

§ 455.185

S=Weight of sample in milligrams.

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

[40 FR 53997, Nov. 20, 1975, as amended at 50 FR 19921, May 13, 1985]

**§ 455.185 Vancomycin hydrochloride oral dosage forms.**

**§ 455.185a Vancomycin hydrochloride for oral solution.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Vancomycin hydrochloride for oral solution is vancomycin hydrochloride packaged in a suitable dispensing container. It may contain a suitable stabilizing agent. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of grams of vancomycin that it is represented to contain. Its moisture content is not more than 5 percent. When reconstituted as directed in the labeling, its pH is not less than 2.5 and not more than 4.5. The vancomycin hydrochloride used conforms to the standards prescribed by § 455.85.

(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 assay on:

(a) The vancomycin hydrochloride used in making the batch for potency, moisture, pH, factor A content, and identity.

(b) The batch for potency, moisture, and pH.

(ii) Samples required:

(a) The vancomycin hydrochloride used in making the batch: 12 packages, each containing approximately 500 milligrams.

(b) The batch: A minimum of six intermediate 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: Empty the contents into an accurately measured volume of distilled water as directed in the labeling of the drug. Further dilute an aliquot with 0.1M passium phosphate buffer, pH 4.5 (solution 4), to the reference

21 CFR Ch. I (4–1–98 Edition)

concentration of 10 micrograms of vancomycin per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the drug reconstituted as directed in the labeling.

[39 FR 19166, May 30, 1974, as amended at 50 FR 19921, May 13, 1985. Redesignated at 51 FR 22072, June 18, 1986, and amended at 59 FR 8399, Feb. 22, 1994]

**§ 455.185b Vancomycin hydrochloride capsules.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Vancomycin hydrochloride capsules contain vancomycin hydrochloride dispersed in polyethylene glycol. Each capsule contains either 125 milligrams or 250 milligrams of vancomycin. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of vancomycin that it is represented to contain. Its moisture is not more than 8 percent. It passes the dissolution test. The vancomycin hydrochloride used conforms to the standards prescribed by § 455.85(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 vancomycin hydrochloride used in making the batch for potency, moisture, pH, factor A content, and identity.

(b) The batch for potency, moisture, and dissolution.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(a) The vancomycin hydrochloride used in making the batch: 12 packages, each containing approximately 500 milligrams.

(b) The batch: A minimum of 100 capsules.

(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 a representative number of capsules into a high-speed

glass blender jar with sufficient distilled water to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with 0.1M potassium phosphate buffer, pH 4.5 (solution 4) to the reference concentration of 10 micrograms of vancomycin per milliliter (estimated).

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter, using the titration procedure described in paragraph (e)(1) of that section, except:

(i) Remove gelatin coating before grinding the capsules; and

(ii) Use solvent C in lieu of solvent A.

(3) *Dissolution*. Proceed as directed in § 436.215 of this chapter. The quantity *Q* (the amount of vancomycin dissolved) is 85 percent within 45 minutes.

[51 FR 22072, June 18, 1986, as amended at 55 FR 11585, Mar. 29, 1990]

#### § 455.188 Rifabutin capsules.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity*. Rifabutin capsules are gelatin capsules containing rifabutin with a suitable and harmless filler and with or without binders, lubricants, and stabilizers. Each capsule contains rifabutin equivalent to 150 milligrams of rifabutin. Its rifabutin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of rifabutin that it is represented to contain. Its content of the four major related substances detected by high-performance liquid chromatography (HPLC) is not more than 1.0 percent each. All other unknown related substances are not more than 0.5 percent. The total of all related substances is not more than 4.5 percent. It passes the dissolution test if the quantity (*Q*) dissolved is 75 percent at 45 minutes. It passes the identity test. The rifabutin used conforms to the standards prescribed by § 455.88(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 rifabutin used in making the batch for potency, related substances, moisture, *N*-isobutylpiperidone, and identity.

(B) The batch for content, related substances, dissolution, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

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

(B) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay—(1) Rifabutin content*. Proceed as directed in § 455.88(b)(1), preparing the sample solution and calculating the rifabutin content as follows:

(i) *Preparation of sample solution*. Empty 20 capsules, collecting the contents quantitatively. Weigh the powder and determine the average capsule fill weight. Mix the powder and accurately weigh a portion containing the equivalent of about 25 milligrams of rifabutin into a 50-milliliter volumetric flask. Add 5 milliliters of acetonitrile. Dilute to volume with mobile phase and mix to yield a solution containing 0.5 milligram of rifabutin per milliliter (estimated). Filter through a suitable filter capable of removing particulate matter 0.5 micron in diameter prior to injection into the chromatographic system.

(ii) *Calculations*. Calculate the rifabutin content as follows:

$$\text{Milligrams of rifabutin per capsule} = \frac{A_U \times C_S \times P_S \times W_a}{A_S \times C_U \times 1,000}$$

where:

$A_U$  = Area of the rifabutin peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

$A_S$  = Area of the rifabutin peak in the chromatogram of the rifabutin working standard;

$C_S$  = Milligrams of rifabutin working standard per milliliter of standard solution;

$C_U$  = Milligrams of sample per milliliter of sample solution;

$P_S$  = Rifabutin activity in the rifabutin working standard solution in micrograms per milliliter; and

$W_a$  = Average capsule fill weight in milligrams.