[0016] In some examples of the above aspects and examples, 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. In some examples, the formulation is stable at about 1°C to about 10 °C for at least about forty-eight months. In some examples, the formulation is stable at about 2 °C to about 8 °C for at least about forty-eight months.

[0017] In some examples, the formulation has a pH of about 4.5 to about 7.0. In some examples, the formulation has a pH of about 4.5 to about 6.0. In some examples, the formulation has a pH of about 6.0.

[0018] In some examples of the above aspects and examples, the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent. In some examples, the formulation is a pharmaceutical formulation suitable for administration to a subject. In some examples, the formulation is pharmaceutical formulation suitable for intravenous, subcutaneous, intramuscular, or intravitreal administration to a subject.

[0019] In some examples, the present disclosure refers to an aqueous formulation comprising a polysorbate and a cyclodextrin, wherein the formulation has been stored at 1 °C to 10 °C for at least six months, wherein the initial w/w ratio of cyclodextrin to polysorbate in the formulation is at least 37.5:1 and less than 67:1; wherein the amount of polysorbate in the formulation is at least 80% of the initial amount of polysorbate in the formulation; and wherein the formulation comprises 0.001% to less than 0.01% polysorbate. In some examples, the disclosure provides an aqueous formulation comprising a polypeptide, 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. In some examples, the present disclosure refers to an aqueous formulation comprising a polysorbate and a cyclodextrin, wherein the formulation has been stored at 1 °C to 10 °C for at least six months, wherein the w/w ratio of cyclodextrin to polysorbate in the formulation is at least 37.5:1 and less than 67:1; and wherein less than 1% of the polysorbate has degraded; and wherein the formulation comprises 0.001% to less than 0.01% polysorbate. In some examples, the disclosure provides an aqueous formulation comprising a polypeptide, 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.

[0020] In some examples of the above aspects, the cyclodextrin is HP-β cyclodextrin, HP-γ cyclodextrin, or sulfobutyl ether β-cyclodextrin. In some examples, the concentration of polysorbate in the formulation is in the range of about 0.01% to 0.4%. In some examples, the concentration of polysorbate in the formulation is in the range of about 0.01% to 0.1%. In some examples, the concentration of polysorbate in the formulation is about 0.02%. In some examples, the concentration of cyclodextrin in the formulation is in the range of about 0.5-30%. In some examples, the concentration of cyclodextrin in the formulation is about 15%.

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 37.5:1 and less than 67:1; wherein the formulation comprises 0.001% to less than 0.01% polysorbate.

2. 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 0.01%-30%, wherein the resulting w/w ratio of cyclodextrin to polysorbate is greater than 37.5:1 and less than 67:1, wherein the formulation comprises 0.001% to less than 0.01% polysorbate.

3. 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 37.5:1 and less than 67:1; wherein the formulation comprises 0.001% to less than 0.01% polysorbate.

4. 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 37.5:1 and less than 67:1; wherein the formulation comprises 0.001% to less than 0.01% polysorbate.

5. The method of any one of claims 1-4, wherein the polysorbate is polysorbate 20 or polysorbate 80.

6. The method of any one of claims 1-5, wherein the cyclodextrin is HP-β cyclodextrin, HP-γ cyclodextrin, or sulfobutyl ether β-cyclodextrin.

7. The method of any one of claims 1-6, wherein the concentration of cyclodextrin in the formulation is in the range of 0.5 to 30%.

8. The method of any one of claims 1-7, wherein the concentration of cyclodextrin in the formulation is about 15%.

9. The method of any one of claims 1-8, wherein the polysorbate degradation is reduced by about 50%, about 75%, about 80%, about 85%, about 90%, about 95% or about 99%.

10. The method of any one of claims 1-9, wherein less than 1,000, 750, 500, 250, 150, 100, 50, or 25 polysorbate particles greater than 2 microns in diameter/mL are formed.

11. The method of any one of claims 1-10, wherein the formulation is stable at 2 °C to 8 °C for at least six months, at least 12 months, at least 18 months, or at least 24 months.

12. The method of any one of claims 1-11, wherein the formulation is stable at 1°C to 10 °C for at least forty-eight months.

13. The method of any one of claims 1-12, wherein the formulation is stable at 2 °C to 8 °C for at least forty-eight months.

14. The method of any one of claims 1-13, wherein the formulation further comprises a polypeptide.

15. The method of claim 14, wherein the polypeptide is an antibody.

16. The method of claim 15, 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.

17. The method of any one of claims 14-16, wherein the polypeptide concentration in the formulation is 1 mg/mL to 250 mg/mL.

18. The method of any one of claims 1-17, wherein the formulation has a pH of 4.5 to 7.0.

19. The method of any one of claims 1-18, wherein the formulation has a pH of 4.5 to 6.0.

20. The method of any one of claims 1-19, wherein the formulation has a pH of about 6.0.

21. The method of any one of claims 1-20, 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.

22. The method of any one of claims 1-21, wherein the formulation is a pharmaceutical formulation suitable for administration to a subject.

23. The method of any one of claims 1-22, wherein the formulation is pharmaceutical formulation suitable for intravenous, subcutaneous, intramuscular, or intravitreal administration to a subject.

24. The method of claim 1, wherein the polysorbate degradation is enzymatic polysorbate degradation.

25. The method of claim 15, wherein the antibody is produced recombinantly.

26. The method of claim 25, wherein the antibody is produced in Chinese hamster ovary cells.