

WHAT IS CLAIMED IS:

1. A method for producing a host cell-protein (HCP) reduced target protein preparation from a sample mixture comprising a target protein and at least one HCP, said method comprising:

- (a) performing Raman spectroscopy analysis of said sample mixture;
- (b) contacting said sample mixture to an affinity chromatography resin in a simulated moving bed chromatographic separation such that the resin is loaded to about 50% -100% of its saturated binding capacity;
- (c) collecting a chromatographic sample; and
- (d) performing Raman spectroscopy analysis of said chromatographic sample to identify it as a HCP-reduced target protein preparation, wherein the target protein is an antibody or an antigen-binding portion thereof.

2. The method of claim 1 wherein the sample mixture is subjected to an additional chromatographic resin selected from the group consisting of an ion exchange chromatographic resin and a hydrophobic interaction chromatographic resin.

3. The method of claim 1 wherein the target protein is selected from the group consisting of: polyclonal antibodies; human monoclonal antibodies; humanized monoclonal antibodies; chimeric monoclonal antibodies; single chain antibodies; Fab antibody fragments; F(ab')₂ antibody fragments; Fd antibody fragments; Fv antibody fragments; and diabodies.

4. The method of claim 1 wherein the chromatography resin is packed into a series of fluidly-connected columns separated by fluid conduits comprising inlet and outlet valves, wherein the number of fluidly connected columns is selected from the group consisting of: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 columns.

5. The method of claim 1 wherein the sample mixture is contacted to the chromatography resin in order to obtain a residence time selected from the group consisting of up to about 0.5, up to about 1, up to about 2, up to about 3, up to about 4, up to about 5, up to about 6, up to about 7, up to about 8, up to about 9, up to about 10, up to about 11, and up to about 12 minutes.

6. The method of claim 1 further comprising the steps of equilibrating the chromatographic resin prior to contact with the sample mixture and washing the chromatographic resin after contact with the sample mixture, where the equilibration and wash buffers are identical buffers.
7. The method of claim 1 further comprising chromatography resin wash, elution, and regeneration steps after step (b) and before step (c), where such steps can be calculated and programmed in order to maintain the step of contacting the sample to the chromatography resin to be from about 20% to about 80% of the time of the process.
8. The method of claim 1 wherein the affinity chromatography resin comprises Protein A.
9. The method of any one of claims 1-8, wherein the antibody or the antigen-binding portion thereof is adalimumab.

WHAT IS CLAIMED IS:

1. A method for producing a host cell-protein (HCP) reduced target protein preparation from a sample mixture comprising a target protein and at least one HCP, said method comprising:

- (a) performing Raman spectroscopy analysis of said sample mixture;
- (b) contacting said sample mixture to an affinity chromatography resin such that the resin is loaded to about 50% -100% of its saturated binding capacity;
- (c) collecting a chromatographic sample; and
- (d) performing Raman spectroscopy analysis of said chromatographic sample to identify it as a HCP-reduced target protein preparation, wherein the target protein is an antibody or an antigen-binding portion thereof.

2. The method of claim 1 wherein the sample mixture is subjected to an additional chromatographic resin selected from the group consisting of an ion exchange chromatographic resin and a hydrophobic interaction chromatographic resin.

3. The method of claim 1 wherein the target protein is selected from the group consisting of: polyclonal antibodies; human monoclonal antibodies; humanized monoclonal antibodies; chimeric monoclonal antibodies; single chain antibodies; Fab antibody fragments; F(ab')₂ antibody fragments; Fd antibody fragments; Fv antibody fragments; and diabodies.

4. The method of claim 1 wherein the chromatography resin is packed into a series of fluidly-connected columns separated by fluid conduits comprising inlet and outlet valves, wherein the number of fluidly connected columns is selected from the group consisting of: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 columns.

5. The method of claim 1 wherein the sample mixture is contacted to the chromatography resin in order to obtain a residence time selected from the group consisting of up to about 0.5, up to about 1, up to about 2, up to about 3, up to about 4,

up to about 5, up to about 6, up to about 7, up to about 8, up to about 9, up to about 10, up to about 11, and up to about 12 minutes.

6. The method of claim 1 further comprising the steps of equilibrating the chromatographic resin prior to contact with the sample mixture and washing the chromatographic resin after contact with the sample mixture, where the equilibration and wash buffers are identical buffers.

7. The method of claim 1 further comprising chromatography resin wash, elution, and regeneration steps, where such steps can be calculated and programmed in order to maintain the step of contacting the sample to the chromatography resin to be from about 20% to about 80% of the time of the process.

8. The method of claim 1 wherein the affinity chromatography resin comprises Protein A.