof.

To reduce frictional effects the collets 42, 44 are ideally provided with domed contact surfaces and washers 43, 34 are ideally smooth. Low frictional materials are ideally used for these components e.g. fluorine polymers such as PTFE, ETFE or polyamides.
In an alternative embodiment, the mounting / demounting of the plunger rod 16 to the collets 42, 44 may be achieved by use of an expanding collet, which expands into a ring shaped recess in the inner housing sleeve 21 to dismount from the plunger rod 16. Suitable expanding collet forms are described hereinafter with reference to Figures 25a to 26b.

A return locking mechanism is also provided to the auto-injector device 1 herein. Thus, the inner housing 21 is provided with a tapered locking flange 39 (e.g. tooth-like) that in the 'syringe retracted and locked' after use position of Figure 6 engages in locking fashion behind tapered flange (e.g. tooth-like) 39 on the inner housing sleeve 21.

Further aspects of the auto-injector device 1 herein may now be appreciated by reference to the following description of a typical use operation.

In a first stage of a typical use operation, the cap 60 is removed from the capped position of Figure 1 via the cap 60 part-removed position of Figure 3 to the cap removed position of Figures 2a and 2b to uncover the needle delivery aperture 25. During the cap 60 removal process it will be seen at Figure 3 that the outer circumference 82 of the O-ring 80 urges (i.e. pushes in) against the needle sheath cover 76 to urge (i.e. push) hooks 77 thereof more deeply into the needle sheath 72. The result is enhanced gripping contact between the hooks 77 and needle sheath 72 during the cap 60 removal operation to thereby, better ensure that the needle sheath 72 unsheathes from the needle tip 15 during this cap 60 removal operation. Once the cap 60 has been removed and in the absence of the needle cover 70, the O-ring 80 expands into the needle receiving cavity 24. As previously described, in this 'ready to use' position the syringe barrel 30 is movable in reciprocating fashion in an axial sense, but subject to the action of the light return spring 36.
In a second use stage, the trigger 48 is released by decoupling from the rear notch 19 of the plunger rod 16. Under the action of the strong spring 40, the washer 43, plunger rod 16 and front 44 and rear 42 collets thereof, and syringe 10 are driven forward to a 'ready to inject' position as shown in Figure 4, in which the needle tip 15 of the syringe protrudes from the needle delivery aperture 25. At this position, the front collet 44 demounts from the plunger rod 16 as a result of the straight/helical track 52 mechanism described above.

In a third use stage, under the continuing action of the strong spring 40, the plunger rod 16 is propelled further forward and plunges the rubber plunger 18 into the syringe barrel 12 to cause delivery of liquid drug formulation 5 from the syringe 10 in a 'delivery' phase. After complete delivery (i.e. at the 'post-injection' position of Figure 5), the rear collet 42 also demounts from the plunger rod 16 as a result of the straight/helical track 56 mechanism described above. The plunger rod 16 may now move freely, and outwith the action of the strong spring 40.

In a fourth use stage, the syringe barrel sleeve 30 experiences the return spring force of the light spring 36 and is propelled rearwards and thereby, also moves the syringe barrel 12 rearwards such that the needle tip 15 is brought back within the needle receiving cavity 24 to the 'syringe retracted and locked' position of Figure 6. Tapered front flange 31 of the barrel sleeve 30 moves over and behind tapered locking flange 39 of the inner housing sleeve 21 such that forward movement of the barrel sleeve 30 is locked. In this position it will be appreciated that syringe 10 is also locked such that the needle tip 15 does not protrude from the needle delivery aperture 25, but rather is safely housed away.

Thus, it will be appreciated that the first auto-injector device 1 includes a locking mechanism 31, 39 for locking the syringe 10 into the syringe retracted and locked position of Figure 6. Further, in this retracted and locked position, it will
be seen that return spring 36 acts such as to bias the syringe barrel sleeve 30 and syringe 10 coupled thereto away from the use position and towards the locking engagement of tapered front flange 31 with tapered locking flange 39. It will also be appreciated that in the rest position, the tapered flange (e.g. tooth-like) 31 on the syringe barrel sleeve 30 is in front of the tapered flange (e.g. tooth-like) 39 on the inner housing sleeve 21 and so the syringe 10 and barrel sleeve 30 can move forward without interference.

Figures 11 to 23 show aspects of a fifth auto-injector herein that may be appreciated to be a variant of the first auto-injector of Figures 1 to 6 and one that employs a similar modus of operation.

Figure 11 shows the outer form of the fifth auto-injector device 501, which defines a generally cylindrical form housing 520 and removable cap 560 provided thereto. Release trigger 548 may be seen to protrude from the rear of the housing 520. The housing 520 is also provided with a viewing window 502 that is of sufficient length such that when the syringe 510 is in both the rest and retract positions the barrel 512 thereof is in registration therewith. By constructing the syringe barrel sleeve 530 of a clear (e.g. colourless material) it means that a user may view the contents of the syringe barrel 512 through the viewing window 502 in both of these positions.

