

CLAIMS

1. A pre-filled syringe (101, 201) comprising a barrel (103, 203) and a  
5 plunger (105, 205), the barrel having an outlet (109, 209), the barrel  
containing a pharmaceutically acceptable solution (113, 213) having a non-  
physiological pH, wherein the syringe further comprises an ion exchange  
material (111, 211, 221) provided such that the pharmaceutically acceptable  
10 solution, when contained within the barrel, does not contact the ion exchange  
material, and wherein the ion exchange material is provided at a position to  
allow contact with the pharmaceutically acceptable solution upon ejection of  
the pharmaceutically acceptable solution from the barrel via the outlet,  
wherein the ion exchange material is adapted to, upon contact with the  
pharmaceutically acceptable solution, adjust the pH of the pharmaceutically  
15 acceptable solution from a first, non-physiological pH to a second pH, wherein  
the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is  
in the range of 6.6-8.0.
2. The pre-filled syringe according to claim 1, wherein the second pH is in  
20 the range of 7.0-8.0.
3. The pre-filled syringe according to claim 2, wherein the second pH is in  
the range of 7.1-8.0.
- 25 4. The pre-filled syringe according to any one of claims claim 1 to 3,  
wherein the pre-filled syringe comprises a separator (115, 215) arranged at a  
position along an ejection path from the barrel, and wherein the  
pharmaceutically acceptable solution is present upstream of said separator  
along said ejection path, and the ion exchange material is provided  
30 downstream of said separator along said ejection path, and the separator is  
adapted to in a first state prevent the pharmaceutically acceptable solution  
from contacting the ion exchange material, and adapted to in a second state

allow fluid communication between the pharmaceutically acceptable solution and the ion exchange material, such as to allow contact therebetween.

5. The pre-filled syringe according to claim 4, wherein the separator is  
5 selected from the group consisting of a collapsible liquid impermeable membrane, a super-hydrophobic material, a valve, a damper and an air pocket.
6. The pre-filled syringe according to any one of the preceding claims,  
10 wherein the syringe comprises an injection needle (107, 207) mounted in fluid communication with said outlet.
7. The pre-filled syringe according to claim 6 wherein the ion exchange material (111, 221) is contained within said needle.  
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8. The pre-filled syringe according to any one of the preceding claims, wherein the ion-exchange material comprises a porous solid material.
9. The pre-filled syringe according to any claim 8, wherein the porous  
20 solid material comprises a zeolite material.
10. The pre-filled syringe according to claim 9, wherein the zeolite is an aluminosilicate zeolite material loaded with  $\text{Na}^+$ ,  $\text{H}^+$  and/or  $\text{Ca}^{2+}$  having  
-a  $\text{SiO}_2/\text{Al}_2\text{O}_3$  molar ratio above 1.5; and/or  
25 -a  $\text{Na}_2\text{O}$  content below 10 wt-% of the total zeolite weight.
11. The pre-filled syringe according to claim 8, wherein the solid porous material comprises a polystyrene material.
- 30 12. The pre-filled syringe according to claim 8, wherein the solid porous material comprises mesoporous silica.

13. The pre-filled syringe according to any one of the preceding claims, wherein the pharmaceutically acceptable solution comprises an acidic buffer solution.
- 5 14. The pre-filled syringe according to claim 13, wherein said acidic buffer solution is a citrate buffer.
15. The pre-filled syringe according to any one of the preceding claims, wherein the pharmaceutically acceptable solution comprises a protein drug or  
10 peptide drug.
16. The pre-filled syringe according to claim 15, wherein the protein or peptide drug is an IL-1 receptor antagonist.
- 15 17. The pre-filled syringe according to claim 16, wherein the IL-1 receptor antagonist is anakinra.
18. A needle unit (222, 322) adapted to be mounted in fluid communication with a syringe, the needle unit comprising an injection needle (207, 307)  
20 adapted for injection of a pharmaceutically acceptable solution into the body of a human or animal, and an ion exchange material (221, 321), wherein the ion exchange material is contained within the needle, wherein the ion exchange material is adapted to, upon contact with a pharmaceutically acceptable solution, adjust the pH of the pharmaceutically acceptable solution  
25 from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, such as in the range of 7.0-8.0, preferably 7.1-8.0.
19. The needle unit according to claim 18, wherein the ion exchange  
30 material is a solid porous material
20. The needle unit according to claim 19, wherein solid porous material is a zeolite material.

