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(54) Title: DEVICE AND PROCESS FOR MIXING A PHARMACEUTICAL COMPOSITION WITH ANOTHER AGENT AND METHOD FOR ORAL ADMINISTRATION OF THE PHARMACEUTICAL PREPARATION			
(57) Abstract			
Device for mixing a pharmaceutical composition stored in a chamber (38) in said device with an agent to be added shortly before administration to form a preparation to be administered. The device should be capable of being shaken without leaking. It comprises a hollow body (2) having an outlet (4), sealed by a removably closure (12) and a plunger (6), which includes a flexible sealing member (20) having a circumferential edge in sealing contact with the inner wall (8) of the hollow body. The plunger (6), the hollow body (2) and the removable closure (12) define said chamber (38). A hollow rod (30) is connected to the plunger (6) for displacing the same in the hollow body (2) and includes at least one opening, which communicates with the interior of the rod (30) with the upper side of the flexible member (20). The flexible member (20) is supported on the plunger (6), so that it can only flex downwards. At a predetermined pressure differential over the upper side and the lower side of the flexible member (20) the flexible member will flex downwards to open a communication at the inner wall (8) of the hollow body into the chamber (38), so that said agent flows into the chamber (38).			

Device and process for mixing a pharmaceutical composition with another agent and method for oral administration of the pharmaceutical preparation.

5 Technical Field

The present invention relates to a device for mixing a pharmaceutical composition, which may be dry and granular, with another agent, which may be a fluid, to form a preparation, which may be a gel or the like, suitable for
10 administration to a living being, e.g. an animal. The invention also relates to a process for preparing a pharmaceutical composition, and to a method for oral administration of that preparation to a living being.

15 Background of the Invention

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The major problem forming the basis for the present invention relates to the handling, the storage and the administration of a pharmaceutical composition to be mixed with another agent, that may adversely affect the stability of the composition to form a preparation suited for administration to a living being, especially an animal.

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It is well known in the veterinary art to administer pharmaceutical compositions in the form of paste-like preparations to horses by means of a syringe-like device. The syringe is then inserted into the mouth of the horse and the preparation is expelled onto the root of the tongue. The viscous nature of the preparation and the placing thereof in the back of the
25 mouth makes it difficult for the horse to spit out the preparation.

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In some cases such preparations, e.g. comprising a mixture of a pharmaceutical composition and a consistency forming agent, will have a short storage stability. Therefore, the components comprised in those preparations must be kept isolated from each other until a
30 short time before use, when they are mixed with each other to form the desired preparation.

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There exists a plurality of solutions to the problem of storing and mixing two components to a preparation, which can not be stored for a longer period of time after mixing.



The most common prior solution is a syringe of the kind disclosed in the US-A-3 340 873, having a plunger, slidably accommodated in a cylindrical body. The two components to be mixed are contained in two different compartments, isolated from each other by a thin diaphragm. Shortly before the preparation is to be used, the diaphragm is
5 ruptured or pierced, so that a communication is established between the two compartments. The syringe, with the mixture is then shaken to form a homogenous preparation. After this operation a cap is removed to open a passage and the content is expelled through a needle by depressing the plunger.

- 10 This kind of prior art has in most cases proved satisfactory and reliable and is moreover relatively easy to manufacture, e.g. by plastics injection moulding, at a low cost.

However, the above syringe is not suitable for the administration of a gel, primarily because of the presence of the needle. But apart from this, generally, mixing devices having two
15 compartments isolated from each other by a thin diaphragm of rubber or plastics could not be used for certain kinds of moisture sensitive pharmaceutical compositions. An example of such a composition is compositions comprising a proton pump inhibitor, such as omeprazole, which degrades during long term storage in the presence of moisture. The
always present molecular migration through a rubber or a plastics diaphragm would be
20 sufficient to cause degradation of such sensitive compositions during long term storage.

Thus, conventional two compartments mixing devices are unsuitable for such compositions.

- DK Patent Specification 112 893 filed July 25, 1966, discloses an injection syringe for the
25 injection of a pharmaceutical composition, that can not be stored in solution for a longer period of time without detrimental effects. The syringe basically corresponds to a standard syringe, the main difference being that the opening in the needle fitting is sealed by a diaphragm. The composition is contained in the syringe in dry form. When the syringe is to be used, a double ended injection needle is mounted on the needle fitting, one end of the

needle piercing the diaphragm. Solvent is aspirated into the syringe through the needle. Then the syringe is shaken and the resulting solution is injected through the needle.