Referring now also to Figures 12 to 14, the fifth auto-injector device 501 is seen to comprise a generally cylindrical form housing 520 that is arranged for receipt of a syringe 510 containing a liquid drug formulation 505. The syringe 510 comprises a barrel 512 for holding the liquid drug formulation 505; a hollow needle 514 at one end of the barrel 512; and a syringe plunger 518 in the form of a rubber stopper that is arranged for axial movement (e.g. in response to plunging motion of plunger rod 516) within the barrel 512 such as to enable the liquid drug formulation 505 to be expelled through the hollow needle 514. The
hollow needle 514 defines a needle bore, which is of circular cross-section (e.g. 23G, 25G or 27G bore diameter) and a needle tip 515.

The housing 520 of the auto-injector device 501 defines a housing cavity within which the syringe 510 is received. In more detail, the housing 520 of the auto-injector defines a barrel receiving cavity 522, plunger rod receiving cavity 523 and needle receiving cavity 524. The needle receiving cavity 524 is provided with a needle delivery aperture 525 through which in use, the hollow needle 514 of the syringe 510 may protrude from the housing 520. It may be seen that the inner wall 526 of needle receiving cavity 524 part of the housing 520 has a stepped form such as to define a needle delivery aperture 525 of reduced diameter compared to the diameter of the needle receiving cavity 524.

In a subtle aspect, the housing 520 may be seen to comprise initially separate front 527 and rear 528 parts that mate at fitting 529. Such a two-part 527, 528 initial structure has been found to be useful from an assembly standpoint in that it allows for ready assembly of parts into the housing 520. However, in both rest and use modes of operation the separate housing parts 527, 528 are joined together and indeed, the fitting 529 may in aspects, be configured to prevent disassembly thereof. The housing 520 also comprises inner housing sleeve 521, which will be described in more detail hereinafter with particular reference to Figures 22 and 23.

Referring now in particular to Figure 14, the removable cap 560 may be appreciated to function such as to close off, the needle delivery aperture 525 (i.e. as shown at Figures 12 to 14). Projecting into the cap 560 interior, from the top inner surface 561 thereof, there is provided a needle cover 570 comprising a natural or synthetic rubber needle sheath 572 that is arranged in the rest configuration for sheathed sealing of the needle tip 515. That needle sheath 572 is also provided with a sheath shell 574 (e.g. of polypropylene), one purpose of
which is to add rigidity and to reduce the tendency of the needle sheath 572 to flex away from the axis defined by the needle 514. The needle sheath 572 and sheath shell 574 are further provided with a needle sheath cover 576 that at its forward end projects away from the top inner surface 561 of the cap 560 and at its rear end defines hooks 577 arranged for gripping receipt of the sheath shell 574 and needle sheath 572. Thus overall, the needle cover 570 comprises needle sheath 572; needle sheath shell 574; and needle sheath cover 576 parts, all of which are defined as an inner extending part of the removable cap 560. The needle sheath 572 is also provided with a polypropylene end ring 578, which comprises an integral moulded part of needle sheath shell 574 and which assists in maintaining rigidity of the end portion thereof.

The needle receiving cavity part 524 of the housing 520 is provided adjacent the stepped inner wall 526 thereof with a flexible element in the form of an O-ring 580 comprised of a plastic polymer or natural or synthetic rubber material. An outer ring circumference of that O-ring 580 attaches to the inner wall of the housing 520. In the rest configuration of Figures 12 to 14, the inner ring circumference 582 thereof contacts the needle sheath cover 576 part of the needle cover 570 and is somewhat compressed (i.e. tensed) inwards as a result of that contact, the effect of which contact is to thereby restrict movement of the needle cover 570. In the use configuration, the cap 560 and needle cover 570 are removed to open up the needle delivery aperture 525. In the absence of compressive contact with the needle cover 570, the O-ring 580 expands outwards into the needle receiving cavity 524 to provide a barrier surface 583 at its syringe-facing wall. The barrier surface 583 may thus, act such as to obstruct the exit of the syringe barrel 512 from the housing cavity 524. This barrier function is assisted by the fact that the diameter of the uncompressed inner ring circumference 582 of the O-ring 580 is less than the diameter of the syringe barrel 512 such that the syringe barrel 512 is unable to pass through the uncompressed O-ring 580. In the event of fracture of the syringe 510, the O-ring
580 thus, acts to obstruct passage of any syringe 510 fragments through the needle delivery aperture 525, and thereby protects the patient from harm.

For ease of assembly the flexible O-ring element 580 of the fifth auto-injector device 501 is arranged such that when needle cover 570 is inserted into the housing 520 for sheathing of the needle tip 515, part thereof interacts with the flexible element 580 such that this flexes (or compresses) towards the inner wall of the housing 520. On completion of that insertion step (i.e. in the rest configuration) the flexible O-ring element 580 is thus, in a somewhat tensed state, which better acts such as to impact on thus, restrict movement of the needle cover 570. Conversely, on removal of the needle cover 570 during a use operation the flexible O-ring element 580 flexes (or compresses) away from the inner wall of the housing 520 and thus further into the housing cavity.

