may be of particular concern regarding biopharmaceuticals because it can cause aggregation of certain proteins, thereby rendering the biopharmaceutical unusable for injection.

[0004] A second aspect is the occurrence of small bumps or asperities on the inner surface of the insertion tube that may be present as a by-product of the insertion tube manufacturing process. Typically, these asperities have no effect on a stopper as the silicone in the insertion tube allows the stopper to pass over the asperities without issue. However, if silicone or another suitable lubricant is not applied or is inadvertently omitted, damage or destruction of the stopper may cause failure in the syringe or similar injectable device.

[0005] Therefore, a need exists for a method of inserting a lubricant free stopper into a lubricant free barrel or a lubricant free cartridge tube in a manner that both reduces the potential for drug contamination and minimizes damage to the stopper.

SUMMARY

[0005a] According to an aspect, the present disclosure refers to a method for inserting a lubricant free stopper into a lubricant free barrel, the method comprising: (A) inserting a stopper that includes at least one sealing rib into a placement region located at a proximal end of an insertion tube, the insertion tube having a body connected to the placement region through a transition zone, wherein the stopper comprises an elastomeric body at least partially covered by a laminate, a polymer, or an expanded polymer, (B) lowering the body of the insertion tube into a syringe barrel having a barrel flange to a position located past the barrel flange, (C) maneuvering the stopper to a distal opening of the insertion tube using an insertion pin, (D) retracting the insertion tube while the stopper remains in a fixed position within the syringe barrel by the insertion pin, where the stopper is securely positioned within the syringe barrel and (E) fully retracting the insertion pin and the insertion tube from the barrel to form a stoppered syringe, wherein at least the stopper, the insertion tube, the body of the insertion tube, the syringe barrel, the barrel flange, and the insertion pin are free of

lubricants, and wherein the insertion tube is modified to have an average surface roughness (Sa) from 20 nm to 400 nm and/or an average kurtosis (Sku) less than 8.

[0005b] According to another aspect, the present disclosure refers to a system comprising: (A) an insertion tube having: a placement region having a diameter for receiving a stopper from a stopper feeder, wherein the stopper is at least partially covered by a laminate, a polymer, or an expanded polymer; a body having a diameter that is smaller than the diameter of the placement region; and a transition zone having a tapered angle for transitioning the stopper from the placement region to the insertion tube body; (B) an insertion pin for maneuvering the stopper through the insertion tube; and (C) a barrel or cartridge tube having an inner surface for receiving the stopper from the insertion tube and a therapeutic substance from a therapeutic feeder, wherein (A) to (C) comprise a system to form a pre-filled syringe or cartridge, and wherein the system and the pre-filled syringe are lubricant free, and wherein the insertion tube is modified to have an average surface roughness (Sa) from 20 nm to 400 nm and/or an average kurtosis (Sku) less than 8.

[0005c] According to another aspect, the present disclosure refers to a method for inserting a lubricant free stopper into a lubricant free cartridge tube, the method comprising: (A) inserting a stopper that includes at least one sealing rib into a placement region located at a proximal end of an insertion tube, the insertion tube having a body connected to the placement region through a transition zone, wherein the stopper is at least partially covered by a laminate, a polymer, or an expanded polymer; (B) lowering the body of the insertion tube into a cartridge tube having an end portion to a position located past the top of the cartridge tube; (C) maneuvering the stopper to a distal opening of the insertion tube using an insertion pin; (D) retracting the insertion tube while the stopper remains in a fixed position within the cartridge tube by the insertion pin, wherein the stopper is securely positioned within the cartridge tube; and (E) fully retracting the insertion pin and the insertion tube from the cartridge tube to form a stoppered cartridge, wherein at least the stopper, the insertion tube, the body of the insertion tube, the cartridge tube, the top of the cartridge tube, and the insertion pin are free of lubricants, and wherein the insertion tube has an average surface roughness (Sa) from 20 nm to 400 nm and/or an average kurtosis (Sku) less than 8.

