CLAIMS

What is claimed is:

1. A method of reducing subvisible and visible particle formation in a drug product, the method comprising:

including at least 100 mg/mL of an IgG antibody in the drug product; and

including a mixture of fatty acid esters of polyoxyethylene sorbitan in the drug product, ~~wherein~~the polyoxyethylene sorbitan having a content of ~~oleic acid esters in the mixture is~~ greater than 98% ~~of all fatty acid~~oleic acid esters ~~in the mixture~~.

2. The method of claim 1, further comprising storing the drug product at a temperature of between 30°C and 50°C for between 1 and 5 months, after which fewer than 3000 particles having a diameter of 10 microns or greater are detectable in the drug product as detected by one of flow imaging microscopy or membrane microscopy.

3. The method of claim 1, further comprising storing the drug product at a temperature of between 2°C and 8°C for between 18 and 36 months, after which fewer than 3000 particles having a diameter of 10 microns or greater are detectable in the drug product as detected by one of flow imaging microscopy or membrane microscopy.

~~4. The method of claim 1, further comprising adding an agent to reduce viscosity to the drug product.~~

~~5.~~4. The method of claim 1, wherein the IgG antibody is an IgG4 antibody.

~~6.~~5. The method of claim 1, wherein the IgG antibody is capable of being co-purified with a lipase, and the drug product includes the lipase.

~~7.~~6. The method of claim 1, wherein the IgG antibody has been purified using an affinity purification step prior to inclusion in the drug product.

~~8.~~7. The method of claim 1, wherein the step of including at least 100 mg/mL of the IgG antibody in the drug product comprises including at least 150 mg/mL of the IgG antibody in the drug product.

~~9.~~8. The method of claim 1, wherein the IgG antibody has not been purified using hydrophobic interaction chromatography (HIC) prior to inclusion in the drug product.

~~10.~~9. The method of claim 1, wherein the IgG antibody is an IgG4 antibody, and the drug product includes phospholipase B-like 2 protein.

~~11.~~10. The method of claim 1, further comprising purifying the IgG antibody using a Protein A purification step before including the IgG antibody in the drug product.

~~12.~~11. The method of claim 1, wherein the content of oleic acid esters in the ~~mixture~~ polyoxyethylene sorbitan is at least 99% ~~of all fatty acid esters in the mixture~~.

~~13.~~12. The method of claim 1, wherein the drug product further includes an esterase.

~~14. A drug product prepared according to the method of claim 1.~~

~~15.~~13. The method of claim 1, wherein the content of oleic acid esters in the mixture is determined by one of gas-liquid chromatography, liquid chromatography, a colorimetric assay, or a fluorometric assay.

~~16.~~14. The method of claim 1, wherein the drug product is configured for parenteral administration.

~~17.~~15. A method of reducing particulate formation in a drug product including an IgG antibody and an esterase, the method comprising:

including in the drug product a mixture of ~~polyoxyethylene sorbitan~~ fatty acid esters of polyoxyethylene sorbitan, ~~wherein~~the polyoxyethylene sorbitan having a content of oleic acid esters ~~in the mixture is~~ greater than 98% ~~of all fatty acid esters in the mixture~~,

wherein the method does not include purifying the IgG antibody using hydrophobic interaction chromatography.

~~18.~~16. The method of claim ~~17~~15, wherein the IgG antibody is an IgG4 antibody and the esterase is a phospholipase B-like 2 protein.

~~19.~~17. A formulation, comprising:

at least 100 mg/mL of an IgG antibody; and

a mixture of fatty acid esters of polyoxyethylene sorbitan, ~~wherein~~the polyoxyethylene sorbitan having a content of oleic acid esters ~~in the mixture is~~ greater than 98% ~~of all fatty acid esters in the mixture~~.

~~20.~~18. The formulation of claim ~~19~~17, comprising at least 150 mg/mL of the IgG antibody.

~~21.~~19. The formulation of claim ~~19~~17, wherein the mixture of fatty acid esters is polysorbate 80.

~~22.~~20. The formulation of claim ~~19~~17, wherein the IgG antibody is an IgG4 antibody, and the formulation includes phospholipase B-like 2 protein.

~~23.~~21. A drug product including the formulation of claim ~~19~~17.

~~24.~~22. The drug product of claim ~~23~~21, wherein fewer than 3000 particles having a diameter of 10 microns or greater are detectable in the drug product by one of flow imaging microscopy or membrane microscopy, after the drug product has been stored at a temperature of between 30°C and 50°C for between 1 and 5 months.

~~25.~~23. The drug product of claim ~~23~~21, wherein fewer than 3000 particles having a diameter of 10 microns or greater are detectable in the drug product by one of flow imaging microscopy or membrane microscopy, after the drug product has been stored at a temperature of between 2°C and 8°C for between 18 and 36 months.

24. The method of claim 1, further comprising storing the drug product at a temperature of between 30°C and 50°C for between 3 months and 5 months.