

(c) *Resolution.* The resolution ( $R$ ) between the clavulanic acid and amoxicillin peaks is satisfactory if it is not less than 3.5.

(d) *Coefficient of variation.* The coefficient of variation ( $S_R$  in percent) of five replicate injections is satisfactory if it is not more than 2.0 percent.

If the system suitability requirements have been met, then proceed as described in § 436.351(b) of this chapter.

(iv) *Calculations.* Calculate the milligrams of amoxicillin or clavulanic acid content per tablet as follows:

$$\text{Milligrams of amoxicillin or clavulanic acid per tablet} = \frac{A_u \times C_s \times V}{A_s \times N}$$

where

$A_u$ =Response of the amoxicillin or clavulanic acid peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

$A_s$ =Response of the amoxicillin or clavulanic acid peak in the chromatogram of the amoxicillin or clavulanic acid working standard;

$C_s$ =Concentration of standards in milligrams of amoxicillin or clavulanic acid per milliliter of the standard solution;

$V$ =Volume of sample solution (milliliters); and

$N$ =Number of tablets taken for assay.

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

(3) *Dissolution.* Proceed as directed in § 436.215 of this chapter. Dissolution rate is determined by dissolution of the amoxicillin component using the high-performance liquid chromatographic assay described in this section.

[50 FR 42933, Oct. 25, 1985; 50 FR 47367, Nov. 17, 1985, as amended at 55 FR 11582, Mar. 29, 1990]

#### § 440.105 Ampicillin oral dosage forms.

##### § 440.105a Ampicillin tablets.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Ampicillin tablets are composed of ampicillin with one or more suitable and harmless diluents and lubricants. Each tablet contains 250 or 500 milligrams of ampicillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to

contain. Its loss on drying is not more than 4 percent. The tablets disintegrate within 15 minutes. The ampicillin used conforms to the standards prescribed by § 440.5(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 ampicillin used in making the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

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

(ii) Samples required:

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

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

(b) *Tests and methods of assay—(1) Potency.* Use either 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 tablets 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 3 to 5 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 a representative number of tablets in a high-speed glass blender jar and add sufficient distilled water to give a convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot with distilled water to the prescribed concentration.

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