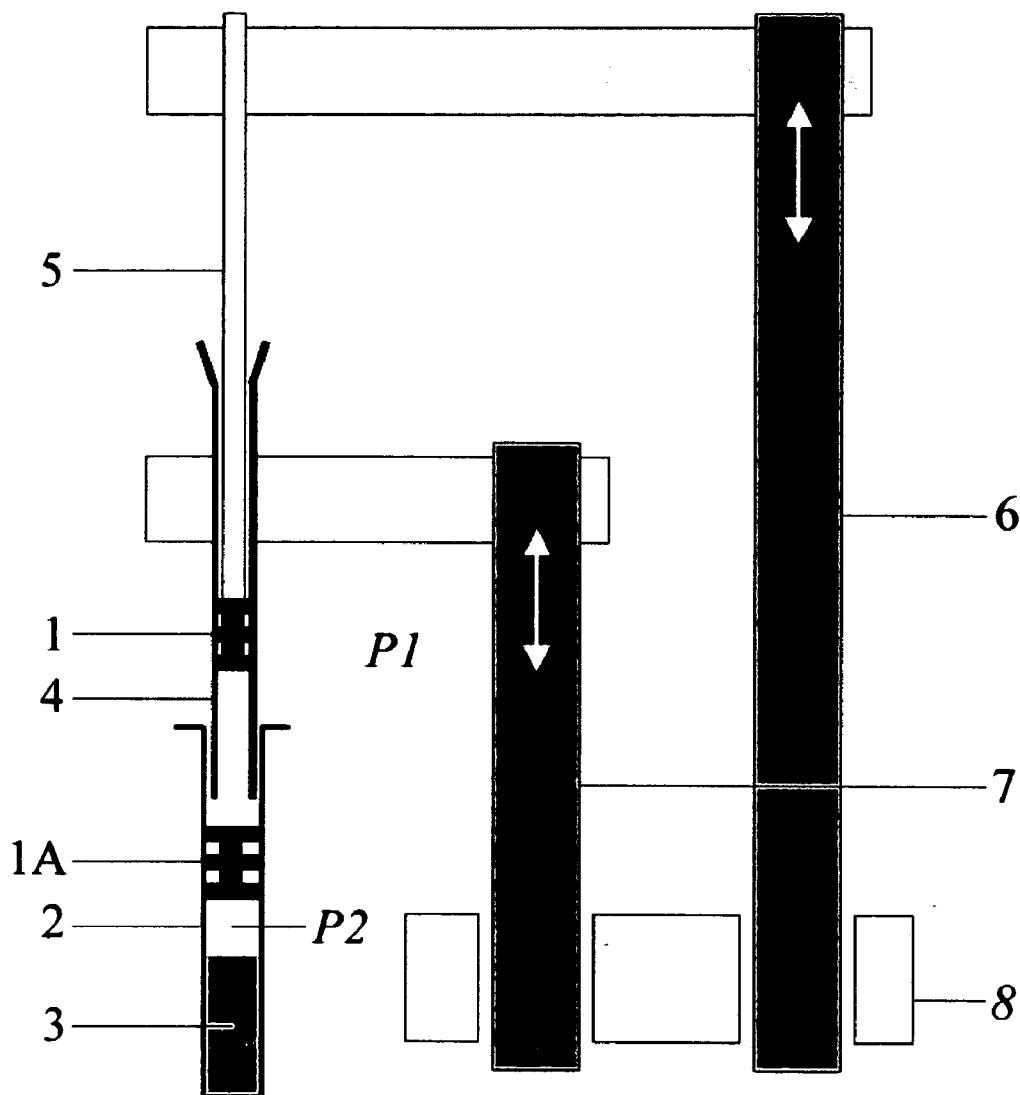




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**Griebel et al.**(10) **Pub. No.: US 2006/0168916 A1**(43) **Pub. Date: Aug. 3, 2006**(54) **METHOD AND APPARATUS TO INSERT STOPPERS INTO PREFILLED SYRINGES****Publication Classification**(76) Inventors: **Robert Andree Emil Griebel**,  
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**Bausch**, Eisenberg (DE)(51) **Int. Cl.**  
**B65B 7/28** (2006.01)  
(52) **U.S. Cl.** ..... **53/489**(57) **ABSTRACT**Correspondence Address:  
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An apparatus and method for inserting a stopper into a medical syringe minimizing the amount of entrapped air between the stopper and the contained liquid. The apparatus in a first embodiment utilizes a vacuum to assist inserting the stopper within the syringe. In a second embodiment a vacuum is used to transport the stopper and cause the insertion into the syringe. This method eliminates a mechanical device that transports the stopper to the syringe.

