One embodiment of the present invention is directed to a method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, an HCP and a viral particle, wherein said sample mixture has not been exposed to Protein A, and wherein the preparation comprises a decreased number of viral particles or decreased viral activity in comparison to the sample mixture, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to a pH of 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to an ion exchange resin and collecting an ion exchange sample;

(d) applying said ion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

One embodiment of the present invention is directed to a method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, and at least one HCP, and wherein said sample mixture has not been exposed to Protein A, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to a cation exchange resin and collecting a cation exchange sample;

(d) applying said cation exchange sample to an anion exchange resin and collecting a anion exchange sample; and

(e) applying said anion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

One embodiment of the present invention is directed to a method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, and at least one HCP, and wherein said sample mixture has not been exposed to Protein A, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to a cation exchange resin and collecting a cation exchange sample;

(d) subjecting said cation exchange sample to filtration and collecting a filtrate;

(e) applying said filtrate from (d) to an anion exchange resin and collecting an anion exchange sample; and

(f) applying said anion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

CLAIMS

What is claimed is:

1. A method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, an HCP and a viral particle, wherein said sample mixture has not been exposed to Protein A, and wherein the preparation comprises a decreased number of viral particles or decreased viral activity in comparison to the sample mixture, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to a pH of 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to an ion exchange resin and collecting an ion exchange sample;

(d) applying said ion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

2. The method of claim 1, wherein said ion exchange resin is a cation exchange resin.

3. The method of claim 2, wherein said cation exchange resin comprises a substituted matrix wherein the substituents are selected from the group consisting of carboxymethyl, sulfoethyl, sulfopropyl, SO_3^-, phosphate and sulfonate.

4. The method of claim 3, wherein said substituent is SO_3^-.

5. The method of claim 1, wherein said ion exchange resin is an anion exchange resin.

6. The method of claim 5, wherein said anion exchange resin comprises a substituted matrix wherein the substituents are selected from the group consisting of diethylaminoethyl, quaternary aminoethyl, and quaternary amine groups.

7. The method of claim 6, wherein said substituent is a quaternary amine.

8. The method of claim 1, wherein said ion exchange sample is applied to a second ion exchange resin and a second ion exchange sample is collected prior to application to the hydrophobic interaction chromatography resin.

9. The method of claim 8, wherein said primary recovery sample is applied to a cation exchange resin and said ion exchange sample is applied to an anion exchange resin.

10. The method of claim 8, further comprising an intermediate step, wherein said intermediate step is a filtration step occurring after said ion exchange sample is collected and before said ion exchange sample is applied to said second ion exchange resin.

11. The method of claim 10, wherein said filtration step is accomplished by capture ultrafiltration/diafiltration.

12. The method of claim 1, wherein said HIC resin comprises a substituted matrix wherein the substituents consist of one or more hydrophobic groups.

13. The method of claim 12, wherein said substituents are selected from the group consisting of alkyl-groups, aryl-groups, and combinations thereof.

14. The method of claim 12, wherein said substituents are selected from the group consisting of: phenyl, 3-octoxypropane-1,2-diol, ether, propyl, methyl, and butyl groups.

15. The method of claim 14, wherein said resin comprises an agarose matrix comprising phenyl substituents.

16. The method of claim 1, further comprising a filtration step, wherein said HIC sample is subjected to filtration to remove viral particles and to facilitate buffer exchange.

17. The method of claim 1, wherein said HCP-reduced antibody, or antigen binding portion thereof, preparation comprises an anti-IL-12 antibody or an anti-IL-18 antibody or antigen-binding portions thereof.

18. The method of claim 17, wherein said anti-IL-18 antibody or antigen-binding portion thereof is a humanized antibody, a chimeric antibody, or a multivalent antibody.

19. The method of claim 18, wherein said anti-IL-18 antibody or antigen-binding portion thereof is a humanized antibody.

20. The method of claim 17, wherein said anti-IL-18 antibody or antigen-binding portion thereof neutralizes IL-18 both *in vivo* and *in vitro*.

21. The method of claim 1, wherein said preparation is substantially free of HCPs.

22. A method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, and at least one HCP, and wherein said sample mixture has not been exposed to Protein A, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to a cation exchange resin and collecting a cation exchange sample;

(d) applying said cation exchange sample to an anion exchange resin and collecting a anion exchange sample; and

(e) applying said anion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

23. A method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, and at least one HCP, and wherein said sample mixture has not been exposed to Protein A, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to a cation exchange resin and collecting a cation exchange sample;

(d) subjecting said cation exchange sample to filtration and collecting a filtrate;

(e) applying said filtrate from (d) to an anion exchange resin and collecting an anion exchange sample; and

(f) applying said anion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

24. The method of claim 1, wherein said HCP-reduced antibody, or antigen binding portion thereof, is adalimumab.

25. The method of claim 22, wherein said HCP-reduced antibody, or antigen binding portion thereof, is adalimumab.

26. The method of claim 23, wherein said HCP-reduced antibody, or antigen binding portion thereof, is adalimumab.