A drawback with this type of syringe is that the filling operation is rather complex, it requires the mounting of a double-ended injection needle for piercing the diaphragm. Furthermore, after the rupture of the diaphragm, the mixing chamber will be open to the air, so that care must be taken during the shaking operation to prevent the mixture from leaking out through the needle. Further, because of the high flow resistance of the syringe due to the narrow passages therein, in particular in the needle, it could not be used for viscous, pasty or gel-like preparations. Moreover, this known apparatus is not suited for oral administration because of the needle. Furthermore, the manufacturing costs for the syringe will be relatively high.

Object of the Invention

An object of the invention is to obviate the disadvantages of the prior art by providing a mixing device, in which a pharmaceutical composition may be stored for a longer period of time and to which a desired agent easily and rapidly can be added immediately before the administration of the preparation. After addition of the agent, the device also should be capable of being vigorously shaken without leaking. Furthermore, the manufacturing cost for the device of the invention should be relatively low.

This object of the invention is attained by a device in accordance with what is set out as the principal feature in the following summary of definitions, said summary including a definition of a process using the device for mixing a pharmaceutical preparation, and a method for administration of a mixed preparation by means of the device.

Definition of the Invention

In accordance with a first aspect of the invention, there is provided a device for mixing a pharmaceutical composition, which may be dry and granular, with another agent, which may be a fluid, to form a preparation, which may be a gel or the like, and subsequently administering said preparation to a living being, e.g. an animal or a human being, said device comprising a hollow body having an outlet sealed by a removable closure, a plunger being displaceably accommodated in said hollow body and in sealing contact with an inner wall of said hollow body, an actuating means being connected to said plunger for displacing the same in said hollow body, said plunger characterized in said hollow body and said removable closure defining a chamber for said composition, and said plunger comprises a sealing member having a flexible edge portion in sealing contact with said inner wall of said hollow body, one side of said edge portion facing said chamber and thus separating said chamber from the opposite side of said flexible edge portion, said edge portion being supported to be able to flex in a sufficient degree in one direction only to lose its sealing contact with said inner wall of said hollow body in order to establish a communication between said chamber and said opposite side of said edge portion, when said plunger is displaced in a direction away from said chamber.

In accordance with a second aspect of the invention, there is provided a process for preparing a pharmaceutical preparation by mixing a pharmaceutical composition, which may be dry and granular, with another agent, which may be a fluid, to form a preparation, which may be a gel or the like, shortly before the administration thereof to a living being, comprising the following steps:

- a) filling said composition into a chamber of a device comprising a hollow body and a plunger displaceable therein in sealing engagement with an inner wall portion of said hollow body, thereby defining a movable end wall of said chamber, the plunger comprising a sealing member having a flexible edge portion in sealing contact with the inner wall of the hollow body, separating the chamber from the

opposite side of the edge portion, the edge portion being able to flex to permit a communication between the chamber and the opposite side of the edge portion,

- b) closing said chamber with a closure,
- 5 c) providing a moisture tight seal to said filled chamber,
- d) storing said device until time of use,
- e) removing said moisture tight seal to said chamber,
- f) expanding said chamber by displacing said plunger thereby establishing communication between the chamber causing the opening
- 10 of said edge portion, thereby transferring fluid agent to said chamber,
- g) if required, shaking said device until said preparation is formed,
- h) providing an opening to said chamber by removing said closure when said preparation is to be administered, allowing said preparation to
- 15 be expelled from said device by displacing said plunger towards said opening.

And in accordance with a third aspect of the invention, there is provided a method for oral administration to a living being of a pharmaceutical preparation, which is achieved by mixing a composition, which may be dry and granular, with an agent, which may be a fluid, by using a device according to the invention as defined above.

Discussion of the Invention

When said device of the invention is to be used for administration of the preparation, a package or a seal which protects the prefilled chamber against moisture during storage first has to be removed. Then the

agent to be mixed with the composition contained in the chamber is supplied, the fluid agent being separated from the chamber by the flexible sealing member. Then the plunger is displaced in opposite direction to the expel direction causing an expansion of the closed chamber defined by the plunger, the side wall portion and the closure, thereby creating a vacuum in the chamber. Initially, the pressure differential over the sealing member will be too low to flex it, but when the plunger continues to be displaced the vacuum in the chamber gradually increases so that the sealing member deforms and loses its contact with the wall, thereby establishing a communication into the chamber. The agent will then be aspirated into the chamber. When the required amount of agent has been drawn into the chamber and the flexible sealing member has flexed back to its rest position, the device is shaken until the preparation is ready for administration. Just before the administration is to be carried out, the closure to the chamber is removed and the device is inserted in for example the mouth of a horse. The content of the device is now expelled by depressing the plunger.