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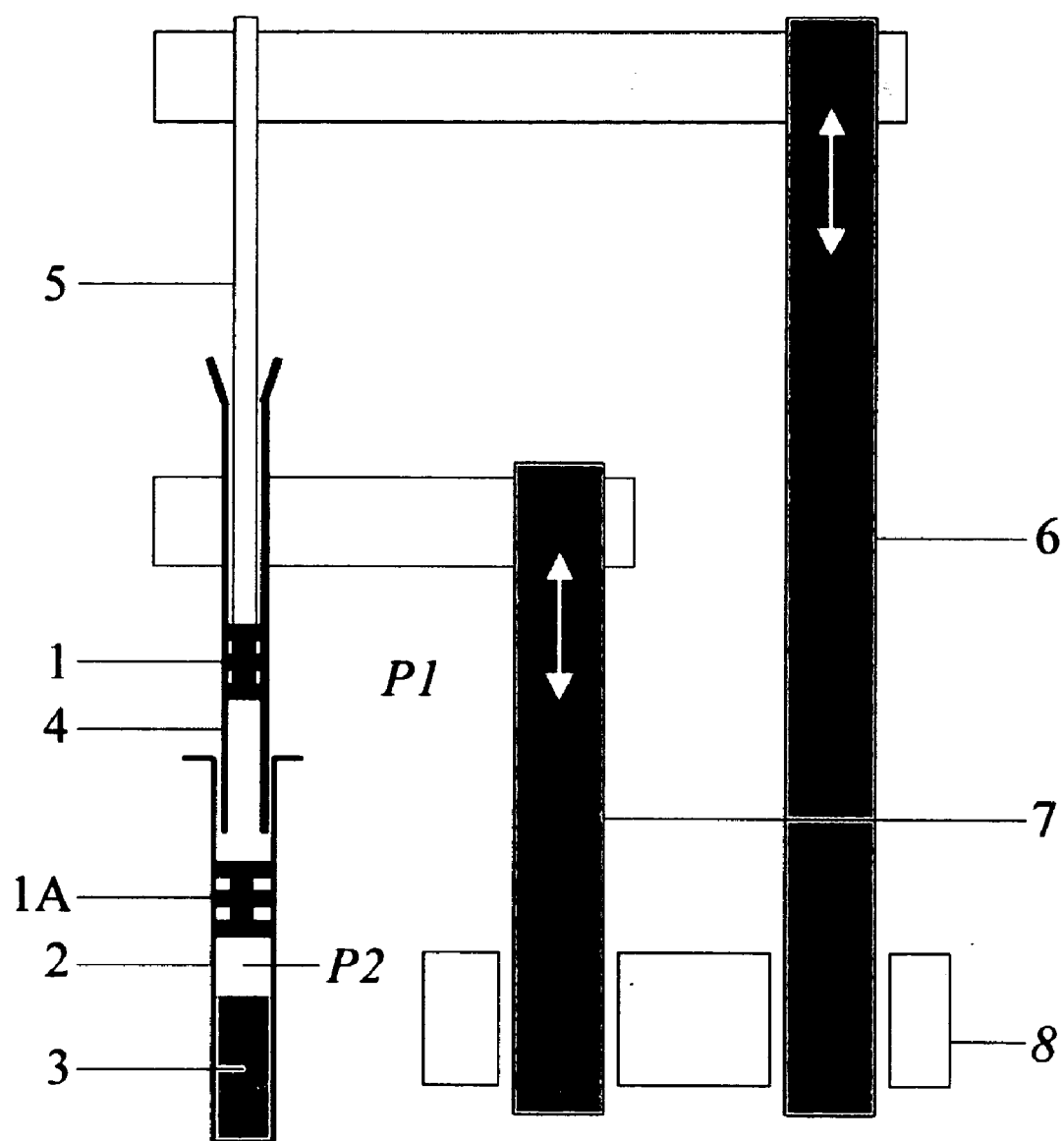


Figure 1

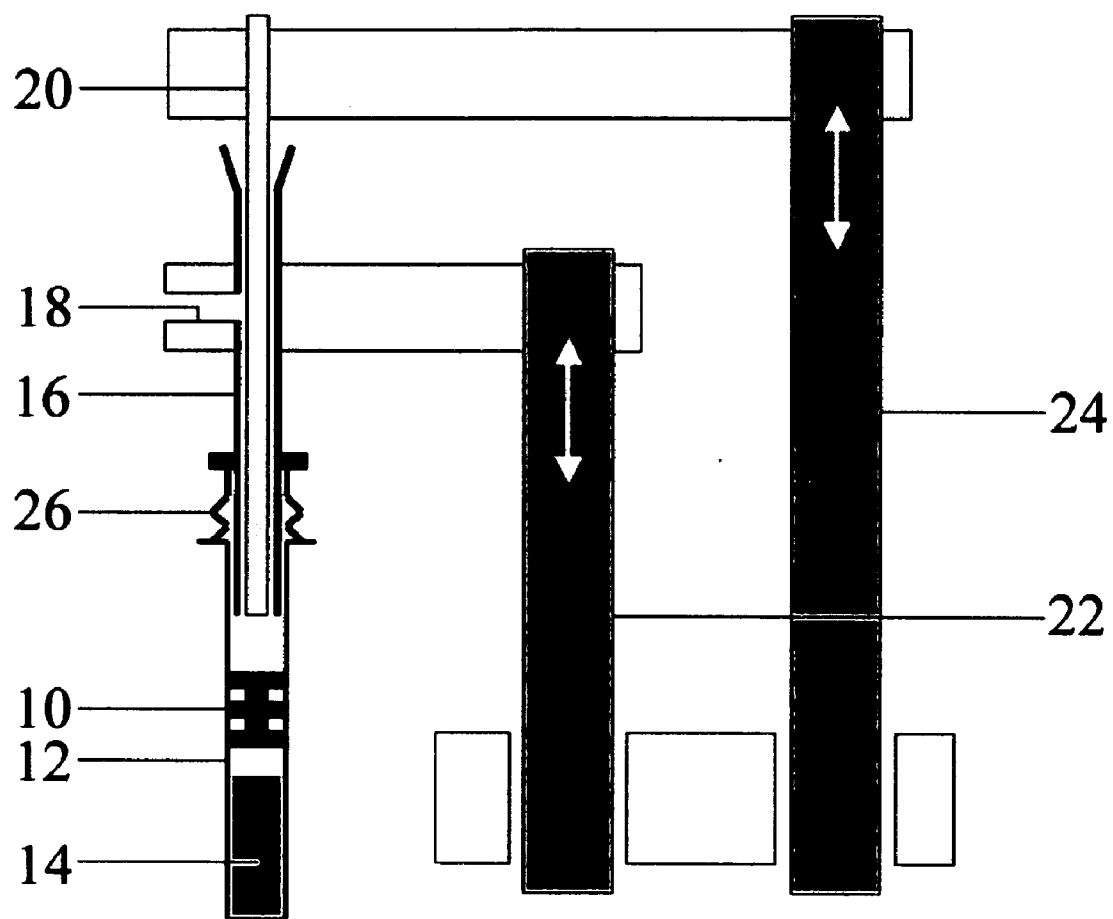


Figure 2

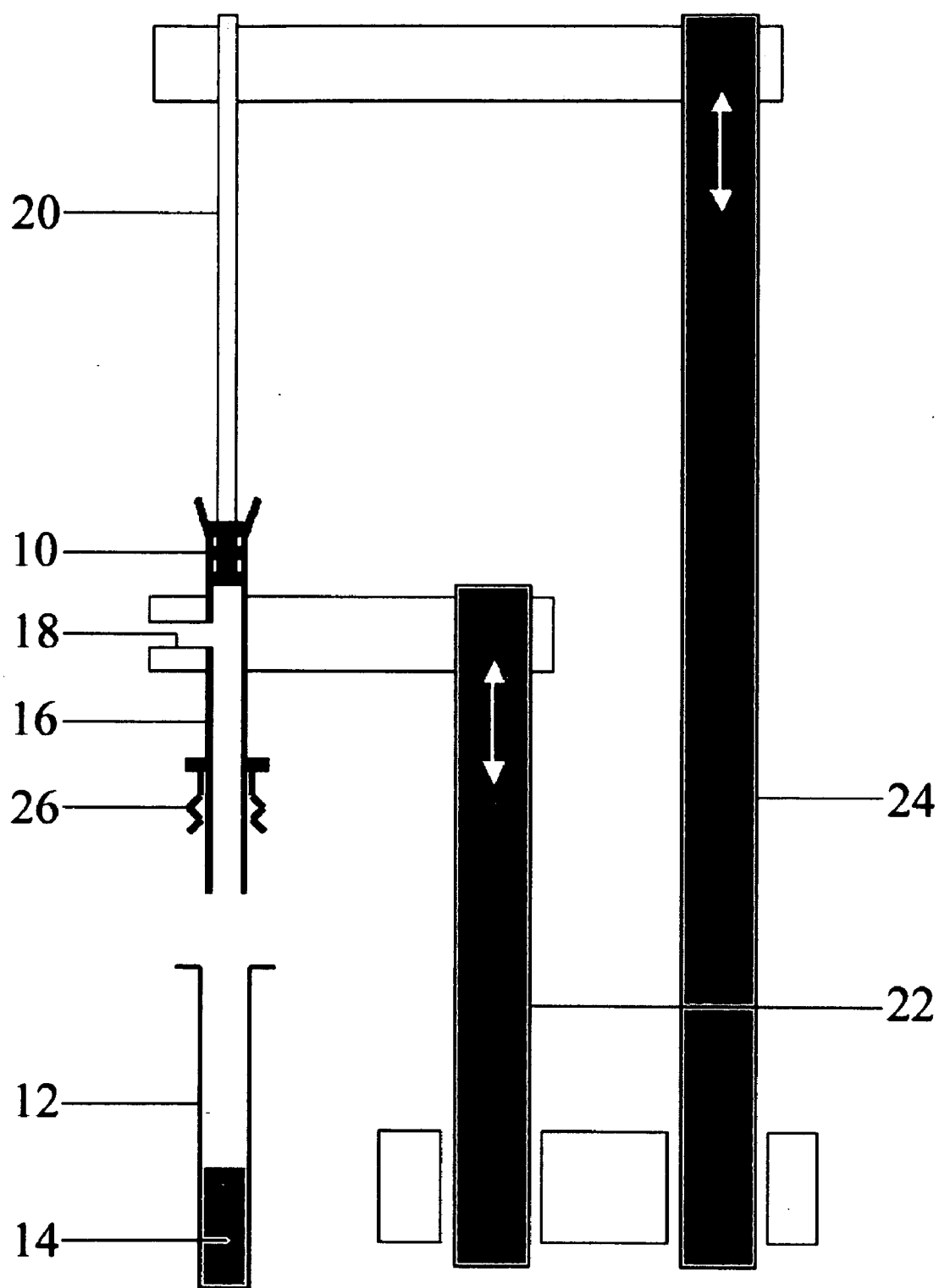


Figure 3

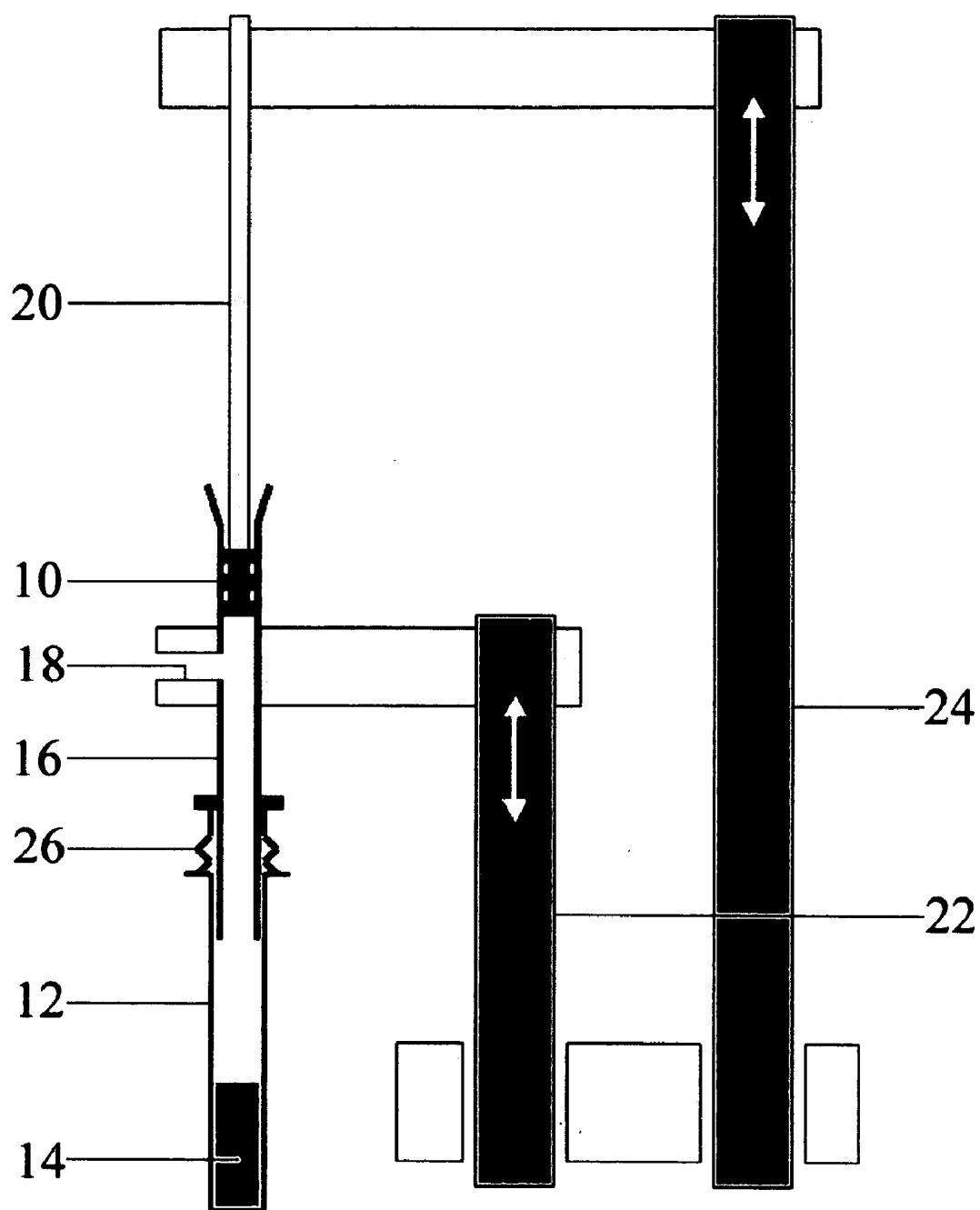


Figure 4

