WHAT IS CLAIMED IS:

1. A stabilized aqueous pharmaceutical composition comprising etanercept and a stabilizer to inhibit instability, misfolding aggregation and/or fragmentation of the etanercept, wherein the composition is free of or is essentially free of arginine, and the stabilizer comprises xylitol or a combination of xylitol and meglumine.

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 composition of claim 2 optionally free or essentially free of arginine, and eliciting 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 composition of claim 2, comprising about 25 to about 75 mg/ml of etanercept; and a stabilizer to inhibit instability, aggregation and/or fragmentation of the etanercept, wherein the stabilizer is xylitol in an amount constituting up to about 10 wt.% of the composition, and wherein the composition is characterized by an SEC analysis at M3 or T2 or T4 of: greater than about 80 wt.% monomer content; less than about 3 wt.% aggregate(s) content; and less than about 6 wt.% fragment 3 content; and having a pH of 6.0 to 6.6.

5. The composition of claim 4 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 composition of claim 3 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 composition of claim 3 comprising: about 25 to 75 mg/ml of etanercept; 1-10 wt.% xylitol; 1 to 30 mM sodium phosphate; optionally up to about 5 wt.% meglumine; optionally up to about 100 mM NaCl; and optionally up to about 5 wt.% sucrose.

8. The composition of claim 7 comprising: about 1-100 mM NaCl; 1 to 5 wt.% sucrose; and wherein the stabilizer further comprises meglumine in an amount of 1-5 wt.% of the composition.

9. The composition of claim 7 comprising: about 50 mg/ml of etanercept; about 10 wt.% xylitol; and 10 to 30 mM sodium phosphate; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

10. The composition of claim 7 comprising: about 50 mg/ml of etanercept; 10 to 30 mM sodium phosphate; 1-3 wt.% xylitol; and 1-3 wt.% meglumine; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

11. The composition of claim 7 comprising: about 50 mg/ml of etanercept; 10-30 mM sodium phosphate; 1-3 wt.% xylitol; 1-3 wt.% meglumine; 1-100 mM sodium chloride; and 1-4 wt. % sucrose; wherein the formulation is

characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

12. The composition of claim 7 comprising: about 50 mg/ml of etanercept; about 6 wt.% xylitol; and 10-30 mM sodium phosphate; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

13. The composition of claim 7 comprising about 50 mg/ml of etanercept; 10-30 mM sodium phosphate; 2-3 wt.% xylitol; about 5% sucrose; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

14. The composition 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 composition 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 composition of claim 3 comprising about 25 to 75 mg/ml of etanercept; 1-10 wt.% xylitol; 1 to 30 mM sodium phosphate; optionally up to about 5 wt.% mannosylglycerate, mannosyllactate, mannosylglycolate, or diglycerolphosphate; optionally up to about 100 mM NaCl; and optionally up to about 5 wt.% sucrose.

17. The composition of claim 1, wherein the composition, at M3 or T2 or T4, 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. A stabilized aqueous pharmaceutical composition comprising etanercept and a stabilizer to inhibit instability, misfolding aggregation and/or fragmentation of the etanercept, wherein the composition is free of arginine, and the stabilizer comprises xylitol or a combination of xylitol and meglumine.

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 composition of claim 2 eliciting 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 composition of claim 2, comprising 25 to 75 mg/ml of etanercept; and a stabilizer to inhibit instability, aggregation and/or fragmentation of the etanercept, wherein the stabilizer is xylitol in an amount constituting up to 10 wt.% of the composition, and wherein the composition is characterized by an SEC analysis at M3 or T2 or T4 of: greater than 80 wt.% monomer content; less than 3 wt.% aggregate(s) content; and less than 6 wt.% fragment 3 content; and having a pH of 6.0 to 6.6.

5. The composition of claim 4 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 composition of claim 3 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 composition of claim 3 comprising: 25 to 75 mg/ml of etanercept; 1-10 wt.% xylitol; 1 to 30 mM sodium phosphate; optionally up to 5 wt.% meglumine; optionally up to 100 mM NaCl; and optionally up to 5 wt.% sucrose.

8. The composition of claim 7 comprising: 1-100 mM NaCl; 1 to 5 wt.% sucrose; and wherein the stabilizer further comprises meglumine in an amount of 1-5 wt.% of the composition.

9. The composition of claim 7 comprising: about 50 mg/ml of etanercept; about 10 wt.% xylitol; and 10 to 30 mM sodium phosphate; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

10. The composition of claim 7 comprising: 50 mg/ml of etanercept; 10 to 30 mM sodium phosphate; 1-3 wt.% xylitol; and 1-3 wt.% meglumine; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

11. The composition of claim 7 comprising: about 50 mg/ml of etanercept; 10-30 mM sodium phosphate; 1-3 wt.% xylitol; 1-3 wt.% meglumine; 1-100 mM sodium chloride; and 1-4 wt. % sucrose; wherein the formulation is

characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

12. The composition of claim 7 comprising: 50 mg/ml of etanercept; 6 wt.% xylitol; and 10-30 mM sodium phosphate; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

13. The composition of claim 7 comprising 50 mg/ml of etanercept; 10-30 mM sodium phosphate; 2-3 wt.% xylitol; 5% sucrose; wherein the formulation is characterized by an SEC analysis at M_3 or T_2 or T_4 of greater than 85 wt.% monomer content.

14. The composition 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 composition 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 composition of claim 3 comprising 25 to 75 mg/ml of etanercept; 1-10 wt.% xylitol; 1 to 30 mM sodium phosphate; optionally up to 5 wt.% mannosylglycerate, mannosyllactate, mannosylglycolate, or diglycerolphosphate; optionally up to 100 mM NaCl; and optionally up to 5 wt.% sucrose.

17. The composition of claim 1, 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 an etanercept composition containing arginine and having the following stability measurements:

(i) SEC analysis of the amounts of etanercept aggregate(s) of 0.59 percent by weight after storage for one week at 40°C and 1.02 percent by weight after storage for two weeks at 40°C;

(ii) SEC analysis of the amount of etanercept monomer in the composition of 92.58 percent by weight after storage for one week at 40°C and 87.64 percent by weight after storage for two weeks at 40°C;

(iii) SEC analysis of the amount of fragment 3 in the composition of 3.30 percent by weight after storage for one week at 40°C and 6.29 percent by weight after storage for two weeks at 40°C; and

(B) an SEC chromatogram containing no peak corresponding to etanercept aggregate(s); and an SEC chromatogram in which the etanercept monomer content represents at least 95 wt% of the composition.