

per-milliliter solution of cefonicid working standard in mobile phase described in paragraph (b)(1)(i)(b) of this section, on a steam bath for 30 minutes. Inject a known volume between 10 and 20 microliters of the desacetyl cefonicid containing solution in the same manner as described for the standard solution. The resolution factor (*R*) between cefonicid and desacetyl cefonicid is satisfactory if it is not less than 1.1.

(d) *Coefficient of variation.* The coefficient of variation (*S<sub>R</sub>* in percent) of five replicate injections is satisfactory if it is not more than 2.0 percent.

If the system suitability parameters have been met, then proceed as described in § 436.350(b) of this chapter.

(iv) *Calculations—(a)* Calculate the micrograms of cefonicid per milligram of sample as follows:

$$\text{Micrograms of cefonicid per milligram} = \frac{A_u \times P_s \times 100}{A_s \times C_u \times (100 - m)}$$

where:

*A<sub>u</sub>*=Area of the cefonicid peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

*A<sub>s</sub>*=Area of the cefonicid peak in the chromatogram of the cefonicid working standard;

*P<sub>s</sub>*=Cefonicid activity in the cefonicid working standard solution in micrograms per milliliter;

*C<sub>u</sub>*=Milligrams of sample per milliliter of sample solution; and

*m*=Percent moisture content of the sample.

(b) Calculate the cefonicid content of the container as follows:

$$\text{Milligrams of cefonicid per container} = \frac{A_u \times P_s \times d}{A_s \times 1,000}$$

where:

*A<sub>u</sub>*=Area of the cefonicid peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

*A<sub>s</sub>*=Area of the cefonicid peak in the chromatogram of the cefonicid working standard;

*P<sub>s</sub>*=Cefonicid activity in the cefonicid 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 meth-

od 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 cefonicid 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 50 milligrams per milliliter.

(6) *Specific rotation.* Dissolve and dilute an accurately weighed sample with sufficient methanol to obtain a concentration of approximately 10 milligrams of cefonicid sodium per milliliter. Proceed as directed in § 436.210 of this chapter, using a 1.0-decimeter polarimeter tube. Calculate the specific rotation on an anhydrous basis.

(7) *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 cefonicid working standard.

[49 FR 34348, Aug. 30, 1984; 49 FR 44460, Nov. 7, 1984, as amended at 54 FR 41824, Oct. 12, 1989; 55 FR 11583, Mar. 29, 1990]

**§ 442.21 Cephaloglycin dihydrate.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cephaloglycin dihydrate is the dihydrate form of 7-(D-α-aminophenylacetamido) cephalosporanic acid. It is a white to off-white powder. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms of cephaloglycin per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its moisture is not less than 8.2 and not more than 12 percent.

(iv) Its pH in an aqueous suspension containing 50 milligrams per milliliter is not less than 3.0 and not more than 5.5.

(v) Its cephaloglycin content is not less than 95 and not more than 104 percent on an anhydrous basis.

(vi) It gives a positive identity test for cephaloglycin dihydrate.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5(b) 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 potency, moisture, pH, cephaloglycin content, identity, and crystallinity.

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

(b) *Tests and methods of assay—(1) Potency.* 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 of 100 micrograms of cephaloglycin per milliliter (esti-

mated). Further dilute an aliquot of the stock solution with 0.1M potassium phosphate buffer, pH 4.5 (solution 4), to the reference concentration of 10 micrograms of cephaloglycin per milliliter (estimated).

(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 suspension containing 50 milligrams per milliliter.

(5) *Cephaloglycin content.* Proceed as directed in §436.213 of this chapter, using the titration procedure described in paragraph (e)(2) of that section. Calculate the cephaloglycin content as follows:

$$\text{Percent cephaloglycin content} = \frac{(A - B) (\text{normality of perchloric acid reagent}) (405.4) (100) (100)}{(\text{Weight of sample in milligrams}) (100 - m)}$$

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.

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

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

[39 FR 19040, May 30, 1974, as amended at 50 FR 19919, May 13, 1985]

#### §442.22a Sterile cefmenoxime hydrochloride.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cefmenoxime hydrochloride is 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-3-[[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-, hydrochloride (2:1), [6R-[6α,7β(Z)]]-. It is so purified and dried that:

(i) Its cefmenoxime content is not less than 869 and not more than 1,015

micrograms of cefmenoxime per milligram on an anhydrous basis.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) Its moisture content is not more than 1.5 percent.

(v) It passes the identity test.

(vi) 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 cefmenoxime content, sterility, pyrogens, moisture, identity, and crystallinity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.

(B) For sterility testing: 1 package containing approximately 6 grams of a composite sample.

(b) *Tests and methods of assay—(1) Cefmenoxime content.* Proceed as directed in §436.363 of this chapter, using