

CLAIMS

1. A therapeutic composition (5,6) comprising an inner portion (7) and a biocompatible
5 membrane (4, 10) fully or partially surrounding the inner portion; wherein the biocompatible
membrane comprises at least two layers:
a first layer (1) of a porous, non-woven network of thermoplastic polyurethane
polymer fibres formed by electrospinning and having a porosity of greater than or equal to
50%; an average pore diameter of less than 5µm; and has a thickness in the range 10 to
10 250µm; and
a second layer (2) of a porous, non-woven network of thermoplastic polymer fibres
formed by electrospinning, the second layer (2) having a porosity which is substantially equal
to or higher than the porosity of first layer (1); and/or wherein the mean average fibre
diameter of the second layer (2) is greater than the mean average fibre diameter in the first
15 layer (1); and/or wherein the average pore diameter of the second layer (2) is greater than
the average pore diameter of the first layer (1); and
wherein the inner portion (7) comprises a therapeutic agent (3).
2. A therapeutic composition according to claim 1, wherein the biocompatible
20 membrane (4, 10) is in the form a pouch or bag (5, 6, 11) which partially or fully
encapsulates the inner portion (7) comprising the therapeutic agent (3).
3. A therapeutic composition according to claim 2, further comprising a carrier (8) on or
in which the therapeutic agent (3) is disposed, preferably wherein the therapeutic agent (3)
25 is:
attached to the surface of the carrier (8);
disposed in pores of the carrier (8); and/or
encapsulated within the carrier (8).
- 30 4. A therapeutic composition according to claim 2 or 3, wherein the pouch or bag (6) is
arranged such that the first layer (1) faces or is in contact with the encapsulated inner portion
(7) and, optionally, the therapeutic agent (3); whilst the second layer (2) faces externally.

5. A therapeutic composition according to claim 2, wherein the pouch or bag (5) is arranged such that the first layer (1) faces externally; whilst the second layer (2) faces or is in contact with the encapsulated inner portion (7) and, optionally, the therapeutic agent (3).
- 5 6. A therapeutic composition according to claim 3, wherein the pouch or bag (5) is arranged such that the first layer (1) faces externally; whilst the second layer (2) faces or is in contact with the encapsulated inner portion (7), the carrier (8) and, optionally, the therapeutic agent (3).
- 10 7. A therapeutic composition according to claim 2 or 3, wherein the biocompatible membrane (10) comprises three layers: a first layer (1) provided between two second layers (2), wherein the inner portion (7) is provided within an internal-facing surface of one of the second layers (2) when the biocompatible membrane (4) is in the form the pouch or bag (11); with the other of the two second layers (2) providing an external-facing surface; and
15 wherein a carrier is optionally disposed within the inner portion (7).
8. A therapeutic composition according to any one of the preceding claims, wherein the first layer (1) has a porosity in the range 50% to 90%, optionally 50 to 80%.
- 20 9. A therapeutic composition according to any one of the preceding claims, wherein the first layer (1) has an average pore diameter of less than 2µm.
10. A therapeutic composition according to any one of the preceding claims, wherein the first layer (1) has a thickness in the range 10 to 150µm, preferably in the range 20 to 150µm,
25 most preferably in the range 50 to 150µm or 50 to 200 µm.
11. A therapeutic composition according to any one of the preceding claims, wherein the mean diameter of the polymer fibres of the first layer (1) is less than 700nm, preferably less than 600nm, preferably less than 500nm and is most preferably in the range 100-500nm,
30 even more preferably in the range 50-500nm.
12. A therapeutic composition according to any preceding claim, wherein the second layer (2) is or comprises polyurethane or any other biocompatible, thermoplastic polymer or polymer blend.

13. A therapeutic composition according to any preceding claim, wherein the first layer (1) and/or the second layer (2) of the biocompatible membrane (4, 10) are non-biodegradable.
- 5 14. A therapeutic composition according to any one of the preceding claims, wherein the therapeutic agent (3) is selected from therapeutic cells, a drug, a nucleic acid, a polynucleotide, a protein, a polypeptide, an antibody, a particle such as lipid nanoparticle, an extracellular vesicle or exosome, optionally wherein the polynucleotide comprises DNA, RNA, RNAi, saRNA or siRNA.
- 10 15. A therapeutic composition according to claim 3, wherein the biocompatible membrane (4) fully or partially surrounds the carrier.
16. A therapeutic composition according to claim 3 or 15, wherein the carrier (8)
- 15 comprises a porous, non-woven network of polymer fibres or a hydrogel, gelatin, collagen (optionally fibres or sponges) or decellularized tissue.
17. A therapeutic composition according to any one of the preceding claims, comprising cells (3), wherein the cells are preferably pancreatic β cells or islet cells.
- 20 18. A therapeutic composition according to claim 4 or 7, wherein the externally-facing second layer further comprises a hydrogel, gelatin or collagen (optionally fibres or sponges), or decellularized tissue.
- 25 19. A therapeutic composition according to any one of the preceding claims, wherein the second layer (2) is formed from electrospun fibres, and
- (i) the porosity is in the range 70 to 98%, preferably in the range 80 to 95%; and/or
- (ii) the average pore diameter is in the range 5 to 80 μ m, preferably in the range 10 to 50 μ m; and/or
- 30 (iii) the mean diameter of the polymer fibres is in the range 1 to 10 μ m, preferably in the range 2 to 8 μ m, most preferably in the range 3 to 7 μ m.

