

CLAIMS

What is claimed is:

1. A method of producing a composition comprising vedolizumab, comprising:
providing a composition comprising vedolizumab at a pH at or greater than pH 6.5,
wherein the composition comprising vedolizumab is derived from a mammalian cell culture expressing vedolizumab; and
incubating the composition comprising vedolizumab for a period of at least 10 hours;
wherein the incubation is performed during vedolizumab purification, and wherein the incubation is performed prior to formulation of vedolizumab in a pharmaceutically acceptable buffer,
thereby producing a composition comprising vedolizumab.
2. The method of claim 1, wherein the method produces a composition comprising vedolizumab having <16%, <15%, <14%, <13%, <12%, <11% or <10% basic vedolizumab isoform species.
3. The method of claim 1 or 2, wherein the incubation is performed during vedolizumab purification, and wherein the incubation is performed prior to ultrafiltration/diafiltration (UF/DF) of the antibody.
4. The method of any one of claims 1-3, wherein the incubation is performed at ambient temperature, or the incubation is performed at 15-30°C, or the incubation is performed at 20-25°C.
5. The method of any one of the previous claims, wherein:
the composition comprising vedolizumab is provided at a pH of about 6.5-8.5.
6. The method of any one of the previous claims, wherein the composition comprising vedolizumab is provided
at a pH of about 7.0-8.0,
at a pH of 7.0-7.5, or

at a pH of about pH 6.5, pH 6.6, pH 6.7, pH 6.8, pH 6.9, pH 7.0, pH 7.1, pH 7.2, pH 7.3, pH 7.4, pH 7.5, pH 7.6, pH 7.7, pH 7.8, pH 7.9, pH 8.0, pH 8.1, pH 8.2, pH 8.3, pH 8.4, or pH 8.5.

7. The method of any one of the previous claims, wherein:
the composition comprising vedolizumab is incubated for a period of 10-120 hours, a period of 12-120 hours, a period of 12-96 hours, a period of 12-72 hours, a period of 12-48 hours, a period of 24-120 hours, a period of 24-96 hours, a period of 24-72 hours, or a period of 24-48 hours;

the composition comprising vedolizumab is incubated for a period of at least 12 hours; or

the composition comprising vedolizumab is incubated for a period of about 12 hours, about 24 hours, about 36 hours, about 48 hours, about 72 hours, about 96 hours, or about 120 hours.

8. The method of any one of the previous claims, wherein the composition comprising vedolizumab comprises a first basic isoform chromatographic peak (BP1) and a second basic isoform chromatographic peak (BP2).

9. The method of claim 8, wherein the method produces a composition comprising vedolizumab having less than 2%, less than 1.5%, less than 1%, or less than 0.7% BP2.

10. The method of claim 1, wherein the mammalian cell culture is a Chinese Hamster Ovary (CHO) cell culture.

11. The method of claim 10, wherein the CHO cell culture comprises CHO cells that lack dihydrofolate reductase (DHFR) expression or CHO cells that lack glutamine synthetase (GS) expression.

12. The method of any one of the previous claims, wherein the method further comprises purifying the composition comprising vedolizumab from mammalian host cell protein (HCP) using one or more chromatographic separation steps selected from the group consisting of affinity chromatography, cation exchange chromatography, anion exchange chromatography, and ceramic hydroxyapatite (CHT) chromatography.

13. The method of claim 12, wherein the composition comprising vedolizumab is purified using affinity chromatography prior to the incubation or following the incubation;
the composition comprising vedolizumab is purified using cation exchange chromatography prior to the incubation or following the incubation;
the composition comprising vedolizumab is purified using anion exchange chromatography prior to the incubation or following the incubation; or
the composition comprising vedolizumab is purified using CHT chromatography prior to the incubation or following the incubation.
14. The method of any one of claims 1-13, wherein the method comprises incorporating the composition into a pharmaceutical formulation.
15. The method of claim 14, wherein the pharmaceutical formulation is a dry, lyophilized pharmaceutical formulation or a liquid pharmaceutical formulation.
16. The method of claim 15, further comprising a step of reconstituting the dry, lyophilized pharmaceutical formulation with a liquid so that it is suitable for administration.
17. A composition comprising vedolizumab, wherein the composition is produced by or is obtainable by the method of any one of claims 1-16.
18. The composition of claim 17, wherein the composition comprises less than 16%, less than 15%, less than 14%, less than 13%, less than 12%, less than 11%, or less than 10% basic vedolizumab isoform species present in the composition.
19. The method of claim 15, wherein the liquid pharmaceutical formulation is suitable for subcutaneous administration to a human.
20. The composition of claim 17 or 18, wherein the amount of HCP in the composition is 8 ppm or less, 7.5 ppm or less, 7 ppm or less, 6.5 ppm or less, 6 ppm or less, 5.5 ppm or less, 5 ppm or less, 4.5 ppm or less, 4 ppm or less, 3.5 ppm or less, 3 ppm or less, 2.5 ppm or less, or 2 ppm or less.