Claims

1. A non-aqueous high concentration suspension formulation, comprising:
   a. a vehicle, comprising a hydrophobic agent and a viscosity-reducing agent; and
   b. an antibody formulated with an excipient.
2. The formulation of claim 1, wherein the antibody is an anti-TNFα antibody.
3. The formulation of claim 1, wherein the hydrophobic agent is sesame oil.
4. The formulation of claim 1, wherein the viscosity-reducing agent is ethyl oleate.
5. The formulation of claim 1, wherein the amount of the viscosity-reducing agent in the vehicle is between 0.2% - 95% by volume (% v/v) of the vehicle.
6. The formulation of claim 2, wherein the anti-TNFα antibody is present at about 0.5%, 1%, 5%, 10%, 20%, 30%, 40%, 50% or 60% by weight (% w/w) of the formulation.
7. The formulation of claim 2, wherein the anti-TNFα antibody is spray dried or lyophilized.
8. The formulation of claim 2, wherein the anti-TNFα antibody comprises a light chain variable region (VL) of SEQ ID NO: 6 and a heavy chain variable region (VH) of SEQ ID NOs: 1 or 2, or a VL of SEQ ID NO: 7 and a VH of SEQ ID NOs: 3, 4, or 5.
9. The formulation of claim 8, wherein the anti-TNFα antibody is of IgG1/κ type.
10. The formulation of claim 1, wherein the injection force of the formulation is equal to or less than 45 Newton (N), wherein the injection force is measured using a 1 mL rigid needle shield glass syringe having a

0.25 inch inside diameter, equipped with a 0.5 inch 26 ½ gauge needle at a 250 mm/min injection speed.

11. The formulation of claim 2 which is stable at 40°C for at least one month.

12. The formulation of claim 2, wherein the excipient is a carbohydrate, an amino acid, a buffer, or a non-ionic surfactant.

13. The formulation of claim 12, wherein the carbohydrate is sucrose, trehalose, mannitol or sorbitol, the amino acid is histidine, isoleucine, methionine, glycine, arginine or lysine, the buffer is a histidine buffer or a citrate buffer, and the non-ionic surfactant is PS-80.

14. The formulation of claim 12, wherein the weight ratio (w/w) of the carbohydrate to the anti-TNFα antibody is between about 0-3 or about 1-2, the weight ratio of the amino acid to the anti-TNFα antibody is between about 0-2 or about 0.3-1.8, the histidine buffer concentration is about 0-40 mM or about 5-10 mM, the citrate buffer concentration is about 0-10 mM or about 5-10 mM, and the non-ionic detergent is present at about 0%-0.5% (%w/v) or about 0.01-0.1% (%w/v).

15. A suspension formulation comprising a particle formulation of anti-TNFα antibody having a light chain variable region (VL) of SEQ ID NO: 6 and a heavy chain variable region (VH) of SEQ ID NOs: 1 or 2, or a VL of SEQ ID NO: 7 and a VH of SEQ ID NOs: 3, 4, or 5, comprising

a. 32.5 mg/mL of the anti-TNFα antibody, 10mM histidine, 27.5mg/mL sucrose, 0.01% (%w/v) PS-80;

b. 16.25 mg/mL of the anti-TNFα antibody, 10mM histidine, 27.5mg/mL sucrose, 0.01% (%w/v) PS-80;

c. 32.5 mg/mL of the anti-TNFα antibody, 10mM citrate, 27.5mg/mL sucrose, 0.01% (%w/v) PS-80;

d. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55 mg/ml sucrose, 10 mg/ml isoleucine, 0.01% (%w/v) PS-80;

e. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 65 mg/ml sucrose, 0.01% (%w/v) PS-80;

f. 32.5 mg/ml of the anti-TNFα antibody, 5 mM histidine, 5 mM citrate, 65mg/ml sucrose, 0.01% (%w/v) PS-80;

g. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 5 mg/ml sucrose, 22.5mg/mL mannitol, 0.01% (%w/v) PS-80;

h. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55 mg/ml trehalose, 10 mg/ml isoleucine, 0.01% (%w/v) PS-80; or

i. 65 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55mg/ml sucrose, 0.01% PS-80,

wherein the formulations shown in a-i are dispersed in a non-aqueous vehicle comprising sesame oil and ethyl oleate, wherein the amount of ethyl oleate in the vehicle is between 0.2% - 95% by volume (% v/v) of the non-aqueous vehicle.

