Claims:

1. A stable aqueous liquid pharmaceutical formulation comprising a glucagon analogue, which is:

Hy-HSQGTFTSDYSKYLD-Aib-ARAEEFVKWLEST-OH

or a pharmaceutically acceptable salt and/or derivative thereof;

wherein the formulation comprises:

(a) the glucagon analogue present at a concentration of about 0.5 mg/mL to about 10 mg/mL;

(b) TRIS, ACES or MES is present as a buffer at a concentration of about 25 mM to about 75 mM, and/or citrate, acetate or succinate is present as a buffer at a concentration of about 1 mM to about 30 mM;

(c) sodium chloride present as a tonicity modifier and at a concentration of about 50 mM to about 600 mM; and

(d) a pH of about 5.6 to about 7.0.

2. The stable aqueous liquid formulation of claim 1, wherein the TRIS, ACES or MES buffer directly chemically stabilise the glucagon analogue independent of the pH of the formulation provided by the buffer.

3. The stable aqueous liquid formulation of claim 1 or claim 2, wherein the formulation provides improved chemical stabilisation relative to a formulation in which the TRIS, ACES, or MES buffer is replaced by a phosphate buffer and/or a histidine buffer of the same concentration and pH evaluated under the same test conditions.

4. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation has a degradation profile following 52 weeks storage at 25ºC after which the formulation contains one or more of less than 5% of Pyro-Glu 4-29, less than 7% of Trp/Tyr oxidation, less than 4% of Kynurenine, less than 5% of F-4-29 + F5-29 and/or less than 2% of F3.29 after storage for 52 weeks at 25ºC, wherein all percentages are determined by HPLC.

5. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation has a degradation profile in which the glucagon analogue is free of succinic acid addition to maleic acid.

6. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation substantially does not include aprotic polar solvent.

7. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation substantially does not include dimethyl sulfoxide (DMSO).

8. The stable aqueous liquid formulation of any one of the preceding claims, wherein the water is the sole solvent used to make the aqueous liquid formulation.

9. The formulation of any one of the preceding claims, wherein the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, is present at a concentration of about 0.5 mg/mL, 0.6 mg/mL, 0.7 mg/mL, 1.0 mg/mL or about 4.0 mg/mL.

10. The stable aqueous liquid formulation of any one of the preceding claims, wherein the TRIS, ACES or MES buffer is present as a buffer at a concentration of about 50 mM.

11. The stable aqueous liquid formulation of any one of the preceding claims, wherein the sodium chloride present as a tonicity modifier at a concentration of about 150 mM to about 200 mM or at a concentration of about 50 mM to about 150 mM.

12. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation has a pH of about 5.8 to 6.7, optionally wherein the formulation has a pH of about 6.5.

13. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation does not include an ionization stabilizing excipient selected from hydrochloric acid, nitric acid, sulphuric acid or a combination thereof.

14. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation is a ready-to-use formulation.

15. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation is stable at 2-8°C for at least 6 months, at least 12 months, at least 18 months or at least 24 months.

16. The stable aqueous liquid formulation of claim 15, wherein the glucagon analogue in the formulation retains at least about 90% of its biological activity after 18 months of storage 2-8°C.

17. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation is sterile and/or free from a reducing agent.

18. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation is formulated for administration to a subject by injection.

19. The stable aqueous liquid formulation of claim 18, wherein the injection is subcutaneous injection.

20. The stable aqueous liquid formulation of any one of the preceding claims, wherein the buffer is TRIS.

21. The stable aqueous liquid formulation of any one of the preceding claims, further comprising a preservative.

22. The stable aqueous liquid formulation of claim 21, wherein the preservative is meta-cresol, optionally at a concentration of about 1.0 mg/mL to about 5.0 mg/mL.

23. The stable aqueous liquid formulation of any one of claims 1 to 19, wherein the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, is present at a concentration of about 0.75 mg/ml to about 1.25 mg/mL, the TRIS, ACES or MES buffer is present at a concentration of about 40 mM to about 60 mM, sodium chloride is present at a tonicity modifier at a concentration of about 150 mM to about 200 mM and the formulation has a pH of about 6.0 to about 6.8.

24. The stable aqueous liquid formulation of claim 23, wherein the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, is present at a concentration of about 1.0 mg/mL, TRIS is present at a concentration of about 50 mM,

sodium chloride is present at a tonicity modifier at a concentration of about 175 mM and the formulation has a pH of about 6.5.

25. The stable aqueous liquid formulation of any one claims 1 to 22, wherein the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, is present at a concentration of about 3.0 to 5.0 mg/mL, TRIS, ACES or MES buffer is present at a concentration of about 40 mM to about 60 mM, sodium chloride is present at a tonicity modifier at a concentration of about 50 mM to about 150 mM, meta-cresol is present as a preservative at a concentration of about 3.0 mg/mL to about 4.0 mg/mL and the formulation has a pH of about 6.0 to 7.0.

26. The stable aqueous liquid formulation of claim 25, wherein the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, is present at a concentration of about 4 mg/mL, TRIS is present at a concentration of about 50 mM, sodium chloride is present at a tonicity modifier at a concentration of about 90 mM, meta-cresol is present as a preservative at a concentration of about 3.0 to about 4.0 mg/mL and the formulation has a pH of about 6.5.

