What is claimed:

1. A method for producing a host cell protein-(HCP) reduced antibody preparation from a mixture comprising an antibody and at least one HCP, the method comprising:

(a) applying the mixture to a first ion exchange resin in an equilibration buffer, wherein greater than 30 grams of antibody per liter of resin are applied;

(b) washing HCP from the resin with a plurality of wash steps; and

(c) eluting the antibody from the resin with an elution buffer to form a first eluate,

such that the HCP-reduced antibody preparation is obtained.

2. The method of claim 1, wherein about 35-70 grams of antibody per liter of resin are applied.

3. The method of claim 1, wherein about 70 grams of antibody per liter of resin are applied.

4. The method of claim 1, wherein the mixture comprising an antibody and at least one HCP is not subjected to protein A capture prior to applying the mixture to the first ion exchange resin.

5. The method of claim 1, wherein the plurality of wash steps comprises at least a first wash and a second wash, wherein there is an increase in conductivity from the first wash to the second wash.

6. The method of claim 5, wherein the first wash is with equilibration buffer and the second wash is with a mixture of elution buffer and water.

7. The method of claim 6, wherein the mixture of elution buffer and water comprises about 40-50% elution buffer and about 50-60% water.

8. The method of claim 7, wherein the mixture of elution buffer and water comprises about 45% elution buffer and about 55% water.

9. The method of claim 8, wherein the elution buffer comprises 20 mM sodium phosphate and 150 mM sodium chloride.

10. The method of claim 1, which is carried out at pH 7.

11. The method of claim 1, which is carried at a pH between about pH 5 and about pH 7.

12. The method of claim 1 which is carried out at pH 5.

13. The method of claim 1, wherein the first ion exchange resin is a cation exchange resin.

14. The method of claim 13, wherein the cation exchange resin is formed into a column and the mixture comprising the antibody and at least one HCP is applied to the column.

15. The method of claim 14, wherein the cation exchange resin comprises a synthetic methacrylate based polymeric resin attached to a sulfonate group.

16. The method of claim 1, which further comprises subjecting the first eluate to a viral inactivation step.

17. The method of claim 16, wherein viral inactivation is achieved by pH viral inactivation to form a virally-inactived preparation.

18. The method of claim 17, wherein the virally-inactivated preparation is applied to a second ion exchange resin, wherein, prior to applying the virally-inactivated preparation to the second ion exchange resin, pH and conductivity of the virally-inactivated preparation is adjusted to be substantially similar to pH and conductivity of the second ion exchange resin.

19. The method of claim 18, wherein the pH of the second ion exchange resin is in a range of about pH 7.7 to about pH 8.3 and the pH of the virally-inactivated preparation is adjusted to be in a range of about pH 7.7 to about pH 8.3.

20. The method of claim 19, wherein the pH of the second ion exchange resin is about pH 8.0 and the pH of the virally-inactivated preparation is adjusted to be about pH 8.0.

21. The method of claim 18, wherein the conductivity of the second ion exchange resin is in a range of about 3.5 mS/cm to about 5.2 mS/cm and the conductivity of the virally-inactivated preparation is adjusted to be in a range of about 3.5 mS/cm to about 5.2 mS/cm.

22. The method of claim 21, wherein the conductivity of the second ion exchange resin is about 5.0 mS/cm and the conductivity of the virally-inactivated preparation is adjusted to be about 5.0 mS/cm.

23. The method of claim 18, wherein the second ion exchange resin is an anion exchange resin.

24. The method of claim 23, wherein the anion exchange resin is a Q sepharose resin.

25. The method of claim 18, wherein the second ion exchange resin is formed into a column and the virally-inactivated preparation is applied to the column such that a first flow through is obtained.

26. The method of claim 25, wherein the first flow through is applied to a hydrophobic interaction column such that a second eluate is obtained.

27. The method of claim 26, wherein the hydrophobic interaction column is a phenyl sepharose column.

28. The method of claim 26, wherein the first flow through applied to the hydrophobic interaction column comprises about 20 to about 40 grams of antibody per liter of hydrophobic interaction column material.

29. The method of claim 28, wherein the first flow through applied to the hydrophobic interaction column comprises about 30 to about 36 grams of antibody per liter of hydrophobic interaction column material.

30. The method of claim 26, wherein the second eluate is not subjected to product peak fractionation.

31. The method of claim 1, which comprises:

(a) applying the mixture to a cation exchange resin in an equilibration buffer, wherein the mixture has not been subjected to protein A capture prior to applying to the cation exchange resin and wherein greater than 30 grams of antibody per liter of resin are applied;

(b) washing HCP from the cation exchange resin with a plurality of wash steps;

(c) eluting the antibody from the cation exchange resin with an elution buffer to form a first eluate;

(d) subjecting the first eluate to a viral inactivation step;

(e) applying the virally-inactivated preparation to an anion exchange resin to obtain a first flow through; and

(f) applying the first flow through to a hydrophobic interaction column such that a second eluate is obtained;

such that the HCP-reduced antibody preparation is obtained.

32. The method of claim 31, wherein the cation exchange resin is at pH 7 and about 35 grams of antibody per liter of resin are applied.

33. The method of claim 31, wherein the cation exchange resin is at pH 5 and about 70 grams of antibody per liter of resin are applied.

34. The method of claim 31, wherein the plurality of wash steps comprises washing the resin with a first wash using the equilibration buffer and a second wash using a mixture of the elution buffer and water.

35. The method of claim 34, wherein the mixture of elution buffer and water comprises about 40-50% elution buffer and about 50-60% water.

36. The method of claim 31, wherein, prior to applying the virally-inactivated preparation to the anion ion exchange resin, pH and conductivity of the virally-inactivated preparation is adjusted to be substantially similar to pH and conductivity of the anion exchange resin.

37. The method of claim 31, wherein the first eluate comprises a range of about 90 to about 100 fold less HCP than the mixture as determined by a HCP ELISA.

38. The method of claim 31, wherein the first flowthrough comprises a range of about 840 to about 850 fold less HCP than the first eluate as determined by a HCP ELISA.

39. The method of claim 31, wherein the second eluate comprises a range of about 3 to about 5 fold less HCP than the first flowthrough as determined by a HCP ELISA.

40. The method of claim 1, which comprises:

(a) applying the mixture to a cation exchange resin in an equilibration buffer, wherein the cation exchange resin is at pH 7 and about 35 grams of antibody per liter of resin are applied, or the cation exchange resin is at a pH in a range of pH 5 to pH 7 and about 35 to about 70 grams of antibody per liter of resin are applied, or the cation exchange resin is at pH 5 and about 70 grams of antibody per liter of resin are applied;

(b) washing HCP from the cation exchange resin with wash steps comprising a first wash using the equilibration buffer and a second wash using a mixture of an elution buffer and water;

(c) eluting the antibody from the cation exchange resin with the elution buffer to form a first eluate;

(d) subjecting the first eluate to a viral inactivation step, wherein viral inactivation is achieved by pH viral inactivation to form a virally-inactived preparation;

(e) applying the virally-inactivated preparation to an anion exchange resin, wherein, prior to applying the virally-inactivated preparation to the anion ion exchange resin, pH and conductivity of the virally-inactivated preparation is adjusted to be substantially similar to pH and conductivity of the anion exchange resin, such that a first flow through is obtained; and

(f) applying the first flow through to a hydrophobic interaction column such that a second eluate is obtained;

such that the HCP-reduced antibody preparation is obtained.

41. The method of claim 40, wherein the antibody mixture has not been subjected to protein A capture prior to applying to the cation exchange resin.

42. The method of claim 40, wherein the mixture of elution buffer and water comprises about 40-50% elution buffer and about 50-60% water.

43. The method of claim 40, wherein the first eluate comprises a range of about 90 to about 100 fold less HCP than the mixture as determined by a HCP ELISA.

44. The method of claim 40, wherein the first flowthrough comprises a range of about 840 to about 850 fold less HCP than the first eluate as determined by a HCP ELISA.

45. The method of claim 40, wherein the second eluate comprises a range of about 3 to about 5 fold less HCP than the first flowthrough as determined by a HCP ELISA.

46. The method of any one of claims 1-45 wherein the HCP comprises procathepsin L such that a procathepsin L-reduced antibody preparation is obtained.

47. The method of claim 46, wherein the first eluate comprises cathepsin L activity ranging from between about 25 to about 60 RFU/s/mg of antibody as measured by a cathepsin L kinetic assay.

48. The method of claim 46, wherein the first flowthrough comprises cathepsin L activity ranging from between about 0.4 to about 4 RFU/s/mg of antibody as measured by a cathepsin L kinetic assay.

49. The method of claim 46, wherein the second eluate comprises cathepsin L activity ranging from between about 0.5 to about 1.5 RFU/s/mg of antibody as measured by a cathepsin L kinetic assay.

50. A method of any one of claims 46-49, wherein the level of procathepsin L is reproducibly low.

51. The method of any one of claims 1-45, wherein the antibody is an anti-tumor necrosis factor-alpha (TNFα) antibody, or antigen-binding portion thereof.

52. The method of claim 51, wherein the anti-TNFα antibody, or antigen-binding portion thereof, is a humanized antibody, a chimeric antibody or a multivalent antibody.

53. The method of claim 51, wherein the anti-TNFα antibody, or antigen-binding portion thereof, is infliximab or golimumab.

54. The method of claim 51, wherein the anti-TNFα antibody, or antigen-binding portion thereof, is a human antibody.

55. The method of claim 54, wherein the anti-TNFα antibody, or antigen-binding portion thereof, is an isolated human antibody that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less.

56. The method of claim 54, wherein the anti-TNFα antibody, or antigen-binding portion thereof, is an isolated human antibody with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

57. The method of claim 54, wherein the anti-TNFα antibody, or antigen-binding portion thereof, is an isolated human antibody with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2

58. The method of claim 54, wherein the anti-TNFα antibody, or antigen-binding portion thereof, is adalimumab.

59. An antibody preparation which is substantially free of HCP as measured by a HCP ELISA produced using the method of any one of claims 1-45.

60. A pharmaceutical composition comprising an HCP-reduced antibody preparation produced using the method of any one of claims 1-45, and a pharmaceutically acceptable carrier.

61. A pharmaceutical composition comprising an HCP-reduced antibody, wherein the level of HCP comprises no greater than about 70 ng of HCP per mg of antibody as measured by a HCP ELISA, and a pharmaceutically acceptable carrier.

62. The pharmaceutical composition of claim 61, wherein the level of HCP comprises no greater than about 13 ng of HCP per mg of antibody as measured by a HCP ELISA.

63. The pharmaceutical composition of claim 61, wherein the level of HCP comprises no greater than about 5 ng of HCP per mg of antibody as measured by a HCP ELISA.

64. A composition comprising an antibody, wherein said composition has no detectable level of HCP as determined by a HCP ELISA assay.

65. An antibody preparation which is substantially free of procathepsin L produced using the method of any one of claims 1-45.

66. A pharmaceutical composition comprising a procathepsin L-reduced antibody preparation produced using the method of any one of claims 1-45, and a pharmaceutically acceptable carrier.

67. A pharmaceutical composition comprising an antibody a procathepsin L-reduced antibody and a pharmaceutically acceptable carrier, wherein the level of procathepsin L is no greater than a cathepsin activity of about 3.0 RFU/s/mg of antibody.

68. The composition or preparation of any one of claims 59-67, wherein the antibody is an anti-tumor necrosis factor-alpha (TNFα) antibody, or antigen-binding portion thereof.

69. A method of treating a disorder in which TNFα activity is detrimental comprising administering to a human subject the composition or preparation of claim 68.

70. An article of manufacture comprising a packaging material, adalimumab, and a label or package insert contained within the packaging material indicating that the

adalimumab formulation comprises no greater than about 70 ng of HCP per mg of adalimumab.

71. An article of manufacture comprising a packaging material, adalimumab, and a label or package insert contained within the packaging material indicating that the adalimumab formulation comprises no greater than about 13 ng of HCP per mg of adalimumab.

72. An article of manufacture comprising a packaging material, adalimumab, and a label or package insert contained within the packaging material indicating that the adalimumab formulation comprises no greater than about 5 ng of HCP per mg of adalimumab.

73. An article of manufacture comprising a packaging material, adalimumab, and a label or package insert contained within the packaging material indicating that the adalimumab formulation comprises no greater a level of procathepsin L than that indicated by a cathepsin L activity of about 3.0 RFU/s/mg adalimumab.

What is claimed:

1. A liquid composition comprising adalimumab, wherein the adalimumab is expressed in a Chinese Hamster Ovary (CHO) cell expression system; and wherein the composition is characterized in that when the composition is assayed in a cathepsin L kinetic assay, a level of cathepsin L activity from 0.4 to less than 1.84 RFU/s/mg of adalimumab is observed, wherein the cathepsin L kinetic assay comprises:

i) diluting the composition in a polystyrene container in a solution containing 25 mM NaOAc, 5 mM DTT and 1 mM EDTA at pH 5.5,

ii) adding dextran sulfate to a concentration of 0.035 µg/mL and incubating at 37°C for six hours,

iii) adding Z-leucine-arginine covalently bound at its C-terminus to a fluorescent 7-amino-4-methyl coumarin (Z-leucine-arginine-AMC), wherein the diluting, adding, and incubating steps are sufficient to permit the measurement of cathepsin L hydrolysis of the Z-leucine-arginine-AMC within a linear range, and

iv) measuring Z-leucine-arginine-AMC hydrolysis in the linear range in RFU/s/mg of adalimumab.

2. The liquid composition of claim 1, wherein the cathepsin L activity is from about 0.4 to 1.0 RFU/s/mg of adalimumab.

3. The liquid composition of claim 1, wherein the cathepsin L activity is from 0.4 to 1.3 RFU/s/mg of adalimumab.

4. The liquid composition of claim 1, wherein the cathepsin L activity is from 0.4 to 0.6 RFU/s/mg of adalimumab.

5. The liquid composition of claim 1, wherein the cathepsin L activity is from 0.4 to 0.85 RFU/s/mg of adalimumab.

6. The liquid composition of claim 1, wherein the cathepsin L activity is from 0.4 to 0.9 RFU/s/mg of adalimumab.

7. The liquid composition of any one of claims 1, 2-6 and 13, wherein the composition is packaged in a pre-filled syringe.

8. The liquid composition of any one of claims 1, 2-6 and 13, wherein the composition comprises 50 mg/ml of adalimumab.

9. The liquid composition of any one of claims 1, 2-6 and 13, wherein the composition is suitable for subcutaneous injection.

10. The liquid composition of any one of claims 1, 2-6 and 13, wherein the diluted composition has an adalimumab concentration of 20 µg/ml.

11. The liquid composition of any one of claims 1, 2-6 and 13, wherein the diluted composition has an adalimumab concentration of 50 µg/ml.

12. The liquid composition of any one of claims 1, 2-6 and 13, wherein step i) of the cathepsin L kinetic assay comprises diluting the composition 600 fold.

13. The liquid composition of claim 1, wherein the cathepsin L activity is from 0.5 to 1.5 RFU/s/mg of adalimumab.