CLAIMS:

1. A pressurized metered dose inhaler comprising:

(a) a canister containing a formulation comprising

an active pharmaceutical ingredient (API) selected from epinephrine and a pharmaceutically acceptable salt thereof;

a liquified propellant; and

a co-solvent; and

(b) an actuator having one or more orifices with an effective diameter of from about 0.12 mm to about 0.33 mm.

2. The pressurized metered dose inhaler of claim 1, wherein the API is in suspension.

3. The pressurized metered dose inhaler of claim 1 or claim 2, wherein the liquified propellant has a vapor pressure of about 5.5 bar to about 5.9 bar (absolute) at 20°C.

4. The pressurized metered dose inhaler of claim 3, wherein the liquified propellant has a vapor pressure of about 5.7 bar absolute at 20°C.

5. The pressurized metered dose inhaler of any one of the preceding claims, wherein the effective diameter of the one or more orifices is from about 0.14 mm to about 0.31 mm.

6. The pressurized metered dose inhaler of claim 5, wherein the effective diameter of the one or more orifices is from about 0.16 mm to about 0.29 mm.

7. The pressurized metered dose inhaler of claim 6, wherein the effective diameter of the one or more orifices is from about 0.18 mm to about 0.27 mm.

8. The pressurized metered dose inhaler of claim 7, wherein the effective diameter of the one or more orifices is from about 0.20 mm to about 0.25 mm.

9. The pressurized metered dose inhaler of claim 8, wherein the effective diameter of the one or more orifices is from about 0.21 mm to about 0.23 mm.

10. The pressurized metered dose inhaler of claim 9, wherein the effective diameter of the one or more orifices is about 0.22 mm.

11. The pressurized metered dose inhaler of any one of claims 1-10, wherein the one or more orifices are circular.

12. The pressurized metered dose inhaler of any one of claims 1-10, wherein the one or more orifices comprise one or more peanut-, clover-, cross- or slot-shaped orifices.

13. The pressurized metered dose inhaler of any one of claims 1-12, wherein the actuator has a single orifice.

14. The pressurized metered dose inhaler of any one of claims 1-13, wherein the co-solvent is present from about 0.1% to about 4% w/w based on the total weight of the formulation.

15. The pressurized metered dose inhaler of claim 14, wherein the co-solvent is present from about 0.1% to about 2% w/w based on the total weight of the formulation.

16. The pressurized metered dose inhaler of any one of claims 1-15, wherein the co-solvent is ethanol, isopropanol, propylene glycol, ethylene glycol, propane, butane, isobutene, pentane, dimethyl ether, diethyl ether, or a mixture thereof.

17. The pressurized metered dose inhaler of claim 16, wherein the co-solvent is ethanol.

18. The pressurized metered dose inhaler of any one of claims 1-17, wherein the liquefied propellant is present from about 95% to about 99.5% w/w based on the total weight of the formulation.

19. The pressurized metered dose inhaler of claim 18, wherein the liquefied propellant is present from about 97% to about 99% w/w based on the total weight of the formulation.

20. The pressurized metered dose inhaler of any one of claims 1-19, wherein the liquefied propellant is 1,1,1,2-tetrafluoroethane (HFA-134A), 1,1,1,2,3,3,3-heptafluoropropane (HFA-227), or a mixture thereof.

21. The pressurized metered dose inhaler of any one of claims 1-20, wherein the API is present from about 0.1% to about 0.5% w/w based on the total weight of the formulation.

22. The pressurized metered dose inhaler of claim 21, wherein the API is present from about 0.1% to about 0.4% w/w based on the total weight of the formulation.

23. The pressurized metered dose inhaler of claim 22, wherein the API is present from about 0.1% to about 0.3% w/w based on the total weight of the formulation.

