

## CLAIMS

1. A process for the preparation of an IgM containing immunoglobulin composition from a plasma fraction comprising immunoglobulins, the process comprising:
  - (a) providing a plasma fraction as a solution containing the immunoglobulins;
  - (b) mixing a C<sub>7</sub> to C<sub>9</sub> carboxylic acid with the solution and treating the mixed solution with a vibrating agitator to precipitate contaminating proteins; and
  - (c) separating the precipitated proteins from the solution to yield the IgM containing immunoglobulin composition.
2. A process according to claim 1 wherein in step (b) the concentration of the C<sub>7</sub> to C<sub>9</sub> carboxylic acid is at least 0.075 kg/kg of plasma fraction.
3. A process according to claim 1 or claim 2 wherein in step (b) the pH of the mixed solution is between 4.5 to 5.5.
4. A process according to any preceding claim wherein in step (b) the temperature of the mixed solution is 10°C to 35°C.
5. A process according to any preceding claim wherein in step (b) the C<sub>7</sub> to C<sub>9</sub> carboxylic acid is incubated with the solution containing immunoglobulins for at least 30 minutes.
6. A process according to any preceding claim wherein the C<sub>7</sub> to C<sub>9</sub> carboxylic acid is octanoic acid.
7. A process according to any preceding claim wherein the immunoglobulins of the plasma fraction comprise at least 5% IgM.
8. A process according to any preceding claim wherein the plasma fraction is a precipitation of Cohn fraction I/III or Kistler/Nitschmann fraction B or B+I.

9. A process according to any preceding claim wherein step (c) comprises ultrafiltration and the immunoglobulin composition comprises a filtered solution.
10. A process according to any preceding claim further comprising a step of incubating the IgM containing immunoglobulin composition from step (c) at between pH 3.5 and pH 4.5 to form an incubated solution.
11. A process according to claim 10 wherein the step of incubating the IgM containing immunoglobulin composition from step (c) is conducted at between 32 and 42°C.
12. A process according to claim 10 or claim 11 further comprising the steps of subjecting the incubated solution to adsorption on DEAE-Sephadex and separating the DEAE Sephadex from the solution by depth filtration.
13. A process according to claim 12 further comprising the step of subjecting the filtrate from the depth filtration to nanofiltration.
14. A process according to claim 13 wherein the nanofiltration is conducted with a filter with a 35 to 75 nm nominal pore size and preferably a 40 to 50 nm nominal pore size.
15. A process according to any one of claims 10 to 14 further comprising a step of treating the incubated solution of claim 10 or claim 11 or the filtrate of any one of claims 12 to 14 with UVC irradiation to form a UVC irradiated solution.
16. A process according to claim 15 wherein the incubated solution or the filtrate is treated with UVC irradiation at 200 to 500 J/m<sup>2</sup>, and preferably at 200 to 300 J/m<sup>2</sup>.
17. A process according to claim 15 or claim 16 further comprising the step of filtering the UVC irradiated solution under sterile conditions to produce an antibody preparation suitable for intravenous administration.

18. A process according to claim 17 comprising formulating the antibody preparation in a glycine-containing buffer at a pH between pH 4 and 5.5.
19. A process according to any one of claims 15 to 18 further comprising a step of filling a container with the UVC irradiated solution of claims 15 or 16 or the antibody preparation of claims 17 or 18 under sterile conditions.
20. A process according to any one of claims 15 to 19 wherein the UVC irradiated solution of claims 15 or 16 or the antibody preparation of claims 17 or 18 has a proteolytic activity of less than 8U/l.
21. A process according to any one of claims 15 to 20 which provides a more than 3 log<sub>10</sub> removal of non-enveloped viruses.
22. An antibody preparation comprising immunoglobulins obtainable by the process of any one of claims 17 to 21.
23. An antibody preparation suitable for intravenous administration in humans comprising immunoglobulins IgG, IgA and IgM, having a proteolytic activity of less than 8U/l, and wherein at least 5% of the total immunoglobulins are IgM.
24. An antibody preparation comprising IgM according to claim 23 which is stable for at least 2 years when stored at 2 to 8°C.
25. An antibody preparation according to any one of claims 22 to 24 wherein the preparation comprises at least 15% IgM.
26. An antibody preparation according to claim 25 wherein the preparation comprises at least 20% IgM

27. An antibody preparation according to claim 26 wherein the preparation comprises 20% to 30% IgM.
28. An antibody preparation according to any one of claims 22 to 27 further comprising a stabilizing agent.
29. An antibody preparation according to claim 28 wherein the stabilizing agent is glycine.
30. An antibody preparation according to any one of claims 22 to 29 wherein the immunoglobulins are not chemically modified.
31. An IgM containing immunoglobulin composition obtainable by the method of any one of claims 1 to 9.
32. An antibody preparation according to any one of claims 22 to 30 for use in medicine.
33. An antibody preparation according to claim 32 for use in the treatment of immunological disorders and bacterial infections.
34. An antibody preparation according to claim 33 wherein the immunological disorder is an IgM deficiency disorder.
35. Use of an antibody preparation according to any one of claims 22 to 30 for the manufacture of a medicament for treatment of immunological disorders and bacterial infections.
36. A method of treatment of a patient comprising administering an antibody preparation according to any one of claims 22 to 30.
37. A method of treatment according to claim 36 wherein the patient is suffering from an immunological disorder or a bacterial infection.

