Claims

1. A method of sanitizing a chromatography medium, the method comprising contacting the medium with an alkaline detergent, wherein the alkaline detergent comprises an alkaline salt and between 0.01% to 10% (w/v) of one or more surfactants and wherein the chromatography medium has been previously contacted with a sample, wherein the sample is plasma or a fraction thereof.

2. The method of claim 1, wherein the alkaline detergent comprises a chelator.

3. The method of claim 2, wherein:
(i) the alkaline salt is selected from the group consisting of potassium hydroxide, sodium hydroxide, sodium carbonate, sodium acetate, sodium sulphide, and sodium bicarbonate, for example, the alkaline salt is potassium hydroxide or sodium hydroxide, preferably wherein the alkaline salt is at a concentration of 75 mM;
(ii) the one or more surfactants is selected from the group consisting of amine ethoxylates, amphocarboxylates, triethanolamine, Octyl-β-Dglucopyranoside (OGP), Polysorbate, Poloxamer, Lauryldimethyl-amine (LDAO), Myristyldimethylamine-N-oxide (TDAO), Sodium-cholate, Decyl-ß-D-glucopyranoside and Dodecyl maltoside; and/or
(iii) the chelator is ethylenediaminetetraacetic acid (EDTA), ethylene glycol-bis(β-aminoethyl ether)-N,N,N′,N′-tetraacetic acid (EGTA), ethylenediamine-N,N'-disuccinic acid (EDDS), iminodisuccinic acid (IDS), methylglycinediacetic acid (MGDA), triethylenetetramine (Trien), iminodiacetic acid (IDA), nitrilotriacetic acid (NTA), tripolyphosphate (TPP), diethylenetriaminepentaacetic acid (DTPA), sodium diethyldithiocarbamate (DDC), L-Glutamic acid N,N-diacetic acid, tetrasodium salt (GLDA), and penicillamine, sodium gluconate, trisodium citrate, DMSA, DMPS, BAPTA, ALA and a salt thereof, for example, the chelator is a biodegradable chelator, such as a biodegradable chelator selected from the group consisting of ethylenediamine-N,N'-disuccinic acid (EDDS), iminodisuccinic acid (IDS), methylglycinediacetic acid (MGDA), nitrilotriacetic acid (NTA), and a salt thereof.

4. The method of any one of claims 1 to 3, wherein the alkaline detergent comprises:
(i) between 0.01% to 1% (w/v) of one or more surfactants;
(ii) between 10 mM and 150 mM of an alkaline salt; and/or
(iii) between 50 mM and 100 mM of an alkaline salt.

5. The method of any one of claims 1 to 4, wherein the alkaline detergent comprises:
(i) TDAO and an alkaline salt selected from sodium hydroxide and potassium hydroxide; optionally
(ii) between 10mM to 150mM of an alkaline salt selected from potassium hydroxide or sodium hydroxide and between 0.01% to 0.1% (w/v) of TDAO.

6. The method of claim 5, wherein the alkaline detergent comprises 75mM of an alkaline salt selected from potassium hydroxide or sodium hydroxide and 0.02% (w/v) of TDAO.

7. The method of any one of claims 1 to 6, wherein the method comprises:
(i) contacting the medium with the alkaline detergent for 60 minutes; and/or
(ii) regenerating the chromatography medium, optionally, regenerating the chromatography medium prior to sanitizing the chromatography medium.

8. The method of claim 7, wherein the chromatography medium is regenerated, the method comprising regenerating the chromatography medium by contacting the medium with a solution comprising ethylene glycol, sodium chloride, sodium hydroxide or a combination of sodium hydroxide and ethanol.

9. The method of any one of claims 1 to 6, wherein the chromatography medium is regenerated before sanitization.

10. The method of any one of claims 1 to 9, wherein the chromatography medium:
(i) is an ion exchange medium, an affinity medium, a hydrophobic interaction chromatography medium, a size exclusion column or a mixed mode chromatography medium; and/or
(ii) comprises a matrix selected from the group consisting of poly(styrene-divinylbenzene), cross-linked poly(styrene-divinylbenzene), silica, agarose, cross-linked agarose, controlled pore glass, polymethacrylate and cellulose, for example, the chromatography medium comprises cross-linked poly(styrene-divinylbenzene), for example, the chromatography medium comprises a VHH antibody fragment capable of specifically binding to a CH3 domain of human IgG conjugated to a cross-linked poly(styrene-divinylbenzene) matrix; and/or
(iii) is an affinity chromatography medium, preferably wherein the affinity chromatography medium binds to an Fc region of an antibody, optionally wherein the

affinity chromatography medium comprises protein A or an antibody binding fragment thereof, protein G or an antibody binding fragment thereof or a ligand capable of specifically binding to a CH1 or a CH3 domain of human IgG, for example, the ligand capable of specifically binding to a CH3 domain of human IgG comprises a camelid-derived single domain [VHH] antibody fragment.

11. The method of any one of claims 1 to 10, comprising contacting a chromatography medium comprising a VHH antibody fragment capable of specifically binding to a CH3 domain of human IgG conjugated to a cross-linked poly(styrene-divinylbenzene) matrix with an alkaline detergent comprising an alkaline salt, one or more surfactants and, optionally, a chelator.

12. The method of any one of claims 1 to 11, comprising regenerating chromatography medium comprising a VHH antibody fragment capable of specifically binding to a CH3 domain of human IgG conjugated to a cross-linked poly(styrene-divinylbenzene) matrix by contacting the medium with a solution comprising a combination of sodium hydroxide and ethanol and sanitizing the medium by contacting the medium with an alkaline detergent comprising an alkaline salt, one or more surfactants and, optionally, a chelator.

13. The method of any one of claims 1 to 12, wherein the method is performed as part of a process of continuous chromatography.

14. The method of any one of claims 1 to 13, wherein the method comprises:

(i) regenerating the chromatography medium by contacting the medium with a regeneration solution comprising a combination of 5-30 mM sodium hydroxide and 5-30% ethanol; and

(ii) sanitizing the chromatography medium by contacting the medium with an alkaline detergent comprising between 0.01% to 1% (w/v) of one or more surfactants and/or between 60 mM and 80 mM of an alkaline salt selected from sodium hydroxide and potassium hydroxide.

15. The method of claim 14, wherein:

(i) the alkaline detergent comprises:

(a) between 75mM of potassium hydroxide or sodium hydroxide and between 0.02% (w/v) of TDAO; or

(b) 2% CIP-100; and/or

(ii) the regeneration solution comprises a combination of 5 mM or 20 mM sodium hydroxide and 20% ethanol.