monoclonal antibodies (mAbs) through a depth filter comprising silica and polyacrylic fiber, to remove a proportion of the NAPRIs from the buffered solution. The amount of NAPRIs is reduced by passing the buffered solution of mAbs through the depth filter.

In another aspect, the present disclosure provides a method of producing a buffered solution of monoclonal antibodies (mAbs) with a reduced amount of non-aggregate product-related impurities (NAPRIs) by passing a buffered solution of monoclonal antibodies (mAbs) through a synthetic depth filter comprising silica and polyacrylic fiber, to produce the buffered solution of monoclonal antibodies (mAbs) with a reduced amount of non-aggregate product-related impurities (NAPRIs), wherein the NAPRIs comprise incompletely or incorrectly assembled mAb polypeptides.

In a further example, this disclosure provides a method of producing a buffered solution of monoclonal antibodies (mAbs) with a reduced amount of non-aggregate product-related impurities (NAPRIs), wherein the method comprises passing a buffered solution of monoclonal antibodies (mAbs) through a depth filter comprising silica and polyacrylic fiber, to produce the buffered solution of monoclonal antibodies (mAbs) with a reduced amount of non-aggregate product-related impurities (NAPRIs). The amount of NAPRIs is reduced by passing the buffered solution of mAbs through the depth filter.

In another aspect, the present disclosure provides a use of a synthetic depth filter comprising silica and polyacrylic fiber to reduce the amount of non-aggregate product-related impurities (NAPRIs) in a buffered solution of monoclonal antibodies (mAbs), wherein the NAPRIs comprise incompletely or incorrectly assembled mAb polypeptides.

In a further example, this disclosure provides use of a depth filter comprising silica and polyacrylic fiber to reduce the amount of non-aggregate product-related impurities (NAPRIs) in a buffered solution of monoclonal antibodies (mAbs).

This disclosure provides a buffered solution of monoclonal antibodies (mAbs) in which the amount of non-aggregate product-related impurities (NAPRIs) has been reduced relative to the amount of the mAbs, produced by performing any of the methods of the disclosure, or by any of the uses of the disclosure.

In yet another aspect, the present disclosure provides a method of producing a mAb, the method comprising the steps of:

Claims

1. A method of reducing the amount of non-aggregate product-related impurities (NAPRIs) in a buffered solution of monoclonal antibodies (mAbs) by passing the buffered solution of monoclonal antibodies (mAbs) through a synthetic depth filter comprising silica and polyacrylic fiber, to remove a proportion of the NAPRIs from the buffered solution,

wherein the NAPRIs comprise incompletely or incorrectly assembled mAb polypeptides.

2. A method of producing a buffered solution of monoclonal antibodies (mAbs) with a reduced amount of non-aggregate product-related impurities (NAPRIs) by passing a buffered solution of monoclonal antibodies (mAbs) through a synthetic depth filter comprising silica and polyacrylic fiber, to produce the buffered solution of monoclonal antibodies (mAbs) with a reduced amount of non-aggregate product-related impurities (NAPRIs),

wherein the NAPRIs comprise incompletely or incorrectly assembled mAb polypeptides.

3. Use of a synthetic depth filter comprising silica and polyacrylic fiber to reduce the amount of non-aggregate product-related impurities (NAPRIs) in a buffered solution of monoclonal antibodies (mAbs),

wherein the NAPRIs comprise incompletely or incorrectly assembled mAb polypeptides.

4. The method according to claim 1 or 2, or the use according to claim 3, wherein the mAb is a multispecific antibody.

5. The method according to any one of claim 1, 2 or 4, or the use according to claim 3 or 4, wherein the mAb is an antibody fusion protein comprising an antibody or antibody fragment and another biologically active polypeptide.

6. The method according to any one of claims 1, 2, 4 and 5, or the use according to any one of claims 3-5, wherein the buffered solution of monoclonal antibodies is passed through the synthetic depth filter at a temperature that is below ambient temperature.

7. The method according to any of claims 1, 2 and 4-6, or the use according to any one of claims 3-6, wherein the NAPRI is a polypeptide lacking one or more polypeptide chains of

the mAb, and/or wherein the NAPRI is a polypeptide comprising a different polypeptide chain arrangement than the mAb.

8. The method according to any one of claims 1, 2 and 4-6, or the use according to any one of claims 3-6, wherein the NAPRI comprises two heavy chains having the same amino acid sequence.

9. The method according to any one of claims 1, 2, and 4-8, or the use according to any one of claims 3-8, wherein the synthetic depth filter is a multi-layer depth filter comprising multiple levels of depth filter media.

10. The method according to any one of claims 1, 2 and 4-9, or the use according to any one of claims 3-9, wherein the synthetic depth filter does not contain diatomaceous earth.

11. The method according to any one of claims 1, 2, and 4-10, or the use according to any one of claims 3-10, further comprising measuring the NAPRI concentration in the buffered solution of mAbs after it has passed through the synthetic depth filter.

12. The method according to any one of claims 1, 2, and 4-11, or the use according to any one of claims 3-11, wherein the buffered solution of mAbs has been subjected to chromatography before passing through the synthetic depth filter.

13. The method or the use according to claim 12, wherein the chromatography comprises one or more of ion exchange chromatography, anion exchange chromatography, cation exchange chromatography, multimodal (mixed mode) chromatography, or affinity chromatography.

14. A method of producing a mAb, the method comprising the steps of:

(a) culturing a host cell comprising a nucleic acid encoding for a mAb so that the mAb is produced along with NAPRIs;

(b) forming a buffered solution of the mAb and NAPRIs;

(c) reducing the amount of NAPRIs by performing the method according to any one of claims 1, 2, and 4-13, or by the use according to any one of claims 3-13 on the buffered solution of mAb and NAPRIs; and

(d) isolating the mAb from the buffered solution.

15. The method according to claim 14, wherein the buffered solution of mAbs has been subjected to chromatography before passing through the synthetic depth filter.

16. The method according to claim 15, wherein the chromatography comprises one or more of ion exchange chromatography, an anion exchange column, a cation exchange column, multimodal (mixed mode) chromatography, or affinity chromatography.

17. The method according to any one of claims 1, 2 and 4-16, or the use according to any one of claims 3-13, wherein the buffered solution of monoclonal antibodies is passed through the synthetic depth filter at a temperature of between 10° C and 21° C, or between 15° C and 20° C.

18. The method according to any one of claims 1, 2 and 4-17, or the use according to any one of claims 3-13 and 17, wherein the buffered solution of monoclonal antibodies is passed through the synthetic depth filter at mass load of in the range of 100 g/m^2 to 2500 g/m^2, 300 g/m^2 to 2000 g/m^2, or 500 g/m^2 to 1500 g/m^2.

19. The method according to any one of claims 1, 2 and 4-18, or the use according to any one of claims 3-13, 17 and 18, wherein the buffered solution of monoclonal antibodies has a pH in the range of 4.0 to 7.5, 4.0 to 7.2, or 4.0 to 5.5 when it passes through the synthetic depth filter.

20. The method according to any one of claims 1, 2 and 4-19, or the use according to any one of claims 3-13 and 17-19, wherein the buffered solution of monoclonal antibodies is passed through the synthetic depth filter at a flow rate in the range of 1 L/min*m^2 to 10 L/min*m^2, 1.5 L/min*m^2 to 8 L/min*m^2, or at a flow rate that is about 4.3 L/min*m^2.