[0006] According to one example, a method for inserting a lubricant free stopper into a lubricant free barrel includes (A) inserting a stopper that includes at least one sealing rib into a placement region located at a proximal end of an insertion tube, the insertion tube having a body connected to the placement region through a transition zone, (B) lowering the body of the insertion tube into a syringe barrel having a barrel flange to a position located past the barrel flange, (C) maneuvering the stopper to a distal opening of the insertion tube using an insertion pin, (D) retracting the insertion tube while the stopper remains in a fixed position within the syringe barrel by the insertion pin, where the stopper is securely positioned within the syringe barrel and (E) fully retracting the insertion pin and the insertion tube from the barrel to form a stoppered syringe. At least the stopper, the insertion tube, the body of the insertion tube, the syringe barrel, the barrel flange, and the insertion pin are free or substantially free of lubricants.

[0007] According to another example, the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.

[0008] According to another example, the body of the insertion tube has an average kurtosis (S_{ku}) less than about 8.

[0009] According to another example, the stopper is inserted into the insertion tube at a peak insertion force ranging from about 10 N to about 200 N.

[0010] According to another example, the stopper includes at least one sealing rib and the sealing rib has a line count of less than 30.

[0011] According to another example, the stoppered syringe has a helium leak rate that is not greater than 6×10^{-6} sccs.

[0012] According to another example, step (A) and step (B) occur sequentially or simultaneously.

[0013] According to another example, in step (B), a gap is located between the insertion tube and an inner surface of the barrel to allow for pressure venting.

[0014] According to another example, in step (D) the insertion tube is retracted prior to the insertion pin.

[0015] According to another example, in step (E) the insertion tube and the insertion pin are retracted sequentially or simultaneously.

[0016] According to another example, the stopper comprises an elastomeric body and a polymer layer thereon.

[0017] According to another example, the expanded fluoropolymer includes an expanded fluoropolymer.

[0018] According to another example, the expanded fluoropolymer includes an expanded polytetrafluoroethylene.

[0019] According to another example, a therapeutic compound is delivered to the syringe barrel prior to lowering the insertion tube into the syringe barrel.

[0020] According to another example, the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

[0021] According to another example, an amount of particles in the barrel is less than about 600 particles / mL for particles greater than 10 µm in size when measured in water for injection (WFI).

[0022] According to another example, an amount of particles in the barrel is less than 60 particles /mL for particles greater than 25 µm in size when measured in water for injection (WFI).

[0023] According to another example, the insertion tube has been electropolished, extrude honed, or a combination thereof.

[0024] According to another example, a system includes an (A) insertion tube having (1) a placement region having a diameter for receiving a stopper from a stopper feeder, (2) a body having a diameter that is smaller than the diameter of the placement region, and (3) a transition zone having a tapered angle for transitioning the stopper from the placement region to the insertion tube body, (B) an insertion pin for maneuvering the stopper through the insertion tube, and (C) a barrel having an inner surface for receiving the stopper from the insertion tube and a therapeutic substance from a therapeutic feeder. (A) to (C) include a system to form a pre-filled syringe or pre-filled cartridge and the system, the pre-filled syringe, and the pre-filled cartridge are lubricant free or substantially lubricant free.

[0025] According to another example, the taper angle is between about 1 degree and about 20 degrees.

[0026] According to another example, the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.

[0027] According to another example, the insertion tube body has an average kurtosis (Sku) less than about 8.

[0028] According to another example, the insertion tube has been electropolished, extrude honed, or a combination thereof.

[0029] According to another example, the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

[0030] According to another example, the stopper comprises an elastomeric body and a polymer layer at least partially covering the elastomeric body.

[0031] According to another example, the polymer layer comprises an expanded fluoropolymer.

[0032] According to another example, the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

[0033] According to another example, a method for inserting a lubricant free stopper into a lubricant free cartridge tube includes (A) inserting a stopper that includes at least one sealing rib into a placement region located at a proximal end of an insertion tube, the insertion tube having a body connected to the placement region through a transition zone, (B) lowering the body of the insertion tube into a cartridge tube having an end portion to a position located past the top of the cartridge tube, (C) maneuvering the stopper to a distal opening of the insertion tube using an insertion pin, (D) retracting the insertion tube while the stopper remains in a fixed position within the cartridge tube by the insertion pin, where the stopper is securely positioned within the cartridge tube, and (E) fully retracting the insertion pin and the insertion tube from the cartridge tube to form a stoppered cartridge. At least the stopper, the insertion tube, the body of the insertion tube, the cartridge tube, the top of the cartridge tube, and the insertion pin are free or substantially free of lubricants.