Description of preferred embodiments

Preferred embodiments of the invention will now be described by way of example with reference to the drawings, in which:

Fig. 1 is an axial section of a first preferred embodiment of the invention.

Fig. 2 shows the encircled portion in Fig. 1 at a larger scale,

Fig. 3 is a cross-section along the line III-III in Fig. 1,

Fig. 4 is an axial section of a further embodiment, which is slightly modified in relation to that of Figs 1-3,

Fig. 5 shows the encircled portion of Fig. 4 at a larger scale,

Fig. 6 is a section along the line VI-VI of Fig. 4,

Fig. 7 shows a part of a slight modification of the embodiment of Fig. 4 at a larger scale,

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Fig. 8 is an axial section of still another embodiment of the invention,

Fig. 9 is a section along the line IX-IX of Fig. 8,

10 Fig. 10 shows the encircled portion of Fig. 8 at a larger scale, and

Fig. 11 discloses a slight modification of the embodiment of Figs 8-10.

As shown in Fig. 1, the syringe-like device of the first preferred embodiment of the invention, comprises a tubular, elongated, cylindrical hollow body 2, which is open at both
15 ends. The lower end in Fig. 1 is the outlet end 4. A plunger 6 is inserted through the open upper end 10. A flange portion or a finger grip portion 13 extends substantially perpendicular to the longitudinal direction of the hollow body 2 around the upper end thereof. The outlet end 4 is closed by a removable lid 12, which has a groove 14, having a diameter
20 corresponding to that of the side wall 8 of the hollow body 2. The groove 14 is constructed with a depth to provide an airtight seal with the lower end 4 of the cylindrical body into the interior of the hollow body 2. The lid 12 has a radially extending lug 16 to facilitate the removal of the lid 12 when the preparation is to be expelled.

25 As best can be seen in Fig. 2, the plunger 6 is comprised by two parts 18, 20, a support means 18 in the form of a flat web, which extends diametrically, perpendicularly to the axis of the hollow body 2 and a sealing member 20 in the shape of a thin, flexible disc, which when unloaded is sized to sealingly contact the inner wall 8 of the hollow body 2, thereby isolating the spaces on each side of the sealing member 20 from each other. The disc 20 is at
30 the centre provided with a peg 22, having a compressible bulged end portion 24, while the

web 18 has a centre aperture 26 having a diameter less than that of the bulge portion 24. The shank 28 of the peg 22 is adapted to the thickness of the web 18, so that the peg 22 may be snapped into the aperture 26, so that the disc 20 will lie close to the web 18.

5 A rod 30 is made integral with the plunger 6. Its external diameter is somewhat smaller than the internal diameter of the hollow body 2, so that the rod 30 is slidably guided therein. The rod 30 is tubular, and its annular end portion 32 is made in one piece with the web 18. The end face of said portion 32 flushes with the end face (the lower face in Fig. 1) of the web 18. At the open end 40 of the rod 30 a radially extending finger grip 23 is provided.

10 The flexible disc 20 is made of a resilient material and will deflect, when subjected to a sufficiently large force and return to its original position upon the removal of said force. When the lid 12 or other seal is placed on the outlet end 4, a closed chamber 38 is defined by the lid 12 or other seal, the flexible disc 20 and the inner wall 8 of the hollow body, the
15 volume of said chamber being variable due to the axially displaceable plunger 6. When snapped into the hole 26, the unloaded disc 20 rests against the web 18 and the annular end portion of the rod 30. Thus, the circumferential edge portion 34 of the disc 20 is prevented from flexing upwards by the web 18 and the annular end portion 32. On the other hand the edge portion 34 is allowed to flex downwardly. If this occurs the edge portion 34 will loose
20 its sealing contact with the inner wall 8 of the hollow body 2, thereby opening a communication at the wall 8 between the upper and lower sides of the flexible disc 20. The disc 20 thus functions as a non-return valve.

