CLAIMS

1. Crystalline psilocybin in the form Polymorph A characterised by one or more of:
   a. peaks in an XRPD diffractogram at 11.5, 12.0,14.5 and 17.5 °2θ±0.1°2θ, ~~and~~ wherein the peak at 17.5 °2θ±0.1°2θ has a relative intensity compared to the peak at 14.5 °2θ±0.1°2θ of at least 5%, and which is substantially absent of a peak in an XRPD diffractogram at 10.1 °2θ±0.1°; and
   b. an endothermic event in a DSC thermogram having a first onset temperature of between 145°C and 155°C and a second onset temperature of between 210 and 220°C; and

   having a chemical purity of greater than 97% by HPLC, and no single impurity of greater than 1% including phosphoric acid as measured by 31P NMR, and psilocin as measured by HPLC.

2. Crystalline psilocybin in the form Polymorph A, according to claim 1 wherein the endothermic event in the DSC thermogram has a second onset temperature of between 210 and 215°C.

3. Crystalline psilocybin in the form Polymorph A, according to claim 1 or 2 further characterised by one or more peaks in an XRPD diffractogram at 19.7, 20.4, 22.2, 24.3 or 25.7 °2θ±0.1°2θ.

4. Crystalline psilocybin in the form Polymorph A, according to claim 3 having peaks in an XRPD diffractogram at each of 19.7, 20.4, 22.2, 24.3 or 25.7 °2θ±0.1°2θ.

5. Crystalline psilocybin in the form Polymorph A, according to any of the preceding claims having peaks in an XRPD diffractogram at each of 5.6, 11.5, 12.0, 14.5, 17.5, 19.7, 20.4, 22.2, 23.2, 24.3, 25.7, 26.8, 27.8, 29.7, 31.2, 32.6 and 33.7 °2θ±0.1°2θ

~~6. Crystalline psilocybin in the form Polymorph A, according to any of the preceding claims which is substantially absent of a peak in an XRPD diffractogram at 10.1 °2θ±0.1°.~~

~~7.~~6. Crystalline psilocybin in the form Polymorph A, according to any of claims 1 to ~~5~~6 having an XRPD diffractogram substantially as illustrated in Figure 7a.

~~8.~~7. Crystalline psilocybin in the form Polymorph A, according to any of claims 1 to ~~6~~7 having a DSC thermogram substantially as illustrated in Figure 8a.

~~9.~~8. Crystalline psilocybin in the form Polymorph A, according to any of the preceding claims further characterised by having either:

i) a water content of <0.5% w/w; or

ii) <0.5% w/w loss in the TGA thermogram between 25°C and 200 °C.

~~10.~~9. Crystalline psilocybin in the form Polymorph A according to any preceding claims wherein the crystalline psilocybin is a white to off white solid comprising rod shaped crystals with a size range of 50 to 200 microns.

~~11.~~10. Crystalline psilocybin according to any preceding claim comprising the acceptance criteria of one or more quality attributes of:

i) a loss on drying of no more than 2% w/w, as measured by European Pharmacopoeia 2.2.32;

ii) residue on ignition of no more than 0.5% w/w, as measured by US Pharmacopoeia <281>;

iii) no single drug related impurities of more than 1.0 area %, as measured by HPLC;

iv) assay (on a dry basis), 95-103 weight %, as measured by HPLC

v) residual solvent content - methanol no more than 3000ppm, ethanol no more than 5000ppm, tetrahydrofuran (THF) no more than 720ppm, and Toluene no more than 890ppm, as measured by HRGC; and

vi) elemental analysis: Cd no more than 1.5ppm, Pb no more than 1.5ppm, As no more than 4.5ppm, Hg no more than 9.0ppm, Co no more than 15ppm, V no more than 30ppm, Ni no more than 60ppm, Li no more than 165ppm, and Pd no more than 30ppm, as measured by ICP-MS US Pharmacopoeia <233>

11. A batch of at least 100g of crystalline psilocybin in the form Polymorph A, as claimed in any of the preceding claims.

~~13.~~12. A pharmaceutical formulation comprising crystalline psilocybin Polymorph A as claimed any of claims 1 to 1~~0~~1 together with one or more excipients.

~~14.~~13. A pharmaceutical formulation as claimed in claim 1~~2~~3 which is an oral dosage form.

~~15.~~14. A pharmaceutical formulation as claimed in claim 1~~2~~3 or 1~~3~~4 wherein the psilocybin is present in an amount providing a dose of from 0.01mg/kg to 1mg/kg.

~~16.~~15. A pharmaceutical formulation as claimed in claim 1~~4~~5 wherein a unit dose is 10mg or 25mg.

~~17.~~16. A pharmaceutical formulation as claimed in any of claims 1~~2~~3 to 1~~5~~6 wherein the one or more excipients comprise microcrystalline cellulose or starch.

~~18.~~17. Crystalline psilocybin Polymorph A as claimed in any of claims 1 to 1~~0~~1 for use in medicine.

~~19.~~18. Crystalline psilocybin as claimed in any of claims 1 to 1~~0~~1 for use in treating a central nervous system disorder.

~~20.~~19. Crystalline psilocybin as claimed in any of claims 1 to 1~~0~~1 for use in treating drug resistant depression.

~~21.~~20. A method for large scale manufacture of psilocybin in the form Polymorph A (12) having a chemical purity of greater than 97% by HPLC, and no single impurity of greater than 1% including phosphoric acid as measured by 31P NMR, and psilocin as measured by HPLC characterised in that the method comprises subjecting psilocybin (12) to a water crystallization step, with controlled drying, to produce a crystalline psilocybin in the form Polymorph A as claimed in of any of claims 1 to 1~~0~~1.