

$f$ =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:

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

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.

(3) *Solubility characteristic test.* Proceed as directed in § 436.317 of this chapter.

[40 FR 41523, Sept. 8, 1975, as amended at 43 FR 22676, May 26, 1978; 46 FR 7275, Jan. 23, 1981; 46 FR 21361, Apr. 10, 1981; 46 FR 46313, Sept. 18, 1981; 47 FR 34132, Aug. 6, 1982; 50 FR 19920, May 13, 1985]

#### § 449.150 Nystatin oral dosage forms.

##### § 449.150a Nystatin tablets.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Nystatin tablets are tablets composed of nystatin and suitable and harmless buffer substances, diluents, binders, lubricants, colorings, and flavorings. Each tablet contains 500,000 units of nystatin. Its potency is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of nystatin that it is represented to contain. The loss on drying is not more than 8 percent. The tablets shall disintegrate within 2 hours. The nystatin used conforms to the standards prescribed by § 449.50(a)(1).

(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 the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The nystatin used in making the batch for potency, loss on drying, pH, and identity.

(b) The batch for potency, loss on drying, and disintegration time.

(ii) Samples required:

(a) The nystatin used in making the batch: 10 packages, each consisting of not less than 300 milligrams.

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

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Blend a representative number of tablets for 3 to 5 minutes in a high-speed glass blender with sufficient dimethylformamide to give a convenient concentration. Dilute an aliquot with sufficient dimethylformamide to give a stock solution containing 400 units of nystatin

per milliliter. Further dilute an aliquot with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

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

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter.

[39 FR 19134, May 30, 1974, as amended at 50 FR 19920, May 13, 1985; 50 FR 52772, Dec. 26, 1985]

##### § 449.150b Nystatin oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Nystatin oral suspension is a suspension containing nystatin and one or more suitable preservatives, suspending agents, surfactants, flavorings, and colorings in purified water. Each milliliter contains 100,000 units of nystatin. Its potency is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of nystatin that it is represented to contain. Its pH is not less than 4.5 and not more than 6.0; except, if the product contains glycerin, its pH is not less than 6.0 and not more than 7.5. The nystatin used conforms to the standards prescribed by § 449.50(a)(1).

(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 nystatin used in making the batch for potency, loss on drying, pH, and identity.

(b) The batch for potency and pH.

(ii) Samples required:

(a) The nystatin used in making the batch: 10 packages, each containing approximately 300 milligrams.

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

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately measured representative aliquot of the sample into a high-speed glass blender jar containing sufficient dimethylformamide to give a convenient concentration. Blend for 3 to 5