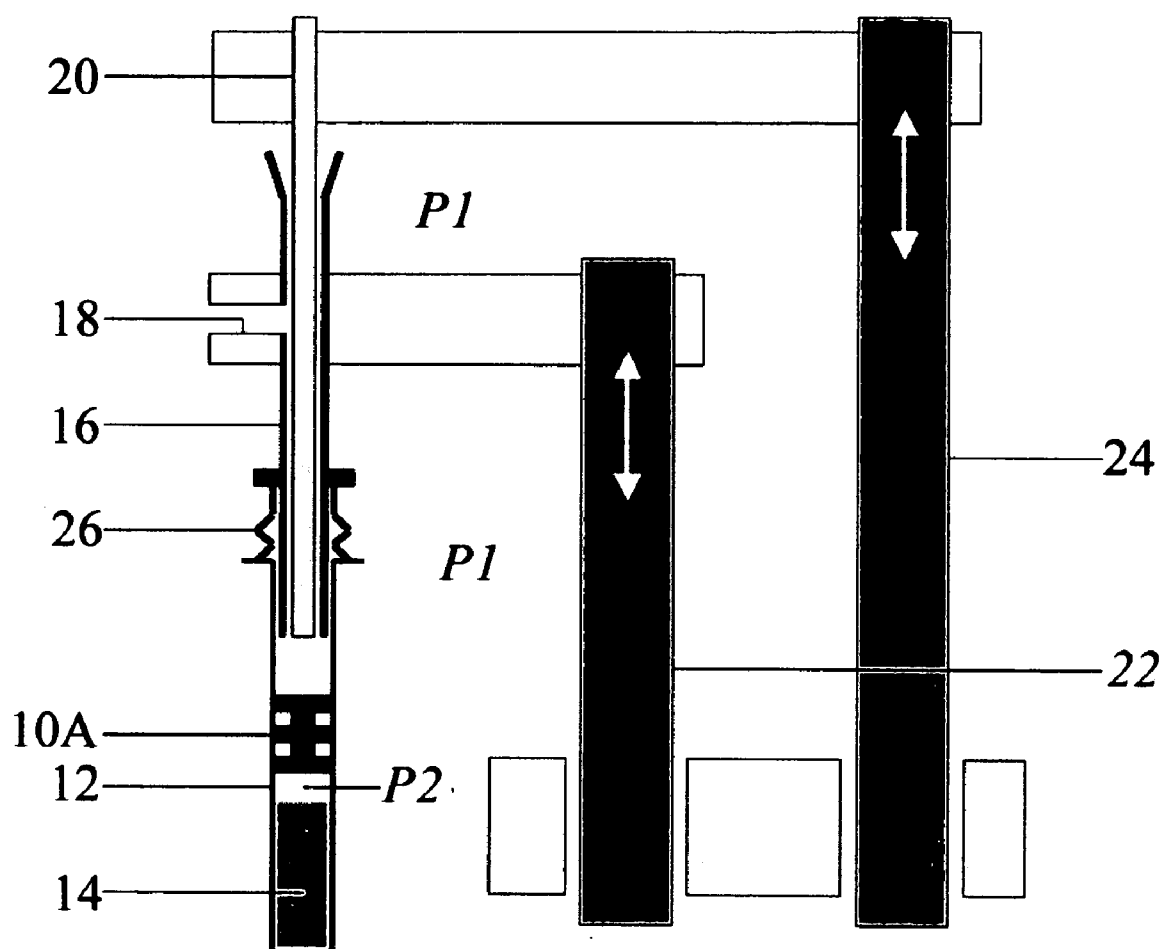


Figure 5

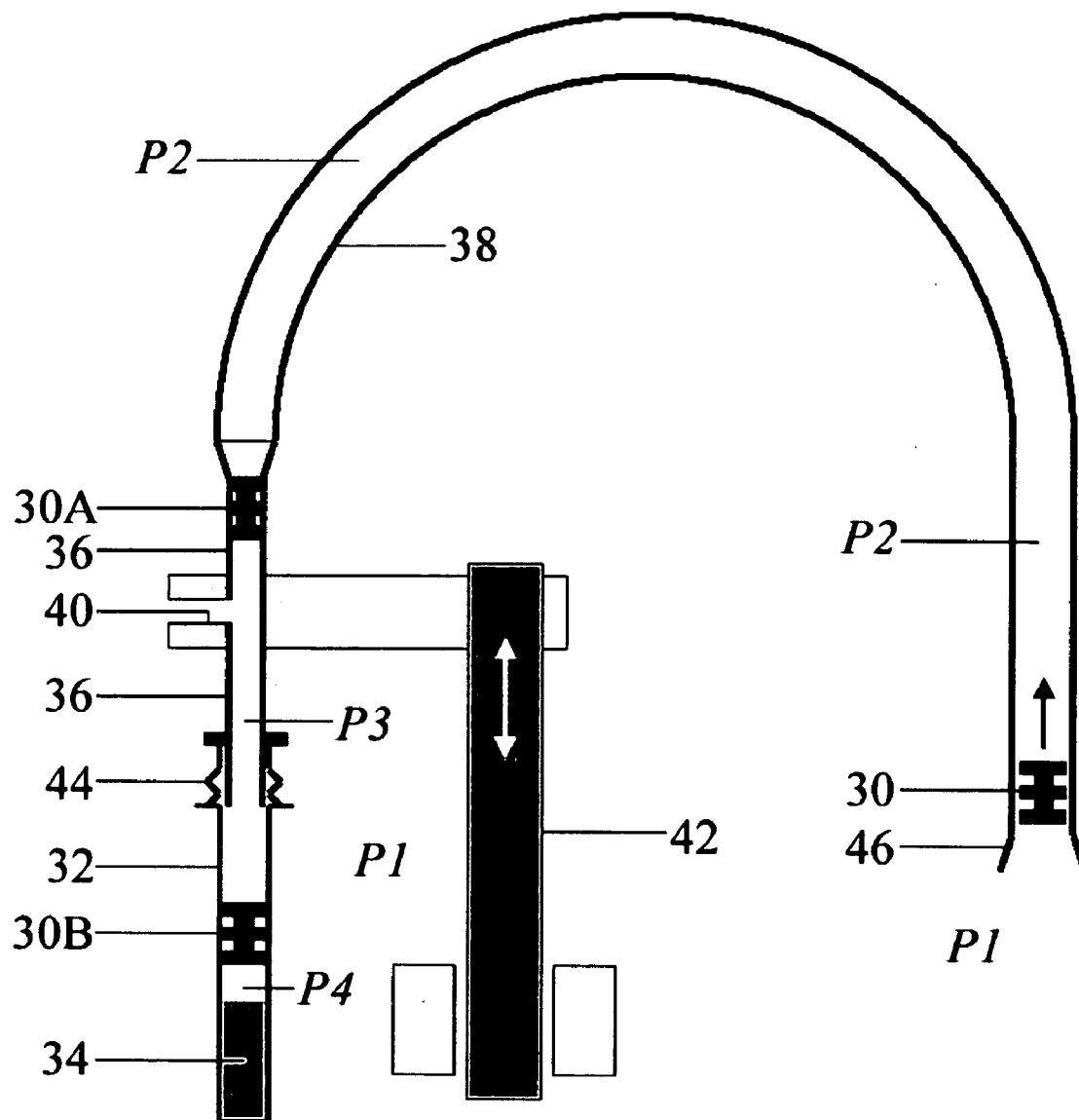


Figure 6

## METHOD AND APPARATUS TO INSERT STOPPERS INTO PREFILLED SYRINGES

### FIELD OF THE INVENTION

[0001] The present invention relates to an apparatus and method for inserting stoppers under a vacuum into a syringe filled with liquid.

