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 ~~Aspect~~example ~~(“Aspect 1”)~~, 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 ~~Aspect (“Aspect 2”) further to Aspect 1~~example, the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.

[0008] According to another exampleAspect ("Aspect 3") further to Aspects 1 and 2, the body of the insertion tube has an average kurtosis (S_{ku}) less than about 8.

[0009] According to another exampleAspect ("Aspect 4") further to any of the preceding Aspects, 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 exampleAspect ("Aspect 5") further to any of the preceding Aspects, the stopper includes at least one sealing rib and the sealing rib has a line count of less than 30.

[0011] According to another exampleAspect ("Aspect 6") further to any of the preceding Aspects, the stoppered syringe has a helium leak rate that is not greater than 6 x 10^{-6} sccs.

[0012] According to another exampleAspect ("Aspect 7") further to any of the preceding Aspects, step (A) and step (B) occur sequentially or simultaneously.

[0013] According to another exampleAspect ("Aspect 8") further to any of the preceding Aspects, 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 exampleAspect ("Aspect 9") further to any of the preceding Aspects, in step (D) the insertion tube is retracted prior to the insertion pin.

[0015] According to another exampleAspect ("Aspect 10") further to any of the preceding Aspects, in step (E) the insertion tube and the insertion pin are retracted sequentially or simultaneously.

[0016] According to another exampleAspect ("Aspect 11") further to any of the preceding Aspects, the stopper comprises an elastomeric body and a polymer layer thereon.

[0017] According to another exampleAspect ("Aspect 12") further to Aspect 11, the expanded fluoropolymer includes an expanded fluoropolymer.

[0018] According to another exampleAspect ("Aspect 13") further to Aspect 12, the expanded fluoropolymer includes an expanded polytetrafluoroethylene.

[0019] According to another exampleAspect ("Aspect 14") further to any of the preceding Aspects, a therapeutic compound is delivered to the syringe barrel prior to lowering the insertion tube into the syringe barrel.

[0020] According to another exampleAspect ("Aspect 15") further to any of the preceding Aspects, the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

[0021] According to another exampleAspect ("Aspect 16") further to any of the preceding Aspects, 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 exampleAspect ("Aspect 17") further to any of the preceding Aspects, 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 exampleAspect ("Aspect 18") further to any of the preceding Aspects, the insertion tube has been electropolished, extrude honed, or a combination thereof.

[0024] According to another exampleAspect ("Aspect 19"), 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 exampleAspect ("Aspect 20") further to Aspect 19, the taper angle is between about 1 degree and about 20 degrees.

[0026] According to another exampleAspect ("Aspect 21") further to Aspects 19 and 20, the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.

[0027] According to another exampleAspect ("Aspect 22") further to Aspects 19-21, the insertion tube body has an average kurtosis (Sku) less than about 8.

[0028] According to another exampleAspect ("Aspect 23") further to Aspects 19-22, the insertion tube has been electropolished, extrude honed, or a combination thereof.

[0029] According to another exampleAspect ("Aspect 24") further to Aspects 19-23, the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

[0030] According to another exampleAspect ("Aspect 25") further to Aspects 19-24, the stopper comprises an elastomeric body and a polymer layer at least partially covering the elastomeric body.

[0031] According to another exampleAspect ("Aspect 26") further to Aspect 25, the polymer layer comprises an expanded fluoropolymer.

[0032] According to another exampleAspect ("Aspect 27") further to Aspect 26, the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

[0033] According to another exampleAspect ("Aspect 28"), 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 exampleAspect ("Aspect 29") further to Aspect 28, 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 exampleAspect ("Aspect 30") further to Aspects 28 and 29, the stopper includes at least one sealing rib and the sealing rib has a line count of less than 30.

[0036] According to another exampleAspect ("Aspect 31") further to Aspects 28-30, (A) and step (B) occur sequentially or simultaneously.

[0037] According to another exampleAspect ("Aspect 32") further to Aspects 28-31, 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 exampleAspect ("Aspect 33") further to Aspects 28-32, in step (D) the insertion tube is retracted prior to the insertion pin.

[0039] According to another exampleAspect ("Aspect 34") further to Aspects 28-33, in step (E) the insertion tube and the insertion pin are retracted sequentially or simultaneously.

[0040] According to another exampleAspect ("Aspect 35") further to Aspects 28-34, the stopper comprises an elastomeric body and a polymer layer thereon.

[0041] According to another exampleAspect ("Aspect 36") further to Aspect 35, the polymer layer comprises an expanded fluoropolymer.

[0042] According to another exampleAspect ("Aspect 37") further to Aspect 36, the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

[0043] According to another exampleAspect ("Aspect 38") further to Aspects 28-37, further including delivering a therapeutic compound to the cartridge tube prior to lowering the insertion tube into the cartridge tube.

[0044] According to another exampleAspect ("Aspect 39") further to Aspect 38, the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

[0045] According to another exampleAspect ("Aspect 40") further to Aspects 28-39, the insertion tube has been electropolished, extrude honed, or a combination thereof.

[0046] According to another exampleAspect ("Aspect 41") further to Aspects 28-40, the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.

[0047] According to another exampleAspect ("Aspect 42") further to Aspects 28-41, the body of the insertion tube has an average kurtosis (S_{ku}) less than about 8.

[0048] According to another exampleAspect ("Aspect 43") further to Aspects 28-42, the stoppered syringe has a helium leak rate that is not greater than 6×10^{-6} sccs.

