

ANNEX A: The Claims of the Patent as proposed to be amended

1.

“1. Microparticles for use in a pharmaceutical composition for pulmonary administration, comprising particles of an active substance having, on their surfaces, particles of a hydrophobic material present as a coating on the surface of the particles of active substance and suitable for promoting the dispersal of the active particles on actuation of an inhaler and suitable for delaying the dissolution of the active substance, wherein the hydrophobic material comprises a metal stearate.

2. Microparticles according to claim 1, wherein the hydrophobic material comprises magnesium stearate.

3. Microparticles according to either of claims 1 or 2, which comprise not more than 90% of the hydrophobic material based on the total weight of the microparticles.

4. Microparticles according to any of claims 1 to 3, having a mass median aerodynamic diameter of not more than 10 μm .

5. Microparticles as claimed in any of claims 1 to 4, which are in the form of agglomerated microparticles.

6. Microparticles as claimed in any of claims 1 to 5, which have at least a partial coating of a film-forming material.

7. Microparticles as claimed in any of claims 1 to 6, being such that, upon inhalation of the microparticles, the active substance exerts its pharmaceutical effect over a period significantly greater than the period over which the active substance exerts its pharmaceutical effect when inhaled alone.

8. Microparticles as claimed in any of claims 1 to 7, comprising an active substance which dissolves rapidly under the conditions obtained in the lung.

9. Microparticles as claimed in any of claims 1 to 8, having a rate of dissolution no greater than 80% of the rate of dissolution of particles of the active substance.

10. Microparticles as claimed in any of claims 1 to 9, comprising an effective amount of an antimuscarinic agent, β -agonist, leukotriene receptor antagonist or steroid.

11. Microparticles as claimed in any of claims 1 to 9, comprising an effective amount of glycopyrrolate.

~~12. Microparticles as claimed in any of claims 1 to 11, in which the particles of hydrophobic material are present as a coating on the surface of the particles of active substance.~~

~~13.12.~~ Microparticles as claimed in claims 1 to 11 in which the coating is a discontinuous coating.

~~14.13.~~ Microparticles as claimed in any of claims 1 to 12, which are suitable for use in a powder for use in a dry powder inhaler.

~~15.14.~~ A method of preparing microparticles exhibiting delayed dissolution for use in a pharmaceutical composition for pulmonary administration, comprising the step of combining particles of an active substance with particles of a hydrophobic material in a spray drying step, wherein the hydrophobic material comprises a metal stearate.

~~16.15.~~ A method as claimed in claim 14, in which the spray-drying step involves spray-drying a suspension comprising the particles of active substance and the particles of hydrophobic material.

~~17.16.~~ A method as claimed in either of claims 14 or 15, in which the active substance comprises an effective amount of glycopyrrolate.

~~18.17.~~ A method as claimed in claim 15, in which a film-forming material is dissolved in the suspension.

~~19.18.~~ A method as claimed in any of claims ~~145-178~~, wherein the droplets formed during the spray-drying process are in the range of 1-20 μm in diameter.

~~20.19.~~ A method as claimed in any of claims ~~145-189~~, wherein the inlet temperature in the spray-drying step is in the range of 50-150 $^{\circ}\text{C}$.

~~21.20.~~ A composition for inhalation, comprising microparticles as claimed in any of claims 1 to ~~134~~.

~~22.21.~~ A composition as claimed in claim ~~201~~, which is a dry powder and is suitable for use in a dry powder inhaler.

~~23.22.~~ A composition as claimed in claim ~~240~~ or ~~212~~, which comprises carrier particles.

~~24.23.~~ A composition as claimed in claim ~~223~~, wherein the composition also includes small excipient particles having a particle size between 5 to 20 μm .

~~25.24.~~ A composition as claimed in claim ~~234~~, wherein the small excipient particles are present in an amount of from 1% to 40% based on the weight of the carrier particles.

~~26.25.~~ A composition as claimed in claim ~~201~~, which comprises a propellant and is suitable for use in a pressurised metered dose inhaler.”

