WHAT IS CLAIMED IS:

1. A stable aqueous pharmaceutical composition comprising etanercept in combination with a stabilizer to reduce instability, aggregation misfolding and/or fragmentation of the etanercept during storage of the formulation; said stabilizer comprising a sugar and a polyol.

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 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 composition of claim 2, optionally free or essentially free of arginine, comprising about 25 to about 75 mg/ml of etanercept; about 1 to about 10 wt.% sucrose, trehalose or dextrose; up to about 10 wt.% mannitol or sorbitol, about 1 mM to about 30 mM sodium phosphate, said composition having pH about 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: the monomer content is greater than about 80 wt.%; aggregates content is less than about 3 wt.%, and fragment 3 content less than about 10 wt.%.

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 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 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 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 composition of claim 3 comprising: about 50 mg/ml of etanercept; about 1 to 5 wt.% sucrose, trehalose or dextrose; about 1-2 wt.% mannitol or sorbitol, about 10-30 mM sodium phosphate, said composition having pH of about 6.3 to 6.5.

8. 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 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.%.

9. The composition 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 5µm.

10. 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 (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 stable aqueous pharmaceutical composition comprising etanercept in combination with a stabilizer to reduce instability, aggregation misfolding and/or fragmentation of the etanercept during storage of the formulation; said stabilizer comprising a sugar and a polyol.

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 about 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, optionally free or essentially free of arginine, comprising about 25 to about 75 mg/ml of etanercept; 1 to 10 wt.% sucrose, trehalose or dextrose; up to 10 wt.% mannitol or sorbitol, 1 mM to 30 mM sodium phosphate, said composition having pH 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: the monomer content is greater than 80 wt.%; aggregates content is less than 3 wt.%, and fragment 3 content less than 10 wt.%.

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 50 mg/ml of etanercept; 1 to 5 wt.% sucrose, trehalose or dextrose; 1-2 wt.% mannitol or sorbitol, 10-30 mM sodium phosphate, said composition having pH of 6.3 to 6.5.

8. 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 3 wt.%.

9. 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.

10. 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 (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.