In one embodiment, there is provided a stable co-formulation composition, wherein:

the composition has a pH of between 6.8 to 7.8; and

the composition comprises:

a) a therapeutically effective amount of a fast-acting insulin;

b) a hyaluronidase in an amount sufficient to render the composition super-fast acting, wherein a super-fast acting insulin composition more closely mimics the endogenous post-prandial insulin release of a nondiabetic subject compared to the fast-acting insulin alone;

c) NaCl at a concentration between 50 mM to 120 mM, inclusive;

d) an anti-microbially effective amount of an antimicrobial preservative or mixture of antimicrobial preservatives, wherein:

at least one preservative is a phenolic preservative; and

the total amount of the one or more preservative agents as a percentage (%) of mass concentration (w/v) in the formulation is or is between 0.1% and 0.4%, inclusive; and

e) a stabilizing agent or agents,

whereby the composition is stable for at least 6 months at a temperature from 2 °C to 8 °C, inclusive, and/or for at least 14 days at a temperature from 20 °C to 30 °C, inclusive.

In one embodiment, there is provided a stable co-formulation composition, wherein:

the composition has a pH of between 6.5 to 7.5;

the composition comprises:

a) a therapeutically effective amount of a fast-acting insulin that is insulin glulisine;

b) a hyaluronidase in an amount sufficient to render the composition super-fast acting, wherein a super-fast acting insulin composition more closely mimics the endogenous post-prandial insulin release of a nondiabetic subject compared to the fast-acting insulin alone;

c) NaCl at a concentration between 120 mM to 200 mM;

d) an anti-microbially effective amount of an antimicrobial preservative or mixture of antimicrobial preservatives, wherein:

at least one preservative is a phenolic preservative; and

the total amount of the one or more preservative agents as a percentage (%) of mass concentration (w/v) in the formulation is or is between 0.1% and 0.4%, inclusive; and

e) a stabilizing agent or agents;

whereby the composition is stable for at least 3 days at a temperature from 32 °C to 40 °C, and/or is stable for at least 3 hours under agitation.

In one embodiment, there is provided a stable co-formulation composition, wherein:

the composition has a pH of between 7.0 to 7.6; and

the composition comprises:

a) a hyaluronidase that is a PH20 in an amount between 100 U/mL to 1000 U/mL, inclusive;

b) a fast-acting insulin analog in an amount between 10 U/mL to 1000 U/mL, inclusive;

c) a Tris buffering agent at a concentration of between 10 mM to 50 mM, inclusive;

d) NaCl at a concentration of between 50 to 200 mM, inclusive;

e) methionine at a concentration between 5 mM to 50 mM, inclusive;

f) glycerin at a concentration from between 0 mM to 50 mM, inclusive;

g) a surfactant that is poloxamer 188, polysorbate 20 or polysorbate 80 at a percentage (%) of mass concentration (w/v) of between 0.01% to 0.5%; and

h) a preservative(s) that comprises phenol at a percentage (%) of mass concentration (w/v) of between 0.1% to 0.25% and m-cresol at a % w/v of between or between about 0.05% to 0.2%,

whereby the composition is stable for at least 6 months at a temperature from 2 °C to 8 °C, inclusive, and/or for at least 14 days at a temperature from 20 °C to 30 °C, inclusive.

In one embodiment, there is provided a stable co-formulation composition, wherein:

the composition has a pH between 7.0 to 7.6; and

the composition comprises:

a) a hyaluronidase that is a PH20 in an amount between or 100 U/mL to 1000 U/mL, inclusive;

b) a fast-acting insulin analog that is insulin lispro in an amount between 10 U/mL to 1000 U/mL, inclusive;

c) a Tris buffering agent at a concentration of between 25 mM to 35 mM, inclusive;

d) NaCl at a concentration of between 50 mM to 120 mM, inclusive;

e) methionine at a concentration between 10 mM to 30 mM, inclusive;

f) glycerin at a concentration from between 40 mM to 60 mM, inclusive;

