CLAIMS

What is claimed is:

1. A method of reducing the level of protein aggregates in an elution pool containing an Fc-containing monomeric protein, the method comprising the steps of:
    (a) providing a sample comprising an Fc-containing monomeric protein and its protein aggregates;
    (b) contacting the sample with a protein A ligand immobilized onto a solid support, wherein the protein A ligand is based on the C domain of Protein A, such that the Fc-region containing monomeric protein and its protein aggregates bind to the protein A ligand;
    (c) obtaining an elution pool containing the Fc-containing monomeric protein using a pH gradient method employing a high pH buffer and a low pH buffer , wherein high pH buffer has a pH of 6.0 and the low pH buffer has a pH of 3.0;

    wherein at least 30% of the protein aggregates are removed prior to the elution of the Fc-containing monomeric protein in addition to protein aggregates that are removed after the elution of the Fc-containing monomeric protein, thereby reducing the level of protein aggregates in the elution pool.
2. A method of reducing the level of protein aggregates in an elution pool containing an Fc-containing monomeric protein, the method comprising the steps of:
    (d) providing a sample comprising an Fc-containing monomeric protein and its protein aggregates;
    (e) contacting the sample with a protein A ligand immobilized onto a solid support, wherein the protein A ligand is based on the C domain of Protein A, such that the Fc-region containing monomeric protein and its protein aggregates bind to the protein A ligand;
    (f) obtaining an elution pool containing the Fc-containing protein using a pH step method employing two or more buffers used sequentially in the order of descending pH values, wherein at least one of the buffers used in the step elution method has a pH ranging from 3.6 to 4.4;

    wherein at least 30% of the protein aggregates are removed prior to the elution of the Fc-containing monomeric protein in addition to protein aggregates that are

removed after the elution of the Fc-containing monomeric protein, thereby reducing the level of protein aggregates in the elution pool.

3. The method of claim 1, wherein the Fc-containing monomeric protein is selected from the group consisting of an antibody or an Fc-fusion protein.
4. The method of claim 2, wherein the Fc-containing monomeric protein is an antibody.
5. The method of claim4, wherein the antibody is a monoclonal antibody.
6. The method of claim 2, wherein the Fc-containing monomeric protein is selected from the group consisting of an antibody or an Fc-fusion protein.
7. The method of claim 9, wherein the antibody is a monoclonal antibody.
8. The method of claim 1, wherein the pH gradient spans 5 column volumes to 30 column volumes.
9. The method of claim 1, wherein the solid support is selected from the group consisting of solid support is selected from the group consisting of controlled pore glass, silica, zirconium oxide, titanium oxide, agarose, polymethacrylate, polyacrylate, polyacrylamide, polyvinylether, polyvinyl alcohol and polystyrene and derivatives thereof.
10. The method of claim 2, wherein the solid support is selected from the group consisting of solid support is selected from the group consisting of controlled pore glass, silica, zirconium oxide, titanium oxide, agarose, polymethacrylate, polyacrylate, polyacrylamide, polyvinylether, polyvinyl alcohol and polystyrene and derivatives thereof.
11. The method of claim 1, wherein the Protein A ligand comprises the amino acid sequence set forth in SEQ ID NO:3 or SEQ ID NO:4.
12. The method of claim 2, wherein the Protein A ligand comprises the amino acid sequence set forth in SEQ ID NO:3 or SEQ ID NO:4.
13. The method of claim 1, wherein the solid support is polyvinyl alcohol or polyvinylether.
14. The method of claim 2, wherein the solid support is polyvinyl alcohol or polyvinylether.