It should be noted that any method for fixing the resilient disc 20 to the rod 30 may be used.
25 For example a keyhole connection could be used. A keyhole aperture is then provided at the bottom end of the rod 30 and, the peg 22 of the sealing disc 20 then being introduced through the wider opening of the keyhole and then being pushed into the narrower slit of the keyhole. In still a further fixing method the flexible disc 20 may be provided with a shank portion at the center thereof which portion then is introduced in an aperture provided

at the lower end of the rod 30. The end of shank is then heated to a softening temperature and thereupon flattened to form a rivet joint-like connection.

As mentioned above and as can be seen in the Figs 1-3, the rod 30 is tubular and has an open bottom and, which normally is sealed by the flexible disc 20. The interior 36 of the rod 30 and the disc 20 form a filling compartment for the agent to be mixed with a composition contained in the chamber.

The function of this first embodiment of the device will now be described by way of an example. Suitable composition for the device is described in WO/SE94/25070. In the following example the pharmaceutical composition is constituted by beads of an active substance, such as enteric coating layered omeprazole pellets mixed with a gelforming agent such as xanthan gum, guar gum, locust bean gum, tragacanth, modified cellulose derivatives or similar, to which mixture of dry components a fluid agent such as for instance water later is added for forming a viscous gel. The use of the device defined by the present invention will not be restricted to use in connection to an omeprazole preparation.

A suitable dosage of a dry mixture of enteric coating layered omeprazole pellets and a gelforming agent is filled into the chamber 38. A buffering or pH-adjusting agent such as citric acid may optionally be added to prevent premature dissolution of the enteric coated beads when water later is added to the composition. This operation could be carried out in two ways, either the plunger 6 is placed in a suitable position in the hollow body 2 with the lid 12 removed, the filling then taking place through the lower end 4, or the lid 12 is applied on the lower end 4 with the plunger 6 removed, the filling then taking place via the upper opening 10. The quantity or the volume of the mixture is optional within certain limits, since the volume of the chamber 38 is variable because of the axially displaceable plunger 6. When the filling is completed, the lid 12 or other seal is applied onto the end 4 or the plunger 6 inserted into the hollow body 2, respectively.

It should be noted that the hollow rod 30 in an advantageous manner serves as a metering device for the agent to be added to the chamber 38. It is transparent and preferably provided with gradation lines, so that the agent to be added precisely could be measured with the device. Superfluous agent may be poured off from the rod 30 before the rod 30 has
5 been displaced to open a communication into the chamber 38. Thus, due to the incorporated metering means provided by the particular design of the rod 20 a very precise measuring of the agent to be added, can be made without the need of any additional means than the syringe itself.

10 In view of the hygroscopic nature of the gelforming agent, and a required durability of several years, for the pharmaceutical composition, the content in the chamber must be protected against penetrating moisture, which else would accumulate in the gelforming agent to sooner or later cause degradation of the omeprazole during long-term storage. Therefore, after the filling operation, the device is enclosed in a moisture tight envelope,
15 preferably having a moisture barrier made of aluminium, but other materials fulfilling the same purpose are of course also conceivable. Suitably a siccative, preferably in a small bag, is enclosed in the envelope as a further protection against moisture. As an alternative to the above package, it might be sufficient providing an impermeable seal or lid of a similar material on top of the open end 40 of the rod 30. A siccative could then be incorporated in
20 the seal or the lid to absorb any penetrating damp. The device could now be stored for several years until use.

When to be used, the device is taken out from the moisture tight package or the seal on top of the tubular rod 30 is removed. A suitable quantity of water to be added to the mixture
25 within the chamber 38 is then filled into the tubular compartment of the rod 30 up to a desired level (marked by a gradation line or level mark). The plunger 6 is then displaced upwardly, thus creating a vacuum in the chamber 38. After a sufficient displacement, the vacuum will be so strong therein, that the flexible disc 20 will flex downwards, the circumferential edge 34 of the flexible disc 20 loosing its sealing contact with the inner wall
30 8, so that a communication is established from the compartment 36 into the chamber 38, so

that the water in the compartment 36 of the rod 30 will be aspirated into the chamber 38. When the water has been transferred thereto, the disc 20 will flex back to its rest position and the device is then shaken until a viscous gel containing the omeprazole pellets has been formed. During the shaking operation, the mixture is prevented by the flexible disc 20 to
5 leak into the compartment 36. The mixture could be stored in the device for a short period of time before administration. Just before administration the lid 12 is removed and the device is placed, where the preparation is to be administered. The preparation is then expelled by depressing the rod 30.

