

Alternate chromatographic conditions are acceptable provided reproducibility and resolution are comparable to the system. However, the sample preparation described in paragraph (b)(1)(ii)(b) of this section should not be changed.

(iv) *Calculations.* (A) Calculate the micrograms of ampicillin or sulbactam per milligram of sample as follows:

$$\begin{array}{l} \text{Micrograms of} \\ \text{ampicillin or} \\ \text{sulbactam per} \\ \text{milligram} \end{array} = \frac{A_u \times P_s \times 100}{A_s \times C_u \times (100 - m)}$$

where:

A_u =Area of the ampicillin or sulbactam peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s =Area of the ampicillin or sulbactam peak in the chromatogram of the ampicillin or sulbactam working standard;

P_s =Ampicillin or sulbactam activity in the ampicillin-sulbactam working standard solution in micrograms per milliliter;

C_u =Milligrams of sample per milliliter of sample solution; and

m =Percent moisture content of the sample.

(B) Calculate the ampicillin or sulbactam content of the container as follows:

$$\begin{array}{l} \text{Milligrams of} \\ \text{ampicillin or sulbactam} \\ \text{per container} \end{array} = \frac{A_u \times P_s \times d}{A_s \times 1,000}$$

where:

A_u =Area of the ampicillin or sulbactam peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s =Area of the ampicillin or sulbactam peak in the chromatogram of the ampicillin or sulbactam working standard;

P_s =Ampicillin or sulbactam activity in the ampicillin-sulbactam working standard solution in micrograms per milliliter; and

d =Dilution factor of the sample.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 20 milligrams of sulbactam and 40 milligrams of ampicillin per milliliter.

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

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams of ampicillin and 5 milligrams of sulbactam per milliliter.

(6) *Identity.* The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the ampicillin-sulbactam working standard.

[52 FR 42288, Nov. 4, 1987, as amended at 54 FR 47205, Feb. 20, 1989; 55 FR 11582, Mar. 29, 1990]

§ 440.210 Benzylpenicilloyl-polylysine injection.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Benzylpenicilloyl-polylysine injection is an aqueous solution of benzylpenicilloyl-polylysine. It contains one or more suitable and harmless buffers. Its benzylpenicilloyl content is satisfactory if it is not less than $5.4 \times 10^{-5} M$ and not more than $7.0 \times 10^{-5} M$, except that for the issuance of a certificate for a batch, the benzylpenicilloyl content must be not less than $6.4 \times 10^{-5} M$. It is sterile. It is nonpyrogenic. Its pH is not less than 6.5 and not more than 8.5. The benzylpenicilloyl-polylysine concentrate used conforms to the standards prescribed by § 440.10(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 benzylpenicilloyl-polylysine concentrate used in making the batch for percent benzylpenicilloyl substitution, benzylpenicilloyl content, penamaldate content, penicillenate content, and pH.

(b) The batch for benzylpenicilloyl content, sterility, pyrogens, and pH.

(ii) Samples required:

(a) The benzylpenicilloyl-polylysine concentrate used in making the batch: 2 vials, each containing not less than 5 milliliters.

(b) The batch:
(1) For all tests except sterility: A minimum of 60 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Benzylpenicilloyl content*. Proceed as directed in § 440.10(b)(1)(ii) except in lieu of § 440.10(b)(1)(ii)(b) prepare the sample solution as follows: Pool contents of 16 immediate containers. Dilute a 3.0-milliliter aliquot to 10 milliliters with saline phosphate buffer, pH 7.6.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens*. Proceed as directed in § 436.32(a) of this chapter, preparing the sample solution as follows: Pool the contents of at least 8 vials to obtain a minimum of 1.5 milliliters of the original preparation. Dilute the 1.5 milliliters to 50 milliliters with diluent 2.

(4) [Reserved]

(5) *pH*. Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[39 FR 35347, Oct. 1, 1974, as amended at 42 FR 14094, Mar. 15, 1977; 50 FR 19918, 19919, May 13, 1985]

§ 440.213 Sterile carbenicillin disodium.

The requirements for certification and the tests and methods of assay for sterile carbenicillin disodium packaged for dispensing are described in § 440.13a.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59867, Nov. 22, 1977]

§ 440.219 Dicloxacillin sodium monohydrate injectable dosage forms.

§ 440.219a Sterile dicloxacillin sodium monohydrate.

The requirements for certification and the tests and methods of assay for sterile dicloxacillin sodium monohydrate packaged for dispensing are described in § 440.19a.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59867, Nov. 22, 1977]

§ 440.219b Dicloxacillin sodium monohydrate for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Dicloxacillin sodium monohydrate for injection is a dry mix-

ture of dicloxacillin sodium monohydrate and lidocaine hydrochloride packaged for dispensing. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of dicloxacillin that it is represented to contain. It is sterile. It is nonpyrogenic. Its moisture content is not more than 5 percent. When reconstituted as directed in the labeling, its pH is not less than 4.5 and not more than 7.5. The dicloxacillin sodium monohydrate used conforms to the standards prescribed by § 440.19a(a)(1).

(2) *Labeling*. In addition to the labeling requirements of § 432.5 of this chapter, this drug shall be labeled “dicloxacillin sodium for injection”.

(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 dicloxacillin sodium monohydrate used in making the batch for potency, moisture, pH, organic chlorine content, free chloride content, crystallinity, and identity.

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

(ii) Samples required:

(a) The dicloxacillin sodium monohydrate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 15 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Sample preparation*. Reconstitute as directed in the labeling. Using a suitable hypodermic needle and syringe remove all of the withdrawable contents if it is represented as a single-dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the sample thus obtained with sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), for the microbiological agar diffusion assay or in distilled water for the iodometric assay and hydroxylamine