WHAT IS CLAIMED IS

1. A method comprising:

providing a syringe including a non-lubricated inner surface and a barrel flange;

inserting a non-lubricated stopper that includes a sealing rib into a placement region located at a proximal end of a vacuum chamber, the non-lubricated stopper being at least partially covered by a polymer layer;

creating a seal between a sealing gasket of the vacuum chamber and the barrel flange of the syringe;

applying vacuum through a vacuum port fluidly connected to the non-lubricated barrel and located at a distal end of the vacuum chamber to translate the stopper through the vacuum chamber from the placement region of the vacuum chamber into a proximal end of the non-lubricated barrel;

translating the stopper through the non-lubricated barrel with an insertion rod until a desired headspace between a front edge of the sealing rib and a liquid solution located in the non-lubricated cartridge tube is achieved;

retracting the insertion rod away from the vacuum chamber; and

retracting the vacuum chamber away from the non-lubricated barrel.

2. The method of claim 1, wherein the non-lubricated stopper comprises an elastomeric material having the polymer layer thereon.

3. The method of claim 1 or claim 2, wherein the polymer layer comprises an expanded fluoropolymer layer.

4. The method of any one of claims 1 to 3, wherein the expanded fluoropolymer layer comprises an expanded polytetrafluoroethylene layer.

5. The method of any one of claims 1 to 4, comprising adding the liquid solution to the non-lubricated barrel prior to creating the vacuum seal between the sealing gasket and the barrel flange.

~~6. The method of any one of claims 1 to 5, wherein the liquid solution is a therapeutic substance.~~

~~7. The method of claim 6, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.~~

~~8. The method of any one of claims 1 to 7, wherein the vacuum chamber has been electropolished, extrude honed, or a combination thereof.~~

~~9. The method of any one of claims 1 to 8, wherein at least the stopper, the vacuum chamber, the syringe barrel, the barrel flange, and the insertion pin are free or substantially free of lubricants.~~

~~10. The method of any one of claims 1 to 9, wherein the vacuum chamber contains a transition zone having a taper angle for transitioning the non-lubricated stopper from the placement region of the vacuum chamber to the proximal end of the barrel.~~

~~11. The method of claim 10, wherein the taper angle is between about 0.1 degree and about 20 degrees.~~

~~12. The method of any one of claims 1 to 11, wherein the desired headspace ranges from about 1 mm to about 25 mm.~~

~~13. The method of any one of claims 1 to 12, wherein the insertion rod includes a pin tip end and the non-lubricated stopper contains therein a cavity to receive the pin tip end.~~

~~14. The method of any one of claims 1 to 13, wherein the vacuum chamber is positioned above and is aligned with the non-lubricated barrel.~~

~~15. The method of any one of claims 1 to 14, comprising lowering the vacuum chamber to create the vacuum seal with the non-lubricated barrel.~~

~~16. The method of any one of claims 1 to 15, wherein the insertion rod and vacuum chamber are retracted simultaneously.~~

~~17. The method of any one of claims 1 to 15, wherein the insertion rod is retracted prior to retracting the vacuum chamber.~~

~~18~~1. A method comprising:

inserting a non-lubricated stopper that includes a sealing rib into a placement region located at a proximal end of a vacuum chamber, the non-lubricated stopper being at least partially covered by a polymer layer;

creating a vacuum seal between the vacuum chamber and an end portion of the non-lubricated cartridge tube;

applying vacuum through a vacuum port fluidly connected to the non-lubricated cartridge tube to vacuum seal the vacuum chamber and sealing gasket of the non-lubricated cartridge tube to translate the non-lubricated stopper through the vacuum chamber from the placement region of the vacuum chamber to a proximal end of the non-lubricated cartridge tube, the vacuum port being located at a distal end of the vacuum chamber;

translating the non-lubricated stopper through the non-lubricated cartridge tube with an insertion rod until a desired headspace between a front edge of the sealing rib and a liquid solution located in the non-lubricated cartridge tube is achieved;

retracting the insertion rod away from the vacuum chamber; and

retracting the vacuum chamber away from the non-lubricated cartridge tube.

~~19~~2. The method of claim ~~18~~1, wherein the stopper comprises an elastomeric material having the polymer layer thereon.

~~20~~3. The method of claim ~~18~~ 1 or claim ~~19~~2, wherein the polymer layer comprises an expanded fluoropolymer layer.

~~21~~4. The method of claim ~~20~~3, wherein the expanded fluoropolymer layer comprises an expanded polytetrafluoroethylene layer.

~~22~~5. The method of any one of claims ~~18~~ 1 to ~~21~~4, comprising adding the liquid solution to the non-lubricated barrel prior to creating the vacuum seal between the sealing gasket and the end portion of the non-lubricated cartridge tube.

~~23~~6. The method of any one of claims ~~18~~ 1 to ~~22~~5, wherein the liquid solution is a therapeutic substance.

~~24~~7. The method of claim ~~23~~6, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

~~25~~8. The method of any one of claims ~~18~~ 1 to ~~24~~7, wherein the vacuum chamber has been electropolished, extrude honed, or a combination thereof.

~~26~~9. The method of any one of claims ~~18~~ 1 to ~~25~~8, wherein at least the stopper, the vacuum chamber, the cartridge tube, the end portion of the cartridge tube, and the insertion pin are free or substantially free of lubricants.

~~27~~10. The method of any one of claims ~~18~~ 1 to ~~26~~9, wherein the vacuum chamber comprises a transition zone having a taper angle for transitioning the non-lubricated stopper from the placement region of the vacuum chamber to the proximal end of the cartridge tube.

~~28~~11. The method of any one of claims ~~18~~ 1 to ~~27~~10, wherein the taper angle is between about 0.1 degree and about 20 degrees.

~~29~~12. The method of any one of claims ~~18~~ 1 to ~~28~~11, wherein the desired headspace is from about 1 mm to about 25 mm.

~~30~~13. The method of any one of claims ~~18~~ 1 to ~~29~~12, wherein the insertion rod has a flat or substantially flat surface and the non-lubricated stopper is a solid stopper.

~~31~~14. The method of any one of claims ~~18~~ 1 to ~~30~~13, wherein the vacuum chamber is positioned above and is aligned with the non-lubricated cartridge tube.

~~32~~15. The method of any one of claims ~~18~~ 1 to ~~31~~14, comprising lowering the vacuum chamber to create the vacuum seal with the non-lubricated cartridge tube.

~~33~~16. The method of any one of claims ~~18~~ 1 to ~~32~~15, wherein the insertion rod and vacuum chamber are retracted simultaneously.

~~34~~17. The method of any one of claims ~~18~~ 1 to ~~32~~16, wherein the insertion rod is retracted prior to retracting the vacuum chamber.

~~35. A method comprising:~~

~~inserting a non-lubricated stopper that includes a sealing rib into a placement region located at a proximal end of a vacuum chamber, the non-lubricated stopper being at least partially covered by a polymer layer;~~

~~creating a seal between a sealing gasket of the vacuum chamber and the barrel flange of the syringe;~~

~~applying vacuum to a headspace by a vacuum port fluidly connected to the non-lubricated barrel and located at a distal end of the vacuum chamber to create a vacuum in the headspace, the non-lubricated barrel having therein a liquid solution;~~

~~translating the non-lubricated stopper through the vacuum chamber from the placement region of the vacuum chamber into a proximal end of the non-lubricated barrel by a first differential pressure created by the vacuum in the headspace;~~

sealing a pressure sealing cap to a proximal end of the vacuum chamber;

maneuvering the non-lubricated stopper through the non-lubricated barrel by a second differential pressure created by the vacuum in the headspace and a pressure applied to the non-lubricated stopper until a final headspace is achieved;

retracting the pressure sealing cap away from the vacuum chamber; and

retracting the vacuum chamber away from the non-lubricated barrel,

wherein the first headspace and the final headspace are each a distance from a liquid surface of the liquid solution to a front edge of the sealing rib of the non-lubricated stopper.

