WHAT IS CLAIMED IS:

1. An aqueous etanercept formulation stabilized to reduce instability, aggregation misfolding and/or fragmentation of the etanercept, said formulation comprising about 25 to about 75 mg/ml of etanercept and one or more stabilizers, wherein the stabilizers are selected from the group consisting of (i) sodium chloride and (ii) sodium chloride in combination with sucrose or trehalose; and (iii) a combination of sodium chloride, sucrose and trehalose.

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

3. The formulation of claim 2 wherein the stabilizer consists essentially of either: (a) sodium chloride; or (b) sodium chloride in combination with sucrose; or (c) sodium chloride in combination with trehalose; and wherein, the formulation, optionally, 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.%.

4. The formulation of claim 2 comprising about 25 to 75 mg/ml etanercept, sodium chloride in an amount up to about 150 mM, about 1 to about 30 mM sodium phosphate; and about 0 to 5 wt.% sucrose or trehalose or combination thereof; wherein the composition has a pH of about 6.0 to about 6.6; and wherein the composition is characterized by SEC analysis at M_3 or T_2 or T_4 in

which: monomer content is greater than about 80 wt.%; aggregate(s) content is less than about 3 wt.%, and fragment 3 content is less than about 8 wt.%.

5. The formulation of claim 4, optionally essentially free of arginine, eliciting long term storage stability characterized by:

(a) an SEC analysis at M_3 or T_2 or T_4 of greater than about 90 wt.% monomer content, and less than about 3 wt.% aggregate(s) content; 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 4 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than about 80 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 20 wt.%; and

6. The formulation of claim 5 having 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 1 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than about 95 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 3 wt.%.

7. The formulation of claim 2 comprising up to about 150 mM sodium chloride, about 1 to 30 mM sodium phosphate, and about 0-5 wt.% sucrose or trehalose, or combination of sucrose and trehalose, and having a pH of about 6.0 to 6.6; and characterized by: an SEC analysis at M_3 or T_2 or T_4 of greater than about 95 wt.% monomer content and less than about 1 wt.% aggregate(s) content; and 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 or equal to about 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than about 82 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than about 15 wt.%.

8. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 75 mM sodium chloride; about 10 to 30 mM sodium phosphate; about 3 wt.% sucrose.

9. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 75mM sodium chloride; about 10 to 30 mM sodium phosphate; about 3 wt.% trehalose.

10. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 75mM sodium chloride; about 10 to 30 mM sodium phosphate; about 3 wt.% sucrose and having pH of about 6.3 to 6.5.

11. The formulation of claim 2 comprising: about 50 mg/ml of etanercept; about 120mM sodium chloride; about 10 to 30 mM sodium phosphate; about 1 wt.% sucrose; about 5 mM arginine, and having pH of about 6.3 to 6.5.

12. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 150 mM sodium chloride; about 10 to 30 mM sodium phosphate, in the absence of sucrose or trehalose.

13. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 100 mM sodium chloride; about 10 to 30 mM sodium phosphate; and about 2 wt.% sucrose.

14. The formulation of claim 3 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 1 wt.%.

15. The formulation of claim 3 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 5um.

16. The formulation 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 (as defined in the specification) and (ii) HIC analysis of amounts of material in the composition corresponding to peaks 1, 2 and 3 of the HIC chromatogram (as defined in the specification); 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 etanercept formulation stabilized to reduce instability, aggregation misfolding and/or fragmentation of the etanercept, said formulation comprising 25 to 75 mg/ml of etanercept and one or more stabilizers, wherein the stabilizers are selected from the group consisting of (i) sodium chloride and (ii) sodium chloride in combination with sucrose or trehalose; and (iii) a combination of sodium chloride, sucrose and trehalose.

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

3. The formulation of claim 2 wherein the stabilizer consists essentially of either: (a) sodium chloride; or (b) sodium chloride in combination with sucrose; or (c) sodium chloride in combination with trehalose; and wherein, the formulation, optionally, 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.%.

4. The formulation of claim 2 comprising 25 to 75 mg/ml etanercept, sodium chloride in an amount up to 150 mM, 1 to 30 mM sodium phosphate; and 0 to 5 wt.% sucrose or trehalose or combination thereof; wherein the composition has a pH of 6.0 to 6.6; and wherein the composition is characterized by SEC analysis at M_3 or T_2 or T_4 in which: monomer content is greater than 80 wt.%; aggregate(s) content is less than 3 wt.%, and fragment 3 content is less than 8 wt.%.

5. The formulation of claim 4, optionally essentially free of arginine, eliciting long term storage stability characterized by:

(a) an SEC analysis at M_3 or T_2 or T_4 of greater than 90 wt.% monomer content; and less than 3 wt.% aggregate(s) content; 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 4 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 formulation of claim 5 having 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 1 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 95 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 3 wt.%.

7. The formulation of claim 2 comprising up to 150 mM sodium chloride, 1 to 30 mM sodium phosphate, and 0-5 wt.% sucrose or trehalose, or combination of sucrose and trehalose, and having a pH of 6.0 to 6.6; and characterized by: an SEC analysis at M_3 or T_2 or T_4 of greater than 95 wt.% monomer content and less than 1 wt.% aggregate(s) content; and 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 or equal to 3 wt.%; the amount of the composition represented by peak 2 of the HIC chromatogram is greater than 82 wt.%; and the amount of the composition represented by peak 3 of the HIC chromatogram is less than 15 wt.%.

8. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 75 mM sodium chloride; 10 to 30 mM sodium phosphate; and about 3 wt.% sucrose.

9. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 75mM sodium chloride; 10 to 30 mM sodium phosphate; and about 3 wt.% trehalose.

10. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 75mM sodium chloride; 10 to 30 mM sodium phosphate; about 3 wt.% sucrose and having pH of 6.3 to 6.5.

11. The formulation of claim 2 comprising: about 50 mg/ml of etanercept; about 120mM sodium chloride; 10 to 30 mM sodium phosphate; about 1 wt.% sucrose; about 5 mM arginine, and having pH of 6.3 to 6.5.

12. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 150 mM sodium chloride; 10 to 30 mM sodium phosphate, in the absence of sucrose or trehalose.

13. The formulation of claim 3 comprising: about 50 mg/ml of etanercept; about 100 mM sodium chloride; 10 to 30 mM sodium phosphate; and about 2 wt.% sucrose.

14. The formulation of claim 3 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 1 wt.%.

15. The formulation of claim 3 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.

16. The formulation 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 (as defined in the specification) and (ii) HIC

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