~~WHAT IS CLAIMED IS:~~

1. A method to minimize inflammation at the injection site during subcutaneous administration of a macromolecule, comprising adding to a formulation containing the macromolecule 2% to 30% cyclodextrin.

2. The method of Claim 1 wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin.

3. The method of Claim 2 wherein the formulation contains 5% to 30% HP-Beta or HP-Gamma cyclodextrin.

4. The method of Claim 3 wherein the formulation contains 5% to 30% HP-Beta cyclodextrin.

5. The method of Claim 3 wherein the formulation contains 5% to 20% HP-Gamma cyclodextrin.

6. The method of Claim 5 wherein the formulation further comprises 50 mM to 200 mM arginine succinate.

7. The method of Claim 2 wherein the formulation contains 2% to 9% SBE cyclodextrin.

8. The method of Claim 1 wherein the macromolecule is a protein.

9. The method of Claim 8 wherein the protein is an antibody.

10. The method of Claim 9 wherein the antibody is a therapeutic antibody.

11. The method of Claim 9 wherein the antibody is a diagnostic antibody.

12. The method of Claim 9 wherein the antibody is an anti-CD20 antibody.

13. The method of Claim 12 wherein the antibody comprises antibody variant A, B, C, D, F, G, H or I as shown in Table 1.

14. The method of Claim 12 wherein the antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-15.

15. The method of Claim 12 wherein the antibody comprises the light chain variable domain of SEQ ID NO:1 and the heavy chain variable domain of SEQ ID NO:2.

16. The method of Claim 12 wherein the antibody comprises the light chain variable domain of SEQ ID NO:3 and the heavy chain variable domain of SEQ ID NO:4.

17. The method of Claim 12 wherein the antibody comprises the light chain variable domain of SEQ ID NO:3 and the heavy chain variable domain of SEQ ID NO:5.

18. The method of Claim 12 wherein the antibody comprises comprises the full-length light chain of SEQ ID NO:6 and the full-length heavy chain of SEQ ID NO:7.

19. The method of Claim 12 wherein the antibody comprises comprises the full-length light chain of SEQ ID NO:6 and the full-length heavy chain of SEQ ID NO:15.

20. The method of Claim 12 wherein the antibody comprises the full-length light chain of SEQ ID NO:9 and the full-length heavy chain of SEQ ID NO:10.

21. The method of Claim 12 wherein the antibody comprises the full-length light chain of SEQ ID NO:9 and the full-length heavy chain of SEQ ID NO:11.

22. The method of Claim 12 wherein the antibody comprises the full-length light chain of SEQ ID NO:9 and the full-length heavy chain of SEQ ID NO:12.

23. The method of Claim 12 wherein the antibody comprises the full-length light chain of SEQ ID NO:9 and the full-length heavy chain of SEQ ID NO:13.

24. The method of Claim 12 wherein the antibody comprises the full-length light chain of SEQ ID NO:9 and the full-length heavy chain of SEQ ID NO:14.

25. A pharmaceutical formulation for subcutaneous administration of an antibody, comprising an antibody at a concentration range of 10mg/ml to 200mg/ml, and 2% to 30% cyclodextrin.

26. The formulation of Claim 25 wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin.

27. The formulation of Claim 26 wherein the formulation contains 5% to 30% HP-Beta or HP-Gamma cyclodextrin.

28. The formulation of Claim 27 wherein the formulation contains 5% to 30% HP-Beta cyclodextrin.

29. The formulation of Claim 27 wherein the formulation contains 5% to 20% HP-Gamma cyclodextrin.

30. The formulation of Claim 29 wherein the formulation further comprises 50 mM to 200 mM arginine succinate.

31. The formulation of Claim 26 wherein the formulation contains 2% to 9% SBE-cyclodextrin.

32. The formulation of Claim 25 wherein the antibody is present at a concentration range of 30 mg/ml to 150 mg/ml.

33. The formulation of Claim 25 wherein the antibody is present at a concentration range of 100 mg/ml to 150 mg/ml.

34. The formulation of Claim 27 comprising a humanized 2H7 antibody at 100 mg/ml and 15% to 30% HP-Beta cyclodextrin.

35. The formulation of Claim 27 comprising a humanized 2H7 antibody at 150 mg/ml and 30% HP-Beta cyclodextrin.

36. The formulation of Claim 27 comprising a humanized 2H7 antibody at 150 mg/ml and 10% HP-Gamma cyclodextrin.

37. The formulation of Claim 36 wherein the formulation further comprises 50 mM to 200 mM arginine succinate.

38. The formulation of Claim 37 wherein the humanized 2H7 antibody comprises antibody variant A, B, C, D, F, G, H or I as shown in Table 1.

