WHAT IS CLAIMED IS:

1. An aqueous pharmaceutical composition comprising etanercept and a stabilizer to inhibit instability, aggregation, misfolding and/or fragmentation of the etanercept, wherein the stabilizer comprises one or more amino acid compounds selected from the group consisting of serine, proline and glutamate.

2. The composition of claim 1, further comprising one or more additional components selected from: a buffer; a tonicity modifier, and an excipient.

3. The stabilized etanercept composition of claim 2 where the stabilizer is glutamate, the formulation is free or essentially free of arginine, and the formulation elicits long term storage stability as characterized by at least one of:

   SEC analysis at M_3 or T_2 or T_4 of: monomer content greater than about 90%; aggregates content of less than about 3 wt%; and fragment 3 content less than about 5 wt%; and

   HIC analysis at M_3 T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than about 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 20 wt.%.

4. The stabilized etanercept composition of claim 2 wherein the stabilizer is glutamate and the formulation comprises about 25 to about 75 mg/ml etanercept; up to about 150 mM glutamate; less than about 6 wt.% sucrose; optionally up to about 100 mM NaCl; about 1 to about 30 mM sodium phosphate, wherein the composition has a pH of about 6.0 to 6.6; and wherein, optionally, the composition contains no arginine or is essentially free of arginine.

5. The glutamate stabilized composition of claim 4 eliciting long term storage stability as characterized by:

SEC analysis at M_3 or T_2 or T_4 of greater than about 90 wt.% monomer content; less than about 3 wt.% aggregate(s) content; and less than about 5 wt% fragment 3; and

HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than about 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 20 wt.%.

6. The glutamate stabilized composition of claim 5 eliciting long term storage stability as characterized by: an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 2 of the HIC chromatogram is greater than or equal to about 95 wt.%; and wherein, if peak 3 is present on the HIC chromatogram, the amount of the composition represented by peak 3 is less than or equal to about 3 wt.%.

7. The glutamate stabilized composition of claim 5 having, at M_3 or T_2 or T_4 no more than, on average, about 10,000 subvisible particles per mL having a size greater than 5µm.

8. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; less than about 150 mM glutamate; about 0 to 3% sucrose; about 1 to 30 mM phosphate buffer, optionally up to about 100 mM NaCl, and having a pH of about 6.0 to 6.6.

9. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; about 100 to about 120 mM glutamate; less than about 4 wt.% sucrose, and about 10 to 30 mM phosphate; and having a pH of about 6.3 to 6.5.

10. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; about 100 mM glutamate; less than about 2 wt.% sucrose, about 100 mM NaCl; about 10-30 mM phosphate; and having a pH of about 6.3 to 6.5.

11. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; about 50 mM glutamate; less than about 2 wt.% sucrose, about 100 mM NaCl; about 10-30 mM phosphate; and having a pH of about 6.3 to 6.5.

12. The stabilized etanercept composition of claim 2 where the stabilizer is serine, the formulation is free or essentially free of arginine, and the formulation elicits long term storage stability as characterized by at least one of:

SEC analysis at M_3 or T_2 or T_4 of: monomer content greater than about 90%; aggregates content of less than about 3 wt%; and fragment 3 content less than about 5 wt%: and

HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than about 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 20 wt.%.

13. The stabilized etanercept composition of claim 2 wherein the stabilizer is serine and the formulation comprises up to about 150 mM serine; about 0.5 to about 3 wt.% sucrose; about 1 to about 30 mM sodium phosphate, and wherein the composition has a pH of about 6.0 to 6.6; and wherein, optionally, the composition contains no arginine or is essentially free of arginine.

14. The serine stabilized composition of claim 13 eliciting long term storage stability as characterized by:

(a) SEC analysis at M_3 or T_2 or T_4 of greater than about 90 wt.% monomer content; less than about 3 wt.% aggregate(s) content; and less than about 5 wt% fragment 3; and

(b) an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than about 3 wt.%; the amount of the composition represented by peak 2 of the

HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 20 wt.%; and

15. The serine stabilized composition of claim 14 which elicits long term storage stability as characterized by: an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 2 of the HIC chromatogram is greater than or equal to about 95 wt.%; and wherein, if peak 3 is present on the HIC chromatogram, the amount of the composition represented by peak 3 is less than or equal to about 3 wt.%.

16. The serine stabilized composition of claim 14 having at M_3 or T_2 or T_4, on average, no more than about 10,000 subvisible particles per mL having a size greater than 5μm.

17. The serine stabilized composition of claim 14 comprising about 50 mg/ml etanercept; about 100-120 mM serine; less than about 4 wt.% sucrose, and about 10-30 mM phosphate; and having a pH of about 6.3 to 6.5.