21. The needle unit according to claim 20, wherein the zeolite material is an aluminosilicate zeolite material loaded with  $\text{Na}^+$ ,  $\text{H}^+$  and/or  $\text{Ca}^{2+}$  having  
-a  $\text{SiO}_2/\text{Al}_2\text{O}_3$  molar ratio above 1.5; and/or  
5 -a  $\text{Na}_2\text{O}$  content below 10 wt-% of the total zeolite weight.
22. The needle unit according to claim 19, wherein the solid porous material comprises a polystyrene material.
- 10 23. The needle unit according to claim 19, wherein the solid porous material comprises mesoporous silica.
24. A method for manufacturing a pre-filled syringe according to any one of the claims 1 to 17 comprising steps of:  
15 a) providing a syringe (101, 201) having a plunger (105, 205) and a barrel (103, 203), the barrel having an interior volume;  
b) providing the syringe with an ion exchange material (111, 211, 221) at a position that is not in fluid communication with the interior volume of the barrel;  
20 c) placing a pharmaceutically acceptable solution (113, 213) within said barrel.
25. The method according to claim 24, wherein the ion exchange material (111, 211) is provided within the barrel.  
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26. The method according to claim 24, wherein the ion exchange material (221) is contained within a needle unit (222), and the step b) involves connecting said needle unit to the barrel.
- 30 27. The method according to claim 26, wherein the ion exchange material is a particulate zeolite material and wherein step b) comprises:  
b-i) sintering the zeolite material to a shape such that it matches to the inner shape of a needle (207) of the needle unit, and

b-ii) placing the sintered zeolite material within the needle.

28. The method according to claim 25, wherein the ion exchange material is a particulate zeolite material and wherein step b) comprises:

5       b-i) sintering a zeolite material to a shape such that it matches to the inner shape of the barrel, and

          b-ii) placing the sintered zeolite material within the barrel.

29. The method according to any one of the claims 25 to 28, wherein the  
10 method further comprises a step of providing a separator (115, 215) in the barrel.

30. A syringe (301) comprising a barrel (303) and a plunger (305), the barrel having an interior volume (314) adapted to contain a pharmaceutically  
15 acceptable solution having a non-physiological pH, wherein the syringe further comprises an ion exchange material (311, 321) provided within the syringe such that it is not in fluid communication with the interior volume of the barrel, and wherein the ion exchange material is provided at a position to, in use, allow contact with the pharmaceutically acceptable solution upon  
20 ejection of the pharmaceutically acceptable solution from the barrel, wherein the ion exchange material is adapted to, upon contact with the pharmaceutically acceptable solution, adjust the pH of the solution from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0.

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31. The syringe according to claim 30, wherein the second pH is in the range of 7.0-8.0.

32. The syringe according to claim 31, wherein the second pH is in the  
30 range of 7.1-8.0

33. The syringe according to any one of claims 30-32, further comprising an injection needle (307) mounted in fluid communication with an outlet of the barrel.

5 34. The syringe according to claim 33, wherein the ion exchange material (321) is provided withinin the injection needle.

35. The syringe according to any one of the claims 30 to 34, wherein the ion exchange material is as defined in any one of claims 8-12.

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36. A method for parental administration of a pharmaceutically acceptable solution to a patient in need thereof, wherein the method comprises the steps of

- 15 a) providing a syringe according to any one of the claims 1 to 17 comprising the pharmaceutically acceptable solution and an ion exchange material;
- b) contacting the solution with the ion exchange material, by pressing the plunger down the barrel of the syringe, whereby the pH of the solution is increased from a first, non-physiological pH to a second pH;
- 20 c) injecting or infusing the solution into the patient, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, such as in the range of 7.0-8.0, preferably 7.1-8.0.

25 37. A method for preventing, avoiding or reducing pain associated with parental administration of a pharmaceutically acceptable solution comprising a buffer having a non-physiological pH in a patient, wherein the method comprises the steps of

- a) providing a syringe according to any one of the claims 1 to 17
- 30 comprising the pharmaceutically acceptable solution and an ion exchange material;

b) contacting the solution with the ion exchange material, by pressing the plunger down the barrel, whereby the pH of the solution is increased from a non-physiological pH to a second pH;

c) injecting or infusing the solution into the patient,

5 wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, such as in the range of 7.0-8.0, preferably 7.1-8.0.

38. A kit (200') comprising:

10 i) a pre-filled syringe (201) according to any one of the claims 1 to 5 or 8 to 12; and  
ii) a needle unit (222) as defined in any one of claims 18 to 23.

39. The kit according to claim 38, wherein the pre-filled syringe comprises  
15 a separator as defined in claim 4.

40. The kit according to any one of claims 38-39, wherein the pharmaceutically acceptable solution is as defined in any one of claims 13-17.

20 41. A kit (300') comprising:

i) a syringe (301) according to any one of claim 30-32;  
ii) a needle unit (322) as defined in any one of claims 18-23.

42. The kit according to claims 41, wherein the syringe comprises a  
25 separator as defined in claim 4.