[0034] According to another example, the stopper is inserted into the insertion tube at a peak insertion force ranging from about 10 N to about 200 N.

[0035] According to another example, the stopper includes at least one sealing rib and the sealing rib has a line count of less than 30.

[0036] According to another example, (A) and step (B) occur sequentially or simultaneously.

[0037] According to another example, in step (B), a gap is located between the insertion tube and an inner surface of the cartridge tube to allow for pressure venting.

[0038] According to another example, in step (D) the insertion tube is retracted prior to the insertion pin.

[0039] According to another example, in step (E) the insertion tube and the insertion pin are retracted sequentially or simultaneously.

[0040] According to another example, the stopper comprises an elastomeric body and a polymer layer thereon.

[0041] According to another example, the polymer layer comprises an expanded fluoropolymer.

[0042] According to another example, the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

[0043] According to another example, further including delivering a therapeutic compound to the cartridge tube prior to lowering the insertion tube into the cartridge tube.

[0044] According to another example, the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

[0045] According to another example, the insertion tube has been electropolished, extrude honed, or a combination thereof.

[0046] According to another example, the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.

[0047] According to another example, the body of the insertion tube has an average kurtosis (S_{ku}) less than about 8.

[0048] According to another example, the stoppered syringe has a helium leak rate that is not greater than 6×10^{-6} sccs.

BRIEF DESCRIPTION OF THE DRAWINGS

[0049] The accompanying drawings are included to provide a further understanding of the disclosure and are incorporated in and constitute a part of this specification,

WHAT IS CLAIMED IS

1. A method for inserting a lubricant free stopper into a lubricant free barrel, the method comprising:

(A) inserting a stopper that includes at least one sealing rib into a placement region located at a proximal end of an insertion tube, the insertion tube having a body connected to the placement region through a transition zone, wherein the stopper comprises an elastomeric body at least partially covered by a laminate, a polymer, or an expanded polymer;

(B) lowering the body of the insertion tube into a syringe barrel having a barrel flange to a position located past the barrel flange;

(C) maneuvering the stopper to a distal opening of the insertion tube using an insertion pin;

(D) retracting the insertion tube while the stopper remains in a fixed position within the syringe barrel by the insertion pin, wherein the stopper is securely positioned within the syringe barrel; and

(E) fully retracting the insertion pin and the insertion tube from the barrel to form a stoppered syringe,

wherein at least the stopper, the insertion tube, the body of the insertion tube, the syringe barrel, the barrel flange, and the insertion pin are free of lubricants, and

wherein the insertion tube is modified to have an average surface roughness (S_a) from 20 nm to 400 nm and/or an average kurtosis (S_{ku}) less than 8.

2. The method of any claim 1, wherein the stopper is inserted into the insertion tube at a peak insertion force ranging from 10 N to 200 N.

3. The method of any one of claims 1-2, wherein the stopper includes at least one sealing rib and the sealing rib is has a line count of less than 30.

4. The method of any one of claims 1-3, wherein the stoppered syringe has a helium leak rate that is not greater than 6×10^{-6} sccs.

5. The method of any one of claims 1-4, wherein step (A) and step (B) occur sequentially or simultaneously.

6. The method of any one of claims 1-5, wherein in step (B), a gap is located between the insertion tube and an inner surface of the barrel to allow for pressure venting.

7. The method of any one of claims 1-6, wherein in step (D) the insertion tube is retracted prior to the insertion pin.

8. The method of any one of claims 1-7, wherein in step (E) the insertion tube and the insertion pin are retracted from the barrel sequentially or simultaneously.

9. The method of any one of claims 1-8, wherein the stopper has a polymer thereon.

10. The method of claim 9, wherein the polymer comprises an expanded fluoropolymer.

11. The method of claim 10, wherein the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

12. The method of any one of claims 1-8, further comprising delivering a therapeutic compound to the syringe barrel prior to lowering the insertion tube into the syringe barrel.

