Claims:

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

Hy-HSQGTFTSDYSKYLD-Aib-ARAEEFVKWLEST-OH

or a pharmaceutically acceptable salt thereof;

wherein the formulation comprises:

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

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

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

(d) a pH of 5.6 to 7.0.

Claim 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.

Claim 3. The stable aqueous liquid formulation of claim 1 or claim 2, wherein the formulation provides:

(i) 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;

(ii) 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;

(iii) has a degradation profile in which the glucagon analogue is free of succinic acid addition to maleic acid;

(iv) substantially does not include aprotic polar solvent; and/or

(v) substantially does not include dimethyl sulfoxide (DMSO).

Claim 4. 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.

Claim 5. The stable aqueous liquid formulation of any one of the preceding claims, wherein:

(i) 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;

(ii) the TRIS, ACES or MES buffer is present as a buffer at a concentration of about 50 mM;

(iii) the sodium chloride present as a tonicity modifier at a concentration of 150 mM to 200 mM or at a concentration of 50 mM to 150 mM; and/or

(iv) has a pH of 5.8 to 6.7, optionally wherein the formulation has a pH of about 6.5.

Claim 6. The stable aqueous liquid formulation of any one of the preceding claims, wherein the formulation:

(i) does not include an ionization stabilizing excipient selected from hydrochloric acid, nitric acid, sulphuric acid or a combination thereof;

(ii) is a ready-to-use formulation;

(iii) is stable at 2-8°C for at least 6 months, at least 12 months, at least 18 months or at least 24 months , optionally wherein the glucagon analogue in the formulation retains at least about 90% of its biological activity after 18 months of storage 2-8°C;

(iv) is sterile and/or free from a reducing agent; and/or

(v) is formulated for administration to a subject by injection, optionally wherein the stable aqueous liquid formulation is formulated for to be administered by subcutaneous injection.

Claim 7. The stable aqueous liquid formulation of any one of the preceding claims, wherein the buffer is TRIS.

Claim 8. The stable aqueous liquid formulation of any one of the preceding claims, further comprising a preservative, optionally wherein the preservative is meta-cresol, optionally at a concentration of 1.0 mg/mL to 5.0 mg/mL.

Claim 9. The stable aqueous liquid formulation of any one of claims 1 to 6, wherein the glucagon analogue, or the pharmaceutically acceptable salt thereof, is present at a concentration of 0.75 mg/ml to 1.25 mg/mL, the TRIS, ACES or MES buffer is present at a concentration of 40 mM to 60 mM, sodium chloride is present as a tonicity modifier at a concentration of 150 mM to 200 mM and the formulation has a pH of 6.0 to 6.8, optionally wherein the glucagon analogue, or the pharmaceutically acceptable salt 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 as a tonicity modifier at a concentration of about 175 mM and the formulation has a pH of about 6.5.

Claim 10. The stable aqueous liquid formulation of any one claims 1 to 8, wherein:

a) the glucagon analogue, or the pharmaceutically acceptable salt thereof, is present at a concentration of 3.0 to 5.0 mg/mL, TRIS, ACES or MES buffer is present at a concentration of 40 mM to 60 mM, sodium chloride is present as a tonicity modifier at a concentration of 50 mM to 150 mM, meta-cresol is present as a preservative at a concentration of 3.0 mg/mL to 4.0 mg/mL and the formulation has a pH of 6.0 to 7.0, optionally wherein the glucagon analogue, or the pharmaceutically acceptable salt 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 as a tonicity modifier at a concentration of about 90 mM, meta-cresol is present as a preservative at a concentration of 3.0 to 4.0 mg/mL and the formulation has a pH of about 6.5; or

b) the glucagon analogue, or the pharmaceutically acceptable salt thereof, is present at a concentration of 3.0 to 5.0 mg/mL, TRIS, ACES or MES is present as a buffer at a concentration of 25 mM to 75 mM, and/or citrate, acetate or succinate is present as a buffer at a concentration of 1 mM to 30 mM, sodium chloride is present as a tonicity modifier at a concentration of 50 mM to 150 mM, meta-cresol is present as a preservative at a concentration of 3.0 mg/mL to 4.0 mg/mL and the formulation has a pH of 6.0 to 7.0, optionally wherein the glucagon analogue, or the pharmaceutically acceptable salt 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 as a tonicity modifier at a concentration of about 90 mM, meta-cresol is present as a preservative at a concentration of 3.0 to 4.0 mg/mL and the formulation has a pH of about 6.5.

Claim 11. The stable aqueous liquid formulation of any one of claims 1 to 10,

wherein the buffer further comprises citrate, acetate or succinate.

Claim 12. The stable aqueous liquid formulation of any one of claims 1 to 11, wherein the citrate, acetate or succinate is present in the formulation at a concentration of 10 mM to 30 mM.

Claim 13. A delivery device comprising the liquid formulation of any one of claims 1 to 12, wherein the delivery device comprises pre-filled syringe, an injector device, an injector pen, an adjustable dose auto-injector, a disposable auto-injector, a wearable injector, an infusion pump, a single-dose or a multi-dose delivery device.

Claim 14. A formulation of the glucagon analogue of any one of claims 1 to 12 for use in therapy.

Claim 15. A formulation of the glucagon analogue of any one of claims 1 to 12 for use in the treatment of a disease or condition selected from 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.

Claim 16. The formulation of the glucagon analogue for use according to claim 14 or claim 15, wherein the disease or condition is hypoglycaemia, optionally wherein the hypoglycaemia is selected from the group consisting of: diabetic hypoglycaemia, acute insulin-induced hypoglycaemia, severe hypoglycaemia, acute hypoglycaemia, chronic hypoglycaemia, non-diabetic hypoglycaemia, reactive hypoglycaemia, fasting hypoglycaemia, drug-induced hypoglycaemia, alcohol-induced hypoglycaemia, gastric bypass-induced hypoglycaemia or hypoglycaemia occurring during pregnancy, optionally wherein the gastric bypass-induced hypoglycaemia is postprandial hypoglycaemia after Roux-en-Y gastric bypass.

Claim 17. The formulation of the glucagon analogue for use according to claim 15 or claim 16, wherein the glucagon analogue is for use in the treatment of a human disease or condition.

Claim 18. 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 thereof;

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