

(ii) Calculate the milligrams of griseofulvin per capsule as follows:

$$\text{Milligrams of griseofulvin per capsule} = \frac{R_u \times W_s \times f \times W_a \times V_u}{R_s \times W_u \times 1,000 \times 50}$$

where:

$R_u$ =Area of the griseofulvin sample peak (at a retention time equal to that observed for the griseofulvin standard)/Area of the internal standard peak;

$R_s$ =Area of the griseofulvin working standard peak/Area of the internal standard peak;

$W_s$ =Weight of the griseofulvin working standard in milligrams;

$f$ =Potency of the griseofulvin working standard in micrograms per milligram;

$W_a$ =Average capsule fill weight in milligrams;

$W_u$ =Weight of the ground tablet powder sample in milligrams;

$V_u$ =Volume of the dissolved capsule powder sample in milliliters.

(2) *Loss of drying.* Proceed as directed in § 436.200(b) of this chapter.

[39 FR 19134, May 30, 1974, as amended at 43 FR 9800, Mar. 10, 1978; 44 FR 20661, Apr. 6, 1979; 50 FR 19920, May 13, 1985]

**§ 449.120c Griseofulvin oral suspension.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Griseofulvin oral suspension is griseofulvin oral suspension with one or more suitable flavorings, colorings, wetting agents, preservatives, and diluents in an aqueous vehicle. Each milliliter contains 25 milligrams of griseofulvin. Its griseofulvin content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of griseofulvin that it is represented to contain. Its pH is not less than 6.5 and not more than 7.5. The griseofulvin used conforms to the standards prescribed by § 449.20(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The griseofulvin used in making the batch for griseofulvin content, loss on drying, melting point, specific rota-

tion, identity, residue on ignition, heavy metals, specific surface area, and crystallinity.

(b) The batch for griseofulvin content and pH.

(ii) Samples required:

(a) The griseofulvin used in making the batch: 10 packages, each containing not less than 1 gram.

(b) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay—(1) Griseofulvin content (gas liquid chromatography).* Proceed as directed in § 436.321 of this chapter, except:

(i) Prepare the sample solution as follows: Transfer an accurately measured portion of the oral suspension equivalent to 100 milligrams of griseofulvin into a 50-milliliter round-bottomed glass-stoppered centrifuge tube. Add 5 milliliters of water and 20 milliliters of a solvent mixture of ethyl acetate and chloroform (85:15). Shake the tube for 1 minute and centrifuge it briefly to separate the layers. Transfer most of the upper layer to a 100-milliliter volumetric flask being careful not to remove any of the lower aqueous layer. Repeat the extraction step with two additional 20-milliliter portions of the solvent mixture combining the extracts in the volumetric flask with the first 20-milliliter extract. Dilute to volume with the solvent mixture and mix. Place 2.0 milliliters of this solution in a conical centrifuge tube and evaporate the contents to dryness on a steam bath under a current of dry air. Add 1.0 milliliter of the internal standard solution to the centrifuge tube and mix vigorously to obtain a uniform solution; and,

(ii) Calculate the milligrams of griseofulvin per milliliter as follows:

$$\text{Milligrams of griseofulvin per milliliter} = \frac{R_u \times W_s \times f \times 2}{R_s \times 1,000 \times V_o}$$

where:

$R_u$ =Area of the griseofulvin sample peak (at a retention time equal to that observed for the griseofulvin standard)/Area of the internal standard peak;

$R_s$ =Area of the griseofulvin working standard peak/Area of the internal standard peak;

$W_s$ =Weight of the griseofulvin working standard in milligrams;

$f$ =Potency of the griseofulvin working standard in micrograms per milligram;  
 $V_o$ =Volume of oral suspension taken in milliliters.

(2) *pH*. Proceed as directed in § 436.202 of this subchapter, using the undiluted suspension.

[39 FR 19134, May 30, 1974, as amended at 44 FR 20662, Apr. 6, 1979; 50 FR 19920, May 13, 1985]

**§ 449.120d Griseofulvin (ultramicrosize) tablets.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Griseofulvin (ultramicrosize) tablets are composed of ultramicrosize crystals of griseofulvin which may or may not be dispersed in polyethylene glycol 6,000. Each tablet contains 125, 165, 250, or 330 milligrams of griseofulvin. The griseofulvin content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of griseofulvin that it is represented to contain. The loss on drying is not more than 5.0 percent. It passes the solubility characteristic test. If it is dispersed in polyethylene glycol 6,000, the griseofulvin used conforms to the standards prescribed by § 449.20(a)(1). If it is not dispersed in polyethylene glycol 6,000, the griseofulvin used conforms to the standards prescribed by § 449.20(a)(1), except specific surface area.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The griseofulvin used in making the batch for potency, loss on drying, melting point, specific rotation, identity, residue on ignition, heavy metals, specific surface area (if it is dispersed in polyethylene glycol 6,000), and crystallinity.

(b) The batch for griseofulvin content, loss on drying, and solubility characteristic.

(ii) Samples required:

(a) The griseofulvin used in making the batch: 10 packages, each containing not less than 1 gram.

(b) The batch: A minimum of 36 tablets.

(b) *Tests and methods of assay—(1) Griseofulvin content (gas liquid chromatography).* Proceed as directed in § 436.321 of this chapter, except:

(i) Prepare the sample solution as follows: Accurately weigh 20 tablets and determine the average tablet weight. Grind the tablets to a fine powder in a mortar and transfer an accurately weighed sample to a volumetric flask of such size that for each 50 milliliters of volume there are 40 milligrams of griseofulvin (estimated). Add chloroform to about one-fourth volume of the flask. Swirl the flask and apply gentle heat to aid in dissolution of the griseofulvin. Allow the mixture to cool and then dilute to volume with chloroform. Mix and allow to settle. Using gentle vacuum, remove and discard the waxy substance that forms on the top of the chloroform. Transfer 2.0 milliliters of the chloroform solution to a conical centrifuge tube and evaporate to dryness under a current of dry air. Add 1.0 milliliter of the internal standard solution to the centrifuge tube and mix vigorously to obtain a uniform solution; and,

(ii) Calculate the milligrams of griseofulvin per tablet as follows:

$$\text{Milligrams of griseofulvin per tablet} = \frac{R_u \times W_s \times f \times W_a \times V_u}{R_s \times W_u \times 1,000 \times 50}$$

where:

$R_u$ =Area of the griseofulvin sample peak (at a retention time equal to that observed for the griseofulvin standard)/Area of the internal standard peak;

$R_s$ =Area of the griseofulvin working standard peak/Area of the internal standard peak;

$W_s$ =Weight of the griseofulvin working standard in milligrams;

$f$ =Potency of the griseofulvin working standard in micrograms per milligram;

$W_a$ =Average tablet weight in milligrams;

$W_u$ =Weight of the ground tablet powder sample in milligrams;

$V_u$ =Volume of the dissolved ground tablet powder sample in milliliters.

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.