13. The method of claim 12, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

14. The method of any one of claims 1-8 and 13, wherein the insertion tube has been electropolished, extrude honed, or a combination thereof.

15. A system comprising:

(A) an insertion tube having:

a placement region having a diameter for receiving a stopper from a stopper feeder, wherein the stopper is at least partially covered by a laminate, a polymer, or an expanded polymer;

a body having a diameter that is smaller than the diameter of the placement region; and

a transition zone having a tapered angle for transitioning the stopper from the placement region to the insertion tube body;

(B) an insertion pin for maneuvering the stopper through the insertion tube; and

(C) a barrel or cartridge tube having an inner surface for receiving the stopper from the insertion tube and a therapeutic substance from a therapeutic feeder,

wherein (A) to (C) comprise a system to form a pre-filled syringe or cartridge, and

wherein the system and the pre-filled syringe are lubricant free, and

wherein the insertion tube is modified to have an average surface roughness (S_a) from 20 nm to 400 nm and/or an average kurtosis (S_{ku}) less than 8.

16. The system of claim 15, wherein the tapered angle is between 1 degree and 20 degrees.

17. The system of any one of claims 15-16, wherein the insertion tube has been electropolished, extrude honed, or a combination thereof.

18. The system of any one of claims 15-17, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

19. The system of any one of claims 15-18, wherein the stopper comprises an elastomeric body and a polymer at least partially covering the elastomeric body.

20. The system of claim 19, wherein the polymer comprises an expanded fluoropolymer.

21. The system of claim 20, wherein the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

22. A method for inserting a lubricant free stopper into a lubricant free cartridge tube, the method comprising:

(A) inserting a stopper that includes at least one sealing rib into a placement region located at a proximal end of an insertion tube, the insertion tube having a body connected to the placement region through a transition zone, wherein the stopper is at least partially covered by a laminate, a polymer, or an expanded polymer;

(B) lowering the body of the insertion tube into a cartridge tube having an end portion to a position located past the top of the cartridge tube;

(C) maneuvering the stopper to a distal opening of the insertion tube using an insertion pin;

(D) retracting the insertion tube while the stopper remains in a fixed position within the cartridge tube by the insertion pin, wherein the stopper is securely positioned within the cartridge tube; and

(E) fully retracting the insertion pin and the insertion tube from the cartridge tube to form a stoppered cartridge,

wherein at least the stopper, the insertion tube, the body of the insertion tube, the cartridge tube, the top of the cartridge tube, and the insertion pin are free of lubricants, and

wherein the insertion tube has an average surface roughness (S_a) from 20 nm to 400 nm and/or an average kurtosis (S_{ku}) less than 8.

23. The method of claim 22, wherein the stopper is inserted into the insertion tube at a peak insertion force ranging from 10 N to 200 N.

24. The method of any claim 22 or claim 23, wherein the stopper includes at least one sealing rib and the sealing rib has a line count of less than 30.

25. The method of any one of claims 22-24, wherein step (A) and step (B) occur sequentially or simultaneously.

26. The method of any one of claims 22-25, wherein in step (B), a gap is located between the insertion tube and an inner surface of the cartridge tube to allow for pressure venting.

27. The method of any one of claims 22-26, wherein in step (D) the insertion tube is retracted prior to the insertion pin.

28. The method of any one of claims 22-27, wherein in step (E) the insertion tube and the insertion pin are retracted sequentially or simultaneously.

29. The method of any one of claims 22-28, wherein the stopper comprises an elastomeric body and a polymer thereon.

30. The method of claim 29, wherein the polymer layer comprises an expanded fluoropolymer.

31. The method of claim 30, wherein the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

32. The method of any one of claims 22-31, further comprising delivering a therapeutic compound to the cartridge tube prior to lowering the insertion tube into the cartridge tube.

33. The method of claim 32, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

34. The method of any one of claims 22-33, wherein the insertion tube has been electropolished, extrude honed, or a combination thereof.

35. The method of any one of claims 22-34 wherein the cartridge has a helium leak rate that is not greater than 6×10^{-6} sccs.