

(a) The ampicillin trihydrate used in making the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(b) The probenecid used in making the batch for all U.S.P. specifications.

(c) The batch for ampicillin content, probenecid content, and loss on drying.

(i) Samples required:

(a) The ampicillin trihydrate 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) *Ampicillin content*. Use any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay*. 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 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 8 to 10 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay*. Proceed as directed in §436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2N hydrochloric acid to both the sample and working standard solutions after the addition of 0.01N iodine solution. Prepare the sample as follows: Place the contents of a representative number of capsules into a high-speed glass blender jar with sufficient distilled water to give a convenient concentration. Blend for 8 to 10 minutes. Filter through Whatman No. 2 filter paper. Further dilute an aliquot of the filtrate with distilled water to the prescribed concentration.

(2) *Probenecid content*—(i) *Preparation of standard solution*. Transfer approximately 25 milligrams of probenecid reference standard U.S.P., accurately weighed, to a 25-milliliter volumetric flask. Dissolve and dilute to volume with 1 percent aqueous sodium carbonate solution.

(ii) *Preparation of sample solution*. Place the contents of a representative

number of capsules into a high-speed glass blender jar with 100 milliliters of 1 percent aqueous sodium carbonate solution for each capsule. Blend for 8 to 10 minutes. Filter a portion through Whatman No. 2 filter paper, discarding the first 10-milliliter portion of the filtrate.

(iii) *Procedure*. Transfer 2.0 milliliters of the clear filtrate to a 125-milliliter separatory funnel and add 8.0 milliliters of 1.0N hydrochloric acid. Extract the solution with four 20-milliliter portions of chloroform, filtering each extract into a 100-milliliter volumetric flask through a glass wool pledget and 6 grams of chloroform-washed anhydrous sodium sulfate. Wash the pledget and sodium sulfate with chloroform, dilute to volume with chloroform and mix. Treat 2.0 milliliters of the standard solution in the same manner. Using a suitable spectrophotometer equipped with a 1-centimeter cell and chloroform washed with 1 percent aqueous sodium carbonate solution as a blank, determine the absorbance of the sample and standard solutions at the peak near 257 nanometers.

(iv) *Calculations*. Calculate the probenecid content as follows:

$$\text{Milligrams probenecid per capsule} = \frac{(\text{Absorbance of sample} \times \text{weight of standard in milligrams} \times \text{percent purity of standard})}{(\text{Absorbance of standard} \times 25)}$$

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

[40 FR 58288, Dec. 16, 1975, as amended at 45 FR 16474, Mar. 14, 1980; 49 FR 3459, Jan. 27, 1984; 50 FR 19919, May 13, 1985]

#### § 440.108 Bacampicillin hydrochloride dosage forms.

##### § 440.108a Bacampicillin hydrochloride tablets.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Bacampicillin hydrochloride tablets are composed of bacampicillin hydrochloride with one or more suitable and harmless diluents and lubricants. Each tablet contains bacampicillin hydrochloride equivalent to either 280 or 560 milligrams of ampicillin. Its potency is satisfactory if it is not less than 90 percent and not more

than 125 percent of the number of milligrams of ampicillin that it is represented to contain. Its moisture content is not more than 2.5 percent. It passes the dissolution test. The bacampicillin hydrochloride used conforms to the standards prescribed by § 440.8(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 bacampicillin hydrochloride used in making the batch for potency, moisture, pH, and identity.

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

(ii) Samples required:

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

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

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Hydroxylamine colorimetric assay.* Proceed as directed in § 440.8(b)(1)(i) of this chapter, except prepare the sample solution and calculate the potency of the sample as follows:

(a) *Preparation of sample solution.* Place one tablet into a high-speed glass blender jar with sufficient distilled water to obtain a concentration of 1.25 milligrams of ampicillin per milliliter (estimated). Blend for 3 to 5 minutes. Filter before using.

(b) *Calculations.* Calculate the ampicillin content in milligrams per tablet as follows:

$$\text{Milligrams of ampicillin per tablet} = \frac{A_u \times P_a \times d}{A_s \times 1,000}$$

where:

$A_u$ =Absorbance of sample solution;

$P_a$ =Potency of working standard in micrograms per milliliter;

$A_s$ =Absorbance of working standard solution;

$d$ =Dilution factor of the sample.

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except use the ampicillin working standard. Prepare the sample as follows: Dissolve and dilute a representative number of tablets with distilled water to the prescribed concentration.

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

(3) *Dissolution.* Proceed as directed in § 436.215 of this chapter, except in lieu of paragraph (d) of that section use the interpretation described in the United States Pharmacopeia XX dissolution test. The quantity,  $Q$  (the amount of ampicillin dissolved) is 85 percent at 30 minutes.

[46 FR 25604, May 8, 1981. Redesignated at 47 FR 23711, June 1, 1982, and amended at 48 FR 51293, 51294, Nov. 8, 1983; 50 FR 19919, May 13, 1985]

#### § 440.108b Bacampicillin hydrochloride for oral suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Bacampicillin hydrochloride for oral suspension is a mixture of bacampicillin hydrochloride with one or more suitable and harmless buffers, diluents, sweetening ingredients, suspending agents, flavorings, and colorings. When reconstituted as directed in the labeling, it contains bacampicillin hydrochloride equivalent to 17.5 milligrams of ampicillin per milliliter. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of ampicillin that it is represented to contain. Its loss on drying is not more than 2.0 percent. When reconstituted as directed in the labeling, its pH is not less than 6.5 and not more than 8.0. It gives a positive identity test for bacampicillin hydrochloride. The bacampicillin hydrochloride conforms to the standards prescribed by § 440.8(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: