plunger deformity. While the VC method may not lead to drug product in the stopper ribs, the VC process is much slower and is impractical when processing prefilled syringes in bulk. For both VA and VC methods, relying on the pressure differential to place the stopper deep in the reservoir 13 results in variable stopper placements and therefore poor process capability scores and longer migration times. Typically, the stopper reaches a final position after 12 to 24 hours, which delays the process of determining whether the prefilled syringes are suitable for use. Consequently, these methods lead to unacceptable rates of prefilled syringe rejections due to plunger deformity, drug product between stopper or plunger ribs, higher rates of stopper migration out of a target placement range – thereby increasing rates of prefilled syringe rejections. These rejections often occur at the sterilization location, different from the filling location, and therefore leads to inefficiency and waste.

SUMMARY

[0006] The proposed methodology of stopper placement in a syringe with a low drug product fill volume involves more predictable and accurate results to place stoppers in prefilled syringes in acceptable ranges by supplementing known vacuum assist and vacuum compression techniques with a mechanical insertion component.

[0007] In accordance with a first aspect of the present disclosure, a method of placing a stopper into a syringe barrel partially filled with a drug product may include aligning a stopper with a longitudinal axis of a syringe barrel. The syringe barrel may include a proximal end, a distal end, and a reservoir. The drug product may be disposed in a distal end of the reservoir at the distal end of the syringe barrel. The method may include applying a vacuum pressure to the reservoir of the syringe barrel. The vacuum pressure may be in a range of approximately 70 mBar to approximately 85 mBar. The method may further include pushing the stopper with a plunger rod into the reservoir of the syringe barrel to a first depth, thereby creating a pressure differential across the stopper. The first depth may be in a range of approximately 20 mm to approximately 40 mm from the distal end of the reservoir. Further, the method may include disengaging the plunger rod from the stopper after pushing the stopper to the first depth, thereby causing the pressure differential across the stopper to displace the stopper to a second depth different than the first depth.

[0008] In accordance with a second aspect of the present disclosure, a method of placing a stopper into a syringe barrel partially filled with a drug product may include aligning a stopper with a longitudinal axis of a syringe barrel. The syringe barrel may include a proximal end, a distal end, and a reservoir. The drug product may be disposed in a distal end of the reservoir at the distal end of the syringe barrel. The method may include applying a vacuum pressure to the reservoir of the syringe barrel and pushing the stopper with a plunger rod into the reservoir of the syringe barrel to a first depth, thereby creating a pressure differential across the stopper. The plunger rod may extend into the reservoir of the syringe barrel. Further, the method may include disengaging the plunger rod from the stopper after pushing the stopper to the first depth, thereby causing the pressure differential across the stopper to displace the stopper to a second depth different than the first depth.

[0009] In further accordance with any one or more of the foregoing first and second aspects, a method for placing a stopper in a syringe barrel may include any one or more of the following forms.

[0010] In one form, pushing the stopper may include inserting the plunger rod into the reservoir of the syringe barrel.

[0011] In another form, applying the vacuum pressure may at least partially coincide with pushing the stopper with the plunger rod into the reservoir of the syringe barrel.

[0012] In yet another form, pushing the stopper may include pushing the stopper into the syringe barrel a distance in a range of approximately 23 mm to 32 mm from the distal end.

[0013] In some forms, pushing the stopper may include pushing the stopper after applying the vacuum pressure to the syringe barrel.