### BACKGROUND OF THE INVENTION

[0002] In order to prepare a medical syringe that will be used to inject liquid into a patient, it is critical that the syringe and fluid are free of contamination, biological and chemical. Apparatus used in the process must be made from non-corrosive materials and be located within a controlled atmosphere. Important to the process and apparatus is the prevention of air being retained within the syringe after the filling and stopper insertion processes. The presence of air in the syringe and its possible injection into a patient is undesirable. One of the objectives of syringe filling and closing systems is to minimize the trapped air above the liquid.

[0003] The syringes and stoppers are often standardized by the use of ISO (International Organization for Standardization), e.g. ISO 11040-4 and 5 for glass barrels and plungers for injectables. It is therefore possible to manufacture apparatus to accommodate the various size barrels or syringes and plungers or stoppers.

[0004] All apparatus described herein is typically part of a larger machine that precisely locates multiple syringes below a series of one or more stopper insertion apparatuses and then delivers and inserts the stoppers within the previous filled syringes. Syringes processed by the traditional method contain a relatively large amount of air or gas above the liquid after filling and stopper insertion. This method also requires moving machinery parts to move stopper rams and stopper tubes, inject the stoppers and place the syringes. This machinery releases particles by wear and interferes with the flow of clean air through the machine.

[0005] A description of a typical prior stopper insertion apparatus will be described by referring to FIG. 1. The basic function of this system is the insertion of stoppers 1 (also called pistons or plungers) into filled syringes 2. The syringes are filled with a liquid medium 3. The main functional elements for this insertion are stopper tubes 4 and stopper rams 5. Each functional element is moved relative to each other according to a specific timing. The movement and timing of stopper tubes 4 and stopper rams 5 is driven for example by mechanical cams, servos or a robot system. A stopper insertion system includes one stopper tube 4 and stopper ram 5 for sealing one syringe 2 at once or more sets for sealing two or more syringes at the same time. The following description of operation is simplified for only one set.

[0006] The stopper 1 is placed concentric above the stopper tube 4. By a vertical movement of the stopper ram 5, the stopper 1 is inserted into the stopper tube 4. The stopper 1 is compressed inside the stopper tube 4. Then the stopper tube 4 and stopper ram 5 move down into the syringe 2 up to a specific depth. As long as the stopper 1 remains in the stopper tube 4, air above the filling level of the filling liquid 3 can escape out of the syringe 2 by passing the gap between

stopper tube 4 and the inner surface of the syringe body. The pressure inside the syringe remains almost equal to the system's environment pressure ( $P1 \approx P2$ ). By starting to move up first, the stopper tube 4 releases the stopper 1 above the filling level. After that release the stopper ram 5 also starts moving up. Both functional elements move back to their home position, and the next cycle can start.

[0007] According to the described function of the system, the final position of the stopper 1A after the insertion into the filled syringe 2 depends on the lowest position of the stopper tube 4 movement and the stopper ram 5 movement. A gas volume between the stopper 1A and filling liquid 3 remains. The pressure of this gas volume is close to the system's environment pressure ( $P1 \approx P2$ ).

### SUMMARY OF THE INVENTION

[0008] It is the purpose of this invention to disclose an apparatus and method for inserting a stopper into a syringe using simplified machinery having less moving parts and that permits a minimum volume of air to remain within the syringe after stopper insertion. In a first embodiment the apparatus provides a stopper insertion system that uses vacuum to assist the insertion of the stopper. This method and apparatus reduces the air entrapped above the liquid in a syringe. A preferred embodiment improves this process by eliminating the stopper ram mechanism and causes insertion of the stopper by controlled use of vacuum. This method and apparatus reduces entrapped air and reduces the moving machinery parts required to insert the stoppers.

### BRIEF DESCRIPTION OF THE DRAWINGS

[0009] FIG. 1 is a side section schematic view of a prior art apparatus for inserting a stopper into a syringe.

[0010] FIG. 2 is a side section of a first embodiment of the present invention for an apparatus for inserting a stopper into a syringe.

[0011] FIG. 3 is a view of the FIG. 2 apparatus at the start of the stopper insertion cycle.

[0012] FIG. 4 is a view of the FIG. 2 apparatus after the start of the stopper insertion cycle.

[0013] FIG. 5 is a view of the FIG. 2 apparatus near completion of the stopper insertion cycle.

[0014] FIG. 6 is a side section schematic of a preferred embodiment of the present invention at the start of the stopper insertion cycle.

### DETAILED DESCRIPTION OF THE INVENTION

[0015] This first embodiment will be described by referring to FIG. 2. The basic function of this system is the insertion of stoppers 10 (also called pistons or plungers) into filled syringes 12 with vacuum assist. The syringes are filled with a liquid medium 14. The main functional elements for this insertion are stopper tubes 16 and stopper rams 20. The stopper tubes 16 have one or more radial ports 18 which are connected to a vacuum system. A vacuum system, for example, could include a vacuum pump and a vacuum valve. Each functional element is moved relative to each other according to a specific timing. Vacuum supplied by the vacuum system is activated and deactivated according to the

stopper tube's 16 and stopper ram's 20 movement. The movements 22 and 24 and timing of stopper tubes 16 and stopper rams 20 are driven for example by mechanical cams, servos, or a robot system. A stopper insertion system can include one stopper tube 16 and stopper ram 20 for sealing one syringe 12 at once or more sets for sealing two or more syringes at the same time. The following description is simplified for only one set. A description of one cycle will refer to FIGS. 3, 4 and 5.

[0016] Referring to FIG. 3: The stopper 10 is placed concentric above the stopper tube 16. By a vertical movement of the stopper ram 20, the stopper 10 is inserted into the stopper tube 16 up to a specific depth as shown. The stopper 10 is compressed inside the stopper tube 16. By reaching this specific depth, the stopper 10 seals the upper opening of the stopper tube 16 but remains above the radial vacuum port(s) 18.