18. The stabilized etanercept composition of claim 2 where the stabilizer is proline, the composition is free or essentially free of arginine, and the composition elicits long term storage stability as characterized by:

SEC analysis at M_3 or T_2 or T_4 of: monomer content greater than about 90%; aggregates content of less than about 3 wt.%; and fragment 3 content less than about 5 wt.%: and

HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than about 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 20 wt.%.

19. The proline stabilized etanercept composition of claim 18 comprising up to about 150 mM proline; said composition further comprising: about 0.5 to

about 3 wt.% sucrose; about 1 to about 30 mM sodium phosphate, about 15 to about 100 mM NaCl; and wherein the composition has a pH of about 6.0 to 6.6; and wherein, optionally, the composition contains no arginine or is essentially free of arginine.

20. The proline stabilized composition of claim 19 which elicits long term storage stability as characterized by:

SEC analysis at M_3 or T_2 or T_4 of greater than about 90 wt.% monomer content; less than about 3 wt.% aggregate(s) content; and less than about 5 wt% fragment 3; and

HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than about 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 20 wt.%.

21. The proline stabilized composition of claim 20 which elicits long term storage stability as characterized by: an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 2 of the HIC chromatogram is greater than or equal to about 95 wt.%; and wherein, if peak 3 is present on the HIC chromatogram, the amount of the composition represented by peak 3 is less than or equal to about 3 wt.%.

22. The proline stabilized composition of claim 20 having at M_3 or T_2 or T_4, on average, no more than about 10,000 subvisible particles per mL having a size greater than 5μm.

23. The proline stabilized composition of claim 20 comprising about 50 mM proline, less than about 4 wt.% sucrose, about 25 mM NaCl, about 10-30 mM phosphate, and having pH of about 6.3 to 6.5.

24. The composition of claim 1, containing no arginine, or essentially free of arginine, wherein the composition, at M_3 or T_2 or T_4, elicits long term storage stability that meets one or both of the following criteria:

(A) stability comparable to or better than commercially available etanercept marketed under the trademark Enbrel®, as measured by (i) SEC analysis of the amounts of aggregate(s), monomer and fragment 3 in the composition and (ii) HIC analysis of amounts of material in the composition corresponding to peaks 1, 2 and 3 of the HIC chromatogram; and

(B) an HIC chromatogram in which (i) peak 3 is absent, or essentially absent and (ii) peak 2 represents greater than about 95 wt% of the composition; an SEC chromatogram containing essentially no peak corresponding to aggregate(s); and an SEC chromatogram in which the monomer content represents at least about 95 wt% of the composition.

WHAT IS CLAIMED IS:

1. An aqueous pharmaceutical composition comprising etanercept and a stabilizer to inhibit instability, aggregation, misfolding and/or fragmentation of the etanercept, wherein the stabilizer comprises one or more amino acid compounds selected from the group consisting of serine, proline and glutamate.

2. The composition of claim 1, further comprising one or more additional components selected from: a buffer; a tonicity modifier, and an excipient.

3. The stabilized etanercept composition of claim 2 where the stabilizer is glutamate, the formulation is free or essentially free of arginine, and the formulation elicits long term storage stability as characterized by at least one of:

   SEC analysis at M_3 or T_2 or T_4 of: monomer content greater than 90%; aggregates content of less than 3 wt%; and fragment 3 content less than 5 wt%: and

   HIC analysis at M_3 T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 20 wt.%.

4. The stabilized etanercept composition of claim 2 wherein the stabilizer is glutamate and the formulation comprises 25 to 75 mg/ml etanercept; up to 150 mM glutamate; less than 6 wt.% sucrose; optionally up to 100 mM NaCl; 1 to 30 mM sodium phosphate, wherein the composition has a pH of 6.0 to 6.6; and wherein, optionally, the composition contains no arginine or is essentially free of arginine.

5. The glutamate stabilized composition of claim 4 eliciting long term storage stability as characterized by:

SEC analysis at M_3 or T_2 or T_4 of greater than 90 wt.% monomer content; less than 3 wt.% aggregate(s) content; and less than 5 wt% fragment 3; and

HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 20 wt.%.

6. The glutamate stabilized composition of claim 5 eliciting long term storage stability as characterized by: an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 2 of the HIC chromatogram is greater than or equal to 95 wt.%; and wherein, if peak 3 is present on the HIC chromatogram, the amount of the composition represented by peak 3 is less than or equal to 3 wt.%.

7. The glutamate stabilized composition of claim 5 having, at M_3 or T_2 or T_4 no more than, on average, 10,000 subvisible particles per mL having a size greater than 5µm.

8. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; less than 150 mM glutamate; 0 to 3% sucrose; 1 to 30 mM phosphate buffer, optionally up to 100 mM NaCl, and having a pH of 6.0 to 6.6.

9. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; 100 to 120 mM glutamate; less than 4 wt.% sucrose, and 10 to 30 mM phosphate; and having a pH of 6.3 to 6.5.

10. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; about 100 mM glutamate; less than 2 wt.% sucrose, about 100 mM NaCl; 10-30 mM phosphate; and having a pH of 6.3 to 6.5.

11. The glutamate stabilized composition of claim 5 comprising about 50 mg/ml etanercept; about 50 mM glutamate; less than 2 wt.% sucrose, about 100 mM NaCl; 10-30 mM phosphate; and having a pH of 6.3 to 6.5.

12. The stabilized etanercept composition of claim 2 where the stabilizer is serine, the formulation is free or essentially free of arginine, and the formulation elicits long term storage stability as characterized by at least one of:

SEC analysis at M_3 or T_2 or T_4 of: monomer content greater than 90%; aggregates content of less than 3 wt%; and fragment 3 content less than 5 wt%: and

HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 20 wt.%.

13. The stabilized etanercept composition of claim 2 wherein the stabilizer is serine and the formulation comprises up to 150 mM serine; 0.5 to 3 wt.% sucrose; 1 to 30 mM sodium phosphate, and wherein the composition has a pH of 6.0 to 6.6; and wherein, optionally, the composition contains no arginine or is essentially free of arginine.

14. The serine stabilized composition of claim 13 eliciting long term storage stability as characterized by:

(a) SEC analysis at M_3 or T_2 or T_4 of greater than 90 wt.% monomer content; less than 3 wt.% aggregate(s) content; and less than 5 wt% fragment 3; and

(b) an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 20 wt.%.

15. The serine stabilized composition of claim 14 which elicits long term storage stability as characterized by: an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 2 of the HIC chromatogram is greater than or equal to 95 wt.%; and wherein, if peak 3 is present on the HIC chromatogram, the amount of the composition represented by peak 3 is less than or equal to 3 wt.%.

16. The serine stabilized composition of claim 14 having at M_3 or T_2 or T_4, on average, no more than 10,000 subvisible particles per mL having a size greater than 5µm.

17. The serine stabilized composition of claim 14 comprising about 50 mg/ml etanercept; 100-120 mM serine; less than 4 wt.% sucrose, and 10-30 mM phosphate; and having a pH of 6.3 to 6.5.

18. The stabilized etanercept composition of claim 2 where the stabilizer is proline, the composition is free or essentially free of arginine, and the composition elicits long term storage stability as characterized by:

    SEC analysis at M_3 or T_2 or T_4 of: monomer content greater than 90%; aggregates content of less than 3 wt.%; and fragment 3 content less than 5 wt.%: and

    HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 20 wt.%.

19. The proline stabilized etanercept composition of claim 18 comprising up to 150 mM proline; said composition further comprising: 0.5 to 3 wt.% sucrose; 1 to 30 mM sodium phosphate, 15 to 100 mM NaCl; and wherein the composition has a pH of 6.0 to 6.6; and wherein, optionally, the composition contains no arginine or is essentially free of arginine.

20. The proline stabilized composition of claim 19 which elicits long term storage stability as characterized by:

SEC analysis at M_3 or T_2 or T_4 of greater than 90 wt.% monomer content; less than 3 wt.% aggregate(s) content; and less than 5 wt% fragment 3; and

HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 1 of the HIC chromatogram is less than 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 20 wt.%.

21. The proline stabilized composition of claim 20 which elicits long term storage stability as characterized by: an HIC analysis at M_3 or T_2 or T_4 wherein the amount of the composition represented by peak 2 of the HIC chromatogram is greater than or equal to 95 wt.%; and wherein, if peak 3 is present on the HIC chromatogram, the amount of the composition represented by peak 3 is less than or equal to 3 wt.%.

22. The proline stabilized composition of claim 20 having at M_3 or T_2 or T_4, on average, no more than 10,000 subvisible particles per mL having a size greater than 5µm.

23. The proline stabilized composition of claim 20 comprising about 50 mM proline, less than 4 wt.% sucrose, about 25 mM NaCl, 10-30 mM phosphate, and having pH of 6.3 to 6.5.

24. The composition of claim 1, containing no arginine, or essentially free of arginine, wherein the composition, at M_3 or T_2 or T_4, elicits long term storage stability that meets one or both of the following criteria:

(A) stability comparable to or better than commercially available etanercept marketed under the trademark Enbrel®, as measured by (i) SEC analysis of the amounts of aggregate(s), monomer and fragment 3 in the composition

and (ii) HIC analysis of amounts of material in the composition corresponding to peaks 1, 2 and 3 of the HIC chromatogram; and

(B) an HIC chromatogram in which (i) peak 3 is absent, or essentially absent and (ii) peak 2 represents greater than 95 wt% of the composition; an SEC chromatogram containing essentially no peak corresponding to aggregate(s); and an SEC chromatogram in which the monomer content represents at least 95 wt% of the composition.