CLAIMS

1. A liquid pharmaceutical formulation comprising: (i) a human antibody that specifically binds to human interleukin-4 receptor alpha (hIL-4Rα); (ii) a buffer at a pH of 5.9 ± 0.5 pH units; (iii) an organic cosolvent; (iv) a thermal stabilizer; and (v) a viscosity reducing agent.

2. The liquid pharmaceutical formulation of claim 1, wherein the antibody is at a concentration of 150 mg/ml ± 50 mg/ml.

3. The liquid pharmaceutical formulation of claim 1 or claim 2, wherein the antibody is at a concentration of 150 mg/ml ± 15 mg/ml.

4. The liquid pharmaceutical formulation of any one of claims 1-3, wherein the buffer comprises a first buffer having an effective pH range within 3.6 – 5.6 and a second buffer having an effective pH range within 5.5 – 7.4.

5. The liquid pharmaceutical formulation of claim 4, wherein the first buffer has a pKa of 4.8 ± 0.3 and the second buffer has a pKa of 6.0 ± 0.3.

6. The liquid pharmaceutical formulation of claim 5, wherein the first buffer is acetate and the second buffer is histidine.

7. The liquid formulation of any one of claims 1-6, wherein the buffer comprises acetate at a concentration of 12.5 mM ± 1.85 mM and histidine at a concentration of 20 mM ± 0.3 mM.

8. The liquid pharmaceutical formulation of any one of claims 1-7, wherein the organic cosolvent is selected from the group consisting of polysorbate 20, poloxamer 181 and polyethylene glycol 3350.

9. The liquid pharmaceutical formulation of any one of claims 1-8, wherein the organic cosolvent is at a concentration of about 0.085% to about 1.15% w/v.

10. The liquid pharmaceutical formulation of any one of claims 1-9, wherein the organic cosolvent is polysorbate 20 at a concentration of 0.2% ± 0.03% w/v.

11. The liquid pharmaceutical formulation of any one of claims 1-10, wherein the thermal stabilizer is selected from the group consisting of sucrose, mannitol and trehalose.

12. The liquid pharmaceutical formulation of any one of claims 1-11, wherein the thermal stabilizer is at a concentration of about 3.5% to about 11% w/v.

13. The liquid pharmaceutical formulation of any one of claims 1-12, wherein the thermal stabilizer is sucrose at a concentration of 5% ± 0.75% w/v.

14. The liquid pharmaceutical formulation of any one of claims 1-13, wherein the viscosity reducing agent is at a concentration that is less than about 100 mM.

15. The liquid pharmaceutical formulation of any one of claims 1-15, wherein the viscosity reducing agent is arginine at a concentration of 25 mM ± 3.75 mM or 50 mM ± 7.5 mM.

16. The liquid pharmaceutical formulation of any one of claims 1-15, wherein the viscosity of the liquid is less than or equal to 35 ± 3.5 cPoise.

17. The liquid pharmaceutical formulation of any one of claims 1-16, wherein the viscosity of the liquid is 21.5 ± 13.5 cPoise.

18. The liquid pharmaceutical formulation of any one of claims 1-16, wherein the viscosity of the liquid is 11 ± 1.1 cPoise or 8.5 ± 0.85 cPoise.

19. The liquid pharmaceutical formulation of any one of claims 1-18, wherein the osmolality of the liquid is 290 ± 20 mOsm/kg.

20. The liquid pharmaceutical formulation of any one of claims 1-19, wherein at least about 90% of the native form of the antibody is recovered after about six months of storage at about 5°C, as determined by size exclusion chromatography

21. The pharmaceutical formulation of any one of claims 1-20, wherein at least about 95% of the native form of the antibody is recovered after about six months of storage at about 5°C, as determined by size exclusion chromatography.

22. The pharmaceutical formulation of any one of claims 1-21, wherein at least about 98% of the native form of said antibody is recovered after about six months of storage at about 5°C, as determined by size exclusion chromatography.

23. The liquid pharmaceutical formulation of any one of claims 1-22, wherein at least about 90% of the native form of the antibody is recovered after about eight weeks of storage at about 45°C, as determined by size exclusion chromatography.

24. The liquid pharmaceutical formulation of any one of claims 1-23, wherein less than about 45% of the antibody recovered after about eight weeks of storage at about 45°C is an acidic form, as determined by cation exchange chromatography.

25. The liquid pharmaceutical formulation of any one of claims 1-24, wherein less than about 4% of the antibody recovered after six months of storage at 25°C is aggregated, as determined by size exclusion exchange chromatography.

26. The liquid pharmaceutical formulation of claim 1, wherein said human antibody that specifically binds to hIL-4R comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein (a) the HCVR comprises heavy chain complementarity determining regions HCDR1, HCDR2 and HCDR3 comprising the amino acid sequence of (i) SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4, respectively, (ii) SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:12, respectively, or (iii) SEQ ID NO:18, SEQ ID NO:19 and SEQ ID NO:20, respectively; and (b) the LCVR comprises light chain complementarity determining regions LCDR1, LCDR2 and LCDR3 comprising the amino acid sequence of (i) SEQ ID NO:6, SEQ ID NO:7 and SEQ ID NO:8, respectively, (ii) SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16, respectively, or (iii) SEQ ID NO:22, SEQ ID NO:23 and SEQ ID NO:24, respectively.

27. The liquid pharmaceutical formulation of claim 26, wherein the HCVR and LCVR comprise amino acid sequences of SEQ ID NO:1 and SEQ ID NO:5, respectively.

28. The liquid pharmaceutical formulation of any one of claims 1-27 contained in a glass vial.

29. The liquid pharmaceutical formulation of any one of claims 1-27 contained in a syringe.

30. The liquid pharmaceutical formulation of any one of claims 1-27 contained in a microinfusor.

31. The liquid pharmaceutical formulation of claim 29, wherein said syringe comprises a fluorocarbon-coated plunger.

32. The liquid pharmaceutical formulation of claim 29 or claim 31, wherein said syringe is a low tungsten syringe.

33. A liquid pharmaceutical formulation comprising: (i) 150 mg/ml ± 50 mg/ml of a human antibody that specifically binds to hIL-4Rα, wherein said antibody comprises a heavy

chain and light chain variable region (HCVR / LCVR) amino acid sequence pair of SEQ ID NOs:1/5; (ii) 12.5 mM ± 2 mM acetate; (iii) 20 mM ± 3 mM histidine; (iv) 5% ± 0.75% sucrose; (v) 0.2% ± 0.03% polysorbate 20; and (vi) 25 mM ± 3.75 mM arginine, at a pH of 5.9 ± 0.5.

34. The liquid pharmaceutical formulation of claim 33, wherein the viscosity of the liquid is 11 ± 1.1 cPoise or 8.5 ± 0.85 cPoise.

35. The liquid pharmaceutical formulation of claim 33 or claim 34, wherein the osmolality of the liquid is 290 ± 20 mOsm/kg.

36. The liquid pharmaceutical formulation of any one of claims 33-35, wherein at least 98% of the native form of said antibody is recovered after six months of storage at 5ºC, as determined by size exclusion chromatography.

37. The liquid pharmaceutical formulation of any one of claims 33-36, wherein at least 90% of the native form of the antibody is recovered after eight weeks of storage at 45ºC, as determined by size exclusion chromatography.

38. The liquid pharmaceutical formulation of any one of claims 33-37, wherein less than 45% of the antibody recovered after eight weeks of storage at 45ºC is an acidic form, as determined by cation exchange chromatography.

39. The liquid pharmaceutical formulation of any one of claims 33-38, wherein less than about 4% of the antibody recovered after six months of storage at 25ºC is aggregated, as determined by size exclusion exchange chromatography.

CLAIMS

1. A stable pharmaceutical formulation comprising:

(i) a human antibody at a concentration of from 100 mg/ml to 200 mg/ml, wherein the antibody specifically binds to human interleukin-4 receptor alpha (hIL-4Rα) and comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:5;

(ii) acetate at a concentration of from 10 mM to 15 mM;

(iii) histidine at a concentration of from 15 mM to 25 mM;

(iv) sucrose at a concentration of from 2.5% w/v to 10% w/v;

(v) polysorbate at a concentration of from 0.1% w/v to 0.3% w/v; and

(vi) arginine at a concentration of from 20 mM to 100 mM,

wherein the formulation has a pH of from 5.6 to 6.2.

2. The pharmaceutical formulation of claim 1, wherein the antibody is at a concentration of 175 mg/ml.

3. The pharmaceutical formulation of claim 1, wherein the antibody is at a concentration of 150 mg/ml ± 15 mg/ml.

4. The pharmaceutical formulation of claim 1, wherein the antibody is at a concentration of 100 mg/ml.

5. The pharmaceutical formulation of claim 1, wherein the acetate is present at a concentration of 12.5 mM ± 1.85 mM and the histidine is present at a concentration of 20 mM ± 0.3 mM.

6. The pharmaceutical formulation of claim 1, wherein the polysorbate is polysorbate 20, or polysorbate 80.

7. The pharmaceutical formulation of claim 6, wherein the polysorbate is polysorbate 20 at a concentration of 0.2% ± 0.03% w/v.

8. The pharmaceutical formulation of claim 6, wherein the polysorbate is polysorbate 80 at a concentration of 0.2% ± 0.03% w/v.

