CLAIMS

1. An etanercept composition prepared by a method comprising a growth phase and a production phase, wherein

(a) the growth phase comprises culturing cells capable of expressing a protein comprising etanercept at a temperature which promotes exponential logarithmic growth of the cells; and

(b) the production phase is conducted in a suitable reaction vessel containing a mixture comprising the cells capable of expressing a protein comprising etanercept and a culture medium suitable for conducting such expression, and wherein the production phase comprises a perfusion method comprising (i) causing the cells to produce the protein comprising etanercept; and (ii) periodically or continuously removing spent culture medium from, and adding fresh culture medium to, the reaction vessel,

wherein the protein comprising etanercept comprises greater than 60 wt.% correctly folded etanercept as determined by hydrophobic interaction chromatography (HIC),

wherein the etanercept composition has sialic acid content of commercially available etanercept described in Physicians' Desk Reference, 2002, and

wherein said etanercept composition comprises 0.75 g/L to about 1 g/L of said protein.

2. The etanercept composition of claim 1, wherein the culture medium comprises a Chinese hamster ovary cell medium as a base feed medium.

3. The etanercept composition of claim 1, wherein the culture medium comprises at least one supplement selected from the group consisting of dexamethasone, N-acetylmannosamine (ManNAc), galactose, glutamine, and cottonseed hydrolysate.

4. The etanercept composition of claim 1, wherein the culture medium comprises a Chinese hamster ovary cell medium as a base feed medium, and wherein the culture medium comprises at least one supplement selected from the group consisting of glutamine, cottonseed hydrolysate, dexamethasone, galactose and N-acetylmannosamine (ManNAc).

5. The etanercept composition of claim 1, wherein:

(1) the growth phase temperature is selected from (i) about 28°C to about 37°C; and (ii) about 35°C to about 36°C; and

(2) the production phase is carried out at a temperature selected from (i) greater than about 32°C; (ii) greater than about 33°C; (iii) greater than about 34°C; (iv) greater than about 35°C; (v) the range of about 33°C to about 36°C; (vi) the range of about 35°C to about 36°C; (vii) 32.5°C; (viii) 33.5°C; (ix) 34.5°C; and (x) 35.5°C.

6. The etanercept composition of claim 5, wherein the production phase temperature is in the range of 33°C to about 36°C.

7. The etanercept composition of claim 6, wherein the production phase temperature is 33.5°C.

8. The etanercept composition of claim 4, wherein the supplement is cottonseed hydrolysate.

9. An etanercept composition comprising 0.75 g/L to about 1 g/L of a protein product consisting of correctly-folded etanercept and incorrectly-folded etanercept, wherein the protein product comprises greater than 60 wt.% correctly folded etanercept, and wherein the etanercept composition has sialic acid content of commercially available etanercept.

10. An etanercept composition comprising 0.2 g/L to about 1 g/L of a protein product consisting of correctly-folded etanercept and incorrectly-folded etanercept, wherein the protein product comprises greater than 60 wt.% correctly folded etanercept, and wherein the etanercept composition has sialic acid content of commercially available etanercept, further comprising dexamethasone, N-acetylmannosamine (ManNAc), galactose, glutamine, and/or cottonseed hydrolysate.

11. The etanercept composition of claim 9, further comprising dexamethasone.

12. The etanercept composition of claim 9, further comprising N-acetylmannosamine (ManNAc).

13. The etanercept composition of claim 9, further comprising galactose.

14. The etanercept composition of claim 9, further comprising glutamine.

15. An etanercept composition comprising 0.2 g/L to about 1 g/L of a protein product consisting of correctly-folded etanercept and incorrectly-folded etanercept, wherein the protein product comprises greater than 60 wt.% correctly folded etanercept, and wherein the etanercept composition has sialic acid content of commercially available etanercept, further comprising cottonseed hydrolysate.