

weighed sample in sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), to obtain a stock solution of convenient concentration; also, if it is packaged for dispensing, reconstitute as directed in the labeling. Then 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 with solution 1 to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 2.0 micrograms of cefotaxime per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except prepare the working standard and sample solutions and calculate the potency of the sample as follows:

(a) *Preparation of the working standard solution.* Dissolve and dilute an accurately weighed portion of the cefotaxime working standard in sufficient distilled water to obtain a concentration of 1 milligram of cefotaxime per milliliter.

(b) *Preparation of sample solution.* Dissolve and dilute an accurately weighed portion of the sample in sufficient distilled water to obtain a concentration of 1 milligram of cefotaxime per milliliter (estimated).

(c) *Calculations—(1)* Calculate the cefotaxime content in micrograms per milligram as follows:

$$\frac{\text{Micrograms of cefotaxime per milligram of sample}}{A_s \times W_u} = \frac{A_u \times P_a}{A_s \times W_u}$$

where:

$A_u$ =Absorbance of sample solution;  
 $P_a$ =Potency of working standard solution in micrograms per milliliter;  
 $A_s$ =Absorbance of working standard solution;  
 $W_u$ =Milligrams of sample per milliliter of sample solution.

(2) Calculate the cefotaxime content of the single-dose vial as follows:

$$\frac{\text{Milligrams of cefotaxime per single-dose vial}}{A_s \times 1,000} = \frac{A_u \times P_a \times d}{A_s \times 1,000}$$

where:

$A_u$ =Absorbance of sample solution;  
 $P_a$ =Potency of working standard solution in micrograms per milliliter;  
 $A_s$ =Absorbance of working standard solution;  
 $d$ =Dilution factor of the sample.

(3) Calculate the cefotaxime content of the multiple-dose vial as follows:

$$\frac{\text{Milligrams of cefotaxime per multiple-dose vial}}{A_s \times 1,000 \times n} = \frac{A_u \times P_a \times d}{A_s \times 1,000 \times n}$$

where:

$A_u$ =Absorbance of sample solution;  
 $P_a$ =Potency of working standard solution in micrograms per milliliter;  
 $A_s$ =Absorbance of working standard solution;  
 $d$ =Dilution factor of the sample;  
 $n$ =Volume of sample solution assayed.

(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 50 milligrams of cefotaxime per milliliter.

(4) [Reserved]

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

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(7) *Identity.* Proceed as directed in § 436.323 of this chapter, except prepare spotting solutions as follows: Prepare solutions of the sample and working standard, each containing 1 milligram of cefotaxime per milliliter in distilled water.

[46 FR 25606, May 8, 1981, as amended at 50 FR 19919, May 13, 1985]

**§ 442.14 Cefoxitin sodium.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cefoxitin sodium is the sodium salt of 3-(hydroxymethyl)-7 $\alpha$ -methoxy-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic

acid carbamate (ester). It is so purified and dried that:

(i) Its cefoxitin content is not less than 850 micrograms and not more than 1,000 micrograms of cefoxitin per milligram.

(ii) Its moisture content is not more than 2.0 percent.

(iii) Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 4.2 and not more than 7.0.

(iv) It gives a positive identity test.

(v) It is crystalline.

(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 the batch for cefoxitin content, moisture, pH, identity, and crystallinity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay—(1) Cefoxitin content.* Proceed as directed in § 436.347 of this chapter, preparing the working standard and sample solutions and calculating the cefoxitin content as follows:

(i) *Working standard solution.* Dissolve an accurately weighed portion of the cefoxitin working standard with water to obtain a solution containing 1 milligram of cefoxitin per milliliter.

(ii) *Sample solution.* Dissolve an accurately weighed portion of the sample with water to obtain a solution containing 1 milligram of cefoxitin per milliliter (estimated).

(iii) *Calculations.* Calculate the micrograms of cefoxitin per milligram of sample as follows:

$$\text{Micrograms of cefoxitin per milligram} = \frac{A_u \times P_s}{A_s \times C_u}$$

where:

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

$A_s$ =Area of the cefoxitin peak in the chromatogram of the cefoxitin working standard;

$P_s$ =Cefoxitin activity in the cefoxitin work-

ing standard solution in micrograms per milliliter; and

$C_u$ =Milligrams of sample per milliliter of sample solution (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 add about 25 milliliters of methanol in lieu of solvent A to a dry titrating vessel and proceed as directed in titration procedure 1.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(4) *Identity.* Proceed as directed in § 436.326 of this chapter.

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

[49 FR 47827, Dec. 7, 1984, as amended at 55 FR 11583, Mar. 29, 1990]

#### § 442.14a Sterile cefoxitin sodium.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cefoxitin sodium is the sodium salt of 3-(hydroxymethyl)-7 $\alpha$ -methoxy-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid carbamate (ester). It is so purified and dried that:

(i) Its potency is not less than 850 micrograms and not more than 1,000 micrograms of cefoxitin per milligram. If it is packaged for dispensing, its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cefoxitin that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 2.0 percent.

(vi) Its pH in an aqueous solution is not less than 4.2 and not more than 7.0.

(vii) It gives a positive identity test.

(viii) It is crystalline.

(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: