CLAIMS

WHAT IS CLAIMED IS:

1. A method of reducing polysorbate degradation in an aqueous formulation comprising a polysorbate, the method comprising adding a cyclodextrin to the formulation, wherein the resulting w/w ratio of cyclodextrin to polysorbate is greater than about 37.5:1.

2. A method of reducing polysorbate degradation in an aqueous formulation comprising a polysorbate, the method comprising adding a cyclodextrin to the formulation wherein the resulting w/w ratio of cyclodextrin to polysorbate is greater than about 37.5:1, wherein the formulation comprises about 0.005%-0.4% polysorbate.

3. A method of reducing polysorbate degradation in an aqueous formulation comprising a polysorbate, the method comprising adding a cyclodextrin to the formulation to a concentration of about 0.01%-30%, wherein the resulting w/w ratio of cyclodextrin to polysorbate is greater than about 37.5:1, wherein the formulation comprises about 0.005% to 0.4% polysorbate.

4. A method of reducing the amount of sub-visible and visible particles in an aqueous formulation comprising polysorbate, comprising adding a cyclodextrin to the formulation, wherein the resulting w/w ratio of cyclodextrin to polysorbate is greater than about 37.5:1.

5. A method to disaggregate and solubilize polysorbate degradation products in an aqueous formulation comprising a polysorbate, the method comprising adding a cyclodextrin to the formulation, wherein the resulting w/w ratio of cyclodextrin to polysorbate is greater than about 37.5:1.

6. The method of any one of claims 1-5, wherein the polysorbate is polysorbate 20 or polysorbate 80.

7. The method of any one of claims 1-6, wherein the cyclodextrin is HP-β cyclodextrin, HP-γ cyclodextrin, or sulfobutyl ether β-cyclodextrin.

8. The method of any one of claims 1-7, wherein the concentration of polysorbate in the formulation is in the range of about 0.01% to 0.4%.

9. The method of any one of claims 1-8, wherein the concentration of polysorbate in the formulation is in the range of about 0.01% to 0.1%.

10. The method of any one of claims 1-9, wherein the concentration of polysorbate in the formulation is about 0.02%.

11. The method of any one of claims 1-10, wherein the concentration of cyclodextrin in the formulation is in the range of about 0.5 to 30%.

12. The method of any one of claims 1-11, wherein the concentration of cyclodextrin in the formulation is about 15%.

13. The method of any one of claims 1-12, wherein the polysorbate degradation is reduced by about 50%, about 75%, about 80%, about 85%, about 90%, about 95% or about 99%.

14. The method of any one of claims 1-4 or 6-13, wherein less than about 1,000, about 750, about 500, about 250, about 150, about 100, about 50, or about 25 polysorbate particles greater than about 2 microns in diameter/mL are formed.

15. The method of any one of claims 1-14, wherein the formulation is stable at about 2 °C to about 8 °C for at least about six months, at least about 12 months, at least about 18 months, or at least about 24 months.

16. The method of any one of claims 1-15, wherein the formulation is stable at about 1°C to about 10 °C for at least about forty-eight months.

17. The method of any one of claims 1-16, wherein the formulation is stable at about 2 °C to about 8 °C for at least about forty-eight months.

18. The method of any one of claims 1-17, wherein the formulation further comprises a polypeptide.

19. The method of claim 18, wherein the polypeptide is an antibody.

20. The method of claim 19, wherein the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody or an antibody fragment.

21. The method of any one of claims 18-20, wherein the polypeptide concentration in the formulation is about 1 mg/mL to about 250 mg/mL.

22. The method of any one of claims 1-21, wherein the formulation has a pH of about 4.5 to about 7.0.

23. The method of any one of claims 1-22, wherein the formulation has a pH of about 4.5 to about 6.0.

24. The method of any one of claims 1-23, wherein the formulation has a pH of about 6.0.

25. The method of any one of claims 1-24, wherein the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent.

26. The method of any one of claims 1-25, wherein the formulation is a pharmaceutical formulation suitable for administration to a subject.

27. The method of any one of claims 1-26, wherein the formulation is pharmaceutical formulation suitable for intravenous, subcutaneous, intramuscular, or intravitreal administration to a subject.

28. An aqueous formulation comprising a polysorbate and a cyclodextrin, wherein the formulation has been stored at about 1 °C to about 10 °C for at least about six months, wherein the initial w/w ratio of cyclodextrin to polysorbate in the formulation is at least about

37.5:1 and wherein the amount of polysorbate in the formulation is at least about 80% of the initial amount of polysorbate in the formulation.

29. An aqueous formulation comprising a polysorbate and a cyclodextrin, wherein the formulation has been stored at about 1 °C to about 10 °C for at least about six months, wherein the w/w ratio of cyclodextrin to polysorbate in the formulation is at least about 37.5:1 and wherein less than about 1% of the polysorbate has degraded.

30. The formulation of claim 28 or 29, wherein the cyclodextrin is HP-β cyclodextrin, HP-γ cyclodextrin, or sulfobutyl ether β-cyclodextrin.

31. The formulation of any one of claims 28-30, wherein the concentration of polysorbate in the formulation is in the range of about 0.01% to 0.4%.

32. The formulation of any one of claims 28-31, wherein the concentration of polysorbate in the formulation is in the range of about 0.01% to 0.1%

33. The formulation of any one of claims 28-32, wherein the concentration of polysorbate in the formulation is about 0.02%.

34. The formulation of any one of claims 28-33, wherein the concentration of cyclodextrin in the formulation is in the range of about 0.5 to 30%.

35. The formulation of any one of claims 28-34, wherein the concentration of cyclodextrin in the formulation is about 15%.

36. The formulation of any one of claims 28-35, wherein the polysorbate degradation is reduced by about 50%, about 75%, about 80%, about 85%, about 90%, about 95% or about 99%.

37. The formulation of any one of claims 28-36, wherein less than about 1,000, about 750, about 500, about 250, about 150, about 100, about 50, or about 25 polysorbate particles greater than about 2 microns in diameter/mL are formed.

38. The formulation of any one of claims 28-37, wherein the formulation further comprises a polypeptide.

39. The formulation of claim 38, wherein the polypeptide is an antibody.

40. The formulation of claim 39, wherein the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody or an antibody fragment.

41. The formulation of any one of claims 38-40, wherein the polypeptide concentration in the formulation is about 1 mg/mL to about 250 mg/mL.

42. The formulation of any one of claims 28-41, wherein the formulation is stable at about 2 °C to about 8 °C for at least about six months.

43. The formulation of any one of claims 28-42, wherein the formulation is stable at about 1°C to about 10 °C for at least about forty-eight months.

44. The formulation of any one of claims 28-43, wherein the formulation is stable at about 2 °C to about 8 °C for at least about forty-eight months.

45. The formulation of any one of claims 28-44, wherein the formulation has a pH of about 4.5 to about 7.0.

46. The formulation of any one of claims 28-45, wherein the formulation has a pH of about 4.5 to about 6.0.

47. The formulation of any one of claims 28-46, wherein the formulation has a pH of about 6.0.

48. The formulation of any one of claims 28-47, wherein the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent.

49. The formulation of any one of claims 28-48, wherein the formulation is a pharmaceutical formulation suitable for administration to a subject.

50. The formulation of any one of claims 28-49, wherein the formulation is a pharmaceutical formulation suitable for intravenous, subcutaneous, intramuscular, or intravitreal administration to a subject.