36. The method of claim 35, wherein the pressure is applied to the non-lubricated stopper through a pressure port in the pressure sealing cap.

37. The method of claim 35 or claim 36, comprising lowering the pressure sealing cap, the pressure sealing cap being positioned above and aligned with the vacuum chamber.

38. The method of any one of claims 35 to 37, comprising lowering the vacuum chamber to create the seal between the sealing gasket and the barrel flange of the non-lubricated barrel, the vacuum chamber being positioned above and aligned with the non-lubricated barrel.

39. The method of any one of claims 35 to 38, wherein the polymer layer comprises an expanded fluoropolymer layer.

40. The method of claim 39, wherein the expanded fluoropolymer layer comprises an expanded polytetrafluoroethylene layer.

41. The method of any one of claims 35 to 40, comprising adding the liquid solution to the non-lubricated barrel prior to creating the vacuum seal between the sealing gasket and the barrel flange.

~~42. The method of any one of claims 35 to 41, wherein the liquid solution is a therapeutic substance.~~

~~43. The method of claim 42, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.~~

~~44. The method of any one of claims 35 to 43, wherein the vacuum chamber has been electropolished, extrude honed, or a combination thereof.~~

~~45. The method of any one of claims 35 to 44, wherein at least the stopper, the vacuum chamber, the barrel, the barrel flange, and the pressure sealing cap are free or substantially free of lubricants.~~

~~46. The method of any one of claims 35 to 45, wherein the vacuum chamber contains a transition zone having a taper angle for transitioning the non-lubricated stopper from the placement region of the vacuum chamber to the proximal end of the non-lubricated barrel.~~

~~47. The method of claim 46, wherein the taper angle is between about 0.1 degree and about 20 degrees.~~

~~48. The method of any one of claims 35 to 47, wherein the final headspace is from about 1 mm to about 25 mm.~~

~~49. The method of any one of claims 35 to 47, wherein the pressure sealing cap and vacuum chamber are retracted simultaneously.~~

~~50. The method of any one of claims 35 to 47, wherein the pressure sealing cap is retracted prior to retracting the vacuum chamber.~~

~~51. A method comprising:~~

~~inserting a non-lubricated stopper that includes a sealing rib into a placement region located at a proximal end of a vacuum chamber, the non-lubricated stopper being at least partially covered by a polymer layer;~~

~~creating a seal between a sealing gasket of the vacuum chamber and an end portion of a cartridge tube;~~

~~applying vacuum to a headspace by a vacuum port fluidly connected to the non-lubricated cartridge tube and located at a distal end of the vacuum chamber to create a vacuum in the headspace, the non-lubricated cartridge tube having therein a liquid solution;~~

~~translating the non-lubricated stopper through the vacuum chamber from the placement region of the vacuum chamber into a proximal end of the non-lubricated cartridge tube by a first differential pressure created by the vacuum in the headspace;~~

~~sealing a pressure sealing cap to a proximal end of the vacuum chamber;~~

~~maneuvering the non-lubricated stopper through the non-lubricated cartridge tube by a second differential pressure created by the vacuum in the headspace and a pressure applied to the non-lubricated stopper until a final headspace is achieved;~~

~~retracting the pressure sealing cap away from the vacuum chamber; and~~

~~retracting the vacuum chamber away from the non-lubricated cartridge tube,~~

~~wherein the first headspace and the final headspace are each a distance from a liquid surface of the liquid solution to a front edge of the sealing rib of the non-lubricated stopper.~~

~~52. The method of claim 51, wherein the pressure is applied to the non-lubricated stopper through a pressure port in the pressure sealing cap.~~