10 Conveniently, the rod 30 has such an axial length, that when fully depressed, all of the preparation is expelled from the device. Preferably the flexible disc 20 has an even surface to expel the composition completely, thereby avoiding the risk for any residues, pellets or gel, being left in openings or slits, which could happen with a slitted disc.

15 Instead of the plastic lid 12, a tear-off or a rupturable seal could be provided to seal the chamber 38.

Fig. 4 demonstrates a slight modification of the embodiment of Figs 1-3. Instead of being open at the bottom end the tubular rod 30a has two opposed longitudinal slits 42, which
20 extend from the bottom portion of the rod 30a up to about half the height of the rod 30a, thereby providing a communication between the interior 36a of the rod 30a and the upper side of the disc 20a. The bottom portion comprises an aperture 26a in the centre, which functions in a similar way as the aperture 26 in the embodiment of Fig. 1. The bottom portion of the rod 30 is circular and provides a support for the middle portion of the flexible
25 disc 20a.

In a further modification of the Fig. 4 embodiment, the sealing member 20'a is integral with the rod 30'a and consists of an annular flexible ring, see Fig. 7. The advantage of this embodiment is that it only requires a single operation in the manufacture of the rod 30'a and
30 the sealing member 20'a.

In still a further modification (Figs. 8-10) of the previously described embodiments the upper part of the rod 30b is tubular, while the lower part 46 thereof has a section in the shape of a cross, as clearly could be seen in Fig. 9. Thus, the lower part consists of two
5 longitudinally extending, perpendicular wall portions 48, 50, which extend from the bottom portion of the rod 30b up to about half the height of the rod 30b. From the tubular portion 44 and extending downwards the cross-shaped portion 46 includes a first part having a constant section to provide sufficient stiffness and guidance against the inner wall 8. The following part 56 tapers downwards towards the bottom portion, which in turn comprises
10 an annular rim 60 to support the flexible disc 20b and prevent it from being flexed upwardly. The bottom portion also includes an aperture 62, into which the bulge 24b of the flexible disc 20b is snapped (cf. Fig. 10).

A modification of the Figs. 8-10 embodiment is shown in Fig. 11. As in Fig. 7 the flexible
15 sealing member 34'b is integral with the rod 30b, which has a radially protruding annular rim 60', which is prolonged by a thinner flexible annular edge 34'b in sealing contact with the inner wall 8 of the hollow body 2.

In the embodiment of Figs. 8-11 the water to be added is introduced as before through the
20 open end 40 of the rod 30b but in opposition to the previously described embodiments the water will not be contained in a lower tubular portion of the rod, but will rise along the cross-shaped portion up to a desired level. In this case the cross-shaped portion could be provided with coloured lines to indicate the volume levels. In these embodiments the rod must not be transparent but can be made in an appropriate colour.

25 As should be understood all the embodiments function in a similar manner. A fluid agent, preferably water, is filled into the upper end 40 of the rod 30, which water then flows through the opening provided in the rod and subsequently reaches the upper side of the flexible sealing member. The sealing member prevents the water from reaching the chamber
30 38. The rod will then be displaced backwards, thereby creating a vacuum in the chamber 38.

The combined action of the weight of the water and the vacuum will flex the sealing member downwards, so that water will be aspirated into the chamber 38. When the water has disappeared from above the flexible sealing member into the chamber, said member will flex back to its original rest position and seal off the chamber 38.

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The described solutions offer different advantages. If the sealing member is a separate constructional detail, it offers a great freedom in the choice of material. The material in the sealing member can be chosen to have optimal sealing and elastic properties, while the material in the rod can be chosen to provide sufficient stiffness and support for the sealing member. If the rod and the sealing member are made integral, the choice of material must be a compromise between required stiffness of the rod and needed flexibility and elasticity of the sealing member. However, this latter solution offers advantages as regards manufacturing costs.

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It should further be noted that in the two embodiments all the elements can be made of polymeric materials, such as for instance polyethylene, polypropylene, polyester, elastomer, polycarbonate, rubber or silicone, and manufactured by conventional and cheap methods, such as injection moulding. Moreover, all the details have a simple construction and are easy to assemble. Consequently, the devices can be produced at a low cost.