Figure 29 shows a detail of the assembly of the front part of the fifth auto-injector device 501. Thus, the syringe 510 and syringe barrel sleeve 530 are within the rear part 528 of the housing 520. The needle cover 570 comprising needle sheath 572; needle sheath shell 574; and needle sheath cover 576 parts has been provided to sheath the needle tip (not visible in Figure 29). The flexible O-ring element 580 has been provided around the needle cover 570, and in particular interacts with the needle sheath cover 576. In a first subsequent assembly step, this whole sub-assembly is inserted into the front part 527 of the housing 520. During this insertion the flexible element 580 flexes (or compresses) towards the inner wall of the front part 527 of housing 520 and eventually seats against the stepped part 526 of that inner wall. It will be appreciated that as a result of this tensing of the flexible O-ring element 580 inwards pressure is applied to the needle sheath cover 576, which also flexes inwards such that the hook elements 577 thereof (see Figures 12 to 14) grip the needle sheath 572. The cap 560 is then placed in the capped position and peg 562 is used to secure the needle sheath cover 576 to the inner top surface 561.
of the cap 560 (see also Figures 12 to 14). In alternative embodiments, the front and/or rear parts 528, 529 of the housing may have clam-shell form (e.g. having a longitudinal split between the clam-shell halves) and be arranged for clam-shell fixing (e.g. by snap-fitting) together during assembly of the device 501.

The rear part 528 of the housing 520 may be seen to be provided with an inner housing sleeve 521 that fixes to the front part 527 of the housing 520. A barrel sleeve 530 having front 531 and rear 532 flanges is provided within the inner housing sleeve 521 at a position corresponding to the barrel receiving part 522. The barrel sleeve 530 is cylindrical and arranged for receipt of the syringe barrel 512, wherein an end circular barrel lip 513 of the syringe barrel 512 seats between the rear flange 532 thereof and the inner housing sleeve 521. In embodiments, the barrel lip 513 may be of truncated circular or other suitable form. Light compression return spring 536 fits over a rearmost part of the barrel sleeve 530 such that a first spring end thereof contacts the rear flange 532 of the barrel sleeve 530 and a second spring end thereof contacts a rigid washer 535 provided exterior to the barrel sleeve 530 and interior to the inner housing sleeve 521. In the rest configuration the rigid washer 535 also seats up against the rear perpendicular face of tapered flange 538, which protrudes from the inner housing sleeve 521. Overall, the effect is that in the rest configuration, the barrel sleeve 530 may reciprocate within the inner housing sleeve 521 under the influence of the return spring 536. As is described in more detail hereinafter, during actuation of the syringe 510 the biasing action of the light compression return spring 536 is overcome and the syringe barrel 512 and needle 514 move axially such that the tip 515 of the needle 514 protrudes out through the delivery aperture 525 of the needle-receiving part 524 of the housing 520 to enable the liquid drug formulation 505 to be delivered by injection to a patient.

The syringe barrel 512 is provided with a rubber plunger 518, which may abut, but is not otherwise connected to, the forward end 517 of plunger rod 516. It
may be appreciated that in general terms, actuation of the syringe 510 occurs in response to plunging of the plunger rod 516 against the rubber plunger 518, thereby plunging both 516, 518 of the parts into the barrel 512 of the syringe 510, which causes the liquid drug formulation 505 to be expelled through the tip 515 of the hollow needle 514. By not physically attaching the plunger rod 516 to the rubber plunger 518 it means that the syringe 510 can move in the housing 520 with respect to the plunger rod 516, but without risk of pulling the rubber plunger 518 from the syringe barrel 512, which may risk breach of sterility or leakage of liquid drug formulation 505 contents therefrom.

The auto-injector device 501 is provided with both an actuating mechanism and an after use, locking mechanism, both of which are now described in more detail.

Referring now also to Figures 15 to 20, the actuating mechanism of the auto-injector device 501 comprises a strong drive compression spring 540 that fits around the rear end of the plunger rod 516 and seats at a rear spring end thereof against the end wall 521a of the inner sleeve housing and at a front end thereof against rear collet 542. The rear collet 542 mounts (but, in a de-mountable sense as described hereinafter) by peg elements 547 thereof to front collar mount 591 of the plunger rod 516 such that spring force experienced thereby will cause plunging of the rod 516 towards the rubber plunger 518 of the syringe 510. Such movement of the plunger rod is normally prevented by push trigger release 548, which in a non-trigger released position (e.g. of Figures 12 to 14) seats firmly within rear notch 519 of the plunger rod 516.

Referring now also to Figure 21, the plunger rod 516 is also provided with front collet 544, which mounts (but, in a de-mountable sense as described hereinafter) by peg elements 545 thereof to rear collar mount 592 of the plunger rod 516 at a forward position thereof. In the rest position, the front collet 544
seats up against end circular barrel lip 513 of the syringe barrel 512. The effect is that during actuation, when the plunger rod 516 plunges forward the collet 544 (when so-mounted) moves forward to also drive the syringe barrel 512 forward.

The de-mounting mechanism of the front collet 544 is now described by reference now also to Figures 22 and 23: Thus, the front collet 544 is provided with two or more lugs 550 disposed arranged around its circumference, which in the rest configuration engage in slot form tracks 552 provided to the inner sleeve housing 521. These tracks 552 define helical paths running parallel to the axis of the syringe 510, which serve to rotate the front collet 544 to disengage the peg elements 545 from the plunger rod 516 such that the front collet 544 is now dismounted from the front collar mount 591 of the plunger rod 516. The effect of this dismounting is that further forward plunging movement of the plunger rod 516 no longer results in forward movement of the syringe barrel 513, but rather only plunges the rubber syringe plunger 518 forward for expelling the liquid drug formulation 505 contents of the syringe barrel 512 through the tip 515 of the hollow needle 514.