16. The suspension formulation of claim 15, wherein the amount of ethyl oleate in the vehicle is 5%, 10%, 15%, 30% or 50% (% v/v) of the non-aqueous vehicle.

17. The suspension formulation of claim 15, wherein the anti-TNFα antibody is of IgG1/k type.

18. A suspension formulation comprising a particle formulation of an anti-TNFα antibody having a light chain variable region (VL) of SEQ ID NO: 6 and a heavy chain variable region (VH) of SEQ ID NOs: 1 or 2, or a

VL of SEQ ID NO: 7 and a VH of SEQ ID NOs: 3, 4, or 5, comprising

a. 32.5 mg/mL of the anti-TNFα antibody, 10mM histidine, 27.5mg/mL sucrose, 0.01% (%w/v) PS-80;

b. 16.25 mg/mL of the anti-TNFα antibody, 10mM histidine, 27.5mg/mL sucrose, 0.01% (%w/v) PS-80;

c. 32.5 mg/mL of the anti-TNFα antibody, 10mM Citrate, 27.5mg/mL sucrose, 0.01% (%w/v) PS-80;

d. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55 mg/ml sucrose, 10 mg/ml isoleucine, 0.01% (%w/v) PS-80;

e. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 65 mg/ml sucrose, 0.01% (%w/v) PS-80;

f. 32.5 mg/ml of the anti-TNFα antibody, 5 mM histidine, 5 mM citrate, 65mg/ml sucrose, 0.01% (%w/v) PS-80;

g. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 5 mg/ml sucrose, 22.5mg/mL mannitol, 0.01% (%w/v) PS-80;

h. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55 mg/ml trehalose, 10 mg/ml isoleucine, 0.01% (%w/v) PS-80; or

i. 65 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55mg/ml sucrose, 0.01% (%w/v) PS-80,

wherein the formulations shown in a-i are dispersed in a non-aqueous vehicle comprising ethyl oleate.

19. The suspension formulation of claim 18, wherein the anti-TNFα antibody is of IgG1/k type.

20. A method of reducing an injection force to about 45 Newton (N) or less of a formulation containing ≧50 mg/ml of anti-TNFα antibody in a vehicle comprising a hydrophobic agent, comprising:

a. adding at least 28% by volume of a viscosity reducing agent into the vehicle comprising a hydrophobic agent; or

b. utilizing protein particles having particle size between about 2 μm - 13 μm to prepare the formulation,

wherein the injection force is measured using a 1 mL rigid needle shield glass syringe having a 0.25 inch inside diameter, equipped with a 0.5 inch 26 ½ gauge needle at a 250 mm/min injection speed.

21. The method of claim 20, wherein the anti-TNFα antibody has a light chain variable region (VL) of SEQ ID NO: 6 and a heavy chain variable region (VH) of SEQ ID NOs: 1 or 2, or a VL of SEQ ID NO: 7 and a VH of SEQ ID NOs: 3, 4, or 5.

22. The method of claim 21, wherein the anti-TNFα antibody is of IgG1/k type.

23. A method of making a non-aqueous high concentration suspension formulation of a an anti-TNFα antibody having a light chain variable region (VL) of SEQ ID NO: 6 and a heavy chain variable region (VH) of SEQ ID NOs: 1 or 2, or a VL of SEQ ID NO: 7 and a VH of SEQ ID NOs: 3, 4, or 5, comprising

a. providing the anti-TNFα antibody;

b. providing a hydrophobic agent;

c. providing a viscosity reducing agent;

d. mixing the hydrophobic agent and the viscosity reducing agent to form a vehicle; and

e. adding the anti-TNFα antibody into the vehicle formed in step d at a concentration of equal to or more than 50 mg/mL.

24. The method of claim 23, wherein the anti-TNFα antibody is of IgG1/k type.

The invention claimed is:

1. A non-aqueous high concentration suspension formulation, consisting of:

a. a vehicle, consisting of sesame oil as a hydrophobic agent and ethyl oleate as a viscosity-reducing agent; and

b. an antibody formulated with an excipient.

2. The formulation of claim 1, wherein the antibody is an anti-TNFα antibody.

3. The formulation of claim 1, wherein the amount of the viscosity-reducing agent in the vehicle is between 0.2%-95% by volume (% v/v) of the vehicle.