2.

“Microparticles for use in a pharmaceutical composition for pulmonary administration, comprising particles of an active substance having, on their surfaces, particles of a hydrophobic material present as a coating on the surface of the particles of active substance and suitable for promoting the dispersal of the active particles on actuation of an inhaler and suitable for delaying the dissolution of the active substance, wherein the hydrophobic material comprises a metal stearate, wherein the coating covers at least 50% of the total surface area of the active particles.”

2. Microparticles according to claim 1, wherein the hydrophobic material comprises magnesium stearate.
3. Microparticles according to either of claims 1 or 2, which comprise not more than 90% of the hydrophobic material based on the total weight of the microparticles.
4. Microparticles according to any of claims 1 to 3, having a mass median aerodynamic diameter of not more than 10 μm .
5. Microparticles as claimed in any of claims 1 to 4, which are in the form of agglomerated microparticles.
6. Microparticles as claimed in any of claims 1 to 5, which have at least a partial coating of a film-forming material.
7. Microparticles as claimed in any of claims 1 to 6, being such that, upon inhalation of the microparticles, the active substance exerts its pharmaceutical effect over a period significantly greater than the period over which the active substance exerts its pharmaceutical effect when inhaled alone.
8. Microparticles as claimed in any of claims 1 to 7, comprising an active substance which dissolves rapidly under the conditions obtained in the lung.
9. Microparticles as claimed in any of claims 1 to 8, having a rate of dissolution no greater than 80% of the rate of dissolution of particles of the active substance.
10. Microparticles as claimed in any of claims 1 to 9, comprising an effective amount of an antimuscarinic agent, β -agonist, leukotriene receptor antagonist or steroid.
11. Microparticles as claimed in any of claims 1 to 9, comprising an effective amount of glycopyrrolate.

~~12.~~ ~~Microparticles as claimed in any of claims 1 to 11, in which the particles of hydrophobic material are present as a coating on the surface of the particles of active substance.~~

~~13.~~12. Microparticles as claimed in claims 1 to 11 in which the coating is a discontinuous coating.

~~14.~~13. Microparticles as claimed in any of claims 1 to 12, which are suitable for use in a powder for use in a dry powder inhaler.

~~15.~~14. A method of preparing microparticles according to any of claims 1 to 13 exhibiting delayed dissolution for use in a pharmaceutical composition for pulmonary administration, comprising the step of combining particles of an active substance with particles of a hydrophobic material in a spray drying step, wherein the hydrophobic material comprises a metal stearate.

~~16.~~15. A method as claimed in claim 14, in which the spray-drying step involves spray-drying a suspension comprising the particles of active substance and the particles of hydrophobic material.

~~17.~~16. A method as claimed in either of claims 14 or 15, in which the active substance comprises an effective amount of glycopyrrolate.

~~18.~~17. A method as claimed in claim 15, in which a film-forming material is dissolved in the suspension.

~~19.~~18. A method as claimed in any of claims 14-17, wherein the droplets formed during the spray-drying process are in the range of 1-20 μm in diameter.

~~20.~~19. A method as claimed in any of claims 14-18, wherein the inlet temperature in the spray-drying step is in the range of 50-150 $^{\circ}\text{C}$.

~~21.~~20. A composition for inhalation, comprising microparticles as claimed in any of claims 1 to 13.

~~22.21.~~ A composition as claimed in claim ~~201~~, which is a dry powder and is suitable for use in a dry powder inhaler.

~~23.22.~~ A composition as claimed in claim ~~210~~ or ~~212~~, which comprises carrier particles.

~~24.23.~~ A composition as claimed in claim ~~223~~, wherein the composition also includes small excipient particles having a particle size between 5 to 20 μm .

~~25.24.~~ A composition as claimed in claim ~~234~~, wherein the small excipient particles are present in an amount of from 1% to 40% based on the weight of the carrier particles.

~~26.25.~~ A composition as claimed in claim ~~201~~, which comprises a propellant and is suitable for use in a pressurised metered dose inhaler.”