Thus overall, the front collet 544 and helical track 552 mechanism described above facilitates a two-stage actuating process. In the first stage, when the front collet 544 mounts to the plunger rod 516, release of spring force from the strong spring 540 to move the rear collet 542 and plunger rod 516 forward also causes the syringe 510 to be advanced to move the needle tip 515 thereof through the needle delivery aperture 525 to a delivery position. In the second stage, when the front collet 544 has become dismounted from front collar mount 591 of the plunger rod 516, further forward movement of the plunger rod 516 only causes plunging of the rubber plunger 518 within the syringe barrel 512 to cause delivery of liquid drug formulation 505 from the syringe 510.
In a detailed aspect, the rear collet 542 is also provided with two or more lugs 555 disposed arranged around its circumference, which in the rest configuration engage in slot form helical tracks 556 provided to the rear of the inner sleeve housing 521. These helical tracks 556 serve to rotate the rear collet 542 to disengage the peg elements 547 from the rear collar mount 592 of the plunger rod 516 at the end of the injection stroke such that the rear collet 544 is now dismounted from the plunger rod 516. It will be appreciated that the dismounting of the rear collet 544 occurs at a later stage (i.e. at end of injection stroke) than the similar dismounting of the front collet 542 (i.e. at the point at which the needle tip 515 protrudes from the needle delivery aperture 525, but prior to dispensing of liquid drug formulation 505 therefrom. Once both collets 542, 544 are dismounted from their respective collar mounts 591, 592 the plunger rod 516 is released from the influence of the strong drive spring 540, and the syringe 510 may thus, be returned to its rest position or beyond under the action of the return spring 536.

To reduce frictional effects the collets 542, 544 are ideally provided with domed contact surfaces and are ideally smooth. Low frictional materials are ideally used for these components e.g. fluorine polymers such as PTFE, ETFE or polyamides.

In an alternative embodiment, the mounting / demounting of the plunger rod 516 to the collets 542, 544 may be achieved by use of an expanding collet, which expands into a ring shaped recess in the inner housing sleeve 521 to dismount from the plunger rod 516. Suitable expanding collet forms are described hereinafter with reference to Figures 25a to 26b.

A return locking mechanism is also provided to the fifth auto-injector device 501 herein. Thus, the barrel sleeve 530 is provided with a tapered locking flange 539 (e.g. tooth-like) that in a 'locked after use' position engages in locking fashion
behind tapered flange 538 (e.g. tooth-like) of the inner housing sleeve 521. It may be appreciated that the tapered locking flange 539 and/or the tapered flange 538 are suitably comprised of a flexible and/or resilient material. It may also be appreciated that, although the tapered locking flange 539 is shown as a continuous circumferential flange, in other embodiments this may be replaced by an intermittent (e.g. crenellated or toothed) flange. In addition, an undercut may be provided to the tapered locking flange 539 to enhance the inward give thereof.

Further aspects of the fifth auto-injector device 501 herein may now be appreciated by reference to Figures 24a to 24e and to the following description of a typical use operation.

In a first stage of a typical use operation, the device 501 (e.g. as shown in Figure 13) is taken and the cap 560 is removed to uncover the needle delivery aperture 525 as shown at Figure 24a. In the absence of the needle cover 570, the O-ring 580 expands into the needle receiving cavity 524. As previously described, in this 'ready to use' position the syringe barrel 530 is movable in reciprocating fashion in an axial sense, but subject to the action of the light return spring 536.

In a second use stage, the trigger 548 is released by decoupling from the rear notch 519 of the plunger rod 516. Under the action of the strong spring 540, the plunger rod 516 and front 544 and rear 542 collets thereof, and syringe 510 are driven forward to a 'ready to inject' position of Figure 24b, in which the needle tip 515 of the syringe protrudes from the needle delivery aperture 525. In this position, the end-shoulder 511 of the syringe 510 seats up against the syringe-facing wall 583 of the O-ring 580, thereby acting to somewhat compress (e.g. 'squash') the O-ring 580 which thus, tends to flex inwards e.g. to block/grip the syringe 510. In alternative embodiments, a forward end of the syringe barrel 530
seats up against the syringe-facing wall 583 of the O-ring 580 in this position, which again acts such as to somewhat compress (e.g. 'squash') the O-ring 580 which thus, tends to flex inwards e.g. to block/grip the syringe 510. The syringe barrel 530 may thus, be provided with shaped end-features (e.g. lip or flange form) which facilitate this seating up against the O-ring 580 and compression thereof. Also at this 'ready to inject' position, the front collet 544 begins to demount from the front collar mount 591 of plunger rod 516 as a result of the helical track 552 mechanism described above.

In a third use stage, under the continuing action of the strong spring 540, the plunger rod 516 is propelled further forward and plunges the rubber plunger 518 into the syringe barrel 512 as shown at Figure 24c to cause delivery of liquid drug formulation 505 from the syringe 510. After complete delivery (i.e. at the 'post-injection' position of Figure 24d), the rear collet 542 also begins to demount from the rear collar mount 592 of plunger rod 516 as a result of the helical track 556 mechanism described above. The plunger rod 516 may now move freely, and outwith the action of the strong spring 540.