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 ~~or substantially 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 claim 1, wherein the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.~~

~~3. The method of claim 1 or claim 2, wherein body of the insertion tube has an average kurtosis (S_{ku}) less than about 8.~~

4~~2~~. The method of any ~~one of~~ claim~~s~~ 1~~-3~~, wherein the stopper is inserted into the insertion tube at a peak insertion force ranging from ~~about~~ 10 N to ~~about~~ 200 N.

~~53~~. The method of any one of claims 1-24, wherein the stopper includes at least one sealing rib and the sealing rib is has a line count of less than 30.

~~64~~. The method of any one of claims 1-~~53~~, wherein the stoppered syringe has a helium leak rate that is not greater than 6 x 10^{-6} sccs.

~~75~~. The method of any one of claims 1-~~64~~, wherein step (A) and step (B) occur sequentially or simultaneously.

~~86~~. The method of any one of claims 1-~~75~~, wherein in step (B), a gap is located between the insertion tube and an inner surface of the barrel to allow for pressure venting.

~~97~~. The method of any one of claims 1-~~86~~, wherein in step (D) the insertion tube is retracted prior to the insertion pin.

~~108~~. The method of any one of claims 1-~~97~~, wherein in step (E) the insertion tube and the insertion pin are retracted from the barrel sequentially or simultaneously.

~~119~~. The method of any one of claims 1-~~108~~, wherein the stopper has~~comprises an elastomeric body and~~ a polymer ~~layer~~ thereon.

~~1210~~. The method of claim ~~119~~, wherein the polymer ~~layer~~ comprises an expanded fluoropolymer.

~~1311~~. The method of claim ~~1210~~, wherein the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

~~1412~~. The method of any one of claims 1-~~108~~, further comprising delivering a therapeutic compound to the syringe barrel prior to lowering the insertion tube into the syringe barrel.

~~1513~~. The method of claim ~~1412~~, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

~~16. The method of claim 14, wherein 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).~~

~~17. The method of claim 14, wherein 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).~~

~~18~~14. The method of any one of claims 1-~~10~~ 8 and ~~15~~13, wherein the insertion tube has been electropolished, extrude honed, or a combination thereof.

~~19~~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~~ or substantially 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.

~~20~~16. The system of claim ~~19~~15, wherein the taper~~ed~~ angle is between ~~about~~ 1 degree and ~~about~~ 20 degrees.

~~21. The system of claim 19 or claim 20, wherein the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.~~

~~22. The system of any one of claims 19-21, wherein the insertion tube body has an average kurtosis (Sku) less than about 8.~~

~~23~~17. The system of any one of claims ~~19~~15-~~22~~16, wherein the insertion tube has been electropolished, extrude honed, or a combination thereof.

~~24~~18. The system of any one of claims ~~19~~15-~~23~~17, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

~~25~~19. The system of any one of claims ~~19~~15-~~24~~18, wherein the stopper comprises an elastomeric body and a polymer ~~layer~~ at least partially covering the elastomeric body.

~~26~~20. The system of claim ~~25~~19, wherein the polymer ~~layer~~ comprises an expanded fluoropolymer.

~~27~~21. The system of claim ~~26~~20, wherein the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

~~28~~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 ~~or substantially 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.

~~29~~23. The method of claim ~~28~~22, wherein the stopper is inserted into the insertion tube at a peak insertion force ranging from ~~about~~ 10 N to ~~about~~ 200 N.

~~30~~24. The method of any claim ~~28~~ 22 or claim ~~29~~23, wherein the stopper includes at least one sealing rib and the sealing rib has a line count of less than 30.

~~31~~25. The method of any one of claims ~~27~~22-~~30~~24, wherein step (A) and step (B) occur sequentially or simultaneously.

~~32~~26. The method of any one of claims ~~28~~22-~~31~~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.

~~33~~27. The method of any one of claims ~~28~~22-~~32~~26, wherein in step (D) the insertion tube is retracted prior to the insertion pin.

~~34~~28. The method of any one of claims ~~28~~22-~~33~~27, wherein in step (E) the insertion tube and the insertion pin are retracted sequentially or simultaneously.

~~35~~29. The method of any one of claims ~~28~~22-~~34~~28, wherein the stopper comprises an elastomeric body and a polymer ~~layer~~ thereon.

~~36~~30. The method of claim ~~35~~29, wherein the polymer layer comprises an expanded fluoropolymer.

~~37~~31. The method of claim ~~36~~30, wherein the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.

~~38~~32. The method of any one of claims ~~28~~22-~~37~~31, further comprising delivering a therapeutic compound to the cartridge tube prior to lowering the insertion tube into the cartridge tube.

~~39~~33. The method of claim ~~38~~32, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

~~40~~34. The method of any one of claims ~~28~~22-~~39~~33, wherein the insertion tube has been electropolished, extrude honed, or a combination thereof.

~~41. The method of any one of claims 28-40, wherein the insertion tube has an average surface roughness (Sa) from about 20 nm to about 400 nm.~~

~~42. The method of any one of claims 28-41, wherein body of the insertion tube has an average kurtosis (S_{ku}) less than about 8.~~

~~43~~35. The method of any one of claims ~~28~~22-~~42~~,34 wherein the cartridge has a helium leak rate that is not greater than 6 x 10^{-6} sccs.