CLAIMS:

1. A ~~preparation~~ method for preparing sealed vials, comprising:

housing a plurality of vials in a temperature-controlled environment, which is a lyophilisation apparatus in which the condenser is disabled or which is an apparatus that is not specifically configured for lyophilisation, wherein the plurality of vials each have a volume of a substance therein and each defines an unfilled volume therein, each vial having a stopper partially inserted into an opening of the vial so that gas can transfer between the unfilled volume and an external volume;

applying a vacuum to the environment to reduce pressure in the environment and in the unfilled volume of each vial to a first pressure level;

venting an inert gas into the environment to raise the pressure in the environment and in the unfilled volume of each vial to a second pressure level;

allowing the vials to rest in the environment at the second pressure level for a predetermined period;

repeating the applying, venting and allowing at least once; and

fully inserting the stopper into each opening to seal each vial after the repeating.

2. The method of claim 1, further comprising, prior to the fully inserting, once repeating only the applying and venting; or ~~.~~

~~3. The method of claim 1 or claim 2,~~ further comprising, after the fully inserting, capping each vial with a cap to retain the stopper in each vial.

3. The method of claim 1 or 2, wherein the vials are housed in a closed chamber of a lyophilisation apparatus.

~~4. The method of any one of claims 1 to 3, wherein the housing comprises housing the vials in lyophilization apparatus.~~

~~5~~4. The method of any one of claims 1 to ~~4~~3, further comprising, before the applying, controlling the temperature in the environment to be at or about ~~or around~~ a temperature set-point, optionally wherein the repeating comprises repeating the controlling.

~~6~~5. The method of claim ~~5~~4, wherein the temperature set-point is a first temperature set-point and the method further comprises, after the venting, controlling the temperature in the environment to be at or about ~~or around~~ a second temperature set-point that is different from the first temperature set-point, optionally ~~.~~

~~7. The method of claim 5 or claim 6, wherein the repeating comprises repeating the controlling.~~

~~8. The method of claim 6 or claim 7,~~ wherein at least one of:

the first temperature set-point is less than about 10°C, optionally less than about 8°C, optionally about 5°C; and

the second temperature set-point is between about 17°C and about 26°C.

~~9~~6. The method of claim 5~~8~~ wherein the first temperature set-point is at or below a freezing temperature of the substance, optionally ~~.~~

~~10. The method of claim 9,~~ wherein the first pressure level is between about 0.0001 mbar and about 10 mbar; or~~.~~

~~11. The method of any one of claims 5 to 8,~~ wherein the temperature set-point is above a freezing temperature of the substance and wherein the first pressure level is greater than about 10 mbar and less about 500 mbar, optionally between about 10 mbar and about 300 mbar.

~~12~~7. The method of any one of claims 6 to 8, further comprising allowing the vials to rest in the environment for another predetermined period at or about ~~or around~~ the second temperature set-point, optionally ~~.~~

~~13. The method of claim 12,~~ wherein the another period is between about 15 minutes and about 45 or 60 minutes, optionally between about 25 and about 35 minutes, optionally about 30 minutes.

~~14~~8. The method of any one of claims 1 to 7~~13~~, wherein at least one of:

the second pressure level is between about 800 mbar and about 1000 mbar, optionally between about 900 mbar and 950 mbar;~~.~~

~~15. The method of any one of claims 1 to 14, wherein~~ the housing is performed at ambient pressure~~;~~.

~~16. The method of any one of claims 1 to 15, wherein~~ the repeating of the applying, venting and allowing is performed at least twice; optionally ~~.~~

~~17. The method of claim 16,~~ wherein the repeating of the applying, venting and allowing is performed at least eight times~~;~~.

~~18. The method of any one of claims 1 to 17, wherein the~~ repeating is performed a number of times effective to reduce a dissolved oxygen content of the substance to about 0.4% or less; and~~.~~

~~19. The method of any one of claims 1 to 18, wherein~~ the repeating is performed a number of times effective to reduce an oxygen gas content in the unfilled volume to less than or equal to about one percent, optionally ~~.~~

~~20. The method of claim 19,~~ wherein the repeating is performed a number of times effective to reduce the oxygen gas content in the unfilled volume to between about 0.01% and about 0.6%.

~~21~~9. The method of any one of claims 1 to ~~20~~8, wherein prior to the applying, the unfilled volume contains a substantially atmospheric level of oxygen gas and/or the substance contains a substantially atmospheric level of dissolved oxygen; or wherein a volume of the substance in liquid form remains substantially the same between the housing and the fully inserting, apart from a slight amount of evaporation.

~~22~~10. The method of any one of claims 1 to ~~21~~9, wherein the predetermined time period is between about 15 minutes and about 45 or 60 minutes, optionally between about 25 minutes and about 35 minutes.

~~23~~11. The method of any one of claims 1 to ~~22~~10, wherein at least one of:

the substance in a liquid form comprises an oxygen-sensitive solution~~;~~.

~~24. The method of any one of claims 1 to 23, wherein~~ the substance in a liquid form is an aqueous solution free of volatile constituents; and ~~.~~

~~25. The method of any one of claims 1 to 24, wherein~~
~~-~~the substance in a liquid form is stable at temperatures between about 1°C and about 26°C and pressures between about 10 mbar and 1000 mbar.

~~26. A preparation method, comprising:~~
~~filling a plurality of vials with a predetermined volume of liquid so that an unfilled volume remains in each vial;~~
~~partially inserting a stopper into an opening of each vial so that gas can transfer between the unfilled volume of the vial and an external volume;~~
~~housing the vials in a temperature-controlled environment;~~
~~applying a vacuum to the environment to reduce pressure in the environment and in the unfilled volume of each vial to a first pressure level;~~
~~venting an inert gas into the environment to raise the pressure in the environment and in the unfilled volume of each vial to a second pressure level;~~
~~allowing the vials to rest in the environment at the second pressure level for a predetermined period;~~
~~repeating the applying, venting and allowing at least once; and~~
~~fully inserting the stopper into each opening to seal each vial after the repeating.~~

~~27. The method of claim 26, further comprising, prior to the fully inserting, once repeating only the applying and venting.~~

~~28. The method of claim 26 or claim 27, further comprising, after the fully inserting, capping each vial with a cap to retain the stopper in each vial.~~

~~29. The method of any one of claims 26 to 28, wherein the housing comprises housing the vials in lyophilization apparatus.~~

~~30. The method of any one of claims 26 to 29, further comprising, before the applying, controlling the temperature in the environment to be at or around a temperature set-point.~~

~~31. The method of claim 30, wherein the temperature set-point is a first temperature set-point and the method further comprises, after the venting, controlling the temperature in the environment to be at or around a second temperature set-point that is different from the first temperature set-point.~~

~~32. The method of any one of claims 30 or claim 31, wherein the repeating comprises repeating the controlling.~~

~~33. The method of any one of claims 30 to 32, wherein at least one of:~~

~~the first temperature set-point is above freezing and less than about 10°C, optionally between about 3°C and about 8°C, optionally about 5°C; and~~

~~the second temperature set-point is between about 17°C and about 26°C.~~

~~34. The method of any one of claims 30 to 33, further comprising allowing the vials to rest in the environment for another predetermined period at or around the temperature set-point.~~

~~35. The method of claim 34, wherein the another period is between about 15 minutes and about 45 or 60 minutes, optionally between about 25 and about 35 minutes, optionally about 30 minutes.~~

~~36. The method of any one of claims 26 to 35, wherein the first pressure level is between about 10 mbar and about 500 mbar, optionally between about 40 mbar and about 300 mbar.~~

~~37. The method of any one of claims 26 to 36, wherein the second pressure level is between about 800 mbar and about 1000 mbar.~~

~~38. The method of claim 37, wherein the second pressure level is between about 900 mbar and 950 mbar.~~

~~39. The method of any one of claims 26 to 38, wherein at least one of the filling, partially inserting and housing is performed at ambient pressure.~~

~~40. The method of any one of claims 26 to 39, wherein the repeating of the applying, venting and allowing is performed at least twice.~~

~~41. The method of claim 40, wherein the repeating of the applying, venting and allowing is performed at least eight times.~~

~~42. The method of any one of claims 26 to 41, wherein the repeating is performed a number of times effective to reduce a dissolved oxygen content of the liquid to about 0.4% or less.~~

~~43. The method of any one of claims 26 to 42, wherein the repeating is performed a number of times effective to reduce an oxygen gas content in the unfilled volume to less than or equal to about one percent.~~

~~44. The method of claim 43, wherein the repeating is performed a number of times effective to reduce the oxygen gas content in the unfilled volume to between about 0.01% and about 0.6%.~~

~~45. The method of any one of claims 26 to 44, wherein prior to the applying, the unfilled volume contains a substantially atmospheric level of oxygen gas and/or the liquid contains a substantially atmospheric level of dissolved oxygen.~~

~~46. The method of any one of claims 26 to 45, wherein the predetermined time period is between about 15 minutes and about 45 or 60 minutes, optionally between about 25 minutes and about 35 minutes.~~

~~47. The method of any one of claims 26 to 46, wherein the liquid comprises an oxygen-sensitive solution.~~

~~48. The method of any one of claims 26 to 47, wherein the liquid is an aqueous solution free of volatile constituents.~~

~~49. The method of any one of claims 26 to 48, wherein the liquid is stable at temperatures between about 1°C and about 26°C and pressures between about 10 mbar and 1000 mbar.~~

~~50. A preparation method, comprising:~~

~~filling a plurality of vials with a predetermined volume of liquid so that an unfilled volume remains in each vial;~~

~~partially inserting a stopper into an opening of each vial so that gas can transfer between the unfilled volume of the vial and an external volume;~~

~~housing the vials in an environment in which the temperature is fixed at a selected temperature;~~

~~applying a vacuum to the environment to reduce pressure in the environment and in the unfilled volume of each vial to a first pressure level;~~

~~venting an inert gas into the environment to raise the pressure in the environment and in the unfilled volume of each vial to a second pressure level;~~

~~allowing the vials to rest in the environment at the second pressure level for a predetermined period;~~

~~repeating the applying, venting and allowing at least once; and~~

~~fully inserting the stopper into each opening to seal each vial after the repeating.~~

~~51. The method of claim 50 further comprising, prior to the fully inserting, once repeating only the applying and venting.~~

~~52. The method of claim 50 or claim 51, further comprising, after the fully inserting, capping each vial with a cap to retain the stopper in each vial.~~

~~53. The method of any one of claims 50 to 52, wherein the housing comprises housing the vials in lyophilization apparatus.~~

~~54. The method of any one of claims 50 to 53, wherein the selected temperature is around room temperature.~~

~~55. The method of any one of claims 50 to 54, wherein the selected temperature is between about 17°C and about 26°C.~~

~~56. The method of any one of claims 50 to 55, wherein the first pressure level is between about 200 mbar and about 500 mbar.~~

~~57. The method of claim 56, wherein the first pressure level is between about 300 mbar and about 350 mbar.~~

~~58. The method of any one of claims 50 to 57, wherein the second pressure level is between about 800 mbar and about 1000 mbar.~~

~~59. The method of claim 58, wherein the second pressure level is between about 900 mbar and 950 mbar.~~

~~60. The method of any one of claims 50 to 59, wherein at least one of the filling, partially inserting and housing is performed at ambient pressure.~~

~~61. The method of any one of claims 50 to 60, wherein the repeating of the applying, venting and allowing is performed at least twice.~~

~~62. The method of claim 61, wherein the repeating of the applying, venting and allowing is performed at least eight times.~~

~~63. The method of any one of claims 50 to 62, wherein the repeating is performed a number of times effective to reduce a dissolved oxygen content of the liquid to about 0.4% or less.~~

~~64. The method of any one of claims 50 to 63, wherein the repeating is performed a number of times effective to reduce an oxygen gas content in the unfilled volume to less than or equal to about one percent.~~

~~65. The method of claim 64, wherein the repeating is performed a number of times effective to reduce the oxygen gas content in the unfilled volume to between about 0.5% and about 0.6%.~~

~~66. The method of any one of claims 50 to 65, wherein prior to the applying, the unfilled volume contains a substantially atmospheric level of oxygen gas and/or the liquid contains a substantially atmospheric level of dissolved oxygen.~~

~~67. The method of any one of claims 50 to 66, wherein the predetermined time period is between about 15 minutes and about 45 or 60 minutes.~~

~~68. The method of claim 67, wherein the predetermined time period is between about 25 minutes and about 35 minutes.~~

~~69. The method of any one of claims 50 to 68, wherein the liquid comprises an oxygen-sensitive solution.~~

~~70. The method of any one of claims 50 to 69, wherein the liquid is an aqueous solution free of volatile constituents.~~

~~71. The method of any one of claims 50 to 70, wherein the liquid is stable at temperatures between about 17°C and about 26°C and pressures between about 200 mbar and 1000 mbar.~~

~~72. Use of lyophilization apparatus to prepare a plurality of stoppered vials containing a liquid by a method comprising:~~

~~housing the plurality of vials containing the liquid in a closed chamber of the lyophilization apparatus, the vials each arranged to have a stopper partially inserted into an opening of the vial so that gas can transfer between an unfilled internal volume of the vial and an external volume;~~

~~controlling the lyophilization apparatus to substantially maintain a selected temperature above freezing in the chamber;~~

~~applying a vacuum to the chamber to reduce pressure in the chamber and in the unfilled volume of each vial to a first pressure level;~~

~~venting an inert gas into the chamber to raise the pressure in the chamber and in the unfilled volume of each vial to a second pressure level;~~

~~allowing the vials to rest in the chamber at the second pressure level for a predetermined time period;~~

~~repeating the applying, venting and allowing at least once; and~~

~~fully inserting the partially inserted stopper into the opening of each vial to seal each vial after the repeating.~~

~~73. Use of lyophilization apparatus to prepare a plurality of stoppered vials containing a substance by a method comprising:~~

~~housing the plurality of vials containing the substance in a closed chamber of the lyophilization apparatus, the vials each arranged to have a stopper partially inserted into an~~

~~opening of the vial so that gas can transfer between an unfilled internal volume of the vial and an external volume;~~

~~applying a vacuum to the chamber to reduce pressure in the chamber and in the unfilled volume of each vial to a first pressure level;~~

~~venting an inert gas into the chamber to raise the pressure in the chamber and in the unfilled volume of each vial to a second pressure level;~~

~~allowing the vials to rest in the chamber at the second pressure level for a predetermined time period;~~

~~repeating the applying, venting and allowing at least once; and~~

~~fully inserting the partially inserted stopper into the opening of each vial to seal each vial after the repeating.~~

~~74. The use of claim 72 or claim 73, wherein the vials are initially positioned on vertically spaced shelves in the chamber and the stoppers are fully inserted into the vials by vertically compacting the shelves together.~~

~~75. The use of any one of claims 72 to 74, further comprising, prior to the fully inserting, once repeating only the applying and venting.~~

~~76. The use of any one of claims 72 to 75, wherein the controlling comprises controlling the lyophilization apparatus to substantially maintain a first selected temperature for a first time period and to substantially maintain a second selected temperature for a second time period, wherein the first selected temperature is different from the second selected temperature.~~

~~77. The use of claim 76, wherein the first selected temperature is above freezing and less than around 15°C, optionally less than around 12°C, optionally less than around 10°C .~~

~~78. The use of claim 76 or claim 77, wherein the second selected temperature is between about 17°C and about 26°C.~~

~~79. The use of any one of claims 76 to 78, wherein the first time period occurs before and/or during the applying and the second time period occurs during the allowing.~~

~~80. The use of any one of claims 72 to 79, wherein the first pressure level is between about 10 mbar and about 500 mbar, optionally between about 40 or 50 mbar and about 300 mbar.~~

~~81. The use of any one of claims 76 to 79, wherein the first temperature set-point is at or below a freezing temperature of the substance and optionally wherein the first pressure level is between about 0.0001 mbar and about 10 mbar.~~

~~82. The use of any one of claims 72 to 81, wherein the second pressure level is between about 800 mbar and about 1000 mbar, optionally about 900 mbar and 950 mbar.~~

~~83. The use of any one of claims 72 to 82, wherein at least one of the filling, partially inserting and housing is performed at ambient pressure.~~

~~84. The use of any one of claims 72 to 83, wherein the repeating of the applying, venting and allowing is performed at least twice.~~

~~85. The use of any one of claims 72 to 84, wherein the repeating of the applying, venting and allowing is performed at least eight times.~~

~~86. The use of any one of claims 72 to 85, wherein the repeating is performed a number of times effective to reduce a dissolved oxygen content of the liquid to about 0.4% or less.~~

~~87. The use of any one of claims 72 to 86, wherein the repeating is performed until an oxygen gas content in the unfilled volume is less than about one percent.~~

~~88. The use of claim 87, wherein the repeating is performed until the oxygen gas content in the unfilled volume is between about 0.01% and about 0.6%.~~

~~89. The use of any one of claims 72 to 88, wherein prior to the applying, the unfilled volume contains a substantially atmospheric level of oxygen gas.~~

~~90. The use of any one of claims 72 to 89, wherein the predetermined time period is between about 15 minutes and about 45 or 60 minutes, optionally between about 25 minutes and about 35 minutes, optionally about 30 minutes.~~

~~91. The use of any one of claims 72 to 90, wherein the repeating includes repeating the controlling.~~

~~92. The use of any one of claims 72 to 91, wherein the liquid comprises an oxygen-sensitive solution.~~

~~93. The use of any one of claims 72 to 92, wherein the liquid is an aqueous solution free of volatile constituents.~~

~~94. The use of any one of claims 72 to 93, wherein the liquid is stable at temperatures between about 1°C and about 26°C and pressures between about 10 mbar and 1000 mbar.~~

~~95. The use of any one of claims 72 to 94, further comprising use of a stopper for each vial, the stopper having a disc-shaped top and at least one projection receivable within the opening of each vial, the projection defining at least one gap so that, when the stopper is partially inserted into the opening, gas can flow between the unfilled volume and the external volume through parts of the at least one gap not occluded by a rim of the vial.~~

~~96. The use of claim 95, wherein, when the stopper is fully inserted into the opening, the disc-shaped top overlies the rim and the at least one gap is fully occluded by the rim, thereby sealing the vial from gas transfer between the unfilled volume and the external volume.~~

~~97. Use of lyophilization apparatus to perform the method of any one of claims 1 to 25.~~

~~98. A vial comprising:~~
~~a body having a neck and a single opening defined by the neck;~~
~~a stopper partly received in and sealing the opening;~~
~~a liquid contained by the body and the stopper, the liquid comprising an oxygen-sensitive formulation; and~~
~~a headspace defined between the body, the liquid and the stopper;~~
~~wherein the stopper has at least one projection received in the opening, wherein the projection defines at least one gap or aperture which, when the projection is partially inserted into the opening, allows gas transfer between the headspace and a volume external of the vial.~~