In a fourth use stage, the syringe barrel 530 experiences the return spring force of the light spring 536 and is propelled rearwards and thereby, also moves the syringe barrel 512 rearwards such that the needle tip 515 is brought back within the needle receiving cavity 524 to the 'syringe retracted and locked' position of Figure 24e. Tapered locking flange 539 moves over and behind tapered flange 538 of the inner housing sleeve 521 such that forward movement of the barrel sleeve 530 is locked. In this 'locking position' it will be appreciated that syringe 510 is also locked such that the needle tip 515 does not protrude from the needle delivery aperture 525, but rather is safely housed away. Further, in this retracted and locked position, it will be seen that light spring 536 acts such as to bias the syringe barrel sleeve 530 and syringe 510 coupled thereto away from
the use position and towards the locking engagement of the tapered flanges 538, 539.

In variations of the first and fifth auto-injector devices 1; 501 herein the mounting / demounting of the plunger rod 16; 516 to the front and rear collets 42, 44; 542, 544 may be achieved by use of an expanding front or rear collet, which expands into a ring shaped recess in the inner housing sleeve 21; 521 to dismount from the plunger rod 16; 516. Suitable expanding collet forms are described hereinafter with reference to Figures 25a to 26b.

Thus, ring-shaped collet 644 is provided with three dumb-bell form lugs 694 that are arranged radially at 120° radial spacing relative to each other and spring loaded by means of light lug springs 695. The lugs are movable from the 'lugs in' position of Figures 25a and 26a, in which three equally-spaced inner lug elements 645 protrude into the inner circumference thereof to the 'lugs out' position of Figures 25b and 26b, in which three equally-spaced outer lug elements 650 protrude from the outer circumference thereof.

It will be appreciated that, as before, the inner lug elements 645 are arranged for interaction with mounts (e.g. track or slot form) provided to the plunger rod 16; 516 and the outer lug elements 650 are arranged for interaction with mounts (e.g. track or slot form) provided to the inner sleeve housing 21; 521 of the device 1; 501. It will also be appreciated that the lug springs 695 tend to bias the lugs 694 to the 'lugs out' position. However, when located in the device 1; 501 the inner housing sleeve 21; 521 would tend to push them in so that they engage in mounts (e.g. track, slot or hole form) in the plunger rod 16; 516 therefore coupling to it. As described in relation to the first and fifth auto-injector devices 1; 501, the inner housing sleeve 21; 521 would have a recess, a slot or holes into which, at the desired position for de-coupling, the lugs 694 would spring outwards and de-couple from the plunger rod 16; 516, when the
expanding collet 644 reaches them. Where the expanding collet 644 is employed as the rear collet 42; 542 this action need not be reversible because this is the final position of the rear collet 42; 542. However, where the expanding collet 644 is used as the front collet 44; 544 to achieve the retraction action, the expansion of the lugs 694 would need to be reversible. This could be achieved in principle with a ramped track 52; 552 within the inner housing sleeve 21; 521 into which the outer lug elements 650 engage in so that they are progressively released/engaged depending on their position along the track 52; 552.

In an alternative to the form shown in Figures 25a to 26b, the lugs 694 could always partially protrude from the outer circumference of the collet 644 so that they could positively locate on straight slots provided on the inner housing sleeve 21; 521. In embodiments, both conventional collets and expanding collets could be used together in the same device. Thus, in embodiments there may be provided expanding collet 644 for the rear coupling and helical track and follower for the front coupling (as the reversing retracting mechanism is probably simpler in this form than with the ramped track/expanding collet). By having the expanding collet 644 coupled to the plunger rod 16; 516 and engaged in a slot 52; 552 in the inner housing sleeve 21; 521, this has the advantage of fixing the orientation of the plunger rod 16; 516, which is important for the helical track/follower mechanism: it must not rotate or else the synchronisation of the de-coupling is lost. Using the expanding collet 644 for the rear coupling may be easier to manufacture than the helical track/follower.

In developments, means may be provided for positively orientating the plunger rod 16; 516 so that it does not rotate and lose synchronisation (e.g. fail to de-couple/prematurely de-couple). Such an arrangement is particularly suitable for use with an expanding collet 644 type set-up since the expanding collets do not need to rotate for coupling/decoupling to occur. orientation means as shown in
Figure 27 may comprise an additional washer 784 (which may actually be a part of the inner housing sleeve 21; 521 made in two halves), located between the final positions of both of the collets 644 and which has a key slot 785 which engages with a rib 786 on the plunger rod 716 to form a slot and key type 785, 786 mechanism to prevent rotation of the plunger rod 716. Other elements of the auto-injector device 701 may in embodiments, correspond to those of the first or fifth auto-injector device 1; 501 herein.

In still other developments, means may be provided for positively orientating the plunger rod 16; 516 so that it might however, still rotate. Such an arrangement is particularly suitable for use with a rotating collet 42, 44; 542; 544 type set-up since these do need to rotate for coupling/decoupling to occur. Such orientation means as shown in Figure 30 may comprise an additional washer 984 (which may actually be a part of the inner housing sleeve 21; 521 made in two halves), located between the final positions of both of the collets 542, 544 and which has a rib 986 protruding into the circular aperture thereof, and which engages with a key slot 985 on the plunger rod 916 to form a slot and key type 985, 986 mechanism that allows for rotation of the plunger rod 716. Other elements of the auto-injector device 901 may in embodiments, correspond to those of the first or fifth auto-injector device 1; 501 herein.

The fifth auto-injector device 501 includes a locking mechanism 538, 539 for locking the syringe 510 into the syringe retracted position. In the rest position, the tapered flange (e.g. tooth-like) 539 on the syringe barrel sleeve 530 are in front of the tapered flange (e.g. tooth-like) 538 on the inner housing sleeve 521 and so the syringe 510 and barrel sleeve 530 can move forward without interference. In embodiments, the initial position of the syringe barrel sleeve 530 is defined by the equilibrium of the two sets of flanges 538, 539 resting against each other, under the action of the return spring 536.
In other embodiments, the plunger rod 16; 516 and front collet/follower 42, 542; 45; 545 may be arranged to prevent the return spring 36; 536 from pushing the syringe barrel sleeve 30; 530 any further back so there does not need to be any contact between the two sets of flanges 38, 39; 538, 539. This requires therefore that the final locked position of the syringe barrel sleeve 30; 530 lies behind the starting position. This is easily achieved by having the front follower/collet 42, 542; 45; 545 when in its starting position, not being at the rearmost end of its track 52; 552 so that on de-coupling the return spring 36; 536 can push it all of the way back (to the end of its track 52; 552), whereas in the start position it is prevented from further rearward movement by the plunger rod follower 47; 547. A suitable arrangement to achieve this purpose is shown at Figures 28a to 28c, which show an alternative inner housing sleeve 821 and its relationship to the syringe plunger 516 and lugs 550, 555 of the front and rear collets 544, 542 of the fifth auto-injector herein.

Thus, Fig 28a to 28c show the alternative inner housing sleeve provided with front slot form tracks 852 (only one visible) arranged for interaction with the lugs 550 of the front collet 544 and rear slot form tracks 856 (only one visible) arranged for interaction with the lugs 555 of the rear collet 542. The form of the rear slot form tracks 856 corresponds to those rear slot form tracks 556 previously described in relation to Figures 22 and 23. The form of the front slot form tracks 852 however, differs slightly from those of the front slot form tracks 552 previously described in relation to Figures 22 and 23 in that a heel 853 is provided thereto, wherein the heel 853 is defined by a straight form track running parallel to the principal axis (i.e. the plunging/injection axis) of the device 501.

Figure 28a shows the relationship between lug 550 of the front collet 544 when the device 501 is in the rest position. Thus, in this rest position the lug 550 is at the point where the helical track 853 meets the heel 853. Figure 28b shows the
relationship between lug 550 of the front collet 544 when the device 501 is in the 'ready to inject' and 'delivery' positions, in which the syringe 510 is moved forward and the needle tip 515 thereof protrudes from the front aperture 525.

Figure 28c shows the relationship between lug 550 of the front collet 544 when the device 501 is in the 'syringe retracted and locked' position when the syringe 510 is retracted back into the housing 510. It will be appreciated that the presence of the straight form, axially aligned track provided by the heel 853 particularly enables the syringe 510 to retract sufficiently back under the influence of the return spring 536 that it may be locked by the locking mechanism 538, 539 as previously described. It will also be appreciated that the end of the heel 853 may in embodiments, be employed to limit the extent of rearward travel. In embodiments, the opposing sets of tapered flanges 538, 539 may be arranged to snap over each other irreversibly to lock the syringe 510 and its syringe barrel sleeve 530 in its rearward position. In embodiments, at least one of the sets of teeth 538, 539 is flexible in order that they snap over each other. In embodiments, the syringe barrel sleeve 530 may be specifically oriented within the housing to make the locking mechanism work 538, 539 reliably. In particular, the inner housing sleeve 521; 821 and syringe barrel sleeve 530 may be provided with means ensuring positive alignment so that the teeth 538, 539 will engage correctly. Such alignment means may in embodiments, comprise additional slots/ribs provided to the inner housing sleeve 521; 821 and/or to the syringe barrel sleeve 530.

The auto-injector of the invention is suitable for the injected delivery of drug, particularly for the treatment and/or prophylaxis of a number of diseases, disorders or conditions, including infections (viral, e.g. HIV infection, bacterial, fungal and parasitic); endotoxic shock associated with infection; inflammatory diseases/autoimmunity such as osteoarthritis, rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus (SLE), ankylosing spondilitis, COPD, asthma, Alzheimer's Disease, Crohn's disease, ulcerative colitis, irritable bowel
syndrome and psoriasis; immune mediated inflammatory disorders of the central and peripheral nervous system such as multiple sclerosis and Guillain-Barr syndrome; graft-versus-host disease; organ transplant rejection; pain; cancer (including solid tumours such as melanomas, hepatoblastomas, sarcomas, squamous cell carcinomas, transitional cell cancers, ovarian cancers and hematologic malignancies, acute myelogenous leukaemia, chronic myelogenous leukemia, gastric cancer and colon cancer); congenital disorders, e.g. cystic fibrosis and sickle cell anaemia; growth disorders; epilepsy; treatment of infertility; heart disease including ischaemic diseases such as myocardial infarction as well as atherosclerosis and intravascular coagulation; bone disorders such as osteopenia and osteoporosis; and metabolic/idiopathic disease, e.g. diabetes.