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In the above described embodiments of the invention the lid 12 is provided with an radially protruding lug 16, which extends around a part of the circumference of the lid 12 and forms a grip portion for facilitating the removal of said element. It should be realized that the grip portion may have any suitable configuration. For example, it could be oval, or it could be

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constituted by a protruding flange extending over the whole circumference of the lid.

The devices are in particular suited for oral administration to an animal, especially a horse, in particular of an aqueous gel containing a formulation of a proton pump inhibitor e.g. omeprazole or a similar composition. However, it should be evident to the man skilled in the art that the use of the device is not restricted to this field, since it can be used for mixing

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various kinds of pharmaceutical compositions with other agents, and for oral, rectal or any other suitable administration to many different kinds of living beings, including humans.

It should also be noted that a pharmaceutical composition in the sense of this application
5 does not solely mean a drug, also other kinds of beneficial agents, for instance essential nutrients are intended to be included by this expression.

The claims defining the invention are as follows:

1. Device for mixing a pharmaceutical composition, which may be dry and granular, with another agent, which may be a fluid, to form a preparation, which may be a gel or the like, and subsequently administering said preparation to a living being, e.g. an animal or a human being, said device comprising a hollow body (2) having an outlet (4) sealed by a removable closure (12), a plunger (6, 6a, 6'a, 6b, 6'b) being displaceably accommodated in said hollow body (2) and in sealing contact with an inner wall of said hollow body (8), an actuating means (30, 30a, 30b) being connected to said plunger (6, 6a, 6'a, 6b, 6'b) for displacing the same in said hollow body (2), said plunger characterized in said hollow body and said removable closure defining a chamber for said composition, and said plunger (6, 6a, 6'a, 6b, 6'b) comprises a sealing member (20, 20a, 20'a, 20b, 20'b) having a flexible edge portion (34, 34a, 34'a, 34b, 34'b) in sealing contact with said inner wall (8) of said hollow body (2), one side of said edge portion facing said chamber (38) and thus separating said chamber from the opposite side of said flexible edge portion, said edge portion being supported to be able to flex in a sufficient degree in one direction only to lose its sealing contact with said inner wall (8) of said hollow body (2) in order to establish a communication between said chamber (38) and said opposite side of said edge portion, when said plunger is displaced in a direction away from said chamber (38).
2. Device according to claim 1, characterized in that said actuating means is a tubular rod (30, 30a, 30b), provided with at least one opening at a bottom portion thereof.
3. Device according to claim 2, characterized in that said rod (30, 30a, 30b) has a diametrically extending web (18), with openings defined between the side edges of said web (18) and the inner wall of said tubular rod (30).
4. Device according to claim 3, characterized in that said web (18) has a centre aperture (26) adapted for detachably connecting said flexible

sealing member (20) to said rod (30), said sealing member being circular and extending at least to the outer wall of said tubular rod.

5 5. Device according to claim 2, characterized in that said tubular rod (30a) has a closed bottom portion and axial slits (42) extending from said bottom portion.

10 6. Device according to claim 5, characterized in that said flexible sealing member is a circular disc (20a), detachably fixed to said bottom portion.

15 7. Device according to claim 6, characterized in that said flexible sealing member is integral with said tubular rod (30'a) and consists of a flexible annular ring (34'a) extending radially from said bottom portion to said inner wall (8) of said hollow body (2).

20 8. Device according to any one of claims 2-7, characterized in that said tubular rod (30, 30a, 30a') includes a volume measurement means for said agent to be added.

25 9. Device according to claim 8, characterized in that said tubular rod (30, 30a, 30a') has level gradations for said agent to be added.

30 10. Device according to claim 8 or 9, characterized in that said tubular rod (30, 30a, 30a') is transparent.

35 11. Device according to claim 2, characterized in that said rod (30b) includes a tubular first part (44) connected to a second part (46) having a cross-shaped section.

12. Device according to claim 11, characterized in that said second part (46) tapers towards the bottom portion of said rod (30b).

13. Device according to claim 11 or 12, characterized in that said rod has a plate-formed bottom portion having a centre aperture (62) adapted

for detachably connecting said flexible sealing member (20b) to said rod (30b), said sealing member being circular and extending to the inner wall of said hollow body (2).