4. The formulation of claim 2, wherein the anti-TNFα antibody is present at about 0.5%, 1%, 5%, 10%, 20%, 30%, 40%, 50% or 60% by weight (% w/w) of the formulation.

5. The formulation of claim 2, wherein the anti-TNFα antibody is spray dried or lyophilized.

6. The formulation of claim 2, wherein the anti-TNFα antibody comprises a light chain variable region (VL) of SEQ ID NO: 6 and a heavy chain variable region (VH) of SEQ ID NOs: 1 or 2, or a VL of SEQ ID NO: 7 and a VH of SEQ ID NOs: 3, 4, or 5.

7. The formulation of claim 6, wherein the anti-TNFα antibody is of IgG1/k type.

8. The formulation of claim 1, wherein the injection force of the formulation is equal to or less than 45 Newton (N), wherein the injection force is measured using a 1 mL rigid needle shield glass syringe having a 0.25 inch inside diameter, equipped with a 0.5 inch 26½ gauge needle at a 250 mm/min injection speed.

9. The formulation of claim 2 which is stable at 40° C. for at least one month.

10. The formulation of claim 2, wherein the excipient is a carbohydrate, an amino acid, a buffer, or a non-ionic surfactant.

11. The formulation of claim 10, wherein the carbohydrate is sucrose, trehalose, mannitol or sorbitol, the amino acid is histidine, isoleucine, methionine, glycine, arginine or lysine, the buffer is a histidine buffer or a citrate buffer, and the non-ionic surfactant is PS-80.

12. The formulation of claim 10, wherein the weight ratio (w/w) of the carbohydrate to the anti-TNFα antibody is between about 0-3 or about 1-2, the weight ratio of the amino acid to the anti-TNFα antibody is between about 0-2 or about

0.3-1.8, the histidine buffer concentration is about 0-40 mM or about 5-10 mM, the citrate buffer concentration is about 0-10 mM or about 5-10 mM, and the non-ionic detergent is present at about 0%-0.5% (% w/v) or about 0.01-0.1% (% w/v).

13. A suspension formulation consisting of a particle formulation of anti-TNFα antibody having a light chain variable region (VL) of SEQ ID NO: 6 and a heavy chain variable region (VH) of SEQ ID NOs: 1 or 2, or a VL of SEQ ID NO: 7 and a VH of SEQ ID NOs: 3, 4, or 5, consisting of

a. 32.5 mg/mL of the anti-TNFα antibody, 10 mM histidine, 27.5 mg/mL sucrose, 0.01% (% w/v) PS-80;
b. 16.25 mg/mL of the anti-TNFα antibody, 10 mM histidine, 27.5 mg/mL sucrose, 0.01% (% w/v) PS-80;
c. 32.5 mg/mL of the anti-TNFα antibody, 10 mM citrate, 27.5 mg/mL sucrose, 0.01% (% w/v) PS-80;
d. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55 mg/ml sucrose, 10 mg/ml isoleucine, 0.01% (% w/v) PS-80;
e. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 65 mg/ml sucrose, 0.01% (% w/v) PS-80;
f. 32.5 mg/ml of the anti-TNFα antibody, 5 mM histidine, 5 mM citrate, 65 mg/ml sucrose, 0.01% (% w/v) PS-80;
g. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 5 mg/ml sucrose, 22.5 mg/mL mannitol, 0.01% (% w/v) PS-80;
h. 32.5 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55 mg/ml trehalose, 10 mg/ml isoleucine, 0.01% (% w/v) PS-80; or
i. 65 mg/ml of the anti-TNFα antibody, 10 mM histidine, 55 mg/ml sucrose, 0.01% PS-80,

wherein the formulations shown in a-i are dispersed in a non-aqueous vehicle consisting of sesame oil and ethyl oleate, wherein the amount of ethyl oleate in the vehicle is between 0.2%-95% by volume (% v/v) of the non-aqueous vehicle.

14. The suspension formulation of claim **13**, wherein the amount of ethyl oleate in the vehicle is 5%, 10%, 15%, 30% or 50% (% v/v) of the non-aqueous vehicle.

15. The suspension formulation of claim **13**, wherein the anti-TNFα antibody is of IgG1/k type.