In a further example of all aspects the chromatography material is an affinity chromatography material, a cation exchange chromatography material, an anion exchange chromatography material, a hydrophobic interaction chromatography material or a mixed mode chromatography material.

In a further example of all aspects the chromatography material is an affinity chromatography material or a cation exchange chromatography material.

In a further example of all aspects the chromatography material is an affinity chromatography material or a strong cation exchange chromatography material.

In a further example of all aspects the chromatography material is an affinity chromatography material selected from Protein A chromatography or a chromatography material with a camelid-derived single domain antibody fragment as ligand.

In a further example of all aspects the affinity chromatography material is CaptureSelect FcXL or MabSelect SuRe.

In a further example of all aspects the cation exchange chromatography material is SP Sepharose Fast Flow or Poros XS or Poros 50 HS.

In a further example of all aspects the protein is a monoclonal antibody.

In a further example of all aspects the protein is a humanized Type II anti-CD20 antibody or an anti-VEGF/Ang2 antibody or an anti-HER2 antibody.

~~One aspect as reported~~Reported herein is a liquid antibody preparation with reduced hydrolytic activity (increased polysorbate degradation stability/reduced polysorbate degradation) obtained by a method as reported herein.

In an example, there is provided a liquid antibody preparation with increased stability obtained by a method as reported herein.

In an example, there is provided a liquid antibody preparation with reduced particle formation (by free fatty acid assemblies) obtained by a method as reported herein.

One aspect as reported herein is a method for producing a protein comprising the following steps:

a) cultivating a mammalian cell comprising a nucleic acid encoding the protein,

b) recovering the protein from the cell or the cultivation medium, and

c) purifying the protein with a method as reported herein,

and thereby producing the protein.

~~One aspect as reported~~Reported herein is a liquid composition comprising an antibody and a polysorbate, wherein the polysorbate is degraded during storage of the liquid composition by 20% or less per year.

## Patent Claims

1. A method for purifying a protein from a sample comprising the protein and at least one impurity with hydrolytic activity, comprising the following steps:

i)

a) applying the sample comprising the protein and at least one impurity with hydrolytic activity to a chromatography material,

b) applying a solution which comprises a polysorbate to the chromatography material, and

c) recovering the protein from the chromatography material, or

ii)

a) adding a polysorbate to the sample comprising the protein and at least one impurity with hydrolytic activity,

b) applying the mixture of step a) to a chromatography material, and

c) recovering the protein from the chromatography material, or

iii)

a) adding a polysorbate to the sample comprising the protein and at least one impurity with hydrolytic activity,

b) applying the mixture of step a) to a chromatography material,

c) applying a solution which comprises a polysorbate to the chromatography material, and

d) recovering the protein from the chromatography material.

2. A method for reducing the hydrolytic activity in a sample comprising a protein and at least one impurity with hydrolytic activity, comprising the following steps:

i)

a) applying the sample comprising the protein and at least one impurity with hydrolytic activity to a chromatography material,

b) applying a solution which comprises a polysorbate to the chromatography material, and

c) recovering the protein from the chromatography material, or

ii)

a) adding a polysorbate to the sample comprising the protein and at least one impurity with hydrolytic activity,

b) applying the mixture of step a) to a chromatography material, and

c) recovering the protein from the chromatography material, or

iii)

a) adding a polysorbate to the sample comprising the protein and at least one impurity with hydrolytic activity,

b) applying the mixture of step a) to a chromatography material,

c) applying a solution which comprises a polysorbate to the chromatography material, and

d) recovering the protein from the chromatography material.

3. The method according to any one of claims 1 to 2, wherein the impurity is a hydrolase.

4. The method according to any one of claims 1 to 3, wherein the impurity is an esterase.

5. The method according to any one of claims 1 to 4, wherein the polysorbate is selected from the group comprising polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 65 or polysorbate 80.

6. The method according to any one of claims 1 to 5, wherein the polysorbate is polysorbate 20 or polysorbate 80.

7. The method according to any one of claims 1 to 6, wherein the polysorbate is added to a final concentration of at least about 0.001% (w/v).

8. The method according to any one of claims 1 to 7, wherein the polysorbate is added to a final concentration of from about 0.001% (w/v) to about 10% (w/v).

9. The method according to any one of claims 1 to 8, wherein the chromatography material is an affinity chromatography material, a cation exchange chromatography material, an anion exchange chromatography material, a hydrophobic interaction chromatography material or a mixed mode chromatography material.

10. The method according to any one of claims 1 to 9, wherein the chromatography material is an affinity chromatography material or a cation exchange chromatography material.

11. The method according to any one of claims 1 to 10, wherein the chromatography material is an affinity chromatography material selected from Protein A chromatography or a chromatography material with a camelid-derived single domain antibody fragment as ligand.

12. The method according to any one of claims 1 to 11, wherein the affinity chromatography material is CaptureSelect FcXL or MabSelect SuRe.

13. The method according to any one of claims 1 to 10, wherein the cation exchange chromatography material is SP Sepharose Fast Flow or Poros 50HS or Poros XS.

14. The method according to any one of claims 1 to 13, wherein the protein is a monoclonal antibody.

15. The method according to any one of claims 1 to 14, wherein the protein is a humanized Type II anti-CD20 antibody, or an anti-VEGF/Ang2 antibody or an anti-HER2 antibody.

~~16. A liquid antibody preparation with reduced hydrolytic activity obtained by a method according to any one of the preceding claims.~~

~~17~~16. A method for producing a protein comprising the following steps:

a) cultivating a mammalian cell comprising a nucleic acid encoding the protein,

b) recovering the protein from the cell or the cultivation medium, and

c) purifying the protein with a method according to any one of claims 1 to 15,

and thereby producing the protein.

~~18. A liquid composition comprising an antibody and a polysorbate, wherein the polysorbate is degraded during storage of the liquid composition by 20% or less per year.~~

~~19. A liquid composition according to claim 18, wherein the antibody is a humanized Type II anti-CD20 antibody, or an anti-VEGF/Ang2 antibody or an anti-HER2 antibody.~~

~~20. A liquid composition according to any one of claims 18 or 19, wherein the antibody is obinutuzumab, faricimab, trastuzumab or pertuzumab.~~