Appropriate drugs may thus be selected from biologically active agents, including chemical entities, polysaccharides, steroids and, especially, naturally occurring and recombinant proteins, including glycoproteins, polypeptides and oligopeptides and polymeric derivatives thereof. Particular proteins, polypeptides and oligopeptides include hormones, such as insulin, epinephrine, norepinephrine, adrenocorticotropic, somatotropin, erythropoietin and oxytocin; cytokines, such as lymphokines, chemokines and interleukins and receptors therefor, e.g. interleukin (IL)-1α, IL-1β, IL-1R, IL-2, IL-3, IL-4, IL-5, IL-6, IL-13, IL17, interferon (IFN)-α, IFN-β, IFN-γ, granulocyte monocyte colony stimulating factor, tumour necrosis factor-α; growth factors, such as nerve growth factor and platelet-derived growth factor; enzymes, such as tissue plasminogen activator; and, especially, immunoglobulins. Immunoglobulins include whole antibodies and functionally active fragments and/or derivatives thereof, for example polyclonal, monoclonal, recombinant, multi-valent, mono- or multi-specific, humanised or chimeric antibodies, single chain antibodies, Fab fragments, Fab' and F(ab')2 fragments. Polymeric derivatives of such proteins, polypeptides and oligopeptides include derivatives formed between the protein, polypeptide or
oligopeptide and a naturally occurring or synthetic polymer, e.g. a polysaccharide or a polyalylklene polymer such as a poly(ethylene glycol) [PEG] or derivative thereof, e.g. methoxypoly(ethylene glycol) [mPEG]. Particular agents include growth hormones and hormones for the treatment of infertility.

Other particular agents are for the treatment of epilepsy such as brivaracetam and seletracetam.

The auto-injector device herein has been found to be of particular utility where the drug is an immunoglobulin or a fragment thereof, especially a PEGylated or mPEGylated antibody fragment.

The liquid drug formulations herein are typically aqueous formulations, which comprise the drug in solution and additionally other optional formulation components, which may include buffers (e.g. lactate, acetate), NaCl, and pH modifiers (e.g. NaOH).

The auto-injector device herein has been found to be of particular utility wherein the concentration of the drug (e.g. a therapeutic biologic type drug) in the liquid drug formulation is quite high. In particular, where the drug is a pegylated antibody the auto-injector device has been found to be of particular utility wherein the concentration of the drug is greater than 100mg/ml, particularly greater than 150mg/ml such as 200mg/ml.

It will be understood that the present disclosure is for the purpose of illustration only and the invention extends to modifications, variations and improvements thereto.

The application of which this description and claims form part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or combination of
features described therein. They may take the form of product, method or use claims and may include, by way of example and without limitation, one or more of the following claims:
Claims

1. An auto-injector comprising

   a housing defining a housing cavity arranged for receipt of a syringe comprising
   a barrel for containing a volume of a liquid drug formulation;

   a hollow needle at a front end of said barrel, said hollow needle defining a needle tip for dispensing of said liquid drug formulation; and

   a plunger that is axially movable within the barrel,

   wherein the housing defines a needle delivery aperture through which the needle tip of the syringe protrudes during dispensing of the liquid drug formulation, the auto-injector further comprising

   a needle sheath for covering of said needle tip of the syringe;

2. a removable cap that in a capped position acts to close off said needle delivery aperture of the housing, wherein said removable cap defines an inwardly projecting needle sheath cover for covering said needle sheath that includes one or more gripping elements arranged for gripping of the needle sheath; and

   provided to the housing, one or more flexible elements extending into said housing cavity thereof,

   wherein the needle sheath cover and/or the one or more flexible elements are shaped for interaction with each other such that on moving the removable cap
away from the capped position the one or more flexible elements are in urging contact with the needle sheath cover to thereby urge the one or more gripping elements into gripping contact with the needle sheath.

2. An auto-injector according to claim 1, wherein in said capped position, the one or more flexible elements contact the needle sheath cover to thereby bring the one or more gripping elements into at least light contact with the needle sheath.

3. An auto-injector according to either of claims 1 or 2, wherein the needle sheath cover defines a tapering surface at an outer part thereof arranged for contact with the one or more flexible elements.

4. An auto-injector according to any of claims 1 to 3, wherein the one or more flexible elements define a tapering surface arranged for contact with an outer part of the needle sheath cover.

5. An auto-injector according to any of claims 1 to 4, wherein the removable cap defines a cylindrical cap chamber and the needle sheath cover is provided along the axis of that cylindrical cap chamber.

6. An auto-injector according to claim 5, wherein the needle sheath cover defines a cylindrical needle sheath-receiving chamber.

7. An auto-injector according to claim 6, wherein said cylindrical needle sheath-receiving chamber has at least partly tapering form.

8. An auto-injector according to any of claims 1 to 7, wherein the one or more gripping elements are of hook form.
9. An auto-injector according to any of claims 1 to 8, wherein the needle sheath is provided with one or more grip-receiving features arranged for receipt of the one or more gripping elements.

10. An auto-injector according to claim 9, wherein the or each of said one or more grip receiving features comprises an indent, groove or cavity.

11. An auto-injector according to any of claims 1 to 10, wherein the needle sheath is comprised of a natural or synthetic rubber material.