27. The stable aqueous liquid formulation of any one claims 1 to 22, wherein the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, is present at a concentration of about 3.0 to 5.0 mg/mL, TRIS, ACES or MES is present as a buffer at a concentration of about 25 mM to about 75 mM, and/or citrate, acetate or succinate is present as a buffer at a concentration of about 1 mM to about 30 mM, sodium chloride is present at a tonicity modifier at a concentration of about 50 mM to about 150 mM, meta-cresol is present as a preservative at a concentration of about 3.0 mg/mL to about 4.0 mg/mL and the formulation has a pH of about 6.0 to 7.0.

28. The stable aqueous liquid formulation of claim 27, wherein the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, is present at a concentration of about 4 mg/mL, TRIS, ACES, MES buffer is present at a concentration of about 50 mM or citrate, acetate and/or succinate buffer is present at a concentration of about 15 mM, sodium chloride is present at a tonicity modifier at a concentration of about 90 mM, meta-cresol is present as a preservative at a concentration of about 3.0 to about 4.0 mg/mL and the formulation has a pH of about 6.5.

29. The stable aqueous liquid formulation of any one of claims 1 to 28, wherein the buffer further comprises citrate, acetate or succinate.

30. The stable aqueous liquid formulation of any one of claims 1 to 29, wherein the citrate, acetate or succinate is present in the formulation at a concentration of 10 mM to 30 mM.

31. A delivery device comprising the liquid formulation of any one of claims 1 to 30.

32. The delivery device of claim 30, wherein the delivery device is pre-filled syringe, an injector device, an injector pen, an adjustable dose auto-injector, a disposable auto-injector, a wearable injector, or an infusion pump.

33. A formulation of the glucagon analogue of any one of claims 1 to 30 for use in therapy.

34. A formulation of the glucagon analogue of any one of claims 1 to 30 for use in the treatment of a disease or condition selected from hypoglycaemia (including, but not limited to, severe hypoglycaemia, acute hypoglycaemia, chronic hypoglycaemia), type 2 diabetes, impaired glucose tolerance, type 1 diabetes, obesity, coronary heart disease, atherosclerosis, hypertension, dyslipidemia, hepatic steatosis, β-blocker poisoning, insulinoma or Von Gierkes disease.

35. The formulation of the glucagon analogue for use in the method of treatment of claim 33 or claim 34, wherein the disease or condition is hypoglycaemia.

36. The formulation of the glucagon analogue for use in the method of treatment of claim 35, wherein the hypoglycaemia is selected from the group consisting of: diabetic hypoglycaemia, acute insulin-induced hypoglycaemia, severe hypoglycaemia, non-diabetic hypoglycaemia, reactive hypoglycaemia, fasting hypoglycaemia, drug-induced hypoglycaemia, alcohol-induced hypoglycaemia, gastric bypass-induced hypoglycaemia (including, but not limited, to postprandial hypoglycaemia after Roux-en-Y gastric bypass) or hypoglycaemia occurring during pregnancy.

37. The formulation of the glucagon analogue for use in the method of treatment of any one of claims 33 to 36, wherein the glucagon analogue is used for the treatment of a human patient.

38. A method of treating a patient, the method comprising administering a formulation

of any one of claims 1 to 30 to a patient in need thereof.

39. A method of treating a disease or condition selected from hypoglycaemia (including, but not limited to, severe hypoglycaemia, acute hypoglycaemia, chronic hypoglycaemia), type 2 diabetes, impaired glucose tolerance, type 1 diabetes, obesity, coronary heart disease, atherosclerosis, hypertension, dyslipidemia, hepatic steatosis, β-blocker poisoning, insulinoma or Von Gierkes disease in a patient, the method comprising administering a formulation of any one of claims 1 to 30 to a patient in need thereof.

40. The method of claim 39, wherein the disease or condition is hypoglycaemia.

41. The method of claim 40, wherein the hypoglycaemia is selected from the group consisting of: diabetic hypoglycaemia, acute insulin-induced hypoglycaemia, severe hypoglycaemia, non-diabetic hypoglycaemia, reactive hypoglycaemia, fasting hypoglycaemia, drug-induced hypoglycaemia, alcohol-induced hypoglycaemia, gastric bypass-induced hypoglycaemia (including, but not limited, to postprandial hypoglycaemia after Roux-en-Y gastric bypass) or hypoglycaemia occurring during pregnancy.

42. The method of any one of claims 38 to 41, wherein the patient is a human.

43. A process for producing a stable aqueous liquid pharmaceutical formulation comprising a glucagon analogue which is:

Hy-HSQGTFTSDYSKYLD-Aib-ARAEEFVKWLEST-OH

or a pharmaceutically acceptable salt and/or derivative thereof;

the process comprising formulating (a) the glucagon analogue, or the pharmaceutically acceptable salt and/or derivative thereof, present at a concentration of about 0.5 mg/mL to about 10 mg/mL; (b) TRIS, ACES or MES is present as a buffer at a concentration of about 25 mM to about 75 mM, and/or citrate, acetate or succinate is present as a buffer at a concentration of about 1 mM to about 30 mM; (c) sodium chloride present as a tonicity modifier and at a concentration of about 50 mM to about 600 mM; (d) a pH of about 6.0 to about 7.0; and optionally (e) meta-cresol at a concentration of about 1.0 mg/mL to about 5.0 mg/mL to produce the stable aqueous liquid pharmaceutical formulation.

44. A formulation produced by the process of claim 43, wherein the formulation is a stable aqueous liquid formulation of any one of claims 1 to 30.