WHAT IS CLAIMED:

1. A method of preparing a lyophilized formulation, the method comprising:

(a) cooling a lyophilization chamber containing a liquid formulation comprising a protein, a saccharide, and a surfactant to a temperature ranging from ~~about~~ -35 °C to ~~about~~ -50 °C to produce a frozen formulation, and holding the chamber at a temperature ranging from ~~about~~ -40 °C to ~~about~~ -50 °C for a time period of ~~about~~ 2 hours to ~~about~~ 24 hours;

(b) heating the chamber to a temperature ranging from ~~about~~ -30 °C to ~~about~~ -20 °C and a pressure ranging from ~~about~~ 25 mTorr to ~~about~~ 100 mTorr to produce a primary dried formulation, and holding the chamber at a temperature ranging from ~~about~~ -30 °C to ~~about~~ -20 °C and a pressure ranging from ~~about~~ 25 mTorr to ~~about~~ 100 mTorr for a time period of ~~about~~ 45 hours to ~~about~~ 60 hours;

(c) heating the chamber to a temperature ranging from ~~about~~ 20 °C to ~~about~~ 35 °C to produce a secondary dried formulation, and holding the chamber at a temperature ranging from ~~about~~ 20 °C to ~~about~~ 30 °C and a pressure ranging from ~~about~~ 25 mTorr to ~~about~~ 100 mTorr for a time period of ~~about~~ 5 hours to ~~about~~10 hours to produce the lyophilized formulation;

wherein the liquid formulation has a pH of ~~about~~ 3-7 and does not contain mannitol; and the method lacks an annealing step.

2. The method of claim 1, wherein, the cooling of step (a) occurs to a temperature of about -45 °C, the holding of step (a) occurs, at a temperature of about -45°C, or both.

3. The method of claim 1 or 2, wherein the cooling of step (a) occurs at a rate ranging from ~~about~~0.5 °C/min to ~~about~~ 1 °C/min, preferably 0.5 °C/min.

~~4. The method of claim 3, wherein the cooling of step (a) occurs at a rate of about 0.5 °C/min.~~

~~5. The method of any one of claims 1-4, wherein the holding of step (a) occurs at a temperature of about -45 °C.~~

~~6. The method of any one of claims 1-5, wherein the holding of step (a) occurs for a time period of about 2 hours to about 5 hours.~~

~~7. The method of claim 6, wherein the holding of step (a) occurs for about 2 hours.~~

8.4. The method of any one of claims 1-73, wherein the heating of step (b) occurs to a temperature of about -25 °C, the holding of step (b) occurs at a temperature of about -25 °C, or both.

9.5. The method of any one of claims 1-84, wherein the heating of step (b) occurs at a rate ranging from about 0.1 °C/min to about 1 °C/min, 0.1 °C/min to 0.5 °C/min, or about 0.3 °C/min.

10. The method of claim 9, wherein the heating of step (b) occurs at a rate ranging from about 0.1 °C/min to about 0.5 °C/min.

11. The method of claim 10, wherein the heating of step (b) occurs at a rate of about 0.3 °C/min.

12.6. The method of any one of claims 1-115, wherein the heating of step (b), the holding of step (b), or both occurs at a pressure ranging from about 70 mTorr to about 100 mTorr, preferably about 70 mTorr.

13. The method of claim 12, wherein the heating of step (b) occurs at a pressure of about 70 mTorr.

14. The method of any one of claims 1-13, wherein the holding of step (b) occurs at a temperature of about -25 °C.

15. The method of any one of claims 1-14, wherein the holding of step (b) occurs at a pressure ranging from about 70 mTorr to about 100 mTorr.

16. The method of claim 15, wherein the holding of step (b) occurs at a pressure of about 70 mTorr.

17. The method of any one of claims 1-16, wherein the holding of step (b) occurs for a time period of about 50 hours to about 55 hours

18. The method of claim 17, wherein the holding of step (b) occurs for about 52 hours.

19.7. The method of any one of claims 1-186, wherein the heating of step (c) occurs to a temperature of about 30 °C, the holding of step (c) occurs at a temperature of about 30°C, or both.

20.8. The method of any one of claims 1-197, wherein the heating of step (c) occurs at a rate ranging up to about 0.5 °C/min, for example at a rate ranging from 0.05 °C/min to 0.5 °C/min, preferably at a rate of about 0.1 °C/min.

~~21. The method of claim 20, wherein the heating of step (c) occurs at a rate ranging from about 0.05 °C/min to about 0.5 °C/min.~~

~~22. The method of claim 21, wherein the heating of step (c) occurs at a rate of about 0.1 °C/min.~~

~~23. The method of any one of claims 1-22, wherein the holding of step (c) occurs at a temperature of about 30 °C.~~

~~24.~~9. The method of any one of claims 1-~~23~~8, wherein the holding of step (c) occurs at a pressure ranging from ~~about~~ 70 mTorr to ~~about~~ 100 mTorr, preferably at about 70 mTorr.

~~25. The method of claim 24, wherein the holding of step (c) occurs at a pressure of about 70 mTorr.~~

~~26. The method of any one of claims 1-25, wherein, the holding of step (c) occurs for about 8 hours.~~

~~27.~~10. The method of any one of claims 1-~~26~~9, wherein the protein is an antibody or a bispecific antibody construct.

~~28. The method of any one of claims 1-26, wherein the protein is a bispecific antibody construct.~~

~~29.~~11. The method of claim ~~28~~10, wherein the bispecific antibody construct is a half-life extended (HLE) bispecific antibody construct, optionally comprising an amino acid sequence set forth in SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 33, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 55, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 55, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 87, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 131, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 156, SEQ ID NO: 165, SEQ ID NO: 174, SEQ ID NO: 183, SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 187, or SEQ ID NO: 188.

~~30. The method of claim 29, wherein the HLE bispecific antibody construct comprises an amino acid sequence set forth in SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 33, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 55, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 55, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 87, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 131, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 156, SEQ ID NO: 165,~~

~~SEQ ID NO: 174, SEQ ID NO: 183, SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 187, or SEQ ID NO: 188.~~

~~31. The method of claim 30, wherein the HLE bispecific antibody construct comprises an amino acid sequence set forth in SEQ ID NO: 22, SEQ ID NO: 77, SEQ ID NO: 87, or SEQ ID NO: 97.~~

~~32.~~12. The method of any one of claims 1-~~31~~11, wherein the protein is present in the liquid formulation at a concentration ranging from ~~about~~ 0.1 mg/mL to ~~about~~ 100 mg/mL, or from 0.1 mg/mL to 70 mg/mL, or from 0.5 mg/mL to 30 mg/mL, or from 1 mg/ml to 20 mg/mL, or about 1 mg/mL.

~~33. The method of claim 32, wherein the protein is present at a concentration ranging from about 0.1 mg/mL to about 70 mg/mL.~~

~~34. The method of claim 33 wherein the protein is present at a concentration ranging from about 0.5 mg/mL to about 30 mg/mL.~~

~~35. The method of claim 34, wherein the protein is present at a concentration ranging from about 1 mg/ml to about of 20 mg/mL.~~

~~36. The method of claim 35, wherein the protein is present at a concentration of about 1 mg/mL.~~

~~37.~~13. The method of any one of claims 1-~~36~~12, wherein the liquid formulation of step (a) has a pH of ~~about~~ 4-6, or 4-5, and optionally further comprises a buffer wherein the buffer is an acetate buffer, a glutamate buffer, a citrate buffer, a lactate buffer, a succinate buffer, a tartrate buffer, a fumarate buffer, a maleate buffer, a histidine buffer, a phosphate buffer, a 2-(N-morpholino) ethanesulfonate buffer, or any combination thereof.

~~38. The method of any one of claims 1-37, wherein the liquid formulation of step (a) further comprises a buffer.~~

~~39. The method of claim 38, wherein the buffer is an acetate buffer, a glutamate buffer, a citrate buffer, a lactate buffer, a succinate buffer, a tartrate buffer, a fumarate buffer, a maleate buffer, a histidine buffer, a phosphate buffer, a 2-(N-morpholino)ethanesulfonate buffer, or any combination thereof.~~

~~40. The method of claim 39, wherein the buffer comprises glutamic acid.~~

41.14. The method of any one of claims 38-40 claim 13, wherein the buffer is present at a concentration ranging from about 5 mM to about 200 mM, from 10 mM to 50 mM, or about 10 mM.

42. The method of claim 41, wherein the buffer is present at a concentration ranging from about 10 mM to about 50 mM.

43. The method of claim 42, wherein the buffer is present at a concentration of about 10 mM.

44.15. The method of any one of claims 1-4314, wherein the saccharide is a monosaccharide or a disaccharide.

45. The method of claim 44, wherein the saccharide is glucose, galactose, fructose, xylose, sucrose, lactose, maltose, trehalose, or any combination thereof.

46. The method of claim 45, wherein the saccharide is sucrose.

47.16. The method of any one of claims 1-4615, wherein the saccharide is present in the liquid formulation at a concentration ranging from about 1 to about 15% (w/v), from 6% to 12% (w/v), or about 9% (w/v).

48. The method of claim 47, wherein the saccharide is present at a concentration ranging from about 6% to 12% (w/v).

49. The method of claim 48, wherein the saccharide is present at a concentration of about 9% (w/v).

50.17. The method of any one of claims 1-4916, wherein the surfactant is polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, poloxamer 188, poloxamer 407, triton X-100, polyoxyethylene, PEG 3350, PEG 4000, or a combination thereof and the surfactant is present in the liquid formulation at a concentration ranging from 0.001% to 0.5% (w/v), from 0.001% to 0.01% (w/v), or about 0.01% (w/v).

51. The method of claim 50, wherein the surfactant is polysorbate 80.

52. The method of any one of claims 1-51, wherein the surfactant is present in the liquid formulation at a concentration ranging from about 0.001% to 0.5% (w/v).

53. The method of claim 52, wherein the surfactant is present at a concentration ranging from about 0.001% to 0.01% (w/v).

54. The method of claim 53, wherein the surfactant is present at a concentration of about 0.01% (w/v).

~~55. The method of any one of claims 1-54, wherein the liquid formulation of step (a) has a pH from about 4 to about 5.~~

~~56.~~18. The method of any one of claims 1-~~55~~17, wherein the liquid formulation of step (a) has a pH of about 4.2 and comprises about 10 mM L-glutamic acid, about 9.0% (w/v) sucrose, and about 0.010% (w/v) polysorbate 80.

~~57.~~19. The method of any one of claims 1-~~56~~18, wherein the lyophilized formulation, upon reconstitution, exhibits a 0.5% or less increase in the percentage of high molecular weight species after storage for one month at 40 °C, or exhibits a 0.3% or less increase in the percentage of high molecular weight species after storage for one month at 40 °C.

~~58. The method of claim 57, wherein the lyophilized formulation, upon reconstitution, exhibits a 0.3% or less increase in the percentage of high molecular weight species after storage for one month at 40 °C.~~

~~59.~~20. A lyophilized protein formulation prepared by the method according to any one of claims 1-~~58~~19.