12. An auto-injector according to any of claims 1 to 11, wherein the housing defines a barrel receiving part for receiving the barrel of the syringe; a plunger receiving part for receiving the plunger of the syringe; and a needle receiving part for receiving the hollow needle of the syringe, and wherein the one or more flexible elements are provided to said needle receiving part.

13. An auto-injector according to claim 12, wherein said plunger receiving part of the housing allows for the plunger of the syringe to be movable therein from a first position, in which it is somewhat withdrawn from the barrel to a second position, in which it is moved somewhat into the barrel.

14. An auto-injector according to any of claims 1 to 13, wherein the one or more flexible elements are provided as separate parts that attach or fix to an inner wall of the housing.

15. An auto-injector according to any of claims 1 to 14, wherein one or each of the flexible elements comprises a ring comprised of a flexible material.

16. An auto-injector according to claim 15, wherein said flexible material is a plastic polymer or natural or synthetic rubber material.
17. An auto-injector according to either of claims 15 or 16, wherein an outer ring circumference of said ring attaches to said inner wall of the housing.

18. An auto-injector according to any of claims 15 to 17, wherein the diameter of the inner ring circumference of the ring when in an uncompressed state is less than the outer diameter of the syringe barrel.

19. An auto-injector according to any of claims 1 to 14, wherein one or each of the flexible elements comprises a flexible finger element.

20. An auto-injector according to claim 19, wherein the inner wall of the housing is provided with a circular arrangement of flexible finger elements.

21. An auto-injector according to claim 20, wherein the diameter of the inner circumferential aperture defined by the finger tips of the flexible finger elements when in an un-flexed state is less than the outer diameter of the syringe barrel.

22. An auto-injector according to any of claims 1 to 21, wherein the one or more flexible elements are arranged such that during a capping operation, on bringing the removable cap into the capped position the needle sheath cover projects into the housing for sheathing of the needle tip and an outer part thereof interacts with the one or more flexible elements.

23. An auto-injector according to any of claims 1 to 22, additionally comprising a barrel sleeve that in use, is arranged to fit over part or all of the length of the barrel of the syringe.
24. An auto-injector according to claim 23, wherein the barrel sleeve extends out beyond the syringe barrel to wholly or partly enclose a length of an end-shoulder of the syringe barrel and/or the hollow needle of the syringe.

25. An auto-injector according to any of claims 1 to 24, additionally comprising an actuating mechanism for actuating the syringe to deliver the liquid drug formulation to a patient;

26. An auto-injector according to claim 25, wherein the actuating mechanism includes an energy store for storing energy that is releasable to actuate the syringe.

27. An auto-injector according to claim 26, wherein the energy store comprises a spring.

28. An auto-injector according to claim 26, wherein the energy store comprises a container of compressed liquid or gas.

29. An auto-injector according to any of claims 12 to 28, wherein the needle receiving part of the housing allows for the needle of the syringe to be axially moveable therein from a rest position, in which the needle is wholly housed by the needle receiving part, to a use position, in which at least the tip of the needle protrudes from the needle receiving part of the housing.

30. An auto-injector according to claim 29, wherein the housing includes biasing means arranged such that the needle is normally biased towards said rest position, wherein such biasing means are overcome during the actuation of the syringe by the actuating mechanism to allow for movement of the needle to the use position.
31. An auto-injector according to any of claims 1 to 30, wherein the housing receives a syringe containing a liquid drug formulation.

32. An auto-injector according to claim 31, wherein the barrel of said syringe has a volume corresponding to a single dose of said liquid drug formulation.

33. An auto-injector according to either of claims 31 or 32, wherein said liquid drug formulation is arranged for rest at from 2-8°C and for injected delivery at from 18-30°C.

34. An auto-injector according to claim 33, wherein the liquid drug formulation has a viscosity of less than 120 mPa.s at a delivery temperature of 20°C.

35. An auto-injector according to any of claims 31 to 34, wherein the liquid drug formulation comprises an aqueous formulation of a therapeutic biologic type drug.

36. An auto-injector according to claim 35, wherein said biologic type drug comprises an immunoglobulin or a fragment thereof.

37. An auto-injector according to claim 36, wherein said biologic type drug comprises a PEGylated or mPEGylated antibody fragment.

38. An auto-injector according to any of claims 35 to 37, wherein said aqueous formulation comprise additional formulation component selected from the group consisting of buffers, NaCl, and pH modifiers.
39. An auto-injector according to any of claims 35 to 38, wherein the concentration of the drug in the liquid drug formulation is greater than 100mg/ml.

40. A kit of parts comprising an auto-injector according to any of claims 1 to 30; and a syringe containing a liquid drug formulation.
**INTERNATIONAL SEARCH REPORT**

International application No
PCT/GB2008/004212

**A CLASSIFICATION OF SUBJECT MATTER**

INV. A61M5/20 A61M5/32

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)

A61H

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**

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* Further documents are listed in the continuation of Box C

**Date of the actual completion of the international search**

24 March 2009

**Date of mailing of the international search report**

01/04/2009

Name and mailing address of the ISA/Authorized officer

European Patent Office P B 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Fax (+31-70) 340-3013

Reinbold, Sylvie

Form PCT/ISA/210 (second sheet) (April 2005)
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