[0017] Referring to FIG. 4: The stopper tube 16 and stopper ram 20 move down until the sealing element 26 touches the syringe's 12 body. The stopper tube 16 follows the movement of the stopper ram 20, so there is no relative movement between these two components. The stopper 10 remains in its specific position proportional to the stopper tube 16. The sealing element 26 seals the stopper tube against the syringe 12. A vacuum chamber is formed including the stopper tube 16 and syringe 12. After the vacuum chamber is formed, the vacuum is activated for the duration of 0.01 seconds to 4 seconds. The vacuum chamber is evacuated up to a pressure between 0.01 millibar and 300 millibar. During the evacuation the stopper tube 16, stopper ram 20 and stopper 10 remain in position as shown.

[0018] Referring to FIG. 5: After that specific duration of evacuation the stopper tube 16 and sealing element 26 remain in position. The stopper ram 20 moves down until the stopper 10 is released out of the stopper tube 16. When the stopper 10 reaches the vacuum connection port 18, no further vacuum in the syringe 12 can be reached by evacuating the vacuum chamber. After the stopper 10 has passed the depth of the vacuum connection port 18 the stopper tube's 16 section above the stopper 10 (including the vacuum connection port 18) is vented up to the system's environment pressure  $P_1$ . A force which is caused by the pressure difference between inside the syringe 12 and the environment ( $P_1 > P_2$ ) moves the stopper 10 down to a final position where the pressure difference is almost equalized with ambient pressure by the compression of the remaining gas volume between the filling liquid 14 and the stopper 10. The stopper ram 20 and stopper tube 16 return to their home position by upward movements 22 and 24. A new cycle can start.

[0019] According to the described function of the system, the final position of the stopper 10A after the insertion into the filled syringe 12 does not depend on the lowest position of the stopper tube 16 movement and the stopper ram 20 movement. After the stopper 10 is released out of the stopper tube 16, different forces act on the stopper 10. The first resultant force is caused by the pressure difference between inside the syringe 12 ( $F_{\text{Inside}} = P_2 \cdot A$ ) and the system's environment pressure ( $F_{\text{Outside}} = P_1 \cdot A$ ). "A" is the cross-sectional area of the inserted stopper 10A. The second force is friction between the syringe 12 and the moving stopper 10. The stopper 10 is forced to move down until these forces

are balanced. By this way the remaining gas volume between the filling liquid 14 and the stopper 10 can be reduced in comparison to the stopper insertion prior art.

[0020] The preferred embodiment vacuum stopper insertion apparatus description refers to FIG. 6. The apparatus can have one or more devices, but one will be described for simplicity. The basic function of this system is the insertion of stoppers 30 into filled syringes 32 using a vacuum. The syringes are filled with a liquid medium 34. The main functional elements for this insertion are a stopper tube 36 and a flexible stopper transport device 38. The stopper tube 36 has one or more radial ports 40 which are connected to a vacuum system. A vacuum system, for example, can include a vacuum pump and a vacuum valve. The stopper tube 36 is moved according to a specific timing. Vacuum is supplied by the vacuum system and is activated and deactivated according to the stopper tube 36 movement and the flexible stopper transport device 38 movement. The movement and timing of the stopper tube 36 and flexible stopper transport device 38 is driven, for example, by mechanical cams, servos, or a robot system. A stopper insertion system can include one stopper tube 36 and flexible stopper transport device 38 for sealing one syringe 32 at one time or more sets for sealing two or more syringes at the same time. The following operational description is simplified for only one set. A description of one cycle follows:

[0021] The stopper tube 36 is moved down until a sealing element 44 touches the syringe 32 body. The sealing element 44 seals the stopper tube 36 against the syringe 32. A stopper 30 is fed into the flexible stopper transport device entrance 46. Vacuum between 10 and 800 millibars is activated at port 40. In comparison to the environment's pressure  $P_1$ , the pressure  $P_2$  inside the flexible stopper transport device 38 is reduced ( $P_1 > P_2$ ) by evacuation. This pressure difference forces the stopper 30 to move through the flexible stopper transport device 38. The stopper 30 is compressed as shown at 30A when it enters the stopper tube 36. The stopper 30A seals the stopper tube 36 from the flexible stopper transport device 38. In that stage, an optional higher vacuum between 0.01 and 300 millibars,  $P_3$  ( $P_1 > P_2 > P_3$ ) can be provided by the vacuum system. Also in that stage, the stopper 30A can be held on this position by an optional holding device for a specific duration of evacuation. After the evacuation of the smaller vacuum chamber between the stopper 30A, stopper tube 36 and the syringe 32, the pressure difference between inside the syringe 32 and above the stopper 30A (inside the flexible stopper transport device 38 and the upper section of the stopper tube 36) forces the stopper 30A to move down through the stopper tube 36 into the syringe 32 to position 30B. As an option, the pressure inside the flexible stopper transport device 38 and the upper section of the stopper tube 36 can be increased by venting or providing an additional air pressure supply at port 40 at that stage. The stopper tube 36 returns to its home position by movement 42, and a new cycle can start. Similar to the vacuum assisted stopper insertion previously described, the final position of the stopper 30B after the insertion into the filled syringe 32 depends also on the pressure difference  $P_1 > P_4$ . After the stopper 30B reaches the lowest position, a gas volume between the stopper 30B and filling liquid 34 can remain. The pressure  $P_4$  of this gas volume would be close to the system's environment pressure  $P_1$ . Also similar to the vacuum assisted stopper insertion previously described, the final position of the stopper 30B after the insertion into the

filled syringe 32 depends on different forces that act on the stopper 30B. The first resultant force is caused by the pressure difference between inside the syringe 32 ( $F_{\text{Inside}} = P4 \cdot A$ ) and the system's environment pressure ( $F_{\text{Outside}} = P1 \cdot A$ ). "A" is the cross-sectional area of the inserted stopper 30B. The second force is friction between the syringe 32 and the moving stopper 30B. The stopper 30B is forced to move down until these forces are balanced. In this way the remaining gas volume between the filling liquid 34 and the stopper 30B is reduced in comparison to the traditional stopper insertion previously described.

