

cloxacillin in the sample by means of the following calculation:

$$\text{Percent cloxacillin} = \frac{A_1 \times \text{weight of standard in milligrams, on an "as is" basis} \times \text{percent cloxacillin in the standard}}{A_2 \times \text{weight of sample in milligrams on an "as is" basis} \times 100}$$

where:

A<sub>1</sub>=Difference in absorbance for the sample between 257 nanometers and 282 nanometers;

A<sub>2</sub>=Difference in absorbance for the cloxacillin working standard, similarly treated.

(6) *Identity*. Proceed as directed in § 436.211 of this subchapter, using the 0.5 percent potassium bromide disc described in paragraph (b)(1) of that section.

(7) *Crystallinity*. Proceed as directed in § 436.203 of this subchapter.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59857, Nov. 22, 1977; 50 FR 19918, May 13, 1985]

**§ 440.17 Cyclacillin.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cyclacillin is 6-(1-aminocyclohexanecarboxamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid. It is a white to off-white powder. It is so purified and dried that:

(i) It contains not less than 900 micrograms and not more than 1,050 micrograms of cyclacillin per milligram.

(ii) [Reserved]

(iii) Its moisture content is not more than 1.0 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 4.0 and not more than 6.5.

(v) Its cyclacillin content is not less than 90 percent on an anhydrous basis.

(vi) The acid-base titration concordance is such that the difference between the percent cyclacillin content when determined by nonaqueous acid titration and nonaqueous base titration is not more than six. The potency-acid titration concordance is such that

the difference between the potency value divided by 10 and the percent cyclacillin content of the sample determined by the nonaqueous acid titration is not more than six. The potency base titration concordance is such that the difference between the potency value divided by 10 and the percent cyclacillin content of the sample determined by the nonaqueous base titration is not more than six.

(vii) It is crystalline.

(viii) It gives a positive identity test for cyclacillin.

(2) *Labeling*. In addition to the labeling requirements of § 432.5 of this chapter, each package shall bear on its outside wrapper or container and the immediate container the following statement, "For use in the manufacture of nonparenteral drugs only."

(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 the batch for potency, moisture, pH, cyclacillin content, concordance, crystallinity, and identity.

(ii) Samples required: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay—(1) Potency*. Assay for potency by any of the following methods; however, the results obtained from the iodometric 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: Dissolve an accurately weighed portion of the sample in sufficient sterile distilled water to give a stock solution containing 1 milligram of cyclacillin per milliliter (estimated). Further dilute an aliquot of the stock

solution with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 1.0 microgram of cyclacillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in §436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in §436.205 of this chapter.

(2) [Reserved]

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

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

(5) *Cyclacillin content.* Proceed as directed in §436.213 of this chapter, using both the titration procedures described in paragraph (e)(1) and (2) of that section. Calculate the percent cyclacillin content as follows:

(i) *Acid titration.*

$$\text{Percent cyclacillin content} = \frac{(A - B)(\text{normality of perchloric acid reagent})(341.4)(100)}{(\text{Weight of sample in milligrams})(100 - m)}$$

where:

A=Milliliters of lithium methoxide reagent used in titrating the sample;

B=Milliliters of lithium methoxide reagent used in titrating the blank;

m=Percent moisture content of the sample.

Calculate the difference between the potency and the cyclacillin content as follows:

$$\text{Difference} = \frac{\text{Potency in micrograms per milligram}}{10} - \text{percent cyclacillin content}$$

(ii) *Base titration.*

$$\text{Percent cyclacillin content} = \frac{(A - B)(\text{normality of perchloric acid reagent})(341.4)(100)(100)}{(\text{Weight of sample in milligrams})(100 - m)}$$

where:

A=Milliliters of perchloric acid reagent used in titrating the sample;

B=Milliliters of perchloric acid reagent used in titrating the blank;

m=Percent moisture content of the sample.

Calculate the difference between the potency and the cyclacillin content as follows:

$$\text{Difference} = \frac{\text{Potency in micrograms per milligrams}}{10} - \text{percent cyclacillin content}$$

(6) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

(7) *Identity.* Proceed as directed in §436.211 of this chapter, using a 1-percent potassium bromide disc prepared as described in paragraph (b)(1) of that section.

[46 FR 2981, Jan. 13, 1981; 46 FR 15880, Mar. 10, 1981, as amended at 50 FR 19918, May 13, 1985]

#### §440.19 Dicloxacillin sodium monohydrate.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Dicloxacillin sodium monohydrate is the monohydrated sodium salt of 5-methyl-3-(2,6-dichlorophenyl)-4-isoxazolyl penicillin. It is so purified and dried that: