

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 any one of the preceding claims, or the use according to claim 3, wherein the mAb is a multispecific antibody.
5. The method according to any one of the preceding claims, or the use according to any one of the preceding claims, 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 the preceding claims, or the use according to any one of the preceding claims, wherein the buffered solution of monoclonal antibodies is passed through the depth filter at a temperature that is below ambient temperature.
7. The method according to any of the preceding claims, or the use according to any one of the preceding claims, wherein the NAPRI is a polypeptide lacking one or more polypeptide chains of the mAb.

8. The method according to any of the preceding claims, or the use according to any one of the preceding claims, wherein the NAPRI is a polypeptide comprising a different polypeptide chain arrangement than the mAb.

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

10. The method according to any one of the preceding claims, or the use according to any one of the preceding claims, wherein the buffered solution of mAbs has been subjected to affinity chromatography.

11. The method according to any one of the preceding claims, or the use according to any one of the preceding claims, wherein the depth filter is a multi-layer depth filter comprising multiple levels of depth filter media.

12. The method according to any one of the preceding claims, or the use according to any one of the preceding claims, wherein the depth filter does not contain diatomaceous earth.

13. The method according to any one of the preceding claims, or the use according to any one of the preceding claims, further comprising measuring the NAPRI concentration in the buffered solution of mAbs after it has passed through the depth filter.

14. The method according to any one of the preceding claims, or the use according to any one of the preceding claims, wherein the buffered solution of mAbs has been subjected to chromatography before passing through the synthetic depth filter.

15. The method or the use according to claim 14, wherein the chromatography is affinity chromatography, anion exchange chromatography, cation exchange chromatography or multimodal (mixed mode) chromatography.

16. The method or the use according to claim 15, wherein the chromatography is affinity chromatography using a Protein A resin, a Protein L resin, an Fc-selective resin, a Kappa light chain-selective resin, or a Lambda light chain-selective resin.

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17. The method or the use according to any one of claims 14-16, wherein the chromatography is ion exchange chromatography.

18. The method or the use according to claim 17, wherein the ion exchange chromatography used an anion exchange column, a cation exchange column, or multimodal (mixed mode) chromatography.

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19. 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 the method according to any one of the preceding claims, or by the use according to any one of the preceding claims.

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20. 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;

15 (c) reducing the amount of NAPRIs by performing the method according to any one of the preceding claims, or by the use according to any one of the preceding claims on the buffered solution of mAb and NAPRIs; and

(d) isolating the mAb from the buffered solution.

20 21. The method according to claim 20, wherein the buffered solution of mAbs has been subjected to chromatography before passing through the synthetic depth filter.

22. The method according to claim 20, wherein the chromatography is affinity chromatography, anion exchange chromatography, cation exchange chromatography or
25 multimodal (mixed mode) chromatography.

23. The method according to claim 22, wherein the chromatography is affinity chromatography using a Protein A resin, a Protein L resin, an Fc-selective resin, a Kappa light chain-selective resin, or a Lambda light chain-selective resin.

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24. The method according to any one of claims 21-23, wherein the chromatography is ion exchange chromatography.

25. The method according to claim 24, wherein the ion exchange chromatography used an
35 anion exchange column, a cation exchange column, or multimodal (mixed mode) chromatography.

26. The method or the use according to any one of the preceding claims, wherein the buffered solution of monoclonal antibodies is passed through the depth filter at a temperature of between about 10° C and about 21° C, or between about 15° C and about 20° C.

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27. The method or the use according to any one of the preceding claims, wherein the buffered solution of monoclonal antibodies is passed through the depth filter at mass load of in the range of about 100 g/m² to about 2500 g/m², about 300 g/m² to about 2000 g/m², or about 500 g/m² to about 1500 g/m².

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28. The method or the use according to any one of the preceding claims, wherein the buffered solution of monoclonal antibodies has a pH in the range of about 4.0 to about 7.5, about 4.0 to about 7.2, or about 4.0 to about 5.5 when it passes through the depth filter.

15 29. The method or the use according to any one of the preceding claims, wherein the buffered solution of monoclonal antibodies is passed through the depth filter at a flow rate in the range of about 1 L/min*m² to about 10 L/min*m², about 1.5 L/min*m² to about 8 L/min*m², or at a flow rate that is about 4.3 L/min*m².