Claims:

1. A process for the preparation of an IgM containing immunoglobulin composition from a plasma fraction comprising immunoglobulins, the process comprising:
  - (a) providing a plasma fraction as a solution containing the immunoglobulins;
  - (b) mixing a C<sub>7</sub> to C<sub>9</sub> carboxylic acid with the solution and treating the mixed solution with a vibrating agitator to precipitate contaminating proteins; and
  - (c) separating the precipitated proteins from the solution to yield the IgM containing immunoglobulin composition.
2. A process according to claim 1 wherein in step (b):
  - (i) the concentration of the C<sub>7</sub> to C<sub>9</sub> carboxylic acid is at least 0.075 kg/kg of plasma fraction; and/or
  - (ii) the pH of the mixed solution is between 4.5 to 5.5; and/or
  - (iii) the temperature of the mixed solution is 10°C to 35°C; and/or
  - (iv) the C<sub>7</sub> to C<sub>9</sub> carboxylic acid is incubated with the solution containing immunoglobulins for at least 30 minutes.
3. A process according to claim 1 or claim 2 wherein:
  - (i) the C<sub>7</sub> to C<sub>9</sub> carboxylic acid is octanoic acid; and/or
  - (ii) the immunoglobulins of the plasma fraction comprise at least 5% IgM; and/or
  - (iii) the plasma fraction is a precipitation of Cohn fraction I/III or Kistler/Nitschmann fraction B or B+I; and/or
  - (iv) step (c) comprises ultrafiltration and the immunoglobulin composition comprises a filtered solution.
4. A process according to any preceding claim further comprising a step of incubating the IgM containing immunoglobulin composition from step (c) at between pH 3.5 and pH 4.5 to form an incubated solution, and preferably wherein the step of incubating the IgM containing immunoglobulin composition from step (c) is conducted at between 32 and 42°C.
5. A process according to claim 4 further comprising the steps of subjecting the incubated solution to adsorption on DEAE-Sephadex and separating the DEAE Sephadex from the solution by depth filtration.

6. A process according to claim 5 further comprising the step of subjecting the filtrate from the depth filtration to nanofiltration, and preferably wherein the nanofiltration is conducted with a filter with a 35 to 75 nm nominal pore size and more preferably a 40 to 50 nm nominal pore size.

7. A process according to any one of claims 4 to 6 further comprising a step of treating the incubated solution of claim 4 or the filtrate of claim 5 or claim 6 with UVC irradiation to form a UVC irradiated solution, and preferably wherein the incubated solution or the filtrate is treated with UVC irradiation at 200 to 500 J/m<sup>2</sup>, and more preferably at 200 to 300 J/m<sup>2</sup>.

8. A process according to claim 7 further comprising the step of filtering the UVC irradiated solution under sterile conditions to produce an antibody preparation suitable for intravenous administration, and preferably further comprising formulating the antibody preparation in a glycine-containing buffer at a pH between pH 4 and 5.5.

9. A process according to claim 7 or claim 8, wherein:

(i) the process further comprises a step of filling a container with the UVC irradiated solution of claim 7 or the antibody preparation of claim 8 under sterile conditions; and/or

(ii) the UVC irradiated solution of claim 7 or the antibody preparation of claim 8 has a proteolytic activity of less than 8U/l; and/or

(iii) the process provides a more than 3 log<sub>10</sub> removal of non-enveloped viruses.

10. An antibody preparation comprising immunoglobulins obtainable by the process of claim 8 or claim 9, preferably wherein at least 15% of the total immunoglobulins are IgM.

11. An antibody preparation comprising immunoglobulins IgG, IgA and IgM, wherein at least 15% of the total immunoglobulins are IgM, wherein the antibody preparation is virus safe with respect to enveloped and non-enveloped virus, has an anticomplementary activity of  $\leq 1$  CH 50/mg protein, and is stable in liquid form for at least 6 months when stored at 2 to 8°C.

12. An antibody preparation according to claim 11, which has a proteolytic activity of less than 8U/l.

13. An antibody preparation according to any one of claims 10 to 12 wherein:
- (i) the preparation comprises at least 20% IgM and preferably 20% to 30% IgM; and/or
  - (ii) the preparation further comprising a stabilizing agent, preferably wherein the stabilizing agent is glycine; and/or
  - (iii) wherein the preparation is stable for at least 2 years when stored at 2 to 8°C.; and/or
  - (iv) wherein the immunoglobulins are not chemically modified, or wherein the preparation has not been treated during its process of production with  $\beta$ -propiolactone or with an added protease such as pepsin.
14. An IgM containing immunoglobulin composition obtainable by the method of any one of claims 1 to 3.
15. An antibody preparation according to any one of claims 10 to 13 for use in medicine.
16. An antibody preparation according to claim 15 for use in the treatment of immunological disorders or bacterial infections, preferably wherein the immunological disorder is an IgM deficiency disorder.
17. Use of an antibody preparation according to any one of claims 10 to 13 for the manufacture of a medicament for treatment of immunological disorders and bacterial infections.