[0022] The above embodiments describe a simplified apparatus and method for closing a filled syringe with a stopper that has a minimum of entrapped air.

We claim:

1. An apparatus for inserting stoppers into prefilled syringes comprising:

- (a) a stopper tube movement within a base;
- (b) a stopper tube attached to the stopper tube movement;
- (c) at least one radial vacuum port in the stopper tube, said ports connecting to a vacuum means;
- (d) a sealing element attached to the circumference of the stopper tube;
- (e) a stopper ram movement within the base, mounted adjacent to the stopper tube movement;
- (f) a stopper ram affixed to the stopper ram movement, aligned within the stopper tube; and
- (g) stoppers temporarily affixed to the stopper ram movement, wherein sequential timed motion of the stopper tube movement and the stopper ram movement, with vacuum application, inserts the stoppers into the syringe above a prefilled liquid.

2. The apparatus of claim 1 wherein the apparatus comprises two or more of the following elements: stopper tubes, stoppers, sealing elements, stopper rams, and syringes; thereby able to insert stoppers into multiple syringes simultaneously.

3. The apparatus of claim 1 wherein the vacuum application to insert the stoppers is between 0.01 and 4 seconds duration and to an absolute pressure of 0.01 to 300 millibars.

4. A method for inserting stoppers into prefilled syringes in an apparatus comprising a stopper tube having a vacuum means port and a sealing element, a stopper tube movement affixed to the stopper tube, a stopper ram, and a stopper ram movement affixed to the stopper ram, the method comprising the steps of:

- (a) inserting the stopper into the stopper tube above the vacuum means port by lowering the stopper ram movement, stopper tube movement and attached stopper;
- (b) lowering the stopper tube movement and the stopper ram movement until the sealing element seals against the syringe thereby creating a vacuum chamber including the syringe and stopper tube;
- (c) evacuating the chamber to a vacuum;
- (d) lowering the stopper ram and stopper below the vacuum means port and out of the stopper tube into the syringe;

(e) venting to atmospheric pressure, the stopper tube and space above the stopper thereby forcing the stopper to a position close to a prefilled liquid; and then

(f) raising the stopper ram and stopper tube up to the home position immediately prior to step (a).

5. The method of claim 4 wherein the chamber is evacuated for a period between 0.01 and 4 seconds to an absolute pressure of 0.01 to 300 millibars.

6. The method of claim 4 wherein the apparatus comprises two or more of the following elements: stopper tubes, stoppers, sealing elements, stopper rams, and syringes; thereby able to insert stoppers into multiple syringes simultaneously.

7. An apparatus for inserting stoppers into prefilled syringes using a vacuum, the apparatus comprising:

- (a) a stopper tube movement within a base;
- (b) a stopper tube attached to the stopper tube movement;
- (c) at least one radial vacuum port in the stopper tube, said ports connecting to vacuum means;
- (d) a sealing element attached to the circumferences of the stopper tube;
- (e) stopper transport device having a first end attached to the top of the stopper tube; and
- (f) means for feeding stoppers into a second end of the stopper transport device, wherein sequential operation of the stopper tube movement and application of vacuum and atmospheric pressure inserts the stoppers into the syringes.

8. The apparatus of claim 7 wherein the apparatus comprises two or more of the following elements: stopper tubes, stoppers, sealing elements, syringes, and stopper transport devices, thereby able to insert stoppers into multiple syringes simultaneously.

9. The apparatus of claim 7 wherein the vacuum application is to an absolute pressure of between 0.01 and 800 millibars.

10. A method for inserting stoppers into prefilled syringes in an apparatus comprising a stopper tube having a vacuum means port and a sealing element, a mechanical arm affixed to the stopper tube, and a stopper transport device affixed to the top of the stopper tube, the method comprising the steps of:

- (a) lowering the mechanical arm and stopper tube until the sealing element seals at the top of the syringe;
- (b) feeding a stopper into an open end of the stopper transport device;
- (c) activating a vacuum in the stopper tube, syringe and transport device thereby transporting the stopper to the top of the stopper tube;
- (d) activating a higher vacuum in the stopper tube and syringe thereby inserting the stopper into the syringe above a prefilled liquid; and then
- (e) raising the mechanical arm and stopper tube up to the home position immediately prior to step (a).

11. The method of claim 10 wherein the apparatus comprises two or more of the following elements: stopper tubes,

stoppers, sealing elements, syringes, and stopper transport devices, thereby able to insert stoppers into multiple syringes simultaneously.

**12.** The method of claim 10 wherein a step is added after step (d) to increase the pressure in the stopper tube transport device thereby forcing the stopper further into the syringe.

**13.** The method of claim 10 wherein the actuating vacuum of step (c) is between 10 and 800 millibars.

**14.** The method of claim 10 wherein the actuating higher vacuum of step (d) is between 0.01 and 300 millibars.

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