~~53. The method of claim 51 or claim 52, comprising lowering the pressure sealing cap, the pressure sealing cap being positioned above and aligned with the vacuum chamber.~~

~~54. The method of any one of claims 51 to 53, comprising lowering the vacuum chamber to create the seal between the sealing gasket and the end portion of the non-lubricated cartridge tube, the vacuum chamber being positioned above and aligned with the non-lubricated cartridge tube.~~

~~55. The method of any one of claims 51 to 54, wherein the polymer layer comprises an expanded fluoropolymer layer.~~

~~56. The method of claim 55, wherein the expanded fluoropolymer layer comprises an expanded polytetrafluoroethylene layer.~~

~~57. The method of any one of claims 51 to 56, comprising adding the liquid solution to the non-lubricated cartridge tube prior to creating the vacuum seal between the sealing gasket and the end of the non-lubricated cartridge tube.~~

~~58. The method of any one of claims 51 to 57, wherein the liquid solution is a therapeutic substance.~~

~~59. The method of claim 58, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.~~

~~60. The method of any one of claims 51 to 59, wherein the vacuum chamber has been electropolished, extrude honed, or a combination thereof.~~

~~61. The method of any one of claims 51 to 60, wherein at least the stopper, the vacuum chamber, the cartridge tube, the end portion, and the pressure sealing cap are free or substantially free of lubricants.~~

~~62. The method of any one of claims 51 to 61, wherein the vacuum chamber contains a transition zone having a taper angle for transitioning the non-lubricated~~

stopper from the placement region of the vacuum chamber to the proximal end of the non-lubricated cartridge tube.

63. The method of claim 62, wherein the taper angle is between about 0.1 degree and about 20 degrees.

64. The method of any one of claims 51 to 63, wherein the final headspace is from about 1 mm to about 25 mm.

65. The method of any one of claims 51 to 64, wherein the pressure sealing cap and vacuum chamber are retracted simultaneously.

66. The method of any one of claims 51 to 64, wherein the pressure sealing cap is retracted prior to retracting the vacuum chamber.

67. A system comprising:

(A) a vacuum chamber having:

a placement region having a diameter for receiving a non-lubricated stopper from a stopper feeder;

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

a transition zone having a taper angle for transitioning a syringe stopper from the placement region to the vacuum chamber; and

a vacuum port for drawing a vacuum;

(B) a syringe barrel or cartridge tube having an inner surface for receiving the stopper from the vacuum chamber and a therapeutic substance from a therapeutic feeder;

(C) a mechanism for lowering the vacuum chamber to sealably attach the syringe barrel or cartridge tube to the vacuum chamber;

(D) a first pressure member for maneuvering the syringe stopper through the vacuum chamber;

(E) a second pressure member for translating the stopper through the syringe barrel or cartridge tube;

(F) a first mechanism for removing the vacuum chamber from the syringe barrel or cartridge tube;

(G) a second mechanism for removing a pressure sealing cap or insertion rod from the vacuum chamber;

wherein (A) to (G) 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.

68. The system of claim 67, wherein the taper angle is between about 1 degree and about 20 degrees.

69. The system of claim 67 or claim 68, wherein the first pressure member is differential pressure, an insertion pin, or a combination thereof.

70. The system of any one of claims 67 to 69, wherein the second pressure member is a differential in pressure between a vacuum in the headspace and a pressure applied to the stopper, or an insertion pin.

71. The system of any one of claims 67 to 70, wherein the vacuum chamber has been electropolished, extrude honed, or a combination thereof.

72. The system of any one of claims 67 to 71, wherein the therapeutic substance contains therein a biologic, a therapeutic compound, or a combination thereof.

73. The system of any one of claims 67 to 72, wherein the stopper comprises an elastomeric body and a polymer layer at least partially covering the elastomeric body.

74. The system of claim 73, wherein the polymer layer comprises an expanded fluoropolymer.

~~75. The system of claim 74, wherein the expanded fluoropolymer comprises an expanded polytetrafluoroethylene.~~