- 5 14. Device according to claim 11 or 12, characterized in that said flexible sealing member is integral with said rod (30b) and consists of a flexible annular ring (34'b) extending radially from said bottom portion to said inner wall (8) of said hollow body (2).
- 10 15. Device according to any one of claims 11-14, characterized in that said cross-shaped second part (46) includes a volume measurement means for said agent to be added.
- 15 16. Device according to claim 15, characterized in that said second part (46) has level gradation for said agent to be added.
17. Device according to claim 16, characterized in that said level gradations are coloured lines.
- 20 18. Device according to any one of claims 11-17, characterized in that said second part (46) is coloured.
- 25 19. Device according to any one of claims 2-18, characterized in that said tubular rod (30, 30a, 30b) includes an open end (40) remote from said plunger (6), which is closed by a moisture proof seal.
20. Device according to any one of claims 1-19, characterized in that said closure is a removable lid (12).
- 30 21. Device according to any one of claims 1-19, characterized in that said removable closure (12) is a rupturable or a tear-off closure.
22. Device according to any preceding claim, characterized in that said chamber (38) is prefilled with said pharmaceutical composition and said device is enclosed in a moisture proof envelope comprising at least one moisture barrier.
- 35

23. Device according to claim 22, characterized in that said at least one moisture barrier is comprised by an aluminium layer.

24. Device according to claim 22 or 23, characterized in that a siccative is contained in said envelope.

25. Device according to any preceding claim, characterised in that said pharmaceutical composition is constituted by enteric coating layered pellets comprising a proton pump inhibitor, e.g. omeprazole pellets, mixed with a dry gelforming agent.

26. Process for preparing a pharmaceutical preparation by mixing a pharmaceutical composition, which may be dry and granular, with another agent, which may be a fluid, to form a preparation, which may be a gel or the like, shortly before the administration thereof to a living being, comprising the following steps:

- a) filling said composition into a chamber (38) of a device comprising a hollow body (2) and a plunger (6) displaceable therein in sealing engagement with an inner wall portion of said hollow body (2), thereby defining a movable end wall of said chamber (38), the plunger (6) comprising a sealing member (20) having a flexible edge portion (34) in sealing contact with the inner wall (8) of the hollow body (2), separating the chamber (38) from the opposite side of the edge portion, the edge portion (34) being able to flex to permit a communication between the chamber (38) and the opposite side of the edge portion (34),
- b) closing said chamber with a closure (12),
- c) providing a moisture tight seal to said filled chamber (38),
- d) storing said device until time of use,
- e) removing said moisture tight seal to said chamber (38),

- f) expanding said chamber (38) by displacing said plunger (6) thereby establishing communication between the chamber (38) causing the opening of said edge portion (34), thereby transferring fluid agent to said chamber (38),
- g) if required, shaking said device until said preparation is formed,
- h) providing an opening to said chamber (38) by removing said closure (12) when said preparation is to be administered, allowing said preparation to be expelled from said device by displacing said plunger (6) towards said opening.

27. Process according to claim 26, characterized in that said moisture tight seal in step c) to said chamber (38) is accomplished by enclosing said device in a moisture proof envelope, which comprises at least one moisture barrier.

28. Process according to claim 27, characterized in that said at least one moisture proof barrier is an aluminium layer.

29. Process according to any one of claims 26-28, characterised in that said pharmaceutical composition is constituted by enteric coated pellets of a proton pump inhibitor, e.g. omeprazole pellets, mixed with a dry gelforming agent and that said fluid agent is water.

30. A pharmaceutical preparation obtained by the process of any one of claims 26 to 29.

31. Method for oral administration to a living being of a pharmaceutical preparation, which is achieved by mixing a composition, which may be dry and granular, with an agent, which may be a fluid, by using a device according to any one of claims 1-25.

32. Method according to claim 30, characterized in that said living being is an animal, e.g. a horse.

DATED this 26th day of October 1998

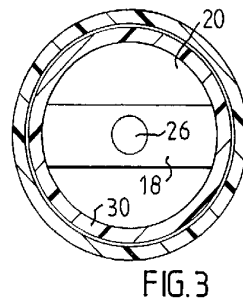
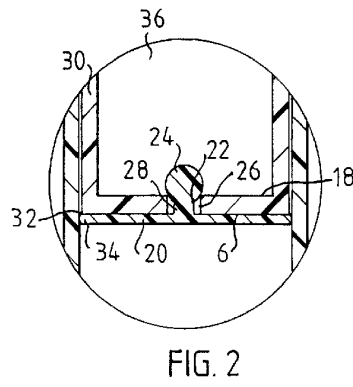
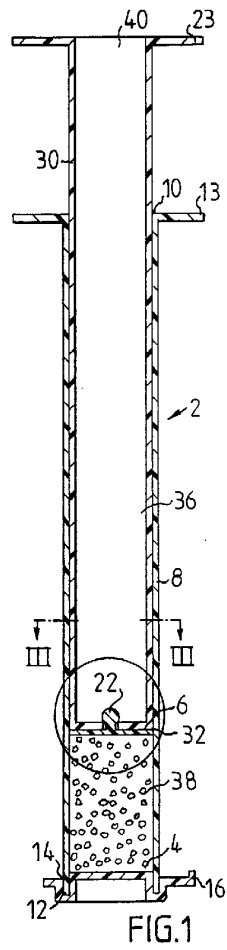
ASTRA AKTIEBOLAG,
By its Patent Attorneys,
E. F. WELLINGTON & CO.,
By:

(Bruce Wellington)

Figure 6

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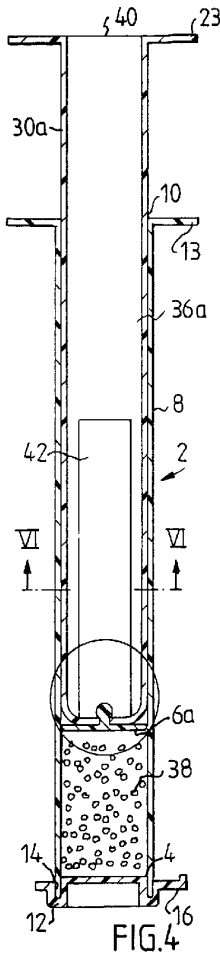


FIG. 4

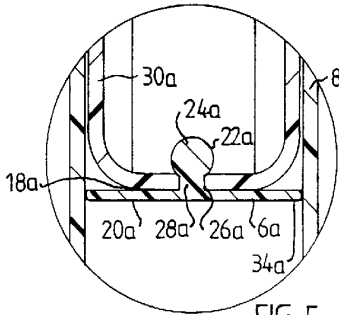


FIG. 5

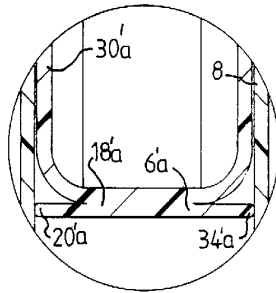


FIG. 7

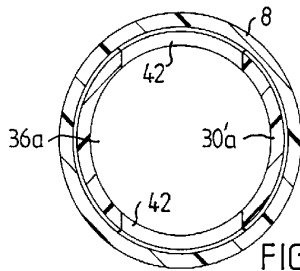


FIG. 6

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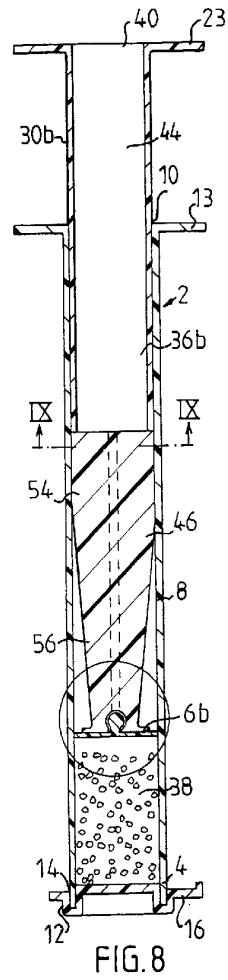


FIG. 8

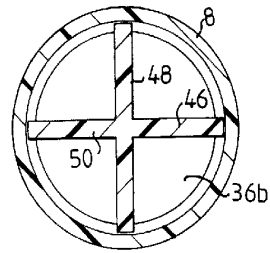


FIG. 9

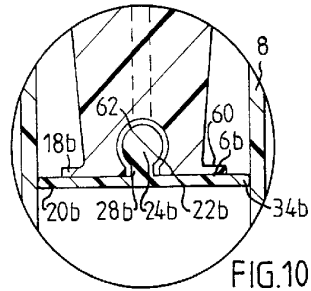


FIG. 10

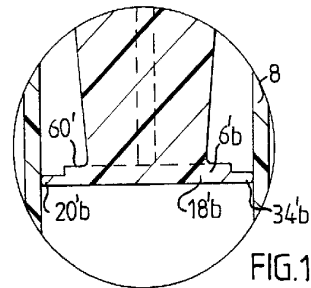


FIG. 11