~~99. The vial of claim 98, wherein the liquid is an aqueous solution free of volatile constituents.~~

~~100. The vial of claim 98 or claim 99, wherein the liquid is stable at temperatures between about 1°C and about 26°C and pressures between about 10 mbar and 1000 mbar.~~

~~101. The vial of any one of claims 98 to 100, wherein an oxygen gas content in the headspace is less than or equal to about one percent.~~

~~102. The vial of claim 101, wherein the oxygen gas content in the headspace is between about 0.01% and about 0.6%.~~

~~103. The vial of any one of claims 98 to 102, wherein a dissolved oxygen content in the liquid is about 0.4% or less.~~

~~104. The vial of any one of claims 98 to 103, further comprising a cap to hold the stopper onto the neck.~~

~~105. The vial of any one of claims 98 to 104, wherein the stopper and vial body are arranged so that, when the stopper is fully inserted into the opening, the disc-shaped top overlies a rim around the opening and the at least one gap is fully occluded by the rim, thereby sealing the vial from gas transfer between the unfilled volume and the external volume.~~

~~106~~12. A vial comprising:

a body having a neck and a single opening defined by the neck;

a stopper partly received in and sealing the opening;

a substance contained by the body and the stopper, the substance comprising an oxygen-sensitive formulation; and

a headspace defined between the body, the substance and the stopper;

wherein the stopper has at least one projection received in the opening, wherein the projection defines at least one gap or aperture which, when the projection is partially inserted into the opening, allows gas transfer between the headspace and a volume external of the vial, wherein the substance is in a liquid state or a frozen state and wherein an oxygen gas content in the headspace is less than or equal to about one percent.

~~107. The vial of claim 106, wherein the substance is in a liquid state or a frozen state.~~

~~108~~13. The vial of claim ~~107~~12, wherein at least one of

_____the substance in the liquid state is an aqueous solution free of volatile constituents;~~.~~

_____

~~109. The vial of claim 107 or claim 108, wherein~~ the substance in the liquid state is stable at temperatures between about 1°C and about 26°C and pressures between about 10 mbar and 1000 mbar;~~.~~

~~110. The vial of any one of claims 106 to 109, wherein an oxygen gas content in the headspace is less than or equal to about one percent.~~

~~111. The vial of claim 110, wherein~~ the oxygen gas content in the headspace is between about 0.01% and about 0.6%;~~.~~

~~112. The vial of any one of claims 106 to 111, wherein~~ a dissolved oxygen content in the substance is about 0.4% or less; and~~.~~

~~113. The vial of any one of claims 106 to 112,~~ the vial further comprises~~ing~~ a cap to hold the stopper onto the neck.

~~114. The vial of any one of claims 106 to 113, wherein~~ the stopper and vial body are arranged so that, when the stopper is fully inserted into the opening, the disc-shaped top overlies a rim around the opening and the at least one gap is fully occluded by the rim, thereby sealing the vial from gas transfer between the unfilled volume and the external volume.

~~115. A vial prepared according to the method of any one of claims 1 to 71.~~

~~116. The method of any one of claims 1 to 71 or the use of any one of claims 72 to 97, wherein a volume of the liquid or the substance in liquid form remains substantially the same between the housing and the fully inserting, apart from a slight amount of evaporation.~~

~~117. A method substantially as hereinbefore described with reference to the accompanying drawings and/or examples.~~

~~118. A system substantially as hereinbefore described with reference to the accompanying drawings and/or examples.~~

~~119. Apparatus substantially as hereinbefore described with reference to the accompanying drawings and/or examples.~~

~~120. A vial containing a liquid substantially as hereinbefore described with reference to the accompanying drawings and/or examples.~~

~~121. A system comprising means for performing the method of any one of claims 1 to 71, 116 and 117.~~

~~122. The steps, features, elements, acts, compositions, components, examples, arrangements and structure described or depicted herein, individually or in any combination or subcombination thereof.~~