24. The pressurized metered dose inhaler of any one of claims 1-24, wherein the API is epinephrine free base.

25. The pressurized metered dose inhaler of any one of claims 1-24, wherein the API is selected from the hydrochloric, hydrobromic, phosphoric, sulfuric, perchloric, acetic, oxalic, maleic, tartaric, citric, succinic and malonic acid salts of epinephrine and the adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate, hemisulfate, heptanoate, hexanoate, hydroiodide, 2–hydroxy–ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2–naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3–phenylpropionate, phosphate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, p–toluenesulfonate, undecanoate and valerate salts of epinephrine.

26. The pressurized metered dose inhaler of any one of claims 1-25, wherein the formulation further comprises a surfactant.

27. The pressurized metered dose inhaler of any one of claims 1-26, wherein the formulation further comprises an antioxidant

28. The pressurized metered dose inhaler of any one of claims 1-13,
wherein:

the API is epinephrine free base in suspension at a concentration of 1.9% w/w based on

the total weight of the formulation;

the liquefied propellant is 1,1,1,2-tetrafluoroethane (HFA-134a);

the co-solvent is ethanol at about 1% w/w based on the total weight of the formulation;

wherein the formulation further comprises

polysorbate 80; and

thymol,

and wherein the formulation is free of sulfites.

29. The pressurized metered dose inhaler of any one of claims 1-28, which is capable of delivering a dose of epinephrine or pharmaceutically acceptable salt thereof such that the proportion of the delivered dose that reaches the larynx, pharynx, and lungs when the metered dose inhaler is in a transverse orientation is at least 90% of the proportion of the delivered dose that reaches the larynx, pharynx, and lungs when the metered dose inhaler is in an coaxial orientation, as determined with the Sectioned Alberta Idealized Throat at a flowrate of 30 L/min.

30. The pressurized metered dose inhaler of any one of claims 1-29, which is a limited-dose metered dose inhaler adapted for emergency use and provides up to 50 inhalation doses.

31. The pressurized metered dose inhaler of claim 30, which provides up to 20 inhalation doses.

32. The pressurized metered dose inhaler of claim 31, which provides up to 10 inhalation doses.

33. Use of a formulation in the manufacture of a medicament for treating an acute allergic reaction, said formulation comprising:

an active pharmaceutical ingredient (API) selected from epinephrine and a pharmaceutically acceptable salt thereof;

a liquefied propellant; and

a co-solvent;

and wherein said formulation is to be administered to a patient by oral inhalation using the pressurized metered dose inhaler as defined in any one of claims 1-32.

34. The use according to claim 33 wherein the acute allergic reaction is anaphylaxis.

35. The use according to claim 34, wherein two puffs of epinephrine are to be administered periodically until the patient shows a physiological response to the treatment.

36. The use according to claim 35 wherein the physiological response is:
(a) tachycardia, tremor or both; or
(b) the patient's subjective awareness of body or hand tremor or patient's subjective awareness of increased heart rate.

37. The use according to claim 34, wherein a therapeutically effective amount of epinephrine is to be administered using two puffs of the pressurized metered dose inhaler once every 2 minutes until the anaphylactic reaction ameliorates.

38. The use according to claim 34, wherein two puffs of epinephrine are to be administered every 60 seconds until clinical resolution of allergic symptoms is obtained.

39. The use according to claim 33 or 34, wherein the administration is by oral inhalation of 250 μg epinephrine (for example two puffs) periodically until the patient experiences subjective awareness of a physiological response to treatment.

40. The use according to claim 39, wherein the administration is by oral inhalation of 250 μg epinephrine (for example two puffs) every 30-90 seconds until the patient experiences subjective awareness of a physiological response to treatment.

41. The use according to claim 39, wherein the administration is by oral inhalation of 250 μg epinephrine (for example two puffs) about every 60 seconds until the patient experiences subjective awareness of a physiological response to treatment.

42. The use according to any one of claims 39-41, wherein the awareness of a physiological response is awareness of increased heart rate, awareness of body or hand tremor, or awareness of both increased heart rate and body or hand tremor.