20. A therapeutic composition according to any one of the preceding claims, wherein
- (i) the porosity of the second layer (2) is within at least 120%, 110%, 100% of the porosity of the first layer (1), optionally 100% to 110%, 100% to 150%, 100% to 175%, or 100% to 190%, or 100% up to 199% or 200% compared to the porosity of the first layer (1);
- 5 and/or
- (ii) the average pore size/diameter of the second layer (2) is at least 2 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times or at least 100 times the pore size/diameter of the first layer (1); and/or
- (iii) the mean diameter of the polymer fibres of the second layer (2) is at least 2 times, at
- 10 least 5 times, at least 10 times, at least 20 times, at least 50 times or at least 100 times the diameter of the first layer (1).
21. A therapeutic composition according to any one of the preceding claims, which further comprises one or more additives, wherein the additives are preferable disposed
- 15 within the carrier (8) or one or both of the first layer (1) or the second layer (2), further wherein the additives are selected from growth factors such as VEGF, crosslinking agents, Growth factors, Catalase and other enzymes; or an oxygen- releasing material such as CaO₂ or Haemoglobin, Peroxides (for instance, H₂O₂, CaO₂, MgO₂, Li₂O₂, Na₂O₂), Sodium Percarbonate (Na₂CO₃), Perfluorocarbons, Hydroxyapatite, Tricalcium phosphate (bone
- 20 growth promoting materials), most preferably CaO₂ and/or MgO₂.
22. A membrane comprising at least two layers, wherein
- (i) the first layer (1) is a biocompatible membrane comprising a porous, non-woven network of thermoplastic polyurethane polymer fibres formed by electrospinning,
- 25 wherein the biocompatible membrane has a porosity of greater than or equal to 50%; an average pore diameter of less than 5µm; and has a thickness in the range 10 to 250µm; and
- (ii) the second layer (2) is disposed on the first layer and wherein the second layer (2) is of a porous, non-woven network of thermoplastic polymer fibres formed by
- 30 electrospinning, which fibres of the second layer (2) may or may not be polyurethane, the second layer (2) having a mean average fibre diameter of the second layer (2) greater than the mean average fibre diameter in the first layer (1), and/or wherein the

average pore diameter of the second layer (2) is greater than the average pore diameter of the first layer (1);.

23. A membrane according to claim 22, wherein the first layer (1) and/or the second layer
5 (2) is as defined in any of claims 1 to 21.

24. A membrane or a therapeutic composition according to any one of the preceding claims for use in a method for treatment of the human or animal body by therapy.

10 25. A membrane or a therapeutic composition according to claim 24 for use in a method of immunoprotecting therapeutic cells or in a method of treating (preferably type I) diabetes.

26. A method of treatment of the human or animal body in need thereof comprising administering to the human or animal body a therapeutically effective amount of a
15 therapeutic composition or membrane according to any one of the preceding claims.

27. A device comprising a therapeutic composition according to any one of claims 1 to 21, wherein the inner portion (7) comprises pancreatic beta or islet cells, with or without the carrier material (8).

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28. A device comprising a therapeutic composition according to any one of claims 1 to 21, wherein the inner portion (7) comprises hepatocytes.

29. A device comprising a therapeutic composition according to any one of claims 1 to
25 21, wherein the inner portion comprises erythrocytes and/or leukocytes, preferably engineered leukocytes such as CAR-T cells.

30. A process for producing a therapeutic composition according to any one of claims 1 to 21 comprising

- (i) an electrospinning process to produce a biocompatible membrane (4) comprising a porous, non-woven network of thermoplastic polyurethane polymer fibres; and
- (ii) shaping the biocompatible membrane to produce a therapeutic composition in which an inner portion (7) is fully or partially surrounded; the shaping being optionally by welding edges.

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