39. The formulation of Claim 37 further comprising 30 mM sodium acetate; 5% trehalose dihydrate; and 0.03% Polysorbate 20, at pH 5.3.

40. The formulation of Claim 39 wherein the humanized 2H7 antibody comprises antibody variant A, B, C, D, F, G, H or I as shown in Table 1.

41. The formulation of Claim 27 wherein the formulation comprises humanized 2H7 antibody variant A as shown in Table 1 at a concentration range of 100 mg/ml to 150 mg/ml, 15% to 30% HP-Gamma cyclodextrin, and 50 mM to 100 mM arginine succinate.

42. A method of treating a CD20 positive B cell cancer, comprising administering to a patient having the cancer a therapeutically effective amount of a humanized 2H7 antibody of Table 1 in a pharmaceutical formulation comprising 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin.

43. The method of Claim 42 wherein the CD20 positive B cell cancer is a B cell lymphoma or leukemia.

44. The method of Claim 43 wherein the CD20 positive B cell cancer is selected from the group consisting of non-Hodgkin's lymphoma (NHL), relapsed indolent

NHL and rituximab-refractory indolent NHL, lymphocyte predominant Hodgkin's disease (LPHD), small lymphocytic lymphoma (SLL), and chronic lymphocytic leukemia (CLL).

45. The method of Claim 42 wherein the humanized 2H7 antibody is variant A, B, C, D or H from Table 1.

46. A method of treating an autoimmune disease, comprising administering to a patient having the autoimmune disease a therapeutically effective amount of a humanized 2H7 antibody of Table 1 in a pharmaceutical formulation comprising 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin.

47. The method of Claim 46 wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis (RA) and juvenile rheumatoid arthritis, including methotrexate (Mtx)- inadequate responders and TNFα– antagonist inadequate responders, systemic lupus erythematosus (SLE) including lupus nephritis, multiple sclerosis (MS), including relapsing remitting multiple sclerosis (RRMS), Wegener's disease, inflammatory bowel disease, ulcerative colitis, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, myasthenia gravis, ANCA associated vasculitis, diabetes mellitus, Reynaud's syndrome, Sjogren's syndrome, Neuromyelitis Optica (NMO) and glomerulonephritis.

48. The method of Claim 46 wherein the humanized 2H7 antibody is variant A, B, C, D or H from Table 1.

49. A method of improving or maintaining solubilization of or minimizing precipitation of an antibody in an aqueous subcutaneous formulation upon injection at the injection site of a patient, comprising adding 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin, to the aqueous subcutaneous formulation.

50. The method of Claim 49 wherein the antibody is a humanized anti-CD20 antibody variant A, B, C, D, F, G, H or I as shown in Table 1.

51. A method of increasing the bioavailability of an antibody to be administered subcutaneously, comprising adding 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin, to an aqueous subcutaneous formulation comprising the antibody.

52. The method of Claim 51 wherein the antibody is a humanized anti-CD20 antibody variant A, B, C, D, F, G, H or I as shown in Table 1.

53. An *in vitro* dialysis method for evaluating the ability of an excipient to reduce aggregation of an antibody or other macromolecule under physiological conditions, comprising:

(a) dialyzing formulations of the macromolecule with and without the test excipient against modified PBS solution (167mM Sodium, 140mM Chloride, 17mM Phosphate, 4mM Potassium) at 37°C with constant stirring;