9. The pharmaceutical formulation of claim 1, wherein the sucrose is present at a concentration of 5% ± 0.75% w/v.

10. The pharmaceutical formulation of claim 1, wherein the arginine is present at a concentration of 25 mM ± 3.75 mM.

11. The pharmaceutical formulation of claim 1, wherein the arginine is present at a concentration of 50 mM ± 7.5 mM.

12. The pharmaceutical formulation of claim 1, wherein the viscosity of the liquid is 11 ± 1.1 cPoise or 8.5 ± 0.85 cPoise.

13. The pharmaceutical formulation of claim 1, wherein the osmolality of the liquid is 290 ± 20 mOsm/kg.

14. The pharmaceutical formulation of claim 1, wherein:

(a) at least about 98% of the native form of said antibody is recovered after about six months of storage at about 5ºC, as determined by size exclusion chromatography;

(b) at least about 90% of the native form of the antibody is recovered after about eight weeks of storage at about 45ºC, as determined by size exclusion chromatography;

(c) less than about 45% of the antibody recovered after about eight weeks of storage at about 45ºC is an acidic form, as determined by cation exchange chromatography; or

(d) less than about 4% of the antibody recovered after six months of storage at 25ºC is aggregated, as determined by size exclusion exchange chromatography.

15. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is contained in a glass vial.

16. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is contained in a syringe.

17. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is contained in a microinfusor.

18. The pharmaceutical formulation of claim 16, wherein said syringe comprises a fluorocarbon-coated plunger.

19. The pharmaceutical formulation of claim 16, wherein said syringe is a low tungsten syringe.

20. A stable pharmaceutical formulation comprising:

(i) 150 mg/ml ± 50 mg/ml of a human antibody that specifically binds to hIL-4Rα, wherein said antibody comprises a heavy chain and light chain variable region (HCVR / LCVR) amino acid sequence pair of SEQ ID NOs:1/5;

(ii) 12.5 mM ± 2 mM acetate;

(iii) 20 mM ± 3 mM histidine;

(iv) 5% ± 0.75% sucrose;

(v) 0.2% ± 0.03% polysorbate 20; and

(vi) 25 mM ± 3.75 mM arginine,

at a pH of 5.9 ± 0.5.

21. The pharmaceutical formulation of claim 20, wherein the viscosity of the liquid is 11 ± 1.1 cPoise or 8.5 ± 0.85 cPoise, and the osmolality of the liquid is 290 ± 20 mOsm/kg.

22. The pharmaceutical formulation of claim 20, wherein:

(a) at least about 98% of the native form of said antibody is recovered after six months of storage at 5ºC, as determined by size exclusion chromatography;

(b) at least about 90% of the native form of the antibody is recovered after eight weeks of storage at 45ºC, as determined by size exclusion chromatography;

(c) less than about 45% of the antibody recovered after eight weeks of storage at 45ºC is an acidic form, as determined by cation exchange chromatography; or

(d) less than about 4% of the antibody recovered after six months of storage at 25ºC is aggregated, as determined by size exclusion exchange chromatography.

23. A stable pharmaceutical formulation comprising:

(i) 175 mg/ml of a human antibody that specifically binds to hIL-4Rα, wherein said antibody comprises a heavy chain and light chain variable region (HCVR / LCVR) amino acid sequence pair of SEQ ID NOs:1/5;

(ii) 12.5 mM ± 2 mM acetate;

(iii) 20 mM ± 3 mM histidine;

(iv) 5% ± 0.75% sucrose;

(v) 0.2% ± 0.03% polysorbate 20; and

(vi) 50 mM ± 3.75 mM arginine,

at a pH of 5.9 ± 0.5.

24. A stable pharmaceutical formulation comprising:

(i) 175 mg/ml of a human antibody that specifically binds to hIL-4Rα, wherein said antibody comprises a heavy chain and light chain variable region (HCVR / LCVR) amino acid sequence pair of SEQ ID NOs:1/5;

(ii) 12.5 mM ± 2 mM acetate;

(iii) 20 mM ± 3 mM histidine;

(iv) 5% ± 0.75% sucrose;

(v) 0.2% ± 0.03% polysorbate 80; and

(vi) 50 mM ± 3.75 mM arginine,

at a pH of 5.9 ± 0.5.

25. A stable pharmaceutical formulation comprising:

(i) 150 mg/ml ± 50 mg/ml of a human antibody that specifically binds to hIL-4Rα, wherein said antibody comprises a heavy chain and light chain variable region (HCVR / LCVR) amino acid sequence pair of SEQ ID NOs:1/5;

(ii) 12.5 mM ± 2 mM acetate;

(iii) 20 mM ± 3 mM histidine;

(iv) 5% ± 0.75% sucrose;

(v) 0.2% ± 0.03% polysorbate 80; and

(vi) 25 mM ± 3.75 mM arginine,

at a pH of 5.9 ± 0.5.