g) a surfactant that is poloxamer 188, polysorbate 20 or polysorbate 80 at a percentage (%) of mass concentration (w/v) of between 0.01% to 0.05%, inclusive;

f) zinc at a concentration of 0.017 to 0.024 mg per 100 units of insulin (mg/100U); and

g) a preservative(s) that comprises phenol at a percentage (%) of mass concentration (w/v) of between 0.08% to 0.17%, inclusive, and m-cresol at a % w/v of between 0.07% to 0.17%,

whereby the composition is stable for at least 6 months at a temperature from 2 °C to 8 °C, inclusive, and/or for at least 14 days at a temperature from 20 °C to 30 °C, inclusive.

In one embodiment, there is provided a stable co-formulation composition, wherein:

the composition has a pH between 7.0 to 7.6; and

the composition comprises:

a) a hyaluronidase that is a PH20 in an amount between 100 U/mL to 1000 U/mL, inclusive;

b) a fast-acting insulin analog that is insulin aspart in an amount between 10 U/mL to 1000 U/mL, inclusive;

c) a Tris buffering agent at a concentration of between 25 mM to 35 mM, inclusive;

d) NaCl at a concentration of between 80 mM to 160 mM, inclusive;

e) methionine at a concentration between 10 mM to 30 mM, inclusive;

f) glycerin at a concentration from between 20 mM to 50 mM, inclusive;

g) a surfactant that is poloxamer 188, polysorbate 20 or polysorbate 80 at a percentage (%) of mass concentration (w/v) of between 0.01% to 0.05%, inclusive;

f) zinc at a concentration of 0.017 to 0.024 mg per 100 units of insulin (mg/100U); and

g) a preservative(s) that comprises phenol at a percentage (%) of mass concentration (w/v) of between 0.08% to 0.17%, inclusive, and m-cresol at a % w/v of between 0.07% to 0.17%,

whereby the composition is stable for at least 6 months at a temperature from 2 °C to 8 °C, inclusive, and/or for at least 14 days at a temperature from 20 °C to 30 °C, inclusive.

In one embodiment, there is provided a stable co-formulation composition, wherein:

the composition has a pH between 7.0 to 7.6; and

the composition comprises:

a) a hyaluronidase that is a PH20 in an amount between 100 U/mL to 1000 U/mL, inclusive;

b) a fast-acting insulin analog that is insulin glulisine in an amount between 10 U/mL to 1000 U/mL, inclusive;

c) a Tris buffering agent at a concentration of between 25 mM to 35 mM, inclusive;

d) NaCl at a concentration of between 80 mM to 200 mM, inclusive;

e) methionine at a concentration between 10 mM to 30 mM, inclusive;

f) glycerin at a concentration from between 40 mM to 60 mM, inclusive;

g) a surfactant that is poloxamer 188 at a percentage (%) of mass concentration (w/v) of between 0.01% to 0.05%, inclusive; and

h) a preservative(s) that comprises phenol at a percentage (%) of mass concentration(w/v) of between 0.08% to 0.17%, inclusive, and m-cresol at a % w/v of between 0.07% to 0.17%,

whereby the composition is stable for at least 6 months at a temperature from 2 °C to 8 °C, inclusive, and/or for at least 14 days at a temperature from 20 °C to 30 °C, inclusive.

In one embodiment, there is provided a syringe or vial, comprising the stable co-formulation or composition as defined above.

In one embodiment, there is provided a closed loop system, comprising the stable co-formulation as defined above.

In one embodiment, there is provided an insulin pump, comprising the stable co-formulation as defined above.

In one embodiment, there is provided an insulin pen, comprising the stable co-formulation as defined above.

In one embodiment, there is provided a stable co-formulation as defined above for use in treating diabetes or for use in controlling blood glucose levels in a subject.

In one embodiment, there is provided the use of a stable co-formulation as defined above for the manufacture of a medicament for treating diabetes or for controlling blood glucose levels in a subject.