(b) removing test samples of the modified PBS solution; and

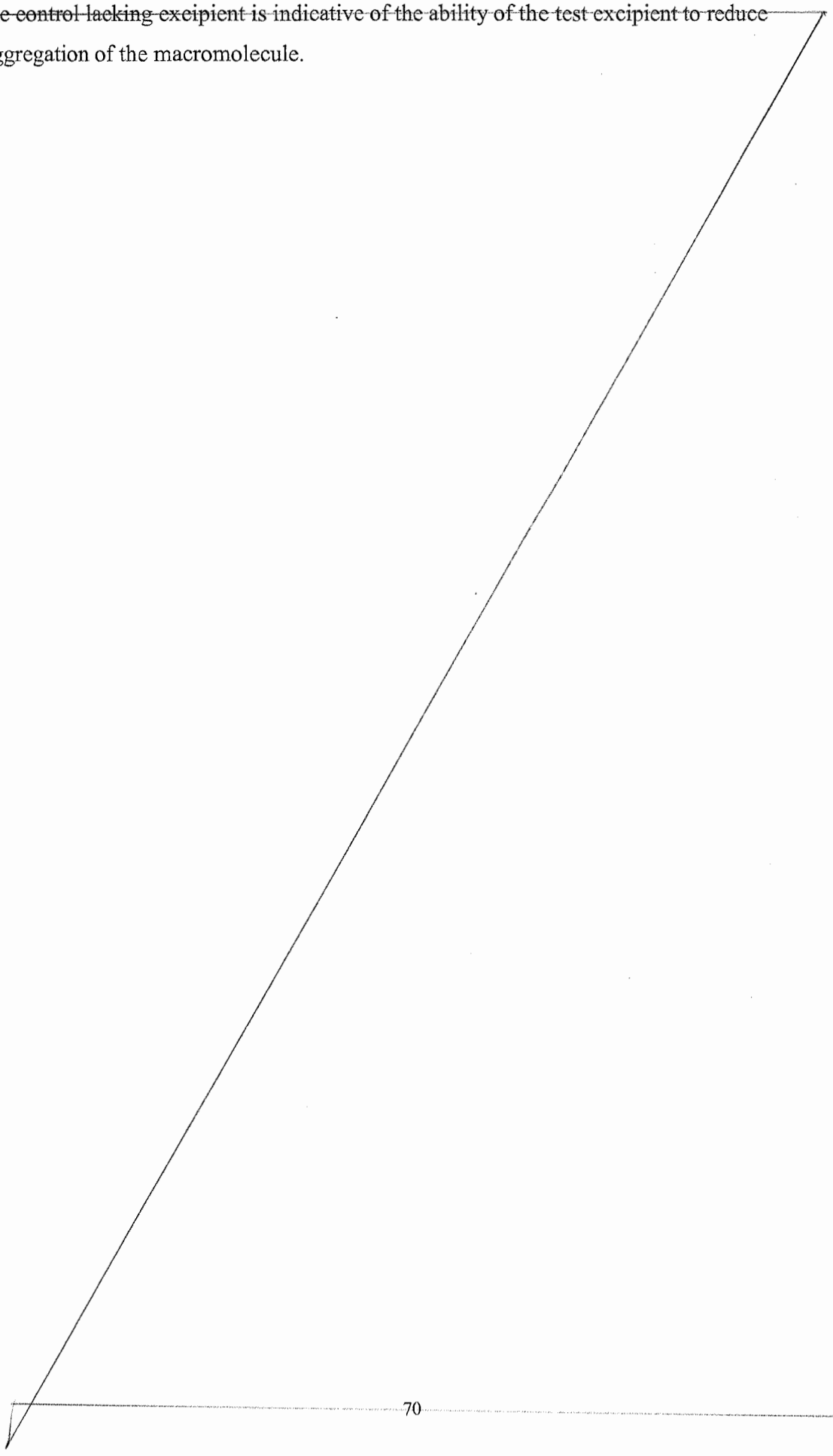
(c) measuring the turbidity and the amount of protein present in the test samples, wherein increased protein concentration and decreased turbidity in the samples in the assay containing the test excipient as compared to the control lacking excipient are indicative of the ability of the test excipient to reduce aggregation of the macromolecule.

54. The method of Claim 53 wherein the formulation is dialyzed in dialysis tubing having a 1 million Dalton molecular weight cut-off.

55. The method of Claim 53 wherein the protein concentration and turbidity in the test samples are measured using UV spectrometry.

56. The method of Claim 53 further comprising visually inspecting the modified PBS solution and the solution inside the dialysis tubing for precipitation, wherein decreased precipitation in the dialysis tubing containing the test excipient as compared to

the control lacking excipient is indicative of the ability of the test excipient to reduce aggregation of the macromolecule.



WHAT IS CLAIMED IS:

1. A pharmaceutical formulation for subcutaneous administration of a humanized 2H7 antibody, comprising an antibody at a concentration range of 10mg/ml to 200mg/ml, and 2% to 30% cyclodextrin.

2. The formulation of Claim 1 wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE- cyclodextrin.

3. The formulation of Claim 2 wherein the formulation contains 5% to 30% HP - Beta or HP-Gamma cyclodextrin.

4. The formulation of Claim 3 wherein the formulation is selected from the group consisting of
(a) a formulation containing 5% to 30% HP -Beta cyclodextrin; and
(b) a formulation containing 5% to 20% HP-Gamma cyclodextrin.

5. The formulation of Claim 4 wherein the formulation in (b) further comprises 50 mM to 200 mM arginine succinate.

6. The formulation of Claim 2 wherein the formulation contains 2% to 9% SBE-cyclodextrin.

7. The formulation of Claim 1 wherein the antibody is present at a concentration range selected from the group consisting of
(a) a concentration range of 30 mg/ml to 150 mg/ml; and
(b) a concentration range of 100 mg/ml to 150 mg/ml.

8. The formulation of Claim 3, wherein the formulation is selected from the group consisting of
(a) a formulation comprising a humanized 2H7 antibody at 100 mg/ml and 15% to 30% HP-Beta cyclodextrin;

(b) a formulation comprising a humanized 2H7 antibody at 150 mg/ml and 30% HP-Beta cyclodextrin; and
(c) a formulation comprising a humanized 2H7 antibody at 150 mg/ml and 10% HP-Gamma cyclodextrin.

9. The formulation of Claim 8 wherein the formulation in (c) further comprises 50 mM to 200 mM arginine succinate.

10. The formulation of Claim 9 further comprising 30 mM sodium acetate; 5% trehalose dihydrate; and 0.03% Polysorbate 20, at pH 5.3.

11. The formulation of Claim 9 or 10 wherein the humanized 2H7 antibody comprises antibody variant A, B, C, D, F, G, H or I as shown in Table 1.

12. The formulation of Claim 3 wherein the formulation comprises humanized 2H7 antibody variant A as shown in Table 1 at a concentration range of 100 mg/ml to 150 mg/ml, 15% to 30% HP-Gamma cyclodextrin, and 50 mM to 100 mM arginine succinate.

13. Use of a humanized 2H7 antibody of Table 1 in a pharmaceutical formulation comprising 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP- Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin, in the manufacture of a medicament for treating a CD20 positive B cell cancer in a patient having the cancer.

14. The use of Claim 13 wherein the CD20 positive B cell cancer is a B cell lymphoma or leukemia.

15. The use of Claim 14 wherein the CD20 positive B cell cancer is selected from the group consisting of non-Hodgkin's lymphoma (NHL), relapsed indolent

NHL and rituximab -refractory indolent NHL, lymphocyte predominant Hodgkin's disease (LPHD), small lymphocytic lymphoma (SLL), and chronic lymphocytic leukemia (CLL).

16. Use of a humanized 2H7 antibody of Table 1 in a pharmaceutical formulation comprising 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin, in the manufacture of a medicament for treating an autoimmune disease.

17. The use of Claim 16 wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis (RA) and juvenile rheumatoid arthritis, including methotrexate (Mtx)- inadequate responders and TNFα- antagonist inadequate responders, systemic lupus erythematosus (SLE) including lupus nephritis, multiple sclerosis (MS), including relapsing remitting multiple sclerosis (RRMS), Wegener's disease, inflammatory bowel disease, ulcerative colitis, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, myasthenia gravis, ANCA associated vasculitis, diabetes mellitus, Reynaud's syndrome, Sjogren's syndrome, Neuromyelitis Optica (NMO) and glomerulonephritis.

18. The use of Claim 13 or 16 wherein the humanized 2H7 antibody is variant A, B, C, D or H from Table 1.

19. A method of improving or maintaining solubilization of or minimizing precipitation of a humanized 2H7 antibody in an aqueous subcutaneous formulation upon injection at the injection site of a patient, comprising adding 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin, to the aqueous subcutaneous formulation.

20. A method of increasing the bioavailability of a humanized 2H7 antibody to be administered subcutaneously, comprising adding 2% to 30% cyclodextrin, wherein the cyclodextrin is selected from the group consisting of HP-Beta cyclodextrin, HP-Gamma cyclodextrin, and SBE-cyclodextrin, to an aqueous subcutaneous formulation comprising the antibody.

21. The method of Claim 19 or 20 wherein the antibody is a humanized anti-CD20 antibody variant A, B, C, D, F, G, H or I as shown in Table 1.